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Synthesis of new acyl, furoyl, and benzoylthiocarbamates as polydentate systems. Structural study of isopropyl *N*-(2-furoyl)thiocarbamate

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Abstract—Synthesis of new acylthiocarbamates has been carried out. To establish the preferential conformation and to explain the behaviour chemically, the structure of isopropyl *N*-(2-furoyl)thiocarbamate **3m** has been determined by single-crystal X-ray analysis. The most stable conformation *E*,*Z*′ established by X-ray analysis was corroborated by semiempirical theoretical calculations.

1. Introduction

Some organic sulfur compounds such as thiocarbamates show important biological activity.[1] Most notably, acylthiocarbamates are used as biosensors,[2] elastase inhibitors,[3] and they can exhibit antineoplasic and antiinflammatory or antiarthritic[1] effects. Also molecular modelling studies of related acylthiocarbamates has been previously carried out due to they are potent non-nucleoside HIV-1 reverse transcriptase inhibitors.[4]

In addition, acylthiocarbamates have also been employed as starting compounds to obtain different heterocyclic compounds such as aminothiazoles, thietanes, aminotetrazoles, thiadiazoles, or thiadiazolines.[5] Some of these compounds are important since they are intermediates en route to variety of drugs.[6]

Thiocarbamates can react with weak bases, such as sodium or potassium carbonate, generating the corresponding anion, which can be represented through four plausible conformations as shown in Figure 1.[7] Molecular mechanics calculations onto *N*-acylthiocarbamate predict that *E*,*Z*′ is the most stable conformation.[8] Likewise, Schroeder et al. established, by using nuclear magnetic resonance, that *E*,*Z*′ was the most stable conformation in *N*-benzoyl-*O*-alkylthiocarbamates.[7] X-ray and semiempirical calculations would complete the structural determination of acylthiocarbamates in the literature and would be useful to understand the behaviour of these compounds versus electrophiles.

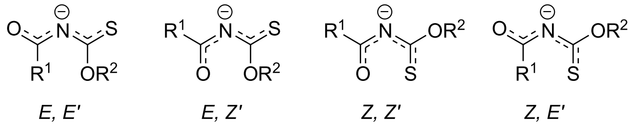
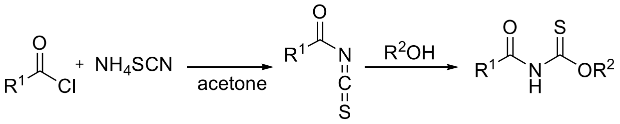


Figure 1.

Previously, we reported the synthesis of 1-benzoyl-3-alkylureas, using microwaves, through transamidation reactions,[9] and the alkylation of benzoyl and furoylthioureas as polydentate systems.[10] Here, we describe the synthesis of new acyl, furoyl and benzoylthiocarbamates and we have determined the structure of isopropyl *N*-(2-furoyl)thiocarbamate **3m** by single-crystal X-ray analysis. We have also confirmed that *E*,*Z*′ is the most stable conformation using the X-ray data and semiempirical theoretical calculations.



1 2 3

Scheme 1.

Keywords: Thiocarbamates; Acylthiocarbamates; Structural studies; Semiempirical methods.

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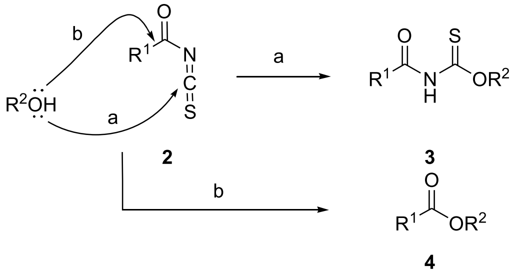
Table 1. Synthesis of compounds **3**

Entry	3	R^1	R^2	Yield (%)
1	**3a**	*t*-Bu	Me	68
2	**3b**	*t*-Bu	Et	67
3	**3c**	*t*-Bu	*i*-Pr	70
4	**3d**	Ph	*n*-C_5H_{11}	74
5	**3e**	Ph	*s*-C_5H_{11}	78
6	**3f**	Ph	*i*-C_5H_{11}	76
7	**3g**	Ph	*n*-$C_{18}H_{37}$	72
8	**3h**	Ph	Bn	81
9	**3i**	*p*NO_2–C_6H_4	*i*-Pr	71
10	**3j**	*p*F–C_6H_4	*i*-Pr	74
11	**3k**	Furyl	Me	72
12	**3l**	Furyl	Et	74
13	**3m**	Furyl	*i*-Pr	73
14	**3n**	Furyl	Bn	78
15	**3o**	2-(2-Furyl)vinyl	Me	78
16	**3p**	2-(2-Furyl)vinyl	Et	78
17	**3q**	2-(2-Furyl)vinyl	*i*-Pr	78

2. Results and discussion

The thiocarbamates were prepared by using acid chlorides **1** and ammonium thiocyanate in acetone. The intermediate isothiocyanate **2** reacts in situ with the corresponding alcohol affording the thiocarbamate **3** (Scheme 1 and Table 1).

Although there are two electrophilic carbon centres in **2**, the major product obtained is **3**, a consequence of the alcohol addition to the isocyanate electrophilic carbon (Scheme 2).



Scheme 2.

AM1, and PM3 semiempirical calculations predict a slightly negative charge value (−0.035, and −0.00075, respectively) on the carbon in the thiocarbamoyl group in products **2** (R^1 = Ph). However, steric effects on the carbonyl group lead to products **3** in high yields instead of compounds **4**. In the case of net charges values on *C*═O, AM1 and PM3 methods predict 0.418 and 0.408, respectively.

Synthesis of acylthiocarbamates seems to be general: a variety of aliphatic and aromatic alcohols were shown to be applicable. In general, slightly higher yields were obtained from aromatic, or conjugated alcohols **3d–q** in comparison to aliphatic alcohols **3a–c**. This result could be explained taking into account that aliphatic acylisothiocyanates are more reactive than conjugated or aromatic equivalents: the decomposition of these products afforded the corresponding acid. Scheme 2 illustrates the two possible mechanisms of the reaction of alcohols with isothiocyanates **2**. When the aliphatic chain in alcohols is branched, better yields were observed in the reaction to afford **3**. When alcohols with smaller aliphatic chain were used, products **3** were obtained in lower yields due to the generation of **4**. This fact could be explained assuming steric effects, as stated before.

To study the structure of acylthiocarbamates, isopropyl *N*-(2-furoyl)thiocarbamate (**3m**) was used as compound model. Thus, X-ray diffraction and semiempirical methods were employed to reveal the most stable conformation of **3m** (Fig. 1).

X-ray analysis of **3m** shows that fragments S1═C6–N1–C5═O2 are in a nearly planar alignment with a torsion angle S1–C6–N1–C5 = −177(2)° and C6–N1–C5–O2 = −3(4)° (Fig. 2).

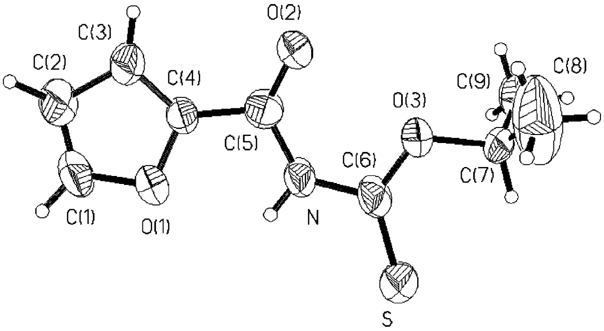


Figure 2. X-ray structure of compound **3m** showing the numbering scheme.

Asymmetry in angles C3–C4–C5 and O1–C4–C5 [131.8(5) and 118.9(4)°, respectively] could be due to the repulsion in the C3–H3···O2 system [C3·O2 = 3.006(6), H3···O2 = 2.96 Å] and the attraction in the NH···O1 system [N···O1 = 2.654(6) Å, H···O1 = 2.19 Å]. Taking into account that distances in C5–N1 and C6–N1 are 1.389(6) and 1.377(6) Å, respectively, it is possible to assume an electronic delocalization in that part of the molecule. In addition, C6–O3 bond distance [1.300(7) Å] indicates a partial double bond and a π-type conjugation in the whole system, this observation is in agreement with the previously reported results.[7]

In order to predict the minimum energy conformation, and relative stability of the possible conformers for **3m**, the

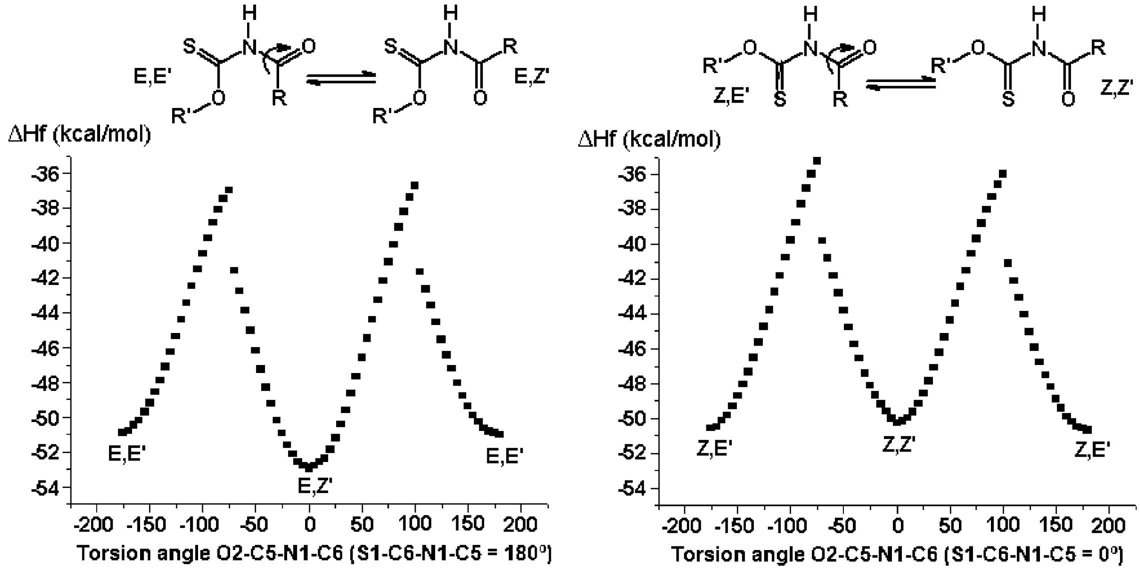


Figure 3. Heat of formation versus torsion angle O2–C5–N1–C6 (S1–C6–N1–C5 = 180 and 0°, respectively) for compound **3m**.

semiempirical PM3 method was used. The strategy was to study the heat of formation against the torsion angle related to the interconversion of these conformations.[11] Figure 3 represents the variation of the torsion angle that corresponds to the interconversion *E*,*E*′ *E*,*Z*′ and *Z*,*E*′ *Z*,*Z*′, respectively.

In the first case (Fig. 3a), the torsion angle O2–C5–N1–C6 was rotated every 5° from −180° (*E*,*E*′) to 180° (*E*,*E*′) passing through 0° (*E*,*Z*′), the torsion angle S1–C6–N1–C5 being fixed at 180°.

In the second case (Fig. 3b), the torsion angle O2–C5–N1–C6 was again rotated every 5° from −180° (*Z*,*E*′) to 180° (*Z*,*E*′) passing through 0° (*Z*,*Z*′), and the torsion angle S1–C6–N1–C5 was fixed at 0°.

In this sense, Figure 3 shows that the four conformers are consistent with the minimum energy in the curve and are close in energy (heat of formation around −50 kcal/mol). A complete optimisation onto the geometry corresponding to the energetic minimum was carried out and

Table 2. Bond distances, valence angles, and torsion angles for compound **3m** (the numbering scheme is shown in Figure 2). Bond distances are given in Å and angles in degrees (standard deviations in parenthesis)

3m	PM3	X-ray	3m	PM3	X-ray
Bond distances					
C1–C2	1.375	1.317(9)	C6–O3	1.344	1.300(7)
C1–O1	1.370	1.382(6)	C6–N1	1.404	1.377(6)
C2–C3	1.437	1.411(8)	C6–S1	1.654	1.635(6)
C3–C4	1.379	1.343(7)	C7–C9	1.523	1.46(3)
C4–O1	1.393	1.362(7)	C7–O3	1.449	1.486(8)
C4–C5	1.476	1.466(7)	C7–C8	1.523	1.50(4)
C5–O2	1.215	1.198(6)	N1–H1	1.001	0.8600
C5–N1	1.445	1.389(6)			
Valence angles					
C2–C1–O1	110.8	111.1(6)	O3–C6–S1	131.5	127.8(5)
C1–C2–C3	106.4	106.1(6)	N1–C6–S1	120.9	119.8(4)
C4–C3–C2	106.4	107.5(5)	C9–C7–O3	107.1	108.3(15)
C3–C4–O1	109.8	109.6(5)	C9–C7–C8	111.5	112.3(7)
C3–C4–C5	129.6	131.9(5)	O3–C7–C8	107.1	103.0(2)
O1–C4–C5	120.6	118.3(5)	C4–O1–C1	106.6	105.3(5)
O2–C5–N1	121.0	124.3(5)	C6–O3–C7	118.3	120.3(4)
O2–C5–C4	122.4	122.4(5)	C6–N1–C5	129.9	131.7(4)
N1–C5–C4	116.6	113.0(5)	C6–N1–H1	112.8	114.2
O3–C6–N1	107.5	111.5(5)	C5–N1–H1	117.1	114.2
Torsion angles					
O1–C1–C2–C3	0.0	6(4)	C2–C1–O1–C4	−0.1	−7(4)
C1–C2–C3–C4	0.1	−3(3)	N1–C6–O3–C7	180.0	−173(2)
C2–C3–C4–O1	−0.2	−1(3)	S1–C6–O3–C7	1.0	−4(5)
C2–C3–C4–C5	−179.3	−177(3)	C9–C7–O3–C6	120.0	129(2)
C3–C4–C5–O2	8.8	4(5)	C8–C7–O3–C6	−120.3	−112(3)
O1–C4–C5–O2	−170.2	−170(3)	O3–C6–N1–C5	7.7	−7(4)
C3–C4–C5–N1	−170.1	178(3)	S1–C6–N1–C5	−173.3	−177(2)
O1–C4–C5–N1	0.8	3(3)	O2–C5–N1–C6	7.2	−3(4)
C3–C4–O1–C1	0.2	5(4)	C4–C5–N1–C6	−173.7	−177(3)
C5–C4–O1–C1	179.4	−179(2)			

$E,E' = -51.3$ kcal/mol; $E,Z' = -54.4$ kcal/mol; $Z,E' = -51.2$ kcal/mol and $Z,Z' = -51.9$ kcal/mol heats of formation were found. This lead us to state that E,Z' conformation is the most stable. This result is in agreement with the experimental data from X-ray analysis, in which the torsion angles are S1–C6–N1–C5 = −177(2) and O2–C5–N1–C6 = −3(4)°. This also explains that the carbonyl and thiocarbonyl groups are in opposite positions, the molecule being in a E,Z' conformation (Fig. 2).

Table 2 shows selected data of bond distances, bond angles and torsion angles, obtained from X-ray diffraction studies and values from the semiempirical method PM3 for **3m**. Both methods showed a satisfactory correspondence. These results confirmed that the semiempirical method PM3, reports a reliable geometry for the propose systems.

3. Conclusion

In conclusion, a synthesis of new acythiocarbamates has been carried out. X-ray analysis and semiempirical theoretical calculations, established that the most stable conformation in acylthiocarbamates as E,Z'.

4. Experimental

4.1. General experimental

Reactions which required an inert atmosphere were conducted under dry nitrogen, and the glassware was oven dried (120 °C). All reagents were purchased from Aldrich or Merck and were used without further purification. Silica gel for flash chromatography was purchased from Scharlau or Merck (200–450 mesh), and compounds were visualized (UV light, 254 nm) on analytical thin layer chromatograms (TLC) and using benzene/methanol (9/1) as eluent. ^{1}H NMR spectra were recorded on a Bruker AC spectrometer at 250 MHz. ^{13}C NMR spectra and DEPT experiments were determined at 62 MHz. Chemical shifts are given in ppm relative to tetramethylsilane (TMS), which was used as an internal standard, and coupling constants J are reported in Hz. Melting points (mp) were determined on an Electrothermal C14500 apparatus and are uncorrected. IR spectra (ν_{max}/cm^{-1}) were recorded on a Bruker IRS48 instrument using KBr disc. MS (electronic impact) spectra were measured at 70 eV. Only the most important IR absorptions (cm^{-1}) and the molecular ions and/or base peaks in MS are given. Microanalyses were performed by the Servicio de Microanálisis of Universidad Complutense de Madrid.

4.2. Synthesis of acylthiocarbamates 3

The corresponding acyl chlorides (0.02 mol) were dissolved in dry acetone. To that solution, 0.02 mol of thiocyanate in acetone was added slowly. The mixture was stirred until a precipitate of ammonium chloride appeared. The precipitate indicated the formation of the corresponding organic isothiocyanate. So, to 0.02 mol of the generated isothiocyanate was slowly added the corresponding alcohol dissolved in acetone. The mixture was stirred for between 3 and 8 h. The progress of the reaction was monitored by TLC (using benzene/methanol (9/1) as eluent). When the reaction was completed the product was poured into 100 mL of cold water. The solid acylthiocarbamates were filtered out. Purification of compounds **3** were performed by recrystallization using acetone–H_2O as solvent.

4.2.1. Methyl *N*-pivaloylthiocarbamate 3a. 68% Yield; mp 69–70 °C; ν_{max}/cm^{-1} 3282 (NH), 2966 (C–H), 1714 (C=O), 1525 (NH), 1278 (C=S); δ_H (d_6-DMSO, 250 MHz), 8.72 (br s, 1H), 4.09 (s, 3H), 1.22 (s, 9H); δ_C (d_6-DMSO, 62 MHz), 190.7 (CS), 173.6 (CO), 59.5 (OCH_3), 40.3 (C), 27.1 (CH_3).

4.2.2. Ethyl *N*-pivaloylthiocarbamate 3b. 67% Yield; mp 90–92 °C; ν_{max}/cm^{-1} 3314 (NH), 2983 (CH), 1709 (C=O), 1518 (NH), 1272 (C=S); δ_H (d_6-DMSO, 250 MHz), 8.67 (br s, 1H), 4.58 (q, $J=6$ Hz, 2H), 1.41 (t, $J=6$ Hz, 3H), 1.22 (s, 9H); δ_C (d_6-DMSO, 62 MHz), 189.9 (CS), 173.5 (CO), 69.5 (CH_2), 40.3 (C), 27.1 [$(CH_3)_3C$], 13.8 (CH_3).

4.2.3. *Iso*propyl *N*-pivaloylthiocarbamate 3c. 70% Yield; mp 76–78 °C; ν_{max}/cm^{-1} 3207 (NH), 2980 (CH), 1720 (C=O), 1523 (NH), 1290 (C=S); δ_H (d_6-DMSO, 250 MHz), 8.57 (br s, 1H), 5.54 (hept, $J=6.5$ Hz, 1H), 1.42 (d, $J=6.5$ Hz, 6H), 1.24 (s, 9H); δ_C (d_6-DMSO, 62 MHz), 189.1 (CS), 173.3 (CO), 77.6 [$CH(CH_3)_2$], 40.2 [$C(CH_3)_3$], 27.1 [$C(CH_3)_3$], 21.2 (CH_3).

4.2.4. *n*-Pentyl *N*-benzoylthiocarbamate 3d. 74% Yield; mp 69–71 °C; ν_{max}/cm^{-1} 3208 (NH), 3063 (CH), 2956 (CH), 1696 (C=O), 1601 (C=C), 1300 (C=S), 1462 (CH_3); δ_H ($CDCl_3$, 250 MHz), 9.32 (br s, 1H), 7.90–7.40 (m, 5H), 4.60 (t, $J=6.2$ Hz, 2H), 1.85–1.75 (m, 2H), 1.40–1.35 (m, 4H), 0.95 (t, $J=6.2$ Hz, 3H); δ_C ($CDCl_3$, 62 MHz) 189.7 (CS), 162.8 (CO), 133.1 (C8), 133.0 (C5), 128.9 (C6 and C10), 127.8 (C7 and C9), 73.7 (OCH_2), 27.9 ($(CH_2)_2CH_2O$), 22.3 (CH_2CH_3), 13.9 (CH_3); MS (EI): m/z (%), 251 (5), 181 (25), 121 (18), 105 (100), 77 (72), 51 (34); elemental analysis calcd (%) for $C_{13}H_{17}NO_2S$: C, 62.12; H, 6.82; N, 5.57. Found: C, 62.04; H, 6.96; N, 5.41.

4.2.5. 2-Pentyl *N*-benzoylthiocarbamate 3e. 78% Yield; mp 64–65 °C; δ_H ($CDCl_3$, 250 MHz), 9.28 (br s, 1H), 7.90–7.40 (m, 5H), 5.60–5.55 (m, 1H), 1.80–1.60 (m, 2H), 1.45–1.40 (m, 4H), 0.90–0.85 (m, 3H); δ_C ($CDCl_3$, 62 MHz), 189.6 (CS), 162.8 (CO), 133.1 (C8), 133.0 (C5), 128.9 (C6 and C10), 127.8 (C7 and C9), 81.1 (OCH_2), 37.5 (OCH_2CH_2), 19.1 [$CH(CH_3)_2$], 18.4 (CH_3), 13.9 (CH_3).

4.2.6. *Iso*pentyl *N*-benzoylthiocarbamate de 3f. 76% Yield; mp 77–78 °C; ν_{max}/cm^{-1} 3263 (NH), 3059 (CH), 2958 (CH), 1700 (C=O), 1601 (C=C), 1300 (C=S), 1456 (CH_3); δ_H ($CDCl_3$, 250 MHz), 9.22 (br s, 1H), 7.90–7.35 (m, 5H), 4.60 (t, $J=6.2$ Hz, 2H), 2.00–1.60 (m, 3H), 0.95 (d, $J=6.4$ Hz, 6H); δ_C ($CDCl_3$, 62 MHz), 189.7 (CS), 162.7 (CO), 133.1 (C8), 133.0 (C5), 129.0 (C6 and C10), 127.8 (C7 and C9), 72.3 (OCH_2), 36.8 (OCH_2CH_2), 24.9 (CH), 22.4 (CH_3); MS (EI): m/z (%), 251 (2), 181 (14), 121 (9), 105 (100), 77 (63), 51 (14); elemental analysis calcd (%) for $C_{13}H_{17}NO_2S$: C, 62.12; H, 6.82; N, 5.57. Found: C, 62.19; H, 6.88; N, 5.43.

4.2.7. Octadecyl *N*-benzoylthiocarbamate 3g. 72% Yield; mp 68–69 °C; ν_{max}/cm^{-1} 3256 (NH), 3021 (CH), 2951 (CH), 1704 (C=O), 1604 (C=C), 1300 (N–C=S); δ_H (CDCl$_3$, 250 MHz), 9.18 (br s, 1H), 7.90–7.41 (m, 5H), 4.60–4.55 (m, 2H), 1.80–1.75 (m, 2H), 1.55–1.0 (m, 30H), 0.90–0.85 (m, 3H); δ_C (CDCl$_3$, 62 MHz), 189.7 (CS), 162.7 (CO), 133.1 (C5 and C8), 129.0 (C6 and C10), 127.7 (C7 and C9), 73.8 (OCH$_2$), 31.9 (CH$_2$(CH$_2$)$_{14}$, 31.9 (CH$_2$(CH$_2$)$_{14}$ 22.7 [CH$_2$(CH$_2$)$_{14}$$CH_2$], 14.1 (CH$_3$); elemental analysis calcd (%) for $C_{26}H_{43}NO_2S$: C, 72.01; H, 9.99; N, 3.23. Found: C, 72.19; H, 9.85; N, 3.34.

4.2.8. Benzyl *N*-benzoylthiocarbamate 3h. 81% Yield; mp 104–106 °C; ν_{max}/cm^{-1}: 3314 (NH), 3073 (CH), 2968 (CH), 1693 (C=O), 1601 (C=C), 1269 (C=S); δ_H (CDCl$_3$, 250 MHz), 9.24 (br s, 1H), 7.83–7.25 (m, 10H), 5.62 (s, 2H); δ_C (CDCl$_3$, 62 MHz), 188.9 (CS), 162.8 (CO), 137.4 (C5 and C8), 131.1 (1C), 128.3 (1C), 127.3 (1C), 127.1 (1C) (aromatic), 129.0 (C6 and C10), 127.7 (C7 and C9), 74.2 (CH$_2$); elemental analysis calcd (%) for $C_{15}H_{13}NO_2S$: C, 66.40; H, 4.83; N, 5.16. Found: C, 66.29; H, 4.99; N, 5.27.

4.2.9. *Iso*propyl *N*-(4-nitrobenzoyl)thiocarbamate 3i. 71% Yield; mp 101–103 °C; ν_{max}/cm^{-1} 3209 (NH), 3120 (=CH), 3060 (CH), 2976 (CH), 1698 (C=O), 1601 (C=C), 1550 (NO$_2$), 1280 (C=S); δ_H (CDCl$_3$, 250 MHz), 9.45 (br s, 1H), 8.30 (d, J=8.1 Hz, 2H), 8.04 (d, J=8.1 Hz, 2H), 5.65 (hept, J=6.2 Hz, 1H), 1.40 (d, J=6.2 Hz, 6H); δ_C (CDCl$_3$, 62 MHz), 187.7 (CS), 161.7 (CO), 150.0 (C8), 138.7 (C5), 128.9 (C6, C10), 123.8 (C7, C9), 77.9 [CH(CH$_3$)$_2$], 21.0 (CH$_3$); MS (EI): m/z (%), 268 (<1), 226 (3), 166 (5), 150 (100), 122 (7); elemental analysis calcd (%) for $C_{11}H_{12}N_2O_4S$: C, 49.25; H, 4.51; N, 10.44. Found: C, 49.45; H, 4.72; N, 10.50.

4.2.10. *Iso*propyl *N*-(4-fluorobenzoyl)thiocarbamate 3j. 74% Yield; mp 111–112 °C; ν_{max}/cm^{-1} 3256 (NH), 3080 (=CH), 3100 (C–H), 2974 (C–H), 1696 (C=O), 1604 (C=C), 1287 (C=S); δ_H (CDCl$_3$, 250 MHz), 9.22 (br s, 1H), 7.87 (q, J=5.2 Hz, 2H), 7.16 (t, J=8.1 Hz, 2H), 5.63 (hept, J=6.1 Hz, 1H), 1.43 (d, J=6.1 Hz, 6H); δ_C (CDCl$_3$, 62 MHz), 188.6 (CS), 167.6 (CO), 167.6, 163.6 (C8), 130.7 (C5), 130.4, 129.3 (C6, C10), 116.2, 115.9 (C7, C9), 77.9 OCH, 21.2 (CH$_3$); MS (EI): m/z (%), 241 (3), 199 (15), 139 (22), 123 (100), 95 (46), 75 (19); elemental analysis calcd (%) for $C_{11}H_{12}FNO_2S$: C, 54.76; H, 5.01; N, 5.81. Found: C, 54.88; H, 5.12; N, 5.76.

4.2.11. Methyl *N*-(2-furoyl)thiocarbamate 3k. 72% Yield; mp 97–100 °C; ν_{max}/cm^{-1} 3416 (NH), 3120, (=CH), 2970 (CH), 1712 (C=O), 1581 (C=C), 1298 (C=S), 1025 (C–O–C); δ_H (CDCl$_3$, 250 MHz), 9.46 (br s, 1H), 7.55–7.47 (m, 1H), 7.31–7.26 (m, 1H); 6.58–6.54 (m, 1H), 4.17 (s, 3H); δ_C (CDCl$_3$, 62 MHz), 189.4 (CS), 152.3 (CO), 145.9 (C2), 145.7 (C5), 118.3 (C3), 113.3 (C4), 59.4 (CH$_3$); elemental analysis calcd (%) for $C_7H_7NO_3S$: C, 45.40; H, 3.81; N, 7.56. Found: C, 45.88; H, 3.92; N, 7.60.

4.2.12. Ethyl *N*-(2-furoyl)thiocarbamate 3l. 74%; mp 98–99 °C; ν_{max}/cm^{-1} 3411 (NH), 3122 (=CH), 2970 (CH); 1712 (C=O), 1583 (C=C), 1310 (C=S), 1025 (C–O–C); δ_H (CDCl$_3$, 250 MHz), 9.49 (br s, 1H), 7.54–7.53 (m, 1H), 7.31–7.27 (m, 1H), 6.58–6.55 (m, 1H), 4.60 (q, J=7.1 Hz, 2H), 1.50 (t, J=7.1 Hz, 3H); δ_C (CDCl$_3$, 62 MHz), 188.1 (CS), 152.3 (CO), 145.7 (C2), 145.5 (C5), 117.8 (C3), 112.6 (C4), 68.7 (CH$_2$), 13.4 (CH$_3$); MS (EI): m/z (%), 199 (2), 171 (1), 111 (1), 95 (100), 67 (6), 54 (2); elemental analysis calcd (%) for $C_8H_9NO_3S$: C, 48.23; H, 4.55; N, 7.03. Found: C, 48.58; H, 4.92; N, 7.30.

4.2.13. *Iso*propyl *N*-(2-furoyl)thiocarbamate 3m. 73% Yield; mp 76–78 °C; ν_{max}/cm^{-1} 3415 (N–H), 3132 (=CH), 2988 (CH), 1715 (C=O), 1584 (C=C), 1298 (C=S), 1013 (C–O–C); δ_H (CDCl$_3$, 250 MHz), 9.27 (br s, 1H), 7.51–7.50 (m, 1H), 7.27–7.25 (m, 1H), 6.53–6.52 (m, 1H), 5.55 (hept, J=6.2 Hz, 1H), 1.39 (d, J=6.3 Hz, 6H,); δ_C (CDCl$_3$, 62 MHz), 187.7 (CS), 152.3 (CO), 146.1 (C2), 145.5 (C5), 118.1 (C3), 113.3 (C4), 77.65 [CH(CH$_3$)$_2$], 21.3. (CH$_3$); MS (EI): m/z (%), 213 (6), 171 (23), 111 (40), 109 (1), 95 (100), 67(4), 55 (16); elemental analysis calcd (%) for $C_9H_{11}NO_3S$: C, 50.69; H, 5.20; N, 6.57. Found: C, 50.88; H, 5.72; N, 6.69.

4.2.14. Benzyl *N*-(2-furoyl)thiocarbamate 3n. 78% Yield; mp 114–116 °C; ν_{max}/cm^{-1} 3418 (NH), 3130 (=CH), 2990 (CH), 1718 (C=O), 1609 (C=C), 1290 (C=S), 1012 (C–O–C); δ_H (CDCl$_3$, 250 MHz), 9.39 (s, 1H), 7.50–7.49 (m, 1H), 7.26–7.25 (m, 1H), 6.65–6.60 (m, 1H), 5.63 (s, 2H), 7.46–7.30 (m, 5H); δ_C (CDCl$_3$, 62 MHz), 184.5 (CS), 154.7 (CO), 149.9 (C2), 142.0 (C5), 137.4 (1C), 128.3 (1C), 127.3 (1C), 127.1 (1C), (Ph), 119.7 (C3), 109.5 (C4), 71.9 (CH$_2$); MS (EI): m/z (%), 261 (<1), 171 (2), 111 (2), 95 (100), 67 (8); elemental analysis calcd (%) for $C_{13}H_{11}NO_3S$: C, 59.76; H, 4.24; N, 5.36. Found: C, 59.88; H, 4.92; N, 5.60.

4.2.15. Methyl *N*-[3-(2-furylacryloyl)]thiocarbamate 3o. 53% Yield; mp 117–118 °C; ν_{max}/cm^{-1} 3254 (NH), 3118 (=CH), 2980, (C–H), 1713 (C=O), 1626 (C=C), 1278 (C=S), 1023 (C–O–C); δ_H (CDCl$_3$, 250 MHz), 11.83 (br s, 1H), 7.84 (d, J=1.7 Hz, 1H), 7.46 (d, J=15.4 Hz, 1H), 6.92 (d, J=3.4 Hz, 1H), 6.69 (d, J=15.4 Hz, 1H), 6.65 (dd, J=3.4, 1.7 Hz, 1H), 4.02 (s, 3H); δ_C (CDCl$_3$, 62 MHz), 189.8 (CS), 162.5 (CO), 151.0 (C2), 145.4 (C5), 132.5 (C6), 116.5 (C3), 116.2 (C7), 112.7 (C4), 59.4 (CH$_3$); elemental analysis calcd (%) for $C_9H_9NO_3S$: C, 51.17; H, 4.29; N, 6.63. Found: C, 51.48; H, 4.12; N, 6.30.

4.2.16. Ethyl *N*-[3-(2-furyl)acryloyl]thiocarbamate 3p. 78% Yield; mp 114–116 °C; ν_{max}/cm^{-1} 3250 (NH), 3030 (=CH), 2982 (CH), 1716 (C=O), 1630 (C=C), 1336 (CH$_3$), 1275 (C=S); δ_H (CDCl$_3$, 250 MHz), 11.76 (br s, 1H), 7.83 (d, J=1.6 Hz, 1H), 7.50 (d, J=15.4 Hz, 1H), 6.92 (d, J=3.4 Hz, 1H), 6.68 (d, J=15.4 Hz, 1H), 6.65 (dd, J=3.4, 1.6 Hz, 1H), 4.50 (q, J=7.1 Hz, 2H), 1.31 (t, J=7.1 Hz, 3H); δ_C (CDCl$_3$, 62 MHz), 188.7 (CS), 161.9 (CO), 150.4 (C2), 145.7 (C5), 130.1 (C6), 117.3 (C3), 116.2 (C7), 112.6 (C4), 67.1 (CH$_2$), 13.4 (CH$_3$); elemental analysis calcd (%) for $C_{10}H_{11}NO_3S$: C, 53.32; H, 4.92; N, 6.22. Found: C, 53.58; H, 4.82; N, 6.32.

4.2.17. *Iso*propyl *N*-[3-(2-furyl)acryloyl]thiocarbamate 3q. 62% Yield; mp 70–72 °C; ν_{max}/cm^{-1} 3251 (NH), 3120 (=CH), 2987 (CH), 1718 (C=O), 1630 (C=C), 1280 (C=S), 1020 (C–O–C); δ_H (CDCl$_3$, 250 MHz), 11.76 (br s, 1H), 7.83 (d, J=1.6 Hz, 1H), 7.43 (d, J=15.4 Hz, 1H), 6.92

(d, $J=3.4$ Hz, 1H), 6.69 (d, $J=15.4$ Hz, 1H), 6.65 (dd, $J=3.4$, 1.6 Hz, 1H), 5.54 (hept, $J=6.1$ Hz, 1H), 1.37 (d, $J=6.1$ Hz, 6H); δ_C ($CDCl_3$, 62 MHz), 188.0 (CS), 161.9 (CO), 150.4 (C5), 145.6 (C2), 130.1 (C7), 117.4 (C6), 116.2 (C4), 112.6 (C3), 77.6 [$OCH(CH_3)$], 21.7 (CH_3); MS (EI): *m*/*z* (%), 239 (<1), 197 (2), 137 (3), 121 (100); elemental analysis calcd (%) for $C_{11}H_{13}NO_3S$: C, 55.21; H, 5.48; N, 5.85. Found: C, 55.48; H, 5.62; N, 5.60.

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