Quinone Epoxides. Part VII.[1] Stereospecific Elaboration of 2-Acetyl-1,4-naphthoquinone Epoxides

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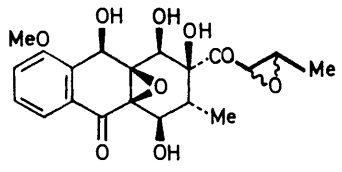
The reductive elaboration of 2-acetyl-3-methyl-1,4-naphthoquinone epoxide has been examined in an investigation into the potential of quinone epoxides as intermediates in the stereospecific syntheses of alicyclic compounds from aromatic starting materials. A series of products is obtained by stereospecific and selective reduction with borohydride: these are further transformed stereospecifically. Direct reductive opening of the epoxide ring has not been achieved. Catalytic reduction of the bromohydrin (XIV) obtained in these transformations is stereospecific but not selective. Catalytic reduction of the 3-acetyl-3.4-dihydroxy-2-methyltetralone (XVI) also leads to a mixture of products, one of which undergoes ring expansion under mild conditions to form the benzocycloheptenone derivative (XXVII).

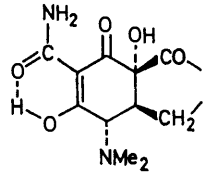
THE use of appropriately substituted aromatic intermediates in the synthesis of alicyclic structures which are polyfunctional and contain six-membered rings is particularly attractive in view of the high specificity with which aromatic compounds can be substituted and the substituents further modified. Nature, recognising the value of this approach, has adopted it for the biosynthesis of several classes of alkaloid [2] and the tetracycline antibiotics.[3] In the laboratory, elaborations of aromatic systems by the Birch reduction and the oxidative coupling of phenols [4] have featured in many syntheses. A particularly useful route to cyclohexa-2,5-dienones, which involves the 1,4-addition to the aromatic ring of an external electrophile and an internal nucleophile has been described recently.[5]

The potential value of the foregoing synthetic approach is largely determined by the ease with which the required stereochemistry of the ring substituents can be introduced at post-aromatic stages. In earlier studies we established that simple quinone epoxides, readily formed from aromatic precursors, can be modified in a highly stereospecific manner.[1,6] † Further work on the stereochemistry of products resulting from reductive modification of more elaborate compounds in this class is reported in this paper. In particular, we describe attempts to convert 2-acetyl-3-methylnaphthalene-1,4-diol (IV; R^1 = Me, R^2 = H) into the tetralone diol (X; R = Me) ‡ and the tetralin triol (XI; R = Me) by the route outlined in Scheme 1. These primary objectives were chosen for two reasons. There is a marked stereochemical and functional similarity between the hydroxylated ring of the triol (XI; R = Me) and the saturated ring in the antitumour antibiotic cervicarcin (I),[8] and there is a clear but less direct relationship between the ketonic ring of the tetralone (X; R = Me) and the A ring, (II), of the tetracycline antibiotics. Parallel studies were also carried out on 2-acetylnaphthalene-1,4-diol (IV; R^1 = R^2 = H).

The acetyl quinone (V; R = H) [9] was readily prepared from 1,4-diacetoxynaphthalene, but aluminium trichloride was needed to effect the Fries rearrangement



(I)



(II)

of the methyl derivative (III; R = Me) to the monoester (IV; R^1 = Me, R^2 = Ac), whereas zinc chloride in acetic acid smoothly promoted the corresponding conversion for the lower homologue. In both series oxidation of the quinol to the quinone was effected with silver oxide in ether. Epoxidation of 2-acetyl-1,4-napthoquinone with sodium perborate at pH 10·0 gave higher yields than with alkaline hydrogen peroxide.[10] However, the 3-methyl quinone (V; R = Me) was less sensitive to alkali and nearly quantitative yields of the epoxide (VI; R = Me) were obtained when alkaline hydrogen peroxide was used.

Reduction of the epoxide (VI; R = H) with 1 equiv. of sodium borohydride gave a 5 : 1 mixture of the dihydroquinone epoxides (VII; R = H) and (VIII; R = H) which were clearly distinguished by their i.r. and n.m.r. spectra. The acetyl carbonyl stretching absorption of (VII; R = H) was at 1730 cm^{-1}, *ca.* 20 wavenumbers higher than that normally found for an α-epoxy-ketone with an '*s-trans*'-conformation [11] and the n.m.r. spectrum showed vicinal coupling (1·7 Hz) between H-3 and H-4. The structures of the dihydroquinone epoxides (VII; R = Me) and (VIII; R = Me), obtained in an

† Unequivocal evidence has been obtained [7] for the triol designated (VIII; R = H) in ref. 6 being 1,2,3,4-tetrahydronaphthalene-*r*-1,*c*-2,*c*-4-triol.

‡ Throughout this paper only one enantiomer will be depicted when racemic modifications are discussed.

[1] Part VI, G. Read and V. M. Ruiz, *J. Chem. Soc.* (*C*), 1970, 1945.

[2] D. H. R. Barton, G. W. Kirby, J. B. Taylor, and G. M. Thomas, *J. Chem. Soc.*, 1963, 4545; F. R. Stermitz and H. Rapoport, *J. Amer. Chem. Soc.*, 1961, **83**, 4045.

[3] J. R. D. McCormick in 'Antibiotics,' vol. 2, eds. D. Gottleib and P. D. Shaw, Springer, New York, 1967.

[4] A. I. Scott, *Quart. Rev.*, 1965, **19**, 1.

[5] E. J. Corey, S. Barcza, and G. Klotmann, *J. Amer. Chem. Soc.*, 1969, **91**, 4782.

[6] A. Rashid and G. Read, *J. Chem. Soc.* (*C*), 1969, 2053.

[7] V. M. Ruiz, Ph.D. Thesis, Exeter, 1969.

[8] S. Marumo, N. Harada, K. Nakamishi, and T. Nishida, *Chem. Comm.*, 1970, 1693.

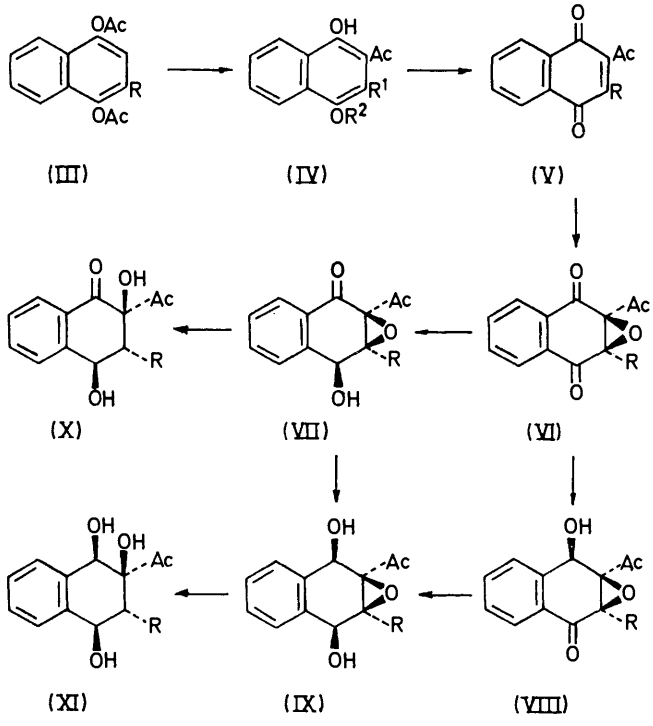
[9] C. J. P. Spruit, *Rec. Trav. chim.*, 1947, **66**, 655.

[10] D. J. Cram, *J. Amer. Chem. Soc.*, 1949, **71**, 3953.

[11] M. E. Kuehne and J. A. Nelson, *J. Org. Chem.*, 1970, **35**, 161; J. Carnduff, D. G. Leppard, *Chem. Comm.*, 1968, 822; S. Danishefsky and G. A. Koppel, *ibid.*, 1971, 367.

analogous manner from (VI; R = Me), were apparent from correlation of their i.r. and n.m.r. spectra with those of their lower homologues. High yields of the tetrahydroquinone epoxides (IX; R = H) and (IX; R = Me) were obtained when the corresponding quinone epoxides (VI; R = H) and (VI; R = Me) were reduced with 2 equiv. of sodium borohydride or when corresponding dihydroquinone epoxides were reduced with 1 equiv. of borohydride.

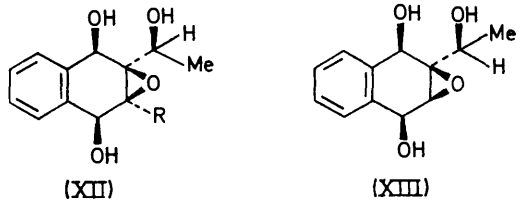
In these reductions we consider that each aryl keto-group has been stereospecifically converted into a benzylic hydroxy-group which has a *cis*-orientation with respect to the epoxide ring. This assignment is based largely on previous reductions of quinone epoxides, where the *cis*-isomer was formed in high yield and only small quantities of stereoisomeric material could be detected in the crude products. There has been no evidence for stereoisomer formation in the cases reported



SCHEME 1

here and we consider that the introduction of a 2-acetyl group in, for example, the quinone epoxide (VI; R = H), is not likely to cause a virtual reversal of the stereospecificity. The evidence for the stereochemistry of the tetralone (XIX) (see later) provides further support for this view.

The rate of reduction of acetone by borohydride is several times greater than that of acetophenone,[12] but in these cases no evidence for competing reduction at the acetyl carbonyl group was obtained unless the reagent was in excess. The diol (IX; R = H) was reduced with borohydride to a mixture of the epimeric triols (XII; R = H) and (XIII) but the diol (IX; R = Me) gave only one triol with this reagent, which for steric reasons we consider to be (XII; R = Me).

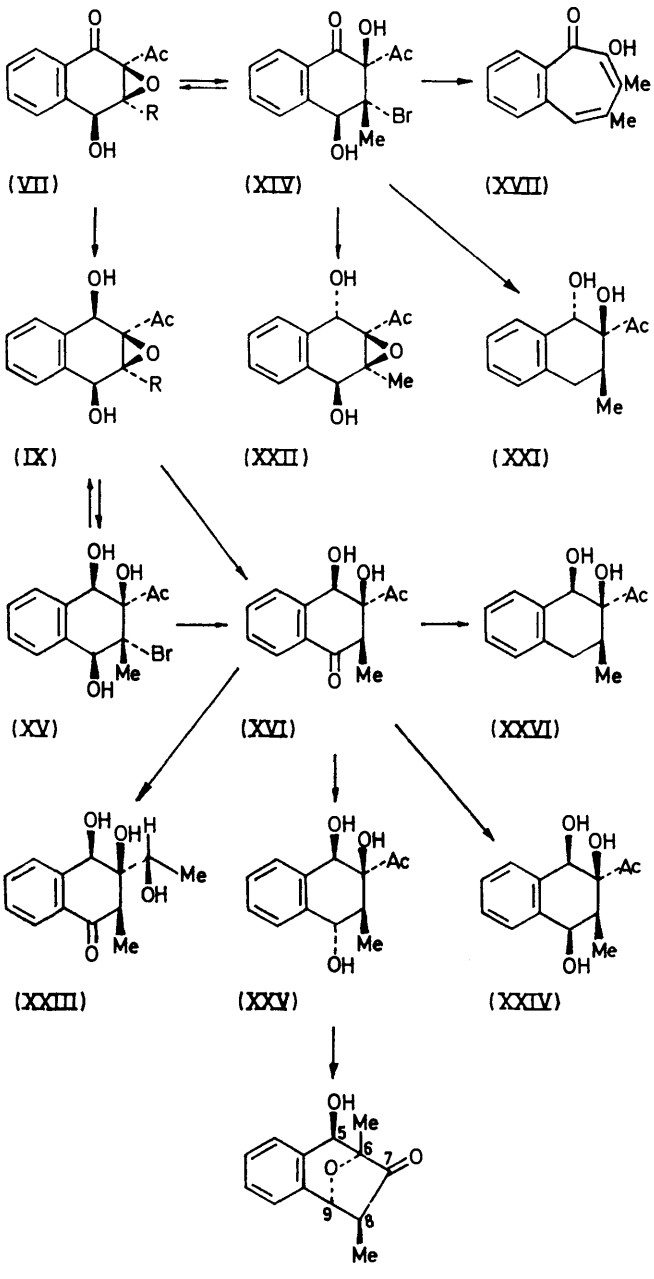


Initial attempts were made to open reductively the epoxide ring in the dihydroquinone epoxide (VII; R = Me) using hydrogen, with 5% palladium–charcoal as the catalyst, but only the dihydroxynaphthalene (IV; R^1 = Me, R^2 = H) and the corresponding quinone could be isolated. Reduction with the less active palladium oxide–barium carbonate [13,14] gave the same product. The dihydroquinone epoxide (VII; R = H) behaved in an analogous manner when reduced in the presence of these catalysts. Attempts to reduce the tetrahydroquinone epoxide (IX; R = Me) over the same catalysts and over palladised charcoal in acetic acid and palladised charcoal in acetic acid containing a little perchloric acid were unsuccessful. No hydrogen uptake was detected.

Attention was turned to preparing the bromohydrins (XIV) and (XV) (Scheme 2) from the two epoxides (VII; R = Me) and (IX; R = Me), respectively, with a view to obtaining the α-hydroxy-ketones (X) and (XI) by reductive removal of bromine; this approach has met with considerable success in the steroid field.[15] The bromohydrin (XIV) was prepared by treating the dihydroquinone epoxide (VII; R = Me) with hydrogen bromide in acetic acid. Similar treatment of the tetrahydroquinone epoxide (IX; R = Me) gave exclusively the quinol (IV; R^1 = Me, R^2 = H) but this aromatisation could be avoided by using hydrogen bromide in benzene. With this reagent a mixture of the bromohydrin (XV) and the tetralone (XVI) was obtained but the ratio of the products was very sensitive to conditions and in some runs only traces of the former compound were detected. This was probably due to the instability of the bromohydrin, which slowly decomposed in the dark at room temperature. The bromohydrins (XIV) and (XV) could be smoothly converted back into their epoxide precursors under mildly basic conditions, confirming that normal *trans* diaxial ring opening had taken place. In both cases the orientation of the bromine and newly formed hydroxy-group could not be readily deduced from spectral properties. However, the smooth conversion of the bromohydrin from (IX) into the tetralone (XVI) on reduction with 10% palladium–calcium carbonate confirmed that this bromohydrin was an α-ketol. The α-hydroxy-ketone grouping in the

[12] H. C. Brown, O. H. Wheeler, and K. Ichikawa, *Tetrahedron*, 1957, **1**, 214.
[13] R. Kuhn and H. J. Haas, *Angew. Chem.*, 1955, **67**, 785.
[14] O. Dann and H. Hofmann, *Chem. Ber.*, 1963, **96**, 320.
[15] *Cf.* N. L. Wendler, D. Taub, S. Dobriner, and D. K. Fukushima, *J. Amer. Chem. Soc.*, 1956, **78**, 5027; D. Taub, R. D. Hoffsommer, H. L. Slater, and N. L. Wendler, *J. Org. Chem.*, 1961, **26**, 2852.

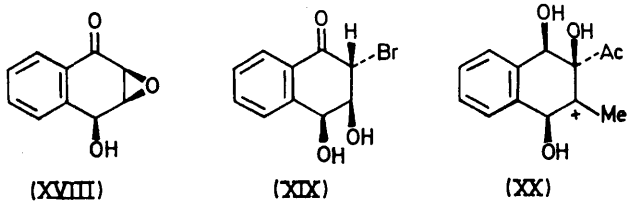
bromohydrin from (XIV) followed, less directly, from the unanticipated conversion of the bromohydrin into the benzotropolone (XVII) in the presence of zinc and



SCHEME 2

acetic acid, a reaction which will be reported in detail in a later paper. The direction of these epoxide ring openings contrasts with that found for the simple dihydronaphthoquinone epoxide (XVIII) in ethanolic hydrogen bromide, where the product is the α-tetralone (XIX). A full appraisal of the factors influencing acid-catalysed opening of the epoxide rings has yet to be made [16] but it seems clear that in the case of the tetrahydroquinone epoxide (IX) an intermediate species closely corresponding to the fully developed carbonium ion (XX) is formed under the conditions used. This can either lose the benzylic proton to the incoming bromide or bond to the latter. Interestingly, the same species appears to have been formed at the surface of the palladium catalyst when the bromohydrin (XV) was catalytically reduced with hydrogen, for the ketone (XVI) was obtained in a high yield rather than the required triol (XI; R = Me). The structure of (XVI) followed from its elemental analysis and spectroscopic properties. For convenience we defer discussion of its stereochemistry and the stereochemistry of the products now described until the end of this paper.

An attempt to form the tetralone (X) from the bromohydrin (XIV) by reductively removing the bromine over palladium–calcium carbonate was unsuccessful. It is clear that competing reactions also took place on the surface of the catalyst. Slow absorption hydrogen virtually ceased after 1 equiv. had been taken up but a significant amount of unchanged starting material was recovered together with two major products, the diol (XXI) and the tetrahydroquinone epoxide (XXII).



In view of the difficulty in obtaining the bromohydrin (XV) in high yield, the instability of this product, and the fact that it was not reduced smoothly over palladium, we turned our attention to reduction of the tetralone (XVI). With 1 equiv. of sodium borohydride, (XVI) gave the triol (XXIII) in high yield; this reaction contrasts with the reduction of the dihydroquinone epoxide (VIII; R = Me), where the aromatic carbonyl group was reduced. The aromatic carbonyl group of the tetralone was successfully reduced with hydrogen over palladium but the reduction was not stereospecific. Chromatographic separation gave a triol which we formulate as (XXIV), a more polar compound which we believe to be its epimer (XXV), and the diol (XXVI). The first two compounds had virtually identical i.r. spectra as expected from epimers of this complexity, but an unexpected property of the more polar material was its slow dehydration when heated under vacuum at a temperature some 60° below its m.p. A major portion of the specimen was lost by this process but the product, which sublimed under the dehydration conditions, was recovered. The residual material was clearly contaminated and had a rather high carbon content for $C_{13}H_{16}O_4$. The evidence for structure (XXV) is therefore incomplete but is supported by the structure of its decomposition product (see later), its mode of formation, and the i.r. evidence.

[16] (*a*) R. E. Parker and N. S. Isaacs, *Chem. Rev.*, 1959, **59**, 737; (*b*) S. O. Chan and E. J. Wells, *Canad. J. Chem.*, 1967, **45** 2123.

The analytical and mass spectroscopic evidence for the product obtained on heating (XXV) under reduced pressure indicated the molecular formula $C_{13}H_{14}O_3$. On the basis of the i.r. evidence, two of the oxygen atoms were accommodated in a keto-group associated with a five-membered ring and a hydroxy-group. The u.v. evidence indicated a benzenoid chromophore without further conjugation. Two benzylic methine systems which were bound to oxygen atoms were apparent from the n.m.r. spectrum, and deuterium exchange showed that one of these was not carrying a hydroxy-group but was vicinally coupled to a further methine system. The second benzylic methine group, which showed a broad doublet, was vicinally coupled to a hydroxy-proton. Signals from two methyl groups, a singlet and a doublet, were also observed. Collectively, this evidence is only compatible with the tricyclic ketone structure (XXVII).

Before examining in detail the evidence for the stereochemistry of the foregoing compounds, it is necessary to establish some relationships between the stereochemistry and the physical properties of the two dihydroquinone epoxides (VIII; R = H) and (VIII; R = Me) and the two tetrahydroquinone epoxides (IX; R = H) and (IX; R = Me). The acetyl groups in (VIII; R = H) and (IX; R = H) can rotate freely with the ring in the ' O-axial ' conformation,[6] but preferential stabilisation of conformation (A) (see Figure 1) by conjugation of the carbonyl group to the epoxide ring,[17] and conformation (B) (in which the 2,3-bond is eclipsed) by hydrogen bonding, is expected. However, in structures (VIII; R = Me) and (IX; R = Me) there will be considerable steric interaction between the acetyl methyl groups and the methyl groups at C-3, and it is important for our later arguments to establish that conformations (A) and (B) are not significantly occupied in these compounds. Several pieces of spectroscopic evidence support this view. The carbonyl stretching frequencies of (VIII; R = H) and (IX; R = H) (1712 and 1705 cm^{-1}, respectively) are significantly lower than those of (VIII; R = Me) and (IX; R = Me) (1720 and 1718 cm^{-1}, respectively), indicating some hydrogen bonding in the former pair. Also, for the hydrogen bonded conformation (B), an HCOH dihedral angle of 90° is required which should result in a very small vicinal coupling.[18] Several examples indicate that $J_{H,OH}$ normally falls between 11 and 12 Hz (in $CDCl_3$) when intramolecular hydrogen bonding is not possible, and the extent of any hydrogen bonding should be reflected in a lowering of this value in the time-averaged n.m.r. spectrum. This is particularly apparent in the spectra of the tetrahydroquinone epoxides where $J_{H,OH}$ is 11·0 and 12·0 Hz for the C-4 positions of (IX; R = H) and (IX; R = Me), respectively, but is 8·0 and 11·2 Hz, respectively, for the C-1 positions. In the dihydroquinone epoxide series $J_{H,OH}$ is 8·0 Hz for (VIII; R = H) and 10·4 Hz for (VIII; R = Me). We conclude that moderate populations of the hydrogen-bonding conformations occur in (VIII; R = H) and (IX; R = H) only. Evidence for the relative populations of conformation (A) comes from the resonances of the acetyl methyl groups of (VIII; R = H) and (IX; R = H), which occur at higher field than those of (VIII; R = Me) and (IX; R = Me), indicating that only in the former pair are the acetyl methyl groups subjected to long-range shielding from the epoxide ring,[19] and from the chemical shifts of the axial protons at C-1 in all four compounds, which will be subjected to the greatest long range deshielding by the acetyl carbonyl groups in this conformation. For compound (VIII; R = H) this signal is 0·29 p.p.m. to lower field than the corresponding signal for compound (VIII; R = Me), and in the tetrahydroquinone epoxide series the difference is 0·25 p.p.m.

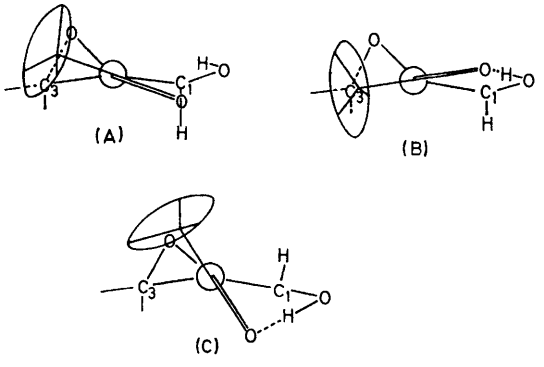


FIGURE 1

The tetrahydroquinone epoxide (XXII) shows spectral properties which are consistent with a *cis* relationship between the C-1 hydroxy- and the C-2 acetyl group. In addition to the i.r. evidence (carbonyl stretching frequency of 1699 and a shoulder at 1715 cm^{-1}), support for the C-1 hydroxy-group being predominantly hydrogen-bonded comes from the n.m.r. spectrum, which gives $J_{H,OH}$ for the C-1 position as 1·8 Hz compared with $J_{H,OH}$ for the C-4 position as 11·5 Hz. Appreciable hydrogen bonding in (XXII) is not expected, if the ring maintains the ' O-axial ' conformation, for the O · · · O distance of about 2·9 Å is marginally greater than that found in structure (IX; R = H), where the hydrogen bonding is discernible but not strong. A much higher degree of hydrogen bonding is possible if the ring adopts the ' O-equatorial ' conformation. However, in the optimum conformation for hydrogen bonding (O · · · O distance *ca.* 2·3 Å) the methyl group will interact strongly with the C-3 methyl group and be shielded by the epoxide ring. No shielding is observed in the n.m.r. spectrum and the most stable conformation appears to be (C) (Figure 1) in which the ring is ' O-equatorial ' and a longer hydrogen bond is formed (O · · · O distance 2·5 Å). Not only is the acetyl methyl group outside the

[17] C. Djerassi, N. Klyne, T. Norin, G. Ohloff, and E. Klein, *Tetrahedron*, 1965, **21**, 163; *cf.* R. C. Hahn, P. Howard, S.-M. Kong, G. A. Lorenzo, and N. L. Miller, *J. Amer. Chem. Soc.*, 1969, **91**, 3558.

[18] C. P. Rader, *J. Amer. Chem. Soc.*, 1969, **91**, 3248.

[19] L. M. Jackman and S. Sternhell, ' Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry,' Pergamon, Oxford, 1969.

shielding zone of the epoxide ring * in this conformation but the axial C-1 proton is well removed from the deshielding influence of the acetyl carbonyl group, which is consistent with its relatively high τ value of 4·90. The configuration at C-4 in this compound is thought to be the same as that of C-4 in the precursor (XIV) and the chemical shift of H-4 supports this view.

The n.m.r. spectrum of the diol obtained in the same reaction as (XXII) shows the three protons at C-3 and C-4 as a complex signal which is altered to an ABC spectrum when the C-3 methyl signal is spin decoupled. The resulting spectrum is almost symmetrical and is consistent with a situation in which $2(\nu_A - \nu_B) \simeq \nu_A - \nu_C$ and $J_{AB} \simeq J_{BC} > J_{AC}$.[20] The decoupling experiment indicates that the C proton of the ABC spectrum is H-3, which must occupy an axial position in order to have a large coupling constant (*trans* diaxial) similar in magnitude to the geminal coupling expected at C-4, and a small coupling constant (axial–equatorial). The predominant conformation of this compound is therefore one in which the C-3 methyl group is equatorial. It is clear from the carbonyl stretching frequency of the acetyl group in this diol (1696 cm^{-1}) and from the small coupling constant for the C-1 hydroxy-group ($J_{H.OH}$ 4·4 Hz), that the C-1 hydroxy-group is strongly bound to the acetyl carbonyl group. Hydrogen bonding between the C-2 acetyl and the C-2 hydroxy-group is also possible but this would not result in a lowering of the carbonyl stretching frequency.[21] The C-2 acetyl group must also be equatorial in the predominant conformation, for, if it were axial, hydrogen bonding would not be possible in the case of a *trans* disposed hydroxy-group at C-1 and, in the case of a *cis* hydroxy-group, the HCOH dihedral angle of the hydrogen-bonded hydroxy-group would be close to 180° and would not reduce $J_{H.OH}$ to a significant extent. The latter isomer may also be eliminated on steric grounds, for the important interatomic distances are almost identical to those in conformation (B). Approximately the same dimensions are also found in the hydrogen-bonded conformation of the isomer with an equatorial acetyl and a *trans*-disposed C-1 hydroxy-group. We therefore suggest the structure with the equatorial acetyl and *cis*-disposed C-1 hydroxy-group, *i.e.* (XXI), for the diol. In this case there is no steric restriction on hydrogen bonding. The shielding of the acetyl methyl group, indicated by the τ value of 8·05, appears to be due to the long-range influence of the C-2 hydroxy-group.[22] It would appear from these results that catalytic reduction of the bromohydrin (XIV) involves several reactions, including the stereospecific reduction of the C-1 carbonyl by hydrogen approaching from the same side of the molecule as the C-2 hydroxy-group.

The stereochemistry assigned to the tetralone (XVI) is based on the following considerations. Attempts to epimerise the C-3 centre with toluene-*p*-sulphonic acid in chloroform (room temp. for 48 h) and perchloric acid–sodium perchlorate in dioxan water (room temp. 15 h) [23] were unsuccessful, suggesting that the thermodynamically more stable equatorial methyl group was present.[24] If the ketonic function was formed by the collapse of an enol (see before) this stereochemistry is also more probable on kinetic grounds.[25] There is no i.r. or n.m.r. evidence for hydrogen bonding between the C-2 acetyl and the C-1 hydroxy-group in this tetralone. Therefore the acetyl group is expected to adopt a preferred conformation which allows hydrogen bonding to the C-2 hydroxy-group.[26] For an axial acetyl group in this conformation the acetyl methyl would lie in the strong shielding zone of the benzene ring, which is not consistent with the n.m.r. evidence. We therefore formulate (XVI) with an equatorial acetyl at C-2 and a *trans*-disposed hydroxy-group at C-1, for, as we have already noted, hydrogen bonding is possible if the hydroxy-group at C-1 is *cis*-disposed. Support for this stereochemical assignment also came from dehydration studies which showed that the stereochemistry favoured dehydration under conditions which are considered to give rise to *E2 trans* diaxial eliminations.[27]

The configuration assigned to the alcoholic function formed on reducing (XVI) with sodium borohydride is based on the belief that the predominant and most reactive conformation of the acetyl group in (XVI) is the one in which the acetyl oxygen is hydrogen bound to the C-2 hydroxy-group. For this conformation, hydride attack on the opposite face of the carbonyl to the equatorial C-3 methyl group would be expected, which leads to stereoisomer (XXIII). Inversion of the C-3 centre in (XVI) during the catalytic conversion of this compound into the triols (XXIV) and (XXV), and into the diol (XXVI), was not anticipated and the physical properties of (XXIV) and (XXVI) support this view. The relative orientation of the C-4 hydroxy-group with respect to the equatorial C-3 methyl group in the triol (XXIV) is revealed by the vicinal coupling constant of 4·4 Hz, for the axial H-3 and H-4, which is consistent with an axial–equatorial relationship. The two triols are therefore formulated as (XXIV) and (XXV).

The tricyclic ketone obtained from the triol (XXV) by heating under reduced pressure shows a relatively high coupling constant of 7·2 Hz for the protons at C-6 and C-7 which points strongly to the 33° dihedral angle between these protons rather than the alternative 87° angle for this ring system. We have no direct evidence

* On the basis of the π-electron distribution in the epoxide ring [16a] the anisotropy would be expected to be greatest close to the 2,3-bond.

[20] F. A. Bovey, 'Nuclear Magnetic Resonance Spectroscopy,' Academic Press, New York, 1969, p. 323, spectrum 51.

[21] W. G. Cole and D. H. Williams, *J. Chem. Soc.* (*C*), 1968, 1849.

[22] J. A. Pople, *J. Chem. Phys.*, 1962, **37**, 60.

[23] G. E. Lienhard and T.-C. Wang, *J. Amer. Chem. Soc.*, 1969, **91**, 1146.

[24] N. L. Allinger and H. M. Blatter, *J. Amer. Chem. Soc.*, 1961, **83**, 994; B. Rickborn, *ibid.*, 1962, **84**, 2414.

[25] E. J. Corey and R. A. Sneen, *J. Amer. Chem. Soc.*, 1956, **78**, 6269.

[26] L. Joris and P. von R. Schleyer, *J. Amer. Chem. Soc.*, 1968, **90**, 4599.

[27] D. V. Banthorpe, 'Elimination Reactions,' Elsevier, Amsterdam, 1963, p. 155.

which bears on the stereochemistry at C-3 in this compound but we consider that this remarkable ring expansion involves an internally catalysed tertiary ketol rearrangement [28] (see Figure 2) to give, as an intermediate,

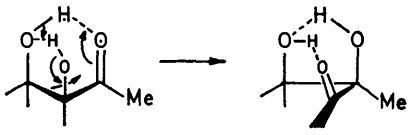
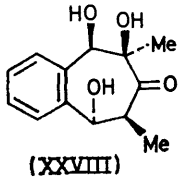


FIGURE 2

the benzocycloheptenone (XXVIII), which has the correct stereochemistry and can adopt the correct conformation for an intramolecular S_N2 substitution of the tertiary hydroxy-group at C-6 to give (XXVII). This latter reaction may also be internally catalysed by the C-5 hydroxy-group. No inversion of the C-5 centre would be expected on the basis of this mechanism.



(XXVIII)

Although the precise objectives of this work have not been achieved, it is clear that quinone epoxides can be converted with a high degree of stereospecificity into polyfunctional alicyclic systems not readily obtained by other routes. However, the synthetic potential of such intermediates could be limited by the ease with which the products derived from the quinone epoxides are rearranged and dehydrated. A further feature of several of the compounds described in this paper, ready deacetylation, will be discussed in a later paper.

EXPERIMENTAL

U.v. spectra were measured with a Hilger Ultrascan recording spectrophotometer H999 Mark II, and i.r. spectra were determined for potassium bromide discs, unless otherwise stated, with a Hilger Infrascan recording spectrophotometer H900. N.m.r. spectra were recorded with a Perkin-Elmer R10 instrument at 60 MHz and a JEOL JNM-MH-100 at 100 MHz. Mass measurements were made with a Hitachi–Perkin-Elmer RMU-6 instrument.

For column chromatography Mallinckrodt silicic acid and Merck silica gel were used. Merck DC-Fertigplatten Kieselgel F_{254} were used for the t.l.c. Unless otherwise stated, R_F values refer to samples run in chloroform–ethanol (19 : 1).

4-Acetoxy-2-acetyl-1-naphthol (IV; R^1 = H, R^2 = Ac).—1,4-Diacetoxynaphthalene (27 g) was added to a solution of anhydrous zinc chloride (27 g) in glacial acetic acid (60 ml). The solution was refluxed for 30 min, cooled, poured into cold water (4 l) and stirred for 15 min. The oily residue crystallised and gave 4-acetoxy-2-acetyl-1-naphthol (21 g, 78%) as pale green plates, m.p. 102—103° (from 70% ethanol); $\nu_{max.}$ 1760 (acetoxy C=O str.), 1723 (acetyl C=O str.), and 1623 cm^{-1} (lit.,[9] m.p. 103—104°).

4-Acetoxy-2-acetyl-3-methyl-1-naphthol (IV; R^1 = Me, R^2 = Ac).—Anhydrous aluminium chloride (24 g) was added to a solution of 1,4-diacetoxy-2-methylnaphthalene (34 g) in 1,2-dichloroethane (200 ml). The solution was refluxed under anhydrous conditions for 1 h, then allowed to cool and poured on crushed ice (1 kg). The aqueous solution obtained was stirred, acidified with 2M-hydrochloric acid (80 ml), and extracted with chloroform (3 × 200 ml). Evaporation of the dried extract gave *4-acetoxy-2-acetyl-3-methyl-1-naphthol* (IV; R^1 = Me, R^2 = Ac) (30 g, 88%), which formed pale yellow needles, m.p. 95·5—96° (from propan-1-ol) (Found: C, 70·0; H, 5·5. $C_{15}H_{14}O_4$ requires C, 69·8; H, 5·5%); $\nu_{max.}$ 1760 (acetoxy C=O str.), 1625 (acetyl C=O str.), and 1205 cm^{-1}; $\lambda_{max.}$ 220, 261, 270, and 274 nm (log ε 4·62, 4·38, 4·33, and 3·58).

2-Acetylnaphthalene-1,4-diol (IV; R^1 = R^2 = H).—4-Acetoxy-2-acetyl-1-naphthol (15 g) in 50% aqueous ethanol was hydrolysed in the presence of hydrochloric acid (80 ml; *d* 1·19). The solution was refluxed for 15 min and poured into ice-cold water (4 l). The diol (12·4 g, 100%), which separated as a yellow solid, had m.p. 210—211° (from 5% ethanol–benzene); $\nu_{max.}$ 3275 (OH str.) and 1638 cm^{-1} (C=O str. chelated acetyl) (lit.,[9] m.p. 206°; lit.,[10] m.p. 216—217°).

2-Acetyl-3-methylnaphthalene-1,4-diol (IV; R^1 = Me, R^2 = H).—4-Acetoxy-2-acetyl-3-methyl-1-naphthol (18 g) was hydrolysed in propan-1-ol (100 ml) and 2M-hydrochloric acid (100 ml) under nitrogen. The solution was refluxed for 2 h, allowed to cool, and poured into ice–water (*ca.* 3 l). The suspension was extracted with chloroform (4 × 200 ml); the extract was dried ($MgSO_4$) and evaporated. The residue, which was oxidised readily in air, was crystallised twice from benzene to give 2-acetyl-3-methylnaphthalene-1,4-diol (IV; R^1 = Me, R^2 = H) as orange needles (13 g, 87%), m.p. 134·5—135·5° (Found: C, 73·3; H, 5·7. Calc. for $C_{13}H_{12}O_3$: C, 72·2; H, 5·6%); $\nu_{max.}$ 3410 (phenol OH str.), 1620 (chelated acetyl C=O str.), and 1585 and 1563 cm^{-1} (phenyl ring); $\lambda_{max.}$ 215, 242, 275, and 396 nm (log ε 4·56, 4·17, 4·17, and 3·49); τ ($CDCl_3$–D_2O) 7·43 (3H, s, 3-Me), 7·32 (3H, s, Ac), and 1·40—2·70 (4H, m, aryl H).

2-Acetyl-1,4-naphthoquinone (V; R = H).—Naphthalene-1,4-diol (10·5 g) in ether (900 ml) was stirred with silver oxide [from silver nitrate (30 g)] [29] in the presence of anhydrous sodium sulphate (35 g) for 15 min. The solids were filtered off and the filtrate evaporated under reduced pressure to *ca.* 15—20 ml. Crystallisation from light petroleum (charcoal) gave 2-acetyl-1,4-naphthoquinone (8 g, 80%), m.p. 83·5—84°; $\nu_{max.}$ 1690 (C=O str. acetyl) and 1670br cm^{-1} (C=O str. quinone) (lit.,[9] m.p. 84°, lit.,[10] 80—81°).

2-Acetyl-3-methyl-1,4-naphthoquinone (V; R = Me).—2-Acetyl-3-methylnaphthalene-1,4-diol (13 g) was oxidized in ether with silver oxide [from silver nitrate (34 g)]. Evaporation and crystallisation of the product from petroleum (b.p. 80—100°) gave *2-acetyl-3-methyl-1,4-naphthoquinone* (V; R = Me) as yellow needles (10·1 g, 78%), m.p. 88—89° (Found: C, 72·8; H, 4·7. $C_{13}H_{10}O_3$ requires C, 72·8; H, 4·7%); $\nu_{max.}$ 1703 (acetyl C=O str.) and 1663 cm^{-1} (quinone C=O str.); $\lambda_{max.}$ 220, 254, and 337 nm (log ε 3·98, 4·31, and 3·46).

2-Acetyl-2,3-epoxy-2,3-dihydro-1,4-naphthoquinone (VI; R = H).—2-Acetyl-1,4-naphthoquinone (3·36 g) in ethanol (240 ml) was treated with sodium perborate (3·3 g) in water (240 ml). After 1 min at room temperature the reaction

[28] S. Selman and J. F. Eastham, *Quart. Rev.*, 1960, **14**, 221.
[29] J. Cason, *Org. Reactions*, 1948, **4**, 314.

was stopped by adjusting the pH to 3—3·5 with hydrochloric acid. The solution was poured into 10% sodium chloride solution (2 l) and extracted with chloroform (4 × 80 ml). The chloroform solution was dried ($MgSO_4$) and evaporated to yield an oily residue which was dissolved in ethanol and boiled with charcoal. After removal of the decolourizing agent the solution was evaporated to a small volume to give 2-acetyl-2,3-epoxy-2,3-dihydro-1,4-naphthoquinone as needles (1·92 g, 53%), m.p. 125·5—126°;' $\nu_{max.}$ 1700 (quinone C=O str.), 1251, 905, and 852 cm^{-1} (epoxide ring str.); τ [$(CD_3)_2SO$] 7·52 (3H, s, Me), 5·58 (1H, s, H-3), and 1·97 (4H, s, aryl H) (lit.,[10] m.p. 125—126°).

2-Acetyl-2,3-epoxy-2,3-dihydro-3-methyl-1,4-naphthoquinone (VI; R = Me).—2-Acetyl-3-methyl-1,4-naphthoquinone (32 g) in ethanol (800 ml) was treated, at 15°, with 30% hydrogen peroxide (30 ml) and 15% sodium carbonate solution (30 ml). After 5 min the solution was acidified to pH 5 with dilute hydrochloric acid and poured into ice–water (*ca.* 4 l). After a few minutes the solid which separated was collected, washed with water, and crystallised from ethanol to give *2-acetyl-2,3-epoxy-2,3-dihydro-3-methyl-1,4-naphthoquinone* (32 g, 92%), m.p. 90—91°, R_F 0·56 ($CHCl_3$) (Found: C, 67·9; H, 4·4. $C_{13}H_{10}O_4$ requires C, 67·8; H, 4·3%); $\nu_{max.}$ 1725 (acetyl C=O str.), 1712 (quinone C=O str.), 1265, 907, and 850 cm^{-1} (epoxide ring str.); $\lambda_{max.}$ 234, 262, and 308 nm (log ε 4·23, 376, and 3·34); τ ($CDCl_3$) 8·39 (3H, s, 3-Me), 7·55 (3H, s, Ac) and 1·70—2·40 (4H, m, aryl H).

Reduction of 2-Acetyl-2,3-epoxy-2,3-dihydro-1,4-naphthoquinone with Sodium Borohydride (1·1 *Equiv.*).—The epoxy quinone (0·43 g) dissolved in ethanol (35 ml) was treated with sodium borohydride (20·5 mg) in ethanol (10 ml). After 20 min at room temperature, the solution was diluted with water (150 ml), acidified to pH 3—3·5 with 2M-hydrochloric acid, and extracted with chloroform (4 × 50 ml.). The extract was dried ($MgSO_4$) and evaporated to give the crude product (0·5 g), which was dissolved in 50% benzene–chloroform (15 ml) and chromatographed on a silic acid (20 g) column (1·5 cm int. diam.). Elution with 50% benzene–chloroform gave *3-acetyl-r-2,3-epoxy-3,4-dihydro-c-4-hydroxynaphthalen-1(2H)-one* (VIII; R = H) as needles (33 mg, 7·6%), m.p. 163·5—164° (from benzene) (Found: C, 66·0; H, 4·7. $C_{12}H_{10}O_4$ requires C, 66·0; H, 4·6%); $\nu_{max.}$ ($CHCl_3$) 3590 (alcoholic OH str.), 1712 (acetyl C=O str.), and 1693 cm^{-1} (aryl ketone C=O str.); $\lambda_{max.}$ 217, 256, and 292 nm (log ε 3·86, 4·04, and 3·17); τ ($CDCl_3$), 7·79 (3H, s, Ac), 7·10 (1H, d, $J_{H,OH}$ 8·0 Hz, OH), 6·14 (1H, s, H-2), 4·25 (1H, d, $J_{H.OH}$ 8·0 Hz, H-4), and 2·04—2·75 (4H, m, aryl H); R_F 0·50.

Elution with chloroform gave *2-acetyl-r-2,3-epoxy-3,4-dihydro-c-4-hydroxynaphthalen-1(2H)-one* (VII; R = H) as prisms (94·7 mg, 22%), m.p. 123·5—124° (from benzene) (Found: C, 66·0; H, 4·7. $C_{12}H_{10}O_4$ requires C, 66·0; H, 4·6%); $\nu_{max.}$ ($CHCl_3$) 3570 (alcoholic OH str.), 1730 (acetyl C=O str.), and 1686 cm^{-1} (aryl ketone C=O str.); $\lambda_{max.}$ 218, 258, and 292 nm (log ε 3·80, 4·02, and 3·14); τ [$(CD_3)_2SO$–D_2O] 7·58 (3H, s, Ac), 5·85 (1H, d, *J* 1·7 Hz, H-3), 4·68 (1H, d, *J* 1·7 Hz, H-4), and 1·95—2·6 (4H, m, aryl H); R_F 0·41.

2-Acetyl-c-2,3-epoxy-1,2,3,4-tetrahydronaphthalene-r-1,c-4-diol (IX; R = H).—The epoxy-ketone (VIII; R = H) (130 mg) dissolved in ethanol (10 ml), was reduced with sodium borohydride (6·2 mg, 1·1 equiv.) in ethanol (6·2 ml). After 30 min at room temperature the solution was diluted with water (*ca.* 50 ml), acidified to pH 3·5—4 with dilute hydrochloric acid, saturated with sodium chloride, and extracted with ethyl acetate (7 × 30 ml). The extract was dried ($MgSO_4$) and evaporated to give the crude product, which on t.l.c. showed a single spot, R_F 0·24. Crystallisation from chloroform or hexan-1-ol gave the *diol* (IX; R = H) as feathery needles (67 mg, 50%), m.p 177—178·7°, which contained water of crystallisation (0·25—0·33 mol. equiv.). Sublimation of a sample under high vacuum gave material, m.p. 168—169° (Found: C, 64·9; H, 5·3%; *m/e* 220·0740. $C_{12}H_{12}O_4$ requires C, 65·4; H, 5·5%; *m/e* 220·0736); $\nu_{max.}$ 3425, 3300 (alcoholic OH str.), and 1705 cm^{-1} (acetyl C=O str.); $\lambda_{max.}$ 222 and 261 nm (log ε 3·04 and 2·32); τ ($CDCl_3$) 7·80 (3H, s, Ac), 7·70 (1H, d, $J_{H.OH}$ 11·0 Hz, 4-OH), 7·34 (1H, d, $J_{H.OH}$ 8·0 Hz, 1-OH), 6·15 (1H, d, $J_{3,4}$ 1·2 Hz, H-3), 5·08br (1H, d, $J_{H.OH}$ 11·0 Hz, H-4), 4·43 (1H, d, $J_{H.OH}$ 8·0 Hz, H-1), and 2·26—2·75 (4H, m, aryl H).

Reduction of the epoxy-ketone (VII; R = H) with 1·1 equiv. of sodium borohydride, and 2-acetyl-2,3-epoxy-1,4-naphthoquinone with 2·2 equiv. of sodium borohydride, by procedures similar to that just described, gave the same product in yields of 65 and 75%, respectively.

Reduction of 2-Acetyl-2,3-epoxy-2,3-dihydro-3-methyl-1,4-naphthoquinone with Sodium Borohydride (1·1 *Equiv.*).—The epoxy-quinone (13·8 g), dissolved in ethanol (800 ml), was reduced with sodium borohydride (630 mg) in ethanol (250 ml). After 20 min at room temperature the solution was evaporated under reduced pressure (to *ca.* 60 ml), diluted with water (500 ml), acidified to pH 4·0—4·5 with dilute hydrochloric acid, and extracted with ethyl acetate (5 × 150 ml). The extract was dried ($MgSO_4$), and evaporated. The residue (12·3 g) was dissolved in benzene (100 ml) and treated with charcoal. T.l.c. (ethyl acetate) showed the presence of three major components. When the solution was evaporated to half volume and allowed to cool, crystals of *2-acetyl-r-2,3-epoxy-3,4-dihydro-c-4-hydroxy-3-methylnaphthalen-1(2H)-one* (VII; R = Me) (7·2 g, 51%) were obtained; m.p. 149·5—150·5° (Found: C, 67·0; H, 5·2. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2%); $\nu_{max.}$ ($CHCl_3$) 3580 (alcoholic OH str.), 1732 (acetyl C=O str.), and 1685 cm^{-1} (aryl ketone C=O str.); $\lambda_{max.}$ 218, 257, and 293 nm (log ε 3·83, 4·01, and 3·17); τ ($CDCl_3$) 8·45 (3H, s, 3-Me), 7·66 (3H, s, Ac), 7·34 (1H, d, $J_{H,OH}$ 10·4 Hz, 4-OH), 5·13 (1H, d, $J_{H.OH}$ 10·4 Hz, H-4), and 2·04—2·76 (4H, m, aryl H).

The residue obtained on evaporation of the mother liquors from the foregoing crystallisation was crystallised twice from chloroform to give *2-acetyl-c-2,3-epoxy-1,2,3,4-tetrahydro-3-methylnaphthalene-r-1,c-4-diol* (IX; R = Me) (0·42 g, 3%), as plates, m.p. 180—181° (Found: C, 66·7; H, 6·1. $C_{13}H_{14}O_4$ requires C, 66·6; H, 6·0%); $\nu_{max.}$ 3450 (alcoholic OH str.) and 1718 cm^{-1} (acetyl C=O str.); $\lambda_{max.}$ 211 nm (log ε 3·73); τ ($CDCl_3$) 8·46 (3H, s, 3-Me), 7·99 (1H, d, $J_{H.OH}$ 12·0 Hz, 4-OH), 7·77 (1H, d, $J_{H.OH}$ 11·2 Hz, 1-OH), 7·67 (3H, s, Ac), 5·38 (1H, d, $J_{H.OH}$ 12·0 Hz, H-4), 4·68 (1H, d, $J_{H.OH}$ 11·2, H-1), and 2·28—2·77 (4H, m, aryl H).

Evaporation of the mother liquors from the second crystallisation from chloroform yielded a residue which after several crystallisations from benzene gave *3-acetyl-r-2,3-epoxy-3,4-dihydro-c-4-hydroxy-3-methylnaphthalen-1(2H)-one* (VIII; R = Me) as needles (1·2 g, 8·5%), m.p. 134·5—135·5° (Found: C, 67·1; H, 5·2. $C_{13}H_{12}O_4$ requires C, 67·2; H, 5·2%); $\nu_{max.}$ ($CHCl_3$) 3570 (alcoholic OH str.), 1720 (C=O str.), and 1695 cm^{-1} (aryl ketone C=O str.); $\lambda_{max.}$ 216, 254, and 291 nm (log ε 3·89, 4·01, and 3·17); τ ($CDCl_3$) 8·51 (3H, s, 2-Me), 7·66 (3H, s, Ac), 6·69 (1H, d, $J_{H.OH}$ 10·4 Hz, 4-OH), 4·54 (1H, d, $J_{H,OH}$ 10·4 Hz, H-4), and 2·08—2·76 (4H, m, aryl H).

Reduction of 2-*Acetyl*-r-2,3-*epoxy*-3,4-*dihydro*-c-4-*hydroxy*-3-*methylnaphthalen*-1(2H)-*one*.—The epoxy-ketone (93 mg) in ethanol (20 ml) was treated with sodium borohydride (4·16 mg) in ethanol (4·16 ml). After 25 min at room temperature the solution was evaporated to half volume, diluted with water (50 ml), acidified with 2M-hydrochloric acid to pH 4, and extracted with ethyl acetate (5 × 30 ml). The extract was dried ($MgSO_4$) and evaporated and the residue crystallised from chloroform to give plates of 2-acetyl-*c*-2,3-epoxy-1,2,3,4-tetrahydro-3-methylnaphthalene-*r*-1,*c*-4-diol (68 mg, 72%), m.p. 178·5—179·5°, identical (u.v., i.r., and n.m.r. spectra) with the material obtained by reduction of 2-acetyl-2,3-epoxy-3-methyl-1,4-naphthoquinone.

The same diol was obtained when 2-acetyl-2,3-epoxy-3-methyl-1,4-naphthoquinone was reduced with 2·2 equiv. of sodium borohydride (91% yield).

Reduction of 2-*Acetyl*-c-2,3-*epoxy*-1,2,3,4-*tetrahydronaphthalene*-r-1,c-4-*diol with Sodium Borohydride* (1·1 *Equiv.*).—The epoxy-diol (68 mg) dissolved in ethanol (10 ml) was reduced with sodium borohydride (3·1 mg) in ethanol (3·1 ml). After 30 min at room temperature the solution was diluted with water (*ca.* 50 ml), acidified to pH 3·5 with dilute hydrochloric acid, saturated with sodium chloride, and extracted with ethyl acetate (7 × 30 ml). The extract was dried ($MgSO_4$) and evaporated to give the crude product (61 mg) which on t.l.c. showed two overlapped spots (R_F 0·10). Recrystallisation from ethyl acetate gave an epimeric mixture of *c*-2,3-epoxy-2-(1-hydroxyethyl)-1,2,3,4-tetrahydronaphthalene-*r*-1,*c*-4-diols [(XII; R = H) and (XIII; R = H)] (53 mg, 77%), m.p. 164—166° (decomp.) (Found: C, 62·6; H, 6·2. Calc. for $C_{12}H_{14}O_4$,-$0·5H_2O$: C, 62·4; H, 6·5%); $\nu_{max.}$ 3400 cm^{-1} (alcoholic OH str.); τ [$(CD_3)_2SO$–D_2O] 8·88 and 8·69 [3H, two d (ratio 9 : 11); *J* 6·6 Hz and 6·6 Hz; Me (isomer a) and Me (isomer b)], 6·43 (1H, m, H-3), 5·76 (1H, m, C*H*Me), 5·10 and 4·96 (1H, two s, H-1, isomer b and isomer a, respectively), 5·15 (1H, m, H-4, isomer b and isomer a), and 2·61 (4H, m, aryl H).*

c-2,3-*Epoxy*-2-(1-*hydroxyethyl*)-1,2,3,4-*tetrahydro*-3-*methylnaphthalene*-r-1,c-4-*diol* (XII; R = Me).—2-Acetyl-2,3-epoxy-3-methyl-1,4-naphthoquinone (230 mg) dissolved in ethanol (15 ml) was reduced with sodium borohydride (30·1 mg, 3·1 equiv.) in ethanol (15 ml). After 45 min at room temperature the solution was evaporated under reduced pressure to half volume, diluted with water (50 ml), acidified to pH 3·5—4 with dilute hydrochloric acid, saturated with sodium chloride, and extracted with ethyl acetate (7 × 30 ml). The extract was dried ($MgSO_4$) and evaporated and the residue crystallised from acetone to give the *triol* (XIII; R = Me) as feathery needles (188 mg, 80%), m.p. 194·5—195° (decomp.) (Found: C, 66·1; H, 6·8. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%); $\nu_{max.}$ 3390 cm^{-1} (alcoholic OH str.); τ [$(CD_3)_2SO$–D_2O] 8·61 (3H, d, *J* 7·3 Hz, CH*Me*), 8·38 (3H, s, 3-Me), 5·76 (1H, q, *J* 7·3 Hz, C*H*Me), 5·44 (1H, s, H-4), 5·04 (1H, s, H-1), and 2·62 (4H, m, aryl H); R_F 0·16.

2-*Acetyl*-t-3-*bromo*-3,4-*dihydro*-r-2,c-4-*dihydroxy*-3-*methylnaphthalen*-1(2H)-*one* (XIV).—2-Acetyl-r-2,3-epoxy-3,4-dihydro-*c*-4-hydroxy-3-methylnaphthalen-1(2*H*)-one (2·0 g) in acetic acid (30 ml) was treated with a 45% solution of hydrogen bromide in acetic acid (5·6 ml). After 3 h at room temperature, the solution was poured into water (300 ml) and extracted with chloroform (4 × 100 ml). The extract was washed with water (2 × 30 ml), dried ($MgSO_4$), and evaporated. The residue was dissolved in hot benzene and treated with charcoal. On cooling, the solution deposited plates of the *bromohydrin* (XIV) (0·95 g, 37%), m.p. 131—133° (Found: C, 49·9; H, 4·3. $C_{13}H_{13}BrO_4$ requires C, 49·9; H, 4·2%); $\nu_{max.}$ 3485, 3390 (alcoholic OH str.), 1713 (acetyl C=O str.), and 1693 cm^{-1} (aryl ketone C=O str.); $\lambda_{max.}$ 217, 256, and 296 nm (log ε 3·97, 4·05, and 3·08); τ ($CDCl_3$–D_2O), 8·35 (3H, s, 3-Me), 7·54 (3H, s, Ac), 4·13 (1H, s, H-4), and 2·25 (4H, m, aryl H).

Reaction of 2-*Acetyl*-t-3-*bromo*-3,4-*dihydro*-r-2,c-4-*dihydroxy*-3-*methylnaphthalen*-1(2H)-*one with Hydrogen Bromide in Benzene*.—2-Acetyl-*c*-2,3-epoxy-1,2,3,4-tetrahydro-3-methylnaphthalene-*r*-1,*c*-4-diol (3·7 g) in ethyl acetate (100 ml) was treated with 0·74M-hydrogen bromide in benzene (20 ml). After 15 min at room temperature the solvent was removed and the residue was dissolved in chloroform–benzene (1 : 1; 10 ml). The two major products were separated on a column of silicic acid (3·0 cm int. diam.; 200 g) with chloroform–benzene (3 : 1) as eluant. From the first fractions fine needles of 2-*acetyl*-t-3-*bromo*-1,2,3,4-*tetrahydro*-3-*methylnaphthalene*-r-1,c-2,c-4-*triol* (XV) were obtained (0·75 g, 15%); m.p. 134—135° (from benzene) (Found: C, 49·3; H, 4·8. $C_{13}H_{15}BrO_4$ requires C, 49·5; H, 4·8%); $\nu_{max.}$ 3480, 3340 (alcoholic OH str.), and 1713 cm^{-1} (acetyl C=O str.); $\lambda_{max.}$ 218 nm (log ε 3·86); τ ($CDCl_3$–D_2O), 8·19 (3H, s, 3-Me), 7·30 (3H, s, Ac), 5·22 (1H, s, H-1), 4·43 (1H, s, H-4), and 2·50 (4H, m, aryl H); R_F 0·50.

Fractions which contained a mixture of (XV) and the second component were combined and washed with aqueous 5% sodium hydrogen carbonate (100 ml). The washing was extracted with ethyl acetate (3 × 50 ml) and the ethyl acetate solution was worked up to give a small amount of regenerated starting material (220 mg, 6%). Concentration of the washed chloroform–benzene solution gave 3-*acetyl*-3,4-*dihydro*-c-3,c-4-*dihydroxy*-r-2-*methylnaphthalen*-1(2H)-*one* (XVI) (0·89 g, 24%), m.p. 104—106° (decomp.) (from benzene) (Found: C, 66·6; H, 6·0. $C_{13}H_{14}O_4$ requires C, 66·6; H, 6·0%); $\nu_{max.}$ ($CHCl_3$) 3557 and 3453 (alcoholic OH str.), 1717 (acetyl C=O str.), and 1696 cm^{-1} (aryl ketone C=O str.); $\lambda_{max.}$ 249 and 290 nm (log ε 4·00 and 3·17); τ ($CDCl_3$) 8·93 (3H, d, $J_{H,Me}$ 7·2 Hz, 2-Me), 7·60 (3H, s, Ac), 7·19 (1H, d, $J_{H,OH}$ 12·0 Hz, 4-OH), 6·98 (1H, q, $J_{H,Me}$ 6·6 Hz, H-2), 5·80 (1H, s, 3-OH), 4·65 (1H, d, $J_{H,OH}$ 12·0 Hz, H-4), and 1·80—2·80 (4H, m, aryl H); *m/e* 234 ($M^{+\cdot}$), 216 ($M^{+\cdot}$ − 18), and 191 ($M^{+\cdot}$ − 43); R_F 0·38.

Catalytic Hydrogenation of 2-*Acetyl*-t-3-*bromo*-1,2,3,4-*tetrahydro*-3-*methylnaphthalene*-r-1,c-2,c-4-*triol*.—The triol (158 mg) in ethanol (20 ml) was hydrogenated over 10% palladium–calcium carbonate (50 mg) at 1 atm and room temperature. After 30 min the hydrogen uptake (18 ml) stopped; filtration and evaporation gave 3-acetyl-3,4-dihydro-*c*-3,*c*-4-dihydroxy-*r*-2-methylnaphthalen-1(2*H*)-one (XVI) (0·11 g, 93%) (from benzene), indistinguishable from the compound obtained before.

Reduction of 3-*Acetyl*-3,4-*dihydro*-c-3,c-4-*dihydroxy*-r-2-*methylnaphthalen*-1(2H)-*one*.—The dihydroxy-ketone (575 mg) in ethanol (15 ml) was reduced with sodium borohydride (50 mg) in ethanol (30 ml). After 90 min the solution was evaporated under reduced pressure to approximately half volume, acidified with 2M-hydrochloric acid to pH 3, diluted with water (50 ml), and extracted with ethyl acetate (10 × 20 ml). The extract was dried ($MgSO_4$) and evaporated.

* Assignments based on spectrum of sample in which isomer a : isomer b = 2 : 1.

The product was separated from some starting material on a column of silicic acid (2·3 cm int. diam.; 75 g) with chloroform as eluant. Starting material was recovered from the first fractions (187 mg, 33%) and subsequent fractions gave 3,4-*dihydro*-c-3,c-4-*dihydroxy*-2-(1-*hydroxyethyl*)-r-2-*methylnaphthalen*-1(2H)-*one* (XXIII) (230 mg, 40%) as a feathery solid, m.p. 151·5—152·5° (from chloroform) (Found: C, 65·9; H, 6·7. $C_{13}H_{16}O_4$ requires C, 66·1; H, 6·8%); $\nu_{max.}$ 3400br (alcoholic OH str.) and 1695 cm^{-1} (aryl ketone C=O str.); τ [$(CD_3)_2SO$–D_2O)] 8·86 (3H, d, *J* 6·8 Hz, 2-Me), 8·69 (3H, d, *J* 6·8 Hz, C*H*$_3$·C·OH), 7·21 (1H, q, *J* 6·8 Hz, H-2), 6·05 (1H, q, *J* 6·8 Hz, MeC*H*·OH), 4·80 (1H, s, H-4), and 2·34 (4H, m, aryl H).

Reduction of 2-*Acetyl*-t-3-*bromo*-3,4-*dihydro*-r-2,c-4-*dihydroxy*-3-*methylnaphthalen*-1(2H)-*one over Palladium–Calcium Carbonate*.—The bromohydrin (XIV) (344 mg) was hydrogenated over 10% palladium–calcium carbonate (65 mg) in ethanol [uptake 26 ml (1 equiv.) in 14 h]. A solution of the products in benzene gave crystalline starting material (44 mg). The residue was chromatographed on a column of silica gel (12 × 240 mm). Elution with benzene gave starting material (13 mg) followed by 2-*acetyl*-t-1,2,3,4-*tetrahydro*-3-*methylnaphthalene*-r-1,t-2-*diol* (XXI) (34 mg), as blades, m.p. 132—134° (from benzene–petroleum) (Found: C, 71·0, 71·2; H, 7·3, 7·4. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%); $\lambda_{max.}$ 264 and 271 nm (log ε 2·66 and 2·59); $\nu_{max.}$ ($CHCl_3$) 3560 (OH str.), 3440 (chelated OH str.), and 1696 cm^{-1} (chelated C=O str.); τ ($CDCl_3$) 2·26—3·00 (4H, m, aryl H), 5·10 (1H, d, $J_{1,OH}$ 4·4 Hz, H-1), 5·34 (1H, s, 2-OH), 6·64—7·90 (3H, m, CH_2·CH), 7·10 (1H, d, $J_{1.OH}$ 4·4 Hz, 1-OH), 8·05 (3H, s, Ac), and 9·02 (3H, d, $J_{3,Me}$, 7·2 Hz, 3-Me); *m/e* 220 ($M^{+\bullet}$) and 177 ($M^{+\bullet}$ − 43); R_F 0·72. Elution with benzene–ethyl acetate (19 : 1) gave 2-*acetyl*-t,2,3-*epoxy*-1,2,3,4-*tetrahydro*-3-*methylnaphthalene*-r-1,t-4-*diol* (XXII) (30 mg), as needles, m.p. 153—155° (from benzene–petroleum) (Found: C, 65·1; H, 6·1. $C_{13}H_{14}O_4$,$\frac{1}{3}H_2O$ requires C, 65·1; H, 6·1%); $\lambda_{max.}$ 242, 254, and 271 nm (log ε 2·48, 2·53, and 2·40); $\nu_{max.}$ ($CHCl_3$) 3583 (OH str.), 3500 (chelated OH str.), and 1699 (chelated C=O str.) cm^{-1}; τ ($CDCl_3$) 2·76—2·88 (4H, m, aryl H), 4·90 (1H, d, $J_{1.OH}$ 1·8 Hz, H-1), 5·03 (1H, d, $J_{H.OH}$ 11·5 Hz, H-4), 6·14 (1H, d, $J_{1.OH}$ 1·8 Hz, 1-OH), 7·66 (3H, s, Ac), 7·78 (1H, d, $J_{4.OH}$ 11·5 Hz, 4-OH), and 8·38 (3H, s, 3-Me); *m/e* 216 ($M^{+\cdot}$ − 18) and 173 ($M^{+\cdot}$ − 18 − 43); R_F 0·57.

Reduction of 3-*Acetyl*-3,4-*dihydro*-c-3,c-4-*dihydroxy*-r-2-*methylnaphthalen*-1(2H)-*one over Palladium–Charcoal*.—The tetralone (XVI) (114 mg) was reduced with hydrogen over 5% palladium–charcoal (35 mg) in ethanol [uptake 18·9 ml (1·5 equiv.) in 4·8 h]. T.l.c. revealed three products (R_F 0·35, 0·51, and 0·71) which were partly separated on a silicic acid column (30 × 1·8 cm) with chloroform–ethanol (97 : 3) as eluant.

The most polar (16 mg) separated cleanly and crystallised from benzene as plates, m.p. 126—128°; $\nu_{max.}$ 3400vs and 3460vs (chelated OH str.) and 1712 cm^{-1} (C=O str.). This compound, considered to be 2-acetyl-1,2,3,4-tetrahydro-c-3-methylnaphthalene-*r*-1,*c*-2,*t*-4-triol (XXV) began to decompose slowly at 60° under reduced pressure to give volatile products. Repurification attempts were unsuccessful (Found for partially decomposed sample: C, 67·2; H, 6·8. Calc. for $C_{13}H_{16}O_4$: C, 66·1; H, 6·8%). The small amount of remaining sample was heated in a sublimation tube (75°; 0·1 mmHg) to give *t*-6,9-epoxy-5,6,8,9-tetrahydro-*r*-5-hydroxy-6,*c*-8-dimethylbenzocyclohepten-7-one (XXVII) as large prisms, m.p. 115—116°, contaminated with a trace of oil (Found: C, 72·4; H, 7·0. Calc. for $C_{13}H_{14}O_3$: C, 71·5; H, 6·5%); $\lambda_{max.}$ 258, 266, and 274 nm (log ε 2·47, 2·49, and 2·40); $\nu_{max.}$ 3460 (OH str.) and 1740 cm^{-1} (five-membered ring C=O str.); τ ($CDCl_3$) 2·35—3·25 (4H, m, aryl H), 4·75 (1H, d, $J_{8.9}$ 7·2 Hz, H-9), 5·27br (1H, d, $J_{5.OH}$ 11·4 Hz, H-5), 6·85 (1H, q, $J_{8.9} = J_{8.Me}$ = 7·2 Hz, H-8), 7·85 (1H, d, $J_{5.OH}$ 11·4 Hz, 5-OH), 8·45 (3H, s, 6-Me), and 9·28 (3H, d, $J_{8,Me}$ 7·8 Hz, 8-Me); *m/e* 218 ($M^{+\cdot}$).

Separation of the two other products was incomplete but the least polar material was purified further by sublimation under reduced pressure. Resublimation gave 2-*acetyl*-1,2,3,4-*tetrahydro*-3-*methylnaphthalene*-r-1,c-2-*diol* (XXVI) as prisms, m.p. 116° (Found: C, 70·8; H, 7·5. $C_{13}H_{16}O_3$ requires C, 70·9; H, 7·3%); $\lambda_{max.}$ 251, 264, and 272 nm (log ε 2·57, 2·61, and 2·58); $\nu_{max.}$ 3400 and 3460 (OH str.) and 1715 cm^{-1} (C=O str.); τ ($CDCl_3$–D_2O) 2·23—3·08 (4H, m, aryl H), 5·02br (1H, H-1), 7·08—7·98 (3H, m, CH_2·CH), 7·7 (3H, s, Ac), and 9·16 (3H, d, $J_{3,Me}$ 7·0 Hz, 3-Me); *m/e* 220 ($M^{+\cdot}$), 203 ($M^{+\cdot}$ − 17), and 177 ($M^{+\cdot}$ − 43).

Chromatographic fractions containing the product of intermediate polarity were obtained, virtually free from the diol (XXVI). Cold benzene solutions of these gave, on slow evaporation, 2-*acetyl*-1,2,3,4-*tetrahydro*-c-3-*methylnaphthalene*-r-1,c-2,c-4-*triol* (XXIV) as prisms which when heated changed to an oil (125—140°), partly recrystallised, and finally melted at 159° (Found: C, 64·9, 64·7, H, 7·1, 7·1. $C_{13}H_{16}O_4$,$\frac{1}{3}H_2O$ requires C, 64·9; H, 6·9%); $\lambda_{max.}$ 255, 262, 267·5, and 272 nm (log ε 2·35, 2·42, 2·31, and 2·13); $\nu_{max.}$ 3460vs (OH str.) and 1712 cm^{-1} (C=O str.); τ ($CDCl_3$) 2·23—2·92 (4H, m, aryl H), 5·01 (1H, d, $J_{1.OH}$ 12 Hz, H-1), 5·42 (1H, s, 2-OH), 5·47 (1H, dd, $J_{4.OH}$ 10·5, $J_{3.4}$ 4–5 Hz, H-4), 6·67 (1H, d, $J_{1.OH}$ 11·5 Hz, 1-OH), 7·3—7·91 (1H, complex, H-3), 7·53 (1H, d, $J_{4.OH}$ 10·5 Hz, 4-OH), 7·65 (3H, s, Ac), and 8·94 (3H, d, $J_{3,Me}$ 7·2, 3-Me); *m/e* 218 ($M^{+\cdot}$ − 18).

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