On the Selective *O*-Alkylation of Ambident Nucleophiles – The Synthesis of Thiohydroxamic Acid *O*-Esters by Phase-Transfer Reactions

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In memoriam of Prof. Dr. Sir Derek H. R. Barton

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O-Alkylation of cyclic thiohydroxamic acids **1** and **3–5** has been studied with a view to developing an efficient method for the synthesis of *N*-(alkoxy)pyridine-2(1*H*)-thiones and *N*-(alkoxy)thiazole-2(3*H*)-thiones. Four issues have been addressed and the following conclusions can be drawn: (i) Thiones **1** and **5** exist as O–H acids in the solid state. (ii) According to NMR investigations (^{1}H, ^{13}C), the thione structures should be largely retained in $CDCl_3$, [D$_6$]DMSO, and CD_3OD solutions of acids **1**, **3–5**, as is also the case for pyridinethione salts **2a–h**. (iii) *O*-Alkylation of pyridinethione salts occurs in competition with *S*-alkylation. Selective *O*-alkylation is however possible, if thiohydroxamate salts with large countercations, such as M = NBu_4, are treated with hard alkylating reagents in polar aprotic media. (iv) As tetrabutylammonium thiohydroxamates, such as **2f**, are highly useful in the synthesis of cyclic thiohydroxamic acid *O*-esters, we have developed an efficient protocol for the preparation of *N*-(alkoxy)pyridine-2(1*H*)-thiones directly from acid **1** using phase-transfer conditions (alkyl halide or sulfonic acid ester, CH_3CN, K_2CO_3, Bu_4NHSO_4). This method has proved particularly successful for the synthesis of *N*-(alkoxy)thiazole-2(3*H*)-thiones **11**, **20–28**, which were obtained in yields of up to 87%.

Introduction

Recently, *O*-esters of cyclic thiohydroxamic acids,[1] e.g. *N*-(alkoxy)pyridine-2(1*H*)-thiones or *N*-(alkoxy)thiazole-2(3*H*)-thiones (Figure 1), have been successfully employed as sources of oxygen-centred radicals, both in synthetic procedures as well as in mechanistic studies.[2−6] Although alkoxyl radicals have been less extensively studied than carbon[7] or nitrogen[8] radicals, it is obvious from the literature that increasing numbers of transformations are being developed that rely on selective transformations involving *O*-radicals.[4] In 1988, Beckwith and Hay developed a method for the preparation of *N*-(alkoxy)pyridine-2(1*H*)-thiones, which constituted a new class of alkoxyl radical precursors at that time (Figure 1).[2] Although an alternative synthetic access to *N*-(alkoxy)pyridine-2(1*H*)-thiones has since been developed, starting from 2,2′-dithiopyridine 1,1′-dioxide,[9][10] further methods for the synthesis of *O*-esters of cyclic thiohydroxamates that avoid the use of highly hygroscopic tetraethylammonium salts such as **2f**[3b] or **6−8** should be useful, especially for the synthesis of *N*-(alkoxy)thiazole-2(3*H*)-thiones. The latter compounds are of considerable importance, since thiazolethione-derived thiohydroxamic acid *O*-esters represent a new type of alkoxyl radical precursors. They offer a number of advantages in terms of ease of handling and application in radical chemistry in comparison with pyridinethiones.[11] In order to devise a new method for the synthesis of *O*-esters of cyclic thiohydroxamic acids, we addressed two major issues: (i) *O*-Alkylation of thiohydroxamic acids requires an activation step (Figure 1). The principal means of activation is usually deprotonation of the acid, which leads to the formation of ambident thiohydroxamate anions. Alkylation of these anions with, e.g., alkyl tosylates, mesylates, triflates, or halides usually affords the desired thiohydroxamic acid *O*-esters along with *S*-alkylthiohydroximinic acids (Figure 1).[11] By carrying out structural studies of thiohydroxamic acids and derived salts, it should be possible to gain insight into the factors that lead to preferential *O*-alkylation of thiohydroxamates and minimize the formation of heterocyclic *N*-oxides. (ii) Preparation of tetraethylammonium thiohydroxamates (Scheme 1), which are generally used as starting materials for the synthesis of *N*-(alkoxy)pyridine-2(1*H*)-thiones or the corresponding thiazole-2(3*H*)-thiones, requires freeze-drying of the salts in order to obtain material of satisfactory quality. Suitable facilities for this are, however, not available in every laboratory. Therefore, we sought an improved procedure for the synthesis of cyclic

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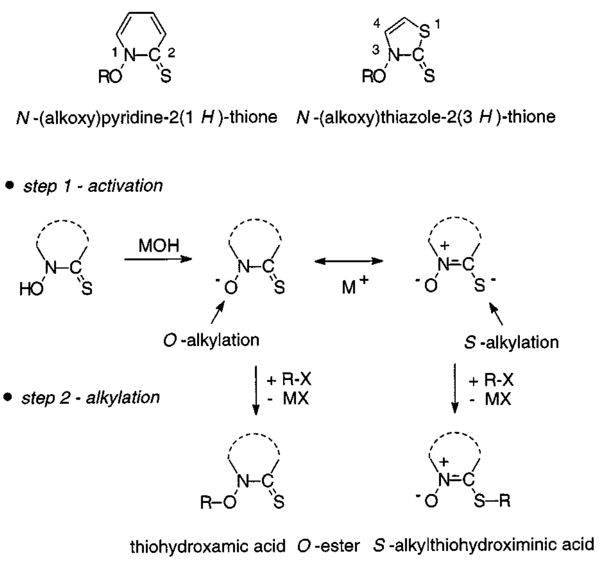


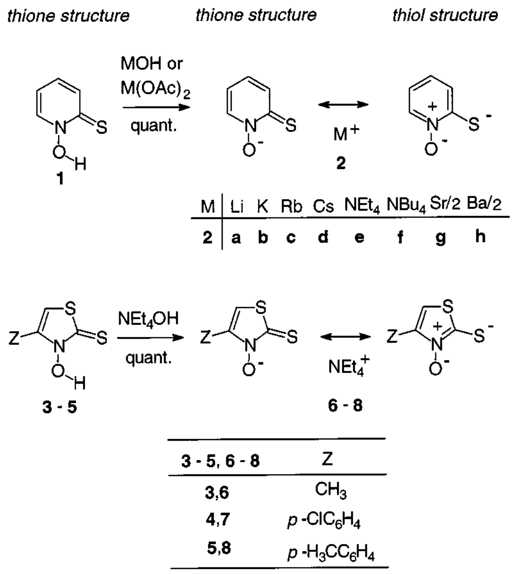
Figure 1. Schematic representation of competing pathways in alkylation reactions of ambident thiohydroxamate nucleophiles

thiohydroxamic acid *O*-esters, starting directly from *N*-(hydroxy)pyridinethione **1**, that would also be applicable to other acids, in particular thiazolethiones **3−5** (Scheme 1).

Results and Discussion

Synthesis and Structural Studies of Thiohydroxamic Acids and Derived Salts

Neutralization of solutions of *N*-(hydroxy)pyridine-2(1*H*)-thione (**1**)[12] in ethanol with 1 equiv. of the respective hydroxides [except for the synthesis of **2g**: 0.5 equiv. of $Sr(OAc)_2$; **2h**: 0.5 equiv. of $Ba(OH)_2 \cdot 8\ H_2O$] afforded salts **2a−h** as colorless to yellowish powders.[13] Apart from the lithium salt **2a**, the potassium salt **2b**, and thiohydroxamate derivatives of divalent cations (i.e. **2g** and **2h**), all compounds **2** were found to be hygroscopic and had to be stored under protection from moisture. Likewise, the thiazolethione-derived acids **3−5**[11,14] were treated with 1 equiv. of NEt_4OH to afford the corresponding tetraethylammonium salts **6−8** as tan-colored hygroscopic powders. In order to create a sound basis for structural investigations, two thiohydroxamic acids were studied by X-ray diffraction. To the best of our knowledge, none of these compounds have previously been studied in the solid state. Crystals of *N*-(hydroxy)pyridine-2(1*H*)-thione (**1**) suitable for X-ray analysis were grown from ethanol, while suitable specimens of *N*-hydroxy-4-(*p*-tolyl)thiazole-2(3*H*)-thione (**5**) were obtained from a saturated solution of **5** in methanol protected from light. The results of our X-ray experiments are presented in Figure 2. Selected connectivities, bond and torsion angles are summarized in Table 1.



Scheme 1. Formation of thiohydroxamate salts **2**, **6−8** from parent acids **1**, **3−5**

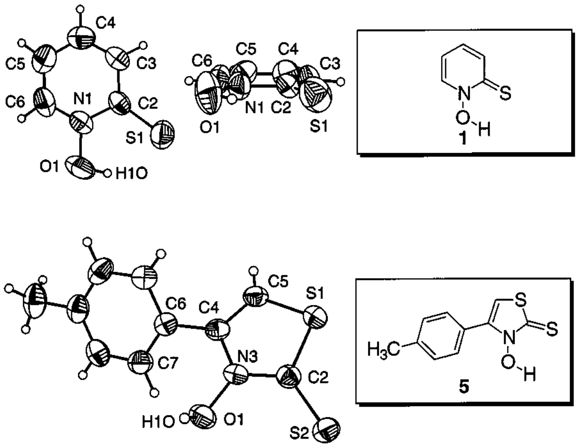


Figure 2. View of a) *N*-(hydroxy)pyridine-2(1*H*)-thione (**1**) and b) *N*-hydroxy-4-(*p*-tolyl)thiazole-2(3*H*)-thione (**5**) in the solid state, showing labelling of selected non-H atoms (see Table 1); thermal ellipsoids are drawn at 50% levels; hydrogen atoms are depicted as small circles of arbitrary radius

Ellipsoid graphics (Figure 2) show an almost planar substituted heterocyclic core in pyridinethione **1** [C2−N1−C6−C5 = −0.2(4)°; N1−C2−C3−C4 = 1.2(4)°]. The acidic H1O, which was located on a difference Fourier map, is bound to O1 and is directed towards the sulfur atom so as to form an intramolecular hydrogen bond [O1−H1O−S1 = 134.1(2)°, O1−H1O = 0.89(4) Å, H1O−S1 = 2.105(2) Å]. The C−S bond length in **1** [C2−S1 = 1.684 (2) Å] is indicative of a C−S double bond. Within experimental uncertainties, C−S and N−O distances [N1−O1 = 1.377(3) Å] compare well with recently obtained values for an *N*-(alkoxy)pyridine-2(1*H*)-thione.[15] C−C bond lengths in heterocycle **1** show alternating distances, although their variation is less pronounced than in *N*-(alkoxy)- or *N*-(acyloxy)pyridine-2(1*H*)-thiones.

The structure of *N*-hydroxy-4-(*p*-tolyl)thiazole-2(3*H*)-thione (**5**) (Figure 2, Table 1) reveals an almost planar heterocyclic framework [C4−N3−C2−S1 = 2.7(3)°; C2−N3−C4−C5 = −1.9(3)°]. Connectivities within the thiohydroxamate group of **5** in the solid state are similar to

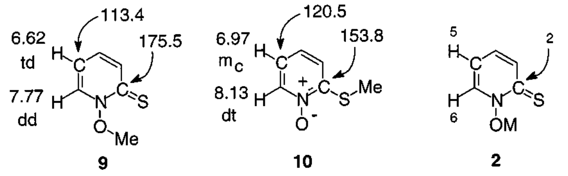
Table 1. Selected bond lengths [Å], bond angles [°] and torsion angles [°] of *N*-(hydroxy)pyridine-2(1*H*)-thione (**1**) and *N*-hydroxy-4-(*p*-tolyl)thiazole-2(3*H*)-thione (**5**)

Parameter	1	Parameter	5
S1−C2	1.684(2)	C2−S2	1.672(3)
C2−C3	1.400(4)	S1−C2	1.708(3)
C3−C4	1.349(4)	S1−C5	1.707(3)
C4−C5	1.372(5)	C2−N3	1.341(3)
N1−O1	1.377(3)	N3−O1	1.369(3)
N1−C2	1.367(3)	N3−C4	1.390(3)
N1−C6	1.340(4)	C4−C5	1.334(4)
N1−C2−C3	113.5(2)	N3−C2−S2	127.7(2)
C2−C3−C4	122.1(3)	N3−C2−S1	108.0(2)
C3−C4−C5	120.8(3)	C2−S1−C5	91.9(1)
C4−C5−C6	118.6(3)	S1−C5−C4	113.0(2)
C5−C6−N1	119.5(3)	C5−C4−N3	109.4(2)
C6−N1−C2	125.5(2)	C4−N3−C2	117.6(2)
C2−N1−O1	117.3(2)	C4−N3−O1	120.8(2)
C6−N1−O1	117.3(2)	C2−N3−O1	121.6(2)
C3−C2−S1	128.5(2)	S1−C2−S2	124.3(2)
O1−N1−C2−S1	−0.1(3)	S2−C2−N3−C4	−177.9(2)
S1−C2−N1−C6	179.2(2)	S2−C2−N3−O1	0.7(3)
C2−N1−O1−H1O	4(1)	C2−N3−O1−H1O	−86(2)
		N3−C4−C6−C7	−41.2(4)

the distances observed in **1** [C2−S2 = 1.672(3) Å, N3−O1 = 1.369(3) Å]. The bond length C4−C5 = 1.334(4) Å is indicative of an olefinic C−C double bond. The *p*-tolyl group and H1O are both twisted out of the plane of the heterocycle [N3−C4−C6−C7 = 41.2(4)°, C2−N3−O1−H1O = −85.8(9)°]. In the solid state, the hydroxy group in thiazolethione **5** is part of an intermolecular hydrogen bond, which is directed towards a thiocarbonyl group of a neighbouring thione **5** [O1−H1O = 1.22(8) Å, S1(molecule A)−H1O(molecule B) = 1.959(2) Å, O1(A)−S2(B) = 3.148(4) Å, O1(A)−H1O(A)−S1(B) = 163.7(6)°].

Of the possible thione or thiol tautomers, acids **1** and **5** preferentially adopt thione structures.[16] This had been predicted for **1** in the solid state by Katritzky et al. on the basis of IR absorptions.[16][17] In the ^{1}H-NMR spectra in $CDCl_3$ solution, the signals of the acidic hydrogen atoms of thiones **1** and **5** are seen to be strongly downfield shifted ($\delta \approx 12-14$). In both cases, these shifts can most probably be attributed to intramolecular hydrogen bonds. We had also intended to grow crystals of thiohydroxamate salts **2** or **6−8**, in order to analyze by X-ray diffraction the structural changes that occur upon deprotonation of acids **1** or **3−5**, but so far we have not succeeded in this matter. For reasons outlined previously,[17] we refrained from using IR analysis but restricted ourselves to NMR experiments in solution. Thus, acids **1** and **3−5** and the derived salts **2** and **6−8** were subjected to an NMR study in order to derive structural information allowing us to ascertain whether salts **2**, **6−8** preferentially adopt thiol or thione structures in solution. NMR data on *N*-(methoxy)pyridine-2(1*H*)-thione (**9**)[15] and 2-(methylsulfanyl)pyridine *N*-oxide (**10**)[14] have been published previously and served as reference values for the two structure types (**9**: thione, **10**: thiol). NMR experiments on *N*-(hydroxy)pyridinethione **1** were carried out in both aprotic ($CDCl_3$, [D$_6$]DMSO) and protic solvents (CD_3OD). The signals due to C-2 ($\delta = 175.5$ in **9**; 153.8 in **10**), C-5 ($\delta = 113.4$ in **9**; 120.5 in **10**), 5-H, and 6-H were selected for analysis (Table 2), as the most significant differences in chemical shifts between compounds **9** and **10** were observed for the nuclei in these positions. Our data show that the resonance of C-2 in **1** ($\delta = 167.2-169.1$) is almost independent of the solvent ($CDCl_3$, [D$_6$]DMSO, CD_3OD). When salts **2** are studied by NMR (CD_3OD, [D$_6$]DMSO, D_2O), the C-2 signal is again observed between $\delta = 165.1$ (**2h**: M = Ba/2) and $\delta = 175.0$ (**2f**: M = NBu_4), and that of C-5 between $\delta = 114.1$ (**2e**: M = NEt_4) and $\delta = 116.9$ (**2b**: M = K), with $\delta = 119.2-119.6$ (**2f**, M = NBu_4, **2h**: M = Ba/2) being exceptions (Table 2). According to this correlation, salts **2** are best described as thione derivatives and should have highest charge density located on the oxygen atom. These findings are in accord with the conclusions that Beckwith and Hay drew from results of their alkylation experiments on the sodium salt of *N*-(hydroxy)pyridine-2(1*H*)-thione (**1**) and the ammonium salt **2e**.[2][3]

Table 2. Selected ^{1}H- and ^{13}C-NMR chemical shifts [ppm] of thiohydroxamic acid **1** and derivatives **2** (Scheme 1)

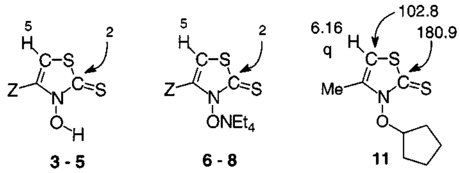


Entry	Compound	M	Solvent	5-H	6-H	C-2	C-5
1	**1**	–	$CDCl_3$	6.77	8.08	167.2	114.4
2	**1**	–	[D$_6$]DMSO	6.91	8.46	169.1	115.3
3	**1**	–	CD_3OD	6.89	8.31	167.8	114.7
4	**2a**	Li	CD_3OD	6.78	8.05	166.8	115.8
5	**2b**	K	CD_3OD	7.02	8.05	168.0	116.9
6	**2c**	Rb	CD_3OD	6.73	8.03	167.6	116.6
7	**2d**	Cs	[D$_6$]DMSO	6.67	8.03	174.1	114.5
8	**2e**	NEt_4	[D$_6$]DMSO	6.00	7.27	165.9	114.1
9	**2f**	NBu_4	$CDCl_3$	6.39	7.76	175.0	119.6
10	**2g**	Sr/2	[D$_6$]DMSO	6.63	8.01	167.5	115.2
11	**2h**	Ba/2	D_2O	6.84	7.96	165.1	119.2

A similar relationship between chemical shift values (^{1}H- and ^{13}C-NMR) was determined for *N*-(hydroxy)thiazole-2(3*H*)-thiones **3−5** and the derived tetraethylammonium salts **6−8**. (Table 3). *N*-(Cyclopentoxy)thiazole-2(3*H*)-thione **11** served as a reference for thione structures, whereas data for 2-(2-methyl-2-propenyl-1-sulfanyl)-4-(4-chlorophenyl)thiazole *N*-oxide (C-2: $\delta = 164.6$; C-5: $\delta = 112.9$) were used as a rough guide for assessing whether the observed shifts could be assigned to the possible thiol isomers of heterocycles **3−8**.[12] The signal of thiocarbonyl carbon atom C-2 is downfield shifted by 10 ppm upon *O*-alkylation of, e.g., 4-methylthiazolethione **3**, while an upfield shift of 10 ppm is observed upon deprotonation of **3** to afford the salt **6** (Table 3). ^{13}C-NMR chemical shifts of C-5 appear at $\delta = 102-106$ in acids **3−5** and at $\delta = 100-104$ in tetraethylammonium salts **6−8**. Thus, it is difficult to draw a firm conclusion on the basis of these data, since the positions of the resonances for C-2 seemingly favor a thiol structure, while those for C-5 are appropriate for a thione.

Our results from structural studies of pyridinethione **1**, and its deprotonated derivatives **2a−h**, as well as of thiazole-derived acids **3−5** and their respective ammonium salts **6−8**, can be summarized as follows: (i) Cyclic thiohydroxamic acids **1**, **3−5** should prefer thione to thiol structures. Similar arguments can be applied in the case of pyridinethione-derived salts **2**, whereas data for deprotonated *N*-hydroxythiazole-2(3*H*)-thiones can be interpreted in terms of mesomeric thiol and thione structures contributing to the ground state descriptions of salts **6−8**. (ii) The most efficient methods for *O*-alkylation of thiohydroxamate anions should therefore be predictable from Pearson's hard-soft acid-base (HSAB) concept.[18] Thus, selective formation of thiohydroxamic acid *O*-esters is best achieved by reactions of thiohydroxamate salts possessing large countercations with hard electrophiles.

Table 3. Selected ^{1}H- and ^{13}C-NMR chemical shifts [ppm] of thiazolethiones **3−5** and derived tetraethylammonium salts **6−8** in $CDCl_3$ (Scheme 1)



Entry	Compound	Z	5-H	C-2	C-5
1	**3**	CH_3	6.31	171.2	102.1
2	**4**	p-ClC_6H_4	6.68	179.2[a]	106.4[a]
3	**5**	p-$H_3CC_6H_4$	6.64	178.9[a]	104.8[a]
4	**6**	CH_3	5.95	161.7[a]	99.8[a]
5	**7**	p-ClC_6H_4	6.40	164.5	104.1
6	**8**	p-$H_3CC_6H_4$	6.53	162.1[b]	102.3[b]

[a] $[D_6]$DMSO. − [b] $[D_6]$DMSO/$CDCl_3$ (1:1).

Alkylation of Pyridinethione Salts 2 and Phase-Transfer Alkylation of Cyclic Thiohydroxamic Acids 1, 3−5

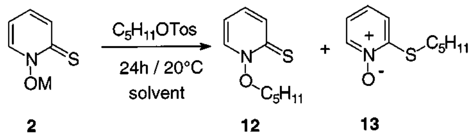
Initially, thiohydroxamate salts **2** were treated with *n*-pentyl tosylate in various solvents in order to study the effects of the countercation in **2** and the reaction medium on the efficiency of synthesis of *n*-(pentoxy)pyridinethione **12**. Alkyl tosylates were chosen as substrates because they are useful alkylating reagents in the synthesis of thiohydroxamic acid *O*-esters[4,5] and are nowadays accessible in excellent yields using a pyridine-free methodology that does not necessarily require halogenated solvents.[19] Reaction mixtures of **2** and the alkylating reagent were stirred in the dark (Table 4) and worked-up as described in the Experimental Section. Apart from the lithium salt **2a** (M = Li) and the pyridinethione salts **2** having divalent counterions (M = Sr/2, Ba/2), alkylation of the other derivatives (**2b−2e**: M = K, Rb, Cs, NEt_4) in DMF solution afforded *n*-pentyl ester **12** in comparable yields (33−43%) (Table 4). This observation is in line with data compiled in Table 2. If chemical shift values are taken as a guide for charge distributions in organic anions,[20] **2b−2e** should indeed exhibit comparable reactivities in alkylation reactions in DMF.

Besides **12**, 2-(*n*-pentylsulfanyl)pyridine *N*-oxide (**13**) was obtained in 19−44% yield as a further reaction product (Table 4). Lithium salt **2a** and salts of alkaline earth metals **2g** and **2h** were found to be less reactive, presumably due to a strong polar interaction between the cations and anions. Typical coordination compounds of *N*-(hydroxy)pyridine-2(1*H*)-thione (**1**), such as palladium(II), nickel(II), or copper(II) complexes[21][22] did not afford *O*-alkylated product **12** or *N*-oxide **13**, even after prolonged treatment with alkyl tosylates at ambient (20°C) or at elevated temperatures (80°C; data not included in Table 4).

A change in the reaction medium had a dramatic effect on the yield of pyridinethione **12**. When tetraethylammonium salt **2e** was treated with *n*-pentyl tosylate, yields of **12** were found to increase from 10% to 68% in the series EtOH < THF < CH_3NO_2 < DMF < CH_3CN < DMSO < DMPU.[23] Thus, the use of solvents that interact strongly with cations [i.e. polar aprotic solvents with high Gutmann donor values combined with low acceptor properties (small acceptor numbers)][24] resulted in the production of primary ester **12** in yields of up to 68% (entry 11, Table 4). As the tetraethylammonium salt **2e** is seen to be almost as efficient for the synthesis of **12** as potassium derivative **2b**, salts with even larger counterions than NEt_4^+ should also be of interest for our purposes. Thus, tetrabutylammonium salt **2f** (M = NBu_4) was prepared and tested for its utility as a reagent in the synthesis of **12** (entry 12, Table 4). We obtained ester **12** in 49% yield (compared to 68% using **2e** in DMPU). Subsequently, we considered the use of tetrabutylammonium salt **2f**, which can be generated in situ from **1**, under phase-transfer conditions[25] as a means of improving the synthesis of **12**. Thus, *n*-pentyl halides or sulfonic acid esters were treated with *N*-(hydroxy)pyridine-2(1*H*)-thione (**1**) using NBu_4HSO_4, $N(n\text{-}C_6H_{13})_4HSO_4$, or PPh_4Cl as phase-transfer reagents and K_2CO_3 as the base (Table 5). This procedure was indeed found to work well. Work-up of the reaction mixtures led to the isolation of pyridinethione **12** in yields of up to 41%.[26] This value corresponds to the yield obtained from the reaction of the NEt_4 salt **2e** with n-$C_5H_{11}OTos$ in CH_3CN (entry 7, Table 4). In the absence of NBu_4HSO_4, the yield of ester **12** dropped to 13%. Tosylates proved to be as effective as mesylates and both leaving groups were by far more useful than halides. Changing the cation of the phase-transfer reagent from tetrabutylammonium to larger groups did not improve yields of ester **12** (entries 13 and 14, Table 5). CH_2Cl_2 or 1,4-dioxane (entries 4−6, Table 5) proved inferior to CH_3CN as reaction media. An optimized procedure involves the use of CH_3CN as solvent, 0.10 equiv. of NBu_4HSO_4, 3 equiv. of K_2CO_3, and a sulfonic acid ester as the alkylating reagent (entries 1, 2, Table 5).

Numerous examples of phase-transfer alkylations have been reported in the literature where alkyl halides are preferred to tosylates as electrophiles.[25] Therefore, some ad-

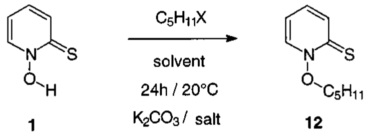
Table 4. Alkylation of *N*-(hydroxy)pyridinethione salts **2** in various solvents



Entry	M	**2**	Solvent	Conversion (%)[a]	**12** (%)	**13** (%)
1	Li	**2a**	DMF	54	12	6
2	K	**2b**	DMF	96	43	35
3	Rb	**2c**	DMF	quant.	34	27
4	Cs	**2d**	DMF	quant.	33	19
5	NEt_4	**2e**	DMF	quant.	40	44
6	NEt_4	**2e**	DMSO	quant.	50	49
7	NEt_4	**2e**	CH_3CN	quant.	43	51
8	NEt_4	**2e**	CH_3NO_2	98	35	54
9	NEt_4	**2e**	THF	73	22	41
10	NEt_4	**2e**	EtOH	90	10	67
11→	NEt_4	**2e**	DMPU	quant.	68	11
12→	NBu_4	**2f**	DMPU	quant.	49	15
13	Sr/2	**2g**	DMPU	56	6	26
14	Ba/2	**2h**	DMPU	61	6	24

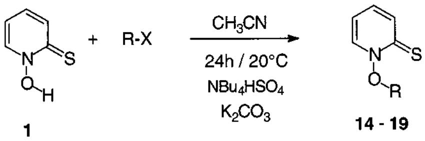
[a] Of *n*-pentyl tosylate (^{1}H-NMR).

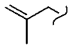
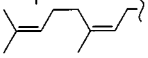
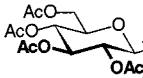
Table 5. Preparation of pyridinethione **12** by phase-transfer alkylation of acid **1**



Entry	Solvent	X	Salt	equiv.	Yield (%)
1→	CH_3CN	OTos	NBu_4HSO_4	0.10	41
2→	CH_3CN	OMs	NBu_4HSO_4	0.10	41
3	CH_3CN	Br	NBu_4HSO_4	0.10	10
4	CH_3CN	Cl	NBu_4HSO_4	0.10	21
5	CH_2Cl_2	OMs	NBu_4HSO_4	0.10	9
6	1,4-dioxane	OMs	NBu_4HSO_4	0.10	29
7	CH_3CN	OMs	NBu_4HSO_4	1.00	28
8	CH_3CN	OMs	NBu_4HSO_4	0.70	31
9	CH_3CN	OMs	NBu_4HSO_4	0.50	32
10	CH_3CN	OMs	NBu_4HSO_4	0.30	37
11	CH_3CN	OMs	NBu_4HSO_4	0.05	30
12	CH_3CN	OMs	NBu_4HSO_4	–	13
13	CH_3CN	OMs	$N(n\text{-}C_6H_{13})_4HSO_4$	0.10	40
14	CH_3CN	OMs	PPh_4Cl	0.10	40

Table 6. Phase-transfer alkylation for the synthesis of pyridinethiones from alkyl halides and cyclopentyl tosylate (for conditions, see entry 2, Table 5)



Entry	R	X	Pyridinethione	Yield
1		Cl	**14**	6%
2		Cl	**15**	5%
3	$C_6H_5CH_2$	Cl	**16**	6%
4	$C_6H_5CHCH_3$	Cl	**17**	59%
5	*c*-C_5H_9	Cl	**18**	10%
6	*c*-C_5H_9	OTos	**18**	64%
7		Br[a]	**19**	56%

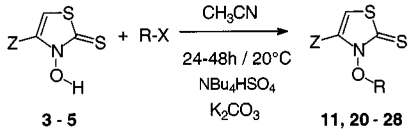
[a] 2,3,4,6-Tetra-*O*-acetyl-1-bromo-α-D-glucopyranoside was used as alkylating reagent R−X

ditional, more reactive allylic, benzylic, or carbohydrate-derived halides were tested as reagents in the phase-transfer alkylation of acid **1** (Table 6). Experiments using α-methylallyl, geranyl, or benzyl chloride afforded the corresponding thiones **14−16** in unexpectedly poor yields (entries 1−3, Table 6). The reasons for these findings are as yet unclear, especially in view of the fact that secondary benzyl ester **17** is accessible in significantly higher yield (59%). In order to prepare compounds **14−16** more efficiently, we strongly recommend use of the alternative protocol,[9] which requires 2,2′-dithiopyridine 1,1′-dioxide, PBu_3, and an allylic or benzylic alcohol to prepare *O*-allyl esters of **1** or *N*-(benzyloxy)pyridinethione **16**. Phase-transfer reaction of acid **1** with α-acetobromoglucose (Table 6, entry 7) afforded carbohydrate-derived pyridinethione **19** in 56% yield. According to ^{1}H-NMR analysis, none of the acetyl groups in **19** were cleaved during synthesis or work-up of the reaction mixture, in spite of the large excess of K_2CO_3 required as base. A large vicinal coupling constant $^3J_{\mathrm{H}1\text{-}\mathrm{H}2} = 8.1$ Hz between hydrogen atoms at C-1 (anomeric centre, $\delta = 5.68$) and C-2, and distinctive nuclear Overhauser enhancements (^{1}H-NMR), are indicative of the β-configuration for **19**. The α-isomer was not detected.

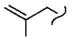
In the light of these encouraging results, we focused on the application of phase-transfer alkylation in the synthesis of *N*-(alkoxy)thiazole-2(3*H*)-thiones **11**, **20−28**. Reactions of primary chlorides or sulfonic acid esters, secondary sulfonates, allylic or benzylic chlorides with methyl-, *p*-tolyl-, or *p*-chlorophenyl-substituted *N*-(hydroxy)thiazole-2(3*H*)-thiones **3−5** afforded the corresponding *O*-esters **11**, **20−28** in good to excellent yields (Table 7).[27] The highest yields of *N*-(alkoxy)thiazole-2(3*H*)-thiones achieved to date were obtained using 4-methyl-substituted acid **3** as the starting material (**11**, **20−21**: 76−87%). Other than the newly formed thiones **11**, **20−21**, TLC studies did not reveal the presence of any additional compounds that might have been indicative of the formation of alkylsulfanylthiazole *N*-oxide isomers of **11**, **20−21** (i.e. *S*-alkylated products). These findings are in accord with previous studies on the synthesis of *N*-alkoxy-*p*-chlorophenylthiazole-2(3*H*)-thiones, e.g. of **25** from the corresponding tetraethylammonium salt, which showed that *S*-alkylation occurs to a lesser extent in the thiazolethione than in the pyridinethione series.[11] Alkylations of 4-aryl-substituted thiazolethiones **4−5** afford the corresponding esters **22−28**. Yields are lower compared to those achieved in the syntheses of *N*-alkoxy-4-methylthiazolethiones **11**, **20−21** (entries 4−11, Table 7). This may be attributed to differential steric congestion at the N−O faces of the anionic derivatives of thiazole-2(3*H*)-thiones **3−5**, which should be least significant in the 4-methyl-substituted thiohydroxamate.

Remarkably, all the studied chlorides, with the exception of cyclopentyl chloride for reasons which remain unclear, are satisfactory to good substrates and provide a simple and convenient access to *N*-(alkoxy)thiazolethiones for the future development of alkoxyl radical chemistry and its application in synthesis.[12,27]

Table 7. Application of phase-transfer alkylation in the synthesis of *N*-alkoxythiazolethiones



3 - 5 **11, 20 - 28**

Entry	Z	R	X	Thiazole	Yield
1	CH_3	n-C_5H_{11}	OMs	**20**	82%
2	CH_3	c-C_5H_9	OTos	**11**	87%
3	CH_3	$C_6H_5CHCH_3$	Cl	**21**	76%
4	p-ClC_6H_4	n-C_5H_{11}	Cl	**22**	55%
5	p-ClC_6H_4	n-C_5H_{11}	OTos	**22**	62%
6	p-ClC_6H_4		Cl	**23**	35%
7	p-ClC_6H_4	$C_6H_5CH_2$	Cl	**24**	36%
8	p-ClC_6H_4	$C_6H_5CHCH_3$	Cl	**25**	63%
9	p-$H_3CC_6H_4$	n-C_5H_{11}	Cl	**26**	39%
10	p-$H_3CC_6H_4$	$CH(CH_3)_2$	OTos	**27**	70%
11	p-$H_3CC_6H_4$	$C_6H_5CHCH_3$	Cl	**28**	70%

Conclusion

Reactions of *N*-(hydroxy)pyridine-2(1*H*)-thione (**1**) or *N*-(hydroxy)thiazole-2(3*H*)-thiones **3−5** with alkyl, allyl, benzyl, or carbohydrate-derived halides (chlorides, bromides) or primary or secondary sulfonic acid esters (tosylates or mesylates) under phase-transfer conditions (CH_3CN, K_2CO_3, NBu_4HSO_4) afford alkyl, allyl, benzyl, or carbohydrate-derived thiohydroxamic acid *O*-esters. In most cases, the recommended procedure represents a significant improvement on the existing method for *O*-alkylation of thiohydroxamate salts **2**, **6−8**, since it circumvents preparation of hygroscopic thiohydroxamate compounds themselves. Yields of *N*-(alkoxy)thiazole-2(3*H*)-thiones of up to 87% highlight the efficiency of the new method. Detailed spectroscopic and preparative studies using metal derivatives **2** of *N*-(hydroxy)pyridine-2(1*H*)-thione (**1**) in various solvents provide evidence for the intermediacy of the *N*-(hydroxy)pyridinethione tetrabutylammonium salt **2f** (M = NBu_4), and presumably also of NBu_4 salts of thiazolethiones **3−5**, in phase-transfer reactions.

Experimental Section

General Aspects: ^1H- and ^{13}C-NMR spectra were recorded with Bruker AC 200, AC 250, and WM 400 instruments at 20°C in $CDCl_3$ solution unless otherwise noted. Residual protons of deuterated solvents {$\delta_H = 7.26$ ($CDCl_3$), $\delta_H = 2.50$ ([D_6]DMSO), $\delta_H = 3.38$ (CD_3OD)} and the corresponding carbon resonances in ^{13}C-NMR spectra {$\delta_C = 77.0$ ($CDCl_3$), $\delta_C = 39.5$ ([D_6]DMSO), $\delta_C = 49.3$ (CD_3OD)} were taken as internal standards. 1,4-Dioxane ($\delta_C = 67.6$, $\delta_H = 3.71$) was used as an internal standard for NMR spectra recorded in D_2O. − IR: Spectra were recorded either from CCl_4 solutions in NaCl cuvettes (0.5 mm), from films (Nujol) on NaCl plates, or from KBr pellets, using a Perkin-Elmer 1600 FT-IR spectrometer. − UV/Vis: Ethanol solutions in 1-cm quartz cuvettes with a Perkin-Elmer 330 spectrophotometer. − MS: Varian MATCH 7 spectrometer [electroimpact, EI, 70 eV, chemical ionization DCI (NH_3)]. − DTA: DuPont thermal analyzer 9000; scanning rate 10° min^{-1}; samples were enclosed in metal containers under nitrogen. − C,H,N,S analyses: Microanalytical Laboratory, University of Würzburg, Carlo Erba 1106 or LECO CHNS-932. − Solvents were purified according to standard procedures.[28] *N*-(Hydroxy)pyridine-2(1*H*)-thione (**1**),[12] *N*-hydroxy-4-methylthiazole-2(3*H*)-thione (**3**),[14] *N*-hydroxy-4-(*p*-chlorophenyl)thiazole-2(3*H*)-thione (**4**),[11] *N*-(methoxy)pyridine-2(1*H*)-thione (**9**),[15] 2-(methylthio)pyridine-*N*-oxide (**10**),[14] *N*-(hydroxy)pyridine-2(1*H*)-thione tetraethylammonium salt (**2e**),[3b] and α-phenylethyl chloride[29] were prepared according to literature procedures. Phase-transfer reagents [NBu_4HSO_4, $N(n\text{-}C_6H_{13})_4HSO_4$, NBu_4Cl, NBu_4Br, PPh_4Cl] were purchased from Fluka and used as received. CH_3CN was distilled under argon from CaH_2 and stored under argon. Petroleum ether was distilled prior to use (b.p. 55−60°C).

Preparation of *N*-Hydroxpyridine-2(1*H*)-thione Salts 2:[13] Pyridinethione **1** (2.00 g, 16.0 mmol) was dissolved in 95% aqueous[30] EtOH (50 mL) and treated with equimolar amounts of MOH {LiOH (0.38 g, 16.0 mmol), KOH (0.90 g, 16.0 mmol), RbOH [1.9 mL of a 50% aqueous solution (w/w), 16.0 mmol], $CsOH \cdot H_2O$ (2.60 g, 16.0 mmol), NEt_4OH (10.7 mL of a 1.5 M solution in MeOH, 16.0 mmol), NBu_4OH (20.0 mL of a 0.8 M solution in MeOH, 16.0 mmol), $Sr(OAc)_2$ (1.65 g, 8.00 mmol), $Ba(OH)_2 \cdot 8\,H_2O$ (2.52 g, 8.00 mmol dissolved in 30 mL of H_2O)}. The resulting colorless to pale-yellow clear solutions of **2** were stirred for 10 min at 20°C and were subsequently concentrated in vacuo. Colorless to yellowish powders of **2** (quantitative yield, ^1H-NMR) were obtained by thorough freeze-drying of the residues (3 d at 10^{-3} mbar). According to ^{1}H-NMR analysis, prepared samples of the lithium salt **2a** contained 0.5 equiv. of EtOH. − **2a** (M = Li): ^{1}H NMR (250 MHz, CD_3OD): δ = 6.78 (td, J_d = 2.1 Hz, J_t = 7.3 Hz, 1 H, 5-H), 7.04 (ddd, *J* = 1.5, 7.3, 8.6 Hz, 1 H, 4-H), 7.58 (ddd, *J* = 0.9, 1.8, 8.2 Hz, 1 H, 3-H), 8.05 (dd, *J* = 1.5, 6.1 Hz, 1 H, 6-H). − ^{13}C NMR (63 MHz, CD_3OD): δ = 115.8, 127.1, 132.7, 138.7, 166.8. − **2b** (M = K): ^{1}H NMR (200 MHz, CD_3OD): δ = 6.76 (ddd, *J* = 2.0, 7.1, 8.7 Hz, 1 H, 5-H), 7.02 (td, J_d = 1.4 Hz, J_t = 8.3 Hz, 1 H, 4-H), 7.56 (dd, *J* = 1.8, 8.3 Hz, 1 H, 3-H), 8.05 (d, *J* = 6.6 Hz, 1 H, 6-H). − ^{13}C NMR (50 MHz, CD_3OD): δ = 116.9, 128.4, 134.0, 139.6, 167.0. − **2c** (M = Rb): ^{1}H NMR (250 MHz, CD_3OD): δ = 6.73 (td, J_d = 2.0 Hz, J_t = 7.1 Hz, 1 H, 5-H), 6.98 (ddd, *J* = 1.5, 7.2, 8.4 Hz, 1 H, 4-H), 7.56 (dd, *J* = 1.8, 8.3 Hz, 1 H, 3-H), 8.03 (dd, *J* = 1.2, 6.6 Hz, 1 H, 6-H). − ^{13}C NMR (50 MHz, CD_3OD): δ = 116.6, 127.5, 133.7, 139.7, 167.6. − **2d** (M = Cs): ^{1}H NMR (250 MHz, $[D_6]DMSO$): δ = 6.67 (br. s, 1 H), 6.88 (br. s, 1 H), 7.35 (d, *J* = 7.0 Hz, 1 H), 8.03 (br. s, 1 H). − ^{13}C NMR (50 MHz, $[D_6]DMSO$): δ = 114.5, 125.8, 139.2, 139.3, 174.1. − **2f** (M = NBu_4): ^{1}H NMR (250 MHz): δ = 0.95 (t, *J* = 7.3 Hz, 12 H, CH_3), 1.32 (sext, *J* = 7.3 Hz, 8 H, CH_2), 1.59 (m, 8 H, CH_2), 3.22 (m_c, 8 H, CH_2), 6.39 (dt, J_d = 2.1 Hz, J_t = 7.0 Hz, 1 H, 5-H), 6.54 (dt, J_d = 1.8 Hz, J_t = 8.2 Hz, 1 H, 4-H), 7.23 (dd, *J* = 1.8, 7.9 Hz, 1 H, 6-H), 7.76 (dd, *J* = 1.2, 6.4 Hz, 1 H, 3-H). − ^{13}C NMR (63 MHz): δ = 20.3, 26.1, 29.9, 64.4, 119.6, 127.5, 138.0, 144.8, 175.0. − **2g** (M = Sr/2): ^{1}H NMR (250 MHz, $[D_6]DMSO$): δ = 6.63 (dt, J_d = 2.1 Hz, J_t = 7.0 Hz, 1 H, 5-H), 6.88 (t, *J* = 7.3 Hz, 1 H, 5-H), 7.34 (dd, *J* = 1.8, 8.2 Hz, 1 H, 3-H), 8.01 (d, *J* = 6.4 Hz, 1 H, 6-H). − ^{13}C NMR (63 MHz, $[D_6]DMSO$): δ = 115.2, 128.0, 131.9, 138.8, 167.5. − **2h** (M = Ba/2): ^{1}H NMR (250 MHz, D_2O): δ = 6.84 (dt, J_d = 1.8 Hz, J_t = 7.0 Hz, 1 H, 5-H), 7.10 (m_c, 1 H, 4-H), 7.49 (dd, *J* = 1.8, 8.4 Hz, 1 H, 3-H), 7.96 (dd, *J* = 1.2, 6.7 Hz, 1 H, 6-H). − ^{13}C NMR (63 MHz, D_2O): δ = 119.2, 130.7, 134.2, 140.3, 165.1.

***O*-Ethyl *S*-[2-(*p*-Methylphenyl)-2-oximinoethyl] Dithiocarbonate:** At 0°C, a solution of 2-bromo-*p*-methylacetophenone oxime[31] (7.74 g, 33.9 mmol) in acetone (50 mL) was added dropwise to a solution of potassium *O*-ethyl dithiocarbonate (5.98 g, 37.3 mmol) in acetone (38 mL). The reaction mixture was stirred for 6 h at 20°C and the resulting precipitate was removed by suction and washed with acetone (2 × 20 mL). The combined filtrate and washings were concentrated in vacuo. The residual yellow solid was dissolved in diethyl ether, the solution was washed with an equivalent volume of water, and then dried ($MgSO_4$). The ether was removed in vacuo to afford *O*-ethyl *S*-[2-(*p*-methylphenyl)-2-oximinoethyl] dithiocarbonate as a yellow powder (8.01 g, 88%), which was sufficiently pure for the subsequent synthesis of thiazolethione **5**. An analytical sample was recrystallized from toluene/*n*-pentane, m.p. 105−109°C. − IR (CCl_4): ṽ = 3590 cm^{-1}, 3296, 2928, 1640, 1610, 1548, 1517, 1445, 1219, 1114, 1051. − ^{1}H NMR (250 MHz): δ = 1.39 (t, *J* = 7.3 Hz, 3 H, CH_3), 2.37 (s, 3 H, $ArCH_3$), 4.51 (s, CH_2S), 4.65 (q, *J* = 7.3 Hz, 2 H, OCH_2), 7.20 (m_c, 2 H, Ar-H), 7.59 (m_c, 2 H, Ar-H). − ^{13}C NMR (100 MHz): δ = 13.7, 21.4, 29.8, 70.4, 126.2, 128.1, 129.4, 140.0, 154.0, 213.6. − MS (70 eV, EI); *m/z* (%): 269 (3) [M^+], 252 (43) [M^+ − OH], 208 (17) [$C_{10}H_{10}NS_2^+$], 163 (100) [$C_9H_9NS^+$], 148 (23) [$C_9H_8S^+$], 118 (81) [$C_8H_8N^+$], 91 (53) [$C_7H_7^+$]. − $C_{12}H_{15}NO_2S_2$ (269.4): calcd. C 53.50, H 5.61, N 5.20, S 23.80; found C 53.24, H 5.63, N 5.21, S 23.66.

***N*-Hydroxy-4-(*p*-methylphenyl)thiazole-2(3*H*)-thione (5):** At 20°C, anhydrous $ZnCl_2$ (2.54 g, 18.6 mmol) was added to a solution of *O*-ethyl *S*-[2-(*p*-methylphenyl)-2-oximinoethyl] dithiocarbonate (1.66 g, 6.20 mmol) in diethyl ether (6 mL) and the resulting dark-brown reaction mixture was stirred for 14 h at 20°C. At the end of this period, the mixture had solidified. The flask was then immersed in an ice bath and the contents were treated dropwise with dilute aqueous HCl (prepared from 2.6 mL of conc. HCl and 2 mL of H_2O), whereupon the precipitate dissolved. The resulting brown solution was stirred for 1 h at 0°C and the newly formed precipitate was collected by suction, washed with cold diethyl ether (2 × 2 mL), and dried in vacuo to afford 1.03 g (74%) of thione **5** as a greenish-yellow solid. An analytical sample was recrystallized from methanol, 164 ± 2°C dec. (DTA). − IR (CCl_4): ṽ = 3296 cm^{-1}, 2927, 2855, 1640, 1552, 1512, 1498, 1357, 1298, 1220, 1166, 1062. − UV/Vis (EtOH): λ_{max} (lg ε) = 309 nm (4.10), 240 (4.17). − ^{1}H NMR (250 MHz): δ = 2.42 (s, 3 H, $ArCH_3$), 6.64 (s, 1 H, 5-H), 7.29 (m_c, 2 H, Ar-H), 7.52 (m_c, 2 H, Ar-H), 10.03 (br. s, 1 H, OH). − ^{13}C NMR (100 MHz, $[D_6]DMSO$): δ = 20.6, 104.8, 125.8, 127.9, 128.8, 138.9, 141.3, 178.9. − MS (70 eV, EI); *m/z* (%): 223 (63) [M^+], 207 (25) [M^+ − O], 206 (11) [M^+ − OH], 148 (100) [$C_9H_8S^+$], 147 (30) [$C_9H_7S^+$], 119 (15) [$C_8H_9N^+$], 91 (13) [$C_7H_7^+$]. − $C_{10}H_9NOS_2$ (223.31): calcd. C 53.78, H 4.06, N 6.27, S 28.72; found C 53.96, H 4.02, N 6.17, S 28.76.

***N*-Hydroxy-4-methylthiazole-2(3*H*)-thione Tetraethylammonium Salt (6):** A round-bottomed flask was charged with *N*-hydroxy-4-methylthiazole-2(3*H*)-thione (**3**) (2.36 g, 16.0 mmol) and tetraethylammonium hydroxide (10.7 mL of a 1.5 M solution in methanol, 16.0 mmol). After stirring for 30 min, the solvent was removed in vacuo and the residue was freeze-dried (3 d, 10^{-3} mbar) to afford the thiohydroxamate salt in quantitative yield. − UV/Vis: λ_{max} (lg ε) = 231 (4.07), 317 (4.06). − ^{1}H NMR (400 MHz): δ = 1.11 (t, *J* = 7.4 Hz, 12 H, CH_3), 2.00 (s, 3 H, CH_3), 3.15 (q, *J* = 7.4 Hz, 8 H, CH_2), 5.95 (s, 1 H, 5-H). − ^{13}C NMR (100 MHz, $[D_6]DMSO$): δ = 7.0, 14.2, 51.4, 99.8, 141.8, 161.7. − MS (DCI; NH_3); *m/z* (%): 277 (48) [M^+], 261 (16) [M^+ − O], 130 (22) [NEt_4^+].

***N*-Hydroxy-4-(*p*-methylphenyl)thiazole-2(3*H*)-thione Tetraethylammonium Salt (8):** A solution of NEt_4OH in MeOH (Fluka 1.5 M; 1.4 mL, 2.09 mmol) was diluted with reagent-grade MeOH (15 mL) and treated with thiazolethione **5** (470 mg, 2.09 mmol). The resulting brown solution was stirred for 1 h at 20°C and then concentrated in vacuo. The residue was freeze-dried (3 d, 10^{-3} mbar) to afford the salt **8** in quantitative yield as a tan-colored hygroscopic powder. − IR (Nujol): ṽ = 1640 cm^{-1}, 1605, 1550, 1377, 1299, 1248, 1218, 1173, 1044. − UV/Vis (EtOH): λ_{max} (lg ε) = 295 nm (3.73), 260 (4.02). − ^{1}H NMR (200 MHz): δ = 1.14 (t, *J* = 7.2 Hz, 12 H, CH_3), 2.32 (s, 3 H, $ArCH_3$), 3.21 (q, *J* = 7.2 Hz, 8 H, NCH_2), 6.40 (s, 1 H, 5-H), 7.08 (m_c, 2 H, Ar-H), 7.66 (m_c, 2 H, Ar-H). − ^{13}C NMR (50 MHz, $CDCl_3/[D_6]DMSO$): δ = 6.7, 20.4, 51.5, 102.3, 127.0, 128.0, 137.2, 143.0, 162.1.

Alkylation of *N*-(Hydroxy)pyridine-2(1*H*)-thione Salts 2[13] **with *n*-Pentyl Tosylate**[19,32] was performed as described previously.[5]

***N*-(1-Pentoxy)pyridine-2(1*H*)-thione (12):** Yellow oil. − IR: ṽ = 2959 cm^{-1}, 2874, 1960, 1847, 1609, 1525, 1446, 1410, 1226, 1177, 1134. − UV/Vis: λ_{max} (lg ε) = 361 nm (3.71), 289 (4.08). − ^{1}H NMR (200 MHz): δ = 0.84 (t, *J* = 6.8 Hz, 3 H, CH_3), 1.28−1.46 (m, 4 H, CH_2), 1.67−1.81 (m, 2 H, CH_2), 4.32 (t, *J* = 6.8 Hz, 2 H, O-CH_2), 6.55 (td, J_d = 1.8 Hz, J_t = 6.7 Hz, 1 H, 4-H), 7.06 (td, J_d = 1.7 Hz, J_t = 6.8 Hz, 1 H, 5-H), 7.55 (dd, *J* = 1.8, 8.7 Hz, 1 H, 3-H), 7.69 (dd, *J* = 1.7, 6.9 Hz, 1 H, 6-H). − ^{13}C NMR (50 MHz): δ = 13.7, 22.2, 27.1, 27.6, 76.4, 113.1, 132.7, 137.7, 137.9, 175.5. − MS (70 eV, EI); *m/z* (%): 197 (11) [M^+], 127 (100) [M^+ − C_5H_{10}]. − $C_{10}H_{15}NOS$ (197.3): calcd. C 60.88, H 7.66, N 7.10, S. 16.25; found C 60.54, H 7.41, N 7.17, S 16.50.

2-(1-Pentylsulfanyl)pyridine *N*-Oxide (13): Colorless, block-shaped crystals (petroleum ether/CH_2Cl_2), m.p. 58−59°C. − ^1H NMR (250 MHz): δ = 0.87 (t, J = 7.0 Hz, 3 H, CH_3), 1.22−1.50 (m, 4 H, CH_2), 1.73 (quint, J = 7.6 Hz, 2 H, CH_2), 2.84 (t, J = 7.3 Hz, 2 H, CH_2S), 6.99 (m_c, 1 H, CH), 7.08 (dd, J = 1.8, 8.2 Hz, 1 H, 3-H), 7.20 (ddd, J = 1.2, 7.3, 8.5 Hz, 1 H, 4-H), 8.20 (dd, J = 0.9, 6.1 Hz, 1 H, 6-H). − ^{13}C NMR (50 MHz): δ = 14.3, 22.7, 28.1, 30.9, 31.5, 120.5, 121.7, 126.1, 139.2, 153.2. − MS (70 eV, EI); *m/z* (%): 197 (5) [M^+ − OH], 127 (100) [$C_5H_5NOS^+$], 112 (79) [$C_5H_6NS^+$]. − $C_{10}H_{15}NOS$ (197.3): calcd. C 60.88, H 7.66, N 7.10, S 16.25; found C 60.34, H 8.02, N 7.04, S 15.99.

Synthesis of Thiohydroxamic Acid *O*-Esters by Phase-Transfer Alkylation. − General Procedure: Cyclic thiohydroxamic acid **1** (5.00 mmol) or **3**−**5** (2.00 mmol) was dissolved in anhydrous CH_3CN (10 mL for **1**, 4 mL for **3**−**5**). K_2CO_3 (2.08 g, 15.0 mmol for **1**; 830 mg, 7.50 mmol fo **3**−**5**) and NBu_4HSO_4 (170 mg, 0.50 mmol for **1**; 68.0 mg, 0.20 mmol for **3**−**5**) were added at 20°C and the slurry was stirred (750 min^{-1}) for 15 min. The alkylating reagent [3.90 mmol for **1**, 1.56 mmol for **3**−**5**; neat] was then added and the reaction mixture, which remained a viscous slurry, was stirred for 24−48 h at 20°C in the dark. The pale-yellow (pyridinethione) or dark-orange to brown (thiazolethiones) reaction mixture was subsequently diluted with water (25 mL) and extracted with *tert*-butyl methyl ether (MTB, 3 × 25 mL) or with diethyl ether (thiones **11**, **20**−**28**). The combined organic phases were washed with 2 N aqueous NaOH solution, dried ($MgSO_4$), and concentrated in vacuo to afford an orange to brown oil, which was purified by column chromatography [SiO_2, MTB for pyridinethione **12**, **14**−**19** diethyl ether for **11**, **20**−**21**, R_f = 0.3−0.6, yellow spots; SiO_2, CH_2Cl_2 for thiazolethiones **22**−**28**, R_f = 0.3−0.5].

***N*-(2-Methyl-2-propen-1-oxy)pyridine-2(1*H*)-thione (14):** Yield: 42.4 mg (6%), yellow crystals, m.p. 54 ± 2°C, dec. 130 ± 2°C (DTA). − IR: $\tilde{\nu}$ = 3060 cm^{-1}, 3020, 2960, 2940, 1590, 1510, 1440, 1400, 1360, 1270, 1220, 1170, 1120. − ^1H NMR (400 MHz): δ = 1.95 (s, 3 H, CH_3), 4.85 (s, 2 H, 1-H), 5.09 (s, 1 H, 3-H), 5.10 (s, 1 H, 3-H), 6.56 (ddd, J = 1.8, 6.8, 7.0 Hz, 1 H, CH), 7.14 (ddd, J = 1.5, 6.8, 7.0 Hz, 1 H, CH), 7.65−7.67 (m, 2 H, CH). − ^{13}C NMR (100 MHz): δ = 20.1, 79.9, 112.6, 118.4, 132.7, 138.1, 138.4, 175.8. − MS (70 eV, EI); *m/z* (%): 164 (7) [M^+ − OH], 111 (50) [$C_5H_5NS^+$], 78 (33) [$C_5H_4N^+$]. − $C_9H_{11}NOS$ (181.3): calcd. C 59.64, H 6.12, N 7.73, S 17.69; found C 59.80, H 6.18, N 7.59, S 17.38.

***N*-(3,7-Dimethyl-2,6-octadien-1-oxy)pyridine-2(1*H*)-thione (15):** Yield: 51.4 mg (5%), yellow oil. − IR: $\tilde{\nu}$ = 3040 cm^{-1}, 2940, 2900, 2840, 1650, 1460, 1430, 1400, 1370, 1240, 1210, 1130, 1080. − ^1H NMR (400 MHz): δ = 1.58 (d, J = 1.1 Hz, 3 H, CH_3), 1.63 (d, J = 1.3 Hz, 3 H, CH_3), 1.67 (s, 3 H, CH_3), 2.03−2.10 (m, 4 H, 4-H, 5-H), 5.00 (d, J = 8.3 Hz, 2 H, 1-H), 4.99−5.09 (m, 1 H, 6-H), 5.47 (dt, J_d = 1.1 Hz, J_t = 8.3 Hz, 1 H, 2-H), 6.53 (ddd, J = 1.8, 6.8, 7.0 Hz, 1 H, CH), 7.12 (ddd, J = 1.7, 6.8, 7.0 Hz, 1 H, CH), 7.60−7.67 (m, 2 H, CH). − ^{13}C NMR (100 MHz): δ = 16.6, 17.7, 25.6, 26.1, 39.6, 71.7, 112.2, 115.8, 123.5, 132.0, 132.7, 137.8, 139.3, 148.4, 175.8. − MS (70 eV, EI); *m/z* (%): 111 (10) [$C_5H_5NS^+$], 81 (43) [$C_6H_{11}^+$]. − $C_{15}H_{21}NOS$ (263.4): calcd. C 68.40, H 8.04, N 5.32, S 12.17; found C 68.36, H 8.12, N 4.98, S 11.83.

***N*-(2,3,4,6-Tetra-*O*-acetyl-β-D-glucopyranosyl)pyridine-2(1*H*)-thione (19)** was prepared by application of the general phase-transfer protocol (see above). The reaction mixture was stirred for 24 h at 20°C. Upon addition of water (10 mL), the salts were dissolved and the bulk of **19** precipitated as a yellowish solid, which was removed by suction. The filtrate was extracted as described in the general procedure. The combined yellow residue and precipitate of **19** were purified by column chromatography (SiO_2, acetone, R_f = 0.8). Yield: 999 mg (56%), yellow crystals, dec. 151 ± 2°C (DTA). − IR: $\tilde{\nu}$ = 3100 cm^{-1}, 3000, 2920, 2880, 1740, 1720, 1700, 1590, 1460, 1400, 1350, 1230, 1200, 1130. − ^1H NMR (200 MHz): δ = 2.01 (s, 9 H, CH_3), 2.17 (s, 3 H, CH_3), 3.69 (m_c, 1 H, 5-H), 4.08 (dd, J = 2.4, 12.4 Hz, 1 H, 6-H), 4.26 (dd, J = 5.0, 12.4 Hz, 1 H, 6-H), 5.09 (dd, J = 9.4, 10.1 Hz, 1 H, 4-H), 5.22 (dd, J = 8.1, 9.7 Hz, 1 H, 2-H), 5.35 (dd, J = 9.4, 9.6 Hz, 1 H, 3-H), 5.68 (d, J = 8.1 Hz, 1 H, 1-H), 6.50 (dt, J_d = 1.9 Hz, J_t = 6.9 Hz, 1 H, CH), 7.12 (dt, J_d = 1.6 Hz, J_t = 6.8 Hz, 1 H, CH), 7.62 (dd, J = 1.9, 8.8 Hz, 1 H, CH), 7.75 (dd, J = 1.7, 7.1 Hz, 1 H, CH). − ^{13}C NMR (50 MHz): δ = 20.5, 20.6, 21.0, 61.2, 68.1, 69.2, 71.9, 72.3, 101.6, 111.6, 133.2, 137.8, 140.7, 169.3, 169.7, 169.9, 170.2, 175.6. − MS (70 eV, EI); *m/z* (%): 220 (1) [$C_{10}H_8N_2S_2^+$], 111 (10) [$C_5H_5NS^+$], 43 (100) [$C_2H_3O^+$]. − $C_{19}H_{23}NO_{10}S$ (457.5): calcd. C 49.88, H 5.07, N 3.06, S 7.01; found C 49.85, H 5.26, N 2.71, S 6.43.

***N*-(1-Pentoxy)-4-methylthiazole-2(3*H*)-thione (20):** Yield: 278 mg (82%), brown oil. − IR: $\tilde{\nu}$ = 3060 cm^{-1}, 2920, 2900, 2840, 1580, 1450, 1430, 1370, 1300, 1170, 1130, 1010. − ^1H NMR (250 MHz): δ = 0.92 (t, J = 7.1 Hz, 3 H, 5-H), 1.33−1.50 (m, 4 H, 3-H, 4-H), 1.82 (m_c, 2 H, 2-H), 2.27 (d, J = 1.2 Hz, 3 H, CH_3), 4.38 (t, J = 6.7 Hz, 2 H, 1-H), 6.15 (q, J = 1.2 Hz, 1 H, 5′-H). − ^{13}C NMR (100 MHz): δ = 13.4, 13.8, 22.4, 27.5, 27.8, 76.3, 102.6, 137.7, 180.5. − MS (70 eV, EI); *m/z* (%): 217 (19) [M^+], 147 (38) [$C_4H_5NOS_2^+$], 131 (100) [$C_4H_5NS_2^+$], 86 (40) [$C_5H_{10}O^+$], 71 (34) [$C_5H_{11}^+$]. − $C_9H_{15}NOS_2$ (217.4): calcd. C 49.73, H 6.96, N 6.44, S 29.50; found C 50.04, H 7.01, N 6.34, S 29.39.

***N*-(Cyclopentoxy)-4-methylthiazole-2(3*H*)-thione (11):** Yield: 292 mg (87%), brown oil. − IR: $\tilde{\nu}$ = 3060 cm^{-1}, 2940, 2840, 1580, 1420, 1290, 1160, 1130. − ^1H NMR (250 MHz): δ = 1.62−1.67 (m, 2 H, CH_2), 1.79−1.89 (m, 6 H, CH_2), 2.23 (d, J = 1.2 Hz, 3 H, CH_3), 5.74 (m_c, 1 H, 1-H), 6.16 (q, J = 1.2 Hz, 1 H, 5′-H). − ^{13}C NMR (100 MHz): δ = 13.9, 23.8, 31.3, 88.8, 102.8, 138.8, 180.9. − MS (70 eV, EI); *m/z* (%): 215 (2) [M^+], 131 (100) [$C_4H_5NS_2^+$], 86 (13) [$C_5H_{10}O^+$]. − $C_9H_{13}NOS_2$ (215.3): calcd. C 50.20, H 6.08, N 6.50, S 29.78; found C 50.50, H 6.24, N 6.42, S 29.56.

4-Methyl-*N*-(1-phenyl-1-ethoxy)thiazole-2(3*H*)-thione (21): Yield: 298 mg (76%), tan-colored crystals, m.p. 70 ± 2°C, dec. 119 ± 2°C (DTA). − IR: $\tilde{\nu}$ = 3060 cm^{-1}, 3000, 2960, 1570, 1440, 1360, 1290, 1200, 1150, 1120, 1070. − ^1H NMR (250 MHz): δ = 1.56 (d, J = 1.2 Hz, 3 H, CH_3), 1.78 (d, J = 6.7 Hz, 3 H, 2-H), 5.94 (q, J = 1.2 Hz, 1 H, 5′-H), 6.29 (q, J = 6.7 Hz, 1 H, 1-H), 7.34−7.37 (m, 5 H, Ar-H). − ^{13}C NMR (100 MHz): δ = 13.4, 18.0, 82.3, 101.9, 128.3, 128.6, 129.5, 138.0, 139.2, 180.6. − MS (70 eV, EI); *m/z* (%): 251 (2) [M^+], 147 (36) [$C_4H_5NOS_2^+$], 131 (32) [$C_4H_5NS_2^+$], 105 (100) [$C_8H_9^+$], 77 (32) [$C_6H_5^+$]. − $C_{12}H_{13}NOS_2$ (251.4): calcd. C 57.34, H 5.21, N 5.57, S 25.51; found C 57.72, H 5.39, N 5.47, S 25.81.

4-(*p*-Chlorophenyl)-*N*-(2-methyl-2-propen-1-oxy)thiazole-2(3*H*)-thione (23): Yield: 163 mg (35%), m.p. 92 ± 2°C, colorless solid, R_f = 0.36 (CH_2Cl_2). − IR: $\tilde{\nu}$ = 3310 cm^{-1}, 3112, 3083, 2983, 2944, 2875, 1640, 1482, 1305, 1296, 1213, 1168. − ^1H NMR (250 MHz): δ = 1.60 (dd, J = 0.9, 1.5 Hz, 3 H, CH_3), 4.52 (s, 2 H, 1′-H), 4.93 (m_c, 1 H, 3′-H), 4.97 (quint, J = 1.5 Hz, 1 H, 3′-H), 6.50 (s, 1 H, 5-H), 7.44 (m_c, 2 H, Ar-H), 7.53 (m_c, 2 H, Ar-H). − ^{13}C NMR (63 MHz): δ = 20.0, 79.6, 105.2, 118.6, 126.7, 129.1, 129.8, 136.2, 137.7, 140.2, 180.6. − MS (70 eV, EI); *m/z* (%): 297 (12) [M^+], 227 (85) [M^+ − C_4H_6O], 168 (100) [$C_8H_5ClS^+$]. − $C_{13}H_{12}ClNOS_2$ (297.8): calcd. C 52.43, H 4.06, N 4.70, S 21.53; found C 52.50, H 4.16, N 4.69, S 21.38.

***N*-(Benzyloxy)-4-(*p*-chlorophenyl)thiazole-2(3*H*)-thione (24):** Yield: 188 mg (36%), dec. 120 ± 2°C, colorless solid, R_f = 0.47 (CH_2Cl_2).

Table 8. Crystallographic data for thiohydroxamic acids **1** and **5**[a]

	1	**5**
empirical formula	C_5H_5NOS	$C_{10}H_9NOS_2$
formula weight	127.17	223.32
temperature [K]	293(2)	300(2)
wavelength [Å]	0.71093	0.71093
crystal system	monoclinic	orthorhombic
space group	*P*21/*n*	*Pbca*
a [Å]	6.2990(6)	7.329(1)
b [Å]	8.0270(10)	11.694(3)
c [Å]	11.711(2)	23.180(5)
β [°]	91.540(10)	90
V [Å^3]	591.92(14)	1986.6(7)
Z	4	8
$\rho_{calcd.}$ [g cm^{-3}]	1.427	1.493
μ [mm^{-1}]	0.418	0.474
F (000)	264	928
Crystal size [mm]	0.88 × 0.20 × 0.15	0.88 × 0.65 × 0.08
θ range [°]	3.08−22.97	1.76−23.14
Index ranges	$-6 \le h \le 1$ $-8 \le k \le 0$ $-12 \le l \le 12$	$-8 \le h \le 8$ $-12 \le k \le 1$ $-25 \le l \le 1$
Reflections collected	1023	3098
Independent reflections	818	1387
Data/restraints/parameters	818/0/88	1386/0/146
Goodness-of-fit on F^2	1.056	1.072
Final *R* indices [$I > 2\sigma(I)$]	$R1 = 0.0390$, $wR2 = 0.1021$	$R1 = 0.0390$, $wR2 = 0.1166$
R indices (all data)	$R1 = 0.0508$, $wR2 = 0.1126$	$R1 = 0.0423$, $wR2 = 0.1216$
Largest diff. peak and hole [e Å^{-3}]	0.224, −0.235	0.434, −0.255

[a] All data were collected with an Enraf-Nonius CAD4 four-circle diffractometer using Mo-K_α radiation. No absorption corrections were applied. The structures were solved with SHELXS-86[34] and refined with SHELXL-93.[35] All hydrogen atoms were positioned geometrically. Thermal ellipsoids graphics were obtained from Xtal 3.2.[36]

− IR: ṽ = 3296 cm^{-1}, 3069, 3039, 2946, 2864, 1637, 1483, 1305, 1295, 1213, 1164. − ^{1}H NMR (200 MHz): δ = 5.08 (s, 1 H, 1′-H), 6.34 (s, 1 H, 5-H), 7.00−7.30 (m, 9 H, Ar-H). − ^{13}C NMR (63 MHz): δ = 77.4, 104.8, 126.7, 128.5, 128.8, 129.5, 129.6, 130.4, 132.2, 135.9, 140.6, 180.6. − MS (70 eV, EI); *m/z* (%): 333 (2) [M^+], 227 (25), 168 (21) [$C_8H_5ClS^+$], 105 (69), 77 (100) [$C_7H_7^+$]. − $C_{16}H_{12}ClNOS_2$ (333.9): calcd. C 57.56, H 3.62, N 4.20, S 19.21; found C 57.32, H 3.69, S 4.09, N 18.95.

4-(*p*-Methylphenyl)-*N*-(1-pentoxy)thiazole-2(3*H*)-thione (26): Yield: 178 mg (39%), colorless crystals, m.p. 50 ± 2°C (DTA). − IR: ṽ = 3031 cm^{-1}, 2959, 2931, 2873, 1504, 1466, 1380, 1332, 1313, 1302, 1219, 1208, 1168, 1056. − UV/Vis: λ_{max} (lg ε) = 318 nm (4.11), 236 (4.10). − ^{1}H NMR (200 MHz): δ = 0.79 (t, *J* = 6.7 Hz, 3 H, 5-H), 1.29 (m_c, 4 H, CH_2), 1.59 (m_c, 2 H, CH_2), 2.41 (s, 3 H, CH_3), 4.05 (t, *J* = 6.7 Hz, 2 H, 1-H), 6.46 (s, 1 H, 5′-H), 7.23 (m_c, 2 H, Ar-H), 7.48 (m_c, 2 H, Ar-H). − ^{13}C NMR (63 MHz): δ = 13.8, 21.4, 22.2, 27.3, 27.6, 76.2, 104.4, 125.4, 128.2, 129.4, 140.2, 141.3, 180.5. − MS (70 eV, EI); *m/z* (%): 293 (21) [M^+], 223 (10) [$M^+ - C_5H_{10}$], 207 (75) [$M^+ - C_5H_{10}O$], 148 (100) [$C_9H_8S^+$], 44 (39) [$C_3H_8^+$], 41 (50) [$C_3H_5^+$]. − $C_{15}H_{19}NOS_2$ (293.5): calcd. C 61.39, H 6.53, N 4.77, S 21.85; found C 61.70, H 6.69, N 4.70, S 22.06.

4-(*p*-Methylphenyl)-*N*-(2-propoxy)thiazole-2(3*H*)-thione (27): Yield: 290 mg (70%), colorless crystals, m.p. 77 ± 2°C (DTA). − IR: ṽ = 3300 cm^{-1}, 3102, 3026, 2981, 2863, 1637, 1558, 1465, 1382, 1312, 1299, 1219, 1208, 1168, 1148, 1102. − UV/Vis: λ_{max} (lg ε) = 319 nm (4.15), 237 (4.16). − ^{1}H NMR (200 MHz): δ = 1.04 (d, *J* = 6.3 Hz, 6 H, 2-H), 2.41 (s, 3 H, CH_3), 5.03 (sept, *J* = 6.3 Hz, 1 H, 1-H), 6.46 (s, 1 H, 5′-H), 7.26 (m_c, 2 H, Ar-H), 7.45 (m_c, 2 H, Ar-H). − ^{13}C NMR (63 MHz): δ = 21.2, 21.4, 79.3, 104.3, 126.2, 128.4, 129.4, 139.9, 142.7, 181.1. − MS (70 eV, EI); *m/z* (%): 265 (8) [M^+], 207 (33) [$M^+ - C_3H_6O$], 148 (58) [$C_9H_8S^+$], 45 (100) [$C_2H_5O^+$], 43 (23) [$C_3H_7^+$]. − $C_{13}H_{15}NOS_2$ (265.4): calcd. C 58.83, H 5.70, N 5.28, S 24.16; found C 59.11, H 5.75, N 5.24, S 24.09.

4-(*p*-Methylphenyl)-*N*-(1-phenyl-1-ethoxy)thiazole-2(3*H*)-thione (28): Yield: 358 mg (70%); colorless crystals, m.p. 92 ± 2°C (DTA). − UV/Vis: λ_{max} (lg ε) = 320 nm (4.07), 240 (4.04). − IR: ṽ = 3302 cm^{-1}, 3116, 3006, 3034, 2981, 2935, 2868, 1640, 1505, 1458, 1338, 1312, 1300, 1218, 1166, 1119. − ^{1}H NMR (400 MHz): δ = 1.50 (d, *J* = 6.6 Hz, 3 H, CH_3), 2.40 (s, 3 H, CH_3), 6.14 (q, *J* = 6.6 Hz, 1 H, 1-H), 6.21 (s, 1 H, 5-H), 6.90−7.24 (m, 9 H, Ar-H). − ^{13}C NMR (100 MHz): δ = 18.4, 21.3, 82.5, 103.6, 126.2, 128.1, 128.2, 128.4, 128.9, 137.1, 139.4, 142.9, 180.7. − MS (70 eV, EI); *m/z* (%): 327 (2) [M^+], 223 (30) [$M^+ - C_8H_8$], 207 (41) [$M^+ - C_8H_8O$], 148 (38) [$C_9H_8S^+$], 120 (12) [$C_8H_8O^+$], 105 (100) [$C_7H_5O^+$], 91 (8) [$CH_7H_7^+$], 77 (42) [$C_6H_5^+$]. − $C_{18}H_{17}NOS_2$ (327.5): calcd. C 66.02, H 5.23, N 4.28, S 19.58; found C 66.16, H 5.17, N 4.28, S 19.49.

X-ray Structural Analysis of 1 and 5:[33] Suitable crystals of thiones **1** and **5** were obtained by slowly cooling saturated solutions of **1** in ethanol and **5** in methanol. For details see Table 8.

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[1] For reviews on thiohydroxamate chemistry, see ref.[1a]: [1a] W. Walter, E. Schaumann, *Synthesis* **1971**, 111−130. − [1b] D. Crich, L. Quintero, *Chem. Rev.* **1989**, *89*, 1413−1432.

[2] A. L. J. Beckwith, B. P. Hay, *J. Am. Chem. Soc.* **1988**, *110*, 4415−4416.

[3] [3a] A. L. J. Beckwith, B. P. Hay, *J. Am. Chem. Soc.* **1989**, *111*, 230−234. − [3b] B. P. Hay, A. L. J. Beckwith, *J. Org. Chem.* **1988**, *53*, 4330−4334.

[4] For recent applications of alkoxyl radicals in synthesis, see: [4a] J. Hartung, F. Gallou, *J. Org. Chem.* **1995**, *60*, 6706−6716. − [4b] A. Goosen, C. W. McCleland, F. C. Rinaldi, *J. Chem. Soc., Perkin Trans. 2* **1993**, 279−287. − [4c] D. H. R. Barton, J. Cs. Jaszberenyi, A. I. Morrell, *Tetrahedron Lett.* **1991**, *32*, 311−314. − [4d] M. Newcomb, M. U. Kumar, J. Boivin, E. Crépon, S. Z. Zard, *Tetrahedron Lett.* **1991**, *32*, 45−48. − [4e] A. L. J. Beckwith, I. G. E. Davison, *Tetrahedron Lett.* **1991**, *32*, 49−52. − [4f] G. Pattenden, C. W. Ellwood, *Tetrahedron Lett.* **1991**, *32*, 1591−1594. − [4g] C. G. Francisco, R. Freire, C. C. González, E. Súarez, *Tetrahedron: Asymmetry* **1997**, *8*, 1971−1974. − [4h] Y. Guindon, R. C. Denis, *Tetrahedron Lett.* **1998**, *39*, 339−342.

[5] J. Hartung, M. Hiller, P. Schmidt, *Chem. Eur. J.* **1996**, *2*, 1014−1023.

[6] J. Hartung, M. Hiller, P. Schmidt, *Liebigs Ann.* **1996**, 1425−1436.

[7] [7a] B. Giese, *Radicals in Organic Synthesis: Formation of Carbon−Carbon Bonds*, Pergamon Press, Oxford, **1986**. − [7b] D. H. R. Barton, S. I. Parekh, *Half a Century of Free Radical Chemistry*, Cambridge University Press, Cambridge, **1993**.

[8] J. L. Esker, M. Newcomb, *Adv. Heterocycl. Chem.* **1993**, *58*, 1−45.

[9] J. Hartung, *Synlett* **1996**, 1206−1209.

[10] D. H. R. Barton, M. Samadi, *Tetrahedron* **1992**, *48*, 7083−7090.

[11] [11a] J. Hartung, M. Schwarz, *Synlett* **1997**, 848−850. − [11b] J. Hartung, M. Schwarz, *Synlett* **1997**, 1116.

[12] M. Newcomb, T. M. Deeb, D. J. Marquardt, *Tetrahedron* **1990**, *46*, 2137−2328.

[13] [13a] E. N. Shaw, J. Bernstein, U.S. Pat. U.S. 23, 686,786; *Chem. Abstr.* **1955**, *49*, 11025. – [13b] T. Hara, T. Hida, T. Shibatsuji, K. Hirano, JP 02,105,841 [90,105,841]; *Chem. Abstr.* **1990**, *113*, 98842a.

[14] [14a] D. H. R. Barton, D. Crich, G. Kretzschmar, *J. Chem. Soc., Perkins Trans. 1* **1986**, 39−53. – [14b] 4-Methylthiazole-2(3*H*)-thione-derived carbamates have been successfully employed as aminyl radical precursors: M. Newcomb, K. A. Weber, *J. Org. Chem.* **1991**, *56*, 1309−1313.

[15] J. Hartung, M. Hiller, M. Schwarz, I. Svoboda, H. Fueß, *Liebigs Ann.* **1996**, 2091−2097.

[16] A. R. Katritzky, R. A. Jones, *J. Chem. Soc.* **1960**, 2937−2942.

[17] Strong IR bands (C=S stretching mode, $\tilde{\nu}$ = 1130−1200 cm^{-1}) were used in earlier works to assign thione structures to cyclic thiohydroxamic acids.[16] However, this absorption is likely to be attributable to a coupling of N−O and C−S vibrational modes. Thus, IR spectra are probably of little diagnostic value for the determination of C−S bond orders in thiohydroxamic acids. For example, the C−S bond in *N*-(hydroxy)pyridine-4(1*H*)-thione measures 1.718(2) Å, which is a typical value for a carbon−sulfur single bond. Nevertheless, thiohydroxamate absorptions are observed in the IR spectrum of this compound (KBr and CCl$_4$) at 1195 cm^{-1}: J. Hartung, I. Svoboda, M. T. Duarte, *Acta Crystallogr.* **1997**, *C53*, 1631−1634.

[18] [18a] I. Flemming, *Grenzorbitale und Reaktionen organischer Verbindungen*, VCH Weinheim, **1988**, pp. 41−100. – [18b] J. Pearson, *J. Chem. Educ.* **1968**, *45*, 581−587. – [18c] J. Pearson, *J. Chem. Educ.* **1968**, *45*, 643−648. – [18d] T.-L. Ho, *Chem. Rev.* **1975**, *75*, 1−20. – [18e] P. G. Parr, R. G. Pearson, *J. Am. Chem. Soc.* **1983**, *105*, 7512−7516.

[19] J. Hartung, S. Hünig, R. Kneuer, M. Schwarz, H. Wenner, *Synthesis* **1997**, 1433−1438.

[20] H.-O. Kalinowski, S. Berger, S. Braun, ^{13}C-NMR-Spektroskopie, Georg Thieme Verlag, Stuttgart, **1984**, pp. 370−380.

[21] D. R. Brown, D. X. West, *J. Inorg. Nucl. Chem.* **1981**, *43*, 1017−1021.

[22] J. L. Davidson, P. N. Preston, M. V. Russo, *J. Chem. Soc., Dalton Trans.* **1983**, 783−786.

[23] DMPU is short for **D**i**m**ethyl**p**ropylene**u**rea, [IUPAC: 1,3-dimethyltetrahydro-2(1*H*)-pyrimidine]. All attempts to use hygroscopic DMPU as a cosolvent, e.g. with CH$_3$CN or with DMSO, led to the same yields of **12** as those obtained in the corresponding pure solvents, i.e. in the absence of DMPU.

[24] Y. Marcus, *Chem. Soc. Rev.* **1993**, *22*, 409−416.

[25] [25a] M. Makosza, M. Fedorynski, *Polish J. Chem.* **1996**, *70*, 1093−1110. – [25b] M. Makosza, M. Fedorynski, *Adv. Catalysis* **1987**, *35*, 375−422. – [25c] E. V. Dehmlow, S. S. Dehmlow, *Phase Transfer Catalysis*, 3rd ed., VCH, Weinheim, **1993**.

[26] According to TLC analysis, 2-(alkylsulfanyl)pyridine *N*-oxides, e.g. **13** (R_f = 0.0 in *tert*-butyl methyl ether and 0.6 in acetone on SiO$_2$ plates) were formed as side products. No attempts to quantify the amounts of these compounds were undertaken.

[27] Attempted phase-transfer alkylations of *p*-chlorophenylthiazolethione with *tert*-butyl halides were unfortunately not successful.

[28] D. D. Perrin, W. L. F. Armarego, D. R. Perrin, *Purification of Laboratory Chemicals*, 2nd ed., Pergamon Press, Oxford, **1980**.

[29] A. M. Ward, *J. Chem. Soc.* **1927**, *129*, 445−458.

[30] Salts **2** need to be freeze-dried, even when prepared in anhydrous ethanol as solvent.

[31] [31a] H. Korten, R. Scholl, *Ber. Dtsch. Chem. Ges.* **1901**, *34*, 1907. – [31b] M. Masaki, K. Futeni, M. Ohta, *J. Org. Chem.* **1967**, *32*, 3564−3568.

[32] Autorenkollektiv, *Organikum*, 16th ed., VEB Deutscher Verlag der Wissenschaften, Berlin, **1986**, p. 559.

[33] Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publications no. CCDC-101814 (**1**) and -101815 (**5**). Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, U.K. [Fax: (internat.) + 44-1223/336033; E-mail: deposit@ccdc.cam.ac.uk].

[34] G. M. Sheldrick, *SHELXS-86*, *Program for the Solution of Crystal Structures*, Universität Göttingen, **1986**.

[35] G. M. Sheldrick, *SHELXL-93*, *Program for the Refinement of Crystal Structures*, Universität Göttingen, **1993**.

[36] S. R. Hall, H. D. Flack, J. M. Stewart, *Xtal 3.2*, Universities of Western Australia, Geneva and Maryland, **1992**.

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