

Reduction of 5-Hydroxymethylene-*cis*-caran-4-one with Complex Hydrides

By Francesco Bondavalli and Mario Longobardi, Istituto di Chimica Farmaceutica e Tossicologica dell'Università, Genova

Pietro Schenone,* Cattedra di Chimica Organica, Facoltà di Farmacia, Viale Benedetto XV-3, 16132 Genova, Italy

Reduction of 5-hydroxymethylene-*cis*-caran-4-one (I) with lithium aluminium hydride gave 5-methylene-*cis*-caran-*cis*- and -*trans*-4-ols [(III) and (IV)] as main products, and small quantities of *cis*-5-methyl-*cis*-caran-4-one (II) and 5-hydroxymethyl-*cis*-car-4-ene (V), whereas reduction with sodium borohydride gave mainly 5-hydroxymethylcaran-4-ol (VI) with a lesser quantity of compounds (II)–(V). The mechanisms of these reactions are discussed.

REDUCTION of enolisable 1,3-dicarbonyl derivatives of bicyclic terpenes, such as 3-hydroxymethylenebornan-2-one¹ and 1,8-epoxy-3-hydroxymethylene-*p*-menthan-2-one,² by complex metal hydrides, has been investigated as a source of allylic alcohols and carbonyl derivatives. We report here the results of this reduction applied to (–)-5-hydroxymethylene-*cis*-caran-4-one (I).³

Compound (I) was reduced with an excess of lithium aluminium hydride and with sodium borohydride; the products were separated by column and gas chromatography into four components [(II)–(V)] in the former case, and five [(II)–(VI)] in the latter, and were identified from i.r. and n.m.r. spectral data.

cis-5-Methyl-*cis*-caran-4-one (II) shows an i.r. spec-

¹ J.-C. Richer and R. Clarke, *Tetrahedron Letters*, 1964, 935.

² C. Minardi, F. Bondavalli, and P. Schenone, *J. Chem. Soc. Chem. Commun.*, 1974, 1001.

trum similar to that of (–)-*cis*-caran-4-one, and the n.m.r. spectrum shows the C-5 methyl signal at δ 1.04 as a doublet; this deshielding by the carbonyl group indicates a near equatorial or *cis*-configuration.⁴

The i.r. spectra of the epimeric 5-methylene-*cis*-caran-4-ols (III) and (IV) are similar, but the n.m.r. spectra show significant differences. The 5-methylene signal (essentially a singlet at δ 5.10) in the case of (III) is only consistent with an axial position of the C-4 hydroxy-group, which thus does not influence the methylene protons. Moreover, the equatorial C-4 methyne signal (broad singlet) shows deshielding (δ 3.93). In contrast, the equatorial position of the C-4 hydroxy-

³ F. Bondavalli, P. Schenone, and M. Longobardi, *Il Farmaco, Ed. sci.*, 1974, 29, 48.

⁴ M. G. G. P. V. P. Schenone, and P. A. Steriand, *J. Chem. Soc. Chem. Commun.*, 1974, 1001.

group in (IV) causes nonequivalence of the 5-methylene protons (multiplets at δ 4.98 and 5.25; cf. 2-methylene-cyclohexanol⁵), and the C-4 methyne signal (δ 3.45) shows a broad multiplet pattern, typical of an axial proton with several couplings.

I.r. and n.m.r. spectra of 5-hydroxymethyl-*cis*-car-4-ene (V) (see Experimental section) are in agreement with the proposed structure. For the diol (VI) we were unable to assign the stereochemistry at C-4 and C-5 from spectral data.

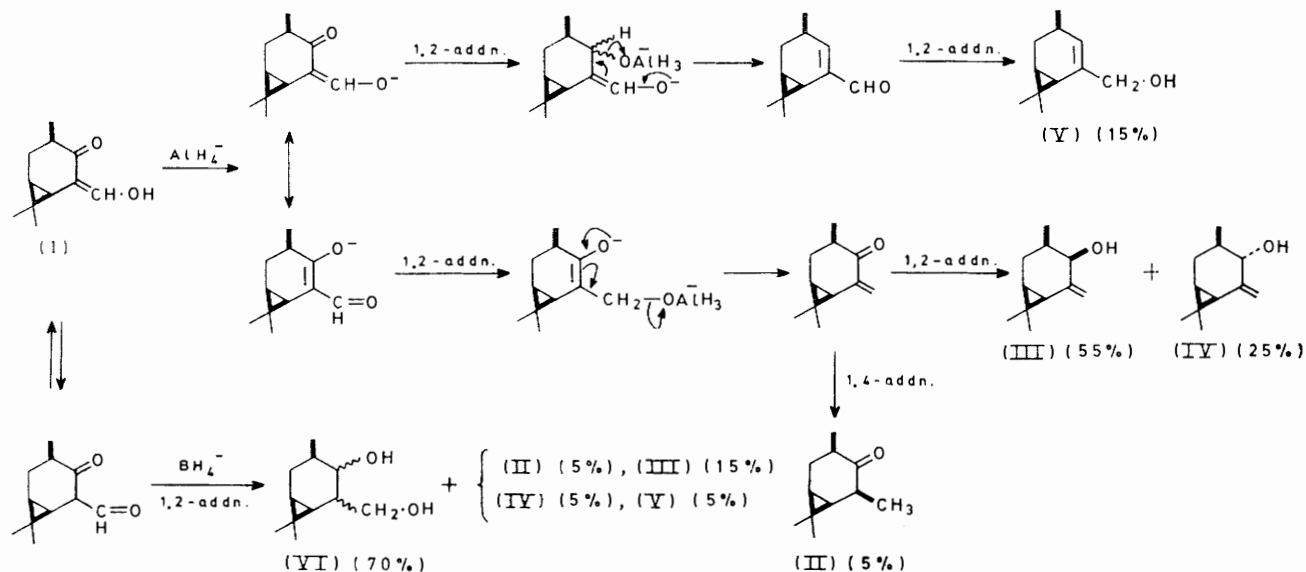
A possible pathway for these reductions is outlined in the Scheme. The 1,3-diol (VI) is the major product of

by acid-catalysed rearrangement of (III) and/or (IV), as was supposed in the case of 3-methylenebornan-2-ol,⁸ can be excluded because of the basicity of the reaction medium.

In both reductions, the ratio (*ca.* 3 : 1) of (III) to (IV) can be explained in terms of easier attack by the reducing anion from the less hindered side.

EXPERIMENTAL

I.r. spectra were measured with a Perkin-Elmer 257 spectrometer, and n.m.r. spectra with a Perkin-Elmer R12



SCHEME

the reduction with sodium borohydride. Under the reaction conditions (with methanol as solvent), protonation of intermediate enolate is possible and the low basicity of the borohydride anion will reduce the tendency for enolate formation.⁶

The reduction of compound (I) with lithium aluminium hydride, as in the cases of 3-hydroxymethylbornan-2-one¹ and 1,8-epoxy-3-hydroxymethylene-*p*-menthan-2-one,² differs from that of 2-hydroxymethylencyclohexanone,⁷ especially in the formation of an α -methyl ketone. The lack of an α -methyl ketone in the case of 2-hydroxymethylencyclohexanone may be ascribed to the occurrence of 1,2-addition only,⁶ whereas in the other cases 1,4-addition also takes place. This 1,4-addition may be a result of steric hindrance at the ketone carbonyl group, very strong in the case of the bornan-2-one (60–65% yield of 3-methylbornan-2-one¹) and weaker in the case of the epoxymenthanone² and in the present instance.

The possibility that the α -methyl ketone (II) is formed

instrument (60 MHz; tetramethylsilane as internal standard). T.l.c. was carried out on silica gel plates, with cyclohexane–benzene–ethyl acetate (4:1:1) as developer. G.l.c. was performed on a Fractovap GI instrument (C. Erba) (2800 \times 4 mm column packed with 2.5% SE 30 on silanized Chromosorb W; temperatures: evaporator 170 $^\circ$ C, column 90 $^\circ$ C; carrier gas helium). M.p.s were determined with a Mettler FP1 apparatus.

*Reduction of 5-Hydroxymethylene-*cis*-caran-4-one.*—(i) *With lithium aluminium hydride.* To a solution of lithium aluminium hydride (2.28 g, 60 mmol) in anhydrous ether (100 ml), a solution of compound (I) (5.41 g, 30 mmol) in the same solvent (25 ml) was added dropwise with stirring. After refluxing for 1 h, the mixture was cooled with ice and decomposed with water (2.5 ml), 15% sodium hydroxide solution (2.5 ml), and finally water again (5 ml). The inorganic precipitate was washed thoroughly with ether and the combined solutions were dried ($MgSO_4$) and evaporated. The liquid residue (5.30 g) exhibited four components on t.l.c. Repeated column chromatography on neutral alumina (grade I) gave the pure components as colourless oils.

⁵ V. S. Joshi, N. P. Damodaran, and S. Dev, *Tetrahedron*, 1968, 24, 5817.

⁶ H. O. House, 'Modern Synthetic Reactions,' Benjamin, Menlo Park, California, 1972, p. 82.

⁷ A. S. Dreiding and J. A. Hartman, *J. Amer. Chem. Soc.*, 1953, 75, 939; W. J. Bailey and J. C. Goossens, *ibid.*, 1956, 78, 2804.

⁸ J.-C. Richer and C. Lamarre, *Canad. J. Chem.*, 1967, 45, 1581.

The relative quantities of the products were ascertained by g.l.c.

cis-5-Methyl-*cis*-*caran*-4-one (II), eluted by light petroleum (b.p. 40–70°), had b.p. 68–70° at 5 mmHg (Found: C, 79.2; H, 10.7. $C_{11}H_{18}O$ requires C, 79.5; H, 10.9%); ν_{\max} (neat) 1 710 cm^{-1} ; δ (CCl_4) 1.04 (3 H, d, J 8 Hz, 5- CH_3), 1.02 (3 H, s, CH_3), 1.00 (3 H, d, J 6 Hz, 3- CH_3), and 0.82 (3 H, s, CH_3). 5-Methylene-*cis*-*caran*-*cis*-4-ol (III), eluted by light petroleum–benzene (4:1), had b.p. 60–63° at 0.5 mmHg (Found: C, 79.2; H, 11.1. $C_{11}H_{18}O$ requires C, 79.5; H, 10.9%); ν_{\max} (neat) 3 470, 3 065, 1 625, and 890 cm^{-1} ; δ (CCl_4) 5.10 (2 H, approx. s, $C=CH_2$) and 3.93br (1 H, s, $CH\cdot OH$). 5-Methylene-*cis*-*caran*-*trans*-4-ol (IV), eluted by benzene, had b.p. 70–73° at 0.5 mmHg (Found: C, 79.4; H, 11.2. $C_{11}H_{18}O$ requires C, 79.5; H, 10.9%); ν_{\max} (neat) 3 320, 3 080, 1 630, and 895 cm^{-1} ; δ (CCl_4) 5.25 and 4.98 (2 H, m, $C=CH_2$) and 3.45br (1 H, m, $CH\cdot OH$). 5-Hydroxymethyl-*cis*-*car*-4-ene (V), eluted by ether, had b.p. 83–85° at 0.5 mmHg (Found: C, 79.6; H, 10.8. $C_{11}H_{18}O$ requires C, 79.5; H, 10.9%); ν_{\max} (neat) 3 300, 1 660, and 825 cm^{-1} ; δ (CCl_4) 5.50 (1 H, m, $C=CH$), 3.93 (2 H, m,

$CH_2\cdot OH$), and 2.13 (1 H, m, OH; disappears with deuterium oxide).

(ii) *With sodium borohydride.* To a solution of compound (I) (5.41 g, 30 mmol) in methanol (50 ml), a solution of sodium borohydride (4.56 g, 0.12 mol) in *n*-sodium hydroxide (12 ml) was added dropwise with stirring. The mixture was refluxed for 2 h, the solvent removed under reduced pressure, and the residue taken up in water and extracted with ether. The combined extracts were dried ($MgSO_4$) and the solvent was distilled off. The semi-solid residue (5.30 g) exhibited five components [(II)–(VI)] on t.l.c. Washing the residue with light petroleum gave 5-hydroxymethyl-*caran*-4-ol (VI) as white needles, m.p. 116° (hexane) (Found: C, 71.8; H, 10.9. $C_{11}H_{20}O_2$ requires C, 71.7; H, 10.9%); ν_{\max} (KBr) 3 420, 1 060, and 1 020 cm^{-1} ; δ ($CDCl_3$) 3.88 (2 H, m, $CH_2\cdot OH$), 3.75 (1 H, approx. s, $CH\cdot OH$), and 2.80–2.20br (2 H, m, 2 OH; disappears with deuterium oxide).

We thank Dr. M. Canepa for the microanalyses and Mr. A. Panaro and Dr. S. Morasso for n.m.r. and i.r. spectra.

[5/1769 Received, 15th September, 1975]