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Efficiency of alkoxyl radical product formation from 5-substituted 3-alkoxy-4-methylthiazole-2(3*H*)-thiones

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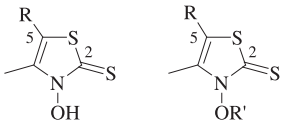
ABSTRACT

In a comparative study, reactions between 5-(*p*-methoxyphenyl)-substituted 3-alkoxy-4-methylthiazole-2(3*H*)-thiones and appropriate mediators ($BrCCl_3$, Bu_3SnH) provided higher yields of alkoxyl radical products (δ-bromohydrins, cyclic ethers, carbonyl compounds) than respective transformations of 5-phenyl- and 5-methyl-substituted derivatives. The unusual selectivity of applied thiohydroxamates to furnish products of O-alkylation, even upon treatment with soft carbon electrophiles, and the marked propensity of 3-alkoxy-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thiones to crystallize, facilitated preparation and purification of the new family of alkoxyl radical precursors in a noteworthy manner.

1. Introduction

Radical precursors share the common property of liberating well defined reactive intermediates upon physical or chemical activation.[1,2] The reagent 3-hydroxy-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione (**1**) in this sense was developed[3] to provide in a sequence of O-alkylation and N,O-homolysis oxygen-centered radicals under non oxidative pH-neutral conditions.[4,5] Its application has contributed to clarify important synthetic,[6] mechanistic,[7,8] and theoretical aspects[9] of alkoxyl radical chemistry that could not adequately be addressed using oxidative methods for oxyl radical generation.[10]

As part of a project directed toward further improving characteristics of thiohydroxamate-based *O*-radical precursors, we recently reported on the synthesis of 5-substituted 3-hydroxythiazole-2(3*H*)-thiones **2** and **3** (Fig. 1).[11] 5-Phenyl-substitution in heterocycle **2** thus was expected to raise efficiency of alkoxyl radical product formation, since the compound shows a similar electronic spectrum (λ_{max}=333 nm) as **1** (λ_{max}=334 nm, both in EtOH) but lacks in comparable weak C,H-bonds originating from the *p*-methoxy substituent. Based on our experience with *N*-hydroxy-4-methylthiazole-2(3*H*)-thione,[12,13] 4,5-dimethyl-substituted heterocycle **3** (λ_{max}=316 nm, in EtOH) was expected to



1–3 **4–6**

R	1–6
p-(H_3CO)C_6H_4 (An)	1 / 4
C_6H_5	2 / 5
CH_3	3 / 6

Figure 1. Structure formulas and indexing of 5-substituted thiazole-2(3*H*)-thiones **1–6** (R′=alkyl, alkenyl, benzyl).

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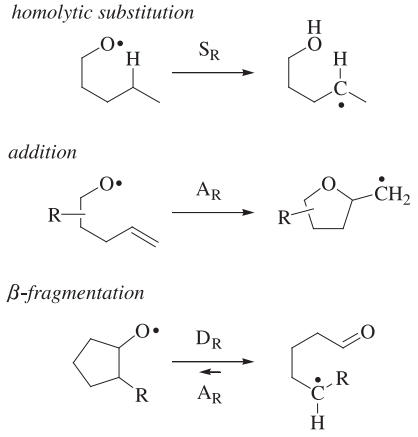
exhibit more pronounced thermal stability compared to aryl-derivatives **1** and **2**, to further reduce the significance of side reactions, for instance fragmentations, that might interfere to N,O-homolysis.[14]

In order to test the hypotheses stated above, acids **1**–**3** were converted into *O*-esters **4**–**6**. The alkyl substituents in those compounds were so chosen as to direct alkoxyl radical reactions into pathways of selective substitution (S_R), addition (A_R), or β-fragmentation (D_R; Scheme 1). Quantitative product radical trapping, target compound analysis, and mass balancing in this approach formed the basis for validating the quality of compounds **4**–**6** regarding their property to serve as alkoxyl radical precursors. The results from such a comparative study showed that 5-(*p*-methoxyphenyl)-substituted thiazolethiones **4** provided higher yields of alkoxyl radical products in reactions with $BrCCl_3$ or Bu_3SnH (δ-bromohydrins, cyclic ethers, carbonyl compounds), than their 5-phenyl- and 5-methyl-substituted congeners **5** and **6**. The latter compounds, however, stood the test to serve as *O*-radical progenitors and therefore merit consideration for selected applications.



Scheme 1. Nomenclature for alkoxyl radical elementary reactions applied in the present study [A=associative step, S=substitution, D=dissociative step; see Sections 2.2.1–2.2.3].[15]

2. Results and interpretation

2.1. Preparation and properties of 3-alkoxythiazole-2(3*H*)-thiones

For reasons of favorable balance between stability and reactivity, *O*-alkyl derivatives of cyclic thiohydroxamic acid **1**[3] have become standard reagents for the pursuit of mechanistic and synthetic alkoxyl radical reactions in this laboratory.[6,7,8] Synthesis of the compounds, which has hitherto not been reported in detail, is feasible via selective O-alkylation of the 5-(*p*-methoxyphenyl)-4-methyl-2-thiooxo-2,3-dihydrothiazol-3-olate ion. It requires conversion of acid **1** into tetraalkylammonium salts **7**–**8** or sodium salt **9** in order to increase nucleophilicity of the thiohydroxamate entity. Salt formation and thus charge transfer onto the heterocyclic subunit is reflected in minor changes of the thiazole-2(3*H*)-thione chromophore (e.g., λ_{max}=335 nm for **9**, EtOH), but marked ^{13}C NMR chemical shift variations of heterocyclic carbons, particularly of C2 (e.g., in DMSO-d_6, Fig. 2).

Ammonium salts **7**–**8** were hygroscopic and difficult to crystallize, whereas powdery sodium salt **9** was stored in open beakers having contact to laboratory atmosphere. In solutions of DMF, salts

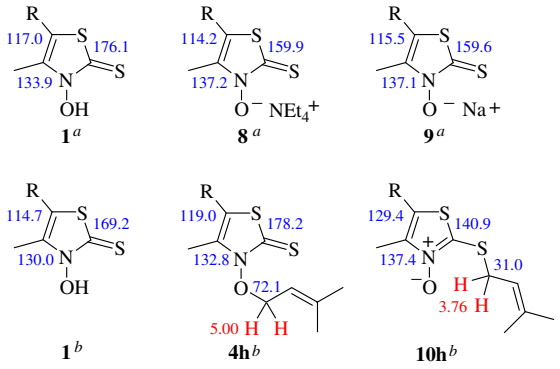
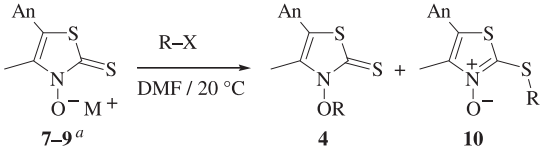


Figure 2. Selected ^{13}C- (blue) and ^{1}H NMR chemical shifts (red) of 5-(*p*-methoxyphenyl)-substituted thiazole-2(3*H*)-thiones [R=*p*-$(H_3CO)C_6H_4$]. [a] in DMSO-d_6. [b] in $CDCl_3$.

7–**9** provided upon treatment with selected alkyl halides and *p*-toluenesulfonates 3-alkoxy derivatives **4a**–**j** as yellowish solids in yields that ranged between 42 and 87% (Table 1; for formation of **10a**, vide infra). The target compounds crystallized upon addition of methanol to materials that were left from organic extractions of underlying reaction mixtures. Recrystallization of likewise obtained solids furnished analytically pure compounds **4a**–**j** that were stored in a refrigerator without noteworthy decomposition.

Yields of O-alkylation product **4** were dependent on substitution and functionalization at the electrophilic carbon atom in R–X, on the nature of the leaving group, and the cation in thiohydroxamates **7**–**9**. Primary allylic and benzylic halides thus were poorer substrates in reactions with NEt_4-salt **8** compared to primary alkyl *p*-toluenesulfonates (Table 1, entries 3, 7–9, 11–13). The effectiveness of *O*-ethyl ester synthesis (formation of **4b**) gradually fell along the series counter cation/leaving group combinations NEt_4^+/OTs^->NEt_4^+/I^->Na^+/OTs^->Na^+/I^- (Table 1, entries 3–6). All alkylations starting from primary and secondary iodoalkanes occurred exclusively (TLC) at oxygen (Table 1, entries 5, 10 and 11). Formation of a mixture of O- and S-alkylation products was restricted in this study to the reaction between 3,3-dimethylallyl bromide and NEt_4-salt **8** (Table 1, entry 12). Alkyl shifts from O to S or vice versa and

Table 1
Preparation of 3-alkoxy-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thiones **4a**–**j**



Entry	R–X	**7**–**9**[a,b]	**4**[b]/%	**10**[b]/%
1	CH_3OTs	**7**	**4a**:[9] 64	—[c]
2	CH_3I	**8**	—[c]	**10a**:46
3	C_2H_5OTs	**8**	**4b**:[4] 87	—[c]
4	C_2H_5OTs	**9**	**4b**:57	—[c]
5	C_2H_5I	**8**	**4b**:64	—[c]
6	C_2H_5I	**9**	**4b**:48	—[c]
7	$C_5H_{11}OTs$	**8**	**4c**:[6] 82	—[c]
8	$Ph(CH_2)_4OTs$	**8**	**4d**:[6] 77	—[c]
9	H_2C=CH–$CH_2CH(Ph)CH_2OTs$[16]	**8**	**4e**:[4] 63	—[c]
10	*c*-C_5H_9I	**8**	**4f**:60	—[c]
11	H_2C=CH–CH_2I	**8**	**4g**:47	—[c]
12	$(H_3C)_2C$=CH–CH_2Br	**8**	**4h**:42	**10h**:26
13	$PhCH_2Br$	**8**	**4i**:54	—[c]
14	$PhCH(CH_3)Cl$	**8**	**4j**:77	—[c]

[a] M=NBu_4 for **7**, NEt_4 for **8** and Na for **9**.
[b] An=*p*-$(H_3CO)C_6H_4$.
[c] Not detected (TLC, ^{1}H NMR).

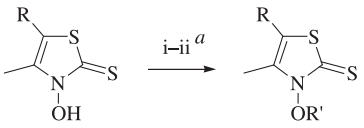
spontaneous fragmentations via carbonyl compound formation[14] were not observed. Iodomethane was the only reagent in the series that gave rise to selective S-alkylation (**10a**; Table 1, entry 2).

Products of O- and S-alkylation were distinguishable via UV- (e.g., λ_{max}=334 nm for **4a** and λ_{max}=311, 254 nm for **10a**) and NMR spectroscopy. The C=S group in, e.g., *O*-esters **4a**–**j**, exhibited diagnostic ^{13}C chemical shifts at ~178 ppm. Magnetic anisotropy exerted by this entity,[17] in combination with the electron withdrawing effect at thioydroxamate O, gave rise to notable deshielding of α-protons of the ester group (e.g., δ=5.00 for O–CH_2 in **4h**; Fig. 2). Resonances of C2 and the α-protons in isomeric *N*-oxides were notably upfield-shifted (e.g., 140.9 ppm and 3.76 ppm for **10h**; Fig. 2).

If compared to other thiohydroxamates, the unusual selectivity of the 5-(*p*-methoxyphenyl)-4-methyl-2-thiooxo-2,3-dihydrothiazol-3-olate ion to furnish products of O-alkylation, even upon treatment with primary or secondary alkyl iodides, merits a comment. Since nucleophilic substitutions commonly are reversible processes, selectivity described above could originate in principle from thermochemical and not only from kinetic preferences as argued on the basis of the principles of hard, soft, acids, bases (HSAB) alone.[18] Tansition states associated with esterification of stabilized anions in **7**–**9** therefore are proposed to be located comparatively late on the associated reaction coordinates. If so, product stability becomes more relevant for explaining selectivity than frontier molecular orbital interactions.[19] According to theory, 3-alkoxythiazole-2(3*H*)-thiones were found at 25 °C to be lower in free energy than *S*-alkylsulfanylthiazole-3-oxide isomers.[14] For open chain and other cyclic thiohydroxamic acids, however, the reverse situation seems to be valid.[20,21] The latter compounds therefore notably favor alkylation at thione sulfur in substitutions with iodoalkanes.[22,23] S-methylation of **8** is expected to take profit from the low steric hinderance at carbon in CH_3I. This circumstance possibly allows soft-soft interactions between the reactants to become more relevant than in slower reactions with primary or secondary iodoalkanes.[24]

The parameters established for the syntheses of 3-alkoxy compounds **4a**–**j** from acid **1** accordingly were applied to prepare *O*-alkyl thiohydroxamates **5**–**6** from selected alkyl- and alkenyl *p*-toluenesulfonates and NEt_4-salts of acids **2** and **3**. The compounds were obtained as yellowish (**5c**, **5d**) to colorless oils (**6c**–**6e**), or as colorless crystalline solid (**5e**). They were stored in a refrigerator without notable decomposition. If the R_f-value of alkylsulfanyl-*N*-oxides **10a** and **10h** (0.01, petroleum ether/Et_2O, 2:1; see Experimental) served as archetype for the mobility of such compounds on TLC-sheets in general, it could be concluded that no products of S-alkylation were formed from *N*-hydroxy compounds **2**–**3** under the chosen conditions (Table 2).

Table 2
Preparation of 5-phenyl- and 5-methyl derivatives of 3-alkoxy-4-methylthiazole-2(3*H*)-thione

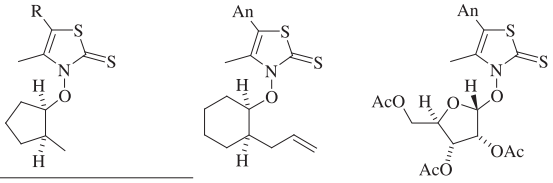


2 / **3** **5** / **6**

Entry	R	**2**/**3**	R′–X	**5**/**6**%
1	C_6H_5	**2**	$C_5H_{11}OTs$	**5c**:80
2	C_6H_5	**2**	$Ph(CH_2)_4OTs$	**5d**:65
3	C_6H_5	**2**	H_2C=CH–$CH_2CH(Ph)CH_2OTs$	**5e**:56
4	CH_3	**3**	$C_5H_{11}OTs$	**6c**:77
5	CH_3	**3**	$Ph(CH_2)_4OTs$	**6d**:76
6	CH_3	**3**	H_2C=CH–$CH_2CH(Ph)CH_2OTs$	**6e**:81

[a]conditions: (i) NEt_4OH, MeOH, 20 °C, then freeze-dry; (ii) R′–X, DMF, 20 °C.

Diastereomerically pure (^1H NMR) *cis*-(2-methylcyclopentyl) *O*-esters (±)-*cis*-**4k**,[4] (±)-*cis*-**5k** (both colorless solids), and (±)-*cis*-**6k** (colorless oil, Fig. 3) for investigating *O*-radical-induced β-fragmentations were prepared from racemic *trans*-(2-methylcyclopentyl) *p*-toluenesulfonate (>98% de) and appropriate NEt_4-thiohydroxamates in DMF at 20 °C. The yields (58–66%, see Experimental) were slightly lower than those of cyclopentyl esters of 4-methylthiazole-2(3*H*)-thiones prepared from cyclopentyl tosylate,[25] presumably for reasons of steric hinderance in case of 2-methyl substitution of the electrophile.



R	compound (yield)	(±)-*cis*-**4l** (7 %)	α-**4m** (59 %)
p-(MeO)C_6H_4	(±)-*cis*-**4k** (66 %)[4]		
C_6H_5	(±)-*cis*-**5k** (58 %)		
CH_3	(±)-*cis*-**6k** (65 %)		

Figure 3. Structure formulas, indexing, and yields of selected carbo- and heterocyclic *O*-esters (±)-*cis*-**4k**–**l**, (±)-*cis*-**5k**–**6k**, and α-**4m** [see Text and Experimental; An=*p*-(H_3CO)C_6H_4].

Treatment of *trans*-2-(prop-2-en-1-yl)-cyclohexyl *p*-toluenesulfonate with NEt_4-salt **8** afforded (±)-*cis*-2-(prop-2-en-1-yl)-cyclohexyl ester (±)-*cis*-**4l** in a highly stereoselective manner. Attempts to raise the comparatively low yield of 7% by elevating the reaction temperature led to quantitative reactant decomposition (not shown). 2,3,5-Tri-*O*-acetyl-β-D-ribofuranosyl chloride[26] underwent stereoselective substitution of thiohydroxamate for chloride upon treatment with NEt_4-salt **8** in DMF, to afford 3-(α-ribosyloxy)-thiazolethione α-**4m** in 59% yield. Stereochemical analysis of this compound was based on diagnostic NMR shift values and coupling constants. The proton attached to the anomeric center, for example, resonated as doublet in α-configured ribose derivative α-**4m** ($^3J_{H,H}$=5.0 Hz), whereas a broad singlet was observed for the same proton in 2,3,5-tri-*O*-acetyl-β-D-ribosylfuranosyl chloride.[26]

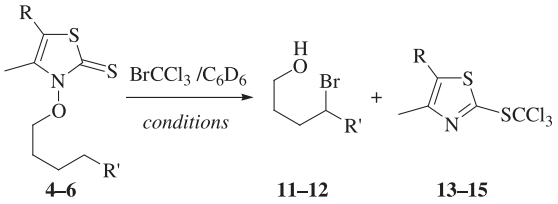
2.2. Generation and trapping of free alkoxyl radicals

3-Alkoxythiazolethiones **4**–**6** were heated or photolyzed in the presence of suitable mediators (i.e., $BrCCl_3$ or Bu_3SnH) for the synthesis of products originating from *O*-radical-mediated C,H-activation (H-atom transfer,[27,28,29] Section 2.2.1), intramolecular addition[30] (Section 2.2.2), and β-C, C cleavage[31] (Section 2.2.3; Scheme 1). Both trapping reagents are able to quantitatively convert carbon radicals that are left from an alkoxyl radical reaction into stable products.[32–34] This circumstance allowed to validate the utility of *O*-radical sources **4**–**6** for conducting these and presumably related transformations[35] on the basis of product quantification.

2.2.1. 1,5-H-Atom transfer (homolytic substitution). Transformations via 1,5-*H*-atom translocation from carbon to oxygen were investigated in the presence of $BrCCl_3$ in order to label the position of the intermediate *C*-radical.

Adequate conditions for preparing 4-bromopentan-1-ol (**11**)[36] required thermal activation (80 °C) of 3-pentoxythiazolethiones **4c**–**6c** in solutions of $BrCCl_3$ and C_6D_6 containing minor amounts (~10 mol %) of AIBN as initiator (Table 3, entries 3–5, 8). Yields were determined via NMR using anisole as internal standard. The

Table 3
Homolytic substitution—formation of δ-bromohydrins **11**/**12**



4–6 **11–12** **13–15**

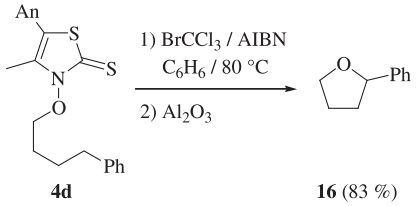
Entry	R	R′	**4–6**	Conditions[a]	**11–12**[b]/%	**13–15**[b]/%
1	*p*-(H_3CO)C_6H_4	CH_3	**4c**	*hν* (350 nm)	**11**:21	**13**:42
2	*p*-(H_3CO)C_6H_4	CH_3	**4c**	*hν* (visible)	**11**:17	**13**:44
3	*p*-(H_3CO)C_6H_4	CH_3	**4c**	AIBN/80 °C	**11**:92 (87)[c]	**13**:94 (89)[c]
4	C_6H_5	CH_3	**5c**	AIBN/80 °C	**11**:81	**14**:90
5	CH_3	CH_3	**6c**	AIBN/80 °C	**11**:77	**15**:88
6	*p*-(H_3CO)C_6H_4	C_6H_5	**4d**	*hν* (350 nm)	**12**:6	**13**:—[d]
7	*p*-(H_3CO)C_6H_4	C_6H_5	**4d**	*hν* (visible)	**12**:5	**13**:—[d]
8	*p*-(H_3CO)C_6H_4	C_6H_5	**4d**	AIBN/80 °C	**12**:91	**13**:93

[a] Quantitative conversion of compounds **4–6** (TLC, ^{1}H NMR).
[b] ^{1}H NMR referenced versus anisole as internal standard.
[c] Number in parentheses refers to yield after chromatographic purification.
[d] Not determined.

reference was added directly after quantitative substrate conversion. Data validation was performed via chromatographic separation of products obtained from a larger batch (1 mmol; Table 3, entry 3). The yields of bromohydrin **11** formed in this set of experiments gradually fell along the series of applied thiones **4c**>**5c**>**6c** from 92 to 77%. The efficiency of trichloromethylsulfanylthiazole formation followed this trend, although the yields of compounds **13**–**15** were slightly higher than those of product **11**.

Photolysis of 3-pentoxy-5-(*p*-methoxyphenyl)-thiazolethione **4c** in the presence of $BrCCl_3$ using a Rayonet®-chamber reactor (λ=350 nm; Table 3, entry 1) or an incandescent light bulb (Table 3, entry 2) was associated with complete consumption of the starting material within 30 min at ~20 °C. The yield of bromoalcohol **11**, however, remained low (17–21%) and the mass balance for unknown reasons erratic.

Reactions of 3-(4-phenylbut-1-oxy)-thiazolethione **4d** and $BrCCl_3$ required thermal reactant activation in order to provide excellent yields of 4-phenyl-4-bromobutanol **12**[4] (91%) and trichloromethylsulfanylthiazole **13** (93%; Table 3, entry 8). Photochemical conditions were less suited for this purpose (Table 3, entry 6–7). Attempts to purify products obtained from a thermally induced reaction via chromatography (SiO_2) afforded mixtures of 4-phenyl-4-bromobutanol **12** and 2-phenyltetrahydrofuran (**16**)[37] with the latter being an artifact due to the selected work up procedure. The material was obtained as sole alkoxyl radical product (83%), e.g., upon adsorptive filtration of a crude reaction mixture (cf. Table 3, entry 8) through basic Al_2O_3 (Scheme 2).



4d **16** (83 %)

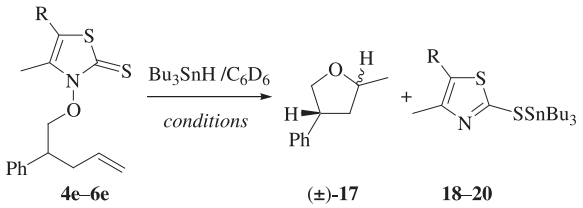
Scheme 2. Synthesis of 2-phenyltetrahydrofuran **16** [An=*p*-(H_3CO)C_6H_4].[37]

The underlying reactivity of 3-pentoxythiazolethiones **4c**–**6c** or 3-phenylbutoxy derivative **4d** in the presence of $BrCCl_3$ is explicable on the basis of 1-pentoxyl- or 4-phenylbut-1-oxyl radical formation in the initial step. *O*-radicals of this type are known to undergo 1,5-*H*-atom transfer to leave respective carbon radicals (cf. Scheme 1, top).[4,38] The 1-hydroxypent-4-yl- or the 1-hydroxy-4-phenylbut-4-yl radical are nucleophilic intermediates that homolytically displace $^{\bullet}CCl_3$ from $BrCCl_3$[33] to furnish bromohydrins **11** or **12**.[32,39] Addition of $^{\bullet}CCl_3$ to thiocarbonyl groups of radical precursors **4c**–**6c** or **4d** has been claimed to induce N,O-homolysis (alkoxyl radical liberation) to leave corresponding trichloromethylsulfanylthiazoles. This mechanistic interpretation was supported in this study by matching yields of organobromine compounds **11**/**12** on one side, and thiazole-derived by-products **13**–**15** on the other.

2.2.2. Addition. The utility of 3-alkenoxythiazolethiones (e.g., **4e**–**6e**) to serve as starting materials for conducting stereoselective tetrahydrofuran synthesis via 5-*exo*-*trig* alkenoxyl radical cyclizations was explored using Bu_3SnH as mediator. Regio- and stereoselectivity of the chosen ring closure provided sufficient information about the chemical nature of the reactive intermediate, and therefore did not require labeling.

Synthetically useful yields of racemic tetrahydrofuran (±)-**17**[40] were obtained from 3-phenylpentenoxy-5-(*p*-methoxyphenyl)-4-methylthiazolethione **4e** and Bu_3SnH, either by photolyzing [Rayonet®-chamber reactor (λ=350 nm) or incandescent light] or heating solutions of the reactants in C_6D_6 (Table 4, entries 1–3). The latter set-up required addition of an initiator (AIBN), to achieve

Table 4
Intramolecular addition under reductive conditions—tetrahydrofuran formation



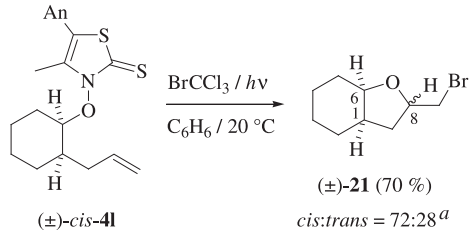
4e–6e (±)-**17** **18–20**

Entry	R	**4e–6e**	Conditions[a]	(±)-**17**[b]%	**18–20**[b]/%
1	*p*-(H_3CO)C_6H_4	**4e**	*hν* (350 nm)	63 (87:13)	**18**:77
2	*p*-(H_3CO)C_6H_4	**4e**	*hν* (visible)	59 (86:14)	**18**:78
3	*p*-(H_3CO)C_6H_4	**4e**	AIBN/80 °C	64 (87:13)	**18**:77
4	C_6H_5	**5e**	AIBN/80 °C	62 (87:13)	**19**:76
5	CH_3	**6e**	AIBN/80 °C	61 (87:13)	**20**:78

[a] Quantitative conversion of compounds **4e–6e** (TLC and ^{1}H NMR).
[b] ^{1}H NMR, referenced versus anisole as internal standard.

quantitative turnover of starting thiones **4e**–**6e** and satisfactory yields of target compound (±)-**17** (64%), besides tributylstannylsulfanylthiazole **18** [77%; R=*p*-(H_3CO)C_6H_4]. This methodology was for reasons of effectiveness applied for converting 3-pentenoxythiazolethiones **5e** or **6e** into tetrahydrofuran (±)-**17** (61–62%) and tributylstannyl-substituted thiazoles **19** (76% from **5e**) or **20** (78% from **6e**) (Table 4, entries 4–5). Tributylstannylsulfanyl-substituted thiazoles **19** and **20** were characterized via NMR directly in solutions obtained from radical reactions, since the compounds decomposed on attempts to separate additionally formed butyl tin compounds via chromatography or distillation (see Experimental and Supplementary Data).

In a synthetic application (±)-3-(*cis*-allylcyclohexyloxy)-thiazolethione (±)-*cis*-**4l** was photolyzed (350 nm, 20 °C) in the presence of $BrCCl_3$ to provide oxabicyclo[4.3.0]nonane (±)-**21**[41] in 70% yield (Scheme 3). This approach refrained from using an initiator and contributed to slightly improve stereoselectivity of the cyclization (6,8-*cis*:6,8-*trans*=72:28).[41]

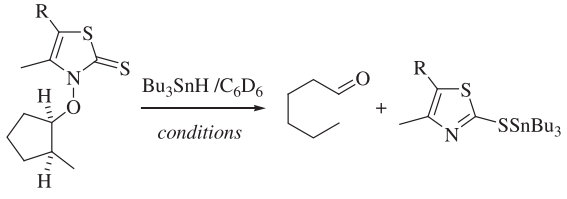


Scheme 3. Stereoselective oxabicyclo[4.3.0]nonane formation[a] refers to positions 6 and 8 [An=*p*-(H_3CO)C_6H_4].

Experiments starting from 3-alkenoxythiazolethiones **4e**–**6e** exemplified that efficiency of alkenoxyl radical product formation via 5-*exo*-*trig* cyclization (Scheme 1, center) was independent from the chemical nature of the substituent in position 5 of the radical precursor, and the applied methodology for activating these molecules. Regio- and diastereoselectivity of tetrahydrofuran synthesis from 3-alkenoxythiazolethiones [**4e**–**6e**, (±)-*cis*-**4l**] and Bu_3SnH or $BrCCl_3$ were consistent with the appearance of free alkenoxyl radicals and their participation in chain reactions. For mechanistic details of both model reactions the reader is referred to appropriate references.[10,40,41]

2.2.3. β-C,C-Fragmentation. Efficiency of 5-substituted 3-alkoxythiazolethiones in the synthesis of carbonyl compounds under reductive conditions was validated in reactions of *O*-(*cis*-2-methylcyclopentyl) thiohydroxamates (±)-*cis*-**4k**–**6k** with Bu_3SnH

Table 5
Fragmentation under reductive conditions—preparation of hexanal (**22**)

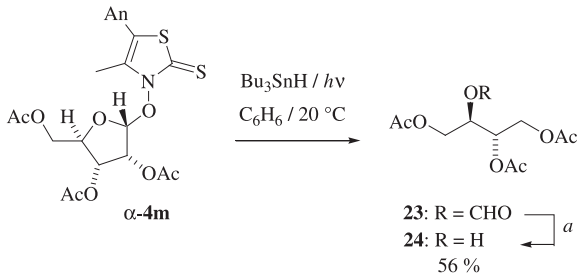


Entry	R	(±)-*cis*-**4k**–**6k**	Conditions[a]	**22**[b]%	**18**–**20**[b]/%
1	*p*-(H_3CO)C_6H_4	**4k**	*hν* (350 nm)	77	**18**: 82
2	*p*-(H_3CO)C_6H_4	**4k**	*hν* (visible)	78	**18**: 80
3	*p*-(H_3CO)C_6H_4	**4k**	AIBN/80 °C	65	**18**: 83
4	C_6H_5	**5k**	*hν* (350 nm)	62	**19**: 79
5	CH_3	**6k**	*hν* (350 nm)	71	**20**: 81

[a] Quantitative conversion of compounds (±)-*cis*-**4k**–**6k** (TLC and ^{1}H NMR).
[b] ^{1}H NMR, referenced versus anisole as internal standard.

(Table 5). All transformations of this type provided hexanal (**22**) and tributylstannyl-substituted thiazoles **18**–**20**, however, in slightly diverging yields. The most effective procedure for hexanal synthesis according to this method started from 5-(*p*-methoxyphenyl)-substituted thiazolethione (±)-*cis*-**4k** and required photochemical reactant activation (Table 5, entries 1–2). The fact that the thermal reaction (80 °C) gave less target compound, however, was correlated with the volatility of aldehyde **22** (bp.=131 °C), which seemed to be no concern in photochemical reactions at ~20 °C. Support for this argumentation arose from analysis of yields of secondary product **18** that differed only marginally across the entire set of experiments (Table 5, entries 1–3). In view of these findings, the remaining two *cis*-2-methylcyclopentyl esters (±)-*cis*-**5k** and (±)-*cis*-**6k** were subjected to photochemical reactions (λ=350 nm, 20 °C) with Bu_3SnH. Hexanal yields (^{1}H NMR) of both experiments were smaller than the value obtained for the reaction of (±)-*cis*-**4k** under identical conditions (Table 5, entries 1, 4 and 5).

Photolysis of *O*-ribosylthiohydroxamate α-**4m** and Bu_3SnH (λ=350 nm, 20 °C; Scheme 4) in a solution of C_6H_6 furnished a mixture of formylester **23** and tri-*O*-acetylerythritol **24**, with the former being transformed into the latter in the course of chromatographic purification (56%).



Scheme 4. Carbohydrate degradation under reductive conditions [[a] chromatographic purification on SiO_2; An=*p*-(H_3CO)C_6H_4].

Alkoxyl radicals having a saturated five-membered ring attached to the *O*-radical center undergo rapid fragmentation into δ-oxo-substituted carbon radicals.[42,43,44] The driving force for this C,C-disconnection originates from a relieve of ring strain and the energy, that is, gained upon C,O-double bond formation at the expense of a C,C-single bond in proximity to an alkoxyl radical center.[35] The reverse reaction, i.e., 5-*exo*-*trig* addition of a δ-formylbutyl radical to a C=O group is slower than the fragmentation, thus shifting the equilibrium onto the side of the open-chain radical.[45] Trapping of intermediates therefore provides ring-opened products (e.g., **22**) as major components. Formation of erythritol **24** is in agreement with this mechanistic interpretation since fragmentation of the α-2,3,5-tri-*O*-acetyloxylribosyloxyl radical (not shown) is expected for thermochemical reasons to occur via breaking of the adjacent C,C- and not of the endocyclic C,O-bond.[46,47] Reduction of the primary intermediate furnished a 3/1-mixture of formylester **23** and erythritol **24**. The former product hydrolyzed upon chromatographic purification to leave alcohol **24**.

3. Concluding remarks

The present report on the efficiency of 5-substituted 3-alkoxy-4-methylthiazole-2(3*H*)-thiones **4**–**6** in alkoxyl radical-based synthesis allows to draw the following conclusions.

(i) The marked propensity to separate as crystalline solids from rather crude reaction mixtures by adding MeOH simplified isolation and subsequent purification of 5-(*p*-methoxyphenyl)-substituted thiazolethiones **4** in comparison to their

5-phenyl and 5-methyl congeners **5** and **6** (predominantly oils) in a noteworthy manner.

(ii) All 3-alkoxythiazolethiones **4**–**6** applied in this study stood the test to serve as alkoxyl radical sources.

(iii) Reactions based on 1,5-*H*-atom transfer from carbon to oxygen required for unknown reasons higher temperatures (~80 °C) to provide good to excellent yields (77–92%) of *O*-radical products (e.g., δ-bromohydrins **11**/**12**).

(iv) Intramolecular additions and β-C,C-homolysis were feasible using any of the 3-alkoxythiazolethiones prepared for this purpose using thermal (~80 °C, AIBN) or photochemical reagent activation (λ=350 nm or incandescent light).

(v) In case of diverging yields (1,5-*H*-atom transfer in Section 2.2.1 and β-fragmentation in paragraph 2.2.3), 5-(*p*-methoxyphenyl)-4-methyl-substituted thiazolethiones **4** consistently were the more effective reagents compared to derivatives **5** and **6**.

The data summarized in this report clearly stressed the utility of the 3-alkoxy-5-(*p*-methoxyphenyl)-4-methylthiazolethiones **4** for alkoxyl radical generation under non oxidative pH-neutral conditions. The results furthermore pointed to the necessity to systematically analyze in future studies effects of the 5 substituent in thiazole-2(3*H*)-thiones onto barriers to N,O-homolysis and the quality of the thione sulfur to serve as carbon radical trap. From an experimental point of view it became obvious that the fundamental 3-alkoxythiazole-2(3*H*)-thione reactivity was largely retained upon substitution of methyl or phenyl for *p*-methoxyphenyl at this site. This conclusion was probably is one of the most important findings from the study. It paves the road toward design of novel *O*-radical precursors having other substituents attached to the thiazole-2(3*H*)-thione core than those applied in the present investigation. Such compounds are expected to contribute to future developments in order to apply the unique reactivity of alkoxyl radicals for quite general or highly specialized purposes.

4. Experimental

4.1. General

For general laboratory practice and instrumentation see Ref. 6 and the Supplementary Data.

4.2. 3-Hydroxythiazole-2(3*H*)-thione salts

4.2.1. General method. A solution of NEt_4OH, NBu_4OH, or NaOH in MeOH (1.10 mmol, 0.73 mL, 1.5 M) was added to a solution of a 3-hydroxythiazole-2(3*H*)-thione **1**–**3** (1.10 mmol) in MeOH (2 mL) at 20 °C. The reaction mixture was stirred for 1 h at 20 °C. The solvent was evaporated under reduced pressure to furnish a residue that was freeze-dried (12 h). The salts were ready for use and taken up in DMF for thiohydroxamate alkylation as described in Section 4.3.1.

*4.2.2. 3-Hydroxy-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione tetraethylammonium salt (**8**).* ^{1}H NMR (DMSO-d_6, 400 MHz) δ 1.14 (t, 12H, *J*=6.4 Hz), 2.18 (s, 3H, 4-CH_3), 3.20 (q, 8H, *J*=7.2 Hz), 3.75 (s, 3H, OCH_3), 6.96 (d, 2H, *J*=8.6 Hz), 7.25 (d, 2H, *J*=8.6 Hz). ^{13}C NMR (DMSO-d_6, 100 MHz) δ 6.8, 13.0 (4-CH_3), 51.5, 55.0 (OCH_3), 114.2, 114.3 (C5), 124.9, 128.4, 137.2 (C4), 158.0, 159.9 (C2).

*4.2.3. 3-Hydroxy-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione sodium salt (**9**).* ^{1}H NMR (DMSO-d_6, 600 MHz) δ 2.23 (s, 3H, 4-CH_3), 3.77 (s, 3H, OCH_3), 6.98 (d, 2H, *J*=8.7 Hz), 7.28 (d, 2H, *J*=8.5 Hz). ^{13}C NMR (DMSO-d_6, 150 MHz) δ 13.4 (4-CH_3), 55.3 (OCH_3), 114.5, 115.5 (C5), 124.6, 129.0, 137.1 (C4), 158.6, 159.6 (C2).

4.3. Alkylation of thiohydroxamate salts

4.3.1. General method. A solution of a 3-hydroxy-5-(*p*-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione salt **7**–**9** (1.10 mmol) or NEt_4-salts of thiazolethiones **2**–**3** (1.10 mmol) in anhydrous DMF (2 mL) was treated at 20 °C with a respective neat alkyl tosylate or an alkyl halide (1.00 mmol). Stirring was continued at 20 °C. until complete substrate conversion had occurred (3–6 days). Water (10 mL) was added. The mixture was extracted with Et_2O (3×5 mL). Combined organic extracts were dried ($MgSO_4$), and concentrated under reduced pressure. MeOH was added for crystallizing the residue. If no solids appeared on standing for 14 h at 5 °C the solvent was evaporated. The remaining oil was purified by column chromatography (SiO_2).

*4.3.2. 5-(p-Methoxyphenyl)-4-methyl-2-(methylsulfanyl)-thiazole-3-oxide (**10a**).* From methyliodide (142 mg, 1.00 mmol). Yield: 124 mg (0.46 mmol, 46%), tan oil. R_f=0.01 [petroleum ether/Et_2O=2:1 (v/v)]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 2.43 (s, 3H, 4-CH_3), 2.61 (s, 3H, SCH_3), 3.85 (s, 3H, OCH_3), 6.98 (m_c, 2H), 7.33 (m_c, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.2 (4-CH_3), 15.4 (SCH_3), 55.4 (OCH_3), 114.6, 122.9, 128.4, 129.8 (C5), 140.9 (C4), 152.8 (C2), 160.3. UV (EtOH) λ_{max} (lg ε/m^2 mol^{-1}) 311 nm (3.38), 253 (3.42). MS (EI) *m*/*z* 267 (M^+, 67), 250 (100), 177 (38). Anal. Calcd for $C_{12}H_{13}NO_2S_2$ (267.36) C, 53.91; H, 4.90; N, 5.24; S, 23.98; Found: C, 53.90; H, 4.91; N, 5.24; S, 23.62.

*4.3.3. 3-Cyclopentoxy-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (**4f**).* From iodocyclopentane (196 mg, 1.00 mmol); yield 193 mg (60%), yellowish solid. R_f=0.28 [petroleum ether/Et_2O=2:1 (v/v)]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.62–1.72 (m, 2H), 1.81–1.92 (m, 4H), 1.92–2.03 (m, 2H), 2.29 (s, 3H, 4-CH_3), 3.83 (s, 3H, OCH_3), 5.75 (m_c, 1H), 6.94 (m_c, 2H), 7.24 (m_c, 2H). ^{13}C NMR ($CDCl_3$, 101 MHz) δ 12.7 (4-CH_3), 23.8, 31.4, 55.4 (OCH_3), 89.1, 114.5, 119.4 (C5), 122.7, 129.9, 133.3 (C4), 159.9, 179.2 (C2). MS (EI) *m*/*z* 321 (M^+, 28), 237 (77), 178 (14), 57 (100). Anal. Calcd for $C_{16}H_{19}NO_2S_2$ (321.45): C, 59.78; H, 5.96; N, 4.36; S, 19.95; Found: C, 59.95; H, 5.98; N, 4.33; S, 20.06.

*4.3.4. 5-(p-Methoxyphenyl)-4-methyl-3-(prop-2-en-1-oxy)-thiazole-2(3H)-thione (**4g**).* From 3-iodopropene (168 mg, 1.00 mmol); yield: 138 mg (47%), yellowish solid. R_f=0.23 [petroleum ether/Et_2O=2:1 (v/v)]. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.32 (s, 3H, 4-CH_3), 3.83 (s, 3H, OCH_3), 5.00 (d, 2H, *J*=6.7 Hz), 5.43 (m, 2H), 6.11 (ddt, 1H, J_d=13.3, 10.1 Hz, J_t=6.7 Hz), 6.94 (m_c, 2H), 7.24 (m_c, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.3 (4-CH_3), 55.4 (OCH_3), 76.7, 114.4, 114.7, 119.2 (C5), 122.9, 129.9, 130.0, 132.4 (C4), 159.1, 178.8 (C2). MS (EI) *m*/*z* 293 (M^+, 1), 262 (8), 237 (100), 163 (18). Anal. Calcd for $C_{14}H_{15}NO_2S_2$ (293.40): C, 57.31; H, 5.15; N, 4.77; S, 21.85; Found: C, 57.57; H, 5.27; N, 4.74; S, 21.39.

*4.3.5. Alkylation of tetraethylammonium salt **8** with 1-bromo-3-methylbut-2-ene (149 mg, 1.00 mmol).* The crude product was purified by column chromatography [petroleum ether/Et_2O=2:1 (v/v)]. *5-(p-Methoxyphenyl)-4-methyl-3-(3-methylbut-2-en-1-oxy)-thiazole-2(3H)-thione* (**4h**). Yield: 135 mg (42%), yellowish solid. R_f=0.28 [petroleum ether/Et_2O=2:1 (v/v)]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.81 (d, 3H, *J*=1.0 Hz), 1.82 (s, 3H), 2.30 (s, 3H, 4-CH_3), 3.84 (s, 3H, OCH_3), 5.00 (d, 2H, *J*=7.8 Hz), 5.53 (m_c, 1H), 6.94 (m_c, 2H), 7.24 (m_c, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4 (4-CH_3), 18.3, 26.0, 55.4 (OCH_3), 72.1, 114.6, 116.3, 119.0 (C5), 122.7, 129.9, 132.8 (C4), 144.7, 159.9, 178.8 (C2). UV (EtOH) λ_{max} (lg ε/m^2 mol^{-1}) 334 nm (3.26). MS (EI) *m*/*z* 321 (M^+, 8), 305 (12), 237 (100), 178 (21). Anal. Calcd for $C_{16}H_{19}NO_2S_2$ (321.45): C, 59.78; H, 5.96; N, 4.36; S, 19.95; Found: C, 59.83; H, 5.87; N, 4.32; S, 20.05. *5-(p-Methoxyphenyl)-4-methyl-2-(3-methyl-2-*

buten-1-ylsulfanyl)-thiazol-3-oxide (**10h**). Yield: 83.6 mg (0.26 mmol, 26%), colorless solid. R_f=0.01 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.63 (s, 3H), 1.73 (s, 3H), 2.43 (s, 3H, 4-CH_3), 3.76 (d, 2H, J=8.1 Hz), 3.86 (s, 3H, OCH_3), 5.32 (m_c, 1H), 6.99 (m_c, 2H), 7.34 (m_c, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.4 (4-CH_3), 17.7, 25.7, 31.0, 55.4 (OCH_3), 114.6, 117.9, 123.0, 129.4 (C5), 129.9, 137.4 (C4), 139.0, 140.9 (C2), 160.4. UV (EtOH) λ_{max} (lg ε/m^2 mol^{-1}) 310 (3.01), 254 (3.07). MS (EI) m/z 321 (M^+, 8), 304 (18), 253 (100), 146 (34). Anal. Calcd for $C_{16}H_{19}NO_2S_2$ (321.45): C, 59.78; H, 5.96; N, 4.36; S, 19.95; Found: C, 59.83; H, 5.97; N, 4.32; S, 20.03.

4.3.6. 3-(1-Benzyloxy)-5-(p-methoxyphenyl)-4-methylthiazole-2(3H)-thione (***4i***). From benzyl bromide (127 mg, 1.00 mmol). Yield: 187 mg (0.54 mmol, 54%), colorless solid. R_f=0.17 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 400 MHz) δ 2.07 (s, 3H, 4-CH_3), 3.83 (s, 3H, OCH_3), 5.52 (s, 2H), 6.92 (m_c, 2H), 7.17 (m_c, 2H), 7.40–7.44 (m, 3H), 7.53–7.57 (m, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.1 (4-CH_3), 55.4 (OCH_3), 77.5, 114.5, 118.9 (C5), 122.6, 128.8, 129.7, 129.9, 130.3, 132.8 (C4), 133.3, 159.9, 178.7 (C=S). MS (EI) m/z 343 (M^+, 3), 237 (21), 106 (87), 91 (17), 77 (100). Anal. Calcd for $C_{18}H_{17}NO_2S_2$ (343.46): C, 62.95; H, 4.99; N, 4.08; S, 18.67; Found: C, 62.96; H, 4.99; N, 4.11; S, 18.37.

*4.3.7. (±)-5-(p-Methoxyphenyl)-4-methyl-3-(1-phenyleth-1-oxy)-thiazole-2(3H)-thione (±)-(**4j**).* From 1-chloro-1-phenylethane (141 mg, 1.00 mmol). Yield: 275 mg (0.77 mmol, 77%), colorless solid. R_f=0.42 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.61 (s, 3H, 4-CH_3), 1.84 (d, 3H, J=6.7 Hz), 3.79 (s, 3H, OCH_3), 6.33 (q, 1H, J=6.7 Hz), 6.87 (m_c, 2H), 7.03 (m_c, 2H), 7.38–7.44 (m, 5H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.1 (4-CH_3), 17.9, 55.4 (OCH_3), 82.5, 114.4, 118.4 (C5), 122.7, 128.5, 128.6, 129.6, 129.8, 133.8 (C4), 138.0, 159.7, 178.7 (C2). MS (EI) m/z 357 (M^+, 2), 253 (8), 237 (21), 178 (5), 120 (36), 105 (100), 77 (98). Anal. Calcd for $C_{19}H_{19}NO_2S_2$ (357.49): C, 63.84; H, 5.36; N, 3.92; S, 17.94; Found: C, 63.49; H, 5.19; N, 3.95; S, 17.46.

*4.3.8. (±)-5-(p-Methoxyphenyl)-4-methyl-3-[cis-2-(prop-2-en-1-yl)-cyclohexyl-1-oxy]-thiazole-2(3H)-thione (±)-cis-(**4l**).* From (±)-*trans*-2-(prop-2-en-1-yl)cyclohexyltosylate (294 mg, 1.00 mmol). The crude product was purified by column chromatography [petroleum ether/Et_2O=2:1 (v/v)]. Yield: 24.4 mg (74.0 μmol, 7%), yellowish solid. R_f=0.45 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.30–1.50 (m, 4H), 1.72–1.84 (m, 4H), 2.20–2.40 (m, 2H), 2.30 (s, 3H, 4-CH_3), 2.60–2.64 (m, 1H), 3.84 (s, 3H, OCH_3), 5.02–5.12 (m, 2H), 5.30–5.35 (m, 1H), 5.77–5.85 (m, 1H), 6.95 (m_c, 2H), 7.24 (m_c, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.9 (4-CH_3), 20.5, 23.9, 26.3, 26.9, 30.6, 37.6, 55.4 (OCH_3), 85.5, 114.5, 116.1, 119.9 (C5), 122.8, 129.9, 133.6, 137.3 (C4), 159.9, 179.0 (C2). MS (EI) m/z 375 (M^+, 3), 253 (15), 237 (57), 138 (37), 79 (100). Anal. Calcd for $C_{20}H_{25}NO_2S_2$ (375.54): C, 63.97; H, 6.71; N, 3.73; S, 17.07; Found: C, 64.37; H, 6.97; N, 3.80; S, 17.15.

*4.3.9. 5-(p-Methoxyphenyl)-4-methyl-3-(2,3,5-tri-O-acetyl-α-D-ribofuranosyl-1-oxy)- thiazole-2(3H)-thione α-(**4m**).* From 2,3,5-tri-*O*-acetyl-β-D-ribofuranosyl chloride (295 mg, 1.00 mmol). Yield: 302 mg (0.59 mmol, 59%), colorless solid. R_f=0.08 [petroleum ether/Et_2O=2:1 (v/v)]. $[\alpha]_D^{25}$ 159.6 (*c* 0.54, CH_2Cl_2). ^1H NMR ($CDCl_3$, 400 MHz) δ 2.11 (s, 3H), 2.16 (s, 3H), 2.21 (s, 3H), 2.31 (s, 3H, 4-CH_3), 3.83 (s, 3H, OCH_3), 4.23 (dd, 1H, J=12.1, 3.7 Hz), 4.36 (dd, 1H, J=12.1, 3.4 Hz), 4.64 (m_c, 1H), 5.37 (dd, 1H, J=6.3, 1.8 Hz), 5.50 (dd, 1H, J=6.3, 5.0 Hz), 6.39 (d, 1H, J=5.0 Hz), 6.94 (m_c, 2H), 7.23 (m_c, 2H). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 12.5 (4-CH_3), 20.6, 20.7, 20.8, 55.4 (OCH_3), 63.2, 69.5, 70.2, 82.4, 104.4, 114.5, 118.8 (C5), 122.5, 130.0, 133.0 (C4), 160.0, 169.6 (C=O), 170.2 (C=O), 170.3 (C=O), 179.3 (C2). Anal. Calcd for $C_{22}H_{25}NO_9S_2$ (511.56): C, 51.65; H, 4.93; N, 2.74; S, 12.53; Found: C, 51.03; H, 5.11; N, 2.72; S, 12.49.

4.3.10. 4-Methyl-3-(pent-1-oxy)-5-phenylthiazole-2(3H)-thione (***5c***). From pentyl tosylate (242 mg, 1.00 mmol). The crude product was purified by column chromatography [petroleum ether/Et_2O=2:1 (v/v)]. Yield: 235 mg (0.80 mmol, 80%), yellowish oil. R_f=0.53 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 250 MHz) δ 0.94 (t, 3H, J=7.2 Hz), 1.30–1.58 (m, 4H), 1.87 (m_c, 2H), 2.37 (s, 3H, 4-CH_3), 4.46 (t, 2H, J=6.6 Hz), 7.29–7.46 (m, 5H). ^{13}C NMR ($CDCl_3$, 63 MHz) δ 12.1 (4-CH_3), 13.9, 22.5, 27.6, 27.8, 76.5, 119.3 (C5), 128.5, 128.7, 129.1, 130.4, 132.9 (C4), 179.0 (C2). UV (EtOH) λ_{max} (lg ε/m^2 mol^{-1}) 332 nm (3.45), 284 nm (2.77). Anal. Calcd for $C_{15}H_{19}NOS_2$ (293.44): C, 61.40; H, 6.53; N, 4.77; S, 21.85; Found: C, 61.40; H, 6.41; N, 4.81; S, 21.65.

4.3.11. 4-Methyl-5-phenyl-3-(4-phenylbut-1-oxy)-thiazole-2(3H)-thione (***5d***). From 4-phenylbutyl tosylate (304 mg, 1.00 mmol). The crude product was purified by column chromatography [petroleum ether/Et_2O=2:1 (v/v)]. Yield: 231 mg (0.65 mmol, 65%), yellowish oil. R_f=0.51 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 250 MHz) δ 1.33–1.55 (m, 4H), 2.34 (s, 3H, 4-CH_3), 2.73 (t, 2H, J=7.1 Hz), 4.49 (t, 2H, J=6.0 Hz), 7.19–7.22 (m, 3H), 7.28–7.33 (m, 4H), 7.36–7.46 (m, 3H). ^{13}C NMR ($CDCl_3$, 63 MHz) δ 12.1 (4-CH_3), 27.5, 27.5, 35.5, 76.0, 119.3 (C5), 125.9, 128.4, 128.5, 128.5, 128.7, 129.1, 130.4, 132.8 (C4), 141.8, 179.0 (C2). UV (EtOH) λ_{max} (lg ε/m^2 mol^{-1}) 334 nm (3.17), 289 nm (2.91). MS (EI) m/z 355 (M^+, 4), 207 (50), 147 (16), 104 (100), 91 (69). Anal. Calcd for $C_{20}H_{21}NOS_2$ (355.51): C, 67.57; H, 5.95; N, 3.94; S, 18.04; Found: C, 67.44; H, 6.22; N, 3.91; S, 17.54.

*4.3.12. (±)-4-Methyl-5-phenyl-3-(2-phenylpent-4-en-1-oxy)-thiazole-2(3H)-thione (±)-(**5e**).* From (±)-2-phenyl-4-penten-1-yl tosylate (316 mg, 1.00 mmol). The crude product was purified by column chromatography [petroleum ether/Et_2O=2:1 (v/v)]. Yield: 206 mg (0.56 mmol, 56%), colorless solid. R_f=0.51 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 250 MHz) δ 2.00 (s, 3H, 4-CH_3), 2.55 (ddd, 1H, J=14.4, 7.2, 7.0 Hz), 2.72 (ddd, 1H, J=14.4, 7.2, 7.0 Hz), 3.30 (quint, 1H, J=7.2 Hz), 4.51 (t, 1H, J=7.2 Hz), 4.78 (t, 1H, J=7.2 Hz), 5.05 (m_c, 2H), 5.76 (m_c, 1H), 7.21–7.42 (m, 10H). ^{13}C NMR ($CDCl_3$, 63 MHz) δ 11.7 (4-CH_3), 36.5, 44.3, 79.2, 117.1, 119.1 (C5), 127.1, 128.0, 128.4, 128.5, 128.6, 129.0, 130.3, 132.9, 135.4 (C4), 140.7, 179.0 (C2). UV (EtOH) λ_{max} (lg ε/m^2 mol^{-1}) 333 nm (3.18), 285 (2.52). MS (EI) m/z 367 (M^+, 1), 207 (46), 131 (76), 91 (100). Anal. Calcd for $C_{21}H_{21}NOS_2$ (367.52): C, 68.63; H, 5.76; N, 3.81; S, 17.45; Found: C, 68.36; H, 5.73; N, 3.88; S, 16.95.

*4.3.13. (±)-4-Methyl-3-(cis-2-methylcyclopent-1-oxy)-5-phenylthiazole-2(3H)-thione (±)-cis-(**5k**).* From (±)-*trans*-2-methylcyclopentyl tosylate (254 mg, 1.00 mmol). The crude product was purified by column chromatography [petroleum ether/Et_2O=2:1 (v/v)]. Yield: 177 mg (0.58 mmol, 58%), colorless solid. R_f=0.78 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 250 MHz) δ 1.28 (d, 3H, J=6.9 Hz), 1.50–1.98 (m, 6H), 2.12–2.25 (m, 1H), 2.32 (s, 3H, 4-CH_3), 5.64 (dt, 1H, J=4.9, 4.8 Hz), 7.30–7.45 (m, 5H). ^{13}C NMR ($CDCl_3$, 63 MHz) δ 12.6 (4-CH_3), 13.6, 21.9, 29.6, 31.4, 39.3, 89.8, 119.3 (C5), 128.5, 128.6, 129.1, 130.5, 134.3 (C4), 179.6 (C2). UV (EtOH) λ_{max} (lg ε/m^2 mol^{-1}) 334 nm (3.38), 285 (2.69). MS (EI) m/z 305 (M^+, 22), 223 (85), 207 (100), 147 (43), 130 (40), 115 (32). Anal. Calcd for $C_{16}H_{19}NOS_2$ (305.45): C, 62.92; H, 6.27; N, 4.59; S, 20.99; Found: C, 62.58; H, 6.56; N, 4.49; S, 20.54.

4.3.14. 4,5-Dimethyl-3-(pent-1-oxy)-thiazole-2(3H)-thione (***6c***). From pentyl tosylate (242 mg, 1.00 mmol). The crude product was purified by column chromatography [petroleum ether/Et_2O=2:1 (v/v)]. Yield: 178 mg (0.77 mmol, 77%), colorless oil. R_f=0.28 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 250 MHz) δ 0.93 (t, 3H, J=7.1 Hz), 1.31–1.53 (m, 4H), 1.82 (m_c, 2H), 2.12 (s, 3H, 4-CH_3), 2.18 (s, 3H, 5-CH_3), 4.37 (t, 2H, J=6.7 Hz). ^{13}C NMR ($CDCl_3$, 63 MHz) δ 11.0 (4-CH_3), 12.0 (5-CH_3), 13.9, 22.5, 27.5, 27.8, 76.2, 114.4 (C5), 132.6 (C4), 178.3 (C2). UV (EtOH) λ_{max} (lg ε/m^2 mol^{-1}) 320 nm (3.13).

Anal. Calcd for $C_{10}H_{17}NOS_2$ (231.37): C, 51.91; H, 7.41; N, 6.05; S, 27.71; Found: C, 52.13; H, 7.32; N, 6.11; S, 27.63.

*4.3.15. 4,5-Dimethyl-3-(4-phenylbut-1-oxy)-thiazole-2(3H)-thione (**6d**).* From 4-phenylbutyl tosylate (304 mg, 1.00 mmol). The crude product was purified by column chromatography [petroleum ether/Et_2O=2:1 (v/v)]. Yield: 223 mg (0.76 mmol, 76%), colorless oil. R_f=0.29 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 250 MHz) δ 1.84 (m_c, 4H), 2.11 (q, 3H, J=0.9 Hz, 4-CH_3), 2.16 (q, 3H, J=0.9 Hz, 5-CH_3), 2.70 (t, 2H, J=7.1 Hz), 4.38 (t, 2H, J=6.0 Hz), 7.33–7.14 (m, 5H). ^{13}C NMR ($CDCl_3$, 63 MHz) δ 11.0 (4-CH_3), 12.0 (5-CH_3), 27.4, 27.5, 35.5, 75.8, 114.4 (C5), 125.9, 128.3, 128.4, 132.5 (C4), 141.0, 178.3 (C2). UV (EtOH) λ_{max} (lg ε/m^2 mol^{-1}) 321 nm (2.98). Anal. Calcd for $C_{15}H_{19}NOS_2$ (293.44): C, 61.40; H, 6.53; N, 4.77; S, 21.85; Found: C, 60.95; H, 6.41; N, 4.67; S, 21.75.

*4.3.16. (±)-4,5-Dimethyl-3-(2-phenylpent-4-en-1-oxy)-thiazole-2(3H)-thione (±)-(**6e**).* From (±)-2-phenyl-4-penten-1-yl tosylate (316 mg, 1.00 mmol). The crude product was purified by column chromatography [petroleum ether/Et_2O=2:1 (v/v)]. Yield: 247 mg (0.81 mmol, 81%), colorless oil. R_f=0.36 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 250 MHz) δ 1.82 (q, 3H, J=0.9 Hz, 4-CH_3), 2.06 (q, 3H, J=0.9 Hz, 5-CH_3), 2.51 (m_c, 1H), 2.70 (m_c, 1H), 3.25 (dddd, 1H, J=8.5, 7.5, 6.4, 6.3 Hz), 4.41 (t, 1H, J=7.5 Hz), 4.68 (dd, 1H, J=7.5, 6.4 Hz), 4.95–5.10 (m, 2H), 5.74 (m_c, 1H), 7.20–7.37 (m, 5H). ^{13}C NMR ($CDCl_3$, 63 MHz) δ 10.5 (4-CH_3), 11.9 (5-CH_3), 36.5, 44.3, 79.0, 114.3 (C5), 117.1, 127.0, 128.0, 128.5, 132.6, 135.4 (C4), 140.8, 178.3 (C2). UV (EtOH) λ_{max} (lg ε/m^2 mol^{-1}) 321 nm (3.32). Anal. Calcd for $C_{16}H_{19}NOS_2$ (305.45): C, 62.92; H, 6.27; N, 4.59; S, 20.99; Found: C, 62.87; H, 6.45; N, 4.35; S, 20.50.

*4.3.17. (±)-4,5-Dimethyl-3-(cis-2-methylcyclopent-1-oxy)-thiazole-2(3H)-thione (±)-cis-(**6k**).* From (±)-*trans*-2-methylcyclopentyl tosylate (254 mg, 1.00 mmol). The crude product was purified by column chromatography [petroleum ether/Et_2O=2:1 (v/v)]. Yield: 157 mg (0.65 mmol, 65%), colorless oil. R_f=0.41 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 250 MHz) δ 1.24 (d, 3H, J=7.0 Hz), 1.51–1.64 (m, 1H), 1.64–1.76 (m, 2H), 1.79–1.94 (m, 3H), 2.11 (q, 3H, J=0.8 Hz, 4-CH_3), 2.13 (q, 3H, J=0.8 Hz, 5-CH_3), 2.12–2.18 (m, 1H), 5.57 (dt, 1H, J=4.7, 2.2 Hz). ^{13}C NMR ($CDCl_3$, 63 MHz) δ 11.3 (4-CH_3), 12.1 (5-CH_3), 13.5, 21.8, 29.4, 31.4, 39.2, 89.5, 114.4 (C5), 134.0 (C4), 178.9 (C2). UV (EtOH) λ_{max} (lg ε/m^2 mol^{-1}) 321 nm (3.22). Anal. Calcd for $C_{11}H_{17}NOS_2$ (243.38): C, 54.29; H, 7.04; N, 5.76; S, 26.35; Found: C, 54.21; H, 7.28; N, 5.61; S, 26.12.

4.4. Radical reactions

4.4.1. General remarks. Product analysis was performed via ^1H NMR. Yields were determined via integration of ^1H NMR signals versus anisole (δ 3.29 ppm; C_6D_6, 400 MHz) as internal standard.

4.4.2. Standard procedures. Bu_3SnH (3.7 equiv) or $BrCCl_3$ (10.0 equiv) was added under Ar to an oxygen-free solution of 3-alkoxythiazole-2(3*H*)-thione **4**, **5**, or **6** in anhydrous C_6D_6 or C_6H_6 (20 mL/1.0 mmol thiazolethione; standard glassware).

A. *Photochemical reaction I* (*λ=350 nm*). The reaction mixture was photolyzed for 30 min at 20 °C in a Southern New England Rayonet® chamber photo reactor equipped with 350 nm light bulbs.

B. *Photochemical reaction II* (*visible light*). The reaction mixture was photolyzed with external cooling for 30 min at 15 °C with a 250 W Osram Power Star HQI/D discharge lamp (visible light spectrum).

C. *Thermal reaction*. AIBN (5.00 mg, 30.4 μmol/1.0 mmol thiazolethione) was added under Ar to the boiling reaction mixture. If N_2 evolution ceased prior to quantitative 3-alkoxythiazolethione consumption (TLC), additional small portions of AIBN were added (spatula tip) until the starting material was completely consumed.

4.5. 3-Alkoxythiazolthione reactions with $BrCCl_3$

*4.5.1. Conversion of 5-(p-methoxyphenyl)-4-methyl-3-(pent-1-oxy)-thiazole-2(3H)-thione (**4c**). 4.5.1.1. Analytic scale experiments.* Reactants: **4c** (16.1 mg, 50.0 μmol), $BrCCl_3$ (98.8 mg, 500 μmol, 50 μL) in C_6D_6 (1 mL). According to procedure 4.4.2.A: Yield: 1.8 mg (21 %) of 4-bromopentan-1-ol (**11**). ^1H NMR (C_6D_6, 250 MHz) δ 1.29–1.68 (m, 7H), 3.21 (t, 2H, J=7.0 Hz), 3.77 (sext, 1H, J=6.9 Hz). 7.4 mg (42%) of 5-(*p*-methoxyphenyl)-4-methyl-2-(trichloromethylsulfanyl)-thiazole (**13**). According to procedure 4.4.2.B: Yield: 1.4 mg (17%) of **11** and 7.7 mg (44%) of **13**. According to procedure 4.4.2.C: Yield: 7.7 mg (92%) of **11** and 16.7 mg (94%) of **13**.

4.5.1.2. Preparative scale experiment. Reactants: **4c** (161 mg, 500 μmol), $BrCCl_3$ (988 mg, 5.00 mmol, 0.49 mL), AIBN in C_6H_6 (6.00 mL). According to procedure 4.4.2.C. The solvent was evaporated under reduced pressure and the reaction mixture purified by column chromatography [petroleum ether/Et_2O=2:1 (v/v)]. Yield: 72.4 mg (87%) of **11** and 158 mg (89%) of **13**, yellowish powder. Mp 61–62 °C (dec). R_f=0.45 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 600 MHz) δ 2.57 (s, 3H, 4-CH_3), 3.86 (s, 3H, OCH_3), 6.89 (d, 2H, J=8.5 Hz), 7.41–7.49 (d, 2H, J=8.8 Hz). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 16.4 (4-CH_3), 55.5 (OCH_3), 97.3 ($SCCl_3$), 114.5, 123.1 (C5), 130.6, 141.7, 149.9 (C4), 150.4 (C2), 160.1. UV (MeOH) λ_{max} (lg ε/m^2 mol^{-1}) 324 nm (3.44), 227 nm (3.36), 203 nm (3.62). MS (EI) *m*/*z* 359 (1), 357 (7), 355 (19), 353 (18), 321 (3), 319 (4), 248 (8), 238 (10), 236 (100), 203 (27), 192 (17), 179 (5), 177 (38), 160 (21), 145 (26), 134 (8), 121 (3), 119 (5), 117 (5), 108 (10). Anal. Calcd for $C_{12}H_{10}NOS_2Cl_3$ (354.69): C, 40.64; H, 2.84; N, 3.95; S, 18.06; Found: C, 40.81; H, 2.99; N, 3.90; S, 18.51.

*4.5.2. Conversion of 5-(p-methoxyphenyl)-4-methyl-3-(4-phenylbut-1-oxy)-thiazole-2(3H)-thione (**4d**). 4.5.2.1. Analytic scale experiments.* Reactants: **4d** (17.8 mg, 50.0 μmol), $BrCCl_3$ (98.8 mg, 500 μmol, 50 μL) in C_6D_6 (1 mL). According to procedure 4.4.2.A: Yield: 0.7 mg (3.0 μmol, 6%) of 4-bromo-4-phenyl-1-butanol (**12**), R_f=0.12 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR (C_6D_6, 400 MHz) δ 1.18–1.47 (m, 2H), 1.91–2.20 (m, 2H), 3.18 (t, 2H, J=6.2 Hz), 4.71 (t, 1H, J=7.6 Hz), 6.94–7.10 (m, 5H). ^{13}C NMR (C_6D_6, 100 MHz) δ 31.6, 36.9, 55.8 (C-Br), 61.5, 121.4, 127.6, 128.1, 131.1. According to procedure 4.4.2.B: Yield: 0.6 mg (5%) of **12**. According to procedure 4.4.2.C: Yield: 10.4 mg (91%) of **12** and 16.5 mg (93%) of **13**.

*4.5.2.2. 2-Phenyltetrahydrofuran (**16**).* From a solution of 4-methyl-5-(*p*-methoxyphenyl)-3-(4-phenyl-1-butoxy)-thiazole-2(3*H*)-thione (**4d**) (17.8 mg, 50.0 μmol), $BrCCl_3$ (98.8 mg, 500 μmol, 50 μL), and AIBN in C_6H_6 (1 mL). According to procedure 4.4.2.C. The crude product was filtered through basic Al_2O_3 and eluted with Et_2O. The filtrate was concentrated under reduced pressure to furnish 6.2 mg (83%) of **16**.

*4.5.3. Conversion of (±)-5-(p-methoxyphenyl)-4-methyl-3-[cis-2-(prop-2-en-1-yl)cyclohexyl-1-oxy]-thiazole-2(3H)-thione (±)-cis-(**4l**).* Reactants: (±)-*cis*-**4l** (188 mg, 500 μmol), $BrCCl_3$ (988 mg, 5.00 mmol, 0.49 mL) in C_6H_6 (6.00 ml). According to procedure 4.4.2.A. The solvent was evaporated under reduced pressure and the residue purified by chromatography [petroleum ether/Et_2O=5:1 (v/v)]. Yield: 76.7 mg (70%) of 8-bromomethyl-7-oxabicyclo[4.3.0]nonane (±)-(**21**), 6,8-*cis*:6,8-*trans*=72:28, R_f=0.77 [petroleum ether/Et_2O=5:1 (v/v)].

*4.5.4. Conversion of 4-methyl-3-(pent-1-oxy)-5-phenylthiazole-2(3H)-thione (**5c**).* Reactants: **5c** (14.7 mg, 50.0 μmol), $BrCCl_3$

(98.8 mg, 500 μmol, 50 μL), and AIBN in C_6D_6 (1 mL). According to procedure 4.4.2.C: Yield: 6.8 mg (81%) of **11** and 14.5 mg (90%) of 4-methyl-5-phenyl-2-(trichloromethylsulfanyl)-thiazole (**14**), yellowish oil. R_f=0.59 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 400 MHz) δ 2.60 (s, 3H, 4-CH_3), 7.41–7.49 (m, 5H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 16.5 (4-CH_3), 97.2 ($SCCl_3$), 128.9 (C5), 129.1, 129.4, 130.9, 141.6, 150.8 (C4), 151.0 (C2). UV (MeOH) λ_{max} (lg ε/m^2 mol^{-1}) 310 nm (3.46). [$C_{11}H_8NOS_2Cl_3$ (324.66)] MS (EI) *m*/*z* 329 (1), 327 (10), 325 (29), 323 (24), 290 (7), 288 (10), 218 (6), 206 (100), 173 (16), 162 (10), 147 (86), 130 (37), 121 (36), 119 (12), 117 (13), 115 (84), 103 (34).

*4.5.5. Conversion of 4,5-dimethyl-3-(pent-1-oxy)-thiazole-2(3H)-thione (**6c**).* Reactants: **6c** (11.6 mg, 50.0 μmol), $BrCCl_3$ (98.8 mg, 500 μmol, 50 μL), and AIBN in C_6D_6 (1 mL). According to procedure 4.4.2.C: Yield: 6.43 mg (77%) of **11** and 11.5 mg (88%) of 4,5-dimethyl-2-(trichloromethylsulfanyl)-thiazole (**15**), yellowish oil. R_f=0.51 [petroleum ether/Et_2O=2:1 (v/v)]. ^1H NMR ($CDCl_3$, 400 MHz) δ 2.44 (s, 3H, 4-CH_3), 2.45 (s, 3H, 5-CH_3). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 11.9 (4-CH_3), 15.0 (5-CH_3), 97.4 ($SCCl_3$), 136.8 (C5), 148.7 (C4), 152.1 (C2). UV (MeOH) λ_{max} (lg ε/m^2 mol^{-1}) 295 nm (2.90), 224 nm (2.60), 202 nm (2.68). [$C_6H_6NOS_2Cl_3$ (262.60)] MS (EI) *m*/*z* 265 (11), 263 (12), 261 (3), 228 (14), 226 (18), 144 (100), 121 (2), 119 (8), 117 (9), 100 (17).

4.6. 3-Alkoxythiazolthione reactions with Bu_3SnH

*4.6.1. Conversion of (±)-5-(p-methoxyphenyl)-4-methyl-3-(2-phenylpent-4-en-1-oxy)- thiazole-2(3H)-thione (±)-(**4e**).* Reactants: (±)-**4e** (19.9 mg, 50.0 μmol), Bu_3SnH (53.8 mg, 185.0 μmol, 50 μL) in C_6D_6 (1 mL). According to procedure 4.4.2.A: Yield: 5.1 mg (63%) of 2-methyl-4-phenyltetrahydrofuran (±)-(**17**), *cis*:*trans*=87:13, and 21.2 mg (77%) of 5-(*p*-methoxyphenyl)-4-methyl-2-(tributylstannylsulfanyl)-thiazole (**18**), colorless oil, R_f=0.45 [petroleum ether/Et_2O=5:1 (v/v)]. According to 4.4.2.B: Yield: 4.8 mg (59%) of (±)-**17**, *cis*:*trans*=86:14, and 21.6 mg (78%) of **18**. According to 4.4.2.C: Yield: 5.2 mg (64%) of (±)-**17**, *cis*:*trans*=87:13, and 21.2 mg (77%) of **18**.

*4.6.2. Conversion of (±)-5-(p-methoxyphenyl)-4-methyl-3-[cis-(2-methylcyclopent-1-oxy)]-thiazole-2(3H)-thione (±)-cis-(**4k**).* Reactants: (±)-*cis*-(**4k**) (16.8 mg, 50.0 μmol), Bu_3SnH (53.8 mg, 185 μmol, 50 μL) in C_6D_6 (1 mL). According to procedure 4.4.2.A: Yield: 3.9 mg (77%) of hexanal (**22**). ^1H NMR (C_6D_6, 250 MHz) δ 0.77 (t, 3H, *J*=7.3 Hz), 1.19–1.39 (m, 6H), 1.78 (dt, 2H, J_t=7.3 Hz, J_d=1.7 Hz), 9.30 (t, 1H, *J*=1.7 Hz), and 22.6 mg (82%) of **18**. According to 4.4.2.B: 3.9 mg (78%) of **22** and 22.1 mg (80%) of **18**. According to 4.4.2.C: Yield: 3.3 mg (65%) of **22** and 22.9 mg (83%) of **18**.

*4.6.3. Conversion of 5-(p-methoxyphenyl)-4-methyl-3-(2,3,5-tri-O-acetyl-α-D-ribofuranosyl-1-oxy)- thiazole-2(3H)-thione α-(**4m**).* Reactants: α-**4m** (256 mg, 500 μmol), Bu_3SnH (538 mg, 1.85 mmol, 0.49 mL) in C_6H_6 (10 mL). According to procedure 4.4.2.A. After complete substrate consumption (TLC), the solvent was distilled off under reduced pressure to furnish a residue that consisted of a 3/1-mixture of formylester **23**/erythritol **24**. Erythro-butan-1,2,3,4-tetrayl 1,2,4-triacetate-3-formate (**23**). R_f=0.29 [*tert*-butyl methyl ether/pentane=1:1 (v/v)]. ^1H NMR ($CDCl_3$, 600 MHz) δ 2.00 (s, 6H), 2.02 (s, 3H), 4.10 (dd, 1H, *J*=12.3, 5.5 Hz), 4.16 (dd, 1H, *J*=12.4, 5.9 Hz), 4.29 (ddd, 2H, *J*=12.3, 7.9, 3.3 Hz), 5.20 (dt, 1H, *J*=5.9, 3.4 Hz), 5.34 (dt, 1H, *J*=6.1, 3.2 Hz), 8.01 (s 1H). ^{13}C NMR ($CDCl_3$, 150 MHz) δ 20.4, 20.5, 61.3, 61.4, 68.6, 68.8, 159.4, 169.5, 170.2, 170.2. MS (EI) *m*/*z* 203 (50), 161 (20), 145 (77), 128 (52), 115 (100), 103 (75). The residue was purified by chromatography [SiO_2, *tert*-butyl methyl ether/pentane=1:1 (v/v)]. Yield: 69.2 mg (56%) of 1,2,4-tri-*O*-acetyl-D-erythritol (**24**), yellowish oil, R_f=0.16 [methyl tert-butyl ether/pentane=1:1 (v/v)]. ^1H NMR ($CDCl_3$, 600 MHz) δ 2.09 (s, 3H), 2.10 (s, 3H), 2.11 (s, 3H), 3.97 (ddd, 1H, *J*=7.8, 5.3, 3.5 Hz), 4.16 (dd, 1H, *J*=11.8, 5.3 Hz), 4.21 (dd, 1H, *J*=11.8, 3.5 Hz), 4.32 (dd,1H, *J*=12.4, 4.7 Hz), 4.42 (dd, 1H, *J*=12.4, 3.2 Hz), 5.02 (ddd, 1H, *J*=7.8, 4.7, 3.2 Hz). ^{13}C NMR ($CDCl_3$, 63 MHz) δ 20.8, 20.9, 62.3, 65.0, 68.3, 71.1, 170.0, 171.2, 171.3. MS (EI) *m*/*z* 145 (53), 128 (10), 115 (100), 103 (73). Anal. Calcd for $C_{10}H_{16}O_7$ (248.23): C, 48.58; H, 6.12; Found C, 48.52; H, 5.71.

*4.6.4. Conversion of (±)-4-methyl-5-phenyl-3-(2-phenylpent-4-en-1-oxy)-thiazole-2(3H)-thione (±)-(**5e**).* Reactants: (±)-**5e** (18.4 mg, 50.0 μmol), Bu_3SnH (53.8 mg, 185.0 μmol, 50 μL), and AIBN in C_6D_6 (1 mL). According to procedure 4.4.2.C: Yield: 5.0 mg (62%) of 2-methyl-4-phenyltetrahydrofuran (±)-**17**, *cis*:*trans*=87:13 and 19.9 mg (76%) of 4-methyl-5-phenyl-2-(tributylstannylsulfanyl)-thiazole (**19**). ^1H NMR ($CDCl_3$, 200 MHz) δ 0.87–0.94 (t, 9H, *J*=7.1 Hz), 1.26–1.44 (m, 12H), 1.55–1.67 (m, 6H), 2.36 (s, 3H, 4-CH_3), 7.30–7.41 (m, 5H). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 13.6, 16.0 (4-CH_3), 27.0, 27.9, 28.6, 127.2 (C5), 128.5, 128.9, 132.0, 132.5, 146.7 (C4), 162.1 (C2).

*4.6.5. Conversion of (±)-4-methyl-3-(cis-2-methylcyclopentoxy)-5-phenylthiazole-2(3H)-thione (±)-cis-(**5k**).* Reactants: (±)-*cis*-(**5k**) (15.3 mg, 50.0 μmol), Bu_3SnH (53.8 mg, 185.0 μmol, 50 μL) in C_6D_6 (1 mL). According to procedure 4.4.2.A: Yield: 3.10 mg (66%) of **22** and 20.6 mg (79%) of **19**.

*4.6.6. Conversion of (±)-4,5-dimethyl-3-(2-phenylpent-4-en-1-oxy)-thiazole-2(3H)-thione (±)-(**6e**).* Reactants: (±)-**6e** (15.3 mg, 50.0 μmol), Bu_3SnH (53.8 mg, 185.0 μmol, 50 μL), and AIBN in C_6D_6 (1 mL). According to procedure 4.4.2.C: Yield: 5.0 mg (61%) of (±)-**17**, *cis*:*trans*=87:13 and 17.0 mg (78%) of 4,5-dimethyl-2-(tributylstannylsulfanyl)-thiazole-2(3*H*)-thione (**20**). ^1H NMR ($CDCl_3$, 400 MHz) δ 0.87–0.92 (m, 9H), 1.22–1.36 (m, 12H), 1.54–1.61 (m, 6H), 2.16 (s, 3H, 4-CH_3), 2.22 (s, 3H, 5-CH_3). ^{13}C NMR ($CDCl_3$, 50 MHz) δ 11.2 (4-CH_3), 13.6, 14.4 (5-CH_3), 27.0, 27.8, 28.6, 126.3 (C5), 147.1 (C4), 159.2 (C2).

*4.6.7. Conversion of (±)-4,5-dimethyl-3-(cis-2-methylcyclopent-1-oxy)-thiazole-2(3H)-thione (±)-cis-(**6k**).* Reactants: (±)-*cis*-(**6k**) (12.2 mg, 50.0 μmol), Bu_3SnH (53.8 mg, 185.0 μmol, 50 μL) in C_6D_6 (1 mL). According to procedure 4.4.2.C: Yield: 3.6 mg (71%) of **22** and 17.6 mg (81%) of **20**.

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Supplementary data

Instrumentation, spectra of 3-alkoxythiazolethione α-**4m**, trichloromethylsulfanylthiazoles **13**–**15**, tributylstannylsulfanylthiazoles **19**–**20**, formylester **23**, and erythritol **24** (7 pages). Supplementary data associated with this article can be found in the online version at doi:10.1016/j.tet.2009.11.113.

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