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***Cis* and *Trans*-2,2-Dimethyloctahydrobenzofuran (1)**

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In connection with another problem it was necessary to prepare and characterize the isomeric title compounds. An independent synthesis of each isomer was developed which involves some noteworthy stereospecific transformations.

The *cis*-ether, 2, was prepared very conveniently by the low pressure hydrogenation of the benzofuran, (2) 1, in acetic acid using 5% rhodium-on-alumina as the catalyst. The reduction was complete in about 2 hours and the yield of 2 was 94%. This facile hydrogenation of the aromatic nucleus has also been applied to the reduction of 1- and 2-naphthols to their corresponding decalols and shown to be highly stereoselective (3). The isomeric purity of the product was confirmed by its n.m.r. spectrum (4) which exhibited a single proton sextet (poorly resolved) at 6.14 τ . This chemical shift is due to the proton on the carbon bearing the ether linkage. Its field position is in good agreement with equatorially placed protons in similar systems (5). Since it is a well-known fact that equatorial protons resonate at lower fields than their axial counterparts, the absence of a signal at slightly higher fields (6.8-7.2 τ) would confirm the purity of the *cis*-configuration. This was indeed found to be the case. Actually, no signals appeared upfield from 6.14 τ until the hydrocarbon region (8.2-9.0 τ) was reached. Also appearing in the spectrum was the *gem*-dimethyl doublet at 8.72 and 8.87 τ .

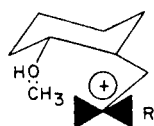
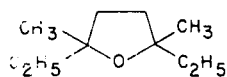
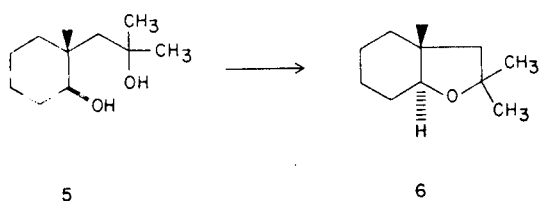
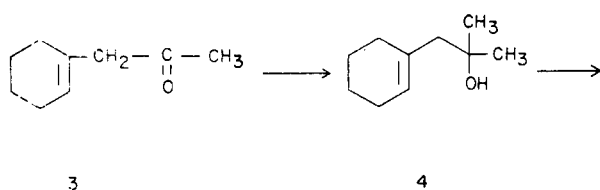
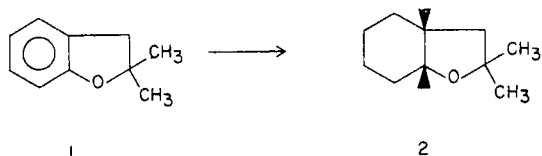
The *trans*-ether, 6, was obtained by first converting the unsaturated ketone, 3, to the corresponding tertiary alcohol, 4, by use of methyl magnesium bromide. Hydroboration of the unsaturated alcohol gave the *trans*-glycol uncontaminated by any other isomers (6). Stereospecific formation of the glycol is consistent with many hydroboration reactions (7) and the results of this experiment were further supported by the sharp melting point of 5 and examination of its n.m.r. spectrum. The key feature was the very broad signal (half-band width 15-17 c.p.s.) which peaked at 6.90 τ typical of an axial carbinol proton (5). Contamination by the *cis*-glycol would have given rise to a downfield signal due to the axial proton. The only signal downfield from the one at 6.90 τ was a two proton broad peak (half-band width 7 c.p.s.) at 4.34 τ due to the equivalency of the hydroxyl protons. This peak vanished from the spectrum upon the addition of deuterium oxide to the sample. The *gem*-dimethyl group appeared as a six proton singlet at 8.82 τ .

When the glycol, 5, was heated in dimethyl sulfoxide at 165-180° for 20 hours, the pure *trans* ether

was obtained in 78% yield with no evidence of concurrent olefin production due to elimination reactions. The use of dimethyl sulfoxide as a dehydrating agent for tertiary and benzylic alcohols has been described by Traynelis *et. al.*, (8). A further study of this reaction by Gillis and Beck (9) has shown that various 1,4-diols can readily be cyclized to tetrahydrofuran derivatives. More recently (10) the scope of this reaction has been increased to include the successful catalysis of pinacol rearrangements, dioxolane formation and *bis*-amide syntheses.

The transformation of the glycol, 5, to the ether, 6, stereospecifically represents still another example of the use of this unique solvent-catalyst. Proof of the purity of the *trans* ether was based upon its n.m.r. spectrum. Most striking was the fact that the broad signal present in the spectrum of the glycol at 6.90 τ was present at exactly the same field position for the ether. In fact, the 6.90 τ signals were superimposable. The major distinction between the glycol and ether spectra was the *gem*-dimethyl signal which was split in the ether. This, as expected, is due to the non-equivalency of the methyl groups in the rigid ether system.

The stereospecific cyclization of the glycol to the ether deserves further comment. The only information regarding the stereochemical nature of the dimethyl sulfoxide-catalyzed ether formation was reported by Gillis and Beck (9) who have observed that 3,6-dimethyl-3,6-octanediol cyclized to a mixture of the *cis* and *trans* tetrahydrofuran, 7, along with noticeable amounts of olefinic products. The non-stereospecific result of this reaction is to be expected however due to the freely rotating open chain glycol. In the case at hand the glycol contains both substituents in the preferred equatorial position, 8. Regarding the role of the dimethyl sulfoxide in catalyzing the ether formation (or other "acid-catalyzed" reactions previously mentioned) Traynelis (10) has presented much evidence for a carbonium ion mechanism. The fact that cyclohexanol is recovered unchanged after heating in dimethyl sulfoxide whereas tertiary alcohols dehydrate readily to olefins is consistent with the stable carbonium ion concept and also with the findings of this study. If these reactions all proceed *via* an initial carbonium ion (or a highly polarized C-O bond) then it is reasonable to assume that 8 (R=CH₃) is an intermediate in the formation of the *trans* ether. One would expect the tertiary carbonium ion to form before any significant C-O polarization occurs in the secondary hydroxyl group. It would be interesting to see the results

R = CH₃

R = H

of dimethyl sulfoxide treatment of the pure *trans* secondary alcohol derived from 8 (R=H). It would be reasonable to expect that such a glycol would lead to a mixture of the *cis* and *trans* ethers.

EXPERIMENTAL

trans-2-Hydroxy- α, α -dimethylcyclohexaneethanol, 5.

This compound was prepared by a published procedure (6) via the cyclohexenyl acetone, 3, and the unsaturated alcohol, 4. B.p. 121-125° (1.5 mm); n_D^{25} 1.4725, m.p. 55-56°.

trans-2,2-Dimethyloctahydrobenzofuran, 6.

A mixture of 57.3 g. (0.3 mole) of the glycol and 224 g. (3.0 mole) of dimethyl sulfoxide was heated for 20 hours at 165-180°. There was present above the reaction flask a distilling head to collect any volatile products (olefins) which may arise from the dehydration. No material was collected in this manner during the heating period. After cooling the reaction mixture, it was diluted with water. The oil that had separated was removed by extraction with ether. The ethereal extracts were dried with sodium sulfate and then concentrated. Distillation gave 40 g. (78%) of a colorless oil, b.p. 57-58° (6 mm); n_D^{25} 1.4536. The infrared spectrum showed no evidence of the OH stretching frequency.

Anal. Calcd. for C₁₀H₁₈O: C, 77.87; H, 11.76. Found: C, 77.82; H, 11.75.

2,2-Dimethylbenzofuran, 1.

This compound was prepared according to Adams *et al.*, (2); b.p. 28-29° (0.2 mm), n_D^{22} 1.5194 (reported (2) b.p. 67° (7 mm), n_D^{20} 1.5190). An improved procedure by Shales (11) was employed to prepare the precursor to the benzofuran; *o*-isobutylenephenol.

cis-2,2-Dimethyloctahydrobenzofuran, 2.

To a solution of 56.5 g. of the dimethylbenzofuran, 1, in 150 ml. glacial acetic acid was added 28 g. of 5% rhodium-on-alumina (12). The mixture was hydrogenated in a low-pressure Parr apparatus with initial hydrogen pressure of 60 p.s.i. The hydrogen pressure was replenished each time the bottle pressure dropped below 25 p.s.i. The theoretical hydrogen uptake (96 p.s.i.) was complete in 2.25 hours. The catalyst was removed by filtration (13) and the acetic acid solution neutralized with 20% sodium hydroxide. The oil that appeared was taken up in ether and the ether extracts washed with 5% sodium hydroxide solution then with water. After drying with sodium sulfate and concentration, the residue was distilled. There was obtained 52 g. (94%) of a colorless liquid, b.p. 77-78° (20 mm); n_D^{25} 1.4590. The infrared spectrum of this product was also devoid of -OH stretching bands.

Anal. Calcd. for C₁₀H₁₈O: C, 77.87; H, 11.76. Found: C, 77.78; H, 11.63.

The infrared spectra of the *cis* and *trans* ethers exhibited distinct difference only in the C-O stretch region. The *trans* ether possessed a strong doublet at 9.25 μ and 9.41 μ whereas the *cis* shows no absorption in this region. This *cis* isomer however, shows three strong peaks at 9.60, 10.05, and 10.41 μ where the *trans* exhibits only transparency.

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- (13) The catalyst may be re-used if washed first with acetic acid then with methanol and heated to 300° for 24 hours.

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