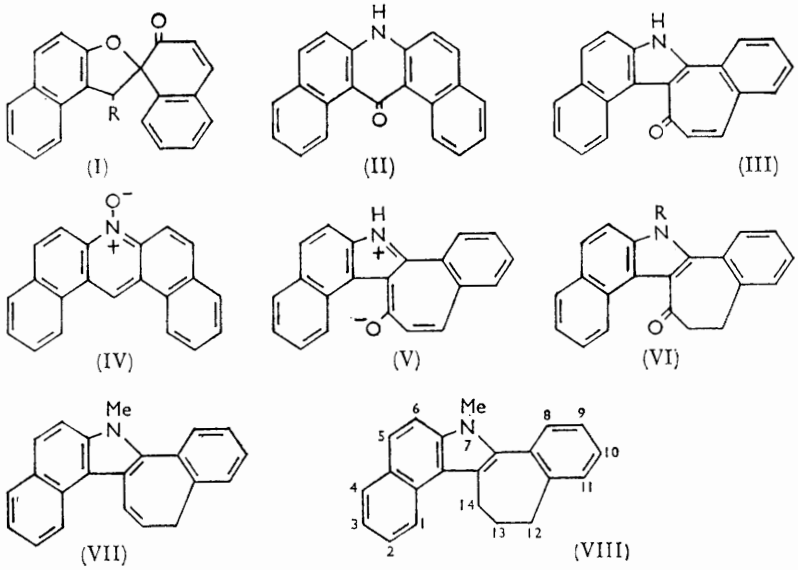
978. *Spirans. Part VI.*[1] *The "Anhydro-oxime" from Abel's Spiro-ketone.*

By F. M. Dean, Colin Fletcher, and H. D. Locksley.

The compound made by oximation of Abel's ketone (I; R = H) is the dibenzocyclohepta[*b*]indole (III).

Structure (I; R = H) is accepted for a ketone prepared by Abel,[1,2a,3] but the anomalous oximation discovered[4] in 1892 has been difficult to explain. The only crystalline product is apparently an anhydro-oxime with an empirical formula $C_{21}H_{13}NO$, a high melting point, a yellow colour, and low solubility in a range of solvents. Dischendorfer's claim[5] that zinc-dust distillation gives di-β-naphthylamine encouraged the belief that the product might be the dibenzacridone (II) until Chatterjea[2b] synthesised this and found it to be different. The latter worker[2b] then suggested other structures, but these also seemed to us inadequate and we now offer evidence that the "anhydro-oxime" has structure (III) with fused tropone and indole rings.



In the preliminary studies we failed to identify carbonyl absorption in the infrared spectrum of "anhydro-oxime" and therefore prepared the *N*-oxide (IV) isomeric with the dibenzo-acridone (II). This oxide was also different from the anhydro-oxime. We then confirmed Chatterjea's observation[2b] that zinc-dust distillation merely causes the latter to sublime.

The very low solubility of the cycloheptaindole (III) may account for the reported absence of active hydrogen,[2b] while the failure to undergo acylation (which we confirmed) can be attributed to electronic interactions leading to a charge distribution as in (V) which would also account for the high m. p. and low solubility. The presence of active hydrogen (OH or NH groups) is required to explain absorption at 3205 cm.$^{-1}$ and the formation, by Purdie's method, of a methyl derivative lacking it. The dihydro-derivative (VI; R = H)

[1] Part V, Dean and Locksley, *J.*, 1963, 393.
[2] Chatterjea, *J. Indian Chem. Soc.*, (*a*) 1950, **27**, 375; 1958, **35**, 37; (*b*) 1958, **35**, 41.
[3] Sestanj, *Arhiv Kem.*, 1951, **23**, 81.
[4] Abel, *Ber.*, 1892, **25**, 3483.
[5] Dischendorfer, *Ber.*, 1926, **59**, 774.

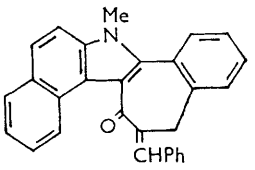
was obtained by hydrogenation. Chatterjea [2b] states that this ketone is also formed on reduction with lithium aluminium hydride, an unusual reaction which, however, is consistent with the survival of the carbonyl group of tropone itself in similar conditions.[6] Hydrogenation of the methyl derivative, or methylation of the dihydro-derivative, led to compound (VI; R = Me) so that, contrary to earlier belief, one active hydrogen atom is already present in the original ketone and hydrogenation does not introduce another. It follows that hydrogenation affects an olefinic system.

Attempts at selective oxidation failed, the cycloheptaindole either resisting or disintegrating. The dihydro-derivatives behaved similarly, probably because they are easily dehydrogenated. Thus, while the picrate and trinitrobenzene adduct of the methyl derivative (VI; R = Me) were stable, the perchlorate was transformed into the salt of (III; NMe for NH) when attempts were made to recrystallise it. Such ready dehydrogenation indicates considerable aromaticity in the parent compound (III).

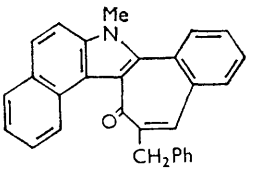
The carbonyl group in structure (III) is (i) part of a tropone ring, (ii) part of a vinylogous amide system, and (iii) shielded on one side by the naphthalene nucleus, so the lack of chemical reactivity is amply explained. The compound appears to form salts with strong acids and bases though they could not be isolated. It resisted hydrolysis by acid or base under very vigorous conditions. Attempted reduction with phosphorus and hydriodic acid was ineffective, and reduction by borohydride was extremely slow, giving ill-defined products.

The derivative (VI; R = Me) also failed to react with carbonyl reagents even though it is no longer a tropone. Proof that a carbonyl group is, however, present was obtained by vigorous reduction with lithium aluminium hydride, which gave an unstable alcohol converted during purification into an olefin. This product is formulated as (VII) although the nuclear magnetic resonance (n.m.r.) spectrum suggested that a mixture of isomers or tautomers was present. It was unstable, especially in air, so it was purified through the relatively stable picrate. Despite these difficulties it was now clear that the methyl group, which had survived these reactions, must be attached to nitrogen and not oxygen, and consequently that a carbonyl group must be present. That the methyl derivatives (III; NMe for NH) and (VI; R = Me) contain methylimino-groups had been indicated by the negative Ziesel determinations but obscured by the n.m.r. spectra which possessed bands of the appropriate intensity at 5·63 τ, that is, at fields usually appropriate to methoxyl groups, as was confirmed by the spectrum of 2-methoxy-*N*-methylbenzaldimine. The unusual position of this absorption now indicated that a pyrrole or indole ring might be present. Accordingly, the olefin (VII) was hydrogenated, giving the indole derivative (VIII) identical with an authentic specimen. The latter was made by alkylating the unmethylated parent, a compound already synthesised by Buu-Hoï and Xuong [7] who used the Fischer method with β-naphthylhydrazine and benzosuberone as components.

The n.m.r. spectrum of the ketone (VI; R = Me) showed a single band at 6·92 τ, appropriate to four protons all having the same chemical shift, two of which corresponded



(IX)



(X)

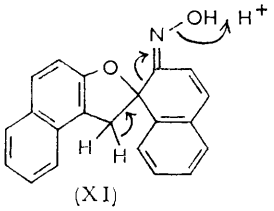
to an active methylene group since the intensity fell to half by base-catalysed deuteration. In agreement, the ketone condensed with benzaldehyde, but the product appeared from its spectrum to be a mixture of isomers or tautomers such as (IX) or (X). Hence the carbonyl group of ketone (VI; R = Me) cannot be at position 13 in structure (VIII) and must be at

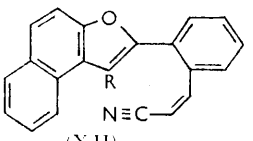
[6] Chapman, Pasto, and Griswold, *J. Amer. Chem. Soc.*, 1962, **84**, 1213.
[7] Buu-Hoï and Xuong, *J.*, 1952, 2225.

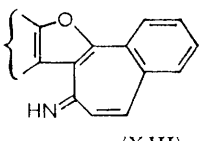
position 14 or 12. The last-mentioned position leads to an acetophenone grouping, with the usual carbonyl activity and spectral properties widely different from those exhibited by ketone (VI; R = Me), so that position 14 must be the correct location, and the parent must have structure (III).

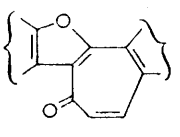
We have no strong evidence that the cycloheptaindole (III) should be formulated as shown rather than as the isomer containing a hydroxyl group and a double bond distribution as in (V): by analogy with pyridones and quinolones, however, structure (III) is preferable. In that case the relatively weak absorption bands at 1621 cm.$^{-1}$ in the spectrum of (III) and at 1610 cm.$^{-1}$ in that of the *N*-methyl derivative might be attributed to the double bond at position 12 since these bands are absent after hydrogenation. Though far from the usual carbonyl region, even of tropones, a relatively strong band at 1558 cm.$^{-1}$ might now be assigned to the carbonyl group in (III) greatly modified by both hydrogen bonding and the interaction indicated in (V): thus strong absorption is found in the dihydro-derivative (VI; R = H) at 1610, in the methyl derivative (III; NMe for NH) at 1626, and in the ketone (VI; R = Me) at 1640 cm.$^{-1}$.

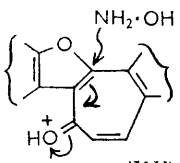
Since Abel's ketone (I; R = H) forms a semicarbazone, a phenylhydrazone,[8] and a 2,4-dinitrophenylhydrazone, the first stage in the transformation of Abel's ketone into structure (III) is almost certainly oximation. The next stage might involve a Beckmann transformation but, if so, it would be difficult to explain why the oximes from the substituted ketones (I; R = Ph) are stable. As the second stage, then, the fission indicated in (XI) can be considered: it leads to the cyanide (XII; R = H) in the case of Abel's ketone,

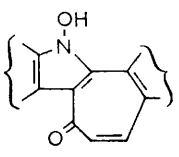

(XI)

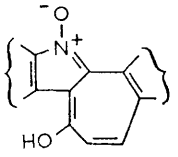

(XII)


(XIII)


(XIV)


(XV)


(XVI)


(XVII)

but in the oximes from the substituted ketones (I; R = Ph) it would be opposed by bringing into coplanarity three adjacent benzene residues in (XII; R = Ph). Generally, fissions of this kind occur in more vigorous conditions than those required here,[9] and the concurrent development of the naphthofuran ring is therefore regarded as important in promoting the present example.

The functional group in the cyanide (XII; R = H) is favourably placed for an internal Hoesch reaction [10] leading to imine (XIII), this reaction being aided further by the nucleophilic character of the furan ring. Both this cyclisation and the preceding fission usually need strongly acidic conditions whereas oximation of the ketone (I; R = H) has always been conducted in weakly acidic conditions. The yields have been correspondingly poor. When we conducted oximation in relatively concentrated hydrochloric acid the yields increased to nearly 60%, while in pyridine only tars resulted. We presume these tars to arise from the cyanide (XII; R = H), in part, since this could arise from the base-catalysed

[8] Pummerer and Cherbuliez, *Ber.*, 1914, **47**, 2957.
[9] Hill and Conley, *J. Amer. Chem. Soc.*, 1960, **82**, 645; Cottingham, *J. Org. Chem.*, 1960, **25**, 1473; Conley and Lange, *ibid.*, 1963, **28**, 210; Lukes and Hofman, *Coll. Czech. Chem. Comm.*, 1961, **26**, 523.
[10] Spoerri and DuBois, *Org. Reactions*, 1949, **5**, 387.

counterpart of the fission in (XI); but we failed to isolate the cyanide or to trap it by condensation.

The conditions used would permit rapid hydrolysis of the imine (XIII) to ammonia and the ketone (XIV) in which exchange of the cyclic oxygen for nitrogen would complete the transformation. The mechanism of the exchange would be related on the one hand to the conversion of pyrones into pyridones, and on the other to the Bucherer reaction. Although the reaction mixture does contain ammonium salts we think the nitrogen is more probably supplied by hydroxylamine for several reasons. Added ammonium salts do not improve the yield of the tropone-indole (III), whereas more than two mols. of hydroxylamine have to be supplied to give the best results. Ammonia being more basic than hydroxylamine, the concentration of the free base is less: moreover, hydroxylamine is the better nucleophile because of the α-effect.[11] After nucleophilic substitution as indicated in (XV) and some form of a Bucherer reaction, the product would be the *N*-hydroxyindole (XVI) or its tautomer, the *N*-oxide (XVII). The final reduction yielding structure (III) might be effected in part by oxidation–reduction reactions, since phenylhydroxylamine gives considerable quantities of aniline in strongly acidic media. It might also be effected by surviving hydroxylamine, since we have found in parallel work that this reagent will convert *N*-oxides such as (IV) into the corresponding amines in acid solution.

Experimental

Dibenzo[e:3′,4′]*cyclohepta*[b]*indol*-14-*one* (*Abel's "Anhydro-oxime"*) (III).—Hydroxylamine hydrochloride (12 g.) in ethanol (300 ml.) was added to Abel's ketone (20 g.) in tetrahydrofuran (100 ml.), and the mixture heated under reflux with concentrated hydrochloric acid (1 ml.) for 1 hr. The solid (13·3 g.) which slowly separated was washed with ethanol and recrystallised from dimethylformamide, giving the "anhydro-oxime" (III) in golden-yellow rhombs, m. p. >360° (decomp.) (Found: C, 85·6; H, 4·6; N, 4·5. Calc. for $C_{21}H_{13}NO$: C, 85·4; H, 4·4; N, 4·7%).

Shaken under hydrogen with 10% palladium–charcoal (0·11 g.), a suspension of the powdered cycloheptaindole (III) (4·0 g.) in dimethylformamide (150 ml.) slowly gave a clear solution (about 12 hr.). The catalyst and solvent were then removed, leaving the 12,13-*dihydroketone* (VI; R = H) which crystallised from acetic acid in pale yellow plates (1·8 g.), m. p. ~330° (decomp. from 310°) (Found: C, 84·7; H, 5·3; N, 4·6. $C_{21}H_{15}NO$ requires C, 84·8; H, 5·1; N, 4·7%). This was unaffected by boiling acetic anhydride, potassium hydroxide in boiling ethanol, and the usual carbonyl reagents.

The cycloheptaindole (III) (4·2 g.) in dimethylformamide (100 ml.) was shaken with methyl iodide (15 ml.) and silver oxide (4 g.). The silver oxide was renewed on the second and again on the third day: then the mixture was filtered and concentrated under reduced pressure. That part of the residue soluble in benzene was chromatographed on a column of alumina, and the fraction eluted by benzene was crystallised from acetic acid, giving 7-*methyldibenzo*[e:3′,4′]-*cyclohepta*[b]*indol*-14-*one* in yellow blades (3·1 g.), m. p. 219—221° (Found: C, 85·3; H, 5·0; N, 4·6; NMe, 5·4; OMe, 0. $C_{21}H_{12}O{\cdot}NMe$ requires C, 85·4; H, 4·9; N, 4·5; NMe, 9·4%). The *picrate* separated from acetic acid in bright red needles, m. p. 221—224° (decomp.) (Found: C, 62·2; H, 3·4; N, 10·3. $C_{28}H_{18}N_4O_8$ requires C, 62·45; H, 3·4; N, 10·4%). The *trinitrobenzene adduct* separated from acetic acid in orange-red needles, m. p. 250—252° (Found: C, 64·1; H, 3·5; N, 10·8. $C_{28}H_{18}N_4O_7$ requires C, 64·4; H, 3·5; N, 10·7%). Formed in acetic acid at 80°, the *perchlorate* crystallised in orange needles, m. p. 242° (decomp.) (Found: C, 64·1; H, 4·1; N, 3·2. $C_{22}H_{16}ClNO_5$ requires C, 64·5; H, 3·9; N, 3·4%). Attempts to oxidise this cycloheptaindole with ozone, osmium tetroxide, ruthenium tetroxide, or plumbic acetate failed to give useful results.

12,13-*Dihydro*-7-*methyldibenzo*[e:3′,4′]*cyclohepta*[b]*indol*-14-*one* (VI; R = Me).—(*a*) The dihydro-derivative (IV; R = H) (0·51 g.) was methylated by methyl iodide and silver oxide in dimethylformamide, giving a product which, purified from ethanol, afforded the 7-*methyl-derivative* in needles (0·33 g.), m. p. 184° (Found: C, 84·7; H, 5·8; N, 4·4; NMe, 6·8; OMe, 0·2%. $C_{21}H_{14}O{\cdot}NMe$ requires C, 84·9; H, 5·5; N, 4·5; NMe, 9·3%). The *picrate* crystallised from ethanol in dark red plates, m. p. 161—163° (Found: C, 62·0; H, 3·8; N, 10·0. $C_{28}H_{20}N_4O_8$

[11] Edwards and Pearson, *J. Amer. Chem. Soc.*, 1962, **84**, 16.

requires C, 62·2; H, 3·7; N, 10·4%). The *trinitrobenzene adduct* crystallised from acetic acid in bright red needles, m. p. 190—192° (Found: C, 64·1; H, 4·0; N, 10·5. $C_{28}H_{20}N_4O_7$ requires C, 64·1; H, 3·8; N, 10·7%). The *perchlorate*, m. p. 185° (decomp.), separated when 70% perchloric acid (2 ml.) in acetic acid (3 ml.) was added to the dihydro-*N*-methyl derivative (0·22 g.) in acetic acid (5 ml.) at 80° and the mixture cooled at once (Found: N, 3·5; 3·2. $C_{22}H_{18}ClNO_5$ requires N, 3·4%); attempted recrystallisation led to a dark solution which deposited the perchlorate, m. p. 242°, of the *N*-methyl derivative of the cycloheptaindole (III), identified spectroscopically.

(*b*) The *N*-methyl derivative (0·28 g.) of the cycloheptaindole (III) in ethanol, was shaken under hydrogen with palladium–charcoal for 17 hr., giving the dihydro-*N*-methyl derivative which crystallised from ethanol in needles (0·20 g.), m. p. 184°, identical with a specimen prepared as in (*a*). Attempts to oxidise this compound with dimethyl-*p*-nitrosoaniline led only to tars. No methylamine was liberated on fusion with potassium hydroxide, but with benzaldehyde (0·5 ml.) in ethanol (25 ml.) containing sodium ethoxide (0·2 g.), this compound (0·26 g.) reacted during 1 min. at 70° and, when cool, the mixture supplied the *benzylidene derivative* (IX) or (X), as bright yellow needles (0·14 g.), m. p. 179—181° (sometimes 227—230°) (Found: C, 87·5; H, 5·5; N, 3·5. $C_{29}H_{21}NO$ requires C, 87·2; H, 5·3; N, 3·5%). The n.m.r. spectrum exhibited absorption due to aromatic protons (relative intensity 16) and a complex band (relative intensity 4·6) consisting of a sharp peak due to *N*-Me at τ 6·22 together with two weaker, broader bands (τ 6·05 and τ 6·17) attributed to methylene groups in structures (IX) and (X).

12,13-*Dihydro*-7-*methyldibenzo*[e:3′,4′]*cyclohepta*[b]*indole* (VIII).—(*a*) The dihydro-*N*-methyl derivative (VI; R = Me) (1·0 g.) was treated, in tetrahydrofuran (50 ml.), with lithium aluminium hydride (0·4 g.). There was little change until the mixture was heated. After an hour, the mixture was cooled and residual hydride was destroyed by means of wet tetrahydrofuran. Ether (200 ml.) was added, and inorganic materials were removed by 2N-sulphuric acid and then water. The ether was dried (Na_2SO_4) and evaporated *in vacuo*, leaving a yellowish oil with the spectroscopic properties of an alcohol. This oil, in benzene, was chromatographed on silica. The first fractions were small and highly fluorescent, and were discarded: the next fractions contained the major product, a clear gum with a pale blue fluorescence but devoid of hydroxylic absorption. An unwanted component of this gum was removed by repeated extraction with boiling methanol. The residue appeared to be unstable in air and could not be purified easily, but with picric acid it gave a derivative crystallising readily from benzene in long, thin, blood-red or black prisms (1·3 g.), m. p. ~140° (Found: C, 55·95, 56·0; H, 3·4, 3·3; N, 12·2%): this substance appeared to be an unstable dipicrate, which readily lost picric acid, so the analyses were unsatisfactory. Obtained as the sole product from the picrate by chromatography from benzene on alumina, *compound* (VII) formed a glass which gradually deposited prisms, m. p. 130°, difficult to purify further (Found: C, 89·6; H, 5·9; N, 4·7. $C_{22}H_{17}N$ requires C, 89·5; H, 5·8; N, 4·7%). In addition to absorption in the aromatic region, the n.m.r. spectrum contained a sharp band (τ 6·41) due to *N*-Me and multiplets between τ 6·4 and 7·4 attributed to methylene and methine groups in tautomeric structures.

This cycloheptaindole (0·5 g.) in ethyl acetate (20 ml.) was shaken with 10% palladium–charcoal (0·2 g.) and hydrogen until uptake (~40 ml.) ceased. The catalyst and solvent were removed, leaving a yellowish solid which, purified through the picrate, gave 12,13-*dihydro*-7-*methyldibenzo*[e:3′,4′]*cyclohepta*[b]*indole* as rectangular plates (0·3 g.), having m. p. 145—146° after crystallisation from ethanol (Found: C, 88·7; H, 6·6; N, 4·8%. $C_{22}H_{19}N$ requires C, 88·85; H, 6·45; N, 4·7%). The *picrate* formed deep red needles, m. p. 184—185° (from ethanol) (Found: C, 63·5; H, 4·1; N, 10·6. $C_{28}H_{20}N_4O_7$ requires C, 64·1; H, 3·9; N, 10·7%).

(*b*) Prepared by the method of Buu-Hoï and Xuong [7] and purified through the picrate, 12,13-dihydrodibenzo[*e*:3′,4′]cyclohepta[*b*]indole (1·9 g.), in ether, was added to a stirred solution of potassium (0·3 g.) in liquid ammonia (50 ml.) containing ferric nitrate (0·05 g.). An hour later, methyl iodide (0·4 ml.) was added and, after another 20 min., volatile materials were permitted to escape. The residue was mixed with water (50 ml.) and ether (50 ml.), and the organic layer was washed with water, dried, and evaporated. The residue crystallised from ethanol, giving the dihydro-7-methyl derivative in plates, m. p. and mixed m. p. 145—146°, further identified spectroscopically (Found: C, 88·6; H, 6·5; N, 4·8%).

Dibenz[,aj]*acridine* 7-*Oxide* (IV).—The dibenzacridine (4·0 g.) in acetic acid (50 ml.) was treated with hydrogen peroxide (100-vol.; 6 ml.) at 80° for 1 hr. Next day the crystalline product was collected and, when purified from acetic acid, gave an unstable acetate as yellow

prisms, m. p. ~270° (decomp.), a solution of which in pyridine deposited the *oxide* in yellow needles (2·9 g.), m. p. 264—265° (decomp.) (Found: C, 85·2; H, 4·7; N, 4·75. $C_{21}H_{13}NO$ requires C, 85·4; H, 4·4; N, 4·7%). Interaction of this oxide (1·4 g.) with methyl sulphate (2 ml.) in xylene (100 ml.) at 100° for 6 hr. gave 7-*methoxydibenz*[a,j]*acridinium methyl sulphate*, which separated from aqueous methanol in yellow prisms (2·6 g.), m. p. 318—320° (decomp.) (Found: C, 65·5; H, 5·3; N, 3·35. $C_{23}H_{19}NO_4S$,MeOH requires C, 65·9; H, 5·3; N, 3·2%).

o-*Methoxy*-N-*methylbenzaldimine*.—Prepared by the interaction of *o*-methoxybenzaldehyde and methylamine in ethanol, this imine had b. p. 78—80°/0·7 mm. (lit., 134°/20 mm.) and was spectroscopically pure after three redistillations (Found: C, 72·3; H, 7·1; N, 9·3. Calc. for $C_9H_{11}NO$: C, 72·45; H, 7·4; N, 9·4%). It rapidly liberated methylamine when mixed with aqueous-ethanolic potassium hydroxide, and absorbed at τ 4·22 (OMe). A second band at τ 4·55 (>NMe) showed slight splitting (J 3 c./sec.).

We thank Unilever Ltd. for financial support for C. F. and H. D. L.

UNIVERSITY OF LIVERPOOL. [*Received, January* 14*th*, 1964.]