Synthesis and Characterization of 2(3H)-Furanones, 2(3H)-Pyrrolones, Quinolinones, Thienochromenones, Thienopyridinones and Biological Activity of Some Selective Compounds

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in

Organic Chemistry

by

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IN THE NAME OF ALLAH
THE COMPASSIONATE
THE MERCIFUL
Dedicated to

My Loving Mother
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Abstract:

Reaction of 3-(4-substitutedbenzoyl)propionic acid with appropriate aromatic aldehydes in the presence of triethylamine in acetic anhydride gave 3-arylidene-5-(4-substitutedphenyl)furan-2(3H)-ones. Reaction of furanones with benzylamine gave γ-ketobenzylamides which were then cyclized to 1-benzyl-3-arylidene-5-(4-substituted phenyl)-1H-pyrrol-2-(3H)-ones by refluxing with 6N-HCl. Two series of furanones and pyrrolones were synthesized. The synthesized compounds were evaluated for antioxidant, cytotoxicity and urease inhibition activities. These compounds showed non significant antioxidant activity, nil brine shrimp lethality and low to moderate urease inhibition activity.

Reaction of hitherto unknown 4-chloro-3-(2,2,2-trifluoroacetyl)-2H-chromen-2-one with different commercially available anilines gave 3-(trifluoroacetyl)-4-(arylamino)-2H-chromen-2-ones which were then successfully cyclized to 7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-ones with conc. H$_2$SO$_4$.

Suzuki cross-coupling reaction of methyl-3-bromothiophene-2-carboxylate and ethyl-2-bromo-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate with o-methoxy phenylboronic acids gave the arylated products which were then successfully cyclized to thieno[2,3-c]chromen-4-ones and 7,8,9,10-tetrahydrobenzothieno[3,2-c]chromen-6-ones via BBr$_3$ mediated lactonization.

The Sonogashira cross-coupling reaction of methyl-3-bromothiophene-2-carboxylate and 2-bromo-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonitrile with terminal alkynes gave respective alkynyl products. The ester and nitrile groups of these substituted thiophenes were then converted into amides which were then cyclized to 5-substituted-thieno[2,3-c]pyridin-7(6H)-ones and 3-substituted-5,6,7,8-tetrahydrobenzothieno[3,2-c]pyridin-1(2H)-ones via base-promoted-cyclization.

4,5-Disubstituted thieno[3,2-b]pyridin-7(4H)-ones were synthesized by Pd-catalyzed tandem amination reaction of α,β-ynone with commercially available anilines/amines. The method provides an efficient approach to a wide range of thienopyridinones.
Abbreviations

Ar    Aromatic
Ac₂O  Acetic Anhydride
BINAP 2,2’-bis(diphenylphosphino)-1,1’-binaphthyl
dba   Dibenzylideneacetone
dppe  1,2-Bis(diphenylphosphino)ethane
dppp  1,3-Bis(diphenylphosphino)propane
dppf  1,1’-Bis(diphenylphosphino)ferrocene
DIPA  Di-isopropylamine
DMF   Dimethylformamide
DEPT  Distortionless Enhancement by Polarization Transfer
ESI   Electro Spray Ionization
EI    Electronic Impact
EtOAc Ethyl acetate
GC-MS Gas Chromatography-Mass Spectrometry
HRMS  High Resolution Mass Spectroscopy
IC₅₀  Half maximal inhibitory concentration
IR    Infrared Spectroscopy
mp.   Melting Point
NEt₃  Triethylamine
NMR   Nuclear Magnetic Resonance
OD    Optical density
Ph    Phenyl
Py    Pyridine
SEM   Standard error of the mean
TMS   Trimethylsilane
TMSCl Trimethylsilylchloride
TFA   Trifluoroacetic Acid
TFAA  Trifluoroacetic Anhydride
THF   Tetrahydrofuran
TLC   Thin Layer Chromatography
UV    Ultraviolet Spectroscopy
1.1 General Introduction:

Chemists have always been interested in finding new methods for C-C bond formation. For the last three decades, palladium-catalyzed cross-coupling reactions have gained much importance for C-C bond formation. This has allowed chemists to assemble complex molecular frameworks from simple precursors, of diverse interests like total synthesis of natural products, medicinal chemistry and material science. The most commonly used palladium catalyzed cross coupling reactions in organic synthesis are Heck reaction, Suzuki-Miyaura reaction, Stille reaction, Nigishi reaction and Sonogashira reaction. The importance of palladium catalyzed cross coupling reactions was recognized by awarding Nobel prize in chemistry in 2010 to Richard Heck, Ei-ichi Negishi, and Akira Suzuki “for palladium-catalyzed cross-couplings in organic synthesis”. A brief discussion on Suzuki and Sonogashira reactions is given below, as these coupling reactions have been used in the present synthetic work. The mechanisms of the Suzuki and Sonogashira reactions are similar: The first step is usually the oxidative addition of organic halides to the Pd(0) complex to form organopalladium halides. The next step is often a transmetallation with nucleophilic compounds to give a diorganopalladium complex. In the last step, the complex undergoes reductive elimination to create carbon-carbon bond and regeneration of the catalyst.

Suzuki Reaction:

The basic reaction was first published by Miyaura and Suzuki in 1979 using alkenyl boronates and alkenyl halides, but after the classical reaction of phenyl boronic acid and aryl halide in 1981, this chemistry has been greatly expanded and elaborated over the years. Advances in this area include the development of new catalysts and modern methods and is now considered to be a very general procedure for a wide range of selective carbon-carbon bond formations. The scope of the reaction partners is not limited to arenes, but also includes alkyl, alkenyl and alkynyl compounds. The selection of an appropriate catalyst plays an important role in the success of the desired reaction. The common sources of palladium include, for example, Pd(OAc)$_2$, PdCl$_2$, Ph(PPh$_3$)$_2$Cl$_2$, and Pd(dba)$_2$. The use of bulky electron-
rich ligands is often the key for a successful reaction. The ferrocenylphosphine\textsuperscript{14}, \textit{N}-heterocyclic carbenes\textsuperscript{15}, P(tBu)\textsubscript{3}\textsuperscript{16} often gives good yield. The reactivity order of aryl halides and aryl triflates, which works as electrophiles, is Ar-I > Ar-OTf > Ar-Br > Ar-Cl. The use of base usually accelerates the transmetalation. This is due to the fact that the carbanion character of the organoborane moiety is increased by formation of an organoborate containing a tetravalent boron atom. Suzuki–Miyaura couplings have a much broader scope in that a potentially huge range of alkyl boranes (typically prepared through the regio- and chemoselective hydroboration of readily available alkene precursors) can be used in the reaction.\textsuperscript{17} The interest of the chemists in this area is clear from the continuous developments in the use of new reaction conditions, catalysts and ligands.\textsuperscript{18-20}

\textbf{Fig 1.1}: A general catalytic cycle for Suzuki-Miyaura reaction

\textbf{Sonogashira reaction:}

Although coupling of aryl halides and alkynes had been reported previously, the condition of using Cu as cocatalyst in 1975 by Sonogashira greatly improved the attractiveness of the reaction.\textsuperscript{21} Since then there has been much development in the protocol for Sonogashira reactions. Nowadays, the Sonogashira reaction can be carried out under mild conditions, even at room temperature, with high yields. Modern variations has enabled to carry out the reaction even in copper-free conditions. Typical reactions are carried out using a palladium(0)-phosphane complex in the presence of a cocatalytic amount of a copper (I) salt and an amine (used as a solvent.
or in large excess) under homogeneous conditions. The catalysts that are in use are triphenylphosphane-related complexes, such Pd(PPh₃)₄, Pd(PPh₃)₂Cl₂, Pd(dppe)Cl₂, Pd(dppp)Cl₂ or Pd(dppf)Cl₂. The reaction medium should be basic in order to neutralize the hydrogen halide produced as a byproduct of this coupling reaction. Thus, alkyl amine compounds such as triethylamine, diethylamine and diisopropylamine are often used. Other bases such as potassium carbonate or cesium carbonate are also sometimes used. The general order of reactivity of organic electrophiles relative to the leaving groups is: vinyl iodide > vinyl triflate > vinyl bromide > aryl iodide > aryl triflate > aryl bromide >> aryl chloride; the use of aryl or vinyl iodides often results in fast rate of Sonogashira reaction.

In general, Sonogashira reactions have great importance in organic synthesis and a number of applications in various fields like synthesis of natural products, electronic and electrooptical molecules for nanostructures.

![Fig 1.2: A general catalytic cycle for Sonogashira reaction](image-url)
1.2 Furanones and Pyrrolones:

1.2.1 Introduction:

Furanones, also called butenolides, are unsaturated $\gamma$-lactones and mainly exist in two isomeric forms i.e. 2,3- and 2,5-dihdrofuran-2-ones. They are valuable synthetic intermediates and key structural subunits of a variety of natural products. They are typical products of polyketide biochemical synthesis pathways. They are ubiquitous chemical moieties found in a large number of natural products many of which are biologically active like rubrolide O.

Furanone derivatives possess a broad spectrum of biological activities like anti-inflammatory, anti-tumor, anticonvulsant, antimalarial, anti-platelet, anti-oxidant, anti-HCV, antibacterial, and antifungal agents. They are also used as potent and selective antagonist of endothelin (ET) for preventing acute hypoxia induced pulmonary hypertension. They also act as 4-hydroxyphenylpyruvate dioxygenase (4-HPPD) inhibitors for the treatment of life threatening tyrosinaemia type I disease and also have the potential to serve as a new class of herbicides for control of grass and broad leaf weeds. They also show platelet-activating factor receptor binding inhibitory activity. A number of furanone containing compounds have been successfully commercialized, such as Rofecoxib (Vioxx®).

Pyrrolones also represents an important class of heterocycles. They are also found in many natural products like Sarcotrine F and Strobilinin.
Pyrrolone derivatives possess numerous biological activities. They act as inhibitor of cardiac cAMP phosphodiesterase. They also act as modulator of GABA receptor with anticonvulsant activity. They have been shown to possess immunosuppressive activity. They also show analgesic and anti-inflammatory activity with reduced gastrointestinal toxicity and lipid peroxidation. They act as antibacterial and antifungal agents. They also act as Pim1 inhibitors for cancer therapy.

1.2.2 Synthetic methods:

A number of methods have been developed for the synthesis of furanones and pyrrolones. Lee et al. have shown synthesis of furanones via boron-catalyzed direct aldol reaction of pyruvic acids. Reaction takes place in water at room temperature with low catalyst loadings. A wide range of aldehydes may be used giving furanones in high yields.

Ma et al. have described an efficient method for the synthesis of substituted furanones via \( \Gamma \)-catalyzed methyl-oxygen bond cleavage in 2-methoxyfurans and subsequent C-C bond formation at the 5-position. Due to easy availability of the starting materials, simple operation and mild conditions, this method will show its utility in the synthesis of furanones.
Surmont et al. have described efficient synthesis of 3,4,5-trimethyl-2(5H)-furanone, a new seed germination inhibitor, from 2,3-dimethylmaleic anhydride via nucleophilic addition of methyl-lithium followed by reduction using borohydride. This two-step method is straightforward and high-yielding and permits the large scale preparation of the seed germination inhibitor.\textsuperscript{53}

Langer et al. have carried out a new and efficient method for butenolide synthesis via $\text{Me}_3\text{SiOTf}$-catalyzed cyclization of 1,3-bis(trimethylsiloxy)-1,3-butadiene with oxalyl chloride.\textsuperscript{54}

Beck et al. have shown 5-acylamino butenolide synthesis by a novel three component reaction of isocyanides, glyoxals, and acetophosphonic acid diethyl esters. The one pot multicomponent reaction has advantages over multistep synthesis.\textsuperscript{55}
Just and Larock have described synthesis of highly substituted 2(3H)-furanones from 3-alkynoate esters and the corresponding acids via electrophilic cyclization. This highly efficient process proceeds under mild conditions, tolerates various functional groups, and generally provides substituted 2(3H)-furanones in good to excellent yields. 56

Nair et al. have shown a facile synthesis of highly functionalized furanones by a multicomponent reaction of 1,3-dimesityl imidazol-2-ylidene/imidazol-2-ylidene, dimethyl acetylenedicarboxylate (DMAD), and aldehyde. 57

Rousset et al. have carried out stereoselective synthesis of E-γ-tributylstannylmethylidene furanone via palladium-catalyzed cross-coupling/cyclization reaction of tributylstannyl 3-iodopropenoate derivatives with tributyltinacetylene. 58
Ma et al. have shown palladium(0)-catalyzed cyclization reaction of polymer-supported aryl iodides with 1,2-allenyl carboxylic acid to give polymer supported butenolides which could be easily cleaved by Lewis acid-catalyzed process in good yields and purities.\textsuperscript{59}

Rondla et al. have used palladium-catalyzed C-CN activation for intramolecular cyanoesterification of alkynes for the synthesis of butenolides in good to excellent yield.\textsuperscript{60}

Huang and Zhou have described CuX\textsubscript{2}-mediated cyclization reaction of cyclopropylideneacetic acid/ester for the facile synthesis of 4-halomethyl-2(5\textit{H})-furanones.\textsuperscript{61}
Recently Qi et al. have shown a novel carbon dioxide triggered and copper-catalyzed domino reaction for the efficient synthesis of highly substituted furanones. Nitriles not only act as solvent but also as reactant. This method has the advantage of low cost, readily available catalyst and starting materials and its simple experimental procedure.62

\[
\begin{align*}
 R = H, \text{Alkyl} \\
 R^1 = H, \text{Et} \\
 X = \text{Br, I} \\
 \end{align*}
\]

Chen et al. have described a one pot high stereoselective synthesis of furanones via Pd(OAc)\(_2\)-catalyzed cyclization of 2,3-allenoic acid in the presence of terminal \(\alpha,\beta\)-unsaturated alkynones.63

\[
\begin{align*}
 R^1 &= \text{Py, Ph, subst-Ph} \\
 R^2, R^3 &= \text{alkyl} \\
 R^4 &= \text{Me, } n\text{-Bu, c-Pr, Ph} \\
\end{align*}
\]

Ma and Yu have studied an efficient methodology for the synthesis of \(\beta\)-allylic furanones via palladium(II)-catalyzed coupling-cyclization reaction of 2,3-allenoic acids with allylic halides.64
Alam et al.\textsuperscript{49a} and Husain et al.\textsuperscript{49b} have shown efficient synthesis of 2(3\textit{H})-furanones and their nitrogen analogs 2(3\textit{H})-pyrrolones. The compounds were evaluated for different activities and some showed promising activities.

Hasse and Langer have described a convenient synthesis of a variety of pyrrolones via acid-mediated reaction of amines with furanones.\textsuperscript{65a}

Similarly Goh \textit{et al.} have shown efficient method for conversion of furanones to pyrrolones. This method has the advantage of higher yields and can be used for synthesis of a series of new dihydropyrrol-2-ones with anti-bacterial properties.\textsuperscript{65b}
1.3 Chromenoquinoliones:

1.3.1 Introduction:

Quinolines are important class of heterocycles with unique biological activities. They are valuable synthetic intermediates and key structural subunits of a variety of natural products in the form of quinoline alkaloids like 2-acetylevolitrine and 6-hydroxyquinoline-8-carboxylic acid. Quinoline derivatives represent privileged moieties in medicinal chemistry and possess diverse range of biological activities including antimalarial, anticancer, antituberculosis, anti-inflammatory, anti-Alzheimer, anti-HIV, anti-HBV, anti-HCV, antioxidant, antifungal and antibacterial. They are also found in active pharmaceutical ingredients including Cetromycin (antibacterial), Pitavastatin (statin), Montelukast (asthma and allergy) and many antimalarial drugs. They are used as estrogen receptor ligands and also for the treatment of estrogen dependent diseases. Quinoline derivatives also act as potent liver X receptor (LXR) agonists. They also find applications in agrochemicals and effect chemicals such as dye stuffs and corrosion inhibitors.

Differently fused chromenopyridin-5-ones are also under study due to their biological activities. Some of them make the backbone of naturally occurring alkaloids, for example, of Santiagonamine. Several chromeno[4,3-b] pyridin-5-ones, both natural and non-natural products are currently under clinical trials and have attracted much attention in the recent years. The related 6H-chromeno[4,3-b]quinolines have also been studied in medicinal chemistry, such as a new series of
estrogen receptor β-selective ligands. The attachment of fluorine-containing functional groups to biomolecules often leads to the development of new physiologically active compounds. Langer group has some recent achievements related to the synthesis of fluorinated drug like scaffolds.

1.3.2 Synthetic methods:

A number of strategies have been devised for the synthesis of quinoline ring system. Horn et al. have reported a convergent, regiospecific two component synthesis of quinolines from α,β-unsaturated ketones and o-aminophenylboronates.

\[
\begin{align*}
\text{B(OR)}_2^+\text{NH}_2 + \text{R}^1\text{R}^2\text{O} & \xrightarrow{\text{toluene, rt}} \xrightarrow{\text{then Pd/C, air, reflux}} \text{R}^3\text{R}^2\text{R}^1 \\
\text{R}^1 &= \text{Me, Ph, 4-MeOC}_6\text{H}_4, 1\text{-napthyl, 3-thienyl, 2-pyridyl} \\
\text{R}^2 &= \text{H, Me} \\
\text{R}^3 &= \text{H, C}_5\text{H}_11, \text{Ph, 4-MeOC}_6\text{H}_4, 4\text{-ClC}_6\text{H}_4, 4\text{-NO}_2\text{C}_6\text{H}_4
\end{align*}
\]

Suginome et al. have shown a new method for the synthesis of 2,3-disubstituted quinolines through nucleophile triggered cyclization of o-alkynylisocyanobenzenes.

\[
\begin{align*}
\text{NC}_R & \xrightarrow{\text{Nu}^- \text{or NuH}} \xrightarrow{\text{Nu} = \text{OMe, NEt}_2, \text{or HC(CO}_2\text{Et})_2} \\
\text{R} &= \text{t-Bu, c-Hex, CH}_2\text{OCH}_3, \text{Ph}
\end{align*}
\]

Isobe et al. have studied synthesis of 4-chloroquinolines via palladium-catalyzed chloroimination of imidoyl chlorides to a triple bond. This novel Pd-catalyzed chloroimination reaction expands the scope of palladium chemistry.
Majumder *et al.* have shown a titanium-catalyzed three-component coupling reaction for direct access to substituted quinolines. The primary amines employed can be substituted anilines, aminonapthalenes, or even heterocyclic amines, which leads to a variety of substituted quinolines.\(^{94}\)

Banwell *et al.* have described synthesis of quinolines via palladium(0)-mediated Ullmann cross-coupling of 1-bromo-2-nitroarenes with \(\beta\)-halo-enals and then reaction with dihydrogen in the presence of Pd on C. This synthesis highlight the utility of Pd(0)-mediated Ullmann cross-coupling in the synthesis of heterocycles.\(^{95}\)

Stone has shown an improved Larock method for the one-pot synthesis of substituted quinolines via a Heck reaction of 2-bromoanilines and allylic alcohols followed by dehydrogenation with diisopropyl azodicarboxylate (DIAD).\(^{96}\)
Gao et al. developed a domino reaction for the synthesis of quinolines via palladium-catalyzed Sonogashira coupling of benzimidoyl chlorides with 1,6-enynes and then cyclization. The procedure is simple, rapid and general, and the substrates are readily available. ⁹⁷

Hogan and O’Shea have studied application of the carbolithiation/electrophile reaction methodology for the synthesis of quinolines. ⁹⁸

Jiang and Si have shown a one pot synthesis of 4-trifluoromethyl-substituted quinoline via zinc-mediated alkynylation-cyclization of o-trifluoroacetyl anilines. The salient features of the procedure are facile synthesis under mild conditions and rapid access to a wide range of functionalized 4-trifluoromethylated quinolines. ⁹⁹
Korivi and Cheng have described an efficient and convenient route to 2,4-disubstituted quinoline synthesis by nickel catalyzed cyclization of 2-iodoanilines with aroylalkynes. The reaction can be employed for the synthesis of naturally occurring quinolines derivatives in good yields.\textsuperscript{100}

\[
\begin{align*}
\text{R}^1 &= \rho\text{-Cl}, \rho\text{-MeO}, \alpha\text{-MeO}, \text{H}, \rho\text{-CF}_3 \\
\text{R}^2 &= \text{Ph}, \alpha\text{-C}_3\text{H}_5
\end{align*}
\]

Wu et al. have found a reversal of the standard regiochemistry of the Skraup-Doebner-Von Miller quinoline synthesis when anilines were condensed with γ-aryl-β,γ-unsaturated α-ketoesters in refluxing TFA.\textsuperscript{101}

\[
\begin{align*}
\text{X} &= \text{H, 4-OMe, 4-Me, 4-F, 4-NO}_2
\end{align*}
\]

Sakai et al. have described a direct method for the synthesis of polysubstituted quinolines by \textit{InBr}_3-promoted dimerization of 2-ethynylaniline derivatives. This is the first direct synthesis of quinolines skeleton via dimerization of identical molecules.\textsuperscript{102}
Plaskon et al. have shown a facile synthesis of quinolines based on TMSCl-mediated recyclization of 3-formylchromone with various anilines. TMSCl acts as a promoter and water scavenger. The developed procedure can be applied for the synthesis of diverse sets of functional drug like quinolines.\textsuperscript{103}

Mulakayala et al. have reported ultrasound-promoted catalyst free synthesis of 6\textit{H}-1-benzopyrano[4,3-\textit{b}]quinolines-6-one via the reaction of 4-chloro-2-oxo-2\textit{H}-chromene-3-carbaldehyde with anilines. Many of the compounds were found to be active for anti-proliferative properties.\textsuperscript{104a}

1.4 Dibenzopyranones:

1.4.1 Introduction:

Coumarins (2\textit{H}-1-benzopyran-2-ones, 2\textit{H}-chromen-2-ones) constitute an important class of heterocycles. They are subunits of many natural products and a range of relevant pharmaceuticals with unique biological activities. These compounds
are well known aromatic lactones isolated from a variety of plant sources\textsuperscript{105} and are associated with diverse range of bioactivities.\textsuperscript{106,107} On the other hand, the coumarin framework is present in potential drug candidates as nonpeptidic HIV protease inhibitors,\textsuperscript{108} topoisomerase II\textsuperscript{109} and tyrosine kinase\textsuperscript{110} inhibitors. Many coumarins (natural, semi-synthetic and synthetic) have occupied an important place in drug discovery, as one of the so-called privileged drug scaffold. Moreover, heterocyclic composites, with coumarin subunit are of particular interest as fluorescent dyes that have gained wide applications in material science.\textsuperscript{111} Fluorescent compounds containing coumarin moiety are currently using for DNA and RNA labelling.\textsuperscript{105}

The related dibenzopyranone is also a privileged scaffold in many natural products\textsuperscript{112} such as alternariol, autumnariol, autumnariniol, altenuisol and in biologically active compounds like gilvocarcin V.\textsuperscript{113}

They possess diverse range of biological properties like anticancer, cardioprotective and anti-oxidant activity.\textsuperscript{114-116} In addition dibenzopyranones have been used as intermediated in the synthesis of several pharmacologically interesting compounds including progesterone, glucocorticoid receptor agonists\textsuperscript{117} and endothelial cell proliferation inhibitors.\textsuperscript{118} Furthermore dibenzopyranones occur naturally in many food sources including citrus fruits, herbs and vegetables.\textsuperscript{119}
Heteroaryl-fused benzopyranones constitute sizable group of heterocyclic compounds found in many natural products like lamellarin D and coumestrol. They show biological properties like activity against breast cancer cell lines, benzodiazepine receptor ligands and HIV-1 integrase inhibitors etc.

1.4.2 Synthetic methods:

Several methods have been developed for the synthesis of dibenzopyranones. The most popular method for their synthesis involves Suzuki-Miyaura cross-coupling reaction followed by Lewis acid mediated lactonization.

\[
\text{OMe} \quad \text{O} \quad \text{OMe} \\
\text{X} \quad \text{MeO} \quad \text{B(OH)_2} \quad \text{Pd(PPh}_3\text{)}_4 \quad \text{base} \quad \text{MeO} \quad \text{R}^1 \quad \text{R}^2 \\
\text{R}^1 = \text{Cl, Br, Me, OCH}_3 \\
\text{R}^2 = \text{H, Me, OCH}_3, \text{Cl} \\
\text{Lewis acid} \\
\text{base}
\]

Thasana et al. have shown a simple and effective microwave assisted C–O\text{caboxylic coupling reaction catalyzed by copper(I) salts for the synthesis of dibenzopyranones. The reaction of various 2-halobiarylcarboxylic acids was examined using microwave irradiation.}

\[
\text{X} \quad \text{COOH} \\
\text{R, R'} = \text{H, OMe, diOMe}
\]

Sanz et al. have described synthesis of dibenzopyranones via tert-butyl-lithium mediated cyclization of bromobenzylhalophenyl ethers followed by \textit{in situ} oxidation. This strategy has been applied to the short and efficient synthesis of Amaryllidaceae alkaloids trisphaeridine and N-methylcrinasiadine.
Teske and Deiters have reported synthesis of dibenzopyranones via microwave mediated ruthenium-catalyzed [2+2+2] cyclotrimerization reaction of aryl diynes. Three members of the cannabinoid class, cannabinol, cannabinol methyl ether, and cannabino diol were synthesis following this strategy.  

Langer et al. have shown synthesis of 7-hydroxydibenzopyranones via the addition of bisilyl enol ethers to chromenones and then treatment with NEt3. The strategy was used for the synthesis of a great variety of dibenzopyranones, including the natural product, autumnariol and a new fluorescence dye, which exhibits promising optical properties.  

Jung and Allen have reported novel synthesis of dibenzopyranones in excellent yield via Diels-Alder reaction of 4-cyanocoumarin with 1-siloxy diene followed by elimination-aromatization with base.
An efficient and general route to the synthesis of heteroaryl dibenzopyranones has been achieved from biaryl-<i>o</i>-carbamates by combined directed <i>ortho</i> and remote metallation-Suzuki cross-coupling strategies.\textsuperscript{128}

Recently Vishnumurthy and Makriyannis have reported a microwave promoted novel and efficient one step parallel synthesis of dibenzopyranones via Suzuki-Miyaura cross-coupling reaction.\textsuperscript{129}

Recently Pottie <i>et al.</i> have shown synthesis of dibenzopyranone via the inverse electron demand Diels-Alder reaction. A set of coumarin-fused electron deficient 1,3-dienes was synthesized which were then reacted with enamines derived from cyclopentanone and pyrrolidine to afford respective dibenzopyranones.\textsuperscript{130}
1.5 Isoquinolinones:

1.5.1 Introduction:

Isoquinolone derivatives are important class of heterocycles with unique biological activities. The Isoquinolone ring system is found in many natural products especially plant alkaloids like ruprechstyril and thalifoline. They have many biological activities like anticancer, JNK inhibitors for the treatment of diabetes, cancer, inflammation, stroke etc, Rho-kinase inhibitors for the treatment of diabetes, neurodegenerative diseases and cancer and non-peptide dipeptidyl peptidase IV inhibitors for the treatment of diabetes.

Thiophene is considered to be bioisostere of benzene ring and can be used for fine tuning of properties of potential drug molecules. Both aromatic rings are similar in size (isostere) and electronic properties. The diameter of sulfur atom is roughly equivalent to the distance between two neighboring carbon atoms in benzene. The physiological effects of thiophene are similar to those of benzene (bioisostere), with frequent superior pharmacodynamic, pharmacokinetic, or toxicological properties.

Thienopyridine derivatives have many biological properties such as potent CHK1 inhibitor and c-Src inhibitors for cancer therapy. Ticlopidine (trade name Ticlid) and Clopidogrel (trade names Plavix and Clopilet) are two antiplatelet drugs derived from the thienopyridine skeleton, often used in the treatment of coronary artery disease, peripheral vascular disease and cerebrovascular disease. Similarly
thienopyridinone derivatives also have found various biological applications as potent GSK 3β inhibitor\textsuperscript{140} for the treatment of neurodegenerative diseases such as Alzheimer and neurological diseases such as bipolar disorders, as potent CDC7 inhibitors\textsuperscript{141} for cancer therapy and as a cytoprotectant.

1.5.2 Synthetic methods:

A number of strategies have been developed for the synthesis of isoquinolinones. Some of the strategies are as follows:

Davis \textit{et al.} have shown synthesis of isoquinolinones via double lithiation of arylbenzamides and the resulting polyanion-type intermediate were condensed with aromatic esters followed by acid cyclization.\textsuperscript{142}

\[
\begin{align*}
\text{R} &= \text{-Ar, -CH}_2\text{Ar, or -N(CH}_3)_2 \\
\text{R'} &= \text{Phenyl or subst. Phenyl}
\end{align*}
\]

Guastavino \textit{et al.} have reported synthesis of isoquinolinones and fused isoquinolinones via photostimulated S\textsubscript{RN}1 reaction of 2-iodobenzamide with enolates of aromatic, aliphatic and cyclic ketones in DMSO. Due to the availability of the starting materials and mild conditions of the procedure, this methodology can be used as a general method for the synthesis of isoquinolinones.\textsuperscript{143}

\[
\begin{align*}
\text{R} &= \text{-Ar, -CH}_2\text{Ar, or -N(CH}_3)_2 \\
\text{R'} &= \text{Phenyl or subst. Phenyl}
\end{align*}
\]

Snow \textit{et al.} have shown a versatile method for the synthesis of isoquinolinone via reaction of 2-chlorobenzonitriles with β-ketoesters in an S\textsubscript{N}Ar reaction. The compounds have been shown to possess kinase inhibitor activity.\textsuperscript{144}
Miura et al. have reported facile synthesis of isoquinolones in high yields by reaction of 1,2,3-benzotriazin-4(3H)-ones with terminal alkynes in the presence of nickel(0)/phosphine catalyst. A wide range of alkynes were regioselectively incorporated into 1,2,3-benzotriazin-4(3H)-ones with loss of a nitrogen molecule.  

\[
\begin{align*}
\text{R} &= \text{H, Me, Bn, subst-Ph} \\
\text{R}^1 &= \text{Me, i-Pr, n-Bu, Ph, TMS} \\
\text{R}^2 &= \text{Me, CO}_2\text{Et, Ph, subst-Ph}
\end{align*}
\]

Sakamoto et al. have shown synthesis of napthyridine derivatives by cyclization of pyridinecarboxamides having an ethynyl group adjacent to the carbamoyl group. The synthesis of the starting pyridine derivatives were easily accomplished by cross-coupling of the corresponding halopyridines with acetylenes.

Zheng and Alper have described a novel and efficient route to substituted isoquinolones via palladium catalyzed carboxylation–decarboxylation of diethyl(2-iodoaryl)malonates with imidoyl chlorides. The reaction is compatible with a variety of functional groups and affords isoquinolinones in good yield.
Liu et al. have shown an easy and convenient method for the synthesis of highly substituted isoquinolones by nickel-catalyzed annulation of substituted 2-halobenzamides with alkynes. This protocol is successfully applied to the total synthesis of oxyavicine with excellent yield.\(^{148}\)

Jagtap et al. have reported a facile and convenient synthesis of substituted isoquinolinones by the base-promoted condensation reaction of homophthalic anhydride and 2-(bromomethyl)-benzonitrile.\(^{149}\)

Xiang et al. have studied a concise synthesis of isoquinolinone via the Ugi four-component reaction and then palladium-catalyzed intramolecular Heck reaction. This two step synthetic route allows easy synthesis of a variety of isoquinolinones.\(^{150}\)
Thansandote et al. have shown a new and efficient route to the synthesis of functionalized isoquinolinones in good yields via palladium-catalyzed annulation of substituted halobenzamides with norbornadiene.\textsuperscript{151}

Kajita et al. have described a new synthesis of substituted isoquinolinones via nickel-catalyzed decarbonylative addition of phthalimides to alkynes.\textsuperscript{152}

Guimond et al. have reported synthesis of isoquinolones via rhodium-catalyzed reaction. This synthesis operates under mild conditions, and is not sensitive to air or moisture.\textsuperscript{153}
Wang et al. have described an efficient one-pot copper-catalyzed method for the synthesis of substituted isoquinolones via cascade reactions of substituted 2-halo-benzamides with β-keto esters under mild conditions.\(^\text{154}\)

\[
\begin{align*}
\text{R}^1 \text{H, Me, OMe, Cl} \\
\text{R}^2 \text{Me, n-Pr, iso-Pr} \\
\text{R}^3 \text{Et, t-Bu}
\end{align*}
\]

1.6 4-Quinolinones:

1.6.1 Introduction:

Quinolinones represent one of the most important class of nitrogen containing heterocycles. They are found in a large number of natural products many of which are biologically active like Aurachin C and Transtorine.\(^\text{155}\)

\[
\begin{align*}
\text{Aurachin C (R=OH)} & \quad \text{Aurachin D (R=H)} \\
\text{Transtorine (antibacterial)}
\end{align*}
\]

(antiplasmodial)

Quinolinones are also integral to a large number of synthetic compounds with activities including anticancer,\(^\text{156}\) anti-HIV,\(^\text{157}\) anti-HCV,\(^\text{158}\) antioxidant,\(^\text{159}\) anti-inflammatory,\(^\text{159,160}\) antimalarial\(^\text{161}\) and anti-depressant.\(^\text{162}\) They also represent an important category of antibacterial agents\(^\text{163}\) and some show antimycobacterial activities.\(^\text{164}\) They also act as potential agents for the treatment of Alzheimer disease.\(^\text{165}\) They also act as selective androgen receptor modulator\(^\text{166}\) and as selective human neuronal nitric oxide synthase inhibitors.\(^\text{167}\) They also show cardiac stimulant\(^\text{168}\) and diuretic activity.\(^\text{169}\)
Thienopyridinones also have interesting biological properties like they act as antibiotics,\textsuperscript{170} as AMP-activated protein kinase (AMPK) activator\textsuperscript{171} for the treatment of diabetes, metabolic disorders, obesity, and protects the heart against ischemia-reperfusion injury and as inhibitor of $[3H]$Glycine binding to the N-methyl-D-aspartase (NMDA) receptor.\textsuperscript{172}

1.6.2 Synthetic methods:

Many methods have been developed for the synthesis of 4-quinolines. The most widely used method for the synthesis of 4-quinolone is base promoted cyclization of N-(ketoaryl)-amides (Camps cyclization). Ding \textit{et al.} have shown microwave assisted synthesis of 4-quinolones by exposing corresponding acylated 2-aminoacetophenone to microwave irradiation in the presence of NaOH. This is a rapid and straightforward method giving 4-quinolones in high yields.\textsuperscript{173a}

\[
\begin{array}{c}
\text{NaOH/t-BuOH} \\
\text{MW/ 120 °C}
\end{array}
\]

\[
\text{R= H, 4-Cl, 4,5-OMe, 3,4,5-OMe}
\]

Jones \textit{et al.} have shown a direct two step method for the synthesis of 4-quinolones involving Cu-catalyzed amidation-base-mediated Camps-cyclization. With CuI, a diamine ligand, and base as the catalyst system, the amidation reactions proceed in good yields for a range of aryl, heteroaryl, and vinyl amides.\textsuperscript{173b}

\[
\begin{array}{c}
\text{CuI, ligand} \\
\text{base, toluene} \\
\text{90-110 °C}
\end{array}
\]

\[
\text{X = Br, I}
\]

Haradil \textit{et al.} have reported an efficient method for the synthesis of substituted 4-quinolones via reaction of isatoic anhydride with ketone derived enolates and then cyclization of anthranilamides with polyphosphoric acid. The method provides an
efficient and straightforward pathway for the synthesis of substituted 4-quinolones.\textsuperscript{174a}

\begin{center}
\includegraphics[width=\textwidth]{synthesis.png}
\end{center}

Abdou and Kamel have shown synthesis of 4-quinolones by reaction of isatoic anhydride with triphenylphosphonium salts.\textsuperscript{174b}

Yoshino \textit{et al.} have demonstrated a new nickel-catalyzed reaction of isatoic anhydride with alkynes to afford 4-quinolones.\textsuperscript{174c}

\begin{center}
\includegraphics[width=\textwidth]{catalysis.png}
\end{center}

Zewge \textit{et al.} have shown efficient synthesis of 4-quinolones by cycloacylation of aniline derivatives in the presence of Eaton’s reagent. This high yielding methodology is applicable to a wide variety of anilines and requires milder conditions than those traditionally employed and is characterized by relatively low reaction temperature and ease of product isolation.\textsuperscript{175}

\begin{center}
\includegraphics[width=\textwidth]{cycloacylation.png}
\end{center}

Haddad \textit{et al.} have reported convergent synthesis of 4-quinolone (key substructure of
the protease inhibitor BILN 2061) via palladium-catalyzed carbonylative Sonogashira coupling/cyclization of 2-iodomethoxyaniline with thiazolylacetylene.\textsuperscript{176}

Bernini \textit{et al.} have studied synthesis of 4-quinolones via Cu-catalyzed cyclization of 1-(2-halophenyl)-2-en-3-amin-1-one. The reaction tolerates a variety of useful functionalities including ester, keto, cyano and chloro substituents.\textsuperscript{177}

Al-Hiari \textit{et al.}\textsuperscript{178a} and Guillou \textit{et al.}\textsuperscript{178b} have shown base promoted cyclization of enamines for the synthesis of 4-quinolones.

Huang \textit{et al.} have reported a mild, one pot synthesis of 4-quinolones via Pd-catalyzed amidation of 2-acetylbromoarenes and the subsequent base promoted cyclization. The easily available starting materials, mild reaction conditions, and simple manipulation makes this an attractive method for the synthesis of 4-quinolones.\textsuperscript{179}
Zhao and Xu have carried out an efficient Pd-catalyzed tandem amination reaction for the synthesis of 4-quinolones in good to excellent yield from easily accessible ortho-haloaryl acetylenic ketones and primary amines.\textsuperscript{180}

1.7 Plan of work:

In view of the extensive literature survey, it was revealed that 2-(3\textit{H})furanones, 2-(3\textit{H})pyrrolones, chromenoquinolinones, thienochromenones, and thienopyridinones belong to a very important class of heterocycles that exhibit a vast range of biological activities. These heterocycles were synthesized following the synthetic methods as shown in (Scheme 1.1). 2(3\textit{H})-Furanones were synthesized by condensation reaction of 4-(substituted benzoyl)propionic acid with aromatic aldehydes in the presence of Ac\textsubscript{2}O/Et\textsubscript{3}N.\textsuperscript{49} Reaction of furanones with benzylamine and then cyclization of resulting intermediates with 6-N HCl gave 2(3\textit{H})-Pyrrolones.\textsuperscript{49} 7-(Trifluoromethyl)-6\textit{H}-chromeno[4,3-\textit{b}]quinolin-6-ones were synthesized by reaction of anilines with 4-chloro-3-(2,2,2-trifluoroacetyl)-2\textit{H}-chromen-2-one and then acidic annulation. Thieno[2,3-\textit{c}]chromen-4-one and 7,8,9,10-tetrahydrobenzothieno[3,2-\textit{c}]chromen-6-one were prepared by Suzuki-Miyaura cross-coupling followed by BBr\textsubscript{3}-mediated lactonization.\textsuperscript{122} 5-Substituted thieno[2,3-\textit{c}]pyridin-7(6\textit{H})-one and 3-substituted-5,6,7,8-tetrahydrobenzothiophen-3,2-\textit{c}pyridin-1(2\textit{H})-one were synthesized by first Sonogashira cross-coupling reaction of halothiophens with terminal alkynes, then conversion of ester and nitrile functionality into amide and finally base mediated
cyclization. 4,5-Disubstituted thieno[3,2-b]pyridin-7(4H)-one were prepared by Pd-catalyzed tandem amination reaction of α,β-ynones and commercially available anilines/amines. The present study was carried out in the quest to synthesize furanones, pyrrolones, chromenoquinolinones, thienochromenones and thienopyridinones, not synthesized earlier.

Scheme 1.1: Content of present thesis
2.1 Synthesis of 3-Arylidene-5-(4-substituted phenyl)furan-2(3H)-ones and 1-Benzyl-3-arylidene-5-(4-substituted phenyl)-1H-pyrrol-2-(3H)-ones:

2.1.1 Results and Discussion:

In this section of the thesis results related to the synthesis of 2(3H)-furanones and its nitrogen analogs 2(3H)-pyrrolones are discussed. 2(3H)-Furanones were synthesized by condensation reaction of aromatic aldehydes with benzoylpropionic acid which in turn was synthesized by Friedel-Craft’s acylation reaction of substituted benzene. When ethoxybenzene (phenetole) 1 or bromobenzene 2 was treated with succinic anhydride 3 in the presence of anhydrous aluminum chloride, 4-(ethoxybenzoyl)propionic acid 4 and 4-(bromobenzoyl)propionic acid 5 were obtained in good yield (Scheme 2.1).

![Scheme 2.1](attachment://Scheme_2.1.png)

**Scheme 2.1** Synthesis of 4, 5: *Reagents and conditions: i) 1, 2 (15 mL), 3 (1 equiv.), anhydrous AlCl₃ (2.2 equiv.), 100 °C, 2 h.*

In the IR spectrum the appearance of a broad band for O-H centered at 3000 cm⁻¹ along with C=O absorption at 1700 cm⁻¹ shows the formation of the acids 4, 5. Reaction of 3-(4-ethoxybenzoyl)propionic acid 4 with different aromatic aldehydes 6 in the presence of acetic anhydride and triethylamine under anhydrous conditions resulted in the formation of 3-arylidene-5-(4-ethoxyphenyl)furan-2(3H)-one 7a-q in
65-78% yield. Similarly reaction of 3-(4-bromobenzoyl)propionic acid 5 with
different aromatic aldehydes 6 in the presence of acetic anhydride and triethylamine
under anhydrous conditions gave 3-arylidene-5-(4-bromophenyl)furan-2(3\(H\))-one 8a-l
in 65-80% yield (Scheme 2.2, Table 2.1).

![Reaction Scheme](image)

**Scheme 2.2** Synthesis of 7a-q and 8a-l: *Reagents and conditions: i) 4, 5 (1 equiv.), 6 (1 equiv.), Ac\(_2\)O, triethylamine, reflux, 4 h.*

**Table 2.1** Synthesis of 7a-q and 8a-l

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<tr>
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<th>% (7)(^a)</th>
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<th>Ar</th>
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<tr>
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<td>69</td>
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<tr>
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<td>65</td>
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<td>69</td>
<td>k</td>
<td>2,4-diClC(_6)H(_3)</td>
<td>74</td>
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The structures of the 2(3H)-furanones were confirmed by spectral analysis i.e. IR, $^1$H NMR, $^{13}$C NMR, GC-MS and elemental analysis. In the IR spectrum, all the compounds show absorption peaks at around 1750 cm$^{-1}$ and 1250 cm$^{-1}$ for stretching vibration frequencies of carbonyl and C-O of the lactone ring. The $^1$H NMR of the furanones showed two characteristic peaks in the range $\delta$ 6.76-6.90 and 7.34-7.50 ppm for lactone ring $\beta$-H and olefinic-H of the arylidene substituent respectively. The $^{13}$C NMR spectra of all the compounds showed characteristic peak in the range $\delta$ 97-100 ppm for the lactone ring $\beta$-C. In the mass spectrum, all the compounds give molecular ion peak (M$^+$) with reasonable intensities. There also appear peaks with good intensities at m/z 149 (OEt-C$_6$H$_4$-C$^+$=O) and 180 (Br-C$_6$H$_4$-C$^+$=O) which on subsequent loss of CO give peaks at m/z 121 (OEt-C$_6$H$_4^+$) and 155 (Br-C$_6$H$_4^+$) respectively. Molecular ion or other ions containing halogen, appear as a cluster of peaks due to isotopic abundances.

Some of the 2(3H)-furanones were then converted into their nitrogen analogs 2(3H)-pyrrolones. Reaction of some of the 3-arylidene-5-(4-ethoxyphenyl)furan-2(3H)-one 7 and 3-arylidene-5-(4-bromophenyl)furan-2(3H)-one 8 with benzylamine 9 in dry benzene gave $\gamma$-keto benzylamide 10a-f and 11a-f respectively which were then cyclized to 1-benzyl-3-arylidene-5-(4-ethoxyphenyl)-1H-pyrrol-2-(3H)-one 12a-f and 1-benzyl-3-arylidene-5-(4-bromophenyl)-1H-pyrrol-2-(3H)-one 13a-f respectively by refluxing in 6N-hydrochloric acid (Scheme 2.3, Table 2.2).

<p>| | | | |</p>
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<td>75</td>
<td>l</td>
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<tr>
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<td>q</td>
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<td>78</td>
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</table>

$^a$ Yields of isolated products
Scheme 2.3 Synthesis of 12a-f and 13a-f: Reagents and conditions: i) 7, 8 (1 equiv.), 9 (1.3 equiv.), dry benzene, reflux, 2h (ii) 6N-HCl, reflux, 1 h.

Table 2.2 Synthesis of 12a-f and 13a-f

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<th>No</th>
<th>Ar</th>
<th>% (13)</th>
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<td>3-ClC₆H₄</td>
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*Yields of isolated products

The structures of the 2(3H)-pyrrolones were confirmed by spectral analysis i.e. IR, ¹H NMR, ¹³C NMR, GC-MS and elemental analysis. In the IR spectrum carbonyl bond give stretching absorption at around 1700 cm⁻¹ with disappearance of ether C-O absorption and appearance of C-N absorption around 1250 cm⁻¹. In the ¹H NMR, β-H of the lactone ring and olefinic-H of the aryldene substituent appear at around the same δ values. The benzylic protons appear in the range δ 4.83-4.87 ppm. In the mass spectrum the molecular ion peak appears at reasonable intensity. Also there appears
major peak at m/z 91 corresponding to tropylium ion. The molecular ion or other ions containing halogen appear as a cluster of peaks due to isotopic abundances.

2(3H)-furanones and 2(3H)-pyrrolones were then evaluated for their antioxidant, cytotoxicity and urease inhibition activities (chapter4). These compounds showed non significant antioxidant activity, nil brine shrimp lethality and low to moderate urease inhibition activity.

2.1.2 Conclusion:

In conclusion, an efficient method was reported for the synthesis of some new 3-arylidene-5-(4-substitutedphenyl)furan-2(3H)-ones by condensation of different aromatic aldehydes with 3-(4-substitutedbenzoyl)propionic acid. Some of the furanones were then converted into their nitrogen analogs 1-benzyl-3-arylidene-5-(4-substitutedphenyl)-1H-pyrrol-2-(3H)-one.

2.2 Synthesis of 7-(Trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-ones:

2.2.1 Results and discussion:

Herein results related to the synthesis of 7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one ring system by annulation of the aniline moiety to the pyridine ring is reported. For this purpose specially designed novel trifluoroacetyl-containing building block 17a was used. The synthesis of 6H-chromeno[4,3-b]quinolines heterocyclic framework, by reaction of 4-chloro-2-oxo-2H-chromene-3-carbaldehyde with anilines, using a related strategy was previously reported.\(^{104b}\) In the initial study, synthesis of todate unknown 4-chloro-3-(2,2,2-trifluoroacetyl)-2H-chromen-2-one 17a has been developed starting from commercially available 4-hydroxy-2H-chromen-2-one 14, by a one pot procedure shown in Scheme 2.4. The synthetic scheme consists of three steps: firstly, 4-hydroxycoumarin 14 was sylilated by TMSCl in 1,4-dioxane using dry pyridine as the base; secondly, acylation by TFAA \textit{in situ} delivers the corresponding intermediate 16. The later was then treated with POCl\(_3\) to give 4-chloro-3-(2,2,2-trifluoroacetyl)-2H-
chromen-2-one 17a ($\delta^{19}$F= - 75.8 ppm) in 93% yield (Scheme 2.4).

**Scheme 2.4** Synthesis of 4a. **Reagents and conditions:** (i) 1,4-dioxane, Py (2.1 eq.) 30 min, TMSCl (1.2 eq), 60 min r.t. (ii) 1.3 eqv. TFAA, 2h. 80-90 °C. (iii) POCl$_3$ (1.0 eq), 60 °C, 2 h.

The exact structure of product 17a was not clear, since theoretically this compound can exist in a form of another possible isomer, namely as 3-(1-chloro-2,2,2-trifluoroethylidene)-3H-chromene-2,4-dione 17b. The structure of 17a could be clearly confirmed by X-ray crystal structure analysis.

**Figure 2.1.** Ortep plot of 17a.

With compound 17a in hand, its reactions with a variety of commercially available $o$-, $m$-, $p$- substituted anilines 18 were studied to give 3-(trifluoroacetyl)-4-(arylamino)-2H-chromen-2-one 19 (Scheme 2.5, Table 2.3). First the reaction was conducted in dry solvents, such as DMF, CH$_2$Cl$_2$, toluene, 1,4-dioxane, with triethyl amine as base,
but the yields were less than 50%. At this stage, focus was turned towards the use of a new condensing media, namely DMF/TMSCl. This reaction condition gave the highest yields for the synthesis of 19 (Table 2.3). In the ¹H NMR spectra, the appearance of an NH peak at around δ 12.70-12.80 ppm supports formation of the product.

As regards the second step, by testing a number of reaction conditions (stirring with 37% HCl, POCl₃, PPA, Conc. H₂SO₄), concentrated sulfuric acid was found to be reaction media of choice for the intramolecular cyclization of 19 to give 7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-ones 20 (Scheme 2.5).

![Scheme 2.5](image)

Scheme 2.5. Synthesis of 19a-l and 20a-l; Reagents and conditions: (i) 17 (1 equiv.), 18 (1 equiv.), DMF/TMSCl, 120 °C, 12-24 h.; (ii) conc. H₂SO₄, 70 °C, 2 h.

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Table 3: Yields of isolated products

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ᵇ This compound was formed directly on the first step in DMF/TMSCl at 120 °C.

Reaction of 17a with meta substituted anilines i.e. m-anisidine and 2,3,4-trimethoxyaniline, in DMF/TMSCl gave the cyclized products 7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-ones 20 in a single step (Table 3), which could be explained on the basis of electron donating effect of the methoxy group.

The structures of the cyclized products were confirmed by spectral analysis i.e. IR, ¹H NMR, ¹³C NMR, GC-MS and elemental analysis. In the ¹H NMR spectra, disappearance of NH signal at around δ 12.70-12.80 ppm and in ¹³C NMR also disappearance of carbonyl C signal of the trifluoroacetyl group at around δ 181-182 ppm support formation of the cyclized products. In the mass spectral analysis, the molecular ion peak (M⁺) usually appeared as the base peak (100%). Finally the structure of one of the cyclized product 20k was unambiguously established by crystal structure investigation (Figure 2.2).

![Figure 2.2. Ortep plot of compound 20k.](image)
2.2.2 Conclusion:

In summary, synthesis of 4-chloro-3-(2,2,2-trifluoroacetyl)-coumarin 17a, a novel flourine-containing 1,3-CCC-dielectrophile on the basis of commercially available 4-hydroxycoumarin was developed. The reaction of 17a with a number of o-, m-, p- substituted anilines was studied. The method reported here in provides a straightforward approach to a wide range of 4-(trifluoromethyl)-5H-chromeno[4,3-b]pyridin-5-one ring system, which are not easily accessible by other methods.

2.3 Synthesis of Thieno[2,3-c]chromen-4-one and 7,8,9,10-Tetrahydrobenzothieno[3,2-c]chromen-6-one via Suzuki-Miyaura cross-coupling reaction followed by lactonization:

2.3.1 Results and discussion:

In this section results related to the synthesis of thienochromenones will be discussed. For the project, the amine methyl-3-aminothiophene-2-carboxylate 21 and ethyl-2-amino-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate 22 were commercially available. In the first step, amines 21 and 22 were converted into respective brominated products i.e. methyl-3-bromothiophene-2-carboxylate 23 and ethyl-2-bromo-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate 24 in good yields (83-86%) by treatment with tBuONO and CuBr₂ in acetonitrile¹⁸¹ (Scheme 2.6).

![Scheme 2.6 Synthesis of 23 and 24. Reagents and conditions: i) (1) tBuONO, CuBr₂, CH₃CN, 65 °C. (2) HCl](image)

In the ¹H NMR spectra, disappearance of the NH₂ peak at δ 3.78 ppm for 23 and 5.99
ppm for 24 supports formation of the brominated products.

The Suzuki–Miyaura (S-M) reaction of 23 and 24 with variously substituted aryl boronic acids 25 resulted in the formation of arylated thiophene carboxylates 26a-o and 27a-o respectively in 60-85% yields (Scheme 2.7, Table 2.4). The conditions of the reaction were optimized to have better yields of products. The best combination found was Pd(PPh₃)₄ (3 mol%) as catalyst, boronic acid (1.3 equiv.) and use of K₃PO₄ (1.5 equiv.) as base and 1,4-dioxane solvent (at 100-110 °C, 4-6 hours). It was also found that the products derived from aryl boronic acids containing electron-withdrawing substituents gave better yields than those derived from electron-rich boronic acids.

![Scheme 2.7 Synthesis of 26a-o and 27a-o. Reagents and conditions: (i) 23, 24 (1.0 equiv), 25 (1.3 equiv), K₃PO₄ (1.5 equiv), Pd(PPh₃)₄ (3 mol%), 1,4-dioxane, 100-110 °C, 4-6 h.](image)

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Yields of isolated products

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*Spectral analysis confirmed the formation of arylated products. The X-ray crystal structure of two of the Suzuki–Miyaura products i.e. 26a and 27i are shown below (Figures 2.3 and 2.4).*
Figure 2.4 Ortep plot of 27i

Treatment of variably substituted 2-methoxyphenylthiophene-carboxylates 26i-n and 27i-n with Lewis acid BBr₃ and subsequent addition of an aqueous solution of potassium tert-butoxide (KOrBu), resulted in the formation of thienochromenones 28i-n and 29i-n respectively in 75-86% yields (Scheme 2.8, Table 2.5).

Scheme 2.8 Synthesis of 28i-n and 29i-n. Reagents and conditions: i) (1) BBr₃ (4.0 equiv), CH₂Cl₂, 0→20 °C, 18 h (2). KOrBu, H₂O, 15 min, 20 °C.
Table 2.5 Synthesis of 28i-n and 29i-n

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$^a$ Yields of isolated products

The formation of the products proceeds by cleavage of the aryl methyl ether and subsequent base mediated lactonization. The structures of the thienochromenones were confirmed by spectral analysis i.e. IR, $^1$H NMR, $^{13}$C NMR and GC-MS. In IR spectrum, the C=O of lactone ring show absorption in the range 1671-1700 cm$^{-1}$. In $^1$H-NMR spectra, the signals for OCH$_3$ and OCH$_2$CH$_3$ disappear. In the $^{13}$C NMR spectra carbonyl group C give signal at around $\delta$ 156 ppm. In mass spectrum the molecular ion peak (M$^+$) also appears as the base peak (100%).

The structure of 28a and 28n were independently confirmed by X-ray crystal structure analysis (Figures 2.5 and 2.6).

![Ortep plot of 28a](image-url)
2.3.2 Conclusion:

In conclusion a simple, convenient and high yield method has been developed for the synthesis of some novel thienochromenones. The C-C bond formation via Suzuki-Miyaura reaction followed by lactonization afforded the target thienochromenones which could be of biological importance.

2.4 Synthesis of 5-Substituted thieno[2,3-c]pyridin-7(6H)-one and 3-Substituted-5,6,7,8-tetrahydrobenzothieno[3,2-c]pyridin-1(2H)-one based on Sonogashira cross-coupling-annulation procedure:

2.4.1 Results and Discussion:

Compounds 23 and 30 were synthesized by deaminative bromination reaction of their respective amines, which were commercially available. They were then subjected to Sonogashira cross-coupling reactions to give the respective alkynyl derivatives i.e. methyl 3-(alkynyl)thiophene-2-carboxylates 32a-j and 2-(alkynyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonitriles 33a-g in 50-78% yield (Scheme 2.9, Table 2.6). Different reaction conditions were examined and it was found that the best yields were obtained with the combination of Pd(PPh₃)₂Cl₂ (5 mol %), CuI (5
mol %), acetylene (1.5 equiv.), and di-isopropylamine at 70 °C, 2 h. In the Sonogoshira cross-coupling reaction, aliphatic alkynes gave less yields than aromatic alkynes.

Scheme 2.9 Synthesis of 32a-j and 33a-g. Reagents and conditions: i) 23, 30 (1.0 equiv), 31 (1.5 equiv), CuI (5 mol%), Pd(PPh₃)₂Cl₂ (5 mol %), DIPA, 70 °C, 2 h.

In the ¹³C NMR spectra, characteristic signals appear for acetylenic carbons at around δ 51 and 82 ppm for 32 and at around δ 79 and 100 ppm for 33.

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⁵ Yields of isolated products
When methyl 3-(alkynyl)thiophene-2-carboxylates 32a-j were heated with an excess amount of aqueous ammonia in ethanol in a pressure tube for 10-12 hours, 3-(alkynyl)thiophene-2-carboxamides 34a-j were obtained in excellent yields (80-90%) (Scheme 2.10, Table 2.7).

![Scheme 2.10 synthesis of 34a-j](image1)

**Scheme 2.10** Synthesis of 34a-j. *Reagents and conditions:* i) Aq. NH$_3$, EtOH, 80 °C, 10-12 h.

Similarly 2-(alkynyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonitrile 33a-g were converted by indirect acid catalyzed hydration, into corresponding amides i.e. 2-(alkynyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamides 35a-g in 69-79% yield, using a TFA-H$_2$SO$_4$ mixture as a reagent system (Scheme 2.11, Table 2.7).

![Scheme 2.11 synthesis of 35a-g](image2)

**Scheme 2.11** Synthesis of 35a-g. *Reagents and conditions:* (i) 1). TFA–H$_2$SO$_4$, 75 °C, 4-8 h 2). H$_2$O
Table 2.7 Synthesis of 34a-j and 35a-g

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a Yields of isolated products

In the IR spectrum, NH group shows two absorption bands in the range 3350-3180 cm⁻¹ while the carbonyl group show strong absorption in the range 1634-1650 cm⁻¹. In the ¹H-NMR spectrum, a singlet for (OCH₃) at around δ 3.85 ppm disappears while a signal appears in the range δ 6.21-6.66 ppm (NH₂) for 34. In the case of 35, in ¹H NMR, a signal appears in the range δ 5.67-5.86 ppm for (NH₂) while in ¹⁳C NMR peak for carbonyl carbon appears in the range 165.1-165.2. The structure of 34c was independently confirmed by X-ray crystal structure analysis (Figure 2.7).

Figure 2.7 Ortep plot of 34c
Finally cyclization of 3-(alkynyl)thiophene-2-carboxamides 34a-j and 2-(alkynyl)-4,5,6,7-tetrahydrobenz[6]thiophene-3-carboxamide 35a-g was carried out with sodium methoxide in methanol and the cyclized products i.e. 5-substituted thieno[2,3-c]pyridin-7(6H)-ones 36a-j and 3-substituted-5,6,7,8-tetrahydrobenzothieno[3,2-c]pyridin-1(2H)-ones 37a-g were obtained in 70-80% yield (Scheme 2.12, Table 2.8).

Scheme 2.12 Synthesis of 36a-j and 37a-g. Reagents and conditions: i) NaOMe, MeOH, 40-50 °C, 3-4 h.

Table 2.8 Synthesis of 36a-j and 37a-g

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*Yields of isolated products
The structures of the thienopyridinones were confirmed by spectral analysis i.e. IR, $^1$H NMR, $^{13}$C NMR, GC-MS and elemental analysis. In the IR spectrum NH gives one absorption band at around 3300 cm$^{-1}$ plus the appearance of a strong band in the range 1620-1630 cm$^{-1}$ for the C=O group supports formation of the cyclized products. In the $^1$H NMR, the NH signals appear in the range $\delta$ 9.49-11.99 ppm for 36 while in the range $\delta$ 10.20-10.11.07 ppm for 37. Also the vinylic proton appear as a signal in the range $\delta$ 6.42-7.03 ppm for 36 and in the range $\delta$ 6.81-6.86 ppm for 37. In the $^{13}$C NMR, the acetylenic-C signals disappear. In the mass spectrum, for 36, in cases with phenyl substituent the molecular ion peak (M$^+$) also appear as the base peak (100%), while in cases with alkyl side chain, the base peak (100%) appears at m/z 165. For 37, with phenyl side chain, the molecular ion peak appears as the base peak (100%). Finally the structure 36d was independently confirmed by X-ray crystal structure analysis (Figure 2.8).

![Figure 2.8 Ortep plot of 36d](image)

### 2.4.2 Conclusion:

To sum up, an efficient method for was reported for the the synthesis of some novel 5-substitutedthieno[2,3-c]pyridin-7(6$H$)-ones and 3-substituted-5,6,7,8-tetrahydro benzothieno[3,2-c]pyridin-1(2$H$)-ones by a cross coupling-annulation procedure. These compounds could be of biological importance.
2.5 Synthesis of 4,5-Disubstituted thieno[3,2-b]pyridin-7(4H)-one via palladium catalyzed tandem amination reaction:

2.5.1 Results and discussion:

In this section, Pd catalyzed tandem amination reaction is reported, consisting of sequential double C-N bond formation, to give 4,5-disubstituted thieno[3,2-b]pyridin-7(4H)-ones from α,β-ynones and commercially available anilines/amines. Methyl-3-bromothiophene-2-carboxylate 23 was prepared from commercially available methyl-3-aminothiophene-2-carboxylate by treatment with tBuONO and CuBr$_2$. Ester 23 was then converted into the corresponding acid 38 by hydrolysis with NaOH in EtOH/H$_2$O and then treating with HCl. In the IR spectrum, acidic O-H gave a broad band centered at 3100 cm$^{-1}$. Acid 38 was then converted into corresponding acid halide 39 by treatment with thionyl chloride (Scheme 2.13).

![Scheme 2.13 Synthesis of 38 and 39. Reagents and conditions: i) (1). 23 (1.0 equiv), NaOH (5 equiv.), H$_2$O/EtOH, 70-80 °C, 1-2 h (2) HCl. ii) SOCl$_2$ (excess), 70 °C, 4-6 h](image)

Sonogashira cross-coupling reaction of acid halide 39 with terminal alkynes 40a-e resulted in the formation of α,β-ynones 41a-e in 65-77% yield (Scheme 2.14, Table 2.9). Sonogashira cross-coupling of acid halide (1 equiv.) with PdCl$_2$(PPh$_3$)$_2$ (2 mol%), CuI (5 mol%), Et$_3$N (1 equiv.) in THF at room temperature gave best yield of α,β-ynones.
Scheme 2.14 Synthesis of 41a-e. Reagents and conditions: (i) 39 (1.0 equiv), 40 (1 equiv), Pd(PPh₃)₃Cl₂ (2 mol %), CuI (5 mol%), Et₃N (1 equiv.), THF, r.t., 2 h.

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*Yields of isolated products*

The synthesis of ynones was confirmed by spectral analysis. In $^{13}$C NMR, characteristic signals appear for acetylenic carbons at around δ 87 and 94 ppm. In the mass spectrum the molecular ion peak appears in reasonable intensity. With different α,β-ynones in hand, its reactions with different commercially available anilines/amines were studied. Conditions were optimized to have better yields of thienopyridinones. Palladium catalyst, ligand, solvent, base, temperature and stoichiometry were optimized. Some of the observations are summarized as follows:

1. No products were formed in the absence of either catalyst or ligand.
2. Pd₂(dba)₃ and Pd(OAc)₂ were found to be an effective Pd source for reaction.
3. BINAP was found to be a superior ligand for the reaction.
4. Toluene and dioxane were found to be the best solvents for the reaction.
5. No other metal carbonate other than Cs₂CO₃ was found to be the superior
base for the reaction.

6. The best yields of products were obtained with the stoichiometry $\alpha,\beta$-ynones (1 equiv), aniline/amine (1.2 equiv), $\text{Cs}_2\text{CO}_3$ (1.4 equiv), $\text{Pd}_2(\text{dba})_3$ (5 mol%), and BINAP (10 mol%) and at 110 °C for 10-12 hours.

7. Lower temperatures gave very poor yield of products.

With the optimized conditions in hand, reactions of $\alpha,\beta$-ynones 41a-e with different commercially available anilines/amines 42a-z were studied, giving thieno[3,2-b]pyridin-7(4H)-ones 43a-z in 69-86% yield (Scheme 2.15, Table 2.10).

![Scheme 2.15 Synthesis of 43a-z. Reagents and conditions: (i) 41 (1 equiv), 42 (1.2 equiv), $\text{Cs}_2\text{CO}_3$ (1.4 equiv), $\text{Pd}_2(\text{dba})_3$ (5 mol%), BINAP (10 mol%), toluene, 110 °C, 10-12 h.](image)

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\text{l} & \quad \text{C}_6\text{H}_5 & \quad p\text{-EtC}_6\text{H}_4 & \quad 82 \\
\text{m} & \quad \text{C}_6\text{H}_5 & \quad \text{cyclohexyl} & \quad 70 \\
\text{n} & \quad \text{C}_6\text{H}_5 & \quad n\text{-hept} & \quad 69 \\
\text{o} & \quad \text{C}_6\text{H}_5 & \quad p\text{-MeC}_6\text{H}_4 & \quad 77 \\
\text{p} & \quad \text{C}_6\text{H}_5 & \quad p\text{-ClC}_6\text{H}_4 & \quad 85 \\
\text{q} & \quad \text{C}_6\text{H}_5 & \quad p\text{-OMeC}_6\text{H}_4 & \quad 75 \\
\text{r} & \quad \text{C}_6\text{H}_5 & \quad p\text{-MeC}_6\text{H}_4 & \quad 83 \\
\text{s} & \quad \text{C}_6\text{H}_5 & \quad p\text{-FC}_6\text{H}_4 & \quad 81 \\
\text{t} & \quad \text{C}_6\text{H}_5 & \quad p\text{-OMeC}_6\text{H}_4 & \quad 75 \\
\text{u} & \quad \text{C}_6\text{H}_5 & \quad p\text{-MeC}_6\text{H}_4 & \quad 80 \\
\text{v} & \quad \text{C}_6\text{H}_5 & \quad p\text{-ClC}_6\text{H}_4 & \quad 82 \\
\text{w} & \quad \text{C}_6\text{H}_5 & \quad p\text{-EtC}_6\text{H}_4 & \quad 79 \\
\text{x} & \quad \text{C}_6\text{H}_5 & \quad p\text{-OMeC}_6\text{H}_4 & \quad 83 \\
\text{y} & \quad \text{C}_6\text{H}_5 & \quad p\text{-ClC}_6\text{H}_4 & \quad 82 \\
\text{z} & \quad \text{C}_6\text{H}_5 & \quad p\text{-EtC}_6\text{H}_4 & \quad 79 \\
\end{align*}

\textit{a} Yields of isolated products;

The structures of the thieno[3,2-b]pyridin-7(4H)-one were confirmed by spectral analysis i.e. IR, \textsuperscript{1}H NMR, \textsuperscript{13}C NMR, GC-MS and elemental analysis. In the \textsuperscript{1}H NMR, signals for vinylic H appear in the range 6.13-6.50 ppm. In \textsuperscript{13}C NMR spectra, signals for the acetylenic carbons are absent. In mass spectrum, the molecular ion peak usually appears as the base peak. The structure of two of the thieno[3,2-b]pyridin-7(4H)-one i.e. 43\textit{a} and 43\textit{m} were also independently confirmed by X-ray crystal structure analysis (Figures 2.9 and 2.10).
2.5.2 Conclusion:

In summary, an efficient palladium catalyzed tandem amination protocol for the synthesis of a wide range of 4,5-disubstituted thieno[3,2-b]pyridin-7(4H)-ones was developed. These compounds could be of biological importance.
2.6 Summary:

The thesis can be summarized as follows:

1. Synthesis of 3-arylidene-5-(4-substituted phenyl)furan-2(3H)-ones and 1-benzyl-3-arylidene-5-(4-substituted phenyl)-1H-pyrrol-2-(3H)-ones: In this section, synthesis of 3-arylidene-5-(4-substituted phenyl)furan-2(3H)-one and their nitrogen analogs 1-benzyl-3-arylidene-5-(4-substituted phenyl)-1H-pyrrol-2-(3H)-one was described. The synthesized compounds were then evaluated for their antioxidant, cytotoxicity and urease inhibition activities. These compounds showed non significant antioxidant activity, nil brine shrimp lethality and low to moderate urease inhibition activity.

2. Synthesis of 7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-ones: This section included the synthesis of 7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-ones by the reaction of 4-chloro-3-(2,2,2-trifluoroacetyl)-2H-chromen-2-one with commercially available anilines in a two step method.

3. Synthesis of thieno[2,3-c]chromen-4-ones and 7,8,9,10-tetrahydrobenzothieno[3,2-c]chromen-6-ones via Suzuki–Miyaura cross coupling followed by lactonization: This section reported synthesis of thienochromenones via Suzuki–Miyaura cross-coupling reaction of bromo thienocarboxylates with o-methoxyarylboronic acids followed by boron-tribromide mediated lactonization.

4. Synthesis of 5-substituted thieno[2,3-c]pyridin-7(6H)-ones and 3-substituted-5,6,7,8-tetrahydrobenzothieno[3,2-c]pyridin-1(2H)-ones based on Sonogashira cross coupling-annulation procedure: In this section, efficient synthesis of some novel 5-substituted thieno[2,3-c]pyridin-7(6H)-ones and 3-substituted-5,6,7,8-tetrahydro benzothieno[3,2-c] pyridine-1(2H)-ones was described which could of relevant biological importance.

5. Synthesis of 4,5-disubstituted thieno[3,2-b]pyridin-7(4H)-ones via palladium catalyzed tandem amination reaction: This section included the palladium catalyzed tandem amination reaction, consisting of sequential double C-N bond formation to give 4,5-disubstitutedthieno[3,2-b]pyridin-7(4H)-ones from α,β-yrones and commercially available anilines/amines which could be of considerable pharmacological relevance.
3.1 General: Equipment, chemicals and work technique:

$^1$H NMR Spectroscopy:
Bruker: AM 250, Bruker ARX 300, Bruker ARX 500; $\delta = 0.00$ ppm for Tetramethylsilane; $\delta = 2.04$ ppm for Acetone-$d_6$; $\delta = 7.26$ ppm for (CDCl$_3$); 2.50 ppm for DMSO-$d_6$; Characterization of the signal fragmentations: s = singlet, d = doublet, dd = doublet of doublet, ddd = doublet of a double doublet, t = triplet, q = quartet, quint = quintet; sext = sextet, sept = septet, m = multiplet, br = broadly. Spectra were evaluated according to first order rule. All coupling constants are indicated as $(J)$.

$^{13}$C NMR Spectroscopy:
Bruker: AM 250, (62.9 MHz); Bruker: ARX 300, (75 MHz), Bruker: ARX 500, (125 MHz) Ref: 29.84 ± 0.01 ppm and 206.26 ± 0.13 ppm for (CD$_3$)$_2$CO. $\delta = 128.00$ ppm for benzene-$d_6$; $\delta = 77.00$ ppm for CDCl$_3$. The multiplicity of the carbon atoms was determined by the DEPT 135 and APT technique (APT = Attached Proton Test) and quoted as CH$_3$, CH$_2$, CH and C for primary, secondary, tertiary and quaternary carbon atoms. Characterization of the signal fragmentations: quart = quartet the multiplicity of the signals was determined by the DEPT recording technology and/or the APT recording technology.

Mass Spectroscopy:
AMD MS40, AMD 402 (AMD Intectra), Varian MAT CH 7, MAT 731.

High Resolution mass spectroscopy:
Finnigan MAT 95 or Varian MAT 311; Bruker FT CIR, AMD 402 (AMD Intectra).

Infrared spectroscopy (IR):
Bruker IFS 66 (FT-IR), Nicolet 205 FT-IR; Nicolet Protege 460, Nicolet 360 Smart Orbit (ATR); KBr, KAP, Nujol, and ATR; Abbreviations for signal allocations: w = weak, m = medium, s = strong, br = broad.
Elementary analysis:
LECO CHNS-932, Thermoquest Flash EA 1112.

X-ray crystal structure analysis:
Bruker X8Apex Diffractometer with CCD-Kamera (Mo-K$_\alpha$ und Graphit Monochromator, $\lambda = 0.71073$ Å).

Melting points:
Micro heating table HMK 67/1825 Kuestner (Büchi apparatus); Melting points are uncorrected.

Column chromatography:
Chromatography was performed over Merck silica gel 60 (0,063 - 0,200 mm, 70 - 230 mesh) as normal and/or over mesh silica gel 60 (0,040 - 0,063 mm, 200 - 400 mesh) as Flash Chromatography. All solvent were distilled before use.

TLC:
Merck DC finished foils silica gel 60 F254 on aluminum foil and Macherey finished foils Alugram® Sil G/UV254. Detection under UV light with 254 nm and/or 366 nm without dipping reagent, as well as with anisaldehyde sulfuric acid reagent (1 mL anisaldehyde consisting in 100 mL stock solution of 85% methanol, 14% acetic acid and 1% sulfuric acid).

Chemicals and work technique:
All solvents were distilled by standard methods before use. All reactions were carried out under an inert atmosphere, oxygen and humidity exclusion. All of the chemicals are standard, commercially available from Merck®, Aldrich®, Arcos® and others.
3.2 Procedures and Spectroscopic Data:

3.2.1 Synthesis of 3-(Arylidene)-5-(4-substitutedphenyl)furan-2(3H)-ones:

General procedure for the synthesis of compound (4, 5):

Succinic anhydride (2 g, 20 mmol) was reacted with 4-substituted benzene (15 mL) in the presence of anhydrous aluminium chloride (6 g, 44 mmol). The reaction mixture was refluxed for 4 h. After completion of the reaction, excess solvent (4-substituted benzene) was removed by steam distillation. The product was purified by dissolving in sodium hydroxide solution (5%, w/v), and was filtered followed by addition of hydrochloric acid. The solid mass so obtained was filtered, washed with cold water, dried and crystallized from methanol to give the desired product as a white crystalline solid.

4-(Ethoxybenzoyl)propionic acid (4):

Chemical Formula: C_{12}H_{14}O_{4}

Starting with succinic anhydride 3 (2 g, 20 mmol), phenetole 1 (15 mL) and anhyd. AlCl₃ (6 g, 45 mmol), 4 was obtained as a white solid, yield (2.9 g, 65%), mp. 131-132 °C; ¹H NMR (300MHz, CDCl₃): δ = 1.46 (t, 3J = 7.2 Hz, CH₃), 2.81 (t, 3J = 6.6 Hz, CH₂), 3.29 (t, 3J = 6.6 Hz, CH₂), 4.12 (q, 3J = 7.2 Hz, CH₂), 6.94 (d, 3J = 9 Hz, 2H), 7.97 (d, 3J = 9 Hz, 2H), 11.1 (s, O-H); ¹³C NMR (75.4 MHz, CDCl₃): δ = 14.7 (CH₃), 28.1 (C-2), 32.8 (C-3), 63.8 (OCH₂), 114.2 (C-1'), 129.3 (C-2',6'), 130.4 (C-3',5'), 163.1 (C-4'), 178.4 (C-1), 196.5 (C-4); GC-MS (EI, 70eV): m/z (%) = 222 (17), 149 (100), 121 (60), 93 (16), 65 (15); IR (cm⁻¹): 3104, 2979, 1709, 1601, 1244, 1040; Anal. Calcd. for C_{12}H_{14}O_{4}: C, 64.85; H, 6.35. Found: C, 64.80; H, 6.30.

4-(Bromobenzoyl)propionic acid (5):

Chemical Formula: C_{10}H_{9}BrO_{3}

Starting with succinic anhydride 3 (2 g, 20 mmol), bromobenzene 2 (15 mL) and anhyd. AlCl₃ (6 g, 45 mmol), 5 was obtained as a white solid, yield (3.6 g, 70%), mp. 139-140 °C; ¹H NMR (300MHz, CDCl₃): δ = 2.83 (t, 3J = 6.6 Hz, CH₂), 3.29 (t, 3J = 6.6 Hz, CH₂),
7.64 (d, $^3J = 8.4$ Hz, 2H), 7.86 (d, $^3J = 8.7$ Hz, 2H), 11.1 (s, O-H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta = 27.9$ (C-2), 33.1 (C-3), 128.6 (C-4'), 129.6 (C-2',6'), 132.0 (C-3',5'), 135.0 (C-1'), 178.4 (C-1), 196.8 (C-4); GC-MS (EI, 70eV): $m/z$ (%) = 258 [M$^+$, 81Br, 9], 256 [M$^+$, 79Br, 9], 183 (100), 155 (28), 104 (9), 76(23), 50 (15); IR (cm$^{-1}$): 3059, 1700, 1674, 1584, 1447, 1411, 1335, 1201, 1072, 1013; Anal. Calcd. for C$_{10}$H$_9$BrO$_3$: C, 46.72; H, 3.53. Found: C, 46.90; H, 3.55.

General procedure for the synthesis of compounds (7a-q) and (8a-l):

A solution of 3-(4-substitutedbenzoyl)propionic acid (0.5 g, 2.2 mmol) and aromatic aldehyde (equiv.) in acetic anhydride (5 mL) with triethyl amine (3-4 drops) was refluxed for 4h under anhydrous conditions. After completion of reaction, the mixture was poured onto crushed ice and a colored solid mass, which separated out, was filtered, washed, dried and crystallized from methanol: chloroform mixture (1:1) to give furanones.

3-(2-Chlorobenzylidene)-5-(4-ethoxyphenyl)furan-2(3$H$)-one (7a):

Starting with benzyol propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (0.25 mL, 2.2 mmol), 7a was obtained as a yellow solid, yield (550 mg, 75%), mp. 172-173 °C; $^1$H NMR (300MHz, CDCl$_3$): $\delta = 1.46$ (t, $^3J = 7.2$ Hz, CH$_3$), 4.10 (q, $^3J = 7.2$ Hz, CH$_2$), 6.69 (s, 1H), 6.96 (d, $^3J = 8.7$ Hz, 2H), 7.32-7.41 (m, 2H), 7.47-7.50 (m, 1H), 7.67-7.72 (m, 4H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta = 14.7$ (CH$_3$), 63.7 (OCH$_2$), 97.4 (C-4), 114.9 (C-3',5'), 120.3 (C-1'), 127.1 (C-5''), 127.2 (C-6''), 127.7 (C-2',6'), 129.6 (C-4''), 129.8 (C-3''), 130.3 (C-3), 130.7 (C-1''), 133.7 (C-2''), 135.5 (C-6), 157.9 (C-5), 161.1 (C-4''), 168.9 (C-2); GC-MS (EI, 70eV): $m/z$ (%) = 328 [M$^+$, 37Cl, 19], 326 [M$^+$, 35Cl, 52], 291 (100), 263 (20), 149 (66), 121 (62), 93 (19), 76 (4), 65 (17); IR (cm$^{-1}$): 2988, 1786, 1604, 1509, 1267, 1245, 1174, 1120, 1043; Anal. Calcd. for C$_{19}$H$_{15}$ClO$_3$: C, 69.84; H, 4.63. Found: C, 70.10; H, 4.58.
3-(4-Chlorobenzylidene)-5-(4-ethoxyphenyl)furan-2(3H)-one (7b):

Starting with benzoyl propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (309 mg, 2.2 mmol), 7b was obtained as a yellow solid, yield (515 mg, 70%), mp. 205-206 °C; ¹H NMR (300MHz, CDCl₃): δ =1.47 (t, 3J = 6.9 Hz, CH₃), 4.11 (q, 3J = 6.9 Hz, CH₂), 6.76 (s, 1H), 6.98 (d, 3J = 9 Hz, 2H), 7.31 (s, 1H), 7.44 (d, 3J = 8.4 Hz, 2H), 7.57 (d, 3J = 8.4 Hz, 2H), 7.72 (d, 3J = 9 Hz, 2H); ¹³C NMR (75.4 MHz, CDCl₃): δ = 14.7 (CH₃), 63.7 (OCH₂), 97.6 (C-4), 114.9 (C-3′,5′), 120.3 (C-1′), 126.0 (C-2′,6′), 127.2 (C-3″,5″), 129.3 (C-3), 131.0 (C-1″), 132.0 (C-4″), 133.9 (C-2″,6″), 135.8 (C-6), 157.5 (C-5), 161.1 (C-4′), 169.5 (C-2); GC-MS (EI, 70eV): m/z (%) = 328 [M +, 35Cl, 35], 326 [M+, 37Cl, 35], 298 (8), 149 (80), 121 (75), 93 (14), 76 (3), 65 (11); IR (cm⁻¹): 2983, 1759, 1625, 1508, 1255, 1173, 1092; Anal. Calcd. for C₁₉H₁₅ClO₃: C, 69.84; H, 4.63. Found: C, 69.96; H, 4.50.

3-(3-Bromobenzylidene)-5-(4-ethoxyphenyl)furan-2(3H)-one (7c):

Starting with benzoyl propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (0.25 mL, 2.2 mmol), 7c was obtained as a yellow solid, yield (585 mg, 70%), mp. 166-167 °C; ¹H NMR (300MHz, CDCl₃): δ =1.47 (t, 3J = 7.2 Hz, CH₃), 4.11 (q, 3J = 7.2 Hz, 2H), 6.75 (s, 1H), 6.97 (d, 3J = 8.7 Hz, 2H), 7.25 (s, 1H), 7.31-7.36 (m, 1H), 7.51-7.54 (m, 2H), 7.69-7.74 (m, 3H); ¹³C NMR (75.4 MHz, CDCl₃): δ = 14.7 (CH₃), 63.7 (OCH₂), 97.5 (C-4), 114.9 (C-3′,5′), 120.2 (C-1′), 123.2 (C-3′), 126.8 (C-6′), 127.3 (C-2′,6′), 128.5 (C-5′), 130.5 (C-2″), 131.5 (C-3), 132.3 (C-4″), 132.6 (C-1″), 137.4 (C-6), 157.9 (C-5), 161.2 (C-4′), 169.3 (C-2); GC-MS (EI, 70eV): m/z (%) = 372 [M⁺, 81Br, 52], 370 [M+, 79Br, 52], 342 (4), 149 (95), 121 (100), 93 (19), 76 (5), 65 (17); IR (cm⁻¹): 2979, 1761, 1608, 1504, 1262, 1172, 1069, 1044; Anal. Calcd. for C₁₉H₁₅BrO₃: C, 61.47; H, 4.07 Found: C, 61.62; H, 4.53.
3-(4-Bromobenzylidene)-5-(4-ethoxyphenyl)furan-2(3H)-one (7d):

Starting with benzoyl propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (407 mg, 2.2 mmol), 7d was obtained as a yellow solid, yield (595 mg, 71%), mp. 208-209 °C; 1H NMR (300MHz, CDCl3): δ = 1.47 (t, 3J = 6.9 Hz, CH3), 4.11 (q, 3J = 6.9 Hz, CH2), 6.76 (s, 1H), 6.97 (d, 3J = 9 Hz, 2H), 7.27 (s, 1H), 7.49 (d, 3J = 8.4 Hz, 2H), 7.60 (d, 3J = 8.4 Hz, 2H), 7.72 (d, 3J = 9 Hz, 2H); 13C NMR (75.4 MHz, CDCl3): δ = 14.8 (CH3), 63.8 (OCH2), 97.6 (C-4), 114.9 (C-3′,5′), 120.6 (C-1′), 126.8 (C-4′), 127.2 (C-2′,6′), 131.2 (C-3), 132.1 (C-3″,5″), 132.3 (C-1″), 134.3 (C-2″,6″), 135.2 (C-6), 157.6 (C-5), 161.4 (C-4′), 169.9 (C-2); GC-MS (EI, 70eV): m/z (%) = 372 [M+81Br, 74], 370 [M+, 79Br, 74], 149 (100), 121 (95), 93 (21), 76 (5), 65 (20); IR (cm⁻¹): 2980, 1758, 1509, 1256, 1175, 1049, 997; Anal. Calcd. for C19H15BrO3: C, 61.47; H, 4.07. Found: C, 61.53; H, 4.21.

3-(2-Fluorobenzylidene)-5-(4-ethoxyphenyl)furan-2(3H)-one (7e):

Starting with benzoyl propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (0.23 mL, 2.2 mmol), 7e was obtained as a yellow solid, yield (505 mg, 72%), mp. 146-147 °C; 1H NMR (300MHz, CDCl3): δ = 1.46 (t, 3J = 6.9 Hz, CH3), 4.11 (q, 3J = 6.9 Hz, CH2), 6.74 (s, 1H), 6.96 (d, 3J = 9 Hz, 2H), 7.13-7.25 (m, 2H), 7.37-7.45 (m, 1H), 7.54 (s, 1H), 7.66-7.74 (m, 3H); 13C NMR (75.4 MHz, CDCl3): δ = 14.8 (CH3), 63.8 (OCH2), 97.6 (C-4), 114.9 (C-3′,5′), 120.6 (C-1′), 126.8 (C-4′), 127.2 (C-2′,6′), 131.2 (C-3), 132.1 (C-3″,5″), 132.3 (C-1″), 134.3 (C-2″,6″), 135.2 (C-6), 157.6 (C-5), 161.4 (C-4′), 169.9 (C-2); GC-MS (EI, 70eV): m/z (%) = 372 [M+, 81Br, 74], 370 [M+, 79Br, 74], 149 (100), 121 (95), 93 (21), 76 (5), 65 (20); IR (cm⁻¹): 2980, 1758, 1509, 1221, 1265, 1175, 1049, 997; Anal. Calcd. for C19H15BrO3: C, 61.47; H, 4.07. Found: C, 61.53; H, 4.21.
3-(3-Fluorobenzylidene)-5-(4-ethoxyphenyl)furan-2(3H)-one (7f):

Starting with benzoyl propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (0.23 mL, 2.2 mmol), 7f was obtained as a yellow solid, yield (490 mg, 70%), mp.169-170 °C; ¹H NMR (300MHz, CDCl₃): δ =1.46 (t, ³J = 6.9 Hz, CH₃), 4.11 (q, ³J = 6.9 Hz, CH₂), 6.77 (s, 1H), 6.97(d, ³J = 9 Hz, 2H), 7.08-7.14 ( m, 1H), 7.30 (s, 1H), 7.34-7.48 (m, 3H), 7.72 (d, ³J = 9 Hz, 2H); ¹³C NMR (75.4 MHz, CDCl₃): δ = 14.7 (CH₃), 63.7 (OCH₂), 97.6 (C-4), 114.9 (C-3′,5′), 115.9 (d, ²JCF = 21.8 Hz, C-2″), 116.8 (d, ²JCF = 21 Hz, C-4″), 120.2 (C-1′), 125.9 (d, ⁴JCF = 3 Hz, C-6″), 126.7 (C-2′,6′), 127.3 (C-3), 130.6 (d, ³JCF = 8.3 Hz, C-5″), 131.9 (d, ⁴JCF = 3 Hz, C-6), 137.5 (d, ³JCF = 7.5 Hz, C-1″), 157.8 (C-5), 161.2 (C-4′), 162.9 (d, ¹JCF = 245.4 Hz, C-3″), 169.4 (C-2); GC-MS (EI, 70eV): m/z (%) = 310 [M+, 100], 282 (8), 149 (71), 121 (80), 93 (20), 76 (3), 65 (15); IR (cm⁻¹): 2980, 1758, 1582, 1507, 1258, 1233, 1177, 1117, 1049; Anal. Calcd. for C₁₉H₁₄FO₃: C, 73.54; H, 4.87. Found: C, 73.45; H, 4.57.

3-(4-Fluorobenzylidene)-5-(4-ethoxyphenyl)furan-2(3H)-one (7g):

Starting with benzoyl propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (0.23 mL, 2.2 mmol), 7g was obtained as a yellow solid, yield (485 mg, 69%) mp.161-162 °C; ¹H NMR (300MHz, CDCl₃): δ =1.46 (t, ³J = 6.9 Hz, CH₃), 4.11 (q, ³J = 6.9 Hz, CH₂), 6.76 (s, 1H), 6.96 (d, ³J = 9 Hz, 2H), 7.14-7.19 (m, 2H), 7.33 (s, 1H), 7.61-7.65 (m, 2H) 7.71 (d, ³J = 9 Hz, 1H); ¹³C NMR (75.4 MHz, CDCl₃): δ = 14.7 (CH₃), 63.7 (OCH₂), 97.5 (C-4), 114.9 (C-3′,5′), 116.3 (d, ²JCF = 22.5 Hz, C-3″,5″), 120.4 (C-1′), 125.3 (C-2′,6′), 127.1 (C-3), 131.7 (d, ⁴JCF = 3.8 Hz, C-1″), 131.9 (d, ³JCF = 8.3 Hz, C-2″,6″), 132.4 (C-6), 157.2 (C-5), 161.0 (C-4′), 163.4 (d, ¹JCF = 251.3 Hz, C-4″), 169.6 (C-2); GC-MS (EI, 70eV): m/z (%) = 310 [M+, 100], 282 (10), 149 (67), 121 (66), 93 (20), 76 (3), 65 (11); IR (cm⁻¹): 2980, 1758, 1582, 1507, 1258, 1233, 1177, 1117, 1049; Anal. Calcd. for C₁₉H₁₄FO₃: C, 73.54; H, 4.87. Found: C, 73.12; H, 4.90.
3-(2-Methoxybenzylidene)-5-(4-ethoxyphenyl)furan-2(3H)-one (7h):

Starting with benzoic propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (299 mg, 2.2 mmol), 7h was obtained as a yellow solid, yield (475 mg, 65%), mp. 137-138 °C; $^1$H NMR (300MHz, CDCl$_3$): $\delta = 1.46$ (t, $^3J = 6.9$ Hz, CH$_3$), 4.10 (q, $^3J = 6.9$ Hz, CH$_2$), 3.91 (s, OCH$_3$), 6.76 (s, 1H), 6.93-6.97 (m, 3H), 7.03-7.08 (m, 1H), 7.37-7.43 (m, 1H), 7.66-7.72 (m, 3H), 7.85 (s, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta = 14.8$ (CH$_3$), 55.6 (OCH$_3$), 63.7 (OCH$_2$), 98.2 (C-4), 111.1 (C-3'), 114.8 (C-3',5'), 120.7 (C-5''), 124.6 (C-1'), 125.2 (C-1''), 126.9 (C-2',6'), 129.2 (C-4''), 129.3 (C-3), 131.6 (C-6''), 136.3 (C-6), 156.4 (C-5), 158.6 (C-4'), 160.7 (C-2''), 169.8 (C-2); GC-MS (EI, 70eV): m/z (%) = 322 [M+, 100], 294 (5), 149 (100), 121 (65), 93 (14), 76 (5), 65 (11); IR (cm$^{-1}$): 2975, 1778, 1618, 1504, 1302, 1263, 1244, 1175, 1115, 1024; Anal. Calcd. for C$_{20}$H$_{18}$O$_4$: C, 74.52; H, 5.63. Found: C, 74.08; H, 5.77.

3-(3-Methoxybenzylidene)-5-(4-ethoxyphenyl)furan-2(3H)-one (7i):

Starting with benzoic propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (0.26 mL, 2.2 mmol), 7i was obtained as a yellow solid, yield (530 mg, 73%), mp. 124-125 °C; $^1$H NMR (300MHz, CDCl$_3$): $\delta = 1.46$ (t, $^3J = 7.2$ Hz, CH$_3$), 3.88 (s, OCH$_3$), 4.11 (q, $^3J = 7.2$ Hz, CH$_2$), 6.80 (s, 1H), 6.95-6.98 (m, 3H), 7.13-7.15 (m, 1H), 7.22-7.25 (m, 1H), 7.34 (s, 1H), 7.36-7.42 (m, 2H), 7.71 (d, $^3J = 9$ Hz, 2H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta = 14.7$ (CH$_3$), 55.4 (OCH$_3$), 63.7 (OCH$_2$), 97.9 (C-4), 114.9 (C-2''), 115.4 (C-4''), 120.5 (C-3',5'), 122.5 (C-6''), 125.9 (C-1'), 127.1 (C-2',6'), 130.1 (C-5''), 133.7 (C-3), 136.7 (C-1''), 157.1 (C-6), 158.0 (C-5), 159.9 (C-4), 160.9 (C-3''), 169.7 (C-2); GC-MS (EI, 70eV): m/z (%) = 322 [M+, 81], 294 (5), 149 (88), 121 (66), 93 (19), 76 (6), 65 (15); IR (cm$^{-1}$): 2975, 1778, 1618, 1504, 1302, 1263, 1244, 1175, 1115, 1024; Anal. Calcd. for C$_{20}$H$_{18}$O$_4$: C, 74.52; H, 5.63. Found: C, 74.08; H, 5.77.
3-(4-Ethoxybenzylidene)-5-(4-ethoxyphenyl)furan-2(3H)-one (7j):

Starting with benzoyle propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (0.30 mL, 2.2 mmol), 7j was obtained as a yellow solid, yield (508 mg, 67%), mp. 181-182 °C; \(^1\)H NMR (300MHz, CDCl\(_3\)): δ = 1.44-1.49 (m, 2xCH\(_3\)), 4.07-4.15 (m, 2xCH\(_2\)), 6.80 (s, 1H), 6.93-7.00 (m, 4H), 7.34 (s, 1H), 7.59 (d, 3\(^J\) = 9 Hz, 2H), 7.70 (d, 3\(^J\) = 9 Hz, 2H); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): δ = 14.8 (OCH\(_3\)×2), 63.6 (OCH\(_2\)×2), 97.9 (C-4), 114.8 (C-3′,5′), 115.1 (C-3″,5″), 120.8 (C-1′), 123.0 (C-1″), 126.9 (C-2′,6′), 128.0 (C-2″,6″), 131.9 (C-3), 134.1 (C-6), 155.9 (C-5), 160.6 (C-4′), 160.7 (C-4″), 170.2 (C-2); GC-MS (EI, 70eV): m/z (%) = 336 [M+, 100], 308 (19), 149 (76), 121 (52), 93 (15), 76 (4), 65 (10); IR (cm\(^{-1}\)): 2978, 1752, 1603, 1506, 1393, 1250, 1167, 1049; Anal. Calcd. for C\(_{21}\)H\(_{20}\)O\(_4\): C, 74.98; H, 5.99. Found: C, 74.76; H, 5.67.

2-[[5-(4-Ethylphenyl)-2-oxofuran-3(2H)-ylidene]methyl]phenylacetate (7k):

Starting with benzoyle propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (0.23 mL, 2.2 mmol), 7k was obtained as a yellow solid, yield (550 mg, 69%), mp. 142-143 °C; \(^1\)H NMR (300MHz, CDCl\(_3\)): δ = 1.46 (t, 3\(^J\) = 6.9Hz, CH\(_3\)), 2.39 (s, CH\(_3\)), 4.11 (q, 3\(^J\) = 6.9 Hz, CH\(_2\)), 6.73 (s, 1H), 6.96 (d, 3\(^J\) = 9 Hz, 2H), 7.19 (dd, 3\(^4\)J = 7.8, 1.2 Hz, 1H), 7.33-7.39 (m, 1H), 7.40 (s, 1H), 7.45 (td, 3\(^4\)J= 7.8,1.8 Hz, 1H), 7.70 (d, 3\(^J\) = 9Hz, 2H), 7.75 (dd, 3\(^4\)J = 7.5, 1.8 Hz, 1H); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): δ = 14.7 (CH\(_3\)), 21.0 (COCH\(_3\)), 63.7 (OCH\(_2\)), 97.8 (C-4), 114.9 (C-3′,5′), 120.3 (C-1″), 123.2 (C-3″), 126.4 (C-1), 126.7 (C-5″), 127.2 (C-6″), 127.4 (C-4′), 128.4 (C-2′,6′), 129.4 (C-3), 130.9 (C-6), 149.7 (C-5), 157.6 (C-2″), 161.1 (C-4′), 169.1 (C-2), 169.2 (C); GC-MS (EI, 70eV): m/z (%) = 350 [M+, 40], 308 (38), 279 (10), 186 (100), 149 (35), 121 (40), 93 (15), 76 (5), 65 (10); IR (cm\(^{-1}\)): 2982, 1762, 1620, 1587, 1506, 1258, 1207, 1173, 1045; Anal. Calcd. for C\(_{21}\)H\(_{18}\)O\(_5\): C, 71.99; H, 5.18. Found: C, 74.58; H, 5.34.
3-[(5-(4-Ethylphenyl)-2-oxofuran-3(2H)-ylidene)methyl]phenylacetate (7l):

Starting with benzoyl propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (268 mg, 2.2 mmol), 7l was obtained as a yellow solid, yield (595 mg, 75%), mp.137-138 °C; \(^1\)H NMR (300MHz, CDCl\(_3\)): \(\delta = 1.46 (t, \(3^J = 6.9 \text{ Hz}, \text{CH}_3\)), 2.38 (s, \text{CH}_3), 4.11 (q, \(3^J = 6.9 \text{ Hz}, \text{CH}_2\)), 6.77 (s, 1H), 6.97 (d, \(3^J = 9 \text{ Hz}, \text{2H}\)), 7.14-7.17 (m, 1H), 7.36-7.37 (m, 1H), 7.33 ( s, 1H), 7.45 (d, \(3^J = 4.8 \text{ Hz}, \text{2H}\)), 7.72 (d, \(3^J = 9 \text{ Hz}, \text{2H}\)); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 14.7 (\text{CH}_3), 21.3 (\text{COCH}_3), 63.7 (\text{OCH}_2), 97.7 (\text{C-4}), 114.9 (\text{C-3',5'}), 120.3 (\text{C-4''}), 122.5 (\text{C-2''}), 122.9 (\text{C-1'}), 126.6 (\text{C-6''}), 127.2 (\text{C-2',6'}), 127.4 (\text{C-5''}), 130.0 (\text{C-3}), 132.4 (\text{C-1''}), 136.9 (\text{C-6}), 151.0 (\text{C-5}), 157.6 (\text{C-3'}), 161.1 (\text{C-4'}), 169.3 (\text{C}-2), 169.4 (\text{C}); GC-MS (EI, 70eV): \(m/z\) (%): 350 (M+, 100), 308 (36), 280 (7), 186 (20),149 (90), 121 (80), 93 (20), 76 (6), 65 (15); IR (cm\(^{-1}\)): 3068, 2985, 1785, 1763, 1624, 1511, 1256, 1207, 1173, 1118, 1047; Anal. Calcd. for C\(_{21}\)H\(_{18}\)O\(_5\): C, 71.99; H, 5.18. Found: C, 73.41; H, 5.20.

4-[(5-(4-Ethylphenyl)-2-oxofuran-3(2H)-ylidene)methyl]phenylacetate (7m):

Starting with benzoyl propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (268 mg, 2.2 mmol), 7m was obtained as a yellow solid, yield (595 mg, 75%), mp.190-191 °C; \(^1\)H NMR (300MHz, CDCl\(_3\)): \(\delta = 1.46 (t, \(3^J = 6.9 \text{ Hz}, \text{CH}_3\)), 2.36 (s, \text{CH}_3), 4.11 (q, \(3^J = 6.9 \text{ Hz}, \text{CH}_2\)), 6.78 (s, 1H), 6.97 (d, \(3^J = 9 \text{ Hz}, \text{2H}\)), 7.21 (d, \(3^J = 8.7 \text{ Hz}, \text{2H}\)), 7.34 (s, 1H), 7.65 (d, \(3^J = 8.7 \text{ Hz}, \text{1H}\)), 7.71 (d, \(3^J = 9 \text{ Hz}, \text{2H}\)); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 14.7 (\text{CH}_3), 21.2 (\text{COCH}_3), 63.7 (\text{OCH}_2), 97.7 (\text{C-4}), 114.9 (\text{C-3',5'}), 120.4 (\text{C-3''},5''), 122.4 (\text{C-1'}), 125.7 (\text{C-2',6'}), 127.1 (\text{C-2'',6''}), 131.1 (\text{C-1''}), 132.6 (\text{C-3}), 133.1 (\text{C-6}), 151.6 (\text{C-5}), 157.3 (\text{C-4'}), 161.0 (\text{C-4'}), 169.2 (\text{C}-2), 169.6 (\text{C}); GC-MS (EI, 70eV): \(m/z\) (%): 350 [M+, 45], 308 (100), 280 (8), 149 (60), 121 (52), 93 (13), 76 (3), 65 (12); IR (cm\(^{-1}\)): 3053, 2979, 1758, 1603, 1505, 1256, 1219, 1166, 1113, 1049; Anal. Calcd. for C\(_{21}\)H\(_{18}\)O\(_5\): C, 71.99; H, 5.18. Found: C, 74.92; H, 5.54.
3-(3-Nitrobenzylidene)-5-(4-ethoxyphenyl)furan-2(3H)-one (7o):

Starting with benzyol propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (332 mg, 2.2 mmol), 7o was obtained as a red solid, yield (595 mg, 78%), mp.175-176 °C; \(^1\)H NMR (300MHz, CDCl\(_3\)): \(\delta =1.47\) (t, \(^3\)J = 6.9Hz, CH\(_3\)), 4.12 (q, \(^3\)J = 6.9 Hz, CH\(_2\)), 6.80 (s, 1H), 7.99 (d, \(^3\)J = 9 Hz, 2H), 7.34 (s, 1H), 7.63-7.68 (m, 1H), 7.75 (d, \(^3\)J = 8.7 Hz, 2H), 7.89 (d, \(^3\)J = 7.8 Hz, 1H), 8.24 (dd, \(^3\),\(^4\)J = 8.4, 1.2 Hz, 1H), 8.48 (m, 1H); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 14.7\) (CH\(_3\)), 63.8 (OCH\(_2\)), 97.0 (C-4), 114.9 (C-3’,5’), 119.8 (C-1’), 123.7 (C-4”), 123.9 (C-6”), 127.6 (C-2”), 128.0 (C-2’,6’), 129.7 (C-5”), 130.1 (C-3), 135.5 (C-1”), 137.0 (C-6), 148.7 (C-5), 158.9 (C-3”), 161.5 (C-4’), 168.9 (C-2); GC-MS (EI, 70eV): \(m/z\) (%) =337 [M+, 100], 309 (8), 149 (90), 121 (52), 93 (20), 76 (5), 65 (15); IR (cm\(^{-1}\)): 2990, 1758, 1602, 1561, 1528, 1350, 1249, 1172, 1023; Anal. Calcd. for C\(_{19}\)H\(_{15}\)NO\(_5\): C, 67.65; H, 4.48; N, 4.15. Found: C, 67.26; H, 4.34; N, 4.03.

3-(4-Nitrobenzylidene)-5-(4-ethoxyphenyl)furan-2(3H)-one (7p):

Starting with benzyol propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (332 mg, 2.2 mmol), 7p was obtained as a red solid, yield (575 mg, 75%), mp. 252-253 °C; \(^1\)H NMR (300MHz, CDCl\(_3\)): \(\delta =1.48\) (t, \(^3\)J = 6.9Hz, CH\(_3\)), 4.12 (q, \(^3\)J = 6.9 Hz, CH\(_2\)), 6.81 (s, 1H), 6.99 (d, \(^3\)J = 8.7 Hz, 1H), 7.34 (s, 1H), 7.47-7.78 (m, 4H), 8.32 (d, \(^3\)J = 9 Hz, 2H); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 14.7\) (CH\(_3\)), 63.8 (OCH\(_2\)), 97.0 (C-4), 114.9 (C-3’,5’), 121.0 (C-1’), 122.0 (C-3”,5”), 127.0 (C-2’,6’), 127.3 (C-3), 130.5 (C-2”,6”), 137.5 (C-1”), 141.3 (C-6), 146.2 (C-5), 158.6 (C-4”), 161.7 (C-4’), 168.3 (C-2); GC-MS (EI, 70eV): \(m/z\) (%) = 337 [M+, 100], 309 (10), 149 (52), 121 (95), 93 (20), 76 (5), 65 (5). IR (cm\(^{-1}\)): 2983, 1763, 1601, 1563, 1339, 1249, 1173, 1043; Anal. Calcd. for C\(_{19}\)H\(_{15}\)NO\(_5\): C, 67.65; H, 4.48; N, 4.15. Found: C, 67.93; H, 4.43; N, 4.52.
3-(4-Methylbenzylidene)-5-(4-ethoxyphenyl)furan-2(3H)-one (7q):

Starting with benzooyl propionic acid 4 (500 mg, 2.2 mmol) and benzaldehyde (0.26 mL, 2.2 mmol), 7q was obtained as a yellow solid, yield (540 mg, 78%), mp.164-165 °C; $^1$H NMR (300MHz, CDCl$_3$): $\delta$ =1.46 (t, $^3J = 6.9$ Hz, CH$_3$), 2.43 (s, CH$_3$), 4.11 (q, $^3J = 6.9$ Hz, CH$_2$), 6.81 (s, 1H), 6.96 ( d, $^3J = 9$ Hz, 2H), 7.28 (d, $^3J = 8.1$ Hz, 2H) 7.55 (d, $^3J = 8.1$ Hz, 2H), 7.71(d, $^3J = 9$ Hz, 2H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta$ = 14.8 (CH$_3$), 21.6 (CH$_3$), 63.7 (OCH$_2$), 98.0 (C-4), 114.8 (C-3',5'), 120.6 (C-1'), 124.7 (C-2',6'), 126.9 (C-3''5''), 129.9 (C-1''), 130.1 (C-3), 132.7 (C-2'',6''), 134.1 (C-4''), 140.7 (C-6), 156.5 (C-5), 160.8 (C-4'), 169.9 (C-2); GC-MS (EI, 70eV): m/z (%) =306 [M+, 100], 278 (10), 149 (85), 121 (57), 93 (15), 76 (3), 65 (11); IR (cm$^{-1}$): 2980, 1759, 1626, 1605, 156.5 (C-5), 167.3 (C-2); Anal. Calcd. for C$_{20}$H$_{18}$O$_3$: C, 78.41; H, 5.92. Found: C, 78.96; H, 5.82.

5-(4-Bromophenyl)-3-(2-chlorobenzylidene)furan-2(3H)-one (8a):

Starting with benzooyl propionic acid 5 (500 mg, 1.9 mmol) and benzaldehyde (0.21 mL, 1.9 mmol), 8a was obtained as a yellow solid, yield (490 mg, 70%), mp. 235-236 °C; $^1$H NMR (300MHz, CDCl$_3$): $\delta$ = 6.87 (s, 1H), 7.08-7.09 (m, 2H), 7.19 (d, $^3J = 8.4$ Hz, 2H), 7.22 (d, $^3J = 8.4$ Hz, 2H), 7.24-7.38 (m, 2H), 7.86 (s, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta$ = 99.2 (C-4), 122.3 (C-4'), 124.9 (C-5''), 125.5 (C-6''), 126.9 (C-4''), 127.8 (C-1'), 128.6 (C-3''), 129.6 (C-3), 131.2 (C-3',5'), 132.0 (C-2',6'), 132.2 (C-1''), 133.8 (C-2''), 137.0 (C-6), 146.2 (C-5), 167.3 (C-2); GC-MS (EI, 70eV): m/z (%) = 364 [M$^+$, $^{81}$Br$^{37}$Cl, 8], 362 [M$^+$, $^{81}$Br$^{35}$Cl, 27], 360 [M$^+$, $^{79}$Br$^{35}$Cl, 20], 325 (100), 246 (8), 218 (4), 183 (84), 155 (37), 114 (19), 94 (11), 76 (31), 63 (11), 50 (14); IR (cm$^{-1}$): 3122, 1775, 1618, 1584, 1486, 1443, 1405, 1380, 1277, 1178, 1069, 1051, 998, 818; Anal. Calcd. for C$_{17}$H$_{10}$BrClO$_2$: C, 56.46; H, 2.79. Found: C, 56.54; H, 3.11.
5-(4-Bromophenyl)-3-(3-chlorobenzylidene)furan-2(3H)-one (8b):

Starting with benzoyl propionic acid 5 (500 mg, 1.9 mmol) and benzaldehyde (266 mg, 1.9 mmol), 8b was obtained as a yellow solid, yield (475 mg, 65%), mp. 173-174 °C; $^1$H NMR (300MHz, CDCl$_3$): $\delta =$ 6.92 (s, 1H), 7.40-7.43 (m, 3H), 7.47-7.52 (m, 2H), 7.60-7.68 (m, 4H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta =$ 99.9 (C-4), 125.3 (C-4’), 125.6 (C-2’), 126.3 (C-6’), 126.7 (C-1’), 128.3 (C-5’), 129.5 (C-3), 130.3 (C-3’,5’), 130.4 (C-2’,6’), 132.3 (C-3’), 135.2 (C-1’”), 136.7 (C-6), 156.7 (C-5), 168.7 (C-2); GC-MS (EI, 70eV): m/z (%) = 364 [M$^+$, 81Br$^{37}$Cl, 12], 362 [M$^+$, 81Br$^{35}$Cl, 47], 360 [M$^+$, 79Br$^{35}$Cl, 36], 183 (100), 155 (30), 114 (12), 94 (10), 76 (24); IR (cm$^{-1}$): 1765, 1725, 1590, 1485, 1430, 1280, 1180, 1070, 1000; Anal. Calcd. for C$_{17}$H$_{10}$BrClO$_2$: C, 56.46; H, 2.79. Found: C, 56.90; H, 2.50.

5-(4-Bromophenyl)-3-(3-bromobenzylidene)furan-2(3H)-one (8c):

Starting with benzoyl propionic acid 5 (500 mg, 1.9 mmol) and benzaldehyde (0.22 mL, 1.9 mmol), 8c was obtained as a yellow solid, yield (555 mg, 70%), mp. 193-194 °C; $^1$H NMR (300MHz, CDCl$_3$): $\delta =$ 6.90 (s, 1H), 7.34-7.39 (m, 2H), 7.54-7.60 (m, 2H), 7.63-7.67 (m, 2H), 7.76 (s, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta =$ 99.9 (C-4), 123.3 (C-4’), 126.3 (C-3’), 126.7 (C-1’), 128.3 (C-5’), 129.5 (C-3), 130.3 (C-3’,5’), 130.4 (C-2’,6’), 132.3 (C-3’), 135.2 (C-1’”), 136.7 (C-6), 156.7 (C-5), 168.7 (C-2); GC-MS (EI, 70eV): m/z (%) = 408 [M$^+$, 81Br$^{37}$Br, 25], 406 [M$^+$, 81Br$^{35}$Br, 54], 404 [M$^+$, 79Br$^{35}$Br, 25], 281 (14), 207 (47), 183 (100), 155 (29), 114 (16), 95 (10), 76 (23); IR (cm$^{-1}$): 1765, 1622, 1590, 1485, 1430, 1280, 1180, 1070, 1000; Anal. Calcd. for C$_{17}$H$_{10}$Br$_2$O$_2$: C, 50.28; H, 2.48. Found: C, 50.10; H, 2.52.
5-(4-Bromophenyl)-3-(2-methoxybenzylidene)furan-2(3H)-one (8e):

Starting with benzoyl propionic acid 5 (500 mg, 1.9 mmol) and benzaldehyde (258 mg, 1.9 mmol), 8e was obtained as a yellow solid, yield (525 mg, 75%), mp. 193-194 °C; $^1$H NMR (300MHz, CDCl$_3$): $\delta$ = 3.92 (s, OCH$_3$), 6.92 (s, 1H), 6.98 (d, $^3$$J$ = 8.4 Hz, 1H), 7.04-7.09 (m, 1H), 7.41-7.47 (m, 1H), 7.57-7.68 (m, 5H), 7.92 (s, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta$ = 55.7 (OCH$_3$), 100.7 (C-4), 111.2 (C-3”), 120.8 (C-5”), 124.3 (C-1”), 124.5 (C-4), 124.7 (C-4”), 126.6 (C-2”), 127.2 (C-3), 129.5 (C-3’,5’), 131.7 (C-2’,6’), 132.1 (C-6”), 132.2 (C-6), 155.2 (C-6”), 158.8 (C-2’”), 169.2 (C-2); GC-MS (EI, 70eV): $m/z$ (%) = 358 [M$^+$, $^{81}$Br, 55], 356 [M$^+$, $^{79}$Br, 56], 250 (33), 183 (100), 155 (31), 115 (26), 102 (18), 89 (13), 76 (33); IR (cm$^{-1}$): 1755, 1620, 1580, 1480, 1460, 1305, 1242, 1070, 1040, 999; Anal. Calcd. for C$_{18}$H$_{13}$BrO$_3$: C, 60.52; H, 3.67. Found: C, 60.32; H, 3.25.

5-(4-Bromophenyl)-3-(3-methoxybenzylidene)furan-2(3H)-one (8f):

Starting with benzoyl propionic acid 5 (500 mg, 1.9 mmol) and benzaldehyde (0.23 mL, 1.9 mmol), 8f was obtained as a yellow solid, yield (495 mg, 71%), mp. 179-180 °C; $^1$H NMR (300MHz, CDCl$_3$): $\delta$ = 3.89 (s, OCH$_3$), 6.95 (s, 1H), 6.99-7.02 (m, 1H), 7.14-7.15 (m, 1H), 7.24-7.26 (m, 1H), 7.38-7.44 (m, 1H), 7.46 (s, 1H), 7.58-7.66 (m, 4H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta$ = 55.5 (OCH$_3$), 100.4 (C-4), 115.7 (C-2”), 115.8 (C-5”), 122.6 (C-6”), 124.9 (C-4’), 125.5 (C-1’), 126.7 (C-5”), 130.2 (C-3), 132.2 (C-3’,5’), 136.1 (C-2’,6’), 136.3 (C-1”), 155.9 (C-6), 159.9 (C-5), 162.2 (C-3”) 169.0 (C-2); GC-MS (EI, 70eV): $m/z$ (%) = 358 [M$^+$, $^{81}$Br, 40], 356 [M$^+$, $^{79}$Br, 40], 207 (11), 185 (100), 173 (11), 155 (28), 115 (10), 102 (19), 76 (23); IR (cm$^{-1}$): 3128, 2930, 1754, 1620, 1589, 1484, 1402, 1331, 1304, 1263, 1182, 1069, 1038; Anal. Calcd. for C$_{18}$H$_{13}$BrO$_3$: C, 60.52; H, 3.67. Found: C, 60.20; H, 3.55.
5-(4-Bromophenyl)-3-(4-methoxybenzylidene)furan-2(3H)-one (8g):

Starting with benzoyl propionic acid 5 (500 mg, 1.9 mmol) and benzaldehyde (0.23 mL, 1.9 mmol), 8g was obtained as a yellow solid, yield (555 mg, 80%), mp. 224-225 °C; $^1$H NMR (300MHz, DMSO): $\delta$ = 3.86 (s, OCH$_3$), 7.07 (d, $^3J$ = 8.7 Hz, 2H), 7.40 (s, 1H), 7.71-7.74 (m, 3H), 7.82 (d, $^3J$ = 8.7 Hz, 2H), 7.91 (d, $^3J$ = 8.7 Hz, 2H); $^{13}$C NMR (75.4 MHz, DMSO): $\delta$ = 55.9 (OCH$_3$), 102.5 (C-4), 115.2 (C-3″,5″), 122.1 (C-4′), 123.9 (C-1″), 127.4 (C-1′), 127.6 (C-2″,6″), 127.7 (C-3), 132.5 (C-3′,5′), 133.5 (C-2′,6′), 136.5 (C-6), 154.2 (C-5), 161.9 (C-4″), 169.4 (C-2); GC-MS (EI, 70eV): m/z (%) = 358 [M$^+$, 81Br, 76], 356 [M$^+$, 79Br, 77], 328 (9), 183 (76), 145 (100), 102 (28), 76 (27); IR (cm$^{-1}$): 1751, 1604, 1512, 1481, 1263, 1247, 1170, 1068, 1037, 993; Anal. Calcd. for C$_{18}$H$_{13}$BrO$_3$: C, 60.52; H, 3.67. Found: C, 60.77; H, 3.93.

2-[[5-(4-Bromophenyl)-2-oxofuran-3(2H)-ylidene]methyl]phenyl acetate (8h):

Starting with benzoyl propionic acid 5 (500 mg, 1.9 mmol) and benzaldehyde (0.20 mL, 1.9 mmol), 8h was obtained as a yellow solid, yield (560 mg, 75%), mp. 175-176 °C; $^1$H NMR (300MHz, CDCl$_3$): $\delta$ = 2.39 (s, CH$_3$), 6.87 (s, 1H), 7.21 (dd, $^3J$ = 7.8, 1.5 Hz, 1H), 7.34-7.40 (m, 1H), 7.47 (dd, $^3J$ = 8.1, 1.8 Hz, 1H), 7.52 (s, 1H), 7.58-7.65 (m, 4H), 7.74 (dd, $^3J$ = 7.8, 1.5 Hz, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta$ = 21.0 (CH$_3$), 6.87 (s, 1H), 7.21 (dd, $^3J$ = 7.8, 1.5 Hz, 1H), 7.34-7.40 (m, 1H), 7.47 (dd, $^3J$ = 8.1, 1.8 Hz, 1H), 7.52 (s, 1H), 7.58-7.65 (m, 4H), 7.74 (dd, $^3J$ = 7.8, 1.5 Hz, 1H); GC-MS (EI, 70eV): m/z (%) = 386 [M$^+$, 81Br, 20], 384 [M$^+$, 79Br, 20], 342 (100), 218 (9), 205 (14), 183 (82), 155 (35), 131 (14), 102 (17), 76 (33); IR (cm$^{-1}$): 1762, 1614, 1582, 1484, 1451, 1405, 1276, 1206, 1175, 1070, 1001; Anal. Calcd. for C$_{19}$H$_{13}$BrO$_4$: C, 59.24; H, 3.40. Found: C, 59.60; H, 3.21.
5-(4-Bromophenyl)-3-(2-methylbenzylidene)furan-2(3H)-one (8j):

Starting with benzoyl propionic acid 5 (500 mg, 1.9 mmol) and benzaldehyde (0.22 mL, 1.9 mmol), 8j was obtained as yellow solid, yield (490 mg, 73%), mp. 170-171 °C; \(^1\)H NMR (300MHz, CDCl\(_3\)): \(\delta = 2.43\) (s, CH\(_3\)), 7.32-7.40 (m, 3H), 7.55 (s, 1H), 7.59 (s, 1H), 7.72 (d, \(^3\)J = 8.7 Hz, 2H), 7.81-7.85 (m, 3H); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 20.0\) (CH\(_3\)), 102.3 (C-4), 124.4 (C-4'), 125.6 (C-5''), 127.1 (C-6''), 127.4 (C-3''), 127.7 (C-4''), 129.6 (C-1''), 131.1 (C-3), 131.3 (C-3',5'), 132.5 (C-2',6'), 133.6 (C-2''), 133.8 (C-1''), 139.3 (C-6), 155.6 (C-5), 168.8 (C-2); GC-MS (EI, 70eV): \(m/z\) (%) = 342 [M\(^+\), 81Br, 45], 340 [M\(^+\), 79Br, 46], 185 (100), 157 (39), 128 (32), 104 (11), 76 (21); IR (cm\(^{-1}\)): 1770, 1622, 1585, 1483, 1402, 1276, 1195, 1174, 1070, 997; Anal. Calcd. for C\(_{18}\)H\(_{13}\)BrO\(_2\): C, 63.36; H, 3.84. Found: C, 63.03; H, 3.46.

5-(4-Bromophenyl)-3-(2,6-dichlorobenzylidene)furan-2(3H)-one (8l):

Starting with benzoyl propionic acid 5 (500 mg, 1.9 mmol) and benzaldehyde (332 mg, 1.9 mmol), 8l was obtained as a yellow solid, yield (575 mg, 75%), mp. 204-205°C; \(^1\)H NMR (300MHz, CDCl\(_3\)): \(\delta = 6.33\) (s, 1H), 7.30-7.33 (m, 1H), 7.41-7.46 (m, 3H), 7.58 (m, 3H), 7.71-7.74 (m, 1H); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 101.6\) (C-4), 125.3 (C-5), 125.6 (C-4''), 126.7 (C-3'',5''), 126.9 (C-1''), 128.6 (C-3), 129.9 (C-3',5'), 130.5 (C-2',6'), 130.9 (C-2'',6''), 132.2 (C-1''), 134.5 (C-6), 156.1 (C-5), 167.3 (C-2); GC-MS (EI, 70eV): \(m/z\) (%) = 400 [M\(^+\), 81Br\(^{37}\)Cl\(^{37}\)Cl, 1], 398 [M\(^+\), 81Br\(^{37}\)Cl\(^{35}\)Cl, 7], 396 [M\(^+\), 81Br\(^{35}\)Cl\(^{35}\)Cl, 15], 394 [M\(^+\), 79Br\(^{35}\)Cl\(^{35}\)Cl, 9], 361 (100), 280 (9), 183 (61), 155 (31), 113 (15), 76 (22); IR (cm\(^{-1}\)): 1784, 1580, 1540, 1427, 1270, 1174, 997; Anal. Calcd. for C\(_{17}\)H\(_{9}\)BrCl\(_2\)O\(_2\): C, 51.55; H, 2.29. Found: C, 51.67; H, 2.34.
3.2.2 Synthesis of 1-Benzyl-3-arylidene-5(4-substitutedphenyl)-1H-pyrrol-2-(3H)-one:

General procedure for the synthesis of compounds (12a-f) and (13a-f):

Synthesis of γ-Ketobenzylamide
Furanone (0.5 mmol) and benzylamine (0.66 mmol) were refluxed in dry benzene for 2h. On completion of the reaction, excess benzene was distilled off and a solid mass so obtained was washed with petroleum ether and dried. The compound obtained was used without crystallization.

Cyclization of γ-Ketobenzylamide
γ-Ketobenzylamide was refluxed in 6N-hydrochloric acid (20 mL) for 1h. The contents were then cooled and a solid mass so obtained was collected, washed with water and crystallized from methanol to give pyrrolone.

1-Benzyl-3-(3-bromobenzylidene)-5-(4-ethoxyphenyl)-1H-pyrrole-2(3H)-one (12b):
Starting with furanone 7c (185 mg, 0.5 mmol) and benzylamine (0.07 mL, 0.66 mmol), 12b was obtained as an orange solid, yield (161 mg, 70%), mp. 149-150 °C; ¹H NMR (300MHz, CDCl₃): δ = 1.45 (t, 3J = 6.9 Hz, CH₃), 4.07 (q, 3J = 6.9 Hz, CH₂), 4.86 (s, CH₂), 6.16 (s, 1H), 6.89 (d, 3J = 8.7 Hz, 2H), 7.10-7.13 (m, 2H), 7.23-7.33 (m, 6H), 7.38 (s, 1H), 7.47-7.51 (m, 1H); ¹³C NMR (75.4 MHz, CDCl₃): δ = 14.8 (CH₃), 44.7 (CH₂), 63.6 (OCH₂), 99.5 (C-4), 114.6 (C-3′,5′), 122.9 (C-3″), 123.1 (C-4″′), 126.9 (C-2″′,6″′), 127.2 (C-6″), 128.6 (C-3″′,5″′), 128.8 (C-2′,6′), 129.4 (C-5″), 129.9 (C-1″′), 130.4 (C-2″′), 130.9 (C-4″), 132.0 (C-3), 132.5 (C-6), 137.7 (C-1″′), 138.1 (C-5), 150.6 (C-1″), 160.1 (C-4″), 170.9 (C-2); GC-MS (EI, 70eV): m/z (%) = 461 [M+, ⁷⁹Br, 100], 463 [M+, ⁸¹Br, 100]. 261 (28), 233 (9), 218 (14), 204 (9), 189 (11), 91 (85), 65 (9); IR (cm⁻¹): 3059, 2975, 1693, 1602, 1504, 1427, 1354, 1324, 1290, 1248, 1182, 1146, 1107, 1041; Anal. Calcd. for C₂₆H₂₂BrNO₂: C, 67.83; H, 4.82; N, 3.04. Found: C, 68.11; H, 4.55; N, 3.01.
1-Benzyl-5-(4-ethoxyphenyl)-3-(3-methoxybenzylidene)-1H-pyrrol-2(3H)-one (12c):

Starting with furanone 7i (161 mg, 0.5 mmol) and benzylamine (0.07 mL, 0.66 mmol), 12c was obtained as a brown solid, yield (147 mg, 68%), mp.127-128 °C; 

$^1$H-NMR (300MHz, CDCl$_3$): $\delta$ =1.45 (t, $^3J = 6.9$ Hz, CH$_3$), 3.86 (s, CH$_3$), 4.06 (q, $^3J = 6.9$ Hz, CH$_2$), 4.86 (s, CH$_2$), 6.20 (s, 1H), 6.88 (d, $^3J = 9$ Hz, 2H), 6.91-6.96 (m, 1H), 7.10-7.14 (m, 2H), 7.18-7.19 (m, 1H), 7.22-7.29 (m, 6H), 7.32-7.38 (m, 1H), 7.47 (s, 1H); 

$^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta$ = 14.8 (CH$_3$), 44.7 (CH$_2$), 55.4 (OCH$_3$), 63.6 (OCH$_2$), 99.9 (C-4), 114.6 (C-2”), 115.1 (C-4”), 115.3 (C-3′,5′), 122.9 (C-6”), 123.4 (C-1”’), 127.0 (C-2′′,”’), 127.1 (C-3′′,”’), 128.5 (C-2′,”’), 129.4 (C-5”), 129.8 (C-1”), 130.1 (C-3), 132.0 (C-6), 137.3 (C-5), 137.8 (C-1”), 149.6 (C-1”’), 159.8 (C-4’), 159.9 (C-3”), 171.1 (C-2); GC-MS (EI, 70eV): m/z (%) =411 [M+ , 100], 320 (5), 292 (5), 277 (9), 249 (12), 91 (37), 65 (5); IR (cm$^{-1}$): 2972, 1697, 1597, 1570, 1504, 1434, 1355, 1246, 1175, 1156, 1110, 1046; Anal. Calcd. for C$_{27}$H$_{25}$NO$_3$: C, 78.81; H, 6.12; N, 3.40. Found: C, 78.51; H, 6.02; N, 3.10.

1-Benzyl-5-(4-ethoxyphenyl)-3-(2-hydroxybenzylidene)-1H-pyrrol-2(3H)-one (12d):

Starting with furanone 7k (175 mg, 0.5 mmol) and benzylamine (0.07 mL, 0.66 mmol), 12d was obtained as a red solid, yield (135 mg, 68%), mp.192-193 °C; 

$^1$H-NMR (300MHz, CDCl$_3$): $\delta$ =1.45 (t, $^3J = 6.9$ Hz, CH$_3$), 4.07 (q, $^3J = 6.9$ Hz, CH$_2$), 4.92 (s, CH$_2$), 6.26 (s, 1H), 6.86-6.97 (m, 4H), 7.13-7.16 (m, 2H), 7.21-7.31 (m, 6H), 7.71 (d, $^3J = 6.6$ Hz, 1H), 8.41 (s, 1H), 9.18 (s, OH); 

$^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta$ = 14.8 (CH$_3$), 44.8 (CH$_2$), 63.6 (OCH$_2$), 100.8 (C-4), 114.5 (C-3′,5′), 116.6 (C-3”), 119.9 (C-1”), 123.4 (C-5”), 123.4 (C-4’”), 127.0 (C-2′′,”’), 127.1 (C-3′′,”’), 128.4 (C-2′,”’), 128.6 (C-4’), 129.5 (C-1”), 129.6 (C-6”), 130.9 (C-3), 131.6 (C-6), 137.7 (C-1”’), 147.6 (C-5), 157.4 (C-2”), 159.8 (C-4’), 172.2 (C-2); GC-MS (EI, 70eV): m/z
(%) = 397 [M+, 30], 305 (10), 292 (64), 207 (12), 131 (9), 107 (9), 91 (100), 77 (9), 65 (9); IR (cm\(^{-1}\)): 3076, 1663, 1592, 1506, 1454, 1338, 1307, 1268, 1241, 1176, 1152, 1030; Anal. Calcd. for C\(_{26}\)H\(_{23}\)N\(_2\)O\(_3\): C, 78.57; H, 5.83; N, 3.52. Found: C, 78.67; H, 5.58; N, 3.21.

1-Benzyl-5-(4-ethoxyphenyl)-3-(2-nitrobenzylidene)-1\(H\)-pyrrol-2(3\(H\))-one (12e):

Starting with furanone 7h (168 mg, 0.5 mmol) and benzylamine (0.07 mL, 0.66 mmol), 12e was obtained as a red solid, yield (153 mg, 72%), mp. 139-140 °C; \(^1\)H-NMR (300MHz, CDCl\(_3\)): \(\delta = 1.46\) (t, \(^3J = 6.9\) Hz, CH\(_3\)), 4.08 (q, \(^3J = 6.9\) Hz, CH\(_2\)), 4.87 (s, CH\(_2\)), 6.19 (s, 1H), 6.91 (d, \(^3J = 8.7\) Hz, 2H), 7.10-7.13 (m, 2H), 7.23-7.32 (m, 5H), 7.46 (s, 1H), 7.58-7.64 (m, 1H), 7.92 (d, \(^3J = 7.8\) Hz, 1H), 8.21 (dd, \(^3,4J = 8.1, 1.2\) Hz, 1H), 8.51 (m, 1H); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 14.8\) (CH\(_3\)), 44.8 (CH\(_2\)), 63.7 (OCH\(_2\)), 98.9 (C-4), 114.7 (C-3',5'), 122.8 (C-3''), 123.4 (C-4''), 123.9 (C-2'',6''), 126.9 (C-3''',5'''), 127.3 (C-4'''), 128.2 (C-2',6'), 128.6 (C-1''), 129.5 (C-1''), 129.9 (C-6''), 132.2 (C-3), 135.8 (C-5'), 137.5 (C-6), 137.9 (C-1''''), 148.6 (C-5), 151.9 (C-2''), 160.3 (C-4'), 170.8 (C-2); GC-MS (EI, 70eV): \(m/z\) (%): 426 [M+, 83], 189 (8), 91 (100), 65 (8); IR (cm\(^{-1}\)): 1706, 1599, 1523, 1502, 1467, 1388, 1344, 1291, 1256, 1177, 1108, 1046; Anal. Calcd. for C\(_{26}\)H\(_{22}\)N\(_2\)O\(_4\): C, 73.23; H, 5.20; N, 6.57. Found: C, 73.56; H, 5.40; N, 6.89.

1-Benzyl-5-(4-ethoxyphenyl)-3-(4-nitrobenzylidene)-1\(H\)-pyrrol-2(3\(H\))-one (12f):

Starting with furanone 7l (168 mg, 0.5 mmol) and benzylamine (0.07 mL, 0.66 mmol), 12f was obtained as a red solid, yield (146 mg, 69%), mp. 159-160 °C; \(^1\)H-NMR (300MHz, CDCl\(_3\)): \(\delta = 1.46\) (t, \(^3J = 6.9\) Hz, CH\(_3\)), 4.07 (q, \(^3J = 6.9\) Hz, CH\(_2\)), 4.87 (s, CH\(_2\)), 6.17 (s, 1H), 6.90 (d, \(^3J = 8.7\) Hz, 2H), 7.10-7.13 (m, 2H), 7.23-7.31 (m, 5H), 7.43 (s, 1H), 7.78 (d, \(^3J = 9\) Hz, 2H), 8.28 (d, \(^3J = 9\) Hz, 2H); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 14.8\) (CH\(_3\)), 44.8 (CH\(_2\)), 63.7 (OCH\(_2\)), 98.9 (C-4), 114.7 (C-3',5'), 122.8 (C-3''), 123.4 (C-4''), 123.9 (C-2'',6''), 126.9 (C-3''',5'''), 127.3 (C-4'''), 128.2 (C-2',6'), 128.6 (C-1''), 129.5 (C-1''), 129.9 (C-6''), 132.2 (C-3), 135.8 (C-5'), 137.5 (C-6), 137.9 (C-1''''), 148.6 (C-5), 151.9 (C-2''), 160.3 (C-4'), 170.8 (C-2); GC-MS (EI, 70eV): \(m/z\) (%): 426 [M+, 83], 189 (8), 91 (100), 65 (8); IR (cm\(^{-1}\)): 1706, 1599, 1523, 1502, 1467, 1388, 1344, 1291, 1256, 1177, 1108, 1046; Anal. Calcd. for C\(_{26}\)H\(_{22}\)N\(_2\)O\(_4\): C, 73.23; H, 5.20; N, 6.57. Found: C, 73.56; H, 5.40; N, 6.89.
99.3 (C-4), 114.7 (C-3’,5’), 122.8 (C-3”,5”), 124.1 (C-4”), 126.9 (C-2”,6”), 127.3 (C-3”,5”), 128.0 (C-2’,6’), 128.6 (C-1’), 129.4 (C-2”,6”), 130.5 (C-3), 132.9 (C-6), 137.4 (C-1”), 142.5 (C-5), 147.3 (C-1”), 152.6 (C-4”), 160.4 (C-4’), 170.8 (C-2); GC-MS (EI, 70eV): m/z (%) = 426 [M+, 59], 261 (5), 189 (5), 91 (100), 65 (9); IR (cm⁻¹): 3064, 2980, 1698, 1603, 1504, 1391, 1334, 1289, 1250, 1179, 1097, 1045; Anal. Calcd. for C₂₆H₂₂N₂O₄: C, 73.23; H, 5.20; N, 6.57. Found: C, 73.50; H, 5.29; N, 6.21.

1-Benzyl-5-(4-bromophenyl)-3-(2-chlorobenzylidene)-1H-pyrrol-2(3H)-one (13a):

Starting with furanone 8a (180 mg, 0.5 mmol) and benzylamine (0.07 mL, 0.66 mmol), 13a was obtained as a yellow solid, yield (154 mg, 68%), mp. 149-150 °C; ¹H NMR (300MHz, CDCl₃): δ = 4.84 (s, CH₂), 6.12 (s, 1H), 7.07-7.11 (m, 2H), 7.15-7.20 (m, 2H), 7.23-7.33 (m, 4H), 7.39-7.42 (m, 1H), 7.46-7.52 (m, 2H), 7.58-7.60 (m, 1H), 7.69-7.72 (m, 1H), 7.87 (s, 1H); ¹³C NMR (75.4 MHz, CDCl₃): δ = 44.7 (CH₂), 100.7 (C-4), 123.9 (C-4’), 126.9 (C-5”), 127.0 (C-4”), 127.3 (C-2”,6”), 128.6 (C-6”), 129.2 (C-3”,5”), 129.4 (C-2’,6’), 129.6 (C-4”), 130.0 (C-3”), 130.2 (C-3’,5’), 130.4 (C-1”), 131.4 (C-3), 131.9 (C-2”), 134.0 (C-6), 135.7 (C-1”), 137.3 (C-5), 149.3 (C-1’), 170.2 (C-2); GC-MS (EI, 70eV): m/z (%) = 453 [M⁺, 8¹Br 3⁷Cl, 8], 451 [M⁺, 8¹Br 3⁵Cl, 30], 449 [M⁺, 3⁵Cl 7¹Br, 22], 279 (16), 244 (3), 216 (8), 202 (8), 114 (4), 91 (100), 77 (2), 65 (9); IR (cm⁻¹): 3028, 1697, 1583, 1506, 1485, 1355, 1317, 1282, 1263, 1220, 1195, 1143, 1068, 1006; Anal. Calcd. for C₂₆H₁₇BrClINO: C, 63.95; H, 3.80; N, 3.11. Found: C, 64.31; H, 3.96; N, 3.45.

1-Benzyl-5-(4-bromophenyl)-3-(3-chlorobenzylidene)-1H-pyrrol-2(3H)-one (13b):

Starting with furanone 8b (180 mg, 0.5 mmol) and benzylamine (0.07 mL, 0.66 mmol), 13b was obtained as a red solid, yield (158 mg, 70%), mp. 189-190 °C; ¹H NMR (300MHz, CDCl₃): δ = 4.83 (s, CH₂), 6.22 (s, 1H), 7.06-7.09 (m, 2H), 7.19 (d, 3J = 8.4 Hz, 2H), 7.23-7.30 (m, 4H), 7.34-7.38
(m, 2H), 7.47 (s, 1H), 7.51 (d, 3J = 8.4 Hz, 2H), 7.63 (m, 1H); 13C NMR (75.4 MHz, CDCl₃): δ = 44.7 (CH₂), 100.8 (C-4), 124.0 (C-4'), 126.9 (C-2''), 127.0 (C-6''), 127.3 (C-4''), 128.4 (C-2'',6''), 128.6 (C-4''), 129.4 (C-3'',5''), 129.5 (C-2',6'), 129.6 (C-5''), 130.1 (C-3',5'), 130.6 (C-3), 131.6 (C-3''), 131.9 (C-6), 134.8 (C-1''), 137.2 (C-1''), 137.4 (C-5), 149.3 (C-1'), 170.6 (C-2); GC-MS (EI, 70eV): m/z (%) = 453 [M⁺, 81Br, 37Cl, 7], 451 [M⁺, 81Br, 35Cl, 26], 449 [M⁺, 35Cl, 79Br, 19], 279 (6), 244 (3), 216 (6), 202 (8), 189 (2), 114 (3), 91 (100), 77 (2), 65 (9); IR (cm⁻¹): 3028, 1745, 1697, 1615, 1582, 1483, 1350, 1321, 1261, 1221, 1149, 1107, 1070, 1006; Anal. Calcd. for C₂₄H₁₇Br₂ClNO: C, 63.95; H, 3.80; N, 3.11. Found: C, 63.44; H, 3.89; N, 3.50.

1-Benzyl-3-(4-bromobenzylidene)-5-(4-bromophenyl)-1H-pyrrol-2(3H)-one (13c):

Starting with furanone 8d (203 mg, 0.5 mmol) and benzylamine (0.07 mL, 0.66 mmol), 13c was obtained as an orange solid, yield (172 mg, 69%), mp. 143-144 °C. 1H NMR (300MHz, CDCl₃): δ = 4.83 (s, CH₂), 6.20 (s, 1H), 7.06-7.09 (m, 2H), 7.18 (d, 3J = 8.4 Hz, 1H), 7.23-7.28 (m, 3H), 7.47-7.58 (m, 7H); 13C NMR (75.4 MHz, CDCl₃): δ = 44.7 (CH₂), 100.8 (C-4), 123.9 (C-4'), 124.0 (C-4''), 126.9 (C-4''), 127.0 (C-2'',6''), 127.3 (C-2',6'), 128.6 (C-3'',5''), 129.4 (C-3',5'), 130.0 (C-3'',5''), 131.5 (C-1''), 131.9 (C-3), 132.2 (C-2'',6''), 134.5 (C-6), 134.7 (C-1''), 137.3 (C-5), 148.9 (C-1'), 170.6 (C-2); GC-MS (EI, 70eV): m/z (%) = 497 [M⁺, 81Br, 15], 495 [M⁺, 81Br, 28], 493 [M⁺, 79Br, 15], 323 (10), 244 (3), 216 (8), 202 (9), 189 (5), 114 (5), 91 (100), 77 (2), 65 (9); IR (cm⁻¹): 3028, 1695, 1615, 1582, 1483, 1350, 1321, 1261, 1221, 1149, 1107, 1070, 1006; Anal. Calcd. for C₂₄H₁₇Br₂NO: C, 58.21; H, 3.46; N, 2.83. Found: C, 58.47; H, 3.78; N, 2.43.
1-Benzyl-5-(4-bromophenyl)-3-(2-nitrobenzylidene)-1H-pyrrol-2(3H)-one (13d):

Starting with furanone 8i (186 mg, 0.5 mmol) and benzylamine (0.07 mL, 0.66 mmol), 13d was obtained as a red solid, yield (151 mg, 65%), mp.199-200 °C; \(^1\)H NMR (300MHz, CDCl\(_3\)): \(\delta = 4.82\) (s, CH\(_2\)), 5.92 (s, 1H), 7.08-7.16 (m, 2H), 7.24-7.38 (m, 6H), 7.47-7.50 (m, 2H), 7.68-7.70 (m, 2H), 7.90 (s, 1H), 8.14-8.17 (m, 1H); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 44.8\) (CH\(_2\)), 100.2 (C-4), 124.0 (C-4'), 125.3 (C-3”), 127.0 (C-4'”), 127.4 (C-2”,”6””), 128.7 (C-3’,”5””), 128.8 (C-2’,”6’”), 129.4 (C-4’”), 129.7 (C-1”), 131.4 (C-6”), 131.7 (C-3’,”5’”), 131.9 (C-3), 132.8 (C-5””), 133.4 (C-6), 137.2 (C-1’’”), 145.3 (C-5), 146.1 (C-1’), 147.6 (C-2”), 169.6 (C-2); GC-MS (EI, 70eV): \(m/z\) (%) = 462 [M\(^+\), 81Br,14], 460 [M\(^+\), 81Br, 15], 338 (8), 281 (4), 231 (3), 207 (9), 113 (3), 102 (3), 91 (100), 76 (5), 65 (9); IR (cm\(^{-1}\)): 3028, 1766, 1697, 1585, 1521, 1485, 1440, 1396, 1342, 1259, 1070, 1008; Anal.Calcd. for C\(_{24}\)H\(_{17}\)BrN\(_2\)O\(_3\): C, 62.49; H, 3.71; N, 6.07. Found: C, 62.13; H, 3.34; N, 5.65.

1-Benzyl-5-(4-bromophenyl)-3-(2,6-dichlorobenzylidene)-1H-pyrrol-2(3H)-one (13f):

Starting with furanone 8l (198 mg, 0.5 mmol) and benzylamine (0.07 mL, 0.66 mmol), 13f was obtained as a red solid, yield (179 mg, 70%), mp.157-158 °C; \(^1\)H NMR (300MHz, CDCl\(_3\)): \(\delta = 4.81\) (s, CH\(_2\)), 5.63 (s, 1H), 7.11-7.15 (m, 4H), 7.22-7.33 (m, 5H), 7.38-7.40 (m, 2H), 7.44-7.47 (m, 2H), 7.50 (s, 1H); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 44.8\) (CH\(_2\)), 102.3 (C-4), 123.9 (C-4’), 126.9 (C-4”), 127.1 (C-4'”), 127.3 (C-3’,”5’”), 128.3 (C-3’,”5’’”), 128.5 (C-3’’,”5’’’”), 128.6 (C-2’,”6’”), 129.5 (C-3’,”5’’”), 129.8 (C-2’,”6’”), 131.8 (C-3), 133.3 (C-6), 134.6 (C-1’”), 134.7 (C-1’’’”), 137.3 (C-5), 148.6 (C-1’), 169.4 (C-2’); GC-MS (EI, 70eV): \(m/z\) (%) = 482 [M\(^+\), 81Br\(^{37}\)Cl\(^{37}\)Cl, 1], 480 [M\(^+\), 81Br\(^{37}\)Cl\(^{35}\)Cl, 10], 478 [M\(^+\), 81Br\(^{37}\)Cl\(^{35}\)Cl, 37], 476 [M\(^+\), 79Br\(^{35}\)Cl\(^{35}\)Cl, 30], 373 (4), 359 (10), 281 (5), 135.
243 (3), 207 (12), 91 (100), 77 (6), 65 (10); IR (cm⁻¹): 3028, 1701, 1480, 1420, 1350, 1261, 1190, 1140, 1070, 1010, 950; Anal. Calcd. for C₂₄H₁₆BrCl₂NO: C, 59.41; H, 3.32; N, 2.89. Found: C, 59.15; H, 3.39; N, 3.17.

3.2.3 Synthesis of 7-(Trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-ones:

General procedure for the synthesis of compound (17a):

Synthesis was conducted in a pressure tube. To the suspension of 4-hydroxy coumarin 14 (2.5 g, 15.4 mmol) in dry 1,4-dioxane was added (2.56 g, 32.4 mmol) of dry pyridine. After a brief stirring when the mixture became completely homogenous, was added (2.01 g, 18.5 mmol) of TMSCl. The reaction mixture was stirred for 1 hour at room temperature. Then was added (4.21 g, 20.0 mmol) of trifluoroacetic anhydride and the mixture was stirred for another 2 hour at 80–90 °C. To the cooled reaction mass was added (2.36 g, 15.4 mmol) of POCl₃ and the mixture was stirred 2 hour at 60 °C. Then the reaction mass was diluted with ice water and extracted with chloroform (50 mL). The chloroform layer was separated and the aqueous phase was extracted two times with chloroform (50 mL). The combined extract was dried (Na₂SO₄), chloroform was removed and product dried under vacuum.

4-Chloro-3-(2,2,2-trifluoroacetyl)-2H-chromen-2-one (17a):

Starting with 4-hydroxycoumarin 14 (2.5 g, 15.4 mmol), 17a was obtained as a white solid (3.943 g, 93%), mp. 115–117 °C; ¹H NMR (300 MHz, CDCl₃): δ = 7.42-7.50 (m, 2H), 7.73-7.78 (m, 1H), 7.97-8.00 (m, 1H); ¹³C NMR (62.9 MHz, DMSO): δ = 114.4 (q, J_C-F = 290 Hz, CF₃), 116.9 (C-8), 117.4 (C-3), 120.8 (C-6), 125.8 (C-5), 126.7 (C-7), 135.5 (C-10), 150.2 (C-4), 152.9 (C-9), 155.9 (C-2), 180.9 (q, J_C-F = 40 Hz, C=O); ¹⁹F NMR (282.4 MHz, CDCl₃): δ = -75.8 (s, CF₃); GC-MS (EI, 70eV): m/z (%) = 276 (M⁺, 15), 209 (33), 208 (12), 207 (100), 135 (18), 123 (11); HRMS (ESI): calcd for C₁₁H₄ClF₃O₃ (M+H) 277.0072, found 277.0070; IR (ATR, cm⁻¹): ν = 3084 (w), 1727 (m), 1605 (w), 1584 (m), 1480 (w), 1453 (m), 1315 (s), 1276 (w), 1237 (w), 1195 (m), 1170 (s), 1156 (s), 1135 (m), 1073 (m), 1034 (w), 974 (m), 851 (m), 820 (m), 766 (s), 723 (s).
General procedure for the synthesis of compounds (19a-j):

Synthesis was carried out in a pressure tube. To a solution of compound 17a (300 mg, 1.08 mmol) and equimolar amount of aniline in DMF (15 mL) was added TMSCl (1 mL) dropwise. The reaction was heated for 12-24 h at 110-120 °C (controlled by TLC). After cooling the pressure tube, the reaction mixture was poured onto cooled water. The precipitate formed was filtered and dried. The product was purified by column chromatography (silica gel, EtOAc/hexane). The products were obtained in good to excellent yield (60-85%).

4-(4-Fluorophenylamino)-3-(2,2,2-trifluoroacetyl)-2H-chromen-2-one (19a):

Starting with 17a (300 mg, 1.08 mmol), aniline (0.103 mL, 1.08 mmol), 19a was obtained as a yellow solid (260 mg, 68%), mp. 184–185 °C; 1H NMR (300 MHz, CDCl3): δ = 6.81-6.87 (m, 1H), 7.04-7.25 (m, 6H), 7.44-7.50 (m, 1H), 12.80 (s, NH); 13C NMR (75.4 MHz, DMSO): δ = 95.8 (C-3), 112.2 (C-10), 116.9 (q, 1JCF = 287.9 Hz, CF3), 117.4 (d, 2JCF = 22.9 Hz, C-3‘,5’), 118.5 (C-8), 123.2 (C-5), 127.2 (d, 3JCF = 8.60 Hz, C-2‘,6’), 127.8 (C-6), 134.5 (d, 4JCF = 3.53 Hz, C-1’), 135.4 (C-7), 155.1 (C-4), 157.9 (C-9), 161.0 (C-2), 162.1 (d, 1JCF = 249 Hz, C-4’), 182.2 (q, 2JCF = 37.1 Hz, C=O); 19F NMR (282.4 MHz, CDCl3): δ = -72.68 (s, CF3), -111.45 (s, CF); GC-MS (EI, 70eV): m/z (%) = 351 (M+, 40.29), 333 (25.94), 305 (10.16), 282 (100), 254 (11.13), 214 (12.44), 183 (7.08), 95 (12.28); HRMS (ESI): calcd for C17H9F4NO3 (M+H) 352.0386, found 352.0389; IR (ATR, cm⁻¹): 3320 (w), 2925 (s), 1715 (s), 1655 (s), 1612 (m), 1544 (m), 1412 (m), 1375 (m), 1296 (m), 1270 (w), 1210 (s), 1180 (s), 1150 (s), 991 (s), 875 (m), 824 (m), 762 (s), 746 (s), 713 (s), 690 (w), 638 (m); Anal. Calcd. for C17H9F4NO3: C, 58.13; H, 2.58; N, 3.99. Found: C, 55.48; H, 2.28; N, 3.23.

4-(4-Methoxyphenylamino)-3-(2,2,2-trifluoroacetyl)-2H-chromen-2-one (19b):

Starting with 17a (300 mg, 1.08 mmol), aniline (133 mg, 1.08 mmol), 19b was obtained as a yellow solid (337 mg, 85%), mp. 188–190 °C; 1H NMR (300 MHz, CDCl3): δ = 3.79 (s, OCH3), 6.79-6.84
(m, 1H), 6.89 (d, \(^3J = 8.9\) Hz, 2H), 7.08-7.13 (m, 3H), 7.19 (dd, \(^4J = 8.4, 1.1\) Hz, 1H), 7.41-7.47 (m, 1H), 12.83 (s, NH); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 55.6\) (C-OCH\(_3\)), 95.1 (C-3), 112.5 (C-10), 115.5 (C-3',5'), 117.1 (q, \(^1J_{C-F} = 287\) Hz, CF\(_3\)), 118.3 (C-8), 123.1 (C-2',6'), 126.5 (C-5), 127.9 (C-6), 130.8 (C-7), 135.1 (C-1'), 155.0 (C-4), 158.3 (C-9), 159.6 (C-4'), 160.8 (C-2), 181.8 (q, \(^2J_{C-F} = 36.8\) Hz, C=O); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta = -72.5\) (s, CF\(_3\)); GC-MS (EI, 70eV): \(m/z\) (%) = 363 (M\(^+\), 100), 345 (33.77), 302 (12.91), 294 (86.36), 266 (12.92), 251 (35.57), 226 (16.05); HRMS (ESI): calcd for C\(_{18}\)H\(_{12}\)F\(_3\)NO\(_4\) (M\(^+\)) 364.0791, found 363.0795; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3067\) (w), 2941 (w), 1730 (s), 1607 (s), 1563 (m), 1508 (m), 1463 (m), 1287 (w), 1241 (m), 1170 (s), 1148 (s), 1064 (w), 1026 (m), 981 (s), 905 (w), 861 (w), 831 (m), 806 (m), 780 (m), 754 (s), 724 (s), 668 (w), 600 (w); Anal. Calcd. for C\(_{18}\)H\(_{12}\)F\(_3\)NO\(_4\): C, 59.51; H, 3.33; N, 3.86. Found: C, 59.67; H, 3.20; N, 3.58.

\[ \text{4-(4-Ethylphenylamino)-3-(2,2,2-trifluoroacetyl)-2H-chromen-2-one (19c):} \]

\[
\begin{align*}
\text{Chemical Formula: C}_{19}\text{H}_{14}\text{F}_{3}\text{NO}_{3} \\
\text{Exact Mass: 361.09}
\end{align*}
\]

Starting with 17a (300 mg, 1.08 mmol), aniline (0.135 mL, 1.08 mmol), 19c was obtained as a yellow solid (300 mg, 76%), mp. 112–113 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 1.19\) (t, \(^3J = 7.6\) Hz, CH\(_3\)), 2.63 (q, \(^3J = 7.6\) Hz, CH\(_2\)), 6.76-6.82 (m, 1H), 7.06-7.12 (m, 2H), 7.16 (m, 2H), 7.20 (d, \(^3J = 8.4\) Hz, 2H), 7.39-7.45 (m, 1H), 12.82 (s, NH); \(^{13}\)C NMR (62.9 MHz, CDCl\(_3\)): \(\delta = 14.3\) (CH\(_3\)), 27.4 (CH\(_2\)), 94.2 (C-3), 111.4 (C-10), 116.0 (q, \(^1J_{C-F} = 283.6\) Hz, CF\(_3\)), 117.1 (C-2',6'), 122.1 (C-8), 124.0 (C-5), 127.0 (C-6), 128.7 (C-7), 134.1 (C-3',5'), 134.8 (C-1'), 144.1 (C-4'), 153.9 (C-4), 157.2 (C-9), 159.8 (C-2), 180.7 (q, \(^2J_{C-F} = 36.7\) Hz, C=O); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta = -72.5\) (s, CF\(_3\)); GC-MS (EI, 70eV): \(m/z\) (%) = 361 (M\(^+\), 60.47), 343 (16.95), 328 (19.54), 292 (100), 277 (28.26), 264 (36.83), 77 (9.16); HRMS (ESI): calcd for C\(_{19}\)H\(_{14}\)F\(_3\)NO\(_3\) (M+H) 362.0999, found 362.1005; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3045\) (w), 2932 (w), 1733 (s), 1610 (s), 1562 (m), 1495 (m), 1337 (w), 1314 (w), 1285 (w), 1233 (m), 1213 (m), 1152 (s), 1076 (w), 1049 (w), 985 (s), 904 (w), 862 (m), 814 (m), 761 (s), 723 (s), 666 (m), 601 (m); Anal. Calcd. for C\(_{19}\)H\(_{14}\)F\(_3\)NO\(_3\): C, 63.16; H, 3.91; N, 3.88. Found: C, 63.10; H, 3.95; N, 3.55.
**4-(4-Nitrophenylamino)-3-(2,2,2-trifluoroacetyl)-2H-chromen-2-one (19d):**

Starting with 17a (300 mg, 1.08 mmol), aniline (149 mg, 1.08 mmol), **19d** was obtained as a yellow solid (250 mg, 60%), mp. 203–204 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 6.89-6.94$ (m, 1H), 7.12 (dd, $^3$$^A$$J$ = 8.36, 1.37 Hz, 1H), 7.28-7.34 (m, 3H), 7.52-7.57 (m, 1H), 8.24 (d, $^3$$J$ = 8.94 Hz, 2H), 12.52 (s, NH); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta = 98.4$ (C-3), 111.9 (C-10), 116.7 (q, $^1$$J$$_{C-F}$ = 288 Hz, CF$_3$), 118.7 (C-2′,6′), 123.5 (C-8), 125.1 (C-5), 125.7 (C-3′,5′), 127.7 (C-7), 136.0 (C-4′), 144.6 (C-1′), 146.4 (C-4), 157.4 (C-9), 160.6 (C-2), 182.8 (q, $^2$$J$$_{C-F}$ = 37.9 Hz, C=O); $^1$F NMR (282.4 MHz, CDCl$_3$): $\delta = -72.8$ (s, CF$_3$); GC-MS (EI, 70 eV): $m/z$ (%) = 378 (M$^+$, 100), 361 (25.94), 331 (10.16), 309 (9.31), 281 (11.13); HRMS (ESI): calcd for C$_{17}$H$_9$F$_3$N$_2$O$_5$ (M+H) 379.0536, found 379.0535; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 3082$ (w), 1715 (s), 1641 (w), 1604 (s), 1588 (s), 1556 (m), 1523 (s), 1492 (s), 1460 (m), 1440 (m), 1342 (s), 1280 (w), 1251 (m), 1212 (m), 1180 (s), 1152 (s), 1108 (w), 1065 (w), 1040 (w), 990 (s), 904 (w), 877 (m), 857 (m), 804 (m), 764 (s), 707 (s), 621 (w). Anal. Calcd. for C$_{17}$H$_9$F$_3$N$_2$O$_5$: C, 53.98; H, 2.40; N, 7.41. Found: C, 54.00; H, 2.16; N, 6.79.

**4-(4-Chlorophenylamino)-3-(2,2,2-trifluoroacetyl)-2H-chromen-2-one (19e):**

Starting with 17a (300 mg, 1.08 mmol), aniline (138 mg, 1.08 mmol), **19e** was obtained as a yellow solid (290 mg, 72%), mp. 157–158 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 6.84-6.89$ (m, 1H), 7.09-7.15 (m, 3H), 7.23 (dd, $^3$$^A$$J$ = 8.41, 1.10 Hz, 1H), 7.37 (d, $^3$$J$ = 8.68 Hz, 2H), 7.45-7.51 (m, 1H) 12.74 (s, NH); $^{13}$C NMR (62.9 MHz, CDCl$_3$): 96.1 (C-3), 112.1 (C-10), 116.9 (q, $^1$$J$$_{C-F}$ = 287.2 Hz, CF$_3$), 118.4 (C-8), 123.2 (C-2′,6′), 126.5 (C-5), 127.8 (C-7), 130.5 (C-4′), 134.3 (C-7), 135.4 (C-3′,5′), 137.1 (C-1′), 155.1 (C-4), 157.9 (C-9), 160.8 (C-2), 182.2 (q, $^2$$J$$_{C-F}$ = 37.1 Hz, C=O); $^1$F NMR (282.4 MHz, CDCl$_3$): $\delta = -72.6$ (s, CF$_3$); GC-MS (EI, 70eV): $m/z$ (%) = 369 (M$^+$, 100), 367 (M$^+$, $^{35}$Cl, 44.46), 349 (18.56), 298 (100), 270 (14.56), 230 (11.51), 111 (11.63); HRMS (ESI): calcd for C$_{17}$H$_9$CIF$_3$NO$_3$ (M+H) 368.0296, found 368.00302; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 3082$ (w), 1715 (s), 1641 (w), 1604 (s), 1588 (s), 1556 (m), 1523 (s), 1492 (s), 1460 (m), 1440 (m), 1342 (s), 1280 (w), 1251 (m), 1212 (m), 1180 (s), 1152 (s), 1108 (w), 1065 (w), 1040 (w), 990 (s), 904 (w), 877 (m), 857(m), 804 (m), 764 (s), 707 (s), 621 (w). Anal. Calcd. for C$_{17}$H$_9$ClF$_3$NO$_3$: C, 53.98; H, 2.40; N, 7.41. Found: C, 54.00; H, 2.16; N, 6.79.

**4-(4-Chlorophenylamino)-3-(2,2,2-trifluoroacetyl)-2H-chromen-2-one (19e):**

Starting with 17a (300 mg, 1.08 mmol), aniline (138 mg, 1.08 mmol), **19e** was obtained as a yellow solid (290 mg, 72%), mp. 157–158 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 6.84-6.89$ (m, 1H), 7.09-7.15 (m, 3H), 7.23 (dd, $^3$$^A$$J$ = 8.41, 1.10 Hz, 1H), 7.37 (d, $^3$$J$ = 8.68 Hz, 2H), 7.45-7.51 (m, 1H) 12.74 (s, NH); $^{13}$C NMR (62.9 MHz, CDCl$_3$): 96.1 (C-3), 112.1 (C-10), 116.9 (q, $^1$$J$$_{C-F}$ = 287.2 Hz, CF$_3$), 118.4 (C-8), 123.2 (C-2′,6′), 126.5 (C-5), 127.8 (C-7), 130.5 (C-4′), 134.3 (C-7), 135.4 (C-3′,5′), 137.1 (C-1′), 155.1 (C-4), 157.9 (C-9), 160.8 (C-2), 182.2 (q, $^2$$J$$_{C-F}$ = 37.1 Hz, C=O); $^1$F NMR (282.4 MHz, CDCl$_3$): $\delta = -72.6$ (s, CF$_3$); GC-MS (EI, 70eV): $m/z$ (%) = 369 (M$^+$, $^{35}$Cl, 44.46), 349 (18.56), 298 (100), 270 (14.56), 230 (11.51), 111 (11.63); HRMS (ESI): calcd for C$_{17}$H$_9$ClF$_3$NO$_3$ (M+H) 368.0296, found 368.00302; IR (ATR,
cm⁻¹): \( \tilde{\nu} = 3316 \text{ (m)}, 1672 \text{ (s)}, 1613 \text{ (m)}, 1586 \text{ (m)}, 1519 \text{ (s)}, 1492 \text{ (s)}, 1409 \text{ (m)}, 1373 \text{ (m)}, 1322 \text{ (m)}, 1297 \text{ (w)}, 1216 \text{ (m)}, 1185 \text{ (s)}, 1154 \text{ (s)}, 1088 \text{ (m)}, 1014 \text{ (w)}, 992 \text{ (s)}, 950 \text{ (w)}, 904 \text{ (w)}, 871 \text{ (m)}, 825 \text{ (m)}, 780 \text{ (w)}, 761 \text{ (s)}, 730 \text{ (s)}, 685 \text{ (m)}, 633 \text{ (w)}; \)

Anal. Calcd. for C\textsubscript{17}H\textsubscript{9}F\textsubscript{3}ClNO\textsubscript{3}: C, 55.53; H, 2.47; N, 3.81. Found: C, 55.35; H, 2.47; N, 3.34.

4-(2-Iodophenylamino)-3-(2,2,2-trifluoroacetyl)-2\textit{H}-chromen-2-one (19f):

Starting with \textit{17a} (300 mg, 1.08 mmol), aniline (236 mg, 1.08 mmol), \textit{19f} was obtained as a yellow solid (325 mg, 65\%), mp. 155–156 °C; \(^1\text{H} \ \text{NMR} \) (300 MHz, CDCl\textsubscript{3}): \( \delta = 6.79-6.85 \text{ (m, 1H)}, 6.91 \text{ (dd, } \text{J} = 8.4, 1.5 \text{ Hz, 1H)}, 7.05-7.16 \text{ (m, 2H)}, 7.23 \text{ (dd, } \text{J} = 8.43, 1.02 \text{ Hz, 1H)}, 7.31-7.37 \text{ (m, 1H)}, 7.45-7.50 \text{ (m, 1H)}, 7.94 \text{ (dd, } \text{J} = 7.95, 1.32 \text{ Hz, 1H)}, 12.70 \text{ (s, NH)}; \( ^{13} \text{C} \ \text{NMR} \) (75.4MHz, CDCl\textsubscript{3}): \( \delta = 94.6 \text{ (C-2′)}, 95.1 \text{ (C-3), 111.5 \text{ (C-10), 115.9 \text{ (q, } J_{C-F} = 288.3 \text{ Hz, CF}_3), 117.4 \text{ (C-8), 122.5 \text{ (C-6′), 126.0 \text{ (C-4′), 126.3 \text{ (C-5), 128.8 \text{ (C-6), 128.9 \text{ (C-7), 134.4 \text{ (C-3′), 139.5 \text{ (C-4), 140.1 \text{ (C-9), 153.9 \text{ (C-1′), 159.8 \text{ (C-2), 181.3 \text{ (q, } J_{C-F} = 37.0 \text{ Hz, C}=O)}, 19^\text{F} \ \text{NMR} \) (282.4 MHz, CDCl\textsubscript{3}): \( \delta = -72.6 \text{ (s, CF}_3)); \) \( \text{GC-MS (EI, 70eV): } m/z \text{ (%) = 459 (M}^+ \text{, 33.59), 441 (56.10), 332 (50.18), 263 (100), 235 (46.23), 178 (13.51), 76 (15.79); HRMS (ESI): calcd for C\textsubscript{17}H\textsubscript{9}F\textsubscript{3}INO\textsubscript{3} (M+H) 460.0456, found 460.0459; IR (ATR, cm⁻¹): \( P = 3102 \text{ (w), 2923 \text{ (w), 1743 \text{ (s), 1608 \text{ (s), 1597 \text{ (s), 1552 \text{ (s), 1494 \text{ (m), 1471 \text{ (m), 1437 \text{ (s), 1336 \text{ (w), 1318 \text{ (w), 1287 \text{ (w), 1239 \text{ (w), 1212 \text{ (m), 1152 \text{ (s), 1067 \text{ (w), 1016 \text{ (w), 981 \text{ (m), 904 \text{ (w), 863 \text{ (w), 804 \text{ (m), 759 \text{ (s), 719 \text{ (s), 645 \text{ (m), 610 \text{ (m); Anal. Calcd. for C}_{17}H_9F_3NO_3: C, 44.47; H, 1.98; N, 3.05. Found: C, 44.68; H, 1.89; N, 2.80.}

4-(3-Fluorophenylamino)-3-(2,2,2-trifluoroacetyl)-2\textit{H}-chromen-2-one (19g):

Starting with \textit{17a} (300 mg, 1.08 mmol), aniline (0.103 mL, 1.08 mmol), \textit{19g} was obtained as a yellow solid (270 mg, 71\%), mp. 154–156 °C; \(^1\text{H} \ \text{NMR} \) (300 MHz, CDCl\textsubscript{3}): \( \delta = 6.83-6.89 \text{ (m, 1H)}, 6.93 \text{ (dt, } J = 9.0, 1.26 \text{ Hz, 1H)}, 6.97-7.01 \text{ (m, 1H)}, 7.04-7.13 \text{ (m, 2H)}, 7.23 \text{ (dd, } J = 8.43, 1.11 \text{ Hz, 1H}), 7.33-7.41 \text{ (m, 1H)}, 7.45-7.50 \text{ (m, 1H)}, 7.94 \text{ (dd, } J = 7.95, 1.32 \text{ Hz, 1H)}, 12.70 \text{ (s, NH)}; \( ^{13} \text{C} \ \text{NMR} \) (75.4MHz, CDCl\textsubscript{3}): \( \delta = 94.6 \text{ (C-2′), 95.1 \text{ (C-3), 111.5 \text{ (C-10), 115.9 \text{ (q, } J_{C-F} = 288.3 \text{ Hz, CF}_3), 117.4 \text{ (C-8), 122.5 \text{ (C-6′), 126.0 \text{ (C-4′), 126.3 \text{ (C-5), 128.8 \text{ (C-6), 128.9 \text{ (C-7), 134.4 \text{ (C-3′), 139.5 \text{ (C-4), 140.1 \text{ (C-9), 153.9 \text{ (C-1′), 159.8 \text{ (C-2), 181.3 \text{ (q, } J_{C-F} = 37.0 \text{ Hz, C}=O)}, 19^\text{F} \ \text{NMR} \) (282.4 MHz, CDCl\textsubscript{3}): \( \delta = -72.6 \text{ (s, CF}_3)); \) \( \text{GC-MS (EI, 70eV): } m/z \text{ (%) = 459 (M}^+ \text{, 33.59), 441 (56.10), 332 (50.18), 263 (100), 235 (46.23), 178 (13.51), 76 (15.79); HRMS (ESI): calcd for C\textsubscript{17}H\textsubscript{9}F\textsubscript{4}NO\textsubscript{3} (M+H) 461.0465, found 461.0459; IR (ATR, cm⁻¹): \( P = 3102 \text{ (w), 2923 \text{ (w), 1743 \text{ (s), 1608 \text{ (s), 1597 \text{ (s), 1552 \text{ (s), 1494 \text{ (m), 1471 \text{ (m), 1437 \text{ (s), 1336 \text{ (w), 1318 \text{ (w), 1287 \text{ (w), 1239 \text{ (w), 1212 \text{ (m), 1152 \text{ (s), 1067 \text{ (w), 1016 \text{ (w), 981 \text{ (m), 904 \text{ (w), 863 \text{ (w), 804 \text{ (m), 759 \text{ (s), 719 \text{ (s), 645 \text{ (m), 610 \text{ (m); Anal. Calcd. for C}_{17}H_9F_3NO_3: C, 44.47; H, 1.98; N, 3.05. Found: C, 44.68; H, 1.89; N, 2.80.}
1H), 7.46-7.52 (m, 1H), 12.71 (s, NH); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)):\ \(\delta = 96.3\) (C-3), 112.1 (C-10), 112.8 (d, \(^2\)J\(_{C\text{-}F}\) = 23.8 Hz, C-4’), 115.6 (d, \(^2\)J\(_{C\text{-}F}\) = 20.9 Hz, C-2’), 116.9 (q, \(^1\)J\(_{C\text{-}F}\) = 288.1 Hz, CF\(_3\)), 118.4 (C-8), 121.4 (d, \(^4\)J\(_{C\text{-}F}\) = 3.3 Hz, C-6’), 123.3 (C-5), 127.9 (C-6), 131.6 (d, \(^3\)J\(_{C\text{-}F}\) = 9.9 Hz, C-5’), 135.5 (C-7), 139.9 (d, \(^3\)J\(_{C\text{-}F}\) = 9.5 Hz, C-1’), 155.1 (C-4), 157.9 (C-9), 160.9 (C-2), 163.3 (d, \(^4\)J\(_{C\text{-}F}\) = 249 Hz, C-3’), 182.3 (q, \(^2\)J\(_{C\text{-}F}\) = 37.10 Hz, C=O); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)):\ \(\delta = -72.7\) (s, CF\(_3\)), -108.7 (s, CF).

GC-MS (EI, 70eV): m/z (%): 351 (M\(^+\), 22.43), 333 (18.75), 305 (9.95), 282 (100), 254 (24.57), 214 (11.14), 183 (10.15), 95 (13.82); HRMS (ESI): calcd for C\(_{17}\)H\(_9\)F\(_4\)NO\(_3\) (M+H): 352.0591, found: 352.0589; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3259\) (w), 3076 (w), 1668 (s), 1593 (m), 1544 (m), 1513 (s), 1488 (s), 1438 (m), 1378 (m), 1323 (w), 1260 (w), 1219 (m), 1196 (w), 1147 (s), 1048 (w), 997 (m), 948 (m), 907 (w), 881 (w), 840 (w), 783 (m), 758 (s), 746 (s), 726 (m), 704 (m), 673 (m), 618 (w); Anal. Calcd. for C\(_{17}\)H\(_9\)F\(_4\)NO\(_3\): C, 58.13; H, 2.58; N, 3.99. Found: C, 58.50; H, 2.64; N, 3.78.

4-(3,4-Dimethoxyphenylamino)-3-(2,2,2-trifluoroacetyl)-2\(^{\text{H}}\)chromen-2-one (19h):

Starting with \(17a\) (300 mg, 1.08 mmol), aniline (165 mg, 1.08 mmol), \(19h\) was obtained as a yellow solid (300 mg, 70%), mp. 166–168 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)):\ \(\delta = 3.76\) (s, OCH\(_3\)), 3.87 (s, OCH\(_3\)), 6.9 (d, \(^4\)J = 2.34 Hz, 1H), 6.74-6.86 (m, 3H), 7.14 (dd, \(^3\)J\(_{C\text{-}H}\) = 8.43, 1.35 Hz, 1H), 7.20-7.22 (m, 1H), 7.42-7.48 (m, 1H), 12.86 (s, NH); \(^{13}\)C NMR (62.9 MHz, CDCl\(_3\)):\ \(\delta = 56.1\) (OCH\(_3\)), 56.2 (OCH\(_3\)), 95.1 (C-2’), 108.7 (C-3), 111.8 (C-6’), 112.4 (C-5’), 116.9 (q, \(^1\)J\(_{C\text{-}F}\) = 287.7 Hz, CF\(_3\)), 117.5 (C-10), 118.3 (C-8), 123.1 (C-5), 127.9 (C-6), 130.9 (C-7), 135.1 (C-1’), 149.2 (C-4’), 150.2 (C-4), 154.9 (C-3’), 158.2 (C-9), 160.8 (C-2), 181.9 (q, \(^2\)J\(_{C\text{-}F}\) = 36.82 Hz, C=O); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)):\ \(\delta = -72.6\) (s, CF\(_3\)). GC-MS (EI, 70eV): m/z (%): 393 (M\(^+\), 0.01), 375 (100), 332 (19.87), 261 (10.20); HRMS (ESI): calcd for C\(_{19}\)H\(_{14}\)F\(_3\)NO\(_5\) (M+H): 394.0897, found 394.0904; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3090\) (w), 2992 (w), 1727 (s), 1601 (s), 1557 (m), 1514 (m), 1462 (s), 1442 (s), 1421 (w), 1337 (w), 1265 (w), 1240 (m), 1213 (m), 1152 (s), 1077 (w), 1036 (w), 1023 (m), 995 (m), 955 (m), 896 (w), 874 (m), 809 (m), 755 (s), 725 (s), 671 (w), 607 (w); Anal. Calcd. for C\(_{19}\)H\(_{14}\)F\(_3\)NO\(_5\): C, 58.02; H, 3.59; N, 3.56. Found: C, 57.72; H, 3.48; N, 3.34.
4-(3-Nitrophenylamino)-3-(2,2,2-trifluoroacetyl)-2H-chromen-2-one (19i): Starting with 17a (300 mg, 1.08 mmol), aniline (149 mg, 1.08 mmol), 19i was obtained as a yellow solid (260 mg, 63%), mp. 168–170 °C; ¹H NMR (300 MHz, CDCl₃): δ = 6.87-6.90 (m, 1H), 7.06 (dd, ³J = 8.43, 1.38 Hz, 1H), 7.28 (dd, ³J = 8.43, 1.05 Hz, 1H), 7.50-7.63 (m, 3H), 8.06-8.07 (m, 1H), 8.17-8.20 (m, 1H), 12.70 (s, NH); ¹³C NMR (75.4 MHz, CDCl₃): δ = 97.5 (C-3), 111.8 (C-2’), 116.8 (q, ¹JCF = 287.5 Hz, CF₃), 118.8 (C-4’), 119.9 (C-10), 122.8 (C-8), 123.5 (C-6’), 127.5 (C-5), 130.8 (C-6), 131.2 (C-7), 135.9 (C-5’), 140.1 (C-1’), 149.2 (C-3’), 155.2 (C-4), 157.7 (C-9), 160.8 (C-2), 182.6 (q, ²JCF = 37.6 Hz, C=O); ¹⁹F NMR (282.4 MHz, CDCl₃): δ = -72.8 (s, CF₃). GC-MS (EI, 70eV): m/z (%) = 378 (M⁺, 45.28), 309 (93.97), 263 (100), 235 (37.69), 195 (17.05), 176 (18.80); HRMS (ESI): calcd for C₁₇H₉F₃N₂O₅ (M+H) 379.0536, found 379.0539; IR (ATR, cm⁻¹): ν = 3306 (w), 3090 (w), 1725 (m), 1599 (s), 1563 (w), 1557 (w), 1527 (s), 1462 (w), 1444 (w), 1351 (s), 1301 (w), 1277 (w), 1241 (m), 1212 (m), 1152 (s), 1075 (w), 1044 (w), 987 (m), 936 (w), 886 (w), 835 (w), 807 (m), 763 (m), 714 (m), 666 (m), 612 (w); Anal. Calcd. for C₁₇H₉F₃N₂O₅: C, 53.98; H, 2.40; N, 7.41. Found: C, 53.75; H, 2.48; N, 6.89.

4-(4-(Diethylamino)phenylamino)-3-(2,2,2-trifluoroacetyl)-2H-chromen-2-one (19j): Starting with 17a (300 mg, 1.08 mmol), aniline (0.179 mL, 1.08 mmol), 19j was obtained as a red solid (350 mg, 85%), mp. 154–155 °C; ¹H NMR (300 MHz, CDCl₃): δ = 1.13 (t, ³J = 7.1 Hz, 2CH₃), 3.32 (q, ³J = 7.1 Hz, 2CH₂), 6.59 (d, ³J = 8.9 Hz, 2H), 6.80-6.86 (m, 1H), 6.95 (d, ³J = 8.9 Hz, 2H), 7.18 (dd, ³J = 8.4, 1.4 Hz, 1H), 7.30 (dd, ³J = 8.4, 1.4 Hz, 1H), 7.39-7.44 (m, 1H), 12.86 (s, NH); ¹³C NMR (75.4 MHz, CDCl₃): δ = 12.4 (CH₃×2), 44.5 (CH₂×2), 94.6 (C-3), 112.2 (C-3’,5’), 112.9 (C-10), 117.2 (q, ¹JCF = 287.0 Hz, CF₃), 118.1 (C-8), 123.0 (C-2’,6’), 125.4 (C-5), 126.1 (C-6), 128.1 (C-1’), 134.8 (C-7), 147.7 (C-4’), 154.9 (C-4), 158.5
(C-9), 160.3 (C-2), 181.4 (q, $^2J_{C\text{-}F} = 36.4$ Hz, C=O); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta = -72.5$ (s, CF$_3$). GC-MS (EI, 70eV): $m/z$ (%) = 404 (M$^+$, 56.92), 389 (100), 371 (11.54), 291 (15.37); HRMS (ESI): calcd for C$_{21}$H$_{19}$F$_3$N$_2$O$_3$ (M+H) 405.1421, found 405.1421; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 3119$ (w), 2968 (w), 1740 (m), 1598 (s), 1564 (m), 1519 (m), 1463 (m), 1403 (w), 1349 (m), 1276 (m), 1238 (m), 1214 (m), 1153 (s), 1093 (w), 1079 (w), 1048 (w), 982 (m), 936 (w), 905 (w), 851 (w), 818 (m), 785 (w), 760 (s), 723 (s), 665 (m), 597 (m); Anal. Calcd. for C$_{21}$H$_{19}$F$_3$N$_2$O$_3$: C, 62.37; H, 4.74; N, 6.93. Found: C, 62.38; H, 4.74; N, 6.62.

**General procedure for the synthesis of compounds (20a-j):**

The intermediate 19a-j (0.5 mmol) was heated at 70 $^\circ$C for 2 h in conc. H$_2$SO$_4$ under inert atmosphere. Then reaction mixture was poured onto cooled water and the precipitate formed was filtered off, washed with dilute sodium carbonate solution, then water and finally dried. The product was purified by column chromatography. The products were obtained in excellent yield (85-95%).

**Note:** Compound 20k and 20l were formed directly on the first step in DMF/TMSCl at 120 $^\circ$C.

**9-Fluoro-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20a):**

Starting with 19a (175 mg, 0.5 mmol), 20a was obtained as a yellow solid (150 mg, 90%), mp. 202–203 $^\circ$C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 7.27$-7.37 (m, 2H), 7.50-7.56 (m, 1H), 7.63-7.69 (m, 1H), 7.92-7.97 (m, 1H), 8.21 (dd, $^1J_{C\text{-}F} = 9.35$, 5.73 Hz, 1H), 8.63 (dd, $J = 7.92$, 1.64 Hz, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta = 108.5$ (d, $^2J_{C\text{-}F} = 25.0$ Hz, C-8), 108.9 (C-1’), 114.1 (C-4), 115.9 (C-6’), 117.4 (C-2), 121.7 (q, $^1J_{C\text{-}F} = 278.17$ Hz, CF$_3$), 123.2 (d, $^2J_{C\text{-}F} = 26.82$ Hz, C-10), 123.5 (C-3), 123.9 (C-3’), 124.5 (C-1), 131.9 (d, $^3J_{C\text{-}F} = 9.53$ Hz, C-11), 132.0 (C-5’), 137.8 (q, $^2J_{C\text{-}F} = 32.69$ Hz, C-7), 148.2 (C-2’), 151.2 (C-4’), 156.3 (C-6), 160.3 (d, $^1J_{C\text{-}F} = 253.2$ Hz, C-9); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta = -53.9$ (s, CF$_3$), -106.9 (s, CF). GC-MS (EI, 70eV): $m/z$ (%) = 333 (M$^+$, 100), 305 (38.95), 286 (21.19); HRMS (ESI): calcd for C$_{17}$H$_7$F$_4$NO$_2$ (M+H) 334.0486, found 334.0488; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 3089$ (w), 1742 (s), 1625 (m), 1608 (w), 1593 (m), 1573 (m), 1551 (m), 1495 (m), 1462 (s), 86
1400 (w), 1367 (s), 1289 (m), 1228 (m), 1209 (s), 1183 (s), 1142 (s), 1034 (m), 1000 (m), 980 (w), 958 (w), 902 (w), 863 (m), 838 (s), 810 (m), 771 (s), 751 (s), 715 (s), 686 (m), 645 (m), 631 (m), 619 (m); Anal. Calcd. for C_{17}H_{2}F_{4}NO_{2}: C, 61.27; H, 2.12; N, 4.20. Found: C, 61.53; H, 1.98; N, 3.93.

9-Methoxy-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20b):

Starting with 19b (181 mg, 0.5 mmol), 20b was obtained as a yellow solid (155 mg, 90%), mp. 248–249 °C; \(^{1}\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 3.90 \) (s, OCH\(_3\)), 7.30-7.36 (m, 2H), 7.47-7.54 (m, 3H), 8.08 (d, \(^{3}\)J = 9.24 Hz, 1H), 8.63 (dd, \(^{3,4}\)J = 7.92, 1.59 Hz, 1H); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 54.8 \) (OCH\(_3\)), 101.6 (C-8), 113.6 (C-1\(^{1}\)), 115.7 (C-4), 117.8 (C-10), 122.3 (q, \(^{1}\)J\(_{C-F}\) = 277.43 Hz, CF\(_3\)), 123.8 (C-6\(^{1}\)), 124.2 (C-2), 124.5 (C-3), 126.3 (C-3\(^{2}\)), 130.7 (C-1), 131.3 (C-11), 134.7 (q, \(^{2}\)J\(_{C-F}\) = 32.55 Hz, C-7), 146.4 (C-5\(^{1}\)), 147.4 (C-2\(^{1}\)), 150.9 (C-4\(^{1}\)), 156.8 (C-6), 158.2 (C-9); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta = -53.9 \) (s, 3F, CF\(_3\)); GC-MS (EI, 70eV): \(m/z \) (%) = 345 (M\(^{+}\), 100), 302 (41.65), 274 (15.04); HRMS (ESI): calcd for C\(_{18}\)H\(_{10}\)F\(_{3}\)NO\(_{3}\) (M+H) 346.0686, found 346.0686; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3077 \) (w), 1738 (s), 1622 (s), 1567 (w), 1550 (w), 1496 (m), 1469 (m), 1455 (m), 1417 (s), 1366 (s), 1296 (w), 1261 (w), 1222 (m), 1173 (m), 1151 (s), 1126 (s), 1023 (m), 996 (m), 972 (m), 902 (w), 856 (w), 833 (s), 808 (w), 776 (w), 759 (s), 750 (s), 715 (m), 686 (m), 635 (m), 620 (m); Anal. Calcd. for C\(_{18}\)H\(_{10}\)F\(_{3}\)NO\(_{3}\): C, 62.62; H, 2.92; N, 4.06. Found: C, 62.50; H, 2.80; N, 3.81.

9-Ethyl-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20c):

Starting with 19c (180 mg, 0.5 mmol), 20c was obtained as a yellow solid (153 mg, 90%), mp. 212–213 °C; \(^{1}\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 1.30 \) (t, \(^{3}\)J = 7.56 Hz, CH\(_3\)), 2.83 (q, \(^{3}\)J = 7.56 Hz, CH\(_2\)), 7.25-7.35 (m, 2H), 7.47-7.53 (m, 1H), 7.72 (d, \(^{3}\)J = 8.76 Hz, 1H), 8.05-8.10 (m, 2H), 8.64 (d, \(^{3}\)J = 7.89 Hz, 1H); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 15.0 \) (CH\(_3\)), 29.5 (CH\(_2\)), 114.3 (C-1\(^{1}\)), 116.8 (C-4), 118.8 (C-8), 123.1 (q, \(^{1}\)J\(_{C-F}\) = 278.2 Hz, CF\(_3\)), 87
123.2 (C-6'), 124.2 (C-2), 124.8 (C-3), 125.5 (C-3'), 130.1 (C-11), 132.6 (C-1), 134.7 (C-10), 137.7 (q, $^J_{\text{C-F}} = 32.9$ Hz, C-7), 145.1 (C-9), 148.8 (C-5'), 150.5 (C-2'), 152.2 (C-4'), 157.7 (C-6); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta = -53.3$ (s, CF$_3$). GC-MS (EI, 70eV): $m/z$ (%) = 343 (M$^+$, 95.65), 328 (100), 300 (7.14); HRMS (ESI): calcd for $C_{19}H_{12}F_3NO_2 (M+H)$ 344.0893, found 344.0895; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 2972$ (w), 1754 (s), 1622 (w), 1611 (w), 1594 (m), 1547 (m), 1486 (w), 1460 (s), 1360 (s), 1324 (w), 1290 (w), 1228 (m), 1176 (m), 1153 (s), 1133 (s), 1032 (m), 1000 (m), 951 (w), 902 (m), 838 (s), 789 (w), 753 (s), 714 (s), 684 (m), 651 (w), 634 (m), 617 (m); Anal. Calcd. for $C_{19}H_{12}F_3NO_2$: C, 66.47; H, 3.52; N, 4.08. Found: C, 66.14; H, 3.19; N, 3.77.

9-Nitro-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20d):  

![Chemical Structure of 9-Nitro-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20d)](image)

Starting with 19d (189 mg, 0.5 mmol), 20d was obtained as a yellow solid (153 mg, 85%), mp. 275–276 °C; $^1$H NMR (300 MHz, DMSO): $\delta = 7.53-7.59$ (m, 2H), 7.79-7.84 (m, 1H), 8.54 (d, $^3J = 9.31$ Hz, 1H), 8.72-8.79 (m, 2H), 9.16-9.17 (m, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta = 115.1$ (C-8), 116.2 (C-1'), 117.0 (C-4), 117.4 (C-6'), 122.0 (C-10), 122.1 (q, $^1J_{\text{C-F}} = 278.4$ Hz, CF$_3$), 123.2 (C-2), 124.4 (C-3), 125.2 (C-3'), 125.3 (C-1), 131.1 (C-11), 133.4 (C-5'), 136.8 (C-9), 138.2 (q, $^2J_{\text{C-F}} = 33.5$ Hz, C-7), 147.2 (C-2'), 151.9 (C-4'), 155.5 (C-6'); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta = -52.5$ (s, CF3); GC-MS (EI, 70eV): $m/z$ (%) = 351 (M$^+$, 40.29), 333 (25.94), 305 (10.16), 282 (100), 254 (11.13), 214 (12.44), 183 (7.08), 95 (12.28), 75 (6.11); HRMS (ESI): calcd for $C_{17}H_{7}F_3N_2O_4 (M+H)$ 361.0182, found 361.0189; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 3141$ (w), 2921 (m), 1761 (s), 1623 (m), 1607 (m), 1593 (m), 1555 (s), 1533 (s), 1484 (w), 1459 (s), 1362 (m), 1340 (s), 1285 (m), 1226 (m), 1199 (m), 1174 (s), 1142 (s), 1095 (m), 1031 (m), 998 (m), 965 (m), 895 (m), 853 (s), 834 (w), 802 (w), 768 (s), 735 (s), 715 (s), 670 (w), 641 (m), 618 (m); Anal. Calcd. for $C_{17}H_{7}F_3N_2O_4$: C, 56.68; H, 1.96; N, 7.78. Found: C, 59.38; H, 2.82; N, 6.27.
9-Chloro-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20e):

![Chemical formula for 9-Chloro-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20e).]

Starting with 19e (183 mg, 0.5 mmol), 20e was obtained as a yellow solid (155 mg, 89%), mp. 226–227 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 7.29$ (d, $^3J = 8.28$ Hz, 1H), 7.33-7.38 (m, 1H), 7.52-7.58 (m, 1H), 7.80 (dd, $^{3,4}J = 9.09$, 2.16 Hz, 1H), 8.15 (d, $^3J = 9.09$ Hz, 1H), 8.30-8.31 (m, 1H), 8.65 (dd, $^{3,4}J = 7.95$, 1.53 Hz, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta = 114.21$ (C-1'), 115.9 (C-4), 117.3 (C-8), 121.6 (q, $^1J_{C-F} = 278.37$ Hz, CF$_3$), 123.3 (C-6'), 123.7 (C-2), 124.0 (C-3), 124.7 (C-3'), 130.7 (C-1), 132.2 (C-11), 133.2 (C-10), 134.2 (C-9), 137.0 (q, $^2J_{C-F} = 33.53$ Hz, C-7), 148.7 (C-5'), 148.8 (C-2'), 151.4 (C-4'), 156.2 (C-6); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta = -53.5$ (s, CF$_3$); GC-MS (EI, 70eV): $m/z$ (%) = 351 (M$^+$, 37Cl, 34.90), 349 (M$^+$, 37Cl, 100), 321 (29.08), 302 (15.78), 286 (7.17); HRMS (ESI): calcd for C$_{17}$H$_7$ClF$_3$NO$_2$ (M+H) 350.019, found 350.0189; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 3114$ (w), 3078 (w), 1742 (s), 1610 (m), 1564 (s), 1544 (m), 1480 (m), 1460 (s), 1390 (w), 1360 (s), 1350 (s), 1285 (m), 1249 (w), 1227 (m), 1170 (s), 1157 (s), 1131 (s), 1083 (m), 1033 (m), 998 (m), 958 (w), 903 (w), 840 (s), 815 (m), 765 (m), 755 (s), 714 (s), 676 (m), 641 (m), 615 (m); Anal. Calcd. for C$_{17}$H$_7$ClF$_3$NO$_2$: C, 58.39; H, 2.02; N, 4.01. Found: C, 57.85; H, 1.70; N, 3.73.

11-Iodo-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20f):

![Chemical formula for 11-Iodo-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20f).]

Starting with 19f (229 mg, 0.5 mmol), 20f was obtained as a yellow solid (179 mg, 89%), mp. 221–222 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 7.25-7.38$ (m, 3H), 7.51-7.56 (m, 1H), 8.27-8.31 (m, 1H), 8.46 (dd, $^{3,4}J = 7.30$, 1.02 Hz, 1H), 8.74 (dd, $^{3,4}J = 7.95$, 1.61 Hz, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta = 104.3$ (C-11), 115.2 (C-1'), 116.9 (C-4), 118.4 (C-2), 122.6 (q, $^1J_{C-F} = 278.7$ Hz, CF$_3$), 124.4 (C-6'), 125.2 (C-3), 126.4 (C-8), 126.5 (C-3'), 129.4 (C-1), 133.4 (C-9), 139.3 (q, $^2J_{C-F} = 33.3$ Hz, C-7), 143.7 (C-10), 149.3 (C-5'), 150.3 (C-2'), 152.5 (C-4'), 157.1 (C-6); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta = -53.1$ (s, CF$_3$); GC-MS (EI, 70eV): $m/z$ (%) = 441 (M$^+$, 100), 413 (6.09), 394 (7.50), 286 (12.08); HRMS (ESI): calcd for C$_{17}$H$_7$F$_3$INO$_2$ (M+H) 441.9546, found 441.9545; IR (ATR, cm$^{-1}$): $\tilde{\nu}$
= 3099 (w), 3065 (w), 1750 (m), 1732 (s), 1611 (m), 1563 (m), 1538 (m), 1483 (m), 1461 (s), 1352 (s), 1282 (m), 1226 (s), 1206 (m), 1184 (w), 1127 (s), 1031 (m), 1003 (m), 962 (w), 931 (m), 896 (m), 849 (m), 809 (w), 787 (m), 763 (s), 725 (m), 706 (m), 675 (s), 650 (m), 613 (m); Anal. Calcd. for C_{17}H_{7}F_{3}INO_{2}: C, 46.28; H, 1.60; N, 3.18. Found: C, 45.72; H, 1.51; N, 2.89.

10-Fluoro-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20g-1):

Starting with 19g (175 mg, 0.5 mmol), 20g-1 was obtained as a yellow solid (0.100g, 60%), mp. 225–227 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 7.27-7.46\) (m, 3H), 7.52-7.58 (m, 1H), 7.80 (dd, \(J = 9.19, 2.68\) Hz, 1H), 8.32-8.38 (m, 1H), 8.64 (dd, \(J = 7.95, 1.52\) Hz, 1H); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 112.5\) (d, \(J_{C,F} = 20.38\) Hz, C-11), 115.9 (C-1'), 117.3 (C-6'), 118.7 (d, \(J_{C,F} = 26.0\) Hz, C-9), 120.1 (C-4), 121.8 (q, \(J_{C,F} = 278.49\) Hz, CF\(_3\)), 123.9 (C-2), 124.7 (C-3), 127.6 (d, \(J_{C,F} = 9.76\) Hz, C-8), 132.3 (C-3'), 137.8 (q, \(J_{C,F} = 32.69\) Hz, C-7), 149.7 (C-1), 151.5 (C-5'), 151.9 (C-2'), 152.1 (C-4'), 156.3 (C-6'), 163.9 (d, \(J_{C,F} = 259.15\) Hz, C-10); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta = -53.2\) (s, CF\(_3\)), -102.2 (s, CF). GC-MS (EI, 70eV): \(m/z\) (%) = 333 (M\(^+\), 100), 305 (45.46), 286 (16.33); HRMS (ESI): calcd for C_{17}H_{7}F_{4}NO_{2} (M+H) 334.0486, found 334.0483; IR (ATR, cm\(^{-1}\)): \(\nu = 3144\) (w), 2923 (w), 1749 (s), 1625 (m), 1611 (m), 1594 (m), 1562 (m), 1503 (m), 1466 (m), 1437 (w), 1417 (w), 1362 (s), 1313 (w), 1279 (w), 1260 (w), 1220 (m), 1198 (m), 1166 (s), 1151 (s), 1131 (s), 1032 (m), 999(m), 969 (m), 958 (m), 916 (w), 867 (s), 816 (w), 795 (s), 759 (s), 717(m), 669 (w), 645 (m), 614 (m); Anal. Calcd. for C_{17}H_{7}F_{4}NO_{2}: C, 61.27; H, 2.12; N, 4.20. Found: C, 60.00; H, 2.37; N, 3.83.

8-Fluoro-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20g-2):

Starting with 19g (175 mg, 0.5 mmol), 20g-2 was obtained as a yellow solid (50 mg, 30%), mp. 205–207 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 7.25-7.35\) (m, 3H), 7.50-7.56 (m, 1H), 7.75-7.82 (m, 1H), 7.98 (d, \(J = 8.43\) Hz, 1H), 8.61 (dd, \(J = 7.93, 1.56\) Hz, 1H); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 113.0\) (d, \(J_{C,F} = 23.54\) Hz, C-11), 115.9 (C-1'), 117.3 (C-6'), 118.7 (d, \(J_{C,F} = 26.0\) Hz, C-9), 120.1 (C-4), 121.8 (q, \(J_{C,F} = 278.49\) Hz, CF\(_3\)), 123.9 (C-2), 124.7 (C-3), 127.6 (d, \(J_{C,F} = 9.76\) Hz, C-8), 132.3 (C-3'), 137.8 (q, \(J_{C,F} = 32.69\) Hz, C-7), 149.7 (C-1), 151.5 (C-5'), 151.9 (C-2'), 152.1 (C-4'), 156.3 (C-6'), 163.9 (d, \(J_{C,F} = 259.15\) Hz, C-10); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta = -53.2\) (s, CF\(_3\)), -102.2 (s, CF). GC-MS (EI, 70eV): \(m/z\) (%) = 333 (M\(^+\), 100), 305 (45.46), 286 (16.33); HRMS (ESI): calcd for C_{17}H_{7}F_{4}NO_{2} (M+H) 334.0486, found 334.0483; IR (ATR, cm\(^{-1}\)): \(\nu = 3144\) (w), 2923 (w), 1749 (s), 1625 (m), 1611 (m), 1594 (m), 1562 (m), 1503 (m), 1466 (m), 1437 (w), 1417 (w), 1362 (s), 1313 (w), 1279 (w), 1260 (w), 1220 (m), 1198 (m), 1166 (s), 1151 (s), 1131 (s), 1032 (m), 999(m), 969 (m), 958 (m), 916 (w), 867 (s), 816 (w), 795 (s), 759 (s), 717(m), 669 (w), 645 (m), 614 (m); Anal. Calcd. for C_{17}H_{7}F_{4}NO_{2}: C, 61.27; H, 2.12; N, 4.20. Found: C, 60.00; H, 2.37; N, 3.83.
Hz, C-9), 114.3 (C-6'), 115.1 (C-1'), 116.0 (C-4), 117.1 (C-2), 120.8 (q, \(^1J_{C-F} = 277.72\) Hz, CF\(_3\)), 124.0 (C-3), 124.8 (C-3'), 125.0 (d, \(^4J_{C-F} = 4.29\) Hz, C-11), 131.9 (d, \(^3J_{C-F} = 9.76\) Hz, C-10), 132.4 (C-1), 136.5 (q, \(^2J_{C-F} = 33.0\) Hz, C-7), 149.2 (C-5'), 150.8 (C-2'), 151.5 (C-4'), 155.8 (d, \(^1J_{C-F} = 262.64\) Hz, C-8), 156.2 (C-6); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta = -55.7\) (s, CF\(_3\)), -102.9; GC-MS (EI, 70eV): \(m/z\) (%) = 333 (M\(^{+}\), 100), 314 (10.44), 305 (20.67), 286 (65.58); HRMS (ESI): calcld for C\(_{17}\)H\(_7\)F\(_4\)NO\(_2\) (M) 333.04074, found 334.040717; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3489\) (w), 2923 (w), 1749 (s), 1611 (m), 1592 (m), 1553 (s), 1492 (m), 1459 (s), 1361 (s), 1345 (s), 1283 (w), 1246 (w), 1212 (s), 1149 (s), 1075 (m), 1046 (m), 996 (w), 961 (s), 919 (w), 892 (s), 868 (w), 825 (s), 797 (s), 746 (s), 712 (s), 679 (m), 649 (w), 621 (m); Anal. Calcd. for C\(_{17}\)H\(_7\)F\(_4\)NO\(_2\): C, 61.27; H, 2.12; N, 4.20. Found: C, 61.88; H, 2.02; N, 3.92.

8,9-Dimethoxy-7-(trifluoromethyl)-6\(H\)-chromeno[4,3-\(b\)]quinolin-6-one (20h):

Starting with 19h (196 mg, 0.5 mmol), 20h was obtained as a yellow solid (160 mg, 85%), mp. 283–285 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 4.00\) (s, OCH\(_3\)), 4.07 (s, OCH\(_3\)), 7.25-7.34 (m, 2H), 7.43-7.52 (m, 3H), 8.59 (dd, \(^3J = 7.9, 1.5\) Hz, 1H); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 55.2\) (OCH\(_3\)), 55.6 (OCH\(_3\)), 101.8 (C-6'), 106.8 (C-1'), 115.7 (C-4), 117.8 (C-11), 119.9 (C-10), 122.4 (q, \(^1J_{C-F} = 277.75\) Hz, CF\(_3\)), 123.6 (C-2), 124.1 (C-3), 127.9 (C-3'), 131.1 (C-1), 133.9 (q, \(^2J_{C-F} = 32.80\) Hz, C-7), 147.1 (C-5'), 149.3 (C-9), 150.6 (C-2'), 151.1 (C-8), 154.8 (C-4'), 156.9 (C-6); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta = -75.8\) (s, CF\(_3\)); GC-MS (EI, 70eV): \(m/z\) (%) = 375 (M\(^{+}\), 100), 332 (19.85), 261 (9.40). HRMS (ESI): calcld for C\(_{19}\)H\(_{12}\)F\(_3\)NO\(_4\) (M+H) 376.0791, found 376.0793; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 2919\) (s), 2850 (m), 1742 (s), 1621 (w), 1596 (w), 1546 (w), 1495 (s), 1454 (s), 1431 (m), 1414 (s), 1372 (m), 1358 (m), 1303 (w), 1278 (w), 1244 (m), 1221 (m), 1202 (w), 1184 (w), 1171 (w), 1135 (s), 1101 (m), 1010 (m), 987(s), 929 (w), 884 (w), 851 (s), 808 (m), 764 (s), 720 (m), 698 (w), 657 (w), 637(m); Anal. Calcd. for C\(_{19}\)H\(_{12}\)F\(_3\)NO\(_4\): C, 60.81; H, 3.22; N, 3.73. Found: C, 62.81; H, 4.66; N, 2.95.
10-Nitro-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20i-1):

Starting with 19i (189 mg, 0.5 mmol), 20i-1 was obtained as a yellow solid (100 mg, 55%), mp. 261–263 °C; ^1^H NMR (300 MHz, CDCl$_3$): δ = 7.34 (dd, $^{3,4}J = 8.38$, 0.94 Hz, 1H), 7.39-7.44 (m, 1H), 7.59-7.65 (m, 1H), 7.34 (dd, $^{3,4}J = 9.62$, 2.40 Hz, 1H), 8.51 (dq, $^{3,4}J = 9.54$, 1.95 Hz, 1H), 8.71 (dd, $^{3,4}J = 7.95$, 1.59 Hz, 1H), 9.07 (d, $^{4}J = 2.04$ Hz, 1H); ^13^C NMR (75.4 MHz, CDCl$_3$): δ = 115.2 (C-11), 116.1 (C-4), 116.8 (C-9), 119.5 (C-1’), 120.4 (q, $^{1}J_{C:F} = 278.02$ Hz, CF$_3$), 124.4 (C-2), 124.7 (C-6’), 124.9 (C-3), 127.1 (C-8), 127.2 (C-3’), 129.3 (C-1), 133.1 (C-5’), 138.4 (q, $^{2}J_{C:F} = 35.5$ Hz, C-7), 149.7 (C-2’), 150.8 (C-10), 151.6 (C-4’), 157.2 (C-6’); ^19^F NMR (282.4 MHz, CDCl$_3$): δ = -53.5 (s, CF$_3$); GC-MS (EI, 70eV): m/z (%) = 360 (M$^+$, 100), 314 (16.40), 286 (9.51), 270 (21.91), 258 (7.06), 214; HRMS (ESI): calcd for C$_{17}$H$_7$F$_3$N$_2$O$_4$ (M+H) 361.0431, found 361.0431; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3097 (w), 2923 (w), 1754 (s), 1613 (m), 1595 (m), 1565 (s), 1528 (s), 1491 (w), 1434 (w), 1411 (w), 1350 (s), 1210 (m), 1101 (s), 999 (s), 967 (w), 898 (m), 873 (m), 828 (m), 809 (m), 770 (s), 753 (m), 736 (m), 717 (m), 642 (m); Anal. Calcd. for C$_{17}$H$_7$F$_3$N$_2$O$_4$: C, 56.68; H, 1.96; N, 7.78. Found: C, 55.68; H, 2.91; N, 6.19.

8-Nitro-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20i-2):

Starting with 19i (189 mg, 0.5 mmol), 20i-2 was obtained as a yellow solid (54 mg, 30%), mp. 252–254 °C; ^1^H NMR (300 MHz, CDCl$_3$): δ = 7.34 (dd, $^{3,4}J = 8.30$, 0.75Hz, 1H), 7.37-7.42 (m, 1H), 7.59-7.65 (m, 1H), 7.87-7.92 (m, 1H), 8.24 (dd, $^{3,4}J = 7.44$, 1.17 Hz, 1H), 8.42 (dd, $^{3,4}J = 8.61$, 1.27 Hz, 1H), 8.70 (dd, $^{3,4}J = 8.07$, 1.58 Hz, 1H); ^13^C NMR (75.4 MHz, CDCl$_3$): δ = 115.4 (C-6’), 116.0 (C-4), 116.4 (C-9), 116.6 (C-1’), 120.9 (q, $^{1}J_{C:F} = 278.13$ Hz, CF$_3$), 124.3 (C-3), 125.1 (C-3’), 125.2 (C-1), 129.9 (C-11), 133.1 (C-10), 134.6 (C-9), 138.5 (q, $^{2}J_{C:F} = 35.73$ Hz, C-7), 147.1 (C-5’), 150.2 (C-8), 150.9 (C-2’), 151.6 (C-4’), 155.3 (C-6’); ^19^F NMR (282.4 MHz, CDCl$_3$): δ = -75.8 (s, CF$_3$); GC-MS (EI, 70eV): m/z (%) = 360 (M$^+$, 100), 314 (73.66), 291 (33.87), 286 (14.70), 86 (100).
257 (8.69), 238 (11.96), 208 (12.50); HRMS (ESI): calcd for C_{17}H_{2}F_{3}N_{2}O_{4} (M+H) 361.0431, found 361.0431; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3079\) (w), 1737 (s), 1610 (m), 1595 (m), 1537 (s), 1485 (m), 1455 (m), 1359 (s), 1340 (m), 1282 (m), 1259 (w), 1226 (s), 1158 (s), 1041 (m), 1021 (w), 997 (w), 959 (w), 919 (w), 883 (w), 872 (w), 832 (s), 803 (m), 752 (s), 718 (m), 684 (w), 670 (w), 617 (m); Anal. Calcd. for C_{17}H_{7}F_{3}N_{2}O_{4}:

C, 56.68; H, 1.96; N, 7.78. Found: C, 56.04; H, 1.88; N, 7.38.

9-(Diethylamino)-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20j):

Starting with 19j (202 mg, 0.5 mmol), 20j was obtained as a red solid (170 mg, 95%), mp. 153–155 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 1.19\) (t, \(3J = 7.10\) Hz, 2\(\times\)CH\(_3\)), 3.42 (q, \(3J = 7.10\) Hz, 2\(\times\)CH\(_2\)), 6.98-7.00 (m, 1H), 7.16-7.19 (m, 1H), 7.21-7.26 (m, 1H), 7.35-7.41 (m, 2H), 7.87 (d, \(3J = 9.60\) Hz, 1H), 8.48 (dd, \(3,4J = 7.90, 1.61\) Hz, 1H); \(^{13}\)C NMR (62.9 MHz, CDCl\(_3\)): \(\delta = 12.6\) (CH\(_3\)\(\times\)2), 44.9 (CH\(_2\)\(\times\)2), 100.0 (C-8), 114.6 (C-1'), 116.4 (C-4), 119.3 (C-11), 123.2 (C-2), 123.6 (q, \(1J_{C-F} = 277.4\) Hz, CF\(_3\)), 124.5 (C-6'), 124.7 (C-3), 126.6 (C-3'), 130.3 (C-10), 131.1 (C-1), 132.1 (q, \(2J_{C-F} = 32.2\) Hz, C-7), 144.3 (C-5'), 146.3 (C-2'), 146.7 (C-9), 151.4 (C-4'), 158.4 (C-6); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta = -54.6\) (s, CF\(_3\)); GC-MS (EI, 70eV): \(m/z\) (%) = 386 (M\(^+\), 43.47), 371 (100), 343 (17.13); HRMS (ESI): calcd for C\(_{21}\)H\(_{17}\)F\(_3\)N\(_2\)O\(_2\) (M+H) 387.1315, found 387.1319; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3075\) (w), 2975 (w), 1740 (s), 1615 (s), 1556 (w), 1505 (s), 1486 (m), 1466 (m), 1426 (m), 1353 (s), 1339 (s), 1260 (s), 1227 (m), 1180 (m), 1145 (s), 1033 (m), 993 (m), 973 (m), 905 (w), 887 (w), 852 (w), 838 (w), 822 (m), 788 (w), 750 (s), 714 (m), 644 (w), 621 (m); Anal. Calcd. for C\(_{21}\)H\(_{17}\)F\(_3\)N\(_2\)O\(_2\): C, 65.28; H, 4.43; N, 7.25. Found: C, 64.00; H, 4.44; N, 6.69.

10-Methoxy-7-(trifluoromethyl)-6H-chromeno[4,3-b]quinolin-6-one (20k):

Starting with 17a (300 mg, 1.08 mmol), aniline (133 mg, 0.121 mL, 1.08 mmol), 20k was obtained as a yellow solid (245 mg, 65%), mp. 202–204 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 3.97\) (s, OCH\(_3\)), 7.16-7.27 (m, 4H), 7.38-7.42 (m, 2H), 7.55 (d, \(3J = 8.90\) Hz, 1H), 7.90 (d, \(3J = 8.90\) Hz, 1H), 8.00 (dd, \(3,4J = 7.90, 1.61\) Hz, 1H); \(^{13}\)C NMR (62.9 MHz, CDCl\(_3\)): \(\delta = 19.4\) (CH\(_3\)O), 50.6 (CH\(_3\)), 100.0 (C-8), 114.6 (C-1'), 116.6 (C-4), 119.3 (C-11), 123.2 (C-2), 123.6 (q, \(1J_{C-F} = 277.4\) Hz, CF\(_3\)), 124.5 (C-6'), 124.7 (C-3), 126.6 (C-3'), 130.3 (C-10), 131.1 (C-1), 132.1 (q, \(2J_{C-F} = 32.2\) Hz, C-7), 144.3 (C-5'), 146.3 (C-2'), 146.7 (C-9), 151.4 (C-4'), 158.4 (C-6); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \(\delta = -54.6\) (s, CF\(_3\)); GC-MS (EI, 70eV): \(m/z\) (%) = 345 (M\(^+\), 100), 329 (50), 307 (20), 297 (w), 1740 (s), 1615 (s), 1556 (w), 1505 (s), 1486 (m), 1466 (m), 1426 (m), 1353 (s), 1329 (s), 1260 (s), 1227 (m), 1180 (m), 1145 (s), 1033 (m), 993 (m), 973 (m), 905 (w), 887 (w), 852 (w), 838 (w), 822 (m), 788 (w), 750 (s), 714 (m), 644 (w), 621 (m); Anal. Calcd. for C\(_{18}\)H\(_{10}\)F\(_3\)NO\(_3\): C, 65.28; H, 4.43; N, 7.25. Found: C, 64.00; H, 4.44; N, 6.69.
7.24 (m, 2H), 7.26-7.31 (m, 1H), 7.36 (d, $^3J = 2.66$ Hz, 1H), 7.45-7.50 (m, 1H), 8.13 (dq, $^3J = 9.69$, 2.19 Hz, 1H), 8.54 (dd, $^3J = 7.94$, 1.56 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta = 55.9$ (OCH$_3$), 106.9 (C-11), 111.7 (C-1′), 116.6 (C-9), 118.5 (C-6′), 119.5 (C-4), 122.7 (C-2), 123.1 (q, $^1J_{C-F} = 278.2$ Hz, CF$_3$), 124.6 (C-8), 125.4 (C-3), 126.9 (C-3′), 132.6 (C-1), 137.8 (q, $^2J_{C-F} = 33.0$ Hz, C-7), 149.9 (C-5′), 152.2 (C-10), 153.7 (C-2′), 157.6 (C-4′), 163.3 (C-6); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta = -53.08$ (s, CF$_3$); GC-MS (EI, 70eV): m/z (%) = 345 (M$^+$, 100), 317 (8.52), 298 (5.42), 274 (28.87); HRMS (ESI): calcd for C$_{18}$H$_{10}$F$_3$NO$_3$ (M+H) 346.0686, found 346.0486; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 2944$ (w), 1740 (s), 1614 (m), 1594 (m), 1555 (m), 1502 (m), 1468 (m), 1439 (m), 1417 (m), 1359 (m), 1320 (w), 1286 (w), 1243 (w), 1210 (m), 1132 (s), 1016 (m), 959 (m), 917 (m), 799 (m), 748 (s), 718 (s), 699 (w), 669 (w), 647 (m), 627 (w); Anal. Calcd. for C$_{18}$H$_{10}$F$_3$NO$_3$: C, 62.62; H, 2.92; N, 4.06. Found: C, 63.36; H, 2.68; N, 3.63.

8,9,10-Trimethoxy-7-(trifluoromethyl)-6$^H$-chromeno[4,3-b]quinolin-6-one (20l):

Starting with 17a (300 mg, 1.08 mmol), aniline (198 mg, 1.08 mmol), 20l was obtained as a yellow solid (285 mg, 64%), mp. 240–241 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 3.94$ (s, OCH$_3$), 3.97 (s, OCH$_3$), 4.04 (s, OCH$_3$), 7.27-7.35 (m, 3H), 7.48-7.54 (m, 1H), 8.61 (dd, $^3J = 7.96$, 1.44 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta = 56.5$ (OCH$_3$), 61.4 (OCH$_3$), 61.9 (OCH$_3$), 103.8 (C-11), 113.9 (C-6′), 116.9 (C-1′), 117.7 (C-4), 118.6 (C-2), 122.5 (q, $^1J_{C-F} = 276.4$ Hz, CF$_3$), 124.7 (C-3), 125.3 (C-3′), 132.5 (C-1′), 137.9 (q, $^2J_{C-F} = 35.9$ Hz, C-7), 144.1 (C-9), 148.1 (C-5′), 149.1 (C-2′), 150.1 (C-8), 152.4 (C-4′), 158.1 (C-6′), 159.2 (C-10); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta = -54.5$ (s, CF$_3$); GC-MS (EI, 70eV): m/z (%) = 405 (M$^+$, 100), 390 (45.30), 362 (58.03), 332 (19.91), 276 (10.80), 248 (11.61); HRMS (ESI): calcd for C$_{20}$H$_{14}$F$_3$NO$_5$ (M+H) 406.0897, found 406.0899; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 2958$ (w), 1746 (s), 1606 (m), 1596 (m), 1547 (s), 1494 (w), 1457 (s), 1401 (s), 1361 (s), 1278 (w), 1262 (w), 1225 (m), 1202 (m), 1136 (s), 1041 (m), 1001 (s), 979 (s), 951 (w), 940 (w), 915 (w), 895 (w), 830 (s), 785 (w), 755 (s), 715 (s), 658 (m), 631 (m), 615 (w); Anal. Calcd. for C$_{20}$H$_{14}$F$_3$NO$_5$: C, 59.26; H, 3.48; N, 3.46. Found: C, 58.82; H, 3.22; N, 3.20.
3.2.4 Synthesis of Thieno[2,3-\c]chromen-4-ones and 7,8,9,10-Tetrahydrobenzo[3,2-\c]chromen-6-ones:

General procedure for deaminative bromination of Arylamine:

In this procedure anhydrous copper(II) bromide (12 mmol), tert-butyl nitrite (15 mmol), and anhydrous acetonitrile (40 mL) were added to a three necked round bottom flask that was equipped with a reflux condenser, addition funnel or solid inlet tube, and a gas outlet tube. The amine (10 mmol) in 5 mL of acetonitrile or as a solid was slowly added over a period of 5 min to the reaction solution. During this addition, the reaction solution turned completely black from the initial green color as nitrogen was evolved. After complete gas evolution, the reaction mixture was then poured into 200 mL of 20% aqueous HCl and extracted with 200 mL of ether and organic layer was washed once with 200 mL of 20% aqueous HCl. The resulting ether solution was dried over anhydrous magnesium sulfate and the ether was removed under reduce pressure. The product was then purified by silica gel column chromatography.

Methyl 3-bromothiophene-2-carboxylate (23):

Starting with CuBr$_2$ (5.36 g, 12 mmol), tert-butyl nitrite (3.56 mL, 15 mmol) and amine 21 (3.14 g, 10 mmol), 23 was obtained as a colorless solid, (3.80 g, 86%), mp. 50–51 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 3.82 (s, OCH$_3$), 7.01 (d, $^3$J = 5.25 Hz, 1H), 7.39 (d, $^3$J = 5.25 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 52.2 (OCH$_3$), 7.01 (d, $^3$J = 5.25 Hz, 1H), 7.39 (d, $^3$J = 5.25 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 52.2 (OCH$_3$), 117.0 (C-3), 127.3 (C-4), 131.2 (C-5), 132.9 (C-2), 161.1 (C=O); GC-MS (EI, 70eV): $m/z$ (%) = 222 (M$^+$, $^{81}$Br, 44.14), 220 (M$^+$, $^{79}$Br, 42.88), 191 (100), 161 (5.53), 119 (5.00), 82 (26.38), 45 (8.25); HRMS (ESI): calcd for C$_6$H$_5$O$_2$Br$_{1}S_1$ 219.91881, found 219.919086 and calcd for C$_6$H$_5$O$_2$S$^{81}$Br$_1$S$_1$ 221.91677, found 221.917148; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3119 (w), 2992 (w), 1711 (s), 1536 (w), 1503 (s), 1463 (w), 1434 (s), 1408 (s), 1353 (s), 1230 (s), 1188 (m), 1156 (m), 1091 (m), 1071 (s), 969 (w), 878 (s), 816 (m), 762 (s).

Ethyl 2-bromo-4,5,6,7-tetrahydrobenzo[\b]thiophene-3-carboxylate (24):

Starting with CuBr$_2$ (2.68 g, 12 mmol), tert-butyl nitrite (1.78 mL, 15 mmol) and amine 22 (2.25 g, 10
mmol), 24 was obtained as a colorless oil, (2.40 g, 83%); \(^1\)H NMR (250 MHz, CDCl\(_3\)): \(\delta = 1.29\) (t, \(^3J = 7.18\) Hz, CH\(_3\)), 1.65-1.72 (m, 4H, CH\(_2\times2\)), 2.52-2.56 (m, 2H, CH\(_2\)), 2.64-2.69 (m, 2H, CH\(_2\)), 4.25 (q, \(^3J = 7.18\) Hz, CH\(_2\)); \(^13\)C NMR (62.9 MHz, CDCl\(_3\)): \(\delta = 14.2\) (CH\(_3\)), 22.4 (C-4), 22.7 (C-5), 24.9 (C-6), 26.1 (7), 60.6 (OCH\(_2\)), 115.3 (C-2), 130.7 (C-8), 136.0 (C-3), 137.2 (C-9), 162.8 (C=O); GC-MS (EI, 70eV): \(m/z\) (%) = 290 (M\(^+\), 81 Br, 100), 288 (M\(^+\), 79 Br 96.73), 261 (90.54), 244 (73.69), 234 (21.14), 216 (29.82), 180 (48.69), 135 (39.84), 91 (20.41); HRMS (ESI): calcd for C\(_{11}\)H\(_{13}\)O\(_2\)S\(_2\)Br 287.98141, found 287.981030 and calcd for C\(_{11}\)H\(_{13}\)O\(_2\)S\(_2\)Br 289.97937, found 289.979393; IR (ATR, cm\(^{-1}\)): \(~\nu = 2932\) (m), 1707 (s), 1599 (w), 1552 (w), 1446 (s), 1383 (m), 1336 (w), 1314 (m), 1262 (s), 1178 (m), 1144 (s), 1094 (w), 1069 (w), 1030 (s), 947 (m), 975 (w), 839 (w), 819 (w), 737 (m).

2-Bromo-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonitrile (30):
Starting with CuBr\(_2\) (2.68 g, 12 mmol), tert-butyl nitrite (1.78 mL, 15 mmol) and amine (1.78 g, 10 mmol), 30 was obtained as a colorless solid, (1.80 g, 74%), mp. 62–64 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 1.75-1.77\) (m, 4H, CH\(_2\)/uni0445\(_2\)), 2.56-2.60 (m, 4H, CH\(_2\)/uni0445\(_2\)); \(^13\)C NMR (62.9 MHz, CDCl\(_3\)): \(\delta = 21.8\) (C-4), 22.8 (C-5), 24.5 (C-6), 24.7 (C-7), 113.7 (C-CN), 114.1 (C-3), 119.6 (C-2), 136.8 (C-8), 138.6 (C-9); GC-MS (EI, 70eV): \(m/z\) (%) = 243 (M\(^+\), 81 Br, 49.29), 241 (M\(^+\), 79 Br, 48.76), 215 (100), 162 (45.73), 134 (26.47); HRMS (ESI): calcd for C\(_9\)H\(_8\)N\(_1\)Br\(_1\)S\(_1\) 240.96; found 240.955427 and calcd for C\(_9\)H\(_8\)N\(_1\)Br\(_1\)S\(_1\) 240.95553, found 240.955427 and calcd for C\(_9\)H\(_8\)N\(_1\)Br\(_1\)S\(_1\) 242.95349, found 242.953794; IR (ATR, cm\(^{-1}\)): \(\nu = 3100\) (w), 2928 (s), 2225 (s), 1555 (m), 1448 (s), 1431 (s), 1332 (m), 1306 (w), 1253 (w), 1166 (w), 1134 (w), 1033 (s), 757 (m), 865(w), 817(s); C\(_9\)H\(_8\)N\(_1\)Br\(_1\)S\(_1\) (239.34) Calcd C 44.64, H 3.33, N 5.78, S 13.24, found C 45.79, H 3.57, N 5.90, S 13.37.

**General procedure for the synthesis of compounds (26a-o) and (27a-o):**
A 1, 4-dioxane solution (5–6 mL) of 23 (1.0 equiv, 110 mg, 0.5 mmol) or 24 (1.0 equiv, 144 mg, 0.5 mmol), aryl boronic acid (1.3 equiv.), K\(_3\)PO\(_4\) (1.5 equiv.), and Pd(PPh\(_3\))\(_4\) (3 mol%) was heated at 100–110 °C for 4-6 h. After cooling to 20 °C, a saturated aqueous solution of NH\(_4\)Cl was added. The organic and aqueous layers were separated and the latter was extracted with CH\(_2\)Cl\(_2\). The combined organic layers were dried (Na\(_2\)SO\(_4\)), filtered and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography.
Methyl-3-phenylthiophene-2-carboxylate (26a):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (79 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 26a was obtained as a colorless solid (0.085 g, 78%), mp. 40–41 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 3.68 (s, OCH$_3$), 7.00 (d, $^3J$ = 5.07 Hz, 1H), 7.27-7.39 (m, 5H), 7.41 (d, $^3J$ = 5.07 Hz, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta$ = 51.9 (OCH$_3$), 126.9 (C-4), 127.8 (C-2',6'), 127.9 (C-4'), 129.2 (C-3',5'), 130.2 (C-2), 131.6 (C-1'), 135.6 (C-5), 148.7 (C-3), 162.4 (C=O); GC-MS (EI, 70eV): m/z (%) = 218 (M$^+$, 82.29), 187 (100), 158 (7.96), 115 (46.95), 89 (7.79), 79 (5.83); HRMS (ESI): calcd for C$_{12}$H$_{10}$O$_2$S $^{1218.03960}$, found 218.039633; IR (ATR, cm$^{-1}$): $\nu$ = 3103 (w), 2949 (w), 1703 (s), 1599 (w), 1573 (w), 1573 (m), 1486 (m), 1435 (s), 1399 (m), 1372 (m), 1315 (w), 1277 (s), 1231 (s), 1189 (w), 1158 (w), 1084 (s), 1065 (s), 966 (w), 919 (w), 888 (s).

Methyl-3-p-tolylthiophene-2-carboxylate (26b):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (88 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and (34 mg, 0.03 mmol), 26b was obtained as a colorless oil (0.090 g, 78%); $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 2.30 (s, CH$_3$), 3.68 (s, OCH$_3$), 6.98 (d, $^3J$ = 5.05 Hz, 1H), 7.13 (d, $^3J$ = 7.94 Hz, 2H), 7.27 (d, $^3J$ = 8.05 Hz, 2H), 7.39 (d, $^3J$ = 5.08 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 21.3 (CH$_3$), 51.8 (OCH$_3$), 126.5 (C-4), 128.5 (C-2',6'), 129.1 (C-3',5'), 130.1 (C-2), 131.5 (C-4'), 132.6 (C-1'), 137.7(C-5), 148.8(C-3), 162.5 (C=O); GC-MS (EI, 70eV): m/z (%) = 232 (M$^+$, 100), 201 (71.49), 171 (19.04), 158 (9.64), 129 (17.68), 115 (6.97); HRMS (ESI): calcd for C$_{13}$H$_{12}$O$_2$S $^{1232.05525}$, found 232.055510; IR (ATR, cm$^{-1}$): $\nu$ = 3106 (w), 2949 (w), 1704 (s), 1614 (w), 1567 (w), 1536 (m), 1501 (m), 1436 (s), 1399 (m), 1368 (m), 1349 (w), 1308 (w), 1278 (s), 1231 (s), 1184 (w), 1109 (m), 1083 (s), 1066 (s), 1021 (w), 966 (w), 888 (s), 852 (w), 777 (s).
Methyl-3-(4-chlorophenyl)thiophene-2-carboxylate (26c):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (101 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and (34 mg, 0.03 mmol), 26c was obtained as a colorless oil (0.1 g, 80%); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 3.69 (s, OCH$_3$), 6.96 (d, $^3$$J$ = 5.11 Hz, 1H), 7.26-7.33 (m, 4H), 7.43 (d, $^3$$J$ = 5.09 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 51.9 (OCH$_3$), 127.1 (C-4), 128.0 (C-2,6'), 130.5 (C-3,5'), 130.6 (C-2), 131.3 (C-4'), 133.9 (C-1'), 134.0 (C-5), 147.3 (C-3), 162.3 (C=O); GC-MS (EI, 70eV): $m/z$ (%) = 252 (M$^+$, 83.77), 221 (100), 186 (19.31), 158 (25.94), 149 (14.44), 113 (7.14); HRMS (ESI): calcd for C$_{12}$H$_9$ClO$_2$S, 252.00063, found 252.001160 and calcd for C$_{12}$H$_9$ClO$_2$S$^{13}$, 253.99768, found 253.998204; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3108 (w), 2952 (w), 1699 (s), 1595 (w), 1567 (w), 1537 (m), 1478 (m), 1433 (s), 1405 (m), 1373 (m), 1277 (s), 1233 (s), 1185 (w), 1119 (m), 1086 (m), 1067 (s), 1015 (m), 963 (w), 779 (s).

Methyl-3-(4-methoxyphenyl)thiophene-2-carboxylate (26d):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (98 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 26d was obtained as a colorless oil (0.095 g, 77%); $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 3.70 (s, OCH$_3$), 3.76 (s, OCH$_3$), 6.86 (d, $^3$$J$ = 8.75 Hz, 2H), 6.98 (d, $^3$$J$ = 5.11 Hz, 1H), 7.33 (d, $^3$$J$ = 8.77 Hz, 2H), 7.39 (d, $^3$$J$ = 5.08 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 51.8 (OCH$_3$), 52.2 (OCH$_3$), 113.2 (C-3',5'), 127.9 (C-1'), 130.1 (C-2,6'), 130.5 (C-2), 131.5 (C-5), 148.5 (C-3), 159.4 (C-4'), 162.5 (C=O); GC-MS (EI, 70eV): $m/z$ (%) = 248 (M$^+$, 100), 233 (5.00), 217 (62.11), 202 (5.00), 189 (6.08), 174 (10.39), 145 (13.84), 102 (7.38); HRMS (ESI): calcd for C$_{13}$H$_{12}$O$_3$S, 248.05017, found 248.050234; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3103 (w), 2949 (w), 2912 (s), 1607 (m), 1574 (w), 1538 (w), 1501 (m), 1464 (w), 1444 (m), 1404 (m), 1368 (w), 1276 (m), 1225 (s), 1190 (w), 1177 (m), 1113 (m), 1070 (s), 1024 (s), 964 (w), 821 (s), 776 (s).
Methyl-3-(4-ethylphenyl)thiophene-2-carboxylate (26e):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (97 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 26e was obtained as a colorless oil (0.095 g, 78%); $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 1.19 (t, $^3J$ = 7.58 Hz, CH$_3$), 2.61 (q, $^3J$ = 7.58 Hz, CH$_2$), 3.70 (s, OCH$_3$), 7.00 (d, $^3J$ = 5.07 Hz, 1H), 7.16 (d, $^3J$ = 8.06 Hz, 2H), 7.31 (d, $^3J$ = 8.15 Hz, 2H), 7.40 (d, $^3J$ = 5.08 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 15.3 (CH$_3$), 28.6 (CH$_2$), 51.8 (OCH$_3$), 126.4 (C-4), 127.3 (C-2',6'), 129.1 (C-3',5'), 130.1 (C-2), 131.6 (C-1'), 132.8 (C-5), 144.0 (C-4'), 148.8 (C-3), 162.5 (C=O); GC-MS (EI, 70eV): m/z (%) = 246 (M$^+$, 100), 231 (86.16), 215 (20.81), 199 (5.00), 187 (11.77), 171 (26.42), 158 (5.00), 128 (5.79), 115 (12.75), 100 (7.05); HRMS (ESI): calcd for C$_{14}$H$_{14}$O$_2$S 246.07090, found 246.071566; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3102 (w), 2962 (w), 1716 (s), 1612 (w), 1537 (w), 1503 (m), 1433 (m), 1404 (m), 1372 (m), 1274 (m), 1218 (s), 1185 (w), 1110 (m), 1067 (s), 1020 (w), 965(w), 773 (s).

Methyl-3-(3-(trifluoromethyl)phenyl)thiophene-2-carboxylate (26f):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (123 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 26f was obtained as a colorless oil (0.122 g, 85%); $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 3.67 (s, OCH$_3$), 6.99 (d, $^3J$ = 5.11 Hz, 1H), 7.39-7.62 (m, 5H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 50.9 (OCH$_3$), 122.9 (q, $^1J_{C-F}$ = 272.57 Hz, CF$_3$), 123.57 (q, $^3J_{C-F}$ = 3.76 Hz, C-4'), 125.1 (q, $^3J_{C-F}$ = 3.90 Hz, C-2'), 126.8 (C-4), 127.1 (C-5'), 129.20 (q, $^2J_{C-F}$ = 32.18 Hz, C-3'), 129.7 (C-2), 130.1 (C-6'), 131.6 (C-1'), 135.3 (C-5), 145.6 (C-3), 161.1 (C=O); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ = -61.33 (s, CF$_3$); GC-MS (EI, 70eV): m/z (%) = 286 (M$^+$, 82.34), 267 (8.05), 255 (100), 235 (6.45), 207 (15.40), 183 (22.21), 158 (11.30), 133 (5.00); HRMS (ESI): calcd for C$_{13}$H$_9$F$_3$O$_2$S 286.02699, found 286.026527; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3102 (w), 2962 (w), 1716 (s), 1614 (w), 1538 (w), 1483 (w), 1435 (m), 1406 (m), 1379 (w), 1325 (s), 1266 (m), 1223 (m), 1162 (m), 1116 (s), 1066 (s), 1001 (w), 970 (w), 848 (w), 769 (s).
Methyl-3,2'-bithiophene-2-carboxylate (26g):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (83 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 26g was obtained as a colorless oil (0.073 g, 65%); $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 3.77 (s, OCH$_3$), 6.99-7.03 (m, 1H), 7.17 (d, $^3J$ = 5.22 Hz, 1H), 7.30 (dd, $^{3,4}J$ = 5.15, 1.17 Hz, 1H), 7.39 (d, $^3J$ = 5.17 Hz, 1H), 7.50 (dd, $^{3,4}J$ = 3.65, 1.17 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 51.0 (OCH$_3$), 161.1 (C-5′), 125.5 (C-4′), 126.1 (C-4), 127.8 (C-3′), 129.1 (C-2), 130.4 (C-1′), 131.9 (C-5), 139.1 (C-3), 161.3 (C=O); GC-MS (EI, 70eV): $m/z$ (%) = 224 (M$^+$, 90.18), 193 (100), 166 (9.23), 121 (28.99); HRMS (ESI): calcd for C$_{10}$H$_8$O$_2$S$_2$: 223.99602, found 223.995873; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3105 (w), 2950 (w), 1716 (s), 1536 (w), 1506 (m), 1435 (s), 1411 (m), 1379 (w), 1353 (w), 1344 (w), 1234 (s), 1192 (w), 1158 (w), 1070 (s), 1043 (w), 960 (w), 932 (w), 768 (s).

Methyl-3-(4-vinylphenyl)thiophene-2-carboxylate (26h):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (96 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 26h was obtained as a colorless oil (0.1 g, 82%); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 3.68 (s, OCH$_3$), 5.18 (dd, $^{3,3}J$ = 10.86, 8.87 Hz, 1H), 5.70 (dd, $^{3,2}J$ = 17.55, 0.99 Hz, 1H), 6.65 (dd, $^{3,3}J$ = 17.62, 10.89 Hz, 1H), 6.98 (d, $^3J$ = 5.11 Hz, 1H), 7.31-7.34 (m, 4H), 7.39 (d, $^3J$ = 5.07 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 50.8 (OCH$_3$), 113.1 (CH), 124.6 (C-4), 128.4 (C-3′,5′), 129.2 (C-2′,6′), 130.4 (C-2), 131.9 (C-1′), 133.9 (CH), 135.4 (C-4′), 136.1 (C-5), 147.2 (C-3), 161.3 (C=O); GC-MS (EI, 70eV): $m/z$ (%) = 244 (100), 213 (31.99), 184 (26.46), 171 (12.63), 152 (8.30), 139 (7.33), 115 (7.26); HRMS (ESI): calcd for C$_{14}$H$_{12}$O$_2$S: 244.05525, found 244.055476; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3097 (w), 2944 (w), 1717 (s), 1627 (w), 1556 (w), 1498 (m), 1455 (w), 1433 (m), 1409 (m), 1372 (w), 1317 (w), 1280 (s), 1228 (s), 1187 (w), 1110 (w), 1074 (m), 988 (m), 928 (m), 888 (m), 851 (m), 783 (s).
Methyl-3-(2-methoxyphenyl)thiophene-2-carboxylate (26i):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (98 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 26i was obtained as a colorless oil (0.096 g, 78%); $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 3.66 (s, OCH$_3$), 3.68 (s, OCH$_3$), 6.87-6.95 (m, 2H), 6.99 (d, $^3$J = 5.06 Hz, 1H), 7.16-7.31 (m, 2H), 7.41 (d, $^3$J = 5.08 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 51.7 (OCH$_3$), 55.4 (OCH$_3$), 110.8 (C-3'), 120.1 (C-5'), 123.3 (C-4), 125.0 (C-1'), 129.3 (C-4'), 129.4 (C-6'), 130.6 (C-2), 144.2 (C-3), 156.6 (C-2'), 161.3 (C=O); GC-MS (EI, 70eV): m/z (%) = 248 (M$^+$, 63.35), 217 (100), 202 (45.28), 187 (13.85), 174 (20.80), 155 (27.90), 145 (12.11), 128 (5.00), 115 (9.35), 102 (9.38); HRMS (ESI): calcd for C$_{13}$H$_{12}$O$_3$S: 248.05017, found 248.050367; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3107 (w), 2954 (w), 1704 (s), 1600 (w), 1579 (w), 1537 (w), 1486 (m), 1466 (w), 1434 (m) 1401 (m), 1371 (w), 1269 (m), 1227 (s), 1178 (w), 1159 (w), 1123 (w), 1104 (m), 1080 (m), 1067 (m), 1018 (m), 964 (w), 945 (w), 763 (s).

Methyl-3-(2,3-dimethoxyphenyl)thiophene-2-carboxylate (26j):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (118 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 26j was obtained as a colorless oil (0.107 g, 77%); $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 3.49 (s, OCH$_3$), 3.67 (s, OCH$_3$), 3.82 (s, OCH$_3$), 6.78 (dd, $^3$J = 7.64, 1.59 Hz, 1H), 6.85-7.01 (m, 2H), 7.42 (d, $^3$J = 5.05 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 51.8 (OCH$_3$), 55.8 (OCH$_3$), 60.6 (OCH$_3$), 111.6 (C-4'), 112.2 (C-5'), 122.5 (C-6'), 123.3 (C-4), 129.4 (C-1'), 130.5 (C-2), 131.5 (C-5), 144.1 (C-3), 146.5 (C-2'), 152.6 (C-3'), 162.4 (C=O); GC-MS (EI, 70eV): m/z (%) = 278 (M$^+$, 60.42), 247 (100), 232 (17.76), 217 (7.63), 204 (17.21), 189 (9.52), 155 (8.80), 133 (5.00), 89 (5.27); HRMS (ESI): calcd for C$_{14}$H$_{14}$O$_4$S: 278.06073, found 278.060567; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3103 (w), 2943 (w), 1600 (w), 1576 (w), 1537(w), 1469 (m), 1425 (m), 1404 (m), 1374 (w), 1305 (m), 1247 (s), 1191 (w), 1169 (w), 1144 (m), 1074 (m), 1054 (m), 999 (s), 926 (m), 852 (m), 764 (s).

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Methyl-3-(2,5-dimethoxyphenyl)thiophene-2-carboxylate (26k):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (118 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 26k was obtained as a colorless oil (0.108 g, 78%); $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 3.62 (s, OCH$_3$), 3.66 (s, OCH$_3$), 3.71 (s, OCH$_3$), 6.75-6.76 (m, 1H), 6.79-6.82 (m, 2H), 6.98 (d, $^3J = 5.05$ Hz, 1H), 7.41 (d, $^3J = 5.05$ Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 51.7 (OCH$_3$), 55.7 (OCH$_3$), 56.1 (OCH$_3$), 111.9 (C-6'), 113.3 (C-3'), 113.8 (C-4'), 116.4 (C-4), 117.1 (C-1'), 125.9 (C-2), 128.6 (C-5), 129.4 (C-3), 131.5 (C-2'), 143.8 (C-5'), 162.4 (C=O); GC-MS (EI, 70eV): m/z (%) = 278 (M$^+$, 100), 263 (10.53), 247 (59.99), 232 (16.75), 217 (14.92), 204 (21.65), 189 (9.49), 161 (8.15), 147 (5.96), 89 (5.00); HRMS (ESI): calcd for C$_{14}$H$_{14}$O$_4$S $^{278.06073}$, found 278.060954; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3106 (w), 2936 (w), 2830 (w), 1710 (s), 1583 (w), 1537 (w), 1500 (s), 1435 (s), 1373 (w), 1309 (w), 1295 (w), 1223 (s), 1104 (m), 1070 (m), 1020 (s), 927 (m), 881 (m), 854 (m), 784 (s).

Methyl-3-(2,6-dimethoxyphenyl)thiophene-2-carboxylate (26l):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (118 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 26l was obtained as a colorless oil (0.104 g, 75%); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 3.61 (s, OCH$_3$), 3.62 (s, OCH$_3$), 6.53 (d, $^3J = 8.40$ Hz, 2H), 6.94 (d, $^3J = 5.07$ Hz, 1H), 7.19 (t, $^3J = 8.36$ Hz, 1H), 7.38 (d, $^3J = 5.04$ Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 51.6 (OCH$_3$), 55.8 (OCH$_3$×2), 103.9 (C-3',5'), 104.4 (C-1'), 113.8 (C-4), 128.9 (C-2), 129.3 (C-4'), 132.1 (C-5), 140.0 (C-3), 157.7 (C-2',6'), 162.4 (C=O); GC-MS (EI, 70eV): m/z (%) = 278 (M$^+$, 69.57), 247 (100), 232 (35.75), 217 (12.03), 203 (5.12), 189 (21.88), 155 (26.54), 125 (6.71); HRMS (ESI): calcd for C$_{14}$H$_{14}$O$_4$S $^{278.06073}$, found 278.060954; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3105 (w), 2936 (w), 1710 (s), 1583 (w), 1537 (w), 1500 (s), 1435 (s), 1373 (w), 1309 (w), 1295 (w), 1223 (s), 1104 (m), 1070 (m), 1020 (s), 927 (m), 881 (m), 854 (m), 784 (s).
Methyl-3-(5-fluoro-2-methoxyphenyl)thiophene-2-carboxylate (26m):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (110 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 26m was obtained as a colorless oil (0.106 g, 80%); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 3.63 (s, OCH$_3$), 3.65 (s, OCH$_3$), 6.75-6.80 (m, 1H), 6.87-6.97 (m, 2H), 6.95 (d, $^3J$ = 5.05 Hz, 1H), 7.40 (d, $^3J$ = 5.08 Hz, 1H). $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta$ = 51.8 (OCH$_3$), 55.8 (OCH$_3$), 111.9 (C-3'), 125.0 (C-4), 126.6 (C-1'), 128.9 (C-6'), 129.7 (C-2), 130.2 (C-4'), 131.2 (C-5), 142.5 (C-3), 152.9 (C-2'), 155.4 (C-2'), 162.2 (C=O); GC-MS (EI, 70eV): m/z (%) = 266 (60.40), 235 (100), 220 (41.26), 205 (13.48), 192 (20.47), 155 (11.42), 133 (7.01), 120 (8.50); HRMS (ESI): calcd for C$_{13}$H$_{11}$O$_3$F$_1$S$_1$ 266.04074, found 266.040926; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3109 (w), 2957 (w), 1709 (s), 1621 (w), 1595 (w), 1492 (s), 1463 (m), 1434 (m), 1395 (m), 1284 (m), 1259 (w), 1234 (s), 1176 (s), 1126 (m), 1100 (m), 1073 (m), 1023 (m), 976 (w), 937 (w), 858 (m), 817 (m), 782 (m), 729 (s).

Methyl-3-(5-chloro-2-methoxyphenyl)thiophene-2-carboxylate (26n):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (121 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 26n was obtained as a colorless oil (0.126 g, 85%); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 3.63 (s, OCH$_3$), 3.80 (s, OCH$_3$), 6.78 (d, $^3J$ = 8.77 Hz, 1H), 6.95 (d, $^3J$ = 5.04 Hz, 1H), 7.14 (d, $^4J$ = 2.61 Hz, 1H), 7.21 (dd, $^3J$ = 8.76, 2.67 Hz, 1H), 7.42 (d, $^3J$ = 5.07 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 51.8 (OCH$_3$), 55.8 (OCH$_3$), 111.9 (C-3'), 125.0 (C-4), 126.6 (C-1'), 128.9 (C-6'), 129.7 (C-2), 130.2 (C-4'), 131.2 (C-5), 142.5 (C-3), 155.4 (C-2'), 162.2 (C=O); GC-MS (EI, 70eV): m/z (%) = 266 (60.40), 235 (100), 220 (41.26), 205 (13.48), 192 (20.47), 155 (11.42), 133 (7.01), 120 (8.50); HRMS (ESI): calcd for C$_{13}$H$_{11}$O$_3$Cl$_1$S$_1$ 282.01119, found 282.010461 and calcd for C$_{13}$H$_{11}$O$_3$Cl$_1$S$_1$ 282.01119.
Methyl-3-(2,3,4-trimethoxyphenyl)thiophene-2-carboxylate (26o):

Starting with 23 (110 mg, 0.5 mmol), boronic acid (137 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 26o was obtained as a colorless oil (0.1 g, 65%); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 3.56 (s, OCH$_3$), 3.67 (s, OCH$_3$), 3.82 (s, OCH$_3$), 3.83 (s, OCH$_3$), 6.63 (d, $^3$J = 8.61 Hz, 1H), 6.89 (d, $^3$J = 8.62 Hz, 1H), 6.98 (d, $^3$J = 5.05 Hz, 1H), 7.41 (d, $^3$J = 5.07 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 51.8 (OCH$_3$), 55.9 (OCH$_3$), 60.9 (OCH$_3$), 61.0 (OCH$_3$), 105.2 (C-5'), 106.7 (C-1'), 122.8 (C-6'), 124.9 (C-4), 129.4 (C-2), 131.7 (C-5), 142.0 (C-3'), 144.0 (C-2'), 151.4 (C-3), 153.6 (C-4'), 162.6 (C=O); GC-MS (EI, 70eV): m/z (%) = 308 (100), 293 (8.41), 277 (55.68), 262 (10.09), 247 (13.23), 235 (12.89), 219 (13.58), 207(6.93), 179(6.22), 155(7.07); HRMS (ESI): calcd for C$_{15}$H$_{16}$O$_5$S: 308.07130, found 308.071675; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 2933 (m), 2834 (w), 1695 (s), 1586 (m), 1507 (w), 1472 (s), 1439 (w), 1430 (w), 1406 (m), 1388 (w), 1360 (w), 1318 (m), 1284 (w), 1236 (s), 1178 (w), 1142 (w), 1095 (m), 1066 (m), 1022 (s), 966 (w), 932 (w), 785 (s).

Ethyl-2-p-tolyl-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (27a):

Starting with 24 (144 mg, 0.5 mmol), boronic acid (88 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 27a was obtained as a colorless oil, (0.12 g, 80%); $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 1.01 (t, $^3$J = 7.15 Hz, CH$_3$), 1.68-1.76 (m, 4H, CH$_2$), 2.27 (s, CH$_3$), 2.62-2.70 (m, 4H, CH$_2$), 4.05 (q, $^3$J = 7.18 Hz, CH$_2$), 7.06 (d, $^3$J = 7.89 Hz, 2H), 7.19 (d, $^3$J = 8.12 Hz, 2H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 13.9 (CH$_3$), 21.2 (CH$_3$), 22.6 (C-5), 23.1 (C-6), 25.0 (C-4), 25.8 (C-7), 60.2 (OCH$_3$), 127.9 (C-3',5'), 128.7 (C-8), 129.0 (C-2',6'), 130.3 (C-1'), 131.4 (C-4'), 135.9 (C-3), 137.7 (C-9), 145.7 (C-2), 164.9 (C=O); GC-MS (EI, 70eV): m/z (%) =
300 (M⁺, 100), 271 (11.83), 253 (32.31), 243 (5.00), 226 (15.39), 198 (5.94), 178 (5.02), 165 (5.00); HRMS (ESI): calcd for C₁₈H₂₀O₂S₁ 300.11785, found 300.118484; IR (ATR, cm⁻¹): ν = 2930 (m), 1705 (s), 1556 (w), 1518 (m), 1439 (m), 1407 (m), 1363 (w), 1348 (w), 1320 (m), 1270 (s), 1240 (w), 1192 (s), 1144 (s), 1112 (w), 1069 (w), 1030 (s), 993 (w), 954 (w), 934 (w), 875 (w), 814 (s).

Ethyl-2-(4-ethylphenyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (27b):

Starting with 24 (144 mg, 0.5 mmol), boronic acid (97 mg, 0.65 mmol), K₃PO₄ (159 mg, 0.75 mmol) and Pd(PPh₃)₄ (34 mg, 0.03 mmol), 27b was obtained as a colorless oil, (0.124 g, 79%); ¹H NMR (250 MHz, CDCl₃): δ = 1.00 (t, 3J = 7.12 Hz, CH₃), 1.16 (t, 3J = 7.61 Hz, CH₃), 1.69-1.77 (m, 4H, CH₂), 2.57 (q, 3J = 7.60 Hz, CH₂), 2.63-2.71 (m, 2H, CH₂), 4.05 (q, 3J = 7.10 Hz, CH₂), 7.09 (d, 3J = 8.35 Hz, 2H), 7.22 (d, 3J = 8.23 Hz, 2H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 13.8 (CH₃), 22.6 (C-5), 23.1 (C-6), 25.0 (C-4), 25.8 (C-7), 28.6 (CH₂), 60.2 (OCH₂), 127.4 (C-8), 127.9 (C-3',5'), 129.0 (C-2',6'), 130.3 (C-1'), 131.7 (C-3), 135.9 (C-9), 144.1 (C-2), 145.7 (C-4'), 164.9 (C=O); GC-MS (EI, 70eV): m/z (%) = 314 (M⁺, 100), 285 (10.22), 267 (20.32), 240 (14.99), 212 (7.41), 178 (5.00); HRMS (ESI): calcd for C₁₉H₂₂O₂S₁ 314.13350, found 314.133814; IR (ATR, cm⁻¹): ν = 2930 (m), 1704 (s), 1610 (w), 1555 (w), 1518 (m), 1455 (m), 1407 (m), 1384 (w), 1363 (w), 1348 (w), 1320 (m), 1271 (m), 1239 (w), 1193 (s), 1144 (s), 1114 (m), 1094 (w), 1069 (w), 1031 (s), 955 (w), 875 (w), 829 (s).

Ethyl-2-(4-fluorophenyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate(27c):

Starting with 24 (144 mg, 0.5 mmol), boronic acid (90 mg, 0.65 mmol), K₃PO₄ (159 mg, 0.75 mmol) and Pd(PPh₃)₄ (34 mg, 0.03 mmol), 27c was obtained as a colorless oil, (0.126 g, 83%); ¹H NMR (300 MHz, CDCl₃): δ = 1.00 (t, 3J = 7.16 Hz, CH₃), 1.16 (t, 3J = 7.61 Hz, CH₃), 1.69-1.77 (m, 4H, CH₂), 2.63-2.71 (m, 2H, CH₂x2), 4.05 (q, 3J = 7.16 Hz, CH₂), 6.91-6.97 (m, 2H), 7.24-7.29 (m, 2H); ¹³C NMR (75.4 MHz, CDCl₃): δ = 13.8 (CH₃), 22.5 (C-5), 23.0 (C-6), 25.0 (C-4), 25.9 (C-7), 60.3 (OCH₂), 114.9 (d, 3J_C,F = 21.63 Hz, C-3',5').
128.3 (C-8), 130.5 (d, \(J_{C-F} = 3.36 \text{ Hz}, \text{C-1}'\)), 130.9 (d, \(J_{C-F} = 8.19 \text{ Hz}, \text{C-2'6'}\)), 135.9 (C-3), 136.2 (C-9), 144.5 (C-2), 162.6 (d, \(J_{C-F} = 247.4 \text{ Hz}, \text{C-4'}\)), 164.5 (C=O);

\(^{19}\text{F} \text{ NMR (282.4 MHz, CDCl}_3\):} \delta = -113.96 (s, CF); \text{GC-MS (EI, 70eV):} \text{ } m/z (\%) = 304 (M\text{ }^+, 100), 275 (23.27), 257 (33.73), 248 (7.18), 230 (25.66), 196 (7.40), 183 (6.47), 139 (6.20); \text{HRMS (ESI):} \text{calcd for C}_{17}\text{H}_{17}\text{O}_2\text{F}_3\text{S}_1 304.09278, \text{found 304.1093178; IR (ATR, cm}^{-1}):}  \tilde{\nu} = 2931 (m), 1705 (s), 1601 (m), 1556 (w), 1515 (s), 1456 (m), 1408 (m), 1384 (w), 1363 (w), 1348 (w), 1320 (m), 1270 (m), 1217 (m), 1190 (s), 1144 (m), 1114 (w), 1094 (w), 1078 (w), 1069 (w), 1028 (m), 994 (w), 955 (w), 876 (w), 831 (s).

\text{Ethyl-2(2-chlorophenyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate(27d):}

![Chemical structure](image)

\text{Starting with 24 (144 mg, 0.5 mmol), boronic acid (101 mg, 0.65 mmol), K}_3\text{PO}_4 (159 mg, 0.75 mmol) and Pd(PPh}_3)_4 (34 mg, 0.03 mmol), 27d was obtained as a colorless oil, (0.131 g, 82%); \text{^1H NMR (300 MHz, CDCl}_3\):} \delta = 0.85 (t, \(J = 7.10 \text{ Hz}, \text{CH}_3\)), 1.70-1.80 (m, 4H, CH\_2/uni0445\_2), 2.66-2.71 (m, 2H, CH\_2), 2.77-2.81 (m, 2H, CH\_2), 3.96 (q, \(J = 7.12 \text{ Hz}, \text{CH}_2\)), 7.16-7.26 (m, 3H), 7.31-7.34 (m, 1H); \text{\textsuperscript{13}C NMR (75.4 MHz, CDCl}_3\):} \delta = 12.5 (CH\_3), 21.5 (C-5), 21.9 (C-6), 24.0 (C-4), 25.0 (C-7), 58.9 (OCH\_2), 125.1 (C-5'), 128.1 (C-6'), 128.2 (C-3'), 128.6 (C-8), 130.5 (C-4'), 133.1 (C-3), 133.2 (C-2'), 135.1 (C-1'), 135.4 (C-9), 141.7 (C-2), 162.5 (C=O); \text{GC-MS (EI, 70eV):} \text{ } m/z (\%) = 322 (M\text{ }^+, 37\text{Cl },2.71), 320 (M\text{ }^+, 35\text{Cl },7.30), 285 (100), 257 (90.45), 229 (6.89), 212 (7.27), 184 (4.83), 178 (4.95), 165 (4.79); \text{HRMS (ESI):} \text{calcd for C}_{17}\text{H}_{17}\text{ClO}_2\text{S}_1 320.06323, \text{found 320.062797, and calcd for C}_{17}\text{H}_{17}\text{O}_2\text{Cl}_{3}\text{S}_1 322.06028, found 322.060607; IR (ATR, cm}^{-1}):  \tilde{\nu} = 2932 (m), 1705 (s), 1601 (m), 1556 (w), 1498 (m), 1455 (m), 1410 (m), 1385 (w), 1362 (w), 1348 (w) 1320 (m), 1264 (m), 1241 (m), 1195 (s), 1145 (s), 1079 (w), 1031 (s), 992 (w), 957 (w), 939 (w), 977 (w), 820 (w), 747 (s).

\text{Ethyl-2-{4-(trifluoromethyl)phenyl}-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (27e):}

![Chemical structure](image)

\text{Starting with 24 (144 mg, 0.5 mmol), boronic acid (123 mg, 0.65 mmol), K}_3\text{PO}_4 (159 mg, 0.75 mmol) and Pd(PPh}_3)_4 (34 mg, 0.03 mmol), 27e was}
obtained as a colorless oil, (0.15 g, 85%); $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 1.00$ (t, $^3J = 7.14$ Hz, CH$_3$), 1.69-1.78 (m, 4H, CH$_2$2x), 2.65-2.73 (m, 4H, CH$_2$2x), 4.05 (q, $^3J = 7.14$ Hz, CH$_2$), 7.41 (d, $^3J = 8.08$ Hz, 2H), 7.52 (d, $^3J = 8.17$ Hz, 2H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta = 12.7$ (CH$_3$), 21.4 (C-5), 21.9 (C-6), 24.0 (C-4), 24.8 (C-7), 59.4 (OCH$_2$), 123.0 (q, $^1J$_{CF} = 272.28$ Hz, CF$_3$), 123.8 (q, $^3J$_{CF} = 3.75$ Hz, C-3‘,5’), 128.5 (C-8), 128.8 (q, $^2J$_{CF} = 32.61$ Hz, C-4‘), 129.2 (C-2‘,6‘), 135.5 (C-3), 135.9 (C-1‘), 137.1 (C-9), 142.5 (C-2), 163.3 (C=O); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta = -62.91$ (s, CF$_3$); GC-MS (EI, 70eV): $m/z$ (%) = 354 (M$^+$, 100), 335 (8.52), 325 (34.80), 307 (43.92), 298 (9.57), 280 (31.58), 239 (5.71), 213 (5.92), 189 (6.16); HRMS (ESI): calcd for C$_{18}$H$_{17}$O$_2$F$_3$S$_3$: 554.08959, found 554.089330; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 2934$ (m), 1707 (s), 1614 (m), 1556 (w), 1521 (w), 1471 (m), 1407 (m), 1386 (w), 1364 (w), 1319 (s), 1272 (m), 1196 (m), 1163 (m), 1145 (m), 1120 (s), 1065 (s), 1017 (m), 995 (w), 959 (w), 838 (s).

Ethyl-2-(thiophen-2-yl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (27f):

Starting with 24 (144 mg, 0.5 mmol), boronic acid (83 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 27f was obtained as a colorless oil, (0.087 g, 60%); $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 1.14$ (t, $^3J = 7.15$ Hz, CH$_3$), 1.69-1.75 (m, 4H, CH$_2$2x), 2.53-2.58 (m, 4H, CH$_2$2x), 4.15 (q, $^3J = 7.15$ Hz, CH$_2$), 6.93 (dd, $^3J = 5.13$, 3.59 Hz, 1H), 7.10 (dd, $^3J = 3.60$, 1.20 Hz, 1H), 7.23 (dd, $^3J = 5.16$, 1.23 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta = 14.2$ (CH$_3$), 22.7 (C-5), 22.9 (C-6), 25.7 (C-4), 26.1 (C-7), 60.7 (OCH$_2$), 115.3 (C-5‘), 126.4 (C-3‘), 126.9 (C-4‘), 127.6 (C-8), 136.0 (C-3), 136.1 (C-1‘), 136.2 (C-9), 137.3 (C-2), 164.5 (C=O); GC-MS (EI, 70eV): $m/z$ (%) = 292 (M$^+$, 100), 264 (8.24), 245 (29.42), 235 (6.04), 218 (30.39), 184 (8.89), 147 (3.29), 127 (4.62); HRMS (ESI): calcd for C$_{15}$H$_{10}$O$_2$S$_2$: 292.05862, found 292.059107; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 2931$ (m), 1705 (s), 1554 (w), 1529 (w), 1493 (m), 1418 (w), 1383 (w), 1336 (w), 1314 (m), 1265 (m), 1217 (s), 1179 (m), 1144 (s), 1113 (w), 1094 (w), 1078 (w), 1027 (s), 947 (w), 911 (w), 693 (s).
Ethyl-2-(4-vinylphenyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (27g):

Starting with 24 (144 mg, 0.5 mmol), boronic acid (96 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 27g was obtained as a colorless oil, (0.116 g, 75%); $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 1.02 (t, $^3J$ = 7.16 Hz, CH$_3$), 1.69-1.75 (m, 4H, CH$_2$/uni0445 2), 2.64-2.71 (m, 4H, CH$_2$/uni0445 2), 4.07 (q, $^3J$ = 7.16 Hz, CH$_2$), 5.17 (dd, $^3J = 10.89, 0.75$ Hz, 1H), 5.68 (dd, $^3J = 17.59, 0.80$ Hz, 1H), 6.63 (dd, $^3J = 17.61, 10.90$ Hz, 1H), 7.24-7.29 (m, 4H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 13.8 (CH$_3$), 22.5 (C-5), 23.0 (C-6), 25.0 (C-4), 25.7 (C-7), 60.3 (OCH$_2$), 114.1 (C-CH), 125.8 (C-3’,5’), 128.1 (C-2’,6’), 129.2 (C-8), 133.8 (C-3), 135.9 (C-1’), 136.1 (C-CH), 136.3 (C-4’), 137.1 (C-9), 145.1 (C-2), 164.8 (C=O); GC-MS (EI, 70eV): $m/z$ (%) = 312 (M$^+$, 100), 283 (10.44), 265 (20.39), 238 (13.71), 210 (5.00), 165 (5.10), 152 (5.00); HRMS (ESI): calcd for C$_{19}$H$_{20}$O$_2$S$_1$ 312.11785, found 312.117730; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 2931 (m), 1704 (s), 1627 (m), 1557 (w), 1516 (m), 1439 (m), 1303 (m), 1270 (s), 1193 (s), 1144 (s), 1094 (w), 1070 (w), 1028 (m), 987 (m), 955 (w), 939 (w), 875 (s).

Ethyl-2-m-tolyl-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (27h):

Starting with 24 (144 mg, 0.5 mmol), boronic acid (88 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 27h was obtained as a colorless oil, (0.105 g, 70%); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 0.99 (t, $^3J$ = 7.15 Hz, CH$_3$), 1.73-1.75 (m, 4H, CH$_2$/uni0445 2), 2.27 (s, CH$_3$), 2.66-2.69 (m, 4H, CH$_2$/uni0445 2), 4.05 (q, $^3J = 7.15$ Hz, CH$_2$), 7.03-7.12 (m, 4H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 13.8 (CH$_3$), 21.3 (CH$_3$), 22.5 (C-5), 23.1 (C-6), 25.0 (C-4), 25.7 (C-7), 60.2 (OCH$_2$), 126.2 (C-2’), 127.8 (C-4’), 128.1 (C-3’), 128.6 (C-8), 129.8 (C-6’), 134.3 (C-3), 135.7 (C-1’), 136.0 (C-9), 137.5 (C-5’), 145.5 (C-2), 164.9 (C=O); GC-MS (EI, 70eV): $m/z$ (%) = 300 (M$^+$, 100), 271 (11.67), 253 (35.15), 243 (5.00), 226 (19.88), 198 (7.99), 178 (5.44), 165 (5.13); HRMS (ESI): calcd for C$_{18}$H$_{20}$O$_2$S$_1$ 300.11785, found 300.117988; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 2930 (m), 1704 (s), 1603 (m), 1584 (w), 1556 (w), 1498 (m), 1440 (m), 1406 (m), 1384 (w), 1363 (w), 1348 (w), 1320 (m).
1275 (m), 1210 (s), 1178 (s), 1143 (w), 1114 (w), 1070 (w), 1033 (m), 987 (w), 956 (m), 908 (w), 780 (s).

**Ethyl-2-(2-methoxyphenyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (27i):**

Starting with 24 (144 mg, 0.5 mmol), boronic acid (98 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 27i was obtained as a colorless solid, (0.119 g, 75%) mp. 39 – 40 °C; $^1$H NMR (250 MHz, CDCl$_3$): $\delta = 0.91$ (t, $^3J = 7.15$ Hz, CH$_3$), 1.69-1.78 (m, 4H, CH$_2$/uni0445), 2.64-2.75 (m, 4H, CH$_2$/uni0445), 3.67 (s, OCH$_3$), 3.97 (q, $^3J = 7.15$ Hz, CH$_2$), 6.79-6.90 (m, 2H), 7.15-7.24 (m, 2H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta = 13.7$ (CH$_3$), 22.5 (C-5), 23.0 (C-6), 25.0 (C-4), 25.8 (C-7), 55.4 (C-OCH$_3$), 59.8 (OCH$_2$), 110.4 (C-3'), 120.2 (C-5'), 123.8 (C-1'), 129.3 (C-6'), 129.4 (C-8), 129.6 (C-4'), 130.8 (C-3), 135.8 (C-9), 141.0 (C-2), 156.5 (C-2'), 164.6 (C=O); GC-MS (EI, 70eV): $m/z$ (%) = 316 (M$^+$, 100), 285 (14.39), 271 (13.95), 255 (45.00), 243 (33.79), 228 (12.38), 209 (8.57), 165 (7.19); HRMS (ESI): calcd for C$_{18}$H$_{20}$O$_3$S, found 316.11277.

**Ethyl-2-(2,3-dimethoxyphenyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (27j):**

Starting with 24 (144 mg, 0.5 mmol), boronic acid (118 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 27j was obtained as a colorless oil, (0.120 g, 70%); $^1$H NMR (250 MHz, CDCl$_3$): $\delta = 0.91$ (t, $^3J = 7.13$ Hz, CH$_3$), 1.69-1.81 (m, 4H, CH$_2$/uni0445), 2.66-2.76 (m, 4H, CH$_2$/uni0445), 3.55 (s, OCH$_3$), 3.80 (s, OCH$_3$), 4.00 (q, $^3J = 7.13$ Hz, CH$_2$), 6.78-6.85 (m, 2H), 6.92-6.98 (m, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta = 13.6$ (CH$_3$), 22.5 (C-5), 23.0 (C-6), 25.0 (C-4), 25.7 (C-7), 55.9 (OCH$_3$), 59.9 (OCH$_3$), 60.5 (OCH$_2$), 112.4 (C-4'), 123.0 (C-6'), 123.4
(C-5’), 129.2 (C-1’), 129.6 (C-8), 135.7 (C-3), 136.0 (C-9), 140.8 (C-2), 146.7 (C-2’), 152.7 (C-3’), 164.4 (C=O); GC-MS (EI, 70eV): \( m/z \) (%) = 346 (M\(^+\), 88.09), 315 (51.60), 285 (100), 273 (21.55), 258 (15.35), 230 (12.59), 215 (5.00), 115 (5.00); HRMS (ESI): calcd for C\(_{19}\)H\(_{22}\)O\(_4\)S\(_3\) 346.12333, found 346.122952; IR (ATR, cm\(^{-1}\)): \( \tilde{\nu} \) = 2931 (m), 1705 (s), 1596 (w), 1576 (m), 1557 (w), 1497 (m), 1472 (s), 1423 (m), 1385 (w), 1363 (w), 1301 (w), 1261 (s), 1205 (s), 1146 (s), 1094 (s), 1001 (s), 963 (w), 906 (w), 867 (w), 848 (w), 743 (s).

**Ethyl-2-(2,5-dimethoxyphenyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (27k):**

Starting with 24 (144 mg, 0.5 mmol), boronic acid (118 mg, 0.65 mmol), K\(_3\)PO\(_4\) (159 mg, 0.75 mmol) and Pd(PPh\(_3\))\(_4\) (34 mg, 0.03 mmol), 27k was obtained as a colorless oil, (0.120 g, 70%); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta \) = 0.95 (t, \( \tilde{J} = \) 7.14 Hz, CH\(_3\)), 1.69-1.79 (m, 4H, CH\(_2\)/uni), 2.65-2.74 (m, 4H, CH\(_2\)/uni), 3.62 (s, OCH\(_3\)), 3.69 (s, OCH\(_3\)), 3.99 (q, \( \tilde{J} = \) 7.14 Hz, CH\(_2\)), 6.71-6.75 (m, 2H), 6.78-6.81 (m, 1H); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \( \delta \) = 13.8 (CH\(_3\)), 22.5 (C-5), 23.0 (C-6), 25.0 (C-4), 25.8 (C-7), 55.7 (OCH\(_3\)), 56.0 (OCH\(_3\)), 59.9 (OCH\(_2\)), 111.6 (C-6’), 114.1 (C-3’), 116.6 (C-4’), 124.5 (C-1’), 129.8 (C-8), 135.8 (C-3), 135.9 (C-9), 140.6 (C-2), 150.8 (C-2’), 153.2 (C-5’), 164.5 (C=O); GC-MS (EI, 70eV): \( m/z \) (%) = 346 (M\(^+\), 100), 315 (28.60), 301 (7.91), 285 (43.98), 273 (16.59), 258 (19.69), 243 (6.93), 230 (13.76); HRMS (ESI): calcd for C\(_{19}\)H\(_{22}\)O\(_4\)S\(_3\) 346.12333, found 346.122860; IR (ATR, cm\(^{-1}\)): \( \tilde{\nu} \) = 2931 (m), 1706 (s), 1615 (w), 1606 (w), 1581 (m), 1556 (w), 1484 (m), 1440 (m), 1408 (m), 1383 (w), 1360 (w), 1319 (m), 1281 (m), 1268 (m), 1219(s), 1166(s), 1112(w), 1071(w), 1022(s), 999(w), 897(w), 803(s).

**Ethyl-2-(2,6-dimethoxyphenyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (27l):**

Starting with 24 (144 mg, 0.5 mmol), boronic acid (118 mg, 0.65 mmol), K\(_3\)PO\(_4\) (159 mg, 0.75 mmol) and Pd(PPh\(_3\))\(_4\) (34 mg, 0.03 mmol), 27l was obtained as a colorless oil, (0.130 g, 75%); \(^1\)H NMR (300 MHz,
CDCl$_3$): $\delta = 0.86$ (t, $^3J = 7.14$ Hz, CH$_3$), 1.70-1.81 (m, 4H, CH$_2$), 2.67-2.79 (m, 4H, CH$_2$), 3.67 (s, OCH$_3$), 3.93 (q, $^3J = 7.09$ Hz, CH$_2$), 6.51 (d, $^3J = 8.35$ Hz, 2H), 7.19 (d, $^3J = 8.34$ Hz, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta = 12.6$ (CH$_3$), 21.6 (C-5), 22.0 (C-6), 21.7 (C-7), 54.9 (OCH$_3$), 58.4 (OCH$_2$), 102.7 (C-1’), 128.4 (C-3’,5’), 129.2 (C-8), 133.5 (C-4’), 134.4 (C-3), 135.3 (C-9), 136.4 (C-2), 157.0 (C-2’,6’), 163.1 (C=O); GC-MS (EI, 70eV): m/z (%) = 346 (M$^+$, 98.64), 315 (38.41), 301 (11.00), 285 (100), 273 (28.88), 258 (14.30), 243 (7.25), 230 (7.37), 215(8.79), 195(3.76), 115(4.61); HRMS (ESI): calcd for C$_{19}$H$_{22}$O$_2$S $346.12333$, found $346.123007$; IR (ATR, cm$^{-1}$): $\tilde{\nu} = $ 2937 (m), 1718 (s), 1597 (m), 1537 (m), 1433 (s), 1374 (m), 1294 (m), 1268 (w), 1229 (s), 1186 (w), 1172 (w), 1087 (s), 1011 (m), 974 (w), 937 (w), 906 (w), 852 (m).

Ethyl-2-(5-fluoro-2-methoxyphenyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxylate (27m):

Starting with 24 (144 mg, 0.5 mmol), boronic acid (110 mg, 0.65 mmol), K$_3$PO$_4$ (159 mg, 0.75 mmol) and Pd(PPh$_3$)$_4$ (34 mg, 0.03 mmol), 27m was obtained as a colorless oil, (0.129 g, 77%); $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 0.95$ (t, $^3J = 7.13$ Hz, CH$_3$), 1.69-1.79 (m, 4H, CH$_2$), 3.64 (s, OCH$_3$), 3.99 (q, $^3J = 7.13$ Hz, CH$_2$), 6.70-6.75 (m, 1H), 6.87-6.96 (m, 2H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta = 13.7$ (CH$_3$), 22.5 (C-5), 23.0 (C-6), 25.0 (C-4), 25.7 (C-7), 55.9 (OCH$_3$), 59.9 (OCH$_2$), 111.3 (d, $^3J_{C\text{-}F} = 8.37$ Hz, C-3’), 115.0 (d, $^2J_{C\text{-}F} = 22.58$ Hz, C-4’), 117.6 (d, $^2J_{C\text{-}F} = 23.90$ Hz, C-6’), 125.1 (d, $^3J_{C\text{-}F} = 8.29$ Hz, C-1’), 130.0 (C-8), 136.0 (C-3), 136.4 (C-9), 139.4 (C-2), 152.8 (d, $^4J_{C\text{-}F} = 2.14$ Hz, C-2’), 156.4 (d, $^1J_{C\text{-}F} = 238.76$ Hz, C-5’), 164.3 (C=O); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta = -124.42$ (s, CF); GC-MS (EI, 70eV): m/z (%) = 334 (M$^+$, 100), 303 (20.56), 273 (46.23), 261 (37.14), 246 (14.98), 227 (8.64), 218 (10.12), 183 (7.36); HRMS (ESI): calcd for C$_{18}$H$_{19}$O$_2$F$_3$S$_1$ 334.10334, found 334.103190; IR (ATR, cm$^{-1}$): $\tilde{\nu} = $ 2932 (m), 1707(s), 1610 (w), 1592 (w), 1557 (w), 1484 (s), 1438 (m), 1404 (m), 1385 (w), 1363 (w), 1348 (w), 1320 (m), 1281 (m), 1258 (m), 1233 (m), 1208 (s), 1262 (s), 1242 (s), 1095 (w), 1070 (w), 1028 (s), 954 (m), 911 (m), 867 (m).
Ethyl-2-(5-chloro-2-methoxyphenyl)-4,5,6,7-tetrahydrobenzo[\textit{b}]thiophene-3-carboxylate (27\textit{n}):  

\begin{center}
\includegraphics[width=0.8\textwidth]{chem.png}
\end{center}

**Chemical Formula:** C\textsubscript{18}H\textsubscript{19}ClO\textsubscript{3}S  
**Exact Mass:** 350.07  
Starting with 24 (144 mg, 0.5 mmol), boronic acid (121 mg, 0.65 mmol), K\textsubscript{3}PO\textsubscript{4} (159 mg, 0.75 mmol) and Pd(PPh\textsubscript{3})\textsubscript{4} (34 mg, 0.03 mmol), 27\textit{n} was obtained as a colorless oil, (0.136 g, 78%); \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ = 0.95 (t, \textit{J} = 7.13 Hz, CH\textsubscript{3}), 1.70-1.79 (m, 4H, CH\textsubscript{2}/uni0445), 2.65-2.75 (m, 4H, CH\textsubscript{2}/uni0445), 3.66 (s, OCH\textsubscript{3}), 4.00 (q, \textit{J} = 7.13 Hz, CH\textsubscript{2}), 6.71-6.74 (m, 1H), 7.15-7.19 (m, 2H); 
\textsuperscript{13}C NMR (62.9 MHz, CDCl\textsubscript{3}): δ = 13.8 (CH\textsubscript{3}), 22.5 (C-5), 23.0 (C-6), 25.0 (C-4), 25.8 (C-7), 55.7 (OCH\textsubscript{3}), 111.6 (C-3'), 125.0 (C-1'), 125.4 (C-5'), 128.8 (C-6'), 130.0 (C-8), 130.5 (C-4'), 136.0 (C-3), 136.4 (C-9), 139.2 (C-2), 155.2 (C-2'), 164.2 (C=O); GC-MS (EI, 70eV): \textit{m/z} (%) = 350 (M\textsuperscript{+}, 100), 319 (21.24), 305 (19.30), 289 (45.11), 277 (38.22), 262 (14.66), 243 (9.34), 234 (9.14); HRMS (ESI): calcd for C\textsubscript{18}H\textsubscript{19}O\textsubscript{3}35ClS: 350.07379, found 350.07287; IR (ATR, cm\textsuperscript{-1}): \textit{\nu} = 2933 (m), 1707 (s), 1594 (w), 1555 (w), 1498 (m), 1476 (m), 1437 (m), 1410 (m), 1382 (m), 1362 (w), 1348 (w), 1321 (m), 1270 (s), 1190 (s), 1147 (s), 1096 (w), 1027 (s), 955 (w), 876 (m), 806 (m).

Ethyl-2-(2,3,4-trimethoxyphenyl)-4,5,6,7-tetrahydrobenzo[\textit{b}]thiophene-3-carboxylate (27\textit{o}):  

\begin{center}
\includegraphics[width=0.8\textwidth]{chem.png}
\end{center}

**Chemical Formula:** C\textsubscript{20}H\textsubscript{24}O\textsubscript{5}S  
**Exact Mass:** 376.13  
Starting with 24 (144 mg, 0.5 mmol), boronic acid (137 mg, 0.65 mmol), K\textsubscript{3}PO\textsubscript{4} (159 mg, 0.75 mmol) and Pd(PPh\textsubscript{3})\textsubscript{4} (34 mg, 0.03 mmol), 27\textit{o} was obtained as a colorless oil, (0.131 g, 70%); \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): δ = 0.97 (t, \textit{J} = 7.14 Hz, CH\textsubscript{3}), 1.72-1.79 (m, 4H, CH\textsubscript{2}/uni0445), 2.66-2.74 (m, 4H, CH\textsubscript{2}/uni0445), 3.66 (s, OCH\textsubscript{3}), 4.00 (q, \textit{J} = 7.13 Hz, CH\textsubscript{2}), 6.71-6.74 (m, 1H), 7.15-7.19 (m, 2H); 
\textsuperscript{13}C NMR (75.4 MHz, CDCl\textsubscript{3}): δ = 13.8 (CH\textsubscript{3}), 22.5 (C-5), 23.1 (C-6), 25.0 (C-4), 25.8 (C-7), 56.0 (OCH\textsubscript{3}), 59.9 (OCH\textsubscript{3}), 60.2 (OCH\textsubscript{3}), 60.9 (OCH\textsubscript{3}), 106.7 (C-5'), 121.7 (C-1'), 125.2 (C-6'), 129.4 (C-8), 135.6 (C-3), 135.7 (C-9), 140.9 (C-2), 142.1 (C-3'), 151.4 (C-2'), 153.8 (C-4'), 164.6 (C=O); GC-MS (EI, 70eV): \textit{m/z} (%) = 376 (M\textsuperscript{+}, 100), 345 (11.75), 315 (57.03), 303 (10.94), 112
288 (7.23), 273 (8.80); HRMS (ESI): calcd for C_{20}H_{24}O_{5}S_{1} 376.13390, found 376.133274; IR (ATR, cm⁻¹): \( \tilde{\nu} = 2931 \) (m), 1706 (s), 1596 (m), 1556 (w), 1505 (m), 1461 (s), 1410 (s), 1385 (w), 1363 (w), 1348 (w), 1321 (m), 1291 (s), 1215 (m), 1196 (m), 1178 (w), 1167 (w), 1146 (m), 1099 (s), 1072 (m), 997 (m), 915 (w), 797 (m).

**General procedure for the synthesis of Lactones (28a-f) and (29a-f):**

To a dichloromethane solution of 26i-n or 27i-n (100 mg), was added BBr₃ in CH₂Cl₂ (1M solution, 4.0 equiv.) at 0 °C. The solution was warmed to 20 °C during 18 h. An aqueous solution of KOtBu (0.1 M) was added to the reaction mixture and was stirred for 15 min. The organic and the aqueous layers were separated and the latter was extracted with dichloromethane. The combined organic layers were dried (Na₂SO₄), filtered and the filtrate was concentrated in vacuo. The product was purified by silica gel column chromatography.

**4H-Thieno[2,3-c]chromen-4-one (28i):**

![Chemical Structure](image)

Chemical Formula: C_{11}H_{6}O_{2}S

Exact Mass: 202.01

Starting with 26i (100 mg, 0.4 mmol) and BBr₃ (1.6 mL, 1.6 mmol), 28i was obtained as a colorless solid (0.070 g, 86%), mp. 128–130 °C; \(^1\)H NMR (300 MHz, CDCl₃): \( \delta = 7.21-7.27 \) (m, 1H), 7.31-7.42 (m, 2H), 7.54 (d, \(^3\)J = 5.19 Hz, 1H), 7.73 (dd, \(^3\)J,\(^4\)J = 7.77, 1.40 Hz, 1H), 7.83 (d, \(^3\)J = 5.19 Hz, 1H); \(^13\)C NMR (62.9 MHz, CDCl₃): \( \delta = 116.3 \) (C-6), 116.4 (C-1), 121.3 (C-8), 122.7 (C-7), 123.3 (C-9), 123.5 (C-1’), 129.1 (C-3’), 135.8 (C-2), 143.9 (C-2’), 151.5 (C-4’), 156.1 (C=O); GC-MS (EI, 70eV): m/z (%) = 202 (M⁺, 100), 174 (36.84), 145 (15.12), 120 (3.48), 102 (12.73), 87 (4.43); HRMS (ESI): calcd for C_{11}H_{6}O_{2}S 202.00830, found 202.008620; IR (ATR, cm⁻¹): \( \tilde{\nu} = 3125 \) (w), 2921 (w), 1704 (s), 1604 (w), 1585 (w), 1529 (w), 1494 (m), 1752 (m), 1415 (m), 1384 (w), 1312 (w), 1300 (m), 1258 (m), 1202 (m), 1137 (m), 1095 (m), 1070 (m), 1037 (m), 1010 (m), 936 (w), 909 (w), 745 (s), 727 (s).

**6-Hydroxy-4H-thieno[2,3-c]chromen-4-one (28j):**

![Chemical Structure](image)

Chemical Formula: C_{11}H_{6}O_{2}S

Exact Mass: 218.00

Starting with 26j (100 mg, 0.35 mmol) and BBr₃ (1.4 mL, 1.4 mmol), 28j was obtained as a colorless solid (0.063 g, 80%), mp. 198–200 °C; \(^1\)H NMR (300 MHz, DMSO): \( \delta = 7.09 \) (dd, \(^3\)J,\(^4\)J = 8.01, 1.45 Hz, 1H), 7.23 (d,
$^{3}J = 7.91 \text{ Hz, 1H}$, $7.59 \text{ (dd,}^{3,4}J = 7.83, 1.44 \text{ Hz, 1H)}, 8.02 \text{ (d,}^{3}J = 5.19 \text{ Hz, 1H), 8.39} \text{ (d,}^{3}J = 5.17 \text{ Hz, 1H)}, 10.23 \text{ (s, OH);}^{13}\text{C NMR (62.9 MHz, DMSO):} \delta = 114.4 \text{ (C-7), 116.8 (C-1), 118.0 (C-9), 123.2 (C-8), 123.8 (C-1'), 124.7 (C-3'), 138.4 (C-4'), 140.8 (C-2), 145.3 (C-6), 145.5 (C-2'), 156.2 (C=O); GC-MS (EI, 70eV):} m/z (%) = 218 (100), 190 (13.78), 162 (16.60), 134 (26.77), 108 (5.88), 89 (7.57), 63 (5.00); HRMS (ESI): calcd for C$_{11}$H$_{6}$O$_{3}$S$_{1}$ 218.00322, found 218.003296; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 3247 (m), 3094 (w), 1678(s), 1633 (w), 1620 (w), 1556 (w), 1467 (s), 1425 (m), 1415 (m), 1351 (m), 1299 (m), 1217 (m), 1181 (m), 1157 (w), 1149 (w), 1093 (m), 1044 (s), 953 (w), 904 (w), 956 (s).

8-Hydroxy-4H-thieno[2,3-c]chromen-4-one (28k):

Starting with 26k (100 mg, 0.35 mmol) and BBr$_3$ (1.4 mL, 1.4 mmol), 28k was obtained as a colorless solid (0.06 g, 76%), mp. 187–189 °C; $^1$H NMR (300 MHz, DMSO): $\delta = 6.95 \text{ (dd,}^{3,4}J = 8.94, 2.85 \text{ Hz, 1H)}, 7.28 \text{ (d,}^{3}J = 8.94 \text{ Hz, 1H), 7.38} \text{ (d,}^{3}J = 2.82 \text{ Hz, 1H), 7.89} \text{ (d,}^{3}J = 5.19 \text{ Hz, 1H), 8.29} \text{ (d,}^{3}J = 5.16 \text{ Hz, 1H), 9.71} \text{ (s, OH);}^{13}\text{C NMR (75.4 MHz, DMSO):} \delta = 109.1 \text{ (C-9), 117.6 (C-7), 117.8 (C-1), 118.1 (C-6), 123.5 (C-1'), 123.6 (C-3'), 138.3 (C-2), 144.9 (C-4'), 145.3 (C-2'), 154.1 (C-8), 156.6 (C=O); GC-MS (EI, 70eV):} m/z (%) = 218 (100), 190 (19.41), 161 (5.62), 145 (2.83), 134 (13.32), 109 (3.75), 89 (7.58), 63 (8.25); HRMS (ESI): calcd for C$_{11}$H$_{6}$O$_{3}$S$_{1}$ (M+H) 219.01104, found 219.01043; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 3307 (m), 3117 (w), 2920 (s), 2872 (w), 1985 (s), 1858 (s), 1617 (s), 1591 (m), 1494 (m), 1467 (s), 1177 (w), 1082 (s), 916 (m), 801 (s), 769 (s).

9-Hydroxy-4H-thieno[2,3-c]chromen-4-one (28l):

Starting with 26l (100 mg, 0.35 mmol) and BBr$_3$ (1.4 mL, 1.4 mmol), 28l was obtained as a colorless solid (0.063 g, 80%), mp. 235–237 °C; $^1$H NMR (300 MHz, DMSO): $\delta = 6.91 \text{ (d,}^{3}J = 8.16 \text{ Hz, 1H), 6.96} \text{ (d,}^{3}J = 8.29 \text{ Hz, 1H), 7.39} \text{ (t,}^{3}J = 8.22 \text{ Hz, 1H), 8.20} \text{ (d,}^{3}J = 5.16 \text{ Hz, 1H), 10.96} \text{ (s, OH).}^{13}\text{C NMR (62.9 MHz, DMSO):} \delta = 106.4 \text{ (C-8), 107.3 (C-6), 110.9 (C-3'), 122.2 (C-
1), 127.1 (C-7), 13.2 (C-1’), 137.6 (C-2), 143.2 (C-2’), 153.3 (C-4’), 154.5 (C-9), 156.5 (C=O); GC-MS (EI, 70eV): \( m/z \) (%) = 218 (100), 190 (14.69), 174 (7.79), 162 (5.71), 145 (2.83), 134 (14.59), 108 (4.59), 102 (3.65), 89 (7.08); HRMS (ESI): calcd for \( \text{C}_{11}\text{H}_6\text{O}_3\text{S}_1 \) 218.00322, found 218.002985; IR (ATR, \( \text{cm}^{-1} \)): \( \tilde{\nu} \) = 3357 (m), 3093 (w), 1677 (s), 1614 (m), 1594 (m), 1520 (m), 1503 (w), 1469 (s), 1402 (m), 1345 (m), 1303 (w), 1279 (m), 1205 (w), 1171 (w), 1125 (w), 1075 (m), 1047 (m), 1024 (s), 898 (w), 790 (s), 722 (s).

**8-Fluoro-4\( H \)-thieno[2,3-\( c \)]chromen-4-one (28m):**

Starting with 26m (100 mg, 0.37mmol) and BBr\(_3\) (1.48 mL, 1.48 mmol), 28m was obtained as a colorless solid (0.065 g, 79%), mp. 163–164 °C; \(^1\)H NMR (300 MHz, DMSO): \( \delta \) = 7.09-7.16 (m, 1H), 7.34 (dd, \( J = 9.10, 4.53 \) Hz, 1H), 7.42 (dd, \( J = 8.26, 2.93 \) Hz, 1H), 7.52 (d, \( J = 5.20 \) Hz, 1H), 7.87 (d, \( J = 5.17 \) Hz, 1H); \(^{13}\)C NMR (75.4 MHz, DMSO): \( \delta \) = 109.6 (d, \( 2^J_{C-F} = 24.6 \) Hz, C-7), 117.4 (d, \( 2^J_{C-F} = 24.43 \) Hz, C-9), 118.2 (d, \( 3^J_{C-F} = 8.93 \) Hz, C-6), 119.1 (d, \( 3^J_{C-F} = 8.66 \) Hz, C-3’), 122.4 (C-1), 125.2 (C-1’), 137.1 (C-2), 144.0 (d, \( 4^J_{C-F} = 2.75 \) Hz, C-4’), 148.7 (d, \( 4^J_{C-F} = 2.17 \) Hz, C-2’), 156.8 (C=O), 159.1 (d, \( 1^J_{C-F} = 244.54 \) Hz, C-8); \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \( \delta \) = -116.93 (s, CF); GC-MS (EI, 70eV): \( m/z \) (%) = 220 (100), 192 (37.52), 163 (13.57), 147 (3.00), 138 (5.00), 120 (13.70); HRMS (ESI): calcd for \( \text{C}_{11}\text{H}_5\text{FO}_1\text{S}_1 \) 220.00, found 220.000; IR (ATR, \( \text{cm}^{-1} \)): \( \tilde{\nu} \) = 3081 (w), 2917 (w), 1713 (s), 1650 (w), 1594 (m), 1531 (m), 1496 (m), 1415 (s), 1310 (w), 1295 (m), 1269 (m), 1251(m), 1224 (w), 1174 (m), 1065 (w), 1030 (s), 971 (w), 906 (w), 773 (s).

**8-Chloro-4\( H \)-thieno[2,3-\( c \)]chromen-4-one (28n):**

Starting with 26n (100 mg, 0.35mmol) and BBr\(_3\) (1.4 mL, 1.4 mmol), 28n was obtained as a colorless solid (0.063 g, 79%), mp. 163–164 °C; \(^1\)H NMR (300 MHz, DMSO): \( \delta \) = 7.57 (d, \( 3^J = 8.85 \) Hz, 1H), 7.65 (dd, \( 3^J = 8.85, 2.39 \) Hz, 1H), 8.17 (d, \( 3^J = 5.16 \) Hz, 1H), 8.37 (d, \( 4^J = 2.37 \) Hz, 1H), 8.46 (d, \( 3^J = 5.19 \) Hz, 1H); \(^{13}\)C NMR (62.9 MHz, DMSO): \( \delta \) = 118.4 (C-1), 118.9 (C-2), 124.4 (C-2’), 137.7 (C-4’), 147.5 (C-7), 156.8 (C=O), 159.1 (d, \( 1^J_{C-F} = 244.54 \) Hz, C-8); \(^{35}\)Cl NMR (35.0 MHz, CDCl\(_3\)): \( \delta \) = 108.7 (s, Cl); GC-MS (EI, 70eV): \( m/z \) (%) = 235 (100), 190 (19.0), 174 (7.79), 162 (5.71), 145 (2.83), 134 (14.59), 108 (4.59), 102 (3.65), 89 (7.08); HRMS (ESI): calcd for \( \text{C}_{11}\text{H}_5\text{ClO}_2\text{S}_1 \) 235.97, found 235.9704; IR (ATR, \( \text{cm}^{-1} \)): \( \tilde{\nu} \) = 3081 (w), 2913 (w), 1714 (s), 1594 (m), 1520 (m), 1503 (w), 1469 (s), 1402 (m), 1345 (m), 1303 (w), 1279 (m), 1205 (w), 1171 (w), 1125 (w), 1075 (m), 1047 (m), 1024 (s), 898 (w), 790 (s), 722 (s).
6), 123.9 (C-9), 124.0 (C-7), 124.1 (C-1'), 128.8 (C-8), 130.0 (C-3'), 138.7 (C-2), 143.8 (C-2'), 150.6 (C-4'), 155.9 (C=O); GC-MS (EI, 70eV): \( m/z \) (%) = 236 (100), 208 (31.50), 173 (7.55), 145 (23.69), 136 (4.00), 119 (3.64); HRMS (ESI): calcd for \( \text{C}_{11}\text{H}_{5}\text{O}_{2}\text{Cl}_{1}\text{S}_{1} \) 235.96933, found 235.969604 and calcd for \( \text{C}_{11}\text{H}_{5}\text{O}_{2}\text{Cl}_{1}\text{S}_{1} \) 237.96638, found 237.965820; IR (ATR, cm\(^{-1}\)): \( \bar{\nu} = 3107 \) (w), 2922 (w), 1699 (s), 1606 (w), 1579 (w), 1528 (w), 1492 (m), 1428 (m), 1406 (m), 1312 (w), 1292 (m), 1261 (m), 1204 (m), 1144 (w), 1112 (w), 1084 (m), 1032 (m), 939 (m), 913 (w), 875 (m).

7,8,9,10-Tetrahydrobenzothieno[3,2-c]chromen-6-one (29i):

Starting with 27i (100 mg, 0.31 mmol) and BBr\(_3\) (1.24 mL, 1.24 mmol), 29i was obtained as a colorless solid (0.068 g, 83%), mp. 221–223 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta = 1.74-1.87 \) (m, 4H, CH\(_2\)/uni0445), 2.72-2.77 (m, 2H, CH\(_2\)), 2.94-2.98 (m, 2H, CH\(_2\)), 7.14-7.19 (m, 1H), 7.26-7.36 (m, 2H), 7.52 (dd, \( ^3\)J = 7.69, 1.08 Hz, 1H), 7.26-7.36 (m, 2H), 7.52 (dd, \( ^3\)J = 7.69, 1.08 Hz, 1H); \(^{13}\)C NMR (62.9 MHz, CDCl\(_3\)): \( \delta = 22.0 \) (C-8), 22.8 (C-9), 25.3 (C-7), 25.5 (C-10), 117.1 (C-4), 117.4 (C-2), 122.9 (C-1), 123.3 (C-3), 124.3 (C-5'), 129.5 (C-3'), 135.9 (C-2'), 137.0 (C-4'), 146.2 (C-1'), 150.8 (C-6'), 157.2 (C=O); GC-MS (EI, 70eV): \( m/z \) (%) = 256 (M\(^+\), 100), 241 (18.21), 228 (78.03), 215 (3.71), 200 (4.78), 171 (8.28), 165 (6.36); HRMS (ESI): calcd for \( \text{C}_{15}\text{H}_{12}\text{O}_{2}\text{S} \) 256.05525, found 256.054556; IR (ATR, cm\(^{-1}\)): \( \bar{\nu} = 3059 \) (w), 2922 (w), 1714 (s), 1628 (w), 1604 (m), 1584 (w), 1551 (m), 1505 (m), 1481 (s), 1454 (m), 1433 (m), 1405 (w), 1333 (m), 1317 (m), 1306 (m), 1267 (m), 1246 (w), 1216 (m), 1182 (m), 1125 (m), 1100 (m), 1067 (m), 1033 (m), 964 (m), 759 (s).

4-Hydroxy-7,8,9,10-tetrahydrobenzothieno[3,2-c]chromen-6-one (29j):

Starting with 27j (100 mg, 0.29 mmol) and BBr\(_3\) (1.16 mL, 1.16 mmol), 29j was obtained as a colorless solid (0.059 g, 75%), mp. 290–291 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta = 1.80-1.81 \) (m, 4H, CH\(_2\)/uni0445), 2.80-2.88 (m, 4H, CH\(_2\)), 7.00-7.05 (m, 1H), 7.12-7.18 (m, 2H), 10.22 (s, OH); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \( \delta = 21.4 \) (C-8), 22.2 (C-9), 24.6 (C-7), 25.4 (C-7), 25.5 (C-10), 117.1 (C-4), 117.4 (C-2), 122.9 (C-1), 123.3 (C-3), 124.3 (C-5'), 129.5 (C-3'), 135.9 (C-2'), 137.0 (C-4'), 146.2 (C-1'), 150.8 (C-6'), 157.2 (C=O); GC-MS (EI, 70eV): \( m/z \) (%) = 272 (M\(^+\), 100), 257 (18.21), 244 (78.03), 231 (3.71), 216 (4.78), 187 (8.28), 171 (6.36); HRMS (ESI): calcd for \( \text{C}_{15}\text{H}_{12}\text{O}_{3}\text{S} \) 272.05525, found 272.05556; IR (ATR, cm\(^{-1}\)): \( \bar{\nu} = 3059 \) (w), 2922 (w), 1714 (s), 1628 (w), 1604 (m), 1584 (w), 1551 (m), 1505 (m), 1481 (s), 1454 (m), 1433 (m), 1405 (w), 1333 (m), 1317 (m), 1306 (m), 1267 (m), 1246 (w), 1216 (m), 1182 (m), 1125 (m), 1100 (m), 1067 (m), 1033 (m), 964 (m), 759 (s).
25.1 (C-10), 112.9 (C-3), 116.4 (C-1), 117.4 (C-2), 122.5 (C-3’), 124.7 (C-5’), 134.9 (C-2’), 137.1 (C-6’), 139.1 (C-4’), 145.1 (C-1’), 145.9 (C-4), 155.9 (C=O); GC-MS (EI, 70eV): \( m/z \) (\%) = 272 (M\(^+\), 100), 257 (12.57), 244 (75.56), 231 (3.10), 216 (4.00), 184 (4.03), 171 (2.91), 149(5.54), 136(4.73), 115(6 .18), 95(3.87); HRMS (ESI): calcd for C\(_{15}\)H\(_{12}\)O\(_3\)S\(_1\) 272.05017, found 272.049827; IR (ATR, cm\(^{-1}\)): \( \tilde{\nu} = 3212 \) (m), 2923 (m), 1678 (s), 1612 (w), 1592 (m), 1552 (m), 1456 (w), 1435 (w), 1353 (m), 1288 (m), 1249 (w), 1214 (w), 1185 (m), 1123 (s), 1074 (m), 1019 (w), 977 (m), 925 (w), 897 (m), 852 (m), 765 (s).

### 2-Hydroxy-7,8,9,10-tetrahydrobenzothieno[3,2-c]chromen-6-one (29k):

Starting with 27k (100 mg, 0.29 mmol) and BBr\(_3\) (1.16 mL, 1.16 mmol), 29k was obtained as a colorless solid (0.059 g, 75%), mp. 245–247 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta = 1.76-1.83 \) (m, 4H, CH\(_2\)), 2.78-2.80 (m, 2H, CH\(_2\)), 2.86-2.88 (m, 2H, CH\(_2\)), 6.94 (dd, \(^3\)J = 8.86, 2.80 Hz, 1H), 6.99 (d, \(^4\)J = 2.64 Hz, 1H), 7.27 (d, \(^3\)J = 8.86 Hz, 1H), 9.79 (s, OH); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \( \delta = 21.4 \) (C-8), 22.2 (C-9), 24.6 (C-7), 25.1 (C-10), 107.1 (C-1), 116.9 (C-3), 117.8 (C-4), 118.0 (C-3’), 122.6 (C-5’), 135.0 (C-2’), 137.0 (C-4’), 143.5 (C-1’), 145.2 (C-6’), 154.0 (C-2), 156.3 (C=O); GC-MS (EI, 70eV): \( m/z \) (\%) = 272 (M\(^+\), 100), 257 (16.67), 244 (77.42), 216 (4.28), 136 (4.36), 115 (3.64), 78 (14.02), 63 (16.44); HRMS (ESI): calcd for C\(_{15}\)H\(_{12}\)O\(_3\)S\(_1\) 272.05017, found 272.049696; IR (ATR, cm\(^{-1}\)): \( \tilde{\nu} = 3185 \) (m), 2933 (m), 1671 (s), 1616 (w), 1592 (m), 1552 (m), 1499 (m), 1451 (m), 1414 (w), 1350 (w), 1275 (w), 1230 (s), 1174 (s), 1131 (s), 1068 (w), 1008 (m), 977 (m), 917 (m), 853 (s), 769 (s).

### 1-Hydroxy-7,8,9,10-tetrahydrobenzothieno[3,2-c]chromen-6-one (29l):

Starting with 27l (100 mg, 0.29 mmol) and BBr\(_3\) (1.16 mL, 1.16 mmol), 29l was obtained as a colorless solid (0.061 g, 78%), mp. 252–254 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta = 1.64-1.66 \) (m, 4H, CH\(_2\)), 2.65-2.75 (m, 4H, CH\(_2\)), 6.69 (dd, \(^3\)J = 8.16, 1.75 Hz, 1H), 6.75 (dd, \(^4\)J = 8.32, 1.75 Hz, 1H), 7.17 (t, \(^3\)J = 8.22 Hz, 1H), 7.62 (d, \(^4\)J = 7.02 Hz, 1H), 7.77 (d, \(^3\)J = 7.02 Hz, 1H), 8.13 (d, \(^4\)J = 7.02 Hz, 1H), 8.22 (d, \(^3\)J = 7.02 Hz, 1H), 8.36 (s, OH); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \( \delta = 21.4 \) (C-8), 22.2 (C-9), 24.6 (C-7), 25.1 (C-10), 107.1 (C-1), 116.9 (C-3), 117.8 (C-4), 118.0 (C-3’), 122.6 (C-5’), 135.0 (C-2’), 137.0 (C-4’), 143.5 (C-1’), 145.2 (C-6’), 154.0 (C-2), 156.3 (C=O); GC-MS (EI, 70eV): \( m/z \) (\%) = 272 (M\(^+\), 100), 257 (16.67), 244 (77.42), 216 (4.28), 136 (4.36), 115 (3.64), 78 (14.02), 63 (16.44); HRMS (ESI): calcd for C\(_{15}\)H\(_{12}\)O\(_3\)S\(_1\) 272.05017, found 272.049696; IR (ATR, cm\(^{-1}\)): \( \tilde{\nu} = 3185 \) (m), 2933 (m), 1671 (s), 1616 (w), 1596 (m), 1552 (m), 1499 (m), 1451 (m), 1414 (w), 1350 (w), 1275 (w), 1230 (s), 1174 (s), 1131 (s), 1068 (w), 1008 (m), 977 (m), 917 (m), 853 (s), 769 (s).
1H), 11.13 (s, OH); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 21.6 (C-8), 22.2 (C-9), 24.2 (C-7), 24.9 (C-10), 106.7 (C-2), 106.8 (C-4), 109.8 (C-5'), 120.4 (C-3'), 129.5 (C-3), 133.3 (C-2'), 137.6 (C-4'), 142.3 (C-1'), 151.3 (C-6'), 153.1 (C-1), 156.4 (C=O); GC-MS (EI, 70eV): $m/z$ (%) = 272 (M$^+$, 100), 257 (11.49), 244 (92.04), 231 (3.43), 216 (3.15), 136 (3.68), 116 (4.70); HRMS (ESI): calcd for C$_{15}$H$_{12}$O$_3$S$_1$ 272.05017, found 272.050064; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3330 (m), 2933 (m), 1681 (s), 1613 (m), 1597 (s), 1549 (m), 1505 (m), 1480 (s), 1414 (w), 1349 (m), 1296 (m), 1271 (m), 1221 (w), 1187 (m), 1124 (m), 1081 (w), 1061 (s), 987 (m), 957 (w), 942 (m), 782 (s), 730 (s).

2-Floro-7,8,9,10-tetrahydrobenzothieno[3,2-c]chromen-6-one (29m):

Starting with 27m (100 mg, 0.3 mmol) and BBr$_3$ (1.2 mL, 1.2 mmol), 29m was obtained as a colorless solid (0.07 g, 85%), mp. 217–218 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 1.76-1.86 (m, 4H, CH$_2$/uni0445), 2.74-2.78 (m, 2H, CH$_2$), 2.93-2.97 (m, 2H, CH$_2$), 7.00-7.06 (m, 1H), 7.17 (dd, $J$ = 2.87, 8.19 Hz, 1H), 7.24 (dd, $J$ = 4.52, 9.06 Hz, 1H). $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 21.9 (C-8), 22.7 (C-9), 25.4 (C-7), 25.5 (C-10), 108.5 (d, $^2$J$_{CF}$ = 25.04 Hz, C-3), 116.7 (d, $^2$J$_{CF}$ = 24.42 Hz, C-1), 118.2 (d, $^3$J$_{CF}$ = 9.30 Hz, C-4), 118.6 (d, $^3$J$_{CF}$ = 8.73 Hz, C-5'), 123.8 (C-3'), 136.2 (C-2'), 138.0 (C-4'), 144.9 (d, $^4$J$_{CF}$ = 6.24 Hz, C-1'), 146.9 (d, $^4$J$_{CF}$ = 2.02 Hz, C-6'), 156.9 (C=O), 158.7 (d, $^1$J$_{CF}$ = 243.9Hz, C-2); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ = -117.25 (s, CF); GC-MS (EI, 70eV): $m/z$ (%) = 274 (M$^+$, 100), 259 (21.07), 246 (75.35), 233 (4.01), 218 (4.54), 189 (8.11), 183 (5.22). HRMS (ESI): calcd for C$_{15}$H$_{11}$FO$_2$S, found 274.045300; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 2925 (m), 1720 (s), 1615 (w), 1592 (m), 1552 (m), 1492 (s), 1456 (w), 1423 (w), 1399 (m), 1334 (m), 1318 (w), 1296 (m), 1249 (m), 1202 (m), 1177 (w), 1158 (s), 1115 (s), 1023 (w), 1002 (s), 963 (s), 872 (w), 856 (m), 963 (m).

2-Chloro-7,8,9,10-tetrahydrobenzothieno[3,2-c]chromen-6-one (29n):

Starting with 27n (100 mg, 0.28 mmol) and BBr$_3$ (1.12 mL, 1.12 mmol), 29n was obtained as a colorless solid (0.067 g, 82%), mp. 205–206 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 1.86-1.95 (m, 4H, CH$_2$/uni0445), 2.74-2.78 (m, 2H, CH$_2$), 2.93-2.97 (m, 2H, CH$_2$), 7.00-7.06 (m, 1H), 7.17 (dd, $J$ = 2.87, 8.19 Hz, 1H), 7.24 (dd, $J$ = 4.52, 9.06 Hz, 1H). $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 21.9 (C-8), 22.7 (C-9), 25.4 (C-7), 25.5 (C-10), 108.5 (d, $^2$J$_{CF}$ = 25.04 Hz, C-3), 116.7 (d, $^2$J$_{CF}$ = 24.42 Hz, C-1), 118.2 (d, $^3$J$_{CF}$ = 9.30 Hz, C-4), 118.6 (d, $^3$J$_{CF}$ = 8.73 Hz, C-5'), 123.8 (C-3'), 136.2 (C-2'), 138.0 (C-4'), 144.9 (d, $^4$J$_{CF}$ = 6.24 Hz, C-1'), 146.9 (d, $^4$J$_{CF}$ = 2.02 Hz, C-6'), 156.9 (C=O), 158.7 (d, $^1$J$_{CF}$ = 243.9Hz, C-2); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ = -117.25 (s, CF); GC-MS (EI, 70eV): $m/z$ (%) = 274 (M$^+$, 100), 259 (21.07), 246 (75.35), 233 (4.01), 218 (4.54), 189 (8.11), 183 (5.22). HRMS (ESI): calcd for C$_{15}$H$_{11}$ClO$_2$S, found 290.045300; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 2925 (m), 1720 (s), 1615 (w), 1592 (m), 1552 (m), 1492 (s), 1456 (w), 1423 (w), 1399 (m), 1334 (m), 1318 (w), 1296 (m), 1249 (m), 1202 (m), 1177 (w), 1158 (s), 1115 (s), 1023 (w), 1002 (s), 963 (s), 872 (w), 856 (m), 963 (m).
CH₂x2), 2.85-2.88 (m, 2H, CH₂), 3.03-3.07 (m, 2H, CH₂), 7.31 (d, 3J = 8.82 Hz, 1H), 7.37 (dd, 3J = 8.82, 2.24 Hz, 1H), 7.58 (d, 4J = 2.19 Hz, 1H); ¹³C NMR (75.4 MHz, CDCl₃): δ = 21.9 (C-8), 22.7 (C-9), 25.4 (C-7), 25.5 (C-10), 118.5 (C-4), 118.6 (C-1), 122.3 (C-3'), 123.8 (C-3), 129.3 (C-5'), 129.6 (C-2), 136.3 (C-2'), 138.2 (C-4'), 144.6 (C-1'), 149.2 (C-6'), 156.7 (C=O); GC-MS (EI, 70eV): m/z (%) = 290 (M⁺, 100), 275 (19.04), 262 (75.72), 249 (4.46), 234 (4.00), 199 (4.00), 171 (7.66); HRMS (ESI): calcd for C₁₅H₁₁O₂ClS₁ 292.01333, found 292.013672; IR (ATR, cm⁻¹): ʋ = 2932 (m), 1722 (s), 1574 (w), 1552 (m), 1480 (s), 1449 (m), 1434 (m), 1417 (w), 1382 (m), 1349 (w), 1329 (m), 1313 (w), 1289 (m), 1257 (m), 1242 (w), 1221 (m), 1181 (m), 1132 (m), 1083 (m), 1024 (w), 993 (m), 961 (m), 819 (s).

3.2.5 Synthesis of 5-Substitutedthieno[2,3-c]pyridin-7(6H)-ones and 3-Substituted-5,6,7,8-tetrahydrobenzothieno[3,2-c]pyridin-1(2H)-ones:

General Procedure for the synthesis of compounds (32a-j) and (33a-i):

A mixture of compound 23 or 30 (1.0 equiv), acetylene (1.5 equiv), PdCl₂(PPh₃)₂ (5 mol%), CuI (5 mol%), and diisopropyl amine (DIPA) (5 mL) were added to a pressure tube under argon and then heated for 2 hours at 70 °C. After cooling, water and ethyl acetate were added and the phases were separated. The aqueous phase was then extracted with ethyl acetate (3 x 10 mL). The combined organic layers were dried (Na₂SO₄), filtered, and the filtrate was concentrated in vacuo. The residue was purified by silica gel column chromatography.

Methyl-3-(phenylethynyl)thiophene-2-carboxylate (32a):

Starting with 23 (221 mg, 1mmol), acetylene (0.164 mL, 1.5 mmol), PdCl₂(PPh₃)₂ (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 32a was obtained as a yellow oil, (175 mg, 72%); ¹H NMR (300 MHz, CDCl₃): δ = 3.85 (s, OCH₃), 7.12 (d, 3J = 5.14 Hz, 1H), 7.26-7.28 (m, 3H), 7.38 (d, 3J = 5.13 Hz, 1H), 7.49-7.52 (m, 2H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 51.1 (OCH₃), 82.9
(C-6), 94.2 (C-7), 121.8 (C-1’), 126.3 (C-4), 127.3 (C-3′,5′), 127.7 (C-4′), 129.4 (C-2′,6′), 130.8 (C-5), 131.0 (C-3), 132.3 (C-2), 160.8 (C=O); GC-MS (EI, 70 eV): m/z (%) = 242 (M+, 100), 227 (72.47), 211 (39.70), 199 (22.54), 184 (6.95), 171 (12.98), 139 (52.38), 113 (8.13), 105 (6.59), 91 (6.38); HRMS (ESI): calcd for C₁₄H₁₀O₂S₁ 242.03960, found 242.039835; IR (ATR, cm⁻¹): ~ν = 3100 (m), 2951 (w), 1702 (s), 1596 (w), 1571 (w), 1521 (m), 1505 (w), 1485 (w), 1432 (m), 1373 (m), 1353 (w), 1288 (m), 1236 (s), 1187 (w), 1097 (m), 1072 (s), 1026 (m), 1003 (w), 994 (m), 934 (m), 878 (m), 845 (m), 784 (s), 755 (s).

Methyl-3-(p-tolylethynyl)thiophene-2-carboxylate (32b):

Starting with 23 (221 mg, 1 mmol), acetylene (0.190 mL, 1.5 mmol), PdCl₂(PPh₃)₂ (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 32b was obtained as a yellow oil, (177 mg, 69%); ¹H NMR (300 MHz, CDCl₃): δ = 2.29 (s, CH₃), 3.85 (s, OCH₃), 7.09 (d, 3J = 7.91 Hz, 2H), 7.12 (d, 3J = 5.13 Hz, 1H), 7.38 (d, 3J = 5.22 Hz, 1H), 7.40 (d, 3J = 8.70 Hz, 2H); ¹³C NMR (75.4 MHz, CDCl₃): δ = 20.5 (CH₃), 51.1 (OCH₃), 82.3 (C-6), 94.6 (C-7), 118.8 (C-1’), 126.6 (C-4), 128.1 (C-3′,5′), 129.3 (C-2′,6′), 130.7 (C-5), 131.0 (C-3), 132.0 (C-2), 137.9 (C-4′), 160.8 (C=O); GC-MS (EI, 70 eV): m/z (%) = 256 (M⁺, 100), 241 (78.54), 225 (26.89), 213 (27.68), 197 (6.02), 185 (9.45), 169 (5.00), 139 (5.00), 112 (9.36), 98 (6.38); HRMS (ESI): calcd for C₁₅H₁₂O₂S₁ 256.05525, found 256.055724; IR (ATR, cm⁻¹): ~ν = 3108 (w), 2949 (w), 2206 (w), 1708 (s), 1604 (w), 1525 (m), 1502 (m), 1429 (m), 1407 (m), 1376 (m), 1284 (m), 1231 (s), 1182 (w), 1118 (w), 1094 (m), 1072 (s), 1021 (w), 999 (w), 936 (m), 893 (w), 878 (w), 814 (s), 772 (s).

Methyl-3-(o-tolylethynyl)thiophene-2-carboxylate (32c):

Starting with 23 (221 mg, 1 mmol), acetylene (0.188 mL, 1.5 mmol), PdCl₂(PPh₃)₂ (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 32c was obtained as a yellow oil, (175 mg, 68%); ¹H NMR (250 MHz, CDCl₃): δ = 2.48 (s, CH₃), 3.83 (s, OCH₃), 7.08-7.17 (m, 4H), 7.36 (d, 3J = 5.10 Hz, 1H), 7.46 (d, 3J = 5.78 Hz, 1H); ¹³C NMR
(62.9 MHz, CDCl$_3$): $\delta$ = 20.6 (CH$_3$), 52.1 (OCH$_3$), 87.6 (C-6), 94.3 (C-7), 122.6 (C-5'), 125.5 (C-1'), 127.4 (C-4), 128.8 (C-4'), 129.5 (C-3'), 130.4 (C-6'), 131.3 (C-5), 132.3 (C-3), 132.9 (C-2), 140.6 (C-2'), 161.8 (C=O); GC-MS (EI, 70eV): $m/z$ (%) = 256 (M$^+$, 43.44), 241 (43.19), 224 (55.68), 213 (100), 195 (46.03), 184 (19.01), 165 (8.16), 152 (43.70), 139 (7.64), 127 (8.04), 112 (1 3.93), 98 (7.97); HRMS (ESI): calcd for C$_{15}$H$_{12}$O$_2$S$_1$ 256.05525, found 256.055634; IR (ATR, cm$^{-1}$): $\nu$ = 2948 (w), 2205 (w), 1716 (m), 1694 (s), 1598 (w), 1454 (w), 1434 (m), 1376 (m), 1298 (m), 1283 (m), 1232 (s), 1200 (w), 1188 (w), 1158 (w), 1096 (m), 1074 (s), 1001 (m), 938 (m), 878 (w), 848 (m), 819 (w), 754 (s).

Methyl-3-((4-propylphenyl)ethynyl)thiophene-2-carboxylate (32d):

Starting with 23 (221 mg, 1mmol), acetylene (0.237 mL, 1.5 mmol), PdCl$_2$(PPh$_3$)$_2$ (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 32d was obtained as a yellow oil, (207 mg, 73%); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 0.86 (t, $^3$J = 7.38 Hz, CH$_3$), 1.57 (sext, $^3$J = 7.55 Hz, 2H), 2.52 (t, $^3$J = 7.82 Hz, 2H), 3.85 (s, OCH$_3$), 7.09 (d, $^3$J = 8.41 Hz, 2H), 7.11 (d, $^3$J = 5.15Hz, 1H), 7.37 (d, $^3$J = 5.13 Hz, 1H), 7.42 (d, $^3$J = 8.25 Hz, 2H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta$ = 12.7 (CH$_3$), 23.2 (CH$_2$), 36.9 (CH$_2$), 51.1 (OCH$_3$), 82.3 (C-6), 94.6 (C-7), 119.0 (C-1'), 127.5 (C-4), 129.3 (C-3',5'), 130.2 (C-2',6'), 130.7 (C-5), 131.0 (C-3), 131.9 (C-2), 142.7 (C-4'), 160.8 (C=O); GC-MS (EI, 70eV): $m/z$ (%) = 284 (M$^+$, 83.09), 269 (10.69), 255 (100), 240 (33.04), 184 (8.94), 170 (7.71), 152 (9.59), 139 (8.07); HRMS (ESI): calcd for C$_{17}$H$_{16}$O$_2$S$_1$ 284.08655, found 284.086871; IR (ATR, cm$^{-1}$): $\nu$ = 2953 (m), 2208 (m), 1697 (s), 1605 (w), 1530 (m), 1503 (m), 1434 (s), 1410 (m), 1379 (m), 1353 (w), 1297 (m), 1232 (s), 1188 (w), 1095 (m), 1074 (s), 1019 (w), 1001 (w), 968 (w), 939 (m), 878 (m), 839 (m), 813 (w), 790 (w), 770 (s).

Methyl-3-{{((4-methoxyphenyl)ethynyl)thiophene-2-carboxylate (32e):

Starting with 23 (221 mg, 1mmol), acetylene (0.194 mL, 1.5 mmol), PdCl$_2$(PPh$_3$)$_2$ (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 32e was obtained as a yellow oil, (192 mg, 70%); $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 3.72 (s, OCH$_3$),
3.83 (s, OCH₃), 6.78 (d, ³J = 8.88 Hz, 2H), 7.08 (d, ³J = 5.13 Hz, 1H), 7.35 (d, ³J = 5.12 Hz, 1H), 7.43 (d, ³J = 8.91 Hz, 2H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 52.1 (OCH₃), 55.2 (OCH₃), 82.9 (C-6), 95.6 (C-7), 114.0 (C-3',5'), 114.9 (C-1'), 127.8 (C-4), 130.4 (C-2',6'), 131.9 (C-5), 132.6 (C-3), 133.3 (C-2), 160.0 (C-4'), 161.9 (C=O); GC-MS (EI, 70eV): m/z (%) = 272 (M⁺, 100), 257 (68.19), 241 (14.07), 229 (11.65), 214 (9.09), 201 (8.45), 186 (6.67), 169 (19.97), 158 (5.75), 144 (5.00), 126 (6.62); HRMS (ESI): calcd for C₁₅H₁₂O₃S₁: 272.050117, found 272.050371; IR (ATR, cm⁻¹): ʋ = 3112 (w), 2953 (w), 2204 (w), 1702 (s), 1650 (w), 1601 (m), 1566 (w), 1526 (m), 1503 (m), 1466 (w), 1452 (w), 1434 (s), 1410 (m), 1373 (m), 1292 (m), 1240 (s), 1179 (m), 1170 (m), 1100 (m), 1073 (m), 1023 (m), 935 (w), 905 (w), 931 (s), 783 (s).

**Methyl-3-[(4-fluorophenyl)ethynyl]thiophene-2-carboxylate (32f):**

Starting with 23 (221 mg, 1mmol), acetylene (0.171 mL, 1.5 mmol), PdCl₂(PPh₃)₂ (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 32f was obtained as a yellow oil, (195 mg, 75%); ¹H NMR (300 MHz, CDCl₃): δ = 3.82 (s, OCH₃), 6.92-6.98 (m, 2H), 7.09 (d, ³J = 5.14 Hz, 1H), 7.36 (d, ³J = 5.16 Hz, 1H), 7.44-7.49 (m, 2H); ¹³C NMR (75.4 MHz, CDCl₃): δ = 52.1 (OCH₃), 83.7 (C-6), 94.2 (C-7), 115.7 (d, ²Jₐ-Cs = 22.09 Hz, C-3',5'), 119.0 (d, ⁴Jₐ-Cs = 2.49 Hz, C-1'), 127.3 (C-4), 130.5 (C-5), 131.9 (C-3), 133.3 (C-2), 133.7 (d, ³Jₐ-Cₐ = 8.51 Hz, C-2',6'), 161.7 (C=O), 162.8 (d, ¹Jₐ-Cₐ = 250.24 Hz, C-4'); ¹⁹F NMR (282.4 MHz, CDCl₃): δ = -110.00 (s, CF); GC-MS (EI, 70eV): m/z (%) = 260 (M⁺, 100), 245 (73.66), 229 (38.06), 217 (30.74), 202 (6.01), 189 (14.45), 157 (55.83), 131 (8.61), 114 (5.75), 100 (5.00); HRMS (ESI): calcd for C₁₄H₉FO₂S₁: 260.03018, found 260.030693; IR (ATR, cm⁻¹): ʋ = 3081 (m), 2949 (w), 2214 (w), 1711 (s), 1673 (w), 1644 (w), 1633 (w), 1599 (m), 1524 (m), 1501 (s), 1469 (w), 1454 (w), 1433 (s), 1409 (m), 1383 (m), 1303 (s), 1219 (s), 1189 (w), 1156 (m), 1102 (m), 1092 (w), 1080 (s), 1015 (w), 1005 (w), 939 (m), 848 (w), 831 (s), 770 (s).
Methyl-3-[(4-tert-butylphenyl)ethynyl]thiophene-2-carboxylate (32g):

Starting with 23 (221 mg, 1mmol), acetylene (0.270 mL, 1.5 mmol), PdCl₂(PPh₃)₂ (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 32g was obtained as a yellow oil, (210 mg, 70%); ¹H NMR (300 MHz, CDCl₃): δ = 1.25 (s, CH₃×3), 3.86 (s, OCH₃), 7.12 (d, 3J = 5.14 Hz, 1H), 7.30 (d, 3J = 8.61 Hz, 2H), 7.38 (d, 3J = 5.14 Hz, 1H), 7.44 (d, 3J = 8.61 Hz, 2H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 31.1 (CH₃×3), 34.8 (C), 52.1 (OCH₃), 83.3 (C-6), 95.5 (C-7), 117.1 (C-1’), 119.8 (C-3’,5’), 125.3 (C-4), 127.2 (C-2’,6’), 131.5 (C-5), 132.1 (C-3), 133.1 (C-2), 152.0 (C-4’), 161.9 (C=O); GC-MS (EI, 70eV): m/z (%) = 298 (M⁺, 45.24), 283 (100), 251 (16.16), 240 (5.82), 179 (6.52), 139 (5.69), 112 (12.09); HRMS (ESI): calcd for C₁₈H₁₈O₂S₁ 298.10220, found 298.102355; IR (ATR, cm⁻¹):  ν = 3106 (w), 2954 (m), 2210 (w), 1922 (w), 1805 (w), 1702 (s), 1650 (w), 1573 (w), 1528 (m), 1503 (m), 1463 (w), 1434 (s), 1409 (m), 1374 (m), 1365 (m), 1354 (w), 1288 (m), 1241 (s), 1188 (w), 1157 (w), 1117 (w), 1099 (m), 1073 (m), 1024 (w), 1015 (w), 970 (w), 895 (w), 879 (m), 846 (w), 830 (m), 784 (s).

Methyl-3-(pent-1-ynyl)thiophene-2-carboxylate (32h):

Starting with 23 (221 mg, 1mmol), acetylene (0.147 mL, 1.5 mmol), PdCl₂(PPh₃)₂ (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 32h was obtained as a yellow oil, (104 mg, 50%); ¹H NMR (300 MHz, CDCl₃): δ = 1.00 (t, 3J = 7.43 Hz, CH₃), 1.59 (sext, 3J = 7.43 Hz, CH₂), 2.39 (t, 3J = 6.99 Hz, CH₂), 3.81 (s, OCH₃), 7.00 (d, 3J = 5.10 Hz, 1H), 7.32 (d, 3J = 5.11 Hz, 1H); ¹³C NMR (75.4 MHz, CDCl₃): δ = 13.5 (C-5’), 21.7 (C-3’), 22.0 (C-4’), 52.0 (OCH₃), 75.3 (C-1’), 97.1 (C-2’), 117.1 (C-4), 128.4 (C-5), 130.1 (C-3), 132.5 (C-2), 161.9 (C=O); GC-MS (EI, 70eV): m/z (%) = 208 (M⁺, 6.45), 193 (13.59), 180 (100), 165 (17.63), 161 (8.90), 149 (18.01), 137 (11.41), 120 (7.86), 108 (7.55), 93 (6.50); HRMS (ESI): calcd for C₁₁H₁₂O₂S₁ 208.05525, found 208.055145; IR (ATR, cm⁻¹):  ν = 2955 (m), 2229 (w), 1717 (s), 1697 (s), 1524 (m), 1505 (m), 1434 (s), 1410 (s), 1377 (m), 1352 (w), 1337 (w), 1268 (m), 1242 (m), 1221 (s), 1188 (w), 1158 (w), 1072 (s), 1022 (w), 879 (m), 846 (w), 830 (m), 784 (s).
Methyl-3-(hex-1-ynyl)thiophene-2-carboxylate (32i):

Starting with 23 (221 mg, 1mmol), acetylene (0.173 mL, 1.5 mmol), PdCl$_2$(PPh$_3$)$_2$ (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 32i was obtained as a yellow oil, (115 mg, 51%); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 0.82 (t, $^3J$ = 7.20 Hz, CH$_3$), 1.29-1.45 (m, CH$_2$/uni0445$_2$), 2.17 (t, $^3J$ = 7.14 Hz, CH$_2$), 3.82 (s, OCH$_3$), 7.01 (d, $^3J$ = 5.13 Hz, 1H), 7.39 (d, $^3J$ = 5.13 Hz, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta$ = 13.4 (C-6$'$), 18.8 (C-5$'$), 21.8 (C-4$'$), 30.3 (C-3$'$), 52.1 (OCH$_3$), 75.1 (C-1$'$), 97.2 (C-2$'$), 117.1 (C-4), 130.1 (C-5), 131.2 (C-3), 132.4 (C-2), 161.1 (C=O); GC-MS (EI, 70eV): m/z (%) = 222 (M$^+$, 8.50), 207 (3.71), 193 (11.20), 180 (100), 165 (23.68), 161 (18.40), 149 (11.60), 137(17.27), 121(9.71), 108(8.37), 93(5.32); HRMS (ESI): calcd for C$_{12}$H$_{14}$O$_2$S $^{222.07090}$, found 222.071350; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 2955 (m), 2231 (w), 1723 (s), 1525 (w), 1506 (w), 1456 (w), 1435 (s), 1411 (s), 1378 (m), 1353 (m), 1317 (w), 1284 (w), 1243 (s), 1189 (w), 1158 (w), 1077 (s), 968 (w), 932 (w), 878 (m), 851 (w), 819 (w), 767 (s).

Methyl-3-(hept-1-ynyl)thiophene-2-carboxylate (32j):

Starting with 23 (221 mg, 1mmol), acetylene (0.196 mL, 1.5 mmol), PdCl$_2$(PPh$_3$)$_2$ (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 32j was obtained as a yellow oil, (131 mg, 55%); $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 0.85 (t, $^3J$ = 7.20 Hz, CH$_3$), 1.26-1.41 (m, CH$_2$/uni0445$_2$, 4H), 1.58 (quint, $^3J$ = 7.62 Hz, CH$_2$), 2.40 (t, $^3J$ = 7.13 Hz, CH$_2$), 3.83 (s, OCH$_3$), 7.02 (d, $^3J$ = 5.25 Hz, 1H), 7.39 (d, $^3J$ = 5.23 Hz, 1H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta$ = 13.9 (C-7$'$), 19.7 (C-6$'$), 22.2 (C-4$'$), 28.2 (C-5$'$), 29.6 (C-3$'$), 52.2 (OCH$_3$), 77.2 (C-1$'$), 95.1 (C-2$'$), 130.1 (C-4), 131.2 (C-5), 132.5 (C-3), 132.9 (C-2), 161.2 (C=O); GC-MS (EI, 70eV): m/z (%) = 236 (M$^+$, 19.65), 204 (12.75), 193 (13.62), 189 (14.15), 180 (100), 175 (20.73), 165 (27.46), 149 (15.64), 137 (21.02), 121 (12.32), 108 (11.16), 93 (6.51); HRMS (ESI): calcd for C$_{13}$H$_{16}$O$_2$S $^{236.08655}$, found 236.087220; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 2929 (m), 1723 (s), 1525 (w), 1456 (w), 1435 (s), 1411 (s), 1378 (m), 1353 (m), 1317 (w), 1284 (w), 1243 (s), 1189 (w), 1158 (w), 1077 (s), 968 (w), 932 (w), 878 (m), 851 (w), 819 (w), 767 (s).
2228 (w), 1720 (s), 1505 (m), 1434 (s), 1411 (s), 1377 (m), 1352 (m), 1269 (m), 1241 (s), 1189 (w), 1158 (w), 1072 (s), 967 (w), 930 (w), 877 (s), 818 (w), 765 (s).

2-(Phenylethynyl)-4,5,6,7-tetrahydrobenzo[\(b\)]thiophene-3-carbonitrile (33a):

Starting with 30 (242 mg, 1mmol), acetylene (0.164 mL, 1.5 mmol), PdCl\(_2\)(PPh\(_3\))\(_2\) (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 33a was obtained as a yellow solid, (205 mg, 77%), mp. 79–80 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 1.75-1.80 (m, 4H, CH_2/uni0445_2), 2.58-2.66 (m, 2H, CH_2/uni0445_2), 7.18-7.29 (m, 3H), 7.46-7.49 (m, 2H); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 20.8 (C-4), 21.8 (C-5), 23.4 (C-6), 23.9 (C-7), 79.0 (C-8'), 98.6 (C-7'), 113.2 (C-3), 113.4 (CN), 120.9 (C-1'), 127.4 (C-3',5'), 128.2 (C-4'), 128.4 (C-2',6'), 130.6 (C-2), 135.3 (C-8), 137.7 (C-9); GC-MS (EI, 70eV): \(m/z (\%) = 263 (M^+ 100), 235 (74.82), 190 (7.72), 145 (5.28); HRMS (ESI): calcd for C\(_{17}\)H\(_{13}\)NS (M+H) 264.0841, found 264.0840; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 2923 (s), 2215 (s), 1939 (w), 1596 (w), 1540 (m), 1494 (w), 1436 (m), 1403 (m), 1349 (w), 1337 (w), 1298 (m), 1260 (w), 1185 (w), 1144 (w), 1109 (m), 1067 (m), 1026 (m), 951 (w), 916 (m), 880 (m), 942 (w), 745 (s), 682 (s).

2-(p-Tolylethynyl)-4,5,6,7-tetrahydrobenzo[\(b\)]thiophene-3-carbonitrile (33b):

Starting with 30 (242 mg, 1mmol), acetylene (0.190 mL, 1.5 mmol), PdCl\(_2\)(PPh\(_3\))\(_2\) (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 33b was obtained as a yellow solid, (215 mg, 77%), mp. 110–112 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 1.74-1.80 (m, 4H, CH_2/uni0445_2), 2.29 (s, CH_3), 2.58-2.65 (m, 2H, CH_2x2), 7.09 (d, \(^3\)J = 7.90 Hz, 2H), 7.36 (d, \(^3\)J = 8.10 Hz, 2H); \(^{13}\)C NMR (62.9 MHz, CDCl\(_3\)): \(\delta = 21.6 (CH_3), 21.8 (C-4), 22.8 (C-5), 24.4 (C-6), 24.9 (C-7), 76.5 (C-8'), 100.0 (C-7'), 114.1 (C-3), 114.3 (CN), 118.8 (C-1'), 129.2 (C-3',5'), 129.8 (C-2',6'), 131.06 (C-2), 136.2 (C-8), 138.4 (C-4'), 13.9.5 (C-9); GC-MS (EI, 70eV): \(m/z (\%) = 277 (M^+ 100), 249 (62.06), 233 (5.00), 190 (5.00); HRMS (ESI): calcd for C\(_{18}\)H\(_{15}\)NS (M+H) 277.0920, found 277.092035; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 2931 (s), 2223 (s), 1547 (m), 1512 (w), 1504 (w), 1445 (m), 1403 (w), 1348 (w), 1294 (m), 1259 (w), 1240 (w), 1178 (w), 1141 (w), 1104 (m), 1077 (w), 1026 (m), 951 (w), 916 (m), 880 (m), 942 (w), 745 (s), 682 (s).
1041 (w), 1017 (w), 949 (w), 900 (w), 880 (m), 844 (w), 813 (s).

2-(α-Tolylethynyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonitrile (33c):

Starting with 30 (242 mg, 1mmol), acetylene (0.188 mL, 1.5 mmol), PdCl$_2$(PPh$_3$)$_2$ (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 33c was obtained as a yellow solid, (216 mg, 78%), mp. 88–89 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 1.75-1.81 (m, 4H, CH$_2$/uni0445), 2.45 (s, CH$_3$), 2.59-2.67 (m, 2H, CH$_2$/uni0445), 7.07-7.22 (m, 3H), 7.43 (d, $^3$J = 7.50Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 19.7 (CH$_3$), 20.8 (C-4), 21.8 (C-5), 23.4 (C-6), 23.9 (C-7), 82.8 (C-8′), 97.7 (C-7′), 113.2 (C-3), 113.3 (CN), 120.7 (C-5′), 124.6 (C-1′), 128.2 (C-4′), 128.6 (C-3′), 128.7 (C-6′), 130.8 (C-2), 135.3 (C-8), 137.5 (C-9), 139.5 (C-2′); GC-MS (EI, 70eV): m/z (%) = 277 (M$^+$, 100), 262 (5.26), 249 (39.98), 221 (5.15), 216 (5.88), 189 (5.36), 115 (6.71); HRMS (ESI): calcd for C$_{18}$H$_{15}$NS$_1$ 277.09197, found 277.091553; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 2917 (m), 2216 (s), 1549 (m), 1494 (w), 1461 (m), 1434 (m), 1402 (w), 1375 (w), 1347 (w), 1305 (w), 1093 (m), 1029 (m), 986 (w), 951 (w), 882 (m), 865 (w), 846 (w), 761 (s).

2-((4-Propylphenyl)ethynyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonitrile (33d):

Starting with 30 (242 mg, 1mmol), acetylene (0.237 mL, 1.5 mmol), PdCl$_2$(PPh$_3$)$_2$ (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 33d was obtained as a yellow solid, (225 mg, 73%), mp. 58–59 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 0.85 (t, $^3$J = 7.35Hz, CH$_2$), 1.56 (sext, $^3$J = 7.29 Hz, CH$_2$), 1.75-1.79 (m, 4H, CH$_2$x2), 2.53 (t, $^3$J = 7.34 Hz, CH$_3$), 2.57-2.64 (m, 2H, CH$_2$x2), 7.08 (d, $^3$J = 8.13 Hz, 2H), 7.38 (d, $^3$J = 8.19 Hz, 2H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 13.7 (CH$_3$), 21.8 (C-4), 22.8 (C-5), 24.2 (C-6), 24.4 (C-7), 24.9 (CH$_3$), 38.0 (CH$_2$), 79.5 (C-8′), 100.1 (C-7′), 114.1 (C-3), 114.3 (CN), 119.0 (C-1′), 128.6 (C-3′,5′), 129.8 (C-2′,6′), 131.6 (C-2), 136.2 (C-8), 138.4 (C-9), 144.3 (C-4′); GC-MS (EI, 70eV): m/z (%) = 305 (M$^+$, 93.52), 276 (100), 260 (5.00), 248 (22.66); HRMS (ESI): calcd for C$_{20}$H$_{19}$NS$_1$ 305.12327, found 305.123071; IR
\[ \nu = 2930 \text{ (s)}, 2221 \text{ (s)}, 1604 \text{ (w)}, 1546 \text{ (m)}, 1459 \text{ (w)}, 1434 \text{ (m)}, 1401 \text{ (w)}, 1348 \text{ (w)}, 1338 \text{ (w)}, 1293 \text{ (m)}, 1258 \text{ (w)}, 1240 \text{ (w)}, 1188 \text{ (w)}, 1178 \text{ (w)}, 1136 \text{ (w)}, 1104 \text{ (m)}, 1053 \text{ (w)}, 985 \text{ (w)}, 950 \text{ (w)}, 903 \text{ (w)}, 880 \text{ (m)}, 809 \text{ (s)}. \]

2-\{(4-Methoxyphenyl)ethynyl\}-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonitrile (33e):

Starting with 30 (242 mg, 1 mmol), acetylene (0.194 mL, 1.5 mmol), \( \text{PdCl}_2(\text{PPh}_3)_2 \) (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 33e was obtained as a yellow solid, (220 mg, 75%), mp. 88–90 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta = 1.75-1.78 \text{ (m, CH}_2\text{)} \), 2.58-2.65 (m, CH\(_2\)), 3.75 (s, OCH\(_3\)), 6.80 (d, \( ^3J = 8.91 \text{ Hz}, 2H \)), 7.41 (d, \( ^3J = 8.85 \text{ Hz}, 2H \)); \(^{13}\)C NMR (62.9 MHz, CDCl\(_3\)): \( \delta = 21.8 \text{ (C-4)}, 22.8 \text{ (C-5)}, 24.4 \text{ (C-6)}, 24.9 \text{ (C-7)}, 55.3 \text{ (OCH}_3\text{)}, 79.0 \text{ (C-8')}, 100.0 \text{ (C-7')}, 113.8 \text{ (C-3)}, 113.9 \text{ (C-3',5')}, 114.1 \text{ (C-1')}, 114.4 \text{ (CN)}, 133.3 \text{ (C-2',6')}, 134.0 \text{ (C-2)}, 136.1 \text{ (C-8)}, 138.1 \text{ (C-9)}, 160.3 \text{ (C-4')}; \text{GC-MS (EI, 70eV)}: m/z (\%) = 293 (M\(^+\), 100), 278 (12.32), 265 (36.78), 250 (9.03), 222 (6.65); HRMS (ESI): calcd for C\(_{18}\)H\(_{15}\)O\(_{}\)N\(_{}\)S\(_{}\) 293.08689, found 293.087508; IR (ATR, cm\(^{-1}\)): \( \nu = 2950 \text{ (m)}, 2839 \text{ (m)}, 2217 \text{ (s)}, 1600 \text{ (s)}, 1563 \text{ (w)}, 1547 \text{ (m)}, 1513 \text{ (w)}, 1459 \text{ (m)}, 1434 \text{ (m)}, 1401 \text{ (w)}, 1348 \text{ (w)}, 1338 \text{ (w)}, 1293 \text{ (m)}, 1258 \text{ (w)}, 1240 \text{ (w)}, 1188 \text{ (w)}, 1178 \text{ (w)}, 1136 \text{ (w)}, 1104 \text{ (m)}, 1053 \text{ (w)}, 1030 \text{ (w)}, 985 \text{ (w)}, 950 \text{ (w)}, 903 \text{ (w)}, 880 \text{ (m)}, 809 \text{ (s)}. \]

2-\{(4-Fluorophenyl)ethynyl\}-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonitrile (33f):

Starting with 30 (242 mg, 1 mmol), acetylene (0.171 mL, 1.5 mmol), \( \text{PdCl}_2(\text{PPh}_3)_2 \) (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 33f was obtained as a yellow solid, (221 mg, 75%), mp. 88–90 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta = 1.75-1.80 \text{ (m, CH}_2\text{)} \), 2.58-2.66 (m, CH\(_2\)), 6.95-7.01 (m, 2H), 7.44-7.48 (m, 2H); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \( \delta = 21.8 \text{ (C-4)}, 22.8 \text{ (C-5)}, 24.4 \text{ (C-6)}, 24.9 \text{ (C-7)}, 79.7 \text{ (C-8')}, 98.5 \text{ (C-7')}, 114.2 \text{ (C-3)}, 114.4 \text{ (CN)}, 115.8 \text{ (d, } ^2J_{\text{C-F}} = 22.31 \text{ Hz, C-3',5'}), 118.0 \text{ (d, } ^4J_{\text{C-F}} = 3.58 \text{ Hz, C-1'}), 129.2 \text{ (C-2)}, 133.7 \text{ (d, } ^3J_{\text{C-F}} = 8.46 \text{ Hz, C-2',6'}), 136.3 \text{ (C-8)}, 138.8 \text{ (C-9)}, 163.0 \text{ (d, } ^1J_{\text{C-F}} = 251.43 \text{ Hz, C-4'}). \(^{19}\)F NMR (282.4 MHz, CDCl\(_3\)): \( \delta = -
109.01 (s, CF); GC-MS (EI, 70eV): $m/z$ (%) = 281 (M$^+$, 100), 253 (82.77), 240 (5.00), 208 (8.17), 163 (6.98); HRMS (ESI): calcld for C$_{17}$H$_{12}$N$_1$F$_1$S$_1$ 281.06690, found 281.067013; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 2908 (m), 2221 (s), 1899 (w), 1598 (s), 1546 (m), 1509 (s), 1456 (m), 1433 (m), 1348 (w), 1335 (w), 1294 (w), 1259 (w), 1233 (s), 1153 (s), 1093 (m), 1025 (w), 985 (w), 950 (w), 879 (m), 833 (s).

2-{{(4-tert-Butylphenyl)ethynyl}-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carbonitrile (33g)}:

Starting with 30 (242 mg, 1mmol), acetylene (0.270 mL, 1.5 mmol), PdCl$_2$(PPh$_3$)$_2$ (35 mg, 0.05 mmol) and CuI (10 mg, 0.05 mmol), 33g was obtained as a yellow solid, (225 mg, 70%), mp. 132–134 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 1.25 (s, CH$_3$/uni0445), 1.75-1.80 (m, 4H, CH$_2$/uni0445), 2.58-2.66 (m, 2H, CH$_2$/uni0445), 7.30 (d, $^3$$J$ = 8.64 Hz, 2H), 7.41 (d, $^3$$J$ = 8.64 Hz, 2H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 21.8 (C-4), 22.8 (C-5), 24.4 (C-6), 24.9 (C-7), 31.1 (CH$_3$/uni0445), 34.9 (C), 79.5 (C-8'), 100.0 (C-7'), 114.1 (C-3), 114.3 (CN), 118.8 (C-1'), 125.4 (C-3',5'), 129.8 (C-2',6'), 131.4 (C-2), 136.2 (C-8), 138.3 (C-9), 152.6 (C-4'); GC-MS (EI, 70eV): $m/z$ (%) = 319 (M$^+$, 57.41), 304 (100), 276 (13.82), 261 (5.00), 235 (5.00), 138 (5.00), 124 (9.86); HRMS (ESI): calcld for C$_{21}$H$_{21}$N$_1$S$_1$ 319.13892, found 319.139308; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 2944 (s), 2218 (s), 1909 (w), 1790 (w), 1660 (w), 1603 (w), 1545 (m), 1505 (w), 1456 (m), 1435 (m), 1403 (m), 1361 (m), 1346 (w), 1334 (w), 1294 (m), 1264 (m), 1200 (w), 1135 (w), 1115 (m), 1095 (m), 1013 (m), 950 (m), 899 (w), 878 (m), 831 (s).

**General Procedure for the synthesis of compounds (34a-j):**

An ethanol solution (10 mL) of 32a-j (100 mg) was saturated with aqueous ammonia and heated for 10-12 hours in a pressure tube. After completion of reaction, solvent was removed under reduced pressure and the residue was purified with silica gel column chromatography.
3-(Phenylethynyl)thiophene-2-carboxamide (34a):

Starting with 32a (100 mg, 0.41 mmol), 34a was obtained as a white solid (80 mg, 86%), mp. 145–147 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 6.46\) (s, NH\(_2\)), 7.13 (d, \(^3\)J = 5.14 Hz, 1H), 7.29-7.35 (m, 3H), 7.41 (d, \(^3\)J = 5.14 Hz, 1H), 7.44-7.47 (m, 2H); \(^13\)C NMR (62.9 MHz, CDCl\(_3\)): \(\delta = 83.2\) (C-6), 96.3 (C-7), 121.3 (C-1\(\prime\)), 121.5 (C-3\(\prime\),5\(\prime\)), 128.6 (C-4\(\prime\)), 129.4 (C-4), 129.9 (C-2\(\prime\),6\(\prime\)), 131.6 (C-5), 131.7 (C-3), 140.4 (C-2), 163.1 (C=O); GC-MS (EI, 70eV): \(m/z\) (%) = 227 (M\(^+\), 100), 211 (18.92), 198 (14.33), 171 (17.87), 139 (37.31), 113 (7.99); HRMS (ESI): calcd for C\(_{13}\)H\(_9\)O\(_1\)N\(_1\)S\(_1\) 227.03994, found 227.039679; IR (ATR, cm\(^{-1}\)): \(\nu = 3428\) (m), 3131 (m), 2957 (w), 2208 (w), 1950 (w), 1656 (s), 1599 (s), 1518 (w), 1485 (m), 1469 (w), 1417 (s), 1397 (m), 1350 (m), 1279 (w), 1238 (w), 1170 (m), 1158 (w), 1127 (m), 1103 (w), 1070 (m), 1048 (w), 1029 (m), 1010 (w), 978 (m), 915 (m), 880 (m), 847 (m), 780 (m), 750 (s), 686(s).

3-(p-Tolylethynyl)thiophene-2-carboxamide (34b):

Starting with 32b (100 mg, 0.39 mmol), 34b was obtained as a white solid, (85 mg, 88%), mp. 143–144 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 2.31\) (s, CH\(_3\)), 6.51 (s, NH\(_2\)), 6.98 (d, \(^3\)J = 5.25 Hz, 1H), 7.12 (d, \(^3\)J = 7.83 Hz, 2H), 7.35 (d, \(^3\)J = 8.12 Hz, 2H), 7.41 (d, \(^3\)J = 5.25 Hz, 1H); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 21.6\) (CH\(_3\)), 82.7 (C-6), 96.7 (C-7), 110.0 (C-1\(\prime\)), 118.4 (C-3\(\prime\),5\(\prime\)), 121.6 (C-4), 129.4 (C-2\(\prime\),6\(\prime\)), 129.9 (C-5), 131.5 (C-3), 131.7 (C-4\(\prime\)), 139.9 (C-2), 163.3 (C=O); GC-MS (EI, 70eV): \(m/z\) (%) = 241 (M\(^+\), 100), 226 (16.99), 212 (20.75), 198 (5.00), 185 (5.00), 171 (8.39), 112 (5.00); HRMS (ESI): calcd for C\(_{14}\)H\(_{11}\)O\(_1\)N\(_1\)S\(_1\) 241.05559, found 241.056212; IR (ATR, cm\(^{-1}\)): \(\nu = 3439\) (m), 3143 (m), 241.05559, found 241.056212; IR (ATR, cm\(^{-1}\)): \(\nu = 3439\) (m), 3143 (m), 2201 (w), 1651 (s), 1594 (s), 1524 (w), 1501 (m), 1462 (w), 1425 (s), 1372 (m), 1349 (m), 1309 (w), 1275 (w), 1240 (w), 1211 (w), 1185 (m), 1160 (w), 1106 (m), 1089 (w), 1044 (w), 975 (m), 877 (m), 817 (s), 774 (s), 709 (s).
3-(o-Tolylethynyl)thiophene-2-carboxamide (34c):

Starting with 32c (100 mg, 0.39 mmol), 34c was obtained as a white solid, (80 mg, 85%), mp. 136–137 °C; 1H NMR (300 MHz, CDCl3): δ = 2.43 (s, CH3), 6.24 (s, NH2), 7.11-7.26 (m, 4H), 7.41-7.43 (m, 2H); 13C NMR (62.9 MHz, CDCl3): δ = 20.8 (CH3), 86.9 (C-6), 95.4 (C-7), 121.3 (C-5′), 121.6 (C-1′), 125.9 (C-4′), 129.5 (C-4), 129.8 (C-3′), 130.0 (C-6′), 131.8 (C-5), 132.1 (C-3), 140.0 (C-2′), 140.2 (C-2), 163.0 (C=O); GC-MS (EI, 70eV): m/z (%) = 241 (M+, 11.73), 224 (100), 212 (33.40), 195 (28.01), 184 (5.44), 171 (5.89), 152 (26.21), 136 (11.85), 112 (6.73), 98 (6.46); HRMS (ESI): calcd for C14H11NOS1 (M+H) 242.006341, found 242.06315; IR (ATR, cm−1): ν = 3423 (m), 3132 (m), 2202 (w), 1657(s), 1600 (s), 1557 (w), 1538 (w), 1516 (w), 1483 (m), 1416 (s), 1394 (m), 1349 (m), 1292 (w), 1271 (w), 1174 (w), 1162 (w), 1100 (m), 1073 (w), 1045 (w), 981 (m), 943 (m), 867 (w), 851 (m), 775 (s), 748 (s), 714 (s).

3-((4-Propylphenyl)ethynyl)thiophene-2-carboxamide (34d):

Starting with 32d (100 mg, 0.35 mmol), 34d was obtained as a white solid, (85 mg, 90%), mp. 158–159 °C; 1H NMR (300 MHz, CDCl3): δ = 0.87 (t, 3J = 7.40 Hz, CH3), 1.58 (sext, 3J = 7.51 Hz, 2H), 2.55 (t, 3J = 7.85 Hz, 2H), 5.95 (s, NH2), 7.12 (d, 3J = 5.16 Hz, 1H), 7.13 (d, 3J = 8.11 Hz, 2H), 7.37 (d, 3J = 8.20 Hz, 2H), 7.41 (d, 3J = 5.13 Hz, 1H); 13C NMR (62.9 MHz, CDCl3): δ = 13.7 (CH3), 24.2 (CH2), 37.9 (CH2), 82.7 (C-6), 96.6 (C-7), 118.6 (C-1′), 121.6 (C-4), 128.8 (C-3′,5′), 129.9 (C-2′,6′), 131.5 (C-5), 131.6 (C-3), 140.1 (C-4′), 144.6 (C-2), 162.9 (C=O); GC-MS (EI, 70eV): m/z (%) = 269 (M+, 59.97), 240 (100), 212 (9.71), 196 (5.00), 184 (5.00), 170 (5.0), 152 (7.56), 139 (5.00); HRMS (ESI): calcd for C16H15N1S1 269.08689, found 269.087562; IR (ATR, cm−1): ν = 3385 (m), 3134 (m), 2926 (m), 2209 (w), 1632 (s), 1608 (s), 1526 (m), 1497 (m), 1436 (s), 1398 (m), 1353 (m), 1278 (w), 1205 (w), 1186 (w), 1167 (w), 1124 (m), 1087 (m), 1072 (w), 1018 (m), 978 (s), 949 (w), 886 (w), 843 (m), 790 (s), 725 (s).
3-{(4-Methoxyphenyl)ethynyl}thiophene-2-carboxamide (34e):

Starting with 32e (100 mg, 0.36 mmol), 34e was obtained as a white solid, (77 mg, 81%), mp. 188–189 °C; 1H NMR (300 MHz, CDCl3): δ = 3.77 (s, OCH3), 6.21 (s, NH2), 6.84 (d, 3J = 8.73 Hz, 2H), 7.11 (d, 3J = 5.14 Hz, 1H), 7.39 (d, 3J = 8.77 Hz, 2H), 7.40 (d, 3J = 5.11 Hz, 1H); 13C NMR (62.9 MHz, CDCl3): δ = 55.3 (OCH3), 82.2 (C-6), 96.6 (C-7), 113.5 (C-3',5'), 114.3 (C-1'), 121.7 (C-4), 128.3 (C-2',6'), 129.9 (C-5), 131.6 (C-3), 133.1 (C-2), 160.5 (C-4'), 163.0 (C=O); GC-MS (EI, 70eV): m/z (%) = 257 (M+ , 100), 242 (81.73), 214 (15.25), 186 (9.76), 169 (12.27), 154 (5.00), 144 (4.99), 136 (5.00), 126 (5.00), 115 (5.71); HRMS (ESI): calcd for C14H11NO2S (M+H) 258.05833, found 258.05846; IR (ATR, cm⁻¹): ~ν = 3425 (m), 3130 (m), 2201 (m), 1657 (s), 1600 (s), 1567 (w), 1558 (w), 1521 (m), 1500 (m), 1453 (w), 1417 (m), 1397 (m), 1348 (m), 1296 (w), 1254 (m), 1180 (m), 1149 (w), 1126 (w), 1110 (m), 1070 (w), 1029 (m), 976 (m), 955 (w), 939 (w), 895 (w), 831 (s), 771 (s).

3-{(4-Fluorophenyl)ethynyl}thiophene-2-carboxamide (34f):

Starting with 32f (100 mg, 0.38 mmol), 34f was obtained as a white solid, (76 mg, 80%), mp. 161–162 °C; 1H NMR (300 MHz, CDCl3): δ = 6.40 (s, NH2), 6.99-7.05 (m, 2H), 7.12 (d, 3J = 5.13 Hz, 1H), 7.42 (d, 3J = 5.19 Hz, 1H), 7.44-7.47 (m, 2H); 13C NMR (75.4 MHz, CDCl3): δ = 83.0 (C-6), 95.2 (C-7), 116.0 (d, 2JCF = 22.24 Hz, C-3',5'), 117.6 (d, 4JCF = 3.64 Hz, C-1'), 121.1 (C-4), 130.0 (C-5), 131.7 (C-3), 133.6 (d, 3JCF = 8.63 Hz, C-2',6'), 140.4 (C-2), 163.0 (C=O), 163.1 (d, 1JCF = 251.75 Hz, C-4'); 19F NMR (282.4 MHz, CDCl3): δ = -108.56 (s, CF); GC-MS (EI, 70eV): m/z (%) = 245 (M+ , 100), 229 (20.27), 216 (13.21), 189 (15.69), 157 (45.34), 131 (8.54), 122 (5.00), 107 (5.00); HRMS (ESI): calcd for C13H8FNO1S1 245.10254, found 245.102721; IR (ATR, cm⁻¹): ~ν = 3429 (m), 3130 (m), 2210 (w), 1893 (w), 1657 (s), 1597 (s), 1556 (w), 1519 (m), 1499 (m), 1469 (w), 1424 (s), 1398 (m), 1349 (m), 1296 (w), 1276 (w), 1254 (m), 1180 (m), 1149 (w), 1126 (w), 1110 (m), 1070 (w), 1029 (m), 976 (m), 955 (w), 939 (w), 895 (w), 831 (s), 771 (s).
1220 (m), 1172 (w), 1154 (m), 1127 (w), 1091 (m), 1072 (w), 1014 (m), 979 (m), 957 (w), 943 (w), 880 (w), 849 (m), 932 (s).

3-{(4-tert-Butylphenyl)ethynyl}thiophene-2-carboxamide (34g):

Starting with 32g (100 mg, 0.33 mmol), 34g was obtained as a white solid, (79 mg, 84%), mp. 179–181 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 1.25\) (s, CH\(_3\) x3), 6.41 (s, NH\(_2\)), 7.12 (d, \(^3J = 5.13\) Hz, 1H), 7.33 (d, \(^3J = 8.67\) Hz, 2H), 7.39 (d, \(^3J = 5.14\) Hz, 1H), 7.39 (d, \(^3J = 8.61\) Hz, 2H); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 30.0\) (CH\(_3\)x3), 33.9 (C), 81.7(C-6), 95.6(C-7), 117.4(C-1′), 120.5(C-3′,5′), 124.6(C-4), 128.8(C-2′,6′), 130.3(C-5), 130.6(C-3), 139.2(C-2), 152.0(C-4′), 162.1 (C=O); GC-MS (EI, 70eV): 
m/z (%) = 283 (M\(^+\), 52.31), 268 (100), 251 (9.02), 240 (5.00), 179 (6.45), 112 (10.86); HRMS (ESI): calcd for C\(_{17}\)H\(_{17}\)O\(_1\)N\(_1\)S\(_1\) 283.10254, found 283.102721; IR (ATR, cm\(^{-1}\)): ~\(\nu = 3443\) (m), 3115 (m), 2954 (m), 1658 (s), 1601 (s), 1552 (w), 1524 (w), 1497 (w), 1462 (w), 1426 (m), 1397 (m), 1362 (m), 1265 (m), 1197 (w), 1170 (w), 1108 (m), 1072 (w), 1016 (m), 981 (m), 946 (w), 850 (w), 834 (s), 777 (s).

3-(Pent-1-ynyl)thiophene-2-carboxamide (34h):

Starting with 32h (100 mg, 0.48 mmol), 34h was obtained as a colorless oil, (80 mg, 86%); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 0.98\) (t, \(^3J = 7.38\) Hz, CH\(_3\)), 1.59 (sext, \(^3J = 7.21\) Hz, CH\(_2\)), 2.40(t, \(^3J = 7.07\) Hz, CH\(_2\)), 6.33 (s, NH\(_2\)), 7.01 (d, \(^3J = 5.13\) Hz, 1H), 7.35 (d, \(^3J = 5.12\) Hz, 1H); \(^{13}\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 13.6\) (C-5′), 21.5 (C-3′), 21.9 (C-4′), 75.5 (C-1′), 98.4 (C-2′), 122.3 (C-4), 129.3 (C-5), 131.9 (C-3), 139.6 (C-2), 163.6 (C=O); GC-MS (EI, 70eV): 
m/z (%) = 193 (M\(^+\), 2.63), 178 (15.08), 165 (100), 147 (4.37), 136 (14.08), 120 (5.67), 109 (6.13), 93 (5.04); HRMS (ESI): calcd for C\(_{10}\)H\(_{11}\)O\(_1\)N\(_1\)S\(_1\) (M+H) 194.06341, found 194.06375; IR (ATR, cm\(^{-1}\)): ~\(\nu = 3456\) (s), 3136 (s), 1656 (s), 1597 (s), 1501 (m), 1462 (w), 1423 (s), 1371 (m), 1350 (m), 1275 (w), 1239 (w), 1159 (w), 1131 (w), 1112 (m), 1089 (m), 1060 (w), 1014 (w), 908 (w), 875 (w), 823 (w), 767 (s).
3-(Hex-1-ynyl)thiophene-2-carboxamide (34i):

Starting with 32i (100 mg, 0.45 mmol), 34i was obtained as a colorless oil, (75 mg, 80%); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 0.88\) (t, \(^3J = 7.23\) Hz, CH\(_3\)), 1.35 (sext, \(^3J = 7.14\) Hz, CH\(_2\)), 1.65 (quint, \(^3J = 7.84\) Hz, CH\(_2\)), 2.41 (t, \(J = 7.14\) Hz, CH\(_2\)), 6.66 (s, NH\(_2\)), 7.00 (d, \(^3J = 5.13\) Hz, 1H), 7.34 (d, \(^3J = 5.13\) Hz, 1H);

\(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 13.5\) (C-6\(^{\prime}\)), 19.2 (C-5\(^{\prime}\)), 22.0 (C-4\(^{\prime}\)), 30.4 (C-3\(^{\prime}\)), 75.3 (C-1\(^{\prime}\)), 98.5 (C-2\(^{\prime}\)), 122.3 (C-4), 129.6 (C-5), 131.9 (C-3), 139.6 (C-2), 163.5 (C=O); GC-MS (EI, 70 eV): \(m/z (\%) = 207 (M^+ + 16.83), 192 (5.24), 178 (24.22), 165 (100), 147 (5.52), 136 (21.54), 121 (6.62), 109(7.49), 93(5.68); HRMS (ESI): calcd for C\(_{11}\)H\(_{13}\)NOS 207.07124, found 207.071472; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3430 \text{ (m)}, 3159 \text{ (m)}, 2929 \text{ (s)}, 2223 \text{ (m)}, 1652 \text{ (s)}, 1596 \text{ (s)}, 1519 \text{ (w)}, 1455 \text{ (w)}, 1419 \text{ (s)}, 1393 \text{ (m)}, 1348 \text{ (m)}, 1323 \text{ (w)}, 1298 \text{ (w)}, 1239 \text{ (w)}, 1209 \text{ (w)}, 1186 \text{ (w)}, 1132 \text{ (w)}, 1105 \text{ (w)}, 1071 \text{ (w)}, 1050 \text{ (w)}, 1035 \text{ (w)}, 992 \text{ (w)}, 978 \text{ (w)}, 959 \text{ (w)}, 928 \text{ (w)}, 898 \text{ (m)}, 770 \text{ (s)}, 711 \text{ (s)}.\)

3-(Hept-1-ynyl)thiophene-2-carboxamide (34j):

Starting with 32j (100 mg, 0.42 mmol), 34j was obtained as a colorless oil, (76 mg, 81%); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 0.83\) (t, \(^3J = 7.20\) Hz, CH\(_3\)), 1.24-1.37 (m, CH\(_2\)/uni0445\(_2\), 4H), 1.54 (quint, \(^3J = 7.62\) Hz, CH\(_2\)), 2.40 (t, \(J = 7.17\) Hz, CH\(_2\)) 6.67 (s, NH\(_2\)), 7.00 (d, \(^3J = 5.14\) Hz, 1H), 7.34 (d, \(^3J = 5.14\) Hz, 1H);

\(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 12.9\) (C-7\(^{\prime}\)), 18.5 (C-6\(^{\prime}\)), 21.1 (C-4\(^{\prime}\)), 27.0 (C-5\(^{\prime}\)), 30.1 (C-3\(^{\prime}\)), 74.3 (C-1\(^{\prime}\)), 97.5 (C-2\(^{\prime}\)), 121.2 (C-4), 128.6 (C-5), 130.9 (C-3), 138.6 (C-2), 162.5 (C=O); GC-MS (EI, 70 eV): \(m/z (\%) = 221 (M^+ + 27.60), 206 (5.26), 192 (10.49), 178 (39.08), 165 (100), 152 (7.25), 141 (7.74), 136 (24.86), 120 (8.56), 109 (8.75), 93 (6.29); HRMS (ESI): calcd for C\(_{12}\)H\(_{15}\)O\(_3\)N\(_3\)S\(_1\) (M+H) 222.09471, found 222.09427; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3431 \text{ (m)}, 3153 \text{ (m)}, 2926 \text{ (s)}, 2223 \text{ (w)}, 1657 \text{ (s)}, 1597 \text{ (s)}, 1538 \text{ (w)}, 1519 \text{ (w)}, 1455 \text{ (w)}, 1421 \text{ (s)}, 1394 \text{ (m)}, 1347 \text{ (m)}, 1325 \text{ (w)}, 1241 \text{ (w)}, 1110 \text{ (w)}, 1071 \text{ (w)}, 1052 \text{ (w)}, 1022 \text{ (w)}, 975 \text{ (w)}, 889 \text{ (w)}, 862 \text{ (w)}, 770 \text{ (s)}, 707 \text{ (s)}.\)
General Procedure for the synthesis of compounds (35a-g):

A solution of compound 33a-g (150 mg) in 7.0 mL of TFA–H₂SO₄ (4:1, v/v) mixture was heated at reflux (75 °C). The progress of the reaction was monitored by TLC analysis. After completion of the reaction (5 h), the reaction mixture was poured onto ice cooled water. The product thus precipitated out was filtered, washed with water and dried.

2-(Phenylethynyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide (35a):

Chemical Formula: C₁₇H₁₅NOS
Exact Mass: 281.09

Starting with 33a (150 mg, 0.57 mmol), 35a was obtained as a white solid (120 mg, 75%), mp. 178–179 °C; ¹H NMR (300 MHz, CDCl₃): δ = 1.69-1.78 (m, 4H, CH₂), 2.64-2.69 (m, 2H, CH₂), 2.79-2.83 (m, 2H, CH₂), 5.75 (s, NH₂), 7.28-7.32 (m, 3H), 7.40-7.44 (m, 2H); ¹³C NMR (75.4 MHz, CDCl₃): δ = 22.3 (C-4), 22.8 (C-5), 25.3 (C-6), 26.2 (C-7), 98.8 (C-7'), 120.2 (C-1'), 122.0 (C-8), 128.5 (C-3',5'), 129.1 (C-4'), 131.3 (C-2',6'), 136.5 (C-2), 137.0 (C-9), 138.8 (C-3), 165.1 (C=O); GC-MS (EI, 70eV): m/z (%) = 281(M⁺, 100), 266 (20.39), 253 (10.52), 234 (5.00), 225 (5.86), 202 (6.00), 176 (6.34), 105 (5.86); HRMS (ESI): calcd for C₁₇H₁₅N₂O₂S₁ 281.08689, found 281.086487; IR (ATR, cm⁻¹): ν = 3373 (m), 3173 (m), 2932 (m), 1639 (s), 1613 (m), 1573 (w), 1546 (w), 1494 (w), 1470 (m), 1433 (m), 1368 (m), 1331 (w), 1294 (m), 1254 (w), 1180 (w), 1165 (w), 1124 (w), 1097 (w), 1070 (w), 1025 (w), 997 (w), 987 (w), 953 (w), 914 (m), 883 (m), 839 (m), 751 (s).

2-(p-Tolylethynyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide (35b):

Chemical Formula: C₁₈H₁₇NOS
Exact Mass: 295.10

Starting with 33b (150 mg, 0.54 mmol), 35b was obtained as a white solid (123 mg, 77%), mp. 209–210 °C; ¹H NMR (300 MHz, CDCl₃): δ = 1.68-1.78 (m, 4H, CH₂), 2.30 (s, CH₃), 2.64-2.68 (m, 2H, CH₂), 2.79-2.83 (m, 2H, CH₂), 5.78 (s, NH₂), 7.10 (d, 3J = 7.93 Hz, 2H), 7.31 (d, 3J = 8.14 Hz, 2H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 21.5 (CH₃), 22.4 (C-4), 22.8 (C-5), 25.3 (C-6), 26.2 (C-7), 98.8 (C-7'), 118.9 (C-1'), 120.6 (C-8), 129.3 (C-3',5'), 131.2 (C-2',6'), 136.1 (C-2), 137.0 (C-4'), 138.5 (C-9), 139.4 (C-3), 165.1 (C=O); GC-MS (El,
70eV): m/z (%) = 295 (M+, 100), 280 (17.91), 267 (8.09), 252 (5.00), 239 (6.15), 203 (7.17), 176 (5.00), 139 (5.00), 119 (9.07); HRMS (ESI): calcd for C₁₈H₁₇O₁N₁S₁ 295.10254, found 295.102731; IR (ATR, cm⁻¹): P = 3374 (m), 3198 (m), 2921 (m), 1635 (s), 1614 (m), 1546 (w), 1469 (m), 1431 (m), 1366 (m), 1333 (w), 1294 (w), 1251 (w), 1179 (w), 1162 (w), 1106 (m), 1068 (w), 1021 (w), 952 (w), 941 (w), 878 (w), 833 (w), 812 (s).

2-(o-Tolylethynyl)-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide (35c):

Starting with 33c (150 mg, 0.54 mmol), 35c was obtained as a white solid, (120 mg, 75%), mp. 169–170 °C; ¹H NMR (300 MHz, CDCl₃): δ = 1.68-1.80 (m, 4H, CH₂), 2.39 (s, CH₃), 2.65-2.69 (m, 2H, CH₂), 2.79-2.83 (m, 2H, CH₂), 5.83 (s, NH₂), 7.08-7.23 (m, 3H), 7.38 (d, 3J = 7.48 Hz, 1H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 20.7 (CH₃), 22.3 (C-4), 22.8 (C-5), 25.3 (C-6), 26.2 (C-7), 85.5 (C-8'), 98.1 (C-7'), 120.6 (C-5'), 121.8 (C-1'), 125.7 (C-8), 128.4 (C-4'), 129.1 (C-3'), 129.7 (C-6'), 131.7 (C-2), 135.9 (C-9), 137.0 (C-2'), 138.7 (C-3), 165.0 (C=O); GC-MS (EI, 70eV): m/z (%) = 295(M+, 100), 278 (47.74), 267 (10.09), 250 (16.23), 234 (12.05), 221 (9.60), 202 (10.42), 178 (8.29), 165 (8.40), 139 (10.09), 119 (10.29), 115 (9.38); HRMS (ESI): calcd for C₁₈H₁₇O₁N₁S₁ 295.10254, found 295.101501; IR (ATR, cm⁻¹): P = 3363 (m), 3173 (m), 2930 (m), 1635 (s), 1614 (m), 1547 (w), 1494 (w), 1468 (m), 1434 (m), 1368 (m), 1294 (m), 1272 (w), 1252 (w), 1180 (w), 1166 (w), 1120 (m), 1040 (m), 951 (w), 939 (w), 879 (w), 817 (w), 803 (w), 749 (s).

2-{(4-Propylphenyl)ethynyl}-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide (35d):

Starting with 33d (150 mg, 0.49 mmol), 35d was obtained as a white solid, (125 mg, 79%), mp. 175–177 °C; ¹H NMR (300 MHz, CDCl₃): δ = 0.86 (t, 3J = 7.39 Hz, CH₃), 1.57 (sext, 3J = 7.44 Hz, CH₂), 1.68-1.78 (m, 4H, CH₂), 2.53 (t, 3J = 7.34 Hz, CH₃), 2.64-2.68 (m, 2H, CH₂), 2.80-2.84 (m, 2H, CH₂), 7.10 (d, 3J = 8.28 Hz, 2H), 7.33 (d, 3J = 8.22 Hz, 2H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 13.6 (CH₃), 22.4 (C-4), 24.6 (CH₃), 25.0 (C-5), 26.3 (C-7), 81.2 (C-8'), 98.1 (C-7'), 120.6 (C-5'), 121.8 (C-1'), 125.7 (C-8), 128.4 (C-4'), 129.1 (C-3'), 129.8 (C-6'), 131.7 (C-2), 135.9 (C-9), 137.0 (C-2'), 138.7 (C-3), 165.0 (C=O); GC-MS (EI, 70eV): m/z (%) = 295(M+, 100), 278 (47.74), 267 (10.09), 250 (16.23), 234 (12.05), 221 (9.60), 202 (10.42), 178 (8.29), 165 (8.40), 139 (10.09), 119 (10.29), 115 (9.38); HRMS (ESI): calcd for C₂₀H₂₁O₁N₁S₁ 323.1356, found 323.13552; IR (ATR, cm⁻¹): P = 3363 (m), 3173 (m), 2930 (m), 1635 (s), 1614 (m), 1547 (w), 1494 (w), 1468 (m), 1434 (m), 1368 (m), 1333 (w), 1294 (m), 1272 (w), 1252 (w), 1180 (w), 1166 (w), 1120 (m), 1040 (m), 951 (w), 939 (w), 879 (w), 817 (w), 803 (w), 749 (s).
22.8 (C-5), 24.2 (C-6), 25.3 (C-7), 26.2 (CH₂), 37.9 (CH₂), 81.4 (C-8’), 99.3 (C-7’),
119.1 (C-1’), 120.6 (C-8), 128.7 (C-3’,5’), 131.2 (C-2’,6’), 136.1 (C-2), 137.0 (C-9),
138.5 (C-4’), 144.2 (C-3), 165.1 (C=O); GC-MS (EI, 70eV): m/z (%) = 323 (M⁺, 100),
308 (14.56), 294 (20.25), 266 (7.19), 203 (7.53), 175 (5.00), 147 (7.04); HRMS (ESI):
calcd for C₂₀H₂₁O₁N₁S₁ 323.13384, found 323.133223; IR (ATR, cm⁻¹): \( \tilde{\nu} = 3367 \) (m),
3176 (m), 2926 (m), 1637 (s), 1613 (s), 1546 (w), 1513 (w), 1463 (m), 1433 (m),
1368 (m), 1334 (w), 1295 (m), 1251 (w), 1242 (w), 1178 (w), 1164 (w), 1095 (m),
1017 (w), 950 (w), 878 (w), 837 (m), 809 (m).

2-{{{(4-Methoxyphenyl)ethynyl}-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide (35e):}}

Starting with 33e (150 mg, 0.51 mmol), 35e was obtained as a white solid, (115 mg, 72%), mp. 212–
214 °C; \(^1\)H NMR (300 MHz, CDCl₃): \( \delta = 1.72-1.77 \) (m, 4H, CH₂/uni0445), 2.64-2.67 (m, 2H, CH₂), 2.80-2.83 (m, 2H, CH₂), 3.76 (s, OCH₃), 5.67 (s, NH₂), 6.81 (d,
\(^3\)J = 8.87 Hz, 2H), 7.36 (d, \(^3\)J = 8.85 Hz, 2H); \(^13\)C NMR (75.4 MHz, CDCl₃): \( \delta = 22.4 \) (C-4), 22.8 (C-5), 25.3 (C-6), 26.3 (C-7), 55.3 (OCH₃), 80.8 (C-8’), 99.2 (C-7’), 114.0 (C-3’,5’), 114.2 (C-1’), 120.8 (C-8), 132.9 (C-2’,6’), 135.9 (C-2), 137.0 (C-9), 138.2 (C-3), 160.3 (C-4’), 165.2 (C=O); GC-MS (EI, 70eV): m/z (%) = 311 (M⁺, 100), 296 (17.74), 283 (11.10), 268 (11.22), 156 (4.00), 121 (4.00); HRMS (ESI): calcd for
C₁₈H₁₇NO₂S 311.10528, found 311.10501; IR (ATR, cm⁻¹): \( \tilde{\nu} = 3387 \) (m),
3177 (m), 2932 (m), 2540 (w), 2203 (w), 1617 (m), 1601 (s), 1558 (w), 1543 (w),
1512 (m), 1543 (w), 1463 (m), 1431 (m), 1369 (w), 1331 (w), 1291 (m), 1249 (s), 1172 (m),
1161 (m), 1098 (m), 1022 (m), 952 (w), 877 (w), 827 (s).

2-{{{(4-Fluorophenyl)ethynyl}-4,5,6,7-tetrahydrobenzo[b]thiophene-3-carboxamide (35f):}}

Starting with 33f (150 mg, 0.53 mmol), 35f was obtained as a white solid, (110 mg, 69%), mp. 170–
172 °C; \(^1\)H NMR (300 MHz, CDCl₃): \( \delta = 1.69-1.78 \) (m, 4H, CH₂x2), 2.64-2.68 (m, 2H, CH₂), 2.78-2.82 (m, 2H, CH₂), 5.86 (s, NH₂), 6.96-7.02 (m, 2H),
7.38-7.43 (m, 2H); \(^13\)C NMR (62.9 MHz, CDCl₃): \( \delta = 22.3 \) (C-4), 22.8 (C-5), 25.3 (C-
$^6$, 26.1 (C-7), 81.7 (C-8’), 97.6 (C-7’), 115.9 (d, $^2J_{CF} = 22.27$ Hz, C-3’,5’), 118.2 (d, $^4J_{CF} = 3.57$ Hz, C-1’), 119.9 (C-8), 133.3 (d, $^3J_{CF} = 8.58$ Hz, C-2’,6’), 136.6 (C-2), 136.9 (C-9), 138.9 (C-3), 163.0 (d, $^1J_{CF} = 250.89$ Hz, C-4’), 165.1 (C=O); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta = -109.18$ (s, CF); GC-MS (EI, 70eV): m/z (%) = 299 (M$^+$, 100), 284 (20.93), 271 (10.67), 243 (7.41), 220 (5.99), 183 (5.00), 176 (6.05), 163 (5.00), 123 (8.93); HRMS (ESI): calcd for C$_{17}$H$_{14}$O$_1$N$_1$F$_1$S$_1$ 299.07746, found 299.077653; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3362 (m), 3174 (m), 2932 (m), 1638 (s), 1615 (m), 1598 (m), 1546 (w), 1510 (m), 1468 (m), 1434 (m), 1368 (w), 1334 (w), 1294 (w), 1226 (s), 1180 (w), 1153 (m), 1093 (m), 1012 (w), 951 (w), 879 (w), 830 (s).

2-{(4-tert-Butylphenyl)ethynyl}-4,5,6,7-tetrahydrobenzof[b]thiophene-3-carboxamide (35g):

Starting with 33g (150 mg, 0.47 mmol), 35g was obtained as a white solid, (113 mg, 71%), mp. 149–150 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 1.25$ (s, CH$_3$×3), 1.72-1.75 (m, 4H, CH$_2$×2), 2.60-2.66 (m, 2H, CH$_2$), 2.80-2.82 (m, 2H, CH$_2$), 5.74 (s, NH$_2$), 7.31 (d, $^3J = 8.70$ Hz, 2H), 7.36 (d, $^3J = 8.67$ Hz, 2H); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta = 22.4$ (C-4), 22.8 (C-5), 25.4 (C-6), 26.3 (C-7), 31.1 (CH$_3$×3), 34.9 (C), 81.4 (C-8’), 99.2 (C-7’), 118.9 (C-1’), 120.6 (C-3’,5’), 125.5 (C-8), 131.1 (C-2’,6’), 136.2 (C-2), 137.0 (C-9), 138.5 (C-3), 152.6 (C-4’), 165.2 (C=O); GC-MS (EI, 70eV): m/z (%) = 337 (M$^+$, 100), 322 (30.42), 304 (10.76), 294 (5.30), 280 (5.34), 203 (6.29), 147 (6.00); HRMS (ESI): calcd for C$_{21}$H$_{23}$N$_1$O$_1$S$_1$ (M+H) 338.15731, found 338.15713; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3452 (m), 3154 (m), 2925 (m), 1665 (s), 1596 (m), 1537 (w), 1504 (w), 1454 (m), 1415 (m), 1360 (m), 1291 (m), 1265 (w), 1250 (m), 1193 (w), 1163 (w), 1112 (m), 1087 (w), 1025 (w), 1015 (w), 956 (w), 878 (w), 830 (s).

General Procedure for the synthesis of compounds (36a-j) and (37a-g):

To the methanol solution of compounds 34a-j or 35a-g (100 mg), was added Sodium methoxide (150 mg, 2.77 mmol) and was refluxed for 3-4 hours. After completion of reaction, methanol was removed under reduced pressure and the residue was diluted with water. The precipitate so formed was filtered, dried and recrystallized from MeOH.
5-Phenylthieno[2,3-c]pyridin-7(6H)-one (36a):

Starting with compound 34a (100 mg, 0.44 mmol) and NaOMe (150 mg, 2.77 mmol), 36a was obtained as a white solid (75 mg, 75%), mp. 169–170 °C; \(^1^H\) NMR (300 MHz, CDCl\(_3\)): \(\delta = 6.88 (s, CH), 7.21 (d, J = 5.16 \text{ Hz}, 1H), 7.39-7.47 (m, 3H), 7.64-7.67 (m, 2H), 7.67 (d, J = 5.18 Hz, 1H), 10.53 (s, NH); \(^1^3^C\) NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 100.6 (C-4), 123.6 (C-3), 125.3 (C-4'), 127.3 (C-2',6'), 128.2 (C-3',5'), 128.5 (C-1'), 132.9 (C-5), 133.1 (C-9), 140.6 (C-2), 146.0 (C-8), 159.0 (C=O); GC-MS (EI, 70eV): \(m/z\) (%) = 227 (M\(^+\), 100), 198 (4.25), 171 (11.88), 149 (5.68), 121 (3.28), 95 (4.52); HRMS (ESI): calcd for C\(_{13}\)H\(_9\)NO\(_1\)S\(_1\) 227.03994, found 227.040380; IR (ATR, cm\(^{-1}\)): \(\nu = 3143 (w), 2917 (w), 1650 (s), 1613 (w), 1600 (w), 1576 (w), 1558 (w), 1538 (w), 1498 (s), 1448 (w), 1425 (w), 1355 (w), 1307 (w), 1259 (m), 1207 (w), 1185 (m), 1157 (w), 1131 (m), 1095 (w), 1078 (w), 1053 (m), 1029 (w), 967 (w), 920 (w), 879 (m), 832 (m), 810 (s).

5-p-Tolylthieno[2,3-c]pyridin-7(6H)-one (36b):

Starting with compound 34b (100 mg, 0.41 mmol) and NaOMe (150 mg, 2.77 mmol), 36b was obtained as a white solid, (77 mg, 77%), mp. 254–255 °C; \(^1^H\) NMR (300 MHz, CDCl\(_3\)): \(\delta = 2.35 (s, CH\(_3\)), 6.85 (s, CH), 7.18-7.25 (m, 3H), 7.49 (d, J = 8.13 Hz, 2H), 7.68 (d, J = 5.14 Hz, 1H), 9.72 (s, NH); \(^1^3^C\) NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 21.2 (CH\(_3\)), 101.2 (C-4), 124.7 (C-3), 126.0 (C-3',5'), 130.1 (C-2',6'), 134.1 (C-1'), 135.3 (C-4'), 137.1 (C-5), 139.9 (C-9), 141.4 (C-2), 147.2 (C-8), 159 (C=O); GC-MS (EI, 70eV): \(m/z\) (%) = 241 (M\(^+\), 100), 226 (3.15), 212 (2.51), 197 (2.07), 184 (2.65), 171 (4.01), 149 (4.06), 121 (3.13), 95 (4.08); HRMS (ESI): calcd for C\(_{14}\)H\(_{11}\)NO\(_1\)S\(_1\) (M+H) 242.06341, found 242.06378; IR (ATR, cm\(^{-1}\)): \(\nu = 3135 (w), 2914 (w), 2914 (s), 1613 (m), 1568 (w), 1511 (m), 1471 (m), 1453 (w), 1303 (w), 1280 (w), 1185 (m), 1153 (w), 1131 (m), 1109 (w), 1057 (w), 1043 (m), 1020 (w), 935 (w), 892 (m), 852 (m), 830 (m), 805 (s).
5-o-Tolylthieno[2,3-c]pyridin-7(6H)-one (36c):

Starting with compound 34c (100 mg, 0.41 mmol) and NaOMe (150 mg, 2.77 mmol), 36c was obtained as a white solid, (77 mg, 77%), mp. 160–161 °C; \(^1\)H NMR (250 MHz, CDCl\(_3\)): \(\delta = 2.31\) (s, CH\(_3\)), 6.59 (s, CH), 7.21-7.31 (m, 5H), 7.70 (d, \(^3\)J = 5.15 Hz, 1H), 9.49 (s, NH); \(^{13}\)C NMR (62.9 MHz, CDCl\(_3\)): \(\delta = 20.0\) (CH\(_3\)), 29.6 (C-4), 104.0 (C-3), 124.5 (C-5), 126.2 (C-6), 129.3 (C-4'), 129.6 (C-3'), 130.9 (C-1'), 134.1 (C-2'), 134.3 (C-5), 136.0 (C-9), 141.4 (C-2), 146.8 (C-8), 159.2 (C=O); GC-MS (EI, 70eV): \(m/z\) (%) = 240 (M\(^+\), 100), 222 (15.88), 212 (4.32), 195 (3.19), 184 (4.06), 152 (4.05), 95 (4.66); HRMS (ESI): calcd for C\(_{14}\)H\(_{11}\)NO\(_2\)S (M+H) 242.06341, found 242.06299; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3451\) (w), 3255 (w), 3126 (w), 3017 (w), 2920 (w), 2851 (w), 1608 (s), 1557 (m), 1524 (w), 1487 (w), 1454 (w), 1403 (w), 1370 (w), 1307 (w), 1292 (w), 1276 (w), 1261 (w), 1159 (w), 1131 (m), 1106 (m), 1039 (m), 939 (w), 880 (m), 859 (w), 830 (m), 756 (s), 715 (s).

5-(4-Propylphenyl)thieno[2,3-c]pyridin-7(6H)-one (36d):

Starting with compound 34d (100 mg, 0.37 mmol) and NaOMe (150 mg, 2.77 mmol), 36d was obtained as a white solid, (72 mg, 72%), mp. 198–199 °C; \(^1\)H NMR (250 MHz, CDCl\(_3\)): \(\delta = 0.90\) (t, \(^3\)J = 7.37 Hz, CH\(_3\)), 1.61(sext, \(^3\)J = 7.26 Hz, CH\(_2\)), 2.58 (t, \(^3\)J = 7.91 Hz, CH\(_2\)), 6.86 (s, CH), 7.19 (d, \(^3\)J = 5.21 Hz, 1H), 7.24 (d, \(^3\)J = 8.28 Hz, 2H), 7.58 (d, \(^3\)J = 8.30 Hz, 2H), 7.66 (d, \(^3\)J = 5.15 Hz, 1H), 10.74 (s, NH); \(^{13}\)C NMR (62.9 MHz, CDCl\(_3\)): \(\delta = 13.8\) (CH\(_3\)), 24.3 (CH\(_2\)), 37.7 (CH\(_2\)), 101.2 (C-4), 124.6 (C-3), 126.2 (C-3',5'), 127.9 (C-2',6'), 129.3 (C-1'), 131.4 (C-5), 133.9 (C-9), 141.8 (C-4'), 144.5 (C-2), 147.2 (C-8), 160.1 (C=O); GC-MS (EI, 70eV): \(m/z\) (%) = 269 (M\(^+\), 71.38), 240 (100), 225 (2.02), 210 (3.35), 184 (3.79), 152 (2.44); HRMS (ESI): calcd for C\(_{16}\)H\(_{15}\)NO\(_2\)S \(269.08689\), found \(269.087494\); IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3451\) (w), 3260 (w), 2951 (w), 2866 (w), 1622 (s), 1601 (m), 1564 (w), 1539 (w), 1514 (m), 1464 (w), 1455 (w), 1433 (w), 1423 (w), 1395 (w), 1349 (w), 1306 (w), 1294 (w), 1273 (w), 1187 (m), 1131 (m), 1107 (w), 964 (w), 949 (w), 884 (m), 834 (m), 796 (s).
5-(4-Methoxyphenyl)thieno[2,3-c]pyridin-7(6H)-one (36e):

Starting with compound 34e (100 mg, 0.39 mmol) and NaOMe (150 mg, 2.77 mmol), 36e was obtained as a white solid, (76 mg, 76%), mp. 141–142 °C; $^1$H NMR (250 MHz, CDCl$_3$): $\delta$ = 3.81 (s, OCH$_3$), 6.87 (s, CH), 6.96 (d, $^3J = 8.88$ Hz, 2H), 7.22 (d, $^3J = 5.18$ Hz, 1H), 7.58 (d, $^3J = 6.78$ Hz, 2H), 7.71 (d, $^3J = 5.15$ Hz, 1H), 10.31 (s, NH); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 55.4 (OCH$_3$), 101.4 (C-4), 114.8 (C-3′,5′), 124.6 (C-3), 126.2 (C-1′), 127.5 (C-2′,6′), 131.4 (C-5), 134.5 (C-9), 141.3 (C-2), 147.6 (C-8), 159.6 (C-4′), 160.9 (C=O); GC-MS (EI, 70eV): m/z (%) = 257 (M$^+$, 100), 242 (23.61), 214 (21.33), 187 (4.84), 128 (3.19), 115 (6.89), 95 (3.95); HRMS (ESI): calcd for C$_{14}$H$_{11}$O$_2$N$_1$S$_1$ 257.05050, found 257.051041; IR (ATR, cm$^{-1}$): $\nu$ = 3255 (w), 3129 (w), 3071 (w), 2831 (w), 1620 (m), 1604 (s), 1556 (w), 1530 (w), 1514 (s), 1468 (w), 1454 (w), 1435 (w), 1394 (w) 1360 (w), 1313 (w), 1287 (m), 1248 (s), 1202 (w), 1179 (m), 1133 (m), 1062 (w), 1044 (m), 937 (w), 921 (w), 882 (m), 856 (m), 812 (s).

5-(4-Fluorophenyl)thieno[2,3-c]pyridin-7(6H)-one (36f):

Starting with compound 34f (100 mg, 0.41 mmol) and NaOMe (150 mg, 2.77 mmol), 36f was obtained as a white solid, (75 mg, 75%), mp. 279–280 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 7.03 (s, CH), 7.32-7.37 (m, 2H), 7.42 (d, $^3J = 5.13$ Hz, 1H), 7.79-7.84 (m, 2H), 8.08 (d, $^3J = 5.11$ Hz, 1H), 11.76 (s, NH); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta$ = 100.9 (C-4), 115.6 (d, $^2J_{C-F} = 21.71$ Hz, C-3′,5′), 125.2 (C-3), 127.8 (C-5), 129.2 (d, $^3J_{C-F} = 8.59$ Hz, C-2′,6′), 130.4 (d, $^4J_{C-F} = 3.06$ Hz, C-1′), 134.3 (C-9), 140.9 (C-2), 146.3 (C-8), 158.9 (C=O), 162.6 (d, $^1J_{C-F} = 246.84$ Hz, C-4′); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ = -112.33 (s, CF); GC-MS (EI, 70eV): m/z (%) = 245 (M$^+$, 100), 218 (5.79), 189 (13.81), 172 (2.00), 149 (5.75), 122 (3.77), 95 (9.90); HRMS (ESI): calcd for C$_{13}$H$_8$F$_2$NOS 245.03051, found 245.030396; IR (ATR, cm$^{-1}$): $\nu$ = 3271 (w), 3146 (w), 3043 (w), 1650 (s), 1615 (m), 1557 (w), 1526 (w), 1506 (s), 1455 (w), 1434 (w), 1424 (w), 1394 (w), 1372 (w), 1360 (w), 1307 (w), 1276 (m), 1221 (s), 1160 (s), 1133 (m), 1107 (m), 1048 (s), 1014 (w), 937 (w), 911 (m), 882 (m), 856 (m), 812 (s).
5-(4-tert-Butylphenyl)thieno[2,3-c]pyridin-7(6H)-one (36g):

Starting with compound 34g (100 mg, 0.35 mmol) and NaOMe (150 mg, 2.77 mmol), 36g was obtained as a white solid, (70 mg, 70%), mp. 246–247 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 1.25 \) (s, CH\(_3\times3\)), 6.87 (s, CH), 7.21 (d, \(^3J = 5.17\) Hz, 1H), 7.45 (d, \(^3J = 8.58\) Hz, 2H), 7.58 (d, \(^3J = 8.61\) Hz, 2H), 7.67 (d, \(^3J = 5.12\) Hz, 1H), 10.26 (s, NH); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 31.2\) (CH\(_3\times3\)), 34.8 (C), 101.3 (C-4), 124.7 (C-3), 125.9 (C-3',5'), 126.3 (C-2',6'), 131.1 (C-1'), 134.0 (C-5), 135.3 (C-9), 141.5 (C-2), 147.2 (C-8), 153.0 (C-4'), 159.9 (C=O); GC-MS (EI, 70eV): \(m/z\) (%) = 283 (M^+ , 64.82), 268 (100), 252 (3.87), 240 (11.60), 210 (3.17), 120 (11.02); HRMS (ESI): calcd for C\(_{17}\)H\(_{17}\)NOS \(M+H\) 284.11036, found 284.10983; IR (ATR, cm\(^{-1}\)): \(\nu = 3261\) (w), 3139 (w), 3040 (w), 2958 (m), 2865 (w), 1626 (s), 1605 (m), 1562 (w), 1537 (w), 1517 (m), 1461 (m), 1423 (w), 1392 (w), 1361 (m), 1305 (w), 1266 (m), 1201 (w), 1126 (m), 1058 (w), 1042 (m), 1016 (w), 950 (w), 906 (m), 887 (m), 839 (m).

5-Propylthieno[2,3-c]pyridin-7(6H)-one (36h):

Starting with compound 34h (100 mg, 0.52 mmol) and NaOMe (150 mg, 2.77 mmol), 36h was obtained as a white solid, (75 mg, 75%), mp. 95–96 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 0.93\) (t, \(^3J = 7.41\) Hz, CH\(_3\)), 1.70 (sext, \(^3J = 7.34\) Hz, CH\(_2\)), 2.60 (t, \(^3J = 7.69\) Hz, CH\(_2\)), 6.42 (s, CH), 7.09 (d, \(^3J = 5.15\) Hz, 1H), 7.60 (d, \(^3J = 5.15\) Hz, 1H), 11.99 (s, NH); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 13.5\) (C-3'), 22.0 (C-2'), 35.0 (C-1'), 101.5 (C-4), 124.1 (C-3), 126.8 (C-9), 133.3 (C-5), 144.2 (C-2), 147.4 (C-8), 161.1 (C=O); GC-MS (EI, 70eV): \(m/z\) (%) = 193 (M^+ , 66.47), 178 (22.19), 165 (100), 151 (4.49), 137 (45.61), 122 (7.17), 109 (14.29), 95 (12.45), 69 (8.13); HRMS (ESI): calcd for C\(_{10}\)H\(_{11}\)NOS \(M+H\) 193.05559, found 193.05538; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3130\) (w), 3059 (w), 2957 (w), 2866 (w), 2800 (w), 1632 (s), 1557 (w), 1524 (m), 1471 (m), 1453 (m), 1427 (w), 1377 (m), 1313 (w), 1228 (w), 1165 (m), 1129 (m), 1077 (m), 1048 (s), 995 (w), 911 (m), 858 (w), 830 (m), 807 (m), 784 (m).

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5-Butylthieno[2,3-c]pyridin-7(6H)-one (36i):

Starting with compound 34i (100 mg, 0.48 mmol) and NaOMe (150 mg, 2.77 mmol), 36i was obtained as a white solid, (73 mg, 73%), mp. 114–115 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 0.83\) (t, \(J = 7.34\) Hz, CH\(_3\)), 1.35 (sext, \(^3\)J = 3 Hz, CH\(_2\)), 1.65 (quint, \(^3\)J = 7.84 Hz, CH\(_2\)), 2.61 (t, \(^3\)J = 7.83 Hz, CH\(_2\)), 6.46 (s, CH), 7.11 (d, \(^3\)J = 5.14 Hz, 1H), 7.64 (d, \(^3\)J = 5.14 Hz, 1H), 11.32 (s, NH); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 13.7\) (C-4'), 22.1 (C-3'), 30.8 (C-2'), 30.9 (C-1'), 32.9 (C-4), 101.9 (C-3), 124.1 (C-9), 133.8 (C-5), 144.0 (C-2), 147.6 (C-8), 160.5 (C=O); GC-MS (EI, 70eV): m/z (%) = 207 (M⁺, 47.17), 192 (3.95), 178 (11.17), 165 (100), 137 (24.22), 122 (7.72), 109 (6.58), 95 (8.04); HRMS (ESI): calcd for C\(_{11}\)H\(_{13}\)NO\(_1\)S\(_1\) 207.07124, found 207.071762; IR (ATR, cm\(^{-1}\)): \(\nu = 3454\) (w), 3267 (w), 2957 (m), 2930 (m), 2860 (m), 1615 (s), 1552 (w), 1528 (m), 1463 (m), 1427 (m), 1372 (m), 1326 (m), 1281 (m), 1259 (w), 1227 (w), 1124 (w), 1101 (w), 1087 (m), 1047 (m), 1016 (m), 981 (w), 894 (m), 848 (m), 835 (m), 773 (s), 722 (s).

5-Pentylthieno[2,3-c]pyridin-7(6H)-one (36j):

Starting with compound 34j (100 mg, 0.45 mmol) and NaOMe (150 mg, 2.77 mmol), 36j was obtained as a white solid, (70 mg, 70%), mp. 142–143 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta = 0.83\) (t, \(^3\)J = 7.05 Hz, CH\(_3\)), 1.28-1.33 (m, CH\(_2\)/uni0445 2, 4H), 1.67 (quint, \(^3\)J = 7.62 Hz, CH\(_2\)), 2.60 (t, \(J = 7.83\) Hz, CH\(_2\)), 6.42 (s, CH), 7.09 (d, \(^3\)J = 5.16 Hz, 1H), 7.60 (d, \(^3\)J = 5.11 Hz, 1H), 11.62 (s, NH); \(^13\)C NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 13.9\) (C-5'), 22.3 (C-4'), 28.4 (C-2'), 31.1 (C-3'), 33.2 (C-1'), 101.4 (C-4), 124.1 (C-3), 131.3 (C-9), 133.4 (C-5), 144.3 (C-2), 147.4 (C-8), 160.9 (C=O); GC-MS (EI, 70eV): m/z (%) = 221 (M⁺, 45.04), 192 (6.15), 178 (20.77), 165 (100), 137 (23.41), 122 (6.08), 109 (6.19), 95 (5.43); HRMS (ESI): calcd for C\(_{12}\)H\(_{15}\)O\(_1\)N\(_1\)S\(_1\) (M+H) 222.09471, found 222.09495; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3128\) (w), 2951 (m), 2853 (m), 1645 (w), 1621 (s), 1529 (m), 1470 (m), 1435 (m), 1386 (w), 1372 (w), 1340 (w), 1316 (w), 1300 (w), 1267 (w), 1241 (w), 1226 (w), 1200 (w), 1169 (m), 1105 (w), 1091 (m), 1049 (m), 1007 (w), 986 (w), 962 (w), 912 (m), 859 (m), 835 (m), 773 (s), 722 (s).
3-Phenyl-5,6,7,8-tetrahydrobenzothieno[3,2-c]pyridin-1(2H)-one (37a):

Starting with compound 35a (100 mg, 0.35 mmol) and NaOMe (150 mg, 2.77 mmol), 37a was obtained as a white solid, (75 mg, 75%), mp. 238–240 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 1.75$-1.84 (m, 4H, CH$_2$/uni0445), 2.72-2.75 (m, 2H, CH$_2$), 3.07-3.08 (m, 2H, CH$_2$), 6.86 (s, CH), 7.32-7.43 (m, 3H), 7.67-7.71 (m, 2H), 10.97 (s, NH); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta = 22.3$ (C-6), 23.0 (C-7), 25.4 (C-8), 26.0 (C-5), 100.5 (C-4), 126.2 (C-9), 128.4 (C-4'), 129.1 (C-2',6'), 129.3 (C-3',5'), 133.8 (C-1'), 134.0 (C-3), 135.1 (C-11), 139.5 (C-10), 148.4 (C-12), 160.9 (C=O); GC-MS (EI, 70eV): m/z (%) = 281(M$^+$, 100), 266 (5.48), 253 (29.19), 225 (9.23), 210 (2.51), 190 (3.98), 165 (3.14), 152 (1.76), 140 (3.00), 117(2.04), 90 (4.29); HRMS (ESI): calcd for C$_{17}$H$_{15}$NO$_1$S$_1$ 281.08689 found 281.087336; IR (ATR, cm$^{-1}$): $\nu$ = 3137 (w), 3074 (w), 3022 (w), 2928 (m), 2847 (w), 1688 (m), 1633 (s), 1594 (m), 1551 (m), 1504 (m), 1443 (m), 1403 (w), 1361 (w), 1334 (w), 1286 (m), 1230 (m), 1178 (w), 1159 (w), 1147 (w), 1066 (w), 1035 (w), 994 (m), 966 (w), 948 (w), 912 (m), 829 (m), 756 (s).

3-(p-Tolyl)-5,6,7,8-tetrahydrobenzothieno[3,2-c]pyridin-1(2H)-one (37b):

Starting with compound 35b (100 mg, 0.34 mmol) and NaOMe (150 mg, 2.77 mmol), 37b was obtained as a white solid, (77 mg, 77%), mp. 254–256 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 1.80$-1.82 (m, 4H, CH$_2$/uni0445), 2.34 (s, CH$_3$), 2.72-2.74 (m, 2H, CH$_2$), 3.06-3.08 (m, 2H, CH$_2$), 6.86 (s, CH), 7.21 (d, $^3$J = 7.99 Hz, 2H), 7.54 (d, $^3$J = 8.18 Hz, 2H), 10.51 (s, NH); $^{13}$C NMR (75.4 MHz, CDCl$_3$): $\delta = 24.8$ (CH$_3$), 26.1 (C-6), 26.8 (C-7), 29.2 (C-8), 29.7 (C-5), 104.7 (C-4), 129.9 (C-9), 130.7 (C-2',6'), 133.7 (C-3',5'), 134.7 (C-1'), 137.4 (C-4'), 139.2 (C-3), 143.6 (C-11), 143.7 (C-10), 153.0 (C-12), 164.9 (C=O); GC-MS (EI, 70eV): m/z (%) = 295(M$^+$, 100), 280 (5.89), 253 (29.19), 225 (9.23), 210 (2.51), 190 (3.98), 165 (3.14), 152 (1.76), 140 (3.00), 117(2.04), 90 (4.29); HRMS (ESI): calcd for C$_{18}$H$_{17}$NO$_1$S$_1$ (M+H) 296.11036, found 296.11088; IR (ATR, cm$^{-1}$): $\nu$ = 3364 (w), 3138 (w), 3077 (w), 3011 (w), 2915 (m), 2837 (w), 2728 (w), 1687 (m), 1635 (s), 1599 (m), 1564 (w), 1552 (w), 1519 (m), 1445 (w), 1424 (w), 1399 (w), 1360 (w), 1335 (w), 1321 (w), 1286 (m), 1247 (m), 1196 (w), 1171 (w), 1128 (m), 1068 (w), 1035 (w), 994 (m), 966 (w), 948 (w), 912 (m), 829 (m), 756 (s).
3-(4-Propylphenyl)-5,6,7,8-tetrahydrobenzothieno[3,2-c]pyridin-1(2H)-one (37d):

Starting with compound 35d (100 mg, 0.31 mmol) and NaOMe (150 mg, 2.77 mmol), 37d was obtained as a white solid, (80 mg, 80%), mp. 228–230 °C; \(^1H\) NMR (300 MHz, CDCl\(_3\)): \(\delta = 0.89 \text{ (t, } ^3J = 7.37 \text{ Hz, CH}\_3)\), 1.60 (sext, \(^3J = 7.42 \text{ Hz, CH}\_2\)), 1.79-1.81 (m, 4H, CH\(_2\)/uni0445\_), 2.57 (t, \(^3J = 7.74 \text{ Hz, CH}\_2\)), 2.73 (m, 2H, CH\(_2\)), 3.07 (m, 2H, CH\(_2\)), 6.82 (s, CH), 7.20 (d, \(^3J = 8.40 \text{ Hz, 2H}\)), 7.60 (d, \(^3J = 8.19 \text{ Hz, 2H}\)), 11.07 (s, NH); \(^{13}C\) NMR (75.4 MHz, CDCl\(_3\)): \(\delta = 13.7 \text{ (CH}\_3\)), 22.4 (C-6), 23.1 (C-7), 24.3 (C-8), 25.4 (C-5), 26.0 (CH\(_2\)), 37.7 (CH\(_2\)), 100.0 (C-4), 126.2 (C-9), 127.1 (C-3',5'), 129.1 (C-2',6'), 131.3 (C-1'), 134.0 (C-3), 134.6 (C-4'), 139.9 (C-11), 144.1 (C-10), 148.5 (C-12), 161.1 (C=O); GC-MS (EI, 70eV): m/z (%) = 323(M\(^+\), 100), 308 (11.42), 294 (21.68), 281 (11.06), 265 (11.56), 249 (7.10), 233 (5.52), 207 (17.11), 186 (5.18), 148 (10.82); HRMS (ESI): calcd for C\(_{20}\)H\(_{21}\)NO\(_3\)S: 323.13384, found 323.133525; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3359 \text{ (w), 3255 \text{ (w), 3138 \text{ (w), 3077 \text{ (w), 3013 \text{ (w), 2925 \text{ (m), 2852 \text{ (w), 1683 \text{ (w), 1632 \text{ (s), 1595 \text{ (m), 1557 \text{ (m), 1517 \text{ (m), 1462 \text{ (w), 1454 \text{ (w), 1434 \text{ (m), 1417 \text{ (w), 1402 \text{ (m), 1376 \text{ (w), 1333 \text{ (m), 1287 \text{ (m), 1247 \text{ (m), 1195 \text{ (w), 1170 \text{ (w), 1125 \text{ (m), 1093 \text{ (w), 1035 \text{ (w), 991 \text{ (m), 952 \text{ (w), 885 \text{ (m), 829 \text{ (m), 787 \text{ (s).}}}}\)

3-(4-Methoxyphenyl)-5,6,7,8-tetrahydrobenzothieno[3,2-c]pyridin-1(2H)-one (37e):

Starting with compound 35e (100 mg, 0.32 mmol) and NaOMe (150 mg, 2.77 mmol), 37e was obtained as a white solid, (73 mg, 73%), mp. 265–268 °C; \(^1H\) NMR (300 MHz, CDCl\(_3\)): \(\delta = 1.80-1.84 \text{ (m, CH}_2\)/uni0445\_2\), 2.72-2.76 (m, 2H, CH\(_2\)), 3.07 (w, 2H, CH\(_2\)), 3.81 (s, OCH\(_3\)), 6.82 (s, CH), 6.92 (d, \(^3J = 8.61 \text{ Hz, 2H}\)), 7.60 (d, \(^3J = 8.72 \text{ Hz, 2H}\)), 10.67 (NH); \(^{13}C\) NMR (75.4 MHz, CDCl\(_3\)): \(\delta = (\text{Due to limited solubility }^{13}C \text{ not measurable}); GC-MS (EI, 70eV): m/z (%) = 311(M\(^+\), 100), 296 (17.29), 283 (21.68), 268 (3.42), 231 (3.09), 181 (5.76), 169 (5.38), 131 (7.90), 119 (8.43); HRMS (ESI): calcd for C\(_{18}\)H\(_{17}\)O\(_2\)N\(_2\)S: 311.09745, found 311.097323; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3271 \text{ (w),}}\)
3134 (w), 3077 (w), 2928 (m), 2832 (w), 1633 (s), 1606 (m), 1567 (m), 1515 (s), 1470 (w), 1451 (m), 1423 (w), 1398 (w), 1361 (w), 1339 (w), 1317 (w), 1285 (m), 1243 (s), 1178 (m), 1138 (m), 1118 (m), 1064 (w), 1028 (m), 993 (m), 938 (w), 879 (m), 851 (w), 806 (s).

3-(4-tert-Butylphenyl)-5,6,7,8-tetrahydrobenzothieno[3,2-c]pyridin-1(2H)-one (37g):

Starting with compound 35g (100 mg, 0.30 mmol) and NaOMe (150 mg, 2.77 mmol), 37g was obtained as a white solid, (70 mg, 70%), mp. 283–285 °C; \textsuperscript{1}H NMR (300 MHz, CDCl\textsubscript{3}): \(\delta = 1.28\) (s, CH\textsubscript{3}/uni0445\textsubscript{3}), 1.75-1.83 (m, 4H, CH\textsubscript{2}/uni0445\textsubscript{2}), 2.71-2.77 (m, 2H, CH\textsubscript{2}), 3.06-3.09 (m, 2H, CH\textsubscript{2}), 6.81 (s, CH), 7.43 (d, \(^3J = 8.66\) Hz, 2H), 7.55 (d, \(^3J = 8.63\) Hz, 2H), 10.20 (s, NH); \textsuperscript{13}C NMR (75.4 MHz, CDCl\textsubscript{3}): \(\delta = 22.3\) (C-6), 23.0 (C-7), 25.4 (C-8), 26.0 (C-5), 31.2 (CH\textsubscript{3}/uni0445\times3), 34.7 (C), 100.3 (C-4), 125.7 (C-3’,5’), 126.2 (C-9), 130.8 (C-2’,6’), 134.0 (C-1’), 134.3 (C-3), 135.0 (C-11), 139.4 (C-10), 148.6 (C-12), 152.8 (C-4’), 160.9 (C=O); GC-MS (EI, 70eV): \(m/z (%) = 337\) (M\textsuperscript{+}, 100); HRMS (ESI): calcd for C\textsubscript{21}H\textsubscript{23}NOS (M+H) 338.15731 found 338.15685; IR (ATR, cm\textsuperscript{-1}): \(\bar{\nu} = 3075\) (w), 2931 (m), 2826 (w), 2778 (w), 2715 (w), 2682 (w), 1682 (w), 1622 (s), 1600 (s), 152 (m), 1516 (m), 1462 (w), 1454 (w), 1442 (w), 1427 (w), 1384 (w), 1361 (s), 1268 (m), 1202 (w), 1170 (w), 1134 (w), 1111 (w), 1066 (w), 1018 (w), 993 (m), 967 (m), 902 (m), 824 (w), 838 (s), 801 (s), 773 (s).

3.2.6 Synthesis of 4,5-Disubstituted-thieno[3,2-b]pyridin-7(4H)-ones:

General procedure for hydrolysis of the ester group into acid:

Ester 23 was treated with NaOH (5 equiv.) in aqueous ethanol. The resulting mixture was refluxed for 1-2 hours, monitored by TLC. The solution was cooled, ethanol evaporated under reduced pressure and finally diluted with water. The solution was then acidified with 1N-HCl solution to precipitate out the acid which was filtered and dried.
3-Bromothiophene-2-carboxylic acid (38):

Starting with 23 (500 mg, 2.26 mmol) and NaOH (452 mg, 11.3 mmol), 38 was obtained as a white solid, (450 mg, 95%), mp. 169–171 °C; \(^1^H\) NMR (300 MHz, CD\(_3\)OD): \(\delta = 4.82\) (s, OH), 7.03 (d, \(^3^J = 5.25\) Hz, 1H), 7.58 (d, \(^3^J = 5.25\) Hz, 1H); \(^1^3^C\) NMR (62.9 MHz, CD\(_3\)OD): \(\delta = 116.1\) (C-3), 127.8 (C-4), 131.4 (C-5), 132.5 (C-2), 161.9 (C=O); GC-MS (EI, 70eV): \(m/z\) (%) = 208 (M\(^+\), 81Br, 100), 206 (M\(^+\), 79Br, 98.63), 189 (94.07), 163 (4.30), 135 (3.15), 119 (5.09), 82 (26.91); HRMS (ESI): calcd for C\(_5\)H\(_3\)O\(_2\)79Br1S1 205.90316, found 205.902783 and calcd for C\(_5\)H\(_3\)O\(_2\)81Br1S1 207.90112, found 207.900748; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3099\) (w), 2929 (w), 2767 (w), 2601 (w), 2516 (w), 1650 (s), 1547 (w), 1504 (s), 1444 (w), 1423 (s), 1390 (w), 1358 (m), 1270 (s), 1164 (w), 1083 (m), 913 (m), 885 (s), 832 (w), 768 (s).

General procedure for conversion of acid into acid halide:

A suspension of acid 38 (207 mg, 1 mmol) in thionyl chloride was refluxed for 3 hours. Excess thionyl chloride was removed under reduced pressure. The acid halide so obtained was used in subsequent reaction without further purification.

3-Bromothiophene-2-carbonyl chloride (39):

Starting with 38 (207 mg, 1 mmol) and SOCl\(_2\) (excess), 39 was obtained as a white solid (220 mg, 98%), mp. 45–46 °C; \(^1^H\) NMR (300 MHz, CDCl\(_3\)):
\(\delta = 7.11\) (d, \(^3^J = 5.22\) Hz, 1H), 7.65 (d, \(^3^J = 5.25\) Hz, 1H); \(^1^3^C\) NMR (62.9 MHz, CDCl\(_3\)): \(\delta = 119.3\) (C-3), 130.7 (C-4), 133.4 (C-2), 135.6 (C-5), 155.7 (C=O); GC-MS (EI, 70eV): \(m/z\) (%) = 228 (M\(^+\), 81Br, 5.03), 226 (M\(^+\), 79Br, 17.41), 224 (M\(^+\), 79Br, 12.93), 191 (100), 163 (5.77), 137 (2.48), 117 (5.04), 82 (24.31); HRMS (ESI): calcd for C\(_5\)H\(_2\)O\(_1\)79Br\(_1\)Cl\(_1\)S\(_1\) 223.86928, found 223.869715 and calcd for C\(_5\)H\(_2\)O\(_1\)81Br\(_1\)Cl\(_1\)S\(_1\) 225.86723, found 225.867580; IR (ATR, cm\(^{-1}\)): \(\tilde{\nu} = 3108\) (w), 3087 (w), 1743 (s), 1673 (m), 1557 (w), 1506 (m), 1473 (s), 1426 (w), 1383 (s), 1349 (s), 1273 (m), 1180 (s), 1106 (w), 1085 (w), 905 (m), 888 (m), 856 (s).
General procedure for synthesis of Ynones (41a-e):

A mixture of acid halide 39 (225 mg, 1 mmol), Et₃N (1 mmol) and PdCl₂(PPh₃)₂ (2 mol%) was stirred in anhydrous THF for 10 min under argon at room temperature. CuI (5 mol%) was added and the reaction mixture was stirred for another 10 min before phenyl acetylene (1 mmol) was added. After 2 h at room temperature the reaction mixture was diluted with ethyl acetate and washed with 0.1-N HCl (2 x 10 mL) and saturated NH₄Cl solution (10 mL). The organic phase was separated, dried (Na₂SO₄), filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography.

1-(3-Bromothiophen-2-yl)-3-phenylprop-2-yn-1-one (41a):

Starting with 39 (225 mg, 1 mmol), PdCl₂(PPh₃)₂ (14 mg, 0.02 mmol), CuI (10 mg, 0.05 mmol), Et₃N (0.14 mL, 1 mmol), and acetylene (0.11 mL, 1 mmol), 41a was obtained as a yellow solid (225 mg, 77%), mp. 81–83 °C; ¹H NMR (300 MHz, CDCl₃): δ = 7.09 (d, 3J = 5.16 Hz, 1H), 7.31-7.42 (m, 3H), 7.54 (d, 3J = 5.16 Hz, 1H), 7.59-7.63 (m, 2H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 87.3 (C-2′), 94.0 (C-3′), 116.4 (C-3), 119.9 (C-1″), 128.7 (C-4), 131.0 (C-3″,5″), 133.0 (C-4″), 133.6 (C-2″,6″), 134.0 (C-5), 137.9 (C-2), 168.2 (C-1); GC-MS (EI, 70eV): m/z (%) = 292 (M+, 81Br, 54.39), 290 (M+, 79Br, 52.42), 264 (100), 183 (3.24), 139 (52.56), 129 (64.41), 101 (9.45), 91 (7.15), 82 (6.79), 75 (17.20); HRMS (ESI): calcld for C₁₃H₇BrO₂S: 289.93955, found 289.940269 and calcld for C₁₃H₇BrO₂S: 291.93750, found 291.938392; IR (ATR, cm⁻¹): ṽ = 3389 (w), 3099 (w), 2959 (w), 2924 (w), 2437 (w), 2350 (w), 2269 (w), 2192 (s), 1985 (w), 1887 (w), 1803 (w), 1651 (w), 1631 (w), 1584 (s), 1557 (w), 1531 (w), 1486 (s), 1440 (m), 1397 (s), 1347 (w), 1328 (w), 1304 (s), 1198 (s), 1095 (w), 1067 (w), 1027 (w), 966 (w), 962 (s), 918 (w), 902 (w), 877 (s).

1-(3-Bromothiophen-2-yl)-3-p-tolylprop-2-yn-1-one (41b):

Starting with 39 (225 mg, 1 mmol), PdCl₂(PPh₃)₂ (14 mg, 0.02 mmol), CuI (10 mg, 0.05 mmol), Et₃N (0.14 mL, 1 mmol), and acetylene (0.13 mL, 1mmol), 41b
was obtained as a yellow solid, (225 mg, 73%), mp. 71–73 °C; 1H NMR (300 MHz, CDCl₃): δ = 2.34 (s, CH₃), 7.09 (d, 3J = 5.20 Hz, 1H), 7.15 (d, 3J = 7.87, 2H), 7.53 (d, 3J = 5.19 Hz, 1H), 7.51 (d, 3J = 8.09 Hz, 2H); 13C NMR (62.9 MHz, CDCl₃): δ = 21.8 (CH₃), 87.3 (C-2”), 94.6 (C-3”), 116.8 (C-1”), 117.0 (C-3), 129.5 (C-4), 133.0 (C-3”,5”), 133.3 (C-2”,6”), 133.9 (C-5), 138.0 (C-4”), 141.8 (C-2), 168.1 (C-1); GC-MS (EI, 70eV): m/z (%) = 306 (M⁺, 81Br, 77.03), 304 (M⁺, 79Br, 75.20), 278 (100), 197 (11.06), 153 (19.46), 143 (49.10), 115 (8.11), 98 (4.28), 89 (7.93), 82 (5.67); HRMS (ESI): calcd for C₁₄H₉O₁79Br₁S₁ 303.95520, found 303.955763 and calcd for C₁₄H₉O₁81Br₁S₁ 305.95315, found 305.953697; IR (ATR, cm⁻¹): ν = 3209 (w), 3105 (w), 3027 (w), 2911 (w), 2859 (w), 2291 (w), 2188 (s), 1903 (w), 1664 (w), 1619 (s), 1602 (m), 1505 (m), 1486 (s), 1454 (w), 1445 (w), 1393 (s), 1351 (s), 1304 (w), 1278 (m), 1238 (w), 1188 (m), 1174 (m), 1148 (m), 1116 (w), 1085 (w), 137 (w), 1010 (s), 962 (w), 945 (w), 900 (w), 879 (s).  

1-(3-Bromothiophen-2-yl)-3-(4-propylphenyl)prop-2-yn-1-one (41c): Starting with 39 (225 mg, 1 mmol), PdCl₂(PPh₃)₂ (14 mg, 0.02 mmol), CuI (10 mg, 0.05 mmol), Et₃N (0.14 mL, 1 mmol), and acetylene (0.16 mL, 1 mmol), 41c was obtained as a yellow oil (250 mg, 75%); 1H NMR (300 MHz, CDCl₃): δ = 0.86 (t, 3J = 7.36 Hz, CH₃), 1.57 (sext, 3J = 7.27 Hz, CH₂), 2.55 (t, 3J = 7.91 Hz, CH₂), 7.08 (d, 3J = 5.20 Hz, 1H), 7.14 (d, 3J = 8.38 Hz, 2H), 7.52 (d, 3J = 5.16 Hz, 1H), 7.52 (d, 3J = 8.22 Hz, 2H); 13C NMR (62.9 MHz, CDCl₃): δ = 13.7 (CH₃), 24.1 (CH₂), 38.1 (CH₂), 87.2 (C-2”), 94.8 (C-3”), 116.1 (C-1”), 117.0 (C-3), 128.9 (C-4), 133.1 (C-3”,5”), 133.4 (C-2”,6”), 133.9 (C-5), 138.0 (C-4”), 146.5 (C-2), 168.2 (C-1); GC-MS (EI, 70eV): m/z (%) = 334 (M⁺, 81Br, 57.12), 332 (M⁺, 79Br, 56.93), 306 (27.28), 277 (100), 195 (18.32), 171 (16.90), 152 (13.99), 142 (12.98), 114 (11.67); HRMS (ESI): calcd for C₁₆H₁₃BrOS₁ 331.98650, found 331.986933 and calcd for C₁₆H₁₃O₁79Br₁S₁ 333.98445, found 333.984964; IR (ATR, cm⁻¹): ν = 3370 (w), 3103 (w), 3083 (w), 2956 (m), 2927 (m), 2868 (m), 2547 (w), 2431 (w), 2273 (w), 2189 (s), 1913 (w), 1625 (m), 1592 (s), 1488 (s), 1463 (w), 1397 (s), 1352 (m), 1302 (m), 1277 (m), 1188 (m), 1174 (s), 1148 (m), 1114 (w), 1085 (w), 1009 (m), 967 (m), 903 (w), 879 (s).
1-(3-Bromothiophen-2-yl)-3-(4-methoxyphenyl)prop-2-yn-1-one (41d):

Starting with 39 (225 mg, 1 mmol), PdCl$_2$(PPh$_3$)$_2$ (14 mg, 0.02 mmol), CuI (10 mg, 0.05 mmol), Et$_3$N (0.14 mL, 1 mmol), and acetylene (0.13 mL, 1mmol), 41d was obtained as a yellow solid (226 mg, 70%), mp. 98–100 °C; $^1$H NMR (250 MHz, CDCl$_3$): δ = 3.78 (s, OCH$_3$), 6.86 (d, $^3$$J = 8.89$ Hz, 2H), 7.07 (d, $^3$$J = 5.17$ Hz, 1H), 7.52 (d, $^3$$J = 5.20$ Hz, 1H), 7.57 (d, $^3$$J = 8.86$ Hz, 2H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): δ = 55.4 (OCH$_3$), 87.4 (C-2'), 95.4 (C-3'), 111.7 (C-3''), 114.4 (C-1''), 115.9 (C-3), 132.7 (C-4), 133.2 (C-2'',6''), 133.4 (C-5), 133.8 (C-2), 161.9 (C-4''), 165.1 (C-1); GC-MS (EI, 70eV): $m/z$ (%) = 322 (M$^+$, $^{81}$Br, 100), 320 (M$^+$, $^{79}$Br, 99.0), 294 (58.31), 277 (67.65), 251 (15.62), 169 (21.03), 159 (62.44), 144 (15.08), 131 (4.06), 116 (14.68); HRMS (ESI): calcd for C$_{14}$H$_9$BrO$_2$S$_1$ 319.95011, found 319.95012; IR (ATR, cm$^{-1}$): $\nu$ = 3099 (w), 2955 (w), 2841 (w), 2587 (w), 2516 (w), 2188 (s), 1893 (w), 1769 (w), 1715 (w), 1668 (m), 1624 (m), 1596 (m), 1567 (m), 1504 (s), 1445 (w), 1423 (m), 1349 (m), 1305 (w), 1253 (s), 1186 (w), 1168 (m), 1106 (w), 1083 (w), 1020 (m), 957 (w), 913 (w), 880 (s).

General procedure for the synthesis of Pyridinones (43a-z):

To the ynone 41a-d (1 mmol), Cs$_2$CO$_3$ (1.4 mmol), Pd$_2$(dba)$_3$ (5 mol%), and BINAP (10 mol%) under argon were added toluene (10 mL) followed by aniline/amine (1.2 mmol) and the reaction was stirred at 110 °C for 10-12 hours. After cooling to room temperature, the reaction mixture was preabsorbed onto silica gel and purified by column chromatography.

4,5-Diphenylthieno[3,2-b]pyridin-7(4H)-one (43a):

Starting with 41a (145 mg, 0.5 mmol), Cs$_2$CO$_3$ (228 mg, 0.7 mmol), Pd$_2$(dba)$_3$ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.05 mL, 0.6 mmol), 43a was obtained as a yellow solid (118 mg, 78%), mp. 233–235 °C; $^1$H NMR (300 MHz, CDCl$_3$): δ = 6.35 (s, CH), 6.52 (d, $^3$$J = 5.49$ Hz, 1H), 7.06-7.14
(m, 7H), 7.20-7.30 (m, 3H), 7.46 (d, \( ^3J = 5.49 \text{ Hz} \), 1H); \(^{13}\)C NMR (62.9 MHz, CDCl\(_3\)): \( \delta = 113.4 \text{ (C-6), 118.9 (C-4'), 128.0 (C-2',6'), 128.3 (C-3), 128.6 (C-4''), 128.7 (C-2'',6''), 129.0 (C-3'',5''), 129.4 (C-3',5'), 129.5 (C-1''), 131.4 (C-2), 134.6 (C-8), 140.1 (C-1'), 146.5 (C-9), 151.7 (C-5), 173.8 (C-7); \) GC-MS (EI, 70eV): \( \text{m/z} \% = 303 \text{ (M}^+ \text{, 100), 275 (42.52), 241 (4.33), 171 (15.85), 136 (3.28), 121 (5.97), 102 (4.32), 77 (8.14); HRMS (ESI): caleed for C\(_{19}\)H\(_{13}\)N\(_1\)O\(_1\)S\(_1\) (M+H) 304.07906, found 304.07893; IR (ATR, cm\(^{-1}\)): \( \nu = 3108 \text{ (w), 3039 (w), 2917 (w), 2850 (w), 1609 (m), 1591 (s), 1574 (m), 1513 (w), 1480 (s), 1451 (m), 1442 (m), 1423 (w), 1384 (m), 1312 (m), 1276 (m), 1249 (m), 1185 (m), 1158 (m), 1113 (m), 1099 (m), 1067 (m), 1049 (m), 1026 (m), 998 (w), 978 (w), 930 (m), 876 (w), 853 (w), 829 (m), 754 (s).

5-Phenyl-4-p-tolylthieno[3,2-b]pyridin-7(4H)-one (43b):

Starting with 41a (145 mg, 0.5 mmol), Cs\(_2\)CO\(_3\) (228 mg, 0.7 mmol), Pd\(_2\)(dba)\(_3\) (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.06 mL, 0.6 mmol), 43b was obtained as a yellow solid (126 mg, 80%), mp. 203–205 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta = 2.23 \text{ (s, CH}_3\text{), 6.35 (s, CH), 6.52 (d, } ^3J = 5.50 \text{ Hz, 1H), 6.95 (d, } ^3J = 8.38 \text{ Hz, 2H), 7.04 (d, } ^3J = 8.14 \text{ Hz, 2H), 7.07-7.15 (m, 5H), 7.44 (d, } ^3J = 5.49 \text{ Hz, 1H]; \) \(^{13}\)C NMR (62.9 MHz, CDCl\(_3\)): \( \delta = 21.1 \text{ (CH}_3\text{), 113.4 (C-6), 119.0 (C-3), 128.0 (C-2',6'), 128.2 (C-4''), 128.5 (C-2'',6''), 128.7 (C-3'',5''), 129.3 (C-3',5'), 130.1 (C-4''), 131.3 (C-1''), 134.7 (C-2), 137.5 (C-8), 139.0 (C-1''), 146.7 (C-9), 151.8 (C-5), 173.8 (C-7); \) GC-MS (EI, 70eV): \( \text{m/z} \% = 317 \text{ (M}^+ \text{, 100), 289 (33.22), 273 (5.87), 214 (5.03), 186 (6.75), 171 (12.21), 137 (4.04), 102 (4.67); HRMS (ESI): caleed for C\(_{20}\)H\(_{15}\)N\(_1\)O\(_1\)S\(_1\) (M+H) 318.09471, found 318.09493; IR (ATR, cm\(^{-1}\)): \( \tilde{\nu} = 3107 \text{ (w), 3051 (w), 2918 (w), 2859 (w), 1607 (m), 1599 (s), 1512 (m), 1480 (s), 1441 (m), 1425 (w), 1384 (m), 1313 (m), 1276 (m), 1250 (w), 1185 (w), 1154 (w), 1112 (m), 1100 (m), 1046 (m), 999 (w), 976 (w), 928 (m), 914 (w), 879 (w), 827 (s), 755 (s).
4-(4-(Diethylamino)phenyl)-5-phenylthieno[3,2-b]pyridin-7(4H)-one (43c):

Starting with 41a (145 mg, 0.5 mmol), Cs₂CO₃ (228 mg, 0.7 mmol), Pd₂(dba)₃ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.1 mL, 0.6 mmol), 43c was obtained as a yellow solid (150 mg, 80%), mp. 194–196 °C; ¹H NMR (250 MHz, CDCl₃): δ = 1.06 (t, ₃J = 7.16 Hz, 2xCH₃), 3.24 (q, ₃J = 7.04 Hz, 2xCH₂), 6.38 (s, CH), 6.43 (d, ₃J = 9.09 Hz, 2H), 6.63 (d, ₃J = 5.49 Hz, 1H), 6.84 (d, ₃J = 9.05 Hz, 2H), 7.11-7.19 (m, 5H), 7.46 (d, ₃J = 5.50 Hz, 1H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 11.3 (CH₃×2), 43.3 (CH₂×2), 110.3 (C-6), 112.2 (C-3′,5′), 118.4 (C-2′,6′), 126.8 (C-3), 126.9 (C-4′), 127.4 (C-2′,6′), 127.7 (C-3′,5′), 128.0 (C-1′), 128.4 (C-1′), 130.0 (C-2), 134.1 (C-8), 146.5 (C-4′), 146.6 (C-9), 151.4 (C-5), 172.8 (C-7); GC-MS (EI, 70eV): m/z (%) = 374 (M⁺, 67.32), 359 (100), 330 (8.91), 302 (8.35), 273 (3.23), 228 (2.61), 171 (6.04), 136 (4.21); HRMS (ESI): calcd for C₂₃H₂₂N₂O₂S₁ 374.14474, found 374.144388; IR (ATR, cm⁻¹): ν = 3541 (w), 3389 (w), 3050 (m), 2963 (m), 2925 (w), 1609 (s), 1517 (s), 1475 (s), 1444 (w), 1422 (w), 1405 (w), 1377 (m), 1355 (m), 1317 (m), 1264 (s), 1197 (m), 1156 (m), 1108 (m), 1073 (m), 1048 (s), 1016 (w), 915 (w), 817 (m), 771 (s).

4-(4-Fluorophenyl)-5-phenylthieno[3,2-b]pyridin-7(4H)-one (43d):

Starting with 41a (145 mg, 0.5 mmol), Cs₂CO₃ (228 mg, 0.7 mmol), Pd₂(dba)₃ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.06 mL, 0.6 mmol), 43d was obtained as a yellow solid (133 mg, 83%), mp. 183–185 °C; ¹H NMR (250 MHz, CDCl₃): δ = 6.33 (s, CH), 6.51 (d, ₃J = 5.49 Hz, 1H), 6.84 (d, ₃J = 9.05 Hz, 2H), 7.06-7.20 (m, 7H), 7.48 (d, ₃J = 5.47 Hz, 1H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 113.5 (C-6), 116.5 (d, ₂J_C-F = 22.99 Hz, C-3′,5′), 126.1 (C-3), 126.8 (C-4′), 128.9 (C-2′,6′), 129.4 (C-3′,5′), 130.4 (d, ₂J_C-F = 8.80 Hz, C-2′,6′), 131.6 (C-1′), 133.4 (C-2), 134.4 (C-8), 136.1 (d, ₄J_C-F = 3.43 Hz, C-1′), 146.5 (C-9), 151.7 (C-5), 162.1 (d, ₁J_C-F = 250.6 Hz, C-4′), 173 (C-7); ¹⁹F NMR (282.4 MHz, CDCl₃): δ = -110.73 (s, CF); GC-MS (EI,
90eV): \( m/z \) (%) = 321 (M\(^+\), 100), 293 (40.13), 259 (3.31), 219 (3.79), 189 (10.0), 171 (8.15), 139 (4.18), 121 (4.41), 102 (4.25), 95 (5.26); HRMS (ESI): calcd for C\(_{10}\)H\(_{15}\)F\(_1\)N\(_1\)O\(_1\)S\(_1\) (M+H) 322.06964, found 322.06965; IR (ATR, cm\(^{-1}\)): \( \nu \approx 3099 \) (w), 3061 (w), 2921 (w), 2851 (w), 1595 (s), 1574 (m), 1538 (w), 1504 (s), 1477 (s), 1441 (m), 1410 (w), 1380 (m), 1310 (m), 1295 (w), 1274 (w), 1234 (w), 1211 (s), 1151 (m), 1113 (m), 1099 (m), 1066 (m), 1041 (m), 996 (w), 958 (w), 881 (w), 844 (s), 832 (s).

4-(4-Methoxyphenyl)-5-phenylthieno[3,2-b]pyridin-7(4H)-one (43e):

Starting with 41a (145 mg, 0.5 mmol), Cs\(_2\)CO\(_3\) (228 mg, 0.7 mmol), Pd\(_2\)(dba)\(_3\) (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (73 mg, 0.6 mmol), 43e was obtained as a yellow solid (130 mg, 78%), mp. 210–212 °C; \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta = 3.70 \) (s, OCH\(_3\)), 6.34 (s, CH), 6.53 (d, \( ^3J = 5.49 \) Hz, 1H), 6.75 (d, \( ^3J = 8.99 \) Hz, 2H), 7.00 (d, \( ^3J = 8.95 \) Hz, 2H), 7.07-7.20 (m, 5H), 7.46 (d, \( ^3J = 5.49 \) Hz, 1H); \(^13\)C NMR (62.9 MHz, CDCl\(_3\)): \( \delta = 55.4 \) (OCH\(_3\)), 113.4 (C-6), 114.5 (C-3’,5’), 119.0 (C-3), 128.0 (C-4”), 128.5 (C-2”,6”), 128.7 (C-3”,5”), 129.4 (C-2’,6’), 129.6 (C-1”), 131.3 (C-2), 132.8 (C-8), 134.8 (C-1’), 147.0 (C-9), 152.0 (C-4’), 159.4 (C-5), 173.8 (C-7); GC-MS (EI, 70eV): \( m/z \) (%) = 333 (M\(^+\), 100), 305 (13.85), 290 (9.83), 260 (3.82), 216 (6.30), 188 (9.00), 160 (7.92), 134 (4.14), 116 (3.12), 102 (4.75); HRMS (ESI): calcd for C\(_{20}\)H\(_{15}\)N\(_1\)O\(_2\)S\(_1\) (M+H) 334.08963, found 334.09029; IR (ATR, cm\(^{-1}\)): \( \tilde{\nu} = 3100 \) (w), 3047 (w), 3011 (w), 2962 (w), 2836 (w), 1599 (s), 1577 (m), 1505 (s), 1478 (s), 1381 (m), 1317 (w), 1297 (m), 1240 (s), 1176 (m), 1104 (m), 1075 (w), 1067 (w), 1046 (m), 1022 (m), 1011 (m), 973 (w), 919 (m), 833 (s), 754 (s).

4-(2,4-Dimethoxyphenyl)-5-phenylthieno[3,2-b]pyridin-7(4H)-one (43f):

Starting with 41a (145 mg, 0.5 mmol), Cs\(_2\)CO\(_3\) (228 mg, 0.7 mmol), Pd\(_2\)(dba)\(_3\) (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (92 mg, 0.6 mmol), 43f was obtained as a yellow gel (127 mg, 70%); \(^1\)H NMR (300 MHz, CDCl\(_3\)): \( \delta = 3.59 \) (s, OCH\(_3\)), 2.75 (s, OCH\(_3\)), 6.35 (d, \( ^4J = 2.55 \) Hz, 1H), 3.67 (s, OCH\(_3\)), 6.35 (d, \( ^4J = 8.95 \) Hz, 2H), 7.00 (d, \( ^3J = 8.95 \) Hz, 2H), 7.07-7.20 (m, 5H), 7.46 (d, \( ^3J = 5.49 \) Hz, 1H); \(^13\)C NMR (62.9 MHz, CDCl\(_3\)): \( \delta = 55.4 \) (OCH\(_3\)), 113.4 (C-6), 114.5 (C-3’,5’), 119.0 (C-3), 128.0 (C-4”), 128.5 (C-2”,6”), 128.7 (C-3”,5”), 129.4 (C-2’,6’), 129.6 (C-1”), 131.3 (C-2), 132.8 (C-8), 134.8 (C-1’), 147.0 (C-9), 152.0 (C-4’), 159.4 (C-5), 173.8 (C-7); GC-MS (EI, 70eV): \( m/z \) (%) = 333 (M\(^+\), 100), 305 (13.85), 290 (9.83), 260 (3.82), 216 (6.30), 188 (9.00), 160 (7.92), 134 (4.14), 116 (3.12), 102 (4.75); HRMS (ESI): calcd for C\(_{20}\)H\(_{15}\)N\(_1\)O\(_2\)S\(_1\) (M+H) 334.08963, found 334.09029; IR (ATR, cm\(^{-1}\)): \( \tilde{\nu} = 3100 \) (w), 3047 (w), 3011 (w), 2962 (w), 2836 (w), 1599 (s), 1577 (m), 1505 (s), 1478 (s), 1381 (m), 1317 (w), 1297 (m), 1240 (s), 1176 (m), 1104 (m), 1075 (w), 1067 (w), 1046 (m), 1022 (m), 1011 (m), 973 (w), 919 (m), 833 (s), 754 (s).
6.39 (dd, $^3J = 8.44$, 2.62 Hz, 1H), 6.40 (s, CH), 6.53 (d, $^3J = 5.48$ Hz, 1H), 7.02 (d, $^3J = 8.55$ Hz, 1H), 7.16-7.22 (m, 5H), 7.50 (d, $^3J = 5.49$ Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 55.4 (OCH$_3$), 55.5 (OCH$_3$), 99.2 (C-6), 104.6 (C-3′), 113.0 (C-5′), 118.9 (C-6′), 121.9 (C-3), 127.7 (C-4′), 128.3 (C-2″,6″), 128.7 (C-3″,5″), 130.1 (C-1″), 131.2 (C-1′), 134.9 (C-2), 147.1 (C-8), 152.9 (C-9), 155.5 (C-2′), 161.3 (C-5), 171.0 (C-4′), 174.1 (C-7); GC-MS (EI, 70eV): $m/z$ (%) = 363 (M$^+$, 100), 335 (7.65), 320 (3.97), 304 (3.12), 289 (3.00), 276 (3.83), 260 (4.88), 218 (2.75), 175 (3.69), 130 (4.61); HRMS (ESI): calcd for C$_{21}$H$_{17}$N$_1$O$_3$S$_1$ (M+H) 364.10019, found 364.10074; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3057 (w), 3004 (w), 2935 (w), 2837 (w), 1732 (w), 1587 (s), 1507 (s), 1476 (s), 1438 (m), 1420 (m), 1384 (m), 1324 (w), 1304 (m), 1280 (m), 1244 (m), 1207 (s), 1159 (m), 1136 (w), 1110 (m), 1067 (w), 1048 (s), 923 (m), 835 (s).

5-Phenyl-4-(3-(trifluoromethyl)phenyl)thieno[3,2-b]pyridin-7(4H)-one (43g):

Starting with 41a (145 mg, 0.5 mmol), Cs$_2$CO$_3$ (228 mg, 0.7 mmol), Pd$_2$(dba)$_3$ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.07 mL, 0.6 mmol), 43g was obtained as a yellow solid (150 mg, 81%), mp. 250–252 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta$ = 6.36 (s, CH), 6.51 (d, $^3J = 5.49$ Hz, 1H), 7.04-7.17 (m, 5H), 7.35-7.47 (m, 4H), 7.51 (d, $^3J = 5.51$ Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta$ = 113.7 (C-6), 118.3 (C-2′), 123.0 (q, $^1J_{C-F} = 272.79$ Hz, CF$_3$), 125.8 (m, 2C, C-4′,6′), 128.2 (C-3), 128.8 (C-4″), 129.0 (C-2″,6″), 129.3 (C-3″,5″), 132.0 (q, $^2J_{C-F} = 33.41$ Hz, C-3′), 132.1 (C-5′), 132.2 (C-1″), 132.3 (C-2), 134.1 (C-8), 140.6 (C-1′), 145.9 (C-9), 151.4 (C-5), 173.8 (C-7); $^{19}$F NMR (282.4 MHz, CDCl$_3$): $\delta$ = -62.93 (s, CF$_3$); GC-MS (EI, 70eV): $m/z$ (%) = 371 (M$^+$, 100), 343 (45.43), 273 (4.49), 241 (3.11), 171 (13.24), 145 (6.59), 121 (2.80); HRMS (ESI): calcd for C$_{20}$H$_{12}$F$_3$NOS (M+H) 372.06645, found 372.06613; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3107 (w), 3047 (w), 2922 (w), 1606 (s), 1578 (m), 1537 (w), 1516 (w), 1480 (m), 1444 (m), 1379 (m), 1330 (s), 1264 (w), 1250 (w), 1234 (w), 1191 (m), 1169 (m), 1156 (w), 1115 (s), 1095 (s), 1075 (m), 1051 (m), 1001 (w), 980 (w), 938 (w), 920 (m), 878 (w), 859 (w), 837 (m), 811 (m), 779 (s).
4-(3-Bromophenyl)-5-phenylthieno[3,2-b]pyridin-7(4H)-one (43h):

Starting with 41a (145 mg, 0.5 mmol), Cs$_2$CO$_3$ (228 mg, 0.7 mmol), Pd$_2$(dba)$_3$ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.07 mL, 0.6 mmol), 43h was obtained as a yellow solid (150 mg, 78%), mp. 206–208 °C; $^1$H NMR (300 MHz, CDCl$_3$): δ = 6.33 (s, CH), 6.53 (d, $^3J = 5.50$ Hz, 1H), 7.04-7.18 (m, 7H), 7.28-7.30 (m, 1H), 7.36-7.40 (m, 1H), 7.49 (d, $^3J = 5.50$ Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): δ = 113.6 (C-6), 118.6 (C-2′), 122.7 (C-4′), 127.4 (C-6′), 128.2 (C-3′), 128.6 (C-3), 129.0 (C-6″), 129.3 (C-2″,3″), 130.7 (C-4″,5″), 131.7 (C-5′), 131.8 (C-1′), 132.2 (C-2), 134.2 (C-8), 141.1 (C-9), 146.0 (C-1′), 151.4 (C-5), 173.7 (C-7); GC-MS (EI, 70eV): m/z (%) = 383 (M$^+$, $^{81}$Br, 100), 381(M$^+$, $^{79}$Br, 96.61), 355 (37.05), 300 (5.62), 273 (13.04), 241 (3.52), 200 (6.35), 171 (19.56), 137 (10.82), 120 (11.82), 102 (8.61), 76 (8.29); HRMS (ESI): calcd for C$_{19}$H$_{12}$BrNOS (M+H) 381.98957, found 381.98951 and calcd for C$_{19}$H$_{12}$BrNOS (M+H) 383.98763, found 383.98752; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3107 (w), 3050 (w), 2917 (w), 2858 (w), 1732 (w), 1609 (m), 1599 (m), 1572 (s), 1515 (w), 1474 (s), 1443 (w), 1418 (w), 1380 (m), 1312 (m), 1277 (w), 1249 (w), 1185 (w), 1138 (w), 1101 (m), 1065 (m), 1048 (m), 1029 (w), 997 (w), 980 (w), 928 (w), 877 (w), 858 (w), 834 (m), 776 (m).

4-(4-Ethoxyphenyl)-5-phenylthieno[3,2-b]pyridin-7(4H)-one (43i):

Starting with 41a (145 mg, 0.5 mmol), Cs$_2$CO$_3$ (228 mg, 0.7 mmol), Pd$_2$(dba)$_3$ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.08 mL, 0.6 mmol), 43i was obtained as a yellow solid (142 mg, 82%), mp. 182–184 °C; $^1$H NMR (300 MHz, CDCl$_3$): δ = 1.31 (t, $^3J = 6.98$ Hz, CH$_3$), 3.91 (q, $^3J = 6.97$ Hz, OCH$_2$), 6.36 (s, CH), 6.54 (d, $^3J = 5.48$ Hz, 1H), 6.73 (d, $^3J = 8.91$ Hz, 2H), 6.98 (d, $^3J = 8.96$ Hz, 2H), 7.07-7.16 (m, 5H), 7.46 (d, $^3J = 5.49$ Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): δ = 13.6 (CH$_3$), 62.7 (OCH$_2$), 112.3 (C-6), 113.9 (C-3′,5′), 118.0 (C-3), 127.0 (C-4″), 127.4 (C-2″,6″), 127.6 (C-3″,5″), 128.3 (C-2′,6′), 128.5 (C-1″), 130.3 (C-2), 131.6 (C-
1'), 133.7 (C-8), 146.0 (C-9), 151.0 (C-4'), 157.9 (C-5), 172.8 (C-7); GC-MS (EI, 70eV): m/z (%) = 347 (M+, 100), 319 (12.04), 318(10.48), 216(9.56), 188(5.64); HRMS (ESI): calcd for C_{21}H_{17}N_{1}O_{2}S_{1} (M+H) 348.10528, found 348.10528; IR (ATR, cm^{-1}): $\nu = 3099$ (w), 3052 (w), 2973 (w), 2928 (w), 1606 (m), 1588 (m), 1509 (m), 1474 (s), 1442 (w), 1379 (m), 1234 (m), 1177 (w), 1105 (w), 1046 (m), 842 (m), 756 (s), 703 (s).

4-(4-Nitrophenyl)-5-phenylthieno[3,2-b]pyridin-7(4H)-one (43j):

Starting with 41a (145 mg, 0.5 mmol), Cs$_2$CO$_3$ (228 mg, 0.7 mmol), 22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (82 mg, 0.6 mmol), 43j was obtained as a yellow solid (150 mg, 86%), mp. 210–212 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 6.41$ (s, CH), 6.54 (d, $^3J = 5.50$ Hz, 1H), 7.08-7.22 (m, 5H), 7.36 (d, $^3J = 8.98$ Hz, 2H), 7.55 (d, $^3J = 5.50$ Hz, 1H), 8.15 (d, $^3J = 8.98$ Hz, 2H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta = 114.0$ (C-6), 118.0 (C-2',6'), 124.8 (C-3), 128.5 (C-3',5'), 128.7 (C-4''), 128.9 (C-2''',6'''), 129.3 (C-3''',5'''), 129.4 (C-1'''), 129.9 (C-2), 132.4 (C-8), 133.9 (C-4'), 145.4 (C-9), 147.3 (C-1'), 151.0 (C-5), 173.6 (C-7); GC-MS (EI, 70eV): m/z (%) = 348 (M+, 100), 320 (24.02), 274(18.09), 273(10.15), 172(7.08); HRMS (ESI): calcd for C_{19}H_{12}N_{2}O_{3}S_{1} (M+H) 349.06414, found 349.06436; IR (ATR, cm^{-1}): $\nu = 3088$ (w), 3054 (w), 1587 (s), 1574 (s), 1509 (m), 1486 (s), 1474 (s), 1443 (w), 1307 (m), 1103 (w), 1088 (m), 1041 (w), 827 (m), 730 (m), 697 (s).

5-Phenyl-4-(3,4,5-trimethoxyphenyl)thieno[3,2-b]pyridin-7(4H)-one (43k):

Starting with 41a (145 mg, 0.5 mmol), Cs$_2$CO$_3$ (228 mg, 0.7 mmol), Pd$_2$(dba)$_3$ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (110 mg, 0.6 mmol), 43k was obtained as a yellow solid (157 mg, 80%), mp. 231–232°C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 3.61$ (s, 2xOCH$_3$), 3.78 (s, OCH$_3$), 6.34 (s, CH), 6.36 (s, 2H), 6.70 (d, $^3J = 5.46$ Hz, 1H), 7.13-7.20 (m, 5H), 7.51 (d, $^3J = 5.46$ Hz, 1H); $^{13}$C NMR (62.9 MHz,
CDCl$_3$): $\delta = 56.4$ (OCH$_3$), 61.0 (OCH$_3$×2), 106.3 (C-2′,6′), 113.3 (C-6), 119.0 (C-3), 128.0 (C-4″), 128.5 (C-2″,6″), 128.9 (C-3″,5″), 129.0 (C-4′), 131.5 (C-1″), 134.8 (C-2), 135.4 (C-8), 138.3 (C-1′), 146.4 (C-9), 151.7 (C-3′,5′), 153.4 (C-5), 173.6 (C-7);

GC-MS (EI, 70eV): $m/z$ (%) = 393 (M$^+$, 100), 378 (37.40), 205 (10.11), 276 (6.5);

HRMS (ESI): calcd for C$_{22}$H$_{19}$N$_1$O$_4$S$_1$ (M+H) 394.1107, found 394.1111; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 3116$ (w), 3058 (w), 2969 (w), 2928 (w), 2840 (w), 1598 (s), 1578 (s), 1501 (m), 1468 (s), 1442 (w), 1417 (s), 1385 (w), 1237 (s), 1178 (w), 1123 (s), 1107 (w), 1010 (m), 842 (m), 773 (m), 756 (s), 702 (s), 695 (s).

4-(4-Ethylphenyl)-5-phenylthieno[3,2-b]pyridin-7(4H)-one (43l):

Starting with 41a (145 mg, 0.5 mmol), Cs$_2$CO$_3$ (228 mg, 0.7 mmol), (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.07 mL, 0.6 mmol), 43l was obtained as a yellow solid (135 mg, 82%), mp. 204–206°C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 1.13$ (t, $J = 6.60$ Hz, CH$_3$), 2.56 (q, $^3J = 7.57$ Hz, CH$_2$), 6.50 (s, CH), 6.57 (d, $^3J = 5.49$ Hz, 1H), 6.99 (d, $^3J = 8.43$ Hz, 2H), 7.07-7.16 (m, 7H), 7.51 (d, $^3J = 5.49$ Hz, 1H);

$^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta = 15.1$ (CH$_3$), 28.3 (CH$_2$), 113.2 (C-6), 119.0 (C-3), 128.0 (C-2′,6′), 128.2 (C-4″), 128.7 (C-2″,6″), 128.8 (C-3′,5′), 129.4 (C-3″,5″), 129.8 (C-1″), 131.7 (C-2), 134.6 (C-8), 137.6 (C-4′), 145.4 (C-1′), 146.9 (C-9), 152.1 (C-5), 173.5 (C-7); GC-MS (EI, 70eV): $m/z$ (%) = 331 (M$^+$, 100), 303 (21.80), 288 (8.00), 274 5.82); HRMS (ESI): calcd for C$_{21}$H$_{17}$N$_1$O$_1$S$_1$ (M+H) 332.1103, found 332.1102; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 3116$ (w), 3052 (w), 2919 (w), 1597 (s), 1480 (m), 1435 (w), 1385 (w), 1312 (w), 1274 (w), 1112 (m), 1010 (m), 834 (m), 700 (s).

4-(4-Methylbenzyl)-5-phenylthieno[3,2-b]pyridin-7(4H)-one (43m):

Starting with 41a (145 mg, 0.5 mmol), Cs$_2$CO$_3$ (228 mg, 0.7 mmol), (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.08 mL, 0.6 mmol), 43m was obtained as a yellow solid (115 mg, 70%), mp. 237–239 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 2.23$ (s, CH$_3$), 5.11 (s, CH$_2$), 6.26 (s, CH), 6.74 (d, $^3J = 8.04$ Hz, 2H),
6.87 (d, $^3J = 5.51$ Hz, 1H), 7.01 (d, $^3J = 7.90$ Hz, 2H), 7.22-7.36 (m, 5H), 7.51 (d, $^3J = 5.49$ Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta = 21.0$ (CH$_3$), 53.5 (CH$_2$), 113.7 (C-6), 118.0 (C-3), 125.4 (C-2,’6’), 128.5 (C-4’), 128.6 (C-2’’6’’), 129.6 (C-3’’5’’), 129.7 (C-3’,5’), 129.9 (C-8), 132.0 (C-1’), 132.9 (C-1’’), 134.4 (C-2), 137.6 (C-4’), 145.5 (C-9), 152.6 (C-5), 173.6 (C-7); GC-MS (EI, 70eV): $m/z$ (%) = 331 (M$^+$, 44.71), 198 (5.54), 171 (2.85), 105 (100), 77 (12.82); HRMS (ESI): calcd for C$_{21}$H$_{17}$N$_1$O$_1$S$_1$ (M+H) 332.11036, found 332.11069; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 3107$ (w), 3052 (w), 3020 (w), 2920 (w), 2852 (w), 1597 (s), 1567 (m), 1537 (w), 1515 (w), 1498 (s), 1442 (m), 1427 (w), 1416 (w), 1389 (m), 1347 (m), 1297 (m), 1244 (m), 1224 (w), 1208 (m), 1123 (w), 1099 (s), 1068 (m), 1034 (w), 998 (w), 969 (m), 920 (m), 858 (w), 831 (s).

4-(3-Methoxybenzyl)-5-phenylthieno[3,2-b]pyridin-7(4H)-one (43n):

Starting with 41a (145 mg, 0.5 mmol), Cs$_2$CO$_3$ (228 mg, 0.7 mmol), Pd$_2$(dba)$_3$ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.08 mL, 0.6 mmol), 43n was obtained as a yellow solid (125 mg, 72%), mp. 122–124 °C; $^1$H NMR (300 MHz, CDCl$_3$): $\delta = 3.63$ (s, OCH$_3$), 5.11 (s, CH$_2$), 6.26 (s, CH), 6.39-6.34 (m, 1H), 6.42-6.45 (m, 1H), 6.69-6.72 (m, 1H), 6.88 (d, $^3J = 5.49$ Hz, 1H), 7.10-7.15 (m, 1H), 7.23-7.36 (m, 5H), 7.51 (d, $^3J = 5.49$ Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): $\delta = 53.6$ (CH$_2$), 55.1 (OCH$_3$), 111.6 (C-6), 112.8 (C-2’), 113.7 (C-4’), 117.7 (C-6’), 117.9 (C-3), 128.5 (C-4’’), 128.7 (C-2’’6’’), 129.6 (C-3’’5’’), 129.8 (C-5’), 130.1 (C-8), 132.0 (C-1’), 134.3 (C-2), 137.6 (C-1’), 145.5 (C-9), 152.5 (C-3’), 160.0 (C-5), 173.5 (C-7); GC-MS (EI, 70eV): $m/z$ (%) = 347 (M$^+$, 71.46), 198 (2.60), 171 (2.06), 121 (100), 91 (19.21), 78 (10.08), 65 (5.10); HRMS (ESI): calcd for C$_{21}$H$_{17}$N$_1$O$_1$S$_1$ (M+H) 348.10528, found 348.10534; IR (ATR, cm$^{-1}$): $\tilde{\nu} = 3107$ (w), 3057 (w), 2956 (w), 2831 (w), 1738 (w), 1604 (m), 1589 (s), 1516 (w), 1492 (s), 1457 (w), 1434 (m), 1386 (m), 1354 (w), 1314 (w), 1289 (m), 1255 (m), 1202 (m), 1182 (w), 1158 (m), 1105 (s), 1078 (w), 1069 (w), 1035 (m), 993 (w), 960 (m), 949 (w), 916 (w), 876 (w), 845 (s).
4-Phenethyl-5-phenylthieno[3,2-b]pyridin-7(4H)-one (43o):

Starting with 41a (145 mg, 0.5 mmol), Cs₂CO₃ (228 mg, 0.7 mmol), Pd₂(dba)₃ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.08 mL, 0.6 mmol), 43o was obtained as a yellow solid (117 mg, 71%), mp. 70–72 °C; ¹H NMR (300 MHz, CDCl₃): δ = 2.81 (t, ³J = 7.49 Hz, CH₂), 4.13 (t, ³J = 7.49 Hz, CH₂), 6.24 (s, CH), 6.64-6.67 (m, 2H), 7.07-7.11 (m, 5H), 7.17 (d, ³J = 5.53 Hz, 1H), 7.17 (d, ³J = 5.53 Hz, 1H), 7.31-7.41 (m, 3H), 7.68 (d, ³J = 5.49 Hz, 1H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 35.6 (CH₂), 51.5 (CH₂), 113.6 (C-6), 117.0 (C-3), 127.0 (C-4′), 128.5 (C-2′,6′), 128.6 (C-4″), 128.7 (C-2″,6″), 128.8 (C-3″,5″), 129.4 (C-3′,5′), 130.0 (C-8), 132.3 (C-1″), 134.5 (C-2), 136.5 (C-1′), 144.8 (C-9), 152.1 (C-5), 173.3 (C-7); GC-MS (EI, 70eV): m/z (%) = 331 (M⁺, 44.21), 138 (18.01), 241 (17.16); HRMS (ESI): calcd for C₂₁H₁₇N₁O₁S₁ (M+H) 332.1103, found 332.1102; IR (ATR, cm⁻¹): ν = 3492 (w), 3053 (w), 1581 (s), 1533 (m), 1493 (m), 1441 (w), 1359 (w), 1304 (w), 1193 (m), 1105 (m), 846 (w), 750 (s), 698 (s).

4-Cyclohexyl-5-phenylthieno[3,2-b]pyridin-7(4H)-one (43p):

Starting with 41a (145 mg, 0.5 mmol), Cs₂CO₃ (228 mg, 0.7 mmol), Pd₂(dba)₃ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.07 mL, 0.6 mmol), 43p was obtained as a yellow solid (108 mg, 70%), mp. 231–233 °C; ¹H NMR (300 MHz, CDCl₃): δ = 0.89-2.24 (m, 10H), 6.13 (s, CH), 7.25-7.28 (m, 2H), 7.38-7.43 (m, 2H), 7.38-7.43 (m, 2H), 7.45 (d, ³J = 5.61 Hz, 1H), 7.62 (d, ³J = 5.58 Hz, 1H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 35.6 (CH₂), 51.5 (CH₂), 113.6 (C-6), 117.0 (C-3), 127.0 (C-4′), 128.5 (C-2′,6′), 128.6 (C-4″), 128.7 (C-2″,6″), 128.8 (C-3″,5″), 129.4 (C-3′,5′), 130.0 (C-8), 132.3 (C-1″), 134.5 (C-2), 136.5 (C-1′), 144.8 (C-9), 152.1 (C-5), 173.3 (C-7); GC-MS (EI, 70eV): m/z (%) = 331 (M⁺, 44.21), 138 (18.01), 241 (17.16); HRMS (ESI): calcd for C₁₉H₁₉N₁O₁S₁ (M+H) 310.12602, found 332.1102; IR (ATR, cm⁻¹): ν = 3080 (w), 2932 (w), 2856 (w), 1737 (w), 1604 (m), 1592 (s), 1538 (w), 1511 (w), 1481 (s), 1447 (s).
(m), 1425 (w), 1389 (m), 1347 (w), 1308 (m), 1253 (m), 1194 (w), 1175 (m), 1149 (w), 1101 (s), 1067 (m), 1019 (w), 997 (m), 934 (w), 897 (w), 845 (s).

4-Heptyl-5-phenylthieno[3,2-b]pyridin-7(4H)-one (43q):

Starting with 41a (145 mg, 0.5 mmol), Cs₂CO₃ (228 mg, 0.7 mmol), Pd₂dba₃ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.09 mL, 0.6 mmol), 43q was obtained as a yellow gel (112 mg, 69%); ¹H NMR (300 MHz, CDCl₃): δ = 0.75 (t, 3J = 7.12 Hz, CH₃), 1.02-1.59 (m, 10H), 3.89 (t, 3J = 7.99 Hz, CH₂), 6.19 (s, CH), 7.11 (d, 3J = 5.49 Hz, 1H), 7.28-7.32 (m, 2H), 7.41-7.43 (m, 3H), 7.67 (d, 3J = 5.48 Hz, 1H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 12.9 (C-7′), 21.3 (C-6′), 25.2 (C-3′), 27.4 (C-2′), 28.4 (C-4′), 30.3 (C-5′), 49.3 (C-1′), 112.5 (C-6), 116.1 (C-3), 127.6 (C-4′), 127.7 (C-2′,6′), 128.4 (C-3′,5′), 128.8 (C-8), 131.1 (C-1′), 133.7 (C-2), 144.0 (C-9), 151.0 (C-5), 172.2 (C-7); GC-MS (EI, 70eV): m/z (%) = 325 (M⁺, 41.53), 227 (32.94), 138 (17.66); HRMS (ESI): calcld for C₂₀H₂₃NOS (M+H) 326.1103, found 326.1102; IR (ATR, cm⁻¹): ~ν = 3057 (w), 2921 (m), 2856 (w), 1737 (w), 1581 (s), 1535 (s), 1493 (m), 1466 (w), 1370 (w), 1299 (w), 1193 (m), 1099 (s), 1019 (w), 845 (m), 768 (s), 703 (s).

4-(4-Chlorophenyl)-5-p-tolylthieno[3,2-b]pyridin-7(4H)-one (43r):

Starting with 41b (152 mg, 0.5 mmol), Cs₂CO₃ (228 mg, 0.7 mmol), (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (76 mg, 0.6 mmol), 43r was obtained as a yellow solid (135 mg, 77%), mp. 104–106 °C; ¹H NMR (300 MHz, CDCl₃): δ = 2.19 (s, CH₃), 6.30 (s, CH), 6.50 (d, 3J = 5.47 Hz, 1H), 6.91 (d, 3J = 9.10 Hz, 2H), 6.97 (d, 3J = 9.17 Hz, 2H), 7.04 (d, 3J = 8.73 Hz, 2H), 7.24 (d, 3J = 8.67 Hz, 2H), 7.46 (d, 3J = 5.47 Hz, 1H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 20.2 (CH₃), 112.5 (C-6), 115.4 (C-3), 117.6 (C-4′), 119.1 (C-2′,6′), 127.7 (C-3′,5′), 127.9 (C-3′,5′), 128.2 (C-1′), 128.7 (C-2′,6′), 128.9 (C-2), 130.7 (C-8), 133.9 (C-4′), 138.1 (C-
1’), 145.2 (C-9), 150.7 (C-5), 172.8 (C-7); GC-MS (EI, 70eV): m/z (%) = 353 (M⁺, 37Cl, 36.44), 351 (M⁺, 35Cl, 100), 323 (38.08), 286 (3.43), 273 (4.63), 235 (3.29), 200 (7.53), 172 (12.38), 137 (12.23), 115 (6.75); HRMS (ESI): calcd for C₂₀H₁₄ClN₁O₁S₁ (M+H) 353.04846, found 353.04852; IR (ATR, cm⁻¹): ~ ν = 3270 (w), 3188 (w), 3033 (w), 2917 (w), 2860 (w), 1731 (w), 1587 (s), 1506 (m), 1475 (s), 1424 (w), 1404 (w), 1377 (m), 1332 (w), 1307 (m), 1271 (w), 1251 (w), 1242 (w), 1184 (w), 1171 (w), 1089 (m), 1067 (w), 1041 (m), 1014 (m), 947 (w), 914 (w), 818 (s).

4-(4-Fluorophenyl)-5-p-tolylthieno[3,2-b]pyridin-7(4H)-one (43s):

Starting with 41b (152 mg, 0.5 mmol), Cs₂CO₃ (228 mg, 0.7 mmol), Pd₂dba₃ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.06 mL, 0.6 mmol), 43s was obtained as a yellow solid (142 mg, 85%), mp. 215–217 °C; ¹H NMR (300 MHz, CDCl₃): δ = 2.15 (s, CH₃), 6.28 (s, CH), 6.48 (d, 3 J = 5.50 Hz, 1H), 6.90–6.98 (m, 6H), 7.08–7.13 (m, 2H), 7.44 (d, 3 J = 5.50 Hz, 1H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 21.1 (CH₃), 113.4 (C-6), 116.5 (d, 2 Jₐ-CF = 22.98 Hz, C-3′,5′), 118.7 (C-3), 128.4 (C-2″,6″), 128.8 (C-3″,5″), 129.2 (C-1″), 130.4 (d, 3 Jₐ-CF = 8.82 Hz, C-2′,6′), 131.5 (C-2), 131.6 (C-8), 136.5 (d, 4 Jₐ-CF = 3.25 Hz, C-1′), 138.9 (C-4″), 146.4 (C-9), 151.8 (C-5), 162.9 (d, 1 Jₐ-CF = 250.34 Hz, C-4′), 173.7 (C-7); ¹⁹F NMR (282.4 MHz, CDCl₃): δ = -110.86 (s, CF); GC-MS (EI, 70eV): m/z (%) = 335 (M⁺, 100), 307 (41.33), 291 (5.09), 219 (6.13), 190 (5.88), 171 (3.70), 146 (5.13), 115 (5.29), 95 (4.15); HRMS (ESI): calcd for C₂₀H₁₄F₁N₁O₁S₁ (M+H) 336.08529, found 336.08595; IR (ATR, cm⁻¹): δ = 3116 (w), 3040 (w), 2919 (w), 2872 (w), 1603 (m), 1595 (s), 1524 (w), 1495 (m), 1479 (s), 1424 (w), 1415 (w), 1384 (m), 1315 (m), 1276 (w), 1254 (w), 1214 (m), 1184 (m), 1158 (m), 1101 (m), 1066 (m), 1041 (m), 1017 (m), 971 (w), 950 (w), 914 (w), 887 (w), 835 (m), 818 (s).
4-(4-Methoxyphenyl)-5-p-tolylthieno[3,2-b]pyridin-7(4H)-one (43t):

Starting with 41b (152 mg, 0.5 mmol), Cs$_2$CO$_3$ (228 mg, 0.7 mmol), Pd$_2$(dba)$_3$ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (73 mg, 0.6 mmol), 43t was obtained as a yellow solid (130 mg, 75%), mp. 175–177 °C; $^1$H NMR (300 MHz, CDCl$_3$): δ = 2.20 (s, CH$_3$), 3.73 (s, OCH$_3$), 6.36 (s, CH), 6.53 (d, $^3$J = 5.49 Hz, 1H), 6.76 (d, $^3$J = 8.97 Hz, 2H), 6.92-7.02 (m, 6H), 7.46 (d, $^3$J = 5.47 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): δ = 21.1 (CH$_3$), 55.4 (OCH$_3$), 113.4 (C-6), 114.5 (C-3’,5’), 118.9 (C-3), 128.5 (C-2”,6”), 128.7 (C-3”,5”), 129.2 (C-2’,6’), 129.5 (C-1”), 131.2 (C-2), 131.9 (C-8), 133.0 (C-4”), 138.6 (C-1’), 147.0 (C-9), 152.1 (C-4’), 159.4 (C-5), 173.9 (C-7); GC-MS (EI, 70eV): m/z (%) = 347 (M$^+$, 100), 319 (16.68), 304 (8.10), 276 (3.05), 260 (2.52), 216 (6.98), 188 (10.01), 160 (8.09), 134 (3.69), 115 (6.61); HRMS (ESI): calcd for C$_{21}$H$_{17}$NO$_2$S (M+H) 348.10528, found 348.10517; IR (ATR, cm$^{-1}$): $\tilde{\nu}$ = 3086 (w), 3044 (w), 3005 (w), 2963 (w), 2916 (w) , 2838 (w), 1737 (w), 1599 (s), 1585 (m), 1537 (w), 1506 (s), 1478 (m), 1380 (m), 1308 (m), 1297 (m), 1274 (w), 1244 (s), 1176 (m), 1147 (w), 1105 (m), 1068 (w), 1046 (m), 973 (w), 915 (w), 878 (w), 837 (m), 825 (s).

4-Phenyl-5-(4-propylphenyl)thieno[3,2-b]pyridin-7(4H)-one (43u):

Starting with 41c (166 mg, 0.5 mmol), Cs$_2$CO$_3$ (228 mg, 0.7 mmol), Pd$_2$(dba)$_3$ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.05 mL, 0.6 mmol), 43u was obtained as a yellow solid (143 mg, 83%), mp. 141–143 °C; $^1$H NMR (300 MHz, CDCl$_3$): δ = 0.75 (t, $^3$J = 7.40 Hz, CH$_3$), 1.46 (sext, $^3$J = 7.35 Hz, CH$_2$), 2.39 (t, $^3$J = 7.85 Hz, CH$_2$), 6.35 (s, CH), 6.51 (d, $^3$J = 5.51 Hz, 1H), 6.89 (d, $^3$J = 8.34 Hz, 2H), 6.96 (d, $^3$J = 8.27 Hz, 2H), 7.05-7.08 (m, 2H), 7.21-7.29 (m, 3H), 7.43(d, $^3$J = 5.48 Hz, 1H); $^{13}$C NMR (62.9 MHz, CDCl$_3$): δ = 13.5 (CH$_3$), 24.0 (CH$_2$), 37.4 (CH$_2$), 113.3 (C-6), 118.9 (C-4’), 128.0 (C-2’,6’), 128.5 (C-3), 128.6 (C-3”,5”), 128.8 (C-2”,6”), 129.2 (C-3’,5’), 129.4 (C-1”), 131.2 (C-2), 131.9 (C-8), 140.2 (C-4”), 143.4 (C-1),
146.4 (C-9), 151.8 (C-5), 173.8 (C-7); GC-MS (EI, 70eV): m/z (%) = 345 (M⁺, 100), 317 (11.62), 288 (49.42), 272 (2.99), 254 (2.40), 201 (3.08), 172 (3.70), 136 (2.60), 115 (3.47); HRMS (ESI): calcd for C₂₂H₁₉N₁O₁S₁ (M+H) 346.12602, found 346.12579; IR (ATR, cm⁻¹): ν = 3120 (w), 3050 (w), 2954 (w), 2928 (w), 2856 (w), 1601 (m), 1587 (s), 1520 (w), 1478 (s), 1453 (m), 1410 (m), 1382 (m), 1338 (w), 1312 (m), 1270 (m), 1206 (w), 1184 (w), 1164 (w), 1107 (m), 1044 (m), 1019 (w), 1000 (w), 961 (w), 916 (w), 871 (w), 829 (s), 759(s).

4-(3-Fluorophenyl)-5-(4-propylphenyl)thieno[3,2-b]pyridin-7(4H)-one (43v):

Starting with 41c (166 mg, 0.5 mmol), Cs₂CO₃ (228 mg, 0.7 mmol), Pd₂(dba)₃ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.06 mL, 0.6 mmol), 43v was obtained as a yellow solid (145 mg, 81%), mp. 138–140 °C; ¹H NMR (300 MHz, CDCl₃): δ = 0.75 (t, ³J = 7.40 Hz, CH₃), 1.46 (sext, ³J = 7.25 Hz, CH₂), 2.40 (t, ³J = 7.87 Hz, CH₂), 6.31 (s, CH), 6.53 (d, ³J = 5.50 Hz, 1H), 6.81-6.85 (m, 1H), 6.90-6.99 (m, 6H), 7.21-7.29 (m, 1H), 7.45 (d, ³J = 5.49 Hz, 1H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 12.5 (CH₃), 23.0 (CH₂), 36.5 (CH₂), 112.4 (C-6), 115.8 (d, ²J_C-F = 20.82 Hz, C-2'), 115.3 (d, ²J_C-F = 23.12 Hz, C-4'), 117.6 (C-3), 123.7 (d, ⁴J_C-F = 3.34 Hz, C-6'), 127.2 (C-3',5'), 127.5(C-2',6''), 128.1 (C-1''), 129.7 (d, ³J_C-F = 8.99 Hz, C-5'), 130.6 (C-2), 130.6 (C-8), 140.4 (d, ³J_C-F = 9.60 Hz, C-1'), 142.7 (C-4''), 145.0 (C-9), 150.6 (C-5), 161.5 (d, ¹J_C-F = 250.17 Hz, C-3'), 172.7 (C-7); ¹⁹F NMR (282.4 MHz, CDCl₃): δ = -109.97 (s, CF); GC-MS (EI, 70eV): m/z (%) = 363 (M⁺, 100), 335 (11.67), 306 (48.30), 272 (2.12), 219 (3.23), 191 (3.44), 139 (3.03), 115 (4.47); HRMS (ESI): calcd for C₂₂H₁₈F₁₁N₁O₁S₁ (M+H) 364.11659, found 364.11671; IR (ATR, cm⁻¹): ν = 3114 (w), 3033 (w), 2958 (w), 2926 (w), 2869 (w), 1615 (m), 1593 (s), 1524 (w), 1480 (s), 1412 (w), 1377 (m), 1340 (w), 1317 (m), 1285 (w), 1269 (w), 1256 (w), 1242 (w), 1186 (s), 1155 (w), 1100 (m), 1077 (m), 1046 (m), 1005 (w), 975 (w), 910 (w), 876 (m), 835 (s).
4-(3,5-Dichlorophenyl)-5-(4-propylphenyl)thieno[3,2-b]pyridin-7(4H)-one (43w):

Starting with 41c (166 mg, 0.5 mmol), Cs₂CO₃ (228 mg, 0.7 mmol), Pd₂dba₃ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (97 mg, 0.6 mmol), 43w was obtained as a yellow solid (155 mg, 75%), mp. 80–82 °C. ¹H NMR (300 MHz, CDCl₃): δ = 0.02 (t, 3J = 7.29 Hz, CH₃), 0.74 (sext, 3J = 7.58 Hz, CH₂), 1.69 (t, 3J = 7.87 Hz, CH₂), 5.57 (s, CH), 5.80 (d, 4J = 5.45 Hz, 1H), 6.21-6.23 (m, 4H), 6.26 (d, 4J = 1.83 Hz, 2H), 7.48 (t, 4J = 1.83 Hz, 1H), 6.76 (d, 3J = 5.50 Hz, 1H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 13.5 (CH₃), 24.0 (CH₂), 37.5 (CH₂), 113.7 (C-6), 118.2 (C-4’), 127.4 (C-3), 128.5 (C-2’,6’), 128.8 (C-3”,5”), 129.1 (C-2”,6”), 129.3 (C-3”,5”), 131.1 (C-1”), 132.0 (C-2”), 135.7 (C-8), 141.8 (C-4”), 144.1 (C-9), 145.6 (C-1’), 151.4 (C-5), 173.8 (C-7); GC-MS (EI, 70eV): m/z (%) = 417 (M⁺, 37Cl³⁷Cl, 14.42), 415(M⁺, ³⁷Cl⁵³Cl, 74.18), 413(M⁺, ³⁵Cl⁵³Cl, 100), 385 (10.05), 356 (3.80), 284 (3.21), 234 (5.46), 206 (10.37), 171 (3.35), 136 (2.84),115 (6.00). HRMS (ESI): calcd for C₂₂H₁₇Cl₂N₂O₂S (M+H) 414.04807, found 414.04721. IR (ATR, cm⁻¹): ν ≈ 3050 (w), 2958 (w), 2927 (w), 2867 (w), 1605 (m), 1568 (s), 1522 (w), 1496 (w), 1475 (m), 1422 (m), 1374 (m), 1338 (w), 1309 (m), 1257 (m), 1202 (w), 1185 (w), 1103 (m), 1061 (s), 1020 (w), 996 (w), 929 (w), 907 (w), 831 (m).

5-(4-Methoxyphenyl)-4-p-tolylthieno[3,2-b]pyridin-7(4H)-one (43x):

Starting with 41d (160 mg, 0.5 mmol), Cs₂CO₃ (228 mg, 0.7 mmol), Pd₂dba₃ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.07 mL, 0.6 mmol), 43x was obtained as a yellow solid (139 mg, 80%), mp. 172–174 °C; ¹H NMR (300 MHz, CDCl₃): δ = 2.26 (s, CH₃), 3.66 (s, OCH₃), 6.33 (s, CH), 6.52 (d, 3J = 5.49 Hz, 1H), 6.63 (d, 3J = 8.83 Hz, 2H), 6.95 (d, 3J = 8.31 Hz, 2H), 7.00 (d, 3J = 8.85 Hz, 2H), 7.06 (d, 3J = 8.04 Hz, 2H), 7.43(d, 3J = 5.48 Hz, 1H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 21.1 (CH₃), 55.1 (OCH₃), 113.3 (C-6), 113.4 (C-3”,5”), 119.0 (C-3), 127.0 (C-1”), 128.2 (C-2’,6’), 128.4 (C-2”,6”), 130.1 (C-3”,5”), 130.7 (C-4”), 131.1 (C-
2), 137.7 (C-8), 138.9 (C-1′), 146.7 (C-9), 151.7 (C-5), 159.6 (C-4″), 173.8 (C-7); GC-MS (EI, 70 eV): m/z (%) = 347 (M⁺, 100), 332 (3.23), 319 (18.32), 304 (12.77), 260 (5.43), 214 (7.10), 186 (7.82), 152 (2.66), 130 (3.93); HRMS (ESI): calcd for C₂₁H₁₇N₁O₂S₁ (M+H) 348.10528, found 348.10458; IR (ATR, cm⁻¹): ν ≈ 3087 (w), 3063 (w), 2932 (w), 2838 (w), 1737 (w), 1590 (s), 1574 (m), 1510 (m), 1473 (m), 1414 (w), 1376 (m), 1312 (m), 1292 (m), 1269 (w), 1248 (s), 1237 (s), 1175 (m), 1151 (w), 1109 (m), 1070 (w), 1042 (m), 961 (w), 940 (w), 915 (w), 870 (w), 825 (s).

4-(4-Chlorophenyl)-5-(4-methoxyphenyl)thieno[3,2-b]pyridin-7(4H)-one (43y):

Starting with 41d (160 mg, 0.5 mmol), Cs₂CO₃ (228 mg, 0.7 mmol), Pd₂(dba)₃ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (76 mg, 0.6 mmol), 43y was obtained as a yellow solid (150 mg, 82%), mp. 84–86 °C; ¹H NMR (300 MHz, CDCl₃): δ = 3.68 (s, OCH₃), 6.31 (s, CH), 6.51 (d, J = 5.47 Hz, 1H), 6.66 (d, J = 8.79 Hz, 2H), 6.99 (d, J = 8.80 Hz, 2H), 7.06 (d, J = 8.67 Hz, 2H), 7.26 (d, J = 8.66 Hz, 2H), 7.47 (d, J = 5.46 Hz, 1H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 55.2 (OCH₃), 113.5 (C-6), 113.6 (C-3″,5″), 118.6 (C-3), 126.6 (C-1″), 128.6 (C-4′), 129.8 (C-3′,5′), 129.9 (C-2″,6″), 130.7 (C-2″,6″), 131.5 (C-2), 134.8 (C-8), 138.8 (C-1′), 146.2 (C-9), 151.4 (C-5), 159.8 (C-4″), 173.8 (C-7); GC-MS (EI, 70 eV): m/z (%) = 369 (M⁺, Cl, 38.61), 367 (M⁺, Cl, 100), 339 (19.58), 324 (18.48), 289 (2.47), 260 (10.49), 235 (6.50), 200 (10.84), 172 (12.10), 152 (3.87), 130 (3.56); HRMS (ESI): calcd for C₂₀H₁₄ClN₁O₂S₁ (M+H) 368.05065, found 368.05043; IR (ATR, cm⁻¹): ν ≈ 3087 (w), 3050 (w), 2930 (w), 2836 (w), 1731 (w), 1598 (s), 1587 (m), 1574 (m), 1520 (m), 1474 (s), 1403 (w), 1376 (m), 1312 (m), 1292 (m), 1246 (s), 1175 (m), 1103 (m), 1088 (m), 1067 (w), 1026 (m), 914 (w), 828 (s).
4-(4-Ethylphenyl)-5-(4-methoxyphenyl)thieno[3,2-b]pyridin-7(4H)-one (43z):

Starting with 41d (160 mg, 0.5 mmol), Cs₂CO₃ (228 mg, 0.7 mmol), Pd₂(dba)₃ (22 mg, 0.025 mmol), BINAP (31 mg, 0.05 mmol) and aniline (0.07 mL, 0.6 mmol), 43z was obtained as a yellow gel (142 mg, 79%); ¹H NMR (300 MHz, CDCl₃): δ = 1.13 (t, ³J = 7.62 Hz, CH₃), 2.55 (q, ³J = 7.60 Hz, CH₂), 3.65 (s, OCH₃), 6.33 (s, CH), 6.53 (d, ³J = 5.49 Hz, 1H), 6.62 (d, ³J = 8.90 Hz, 2H), 6.97 (d, ³J = 8.43 Hz, 2H), 6.99 (d, ³J = 8.84 Hz, 2H), 7.08 (d, ³J = 8.49 Hz, 2H), 7.43(d, ³J = 5.49 Hz, 1H); ¹³C NMR (62.9 MHz, CDCl₃): δ = 15.1 (CH₃), 28.3 (CH₂), 55.1 (OCH₃), 113.3 (C-6), 113.4 (C-3″,5″), 119.1 (C-3), 127.0 (C-1″), 128.3 (C-2′,6′), 128.4 (C-3′,5′), 128.8 (C-2″,6″), 130.7 (C-2), 131.1 (C-8), 137.8 (C-4′), 145.1 (C-1′), 146.7 (C-9), 151.7 (C-5), 159.6 (C-4″), 173.8 (C-7); GC-MS (EI, 70eV): m/z (%) = 361 (M⁺, 100), 333 (15.85), 318 (15.36), 289 (2.58), 273 (2.19), 260 (6.07), 214 (10.71), 185 (2.48); HRMS (ESI): calcd for C₂₂H₁₉NO₂S (M+H) 362.12093, found 362.12142; IR (ATR, cm⁻¹): ʋ = 3041 (w), 2963 (w), 2930 (w), 2836 (w), 1592 (s), 1496 (m), 1473 (s), 1416 (w), 1377 (m), 1311 (w), 1291 (m), 1272 (w), 1246 (s), 1175 (m), 1105 (m), 1066 (w), 1043 (m), 1027 (m), 968 (w), 915 (w), 829 (s).
4.1 Biological screening:

2(3H)-Furanones and 2(3H)-pyrrolones were screened for their anti-oxidant, brine shrimp lethality and urease inhibition activities. The results are shown below:

4.1.1. Antioxidant activity (DPPH radical scavenging assay):

The free radical scavenging ability of the synthesized compounds was measured by modified 1,1-diphenyl-2-picrylhydrazyl (DPPH) method described by Choudhary et al.\textsuperscript{182} n-propyl gallate was used as standard. Test compounds were allowed to react with the stable free radical DPPH for half an hour at 37 °C. The concentration of DPPH was kept at 300 µM. The test compounds were dissolved in DMSO while the DPPH solution was prepared in ethanol. After incubation, the decrease in absorption was measured at 515 nm using multireader, Spectra MAX-384. Percent radical scavenging activity (RSA) of the test compounds was determined in comparison with a DMSO treated control using following formula.

\[
\% \text{ RSA} = 100 - \{\text{OD test compound}/\text{OD control}\} \times 100
\]

Furanones and pyrrolones were screened for DPPH radical scavenging assay. All the compounds showed non-significant activity and is shown in the following (table 4.1). Activity with percent radical scavenging activity (RSA) less than 50 is considered to be nonsignificant.

<table>
<thead>
<tr>
<th>Compd</th>
<th>% RSA</th>
<th>IC_{50}±SEM (µM)</th>
<th>Compd</th>
<th>% RSA</th>
<th>IC_{50}±SEM (µM)</th>
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</thead>
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<tr>
<td>7a</td>
<td>1.30</td>
<td>-</td>
<td>8e</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7b</td>
<td>3.10</td>
<td>-</td>
<td>8f</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7c</td>
<td>0.59</td>
<td>-</td>
<td>8g</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>7d</td>
<td>3.44</td>
<td>-</td>
<td>8h</td>
<td>12.96</td>
<td>-</td>
</tr>
<tr>
<td>7e</td>
<td>8.12</td>
<td>-</td>
<td>8i</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
4.1.2. Cytotoxicity (Brine shrimp lethality bioassay):

The cytotoxicity of the synthesized compounds was studied by the Brine shrimp lethality bioassay method. Brine shrimps (Artemia salvia, leach) were hatched using brine shrimp eggs in a vessel, filled with sterile stimulated sea water (prepared using sea salt 38gL⁻¹ and adjusted to pH 8.5 using 1M NaOH) at room temperature (22-29 °C) under constant aeration for two days. After hatching, thirty active nauplii were drawn through a glass capillary and placed in a vial containing 4.5 mL of brine solution and a drop of yeast suspension. In each experiment, 0.5 mL of

<p>| | | | | | |</p>
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>7f</td>
<td>5.84</td>
<td>–</td>
<td>8j</td>
<td>6.53</td>
<td>–</td>
</tr>
<tr>
<td>7g</td>
<td>11.23</td>
<td>–</td>
<td>8k</td>
<td>11.23</td>
<td>–</td>
</tr>
<tr>
<td>7h</td>
<td>21.73</td>
<td>–</td>
<td>8l</td>
<td>16.52</td>
<td>–</td>
</tr>
<tr>
<td>7i</td>
<td>20.3</td>
<td>–</td>
<td>12a</td>
<td>2.11</td>
<td>–</td>
</tr>
<tr>
<td>7j</td>
<td>19.1</td>
<td>–</td>
<td>12b</td>
<td>-2.28</td>
<td>–</td>
</tr>
<tr>
<td>7k</td>
<td>24.5</td>
<td>–</td>
<td>12c</td>
<td>2.19</td>
<td>–</td>
</tr>
<tr>
<td>7l</td>
<td>22.1</td>
<td>–</td>
<td>12d</td>
<td>40.12</td>
<td>–</td>
</tr>
<tr>
<td>7m</td>
<td>26.66</td>
<td>–</td>
<td>12e</td>
<td>5.22</td>
<td>–</td>
</tr>
<tr>
<td>7n</td>
<td>-1.91</td>
<td>–</td>
<td>12f</td>
<td>4.12</td>
<td>–</td>
</tr>
<tr>
<td>7o</td>
<td>5.23</td>
<td>–</td>
<td>13a</td>
<td>19.23</td>
<td>–</td>
</tr>
<tr>
<td>7p</td>
<td>-14.92</td>
<td>–</td>
<td>13b</td>
<td>22.37</td>
<td>–</td>
</tr>
<tr>
<td>7q</td>
<td>3.12</td>
<td>–</td>
<td>13c</td>
<td>10.68</td>
<td>–</td>
</tr>
<tr>
<td>8a</td>
<td>5.47</td>
<td>–</td>
<td>13d</td>
<td>38.53</td>
<td>–</td>
</tr>
<tr>
<td>8b</td>
<td>23.37</td>
<td>–</td>
<td>13e</td>
<td>20</td>
<td>–</td>
</tr>
<tr>
<td>8c</td>
<td>5.57</td>
<td>–</td>
<td>13f</td>
<td>10.41</td>
<td>–</td>
</tr>
<tr>
<td>8d</td>
<td>1.98</td>
<td>–</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

n-propyl gallate | 90.31 | 30.46±0.27 | n-propyl gallate | 90.31 | 30.46±0.27

–, Not done
the test solution was added to the vial and maintained at ambient temperature for 24 hour. The surviving larvae were counted. All the experiments with different concentrations (1, 10, 100 µg mL\(^{-1}\)) of the test compounds were conducted in triplicate and compared with the control. Data were analyzed with Finney’s probit analysis to determine the LD\(_{50}\).\(^{184}\) Etopside was used as the standard drug.

Furanones and pyrrolones were screened for brine shrimp lethality assay and were found to be inactive.

4.1.3. Urease inhibition studies:

Urease inhibition activity of the synthesized compounds was performed against jack bean urease enzyme using thiourea as the standard inhibitor. Reaction mixtures consisting of 25 µL of enzyme (jack bean urease) and 55 µL of buffers containing 100 mM urea were incubated with 5 µL of the test synthesized compounds (0.5 mM concentration) at 30 °C for 15 min. Urease inhibition activity was determined by measuring ammonia production according to the indophenol method as described by Weatherburn.\(^{185}\) The increase in absorbance at 630 nm was measured after 50 min, using a microplate reader (Molecular Device USA). All the results were performed in triplicate. The results (change in absorbance per min) were processed by using software, soft Max Pro (Molecular Device USA). The entire essays were carried out at pH-6.8. Percentage inhibition of the synthesized compounds was calculated from the formula.

\[
\text{% inhibition} = 100 - \left( \frac{\text{OD testwell}}{\text{OD control}} \right) \times 100
\]

Furanones and pyrrolones were screened for urease inhibition studies. The compounds showed weak to moderate activity and is shown in the following (table 4.2). Activity in the range IC\(_{50} \pm\) SEM 200 is considered moderate. Generally speaking the bromo series of furanones and pyrrolones showed good activity as compared to the ethoxy series of furanones and pyrrolones.
<table>
<thead>
<tr>
<th>Compd</th>
<th>% inhibition</th>
<th>IC$_{50}$±SEM (µM)</th>
<th>Compd</th>
<th>% inhibition</th>
<th>IC$_{50}$±SEM (µM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>7a</td>
<td>84.1</td>
<td>212.1±2.01</td>
<td>8e</td>
<td>60.3</td>
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<tr>
<td>7b</td>
<td>12.7</td>
<td>–</td>
<td>8f</td>
<td>73.4</td>
<td>247.11±1.24</td>
</tr>
<tr>
<td>7c</td>
<td>10.1</td>
<td>–</td>
<td>8g</td>
<td>40.6</td>
<td>–</td>
</tr>
<tr>
<td>7d</td>
<td>72.4</td>
<td>325.1±1.01</td>
<td>8h</td>
<td>82.4</td>
<td>211.96±0.88</td>
</tr>
<tr>
<td>7e</td>
<td>65.2</td>
<td>345.2±1.97</td>
<td>8i</td>
<td>63.1</td>
<td>364.2±3.39</td>
</tr>
<tr>
<td>7f</td>
<td>25.7</td>
<td>–</td>
<td>8j</td>
<td>55.3</td>
<td>419.16±3.93</td>
</tr>
<tr>
<td>7g</td>
<td>12.3</td>
<td>–</td>
<td>8k</td>
<td>68.4</td>
<td>362.1±0.47</td>
</tr>
<tr>
<td>7h</td>
<td>13.9</td>
<td>–</td>
<td>8l</td>
<td>69.1</td>
<td>365.93±0.27</td>
</tr>
<tr>
<td>7i</td>
<td>22</td>
<td>–</td>
<td>12a</td>
<td>35.1</td>
<td>–</td>
</tr>
<tr>
<td>7j</td>
<td>28.1</td>
<td>–</td>
<td>12b</td>
<td>13.1</td>
<td>–</td>
</tr>
<tr>
<td>7k</td>
<td>17.9</td>
<td>–</td>
<td>12c</td>
<td>14</td>
<td>–</td>
</tr>
<tr>
<td>7l</td>
<td>21</td>
<td>–</td>
<td>12d</td>
<td>52.2</td>
<td>480.1±2.11</td>
</tr>
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<td>21.9</td>
<td>–</td>
<td>12e</td>
<td>26.6</td>
<td>–</td>
</tr>
<tr>
<td>7n</td>
<td>24.4</td>
<td>–</td>
<td>12f</td>
<td>28.8</td>
<td>–</td>
</tr>
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<td>7o</td>
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<td>–</td>
<td>13a</td>
<td>58.2</td>
<td>440.63±2.12</td>
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<td>–</td>
<td>13b</td>
<td>39.2</td>
<td>–</td>
</tr>
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<td>7q</td>
<td>21.2</td>
<td>–</td>
<td>13c</td>
<td>9.7</td>
<td>–</td>
</tr>
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<td>8a</td>
<td>21.2</td>
<td>–</td>
<td>13d</td>
<td>66.1</td>
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</tr>
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<td>8b</td>
<td>72.1</td>
<td>254.26±2.19</td>
<td>13e</td>
<td>25</td>
<td>–</td>
</tr>
<tr>
<td>8c</td>
<td>38.4</td>
<td>–</td>
<td>13f</td>
<td>16</td>
<td>–</td>
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<td>8d</td>
<td>63.3</td>
<td>406.76±1.14</td>
<td>thiourea</td>
<td>98.2</td>
<td>21±0.011</td>
</tr>
<tr>
<td>thiourea</td>
<td>98.2</td>
<td>21±0.011</td>
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-, Not done
### 4.2. Data for X-Ray Crystal structures

**Data for compound 20k Chapter 2:**

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<td>Empirical formula</td>
<td>C\textsubscript{18}H\textsubscript{10}F\textsubscript{3}NO\textsubscript{3}</td>
</tr>
<tr>
<td>Formula weight</td>
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</tr>
<tr>
<td>Temperature</td>
<td>173 K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>triclinic</td>
</tr>
<tr>
<td>Space group (H.-M.)</td>
<td>P -1</td>
</tr>
<tr>
<td>Space group (Hall)</td>
<td>-P 1</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 10.9309 (5) Å, b = 11.4227 (5) Å, c = 13.0863 (6) Å</td>
</tr>
<tr>
<td></td>
<td>α = 85.205 (1) ° , β = 69.227 (1) °, γ = 71.674 (1) °</td>
</tr>
<tr>
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<td>1449.54 Å\textsuperscript{3}</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.582 mg/m\textsuperscript{3}</td>
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<tr>
<td>Absorption coefficient</td>
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<td>F(000)</td>
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<tr>
<td>Independent reflections</td>
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<td>Completeness to Θ = 32.50°</td>
<td>99.3%</td>
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<tr>
<td>Absorption correction</td>
<td>Multi-scan</td>
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<td>Max. and min. transmission</td>
<td>0.989 and 0.925</td>
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<td>Refinement method</td>
<td>Full-matrix least-squares on F\textsuperscript{2}</td>
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<td>Data / restraints / parameters</td>
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<td>Goodness-of-fit on F\textsuperscript{2}</td>
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<td>Final R indices [I&gt;2σ(I)]</td>
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<td>Largest diff. peak and hole</td>
<td>0.48 and -0.24 e.Å\textsuperscript{3}</td>
</tr>
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Data for compound 26a Chapter 2:

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<td>173 K</td>
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<td>Wavelength</td>
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</tr>
<tr>
<td></td>
<td>b = 27.5388 (6) Å, ( \beta = 112.033 \degree )</td>
</tr>
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<td></td>
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<td>Max. and min. transmission</td>
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<td>0.48 and -0.24 e.Å(^{-3})</td>
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### Data for compound 27i Chapter 2:

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<th>Property</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Identification code</td>
<td>sa07</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C_{18}H_{20}O_{3}S</td>
</tr>
<tr>
<td>Formula weight</td>
<td>316.40</td>
</tr>
<tr>
<td>Temperature</td>
<td>173 K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>monoclinic</td>
</tr>
<tr>
<td>Space group (H.-M.)</td>
<td>P 21/n</td>
</tr>
<tr>
<td>Space group (Hall)</td>
<td>-P 2yn</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 8.6840 (3) Å, α = 90 °.</td>
</tr>
<tr>
<td></td>
<td>b = 18.1116 (6) Å, β = 107.489 (2) °.</td>
</tr>
<tr>
<td></td>
<td>c = 10.6925 (4) Å, γ = 90 °.</td>
</tr>
<tr>
<td>Volume</td>
<td>1603.99 (10) Å³</td>
</tr>
<tr>
<td>Z</td>
<td>4</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.310 mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.21 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>672</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.43 × 0.27 × 0.21 mm³</td>
</tr>
<tr>
<td>Θ range for data collection</td>
<td>4.6 to 64.3 °.</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-11 ≤ h ≤ 11, -24 ≤ k ≤ 19, -14 ≤ l ≤ 14</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>18978</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>4263 [R(int) = 0.040]</td>
</tr>
<tr>
<td>Completeness to Θ = 29.00°</td>
<td>99.9%</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Multi-scan</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.957 and 0.915</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>3490 / 0 / 201</td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.05</td>
</tr>
<tr>
<td>Final R indices [I&gt;2σ(I)]</td>
<td>R1 = 0.040, wR2 = 0.113</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.80 and -0.23 e Å⁻³</td>
</tr>
</tbody>
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### Data for compound 28a Chapter 2:

<table>
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<tbody>
<tr>
<td>Identification code</td>
<td>sa63l</td>
</tr>
<tr>
<td>Empirical formula</td>
<td>C&lt;sub&gt;11&lt;/sub&gt;H&lt;sub&gt;6&lt;/sub&gt;O&lt;sub&gt;2&lt;/sub&gt;S</td>
</tr>
<tr>
<td>Formula weight</td>
<td>202.22</td>
</tr>
<tr>
<td>Temperature</td>
<td>173 K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>monoclinic</td>
</tr>
<tr>
<td>Space group (H.-M.)</td>
<td>C 2/c</td>
</tr>
<tr>
<td>Space group (Hall)</td>
<td>-C 2yc</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 12.1363 (3) Å, ( \alpha = 90^\circ ), b = 8.2055 (2) Å, ( \beta = 106.099 (1)^\circ ), c = 18.5917 (5) Å, ( \gamma = 90^\circ )</td>
</tr>
<tr>
<td>Volume</td>
<td>1778.84 (1) Å³</td>
</tr>
<tr>
<td>Z</td>
<td>8</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.510 mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.33 mm&lt;sup&gt;-1&lt;/sup&gt;</td>
</tr>
<tr>
<td>F(000)</td>
<td>832</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.62 × 0.40 × 0.23 mm³</td>
</tr>
<tr>
<td>( \Theta ) range for data collection</td>
<td>6.1 to 59.9 °</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-16≤h≤12, -11≤k≤8, -23≤l≤26</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>9561</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>2581 [R(int) = 0.015]</td>
</tr>
<tr>
<td>Completeness to ( \Theta = 29.96^\circ )</td>
<td>99.6%</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Multi-scan</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.929 and 0.823</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F&lt;sup&gt;2&lt;/sup&gt;</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>2288 / 0 / 127</td>
</tr>
<tr>
<td>Goodness-of-fit on F&lt;sup&gt;2&lt;/sup&gt;</td>
<td>1.08</td>
</tr>
<tr>
<td>Final R indices [I&gt;2σ(I)]</td>
<td>R1 = 0.032, wR2 = 0.099</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.37 and -0.20 e.Å&lt;sup&gt;-3&lt;/sup&gt;</td>
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**Data for compound 28n Chapter 2:**

<table>
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<th>Value</th>
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<tbody>
<tr>
<td>Identification code</td>
<td>sa103l</td>
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<tr>
<td>Empirical formula</td>
<td>C_{11}H_{5}ClO_{2}S</td>
</tr>
<tr>
<td>Formula weight</td>
<td>236.66</td>
</tr>
<tr>
<td>Temperature</td>
<td>213 K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>monoclinic</td>
</tr>
<tr>
<td>Space group (H.-M.)</td>
<td>C 2/c</td>
</tr>
<tr>
<td>Space group (Hall)</td>
<td>-C 2yc</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 13.0043 (6) Å, α = 90 °, b = 8.2216 (3) Å, β = 92.290 (2) °, c = 17.8670 (8) Å, γ = 90 °</td>
</tr>
<tr>
<td>Volume</td>
<td>1908.75 (14) Å³</td>
</tr>
<tr>
<td>Z</td>
<td>8</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.647 mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.59 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>960</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.39 × 0.32 × 0.17 mm³</td>
</tr>
<tr>
<td>Θ range for data collection</td>
<td>5.9 to 62.2 °</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-18≤h≤18, -11≤k≤11, -25≤l≤25</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>11222</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>2787 [R(int) = 0.030]</td>
</tr>
<tr>
<td>Completeness to Θ = 30.00°</td>
<td>99.9%</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Multi-scan</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.907 and 0.803</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>2446 / 0 / 136</td>
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<tr>
<td>Goodness-of-fit on F²</td>
<td>1.04</td>
</tr>
<tr>
<td>Final R indices [I&gt;2σ(I)]</td>
<td>R1 = 0.032, wR2 = 0.091</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.36 and -0.33 e.Å⁻³</td>
</tr>
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</table>
Data for compound 34c Chapter 2:

Identification code sa861
Empirical formula C$_{14}$H$_{11}$NOS
Formula weight 241.30
Temperature 173 K
Wavelength 0.71073 Å
Crystal system orthorhombic
Space group (H.-M.) P b c a
Space group (Hall) -P 2ac 2ab
Unit cell dimensions
\[
\begin{align*}
a &= 7.3732 (4) \text{ Å} & \alpha &= 90^\circ \\
b &= 14.0468 (6) \text{ Å} & \beta &= 90^\circ \\
c &= 22.9069 (4) \text{ Å} & \gamma &= 90^\circ \\
\end{align*}
\]
Volume 2372.5 (2) Å$^3$
Z 8
Density (calculated) 1.351 mg/m$^3$
Absorption coefficient 0.25 mm$^{-1}$
F(000) 1008
Crystal size 0.48 × 0.18 × 0.17 mm$^3$
Θ range for data collection 5.8 to 59.8 °
Index ranges -7 ≤ h ≤ 10, -19 ≤ k ≤ 15, -30 ≤ l ≤ 32
Reflections collected 24054
Independent reflections 3432 [R(int) = 0.033]
Completeness to Θ = 29.99° 99.1%
Absorption correction Multi-scan
Max. and min. transmission 0.958 and 0.888
Refinement method Full-matrix least-squares on F$^2$
Data / restraints / parameters 2748 / 0 / 163
Goodness-of-fit on F$^2$ 1.06
Final R indices [I>2σ(I)] R1 = 0.035, wR2 = 0.100
Largest diff. peak and hole 0.37 and -0.27 e.Å$^{-3}$
### Data for compound 36d Chapter 2:

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<td>Identification code</td>
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<tr>
<td>Empirical formula</td>
<td>C\textsubscript{16}H\textsubscript{15}NOS</td>
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<tr>
<td>Formula weight</td>
<td>269.35</td>
</tr>
<tr>
<td>Temperature</td>
<td>173 K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>monoclinic</td>
</tr>
<tr>
<td>Space group (H.-M.)</td>
<td>P 21/n</td>
</tr>
<tr>
<td>Space group (Hall)</td>
<td>P 2yn</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 10.7125 (6) Å, (\alpha = 90^\circ)</td>
</tr>
<tr>
<td></td>
<td>b = 9.0652 (5) Å, (\beta = 107.363 (2)^\circ)</td>
</tr>
<tr>
<td></td>
<td>c = 14.5990 (8) Å, (\gamma = 90^\circ)</td>
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<tr>
<td>Volume</td>
<td>1353.12 (13) Å(^3)</td>
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<tr>
<td>(Z)</td>
<td>4</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.322 mg/m(^3)</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.23 mm(^{-1})</td>
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<tr>
<td>(F(000))</td>
<td>568</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.42 \times 0.29 \times 0.18 mm(^3)</td>
</tr>
<tr>
<td>(\Theta) range for data collection</td>
<td>5.4 to 60.0 (^\circ)</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-13(\leq h \leq 15), -12(\leq k \leq 12), -20(\leq l \leq 8)</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>15165</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>3890 [R(int) = 0.028]</td>
</tr>
<tr>
<td>Completeness to (\Theta = 29.99^\circ)</td>
<td>98.7%</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Multi-scan</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.960 and 0.910</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on (F^2)</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>3320 / 0 / 177</td>
</tr>
<tr>
<td>Goodness-of-fit on (F^2)</td>
<td>1.09</td>
</tr>
<tr>
<td>Final R indices [I&gt;2(\sigma(I))]</td>
<td>R1 = 0.040, wR2 = 0.120</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.47 and -0.34 e.Å(^{-3})</td>
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Data for compound 43a Chapter 2:

<table>
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<th>Property</th>
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</thead>
<tbody>
<tr>
<td>Identification code</td>
<td>sa130</td>
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<tr>
<td>Empirical formula</td>
<td>C_{19}H_{13}NOS</td>
</tr>
<tr>
<td>Formula weight</td>
<td>303.36</td>
</tr>
<tr>
<td>Temperature</td>
<td>173 K</td>
</tr>
<tr>
<td>Wavelength</td>
<td>0.71073 Å</td>
</tr>
<tr>
<td>Crystal system</td>
<td>orthorhombic</td>
</tr>
<tr>
<td>Space group (H.-M.)</td>
<td>P b c a</td>
</tr>
<tr>
<td>Space group (Hall)</td>
<td>-P 2ac 2ab</td>
</tr>
<tr>
<td>Unit cell dimensions</td>
<td>a = 7.1897 (5) Å, b = 16.5759 (10) Å, c = 24.3797 (15) Å</td>
</tr>
<tr>
<td>Volume</td>
<td>2905.5 (3) Å³</td>
</tr>
<tr>
<td>Z</td>
<td>8</td>
</tr>
<tr>
<td>Density (calculated)</td>
<td>1.387 mg/m³</td>
</tr>
<tr>
<td>Absorption coefficient</td>
<td>0.22 mm⁻¹</td>
</tr>
<tr>
<td>F(000)</td>
<td>1264</td>
</tr>
<tr>
<td>Crystal size</td>
<td>0.94 × 0.23 × 0.09 mm³</td>
</tr>
<tr>
<td>Θ range for data collection</td>
<td>4.9 to 55.6 °</td>
</tr>
<tr>
<td>Index ranges</td>
<td>-10≤h≤10, -23≤k≤23, -33≤l≤34</td>
</tr>
<tr>
<td>Reflections collected</td>
<td>18075</td>
</tr>
<tr>
<td>Independent reflections</td>
<td>4232 [R(int) = 0.050]</td>
</tr>
<tr>
<td>Completeness to Θ = 29.99°</td>
<td>100%</td>
</tr>
<tr>
<td>Absorption correction</td>
<td>Multi-scan</td>
</tr>
<tr>
<td>Max. and min. transmission</td>
<td>0.980 and 0.818</td>
</tr>
<tr>
<td>Refinement method</td>
<td>Full-matrix least-squares on F²</td>
</tr>
<tr>
<td>Data / restraints / parameters</td>
<td>2963 / 0 / 199</td>
</tr>
<tr>
<td>Goodness-of-fit on F²</td>
<td>1.04</td>
</tr>
<tr>
<td>Final R indices [I&gt;2σ(I)]</td>
<td>R1 = 0.043, wR2 = 0.108</td>
</tr>
<tr>
<td>Largest diff. peak and hole</td>
<td>0.34 and -0.40 e.Å⁻³</td>
</tr>
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Data for compound 43m Chapter 2:

Identification code  
Empirical formula \(\text{C}_{21}\text{H}_{17}\text{NOS}\)
Formula weight 331.42
Temperature 173 K
Wavelength 0.71073 Å
Crystal system monoclinic
Space group (H.-M.) \(P\ 21/n\)
Space group (Hall) \(-P\ 2yn\)
Unit cell dimensions \(a = 11.3328 (6) \ \text{Å} \quad \alpha = 90^\circ\)
\(b = 9.8191 (4) \ \text{Å} \quad \beta = 94.651 (3)^\circ\)
\(c = 14.7663 (7) \ \text{Å} \quad \gamma = 90^\circ\)
Volume 1637.75 (13) Å³
\(Z\) 4
Density (calculated) 1.344 mg/m³
Absorption coefficient 0.20 mm⁻¹
\(F(000)\) 696
Crystal size 0.42 × 0.28 × 0.13 mm³
\(\Theta\) range for data collection 5.0 to 54.1 °
Index ranges \(-15 \leq h \leq 15, -13 \leq k \leq 13, -19 \leq l \leq 20\)
Reflections collected 18661
Independent reflections 4770 \([R(\text{int}) = 0.051]\)
Completeness to \(\Theta = 30.00^\circ\) 100%
Absorption correction Multi-scan
Max. and min. transmission 0.974 and 0.919
Refinement method Full-matrix least-squares on \(F^2\)
Data / restraints / parameters 3288 / 0 / 218
Goodness-of-fit on \(F^2\) 1.05
Final R indices \([I>2\sigma(I)]\) \(R1 = 0.045, \text{wR}2 = 0.116\)
Largest diff. peak and hole 0.33 and -0.30 e.Å⁻³
References:

31. (a) Pearce, A. N.; Chia, E. W.; Berridge, M. V.; Maas, E. W.; Page, M. J.; Webb, 180


66. (a) I.-S. Chen, H.-F. Chen, M.-J. Cheng, Y.-L. Chang, C.-M. Teng, I. Tsutomu, J.-


140. Gentile, G.; Bernasconi, G.; Pozzan, A.; Merlo, G.; Marzorati, P.; Bamborough, P.; Bax, B.; Bridges, A.; Brough, C.; Carter, P.; Cutler, G.; Neu, M.;


