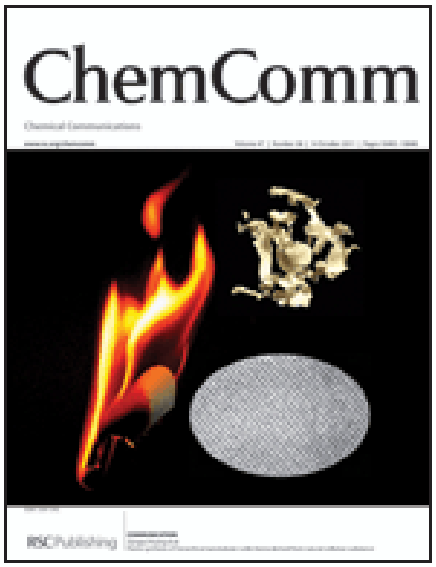

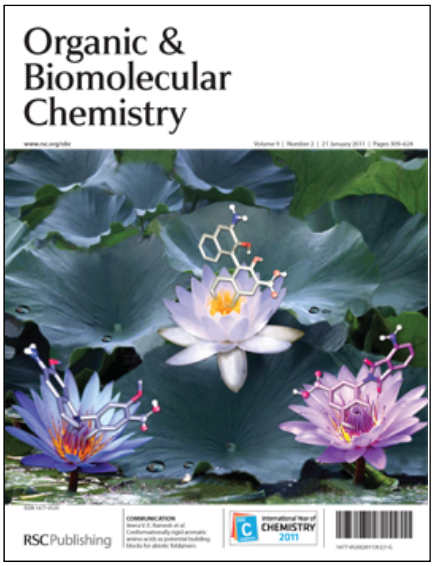

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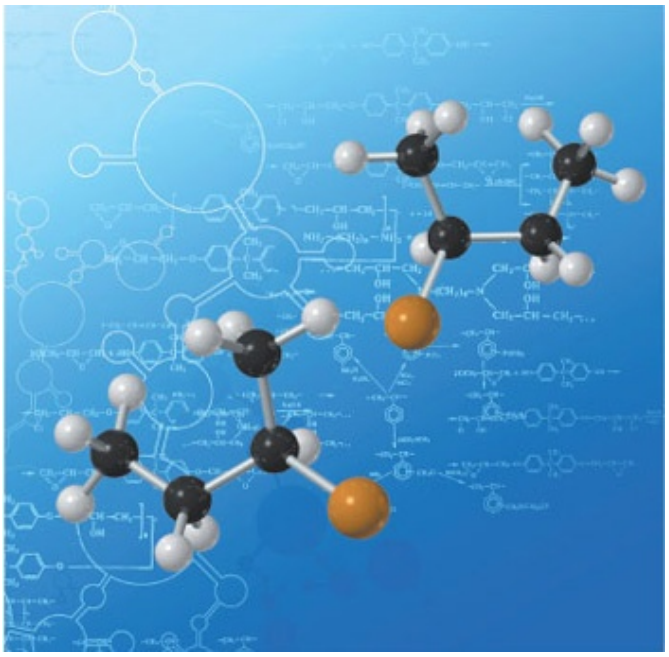

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PAPER

Unprecedented dithiolation of enals *via* their NHC-catalysed umpolung reaction with organic disulfides†

Santosh Singh and Lal Dhar S. Yadav*

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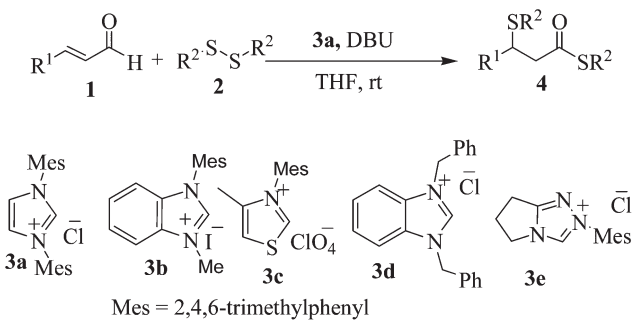
A novel one-pot *N*-heterocyclic carbene (NHC)-catalysed dithiolation of α,β-unsaturated aldehydes (enals) with organic disulfides is reported. The protocol involves homoenolate reactivity of enals, where the homoenolate attacks on the disulfide as a d^3 nucleophile followed by thioesterification to afford β-aryl/alkylsulfanyl thioesters with complete atom economy.

Introduction

The development of mild and efficient new catalytic methods for carbon–sulfur (C–S) bond formation without transition-metal catalyst remains a formidable challenge. Thiolation is among fundamental reactions in biochemistry.[1] Thioethers and thioesters play important roles in biological and chemical processes,[2a] and also serve as useful building blocks for various organosulfur compounds.[2b] Over the past two decades, NHCs have aroused considerable interest due to their continuously growing number of successful and novel applications in organic synthesis.[3] The NHC-catalysed umpolung reactivity of α,β-unsaturated aldehydes (enals) *via* Breslow or homoenolate intermediates has been well documented,[3h,i] where addition of an appropriate NHC to an enal renders it a d^3 nucleophile. The concept of homoenolate anions was introduced by Nickon and Lambert[4] in 1962. Their application in organic synthesis during the last four decades, however, was limited, presumably due to the difficulty in generating homoenolates directly.[5] After the introduction of a conceptually new approach to the generation of homoenolate[6] independently by Bode[6a] and Glorius *et al.*,[6d] the synthetic utility of homoenolate equivalent intermediates of enals has significantly increased. This is because they react with various electrophiles, like aldehydes,[6a] chalcones,[7a] dienones,[7b] diazenes,[7c] imines,[6c] alkyl/acyl halides,[7d,e] epoxides,[7f] aziridines[7g] and activated, polarized C=C double bonds[8] to afford an array of useful products. In the present study organic disulfides have been used, for the first time, as a new class of electrophiles in NHC-catalysed carbonyl umpolung reactions.

The literature scan reveals that no method is available for the direct synthesis of β-aryl/alkylsulfanyl thioesters from enals. However, there are only a few reports on the direct synthesis of β-arylsulfanyl thioesters starting from an enoic acid derivative instead of an enal, *viz.* by conjugate addition of thiols to thiocinnamates,[9a] 1-cinnamoyl-3,5-dimethyl pyrazole,[9b] or an *N*-cinnamoylbenzotriazole.[10] These methods suffer from limitations such as the use of malodorous substrates, thiols and moderate yields. Prompted by our previous efforts to develop synthetically useful processes in the area of NHC-catalysis[7e–g] and the surprising lack of convenient synthetic methods for β-aryl/alkylsulfanyl thioesters, we herein report a novel methodology for an efficient access to chemically and pharmaceutically relevant dithiolated products in a one-pot procedure (Scheme 1). The protocol involves the NHC-catalysed intermolecular thioaryl-/alkylation followed by thioesterification of enals **1** with organic disulfides **2** to afford β-aryl/alkylsulfanyl thioesters **4**. The reaction proceeds with complete atom economy and forms two biologically potent C–S bonds in a one-pot operation.

Thioesters are a useful class of organic compounds due to their wide range of biological activity and considerable applications in drug development[11] and industry.[12] In the past few years they have found increasingly important applications as intermediates for the preparation of heterocycles[13] and diverse ketones,[14] amides,[15] acyl radicals,[16] and biologically active compounds.[17] Moreover, the present reaction products β-aryl-/



Scheme 1 Synthesis of β-aryl/alkylsulfanyl thioesters **4**.

Green Synthesis Lab, Department of Chemistry, University of Allahabad, Allahabad-211 002, India. E-mail: ldsyadav@hotmail.com; Fax: +91 5322460533; Tel: +91 5322500652

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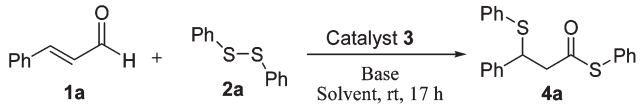
Table 1 Optimization of reaction conditions for the formation of representative compound **4a**[a]

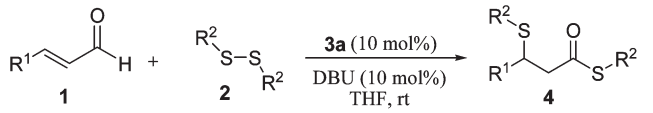


1a **2a** **4a**

Entry	Precatalyst (mol%)	Base	Solvent[b]	Yield[c]
1	**3a** (10)	DBU	THF	81
2	**3b** (10)	DBU	THF	59
3	**3c** (10)	DBU	THF	51
4	**3d** (10)	DBU	THF	0[e]
5	**3e** (10)	DBU	THF	56
6	**3a** (10)	TEA	THF	52
7	**3a** (10)	K_2CO_3	THF	48
8	**3a** (10)	DABCO	THF	34
9	**3a** (10)	DBU	THF–Bu^{t}OH[d]	62
10	**3a** (10)	DBU	THF–H_2O[d]	57
11	**3a** (10)	DBU	CH_2Cl_2	38
12	**3a** (7)	DBU	THF	78
13	**3a** (15)	DBU	THF	81
14	**3d** (30)	DBU	THF	81[f]
15	**3a** (15)	DBU	THF	81[g]
16	—	DBU	THF	0

[a] Reaction conditions: 0.12 mL (1 mmol) cinnamaldehyde, 218 mg (1 mmol) diphenyl disulfide, solvent (5 mL). [b] The different *N*-heterocyclic ammonium salts and bases are soluble in the solvents except potassium carbonate. [c] Yield of isolated and purified product. [d] THF–Bu^{t}OH or THF–H_2O; 10 : 01 were used. [e] Instead of **4a**, 35% of α,β-unsaturated thioester (phenyl thiocinnamate) was obtained. [f] Yield of α,β-unsaturated thioester (phenyl thiocinnamate). [g] Reaction was performed in refluxing solvent.

Table 2 Reaction of enals **1** with organic disulfides **2** yielding β-arylsulfanyl thioesters **4**[a]



1 **2** **4**

Entry	R^1	R^2	Product **4**	Time[b] (h)	Yield[c,d] (%)
1	Ph	Ph	**4a**	17	81
2	4-$NO_2C_6H_4$	Ph	**4b**	12	89
3	4-ClC_6H_4	Ph	**4c**	17	84
4	4-$MeOC_6H_4$	Ph	**4d**	17	78
5	Ph	4-ClC_6H_4	**4e**	18	79
6	4-$NO_2C_6H_4$	4-ClC_6H_4	**4f**	17	88
7	4-$MeOC_6H_4$	4-ClC_6H_4	**4g**	15	82
8	4-ClC_6H_4	4-ClC_6H_4	**4h**	12	86
9	Ph	4-MeC_6H_4	**4i**	19	77
10	4-$NO_2C_6H_4$	4-MeC_6H_4	**4j**	12	84
11	4-$MeOC_6H_4$	4-MeC_6H_4	**4k**	18	76
12	4-ClC_6H_4	4-MeC_6H_4	**4l**	15	82
13	CH_3	Ph	**4m**	19	60
14	CH_3	4-ClC_6H_4	**4n**	18	65
15	CH_3	4-MeC_6H_4	**4o**	20	57
16	Ph	Et	**4p**	23	60
17	4-$NO_2C_6H_4$	Et	**4q**	22	64
18	2-Furyl	Ph	**4r**	23	79
19	2-ClC_6H_4	Ph	**4s**	21	81
20	*p*-$CH_3C_6H_4$	Ph	**4t**	22	76

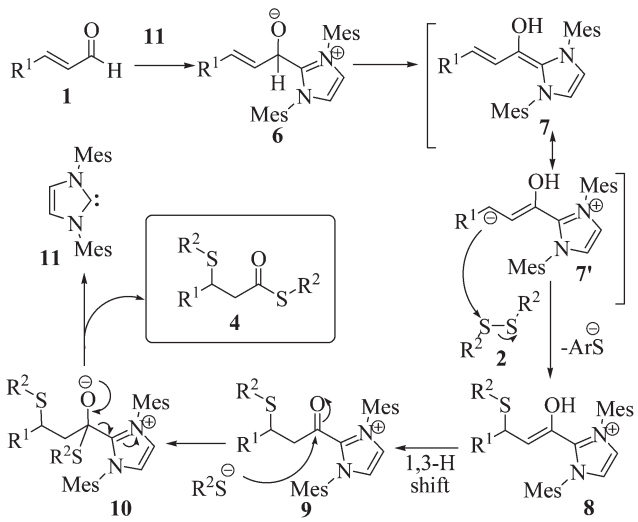
[a] Enal **1** (1 mmol) and disulfide **2** (1 mmol) were used for dithiolation in THF (5 mL) in the presence of bis-1,3-dibenzyl benzimidazolium salt **3d** (10 mol%) and DBU (10 mol%). [b] Stirring time at room temperature. [c] Yield of isolated and purified product **4**. [d] All compounds gave C, H and N analyses within ±0.38% and satisfactory spectral (IR, ^{1}H NMR, ^{13}C NMR and EIMS) data.

alkylsulfanyl thioesters **4** incorporate densely populated chemospecific functional groups including carbonyl, thioaryl, thioalkyl, thioester and active methylene groups, thereby provide handles for further manipulation in a multitude of synthetic organic transformations.

Results and discussion

Initial efforts were directed towards optimization of reaction conditions in regard with NHC-catalyst, base and solvent. Herein, cinnamaldehyde **1a** and diphenyl disulfide **2a** were chosen as model substrates for the synthesis of representative β-arylsulfanyl thioester **4a**, and the reaction was performed at room temperature (Table 1). Different types of *N*-heterocyclic carbene precursors **3a–e** were tested and **3a** was found to be the most effective precatalyst for the preparation of **4a** under the present reaction conditions (Table 1, entry 1). Then, we optimized the base and found that DBU was the best among TEA, K_2CO_3, DABCO, DBU, (Table 1, entries 6–8 and 1). The loading of precatalyst **3a** for the reaction was also optimized and was found to be 10 mol % along with 10 mol% of DBU. When the amount of the precatalyst was decreased from 10 mol% to 7 mol% relative to substrate **1a**, the yield of the β-arylsulfanyl thioester **4a** decreased (Table 1, entry 12), but the use of 15 mol% of **3a** did not affect the yield (Table 1, entries 1 and 13). The reaction did not occur without using the precatalyst **3** (Table 1, entry 16). Optimization of solvents for the synthesis of **4a** employing the precatalyst **3a** revealed that among THF, THF–Bu^{t}OH, THF–H_2O and CH_2Cl_2 (Table 1, entries 1 and 9–11), the best solvent in terms of yield was THF (Table 1, entry 7) and we used this solvent (THF) throughout the present study. It was also noted that a higher reaction temperature, for example, in a refluxing solvent instead of room temperature, did not increase the yield (Table 1, entry 15). Moreover, under the same reaction conditions *N*-heterocyclic carbene precursor **3d** formed α,β-unsaturated thioester (phenyl thiocinnamate) in 35% yield but on increasing the loading of **3d** from 10 to 30 mol%, the yield of the thioester was excellent (81%, Table 1, entry 14).

Encouraged by these results, next, we investigated the scope of this catalytic method for the synthesis of various β-aryl-/alkylsulfanyl thioester derivatives **4** (Table 2). Under the optimal conditions, cinnamaldehyde scaffolds were varied as shown in Table 2. Electron-withdrawing substituents such as 4-nitro, and 4-chloro in enals **1** gave the corresponding β-arylsulfanyl thioester derivatives in good to excellent yields (Table 2, entries 2, 3 compared to 4; 6, 8 compared to 7, and 10, 12 compared to 11). Whereas cinnamaldehyde with an electron-donating substituent such as 4-$MeOC_6H_4$ produced the desired thioesters in relatively lower yields (Table 2, entries 4, 7, 11 and 20). Aliphatic α,β-unsaturated aldehydes such as crotonaldehyde also responded well to this catalytic method, providing the thioesters in moderate yields (57–65%), under the same reaction conditions (Table 2, entries 13–15). Besides these aromatic/aliphatic α,β-unsaturated aldehydes, we also attempted the reaction using heteroaromatic



Scheme 2 A plausible mechanism for the formation of β-aryl/alkylsulfanyl thioesters **4**.

α,β-unsaturated aldehydes such as 3-(furan-2-yl)acrylaldehyde, and found that yields was also good (79%) in this case, under the same reaction conditions (Table 2, entry 18). Next, we extended this catalytic protocol toward other diaryl/dialkyl disulfide component. Diphenyl-, di-*p*-chlorophenyl-, di-*p*-methylphenyl- and diethyl disulfides smoothly underwent this catalytic reaction and gave the desired β-aryl/alkylsulfanyl thioesters in good yields (Table 2, entries 1–12) except in the case of aliphatic enals (Table 2, entries 13–15). But diethyl disulfide produced β-ethylsulfanyl thioesters in moderate yields (Table 2, entries 16 and 17).

The formation of β-aryl-/alkylsulfanyl thioester **4** may be tentatively rationalized by the postulated catalytic cycle (Scheme 2). The α,β-unsaturated aldehyde **1** is attacked by the *in situ* formed carbene **11** and the resulting zwitterionic intermediate **6** generates the conjugated Breslow intermediate **7**. This in turn attacks diaryl disulfide **2** as a d^3-nucleophile to form the intermediate **8**. The tautomerization of **8** to intermediate **9** is followed by an intermolecular attack of the aryl/alkyl sulfide anion at the carbonyl function to afford β-aryl-/alkylsulfanyl thioester **4** and the regeneration of the catalyst **11** (Scheme 2).

Conclusions

In summary, we have developed a novel *N*-heterocyclic carbene catalysed direct dithiolation of enals with organic disulfides to afford β-aryl-/alkylsulfanyl thioesters with complete atom economy. This is the first catalytic method where thioetherification and thioesterification take place in a one-pot operation to form two biologically potent C–S bonds efficiently.

Experimental

General

Melting points were determined by the open glass capillary method and are uncorrected. IR spectra in KBr were recorded on a Perkin-Elmer 993 IR spectrophotometer, ^{1}H NMR spectra were recorded on a Bruker WM-40 C (400 MHz) FT spectrometer in $CDCl_3$ using TMS as internal reference. ^{13}C NMR spectra were recorded on the same instrument at 100 MHz in $CDCl_3$ and TMS was used as internal reference. Mass spectra were recorded on a JEOL D-300 mass spectrometer. Elemental analyses were carried out in a Coleman automatic carbon, hydrogen and nitrogen analyser. All chemicals used were reagent grade and were used as received without further purification. Silica gel-G was used for TLC.

General procedure for the synthesis of β-aryl-/alkylsulfanyl thioesters. A flame-dried round bottom flask was charged with imidazolium salt **3a** (0.1 mmol), α,β-unsaturated aldehyde **1** (1.0 mmol) and 5 mL of THF under positive pressure of nitrogen followed by addition of DBU (0.1 mmol) with a syringe. After stirring at rt for 5 min, a solution of diphenyl disulfide **2** (1.0 mmol) in 1 mL THF was added. The resulting violet-red solution was stirred for 12–23 h at rt. After completion of the reaction (monitored by TLC), the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel column chromatography hexane/EtOAc (20 : 1) to afford analytically pure **4**. The structure of the products was confirmed by their elemental (C, H and N) analyses and spectral (IR, ^{1}H NMR, ^{13}C NMR and EIMS) data.

***S*-Phenyl-3-phenyl-3-(phenylsulfanyl)propanethioate(4a; Table 2; entry 1).** Mp 73–75 °C (Lit.[10] Mp 74–76 °C), IR (KBr): ν_{max} = 3051, 2921, 1708, 1615, 1578, 1509, 1453 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.45–7.19 (m, 15H, Ar–H), 4.81 (t, J = 7.0 Hz, 1H), 3.30 (d, J = 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.7, 142.3, 136.7, 134.6, 130.9, 130.1, 129.1, 128.3, 127.5, 126.6, 125.8, 125.0, 124.1, 51.6, 43.2; MS (EI): m/z = 350 (M^+); Anal. Calcd for $C_{21}H_{18}OS_2$: C, 71.96; H, 5.18%. Found: C, 71.58; H, 5.43%.

***S*-Phenyl-3-(4-nitrophenyl)-3-(phenylsulfanyl)propanethioate (4b; Table 2; entry 2).** Mp 76–77 °C (Lit.[10b] Mp 77–79 °C), IR (KBr): ν_{max} = 3125, 3071, 2938, 2855, 1704, 1605, 1519, 1349 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17–7.98 (m, 2H, Ar–H), 7.11–7.54 (m, 12H, Ar–H), 4.84 (t, J = 7.7 Hz, 1H), 3.36 (d, J = 7.7 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.1, 147.2, 136.7, 135.2, 132.9, 130.5, 129.5, 128.6, 127.7, 126.8, 125.4, 124.6, 121.4, 52.4, 42.9; MS (EI): m/z = 395 (M^+); Anal. Calcd for $C_{21}H_{17}NO_3S_2$: C, 63.77; H, 4.33; N, 3.54%. Found: C, 64.10; H, 4.12; N, 3.25%.

***S*-Phenyl-3-(4-chlorophenyl)-3-(phenylsulfanyl)propanethioate (4c; Table 2; entry 3).** Mp 85–86 °C (Lit.[10b] Mp 86–87 °C), IR (KBr): ν_{max} = 3052, 2909, 1703, 1614, 1456 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.35–7.11 (m, 14H, Ar–H), 4.79 (t, J = 7.6 Hz, 1H), 3.31 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.6, 139.2, 136.7, 134.8, 132.7, 131.4, 130.3, 129.5, 128.8, 127.7, 126.8, 125.7, 124.8, 52.7, 43.5; MS (EI): m/z = 384, 386 (M^+, M + 2). Anal. Calcd for $C_{21}H_{17}ClOS_2$: C, 65.52; H, 4.45%. Found: C, 65.86; H, 4.14%.

***S*-Phenyl-3-(4-methoxyphenyl)-3-(phenylsulfanyl)propanethioate (4d; Table 2; entry 4).** Mp 92–93 °C (Lit.[10b] Mp 93–95 °C), IR (KBr): ν_{max} = 3050, 2904, 1709, 1618, 1454 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.24–6.86 (m, 14H, Ar–H), 4.74 (t, J =

7.6 Hz, 1H), 3.82 (s, 3H), 3.30 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5, 159.4, 135.5, 134.2, 132.1, 130.8, 129.5, 128.8, 127.6, 126.8, 125.9, 125.1, 114.4, 55.1, 52.9, 43.8; MS (EI): m/z = 380 (M^+). Anal. Calcd for $C_{22}H_{20}O_2S_2$: C, 69.44; H, 5.30%. Found: C, 69.68; H, 5.53%.

***S*-4-Chlorophenyl-3-(4-chlorophenylsulfanyl)-3-phenyl-propanethioate (4e; Table 2; entry 5).** Mp 64–65 °C (Lit.[10] Mp 63–65 °C), IR (KBr): ν_{max} = 3058, 2908, 1710, 1618, 1448 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18–7.54 (m, 13H, Ar–H), 4.76 (t, J = 7.6 Hz, 1H), 3.29 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.3, 141.6, 134.5, 133.4, 132.6, 131.9, 131.0, 130.2, 129.4, 128.3, 127.5, 126.6, 125.8, 52.4, 43.8; MS (EI): m/z = 418, 420 (M^+, M + 2); Anal. Calcd for $C_{21}H_{16}Cl_2OS_2$: C, 60.14; H, 3.85%. Found: C, 59.80; H, 4.09%.

***S*-4-Chlorophenyl-3-(4-chlorophenylsulfanyl)-3-(4-nitrophenyl)-propanethioate (4f; Table 2; entry 6).** Mp 101–102 °C, IR (KBr): ν_{max} = 3110, 3070, 2909, 1709, 1612, 1452 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.16–7.96 (m, 2H, Ar–H), 7.42–7.15 (m, 10H, Ar–H), 4.81 (t, J = 7.6 Hz, 1H), 3.33 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.4, 147.9, 146.2, 134.4, 133.5, 132.6, 131.8, 130.7, 129.4, 128.6, 127.8, 126.9, 121.6, 52.8, 43.6; MS (EI): m/z = 463, 465 (M^+, M + 2); Anal. Calcd for $C_{21}H_{15}Cl_2NO_3S_2$: C, 54.31; H, 3.26; N, 3.02%. Found: C, 54.06; H, 3.64; N, 2.78%.

***S*-4-Chlorophenyl-3-(4-chlorophenylsulfanyl)-3-(4-methoxyphenyl)propanethioate (4g; Table 2; entry 7).** Mp 81–83 °C, IR (KBr): ν_{max} = 3105, 2919, 1708, 1614, 1449 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.18–6.81 (m, 12H, Ar–H), 4.77 (t, J = 7.5 Hz, 1H), 3.83 (s, 3H), 3.30 (d, J = 7.5 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.1, 159.7, 135.2, 134.0, 133.2, 132.1, 131.4, 130.5, 129.8, 128.9, 127.6, 126.8, 114.8, 55.2, 52.4, 43.6; MS (EI): m/z = 448, 450 (M^+, M + 2). Anal. Calcd for $C_{22}H_{18}Cl_2O_2S_2$: C, 58.80; H, 4.04%. Found: C, 59.07; H, 3.79%.

***S*-4-Chlorophenyl-3-(4-chlorophenylsulfanyl)-3-(4-chlorophenyl)-propanethioate (4h; Table 2; entry 8).** Mp 97–98 °C, IR (KBr): ν_{max} = 3048, 2903, 1709, 1614, 1452 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.31–7.15 (m, 12H, Ar–H), 4.75 (t, J = 7.6 Hz, 1H). 3.31 (d, J = 7.6 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.7, 139.6, 136.5, 134.5, 133.7, 132.4, 131.6, 130.8, 130.0, 129.2, 128.4, 127.1, 126.2, 52.5, 43.4; MS (EI): m/z = 451, 453 (M^+, M + 2); Anal. Calcd for $C_{21}H_{15}Cl_3OS_2$: C, 55.58; H, 3.33%. Found: C, 55.23; H, 3.59%.

***S*-*p*-Tolyl-3-(*p*-tolylsulfanyl)-3-phenylpropanethioate (4i; Table 2; entry 9).** Mp 83–84 °C (Lit.[10] Mp 82–83 °C), IR (KBr): ν_{max} = 3051, 2911, 1702, 1621, 1454 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.41–7.09 (m, 13H, Ar–H), 4.79 (t, J = 7.5 Hz, 1H), 3.34 (d, J = 7.5 Hz, 2H), 2.34 (s, 3H), 2.38 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.8, 142.1, 135.8, 134.9, 132.2, 131.1, 130.3, 129.3, 128.5, 127.7, 126.8, 126.0, 125.2, 52.5, 43.1, 25.4, 24.6; MS (EI): m/z = 378 (M^+); Anal. Calcd for $C_{23}H_{22}OS_2$: C, 72.97; H, 5.86%. Found: C, 73.24; H, 6.07%.

***S*-*p*-Tolyl-3-(*p*-tolylsulfanyl)-3-(4-nitrophenyl)propanethioate (4j; Table 2; entry 10).** Mp 92–93 °C, IR (KBr): ν_{max} = 3051, 2941, 1703, 1618, 1452 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11–7.99 (m, 2H, Ar–H), 7.11–7.44 (m, 6H, Ar–H), 6.88–7.13 (m, 4H, Ar–H), 4.79 (t, J = 7.6 Hz, 1H), 3.32 (d, J = 7.6 Hz, 2H), 2.39 (s, 3H), 2.31 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.5, 147.9, 146.5, 135.4, 134.8, 133.6, 132.4, 129.7, 128.9, 127.7, 126.7, 125.6, 121.4, 52.6, 42.9, 25.2, 24.1; MS (EI): m/z = 423 (M^+); Anal. Calcd for $C_{23}H_{21}NO_3S_2$: C, 65.22; H, 5.00; N, 3.31%. Found: C, 65.58; H, 5.21; N, 3.05%.

***S*-*p*-Tolyl-3-(*p*-tolylsulfanyl)-3-(4-methoxyphenyl)propanethioate (4k; Table 2; entry 11).** Mp 78–80 °C, IR (KBr): ν_{max} = 3055, 2961, 1701, 1619, 1455 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.22–6.87 (m, 12H, Ar–H), 4.78 (t, J = 7.6 Hz, 1H), 3.84 (s, 3H), 3.28 (d, J = 7.6 Hz, 2H), 2.35 (s, 3H), 2.29 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.3, 159.2, 135.7, 134.9, 133.7, 132.8, 131.6, 130.7, 129.9, 128.9, 127.7, 126.8, 114.7, 55.4, 52.6, 42.9, 25.2, 24.1; MS (EI): m/z = 408 (M^+); Anal. Calcd for $C_{24}H_{24}O_2S_2$: C, 70.55; H, 5.92%. Found: C, 70.24; H, 5.65%.

***S*-*p*-Tolyl-3-(*p*-tolylsulfanyl)-3-(4-chlorophenyl)propanethioate (4l; Table 2; entry 12).** Mp 89–90 °C, IR (KBr): ν_{max} = 3053, 2912, 1704, 1618, 1583, 1509, 1449 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.28–7.09 (m, 12H, Ar–H), 4.78 (t, J = 7.5 Hz, 1H), 3.32 (d, J = 7.5 Hz, 2H), 2.36 (s, 3H), 2.30 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.4, 138.8, 134.9, 133.4, 132.5, 131.6, 130.4, 129.6, 128.9, 128.3, 127.6, 126.9, 125.7, 52.0, 43.2, 25.4, 24.5; MS (EI): m/z = 412, 414 (M^+, M + 2); Anal. Calcd for $C_{23}H_{21}ClOS_2$: C, 66.89; H, 5.13%. Found: C, 66.67; H, 5.33%.

***S*-Phenyl-3-(phenylsulfanyl)butanethioate (4m; Table 2; entry 13).** Yellow oil, IR (KBr): ν_{max} = 3051, 2960, 2928, 2859, 1706, 1578, 1478, 1436 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.44–7.18 (m, 10H, Ar–H), 3.71 (m, 1H), 2.99 (dd, J = 15.5, 5.4 Hz, 1H), 2.71 (dd, J = 15.5, 9.0 Hz, 1H), 1.34 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.9, 137.4, 135.3, 134.7, 129.3, 128.6, 127.9, 126.9, 125.8, 52.3, 37.4, 22.2; MS (EI): m/z = 288 (M^+). Anal. Calcd for $C_{16}H_{16}OS_2$: C, 66.63; H, 5.59%. Found: C, 66.87; H, 5.41%.

***S*-4-Chlorophenyl-3-(4-chlorophenylsulfanyl)butanethioate (4n; Table 2; entry 14).** Yellow oil, IR (KBr): ν_{max} = 3058, 2972, 2932, 2862, 1709, 1584, 1475, 1442 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.48–7.24 (m, 8H, Ar–H), 3.74 (m, 1H), 2.96 (dd, J = 15.4, 5.4 Hz, 1H), 2.75 (dd, J = 15.4, 9.0 Hz, 1H), 1.36 (d, J = 6.9 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.2, 137.1, 135.8, 134.3, 131.9, 130.8, 129.2, 128.4, 127.2, 52.5, 37.1, 21.8; MS (EI): m/z = 356, 358 (M^+, M + 2); Anal. Calcd for $C_{16}H_{14}Cl_2OS_2$: C, 53.78; H, 3.95%. Found: C, 54.05; H, 4.17%.

***S*-*p*-Tolyl-3-(*p*-tolylsulfanyl)butanethioate (4o; Table 2; entry 15).** Yellow oil, IR (KBr): ν_{max} = 3047, 2957, 2930, 2861, 1702, 1574, 1475, 1438 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.11–6.87 (m, 8H, Ar–H), 2.97 (m, 1H), 2.69 (d, J = 7.3 Hz, 2H), 2.38 (s, 3H), 2.32 (s, 3H), 1.43 (d, J = 7.1 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.6, 135.4, 134.8, 132.6, 131.7, 130.9, 130.3, 129.1, 128.6, 52.1, 37.5, 25.8, 25.1, 22.3; MS (EI): m/z = 316 (M^+); Anal. Calcd for $C_{18}H_{20}OS_2$: C, 68.31; H, 6.37%. Found: C, 68.18; H, 6.45%.

***S*-Ethyl-3-(ethylsulfanyl)-3phenylpropanethioate (4p; Table 2; entry 16).** Mp 56–57 °C, IR (KBr): ν_{max} = 3051, 2960, 2933, 2842, 1696, 1576, 1453 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.38–7.06 (m, 5H, Ar–H), 3.81 (t, J = 7.3 Hz, 1H), 3.26 (d, J = 7.3 Hz, 2H), 3.03 (q, J = 7.1 Hz, 2H), 2.49 (q, J = 7.0, 2H), 1.27 (t, J = 7.0, 3H), 1.32 (t, J = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.4, 138.2, 130.6, 129.4, 128.8, 52.2, 42.3, 30.6, 28.4, 15.2, 12.8; MS (EI): m/z = 254 (M^+); Anal. Calcd for $C_{13}H_{18}OS_2$: C, 61.37; H, 7.13%. Found: C, 61.59; H, 6.91%.

***S*-Ethyl-3-(ethylsulfanyl)-3-(4-nitrophenyl)propanethioate (4q; Table 2; entry 17).** Mp 64–65 °C, IR (KBr): ν_{max} = 3062, 2955, 2941, 2848, 1694, 1582, 1455 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 8.19–8.02 (m, 2H, Ar–H), 7.28–7.41 (m, 2H, Ar–H), 3.84 (t, J = 7.3 Hz, 1H), 3.23 (d, J = 7.3 Hz, 2H), 3.06 (q, J = 7.1 Hz, 2H), 2.51 (q, J = 7.0, 2H), 1.26 (t, J = 7.0, 3H), 1.30 (t, J = 7.1, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 198.7, 145.2, 143.6, 130.4, 122.5, 51.9, 42.1, 30.8, 28.6, 14.8, 13.1; MS (EI): m/z = 299 (M^+); Anal. Calcd for $C_{13}H_{17}NO_3S_2$: C, 52.15; H, 5.72; N, 4.68%. Found: C, 51.89; H, 5.57, N, 4.86%.

***S*-Phenyl 3-(furan-2-yl)-3-(phenylsulfanyl)propanethioate (4r; Table 2; entry 18).** Mp 49–51 °C, IR (KBr): ν_{max} = 3117, 3055, 2942, 1714, 1627, 1569, 1451 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.49–7.18 (m, 13H, Ar–H), 4.97 (t, J = 7.0 Hz, 1H), 3.41 (d, J = 7.0 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.1, 152.7, 141.8, 137.8, 134.7, 134.1, 129.6, 128.5, 127.4, 126.9, 125.5, 111.4, 108.6, 51.7, 43.8; MS (EI): m/z = 340 (M^+). Anal. Calcd for $C_{19}H_{16}O_2S_2$: C, 67.03; H, 4.74%. Found: C, 67.28; H, 4.86%.

***S*-Phenyl-3-(2-chlorophenyl)-3-(phenylsulfanyl)propanethioate (4s; Table 2; entry 19).** Mp 71–73 °C, IR (KBr): ν_{max} = 3052, 2917, 1710, 1614, 1580, 1455 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.39–7.18 (m, 14H, Ar–H), 5.30 (t, J = 7.2 Hz, 1H), 3.30 (d, J = 7.2 Hz, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.6, 138.2, 135.1, 134.2, 133.4, 132.6, 131.4, 130.1, 129.5, 128.8, 128.2, 127.5, 126.8, 126.1, 125.5, 47.8, 45.5; MS (EI): m/z = 384, 386 (M^+, M + 2). Anal. Calcd for $C_{21}H_{17}ClOS_2$: C, 65.52; H, 4.45%. Found: C, 65.33; H, 4.31%.

***S*-Phenyl-3-(phenylsulfanyl)-3-*p*-tolylpropanethioate (4t; Table 2; entry 20).** Mp 60–62 °C (Lit.[10] Mp 59–61 °C), IR (KBr): ν_{max} = 3056, 3036, 2910, 1701, 1605, 1578, 1450 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 7.20–7.38 (m, 10H, Ar–H), 7.16 (d, J = 7.6 Hz, 2H), 7.04 (d, J = 7.6 Hz, 2H), 4.72 (t, J = 7.1 Hz, 1H), 3.27 (d, J = 7.1 Hz, 2H), 2.33 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 195.4, 138.1, 136.7, 134.6, 133.5, 132.4, 131.1, 130.3, 129.5, 128.6, 127.8, 127.0, 126.1, 50.6, 48.2, 22.1; MS (EI): m/z = 364 (M^+); Anal. Calcd for $C_{22}H_{20}OS_2$: C, 72.49; H, 5.53%. Found: C, 72.61; H, 5.41%.

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