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THE ALUMINUM ALKOXIDE REARRANGEMENT OF EPOXIDES. PART III[1].
REARRANGEMENT OF ISOLONGIFOLENE EPOXIDE

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Concurrent with the reported[2] alumina conversion of isolongifolene epoxide (1) to cyclopropyl alcohol 2 (mp 96-98° and 122-123°) we have isolated an identical compound (mp 126-128°) via the aluminum isopropoxide (AIP) rearrangement of 1. However, the experimental evidence is consistent with and in favor of an endo stereochemical assignment for isolongifolene epoxide in contradistinction with the exo structure recently reported[2].

Treatment of 1 with catalytic amounts of AIP afforded an excellent yield (70%) of a single crystalline alcohol (mp 126-128°), 2,2,7,7-tetramethyltetracyclo[6.2.1.$0^{3,8}0^{3,9}$]-undecan-4-ol (2)(nmr*, 4.3, t, J=4Hz (H α to OH), 0.97, s,(3CH_3), 0.86, s, (CH_3)), which upon chromic oxidation gave the corresponding ketone, 2,2,7,7-tetramethyltetracyclo[6.2.1.$0^{3,8}0^{3,9}$]-undecan-4-one (3) (λ_{max}^{hexane} 195 nm (ε 6000); 2-4-dinitrophenylhydrazone mp 220-222°; Anal. Calcd. for $C_{21}H_{26}O_4N_4$: C, 63.30; H, 6.58; N, 14.06. Found: C, 63.83; H, 6.7; N, 13.92; nmr, 1.13, s,(CH_3), 1.05, s,(CH_3), 1.02,s, (CH_3), 0.97, s,(CH_3)) . The latter was reduced with lithium aluminum hydride (LAH) to liquid alcohol 4 (bp 85-90°(2 mm), n_{20}^{D} 1.5010; nmr, 4.26, t, J=4Hz, (H α to OH), 1.08, s,(2CH_3), 1.00, s,(CH_3), 0.92, s,(CH_3)), which was proven to be an epimer of 2 at C_4 by chromic oxidation to ketone 3.

Reductive cleavage of 3 with lithium in liquid ammonia gave 2,2,7,7-tetramethyltricyclo[6.2.1.$0^{3,8}$]-undecan-4-one (5) (nmr, 1.2, s,(CH_3), 1.0, s,(CH_3), 0.97, s,(2CH_3), 2.22-2.5, m,(3H α to CO)), which was identical to

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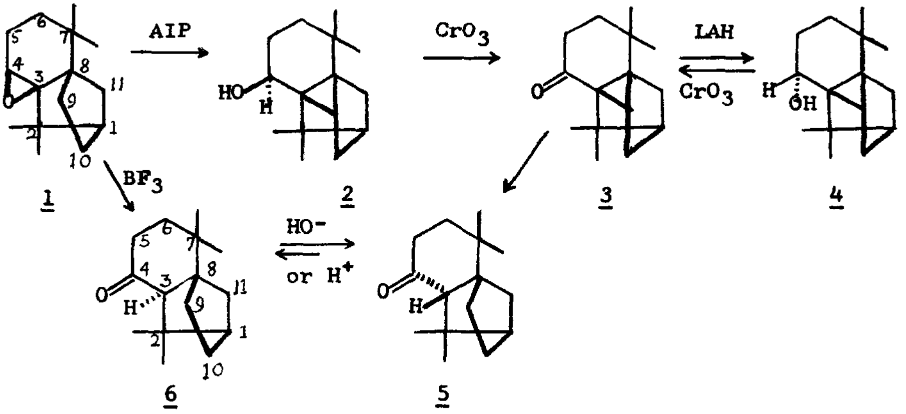
*Nmr Spectra were taken with a Varian A60A in $CDCl_3$ solutions and reported in δ units relative to TMS.

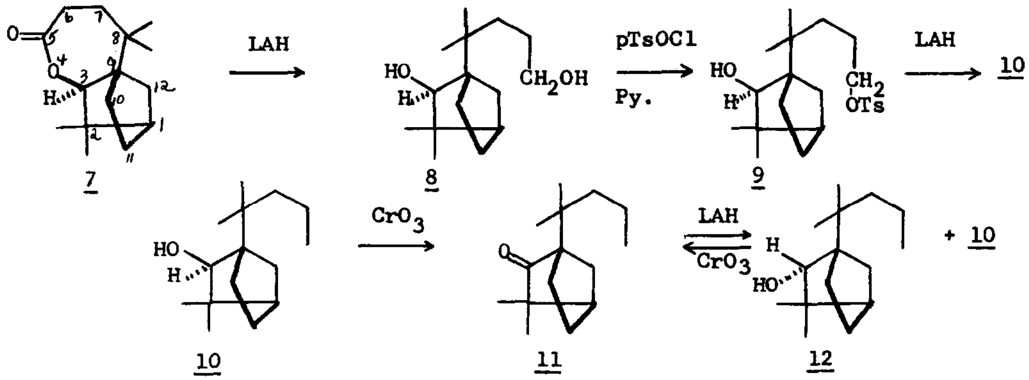
the major (92%) ketone afforded by acid or base equilibration of the epimeric ketone 6 (nmr, 1.22, s,(CH_3), 1.20, s,(CH_3), 1.00, s,(CH_3), 0.96, s,(CH_3), 2.11-2.28, m, (3H α to CO)), which was obtained as the result of BF_3 catalyzed rearrangement of isolongifolene epoxide (1).



Ketone 6, unlike its epimer 5, could easily be converted to the Bayer-Villiger lactone 7 (mp 76-79°)[3]. The stereochemistry at C_3 was established by reduction of 7 with LAH to the corresponding glycol 8 followed by monotosylation to 9 and reductive elimination with LAH to a single homolog of α-fenchyl alcohol 10 (nmr, 0.85, s,(CH_3), 0.90, s,($2CH_3$), 0.97, s,(CH_3), 3.74, s,(H α to OH)).

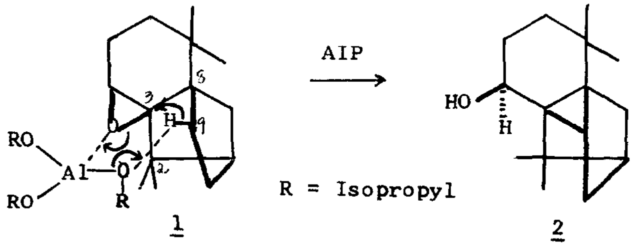
Chromic oxidation of 10 afforded the corresponding ketone 11 which upon reduction with LAH gave a mixture (non separable by vpc on 20M column) which consisted of 40% 10 and 60% of an epimeric alcohol 12 (nmr, methyl region near 1.0 similar, but not identical to 10, 3.35, s, (0.6 H α to OH for 12), 3.74, s, (0.4 H α to OH for 10)). Oxidation of the mixture of 10 and 12 with chromic acid gave back the fenchone homolog 11, thus establishing the epimeric nature of the two alcohols.

The nmr spectra of substituted bornanes[4] have been well studied and the proton α to an *endo*-2-hydroxyl group was shown to resonate at lower field than the corresponding proton of the *exo*-2-hydroxyl isomer. Nmr spectra of the fenchols[5], correlate with the stereochemical assignment made for the bornanes. On this basis the stereochemistry of 10 is assigned the *endo* structure (δ 3.74, s, for the proton α to OH) and the epimeric alcohol 12 obtained as the major product of LAH reduction of 11 is assigned the exo structure (δ 3.35 for αH).

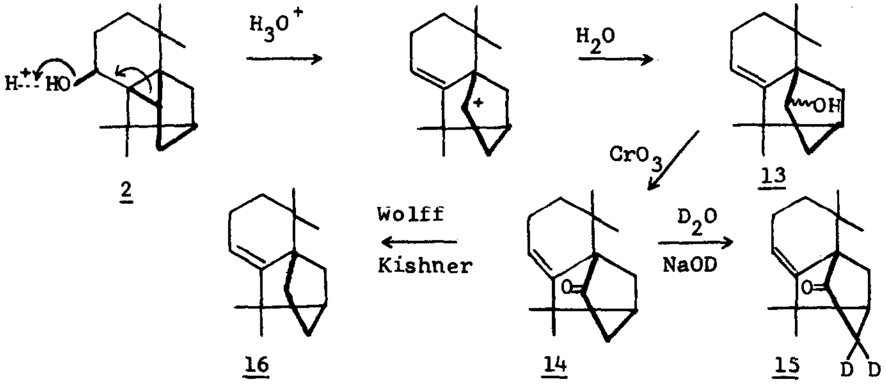


Following this assignment, the correct stereochemistry of the various products derived from the above reaction scheme is opposite to that assigned by the Indian team[2,3].

The concerted mechanism[1] for the aluminum alkoxide rearrangement of epoxides to allylic alcohols, involving the electrophilic cleavage of the most substituted oxygen-carbon bond, accompanied by cis-elimination of a proton from the least substituted vicinal carbon at the cleaved site, is compatible with the endo structure of isolongifolene epoxide (1). The absence in 1, of protons at C_2 and C_8 vicinal to the cleavage point, plus the proximity of the C_9 protons (which, by molecular models, seems very favorable) facilitate the cis-proton elimination at C_9 with the formation of cyclopropyl alcohol 2.



The structure of the cyclopropane ring in 2 resulting from a cis-proton elimination at C_9 in 1 is further confirmed by acid (aq. H_3PO_4 at 25°) cleavage of 2, which affords 2,2,7,7-tetramethyltricyclo[6.2.1.0^{3,8}]-3-undecen-9-ol (13) (mp 95-96°; nmr, 5.22, broad t, J=3Hz (vinyl H), 3.88, m, (H α to OH), 1.16, s,(CH_3), 0.98, broad s, $(2CH_3)$, 0.86, s,(CH_3); nmr in deuterated DMSO, 4.2, d, J=6Hz, (hydroxyl proton)). Chromic oxidation of 13 yields 2,2,7,7-tetramethyltricyclo[6.2.1.$0^{3,8}$]-3-undecen-9-one (14) (nmr, 5.52, t, J=3.5Hz (vinyl H), 1.18, s,(CH_3), 1.07, s,(CH_3), 1.05, s,(CH_3), 0.78, s,(CH_3)), which could be deuterated to dideutero ketone 15 (mass spec. M.W. 220); 14 was further convertedto isolongifolene (16) by Wolff-Kishner reduction.



An AIP trans elimination of a proton at C_{11} in 1, would have resulted in an unstable cyclopropane ring formation between C_3, C_8, and C_{11} which would be inconsistent with our results.

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