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Diisophorone and Related Compounds. Part 19 [1] Synthesis and Reactions of 6,8-Dibromodiisophorones

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Novel 6,8-dibromo-derivatives of diisophor-2(7)-en-1-ol-3-one and the corresponding 1-carboxylic acid methyl ester are readily accessible by the action of 2 mol of N-bromosuccinimide on the respective parent compounds. Treatment with alkali converts the 6,8-dibromo-ketol, by a simultaneous 8-substitution and ring A-aromatisation, into 6-methyl-5-nordiisophora-2(7),3,5-triene-1,3,8-triol; acetolysis and methanolysis produce the corresponding 8-acetoxy- and 8-methoxy-compounds. The 6,8-dibromo-1-carboxylic acid reacts analogously, with the added option of 1,3-lactone formation. The assigned ^{13}C-nmr spectra and fragmentation patterns of the new compounds are in accord with their proposed formulation.

(Keywords: 6,8-Dibromodiisophorones, synthesis of, ring A aromatisation of; Ring A-aromatised tricyclo[7.3.1.0^{2,7}]tridecanes)

Diisophoron und verwandte Verbindungen, 19. Mitt.: Synthese und Reaktionen von 6,8-Dibromdiisophoronen

Neuartige 6,8-Dibrom-Abkömmlinge des Diisophor-2(7)-en-1-ol-3-ons und der entsprechenden 1-Carbonsäure (als Methylester) sind durch Einwirkung von 2 mol N-Bromsuccinimid auf die betreffende Grundverbindung leicht zugänglich. Bei der Umsetzung des 6,8-Dibromketols mit Alkalien entsteht 6-Methyl-5-nordiisophora-2(7),3,5-trien-1,3,8-triol, unter gleichzeitiger 8-Substituierung und Ring-A-Aromatisierung. Acetolyse und Methanolyse ergeben die entsprechenden 8-Acetoxy- und 8-Methoxy-Verbindungen. Die 6,8-Dibrom-1-carbonsäure reagiert analog, mit weiterer Möglichkeit zur 1,3-Lacton-Bildung. Die ^{13}C-Kernresonanz- und Massenspektren der neuen Verbindungen stehen mit den Strukturzuordnungen im Einklang.

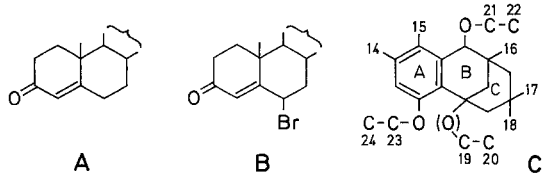
Introduction

The action of nucleophilic reagents on halogenated diisophorones effects the expected replacements [2–6], but is generally attended by more

complex changes, including isomerisations [7, 8], cyclisation [9], aromatisation [2, 10] and ring-contraction [1]. The wide scope of this approach of modifying the tricyclo[7.3.1.$0^{2,7}$]tridecane structure is partly founded on the ready availability of diisophorones containing halogen substituents appropriate in number and location. Thus, halogenation by molecular bromine of the parent ketol **1** or the 1-carboxylic acid **8** yields successively 8-mono- [4, 8, 11], 4,8-di- [6], and 4,4,8-tribromo-diisophorones [12], and specific methods are available for the production of 1-halogeno- [11], 4-monobromo- [5], and 4,6,8-tribromo-compounds [2, 12]. We now report a facile synthesis of novel 6,8-dibromodiisophorones by the *Wohl-Ziegler* reaction [13, 14]; their interaction with nucleophiles is attended by aromatisation of ring A, thus providing a general route to compounds of structure **C**, comprising a condensed bicyclo[3.3.1]nonane and benzene ring system (for nomenclature, see Part 11 [10]).

Results and Discussion

Allylic bromination of alicyclic compounds by N-bromosuccinimide [13, 14] occurs at methylene-groups adjacent to ethylenic as well as ketonic unsaturated centres, as is shown by the conversion of cyclohexene into 1-bromo- and 1,4-dibromo-cyclohex-2-ene [15], and of cyclohexanone into its 2-bromoderivative [16]. In alicyclic α-unsaturated ketones, the directing influence of the ethylenic bond clearly predominates, since 3,5,5-trimethylcyclohex-2-enone (isophorone) gives the 4-bromo-derivative [17], and unsaturated 3-keto-Δ^4-steroids (e.g. testosterone, progesterone) are converted into the 6-substituted products (**A** → **B**) [18]. Homolytic bromination at the two allyl-positions in diisophorones thus appeared to be a potential route to the as yet unknown 6,8-dibromodiisophorones: the synthesis was in fact readily realised in practice.



A B C

Wohl-Ziegler Reaction

Treatment of the parent ketol **1** with *two* moles of N-bromosuccinimide gave 6,8-dibromodiisophor-2(7)-en-1-ol-3-one (**3**) in satisfactory yield. The proposed location of the two halogen substituents, suggested by the method of preparation, is confirmed as follows: The action of *one* mole of

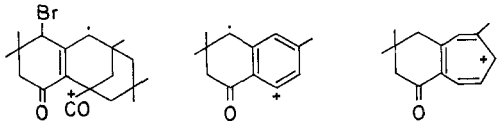
N-bromosuccinimide on the authentic preformed 8-bromodiisophorone (**2**) [2, 11] gave the identical dibromo-compound **3**, showing C-8 to be one of the sites of bromination. The presence of the second halogen substituent in ring A (of **3**) was in accord with the ready aromatisation of this cyclohexane moiety upon dehydrobromination (see below). The non-identity of the dibromo-compound **3** with *either* steric (4α,4β-)forms of the 4,8-dibromo-isomer (compared as their 1-acetates [6]) indicates its 6,8-dibromo-structure by exclusion. The implied assumption of the resistence of ring C to halogenation is justified, in general terms, by its proved inertness in all reactions of diisophorones so far examined, and more specifically in the present example, by its remoteness from the activating unsaturated centre. The 6,8-dibromo-formulation receives additional support from the ^{13}C-nmr spectral data (see below).

Allylic bromination of diisophorone occurs successively at its C-8 and C-6 positions, as is shown by the preferential formation of 8-monobromo-derivatives by the action of *one* mole of N-bromosuccinimide. This reaction, first reported by *Kabas* and *Rutz* [11], produces low yields of the 8-bromoketol **2** (35%), together with much uncrystallisable resin, probably due to the rapid competitive 6-bromination of the 8-monobromo-compound **2** first formed, resulting in intractable mixtures of **1**, **2** and **3**. Finally, the action (on **1**) of an excess of N-bromosuccinimide (e.g. 3 mol) effected the same *di*bromination (**1** → **3**), attack being confined to the two olefinic allyl-positions.

Wohl-Ziegler bromination of the diisophorone-1-carboxylic acid (employed as the soluble methyl ester **9**) similarly afforded the 8-monobromo- (**10**) and 6,8-dibromo-compounds (**12**) successively. The former (**10**), which arose more uniformly in better yield (56%) than the 8-bromoketol **2**, was again the intermediate in the 6,8-dibromination. Because of the limited solubility of diisophorone-1-carboxylic acid **8** in suitable non-polar solvents, the free 6,8-dibromo-1-carboxylic acid **11** was not directly accessible by the present method, but was readily produced by *Koch-Haaf* carboxylation [8, 19] of the 6,8-dibromoketol **3**; its methyl ester **12**, obtained by the action of diazomethane, was identical with the product of the direct dibromination (**9** → **12**). The brominations were promoted by conditions favouring the generation of free radicals, including the presence of benzoyl peroxide [16] or irradiation by ultraviolet light [20], reflecting the established homolytic mechanism [14, 21] of this reaction.

In contrast to their 4,8-disubstituted isomers [6], the 6,8-dibromo-compounds **3**, **11**, and **12** are sterically homogenious: their probable 6α-ax,8β-eq-configuration may be proposed on the basis of the favoured 8β-eq-configuration of 8-monobromodiisophorones, which is supported by ^{1}H-nmr spectral evidence in the case of the 8-bromoketol [2], and the

presumed maximal spatial separation of the halogen substituents in the dibrominated products (compare Ref. [22]). It is noted, however, that a 6α-ax-substituent is subject to a measure of steric hindrance from the 17-methyl-group, which is not encountered in the 6β-eq-conformer.



a *m/e* 364,366 b *m/e* 186 c *m/e* 201

Mass Spectra.—The fragmentation of the 6,8-dibromodiisophorones under electron impact resembles that of the diisophorones in general [23] and that of the 4,8-dibromo-isomer [6] in particular. Elimination of the extranuclear substituents yields fragments such as **a**, while removal of ring C by ejection of the neopentyl radical (.CH_2CMe_3, *m/e* 71) leaves naphthalene-like species (e.g. **b**), or by loss of isopropylidene (CH_2 : CMe_2, *m/e* 56) and rearrangement produces the condensed tropylium ion **c**; the high intensity of the relevant signal (*m/e* 201) suggests, that the contribution of the last process is substantial.

^{13}C-*Nmr Spectra.*—The ^{13}C-nmr spectra of the 6,8-dibromo-compounds **3** and **12**, assigned by reference to established precedents [24, 25], and by their correlation with those of comparable bromodiisophorones [5, 24, 25], corroborate the proposed 6,8-dibromo-structures. Thus, the chemical shifts of their C-3 singlets (**3**, 200.4; **12**, 196.3 ppm) are nearly identical with those of their parent compounds (**1**, 200.7; **9**, 196.6 ppm), confirming the absence of a 4-bromo-substituent, which is known [5] to shield the C-3 carbon (by 7.5 and 7.3 ppm in **1** and **9** respectively). In contrast, the expected shielding of C-7 on introduction of the vicinal 8-bromo-substituent is clearly observed in both the ketol and ester series (Table 2). Its magnitude ($\triangle\delta$, ca. $-$ 4 ppm) is roughly doubled upon entry of the second bromo-substituent at the other available adjacent site (i.e. C-6). The chemical shifts of C-7 in the 4-mono- and 4,8-dibromo-isomers are all consistent with this interpretation (Table 2).

Ring A-Aromatisation

The action of aqueous alkali or methanolic sodium methoxide on the 6,8-dibromoketol **3** gave good yields of products formulated as 6-methyl-5-nordiisophora-2(7),3,5-triene-1,3,8-triol (**4**) (or its 8-methoxy-homologue, **6**) (for nomenclature, see Ref. [10]). Their composition and molecular weight, the benzenoid features of their uv and ir spectra, as well as the characteristics of their ^{13}C-nmr and mass spectra indicated the

Table 1. ^{13}C-*nmr spectra of diisophorones and their assignments*

Compound[a]	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9
				6,8-Dibromodiisophorones					
3	71.8 s	135.8 s	200.4 s	45.0 t	*35.7 s	+61.4 d	149.4 s	+63.3 d	*36.5 s
12	44.9 s	136.0 s	196.3 s	44.8 t	*∅34.0 s	+61.6 d	148.5 s	+62.7 d	*36.6 s
				6-Methyl-5-nordiisophora-2(7),3,5-trienes					
19	75.8 s	*124.2 s	152.9 s	115.9 d	+136.5 s	*124.5 s	+136.7 s	41.5 t	33.3 s
4	74.7 s	*125.7 s	154.9 s	117.7 d	+137.2 s	*126.6 s	+139.7 s	73.1 d	39.3 s
5	75.4 s	*124.8 s	153.3 s	119.1 d	+133.9 s	*127.2 s	+138.3 s	74.8 d	38.6 s
7	81.0 s	130.5 s	145.0 s	125.6 d	*134.7 s	*134.6 s	137.5 s	74.3 d	37.9 s
6	74.6 s	*124.8 s	153.2 s	118.4 d	+135.7 s	*127.0 s	+137.6 s	84.2 d	39.8 s
15	45.9 s	*125.0 s	150.3 s	117.7 d	+136.1 s	*128.3 s	+136.7 s	82.3 d	37.2 s
16	46.2 s	*127.1 s	153.1 s	117.5 d	+136.2 s	*127.3 s	+137.4 s	83.0 d	37.5 s
17	46.1 s	*130.5 s	146.0 s	125.2 d	+135.8 s	*134.2 s	+137.0 s	74.2 d	35.9 s
18	44.7 s	*128.2 s	148.8 s	111.4 d	+133.7 s	*129.4 s	+137.9 s	72.8 d	38.9 s

Compound[a]	C-10	C-11	C-12	C-13	C-14	C-15	C-16	C-17	C-18
				6,8-Dibromodiisophorones					
3	49.6 t	31.5 s	47.5 t	36.3 t	○29.9 q	24.2 q	○31.3 q	34.0 q	34.5 q
12	46.6 t	∅33.9 s	40.8 t	33.7 t	○29.9 q	23.9 q	○30.9 q	33.9 q	34.5 q
				6-Methyl-5-nordiisophora-2(7),3,5-trienes					
19	52.8 t	31.7 s	49.4 t	48.1 t	20.4 q	14.3 q	27.2 q	33.5 q	37.1 q
4	○50.8 t	31.4 s	○50.4 t	42.4 t	20.6 q	14.6 q	∅29.1 q	∅29.5 q	37.9 q
5	○49.2 t	31.3 s	○49.1 t	43.4 t	∅20.7 q	14.6 q	28.2 q	28.5 q	37.4 q
7	48.7 t	31.0 s	47.8 t	37.5 t	○20.8 q	15.2 q	∅28.2 q	∅29.4 q	37.3 q
6	50.1 t	31.1 s	48.5 t	42.6 t	20.8 q	15.3 q	○28.7 q	○29.1 q	37.4 q
15	49.9 t	29.6 s	42.7 t	38.5 t	20.7 q	14.8 q	○29.0 q	○29.8 q	37.7 q
16	49.9 t	29.9 s	43.7 t	38.8 t	20.8 q	15.2 q	○29.4 q	○30.5 q	37.8 q
17	49.2 t	29.6 s	44.4 t	38.6 t	∅20.8 q	14.8 q	○28.3 q	○29.3 q	37.6 q
18	51.6 t	30.6 s	46.4 t	34.7 t	∅20.6 q	14.6 q	○27.3 q	○29.2 q	36.8 q

*+○∅ Signals may be exchanged horizontally. [a] Spectra were determined in deuteriochloroform except those of compounds **4**, **16**, and **17**, for which deuteriopyridine was used

Supplementary Table 1. *Signals of extranuclear carbon atoms*

Compound[a]	C-19	C-20	C-21	C-22	C-23	C-24
			6,8-Dibromodiisophorones			
12	175.9 s	52.1 q	—	—	—	—
			6-Methyl-5-nordiisophora-2(7),3,5-trienes			
5	—	—	170.5 s	∅21.0 q	—	—
7	+170.6 s	○21.9 q	+169.5 s	○21.4 q	+169.1 s	○21.0 q
6	—	—	60.3 q	—	—	—
15	185.2 s	—	58.5 q	—	—	—
16	179.0 s	51.6 q	59.1 q	—	—	—
17	177.3 s	51.8 q	+170.2 s	∅20.7 q	+169.0 s	○20.4 q
18	179.8 s	—	170.2 s	∅20.9 q	—	—

*+○∅ Signals may be exchanged horizontally

[a] Spectra were determined in deuteriochloroform except those of compounds **4**, **16** and **17**, for which deuteriopyridine was used

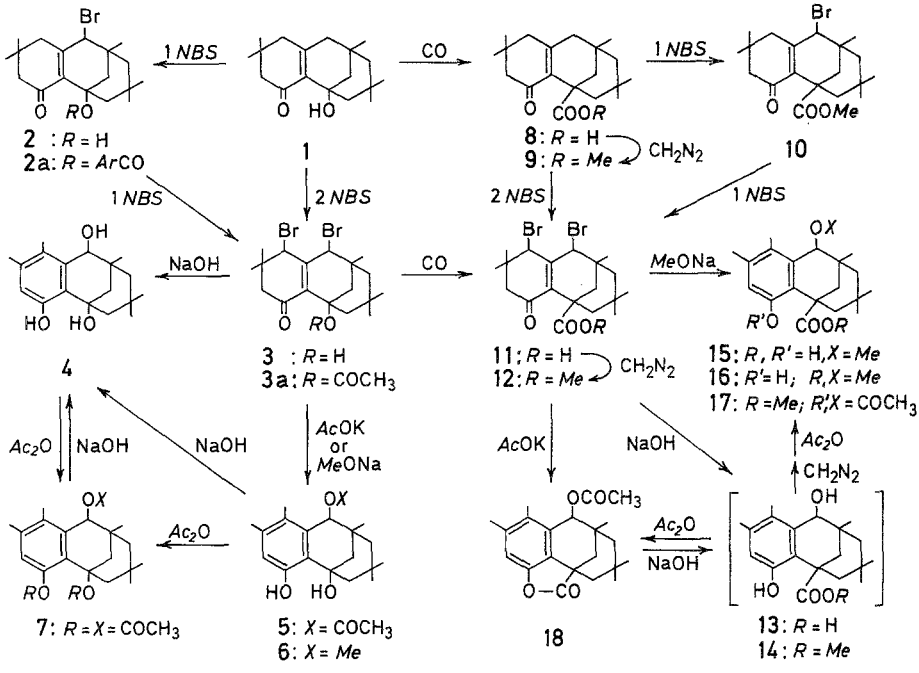
Table 2. *Chemical shifts (in ppm) of C-7 singlets in bromo-diisophorones*

	Ketol	1-Methyl ester
Parent diisophorones (**1**, **9**)	157.5	155.8
8-Bromo-derivatives (**2**, **10**)	153.0	151.7
6,8-Dibromo-derivatives (**3**, **12**)	149.4	148.5
4α-Bromo-derivatives	157.0	157.0
4β-Bromo-derivative	158.9	—
4α-,8-Dibromo-derivatives	153.3	151.6
4β-,8-Dibromo-derivative	152.6	—

contribution of an aromatic moiety to their structure. The seat of this aromaticity is ring A, since the retention of the bridgehead substituents at C-1 and C-9, shown by the ^{13}C-nmr spectral data, precludes aromatisation elsewhere in the molecule. The necessary simultaneous migration of one of the 5-methyl-groups may result in 5,6- or 4,5-dimethyl-structures: the former alternative is adopted, as conforming with the 5,6-dimethyl-structure of a comparable aromatisation product that has been established by X-ray analysis [10].

Acetolysis of the 6,8-dibromoketol **3** by potassium acetate in glacial acetic acid gave high yields of the 8-acetoxy-analogue **5**; on acetylation, this gave the triacetate **7**, identical with that obtained directly from the parent 1,3,8-triol **4**.

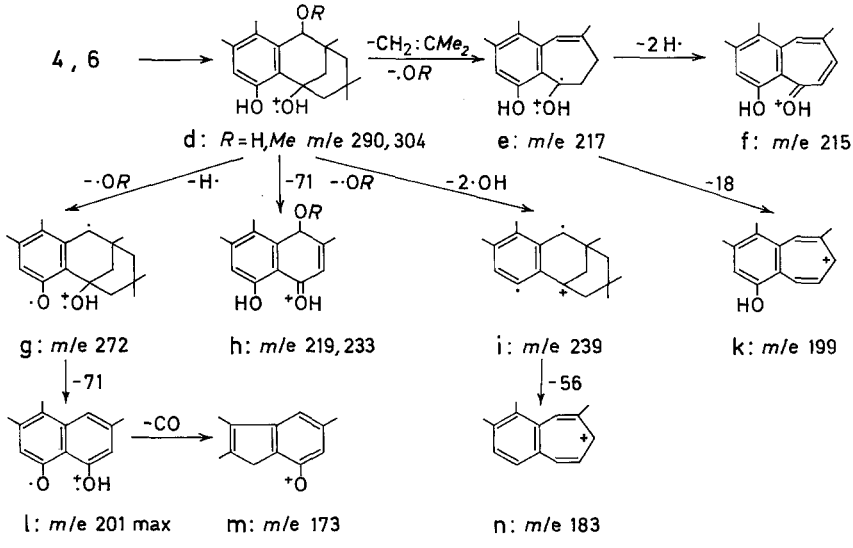
It is recalled that comparable nucleophilic reactions of 8-monobromo-diisophorones yield 4-substituted products, by an apparent migration that may involve an SN2″-mechanism [7]. In the present examples, the substituents (OH, O*Me*, $OCOCH_3$) replacing the 8-bromo-atom retain the 8-position, as shown by the appearance of the appropriate doublets in the ^{13}C-nmr spectra of the products.



Alkaline hydrolysis of 6,8-dibromodiisophor-2(7)-en-3-one-1-carboxylic acid (**11**) gave a product which, though amorphous and resinifying on attempted purification, was the expected aromatised 3,8-dihydroxy-1-carboxylic acid **13**: it was characterised by being subjected to acetylation, with or without preliminary esterification by diazomethane. In the former case, the 3,8-diacetoxy-1-methoxycarbonyl-compound **17** was obtained from the intermediate methyl ester **14**, itself a low-melting uncrystallisable material. Treatment of crude **13** directly with acetic acid-acetic anhydride at room temperature in presence of perchloric acid effected 8-acetylation side by side with dehydration involving the free 1-carboxyl- and 3-hydroxy-groups. The resulting 8-acetoxy-1,3-lactone **18** was also the product of the *acetolysis* of the 6,8-dibromo-1-carboxylic acid **11** (and of its methyl ester, **12**), when 8-substitution and aromatisa-

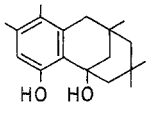
tion is attended by 1,3-lactone formation under the dehydrative (and hydrolytic) conditions. The lactone **18** was reconvertible by alkaline hydrolysis into the parent acid **13** (characterised as **17**). Unlike the amorphous parent acid **13**, its 8-methoxy-homologue **15**, arising in the *methanolysis* of **11**, was readily isolable in high yield. Its methyl ester **16** was identical with material obtained directly from the 6,8-dibromo-1-methyl ester **12** by methanolysis.

Mechanism.—The reactions now described consist in each case of two distinct components, viz. the replacement at C-8, and the aromatisation of ring A by a net dehydrobromination. The former is thought to proceed by an SNl-substitution, the alternative concerted process being disfavoured by the steric constraints that oppose the rear-face approach of the nucleophile. The aromatisation is explicable in terms of a mechanism comprising the tautomerisation of the 3-keto-group, formation of a carbonium ion by loss of bromide ion from C-6, and (5 → 6)-migration of one of the 5-methyl-groups by a *Wagner-Meerwein* rearrangement. This interpretation, first proposed for the comparable conversion by acidic reagents of 6-bromoisophorone into 3,4,5-trimethylphenol [26] and extended to an example in the diisophorone series [10] is directly applicable to the present aromatisation occurring under the acidic conditions of the acetolyses. How far it needs to be modified to account for the aromatisation in alkaline media will be considered in the context of further examples encountered in reactions of tribrominated diisophorones [27].



Mass Spectra.—Since the aromatised diisophorones retain their bicyclo[3.3.1]nonane moiety, i.e. the site of their more specific fragmentation, they produce mass-spectra comparable with those of the fully alicyclic parent structure [1, 6, 23]. A generalised fragmentation pattern, founded on the prominent peaks common to the 1-hydroxy-compounds (**19**, **4**, **6**, **16**), is outlined in Scheme 2. The fission comprises the usual loss of the peripheral substituents and detachment of ring C by ejection of fragments of mass units 56 and 71, resulting in condensed tropylium (e.g. **e**, **k**, **n**) or naphthalene fragments (e.g. **h**, **l**) of the familiar type [1, 6, 23]. The pathway proceeding by the abstraction of gem-dimethylcyclopropane (*m*/e 70), which contributes significantly to the fission of diisophorone ketols [23] and carboxylic acids [6], is apparently not followed to any extent. Furthermore, tropylium ion formation is largely suppressed in the scission of the 1-carboxylic ester **16**.

The following aspects of the fragmentation peculiar to the present series of compounds merit brief notice: The initial stage of the fission appears to be the ejection of the 8-substituent, as is suggested by the production, from the 8-methoxy-compound **6**, of a fragment arising by loss of the elements of methanol, the origin of which is conclusively established. Thereafter, the fragmentation patterns of both **6** and its analogues **4** and **7** resemble in their essentials that of the 1,3-diol **19**, signifying the comparable initiation of the process in the other examples also.



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Under electron bombardment, the strongly held phenolic hydroxyl-group is usually cleaved from the parent compound as carbon monoxide, necessitating a ring contraction, but its removal by loss of water becomes more prominent in alkylated phenols, including cresols and dimethylphenols [28]. Being methylated phenols, the aromatised diisophorones exhibit both modes of fission: their phenolic 3-hydroxy-group is detached (as water) with preservation of the carbon skeleton, as shown by the production in all the examples of a high-intensity peak (*m*/e 239) corresponding to the original ring structure stripped of all its substituents. The strong peak at *m*/e 173 (of **4**, **6**) may be associated with the product of the scission of the abundant naphthalene radical ion **l** (*m*/e 201, max), thus exemplifying a stage (**l** → **m**) proceeding with loss of carbon monoxide.

^{13}C-*Nmr Spectra.*—Our analysis of the ^{13}C-nmr-spectra of diisophorones of various types [24, 25] provides the background for inter-

preting those of the ring A-aromatised series. The numerical results are displayed in the usual way in Table 1; the extranuclear carbon atoms of the structures are numbered as in **C**. The concordant data thus established contribute in some instances towards the formulation of the compounds concerned.

The *singlets* of C-1, C-9 and C-11 are readily identified by their familiar chemical shifts [24, 25], as are those of the phenolic carbon (C-3) which match the established values in phenol [29, 30a, 31] and in the more immediately comparable 2,3,4,5-tetramethylphenol [32]. O-Acetylation (in **7**, **17**) results in the expected small shielding [29, 30b, 33]. The singlets of ring A (C-2,5,6,7) appear in the aromatic range [29] as two pairs of closely spaced signals (at 136–140 and 125–127 ppm). They may be identified with some confidence by reference to the fully assigned

Table 3. ^{13}C-*Nmr spectrum of 2,3,4,5-tetramethylphenol*

	C-1	C-2	C-3	C-4	C-5	C-6	2-*Me*	3-*Me*	4-*Me*	5-*Me*
Calculated[a] [32]	151.9	121.9	139.8	131.2	136.1	112.6	12.1	15.8	15.3	20.6
Calculated[b]	153.3	123.0	140.8	132.1	137.1	113.7				
Found [32]	150.7	119.9	135.6	126.3	133.4	114.4	11.9	16.0	15.2	20.3
Eqlt. posn. in **C**	C-3	C-2	C-7	C-6	C-5	C-4			15-*Me*	14-*Me*

[a] Calculation based on shift increments employed by *Netzel* [32]
[b] Calculation based on shift increments employed in Part 11 [10], taken from *Wehrli* and *Wirthlin* [34]

spectrum of the comparable 2,3,4,5-tetramethylphenol [32]: its chemical shifts, determined experimentally and calculated by the additivity rules employing established shift increments are given in Table 3. In conformity with these data, the lower field signal pair of the aromatised diisophorones is allotted to C-7 and C-5 (corresponding to C-3 and C-5 in the tetramethylphenol, see Table 3), and the higher field signal pair to C-6 and C-2. Although a distinction *within* each closely spaced pair must, in the case of the more complex tricyclic structures **C**, remain uncertain, the signals are tabulated as in the phenol-model, in descending numerical order C-7 > C-5 > > C-6 > C-2; possible interchanges within the closely adjacent signals are marked in the usual manner* (Table 1).

The foregoing assignments receive additional support from a comparison of the effects of O-acetylation in phenol and the aromatised

* Parallel calculations [10] for 2-isopropyl-7-ethyl-4,5-dimethylphenol, being possibly a closer structural approximation to ring A of the aromatised diisophorones (**C**), give a comparable set of figures, but fit the observed results less closely.

diisophorones (at C-3, in **7**, **17**). In the former, acetylation has been shown [30a, b, 31, 33] to deshield the *o*- and *p*-ring carbons (doublets, by ca. 5 ppm), but to leave the *m*-carbons virtually unaffected. In the acetylated aromatised diisophorones (**7**, **17**), the higher-field signal pair, which has undergone a like displacement (by 4–8 ppm, see Table 1), is therefore allotted to the comparable C-2 and C-6 positions, while the lower-field signal pair, unchanged in its chemical shifts, is associated with the C-7 and C-5 carbons (equivalent to the *m*-position).

Of the two *doublets* produced by each of the compounds, the one resonating in the aromatic range [29] is allocated to C-4: its chemical shift (δ, 116–125 ppm) agrees closely with standard values for the *o*-position of phenols [30a, 31, 34]. The chemical shifts of the higher-field signals (δ, 73–75 ppm in 8-hydroxy- or acetoxy-compounds) match those of C-8 doublets of comparable 8-substituted diisophorones [25]. The *triplet* appearing consistently near 50 ppm is allocated as usual [24, 25] to C-10, the ring-methylene most remote from structural changes, while the remaining two triplets (C-12,13) are distributed, for reasons given before [24], so that C-12 is associated with that having the higher resonance. The numerical data relating to the triacetate **7** and the lactone **18** vary slightly from the norm, without however deviating from the general trend.

One of the five *quartets* of the peripheral methyl groups displays the chemical shift (38 ppm) associated with C-18 [24, 25]. The two quartets of the aromatic methyl carbons are identifiable by their resonances (15–21 ppm), which match the standard values in aromatic models [30c, 32]. They are individually assignable by reference to the known resonances of the 4- and 5-methyl-carbons in 2,3,4,5-tetramethylphenol [32] (see Table 3). The two quartets that remain to be allotted to C-16 and C-17 are, at 28–30 ppm, too closely spaced to be separately identified. All singlets and quartets of the extranuclear carbon atoms (C-19 to C-24, forming part of methoxy-, acetoxy- and carboxy-groups) display the characteristics previously established [24, 25] for these substituents (see Table 1, supplement).

It is recalled that the assignment of the aromatic singlets (C-7,6,5,2) and two methyl quartets (C-14,15) IN previously described [10] aromatised diisophorones had remained highly tentative. In the light of the present wider data, these signals are now identifiable with greater assurance, and the revised assignments for the prototype **19** are included in Table 1.

Conclusion

The partial aromatisation of 6,8-dibromodiisophorones by nucleophiles now described appears to be promoted specifically by the participation of the 6-bromo-substituent: under the same conditions, the 4,8-

dibromo-isomers undergo, by an entirely different process, a facile ring A-contraction [1] of the *Favorski* type. The comparable action of nucleophiles on 4- and 8-monobromo-diisophorones terminates with the appropriate replacements [3–6], involving migration in the latter examples [7, 8]. In contrast, the 4- and 8-monobromo-compounds are readily aromatised by mineral acid in boiling acetic acid (e.g. **2** → **19**, [10]), but this procedure failed in the case of the present 6,8-dibromo-compounds; their interaction with nucleophiles thus provides the most versatile route to ring A-aromatised diisophorones so far. A knowledge of the behaviour of 6-monohalogenated diisophorones in this context would be instructive for interpreting this group of reactions as a whole, but these isomers are as yet unavailable.

Experimental

The ring A-aromatised diisophorones are named according to the convention previously used in Part 11 [10], based on the simplified nomenclature originally proposed in Part 1 [35] of this series. In the brominations employing N-bromosuccinimide, the uv source (λ, 2 540 Å) was placed 10 cm from the reaction vessel. Benzoyl peroxide was the commercial "wetted" material, and was air-dried before use. Light petroleum had b.p. 60–80° unless otherwise stated.

The equipment and procedures used in the determination of the ^{13}C-nmr- and mass-spectra have been specified in Part 17 [6]. Unassigned peaks of the ir spectra are not recorded except for the key-compounds **3**, **4**, **11** and **15**.

8-Bromodiisophorone

8-Bromodiisophor-2(7)-en-1-ol-3-one (**2**)

(a) A solution of **1** (8.28 g, 0.03 mol) in carbon tetrachloride (80 ml), treated with N-bromosuccinimide (5.6 g, 0.0315 mol) was boiled under reflux for 2 h, with irradiation by uv light. The residual oil obtained by the usual work-up (see **3**, below) was dissolved in light petroleum (b.p. 40–60°); it slowly deposited prisms (m.p. 98–100°, 3.2–3.7 g, 30–35%, in successive crops) of **2**, m.p. 104–106° (from light petroleum, b.p. 40–60°), identical (mixed m.p., ir) with authentic material obtained by monobromination of **1** by bromine in glacial acetic acid [2, 11].

(b) The use of benzoyl peroxide (0.5 g) as reaction promoter gave, in the foregoing procedure, the same product in comparable yield (36–40%), but after a much shorter time (15 min). In both (a) and (b), evaporation of the crystallisation filtrates at room temperature gave an orange-brown sticky intractable resin, occasionally occluding an additional small solid fraction (ca. 0.5 g).

8-Bromo-1-(3′,5′-dinitrobenzoxy)diisophor-2(7)-en-3-one
[**2a**, *Ar* = 3,5-$(NO_2)_2C_6H_3$]

A solution of **2** (1.78 g, 0.005 mol) in pyridine (25 ml), treated with 3,5-dinitrobenzoyl chloride (1.27 g, 0.0055 mol), was kept at 100° for 30 min, then stirred into ice-water—concentrated hydrochloric acid (25 ml). The soft precipitate (ca. 2.5 g) gave pale-yellow opaque prisms (0.88 g, 32%) of **2a**, m.p. 208–210° (from acetone—ethanol) (Found: C 54.4; H 5.4; N 5.0. $C_{25}H_{29}BrN_2O_7$

requires C 54.65; H 5.3; N 5.1%). ν_{max} 2 950–2 800 s, 1 470 ms (CH_3, CH_2); 1 720 vs (CO of acyl); 1 675 vs (CO ring), 1 630 ms (C=C conjug), 1 555 vs, 755 mw, 735, 725 ms d (? *Ar*); 1 380 ms (.C*Me*$_2$); 1 305 vs–1 295 s br (C—O ester) cm^{-1}. The use of benzoyl chloride in this procedure did not yield a solid derivative.

8-Bromo-1-methoxycarbonyldiisophor-2(7)-en-3-one (**10**)

The interaction of **9** [3, 5] (3.18 g, 0.01 mol) in carbon tetrachloride (40 ml) with N-bromosuccinimide (1.87 g, 0.0105 mol) with uv irradiation for 2 h, and isolation as described for **3** (below) gave a crude product (m.p. 125–128°, 2.22 g, 56%), affording **10**, m.p. 134–136° (from light petroleum), identical (mixed m.p., ir) with authentic material [8].

6,8-Dibromodiisophorone (Ketol)

6,8-Dibromodiisophor-2(7)-en-1-ol-3-one (**3**)

(a) *From diisophor-2(7)-en-1-ol-3-one.*—A solution of **1** (27.6 g, 0.1 mol) in carbon tetrachloride (300 ml), treated with N-bromosuccinimide (37.4 g, 0.21 mol), was boiled under reflux for 1.5 h under uv light. The pale-yellow suspension was set aside at 0° overnight, the succinimide filtered off, and rinsed with carbon tetrachloride—light petroleum (1 : 1). The filtrate gave, on evaporation under reduced pressure, a yellow viscid oil which was dissolved in light petroleum (b.p. 40–60°, 60–80 ml). The solution slowly deposited successive crops of massive yellow prisms (m.p. near 100°, total 23.4–25.2 g, 54–58%) (motherliquors: M). Further crystallisation from light petroleum gave faintly yellow prisms of **3**, m.p. 104–106° (Found: C 49.5; H 6.0; Br 37.0. $C_{18}H_{26}Br_2O_2$ requires C 49.8; H 6.0; Br 36.8%). λ_{max} 258 nm (log ε 3.88). ν_{max} 3 540 s (OH); 2 960–2 860 vs, 1 475–1 455 ms mult, 1 405 s (CH_3, CH_2); 1 660 vs br (CO); 1 615 m (C=C conjug), 1 395 s, 1 370 s (.C*Me*$_2$); 690 m (? Br); 760 ms (? diagnostic for the 6,8-dibromoketol, absent in 4,8-dibromo-isomer); 1 325, 1 315 s d, 1 300 ms, 1 280 ms, 1 225 m d, 1 050 s, 905 m, 875 mw, 815 mw, 800 mw, 665, 655 m cm^{-1}.

The motherliquors M, from which no more crystalline solid was isolable gave, on spontaneous evaporation at room temperature, a viscid sticky orange resin still containing **3**. *Acetylation* of the resin under standard conditions gave 6–8% yields of **3a**, m.p. 133–134°, identical (ir) with authentic material (see below). Alternatively, *acetolysis* (see below) of the resin gave **5** in yields up to 12%, while *methanolysis* (see below) gave **6** in yields up to 10%.

Alternatively, the reaction was performed advantageously in the presence of benzoyl peroxide (1 g) in place of uv irradiation. Bromination was complete after only 20 min boiling, and yields were marginally improved (58–64%).

(b) *From 8-bromodiisophor-2(7)-en-1-ol-3-one.*—Interaction of **2** (0.01 mol) and N-bromosuccinimide (0.0105 mol) in carbon tetrachloride (40 ml) as described above (uv light *or* benzoyl peroxide, with times of refluxing of 3 hr or 30 min, respectively) gave **3**, m.p. 103–106° (in 70% or 60% yield). Uv light-catalysed reaction for shorter periods (e.g. 30 min) was incomplete, giving mixtures of unchanged **2** and **3**. The observations agree with the experience [15] that N-bromosuccinimide introduces a second halogen atom more readily, when the isolated monobromo-derivative is treated with a further 1 mol of the reagent.

(c) The action of 3 or 2 mol of N-bromosuccinimide on **1** or **2** respectively, in the presence of benzoyl peroxide (0.5 g per 0.02 mol reactant; time of reflux 30 min and 2 h, respectively) gave in each case **3** as the sole isolable product (56% and

43%, respectively). In these experiments, the reagent filtered off at 0°, was according to its ir spectrum, a mixture of succinimide and N-bromosuccinimide.

1-Acetoxy-6,8-dibromodiisophor-2(7)-en-3-one (**3a**)

A solution of **3** (2.17 g, 0.005 mol) in glacial acetic acid (20 ml)—acetic anhydride (10 ml), treated with 60% perchloric acid (8 drops), was set aside at room temperature for 3 h, then stirred into warm water (200 ml). The resinous precipitate solidified quickly and gave faintly yellow prisms (1.52 g, 64%) of **3a**, m.p. 133–135° (from methanol) (Found: C 51.0; H 6.0; Br 33.9. $C_{20}H_{28}Br_2O_3$ requires C 50.4; H 5.9; Br 33.6%). ν_{max} 2980 vs–2820 s, 1470 s, 1460 ms (CH_3, CH_2); 1740 vs (CO of *Ac*); 1680 vs (CO, ring); 1615 m (C=C conjug); 1395 ms (.CMe_2); 1265 vs vbr (C—O ester), 680 s (? Br) cm^{-1}.

6-Methyl-5-nordiisophora-2(7),3,5-triene-1,3,8-triol (**4**)

(a) A stirred solution of **3** (4.34 g, 0.01 mol) in dioxan (30 ml) was diluted dropwise with water (15 ml), followed at room temperature with 3 *M* sodium hydroxide (10 ml, 0.03 mol; 10–15 min). The deep yellow solution was stirred for 1.5 h, added to water (500 ml), and acidified with 3 *M* hydrochloric acid (20 ml). The white precipitate, washed neutral, gave on crystallisation from ethanol—light petroleum (ca. 4 and 12 ml per g), microprisms (1.90 g, 66%) of **4**, m.p. 161–164° (Found: C 74.9; H 9.3. $C_{18}H_{26}O_3$ requires C 74.5; H 9.0%). λ_{max} 211 nm (log ε 3.91), 289 (3.27). ν_{max} 3410 vs br, 3300 s br (OH); 2960–2880 vs, 1470 vs br (CH_3, CH_2), 1625 m, 1585 ms, 870 mw, 675 m (? *Ar*), 1390, 1380 ms (.CMe_2); 1300 vs, 1235, 1215 ms d, 1080 s, 995 vs, 800, 780 m mult, 725 mw cm^{-1}. *m/e* 290 s ($M^{+\bullet}$), 272 s ($M-18$, H_2O), 254 ms ($M-2\times18$), 239 s ($M-3\times17$, OH), 219 s ($M-71$, C_5H_{11}), 217 s ($M-56$, C_4H_8-17), 201 vs max ($M-71-18$), 199 vs ($M-56-18-17$), 173 s ($M-71-18-28$, CO), 216 s, 215 vs, 204 ms, 189 ms, 187 ms.

Alkaline treatment was also suitable for recovering material from the final resins obtained in the production of **3** (see above). Performed under the above conditions, it gave again a semisolid crude product, which afforded **4** upon crystallisation, in quantities corresponding to an additional 10–12% yield of the original 6,8-dibromo-compound (**3**).

When a solution of **3** (0.005 mol) in glacial acetic acid (25 ml) containing concentrated hydrochloric acid (2 ml) was boiled under reflux for 30 min and stirred into ice water (i.e. use of the procedure that effects aromatisation of the 4- and 8-monobromo-analogues [10]), a powdery brown low-melting precipitate was obtained, which resinified on attempted crystallisation from the usual solvents. No significant amount of solid material was isolable when the time of refluxing was reduced to 10 min.

(b) A solution of the 8-acetoxy-derivative (**5**, see below) or the 1,3,8-triacetoxy-derivative (**7**, see below) (0.005 mol) in dioxan (40 ml)—water (10 ml) was treated dropwise with 3 *M* sodium hydroxide (6 ml, 0.018 mol), and boiled under reflux for 1 h. The liquid was reduced to half-bulk under reduced pressure, and stirred into ice-water containing 3 *M* hydrochloric acid (10 ml). The white precipitate gave, on crystallisation as above, prisms (75%) of **4**, identical (mixed m.p., ir) with material obtained in (a).

8-Acetoxy-6-methyl-5-nordiisophora-2(7),3,5-triene-1,3-diol (**5**)

A solution of **3** (4.34 g, 0.01 mol) and anhydrous potassium acetate (5.9 g, 0.06 mol) in glacial acetic acid (60 ml) was boiled under reflux for 1 h (separation of

solid and "bumping" after 15 min). Addition to ice-water (400 ml) precipitated a white solid (ca. 3 g) which gave, after two crystallisations from ethanol—light petroleum (1 : 2, 8 ml per g), prismatic needles (2.3 g, 70%) of **5**, m.p. 185–186° (Found: C 71.8; H 8.5. $C_{20}H_{28}O_4$ requires C 72.3; H 8.4%). λ_{max} 210 nm (log ε 4.05), 295 (3.47). ν_{max} 3 390 vs br (OH), 2 980–2 880 vs, 1 475 vs br, 1 415–1 405 ms br (CH_3, CH_2); 1 735 vs (CO of *Ac*); 1 620 mw, 1 585 ms, 880, 860 m d (? *Ar*); 1 375 s (.CMe_2), 1 250–1 225 vs vbr (C—O ester) cm^{-1}.

1,3,8-Triacetoxy-6-methyl-5-nordiisophora-2(7),3,5-triene (**7**)

(a) A solution of **4** (1.45 g, 0.005 mol) in glacial acetic acid—acetic anhydride (8 ml each) was boiled under reflux for 1 h, then added to warm water. The crude resinous product gave, after two crystallisations from ethanol—light petroleum (1 : 2), microplatelets (1.08 g, 52%) of **7**, m.p. 195–197° (Found: C 69.8; H 8.0. $C_{24}H_{32}O_6$ requires C 69.2; H 7.7%). λ_{max} 214 nm (log ε 4.07 br), 275–284 (2.82). ν_{max} 2 980 vs–2 890 s, 1 480 m (CH_3, CH_2); 1 770 vs, 1 745 vs br (CO of *Ac*); 1 380 ms, 1 370 s (.CMe_2); 1 265 s, 1 240 vs, 1 210 vs vbr (C—O ester); 860 w (? *Ar*) cm^{-1}. *m/e* 416 vw ($M^{+\bullet}$), 356 ms ($M - 60$, CH_3COOH), 254 s ($M - 60 - 102$, $CH_3CO.O.COCH_3$), 239 s ($M - 3 \times 59$, $CH_3COO.$), 215 m ($M - 56$, $C_4H_8 - 59 - 2 \times 43$, CH_3CO), 199 vs max ($M - 56 - 59 - 102$ *or* $M - 71$, $C_5H_{11} - 60 - 2 \times 43$), 183 ms ($M - 3 \times 59 - 56$), 198 s.

(b) The 8-acetoxy-1,3-diol **5** (0.83 g, 0.0025 mol) gave, by the foregoing procedure, the same 1,3,8-triacetoxy-derivative **7** (48%), identical (mixed m.p. and ir) with material obtained in (a).

8-Methoxy-6-methyl-5-nordiisophora-2(7),3,5-triene-1,3-diol (**6**)

A solution of **3** (4.34 g, 0.01 mol) in methanol (45 ml), treated with sodium (0.58 g, 0.025 g. atom) in methanol (25 ml), was boiled under reflux for 3 h, the liquid distilled to ca. half-volume under reduced pressure, and stirred into ice-water containing concentrated hydrochloric acid (5 ml). The precipitate (2.5 g) gave, on crystallisation from ethanol—light petroleum (ca. 5 and 10 ml per g), minute prisms (total 2.1 g, 70%) of **6**, m.p. 158–160° (Found: C 75.4; H 9.5. $C_{19}H_{28}O_3$ requires C 75.0; H 9.2%). λ_{max} 214 nm (log ε 4.00); 293 (3.56). ν_{max} 3 370 s, 3 230 vs (OH); 2 960 vs–2 880 s, 1 470 vs br (CH_3, CH_2); 1 625 ms, 1 585 vs, 870 s, 845 m (? *Ar*); 1 325 vs, 1 065 vs, 935 vs cm^{-1}. *m/e* 304 ms ($M^{+\bullet}$), 286 ms ($M - 18$, H_2O), 254 ms ($M - 18 - 32$, *Me*OH), 239 s ($M - 2 \times 17$, OH − 31, *Me*O), 233 s ($M - 71$, C_5H_{11}), 231 s ($M - 56$, $C_4H_8 - 17$), 215 s ($M - 56 - 31 - 2$), 201 s ($M - 71 - 32$), 199 vs max ($M - 56 - 17 - 32$), 173 m ($M - 71 - 32 - 28$, CO), 217 m, 202 s, 187 ms.

6,8-Dibromodiisophorone(1-Carboxylic Acid)

6,8-Dibromo-1-carboxydiisophor-2(7)-en-3-one (**11**)

To externally cooled stirred concentrated sulphuric acid (240 ml), 100% formic acid (5 ml) was added dropwise during 20–30 min, the temperature being kept below 0°. Finely powdered **3** (10.85 g, 0.025 mol) was introduced during 45–60 min; each portion was allowed to dissolve before the next was added, the temperature being maintained below 0°. More 100% formic acid (45 ml) was added dropwise in the same temperature range (1.5–2 h). After further stirring of 15 min, during which effervescence subsided, the pale-yellow liquid was stirred into ice-water (2 l). The white precipitate, washed neutral with water (crude, 10–

11 g, m.p. 165–170° decomp.), gave on crystallisation from acetone—ethanol (1 : 2, ca. 30 ml per g), ivory microprisms (6.5–7.4 g, 56–64%) of **11**, m.p. 228–230° (darkening from ca. 185°, decomp. to deep red melt) (Found: C 49.4; H 5.7; Br 33.8. $C_{19}H_{26}Br_2O_3$ requires C 49.4; H 5.6; Br 34.6%). λ_{max} 265 nm (log ε 3.98). ν_{max} 2 980 vs–2 870 s, 1 475 ms, 1 455 ms (CH_3, CH_2); 2 640 mw (COOH); 1 710 vs (CO of COOH); 1 680 vs (CO, ring); 1 630 m (C=C conjug); 1 395 m, 1 370 s (.C*Me*$_2$); 3 070 m, 1 290, 1 280 s d, 1 220 ms, 1 160, 1 150 ms d, 930 m, 905 m, 875 m, 795 m, 725 m, 690, 670, 650 m tr cm^{-1}.

6,8-Dibromo-1-methoxycarbonyldiisophor-2(7)-en-3-one (**12**)

(a) *From 1-methoxycarbonyldiisophor-2(7)-en-3-one.*—A solution of **9** [3, 5] (3.18 g, 0.01 mol) in carbon tetrachloride (40 ml), treated with N-bromosuccinimide (3.74 g, 0.021 mol) was refluxed for 1.5 h under uv light. The suspended succinimide was filtered off at 0° and rinsed with carbon tetrachloride. Removal from the filtrate of the solvent under reduced pressure gave an oil: its solution in light petroleum (b.p. 40–60°) deposited solid (m.p. 163–165°, 2.85 g, 60%), which afforded **12** as yellow prismatic needles, m.p. 164–166° (from light petroleum, recovery 40%, remainder from filtrates) (Found: C 51.0; H 5.9; Br 34.3. $C_{20}H_{28}Br_2O_3$ requires C 50.4; H 5.9; Br 33.6%). λ_{max} 264 nm (log ε 3.95). ν_{max} 2 990 vs–2 890 s, 1 480 s–1 440 ms br (CH_3, CH_2); 1 740 vs br (CO of COO*Me*), 1 680–1 665 vs br (CO, ring), 1 630 m (C=C conjug), 1 375 s (.C*Me*$_2$), 1 260–1 215 vs mult (C—O ester), 1 160, 1 140 s d, 1 055 s, 740 s cm^{-1}. *m/e* (molecular ion absent), 415, 417, 419 w (*M* − 59, COO*Me*), 395, 397 ms (*M* − Br), 364, 366 ms (*M* − Br − 31, *Me*O), 363, 365 vs max (*M* − Br − 32, *Me*OH), 336, 338 w (*M* − Br − 59), 335, 337 ms (*M* − Br − 59 − 1), 293, 295 ms (*M* − Br − 71, C_5H_{11} − 31), 257 w (*M* − 2 Br − 59), 214 w (*M* − 2 Br − 71 − 31), 213 ms (*M* − 2 Br − 71 − 31 − 1), 201 vs (*M* − 2 Br − 56, C_4H_8 − 59), 199 ms (*M* − 2 Br − 56 − 59 − 2), 187 ms (*M* − 2 Br − 71 − 59 + 1), 186 mw (*M* − 2 Br − 71 − 59), 255 ms.

(b) *From 8-bromo-1-methoxycarbonyldiisophor-2(7)-en-3-one.*—The use of **10** (see above, 0.01 mol) in conjunction with 1 mol of N-bromosuccinimide (1.87 g, 0.0105 mol) in the foregoing procedure gave (56%) **12**, identical (mixed m.p., ir) with material obtained in (a).

(c) *From 6,8-dibromo-1-carboxydiisophor-2(7)-en-3-one.*—A suspension of finely powdered **11** (2.31 g, 0.005 mol) in diethyl ether (50 ml) was treated at room temperature during 5 min with ethereal diazomethane [36] (from toluene-*p*-sulphonylmethylnitrosamide, "Diazald", 0.015 mol). The suspended reactant dissolved with gentle effervescence; the yellow colour of the reagent finally persisted. After 3 h storage at room temperature, the excess of diazomethane was destroyed by the addition of 3 *M* acetic acid. On evaporation under reduced pressure, the washed neutral ethereal solution gave a solid affording needles (1.72 g, 72%) of **12**, m.p. 172–174° (from light petroleum), identical with material obtained in (a).

6,8-Dibromo-1-carboxydiisophor-2(7)-en-3-one (**11**) *Reactions:*

A. Action of alkali

A solution of **11** (2.3 g, 0.005 mol) in *M* sodium hydroxide (25 ml, 0.025 mol) was kept at room temperature for 4 h, then stirred into ice-water (150 ml) containing 3 *M* hydrochloric acid (10 ml, 0.03 mol). The collected air-dried precipitate, forming a white granular solid (of presumed **13**, m.p. 130–135°, after

sintering at 120°; ca. 1.2 g, 76%) gave intractable yellow brittle resins on attempted crystallisation (e.g. from ethanol—light petroleum). The crude hydrolysis product **13** was therefore characterised by being subjected to acetylation (a) without and (b) with preliminary esterification by diazomethane.

(a) Its solution in acetic acid—acetic anhydride (8 ml each), treated with 60% perchloric acid (8 drops), was kept at room temperature for 4 h. Addition of the brown liquid to warm water (120 ml) precipitated a buff solid (ca. 1 g) which gave, on crystallisation from ethanol (20 ml per g), prisms (0.68 g, 40% overall yield for two stages) of the *1,3-lactone* **18**, m.p. 184–186° (Found: C 72.7; 73.0; H 7.6; 7.6. $C_{21}H_{26}O_4$ requires C 73.7; H 7.6%). λ_{max} 220 nm (log ε 4.09); λ_{plat} 283–290 (3.21). ν_{max} 2 980–2 925 vs, 1 470 vs (CH_3, CH_2); 1 820–1 810 vs br (CO, lactone); 1 745 vs (CO of *Ac*); 1 635 s, 870 m (? *Ar*); 1 400 m (.CMe_2); 1 235 vs vbr (C—O ester); 1 370 vs, 970 vs, 950 vs cm^{-1}. *m/e* 342 s ($M^{+\cdot}$), 300 w ($M - 43$, $CH_3CO + 1$), 282 vs max.

The 1,3-lactone **18** was unaffected by diazomethane under the usual conditions [36], being substantially recovered, or by boiling acetic anhydride—acetic acid (1 : 1, 12 ml per 0.0015 mol; 1.5 h; recovery above 90%).

A solution of the lactone **18** (1.03 g, 0.003 mol) in 1.5 *M* sodium hydroxide (15 ml) was boiled under reflux for 1 h, then acidified. The precipitated crude 1-carboxy-3,8-diol (**13**) (m.p. 130–132°, 0.69 g, 72%; ir spectrum identical with that of the foregoing crude hydrolysis product) was identified by its two-step conversion into the 3,8-diacetoxy-1-methoxycarbonyl compound (**17**), m.p. 182–184°, as described in (b) (immediately below) (overall yield for the three stage process, 50%).

(b) A suspension of the crude hydrolysis product **13** in ether (25 ml) was treated with ethereal diazomethane (from 0.012 mol of "Diazald"), when solution occurred rapidly with effervescence. Spontaneous evaporation at room temperature gave a resin (**14**) that could not be crystallised from the usual solvents. It was dissolved in glacial acetic acid—acetic anhydride (6 ml each), treated with 60% perchloric acid (6 drops), the pale brown liquid set aside at room temperature for 3 h, then stirred into water (200 ml). The precipitated resinous material solidified on storage and gave, on crystallisation from light petroleum (with addition of 20% of ethanol) microprisms (0.50 g, 24% overall yield for 3 stages) of *3,8-diacetoxy-1-methoxycarbonyl-6-methyl-5-nordiisophora-2(7),3,5-triene* (**17**), m.p. 180–182° (Found: C 69.2; H 7.9. $C_{24}H_{32}O_6$ requires C 69.2; H 7.7%). λ_{max} 217 nm, broad (log ε 4.05), λ_{plat} 277–284 (2.82). ν_{max} 2 960 vs–2 920 s, 1 480 s, 1 440 s (CH_3, CH_2); 1 770 vs (CO of COO*Me*); 1 735 vs br (CO of 2 *Ac*), 1 245 vs vbr, 1 190 vs vbr (C—O of *Ac*, COO*Me*); 890 ms, 860 s, 795 m, 720 m (? *Ar*); 1 380 vs cm^{-1}.

B. Acetolysis

(a) A suspension of **11** (2.3 g, 0.005 mol) and potassium acetate (2.95 g, 0.03 mol) in glacial acetic acid (45 ml) was boiled under reflux for 1.5 h: complete solution occurred after ca. 15 min, and solid reappeared after a similar period (causing severe "bumping"). The white precipitate (m.p. 150–160°, 1.5 g) obtained on addition of the reaction mixture to water, gave prisms (0.85–0.95 g, 50–56%) of the 1,3-lactone (**18**), m.p. 184–186° (identified by ir, see A, a above). The crystallisation filtrates deposited recovered starting material (up to 10%).

(b) The use of the corresponding methyl ester **12** gave, by the same procedure, prisms (58–64%) of **18**, m.p. 180–184° (from ethanol—light petroleum; identified by ir).

C. Methanolysis

The reactant **11** (2.31 g, 0.005 mol), suspended in methanol (30 ml), dissolved on addition of a solution of sodium (0.5 g, 0.022 g. atom) in methanol (20 ml). The liquid was boiled under reflux for 2 h, distilled to half-volume, and stirred into ice-water containing concentrated hydrochloric acid (2 ml). The resulting precipitate gave faintly yellow prisms (1.15 g, 70%) of *1-carboxy-8-methoxy-6-methyl-5-nordiisophora-2(7),3,5-trien-3-ol* (**15**), m.p. 165–166° (from light petroleum) (Found: C 71.7; H 8.4. $C_{20}H_{28}O_4$ requires C 72.3; H 8.4%). λ_{max} 216 nm (log ε 3.99), λ_{plat} 287–293 (3.48). ν_{max} 3 300 vs br (OH); 2 960–2 880 vs, 1 470 s, 1 420 s (CH_3, CH_2); 2 710 m (COOH); 1 730 vs, 1 690 vs (CO of COOH); 1 610 s, 855 ms, 690 m (? *Ar*); 1 520, 1 510, 1 490 vs t, 1 385 vs, 1 245 vs, 1 205 vs, 1 085, 1 050, 1 040 vs t, 940 ms, 785 m cm^{-1} (all peaks blunt, as is usual for free carboxylic acids).

8-Methoxy-1-methoxycarbonyl-6-methyl-5-nordiisophora-2(7),3,5-trien-3-ol (**16**)

(a) *From the foregoing 1-carboxylic acid.*—A solution of **15** (1.33 g, 0.004 mol) in ether (30 ml) was treated with ethereal diazomethane (from 0.01 mol "Diazald"). The product, isolated in the usual manner, gave microprisms (0.77 g, 56%) of **16**, m.p. 203–204° (from methanol), identical (mixed m.p., ir) with material obtained [1] in the methanolysis of 4,8-dibromo-1-methoxycarbonyldiisophor-2(7)-en-3-one (Found: C 72.8; H 8.8. Calc. for $C_{21}H_{30}O_4$: C 72.8; H 8.7%). *m/e* 346 mw ($M^{+\cdot}$), 315 mw ($M - 31$, *Me*O), 314 vs ($M - 32$, *Me*OH), 287 w ($M - 59$, COO*Me*), 284 ms ($M - 2 \times 31$), 283 vs ($M - 32 - 31$), 255 s ($M - 59 - 32$), 239 vs ($M - 59 - 31 - 17$), 227 ms ($M - 71$, $C_5H_{11} - 31 - 17$), 218 vs max ($M - 70$, gem-dimethylcyclopropane $- 59 + 1$), 199 s ($M - 71 - 59 - 17$), 183 mw ($239 - 56$, C_4H_8), 272 s, 219 s, 211 m, 204 ms.

(b) *By methanolysis.*—A solution of **12** (0.0025 mol) in methanol (25 ml), treated with sodium (0.25 g, 0.011 g. atom) in methanol (10 ml), was boiled under reflux for 1.5 h, distilled to half-volume in a vacuum, and stirred into ice—3 *M* hydrochloric acid (5 ml). The precipitate gave microprisms of **16** (75%; from methanol), identical with material obtained in (a).

6-Methyl-5-nordiisophora-2(7),3,5-triene-1,3-diol (**19**) [10]

Mass-spectrum: *m/e* 274 s ($M^{+\cdot}$), 256 vs ($M - 18$, H_2O), 241 s ($M - 2 \times 17 + 1$), 203 vs ($M - 71$, C_5H_{11}), 202 m ($M - 71 - 1$), 201 vs ($M - 56$, $C_4H_8 - 17$), 200 vs ($M - 56 - 18$), 199 vs ($M - 56 - 18 - 1$), 186 s ($M - 71 - 17$), 185 vs max ($M - 71 - 18$).

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