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Diversity-oriented synthesis of benzo[*b*]thiophenes fused to medium-sized *N*-heterocycles via Friedel–Crafts cyclization processes

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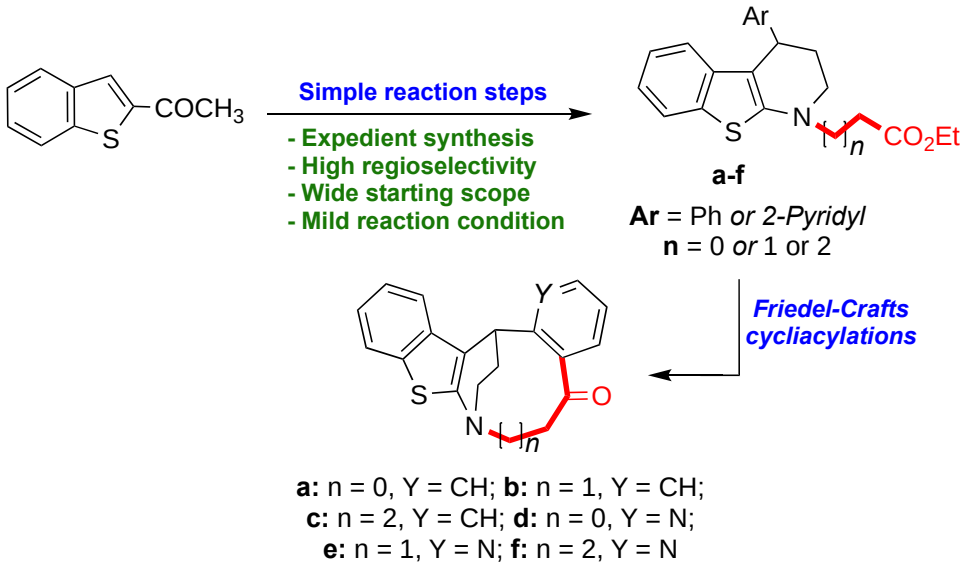
Abstract

An efficient access to benzo[*b*]thiophene-fused or -bridged to medium-sized *N*-heterocycles *e.g.* azocinones, azoninones and azecinones, is described. The process involves cyclization of benzo[*b*]thiophene carboxylic ester precursors, mediated by Lewis and Brønsted acids under suitable conditions. The ring closure precursors were assembled starting from 2-acetylbenzo[*b*]thiophene. The developed strategy allows control of ring size and offers easy access to fused benzo[*b*]thiophene polycycles of promising biological importance in moderate to good yields.



Keywords: Friedel–Crafts cycliacylations, Beckmann rearrangements, thienoazocinones, thienoazoninones, thienoazecinones

Introduction

Condensed carbo- or heterocycles containing a thiophene moiety are valuable structural motifs present in several bioactive natural products[1-3] and pharmaceutically relevant drugs[4-6] (Figure 1). For example, Adrogolide derived diacetate esters of A-86929 (thieno[2,3-*c*]quinolines) acting as a selective dopamine receptor D_1 agonist as a possible treatment for Parkinson's disease and cocaine addiction,[7] Bisulepin is relatively selective antihistamine (H_1 antagonist) with hypnotic, antiadrenergic[8] and very weak anticholinergic effects. Clotiazepam possesses anxiolytic, skeletal muscle relaxant, anticonvulsant and sedative properties.[9] Moreover, these multi-substituted and functionalized thiophene polycycles have also gained popularity in the area of polymer and material sciences. For instance, polythiophene conducting polymers are common components of electroluminescent devices,[10] transistors,[11] nanotubes[12] and optimal imaging devices.[13]

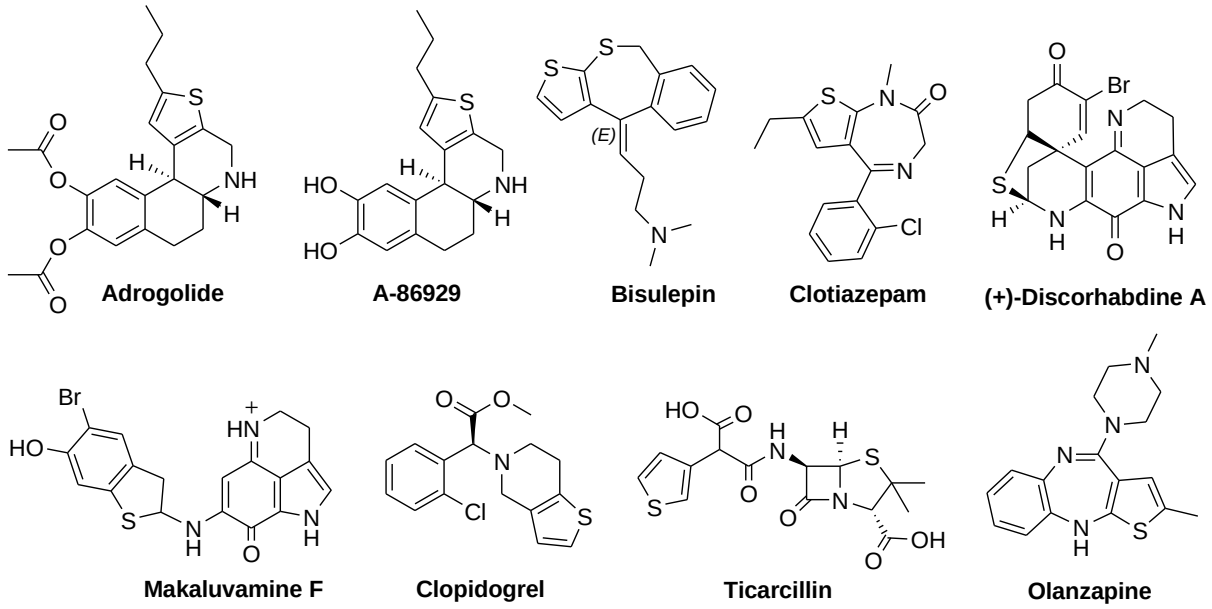


Figure 1. Examples of drugs containing fused thiophene rings in their core structures.

Given the large array of synthetic utility, structural complexity and astonishing biological profile of condensed thiophenes, a flexible route to regioselective access to these significant condensed scaffolds from readily available acyclic precursors is an attractive goal. In the literature, among the most important classical and modern synthetic approaches to functionalized thiophenes are the Paal-Knorr condensation of 1,4-diketones, diesters, or dicarboxylates with P_4S_{10} or elemental sulfur,[14] the Volhard-Erdmann cyclization of γ-oxo acids, 1,4-diketones or chloroacetyl-substituted esters with phosphorus pentasulfide,[15] the Fiesselmann condensation of thioesters with α-chlorocarbonyls,[16] the Gewald reaction of ketones or aldehydes with α-cyanoesters in the presence of a sulfur source,[17] the Hinsberg reaction of dialkyl thioglycolate with α-diketones under basic conditions followed by decarboxylation reactions,[18] Heck or Ullmann couplings,[19] organometallic polycondensation,[20] electrochemical polymerization,[21] the domino fragmentation combined with intramolecular thia-*anti*-Michael addition from α-alkenyl-α'-carbamoyl ketene-(S,S)-acetals,[22] Fort's three-step approach starting from methylthiopyridines,[23] an *N*-acyliminium ion olefin cyclization of hydroxylactam-alcohols,[24] and Dong's combinatorial procedure from the treatment of 1,3-dicarbonyl compounds with CS_2 in the presence of base.[25]

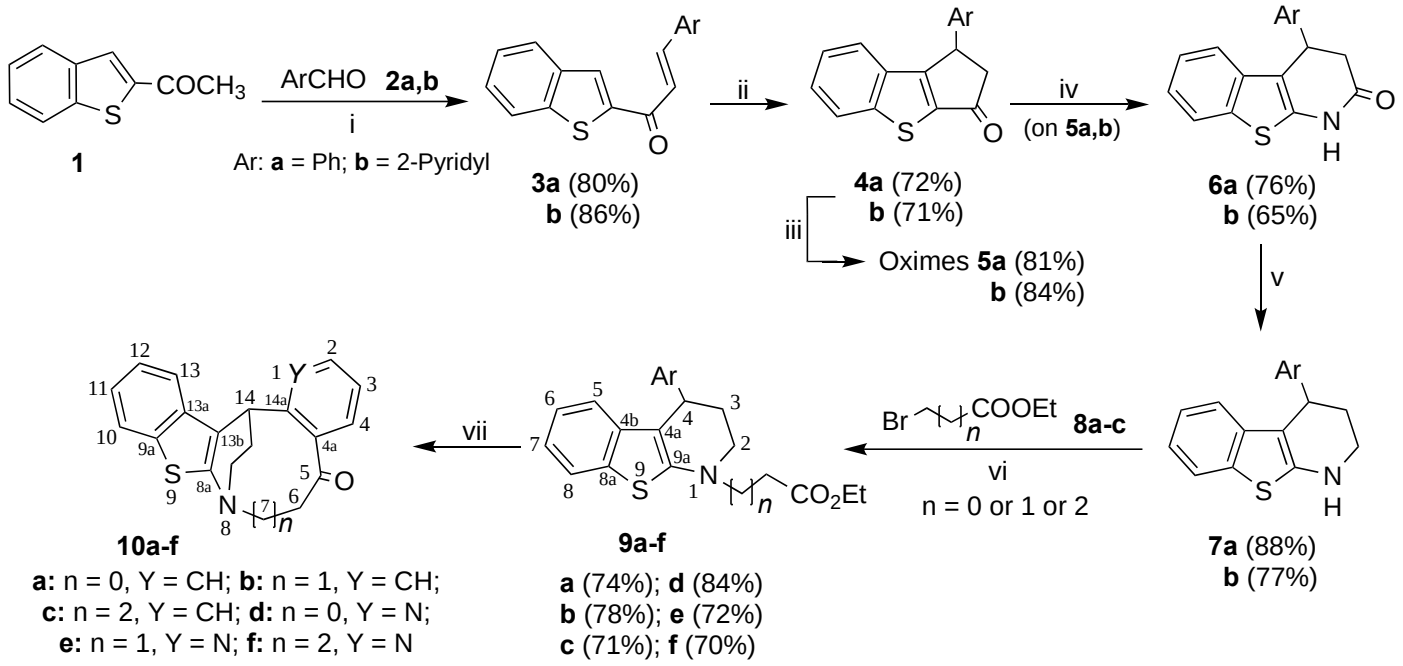
Although these approaches are reliable methods, but they are all multi-step approaches and limited to synthesizing only one type of thiophene. An examination of the literature search over the past four decades for the synthesis of condensed thiophenes is performed and reveals a largest variety of noteworthy methods and reactions are available. Therefore, we give here only literature precedents and applied methodologies relevant to the present work used in the synthesis of thiophene fused seven- or higher-membered *N*-heterocyclic ring compounds. Very few references for the synthesis of thienoazepine regioisomers have been described, and the formation of regioisomeric thienoazocines or higher ring fused systems remains unknown.

Three common approaches used in the construction of thienoazepines are: photolysis of the appropriate azido-substrates such as azidobenzo[*b*]thiophenes or azidodibromobenzo[*b*]thiophene,[26] ring enlargements of the pre-formed fused thiophenones[27] and consequent construction of either azepine-ring or thiophene core via regioselective cyclization of functionalized acyclic chain residue.[28]

In our previous work, we reported the formation and functionalization of tricyclic thiophenes via ring closures of readily accessible precursors.[29] In continuation of our research interests in a Friedel–Crafts approach[30-32] regarding development of an efficient and simple procedures for synthesis of condensed heterocycles,[33,34] herein we report our studies on a common methodology for the synthesis of novel fused and bridged benzo[*b*]thiophene polycycles, in particular benzo- and pyrido-fused thieno[2,3-*b*]azocinones, thieno[2,3-*b*]azoninones and thieno[2,3-*b*]azecinones.

Results and Discussion

In order to develop a useful acyclic precursor to thiophene polycyclic systems **10a-f** containing fused N-heterocyclic rings, we proposed to synthesize the heteroaryl-based ester precursors **9a-f** starting from easily accessible 1-(benzo[*b*]thiophen-2-yl)ethanone (2-acetylbenzo[*b*]thiophene) (**1**)[35] as illustrated in Scheme 1. This ketone was condensed with aldehydes **2a,b** (**a:** PhCHO; **b:** 2-formylpyridine) in the presence of NaOH/EtOH following the Claisen-Schmidt[36] reaction conditions to produce substituted chalcones **3a,b**. Cyclizations of the chalcones were carried out by heating with $AlCl_3$/NaCl in PhCl following standard reaction conditions[37] to furnish the corresponding tricyclic 1,2-dihydrocyclopenta[*d*]-benzo[*b*]thiophen-3-ones **4a,b** in good yields.



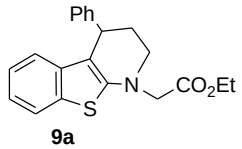
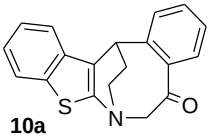
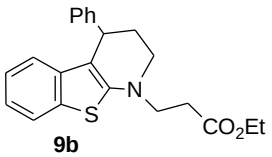
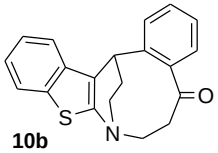
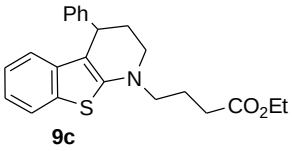
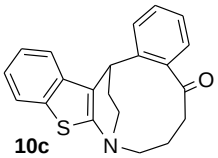
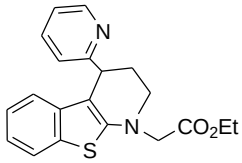
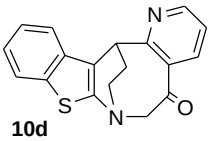
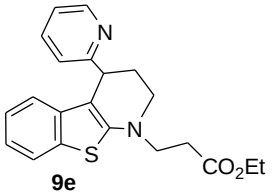
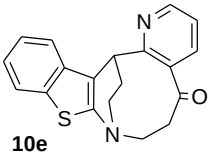
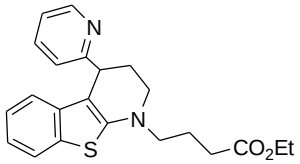
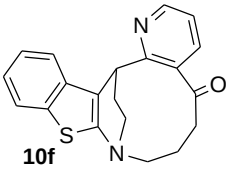
Scheme 1. Reagents and conditions: (i) PhCHO or 2-formylpyridine/NaOH/EtOH, 22 h, 25-30 °C, 80-86%, (ii) $AlCl_3$/NaCl, heated at 60–70 °C, 40 min, 71-72%, (iii) NH_2OH/HCl/NaOH, 10 h, reflux, 81-84%, (iv) PPA, 110–120 °C, 6-8 h, 64-77%, (v) $LiAlH_4$/THF/Et_2O, reflux, 6 h, NaOH, 77-88%, (vi) $BrCH_2CO_2Et$ or $BrCH_2CH_2CO_2Et$, K_2CO_3/DMF, reflux, 6 h, 70-84%, (vii) Cycliacylations of esters **9a-f** mediated by $AlCl_3/CH_3NO_2$ or TfOH or PPA promoters (see Table 1).

Oximation of the ketones **4** using $NH_2OH.HCl$/NaOH in ethanol gave the corresponding oximes **5a,b**. From experimental results, melting ranges, thin layer chromatography and the interpretation of ^1H and ^{13}C NMR spectra of the resulting oximes **5a,b** we assume that these oximes are obtained as single *E*-isomers. However, the rearrangement step of the Beckmann reaction is not stereospecific in nature therefore, the configuration of these intermediates need not be taken into consideration.

The oximes **5a,b** were treated with PPA at high temperature following standard Beckmann[38] ring-expansion conditions resulting in substituted tetrahydro-benzo[4,5]thieno[2,3-*b*]pyridin-2-ones **6a,b**. Reduction of the lactams with $LiAlH_4$ in THF/Et_2O afforded the desired tricyclic amines **7a,b**. *N*-Alkylation of the amines **7** with (α- or β- or γ)-halo-aliphatic esters **8a-c** using DMF/K_2CO_3 at high temperature gave tricyclic-ester precursors **9a-f**.

The pentacyclic benzo[*b*]thiophene-fused carbo- and heterocyclic systems [6-5-6-(8,9,10)-6] **10a–f** namely, benzo- or pyrido-fused thieno[2,3-*b*]azocinones, thieno[2,3-*b*]azoninones and thieno[2,3-*b*]azecinones, were obtained in good to high yields via the Friedel–Crafts cycliacylations of the heterocyclic esters **9a–f** mediated by $AlCl_3/CH_3NO_2$ or trifluoromethanesulfonic acid (TfOH) or polyphosphoric acid (PPA)-promoters, under different reaction conditions. The conditions are summarized in Scheme 1 and Table 1. The initial investigations of this approach were focused on extensive screening of Lewis and Brønsted acids-promoters under different reaction conditions. The choice of these acidic promoters screened was based on the degree of oxophilicity as well as extent of their acidity.

Table 1. Study of cycliacylations of benzo[*b*]thiophene carboxylic esters **9a–f**

Entry	Substrate	Product	Conditions	Yield (%)[A]
1	 **9a**	 **10a**	$AlCl_3/CH_3NO_2$[B], DCM[C], 14 h, rt	81
			TfOH[D], DCE[E], 8 h, 60–70 °C	78
			PPA[F], 6 h, 190-200 °C	73
2	 **9b**	 **10b**	$AlCl_3/CH_3NO_2$, DCM, 13 h, rt	84
			TfOH, DCE, 8 h, 60–70 °C	80
			PPA, 7 h, 190-200 °C	75
3	 **9c**	 **10c**	$AlCl_3/CH_3NO_2$, DCM, 18 h, rt	85
			TfOH, DCE, 8 h, 60–70 °C	80
			PPA, 8 h, 190-200 °C	73
4	 **9d**	 **10d**	$AlCl_3/CH_3NO_2$, DCM, 12 h, rt	78
			TfOH, DCE, 8 h, 60–70 °C	72
			PPA, 8 h, 190-200 °C	70
5	 **9e**	 **10e**	$AlCl_3/CH_3NO_2$, DCM, 11 h, rt	79
			TfOH, DCE, 8 h, 60–70 °C	81
			PPA, 10 h, 190-200 °C	75
6	 **9f**	 **10f**	$AlCl_3/CH_3NO_2$, DCM, 20 h, rt	83
			TfOH, DCE, 8 h, 60–70 °C	74
			PPA, 9 h, 190-200 °C	75

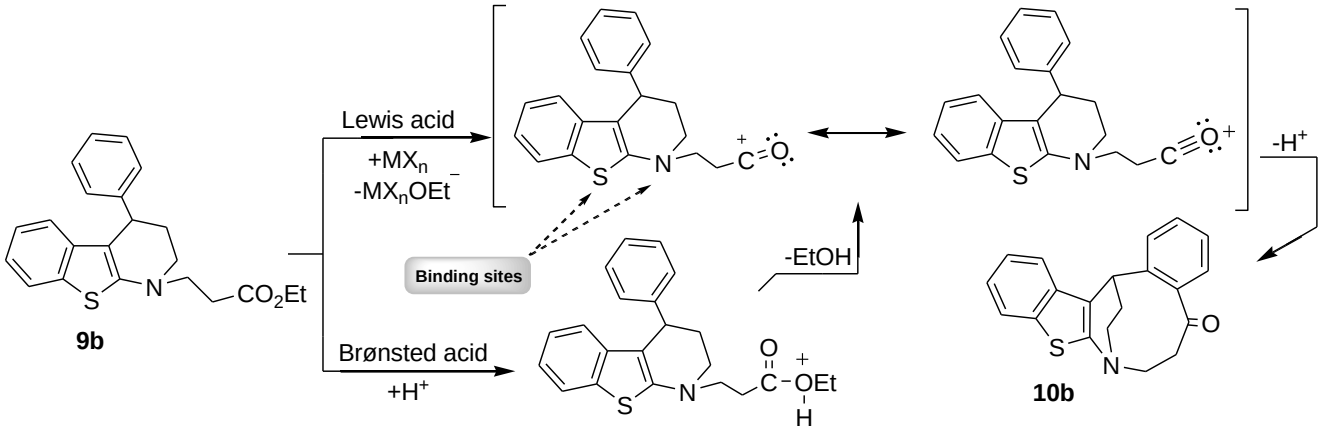
Isolated yields. [B]with $AlCl_3/CH_3NO_2$–catalyst reactant proportions were: acid (2 mmol), $AlCl_3$ (10 mmol) in CH_3NO_2 (80 mmol), solvent (10 mL). [C]dichloromethane. [D]with TfOH–catalyst reactant proportions were: ester (3 mmol) and TfOH (15 mmol), solvent (15 mL). [E]1,2–dichloroethane. [F]with PPA catalyst reactant proportions were: acid (5 mmol) and PPA (15 g).

Our initial extensive attempts in cyclizations of precursor **9a** under mild reaction conditions were successful in the Friedel-Crafts-type transformations. Low stoichiometric loadings of acidic promoters for 30 min affording **10a** in low yields. Flash chromatography (basic alumina, column; *n*-hexane/EtOAc 6:4) allowed separation of the cyclic product (**10a**, 52%) from starting ester (**9a**, 44%). Consequently, stronger conditions were used and, out of several variations tried, the results outlined in Table 1 and Scheme 1 show the exclusive formation of thiophene polycycles in good yields.

Heating ester **9b** with excess of PPA at 180-190 °C for a longer reaction time produced pentacyclic product **10b** but in low yields. The low yields may be attributed to the severity of cyclization conditions, steric hindrance of substrate and the poor acidity of PPA catalyst.

Observations made on the use of Friedel–Crafts catalysts in the cyclization of electron-rich carbo-and heterocyclic substrates[39,40] led to the conclusion that the presence of *sp*^{3}-hybridized heteroatoms was problematic. In an attempt to circumvent this issue, the ease of the cyclization process depends mainly on the binding activity and interaction modes of acidic catalysts on heteroatoms in the substrate molecule.[41] It is presumed that proton H^+ from Brønsted acids protonates the heteroatom or a Lewis acid-substrate complex is formed.[42] These complexities may lead to either alteration in catalyst acidity or reduce its reactivity beside deactivation of a nucleophilic substrate and may also be responsible of slowing the rate of cyclization process.[43] It has been suggested that aromatic substitutions may proceed via a single transition state of strongly electrophilic reagents forming π-complex transition states, whereas less electrophilic reagents providing transition states similar to Wheland intermediates or stabilized σ-complex.[26] The nature of the acylating agent and the strength of the Lewis acid determine the electrophilicity of this complex while the regiochemistry is determined by the transition state leading to the generation of acyl-carbocation. However, under normal Friedel-Crafts conditions the cycliacylating agent reacts with more than stoichiometric loading of oxophilic Lewis acid or weaker promoter strength. These less effectively coordinate with substrate heteroatoms and lead to less catalytic inhibition.[44]

These observations may give some insight into the reaction mechanism.[45] Literature evidence to support the mechanistic hypotheses put forward in this study has been described (Scheme 2). Thus, on treatment of ester precursor with acidic catalysts, a catalyst-substrate complex with a Lewis acid, or protonation of heteroatoms of substrate with Brønsted-catalyst proton, takes place. Subsequently that leads to removal of -EtOH or -EtOMX_{n-1}, generating the acyl-cations. Electrophilic substitution by such acyl-carbocations takes place, with loss of a ring proton to produce the pentacyclic ketones.



Scheme 2. Proposed mechanism for cyclizations of ester **9b**.

The assignment of the chemically inequivalent protons of CH_2-groups in the intermediates and cyclic products was made on the direct inspection of the ^{1}H NMR spectra. Many of the intermediates and pentacyclic frameworks possess a bridged stereogenic center. This creates the stereochemical complexities in the interpretations of diastereotopic[47] protons of CH_2-groups. For example, the ^{1}H NMR signals for the pentacyclic product **10b** is characterized by the presence of diastereotopic protons of the bridged CH_2-group showing as two signals, one with multiplicities of dddd near δ 2.54 ppm with four coupling constants *J* = 14.3, 6.8, 2.3, 1.7 Hz was assigned for the *bridged*–CH*a* proton while the other signal with the same multiplicities as dddd near 2.85 ppm was assigned for the other *bridged*–CH*b* proton. Another CH_2 group next to the chiral nitrogen atom shows two sets of signals, one as a doublet of doublet of doublets near δ 2.83 ppm of

somewhat separated with three coupling constant of *J* = 15.0, 9.3, 3.1 Hz was assumed to be one of *bridged* N–CH. Increasly, the other diastereotopic proton of CH_2-N in the heterocyclic ring of product **10b** shows doublet of triplets near δ 3.36 ppm with inner signals overlapping (*J* = 15.0, 3.7 Hz).

The remaining aliphatic protons show characteristic five signals in the ^{1}H NMR of compound **10b**, two of them are signals for C-$^6H_2$-protons, as two sets of signals with the same splitting as doublet of doublet of doublets near δ 3.77 and 3.82 ppm for the pseudo-equatorial and pseudo-axial protons respectively. Additionally, the two most shielded protons of C-$^7H_2$ group signals appeared upfield as a doublet of doublet of doublets at δ 4.01 and 4.25 ppm with different values of coupling constants. This shielding could be attributed to the coupling between magnetic anisotropic[48] effect of neighbor C=O group with the conformation complexities[49] of the twisted chair conformer of medium sized heterocyclic ring systems. While the other bridged proton C-^{14}H appeared at δ 5.11 ppm and with coupling constants *J* = 3.6, 2.3 Hz with the same splitting.

Conclusions

In conclusion, we have designed unprecedented and concise catalytic protocol to synthesise various banzo[*b*]thiophenes fused with medium-sized *N*-heterocyclic ring systems (8-, 9- and 10-membered *N*-heterocycles) from simple starting materials via Friedel–Crafts cycliacylations of acyclic ester precursors. The results presented herein highlighted simplicity and the broad applicability of the Friedel-Crafts procedures for the construction of pharmaceutically promising heterocyclic compounds.

Experimental Section

General. All chemicals used were of reagent grade and solvents were freshly distilled and dried by standard procedures before use. Melting points were taken on a digital Gallenkamp capillary melting point apparatus and are uncorrected. Infrared (IR) spectra were obtained on a Perkin-Elmer 1600 FT-IR spectrophotometer using KBr wafer and thin-film techniques (ν cm^{-1}) and are in cm^{-1}; The NMR spectra were recorded on JEOL LA 400 MHz FT-NMR (400 MHz for ^{1}H-NMR, 100 MHz for ^{13}C-NMR) using $CDCl_3$ solvent with tetramethylsilane (Me_4Si, TMS) as internal standard. Chemical shifts (δ) and *J* values are reported in ppm and Hz, respectively. Mass spectra were performed by JEOL JMS 600 spectrometer at under electron impact at 70 eV. Elemental analyses of sufficiently pure samples were carried out by a GmbH Vario EL III, 2400, CHNOS-elemental analyzer. Reaction progress was monitored by thin-layer chromatography (TLC) analysis carried out on silica (60 F254) or alumina (60 F254, basic) gel plates with detection by UV light (at 254 and/or 360 nm). The products were purified by flash column chromatography, where necessary, was performed on silica gel (230–400 mesh) or basic alumina (90, standardized). 2-Acetylbenzo[*b*]thiophene **1**, mp 85-88 °C was prepared according to the literature procedure.[35]

General procedure for the Claisen-Schmidt condensations of 2-acetylbenzo[*b*]thiophene 1 with substituted aromatic aldehydes. To a cooled (0 °C) solution of the appropriate 2-acetylbenzo[*b*]thiophene **1** (10 mmol) in absolute EtOH (30 mL) was added dropwise a solution of NaOH (12 mL, 30%) with efficient stirring. The mixture was stirred for 30 min at the same temperature and then a solution of the appropriate aromatic aldehyde **2a** or **2b** (12 mmol) in absolute EtOH (20 mL) was added dropwise over 5 min. After stirring at 0 °C

for 2 h, the ice bath was removed and the mixture was stirred at ambient temperature for 20 h. The suspension was then poured onto crushed ice (200 g) with vigorous stirring for 15 min. The resultant precipitate was filtered off, washed with water and dried to afford crude products **3a,b**.

(*E*)-1-(Benzo[*b*]thiophen-2-yl)-3-phenylprop-2-en-1-one (3a). Yellow crystals; 80%; mp 148-150 °C (ethanol); IR (KBr) ν_{max} 3042, 2972, 2843, 1699, 1615, 1607, 1580, 1446, 1319, 1250, 1120, 765 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 6.72 (1H, d, *J* 15.7 Hz, =C$^{\beta}$H-), 7.42 (2H, dddd, *J* 8.1, 7.5, 2.0, 0.5 Hz), 7.44 (1H, dddd, *J* 7.8, 7.2, 1.9, 0.4 Hz), 7.45 (1H, ddd, *J* 7.8, 7.2, 1.7 Hz), 7.47 (1H, tt, *J* 7.5, 1.5 Hz), 7.51 (1H, d, *J* 15.7 Hz, -COC$^{\alpha}$H=), 7.49 (2H, dddd, *J* 8.1, 2.3, 1.5, 0.5 Hz), 7.82 (1H, dddd, *J* 7.8, 1.9, 1.7, 0.6 Hz), 7.97 (1H, ddt, *J* 7.8, 1.9, 0.5 Hz), 8.04 (1H, ddd, *J* 1.9, 0.5, 0.4 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 122.2, 122.5, 125.6, 127.2 (2C), 127.8, 128.3 (2C), 128.5 (2C), 129.3, 130.3, 139.9, 140.2, 143.6, 144.1, 177.7. Anal. Calcd. for $C_{17}H_{12}OS$ (264); C, 77.27; H, 4.54; S, 12.12. Found; C, 77.09; H, 4.62; S, 12.18%.

(*E*)-1-(Benzo[*b*]thiophen-2-yl)-3-(pyridin-2-yl)prop-2-en-1-one (3b). Brown plates; 86%; mp 161-64 °C (methanol); IR (KBr) ν_{max} 305, 2945, 1695, 1610, 1590, 1480, 1445, 1388, 1240, 1185, 769 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 6.88 (1H, d, *J* 15.6 Hz, =C$^{\beta}$H-), 7.41 (1H, d, *J* 15.6 Hz, -COC$^{\alpha}$H-), 7.44 (1H, dddd, *J* 7.8, 7.2, 1.9, 0.4 Hz), 7.46 (1H, ddd, *J* 7.8, 7.2, 1.7 Hz), 7.56 (1H, ddd, *J* 7.4, 4.7, 1.4 Hz), 7.71 (1H, ddd, *J* 7.7, 7.4, 1.9 Hz), 7.73 (1H, ddd, *J* 7.7, 1.4, 0.5 Hz), 7.83 (1H, dddd, *J* 7.8, 1.7, 1.6, 0.5 Hz), 7.97 (1H, ddt, *J* 7.8, 1.9, 0.5 Hz), 8.04 (1H, ddd, *J* 1.6, 0.5, 0.4 Hz), 8.70 (1H, ddd, *J* 4.7, 1.9, 0.5 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 120.2, 122.2, 122.5 (2C), 122.7, 125.6, 128.4 (2C), 129.3 136.7, 139.9, 140.2, 143.6, 149.1, 155.9, 177.7. Anal. Calcd. for $C_{16}H_{11}NOS$ (265); C, 72.45; H, 4.15; N, 5.28; S, 12.07. Found; C, 72.43; H, 4.31; N, 5.20; S, 12.14%.

General procedure for cyclization of amides 3a,b.

An intimate mixture of amide **3a** or **3b** (20 mmol) with anhydrous $AlCl_3$ (50 mmol) and NaCl (5 g) was warmed with stirring at 60-70 °C for 40 min. The resulting hot molten mixture was poured directly into an excess of well–stirred ice water (100 mL) and then basified with NaOH solution (40 mL, 20%). The mother liquor was diluted with water (100 mL) and extracted with EtOAc (3×30 mL). The combined organic extracts was washed with water, dried over Na_2SO_4, filtered and concentrated in *vacuo*. The residue was purified by flash column chromatography (basic alumina, EtOAc/*n*-hexane, 1/1) to give pure products **4a,b**. The yields and spectral data are given in the following:

1-Phenyl-1,2-dihydrocyclopenta[*d*]benzo[*b*]thiophen-3-one (4a). Yellow crystals; 72%; mp 126–29 °C (n-butanol); IR (KBr) ν_{max} 3062, 2944, 1710, 1600, 1585, 1480, 1445, 1370, 1241, 1139, 788 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 3.16-3.40 (2H, 3.24 (1H, dd, *J* 17.5, 8.1 Hz, C^{2}Ha), 3.33 (1H, dd, *J* 17.5, 4.2 Hz, C^{2}Hb), 5.10 (1H, dd, *J* 8.1, 4.2 Hz, C^{1}H), 7.19 (2H, tt, *J* 7.7, 1.5 Hz), 7.26 (tdd, *J* 7.8, 1.9, 0.5 Hz), 7.27 (2H, dddd, *J* 7.8, 1.5, 1.3, 0.5 Hz), 7.50 (1H, ddd, *J* 8.1, 7.7, 1.7 Hz), 7.58 (1H, ddd, *J* 8.5, 1.7, 0.5 Hz), 7.65 (1H, ddd, *J* 8.5, 7.7, 1.8 Hz), 7.89 (1H, ddd, *J* 8.1, 1.8, 0.5 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 40.7, 41.2, 122.5, 122.8, 127.3, 127.6 (2C), 127.8, 128.4 (2C), 128.5 (2C), 131.6, 138.5, 139.2, 139.4, 194.5. Anal. Calcd. for $C_{17}H_{12}OS$ (264); C, 77.27; H, 4.54; S, 12.12. Found; C, 77.36; H, 4.58; S, 11.97%.

1-Pyridyl-1,2-dihydrocyclopenta[*d*]benzo[*b*]thiophen-3-one (4b). Pale Yellowish brown plates ; 71%; mp 165 °C *dec.* (acetone); IR (KBr) ν_{max} 3066, 2960, 1705, 1585, 1480, 1460, 1444, 1342, 1275, 1128, 760 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 3.28 (1H, dd, *J* 16.4, 8.1 Hz, C^{2}Ha), 3.33 (1H, dd, *J* 16.4, 4.2 Hz, C^{2}Hb), 5.18 (1H, dd, *J* 8.1, 4.2 Hz, C^{1}H), 7.20 (1H, ddd, *J* 7.4, 4.9, 1.2 Hz), 7.27 (1H, ddd, *J* 7.6, 1.2, 0.6 Hz), 7.50 (1H, ddd, *J* 8.1, 7.7, 1.8 Hz), 7.63 (1H, ddd, *J* 8.5, 1.8, 0.5 Hz), 7.65 (1H, ddd, *J* 8.5, 7.7, 1.8 Hz), 7.68 (1H, ddd, *J* 7.6, 7.4, 1.9 Hz), 7.89 (1H, ddd, *J* 8.1, 1.8, 0.5 Hz), 8.52 (1H, ddd, *J* 4.9, 1.9, 0.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 40.7, 41.2, 121.0, 122.5, 122.7 (2C), 127.3 (1C, s), 128.4 (2C), 131.6, 136.7, 138.5, 139.4, 149.1, 164.0, 194.5. Anal. Calcd. for $C_{16}H_{11}NOS$ (265); C, 72.45; H, 4.15; N, 5.28; S, 12.07. Found; C, 72.39; H, 4.05; N, 5.44; S, 12.23%.

General procedure for the synthesis of tricyclic amines 7a,b. The titled compounds were obtained in a series of two reaction steps starting with ketones **4a,b** via Beckmann ring enlargements of oximes **5a,b** followed by reduction of the resulting lactams **6a,b**. A summary of the steps is given in the following:

(i). An ice-cold a solution of ketone **4** (10 mmol) in EtOH (40 mL) was added dropwise with stirring to solution of NH_2OH HCl (12 mmol) in water (10 mL). Afterwards, a solution of NaOH (10 mL, 2 N) was added gradually during 10 min, and then the reaction mixture was stirred for 4 h at rt. The mixture was refluxed in a steam bath at 80-90 °C for 6 h, cooled to rt and finally poured into water (200 mL). The resulting mixture was extracted with AcOEt (3×30 mL) and the combined organic layer was washed with HCl solution (30 mL, 5%), washed with water and dried over Na_2SO_4. The solution was decanted and the solvent was removed in *vacuo* to afford crude oximes. The residue was purified by flash chromatography (basic alumina, column 1×25cm, hexane/EtOAc 3:1) to yield pure oximes. Further purifications, yields and spectral data are presented as the following:

(*E*)-1-Phenyl-1,2-dihydrocyclopenta[*d*]benzo[*b*]thiophen-3-one oxime (5a). Yellow crystals; m.p. 184 °C *dec.*, 81% (ethanol); IR (KBr) ν_{max} 3180, 3140, 2950, 1670, 1440, 1350, 1253, 1180, 782 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 3.21 (1H, dd, *J* 14.2, 8.1 Hz, C^2Ha), 3.29 (1H, dd, *J* 14.2, 4.2 Hz, C^2Hb), 4.91 (1H, dd, *J* 8.1, 4.2 Hz, C^1H), 7.21 (1H, tt, *J* 7.7, 1.3 Hz), 7.22 (1H, dddd, *J* 7.8, 7.7, 1.9, 0.5 Hz), 7.26 (2H, dtd, *J* 7.8, 1.3, 0.5 Hz), 7.38 (2H, ddd, *J* 7.7, 6.9, 1.6 Hz), 7.67 (1H, ddd, *J* 8.5, 6.9, 1.8 Hz), 7.82 (1H, ddd, *J* 8.5, 1.6, 0.5 Hz), 7.96 (1H, ddd, *J* 7.7, 1.8, 0.5 Hz), 10.14 (1H, s, *N*-OH). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 29.2, 40.7, 122.5, 122.8, 127.3, 127.6, 127.8, 128.4 (2C), 128.5 (2C), 131.6, 138.5, 139.2, 139.4, 151.7. Anal. Calcd. for $C_{17}H_{13}NOS$ (279); C, 73.11; H, 4.65; N, 5.01; S, 11.46. Found; C, 73.17; H, 4.51; N, 4.88; S, 11.58%.

***(E)*-1-(Pyridin-2-yl)-1,2-dihydrocyclopenta[*d*]benzo[*b*]thiophen-3-one oxime (5b).** Cream crystals; m.p. 195 °C *dec.*; 84% (ethanol); IR (KBr) ν_{max} 3215, 3248, 2977, 1668, 1440, 1230, 1170, 755 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 3.17 (1H, dd, *J* 11.2, 8.1 Hz, C^2Ha), 3.22 (1H, dd, *J* 11.2, 4.2 Hz, C^2Hb), 4.99 (1H, dd, *J* 8.1, 4.2 Hz, C^1H), 7.20 (1H, ddd, *J* 7.4, 4.9, 1.2 Hz), 7.27 (1H, ddd, *J* 7.6, 1.2, 0.6 Hz), 7.39 (1H, ddd, *J* 7.7, 6.9, 1.6 Hz), 7.67 (1H, ddd, *J* 8.5, 6.9, 1.8 Hz), 7.68 (1H, ddd, *J* 7.6, 7.4, 1.9 Hz), 7.83 (1H, ddd, *J* 8.5, 1.6, 0.5 Hz), 7.96 (1H, ddd, *J* 7.7, 1.8, 0.5 Hz), 8.52 (1H, ddd, *J* 4.9, 1.9, 0.6 Hz), 9.92 (1H, s, *N*-OH). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 29.2, 40.7, 121.0, 122.5, 122.7, 122.8, 127.3, 128.4, 128.5, 131.6, 136.7, 138.5, 139.4, 149.1, 151.7, 164.0. Anal. Calcd. for $C_{16}H_{12}N_2OS$ (280); C, 68.57; H, 4.28; N, 10.00; S, 11.42. Found; C, 68.50; H, 4.45; N, 9.86; S, 11.48%.

(ii). The oxime, **5a** or **5b** (15 mmol), was treated with polyphosphoric acid PPA (20 g) and the mixture was stirred at 110–120 °C for the 6-8 h. The mixture was cooled to rt and diluted with water (50 mL). A sat. $NaHCO_3$ (30 mL) solution was added to the mixture and then left to stand for overnight at refrigerator. The resulting solid was filtered off washed with water to afford the crude lactams. The residue was purified by flash column chromatography (basic alumina, EtOAc/*n*-hexane, 2/1) giving the pure products **6a** or **6b**. Yields, physical and spectral data of the products are given in the following:

4-Phenyl-1,2,3,4-tetrahydro-benzo[4,5]thieno[2,3-*b*]pyridin-2-one (6a). Yellow needles; 76%, m.p. 170-73 °C (AcOEt); IR (KBr) ν_{max} 3434, 3050, 2930, 1703, 1590, 1480, 1440 1371, 1265, 1172, 786 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 2.96 (1H, dd, *J* 16.3, 1.7 Hz, C^3Ha), 3.13 (1H, dd, *J* 16.3, 4.5 Hz, C^3Hb), 4.69 (1H, dd, *J* 4.5, 1.7 Hz, C^4H), 7.21 (2H, tt, *J* 7.7, 1.3 Hz), 7.26 (1H, tdd, *J* 7.8, 1.9, 0.5 Hz), 7.27 (1H, dtd, *J* 7.8, 1.3, 0.5 Hz), 7.32 (2H, ddd, *J* 7.9, 7.5, 1.7 Hz), 7.49 (1H, ddd, *J* 8.6, 7.5, 1.4 Hz), 7.68 (1H, ddd, *J* 8.6, 1.7, 0.4 Hz), 7.88 (1H, ddd, *J* 7.9, 1.4, 0.4 Hz), 9.62 (1H, s, NH). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 39.2, 39.5, 122.5, 122.8, 127.3, 127.6 (2C), 127.8, 128.4 (2C), 128.6 (2C), 136.2, 138.5, 139.3, 151.9, 172.7. Anal. Calcd. for $C_{17}H_{13}NOS$ (279); C, 73.11; H, 4.65; N, 5.01; S, 11.46. Found; C, 73.04; H, 4.60; N, 5.17; S, 11.31%.

4-(Pyridin-2-yl)-1,2,3,4-tetrahydrobenzo[4,5]thieno[2,3-*b*]pyridin-2-one (6b). Buff crystals; 65%, m.p. 190 °C *dec.* (acetone); IR (KBr) ν_{max} 3420, 3070, 2944, 1678, 1605, 1490, 1375, 1260, 1085, 795 cm^{-1}; ^{1}H-NMR (400

MHz, $CDCl_3$, δ, ppm): 2.95 (1H, dd, *J* 16.4, 1.7 Hz, C^3Ha), 3.17 (1H, dd, *J* 16.4, 4.5 Hz, C^3Hb), 4.73 (1H, dd, *J* 4.5, 1.7 Hz, C^4H), 7.21 (1H, ddd, *J* 7.4, 4.9, 1.2 Hz), 7.27 (1H, ddd, *J* 7.9, 1.2, 0.6 Hz), 7.32 (1H, ddd, *J* 7.9, 7.5, 1.7 Hz), 7.49 (1H, ddd, *J* 8.6, 7.5, 1.4 Hz), 7.65 (1H, ddd, *J* 7.9, 7.4, 1.9 Hz), 7.69 (1H, ddd, *J* 8.6, 1.7, 0.4 Hz), 7.88 (1H, ddd, *J* 7.9, 1.4, 0.4 Hz), 8.52 (1H, ddd, *J* 4.9, 1.9, 0.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 38.4, 40.7, 121.0, 122.5, 122.7, 122.8, 127.3, 128.4, 128.6, 136.7, 138.5, 139.3, 149.1, 151.9, 164.0, 172.7. Anal. Calcd. for $C_{16}H_{12}N_2OS$ (280); C, 68.57; H, 4.28; N, 10.00; S, 11.42. Found; C, 68.69; H, 4.32; N, 10.09; S, 11.26%.

(iii). To a cold (0 °C) suspension of $LiAlH_4$ (1.9 g, 50 mmol) in ether (40 mL), was added dropwise with stirring a solution of the lactams **6a** or **6b** (15 mmol) in THF (20 mL). The resulting mixture was refluxed for 6 h on A water bath and then left to stir for overnight. The cooled reaction mixture was carefully decomposed by addition of aqueous NaOH (20 mL, 30 %) and the product was extracted with ether (3×40 mL). The organic layer was separated, washed with saturated NaCl solution and dried over Na_2SO_4. After filtration, the solution was concentrated in *vacuo* to give the free base product **7a** or **7b**. Purifications, yields and spectral data are given in the following:

4-Phenyl-1,2,3,4-tetrahydrobenzo[4,5]thieno[2,3-*b*]pyridine (7a). Yellow crystals; 88%; mp 138-140 °C (ethanol); IR (KBr) ν_{max} 3425, 3047, 2966, 1696, 1600, 1590, 1470, 1440, 1330, 1272, 1113, 769 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 1.96 (1H, dddd, *J* 13.9, 10.2, 10.1, 2.5 Hz, C^3Ha), 2.11 (1H, dddd, *J* 13.9, 3.6, 3.2, 2.4 Hz, C^3Hb), 3.38 (1H, ddd, *J* 14.7, 3.2, 2.5 Hz, C^2Ha), 3.46 (1H, ddd, *J* 14.7, 10.2, 2.4 Hz, C^2Hb), 4.03 (1H, dd, *J* 10.1, 3.6 Hz C^4H), 7.09 (2H, ddd, *J* 7.9, 7.6, 1.6 Hz), 7.19 (1H, dtd, *J* 7.8, 1.2, 0.5 Hz), 7.21 (1H, tt, *J* 7.7, 1.3 Hz), 7.26 (2H, dddd, *J* 7.8, 7.7, 1.9, 0.5 Hz), 7.42 (1H, ddd, *J* 8.6, 7.6, 1.4 Hz), 7.54 (1H, ddd, *J* 8.6, 1.6, 0.5 Hz), 7.83 (1H, ddd, *J* 7.9, 1.4, 0.5 Hz), 10.14 (1H, s, NH). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 29.0, 39.2, 41.6, 122.5, 122.8, 127.3, 127.6 (2C), 127.8, 128.4 (2C), 128.6 (2C), 136.2, 138.5, 139.3, 151.9. Anal. Calcd. for $C_{17}H_{15}NS$ (265); C, 76.98; H, 5.66; N, 5.28; S, 12.07. Found; C, 77.08; H, 5.60; N, 5.26; S, 12.04%.

4-(Pyridin-2-yl)-1,2,3,4-tetrahydrobenzo[4,5]thieno[2,3-*b*]pyridine (7b). Yellow crystals; 77%; mp 130-133 °C (ethanol); IR (KBr) ν_{max} 3442, 3074, 2986, 1692, 1605, 1580, 1475, 1440, 1374, 1278, 1130, 784 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 2.12 (1H, dddd, *J* 13.8, 10.2, 10.1, 2.5 Hz, C^3Ha), 2.54 (1H, dddd, *J* 13.8, 3.6, 3.2, 2.4 Hz, C^3Hb), 3.41 (1H, ddd, *J* 13.4, 10.2, 2.4 Hz, C^2Ha), 3.50 (1H, ddd, *J* 13.4, 3.2, 2.5 Hz, C^2Hb), 4.07 (1H, dd, *J* 10.1, 3.6 Hz), 7.09 (1H, ddd, *J* 7.9, 7.6, 1.6 Hz), 7.20 (1H, ddd, *J* 7.4, 4.9, 1.2 Hz), 7.25 (1H, ddd, *J* 7.6, 1.2, 0.6 Hz), 7.42 (1H, ddd, *J* 8.6, 7.6, 1.4 Hz), 7.55 (1H, ddd, *J* 8.6, 1.6, 0.5 Hz)), 7.68 (1H, ddd, *J* 7.6, 7.4, 1.9 Hz), 7.84 (1H, ddd, *J* 7.9, 1.4, 0.5 Hz), 8.52 (1H, ddd, *J* 4.9, 1.9, 0.6 Hz), 9.95 (1H, s, NH). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 29.0, 40.7, 41.6, 121.0, 122.5, 122.7, 122.8, 127.3, 128.4 (2C), 136.7, 138.5, 139.3, 149.1, 151.9, 164.0. Anal. Calcd. for $C_{16}H_{14}N_2S$ (266); C, 72.18; H, 5.26; N, 10.52; S, 12.03. Found; C, 72.14; H, 5.31; N, 10.50; S, 12.04%.

General procedure for the construction of thiophene based esters 9a–f. To a hot (60-70 °C) and stirred mixture of tricyclic amine **7a** or **7b** (8 mmol) and K_2CO_3 (20 mmol) in DMF (30 mL) was added slowly a solution of haloester **8a-c** (ethyl bromoacetate or ethyl 3-bromopropionate or ethyl 4-bromobutanoate, 9 mmol) in DMF (20 mL) over a period of 10 min. The reaction mixture was refluxed for 6 h. The reaction was maintained at this temperature and monitored by TLC (30% AcOEt/hexane) until complete consumption of starting material was observed. The reaction was then cooled and poured into ice-cold water (200 mL). The resulting solid was filtered off, washed thoroughly with H_2O and dried. The product was directly subjected to flash chromatography (basic alumina, 40%, EtOAc/hexane) gave pure esters **9a-f**. Yields and spectral data of resulting esters are given in the following.

Ethyl 2-(4-phenyl-3,4-dihydro-2*H*-benzo[4,5]thieno[2,3-*b*]pyridin-1(1*H*)-yl)acetate (9a). Pale yellow needles; 74%, mp 105–7 ºC (ethanol); IR (KBr) ν_{max} 3060, 2944, 1732, 1600, 1580, 1470, 1445, 1375, 1281, 786 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 1.17 (3H, t, *J* 7.1 Hz, $CH_2\underline{CH_3}$), 1.94 (1H, dtd, *J* 13.8, 9.9, 1.8 Hz, C^3Ha), 2.26 (1H,

dddd, *J* 13.8, 4.3, 4.0, 1.9 Hz, C^3Hb), 3.29 (ddd, *J* 14.8, 9.9, 1.9 Hz, C^2Ha), 3.40 (ddd, *J* 14.8, 4.0, 1.8 Hz, C^2Hb), 3.86 (2H, s, $C^{\alpha}H_2$), 4.12 (1H, dd, *J* 9.9, 4.3 Hz, C^4H), 4.13 (2H, q, *J* 7.1 Hz, CH_2CH_3), 7.06 (1H, ddd, *J* 7.9, 7.6, 1.6 Hz), 7.20 (2H, dtd, *J* 7.8, 1.2, 0.5 Hz), 7.21 (1H, tt, *J* 7.7, 1.3 Hz), 7.34 (2H, dddd, *J* 7.8, 7.7, 1.9, 0.5 Hz), 7.40 (1H, ddd, *J* 8.6, 7.6, 1.4 Hz), 7.54 (1H, ddd, *J* 8.6, 1.6, 0.5 Hz), 7.83 (1H, ddd, *J* 7.9, 1.4, 0.5 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 14.2, 29.0, 39.2, 50.1, 51.7, 61.2, 122.5, 122.8, 127.3, 127.6 (2C), 127.8, 128.3 (2C), 128.5 (2C), 136.2, 138.5, 139.3, 151.9, 169.2. MS (EI, 70 eV) *m/z* (%), 352 (M^++1, 4), 351 (M^+, 2), 318 (4), 282 (3), 246 (10), 237 (64), 235 (100), 212 (7), 199 (10), 176 (9), 165 (27), 151 (1), 105 (5), 75 (6). Anal. Calcd. for $C_{21}H_{21}NO_2S$ (351); C, 71.79; H, 5.98; N, 3.98; S, 9.11. Found; C, 71.96; H, 5.90; N, 4.14; S, 8.95%.

Ethyl 3-(4-phenyl-3,4-dihydro-2*H*-benzo[4,5]thieno[2,3-*b*]pyridin-1(1*H*)-yl)propanoate (9b). Buff crystals; 78%, mp 132–35 °C (acetone); IR (KBr) ν_{max} 3062, 2949, 1740, 1605, 1590, 1480, 1445, 1373, 1175, 782 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 1.15 (3H, t, *J* 7.1 Hz, $CH_2\underline{CH_3}$), 1.94 (1H, dtd, *J* 13.8, 9.9, 1.8 Hz, C^3Ha), 2.28 (1H, dddd, *J* 13.8, 4.3, 4.0, 1.9 Hz, C^3Hb), 2.50 (2H, t, *J* 6.7 Hz, $C^{\beta}H_2$), 3.32 (1H, ddd, *J* 13.7, 4.0, 1.8 Hz, C^2Ha), 3.41 (1H, ddd, *J* 13.7, 9.9, 1.9 Hz, C^2Hb), 3.56 (2H, t, *J* 6.7 Hz, $C^{\alpha}H_2$), 4.10 (2H, q, *J* 7.1 Hz, $\underline{CH_2}CH_3$), 4.12 (1H, dd, *J* 9.9, 4.3 Hz, C^4H), 7.15 (1H, ddd, *J* 7.9, 7.6, 1.5 Hz), 7.20 (2H, dtd, *J* 7.8, 1.2, 0.5 Hz), 7.21 (1H, tt, *J* 7.7, 1.3 Hz), 7.29 (1H, ddd, *J* 8.6, 7.6, 1.4 Hz), 7.34 (2H, dddd, *J* 7.8, 7.7, 1.9, 0.5 Hz), 7.53 (1H, ddd, *J* 8.6, 1.5, 0.5 Hz), 7.82 (1H, ddd, *J* 7.9, 1.4, 0.5 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 14.2, 29.0, 32.3, 39.2, 50.1 (2C), 61.2, 122.5, 122.8, 127.3, 127.6, 127.8), 128.1 (2C), 128.5 (2C), 136.2, 138.5, 139.3, 151.9, 171.7. MS (EI, 70 eV) *m/z* (%), 366 (M^++1, 5), 365 (M^+, 1), 284 (3), 240 (10), 223 (19), 209 (3), 199 (10), 198 (54), 196 (57), 176 (9), 171 (67), 169 (100), 165 (27), 109 (16), 99 (42), 97 (74), 105 (5), 75 (9), 62 (25), 61 (24). Anal. Calcd. for $C_{22}H_{23}NO_2S$ (365); C, 72.32; H, 6.30; N, 3.83; S, 8.76. Found; C, 72.37; H, 6.35; N, 3.88; S, 8.58%.

Ethyl 4-(4-phenyl-3,4-dihydro-2*H*-benzo[4,5]thieno[2,3-*b*]pyridin-1(1*H*)-yl)butanoate (9c). White plates; 71%, mp 96–99 °C (ethanol); IR (KBr) ν_{max} 3085, 2920, 1735, 1600, 1580, 1480, 1440, 1393, 1171, 769 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 1.15 (3H, t, *J* 7.1 Hz, $CH_2\underline{CH_3}$), 1.92 (1H, dtd, *J* 13.8, 9.9, 1.8 Hz, C^3Ha), 1.91 (2H, quint, *J* 7.4 Hz, $C^{\beta}H_2$), 2.28 (1H, dddd, *J* 13.8, 4.3, 4.0, 1.9 Hz, C^3Hb), 2.33 (2H, t, *J* 7.4 Hz, $C^{\alpha}H_2$), 3.16 (1H, ddd, *J* 13.9, 4.0, 1.8 Hz, C^2Ha), 3.39 (1H, ddd, *J* 13.9, 9.9, 1.9 Hz, C^2Hb), 3.50 (2H, t, *J* 7.5 Hz, $C^{\gamma}H_2$), 4.10 (2H, q, *J* 7.1 Hz, $\underline{CH_2}CH_3$), 4.12 (1H, dd, *J* 9.9, 4.3 Hz, C^4H), 7.15 (1H, ddd, *J* 7.9, 7.6, 1.5 Hz), 7.20 (2H, dtd, *J* 7.8, 1.2, 0.5 Hz), 7.21 (1H, tt, *J* 7.7, 1.3 Hz), 7.29 (2H, ddd, *J* 8.6, 7.6, 1.4 Hz), 7.34 (1H, dddd, *J* 7.8, 7.7, 1.9, 0.5 Hz), 7.53 (1H, ddd, *J* 8.6, 1.5, 0.5 Hz), 7.82 (1H, ddd, *J* 7.9, 1.4, 0.5 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 14.2, 24.9, 29.0, 31.3, 39.2, 50.1 (2C), 61.2, 122.5, 122.8, 127.3, 127.6, 127.8, 128.3 (2C), 128.5 (2C), 136.2, 138.5, 139.3, 151.9, 173.0. MS (EI, 70 eV) *m/z* (%), 381 (M^++2, 3), 379 (M^+, 2), 365 (1), 298 (42), 296 (100), 330 (0.5), 299 (4), 221 (6), 173 (1), 152 (4), 117 (4), 216 (6), 215 (5), 205 (9), 97 (5), 64 (6). Anal. Calcd. for $C_{23}H_{25}NO_2S$ (379); C, 72.82; H, 6.59; N, 3.69; S, 8.44. Found; C, 72.95; H, 6.50; N, 3.82; S, 8.31%.

Ethyl 2-(4-pyridyl-1,2,3,4-tetrahydrobenzo[4,5]thieno[2,3-*b*]pyridine-1(1*H*)-yl)acetate (9d). Pale yellow needles; 84%, mp 140–42 °C (acetone); IR (KBr) ν_{max} 3030, 2965, 1735, 1600, 1580, 1460, 1445, 1360, 1274, 769 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 1.17 (3H, t, *J* 7.1 Hz, $CH_2\underline{CH_3}$), 2.10 (1H, dtd, *J* 13.6, 9.9, 1.8 Hz, C^3Ha), 2.37 (1H, dddd, *J* 13.6, 4.3, 4.0, 1.9 Hz, C^3Hb), 3.28 (1H, ddd, *J* 16.4, 9.9, 1.9 Hz, C^2Ha), 3.35 (1H, ddd, *J* 16.4, 4.0, 1.8 Hz, C^2Hb), 3.91 (2H, s, $C^{\alpha}H_2$), 4.09 (1H, dd, *J* 9.9, 4.3 Hz, C^4H), 4.13 (2H, q, *J* 7.1 Hz, $\underline{CH_2}CH_3$), 7.16 (1H, ddd, *J* 7.9, 7.6, 1.6 Hz), 7.21 (1H, ddd, *J* 7.4, 4.9, 1.2 Hz), 7.26 (1H, ddd, *J* 7.6, 1.2, 0.6 Hz), 7.40 (1H, ddd, *J* 8.6, 7.6, 1.4 Hz), 7.55 (1H, ddd, *J* 8.6, 1.6, 0.5 Hz), 7.68 (1H, ddd, *J* 7.6, 7.4, 1.9 Hz), 7.83 (1H, ddd, *J* 7.9, 1.4, 0.5 Hz), 8.52 (1H, ddd, *J* 4.9, 1.9, 0.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 14.2, 29.0, 40.7, 50.1, 51.7, 61.2, 121.0, 122.5, 122.7, 122.8, 127.3, 128.3, 128.5, 136.7, 138.5, 139.3, 149.1, 151.9, 164.0, 169.2. MS (EI, 70 eV) *m/z* (%), 354 (M^++2, 5), 352 (M^+, 3), 318 (3), 298 (42), 282 (2), 246 (10), 239 (10), 238 (9), 237 (64), 236 (15), 235 (100), 212 (7), 199 (10), 176 (8), 165 (27), 105 (4), 88 (6), 75 (5). Anal. Calcd. for $C_{20}H_{20}N_2O_2S$ (352); C, 68.18; H, 5.68; N, 7.95; S, 9.09. Found; C, 68.15; H, 5.75; N, 7.90; S, 9.14%.

Ethyl 3-(4-pyridyl-1,2,3,4-tetrahydro-benzo[4,5]thieno[2,3-*b*]pyridine-1(1*H*)-yl)propanoate (9e). Brownish needles; 72%, mp 110–13 °C (ethanol); IR (KBr) ν_{max} 3058, 2980, 1733, 1600, 1580, 1470, 1440, 1335, 1295, 1137, 769 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 1.15 (3H, t, *J* 7.1 Hz, $CH_2\underline{CH_3}$), 2.11 (1H, dtd, *J* 13.6, 9.9, 1.8 Hz, C^3Ha), 2.41 (1H, dddd, *J* 13.6, 4.3, 4.0, 1.9 Hz, C^3Hb), 2.50 (2H, t, *J* 6.7 Hz, $C^\alpha H_2$), 3.29 (1H, ddd, *J* 13.3, 9.9, 1.9 Hz, C^2Ha), 3.42 (1H, ddd, *J* 13.3, 4.0, 1.8 Hz, C^2Hb), 3.56 (2H, t, *J* 6.7 Hz, $C^\beta H_2$), 4.06 (1H, dd, *J* 9.9, 4.3 Hz, C^4H), 4.10 (2H, q, *J* 7.1 Hz, $\underline{CH_2}CH_3$), 7.15 (2H, ddd, *J* 7.4, 4.9, 1.2 Hz), 7.26 (1H, ddd, *J* 7.6, 1.2, 0.6 Hz), 7.29 (1H, ddd, *J* 8.6, 7.6, 1.4 Hz), 7.54 (1H, ddd, *J* 8.6, 1.6, 0.5 Hz), 7.68 (1H, ddd, *J* 7.6, 7.4, 1.9 Hz), 7.82 (1H, ddd, *J* 7.9, 1.4, 0.5 Hz), 8.52 (1H, ddd, *J* 4.9, 1.9, 0.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 14.2, 29.0, 32.3, 40.7, 50.1 (2C), 61.2, 121.0, 122.5, 122.8 (2C), 127.3, 128.6 (2C), 136.7, 138.5, 139.3, 149.1, 151.9, 164.0, 171.7. MS (EI, 70 eV) *m/z* (%), 366 (M^+, 5), 355 (3), 321 (2), 240 (9), 223 (18), 198 (54), 196 (57), 176 (9), 171 (67), 169 (100), 109 (12), 99 (42), 97 (74), 75 (5). Anal. Calcd. for $C_{21}H_{22}N_2O_2S$ (366); C, 68.85; H, 6.01; N, 7.65; S, 8.74. Found; C, 68.83; H, 6.11; N, 7.62; S, 8.71%.

Ethyl 4-(4-pyridyl-1,2,3,4-tetrahydro-benzo[4,5]thieno[2,3-*b*]pyridine-1(1*H*)-yl)butanoate (9f). Brown crystals; 70%, mp 102-5 °C (ethanol); IR (KBr) ν_{max} 3083, 2952, 1740, 1600, 1590, 1480, 1440, 1385, 1177, 785 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 1.15 (3H, t, *J* 7.1 Hz, $CH_2\underline{CH_3}$), 1.91 (2H, quint, *J* 7.4 Hz, $C^\beta H_2$), 2.11 (1H, dtd, *J* 13.6, 9.9, 1.8 Hz, C^3Ha), 2.33 (2H, t, *J* 7.4 Hz, $C^\alpha H_2$), 2.41 (1H, dddd, *J* 13.6, 4.3, 4.0, 1.9 Hz, C^3Hb), 3.29 (1H, ddd, *J* 13.7, 4.0, 1.8 Hz, C^2Ha), 3.39 (1H, ddd, *J* 13.7, 9.9, 1.9 Hz, C^2Hb), 3.50 (2H, t, *J* 7.5 Hz, $C^\gamma H_2$), 4.06 (1H, dd, *J* 9.9, 4.3 Hz, C^4H), 4.10 (2H, q, *J* 7.1 Hz, $\underline{CH_2}CH_3$), 7.15 (2H, ddd, *J* 7.4, 4.9, 1.2 Hz), 7.26 (1H, ddd, *J* 7.6, 1.2, 0.6 Hz), 7.29 (1H, ddd, *J* 8.6, 7.6, 1.4 Hz), 7.54 (1H, ddd, *J* 8.6, 1.6, 0.5 Hz), 7.68 (1H, ddd, *J* 7.6, 7.4, 1.9 Hz), 7.82 (1H, ddd, *J* 7.9, 1.4, 0.5 Hz), 8.52 (1H, ddd, *J* 4.9, 1.9, 0.6 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 14.2, 24.9, 29.0, 31.3, 40.7, 50.1 (2C), 61.2, 121.0, 122.5, 122.8 (2C), 127.3, 128.5 (2C), 136.7, 138.5, 139.3, 149.1, 151.9, 164.0, 173.0. MS (EI, 70 eV) *m/z* (%), 380 (M^+, 22), 239 (24), 325 (86), 324 (37), 269 (21), 268 (100), 181 (5), 145 (12), 107 (14), 77 (3), 57 (20). Anal. Calcd. for $C_{22}H_{24}N_2O_2S$ (380); C, 69.47; H, 6.31; N, 7.36; S, 8.42. Found; C, 69.41; H, 6.24; N, 7.41; S, 8.47%.

Cyclizations of heterocyclic ester precursors 9a-f

Method A. General Procedure for $AlCl_3/CH_3NO_2$–mediated cycliacylations

To a solution of $AlCl_3$ (10 mmol) in CH_3NO_2 (100 mmol) was added a solution of required ester **9a**–**f** (2 mmol) in DCM (10 mL) dropwise over 15 min with efficient stirring at rt. The reaction mixture was stirred for a certain time at the required temperature (Table 1), then quenched with addition of ice–cold HCl solution (30 mL, 10%) at 0 °C, extracted with EtOAc (3 × 20 mL), washed with Na_2CO_3 (20 mL, 10%) which was dried over Na_2SO_4, decanted and concentrated under reduced pressure to give the crude products **10a**–**f**.

Method B. General Procedure for TfOH-mediated cycliacylations

To a solution of the indicated ester **9a–f** (3 mmol) in dry 1,2–dichloroethane (20 mL) was added dropwise TfOH (15 mmol) at 0 °C. Afterwards, the mixture was stirred at the required temperature for a certain time as illustrated in Table 1. The reaction mixture was then decomposed with $NaHCO_3$ solution (50 ml, 30%) at room temperature. The reaction mixture was extracted with EtOAc (3×25 mL), and the organic layer was washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to give the crude products **10a**–**f**.

Method C. General Procedure for PPA-mediated cycliacylations

A mixture of ester **9a-f** (3 mmol) and PPA (15 g) was heated on an oil bath at the indicated temperature for the required time (Tables 1) after which TLC analysis (30% AcOEt/hexane) showed the reaction to be complete. The reaction mixture was cooled, basified with addition of $NaHCO_3$ solution (30 ml, 50%) and then extracted with ether (3×30 mL). The combined organics were washed with saturated brine solution, dried over $MgSO_4$, filtered and concentrated in *vacuo* to give the products **10a-f**.

In all procedures, the crude residue was purified by flash chromatography (basic alumina, 25%, EtOAc/hexane) to afford the pure pentacyclic products **10a-f**. Further purification and yields of the products are given in the following.

5,6,13-Trihydro-7*H*-7,13-ethanobenzo[4,5]thieno[2,3-*b*]benzo[*e*]azocin-5-one (10a). Yellow crystals, 81%, mp 152–55 °C (benzene); IR (KBr) ν_{max} 3068, 2955, 1680, 1600, 1570, 1440, 1345, 1281, 1070, 783 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 1.97 (1H, dddd, *J* 13.3, 7.9, 4.4, 1.5 Hz, *bridged*–CH*a*), 2.31 (1H, dddd, *J* 13.3, 8.0, 6.8, 2.6 Hz, *bridged*–CH*b*), 3.47 (ddd, *J* 12.0, 7.9, 2.6 Hz, *bridged*–N–CH), 3.73 (1H, ddd, *J* 12.0, 8.0, 4.4 Hz, *bridged*–N–CH), 4.51 (1H, dd, *J* 6.8, 1.5 Hz, C^{13}H), 4.90 (2H, d, *J* 17.0 Hz, C^{6}H$_2$), 6.85 (1H, td, *J* 7.7, 1.6 Hz), 6.74 (1H, ddd, *J* 7.7, 1.6, 0.5 Hz), 6.95 (1H, td, *J* 7.7, 2.2 Hz), 7.09 (1H, ddd, *J* 7.7, 2.2, 0.5 Hz), 7.35 (2H, m), 7.50 (1H, ddd, *J* 8.0, 7.3, 1.3 Hz), 7.90 (1H, ddd, *J* 7.9, 1.3, 0.5 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 29.0, 39.2, 49.2, 50.1, 122.5, 122.8, 124.1, 126.7, 127.3, 128.4 (2C), 128.5 (2C), 133.0, 138.5, 139.3, 140.3, 151.9, 191.5. MS (EI, 70 eV) *m/z* (%), 306 (M$^+$+1, 12), 305 (M$^+$, 100), 277 (7), 213 (4), 178 (7), 152 (11), 150 (36), 123 (7), 115 (17), 114 (9), 88 (6), 75 (6). Anal. Calcd. for $C_{19}H_{15}NOS$ (305); C, 74.75; H, 4.91; N, 4.59; S, 10.49. Found; C, 74.76; H, 4.97; N, 4.68; S, 10.36%.

5,6,7,14-Tetrahydro-8*H*-8,14-ethanobenzo[4,5]thieno[2,3-*b*]benzo[*e*]azonin-5-one (10b). Yellow crystals; 85%; mp 132–35 °C (acetone); IR (KBr) ν_{max} 3052, 2965, 1695, 1580, 1470, 1440, 1360, 1254, 1122, 1040, 768 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 2.54 (1H, dddd, *J* 14.3, 6.8, 2.3, 1.7 Hz, *bridged*–CH*a*), 2.83 (1H, ddd, *J* 15.0, 9.3, 3.1 Hz, *bridged*–N–CH), 2.85 (dddd, *J* 14.3, 8.1, 4.1, 3.6 Hz, *bridged*–CH*b*), 3.36 (1H, dt, *J* 15.0, 3.7 Hz, *bridged*–N–CH), 3.77 (1H, ddd, *J* 14.2, 4.1, 1.7 Hz, C^{6}H), 3.82 (1H, ddd, *J* 14.5, 9.3, 3.7 Hz, C^{6}H), 4.01 (1H, ddd, *J* 14.5, 3.7, 3.1 Hz, C^{7}H), 4.25 (1H, ddd, *J* 14.2, 8.1, 6.8 Hz, C^{7}H), 5.11 (1H, dd, *J* 3.6, 2.3 Hz, C^{14}H), 7.08 (1H, ddd, *J* 7.9, 7.6, 1.6 Hz), 7.29 (1H, ddd, *J* 8.6, 7.6, 1.4 Hz), 7.36 (1H, ddd, *J* 11.5, 1.8, 0.5 Hz), 7.40 (1H, ddd, *J* 8.7, 7.5, 1.8 Hz), 7.46 (1H, ddd, *J* 11.5, 7.5, 1.3 Hz), 7.54 (1H, ddd, *J* 8.6, 1.6, 0.5 Hz), 7.82 (1H, ddd, *J* 7.9, 1.4, 0.5 Hz), 8.00 (1H, ddd, *J* 8.7, 1.3, 0.5 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 29.0, 37.4, 39.2, 50.1 (2C), 122.5, 122.8, 124.1, 126.7, 127.3, 128.3 (2C), 128.5 (2C), 133.0, 138.5, 139.3, 140.3, 151.9, 198.5. MS (EI, 70 eV) *m/z* (%),319 (M$^+$+1, 6), 318 (M$^+$, 26), 274 (100), 273 (78), 257 (43), 226 (28), 225 (89), 197 (35), 181 (50), 176 (5), 152 (23), 121 (29), 93 (12), 76 (15). Anal. Calcd. for $C_{20}H_{17}NOS$ (319); C, 75.23; H, 5.32; N, 4.38; S, 10.03. Found; C, 75.09; H, 5.30; N, 4.45; S, 10.11%.

5,6,7,8,15-Pentahydro-9*H*,15-ethanobenzo[4,5]thieno[2,3-*b*]benzo[*e*]azecin-5-one (10c). White needles; 90%; mp 149–52 °C (benzene); IR (KBr) ν_{max} 3062, 2948, 1700, 1600, 1485, 1475, 1450, 1347, 1266, 778 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 2.10 (1H, ddddd, *J* 14.0, 8.1, 7.9, 3.2, 2.1 Hz *bridged*–CH*a*), 2.38 (1H, ddddd, *J* 14.0, 6.9, 5.2, 3.6, 2.3 Hz, *bridged*–CH*b*), 2.43 (1H, dddd, *J* 14.2, 7.9, 6.2, 4.8 Hz, *bridged*–N–CH), 2.74 (1H, dddd, *J* 14.2, 8.6, 5.5, 1.4 Hz, *bridged*–N–CH), 2.76 (2H, m, C^{7}H$_2$), 3.60 (1H, ddd, *J* 14.2, 7.9, 5.5 Hz, C^{6}H), 3.87 (1H, ddd, *J* 15.4, 8.1, 3.6 Hz, C^{9}H), 3.90 (1H, ddd, *J* 14.2, 6.2, 1.4 Hz, C^{6}H), 4.01 (1H, ddd, *J* 15.4, 5.2, 3.2 Hz, C^{9}H), 5.17 (1H, dd, *J* 8.6, 4.8 Hz, C^{15}H), 7.08 (1H, ddd, *J* 7.9, 7.6, 1.2 Hz), 7.20 (1H, ddd, *J* 8.6, 1.2, 0.5 Hz), 7.25 (2H, m), 7.36 (1H, ddd, *J* 7.9, 7.3, 1.5 Hz), 7.47 (1H, ddd, *J* 8.0, 7.3, 1.2 Hz), 7.75 (2H, m). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 21.9, 29.0, 35.5, 39.2, 50.3 (2C), 122.5, 122.8, 124.1, 126.7, 127.3, 128.2 (2C), 128.5 (2C), 133.0, 138.5, 139.3, 140.3, 151.9, 206.8. MS (EI, 70 eV) *m/z* (%), 333 (M$^+$, 13), 306 (8), 271 (4), 224 (3), 197 (6), 186 (5), 175 (8), 153 (100), 118 (62), 117 (81), 106 (38), 83 (65), 78 (45), 77 (70). Anal. Calcd. for $C_{21}H_{19}NOS$ (333); C, 75.67; H, 5.70; N, 4.20; S, 9.60. Found; C, 75.65; H, 5.82; N, 4.07; S, 9.64%.

5,6,13-Trihydro-7*H*-7,13-ethanopyrido[2',3'-*e*]benzo[4,5]thieno[2,3-*b*]azocin-5-one (10d). Brownish needles; 92%; mp 174 ºC, *dec.* (AcOEt); IR (KBr) ν_{max} 3060, 2935, 1695, 1600, 1475, 1470, 1440, 1338, 1230, 795 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 2.05 (1H, dddd, *J* 13.3, 7.9, 4.5, 1.5 Hz, *bridged*–CH*a*), 2.36 (1H, dddd, *J* 13.3, 8.0, 6.9, 2.5 Hz, *bridged*–CH*b*), 3.43 (1H, ddd, *J* 12.0, 7.9, 2.5 Hz, *bridged*–N–CH), 3.69 (1H, ddd, *J* 12.0, 8.0, 4.5 Hz, *bridged*–N–CH), 4.68 (1H, dd, *J* 6.9, 1.5 Hz, C^{13}H), 4.94 (1H, d, *J* 17.2 Hz, C^{6}H), 5.07 (1H, d, *J* 17.2 Hz,

C^6H), 6.52 (1H, ddd, *J* 7.7, 1.6, 0.5 Hz), 6.80 (1H, td, *J* 7.7, 1.6 Hz), 6.97 (1H, td, *J* 7.7, 2.2 Hz), 7.11 (1H, ddd, *J* 7.7, 2.2, 0.5 Hz), 7.24 (1H, dd, *J* 7.8, 4.5 Hz), 7.86 (1H, dd, *J* 7.8, 1.9 Hz), 8.74 (1H, dd, *J* 4.5, 1.9 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 29.0, 40.7, 49.2, 50.1, 122.5, 122.8, 123.4, 127.3, 128.3, 128.6 (2C), 135.4, 138.5, 139.3, 149.1, 151.9, 164.9, 191.5. MS (EI, 70 eV) *m/z* (%), 307 (M^++1, 27), 306 (M^+, 4), 307 (26), 275 (26), 246 (12), 218 (4), 171 (22), 143 (100), 129 (24), 128 (28), 115 (74), 102 (18), 101 (19), 89 (13), 77 (25). Anal. Calcd. for $C_{18}H_{14}N_2OS$ (306); C, 70.58; H, 4.57; N, 9.15; S, 10.45. Found; C, 70.62; H, 4.65; N, 9.02; S, 10.40%.

5,6,7,14-Tetrahydro-8*H*-8,14-ethanopyrido[2',3'-*e*]benzo[4,5]thieno[2,3-*b*]azonin-5-one (10e). White needles; 84%; mp 182 °C, *dec.* (AcOEt); IR (KBr) ν_{max} 3090, 2977, 1705, 1600, 1482, 1465, 1435, 1348, 1260, 1162, 758 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 2.40 (1H, dddd, *J* 14.3, 6.8, 2.3, 1.7 Hz, *bridged*–CH*a*), 2.80 (1H, dddd, *J* 14.3, 8.1, 4.1, 3.6 Hz, *bridged*–CH*b*), 2.87 (1H, ddd, *J* 15.5, 9.3, 3.1 Hz, *bridged*–N–CH), 3.40 (1H, dt, *J* 15.5, 3.7 Hz, *bridged*–N–CH), 3.82 (1H, ddd, *J* 14.5, 9.3, 3.7 Hz, C^6H), 3.92 (1H, ddd, *J* 14.5, 3.7, 3.1 Hz, C^6H), 4.09 (1H, ddd, *J* 14.1, 4.1, 1.7 Hz, C^7H), 4.16 (1H, ddd, *J* 14.1, 8.1, 6.8 Hz, C^7H), 5.10 (1H, dd, *J* 3.6, 2.3 Hz, $C^{14}H$), 7.08 (1H, ddd, *J* 7.9, 7.6, 1.6 Hz), 7.24 (2H, m), 7.53 (1H, ddd, *J* 8.6, 1.6, 0.5 Hz), 7.82 (1H, ddd, *J* 7.9, 1.4, 0.5 Hz), 7.89 (1H, dd, *J* 7.8, 1.9 Hz), 8.84 (1H, dd, *J* 4.5, 1.9 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 29.0, 37.4, 40.7, 50.3 (2C),122.5, 122.8, 123.4, 127.3, 128.1, 128.5 (2C), 135.4, 138.5, 139.3, 149.1, 151.9, 164.9, 198.5. MS (EI, 70 eV) *m/z* (%), 322 (M^++2, 60), 320 (M^+, 10), 307 (5), 290 (9), 265 (61), 249 (47), 176 (6), 121 (42), 115 (23), 102 (27), 92 (45), 77 (17), 72 (100), 43 (30). Anal. Calcd. for $C_{19}H_{16}N_2OS$ (320); C, 71.25; H, 5.00; N, 8.75; S, 10.00. Found; C, 71.17; H, 4.96; N, 8.82; S, 10.06%.

5,6,7,8,15-Pentahydro-9*H*,15-ethanopyrido[2',3'-*e*]benzo[4,5]thieno[2,3-*b*]azecin-5-one (10f). creamy crystals; 86%; mp 144–47 °C (ethanol); IR (KBr) ν_{max} 3030, 2969, 1700, 1600, 1590, 1480, 1440, 1375, 1268, 1150, 796 cm^{-1}; ^{1}H-NMR (400 MHz, $CDCl_3$, δ, ppm): 2.10 (1H, ddddd, *J* 14.0, 8.1, 7.8, 3.3, 2.1 Hz, *bridged*–CH*a*), 2.38 (1H, ddddd, *J* 14.0, 7.0, 5.2, 3.6, 2.2 Hz, *bridged*–CH*b*), 2.48 (1H, dddd, *J* 14.4, 8.0, 6.2, 4.8 Hz, *bridged*–N–CH), 2.63 (1H, dddd, *J* 14.4, 8.6, 5.5, 1.4 Hz, *bridged*–N–CH), 2.77 (2H, m, C^7H_2), 3.46 (2H, m, C^6H_2), 3.88 (ddd, *J* 15.4, 8.1, 3.6 Hz, C^8H), 4.00 (ddd, *J* 15.4, 5.2, 3.3 Hz, C^8H), 5.29 (1H, dd, *J* 8.6, 4.8 Hz, $C^{15}H$), 7.55 (2H, m), 7.21 (1H, ddd, *J* 8.6, 1.3, 0.5 Hz), 7.25 (1H, ddd, *J* 8.6, 7.6, 1.2 Hz)), 7.74 (1H, ddd, *J* 7.9, 1.2, 0.5 Hz), 7.89 (1H, dd, *J* 7.9, 1.9 Hz), 8.77 (1H, dd, *J* 4.6, 1.9 Hz). ^{13}C-NMR (100 MHz, $CDCl_3$, δ, ppm): 21.9, 29.0, 35.5, 40.7, 50.1 (2C), 122.5, 122.8, 123.4, 127.3, 128.3, 128.5 (2C), 135.4, 138.5, 139.3, 149.1, 151.9, 164.9, 198.5. MS (EI, 70 eV) *m/z* (%),334 (M^+, 4), 333 (M^+-1, 26), 332 (100), 331 (51), 304 (5), 302 (4), 277 (2), 255 (13), 227 (3), 175 (1), 77 (14), 51 (6). Anal. Calcd. for $C_{20}H_{18}N_2OS$ (334); C, 71.85; H, 5.38; N, 8.38; S, 9.58. Found; C, 71.88; H, 5.43; N, 8.30; S, 9.46%.

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