236. *Experiments on the Preparation of Indolocarbazoles. Part VIII.* The Preparation of 1-Methylindolo(2′ : 3′-2 : 3)carbazole.*

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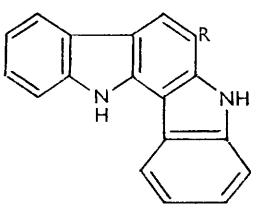
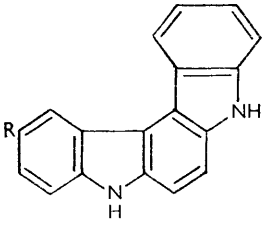
The preparation of 1-methylindolo(2′ : 3′-2 : 3)carbazole from 7-amino-1 : 2 : 3 : 4 : 10 : 11-hexahydro-8-methylcarbazole and 2-hydroxy*cyclo*hexanone is described. It has been shown to be very difficult to acylate 8-chloro-1 : 2 : 3 : 4-tetrahydrocarbazole and the corresponding 8-methyl compound.

THERE are five possible isomeric indolocarbazoles and the literature appears to contain references to simple derivatives of only two of them. Indolo(3′ : 2′-1 : 2)carbazole [1] (I; R = H) and its 3-methyl derivative (I; R = Me[2]) and 6-cyanoindolo(2′ : 3′-3 : 4)carbazole [3] (II; R = CN) have been described. Dobeneck and Maas [4] recently prepared a compound $C_{18}H_{14}N_2$, which they formulated as (III).† This was obtained, in small yield, as a



(I)



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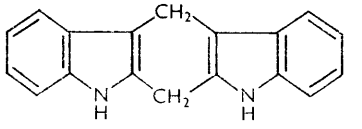


(III)

sparingly soluble yellow compound, m. p. 408°, from indole or 3 : 3′-di-indolylmethane and formaldehyde in the presence of acid. We have failed to obtain this compound from indole but, if the constitution allotted to it is correct, it should give, on dehydrogenation, the parent of the methylindolocarbazole described below.

It has been shown that aromatic amines can often be conveniently converted into tetrahydrocarbazoles by condensation with 2-hydroxy*cyclo*hexanone [5,6,7] and we decided to investigate the preparation of indolo(2′ : 3′-2 : 3)carbazoles from 7-amino-1 : 2 : 3 : 4-tetrahydro- or 7-amino-1 : 2 : 3 : 4 : 10 : 11-hexahydro-carbazoles by this route. This

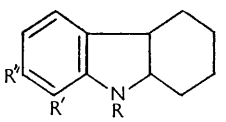
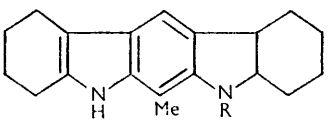
* Part VII, *J.*, 1955, 337.

† The authors named this 5 : 6 : 7 : 12-tetrahydroindolo[2′ : 3′-*b*]carbazole in accordance with the practice of *Chemical Abstracts*.

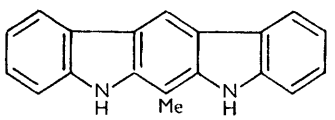
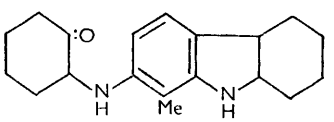
[1] Tomlinson, *J.*, 1951, 809.
[2] Hall and Plant, *J.*, 1953, 116.
[3] Clifton and Plant, *J.*, 1951, 461.
[4] Dobeneck and Maas, *Chem. Ber.*, 1954, **87**, 455.
[5] Jones and Tomlinson, *J.*, 1953, 4114.
[6] Carter, Katritzky, and Plant, *J.*, 1955, 337.
[7] Cummins and Tomlinson, *J.*, 1955, 3475.

will be possible only if the 8-position is blocked, as otherwise ring closure will take place there preferentially and give the " angular " isomer. We did not expect that suitable tetrahydrocarbazoles could be directly nitrated in the 7-position, and indeed 8-chloro-1 : 2 : 3 : 4-tetrahydrocarbazole yielded a yellow amorphous product which may be an *N*-nitro-compound, but it was hoped that 9-acetyl-8-chloro-1 : 2 : 3 : 4-tetrahydrocarbazole and the corresponding 8-methyl compound would be nitrated in the 7-position. It proved extremely difficult to prepare these compounds : all the normal methods of acetylation and benzoylation failed. A small yield of 9-acetyl-8-chloro-1 : 2 : 3 : 4-tetrahydrocarbazole was obtained by treating 8-chloro-1 : 2 : 3 : 4-tetrahydrocarbazolylmagnesium bromide with acetyl chloride but even this method failed with the 8-methyl compound although the indole seemed to react with ethylmagnesium bromide. Further, although 9-acetyl-1 : 2 : 3 : 4-tetrahydrocarbazole affords the 7-nitro-compound readily,[8,9] nitration of this 8-chloro-compound, under a variety of conditions, either converted it into a tar or left it unchanged.

It is known that 1 : 2 : 3 : 4 : 10 : 11-hexahydrocarbazole is nitrated in the 7-position in concentrated sulphuric acid,[9,10] and it seemed likely that nitro-compounds suitable for our purpose could be made by a similar method although an *ortho*- and *para*-directing group in the 8-position might make the nitro-group enter the 5-position instead. 1 : 2 : 3 : 4 : 10 : 11-Hexahydro-8-methylcarbazole (IV; R = R″ = H, R′ = Me) was obtained in good yield by reducing the tetrahydro-compound with tin and hydrochloric acid, but the chloro-compound (IV; R = R″ = H, R′ = Cl) was obtained only in yields too small to be useful. Nitration proceeded as expected to give the product (IV; R = H, R′ = Me, R″ = NO_2) and a compound which is most likely (IV; R = H, R′ = Cl, R″ = NO_2). Reduction of both the compounds (IV; R = H, R′ = Me, R″ = NO_2) and (IV; R = Ac, R′ = Me, R″ = NO_2) gave primary amines which were not solid at room temperature, but both amines afforded the same solid diacetyl compound (IV; R = Ac, R′ = Me, R″ = NHAc).

(IV)   (V)

9-Acetyl-5 : 6 : 7 : 8 : 12 : 13 : 4′ : 5′ : 6′ : 7′-decahydro-1-methylindolo(2′ : 3′-2 : 3)-carbazole (V; R = Ac) was obtained by condensing (IV; R = Ac, R′ = Me, R″ = NH_2) with 2-hydroxy*cyclo*hexanone and this was hydrolysed and dehydrogenated to 1-methylindolo(2′ : 3′-2 : 3)carbazole (VI); m. p. 278—280°. This was different (mixed m. p. and light absorption) from 3-methylindolo(3′ : 2′-1 : 2)carbazole [2] (I; R = Me). It was also found that the secondary amino-group in the compound (IV; R = H, R′ = Me, R″ = NH_2) did not interfere with condensation with 2-hydroxy*cyclo*hexanone. They reacted to give 1 : 2 : 3 : 4 : 10 : 11-hexahydro-8-methyl-7-2′-oxo*cyclo*hexylaminocarbazole (VII), which was dehydrated and dehydrogenated to give the previous material (VI).

(VI)   (VII)

That the linear compound (VI), and not (I), was obtained from the aminohexahydrocarbazole employed proves that 1 : 2 : 3 : 4 : 10 : 11-hexahydro-8-methylcarbazole is nitrated in the 7-position in sulphuric acid.

[8] Perkin and Plant, *J.*, 1921, **119**, 1825; *J.*, 1923, **123**, 676.
[9] Plant, *J.*, 1936, 899.
[10] Gurney and Plant, *J.*, 1927, 1316.

Experimental

9-Acetyl-8-chloro-1 : 2 : 3 : 4-tetrahydrocarbazole.—8-Chloro-1 : 2 : 3 : 4-tetrahydrocarbazole (5·8 g.) in ether, was added gradually to a solution of ethylmagnesium bromide, made by dissolving magnesium (0·8 g.) in ethyl bromide (4·7 g.) and ether (100 c.c.). The yellow solution formed was boiled for 5 min. and slowly treated with acetyl chloride (2·7 g.) in ether. After 1 hr. dilute sulphuric acid was added and the ethereal layer was separated, washed, and dried. After the solvent had been evaporated the residue was distilled and collected in two fractions: that having b. p. 145—155°/0·1 mm. was unchanged chlorotetrahydrocarbazole; that having b. p. 155—165°/0·1 mm. was recrystallised from methanol from which *9-acetyl-8-chloro-1 : 2 : 3 : 4-tetrahydrocarbazole* separated as plates, m. p. 85° raised to 88° by further recrystallisation (Found: C, 67·5; H, 5·8. $C_{14}H_{14}ONCl$ requires C, 67·9; H, 5·7%). The acetyl group could be removed by hydrolysis with aqueous-alcoholic potassium hydroxide.

1 : 2 : 3 : 4 : 10 : 11-Hexahydro-8-methylcarbazole.—1 : 2 : 3 : 4-Tetrahydro-8-methylcarbazole (86 g.), hydrochloric acid (160 c.c.), ethanol (160 c.c.), and tin (160 g.) were heated together on a steam-bath for 4—5 hr. When cold, the solution thus obtained was decanted from the tin and alcohol was removed by steam-distillation. The resulting solution, containing the precipitated stannichloride of the required base, was treated with 40% sodium hydroxide solution (800 c.c.), and *1 : 2 : 3 : 4 : 10 : 11-hexahydro-8-methylcarbazole* was steam-distilled, collected, and recrystallised from aqueous alcohol (75%) from which it separared as needles, m. p. 48°, containing solvent (50 g.). After drying at 70° (loss, 13·8%) it was obtained as a viscous liquid (Found: C, 83·5; H, 9·1. $C_{13}H_{17}N$ requires C, 83·4; H, 9·2%). The *hydrochloride* crystallised from dilute hydrochloric acid as prisms, m. p. 216° (Found: Cl, 15·9. $C_{13}H_{17}N,HCl$ requires Cl, 15·8%). Treatment with acetic anhydride at 100° for 10 min. afforded *9-acetyl-1 : 2 : 3 : 4 : 10 : 11-hexahydro-8-methylcarbazole* which separated from ethanol as plates, m. p. 89° (Found: C, 78·4; H, 8·3. $C_{15}H_{19}ON$ requires C, 78·6; H, 8·3%). Benzoylation (Schotten–Baumann) gave the *9-benzoyl* derivative as needles (from ethanol), m. p. 114° (Found: C, 82·5; H, 7·4. $C_{20}H_{21}ON$ requires C, 82·4; H, 7·3%).

8-Chloro-1 : 2 : 3 : 4 : 10 : 11-hexahydrocarbazole.—This was prepared in a similar manner from the chlorotetrahydrocarbazole (24 g.), hydrochloric acid (40 c.c.), ethanol (40 c.c.), and tin (40 g.). The mixture was vigorously stirred and boiled for 4—5 hr. Hydrochloric acid (20 c.c.) and ethanol (20 c.c.) were then added and at 2-hourly intervals two further similar additions were made before removing alcohol and making the residue alkaline. The product coagulated in the alkaline solution and was removed (by decanting the liquid), dissolved in ether, washed, and dried ($MgSO_4$). After removal of the ether the basic hexahydrocarbazole was extracted from unchanged starting material with dilute hydrochloric acid, liberated with alkali, and re-extracted with ether. When the dried solvent had been removed again, 8-chloro-1 : 2 : 3 : 4 : 10 : 11-hexahydrocarbazole (2 g.) remained as a colourless liquid that did not solidify. The *9-acetyl derivative* separated from aqueous ethanol (70%) as needles, m. p. 78·5—79·5° (Found: C, 67·5; H, 6·5. $C_{14}H_{16}ONCl$ requires C, 67·3; H, 6·5%). Its *hydrochloride* separated from dilute hydrochloric acid as prisms, m. p. 199—206° (decomp.) (Found: C, 59·4; H, 6·5. $C_{12}H_{14}NCl,HCl$ requires C, 59·0; H, 6·2%), and its *picrate* from ethanol as yellow prisms, m. p. 144° (Found: C, 49·7; H, 4·1. $C_{12}H_{14}NCl,C_6H_3O_7N_3$ requires C, 49·5; H, 3·9%).

1 : 2 : 3 : 4 : 10 : 11-Hexahydro-8-methyl-7-nitrocarbazole.—The above hexahydromethylcarbazole (10·8 g.) in sulphuric acid (100 c.c.) was treated at 3° with potassium nitrate (5·8 g.). After 15 min. the solution was poured on ice and neutralised at 0° with aqueous ammonia (*d* 0·88). The product was collected with ether and dried ($MgSO_4$), and, when the solvent had been evaporated, the residue solidified and was recrystallised from aqueous ethanol (75%) from which *1 : 2 : 3 : 4 : 10 : 11-hexahydro-8-methyl-7-nitrocarbazole* separated as yellow plates, m. p. 67—70° (9·6 g.), raised to 71·5—72·5° by further recrystallisation(Found: C, 67·5; H, 7·1. $C_{13}H_{16}O_2N_2$ requires C, 67·2; H, 6·9%). The above product, m. p. 67—70° (3 g.), in light petroleum (b. p. 60—80°), was run on to a column of activated alumina and eluted with solvent containing increasing proportions of benzene, and finally with benzene. Many fractions were collected and separately evaporated. Mixed m. p. determinations with the solids obtained showed that the material was homogeneous and therefore that there was no 5-nitro-compound present. *9-Acetyl-1 : 2 : 3 : 4 : 10 : 11-hexahydro-8-methyl-7-nitrocarbazole*, made by treatment with acetic anhydride at 100°, separated from aqueous ethanol (50%) as prisms, m. p. 178—179° (Found: C, 65·7; H, 6·7. $C_{15}H_{18}O_3N_2$ requires C, 65·7; H, 6·6%).

8-Chloro-1 : 2 : 3 : 4 : 10 : 11-hexahydro-7-nitrocarbazole was prepared in a similar way.

It crystallised from ethanol (75%) as golden needles, m. p. 158—159° (Found, in a sample dried at 130° : C, 57·2; H, 5·4. $C_{12}H_{13}O_2N_2Cl$ requires C, 57·1; H, 5·2%).

*7-Acetamido-9-acetyl-*1 : 2 : 3 : 4 : 10 : 11-*hexahydro-8-methylcarbazole.*—(i) The methylnitro-compound above (1·5 g.) and Adams catalyst (0·01 g.) were shaken in methanol (75 c.c.) in contact with hydrogen at N.T.P. The colour disappeared and hydrogen (435 c.c.) was absorbed. When the catalyst and solvent had been removed, 7-amino-1 : 2 : 3 : 4 : 10 : 11-hexahydro-8-methylcarbazole remained as a liquid that solidified to a glass at 0°. Recrystallisation from light petroleum (b. p. 100—120°) gave light brown prisms, m. p. 125—135° (decomp.), containing solvent which could be removed *in vacuo*, leaving the base as a liquid again. Treatment with acetic anhydride at 100° for 10 min. followed by addition of water gave *7-acetamido-9-acetyl-*1 : 2 : 3 : 4 : 10 : 11-*hexahydro-8-methylcarbazole* as prisms, m. p. 203—204° (Found : C, 70·9; H, 7·8. $C_{17}H_{22}O_2N_2$ requires C, 71·3; H, 7·7%). (ii) Similar reduction of 9-acetyl-1 : 2 : 3 : 4 : 10 : 11-hexahydro-8-methyl-7-nitrocarbazole also gave the corresponding amine as a glass, and acetylation converted this into the diacetyl compound described above.

*9-Acetyl-*5 : 6 : 7 : 8 : 12 : 13 : 4′ : 5′ : 6′ : 7′-*decahydro-*1-*methylindolo*(2′ : 3′-2 : 3)*-carbazole.*—The above 9-acetyl-7-aminohexahydrocarbazole (1·5 g.) was heated with 2-hydroxy*cyclo*hexanone (0·7 g.) at 120—130° until evolution of water ceased. Hydrochloric acid (1 drop) was then added and the temperature was raised to 135—145°; further reaction occurred and the solid formed crystallised in contact with alcohol (40—50 c.c.). Recrystallisation from 90% acetic acid gave *9-acetyl-*5 : 6 : 7 : 8 : 12 : 13 : 4′ : 5′ : 6′ : 7′-*decahydro-*1-*methylindolo*(2′ : 3′-2 : 3)*-carbazole* as prisms, m. p. 284—285° (1·3 g.) (Found : C, 77·9; H, 8·1. $C_{21}H_{26}ON_2$ requires C, 78·2; H, 8·1%).

1-*Methylindolo*(2′ : 3′-2 : 3)*carbazole.*—(i) The above acetyldecahydro-compound (0·5 g.) was boiled for 20 min. with sulphuric acid (10 c.c.) and water (10 c.c.). The solution was cooled and neutralised with ammonia; the dark green powder (0·4 g. after drying) that was collected could not be crystallised. It was heated with palladium–charcoal (0·4 g. containing 10% of palladium) in an atmosphere of carbon dioxide at 320—330° for 1½ hr. The resulting mass was extracted with acetone (50 c.c.), and dilution with water gave a solid, m. p. 268° (0·2 g.). It was sublimed *in vacuo*, giving greenish-yellow needles of 1-*methylindolo*(2′ : 3′-2 : 3)*carbazole*, m. p. 278° raised to 278—280° by recrystallisation from benzene from which it separated as colourless needles, which showed a brilliant green fluorescence in ultraviolet light (Found : C, 84·3; H, 5·3 . $C_{19}H_{14}N_2$ requires C, 84·4; H, 5·2%). The m. p. was depressed to 245—250° on admixture with 3-methylindolo(3′ : 2′-1 : 2)carbazole, m. p. 257°, prepared by dehydrogenation of 3-methyl-5 : 6 : 7 : 8 : 4′ : 5′ : 6′ : 7′-octahydroindolo(3′ : 2′-1 : 2)carbazole (see Jones and Tomlinson [5] and Hall and Plant [2] who gave m. p. 261—262°).

(ii) Condensation of 7-amino-1 : 2 : 3 : 4 : 10 : 11-hexahydro-8-methylcarbazole (0·7 g.) with 2-hydroxy*cyclo*hexanone (0·4 g.) and a little hydrochloric acid at 120—130° gave a product which crystallised when triturated with acetone and was obtained as prisms, m. p. 290—300° (decomp.), from 90% acetic acid (Found : C, 70·5; H, 7·9. $C_{19}H_{26}ON_2,C_2H_4O_2$ requires C, 70·3; H, 8·4%). This therefore appears to be 1 : 2 : 3 : 4 : 10 : 11-*hexahydro-8-methyl-7-2′-oxo*cyclo*hexylaminocarbazole acetate.* It was not possible to isolate the decahydroindolocarbazole by further heating of this compound but, when it (0·4 g.) was treated with palladium–charcoal (0·4 g.) as above, 1-methylindolo(2′ : 3′-2 : 3)carbazole, m. p. 278° (identical with the above), was isolated. Light absorption (log ε in parentheses) : $\lambda_{max.}$ 2400 (4·614), 2650 (4·547), 2750 (4·538), 3060 (4·794), 3440 (4·055), 3600 (4·131) Å; to be compared with $\lambda_{max.}$ 2460 (4·590), 2650 (4·607), 2870 (4·516), 3200 (4·053), 3430 (4·006), 3580 (4·187) Å for the isomeric 3-methylindolo(3′ : 2′-1 : 2)carbazole. It dissolved in sulphuric acid forming a violet solution, changed to bluish-green fading to reddish-brown on addition of a little nitric acid. It was unaffected by boiling it with acetic anhydride and charred if a little sulphuric acid was added to this solution.

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