Monatsh Chem (2009) 140:1199–1204
DOI 10.1007/s00706-009-0154-2

ORIGINAL PAPER

A one-pot synthesis of alkyl acylcarbamodithioates from acid chlorides, thiols, and ammonium thiocyanate

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Received: 22 October 2008 / Accepted: 19 January 2009 / Published online: 21 April 2009

Abstract An efficient synthesis of alkyl acylcarbamodithioates by reaction of acid chlorides with ammonium thiocyanate in the presence of thiols is described. The unusually large values of $^{5}J_{FH} = 12$–15 Hz, observed for alkyl (2-fluorobenzoyl)carbamodithioates provide information about Ar–C–N–H torsion in these compounds.

Keywords Carbamodithioate · Ammonium thiocyanate · Acid chloride · Thiol

Introduction

Alkyl carbamodithioates are a common class of organic molecules with a variety of valuable biological effects, including antibacterial activity [1], antifungal activity [2], and the ability to chelate heavy metals [3, 4]. These esters are bifunctional ligands which have received attention because of their use as agrochemicals [5] and pharmaceuticals [6]. Carbamodithioates have exceptionally strong affinity towards Hg^{2+} ions [7], and have been used for controlled/living free-radical polymerization of methyl acrylate under thermal condition [8]. Synthesis and in-vitro antitumor activity of quinazolinone derivatives with dithiocarbamate side chains have been reported [9]. Carbamodithioates have been used to prepare upper-rim-substituted calix [4] arenes as selective extractants [10].

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As a part of our current studies on the development of new routes in the synthesis of organosulfur compounds [11–14], we report an efficient one-pot method for synthesis of alkyl acylcarbamodithioates.

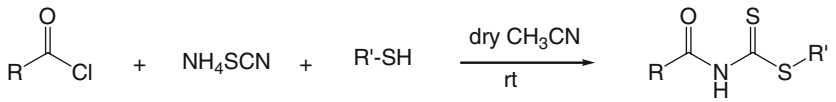
Results and discussion

The reaction of acid chlorides **1** with ammonium thiocyanate in the presence of thiols **2** proceeds smoothly in dry MeCN at rt to produce compounds **3** in good yields (Scheme 1). The structures of compounds **3a**–**3r** were deduced from their IR, ^{1}H NMR, and ^{13}C NMR spectroscopic data. The mass spectra of these compounds contained molecular ion peaks at appropriate *m*/*z* values. The ^{1}H NMR spectrum of **3a** in $CDCl_3$ contained signals for methylene ($\delta = 2.86$ and 3.59 ppm), methoxy ($\delta = 3.73$ ppm), and NH ($\delta = 10.59$ ppm) protons, with multiplets for the aromatic ($\delta = 7.22$–7.64 ppm) protons. The ^{13}C NMR spectrum of **3a** contained 12 signals in agreement with the proposed structure. The ^{1}H and ^{13}C NMR spectra of **3b**–**3r** are similar to those of **3a** except for the alkyl and acyl moieties, which give characteristic signals with appropriate chemical shifts.

The following mechanism (Scheme 2) may be invoked for formation of compounds **3**. Conceivably, the starting point of the reaction is the formation of a 1:1 adduct, **4**, between **1** and ammonium thiocyanate, which undergoes nucleophilic reaction with thiols **2** to produce **3**.

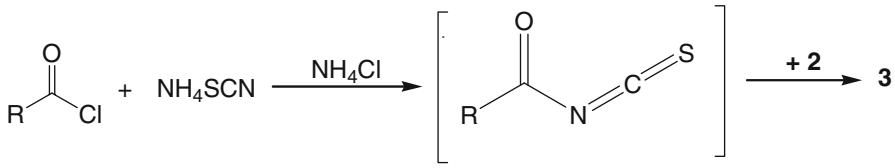
Although the presence of the ^{19}F nucleus complicates both the ^{1}H and ^{13}C NMR spectra of **3a**–**3c**, it helps in assignment of the signals by direct and long range coupling with ^{1}H and ^{13}C nuclei ("Experimental" section). Of particular interest is the observation of an unusually high value for the five-bond fluorine–proton coupling constants,

Scheme 1



	R		R'		R	R'
1a	2-F-C_6H_4	**2a**	$CH_2CH_2CO_2Me$	**3a**	2-F-C_6H_4	$CH_2CH_2CO_2Me$
1b	CMe_3	**2b**	CH_2-C_4H_3O	**3b**	2-F-C_6H_4	CH_2-C_4H_3O
1c	Ph	**2c**	$CH_2CH_2CH_2$-SH	**3c**	2-F-C_6H_4	$CH_2CH_2CH_2$-SH
1d	4-NO_2-C_6H_4			**3d**	CMe_3	$CH_2CH_2CO_2Me$
1e	4-MeO-C_6H_4			**3e**	CMe_3	CH_2-C_4H_3O
1f	CH_3-CH_2			**3f**	CMe_3	$CH_2CH_2CH_2$-SH
				3g	Ph	$CH_2CH_2CO_2Me$
				3h	Ph	CH_2-C_4H_3O
				3i	Ph	$CH_2CH_2CH_2$-SH
				3j	4-NO_2-C_6H_4	$CH_2CH_2CO_2Me$
				3k	4-NO_2-C_6H_4	CH_2-C_4H_3O
				3l	4-NO_2-C_6H_4	$CH_2CH_2CH_2$-SH
				3m	4-MeO-C_6H_4	$CH_2CH_2CO_2Me$
				3n	4-MeO-C_6H_4	CH_2-C_4H_3O
				3o	4-MeO-C_6H_4	$CH_2CH_2CH_2$-SH
				3p	CH_3-CH_2	$CH_2CH_2CO_2Me$
				3q	CH_3-CH_2	CH_2-C_4H_3O
				3r	CH_3-CH_2	$CH_2CH_2CH_2$-SH

Scheme 2

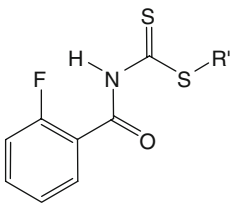


1 **4**

$^5J_{FH}$ = 12.2–15.1 Hz, which provides information about Ar–C–N–H torsion (Scheme 4). It has been suggested [15] that F–H spin coupling can operate not only through the bonds in a molecule but also through space, if the interacting fluorine and proton nuclei are in close proximity. In compounds **3a**–**3c**, the fluorine and the NH proton can come into fairly close proximity in some conformations (Scheme 3), and would be expected to have a large through-space contribution to the coupling. The large observed coupling may thus be explained.

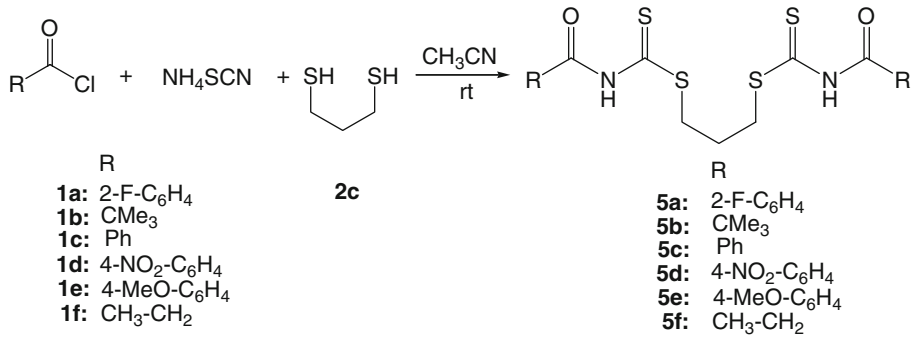
When the reaction was carried out using one equivalent of 1,3-dimercaptopropane (**2c**) and two equivalents of acid chloride **1** in the presence of two equivalents of ammonium thiocyanate, trimethyl bisacylcarbamodithioates **5a**–**5f** were obtained in good yields (Scheme 4). Compounds **5a**–**5f** were identified on the basis of their IR, ^{1}H, and ^{13}C NMR spectral data. The ^{1}H NMR spectrum of **5a** in $CDCl_3$ contained signals for methylene (δ = 2.31 and 3.47 ppm) and NH (δ = 10.58 ppm) protons, with multiplets for the aromatic (δ = 7.19–8.18 ppm) protons. The ^{13}C NMR spectrum of **5a** contained ten signals, in agreement with the proposed structure. The ^{1}H and ^{13}C NMR spectra of **5b**–**5f** are similar to those for **5a**, except for the alkyl and acyl moieties, which give characteristic signals with appropriate chemical shifts.

Scheme 3



In conclusion, we have described a convenient route to the synthesis of alkyl acylcarbamodithioates by reaction of acid chlorides with ammonium thiocyanate in the presence of thiols. Trimethyl bisacylcarbamodithioates were obtained from 1,3-dimercaptopropane and two equivalents of **1** in the presence of ammonium thiocyanate. Unusual large values of $^5J_{FH}$ = 12–15 Hz are observed for alkyl (2-fluorobenzoyl)carbamodithioates; these provide information about Ar–C–N–H torsion in these compounds.

Scheme 4



These alkyl acylcarbamodithioates can be regarded as potentially useful synthetic intermediates. The simplicity of the present procedure makes it an interesting alternative to other approaches.

Experimental

Compounds **1** and **2** were obtained from Fluka and were used without further purification; M.p.: Electrothermal 9100 apparatus; IR spectra: Shimadzu IR-460 spectrometer; ^{1}H and ^{13}C NMR spectra: Bruker DRX-300 Avance instrument; in $CDCl_3$ at 300 MHz and 75 MHz; EI-MS (70 eV): Finningan-MAT-8430 mass spectrometer. Elemental analyses (C, H, and N) were performed with a Heraeus CHN-O-Rapid analyzer. The mass spectral and elemental analysis data were in agreement with the proposed structures.

*General procedure for the preparation of alkyl acylcarbamodithioates **3***

To a stirred solution of 0.15 g NH_4SCN (2 mmol) in 10 cm^3 MeCN were added 2 mmol acid chloride **1**. The mixture was stirred at rt for 30 min. Then, 2 mmol thiol **2** was added and the reaction mixture was stirred for 2 h at rt. The solvent was removed under reduced pressure and the residue was purified by column chromatography (SiO_2, *n*-hexane–EtOAc 3:1) to afford the pure title compounds.

2-(Methoxycarbonyl)ethyl (2-fluorobenzoyl) carbamodithioate (**3a**, $C_{12}H_{12}FNO_3S_2$)
Yellow oil; R_f: 0.61; yield: 0.50 g (83%); IR (KBr): $\bar{\nu}$ = 3384 (NH), 1733, 1693 (C=O), 1151 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 301 (5, M$^+$), 270 (6), 242 (22), 215 (52), 182 (25), 139 (25), 123 (100), 119 (34), 95 (60), 87 (11), 75 (38), 69 (8), 59 (22); ^{1}H NMR: δ = 2.86 (t, $^{3}J_{HH}$ = 7.2 Hz, CH_2), 3.59 (t, $^{3}J_{HH}$ = 7.2 Hz, CH_2S), 3.73 (s, MeO), 7.22–7.27 (m, CH arom), 7.33–7.38 (m, CH arom), 7.59–7.64 (m, CH arom), 8.11–8.16 (m, CH arom), 10.59 (d, $^{5}J_{FH}$ = 15 Hz, NH) ppm; ^{13}C NMR: δ = 31.9 (CH_2), 32.4 (CH_2), 52.4 (MeO), 117.3 (d, $^{2}J_{CF}$ = 24.0 Hz, CH), 119.5 (d, $^{2}J_{CF}$ = 20.5 Hz, C), 125.8 (d, $^{4}J_{CF}$ = 3.2 Hz, CH), 132.4 (d, $^{3}J_{CF}$ = 9.9 Hz, CH), 136.1 (d, $^{3}J_{CF}$ = 9.7 Hz, CH), 160.9 (d, $^{1}J_{CF}$ = 249.0 z, C–F), 163.3 (d, $^{3}J_{CF}$ = 4.1 Hz, C=O), 172.4 (C=O), 203.4 (C=S) ppm.

(Furan-2-yl)methyl (2-fluorobenzoyl) carbamodithioate (**3b**, $C_{13}H_{10}FNO_2S_2$)
Yellow oil; R_f: 0.74; yield: 0.46 g (78%); IR (KBr): $\bar{\nu}$ = 3400 (NH), 1694 (C=O), 1152 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 295 (21, M$^+$), 228 (16), 214 (22), 192 (32), 1722 (25), 123 (100), 81 (11), 67 (38); ^{1}H NMR: δ = 4.61 (s, CH_2), 6.42 (d, $^{3}J_{HH}$ = 1.8 Hz, CH furan), 6.47 (t, $^{3}J_{HH}$ = 3.2 Hz, CH furan), 7.39–7.41 (m, CH arom), 7.43–7.54 (m, CH arom), 7.55 (d, $^{3}J_{HH}$ = 1.3 Hz, CH furan), 7.67–7.72 (m, CH arom), 7.87–7.93 (m, CH arom), 11.48 (d, $^{5}J_{HF}$ = 14.8 Hz, NH) ppm; ^{13}C NMR: δ = 34.1 (CH_2), 109.7 (CH furan), 111.1 (CH furan), 135.4 (CH furan), 117.2 (d, $^{2}J_{CF}$ = 24.2 Hz, CH), 119.4 (d, $^{2}J_{CF}$ = 19.8 Hz, C), 125.9 (d, $^{4}J_{CF}$ = 3.4 Hz, CH), 132.6 (d, $^{3}J_{CF}$ = 9.4 Hz, CH), 136.3 (d, $^{3}J_{CF}$ = 9.7 Hz, CH), 161.0 (d, $^{1}J_{CF}$ = 249.4 Hz, C–F), 163.5 (d, $^{3}J_{CF}$ = 3.3 Hz, C=O), 162.2 (C=O), 202.9 (C=S) ppm.

3-Mercaptopropyl (2-fluorobenzoyl)carbamodithioate (**3c**, $C_{11}H_{12}FNOS_3$)
Yellow oil; R_f: 0.74; yield: 0.49 g (84%); IR (KBr): $\bar{\nu}$ = 3391 (NH), 1688 (C=O), 1153 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 289 (21, M$^+$), 256 (12), 243 (32), 242 (31), 182 (28), 166 (34), 123 (100), 47 (60), 46 (38), 33 (22); ^{1}H NMR: δ = 1.45 (t, $^{3}J_{HH}$ = 7.2 Hz, SH), 2.11 (qui, $^{3}J_{HH}$ = 7.1 Hz, CH_2), 2.70 (q, $^{3}J_{HH}$ = 7.4 Hz, CH_2), 3.43 (t, $^{3}J_{HH}$ = 7.2 Hz, CH_2S), 7.19–7.27 (m, CH arom), 7.33–7.38 (m, CH arom), 7.59–7.66 (m, CH arom), 8.11–8.17 (m, CH arom), 10.59 (d, $^{5}J_{HF}$ = 14.31 Hz, NH) ppm; ^{13}C NMR: δ = 23.9 (CH_2), 31.7 (CH_2), 35.5 (CH_2), 117.2 (d, $^{2}J_{CF}$ = 24.1 Hz, CH), 119.4 (d, $^{2}J_{CF}$ = 9.9 Hz, C), 125.9 (d, $^{4}J_{CF}$ = 3.1 Hz, CH), 132.6 (d, $^{3}J_{CF}$ = 9.4 Hz, CH), 136.3 (d, $^{3}J_{CF}$ = 9.7 Hz, CH), 161.0 (d, $^{1}J_{CF}$ = 248.1 Hz, C–F), 163.5 (d, $^{3}J_{CF}$ = 3.4 Hz, C=O), 203.7 (C=S) ppm.

2-(Methoxycarbonyl)ethyl pivaloylcarbamodithioate (**3d**, $C_{10}H_{17}NO_3S_2$)
Yellow oil; R_f: 0.76; yield: 0.45 g (85%); IR (KBr): $\bar{\nu}$ = 3405 (NH), 1707, 1686 (C=O), 1123 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 263 (9, M^+), 232 (6), 204 (26), 178 (42), 144 (35), 119 (25), 85 (100), 59 (23); ^{1}H NMR: δ = 1.31 (s, C*Me*$_3$), 2.82 (t, $^3J_{HH}$ = 7.2 Hz, CH_2), 3.52 (t, $^3J_{HH}$ = 7.2 Hz, CH_2S), 3.72 (s, MeO), 9.54 (s, NH) ppm; ^{13}C NMR: δ = 27.4 (C*Me*$_3$), 31.9 (CH_2), 32.4 (CH_2), 40.5 (*C*Me$_3$), 52.36 (MeO), 172.3 (C=O), 175.6 (C=O), 204.2 (C=S) ppm.

2-(Furan-2-yl)methyl pivaloylcarbamodithioate (**3e**, $C_{11}H_{15}NO_2S_2$)
Yellow oil; R_f: 0.85; yield: 0.42 g (83%); IR (KBr): $\bar{\nu}$ = 3401 (NH), 1706, 1686, 1148 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 257 (12, M^+), 190 (6), 176 (26), 172 (39), 154 (30), 103 (29), 85 (100), 81 (40), 67 (15); ^{1}H NMR: δ = 1.31 (s, C*Me*$_3$), 4.57 (s, CH_2), 6.32 (d, $^3J_{HH}$ = 1.6 Hz, CH furan), 6.39 (t, $^3J_{HH}$ = 2.8, CH furan), 7.37 (d, $^3J_{HH}$ = 1.4 Hz, CH furan), 9.54 (s, NH) ppm; ^{13}C NMR: δ = 27.7 (C*Me*$_3$), 39.8 (CH_2), 40.1 (*C*Me$_3$), 109.7 (CH furan), 111.2 (CH furan), 142.9 (CH furan), 175.7 (C=O), 203.5 (C=S) ppm.

3-Mercaptopropyl pivaloylcarbamodithioate (**3f**, $C_9H_{17}NO_2S_3$)
Yellow oil; R_f: 0.85; yield: 0.46 g (86%); IR (KBr): $\bar{\nu}$ = 3403 (NH), 1707 (C=O), 1140 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 267 (9, M^+), 234 (8), 221 (28), 220 (58), 160 (42), 107 (31), 85 (100), 47 (21), 46 (12), 33 (17); ^{1}H NMR: δ = 1.31 (s, C*Me*$_3$), 1.43 (t, $^3J_{HH}$ = 7.4 Hz, SH), 2.07 (qui, $^3J_{HH}$ = 7.1 Hz, CH_2), 2.67 (q, $^3J_{HH}$ = 7.4 Hz, CH_2), 3.38 (t, $^3J_{HH}$ = 7.2 Hz, CH_2S), 9.54 (s, NH) ppm; ^{13}C NMR: δ = 24.2 (CH_2), 27.4 (C*Me*$_3$), 31.7 (CH_2), 39.9 (CH_2), 40.0 (*C*Me$_3$), 175.6 (C=O), 204.5 (C=S) ppm.

2-(Methoxycarbonyl)ethyl benzoylcarbamodithioate (**3g**, $C_{12}H_{13}NO_3S_2$)
Yellow oil; R_f: 0.57; yield: 0.47 g (82%); IR (KBr): $\bar{\nu}$ = 3386 (NH), 1734, 1695 (C=O), 1146 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 283 (14, M^+), 252 (18), 224 (28), 178 (43), 164 (35), 119 (23), 105 (100), 59 (19); ^{1}H NMR: δ = 2.86 (t, $^3J_{HH}$ = 7.1 Hz, CH_2), 3.58 (t, $^3J_{HH}$ = 7.1 Hz, CH_2S), 3.71 (s, MeO), 7.51–7.55 (m, 2 CH arom), 7.61–7.64 (m, CH arom), 7.86–7.91 (m, 2 CH arom), 10.08 (br s, NH) ppm; ^{13}C NMR: δ = 31.9 (CH_2), 32.4 (CH_2), 52.4 (MeO), 128.1 (CH arom), 129.6 (CH arom), 133.9 (CH arom), 163.8 (C=O), 172.3 (C=O), 203.8 (C=S) ppm.

(Furan-2-yl)methyl benzoylcarbamodithioate (**3h**, $C_{13}H_{11}NO_2S_2$)
Yellow oil; R_f: 0.74; yield: 0.45 g (82%); IR (KBr): $\bar{\nu}$ = 3380 (NH), 1694 (C=O), 1148 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 277 (9, M^+), 210 (13), 196 (28), 174 (47), 172 (30), 105 (100), 103 (62), 81 (19), 67 (31); ^{1}H NMR: δ = 4.61 (s, CH_2), 6.34 (d, $^3J_{HH}$ = 1.7 Hz, CH furan), 6.38 (t, $^3J_{HH}$ = 3.4 Hz, CH furan), 7.39 (d, $^3J_{HH}$ = 1.5 Hz, CH furan), 7.51–7.56 (m, 2 CH arom), 7.62–7.67 (m, CH arom), 7.89 (m, 2 CH arom), 10.08 (s, NH) ppm; ^{13}C NMR: δ = 35.1 (CH_2), 109.8 (CH furan), 111.9 (CH furan), 128.1 (2 CH arom), 129.6 (CH arom), 133.9 (CH furan), 143.5 (2 CH arom), 1639 (C=O), 203.1 (C=S) ppm.

3-Mercaptopropyl benzoylcarbamodithioate (**3i**, $C_{11}H_{13}NOS_3$)
Yellow oil; R_f: 0.75; yield: 0.45 g (83%); IR (KBr): $\bar{\nu}$ = 3396 (NH), 1689 (C=O), 1146 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 271 (8, M^+), 238 (17), 225 (29), 224 (46), 166 (25), 164 (35), 105 (100), 47 (38), 46 (19), 33 (38); ^{1}H NMR: δ = 1.45 (t, $^3J_{HH}$ = 7.6 Hz, SH), 2.13 (qui, $^3J_{HH}$ = 7.3 Hz, CH_2), 2.69 (q, $^3J_{HH}$ = 7.5 Hz, CH_2), 3.46 (t, $^3J_{HH}$ = 7.3 Hz, CH_2S), 7.51–7.56 (m, 2 CH arom), 7.67–7.69 (m, CH arom), 7.89–7.91 (m, 2 CH arom), 10.07 (s, NH) ppm; ^{13}C NMR: δ = 23.9 (CH_2), 29.2 (CH_2), 36.4 (CH_2), 127.6 (2 CH arom), 129.3 (CH arom), 133.8 (2 CH arom), 163.8 (C=O), 204.1 (C=S) ppm.

2-(Methoxycarbonyl)ethyl (4-nitrobenzoyl) carbamodithioate (**3j**, $C_{12}H_{12}N_2O_5S_2$)
Yellow oil; R_f: 0.61; yield: 0.58 g (88%); IR (KBr): $\bar{\nu}$ = 3364 (NH), 1713, 1690 (C=O), 1154 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 328 (10, M^+), 297 (23), 269 (41), 209 (32), 178 (20), 150 (100), 119 (18), 59 (31); ^{1}H NMR: δ = 2.88 (t, 3J_{HH} = 7.1 Hz, CH_2), 3.61 (t, $^3J_{HH}$ = 7.1 Hz, CH_2S), 3.76 (s, MeO), 8.09 (d, $^3J_{HH}$ = 8.9 Hz, 2 CH arom), 8.41 (d, $^3J_{HH}$ = 8.9 Hz, 2 CH arom), 9.97 (s, NH) ppm; ^{13}C NMR: δ = 31.9 (CH_2S), 32.1 (CH_2), 51.6 (MeO), 128.2 (2 CH arom), 129.5 (2 CH arom), 150.6 (C-NO_2), 163.9 (C=O), 172.4 (C=O), 203.4 (C=S) ppm.

(Furan-2-yl)methyl (4-nitrobenzoyl)carbamodithioate (**3k**, $C_{13}H_{10}N_2O_4S_2$)
Yellow oil; R_f: 0.77; yield: 0.55 g (86%); IR (KBr): $\bar{\nu}$ = 3386 (NH), 1696 (C=O), 1147 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 322 (9, M^+), 255 (6), 241 (22), 219 (42), 172 (25), 150 (100), 103 (38), 81 (27), 67 (22); ^{1}H NMR: δ = 4.61 (s, CH_2), 6.66 (d, $^3J_{HH}$ = 1.6 Hz, CH furan), 6.41 (t, $^3J_{HH}$ = 3.3 Hz, CH furan), 7.80 (d, $^3J_{HH}$ = 1.7 Hz, CH furan), 8.07 (d, $^3J_{HH}$ = 8.5 Hz, 2 CH arom), 8.38 (d, $^3J_{HH}$ = 8.5 Hz, 2 CH arom), 10.00 (s, NH) ppm; ^{13}C NMR: δ = 35.2 (CH_2), 110.1 (CH furan), 111.2 (CH furan), 124.7 (2 CH arom), 129.4 (2 CH arom), 143.2 (CH furan), 151.2 (C-NO_2), 162.1 (C=O), 202.5 (C=S) ppm.

3-Mercaptopropyl (4-nitrobenzoyl)carbamodithioate (**3l**, $C_{11}H_{12}N_2O_3S_3$)
Yellow oil; R_f: 0.77; yield: 0.49 g (78%); IR (KBr): $\bar{\nu}$ = 3434 (NH), 1684 (C=O), 1148 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 316 (8, M^+), 283 (20), 270 (25), 269 (52), 209 (29), 166 (25), 150 (100), 107 (60), 47 (11), 46 (38), 33 (8);

^{1}H NMR: $\delta = 1.46$ (t, $^3J_{HH} = 7.3$ Hz, SH), 2.13 (qui, $^3J_{HH} = 7.2$ Hz, CH_2), 2.73 (q, $^3J_{HH} = 7.3$ Hz, CH_2), 3.46 (t, $^3J_{HH} = 7.3$ Hz, CH_2S), 8.11 (d, $^3J_{HH} = 8.6$ Hz, 2 CH arom), 8.41 (d, $^3J_{HH} = 8.8$ Hz, 2 CH arom), 10.02 (s, NH) ppm; ^{13}C NMR: $\delta = 24.2$ (CH_2), 31.6 (CH_2S), 35.9 (CH_2), 124.7 (2 CH arom), 129.3 (2 CH arom), 151.2 (C-NO_2), 161.9 (C=O), 203.6 (C=S) ppm.

2-(Methoxycarbonyl)ethyl (4-methoxybenzoyl) carbamodithioate (**3m**, $C_{13}H_{15}NO_4S_2$)
Yellow oil; R_f: 0.67; yield: 0.48 g (76%); IR (KBr): $\bar{\nu} = 3427$ (NH), 1729, 1684 (C=O), 1120 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 313 (10, M^+), 282 (6), 254 (22), 194 (52), 178 (25), 135 (100), 119 (31), 59 (22); ^{1}H NMR: $\delta = 2.87$ (t, $^3J_{HH} = 7.2$ Hz, CH_2), 3.59 (t, $^3J_{HH} = 7.2$ Hz, CH_2S), 3.47 (s, MeO), 3.71 (s, MeO), 7.32 (d, $^3J_{HH} = 8.4$ Hz, 2 CH arom), 7.79 (d, $^3J_{HH} = 8.2$ Hz, 2 CH arom), 10.06 (s, NH) ppm; ^{13}C NMR: $\delta = 31.3$ (CH_2), 31.9 (CH_2S), 51.5 (MeO), 54.3 (MeO), 128.1 (2 CH arom), 130.2 (2 CH arom), 145.1 (C), 161.4 (C=O), 169.8 (C=O), 203.3 (C=S) ppm.

(Furan-2-yl)methyl (4-methoxybenzoyl) carbamodithioate (**3n**, $C_{14}H_{13}NO_3S_2$)
Yellow oil; R_f: 0.71; yield: 0.48 g (78%); IR (KBr): $\bar{\nu} = 3391$ (NH), 1693 (C=O), 1145 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 307 (7, M^+), 240 (34), 226 (26), 204 (50), 172 (29), 135 (100), 103 (43), 81 (19), 67 (38); ^{1}H NMR: $\delta = 3.77$ (s, Me*O*), 4.61 (s, CH_2), 6.34 (d, $^3J_{HH} = 1.4$ Hz, CH furan), 6.39 (t, $^3J_{HH} = 3.3$ Hz, CH furan), 7.33 (d, $^3J_{HH} = 8.08$ Hz, 2 CH arom), 7.39 (d, $^3J_{HH} = 1.8$ Hz, CH furan), 7.79 (d, $^3J_{HH} = 8.5$ Hz, 2 CH arom), 10.07 (s, NH) ppm; ^{13}C NMR: $\delta = 34.9$ (CH_2), 53.9 (MeO), 109.8 (CH furan), 111.4 (CH furan), 128.2 (2 CH arom), 130.3 (2 CH arom), 142.9 (CH furan), 144.7 (C), 163.8 (C=O), 203.2 (C=S) ppm.

3-Mercaptopropyl (4-methoxybenzoyl) carbamodithioate (**3o**, $C_{12}H_{15}NO_2S_3$)
Yellow oil; R_f: 0.71; yield: 0.45 g (75%); IR (KBr): $\bar{\nu} = 3382$ (NH), 1690 (C=O), 1149 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 301 (11, M^+), 268 (18), 255 (27), 254 (44), 194 (35), 135 (100), 107 (19), 47 (38), 46 (27), 33 (12); ^{1}H NMR: $\delta = 1.48$ (t, $^3J_{HH} = 7.3$ Hz, SH), 2.12 (qui, $^3J_{HH} = 7.1$ Hz, CH_2), 2.72 (q, $^3J_{HH} = 7.3$ Hz, CH_2), 3. 45 (t, $^3J_{HH} = 7.25$ Hz, CH_2S), 3.61 (s, MeO), 7.33 (d, $^3J_{HH} = 8.5$ Hz, 2 CH arom), 7.80 (d, $^3J_{HH} = 8.5$ Hz, 2 CH arom), 10.07 (s, NH) ppm; ^{13}C NMR: $\delta = 24.3$ (CH_2), 31.8 (CH_2S), 35.8 (CH_2), 54.1 (MeO), 128.4 (2 CH arom), 130.5 (2 CH arom), 145.3 (C), 163.7 (C=O), 204.2 (C=S) ppm.

2-(Methoxycarbonyl)ethyl propionylcarbamodithioate (**3p**, $C_8H_{13}NO_3S_2$)
Yellow oil; R_f: 0.56; yield: 0.36 g (76%); IR (KBr): $\bar{\nu} = 3430$ (NH), 1723, 1693 (C=O), 1152 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 235 (10, M^+), 204 (6), 178 (22), 176 (52), 116 (25), 119 (25), 59 (41), 57 (100), 37 (60); ^{1}H NMR: $\delta = 1.24$ (t, $^3J_{HH} = 9.5$ Hz, *Me*), 2.44 (q, $^3J_{HH} = 9.3$ Hz, CH_2), 2.83 (t, $^3J_{HH} = 7.3$ Hz, CH_2), 3.52 (t, $^3J_{HH} = 7.3$ Hz, CH_2S), 3.73 (s, MeO), 9.47 (s, NH) ppm; ^{13}C NMR: $\delta = 8.9$ (*Me*), 30.5 (CH_2), 31.8 (CH_2S), 32.5 (CH_2), 52.4 (MeO), 170.8 (C=O), 172.3 (C=O), 203.5 (C=S) ppm.

(Furan-2-yl)methyl propionylcarbamodithioate (**3q**, $C_9H_{11}NO_2S_2$)
Yellow oil; R_f: 0.79; yield: 0.34 g (74%); IR (KBr): $\bar{\nu} = 3419$ (NH), 1697 (C=O), 1217 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 229 (9, M^+), 172 (16), 162 (32), 148 (59), 126 (42), 103 (25), 81 (53), 67 (60), 57 (100); ^{1}H NMR: $\delta = 1.25$ (t, $^3J_{HH} = 7.5$ Hz, Me), 2.43 (q, $^3J_{HH} = 7.5$ Hz, CH_2), 4.54 (s, CH_2), 6.34 (d, $^3J_{HH} = 1.7$ Hz, CH furan), 6.36 (t, $^3J_{HH} = 3.6$ Hz, CH furan), 7.38 (d, $^3J_{HH} = 1.8$ Hz, CH furan), 9.54 (s, NH) ppm; ^{13}C NMR: $\delta = 9.1$ (Me), 30.4 (CH_2), 34.8 (CH_2), 109.7 (CH furan), 111.2 (CH furan), 143.0 (CH furan), 171.2 (C=O), 203.8 (C=S) ppm.

3-Mercaptopropyl propionylcarbamodithioate (**3r**, $C_7H_{13}NOS_3$)
Yellow oil; R_f: 0.77; yield: 0.35 g (76%); IR (KBr): $\bar{\nu} = 3430$ (NH), 1710 (C=O), 1152 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 223 (12, M^+), 190 (13), 177 (28), 176 (52), 166 (33), 116 (25), 107 (51), 57 (100), 47 (19), 46 (38), 33 (21); ^{1}H NMR: $\delta = 1.23$ (t, $^3J_{HH} = 8.7$ Hz, Me), 1.45 (t, $^3J_{HH} = 7.2$ Hz, SH), 2.08 (qui, $^3J_{HH} = 7.5$ Hz, CH_2), 2.44 (q, $^3J_{HH} = 7.5$ Hz, CH_2), 2.68 (q, $^3J_{HH} = 8.3$ Hz, CH_2), 3.38 (t, $^3J_{HH} = 7.0$ Hz, CH_2S), 9.46 (s, NH) ppm; ^{13}C NMR: $\delta = 8.9$ (*Me*), 24.2 (CH_2), 30.5 (CH_2), 31.8 (CH_2), 35.6 (CH_2), 170.7 (C=O), 203.8 (C=S) ppm.

General procedure for the preparation of trimethylene bisacylcarbamodithioates **5**

To a stirred solution of 0.30 g NH_4SCN (4 mmol) in 20 cm^3 MeCN was added 4 mmol acid chloride **1**. The mixture was stirred at rt for 30 min. Then, 2 mmol 1,3-propanedithiol (**2c**) was added and the reaction mixture was stirred for 2 h at rt. The solvent was removed under reduced pressure and the residue was purified by column chromatography (SiO_2, *n*-hexane–EtOAc 2:1) to afford the pure title compounds.

Trimethylene bis(2-fluorobenzoyl)carbamodithioate (**5a**, $C_{19}H_{16}F_2N_2O_2S_4$)
Yellow powder; R_f: 0.52; yield: 0.38 g (81%); mp 175–177 °C; IR (KBr): $\bar{\nu} = 3393$ (NH), 1690, 1659 (C=O), 1152 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 470 (M^+, 4), 347 (89), 289 (56), 166 (77), 123 (100), 108 (66), 58 (91), 43 (64); ^{1}H NMR: $\delta = 2.31$ (qui, $^3J_{HH} = 7.5$ Hz, CH_2), 3.47

(t, $^3J_{HH}$ = 7.4 Hz, 2 CH_2S), 7.19–7.26 (m, 2 CH arom), 7.33–7.38 (m, 2 CH arom), 7.59–7.66 (m, 2 CH arom), 8.12–8.18 (m, 2 CH arom), 10.58 (d, $^5J_{HF}$ = 15 Hz, 2 NH) ppm; ^{13}C NMR: δ = 25.5 (CH_2), 36.4 (2 CH_2S), 116.2 (*d*, $^2J_{CF}$ = 24.3 Hz, CH), 118.4 (*d*, $^2J_{CF}$ = 9.6 Hz, C), 125.0 (*d*, $^4J_{CF}$ = 3.0 Hz, CH), 133.6 (*d*, $^3J_{CF}$ = 9.1 Hz, CH), 136.8 (*d*, $^3J_{CF}$ = 9.5 Hz, CH), 159.0 (*d*, $^1J_{CF}$ = 248.4 Hz, C–F), 166.5 (*d*, $^3J_{CF}$ = 3.1 Hz, C=O), 203.4 (2 C=S) ppm.

Trimethylene bispivaloylcarbamodithioate
(**5b**, $C_{15}H_{26}N_2O_2S_4$)
Yellow powder; R_f: 0.83; yield: 0.63 g (80%); mp 143–146 °C; IR (KBr): $\bar{\nu}$ = 3395 (NH), 1700, 1691 (C=O), 1153 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 394 (M^+, 6), 309 (89), 251 (56), 166 (77), 108 (40), 85 (100), 58 (64); ^{1}H NMR: δ = 1.31 (s, 2 *CMe*$_3$), 2.14 (qui, $^3J_{HH}$ = 7.4 Hz, CH_2), 3.42 (t, $^3J_{HH}$ = 7.5 Hz, 2 CH_2S), 9.54 (s, 2 NH) ppm; ^{13}C NMR: δ = 24.2 (CH_2), 27.4 (2 C*Me*$_3$), 31.7 (2 CH_2S), 40.2 (2 *CMe*$_3$), 175.6 (2 C=O), 204.6 (2 C=S) ppm.

Trimethylene bisbenzoylcarbamodithioate
(**5c**, $C_{19}H_{18}N_2O_2S_4$)
Yellow powder; R_f: 0.69; yield: 0.75 g (86%); mp 162–164 °C; IR (KBr): $\bar{\nu}$ = 3406 (NH), 1700, 1686 (C=O), 1145 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 434 (M^+, 3), 329 (59), 271 (38), 166 (61), 105 (100), 58 (41); ^{1}H NMR: δ = 2.32 (qui, $^3J_{HH}$ = 7.5 Hz, CH_2), 3.48 (t, $^3J_{HH}$ = 7.5 Hz, 2 CH_2S), 7.52–7.57 (m, 4 CH arom), 7.62–7.67 (m, 2 CH arom), 7.89–7.92 (m, 4 CH arom), 10.07 (s, 2 NH) ppm; ^{13}C NMR: δ = 25.7 (CH_2), 36.4 (2 CH_2S), 128.1, 129.6, 132.0, 133.9 (2 C_6H_5), 163.8 (2 C=O), 203.9 (2 C=S) ppm.

Trimethylene bis(4-nitrobenzoyl)carbamodithioate
(**5d**, $C_{19}H_{16}N_4O_6S_4$)
Yellow powder; R_f: 0.60; yield: 0.93 g (89%); mp 187–189 °C; IR (KBr): $\bar{\nu}$ = 3386 (NH), 1710, 1694 (C=O), 1149 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 524 (M^+, 4), 374 (89), 316 (56), 166 (77), 150 (100), 108 (42), 58 (51), 43 (34); ^{1}H NMR: δ = 2.45 (qui, $^3J_{HH}$ = 7.5 Hz, CH_2), 3.51 (t, $^3J_{HH}$ = 7.5 Hz, 2 CH_2S), 8.08 (d, $^3J_{HH}$ = 8.9 Hz, 4 CH arom), 8.41 (d, $^3J_{HH}$ = 8.9, 4 CH arom), 9.98 (s, 2 NH) ppm; ^{13}C NMR: δ = 24.1 (CH_2), 31.4 (2 CH_2S), 128.6 (4 CH arom), 130.2 (4 CH arom), 151.7 (2 C-NO_2), 171.3 (2 C=O), 202.9 (2 C=S) ppm.

Trimethylene bis(4-methoxybenzoyl)carbamodithioate
(**5e**, $C_{21}H_{22}N_2O_4S_4$)
Yellow powder; R_f: 0.62; yield: 0.83 g (84%); mp 178–180 °C; IR (KBr): $\bar{\nu}$ = 3430 (NH), 1700, 1731 (C=O), 1151 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 494 (M^+, 5), 359 (39), 301 (50), 166 (57), 135 (100), 108 (61), 58 (46); ^{1}H NMR: δ = 2.31 (qui, $^3J_{HH}$ = 7.5 Hz, CH_2), 3.59 (t, $^3J_{HH}$ = 7.5 Hz, 2 CH_2S), 3.73 (s, 2 MeO), 7.32 (d, $^3J_{HH}$ = 8.5 Hz, 4 CH arom), 7.79 (d, $^3J_{HH}$ = 8.5 Hz, 4 CH arom), 10.06 (s, 2 NH) ppm; ^{13}C NMR: δ = 23.9 (CH_2), 31.9 (2 CH_2S), 54.3 (2 MeO); 128.1 (4 CH arom), 131.4 (4 CH arom), 146.3 (2 C), 164.7 (2 C=O), 204.5 (2 C=S) ppm.

Trimethylene bispropionylcarbamodithioate
(**5f**, $C_{11}H_{18}N_2O_2S_4$)
Yellow powder; R_f: 0.78; yield: 0.55 g (81%); mp 160–162 °C; IR (KBr): $\bar{\nu}$ = 3438 (NH), 1699, 1716, (C=O), 1154 (C=S) cm^{-1}; EI-MS: *m/z* (%) = 338 (M^+, 4), 281 (59), 223 (52), 166 (71), 106 (30), 57 (100); ^{1}H NMR: δ = 1.24 (t, $^3J_{HH}$ = 8.7 Hz, 2 Me), 2.43 (q, $^3J_{HH}$ = 8.5 Hz, 2 CH_2), 2.68 (qui, $^3J_{HH}$ = 7.6 Hz, CH_2), 3.38 (t, $^3J_{HH}$ = 7.5 Hz, 2 CH_2S), 9.49 (s, 2 NH) ppm; ^{13}C NMR: δ = 8.9 (2 Me), 24.2 (CH_2), 31.7 (2 CH_2S), 35.5 (2 CH_2), 170.8 (2 C=O), 203.8 (2 C=S) ppm.

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