

SYNTHESIS OF TERPENE ALCOHOLS FROM ISOPRENE

AND NAPHTHYLLITHIUM

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Introduction

Recently, isoprene has been dimerized by various organometallic complexes, and various new terpenic hydrocarbons can thus be prepared.^{1,2} However, a direct synthesis of terpenic alcohols from isoprene has not yet appeared. It was reported by us that naphthyllithium in tetrahydrofuran dimerizes isoprene to give linear isoprene dimers, a mixture of 2,6-dimethylocta-2,6-diene, 2,7-dimethylocta-2,6-diene, and 2,6-dimethylocta-1,6-diene.³ This paper concerns a new convenient procedure for the preparation of linear terpenic alcohols using naphthyllithium and isoprene.

Experimental

All the reagents were purified, and the experiments were carried out in a dry apparatus under purified nitrogen.

Dimerization of Isoprene and Oxidation of Isoprene Dimer Anions

To 25.6 g (0.2 mol) of naphthalene and 300 ml of tetrahydrofuran, 4.2 g (0.59 mol) of sliced lithium was added and the mixture was then agitated at room temperature for 2 hr under dry nitrogen. Isoprene (40 g, 0.59 mol) was added over 6 hr and the mixture was stirred for 1 hr more. At the conclusion of the reaction, dry oxygen gas was passed slowly into the solution for 5 hr. As the reaction was very exothermic, the introduction of oxygen should be so regulated as to keep the temperature at 20°. It was treated with aqueous methanol, and the organic layer was isolated with isopropyl ether. The ether extracts were washed with water and dried over anhydrous sodium sulphate. Low-boiling fractions, such as isopropyl ether and isoprene, were removed by distillation to give 61 g of viscous oil. This was chromatographed on a silica gel column with n-hexane and methanol as eluents in that order. From the n-hexane eluate was obtained 32 g of a mixture (A) of naphthalene and isoprene oligomers. From the methanol eluate was obtained 28 g of an oily product (B) containing terpenic alcohols.

The fraction (A) contained 15 g of naphthalene and 15 g of isoprene oligomer mixture (b.p. 40–90°/3 Torr). The oligomer mixture consisted of isoprene dimer (10 g), trimer (3 g), and higher polymers (2 g), as shown by gas chromatography. The isoprene dimer was identified as a mixture of 2,6-dimethylocta-2,6-diene, 2,7-dimethylocta-2,6-diene, and 2,6-dimethylocta-1,6-diene by a comparison of their gas chromatographic retention times with those of authentic samples.³

Distillation of (B) gave 14 g of mixed alcohols (b.p. 65–120°/2 Torr). These alcohols were analysed by gas chromatography with a 3-m column of LAC-2R-446 at a temperature of 150°.

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¹ Candlin, J. P., and Jones, W. H., *J. chem. Soc.*, 1968, 1856.

² Watanabe, S., Suga, K., and Kikuchi, H., *Aust. J. Chem.*, 1970, **23**, 385.

³ Suga, K., Watanabe, S., Watanabe, T., and Kuniyoshi, M., *J. appl. Chem.*, 1969, **19**, 318.

using hydrogen and nitrogen as the carrier gas. The gas chromatogram showed eight principal peaks and three minor peaks: (i) 3,7-dimethylocta-1,7-dien-3-ol (1), R_t 6 min, peak area ratio 3%; (ii) unidentified product, R_t 8 min, 1%; (iii) unidentified product, R_t 9 min, 1%; (iv) 2,7-dimethylocta-2,6-dien-1-ol (2), R_t 10 min, 39%; (v) 2,6-dimethylocta-2,6-dien-1-ol (3) (*cis*-form), R_t 12 min, 7%; (vi) 2,6-dimethylocta-2,6-dien-1-ol (3) (*trans*-form), R_t 13 min, 7%; (vii) nerol (4), R_t 14 min, 8%; (viii) geraniol (5), R_t 15 min, 7%; (ix) unidentified product, R_t 26 min, 1%; (x) 2,7-dimethylocta-2,6-diene-1,8-diol (6), R_t 27 min, 15%; (xi) 2,6-dimethylocta-2,6-diene-1,8-diol (7), R_t 29 min, 11%. Redistillation of these alcohols (13 g) gave the following fractions: (A) b.p. 65–70°/2 Torr, yield 8 g, (B) b.p. 93–100°/2 Torr, yield 3 g, and (C) resinous matter, 2 g. The fraction (A) was hydrogenated over palladium-on-carbon in methanol solution at 50° to give the saturated alcohols. 2,7-Dimethyloctanol (50%), tetrahydrogeraniol (20%), tetrahydrolinalool (5%), and 2,6-dimethyloctanol (20%) were confirmed by gas chromatography. 3,7-Dimethylocta-1,7-dien-3-ol (1) was isolated by gas chromatographic trapping from fraction (A) (Found: C, 77.8; H, 11.7. Calc. for $C_{10}H_{18}O$: C, 77.9; H, 11.8%). Quantitative hydrogenation using a Pd-C catalyst required two molar equivalents of hydrogen to give tetrahydrolinalool. 2,7-Dimethylocta-2,6-dien-1-ol (2) was isolated by gas chromatographic trapping from fraction (A) (Found: C, 77.8; H, 11.5. Calc. for $C_{10}H_{18}O$: C, 77.9; H, 11.8%). The catalytic hydrogenation required two molar equivalents of hydrogen to give 2,7-dimethyloctanol. The *cis*-type of 2,6-dimethylocta-2,6-dien-1-ol (3) and the *trans*-isomer were isolated by several attempts of gas chromatographic trapping from fraction (A). The *cis*-alcohol was identified by comparing the infrared spectra and gas chromatographic retention times of authentic samples. The *trans*-alcohol component contained more than 70% of the desired alcohol. Quantitative hydrogenation gave 2,6-dimethyloctanol as a main product. Nerol (4) and geraniol (5) were isolated similarly, and identified by comparing with authentic samples.

2,7-Dimethylocta-2,6-diene-1,8-diol (6) and 2,6-dimethylocta-2,6-diene-1,8-diol (8) were isolated by gas chromatography from fraction (B) (Found for (6): C, 70.5; H, 10.6. Found for (7): C, 70.5; H, 10.6. Calc. for $C_{10}H_{18}O_2$: C, 70.6; H, 10.7%). The catalytic hydrogenation of these glycols required two molar equivalents of hydrogen respectively.

Isolation of the minor products [peaks (ii), (iii), and (ix)] by gas chromatography was unsuccessful.

Spectral Data of Compounds (1), (2), (6), and (7)

3,7-Dimethylocta-1,7-dien-3-ol (1).—I.r. 3300 (OH), 1100 (tert. OH), 920 and 1000 ($CH=CH_2$), 890 cm^{-1} ($C=CH_2$). N.m.r. δ 1.3 (s, 3H, C3-Me), 1.55 [m, 4H, (C4)H₂ and (C5)H₂], 1.65 (m, 1H, OH), 1.7 (s, 3H, C7-Me), 2.0 [2H, (C6)H₂], 4.8 [2H, (C8)H₂], 5.0–6.3 [3H, (C1)H₂ and (C2)H]. M^+ 154.

(E)-2,7-Dimethylocta-2,6-dien-1-ol (2).—I.r. 3350 (OH), 1000 (prim. OH), 830 cm^{-1} ($CH=C<$). N.m.r. δ 1.7 (s, 3H, C2-Me), 1.8 (s, 6H, 2 terminal methyls), 2.15 [4H, (C4)H₂ and (C5)H₂], 3.7 (1H, OH), 4.2 (s, 2H, (CH₂OH)), 5.0 (1H, C6-H), 5.4 (1H, C3-H). M^+ 154.

(2E,6E)-2,7-Dimethylocta-2,6-diene-1,8-diol (6).—I.r. 3300 (OH), 1000 (prim. OH), 830 cm^{-1} ($CH=C<$). N.m.r. δ 1.65 (s, 6H, C2-Me and C7-Me), 2.05 [4H, (C4)H₂ and (C5)H₂], 3.6 (2H, 2OH), 3.95 (s, 4H, 2CH₂OH), 5.2 (2H, C3-H and C6-H).

(2E,6Z)-2,6-Dimethylocta-2,6-diene-1,8-diol (7).—I.r. 3300 (OH), 1000 (OH), 830 cm^{-1} ($CH=C<$). N.m.r. δ 1.65 (3H, C2 or C6-CH₃), 1.70 (3H, C6 or C2-CH₃), 2.05 [4H, (C4)H₂ and (C5)H₂], 3.6 (2H, OH), 3.95 (broad, 4H, 2CH₂OH), 5.2 (2H, C3-H and C7-H).

Preparation of Terpene Alcohols via Boron Compounds

To a naphthyllithium solution prepared from 0.2 mol of lithium, 5 g of naphthalene, and 100 ml of tetrahydrofuran, 14 g of isoprene were slowly added dropwise. Boron trifluoride ether complex (9.5 g, 0.07 mol) was slowly added to this solution over 4 hr. At the conclusion of the reaction, the solution was oxidized by adding a mixture of 3*N* sodium hydroxide solution (30 ml) and 30% hydrogen peroxide (30 ml). This was treated in the usual way to give 9 g (b.p. 80–120°/6 Torr) of a viscous oil. It was chromatographed on a silica gel column with *n*-hexane and methanol as solvents in that order. From the *n*-hexane eluate was obtained isoprene oligomer and naphthalene. From the methanol eluate was obtained 5 g of alcoholic compounds.

Gas chromatography of these alcoholic compounds with a column (3 m) of LAC-2R-446 (25%) on Celite 545 at a temperature of 180° showed the following compositions: 3,7-dimethylocta-1,7-dien-3-ol (1), 3%; 2,7-dimethylocta-2,6-dien-1-ol (2), 36%; 2,6-dimethylocta-2,6-dien-1-ol (3) *cis*-type, 4%; *trans*-type, 4%; nerol (4), 16%; geraniol (5), 9%; 2,7-dimethylocta-2,6-diene-1,8-diol (6), 10%; 2,6-dimethylocta-2,6-diene-1,8-diol (7), 10%; and unidentified alcohol, 8%.

The use of monophenyldifluoroboron and diphenylmonofluoroboron in place of boron trifluoride ether complex gave terpene alcohols in yields of 35% (monohydric alcohol 28%, glycol 7%) and 40% (monohydric alcohol 30%, glycol 10%) respectively.

Results and Discussion

The action of molecular oxygen upon organometallic compounds is typified by the oxidation of phenylmagnesium bromide⁴ and phenyllithium.^{5,6} The present authors reported that naphthyllithium in tetrahydrofuran solution dimerizes isoprene to give linear isoprene dimers.³ It may be considered that dimeric isoprene dianions are produced in this reaction mixture, and the authors have attempted oxidation of dimeric isoprene anions with oxygen.⁷ Thus, through a solution of the reaction mixture prepared from isoprene and naphthyllithium, dry oxygen was slowly passed, followed by decomposition with aqueous methanol to give a mixture of terpenic alcohols in yields of 30–40%. These alcohols contained 70% of C₁₀-terpenic alcohols and 30% of C₁₀-glycols. Details of the composition of these mixtures, and proof of the structures of the components, are given in the Experimental section, which also contains an account of the results obtained when the isoprene dimer anion solution was treated with boron compounds and then oxidized with hydrogen peroxide.

TABLE I
THE EFFECT OF TEMPERATURE ON OXIDATION OF ISOPRENE

Temperature	Monohydric Alcohol	Glycol	Total Yield
40°	83%	17%	30%
20	73	27	35
0	55	45	35
-20	39	61	38
-40	30	70	40
-60	20	80	45

The effects of reaction temperature on the oxidation of isoprene have also been examined; the results are shown in Table I. From these results, it can be said that the reaction at room temperature affords more monohydric alcohol, but that the reaction at lower temperature gives more glycol. This is the same result as the effect of the reaction temperature on the carboxylation of isoprene.⁸ It is surmised that isoprene dimer anion mainly exists in the form of monoanion at higher temperature but that isoprene dimer anion exists in the form of dianion at lower temperature.

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