A Practical Method for O-Acylation of *N*-Hydroxythiazole-2(3*H*)-thiones

Christine Schur, Andreas Groß, Jens Hartung*

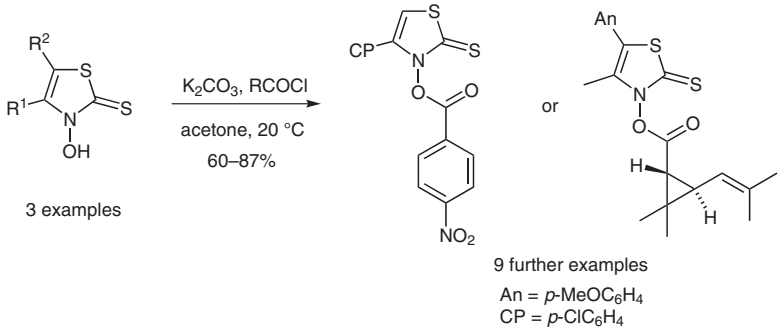
Fachbereich Chemie, Organische Chemie, Technische Universität Kaiserslautern, Erwin-Schrödinger-Straße, 67663 Kaiserslautern, Germany
Fax +49(631)2053921; E-mail: hartung@chemie.uni-kl.de

Received 24 July 2009; revised 9 September 2009

PSP No 177

Abstract: O-Acylation of 4- and 4,5-substituted *N*-hydroxythiazole-2(3*H*)-thiones occurred in solutions of acetone upon treatment with solid K_2CO_3 and a variety of neat acyl chlorides (primary, secondary, and tertiary alkyl, aryl; 60–87% yield; ~10 g scale).

Key words: anhydride, acyl chloride, carbon radical, thiazolethione, thiohydroxamic acid



Scheme 1

Mixed anhydrides composed of carboxylic acids and certain thiohydroxamic acids constitute an important and quite general product class for carbon radical generation in the absence of metal ions under pH neutral conditions.[1] The compounds undergo selective N–O homolysis upon photochemical or thermal activation thus liberating acyloxyl radicals and after decarboxylation, respective carbon radicals.[2,3] The most prominent derivatives of this kind, that is, *O*-acyl derivatives of *N*-hydroxypyridine-2(1*H*)-thione (PTOH, Figure 1), the 'Barton esters',[4] have notably contributed within the past two decades to the progress in synthetic,[3] mechanistic,[5,6] photobiological,[7] and even therapeutic[8] application of free carbon radicals. Thermal and photochemical instability,[9,10] however, precludes the use of *O*-acylpyridine-2(1*H*)-thiones in instances that for technical reasons require synthesis and radical liberation to occur in separate steps. Substantial evidence, however, existed from more recent developments that *O*-acyl derivatives of *N*-hydroxythiazole-2(3*H*)-thiones, for example, **1**–**3**, have the potential to fill this gap.[11,12] Synthesis of cyclic thiohydroxamic acids **1**–**3** is feasible according to well established protocols starting from substituted α-chloro or α-bromo ketones.[11,13,14] This strategy allows to introduce a notable variety of substituents in positions 4 and 5 for controlling photochemical and ground state properties of the thiazole-2(3*H*)-thione entity.[15,16]

Faced with the synthetic task to prepare batches of ~10 g of *N*-acyloxythiazole-2(3*H*)-thiones for reasons outlined above, we realized that none of the available low cost methods was adequate in our hands to solve this simple task in a *satisfactory and reproducible* manner. A scatter of yields ranging from poor (~5%) to satisfactory (~75%) was obtained using established sequences,[11,13] for example, treatment of independently prepared alkali (Li^+, Na^+, K^+) thiohydroxamates with an acyl chloride in solutions of, for example, dichloromethane or acetonitrile.[17] Since others might have encountered similar difficulties, we wish to report here on a modified procedure for the synthesis of *N*-acyloxythiazole-2(3*H*)-thiones. The method is based on a one-pot transformation of thiazole-derived cyclic thiohydroxamic acids, acyl chlorides, and solid potas-

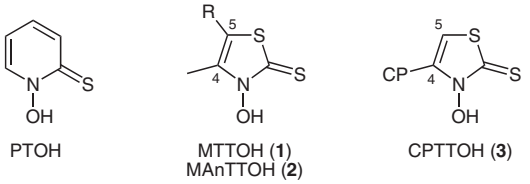


Figure 1 Structural formula of cyclic thiohydroxamic acids **1**–**3** [R = H for **1**, R = *p*-$MeOC_6H_4$ (An) for **2**, CP = *p*-ClC_6H_4 for **3**][15,16]

SYNTHESIS 2010, No. 3, pp 0538–0542
Advanced online publication: 06.11.2009
DOI: 10.1055/s-0029-1217102; Art ID: T14609SS

sium carbonate in acetone at ~20 °C, in combination with a straightforward workup procedure (Scheme 1).

Highest yields of *O*-acylthiazole-2(3*H*)-thiones from the chosen set of substrates (see below) were obtained as follows (Table 1). To a homogeneous solution of a cyclic thiohydroxamic acid (e.g., **1**, **2**, or **3**) in acetone was added an excess of solid potassium carbonate (3 equiv) at ~20 °C in a single batch. This manipulation resulted in a slurry. The temperature of the reaction mixture remained unchanged, even in transformations starting from ~20 mmol of thiohydroxamic acid. The solids changed their appearance from grainy at the beginning to feathery after approximately 30 minutes. At this point, an aliquot of acylating reagent, which was benzoyl chloride (**4a**) in the course of process development, was added. The feathery precipitate almost instantaneously disappeared. Stirring at ambient temperature was continued until complete conversion of acids **1**–**3** had occurred (~30–90 min). This point was evident from spotting of the reaction mixture at intervals of ~15 minutes on iron(II)-stained TLC sheets (Figure 2). The absence of a diagnostic greenish blue color due to complex formation between the transition metal ion and the thiohydroxamate ligand[18] pointed to quantitative consumption of substrates **1**–**3** and thus the moment for terminating the reaction.

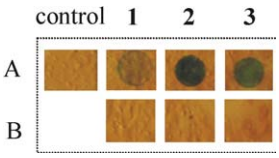
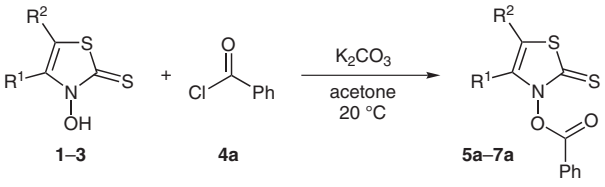


Figure 2 Probing for thiohydroxamic acids via spotting on $FeCl_2$-coated SiO_2 TLC sheets prior to addition of **4a** (A) and after complete consumption of **1**–**3** (B); control refers to a solution of benzoyl chloride and K_2CO_3 in acetone

Table 1 O-Benzoylation of *N*-Hydroxythiazole-2(3*H*)-thiones **1**–**3**

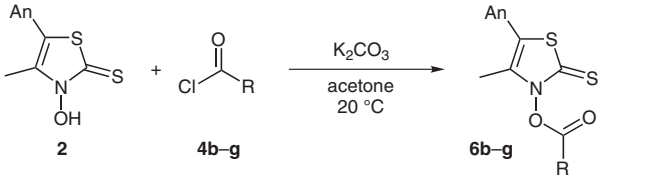


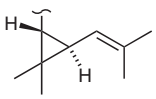
Entry	R^1	R^2	**1**–**3**	Yield (%)
1	Me	H	**1**	**5a**: 84
2	Me	*p*-$MeOC_6H_4$	**2**	**6a**: 81
3	*p*-ClC_6H_4	H	**3**	**7a**: 75

Product isolation was accomplished in two ways. In case of notable salt separation after quantitative thiohydroxamic acid turnover, solids were removed by filtration to afford a clear solution. Volatile components were removed under reduced pressure to furnish a yellowish to dark residue that was (re)crystallized from a mixture of CH_2Cl_2/Et_2O/pentane. In an alternative procedure, the solids were dissolved in a minimum volume of water. The target product was transferred into an organic absorber phase (see experimental section). Analytically pure anhydrides **5a**–**7a** were obtained as tan (**5a** and **7a**) to yellowish (**6a**) solids, which were preferentially kept in amber-colored vials. Anhydride **6a** was expected to be a colorless compound, as judged on the basis of its UV/Vis spectrum. A material showing this appearance was obtained via chromatographic purification [Et_2O–pentane (1:1), $R_f = 0.18$, yellowish spot on silica gel TLC plate], although considerable loss of thione **6a** occurred upon contact with silica gel.

For reasons of favorable stability toward storage in combination with noteworthy reactivity upon photochemical or thermal activation (vide infra), *N*-hydroxy-4-methyl-5-(4-methoxyphenyl)thiazole-2(3*H*)-thione (**2**)[16] was chosen for probing the more general applicability of the O-acylation process. Thus, acyl chlorides **4b**–**g** differing in steric congestion and polar effect of substituents attached to the carboxyl C-atom were subjected to standard conditions to furnish the mixed anhydrides **6b**–**g** in yields between 69–87% (Table 2, entries 1–6). NMR data recorded for mixed anhydride **6g** in $CDCl_3$ or preferentially in C_6D_6 showed a two-fold signal set in a 50:50 intensity ratio. This observation was attributed to slow rotation of the chiral acyl subunit about the stereogenic N–O bond and thus the existence of diastereomers under such conditions.[11] Storage of *N*-acyloxythiazolethiones without significant decomposition was feasible in amber colored vials, preferentially in a refrigerator. Treatment of acid **2** with 4-nitrobenzoyl chloride under established conditions provided the expected product, however, for unknown reasons with a considerable scatter of yields (not shown). The use of acids MTTOH (**1**) and CPTTOH (**3**), on the other hand gave *O*-(4-nitrobenzoyl)thiazole-2(3*H*)-

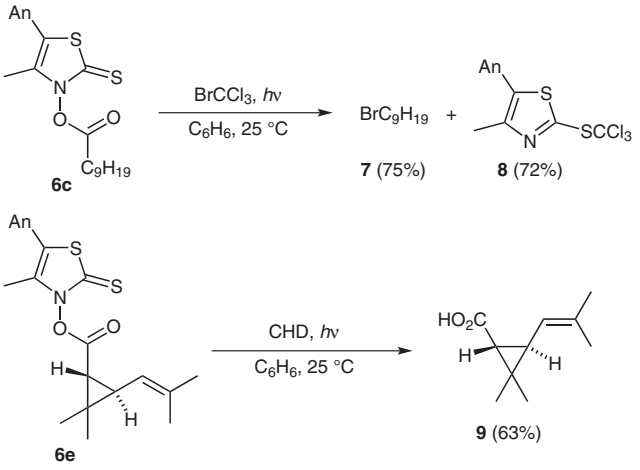
Table 2 Formation of Mixed Anhydrides from MAnTTOH (**2**) and Acyl Chlorides **4b**–**g**



Entry	R	**4**/**6**	Yield (%) of **6**
1	Me	**b**	87
2	*n*-C_9H_{19}	**c**	69
3	*c*-C_6H_{11}	**d**	85
4		**e**	73
5		**f**	79
6	*p*-$MeOC_6H_4$	**g**	74

thiones in 63% (from **1**) and 60% yield (from **3**) as analytically pure compounds (Scheme 1, experimental section).

The ability of *O*-acyl derivatives of MAnTTOH (**2**) to liberate free radicals was clarified with the aid of two diagnostic experiments. Photolysis (350 nm, Rayonet® chamber photoreactor, 25 °C) of *N*-(decanoyloxy)thiazole-2(3*H*)-thione (**6c**) in a solution of $BrCCl_3$ and benzene provided 75% of bromononane (**7**) and 72% of trichloromethylsulfanylthiazole **8** (Scheme 2). The underlying chemistry agrees with reactivity described for the Barton version of the Hunsdiecker reaction.[19] Adapting conditions for the conversion of **6c** to the transformation of *N*-[*trans*-(2,2-dimethyl-3-dimethylvinyl)cyclopropancarbonyloxy] derivative **6e** using cyclohexa-1,4-diene (CHD) as trapping reagent gave *trans*-chrysanthemic acid as a single detectable product from the acyl residue in 63% yield (Scheme 2). The observed reactivity of thione **6e** reflected the propensity of the underlying cyclopropanecarbonyloxyl radical to preferentially abstract a H-atom from a suitable donor, such as CHD. Its decarboxylation is expected to be disfavored due to the σ-character of the cyclopropyl radical[20] that would result.



Scheme 2 Photochemical conversion of *N*-acyloxythiazolethiones **6c** and **6e** in the presence of suitable trapping reagents (see text)

Although the selection of *N*-hydroxythiazole-2(3*H*)-thiones **1**–**3** and acyl chlorides **4a**–**g** reflects preferences from this laboratory and not all permutations were put into practice, we believe that the number of examples suffices to document the utility of a surprisingly simple as much as useful *N*-acyloxythiazole-2(3*H*)-thione synthesis. It saves at least one synthetic step, uses predominantly environmentally benign reagents, and allows a rapid scale-up of the protocol for larger-scale syntheses. The procedure is therefore expected to contribute in a quite general manner to new developments in *O*-acylthiohydroxamate chemistry.

Melting points (°C) were determined on a Koffler hot-plate melting point microscope (Reichert). ^{1}H and ^{13}C NMR spectra were recorded with FT-NMR DPX 200, DPX 400 and DMX 600 instruments (Bruker). Chemical shifts refer to the δ-scale. The resonances of residual protons and those of carbons in deuterated solvents $CDCl_3$ (δ_H = 7.26 ppm, δ_C = 77.0 ppm), C_6D_6 (δ_H = 7.16 ppm, δ_C = 128.06 ppm), DMSO-d_6 (δ_H = 2.50 ppm, δ_C = 39.52 ppm) were used as internal standards. UV/Vis spectra were recorded in 1-cm quartz cuvettes with a Perkin Elmer UV/Vis 330 spectrometer and a Cary 100 Conc, spectrometer (VARIAN). Combustion analysis was performed with a vario Micro cube (analytical laboratory, Technische Universität Kaiserslautern). All solvents were purified according to standard procedures.[21] Unless otherwise indicated, solvent mixtures are given in v/v ratios.

O-Acylation of *N*-Hydroxythiazole-2(3*H*)-thiones 1–3; General Procedure

Solid K_2CO_3 (0.41 g, 3.00 mmol) was added to a solution of thiohydroxamic acid **1**, **2**, or **3** (1.00 mmol) in acetone (9 mL). The slurry was stirred for 10 min at 20 °C leading to a change in the appearance of the precipitate from grainy to feathery. To this suspension was added in one batch the appropriate neat acid chloride (1.10 mmol) and the stirring was continued at 20 °C (30–90 min). Consumption of acids **1**–**3** was followed by spotting the reaction mixture at intervals of ~15 min on $FeCl_2$-coated TLC sheets. The end of the reaction was evident from an absence of greenish blue Fe(II)-thiohydroxamate color (Figure 2).

Product Isolation via Filtration: Excess of solids was filtered off to afford a clear solution, which was evaporated to dryness. Upon addition of Et_2O (5 mL/mmol), the residue immediately solidified. The resulting suspension was stirred for 15 min at 20 °C. The crystalline solids were collected by filtration and dried (40 °C/5 mbar). If no solids appeared, the mixture was allowed to rest at –30 °C.

Product Isolation via Extraction: H_2O (10 mL) was added for dissolving the solids to afford a mixture, which was extracted with Et_2O (2 × 10 mL) and EtOAc (2 × 10 mL). The combined organic extracts were washed with aq 2 M NaOH (10 mL) and brine (10 mL). The combined organic phases were dried ($MgSO_4$) and concentrated under reduced pressure (40 °C/800 → 8 mbar). The residue was taken up in a minimum amount of CH_2Cl_2–Et_2O (1:2). Pentane was added at 20 °C until a slight turbidity remained upon swirling. The mixture was allowed to rest at –30 °C. The solids that separated were collected by suction and dried in aluminum foil wrapped flasks (20 °C/1.5 × 10^{-2} mbar).

N-Benzoyloxy-4-methylthiazole-2(3*H*)-thione (5a)

Yield: 210 mg (84%, 0.84 mmol); yellowish solid; 89–93 °C (dec.).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.21 (s, 3 H, 4-CH_3), 6.30 (s, 1 H, H-5), 7.59–7.51 (m, 2 H), 7.75–7.68 (m, 2 H), 8.25–8.20 (m, 1 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 13.5 (4-CH_3), 102.5 (C-5), 125.3, 129.1, 130.7, 135.2, 137.4 (C-4), 162.4 (C=O), 181.0 (C=S).

UV (CH_2Cl_2): λ_{max} [lg (ε/m^2 mol^{-1})] = 320 nm [3.26].

Anal. Calcd for $C_{11}H_9NO_2S_2$ (363.50): C, 52.57; H, 3.61; N, 5.57. Found: C, 52.51; H, 3.47; N, 5.46.

N-Benzoyloxy-4-methyl-5-(4-methoxyphenyl)thiazole-2(3*H*)-thione (6a)[17]

Yield: 290 mg (81%, 0.81 mmol); yellowish solid; mp 86–89 °C (dec.).

N-Benzoyloxy-4-(4-chlorophenyl)thiazole-2(3*H*)-thione (7a)[13]

Yield: 260 mg (75%, 0.75 mmol); yellowish solid; mp 102–105 °C (dec.).

N-Acetyloxy-4-methyl-5-(4-methoxyphenyl)thiazole-2(3*H*)-thione (6b)

Yield: 258 mg (87%, 0.87 mmol), yellowish solid; mp 79–83 °C (dec.).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 2.16 (d, *J* = 7.8 Hz, 3 H, 4-CH_3), 2.43 (s, 3 H), 3.81 (s, 3 H, OCH_3), 6.92 (m_c, 2 H), 7.22 (m, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 12.0 (4-CH_3), 18.1, 55.5 (OCH_3), 114.7, 119.2 (C-5), 122.2, 130.1, 131.4 (C-4), 160.1, 166.1 (C=O), 179.3 (C=S).

UV (CH_2Cl_2): λ_{max} [lg (ε/m^2 mol^{-1})] = 332 nm [3.17].

Anal. Calcd for $C_{13}H_{13}NO_3S_2$ (295.38): C, 52.86; H, 4.44; N, 4.74. Found: C, 52.21; H, 4.38; N, 4.59.

***N*-Decanoyloxy-4-methyl-5-(4-methoxyphenyl)thiazole-2(3*H*)-thione (6c)**

Yield: 281 mg (69%, 0.69 mmol); reddish oil.

^{1}H NMR (600 MHz, $CDCl_3$): δ = 0.88 (t, *J* = 6.9 Hz, 3 H), 1.27–1.34 (m, 10 H), 1.49–1.46 (m, 2 H), 1.78–1.87 (m, 2 H), 2.19 (s, 3 H, 4-CH_3), 2.71 (m_c, 2 H), 3.83 (s, 3 H, OCH_3), 6.95 (m_c, 2 H), 7.26 (m_c, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.2 (4-CH_3), 22.2, 24.9, 29.4, 29.5, 32.0, 34.1, 55.5 (OCH_3), 68.1, 114.4, 114.5 (C-5), 114.6, 130.5, 130.6, 130.8 (C-4), 160.6, 165.9 (C=O), 178.8 (C=S).

UV (CH_2Cl_2): λ_{max} [lg (ε/m^2 mol^{-1})] = 300 nm [2.95].

Anal. Calcd for $C_{21}H_{29}NO_3S_2$ (407.59): C, 61.88; H, 7.17; N, 3.44. Found: C, 61.75; H, 7.32; N, 3.71.

***N*-Cyclohexylcarbonyloxy-4-methyl-5-(4-methoxyphenyl)thiazole-2(3*H*)-thione (6d)**

Yield: 309 mg (85%, 0.85 mmol); yellowish solid; mp 89–91 °C (dec.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25–1.41 (m, 4 H), 1.64–1.72 (m, 3 H), 1.86 (m_c, 2 H), 2.08–2.10 (m_c, 1 H), 2.17 (s, 3 H, 4-CH_3), 3.83 (s, 3 H, OCH_3), 6.94 (m_c, 2 H), 7.24 (m_c, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 12.0 (4-CH_3), 25.1, 25.3, 29.4, 41.0, 55.5 (OCH_3), 114.7, 119.2 (C-5), 122.4, 130.2, 131.5 (C-4), 160.2, 171.3 (C=O), 179.4 (C=S).

UV (CH_2Cl_2): λ_{max} [lg (ε/m^2 mol^{-1})] = 334 nm [3.33].

Anal. Calcd for $C_{18}H_{21}NO_3S_2$ (363.50): C, 59.48; H, 5.82; N, 3.85. Found: C, 59.14; H, 5.74; N, 3.75.

***N*-[*trans*-2,2-Dimethyl-3-(2-methylpropenyl)cyclopropanecarbonyloxy]-5-(4-methoxyphenyl)-4-methylthiazole-2(3*H*)-thione (6e)**

Yield: 295 mg (73%, 0.73 mmol); yellowish solid; mp 86–87 °C (dec.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.25 (s, 3 H), 1.27 (s, 3 H), 1.34 (s, 3 H), 1.40 (s, 3 H), 1.71 (d, *J* = 7.0 Hz, 2 H), 1.72 (s, 6 H), 1.74 (s, 6 H), 2.17 (s, 3 H, 4-CH_3), 2.20 (s, 3 H, 4-CH_3), 2.23–2.29 (m, 2 H), 3.82 (s, 6 H, OCH_3), 4.98 (d, *J* = 6.2 Hz, 2 H), 6.63 (d, *J* = 8.8 Hz, 4 H), 7.25 (d, *J* = 8.6 Hz, 4 H).

^{1}H NMR (600 MHz, C_6D_6): δ = 0.94 (s, 3 H), 1.03 (s, 3 H), 1.28 (s, 3 H), 1.52 (s, 3 H), 1.57 (s, 3 H), 1.59 (s, 3 H), 1.66 (s, 3 H), 1.74 (s, 4 H), 1.77 (s, 4 H), 2.39 (d, *J* = 5.2 Hz, 2 H), 3.24 (s, 6 H, OCH_3), 4.85 (d, *J* = 8.0 Hz, 2 H), 6.59 (d, *J* = 7.4 Hz, 4 H), 6.81 (d, *J* = 7.4 Hz, 4 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.1 (4-CH_3), 18.7, 18.9, 20.7, 22.0, 22.1, 25.7, 31.2, 31.3, 31.5, 32.6, 35.5, 55.5 (OCH_3), 114.8, 118.8, 119.3 (C-5), 120.0 (C-5), 122.7, 130.2, 131.7, 131.8, 137.3, 138.1 (C-4), 138.2 (C-4), 160.2, 168.1 (C=O), 168.5 (C=O), 179.5 (C=S), 179.6 (C=S).

^{13}C NMR (100 MHz, C_6D_6): δ = 11.6 (4-CH_3), 11.7 (4-CH_3), 18.4, 18.8, 20.6, 20.8, 21.7, 21.9, 25.5, 25.6, 30.7, 31.7, 31.8, 32.1, 35.1, 35.5, 54.7 (OCH_3), 114.6, 117.9, 119.6 (C-5), 120.6 (C-5), 122.9, 130.2, 131.4, 131.6, 136.7, 138.1 (C-4), 160.2, 168.4 (C=O), 168.8 (C=O), 179.8 (C=S), 180.0 (C=S).

UV (MeOH): λ_{max} [lg (ε/m^2 mol^{-1})] = 329 nm [3.09].

Anal. Calcd for $C_{21}H_{25}NO_3S_2$ (403.55): C, 62.50; H, 6.24; N, 3.47. Found: C, 62.30; H, 6.29; N, 3.47.

***N*-Adamantylcarbonyloxy-4-methyl-5-(4-methoxyphenyl)thiazole-2(3*H*)-thione (6f)**

Yield: 328 mg (79%, 0.79 mmol); yellowish solid; mp 106–107 °C (dec.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.81 (m, 6 H), 2.11–2.15 (m, 3 H), 2.17 (s, 3 H, 4-CH_3), 2.20 (m, 6 H), 3.85 (s, 3 H, OCH_3), 6.97 (m_c, 2 H), 7.28 (m_c, 2 H).

^{13}C NMR (150 MHz, $CDCl_3$): δ = 12.0 (4-CH_3), 27.8, 36.3, 38.7, 40.9, 55.5 (OCH_3), 114.7, 119.2 (C-5), 122.4, 130.1, 131.6 (C-4), 160.1, 172.6 (C=O), 179.3 (C=S).

UV (CH_2Cl_2): λ_{max} [lg (ε/m^2 mol^{-1})] = 335 nm [3.36].

Anal. Calcd for $C_{22}H_{25}NO_3S_2$ (415.57): C, 63.58; H, 6.06; N, 3.37. Found: C, 62.98; H, 5.88; N, 3.37.

***N*-(4-Methoxybenzoyl)-4-methyl-5-(4-methoxyphenyl)thiazole-2(3*H*)-thione (6g)**

Yield: 287 mg (74%, 0.74 mmol); yellow solid; mp 112–116 °C (dec.).

^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.25 (s, 3 H, 4-CH_3), 3.84 (s, 3 H, OCH_3), 3.91 (s, 3 H, OCH_3), 6.96 (m_c, 2 H), 7.03 (m_c, 2 H), 7.30 (m_c, 2 H), 8.21 (m_c, 2 H).

^{13}C NMR (100 MHz, $CDCl_3$): δ = 12.2 (4-CH_3), 55.6 (OCH_3), 55.8 (OCH_3), 114.6, 114.9, 119.0 (C-5), 122.7, 126.8, 130.2, 132.4, 133.20 (C-4), 160.3, 162.2, 165.4 (C=O), 179.8 (C=S).

UV (CH_2Cl_2): λ_{max} [lg (ε/m^2 mol^{-1})] = 334 nm [3.27].

Anal. Calcd for $C_{19}H_{17}NO_4S_2$ (387.47): C, 58.90; H, 4.42; N, 3.61. Found: C, 58.74; H, 4.57; N, 3.58.

***N*-(4-Nitrobenzoyl)-4-methylthiazole-2(3*H*)-thione**

Yield: 187 mg (63%, 0.63 mmol); tan solid; mp 127–131 °C (dec.).

^{1}H NMR (200 MHz, DMSO-d_6): δ = 2.26 (s, 3 H, 4-CH_3), 6.93 (s, 1 H, H-5), 8.50–8.40 (m, 4 H).

^{13}C NMR (50 MHz, DMSO-d_6): δ = 12.6 (4-CH_3), 103.9 (C-5), 124.3, 130.1, 131.8, 137.2 (C-4), 151.3, 160.7 (C=O), 179.9 (C=S).

UV (CH_2Cl_2): λ_{max} [lg (ε/m^2 mol^{-1})] = 318 nm [3.02].

Anal. Calcd for $C_{18}H_{14}N_2O_5S_2$ (296.32): C, 44.59; H, 2.72; N, 9.45. Found: C, 44.65; H, 2.73; N, 9.42.

***N*-(4-Nitrobenzoyl)-4-(4-chlorophenyl)thiazole-2(3*H*)-thione**

Yield: 240 mg (61%, 0.61 mmol); tan solid; mp 165–171 °C (dec.).

^{1}H NMR (200 MHz, $CDCl_3$): δ = 6.67 (s, 1 H, H-5), 7.34–7.45 (m, 4 H), 8.23–8.34 (m, 4 H).

^{13}C NMR (50 MHz, $CDCl_3$): δ = 105.4 (C-5), 124.1, 126.1, 129.4, 130.5, 131.8, 136.7, 140.0 (C-4), 151.6, 160.6 (C=O), 181.4 (C=S).

UV(CH_2Cl_2): λ_{max} [lg (ε/m^2 mol^{-1})] = 322 nm [2.99].

Anal. Calcd for $C_{16}H_9ClN_2O_4S_2$ (392.84): C, 48.92; H, 2.31; N, 7.13. Found: C, 48.88; H, 2.22; N, 6.98.

Photoreaction of *N*-Acyloxythiazole-2(3*H*)-thiones; General Procedure

To an oxygen-free solution of *N*-(acyloxy)thiazole-2(3*H*)-thione **6c** or **6e** (1.0 equiv) in anhyd C_6H_6 (12 mL/1.0 mmol thiazolethione) were added CHD (10.0 equiv) or $BrCCl_3$ (10.0 equiv). The reaction mixture was irradiated for 90 min (**6c**) or 7.5 h (**6e**) at 20 °C in a Rayonet® photochamber (λ_{max} = 350 nm). Product analysis was performed by ^{1}H and ^{13}C NMR spectroscopy. Yields were determined

via integration of ^{1}H NMR signals versus pentachlorbenzene (400 MHz, $CDCl_3$: δ = 7.55) as internal standard.

Bromononane (7) and 4-Methyl-5-(4-methoxyphenyl)-2-(trichloromethylsulfanyl)thiazole-2(3*H*)-thione (8)

Transformation of thiazolethione **6c** (363 mg, 0.89 mmol) and $BrCCl_3$ (1.76 g, 0.9 mL, 8.9 mmol) in C_6H_6 (11 mL) was carried out according to the general procedure.

Bromononane (7)[22]

Yield: 138 mg (75%, 0.67 mmol).

4-Methyl-5-(4-methoxyphenyl)-2-(trichloromethylsulfanyl)thiazole-2(3*H*)-thione (8)

Yield: 227 mg (72%, 0.64 mmol); mp 61–62 °C.

^{1}H NMR ($CDCl_3$, 600 MHz): δ = 2.57 (s, 3 H, 4-CH_3), 3.86 (s, 3 H, OCH_3), 6.89 (d, *J* = 8.5 Hz, 2 H), 7.41–7.49 (d, *J* = 8.8 Hz, 2 H).

^{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 (C-5), 130.6, 141.7, 149.9 (C-4), 150.4 (CS), 160.1.

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).

UV (MeOH): λ_{max} [lg (ε/m^2 mol^{-1})] = 324 (3.44), 227 (3.36), 203 nm (3.62).

Anal. Calcd for $C_{12}H_{10}Cl_3NOS_2$ (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.

***trans*-2,2-Dimethyl-3-(2-methylpropen-1-yl)cyclopropanecarboxylic Acid[23]**

Transformation of thiazolethione **6e** (100 mg, 0.25 mmol) and CHD (200 mg, 2.5 mmol) in C_6H_6 (3 mL) was carried out according to the general procedure.

Yield: 26.5 mg (63%, 0.16 mmol).

Acknowledgment

This work is part of Ph.D. theses of C.S. and A.G. It was supported by the state of Rheinland-Pfalz (scholarship for A.G.). We express our gratitude to Prof. Helmut Ritter (Universität Düsseldorf) for stimulating discussions.

References

(1) Barton, D. H. R.; Crich, D.; Motherwell, W. B. *J. Chem. Soc., Chem. Commun.* **1983**, 939.
(2) Motherwell, W. B.; Imboden, C. In *Radicals in Organic Synthesis*, Vol. 1; Renaud, P.; Sibi, M. P., Eds.; Wiley-VCH: Weinheim, **2001**, 109–134.
(3) Crich, D.; Quintero, L. *Chem. Rev.* **1989**, *89*, 1413.
(4) Shaw, E. *J. Am. Chem. Soc.* **1949**, *71*, 67.
(5) Schneiders, N.; Gottwald, T.; Hartung, J. *Eur. J. Org. Chem.* **2009**, 799.
(6) Barton, D. H. R.; Blundell, P.; Jaszberenyi, J. Cs. *J. Am. Chem. Soc.* **1991**, *113*, 6937.
(7) Theodorakis, E. A.; Xiang, X.; Lee, M.; Gibson, T. *Tetrahedron Lett.* **1998**, *39*, 3383.
(8) Castagnino, E.; Cangiotti, M.; Tongiani, S.; Ottaviani, M. F. *J. Controlled Release* **2005**, *108*, 215.
(9) Barton, D. H. R.; Parekh, S. I. In *Half a Century of Free Radical Chemistry*; Cambridge University Press: Cambridge, **1993**, Chap. 5, 46–90.
(10) Garner, P.; Anderson, J. T.; Dey, S. *J. Org. Chem.* **1998**, *63*, 5732.
(11) Hartung, J.; Schur, C.; Kempter, I.; Altermann, S.; Stapf, G.; Bergsträßer, U.; Gottwald, T.; Heubes, M. *Tetrahedron* **2009**, *65*, 7527.
(12) Barton, D. H. R.; Crich, D.; Kretschmar, G. *J. Chem. Soc., Perkin Trans. 1* **1986**, 39.
(13) Hartung, J.; Schwarz, M.; Svoboda, I.; Fueß, H.; Duarte, M.-T. *Eur. J. Org. Chem.* **1999**, 1275.
(14) Hartung, J.; Schwarz, M. *Synlett* **2000**, 371.
(15) Hartung, J.; Schwarz, M. *Org. Synth. Coll. Vol. 10*; Wiley: New York, **2004**, 437–441.
(16) Gross, A.; Schneiders, N.; Daniel, K.; Gottwald, T.; Hartung, J. *Tetrahedron* **2008**, *64*, 10882.
(17) Hartung, J.; Altermann, S.; Svoboda, I.; Fuess, H. *Acta Crystallogr., Sect. E* **2005**, *61*, o1738.
(18) Chimiak, A.; Pryzchodzen, W.; Rachon, J. *Heteroat. Chem.* **2002**, *13*, 169.
(19) Barton, D. H. R.; Lacher, B.; Zard, S. Z. *Tetrahedron* **1987**, *43*, 4321.
(20) Giese, B.; Stellmach, J. *Chem. Ber.* **1980**, *113*, 3294.
(21) Perrin, D. D.; Armarego, W. L. F.; Perrin, D. R. *Purification of Laboratory Chemicals*; 2nd ed., Pergamon Press: Oxford, **1980**.
(22) Midgley, G.; Thomas, C. B. *J. Chem. Soc., Perkin Trans. 2* **1987**, 1103.
(23) Wang, M.-X.; Feng, ; G, Q. *J. Org. Chem.* **2003**, *68*, 621.