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Di-isophorone and Related Compounds. Part 7[1]. Syntheses and Properties of 1-Hydroxydi-isophor-2(7)-ene-3,4-dione

Frederick Kurzer* and **Alan R. Morgan**

Royal Free Hospital School of Medicine, University of London, London W.C. 1., England

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1-Hydroxydi-isophor-2(7)-ene-3,4-dione (**4**), the α-diketone derived from the parent di-isophorone, is obtained by several routes. Its formation by the hydrogenation of the corresponding 2,7-epoxide **3** confirms its assigned structure. The action of alkali on 4-substituted 8-bromodi-isophor-2(7)-en-3-ones yields, presumably by a successive bimolecular (SN2″) substitution and hydrolysis, the 4,4-dihydroxy-precursor, from which the 3,4-diketone **4** arises by loss of water. In yet another approach, **4** is produced by the hydrolysis of its 4-monohydrazone, which is independently accessible from 8-bromo-1-hydroxydi-isophor-2(7)-en-3-one (**8**). In acidic media, the yellow diketone **4** enolises to the stable isolable colourless 1,3-dihydroxydi-isophora-2,7-dien-4-one (**19**); the action of alkali reverses the process. Both forms of the compound yield the same 1-acyl-derivatives and 4-hydrazones.

(Keywords: Di-isophorone, 3,4-diketone, synthesis of; Di-isophorone, nucleophilic substitutions in; Tricyclo[7.3.1.0^{2,7}]tridecanes)

Di-isophoron und verwandte Verbindungen, 7. Mitt. Synthesen und Eigenschaften von 1-Hydroxy-di-isophor-2(7)-en-3,4-dion

1-Hydroxydi-isophor-2(7)-en-3,4-dion (**4**), das vom Grundkörper Di-isophoron abgeleitete α-Diketon, ist auf verschiedene Weise erhältlich. Seine Bildung mittels katalytischer Hydrierung des entsprechenden 2,7-Epoxyds **3** sichert seine Struktur. Es entsteht ferner durch Einwirkung von Alkalien auf 4-substituierte 8-Bromdi-isophor-2(7)-en-3-one, wahrscheinlich über eine bimolekulare Substitution (SN2″) und Hydrolyse, und darauffolgende Wasserabspaltung aus den intermediären 4,4-Dihydroxy-Verbindungen. Weiters erhält man das 3,4-Diketon **4** durch Hydrolyse seines 4-Hydrazons, welches seinerseits unabhängig aus 8-Brom-1-hydroxydi-isophor-2(7)-en-3-on (**8**) darstellbar ist. Im sauren Milieu verwandelt sich das gelbe 3,4-Diketon zum farblosen, isolierbaren 1,3-Dihydroxydi-isophor-2,7-dien-4-on (**19**); diese Enolisierung wird unter dem Einfluß von Alkalien umgekehrt. Beide tautomeren Formen ergeben identische 1-Acyl-Derivate und 4-Hydrazone.

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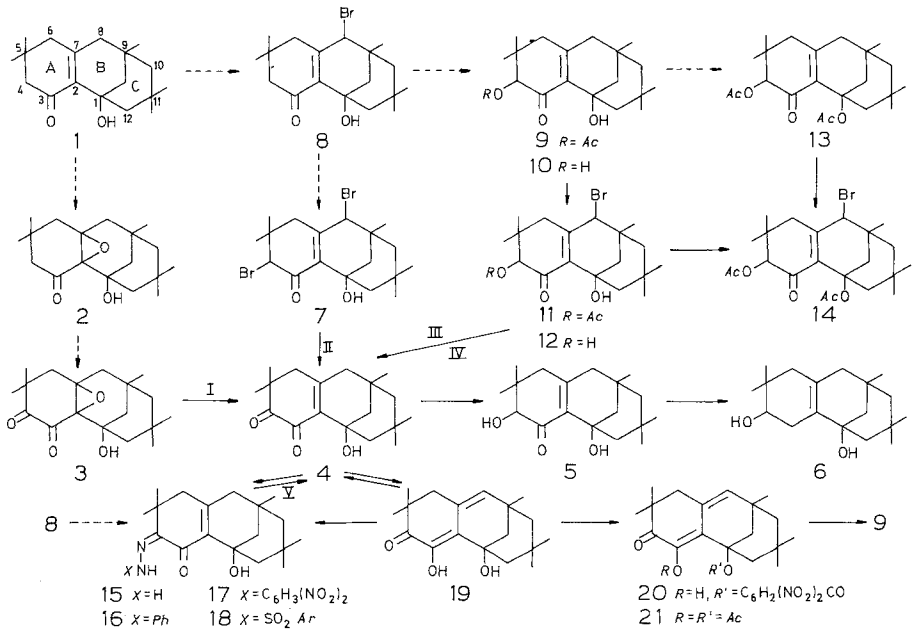
Introduction

The α-diketone corresponding to di-isophorone (**1**), viz. 1-hydroxy-di-isophor-2(7)-ene-3,4-dione (**4**) is of interest from several points of view. Oxidative fission of its ring A should provide a degradation of the tricyclo[7.3.1.$0^{2,7}$]tridecane- to the simpler bicyclo[3.3.1]nonane-ring system[2]. The α-diketone is concerned in several interconversions of di-isophorane-compounds, and has thus become a useful point of reference for assigning or confirming certain structures in this series. A number of synthetic routes to this α-diketone, and some of its relationships with other di-isophorane derivatives are now described.

Results and Discussion

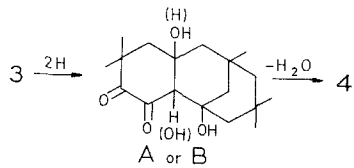
The established method of introducing the 4-keto-function into ring A of the di-isophorone structure by the action of selenium dioxide (e.g. **2** → **3**)[2] proved inapplicable to the parent di-isophorone **1**: The resulting yellow resins were probably mixtures of di- and tri-ketones arising from **1** by multiple oxidation promoted by the activating influence of the 2(7)-double bond.

Scheme 1



Attempts were first made to synthesize the α-diketone **4** by a route that would also establish its structure. 1-Hydroxy-2,7-epoxydi-isophorane-3,4-dione (**3**)[2] appeared to be a suitable source (of **4**), provided its oxirane-ring could be removed[3,4] without affecting its keto-function. Unlike the reduction with zinc, which regenerates the parent ketol **1** in one step[2], catalytic hydrogenation was found to occur in controllable stages, and affected the oxirane moiety first: addition of 1 mol of hydrogen to **3** thus afforded **4** in fair yields (Scheme 1, route I). The 3,4-diketo-system in **3** clearly enhances the susceptibility towards reduction of the 2,7-oxirane ring, since this function remains unaffected in the hydrogenation, or metal hydride reaction of the comparable 1-hydroxy-2,7-epoxydi-isophoran-3-one (**2**)[4].

The mechanism of the hydrogenation is thought to involve, as in the case of **2**[4], the reductive opening of the epoxide ring, followed by the regeneration of the 2(7)-double bond by dehydration of the intermediate tert. alcohol (A or B).

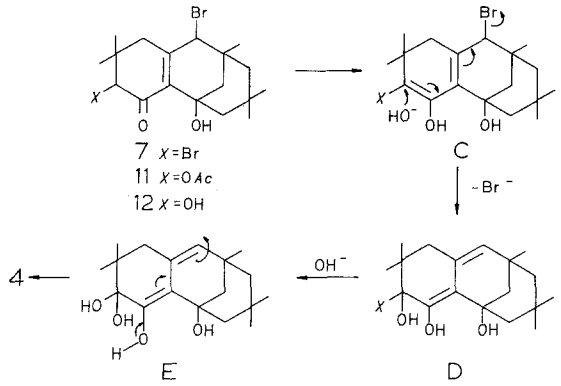


The result of the continued hydrogenation of the epoxydiketone **3** illustrates the superior reactivity of the 4- over that of the 3-oxo-group. Thus, addition of 2 mol of hydrogen gave 1,4α-dihydroxydi-isophor-2(7)-en-3-one (**5**), as did addition of 1 mol of hydrogen to **4**, showing the function of the latter as an intermediate in the process. The product was identified by its comparison with the authentic 1,4α(axial)-diol **5**[1,5]. The stereochemical course of the reaction is in accord with the known[6] preferential formation of axial alcohols from cyclic ketones by hydrogenation under acidic conditions. The maximum uptake of hydrogen by the epoxyketone **3** was 4 mol: the final addition reduced the 3-oxo- to a methylene-group as expected[7,8], producing the known[5] 1,4-dihydroxydi-isophor-2(7)-ene **6**.

The synthesis of the α-diketone **4** by the hydrogenation of the diketoepoxide **3** of known structure is more significant as structural evidence than as a preparative method. The starting material **3** is not very readily available in quantity and tenaciously retains selenium impurities which tend to poison the catalyst[9], and affect the progress of the hydrogenation adversely. Possible alternative routes to the α-diketone **4** were therefore examined.

A general synthesis was suggested by the recent observation[1] that the action of nucleophiles on 8-bromo-1-hydroxydi-isophor-2(7)-en-3-one (**8**) produces, by a presumed SN2″-mechanism, 4-substituted 1-hydroxy-compounds (**9**, **10** etc.). The use as starting materials of 8-bromodi-isophorones containing a suitable 4-substituent could reasonably be expected to yield the 3,4-diketone **4** by way of a 4,4-dihydroxy-precursor. Three variants of this proposed method were in fact successful (Scheme 1, routes II–IV).

Scheme 2



Thus, 4,8-dibromo-1-hydroxydi-isophor-2(7)-en-3-one (**7**) was converted in good yield into **4** by the action of alkali in boiling aqueous dioxan. The reaction is explicable by the following extension of the mechanism proposed[1] for the hydrolysis of the 8-monobromo-analogue **8** (of **7**): After the initial enolisation of the 3-oxo-group (in **7**), producing the bromo-diol (C, X = Br), bimolecular substitution (SN2″), involving attack of hydroxyl at C-4 and concomitant expulsion of the 8-substituent, results in the 4,4-gem-disubstituted intermediate (D, X = Br). Simultaneous or successive hydrolytic replacement of the 4-bromo-group produces the 4,4-diol E which on loss of water, and on reversion of the 2,7-dien-3-ol- to the more stable α,β-unsaturated keto-system yields the 3,4-diketone **4**. The mechanism is equally applicable to, and correlates, the other variants of this synthesis.

Of these, the alkaline hydrolysis of 4α-acetoxy-8-bromo-1-hydroxydi-isophor-2(7)-en-3-one (**11**) to the 3,4-diketone **4** (Scheme 1, route III), which proceeded readily in high yield, is comparable in every respect with that of the 4,8-dibromo-compound **7**, including its presumed mechanism [**11** → C → D → E (X = O*Ac*) → **4**]. The starting ma-

terial **11** was the product of the monobromination of 4α-acetoxy-1-hydroxydi-isophor-2(7)-en-3-one (**9**)[1]. The analogy of its formation with that of the 8-bromoderivative **8** of the parent di-isophorone **1** is the basis of its formulation, which is corroborated by its reaction with alkali. Its further acetylation under restrained conditions[10] gave the bromo-diacetate **14**, which was also obtainable by the monobromination of the known[1] 1,4α-diacetoxy-compound **13**. The α(axial)-conformation of the 4-substituent in all the compounds involved in these interconversions (**9**–**14**) is therefore seen to be maintained throughout.

In the third variant of this synthesis (Scheme 1, route IV), 1,4α-dihydroxydi-isophor-2(7)-en-3-one (**10**) was monobrominated in glacial acetic acid. Although the presumed 8-halogeno-derivative **12** was not isolable as a solid, immediate treatment of the crude intermediate with alkali under the standard conditions gave **4** in ca. 50% yield. Its formation is explicable in the usual way [**12** → C → E → **4**].

The recent conversion of the bromo-derivative **8** into the 4-monohydrazone **15** by the action of hydrazine[1] opens a third synthetic route to **4**. Regeneration (in **15**) of the 4-keto- from the 4-hydrazono-group was readily accomplished by the action of hydrochloric acid, or by a modified form of the method of *Hershberg*[11] using pyruvic acid, and afforded **4** in satisfactory yield (Scheme 1, route V). Conversely, the α-diketone was convertible into 4-monohydrazones by the action of ketonic reagents (see below).

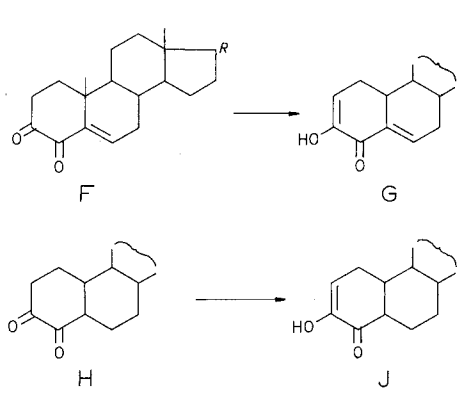
1-Hydroxydi-isophor-2(7)-ene-3,4-dione (**4**) is a bright yellow solid crystallising invariably as the monohydrate, even from non-aqueous solvents. An accurate determination of its molecular weight by high-resolution mass-spectroscopy confirmed its molecular formula ($C_{18}H_{26}O_3$; *M*, 290.1885). Its α-diketo-system produces a single high intensity absorption peak (ν, 1,635 cm^{-1}), as does that of the comparable 2,7-epoxy-3,4-diketone (**3**; ν, 1,720 cm^{-1})[2]: the observed displacement towards lower wave-numbers (in **4**, by 85 cm^{-1}) is attributable to the effect of the 2,7-olefinic bond. A similar, though somewhat smaller shift, encountered on passing from 2,7-epoxydi-isophorone (**2**) to di-isophorone **1** (1,690–1,640 cm^{-1}, i.e. by 50 cm^{-1}) provides a valid correlation, a single keto-group presumably exerting a smaller effect. The abnormally broad hydroxyl absorption at 3,360-3,480 cm^{-1} is attributed in part to the hydrated nature of the solid. The absorption bands of **4** in the u.v. region (at 232 and 329 nm) were of medium intensity, as are those of comparable steroids[12, 13].

1,3-Dihydroxydi-isophora-2,7-dien-4-one (**19**)

In acidic media, the yellow diketone **4** isomerised rapidly and near-quantitatively to a colourless product formulated as the diene-diol **19**, which, like its precursor, was always isolated as the monohydrate. The action of alkali reversed the enolisation. In all the syntheses of **4**

described above, it was in fact usually expedient to isolate part of the product as the enol (**19**, see Experimental).

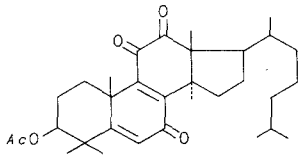
The structural assignment to **19** is in accord with the known analogous conversion, in acid media, of steroid α-diketones into stable isolable enols (e.g. F → G[13]; H → J[14]; and others[15]), and with the spectral and chemical properties of **19**. Its i.r. spectrum included a prominent carbonyl absorption at 1,650 cm^{-1}, with two associated lesser peaks at 1,620 and 1,600 cm^{-1} attributable to the olefinic bonds of the extended conjugated system. Two intense bands (at 3,570 and 3,460 cm^{-1}) indicate the presence of two hydroxyl-groups; the one associated with the absorption at the lower wave-number is probably hydrogen-bonded. The ^1H n.m.r. spectrum of **19** (see Experimental) is consistent with the presence of one methylene- and one methyne-group adjacent to a double bond, and of two hydroxyl-groups; of these, the enolic hydroxyl gives rise to a very broad signal that is displaced from its expected range (δ 12-δ 15) to 4.1-4.5 ppm, reflecting the hydrated state of the compound. In the u.v. range, the position of the absorption maximum (λ_{max} 320 nm) agrees less closely than is usual[1,5] in this series with the value calculated according to the *Fieser-Woodward* rules[16] (λ_{max} 338 nm) for the proposed diene-diolone structure **19**.



Both the ketonic and enolic forms (**4**, **19**) of the 3,4-diketone gave the same monoketonic derivatives **16**–**18**. As in the hydrogenation (**4** → **5**, see above), reaction occurred preferentially at the 4-keto-group of **4**, as shown by the identity of the resulting derivatives and 4-(substituted)hydrazono-1-hydroxydi-isophor-2(7)-en-3-ones (**16**–**18**) of established structure obtained from the parent hydrazone **15** by transhydrazination reactions. Since these derivatives (**16**–**18**) are produced in acid media, i.e. from the enolic form **19** of the reactant, exclusive reaction at C-4 is plausible; subsequent rearrangement of the 2,7-dien-3-ol- to the α,β-unsaturated keto-system produces the observed derivatives. The enol **19** also reacted with hydrazine hydrate giving the known[1] hydrazone **15**.

Similarly, both forms of the α-diketone (**4**, **19**) gave the identical 3,5-dinitrobenzoate. Its formulation as **20** is in accord with its origin from

the ketonic form **4** under the prevailing basic conditions, resulting in substitution at the only available 1-hydroxy-group; isolation of the product in a strongly acid medium causes enolisation to **20**. The appearance of a strong hydroxyl-absorption (at 3,400 cm^{-1}) agrees with the formulation. Acetylation of the enol **19** under restrained conditions[10] yielded the diacetate **21**.



K

Despite incorporating an α-diketone system, **4** did not yield a quinoxaline derivative with *o*-diaminobenzene. In this respect it differs from the closely related 2,7-epoxy-3,4-dione **3**, the ability of which to form such a derivative was held to be evidence for its assigned structure[2]. However, the failure of α-diketones to react in this sense is not without precedent: the dienetrione K[17] of the lanosterol series is such an example, and gives grounds for the surmise that the condensation is inhibited by an adjacent tetrasubstituted olefinic bond.

Hydrogenation of the enol **19** in glacial acetic acid at room temperature produced moderate yields of 1,4α-dihydroxydi-isophor-2(7)-en-3-one (**10**)[5]. The action of zinc in aqueous dimethylformamide on **19** gave an uncrystallisable oil, which was shown to contain the same reduction product **10** by its isolation as the 2,4-dinitrophenylhydrazone[5].

Experimental

General information is given in Part I[18] concerning equipment, standard procedures, reagents, solvents, nomenclature, and abbreviations. Light petroleum had b.p. 60–80° unless otherwise stated. 4,8-Dibromo-1-hydroxydi-isophor-2(7)-en-3-one (**7**) was produced[19] by dibromination of di-isophorone (**1**) in glacial acetic acid. Hydrogenations were performed at room temperature and atmospheric pressure over *Adams'* catalyst[20]. Except for compounds **4** and **19**, unassigned peaks of the i.r. spectra are not recorded.

2,7-Epoxy-1-hydroxydi-isophorane-3,4-dione (**3**)[2]: *Hydrogenation*

(a) *Addition of 1 mol of hydrogen.*—A solution of **3** (3.06 g, 0.01 mol) in ethanol (30 ml) was hydrogenated over *Adams'* catalyst[20] (0.2 g) until 280–300 cc of hydrogen had been absorbed (calc.: 35 and 225 cc at NTP, for uptake by the catalyst and 1 mol) (2–3 h). The filtered solution gave, on dilution with water, basification with 10 *N* sodium hydroxide (3 ml) and storage at 0°, a precipitate which was crystallised (often not without difficulty) from ethanol-light petroleum (2:1, 20 ml per g, recovery ca. 50%), or from light petroleum

alone, to yield yellow prisms (1.60-2,0 g, 52-65%) of *1-hydroxydi-isophor-2(7)-ene-3,4-dione* (**4**), m.p. 260-264° (decomp.). (Found: C 70.7, H 9.0. *M*, by high-resolution mass spectroscopy, 290.1885. $C_{18}H_{26}O_3 \cdot H_2O$ requires C 70.1, H 9.1%, *M* 290.1882.) ν_{max} 3,450 ms (OH); 2,970-2,900 vs, 1,465 s (CH_3, CH_2); 1,635 vs (CO), 1,385 s (.CMe_2); 1,540 s, 1,360 s, 1,295 s, 1,275 s, 1,250 ms, 1,215 ms, 1,180 ms, 1,125 m, 1,080 vs, 1,040 ms, 995 m, 940 m, 805 m cm^{-1}. λ_{max} 232 nm ($\log \varepsilon$, 3.57); 329 (3.71).

m/e 290 m (*M*$^+$), 274 w (*M*$^+$—16), 272 mw (*M*$^+$—18), 258 w (*M*$^+$—2 × 16), 219 w (*M*$^+$—71), 216 s, 203 ms (*M*$^+$—71-16), 201 s (*M*$^+$—71-18), 187 ms (*M*$^+$—71-2 × 16).

Hydrogenation occurred readily in glacial acetic acid (30 ml). Addition of the filtered solution to water, and basification with 10 *N* sodium hydroxide (ca. 60 ml) gave a yellow precipitate from which smaller and variable quantities of the crystallised **4** (up to 1.3 g, 45%) were obtainable.

(b) *Addition of 2 mol of hydrogen.*—(i) A solution of **3** (3.06 g, 0.01 mol) in glacial acetic acid (30 ml) was hydrogenated over *Adams'* catalyst[20] (0.2 g) (uptake: 550 cc; calc. 35 and 450 cc at NTP for catalyst and 2 mol, respectively). Addition of the filtered solution to water (500 ml), and neutralisation with 10 *N* sodium hydroxide slowly deposited a precipitate (m.p. 116-117°, 1.15-1.45 g, 40-50%), which gave platelets of *1,4α-dihydroxydi-isophor-2(7)-en-3-one* (**10**), m.p. 116-118° (from light petroleum), identified by its i.r. spectrum[5]. (Found: C 74.0, H 9.7. Calc. for $C_{18}H_{28}O_3$: C 74.0, H 9.6%). (ii) A solution of **4** (1.45 g, 0.005 mol) in glacial acetic acid (30 ml) was hydrogenated[20] (5 h, uptake 120 cc; calc. 35 + 110 cc at NTP). Isolation of the crude product as in (i) gave a pale-yellow precipitate (0.6 g), which afforded prisms, m.p. 117-119° of (**10**) (0.44 g, 30%) (from light petroleum), identical with authentic material[5].

(c) *Addition of 3 mol of hydrogen.*—A solution of **3** (1.53 g, 0.005 mol) in glacial acetic acid (20 ml) was hydrogenated[20] (uptake 400 cc; first 280 cc within 15 min, the remainder slowly over 3-4 h; calc. 35 + 340 cc at NTP). The (filtered) solution was evaporated under reduced pressure to quarter bulk, stirred into water, basified with 3 *N* sodium hydroxide, and set aside for 12 h. The product was extracted with ether, and the liquid residue therefrom dissolved in light petroleum. The solution deposited *1,4-dihydroxydi-isophor-2(7)-ene* (**6**), m.p. 149-150° (0.7-0.9 g, 25-32%), identified by its i.r. spectrum[5]. (Found: C 77.9, H 11.1. Calc. for $C_{18}H_{30}O_2$: C 77.7, H 10.8%.)

4,8-Dibromo-1-hydroxydi-isophor-2(7)-en-3-one (**7**)[19]. *Action of alkali*

A solution of **7** (4.34 g, 0.01 mol) in dioxan (50 ml)—water (25 ml)—3 *N* sodium hydroxide (12 ml, 0.036 mol) was boiled under reflux for 2.5 h (transient dark green colour), stirred into water (300 ml), and strongly basified with 3 *N* sodium hydroxide (25 ml). The air-dried yellow precipitate was covered with light petroleum and collected, affording a pale yellow crystalline powder (1.6 g, 52%) of **4**, m.p. 260° (decomp.), identified by its i.r. spectrum (see above). The alkaline filtrate from **4** gave, after acidification with concentrated hydrochloric acid, a crystalline precipitate of the enolic form **19** of **4** (see below), m.p. 95-97°, in yields depending on the amount of **4** first isolated, the combined yields of the two forms approaching 75%.

4α-Acetoxy-8-bromo-1-hydroxydi-isophor-2(7)-en-3-one (**11**)

(a) *Preparation.*—A stirred solution of 4α-acetoxy-1-hydroxydi-isophor-2(7)-en-3-one (**9**)[1] (1.67 g, 0.005 mol) in glacial acetic acid (50 ml)—60%hydro-

bromic acid (6 drops) was treated dropwise during 30 min with 1 *M* bromine in glacial acetic acid (5 ml, 0.005 mol). Addition to ice-water precipitated a white solid which gave glass-like prisms (1.32-1.56 g, 64-75%) of **11**; m. p. 111-113° (from light petroleum). (Found: C 58.4, H 7.2, Br 19.5. $C_{20}H_{29}BrO_4$ requires C 58.1, H 7.0, Br 19.35%.) ν_{max} 3,530 vs (OH), 2,960-2,880 vs br, 1,475 s (CH_3, CH_2), 1,745 vs (CO of *Ac*), 1,665 vs (CO), 1,625 ms (C=C, conjug.), 1,395 s, 1,370 vs (. C*Me*$_2$), 1,235 vs br (C—O—C, ester) cm^{-1}.

(b) *Action of alkali.*—A solution of **11** (0.83 g, 0.002 mol) in dioxan (50 ml)—water (25 ml)—1 *N* sodium hydroxide (2.5 ml, 0.0025 mol) was stirred at room temperature for 20 min. The liquid was diluted with water (200 ml), then successively acidified with 3 *N* hydrochloric acid and strongly basified with 3 *N* sodium hydroxide. The yellow precipitate (filtrate: *F'*) was (hydrated) **4** (0.28-0.34 g, 45-55%), m. p. 260° (decomp.), identified by its i.r. spectrum (see above), and by its conversion (75%) into its 2,4-dinitrophenylhydrazone, m. p. 205-207° (decomp.) (from ethanol) (see below). Filtrate *F* gave on acidification a white crystalline precipitate (0.22-0.15 g, 35-25%) of the enolic form **19**, m. p. 95-97°, identified by its i.r. spectrum (see below).

1,4α-Diacetoxy-8-bromodi-isophor-2(7)-en-3-one (**14**)

(i) *By acetylation of* **11**:—A solution of **11** (1.03 g, 0.0025 mol) in acetic acid (8 ml)—acetic anhydride (4 ml)—60% perchloric acid (6 drops) was set aside at room temperature for 2 h, then stirred into water. The white precipitate gave needles (0.74 g, 65%) of **14**, m. p. 142-143° (from light petroleum). (Found: C 58.2, H 7.0, Br 17.8. $C_{22}H_{31}BrO_5$ requires C 58.0, H 6.8, Br 17.6%.) ν_{max} 2,970-2,880 vs br, 1,475 ms (CH_3, CH_2), 1,745, 1,725 vs d (CO of *Ac*), 1,700 s (CO), 1,650 w (C=C, conjug.), 1,380, 1,370 vs (. C*Me*$_2$), 1,255 vs br, 1,235 vs br (C—O—C, ester) cm^{-1}.

(ii) *By bromination of* **13**.—A stirred solution of **13**[1] (1.5 g, 0.004 mol) in glacial acetic acid (50 ml) containing 60% hydrobromic acid (10 drops) was treated dropwise during 30 min with 0.5 *M* bromine in glacial acetic acid (8 ml, 0.004 mol), the colour fading slowly. Addition of the liquid to ice gave a yellow oil, which after extraction with ether and dissolution in light petroleum deposited (after a crop of recovered starting material, 25%), needles (0.58 g, 32%) of **14**, m. p. 142-143°, identical with material obtained in (i).

1,4α-Dihydroxydi-isophor-2(7)-en-3-one (**10**)[5]. *Successive bromination and hydrolysis*

A solution of **10** (2.92 g, 0.01 mol) in glacial acetic acid (35 ml) containing 60% hydrobromic acid (0.25 ml) was treated dropwise with 1 *M* bromine in glacial acetic acid (10 ml, 0.01 mol). The yellow liquid was added to ice-water, and the sticky brown precipitate extracted with ether. The yellow oil remaining on removal of the solvent was dissolved in dioxan (30 ml)—water (20 ml)—10 *N* sodium hydroxide (2.5 ml) and boiled under reflux for 1 h. The liquid was added to water and strongly basified with more 3 *N* sodium hydroxide. The resulting yellow precipitate (1.25-1.55 g, 40-50%) was **4**, m. p. 260° (decomp., darkening from ca. 160°) (from light petroleum), identified by its i.r. spectrum.—Attempts to isolate the initial bromination product by crystallisation from light petroleum gave only oily products.

4-Hydrazono-1-hydroxydi-isophor-2(7)-en-3-one (**15**)[1]

(a) *Action of hydrochloric acid.*—A solution of **15** (1.52 g, 0.005 mol) in acetone (20 ml)—concentrated hydrochloric acid (0.5 ml) was boiled under

reflux for 30 min (colour change deep-orange to pale-yellow), then slowly stirred into ice-water (120 ml). The precipitate, collected at 0°, formed faintly yellow microprisms (1.23 g, 80%) of **19**, m. p. 98–100°, identified by its i.r. spectrum (see below).

(b) *Action of pyruvic acid.*—A solution of **15** (1.52 g, 0.005 mol) in glacial acetic acid (18 ml), treated with pyruvic acid (1.32 g, 0.015 mol)—water (1 ml) was boiled under reflux for 1 h, then added to ice-water (120 ml). The precipitated resin was covered with light petroleum-ethanol (1:1, 10 ml), giving faintly yellow microprisms (0.52 g, 40%) of **19**, m. p. 95–96°, identified by its i.r. spectrum. (Found: C 70.0, H 8.9%.) (See following Section.)

Alternatively, the crude resin, dissolved in ethanol, was treated with 2,4-dinitrophenylhydrazine (1.0 g, 0.005 mol) and concentrated hydrochloric acid (1 ml) and heated to boiling. The reagent dissolved, while the liquid deposited almost immediately orange crystals (ca. 60%) of the *2,4-dinitrophenylhydrazone* of **4**, m. p. 225° (decomp.) (from ethanol).

1,3-Dihydroxydi-isophora-2,7-dien-4-one (**19**)

(a) *Preparation.*—A solution of the 3,4-dione (**4**) (1.54 g, 0.005 mol) in acetone (30 ml), treated with concentrated hydrochloric acid (0.5 ml), was boiled under reflux for 30 min (or set aside at room temperature for 1 h), then stirred into water. A white to faintly yellow crystalline precipitate (1.05–1.25 g, 70–82%) of **19**, m. p. 95–97°, separated rapidly. It was not crystallisable from the common solvents without undergoing decomposition. (Found: C 69.1, H 9.0. $C_{18}H_{26}O_3 \cdot H_2O$ requires C 70.1, H 9.1%.) ν_{max} 3,570 vs, 3,460 vs (OH), 2,970–2,860 vs br (CH_3, CH_2), 1,650 vs (CO), 1,620 s, 1,600 m (C=C, conjug.), 1,395 vs (.CMe_2), 1,360 s, 1,305 vs, 1,210 s, 1,075 s, 1,060 s, 1,040 s, 1,010 m, 995 m, 850 m, 815 m cm^{-1}. λ_{max} 320 nm (log ε 4.05), end absorption at 208 nm (log ε 3.86).

^{1}H-n.m.r.: δ 0.81 (s, 3 H, *Me*), 0.94 (s, 3 H, *Me*), 1.10 (s, 3 H, *Me*), 1.14 (s, 3 H, *Me*), 1.17 (s, 3 H, *Me*), 1.27–2.23 (mult, 6 H), 2.37, 2.39 (d, 2 H, CH_2C:C), 5.61, 5.63 (d, 1 H, CH=C), 4.1–4.5 (s, br, 1 H, OH), 6.95 (s, 1 H, OH) ppm.

(b) *Production.*—A solution of 4,8-dibromo-1-hydroxydi-isophor-2(7)-en-3-one (**7**) (4.34 g, 0.01 mol) in dioxan (50 ml)—water (25 ml)—10 *N* sodium hydroxide (5 ml, 0.05 mol) was boiled under reflux for 4 h. The brown solution was treated with concentrated hydrochloric acid (10 ml) (colour change to pale-yellow) and refluxing continued for 2 h. Slow addition to water (1 l) with good stirring gave a very pale yellow precipitate (2.35–2.6 g, 76–84%) of **19**, m. p. 89–92°, identified by its i.r. spectrum.

(c) *Reconversion into* **4**.—A solution of **19** (0.31 g, 0.001 mol) in ethanol, basified with a little 10 *N* sodium hydroxide, was set aside at room temperature for 15 min, then added to water and strongly basified with more 10 *N* alkali. The separated yellow solid gave, on crystallisation from ethanol-light petroleum, yellow prisms (62%) of **4**, m. p. 260° (decomp.), identified by its i.r. spectrum.

Ketonic Derivatives of 1-Hydroxydi-isophor-2(7)-ene-3,4-dione (**4**) *and of 1,3-Dihydroxydi-isophora-2,7-dien-4-one* (**19**)

1-Hydroxy-4-(ω-2,4-dinitrophenyl)hydrazonodi-isophor-2(7)-en-3-one (**17**)

A solution of **4** or **19** (0.29 g, 0.001 mol) and 2,4-dinitrophenylhydrazine (0.6 g, 0.003 mol) in ethanol (20 ml)—concentrated hydrochloric acid (1 ml) was boiled under reflux for 20 min. The solid gave orange microcrystals (0.26 g, 56%)

of **17**, m.p. 205–207° (decomp.) (from ethanol). (Found: C 60.9, H 6.4, N 12.4. Calc. for $C_{24}H_{30}N_4O_6$: C 61.3, H 6.4, N 11.9%, identified by its i.r. spectrum[1].)

The following derivatives were similarly prepared and were identical (m.p., i.r. spectra) with specimens obtained by transhydrazination[1] from 4-hydrazono-1-hydroxydi-isophor-2(7)-en-3-one (**15**)[1], itself derived from the 8-bromo-compound **8**.

4-(ω-Phenyl)hydrazono-Derivative **16** (from **4** or **19**) (ca. 60%), m.p. 160–162°. (Found: C 76.1, H 8.3, N 7.4. Calc. for $C_{24}H_{32}N_2O_2$: C 75.8, H 8.4, N 7.4%.)

4-(ω-Benzenesulphonyl)hydrazono-Derivative **18** (*Ar* = *Ph*) (from **19**) (45%), m.p. 155–156°. (Found: C 64.8, H 7.2, N 6.4, S 7.6. Calc. for $C_{24}H_{32}N_2O_4S$: C 64.7, H 7.2, N 6.3, S 7.2%.)

4-(ω-Toluene-p-sulphonyl)hydrazono-Derivative **18** (*Ar* = *p-Tol*) (from **19**) (40%), m.p. 152–154°. (Found: C 65.8, H 7.5, N 6.1. Calc. for $C_{25}H_{34}N_2O_4S$: C 65.5, H 7.4, N 6.1%.)

4-Hydrazono-1-hydroxydi-isophor-2(7)-en-3-one (**15**)

A solution of **19** (0.62 g, 0.002 mol) in ethanol (10 ml)—hydrazine hydrate (0.5 g, 0.01 mol) was boiled under reflux for 1 h, evaporated under reduced pressure to small volume, and the residual oil dissolved in ether. The residue from the washed dried extracts gave lustrous yellow platelets (53%) of **15**, m.p. 160–162° (from light petroleum). (Found: C 71.0, H 9.3, N 9.1. Calc. for $C_{18}H_{28}N_2O_2$: C 71.05, H 9.2, N 9.2%, identified by its i.r. spectrum[1].)—Attempts to prepare **15** from **4** under the same conditions, or in the presence of catalytic quantities of hydrochloric acid, failed.

Acyl Derivatives

1,3-Diacetoxydi-isophora-2,7-dien-4-one (**21**)

A solution of **19** (3.08 g, 0.01 mol) in glacial acetic acid (10 ml)—acetic anhydride (5 ml)—60% perchloric acid (0.25 ml) was set aside at room temperature for 2 h, then poured into water. The precipitated soft solid was taken up in light petroleum (after ether extraction, if necessary). The solution deposited massive prisms (1.35–2.1 g, 36–56%) of **21**; m.p. 124–126°. (Found: C 70.5, H 8.3. $C_{22}H_{30}O_5$ requires C 70.6, H 8.0%.) ν_{max} 2,960–2,880 vs br (CH_3, CH_2), 1,765 s, 1,730 vs (CO of *Ac*), 1,680 vs (CO), 1,630 m, 1,605 w (C=C, conjug.), 1,390 ms, 1,370 s (.CMe_2), 1,235 vs (C—O—C, ester) cm^{-1}.

1-(3,5-Dinitrobenzoyl)oxy-3-hydroxydi-isophora-2,7-dien-4-one (**20**)

A solution of **19** (0.62 g, 0.002 mol) in pyridine (15 ml), treated with 3,5-dinitrobenzoyl chloride (0.46 g, 0.002 mol), was kept at 100° for 1 h, then stirred into ice-concentrated hydrochloric acid (15 ml). The precipitate was successively washed with aqueous sodium bicarbonate and water, and gave opaque microcrystalline pale yellow **20**, m.p. 210–213° (from ethanol-light petroleum, 2:1) (0.54 g, 56%). (Found: C 61.9, H 5.8, N 5.7. $C_{25}H_{28}N_2O_8$ requires C 62.0, H 5.8, N 5.8%.) ν_{max} 3,420 vs (OH), 3,130 ms, 730, 720 s (*Ar*), 2,990–2,900 vs, 1,470 m (CH_3, CH_2), 1,730 vs (CO of Acyl), 1,670 vs (CO), 1,630 m (C=C, conjug.), 1,285 vs (C—O—C, ester) cm^{-1}.

1,3-Dihydroxydi-isophora-2,7-dien-4-one (**19**). *Reductions*

(a) A solution of **19** (0.62 g, 0.002 mol) in glacial acetic acid (20 ml) was hydrogenated over *Adams'* catalyst[20] (0.3 g) (2 h, uptake: 150 cc; calc.

55 + 90 cc for catalyst and 2 mol of hydrogen). The filtered solution was added to water and the liquid basified with 10 *N* sodium hydroxide. The yellow resinifying precipitate gave, on crystallisation from light petroleum, prisms (0.15 g, 25%) of 1,4α-dihydroxydi-isophor-2(7)-en-3-one (**10**), m.p. 117–119°, identified by its i.r. spectrum[5].

(b) A solution of **19** (0.62 g, 0.002 mol) in glacial acetic acid (15 ml), treated with zinc dust (1 + 1 g, after 2 hs' interval) was boiled under reflux for 4 h. The filtered liquid was stirred into water, giving an oil which failed to produce solid (from light petroleum). Accordingly, it was converted by the standard procedure (see above and Ref.[18]), into the 2,4-dinitrophenylhydrazone of **10**, forming deep-red prisms (40%), m.p. 235–238° (from ethanol), identified by its i.r. spectrum[5]. (Found: C 60.5, H 6.75, N 12.2. Calc. for $C_{24}H_{32}N_4O_6$: C 61.0, H 6.8, N 11.9%.)

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