248. Photochemistry of 5,5-Dimethyl-2(5*H*)-thiophenone

by **René Kiesewetter** and **Paul Margaretha***

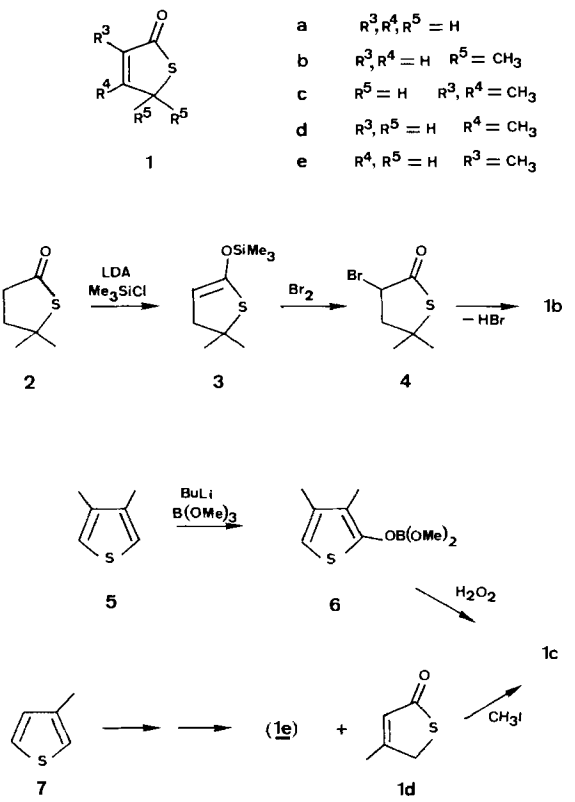
Institut für Organische Chemie, Universität, Martin-Luther-King-Platz 6, D–2000 Hamburg 13

(5.IX.85)

On irradiation (λ > 305 nm) in alcohols, 5,5-dimethyl-2(5*H*)-thiophenone (**1b**) is converted to (*E*)-4-mercapto-4-methyl-2-pentenoates **8**. These esters undergo a consecutive light-induced reaction affording thiolanes when irradiated in the presence of alkenes, and either 2,3-dihydrothiophenes or 3-thiabicyclo[3.1.0]hexanes with alkynes.

We have recently presented results [1] [2] on the photochemical behaviour of 2(5*H*)-thiophenone (**1a**) which, in contrast to the corresponding furan derivative [3], does not

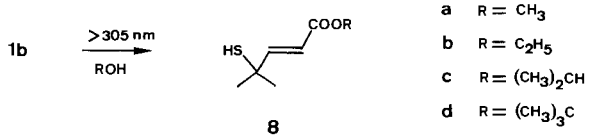
Scheme 1



undergo typical enone reactions as cyclodimerization or [2 + 2] cycloaddition to olefins, but instead reacts with alcohols to give 4-mercaptocrotonates. We have now synthesized 5,5-dimethyl-2(5*H*)-thiophenone (**1b**) and have developed a new synthesis of the 3,4-dimethyl isomer **1c** to investigate their photochemistry and compare it to that of **1a**.

Title compound **1b** was synthesized from thiolactone **2** *via* the ketene O,S-acetal **3** and the bromothiolactone **4**. Compound **1c** was obtained from 3,4-dimethylthiophene (**5**) *via* H_2O_2 oxidation of the boronic ester **6**. Compound **1c** had already been formed together with other isomers by methylation of 4-methyl-2(5*H*)-thiophenone (**1d**) [4], which in turn is obtained as the major product together with the 3-methyl isomer **1e** in a similar sequence starting with 3-methylthiophene (**7**) [5] *(Scheme 1)*.

Scheme 2



Irradiation ($\lambda > 305$ nm) in alcohols affords (*E*)-4-mercapto-4-methyl-2-pentenoates **8** selectively *(Scheme 2)*. The reaction proceeds about twice as fast as the analogous formation of 4-mercaptocrotonates from **1a** and again does not occur in the dark. In contrast, the 3,4-dimethyl isomer **1c** is not converted to a mercapto-ester; even after a tenfold irradiation period (as compared to **1a** or **1b**), less than 5% of starting material is consumed.

On further irradiation, ester **8a** is slowly converted to a new product **9**, whose formation can be monitored by ^{1}H-NMR spectroscopy, but isolation by either chromatography or preparative GC failed due to its decomposition and/or polymerization. The assignment of a ketene-acetal structure to **9** is based on this ^{1}H-NMR data alone and has

Scheme 3

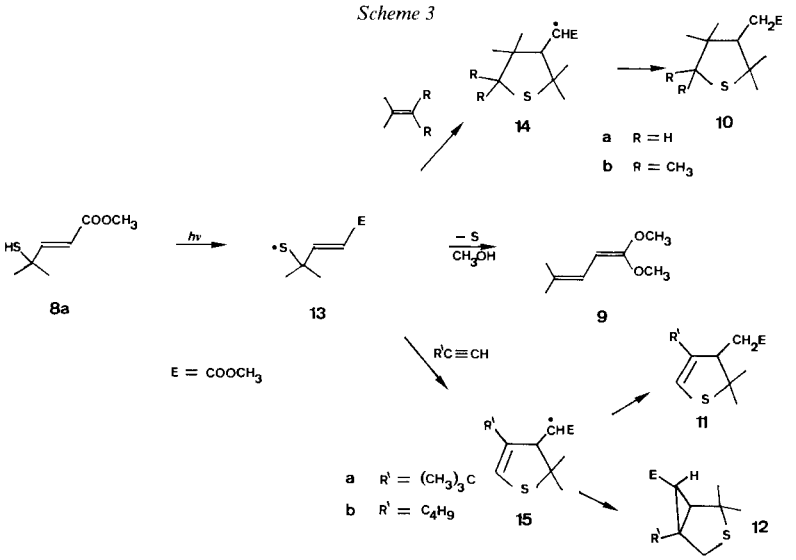


Table. *Spectroscopic Data of* **1b–e** *and of Photoproducts* **8–12**

Compound [a])	UV (Cyclohexane)	IR (Film)	^{1}H-NMR ($CDCl_3$)	^{13}C-NMR ($CDCl_3$)	MS
1b	334 (1.19) 319 (1.64) 267 (3.28)	1680 1600	7.27, 6.12 (*AB*, *J* = 6.0); 1.67 (*s*, CH_3)	198.5 (*s*); 164.7 (*d*); 128.6 (*d*); 58.6 (*s*); 28.0 (*q*)	*128* (M^+)
1c	319 (1.20) 307 (1.67) 255 (3.20) 226 (3.60)	1680 1640	3.85 (*m*, 2 H); 2.15, 1.87 (*m*, CH_3)	200.3 (*s*); 158.7 (*s*); 134.9 (*s*); 38.8 (*t*); 17.5, 10.1 (*q*)	*128* (M^+)
1d	324 (1.18) 311 (1.59) 261 (3.26)	1685 1660 1640	6.07 (*tq*, *J* = 1.2, 1.9); 3.98 (*dq*, *J* = 1.3, 1.2); 2.20 (*dt*, *J* = 1.9, 1.3)		*114* (M^+)
1e	259 (3.25)	1680 1660 1640	7.24 (*tq*, *J* = 3.0, 1.5); 3.94 (*dq*, *J* = 3.0, 2.2); 1.91 (*dt*, *J* = 1.5, 2.2)		*114* (M^+)
8a		1730 1650	7.07, 5.81 (*AB*, *J* = 15.7); 3.74 (*s*, OCH_3); 1.95 (*s*, SH); 1.52 (*s*, CH_3)	[b]) 166.7 (*s*); 155.5 (*d*); 116.3 (*d*); 51.1 (*q*); 42.9 (*s*); 30.5 (*q*)	160 (M^+) *67*
8b		1720 1650	7.10, 5.81 (*AB*, *J* = 15.7); 4.22 (*q*, *J* = 7.0); 2.01 (*s*, SH); 1.55 (*s*, CH_3); 1.33 (*t*, *J* = 7.0)	[b]) 166.3 (*s*); 155.2 (*d*); 116.8 (*d*); 60.2 (*t*); 42.9 (*s*); 30.6 (*q*); 14.3 (*q*)	174 (M^+) *67*
8c		1720 1650	7.04, 5.83 (*AB*, *J* = 15.7); 5.52 (*M*, *J* = 6.3); 1.97 (*s*, SH); 1.54 (*s*, CH_3); 1.25 (*d*, *J* = 6.3)	[b]) 165.9 (*s*); 155.0 (*d*); 117.2 (*d*); 67.6 (*d*); 43.0 (*s*); 30.6 (*q*); 21.9 (*q*)	188 (M^+) *95*
8d		[c]) 1710 1640	6.97, 5.72 (*AB*, *J* = 15.7); 1.97 (*s*, SH); 1.52 (*s*, CH_3); 1.49 (*s*, $C(CH_3)_3$)	[b]) 165.8 (*s*); 154.4 (*d*); 118.5 (*d*); 79.9 (*s*); 42.9 (*s*); 30.8 (*q*); 28.2 (*q*)	202 (M^+) *57*
9			[b]) 5.42 (*dm*, *J* = 10.0, 1.0); 4.47 (*d*, *J* = 10.0); 3.32, 3.17 (*s*, OCH_3) 1.55, 1.47 (*d*, *J* = 1.0, CH_3)		
10a		1740	3.66 (*s*, OCH_3); 2.85, 2.42 (*AB*, *J* = 11.2); 2.13 (*d*, *J* = 7.0, 2 H); 2.07 (*t*, *J* = 7.0); 1.38, 1.29 (*s*, CH_3); 1.04 (*s*, CH_3, 6 H)	173.6 (*s*); 57.5 (*d*); 54.4 (*s*); 51.5 (*q*); 47.3 (*s*); 44.9 (*t*); 34.0 (*q*); 31.2 (*t*); 28.8 (*q*); 27.6 (*q*); 21.8 (*q*)	216 (M^+) *127*
10b		1745	3.70 (*s*, OCH_3); 2.63–2.26 (*ABX*, J_{AB} = 14.6, J_{AX} = 8.3, J_{BX} = 5.8); 1.41, 1.39, 1.27, 1.17, 0.98, 0.82 (*s*, CH_3)	174.0; 56.9; 55.4; 51.6; 51.1; 50.8; 35.6; 31.7; 30.2; 28.1; 23.6; 22.5; 19.8	244 (M^+) *128*
11a		[c]) 1745	5.80 (*s*); 3.71 (*s*, OCH_3); 3.00–2.22 (*ABX*, J_{AB} = 16.8, J_{AX} = 10.0, J_{BX} = 0.8); 1.48, 1.30 (*s*, CH_3); 1.14 (*s*, $C(CH_3)_3$)	173.6 (*s*); 148.8 (*s*); 117.4 (*d*); 60.3 (*s*); 51.8 (*q*); 51.6 (*d*); 34.7 (*s*); 31.7 (*t*); 30.7 (*q*); 29.8 (*q*); 22.3 (*q*)	242 (M^+) *57*
12b	245 (3.31)	1730	3.71 (*s*, OCH_3); 3.19, 3.04 (*AB*, *J* = 11.7); 2.34, 1.79 (*AB*, *J* = 4.2); 1.48, 1.36 (*s*, CH_3); 1.35–0.86 (*m*, 9 H)	172.9 (*s*); 54.3 (*s*); 51.6 (*q*); 45.7 (*d*, *J*(C,H) = 165); 42.3 (*s*); 38.5 (*t*); 31.8 (*q*); 29.9 (*t*); 29.1 (*t*); 26.2 (*q*); 24.7 (*d*, *J*(C,H)) = 166); 22.7 (*t*); 14.0 (*q*)	*242* (M^+)

[a]) All new compounds (except **9**) gave satisfactory elemental analyses. [b]) In C_6D_6. [c]) In KBr.

to be considered as tentative. When the irradiation of **1b** (or **8**) is run in the presence of alkenes, thiolanes **10** are obtained in reasonable yields. Irradiation in the presence of 3,3-dimethyl-1-butyne affords 2,3-dihydrothiophenes **11**. Analogous formations of five-membered sulfur heterocycles had also been observed with **1a** and the mechanism of these conversions have been discussed in detail [2]. However, when 1-hexyne is used as acetylene, selective formation of a new type of product **12** is observed *(Scheme 3)*. The spectroscopic data of the new compounds is summarized in the *Table*.

The photochemistry of five-membered α,β-unsaturated thiolactones is apparently not influenced by Me groups on the saturated C-atom; however, it is strongly affected by Me groups on the C=C bond. The non-reactivity of **1c** as compared to **1a** or **1b** could be due to a much faster radiationless decay of excited **1c**. Such a shortening of the life-time of an excited molecule by additional alkyl groups is known as a 'loose-bolt' effect [6].

On the other hand, the Me groups exert a strong steric effect on the product distribution in the subsequent photochemical step. On irradiation, the (*E*)-4-mercapto-4-methyl-2-pentenoates **8** undergo homolysis of the S–H bond in analogy to the 4-mercaptocrotonates (obtained from **1a**). The Me groups in α-position to sulfur in the alkylthio radical **13** slow down the rate of addition to alkenes or alkynes, and at the same time facilitate the formation of **9** which contains a trisubstituted C=C bond. This explains the lower yields of cycloadducts from **8** (40–15%) as compared to those of the 4-mercaptocrotonates (85–60%) [2]. In addition, the two Me groups also slow down the rate of H transfer to radicals **14** and **15**. This explains the formation of the thiabicyclohexane **12b** from **15b**, where ring closure to a cyclopropane occurs faster. In **15a**, the bulky *t*-Bu group prevents such a cyclization, and, therefore, the 2,3-dihydrothiophene **11a** is formed, again in analogy to the reaction of the mercaptocrotonates with 3,3-dimethyl-1-butyne.

Financial support by the *Deutsche Forschungsgemeinschaft* is gratefully acknowledged.

Experimental Part

General. See [2]. *Tetrahydrothiophen-2-one* (**2**) and *3,4-dimethylthiophene* (**5**) were synthesized according to [7] and [8], resp. 3-Methylthiophene, the alkenes, and alkynes were purchased from *Fluka AG*. All solvents used for photolyses were of spectral grade. GC was performed on a *SE-30* capillary column. Irradiations were performed in an *Applied Photophysics* photoreactor using a 250-W Hg lamp and a liquid filter with cut-off at 305 nm.

Preparation of 5,5-Dimethyl-2(5H)-thiophenone (**1b**). a) *2,2-Dimethyl-5-(trimethylsilyloxy)-2,3-dihydrothiophene* (**3**). To a freshly prepared soln. of lithium diisopropylamide (from 0.15 mol of $(i\text{-Pr})_2NH$ and 96 ml of 1.6M BuLi (0.15 mol)) in dry THF (90 ml) is added a soln. of **2** (19.5 g, 0.15 mol) in THF (50 ml) during 5 min at 0°. After stirring for 30 min, Me_3SiCl (39 ml, 0.30 mol) is added during 5 min, and then the mixture is stirred at r.t. for 30 min. LiCl is filtered under N_2, the solvent evaporated, the residue treated with Et_2O, and Et_2O again evaporated to afford **3** (28.8 g, 95%), which is used as it is for the next step. Purification can be achieved by distillation (b.p. 38–40°/0.4 Torr), ^{1}H-NMR ($CDCl_3$): 4.40 (*t*, 1H); 2.50 (*d*, 2 H); 1.48 (*s*, 6 H); 0.15 (*s*, 9 H).

b) *3-Bromo-5,5-dimethyl-2-thiolanone* (**4**). To a soln. of **3** (28.8 g, 0.142 mol) in $CHCl_3$ (90 ml) at –10° is added Br_2 (7.3 ml, 0.142 mol) in $CHCl_3$ (20 ml). Stirring is continued for 5 h, then 40 ml of H_2O are added, the $CHCl_3$-phase is separated and the aq. phase extracted with Et_2O. The combined org. phases are dried ($MgSO_4$), the solvent evaporated and the residue purified by chromatography (SiO_2, hexane/AcOEt 2:1) to afford 22.5 g (75%) **4**, oil, ^{1}H-NMR ($CDCl_3$): 4.68 (*dd*, J = 10.2, 7.0); 2.67 (*dd*, J = 13.5, 7.0); 2.48 (*dd*, J = 13.5, 10.2); 1.70, 1.68 (*s*, CH_3), ^{13}C-NMR ($CDCl_3$): 199.8 (*s*); 53.3 (*s*); 50.3 (*d*); 49.9 (*t*); 31.3 (*q*); 31.2 (*q*).

c) *5,5-Dimethyl-2(5H)-thiophenone* (**1b**). A mixture of **4** (22.5 g, 0.106 mol), LiBr (32.1 g 0.37 mol), and Li_2CO_3 (20.5 g, 0.276 mol) in dry dimethylacetamide (300 ml) is heated at 100° under N_2 for 3 h. After cooling to

r.t., H_2O (1000 ml) and Et_2O (100 ml) are added; the org. phase is separated and the aq. phase extracted with Et_2O (3×). The combined Et_2O phases are washed with sat. $NaHCO_3$- and NaCl-solns. and dried ($MgSO_4$). The solvent is evaporated and the residue distilled, the fraction boiling at 66–76°/2 Torr being further purified by chromatography (SiO_2, hexane/EtOH 20:1) to afford **1b** (12.6 g, 91%), b.p. 73°/1 Torr.

3,4-Dimethyl-2(5H)-thiophenone (**1c**). 1. *From 3,4-Dimethylthiophene* (**5**). To a soln. of **5** (5.5 g, 0.049 mol) in dry Et_2O (50 ml) under N_2 at r.t. are added 33.5 ml of a 1.6M BuLi soln. in Et_2O. The mixture is refluxed for 30 min, then cooled to −70°, and a soln. of $(MeO)_3B$ (5.6 g, 0.054 mol) in Et_2O (50 ml) is added. The mixture is stirred at −70° for 4 h (formation of **6**). At r.t., 30% H_2O_2 (9.8 ml) is added and the mixture refluxed for 1 h. The org. layer is separated and the aq. phase extracted with Et_2O. The combined org. phases are dried ($MgSO_4$), the solvent evaporated, and the residue chromatographed (SiO_2, hexane/AcOEt 20:1) to afford **1c** (2.9 g, 46%), m.p. 48° (from CCl_4).

2. *From 4-Methyl-2(5H)-thiophenone* (**1d**). a) *4-Methyl-2(5H)-thiophenone* (**1d**) *and 3-methyl-2(5H)-thiophenone* (**1c**). Same procedure as above starting from *3-methylthiophene* (**7**, 4.8 g, 0.049 mol) (metallation, addition of $(MeO)_3B$ and H_2O_2-oxidation). After workup, the residue is distilled, the fraction boiling at 76–88°/3 Torr containing **1d** and **1e** in a 94:6 ratio. This mixture is separated by chromatography (SiO_2, hexane/AcOEt 7:1) to afford **1e** (250 mg, 3%), m.p. 33° (from hexane) and **1d** (4.3 g, 46%), b.p. 63°/0.3 Torr.

b) *Methylation of* **1d**. To a soln. of **1d** (3.85 g, 0.034 mol) and CH_3I (4.3 ml, 0.068 mol) in $CHCl_3$ (35 ml) are added tetrabutylammoniumbisulfate (11.5 g, 0.034 mol) and NaOH (2.7 g, 0.068 mol) in H_2O (35 ml). The mixture is stirred for 60 h at r.t. After addition of 2N HCl (33 ml), the org. layer is separated and the aq. phase extracted with $CHCl_3$ (2×). Evaporation of the solvent and addition of Et_2O leads to precipitation of the ammonium salt. After filtration, the Et_2O soln. is dried ($MgSO_4$), the solvent evaporated, the residue distilled and the fraction boiling at 69–80°/1 Torr recrystallized from CCl_4 to afford **1c** (1.65 g, 43%), m.p. 48°.

(E)-4-Mercapto-4-methyl-2-pentenoates **8**. Ar-degassed solns. of **1b** (256 mg, $2 \cdot 10^{-3}$ mol) in alcohol (MeOH, EtOH, i-PrOH, *t*-BuOH; 10 ml) are irradiated for 24 h to a conversion of about 40%. Evaporation of the solvent, purification by chromatography (SiO_2, hexane/AcOEt 2:1) and bulb-to-bulb distillation (100°/15 Torr) affords **8a** (90 mg, 28%; oil), **8b** (80 mg, 24%; oil), **8c** (80 mg, 22%; oil) and **8d** (100 mg, 26%) m.p. 65°. The yields of **8** corrected for the degree of conversion of starting material are in the order of 55–70%.

Prolonged Irradiation of **1b** *in MeOH (Formation of s-*trans*-1,1-Dimethoxy-4-methyl-1,3-pentadiene* (**9**)). An Ar-degassed soln. of **1b** (64 mg, $5 \cdot 10^{-4}$ mol) in MeOH (5 ml) is irradiated for 80 h. The solvent is evaporated at r.t. and the residue dissolved in Et_2O. The Et_2O soln. is separated from insoluble material, the solvent evaporated, and the residual oil (35 mg) analyzed by ^{1}H-NMR spectroscopy; it contains **9** of about 80% purity.

Irradiation of **1b** *in MeOH in the Presence of Alkenes or Alkynes*. Ar-degassed solns. of **1b** (256 mg, $2 \cdot 10^{-3}$ mol) and 10^{-2} mol of 2,3-dimethyl-2-butene, 3,3-dimethyl-1-butyne, or 1-hexyne in MeOH (10 ml), or a soln. of **1b** (256 mg) in MeOH (10 ml) saturated with 2-methylpropene are irradiated up to total consumption of starting material. After evaporation of the solvent, the residue is purified by bulb-to-bulb distillation and subsequent chromatography on SiO_2.

Methyl 2,2,4,4-Tetramethyl-3-thiolaneacetate (**10a**). Irradiation time: 105 h, 130°/15 Torr, hexane/AcOEt 7:1, 160 mg (36%), oil.

Methyl 2,2,4,4,5,5-Hexamethyl-3-thiolaneacetate (**10b**). Irradiation time: 380 h, 140°/15 Torr, hexane/AcOEt 7:1, 50 mg (10%), oil.

*Methyl 4-(*tert*-Butyl)-2,2-dimethyl-2,3-dihydro-3-thiopheneacetate* (**11a**). Irradiation time: 90 h, 150°/15 Torr, hexane/AcOEt 4:1, 130 mg (28%), m.p. 133°.

Methyl trans*-5-Butyl-2,2-dimethyl-3-thiabicyclo[3.1.0]hexane-6-carboxylate* (**12b**). Irradiation time: 260 h, 150°/15 Torr, hexane/AcOEt 7:1, 110 mg (23%), oil.

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