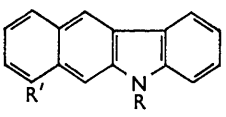
1015. *Carcinogenic Nitrogen Compounds. Part XLVIII.*[1] *Benzo*[b]-*carbazoles, Carbazolocarbazoles, and Carbazoloacridines from Carbazole*

By N. P. Buu-Hoï and G. Saint-Ruf

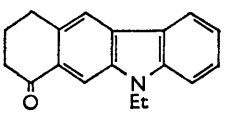
Homologues of 5*H*-benzo[*b*]carbazole have been synthesised by application of the succinic anhydride method to 9-ethylcarbazole *via* 5-ethyl-7,8,9,10-tetrahydro-5-oxo-5*H*-benzo[*b*]carbazole; this intermediate served also for the preparation of carbazolocarbazoles and carbazoloacridines, which represent novel types of heterocycles.

5*H*-Benzo[*b*]carbazole (I) is a well-known constituent of the high-boiling portions of coal tar, but its chemistry has been little investigated.[2] In particular, there is no convenient method for the synthesis of its homologues and derivatives, although several reactions lead to the formation of small amounts of the unsubstituted compound.[3] A method of more general application might be based on the recently reported[4] synthesis of 5-methylbenzo[*b*]carbazole starting from 1,2-dimethylindole and 2-hydroxymethylenecyclohexanone. We now report the possibility of building up the benzo[*b*]carbazole nucleus starting from the readily available 9-alkylcarbazoles.*

Although the Friedel–Crafts reaction of acid anhydrides on 9-alkylcarbazoles was generally believed to lead to disubstitution,[5] Buu-Hoï and Lavit[6] showed that 9-ethyl-



(I: R = R' = H)
(II: R = Et, R' = H)
(III: R = Et, R' = Me)



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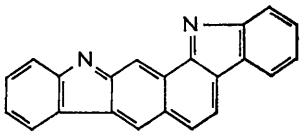


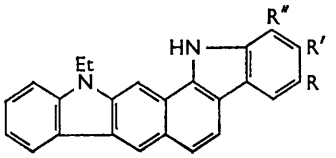
(V)

carbazole could readily undergo monosuccinoylation, the product being converted into γ-(9-ethylcarbazol-3-yl)butyric acid by reduction. This acid undergoes cyclisation with polyphosphoric acid predominantly at position 2, to give a good yield of 5-ethyl-7,8,9,10-tetrahydro-7-oxo-5*H*-benzo[*b*]carbazole (IV); traces of an isomeric ketone, resulting from cyclisation at position 4, were noticeable in the crude product but could not be isolated.

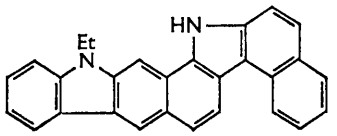
* Since this Paper was submitted, another synthesis of *N*-substituted 2,3-benzocarbazoles has been published (H. Seeboth, H. Neumann, and H. Görsch, *Annalen*, 1965, **683**, 93.)

[1] Part XLVII, preceding Paper.
[2] Cf. Ph. Mabille and N. P. Buu-Hoï, *J. Org. Chem.*, 1960, **25**, 1937.
[3] Recent syntheses include: N. P. Buu-Hoï, N. Hoán, and N. H. Khôi, *J. Org. Chem.*, 1950, **15**, 131; N. P. Buu-Hoï, P. Jacquignon, and D. Lavit, *J.*, 1956, 2593.
[4] W. E. Noland and J. E. Johnson, *Tetrahedron Letters*, 1962, 589.
[5] D. R. Mitchell and S. G. P. Plant, *J.*, 1936, 1295.
[6] N. P. Buu-Hoï and D. Lavit, *Bull. Soc. chim. France*, 1958, 290.

Wolff–Kishner reduction of the ketone (IV), followed by dehydrogenation over palladised charcoal, gave 5-ethyl-5*H*-benzo[*b*]carbazole (II) in excellent yield. The structure of compound (II) [and therefore of (IV)] was established by identification with a sample obtained directly by *N*-ethylation of 5*H*-benzo[*b*]carbazole. From the ketone (IV) and



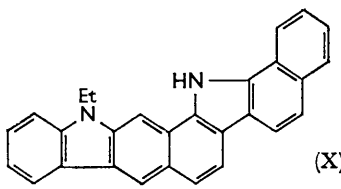
(VI: R = R′ = R″ = H)
(VII: R = Me, R′ = R″ = H)
(VIII: R = H, R′ = R″ = Me)



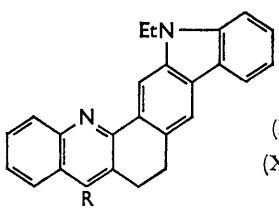
(IX)

methylmagnesium iodide, 5-ethyl-7-methyl-5*H*-benzo[*b*]carbazole (III) was also readily prepared by routine techniques.

The easy preparation of the ketone (IV) gave access to derivatives of the hitherto unknown carbazolo[2,3-*a*]carbazole (V), a nucleus which is interesting in view of its completely aromatic structure. Thus, indolisation of the phenylhydrazone of (IV) afforded 12-ethyl-5,6,12,14-tetrahydrocarbazolo[2,3-*a*]carbazole; dehydrogenation of this compound, even with a drastic reagent like palladium–charcoal, stopped, however, midway, to give 12-ethyl-12,14-dihydrocarbazolo[2,3-*a*]carbazole (VI), instead of carbazolo[2,3-*a*]-carbazole itself (under similar conditions, hydro-derivatives of condensed polycyclic hydrocarbons undergo total aromatisation, with eventual splitting, or displacement, of



(X)



(XI: R = CO_2H)
(XII: R = H)

the encumbering alkyl groups [7]). The 3-methyl and 1,2-dimethyl homologues of (VI) behaved in like manner towards palladium–charcoal, giving only the 12,14-dihydro-compounds, (VII) and (VIII). The two heptacyclic benzo-derivatives, (IX) and (X), of compound (VI) were also obtained, and likewise resisted complete aromatisation.

The ketone (IV) underwent Pfitzinger reactions, giving, with isatin for example, 15-ethyl-6,7-dihydrocarbazolo[2,3-*c*]acridine-8-carboxylic acid (XI), which, on thermal decarboxylation, afforded compound (XII). It is worth noting that this last acridine gave a *mono*picrate. The dihydrocarbazolocarbazoles also gave *mono*picrates, and the deep coloured complexes they formed with tetrachlorophthalic anhydride were also of the 1 : 1 structure.

Results of tests for carcinogenicity will be reported elsewhere.

Experimental

Succinoylation of 9-Ethylcarbazole.—This reaction, performed under various conditions (in nitrobenzene, or in methylene chloride, with 1 or 2 mol. of succinic anhydride per mol. of 9-ethylcarbazole) at room temperature, gave, consistently, only β-(9-ethylcarbazol-3-yl-carbonyl)propionic acid, m. p. 182° (lit.,[6] 182°), the best yield (75%) being obtained with methylene chloride as solvent.

5-Ethyl-7,8,9,10-tetrahydro-7-oxo-5H-benzo[b]*carbazole* (IV).—To a solution of phosphorus pentoxide (43 g.) in 85% orthophosphoric acid (57 g.), γ-(9-ethyl-3-carbazolyl)butyric acid (m. p. 104°; 15 g.) was added in small portions with stirring, and the mixture heated at 105° for 2 hr.;

[7] Cf. L. F. Fieser and M. Fieser, "Natural Products Related to Phenanthrene," Reinhold Publ. Corp., New York, 1949.

after cooling, water was added, the product taken up in chloroform, the organic layer dried (Na_2SO_4), the solvent distilled, and the residue fractionated *in vacuo*. The resin, b. p. 214°/0·25 mm., was triturated with a mixture of acetone and methanol to induce crystallisation, and the *solid* which then formed was recrystallised from methanol, giving pale yellow prisms (9 g.), m. p. 111° (Found: C, 82·3; H, 6·3; N, 5·4. $C_{18}H_{17}NO$ requires C, 82·1; H, 6·5; N, 5·3%). Traces of a non-crystalline isomer could be recovered from the mother-liquors.

5-*Ethyl*-7,8,9,10-*tetrahydro*-5H-*benzo*[b]*carbazole*.—A mixture of the foregoing ketone (2·5 g.), 98% hydrazine hydrate (1 g.), potassium hydroxide (1 g.), and diethylene glycol (20 c.c.) was refluxed for 4 hr., with removal of water; after cooling and dilution with water, the *product* was taken up in benzene, isolated by distillation *in vacuo* (b. p. 240—242°/13 mm.), and recrystallised from ethanol, giving a 96% yield of colourless leaflets, m. p. 88° (Found: C, 86·5; H, 7·5; N, 5·6. $C_{18}H_{19}N$ requires C, 86·7; H, 7·7; N, 5·6%).

5-*Ethyl*-5H-*benzo*[b]*carbazole* (II).—(*a*) The above tetrahydro-compound (1 part) was heated for 3 hr. at 350° over 5% palladised charcoal (5 parts), and the product distilled *in vacuo* (b. p. 258°/15 mm.); recrystallisation from ethanol gave a 70% yield of colourless *needles*, m. p. 143—144° (Found: C, 88·2; H, 6·1. $C_{18}H_{15}N$ requires C, 88·1; H, 6·2%); *picrate*, brown needles, m. p. 135°, from ethanol or benzene (Found: N, 12·0. $C_{24}H_{18}N_4O_7$ requires N, 11·8%).

(*b*) A solution of benzo[*b*]carbazole (3·25 g.) in anhydrous xylene (50 c.c.) was heated with sodamide (1·2 g.) until evolution of ammonia ceased; after cooling, ethyl iodide (4 g.) was added, and the mixture was heated under reflux for a further hr. After decomposition with water, the product was worked up in the usual way, giving, on crystallisation from ethanol, long colourless needles (30% yield), m. p. and mixed m. p. 143—144°.

5-*Ethyl*-9,10-*dihydro*-7-*methyl*-5H-*benzo*[b]*carbazole*.—To an ice-cooled ethereal solution of a Grignard reagent prepared from methyl iodide (6 g.) and magnesium (1 g.), ketone (IV) (5 g.) was added in small portions, and the mixture refluxed for 30 min. on a water-bath. After decomposition with aqueous ammonium chloride, the crude product (1 part) was heated for 3 hr. with formic acid (3 parts); water was then added, the dehydration product taken up in benzene, the benzene layer washed with aqueous sodium hydroxide and dried (Na_2SO_4), and the solvent removed. Crystallisation from ethanol afforded long colourless *needles* (3 g.), m. p. 138° (Found: C, 87·4; H, 6·9; N, 5·6. $C_{19}H_{19}N$ requires C, 87·3; H, 7·3; N, 5·4%); *picrate*, brown needles, m. p. 127°, from ethanol (Found: N, 11·5. $C_{25}H_{22}N_4O_7$ requires N, 11·4%).

5-*Ethyl*-7-*methyl*-5H-*benzo*[b]*carbazole* (III).—Prepared from the above dihydro-compound, either by heating at 280° for 2 hr. over palladised charcoal or by heating with chloranil in boiling xylene for 6 hr., this *carbazole* formed colourless needles, m. p. 141°, from ethanol (Found: C, 87·8; H, 6·7; N, 5·6. $C_{19}H_{17}N$ requires C, 88·0; H, 6·6; N, 5·4%); *picrate*, brown leaflets, m. p. 152°, from ethanol (Found: N, 11·7. $C_{25}H_{20}N_4O_7$ requires N, 11·5%).

12-*Ethyl*-5,6,12,14-*tetrahydrocarbazolo*[2,3-a]*carbazole*.—A solution of the ketone (IV) (2 g.) and phenylhydrazine (0·9 g.) in ethanol (20 c.c.) was refluxed for 45 min. with 1 drop of acetic acid, and the crude phenylhydrazone which precipitated on dilution with water was treated for 1 min. with a boiling solution of hydrogen chloride in acetic acid. After dilution with water, the *indole* obtained in 90% yield was recrystallised from ethanol, to give cream-coloured microneedles, m. p. 276° (Found: C, 85·7; H, 6·1; N, 8·3. $C_{24}H_{20}N_2$ requires C, 85·7; H, 6·0; N, 8·3%). Sublimation of this product (1 part) over palladised charcoal (5 parts) afforded 12-*ethyl*-12,14-*dihydrocarbazolo*[2,3-a]*carbazole* (VI) in 75% yield as colourless leaflets, m. p. 314°, from ethanol–benzene (Found: C, 86·0; H, 5·2; N, 8·5. $C_{24}H_{18}N_2$ requires C, 86·2; H, 5·4; N, 8·4%).

12-*Ethyl*-5,6,12,14-*tetrahydro*-3-*methylcarbazolo*[2,3-a]*carbazole*.—Prepared from *p*-tolylhydrazine, this *indole*, needles, m. p. 218°, from ethanol (Found: N, 7·8. $C_{25}H_{22}N_2$ requires N, 8·0%), was dehydrogenated to 12-ethyl-12,14-*dihydro*-3-*methylcarbazolo*[2,3-a]*carbazole* (VII), needles, m. p. 330°, from ethanol–benzene (Found: C, 86·3; H, 5·8; N, 7·9. $C_{25}H_{20}N_2$ requires C, 86·2; H, 5·8; N, 8·0%); *picrate*, dark brown needles, m. p. 251° (dissoc. > 155°), from ethanol–benzene (Found: N, 11·8. $C_{31}H_{23}N_5O_7$ requires N, 12·1%). The *tetrachlorophthalic anhydride π-complex*,[8] prepared in acetic acid, crystallised from this solvent as brown-violet needles, m. p. 265° (dissoc. > 210°) (Found: C, 62·3; H, 3·4. $C_{33}H_{20}Cl_4N_2O_3$ requires C, 62·5; H, 3·2%).

[8] Cf. N. P. Buu-Hoï and P. Jacquignon, *Compt. rend.*, 1952, **234**, 1056; *Bull. Soc. chim. France*, 1957, 488.

12-*Ethyl*-5,6,12,14-*tetrahydro*-1,2-*dimethylcarbazolo*[2,3-a]*carbazole*.—Prepared from 2,3-xylylhydrazine, this *indole* formed microneedles, m. p. 288°, from ethanol (Found: C, 85·6; H, 6·4; N, 7·8. $C_{26}H_{24}N_2$ requires C, 85·7; H, 6·6; N, 7·7%). 12-*Ethyl*-12,14-*dihydro*-1,2-*dimethylcarbazolo*[2,3-a]*carbazole* (VIII) formed needles, m. p. 295°, from ethanol–benzene (Found: C, 86·3; H, 6·0; N, 7·9. $C_{26}H_{22}N_2$ requires C, 86·1; H, 6·1; N, 7·7%).

14-*Ethyl*-7,8,14,16-*tetrahydrobenzo*[g]*carbazolo*[2,3-a]*carbazole*.—This *indole*, prepared in 70% yield from β-naphthylhydrazine hydrochloride, formed microneedles, m. p. 354°, from ethanol–benzene (Found: C, 86·9; H, 5·8; N, 7·4. $C_{28}H_{22}N_2$ requires C, 87·1; H, 5·7; N, 7·3%). 14-*Ethyl*-14,16-*dihydrobenzo*[g]*carbazolo*[2,3-a]*carbazole* (IX) formed colourless prisms, m. p. 366°, from ethanol–benzene (Found: C, 87·5; H, 5·3; N, 7·4. $C_{28}H_{20}N_2$ requires C, 87·5; H, 5·3; N, 7·3%); *picrate*, brown needles, m. p. 255°, from benzene (Found: N, 11·5. $C_{34}H_{23}N_5O_7$ requires N, 11·4%).

14-*Ethyl*-7,8,14,16-*tetrahydrobenzo*[i]*carbazolo*[2,3-a]*carbazole*.—Prepared in 40% yield from α-naphthylhydrazine hydrochloride, this *indole* formed needles, m. p. 274°, from cyclohexane (Found: C, 87·0; H, 5·8; N, 7·2%).

14-*Ethyl*-14,16-*dihydrobenzo*[i]*carbazolo*[2,3-a]*carbazole* (X) formed needles, m. p. 310°, from ethanol (Found: C, 87·4; H, 5·3%); *picrate*, brown prisms, m. p. 227°, from benzene (Found: N, 11·7%).

15-*Ethyl*-6,7-*Dihydrocarbazolo*[2,3-c]*acridine*-8-*carboxylic Acid* (XI).—A solution of the ketone (IV) (5 g.), isatin (4 g.), and potassium hydroxide (3 g.) in ethanol (20 c.c.) was refluxed for 24 hr., the solvent was distilled, and the residue ground with benzene; the remaining solid was taken up in water and acidified to pH 6. The *product* was recrystallised from ethanol to give a 70% yield of beige prisms, m. p. 336° (Found: C, 76·9; H, 5·6; N, 6·7. $C_{26}H_{20}N_2O_2,C_2H_5OH$ requires C, 76·7; H, 6·0; N, 6·4%). Heating this acid above its m. p. caused decarboxylation, leaving 15-*ethyl*-6,7-*dihydrocarbazolo*[2,3-c]*acridine* (XII), which was purified *via* its *picrate*, bright red needles, m. p. 293°, from nitrobenzene (Found: N, 12·2. $C_{31}H_{23}N_5O_7$ requires N, 12·1%). Treatment with aqueous ammonia afforded the *base*, yellow needles, m. p. 188—190°, from methanol (Found: C, 85·9; H, 5·8. $C_{25}H_{20}N_2$ requires C, 86·2; H, 5·8%).

INSTITUT DE CHIMIE DES SUBSTANCES NATURELLES DU C.N.R.S.,
GIF-SUR-YVETTE (S.-ET-O.), FRANCE.
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