Thioamidoalkylation of 1,3-Dicarbonyl Compounds, Enol Silyl Ethers, and Enamines

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Abstract: Novel syntheses of β-thioamido ketones via thioamidoalkylations of malonates, β-keto esters, β-diketones, enol silyl ethers, and enamines with *N*-(α-thioamidoalkyl)benzotriazoles are described.

Key words: thioamides, *N*-(α-thioamidoalkyl)benzotriazoles, thioamidoalkylation, 1,3-dicarbonyl compounds, enol silyl ethers, enamines

The utility of thioamides as synthetic intermediates is increasingly recognized.[1] In the preparation of heterocycles containing both nitrogen and sulfur two heteroatoms can be introduced in a single step, to provide, for example, oxathiazines,[2] thiadiazines,[3] dithiazines,[4] thiazines,[5] thiazolines[1a] and thiazoles.[1a] Thioamides are precursors for other substrates.[6] Some thioamides possess inhibitory activity against moulds,[7] yeasts,[8] dermatophytes,[9] and phytopathogenic fungi *in vitro*,[10] while others are used as flotation and vulcanization agents, as additives to lubricating oils and greases, and as interesting ligands in coordination chemistry.[1a]

The thioamide linkage in thiopeptides is isosteric to the parent (oxo)amide bond.[11] Although the larger size of the sulfur atom and the longer carbon–sulfur bond length restrict the allowed ϕ and Ψ angles of the amino acids flanking the thioamide group, conformations compatible with the three major types of regular secondary structure (α-helix, β-sheet, and β-turn) are accessible in thiopeptides.[12] The conformational restrictions introduced by the thioamides, together with their ability to confer increased enzymatic stability[13] and increased potency and selectivity,[14] affords thiopeptides potential in drug design. The thioamide moiety also introduces distinctive spectroscopic properties into a peptide, making it a potential probe of local conformations.[15]

Available routes to thioamides of type **1** can be classified according to which of the alternative bonds **a**–**e** is constructed (Figure 1): (i) formation of bond **a** by the thionation of the corresponding amides with the aid of phosphorus pentasulfide,[16] Lawesson's reagents, [17] or sulfur dihydride catalyzed by triflic anhydride (Tf_2O)[18] (although this is limited by the availability of the starting amide); (ii) formation of bond **b** by using isothiocyanate as an electrophile to react with aromatic and hetero(aromatic) compounds under Lewis acid conditions[19] (limited by the availability of isothiocyanates); (iii) formation of bond **c** by treating dithioacids with azides in the presence of a base promoter[20] (limited by the availability of dithioacids); (iv) formation of bond **d** by the N-alkylation of a thioamide $RCSNH_2$ achieved in two steps by *N*-benzotriazolylalkylation of the thioamide to produce adducts of type **2** followed by reductive elimination of the benzotriazolyl group with sodium borohydride;[21] (v) formation of bond **e** achieved by treating **2** with 2.1 equivalents of Grignard reagents;[22] and (vi) formation of both bonds **a** and **c** by three-component Kindler reactions[23] (used mainly for tertiary thioamides).

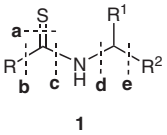

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Figure 1 Classification of available routes to thioamides of type **1**

We now report an efficient extension of method v to prepare novel thioamide derivatives of type **4** by the thioamidoalkylation of malonic esters, β-keto esters, and β-diketones with *N*-(α-thioamidoalkyl)benzotriazoles **2** (Scheme 1 and Table 1). We also describe the reactions of **2** with enol silyl ethers **5**, and enamines **6** which produce novel β-thioamido ketones **7** (Scheme 2 and Table 2).

Thioamidoalkylation of 1,3-Dicarbonyl Compounds

The *N*-(α-thioamidoalkyl)benzotriazoles **2** were prepared by known one-pot reactions from benzotriazole, the appropriate aldehyde and thiobenzamide in refluxing toluene with azeotropic removal of the water.[21] Adducts **2** reacted efficiently with the appropriate malonates **3** in the presence of 1.2 equivalents *t*-BuOK in DMSO at room temperature to afford thioamidoalkylated products **4a**–**f** (80–93%) yields (Scheme 1 and Table 1). The structures of **4a**–**f** were confirmed by their spectral data together with elemental analyses. Because the malonic ester function is attached to a chiral center, in most cases the two

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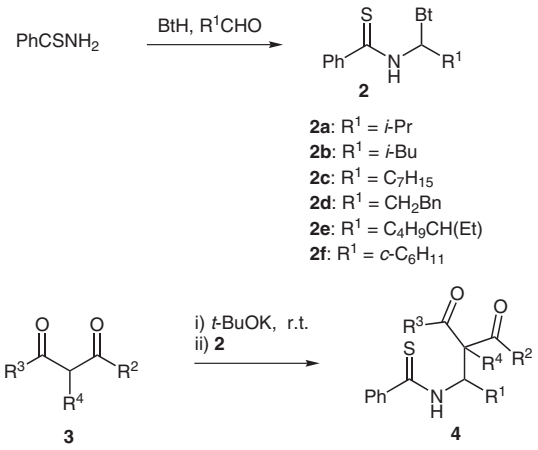
methoxy- or ethoxy-carbonyl groups are pro-chiral and show different chemical shifts in both the ^1H and ^{13}C NMR spectra. Typical downfield doublets were observed for the thioamide NH group coupled with the adjacent CH.



Scheme 1

We examined similar reactions with β-keto esters: ethyl benzoylacetate (**3f**) and methyl (**3g**), and benzyl acetoacetate (**3h**) each reacted with *N*-(α-thioamidoalkyl benzotriazoles **2** under similar conditions (*t*-BuOK/DMSO) to give the thioamidoalkylated products **4g–m** in 57–90% yields. Two diastereoisomers formed for **4g–j**, but a single form was seen for **4k–m**, as indicated in their NMR spectra. The diastereoisomeric ratios were determined from their relative integral values in the ^1H spectra.

We extended the scope of the reaction to include symmetrical and unsymmetrical diketones **3i–l**. Compounds **2a–c** reacted with acetylacetone (**3i**), α-benzoylacetophenone (**3j**), 2,2,6,6-tetramethylheptane-3,5-dione (**3k**), and 1-phenylbutane-1,3-dione (**3l**), under similar conditions to provide the expected thioamidoalkylation products **4n–s** (53–90%) (see Table 1).

Thioamidoalkylation of Enol Silyl Ethers and Enamines

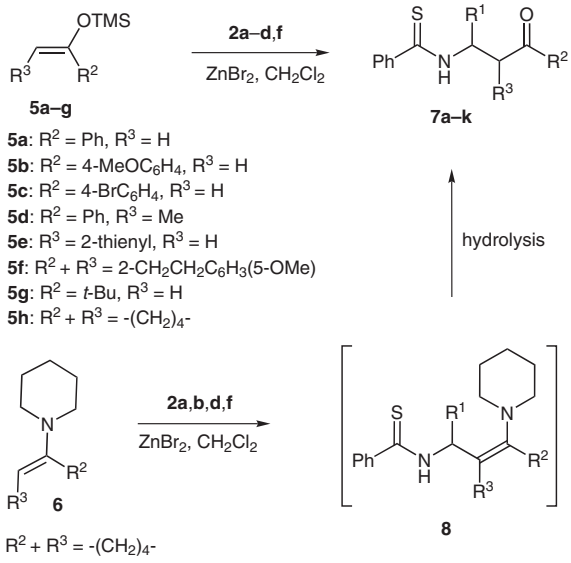
N-Substituted benzotriazoles of type BtCNC=O(R) when treated with Lewis acids form the benzotriazole anion and

Table 1 Thioamidoalkylation of 1,3-Dicarbonyl Compounds **3**

Product	R^1	R^2	R^3	R^4	dr[a]	Yield (%)
4a	*i*-Bu	MeO	MeO	H	–	92
4b	*i*-Pr	EtO	EtO	H	–	93
4c	*c*-C_6H_{11}	*t*-BuO	*t*-BuO	H	–	84
4d	$Me(CH_2)_3CH(Et)$	MeO	MeO	H	–	90
4e	*n*-C_7H_{15}	EtO	EtO	Me	–	86
4f	$BnCH_2$	EtO	EtO	Et	–	80
4g	*i*-Bu	Ph	EtO	H	67:33	66
4h	*i*-Pr	Ph	EtO	H	52:48	70
4i	*i*-Pr	Me	MeO	H	67:33	81
4j	*i*-Bu	Me	MeO	H	67:33	90
4k	*i*-Bu	Me	EtO	H	56:44	79
4l	*n*-C_7H_{15}	Me	BnO	H	60:40	57
4m	$Me(CH_2)_3CH(Et)$	Me	BnO	H	63:37	80
4n	*i*-Pr	Me	Me	H	–	71
4o	*i*-Pr	Ph	Ph	H	–	60
4p	*i*-Bu	CH_3	Me	H	–	90
4q	*i*-Bu	Ph	Ph	H	–	53
4r	*n*-C_7H_{15}	*t*-Bu	*t*-Bu	H	–	70
4s	*i*-Bu	Ph	Me	H	67:33	70

[a] Diastereomeric ratio was evaluated by ^1H NMR analysis.

the corresponding acylimmonium cation which then reacts with nucleophiles.[24] Compounds of type **2** react similarly with enol silyl ether **5** in refluxing CH_2Cl_2 in the presence of 2.0 equivalents of zinc bromide. Enol silyl ethers **5** from aryl **5a**–**d**, heteroaryl **5e**, cyclic **5f**, and acyclic ketones **5g** were all used as nucleophiles affording β-thioamido ketones **7a**–**g** (33–80%) (Scheme 2 and Table 2). However, reaction of cyclohexanone-derived silyl enol ether **5h** with **2a** under the same reaction conditions failed.



For designation of R^1, R^2, R^3 and R^4 in **7** see Table 2

Scheme 2

Table 2 Thioamide Ketones **7** Prepared

Product	R^1	R^2	R^3	Yield (%)
7a	$BnCH_2$	Ph	H	73
7b	*c*-C_6H_{11}	4-$MeOC_6H_4$	H	80
7c	*i*-Bu	4-BrC_6H_4	H	64
7d	*i*-Pr	Ph	Me	77
7e	*c*-C_6H_{11}	2-thienyl	H	51
7f	*n*-C_7H_{15}	2-$CH_2CH_2C_6H_3$(5-OMe)		60[a]
7g	$BnCH_2$	*t*-Bu	H	33
7h	*i*-Pr	-$(CH_2)_4$-		55
7i	*i*-Bu	-$(CH_2)_4$-		66[b]
7j	$BnCH_2$	-$(CH_2)_4$-		69[c]
7k	*c*-C_6H_{11}	-$(CH_2)_4$-		73

[a] Total yield of two isolated diastereoisomers.
[b] Isolated as diastereoisomeric mixture in a ratio of 86:14.
[c] Isolated as diastereoisomeric mixture in a ratio of 55:45.

Treating 1-piperidinocyclohexene (**6**) with **2a**,**b**,**d**,**f** in the presence of zinc bromide in CH_2Cl_2 at room temperature afforded β-thioamido ketones **7h**–**k** in 55–73% yields (Scheme 2 and Table 2). The formation of **7h**–**k** is ascribed to the hydrolysis of the thioamidoalkylation product **8** during the workup.

Structures of **7a**–**k** were confirmed by their ^1H and ^{13}C NMR spectra and by elemental analyses. Their ^1H NMR spectra no longer showed distinctive signals of the benzotriazolyl group. The doublets at 8.31–9.53 ppm and at 8.68–8.8.86 ppm in the ^1H NMR spectra of **7a**–**g** and **7h**–**k**, respectively, were assigned to the NH proton. The multiplets at 4.96–5.31 ppm in the ^1H NMR spectra of **7a**–**g** were assigned to the methine proton next to NH. For **7h**–**k**, the new set signals that appeared in their ^1H NMR spectra in the ranges 1.59–1.75 ppm, 2.03–2.45 ppm, and 2.99–3.08 ppm were assigned to the aliphatic protons of the cyclohexanone ring. The ^{13}C NMR spectra of **7a**–**k** showed new signals at 192.8–199.1 ppm as well as at 198.4–216.9 ppm, corresponding to carbonyl carbon and thiocarbonyl carbon, respectively.

Efforts to extend the methodology to the thioamidoalkylation of nitroalkanes (e.g., nitromethane, nitroethane) acetonitriles (e.g., propionitrile, phenylacetonitrile), esters (e.g., methyl phenylacetate, ethyl naphthylacetate), acetylenes (e.g., hexylacetylene, phenylacetylene), and reactive heterocycles (e.g., thiophene, benzofuran) failed.

In summary, *N*-(α-thioamidoalkyl)benzotriazoles react efficiently with diverse malonates, β-keto esters, β-diketones, enol silyl ethers, and enamines to afford thioamides possessing a carbonyl group at the β position. Our stable and easily prepared starting materials are available from a wide range of aldehydes and react under mild conditions. The high yields in most cases of the previously unknown analogues of thioamide recalls the potential of *N*-(α-thioamidoalkyl)benzotriazoles as advantageous thioamidoalkylating agents. The byproduct benzotriazole formed during the reaction was easily removed by washing the reaction mixture with dilute alkali, making the whole procedure very simple.

All mps are uncorrected. ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini (300 MHz) spectrometer in $CDCl_3$ with TMS as the internal standard. Microanalyses were performed on a Carlo Erba 1106 elemental analyzer. Column chromatography was performed on silica gel 200–425 mesh. CH_2Cl_2 was distilled and DMSO was dried over molecular sieves prior to use. *N*-(α-Thioamidoalkyl)benzotriazoles **2** were prepared according to literature procedures.[21]

Thioamides 4; General Procedure

A mixture of 1,3-dicarbonyl compounds **3** (2 mmol) and t-BuOK (0.45 g, 4 mmol) in DMSO (10 mL) was stirred at r.t. for 40 min. To the resulting mixture, was added dropwise a solution of appropriate *N*-(α-thioamidoalkyl)benzotriazole **2** (2 mmol) in DMSO (10 mL) and the mixture was stirred at r.t. for 10 h. After quenching with H_2O (20 mL) and extraction with EtOAc (4 × 25 mL), the combined organic layers were washed with H_2O, dried ($MgSO_4$) and the solvent was removed under reduced pressure. The resulting oil was

subjected to column chromatography (eluent: hexanes–EtOAc, 3:1) to give the pure thioamides **4**.

2-(3-Methyl-1-thiobenzoylaminobutyl)malonic Acid Dimethyl Ester (4a)
Yield: 0.621 g (92%); colorless microcrystals; mp 85–86 °C.

^{1}H NMR: δ = 8.65 (d, *J* = 9.2 Hz, 1 H), 7.75 (d, *J* = 6.9 Hz, 2 H), 7.48–7.36 (m, 3 H), 5.62–5.56 (m, 1 H), 3.86 (d, *J* = 3.2 Hz, 1 H), 3.83 (s, 3 H), 3.72 (s, 3 H), 1.88–1.66 (m, 2 H), 1.53–1.44 (m, 1 H), 1.02 (d, *J* = 6.5 Hz, 3 H), 0.90 (d, *J* = 6.7 Hz, 3 H).

^{13}C NMR: δ = 199.2, 169.2, 168.1, 142.0, 131.1, 128.6, 126.8, 53.4, 53.2, 53.1, 52.8, 41.6, 25.4, 22.7, 22.6.

Anal. Calcd for $C_{17}H_{23}NO_4S$: C, 60.51; H, 6.87; N, 4.15. Found: C, 60.23; H, 6.86; N, 4.17.

2-(2-Methyl-1-thiobenzoylaminopropyl)malonic Acid Diethyl Ester (4b)
Yield: 0.654 g (93%); colorless microcrystals; mp 101–103 °C.

^{1}H NMR: δ = 9.10 (d, *J* = 9.2 Hz, 1 H), 7.80 (d, *J* = 6.7 Hz, 2 H), 7.44–7.36 (m, 3 H), 5.34 (dt, *J* = 9.5, 2.9 Hz, 1 H), 4.30 (q, *J* = 7.1 Hz, 2 H), 4.13 (*J* = 7.1 Hz, 2 H), 3.90 (d, *J* = 3.0 Hz, 1 H), 2.10–2.03 (m, 1 H), 1.33 (t, *J* = 7.1 Hz, 3 H), 1.23 (t, *J* = 7.1 Hz, 3 H), 1.07 (t, *J* = 7.2 Hz, 6 H).

^{13}C NMR: δ = 199.7, 169.4, 167.8, 142.1, 131.0, 128.5, 126.7, 62.4, 62.0, 60.4, 52.2, 32.2, 19.8, 19.6, 14.0.

Anal. Calcd for $C_{18}H_{25}NO_4S$: C, 60.51; H, 7.17; N, 3.99. Found: C, 60.26; H, 7.27; N, 3.97.

2-(Cyclohexylthiobenzoylaminomethyl)malonic Acid Di-*tert*-butyl Ester (4c)
Yield: 0.752 g (84%); colorless microcrystals; mp 94–96 °C.

^{1}H NMR: δ = 9.23 (d, *J* = 9.3 Hz, 1 H), 7.78 (d, *J* = 6.73 Hz, 2 H), 7.47–7.40 (m, 3 H), 5.32 (dt, *J* = 6.0, 3.3 Hz, 1 H), 7.34 (d, *J* = 3.4 Hz, 1 H), 1.85–1.58 (m, 6 H), 1.53 (s, 9 H), 1.40 (s, 9 H), 1.33–1.19 (m, 5 H).

^{13}C NMR: δ = 199.3, 169.1, 167.2, 142.1, 130.8, 128.4, 126.8, 83.2, 82.9, 59.7, 56.0, 42.2, 30.0, 28.0, 27.7, 26.1, 26.0.

Anal. Calcd for $C_{25}H_{37}NO_4S$: C, 67.08; H, 8.33; N, 3.13. Found: C, 67.30; H, 8.53; N, 3.13.

2-(2-Ethyl-1-thiobenzoylaminohexyl)malonic Acid Dimethyl Ester (4d)
Yield: 0.683 g (90%); yellow oil.

^{1}H NMR: δ = 8.98 (d, *J* = 9.6 Hz, 1 H), 7.78 (d, *J* = 8.1 Hz, 2 H), 7.48–7.37 (m, 3 H), 5.55–5.49 (m, 1 H), 3.88 (t, *J* = 2.5 Hz, 1 H), 3.82 (s, 3 H), 3.69 (s, 3 H), 1.83–1.69 (m, 1 H), 1.54–1.42 (m, 3 H), 1.34–1.22 (m, 5 H), 0.98–0.84 (m, 6 H).

^{13}C NMR: δ = 199.6, 199.5, 169.7, 168.2, 142.2, 142.1, 131.0, 130.9, 128.5, 126.7, 126.6, 57.3, 57.2, 53.0, 52.8, 51.4, 51.3, 41.8, 41.7, 28.9, 28.7, 28.4, 27.4, 23.0, 22.9, 22.2, 22.0, 14.0, 13.9, 11.0, 9.7.

Anal. Calcd for $C_{20}H_{29}NO_4S$: C, 63.30; H, 7.70; N, 3.69. Found: C, 63.11; H, 7.90; N, 3.63.

2-Methyl-2-(1-thiobenzoylaminooctyl)malonic Acid Diethyl Ester (4e)
Yield: 0.725 g (86%); yellow oil.

^{1}H NMR: δ = 8.90 (d, *J* = 9.9 Hz, 1 H), 7.80 (d, *J* = 6.9 Hz, 2 H), 7.52–7.40 (m, 3 H), 5.43 (dt, *J* = 7.3, 2.9 Hz, 1 H), 4.34 (q, *J* = 7.1 Hz, 2 H), 4.16 (q, *J* = 7.1 Hz, 2 H), 1.85–1.82 (m, 1 H), 1.64 (s, 3 H), 1.61–1.40 (m, 2 H), 1.38–1.23 (m, 15 H), 0.91 (t, *J* = 6.6 Hz, 3 H).

^{13}C NMR: δ = 199.3, 171.6, 171.2, 142.2, 131.0, 128.5, 126.7, 62.3, 61.9, 59.4, 58.3, 31.8, 31.2, 29.7, 29.1, 26.2, 22.6, 19.6, 14.1, 14.0, 13.9.

Anal. Calcd for $C_{23}H_{35}NO_4S$: C, 65.52; H, 8.37; N, 3.32. Found: C, 65.19; H, 8.67; N, 3.72.

2-Ethyl-2-(3-phenyl-1-thiobenzoylaminopropyl)malonic Acid Diethyl Ester (4f)
Yield: 0.706 g (80%); yellow microcrystals (80%), mp 55–57 °C

^{1}H NMR: δ = 9.00 (d, *J* = 9.8 Hz, 1 H), 7.77–7.74 (m, 2 H), 7.47–7.37 (m, 3 H), 7.28–7.14 (m, 5 H), 5.61 (dt, *J* = 8.0, 2.4 Hz, 1 H), 4.35–4.23 (m, 2 H), 4.20–4.11 (m, 2 H), 2.90–2.77 (m, 2 H), 2.18–2.10 (m, 2 H), 1.92–1.75 (m, 2 H), 1.32 (t, *J* = 7.1 Hz, 3 H), 1.23 (t, *J* = 7.1, Hz, 3 H), 1.07 (t, *J* = 7.4 Hz, 3 H).

^{13}C NMR: δ = 199.4, 171.2, 170.4, 142.1, 141.6, 131.1, 128.6, 128.4, 128.3, 126.8, 126.0, 62.9, 62.0, 61.0, 58.9, 34.2, 32.8, 27.2, 14.1, 14.1, 10.0.

Anal. Calcd for $C_{25}H_{31}NO_4S$: C, 68.00; H, 7.08; N, 3.17. Found: 67.73; H, 7.15; N, 3.18.

2-Benzoyl-5-methyl-3-thiobenzoylaminohexanoic Acid Ethyl Ester (4g)
This compound was obtained as a 67:33 mixture of two diastereoisomers. Yield: 0.525 g (66%); colorless microcrystals; mp 98–101 °C.

^{1}H NMR: δ = 8.80–8.73 (m, 1 H), 8.10 (d, *J* = 7.4 Hz, 0.67 H), 7.90 (d, *J* = 7.2 Hz, 1 H), 7.80 (d, *J* = 7.1 Hz, 0.33 H), 7.72 (d, *J* = 7.0 Hz, 1 H), 7.65–7.34 (m, 7 H), 5.62–5.57 (m, 1 H), 5.00 (d, *J* = 3.4 Hz, 0.33 H), 4.90 (d, *J* = 3.1 Hz, 0.67 H), 4.28 (q, *J* = 7.1 Hz, 1.32 H), 4.17–4.13 (m, 0.66 H), 2.01–1.91 (m, 1 H), 1.80–1.73 (m, 1 H), 1.65–1.56 (m, 1 H), 1.28 (t, *J* = 7.1 Hz, 2 H), 1.20 (t, *J* = 7.1 Hz, 1 H), 1.05–1.00 (m, 4 H), 0.94 (d, *J* = 6.6 Hz, 1 H), 0.90 (d, *J* = 6.5 Hz, 1 H).

^{13}C NMR: δ = 198.9, 198.8, 195.7, 194.4, 169.6, 168.6, 141.9, 136.0, 135.8, 134.3, 133.9, 131.2, 131.0, 129.1, 129.0, 128.6, 128.6 128.5, 126.8, 62.2, 61.9, 55.6, 55.1, 54.1, 53.4, 42.1, 40.8, 25.5, 22.9, 22.8, 22.8, 22.3, 14.1, 13.9.

Anal. Calcd for $C_{23}H_{27}NO_3S$: C, 69.49; H, 6.85; N, 3.52. Found: C, 69.40; H, 6.88; N, 3.47.

2-Benzoyl-4-methyl-3-thiobenzoylaminopentanoic Acid Ethyl Ester (4h)
This compound was obtained as a 52:48 mixture of two diastereoisomers. Yield: 0.537 g (70%); colorless microcrystals; mp 114–116 °C.

^{1}H NMR: δ = 9.49 (d, *J* = 9.5 Hz, 0.48 H), 9.24 (d, *J* = 9.2 Hz, 0.52 H), 8.00 (d, *J* = 7.6 Hz, 1 H), 7.90–7.77 (m, 3 H), 7.68–7.36 (m, 6 H), 5.47 (dt, *J* = 10, 2.8 Hz, 0.48 H), 5.36 (dt, *J* = 10.0, 2.6 Hz, 0.52 H), 4.94 (d, *J* = 2.6 Hz, 0.52 H), 4.86 (d, *J* = 2.9 Hz, 0.48 H), 4.27 (q, *J* = 7.1 Hz, 1 H), 4.10 (q, *J* = 7.1 Hz, 1 H), 2.25–2.12 (m, 1 H), 1.33–0.97 (m, 9 H).

^{13}C NMR: δ = 199.7, 199.5, 196.3, 194.1, 170.1, 168.1, 142.2, 142.1, 136.0, 135.3, 134.4, 133.8, 130.9, 130.9, 129.1, 128.9, 128.6, 128.5, 128.3, 126.8, 126.8, 62.6, 61.9, 61.7, 60.2, 53.9, 52.7, 32.6, 32.0, 20.1, 19.8, 14.0, 13.9.

Anal. Calcd for $C_{22}H_{25}NO_3S$: C, 68.90; H, 6.57; N, 3.65. Found: C, 69.01; H, 6.71; N, 3.68.

2-Acetyl-4-methyl-3-thiobenzoylaminopentanoic Acid Methyl Ester (4i)
This compound was obtained as a 67:33 mixture of two diastereoisomers. Yield: 0.498 g (81%); colorless microcrystals; mp 116–118 °C.

^{1}H NMR: δ = 9.20 (d, *J* = 8.2 Hz, 0.67 H), 8.86 (d, *J* = 8.7 Hz, 0.33 H), 7.81–7.76 (m, 2 H), 7.75–7.41 (m, 3 H), 5.51 (dt, *J* = 9.6, 2.9 Hz, 0.67 H), 5.33 (dt, *J* = 9.6, 3.1 Hz, 0.33 H), 4.11–4.07 (m, 0.33 H), 4.08 (d, *J* = 2.8 Hz, 0.67 H), 3.90 (s, 2 H), 3.76 (s, 1 H), 2.49 (s, 2 H), 2.38 (s, 1 H), 2.19–2.04 (m, 1 H), 1.16–1.05 (m, 6 H).

^{13}C NMR: δ = 205.0, 202.3, 200.0, 199.9, 170.6, 168.6, 142.2, 141.7, 131.2, 131.0, 128.6, 128.6, 126.8, 126.7, 61.2, 59.7, 59.5, 57.6, 53.1, 52.7, 32.8, 31.7, 31.0, 29.6, 20.1, 20.1, 19.9, 19.8.

Anal. Calcd for $C_{16}H_{21}NO_3S$: C, 62.51; H, 6.89; N, 4.56. Found: C, 62.40; H, 6.81; N, 4.68.

2-Acetyl-5-methyl-3-thiobenzoylaminohexanoic Acid Methyl Ester (4j)

This compound was obtained as a 67:33 mixture of two diastereoisomers. Yield: 0.578 g (90%); colorless microcrystals; mp 105–108 °C.

^{1}H NMR: δ = 8.88 (d, *J* = 9.2 Hz, 0.67 H), 8.45 (d, *J* = 8.9 Hz, 0.33 H), 7.74–7.73 (m, 2 H), 7.48–7.36 (m, 3 H), 5.77–5.68 (m, 0.67 H), 5.70–5.47 (m, 0.33 H), 4.10 (d, *J* = 3.3 Hz, 0.33 H), 3.95 (d, *J* = 3.2 Hz, 0.67 H), 3.82 (s, 2 H), 3.73 (s, 1 H), 2.40 (s, 2 H), 2.33 (s, 1 H), 1.93–1.71 (m, 2 H), 1.69–1.41 (m, 1 H), 1.10–0.95 (m, 6 H).

^{13}C NMR: δ = 203.7, 202.2, 199.0, 198.9, 170.2, 168.6, 141.8, 141.5, 131.2, 128.5, 126.8, 126.8, 61.1, 59.6, 53.4, 52.9, 52.6, 52.5, 42.0, 41.0, 30.8, 29.7, 25.5, 25.3, 23.0, 22.9, 22.4, 22.3.

Anal. Calcd for $C_{17}H_{23}NO_3S$: C, 63.52; H, 7.21; N, 4.36. Found: C, 63.79; H, 7.41; N, 4.35.

2-Acetyl-5-methyl-3-thiobenzoylaminohexanoic Acid Ethyl Ester (4k)

This compound was obtained as a 56:44 mixture of two diastereoisomers. Yield: 0.530 g (79%); colorless microcrystals; mp 86–88 °C.

^{1}H NMR: δ = 8.92 (d, *J* = 8.7 Hz, 0.56 H), 8.51 (d, *J* = 8.7, 0.44 H), 7.23 (d, *J* = 7.1 Hz, 2 H), 7.48–7.35 (m, 3 H), 5.76–5.67 (m, 0.56 H), 5.54–5.45 (m, 0.44 H), 4.28 (q, *J* = 7.1 Hz, 1 H), 4.18 (q, *J* = 7.1 Hz, 1 H), 4.01 (d, *J* = 3.3 Hz, 0.44 H), 3.93 (d, *J* = 3.3 Hz, 0.56 H), 2.39 (s, 2 H), 2.33 (s, 1 H), 1.91–1.71 (m, 1 H), 1.70–1.63 (m, 1 H), 1.45–1.41 (m, 1 H), 1.32 (t, *J* = 7.1 Hz, 1.6 H), 1.25 (t, *J* = 7.1 Hz, 1.4 H), 1.05–0.96 (m, 6 H).

^{13}C NMR: δ = 204.0, 202.3, 199.0, 198.9, 169.7, 168.2, 141.8, 141.5, 131.2, 131.1, 128.5, 128.5, 126.8, 126.7, 62.2, 61.8, 61.1, 59.8, 53.4, 52.6, 42.0, 41.1, 30.9, 29.6, 25.5, 25.3, 23.0, 22.8, 22.4, 22.4, 14.1, 14.0.

Anal. Calcd for $C_{18}H_{25}NO_3S$: C, 64.45; H, 7.51; N, 4.18. Found: C, 64.70; H, 7.69; N, 4.19.

2-Acetyl-3-thiobenzoylaminodecanoic Acid Benzyl Ester (4l)

This compound was obtained as a 60:40 mixture of two diastereoisomers. Yield: 0.501 g (57%); yellow oil.

^{1}H NMR: δ = 8.94 (d, *J* = 9.1 Hz, 0.6 H), 8.50 (d, *J* = 9.2 Hz, 0.4 H), 7.72–7.65 (m, 2 H), 7.47–7.33 (m, 8 H), 5.66–5.63 (m, 0.6 H), 5.44–5.39 (m, 0.4 H), 5.26 (AB system, J_{AB} = 28.2, 12.0 Hz, 1H), 5.13 (s, 1 H), 4.11 (d, *J* = 3.0 Hz, 0.4 H), 3.99 (d, *J* = 3.3 Hz, 0.6 H), 2.35 (s, 1.8 H), 2.31 (s, 1.2 H), 1.92–1.81 (m, 1 H), 1.64–1.54 (m, 1 H), 1.39–1.26 (m, 10 H), 0.87 (t, *J* = 5.2 Hz, 3 H).

^{13}C NMR: δ = 203.8, 202.1, 199.0, 198.9, 169.6, 168.0, 141.7, 141.3, 134.8, 134.7, 131.2, 131.0, 129.0, 128.8, 128.7, 128.6, 128.5, 128.4, 128.3, 126.8, 126.7, 126.4, 67.9, 67.6, 61.1, 59.3, 55.1, 54.2, 33.1, 32.1, 31.7, 30.9, 29.4, 29.2, 29.0, 26.5, 26.2, 22.6, 14.0.

Anal. Calcd for $C_{26}H_{33}NO_3S$: C, 71.04; H, 7.57; N, 3.19. Found: C, 71.86; H, 7.82; N, 3.24.

2-Acetyl-4-ethyl-3-thiobenzoylaminooctanoic Acid Benzyl Ester (4m)

This compound was obtained as a 63:37 mixture of two diastereoisomers. Yield: 0.703 g (80%); yellow oil.

^{1}H NMR: δ = 9.12 (d, *J* = 8.4 Hz, 0.63 H), 8.86 (d, *J* = 6.3 Hz, 0.37 H), 7.74–7.71 (m, 2 H), 7.68–7.21 (m, 8 H), 5.69–5.53 (m, 1 H), 5.39–5.03 (m, 2 H), 4.02–4.05 (m, 1 H), 2.40 (s, 2 H), 2.29 (s, 1 H), 1.77–1.65 (m, 1 H), 1.51–1.24 (m, 8 H), 0.94–0.83 (m, 6 H).

^{13}C NMR: δ = 204.7, 204.6, 199.5, 199.4, 169.8, 168.0, 141.9, 141.6, 134.7, 134.6, 131.1, 131.0, 128.9, 128.7, 128.6, 128.5, 128.4, 128.3, 126.7, 126.6, 126.4, 126.3, 66.7, 66.6, 59.6, 59.5, 57.9, 57.8, 57.7, 57.6, 42.3, 42.2, 41.6, 41.5, 29.6, 29.5, 28.5, 28.4, 22.8, 22.7, 21.9, 21.8, 13.9, 13.8.

Anal. Calcd for $C_{26}H_{33}NO_3S$: C, 71.04; H, 7.57; N, 3.19. Found: C, 70.73; H, 7.80; N, 3.15.

***N*-(2-Acetyl-1-isopropyl-3-oxobutyl)thiobenzamide (4n)**

Yield: 0.414 g (71%); colorless microcrystals; mp 111–112 °C.

^{1}H NMR: δ = 9.09 (d, *J* = 8.0 Hz, 1 H), 7.72–7.69 (m, 2 H), 7.55–7.40 (m, 3 H), 5.42 (dt, *J* = 9.5, 3.0 Hz, 1 H), 4.25 (d, *J* = 3.0 Hz, 1 H), 2.50 (s, 3 H), 2.25 (s, 3 H), 2.10–2.02 (m, 1 H), 1.08–1.04 (m, 6 H).

^{13}C NMR: δ = 206.9, 204.1, 200.0, 141.7, 131.2, 128.5, 126.8, 65.2, 60.5, 32.4, 31.8, 30.3, 20.3, 20.0.

Anal. Calcd for $C_{16}H_{21}NO_2S$: C, 65.94; H, 7.26; N, 4.81. Found: C, 66.18; H, 7.37; N, 4.99.

***N*-(2-Benzoyl-1-isopropyl-3-oxo-3-phenylpropyl)thiobenzamide (4o)**

Yield: 0.499 g (60%); colorless microcrystals; mp 61–62 °C.

^{1}H NMR: δ = 9.54 (d, *J* = 9.2 Hz, 1 H), 8.08 (d, *J* = 8.0 Hz, 2 H), 7.97 (d, *J* = 8.0 Hz, 2 H), 7.87 (d, *J* = 8.0 Hz, 2 H), 7.74–7.45 (m, 9 H), 6.04 (s, 1 H), 5.58 (t, *J* = 8.1 Hz, 1 H), 2.40–2.33 (m, 1 H), 1.20 (t, *J* = 7.8 Hz, 6 H).

^{13}C NMR: δ = 199.7, 197.3, 194.2, 142.2, 136.0, 135.1, 134.1, 134.1, 130.9, 129.2, 129.1, 128.7, 128.4, 128.2, 126.9, 61.7, 54.9, 32.5, 20.4, 20.2.

Anal. Calcd for $C_{26}H_{25}NO_2S$: C, 75.15; H, 6.06; N, 3.37. Found: C, 74.90; H, 6.12; N, 3.76.

***N*-(2-Acetyl-1-isobutyl-3-oxobutyl)thiobenzamide (4p)**

Yield: 0.550 g (90%); colorless microcrystals; mp 91–93 °C.

^{1}H NMR: δ = 8.73 (d, *J* = 8.2 Hz, 1 H), 7.70 (d, *J* = 7.4 Hz, 2 H), 7.48–7.35 (m, 3 H), 5.65–5.60 (m, 1 H), 4.25 (d, *J* = 3.0 Hz, 1 H), 2.38 (s, 3 H), 2.30 (s, 3 H), 1.94–1.84 (m, 1 H), 1.71–1.61 (m, 1 H), 1.43–1.34 (m, 1 H), 1.00 (t, *J* = 7.0 Hz, 6 H).

^{13}C NMR: δ = 206.2, 204.1, 198.9, 141.4, 131.2, 128.5, 126.7, 66.9, 53.2, 41.3, 31.5, 30.4, 25.5, 22.6.

Anal. Calcd for $C_{17}H_{23}NO_2S$: C, 66.85; H, 7.59; N, 4.59. Found: C, 66.08; H, 7.66; N, 4.98.

***N*-[1-(1-Benzoyl-2-oxo-2-phenylethyl)-3-methylbutyl]thiobenzamide (4q)**

Yield: 0.455 g (53%); colorless microcrystals; mp 62–64 °C.

^{1}H NMR: δ = 8.66 (d, *J* = 8.4 Hz, 1 H), 8.20 (d, *J* = 7.42 Hz, 2 H), 7.90 (d, *J* = 7.4 Hz, 2 H), 7.74 (d, *J* = 7.0 Hz, 2 H), 7.68–7.35 (m, 9 H), 6.13 (d, *J* = 3.8 Hz, 1 H), 5.63–5.57 (m, 1 H), 2.28–2.19 (m, 1 H), 1.71–1.68 (m, 1 H), 1.57–1.46 (m, 1 H), 0.95 (d, *J* = 6.6 Hz, 3 H), 0.82 (d, *J* = 6.5 Hz, 3 H).

^{13}C NMR: δ = 198.6, 196.5, 195.3, 141.3, 135.9, 135.5, 134.3, 133.8, 131.2, 129.2, 129.0, 128.8, 128.5, 128.4, 126.8, 56.9, 54.4, 40.5, 25.7, 23.0, 21.9.

Anal. Calcd for $C_{27}H_{27}NO_2S$: C, 75.49; H, 6.33; N, 3.26. Found: C, 75.28; H, 6.24; N, 3.59.

***N*-{1-[1-(2,2-Dimethylpropionyl)-3,3-dimethyl-2-oxobutyl]octyl}thiobenzamide (4r)**
Yield: 0.604 g (70%); yellow oil.

^{1}H NMR: δ = 9.65 (d, *J* = 8.4 Hz, 1 H), 7.83 (d, *J* = 8.2 Hz, 2 H), 7.51–7.40 (m, 3 H), 5.32–5.29 (m, 1 H), 5.06 (d, *J* = 3.0 Hz, 1 H), 1.54–1.41 (m, 3 H), 1.33–1.22 (m, 18 H), 1.21 (s, 9 H), 0.92 (t, *J* = 6.4 Hz, 3 H).

^{13}C NMR: δ = 213.1, 209.8, 197.8, 141.6, 131.0, 128.4, 126.8, 55.7, 54.8, 45.3, 45.2, 33.4, 31.7, 29.3, 29.1, 28.2, 26.6, 26.3, 22.5, 14.0.

Anal. Calcd for $C_{26}H_{41}NO_2S$: C, 72.34; H, 9.57; N, 3.24. Found: C, 72.05; H, 9.65; N, 3.64.

***N*-(2-Benzoyl-1-isobutyl-3-oxobutyl)thiobenzamide (4s)**
This compound was obtained as a 67:33 mixture of two diastereoisomers. Yield: 0.514 g (70%); colorless microcrystals; mp 136–138 °C.

^{1}H NMR: δ = 8.82 (d, *J* = 8.3 Hz, 1 H), 8.14–8.11 (m, 2 H), 7.92–7.89 (m, 1 H), 7.78–7.75 (m, 2 H), 7.68–7.40 (m, 5 H), 5.64–5.60 (m, 1 H), 5.18–515 (m, 1 H), 2.36 (s, 3 H), 2.07–1.88 (m, 1 H), 1.75–1.49 (m, 1 H), 1.02 (d, *J* = 6.5 Hz, 1 H), 0.98 (*J* = 6.6 Hz, 1 H), 0.93 (d, *J* = 6.6 Hz, 2 H), 0.82 (d, *J* = 6.4 Hz, 2 H).

^{13}C NMR: δ = 204.8, 204.2, 199.0, 198.6, 197.5, 195.5, 141.8, 141.4, 136.1, 136.0, 134.4, 134.0, 131.2, 131.1, 129.1, 129.0, 128.6, 128.5, 128.5, 128.4, 126.8, 126.7, 62.6, 61.9, 54.0, 53.8, 41.8, 40.5, 30.4, 30.3, 25.6, 25.5, 23.0, 22.7, 22.4, 22.1.

Anal. Calcd for $C_{22}H_{25}NO_2S$: C, 71.90; H, 6.86; N, 3.81. Found: C, 71.66; H, 6.86; N, 3.79.

β-Thioamido Ketones 7; General Procedure
$ZnBr_2$ (1.1 g, 5 mmol) was added to a mixture of respective silyl enol ether **5** or enamine **6** (2.5 mmol) and appropriate *N*-(α-thioamidoalkyl)benzotriazole **2** (2.0 mmol) in CH_2Cl_2 (20 mL), and the mixture was refluxed with stirring under argon for 12 h (in the case of **5**) or stirred at r.t. for 3 h (in the case of **6**). The mixture was cooled and subsequently washed with aq 10% NaOH (15 mL). The organic phase was dried (Na_2SO_4), and after removal of the solvent, the residue was subjected to column chromatography over silica gel eluting with hexanes–EtOAc (5:1) to give the pure product **7**.

***N*-(3-Oxo-1-phenethyl-3-phenylpropyl)thiobenzamide (7a)**
Yield: 0.583 g (78%); yellow microcrystals; mp 115–117 °C.

^{1}H NMR: δ = 8.62 (d, *J* = 8.5 Hz, 1 H), 7.94–7.92 (m, 2 H), 7.71–7.69 (m, 2 H), 7.59 (t, *J* = 7.4 Hz, 1 H), 7.49–7.42 (m, 3 H), 7.36 (t, *J* = 7.4 Hz, 2 H), 7.27–7.13 (m, 5 H), 5.30–5.25 (m, 1 H), 3.50 (d, *J* = 4.3 Hz, 2 H), 2.78 (t, *J* = 7.7 Hz, 2 H), 2.43–2.36 (m, 1 H), 2.16–2.04 (m, 1 H).

^{13}C NMR: δ = 199.8, 197.9, 141.6, 140.9, 136.6, 133.7, 131.0, 128.7, 128.5, 128.4, 128.3, 128.0, 126.7, 126.1, 53.1, 39.8, 34.5, 33.0.

Anal. Calcd for $C_{24}H_{23}NOS$: C, 77.17; H, 6.21; N, 3.75. Found: C, 77.03; H, 6.26; N, 3.93.

***N*-[1-Cyclohexyl-3-(4-methoxyphenyl)-3-oxopropyl]thiobenzamide (7b)**
Yield: 0.557 g (73%); yellow oil.

^{1}H NMR: δ = 8.82 (d, *J* = 8.9 Hz, 1 H), 8.01–7.79 (m, 4 H), 7.47–7.35 (m, 3 H), 7.13– 6.93 (m, 2 H), 5.02–4.96 (m, 1 H), 3.88 (s, 3 H), 3.59 (dd, *J* = 18.0, 3.6 Hz, 1 H), 3.34 (dd, *J* = 18.0, 4.8 Hz, 1 H), 2.05–1.92 (m, 2 H), 1.74–1.63 (m, 4 H), 1.26–1.12 (m, 5 H).

^{13}C NMR: δ = 198.6, 197.7, 164.0, 141.9, 131.0, 130.4, 129.6, 128.4, 127.8, 126.7, 55.5, 39.7, 36.7, 30.3, 30.1, 25.9, 25.8.

Anal. Calcd for $C_{23}H_{27}NO_2S$: C, 72.40; H, 7.13. Found: C, 72.76; H, 7.14.

***N*-{1-[2-(3-Bromophenyl)-2-oxoethyl]-3-methylbutyl}thiobenzamide (7c)**
Yield: 0.518 g (64%); white microcrystals; mp 72–74 °C.

^{1}H NMR: δ = 8.40 (d, *J* = 8.2 Hz, 1 H), 8.11–8.10 (m, 1 H), 7.90 (d, *J* = 7.8 Hz, 1 H), 7.88–7.70 (m, 3 H), 7.49–7.34 (m, 4 H), 5.31–5.24 (m, 1 H), 3.50 (AB system, J_{AB} = 17.9 Hz, 5.4 Hz, 2 H), 2.02–1.92 (m, 1 H), 1.76–1.66 (m, 1 H), 1.59–1.50 (m, 1 H), 0.98 (d, *J* = 1.4 Hz, 6 H).

^{13}C NMR: δ = 198.4, 197.4, 141.8, 138.4, 136.5, 131.2, 130.4, 128.5, 126.7, 126.6, 123.2, 51.3, 42.0, 40.4, 25.7, 22.9, 22.4.

Anal. Calcd for $C_{20}H_{22}BrNOS$: C, 59.41; H, 5.48; N, 3.64. Found: C, 59.41; H, 5.52; N, 3.42.

***N*-(1-Isopropyl-2-methyl-3-oxo-3-phenylpropyl)thiobenzamide (7d)**
Yield: 0.501 g (77%); yellow microcrystals; mp 125–126 °C.

^{1}H NMR: δ = 9.53 (d, *J* = 8.9 Hz, 1 H), 8.00 (d, *J* = 7.6 Hz, 2 H), 7.91 (d, *J* = 6.7 Hz, 2 H), 7.65 (t, *J* = 7.3 Hz, 1 H), 7.53–7.41 (m, 5 H), 5.08–5.00 (m, 1 H), 4.11 (q, *J* = 2.9 Hz, 1 H), 2.07–2.00 (m, 1 H), 1.39 (d, *J* = 7.3 Hz, 3 H), 1.10 (d, *J* = 6.7 Hz, 3 H), 0.96 (d, *J* = 6.7 Hz, 3 H).

^{13}C NMR: δ = 206.0, 199.4, 141.9, 135.6, 134.0, 130.1, 129.1, 128.5, 128.3, 126.8, 64.8, 40.5, 32.1, 20.2, 20.1, 17.1.

Anal. Calcd for $C_{20}H_{23}NOS$: C, 73.80; H, 7.12; N, 4.30. Found: C, 73.78; H, 7.37; N, 4.29.

***N*-(1-Cyclohexyl-3-oxo-3-thiophen-2-ylpropyl)thiobenzamide (7e)**
Yield: 0.365 g (51%); yellow microcrystals; mp 120–121 °C.

^{1}H NMR: δ = 8.69 (d, *J* = 9.1 Hz, 1 H), 7.79–7.77 (m, 2 H), 7.70 (d, *J* = 7.7 Hz, 1 H), 7.48–7.37 (m, 3 H), 7.26 (s, 1 H), 7.16 (t, *J* = 4.5 Hz, 1 H), 5.30–4.97 (m, 1 H), 3.56 (dd, *J* = 17.7, 3.6 Hz, 1 H), 3.37 (dd, *J* = 17.4, 4.8 Hz, 1 H), 2.03–1.91 (m, 1 H), 1.75–1.67 (m, 4 H), 1.25–1.08 (m, 6 H).

^{13}C NMR: δ = 197.9, 192.8, 143.8, 141.8, 134.6, 132.7, 131.0, 128.5, 126.5, 39.7, 37.8, 30.3, 30.1, 25.8, 25.7.

Anal. Calcd for $C_{20}H_{23}NOS_2$: C, 67.19; H, 6.48; N, 3.92. Found: C, 66.82; H, 6.65; N, 3.88.

***N*-[1-(7-Methoxy-1-oxo-1,2,3,4-tetrahydronaphthalen-2-yl)octyl]thiobenzamide (7f)**
This compound was obtained as a 73:27 mixture of two diastereoisomers.

1st Diastereoisomer: Yield: 0.373 g (44%); yellow oil.

^{1}H NMR: δ = 9.17 (d, *J* = 9.1 Hz, 1 H), 7.98 (d, *J* = 8.8 Hz, 1 H), 7.83 (d, *J* = 6.7 Hz, 2 H), 7.49–7.36 (m, 3 H), 6.83 (dd, *J* = 6.5, 2.3 Hz, 1 H), 6.70 (d, *J* = 2.1 Hz, 1 H) 5.06–4.97 (m, 1 H), 3.86 (s, 3 H), 3.14–2.95 (m, 3 H), 2.24–2.06 (m, 2 H), 1.89–1.81 (m, 1 H), 1.73–1.62 (m, 1 H), 1.45–1.39 (m, 2 H), 1.34–1.24 (m, 8 H), 0.85 (t, *J* = 6.5 Hz, 3 H).

^{13}C NMR: δ = 199.2, 197.1, 164.1, 146.8, 141.9, 131.0, 129.7, 128.5, 126.8, 126.4, 113.5, 112.5, 58.6, 55.5, 50.1, 32.0, 30.0, 29.6, 29.2, 29.1, 27.9, 26.7, 22.6, 14.1.

Anal. Calcd for $C_{26}H_{33}NO_2S$: C, 73.72; H, 7.85; N, 3.31. Found: C, 73.61; H, 7.85; N, 3.29.

2nd Diastereoisomer: Yield: 0.136 g (16%); yellow oil.

^{1}H NMR: δ = 8.31 (d, *J* = 9.3 Hz, 1 H), 7.95 (d, *J* = 8.8 Hz, 1 H), 7.70 (d, *J* = 7.1 Hz, 2 H), 7.45–7.33 (m, 3 H), 6.84 (dd, *J* = 6.5, 2.3 Hz, 1 H), 6.67 (d, *J* = 2.0 Hz, 1 H), 5.29–5.21 (m, 1 H), 3.85 (s, 3 H), 3.09–2.93 (m, 3 H), 2.38–2.31 (m, 1 H), 2.23–2.01 (m, 2 H), 1.91–1.84 (m, 1 H), 1.48–1.38 (m, 2 H), 1.36–1.26 (m, 8 H), 0.87 (t, *J* = 6.5 Hz, 3 H).

^{13}C NMR: δ = 198.8, 196.7, 163.7, 146.2, 14.9, 130.8, 129.5, 128.3, 126.5, 113.3, 112.3, 57.6, 55.4, 51.3, 34.1, 31.7, 29.7, 29.6, 29.4, 29.1, 28.5, 26.5, 22.5, 14.0.

Anal. Calcd for $C_{26}H_{33}NO_2S$: C, 73.72; H, 7.85; N, 3.31. Found: C, 73.48; H, 8.03; N, 3.50.

***N*-(4,4-Dimethyl-3-oxo-1-phenethylpentyl)thiobenzamide (7g)**
Yield: 0.280 g (33%); yellow microcrystals; mp 109–111 °C.

^{1}H NMR: δ = 8.68 (d, *J* = 8.0 Hz, 1 H), 7.71 (d, *J* = 7.1 Hz, 2 H), 7.48–7.30 (m, 3 H), 7.25–7.20 (m, 2 H), 7.17–7.15 (m, 3 H), 5.17–5.10 (m, 1 H), 3.02 (t, *J* = 4.0 Hz, 2 H), 2.75 (t, *J* = 7.0 Hz, 2 H), 2.29–2.18 (m, 1 H), 1.98–1.86 (m, 1 H), 1.14 (s, 9 H).

^{13}C NMR: δ = 216.9, 197.7, 141.6, 141.0, 131.1, 128.5, 128.4, 128.3, 126.7, 126.1, 53.0, 44.7, 38.1, 34.6, 33.1, 26.2.

Anal. Calcd for $C_{22}H_{27}NOS$: C, 74.74; H, 7.70; N, 3.96. Found: C, 74.95; H, 7.88; N, 3.96.

***N*-[2-Methyl-1-(2-oxocyclohexyl)propyl]thiobenzamide (7h)**
Yield: 0.318 g (55%); yellow microcrystals; mp 84–85 °C.

^{1}H NMR: δ = 8.83 (br s, 1 H), 7.76 (d, *J* = 7.1 Hz, 2 H), 7.46–7.37 (m, 3 H), 4.74 (t, *J* = 10.0 Hz, 1 H), 3.08–2.99 (m, 1 H), 2.45–2.14 (m, 5 H), 1.75–1.62 (m, 4 H), 1.00 (t, *J* = 5.8 Hz, 6 H).

^{13}C NMR: δ = 215.4, 199.2, 141.9, 131.0, 128.5, 126.6, 63.3, 52.3, 43.4, 34.1, 31.6, 28.8, 25.3, 20.4, 20.0.

Anal. Calcd for $C_{17}H_{23}NOS$: C, 70.55; H, 8.01; N, 4.84. Found: C, 70.62; H, 8.42; N, 4.79.

***N*-[3-Methyl-1-(2-oxocyclohexyl)butyl]thiobenzamide (7i)**
This compound was obtained as a 86:14 mixture of two diastereoisomers. Yield: 0.400 g (66%); yellow microcrystals; mp 82–83 °C.

^{1}H NMR: δ = 8.68 (d, *J* = 8.8 Hz, 0.86 H), 8.36 (d, *J* = 8.1 Hz, 0.14 H), 7.74 (d, *J* = 6.9 Hz, 2 H), 7.48–7.35 (m, 3 H), 5.18–5.10 (m, 0.86 H), 4.86–4.79 (m, 0.14 H), 3.05–3.01 (m, 0.14 H), 2.82–2.78 (m, 0.86 H), 2.42–2.31 (m, 3 H), 2.19–2.03 (m, 1 H), 2.00–1.85 (m, 2 H), 1.79–1.59 (m, 4 H), 1.48–1.39 (m, 1 H), 1.00 (d, *J* = 6.5 Hz, 3 H), 0.94 (d, *J* = 6.6 Hz, 3 H).

^{13}C NMR: δ = 214.9, 213.3, 198.6, 196.9, 141.9, 141.6, 131.0, 130.9, 128.4, 126.6, 55.7, 55.5, 55.4, 52.3, 43.4, 43.0, 42.4, 38.2, 33.6, 30.5, 28.5, 26.6, 25.7, 25.4, 25.2, 24.7, 23.6, 23.0, 22.7, 21.7.

Anal. Calcd for $C_{18}H_{25}NOS$: C, 71.24; H, 8.30; N, 4.62. Found: C, 71.42; H, 8.61; N, 4.60.

***N*-[1-(2-Oxocyclohexyl)-3-phenylpropyl]thiobenzamide (7j)**
This compound was obtained as a 55:45 mixture of two diastereoisomers. Yield: 0.485 g (69%); yellow microcrystals; mp 98–100 °C.

^{1}H NMR: δ = 8.76 (d, *J* = 9.1 Hz, 0.55 H), 8.47 (d, *J* = 9.1 Hz, 0.45 H), 7.74–7.66 (m, 2 H), 7.44–7.28 (m, 3 H), 7.27–7.13 (m, 5 H), 5.18–5.11 (m, 0.55 H), 4.90–4.83 (m, 0.45 H), 3.03–2.98 (m, 0.45 H), 2.82–2.63 (m, 2.55 H), 2.37–2.22 (m, 3 H), 2.20–1.71 (m, 4 H), 1.67–1.65 (m, 3 H).

^{13}C NMR: δ = 214.9, 213.3, 199.1, 197.6, 141.8, 141.6, 141.4, 141.3, 131.1, 131.0, 128.5, 128.4, 128.3, 128.3, 126.7, 126.7, 126.0, 1226.0, 57.4, 57.3, 54.4, 52.3, 43.3, 42.4, 35.7, 33.5, 33.3, 32.9, 31.1, 30.6, 28.6, 26.7, 25.1, 24.8.

Anal. Calcd for $C_{22}H_{25}NOS$: C, 75.17; H, 7.17; N, 3.98. Found: C, 75.33; H, 7.33; N, 3.95.

***N*-[Cyclohexyl-(2-oxocyclohexyl)methyl]thiobenzamide (7k)**
Yield: 0.481 g (73%); yellow microcrystals; mp 123–124 °C.

^{1}H NMR: δ = 8.82 (d, *J* = 8.7 Hz, 1 H), 7.76 (d, *J* = 6.9 Hz, 2 H), 7.48–7.36 (m, 3 H), 4.80 (dt, *J* = 7.7, 2.0 Hz, 1 H), 3.03–3.01 (m, 1 H), 2.45–2.29 (m, 3 H), 2.17–2.11 (m, 1 H), 1.88–1.60 (m, 10 H), 1.20–1.06 (m, 5 H).

^{13}C NMR: δ = 215.5, 199.1, 141.8, 131.1, 128.4, 126.6, 62.3, 51.8, 43.4, 40.8, 34.1, 30.7, 30.1, 28.8, 26.1, 26.0, 25.8, 25.3.

Anal. Calcd for $C_{20}H_{27}NOS$: C, 72.90; H, 8.26; N, 4.25. Found: C, 73.05; H, 8.57; N, 4.22.

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References

(1) (a) Sheibani, H.; Mosslemin, M. H.; Behzadi, S.; Islami, M. R.; Foroughi, H.; Saidi, K. *ARKIVOC* **2005**, *(xv)*, 88; www.arkat-usa.org. (b) Nair, V.; Wenzel, T. *ARKIVOC* **2004**, *(xiv)*, 128; www.arkat-usa.org. (c) Jagodziński, T. S. *Chem. Rev.* **2003**, *103*, 197. (d) Hurd, R. N.; Delamater, G. *Chem. Rev.* **1961**, *61*, 45.
(2) (a) Giordano, C.; Belli, A. *Synthesis* **1975**, 789. (b) Giordano, C.; Belli, A.; Erbea, R.; Panossian, S. *Synthesis* **1979**, 801.
(3) (a) Giordano, C.; Belli, A. *Synthesis* **1977**, 193. (b) Giordano, C.; Belli, A. *Synthesis* **1977**, 476.
(4) Giordano, C.; Belli, A.; Bellotti, V. *Synthesis* **1978**, 443.
(5) Abis, L.; Giordano, C.; Organica, C. de C.; Edison, M. *J. Chem. Soc., Perkin Trans. 1* **1973**, 771.
(6) (a) Heathcock, C. H.; Davidsen, S. K.; Mills, S. G.; Sanner, M. A. *J. Org. Chem.* **1992**, *57*, 2531. (b) Magnus, P.; Mendoza, J. S.; Stamford, A.; Ladlow, M.; Willis, P. *J. Am. Chem. Soc.* **1992**, *114*, 10232. (c) Kim, G.; Chu-Moyer, M. Y.; Danishefsky, S. J.; Schulte, G. K. *J. Am. Chem. Soc.* **1993**, *115*, 30.
(7) Niewiadomy, A.; Matysiak, J.; Macik-Niewiadomy, G. *Eur. J. Pharm. Sci.* **2001**, *13*, 243.
(8) Matysiak, J.; Niewiadomy, A.; Macik-Niewiadomy, G. *Eur. J. Pharm. Sci.* **2000**, *10*, 119.
(9) Matysiak, J.; Niewiadomy, A.; Macik-Niewiadomy, G.; Kornillowicz, T. *Eur. J. Med. Chem.* **2000**, *35*, 393.
(10) Legocki, J.; Matysiak, J.; Niewiadomy, A.; Kostecka, M. *J. Agric. Food Chem.* **2003**, *51*, 362.
(11) Bardi, R.; Piazzesi, A. M.; Toniolo, C.; Jensen, O. E.; Omar, R. S.; Senning, A. *Biopolymers* **1988**, *27*, 747.
(12) Tran, T. T.; Treutlein, H.; Burgess, A. W. *J. Comput. Chem.* **2001**, *2*, 1026.
(13) Michel, A. G.; Ameziane-Hassani, C.; Boulay, G. *Can. J. Chem.* **1989**, *67*, 1312.
(14) Clausen, K.; Spatola, A. F.; Lemieux, C.; Schiller, P. W.; Lawesson, S.-O. *Biochem. Biophys. Res. Commun.* **1984**, *120*, 305.
(15) Kajtár, M.; Hollósi, M.; Kajtár, J.; Majer, Z.; Kövér, K. E. *Tetrahedron* **1986**, *42*, 3931.
(16) (a) Scheeren, J. W.; Ooms, P. H. J.; Nivard, R. J. F. *Synthesis* **1973**, 149. (b) Curphey, T. J. *J. Org. Chem.* **2002**, *67*, 6461.

(17) (a) Cava, M. P.; Levinson, M. I. *Tetrahedron* **1985**, *41*, 5061. (b) Kaleta, Z.; Makowski, B. T.; Soós, T.; Dembinski, R. *Org. Lett.* **2006**, *8*, 1625.
(18) Charette, A. B.; Chua, P. *Tetrahedron Lett.* **1998**, *39*, 245.
(19) (a) Jagodziński, T. *Synthesis* **1988**, 717. (b) Jagodzicski, T.; Jagodzińska, E.; Jabłoński, Z. J. *Tetrahedron* **1986**, *42*, 3683.
(20) Kolakowski, R. V.; Shangguan, N.; Williams, L. J. *Tetrahedron Lett.* **2006**, *47*, 1163.
(21) Katritzky, A. R.; Drewniak, M. *Tetrahedron Lett.* **1988**, *29*, 1755.
(22) Katritzky, A. R.; Drewniak, M.; Lue, P. *J. Org. Chem.* **1988**, *53*, 5854.
(23) Zbruyev, O. I.; Stiasni, N.; Kappe, O. *J. Comput. Chem.* **2003**, *5*, 145.
(24) (a) Katritzky, A. R.; Pernak, J.; Fan, W.-Q. *Synthesis* **1991**, 868. (b) Katritzky, A. R.; Fali, C. N.; Bao, W.; Qi, M. *Synthesis* **1998**, 1421. (c) Katritzky, A. R.; Ghiviriga, I.; Chen, K.; Dmytro, O.; Tymoshenko, D. O.; Abdel-Fattah, A. A. A. *J. Chem. Soc., Perkin Trans. 2* **2001**, 530. (d) Katritzky, A. R.; Manju, K.; Singh, S. K.; Meher, N. K. *Tetrahedron* **2005**, *61*, 2555.