CHEMISTRY LETTERS, pp. 947-948, 1973. Published by the Chemical Society of Japan

FORMATION OF MONOTERPENOID SKELETON FROM C_9 DIEPOXIDE USING 1,3-DITHIANE

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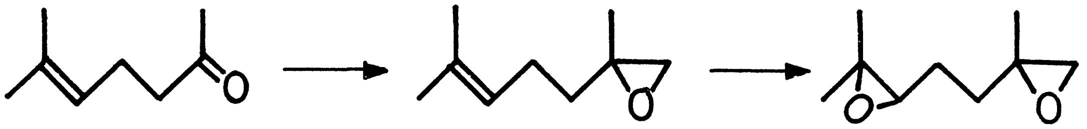
The reaction of 2,2-dilithio-1,3-dithiane with C_9 diepoxide (3) prepared from 6-methyl-5-hepten-2-one (1) afforded precursors of monocyclic and acyclic monoterpenoid compounds (4), (5), (6a), and (6b).

Numerous studies on application of 1,3-dithiane for organic syntheses such as a masking reagent for carbonyl group, reduction of carbonyl function, extention of carbon-carbon linkage, etc., have been carried out in recent years.[1] In this paper, we describe the reaction of diepoxide (3) derived from methylheptenone (1) with 2,2-dilithio-1,3-dithiane, giving monocyclic and acyclic monoterpenoid derivatives.

The monoepoxide (2) (bp 81 °C/45 mmHg, m/e 140 (M$^+$), 60-71%) prepared from (1) by treatment with trimethyloxosulfonium iodide and/or bromide in the presence of methyl sulfinyl carbanion[2] was subjected to oxidation with perbenzoic acid to afford 2,6-dimethylhepta-1,2,5,6-diepoxide (3) (84.0-88.0 °C/14 mmHg, m/e 156 (M$^+$), 70%). The diepoxide (3) was treated with a mixture of 1.6-2.0 equiv mol of *n*-butyllithium and 1.0 equiv mol of 1,3-dithiane in dry THF with stirring for ca. 20 hr and followed by addition of 2.0 equiv mol of *n*-butyllithium or 1.25 equiv mol of *n*-butyllithium-TMEDA complex[3] below -20 °C with stirring additional 40-60 hr to give (4), (5), (6a), and (6b) in 84-85% yield. The reaction conditions and the yields are summerized in Table 1. The proportion of cyclization products (6a) and (6b) was found to increase by addition of *n*-butyllithium-TMEDA complex at ca. -30 °C. TLC analysis of the crude product on silica gel showed presence of four kinds of components (Rf = 0.45, 0.40, 0.25, and 0.15; CH_2Cl_2-AcOEt/9:1).



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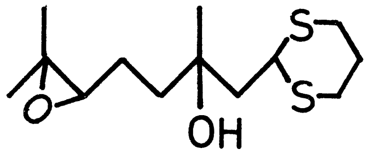

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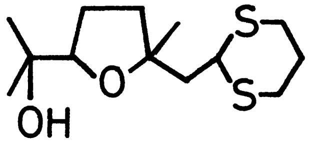

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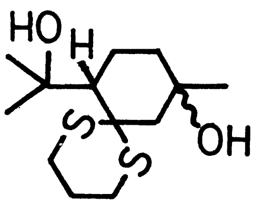


6a, b

The products were separated by column chromatography on silica gel and their structures were characterized by IR, NMR, and Mass spectra.[4]

The upper two spots (Rf 0.45 and 0.40) on TLC were consistent with the compounds (4) and (5) (7 : 3), respectively. Treatment of the compound (5) with an excess amount of n-butyllithium in dry THF afforded a mixture of the compounds (4), (6a), and (6b) along with an appreciable amount of (5). This fact reveals that lithio derivatives of (4) and (5) exist as an equilibrium mixture, which would further cyclize to give (6a) and (6b) in the medium.

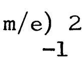
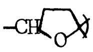
Table 1. Reaction Conditions and Yields $(3) \xrightarrow{\text{Step A}} \xrightarrow{\text{Step B}} (4) + (5) + (6a,b)$

Step A (n-BuLi mmol)	Step B	Temp (° C)	Time (day)	Yield, (%) (4) + (5)	(6a,b)
2.0	2.0	20-25	3	15	36
2.0	1.25[a)]	1-2	5	44	40
1.6	1.25[a)]	-20- -30	3	40	45

a) n-BuLi-TMEDA complex was added.

The lower two spots (Rf 0.25 and 0.15) on TLC were assigned to be compounds (6a) and (6b) (4 : 5). Apparent difference on IR and Mass spectra of the products (6a) and (6b) has not been observed, however, NMR spectra of (6a) and (6b) showed the hydroxy group absorptions at δ 3.02 and 1.67, respectively, exhibiting the presence of configurational isomers (6a) and (6b). Further works on the conversion of the products (6a) and (6b) into several monoterpenes are in progress.

REFERENCES AND FOOTNOTES

1. E. J. Corey and D. Seebach, Angew. Chem., 77, 1134 (1965); D. Seebach, Synthesis, 17 (1969); E. Vedejs and P. L. Fuchs, J. Org. Chem., 36, 366 (1971); S. Rozen, I. Shahak and E. D. Bergmann, Tetrahedron Lett., 1837 (1972); F. Sher, J. L. Isidor, H. R. Taneja, and R. M. Carlson, ibid., 577 (1973) and references are cited therein.
2. E. J. Corey and M. Chaykovsky, J. Amer. Chem. Soc., 87, 1353 (1965).
3. R. J. Crawford, W. F. Erman, and C. D. Broaddus, ibid., 94, 4298 (1972).
4. Spectral data: the compound (4), IR 3486, 1278, 1244, 1176, 1094, 732 cm^{-1}; NMR ($CDCl_3$) δ 4.19 (t, J = 5.8 Hz, 1H, S-CH-S), 3.60-4.00 (m, 1H, -CH); MS (m/e) 276 (M^+), 258, 243, 218, 159. The compound (5), IR 3460, 1280, 1245, 1094, 1060, 894 cm^{-1}; NMR ($CDCl_3$) δ 4.19 (t, J = 5.7 Hz, 1H, S-CH-S), 3.71 (m, 1H, -CH); MS (m/e) 276 (M^+), 258, 243, 218, 159. The compound (6a), IR 3440, 1275, 1160, 1052, 908, 732 cm^{-1}; NMR ($CDCl_3$) δ 1.15-1.53 (m, 9H, 3Me), 3.02 (m, 2H, 2OH); MS (m/e) 276 (M^+), 258, 243, 200, 181, 150. The compound (6b), IR 3440, 1162, 1096, 950, 908, 730 cm^{-1}; NMR ($CDCl_3$) δ 1.08-1.46 (m, 9H, 3Me), 1.67 (m, 2H, 2OH); MS (m/e) 276 (M^+), 258, 243, 200, 181, 150. Satisfactory elemental analyses were obtained for all new compounds.

(Received June 21, 1973)