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DIISOPHORONE AND RELATED COMPOUNDS—III[1]

2,7-EPOXYDIISOPHORANES: PRODUCTION AND REDUCTION

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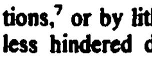
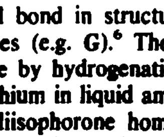
Abstract—Alkaline hydrogen peroxide oxidises diisophor-2(7)-en-1-ol-3-one and its lower homologue to the corresponding 2,7-epoxides. Reduction with LAH or catalytic hydrogenation converts 2,7-epoxydiisophoran-1-ol-3-one into the 1,3-diol, with preservation of the epoxide ring. Reduction by hydrazine (Wharton reaction) cleaves the epoxide ring and affords diisophor-2-ene-1,7-diol, the formulation of which is in accord with its hydrogenation to diisophor-2(7)-en-1-ol of established structure, either directly, or after dehydration to diisophorane-2,7-dien-1-ol.

2,7-Epoxydiisophorones lacking the 3-keto-function are accessible in good yield from 1-hydroxy-, 1-acetoxy- and 1-chlorodiisophor-2(7)-ene by the action of peroxy-acids in dichloromethane. Of these, 2,7-epoxydiisophoran-1-ol is isomerized to diisophor-7-ene-1,2-diol by the combined action of LAH and $AlCl_3$. In the carbon-skeleton of the 2,7-epoxides described, the oxirane ring is likely to project above the plane of the A–B rings, on the side opposite ring C.

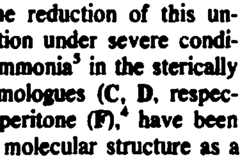
By virtue of its structural environment, the ethylenic bond in diisophor-2(7)-en-1-ol-3-one (E) and related compounds is in many respects chemically inert. Placed between two condensed cyclohexane rings, its usual reactivity is impaired by the steric hindrance exerted by the 3-dimensional folded configuration of the molecule in general, and by the proximity of the semiaxial 5- and 11-Me substituents in particular. The olefinic linkage in E is consequently unaffected by a variety of reduction,[2-4] halogenation[2-5] and other processes[3,4] occurring elsewhere in the molecule, and resembles, in this respect, the 8(9)-unsaturated bond in structurally comparable lanosterol derivatives (e.g. G).[6] The reduction of this unsaturated centre by hydrogenation under severe conditions,[7] or by lithium in liquid ammonia[5] in the sterically less hindered diisophorone homologues (C, D, respectively), and in the dimer of piperitone (F),[4] have been recorded. The influence of the molecular structure as a whole on the reactivity of the "bridged" double bond is also apparent from simpler models: thus, Δ-*4a,8a*-octalin (A) undergoes hydrogenation without difficulty,[8] but dodecahydrophenanthrene (B) requires high temperatures and pressures (Raney Ni, 250°, 200 at) and fails to react with bromine, sulphuric acid, or nitrosyl chloride.[9]



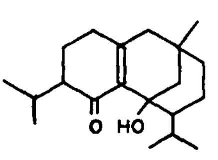
A



B



C: R = R' = H
D: R = Me, R' = H
E: R = R' = Me



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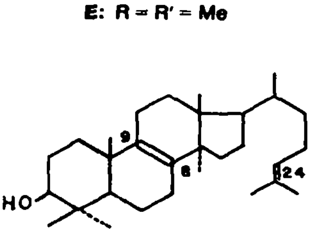


G

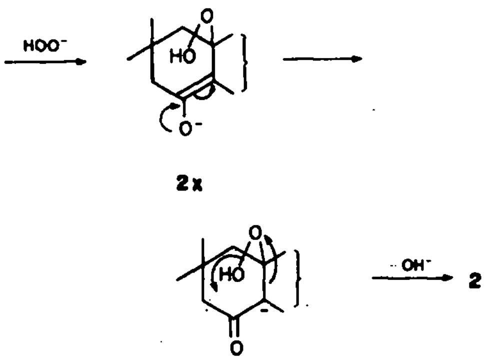
We now describe an approach to the successful opening and removal of the bridged 2(7)-double bond in the diisophorone structure by its epoxidation under carefully controlled conditions. The resulting oxiranes (e.g. 2, 13) have proved versatile intermediates that provide access to hitherto unobtainable compounds in the diisophorane series.

Epoxidation of ethylenes by peroxy-acids[10-12a] or alkaline hydrogen peroxide[12b,13] is in fact favoured by a high degree of substitution by alkyl groups flanking the double bond. Peroxy-acid oxidation is further promoted by electron-releasing groups placed in conjugation with the unsaturated centre, but is impeded or suppressed by conjugated electron-attracting groups.[11b] It is a favourable circumstance, that the latter structures are particularly prone to attack by alkaline hydrogen peroxide,[12b,13] which thus serves as an almost specific reagent for the epoxidation of sterically inaccessible double bonds linked to a CO function.[14] The reactions, particularly peroxy-acid oxidations, have been extensively documented,[10,11] and have often provided decisive structural information. In the present context, brief reference may be made to oxiranes derived from cyclohexenes,[15,16] bridged structures such as bicyclo[2.2.1]heptenes,[15,17] sterols,[10,11,18] and triterpenes (including lanosterol,[19,20] *β*-amyrin,[20] euphol[20,21] and cycloartenol[20]). Both oxidising procedures were employed, where applicable, in the present work.

The action of alkaline hydrogen peroxide at *ca.* 20° converts isophorone into the 2,3-epoxide in 70% yield within 4 hr.[22] The epoxidation of diisophor-2(7)-en-1-ol-3-one (1) was found to proceed much less readily, comparable yields of its epoxide (2) being obtainable under the foregoing conditions only after very prolonged treatment (6–8 weeks). Optimum conversion occurred at 44–46° (50% yield after 6–7 days); above this narrow temperature range, progressive resinification affected yields adversely. Attempts to accelerate the epoxidation by other changes in the conditions (especially the nature and concentration of the basic medium; Experimental) were unsuccessful. Not surprisingly, 3-chloroperoxybenzoic acid failed to effect epoxidation of the double bond of the $\alpha\beta$-unsaturated ketone (1).

The configuration of the oxirane ring (in 2, etc.) is not assigned with certainty, since the double bond is shielded, in the accepted configuration of diisophorone,[4] by the semiaxial C-5–Me *above*, and by the semiaxial C-11–Me group as well as ring C as a whole, *below* the plane of the A–B-ring system. Consideration of a molecular model favours, on balance, the attachment of the oxirane ring *above* the A–B plane, opposite ring C. The steric hindrance imposed on the unsaturated centre (in 1) is also the likely cause of the low rate of epoxidation: the fact that 5,11-bisnordiisophor-2(7)-en-1-ol-3-one (the less hindered lower homologue of 1) was convertible into its 2,7-epoxide (2a) in good yield in a shorter time at lower temperatures, provides support for this view.

The mechanism of the epoxidation is thought, in accordance with established opinion,[12c,13] to involve the hydrogen peroxide anion as the effective reagent. This affords, by a nucleophilic 1,4-attack on the $\alpha\beta$-unsaturated CO-group, the hydroperoxide (2x, 2y), which cyclises to the epoxide (2) with elimination of a hydroxide ion:



2x

2y

The IR spectra of the 2,7-epoxydiisophorones (2, 2a) and their derivatives contain the usual alkane peaks[23] and clearly reflect the structural changes that attend the epoxidation process; they afford incidentally, an excellent means of monotoring the progress of the reaction experimentally. The removal of the conjugated double bond, with its frequency-lowering effect on the CO absorption, results in the disappearance of the multiple bond stretching absorption of the reactant (1; at 1627 cm^{-1}) and the displacement of the prominent CO peak towards higher wave numbers (from 1640 in 1 to 1690 cm^{-1} in 2, 2a). The 3-keto-group, now non-conjugated, forms a weaker H-bond with the 1-OH group in 2, 2a than in 1, revealed by a shift in the HO-absorption from 3475 to 3540 cm^{-1}. The weakened H-bonding may be ascribed in part to the increased distance between the 3-CO and 1-OH-functions, due to distortion of rings A and B. Three spectral regions (near 1250, 910 and 830 cm^{-1}) are generally associated[12d,24] with absorption due to the epoxide ring in a variety of compounds (including sterols[25]). The appearance of a peak of medium to high intensity in the 840–920 cm^{-1} range of the spectra of all the relevant compounds is therefore attributed to this grouping. A peak near 1250 cm^{-1} produced by most (2, 2a, 4, 6, 11, 14, 16), though not all epoxides (3, 7, 13) falls within the first of these relevant regions and is tentatively assigned in this sense. Unlike their parent compound (1, λ_{max} 249 nm), the epoxides (2, 2a) produced no characteristic UV spectra, in agreement with their non-conjugated structure.

2,7-Epoxydiisophoran-1-ol-3-one (2) readily formed an oxime (3) by the standard method. Its oxirane ring was unaffected by boiling acetic acid or anhydride; the latter reagent gave the 1-acetoxy-derivative (4), which was obtained more effectively by perchloric acid-catalysed acylation.[26] The two strong CO absorptions produced by 4 at 1725 and 1710 cm^{-1} are assigned to the Ac- and ring CO-groups, respectively; the displacement of the latter towards higher frequencies reflects the absence, in 4, of H-bonding with the blocked 1-OH-group.

In the systematic study of the behaviour of the 2,7-epoxide (2), its reduction was first examined. Depending on the method employed, it was possible to preserve the oxirane ring, or to remove it.

REDUCTION

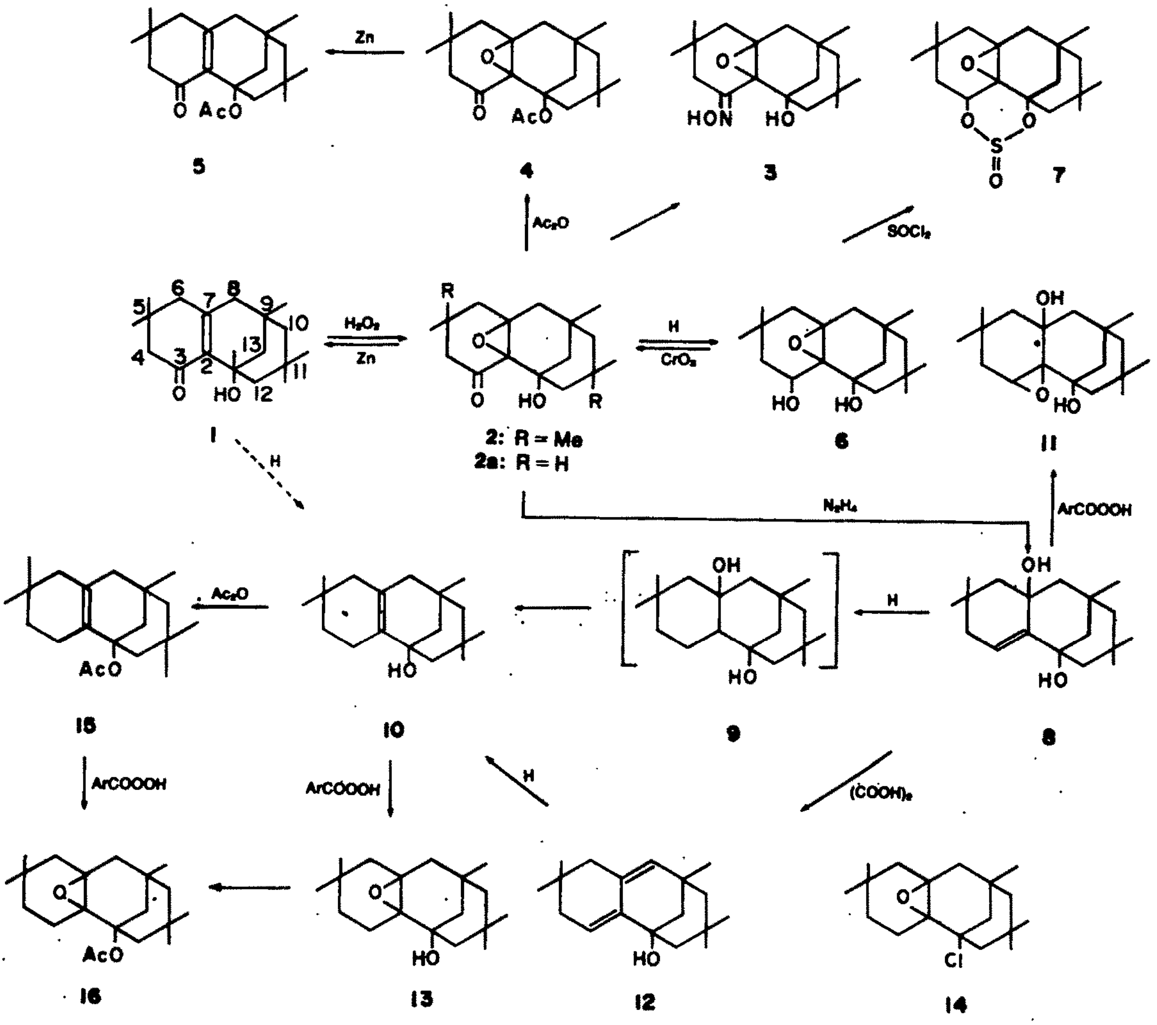
The action of zinc in acetic acid slowly converted 2,7-epoxydiisophoran-1-ol-3-one (2) into the parent olefin (1). The corresponding reaction of the acetates (4→5) occurred even more slowly. The reaction is thought to proceed by the reductive opening of the oxirane ring, followed by dehydration and consequent restoration of the 2(7)-double bond. These results show that no rearrangement occurs in the diisophorone structure during these changes.

Treatment of the 2,7-epoxide (2) with LAH gave high yields of a product formulated as 2,7-epoxydiisophoran-1,3β-diol (6). The same diol (6) arose, again with preservation of the epoxide ring, under the influence of the more vigorous reducing agent aluminium hydride produced *in situ*;[27] this reagent does cleave the oxirane ring of 2,7-epoxydiisophoran-1-ol (13, see below). The same reduction (2→6) was also effected, though in lower yields, by catalytic hydrogenation in the presence of small amounts of perchloric acid. Specimens of 6 obtained by the two procedures differed slightly but consistently in their m.ps but were identical in all other respects (IR spectra, further reactions): this difference may be due to the prevailing configuration of the 3-OH-group in 6, the stereochemical uniformity of which was not established.

2,7-Epoxydiisophoran-1,3-diol (6) was reconverted into its precursor (2) by mild oxidation with chromic acid. The action of thionyl chloride in pyridine gave the cyclic sulphite ester (7); its ready formation implies the proximity of the two hydroxyl groups in 2, and consequently the likely β-configuration of its 3-OH-group, *above* the plane of rings A–B.

The oxirane-ring of $\alpha\beta$-epoxyketones may be cleaved reductively by the action of hydrazine, with formation of an allylic alcohol, and evolution of nitrogen. This specific ring-cleavage, known as the Wharton reaction,[28] was first employed in the sterol field[28,29] in 1961 and has proved applicable to epoxycyclohexanones[30] in general:

Application of the Wharton reaction to 2,7-epoxydiisophoran-1-ol-3-one (2) gave satisfactory yields of a product which is formulated, in accordance with its origin, composition and spectral and chemical properties,



as diisophor-2-ene-1,7-diol (8). 1-Acetoxy-2,7-epoxydiisophoran-3-one (4) gave the same product (8), the 1-ester grouping being simultaneously hydrolysed by the strongly basic hydrazine. The IR spectrum of 8 lacked the CO and epoxide absorption as expected, and featured a broad OH peak, the position of which (3420–3375 cm^{-1}) suggests a measure of intermolecular H-bonding. The trisubstituted double bond of the 1,7-diol (8) is sufficiently accessible and reactive to decolourise bromine, and to react with 3-chloroperoxybenzoic acid: the resulting crystalline 2,3-epoxy-derivative (11) displayed absorption bands at 940 and 1280 cm^{-1} attributable to the oxirane ring.[12d,24,25]

Catalytic hydrogenation in glacial acetic acid converted the 1,7-diol (8) into diisophor-2(7)-en-1-ol (10) of established structure,[3,4] presumably by initial saturation of the trisubstituted 2,3-olefinic bond, followed by dehydration of the intermediate (9) under the acidic conditions.

Of the two OH-groups in the 1,7-diol (8), only one was acylated on benzoylation under the usual conditions. The tertiary 7-OH-group was readily removed by dehydration[31] with oxalic acid at 200°. The resulting diisophor-2,7-dien-1-ol (12) formed an uncrystallisable low-melting pale yellow oil; the position of its UV absorption maximum (λ_{max} 245 nm) agrees with its formulation as 12, and excludes the alternative possible homoannular conjugated 2,5-dien-1-ol-structure, the calculated[32,33] λ_{max} values for tetrasubstituted hetero- and homannular systems of conjugated double bonds being 244 and 283 nm, respectively. Though non-crystalline, the 2,7-dien-1-ol (12) provides a link establishing the relationship between several series of diisophorone compounds. In the present instance, its rapid conversion by catalytic hydrogenation into the known[3,4] diisophor-2(7)-en-1-ol (10) provides supporting evidence for all the foregoing structural interpretations.

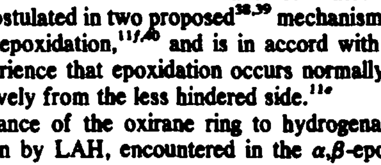
Diisophorones lacking the 3-CO-group (of 1) were convertible into 2,7-epoxides by the action of peroxy-acids.[10,11] 3-Chloroperoxybenzoic acid[11c,34] was the reagent of choice, in view of its ready availability,[35] stability, and its power of epoxidising unsaturated compounds at appreciably higher rates than other peroxy-acids.[36] Diisophor-2(7)-en-1-ol (10),[3,4] the prototype of this series, gave good yields of the 2,7-epoxide (13) on treatment with 3-chloroperoxybenzoic acid in dichloromethane for 12–24 hr at room temperature. The same reaction (10 → 13) occurred more slowly under the influence of 30% hydrogen peroxide in acetic acid;[11d,37] here the active oxidising agent is peroxyacetic acid arising in the equilibrium mixture in moderate but sufficient concentration to effect the epoxidation.

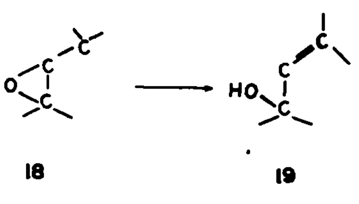
1-Acetoxydiisophor-2(7)-ene (15) was similarly convertible into the 2,7-epoxide (16), which was also accessible by acetylation of 13; the resistance of the oxirane ring to boiling acetic anhydride is noteworthy.

1-Chlorodiisophor-2(7)-ene gave good yields of the appropriate 2,7-epoxide (14) on treatment with 3-chloroperoxybenzoic acid.

The IR spectra of the 2,7-epoxides (13, 14, 16) included, in addition to the usual bands due to the alkane[23] and functional groups, a peak between 835 and 865 cm^{-1}, attributable to the oxirane ring.[12d,24] The factors contributing to steric hindrance of the double bond in 10, etc. do not appear to differ materially from those in 1; the oxirane ring is therefore considered, as in 2, 2a, to project *above* the plane of rings A–B. This configuration takes better account of the considerable spatial requirements of the intermediate transition states that have been postulated in two proposed[38,39] mechanisms of peroxy-acid epoxidation,[11f,40] and is in accord with the general experience that epoxidation occurs normally almost exclusively from the less hindered side.[11e]

The resistance of the oxirane ring to hydrogenation and reduction by LAH, encountered in the *α,β*-epoxyketones (2,2a), is confirmed in the present type of compounds (13, 14, 16), which are substantially recovered in both reactions. The action of a mixture of LAH and $AlCl_3$ did modify the oxirane ring in 2,7-epoxydiisophoran-1-ol (13): the resulting product, formulated as diisophor-7-ene-1,2-diol (17), arises under the influence of the nascent aluminium hydride,[27] since neither constituent had any effect separately. The reaction is effectively an isomerisation process, and resembles formally the isomerisation of 1,2-epoxycyclododecane to 1-hydroxycyclododec-2-ene (18 → 19, and analogous examples) under the influence of diisobutyl aluminium hydride in xylene at 120°.[41] The evidence establishing the structure of 17, which has also been obtained by other routes, will be outlined in another connection.





EXPERIMENTAL

General information is given in Part I[23] concerning standard procedures, apparatus, reagents, solvents and abbreviations. Catalytic hydrogenations were performed at room temp. and atmospheric pressure.

Epoxyketones and derivatives

2,7-*Epoxydiisophoran*-1-*ol*-3-*one* 2

A stirred soln of 1[23] (11.04 g, 0.04 mole) in MeOH (80 ml) was treated at room temp. with ice-cold 30% aqueous H_2O_2 (20 ml, 0.175 mole), followed by 3N NaOH (10 ml, 0.03 mole). The pale yellow soln was set aside at 45° for 48 hr (initial gentle effervescence of O_2, some deepening in colour). It was treated with further portions of MeOH (20 ml), peroxide (20 ml, 0.175 mole) and NaOH (10 ml, 0.03 mole) and kept at 45° for another 48–72 hr. Separation of the crude product was aided by storage at room temp. (24–48 hr). The crystalline solid was collected (filtrate F) and washed with aqueous MeOH (2:1) (crude: m.p. 82–88°, 4.6–5.85 g, 40–50%); it sometimes retained (according to its IR spectrum: slight remaining peak at 1640 cm^{-1}) a very small proportion of 1. This was removed on crystallisation from light petroleum (b.p. 60–80°, *ca.* 5 ml per g), giving 2 as massive prisms (3.25–4.6 g, 28–40%), m.p. 91–93° (Found: C, 74.0; H, 9.55. M, mass-spectrometrically, 292. $C_{18}H_{28}O_3$ requires: C, 74.0; H, 9.6%, M, 292). IR: 3540s (OH); 2970–2880vs (mult); 1475s, 1458m, 1410s (CH_3, CH_2); 1397s, 1370s (·CMe_2); 1690s (CO); 1272m, 840m (C–O–C, epoxide); 1310m, 1185s, 1175s, 1050s, 1000m, 995m, 953m, 867s, 730m, 660m cm^{-1}.

Filtrate F slowly deposited, after dilution with H_2O (*ca.* 10 volumes), a microcrystalline ppt of the same product, raising the yield, after recrystallisation, by 5–8%.

In a slightly higher temp. range (50–55°), the yields were adversely affected. The use of 5N NaOH (2 × 10 ml) also resulted in lower yields. At room temp., some epoxide formation has occurred after 48 hr, but none after 4 hr (IR). To obtain the above yields, reaction times of 45–60 days are required: under these conditions the whole mixture is best poured into H_2O (*ca.* 600 ml) and the crude dried product (65%) directly crystallised from light petroleum (yield, 35–40%).

The use of 2N Na_2CO_3 in place of the NaOH caused a drastic fall in the reaction rates. Estimates (IR) suggested that over 75% of 1 was present after 6 days at 45°. Isolation of the epoxide from the resulting resinous crude products proved difficult and wasteful. In experiments employing 50% H_2O_2 (6 molar excess) in MeOH—"Triton B" (N-benzyltrimethylammonium hydroxide, 40% in MeOH)[42] at room temp., only intractable sticky resinous material was obtained.

The use of the standard epoxidation procedure employing 3-chloroperoxybenzoic acid (see below) did not result in epoxidation, the reactent being recovered (70%, after 3 hr boiling in CH_2Cl_2).

3-*Oximino*-2,7-*epoxydiisophoran*-1-*ol* 3

A soln of 2 (0.58 g, 0.002 mole) and hydroxylamine HCl (0.21 g, 0.003 mole) in EtOH (12 ml)–pyridine (3 ml) was boiled for 2 hr, most of the EtOH removed in a vacuum, and the liquid stirred into ice containing conc. HCl (3 ml). The hardened ppt gave lustrous prisms (0.40 g, 65%) of 3, m.p. 168–171° (from EtOH, with addition of a few drops of H_2O) (Found: C, 70.0; H, 9.3; N, 4.4. $C_{18}H_{29}O_3N$ requires: C, 70.4; H, 9.45; N, 4.6%). IR: 3420m, 3235s (OH); 2960vs, 2920s, 2880ms, 1462–1458s br, 1440m (CH_3, CH_2); 1390m, 1365m (·CMe_2); 1640w (C=N); 880m (C–O–C epoxide); 1180m, 1165m, 1105m, 1050s, 960m, 930m, 913s, 900m, 705m cm^{-1}.

1-*Acetoxy*-2,7-*epoxydiisophoran*-3-*one* 4

A soln of 2 (2.92 g, 0.01 mole) in glacial AcOH (20 ml)–Ac_2O (2.5 ml) was treated dropwise at room temp. with swirling, with 60% perchloric acid (8 drops) (temp. rise), then set aside at room temp. for 1 hr. Addition to ice-water (500 ml) gave a white resin which hardened rapidly and afforded minute prisms (2.74 g, 82%) of 4, m.p. 83–86° (from light petroleum, b.p. 60–80°, 10–12 ml) (Found: C, 71.7; H, 8.9. $C_{20}H_{30}O_4$ requires: C, 71.9; H, 9.0%). IR: 2960–2885s, 1472m (CH_3, CH_2); 1390w, 1365s (·CMe_2); 1725vs, 1255vs, 1235vs (CO–O ester); 1705vs (CO); 1275m, 990m, 840m (C–O–C epoxide); 1025m, 1017m cm^{-1}. The same reaction occurred (66–72%) in boiling Ac_2O (3 hr). The reactant was substantially recovered (70%) after being heated with Ac_2O at 100° for 2 hr.

Reconversion of 2 into diisophor-2(7)-*en*-1-*ol*-3-*one* (1)

A refluxing soln of 2 (0.58 g, 0.002 mole) in glacial AcOH (15 ml) was treated with Zn dust (8 × 0.2 g; 0.025 g atoms, at 2 hr intervals) during 16 hr. The filtered soln was diluted with H_2O and slowly deposited slightly discoloured 1 (0.35 g, 64%), identified by its IR spectrum. Compound 4 was substantially recovered (65%) after 5 hr treatment by this procedure. The IR spectra of appropriate fractions indicated that small quantities of 5 had been formed.

2,7-*Epoxy-5,11-bisnordiisophoran*-1-*ol*-3-*one* 2a

A soln of 5,11-bisnordiisophor-2(7)-en-1-ol-3-one[23] (2.48 g, 0.01 mole) in MeOH (50 ml) was treated with 30% H_2O_2 (3.4 ml, 0.03 mole) and dropwise with 3N NaOH (3.3 ml, 0.01 mole) (external cooling), set aside at room temp. for 5 days, then stirred into H_2O. The ppt gave silky felted needles (1.32–1.7 g, 50–64%) of 2a, m.p. 147–149° (from light petroleum, b.p. 60–80°, 50 ml) (Found: C, 72.25; H, 8.6. $C_{16}H_{24}O_3$ requires: C, 72.7; H, 9.1%). IR: 3545m (OH); 2960s, 1463m, 1380m (CH_3, CH_2); 1690vs (CO); 1280m, 842m (C–O–C, epoxide); 1290m, 1140m, 1040s, 947m, 920m cm^{-1}.

Reduction of epoxyketones

2,7-*Epoxydiisophoran*-1,3-*diol* 6

(a) *By LAH reduction*. A soln of 2 (1.46 g, 0.005 mole) in anhyd. ether (20 ml) was added dropwise to a stirred suspension of LAH (0.57 g, 0.015 mole) in the same solvent (20 ml) at such a rate that the mixture boiled gently (evolution of H_2). After continued refluxing (5 min), the mixture was set aside at room temp. for 1 hr, and the excess of the reducing agent carefully destroyed with 1.5N HCl. The product was extracted with ether; the residual viscid liquid therefrom solidified presently and gave prismatic needles (0.95–1.1 g, 65–75%) of 6, m.p. 124–126° (from light petroleum, b.p. 60–80°) (Found: C, 73.0; H, 10.2. $C_{18}H_{30}O_3$ requires: C, 73.5, H, 10.2%). IR: 3475s, 3360vs (OH); 2960vs, 2925vs, 2890vs, 1470vs, 1460s, 1420s (CH_3, CH_2); 1395s, 1370s (·CMe_2); 1290s, 865vs (C–O–C, epoxide); 1313s, 1180s, 1067s, 1053vs, 1040vs, 1020s, 980s, 955vs, 920s, 690s cm^{-1}. An experiment performed with addition of anhyd. $AlCl_3$ gave the same product (50%).

This reduction provides a useful means of producing 6 from *impure* 2 (containing non-epoxided 1). The latter yields diisophor-2(7),3-dien-1-ol[3] which in contrast to 6 is highly soluble in light petroleum; the reduction mixture thus yields almost pure 6 on crystallisation.

(b) *By catalytic hydrogenation*. A soln of 2 (0.58 g, 0.002 mole) in glacial AcOH (25 ml)–60% $HClO_4$ (6 drops) was hydrogenated in the presence of Adam's catalyst[43] (0.1 g), uptake of H_2 being complete (55 cc; calc. 20 + 25 cc at 20°) after 45 min. The filtered liquid was added to ice water (300 ml) and the product exhaustively extracted with ether; the oily residue gave 6 (0.20 g, 35%) (from light petroleum), identical (IR) with material (a), but having m.p. 132–134°. In the absence of $HClO_4$, no hydrogen uptake occurred.

(c) *Reoxidation*. A stirred soln of the foregoing 1,3-diol 6 (0.29 g, 0.001 mole) in glacial AcOH (6 ml) was treated dropwise with Kiliani's 10% chromic acid[44] (6 ml), set aside at room temp. for 1 hr, added to 0.1N HCl (30 ml), and treated with 10% Na_2SO_3 aq. The resulting crystalline ppt (0.21 g, 72%) was 2 (from light petroleum; identified by m.m.p. and IR spectrum).

Sulphite ester 7 *of* 6

A soln of 6 (0.58 g, 0.002 mole) in anhyd. pyridine (15 ml) at 0° was treated dropwise with $SOCl_2$ (1.4 g, 0.012 mole), kept at 0° for 1 hr, then added to ice-conc. HCl (15 ml). The solidified oil gave 7 as opaque microprisms (0.33 g, 48%), m.p. 106–112° (from light petroleum, b.p. 60–80°) (Found: C, 63.45; H, 8.0; S, 9.1. $C_{18}H_{28}O_4S$ requires: C, 63.5; H, 8.2; S, 9.4%). IR: 2950vs, 2920–2880s-*m* br, 1470*m*, 1425w (CH_3, CH_2); 1395w, 1370*m* (·CMe_2); 1220vs (SO); 840s (C–O–C, epoxide), 1645m, 1025m, 937s, 915s, 790m, 768s, 710s cm^{-1}.

Wharton reaction of epoxyketones

Diisophor-2-en-1,7-diol 8

A soln of 2 (2.92 g, 0.01 mole) in EtOH (20 ml) was treated with hydrazine hydrate (35 ml), boiled under reflux for 2 hr (evolution of N_2), then cooled and stirred into H_2O (400 ml). The pale yellow ppt gave minute needles (1.65 g, 60%) of the 1,7-diol 8, m.p. 143–146° (from light petroleum, b.p. 60–80°) (Found: C, 76.9; H, 10.0. M, mass-spectrometrically, 278. $C_{18}H_{30}O_2$ requires: C, 77.7; H, 10.8%, M, 278). IR: 3420s, 3375s (OH); 2955vs, 2900vs, 1475m, 1460m (CH_3, CH_2); 1390m, 1350m (·CMe_2); 1660w, 850m, 840m (CH of trisub. olefin); 1403m, 1338m, 1200m, 1077m, 1023m, 1000s, 980s, 725w cm^{-1}.

The use of 4 in the foregoing procedure gave the same diol 8 (65%), identified by m.m.p. and IR spectrum.

Monobenzoyl derivative of 8

A soln of 8 (0.56 g, 0.002 mole) in pyridine (15 ml) was treated dropwise with benzoyl chloride (1.4 g, 0.01 mole), set aside for 12 hr, and stirred into ice-conc. HCl (15 ml). The soft brown ppt gave small prisms (0.19 g, 24%) of the derivative, m.p. 139–141° (from EtOH) (Found: C, 78.7; H, 8.9. $C_{25}H_{34}O_3$ requires: C, 78.5; H, 8.9%). IR: 3470s (OH); 2955vs, 2910vs, 1477m, 1460s (CH_3, CH_2); 1390m, 1370m (·CMe_2); 1693vs, 1290vs, 1120s (COO, benzoyl); 1660w (C=C, aliph.); 857m, 840m (CH of trisub. olefin); 3070w, 715vs (CH arom.); 1320s, 1240s, 1070s, 1030m, 960m, 930m cm^{-1}.

2,3-*Epoxydiisophoran*-1,7-*diol* 11

Solns of 8 (0.56 g, 0.002 mole) and 3-chloroperoxybenzoic acid (0.38 g, 0.0022 mole) in CH_2Cl_2 (2 × 10 ml) were mixed and set aside for 24 hr. The usual work-up (see subsequent section) produced a white solid, which gave prisms (0.32 g, 54%) of 11, m.p. 88–90° (from light petroleum, b.p. 60–80°) (Found: C, 73.2; H, 9.8. M, mass spectrometrically 294w, 223s (i.e. M-71). $C_{18}H_{30}O_3$ requires: C, 73.5; H, 10.2%. M, 294). IR: 3575s, 3450s (OH); 2965vs, 2925vs, 2885s, 1467s, 1460m (CH_3, CH_2); 1395m, 1370s (·CMe_2); 1140s, 1067s (C–O of OH); 1280m, 940s (C–O–C, epoxide); 1343s, 745w, 680w cm^{-1}.

Diisophor-2-en-1,7-diol 8 *reactions*:

(a) *Direct catalytic hydrogenation*. A soln of 8 (0.84 g, 0.003 mole) in glacial AcOH (15 ml) was hydrogenated over Adam's[43] catalyst (0.15 g). The rapid H_2-uptake (100 cc) was complete after 20 min (calc. 95 cc, including 27 cc for catalyst). The filtered soln was stirred into H_2O, basified, and the oily product extracted with ether. Removal of the solvent left 10 (0.63 g, 80%), identified by its IR spectrum.

(b) *Successive dehydration* (*to* 12) *and hydrogenation* (*to* 10). An intimate mixture of finely powdered 8 (0.56 g, 0.002 mole) and anhyd. oxalic acid (0.72 g, 0.008 mole) was kept at *ca.* 195° (b.p. of ethanediol used as jacketing liquid) for 2 hr. The resinous *yellow mass was taken up in ether* (2 × 30 *ml*), *the extracts* washed with 3N Na_2CO_3, H_2O, dried (Na_2SO_4) and the solvent removed. The residual yellow oil (diisophorane-2,7-dien-1-ol 12) had the following spectral characteristics: UV: λ_{max} 245 nm. IR: 3435s (OH); 2960vs, 2910–2880vs br, 1465m, 1460m (CH_3, CH_2); 1393m, 1363m (·*CMe_2*); 1650w, 1635w (C:C, conjugated diene); 1030s (C–O of OH); 912m, 820m (CH of trisub. olefin); 1350m, 1120m, 1040m, 1005m cm^{-1}.

It was dissolved in glacial AcOH (15 ml) and hydrogenated over Adam's catalyst[43] (0.1 g); H_2 uptake was rapid. Removal of the solvent and crystallisation of the (washed) oily residue from light petroleum gave 10 (0.34 g, 65%) as prisms, m.p. 83–85°, identified by its IR spectrum.

Epoxides lacking the 3-*keto-function*

2,7-*Epoxydiisophoran*-1-*ol* 13

(a) *Use of* 3-*chloroperoxybenzoic acid*. Compound 1 (13.8 g, 0.05 mole) in glacial AcOH (50 ml) was hydrogenated over Adam's catalyst[43] (0.4 + 0.2 g) until the appropriate amount of H_2 *had been taken up* (*ca.* 2400 + 80 cc, 6–8 hr). The filtered liquid was stirred into H_2O (800 ml), and the product exhaustively extracted with ether. The clear viscid 10 (solidifying below 0°), obtained on evaporating the washed dried extracts, was taken up in CH_2Cl_2 (30 ml) and slowly added to a stirred soln of 3-chloroperoxybenzoic acid (9.0 g, 0.05 mole) in CH_2Cl_2 (75 ml), with external cooling. After 24 hr storage at room temp., the clear colourless liquid was successively shaken with 10% Na_2SO_3 aq., 5% $NaHCO_3$ and sat. NaCl aq., dried (Na_2SO_4), and evaporated under reduced pressure. The residual crystalline solid gave 13 as small lustrous prisms (7.2–9.0 g, 52–65%), m.p. 154–157° (from light petroleum) (Found: C, 77.2; H, 10.2. M mass spectrometrically, 278. $C_{18}H_{30}O_2$ requires: C, 77.7; H, 10.8%. M, 278). IR: 3485s (OH); 2900–2865s br; 1457m, 1445m (CH_3, CH_2); 1387m, 1365s (·CMe_2); 1057s (C–O of OH); 865s (C–O–C, epoxide); 1330m, 1170m, 1155m, 955m, 937m, 875m, 732m, 675m cm^{-1}.

When the starting material was isolated crystalline 10, the yield of 13 rose to 75%.

(b) *Use of peroxyacetic acid formed* in situ. A soln of 10 (0.52 g, 0.002 mole) in glacial AcOH (12 ml) was treated with 30% H_2O_2 (3.4 ml, 0.03 mole), the liquid heated to 100° for 1 min, then set aside at room temp. for 5 days. Addition to H_2O gave a solid affording 13 (0.28 g, 50%) (prisms from light petroleum), identical with (a) by m.m.p. 154–156° and IR spectrum.

1-*Acetoxy*-2,7-*epoxydiisophorane* 16

(a) A soln of 13 (2.78 g, 0.01 mole) in Ac_2O (24 ml) was boiled under reflux for 6 hr, then stirred into H_2O. The crystals which separated gradually gave 16 as platelets, m.p. 75–77° from 75% EtOH (65%) (Found: C, 75.1; H, 9.6. $C_{20}H_{32}O_3$ requires: C, 75.0; H, 10.0%). IR: 2960–2890s br, 1480m, 1460m (CH_3, CH_2); 1390m, 1365s ($\cdot CMe_2$); 1730vs (CO, ester); 1235vs (C–O of acetate): 1253s, 845s (C–O–C, epoxide): 1440m, 1205m, 970s, 880m, 805m, 740m cm^{-1}.

(b) Solns of 15 (1.52 g, 0.005 mole) and 3-chloroperoxybenzoic acid (0.95 g, 0.0055 mole) in CH_2Cl_2 (20 ml each) were mixed, then set aside at room temp. for 24 hr. Isolation of the product by the standard procedure (see above) gave 16 (70%) identified by m.m.p. 73–75° and IR spectrum.

(c) A soln of 15 (0.30 g, 0.001 mole) in glacial AcOH (12 ml) was treated dropwise with 30% H_2O_2 (3.4 ml, 0.03 mole), kept at room temp. for 2 days (the liquid being heated at 100° for 2 min at 12 hr intervals). Dilution with H_2O (60 ml) slowly deposited solid which gave 16 (75%) identical with the product obtained in (a) and (b).

Diisophor-7-ene-1,2-*diol* 17

The turbid liquid obtained on addition of LAH (0.10 g, 0.0025 mole) and anhyd. $AlCl_3$ (0.067 g, 0.0005 mole) to anhyd. ether (30 ml) was treated with stirring with a soln of 13 (0.28 g, 0.001 mole) at such a rate that the liquid boiled gently. The stirred mixture was kept at room temp. for 1 hr then boiled under reflux for 2 hr, and the excess of the hydride decomposed by addition of ·N NaOH (ice). The combined washed dried ether soln (and extracts) gave on evaporation under reduced pressure a sticky semisolid residue which afforded needles (0.11–0.14 g, 40–50%) of 17, m.p. 151–153° (from light petroleum) (Found: C, 77.4, H, 10.7. $C_{18}H_{30}O_2$ requires: C, 77.7; H, 10.8%). IR: 3445m, 3295s (OH); 2950vs, 2870m, 1475m (CH_3, CH_2); 1395m, 1363m ($\cdot CMe_2$); 1110m, 1030s (C–O of OH); 845w (CH of trisub. olefin); 1185w, 1000s, 960m, 910m cm^{-1}. The starting material (13) was substantially unaffected (IR), after reacting under the above conditions with either LAH or $AlCl_3$ separately.

1-*Chloro*-2,7-*epoxydiisophorane* 14

Solns of 1-chlorodiisophor-2(7)-ene[1,3] (1.40 g, 0.005 mole) and 3-chloroperoxybenzoic acid (0.95 g, 0.0055 mole) in CH_2Cl_2 (20 ml each) were slowly mixed, then set aside at room temp. for 18 hr. The standard work-up gave a crystalline solid (m.p. 96–98°) which afforded 14 as massive lustrous prisms (0.95–1.05 g, 64–72%), m.p. 101–103° (from light petroleum, b.p. 60–80°, *ca.* 8 ml per g) (Found: C, 72.95; H, 9.5; Cl, 11.4. $C_{18}H_{29}ClO$ requires: C, 72.9; H, 9.8; Cl, 12.0%). IR: 2965–2900vs br, 2875vs, 1470s, 1455s, 1430m (CH_3, CH_2); 1390m, 1365s, 1355s ($\cdot CMe_2$); 1245m, 835vs (C–O–C, epoxide); 745s (C–Cl); 1025m, 1008m, 990m, 900m, 880s, 865m, 800m cm^{-1}.

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