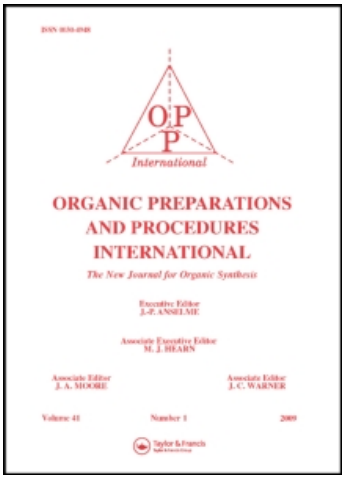

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PREPARATION OF EPOXYOLEFINS EMPLOYING DIMETHYLOXOSULFONIUM METHYLIDE

Benjamin C. Clark Jr.[a]; David J. Goldsmith[a]
[a] Department of Chemistry, Emory University, Atlanta, Georgia

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PREPARATION OF EPOXYOLEFINS[1] EMPLOYING DIMETHYLOXOSULFONIUM METHYLIDE

Benjamin C. Clark, Jr.[2,3] and David J. Goldsmith
Department of Chemistry, Emory University
Atlanta, Georgia 30322

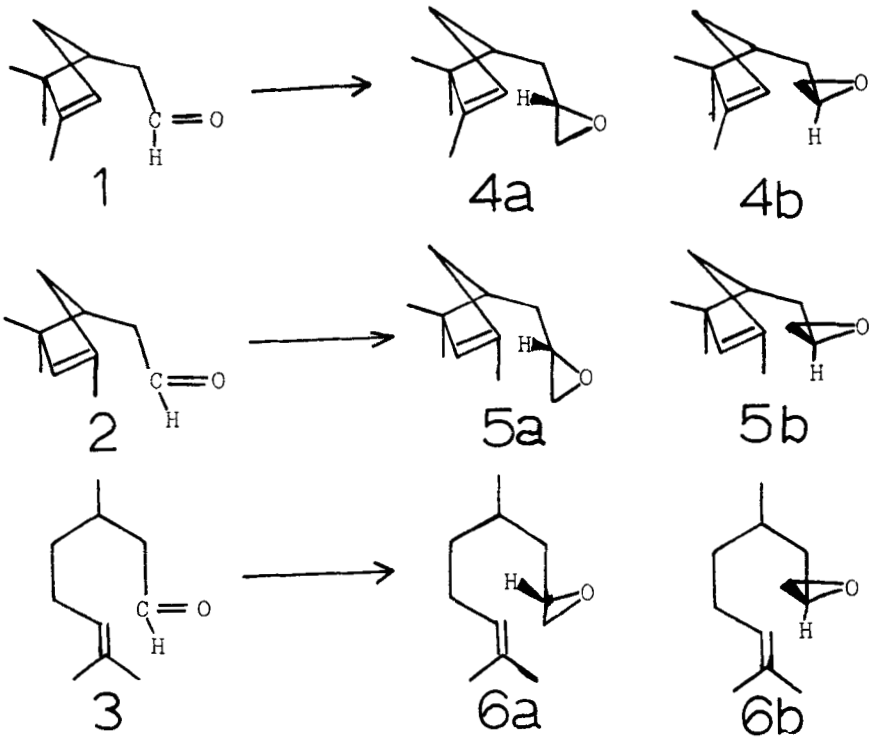
We first reported[4] the cyclization of an acyclic epoxyolefin as a model for lanosterol and cholesterol biosynthesis, a process now shown[5] to be the pathway for the *in vivo* formation of these compounds.

In this paper, we report the syntheses of three new epoxyolefins which have been found[6,7,8] to undergo acid catalyzed cyclizations to yield a variety of new compounds.

The syntheses of 4-(2,3-epoxypropyl)-1,5,5-trimethylcyclopentene (4), 4-(2,3-epoxypropyl)-2,5,5-trimethylcyclopentene (5), and 8,9-epoxy-2,6-dimethyl-2-nonene (6) have been accomplished by treatment of the respective aldehyde precursors 1, 2 and 3 with dimethyloxosulfonium methylide using essentially the procedure of Corey[9].

At the time this work was undertaken, there had apparently been no reported application of this epoxidation procedure to aldehydes with an α-proton. Aldehydes of this type might be expected to undergo aldol-type condensation under the strongly basic conditions of the epoxidation reaction and indeed the only isolated product in addition to epoxide is polymer. It was found, when the aldehydes were dissolved in an equal volume of dimethylsulfoxide and added dropwise to

the ylide rather than injecting the neat aldehyde quickly by syringe, that the yield of epoxide could be increased by ca. 20%.



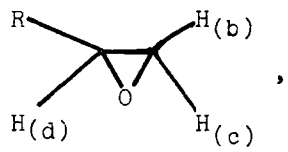
While a mixture of diastereoisomeric epoxides is, no doubt, produced in each case as shown (4a; 4b), no separation could be effected. In the case of epoxide 4, nmr of the LAH reduction products and information from cyclization products indicate the diastereomers to be produced in the ratio of 4a:4b as 3:2.

EXPERIMENTAL[10]

4-(2,3-Epoxypropyl)-1,5,5-trimethylcyclopentene (4). The trimethyloxosulfonium iodide used in this reaction was

prepared by the method of Kuhn[11]. Sodium hydride (24 g, 0.55 mole) (55% dispersion in mineral oil) was placed in a three-necked 1-l flask equipped with a magnetic stirrer, syringe cap, and a gas dispersion tube and washed with pentane. The system was evacuated until the last traces of pentane had evaporated, the flask filled with nitrogen, and trimethyloxosulfonium iodide (124.7 g, 0.556 mole) added. Dimethylsulfoxide (600 ml of Baker "Reagent Grade") (distilled from calcium hydride) was introduced by hypodermic syringe with stirring. A vigorous evolution of gas was observed. The solution became milky white and was allowed to stir one hour. α-Campholenaldehyde[12] (85 g, 0.56 mole) dissolved in 85 ml of dimethylsulfoxide, was added dropwise over a period of one hour. The mixture was then stirred one hour at room temperature and one and one-half hours at 50 to 55°. The mixture was cooled, poured into an equal volume of ice and water, and extracted with ether. The ethereal layer was washed with water, saturated sodium bicarbonate solution, water, brine, and dried over potassium carbonate. The ethereal layer was concentrated <u>in vacuo</u> to yield 91.2 g of crude oxide. Vacuum distillation of the epoxide afforded 65.9 g of <u>4</u> which was greater than 95% pure by glpc (68% yield), bp 68-69° at 2.5 to 2.6 mm. Epoxide <u>4</u> was eluted as a single component on Apiezon L, Carbowax 20-M and Reoplex 400 columns. The epoxide had bp 65° at 2.4 mm; n_D^{23} 1.4656; ir ν_{max}^{neat} 3020, 1650, 932, 846, 757 cm^{-1}. The nmr spectrum (CCl_4) showed two sharp three-proton singlets at δ0.76 and 1.00 ($C\lessdot^{CH_3}_{CH_3}$), a narrow three-proton multiplet at 1.60

(= C - CH_3), a one-proton quartet (J = 2.5 Hz) with additional fine coupling, centered at 2.34 (H_b),



a two-proton broad multiplet centered at 2.7 (H_c and H_d) and a one-proton unresolved vinyl pattern at 5.20.

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.36; H, 10.98.

The structure of epoxide 4 was further confirmed by reduction with LAH to methylcampholenol identical in all respects to authentic material prepared by the method of Ritter and Russell[13].

4-(2,3-epoxypropyl)-2,5,5-trimethylcyclopentene (5). Epoxide 5 was prepared by the above procedure from 2,4,4-trimethylcyclopent-3-enylacetaldehyde[14,15ab] (2) in 55% yield. A pure fraction of 5 (>99.5% by glpc) had bp 61° C at 2.3 mm; ir ν_{max}^{neat} 3020, 1655, 1360, 1380, 930, 840, 825, 755 cm^{-1}; nmr (CCl_4) δ0.80 (s, 3H), 1.05 (s, 3H), 1.67 (m, 3H), 2.3 (q, 1H), 2.68 (m, 2H), 5.14 (m, 1H); mass spectrum m/e, 166(5) (M+), 151(36), 135(63), 109(51), 108(77), 107(97), 93(100), 91(45), 55(40), 41(74).

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.67; H, 10.96.

8,9-Epoxy-2,6-dimethyl-2-nonene, (6). Epoxide 6 was prepared by the above procedure from citronellal[16] in 51% yield. A pure fraction (99.5% by glpc) of 6 had bp 68° at 2.0 mm, 64° at 1.7 mm; n_D^{23} = 1.4508; ir ν_{max}^{neat} 1418, 1380, 835 cm^{-1}; nmr (CCl_4) δ0.96 (d, 3H), 1.60 (s, 3H), 1.68 (s,

3H), 2.44 (m, 1H), 2.55 (t, 1H with additional splitting), 2.78 (m, 1H), 5.07 (t, 1H with additional splitting); mass spectrum, m/e, 168(1) (M+), 109(20), 95(42), 82(38), 61(40), 69(89), 67(38), 56(56), 41(100).

Anal. Calcd. for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.31; H, 12.07.

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