7,10a-Methanocycloocta[c,d]indazoles: Diisophoranes Incorporating the Pyrazole Ring System [1]

Frederick Kurzer* and Stanley S. Langer

Royal Free Hospital School of Medicine, (University of London),
London, NW3 2PF, England

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Compounds of the novel 7,10a-methanocycloocta[*c,d*]indazole ring-system **5**, **7** are obtained by the action of hydrazines on 1-chloro(or hydroxy)diisophor-2,7-en-3-ones **1-3**. Their formulation agrees with their origin and their chemical and spectral characteristics. Analogous syntheses of two comparable ring-systems include the production of a substituted 7,10a-methanocycloocta[*g,h*][2,1]benzisoxazole **10** by a facile cyclodehydration of the oxime of diisophorone **9a**, and that of the indole-analogue **13** by the action of aniline on diisophorone-1-carboxylic acid **11**.

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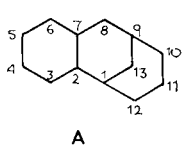
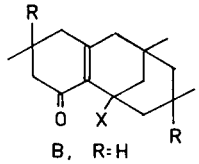
Introduction

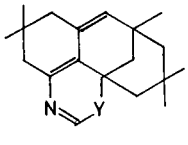
The tricyclo[7.3.1.$0^{2,7}$]tridecane ring-system **A** is readily expanded to condensed tetracyclic structures by the incorporation of an additional ring spanning its 1- and 3-positions. In diisophorones **B** and **C**, the spatial disposition of the replaceable 1-substituent and the enolisable 3-keto-group promotes condensations leading to the introduction of both six- [2] and seven-membered [3] heterorings, three carbons of which are shared with carbon atoms C-1, 2, and 3 of the original tricyclic structure **A**. We have recently used thioureas, ureas and guanidines to incorporate fused 1,3-thiazine [4] and pyrimidine rings [5] into the tricyclotridecane skeleton **C** to produce **D** and **E** and now report the extension of this approach to the synthesis of 7,10a-methanocycloocta[*c,d*]indazoles **F** [6] by the incorporation of a fused pyrazole ring by condensations involving hydrazines.



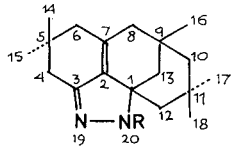
A



B, R=H
C, R=Me



D, Y = S
E, Y = NH



F

Results and Discussion.

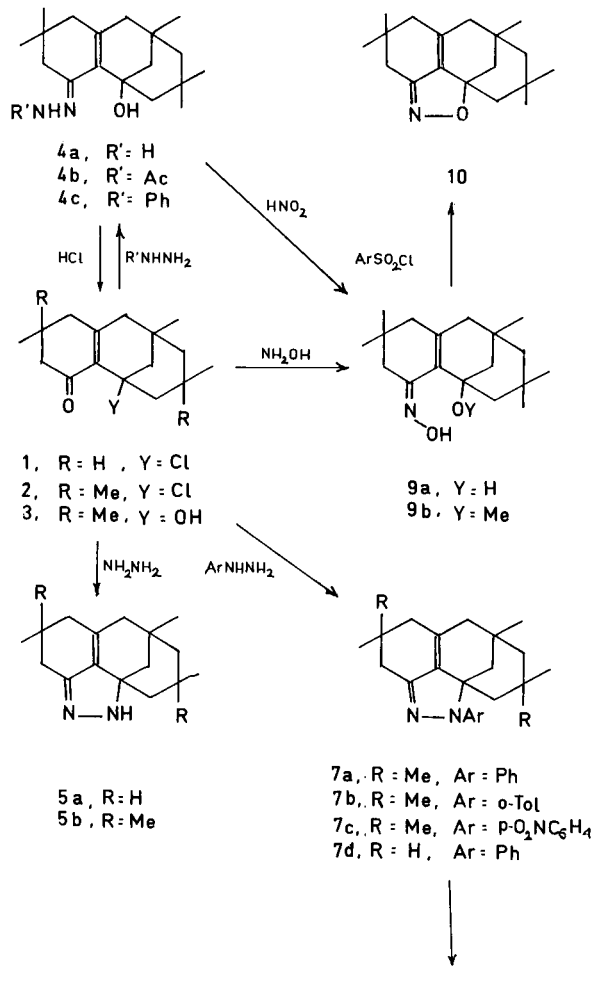
Under standard conditions, diisophorones **1-3** react conventionally with ketonic reagents, yielding 3-oximes, semicarbazones and hydrazones as expected [7]. Their prolonged interaction with hydrazines in boiling trifluoroacetic acid, however, follows the pattern recently established for guanidines and thioureas [4,5], involving the loss of an additional molecule of water from **3** or hydrogen chloride from **1** or **2** and formation of tetracyclic condensation products: these are formulated, on the basis of their origin, and their chemical and spectroscopic properties, as members of the novel 7,10a-methanocycloocta-[*c,d*]indazole ring-system **F** [6].

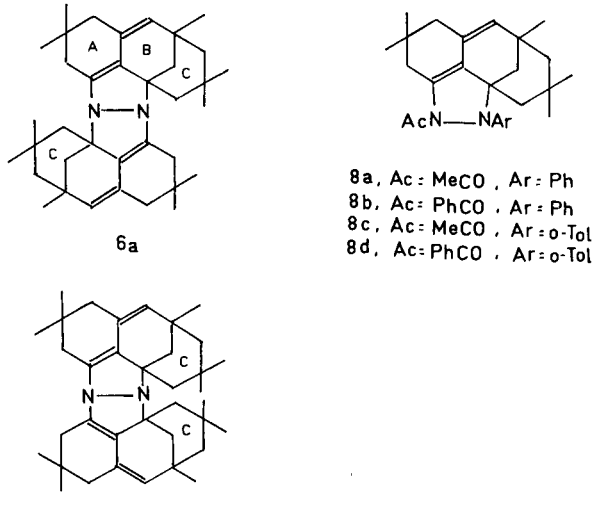
In a typical example, equimolar quantities of **1** and hydrazine hydrochloride gave the methanocycloocta[*c,d*]-indazole **5a** in moderate yield. In the presence of an excess of the diisophorone **2** or **3**, there was formed in addition to **5b**, a condensation product arising from two moles of diisophorone and one of hydrazine. This compound, forming very sparingly soluble platelets with a copper-like metallic lustre, is formulated as the condensed octacyclic structure **6**; in this molecule, the tricyclic precursor moieties may be aligned to one another in the "opposing" **6a** or "concurrent" **6b** sense. Molecular models show that the out-of-plane rings C occupy the *same* side of the approximate plane of the hexacyclic core in **6a**, but *opposite* sides in **6b**, so that neither formulation **6a**, **6b** is prohibited on the grounds of steric hindrance. The observed formation of a dipicrate of **6**, implying free access to both the nitrogen atoms of **6** in thought to favour **6a**.

Arylhydrazines similarly gave fair yields of substituted members of the series, readily isolated as the free bases **7a-d**, and convertible into monoacyl-derivatives **8a-d** by the standard methods. No picrate was obtained, however, from **7a** or **7b**. In the parent bases **7**, the conjugated system of double bonds occupies the exocyclic C=N and the bridged 2(7)-C=C positions, but migrates upon acetylation to **8** into the 2,7-diene position, as is indicated by the absence of an aliphatic doublet in the C-13 nmr spectrum of the former, **7**, and its appearance (at *ca.* 125 ppm) in that of the latter **8**. This shift of the unsaturated centres is also reflected in the marked hypsochromic displacements of the principal uv absorption maxima upon acetylation, **7a,b**→**8a,c**. The preferred heteroan-

nular distribution of the conjugated diene-system over rings A/B in diisophorones has been established [3,8,9] in suitable model structures by the application of the Fieser-Woodward rules [10] to their uv absorption characteristics. The same distribution has been chosen by analogy for more complex derived diisophorone structures [2,4,5] not directly covered by these rules, and is now adopted for the derivatives **8**, as well as the octacyclic diadduct **6**.

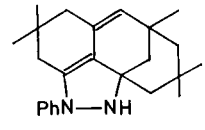
Scheme I





Mechanism.

The synthesis now described, *viz.* **1, 2, 3 → 5, 7** clearly involves condensations at the C-1 and C-3 positions of the tricyclic reactants: it is in all probability initiated by 3-hydrazone-formation, and completed by acid-catalysed cyclodehydration (or cyclodehydrohalogenation) involving the 1-substituent of the intermediate **4**. This proposed sequence is supported by the observations, that the phenylhydrazone **4b** of diisophorone was cyclised to **7** under the conditions of the synthesis, but that 1-chlorodiisophor-2-ene, lacking the 3-keto-group, failed to react with hydrazine. Moreover, in the reverse sequence, an arylhydrazine would presumably react at C-1 preferentially with its more basic amino-group and produce the isomeric 2,7-diene-structure **4x**, which is in fact excluded by the ^{13}C-nmr spectral evidence. The reaction is thus comparable, both in its course and mechanism, with general pyrazole syntheses involving hydrazones (see Conclusion, below).



4x

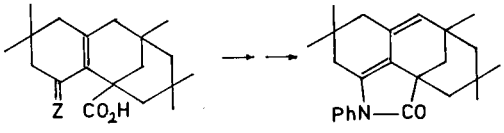
The ready formation of the octacyclic "diadduct" **6a** is rationalised in terms of a condensation between the primarily formed **4a** and an additional molecule of diisophorone, with elimination of two molecules of water. Both components assume their isomeric 2,7-diene-form in the course of the reaction, but the precise sequence of the steps is at present not specified.

Related Syntheses.

Two tetracyclic ring-systems **10,13** closely related to **F** were obtained by comparable reactions. Treatment of 3-oximinodiisophor-2(7)-en-1-ol **(9a)** [7] with *p*-toluenesulphonyl chloride in pyridine gave, instead of the expected tosylate suitable for the production of aminoketones by the Neber rearrangement [11], the substituted 7,10a-methanocycloocta[*g*,*h*][2.1]benzisoxazole **10** by a cyclodehydration that occurred almost quantitatively under exceptionally mild conditions.

The indole-analogue **13** was the product of the action of boiling aniline on diisophor-2(7)-en-3-one-1-carboxylic acid **11**, postulated to arise by cyclodehydration of the intermediate anil **12**. The spectral characteristics of **10** and **13** (Table II) are compatible with the assigned structures;

the appearance of an aliphatic doublet in the spectrum of **13**, and its absence in that of **10** is in accord with the proposed distribution of their conjugated double bond system. The reactions illustrate yet again the versatility of the present synthetic approach for expanding the tricyclo[7.3.1.$0^{2,7}$]tridecane system by a heterocyclic ring.

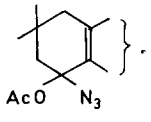


11, Z = O
12, Z = NPh

13

Hydrazones.

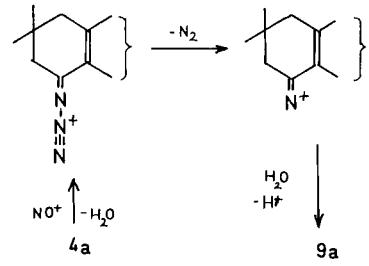
Incidental to the role of hydrazines in the present heterocyclic synthesis, some observations concerning relevant diisophorone hydrazones **4** are briefly reported. The prototype **4a** was readily obtained from its components, into which it was cleaved by acid hydrolysis. Two intense peaks in its ir spectrum (at 3230-3310 and 3430 cm^{-1}) are attributable to the 3-ω-amino- and 1-hydroxy-group, respectively [12a]. The compound was prone to resinification on storage, curiously more so after recrystallisation, presumably by spontaneous cyclisations or condensations involving its reactive substituents; when these were protected, *e.g.* by acylation, or in the ω-phenylhydrazone **4c**, the molecule was stabilised. The monoacetyl-derivative **4b**, obtained under restrained conditions [13], gave rise to a ketonic peak at 1680 cm^{-1} characteristic [12b] of an NHCO- rather than an OCO-group, and consistent with the absence of an ester C-O-C - band in the 1050-1300 cm^{-1} range. Its prominent hydroxyl-peak is displaced towards higher wave numbers, **4a**→**4b**, by 50 cm^{-1}, consequent to the removal of hydrogen bonding [12a,14]. The diacetyl-derivative of **4a**, obtained under more severe conditions, contains one acyl-group at each of its 1- and 3-substituent, as shown by its uv. absorption properties (see Experimental).



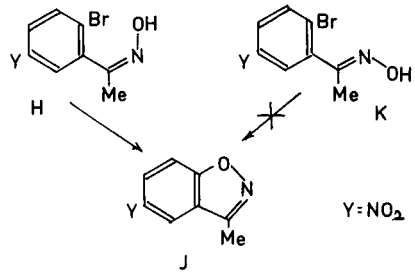
G

The action of nitrous acid in glacial acetic acid on the hydrazone **4a** gave, instead of the expected ketone **3** [15], azine [15], or acetoxyazide **G** [16], excellent yields of the oxime **9a**. This was the more surprising, since oximes are themselves reconverted into their parent carbonyl compounds under these conditions [17]. A proposed mechanism of the reaction (Scheme II) is modelled on that of the comparable conversion of hydrazones into amides [15]: it employs the nitrosonium ion (NO^+) as the effective reagent [18] which is known [19] to attack the hydrazone at its ω-amino-nitrogen.

Scheme II



The remarkably facile cyclisation of the oxime **9a**→**10**, see above, provides a strong argument for assigning the *anti*-configuration to its oximino-group with respect to C-4; in the *syn*-isomer, the reacting components are less favourably placed for interaction. Several precedents support this conclusion, including the cyclisation of 2-bromo-5-nitroacetophenone oxime to the benzisoxazole **J**, which is readily undergone by the anti- **H**, but not by the syn-isomer **K** [20]. This direct chemical evidence would appear to invalidate the syn-configuration assigned by a comparison of C-13 nmr spectra [21] to the oxime of the 5,11-bisnor-homologue of **9a**, which may therefore need to be reversed.



J

Carbon NMR Spectra.

Our systematic determination of the C-13 nmr spectra of a representative selection of diisophorone derivatives [21-28] has provided comprehensive correlations between their structure and spectral characteristics and has on occasion contributed materially to resolving structural problems. The generalisations, initially established for members of the tricyclo[7.3.1.$0^{2,7}$]tridecane ring-system **A-C** [21-24] were subsequently extended to related molecular patterns, including ring-contracted [25], aromatised [24,26,27] and rearranged structures [28] as well as derived tetra- and pentacyclic condensed systems incorporating a fused heterocyclic ring, **D** and **E** [4,5].

The ^{13}C-nmr spectra of the heterocyclic models now reported are displayed in the usual manner [21-24] in accordance with their proposed assignments (Table II). The attribution of their individual signals was facilitated by

Table I

1-Aryldecahydro-7,10a-methanocycloocta[*c,d*]indazoles

Compound	mp °C	Molecular Formula	Yield (%)	Composition Cacld.(%)/Found(%) C	H	N	IR Spectra	UV Spectra λmax (log ε)
7b	152-154 [a,b]	$C_{25}H_{34}N_2$	48	82.9 82.7	9.4 9.8	7.7 7.5	2940-2850 vs, 1460 s, 1420 ms (CH_3,CH_2), 1605 m (C=N, C=C conjug), 1500 vs (?C=N), 1390 ms, 1360 m (CMe_2), 770 vs, 720, 710 ms d (*o*-disub-Ar), 1300 vs	207 (4.03) 321 (4.06)
8c	136-137 [c]	$C_{27}H_{36}N_2O$	70	80.2 80.1	8.9 9.1	6.9 7.1	2950-2880 vs, 1470, 1460 s (CH_3,CH_2), 1685 s, 1665 vs br (CO of Ac, C=C conjug), 1355, 1340 s d (CMe_2), 770 ms, 735 ms (*o*-disub-Ar), 1400 vs br	208 (4.14) 249 (3.94) 299 (4.22)
8d	147-149 [b]	$C_{32}H_{38}N_2O$	75	82.4 82.4	8.15 8.2	6.0 6.0	2950-2880 vs, 1465, 1450 s (CH_3,CH_2), 1690 s, 1660 vs (CO of COPh, C=C conjug), 765 s, 730 ms, 700, 695 s d, 685 m, 670 m (Ph, and *o*-disub-Ar)	209 (4.26) 259 (4.03) 311 (4.11)
7c	159-162 [b,d]	$C_{24}H_{31}N_3O_2$	54	73.3 73.4	7.9 8.0	10.7 10.6	2970-2880 vs, 1475 s (CH_3,CH_2), 1595 vs vbr (C=N, C=C conjug), 1515 vs, 845 vs (NO_2), 1495 vs (?C=N), 1395 ms, 1375 s (CMe_2), 770 m, 760 s, 695 mw (*p*-sub-Ar), 1330-1280 vs mult	206 (4.15) 235 (3.94) sh 310 (3.59) sh 412 (4.44)
7d	158-160 [b,e]	$C_{22}H_{28}N_2$	48	82.5 82.5	8.75 8.8	8.75 8.8	2950-2860 vs, 1460 ms (CH_3,CH_2), 1600 vs (C=N, C=C conjug), 1505 vs (?C=N), 745, 725 m, 690 s (Ph), 1325 s, 1310 s	206 (3.99) 264 (3.86) 336 (4.05)

[a] Pale yellow prisms. [b] From ethanol. [c] From 70% ethanol. [d] Deep–orange prisms [e] Mixture of two conformers; see ^{13}C-nmr spectra. sh = shoulder.

Table II

^{13}C Nuclear Magnetic Resonance Spectra [a]

Compound	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9
3 [b]	71.4 s	135.4 s	200.7 s	51.8 t	32.2 s [c]	45.7 t	157.5 s	44.6 t	32.4 s [c]
7a	67.5 s	130.7 s	149.3 s	37.7 t	34.5 s [c]	43.1 t [d]	138.1 s	42.4 t [d]	33.8 s [c]
8a	70.8 s	130.4 s	122.9 s	50.8 t [c]	38.1 s	41.5 t	133.7 s	128.8 d	33.2 s
8b	71.2 s	130.3 s	124.0 s	50.8 t [f]	38.1 s	41.4 t	135.2 s [c]	124.3 d	33.2 s
7d maj	66.6 s	132.6 s	138.5 s	31.3 t	31.2 d	46.6 t [c]	148.9 s	42.9 t [c]	34.6 s
min	67.3 s	131.8 s	138.0 s	32.1 t	29.7 d	46.2 t [c]	149.4 s	43.0 t [c]	34.3 s
9a [n,p]	73.3 s	129.9 s	156.0 s	35.5 t	29.4 s	45.5 t [c]	141.7 s	44.5 t [c]	32.4 s
9b [p]	77.8 s	129.0 s	151.9 s	36.2 t	29.0 s	45.9 t [c]	144.2 s	45.2 t [c]	32.3 s
4a [n]	72.2 s	131.6 s	150.1 s	35.9 t	29.6 s	45.5 t	138.6 s	43.9 t	32.2 s
4c	72.4 s	131.9 s	145.1 s	36.9 t	29.8 s	45.9 t	139.6 s	43.9 t	32.3 s
10	82.7 s	135.3 s	154.8 s	35.7 t	35.2 s [c]	45.8 t	138.1 s	44.4 t [d]	34.1 s [c]
13	48.1 s	131.4 s	122.1 s	46.6 t	35.5 s [c]	41.8 t	135.2 s [d]	126.2 d	34.0 s [c]
L	56.7 s	132.7 s	160.9 s	45.8 t [c]	30.9 s	46.1 t [c]	136.6 s	48.3 t [d]	31.4 s

reference to the fully mapped spectra of relevant model structures, the interpretation of which was originally acquired by arguments based on a careful collation of numerous appropriate signals. As this reasoning has been detailed previously [21,22], the present discussion is confined to brief individual comments on the spectra of the new structural variants.

The cyclooctabenzisoxazole **10** resembles most closely in structure the oximes **9a,b** and hydrazones **4a,c**, for which mapped spectra are available [22] and provides a

Table II (Continued)

Compound	C-10	C-11	C12	C-13	C-14	C-15	C-16	C-17	C-18
3 [b]	52.1 t	31.4 s	50.3 t	46.6 t	26.8 q	29.7 q	28.2 q	32.7 q	37.1 q
7a	53.7 t	31.8 s	47.2 t	40.9 t	27.2 q	30.4 q	29.0 q	32.9 q	37.3 q
8a	51.6 t [c]	31.9 s	44.2 t	39.2 t	26.4 q	30.8 q [f]	29.4 q	30.8 q [f]	37.1 q
8b	50.8 t [f]	31.8 s	44.1 t	39.5 t	26.5 q	30.7 q	29.5 q	30.8 q	37.1 q
7d maj	50.2 t	25.5 d	38.5 t [d]	36.4 t [d]	[g]	20.8 q	31.2 q	[g]	21.6 q
min	–	25.7 d	38.2 t [d]	36.0 t [d]	[g]	20.8 q	-	[g]	21.7 q
9a [n,p]	52.7 t	31.7 s	49.8 t	47.0 t [c]	26.5 q	30.6 q	27.9 q	32.9 q	37.2 q
9b [p]	52.8 t	31.6 s	46.4 t [c]	43.4 t [c]	26.8 q	30.6 q	28.0 q	33.1 q	37.3 q
4a [n]	52.7 t	31.5 s	50.3 t	47.3 t	26.7 q	30.8 q	27.9 q	33.0 q	37.3 q
4c	52.8 t	31.8 s	50.3 t	47.4 t	26.9 q	30.9 q	27.9 q	33.0 q	37.2 q
10	53.4 t	32.3 s	43.4 t [d]	42.0 t [d]	28.7 q [e]	29.9 q [e]	27.1 q [e]	32.5 q	36.8 q
13	50.3 t	31.3 s	43.8 t	36.9 t [f]	26.1 q	30.9 q [e]	30.1 q [e]	31.2 q [e]	36.9 q [f]
L	53.5 t [e]	31.0 s	52.5 t [e]	49.1 t [d]	26.7 q	29.4 q	27.7 q	32.8 q	37.1 q

Supplement to Table II. Aromatic Signals

Compound	C-X	C-1'	C-2'	C-3'	C-4'	C-5'	C-6'
7a		145.5 s	117.2 d [h]	128.7 d [h]	120.0 d		
8a	170.9 s [i] 22.3 q [k]	147.5 s	124.5 d [h]	129.2 d [h]	119.5 d		
8b	169.0 s [l]	147.6 s 134.8 s [c]	127.3 d [h] 127.2 d [h]	128.4 d [h] 128.3 d [h]	130.0 d 129.8 d		
7d		145.7 s	116.7 d [h]	128.6 d [h] 128.4 d [h]	119.7 d		
4c		144.8 s	112.9 d [h]	129.4 d [h]	120.1 d		
13	181.0 s [m]	134.4 s [d]	124.9 d [h]	128.9 d [h]	127.3 d		
L		144.5 s	139.4 s	126.2 d	120.8 d	131.6 d	119.5 d

[a] Chemical shifts are in ppm downfield from tetramethylsilane ($\delta = 0$). The solvent was deuteriochloroform. [b] The spectrum of the parent ketol **3** is listed for comparison [22]. [c] [d] [e] Signals of very similar numerical value may need to be interchanged in horizontal lines. [f] Superimposed signals with enhanced intensity. [g] The 5,11-bisnor-homolouges lack the C-14 and C-17 positions. [h] Signal of approximately double intesity. [i] Carbonyl carbon of acetyl. [k] Methyl carbon of acetyl. [l] Carbonyl carbon of benzoyl. [m] Carbonyl carbon of hetero-ring. [n] The details of this previously reported spectrum [22] are confirmed, but the assignments of the singlets of C-3 and C-7 are reversed to match the numerical values of those of the now extended series of structures. [p] The spectra of the 5,11-bisnor-homologues of the oximes **9a** and **9b** have been recorded previously [21] and agree satisfactorily with the numerical values of the present examples.

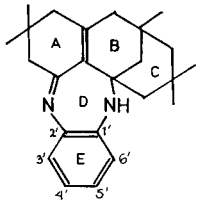
serviceable point of departure for interpreting the spectral characteristics of the group of compounds as a whole. The shieldings of the majority of its signals match those of the ketonic derivatives **4**,**9** and are therefore directly assignable with some confidence. The chemical shift of the C-3 singlet, δ 152-155 in **9a**,**9b**,**10**, agrees with values established for alicyclic oximes, 154-167 ppm [29,30a]. The deshielding of the bridgehead C-1 carbon by *ca.* 10 ppm relative to C-1 in **4** and **9** is attributed to the influence of the hetero-ring D, as are minor changes in the resonances of C-2, 5 and 12.

The spectrum of the cyclooctaindazole-prototype **7a** is comparable with that of **10**, see above, and those of the diisophorone oximes **9a**,**b** and hydrazones **4a**,**c** rather than that of the parent ketol **3**. The exchange at the 3-position of the keto- for an imino-moiety increases the shielding of the proximate carbon atoms of ring A, in accord with the relatively higher electron release from the latter grouping. The C-4 position, for example, is distinctly shielded (by 14 ppm), but the effect disappears in the altered structure of the acyl-derivatives **8a**,**b** as expected. The signal of C-3 itself agrees in its chemical shift (149

ppm) with those of hydrazones in general [31].

The C-13 nmr spectra of most 5,11-bisnor-homologues **B** of diisophorones **C** consist of closely spaced signal pairs, due to the existence of the individual compounds in two stereoisomeric forms differing in the conformation of their ring A and the 5-methyl-group attached to it [21]. The present heterocyclic example **7d** conforms to this pattern consisting, according to the relative intensities of the signal pairs, of the two stereoisomers in the approximate ratio 3:1. Most signals are identifiable unequivocally by reference to standard spectra of 5,11-bisnordiisophorones [21] on the one hand, and of diisophorone oxime **9a**, hydrazone **4a**, and the heterocyclic prototype **7a**, on the other. However, the chemical shifts of four of its high-field triplets, associated with C-6, 8, 12 and 13, and appearing in a narrow range, differ from the values in the comparable structures; their proposed distribution is therefore a collective assignment rather than one specific to the carbon atoms concerned.

The cyclooctaindole **13**, incorporating the 2,7-diene system, produces a spectrum closely resembling those of the acyl-derivatives **8**, except for its shielding of the bridgehead C-1 carbon: bearing a carbonyl-group, this produces a singlet at δ, 48 ppm within the narrow range characteristic of 1-carboxylic acids and esters of this series [23].



L

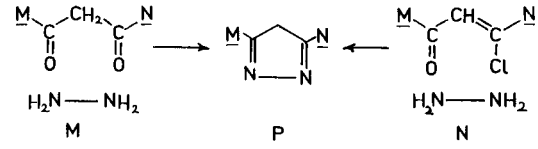
The condensed azepine **L**, synthesized in another context [2] from 1-chlorodiisophor-2(7)-en-3-one **2** and 1,2-diaminobenzene, shares its essential structural and hence spectral features with the methanocycloocta[*c*,*d*]indazoles **7**. However, the distinct shielding of its C-1 and deshielding of its C-3 carbon relative to **7a** marks an electronic displacement towards the former that must ultimately be ascribed to the combined effects of rings D/E. Other significant deviations are confined to two of the triplets, most likely of the 4- and 13-methylene-groups flanking the C-1 and C-3 positions. The absence of an aliphatic doublet demonstrates the distribution of the conjugated double bond system over rings A/D and confirms this formulation originally suggested [2] on the basis of the less decisive ir spectral evidence.

The constancy of the resonances associated with the five extranuclear methyl-groups is a feature common to all members of the tricyclotridecane ring-system **A** and its structural variants [21-28]. The familiar shieldings of these quartets, C-14 - C-18, remain essentially unchanged when the carbon skeleton **A** is extended by fusion with a heterocyclic ring, as has been observed before *e.g.* **D, E** [4,5] and is now further exemplified by the present additional heterocyclic variants, **F, L, 10, 13**.

The signals of the aromatic moieties in each of the structures are readily allocated by reference to standard spectra of aniline [32] and its *N*-alkyl-derivatives [30b,33]. In the phenylene-residue of **L**, the imino-group, -NH-, is chosen as the point of reference for these assignments.

Conclusion.

Our synthesis of methanocycloocta[*c*,*d*]indazoles **7** by the assembly of a three-carbon system with a hydrazine moiety is a formal variant of the classical Knorr synthesis of pyrazoles by the condensation of 1,3-dicarbonyl-compounds, *e.g.* **M**, and hydrazine derivatives [34]. However, our use of β-chloroketones **1,2** as the alternative source of the three-carbon component appears to be without precedent, being equivalent to the participation of substituted β-halo-hydrins or ketones exemplified by **N** in the standard synthesis that would potentially afford pyrazoles at all three levels of ring-saturation.



The present route is clearly capable of further exploitation by being extended to other hydrazine-containing reactants, including amino- and diamino-guanidines, amidrazones, semicarbazides and carbonohydrazides. Not the least interesting aspect of such projected reactions is the fact that their outcome is not obviously predictable [4,5], the nature of the resulting hetero-ring depending in each case on the relative reactivity of the component groups of the multifunctional hydrazines.

EXPERIMENTAL

Compounds are named using our simplified nomenclature [6], but full systematic names are given for the representative structures **5**, **10** and **13**. Details concerning reagents, common procedures, abbreviations are as specified previously [7]. Melting points are uncorrected.

Equipment.

Molecular weights were determined mass-spectrometrically using an AEI MS 902 instrument at 70 eV. The ir spectra were recorded on a Unicam SP 1000 instrument, using potassium bromide discs. Unassigned peaks of the ir spectra are not listed except for the structural prototypes **6**, **5a**, **7a** **10** and **13**. The uv spectra were measured with an SP 800A spectrophotometer, using ethanolic solutions, *ca* 50 mg/litre. Carbon-13 nmr spectra were determined on a Bruker WM 250 Fourier transform instrument operating at 62.89 MHz, with tetramethylsilane as the inter-

nal standard.

1,20-Dehydro-3-hydrazonodiisophor-2(7)-en-1-ol (**5b**) [6,6,10,12,-12-Pentamethyl-2[*H*], 3-diazatetracyclo[6.5.1.1^{1,10}.0^{4,14}]pentadeca-3,8(14)-diene (Baeyer's nomenclature) or 4,4,7,9,9-Pentamethyl-1,3,4,5,6,7,8,9,10,10a-decahydro-7,10a-methanocycloocta[*c,d*]-indazole (IUPAC nomenclature)] and Bis-Condensation Product **6**.

(a) A solution of 1-chlorodiisophor-2(7)-en-3-one [35] (**2**, 2.95 g, 10 mmoles) in trifluoroacetic acid (30 ml) containing hydrazine dihydrochloride (1.16 g, 11 mmoles) was refluxed for 8 hours, the salt dissolving gradually within 2-3 hours. The liquid was distilled to half-bulk, stirred into ice-water (30 ml), the precipitated primrose viscous gum or solid dissolved in ethanol (20 ml), and the deep-red liquid basified with 3*M* sodium hydroxide (10 ml, 30 mmoles). The precipitated gum which hardened on storage gave, on crystallization from 2-ethoxyethanol (6 ml), reddish-brown minute prisms (1.15 g, 45%) of **6**, mp 197-200° sintering at 185°; ir: 2950-2870 vs, 1470 s, 1420 s (CH_3, CH_2), 1660 vs (C=C conjug), 1390 s (CMe_2), 1360 vs (C-N, *tert*-amine), 1305 ms, 1240 s, 1060 s, 990 mw, 915 mw, 810 m, 660 mw cm^{-1}; uv: λ max 212 nm (log ε 3.92), 261 (4.17), 318 (3.94).

Anal. Calcd. for $C_{36}H_{52}N_2$: C, 84.4; H, 10.2; N, 5.5; M, 512. Found: C, 84.0; H, 9.95; N, 5.4. M (mass-spectrometrically) 512.

The base was converted in ethoxyethanol-ethanol into its dipicrate, identical (mixed mp) with this salt described in (b).

(b) In an identical experiment, the crude gum was dissolved in ethanol (15 ml) and treated with picric acid (2.3 g, 10 mmoles) in the same solvent (10 ml). The solution deposited successively deep rust-red solid A, then more slowly, two or three crops of lemon-yellow solid B. The final filtrate contained much intractable red gum. Solid A (mp 191-193°, 1.16 g, 24%) gave, on crystallization from 2-ethoxyethanol, rust-brown prisms (yellow when crushed) of **6** dipicrate, mp 191-193°.

Anal. Calcd. for $C_{36}H_{52}N_2.2C_6H_3N_3O_7$: C, 59.4; H, 6.0; N, 11.55. Found: C, 59.8; H, 6.0; N, 11.4.

Solid B (mp 102-110°, total, 2.0 g, 36%) gave, on crystallization from ethanol (10 ml per g, recovery 80%) yellow platelets of solvated **5b** mono-picrate, mp 109-111°.

Anal. Calcd. for $C_{18}H_{28}N_2.C_6H_3N_3O_7.C_2H_5OH$: C, 57.0; H, 6.8; N, 12.8. Found: C, 57.0; H, 6.6; N, 12.7.

After being kept at 80-100°/1 mm for 6 hours, the desolvated picrate sintered somewhat, but showed the same mp.

Anal. Calcd. for $C_{18}H_{28}N_2.C_6H_3N_3O_7$: C, 57.5; H, 6.2; N, 14.0. Found: C, 56.8; H, 6.6; N, 14.1.

(c) Substantially the same results were obtained when diisophorone **3**, (2.76 g, 10 mmoles) was used in place of **2** in procedure (b).

1-Chlorodiisophor-2(7)-ene (lacking the 3-keto-group in **2**) failed to react with hydrazine dihydrochloride (procedure a, above), as shown by the behaviour of the crude product on tlc. No picrate was obtainable from the ether-extractable product.

1,20-Dehydro-3-hydrazono-5,11-bisnordiisophor-2(7)-en-1-ol (**5a**).

Finely powdered hydrazine dihydrochloride (1.16 g, 11 mmoles) dissolved slowly (2 hours) on being refluxed in trifluoroacetic acid (20 ml). The solution was treated with **1** (2.67 g, 10 mmoles) dissolved in the same solvent (15 ml) and the liquid refluxed for 24 hours. The orange fluoresceing solution was distilled to half volume, stirred into ice-water (40-50 ml), and the precipitated gum dissolved in ethanol (30 ml). The red solution slowly deposited pale-yellow solid (mp 259-263°, 1.0-1.25 g, 28-35%) which gave, on crystallization from the same solvent (40 ml per g, recovery 60%), microprisms of **5a** trifluoroacetate, mp 261-263°; ir: 3390 vs br (NH), 2950-2880 vs, 1460 s, 1415 ms (CH_3, CH_2), 1615, 1600 vs br d (? C=N, C=C conjug), 1200-1170 vs br mult, 1140 vs (CF_3CO_2H), 1250 ms, 1095, 1085 mw d, 1045, 1035 mw d, 1000, 990 mw d, 955, 935 mw d, 770 mw, 705 w cm^{-1}.

Anal. Calcd. for $C_{16}H_{24}N_2.F_3C.CO_2H$: C, 60.3; H, 7.0; N, 7.8; F, 15.9. Found: C, 60.7; H, 7.1; N, 7.7; F, 15.7.

1,20-Dehydro-3-(phenylhydrazono)diisophor-2(7)-en-1-ol (**7a**).

(a) A solution of **2** (2.95 g, 10 mmoles) and phenylhydrazine hydrochloride (1.59 g, 11 mmoles) in trifluoroacetic acid (25 ml) was refluxed for 24 hours, the liquid distilled to half-volume and stirred into ice-water (30 ml). The precipitated red resin was rinsed with water and dissolved in ethanol (10 ml). The liquid deposited large crystals (mp 132-134°, 1.50 g, 60%) which gave, on crystallization from the same solvent (6 ml per g, recovery 70%), pale yellow prisms of **7a**, mp 136-138°; ir: 2960-2860 vs mult, 1460, 1435 ms (CH_3,CH_2), 1600 vs (C=N, C=C conjug), 1500 vs (?C=N), 1390 m (CMe_2), 750 vs, 715 m, 695 s (Ph), 1300 vs, 1035 ms, 1010 ms, 990 ms cm^{-1}; uv: λ max 207 nm (log ε 3.98), 265 (3.84), 338 (4.06).

Anal. Calcd. for $C_{24}H_{32}N_2$: C, 82.8; H, 9.2; N, 8.05. Found: C, 82.3; H, 9.15; N, 7.8.

(b) The use of diisophorone **3** (2.76 g, 10 mmoles) in the identical procedure gave the same product, mp 136-137° in 55-60% yield, identified by mixed mp and tlc.

The base failed to give a picrate, being recovered (80%) from its ethanolic solution containing an equivalent of picric acid (1.5 mmole each in 6 ml).

Acetyl-Derivative **8a**.

A solution of **7a** (0.70 g, 2 mmoles) in acetic anhydride (8 ml) was kept at 100° for 4 hours, then stirred into water (30 ml). The solidified gum gave pale yellow prisms (0.55 g, 70%) of **8a**, mp 139-141° (from ethanol); ir: 2950-2900 vs, 1460 ms (CH_3,CH_2), 1685 vs, 1670 vs (CO of Ac), 1600 ms (C=C conjug), 765 m, 710, 695 mw (Ph), 1400 vs, 1385 vs vbr cm^{-1}; uv λ max 206 nm (log ε 4.05), 232 (3.92), 251 (3.94), 297 (4.18).

Anal. Calcd. for $C_{26}H_{34}N_2O$: C, 80.0; H, 8.7; N, 7.2. Found: C, 79.6; H, 8.8; N, 7.1.

Benzoyl Derivative **8b**.

A solution of **7a** (0.70 g, 2 mmoles) in pyridine (8 ml) was treated with benzoyl chloride (0.34 g, 2.4 mmoles) and kept at 100° for 2 hours. The red liquid was stirred into ice-water containing concentrated hydrochloric acid (8 ml), and the precipitated solid crystallised from ethanol giving yellow prisms (0.72 g, 80%) of **8b**, mp 188-189°; ir : 2950-2870 vs, 1450 s (CH_3,CH_3), 1635 vs (CO of COPh), 1600 ms (C=C conjug), 765 ms, 705, 695 vs, 665 mw (Ph) cm^{-1}; uv: λ max 207 nm (log ε 4.20), 228 (4.13), 2.58 (4.03), 312 (4.06).

Anal. Calcd. for $C_{31}H_{36}N_2O$: C, 82.3; H, 8.0; N, 6.2. Found: C, 82.7; H, 8.1; N, 6.3.

Further aryl-substituted examples, **7b-d**, **8c,d**, are listed in Table I.

4,4,7,9,9-Pentamethyl-4,5,6,7,8,9,10,10a-octahydro-3*H*-7,10a--methanocycloocta[*g,h*] [2,1]benzisoxazole (**10**).

A solution of 3-oximinodiisophor-2(7)-en-1-ol [7] (2.91 g, 10 mmoles) in pyridine (40 ml) was treated in portions at 0° with

p-toluenesulphonyl chloride (1.91 g, 10 mmoles). The liquid was stirred at 0° for 1 hour, then at room temperature for 1 hour, and added to water (200 ml). The solid (mp 68-69°, 2.6 g, 95%) gave, on crystallization from light petroleum (bp 40-60°, 15 ml, recovery 60%), elongated prisms of **10**, mp 67-68°; ir: 2980-2800 vs vbr (CH_3,CH_2), 1695 ms (C=C, conj), 1570 ms (?C=N), 1390, 1365 vs (CMe_2), 1470-1415 vs mult, 1255 s, 1210 s, 1095 m, 950 vs, 915 s, 875 s, 820 vs, 795 vs, 775 s, 715 vs, 680 s cm^{-1} (finger print region very complex).

Anal. Calcd. for $C_{18}H_{27}NO$: C, 79.1; H, 9.9; N, 5.1. Found: C, 79.1; H, 10.2; N, 5.05.

The use of 2 moles *p*-toluenesulphonyl chloride in 50 ml of pyridine gave the same result.

4,4,7,9,9-Pentamethyl-2-phenyl-1,2,3,4,5,7,8,9,10,10a-decahydro-7,10a-methanocycloocta[*c*,*d*]indol-1-one (**13**).

A solution of 1-carboxydiisophor-2(7)-en-3-one (**11**, 1.52 g, 5 mmoles) in aniline (15 ml) was boiled under reflux for 18 hours, allowed to cool, then vigorously stirred into *M* hydrochloric acid (200 ml). The resulting precipitate gave, after two crystallizations from ethanol (*ca.* 5 ml), prisms (0.65-0.86 g, 36-48%) of **13**, mp 113-115°; ir: 2940-2880 vs, 1475, 1465 m d, 1435 ms (CH_3,CH_2), 1390 ms, 1365 vs (CMe_2), 1708 vs (CO), 1660 ms (C=C, conjug), 1600 s, 1505 vs (C=C, arom), 760 vs, 690 s (Ph), 1340, 1330 ms, 1300 ms, 1225 ms, 1090 ms, 1040 ms, 825 m, 720 s cm^{-1}.

Anal. Calcd. for $C_{25}H_{31}NO$: C, 83.1; H, 8.6; N, 3.9. M, 361. Found: C, 83.1; H, 8.3; N, 3.8. M, 361, 359.

The 1-carboxylic acid **11** (3 mmoles) was recovered (90%) after being treated, during 24 hours, with aniline (25 mmoles) in boiling dimethylformamide (15 ml).

3-Hydrazonodiisophor-2(7)-en-1-ol (**4a**).

A solution of **3** (5.52 g, 20 mmoles) in ethanol (30 ml) and hydrazine hydrate (5 g, 100 mmoles) was boiled under reflux for 2 hours. The product crystallizing directly from the reaction mixture slowly on storage (2-3 days, after seeding or addition of a few drops of water to induce crystallization, if necessary), gave large glass-like prisms (yield above 85%) of **4a**, mp 119-121°; ir: 3430 s (OH), 3310-3230 vs (NH), 2940-2850 vs (CH_3,CH_2), 1635 ms (C=N), 1585 m (C=C), 1390 ms, 1365 s (CMe_2), 1440 vs vbr, 1040 vs cm^{-1}. The crystals separating directly are stable indefinitely at room temperature, but material obtained on crystallization (from light petroleum) is liable to change to an orange resin on prolonged storage.

Anal. Calcd. for $C_{18}H_{30}N_2O$: C, 74.5; H, 10.3; N, 9.65. Found: C, 74.1; H, 10.3; N, 9.6.

3-Hydrazonodiisophor-2(7)-en-1-ol.

Acid Hydrolysis.

A solution of **4a** (0.58 g, 2 mmoles) in ethanol (15 ml) and concentrated hydrochloric acid (0.5 ml) was refluxed for 30 minutes, then stirred into ice-water (60 ml). The precipitate (0.48 g, 84%) was **3**, mp 78-80° (from light petroleum), identified by its ir spectrum [7].

Action of Nitrous Acid.

A stirred solution of **4a** (1.45 g, 5 mmoles) in glacial acetic acid (30 ml) was treated dropwise at room temperature with 10% aqueous sodium nitrite until the resulting orange liquid began to effervesce freely (4.3 ml, 6 mmoles). The liquid was stirred for another 10 minutes, then added to ice-water (100 ml). The resulting precipitate (mp 178-179°, 1.23 g, 85%) was 3-oximinodiisophor-2(7)-en-1-ol, **9a**, mp 179-180° (from ethanol-light petroleum), identified by ir [7].

Monoacetyl Derivative **4b**.

A solution of **4a** (1.45 g, 5 mmoles) in glacial acetic acid (25 ml) and acetic anhydride (10 ml) containing 60% perchloric acid (0.25 ml) was set aside at room temperature for 2 hours, then stirred into water. The precipitate gave, on crystallization from light petroleum with addition of a little ethanol, prisms (64%) of **4b**, mp 194-196° (red melt); ir: 3470 ms (OH), 3220 ms, 3120 ms (NH), 2960-2880 s br, 1470 s (CH_3, CH_2), 1675 vs (CO acyl), 1630 s (C=N) cm^{-1}.

Anal. Calcd. for $C_{20}H_{34}N_2O_3$: C, 72.3; H, 9.6; N, 8.4. Found: C, 72.1; H, 9.9; N, 8.4.

Diacetyl Derivative (as the foregoing, but the 1-Acetoxy-analog).

A solution of **4a** (5 mmoles) in acetic anhydride (40 ml) was boiled under reflux for 2 hours, then stirred into warm water. The precipitated red oil was isolated by ether extraction and dissolved in light petroleum with addition of a little ethanol. The solution deposited prisms (1.05 g, 56%) of the diacetyl derivative, mp 220-222°; ir: 3200 s, 3110 ms (NH), 2940, 2900 vs d, 1470 ms (CH_3,CH_2), 1725 vs, 1665 vs (CO acyl), 1630 ms (C=N), 1390 s, 1365 s (CMe_2), 1260 vs (C-O ester) cm^{-1}.

Anal. Calcd. for $C_{22}H_{34}N_2O_3$: C, 70.6; H, 9.0; N, 7.5. Found: C, 70.9; H, 9.3; N, 7.4.

3-ω-Phenylhydrazonodiisophor-2(7)-en-1-ol (**4c**).

A solution of **3** (13.8 g, 50 mmoles) and phenylhydrazine (5.4 g, 50 mmoles) in ethanol (45 ml) and 3 *M* hydrochloric acid (1.5 ml) was refluxed for 3 hours, then set aside. The viscous liquid deposited, after being seeded, massive prisms (mp 195-196°, *ca.* 13.5 g, 75%) which gave, on crystallization from ethanol (8 ml per g, recovery 80%), pale orange plates of **4c**, mp 196-198°; ir: 3360-3260 vs (NH,OH), 2945-2805 vs mult (CH_3,CH_2), 1605 vs (C=N), 1565 s (?C=C), 1390 s, 1365 vs (CMe_2), 740 vs, 685 vs (Ph), 1420 vs, 1315 vs, 1255 vs br, 1150 vs br, 1045, 1035 vs d, 990 vs cm^{-1}.

Anal. Calcd. for $C_{24}H_{34}N_2O$: C, 78.7; H, 9.3; N, 7.65. Found: C, 78.75; H, 9.7; N, 7.6.

The use of boiling glacial acetic acid as solvent with 1-2 hours' refluxing, gave negative results.

Cyclisation to **7a**.

A solution of **4c** (1.83 g, 5 mmoles) in trifluoroacetic acid (15 ml) was refluxed for 2 x 8 hours, distilled to half bulk, and stirred into ice-water (20 ml). The precipitated gum gave (42%) **7a**, mp 136-138° from ethanol, identified by ir, see above.

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[6] Note on Nomenclature. Since the systematic names of diisophorone and its derivatives are excessively cumbersome, we continue to use, in the Experimental, our simplified nomenclature [7,8] based on the trivial name "diisophorane" for the parent hydrocarbon **B**, and suitably modified for derived tetracyclic structures [2,4]. The "1,20-dehydro" component in the present names reflects the relation of the compounds to their presumed precursors **4** by cyclodehydration. The numbering adopted for diisophorones is retained, see **F**, being expedient for direct comparisons, especially of the C-13 nmr spectra.

Systematic names, indispensable for data retrieval, based on both the Baeyer and IUPAC conventions are given for four selected representative structures in the Experimental.

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