124. *Indoles. Part III.** *The Action of* (A) *Ozone, and* (B) *Osmium Tetroxide on Some Indole Derivatives.*

By D. W. OCKENDEN and K. SCHOFIELD.

(*A*) Ozone converted a number of 2 : 3-disubstituted indoles in acetic acid into 2-acylaminoaryl ketones. In ethyl acetate crystalline ozonides were obtained from 3-alkyl-2-aryl-, 2 : 3-dialkyl-, and 2 : 3-diaryl-indoles. Some 1-acylindoles also provided crystalline ozonides.

(*B*) Osmium tetroxide in benzene–pyridine converted 1-acetyl- and 1-benzoyl-indoles into crystalline osmic esters, hydrolysable to indole glycols.

(*A*) OXIDATIVE fissions of the indole 2 : 3-double bond (I $\longrightarrow$ II) have provided routes to various 2-aminoaryl ketones (Schofield and Theobald, *J.*, 1949, 796; 1950, 1505). In extending the synthetic applications of such reactions we considered the use of ozone in certain cases. Various authors have used this reagent in similar reactions, and in some instances the isolation of relatively stable, crystalline ozonides was recorded. Thus (I; R = Ph or *p*-C_6H_4·OMe, R′ = Me, R″ = H, and R = *p*-C_6H_4·OMe, R′ = Me, R″ = OMe) (Mentzer, Molho, and Berguer, *Compt. rend.*, 1949, **229**, 1237; *Bull. Soc. chim.*, 1950, 555), and [I; R = 2-(4 : 5-diethylpyridyl), R′ = Et, R″ = H] (Karrer and Enslin, *Helv. Chim. Acta*, 1949, **32**, 1390) provided crystalline ozonides, hydrolysable to derivatives of type (II). On the other hand, indole, 2-methylindole, skatole, 3-ethylindole, 2 : 3-dimethylindole, and tryptophan (Witkop and Graser, *Annalen*, 1944, **556**, 103), tetrahydrocarbazole (Witkop and Patrick, *J. Amer. Chem. Soc.*, 1951, **73**, 2196), and various other indoles (Scholz, *Helv. Chim. Acta*, 1935, **18**, 923; Mentzer, Molho, and Berguer, *loc. cit.*; *Compt. rend.*, 1950, **230**, 760; *Bull. Soc. chim.*, 1950, 782) evidently did not provide isolable ozonides.

Stable, crystalline ozonides of this class are rarely met (Criegee, " Organische Peroxyde,"

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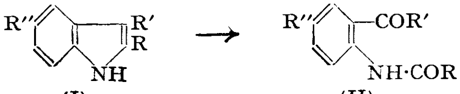
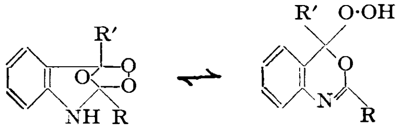
* Part II, *J.*, 1950, 1505.

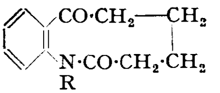
Fortschr. Chem. Forsch., Vol. I, Springer Verlag, Berlin, 1950), and Criegee and Wenner (*Annalen*, 1949, **564**, 9) proved recently that the supposed ozonides from 9 : 10-octalin possessed a different kind of (dimeric) structure. It therefore appeared desirable to determine the molecular weights of representative indole ozonides. Further, since the ozonides described hitherto all arise from 3-alkyl-2-arylindoles, we wished to decide if this type of structure was essential. In view of recent work of Witkop and Patrick (*J. Amer. Chem. Soc.*, 1952, **74**, 3855, 3861) on the interesting reactions of 3-methyl-2-phenylindole ozonide, we record our observations.



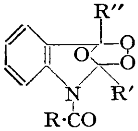
(I) (II)



(III) (IV)



(V)



(VI)

Acetic acid, ethyl acetate, formamide, and methanol were used by the authors mentioned above as solvents in which to effect ozonisation of indoles. Our preliminary experiments indicated that formamide was not a sufficiently powerful solvent to serve generally in this field, and we have ozonised each substance examined in both acetic acid and ethyl acetate.

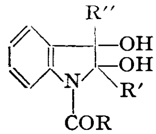
Generally, from experiments in acetic acid, at room temperature, only 2-acylaminoaryl ketones (II) were isolated, as was expected. Thus, 2 : 3-dimethylindole gave 2-acetamidoacetophenone, as described by Witkop and Graser (*loc. cit.*), 2 : 3 : 5- and 2 : 3 : 6-trimethylindole provided 2-acetamido-5- and 2-acetamido-4-methylacetophenone respectively, and 2 : 3-dimethyl-4-nitroindole yielded 2-acetamido-6-nitroacetophenone. The yield (53%) in the last case is considerably better than that (26%) obtained by Schofield and Theobald (*J.*, 1949, 796) by chromic acid oxidation. 3-Methyl-2-phenyl- (cf. Mentzer *et al.*, *loc. cit.*) and 2-methyl-3-phenyl-indole likewise were converted into 2-benzamidoacetophenone and 2-acetamidobenzophenone. Although 2 : 3-diphenyl- and 5-methyl-2 : 3-diphenyl-indole gave 2-benzamido- and 5-methyl-2-benzamido-benzophenone, 6-methyl-2 : 3-diphenylindole gave a mixture.

As was expected from the work of Mentzer *et al.* (*loc. cit.*), our results were in some cases different when ethyl acetate at 0° was used as solvent. Although 2 : 3-dimethyl-, 2 : 3-diphenyl-, 2-methyl-3-phenyl-, 2 : 3-dimethyl-4-nitro-, and 2 : 3 : 5-trimethyl-indole, and tetrahydrocarbazole again yielded ketones (II), 3-methyl-2-phenyl- (as found by Mentzer and his associates) and 5- and 6-methyl-2 : 3-diphenyl-indole yielded crystalline ozonides. Further, although 2 : 3 : 6-trimethylindole in ethyl acetate at 0° gave 2-acetamido-4-methylacetophenone, a similar reaction at —20° provided a small yield of a crystalline ozonide. It should be noted that in this work only the theoretical amount of ozone was passed into the solution, and the method used by Witkop and Patrick (*loc. cit.*) for preparing 3-methyl-2-phenylindole ozonide suggests that for this reason our yields of ozonides were not the maximum obtainable. In addition to the previously known type of ozonide from a 3-alkyl-2-arylindole, it is clear that stable derivatives can arise from 2 : 3-dialkyl- and 2 : 3-diarylindoles. Qualitatively, our experience suggests that ozonides from indoles containing an electron-releasing substituent in the *Bz*-ring are possibly the more stable. The experiments on 2 : 3 : 6-trimethylindole indicate that crystalline ozonides might be obtained from a larger range of indoles provided the reaction conditions were carefully chosen.

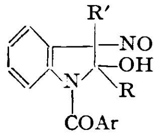
Molecular-weight determinations in chloroform on the ozonides from 3-methyl-2-phenyl- and 5-methyl-2 : 3-diphenyl-indole, the former confirming the recent determination in acetone by Witkop and Patrick (*loc. cit.*), do not conflict with the formulation of these substances in the normal way (III). The American authors adduced evidence that there exists ring-chain tautomerism between (III) and (IV). The ozonides could be crystallised from absolute ethanol or ethyl acetate, but were readily hydrolysed. Thus, 5-methyl-2 : 3-diphenylindole ozonide, when crystallised from non-absolute alcohol, gave 2-benzamido-5-methylbenzophenone. The ozonides decomposed vigorously at the m. p., forming the ketonic products (II) (Witkop and Patrick, *loc. cit.*).

Witkop and Patrick's interpretation of their experiments in terms of tautomerism between (III) and (IV) adds interest to our observations on the action of ozone on 1-acylindoles. In acetic acid, 1-acetyl-2 : 3 : 5-trimethylindole, and 9-acetyltetrahydrocarbazole provided 2-diacetylamino-5-methylacetophenone and the cyclic derivative (V ; R = Me·CO) respectively, whilst 1-acetyl-2 : 3-diphenylindole was unchanged by such treatment. On the other hand, 1-acetyl-2 : 3-dimethyl- and -2 : 3 : 5-trimethyl-indole, and 9-acetyltetrahydrocarbazole, when ozonised in ethyl acetate yielded products crystallisable from absolute alcohol, ethyl acetate, or chloroform–ligroin which were apparently ozonides of the type (VI). The molecular weight of the product from 1-acetyltetrahydrocarbazole showed it to be monomeric. Under the conditions used these products were isolated in poor yield (10—15%). They resembled the previously mentioned ozonides in the vigorous manner in which they decomposed on melting. A few experiments with 1-benzoyltetrahydrocarbazole were not entirely satisfactory. The product of ozonisation in ethyl acetate appears to be an impure ozonide, and that from reaction in acetic acid is of uncertain nature (see Experimental section). If correctly represented by (VI), these *N*-acylated ozonides are clearly incapable of ring-chain tautomerism, and that from 9-acetyltetrahydrocarbazole is especially interesting. Witkop and Patrick (*J. Amer. Chem. Soc.*, 1951, **73**, 2196) who obtained (V; R = H) by ozonising tetrahydrocarbazole in methanol at —79° considered that a true ozonide of tetrahydrocarbazole could not exist for steric reasons. This is evidently not so. The low yield of 2 : 3 : 6-trimethylindole ozonide now obtained suggests that these derivatives of alkyl-substituted indoles are highly reactive, and that only when the mobility of the system is restricted as in *N*-acylation can ozonides of the tetrahydrocarbazole group be isolated. Witkop and Patrick (*loc. cit.*) suggested that (VI ; R = R″ = Me, R′ = Ph) might be an intermediate in the reaction between 3-methyl-2-phenylindole ozonide and pyridine–acetic anhydride. We hope to examine these substances further.

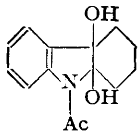
(*B*) Most of the few known glycols of the type (VII) were prepared by Perkin, Plant,



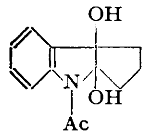
(VII)



(VIII)



(IX)



(X)

and their associates (for a summary see Schofield, *Quart. Reviews*, 1950, **4**, 391) by treating 1-acylindoles with nitric acid in acetic acid. Broadly speaking, 9-acetyl-, 9-cinnamoyl- and 9-carbethoxy-derivatives of 1 : 2 : 3 : 4-tetrahydrocarbazole and 2 : 3-dimethylindole give such glycols, whilst *N*-aroyl derivatives give nitro-alcohols (VIII). 1-Acyl-2 : 3-diphenylindoles merely undergo nuclear nitration, whilst nitro-alcohols are the only addition products to have been isolated from *N*-acyldihydropentindoles. In some cases, though not in the dihydropentindole group, the nitro-alcohols are converted by hot ethanol into the glycol. The compound (X) was prepared by treating *N*-acetyldihydropentindole with chlorine in acetic acid (Plant and Tomlinson, *J.*, 1933, 298). The mode of formation of the glycols, either in nitric–acetic acid, or during halogenation, is unknown. Witkop (*J. Amer. Chem. Soc.*, 1950, **72**, 614) accounted for striking differences between the behaviour of (IX) and (X) by reference to the size of the third ring. Because of the different methods used in preparing (IX) and (X), and to throw some light on the origin of such glycols, it seemed of value to establish their configuration by alternative syntheses.

Initially we attempted the perhydroxylation of some indoles in acetone by means of dilute aqueous potassium permanganate, a reagent known to convert ethylenes into *cis*-

glycols (Raphael, *J.*, 1949, S 44; Cook and Schoental, *J.*, 1950, 47). 2 : 3-Dimethyl- and -diphenyl-indole, and their *N*-acetyl derivatives, all reduced 1% permanganate solution relatively quickly (by comparison with a blank run) but in each case most of the starting material was recovered unchanged. Presumably a small amount of each indole was very highly oxidised. It is noteworthy that Koelsch (*J. Amer. Chem. Soc.*, 1944, **66**, 1983), using hot concentrated permanganate solution, converted 2 : 3-diphenylindole into a C_{40} compound.

We then turned to the Milas reagent (Milas and Sussman, *J. Amer. Chem. Soc.*, 1936, **58**, 1302), which we used in the way described by Mugdan and Young (*J.*, 1949, 2988). Under these conditions, with 2 : 3-diphenyl- and 2 : 3 : 5-trimethyl-indole, tetrahydrocarbazole, or their *N*-acetyl derivatives, only starting material and small amounts of uncrystallisable products were obtained. Application of the reagent under different conditions might be effective (Witkop and Ek, *J. Amer. Chem. Soc.*, 1951, **73**, 5664).

Finally it was found * that the *N*-acetyl derivatives of tetrahydrocarbazole, dihydropentindole, and 2 : 3-dimethyl-, 2 : 3-diphenyl-, and 2 : 3 : 5-trimethyl-indole with osmium tetroxide in pyridine–benzene gave, quantitatively, highly crystalline, fawn-coloured osmic esters, which were hydrolysed to the glycols (VII; R = Me) in moderate yield. In no case was a crystalline product obtained from the *N*-unsubstituted indoles; in such experiments colloidal osmium was liberated. Indole, skatole, tryptophan, and carbazole behaved similarly, and although pyrrole formed a crystalline complex, nothing could be isolated after hydrolysis (the experiments were on a very small scale). The formation of a glycol from 1-acetyl-2 : 3-diphenylindole is interesting since this substance is not attacked at the 2 : 3-double bond by nitric–acetic acid (Fennell and Plant, *J.*, 1932, 2872), ozone (see above), or bromine (Plant and Tomlinson, *J.*, 1933, 955). Also of interest is the preparation by the same method of glycols from 1-benzoyl-2 : 3-dimethylindole, and 9-benzoyltetrahydrocarbazole. As mentioned above, such glycols are not formed from the 1-benzoylindoles and nitric–acetic acid, nitro-alcohols (VIII) being produced. The compound (IX; Bz instead of Ac) results, however, from the reaction between 9-benzoyltetrahydrocarbazole and chlorine in acetic acid (Plant and Tomlinson, *J.*, 1933, 298), and from the corresponding nitro-alcohol in hot ethanol (Plant and Rutherford, *J.*, 1929, 1970).

Criegee's work (*Annalen*, 1936, **522**, 75; 1942, **550**, 99) strongly suggests that the products now described are *cis*-glycols, although the failure of (IX) to provide an acetonyl derivative (Witkop, *J. Amer. Chem. Soc.*, 1950, **72**, 613) is puzzling. If in nitric–acetic acid media the *cis*-glycols arise from ionic processes it is not likely that they are primary products. If their precursors are nitro-alcohols (cf. VIII) the latter would presumably be *trans*-forms. However, Witkop and Ek (*J. Amer. Chem. Soc.*, *loc. cit.*) state that the presence of the nitrogen alone in a related glycol makes the *trans*-form susceptible to easy inversion. There seems to be little evidence on this point, and the nitro-alcohols require investigation.

Some of the indoles used in this work were prepared by the Fischer synthesis with the boron trifluoride-ether complex as the catalyst, in acetic acid solution (Snyder and Smith, *J. Amer. Chem. Soc.*, 1943, **65**, 2454). In this way 2 : 3-dimethyl-, 2-methyl-3-phenyl-, 5-methyl-2 : 3-diphenyl-, and 2 : 3 : 5-trimethyl-indole were obtained in good yield. 2-Methyl-3-phenylindole was previously prepared by Trenkler (*Annalen*, 1888, **248**, 11) who used zinc chloride or alcoholic hydrochloric acid as the catalyst in the cyclisation of phenylacetone phenylhydrazone, and the structure of the compound is now proved by its conversion into 2-acetamidobenzophenone.

EXPERIMENTAL

2 : 3 : 5-*Trimethylindole*.—Ethyl methyl ketone *p*-tolylhydrazone (12·2 g.; obtained by heating equivalent quantities of the ketone and *p*-tolylhydrazine at 95° for 1 hour and then drying the product in ether), boron trifluoride–ether (8·6 g.), and acetic acid (120 c.c.) were refluxed for 3 hours. The hot mixture was filtered and concentrated, giving the indole (6·2 g.; m. p. 120—121°). Further concentration of the mother-liquor and crystallisation of the residue from alcohol brought the yield to 8·75 g. (80%).

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* A preliminary account of this work was given in *Nature*, 1951, **168**, 603.

Alternatively, the hydrazone [from the ketone (6·35 g.) as above] was treated gradually with powdered anhydrous zinc chloride (13·9 g.), and the mixture was heated gently until a vigorous reaction set in. When this had subsided the product was isolated by steam-distillation and extraction of the distillate with ether. Concentration gave the substantially pure indole (10·2 g., 72%). 2 : 3 : 5-Trimethylindole formed fawn plates, m. p. 121—122° (Found : C, 82·4; H, 8·2. Calc. for $C_{11}H_{13}N$: C, 82·9; H, 8·2%). This compound has been obtained previously (Beilstein's "Handbuch der organischen Chemie," 4th edn., Vol. XX; Hickinbottom, *J.*, 1934, 1981; Jenetzky and Verkade, *Rec. Trav. chim.*, 1945, **65**, 691) but not by the Fischer synthesis.

The indole (3 g.), acetic anhydride (20 c.c.), and one drop of 2N-sulphuric acid were refluxed for 12 hours. The solution was poured into iced water, and the product (2·6 g.) was collected. 1-*Acetyl*-2 : 3 : 5-*trimethylindole* separated from aqueous methanol as cream prisms, m. p. 85—86° (Found : C, 77·7; H, 7·5. $C_{13}H_{15}ON$ requires C, 77·6; H, 7·5%).

2-*Methyl*-3-*phenylindole*.—Benzyl methyl ketone phenylhydrazone (1 g.), acetic acid (10 c.c.), and boron trifluoride–ether (0·73 g.) were refluxed for 3 hours. The crude product obtained by filtration and concentration crystallised from light petroleum (b. p. 40—60°) as cream prisms (0·6 g., 65%), m. p. 58—60°. Trenkler (*loc. cit.*) gives m. p. 59—60°. The material from a similar experiment with 6 g. of the hydrazone was passed in benzene over alumina, giving 2-methyl-3-phenylindole in the same yield as above. The column showed a second yellow band, but elution gave only very small amounts of intractable oils. If 2-benzylindole is formed in the experiment it could only be as a trace.

5-*Methyl*-2 : 3-*diphenylindole*.—Deoxybenzoin and *p*-tolylhydrazine were heated in equivalent amounts for 1 hour at 95°; the product crystallised from alcohol as discoloured needles (71%), m. p. 118—120°, which quickly deteriorated. This hydrazone (5 g.), boron trifluoride–ether (2·36 g.), and acetic acid (50 c.c.) were refluxed for 3 hours. The hot solution was filtered and concentrated. Addition of water and crystallisation of the product from aqueous alcohol gave white needles (3·85 g., 82%), m. p. 148—150°. The indole (3·4 g., 73%) was also obtained by heating the hydrazone (5 g.) with concentrated hydrochloric acid (50 c.c.) for 4 hours at 95°, and crystallising the product from aqueous alcohol. 5-Methyl-2 : 3-diphenylindole exhibited deep blue fluorescence in aqueous alcohol, and when pure formed needles, m. p. 150—151° (Found : C, 90·2; H, 6·5. Calc. for $C_{21}H_{17}N$: C, 89·0; H, 6·1%). Ritchie (*Proc. Roy. Soc. N.S. Wales*, 1946, **80**, 33) gives m. p. 153°.

9-*Acetyl*-1 : 2 : 3 : 4-*tetrahydrocarbazole*.—The following method was preferable to that using anhydrous potassium acetate, and appears simpler than that due to Witkop (*J. Amer. Chem. Soc.*, 1950, **72**, 614). Tetrahydrocarbazole (5 g.), acetic anhydride (25 c.c.), and a trace of camphorsulphonic acid were refluxed for 7 hours. The solvent was removed under reduced pressure, and distillation gave the product (b. p. 230—232°/20 mm.), which was crystallised from alcohol, yielding 3·1 g. (50%), m. p. 72—74°.

Experiments with Ozone.—The results (Table 1) were obtained by treating the indole (0·5 g.) with approx. 5% ozonised oxygen until the theoretical amount (as indicated by titration) of ozone had been absorbed. Experiments in acetic acid were carried out at room temperature, those in ethyl acetate at 0°. In the first case the product was isolated by basification and ether-extraction, and in the second by concentration at room temperature. The m. p.s of the ozonides, being decomposition temperatures, depended considerably on the rate of heating.

Products. (2) 2-*Acetamido*-5-*methylacetophenone* gave fawn plates (Found : C, 69·4; H, 6·7. $C_{11}H_{13}O_2N$ requires C, 69·1; H, 6·9%). This compound (0·5 g.) was heated at 95° for 2 hours with concentrated hydrochloric acid (5 c.c.), water (5 c.c.), and alcohol (10 c.c.). After cooling, the solution was basified and chilled, and the resulting 2-amino-5-methylacetophenone was crystallised from ether–light petroleum (b. p. 40—60°), forming yellow plates, m. p. 41—42° (Found: C, 72·5; H, 7·7%). Giacalene and Russo (*Gazzetta*, 1935, **65**, 1127) gave m. p. 50—51°.

(3) 2 : 3 : 6-*Trimethylindole ozonide* formed colourless crystals (Found : C, 64·1; H, 5·9. $C_{11}H_{13}O_3N$ requires C, 63·8; H, 6·3%). The m. p. of 2-acetamido-4-methylacetophenone (Found : C, 69·85; H, 7·0. Calc. for $C_{11}H_{13}O_2N$: C, 69·1; H, 6·85%) was not depressed by admixture with authentic material (Keneford, Morley, and Simpson, *J.*, 1948, 1702).

(5) (V; R = H). This compound has usually been described as being faintly yellow. Our specimen, m. p. 154—156°, was colourless (Found : C, 70·9; H, 6·5. Calc. for $C_{12}H_{13}O_2N$: C, 70·9; H, 6·4%).

(6) 2-Acetamidobenzophenone formed prisms (Found : C, 74·6; H, 5·4. Calc. for $C_{15}H_{13}O_2N$: C, 75·3; H, 5·5%), and did not depress the m. p. of a genuine specimen.

(7) The ozonide [Found : C, 71·5; H, 4·8; N, 4·8%; *M* (in acetone), 246. Calc. for

$C_{15}H_{13}O_3N$: C, 70·6; H, 5·1; N, 5·5%; *M*, 255] was recovered unchanged by evaporation of the solution used in determining the molecular weight. 2-Benzamidoacetophenone (Found : C, 75·3; H, 5·1. Calc. for $C_{15}H_{13}O_2N$ C, 75·3; H, 5·5%).

(9) 5-*Methyl*-2 : 3-*diphenylindole ozonide* formed prisms [Found : C, 75·6; H, 5·2; N, 3·7%; *M*(in acetone), 330. $C_{21}H_{17}O_3N$ requires C, 76·1; H, 5·2; N, 4·2%; *M*, 332] and was recovered unchanged from the mol.-wt. determination. 2-Benzamido-5-methylbenzophenone gave cream prisms, m. p. 115—117° (Found: C, 79·4; H, 5·4. Calc. for $C_{21}H_{17}O_2N$: C, 80·0; H, 5·4%). Chattaway and Lewis (*J.*, 1904, **85**, 589) gave m. p. 118°.

(10) 6-*Methyl*-2 : 3-*diphenylindole ozonide* formed prisms (Found : C, 76·1; H, 5·3%).

(11) 1-*Acetyl*-2 : 3-*dimethylindole ozonide* gave very small crystals (Found : C, 62·1; H, 5·8; N, 5·5. $C_{12}H_{13}O_4N$ requires C, 61·3; H, 5·6; N, 6·0%).

(12) 1-*Acetyl*-2 : 3 : 5-*trimethylindole ozonide* formed small crystals (Found : C, 63·3; H, 6·1. $C_{13}H_{15}O_4N$ requires C, 62·6; H, 6·1%), and 2-*diacetylamino*-5-*methylacetophenone* plates (Found : C, 66·4; H, 6·2. $C_{13}H_{15}O_3N$ requires C, 66·9; H, 6·5%).

(13) Impure 9-acetyltetrahydrocarbazole ozonide gave small crystals [Found : C, 62·8; H, 5·6%; *M* (in chloroform), 240. $C_{14}H_{15}O_4N$ requires C, 64·3; H, 5·8%; *M*, 261], and (V; R = Ac) small prisms (Found : C, 68·7; H, 6·5. $C_{14}H_{15}O_3N$ requires C, 68·55; H, 6·2%).

9-Benzoyltetrahydrocarbazole (0·5 g.) was ozonised in ethyl acetate (25 c.c.), and the oily product obtained by removing the solvent was triturated with alcohol. The *ozonide* (40 mg.) had m. p. 220—225° (decomp.) (from chloroform–ligroin) (Found : C, 68·6; H, 5·2. $C_{19}H_{17}O_4N$ requires C, 70·5; H, 5·3%). A similar experiment in acetic acid (30 c.c.), by working up in the usual way, yielded 0·3 g. of crude product, which after several crystallisations from methanol

TABLE 1.

Indole	EtOAc (c.c.)	AcOH + H_2O (c.c.)		Product [a]	Solvent [b]	Final M. p.	Final Yield, %
(1) 2 : 3-Dimethyl	20	—	—	2-Acetamidoacetophenone	1	67—70° [c]	52
	—	15	5	,,	,,	,,	49
(2) 2 : 3 : 5-Trimethyl	25	—	—	2-Acetamido-5-methylacetophenone	2	123—125	50
	—	25	5	,,	,,	,,	47
(3) 2 : 3 : 6-Trimethyl [d]	25	—	—	Ozonide	3	138	8
	—	25	—	2-Acetamido-4-methylacetophenone	4	75—77	45
(4) 2 : 3-Dimethyl-4-nitro	25	—	—	2-Acetamido-6-nitroacetophenone	5	143—144	53
	—	40	—	,,	,,	,,	,,
(5) Tetrahydrocarbazole	25	—	—	(V; R = H)	6	152—154	40
	—	25	5	,,	,,	154—156	44
(6) 2-Methyl-3-phenyl	25	—	—	Tar [e]	—	—	—
	—	30	5	2-Acetamidobenzophenone	7	71—73	40
(7) 3-Methyl-2-phenyl	25	—	—	Ozonide	3	157—158 [f]	66
	—	25	5	2-Benzamidoacetophenone	7	97—99	48
(8) 2 : 3-Diphenyl	20	—	—	2-Benzamidobenzophenone	5	85—87	55
	—	15	5	,,	,,	,,	57
(9) 5-Methyl-2 : 3-diphenyl	25	—	—	Ozonide	3	158—160	50
	—	50	5	2-Benzamido-5-methylbenzophenone	8	115—117	45
(10) 6-Methyl-2 : 3-diphenyl	25	—	—	Ozonide	6	159—160	52
	—	35	—	Mixture	—	—	—
(11) 1-Acetyl-2 : 3-dimethyl	25	—	—	Ozonide	3	227—228	10
	—	35	—	Small yield of crude ozonide	—	—	—
(12) 1-Acetyl-2 : 3 : 5-trimethyl	25	—	—	Ozonide	6	200—215	25
	—	25	—	2-Diacetylamino-5-methylacetophenone	7	119—121	26
(13) 9-Acetyltetrahydrocarbazole	25	—	—	Ozonide	9	232	10
	—	25	5	(V; R = Ac)	8	127—129	35

[a] See main text for comments. [b] 1, Aq. $COMe_2$. 2, MeOH. 3, Abs. EtOH. 4, C_6H_6–ligroin. 5, Aq. EtOH. 6, EtOAc. 7, Et_2O–ligroin. 8, EtOH. 9, $CHCl_3$–ligroin. [c] Alone and mixed with an authentic specimen. [d] Ockenden and Schofield, unpublished. [e] Even at –20°. [f] Mentzer, Molho, and Berguer, *loc. cit.*

TABLE 2.

Substance	Wt. (g.)	Yield of osmic ester (g.)	Wt. (g.) of crude product	Solvent	M. p. of pure product
(1) 9-Acetyltetrahydrocarbazole	0·084	0·260	0·017	C_6H_6	203—204°
(2) 8-Acetyldihydropentindole	0·079	0·214	0·060	,,	149—151
(3) 1-Acetyl-2 : 3-dimethylindole ...	0·074	0·222	0·060	,,	130—133
(4) 1-Acetyl-2 : 3 : 5-trimethylindole	0·081	0·200	0·061	,,	102—108
(5) 1-Acetyl-2 : 3-diphenylindole	0·123	0·223	0·032	,,	206—208
(6) Pyrrole	0·027	0·130	0·010	—	—
(7) 1-Benzoyl-2 : 3-dimethylindole ...	0·200	0·410	0·100	C_6H_6–ligroin	215—218
(8) 9-Benzoyltetrahydrocarbazole ...	0·216	0·430	0·100	,,	144—147

(1) Leaflets (Found : C, 68·3; H, 7·1. Calc. for $C_{14}H_{17}O_3N$: C, 68·1; H, 6·9%), identical with authentic material (Perkin and Plant, *J.*, 1923, **123**, 676). (2) Prisms (Found : C, 66·9; H, 4·6. Calc. for $C_{13}H_{15}O_3N$: C, 66·9; H, 6·5%), identical with a genuine specimen (Plant and Tomlinson, *J.*, 1933, 298). (3) Prisms (Found : C, 65·9; H, 7·2. Calc. for $C_{12}H_{13}O_3N$: C, 65·1; H, 6·8%). Plant and Whitaker (*J.*, 1940, 283) give m. p. 132—134°. (4) Needles (Found : C, 66·3; H, 7·4. $C_{13}H_{17}O_3N$ requires C, 66·3; H, 7·3%). The m. p. could not be improved. (5) Prisms (Found : C, 76·8; H, 5·6. $C_{22}H_{19}O_3N$ requires C, 76·5; H, 5·5%). (7) Prisms (Found : C, 74·3; H, 6·9. $C_{17}H_{17}O_3N,\frac{1}{2}C_6H_6$ requires C, 74·5; H, 6·3%). (8) Prisms (Found : C, 74·1; H, 6·4. Calc. for $C_{19}H_{19}O_3N$: C, 73·7; H, 6·2%). Plant and Tomlinson (*loc. cit.*) give m. p. 144—146°.

provided needles, m. p. 180—182°, of a *hydrate* (Found : C, 66·1; H, 6·2. $C_{19}H_{17}O_3N,2H_2O$ requires C, 66·4; H, 6·2%).

Experiments with Osmium Tetroxide.—Except in experiments (7) and (8) which were on twice the scale, the indole, osmium tetroxide (0·100 g.), benzene (3·3 c.c.), and pyridine (0·065 c.c.) were left together overnight. The fawn crystals were collected, dried in air, and refluxed with alcohol (5 c.c.), water (5 c.c.), and sodium sulphite (1 g.) for 1 hour. The hot mixture was filtered, the black residue was washed with hot alcohol, and the combined filtrate and washings were concentrated and extracted with chloroform. The extract was dried (Na_2SO_4), the chloroform was removed, and the product was recrystallised (Table 2).

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