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REARRANGEMENTS OF EPOXIDES OF αβ-UNSATURATED KETONES

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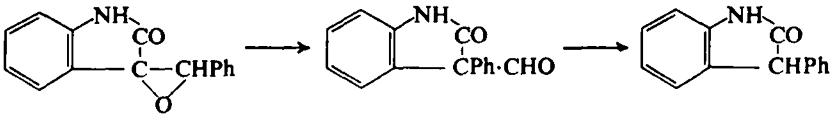
Part I. J. W. AGER and ROBERT ROBINSON

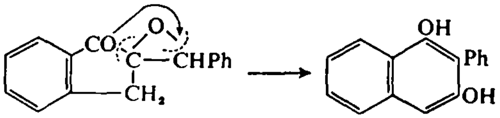
(a) BENZYLIDENE-OXINDOLE was changed into the related expoxide (I) by reaction with hydrogen peroxide and 2N sodium hydroxide in ethanolic solution.[2] The product crystallized from ethanol, m.p. 162–163·5° (dec). A solution of the epoxide in ice-cold concentrated sulphuric acid was kept until gas ceased to be evolved. Addition of water precipitated 3-phenyloxindole, m.p. 182–185° after crystallization from ethanol. For comparison the substance was prepared by the method of Meisenheimer and Lamparter.[3] Clearly the mechanism is as follows:



I

In this example the phenyl group migrated but in all the other cases mentioned below it is the acyl group that wanders. The contrast may be due to the circumstance that the carbonyl is part of an amide system.

(b) 2-*Benzylidene-indanone*-1 *epoxide* was made in a similar manner, m.p. 117–119°, from ethanol. Sulphuric acid at 0° changed it into 1,3-*dihydroxy*-2-*phenylnaphthalene*, which crystallized from benzene, m.p. 164·5–165·5°. The solubility in alkali, ferric reaction and fluorescent phthalein formation were normal for the type.



(c) 2-Benzylidenecyclohexanone-1[4] was reacted with hydrogen peroxide in methanolic solution containing aqueous soldium hydroxide. The temperature was kept below 35° by cooling. The *epoxide* crystallized from ethanol as colourless needles, m.p. 121·5–123°. Solution in sulphuric acid at 0° for a few minutes afforded 2-*phenyl*-cyclo*heptan*-1,3-*dione* which crystallized from ethanol as slender needles, m.p. 70–73°. This substance is soluble in sodium hydrogen carbonate and is hydrolysed by 5N aqueous sodium hydroxide with formation of the salt of 5-*keto*-7-*phenylheptanoic acid.* This substance crystallized from benzene—light pertoleum in

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[1a] D. Phil. Thesis, Oxford, 1955.

[1b] D. Phil. Thesis, Oxford, 1957.

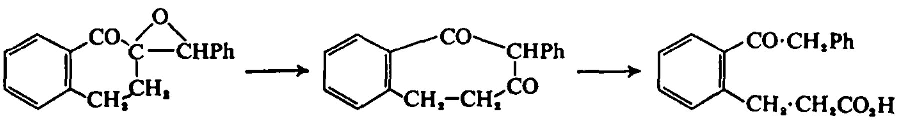
[2] W. Baker and R. Robinson, *J. Chem. Soc.* 1798 (1932).

[3] J. Meisenheimer and Lamparter, *Ber. Dtsch. chem. Ges.* **575**, 276 (1924).

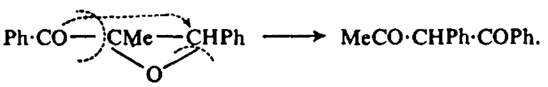
[4] D. Vorländer and K. Kunze, *Ber. Dtsch. Chem. Ges.* **598**, 2078 (1926).

needles, m.p. 52–54°. For comparison the acid was synthesized[5] by reacting potassium phenylacetate with ethylmagnesium bromide and then with the ethyl-ester chloride of adipic acid, throughout in ethereal solution.

(d) The *epoxide* from 2-benzylidenetetralone-1[6] formed colourless needles, m.p. 73·5–75·5°. The product rearranged by sulphuric acid at 0° had m.p. 88–89°, from ethanol. The substance, $C_{17}H_{14}O_6$, is doubtless 6:7-*benzo*-2-*phenylcycloheptan*-1,3-*dione*. It was hydrolysed by hot 1 % aqueous sodium hydroxide to the salt of a keto-acid, $C_{17}H_{16}O_5$.



(e) α-Benzylidenepropiophenone[7] epoxide, made in the usual way, was an oil. It was treated with cold sulphuric acid and thus converted into acetyldeoxybenzoin, colourless needles from ethanol, m.p. 80–82° (ferric reaction). Hydrolysis by means of hot 5 % aqueous sodium hydroxides, followed by steam distillation, afforded benzyl methyl ketone, *semicarbazone*, m.p. 186–188° (mixed m.p. undepressed).



$\mathrm{Ph{\cdot}CO{-}CMe{-}CHPh \longrightarrow MeCO{\cdot}CHPh{\cdot}COPh.}$

It is probable that deoxybenzoin was also formed.[8] Similarly, 5:6-methylenedioxy-2-benzylidene-indanione epoxide, m.p. 139–140°, from ethanol was changed by sulphuric acid at 0° into a substance $C_{17}H_{12}O_4$, m.p. 168–170°, from benzene. This substance, by analogy, should be 1,3-*dihydroxy*-6:7-*methylenedioxy*-2-*phenylnaphthalene* and its properties were consistent with this view. Direct condensation of 5:6-methylenedioxyindan-1-one with potassium opianate in boiling ethanol containing a small amount of potassium hydroxide gave, on cooling, a crystalline potassium salt. The free acid had m.p. 190–192° and may have been an unsaturated ketone. On solution in boiling acetic acid and cooling, colourless plates, m.p. 207·5–209·5° separated. The substance, $C_{20}H_{16}O_7$, was not an acid but probably 2-α-*meconyl*-5:6-*methylenedioxyindan*-1-*one*. In view of this, and in pursance of a synthetic scheme in the chelerythrine group, 5:6-mehylenedioxyindan-1-one was condensed with methyl opianate (CO_2Me form) in hot ethanolic hydrogen chloride solution. The product, $C_{21}H_{18}O_7$, crystallized from ethanol as lemon yellow needles, m.p. 168–169°. This 5:6-*methylenedioxy*-2-(2-'*carbomethoxy*-3',4'-*dimethoxybenzylidene*)*indan*-1-*one* could not be converted into an epoxide.

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[5] Cf. D. Ivanov and N. I. Nikolov, *Bull. Soc. Chim. Fr.* **51**, 1326 (1932).

[6] W. S. Rapson and R. G. Shuttleworth, *J. Chem. Soc.* 636 (1940).

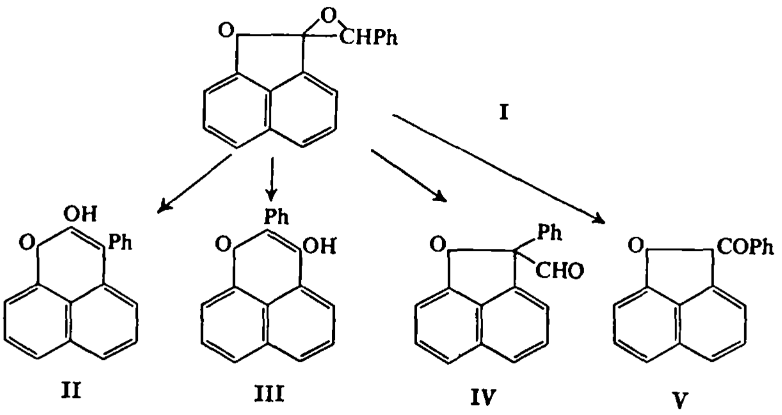
[7] R. D. Abell, *J. Chem. Soc.* 928 (1901).

[8] Cf. H. O. House, *J. Amer. Chem. Soc.* **76**, 1235 (1954); H. O. House and D. J. Reif, *Ibid.* **77**, 6525 (1955); H. O. House, *Ibid.* **78**, 2298 (1956). This work had not been published when J. W. Ager made his experiments (R. R.).

Part II. F. A. Eastwood and Robert Robinson

The studies of House *et al.** which almost synchromized with those of Ager (*v. supra*) cleared up many of the mechanistic and stereochemical problems in the field of rearrangements of epoxides of αβ-unsaturated carbonyl compounds. We were interested in the possible bearing of such processes on the biogenesis of tropolones and made model experiments which later developed a new interest, namely the fixation of unsaturated intermediates, which are normally transitory, by epoxidation.

Benzalacenaphthenone,[9] yellow plates from ethanol, had m.p. 113° (lit. 107°). The oxime, pale yellow needles, had m.p. 203° (lit. for a solidified oil). The epoxide (I) prepared in the usual manner in methanolic solution (with H_2O_2 and NaOH), crystallized from benzene in pale yellow plates, m.p. 201°. Rearrangement with acids could proceed as shown in the scheme.



The action of sulphuric acid on I at 0° and then room temperature over a brief period gave 7% of III, orange platelets, m.p. 214°, identified with an authentic sample[10] prepared by fusion of naphthalic acid with phenylacetic acid. The major product (85%) was *2-hydroxy-3-phenylperinaphtenone* (II), lustrous bronze-coloured needles from ethanol, m.p. 178° (*acetyl* derivative, m.p. 158°; *benzoyl* derivative, m.p. 225°). It formed a copper salt, $C_{38}H_{20}O_4Cu$, deep purple prisms, m.p. 310°. Oxidation with permanganate in acetone afforded 8-benzoyl-1-naphthoic acid, m.p. 129–130° from cyclohexane. This was identified with the substance prepared by Knapp's method.[11]

On the other hand the action of boron trifluoride on benzalacetonaphthenone epoxide in ether solution gave only 1% of II and 2% of III. The main product (50%) was 2-phenylacenaphthenone arising from deformylation of IV. This was compared with an authentic specimen made by the method of Bonner and Collins[12] and found to be identical with it.

A fourth substance (8%) isolated from this reaction crystallized from benzene–ethanol in colourless prisms, m.p. 235–236°. Analysis indicated $C_{35}H_{22}O_2$ and the

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* Ref. 8 and other papers.

[9] C. Graebe and J. Jaquar, *Liebigs Ann.* **290**, 195 (1896).

[10] M. Cesaris, *Gazz. Chim. Ital.* **42**, II, 453 (1912).

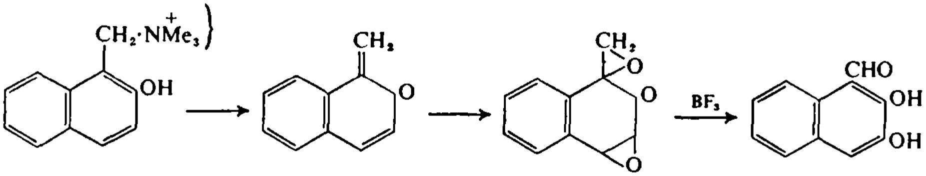
[11] W. Knapp, *Monatsh.* **67**, 332 (1936).

[12] W. A. Bonner and C. J. Collins, *J. Amer. Chem. Soc.* **75**, 2308 (1953).

substance appears therefore to be an artefact from phenylacenaphthenone. It could be an aldol-type condensation product of two molecules or a further transformation product of such.

The endeavour to develop this study in the direction of syntheses of substances analogous to the tropolones focused our attention on the use of Mannich bases as sources of αβ-unsaturated ketones. We found that Mannich bases, or still better the metho-salts derived from them, could be the starting points for the preparation of epoxides of the related unsaturated ketones.

In particular it was found that 1-dimethylamino-2-naphthol reacts with anionoid reagents (HR) to yield $C_{10}H_6(OH)CH_2R$. As one example, on heating with cyclohexanone, 2-(2′-*methylnaphthyl*-1′)*cyclohexan*-1-*one* is obtained, colourless prisms, m.p. 151°. When the Mannich base was treated in methanolic solution with hydrogen peroxide and methyl sulphate at 10°, and then dropwise with aqueous sodium hydroxide at 0°, 1:1,3:4-*diepoxy*-1-*methyl*-2-*tetralone* (VI), along with a little methylenedinaphthol, was obtained. The di-epoxide crystallized from cyclohexanone as colourless plates, m.p. 129°, benzenoid UV and IR absorption at 1725 cm^{-1} (CO).



VI VII

Compound VI is rearranged by boron trifluoride in ether, or less efficiently, by syrupy phosphoric acid, with formation of 2,3-dihydroxy-1-naphthaldehyde[13] (VII), identified with a synthetic specimen.

All the new substances mentioned on this communication gave acceptable results on elementary analysis. The m.ps are uncorrected.

[13] G. T. Morgan and D. C. Vining, *J. Chem. Soc.* **119**, 177 (1921).