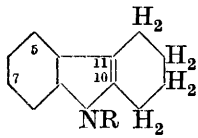
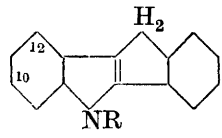
304. *The Action of Halogens on Polycyclic Indole Derivatives. Part II. The Bromination of the Acyl Derivatives of 8 : 9 : 10 : 11-Tetrahydro-α′β′-naphthacarbazole and 7 : 8 : 9 : 10-Tetrahydro-αβ-naphthacarbazole.*

By S. G. P. PLANT and (MISS) M. L. TOMLINSON.

IN Part I (J., 1931, 3324) the authors have shown that while the action of bromine (1 mol.) on the 9-acyltetrahydrocarbazoles (I) leads exclusively to products which are derived from the primary addition of bromine at the 10 : 11-position, the only compounds which have been isolated from the 7-acylbenzopentindoles (II) under similar conditions are monobromo-derivatives with the substituents in the 10- and 12-positions. The bromination of certain 7-acyl-8 : 9 : 10 : 11-tetrahydro-α′β′-naphthacarbazoles (III) and 11-acyl-7 : 8 : 9 : 10-tetrahydro-αβ-naphthacarbazoles (IV) has now



(I.)



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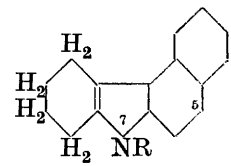
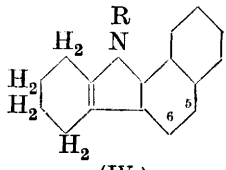


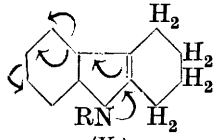
(III.)

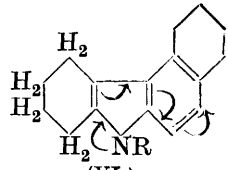
been examined, primarily with the object of discovering whether the replacement of the benzene system in tetrahydrocarbazole by a naphthalene skeleton results in a similar remarkable diminution of the additive properties of the double linkage. The nitration of these derivatives (Oakeshott and Plant, J., 1928, 1840) has suggested that this might be the case, but the frequent failure to obtain more than a small proportion of pure nitration product made it impossible to be certain regarding this point.

When the compounds (III; R = Ac, Bz, and CO_2Et) were treated with bromine in glacial acetic acid, monobromo-derivatives were obtained in good yields and no additive product was detected.

In every case the bromine atom entered the 5-position. This was conclusively proved by applying Fischer's indole synthesis to *cyclo*hexanone-4-bromo-2-naphthylhydrazone, and by converting the 5-*bromo*-8 : 9 : 10 : 11-*tetrahydro*-α'β'-*naphthacarbazole* so formed into its 7-*acetyl*, 7-*benzoyl*, and 7-*carbethoxy*-derivatives, each of which was identical with the respective bromination product.


(IV.)

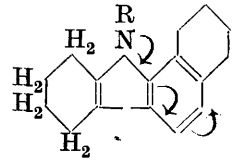
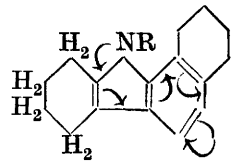

(V.)


(VI.)

Bromination of the compound (IV; R = Ac) in glacial acetic acid gave no crystalline product, but in carbon disulphide the 5-*bromo*-derivative was formed. Similar treatment of the benzoyl compound (IV; R = Bz) gave the 5-*bromo*-derivative in either solvent. The yields of these bromo-compounds were less than those of the isomeric products mentioned above, but again no additive compound was detected. The structures of the products were established by hydrolysis to 5-*bromo*-7 : 8 : 9 : 10-*tetrahydro*-αβ-*naphthacarbazole*, which was itself synthesised by Fischer's method from *cyclo*hexanone and 4-*bromo*-1-*naphthylhydrazine*. Thus, in view of the fact that the reaction of the 9-acyltetrahydrocarbazoles with an equimolecular quantity of bromine is exclusively an additive one, it is now clearly demonstrated that the presence of a fourth ring in the polycyclic indole skeleton, irrespective of its position, results in a very great diminution in the additive properties of the double linkage in question.

The problem of orientation in these more complex indoles is of considerable interest. Substituents enter the 9-acyltetrahydrocarbazoles at the 5- and the 7-position, which, as Professor R. Robinson has pointed out, is readily explained if the orienting effect is transmitted through the double linkage as in (V). It is clear that the results obtained from the bromination of the 7-acylbenzopentindoles may be explained in the same way, while similar considerations, represented in (VI), would account for the formation of the 5-bromo-derivatives of (III). The bromination of the compounds (IV) must, however, be explained by an activation process, represented in (VII), which is more akin to that observed in simple benzene derivatives. If the electromeric effect in the latter compounds did in reality again operate through the double linkage in question, the 6-bromo-derivatives would be expected (VIII). The failure to isolate these and the preferential formation of the 5-bromo-

compounds may very well be due to the excessive length of the path which the activating influence would have to pursue.

(VII.)   (VIII.)

EXPERIMENTAL.

Bromination of 7-Acetyl-8 : 9 : 10 : 11-tetrahydro-α′β′-naphthacarbazole.—When the acetyl compound (Oakeshott and Plant, *loc. cit.*) was treated with Br (1 mol.) in AcOH, *5-bromo-7-acetyl-8 : 9 : 10 : 11-tetrahydro-α′β′-naphthacarbazole* gradually separated; colourless needles, m. p. 199°, from EtOH or AcOH (Found: N, 4·0. $C_{18}H_{16}ONBr$ requires N, 4·1%). Total yield, including that obtained by addition of H_2O to the original AcOH mother-liquor, 80%.

A solution of the bromo-compound in aq.-alc. KOH was boiled for ½ hr. and diluted with H_2O. The pptd. *5-bromo-8 : 9 : 10 : 11-tetrahydro-α′β′-naphthacarbazole* crystallised from petroleum in almost colourless needles, decomp. 115—120° (Found: N, 5·0. $C_{16}H_{14}NBr$ requires N, 4·7%).

These two bromo-derivatives were synthesised as follows. 4-Bromo-β-naphthylamine was converted, by diazotisation and subsequent reduction with $SnCl_2$ and conc. HCl aq., into 4-bromo-2-naphthylhydrazine, which was heated on the steam-bath for a short time with *cyclo*hexanone (1 mol.). The hydrazone was boiled with 18% H_2SO_4 aq. for 5 mins., and the solid product crystallised from petroleum (b. p. 60—80°), 5-bromo-8 : 9 : 10 : 11-tetrahydro-α′β′-naphthacarbazole being obtained in almost colourless needles, decomp. 115—120°. The latter substance, in Me_2CO and 66% KOH aq., was treated with an excess of AcCl. H_2O then pptd. 5-bromo-7-acetyl-8 : 9 : 10 : 11-tetrahydro-α′β′-naphthacarbazole; colourless needles, m. p. (and mixed m. p.) 199°, from EtOH.

Bromination of 7-Benzoyl-8 : 9 : 10 : 11-tetrahydro-α′β′-naphthacarbazole.—The benzoyl derivative (Oakeshott and Plant, *loc. cit.*), brominated in the same way as the corresponding acetyl compound, gave *5-bromo-7-benzoyl-8 : 9 : 10 : 11-tetrahydro-α′β′-naphthacarbazole* in 75% yield; yellow needles, m. p. 158—159°, from EtOH (Found: N, 3·4. $C_{23}H_{18}ONBr$ requires N, 3·5%). A specimen of this substance, prepared from 5-bromo-8 : 9 : 10 : 11-tetrahydro-α′β′-naphthacarbazole and BzCl in Me_2CO and 66% KOH aq., had m. p. (after crystn. from EtOH) and mixed m. p. 158—159°.

Bromination of Ethyl 8 : 9 : 10 : 11-Tetrahydro-α′β′-naphthacarbazole-7-carboxylate.—Mg (2·4 g.) was dissolved in EtBr (8 c.c.) and dry Et_2O (75 c.c.), and 8 : 9 : 10 : 11-tetrahydro-α′β′-naphthacarbazole (12·5 g.) added. After the evolution of C_2H_6 had ceased, ethyl chloroformate (7 g.) was introduced, and the whole warmed on the water-bath for a short time and then treated with ice and dil. HCl aq. *Ethyl 8 : 9 : 10 : 11-tetrahydro-α′β′-naphthacarbazole-7-carboxylate*, which separated as a solid, crystallised from EtOH in colourless needles, m. p. 121° (Found: N, 4·7. $C_{19}H_{19}O_2N$ requires N, 4·8%).

When this ester was brominated by the process already described, *ethyl*

5-bromo-8 : 9 : 10 : 11-tetrahydro-a'β'-naphthacarbazole-7-carboxylate was obtained in 80% yield; colourless needles, m. p. 180—181°, from AcOH (Found: N, 3·8. $C_{19}H_{18}O_2NBr$ requires N, 3·8%). The same compound (mixed m. p.) was obtained synthetically by a process similar to that employed for the corresponding benzoyl derivative, ethyl chloroformate being used in place of BzCl.

Bromination of 11-*Acetyl*-7 : 8 : 9 : 10-*tetrahydro-aβ-naphthacarbazole*.—When this acetyl compound (Oakeshott and Plant, *loc. cit.*) was treated with Br (1 mol.) in CS_2, HBr was evolved. Addition of petroleum (b. p. 40—60°) pptd. a solid which rapidly decomposed. When, however, the CS_2 solution was immediately shaken with KOH aq., and the CS_2 removed in a current of air, a sticky solid remained. This was dried (with K_2CO_3) in Et_2O, recovered, and boiled with EtOH (charcoal). The colourless solid obtained on cooling was recrystallised from EtOH, *5-bromo-11-acetyl-7 : 8 : 9 : 10-tetrahydro-aβ-naphthacarbazole* separating in needles, m. p. 126—127° (Found: C, 63·4; H, 4·2. $C_{18}H_{16}ONBr$ requires C, 63·2; H, 4·7%). Yield, about 45%.

When a solution of this product in aq.-alc. KOH was boiled for ½ hr. and then diluted with H_2O, *5-bromo-7 : 8 : 9 : 10-tetrahydro-aβ-naphthacarbazole* was obtained; pale yellow needles, m. p. 116°, from petroleum (b. p. 60—80°) (Found: N, 4·8. $C_{16}H_{14}NBr$ requires N, 4·7%).

This bromo-compound was synthesised by the following procedure. 4-Bromo-α-naphthylamine (15·4 g.) in 20% HCl aq. was diazotised below 0° ($NaNO_2$, 5 g., in a little H_2O), the solution reduced with cold $SnCl_2$ (50 g.) and conc. HCl aq. (60 c.c.), the solid product dissolved in hot H_2O containing a little HCl aq., freed from Sn by H_2S, and AcONa added. The pptd. *4-bromo-1-naphthylhydrazine* crystallised from EtOH in colourless needles, m. p. 139° (decomp.) (Found: N, 11·8. $C_{10}H_9N_2Br$ requires N, 11·8%). This hydrazine (3 g.) and *cyclo*hexanone (1·4 g.) were heated on the steam-bath, and the hydrazone was boiled for a few mins. with 26% H_2SO_4 aq., and the resulting black mass crystallised from petroleum (b. p. 60—80°), 5-bromo-7 : 8 : 9 : 10-tetrahydro-aβ-naphthacarbazole being obtained in pale yellow needles, m. p. and mixed m. p. 116°.

Bromination of 11-*Benzoyl*-7 : 8 : 9 : 10-*tetrahydro-aβ-naphthacarbazole*.—The benzoyl compound (Oakeshott and Plant, *loc. cit.*) was brominated in CS_2, and the product isolated, by a procedure similar to that used for the corresponding acetyl derivative. On crystn. from EtOH, *5-bromo-11-benzoyl-7 : 8 : 9 : 10-tetrahydro-aβ-naphthacarbazole* was obtained in yellow plates, m. p. 115° (Found: N, 3·6. $C_{23}H_{18}ONBr$ requires N, 3·5%). Yield, about 50%. The same substance was obtained by treating the benzoyl compound with Br (1 mol.) in AcOH; after dilution with H_2O it was isolated and dried in Et_2O and crystallised from EtOH.

When this bromo-compound was hydrolysed by boiling with aq.-alc. KOH as described for the analogous acetyl derivative, 5-bromo-7 : 8 : 9 : 10-tetrahydro-aβ-naphthacarbazole, identical with a synthetical specimen, was obtained.

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