Direct Organocatalytic α-Sulfenylation of Aldehydes and Ketones with Tetramethylthiuram Disulfide

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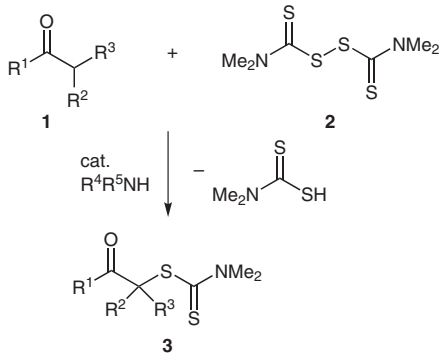
Abstract: The direct pyrrolidine-catalyzed α-sulfenylation of aldehydes and ketones with the commercially available, very cheap chemical tetramethylthiuram disulfide (thiram) is described. The dithiocarbamoyl derivatives are obtained in good to excellent yields (47–98%). In the case of α-substituted aldehydes the protocol allows the generation of quaternary stereocenters. The sensibility of the α-sulfenylated carbonyl compounds for racemization has been investigated.

Key words: organocatalysis, thiram, sulfenylation, dithiocarbamate, enamine

The formation of C–S bonds is a significant task in organic synthesis, since sulfur-containing compounds are known to be important structural motifs in many biologically active substances such as pharmaceuticals and agrochemicals. Especially the synthesis of α-sulfenylated carbonyl compounds from simple and readily available starting materials is an important field as they are commonly used as building blocks in a variety of organic transformations.[1] Besides the broad use of nucleophilic sulfur derivatives in metal-catalyzed cross-coupling reactions[2] or sulfa-Michael additions,[3] electrophilic sulfenylating reagents, which allow a direct α-sulfenylation of aldehydes and ketones, are found frequently in the literature.[1c] Besides the preparation of α-sulfenylated carbonyl compounds via S_N2 displacement of α-halogenated carbonyl compounds with sulfide anions, methods based on the reaction of the parent carbonyl compounds or preformed enolates and enamines with sulfenylating agents such as sulfur, disulfides, *N*-(phenylsulfanyl)succinimide, and sulfenyl chlorides are used.[4] While asymmetric electrophilic α-sulfenylations under stoichiometric conditions are known for quite some time,[5] the catalytic asymmetric protocols employing organocatalysts[6] and enantiopure titanium(IV) or nickel(II) complexes[7] have only been recently reported.

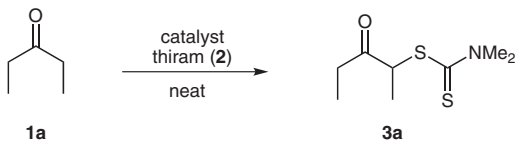
The very cheap, commercially available tetramethylthiuram disulfide (TMTD, thiram, **2**) exhibits broad applications as a fungicide, an animal repellant, in the treatment of human scabies, and as a vulcanization accelerator. Recently thiram has been used in the metal-mediated thiolation of aliphatic and aromatic compounds,[8] the synthesis of sulfur containing heteroaromatics[9] as well as in a copper-catalyzed reaction of 2-haloanilines for the synthesis of 2-aminobenzothiazoles.[10] While thiram has been used in metal- and base-mediated reactions, to the best of our knowledge, no application in organocatalysis has been published so far.

We now wish to report a secondary amine catalyzed α-sulfenylation of aldehydes and ketones with thiram. Earlier work by Fanghänel already showed the reactivity of thiram towards preformed enamines under stoichiometric conditions.[11] With this in mind a catalytic version of this reaction was envisaged, in which an in situ generated enamine attacks the disulfide moiety of thiram with the dithiocarbamic acid anion acting as a leaving group. After hydrolytic regeneration of the catalyst, the desired α-sulfenylated aldehydes and ketones **3** should be obtained along with dithiocarbamic acid (Scheme 1).



Scheme 1 Organocatalytic electrophilic α-sulfenylation of aldehydes and ketones

Our initial investigations started with a screening of frequently used secondary amine catalysts under solvent-free conditions using pentan-3-one (**1a**) as a model substrate (Scheme 2, Table 1). It was expected that an enamine formation is essential for the C–S bond forming step, thus without the addition of any catalyst it came as no surprise that no conversion was observed (Table 1, entry 1). With the addition of a catalytic amount of a cyclic second-



Scheme 2 α-Sulfenylation of pentan-3-one (**1a**) with thiram (**2**)

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ary amine the desired product **3a** was formed, albeit only in low to moderate yields. Piperidine and its sterically hindered analogue tetramethylpiperidine provided poor and no conversion respectively (Table 1, entries 2 and 3). Furthermore morpholine and piperazine showed only low conversions at room temperature or a slightly elevated temperature. A yield of 59% was obtained by employing pyrrolidine as the catalyst. However, (*S*)-proline as an enantiopure pyrrolidine derivative was ineffective in this transformation (Table 1, entry 8).

Table 1 Catalyst Screening for the Synthesis of Dithiocarbamate **3a** (Scheme 2)

Entry[a]	Catalyst (0.3 equiv)	Temp (°C)	Time (h)	Yield (%)[b]
1	–	50	18	–
2	piperidine	50	24	19
3	tetramethylpiperidine	r.t.	17	–
4	morpholine	50	24	7
5	piperazine	r.t.	68	10
6	piperazine	45	48	25
7	pyrrolidine	50	18	59
8	(*S*)-proline	50	24	16

[a] All reactions were performed on a 2.0 mmol scale.
[b] Yield of isolated product **3a**.

Since a reaction under solvent-free conditions could result in insufficient solubility of thiram and would prove impractical for high-boiling carbonyl compounds, a solvent screening was undertaken (Table 2). Polar aprotic solvents proved unsuitable in this reaction and gave no conversion. The best results were achieved in methanol and acetonitrile (Table 2, entries 4 and 6). Attempts to perform the reaction in slightly basic aqueous solution gave only poor yields. Highly nonpolar solvents such as toluene dissolved the reagents only insufficiently and the reaction yield decreased to 20% (Table 2, entry 8).

Table 2 Solvent Screening for the Synthesis of Dithiocarbamate **3a** (Scheme 2)

Entry[a]	Solvent	Temp (°C)	Time (h)	Yield (%)[b]
1	DMSO	r.t.	20	–
2	DMF	r.t.	20	–
3	NMP	r.t. to 50	20	–
4	MeOH	50	24	53
5	THF	50	24	15
6	MeCN	50	24	40
7	K_2CO_3[c]	r.t.	20	12
8	toluene	50	24	20

[a] All reactions were performed on a 2.0 mmol scale.
[b] Yield of isolated product **3a**.
[c] 1 M solution of K_2CO_3 in H_2O.

Next the effects of additives on the catalytic thiram α-sulfenylation reaction were examined (Table 3). Several basic, acidic, oxidizing, and thiophilic additives were screened. Although methanol seemed to be the best solvent in this reaction, further optimization was performed in acetonitrile as no significant increase of yield was achieved in methanol. Additionally the temperature was lowered to suppress a possible reaction in which the dithiocarbamate moiety in thiram is attacked by the catalyst.[12] The addition of trimethylsilyl chloride as thiophile to scavenge the dithiocarbamic acid side product proved to be unsuccessful and resulted in no conversion, most probably resulting from the silylation of the catalyst. The acidic additive trifluoroacetic acid was found to inhibit the catalytic activity completely. Compared to the reaction performed without additive the use of an inorganic base or oxidizing agents gave similar conversion (Table 3, entries 3 and 4). The addition of 1.0 equivalent of triethylamine to the reaction mixture showed no improvement. However the addition of 2.0 equivalents resulted in an increased yield (Table 3, entries 6 and 7).

Table 3 Additive Screening for the Synthesis of Dithiocarbamate **3a** (Scheme 2)

Entry[a]	Additive (equiv)	Temp (°C)	Time (d)	Yield (%)[b]
1	TMSCl (0.1)	−22	0.3	–
2	TFA (0.3)	50	1.0	–
3	K_2CO_3 (0.1)	50	1.0	42
4	$NaIO_4$ (0.3)	−22	7.0	37
5	Et_3N (1.0)	50	1.0	42
6	Et_3N (2.0)	50	1.0	51
7	Et_3N (2.0)	−22	3.0	54
8[c]	Et_3N (2.0)	−22	6.0	84

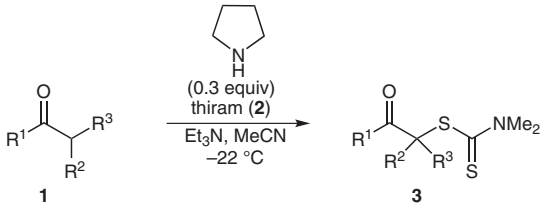
[a] All reactions were performed on a 2.0 mmol scale in MeCN.
[b] Yield of isolated product **3a**.
[c] Reaction was performed in a mixture of MeCN–CH_2Cl_2 (3:1).

After several test reactions two equivalents of triethylamine were found to be optimal. Lowering the reaction temperature to –22 °C significantly improved the yields up to 84% (Table 3, entry 8) even though longer reaction times were necessary for the reactions to go to completion. Substrates that showed poor solubility in pure acetonitrile could be reacted using mixtures of acetonitrile and dichloromethane without a significant change in yield.

Once the reaction conditions had been optimized, we investigated the substrate scope of the organocatalyzed α-sulfenylation of carbonyl compounds with thiram (Table 4). Ketones with various substitution patterns were successfully converted to the desired dithiocarbamates in good to excellent yields. Unfortunately methyl ketones

were found to be unsuitable substrates and gave only low yields of product even when the reactions were performed under solvent-free conditions. Additionally, aldehydes can be employed in this reaction, with α,α-disubstituted aldehydes allowing the creation of quaternary stereocenters in good yields.[13]

Table 4 Scope of the Organocatalyzed α-Sulfenylation of Aldehydes and Ketones with Thiram



Product[a]	R^1	R^2	R^3	Yield (%)[b]
3a	Et	Me	H	84
3b	*n*-Pr	Et	H	90
3c	CF_3	Ph	H	75
3d	Ph	Ph	H	37
3e	H	*i*-Pr	H	98
3f	H	Me	Me	72
3g	H	Me	Et	71
3h	H	Me	*n*-Pr	75
3i	H	Me	Ph	49
3j[c]	$-(CH_2)_3-$		H	47
3k[c]	$-(CH_2)_4-$		H	73
3l[c]	$-(CH_2)_2OCH_2-$		H	83

[a] All reactions were performed on a 2.0 mmol scale at – 22 °C for 6 d in a mixture of MeCN–CH_2Cl_2 (3:1).
[b] Yield of isolated product **3**.
[c] Reactions were performed under neat conditions with 10 equiv of ketone at 50 °C for 1 d.

Interestingly it was discovered that the reaction of cyclic ketones with thiram (**2**) occurs without the addition of a catalyst or an additive (Table 4, **3j–l**,). It was assumed that in this case the reaction proceeds via an enol-type intermediate. To demonstrate the practicability of our protocol, the synthesis of **3a** was performed on a one mole scale to give 172 g of the α-dithiocarbamoylated ketone.

Towards the development of an asymmetric version of this reaction the optical stability of the dithiocarbamates **3** has to be considered as it is conceivable that the product with R^3 = H may racemize by enolization. Therefore, both enantiomers of the cyclohexanone derivative **3k** were separated by preparative chiral HPLC. The enantiomeric excess of a virtually enantiopure sample in a solution of heptane–*i*-PrOH at room temperature slowly diminished over a period of several hours and the half-life for racemization can be estimated to be greater than three days (Table 5). Slightly elevated temperatures, however, led to complete racemization within minutes.

Table 5 Evaluation of the Optical Stability of Dithiocarbamate **3k**

Entry	Temp	Time (h)	ee (%)[a]
1	r.t.	0	96
2	r.t.	16	90
3	r.t.	23	86
4	r.t.	41	82
5	40 °C	0.05	0

[a] Determined by HPLC analysis on a chiral stationary phase (*n*-heptane–*i*-PrOH, 8:2, 1.0 mL/min, Daicel Chiralpak AD column): t_R = 6.7 min (major), t_R = 7.7 min (minor).

In summary, we have developed a direct pyrrolidine-catalyzed α-dithiocarbamoylation of aldehydes and ketones employing the very cheap, commercially available tetramethylthiuram disulfide (thiram) as electrophilic sulfenylation reagent. Besides acyclic and cyclic ketones, aldehydes can be sulfenylated in this way allowing the generation of quaternary stereocenters with good to excellent yields.

Unless otherwise noted, all commercially available compounds were used without further purification. For preparative column chromatography SIL G-25 UV254 from Macherey-Nagel, particle size 0.040–0.063 mm (230–240 mesh, flash) was used. Visualization of the developed TLC plates was performed with ultraviolet irradiation (254 nm) or by staining with a $KMnO_4$ solution. Microanalyses were performed with a Vario EL element analyzer. Mass spectra were measured on a Finnigan SSQ7000 (EI 70 eV) spectrometer and high-resolution mass spectra on a Thermo Fisher Scientific Orbitrap XL. IR spectra were recorded on a PerkinElmer FT-IR Spectrum 100 instrument. ^1H and ^{13}C NMR spectra were recorded at ambient temperature with Varian Mercury 300 or Inova 400 spectrometers with TMS as an internal standard.

α-Sulfenylation of Aliphatic Aldehydes and Ketones; General Procedure 1 (GP 1)

A screw-capped vial was charged with thiram (**2**; 480 mg, 2.0 mmol, 1 equiv) and MeCN–CH_2Cl_2 (3:1; 4 mL, 0.5 M), and the resulting suspension was cooled to –40 °C. Et_3N (405 mg, 4 mmol, 2 equiv), ketone (4.0 mmol, 2 equiv), and pyrrolidine (0.43 mg, 0.6 mmol, 0.3 equiv) were added sequentially. The reaction was stirred at –22 °C for 6 d. The solvent was removed in vacuo and the resulting crude product was purified by flash column chromatography using *n*-pentane–Et_2O as eluent (Table 4).

α-Sulfenylation of Cyclic Ketones; General Procedure 2 (GP 2)

A screw-capped vial was charged with thiram (**2**; 480 mg, 2.0 mmol, 1 equiv) and ketone (20.0 mmol, 10 equiv). The reaction was stirred at 50 °C until a clear solution was obtained. Removal of the unreacted ketone in vacuo and purification of the resulting crude product by flash column chromatography (silica gel, *n*-pentane–Et_2O) afforded the pure product (Table 4).

2-(Dimethylaminothiocarbonylthio)pentan-3-one (3a)
Compound **3a** was synthesized according to GP 1 to yield 349 mg (84%) of a yellowish oil; R_f = 0.69 (*n*-pentane–Et_2O, 1:1).

IR (film): 3408, 2974, 2926, 1713, 1576, 1499, 1450, 1377, 1252, 1149, 1054, 971, 869, 799, 574 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 1.08 (t, *J* = 7.4 Hz, 3 H, CH_2CH_3), 1.48 (d, *J* = 7.4 Hz, 3 H, $CHCH_3$), 2.60 (dq, *J* = 7.2, 7.4 Hz, 1 H, CH_3CHH), 2.80 (dq, *J* = 7.2, 7.4 Hz, 1 H, CH_3CHH), 3.40 (s, 3 H, NCH_3), 3.55 (s, 3 H, NCH_3), 4.90 (q, *J* = 7.4 Hz, 1 H, CH_3CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.2 (CH_3), 16.1 (CH_3), 34.1 (CH_2), 41.8 (NCH_3), 45.8 (NCH_3), 55.1 (CH), 195.2 (C=S), 208.6 (C=O).

MS (EI): *m*/*z* = 205 (8, $[M]^+$), 172 (32), 120 (7), 88 (100), 77 (5), 73 (6), 57 (10).

Anal. Calcd for $C_8H_{15}NOS_2$: C, 46.79; H, 7.36; N, 6.82. Found: C, 46.89; H, 7.56; N, 7.17.

3-(Dimethylaminothiocarbonylthio)heptan-4-one (3b)
The synthesis of **3b** following GP 1 yielded 419 mg (90%) of a yellow oil; R_f = 0.79 (*n*-pentane–Et_2O, 1:1).

IR (film): 3406, 2963, 2924, 2874, 1710, 1578, 1539, 1499, 1458, 1377, 1252, 1148, 1051, 980, 869, 805, 574 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.4 Hz, 3 H, $CH_2CH_2CH_3$), 1.02 (t, *J* = 7.4 Hz, 3 H, $CHCH_2CH_3$), 1.64 (sext, *J* = 7.4 Hz, 2 H, $CH_3CH_2CH_2$), 1.75–1.90 (m, 1 H, CH_2CHH), 1.95–2.09 (m, 1 H, CH_2CHH), 2.51–2.61 (dt, *J* = 6.6, 6.9 Hz, 1 H, CH_3CHHCH), 2.67–2.78 (dt, *J* = 7.1, 7.4 Hz, 1 H, CH_3CHHCH), 3.42 (s, 3 H, NCH_3), 3.56 (s, 3 H, NCH_3), 4.89 (t, *J* = 7.4 Hz, 1 H, CH_2CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 11.9 (CH_3), 13.8 (CH_3), 17.3 (CH_2), 23.7 (CH_2), 41.7 (NCH_3), 43.5 (CH_2), 45.9 (NCH_3), 62.0 (CH), 195.4 (C=S), 207.4 (C=O).

MS (EI): *m*/*z* = 234 (27, $[M + H]^+$), 233 (20, $[M]^+$), 200 (39), 121 (20), 113 (72), 89 (8), 88 (100), 72 (6), 71 (7).

Anal. Calcd for $C_{10}H_{19}NOS_2$: C, 51.46; H, 8.21; N, 6.00. Found: C, 51.92; H, 8.24; N, 6.45.

3-(Dimethylaminothiocarbonylthio)-1,1,1-trifluoro-3-phenylpropan-2-one (3c)
The synthesis of **3c** following GP 1 yielded 290 mg (75%) of a colorless solid; mp 106 °C; R_f = 0.80 (*n*-pentane–Et_2O, 1:1).

IR (ATR): 3075, 2948, 2325, 2101, 1744, 1591, 1500, 1455, 1384, 1316, 1248, 1196, 1138, 1024, 980, 872, 842, 822, 743, 721, 690 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 3.35 (s, 3 H, NCH_3), 3.47 (s, 3 H, NCH_3), 6.20 (s, 1 H, CH), 7.38 (s, 5 H, CH_{arom}).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 42.2 (NCH_3), 45.2 (NCH_3), 60.6 (CH), 115.7 (q, *J* = 292.2 Hz, CF_3), 128.3 (C_{arom}), 129.4 (CH_{arom}, 2 C), 129.6 (CH_{arom}, 2 C), 129.6 (CH_{arom}), 186.2 (q, *J* = 34.4 Hz, C=O), 193.9 (C=S).

^{19}F NMR (376 MHz, $CDCl_3$): δ = 73.95 (s, CF_3).

MS (EI): *m*/*z* = 308 (12, $[M + H]^+$), 307 (36, $[M]^+$), 121 (13), 120 (100), 109 (12), 90 (12), 89 (14), 88 (79), 77 (16).

Anal. Calcd for $C_{12}H_{12}F_3NOS_2$: C, 46.89; H, 3.94; N, 4.56. Found: C, 46.73; H, 3.92; N, 4.52.

2-(Dimethylaminothiocarbonylthio)desoxybenzoin (3d)[11b]
The synthesis of **3d** following GP 1 yielded 235 mg (37%) of a lightly red solid; mp 129 °C; R_f = 0.54 (*n*-pentane–Et_2O, 1:1).

^1H NMR (400 MHz, $CDCl_3$): δ = 3.37 (s, 3 H, NCH_3), 3.48 (s, 3 H, NCH_3), 6.95 (s, 1 H, CH), 7.23–7.51 (m, 8 H, CH_{arom}), 8.08 (d, *J* = 7.8 Hz, 2 H, CH_{arom}).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 41.8 (NCH_3), 45.8 (NCH_3), 62.6 (CH), 128.5 (CH_{arom}), 128.5 (CH_{arom}, 2 C), 129.1 (CH_{arom}, 2 C), 129.1 (CH_{arom}, 2 C), 129.3 (CH_{arom}, 2 C), 133.0 (CH_{arom}), 133.7 (C_{arom}), 136.2 (C_{arom}), 194.3 (C=S), 195.1 (C=O).

2-(Dimethylaminothiocarbonylthio)isovaleraldehyde (3e)[14]
The synthesis of **3e** following GP 1 yielded 3.36 g (98%) of a lightly yellow oil; R_f = 0.39 (*n*-pentane–Et_2O, 1:1).

^1H NMR (300 MHz, $CDCl_3$): δ = 0.99 [d, *J* = 6.8 Hz, 3 H, $CH(CH_3)_2$], 1.05 [d, *J* = 6.8 Hz, 3 H, $CH(CH_3)_2$], 2.47 [d sept, *J* = 6.8, 4.9 Hz, 1 H, $CH(CH_3)_2$], 3.42 (s, 3 H, NCH_3), 3.50 (s, 3 H, NCH_3), 4.80 (dd, *J* = 4.9, 1.3 Hz, 1 H, CH), 9.52 (d, *J* = 1.3 Hz, 1 H, CHO).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 19.9 (CH_3), 20.2 (CH_3), 28.0 [$CH(CH_3)_2$], 41.6 (NCH_3), 45.7 (NCH_3), 67.1 (CH), 194.7 (C=S), 198.0 (CHO).

2-(Dimethylaminothiocarbonylthio)isobutyraldehyde (3f)
The synthesis of **3f** following GP 1 yielded 275 mg (72%) of a colorless solid; mp 63 °C; R_f = 0.51 (*n*-pentane–Et_2O, 1:1).

IR (ATR): 2969, 2927, 2874, 2703, 2106, 1705, 1501, 1450, 1376, 1248, 1156, 1131, 1053, 1013, 983, 902, 813, 711 cm^{-1}.

^1H NMR (400 MHz, C_6D_6): δ = 1.58 [s, 6 H, $C(CH_3)_2$], 3.38 (s, 3 H, NCH_3), 3.47 (s, 3 H, NCH_3), 9.64 (s, 1 H, CHO).

^{13}C NMR (100 MHz, C_6D_6): δ = 22.8 (CH_3, 2 C), 40.9 (NCH_3), 43.7 (NCH_3), 58.6 (C), 192.8 (C=S), 196.5 (CHO).

MS (EI): *m*/*z* = 191 (11, $[M]^+$), 163 (6), 153 (6), 121 (21), 120 (9), 89 (9), 88 (100), 85 (6), 83 (16), 77 (6), 73 (10), 71 (20), 56 (9), 47 (6).

HRMS (ESI): *m*/*z* calcd for $C_7H_{13}NOS_2$: 192.0517 ($[M + H]^+$); found: 192.0511 ($[M + H]^+$).

2-(Dimethylaminothiocarbonylthio)-2-methylbutyraldehyde (3g)
The synthesis of **3g** following GP 1 yielded 290 mg (71%) of a yellow oil; R_f = 0.60 (*n*-pentane–Et_2O, 1:1).

IR (film): 3403, 2970, 2924, 2851, 2707, 1708, 1576, 1500, 1457, 1377, 1252, 1147, 1052, 991, 898, 782, 578 cm^{-1}.

^1H NMR (300 MHz, $CDCl_3$): δ = 1.00 (t, *J* = 7.4 Hz, 3 H, CH_3), 1.63 (s, 3 H, CCH_3), 1.79–1.90 (m, 1 H, CH_3CHH), 2.00–2.15 (m, 1 H, CH_3CHH), 3.40 (s, 3 H, NCH_3), 3.46 (s, 3 H, NCH_3), 9.69 (s, 1 H, CHO).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 8.5 (CH_3), 19.7 (CH_3), 28.3 (CH_2), 42.2 (NCH_3), 44.6 (NCH_3), 63.3 (C), 193.3 (C=S), 198.5 (CHO).

MS (EI): *m*/*z* = 205 (7, $[M]^+$), 122 (5), 121 (23), 120 (7), 90 (5), 89 (8), 88 (100), 85 (24), 77 (6), 73 (8), 72 (6), 71 (5), 57 (13), 56 (6), 55 (10), 45 (5).

Anal. Calcd for $C_8H_{15}NOS_2$: C, 46.79; H, 7.36; N, 6.82. Found: C, 46.95; H, 7.11; N, 6.49.

2-(Dimethylaminothiocarbonylthio)-2-methylvaleraldehyde (3h)
The synthesis of **3h** following GP 1 yielded 327 mg (75%) of a yellow oil; R_f = 0.61 (*n*-pentane–Et_2O, 1:1).

IR (film): 2960, 2928, 2872, 2850, 2703, 1708, 1576, 1499, 1464, 1376, 1252, 1149, 1051, 990, 938, 911, 868, 745, 707, 579, 480 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 0.93 (t, *J* = 7.3 Hz, 3 H, CH_3), 1.36–1.48 (m, 2 H, CH_3CH_2), 1.66 (s, 3 H, CCH_3), 1.71–1.79 (m, 1

H, CH_2CHH), 1.90–1.98 (m, 1 H, CH_2CHH), 3.40 (s, 3 H, NCH_3), 3.46 (s, 3 H, NCH_3), 9.67 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.5 (CH_3), 17.5 (CH_2), 20.4 (CH_3), 37.8 (CH_2), 42.2 (NCH_3), 44.6 (NCH_3), 63.0 (C), 193.2 (C=S), 198.3 (CHO).

MS (EI): *m*/*z* = 220 (23, $[M + H]^+$), 219 (7, $[M]^+$), 122 (10), 121 (35), 120 (12), 99 (28), 90 (6), 89 (11), 88 (100), 77 (5), 73 (5).

Anal. Calcd for $C_9H_{17}NOS_2$: C, 49.28; H, 7.81; N, 6.39. Found: C, 49.78; H, 7.85; N, 6.27.

2-(Dimethylaminothiocarbonylthio)hydratropaldehyde (3i)
The synthesis of **3i** following GP 1 yielded 246 mg (49%) of a red oil; R_f = 0.73 (*n*-pentane–Et_2O, 2:1).

IR (ATR): 3059, 2983, 2930, 2825, 2701, 2324, 2084, 1989, 1950, 1705, 1596, 1494, 1445, 1374, 1250, 1144, 1063, 987, 914, 888, 756, 698 cm^{-1}.

^1H NMR (400 MHz, $CDCl_3$): δ = 2.18 (s, 3 H, CCH_3), 3.38 (s, 3 H, NCH_3), 3.46 (s, 3 H, NCH_3), 7.32–7.40 (m, 3 H, CH_{arom}), 7.53 (dd, *J* = 6.9, 1.5 Hz, 2 H, CH_{arom}), 10.03 (s, 1 H, CHO).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.0 (CH_3), 42.2 (NCH_3), 44.6 (NCH_3), 64.8 (C), 127.5 (CH_{arom}), 128.3 (CH_{arom}, 2 C), 128.9 (CH_{arom}, 2 C), 136.9 (C_{arom}), 192.9 (C=S), 195.9 (CHO).

MS (EI): *m*/*z* = 253 (13, $[M]^+$), 225 (9), 133 (13), 132 (67), 122 (8), 121 (37), 120 (53), 105 (100),104 (12), 103 (25), 88 (95), 79 (16), 78 (14), 77 (55), 73 (11), 59 (7), 56 (6), 51 (16).

2-(Dimethylaminothiocarbonylthio)cyclopentanone (3j)[11b]
The synthesis of **3j** following GP 2 yielded 189 mg (47%) of a brownish solid; mp 94 °C; R_f = 0.42 (*n*-pentane–Et_2O, 1:1).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.92–2.36 (m, 4 H, CH_2), 2.42–2.54 (m, 1 H, C*H*H), 2.62–2.73 (m, 1 H, CH*H*), 3.40 (s, 3 H, NCH_3), 3.56 (s, 3 H, NCH_3), 4.74–4.81 (m, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.6 (CH_2), 31.0 (CH_2), 37.1 (CH_2), 41.7 (NCH_3), 46.1 (NCH_3), 57.7 (CH), 195.2 (C=S), 213.6 (C=O).

2-(Dimethylaminothiocarbonylthio)cyclohexanone (3k)[11b]
The synthesis of **3k** following GP 2 yielded 316 mg (73%) of a colorless solid; mp 111 °C; R_f = 0.50 (*n*-pentane–Et_2O, 1:1).

^1H NMR (400 MHz, $CDCl_3$): δ = 1.65–2.00 (m, 4 H, CH_2), 2.10–2.20 (m, 1 H, C*H*H), 2.50–2.62 (m, 3 H, CH*H*, CH_2), 3.41 (s, 3 H, NCH_3), 3.53 (s, 3 H, NCH_3), 4.97 (m, 1 H, CH).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 25.9 (CH_2), 27.7 (CH_2), 35.4 (CH_2), 41.7 (NCH_3), 42.4 (CH_2), 45.6 (NCH_3), 62.4 (CH), 195.1 (C=S), 205.8 (C=O).

3-(Dimethylaminothiocarbonylthio)tetrahydro-4*H*-pyran-4-one (3l)
The synthesis of **3l** following GP 2 yielded 364 mg (83%) of a colorless solid; mp 75 °C; R_f = 0.42 (*n*-pentane–Et_2O, 1:2).

IR (ATR): 2971, 2913, 2871, 2753, 2069, 1709, 1500, 1376, 1245, 1205, 1147, 1091, 1051, 967, 920, 860, 819, 714, 671 cm^{-1}.

^1H NMR (300 MHz, C_6D_6): δ = 2.59 (dt, *J* = 9.6, 2.5 Hz, 1 H, C*H*H-CO), 2.83–2.94 (m, 1 H, CH*H*CO), 3.43 (s, 3 H, NCH_3), 3.54 (s, 3 H, NCH_3), 3.60 (t, *J* = 10.6 Hz, 1 H, CH), 3.81 (dt, *J* = 11.6, 3.0 Hz, 1 H, CHC*H*HO), 4.32 (m, 1 H, CH_2CHHO), 4.34 (m, 1 H, CH_2CHHO), 5.14 (td, *J* = 10.6, 6.9, 1.0 Hz, 1 H, CHCH*H*O).

^{13}C NMR (75 MHz, C_6D_6): δ = 41.7 (NCH_3), 43.3 (CH_2), 45.8 (NCH_3), 60.4 (CH), 68.2 (CH_2), 72.2 (CH_2), 193.3 (C=S), 201.5 (C=O).

MS (EI): *m*/*z* = 220 (2, $[M + H]^+$), 121 (8), 99 (38), 90 (6), 88 (100), 77 (5), 73 (11), 72 (8), 59 (7), 56 (6), 55 (5), 45 (10).

Anal. Calcd for $C_8H_{13}NO_2S_2$: C, 43.81; H, 5.97; N, 6.39. Found: C, 43.63; H, 5.82; N, 6.64.

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