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Di-isophorone and Related Compounds. Part 6.[1] The Action of Nucleophiles on 8-Bromodi-isophorone

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Hydrolysis and acetolysis of 8-bromo-1-hydroxydi-isophor-2(7)-en-3-one yields both epimeric forms of the corresponding 4-hydroxy and 4-acetoxy-compounds, probably by a mechanism involving a bimolecular (SN2″) displacement. The action of excess of hydrazine on the same reactant occurs with evolution of ammonia, to produce good yields of 4-hydrazono-1-hydroxydi-isophor-2(7)-en-3-one. This is convertible into N- and O-acyl derivatives, but its 3-oxo-group fails to react with the usual ketonic reagents. Instead, its 4-hydrazono-group is displaced by substituted hydrazines and semicarbazides in an exchange process (transhydrazination).

(Keywords: 8-Bromodi-isophorone, action of nucleophiles on; Di-isophorone; Nucleophilic (SN2″) substitution; Tricyclo[7.3.1.0^{2,7}]tridecanes)

Di-isophoron und verwandte Verbindungen, 6. Mitt. Die Einwirkung von Nucleophilen auf 8-Brom-di-isophoron

Die Hydrolyse und Acetolyse des 8-Brom-1-hydroxydi-isophor-2(7)-en-3-ons führt unerwartet, anscheinend über einen bimolekularen (SN2″) Mechanismus, zu epimeren 4-Hydroxy- oder 4-Acetoxy-Verbindungen. Dieselbe 8-Brom-Verbindung ergibt mit Hydrazin, unter Ammoniakentwicklung, gute Ausbeuten von 4-Hydrazono-1-hydroxydi-isophor-2(7)-en-3-on. Hiervon sind N- und O-Acyl-Derivate leicht erhältlich; hingegen reagiert seine 3-Keto-Gruppe nicht mit den gewöhnlichen Keton-Reagentien: stattdessen wird die 4-Hydrazon-Gruppe durch substituierte Hydrazin- oder Semicarbazid-Reste ausgetauscht.

Introduction

Unlike isophorone (**A**), which yields the expected 4- or 6-bromo-derivatives on treatment with N-bromosuccinimide[2] and molecular bromine,[3] respectively, di-isophorone (**1**) is converted by either reagent[4,5] into the 8-bromo-compound [**2**, 8-bromo-1-hydroxydi-isophor-2(7)-en-3-one; for nomenclature, see Ref.[6]].The introduction of

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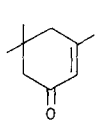
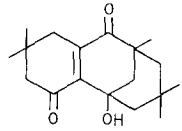
a reactive centre into the 8-position of the di-isophorane framework promised to open a way of further modifying the structure in this region; a potential route to the conjugated 3,8-diketone (**B**), and the resulting activation[7] of the normally unreactive bridged 2(7)-double bond appeared to be of special interest. An example of the type of reaction envisaged is the ethanolysis of **2**, which has been reported[5] to yield a mixture of the 8-ethoxy- and 8-hydroxy-compounds. However, the action of nucleophiles on **2** yields in fact 4-substituted products, as is now shown by our study of the hydrolysis, acetolysis and hydrazinolysis of the 8-halogenated di-isophorone **2**.



A



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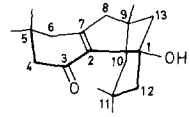

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Results and Discussion

Alkaline Hydrolysis and Acetolysis

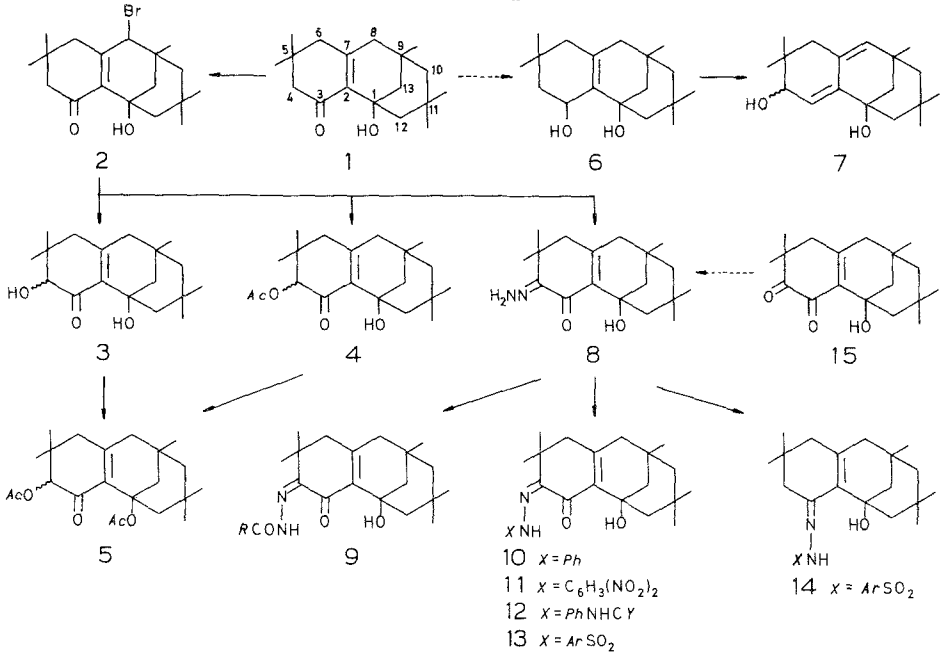
On treatment with alkali under very mild conditions, the 8-bromo-compound **2** was rapidly hydrolysed to a product that proved to be a mixture of the epimeric 1,4α- and 1,4β-dihydroxydi-isophor-2(7)-en-3-ones (**3**). The former, separating as a crystalline solid (36-45%), was identified by its comparison with authentic material[1], and by its perchloric acid-catalysed[8] acetylation to the known[1] 1,4α-diacetoxy-derivative **5** (m.p. 133°[1]). The low-melting 1,4β-epimer **3** was not obtainable as such, but its presence was demonstrated by acetylation of the more soluble oily fraction (from the crystallisation filtrates), when 1,4β-diacetoxydi-isophor-2(7)-en-3-one **5**, (m.p. 188°[1]) was isolable (ca. 12%) (Scheme 1).

Similary, the products of the acetolysis of the 8-bromo-compound **2**, performed by the action of potassium acetate in boiling acetic acid[9], were the 4α- and 4β-acetoxy-1-hydroxydi-isophor-2(7)-en-3-ones (**4**). The structure of the crystallisable α-epimer (42-50%) was in accord with its spectral characteristics (see Experimental), and was established by its conversion into the authentic 1,4α-diacetoxy-derivative **5** (m.p. 133°[1]). The low-melting uncrystallisable residue remaining in the mother-liquors gave, on acetylation, the 1,4β-diacetate **5** (m.p. 188°[1]), showing that the 1,4β-epimer **4** had also been formed (6-12%) in the initial acetolysis.

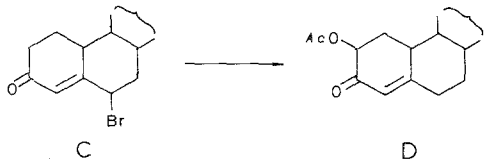
Thus, both the hydrolysis and acetolysis of 8-bromo-1-hydroxydi-isophor-2(7)-en-3-one (**2**) appear to be attended by non-stereospecific

migrations resulting in the appropriate 4-substituted products (**3** and **4**). The observation first gave some grounds for the surmise that the starting material was itself the 4- rather than the 8α-bromo-

Scheme 1



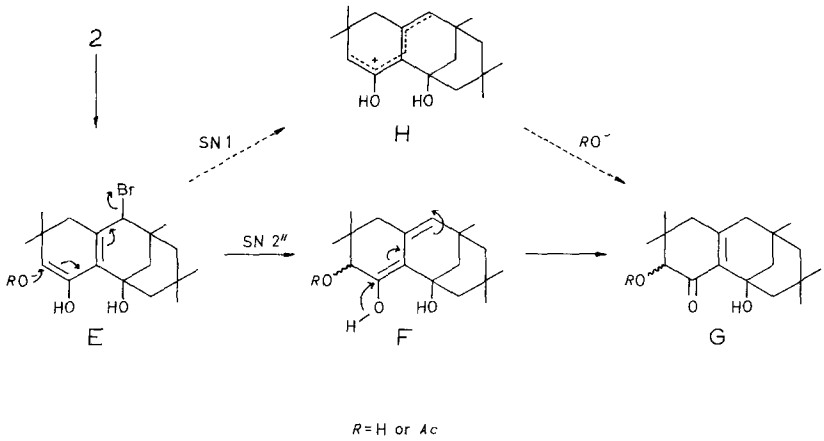
compound[5]. However, the latter structure **2** is upheld by the ready production of the bromo-compound from **1** by the action of N-bromosuccinimide[4,5], allylic halogenation occurring in the 8- in preference to the more hindered 6-position. The fact that molecular bromine unexpectedly attacks the same position[4,5] is explicable in terms of the enolisation of the 3-keto-function (in **1**) under the prevailing acidic conditions[10]: the generation of the system of hetero-annular conjugated double bonds increases the reactivity at C-8 relative to that at C-4[9]. Further support in favour of **2** as the true structure is also provided by the i.r. spectra[5], mass spectra[5], and C-13 n.m.r.[11] spectra of the compound.



The occurrence of apparent migrations attending hydrolyses or acetolyses of the type now described (**2** → **3**, **4**) is not without precedent, and may be correlated with nucleophilic reactions undergone by steroid bromoketones of comparable structures[12–15]. The acetolysis of **6**β-bromo- (**C**) to 2α-acetoxycholest-4-en-3-one (**D**)[13], and parallel reactions in the androstane series[14,15] are particularly relevant and provide guidelines[13,15] for the mechanistic interpretation of the behaviour of the 8-bromodi-isophorone (**2**) now observed.

Thus, after enolisation, the 8-bromoketone **2** may undergo unimolecular substitution involving the mesomeric carbonium ion **H**. Although this interpretation (Scheme 2, **E** → **H** → **G**) agrees with the observed non-stereospecificity of the reaction, it is disfavoured by the fact that isolable quantities of 8(or possibly 6)-substitution products that should have arisen from **H**, where not formed.

Scheme 2



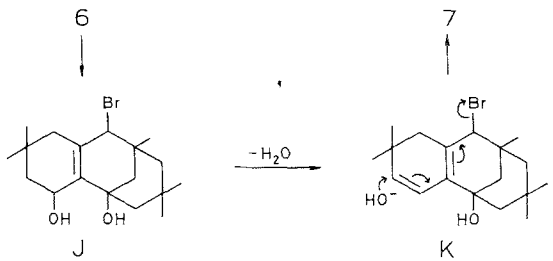
Alternatively, **E** may undergo bimolecular substitution involving the direct attack of the nucleophile at C-4 with simultaneous elimination of the 8-bromo-substituent; reversal of the enolisation (in **F**) produces the more stable α,β-unsaturated ketone (Scheme 2, **E** → **F** → **G**). The initial stage (**E** → **F**) of this sequence appears to be an example of reactions that have been classified as SN2″-substitutions[16], and are thought to operate when SN2 bimolecular replacement at the α-position of an allylic moiety is retarded for steric or other reasons. Unlike the more common SN2′-substitution[17], which takes place *syn*-stereo-specifically[18], the SN2″ process proceeds, according to orbital symmetry considerations[19], by the approach of the reactant and loss of the leaving

group from opposite sides of the reacting molecule. However, because of the increased distance between the reacting centres, a high degree of stereospecificity is not to be expected[19]; this would account for the formation of *both* epimeric 4-substitution products in each case (**2** → **3**, **4**), and obviate the need for postulating a subsequent epimerisation. The analogous nucleophilic replacements in the steroid series[12–15], if similarly classified, would add to the relatively small number of SN2″-substitutions that have so far been recorded in the literature[16].

The solvolysis of **2** by the action of sodium carbonate in aqueous ethanol has been reported[5] to give a mixture of (oily) 1-hydroxy-8-ethoxy- and (solid) 1,8-dihydroxydi-isophor-2(7)-en-3-one. According to its physical properties, the latter is identical with our 1,4α-dihydroxy-compound **3**, and should therefore be re-formulated in this sense. There is little doubt that the analogous solvolysis products ("1,8-dihydroxy-5,11-bisnor- and 1-hydroxy-8-ethoxydi-isophor-2(7)-en-3-one"[5]) are also 1,4- and not 1,8-isomers.

In conclusion we briefly describe the interaction of equimolar quantities of bromine and 1,3-dihydroxydi-isophor-2(7)-ene (**6**)[4,5] in glacial acetic acid, which may be correlated with the foregoing nucleophilic replacements. It gave a low-melting mixture of products, from which small yields of a bromine-free compound ($C_{18}H_{28}O_2$) were isolable. According to its i.r. spectrum (ν, 3.370 cm^{-1}) it contained hydroxy- but lacked keto-groups. Its carbon-13 n.m.r. spectrum[11] indicated the presence of one secondary and one tertiary hydroxyl-function and a pair of double bonds. The position of its absorption maximum in the u.v. range (λ_{max} 246 nm) showed that these formed a heteroannular[20] conjugated system.

The consequent formulation of the product as the 1,4-dihydroxy-2,7-diene **7** is consistent with its formation by the mechanism proposed above. Initial bromination of **6** at C-8 yields **J**; although this lacks an enolisable keto-group, it can form the conjugated 2(7),4-diene-system by loss of water (giving **K**); the synthesis of **6** by the reduction of **1** is in fact accompanied by such dehydration[5]. 4-Hydroxylation and simultaneous loss of bromine completes the process giving **7**.



Hydrazinolysis

With the object of extending the range of nucleophiles, the action of nitrogenous bases on 8-bromo-1-hydroxydi-isophor-2(7)-en-3-one (**2**) was also examined. The reactant was unaffected by liquid ammonia, and several attempted aminolyses gave discouraging results. However, the hydrazinolysis of **2** proceeded rapidly in a manner comparable with that of the other nucleophilic reactions.

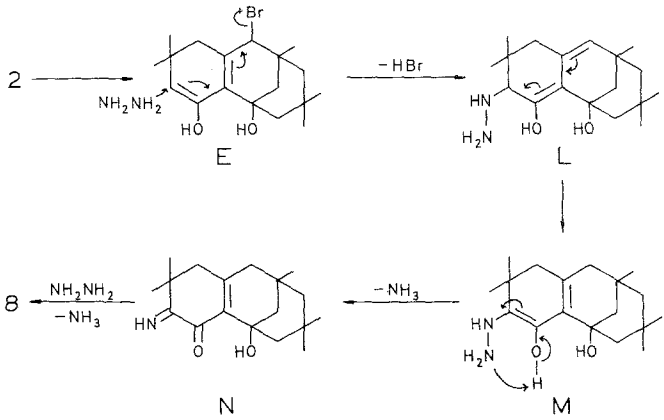
Thus, the interaction of **2** with an excess (preferably three moles) of hydrazine hydrate occurred with evolution of ammonia, giving high yields of a product formulated as 4-hydrazono-1-hydroxydi-isophor-2(7)-en-3-one (**8**). Its composition ($C_{18}H_{28}N_2O_2$) and molecular weight (304.2140) showed that the expected replacement had been accompanied by loss of 2 atoms of hydrogen. That no new ring incorporating the hydrazine residue had been formed was shown by the properties of the compound, which were consistent with the presence of a hydrazono- and hydroxy-group. Thus, absorption bands assignable to these substituents (at 3,360, 3,180 and at 3,430 cm^{-1}) were prominent features of its i.r. spectrum. A peak at 1,640 cm^{-1}, less intense and narrower than the usual characteristic keto-absorption, is thought to be associated with C=N-stretching vibration rather than the 3-keto group, the function of which appears to be suppressed (see below). The mass-spectrum of **8** included peaks that corresponded to the molecular ion, and to fragments derived therefrom by loss of amino-, hydrazono- and the usual[21] C_5H_{11} (mass 71)-moieties.

Unequivocal proof for the structure **8** was finally adduced from the alternative synthesis of the compound by the action of hydrazine on 1-hydroxydi-isophor-2(7)-ene-3,4-dione (**15**)[22]. The 4- (and not the 3-) position is thus established as the site of the hydrazono-group by a consideration of the formation (of **8**) from both sources (**2**, **15**).

In elucidating the nature of the present reaction (**2** → **8**), the observed migration, the apparent oxidation, and the loss of ammonia need to be accounted for. The conversion of α-bromoketones into α-ketohydrazones ($RBrCH \cdot COR' \rightarrow R(NH_2N{:})C \cdot COR'$) has previously been described and a mechanism proposed[23]. By combining this with the SN2″ mechanism adopted above, the action of hydrazine on **2** may be visualised to involve the following steps: the tautomerised reactant **E** yields, by the bimolecular (SN2″) replacement, the 4-hydrazino-compound **L**. Migration of its conjugated double bond system into its original homoannular position provides the intermediate **M**, from which the imino-ketone **N** arises by loss of ammonia (Scheme 3). Displacement of the 4-imino- by a hydrazono-group forms the observed product **8**. Three molecules of hydrazine are thus required for the completion of the process, as is indeed observed experimentally.

On treatment with equimolar quantities of aroyl chlorides, the 4-hydrazono-compound **8** gave mono-N-acyl-derivatives (**9**; $R = Ph$; 3,5-$(NO_2)_2C_6H_3$), as shown by the persistence of the hydroxyl peak in

Scheme 3

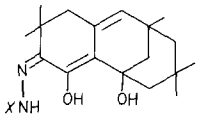


their i.r. spectra. Perchloric acid-catalysed[8] acetylation attacked all its replaceable hydrogen atoms, giving a triacetyl-derivative, though only in moderate yield.

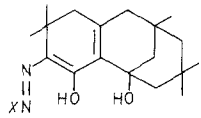
Conventional ketonic reagents, which normally react at the 3-oxo-group of di-isophorones without difficulty[4–6] failed to do so with the 4-hydrazone **8**, but participated in a facile exchange reaction involving the 4-hydrazono-substituent ("transhydrazination"). Thus, the action of arylhydrazines on **8** under standard conditions gave high yields of the corresponding 4-ω-arylhydrazono-analogues **10** and **11**. That migration does not occur during this exchange was established by the observation that the *same* 4-ω-phenylsemicarbazono-compound **12** ($Y = O$) was obtained when the 4-hydrazone **8** undergoes addition with phenyl isocyanate, or the exchange process with 4-phenylsemicarbazide.

The action of arylsulphonylhydrazines on **8** similarly gave the exchange products **13** ($Ar = Ph, p\text{-}Tol$) in very good yield. On more prolonged treatment however, the 3-sulphonylhydrazone **14** ($Ar = Ph$) of the parent di-isophorone (**1**) was the main product of the reaction. Its formation is visualised to involve the reduction of the initial trans-hydrazination product **13** ($Ar = Ph$) to di-isophorone (**1**) by the liberated hydrazine, followed by its conversion into the ketonic derivative **14** ($R = Ph$) in the usual way. The reduction by hydrazine of fluorenone N,N-dimethyl-hydrazone to the parent hydrocarbon

fluorene by a modified *Wolff-Kishner* reaction has been so interpreted[24]. Transhydrazinations of the type now described, but proceeding in the opposite sense, have attracted attention[24,25] because of their usefulness in affording hydrazones free from azines ($RR'C{:}N{-}N{:}CRR'$): aldehyde N,N-dimethylhydrazones yield the pure hydrazones by exchange with hydrazine.



8a X=H
9a X=Ph,$C_6H_3(NO_2)_2$
10a X=Ph
etc.



8b

The 3-oxo-group in **8** and its derivatives clearly does not exert its function fully, their absorption in the i.r. range near 1,640 cm^{-1} being more in accord with the effect of a C=N-moiety, and ketonic derivatives being unobtainable by the conventional methods. These anomalies are explicable by formulating the parent hydrazone **8** and its derivatives **9**–**13** as the enolic tautomers **8a**–**13a** which are probably stabilised by intramolecular hydrogen bonding. The alternative enolic structures (**8b** etc.) lack both carbonyl- and C=N-groups, and are thus inadmissible. The presence of the cumulative system of conjugated double bonds (in either **8** or **8a** etc.) is reflected in the bright yellow colour of the 4-hydrazone **8** and all its monosubstituted derivatives.

Experimental

General information is given in Part I[6] concerning equipment, standard procedures, reagents, solvents, and abbreviations. Light petroleum had b.p. 60–80° unless otherwise stated. Unassigned peaks of the i.r. spectra are not recorded, except for compounds **4**, **7** and **8**.

Hydrolysis and Acetolysis

1,4-Dihydroxydi-isophor-2(7)-en-3-one (**3**)

A stirred solution of 8-bromo-1-hydroxydi-isophor-2(7)-en-3-one (3.55 g, 0.01 mol)[5] in dioxan (40 ml) -water (30 ml) was treated dropwise at room temperature with N-sodium hydroxide (10 ml, 0.01 mol), and stirring continued for 20 min. The liquid was added to ice-water (250 ml), basified with 3 *N*-sodium hydroxide until a pale-yellow precipitate appeared (m.p. 85–90°, up to 2.7 g). This gave, on crystallisation from light petroleum, lustrous prisms (1.05–1.3 g, 36–45%) of the 1,4α-dihydroxy-compound **3**, m.p. 116–119°, identified [1] by its i.r. spectrum. H-NMR: 0.83 δ (s, 6 H, 2 Me), 0.95 (s, 3 H, Me), 1.03 (s, 3 H, Me), 1.20 (s, 3 H, Me), 2.10 (pseudo-s, 4 H, $2CH_2 \cdot C{=}C$), 3.73 (s, 1 H, OH), 4.04 (s, 1 H, OH).

The filtrates therefrom failed to yield more solid on evaporation. The residual oil was dissolved in glacial acetic acid (10 ml), treated with acetic anhydride (4 ml) and 60% perchloric acid (12 drops), set aside at room temperature for 2 h, then stirred into ice water. The soft precipitate, isolated by ether extraction, and crystallised from light petroleum, gave prisms (0.3–0.45 g, 8–12%) of 1,4β-diacetoxydi-isophor-2(7)-en-3-one (**5**), m.p. 185–186°, identified by its i.r. spectrum[1]. A further crop (m.p. 90–92°, ca. 4%) consisted, according to its i.r. spectrum, of a mixture of the 4α- and 4β-epimers of **5**.

Experiments performed at the b.p. of the mixed solvent (30 min) gave yellow oils, from which only low yields (ca. 15%) of the 1,4α-diol-3-one **3** were isolable (from light petroleum). Acetylation of the oily fraction from the motherliquors gave the two epimeric diacetates **5** in a total yield of 45%.

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

A solution of **2** (3.55 g, 0.01 mol) and anhydrous potassium acetate (2.95 g, 0.03 mol) in glacial acetic acid (20 ml) was boiled under reflux for 1.5 h, then stirred into water. The soft (sometimes oily) precipitate was extracted with ether. The washed (Na_2CO_3) dried extracts gave a residue which crystallised from light petroleum (Filtrate: F) to give lustrous platelets (1.4–1.65 g, 42–50%) of the 4α-acetoxy-1-hydroxy-compound **4**, m.p. 107–108°. (Found: C 71.9; H 9.3. $C_{20}H_{30}O_4$ requires C 71.9, H 9.0%). ν_{max} 3520 s (OH), 2970–2900 vs br, 1475 ms (CH_3, CH_2), 1745 vs (CO of *Ac*), 1665 vs br (CO), 1635 s (C=C, conjug.), 1395 s, 1375 vs (.C*Me*$_2$), 1235 vs br (C—O—C ester), 1085 s, 1055 vs, 995 ms, 915 m, 815 m, 690 w cm^{-1}.

The filtrates F from four experiments were evaporated in a vacuum, and the residual oil acetylated in acetic acid (10 ml)-acetic anhydride (5 ml)-60% perchloric acid (6 drops) at room temperature for 2 h. The usual work-up, and crystallisation from light petroleum gave four successive fractions; the first two gave, on further crystallisation from the same solvent, lustrous prisms (1.35 g, 9%) of the 1,4β-diacetate **5**[1], identified by mixed m.p. 186–188° and its i.r spectrum. The last fractions similarly gave minute prisms (1.20 g, 8%) of the 4α-epimer **5**, mixed m.p. 132–133°[1].

The use of sodium acetate (2.5 g, 0.03 mol) in the foregoing procedure gave the same product **4** in ca. 30% yield, or, after acetylation of the total hydrolysis product, and fractional crystallisation as above, 1,4β-diacetoxydi-isophor-2(7)-en-3-one (**5**) (12%), and its 4α-epimer (25%), respectively. U. v. spectra of **5**: 1,4α-Diacetoxy-epimer (m.p. 133°): λ_{max} 247 nm (log ε, 3.95); 1,4β-diacetoxy-epimer (m.p. 186°): λ_{max} 250 nm (log ε, 3.76).

1,4α-Diacetoxydi-isophor-2(7)-en-3-one (**5**)

A solution of 1,4α-dihydroxy- (0.29 g, 0.001 mol) *or* 4α-acetoxy-1-hydroxydi-isophor-2(7)-en-3-one (0.33 g, 0.001 mol) in glacial acetic acid (10 ml)—acetic anhydride (6 ml), treated with 60% perchloric acid (6 drops), was set aside at room temperature for 2 h, then stirred into water. The white precipitate gave minute prisms (ca. 70%) of the 1,4α-diacetoxy-derivative **5** (from light petroleum), identified by mixed m.p. 132–133° and i.r. spectrum[1].

1,4-Dihydroxydiisophora-2,7-diene (**7**)

A solution of 1,3-dihydroxydi-isophor-2(7)-ene[4] (2.78 g, 0.01 mol) in glacial acetic acid (100 ml) containing 60% hydrobromic acid (0.25 ml) was slowly treated dropwise during 2 h with M-bromine in glacial acetic acid (10 ml,

0.01 mol), decolourisation occurring instantly. The liquid was added to ice-water, the separated oily resin extracted with ether, and the oil therefrom dissolved in light petroleum. The solution deposited opaque white prisms (0.33 g, 12%) of **7**, m. p. 168-169° (after recrystallisation from the same solvent) (Found: C 77.8, H 10.4. $C_{18}H_{28}O_2$ requires C 78.3; H 11.6%). ν_{max} 3370 vs tr (OH), 2950-2880 vs br, 1475 m (CH_3, CH_2), 1385 s br (.C*Me*$_2$), 1360 s, 1115 ms, 1040 vs, 900, 895 s.d., 830 s cm^{-1}. *m/e*: 276 ms (M^+), 258 s (M^+—18), 243 s (M^+—18-15), 205 m (M^+—71), 204 m, 203 vs, 202 vs, 187 vs (M^+—71-18). The motherliquors gave, on spontaneous evaporation, uncrystallisable nearly colourless oily residues.

Action of Hydrazine

8-Bromo-1-hydroxydi-isophor-2(7)-en-3-one was recovered (70%), when its solution (0.005 mol) in liquid ammonia (ca. 100 ml) was kept at ca. —50° for 5 h, and the solvent allowed to evaporate spontaneously.

4-Hydrazono-1-hydroxydi-isophor-2(7)-en-3-one (**8**)

(a) *Preparation.*—A solution of 8-bromo-1-hydroxydi-isophor-2(7)-en-3-one (17.75 g, 0.05 mol) in warm ethanol (80 ml) was treated with hydrazine hydrate (7.5 g, 0.15 mol) and boiled under reflux for 3 h, ammonia being evolved during the addition and boiling. The dark-red liquid was stirred into ice-water (1 l), the yellow granular precipitate collected at once, and rinsed with water. It tended to resinify and was quickly added to boiling ethanol (50-60 ml). The greater part dissolved, leaving a variable amount of yellow crystalline solid; the remainder reappeared crystalline on cooling and storage (m. p. 155-157°; 7.6-9.75 g, 50-64%, occasionally 70%). Recrystallisation from the same solvent (3 ml per g, recovery 70-80%) gave **8** as yellow prismatic plates, m. p. 160-162°. (Found: C 71.0; H 9.3; N 9.1. *M*, mass-spectrometrically, 304.2141. $C_{18}H_{28}N_2O_2$ requires C 71.05; H 9.2; N 9.2%. *M* = 304.2151). ν_{max} 3430 s sh (OH); 3360 vs, 3180 s (NH_2), 2960-2850 vs (CH_3, CH_2), 1640 s (C=N), 1395 m, 1380 s d (.C*Me*$_2$), 1560 vs br, 1485 vs, 1470 vs, 1410 vs, 1265 s, 1225 vs, 1185 s, 1045 vs, 995 s, 890 s, 880 s, 780 w br cm^{-1}. *m/e* 305 w (M^+ + 1), 304 ms (M^+), 289 ms (M^+—15), 288 s (M^+—16, ?NH_2), 287 s (M^+—18), 258 s (M^+—16-30, ?:NNH_2), 243 m (M^+—16-30-15), 234 s (M^+ + 1-71), 233 s (M^+—71), 216 ms, 201 s.

(b) *Monobenzoyl Derivative* (**9**, *R* = *Ph*).—A solution of **8** (0.91 g, 0.003 mol) in anhydrous pyridine (12 ml), treated with benzoyl chloride (0.42 g, 0.003 mol), was kept at 100° for 1 h, then stirred into ice-water containing concentrated hydrochloric acid (12 ml), and the (washed) precipitate added to boiling ethanol (20 ml). The resulting crystalline solid (40%) gave deep-yellow prismatic needles of **9**, (*R* = *Ph*), m. p. 182-183° (from light petroleum-ethanol) (Found: C 73.7; H 8.0; N 6.8. $C_{25}H_{32}N_2O_3$ requires C 73.5; H 7.8; N 6.9%). ν_{max} 3540 m (OH), 3250 m br (NH), 2960-2870 vs (CH_3, CH_2), 1700 vs (CO of *Bz*), 1630 s (C=N), 1600 ms (?C=C), 1385 m, 1370 s (.C*Me*$_2$), 695 vs (*Ph*) cm^{-1}.

(c) *3,5-Dinitrobenzoyl Derivative* [**9**, *R* = $C_6H_3(NO_2)_2$-3,5].—The use of 3,5-dinitrobenzoyl chloride (0.69 g, 0.003 mol) in the foregoing procedure produced a solid (m. p. 159-160°, 0.9 g, 64%) which gave lemon-yellow needles of **9** [*R* = $C_6H_3(NO_2)_2$], m. p. 163-164° (from ethanol) (Found: C 60.7; H 6.2; N 11.3. $C_{24}H_{30}N_4O_6$ requires C 61.3; H 6.4; N 11.9%). ν_{max} 3520 s (OH), 3180, 3100 s (NH, *Ar*), 2980-2870 vs (CH_3, CH_2), 1680 vs (CO of aryl), 1620 vs (C=N), 1385 ms, 1345 vs (.C*Me*$_2$), 730 s, 720 s (1,3,5-trisub. *Ar*) cm^{-1}.

(d) *Triacetyl Derivate.*—A solution of **8** (0.91 g, 0.003 mol) in acetic anhydride (10 ml)—60% perchloric acid (3 drops) was set aside at room temperature for

1 h, then stirred into hot water (100 ml). The separated solidified oil gave, on crystallisation from light petroleum (b. p. 40–60°, ca. 50 ml) or ethanol (10 ml), colourless prismatic needles (0.41 g, 32%) of the N,N,O-triacetyl derivate, m. p. 244–246° (Found: C 66.9; H 8.1; N 6.5. $C_{24}H_{34}N_2O_5$ requires C 67.0; H 7.9; N 6.5%). ν_{max} 2960–2870 vs (CH_3, CH_2), 1725 vs (CO of *Ac*), 1685, 1670 vs vbr (?N*Ac*$_2$, CO), 1630 s (C=N), 1395 s, 1370 vs (.C*Me*$_2$), 1275–1240 vs mult (C—O—C, ester) cm^{-1}. *m/e* 430 s (M^+), 387 s (M^+—43, *Ac*), 369 s (M^+—43–18), 344 m (M^+—2 × 43), 327 s (M^+—43–60), 256 s (M^+—2 × 43–60–28).

Transhydrazinations

1-Hydroxy-4-(phenylhydrazono)di-isophor-2(7)-en-3-one (**10**)

A solution of **8** (0.61 g, 0.002 mol) and phenylhydrazine (0.43 g, 0.002 mol) in ethanol (12 ml)-concentrated hydrochloric acid (1 ml) was boiled under reflux for 30 min, then allowed to cool to room temperature. The separated platelets of phenylhydrazine hydrochloride were filtered off. The filtrate deposited, on storage at 0°, a deep yellow solid (m. p. 162–164°, 0.55 g, 72%), which gave elongated orange-yellow prisms of **10**, m. p. 162–163° (from ethanol). (Found: C 76.1; H 8.3; N 7.4. $C_{24}H_{32}N_2O_2$ requires C 75.8; H 8.4; N 7.4%). ν_{max} 3510 vs (OH), 3340 s (NH), 3080 w, 755 vs, 705 vs (*Ph*), 2970–2860 vs (CH_3, CH_2), 1635 s (C=N), 1390 s, 1365 vs (.C*Me*$_2$) cm^{-1}. *m/e* 380 vs (M^+), 309 m (M^+—71), 216 m (M^+—71–93, *Ph*NH_2).

1-Hydroxy-4-(2,4-dinitrophenylhydrazono)di-isophor-2(7)-en-3-one (**11**)

To a warm solution of **8** (0.61 g, 0.002 mol) and 2,4-dinitrophenylhydrazine (0.79 g, 0.004 mol) in ethanol (15 ml), concentrated hydrochloric acid (2 ml) was added. The dark-red liquid was boiled for a few minutes, then set aside, when the product separated nearly quantitatively, giving **11** as a deep yellow microcrystalline powder, m. p. 225° (decomp.) (from ethanol). (Found: C 61.4; H 6.5; N 11.5. $C_{24}H_{30}N_4O_6$ requires C 61.3; H 6.4; N 11.9%). ν_{max} 3550 s (OH), 3200 ms (NH), 3120 ms (*Ar*), 2970–2880 vs (CH_3, CH_2), 1615 vs (C=N), 1390 mw, 1340 vs (.C*Me*$_2$), 895 ms, 885 ms, 855 m, 835 m (1,2,4-trisub. *Ar*) cm^{-1}. *m/e* 470 ms (M^+), 452 vs (M^+—18), 399 vs (M^+—71), 381 s (M^+—71–18), 216 ms [M^+—71–183, $C_6H_3(NO_2)_2NH_2$].

1-Hydroxy-4-(4-phenylsemicarbazono)di-isophor-2(7)-en-3-one (**12**, *Y* = O)

(a) A solution of **8** (0.91 g, 0.003 mol) in pyridine (12 ml), treated with phenyl isocyanate (0.39 g, 0.0033 mol), was kept at 100° for 30 min, then stirred into ice-water containing concentrated hydrochloric acid (12 ml). The precipitate gave yellow prisms (0.91 g, 72%) of **12** (*Y* = O), m. p. 182–183° (from ethanol) (Found: C 71.3; H 8.0; N 9.95. *M*, mass-spectrometrically, 423. $C_{25}H_{33}N_3O_3$ requires C 70.9; H 7.8; N 9.9%. *M* = 423). ν_{max} 3510 s (OH), 3380 ms, 3250 ms (NH), 3050 w, 755 vs, 695 s (*Ph*), 2940–2850 vs (CH_3, CH_2), 1715 vs (CO, amide), 1620 vs br (C=N), 1380 ms, 1355 s (.C*Me*$_2$) cm^{-1}.

(b) A solution of **8** (0.91 g, 0.003 mol) and 4-phenylsemicarbazide (0.68 g, 0.0045 mol) in ethanol (15 ml)-concentrated hydrochloric acid (6 drops) was boiled under reflux for 1 h. The product which sparated on cooling (total, 0.81 g, 64%) formed prisms (from ethanol) identical with the product obtained in (a).

1-Hydroxy-4-(4-phenylthiosemicarbazono)di-isophor-2(7)-en-3-one (**12**, *Y*=S)

The use of phenyl isothiocyanate (0.45 g, 0.0033 mol) in the foregoing procedure (a) gave **12** (*Y*=S) as yellow platelets with a metallic lustre, m.p. 187–188° (from ethanol) (1.06 g, 80%) (Found: C 67,6; H 7.5; N 9.4; S 8.0. $C_{25}H_{33}N_3SO_2$ requires C 68.3; H 7.5; N 9.6; S 7.3%). ν_{max} 3510 s (OH); 3300 vs mult (NH); 3050 mw, 745 vs, 695 vs (Ph); 2970–2850 vs br (CH_3, CH_2), 1630 s (C=N), 1390 s, 1370 s d (.C*Me*$_2$) cm^{-1}. *m/e* 439 s (*M*$^+$), 423 w (*M*$^+$—16), 421 mw (*M*$^+$—18), 346 m (*M*$^+$—93, *Ph*NH_2), 304 ms (*M*$^+$—135, *Ph*NCS), 275 w (*M*$^+$—93-71).

1-Hydroxy-4-(benzenesulphonylhydrazono)di-isophor-2(7)-en-3-one (**13**, *Ar*=*Ph*)

A solution of **8** (0.61 g, 0.002 mol) and benzenesulphonylhydrazine (0.52 g, 0.003 mol) in ethanol (12 ml)-concentrated hydrochloric acid (6 drops) was boiled under reflux for 30 min. The solid separating on storage (0.62 g, 70%) gave pale-yellow prismatic needles of **13** (*Ar*=*Ph*), m.p. 158–159° (Found: C 64.5; H 7.3; N 6.4. $C_{24}H_{32}N_2O_4S$ requires C 64.9; H 7.2; N 6.3%). ν_{max} 3520 s (OH), 3200 s (NH), 3080 w, 750 vs, 685 s (*Ar*), 2960–2860 vs, 1445 ms (CH_3, CH_2), 1615 vs (C=N), 1390 ms, 1365 vs (.C*Me*$_2$), 1305 s, 1165 vs, 1045 s (SO_2) cm^{-1}.

The use of 0.004 mol of benzenesulphonylhydrazine and more prolonged boiling (3 h) gave a product which afforded nearly colourless prisms (0.6 g, 70%) of *3-benzenesulphonylhydrazono-1-hydroxydi-isophor-2(7)-ene* (**14**), m.p. 220–221° (decomp.) (Found: C 67.1; H 8.0; N 6.6; S 7.55. Calc. for $C_{24}H_{34}N_2O_3S$: C 67.0; H 7.9; N 6.5; S 7.4%), identical with material prepared from **1**.

1-Hydroxy-4-(toluene-p-sulphonylhydrazono)di-isophor-2(7)-en-3-one (**13**, *Ar*=*p-Tol*)

The use of toluene-*p*-sulphonylhydrazine[26] (0.56 g, 0.003 mol) in the foregoing procedure gave yellow prismatic needles (64–72%) of **13** (*Ar*=*p-Tol*), m.p. 154–155° (Found: C 65.3; H 7.6; N 6.1. $C_{25}H_{34}N_2O_4S$ requires C 65.5; H 7.4; N 6.1%). ν_{max} 3530 vs (OH), 3200 vs (NH), 3080 w (*Ar*), 2930–2840 vs (CH_3, CH_2), 1615 vs (C=N), 1550 m (?C=C), 1390 ms sh, 1370 vs (.C*Me*$_2$), 1305 vs, 1170 vs br, 1050 vs br (SO_2), 845 vs br (1,4-disub. *Ar*) cm^{-1}.

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