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1-Acyloxy-2(1H)-pyrimidine-2-thiones as Novel Radical Precursors

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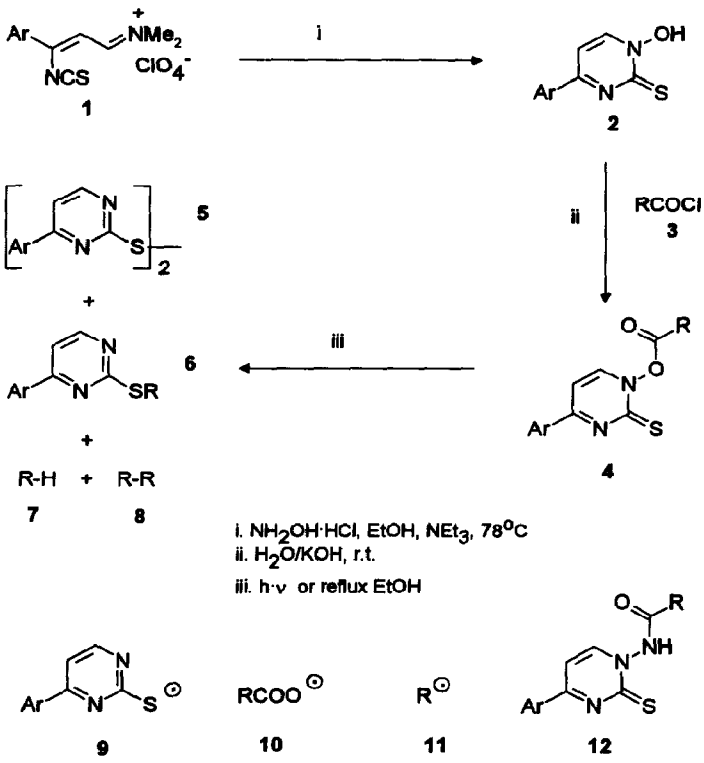
Abstract: Reaction of 3-isothiocyanato-2-propeniminium perchlorates **1** with hydroxylamine gives 1-hydroxy-2(1H)-pyrimidine-2-thiones **2** which can be O-acylated. The resulting 1-acyloxy-2(1H)-pyrimidine-2-thiones **4** are novel precursors for organic radicals. Their photochemical homolysis is studied and affords disulfides **5**, 2-alkylthiopyrimidines **6** and alkanes **7** and **8**.

Heterocyclic O-acyl thiohydroxamates in particular 1-acyloxy-2(1H)-pyridine-2-thiones have been developed by the Barton group as very versatile precursors for radicals suitable to a broad application in organic synthesis.[1] Usually such O-acyl thiohydroxamates are unstable and hence were not isolated. Herein we report on 1-acyloxy-2(1H)-pyrimidine-2-thiones **4** as a novel heterocyclic O-acyl thiohydroxamate system which exhibit both, sufficient stability for isolation and detailed photochemical investigation as well as the ability to serve as radical precursors. The starting 1-hydroxy-2(1H)-pyrimidine-2-thiones **2** were synthesized adapting a synthesis of 1-aryl and 1-amino-2(1H)-pyrimidine-2-thiones previously developed in our group [2,3] that is by reaction of 3-isothiocyanato-2-propeniminium perchlorates **1** [2] with hydroxylamine. The resulting **2** (see Table 1) can be O-acylated with acid chlorides **3** in the presence of KOH affording 1-acyloxy-2(1H)-pyrimidine-2-thiones **4** in excellent yields. The yellow compounds **4** are stable enough to be isolated under the exclusion of light and can be kept in a refrigerator at temperatures below 5°C for some days. Interaction with light or longer heating during the recrystallization process changes the O-acyl thiohydroxamates **4** to colourless bispyrimidinyldisulfides **5** (see Table 1). In addition to the corresponding bispyrimidyl disulfide **5f** the 2-benzylthiopyrimidine **6** (R = benzyl, Ar = 4-tolyl), toluene **7** (R = benzyl) and 1,2-diphenylethane **8** (R = benzyl) were found in the reaction mixture if a solution of **4f** (Ar = 4-tolyl; R = benzyl) in acetonitrile is irradiated using a high pressure mercury lamp. All these products well fit in radical reaction mechanisms running via radical species **9**, **10**, and **11**, like had been proposed in Barton's well explored 1-acyloxy-2(1H)-pyridine-2-thione chemistry.[1,4,5] The proof for the appearance of pyrimidyl radicals **9** was approached by photochemical investigations. Room temperature photolysis revealed that the reaction had gone to completion already after 100 sec. At low temperature photolysis at 78 K (see Fig. 1) the radical intermediate **9** could be detected with an absorption maximum at 263 nm, which disappeared upon warming up to 110 K. The radical nature of this intermediate could be proved by ESR spectroscopy (see Fig. 2a). The ESR pattern , the g-value, and the partially resolved ^{14}N-hyperfine structure confirm the interaction of an unpaired electron (s = ½) with sulfur and nitrogen atoms. Furthermore a superimposition of the ESR data of other radical species (eventually **10** or **11**) is indicated on the wings of the central line.



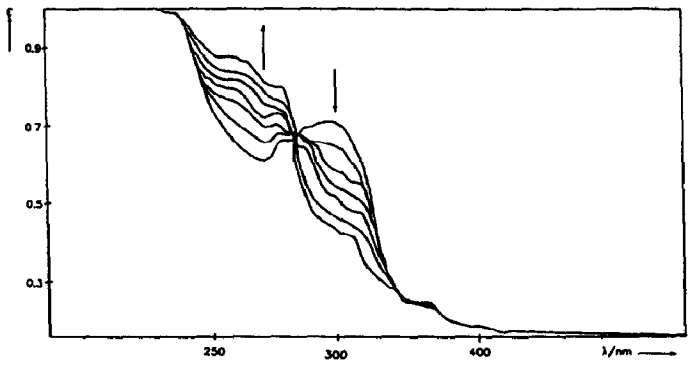


Fig. 1: UV-absorption at 313 nm of **4f** in ethanol/diethyl ether/isopentane (2:5:5) after excitation at 313 at 78K, irradiation times: 0, 2, 7, 12, 22, 92, and 152sec

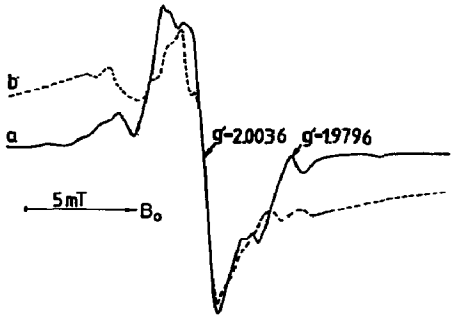


Fig. 2: ESR-spectra (mT) of a) **4f** and b) of the corresponding **12** in CH_2Cl_2 optically excited at 77 K by 200 W high pressure lamp. Internal standard: MgO/Cr^{3+}, corresponds to g´= 1.9796

Table 1: 1-Hydroxy-2(1H)-pyrimidine-2-thiones **2**, 1-Acyloxy-2(1H)-pyrimidine-2-thiones **4** and Bis(pyrimidine-2-yl) disulfides **5**. [8]

	Ar	R	Yield [%]	m. p. [°C]
2a[9]	C_6H_5	-	62	187-189 (EtOH)
2b	4-$CH_3C_6H_4$	-	60	155-157 (EtOH)
2c	4-$CH_3OC_6H_4$	-	55	183-184 (EtOH)
2d	4-ClC_6H_4	-	64	184-186 (EtOH)
4a[10]	C_6H_5	$(CH_2)_4CH_3$	98	86-88 (toluene)
4b	4-$CH_3C_6H_4$	CH_3	98	203-205 (MeOH)
4c	4-$CH_3C_6H_4$	$(CH_2)_2CH_3$	98	139-141 (toluene)
4d	4-$CH_3C_6H_4$	$(CH_2)_4CH_3$	71	131-132 (toluene)
4e	4-$CH_3C_6H_4$	$(CH_2)_{14}CH_3$	95	106-108 (EtOH)
4f	4-$CH_3C_6H_4$	$CH_2C_6H_5$	97	155-157 (toluene)
4g	4-$CH_3C_6H_4$	C_6H_5	95	180-182 (toluene)
5a	C_6H_5	-	55 [11]	170-172 (MeCN))
5b	4-$CH_3C_6H_4$	-	67 [12]	226-228 (AcOEt)
			65 [13]	

Photochemical investigation of the more stable 1-acylamino-2(1H)-pyrimidine-2-thiones **12** revealed a more complex degradation, without the possiblity of detecting bisulfides **5**. On the other hand similar radical species were found in ESR spectroscopy (see Fig. 2b), but the radical yield is about 20 times lower.

Further investigations of the 1-hydroxy-2(1H)-pyrimidine-2-thiones **2** revealed, that these compounds undergo photochemical reactions too. Adopting the conditions used by Boivin et al.[6,7] for 1-hydroxy-2(1H)-pyridine irradiation of a solution of **2b** in isopropanol gave the corresponding bispyrimidyl disulfide **5b** (49%), while acetone could be detected in the reaction mixture. Investigations of the application of 1-acyloxy-2(1H)-pyrimidine-

2-thiones **4** and their precursors in synthetic organic chemistry are currently underway and are to be reported later on.

Acknowledgement

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8. All structures were confirmed by elemental analyses and spectroscopic data. E. g. **2b**: ^{1}H NMR (300 DMSO-d_6, TMS) δ / ppm; J / Hz: 2.36 (s, 2H,)CH_3; 7.34 (m, 2H)C_6H_4; 7.52 (d, 1H, J = 7)5-CH_{pyr}; 7.98 (m, 2H)C_6H_4; 8.79 (d, 1H, J = 7)6-CH_{pyr}; 12.05 (br, 1H)OH. ^{13}C NMR (75 MHz, DMSO-d_6, TMS) δ / ppm: 21.0 (CH_3); 106.2 ($C_{5\text{-pyr}}$); 127.82 (CH_{pyr}); 129.6 (CH_{pyr}); 131.8 (C_{quart}); 142.4 (C_{quart}); 142.8 ($C_{6\text{-pyr}}$); 160.9 (C_{quart}); 175.4 (CS); **4c**: ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ / ppm, J / Hz: 1.55 (t, 3H, J = 7.5)$\underline{CH_3}CH_2$; 1.81 (m, 2H)$\underline{CH_2}CH_3$; 2.36 (s, 3H)$\underline{CH_3}C_6H_4$; 2.65 (t, 2H, J =7.4)$\underline{CH_2}CO$; 7.03 (d, 1H, J = 7.3)$CH_{5\text{-pyr}}$; 7.38 (m, 2H)C_6H_4; 7.86 (d, 1H, J = 7.3)6-CH_{pyr}; 8.40 (m, 2H)C_6H_4. ^{13}C NMR (75 MHz, $CDCl_3$, TMS) δ / ppm: 13.6 ($\underline{C}H_3CH_2$); 17.8 ($\underline{C}H_3CH_2$); 21.4 ($\underline{C}H_3C_6H_4$); 33.5 ($\underline{C}H_2CO$); 105.4 ($C_{5\text{-pyr}}$); 128.5 (CH); 129.6 (CH_{phenyl}); 129.7 (CH_{phenyl}); 131.5 (C_{quart}); 145.1 ($C_{6\text{-pyr}}$); 164.3 (C_{quart}); 169.0 (C=O); 176.8 (C=S). MS (70 eV) *m/z* (%): 288 (M^+, 27); 216 (22); 202 (60); 201 (100); 170 (39); 169 (66); 115 (71); 91 (41); 65 (31); 43 (58); 18 (37). **5b**: ^{1}H NMR (300 MHz, $CDCl_3$, TMS) δ/ ppm, J / Hz: 2.31 (s, 3H)CH_3; 7.09 - 7.20 (m, 2H)C_6H_4; 7.25 (d, 1H, J = 6.3)5-CH_{pyr}; 7.38 - 7.80 (m, 1H)C_6H_4; 7.95 (d, 1H, J = 6.4)6-CH_{pyr}; 8.45 (m, 1H)C_6H_4. MS (70 eV) *m/z* (%): 402 (M^+, 100); 338 (56); 202 (46); 201 (84); 170 (28), 169 (54), 143 (20), 116 (24), 115 (70); 91 (40), 65 (28).
9. General procedure: 1.01g (0.01 mol) triethylamine are added to 0.69g (0.01 mol) of hydroxylamine hydrochloride in 15 ml of ethanol. The mixture is heated to complete solution and is than added to a suspension of 0.01 mol 3-isothiocyanato-2-propeniminium perchlorate **1** in 10 ml ethanol. After cooling **2** is filtered off and recrystallized from EtOH.
10. General procedure: 0.003 mol of **2** are suspended in 10 ml of water. Few drops of methyl red in acetone and 2 ml of **3** are added (exclusion of light). 5molar KOH in water is added dropwise while stirring until the colour changes from yellow to red. The appearing oil solidifies after further addition of KOH and stirring until all excess **3** is hydrolyzed. **4** is filtered off, washed with water and recrystallized from toluene, MeOH, or EtOH with caution (small portions, exclusion of light, short heating).
11. 90 min reflux and irradiation with high pressure mercury lamp of **2a** in isopropanol.
12. 30 min reflux of **4f** in EtOH.
13. 5 min irradiation with high pressure mercury lamp of **4f** in MeCN.

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