A Novel Approach to Pyrrolo[2,1-*b*][1,3]benzothiazines

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Abstract: Alkylation of (3,4-dihydro-4-oxo-2*H*-1,3-benzothiazin-2-ylidene)acetic acid ethyl ester and (3,4-dihydro-4-oxo-2*H*-1,3-benzothiazin-2-ylidene)acetonitrile with phenacyl chlorides in the presence of potassium carbonate was shown to occur at the nitrogen atom yielding the corresponding *N*-phenacyl derivatives. The latter, upon treatment with DMF·$POCl_3$ complex, were converted into 1-aroyl-9-oxo-9*H*-pyrrolo[2,1-*b*][1,3]benzothiazine-3-carboxylic acid ethyl esters and -3-carbonitriles. The structure of the obtained pyrrolobenzothiazine derivatives was confirmed unambiguously by X-ray crystallographic study. Reaction of these pyrrolo[2,1-*b*][1,3]benzothiazines with aliphatic primary amines resulted in the thiazine ring cleavage and formation of 2-[(5-aroyl-3-cyano(or ethoxycarbonyl)-1*H*-pyrrol-2-yl)thio]-*N*-alkylbenzamides.

Key words: alkylations, cleavage, cyclizations, heterocycles, pyrroles

Pyrrolo[2,1-*b*][1,3]benzothiazine is a rare heterocyclic core. To the best of our knowledge only 15 derivatives of this system have been described to date. Apparently, this is because of the lack of good and general procedures for their preparation. Among the known methods, only a single example of pyrrole ring annulation to the benzothiazine moiety was reported.[1] The rest of the published approaches were based on construction of the thiazine ring.[2–5] Most of them included 3*a*C–S bond formation.[2,3] At this step both possible polarities, that is, either the intramolecular attack of electrophilic carbon atom on the sulfur[2] or the intramolecular capture of electrophilic sulfur species produced by Pummerer rearrangement of sulfoxides with electron-rich carbon,[3] were realized. Furthermore, the thermal- or base-induced intramolecular acylation of the nitrogen in the 2-(1*H*-pyrrol-2-yl-thio)benzoic acid derivatives represents another method for the thiazine ring closure[4] during the synthesis of the title system. Finally, a free-radical cyclization of certain *N*-[2-bromo(iodo)benzyl]pyrrolidine derivatives bearing suitable sulfur substituents into pyrrolobenzothiazines was described.[5] However, all these methods[1–5] predominantly afford the singular derivatives of the target core with unique substitution pattern and for different reasons are inapplicable for the preparation of the series of diverse compounds. Moreover, some of the mentioned reactions gave pyrrolobenzothiazines in the mixtures with isomers and side products,[2c,3b,c,5] necessitating a separation procedure. Thus, the current achievements in the synthesis of pyrrolo[2,1-*b*][1,3]benzothiazines are rather limited, and therefore, elaboration of new general approaches to this system is required.

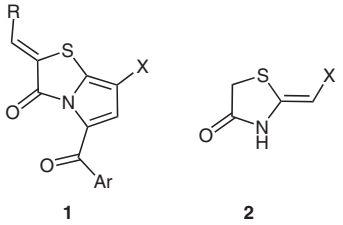
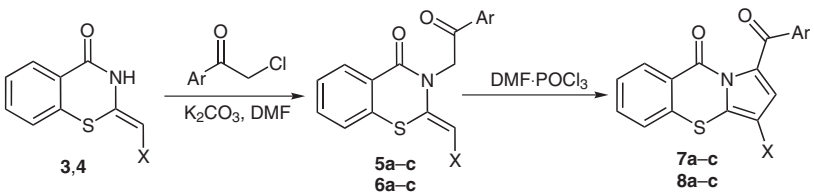


Figure 1 X = CN, CO_2Et, SO_2Ar; Ar = Ph or substituted Ph; R = NMe_2, Ph or substituted Ph

In our recent work,[6] we have prepared pyrrolo[2,1-*b*]thiazoles of type **1** by a two-step pyrrole annulation to the thiazole precursors **2** (Figure 1). Since the closely related benzothiazine derivatives **3**,**4** (Scheme 1) are readily available from 2-mercaptobenzoic ester and ethyl cyanoacetate or malononitrile, respectively,[7] it would be



Scheme 1 X = CO_2Et (**3**, **5**, **7**), X = CN (**4**, **6**, **8**); Ar = Ph (**a**), 4-ClC_6H_4 (**b**), 4-BrC_6H_4 (**c**)

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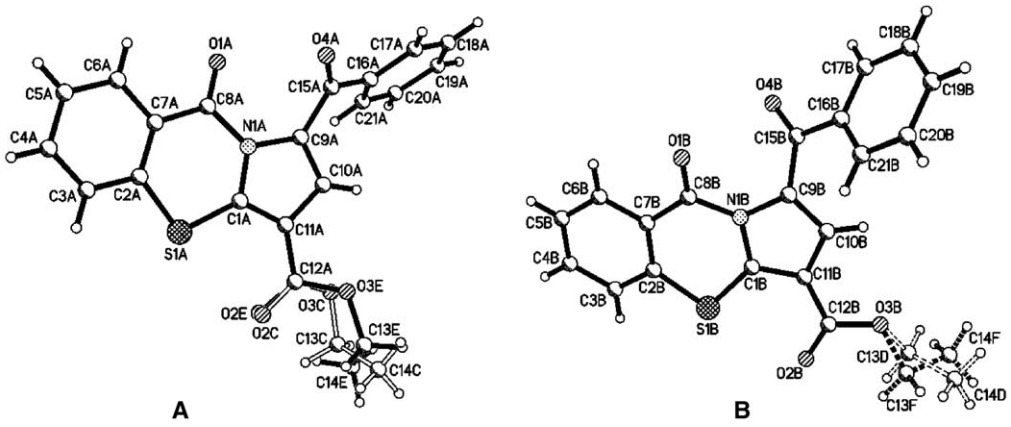


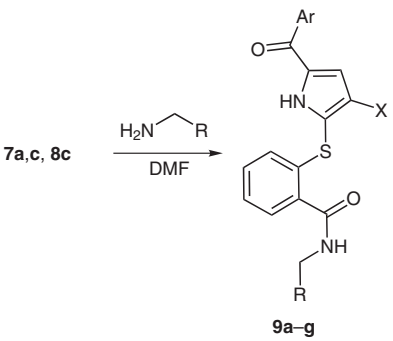
Figure 2 X-ray molecular structures of compound **7a** with the atom numbering used in the crystallographic analysis

reasonable to extend the method to these compounds. Moreover, the alternative route to pyrrolo[2,1-*b*][1,3]benzothiazines based on the pyrrole ring formation seems to be more promising because the previous thiazine ring closure approaches[2–5] revealed their inaptitude providing only 15 derivatives over the last 45 years since the first report[1] of the core synthesis.

Compounds **3**,**4** undergo N-alkylation with simple alkyl halides under basic conditions.[7] Indeed, their reaction with phenacyl chlorides in the presence of K_2CO_3 proceeded smoothly leading to derivatives **5a–c**, **6a–c** in satisfactory yields. Alkylation of the enamine carbon atom was not observed, similar to the case of thiazole analogues **2**.[6] In the next step, the benzothiazines **5**,**6** were treated with a 2.5-fold excess Vilsmeier's complex according to our method[6] to afford the pyrrolobenzothiazines **7a–c**, **8a–c** in good yields. Compounds **7**,**8** were assumed to be formed through initial formylation of the enamine moiety and further intramolecular condensation of the introduced formyl group with the methylene. Compared to the preparation of the pyrrolothiazoles **1** the present reaction occurred slightly faster, but the final yields of the isolated products **7**, **8** were comparable with that of **1**.

The structure of the obtained compounds **7**,**8** was initially deduced from their ^{1}H and ^{13}C NMR spectra and then confirmed unambiguously by X-ray crystallographic study carried out on the derivative **7a** (Figure 2). According to the crystal data, the asymmetric part of crystal unit cell contains the two molecules **A** and **B** differed by certain geometric parameters. In both molecules, the thiazine ring adopts a twist-boat conformation. Deviations of the S(1) and C(8) atoms from the least-squared plane of the rest of the atoms of the ring are +0.15 and +0.19 Å for molecule **A** or –0.12 and –0.19 Å for **B**, respectively. The following puckering parameters[8] have been calculated: S = 0.27, Θ = 72.9°, ψ = 24.6° for molecule **A** and S = 0.28, Θ = 68.0°, ψ = 29.1° for **B**. A repulsion between the neighboring carbonyls of the thiazine moiety and the benzoyl substituent results in considerable elongation of the bonds N(1)–C(8) and N(1)–C(9) compared with their standard values. Thus, the distance N(1)–C(8) is 1.42 Å in both **A** and **B** while the typical length is 1.35 Å;[9] and the distance N(1)–C(9) is 1.41 and 1.42 Å in **A** and **B**, respectively, whereas the standard value is 1.37 Å.[9] Furthermore, in both the molecules the ester group is disordered. In molecule **A** the whole ethoxycarbonyl substituent is disordered over two positions **E** and **C** with a population 70:30% owing to the rotation around C(11)–C(12) bond. In molecule **B**, only the ethyl group is disordered over two positions **F** and **D** with a population of 62:38% at the expense of rotation around C(12)–O(3) bond.

Certain condensed heterocycles containing the *N*-acylpyrrole moiety were reported to undergo cleavage at the CO–N bond upon treatment with highly nucleophilic amines or hydrolysis.[10] Moreover, the two examples of such a cleavage were noted for 9-oxo derivatives of the title system.[3b,4a] Thus, the reaction of compounds **7**,**8** also containing the *N*-acylpyrrole fragment with aliphatic primary amines was examined. It was found that heating derivatives **7a**,**c**, **8c** with amines in DMF furnished 2-(2-pyrrolylthio)benzamides **9a–g** in nearly quantitative yields (Scheme 2, Table 1). The CO–N bond of pyrrolobenzothiazines **7**,**8** is really reactive towards nucleophiles and compounds **7**,**8** can be used as mild acylating agents giving access to unique pyrrole derivatives. The observed reactivity agrees completely with the elongation of the N(1)–C(8) bond revealed by the crystal data.



Scheme 2 For yields and assignments of the groups X, R, Ar, see Table 1

Table 1 Compounds **9a–g** Prepared

Product	X	Ar	R	Yield (%)
9a	CO_2Et	Ph	Ph	96
9b	CO_2Et	Ph	2-furyl	89
9c	CO_2Et	4-BrC_6H_4	Ph	96
9d	CO_2Et	4-BrC_6H_4	2-furyl	93
9e	CN	4-BrC_6H_4	Ph	91
9f	CN	4-BrC_6H_4	2-furyl	91
9g	CO_2Et	4-BrC_6H_4	Bn	95

The structures of compounds **9a–g** were confirmed by ^1H and ^{13}C NMR data. For selected samples the sets of 2D NMR experiments (COSY, NOESY, HSQC, HMBC) were performed to facilitate the signal assignments and to ensure the 2-(2-pyrrolylthio)benzamide structure. As for the spectral data, the downfield shift of the carbonyl signal from 157–158 ppm (9-C) in the starting materials **7**,**8** to 167–168 ppm (CONH) in the products **9** in the ^{13}C NMR spectra as well as appearance of the both pyrrole (12.7–13.5 ppm) and amide (8.6–9.1 ppm) NH signals in the ^1H NMR spectra of derivatives **9** deserve to be mentioned as the most remarkable attributes of the thiazine ring cleavage.

In summary, the present research has resulted in a novel and convenient approach to pyrrolo[2,1-*b*][1,3]benzothiazines. Contrary to the known procedures[1–5] it allows for the preparation of a diverse series of compounds **7**,**8** with at least two points of substituent variation. For the first time, the precise crystallographic data about structure and conformation of pyrrolo[2,1-*b*][1,3]benzothiazine core have been obtained. Furthermore, the possibility of easy nucleophilic cleavage of derivatives **7**,**8** into benzamides **9** has been demonstrated, thus confirming a few previous observations.[3b,4a] In view of our preceding work[6] the two-step pyrrole annulation to heterocyclic enamides of type **2–4** is believed to be general. Further studies in the field are in progress.

The starting compounds **3**,**4** were prepared as described.[7] Phenacyl chlorides were either commercially available or obtained according to the reported procedures.[11] Commercial DMF was kept over P_2O_5 overnight and then distilled under reduced pressure. Other reagents were commercially available and were used without additional purification. All melting points were determined in open capillary tubes in a Thiele apparatus and are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Varian Unity plus 400 spectrometer (400 MHz for ^1H and 100 MHz for ^{13}C) in DMSO-d_6. 2D NMR experiments were performed on a Bruker Avance 500 spectrometer (500 MHz for ^1H and 125 MHz for ^{13}C). Chemical shifts (δ) are given in ppm downfield from internal Me_4Si. *J* values are in Hz. The purity of all compounds obtained was checked by ^1H NMR and LC/MS on an Agilent 1100 instrument.

Benzothiazines 5a–c and 6a–c; General Procedure

Powdered K_2CO_3 (0.76 g, 5.5 mmol) was added to a solution of compound **3**,**4** (5.0 mmol) in DMF (10 mL) and the mixture was stirred at r.t. for 0.5 h. Then an appropriate phenacyl chloride (5.0 mmol) was added in one portion and the stirring was continued for 5–6 h. The mixture was poured into H_2O (20 mL) and the separated solid was filtered and recrystallized from a suitable solvent to give derivatives **5a–c** and **6a–c**.

[3,4-Dihydro-4-oxo-3-(2-oxo-2-phenylethyl)-2*H*-1,3-benzothiazin-2-ylidene]acetic Acid Ethyl Ester (5a)

Yield: 0.88 g (48%); mp 177 °C (EtOH).

^1H NMR: δ = 1.16 (t, *J* = 7.0 Hz, 3 H, CH_3), 4.07 (q, *J* = 7.0 Hz, 2 H, OCH_2), 5.57 (s, 1 H, CHCOO), 5.71 (s, 2 H, NCH_2), 7.43 (t, *J* = 7.5 Hz, 1 H, 6-H), 7.57–7.62 (m, 3 H, 3,5-H_{Ar}, 8-H), 7.68 (t, *J* = 7.5 Hz, 1 H, 7-H), 7.73 (t, *J* = 7.0 Hz, 1 H, 4-H_{Ar}), 8.09 (m, 3 H, 5-H, 2,6-H_{Ar}).

^{13}C NMR: δ = 14.7 (CH_3), 54.3 (NCH_2), 60.0 (OCH_2), 96.3 (*C*HCOO), 122.3 (4a-C), 125.7 (5-C), 127.6 (8-C), 128.8 (3,5-C_{Ar}), 129.4 (2,6-C_{Ar}), 130.4 (6-C), 134.0 (1-C_{Ar}), 134.6 (4-C_{Ar}), 134.7 (7-C), 134.9 (8a-C), 150.6 (2-C), 160.6 (4-CO), 166.4 (COO), 192.6 (*C*OAr).

Anal. Calcd for $C_{20}H_{17}NO_4S$: C, 65.38; H, 4.66; N, 3.81; S, 8.73. Found: C, 65.56; H, 4.73; N, 3.80; S, 8.89.

{3-[2-(4-Chlorophenyl)-2-oxoethyl]-3,4-dihydro-4-oxo-2*H*-1,3-benzothiazin-2-ylidene}acetic Acid Ethyl Ester (5b)

Yield: 1.08 g (54%); mp 190 °C (EtOH).

^1H NMR: δ = 1.16 (t, *J* = 7.5 Hz, 3 H, CH_3), 4.06 (q, *J* = 7.5 Hz, 2 H, OCH_2), 5.61 (s, 1 H, CHCOO), 5.70 (s, 2 H, NCH_2), 7.43 (t, *J* = 8.0 Hz, 1 H, 6-H), 7.58 (d, *J* = 8.0 Hz, 1 H, 8-H), 7.68 (m, 3 H, 7-H, 3,5-H_{Ar}), 8.09 (m, 3 H, 5-H, 2,6-H_{Ar}).

^{13}C NMR: δ = 14.7 (CH_3), 54.3 (NCH_2), 60.0 (OCH_2), 96.4 (*C*HCOO), 122.2 (4a-C), 125.7 (5-C), 127.6 (8-C), 129.5 (3,5-C_{Ar}), 130.4 (6-C), 130.7 (2,6-C_{Ar}), 133.6 (1-C_{Ar}), 134.0 (7-C), 134.7 (8a-C), 139.5 (4-C_{Ar}), 150.6 (2-C), 160.6 (4-CO), 166.4 (COO), 191.8 (*C*OAr).

Anal. Calcd for $C_{20}H_{16}ClNO_4S$: C, 59.78; H, 4.01; N, 3.49; Cl, 8.82; S, 7.98. Found: C, 59.84; H, 3.86; N, 3.70; Cl, 8.80; S, 7.76.

{3-[2-(4-Bromophenyl)-2-oxoethyl]-3,4-dihydro-4-oxo-2*H*-1,3-benzothiazin-2-ylidene}acetic Acid Ethyl Ester (5c)

Yield: 1.13 g (51%); mp 183 °C (EtOH).

^1H NMR: δ = 1.12 (t, *J* = 7.0 Hz, 3 H, CH_3), 4.04 (q, *J* = 7.0 Hz, 2 H, OCH_2), 5.49 (s, 1 H, CHCOO), 5.74 (s, 2 H, NCH_2), 7.51 (t, *J* = 7.5 Hz, 1 H, 6-H), 7.58 (d, *J* = 7.5 Hz, 1 H, 8-H), 7.69 (m, 3 H, 7-H, 3,5-H_{Ar}), 8.05 (m, 3 H, 2,6-H_{Ar}, 5-H).

^{13}C NMR: δ = 12.1 (CH_3), 55.5 (NCH_2), 60.6 (OCH_2), 97.8 (*C*HCOO), 122.5 (4a-C), 126.5 (5-C), 127.2 (8-C), 130.2 (4-C_{Ar}), 130.4 (6-C), 130.9 (3,5-C_{Ar}), 132.5 (7-C), 133.5 (2,6-C_{Ar}), 134.4 (1-C_{Ar}), 134.6 (8a-C), 150.3 (2-C), 163.3 (4-CO), 166.3 (COO), 191.5 (*C*OAr).

Anal. Calcd for $C_{20}H_{16}BrNO_4S$: C, 53.82; H, 3.61; N, 3.14; Br, 17.90; S, 7.18. Found: C, 53.66; H, 3.64; N, 3.18; Br, 17.71; S, 7.35.

[3,4-Dihydro-4-oxo-3-(2-oxo-2-phenylethyl)-2*H*-1,3-benzothiazin-2-ylidene]acetonitrile (6a)

Yield: 1.02 g (64%); mp 153 °C (MeCN).

^1H NMR: δ = 5.24 (s, 1 H, *C*HCN), 5.55 (s, 2 H, NCH_2), 7.37 (t, *J* = 7.5 Hz, 1 H, 6-H), 7.57 (d, *J* = 7.5 Hz, 1 H, 8-H), 7.63–7.68 (m, 3 H, 7-H, 3,5-H_{Ar}), 7.71 (t, *J* = 7.0 Hz, 1 H, 4-H_{Ar}), 8.05 (d, *J* = 7.0 Hz, 2 H, 2,6-H_{Ar}), 8.13 (d, *J* = 7.5 Hz, 1 H, 5-H).

^{13}C NMR: δ = 53.9 (NCH_2), 74.7 (*C*HCN), 115.5 (CN), 121.6 (4a-C), 125.2 (5-C), 128.1 (3,5-C_{Ar}), 128.2 (8-C), 131.4 (2,6-C_{Ar}), 132.8 (6-C), 133.5 (7-C), 134.1 (1-C_{Ar}), 134.3 (4-C_{Ar}), 135.4 (8a-C), 153.8 (2-C), 160.5 (4-CO), 193.1 (*C*OAr).

Anal. Calcd for $C_{18}H_{12}N_2O_2S$: C, 67.48; H, 3.78; N, 8.74; S, 10.01. Found: C, 67.47; H, 3.72; N, 8.61; S, 9.97.

{3-[2-(4-Chlorophenyl)-2-oxoethyl]-3,4-dihydro-4-oxo-2*H*-1,3-benzothiazin-2-ylidene}acetonitrile (6b)
Yield: 0.80 g (45%); mp 184 °C (MeCN).

^{1}H NMR: δ = 5.28 (s, 1 H, *C*HCN), 5.55 (s, 2 H, NCH_2), 7.38 (t, *J* = 7.5 Hz, 1 H, 6-H), 7.46 (d, *J* = 7.5 Hz, 1 H, 8-H), 7.53 (d, *J* = 8.5 Hz, 2 H, 3,5-H_{Ar}), 7.61 (t, *J* = 7.5 Hz, 1 H, 7-H), 8.06 (d, *J* = 8.5 Hz, 2 H, 2,6-H_{Ar}), 8.14 (d, *J* = 7.5 Hz, 1 H, 5-H).

^{13}C NMR: δ = 53.5 (NCH_2), 75.8 (*C*HCN), 117.2 (CN), 122.3 (4a-C), 125.7 (5-C), 128.1 (8-C), 129.5 (3,5-C_{Ar}), 130.7 (2,6-C_{Ar}), 131.1 (6-C), 131.2 (7-C), 133.5 (1-C_{Ar}), 135.0 (8a-C), 139.6 (4-C_{Ar}), 152.2 (2-C), 160.2 (4-CO), 191.1 (*C*OAr).

Anal. Calcd for $C_{18}H_{11}ClN_2O_2S$: C, 60.93; H, 3.12; N, 7.90; Cl, 9.99; S, 9.04. Found: C, 60.84; H, 3.20; N, 7.80; Cl, 10.01; S, 8.95.

{3-[2-(4-Bromophenyl)-2-oxoethyl]-3,4-dihydro-4-oxo-2*H*-1,3-benzothiazin-2-ylidene}acetonitrile (6c)
Yield: 0.92 g (46%); mp 185 °C (MeCN).

^{1}H NMR: δ = 5.52 (s, 1 H, CHCN), 5.58 (s, 2 H, NCH_2), 7.47 (t, *J* = 8.0 Hz, 1 H, 6-H), 7.65 (d, *J* = 8.0 Hz, 1 H, 8-H), 7.71 (t, *J* = 8.0 Hz, 1 H, 7-H), 7.82 (d, *J* = 7.0 Hz, 2 H, 3,5-H_{Ar}), 8.00 (d, *J* = 7.0 Hz, 2 H, 2,6-H_{Ar}), 8.09 (d, *J* = 8.0 Hz, 1 H, 5-H).

^{13}C NMR: δ = 53.4 (NCH_2), 75.8 (*C*HCN), 117.2 (CN), 122.3 (4a-C), 125.7 (5-C), 128.1 (8-C), 128.8 (4-C_{Ar}), 130.8 (3,5-C_{Ar}), 131.1 (6-C), 131.2 (7-C), 132.4 (2,6-C_{Ar}), 133.8 (1-C_{Ar}), 135.0 (8a-C), 152.2 (2-C), 160.2 (4-CO), 191.4 (*C*OAr).

Anal. Calcd for $C_{18}H_{11}BrN_2O_2S$: C, 54.15; H, 2.78; N, 7.02; Br, 20.01; S, 8.03. Found: C, 53.93; H, 2.74; N, 7.17; Br, 19.98; S, 7.87.

Pyrrolo[2,1-*b*][1,3]benzothiazines 7a–c and 8a–c; General Procedure
The appropriate compound **5a–c**, **6a–c** (3.0 mmol) was added to a cold solution of $POCl_3$ (1.15 g, 7.5 mmol) in DMF (10 mL) and the mixture was gently warmed to dissolve the starting material and then heated at 60–70 °C for 1–1.5 h. After cooling, the mixture was diluted with H_2O (20 mL) and the precipitate formed was filtered and recrystallized from aq DMF yielding derivatives **7a–c** and **8a–c**.

1-Benzoyl-9-oxo-9*H*-pyrrolo[2,1-*b*][1,3]benzothiazine-3-carboxylic Acid Ethyl Ester (7a)
Yield: 0.88 g (78%); mp 153 °C (DMF–H_2O).

^{1}H NMR: δ = 1.32 (t, *J* = 7.0 Hz, 3 H, CH_3), 4.31 (q, *J* = 7.0 Hz, 2 H, OCH_2), 7.23 (s, 1 H, 2-H), 7.50 (t, *J* = 7.5 Hz, 2 H, 3,5-H_{Ar}), 7.55 (t, *J* = 8.0 Hz, 1 H, 7-H), 7.63 (t, *J* = 7.5 Hz, 1 H, 4-H_{Ar}), 7.81 (m, 3 H, 6-H, 2,6-H_{Ar}), 7.91 (d, *J* = 8.0 Hz, 1 H, 5-H), 8.22 (d, *J* = 8.0 Hz, 1 H, 8-H).

^{13}C NMR: δ = 14.8 (CH_3), 61.1 (OCH_2), 112.8 (3-C), 118.7 (2-C), 121.9 (8a-C), 126.9 (8-C), 128.0 (5-C), 129.2 (3,5-C_{Ar}), 129.5 (2,6-C_{Ar}), 130.8 (7-C), 132.3 (6-C), 133.7 (4a-C), 133.8 (4-C_{Ar}), 134.8 (1-C_{Ar}), 134.9 (1-C), 137.7 (3a-C), 157.8 (9-CO), 162.9 (COO), 186.0 (*C*OAr).

Anal. Calcd for $C_{21}H_{15}NO_4S$: C, 66.83; H, 4.01; N, 3.71; S, 8.50. Found: C, 66.91; H, 4.10; N, 3.72; S, 8.28.

1-(4-Chlorobenzoyl)-9-oxo-9*H*-pyrrolo[2,1-*b*][1,3]benzothiazine-3-carboxylic Acid Ethyl Ester (7b)
Yield: 0.76 g (62%); mp 196 °C (DMF–H_2O).

^{1}H NMR: δ = 1.32 (t, *J* = 7.5 Hz, 3 H, CH_3), 4.32 (q, *J* = 7.5 Hz, 2 H, OCH_2), 7.28 (s, 1 H, 2-H), 7.56 (m, 3 H, 7-H, 3,5-H_{Ar}), 7.82 (m, 3 H, 6-H, 2,6-H_{Ar}), 7.92 (d, *J* = 7.5 Hz, 1 H, 5-H), 8.23 (d, *J* = 7.5 Hz, 1 H, 8-H).

^{13}C NMR: δ = 14.7 (CH_3), 61.1 (OCH_2), 113.0 (3-C), 118.9 (2-C), 121.9 (8a-C), 126.9 (8-C), 128.0 (5-C), 129.3 (3,5-C_{Ar}), 130.8 (7-C), 131.2 (2,6-C_{Ar}), 131.8 (6-C), 133.9 (4a-C), 134.8 (1-C_{Ar}), 134.9 (1-C), 136.7 (3a-C), 138.6 (4-C_{Ar}), 157.9 (9-CO), 162.9 (COO), 184.9 (*C*OAr).

Anal. Calcd for $C_{21}H_{14}ClNO_4S$: C, 61.24; H, 3.43; N, 3.40; Cl, 8.61; S, 7.79. Found: C, 61.30; H, 3.21; N, 3.30; Cl, 8.60; S, 7.64.

1-(4-Bromobenzoyl)-9-oxo-9*H*-pyrrolo[2,1-*b*][1,3]benzothiazine-3-carboxylic Acid Ethyl Ester (7c)
Yield: 0.85 g (62%); mp 190–191 °C (DMF–H_2O).

^{1}H NMR: δ = 1.32 (t, *J* = 7.0 Hz, 3 H, CH_3), 4.32 (q, *J* = 7.0 Hz, 2 H, OCH_2), 7.29 (s, 1 H, 2-H), 7.57 (t, *J* = 7.5 Hz, 1 H, 7-H), 7.71 (m, 4 H_{Ar}), 7.83 (t, *J* = 7.5 Hz, 1 H, 6-H), 7.94 (d, *J* = 7.5 Hz, 1 H, 5-H), 8.24 (d, *J* = 7.5 Hz, 1 H, 8-H).

^{13}C NMR: δ = 14.7 (CH_3), 61.1 (OCH_2), 112.9 (3-C), 119.0 (2-C), 121.8 (8a-C), 126.9 (8-C), 127.8 (4-C_{Ar}), 128.0 (5-C), 130.8 (7-C), 131.3 (2,6-C_{Ar}), 131.8 (6-C), 132.3 (3,5-C_{Ar}), 133.9 (4a-C), 134.7 (1-C_{Ar}), 134.8 (1-C), 136.9 (3a-C), 157.9 (9-CO), 162.9 (COO), 185.1 (*C*OAr).

Anal. Calcd for $C_{21}H_{14}BrNO_4S$: C, 55.28; H, 3.09; N, 3.07; Br, 17.51; S, 7.03. Found: C, 55.30; H, 3.16; N, 3.10; Br, 17.50; S, 7.13.

1-Benzoyl-9-oxo-9*H*-pyrrolo[2,1-*b*][1,3]benzothiazine-3-carbonitrile (8a)
Yield: 0.66 g (67%); mp 208–209 °C (DMF–H_2O).

^{1}H NMR: δ = 7.50 (m, 3 H, 2-H, 3,5-H_{Ar}), 7.59 (t, *J* = 8.0 Hz, 1 H, 7-H), 7.65 (t, *J* = 7.0 Hz, 1 H, 4-H_{Ar}), 7.81–7.88 (m, 3 H, 6-H, 2,6-H_{Ar}), 7.96 (d, *J* = 8.0 Hz, 1 H, 5-H), 8.25 (d, *J* = 8.0 Hz, 1 H, 8-H).

^{13}C NMR: δ = 91.4 (3-C), 113.9 (CN), 119.6 (2-C), 121.8 (8a-C), 126.9 (8-C), 128.3 (5-C), 129.2 (3,5-C_{Ar}), 129.7 (2,6-C_{Ar}), 131.3 (7-C), 132.0 (4-C_{Ar}), 132.5 (6-C), 134.1 (1-C_{Ar}), 135.1 (1-C), 135.6 (4a-C), 137.4 (3a-C), 157.4 (9-CO), 185.8 (*C*OAr).

Anal. Calcd for $C_{19}H_{10}N_2O_2S$: C, 69.08; H, 3.05; N, 8.48; S, 9.71. Found: C, 69.15; H, 3.16; N, 8.62; S, 9.89.

1-(4-Chlorobenzoyl)-9-oxo-9*H*-pyrrolo[2,1-*b*][1,3]benzothiazine-3-carbonitrile (8b)
Yield: 0.68 g (62%); mp 184 °C (DMF–H_2O).

^{1}H NMR: δ = 7.53 (s, 1 H, 2-H), 7.55 (d, *J* = 8.5 Hz, 2 H, 3,5-H_{Ar}), 7.60 (t, *J* = 8.0 Hz, 1 H, 7-H), 7.83 (d, *J* = 8.5 Hz, 2 H, 2,6-H_{Ar}), 7.86 (t, *J* = 8.0 Hz, 1 H, 6-H), 7.96 (d, *J* = 8.0 Hz, 1 H, 5-H), 8.26 (d, *J* = 8.0 Hz, 1 H, 8-H).

^{13}C NMR: δ = 91.5 (3-C), 113.8 (CN), 119.9 (2-C), 121.8 (8a-C), 126.9 (8-C), 128.4 (5-C), 129.4 (3,5-C_{Ar}), 131.3 (7-C), 131.4 (2,6-C_{Ar}), 131.6 (1-C_{Ar}), 132.5 (6-C), 135.1 (1-C), 135.9 (4a-C), 136.3 (3a-C), 138.9 (4-C_{Ar}), 157.5 (9-CO), 184.7 (*C*OAr).

Anal. Calcd for $C_{19}H_9ClN_2O_2S$: C, 62.56; H, 2.49; N, 7.68; Cl, 9.72; S, 8.79. Found: C, 62.77; H, 2.68; N, 7.60; Cl, 9.70; S, 8.70.

1-(4-Bromobenzoyl)-9-oxo-9*H*-pyrrolo[2,1-*b*][1,3]benzothiazine-3-carbonitrile (8c)
Yield: 0.92 g (75%); mp 189–190 °C (DMF–H_2O).

^{1}H NMR: δ = 7.52 (s, 1 H, 2-H), 7.59 (t, *J* = 7.5 Hz, 1 H, 7-H), 7.69 (d, *J* = 8.5 Hz, 2 H, 3,5-H_{Ar}), 7.74 (d, *J* = 8.5 Hz, 2 H, 2,6-H_{Ar}), 7.86

(t, *J* = 7.5 Hz, 1 H, 6-H), 7.95 (d, *J* = 7.5 Hz, 1 H, 5-H), 8.25 (d, *J* = 7.5 Hz, 1 H, 8-H).

^{13}C NMR: δ = 91.5 (3-C), 113.8 (CN), 119.9 (2-C), 121.8 (8a-C), 126.9 (8-C), 128.2 (4-C_{Ar}), 128.4 (5-C), 131.3 (7-C), 131.4 (3,5-C_{Ar}), 131.5 (1-C_{Ar}), 132.3 (2,6-C_{Ar}), 132.6 (6-C), 135.1 (1-C), 135.9 (4a-C), 136.6 (3a-C), 157.5 (9-CO), 185.0 (*C*OAr).

Anal. Calcd for $C_{19}H_9BrN_2O_2S$: C, 55.76; H, 2.22; N, 6.84; Br, 19.52; S, 7.83. Found: C, 55.70; H, 2.30; N, 6.80; Br, 19.52; S, 7.75.

2-(2-Pyrrolylthio)benzamides 9a–g; General Procedure

An appropriate amine (1.8 mmol) was added to a solution of compound **7a**,**c**, **8c** (1.5 mmol) in DMF (5 mL) and the mixture was refluxed for 2 h. Upon cooling, the mixture was poured into H_2O (15 mL) to give an oily precipitate, which slowly solidified overnight. The solid was filtered and recrystallized from an appropriate solvent affording derivatives **9a**–**g** (Table 1).

5-Benzoyl-2-({2-[(benzylamino)carbonyl]phenyl}thio)-1*H*-pyrrole-3-carboxylic Acid Ethyl Ester (9a)

Mp 119 °C (*i*-PrOH–H_2O).

^{1}H NMR: δ = 1.20 (t, *J* = 7.0 Hz, 3 H, CH_3), 4.13 (q, *J* = 7.0 Hz, 2 H, OCH_2), 4.53 (d, *J* = 5.0 Hz, 2 H, NCH_2), 6.99 (d, *J* = 7.0 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.12 (s, 1 H, 4-H), 7.22–7.30 (m, 5 H, 3 H_R, 2 $H_{o\text{-phenylene}}$), 2.47 (d, *J* = 6.5 Hz, 2 H, 2 H_R), 7.52 (t, *J* = 7.0 Hz, 2 H, 3,5-H_{Ar}), 7.59 (m, 2 H, 4-H_{Ar}, $H_{o\text{-phenylene}}$), 7.82 (d, *J* = 7.0 Hz, 2 H, 2,6-H_{Ar}), 8.92 (t, *J* = 5.0 Hz, 1 H, CONH), 12.73 (br s, 1 H, NH).

^{13}C NMR: δ = 14.6 (CH_3), 43.1 (NCH_2), 60.2 (OCH_2), 120.1 (4-C_{Py}), 121.4 (3-C_{Py}), 126.2 (4-$C_{o\text{-phenylene}}$), 127.3 (4-C_R), 127.7 (2,6-C_R), 128.4 (6-$C_{o\text{-phenylene}}$), 128.8 (3,5-C_R), 128.9 (5-$C_{o\text{-phenylene}}$), 129.1 (3,5-C_{Ar}), 129.2 (2,6-C_{Ar}), 131.3 (3-$C_{o\text{-phenylene}}$), 132.6 (1-$C_{o\text{-phenylene}}$), 132.7 (1-C_R), 132.8 (4-C_{Ar}), 134.7 (2-$C_{o\text{-phenylene}}$), 137.1 (1-C_{Ar}), 137.9 (5-C_{Py}), 139.8 (2-C_{Py}), 162.8 (COO), 167.8 (CONH), 184.2 (*C*OAr).

Anal. Calcd for $C_{28}H_{24}N_2O_4S$: C, 69.40; H, 4.99; N, 5.78; S, 6.62. Found: C, 69.29; H, 4.86; N, 5.75; S, 6.77.

5-Benzoyl-2-[(2-{[(2-furanylmethyl)amino]carbonyl}phenyl)thio]-1*H*-pyrrole-3-carboxylic Acid Ethyl Ester (9b)

Mp 134 °C (*i*-PrOH–H_2O).

^{1}H NMR: δ = 1.21 (t, *J* = 4.5 Hz, 3 H, CH_3), 4.13 (q, *J* = 4.5 Hz, 2 H, OCH_2), 4.51 (d, *J* = 3.0 Hz, 2 H, NCH_2), 6.33 (m, 2 H, H_R), 6.97 (d, *J* = 7.0 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.13 (s, 1 H, 4-H), 7.27 (m, 2 H, 2 $H_{o\text{-phenylene}}$), 7.45 (d, *J* = 0.5 Hz, 1 H, H_R), 7.52–7.61 (m, 4 H, 3,4,5-H_{Ar}, $H_{o\text{-phenylene}}$), 7.83 (d, *J* = 6.5 Hz, 2,6-H_{Ar}), 8.87 (t, *J* = 3.0 Hz, 1 H, CONH), 12.75 (s, 1 H, NH).

^{13}C NMR: δ = 14.5 (CH_3), 36.7 (NCH_2), 60.2 (OCH_2), 107.4 (3-C_R), 111.0 (4-C_R), 120.2 (4-C_{Py}), 121.4 (3-C_{Py}), 126.1 (4-$C_{o\text{-phenylene}}$), 128.5 (6-$C_{o\text{-phenylene}}$), 128.7 (5-$C_{o\text{-phenylene}}$), 129.1 (3,5-C_{Ar}), 129.2 (2,6-C_{Ar}), 131.4 (3-$C_{o\text{-phenylene}}$), 132.5 (1-$C_{o\text{-phenylene}}$), 132.6 (5-C_R), 132.8 (4-C_{Ar}), 134.3 (2-$C_{o\text{-Phenylene}}$), 137.2 (1-C_{Ar}), 137.9 (5-C_{Py}), 142.6 (2-C_{Py}), 152.6 (2-C_R), 162.8 (COO), 167.6 (CONH), 184.2 (*C*OAr).

Anal. Calcd for $C_{26}H_{22}N_2O_5S$: C, 65.81; H, 4.67; N, 5.90; S, 6.76. Found: C, 65.80; H, 4.58; N, 6.08; S, 6.59.

5-(4-Bromobenzoyl)-2-({2-[(benzylamino)carbonyl]phenyl}thio)-1*H*-pyrrole-3-carboxylic Acid Ethyl Ester (9c)

Mp 186–187 °C (*i*-PrOH).

^{1}H NMR: δ = 1.07 (t, *J* = 7.0 Hz, 3 H, CH_3), 4.07 (q, *J* = 7.0 Hz, 2 H, OCH_2), 4.50 (d, *J* = 5.5 Hz, 2 H, NCH_2), 6.84 (d, *J* = 8.0 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.16 (s, 1 H, 4-H), 7.25 (m, 2 H, $H_{o\text{-phenylene}}$), 7.33 (m, 3 H, 3,4,5-H_R), 7.37 (d, *J* = 7.0 Hz, 2 H, 2,6-H_R), 7.66 (d, *J* = 7.5 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.78 (m, 4 H, H_{Ar}), 9.10 (t, *J* = 5.5 Hz, 1 H, CONH), 12.89 (br s, 1 H, NH).

^{13}C NMR: δ = 14.6 (CH_3), 43.1 (NCH_2), 60.2 (OCH_2), 120.2 (4-C_{Py}), 121.5 (3-C_{Py}), 126.2 (4-$C_{o\text{-phenylene}}$), 126.8 (4-C_{Ar}), 127.3 (4-C_R), 127.7 (2,6-C_R), 128.4 (6-$C_{o\text{-phenylene}}$), 128.7 (3,5-C_R), 128.8 (5-$C_{o\text{-phenylene}}$), 131.2 (3,5-C_{Ar}), 131.3 (3-$C_{o\text{-phenylene}}$), 132.2 (2,6-C_{Ar}), 132.3 (1-$C_{o\text{-phenylene}}$), 133.1 (1-C_R), 134.6 (2-$C_{o\text{-phenylene}}$), 136.9 (1-C_{Ar}), 137.1 (5-C_{Py}), 139.8 (2-C_{Py}), 162.7 (COO), 167.7 (CONH), 183.1 (*C*OAr).

Anal. Calcd for $C_{28}H_{23}BrN_2O_4S$: C, 59.69; H, 4.11; N, 4.97; Br, 14.18; S, 5.69. Found: C, 59.52; H, 4.11; N, 5.09; Br, 14.15; S, 5.53.

5-(4-Bromobenzoyl)-2-[(2-{[(2-furanylmethyl)amino]carbonyl}phenyl)thio]-1*H*-pyrrole-3-carboxylic Acid Ethyl Ester (9d)

Mp 172 °C (*i*-PrOH).

^{1}H NMR: δ = 1.07 (t, *J* = 7.5 Hz, 3 H, CH_3), 4.07 (q, *J* = 7.5 Hz, 2 H, OCH_2), 4.48 (d, *J* = 5.5 Hz, 2 H, NCH_2), 6.33 (dd, *J* = 2.5, 1.5 Hz, 1 H, 4-H_R), 6.40 (d, *J* = 1.5 Hz, 1 H, 3-H_R), 6.82 (d, *J* = 8.0 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.16 (s, 1 H, 4-H), 7.25 (t, *J* = 8.0 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.32 (t, *J* = 8.0 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.58 (d, *J* = 2.5 Hz, 1 H, 5-H_R), 7.62 (d, *J* = 8.0 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.78, (m, 4 H, H_{Ar}), 9.03 (t, *J* = 5.5 Hz, 1 H, CONH), 13.01 (br s, 1 H, NH).

^{13}C NMR: δ = 14.5 (CH_3), 36.7 (NCH_2), 60.2 (OCH_2), 107.4 (3-C_R), 111.0 (4-C_R), 120.3 (4-C_{Py}), 121.5 (3-C_{Py}), 126.1 (4-$C_{o\text{-phenylene}}$), 126.7 (4-C_{Ar}), 128.5 (6-$C_{o\text{-phenylene}}$), 128.7 (5-$C_{o\text{-phenylene}}$), 131.2 (3,5-C_{Ar}), 131.4 (3-$C_{o\text{-phenylene}}$), 132.2 (2,6-C_{Ar}), 132.3 (1-$C_{o\text{-phenylene}}$), 133.0 (5-C_R), 134.2 (2-$C_{o\text{-phenylene}}$), 136.9 (1-C_{Ar}), 137.2 (5-C_{Py}), 142.6 (2-C_{Py}), 152.6 (1-C_R), 162.7 (COO), 167.7 (CONH), 183.1 (*C*OAr).

Anal. Calcd for $C_{26}H_{21}BrN_2O_5S$: C, 56.43; H, 3.82; N, 5.06; Br, 14.44; S, 5.79. Found: C, 56.59; H, 3.65; N, 4.96; Br, 14.60; S, 5.70.

2-{[5-(4-Bromobenzoyl)-3-cyano-1*H*-pyrrol-2-yl]thio}-*N*-benzylbenzamide (9e)

Mp 115–116 °C (*i*-PrOH).

^{1}H NMR: δ = 4.54 (d, *J* = 5.0 Hz, 2 H, NCH_2), 6.91 (d, *J* = 7.5 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.19 (s, 1 H, H_{Py}), 7.22 (t, *J* = 7.5 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.27–7.32 (m, 4 H, 3,4,5-H_R, $H_{o\text{-phenylene}}$), 7.39 (d, *J* = 6.5 Hz, 2,6-H_R), 7.67 (m, 3 H, 3,5-H_{Ar}, $H_{o\text{-phenylene}}$), 7.79 (d, *J* = 7.5 Hz, 2 H, 2,6-H_{Ar}), 9.02 (t, *J* = 5.0 Hz, 1 H, CONH), 13.48 (br s, 1 H, NH).

^{13}C NMR: δ = 43.2 (NCH_2), 102.1 (3-C_{Py}), 115.2 (CN), 122.9 (4-C_{Py}), 126.4 (5-C), 127.2 (4-C_{Ar}), 127.3 (4-C_R), 127.7 (2,6-C_R), 127.8 (1-C_R), 127.9 (3-C), 128.7 (4-C), 128.8 (3,5-C_R), 131.5 (3,5-C_{Ar}), 131.8 (6-C), 132.2 (2,6-C_{Ar}), 133.5 (2-C), 134.8 (1-C), 136.4 (1-C_{Ar}), 136.9 (5-C_{Py}), 139.7 (2-C_{Py}), 167.4 (CONH), 182.9 (*C*OAr).

Anal. Calcd for $C_{26}H_{18}BrN_3O_2S$: C, 60.47; H, 3.51; N, 8.14; Br, 15.47; S, 6.21. Found: C, 60.52; H, 3.37; N, 8.20; Br, 15.68; S, 6.24.

2-{[5-(4-Bromobenzoyl)-3-cyano-1*H*-pyrrol-2-yl]thio}-*N*-(2-furanylmethyl)benzamide (9f)

Mp 85 °C (*i*-PrOH).

^{1}H NMR: δ = 4.51 (d, *J* = 5.5 Hz, 2 H, NCH_2), 6.32 (m, 2 H, 3,4-H_R), 6.87 (d, *J* = 8.0 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.19 (s, 1 H, H_{Py}), 7.26 (t, *J* = 8.0 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.32 (t, *J* = 8.0 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.43 (d, *J* = 1.0 Hz, 1 H, 5-H_R), 7.62 (d, *J* = 8.0 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.67 (d, *J* = 8.5 Hz, 2 H, 3,5-H_{Ar}), 7.79 (d, *J* = 8.5 Hz, 2 H, 2,6-H_{Ar}), 8.96 (t, *J* = 5.5 Hz, 1 H, CONH), 13.48 (s, 1 H, NH).

^{13}C NMR: δ = 45.3 (NCH_2), 102.8 (3-C_{Py}), 105.1 (3-C_R), 111.6 (4-C_R), 115.9 (CN), 121.4 (4-C_{Py}), 126.4 (5-C), 127.7 (3-C), 128.4 (4-C_{Ar}), 128.7 (4-C), 130.5 (3,5-C_{Ar}), 130.6 (2,6-C_{Ar}), 131.8 (5-C_R),

132.5 (6-C), 134.9 (2-C), 135.7 (1-C), 137.1 (5-C_{Py}), 137.2 (1-C_{Ar}), 139.3 (2-C_{Py}), 151.9 (1-C_R), 167.8 (CONH), 182.6 (*C*OAr).

Anal. Calcd for $C_{24}H_{16}BrN_3O_3S$: C, 56.93; H, 3.18; N, 8.30; Br, 15.78; S, 6.33. Found: C, 57.04; H, 3.04; N, 8.39; Br, 15.72; S, 6.48.

5-(4-Bromobenzoyl)-2-[(2-{[(2-phenylethyl)amino]carbonyl}phenyl)thio]-1*H*-pyrrole-3-carboxylic Acid Ethyl Ester (9g)
Mp 133 °C (*i*-PrOH–H_2O).

^{1}H NMR: δ = 1.08 (t, *J* = 6.5 Hz, 3 H, CH_3), 2.87 (t, *J* = 6.5 Hz, 2 H, CH_2), 3.50 (m, 2 H, NCH_2), 4.07 (q, *J* = 6.5 Hz, 2 H, OCH_2), 6.85 (d, *J* = 7.5 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.16 (s, 1 H, 4-H), 7.19 (t, *J* = 7.5 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.27 (m, 6 H, 5 H_R, $H_{o\text{-phenylene}}$), 7.52 (d, *J* = 7.5 Hz, 1 H, $H_{o\text{-phenylene}}$), 7.78 (m, 4 H, H_{Ar}), 8.63 (t, *J* = 5.5 Hz, 1 H, CONH), 12.99 (s, 1 H, NH).

^{13}C NMR: δ = 14.6 (CH_3), 35.5 (CH_2), 41.3 (NCH_2), 60.2 (OCH_2), 120.1 (4-C_{Py}), 121.5 (3-C_{Py}), 126.3 (4-$C_{o\text{-phenylene}}$), 126.6 (4-C_R), 126.7 (4-C_{Ar}), 128.3 (6-$C_{o\text{-phenylene}}$), 128.8 (2,6-C_R), 129.0 (5-$C_{o\text{-phenylene}}$), 129.2 (3,5-C_R), 131.1 (3-$C_{o\text{-phenylene}}$), 131.2 (3,5-C_{Ar}), 132.2 (2,6-C_{Ar}), 132.3 (1-$C_{o\text{-phenylene}}$), 133.3 (1-C_R), 135.1 (2-$C_{o\text{-phenylene}}$), 136.7 (1-C_{Ar}), 136.9 (5-C_{Py}), 139.9 (2-C_{Py}), 162.7 (COO), 167.7 (CONH), 183.0 (*C*OAr).

Anal. Calcd for $C_{29}H_{25}BrN_2O_4S$: C, 60.32; H, 4.36; N, 4.85; Br, 13.84; S, 5.55. Found: C, 60.30; H, 4.46; N, 4.71; Br, 13.64; S, 5.51.

X-ray Crystal Structure Determination of Compound 7a
Colorless single crystals of **7a** were obtained from DMF. Intensities of 18956 reflections (6131 independent, R_{int} = 0.044) were measured with 'Xcalibur-3' diffractometer operating in the ω-2θ scan mode, $2\theta_{max}$ = 50°, and using graphite monochromated MoKα radiation (λ = 0.71073 Å). Crystal data: $C_{21}H_{15}O_4NS$, M_r = 377.40, monoclinic, *a* = 21.977(1), *b* = 10.833(1), *c* = 15.888(1) Å, β = 110.08(1)°, V = 3552.8(3) Å^3, T = 293 K, space group $P2_1/c$, *Z* = 8, μ(MoKα) = 0.210 mm^{-1}. The structure was solved by direct method with the SHELXTL program package.[12,13] Hydrogen atoms were placed geometrically and refined by riding model with $U_{iso} = nU_{eq}$ of nonhydrogen atom bonded with the hydrogen atom given (n = 1.5 for methyl group and n = 1.2 for the rest of hydrogens). During the refinement the following restraints were placed on the bonds length of the disordered fragments: C=O 1.21 Å, Csp^2–O 1.32 Å, Csp^3–O 1.43 Å, Csp^3–Csp^3 1.53 Å. Full-matrix least-squares refinement against F^2 in anisotropic approximation using 5902 reflections was converged to *wR*2 = 0.112, *R*1 = 0.079 [for 4078 reflections with F>4σ(F)], S = 1.041.

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(13) Full crystallographic parameters have been deposited at Cambridge Crystallographic Data Center under reference number CCDC 681250. Copies of the data may be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44 1223 33603 or e-mail: deposit@ccdc.cam.ac.uk).