256. Synthesis of Thiolanes from (*E*)-4-Mercapto-2-butenoates *via* Consecutive *Michael* Additions

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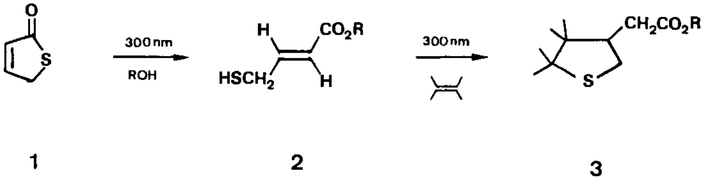
Summary

Methyl 4-mercaptocrotonate (**4**) adds to α,β-unsaturated nitriles or carbonyl compounds in the presence of *Triton B* as base. Several of the primary adducts **10** cyclize to thiolanes **11** in a second (base-catalyzed) *Michael* addition. Dimerization of **4** under these conditions affords a mixture of the diastereomeric 1,4-dithianes **7** and **8**.

We have recently found [1] that 4-mercaptocrotonates **2** were formed photochemically from dihydro-2(5*H*)-thiophenone (**1**), and that they underwent a further light-induced reaction with alkenes to afford the thiolanes **3** *(Scheme 1)*. We now report on the thermal reactivity of these interesting polyfunctional synthetic intermediates.

Scheme 1

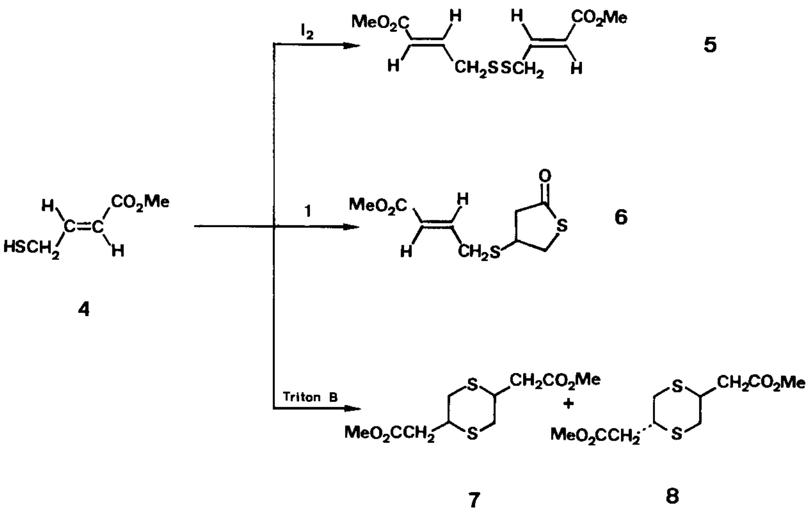


Already in the photochemical experiments, we had observed the formation of byproducts when the solutions were either not properly cooled or when they were exposed to air. Therefore, we have first investigated the reactions of **2** with oxidants, its precursor **1**, and itself.

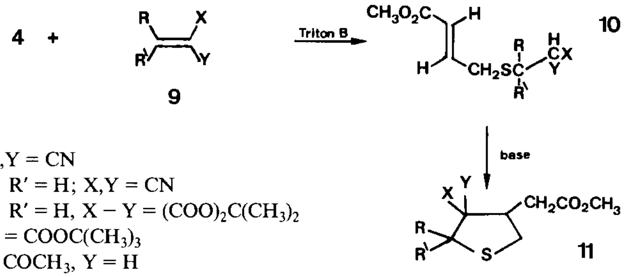
When air is bubbled through a solution of **4** in EtOH, one new product **5**, easily identified as the corresponding disulfide, is formed. The best yields of **5** were obtained when **4** was oxidized with I_2 in EtOH. Addition of traces of *Triton B* to an equimolar mixture of **1** and **4** leads to the formation of **6**. Treatment of **4** alone with the same base affords a 1:1 mixture of the 1,4-dithianes **7** and **8** *(Scheme 2)*.

The ease of addition of the thiolate anion of **2** to **1** and to a second molecule of **2** led us to investigate the addition of **4** to some typical *Michael* acceptors **9**. The primary adducts **10a–c** could not be isolated as they underwent a consecutive intramolecular *Michael* addition to afford the thiolanes **11a–c**. The malonate **10d** cyclizes to **11d** when

Scheme 2



Scheme 3



a R,R′ = CH_3; X,Y = CN
b R = $(CH_3)_2CH$, R′ = H; X,Y = CN
c R = $(CH_3)_2CH$, R′ = H, X – Y = $(COO)_2C(CH_3)_2$
d R,R′ = H; X,Y = $COOC(CH_3)_3$
e R,R′ = H; X = $COCH_3$, Y = H
f R,R′ = H; X = $COOCH_3$, Y = H

using stronger bases, e.g. $NaOCH_3$. Under these conditions the ketoester **10e** and the diester **10f** afford complex product mixtures. This different reactivity of compounds **10** correlates with their different CH acidities [2] [3]. The reaction sequence **4** + **9**→**11** *(Scheme 3)* thus represents a complementary method for the synthesis of thiolanes starting from **2**. The spectroscopic data of all the new compounds are summarized in the *Table*.

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Experimental Part

General. Absorptions in the IR spectra are given in cm^{-1}. Chemical shifts in the 400-MHz ^1H- and 100.63-MHz ^{13}C-NMR spectra are given in ppm relative to TMS (= 0 ppm) as internal standard. The mass spectra were measured at 70 eV. GC-analysis was performed on a *SE30* capillary column.

Table. *Spectroscopic Data of Compounds* (**5**–**8**, **10** *and* **11**)

Compound[a])	IR (CCl_4)	^{1}H-NMR ($CDCl_3$)	^{13}C-NMR ($CDCl_3$)	MS
5	1732	6.84 (*dt*, *J* = 15.4, 7.4); 5.92 (*dt*, *J* = 15.4, 1.2); 3.72 (*s*, 3H); 3.35 (*dd*, *J* = 7.2, 1.2, 2H)	166.1 (*s*); 142.0 (*d*); 124.2 (*d*); 51.5 (*q*); 40.5 (*t*)	262 (M^+) *99*
6	1730	6.92 (*dt*, *J* = 15.2, 7.2); 5.97 (*dt*, *J* = 15.2, 1.5); 3.79 (*s*, 3H); 3.61 (*dd*, *J* = 10.4, 1.9); 3.52 (*dddd*, *J* = 9.6, 6.4, 5.5, 1.9); 3.47 (*dd*, *J* = 10.4, 5.5); 3.38 (*dd*, *J* = 7.2, 1.5, 2H); 2.85 (*dd*, *J* = 16.6, 6.4); 2.57 (*dd*, *J* = 16.6, 9.6)	–	232 (M^+) *101*
7 and **8**	1735	3.65 and 3.64 (*s*, 3H and 3H)[b]); 2.75, 2.72, 2.63 and 2.58 (*dd*, *J* = 16.0, 7.1); 3.24 (*ddt*, *J* = 7.2, 2.6, 7.1); 3.06 (*dd*, *J* = 14.0, 2.6); 2.08 (*dd*, *J* = 14.0, 7.2) and 3.23 (*ddt*, *J* = 8.8, 2.2, 7.1); 3.03 (*dd*, *J* = 13.8, 2.2); 2.80 (*dd*, *J* = 13.8, 8.8)	171.2 and 171.0 (*s*); 51.9 and 51.8 (*q*); 39.0 and 38.9 (*t*); 36.4 and 35.3 (*d*); 34.2 and 32.7 (*t*)	264 (M^+) *133*
10d	1735	6.78 (*dt*, *J* = 15.2, 7.4); 5.84 (*dt*, *J* = 15.2, 1.0); 3.67 (*s*, 3H); 3.24 (*t*, *J* = 7.3); 3.16 (*dd*, *J* = 7.4, 1.0, 2H); 2.78 (*d*, *J* = 7.3, 2H); 1.38 (*s*, 18H)	–	360 (M^+) *57*
10e	1730 1715	6.78 (*dt*, *J* = 15.2, 7.4); 5.82 (*dt*, *J* = 15.2, 1.6); 3.67 (*s*, 3H); 3.16 (*dd*, *J* = 7.4, 1.6, 2H); 2.65 (*t*, 2H); 2.58 (*t*, 2H); 2.10 (*s*, 3H)	–	202 (M^+) *43*
10f	1735	6.87 (*dt*, *J* = 15.4, 7.4); 5.90 (*dt*, *J* = 15.4, 1.6); 3.72 (*s*, 3H); 3.66 (*s*, 3H); 3.27 (*dd*, *J* = 7.4, 1.6, 2H); 2.71 (*t*, 2H); 2.57 (*t*, 2H)	–	218 (M^+) *71*
11a	2250 1735	3.76 (*s*, 3H); 3.40 (*dd*, *J* = 11.2, 7.6)[c]); 3.39 (*dddd*, *J* = 10.2, 9.8, 7.6, 4.4); 3.05 (*dd*, *J* = 16.4, 4.4); 2.92 (*dd*, *J* = 11.2, 10.2); 2.75 (*dd*, *J* = 16.6, 9.8); 1.78 and 1.70 (*s*, CH_3)	–	238 (M^+) *74*
11b[d])	2250 1735	3.75 (*s*, 3H); 3.45 (*d*, *J* = 8.6); 3.31 (*dd*, *J* = 10.4, 6.4); 3.18 (*dddd*, *J* = 10.0, 9.6, 6.4, 4.4); 3.04 (*dd*, *J* = 16.4, 4.4); 2.98 (*dd*, *J* = 10.4, 10.0); 2.72 (*dd*, *J* = 16.4, 9.6); 2.26 (*m*, *J* = 8.6, 6.6); 1.23 and 1.09 (*d*, *J* = 6.6, CH_3)	–	252 (M^+) *74*
11c[d])	1780 1735	4.13 (*d*, *J* = 8.6); 3.70 (*s*, 3H), 3.50 (*ddt*, *J* = 7.2, 4.8, 10.3); 3.18 (*dd*, *J* = 11.2, 7.2); 3.08 (*dd*, *J* = 11.2, 10.3); 2.51 (*dd*, *J* = 15.4, 4.8); 2.40 (*dd*, *J* = 15.4, 10.3); 1.90 (*m*, *J* = 8.6, 6.6); 1.80 and 1.75 (*s*, CH_3); 1.16 and 0.98 (*d*, *J* = 6.6, CH_3)	–	330 (M^+) *143*
11d	1735	3.58 (*s*, 3H); 3.15 and 3.10 (*AB*, *J* = 11.2); 3.12 (*dd*, *J* = 10.4, 8.8); 3.09 (*dddd*, *J* = 10.4, 8.8, 5.6, 2.8); 2.61 (*dd*, *J* = 10.4, 5.6); 2.48 (*dd*, *J* = 16.2, 2.8); 2.35 (*dd*, *J* = 16.2, 10.4); 1.38 (*s*, 18H)	–	360 (M^+) *57*

[a]) All new compounds gave satisfactory elemental analyses.

[b]) In CD_3CN.

[c]) Coupling constants (Hz) from measurement in C_6D_6.

[d]) ^{1}H-NMR data for major (probably *trans*-)isomer.

Starting Materials. Compounds **1** [1], **4** [1], **9a** [4], **9b** [5], **9c** [6] and **9d** [7] were synthesized according to the ref. indicated. Methyl vinyl ketone (**9e**) and methyl acrylate (**9f**) were purchased from *Fluka AG.*

*Dimethyl (2*E*,8*E*)-5,6-Dithia-2,8-decadienedioate* (**5**). A soln. of 132 mg (10^{-3} mol) **4** and 504 mg ($2 \cdot 10^{-3}$ mol) I_2 in 5 ml EtOH was stirred at r.t. for 30 min. After addition of 50 ml H_2O the soln. was extracted 3 × 10 ml Et_2O. The combined Et_2O-phases were washed with aq. $Na_2S_2O_3$, with H_2O and dried ($MgSO_4$). Evaporation of the solvent and chromatography (SiO_2, Et_2O/pentane 1:1) afforded 118 mg (90%) **5** as a colorless oil.

*Methyl (*E*)-5-Thia-5-(2'-oxo-3'-tetrahydrothienyl)-2-pentenoate* (**6**). A soln. of 132 mg (10^{-3} mol) **4**, 100 mg (10^{-3} mol) **1** and 1 µl 40% methanolic *Triton B* in 2 ml $CHCl_3$ was stirred at r.t. for 15 min. Evaporation of the solvent and chromatography (SiO_2, Et_2O/pentane 1:1) afforded 140 mg (60%) **6** as a colorless oil.

Dimethyl cis- *and* trans-*1,4-Dithiane-2,5-diacetate*[1]) (**7** and **8**). A soln. of 132 mg (10^{-3} mol) **4** and 1 µl *Triton B* in 2 ml $CHCl_3$ was refluxed for 15 min. Evaporation of the solvent and chromatography (SiO_2, Et_2O/pentane 9:1) afforded 105 mg (80%) of a 1:1 mixture (GC, NMR) of **7** and **8** as a colorless oil.

Methyl 4,4-Dicyano-5,5-dimethyl-3-thiolaneacetate (**11a**). A soln. of 132 mg (10^{-3} mol) **4**, 106 mg (10^{-3} mol) **9a** and 1 µl *Triton B* in 4 ml benzene was stirred at r.t. for 15 min. Evaporation of the solvent and bulb-to-bulb distillation (210°/0.1 mm) afforded 196 mg (82%) **11a** as a colorless oil.

cis- *and* trans-*4,4-Dicyano-5-isopropyl-3-thiolaneacetate* (**11b**). A soln. of 132 mg (10^{-3} mol) **4**, 120 mg (10^{-3} mol) **9b** and 1 µl *Triton B* in 3 ml benzene was stirred at r.t. for 30 min. Evaporation of the solvent and chromatography (SiO_2, Et_2O/pentane 1:1) afforded 180 mg (70%) of a 2:1 mixture (GC, NMR) of diastereomeric products **11b** as a colorless oil.

Methyl cis- *and* trans-*4-Isopropyl-8,8-dimethyl-6,10-dioxo-7,9-dioxa-3-thiaspiro[4,5]decane-1-acetate* (**11c**). Preparation from **4** and **9c** as for **11b** afforded 200 mg (60%) of a 3:1 mixture (NMR) of diastereomeric products **11c** as a colorless oil.

Preparation of **10d–f**. A soln. of 10^{-3} mol **4**, 10^{-3} mol **9d**, **9e** or **9f** and 1 µl *Triton B* in 2 ml $CHCl_3$ was stirred at r.t. for 30 min. Evaporation and bulb-to-bulb distillation (180°/0.1 mm) afforded: *di(tert-butyl) [(*E*)-5-methoxycarboxyl-2-thia-4-pentenyl]malonate* (**10d**, 85%); *methyl(*E*)-5-thia-8-oxo-2-nonenoate* (**10e** 87%); *dimethyl(*E*)-5-thia-2-octenedioate* (**10f**, 92%), all as colorless oils.

Methyl-4,4-dicarbo-t-butoxy-3-thiolaneacetate (**11d**). A soln. of 2.3 mg Na (10^{-4} mol) and 10^{-3} mol **10d** in 3 ml MeOH was stirred at 40° for 2 h. Addition of 30 ml H_2O, extraction with Et_2O (4 times 5 ml), drying and evaporation of the solvent and chromatography (SiO_2, Et_2O/pentane 1:9) afforded 250 mg (70%) **11d** as a colorless oil.

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[1]) The preparation of a mixture of the corresponding dinitriles has been reported [8].