

Base-catalysed Rearrangements of Bicyclic δ -Hydroxy- $\alpha\beta$ -enones. Part V.¹

By P. V. Ramani, J. P. John, K. V. Narayanan, and S. Swaminathan,* Department of Organic Chemistry, University of Madras, Madras 25, India

4,4a,5,6,7,8-Hexahydro-5 β -hydroxy-4a β -methylnaphthalen-2(3*H*)-one (1) and its 4a β -ethyl analogue (6) rearrange in the presence of base to give a mixture of 4-alkyl-3,4-dihydronaphthalen-1(2*H*)-one and 4-alkyl-3,4,5,6,7,8-hexahydronaphthalen-1(2*H*)-one. 4a β -Ethyl-4,4a,5,6,7,8-hexahydro-5 β -hydroxy-5 α -vinylnaphthalen-2(3*H*)-one (7) is similarly converted into 4-ethyl-3,4,6,7,9,10-hexahydrobenzocyclo-octene-1(2*H*),8(5*H*)-dione (16).

BICYCLIC δ -hydroxy- $\alpha\beta$ -enones of the type (1)—(3) have been shown to undergo rearrangements catalysed by acids and bases^{2,3} and by u.v. light.⁴

The ketol (1) is transformed into the phenol (4) and the ether (5) by toluene-*p*-sulphonic acid, but with aqueous methanolic alkali, a mixture of products⁵⁻⁷ is obtained. We describe here the separation of these products and the course of the rearrangement of the ketol (1) and the related compounds (6) and (7).

When refluxed with 1 mol. equiv. of methanolic potassium hydroxide, the ketol (1) gave a liquid consist-

¹ Part IV, S. Swaminathan, K. G. Srinivasan, and P. S. Venkataramani, *Tetrahedron*, 1970, **26**, 1453.

² S. Swaminathan, J. P. John, and S. Ramachandran, *Tetrahedron Letters*, 1962, 729.

³ S. Swaminathan, R. K. Natarajan, S. Ramachandran, and S. K. Sankarappa, *J. Org. Chem.*, 1966, **31**, 656.

ing of two major ketonic components with similar R_F values and four minor components. Distillation gave a liquid mixture of the ketones (*ca.* 42%) and a polymeric residue. The ketones were separated as their 2,4-dinitrophenylhydrazone derivatives on a Kieselguhr-Bentonite column and also by careful chromatography of the ketones themselves on silica gel. The ketone of higher R_F value (t.l.c.) was identified as 3,4-dihydro-4-methylnaphthalen-1(2*H*)-one (8) by spectra and by comparison (mixed m.p.) of the 2,4-dinitrophenylhydrazone with an authentic sample. From its analyti-

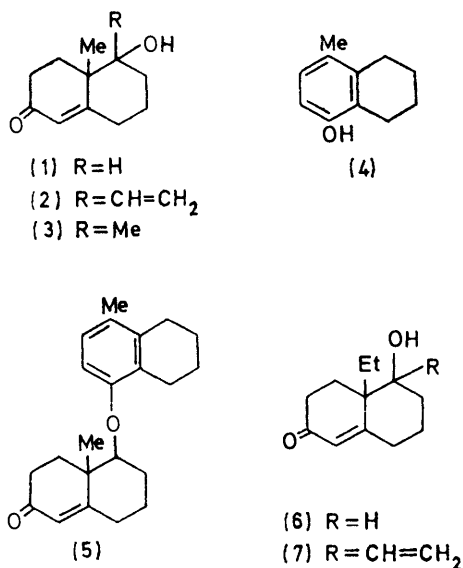
⁴ D. Gravel and J. Gauthier, *Tetrahedron Letters*, 1968, 5489.

⁵ J. D. Cocker and T. G. Halsall, *J. Chem. Soc.*, 1957, 3441.

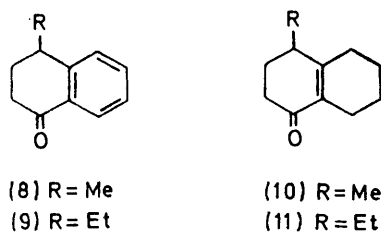
⁶ J. P. John, Ph.D. Thesis, University of Madras, 1963.

⁷ C. H. Heathcock and R. Ratchiffe, *J. Amer. Chem. Soc.*, 1971, **93**, 1748.

cal data, molecular weight,* and spectra, the slower-moving ketone was assigned structure (10).



The same products were formed even when the reaction was carried out under nitrogen, thereby proving



that the ketones (8) and (10) were not formed by aerial

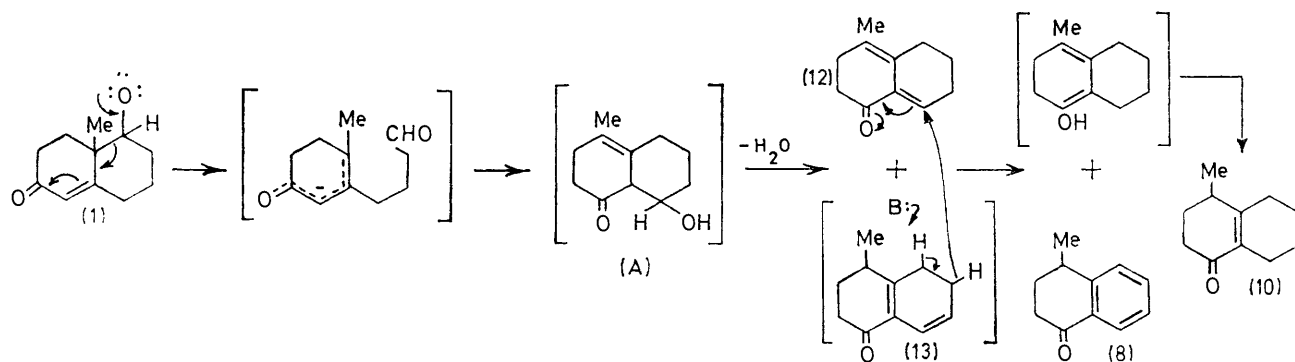
whereas at room temperature it was incomplete even after 24 h.

The formation of the two ketones (8) and (10) may be rationalised as shown in Scheme 1 (*cf.* ref. 8). Dehydration of the intermediate ketol (A) could give a mixture of the ketones (12) and (13). The latter could then undergo aromatisation to give the ketone (8) by base-induced hydride transfer to the cross-conjugated dienone (12) in a 1,4-fashion, leading to the enone (10); hydride ion is known⁹ to add to conjugated ketones in a 1,4-manner. The same mixture of ketones (8) and (10) could also be obtained by the action of aqueous methanolic alkali on the known¹⁰ dienone (12). The complete absence of the phenol (4) [which is formed in the acid-catalysed rearrangement of ketol (1) or dienone (12)†] in these rearrangements is surprising and is probably the result of enolisation in different directions¹¹ when the dienone (12) is treated with acid or base.

The polymeric residue mentioned earlier could not be separated by column chromatography. Attempts to hydrogenate the mixture under high pressure were also unsuccessful. Dehydrogenation (Pd-C) in *p*-cymene gave a u.v.-fluorescent yellow solid.

Base-catalysed rearrangement of the ethyl-substituted ketol (6) similarly gave a mixture of ketones [(9) and (11)] and a non-volatile fraction. Dehydrogenation of the latter gave a yellow solid. The structures of the two yellow dehydrogenation products will be discussed in a later paper.

The enone (7), whose rearrangement was also studied next, was prepared as in Scheme 2. Michael addition of methyl vinyl ketone to 2-ethylcyclohexane-1,3-dione¹² and cyclisation of the resulting crude trione with pyrrolidine yielded the enedione (14) (50%). The latter reacted incompletely with lithium acetylide giving, even

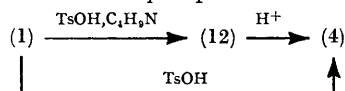


SCHEME 1

oxidation. When refluxed with aqueous alkali, the rearrangement of the ketol (1) was complete in 15 min,

* We thank Dr. K. G. Das, National Chemical Laboratory, Poona, for recording the mass spectrum.

† The dienone (12) is formed¹⁰ when the ketol (1) is treated with pyrrolidine and toluene-*p*-sulphonic acid:



under the best of conditions (1 h at -78°) only 35% yield of the carbinol (15). Starting material (27%) and a by-product (20%), believed to be impure (15a), were also

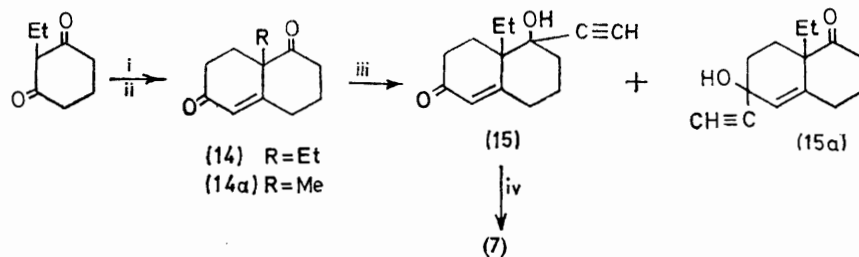
⁸ K. H. Bell, *Tetrahedron Letters*, 1968, 3979.

⁹ M. R. Johnson and B. Rickborn, *J. Org. Chem.*, 1970, **35**, 1041.

¹⁰ M. Los and A. D. Mighell, *Tetrahedron*, 1965, **21**, 2297.

¹¹ A. Liberles, 'Introduction to Theoretical Organic Chemistry,' MacMillan, New York, 1968, p. 533.

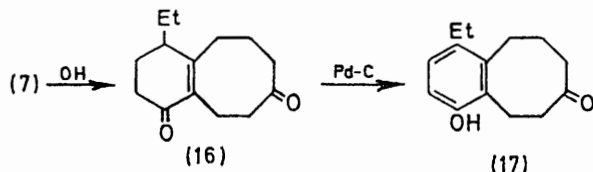
¹² H. Stetter and W. Dierichs, *Chem. Ber.*, 1952, **85**, 61.



SCHEME 2 Reagents: i, MeCO·CH₂CH₃; ii, pyrrolidine; iii, LiC≡CH, liq. NH₃; iv, H₂, Pd-BaSO₄.

obtained. By analogy¹³ with the reaction of the dione (14a) with lithium acetylide, the carbinol (15) may be assigned the β-hydroxy-structure. Selective reduction of the carbinol (15) (Pd-BaSO₄ catalyst) gave the vinyl carbinol (7) in high yield.

When treated with methanolic potassium hydroxide, the carbinol (7) rearranged to the isomeric dione (16) (50%). This rearrangement is similar to that of the lower homologue (2). The structure of the dione (16) was confirmed by dehydrogenation to the phenol (17), which showed the expected spectroscopic behaviour.



EXPERIMENTAL

4,4a,5,6,7,8-Hexahydro-5β-hydroxy-4aβ-methylnaphthalen-2(3H)-one (1)¹⁴ and 8a-ethyl-3,4,8,8a-tetrahydronaphthalene-1(2H),6(7H)-dione (14)¹⁵ [m.p. 67–68° (lit.,¹⁶ 69–70°)] were prepared as described in the literature. The latter has been prepared independently¹⁷ by an essentially similar method.

Reaction of the Ketol (1) with Aqueous Methanolic Alkali.—A solution of the ketol (1) (4.95 g) in methanol (150 ml) was refluxed with aqueous 5.6% potassium hydroxide (25 ml, 1 equiv.) for 2 h. Solvents were then removed under vacuum and the residue was diluted with water and extracted with chloroform. Work-up of the extract furnished a viscous liquid (4.1 g, 88%); distillation gave a colourless liquid (1.7 g, 42%), b.p. 98–102° at 0.7–0.8 mmHg, R_F 0.65 and 0.7 (t.l.c. in 8:92 ethyl acetate-petroleum) and much pot residue (2.38 g). This residue was obtained even when the crude reaction mixture was steam-distilled, indicating that vacuum distillation was not responsible for the large amount of pot residue.

Separation of the Components of the Distillate.—(a) The distillate (4 g) was dissolved in ethanol (25 ml) and mixed with excess of 2,4-dinitrophenylhydrazine reagent. The precipitate, m.p. 200–215° (from chloroform-ethanol) (4 g) was transferred to a column of Bentonite (72 g) and Kieselguhr (18 g) and was eluted with chloroform (100 ml fractions at a rate of 100 ml h⁻¹). The first few fractions gave a solid (0.8 g), m.p. 226–229° [from chloroform-ethyl acetate (1:2)] (Found: C, 59.2; H, 6.1; N, 16.5. C₁₇H₂₀N₄O₄ re-

quires C, 59.3; H, 5.9; N, 16.3%). The later fractions gave another solid (0.8 g), m.p. 213–215° [from ethyl acetate-chloroform (1:1)], identical (mixed m.p.) with the 2,4-dinitrophenylhydrazone of authentic 3,4-dihydro-4-methylnaphthalen-1(2H)-one (Found: C, 60.2; H, 4.9; N, 16.6. Calc. for C₁₇H₁₆N₄O₄: C, 60.0; H, 4.7; N, 16.7%).

(b) The distillate (2 g) was dissolved in a little petroleum, transferred to a column of silica gel (250 g, 42 × 1 in), and eluted first with petroleum (2 l), followed by ethyl acetate-petroleum (2:98) at 100 ml h⁻¹. Fractions were monitored with 2,4-dinitrophenylhydrazine reagent. The first few fractions gave a liquid (500 mg), homogeneous on t.l.c. Distillation (bath temp. 60–62° at 0.7 mmHg) of this gave 3,4-dihydro-4-methylnaphthalen-1(2H)-one (8) (Found: C, 82.0; H, 7.9. Calc. for C₁₁H₁₂O: C, 82.4; H, 7.5%), ν_{max} (CHCl₃) 1680 cm⁻¹, λ_{max} (EtOH) 249 (ε 11,520) and 291 nm (1880), δ (CCl₄) 1.38 (3H, Me), 1.5–3.2 (5H, CH₂·CH₂·CH), 7.25 (3H, aromatic protons), and 8.0 p.p.m. (1H, *peri*-aromatic proton), identified by comparison (t.l.c.; u.v. and i.r. spectra) with an authentic sample and also as the 2,4-dinitrophenylhydrazone, m.p. 213–215°.

The next few fractions were mixtures of ketones and were rejected. The last few fractions (single spot on t.l.c.) were combined to furnish 3,4,5,6,7,8-hexahydro-4-methylnaphthalen-1(2H)-one (10) (500 mg), purified by distillation (bath temp. 70–72° at 0.6–0.7 mmHg) (Found: C, 80.7; H, 10.0. C₁₁H₁₆O requires C, 80.4; H, 9.8%), ν_{max} (neat) 1650 and 1620 cm⁻¹, λ_{max} (EtOH) 245 nm (ε 10,140) [lit.,¹⁸ 247 nm (ε 11,900)], δ (CCl₄) 1.11–1.2 (3H, Me) and 1.53–2.5 p.p.m. (13H), *m/e* 164 (M⁺); 2,4-dinitrophenylhydrazone, m.p. 228–229° (from chloroform-ethyl acetate), identical with the derivative of m.p. 226–229° described in (a).

Dehydrogenation of the Pot Residue.—A solution of the residue (4 g) in *p*-cymene (40 ml) was refluxed for 3 h with palladium-charcoal with (30%; 400 mg). The mixture was filtered and the filtrate was diluted with ether. The organic layer was washed with sodium hydroxide solution (20%; 100 ml) and water, dried, and evaporated to leave a viscous residue (3 g). This was adsorbed on a column of alumina (40 g) and eluted with petroleum; a u.v.-fluorescent solid (500 mg), m.p. 186–187°, was obtained (Found: C, 87.5; H, 6.9. Calc. for C₂₂H₂₀O: C, 87.9; H, 6.7%), *m/e* 300 (M⁺).

Rearrangement of 4aβ-Ethyl-4,4a,5,6,7,8-hexahydro-5β-hydroxynaphthalen-2(3H)-one (6) with Methanolic Alkali.—Reduction of the dione (14) with sodium borohydride as reported¹⁷ gave the ketol (6).

By the procedure used for the rearrangement of com-

¹³ S. Swaminathan, S. Ramachandran, and S. K. Sankarappa, *Tetrahedron*, 1964, **20**, 1119.

¹⁴ C. B. C. Boyce and J. C. Whitehurst, *J. Chem. Soc.*, 1960, 2680.

¹⁵ K. V. Narayanan, Ph.D. Thesis, University of Madras, 1966.

¹⁶ A. J. Birch, M. Kocor, and D. C. C. Smith, *J. Chem. Soc.* 1962, 782.

¹⁷ J. N. Gardner, B. A. Anderson, and E. P. Oliveto, *J. Org. Chem.*, 1969, **34**, 107.

¹⁸ P. S. Wharton and B. T. Aw, *J. Org. Chem.*, 1966, **31**, 3787.

pound (1), the enone (6) (5 g) gave a distillate, b.p. 96—98° at 0.5 mmHg (1.35 g), and a pot residue (2.68 g). Chromatography of the distillate over silica gel gave only mixtures. The material eluted first from the column gave a 2,4-dinitrophenylhydrazone, m.p. 186—187° (from ethyl acetate-chloroform) (Found: C, 61.0; H, 5.6. Calc. for $C_{18}H_{18}N_4O_4$: C, 61.0; H, 5.1%), identical (m.p. and mixed m.p.) with the 2,4-dinitrophenylhydrazone of 4-ethyl-3,4-dihydro-naphthalen-1(2H)-one. The later fractions furnished another ketone, believed to be 4-ethyl-3,4,5,6,7,8-hexahydro-naphthalen-1(2H)-one (11) on the basis of spectral data and analogy. It was characterised as its 2,4-dinitrophenylhydrazone, m.p. 206—208° (from ethyl acetate-chloroform) (Found: C, 60.1; H, 6.0. $C_{18}H_{22}N_4O_4$ requires C, 60.3; H, 6.2%).

The pot residue (2 g) was dehydrogenated neat with palladium-charcoal (300 mg) at 260—280° for 3 h. Work-up and chromatography gave a u.v.-fluorescent solid, m.p. 147—148° (200 mg) (from petroleum) (Found: C, 88.5; H, 6.3. Calc. for $C_{24}H_{20}O$: C, 88.8; H, 6.2%), m/e 324 (M^+).

4 α \beta-Ethyl-5 α -ethynyl-4,4a,5,6,7,8-hexahydro-5 β -hydroxy-naphthalen-2(3H)-one (15).—A solution of the dione (14) (30 g) in dry ether (100 ml) was added with stirring during 10 min to a solution of lithium acetylide [from lithium (2.5 g)] in liquid ammonia at -78°. The orange solution was stirred for 1 h with cooling, then decomposed with ammonium chloride (25 g). The ammonia was evaporated off and the residue was diluted with water and extracted with chloroform. The extract was washed with water, dried, and evaporated to leave a viscous liquid (30 g). This was adsorbed on a column of silica gel (200 g). Elution with benzene-petroleum (1:19; 10 l) gave a liquid (5 g), believed to have structure (15a) (i.r. spectrum). Elution with benzene-petroleum (3:1 and 9:1; 15 l) then gave the starting material (14) (8 g). Further elution, with benzene-ether (9:1; 10 l) gave the acetylenic alcohol (15) (8 g), m.p. 114—115° (from ethyl acetate-petroleum) (Found: C, 77.0; H, 8.3. $C_{14}H_{18}O_2$ requires C, 77.0; H, 8.7%), ν_{max} (KBr) 3225, 2105, and 1680 cm^{-1} , λ_{max} (EtOH) 242 nm (ϵ 12,770), δ ($CDCl_3$) 0.8—1.03 (3H, Me), 2.63 (13H, C \equiv CH and methylenes), 2.8 (1H, OH), and 6.0 p.p.m. (1H, =CH).

4 α \beta-Ethyl-4,4a,5,6,7,8-hexahydro-5 β -hydroxy-5 α -vinyl-naphthalen-2(3H)-one (7).—Hydrogenation of compound (15) (1 g) in pyridine (5 ml) over palladium-barium sulphate (200 mg) gave the vinyl carbinol (7), m.p. 104—105° (from ether) (800 mg) (Found: C, 76.2; H, 9.1. $C_{14}H_{20}O_2$ requires C, 76.2; H, 9.2%), ν_{max} ($CHCl_3$) 3600 and 1650 cm^{-1} , λ_{max} (EtOH) 247 nm (ϵ 11,910), δ ($CDCl_3$) 0.75—1.0 (3H, Me), 1.66—2.5 (13H, methylenes and OH), and 5.05—6.5 p.p.m. (4H, vinyl protons).

Rearrangement of the Enone (7) to 4-Ethyl-3,4,6,7,9,10-hexahydrobenzocyclo-octene-1(2H),8(5H)-dione (16).—The carbinol (7) (600 mg) in methanol (20 ml) and aqueous potassium hydroxide (5.6%; 15 ml) was refluxed for 2 h. The solvents were removed and the residue was diluted with water and extracted with ether. Work-up of the extract gave a viscous liquid (300 mg). Distillation (bath temp. 140—150° at 0.5 mmHg) gave a solid (16), m.p. 54—55° (from petroleum-ethyl acetate) (Found: C, 76.3; H, 9.4. $C_{14}H_{20}O_2$ requires C, 76.3; H, 9.2%), ν_{max} ($CHCl_3$) 1695 and 1650 cm^{-1} , λ_{max} (EtOH) 248 nm (ϵ 10,210), δ ($CDCl_3$) 0.8—1.1 (3H, Me) and 1.28—3.10 p.p.m. (17H).

Dehydrogenation of the Dione (16): 1-Ethyl-5,6,9,10-tetrahydro-4-hydroxybenzocyclo-octen-7(8H)-one (17).—A solution of the dione (16) (2.3 g) in *p*-cymene (20 ml) was refluxed for 2 h with palladium-charcoal (250 mg, 30%). The mixture was filtered hot and the filtrate was cooled. Compound (17) separated as crystals, m.p. 148—149° (from ether-petroleum) (1.8 g) (Found: C, 76.9; H, 8.6. $C_{14}H_{18}O_2$ requires C, 77.0; H, 8.3%), ν_{max} (CCl_4) 3603, 1695, and 1600 cm^{-1} , λ_{max} (EtOH) 222 nm (ϵ 7602), δ ($CDCl_3$) 1.0—1.25 (3H, Me), 1.63—3.23 (12H, methylenes), 6.55—6.93 (2H, aromatic protons), and 8.25 p.p.m. (1H, OH).

We thank Professor T. R. Govindachari, CIBA Research Centre, Bombay, for the n.m.r. spectra, Mr. R. Balasubramanian for microanalyses, and Drs. K. Nagarajan and K. K. Balasubramanian for discussions. P. V. R. and J. P. J. thank the C.S.I.R., New Delhi, India, for financial support.

[2/011 Received, 3rd January, 1972]