

A Base-induced Transannular 1,4-Hydride Shift in a Cyclohexanone

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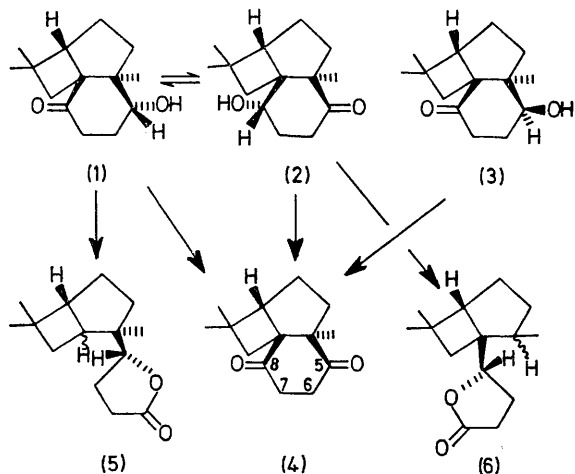
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Summary The ketol (**1**) is transformed into the ketol (**2**) by an unusual base-induced intramolecular 1,4-hydride shift.

ALTHOUGH there are examples of base-induced transannular hydride shifts to ketonic carbon across fused common rings¹ and across a seven-membered ring,² such hydride shifts within the cyclohexyl system appear not to have been observed previously. An unambiguous case of a 1,4-hydride shift in a cyclohexanone is reported here.

When the ketol (**1**),³ m.p. 146 °C, is refluxed (*ca.* 80 °C) with KOH in Bu^tOH—H₂O (35:1), it is partially transformed into an isomeric ketol, m.p. 119 °C. Similar treatment of the pure isomer yields mostly (**1**), and the equilibrium ratio of (**1**):isomer is 65:35. These reactions also occur in refluxing KOH—PrⁱOH, and, much more slowly, in refluxing KOH—MeOH. Oxidation of this isomeric ketol produces the same diketone (**4**) that was obtained from (**1**).³ However, the isomeric ketol is not merely the hydroxy-epimer of (**1**), because this epimer (**3**), m.p. 130 °C, has quite

different properties.† The only remaining possibility involves interchange of the ketone and hydroxy-groups in (1) to produce either (2) or its hydroxy-epimer. Functional group interchange was proved to have occurred by photochemical cleavage of the two ketols.⁴ On irradiation in



benzene the ketol (1) was easily transformed into the lactone (5), while the ketol (2) produced the lactone (6). The ¹H n.m.r. spectrum of (6) (a single stereoisomer) contained the requisite methyl doublet at δ (CDCl₃) 0.91 (*J* 6 Hz).

That the hydrogen migration does not involve proton

transfer (*e.g.*, homoenolisation) is shown by the reaction of (1) in Bu^tOD-D₂O-KOD. Both of the products, [²H₄]-**(1)** and [²H₄]-**(2)**, have undergone exchange of both methylene groups in the cyclohexanone ring, but no exchange of the CHOH. Therefore, the change of (1) into (2) is a 1,4-hydride transfer which must be intramolecular for the following reasons: (i) the absence of traces of other products [dione (4), (3), the OH epimer of (2), or a diol] to be expected from an intermolecular process, (ii) the failure of (1) or (2) to accept hydride from PrⁱOH or to donate hydride to other carbonyl compounds such as fluorenone⁵ and 2,2-dimethyl-cyclohexanone, and (iii) the failure of the ketol (3) to undergo a similar hydride transfer under the same conditions. Certainly, the *cis*-fusion of the cyclopentane ring would favour easy attainment of the boat conformation necessary for an intramolecular hydride transfer, and the crowded steric situation around the carbonyl function would inhibit an intermolecular process. An intramolecular hydride transfer in (1) would have to be suprafacial and produce the hydroxy-configuration depicted in (2) which is in agreement with the results of reduction of the 5,5-ethylenedioxy-derivative of (4).⁴

There would appear to be no reason why such readily occurring hydride shifts should not be quite general provided that the appropriate conformation can be attained.

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† Compound (3) was produced by the reaction of isocaryophyllene keto oxide-a with KOH and also by the NaBH₄ reduction of the 8,8-ethylenedioxy-derivative of (4). It is also oxidized to the diketone (4).⁴

¹ W. Acklin and V. Prelog, *Helv. Chim. Acta*, 1959, **42**, 1239; W. Parker and J. R. Stevenson, *Chem. Comm.*, 1969, 1289; J. M. Shepherd, D. Singh, and P. Wilder, *Tetrahedron Letters*, 1974, 2473.

² P. T. Lansbury and F. D. Saeva, *J. Amer. Chem. Soc.*, 1967, **89**, 1890.

³ D. H. R. Barton and A. S. Lindsey, *J. Chem. Soc.*, 1951, 2988.

⁴ E. W. Warnhoff and V. Srinivasan, *Canad. J. Chem.*, submitted for publication.

⁵ E. W. Warnhoff and P. Reynolds-Warnhoff, *J. Org. Chem.*, 1963, **28**, 1431.