Tetrahedron Letters No.5, pp. 397-400, 1967. Pergamon Press Ltd. Printed in Great Britain.

REARRANGEMENT OF 10-ETHYL-2-KETO-$\Delta^{1(9);3(4)}$-HEXAHYDRONAPHTHALENE

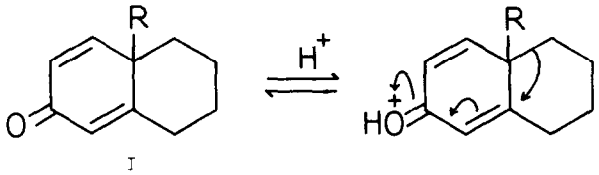
K.H. Bell

Dept. of Chemistry, University of Newcastle, N.S.W., Australia.

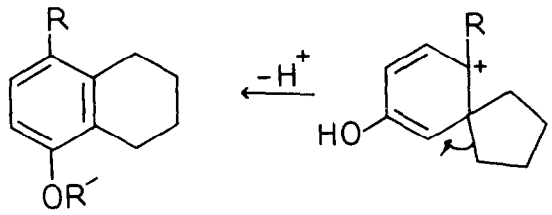
(Received 19 November 1966)

The acid catalysed dienone-phenol rearrangement of I (R=Me), or the related steroid derivative, has been shown to proceed by two pathways (1).

Pathway A

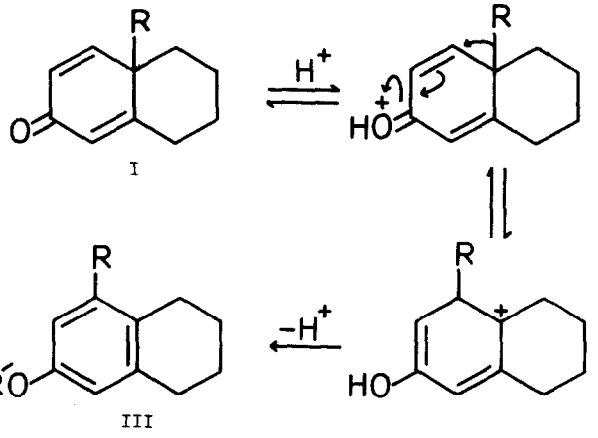


I



II

Pathway B



Under "normal" anhydrous conditions (e.g. concentrated sulphuric acid in acetic anhydride) the reaction follows pathway A. However, the course of the reaction is drastically altered by the use of aqueous conditions or the introduction of even subtle structural or electronic variations in the molecule and usually follows pathway B (1 and references cited therein).

The preference for pathway A in the case of I (R=Me) above has been attributed to the greater migratory aptitude of the secondary ring centre (or tertiary in the steroid case) over the primary methyl group. Thus, it was deemed of interest to examine the rearrangement of the dienone I (R=Et), in which both the potential migrating centres have the same aptitude, to see which of the two possible pathways would predominate.

The required dienone I (R=Et) was prepared in two steps from 2-ethylcyclohexanone. Robinson annelation with the methiodide of 4-diethylamino-2-butanone (2) gave 10-ethyl-2-keto-$\Delta^{1(9)}$-octahydronaphthalene, b.p. 130-132°/0.2 mm, $\nu_{max.}$ (film) 1675, 1618 cm^{-1} (2,4-DNP, m.p. 148-149°) in 26% yield (based on recovered

2-ethylcyclohexanone). Dehydrogenation with selenium dioxide in t-butyl alcohol containing a small amount of pyridine (3) yielded the dienone I (R=Et), b.p. 117-118°/1 mm, $\nu_{max.}$(film) 1662, 1625, 1608 cm^{-1} (2,4-DNP, m.p. 122-124°) in 61% yield.

Rearrangement of I (R=Et) in acetic anhydride containing a catalytic amount of sulphuric acid at room temperature gave an oily acetate, $\nu_{max.}$(film) 1765, 1215 cm^{-1}, which appeared homogeneous by t.l.c. The n.m.r. spectrum (CCl_4) showed a slightly broadened aromatic proton peak (3.4 τ) suggesting the compound was III (R=Et, R'=$COCH_3$) in which the aromatic protons are in a similar environment. The corresponding aromatic protons of II (R=Et,R'=$COCH_3$) would be expected to have significantly different chemical shifts.

As final proof, the acetate was hydrolysed to the corresponding phenol with 2% aqueous ethanolic sodium hydroxide, methylated directly with dimethyl sulphate, and the product isolated by steam distillation. The resulting methyl ether, which appeared homogeneous by t.l.c. and v.p.c., was then compared with a sample of III (R=Et,R'=Me) obtained by the following unambiguous route.

Friedel-Crafts succinoylation of meta-ethylanisole gave a mixture of the ortho and para isomers (relative to the methoxyl group) from which the less soluble and predominant 3-(2-ethyl-4-anisoyl) propionic acid, m.p. 144-145°, was isolated by crystallization from acetone or aqueous alcohol(4). That the compound isolated was indeed the desired isomer was shown by its degradation with alkaline sodium hypobromite (5) to the known (6) 2-ethylanisic acid, m.p.120-121°. Clemmensen reduction (Martin modification) gave the aryl butyric acid, b.p. 151-152°/0.3 mm, which yielded the corresponding tetralone, b.p. 116-118°/0.2 mm (2,4-DNP, m.p. 214-215°) on cyclization with

polyphosphoric acid. Wolff-Kishner reduction (Huang-Minlon modification) gave the desired product III (R=Et, R'=Me), b.p. 115-116°/1.5 mm, in an overall yield of 17%.

The i.r. spectrum (film or CCl_4 solution) of the synthetic product was identical with that of the methyl ether produced via the rearrangement.

To check for possible traces of the other isomer II (R=Et, R'=$COCH_3$) in the rearranged product, a sample of the corresponding methyl ether was prepared from para-ethylanisole by the same route used for the isomer above. The final product, obtained in an overall yield of 52%, had b.p. 97-98°/0.15 mm, but comparison with the methyl ether produced via the rearrangement using i.r., t.l.c., and v.p.c. analysis showed the complete absence of this isomer.

The exclusive formation of isomer III provides yet another example of the extreme sensitivity of the course of the dienone-phenol rearrangement to a small structural change in the molecule.

References

1. N.L. Wendler in Molecular Rearrangements, Part II (Ed.P.de Mayo), p.1028, Interscience, New York (1964).
R.H.Shapiro in Steroid Reactions, (Ed.C.Djerassi), Ch.9, Holden-Day, San Francisco (1963).
2. E.C. du Feu, F.J.McQuillin, and R.Robinson, J.Chem.Soc.53 (1937).
3. R.Owyang in Steroid Reactions, p. 233.
4. The corresponding isomers from the succinoylation of meta-methylanisole have been separated by crystallization from acetone. P.J. Kropp, J.Amer.Chem.Soc. 85, 3280 (1963).
5. R.Levine and J.R.Stephens, J.Amer.Chem.Soc.72,1642 (1950).
6. M.Oki and T.Sato, Bull.Chem.Soc. Japan 30, 508 (1957).
H.Richtzenhain, Ber. 82, 405 (1949).