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Aspects of structural thiohydroxamate chemistry—on a systematic in the 5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione series

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ABSTRACT

Bond angles at thiohydroxamate oxygen in crystal structures of 3-alkoxy-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thiones gradually increased with the size of the 3-alkoxy substituent. This effect was attributed to strain on the basis of (i) a linear free energy relationship (Taft–Dubois correlation) and (ii) signal coalescence from resonances of diastereotopic CH_3 groups in solution (*O*-cumyl substituent; DNMR). Substitution at oxygen along the sequence OR (R=*prim*-, *sec*-, and *tert*-alkyl), OH, and OLi was reflected in a gradual decrease of N,O distances and lengthening of associated C,S bonds. The responsivity for these changes was more pronounced in the thiazole-2(3*H*)-thione than in the pyridine-2(1*H*)-thione series.

1. Introduction

Structural thiohydroxamate chemistry so far is dominated by studies on transition metal complexes.[1,2] Considerably less is known about thiohydroxamic acid solid state chemistry[3,4] and systematics within series of *O*-alkyl- (esters)[5,6] and *O*-acyl-derivatives (mixed anhydrides).[7] This lack in structural information makes it difficult to convincingly answer long standing questions, for example, on the origin of inherent problems in tertiary *O*-ester synthesis,[8,15] or rationalization of notable changes in alkylation selectivity that occur upon rather subtle structural changes in heterocyclic thiohydroxamate subunits,[9,10] although major aspects of this chemistry in the fields of biocides,[11,12,13,14] organic reagents,[15,16] and radical reactions[9,17,18] have been pursued for decades.[1,5,7]

Based on recent progress in the synthesis of primary, secondary, and even tertiary *O*-esters of the cyclic thiohydroxamic acid 3-hydroxy-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione (**1a**) (Fig. 1),[10,19,20] structural thiohydroxamate chemistry began to attract our attention. The compounds (e.g., **1b**–**f**) (Fig. 1) are applied as valuable alkoxyl radical precursors under neutral pH and non-oxidative conditions. Alkali salts (e.g., **2**; Fig. 1) of acid **1a** form non-hygroscopic crystalline solids that serve as starting materials for the synthesis of *O*-acyl derivatives (e.g., **1g**).[21] The latter compounds constitute a potential new class of carbon radical progenitors, to be stored and applied on demand.

The present study dealing with solid state chemistry of *N*-oxy-substituted thiazole-2(3*H*)-thiones (**1**, **2**) and their more prominent pyridine-2(1*H*)-thione congeners (e.g., **3**, **4**) (Fig. 1) now showed that steric effects exerted by *O*-alkyl groups were predominantly reflected by N–O–R angle widening. Variation of substitution at oxygen along the sequence OR (R=*prim*-, *sec*-, *tert*-alkyl), OH, and OLi was paralleled by a gradual decrease in N,O bond lengths, while thiohydroxamate C,S distances increased. The exocyclic C,S-connectivity was in favor for a double bond in chelated *N*-(hydroxy)-thiazole-2(3*H*)-thione-derived lithium salt **2**B but close to the value for a sulfanyl group for pyridine-2(1*H*)-thione analogue **3**. Observed systematics are summarized and discussed in the following sections.

2. Results and interpretation

2.1. Preparation of *N*-(alkoxy)thiazole-2(3*H*)-thiones

Primary and secondary *N*-(alkoxy)thiazolethiones **1b**–**e** were prepared from 3-hydroxy-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione tetrabutylammonium salt and corresponding alkyl

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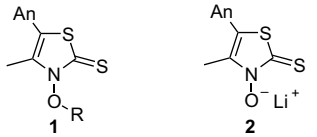
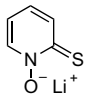


1	R
a	H
b	CH_3
c	$(CH_2)_4CH_3$
d	$(CH_2)_4C_6H_5$
e	$CH(CH_3)_2$
f	$C(CH_3)_2C_6H_5$
g	$C(O)C_6H_5$



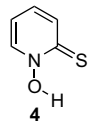


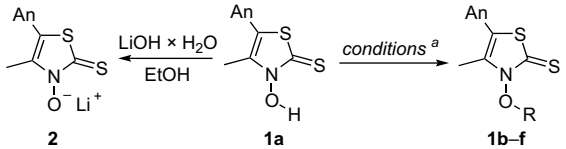
Figure 1. Structural formulae and indexing of cyclic thiohydroxamates **1**–**4** (An=*p*-$MeOC_6H_4$).[10,21,22]

tosylates in solutions of dry DMF (Table 1).[22] The yields of target compounds increased along the series of introduced *O*-alkyl groups $(CH_2)_4C_6H_5$ (**1d**)<CH_3 (**1b**)<*n*-C_5H_{11} (**1c**)<$CH(CH_3)_2$ (**1e**)[10] (Table 1, entries 1–5) thus reflecting the propensity of secondary alkyl tosylates to afford most effective substitution at oxygen in thiohydroxamates.[23] *N*-Cumyloxythiazolethione **1f** was obtained in gram quantities upon treatment of acid **1a** with in situ prepared *O*-cumyl *N*,*N*′-diisopropylisourea[20,24–26] in a solution of CH_2Cl_2. The reaction between LiOH×H_2O and *N*-(hydroxy)thiazole-2(3*H*)-thione **1a** in a solution of EtOH afforded lithium salt **2** in quantitative yield as yellowish non-hygroscopic powder (Table 1, entry 6).

Thiones **1** were characterized via NMR spectroscopy showing diagnostic resonances at ~2.3 ppm for the 4-CH_3 singlet and at ~3.8 ppm for the *p*-OCH_3 group. The former signal in *N*-cumyloxy derivative **1f** was high field-shifted (1.57 ppm), presumably due to its proximity to the phenyl group (see also Fig. 4). The low field shift experienced by α-alkoxy protons (e.g., in **1b**–**e**) (Table 1, entries 1–4) and to some extend by β-protons (e.g., in **1c**–**f**) (Table 1, entries 3–5) was attributed to anisotropy exerted by the thiocarbonyl group.[3,27,28] Resonances of thiohydroxamate C atoms showed a gradual low field shift in going from Li salt **2** (165.5 ppm) to *O*-esters **1b**–**f** (178.9±0.3 ppm).

A broad singlet at δ=2.04 pointed to slow topomerization of diastereotopic CH_3 groups in *N*-cumyloxythiazolethione **1f** at 25 °C (Fig. 2). The associated ^{13}C NMR signal surprisingly was not

Table 1
Yields and selected spectral properties of *N*-(alkoxy)thiazolethiones **1**



Entry	Compound	Conditions[a]	Yield (%)	$\delta_{C=S}$[b]	δ $^1H^{\alpha}$ (ppm[c])	δ $^1H^{\beta}$ (ppm[c])
1	**1b**	i, ii	64	178.6	4.20	—[d]
2	**1c**	i, ii	71	179.1	4.45	—[e]
3	**1d**	i, ii	44	179.1	4.45	2.72
4	**1e**	i, ii	73	179.1	5.50	1.36
5	**1f**	iii	15	179.2	—[d]	2.60
6	**2**	—	Quant.	165.5	—[d]	—[d]

[a] Reagents and conditions: i: NBu_4OH, CH_3OH; ii: TsOR, DMF, 25 °C; iii: 2-phenyl-2-propanol, diisopropylcarbodiimide (DIC), CuCl, CH_2Cl_2, 25 °C, then **1a**.
[b] In $CDCl_3$; $\delta_{C=S}$=172.0 for **1a** and 182.3 for **1g**.
[c] In $CDCl_3$; O–CH^{α}; O–C–CH^{β}.
[d] Not available.
[e] Not resolved.

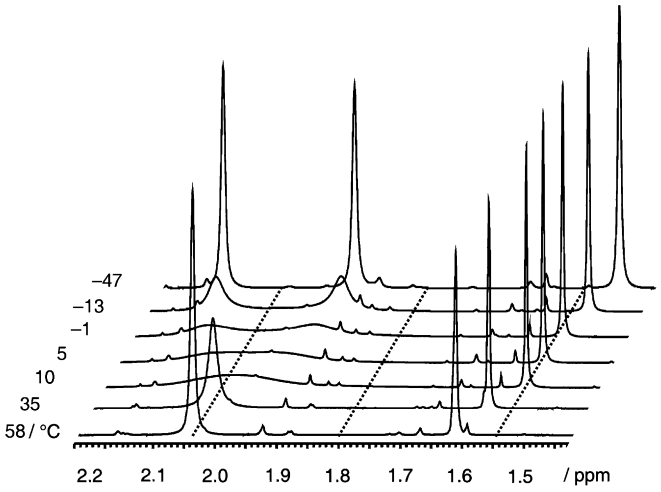


Figure 2. ^1H NMR spectra (stacking plot, $CDCl_3$) of *N*-cumyloxythiazolethione **1f** in the temperature range of −47 to +58 °C showing coalescence of cumyl CH_3 signals at 5 °C (left) and shifting of 4-CH_3 signal (right).

observed at that temperature. At −47 °C (referenced vs the MeOH NMR thermometer),[29,30] base line separated signals for CH_3 resonances were observed at δ_H=1.90 and 2.12, being correlated with ^{13}C NMR resonances at 22.4 and 31.8 ppm (HMQC). Signal coalescence (^1H NMR) occurred at 5 °C. A sharp singlet at δ=2.04 due to fast CH_3-exchange was observed at 58 °C. The associated ^{13}C NMR signal at 27.6 ppm remained surprisingly low in intensity. Attempts to further elevate the temperature for increasing its magnitude were paralleled by decomposition of **1f**, as evident from α-methyl styrene formation.[31] The observed temperature effects were interpreted as hindered rotation of the cumyl substituent about the stereogenic N,O axis in **1f**. The approximated free energy of activation derived from coalescence temperature and $\Delta\nu_i$ values for this process ($\Delta G^{\ddagger}_{278}$=44 kJ mol^{-1}) was comparable to barriers derived from line shape analysis (variable temperature NMR) for *N*-isopropoxy-4-methyl- and -4-(*p*-chlorophenyl)-substituted thiazolethiones ($\Delta G^{\ddagger}_{200}$=42–46 kJ mol^{-1}).[6]

Lowest energy UV–vis absorptions (EtOH or MeOH) remained almost unchanged in going from *N*-methoxy compound **1b** via *N*-cumyloxy derivative **1f** (both λ_{max}=333 nm) to Li salt **2** (λ_{max}=335), pointing to similar chromophores. Macroscopic appearance of the compounds varied from colorless (**1a**,**b**,**d**) to yellowish (**1c**,**f**, **2**).

2.2. X-ray crystallography—*N*-oxy-substituted thiazole-2(3*H*)-thiones

X-ray diffraction experiments were conducted at 100 K (**2**) and in the range of 293–299 K (**1b**–**f**) (Table 2, entry 1). Selected bond lengths, bond and torsion angles are listed in Tables 2 and 3.

N-Methoxythiazolethione **1b** (Fig. 3) crystallized in acentric space group $Pna2_1$. Thiones **1c**–**f** and **2** (Figs. 3 and 4) formed centrosymmetric crystal lattices. Absolute structure determination of **1b** was feasible with the aid of the Flack parameter.[32] The two independent molecules of **1b**, i.e., **1b**A and **1b**B, showed almost similar bond lengths and angles. Molecule **1b**A was arbitrarily selected for presentation and data analysis. Both molecules of **1b** exhibited (*P*)-configuration at the N,O-bond,[33] whereas **1c**–**f** were racemic. The angle C2–N3–O1–C14 describing the offset of the ester substituent from the thiazole-2(3*H*)-thione plane was approximately independent of steric size of the alkyl group attached to oxygen (88±5°; Table 3, entry 9). In a similar manner, a comparatively small variation of torsion angle C4–C5–C7–C8 (42±5°), reflecting the twist between *p*-methoxyphenyl and thiazolethione planes, was noted (Table 3, entry 10, Fig. 3).

Table 2
Selected parameters of *N*-substituted thiazole-2(3*H*)-thiones **1b–f** and lithium salt **2**—part I: heterocycle core

Entry	Parameter	**1b**A R=CH_3	**1c** R=*n*-C_5H_{11}	**1d** R=$(CH_2)_4Ph$	**1e** R=$CH(CH_3)_2$	**1f** R=CMe_2Ph	**2**A (monodentate)	**2**B (bidentate)
1	*T* [K]	293(2)	299(2)	299(2)	299(2)	293(2)	100(2)	100(2)
2	S1–C2 [Å]	1.731(3)	1.717(6)	1.726(2)	1.728(2)	1.726(3)	1.738(2)	1.742(2)
3	C2–N3 [Å]	1.339(4)	1.343(6)	1.346(3)	1.357(3)	1.359(3)	1.345(2)	1.345(2)
4	N3–C4 [Å]	1.400(4)	1.394(6)	1.401(3)	1.402(3)	1.405(3)	1.409(2)	1.401(2)
5	C4–C5 [Å]	1.339(4)	1.355(6)	1.351(3)	1.347(3)	1.347(4)	1.366(2)	1.357(2)
6	C5–S1 [Å]	1.741(3)	1.741(5)	1.748(2)	1.748(2)	1.740(3)	1.752(2)	1.753(2)
7	S1–C2–N3 [°]	105.7(2)	107.0(4)	106.7(2)	106.4(2)	106.6(2)	108.5(2)	108.1(1)
8	C2–N3–C4 [°]	120.0(3)	118.4(4)	118.7(2)	118.6(2)	118.4(2)	117.0(1)	117.1(1)
9	N3–C4–C5 [°]	109.8(3)	111.1(4)	110.9(2)	110.9(2)	110.3(3)	111.4(2)	112.0(2)
10	C4–C5–S1 [°]	111.1(2)	109.8(4)	110.1(2)	110.5(2)	111.3(2)	110.3(1)	110.2(1)
11	C5–S1–C2 [°]	93.3(2)	93.6(2)	93.5(1)	93.5(1)	93.3(1)	92.6(1)	92.5(1)

Lithium salt **2** crystallized as monohydrate in space group *C*2/*c*. Layers of 5-(4-methoxyphenyl)-4-methyl-2-thiooxo-2,3-dihydrothiazole-3-olate were composed of two independent molecules, i.e., **2**A and **2**B, which formed coordination polymers due to Li-bridging and an extensive array of H-atom bonds originating from metal-coordinated aqua ligands (Fig. 4). The distance Li1⋯S2=3.625(4) Å was equivalent to the sum of associated van der Waals radii [3.62 Å][34] thus pointing to monodentate thiohydroxamate binding to Li1 in molecule **2**A [Li1⋯O1=1.926(3) Å]. Chelating of Li1′ by the thiohydroxamate ligand occurred in **2**B [Li1′⋯S2′=2.649(3) Å, Li1′⋯O1′=2.098(3) Å].

2.2.1. The heterocyclic core

Endocyclic bond lengths (Table 2, entries 2–6) and angles in *N*-alkoxy compounds **1b–f** and lithium salt **2** (Table 2, entries 7–11) corresponded to parameters reported for *N*-alkyl-substituted thiazole-2(3*H*)-thiones,[35,36] cyclic conjugated thioureas,[37] and cyclic dithiocarbonic acid amides.[38,39] Compared to the structure of 1,3-thiazole,[40] thiazole-2(3*H*)-thiones showed a more acute bond angle at C2, a larger at N3, and more pronounced alternation of bond lengths, probably due to less extensive cyclic conjugation.

2.2.2. The thiohydroxamte functionality in thiazole-2(3H)-thiones

N3–O2–C14 bond angles (Table 3, entry 3) gradually increased with the steric size of the alkyl substituent at oxygen in *N*-alkoxythiazolethiones **1b–f**. Geometric changes were linearly reflected in a correlation with Taft–Dubois parameters[41–43] E_S' of associated ester substituents (Fig. 5). The E_S' value for the cumyl group thereby was approximated with the corresponding parameter of the *tert*-butyl substituent. The use of alternative parameters, for instance the Winstein–Holness *A*-value for 1,3-interactions in cyclohexanes,[44,45] or the solid angle Ω_S for description of minimum steric substituent effects,[46] provided less satisfactory correlations (not shown). This analysis suggested that the magnitude of the N–O–C bond angle in cyclic thiohydroxamic acid *O*-esters was guided by strain, experienced by substituents in molecular environments of restricted conformational flexibility.

Exocyclic bond lengths (Table 3, entries 1 and 2) showed a gradual decrease of the N3–O1 distance along the sequence of *O*-alkyl derivatives **1b–f**, thiohydroxamic acid **1a**, and lithium salt **2**. These changes were paralleled by C2–S2 lengthening as evident from the relationship $d_{N3-O1}=-0.66d_{C2-S2}+2.5$ Å (correlation coefficient $r=0.87$; Fig. 6). The distance C2–N3 remained approximately unchanged. Gradient and intercept were surprisingly similar to a N3–O1/C2–S2 correlation using structural data of *N*-alkoxy-4-(*p*-chlorophenyl)thiazole-2(3*H*)-thiones (primary and secondary esters, 6 examples), *N*-hydroxy-4-(*p*-chlorophenyl)thiazole-2(3*H*)-thione, and sodium 4-(4-chlorophenyl)-2-thiooxo-2,3-dihydrothiazole-3-olate ($d_{N3-O1}=-0.69d_{C2-S2}+2.5$ Å; $r=0.71$, not shown).[33,47–49]

2.3. *N*-Oxy-substituted pyridine-2(1*H*)-thiones

In order to test the generality of the N3–O1/C2–S2-systematic, lithium salt **3** was prepared from *N*-(hydroxy)pyridine-2(1*H*)-thione (**4**),[23] crystallized, and investigated via X-ray diffraction (Fig. 7). The compound crystallized in $P2_1/m$. The metal was chelated by the 2-thiooxo-1,2-dihydropyridine-1-olate ligand [Li1–O1=1.930(6) Å, Li1–S1=2.431(5) Å]. One water molecule was attached to the fourth site of Li1. It participated in H-atom bonding toward O1 and S1 of two non-identical proximate molecules of **3** (not shown).

A plot of N1–O1 bond lengths of salt **3**, corresponding acid **4**,[23] *N*-[4-*trans*-(*tert*-butylcyclohexyl-1-oxy)]pyridine-2(1*H*)-thione (**5**),[3] and *N*-[4-*trans*-(*tert*-butylcyclohexyl-1-carbonyloxy)]pyridine-2(1*H*)-thione (**6**)[3] (the latter two compounds are not shown) against associated C2–S1 distances were fitted with a first order equation thus providing the correlation $d_{N1-O1}=-0.48d_{C2-S1}+2.2$ Å ($r=0.98$) (Fig. 8).

2.4. Comparison between thiazole-2(3*H*)-thiones and pyridine-2(1*H*)-thiones

Major structural differences between *N*-(Hydroxy)thiazole-2(3*H*)-thiones (e.g. **1**a) and *N*-(hydroxy)pyridin-2(1*H*)-thione (**4**)

Table 3
Selected parameters of *N*-substituted thiazole-2(3*H*)-thiones **1b–f** and lithium salt **2**—part II: substituents

Entry	Parameter	**1bA** R=CH_3	**1c** R=*n*-C_5H_{11}	**1d** R=$(CH_2)_4Ph$	**1e** R=$CH(CH_3)_2$	**1f** R=CMe_2Ph	**2**A Li (monodentate)	**2**B Li (bidentate)
1	C2–S2 [Å]	1.650(3)	1.671(7)	1.663(3)	1.657(2)	1.649(3)	1.701(2)	1.685(2)
2	N3–O1 [Å]	1.391(3)	1.370(6)	1.381(2)	1.389(2)	1.376(3)	1.354(2)	1.367(2)
3	N3–O1–R [°]	110.7(3)	111.0(4)	112.0(2)	112.4 (2)	116.0(2)	123.9(1)	119.8(1)
4	C4–N3–O1 [°]	119.1(3)	120.0(4)	119.4(2)	120.6(2)	120.8(2)	120.2(1)	120.9(1)
5	C2–N3–O1 [°]	120.1(3)	121.0(4)	120.9(2)	120.1(2)	120.1(2)	122.8(1)	121.9(1)
6	S2–C2–N3 [°]	128.5(3)	127.0(4)	127.7(2)	128.1(2)	128.4(2)	128.0(1)	125.8(1)
7	S1–C2–S2 [°]	125.8(2)	125.9(3)	125.6(2)	125.5(1)	125.0(2)	123.5(1)	126.0(1)
8	N3–C4–C6 [°]	119.4(3)	119.0(4)	118.7(2)	119.4(2)	120.4(3)	117.6(1)	117.9(1)
9	C2–N3–O1–R [°]	89.3(4)	−90.4(5)	83.4(3)	81.4(2)	95.7(3)	−63.0(2)	104.9(2)
10	C4–C5–C7–C8 [°]	44.5(5)	−44.3(7)	−37.2(4)	38.0(3)	49.9(5)	−31.4(3)	−39.7(3)

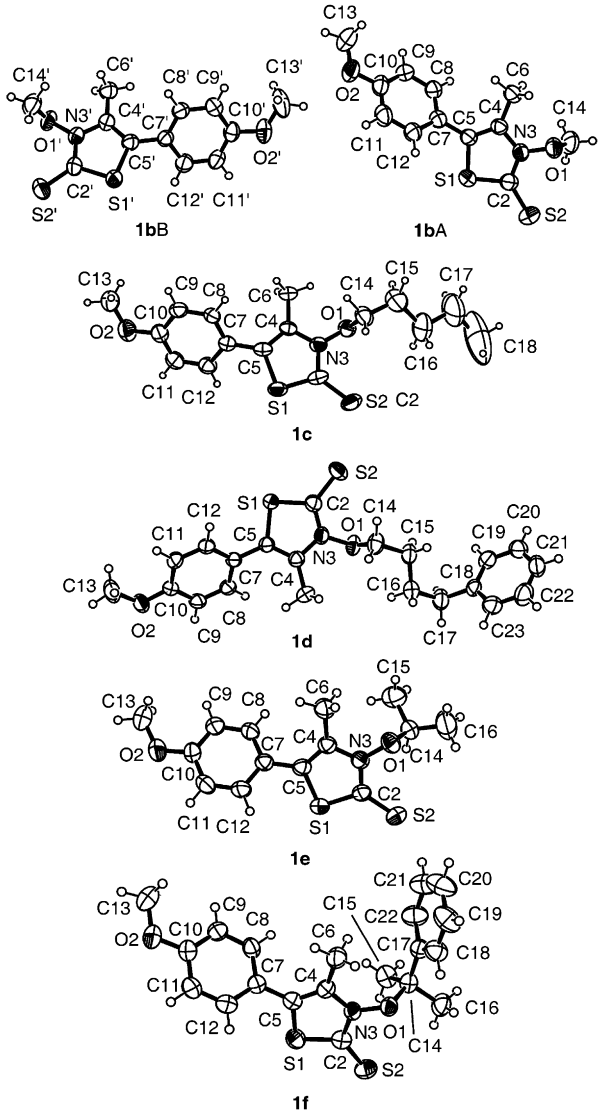


Figure 3. Ellipsoid graphics (50% probability level) of *N*-(alkoxy)thiazolethiones **1b–f**. Hydrogen atoms are drawn as circles of an arbitrary radius.

differed in structural responsivity upon variation of the thiohydroxamate oxygen-bound substituent.

The stronger gradient of inverse N,O/C,S-bond length correlations pointed to a more pronounced responsivity of *N*-oxy-substituted thiazole-2(3*H*)-thiones upon substitution at oxygen than in the pyridine-2(1*H*)-thione series (Figs. 6 and 8). This

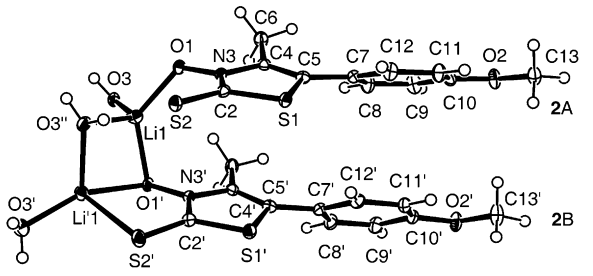


Figure 4. Ellipsoid graphics (50% probability level) of lithium 5-(4-methoxyphenyl)-4-methyl-2-thiooxo-2,3-dihydrothiazole-3-olate monohydrate (**2**)×H_2O. Hydrogen atoms are drawn as circles of an arbitrary radius.

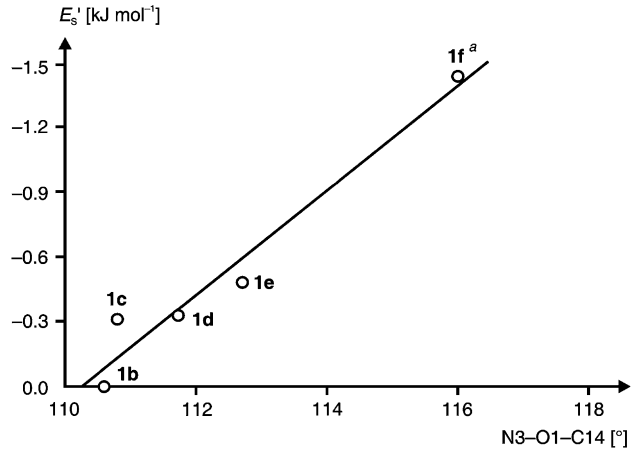


Figure 5. Correlation of N3–O1–C14 angles and Taft–Dubois parameter[41–43] E_S' [kJ mol^{-1}] (correlation coefficient r=0.98). E_S' for the cumyl group was approximated with the value for the *tert*-butyl substituent.

observation suggested that strain imposed by sterically demanding substituents at thiohydroxamate oxygen, for instance from a tertiary alkyl group, should be more effectively compensated by structural parameter variation in the former than in the latter type of cyclic thiohydroxamic acid *O*-ester. This interpretation offers a possible explanation for the diverse chemistry of tertiary *O*-esters in the thiazole-2(3*H*)-thione series,[10,20,24,31] which in turn is rather limited for *N*-(hydroxy)pyridine-2(1*H*)-thione (**4**).[3,9]

The N,O-distance shortening seemed to be correlated with the propensity of substituents attached to oxygen to withdraw negative charge. The most pronounced effect was observed for Li and least for alkyl groups, leaving the hydrogen atom in between. The N,O bond in *N*-cumylthiazolethione **1f** would have been expected to be the longest, since steric congestion added to polar contributions from the substituent. The value of N3–O1=1.376(3) Å, however, was located at the lower end of N,O distances for alkyl substitution (Fig. 6). From the unusual C14–O1 distance in **1f** [1.512(3) Å, compared to 1.434(4) Å for **1b**] and a noteworthy deshielding at C14 (92.6 ppm, compared to 64.1 for **1b**) it seemed that additional parameter existed that contributed to exact data point positioning in N,O/C,S-bond length correlation diagrams. Clarification of these aspects was not possible on the basis of the existing data and therefore deserves a separate computational analysis.

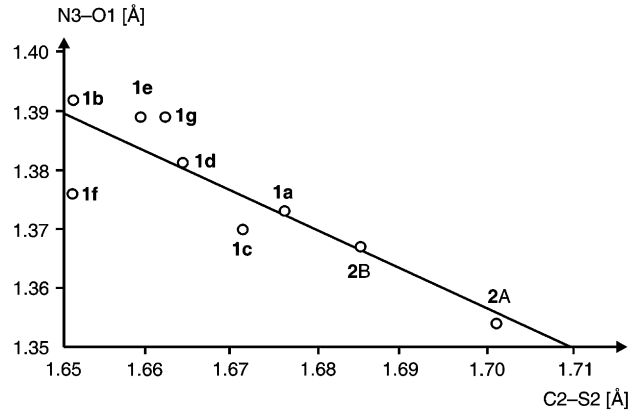
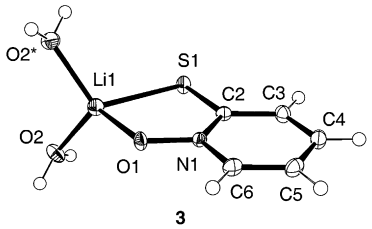


Figure 6. Correlation of N3–O1 and C2–C2 distances of thiazolethiones **1a** [N3–O1=1.373(3) Å, C2–S2=1.676(3) Å at 299(2) K],[22] **1b–f** (Table 1), and *N*-benzoyl-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione **1g** [N3–O1=1.389(2) Å, C2–S2=1.662(2) Å at 100(2) K][21] (d_{N3-O1}=−0.66 d_{C2-S2}+2.5 Å; r=0.87).



3

Figure 7. Ellipsoid graphics (50% probability level) of lithium 2-thiooxo-1,2-dihydropyridine-1-olate monohydrate (**3**) [100(2) K, symmetry code for O2*: x, $-y+1/2$, z]. Hydrogen atoms are drawn as circles of an arbitrary radius. Selected bond lengths [Å]: C2–S1=1.723(3), N1–O1=1.360(3), N1–C2=1.371(4), C2–C3=1.416(4), C3–C4=1.376(4), C4–C5=1.399(4), C5–C6=1.367(4), C6–N1=1.365(4). Selected angles [°]: N1–O1–Li1=121.2(2), C2–N1–O1=120.3(2), C6–N1–O1=117.1(2), S1–C2–N1=120.1(2), S1–C2–C3=123.4(2), N1–C2–C3=116.6(3), C2–C3–C4=121.4(3), C3–C4–C5=119.6(3), C4–C5–C6=119.1(3), C5–C6–N1=120.8(3), C6–N1–C2=122.6(3), C2–N1–O1–Li1=0.0(2).

The distance C2–S2 in thiazolethione **2**B [chelating, 1.685(2) Å] was closer to the mean value of a thiocarbonyl group, whereas distance C2–S1 in pyridinethione **3** [chelating, 1.723(3) Å] approximately agreed with the mean value for a Csp^2, S-single bond, e.g., in 2-alkylsulfanylpyridine-*N*-oxides.[50,51] If interpreted in terms of charge distribution, a major fraction of the negative charge was expected to be localized at thiohydroxamate oxygen in thiazole derivative **2**B and at sulfur in pyridine analogue **3**. Hard electrophiles therefore should favor substitution of, e.g., *p*-toluenesulfonate for thiohydroxamate at oxygen, if derivatives of thiazole-2(3*H*)-thione served as ambident nucleophile. Structure and bonding of pyridinethione-derived lithium salt **3** suggested that thiohydroxamate alkylation should occur to notable extend at sulfur, even if treated with a hard alkylating reagent. These interpretations are consistent with experimental findings.[23,31,52] Since bond lengths in the present work showed a marked dependency on the mode of thiohydroxamate binding to lithium, a similar change is expected to occur in case of complete separation of anion and cation, e.g., in solvents of strong donicity. If the trends outlined for thiohydroxamate salts **2**A and **3** prevailed in case of solvation, the present findings offered an explanation for notable differences in alkylation selectivity for the investigated types of thiohydroxamates on a structural basis.

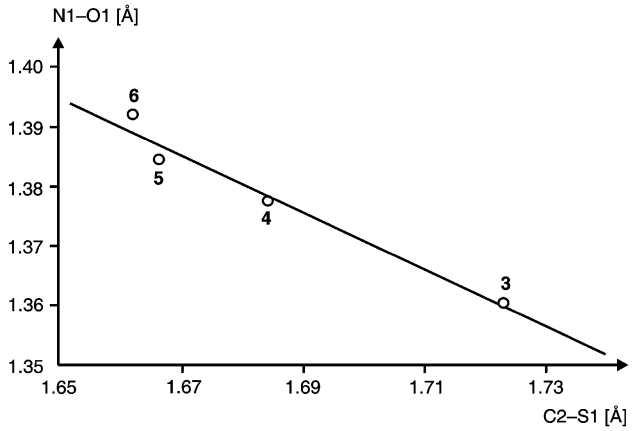


Figure 8. Correlation of N1–O1 and C2–S1 distances of pyridinethione **3** (Fig. 4), *N*-hydroxypyridinethione **4** [N1–O1=1.377(3) Å, C2–S1=1.684(2) Å at 297(2) K],[23] *N*-[4-*trans*-(*tert*-butylcyclohexyl-1-oxy)]pyridine-2(1*H*)-thione **5** [N1–O1=1.384(4) Å, C2–S1=1.666(4) Å at 297(2) K],[3] and *N*-[4-*trans*-(*tert*-butylcyclohexyl-1-carbonyloxy)]pyridine-2(1*H*)-thione **6** [N1–O1=1.392(5) Å, C2–S1=1.662(6) Å at 300(2) K][3] (d_{N1-O1}=−0.48 d_{C2-S1}+2.2 Å; r=0.98).

3. Concluding remarks

The pursuit of structural chemistry in the series of *N*-alkoxy-5-(*p*-methoxyphenyl)-4-methylthiazolethiones **1b–f**, acid **1a**, lithium salt **2** and its pyridinethione congener **3** provided three distinctive results.

(i) Bond angles at thiohydroxamate oxygen gradually increased along the series of substituents CH_3 (**1b**) via primary alkyl (e.g., **1c**,**d**), secondary alkyl (**1e**) to tertiary alkyl (**1f**). The magnitude of angle widening correlated with Taft–Dubois parameter of associated ester substituents thus pointing to strain as major effect.

(ii) In a set of *N*-hydroxy-, *N*-alkoxy-, and *N*-benzoyloxy-substituted compounds **1a–g** and lithium salt **2**, N,O and C,S bond lengths were inversely correlated. The stronger gradient of underlying N,O/C,S relationships upon substitution at exocyclic oxygen pointed to a more pronounced structural responsivity in the thiazole-2(3*H*)-thione than in the pyridine-2(1*H*)-thione series. This aspect is considered to facilitate O-alkylation with sterically demanding, e.g., tertiary substituents in thiazole-2(3*H*)-derived thiohydroxamates.

(iii) Exocyclic C,S-bonds in lithium salts of a *N*-hydroxythiazole-2(3*H*)-thione (compound **2**) and *N*-hydroxypyridine-2(1*H*)-thione (compound **3**) differed notably in length, being in favor for a thione group in the former and a sulfanyl entity in the latter case. If interpreted in terms of charge distribution, this picture correlated with the unusual *O*-selectivity in alkylations of thiazolethione-derived thiohydroxamate salts.

The results outlined in the present study are expected to guide reagent selection, particularly for the synthesis of tertiary thiohydroxamic acid *O*-esters. These compounds serve as valuable sources of derived oxyl radicals and have the potential to further developments in this area of research.

4. Experimental

4.1. General

For spectroscopic equipment and general laboratory practice see Ref. 10. UV–vis spectra: Varian Cary 100 spectrophotometer at 20 °C using analytical grade solvents in 1 cm quartz cuvettes. Single crystal analysis: Xcalibur diffractometer (Oxford Diffraction) equipped with the fine-focus sealed tube and Sapphire CCD detector in φ and ω-scan mode (compounds **1c–e**) and a STOE-IPDS diffractometer (**1b**,**f**). For single crystal data collection of lithium salts **2** and **3**, crystals were placed in pre-mounted cryoloops from Hampton Research. *N*-Hydroxy-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione (**1a**),[10] *N*-methoxy-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione (**1b**),[22] lithium 2-thiooxo-1,2-dihydropyridine-1-olate (**3**),[23] and *N*-hydroxy-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione tetraalkylammonium salt were prepared according to published procedures.[22] Isopropyl *p*-toluenesulfonate, 1-pentyl *p*-toluenesulfonate, and 4-phenyl-1-butyl *p*-toluenesulfonate were prepared according to procedure given in Section 4.2.1.

4.2. Alkyl *para*-toluenesulfonates

4.2.1. General procedure[53]

A solution of an alcohol (2.5 mmol) and 1,4-diazabicyclooctane (5.0 mmol) in CH_2Cl_2 (30 mL) was treated in small portions at 0 °C with *p*-toluenesulfonic acid chloride (3.75 mmol). The slurry was stirred for 2 h at 25 °C and poured into a mixture of *tert*-butyl

methyl ether (TBM)/H_2O [60 mL, 2:1, (v/v)]. The layers were separated. The aqueous phase was extracted with TBM (3×30 mL). Combined organic washings were extracted with aq HCl (2 M), satd aq $NaHCO_3$, and H_2O (20 mL each). The solvent was dried ($MgSO_4$) and removed under reduced pressure. The residue was purified by column chromatography [SiO_2, petroleum ether/Et_2O] to afford analytically pure alkyl tosylates.

4.3. *N*-(Alkoxy)thiazole-2(3*H*)-thiones

4.3.1. General method

A solution of an alkyl tosylate (2.20 mmol) in dry DMF (2 mL) was added to a solution of *N*-(hydroxy)thiazole-2(3*H*)-thione tetraalkylammonium salt (2.20 mmol) in dry DMF (5 mL) in an atmosphere of Ar. The mixture was stirred at 20 °C for 4–6 days in the dark. It was poured into a mixture of H_2O/TBM [60 mL, 2:1 (v/v)]. The phases were separated and the aqueous phase was extracted with MTB (3×20 mL). Combined organic washings were extracted with satd aq $NaHCO_3$ solution and brine (10 mL each). The organic phase was dried ($MgSO_4$) and concentrated under reduced pressure. The residual oil was purified by column chromatography [SiO_2, petroleum ether/Et_2O] or crystallized from petroleum ether/Et_2O to afford *N*-alkoxythiazolethione **1** as colorless to yellowish crystalline solid.

4.3.2. N-(1-Pentoxy)-5-(p-methoxyphenyl)-4-(methyl)thiazole-2(3H)-thione (**1c**)

Yield of 0.80 g (71%) from *N*-(hydroxy)-5-(*p*-methoxyphenyl)-4-(methyl)thiazole-2(3*H*)-thione tetraethylammonium salt [1.33 g (3.48 mmol)] and 1-pentyl *p*-toluenesulfonate [0.84 g (3.48 mmol)], colorless solid, R_f=0.35 [SiO_2, petroleum ether/Et_2O=2:1 (v/v)]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 0.94 (t, J=7.2 Hz, 3H), 1.41 (ddd, J=6.9, 7.7, 14.7 Hz, 2H), 1.53–1.45 (m, 2H), 1.85 (m_c, 2H), 2.32 (s, 3H, CH_3), 3.83 (s, 3H, OCH_3), 4.45 (t, J=6.7 Hz, 2H), 6.94 (m_c, 2H, Ar–H), 7.22 (m_c, 2H, Ar–H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4, 14.3, 22.9, 28.0, 28.2, 55.8 (OCH_3), 76.8, 114.7, 119.7, 123.0, 130.2, 132.6, 160.3, 179.1 (C=S). Anal. Calcd for $C_{16}H_{21}NO_2S_2$: C, 59.41; H, 6.54; N, 4.33; S, 19.82. Found: C, 59.64; H, 6.42; N, 4.34; S, 19.48.

4.3.3. N-(4-Phenyl-1-butoxy)-5-(p-methoxyphenyl)-4-(methyl) thiazole-2(3H)-thione (**1d**)

Yield of 0.45 g (44%) from *N*-(hydroxy)-5-(*p*-methoxyphenyl)-4-(methyl)thiazole-2(3*H*)-thione tetraethylammonium salt [1.01 g (2.65 mmol)] and 4-phenyl-1-butyl *p*-toluenesulfonate [0.81 g (2.65 mmol)], colorless solid, R_f=0.40 [SiO_2, petroleum ether/Et_2O=2:1 (v/v)]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.88 (m_c, 4H), 2.30 (s, 3H, CH_3), 2.72 (t, J=7.1 Hz, 2H), 3.84 (s, 3H, OCH_3), 4.45 (t, J=5.9 Hz, 2H), 6.94 (m_c, 2H, Ar–H), 7.22 (m_c, 2H, Ar–H), 7.18–7.32 (m, 5H, Ph). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4 (CH_3), 27.9, 27.9, 31.3, 55.8 (CH_3O), 76.4, 114.9, 119.7, 122.9, 126.3, 128.7, 128.8, 130.2, 132.5, 142.2, 160.3, 179.1 (C=S). MS (EI) m/z 237 (2), 148 (8), 104 (100), 91 (43). Anal. Calcd for $C_{21}H_{23}NO_2S_2$: C, 65.43; H, 6.02; N, 3.64; S, 16.60. Found: C, 64.85; H, 5.89; N, 3.68; S, 16.35.

4.4. Lithium 5-(4-methoxyphenyl)-4-methyl-2-thiooxo-2, 3-dihydrothiazole-3-olate (2)

A solution of *N*-hydroxythiazolethione **1a** (243 mg, 959 μmol) in EtOH (5 mL) was treated with LiOH×H_2O (40.2 mg, 959 μmol) and stirred for 1 h at 25 h. The reaction mixture was protected with aluminum foil from light. The solvent was removed under reduced pressure (200 mbar, 40 °C) to furnish lithium salt **2** as yellow powder. UV (MeOH) λ_{max} (lg ε/m^2 mol^{-1}) 335 nm (3.15), 251 (3.17). ^{1}H NMR (CD_3OD, 600 MHz) δ 2.30 (s, 3H, 4-CH_3), 3.81 (s, 3H, OCH_3), 6.97 (m_c, 2H, Ar–H), 7.28 (m_c, 2H, Ar–H). ^{13}C NMR (CD_3OD, 150 MHz) δ 13.2 (4-CH_3), 55.8 (OCH_3), 115.4 (Ar–C), 120.1, 125.6, 130.7 (Ar–C), 138.2, 161.0 (Ar–C), 165.5 (2-C).

4.5. X-ray crystallography

4.5.1. N-(Methoxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (**1b**)

Crystals suitable for X-ray diffraction were grown from a satd solution of **1b** in Et_2O. $C_{12}H_{13}NO_2S_2$ (267.35), T=293(2) K, λ=0.71073 Å, orthorhombic, $Pna2_1$, a=13.352(3) Å, b=7.9280(16) Å, c=24.621(5) Å, Z=8, μ=0.397 mm^{-1}, completeness to 2θ=99.7%, goodness-of-fit on F^2=0.780, final R indices [$I>2\sigma(I)$]: R_1=0.0336 and wR_2=0.0648, absolute structure parameter=0.06(7).

4.5.2. N-(Pentoxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (**1c**)

Crystals suitable for X-ray diffraction were grown by slowly allowing petroleum ether to diffuse into a satd solution of **1c** in CH_2Cl_2. $C_{16}H_{21}NO_2S_2$ (323.46), T=299(2) K, λ=0.71073 Å, monoclinic, $C2/c$, a=35.499(1) Å, b=7.844(1) Å, c=13.536(1) Å, β=111.85 (1)°, Z=8, μ=0.308 mm^{-1}, completeness to 2θ=97.4%, goodness-of-fit on F^2=1.060, final R indices [$I>2\sigma(I)$]: R_1=0.0733, wR_2=0.1966.

4.5.3. N-(4-Phenylpent-1-oxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (**1d**)

Crystals suitable for X-ray diffraction were grown by slowly allowing petroleum ether to diffuse into a satd solution of **1d** in CH_2Cl_2. $C_{21}H_{23}NO_2S_2$ (385.52), T=299(2) K, λ=0.71073 Å, monoclinic, $P2_1/c$, a=9.916(1) Å, b=12.725(1) Å, c=16.483(1) Å, β=105.68(1)°, Z=4, μ=0.281 mm^{-1}, completeness to 2θ=99.8%, goodness-of-fit on F^2=1.120, final R indices [$I>2\sigma(I)$]: R_1=0.0472, wR_2=0.1374.

4.5.4. N-(2-Propoxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (**1e**)

Crystals suitable for X-ray diffraction were grown by slowly allowing petroleum ether to diffuse into a satd solution of **1e** in CH_2Cl_2. $C_{14}H_{17}NO_2S_2$ (295.41), T=299(2) K, λ=0.71073 Å, triclinic, $P\bar{1}$, a=7.713(1) Å, b=9.883(1) Å, c=10.781(2) Å, α=87.56(1)°, β=79.13(1)°, γ=70.04(1)°, Z=2, μ=0.348 mm^{-1}, completeness to 2θ=96.5%, goodness-of-fit on F^2=1.059, final R indices [I>2σ(I)]: R_1=0.0364, wR_2=0.0959.

4.5.5. 5-(p-Methoxyphenyl)-4-methyl-3-(1-phenyl-1-methyleth-1-oxy)-thiazole-2(3H)-thione (**1f**)

Crystals suitable for X-ray diffraction were from a satd solution of **1f** in Et_2O. $C_{20}H_{21}NO_2S_2$ (371.50), T=293(2) K, λ=0.71073 Å, monoclinic, $C2/c$, a=22.938(5) Å, b=8.5795(17) Å, c=20.167(4) Å, β=105.76(3)°, Z=8, μ=0.291 mm^{-1}, completeness to 2θ=99.4%, goodness-of-fit on F^2=0.679, final R indices [$I>2\sigma(I)$]: R_1=0.0358, wR_2=0.0655.

4.5.6. Lithium 5-(4-methoxyphenyl)-4-methyl-2-thiooxo-2, 3-dihydrothiazole-3-olate monohydrate (**2**)×H_2O

Crystals suitable for X-ray diffraction were grown from a satd solution of lithium salt **2** in CH_3CN, which was kept in an atmosphere of pentane. $C_{44}H_{50}Li_4N_4O_{13}S_8$ (1127.12), T=100(2) K, λ=0.71073 Å, monoclinic, $C2/c$, a=25.7198(10) Å, b=16.4021(9) Å, c=12.2578(6) Å, β=95.706(4)°, Z=4, μ=0.412 mm^{-1}, completeness to 2θ=99.5%, goodness-of-fit on F^2=1.049, final R indices [$I>2\sigma(I)$]: R_1=0.0284, wR_2=0.0690.

4.5.7. Lithium 2-thiooxo-1,2-dihydropyridine-1-olate monohydrate (**3**)×H_2O

Crystals suitable for X-ray diffraction were grown from a saturated solution of lithium salt **3** in CH_3CN, which was kept in an

atmosphere of pentane. $C_5H_8LiNO_3S$ (169.12), T=100(2) K, λ=0.71073 Å, monoclinic, $P2_1/m$, a=7.5034(11) Å, b=6.9955(8) Å, c=8.1024(13) Å, β=114.554(19)°, Z=2, μ=0.369 mm^{-1}, completeness to 2θ=99.5%, goodness-of-fit on F^2=1.067, final R indices [$I>2\sigma(I)$]: R_1=0.0398, wR_2=0.0957.

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication [**1b** CCDC 708992, **1c** CCDC 708986, **1d** CCDC 708987, **1e** CCDC 708988, **1f** 708991, **2**×H_2O CCDC 708989, **3**×H_2O CCDC 708990]. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: +44 (0)1223 336033 or e-mail: deposit@ccdc.cam.ac.uk).

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References and notes

1. Chmiak, A.; Przychodzen, W.; Rachon, J. *Heteroat. Chem.* **2002**, *13*, 169–194.
2. Bond, A. D.; Jones, W. *J. Chem. Soc., Dalton Trans.* **2001**, 3045–3051.
3. Hartung, J.; Hiller, M.; Schwarz, M.; Svoboda, I.; Fuess, H. *Liebigs Ann. Chem.* **1996**, 2091–2097.
4. Bond, A. D.; Feeder, N.; Teat, S. J.; Jones, W. *Tetrahedron* **2000**, *56*, 6617–6624.
5. Hartung, J.; Gottwald, T.; Špehar, K. *Synthesis* **2002**, 1469–1498.
6. Hartung, J.; Kneuer, R.; Schwarz, M.; Heubes, M. *Eur. J. Org. Chem.* **2001**, 4733–4736.
7. Crich, D.; Quintero, L. *Chem. Rev.* **1989**, *89*, 1413–1432.
8. Hartung, J. *Synlett* **1996**, 1206–1209.
9. Beckwith, A. L. J.; Hay, B. P. *J. Am. Chem. Soc.* **1989**, *111*, 230–234.
10. Hartung, J.; Daniel, K.; Gottwald, T.; Groß, A.; Schneiders, N. *Org. Biomol. Chem.* **2006**, *4*, 2313–2322.
11. Shaw, E. *J. Am. Chem. Soc.* **1949**, *71*, 67–73.
12. Omae, I. *Chem. Rev.* **2003**, *103*, 3431–3488.
13. Turley, P. A.; Fenn, R. J.; Ritter, J. C. *Biofouling* **2000**, *15*, 175–182.
14. Doose, C. A.; Ranke, J.; Stock, F.; Bottin-Weber, U.; Jastorff, B. *Green Chem.* **2004**, *6*, 259–266.
15. Walter, W.; Schaumann, E. *Synthesis* **1971**, 111–130.
16. Bailén, M. A.; Chinchilla, R.; Dodsworth, D. J.; Nájera, C. *J. Org. Chem.* **1999**, *64*, 8936–8939.
17. Barton, D. H. R.; Crich, D.; Kretschmar, G. *J. Chem. Soc., Perkin Trans. 1* **1986**, 39–53.
18. Hartung, J. *Eur. J. Org. Chem.* **2001**, 619–632.
19. Hartung, J.; Gottwald, T.; Špehar, K. *Synlett* **2003**, 227–229.
20. Groß, A.; Schneiders, N.; Gottwald, T.; Daniel, K.; Hartung, J. *Tetrahedron* **2008**, *64*, 10882–10889.
21. Hartung, J.; Altermann, S.; Svoboda, I.; Fuess, H. *Acta Crystallogr.* **2005**, *E61*, o1738–o1740.
22. Hartung, J.; Špehar, K.; Svoboda, I.; Fuess, H.; Arnone, M.; Engels, B. *Eur. J. Org. Chem.* **2005**, 869–881.
23. Hartung, J.; Kneuer, R.; Schwarz, M.; Svoboda, I.; Fuess, H. *Eur. J. Org. Chem.* **1999**, 97–106.
24. Hartung, J.; Schneiders, N.; Bergsträßer, U. *Acta Crystallogr.* **2006**, *E62*, o4713–o4714.
25. Mathias, L. J.; Fuller, W.; Nissen, D.; Goodman, M. *Macromolecules* **1978**, *11*, 534–539.
26. Mathias, L. J. *Synthesis* **1979**, 561–576.
27. Walter, W.; Rueß, K.-P. *Liebigs Ann. Chem.* **1971**, *743*, 167–176.
28. Walter, W.; Schaumann, E.; Paulsen, H. *Liebigs Ann. Chem.* **1969**, *727*, 61–70.
29. Van Geet, A. L. *Anal. Chem.* **1970**, *42*, 679–680.
30. Hansen, E. W. *Anal. Chem.* **1985**, *57*, 2993–2994.
31. Hartung, J.; Schneiders, N.; Gottwald, T. *Tetrahedron Lett.* **2007**, *48*, 6327–6330.
32. Flack, H. D. *Acta Crystallogr.* **1983**, *A39*, 876–881.
33. Hartung, J.; Schwarz, M.; Svoboda, I.; Fuess, H. *Acta Crystallogr.* **2003**, *C59*, 682–684.
34. Bondi, A. *J. Phys. Chem.* **1964**, *68*, 441–452.
35. Estrada, M. D.; López-Castro, A. *Acta Crystallogr.* **1989**, *C45*, 1977–1979.
36. Pèpe, G.; Pierrot, M. *Acta Crystallogr.* **1976**, *B32*, 1321–1325.
37. Schwindinger, W.; Fawcett, T. G.; Potenza, J. A.; Schugar, H. J.; Lalancette, R. A. *Acta Crystallogr.* **1980**, *B36*, 1232–1234.
38. Pèpe, G.; Pierrot, M. *Acta Crystallogr.* **1976**, *B32*, 1317–1320.
39. Hartung, J.; Daniel, K.; Svoboda, I.; Fuess, H. *Acta Crystallogr.* **2005**, *E61*, o1744–o1746.
40. Nygaard, L.; Asmussen, E.; Høg, J. H.; Maheshwari, R. C.; Nielsen, C. H.; Petersen, I. B.; Rastrup-Andersen, J.; Sørensen, G. O. *J. Mol. Struct.* **1971**, *8*, 225–233.
41. Taft, R. W. In *Steric Effects in Organic Chemistry*; Neman, M. S., Ed.; Wiley: New York, NY, 1956; p 556.
42. McPhee, J. A.; Panaye, A.; Dubois, J.-E. *Tetrahedron* **1978**, *34*, 3553–3562.
43. White, D. P.; Anthony, J. C.; Oyefeso, A. *J. Org. Chem.* **1999**, *64*, 7707–7716.
44. Winstein, S.; Holness, N. *J. Am. Chem. Soc.* **1955**, *77*, 5562–5578.
45. Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; Wiley: New York, NY, 1994; Chapter 11.
46. Komatsuzaki, T.; Akai, I.; Sakakibara, K.; Hirota, M. *Tetrahedron* **1992**, *48*, 1539–1556.
47. Hartung, J.; Schwarz, M.; Svoboda, I.; Fuess, H.; Duarte, M.-T. *Eur. J. Org. Chem.* **1999**, 1275–1290.
48. Hartung, J.; Bachmann, J.; Svoboda, I.; Fuess, H. *Acta Crystallogr.* **2008**, *E64*, m299.
49. Hartung, J.; Schwarz, M.; Paulus, E. F.; Svoboda, I.; Fuess, H. *Acta Crystallogr.* **2006**, *C62*, o386–388.
50. Hartung, J.; Svoboda, I.; Fuess, H. *Acta Crystallogr.* **1996**, *C52*, 2841–2844.
51. Allen, F. H.; Kennard, O.; Waston, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1987**, S1–S19.
52. Hay, B. P.; Beckwith, A. L. J. *J. Org. Chem.* **1988**, *53*, 4330–4334.
53. Hartung, J.; Hünig, S.; Kneuer, R.; Schwarz, M.; Wenner, H. *Synthesis* **1997**, 1433–1438.