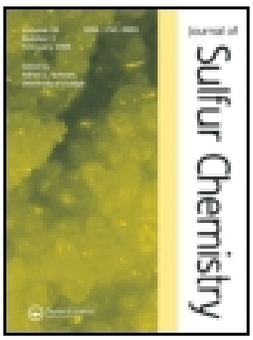

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An efficient, four-component reaction for the synthesis of novel carbamodithioates

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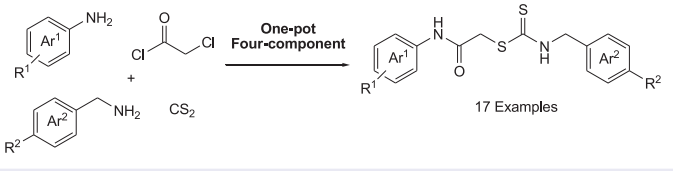
ABSTRACT

A series of substituted phenylcarbamoyl methyl benzylcarbamodithioates have been synthesized using the multicomponent condition. The reaction proceeded under mild practical condition and afforded the desired products in good yields.



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Dithiocarbamate; four-component; one-pot; CS_2; chloroacetyl chloride

1. Introduction

The multi-component reaction (MCR) plays an undeniable role for the interfacing of chemistry with biology to introduce novel biologically active molecules [1]. The advantageous features of this reaction make this protocol well suited for the one-pot generation of drug targets. Despite the presence of few drugs based on multicomponent synthesis in the market [2], there is an ever increasing effort directed toward combinatorial library construction [3,4] with the hopes for finding interesting scaffolds, exhibiting reasonable levels of bioactivities.

In the literature, dithiocarbamates have been identified as a potent building block in a number of useful biomolecules [5–16]. The presence of this moiety in phytoalexins brassinin [17–22], the antimicrobial agent produced by genus *Brassica* in the case of exposure to chemical and biological stress [23,24], along with its incorporation as a side chain into various cores [25] like quinazoline [26–29] and pyrrolidine [30] led to the significant

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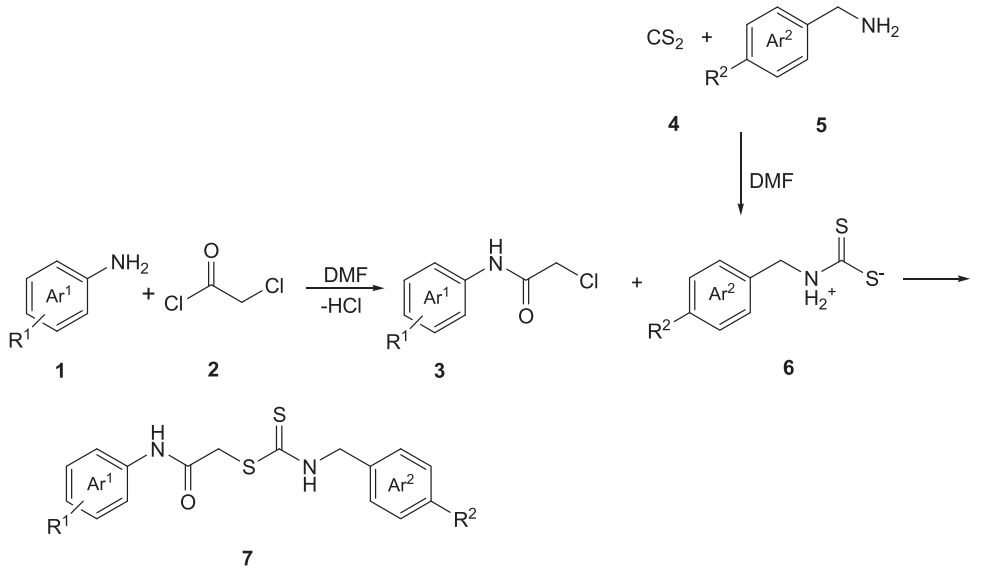
cancer chemopreventive and cytotoxic activities. Dithiocarbamates have also found applications in organic synthesis mainly relying on their role as a mediator in carbamoyl radical cyclization reactions [31]. Because of the important biological and synthetic applications of dithiocarbamates, it is a highly desirable endeavor to synthesize such an important building block in a simple and one-pot manner.

As part of our ongoing research program aimed at the synthesis of novel molecules, [32–38] in this paper, we present a simple, four-component synthesis of substituted phenylcarbamoyl methyl benzylcarbamodithioates by the reaction of aniline derivatives, benzyl amines, chloroacetyl chloride, and carbon disulfide.

2. Results and discussion

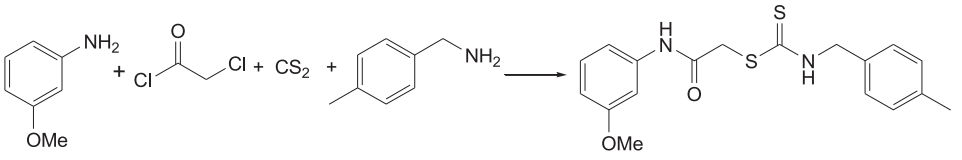
The reaction of anilines and chloroacetyl chloride produced compounds **3** upon stirring at room temperature. The addition of carbon disulfide and benzyl amines to this pot generated compounds **7** in good yields (Scheme 1).

In an effort to find the optimal reaction condition, we chose *meta*-anisidine **1b**, chloroacetyl chloride **2**, carbon disulfide **4** and 4-methyl benzylamine **5b** as model substrates and tested the reaction in different solvents (including DMF, acetonitrile, acetone, THF, ethanol and methanol) at room temperature. The sequence of the addition was also important to achieve high yields in short reaction times. The results are given in Table 1. By employing DMF as the medium, the reaction proceeded rapidly and afforded the product in high yield (Table 1, entry 1). DMF is effective for this reaction, due to the stabilizing effect of this solvent and its ability to solubilize intermediate salt **6**. Other solvents were less effective in terms of the isolated yields and reaction times (Table 1, entries **2**–**6**).



Scheme 1. One-pot, four-component synthesis of carbamodithioates.

Table 1. Solvent screening.[a]



Entry	Solvent	Time (h)	Yield (%)[b]
1	DMF	1	81
2	Acetonitrile	3	54
3	Ethanol	8	51
4	Methanol	6	47
5	Acetone	12	38
6	THF	12	31

[a]Reactions were run at room temperature.
[b]Isolated yields.

Table 2. Substrate scope of the reaction (Scheme 1).

Compound	Ar^1	Ar^2	Time (min)	Yield (%)[a]
7a	C_6H_5	C_6H_5	70	70
7b	C_6H_5	4-MeC_6H_4	90	75
7c	C_6H_5	4-ClC_6H_4	120	68
7d	3-$MeOC_6H_4$	C_6H_5	90	74
7e	3-$MeOC_6H_4$	4-MeC_6H_4	60	81
7f	3-$MeOC_6H_4$	4-ClC_6H_4	105	70
7g	2-FC_6H_4	C_6H_5	140	68
7h	2-FC_6H_4	4-MeC_6H_4	100	69
7i	2-FC_6H_4	4-ClC_6H_4	160	65
7j	3-ClC_6H_4	4-MeC_6H_4	120	71
7k	2,5-$Cl_2C_6H_3$	C_6H_5	130	70
7l	2,5-$Cl_2C_6H_3$	4-MeC_6H_4	110	75
7m	2,5-$Cl_2C_6H_3$	4-ClC_6H_4	170	69
7n	3,4-$Cl_2C_6H_3$	C_6H_5	130	71
7o	3,4-$Cl_2C_6H_3$	4-MeC_6H_4	120	76
7p	3,4-$Cl_2C_6H_3$	4-ClC_6H_4	150	70
7q	4-BrC_6H_4	C_6H_5	180	67

[a]Isolated yields.

For library construction, the optimized condition was used for different commercially available primary amines. The presence of both electron-withdrawing and electron-donating groups in these compounds at different positions led to the easy generation of the desired products **7a–7q** (Table 2). Electron-donating groups gave rise to the corresponding products in higher yields.

The structure of compounds **7a–7q** were confirmed by IR, ^{1}H-NMR and ^{13}C-NMR spectroscopy. The ^{1}H-NMR spectrum of compound **7p** exhibited two singlet peaks for the methylene groups at 4.26 and 4.83 ppm along with characteristic signals for aryl and NH protons (9.99 and 10.62 ppm). The ^{13}C NMR spectrum of this compound exhibited characteristic signals for CH_2S at 40 ppm and CH_2N at 49 ppm in the aliphatic region. The C=O and C=S groups appeared at 166 and 196 ppm, respectively, along with 10 aromatic carbons.

3. Conclusion

In conclusion, we have developed an efficient one-pot, four-component synthesis of substituted phenylcarbamoyl methyl benzylcarbamodithioates. Given the large number of commercially available aniline and benzyl amines derivatives, this method was applicable for the synthesis of a library of compound **7**.

4. Experimental

Melting points were taken on a Kofler hot-stage apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker FT-500, using tetramethylsilane (TMS) as an internal standard. The infrared (IR) spectra were obtained on a Nicolet Magna FT-IR 550 spectrophotometer (KBr disks). Mass spectra were recorded on an Agilent Technology (HP) mass spectrometer operating at an ionization potential of 70 eV. Elemental analyses were carried out with a Perkin-Elmer model 240-C apparatus.

4.1. General procedure for the synthesis of compounds 7a–7q

To a stirred solution of substituted aniline (1 mmol) and chloroacetyl chloride (1 mmol) which was stirred in 5 mL DMF for 20 min, were added benzyl amine derivatives (1.3 mmol) and CS_2 (5 mmol). The reaction mixture was allowed to stir for required additional time (Table 2). Then, 5 mL of water was added and the solution was extracted with ethyl acetate and dried over sodium sulfate and purified by passing over a silica gel column chromatography using petroleum ether/ethyl acetate (8:2).

4.1.1. (Phenylcarbamoyl)methyl benzylcarbamodithioate (7a)

Colorless powder; Yield 70%; mp 122–124°C; IR (KBr, cm^{-1}): 3206, 1666, 1600, 1537, 1495, 1442, 1394, 1328, 922, 750, 690; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.07 (s, 2H, CH_2S), 4.92 (d, J = 5.0 Hz, 2H, CH_2NH), 7.10 (t, J = 7.5 Hz, 1H, H_{4Ar^1}), 7.25–7.36 (m, 7H), 7.49 (d, J = 8.5 Hz, 2H, $H_{2,6Ar^1}$), 7.82 (brs, NH), 8.76 (s, NH). EI-MS: 316 (M^+, 18), 182 (33), 134 (100), 106 (56), 92 (62), 77 (45). Anal. calcd. for $C_{16}H_{16}N_2OS_2$: C 60.73, H 5.10, N 8.85; found: C 60.64, H 5.19, N 8.78.

4.1.2. (Phenylcarbamoyl)methyl 4-methylbenzylcarbamodithioate (7b)

Colorless powder; Yield 75%; mp 115–117°C; IR (KBr, cm^{-1}): 3148, 1676, 1601, 1546, 1518, 1497, 1442, 1356, 941, 831, 750; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.17 (s, 3H, CH_3), 4.08 (s, 2H, CH_2S), 4.87 (d, J = 5.0 Hz, 2H, CH_2NH), 7.11 (t, J = 7.5 Hz, 1H, H_{4Ar^1}), 7.17 (d, J = 8.5 Hz, 2H, $H_{3,5Ar^2}$), 7.22 (d, J = 8.5 Hz, 2H, $H_{2,6Ar^2}$), 7.31 (t, J = 7.5 Hz, 2H, $H_{3,5Ar^1}$), 7.50 (d, J = 7.5 Hz, 2H, $H_{2,6Ar^1}$), 7.73 (brs, NH), 8.79 (s, NH). Anal. calcd. for $C_{17}H_{18}N_2OS_2$: C 61.79, H 5.49, N 8.48; found: C 61.86, H 5.60, N 8.55.

4.1.3. (Phenylcarbamoyl)methyl 4-chlorobenzylcarbamodithioate (7c)

Colorless powder; Yield 68%; mp 130–131°C; IR (KBr, cm^{-1}): 3247, 1643, 1600, 1519, 1497, 1443, 1326, 918, 832, 754; ^{1}H NMR (500 MHz, DMSO-d_6): δ 4.20 (s, 2H, CH_2S), 4.83 (s, 2H, CH_2NH), 7.06 (t, J = 7.5 Hz, 1H, H_{4Ar^1}), 7.29 (d, J = 8.0 Hz, 2H, $H_{2,6Ar^2}$), 7.33 (d, J = 8.0 Hz, 2H, $H_{3,5Ar^2}$), 7.39 (t, J = 8.0 Hz, 2H, $H_{3,5Ar^1}$), 7.57 (d, J = 8.0 Hz, 2H,

$H_{2,6Ar^1}$), 10.22 (s, NH), 10.59 (brs, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 39.4 (CH_2S), 48.9 (CH_2N), 119.1, 123.4, 127.9, 128.8, 129.1, 131.7, 136.1, 138.8, 165.7 (C=O), 196.2 (C=S). Anal. calcd. for $C_{16}H_{15}ClN_2OS_2$: C 54.77, H 4.31, N 7.98; found: C 54.83, H 4.40, N 8.06.

4.1.4. (3-Methoxyphenylcarbamoyl)methyl benzylcarbamodithioate (7d)

Colorless powder; Yield 74%; mp 80–82°C; IR (KBr, cm^{-1}): 3142, 1677, 1610, 1521, 1495, 1326, 1283, 1206, 1085, 936, 752, 694; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.79 (s, 3H, OCH_3), 4.06 (s, 2H, CH_2S), 4.91 (d, J = 5.0 Hz, 2H, CH_2NH), 6.6 (d, J = 8.0 Hz, 1H, H_{4Ar^1}), 6.97 (d, J = 8.0 Hz, 1H, H_{6Ar^1}), 7.19 (t, J = 8.0 Hz, 1H, H_{5Ar^1}), 7.25 (d, J = 3.0 Hz, 1H, H_{2Ar^1}), 7.32–7.36 (m, 5H), 8.02 (brs, NH), 8.83 (s, NH). Anal. calcd. for $C_{17}H_{18}N_2O_2S_2$: C 58.93, H 5.24, N 8.09; found: C 58.99, H 5.17, N 8.16.

4.1.5. (3-Methoxyphenylcarbamoyl)methyl 4-methylbenzylcarbamodithioate (7e)

Colorless powder; Yield 81%; mp 114–116°C; IR (KBr, cm^{-1}): 3266, 1660, 1611, 1548, 1514, 1464, 1322, 1212, 916, 845, 753; ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.28 (s, 3H, CH_3), 3.73 (s, 3H, OCH_3), 4.17 (s, 2H, CH_2S), 4.78 (d, J = 5.5 Hz, 2H, CH_2NH), 6.64 (dd, J = 8.5, 2.3 Hz, 1H, H_{4Ar^1}), 7.08 (d, J = 7.5 Hz, 1H, H_{6Ar^1}), 7.13 (d, J = 8.5 Hz, 2H, $H_{3,5Ar^2}$), 7.19 (d, J = 8.5 Hz, 2H, $H_{2,6Ar^2}$), 7.22 (m, 1H, H_{2Ar^1}), 7.26 (m, 1H, H_{5Ar^1}), 10.19 (s, NH), 10.52 (t, J = 5.5 Hz, NH). Anal. calcd. for $C_{18}H_{20}N_2O_2S_2$: C 59.97, H 5.59, N 7.77; found: C 60.04, H 5.66, N 7.89.

4.1.6. (3-Methoxyphenylcarbamoyl)methyl 4-chlorobenzylcarbamodithioate (7f)

Colorless powder; Yield 70%; mp 104–106°C; IR (KBr, cm^{-1}): 3220, 1674, 1609, 1523, 1494, 1426, 1326, 1283, 1088, 931, 843; ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.78 (s, 3H, OCH_3), 4.03 (s, 2H, CH_2S), 4.89 (d, J = 5.0 Hz, 2H, CH_2NH), 6.67 (dd, J = 7.5, 2.0 Hz, 1H, H_{4Ar^1}), 6.95 (d, J = 7.5 Hz, 1H, H_{6Ar^1}), 7.18–7.22 (m, 2H), 7.26–7.27 (m, 2H), 7.32 (d, J = 8.0 Hz, 2H, $H_{2,6Ar^2}$), 8.33 (brs, NH), 8.78 (s, NH). Anal. calcd. for $C_{17}H_{17}ClN_2O_2S_2$: C 53.60, H 4.50, N 7.35; found: C 53.71, H 4.57, N 7.47.

4.1.7. (2-Fluorophenylcarbamoyl)methyl benzylcarbamodithioate (7g)

Colorless powder; Yield 68%; mp 128–130°C; IR (KBr, cm^{-1}): 3200, 1704, 1617, 1536, 1496, 1376, 1346, 1299, 1193, 754; ^{1}H NMR (500 MHz, DMSO-d_6): δ 4.26 (s, 2H, CH_2S), 4.85 (s, 2H, CH_2NH), 7.15–7.18 (m, 2H), 7.23–7.26 (m, 2H), 7.28–7.35 (m, 4H), 7.88–7.90 (m, 1H), 9.99 (s, NH), 10.59 (brs, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 40.3 (CH_2S), 49.8 (CH_2N), 115.4, 123.7, 124.3, 125.3, 125.8, 127.3, 128.2, 128.4, 137.1, 154.4 (d, J_{C-F} = 225 Hz), 166.4 (C=O), 195.9 (C=S). Anal. calcd. for $C_{16}H_{15}FN_2OS_2$: C 57.46, H 4.52, N 8.38; found: C 57.38, H 4.65, N 8.29.

4.1.8. 4(2-Fluorophenylcarbamoyl)methyl 4-methylbenzylcarbamodithioate (7h)

Colorless powder; Yield 69%; mp 119–121°C; IR (KBr, cm^{-1}): 3185, 1665, 1539, 1525, 1490, 1457, 1330, 908, 824, 760; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.35 (s, 3H, CH_3), 4.15 (s, 2H, CH_2S), 4.87 (s, 2H, CH_2NH), 7.06–7.11 (m, 3H), 7.16–7.58 (m, 4H), 7.58 (m, 1H), 8.25 (brs, NH), 8.77 (s, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.1 (CH_3), 39.2 (CH_2S), 52.0 (CH_2N), 114.8, 115.0, 121.9, 124.5, 128.0, 128.3, 129.7, 132.5, 138.2, 156.9

(d, J_{C-F} = 250 Hz), 167.1 (C=O), 196.0 (C=S). Anal. calcd. for $C_{17}H_{17}FN_2OS_2$: C 58.60, H 4.92, N 8.04; found: C 58.53, H 5.01, N 8.11.

4.1.9. (2-Fluorophenylcarbamoyl)methyl 4-chlorobenzylcarbamodithioate (7i)

Colorless powder; Yield 65%; mp 100–103°C; IR (KBr, cm^{-1}): 1676, 1633, 1489, 1456, 1328, 1083, 925, 752; ^{1}H NMR (500 MHz, DMSO-d_6): 4.26 (s, 2H, CH_2S), 4.85 (d, J = 5.5 Hz, 2H, CH_2NH), 7.15–7.17 (m, 2H), 7.23–7.26 (m, 1H), 7.30 (d, J = 7.5 Hz, 2H, $H_{2,6Ar^2}$), 7.39 (d, J = 7.5 Hz, 2H, $H_{3,5Ar^2}$), 7.86–7.90 (m, 1H), 9.98 (s, NH), 10.61 (t, J = 5.5 Hz, NH). ^{13}C NMR (125 MHz, DMSO-d_6): 49.0 (CH_2S), 66.9 (CH_2N), 115.4, 123.7, 124.3, 125.3, 125.9, 128.1, 128.4, 129.2, 136.1, 159.2 (d, J_{C-F} = 212 Hz), 166.4 (C=O), 196.1 (C=S). Anal. calcd. for $C_{16}H_{14}ClFN_2OS_2$: C 52.10, H 3.83, N 7.59; found: C 51.99, H 3.92, N 7.48.

4.1.10. (3-Chlorophenylcarbamoyl)methyl 4-methylbenzylcarbamodithioate (7j)

Colorless powder; Yield 71%; mp 115–117°C; IR (KBr, cm^{-1}): 3225, 1657, 1643, 1592, 1532, 1426, 1368, 1319, 916, 822, 781; ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.28 (s, 3H, CH_3), 4.20 (s, 2H, CH_2S), 4.78 (d, J = 4.0 Hz, 2H, CH_2NH), 7.12 (d, J = 7.5 Hz, 2H, $H_{3,5Ar^2}$), 7.18 (d, J = 7.5 Hz, 2H, $H_{2,6Ar^2}$), 7.32–7.35 (m, 2H), 7.43 (d, J = 7.5 Hz, 1H, H_{4Ar^1}), 7.79 (s, 1H, H_{2Ar^1}), 10.42 (brs, NH), 10.55 (s, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 20.6 (CH_3), 40.6 (CH_2S), 49.6 (CH_2N), 118.5, 123.0, 127.7, 128.8, 130.3, 130.5, 133.0, 134.0, 136.3, 140.3, 166.2 (C=O), 195.6 (C=S). Anal. calcd. for $C_{17}H_{17}ClN_2OS_2$: C 55.95, H 4.70, N 7.68; found: C 56.03, H 4.59, N 7.76.

4.1.11. (2,5-Dichlorophenylcarbamoyl)methyl benzylcarbamodithioate (7k)

Colorless powder; Yield 70%; mp 107–109°C; IR (KBr, cm^{-1}): 3210, 1680, 1582, 1519, 1452, 1404, 1368, 1093, 1058, 917, 754; ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.23 (s, 2H, CH_2S), 4.92 (d, J = 4.5 Hz, 2H, CH_2NH), 7.32–7.37 (m, 7H), 7.51 (s, 1H, H_{6Ar^1}), 8.87 (s, NH), 8.93 (brs, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 39.4 (CH_2S), 52.2 (CH_2N), 121.7, 124.8, 125.4, 128.3, 128.4, 129.0, 129.8, 129.8, 134.5, 135.5, 167.0 (C=O), 195.6 (C=S). Anal. calcd. for $C_{16}H_{14}Cl_2N_2OS_2$: C 49.87, H 3.66, N 7.27; found: C 49.98, H 3.73, N 7.16.

4.1.12. (2,5-Dichlorophenylcarbamoyl)methyl 4-methylbenzylcarbamodithioate (7l)

Colorless powder; Yield 75%; mp 131–133°C; IR (KBr, cm^{-1}): 3215, 1673, 1579, 1523, 1448, 1409, 1369, 1089, 1043, 927, 854, 742; ^{1}H NMR (500 MHz, DMSO-d_6): δ 2.27 (s, 3H, CH_3), 4.27 (s, 2H, CH_2S), 4.79 (d, J = 5.5 Hz, 2H, CH_2NH), 7.13 (d, J = 8.0 Hz, 2H, $H_{3,5Ar^2}$), 7.18 (d, J = 8.0 Hz, 2H, $H_{2,6Ar^2}$), 7.26 (dd, J = 9.0, 2.0 Hz, 1H, H_{4Ar^1}), 7.54 (d, J = 9.0 Hz, 1H, H_{3Ar^1}), 7.95 (d, J = 2.0 Hz, 1H, H_{6Ar^1}), 9.77 (s, NH), 10.61 (t, J = 5.5 Hz, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 20.6 (CH_3), 38.7 (CH_2S), 49.7 (CH_2N), 125.4, 125.6, 127.7, 128.8, 130.7, 130.8, 131.6, 133.9, 135.8, 136.4, 166.9 (C=O), 195.3 (C=S). Anal. calcd. for $C_{17}H_{16}Cl_2N_2OS_2$: C 51.13, H 4.04, N 7.01; found: C 51.18, H 4.09, N 6.92.

4.1.13. (2,5-Dichlorophenylcarbamoyl)methyl 4-chlorobenzylcarbamodithioate (7m)

Colorless powder; Yield 69%; mp 129–131°C; IR (KBr, cm^{-1}):1680, 1583, 1519, 1490, 1453, 1366, 1093, 1072, 920, 842; ^{1}H NMR (500 MHz, DMSO-d_6): δ 4.28 (s, 2H, CH_2S), 4.82 (s, 2H, CH_2NH), 7.25 (d, J = 9.0 Hz, 1H, H_{4Ar^1}), 7.30 (d, J = 7.5 Hz, 2H, $H_{2,6Ar^2}$), 7.39 (d, J = 7.5 Hz, 2H, $H_{3,5Ar^2}$), 7.55 (d, J = 9.0 Hz, 1H, H_{3Ar^1}), 7.90 (s, 1H, H_{6Ar^1}), 9.96 (s, NH), 10.67 (brs, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 40.1 (CH_2S), 49.1 (CH_2N), 123.7,

124.8, 125.5, 126.4, 128.1, 129.6, 130.8, 131.6, 135.4, 145.9, 166.8 (C=O), 195.9 (C=S). Anal. calcd. for $C_{16}H_{13}Cl_3N_2OS_2$: C 45.78, H 3.12, N 6.67; found: C 45.84, H 3.04, N 6.72.

4.1.14. (3,4-Dichlorophenylcarbamoyl)methyl benzylcarbamodithioate (7n)

Colorless powder; Yield 71%; mp 102–104°C; IR (KBr, cm^{-1}):3201, 1680, 1588, 1530, 1474, 1453, 1391, 1335, 811, 702; ^{1}H NMR (500 MHz, DMSO-d_6): δ 4.23 (s, 2H, CH_2S), 4.84 (d, J = 5.5 Hz, 2H, CH_2NH), 7.31–7.36 (m, 5H), 7.49 (dd, J = 9.0, 3.0 Hz, 1H, H_{6Ar^1}), 7.56 (d, J = 9.0 Hz, 1H, H_{5Ar^1}), 7.98 (s, 1H, H_{2Ar^1}), 10.57 (s, NH), 10.61 (t, J = 5.5 Hz, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 40.1 (CH_2S), 49.8 (CH_2N), 119.2, 120.3, 124.8, 127.8, 128.2, 128.4, 130.6 (2C), 137.1, 138.9, 166.3 (C=O), 195.8 (C=S). Anal. calcd. for $C_{16}H_{14}Cl_2N_2OS_2$: C 49.87, H 3.66, N 7.27; found: C 49.94, H 3.58, N 7.33.

4.1.15. (3,4-Dichlorophenylcarbamoyl)methyl 4-methylbenzylcarbamodithioate (7o)

Colorless powder; Yield 76%; mp 120–122°C; IR (KBr, cm^{-1}): 3197, 1670, 1595, 1536, 1476, 1392, 1378, 919, 894; ^{1}H NMR (500 MHz, $CDCl_3$): δ 2.32 (s, 3H), 4.07 (s, 2H, CH_2S), 4.87 (s, 2H, CH_2NH), 7.17 (d, J = 8.0 Hz, 2H, $H_{3,5Ar^2}$), 7.23 (d, J = 8.0 Hz, 1H, H_{6Ar^1}), 7.30–7.33 (m, 3H, $H_{2,6Ar^2}$, H_{5Ar^1}), 7.64 (s, NH), 7.71 (s, 1H, H_{2Ar^1}), 9.06 (brs, NH). ^{13}C NMR (125 MHz, $CDCl_3$): δ 21.1 (CH_3), 38.9 (CH_2S), 50.9 (CH_2N), 119.1, 121.5, 128.0, 128.3, 129.7, 129.9, 130.4, 132.2, 137.3, 138.4, 167.2 (C=O), 196.7 (C=S). Anal. calcd. for $C_{17}H_{16}Cl_2N_2OS_2$: C 51.13, H 4.04, N 7.01; found: C 51.19, H 4.00, N 6.95.

4.1.16. (3,4-Dichlorophenylcarbamoyl)methyl 4-chlorobenzylcarbamodithioate (7p)

Colorless powder; Yield 70%; mp 103–105°C; IR (KBr, cm^{-1}): 3209, 1675, 1532, 1489, 1455, 1374, 1327, 1257, 1082, 830, 751, 623; ^{1}H NMR (500 MHz, DMSO-d_6): δ 4.26 (s, 2H, CH_2S), 4.83 (s, 2H, CH_2NH), 7.15 (dd, J = 6.0, 3.0 Hz, 1H, H_{6Ar^1}), 7.30–7.33 (m, 3H), 7.40 (d, J = 8.5 Hz, 2H, $H_{3,5Ar^2}$), 7.49 (s, 1H, H_{2Ar^1}), 9.99 (s, NH), 10.62 (brs, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 40.4 (CH_2S), 49.0 (CH_2N), 115.4, 123.8, 124.2, 125.3, 128.1, 128.4, 129.3, 129.6, 131.7, 136.1, 166.4 (C=O), 196.1 (C=S). Anal. calcd. for $C_{16}H_{13}Cl_3N_2OS_2$: C 45.78, H 3.12, N 6.67; found: C 45.69, H 3.21, N 6.72.

4.1.17. (4-Bromophenylcarbamoyl)methyl benzylcarbamodithioate (7q)

Colorless powder; Yield 67%; mp 126–128°C; IR (KBr, cm^{-1}): 3182, 1662, 1535, 1488, 1394, 1354, 1322, 922, 825, 699 ; ^{1}H NMR (500 MHz, DMSO-d_6): δ 4.21 (s, 2H, CH_2S), 4.84 (d, J = 5.5 Hz, 2H, CH_2NH), 7.27–7.36 (m, 5H), 7.49 (d, J = 8.5 Hz, 2H, $H_{2,6Ar^2}$), 7.55 (d, J = 8.5 Hz, 2H, $H_{3,5Ar^2}$), 10.38 (s, NH), 10.60 (t, J = 5.5 Hz, NH). ^{13}C NMR (125 MHz, DMSO-d_6): δ 40.1 (CH_2S), 49.8 (CH_2N), 114.9, 121.0, 127.3, 127.8, 128.4, 131.4, 131.6, 137.1, 166.0 (C=O), 195.9 (C=S). Anal. calcd. for $C_{16}H_{15}BrN_2OS_2$: C 48.61, H 3.82, N 7.09; found: C 48.56, H 3.75, N 7.00.

Disclosure statement

No potential conflict of interest was reported by the authors.

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