Solvent-free Synthesis of Unsymmetrical Benzoyldisulfides and Related Novel Biscarbonyldisulfides

Kiyoko Fujiki,* Shizuka Akieda, Hironobu Yasuda, Yohei Sasaki

Department of Agricultural Chemistry, Meiji University, Kawasaki 214–8571, Japan
Fax +81(44)9347831; E-mail: fujiki@isc.meiji.ac.jp

Received 7 December 2000; revised 12 March 2001

Abstract: Under solvent-free conditions, various unsymmetrical benzoyldisulfides and symmetrical novel biscarbonyldisulfides were easily prepared in good yields at room temperature by the mixing of thiosulfonates with thiocarboxylic *S*-acids in the absence or presence of an amine.

Key words: benzoyldisulfides, thiocarboxylic *S*-acid, carbonyldisulfides, thiosulfonates, sulfenylation

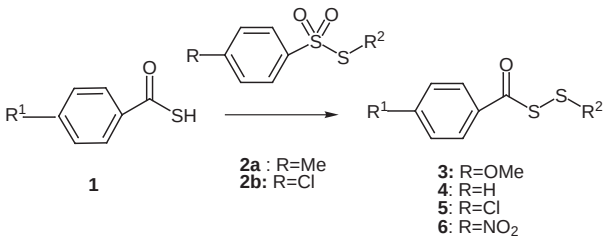
Acyldisulfides are of pharmaceutical or physiological interest because of their biological activities. Some of these disulfides proved to have significant activities in controlling the growth of bacteria or fungi.[1] Recently, monoacyl disulfides have come into use as a mediator of the peptide bond formation between the unprotected peptide segments.[2] However, only a few reports on the monoacyl disulfides are known compared with those of the symmetric diacyl disulfides.[3] These reports include the reaction of acetyl sulfenyl chloride with thiols[4a,b] or with activated aromatic compounds[4c] to give monoacetyl disulfides, and the reaction of thiocarboxylic *S*-acids with sulfenyl chlorides,[5,1b] thiosulfonates[6,1b] or alkyl thiosulfates.[7] Recently, it was shown that sulfines from aliphatic dithioesters undergo rearrangement to monoacyl disulfides.[8] Among these reagents, thiosulfonates are the most stable and powerful sulfenylating agent unlike the sulfenyl halides or acylsulfenyl halides. However, the synthetic examples of monoacyl disulfides by use of the thiosulfonates as a sulfenylating agent are few in the usual solution state, especially only two benzoyl disulfides have been reported,[6] and it was noted that the purification of some unsymmetrical carbonyldisulfides was difficult.[1b]

Previously, we succeeded in developing the new preparation of aryl thiocyanates[9] and unsymmetrical aryldisulfides[10], the latter have a tendency to disproportionate in solvent, by the reaction of thiosulfonates with nucleophiles under solvent-free conditions, with recognition that in some cases, the reaction may proceed more efficiently and even more selectively in the solvent-free or solid state.[11] Now we report the solvent-free synthesis of unsymmetrical benzoyldisulfides and related novel biscarbonyldisulfides at room temperature.

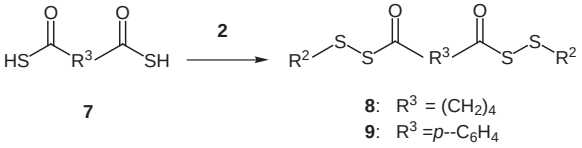
Synthesis 2001, No. 7, 01 06 2001. Article Identifier:
1437-210X,E;2001,0,07,1035,1042,ftx,enF06800SS.pdf.

ISSN 0039-7881

Scheme 1 shows the general reaction for the preparation of monobenzoyl disulfides **3**–**6** by the sulfenylation of thiobenzoic *S*-acids **1** with thiosulfonates **2** in the absence or presence of an amine as an activator. Novel biscarbonyldisulfides **8** and **9** were also prepared from thiocarboxylic acids having two SH groups such as adipoyl dithiol **7a** and terephthaloyl dithiol **7b** in the solid state (Scheme 2).



Scheme 1



Scheme 2

When **1** and **2** were mixed in the molar ratio of 1:1.2, the reaction proceeded and the spot on the TLC plate corresponding to **1**, and its odor disappeared (= reaction time). Nucleophilic S-S bond scission of the *p*-toluenethiosulfonate **2a** with thiobenzoic *S*-acids **1** bearing an electron-donating group such as a methoxy group at their *p*-position (R^1), rapidly occurred (**3a**–**3f**, Table 1). In contrast, the *p*-nitro and *p*-chlorothiobenzoic *S*-acids needed a long reaction time (over 1.5 h) even in the presence of an amine, as an activator of the thiol and as a trapping agent of the liberated sulfinic acid. Thiobenzoic *S*-acid itself also needed the aid of the amine to complete the reaction within a few minutes (**4a**–**4i**, Table 1). The amine, *p*-aminoacetanilide, was much preferred, over other stronger basic amines such as *p*-toluidine and *p*-chloroaniline, for prevention of the formation of amides[1,12] with the thiocarboxylic *S*-acid. The reactivity depended not only on the electronegativity of R^1 in **1** but also on the *p*-substituted group R at the sulfonyl phenyl in the thiosulfonates **2**. The electron-donating groups R such as a Me group increased the reaction time, whereas the electron-withdrawing

Table 1 Benzoyl Disulfides **3** and **4** from Thiobenzoic *S*-Acid and *p*–Toluenethiosulfonate Prepared[a]

Compd	R^1	R^2	Yield (%)[b]
3a	OMe[c]	Me	70
3b	OMe[c]	Bn	68
3c	OMe[c]	Cy	71
3d	OMe[c]	Ph	73
3e	OMe[c]	*p*-Tolyl	70
3f	OMe[c]	*p*-FluoroPh	81
4a	H[d]	Me	67
4b	H[d]	*i*-Pr	77
4c	H[d]	Bn	76
4d	H[d]	Cy	71
4e	H[d]	Ph	72
4f	H[d]	*p*-Tolyl	71
4g	H[d]	*p*-FluoroPh	74
4h	H[d]	*p*-BromoPh	69
4i	H[d]	2-Naphthyl	75

[a] Reaction time: 1 min at r.t.
[b] Isolated yield is based on the amount of thiobenzoic *S*-acid **1** used.
[c] Reaction conditions: The molar ratio of **1** to *p*-toluenethiosulfonate **2a** = 0.3:0.36 mmol.
[d] Reaction conditions: **1**:**2a**:amine (*p*-aminoacetanilide) = 0.3:0.36:0.9 mmol.

Table 2 Benzoyl Disulfides **5** and **6** from Thiobenzoic *S*-Acid and *p*-Chlorobenzenethiosulfonate Prepared[a]

Compd	R^1	R^2	Reaction time (h)	Yield[b] (%)
5a	Cl	Me	1	65
5b	Cl	Bn	1	63
5c	Cl	Cy	2	99
5d	Cl	Ph	4	68
5e	Cl	*p*-Tolyl	1	59
5f	Cl	*p*-FluoroPh	1.5	88
6a[c]	NO_2	Me	1[c]	45
6a'	NO_2	Me	5	46
6b	NO_2	Bn	2	73
6c[c]	NO_2	Cy	2[c]	66
6c'	NO_2	Cy	4	50
6d[c]	NO_2	Ph	3[c]	63
6e[c]	NO_2	*p*-Tolyl	2[c]	60
6e'	NO_2	*p*-Tolyl	8	29
6f[c]	NO_2	*p*-FluoroPh	5[c]	62
6f'	NO_2	*p*-FluoroPh	6	41

[a] Reaction conditions: The molar ratio of thiobenzoic *S*-acid **1** to *p*-chlorobenzenethiosulfonate **2b** = 0.3:0.36 mmol.
[b] Isolated yield is based on the amount of **1** used.
[c] Further 0.9 mmol of *p*-aminoacetanilide was added.

groups decreased it. When *p*-chlorobenzenethiosulfonate **2b** was used instead of *p*-toluenethiosulfonate **2a**, the reaction time dramatically decreased (several hours to 1–2 h) even in the absence of the amine (*p*-chlorothiobenzoic *S*-acid series **5a**–**5f**, Table 2). Furthermore, **2b** was very effective in decreasing the reaction time even for the *p*-nitrothiobenzoic *S*-acid series (1 day to several hours), where the presence of the amine somewhat enhanced the reaction (**6a**–**6f'**, Table 2).

For terephthaloyl dithiol **7b**, only reactive **2b** was effective to form dithioperoxyterephthalate **9** within a few minutes, although adipoyl dithiol **7a** rapidly reacted with **2a** to give dithioperoxyadipate **8** (Scheme 2, Table 3).

The benzoyl disulfides shown in Tables 1 and 2 demonstrate the scope of the sulfenylation, namely each of the thiobenzoic *S*-acids bearing an electron-donating or withdrawing groups can react with various types of thiosulfonates in good yields at room temperature.

The similar sulfenylation with thiosulfonates was examined in the solvent system. The results are of interest. The thiobenzoic *S*-acids having an electron-attracting group at their *p*-position rapidly reacted with **2a**, but in contrast, for those having an electron-donating group, disproportionation competed with desired sulfenylation. The yields for the corresponding disulfides were low and the purification was difficult. That is, under the solvent or solvent-free system, the reactivity complemented each other.

The reaction of thioacetic *S*-acid with thiosulfonates in a similar way reached no end-point along with the formation of diacetyl disulfide in both the presence and absence of solvent.

In conclusion, the stable unsymmetrical benzoyldisulfides and novel biscarbonyldisulfides were successfully prepared under solvent-free conditions using thiosulfonates, especially *p*-chlorobenzene thiosulfonate, as the strong sulfenylating agent toward a (C=O)SH group. The present method has some advantages, such as avoiding the use of the unstable and unavailable reagents, facile procedure without the byproducts and good yields.

Mps (uncorrected) were determined using a Yanagimoto micro melting point apparatus Mp-S3. ^{1}H and ^{13}C NMR spectra: JNM-AL 30 (JOEL), chemical shift (δ) are relative to TMS. IR spectra: Hitachi-Nicolet FT-IR 5020. Mass spectra: JMS SX-102(JOEL). Elemental analyses were performed at the Elemental Analysis Center, University of Tsukuba. Chromatography: SEP-PAK cartridge SILICA PLUS (Waters). The starting materials **1**, **7** and **2** were pre-

Table 3 Biscarbonyldisulfides **8** and **9** Prepared from Thiosulfonates and Adipoyl or Terephthaloyl Dithiols

Compd	R^3	R^2	Reaction time (min)	Yield[a] (%)
8a	$(CH_2)_4$[b]	Me	1	88
8b	$(CH_2)_4$[b]	Bn	1	82
8c	$(CH_2)_4$[b]	Cy	1	87
8d	$(CH_2)_4$[b]	Ph	1	67
8e	$(CH_2)_4$[b]	*p*-Tolyl	1	82
8f	$(CH_2)_4$[b]	*p*-FluoroPh	1	78
9a	*p*-C_6H_4[c]	Me	1	81
9b	*p*-C_6H_4[c]	Bn	2	82
9c	*p*-C_6H_4[c]	Cy	2	66
9d	*p*-C_6H_4[c]	Ph	3	67
9e	*p*-C_6H_4[c]	*p*-Tolyl	2	79
9f	*p*-C_6H_4[c]	*p*-FluoroPh	5	62

[a] Isolated yield is based on the amount of adipoyl dithiol used (**8a**–**8f**), and of *p*-chlorobenzenethiosulfonates **2b** used (**9a**–**9f**).
[b] Reaction conditions: The molar ratio of adipoyl dithiol to *p*-toluenethiosulfonate **2a** = 0.3:0.66 mmol.
[c] Reaction conditions: The molar ratio of terephthaloyl dithiol to **2b** = 0.24:0.4 mmol.

pared according to the literature procedure[13] and by the reaction of sulfinic acid with disulfides,[10] respectively.

Monoacyl Disulfides and Biscarbonyldisulfides; Typical Procedures

Method 1: *p*-Chlorobenzoyl *p*-Fluorophenyl Disulfide (5f)

A mixture of *p*-chlorothiobenzoic *S*-acid (51.8 mg, 0.3 mmol) and (*S*)-*p*-fluorophenyl *p*-chlorobenzenethiosulfonate (109.0 mg, 0.36 mmol) was allowed to stand at 25 °C and occasionally stirred. After disappearance of the thioacid spot a TLC plate, the reaction mixture was extracted with hexane (6 × 5 mL) followed by filtration and concentration at reduced pressure. The residue was recrystallized from EtOH–H_2O.

Method 2: Benzoyl Cyclohexyl Disulfide (4d)

A mixture of thiobenzoic *S*-acid (41.5 mg, 0.3 mmol), (*S*)-cyclohexyl *p*-toluenethiosulfonate (97.4 mg, 0.36 mmol) and *p*-aminoacetanilide (135.2 mg, 0.9 mmol) was allowed to stand at 25 °C and occasionally stirred. The work-up was carried out as described in Method 1. The residue was subjected to chromatography (CCl_4) with a Sep-Pak cartridge.

Method 3: Bis(*p*-fluorophenyl)dithioperoxyterephthalate (9f)

After stirring a mixture of the finely powdered thioterephthalic (*S*)-acid (237.9 mg, 1.2 mmol) and (*S*)-*p*-fluorophenyl *p*-chlorobenzenethiosulfonate (605.3 mg, 2.0 mmol), the reaction mixture was extracted with hexane (50 + 15 mL), followed by filtration and concentration at reduced pressure. The concentrate was dissolved in $CHCl_3$ (2 mL), and MeOH (4 mL) was added. Colorless crystals were formed as a precipitate.

Compounds 3 (R^1 = OMe)

Prepared by Method 1 with **2a**. An oily product was obtained after chromatography (Method 2).

3a (R^2 = Me)
Colorless.

Mp 64.0–65.0 °C.

IR (KBr): ν = 1662.85 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97 (d, 2H, *J* = 9.0 Hz, Bz-2,6), 6.95 (d, 2H, *J* = 9.0 Hz, Bz-3,5), 3.88 (s, 3H, OCH_3), 2.46 (s, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ =188.30 (*C*=O), 164.31 (Bz-4), 129.99 (Bz-2,6), 128.47 (Bz-1), 114.08 (Bz-3,5), 55.58 (O*C*H$_3$), 22.76 (*C*H$_3$).

MS (FAB): *m/z* (%) = 215 (4.30) $[M + H]^+$, 151 (7.96), 135 (100) $[MeOPhCO]^+$, 121 (3.23), 107 (2.57).

Anal. Calcd for $C_9H_{10}O_2S_2$: C, 50.44; H, 4.70. Found: C, 50.74; H, 4.78.

3b (R^2 = benzyl)
Colorless.

Mp 56.0–57.0 °C.

IR (KBr): ν = 1691.79 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.95 (d, 2H, *J* = 9.0 Hz, Bz-2,6), 7.36−7.26(m, 5H, Bn), 6.94 (d, 2H, *J* = 9.0 Hz, Bz-3,5), 3.99 (s, 2H, Bn-CH_2), 3.87 (s, 3H, OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.21 (*C*=O), 164.33 (Bz-4), 136.28 (Bn-1), 130.05 (Bn-3,5), 129.52 (Bz-2,6), 128.55 (Bn-2,6), 128.48 (Bz-1), 127.70 (Bn-4), 114.10 (Bz-3,5), 55.59 (O*C*H$_3$), 42.85 (Bn-*C*H$_2$).

MS (FAB): *m/z* (%) = 291 (11.53) $[M + H]^+$, 151 (24.76), 135 (100) $[MeOPhCO]^+$, 121 (7.41), 107 (6.21), 91 (29.64).

Anal. Calcd for $C_{15}H_{14}O_2S_2$: C, 62.04; H, 4.86. Found: C, 61.62; H, 5.02.

3c (R^2 = cyclohexyl)
Colorless oil.

IR (thin film): ν = 1691.79 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00 (d, 2H, *J* = 9.0 Hz, Bz-2,6), 6.94 (d, 2H, *J* = 9.0 Hz, Bz-3,5), 3.87 (s, 3H, OCH_3), 2.84 (nonet, 1H, *J* = 3.6 Hz, Cy-1), 2.05 (2H), 1.77 (2H), 1.59 (1H), 1.46–1.15 (m, 5H, Cy).

^{13}C NMR (75 MHz, $CDCl_3$): δ =188.96 (*C*=O), 164.22 (Bz-4), 130.00 (Bz-2,6),128.55 (Bz-1), 114.02 (Bz-35), 55.57 (O*C*H$_3$), 49.60 (Cy-1), 32.60 (Cy-2,6), 25.99 (Cy-3,5), 25.51 (Cy-4).

MS (FAB): *m/z* (%) =283 (27.99) $[M + H]^+$, 151 (23.00), 135 (100) $[MeOPhCO]^+$, 121 (9.84), 107 (6.08), 83 (10.91).

Anal. Calcd for $C_{14}H_{18}O_2S_2$: C, 59.54; H, 6.42. Found: C, 59.63; H, 6.40).

3d (R^2 = phenyl)
Colorless.

Mp 51.0–52.0 °C.

IR (KBr): ν = 1693.72 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.99 (d, 2H, *J* = 9.0 Hz, Bz-2,6), 7.56 (dd, 2H, *J* = 2.0, 8.5 Hz, Ph-2,6), 7.33–7.25 (m, 3H, Ph-3,4,5), 6.95 (d, 2H, *J* = 9.0 Hz, Bz-3,5), 3.88 (s, 3H, OCH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ =187.26 (*C*=O), 164.46 (Bz-4), 136.11 (Ph-1), 130.24 (Bz-2,6), 130.16 (Ph-2,6), 129.08,(Ph-3,5), 128.13 (Bz-1), 128.07 (Ph-4), 114.16 (Bz-3,5), 55.62 (O*C*H$_3$).

MS (FAB): *m/z* (%) = 277 (13.03) $[M + H]^+$, 151 (24.53), 135 (100) $[MeOPhCO]^+$, 121 (4.77), 107 (5.15).

Anal. Calcd for $C_{14}H_{12}O_2S_2$: C, 60.84; H, 4.38. Found: C, 60.70; H, 4.52.

3e (R^2 = *p*-tolyl)
Colorless.

Mp 59.0–60.0 °C.

IR (KBr): ν = 1699.50 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97 (d, 2H, *J* = 9.0 Hz, Bz-2,6), 7.49 (d, 2H, *J* = 8.1 Hz, tolyl-2,6), 7.10 (d, 2H, *J* = 8.1 Hz, tolyl-3,5), 6.94 (d, 2H, *J* = 9.0 Hz, Bz-3,5), 3.87 (s, 3H, OC*H*$_3$), 2.31 (s, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 187.59 (*C*=O), 164.37 (Bz-4), 138.67 (tolyl-4), 132.69 (tolyl-1), 131.24 (tolyl-3,5), 130.18 (tolyl-2,6), 129.87 (Bz-2,6), 128.23 (Bz-1), 114.11 (Bz-3,5), 55.59 (O*C*H$_3$), 21.17 (*C*H$_3$).

MS (FAB): *m/z* (%) = 291 (20.91) $[M + H]^+$, 151 (21.21), 135 (100) $[MeOPhCO]^+$, 121 (3.19), 107 (4,71).

Anal. Calcd for $C_{15}H_{14}O_2S_2$: C, 62.04; H, 4.86; S, 22.08. Found: C, 62.04; H, 4.95; S, 21.80.

3f (R^2 = *p*- fluorophenyl)
Colorless.

Mp 83.0–84.0 °C.

IR (KBr): ν = 1693.72 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96 (d, 2H, *J* = 8.6 Hz, Bz-2,6), 7.60 [dd, 2H, *J* = 9.0 Hz, Ph-2,6, $J^m_{H\text{-}F}$ = 5.3 Hz], 7.00 (d, 2H, *J* = 8.6 Hz, Bz-3,5), 6.96 [t, 2H, *J* = 9.0 Hz, Ph-3.5, $J^o_{H\text{-}F}$ = 9.0 Hz], 3.87 (s, H, OC*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 187.29 (*C*=O), 164.50 (Bz-4), 162.99 ($J_{4C\text{-}F}$ = 247.3 Hz), 133.62 ($J^m_{C\text{-}F}$ = 8.0 Hz), 131.45 ($J^p_{C\text{-}F}$ = 3.2 Hz), 130.22 (Bz-2,6), 128.03 (Bz-1), 116.25 ($J^o_{C\text{-}F}$ = 22.3 Hz), 114.18 (Bz-3,5), 55.62 (O*C*H$_3$).

MS (FAB): *m/z* (%) = 295 (15.53) $[M + H]^+$, 151 (31.01), 135 (100) $[MeOPhCO]^+$, 121 (3.55), 107 (7.17).

Anal. Calcd for $C_{14}H_{11}FO_2S_2$: C, 57.13; H, 3.77. Found: C, 57.06; H, 3.73.

Compounds 4 (R^1 = H)
Prepared by Method 2 with **2a**.

4a (R^2 = Me)
Colorless oil.

IR (thin film): ν = 1687.93 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98 (d, 2H, *J* = 7.5 Hz, Bz-2,6), 7.62 (t, 1H, *J* = 7.5 Hz, Bz-4), 7.48 (t, 2H, *J* = 7.5 Hz, Bz-3,5), 2.48 (s, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 190.09 (*C*=O), 135.76 (Bz-1), 134.05 (Bz-4), 128.89 (Bz-3,5), 127.69 (Bz-2,6), 22.61 (*C*H$_3$).

MS (EI): *m/z* (%) = 184 (0.71) $[M]^+$, 105 (100) $[PhCO]^+$, 77 (50.41).

Anal. Calcd for $C_8H_8OS_2$: C, 52.15; H, 4.38. Found: C, 52.27; H, 4.50.

4b (R^2 = *i*-Pr)
Colorless oil.

IR (thin film): ν = 1691.79 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02 (d, 2H, *J* = 8.0 Hz, Bz-2,6), 7.62 (t, 1H, *J* = 8.0 Hz, Bz-4), 7.49 (t, 2H, *J* = 8.0 Hz, Bz-3,5), 3.14 (sept, 1H, *J* = 7.0 Hz), 1.32 (d, 6H, *J* = 7.0 Hz, 2 C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 190.56 (*C*=O), 135.84 (Bz-1), 133.96 (Bz-4), 128.85 (Bz-3,5), 127.74 (Bz-2,6), 41.54 (*i*-Pr *C*H), 22.48 (*C*H$_3$).

MS (EI): *m/z* (%) = 212 (5.93) $[M]^+$, 105 (100) $[PhCO]^+$, 77 (30.28).

Anal. Calcd for $C_{10}H_{12}OS_2$: C, 56.57; H, 5.70. Found: C, 56.21; H, 5.67.

4c (R^2 = benzyl)
Colorless.

Mp 52.0–53.0 °C.

IR (KBr): ν = 1682.14 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.96 (d, 2H, *J* = 7.5 Hz, Bz-2,6), 7.61 (t, 1H, *J* = 7.5 Hz, Bz-4), 7.48 (t, 2H, *J* = 7.5 Hz, Bz-3,5), 7.36–7.25 (m, 5H, Bn), 4.00 (s, 2H, Bn-C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.98 (*C*=O), 136.14 (Bn-1), 135.76 (Bz-1), 134.03 (Bz-4), 129.51 (Bn-3,5), 128.88 (Bz-3,5), 128.58 (Bn-2,6), 127.73 (Bz-2,6), 127.73 (Bn-4), 42.72 (Bn-*C*H$_2$).

MS (EI): *m/z*(%)= 260 (2.89) $[M]^+$, 246 (2.73), 105 (100) $[PhCO]^+$, 91 (45.14), 77 (66.76).

Anal. Calcd for $C_{14}H_{12}OS_2$: C, 64.58; H, 4.65. Found: C, 64.39; H, 4.71.

4d (R^2 = cyclohexyl)
Colorless oil.

IR (thin film): ν = 1691.79 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.01 (d, 2H, *J* = 7.5 Hz, Bz-2,6), 7.61 (t, 1H, *J* = 7.5 Hz, Bz-4), 7.48 (t, 2H, *J* = 7.5 Hz, Bz-3,5), 2.87 (nonet, 1H, *J* = 3.5 Hz, Cy-1), 2.05 (2H), 1.79 (2H), 1.60 (1H), 1.44–1.18 (m, 5H, Cy).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 190.77 (*C*=O), 135.87 (Bz-1), 133.91 (Bz-4), 128.83 (Bz-3,5), 127.13 (Bz-2,6), 49.66 (Cy-1), 32.68 (Cy-2,6), 26.00 (Cy-3,5), 25.50 (Cy-4).

MS (EI): *m/z* (%) = 252 (1.99) $[M]^+$, 105 (100) $[PhCO]^+$, 83 (2.72), 77 (23.66).

Anal. Calcd for $C_{13}H_{16}OS_2$: C, 61.87; H, 6.39. Found: C, 62,09; H, 6.48.

4e (R^2 = phenyl)
Colorless.

Mp 29.5–30.0 °C (Lit.[4a,6] 52–53 °C).

IR (KBr): ν = 1693.72 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.01 (d, 2H, *J* = 7.5 Hz, Bz-2,6), 7.62 (t, 1H, *J* = 7.5 Hz, Bz-4), 7.58 (d, 2H, *J* = 7.5 Hz, Ph-2,6), 7.49 (t, 2H, *J* = 7.5 Hz, Bz-3,5), 7.32–7.27 (m, 3H, Ph-3,4,5).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.09 (*C*=O), 135.79 (Bz-1), 135.43 (Ph-1), 134.22 (Bz-4), 130.42 (Ph-2,6), 129.13 (Ph-3,5), 128.94 (Bz-3,5), 128.25 (Ph-4), 127.89 (Bz-2,6).

MS(EI): *m/z* (%)= 246 (5.32) $[M]^+$, 218 (1.60), 141 (5.81), 105 (100) $[PhCO]^+$, 77 (76.47).

Anal. Calcd for $C_{13}H_{10}OS_2$: C, 63.38; H, 4.09. Found: C, 63.55; H, 4.31.

4f (R^2 = *p*-tolyl)
Colorless.

Mp 37.5–38.0 °C (Lit.[5] 37–39 °C).

IR (KBr): ν = 1691.79 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98 (d, 2H, *J* = 7.5 Hz, Bz-2,6),7.60 (t, 1H, *J* = 7.5 Hz, Bz-4), 7.51 (d, 2H, *J* = 8.0 Hz, tolyl-2,6), 7.47 (t, 2H, *J* = 7.5 Hz, Bz-3,5), 7.11 (d, 2H, *J* = 8.0 Hz, tolyl-3,5), 2.31 (s, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.38 (*C*=O), 138.86 (tolyl-4), 135.56 (Bz-1), 134.10 (Bz-4), 132.39 (tolyl-1), 131.48 (tolyl-3,5), 129.92 (tolyl-2,6), 128.84 (Bz-3,5), 127.8 4 (Bz-2,6), 21.17 (*C*H$_3$).

MS (EI): *m/z* (%)= 260 (3.55) [M]$^+$, 246 (8.23), 123 (15.50), 105 (100) [PhCO]$^+$, 77 (36.43).

Anal. Calcd for $C_{14}H_{12}OS_2$: C, 64.58; H, 4.65. Found: C, 64.52; H, 4.77.

4g (R^2 = *p*- fluorophenyl)
Colorless oil.

IR (thin film): ν = 1691.79 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.98 (d, 2H, *J* = 7.5 Hz, Bz-2,6), 7.63 (t, 1H, *J* = 7.5, Bz-4), 7.61 (d, 2H, *J* = 8.5 Hz, Ph-2,6), 7.48 (t, 2H, *J* = 7.5 Hz, Bz-3,5),7.00 (dd, 2H, *J* = 8.5 Hz, Ph-3,5, $J^o_{H\text{-}F}$ = 9.0 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.11 (*C*=O), 164.08 ($J_{C\text{-}F}$ = 247.5 Hz), 135.36 (Bz-1), 134.28 (Bz-4), 133.90 ($J^m_{C\text{-}F}$ = 8.3 Hz), 131.14 ($J^P_{C\text{-}F}$ = 2.8 Hz), 128.96 (Bz-3,5), 127.86 (Bz-2,6), 116.31 ($J^o_{C\text{-}F}$ = 21.9 Hz).

MS (EI): *m/z* (%) = 264 (1.98) [M]$^+$, 159 (3.91), 127 (25.28), 105 (100) [PhCO]$^+$, 77 (56.68).

Anal. Calcd for $C_{13}H_9FOS_2$: C, 59.07; H, 3.43. Found: C, 58.85; H, 3.52.

4h (R^2 = *p*-bromophenyl)
Colorless.

Mp 45.5–47.0 °C.

IR (KBr): ν = 1693.72 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.79 (d, 2H, *J* = 8.0 Hz, Bz-2,6), 7.63 (t, 1H, *J* = 8.0 Hz, Bz-4), 7.49 (t, 2H, *J* = 8.0 Hz, Bz-3,5), 7.45 (d, 2H, *J* = 8.5, Ph-3,5), 7.42 (d, 2H, *J* = 8.5 Hz, Ph-2,6).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.70 (*C*=O), 135.24 (Bz-1), 135.01 (Ph-1), 134.39 (Bz-4), 132.22 (Ph-3,5), 132.06 (Ph-2,6), 129.01 (Bz-3,5), 127.92 (Bz-2,6), 122.59 (Ph-4).

MS (EI): *m/z* (%) = 324 (0.66) [M]$^+$, 219 (0.37), 187 (7.21), 105 (100) [PhCO]$^+$, 77 (29.02).

Anal. Calcd for $C_{13}H_9BrOS_2$: C, 48.01; H, 2.79. Found: C, 48.15; H, 2.87.

4i (R^2 = 2-naphthyl)
Colorless.

Mp 69.0–70.0 °C (Lit.[4a] 69 °C).

IR (KBr): ν = 1695.64 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.09 (s, 1H, naph-1), 8.02 (d, 2H, *J* = 7.5 Hz, Bz-2,6), 7.78 (d, 3H, *J* = 7.5 Hz, naph-4,5,8), 7.62(t, 2H, *J* = 7.5 Hz, naph-6,7), 7.49 (t, 3H, *J* = 7.5 Hz, Bz-3,4,5), 7.47 (d, 1H, *J* = 7.5 Hz, naph-3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.12 (*C*=O), 135.47 (Bz-1), 135.46 (naph-9), 134.24 (Bz-4), 133.34 (naph-10), 132.91 (naph-2), 129.95 (naph-1), 129.05 (Bz-3,5), 128.96 (naph-4), 127.91 (naph-5,8), 127.74 (Bz-2,6), 126.76 (naph-6,7), 126.72 (naph-3).

MS (EI): *m/z* (%) = 296 (7.69) [M]$^+$, 219 (0.37), 187 (7.21), 105 (100) [PhCO]$^+$, 77 (29.02).

Anal. Calcd for $C_{17}H_{12}OS_2$: C, 68.89; H, 4.08. Found: C, 68.56; H, 4.20.

Compounds 5 (R^1 = Cl)
Prepared by Method 1 with **2b**. The oily products were subjected to chromatography (method 2).

5a (R^2 = Me)
Colorless oil.

IR (thin film): ν = 1686.00 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92 (d, 2H, *J* = 9.0 Hz, Bz-2,6), 7.46 (d, 2H, *J* = 9.0 Hz, Bz-3,5), 2.48 (s, 3H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ =189.14 (*C*=O), 140.58 (Bz-4), 134.04 (Bz-1), 129.25 (Bz-2,6), 129.02 (Bz-3,5), (22.60, *C*H$_3$).

MS (EI): *m/z* (%) = 218 (0.45) [M]$^+$, 139 (100) [ClPhCO]$^+$, 111 (28.77).

Anal. Calcd for $C_8H_7ClOS_2$: C, 43.93; H, 3.23. Found: C, 44.03; H, 3.39.

5b (R^2 = benzyl)
Colorless.

Mp 65.0–66.0 °C.

IR (KBr): ν = 1695.64 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.88 (d, 2H, *J* = 9.0 Hz, Bz-2,6), 7.45 (d, 2H, *J* = 9.0 Hz, Bz-3,5), 7.33–7.27 (m, 5H, Bn), 4.00 (s, 2H, Bn-C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.01 (*C*=O), 140.58 (Bn-1), 136.00 (Bz-4), 134.07 (Bz-1), 129.52 (Bz-2,6), 129.23 (Bz-3,5), 129.05 (Bn-3,5), 128.60 (Bn-2,6), 127.83 (Bn-4), 42.73 (Bn *C*H$_2$).

MS (EI): *m/z* (%) = 294 (0.69) [M]$^+$, 139 (100) [ClPhCO]$^+$, 111 (20.52), 91 (25.94).

Anal. Calcd for $C_{14}H_{11}ClOS_2$: C, 57.04; H, 3.76. Found: C, 56.85; H, 3.85.

5c (R^2 = cyclohexyl)
Colorless oil.

IR (thin film): ν = 1689.86 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.95 (d, 2H, *J* = 8.5 Hz, Bz-2,6), 7.46 (d, 2H, *J* = 8.5 Hz, Bz-3,5), 2.87 (nonet, 1H, *J* = 3.6 Hz, Cy-1), 2.05 (2H), 1.80 (2H), 1.61 (1H), 1.46–1.29 (m, 5H, Cy).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.84 (*C*=O), 140.45 (Bz-4),134.18 (Bz-1),129.17 (Bz-2,6), 129.06 (Bz-3,5), 49.75 (Cy-1), 32.64 (Cy-2,6), 25.99 (Cy-3,5), 25.48 (Cy-4).

MS (EI): *m/z* (%) = 286 (1.58) [M]$^+$, 139 (100) [ClPhCO]$^+$, 111 (14.43), 83 (2.84).

Anal. Calcd for $C_{13}H_{15}ClOS_2$: C, 54.44; H, 5.27. Found: C, 54.50; H, 5.37.

5d (R^2 = phenyl)
Colorless.

Mp 79.0–80.0 °C.

IR (KBr): ν = 1686.00 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.94 (d, 2H, *J* = 8.4 Hz, Bz-2,6), 7.57 (dd, 2H, *J* = 2.0, 7.5 Hz, Ph-2,6), 7.46 (d, 2H, *J* = 8.4 Hz, Bz-3,5), 7.31–7.28 (m, 3H, Ph-3,4,5).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.19 (*C*=O), 140.77 (Bz-4), 135.53 (Ph-1), 133.75 (Bz-1), 130.69 (Bz-2,6), 129.30 (Ph-2,6), 129.20 (Bz-3,5), 129.20 (Ph-3,5), 128.47 (Ph-4).

MS (EI): *m/z* (%) = 280 (2.08) [M]$^+$, 248, 139 (100) [ClPhCO]$^+$, 111 (19.98), 109 (11.75).

Anal. Calcd for $C_{13}H_9ClOS_2$: C, 55.61; H, 3.23. Found: C, 55.27; H, 3.31.

5e (R^2 = *p*-tolyl)
Colorless.

Mp 61.5–63.5 °C.

IR (KBr): ν = 1682.14 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.92 (d, 2H, *J* = 8.4 Hz, Bz-2,6), 7.51 (d, 2H, *J* = 8.1 Hz, tolyl-2,6), 7.45 (d, 2H, *J* = 8.4 Hz, Bz-3,5), 7.12 (d, 2H, *J* = 8.1 Hz, tolyl-3,5), 2.32 (s, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.50 (*C*=O), 140.64 (Bz-4), 139.14 (tolyl-4), 133.87 (Bz-1), 132.12 (tolyl-1), 131.75 (tolyl-3,5), 129.98 (Bz-2,6), 129.25 (tolyl-2,6), 129.16 (Bz-3,5), 21.20 (*C*H_3).

MS (EI): *m/z* (%) = 294 (2.85) $[M]^+$, 155 (2.58), 139 (100) $[ClPhCO]^+$, 123 (15.68), 111 (19.90), 91 (10.67).

Anal. Calcd for $C_{14}H_{11}ClOS_2$: C, 57.04; H, 3.76. Found: C, 57.18; H, 3.89.

5f (R^2 = *p*-fluorophenyl)
Colorless.

Mp 64.0–65.5 °C.

IR (KBr): ν = 1687.93 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 7.94 (d, 2H, *J* = 8.7 Hz, Bz-2,6), 7.62 [dd, 2H, *J* = 8.7 Hz, Ph-2,6, $J^m_{H\text{-}F}$ = 5.3 Hz], 7.46 (d, 2H, *J* = 8.7 Hz, Bz-3,5), 7.01 [dd, 2H, *J* = 8.7 Hz, Ph-3,5, $J^o_{H\text{-}F}$ = 8.7 Hz].

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.21 (*C*=O), 163.23 ($J_{C\text{-}F}$ = 247.7 Hz), 140.85 (Bz-4), 134.20 ($J^m_{C\text{-}F}$ = 8.0 Hz), 133.7 (Bz-1), 130.90 ($J^p_{C\text{-}F}$ = 3.8 Hz), 129.33 (Bz-2,6), 129.18 (Bz-3,5), 116.39 ($J^o_{C\text{-}F}$ = 22.3 Hz).

MS (EI): *m/z* (%) = 298 (0.76) $[M]^+$, 159 (16.22), 139 (100) $[ClPhCO]^+$, 127 (16.22), 111 (24.70), 95 (4.09).

Anal. Calcd for $C_{13}H_8ClFOS_2$: C, 52.26; H, 2.70. Found: C, 52,23; H, 2,72.

Compounds 6 (R^1 = NO_2)
Prepared by Method 1 or Method 2 with **2b**

6a (6a') (R^2 = Me)
Pale yellow.

Mp 65.0 °C.

IR (KBr): ν = 1674.43 (C=O), 1522.03 (NO_2), 1348.41 (NO_2) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.34 (d, 2H, *J* = 9.0 Hz, Bz-3,5), 8.14 (d, 2H, *J* = 9.0 Hz, Bz-2,6), 2.52 (s, 3H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.30 (*C*=O), 150.85 (Bz-4), 140.34 (Bz-1), 128.69 (Bz-2,6), 124.13 (Bz-3,5), 22.48 (*C*H_3).

MS (EI): *m/z* (%) = 229 (2.39) $[M]^+$, 150 (100) $[NO_2PhCO]^+$, 120 (5.00), 104 (25.27).

Anal. Calcd for $C_8H_7NO_3S_2$: S, 27.97. Found: S, 28.03.

6b (R^2 = benzyl)
Colorless.

Mp 111.0–112.5 °C.

IR (KBr): ν = 1693.72 (C=O), 1525.89 (NO_2), 1350.34 (NO_2) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.32 (d, 2H, *J* = 8.7 Hz, Bz-3,5), 8.09 (d, 2H, *J* = 8.7 Hz, Bz-2,6), 7.34–7.29 (m, 5H, Bn), 4.03 (s, 2H, Bn-CH_2).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.18 (*C*=O), 150.82 (Bz-4), 140.34 (Bz-1), 135.66 (Bn-1), 129.54 (Bz-2,6), 128.69 (Bn-3,5), 128.66 (Bn-2,6), 127.98 (Bn-4), 124.10 (Bz-3,5), 42.63 (Bn *C*H_2).

MS (EI): *m/z* (%) = 305 (4.17) $[M]^+$, 150 (100) $[NO_2PhCO]^+$, 123 (4.34), 120 (5.80), 104 (18.52), 91 (42.67).

Anal. Calcd for $C_{14}H_{11}NO_3S_2$: C, 55.07; H, 3.63; N, 4.59. Found: C, 55.27, H, 3.69; N, 4.53.

6c (6c') (R^2 = cyclohexyl)
Cream yellow.

Mp 72.0–73.0 °C.

IR (KBr): ν = 1682.14 (C=O), 1522.03 (NO_2), 1350.34 (NO_2) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.34 (d, 2H, *J* = 9.0 Hz, Bz-3,5), 8.17 (d, 2H, *J* = 9.0 Hz, Bz-2,6), 2.91 (nonet, 1H, *J* = 3.6 Hz, Cy-1), 2.05 (2H), 1.82 (2H), 1.61 (1H), 1.47–1.21 (m, 5H, Cy).

^{13}C NMR (75 MHz, $CDCl_3$,): δ = 190.06 (*C*=O), 150.81 (Bz-4), 140.55 (Bz-1), 128.73 (Bz-2,6), 124.07 (Bz-3,5), 49.98 (Cy-1), 32.70 (Cy-2,6), 25.98 (Cy-3,5), 25.43 (Cy-4).

MS (EI): *m/z* (%) = 297 (4.47) $[M]^+$, 150 (100) $[NO_2PhCO]^+$, 120 (5.03), 104 (15.05), 92 (5.98), 83 (6.63).

Anal. Calcd for $C_{13}H_{15}NO_3S_2$: C, 52.51; H, 5.08; N, 4.71. Found: C, 52.43; H, 5.11; N, 4.52.

6d (R^2 = phenyl)
Colorless.

Mp 74.0–76.0 °C.

IR (KBr): ν = 1684.07 (C=O), 1522.03 (NO_2), 1344.56 (NO_2) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.33 (d, 2H, *J* = 8.7 Hz, Bz-3,5), 8.14 (d, 2H, *J* = 8.7 Hz, Bz-2,6), 7.61 (dd, 2H, *J* = 2.4, 7.5 Hz, Ph-2,6), 7.35–7.31 (m, 3H, Ph-3,4,5).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.45 (*C*=O), 150.92 (Bz-4), 140.12 (Bz-1), 134.97 (Ph-1), 131.33 (Ph-2,6), 129.34 (Ph-3,5), 128.95 (Ph-4), 128.86 (Bz-2,6), 124.14 (Bz-3,5).

MS (EI): *m/z* (%) = 291 (5.11) $[M]^+$, 150 (100) $[NO_2PhCO]^+$, 141 (6.27), 120 (5.71), 109 (17.51), 104 (20.19).

Anal. Calcd for $C_{13}H_9NO_3S_2$: C, 53.59; H, 3.11; N, 4.81; S, 22.01. Found: C, 53.61; H, 3.18; N, 4.64; S, 22.01.

6e (6e') (R^2 = *p*-tolyl)
Colorless.

Mp 98.5–100.5 °C.

IR (KBr): ν = 1689.86 (C=O), 1529.75 (NO_2), 1348.41 (NO_2) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.32 (d, 2H, *J* = 9.0 Hz, Bz-3,5), 8.13 (d, 2H, *J* = 9.0 Hz, Bz-2,6), 7.54 (d, 2H, *J* = 8.1 Hz, tolyl-2,6), 7.14 (d, 2H, *J* = 8.1 Hz, tolyl-3,5), 2.34 (s, 3H, CH_3).

^{13}C NMR(75 MHz, $CDCl_3$): δ = 188.73 (*C*=O), 150.84 (Bz-4), 140.24 (Bz-1), 139.69 (tolyl-4), 132.33 (toly-3,5), 131.51 (tolyl-1), 130.11 (tolyl-2,6), 128.81 (Bz-2,6), 124.10 (Bz-3,5), 21.24 (*C*H_3).

MS (EI): *m/z* (%) = 305 (7.40) $[M]^+$, 273 (2.55), 246 (8.67), 150 (100) $[NO_2PhCO]^+$, 123 (18.20), 120 (6.29), 104 (18.46), 91 (10.67).

Anal. Calcd for $C_{14}H_{11}NO_3S_2$: C, 55.07; H, 3.63; N, 4.59. Found: C, 54.75; H, 3.38; N, 4.46.

6f (6f') (R^2 = *p*-fluorophenyl)
Colorless.

Mp 86.5–87.5 °C.

IR (KBr): ν = 1697.57 (C=O), 1545.18 (NO_2), 1350.34 (NO_2) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.33 (d, 2H, *J* = 8.8 Hz, Bz-3,5), 8.12 (d, 2H, *J* = 8.8 Hz, Bz-2,6), 7.66 (dd, 2H, *J* = 8.7 Hz, Ph-2,6, $J^m_{H\text{-}F}$ = 5.1 Hz), 7.03 (dd, 2H, *J* = 8.7 Hz, Ph-3,5, $J^{o=}{}_{H\text{-}F}$ = 8.7 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.45 (C=O), 163.46 (d, Ph-4, $J_{C\text{-}F}$ = 248.5 Hz), 150.95 (Bz-4), 140.06 (Bz-1), 134.84 (d, $J^m_{C\text{-}F}$ =

8.0 Hz), 130.29 (d, $J^{p}_{C\text{-}F}$ = 3.8 Hz), 128.84 (Bz-2,6), 124.17 (Bz-3,5), 116.55 (d, $J^{o}_{C\text{-}F}$ = 22.3 Hz).

MS (EI): *m/z* (%) = 309 (3.95) $[M]^+$, 159 (5.05), 150 (100) $[NO_2PhCO]^+$, 127 (21.25), 120 (6.71), 104 (21.96), 95 (3.72), 92 (9.10), 83 (13.28), 76 (14.26).

Anal. Calcd for $C_{13}H_8FNO_3S_2$: C, 50.48; H, 2.61; N, 4.53. Found: C, 50.43; H, 2.69; N, 4.32.

Compounds 8 (R^3 = Tetramethylene)
Prepared by Method 3 with **2a**

8a (R^2 = Me)
Colorless.

Mp 24.0–25.0 °C.

IR (KBr): ν = 1718.79 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.70 (t, 4H, *J* = 6.9 Hz), 2.41 (s, 6H, C*H*$_3$), 1.76 (quint, 4H, *J* = 3.6 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.37 (*C*=O), 41.91 (1-*C*H_2), 24.59 (2-*C*H_2), 22.74 (CH_3).

MS (FAB): *m/z* (%) = 271 (5.15) $[M + H]^+$, 191 (71.95), 145 (29.83), 111 (100) $[(CH_2)_4(CO)_2]^+$.

Anal. Calcd for $C_8H_{14}O_2S_4$: C, 35.53; H, 5.22. Found: C, 35.63; H, 5.00.

8b (R^2 = benzyl)
Colorless.

Mp 39.0–40.0 °C.

IR (KBr): ν = 1720.72 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.33–7.27 (m, 10H, Bn), 3.92 (s, 4H, Bn-C*H*$_2$), 2.56 (t, 4H, *J* = 7.2 Hz), 1.61 (quint, 4H, *J* = 3.6 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.49 (*C*=O), 136.05 (Bn-1), 129.48 (Bn-3,5), 128.58 (Bn-2,6), 127.80 (Bn-4), 42.88 (Bn-*C*H_2), 41.58 (1-*C*H_2), 24.45 (2-*C*H$_2$)

MS (FAB): *m/z* (%) = 423 (0.42) $[M + H]^+$, 267 (33.01), 221 (14.09), 155 (1.99), 123 (6.53), 111 (54.84), 91 (100) $[PhCH_2]^+$.

Anal. Calcd for $C_{20}H_{22}O_2S_4$: C, 56.84; H, 5.25. Found: C, 56.74; H, 5.24.

8c (R^2 = cyclohexyl)
Colorless.

Mp 48.0–49.0 °C.

IR (KBr): ν = 1724.58 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ =2.74 (nonet, 2H, *J* = 3.9 Hz, Cy-1), 2.71 (t, 4H, *J* = 6.9 Hz), 1.98 (4H, Cy), 1.76 (quint, 4H + 4H, Cy), 1.60 (2H, Cy), 1.40–1.16 (m, 10H, Cy).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 198.24 (*C*=O), 49.71 (Cy-1), 41.79 ((1-*C*H_2), 32.58 (Cy-2,6), 25.96 (Cy-3,5), 25.45 (Cy-4), 24.68 (2-*C*H_2).

MS (FAB): *m/z* (%) = 407 (1.64) $[M + H]^+$, 259 (71.49), 213 (9.22), 177 (15.31), 159 (5.94), 131 (7.78), 111 (100) $[CO(CH_2)_4CO]^+$, 83 (28.23) $[C_6H_{11}]^+$.

Anal. Calcd for $C_{18}H_{30}O_2S_4$: C, 53.16; H, 7.44. Found: C, 53.19; H, 7.33.

8d (R^2 = phenyl)
Colorless.

Mp 66.0–67.5 °C.

IR (KBr): ν = 1732.30 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.48 (dd, 4H, *J* = 2.4, 7.8 Hz, Ph-2,6), 7.30–7.28 (m, 6H, Ph-3,4,5), 2.71 (t, 4H, *J* = 6.6 Hz), 1.73 (quint, 4H, *J* = 3.3 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.70 (*C*=O), 135.67 (Ph-1), 130.28 (Ph-2,6), 129.19 (Ph-3,5), 128.33 (Ph-4), 41.60 (1-*C*H_2), 24.50 (2-*C*H_2).

MS (FAB): *m/z* (%) = 395 (0.60) $[M + H]^+$, 253 (36.18), 207 (30.32), 141 (19.15), 111 (100) $[CO(CH_2)_4CO]^+$.

Anal. Calcd for $C_{18}H_{18}O_2S_4$: C, 54.79; H, 4.60. Found: C, 54.53; H, 4.69.

8e (R^2 = *p*-tolyl)
Colorless.

Mp 54.0–55.0 °C.

IR (KBr): ν = 1710.79 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.41 (d, 4H, *J* = 8.1 Hz, tolyl-2,6), 7.11 (d, 4H, *J* = 8.1 Hz, tolyl-3,5), 2.68 (t, 4H, *J* = 6.9 Hz), 2.32 (s, 6H, C*H*$_3$), 1.72 (quint, 4H, *J* = 3.6 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.96 (*C*=O), 138.94 (tolyl-4), 132.30 (tolyl-1), 131.30 (toly-3,5), 129.97 (tolyl-2,6), 41.60 (1-*C*H_2), 24.51 (2-*C*H_2), 21.17 (*C*H_3).

MS (FAB): *m/z* (%) = 421 (1.22) $[M – 1]^+$, 267 (44.25), 221 (23.85), 155 (18.87), 123 (29.65), 111 (100) $[CO(CH_2)_4CO]^+$.

Anal. Calcd for $C_{20}H_{22}O_2S_4$: C, 56.84; H, 5.25. Found: C, 56.62; H, 5.26.

8f (R^2 = *p*-fluorophenyl)

Colorless.

Mp 57.0–58.0 °C.

IR (KBr): ν = 1713.01 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.53 (dd, 4H, *J* = 8.7 Hz, Ph-2,6, $J^{m}_{H\text{-}F}$ = 5.1 Hz), 7.00 (dd, 4H, *J* = 8.7 Hz, Ph-3,5, $J^{o}_{H\text{-}F}$ = 8.1 Hz), 2.68 (t, 4H, *J* = 6.9 Hz, 1-C*H*$_2$), 1.73 (quint, 4H, *J* = 3.6 Hz, 2-C*H*$_2$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 196.44 (*C*=O), 163.11 (d, Ph-4, $J_{C\text{-}F}$ = 247.9 Hz), 133.85 (d, $J^{m}_{C\text{-}F}$ = 8.6), 131.03 (d, $J^{p}_{C\text{-}F}$ = 3.7 Hz), 116.38 (d, $J^{o}_{C\text{-}F}$ = 22.2 Hz), 41.71 (1-*C*H_2), 24.49 (2-*C*H_2).

MS (FAB): *m/z* (%) = 429 (0.28) $[M – 1]^+$, 271 (24.77), 225 (22.27), 159 (20.25), 127 (24.93), 111 (100) $[CO(CH_2)_4CO]^+$, 95 (3.49), 83 (17.87).

Anal. Calcd for $C_{18}H_{16}F_2O_2S_4$: C, 50.21; H, 3.75. Found: C, 50.00; H, 3.76.

Compounds 9 (R^3 = *p*-Phenylene)
Prepared by Method 3 with **2b**.

9a (R^2 = Me)
Pale yellow.

Mp 152.0–153.0 °C.

IR (KBr): ν = 1684.07 (C=O) cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07 (s, *p*-phenylene-4H), 2.50 (s, 6H, C*H*$_3$).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.73 (*C*=O), 139.69 (*p*- phenylene-1,4), 128.08 (*p*-phenylene-2,3,5,6), 22.52 (*C*H_3).

MS (EI): *m/z* (%) = 290 (0.39) $[M]^+$, 211 (100), 179 (10.89), 132 (48.30), 104 (55.00),76 (23.65).

Anal. Calcd for $C_{10}H_{10}O_2S_4$: C, 41.35; H, 3.47. Found: C, 40.89; H, 3.49.

9b (R^2 = benzyl)
Colorless.

Mp 156–157.5 °C.

IR (KBr): ν = 1689.86 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.02 (s, *p*-phenylene-4H), 7.35–7.26 (m, 10H, Bn), 4.02 (s, 4H, Bn-CH_2),

^{13}C NMR (75 MHz, $CDCl_3$): δ = 189.62 (*C*=O), 139.68 (*p*-phenylene-1,4), 135.84 (Bn-1), 129.53 (Bn-3,5), 128.64 (Bn-2,6), 128.08 (*p*-phenylene-2,3,5,6), 127.91 (Bn-4), 42.67 (Bn-*C*H_2).

MS (EI): *m/z* (%) = 442 (0.24) $[M]^+$, 287 (30.49), 255 (61.05), 132 (16.02), 104 (22.68), 91 (100).

Anal. Calcd for $C_{22}H_{18}O_2S_4$: C, 59.70; H, 4.10; S, 28.97. Found: C, 59.28; H, 4.04, S, 28.63.

9c (R^2 = cyclohexyl)
Colorless.

Mp 93.5–95.5 °C.

IR (KBr): ν = 1691.79 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.09 (s, *p*-phenylene-4H), 2.90 (nonet, 2H, *J* = 3.6 Hz, Cy-1), 2.06 (4H), 1.79 (4H), 1.58 (2H), 1.48–1.21 (m, 10H, Cy).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 190.51 (C=O), 139.75 (*p*-phenylene-1,4), 128.08 (*p*-phenylene-2,3,5,6), 49.85 (Cy-1), 32.67 (Cy-2,6), 25.79 (Cy-3,5), 25.46 (Cy-4).

MS (EI): *m/z* (%) = 426 (1.39) $[M]^+$, 279 (100), 247 (53.21), 165 (19.36), 132 (42.14), 104 (34.31), 83 (22.50),76 (9.58).

Anal. Calcd for $C_{20}H_{26}O_2S_4$: S, 30.06. Found: S, 29.55.

9d (R^2 = phenyl)
Pale yellow.

Mp 97.0–99.0 °C.

IR (KBr): ν = 1687.93 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.07 (s, *p*-phenylene-4H), 7.61 (dd, 4H, *J* = 2.4, 7.9 Hz, Ph-2,6), 7.34−7.30 (m, 6H, Ph-3,4,5).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.83 (*C*=O), 139.51 (*p*-phenylene-1,4), 135.22 (Ph-1), 131.03 (Ph-2,6), 129.26 (Ph-3,5), 128.71 (Ph-4), 128.27 (*p*-phenylene-2,3,5,6).

MS (EI): *m/z* (%) = 414 (0.20) $[M]^+$, 350 (3.94), 273 (4.51), 241 (100), 165 (4.80), 141 (13.92), 132 (18.11), 109 (25.19), 104 (35.87), 76 (14.04).

Anal. Calcd for $C_{20}H_{14}O_2S_4$: C, 57.94; H, 3.40. Found: C, 57.50; H, 3.45.

9e (R^2 = *p*-tolyl)
Yellow.

Mp 131.0–133.0 °C.

IR (KBr): ν = 1686.00 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.04 (s, *p*-phenylene-4H), 7.52 (d, 4H, *J* = 8.1 Hz, tolyl-2,6), 7.13 (d, 4H, *J* = 8.1 Hz, tolyl-3,5), 2.32 (s, 6H, CH_3).

^{13}C NMR (75 MHz, $CDCl_3$,): δ = 189.12 (*C*=O), 139.59 (*p*-phenylene-1,4), 139.41 (tolyl-4), 132.07 (tolyl-1), 131.83 (tolyl-3,5), 130.05 (tolyl-2,6), 128.27 (*p*-phenylene-2,3,5,6), 21.21 (*C*H_3).

MS (EI): m/z (%) = 442 (1.03) $[M]^+$, 287 (20.48), 255 (100), 184 (4.91), 165 (11.68), 155 (5.59), 132 (27.09), 123 (28.20), 104 (42.29). 91 (17.11), 76 (14.08).

Anal. Calcd for $C_{22}H_{18}O_2S_4$: S, 28.97. Found: S, 28.80.

9f (R^2 = *p*-fluorophenyl)
Colorless.

Mp 115.5–117 °C.

IR (KBr): ν = 1687.93 (C=O) cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 8.05 (s, *p*-phenylene-4H), 7.64 (dd, 4H, *J* = 8.7 Hz, Ph-2,6, $J^m_{H\text{-}F}$ = 5.1 Hz), 7.02 (t, 4H, *J* = 8.7 Hz, Ph-3,5, $J^o_{H\text{-}F}$ = 9.0 Hz).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 188.84 (*C*=O), 163.34 (d, Ph-4, $J_{C\text{-}F}$ = 248.6 Hz), 139.48 (*p*-phenylene-1,4), 134.57 (d, $J^m_{C\text{-}F}$ = 8.0 Hz), 130.53 (d, $J^p_{C\text{-}F}$ = 3.1 Hz), 128.27 (*p*-phenylene-2,3,5,6), 116.48 (d, $J^o_{C\text{-}F}$ = 22.2 Hz).

MS (EI): *m/z* (%) = 450 (0.18) $[M]^+$, 291 (9.17), 259 (100), 159 (13.89), 136 (3.75), 132 (28.19), 127 (51.11), 104 (43.64), 95 (4.18), 83 (25.13), 76 (16.59).

Anal. Calcd for $C_{20}H_{12}F_2O_2S_4$: C, 53.32; H, 2.68. Found: C, 53.37; H, 2.88.

References

(1) (a) Buckmann, J. D.; Johnson, B. S.; Field, L. *Can. J. Microbiol.* **1966**, *12*, 1263. (b) Field, L.; Hanley, W. S. *J. Med. Chem.* **1971**, *14*, 202; and references cited therein.
(2) Chuan-Fa, L.; Chang, R.; Tam, J. P. *Tetrahedron Lett.* **1996**, *37*, 933.
(3) (a) Flank, R. L.; Blegen, J. R. *Org. Synth. Coll.*, Vol. 3; Wiley: Chichester, **1955**, 116–118. (b) Tanaka, S.; Masue, K.; Okano, M. *Bull. Chem. Soc. Jpn.* **1978**, *51*, 659. (c) Kodamari, M.; Fukuda, M.; Yoshitomi, S. *Synthesis* **1981**, 637. (d) Kato, S. *Phosphorus, Sulfur Silicon Relat. Elem.* **1997**, *120 & 121*, 213. (e) Robert, J.; Anouti, M.; Abarbi, M.; Paris, J. *J. Chem. Soc., Perkin Trans. 2* **1997**, 1759. (f) Niyomura, O.; Kitoh, Y.; Nagayama, K.; Kato, S. *Sulfur Letters* **1999**, *22*, 195.
(4) (a) Böhme, H.; Clement, M. *Liebigs Ann. Chem.* **1952**, *576*, 61. (b) Böhme, H.; Zinner, G. *Liebig Ann. Chem.* **1954**, *585*, 142. (c) Fujisawa, T.; Kobayashi, N. *J. Org. Chem.* **1971**, *36*, 3546.
(5) (a) Field, L.; Hanley, W. S.; McVeigh, I. *J. Org. Chem.* **1971**, *36*, 2735. (b) Neumann, W. P.; Schwindt, J. *Chem. Ber.* **1975**, *108*, 1339.
(6) Field, L.; Buckmann, J. D. *J. Org. Chem.* **1967**, *32*, 3467.
(7) Milligan, B.; Saville, B.; Swan, J. M. *J. Chem. Soc.* **1961**, 4850.
(8) Metzner, P.; Thinhan, P. *J. Chem. Soc., Chem. Commun.* **1988**, 390.
(9) Fujiki, K.; Yoshida, E. *Synth. Commun.* **1999**, *29*, 3289.
(10) Manuscript in preparation.
(11) (a) Toda, F. *Synlett* **1993**, 303. (b) Toda, F. *Acc. Chem. Res.* **1995**, 480. (c) Dittmwe, D. *Chem. Ind.* **1997**, 779. (d) Tanaka, K.; Toda, F. *Chem. Rev.* **2000**, 1025.
(12) Hirabayashi, Y.; Mizuta, M.; Kojima, M.; Horio, Y. *Bull. Chem. Soc. Jpn.* **1971**, *44*, 791; and references cited therein.
(13) Kobayashi, Y.; Itabashi, K. *Synthesis* **1985**, 671.