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Reaction of 2,2,4,4-Tetramethyl-3-thioxocyclobutanone with Dimethyl Diazomalonate Catalyzed by $Rh_2(OAc)_4$

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The reaction of 2,2,4,4-tetramethyl-3-thioxocyclobutanone (**1**) with dimethyl diazomalonate in the presence of $Rh_2(OAc)_4$ in toluene at 50°C yielded a mixture of three products **10**, **11**, and **12**. Thiocarbonyl ylide **8** is believed to be the common intermediate. The formation of **10** is rationalized by the 1,3-dipolar electrocyclization of **8** to give spirocyclic thiirane **9**, which spontaneously eliminated sulfur. On the other hand, the 1,5-dipolar electrocyclization of **8** led to 1,3-oxathiole **11**, which is converted into lactone **12** by hydrolysis.

Key words: carbenoids, 1,3- and 1,5-dipolar electrocyclization, 1,3-oxathioles, thiiranes, thiocarbonyl ylides

In previous studies, we have shown that thioketones easily undergo reactions with electrophilic carbenes and carbenoids to give thiiranes [1–4]. The reactions proceed *via* thiophilic addition of the carbenes to give reactive thiocarbonyl ylides as intermediates [5]. In a recent paper, the reaction of adamantanethione with the nucleophilic dimethoxycarbene leading to the corresponding 2,2-dimethoxythiirane was reported [6].

One of the best models for studies of reactions of thioketones with carbenoid species is "monothione" **1**. Whereas 2,2,4,4-tetramethylcyclobutane-1,3-dione (**2**) in the two-phase system $CHCl_3$/aqueous NaOH undergoes ring enlargement to give **3** [7], the monothio analogue **1** smoothly reacts to give spirothiirane **4** [3]. The reaction with difluorocarbene, generated by thermolysis of $PhHgCF_3$ (Seyferth's reagent), leads to the stable *gem*-difluorothiirane **5** [4]. In contrast to electrophilic carbenes, dimethoxycarbene reacts with **1** by ring enlargement to give the cyclopentane derivatives **6** and **7** (Scheme 1). Remarkably, the ring expansion occurred regioselectively in favour of the isomer **6**. In the crude reaction mixture, a 10:1 ratio of **6**/**7** was established [8].

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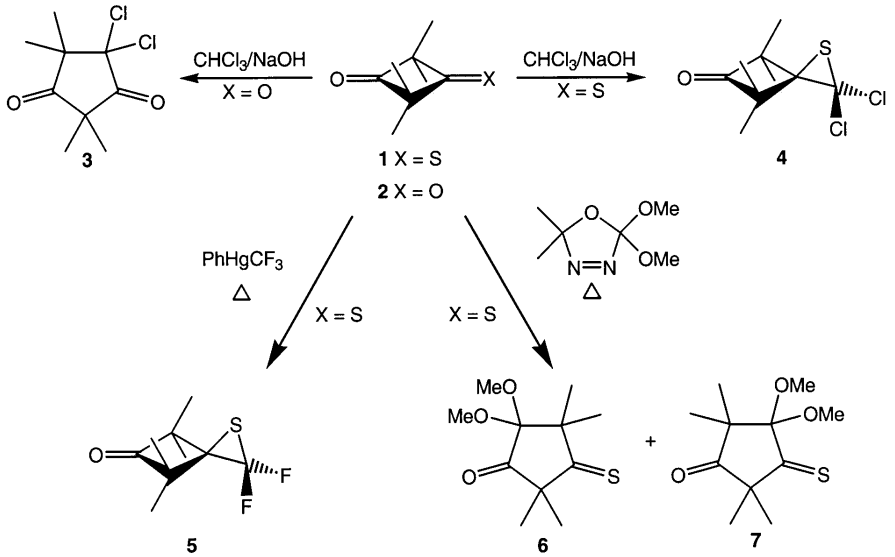
Scheme 1



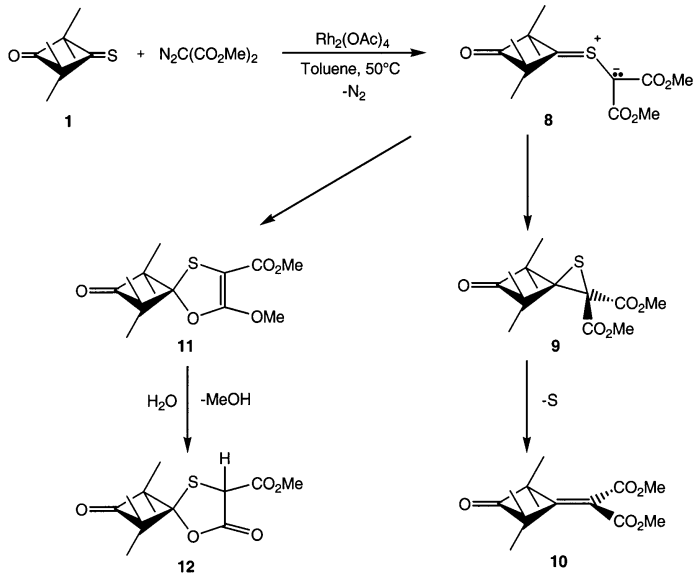
Many years ago, 1,3-dipolar cycloaddition of diazomethane with **1** was reported to give a relatively stable 2,5-dihydro-1,3,4-thiadiazole derivative [9]. Since, this cycloadduct has frequently been used as a convenient precursor of a reactive thiocarbonyl ylide, generated under mild and neutral conditions [10,11]. On the other hand, diazomalonates belong to the less reactive 1,3-dipoles and can be used for the generation of thiocarbonyl ylides only in the presence of $Rh_2(OAc)_4$ as a catalyst. Under these conditions, an intermediate carbenoid is believed to add to the S-atom of a thioketone. Recently, a series of reactions of this type using dimethyl diazomalonate and aromatic thioketones or 1,3-thiazole-5(4*H*)-thiones have been reported to give the corresponding thiiranes [2].

RESULTS AND DISCUSSION

In accordance with the known low reactivity of diazomalonates as 1,3-dipoles, no reaction occurred with **1** in toluene, neither at room temperature, nor at 50°C. But addition of catalytic amounts of $Rh_2(OAc)_4$ at elevated temperature started immediately a reaction which was monitored by control of N_2 evolution. After 48 h, the reaction was completed and the mixture was separated by column chromatography to give three products. From the least polar fraction, colorless crystals were isolated and the product was identified as **10** (Scheme 2). The high symmetry of the molecule was reflected by the NMR spectra: the ^{1}H-NMR spectrum showed two singlets at 3.82 and 1.41 ppm for two MeO and four Me groups, respectively. Characteristic signals in the ^{13}C-NMR spectrum appeared at 218.0 ppm (C=O, cyclobutanone), 166.1 ppm (C=O,

α,β-unsaturated ester), and 171.0 and 122.1 ppm (two olefinic C-atoms). The formation of **10** corresponds to the typical sequence of conversions of thiocarbonyl ylides (*e.g.* **8**) undergoing a 1,3-dipolar electrocyclization to give a thiirane (*e.g.* **9**) that subsequently desulfurize. In many instances, elimiation of sulfur occurs spontaneously under the reaction conditions [5].

Scheme 2



The second product, obtained as colorless crystals, showed in the ^{1}H-NMR spectrum two singlets for MeO groups at 4.03 and 3.74 ppm, respectively, as well as two singlets at 1.32 and 1.31 ppm (1:1) for four Me groups. The CI-MS (NH_3) with $[M+18]^+$ at *m/z* 304 confirmed the molecular formula $C_{13}H_{18}O_5S$ which corresponds to a molecule isomeric with **9** or its precursor **8**. The ^{13}C-NMR spectrum is in good agreement with structure **11**, and similar to other spirocyclic 1,3-oxathiole derivatives reported earlier [12,13]. In the IR spectrum (KBr), structure **11** is supported by three strong absorptions between 1800 and 1600 cm^{-1}. The most intensive one (1628 cm^{-1}) is characteristic for the C=C stretching of the ketene acetal. The formation of 1,3-oxathioles from thiocarbonyl ylides has been observed when a carbonyl group was conjugated with the dipolar system [5,12,13]. But it is important to mention that this type of 1,5-dipolar electrocyclization involving an ester C=O group leading to a product which could be isolated has never been observed so far. In preceeding papers, however, we have described cascade reactions of some ester-substituted thiocarbonyl ylides in which analogous 1,3-oxathiole formations were proposed as key steps of the reaction mechanism [14,15].

The third product of the reaction was identified as lactone **12** on the basis of its spectroscopic data. In the ^{13}C-NMR spectrum, three C=O absorptions at 216.6 ppm (cyclobutanone), 167.4 and 167.3 ppm (ester, lactone) and a doublet for HC(7) at 48.8 ppm were characteristic. A plausible interpretation for the formation of **12** is the hydrolysis of the ketene acetal function of **11**. This conversion also took place slowly when a solution of **11** was kept at room temperature.

In conclusion, the first example of a 1,5-dipolar electrocyclization of a thiocarbonyl ylide *via* an ester carbonyl group leading to an isolable 1,3-oxathiole was found. Under similar conditions, aromatic thioketones and 1,3-thiazole-5(4*H*)-thiones have been shown to undergo 1,3-dipolar electrocyclization to give thiiranes exclusively [2].

EXPERIMENTAL

General. M.p.'s were determined on a Mettler-FP-5 apparatus and are not corrected. IR spectra were registered with a Perkin-Elmer-1600-Series spectrophotometer (in KBr). NMR-spectra were recorded in $CDCl_3$ on a Bruker-AC-300 (^{1}H, 300 MHz) or a Bruker-ARX-300 (^{13}C, 75.6 MHz) instrument. CI-MS-spectra were registered with a Varian-MAT-112S spectrometer (with NH_3). Elemental analyses were performed in the microanalytical laboratory of the Institute of Organic Chemistry of the University of Zürich.

Starting materials. The 2,2,4,4-tetramethyl-3-thioxocyclobutanone (**1**) was prepared by thionation of 2,2,4,4-tetramethylcyclobutane-1,3-dione (**2**) using P_4S_{10} and pyridine as a solvent [16]. Dimethyl diazomalonate was synthesized by diazo transfer method according to a known protocol starting with methyl malonate and tosyl azide [17].

Catalyzed decomposition of dimethyl diazomalonate in the presence of monothione 1. To a solution of **1** (156 mg, 1.0 mmol) and methyl diazomalonate (174 mg, 1.1 mmol) in 1 ml of dry toluene was added $Rh_2(OAc)_4$ (*ca*. 10 mg), and the solution was stirred under heating in an oil bath (50°C). The evolution of N_2 was controlled volumetrically with a gas burette combined with the reaction flask. After 48 h, the evolution of N_2 ceased when 22 ml of N_2 were collected (*ca*. 80% of theoretical amount). The solvent was evaporated, and the thick residue was separated on prep. TLC plates (SiO_2; hexane/ethyl acetate (4:1) as eluant, 2x developed). Three fractions were isolated and identified as products **10** (R_f 0.60), **11** (R_f 0.35), and **12** (R_f 0.25), respectively. The reported yields refer to isolated material.

Dimethyl 2-(2′,2′,4′,4′-Tetramethyl-3′-oxocyclobutan-1′-ylidene)propanoate (**10**). Colorless solid, m.p. 61–62°C (recrystallized from MeOH at –20°C). Yield: 51 mg (20%). ^{1}H-NMR: 1.41 (*s*, 4 Me); 3.82 (*s*, 2 MeO). ^{13}C-NMR: 20.9 (*q*, 4 Me); 52.2 (*q*, 2 MeO); 64.7 (*s*, C(2′), C(4′)); 122.1 (*s*, C(2)); 166.1 (*s*, 2 C=O (ester)); 171.0 (*s*, C(1′)); 218.0 (*s*, C=O (ketone)). IR: 1808*s* (C=O (ketone)), 1732*vs* (2 C=O (ester)), 1655*m* (C =C), 1445*s*, 1295*s*, 1247*vs*, 1092*s*, 1030*m*, 1013*s*. CI-MS: 272 (100, $[M+NH_4]^+$), 255 (20, $[M+1]^+$). Anal. Calc. for $C_{13}H_{18}O_5$ (254.28): C 61.40, H 7.14; found: C 61.27, H 6.99.

Methyl 6-Methoxy-1,1,3,3-tetramethyl-2-oxo-5-oxa-8-thiaspiro[3.4]oct-6-ene-7-carboxylate (**11**). Colorless solid, m.p. 72–73°C (crystallized from hexane). Yield: 129 mg (45%). During storage at room temperature, **11** slowly decomposed to give **12**. ^{1}H-NMR: 1.31, 1.32 (2*s*, 4 Me); 3.74 (*s*, MeO (ester)); 4.03 (*s*, MeO). ^{13}C-NMR: 18.5, 22.2 (2*q*, 4 Me); 51.4 (*q*, MeO (ester)); 57.9 (*q*, MeO); 66.4 (*s*, C(1), C(3)); 75.5 (*s*, C(7)); 99.1 (*s*, C(4)); 159.0 (*s*, C(6)); 162.6 (*s*, C=O (ester)); 217.3 (*s*, C=O (ketone)). IR: 1782*s* (C=O (ketone)), 1675*s* (C=O (ester)), 1625*vs* (C=C), 1460*s*, 1440*m*, 1360*vs* (MeO), 1100*s*, 1080*s*, 1040*s*. CI-MS: 304 (62, $[M+NH_4]^+$), 287 (100, $[M+1]^+$). Anal. Calc. for $C_{13}H_{18}O_5S$ (286.35): C 54.53, H 6.33; found: C 53.91, H 6.19.

Methyl 1,1,3,3-Tetramethyl-2,6-dioxo-5-oxa-8-thiaspiro[3.4]octane-7-carboxylate (**12**). Colorless crystals, m.p. 79–80°C (crystallized from MeOH at –20°C). Yield: 27 mg (10%). ^{1}H-NMR: 1.28, 1.30, 1.31, 1.35 (4*q*, 4 Me); 3.85 (*q*, MeO); 4.57 (*d*, CH). ^{13}C-NMR: 18.1, 18.2, 21.5, 23.3 (4*q*, 4 Me); 48.8 (*d*,

CH); 53.6 (*q*, MeO); 65.2, 65.1 (2*s*, C(1), C(3)). IR: 1785*vs* (C=O (ketone)), 1748*vs* (C=O (ester)), 1475*m*, 1275*m*, 1230*vs*, 1180*vs*, 1065*s*, 1035*w*, 1010*s*, 950*w*, 745*w*. CI-MS: 290 (100, $[M+NH_4]^+$). Anal. Calc. for $C_{12}H_{16}O_5S$ (272.32): C 52.93, H 5.92; found: C 52.77, H 5.69.

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