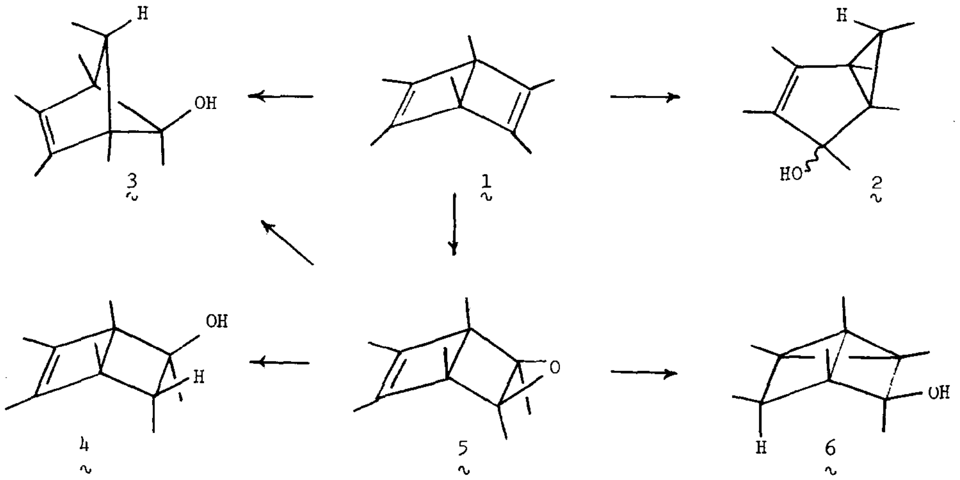
Tetrahedron Letters No. 19, pp 1561 - 1564, 1975. Pergamon Press. Printed in Great Britain.

ANOMALOUS HYDRIDE REDUCTION OF HEXAMETHYLDEWARBENZENE EPOXIDE. 1,2,3,4,5,6-HEXAMETHYLTRICYCLO[2.2.0.0^{2,6}]HEXAN-3-OL

Grant R. Krow and James Reilly
Department of Chemistry, Temple University, Phila., Pa. 19122

(Received in USA 17 February 1975; received in UK for publication 1 April 1975)

Hexamethyldewarbenzene 1 is the precursor of several strained bicyclic alcohols 2-4 whose molecular formulae correspond to hydration of the parent hydrocarbon. Marked isomeric selectivity in the syntheses of 2-4 has been obtained by appropriate choices of synthetic sequences. Starting with 1 the alcohol 2 has been prepared with mercuric acetate/sodium borohydride[1], alcohol 3 with HCl followed by ethanolic KOH workup[2], and alcohol 4 with diborane/hydrogen peroxide[3]. Alcohol 4 has also been synthesized by oxidation of 1 with peracid[4] to give epoxide 5 followed by reduction of 5 with lithium metal[3]. We wish to report (1) selective syntheses of bicyclic alcohol 3 and a new alcohol 1,2,3,4,5,6-hexamethyltricyclo[2.2.0.0^{2,6}]-hexan-3-ol 6, and (2) a comparison of the hydride reductions of hexamethyldewarbenzene epoxide 5 with the anomalous hydride reduction[5] of cyclobutene epoxide 10.



Hexamethyldewarbenzene epoxide 5[4] was reacted with excess lithium aluminum hydride or aluminum hydride under the conditions shown in Table 1 to afford compounds 3, 6, and 7, shown in Scheme 1. Compound 3 was identified by spectral comparison with an authentic sample[2]. Alcohol 6, mp 55-56.5°, was identified via its spectral parameters, ir (CCl_4) 3520 cm^{-1}; pmr spectrum ($CDCl_3$) δ0.80 (s,3), 0.98 (s,3), 1.07 (s,6), 1.34 (s,3), 1.13 (d, J=6.5Hz, C_5-methyl), 2.12 (q, J=6.5Hz, H_5), 1.50 (OH); Eu(dpm)$_3$ shift ratio for H_5/C_5-methyl protons equals 1.95[6]. Ketone 7, 2,4-dinitrophenylhydrazone mp 163-164.5° (ethyl acetate), was also identified via spectral data; ir (CCl_4) 1710 cm^{-1}; pmr ($CDCl_3$) δ0.86 (t, J=6Hz, 6), 1.00 (s,3), 1.48 (m, J=1Hz, 3), 1.63 (m, J=1Hz, 3), 2.01 (s, 3), 2.54 (m, 2 allylic protons); irradiation at δ2.54 collapses the δ0.86 triplet to two singlets at δ0.90 and δ0.83. The slight chemical shift difference indicates a trans relationship of these methyl groups in 7, since they would be equivalent in the cis isomer by virtue of a molecular plane of symmetry.

Table 1. Hydride Reductions of Epoxide 5.

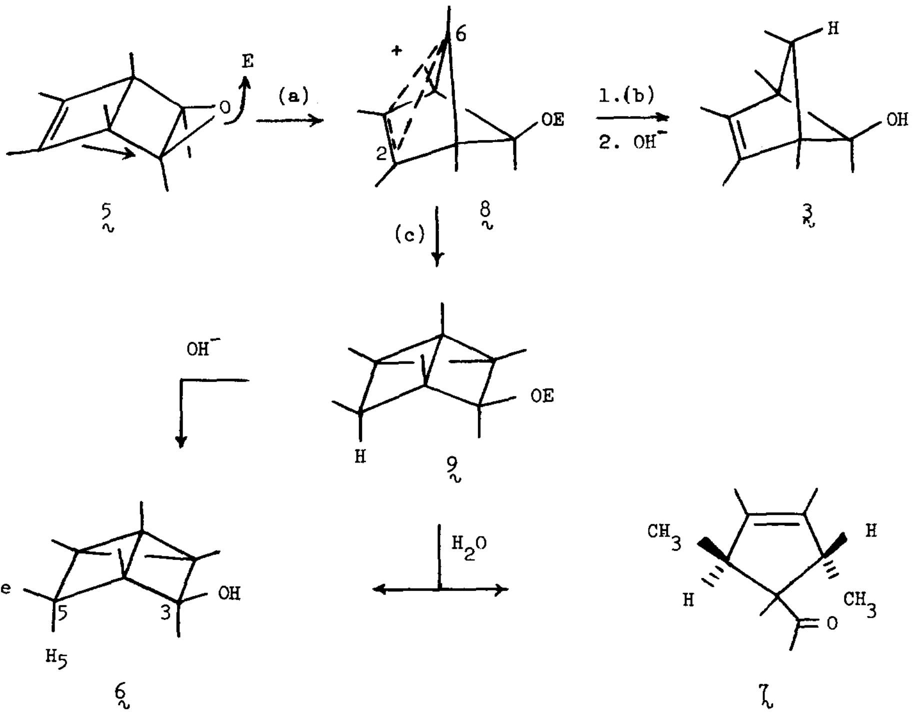
Reducing agent	Conditions	Workup	Major products (% of total product)[a]		
$LiAlH_4$	THF, reflux, two days[b,c]	H_2O		6 (40%)	7 (40%)
$LiAlH_4$	THF, 130°, sealed tube, one day[c,d]	H_2O		6 (40%)	7 (40%)
AlH_3 ($LiAlH_4$/100% H_2SO_4)[e]	THF/ether, 0-4°, 3hr[d]	H_2O		6 (47%)	7 (53%)
		10% NaOH		6 (100%)	
AlH_3 ($LiAlH_4$/oleum[f])	THF/ether, 0-4°, 3hr[d]	15% NaOH	3 (95%)	6 (5%)	

THF= tetrahydrofuran, (a) Glpc (2m x 1/4" 10% DC550 on Chrom W at 110°) and pmr of crude reaction mixtures, (b) 20% reduction, (c) complex mixture of products, (d) complete reduction, (e) N. M. Yoon and H. C. Brown, J. Amer. Chem. Soc., 90, 2927 (1968), (f) fuming sulfuric acid, i.e. 65% SO_3.

A mechanism which accounts for formation of products is shown in Scheme 1. Initial nucleophilic attack by hydride on epoxide 5 is blocked by endo methyl groups. Epoxide 5 ring opening can be facilitated, however, by coordination of oxygen with an electrophilic hydride reducing agent[5] or associated Lewis acid. Opening of epoxide 5 by an electrophile should lead readily to the bicyclo[2.1.1]hexenyl cation 8[7]. This cation can by attacked by nucleophile at C_6 to yield alcohol 3 on workup[7,8]. Under other conditions attack from the endo position at C_2 can lead to intermediate 9[7,8]. Basic quenching of ion 9 leads without rearrangement to alcohol 6. Neutral aqueous quenching of 9 affords in addition to 6 the less strained ring-opened ketone 7. Formally, ketone 7 is derived by protonation of 9 at a cyclopropyl carbon during or following bond reorganization.

Ion 8[7] has previously been trapped by attack of hydroxide ion at C_2 from an endo direction. Similar attack on 8 by a hydride nucleophile would result in alcohol 6 with the stereochemistry shown. The observed lanthanide pmr shift ratio for the proton H_5 versus the C_5-methyl proton is qualitatively consistent with this structural assignment[9].

Scheme 1

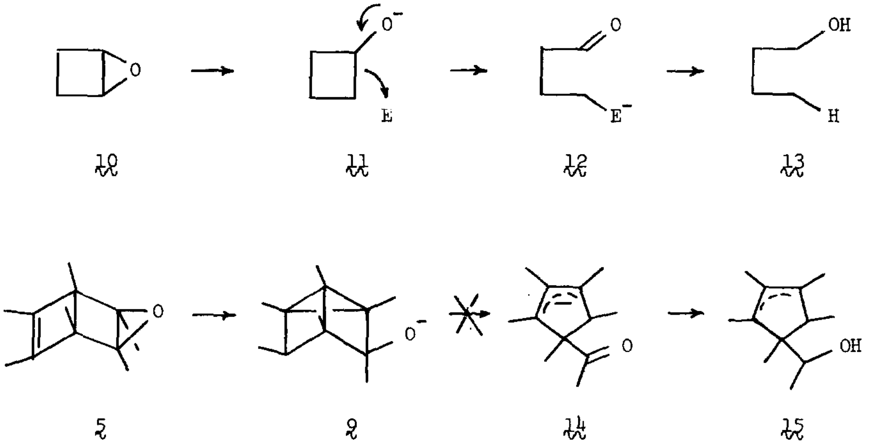


E= electrophile, (a) AlH_3, AlH_3/SO_3, or $LiAlH_4$, (b) AlH_3/SO_3, (c) AlH_3 or $LiAlH_4$

The mode of structural rearrangement during the hydride reduction of epoxide **5** can be contrasted with rearrangement during the anomalous hydride reduction[5] of cyclobutene epoxide **10** shown in Scheme 2. The cyclobutane alkoxide **11**, formed by nucleophilic attack on **10** with epoxide ring opening, undergoes ring cleavage to give carbanion **12**. Further reduction and hydrolytic workup gives **13**. The importance of ring strain in the opening of alkoxide **11**[5], suggested to us that the strain inherent in alkoxide **9** might result in ring opening to a carbanion such as **14**. Such a cleavage process was not observed with AlH_3; and, although the vigorous reaction conditions used for the $LiAlH_4$ reductions resulted in observation of eight or more products by glpc, the major products **6** and **7** were formed during hydrolytic workup from unrearranged **9**.

Scheme 2

E= electrophile



FOOTNOTES AND REFERENCES

(1) E. Müller, *Chem. Ber.*, **106**, 3920 (1973).

(2) H. Hogeveen and P. W. Kwant, *Tetrahedron Lett.*, **1972**, 5357.

(3) L. A. Paquette, S. A. Lang, Jr., S. K. Porter, and J. Clardy, *ibid.*, **1972**, 3141.

(4) H. N. Junker, W. Schäfer, and N. Niedenbruck, *Chem. Ber.*, **100**, 2508 (1967).

(5) L. A. Paquette, A. A. Youssef, M. L. Wise, *J. Amer. Chem. Soc.*, **89**, 5246 (1967); A. C. Cope and R. W. Gleason, *ibid.*, **84**, 1928 (1962).

(6) Shift ratios were determined using the ratio of slopes obtained by plotting lanthanide induced shift versus lanthanide/**6** mole ratios between 0.1 and 0.6.

(7) H. Hogeveen and P. W. Kwant. *ibid.*. **95**, 7315 (1973), note especially refs. 1-8 therein.

(8) H. Hogeveen, P. W. Kwant, and J. Thio, *Rec. Trav. Chim.*, **93**, 152 (1974).

(9) The H_5 *endo* hydrogen in **6** is closer to an *exo* hydroxyl substituent than is the C_5-methyl group in an *exo* position. In the *endo* C_5-methyl isomer this situation is reversed. In the model compound isoborneol (*exo*-hydroxyl) the more remote H_6 *exo* proton is shifted less than the closer H_6 *endo* proton[10]. Based on measurements of internuclear oxygen-proton distances, the magnitude of the shift ratio for the C_5 substituents in **6** appears to be inconsistent with an *endo* hydroxyl group.

(10) G. E. Hawkes, D. Leibfritz, D. W. Roberts, J. D. Roberts, *J. Amer. Chem. Soc.*, **95**, 1659 (1973).