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Di-isophorone and Related Compounds. Part 9[1] 1-(Substituted)aminodi-isophoranes and Their Cyclodehydration Products

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The interaction of 1-chlorodi-isophor-2(7)-en-3-one (or its 5,11-bisnor-homologue) with aromatic, heteroaromatic, or saturated heterocyclic amines produces 1-(substituted)aminodi-isophor-2(7)-en-3-ones by nucleophilic replacement of the bridgehead halogen. Subsequent cyclodehydration affords, in certain examples, substituted 2,3,5,6,7,8-hexahydro-1*H*,9*H*-5,8a-methanocycloocta[gh]phenanthridines ("2′,3-dehydro-1-anilinodi-isophor-2,7-dien-3-ols"). Some physical and chemical properties of these novel amines and condensed pentacyclic bases are described.

(Keywords: Di-isophorones, 1-arylamino, synthesis and cyclodehydration; 2,3,5,6,7,8-Hexahydro-1H,9H-5,8a-methanocycloocta[g,h]phenanthridines; Tricyclo[7.3.1.0^{2,7}]tridecanes)

Di-isophoron und verwandte Verbindungen, 9. Mitt.:
1-Substituierte Aminodi-isophorone und ihre Cyclisierungsprodukte

Die Umsetzung von 1-Chlor-di-isophor-2(7)-en-3-on oder der entsprechenden 5,11-Bis-nor-verbindung mit aromatischen, heteroaromatischen oder gesättigten heterocyclischen Aminen führt durch nucleophile Substitution des Brückenkopf-Halogens zu 1-(substituierten) Aminodi-isophor-2(7)-en-3-onen. Darauffolgende cyclisierende Wasserabspaltung ergibt in gewissen Fällen substituierte 2,3,5,6,7,8-Hexahydro-1*H*,9*H*-5,8a-methanocycloocta[gh]phenathridine („2′,3-Dehydro-1-anilino-di-isophor-2,7-dien-3-ole"). Einige physikalische und chemische Eigenschaften der Amine und dieser neuen Type von kondensierten heterocyclischen Basen werden beschrieben.

Introduction

The first objective of our study of 1-(substituted)aminodi-isophoranes was their synthesis by the ammonolysis and aminolysis of the corresponding 1-halogen-compounds. The former reaction, resulting in

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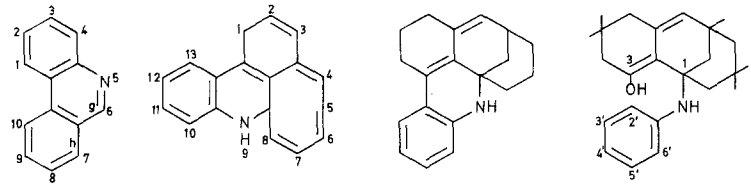
unsubstituted 1-aminodi-isophoranes, was achieved indirectly[1] by the application of the *Gabriel* and *Ritter* syntheses. Aminolysis, on the other hand, effects the desired substitution directly. The resulting 1-(hetero)arylaminodi-isophoranes (**3**) may undergo immediate dehydrative cyclisation to novel condensed pentacyclic nitrogenous bases (**4**, **14**). The stage at which the process terminates is governed partly by the reaction conditions, but principally by the nature of the amine employed.

The nomenclature of the novel pentacyclic structures calls for brief comment. The simplified scheme that was adopted[2] for the 5,5,9,11,11-pentamethyltricyclo[7.3.1.$0^{2,7}$]tridecanes (i.e. di-isophoranes) (**1**-**3**) ceases to be applicable to structures incorporating additional rings fused with this system (e.g. **4**, **5**, **14**). According to the IUPAC rules[3,4], the systematic name of **4** is derived from the appropriate fully unsaturated hydrocarbon (i.e. **B**), which itself originates from phenanthridine (**A**). This new ring-system (**B**) is renumbered as shown and its saturated centres duly enumerated. The official name of the parent base **C** is therefore 2,3,5,6,7,8-hexahydro-1*H*,9*H*-5,8a-methanocycloocta[gh]phenanthridine and may serve as the starting point for systematically naming all members of this series. As alternative to these unwieldy names, we adopt for ordinary usage the trivial name 2′,3-dehydro-1-anilinodi-isophor-2,7-dien-3-ol (for **4**). This extension of our original proposals[2] provides a succinct and unequivocal name for each compound, defining it in terms of its origin from the hypothetical intermediate **D**.



Results and Discussion

The aminolysis is illustrated in all its aspects by the interaction of 1-chlorodi-isophor-2(7)-en-3-one (**1**) and aniline: this was the prototype most closely studied, and proved to be the only example that could be terminated at the initial substitution- (**3**) or the final cyclised stage (**4**) by a choice of suitable conditions. Thus, brief interaction of equimolar quantities of the reactants in boiling dimethylformamide gave, by the nucleophilic replacement of the bridgehead halogen, 1-anilinodi-isophor-2(7)-en-3-one (**3**, 50-65%). The formulation of the product is in accord with its mode of formation, composition, and spectral characteristics (see Experimental). It is readily cyclodehydrated (to **4**), e.g. under the conditions of its synthesis on more prolonged interaction, or

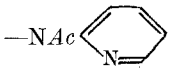
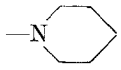
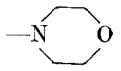
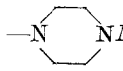
even in boiling ethanol during recrystallisation. Its elusiveness would have made its existence doubtful, had not other amines given stable analogues that were not prone to cyclodehydration (see Table 1).

The action on **1** of a large excess of boiling aniline acting both as nucleophile and solvent, gave the cyclodehydrated product directly (ca. 50%). Its formulation (and hence that of its analogues, see Table 2) as the condensed pentacyclic structure **4** agrees with its properties as follows. The compound ($C_{24}H_{31}N$, $M = 333$) forms a yellow solid, which displays a strong blue fluorescence in organic solvents, and a brilliant silvery-blue metallic lustre when exposed in its solid state to u.v. light, suggestive of the presence of an extended system of conjugated double bonds[5]. Its i.r. spectrum indicates the removal of the original keto- and the introduction of an amino-group (ν3370 s, 1310 vs cm^{-1}), the secondary nature of which is shown by the disappearance of the band (at 3370 cm^{-1}) associated with the N—H stretch in the mono-acyl and alkyl-derivatives (**6**-**9**). These, as well as a monopicrate, were readily accessible by conventional methods; the N-benzyl-compound (**9**) was obtained in improved yield under the catalytic influence of benzyltrimethylammonium hydroxide (Triton *B*)[6]. Although these properties would also be shown by the structural isomer **16** originating from the hypothetical *Schiff*s base **15**, this formulation may be rejected because of the demonstrated preferential formation of **3** (from **1**) and its ready conversion into **4**. The postulated distribution of the olefinic double bonds in **4** as a hetero- rather than a homo-annular conjugated system (**4 A**) cannot be verified by u.v. spectroscopy, since the introduction of the extended conjugation with the aromatic ring, and the presence of the nitrogenous centre precludes the direct application of the *Fieser-Woodward* rules[7]. However, since the preferred heteroannular disposition of conjugated olefinic bonds has been established in comparable examples (e.g. **17**[8,9], **19**[8]), it is also adopted in the present case.

There is scope for additional stereoisomerism in the 5,11-bisnor-homologue (**5**) of **4**, because of the possible axial or equatorial conformation of its single 5- and 11-methyl groups. The product (**5**) obtained from **2** and boiling aniline was indeed stereochemically non-uniform, as shown by its behaviour on fusion, and its separation into higher and lower melting isomeric components on fractional crystallisation. Beyond its conversion into a derivative (**10**), it was not further examined.

Reduction of 2′,3-dehydro-1-anilinodi-isophor-2,7-dien-3-ol (**4**) by red phosphorus and hydriodic acid, or more effectively by catalytic hydrogenation, saturated one double bond to give a product ($C_{24}H_{33}N$, $M = 335$) formulated as **11**. The new location of its remaining olefinic bond in the „stable"[9] 2(7)-position is in accord with its inertness to further reduction. The consequent simultaneous removal (from **4**) of the

Table 1. *1-(Substituted)amino*

Compound	1-Substituent[a]	Procedure Time of Reflux	m.p. (°C) Yield	Molecular Formula
3a	—NHC$_6$H$_4$NO$_2$-*p*	X 4 h	238-240[b, c] 64%[d]	$C_{24}H_{32}N_2O_3$
3b	—NHC$_6$H$_4$Cl-*p*	X 4 h	136-140[c] 60%[d]	$C_{24}H_{32}ClNO$
3c		X 4 h Y 0.5 h	114-116[c] 50% 35%	$C_{23}H_{32}N_2O$
3d[f]		—	185-188[c] 80%	$C_{25}H_{34}N_2O_2$
3e		X 4 h	211-213[c] 60%	$C_{23}H_{32}N_2O$
3f		Y 48 h 24 h	129-132[c, g] 52% 14%	$C_{23}H_{37}NO$
3g		Y 24 h	110-112[c, g] 50%	$C_{22}H_{35}NO_2$
3h		Y 5 h	111-113[h, g] 32%	$C_{23}H_{38}N_2O$

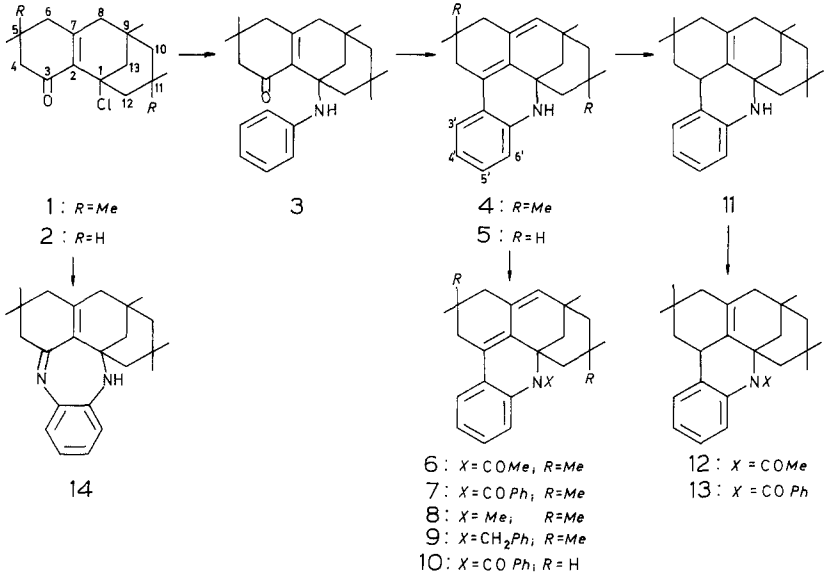
[a] Replaces —NH*Ph* in **3**.
[b] From dimethylformamide.
[c] From ethanol.
[d] Insoluble in 3*N*—HCl.
[e] Molecular weight determined mass-spectrometrically.

diisophor-2(7)-en-3-ones (**3**)

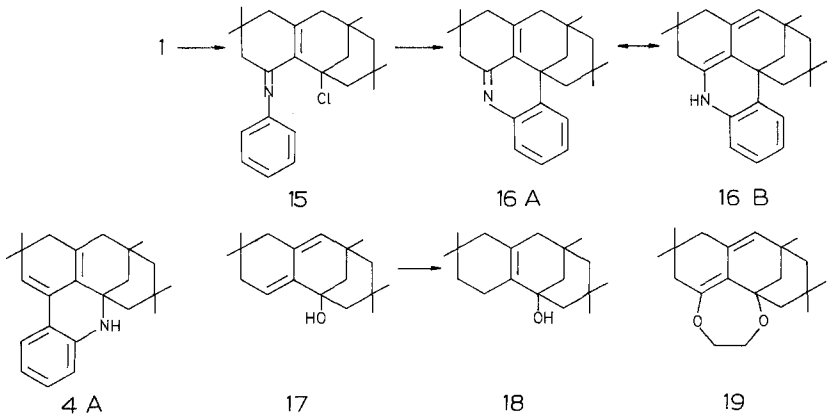
	Found %	Required %	IR: ν cm^{-1} [i]
C	72.5	72.7	3400 vs (NH); 2960-2900 vs, 1475 s (CH_3, CH_2); 1395 m,
H	7.9	8.1	1370 ms (CMe_2); 1665 vs (CO); 1320-1310 vs mult
N	7.5	7.1	(NO_2); 1630 m (C=C, conjug. olefin); 1610 vs, 1590 vs sh, 1510 ms (C=C, arom.); 845 s (CH, arom.); 1535 m, 1285 vs, 1115 vs, 755 m, 730 w, 700 w.
C	74.2	74.7	3400 s (NH); 2970-2860 vs, 1465 s (CH_3, CH_2); 1385-
H	8.1	8.3	1370 vs (CMe_2); 1665, 1655 vs d (CO); 1625 vs
Cl	8.6	9.2	(C=C, conjug. olefin); 1600 vs, 1495 vs (C=C arom.);
N	3.5	3.6	3110 w, 820 vs (CH arom); 650 vs (?C—Cl), 1520 vs, 1340-1325 vs br, 1260 vs, 1095 ms, 1055 ms, 800 m.
C	78.1	78.4	3410 s (NH); 2960-2850 vs, 1475 m, 1360-1345 vs mult
H	8.6	9.1	(CH_3, CH_2); 1390 s, 1375 vs (CMe_2); 1665 vs (CO);
N	7.9	7.95	1635 s (C=C, conjug. olefin); 1610, 1605 s d, 1575 s,
Me	352	352	1525 vs, 1490 vs (C=C, arom.); 3020 m, 765 vs, 730 vs, (CH arom.); 1425 vs, 1285 vs, 1265 vs, 1140 s, 1060 s, 850 s.
C	76.15	76.1	2940-2860 vs, 1475 vs (CH_3, CH_2); 1385 vs, 1375 vs
H	8.6	8.6	(CMe_2); 1680-1660 vs (CO, ring and acyl);
N	7.4	7.1	1640 vs (C=C, conjug. olefin); 1585 vs, 1565 s (C=C, heteroaryl); 3050 w, 3000 m, 765 s (CH, arom.).
C	78.0	78.4	3400 s (NH); 2970-2880 vs mult, 1475 s (CH_3, CH_2);
H	8.5	9.1	1395 ms, 1375 vs (CMe_2); 1670 vs br (CO); 1630 s
N	7.7	7.95	(C=C, conjug. olefin); 1600 vs br, 1525 s (C=C, heteroaryl); 3090 w, 815 vs (CH, arom.).
C	80.1	80.5	2960-2820 vs vbr, 1475, 1455, 1445 vs tr (CH_3, CH_2);
H	10.2	10.8	1385 s, 1365 vs (CMe_2); 1670 vs vbr (CO);
N	4.3	4.1	1625 vs (C=C, conjug. olefin).
Me	343	343	
C	76.9	76.5	2970-2855 vs mult, 2810 vs, 1480-1460 vs mult (CH_3,
H	9.6	10.1	CH_2); 1390, 1385 s d, 1375 vs (CMe_2); 1660 vs (CO);
N	3.9	4.1	1625 s (C=C, conjug. olefin).
Me	345	345	
C	77.4	77.1	2950 vs-2860 vs mult, 2790 s, 1470, 1460 s d (CH_3, CH_2);
H	10.5	10.6	1390 m, 1375 vs (CMe_2); 1670 s sh, 1660 vs (CO);
N	7.5	7.8	1615 s (C=C, conjug. olefin); 1425 m (CH of N*Me*).
Me	358	358	

[f] Prepared from **3c** by the action of boiling Ac_2O (3 h).
[g] Soluble in 3*N*—HCl.
[h] Crystallized successively from *Et*O*Ac* and *Et*OH.
[i] For **3a–c**, spectra are recorded in full, for **3d–h**, the unassigned peaks are omitted.

extended conjugation, and of the trisubstituted olefinic group was shown, as expected, in the loss of colour and fluorescing power, and in the disappearance of the peak (at 840 cm^{-1}) characteristic of the C—H bending vibration of a $RR'C=CHR''$-group. The reduction thus resem-



bles the hydrogenation of di-isophor-2,7-dien-1-ol (**17**) to **18**, where the conversion of the 2,7-diene- into the 2(7)-mono-olefin system has been established[9]. The reduction product (**11**), being a secondary amine,



showed the expected spectral properties, and was convertible into a picrate, and into mono-N-acyl-derivatives (**12**, **13**). Curiously, the N-methyl-derivative (**8**) of **4** failed to undergo hydrogenation.

The successful condensation of 1-chlorodi-isophor-2(7)-en-3-one with a number of aromatic, heteroaromatic and saturated heterocyclic amines demonstrated the general applicability of the reaction (see Tables 1 and 2). It was performed under two sets of conditions (see Experimental), the more restrained procedure (X) generally giving better yields of purer products (see, for example, Table 1, compound **3c**). The stage to which the reaction progresses (**3** or **4**) appears to be largely independent of these conditions, but is controlled principally by the nature of the amine employed. Thus, interaction under the more restrained conditions gave exclusively the cyclodehydrated bases (**4**) in some examples, while conversely, more vigorous and prolonged action did not drive the reaction beyond the substitution stage (**3**) in others. This characteristic of the reaction is further emphasised by the resistance of 1-(hetero)arylamino-di-isophorones (**3**), once formed, to cyclisation by conventional methods: thus, the action of polyphosphoric acid or phosphorus pentoxide (on **3c**) gave amorphous substances of uncertain composition, while acetic anhydride afforded merely the N-acetyl derivative (**3d**). The 1-(*p*-nitranilino)-compound (**3a**) resisted the action of concentrated sulphuric acid or acetic anhydride, being neither cyclodehydrated nor acetylated.

The reaction involving 4-nitro- and 4-chloro-aniline, 2- and 4-aminopyridine, or saturated heterocyclic amines terminated at the initial substitution stage (**3**, **a**–**h**). The non-aromatic amines reacted only slowly, requiring 24–48 h at their boiling point to produce maximum, though still only moderate yields (of **3**, **f**–**h**). A number of failures (see Experimental) may be ascribed either to the entire inhibition of the reaction, or to difficulties of isolation. 2,4,6-Tribromo- and 2,6-dimethyl-aniline, for example, intended to provide uncyclised substitution products (**3**) because of their blocked *ortho*-positions, did not react at all, probably because of the effect of steric hindrance. The hope that N-methyl-2′,3-dehydroanilinodi-isophor-2,7-dien-3-ol (**8**), the methylation product of **4**, could be synthesised directly from **1** and N-methylaniline, was not realised.

The products arising from aromatic amines bearing electron-releasing substituents were the cyclodehydrated bases (**4**, Table 2), forming pale to greenish yellow fluorescent solids. Their i.r. spectra contained, in addition to the usual absorption characteristics of the di-isophorane ring system[2], bands attributable to their imino-, diene-, trisubstituted olefin, and aromatic functions (see Table 2). The products derived from *m*-substituted anilines may bear these substituents in positions 3′ or 5′

Table 2. *2′,3-Dehydro-1-(substituted)*

Compound	Substituent 4′	Substituent 3′ or 6′	Procedure Time of Reflux	m.p. (°C)[a] Yield	Molecular Formula
4a	*Me*	H	X 4 h	133–135 56%	$C_{25}H_{33}N$
4b	O*Me*	H	X 4 h	156–158 36%	$C_{25}H_{33}NO$
4c	H	*Me*	Y 2 h[b]	181–184 42%	$C_{25}H_{33}N$
4d	H	O*Me*	Y 0.5 h[d]	175–177 28%	$C_{25}H_{33}NO$
4e	H	Cl	X 4 h	198–201 24%	$C_{24}H_{30}ClN$

[a] From *Et*OH.
[b] Refluxed under N_2.

(of **4d, e, f**): the latter formulation, though not proved, is thought to be the correct one on steric grounds.

The condensation of **1** and 1,2-diaminobenzene occurred with the usual loss of the elements of hydrogen chloride and water to give a product ($C_{24}H_{32}N_2$), which appears to be the condensed diazepine (**14**) rather than the pentacyclic base (**4**, NH_2 at C-6). That it was not a primary amine was indicated by a negative diazo-test, and by the presence of only one N—H stretching absorption (3380 cm^{-1}). It also lacked the peak at 830–840 cm^{-1} associated with the trisubstituted olefinic moiety ($RR'C=CHR''$), which is produced by all members of the series **4**. The observation excludes, incidentally, alternative distributions of the conjugated system of double bonds (in **14**) over rings A or A

anilinodiisophor-2.7-dien-3-ols (**4**)

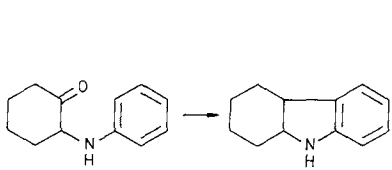
	Found %	Required %	IR: ν cm^{-1}
C	85.9	86.45	3380 s (NH); 2980-2870 vs br, 1475 vs, 1460 vs (CH_3,
H	9.3	9.5	CH_2); 1390 vs, 1365 vs (CMe_2); 1620 ms, 1580 m,
N	3.7	4.0	1505 vs (C=C); 3020 m, 825 vs, 810 vs (CH arom.); 840 m (CH, trisub. olefin); 1300 vs, 1130 ms, 1055 ms, 910 ms, 725 s, 685 m, 670 m.
C	83.1	82.6	3360 m (NH); 2960-2870 vs, 2820 ms, 1460 vs br
H	8.8	9.1	(CH_3, CH_2); 1395 ms, 1365 ms (CMe_2); 1620 w, 1580 ms,
N	3.3	3.9	1500 vs (C=C); 1205 vs (C—O*Me*); 840 m (CH, trisub. olefin); 815 m (CH arom.); 1300 vs, 1165 s, 1130 ms, 1055 s, 1025 ms, 725 m, 690 w.
C	86.2	86.45	3370 ms (NH); 2970-2880 vs br, 1475 vs, 1460 vs br,
H	9.1	9.5	1395 ms (CH_3, CH_2); 1385 vs, 1360 s (CMe_2); 1615 s
N	4.2	4.0	(C=C, conjug. diene); 1600 s, 1565 w, 1515 w
M[c]	347	347	(C=C, arom.); 830 s (CH. trisub. olefin); 805 vs (CH, arom.); 1310 s, 1145 ms, 905 ms, 875 m, 725 ms.
C	82.0	82.6	3350 ms (NH); 2950-2890 vs, 1475-1460 s tr (CH_3, CH_2);
H	9.2	9.1	1395 m, 1385 ms, 1365 ms (CMe_2); 2820 ms (CH of O*Me*);
N	3.5	3.9	1620 vs, 1575 m, 1520 s (C=C, arom.); 835 vs (CH,
M[c]	364	363	trisub. olefin); 1290-1285 s (C—N); 1260 s (CO of C—O*Ar*); 1330 ms, 1205 vs, 1170 s, 1035 ms, 810 m.
C	78.2	78.4	3350 s (NH); 2950-2880 vs, 1480 s, 1460 vs (CH_3, CH_2);
H	8.2	8.2	1390 s, 1365 ms (CMe_2); 1610 ms d, 1595 s, 1500 s
Cl	9.5	9.65	(C=C, arom.); 805 vs (CH arom.); 840 m (CH,
N	3.7	3.8	trisub. olefin); 1310 m, 1250 m, 1090 m, 938, 935 s d, 905 ms, 870 m, 745 m.

[c] Molecular weight determined mass-spectrometrically.
[d] Short reaction time because of excessive darkening of the boiling liquid.

and B (not shown). The structural assignment (**14**) implies that in this instance cyclisation occurs with the formation of an azine-link involving the 3-keto- and the *o*-amino-group rather than the usual *o*-hydrogen of the benzene ring. In this respect, the reaction is at variance with the observation that di-isophor-2(7)-en-1-ol-3-one and aniline did not react under the same conditions to give either the *Schiffs* base, or its cyclodehydration product (**16**), or indeed the base **4**.

Condensations that are formally comparable with the present synthesis (of **4**), though resulting in different ring systems, have previously been reported. The production of tetrahydrocarbazoles (**21**) from 2-halogenocyclohexanones and arylamines probably involves the analogous cyclodehydration of intermediate 2-anilinocyclohexanones

(**20**)[10]. A steroid structure incorporating an indole moiety (**22**) has been similarly obtained[11], but in that example the reaction sequence and mechanism are less clear.



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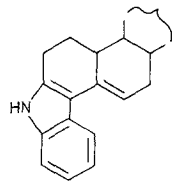

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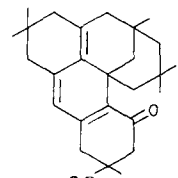

23

The ready formation of the condensed pentacyclic bases (**4**, **14**) now described illustrates the ease with which an additional ring may be fused with the di-isophorane structure at C-1 and C-3. Condensations involving suitable reactive groups at these centres may introduce a five-, six- or seven-membered ring into this near-planar region without imposing any appreciable strain. Comparable extensions to the di-isophorane skeleton that have previously been reported include the synthesis of the tetracyclic dioxepan (**19**)[8] by the action of ethylene glycol on di-isophor-2(7)-en-1-ol-3-one, and the remarkable formation of the trimeric by-product **23** in the base-catalysed dimerisation of isophorone[12]. Other readily accessible variants incorporating 5- and 6-membered nitrogen-containing rings will be described in another connection[13].

Acknowledgements

We thank Dr. *A. D. McNaught*, Editor, of the Chemical Society, London, for his expert advice concerning the systematic nomenclature of the condensed pentacyclic structures **C**. Our original acknowledgements[2] to Dr. *M. Gordon*, Professor *J. F. McGhie*, and Mr. *D. Carter*, and to Bristol Laboratories of Syracuse, New York, for financial support, are renewed with our sincere thanks.

Experimental

General information is given in Part I[2] concerning standard procedures, apparatus, reagents, solvents, and abbreviations. Light petroleum had b.p. 60-80° unless otherwise specified.

1-Anilinodi-isophor-2(7)-en-3-one (**3**)

A solution of 1-chlorodi-isophor-2(7)-en-3-one (**1**) (2.95 g, 0.01 mol) and aniline (1.02 g, 0.011 mol) in dimethylformamide (18 ml) was boiled under reflux for 15 min, then stirred into water (200 ml). The precipitated resin, which hardened on storage at 0°, was rinsed with water, drained, air-dried and *quickly*

dissolved with stirring in warm ethanol (6–8 ml), affording lustrous amber prisms (1.75–1.90 g, 50–55%) of **3**, m.p. 102–108°. The ethanolic filtrate deposited more of the same material (ca. 10%, m.p. 95–100°) on storage. Since **3** is cyclodehydrated in boiling ethanol (see below), rapid crystallisation at the lowest possible temperature is essential. (Found: C 81.6; H 8.9; N 3.8. $C_{24}H_{33}NO$ requires C 82.05; H 9.4; N 4.0%). ν_{max} 3400 s, 1535 s (NH), 2950–2860 vs, 1470 s (CH_3, CH_2), 1395, 1385 ms d, 1370 vs (CMe_2), 1680 vs (CO), 1635 s (C=C, conjug.), 1605 vs, 1505 s (C=C, arom.), 3020 m, 740 vs, 695 vs (CH arom.), 1340, 1330 vs d, 1300 s, 1265 vs, 1180 ms, 1140 ms, 1060 ms, 870 m, 730 ms cm^{-1}.

More prolonged boiling (30 min) tended to give a mixture of **3** and its cyclodehydrated product **4**. Reaction did not occur noticeably in dimethylformamide at 100° (30 min), or in boiling pyridine (1 h), or in boiling ethanol (4 h), the reactant being substantially recovered (identified by its i.r. spectrum).

2,2,5,7,7-Pentamethyl-2,3,5,6,7,8-hexahydro-1H,9H-5,8a-methanocycloocta[gh]phenanthridine (2',3-Dehydro-1-anilinodi-isophor-2,7-dien-3-ol) (**4**)

A solution of **1** (14.72 g, 0.05 mol) in redistilled aniline (60 ml) was boiled under reflux for 3 h, the liquid darkening rapidly. The cooled deep reddish-brown solution was stirred into 3*N*-hydrochloric acid (350 ml), the precipitated brown solid collected, washed with water, air-dried and crystallised from ethanol (120 ml), giving **4** as pale yellow prismatic needles, m.p. 152–154° (7.5–9.7 g, 45–58%) (Found: C 86.35; H 9.3; N 4.3. *M*, mass-spectrometrically, 333. $C_{24}H_{31}N$ requires C 86.5; H 9.3; N 4.2%. *M*, 333). ν_{max} 3370 s (NH), 2940–2880 vs, 1475, 1470 vs d (CH_3, CH_2), 1395 ms, 1385 s, 1365 s (CMe_2), 1620 s (C=C, diene), 1600 ms, 1505 m (C=C, arom.), 755–745 vs br (CH arom.), 1310 vs (C—N), 840 ms (trisub. olefin), 1255 m, 1135 s, 1055 ms, 927, 920 m d, 665 m cm^{-1}.

λ_{max} 252 nm (log ε 4.25), 357 (3.79), plateau 288–295 (3.60), λ_{min} 282, 322 nm. Nmr: δ[$CDCl_3$] 7.25–6.45 (4H, C_6H_4), 5.27 (1H, —CH=), 3.45 (1H, shallow, NH, exchanged by D_2O), 2.3–0.8 (25H, mult, CH aliph.) including three intense signals at 1.05 (6H, $2CH_3$), 0.93 (3H, CH_3) and 0.85 (6H, $2CH_3$).

Solutions of the compound in methanol, ethanol or ethoxyethanol showed a strong blue fluorescence. It was sparingly soluble in 5*N*-hydrochloric acid; the solution, treated at 0° with aqueous sodium nitrite, followed by alkaline α-naphthol, gave an orange-brown precipitate which resinified rapidly. Shorter reaction times (e.g. 30 min) lowered the yield considerably (to ca. 10%).

The *picrate*, obtained (64%) from equimolar proportions of the components in ethanol, formed prismatic needles, m.p. 164–168° (from ethanol). (Found: C 64.7; H 5.6; N 9.8. $C_{24}H_{31}N$. $C_6H_3N_3O_7$ requires C 64.1; H 6.05; N 10.0%).

The use of di-isophor-2(7)-en-1-ol-3-one ("di-isophorone") in the foregoing procedure gave no isolable product except recovered starting material (10–15%).

2',3-Dehydro-1-anilinodi-isophor-2,7-dien-3-ol: Derivatives

N-Acetyl Derivative (**6**). A solution of **4** (0.33 g, 0.001 mol) in acetic anhydride (5 ml) was boiled under reflux for 5 h. The resulting dark liquid was stirred into water and the precipitated discoloured solid crystallised from ethanol, yielding **6** (0.21 g, 56%) as lustrous prisms, m.p. 138–141°. (Found: C 83.5; H 8.6; N 3.6. *M*, mass-spectrometrically 375. $C_{26}H_{33}NO$ requires C 83.2; H 8.8; N 3.7%. *M*, 375). ν_{max} 2970 2890 vs, 1490 s (CH_3, CH_2), 1390 s d, 1365 vs

(CMe_2), 1660 vs, 1240 vs (CO), 1645 vs (C=C, diene), 1610 s, 1495 s, 1455 s (C=C, arom.), 770 vs br (CH arom.), 835 s (CH, trisub. olefin) cm^{-1}.

N-Benzoyl Derivative (**7**). A solution of **4** (0.33 g, 0.001 mol) in pyridine (5 ml), treated with benzoyl chloride (0.7 g, 0.005 mol) was kept at 100° for 30 min, then stirred into ice-water — concentrated hydrochloric acid (5 ml). The precipitated solidified brown resin gave **7** as pale yellow prisms (0.2 g, 45%), m.p. 202–204° (from ethanol). (Found: C 84.75; H 7.7; N 3.6. *M*, mass-spectrometrically, 437. $C_{31}H_{35}NO$ requires C 85.1; H 8.0; N 3.2%. *M*, 437). ν_{max} 2960–2870 vs, 1460, 1455 s d (CH_3, CH_2), 1390 ms, 1365 s (CMe_2), 1655 vs br (CO); 1605 ms, 1500 vs (C=C, arom.), 3090 m, 765 vs, 740 s, 705 vs (CH arom.), 845 mw (CH, trisub. olefin), 1335–1290 vs mult, 1265 vs br cm^{-1}.

N-Methyl Derivative (**8**). A suspension of **4** (6.66 g, 0.02 mol) in methanol (100 ml) was treated with sodium (0.46 g, 0.02 g-atom) dissolved in methanol (20 ml), followed by methyl iodide (35.5 g, 0.25 mol) and the solution boiled under reflux for 3 h. The liquid was evaporated to half volume under reduced pressure (removal of *Me*I), and stirred into ice-water. The precipitate gave greenish-yellow lustrous prisms (3.9–4.3 g, 56–62%) of **8**, m.p. 96–98° (from ethanol). (Found: C 86.4; H 9.2; N 4.2. *M*, mass-spectrometrically, 347. $C_{25}H_{33}N$ requires C 86.45; H 9.5; N 4.0%. *M*, 347). ν_{max} 2960–2870 vs mult, 1475 s d (CH_3, CH_2), 1390 s, 1365 s (CMe_2), 1615 ms (C=C, diene), 1595 ms, 1570 w, 1495 ms (C=C, arom.), 3030 m, 745 vs (CH arom.), 840 ms (CH, trisub. olefin), 1305 vs (C—N) cm^{-1}.

The *picrate* of **8** (80%) formed lemon-yellow microprisms, m.p. 185–188° (from ethanol) (Found: C 64.8; H 6.6; N 9.2. $C_{25}H_{33}N$. $C_6H_3N_3O_7$ requires C 64.6; H 6.25; N 9.7%).

N-Benzyl Derivative (**9**). A solution of **4** (1.0 g, 0.003 mol) in boiling methanol (20 ml) — benzyl bromide (0.62 g, 0.0036 mol) was treated with benzyltrimethylammonium hydroxide in methanol ("Triton *B*") (2 ml). On continued boiling (10–15 min), crystalline solid began to separate, which was collected at 0° (m.p. 193–196°, 0.83 g, 65%) and gave **9** as faintly yellow prismatic needles, m.p. 189–192° (from 1:1 ethyl acetate—ethanol). (Found: C 87.5; H 8.4; N 2.8. $C_{31}H_{37}N$ requires C 87.9; H 8.7; N 3.3%). ν_{max} 2960–2880 vs mult, 1460 s (CH_3, CH_2), 1390 ms, 1365 ms (CMe_2), 1620 m (C=C, diene), 1600 m, 1590 m, 1500 s (C=C, arom.), 3040 m, 745 vs, 730 s (CH arom.), 840 mw (CH of trisub. olefin), 1295 ms (C—N) cm^{-1}. Nmr: δ[$CDCl_3$]: 7.85–6.50 (9H, C_6H_4, Ph), 5.32 (1H, —CH=), 4.7, 4.43 (2H, CH_2 of $PhCH_2$), 2.45–0.8 (25H, mult, CH aliph.) including four intense signals at 1.10 (3H, CH_3), 1.02 (3H, CH_3), 0.96 (3H, CH_3) and 0.83 (6H, $2CH_3$).

2′,3-Dehydro-1-anilinodi-isophor-2(7)-en-3-ol (**11**)

(a) *By hydrogenation of* **4**. A solution of **4** (3.33 g, 0.01 mol) in glacial acetic acid (120 ml) was hydrogenated over *Adams* catalyst[14] (0.4 g) at room temperature and atmospheric pressure. Uptake of hydrogen was complete after 2–3 h (observed: 90 cm^3 rapid, 300 cm^3 slow; calc.: 75 cm^3 by catalyst, 225 cm^3 by reactant at *NTP*). The filtered dark brown liquid, usually still containing colloidal platinum, was stirred into water (500 ml), and the finely divided buff precipitate coagulated, if necessary, by the addition of 3*N*-sodium hydroxide (100 ml) and solid sodium chloride. The crude product (2.5–3 g) gave **11** as lustrous microprisms, m.p. 168–171° (from ethanol, ca. 5 ml per g) (1.5–1.9 g, 45–56%). (Found: C 85.7; H 9.7; N 4.4. *M*, mass-spectrometrically 335. $C_{24}H_{33}N$ requires C 86.0; H 9.85; N 4.2%. *M*, 335). ν_{max} 3365 s (NH), 2950–2870 vs mult, 1470 vs, 1455 s (CH_3, CH_2), 1395 m, 1365 m (CMe_2), 1600 ms, 1575 w, 1500 ms

(C=C, arom.), 3060 w, 750 vs (CH arom.) cm^{-1}. λ_{max} 235 nm (log ε 4.07), 337 (3.3, shallow). — The use of methanol-ethoxyethanol (1:1) as solvent inhibited the uptake of hydrogen.

(b) *By the Action of Hydriodic Acid* on **4**. A mixture of **4** (1.67 g, 0.005 mol), glacial acetic acid (18 ml), 66% hydriodic acid (10 ml) and red phosphorus (0.47 g, 0.015 g atom) was boiled under reflux for 4 h and the filtered red liquid added to water (500 ml). The (coagulated) precipitate gave faintly green microprisms (1.39 g, 60%) of the *hydriodide* of **11**, m.p. 256-260° (after darkening from 230°, emitting brown vapour on decomp.) (from ethanol). (Found: C 62.3; H 7.3; N 3.25; I 28.0. $C_{24}H_{33}N \cdot HI$ requires C 62.2; H 7.3; N 3.0; I 27.4%). ν_{max} 3450 s br (NH_2^+), 2970-2400 vs vbr mult (CH_3, CH_2, NH_2^+), 1465 vs br (CH_3, CH_2), 1395 s, 1370 vs (CMe_2), 1620 m, 1505 s (C=C, arom.), 765 vs (CH arom.), 1350 vs (C—N) cm^{-1}.

Dissolution of the hydriodide (0.003 mol) in the minimum of hot ethanol, addition of 3*N*-sodium hydroxide (0.003 mol), and dilution with water deposited a resin which gave low yields of **11**, m.p. 168-171° (from ethanol), identical with the product obtained in (a).

(c) The reactant **4** was recovered (75%) after being boiled under reflux in glacial acetic acid containing amalgamated zinc for 1 h.

2',3-Dehydro-1-anilinodi-isophor-2(7)-en-3-ol (**11**): *Derivatives*

The *picrate* separated slowly (60%) from equimolar quantities of the components (0.001 mol) in ethanol (8 ml), forming yellow prisms, m.p. 138-141° (from ethanol). (Found: C 63.9; H 7.3. $C_{24}H_{33}N$. $C_6H_3N_3O_7$ requires C 63.8; H 6.4%).

The *N-acetyl derivative* (**12**) obtained (75%) from **11** (0.001 mol) in boiling acetic anhydride (5 ml, 5 h) formed prisms, m.p. 124-127° (from ethanol). (Found: C 82.0, H 8.6; N 3.6. $C_{26}H_{35}NO$ requires C 82.8; H 9.3; N 3.7%). ν_{max} 2960-2890 vs br, 1460 s (CH_3, CH_2), 1390 s, 1370 vs (CMe_2), 1660 vs, 1245 vs (CO), 1570 m, 1495 s (C=C, arom.), 3070 mw, 765 vs, 745 s (CH arom.), 1300 s (C—N) cm^{-1}.

The *N-benzoyl derivative* (**13**) (prepared as **7**) formed small prisms (65%), m.p. 195-198° (from ethanol) (Found: C 84.6; H 8.1; N 3.0. $C_{31}H_{37}NO$ requires C 84.7; H 8.4; N 3.2%). ν_{max} 2950-2860 vs br, 1460 s, 1455 s (CH_3, CH_2), 1390 ms, 1365 s (CMe_2), 1665 vs br (CO), 1600 m, 1575 s, 1500 vs (C=C, arom.), 3080 mw, 765 vs, 745 s, 705 vs (CH arom.), 1340-1240 vs (complex mult), 1175 s cm^{-1}.

2',3-Dehydro-1-anilino-5,11-bisnordi-isophor-2,7-dien-3-ol (**5**)

The use of **2** (2.65 g, 0.01 mol) in conjunction with boiling aniline (12 ml) in the procedure described for **4** gave **5** as pale-yellow prismatic needles, m.p. 162-164° (after sintering at 148-150°) (from ethanol) (1.46 g, 48%). (Found: C 86.2; H 8.6; N 4.6. *M*, mass-spectrometrically, 305. $C_{22}H_{27}N$ requires C 86.6; H 8.85; N 4.6%. *M*, 305). ν_{max} 3370 s (NH), 2940-2895 vs mult, 1475 s, 1395 ms, 1350 ms (CH_3, CH_2), 1610 s, 1500 m (C=C, arom.), 3070 w, 750 vs br (CH, arom.), 1460 s, 1320, 1310 s d cm^{-1}. — Fractional crystallisation from ethanol partially separated the material into the less soluble higher-melting (162-164°) and more soluble lower-melting (146-148°) components; their i.r. spectra were identical with that of the unfractionated crystals.

The *N-benzoyl derivative* (**10**), obtained by the usual procedure, formed lustrous felted needles (35%), m.p. 193-195° (from ethanol). (Found: C 84.6; H 7.8; N 3.25. *M*, mass-spectrometrically, 409. $C_{29}H_{31}NO$ requires C 85.1; H 7.6;

N 3.4%. *M*, 409). ν_{max} 2960-2870 vs mult, 2830 s, 1455 s, 1390 ms (CH_3, CH_2), 1665 vs br (CO), 1630 m (C=C, conjug.), 1600 s, 1585 m, 1490 s (C=C, arom.), 3060 m, 740 vs br, 715 vs (CH, arom.), 840 ms (CH, trisub. olefin), 1330-1250 vs mult cm^{-1}.

1-(Substituted)aminodi-isophor-2(7)-en-3-ones (**3**) *(Table 1) and 2',3-Dehydro-1-(substituted)anilinodi-isophor-2,7-dien-3-ols* (**4**) *(Table 2)*

General Procedure X: A solution of **1**-chlorodi-isophor-2(7)-en-3-one (**1**) (2.95 g, 0.01 mol) and the appropriate primary or secondary amine (0.011 mol) in dimethylformamide (30 ml) was boiled under reflux for the time specified (see Tables 1 and 2). The cooled liquid was stirred into water (300-500 ml), and the precipitated crude material crystallised from ethanol. Products **3** or **4** thus obtained are listed in Tables **1** and 2.

General Procedure Y: A solution of **1** (0.01 mol) in the appropriate amine (0.15-0.2 mol) was boiled under reflux in an atmosphere of nitrogen for the specific period (see Tables 1 and 2). The resulting dark liquid was stirred into an excess of *N*-hydrochloric acid, and the solidified resinous crude material crystallised from ethanol. Products **3** and **4** thus obtained are listed in Tables **1** and 2.

The following amines failed to react (procedure in parentheses): 2,4,6-Tribromoaniline (Y), 2,6-dimethylaniline (X, Y), N-methyl (and ethyl)aniline (X), pyrrole (Y, 0.5 h). — The following failed to yield isolable products: 2-Methoxyaniline (X, Y), 2- and 4-aminophenol (X), ethylenediamine (Y), benzylamine (Y), and pyrrolidine (Y).

2',3-Dehydro-1-(4'-methoxyanilino)di-isophor-2,7-dien-3-ol (**4b**)

The *N-acetyl derivative* (**6**, O*Me* in C-4'), obtained (75%) by refluxing **4b** (0.36 g, 0.001 mol) in acetic anhydride (6 ml) for 5 h, and adding the liquid to water, formed lemon-yellow prisms, m.p. 139-142° (Found: C 80.2; H 8.9; N 3.6. $C_{27}H_{35}NO_2$ requires C 80.0; H 8.6; N 3.5%). ν_{max} 2960 s, 2920 s-2860 ms, 1470-1455 m mult (CH_3, CH_2), 1385 m, 1365 s (CMe_2), 1665 vs (CO), 1610 m br, 1505 vs (C=C, conjug. diene), 1210 vs (C—O*Me*), 870 m, 840 m, 820, 815 m d, (CH arom.), 1290 vs br d, 1240 s cm^{-1}.

Compound **3a** (see Table 1)

Nmr: δ[$CDCl_3$]: 8.03, 7.86, 6.58, 6.43 (4H, C_6H_4), 5.05 (1H, shallow, NH, exchanged by D_2O), 2.9-0.8 (27H, mult, CH aliph.) including four intense signals at 1.05, 1.00 (9H, $3CH_3$), 0.95 (3H, CH_3), 0.80 (3H, CH_3).

Compound **4a** (see Table 2)

Nmr: δ[$CDCl_3$]: 7.0-6.65 (3H, C_6H_3), 5.25 (1H, —CH=), 2.0-0.8 (25H, mult, CH aliph.) including three intense signals 1.05 (6H, $2CH_3$), 0.92 (3H, CH_3), 0.83 (6H, $2CH_3$).

Compound **14**

A solution of **1** (1.47 g, 0.005 mol) and 1,2-diaminobenzene (0.6 g, 0.0055 mol) in dimethylformamide (15 ml) was boiled under reflux for 4 h, then stirred into water, and the yellow precipitate coagulated by the addition of sodium chloride. Crystallisation from ethanol (30 ml per g, recovery 50%) gave **14** as pale orange-brown prisms (40%), m.p. 169-172° (Found: C 82.25; H 8.95;

N 7.4. $C_{24}H_{32}N_2$ requires C 82.8; H 9.2; N 8.0%). ν_{max} 3380 m (NH), 2960-2850 vs br, 1485 vs, 1475 vs, 1460 s (CH_3, CH_2), 1390 m, 1370 s (CMe_2), 1643 mw (C=C, conjug. diene), 1620 vs (C=N), 1600 vs, 1575 s, 1500 m sh (C=C, arom.), 3060 m, 3000 m, 770 vs (CH arom.) cm^{-1}. The compound was soluble in 3*N*-hydrochloric acid; the yellow solution, treated at 0° with aqueous sodium nitrite and alkaline 2-naphthol, gave a pale orange precipitate.

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