*Hydroxycarbazoles and Tetrahydrohydroxycarbazoles. Part III.**

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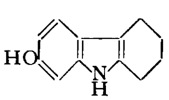
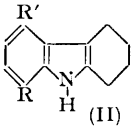
The hitherto unknown 4-hydroxy-, 4-methoxy-, and 1 : 2 : 3 : 4-tetrahydro-5-methoxy-carbazole are described. The compound previously described as 1 : 2 : 3 : 4-tetrahydro-7(or 5)-hydroxycarbazole is shown to be the 7-hydroxy-compound.

Jones and Tomlinson (*J.*, 1953, 4114) showed that 1 : 2 : 3 : 4-tetrahydro-7(or 5)-hydroxycarbazole (I), m. p. 163—164°, could be obtained from *m*-aminophenol and 2-hydroxy*cyclo*hexanone. A substance, m. p. 164°, made from *cyclo*hexanone and *m*-hydroxyphenylhydrazine (D.R.P., 574,840; *Chem. Zentr.*, 1933, II, 622), has been described as the 7-hydroxy-compound but no proof of the position of the hydroxy-group appears to have been reported.

Authentic 1 : 2 : 3 : 4-tetrahydro-5-methoxycarbazole (II; R′ = OMe, R = H) has now been prepared by removing chlorine, by catalytic reduction, from 8-chloro-1 : 2 : 3 : 4-tetrahydro-5-methoxycarbazole (II; R′ = OMe, R = Cl) which was obtained by condensing 3-amino-4-chloroanisole with 2-hydroxy*cyclo*hexanone. This substance, m. p. 126—127°, is different from the methoxy-compound, m. p. 148—149°, prepared from Jones and Tomlinson's compound (I) which must therefore be 1 : 2 : 3 : 4-tetrahydro-7-hydroxycarbazole.

Dehydrogenation of 1 : 2 : 3 : 4-tetrahydro-7-hydroxycarbazole has yielded 2-hydroxycarbazole, m. p. 277°, most of the references to which are in patent literature (*e.g.*, B.P., 303,502; *Chem. Zentr.*, 1930, II, 470, which describes its preparation from 2-aminocarbazole and gives m. p. 276°). Hoshino and Takiura (*Bull. Chem. Soc. Japan*, 1936, **11**, 218) describe the preparation of 2-hydroxycarbazole, m. p. 273—274°, by dehydrogenation and dealkylation of the tetrahydrocarbazole which they obtained by the Fischer method from *cyclo*hexanone *m*-ethoxyphenylhydrazone. They give no evidence to prove that it is the 2- and not the 4-hydroxy-compound. (See also B.P., 337,821; *Chem. Zentr.*, 1931, II, 1761.) The hitherto unknown 4-hydroxycarbazole has now been obtained by dehydrogenation of 1 : 2 : 3 : 4-tetrahydro-4-oxocarbazole and it has m. p. 169—170°. The product described by the Japanese authors is therefore proved to be 2-hydroxycarbazole.


(I)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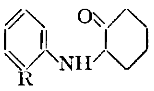
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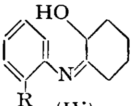
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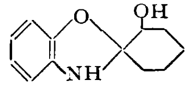
(V)

It has now been found (compare Carter, Katritzky, and Plant, *J.*, 1955, 338) that condensation of aromatic amines with 2-hydroxy*cyclo*hexanone frequently proceeds in two stages. Infrared absorption spectra indicate that the intermediate compounds are 2-oxo*cyclo*hexylanilines (III) rather that the isomeric 2-hydroxy*cyclo*hexylideneanilines (IV). Condensation of *m*-aminophenol with 2-hydroxy*cyclo*hexanone proceeds exceptionally easily, without any catalyst, and no intermediate has been isolated. Moreover no trace of 4-methoxycarbazole could be found with the 2-methoxycarbazole prepared by methylating and dehydrogenating the crude reaction product. (The peroxidation which occurs rapidly in solution makes a search for the tetrahydro-5-methoxy-compound unsatisfactory.) 4-Methoxycarbazole has been prepared by removal of chlorine and hydrogen from the chloro-compound (II; R = Cl, R′ = OMe). The compound (III; R = OMe)

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* *J.*, 1952, 2789, and *J.*, 1954, 1414, are regarded as Parts I and II.

prepared from *o*-anisidine, could not be converted into 1 : 2 : 3 : 4-tetrahydro-8-methoxycarbazole (II; R = OMe, R′ = H).

It is interesting to note that *o*-aminophenol condenses easily with 2-hydroxy*cyclo*hexanone (no catalyst) to give a substance, $C_{12}H_{15}O_2N$, which does not appear to be (III; R = OH). It does not react with sodium hydroxide, and consideration of its infrared absorption spectrum indicates that it may be 2-hydroxy*cyclo*hexane*spiro*benzoxazoline (V). It certainly contains no carbonyl group but it does give a ferric chloride reaction so the aniline (IV; R = OH) may not be ruled out.

1 : 2 : 3 : 4-Tetrahydro-5-methylcarbazole was prepared while using the chloro-compound (II; R = Cl, R′ = Me) as a model, before attempting to make the corresponding methoxy-compound. The m. p. and the rapid peroxidation recorded by Coldham, Lewis, and Plant (*J.*, 1954, 4528) were confirmed, and the substance has now been obtained analytically pure.

EXPERIMENTAL

1 : 2 : 3 : 4-*Tetrahydro*-7-*methoxycarbazole*.—1 : 2 : 3 : 4-Tetrahydro-7-hydroxycarbazole (1·3 g.) was methylated in acetone (12 c.c.) with methyl sulphate (1·8 g.) and sodium hydroxide (0·6 g. in a little water). The *ether* crystallised from ethanol as plates, m. p. 148—149° (Found: C, 77·7; H, 7·4. $C_{13}H_{15}ON$ requires C, 77·6; H, 7·4%).

3-*Amino*-4-*chloroanisole*.—4-Chloro-3-nitroanisole (32 g.), water (320 c.c.), iron powder (32 g.), and hydrochloric acid (4 c.c.) were boiled for 1½ hr., and after the mixture had been neutralised it was extracted with ether. The ethereal layer was extracted with dilute acid and the amine was again collected with ether from the basified aqueous extract. 3-*Amino*-4-*chloroanisole* (20·5 g.) distilled at 140—145°/18 mm. It solidified to an almost colourless mass of needles, m. p. 27° (Found: N, 9·1. C_7H_8ONCl requires N, 8·9%). With acetic anhydride it gave 3-*acetamido*-4-*chloroanisole* which separates from dilute acetic acid (50%) as needles, m. p. 99° (Found: C, 54·3; H, 5·3. $C_9H_{10}O_2NCl$ requires C, 54·1; H, 5·0%).

8-*Chloro*-1 : 2 : 3 : 4-*tetrahydro*-5-*methoxycarbazole*.—An intimate mixture of 3-amino-4-chloroanisole (1·0 g.), 2-hydroxy*cyclo*hexanone (0·72 g.), and a trace of the amine hydrochloride was heated at 120—125°. Recrystallisation from ethanol of the mass formed gave 4-*chloro*-3-2′-*oxo*cyclo*hexylaminoanisole* as needles, m. p. 72° (Found: C, 61·7; H, 6·3. $C_{13}H_{16}O_2NCl$ requires C, 61·5; H, 6·3%). The infrared spectra showed max. at 2·96 and 5·84 μ. The compound could be distilled *in vacuo* unchanged, but when it was heated at 190—200° with a drop of hydrochloric acid it was converted into 8-*chloro*-1 : 2 : 3 : 4-*tetrahydro*-5-*methoxycarbazole* which crystallised from methanol as plates, m. p. 99° (Found: C, 66·3; H, 6·1. $C_{13}H_{14}ONCl$ requires C, 66·2; H, 5·9%).

1 : 2 : 3 : 4-*Tetrahydro*-5-*methoxycarbazole*.—The above chloro-compound (0·5 g.), in methyl alcohol (50 c.c.) containing potassium hydroxide (0·5 g. in a little water), was shaken in hydrogen with palladium–charcoal (Norite containing 10% of palladium). Hydrogen (approx. 50 c.c.) was absorbed. The solution was filtered and diluted with water, and the precipitate was rapidly recrystallised from aqueous ethanol, from which 1 : 2 : 3 : 4-*tetrahydro*-5-*methoxycarbazole* separated as plates, m. p. 126—127°, sintering at 121°, and depressed by admixture with the above 7-methoxy-compound (Found: C, 77·7; H, 7·4. $C_{13}H_{15}ON$ requires C, 77·6; H, 7·5%).

1 : 2 : 3 : 4-*Tetrahydro*-5-*methylcarbazole*.—This was prepared in the same way from the corresponding methyl compound and was obtained from aqueous ethanol as plates, m. p. 147°, sintering at 140° (Found: 84·1; H, 8·1. $C_{13}H_{15}N$ requires C, 84·3; H, 8·1%).

1-*Chloro*-4-*methoxycarbazole*.—The corresponding tetrahydro-compound (2·0 g.) was refluxed with chloranil (4·0 g.) in sulphur-free xylene for 6 hr. The cooled solution was filtered from tetrachloroquinone, diluted with ether, and washed with sodium hydroxide. The residue left after solvents had been removed was dissolved in benzene and light petroleum (equal parts) and passed through activated alumina. 1-*Chloro*-4-*methoxycarbazole*, obtained from this solution, crystallised from light petroleum (b. p. 60—80°) as plates, m. p. 100—101° (Found: C, 67·4; H, 4·3. $C_{13}H_{10}ONCl$ requires C, 67·4; H, 4·3%).

4-*Hydroxycarbazole*.—1 : 2 : 3 : 4-Tetrahydro-4-oxocarbazole (1·0 g.), mixed with palladium–charcoal (0·5 g. containing 10% of palladium), was heated at 270° in carbon dioxide for 1 hr. A small quantity of carbazole sublimed and the main product was extracted from the charcoal with sodium hydroxide solution (4%). Acidification afforded 4-*hydroxycarbazole* which was recrystallised from water containing a little hydrochloric acid. It separated as almost colourless needles, m. p. 169—170° (with blackening) (Found: C, 78·5; H, 5·1. $C_{12}H_9ON$ requires 78·7; H, 4·9%). It gives a violet ferric chloride reaction. 1-Hydroxycarbazole, m. p. 160—162° (together with a little carbazole), was obtained from similar treatment of 1 : 2 : 3 : 4-tetrahydro-1-oxocarbazole at 245° (Found: C, 78·9; H, 4·9. Calc. for $C_{12}H_9ON$: C, 78·7; H, 4·9%). In aqueous alcohol it gives a green precipitate with ferric chloride.

2-*Hydroxycarbazole.*—Similar dehydrogenation of 1 : 2 : 3 : 4-tetrahydro-7-hydroxycarbazole gave 2-hydroxycarbazole, m. p. 277° (black liquid and previous darkening) (Found, in sample dried *in vacuo* at 125°: C, 78·7; H, 4·9. Calc. for $C_{12}H_9ON$: C, 78·7; H, 4·9%).

4-*Methoxycarbazole.*—8-Chloro-1 : 2 : 3 : 4-tetrahydro-5-methoxycarbazole (0·7 g.) was dehydrogenated as above in carbon dioxide at 200—210° for 30 min. Hydrogen was then substituted for carbon dioxide and the temperature was raised to 240—250° for a further 30 min. Hydrogen chloride was evolved. The product was extracted with benzene, and the solution, diluted with an equal volume of light petroleum (b. p. 60—80°), was passed through activated alumina. From a band which showed greenish-yellow fluorescence in ultraviolet light, a solid was isolated; it crystallised from ethanol giving prisms of 4-*methoxycarbazole*, m. p. 135° (Found: C, 78·7; H, 5·7. $C_{13}H_{11}ON$ requires C, 79·2; H, 5·6%). (More vigorous dehydrogenation converted both 1-chloro-4-methoxycarbazole and the corresponding tetrahydro-compound into carbazole.)

2-*Methoxycarbazole.*—*m*-Aminophenol (2·2 g.) and 2-hydroxy*cyclo*hexanone (2·3 g.) were heated at 125—135°. The solid which resulted was methylated in acetone solution. Water precipitated the product, and the dried, crude, tetrahydromethoxycarbazole thus prepared was dehydrogenated as above at 180—200° in carbon dioxide. When the benzene extract of the product was diluted with an equal amount of light petroleum (b. p. 60—80°) 2-*methoxycarbazole* separated. It crystallised from alcohol as needles, m. p. 234° (Found: C, 79·0; H, 5·7. $C_{13}H_{11}ON$ requires C, 79·2; H, 5·6%). The mother liquor was passed through activated alumina which was then eluted with benzene and light petroleum until the alumina ceased to fluoresce in ultraviolet light. More 2-methoxycarbazole was isolated but no 4-methoxycarbazole was found.

2-2′-*Oxo*cyclo*hexylaminoanisole.*—*o*-Anisidine (1·0 g.) and 2-hydroxy*cyclo*hexanone (1·0 g.) reacted at 140—145° to give 2-2′-*oxo*cyclo*hexylaminoanisole* which crystallised from alcohol as plates, m. p. 72—74° (Found: C, 71·1; H, 7·8. $C_{13}H_{17}O_2N$ requires C, 71·2; H, 7·7%). Infrared spectrum showed bands at 2·97 and 5·86 μ. Similarly, *o*-aminophenol and 2-hydroxy*cyclo*hexanone reacted at 135—140° to give a solid which crystallised from alcohol as plates, m. p. 171° (Found: C, 70·5; H, 7·3. $C_{12}H_{15}O_2N$ requires C, 70·2; H, 7·3%). Infrared spectrum showed bands at 2·93, 3·02, 3·09, 3·32, 3·77 μ and a number of big bands usually ascribed to $>C-O-C$ in the 8—10 μ region. There was no band indicative of a carbonyl group. The substance may therefore be 2-*hydroxy*cyclo*hexane*spiro*benzoxazoline.* It forms a sparingly soluble hydrochloride that can be recrystallised from dilute hydrochloric acid. It gives a greenish-black colour with ferric chloride in aqueous alcohol and it can be recrystallised, unchanged, from aqueous sodium hydroxide solution.

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