

Reaction of Lithiated 2-Trimethylsilyl-1,3-dithiane with (±)-Pantolactone with (±)-Pantolactone

V. Z. Vasikov, I. A. Serbaev, A. M. Gimazetdinov, and M. S. Miftakhov

*Institute of Organic Chemistry, Ufa Research Center, Russian Academy of Sciences,
pr. Oktyabrya 71, Ufa, 450054 Bashkortostan, Russia
e-mail: bioreg@anrb.ru*

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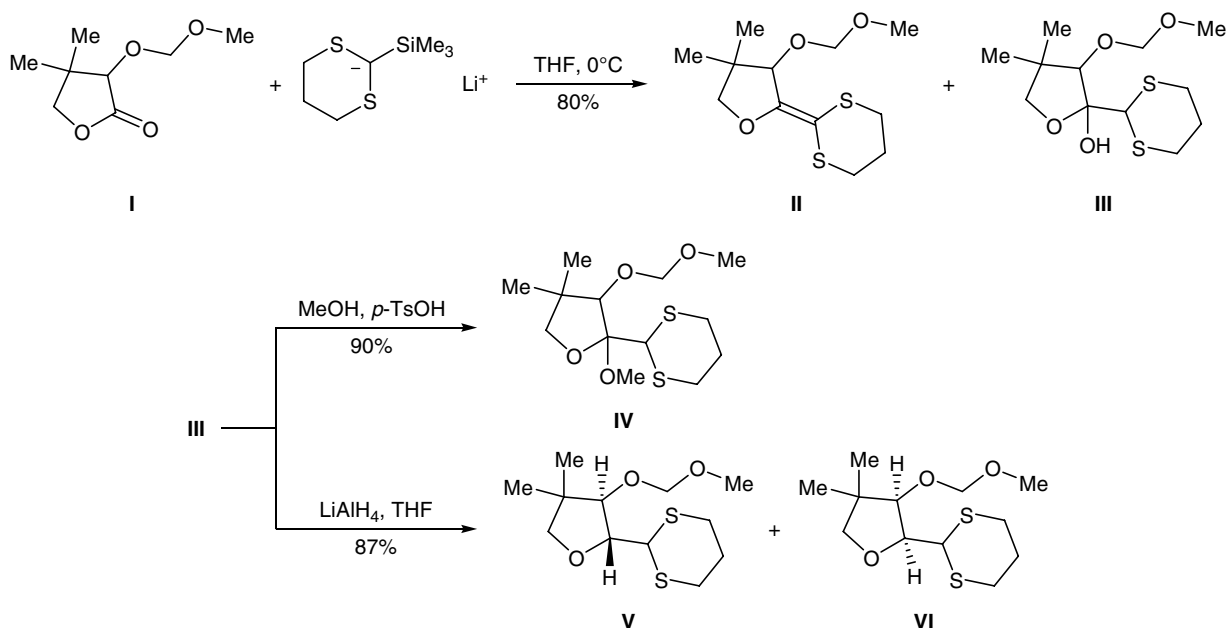
Abstract—Pantolactone methoxymethyl ether reacted with lithiated 2-trimethylsilyl-1,3-dithiane to give the corresponding ketene dithioacetal and formal monoaddition product of silicon-free 2-lithio-1,3-dithiane at a ratio of 2:1. Possible ways of formation of the latter are discussed.

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With the goal of obtaining functional derivatives of pantolactone at the C¹ atom we examined the reaction of its methoxymethyl ether **I** with 2-trimethylsilyl-1,3-dithiane lithium salt [1, 2]. It is known that the latter is used as reagent in the Peterson olefination of aldehydes and ketones [3] to obtain the corresponding ketene dithioacetals [4]. In our experiments, the reaction of equimolar amounts of compound **I** and 2-trimethylsilyl-1,3-dithiane lithium salt in THF at 0°C led to the formation of a mixture of two products, ketene dithioacetal **II** and hydroxy derivative **III**, at a ratio of

2:1 (Scheme 1). Compounds **II** and **III** were separated by column chromatography on silica gel and were subjected to reduction and acetalization. The reaction of **III** with methanol in the presence of *p*-toluenesulfonic acid gave methoxy derivative **IV** in quantitative yield. Although we failed to reduce the double bond in molecule **II** with LiAlH₄ in THF at 65°C, compound **III** under analogous conditions was smoothly converted into a mixture of epimeric substituted tetrahydrofurans **V** and **VI** which can be separated by chromatography on silica gel. Signals from the C², C³, and C^{2'} atoms in

Scheme 1.



2-(1,3-Dithian-2-yl)-2-methoxy-3-methoxymethoxy-4,4-dimethyltetrahydrofuran (IV). *p*-Toluene-sulfonic acid, 0.001 g, was added to a solution of 0.1 g (0.34 mmol) of compound **III** in 4 ml of anhydrous methanol, and the mixture was stirred for 4 h. The mixture was then treated with 0.01 g of NaHCO₃ and evaporated under reduced pressure. The residue was subjected to column chromatography on silica gel to isolate 0.104 g (99%) of compound **IV** as an oily substance. IR spectrum, ν , cm⁻¹: 1060, 1470, 2910. ¹H NMR spectrum, δ , ppm: 1.13 s (3H, CH₃), 1.16 s (CH₃), 1.80 m and 2.10 m (2H, SCH₂CH₂), 2.80–2.90 m (4H, SCH₂), 3.41 s (3H, OCH₃), 3.43 s (3H, OCH₃), 3.67 d (1H, CH₂O, J = 8.5 Hz), 3.73 d (1H, CH₂O, J = 8.5 Hz), 4.06 s (1H, 2'-H), 4.68 s (1H, 3-H), 4.71 d (1H, OCH₂O, J = 5.76 Hz), 4.75 d (1H, OCH₂O, J = 5.76 Hz). ¹³C NMR spectrum, δ_c , ppm: 22.04 (CH₃), 26.97 (CH₃), 25.76 (SCH₂CH₂), 30.32 (SCH₂), 30.72 (SCH₂), 39.63 (C⁴), 48.26 (C²), 51.32 (OCH₃), 56.17 (OCH₃), 79.33 (C⁵), 86.62 (C³), 98.12 (OCH₂O), 105.85 (C²). Found, %: C 51.05; H 7.95; S 19.50. C₁₃H₂₄O₄S₂. Calculated, %: C 50.62; H 7.84; S 20.79.

2-(1,3-Dithian-2-yl)-3-methoxymethoxy-4,4-dimethyltetrahydrofurans V and VI. A solution of 0.100 g (0.34 mmol) of compound **III** in 2 ml of anhydrous THF was added to a suspension of 0.023 g (0.68 mmol) of LiAlH₄ in 4 ml of anhydrous THF, and the mixture was stirred for 1 h. Excess LiAlH₄ was quenched by treatment with 3 ml of a saturated solution of sodium chloride, the aqueous phase was extracted with chloroform (3×10 ml), the extracts were combined, dried over Na₂SO₄, and evaporated, and the residue was separated by column chromatography on silica gel to isolate 0.04 g (43%) of compound **V** and 0.041 g (44%) of stereoisomer **VI** as colorless oily substances.

trans Isomer **V**. IR spectrum, ν , cm⁻¹: 1050, 1440, 2950. ¹H NMR spectrum, δ , ppm: 1.00 s (3H, CH₃), 1.02 s (CH₃), 1.90 m and 2.10 m (2H, SCH₂CH₂), 2.80–3.00 m (4H, SCH₂), 3.48 s (3H, OCH₃), 3.42 d (1H, CH₂O, J = 11.3 Hz), 3.50 d (1H, CH₂O, J =

11.3 Hz), 3.60 d (1H, 2'-H, J = 7.0 Hz), 3.95 d.d (1H, 2-H, J = 7.0, 2.86 Hz), 4.45 d (1H, 3-H, J = 2.86 Hz), 4.75 d (1H, OCH₂O, J = 6.24 Hz), 4.87 d (1H, OCH₂O, J = 6.24 Hz). ¹³C NMR spectrum, δ_c , ppm: 21.06 (CH₃), 22.27 (CH₃), 25.68 (SCH₂CH₂), 29.13 (SCH₂), 30.21 (SCH₂), 40.03 (C⁴), 51.20 (C^{2'}), 56.50 (OCH₃), 69.65 (C⁵), 75.14 (C²), 85.16 (C³), 99.71 (OCH₂O). Found, %: C 51.24; H 7.55; S 22.43. C₁₂H₂₂O₃S₂. Calculated, %: C 51.76; H 7.96; S 23.03.

cis Isomer **VI**. IR spectrum, ν , cm⁻¹: 1020, 1480, 2950. ¹H NMR spectrum, δ , ppm: 0.98 s (3H, CH₃), 0.99 s (CH₃), 2.10–2.30 m (2H, SCH₂CH₂), 2.7 m (2H, SCH₂), 2.9 m (2H, SCH₂), 3.40 s (3H, OCH₃), 3.31 d (1H, CH₂O, J = 11.61 Hz), 3.45 d (1H, CH₂O, J = 11.61 Hz), 3.84 s (1H, 2'-H), 3.96 d (1H, 2-H, J = 9.62 Hz), 4.06 d (1H, 3-H, J = 9.62 Hz), 4.72 d (1H, OCH₂O, J = 6.57 Hz), 4.80 d (1H, OCH₂O, J = 6.57 Hz). ¹³C NMR spectrum, δ_c , ppm: 20.82 (CH₃), 23.51 (CH₃), 25.45 (SCH₂CH₂), 27.32 (SCH₂), 27.71 (SCH₂), 40.02 (C⁴), 49.28 (C^{2'}), 56.37 (OCH₃), 67.94 (C⁵), 68.86 (C²), 83.08 (C³), 99.45 (OCH₂O). Found, %: C 51.20; H 7.79; S 22.41. C₁₂H₂₂O₃S₂. Calculated, %: C 51.76; H 7.96; S 23.03.

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