New Syntheses of Aliphatic Thioamides and Oxalic, Malonic, or Succinic Monothio- and Dithioamides

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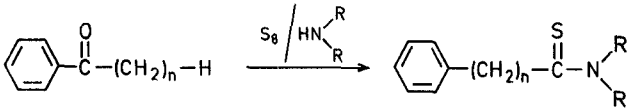
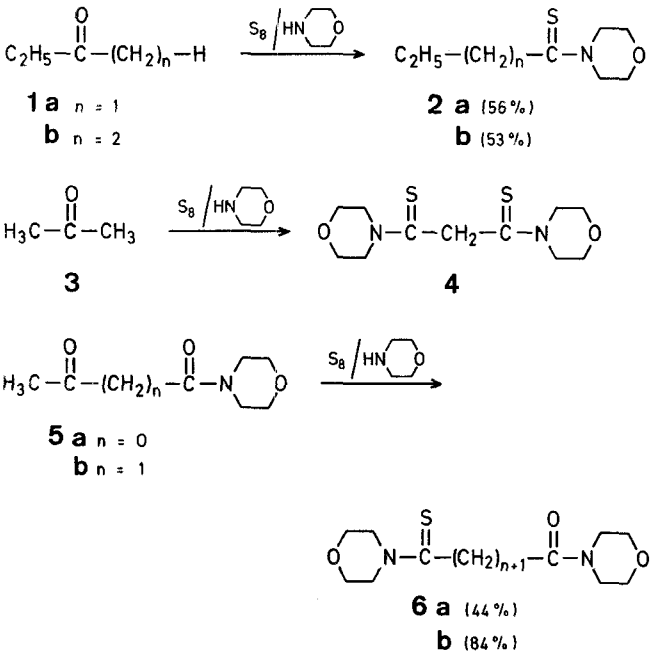
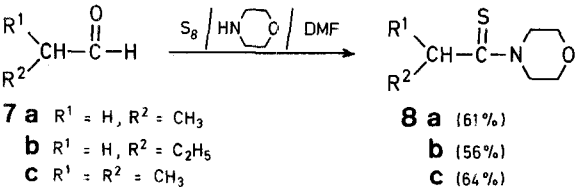
One recent study on the reactivity of captodative *(cd)* methylene groups towards elementary sulfur[1] had familiarised us with the chemistry of thioamides accessible by the Willgerodt-Kindler reaction[2]. In this reaction arylaliphatic ketones in presence of elementary sulfur and secondary amines lead, by oxidation and rearrangement, to the terminal thioamides.



We have now developed an extension of the Willgerodt-Kindler reaction in to aliphatic chemistry. Aliphatic ketones **1** generally furnish, with elementary sulfur and morpholine at 130 °C, the respective monothioamide derivatives **2**. Acetone **(3)** is exceptional in leading to dimorpholinomalonodithioamide **(4)**. Monothiomalonamide **6a** or monothiosuccinamide **6b** are obtained by this method from pyruvic amide **5a** or from acetoacetamide **5b**.



The Willgerodt-Kindler reaction, when extented to aliphatic aldehydes[3] **7** gives, under milder conditions than are necessary for ketones, access to the corresponding monothioamides **8**.



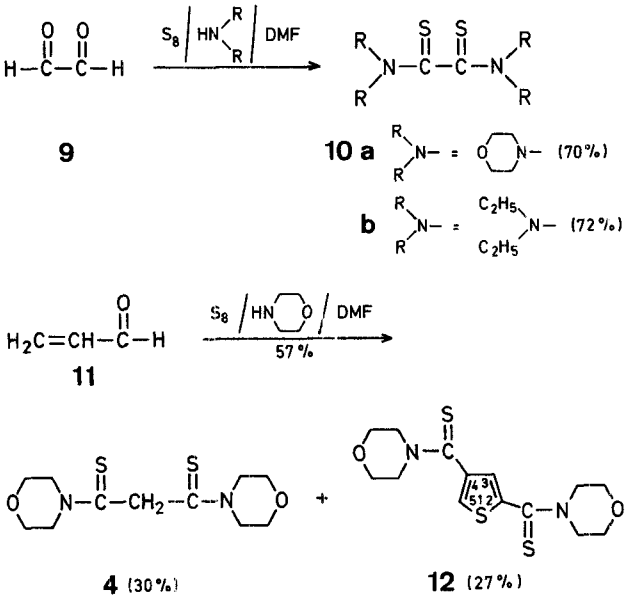
Dithiooxalamides **10** are obtained from glyoxal **(9)**[4]. Acrolein **(11)** at 20 °C, leads to two products: the dithiomalonamide **4** and the 2,4-disubstituted thiophene **12**.

Table. Mono- and Dithioamides from Aliphatic Ketones and Aldehydes

Product	Reaction Time/Temp.	Yield [%]	m.p. [°C] (solvent) and/or b.p. [°C]/torr	Molecular or Lit. Data	I.R. ($CHCl_3$) ν[cm^{-1}]	^{1}H-N.M.R. ($CDCl_3$/TMS) δ[ppm]	M.S. *m/e*
2a	3 h/130 °C	56	40–42° (C_2H_5OH)	46°[5]	1485	1.0 (t, 3H); 1.65 (m, 2H); 2.8 (m, 2H, $CSCH_2$); 3.7–3.8 (m, 6H); 4.3 (m, 2H, NCH_2)	173 (M^+), 158, 144, 140, 130, 112, 110, 86
2b	3 h/130 °C	53	100°/0.1	106–114°/0.2[6]	1485	1.0 (m, 3H); 1.5–1.6 (m, 4H); 2.8 (m, 2H, $CSCH_2$); 3.7–3.8 (m, 6H); 4.3 (m, 2H, NCH_2)	187 (M^+), 158, 154, 145, 130, 112, 86
4	1 h/80 °C	53	205–206° (C_6H_6)	208°[7]	1480	3.7–3.9 (m, 12H); 4.3 (m, 4H, NCH_2); 4.38 (s, 2H, $CSCH_2$)	274 (M^+), 241, 208, 144, 130, 86
4 (from **11**)	0.5 h/20 °C	30					
6a	3 h/130 °C	44	124–126° (c-C_6H_{12})	$C_{11}H_{18}N_2O_3S$ (258.3)	1490	3.6–3.9 (m, 14H); 4.0 (s, 2H, $CSCH_2$); 4.3 (m, 2H, NCH_2)	258 (M^+)
6b	2 h/110 °C	84	120–122° (C_6H_6)	$C_{12}H_{20}N_2O_3S$ (272.4)	1645, 1460	2.9–2.94 (m, 4H, $CSCH_2$); 3.5–3.8 (m, 14H); 4.3 (m, 2H, NCH_2)	272 (M^+), 256, 185, 170, 132, 86
8a	1 h/20 °C	61	18° (C_2H_5OH) 105°/0.1	15–17°[8], 23°[3]; 121°/0.2[3]	1485	1.27 (t, 3H); 2.85 (q, 2H); 3.7–3.8 (m, 6H); 4.3 (m, 2H, NCH_2)	159 (M^+), 135, 100, 72, 44, 28
8b	2 h/20 °C	56	see **2a**	–	–	–	–
8c	4 h/80 °C	64	39–41°	36°[3], 41–42°[9]	1465	1.25 (d, 6H); 3.14 (sept, 1H); 3.7–3.9 (m, 6H); 4.4 (m, 2H, NCH_2)	173 (M^+), 140, 130, 86, 43
10a	2 h/60 °C	91	> 260° (C_6H_6)	263–265°[10a], 255°[10b]	1480	3.9–4.3 (m)	260 (M^+), 130, 88, 86
10b	1 h/50 °C	72	88–90° (c-C_6H_{12})	88–90°[11]	1490	1.35 (t, 12H); 3.6 (q, 4H); 3.8 (m, 2H); 4.0 (m, 2H)	232 (M^+)
12[b]	0.5 h/20 °C	27	189–191° (C_2H_5OH)	$C_{14}H_{18}N_2O_2S_3$ (342.5)	2860, 1470	3.7–4.1 (m, 16H); 6.95 (d, 1H); 7.3 (d, 1H); $J_{H\text{-}3,H\text{-}5}$ = 1.5 Hz	342 (M^+); 309, 257, 224, 171, 130, 127, 86

[a] Satisfactory microanalyses obtained: C ±0.14, H ±0.14, N ±0.13, S ±0.16.

[b] ^{13}C-N.M.R. ($CDCl_3$/TMS): δ = 51.5 (T.m, NCH_2); 66.6 (T.m, OCH_2); 125.3 (C-3, D.d, ^1J = 171.2 Hz, ^3J = 7.7 Hz); 127.2 (C-5, D.d, ^1J = 186.3 Hz, ^3J = 9.7 Hz); 141.6 and 144.9 (C-2 and 4, S.m); 190.9 (S.m, CS); 193.4 ppm (S.m, CS).



***N,N*-Disubstituted Thioamides from Ketones or Aldehydes; General Procedure:**

The aldehyde (0.01 mol) or ketone (0.01 mol), amine (0.02 mol), and elementary sulfur (0.025 g-atom) are placed in a flask fitted with a reflux condenser and a magnetic stirrer. When starting form aldehydes, dimethylformamide (50 ml) is added to the mixture. For substrates **3**, **9**, and **11**, 0.04 mol of amine and 0.05 g-atom of sulfur are utilized. Temperatures and reaction times are indicated in the Table. Thioamides **4**, **6b**, **8c**, **10a**, **10b**, and **12** are isolated from resulting mixture by precipitation with cold water. Thioamides **2a**, **2b**, and **8b** are obtained by distillation of the reaction products under reduced pressure. Thioamides **6a** and **8a** are extracted by addition of water (100 ml) to the mixture and extraction with chloroform (100 ml). The organic phase is washed successively with water (50 ml), dilute hydrochloric acid (20 ml), and water (50 ml), then dried with magnesium sulfate, and evaporated.

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