*Experiments on the Preparation of Indolocarbazoles. Part VII.** *Some Derivatives of 5-Amino-1-phenylbenzotriazole.*

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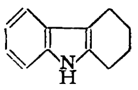
Some derivatives of 5 : 6 : 7 : 8-tetrahydro-1′-phenyltriazolo(5′ : 4′-3 : 4)-carbazole have been prepared by an extension of Jones and Tomlinson's reaction (*J.*, 1953, 4114) to the appropriate 5-amino-1-phenylbenzotriazoles, and further information has been obtained about this approach to substituted tetrahydrocarbazoles. 5-Amino-1-phenylbenzotriazole has also been converted by other reactions into various substances of quinoline type.

The reaction by which 1 : 2 : 3 : 4-tetrahydrocarbazole (I) was obtained from aniline and 2-chloro*cyclo*hexanone (D.R.-P. 374,098; *Chem. Zentr.*, 1923, IV, 724) has been used by Campbell and McCall (*J.*, 1950, 2870) for the preparation of a number of simple tetrahydrocarbazoles from the appropriate anilines in yields of 30—60%, but it has given very small yields, if any, of the corresponding product when applied to more complex amines such as the aminotetrahydrocarbazoles and *m*-phenylenediamine (Hall and Plant, *J.*, 1953, 116; Jones and Tomlinson, *ibid.*, p. 4114). It has been found by Jones and Tomlinson (*loc. cit.*) that tetrahydrocarbazoles can be very conveniently obtained, often in good yield, by the somewhat analogous process of heating anilines with 2-hydroxy*cyclo*hexanone and a trace of hydrochloric acid, and they have applied the reaction to the preparation of indolocarbazoles from certain diamines which gave none of the desired product when 2-chloro*cyclo*hexanone was used. Katritzky and Plant (*J.*, 1953, 412) prepared 5 : 6 : 7 : 8-tetrahydro-1′-phenyltriazolo(5′ : 4′-3 : 4)carbazole (III) from 5-amino-1-phenylbenzotriazole (II; R = NH_2) and 2-chloro*cyclo*hexanone, but further experience has shown that



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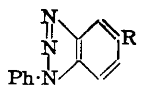

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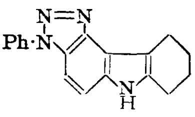

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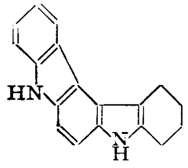

(IV)

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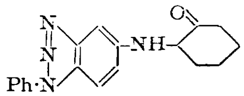
* Part VI, *J.*, 1953, 412.

the yields are very variable and the product difficult to purify. Coker, Plant, and Turner (*J.*, 1951, 110) have found that the yields of the resulting carbazoles are profoundly affected by substituents in the phenyl group in the application of the Graebe–Ullmann reaction to 5-cyano- (II; R = CN) and 5-nitro-1-phenylbenzotriazoles (II; R = NO_2). It therefore seemed possible that tetrahydroindolo(2′ : 3′-3 : 4)carbazoles of the type (IV) would result from the elimination of nitrogen from derivatives of the compound (III) with substituents in the phenyl group, and that the latter might be conveniently prepared from the correspondingly substituted 5-amino-1-phenylbenzotriazoles and 2-hydroxy*cyclo*hexanone. Although the ultimate objective was not achieved, the preparation of the required substances (of the type III) has led to useful observations on the Jones and Tomlinson reaction. In its earlier applications the tetrahydrocarbazoles were prepared in a single operation, but the examples now studied have been employed in two stages. The first took place when the reactants were heated together without a catalyst and involved the formation of an intermediate which, although there are possibilities for isomerism, seemed likely to be represented in the case of the parent compound by the structure (V), a view confirmed by its infra-red spectrum. The second stage occurred at a slightly higher temperature in the presence of a catalyst. Concentrated hydrochloric acid was used for this purpose, but was not universally satisfactory, and it was sometimes, but not always, better to replace it by a trace of the dry hydrochloride of the corresponding amine. Attempts to combine the two stages into one operation gave poorer results, and it was an advantage to purify the intermediate. The well-known synthesis of indoles from aromatic amines and 2-halogeno-ketones proceeds through the intermediate 2-anilino-ketones (Crowther, Mann, and Purdie, *J.*, 1943, 58; Brown and Mann, *J.*, 1948, 847, 858; Campbell and McCall, *loc. cit.*), and the close connexion between the reactions is obvious.

During other work, which has been discontinued, the base (II; R = NH_2) and 1-*p*-aminophenylbenzotriazole (VI) have been condensed with ethyl acetoacetate with the formation of the corresponding 4-quinolones through the Conrad–Limpach reaction. The base (II; R = NH_2) has also been converted into 5-acetoacetamido-1-phenylbenzotriazole (II; R = $NH{\cdot}CO{\cdot}CH_2Ac$), but attempts to obtain the corresponding 2-quinolone with sulphuric acid under the conditions ordinarily used for the Knorr reaction (Ewins and King, *J.*, 1913, **103**, 104) led to hydrolysis with the formation of the original amine. 5-Acetamido-1-phenylbenzotriazole was similarly hydrolysed. It was possible however to convert the benzotriazole (II; R = $NH{\cdot}CO{\cdot}CH_2Ac$) directly into 2-chloro-4-methyl-1′-phenyltriazolo(4′ : 5′-5 : 6)quinoline (VII; R = Cl; R′ = Me) with phosphorus oxychloride. 5-Chloro-1′-phenyltriazolo(5′ : 4′-3 : 4)acridine (VIII) has been prepared by the action of phosphorus oxychloride on the product obtained by condensing the base (II; R = NH_2) with *o*-chlorobenzoic acid.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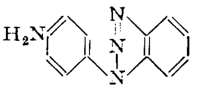
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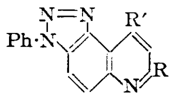
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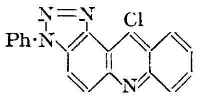
(VIII)

In these various cyclisations with the base (II; R = NH_2) and its derivatives there are two possible structures for the product, but on theoretical grounds and from general experience of related reactions the " linear " form is extremely unlikely. In fact it has been proved by Kulka and Manske (*Canad. J. Chem.*, 1952, **30**, 711) that the product of the Skraup reaction with the base (II; R = NH_2) has the " angular " structure (VII; R = R′ = H).

EXPERIMENTAL

Substituted 5-*Amino*-1-*phenylbenzotriazoles*.—The amines required for the work described below were prepared by condensation of the appropriate substituted aniline with 1-chloro-2 : 4-dinitrobenzene, reduction with sodium sulphide in hot ethanol to the corresponding derivative of 2-amino-4-nitrodiphenylamine (cf. D.R.-P. 85,388), conversion into the 5-nitro-

1-phenylbenzotriazole (cf. Fries and Empson, *Annalen*, 1912, **389**, 350), and subsequent reduction with zinc dust and aqueous-ethanolic calcium chloride (cf. Beretta, *Gazzetta*, 1925, **55**, 788). The following are new: 5-*amino*-1-p-*chlorophenylbenzotriazole* (Blom, *Helv. Chim. Acta*, 1921, **4**, 1036, obtained a crude amine, stated to be unstable, which he converted into the corresponding acetamido-compound without purification), pale brown needles, m. p. 170—171° (from aqueous ethanol) (Found: C, 58·9; H, 3·9. $C_{12}H_9N_4Cl$ requires C, 58·9; H, 3·7%); 2-*amino-2′-methoxy-4-nitrodiphenylamine*, orange-red plates, m. p. 146—147° (from carbon tetrachloride) (Found: C, 60·2; H, 4·9. $C_{13}H_{13}O_3N_3$ requires C, 60·2; H, 5·0%); 1-o-*methoxyphenyl*-5-*nitrobenzotriazole*, needles, m. p. 152—153° (from ethanol) (Found: C, 58·3; H, 3·8. $C_{13}H_{10}O_3N_4$ requires C, 57·8; H, 3·7%); 5-*amino*-1-o-*methoxyphenylbenzotriazole*, pale brown rods, m. p. 149° (from aqueous ethanol) (Found: C, 64·5; H, 5·1. $C_{13}H_{12}ON_4$ requires C, 65·0; H, 5·0%); 2-*amino-3′-methoxy-4-nitrodiphenylamine*, chocolate-brown needles, m. p. 151—152° (from ethanol) (Found: C, 60·0; H, 5·0%); 1-m-*methoxyphenyl*-5-*nitrobenzotriazole*, needles, m. p. 201° (from ethanol) (Found: C, 57·8; H, 4·0%); 5-*amino*-1-m-*methoxyphenylbenzotriazole*, needles, m. p. 108—109° (from aqueous ethanol) (Found: C, 64·8; H, 5·2%); 5-*amino*-1-o-*tolylbenzotriazole*, brown prisms, m. p. 93° (from ethanol) (Found: C, 69·6; H, 5·4. $C_{13}H_{12}N_4$ requires C, 69·6; H, 5·4%). The last-named was converted into 5-*acetamido*-1-o-*tolylbenzotriazole*, needles, m. p. 204° (from acetic acid) (Found: C, 67·4; H, 5·5. $C_{15}H_{14}ON_4$ requires C, 67·7; H, 5·3%), by warm acetic anhydride.

*5-(2-Oxo*cyclo*hexyl)amino-1-phenylbenzotriazole and its Derivatives.*—When a mixture of 5-amino-1-phenylbenzotriazole (1 g.) and 2-hydroxy*cyclo*hexanone (0·6 g.) was gradually heated in a paraffin bath, it became completely molten at 126°, and, with continued heating and stirring, solidified at 132° with evolution of water. After the whole had been stirred with hot ethanol, the solid, when cold, was collected and recrystallised from *cyclo*hexanone, from which 5-(2-*oxo*cyclo*hexyl)amino*-1-*phenylbenzotriazole* separated in plates (55%), m. p. 169° (Found: C, 70·5; H, 5·8. $C_{18}H_{18}ON_4$ requires C, 70·6; H, 5·9%) [the infra-red spectrum, in Nujol suspension, showed bands at 2·98 μ (>NH) and 5·85 μ (>CO)]. The following were similarly prepared, the temperature reached in the reaction being given in each case in parentheses after the name: 1-p-*chlorophenyl*- (150°), needles (53%), m. p. 200—201° (from *cyclo*hexanone and then ethanol) (Found: C, 63·5; H, 5·1. $C_{18}H_{17}ON_4Cl$ requires C, 63·4; H, 5·0%), 1-o-*methoxyphenyl*- (140°), prisms (55%), m. p. 129—130° [from ethanol (charcoal)] (Found: C, 67·7; H, 6·1. $C_{19}H_{20}O_2N_4$ requires C, 67·9; H, 6·0%), 1-m-*methoxyphenyl*- (145°), plates (46%), m. p. 178° [from ethanol (charcoal)] (Found: C, 68·0; H, 6·0%), and 1-p-*methoxyphenyl*-5-(2-*oxo*cyclo*hexyl)aminobenzotriazole* (145°), needles (45%), m. p. 178—179° [from ethanol (charcoal)] (Found: C, 68·0; H, 6·0%), and 5-(2-*oxo*cyclo*hexyl)amino*-1-o-*tolylbenzotriazole* (140°), pale brown prisms (51%), m. p. 106—107° [from ethanol (charcoal)] (Found: C, 71·2; H, 6·2. $C_{19}H_{20}ON_4$ requires C, 71·3; H, 6·2%).

5 : 6 : 7 : 8-*Tetrahydro-1′-phenyltriazolo*(5′ : 4′-3 : 4)*carbazole and its Derivatives.*—When 5-(2-oxo*cyclo*hexyl)amino-1-phenylbenzotriazole (0·8 g.) was gradually heated with a few drops of concentrated hydrochloric acid, the mixture became molten at 145—150° and solidified again within a few seconds with the evolution of water. After the product had been crystallised from ethanol, 5 : 6 : 7 : 8-tetrahydro-1′-phenyltriazolo(5′ : 4′-3 : 4)carbazole was obtained in prisms (0·2 g.), m. p. 221—222°, identical (mixed m. p.) with the substance described by Katritzky and Plant (*loc. cit.*). The following were similarly prepared (the reaction temperature being indicated as before), except that the catalyst in each case was a small amount of the dry hydrochloride of the corresponding amine (prepared by passing dry hydrogen chloride through a suspension of the base in ether): 1′-p-*chlorophenyl*-5 : 6 : 7 : 8-*tetrahydrotriazolo*(5′ : 4′-3 : 4)*carbazole* (180°), prisms (70%), m. p. 251—252° (from ethanol) (Found: C, 66·7; H, 4·9. $C_{18}H_{15}N_4Cl$ requires C, 67·0; H, 4·7%), and 5 : 6 : 7 : 8-*tetrahydro*-1′-o-*methoxyphenyl*- (150°), prisms (16%), m. p. 193° [from ethanol (charcoal)] (Found: C, 71·5; H, 6·0. $C_{19}H_{18}ON_4$ requires C, 71·7; H, 5·7%), -1′-m-*methoxyphenyl*- (180°), needles (30%), m. p. 203—204° [from ethanol (charcoal)] (Found: C, 71·4; H, 5·9%), -1′-p-*methoxyphenyl*- (170°), plates (8%), m. p. 245—246° [from ethanol (charcoal)] (Found: C, 71·6; H, 5·8%) (use of concentrated hydrochloric acid as catalyst led to hydrolysis of the 2-oxo*cyclo*hexylamino-group with the isolation of the hydrochloride of 5-amino-1-*p*-methoxyphenylbenzotriazole), and -1′-o-*tolyltriazolo*(5′ : 4′-3 : 4)*carbazole* (160°), prisms (53%), m. p. 226—227° [from ethanol (charcoal)] (Found: C, 75·2; H, 6·2. $C_{19}H_{18}N_4$ requires C, 75·5; H, 6·0%).

Although these triazolocarbazoles were heated at different temperatures under various conditions, nothing pure could be isolated from any of the products, except when the conditions were such as to leave unchanged material.

2-*Methyl*-1′-*phenyltriazolo*(4′ : 5′-5 : 6)*quinol*-4-*one*.—After 5-amino-1-phenylbenzotriazole (5 g.), ethyl acetoacetate (5 c.c.), and a few drops of concentrated hydrochloric acid had been left at room temperature for 12 hr. and the solid crystallised from ethanol, *ethyl* β-(1-*phenylbenzotriazol*-5-*ylamino*)*crotonate* was obtained in plates (5·5 g.), m. p. 127—128° (Found : C, 67·4; H, 5·8. $C_{18}H_{18}O_2N_4$ requires C, 67·1; H, 5·6%). When the ester (6 g.) was heated for 5 min. at 265°, the product pulverised and extracted with hot benzene, and the residual solid crystallised from nitrobenzene, 2-*methyl*-1′-*phenyltriazolo*(4′ : 5′-5 : 6)*quinol*-4-*one* was obtained in prisms (2·7 g.), decomp. 325—335° (Found : C, 69·4; H, 4·4. $C_{16}H_{12}ON_4$ requires C, 69·6; H, 4·3%).

The quinolone (1·2 g.), phosphorus oxychloride (10 c.c.), and phosphorus pentachloride (2 g.) were refluxed together for 1½ hr., cooled, and poured into ice and dilute hydrochloric acid. After 1 hr., the solution was filtered and made alkaline with ammonia, and the solid crystallised from aqueous ethanol, to give 4-*chloro*-2-*methyl*-1′-*phenyltriazolo*(4′ : 5′-5 : 6)-*quinoline* in prisms (0·8 g.), m. p. 183—184° (Found : C, 65·1; H, 3·8. $C_{16}H_{11}N_4Cl$ requires C. 65·2; H, 3·7%).

2-*Methyl*-6-(*benzotriazol*-1-*yl*)*quinol*-4-*one*.—Prepared from 1-*p*-aminophenylbenzotriazole as described above for their isomers, *ethyl* β-(p-*benzotriazol*-1-*ylanilino*)*crotonate*, first purified by boiling in benzene with charcoal and recovered by evaporation of the filtered solution, was obtained from ethanol in needles (66%), m. p. 130° (Found : C, 67·0; H, 5·7%), and 2-*methyl*-6-(*benzotriazol*-1-*yl*)*quinol*-4-*one* from nitrobenzene in pale brown prisms (45%) which decomposed at 320—340° (Found : C, 69·6; H, 4·4%).

2-*Chloro*-4-*methyl*-1′-*phenyltriazolo*(4′ : 5′-5 : 6)*quinoline*.—When the solid obtained by heating 5-amino-1-phenylbenzotriazole (1·1 g.) with ethyl acetoacetate (0·7 g.) at 180° for 2 min. was crystallised twice from ethanol, 5-*acetoacetamido*-1-*phenylbenzotriazole* was isolated in almost colourless plates (1·2 g.), m. p. 210° (decomp.) (Found : C, 65·0; H, 4·8. $C_{16}H_{14}O_2N_4$ requires C, 65·3; H, 4·8%). After this substance (1·3 g.) had been heated at 100° for 20 min. with concentrated sulphuric acid (25 c.c.), and the whole poured into water, the sulphate (1 g.) of 5-amino-1-phenylbenzotriazole was precipitated. The free base, identified by mixed m. p., was obtained from the salt by adding alkali to its solution in hot water.

5-Acetoacetamido-1-phenylbenzotriazole (2·5 g.) was refluxed with phosphorus oxychloride (12 c.c.) for 4 hr., diluted with chloroform (150 c.c.), and poured into ammonia (150 c.c. of *d* 0·88), and the whole stirred for ½ hr. After the chloroform layer had been dried (Na_2SO_4) and evaporated, the residue was boiled in ethanol with charcoal, and the filtered solution diluted with water. When the precipitate was crystallised first from ethanol and then from light petroleum, 2-*chloro*-4-*methyl*-1′-*phenyltriazolo*(4′ : 5′-5 : 6)*quinoline* separated in almost colourless prisms (0·2 g.), m. p. 180° (Found : C, 65·3; H, 4·1; Cl, 11·7. $C_{16}H_{11}N_4Cl$ requires Cl, 12·1%).

5-*Chloro*-1′-*phenyltriazolo*(5′ : 4′-3 : 4)*acridine*.—5-Amino-1-phenylbenzotriazole (5 g.), *o*-chlorobenzoic acid (3·5 g.), potassium carbonate (4·5 g.), and a little copper bronze were refluxed with amyl alcohol (30 c.c.) for 3 hr., the solvent removed in steam, the residual solution filtered, and the filtrate acidified with acetic acid. The precipitate was dried, refluxed for 2 hr. with phosphorus oxychloride (12 c.c.), and, after the addition of chloroform (150 c.c.), the whole, when cold, was added to a mixture of ice (300 g.) and ammonia (500 c.c. of *d* 0·88). After the mixture had been stirred for ½ hr., the chloroform layer was dried and evaporated. The residual 5-*chloro*-1′-*phenyltriazolo*(5′ : 4′-3 : 4)*acridine* was purified by absorption from benzene on alumina, and it then separated from benzene in prisms (1·5 g.), m. p. 219—221°, which changed above 200° to a polymorphic form, m. p. 229—230° (Found : C, 68·9; H, 3·6. $C_{19}H_{11}N_4Cl$ requires C, 69·0; H, 3·3%).

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