α-Methylene β-*S*-Thiolactones: Synthesis of a New Heterocycle by Sulfurization of an α-Methylene β-Lactone and Its Structure

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An α-methylene β-*S*-thiolactone, a new sulfur heterocycle, is prepared by sulfurization of the corresponding α-methylene β-lactone using Lawesson's reagent as sulfur source.

β-Thiolactones represent a well-known class of substances whose reactivity has been thoroughly investigated[1]. Although numerous methods for the synthesis of β-thiolactones have been developed in the past, it is surprising that heterocycles such as the thiolactones **1** are not mentioned in the literature, despite the fact that the regioisomer **2** has been known for a long time[2].

1

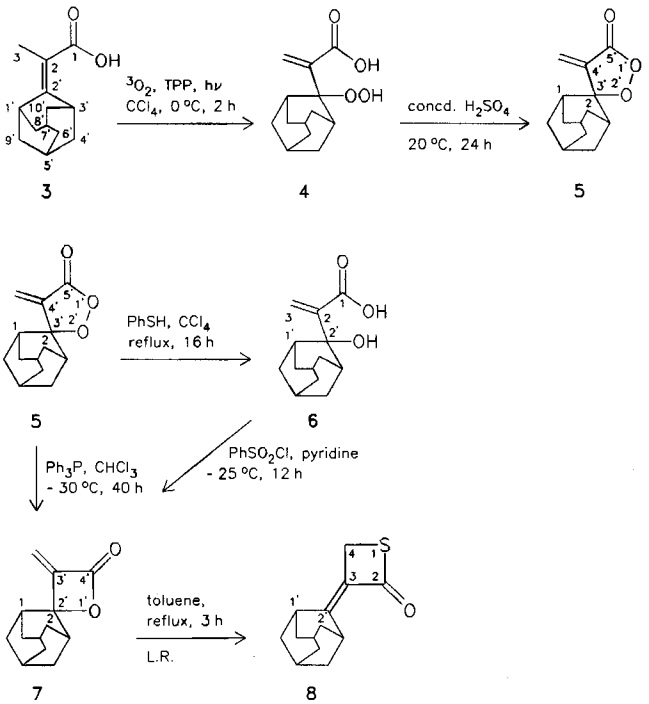
2

Recently, we have shown that α-methylene β-lactones[3] can be conveniently prepared by deoxygenation of the corresponding α-methylene β-peroxy lactones, which in turn are readily available by photooxygenation of the appropriate methacrylic acids[4a]. Based on this synthetic methodology, we report in this paper on the first member of this new sulfur heterocycle, namely the α-methylene β-*S*-thiolactone **8** by employing the Lawesson reagent in the sulfurization step (Scheme 1).

The photooxygenation of the previously unknown methacrylic acid **3**, which is prepared according to the procedure developed by Brittelli[5], is carried out in CCl_4 at 0°C by irradiation with a 400-W sodium street lamp, using an immersion well and tetraphenylporphine (TPP) as sensitizer[6]. The resulting hydroperoxide **4** is not isolated, but on acid catalysis directly cyclized in 35% yield to the new β-peroxy lactone **5**, one of the few β-disubstituted derivatives[4b].

Subsequent deoxygenation of the β-peroxy lactone **5** with triphenylphosphine leads to the hitherto unknown α-methylene β-lactone **7** in 59% yield, the first disubstituted derivative (Figure 1). An alternative way of preparation is the direct cyclization of the β-hydroxy acid **6** by our $PhSO_2Cl$/pyridine method[7], affording the desired α-methylene β-lactone **7** in 71% yield. The required hydroxy acid **6** was generated by reducing the β-peroxy lactone **5** with thiophenol. Although the spectral data speak for the proposed structure, an X-ray structure determination[8] (Figure 1) unequivocally confirms the existence of this unusual class of strained β-lactones, revealing the α-methylene β-lactone moiety to occur as a planar ring.

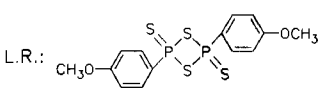
Scheme 1



3 4 5 6 7 8

TPP: tetraphenylporphine

L.R.:



Treatment of the β-lactone **7** with Lawesson's reagent (L. R.)[9] affords a pale yellow solid in 40% yield whose spectral data suggest the α-methylene β-*S*-thiolactone structure **8**. Definitive evidence is provided again by an X-ray structure determination[8] (Figure 1), which exhibits the novel pla-

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nar sulfur ring system, but the bond angles of the β-*S*-thiolactone heterocycle are significantly distorted as compared with those of the β-lactone due to the significantly longer carbon–sulfur bonds.

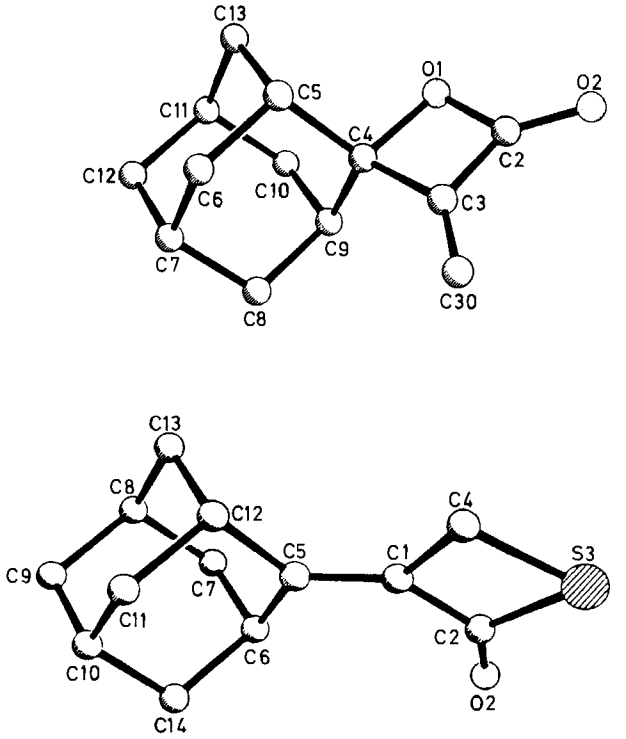
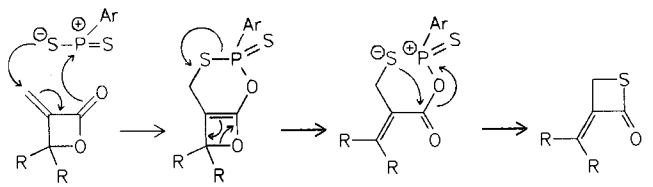


Figure 1. X-ray structures of **7** (top) and **8** (bottom)[8]

In view of the mechanism of sulfurization, a direct exchange of the carbonyl oxygen atom by the sulfur atom, followed by isomerization of the resulting β-*O*-thiolactone to the observed β-*S*-thiolactone **8**, is unlikely, because β-lactones do not undergo direct carbonyl sulfurization with the Lawesson reagent[10]. Instead, since it has been postulated[11] that the monomeric Lawesson reagent[11,12] serves as a dienophile in the reactions with α,β-enones leading to sulfur-containing, six-membered ring heterocycles, we propose the [4 + 2] cycloaddition depicted in Scheme 2.

Scheme 2



Of course, in view of the dipolar nature of the monomeric Lawesson reagent, an alternative Michael-type addition to the α,β-enone is also feasible. Electrophilic ring opening of the strained oxetene and subsequent sulfur–phosphorus bond scission lead to the 1,6-dipole. The latter conveniently cyclizes to the β-*S*-thiolactone **1** by expulsion of the phosphorus moiety through nucleophilic sulfur attack at the activated carbonyl group. Although conjecture, the mechanism in Scheme 2 provides a consistent rationale for the unprecedented transformation of the α-methylene β-lactone **7** into the corresponding β-*S*-thiolactone **8**.

In summary, the first α-methylene β-*S*-thiolactone reported in this paper constitutes a novel sulfur heterocycle which should, due to the activated α-methylene group, exhibit diversified chemical reactivity. Such a new, highly functionalized heterocyclic four-membered ring system should provide interesting opportunities for synthetic applications.

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Experimental

All reactions were carried out with dried solvents. – **IR**: Perkin-Elmer 1420. – ^{1}H and ^{13}C NMR: Bruker AC 200, WM 250; $CDCl_3$ solutions with tetramethylsilane as internal standard. – The solvents were removed by rotary evaporation at 20°C/15 Torr. – Melting points: (uncorrected) Reichert Thermovar.

2-(2-Adamantylidene)propionic Acid (**3**): A mixture of 9.00 g (0.300 mol) of sodium hydride (80% suspension in paraffin oil) and 13.8 g (0.100 mol) of diethyl phosphite in 250 ml of absolute THF under nitrogen was treated with a solution of 15.3 g (0.100 mol) of α-bromopropionic acid in 100 ml of absolute THF. After hydrogen gas evolution had ceased, 15.0 g (0.100 mol) of adamantanone in 30 ml of absolute THF was added and the mixture stirred for 2 d. After the addition of 10 ml of ethanol, the mixture was poured into 800 ml of water. The strongly basic solution was washed with methyl *tert*-butyl ether (MTB) to remove the paraffin oil (ether extracts were discarded), acidified to pH = 2–3 with ca. 10% aqueous hydrochloric acid and extracted with MTB (3 × 150 ml). The latter ether solution was washed with satd. sodium chloride solution (1 × 150 ml), with water (1 × 100 ml), dried ($MgSO_4$) and rotary-evaporated. The crude product was purified by recrystallization from ethanol yielding 4.25 g (28%) of colorless needles, mp 188–189°C. – IR (CCl_4): $\tilde{\nu}$ = 3500–2500 cm^{-1} (O–H), 2930, 2870 (C–H), 1700 (C=O), 1655 (C=C), 1460, 1420, 1280, 1020, 880. – ^{1}H-NMR ($CDCl_3$, 200 MHz): δ = 1.89 (m, 15H, CH_3, 4′-, 5′-, 6′-, 7′-, 8′-, 9′-, 10′-H), 2.92 (br. s, 1H, 1′-H), 3.67 (br. s, 1H, 3′-H), 9.32 (br. s, 1H, OH). – ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 14.5 (q), 27.6 (2 d), 34.4 (d), 34.6 (d), 36.7 (t), 38.9 (2 t), 39.4 (2 t), 115.1 (s), 160.8 (s), 176.0 (s). – MS (70 eV): *m/z* (%) = 206 (100) [M^+], 191 (4) [$M^+ - CH_3$], 161 (20), 160 (33), 146 (15) [$M^+ - CH_3 - CO_2H$], 133 (21), 119 (23), 105 (34), 91 (46), 79 (45), 77 (27), 55 (19), 43 (17). $C_{13}H_{18}O_2$ (206.3) Calcd. C 75.69 H 8.79 Found C 75.73 H 8.54

4′-Methylenespiro[adamantane-2,3′-[1,2]dioxolan]-5′-one (**5**): A solution of 2.00 g (9.70 mmol) of **3** in 30 ml of CCl_4 containing tetraphenylporphine (ca. 2 mg) as sensitizer was photooxygenated at ca. 0°C for 2 h. After addition of 1 ml of concd. sulfuric acid, the mixture was stirred for 24 h, subsequently washed with water (15 ml), dried ($MgSO_4$), and rotary-evaporated. The crude product was purified by column chromatography [silica gel (63–230 mesh), adsorbant/substrate ratio 25:1, ca. 20°C, CH_2Cl_2 as eluent, R_f = 0.67] to yield 700 mg (35%) of colorless prisms, mp 97–99°C. –

IR (CCl_4): $\tilde{\nu}$ = 3020 cm^{-1} (=C–H), 2910, 2860 (C–H), 1780 (C=O), 1655 (C=C), 1450, 1270, 1210, 1145, 1090, 950. – ^{1}H-NMR ($CDCl_3$, 200 MHz): δ = 1.62–2.20 (m, 14H, adamantyl H), 6.03 (s, 1H, $=CH_a$), 6.38 (s, 1H, $=CH_b$). – ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 26.2 (d), 26.4 (d), 32.8 (2 t), 33.6 (2 t), 34.6 (2 d), 37.2 (t), 91.8 (s), 123.9 (t), 140.6 (s), 170.0 (s). – MS (70 eV): *m/z* (%) = 220 (3) [M^+], 192 (3) [$M^+ - CO$], 176 (11) [$M^+ - CO_2$], 150 (26) [$M^+ - C_3H_2O_2$], 134 (7) [$M^+ - C_3H_2O_3$], 107 (26), 105 (28), 93 (39), 91 (58), 80 (41), 79 (100) [$C_6H_7^+$], 77 (41), 67 (34), 55 (34), 41 (54), 39 (35).

$C_{13}H_{16}O_3$ (220.3) Calcd. C 70.88 H 7.32
Found C 70.77 H 7.52

2-(2-Hydroxyadamantyl)-2-propenoic Acid (**6**): 538 mg (5.30 mmol) of thiophenol in 10 ml of CCl_4 was added to a solution of 538 mg (2.65 mmol) of **5** in 15 ml of CCl_4 at 0°C and stirred for 1 h. After heating at reflux for 18 h, ca. 30% conversion was observed; the solvent was rotary-evaporated (ca. 20°C/20 Torr) and the residue taken up in 20 ml of ether. The ether solution was washed with satd. aqueous $NaHCO_3$ (5 × 5 ml), the combined aqueous extracts were acidified with HCl to pH = 2 and extracted with ether (4 × 5 ml). The combined ether layers were washed with satd. aqueous sodium chloride (5 ml) and water (5 ml), dried ($MgSO_4$), and the solvent was rotary-evaporated (20°C/20 Torr). The crude product was recrystallized from ethyl acetate/petroleum ether (boiling range 30–50°C) affording 124 mg (70% corrected for 30% conversion) of colorless prisms, mp 126–128°C. – IR (KBr): $\tilde{\nu}$ = 3550 cm^{-1} (OH), 3600–2500 (OH), 2930, 2860 (C–H), 1685 (C=O), 1655 (C=C), 1455, 1400, 1308, 1190, 1100, 1065, 1020, 995, 935. – ^{1}H-NMR ($CDCl_3$, 250 MHz): δ = 1.55–2.40 (m, 14H, adamantyl H), 5.88 (s, 1H, $=CH_a$), 6.32 (s, 1H, $=CH_b$). – ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 26.6 (d), 27.5 (d), 32.5 (2 t), 33.6 (2 t), 34.6 (2 d), 37.6 (t), 75.6 (s), 126.5 (t), 143.8 (s), 173.1 (s). – MS (70 eV): *m/z* (%) = 222 (2) [M^+], 204 (100) [$M^+ - H_2O$], 177 (4) [$M^+ - CO_2H$], 176 (17), 160 (3) [$M^+ - CO_2 - H_2O$], 151 (12), 148 (12), 117 (11), 109 (8), 91 (14), 79 (22), 77 (10), 67 (12), 55 (8), 41 (10). $C_{13}H_{18}O_3$ (222.19) Calcd. C 70.27 H 8.16
Found C 70.21 H 8.09

3'-Methylenespiro[adamantane-2,2'-oxetan]-4'-one (**7**). – a) *By Reduction of* **5** *with Triphenylphosphine.* – To a solution of 0.500 g (2.27 mmol) of **5** in 20 ml of $CHCl_3$ at –30°C was added within 10 min a solution of 0.595 g (2.27 mmol) of triphenylphosphine in 15 ml of $CHCl_3$. The mixture was allowed to warm up to ca. 20°C and stirred (ca. 40 h) until a peroxide test was negative (detected by TLC using a KI spray). The solvent was mostly rotary-evaporated and the triphenylphosphine oxide was precipitated by adding ca. 100 ml of petroleum ether (boiling range 30–50°C). The residue was purified by column chromatography [silica gel (63–230 mesh), adsorbant/substrate ratio 20:1, ca. 20°C, CH_2Cl_2 as eluent, R_f = 0.55] to yield 273 mg (59%) of colorless prisms, mp 97.5–98.5°C. – IR (CCl_4): $\tilde{\nu}$ = 2930 cm^{-1}, 2865 (C–H), 1835 (C=O), 1455, 1410, 1208, 1155, 1071, 1060, 958, 940, 860. – ^{1}H-NMR ($CDCl_3$, 200 MHz): δ = 1.65–2.18 (m, 14H, adamantyl-H), 5.55 (d, $J_{a,b}$ = 1.7 Hz, 1H, $=CH_a$), 5.86 (d, $J_{b,a}$ = 1.7 Hz, 1H, $=CH_b$). – ^{13}C NMR ($CDCl_3$, 50 MHz): δ = 26.4 (2 d), 32.9 (2 t), 34.9 (2 t), 35.7 (2 d), 36.6 (t), 92.0 (s), 114.0 (s), 149.5 (s), 164.3 (s). – MS (70 eV): *m/z* (%) = 204 (3) [M^+], 176 (14) [$M^+ - CO$], 160 (100) [$M^+ - CO_2$], 150 (8) [$M^+ - C_3H_2O$], 131 (16), 118 (20), 117 (35), 105 (23), 91 (47), 79 (60), 77 (31), 55 (21), 41 (44), 39 (31).

$C_{13}H_{16}O_2$ (204.3) Calcd. C 76.44 H 7.89
Found C 76.58 H 7.70

b) *By Direct Cyclization of* **6**: A solution of 32.0 mg (0.144 mmol) of **6** in 25 parts 0.8 ml of anhydrous pyridine was cooled to 0–5°C, and 51.0 mg (0.288 mmol) benzenesulfonyl chloride was added. The mixture was well shaken, the flask sealed and placed into the freezer (–25°C) for ca. 12 h. After pouring onto ca. 5 g of crushed ice, the mixture was extracted with ether (5 × 5 ml). The combined ether layers were washed with satd. aqueous. $NaHCO_3$ (5 ml) and water (5 ml), dried ($MgSO_4$), and the ether was rotary-evaporated (20°C/20 Torr). The crude product was sublimed (130–150°C/0.01 Torr) affording 21.0 mg (71%) of pure **7**. The physical and spectral data are in good agreement with those of the deoxygenation procedure with triphenylphosphine.

3-(2-Adamantylidene)-2-thietanone (**8**): 150 mg (0.730 mmol) of **7** and 148.5 mg (0.365 mmol) of Lawesson's reagent (L. R.) in 20 ml of absolute toluene were stirred under reflux for 3 h. The solvent was rotary-evaporated at 40°C/15 Torr and the residue purified by double column chromatography [silica gel (32–63 mesh), adsorbant/substrate ratio 50:1, ca. 20°C, CH_2Cl_2 as eluent, R_f = 0.69; the second column chromatography was performed under the same conditions, except that CH_2Cl_2/petroleum ether (boiling range 30–50 (1:1) was used as eluent, R_f = 0.31) affording 60.0 mg (37%) of pale yellow prisms, mp 128–130°C. – IR (CCl_4): $\tilde{\nu}$ = 2940 cm^{-1}, 2860 (C–H), 1755 (C=O), 1660 (C=C), 1450, 1135, 1070, 945, 870. – ^{1}H-NMR ($CDCl_3$, 250 MHz): δ = 1.80–2.05 (m, 12H, adamantyl H), 2.43 (br. s, 1H, 1'-H), 3.54 (s, 2H, 4-H), 3.58 (br. s, 1H, 3'-H). – ^{13}C NMR ($CDCl_3$, 63 MHz): δ = 24.2 (t), 27.6 (2 d), 34.3 (d), 34.8 (d), 36.6 (t), 39.3 (2 t), 39.5 (2 t), 134.7 (s), 158.8 (s), 185.5 (s). – MS (70 eV): *m/z* (%) = 220 (100) [M^+], 192 (90) [$M^+ - CO$], 160 (36) [$M^+ - CO - S$], 149 (36), 136 (16), 131 (17), 117 (42), 115 (17), 105 (16), 91 (47), 79 (36), 77 (31), 67 (17), 65 (19), 53 (15), 41 (32), 39 (25).

$C_{13}H_{16}OS$ (220.3) Calcd. C 70.87 H 7.32
Found C 70.59 H 7.30

CAS Registry Numbers

3: 126255-67-2 / **5**: 126255-68-3 / **6**: 126255-69-4 / **7**: 126255-70-7 / **8**: 126255-71-8 / α-bromopropionic acid: 598-72-1 / adamantanone: 700-58-3

[1] [1a] Y. Etienne, N. Fischer in *The Chemistry of Heterocyclic Compounds* (A. Weissberger, Ed.), vol. 19(II), p. 849, Interscience, New York 1964. – [1b] D. C. Dittmer, T. C. Sedergran in *The Chemistry of Heterocyclic Compounds* (A. Hassner, Ed.), vol. 42(III), p. 547, Interscience, New York 1984.
[2] H. Gotthardt, *Tetrahedron Lett.* **15** (1973) 1221.
[3] W. Adam, L. Hasemann, F. Prechtl, *Angew. Chem.* **100** (1988) 1594; *Angew. Chem. Int. Ed. Engl.* **27** (1988) 1536.
[4] [4a] W. Adam, A. Griesbeck, *Angew. Chem.* **97** (1985) 1071; *Angew. Chem. Int. Ed. Engl.* **24** (1985) 1070. – [4b] W. Adam, A. Griesbeck, D. Kappes, *J. Org. Chem.* **51** (1986) 4479.
[5] D. R. Brittelli, *J. Org. Chem.* **46** (1981) 2514.
[6] W. Adam, G. Klug, E.-M. Peters, K. Peters, H. G. von Schnering, *Tetrahedron* **41** (1985) 2045.
[7] W. Adam, J. Baeza, C. J. Liu, *J. Am. Chem. Soc.* **94** (1972) 2000.
[8] Data can be obtained from Dr. K. Peters, Max-Planck-Institut für Festkörperforschung, Heisenbergstraße 1, D-7000 Stuttgart, F.R.G.; the crystallographic data will be published separately.
[9] S. Scheibye, J. Kristensen, S.-O. Lawesson, *Tetrahedron* **35** (1979) 1339.
[10] M. P. Cava, M. I. Levinson, *Tetrahedron* **41** (1985) 5061.
[11] S. Scheibye, R. Shabana, S.-O. Lawesson, C. Roemming, *Tetrahedron* **38** (1982) 993.
[12] S. Kametani, H. Ohmura, H. Tanaka, S. Motoki, *Chem. Lett.* **1982**, 793.

[56/90]