

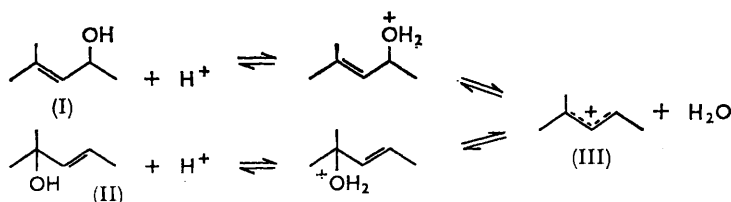
682. The Reduction of Mesityl Oxide to 4-Methylpent-3-en-2-ol.

By M. E. CAIN.

Good yields of 4-methylpent-3-en-2-ol are obtained by reduction of mesityl oxide only if, during isolation, acid treatment (which yields predominantly the isoallylic 2-methylpent-3-en-2-ol) is avoided. Lithium aluminium hydride is the preferred reductant, lithium tri-*t*-butoxyhydroaluminate, sodium borohydride, and aluminium isopropoxide giving varying amounts of isomeric alcohols and ketones as impurities.

REDUCTION of mesityl oxide (4-methylpent-3-en-2-one) by lithium aluminium hydride has been claimed¹ to give 4-methylpent-3-en-2-ol (I), Larsson^{1a} ascribing the inhomogeneity of the product to the presence of isomesityl oxide (4-methylpent-4-en-2-one) in the starting material. Repetition of Larsson's procedure gave mainly the isoallylic *trans*-2-methylpent-3-en-2-ol (II), but when mineral acid was omitted from the working-up process it was possible to obtain pure (I). Previous workers¹ may have obtained a mixture of these isomers.

Rapid isomerisation of (I) \rightleftharpoons (II) in presence of 2*N*-sulphuric acid has been confirmed separately, the equilibrium mixture (I : II \approx 1 : 2) being reached in just over five minutes



at room temperature. Acetic acid (2*N*) gives slower equilibration (I : II = 2.5 : 1 after 70 minutes). Diene formation was also observed in the former case,^{1b} the amount increasing with time. A similar equilibrium mixture is obtained by the neutral hydrolysis of

¹ (a) Larsson, *Trans. Chalmers Univ. Technol., Gothenburg*, 1950, No. 94, 15; (b) Green and Hickinbottom, *J.*, 1957, 3262; (c) Knights and Waite, *J.*, 1955, 2830.

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





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S-1,3-dimethylbut-2-enylthiouronium bromide, and obviously arises from different rates of attack by water molecules at the two positions of the 1,3,3-trimethylallyl carbonium ion (III).

Similar results were observed with lithium tri-*t*-butoxyhydroaluminat² as reductant, although the product obtained by neutral work-up also contained both the saturated alcohol, 4-methylpentan-2-ol, and ketone (4-methylpentan-2-one), as well as more 4-methylpent-4-en-2-ol than could be accounted for by the small amount (2%) of isomesityl oxide in the starting material. Two other reductants, sodium borohydride³ and aluminium isopropoxide,⁴ were also examined, giving the results compared in the Table. In both cases the

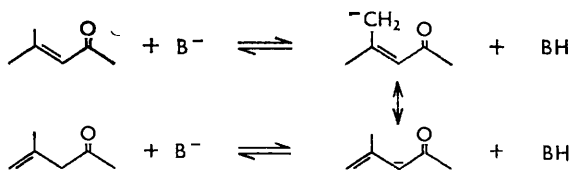
Composition of mesityl oxide reduction products.

Reductant	Solvent	Product (%) *					
							
LiAlH ₄ †	Et ₂ O	—	1.6	2.2	1.9	63.4	30.9
LiAlH ₄	Et ₂ O	—	—	0.4	2.0	0.2	97.4
LiAl(OBu ^t) ₃ H	THF	3.4	—	4.4	9.2	—	83.0
NaBH ₄	MeOH-H ₂ O	—	0.8	17.2	7.2	—	74.7
Al(OPr ⁱ) ₃	Pr ⁱ OH	—	7.5	1.3	6.3	1.9	83.0

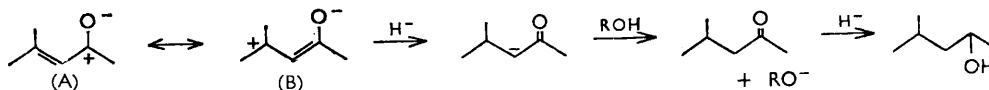
* Area % by gas-liquid chromatography (see Experimental section). † Dilute mineral acid used in work-up.

main product is 4-methylpent-3-en-2-ol, but the borohydride gives a large amount of the saturated alcohol, while both give enhanced amounts of the terminally unsaturated alcohol.

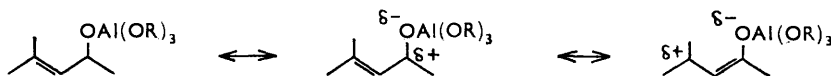
These observations may be explained by considering the effects of both basicity and polarity of the reducing media. Terminally unsaturated alcohol could arise in the more basic media (containing PrⁱO⁻, BH₄⁻, Bu^tO⁻) from an isomerisation process such as:



with subsequent reduction of the isomerised ketone. In polar media, attack by hydride ion at the tertiary carbon atom of the π -electron system of mesityl oxide could be enhanced by solvation supporting the existence of the larger dipole (B) at the expense of the smaller (A):



Consistently, the highest yield of saturated alcohol is obtained with sodium borohydride in aqueous methanol. In the less polar media, some contribution from polarisation of the C-O bond by aluminium alkoxide⁵ could account for the small amounts of this component:



² H. C. Brown and McFarlin, *J. Amer. Chem. Soc.*, 1956, **78**, 252.

³ Chaiken and W. G. Brown, *J. Amer. Chem. Soc.*, 1949, **71**, 122.

⁴ (a) Rouvé and Stoll, *Helv. Chim. Acta*, 1947, **30**, 2216; (b) Kenyon and Young, *J.*, 1940, 1547; Macbeth and Mills, *J.*, 1949, 2646.

⁵ Lee and Bhardwaj, *Canad. J. Chem.*, 1963, **41**, 1031.

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The saturated ketone obtained by reduction with tri-*t*-butoxyhydroaluminate could arise by this mechanism, insufficient reducing agent being present to complete the reduction to saturated alcohol.

These results show clearly that preparation of 4-methylpent-3-en-2-ol is best achieved by reduction of pure mesityl oxide with lithium aluminium hydride in ether, *strictly* avoiding the use of any acid during the working-up process.

EXPERIMENTAL

Materials.—Mesityl oxide (Kodak, London, Ltd.) contained 2% of isomesityl oxide (gas-liquid chromatography). Aluminium isopropoxide, *t*-butyl alcohol, and AnalaR isopropyl alcohol were redistilled, the last from aluminium isopropoxide. Tetrahydrofuran was dried by shaking it with an equal volume of glycerol, followed by redistillation, and stored over Linde molecular sieve 5A.

Analysis.—Products were examined by gas-liquid chromatography on 5 ft. \times 4 mm. columns of 20% polyethylene glycol (Carbowax 400) on acid-washed Celite at 65°, peaks being identified by retention indices with hexan-2-ol as internal standard.⁶ Normalised area percentages were determined in duplicate, peaks due to solvents being neglected. Infrared spectroscopy of the products from reduction with lithium tri-*t*-butoxyhydroaluminate and aluminium isopropoxide gave good agreement with gas-liquid chromatography.

Reduction Procedures.—*Lithium aluminium hydride.*^{1a} (a) Mesityl oxide (0.1 mole) in dry ether (25 ml.) was added to lithium aluminium hydride (0.05 mole) in dry ether (25 ml.) to cause gentle refluxing. Ice-cold water (10 ml.) was added cautiously, followed by 2*N*-sulphuric acid (50 ml.). The layers were separated and the product extracted in ether, the solvent being distilled through a 40 \times 1.5 cm. column packed with glass helices.

(b) Water (50 ml.) was added in place of the dilute acid, the organic layer decanted, and the slurry washed with ether by decantation.

*Lithium tri-*t*-butoxyhydroaluminate.*² *t*-Butyl alcohol (0.3 mole) was added slowly to an ice-cold suspension of lithium aluminium hydride (0.1 mole) in tetrahydrofuran (100 ml.). The cooling bath was removed and mesityl oxide (0.075 mole) added as above, the mixture then being heated under reflux for 2 hr. After cooling it was worked up by both methods described above.

*Sodium borohydride.*³ Mesityl oxide (0.1 mole) was added slowly to a solution of the borohydride (0.05 mole) in 30% aqueous methanol (20 ml.) at 60°, the exothermic reaction maintaining this temperature for 20 min. After a further 10 min. the layers were separated and the product isolated with ether.

Aluminium isopropoxide.^{4a} Aluminium isopropoxide (0.37 mole) in isopropyl alcohol (180 ml.) was heated to reflux through a 30-cm. Widmer column whose central tube was packed with glass helices. Mesityl oxide (0.37 mole) in isopropyl alcohol (40 ml.) was added during 3 hr., slow distillation maintaining b. p. 77—78°. Addition of isopropyl alcohol during distillation at 81—82° was continued for 50 hr., a total of 350 ml. being collected. The residue was freed from most of the alcohol by distillation, added to crushed ice, the layers separated, and the slurry washed with ether.

Preparation of 4-Methylpent-3-en-2-ol.—Mesityl oxide (1 mole) in dry ether (250 ml.) was added to lithium aluminium hydride (0.5 mole) in dry ether (250 ml.) so as to maintain gentle reflux. Excess of hydride was cautiously destroyed with ice-cold water, and more water (500 ml.) added. The aqueous slurry was washed with ether (3 \times 250 ml.), and the ether layers washed, dried, and distilled. The product (75 g., 75% yield) had b. p. 44.5—45°/15 mm., n_D^{20} 1.4404 (Found: C, 71.9; H, 11.9. Calc. for C₆H₁₂O: C, 71.9; H, 12.1%), purity 98% (gas-liquid chromatography).

Acid-catalysed Isomerisation of 4-Methylpent-3-en-2-ol.—The alcohol (2 ml.) in ether (20 ml.) was magnetically stirred with 2*N*-acid (20 ml.) at room temperature. Aliquot parts (5 ml.) of the ether layer were removed at various times, shaken with 2*N*-aqueous sodium hydroxide (10 ml.), washed with water (5 ml.), dried, and examined by gas-liquid chromatography.

*4-Methylpent-4-en-2-ol.*⁷—2-Methylpentane-2,4-diol (200 ml.) was dehydrated by rapid distillation from aniline (3 ml.) and hydrobromic acid (4 ml.). The organic layer was washed free from acid, dried, and redistilled, giving a product (35 g., 22% yield) having b. p. 42°/15 mm.,

⁶ Evans, *J. Chromatog.*, 1963, **12**, 2.

⁷ Kenyon and Young, *J.*, 1938, 1452.

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n_D^{20} 1.4342 (Found: C, 71.6; H, 11.9. Calc. for $C_6H_{12}O$: C, 71.9; H, 12.1%), purity 94% by gas-liquid chromatography. The infrared spectrum showed strong bands at 1635 and 888 cm^{-1} typical of $CH_2=CR_2$ unsaturation.

2-Methylpent-3-en-2-ol.—3,4-Epoxy-4-methylpentan-2-one, b. p. 50–52.5°/11 mm., n_D^{20} 1.4260 (Found: C, 62.9; H, 8.6. Calc. for $C_6H_{10}O_2$: C, 63.1; H, 8.8%), was obtained in 47% yield as previously described.⁸ Addition of this epoxide (0.2 mole) to a stirred solution of hydrazine hydrate (0.6 mole) in ethanol (150 ml.) containing acetic acid (1 ml.) gave an immediate exothermic evolution of nitrogen.⁹ Distillation of the ether extract gave a product (4 g., 20%), b. p. 120–122°, n_D^{20} 1.4320 (Found: C, 71.2; H, 12.1%). Gas-liquid chromatography showed the presence of main components of 37.3 and 61.4%. The infrared spectrum included the following characteristic bands: 3500 cm^{-1} (broad, -OH); 1675, 1661 cm^{-1} (C=C); 1380, 1364 cm^{-1} (*gem*-dimethyl and methyl); 967 cm^{-1} (*trans*-CH:CH). The intensity of the 967 cm^{-1} band showed that the major component had the *trans*-structure, and bands between 800 and 700 cm^{-1} were consistent with the presence of *cis*-CH:CH groups.¹⁰

Neutral Hydrolysis of S-1,3-Dimethylbut-2-enylthiuronium Bromide.—The bromide¹¹ (0.42 mole) was stirred with a solution of sodium acetate (0.63 mole) in water (500 ml.) at room temperature for 5 hr., when all had dissolved. Ether extraction after 4 days gave a product, b. p. 64–86°/54 mm., shown by gas-liquid chromatography to be a mixture of *cis*- (10%) and *trans*-2-methylpent-3-en-2-ol (50%) and 4-methylpent-3-en-2-ol (30%).

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⁸ Payne, *J. Org. Chem.*, 1958, **23**, 310.

⁹ Wharton and Bohlen, *J. Org. Chem.*, 1961, **26**, 3615.

¹⁰ Bellamy, "Infra-red Spectra of Complex Molecules," Methuen and Co., London, 2nd edn., 1960, p. 48.

¹¹ Saville, *J.*, 1962, 5040.