316. *A Relationship between β-Naphthylamine and Ethyl β-Aminocrotonate.*

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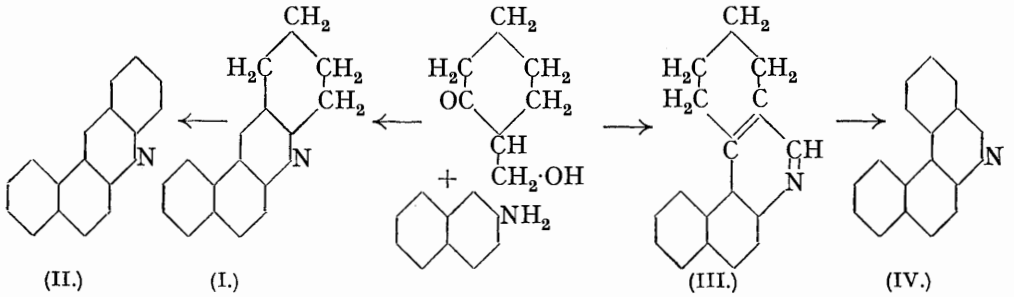
Extension of the recently described synthesis of 5 : 6 : 7 : 8-tetrahydrophenanthridine to β-naphthylamine unexpectedly yields two isomeric bases of the desired composition, and the same products are obtained from 1-bromo-β-naphthylamine. One of these furnishes β-naphthacridine on dehydrogenation, and is therefore the tetrahydro-β-naphthacridine. The isomer is doubtless the expected tetrahydro-

phenanthridine derivative, since the dehydrogenated base in concentrated sulphuric acid exhibits the blue fluorescence characteristic of phenanthridine bases.

This exceptional behaviour of β-naphthylamine is indicative of its specially close relationship to ethyl β-aminocrotonate, since the latter furnishes ethyl hexahydroquinaldine-3-carboxylate on condensation with 2-methylol*cyclo*hexanone.

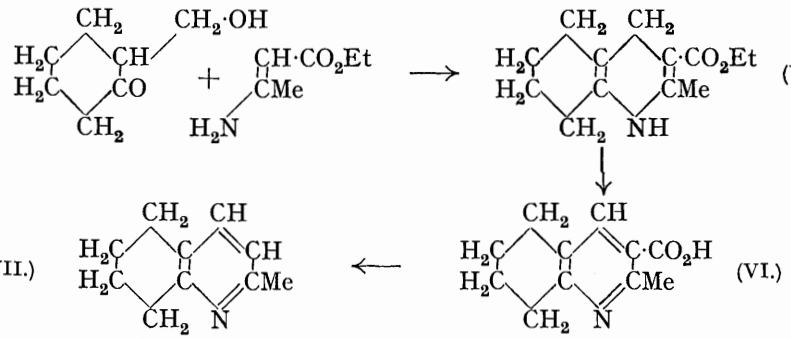
It was recently shown (Kenner, Ritchie, and Statham, this vol., p. 1169) that 5 : 6 : 7 : 8-tetrahydrophenanthridine and its derivatives resulted from the condensation of 2-methylol*cyclo*hexanone with aromatic amines. From β-naphthylamine, however, two isomerides of the expected composition have been obtained. Furthermore, the same isomerides, though in smaller yield, resulted from the use of 1-bromo-β-naphthylamine in place of β-naphthylamine itself. Similarly, 3-bromo-β-naphthylamine furnished two isomeric bases, but each containing bromine. It was therefore apparent that in each case ring-closure involved the 1-position of the naphthalene nucleus. The suspicion that one of the two products in each case might be a tetrahydronaphthacridine (I) was readily confirmed, since one of the dehydrogenated bases exhibited the characteristic green fluorescence of acridine derivatives in concentrated sulphuric acid and proved to be identical with β-naphthacridine (II; Ullmann, *Annalen*, 1907, **355**, 350). Since the solution of its isomeride in sulphuric acid showed the usual blue fluorescence of phenanthridines, it was doubtless the expected β-naphthaphenanthridine (IV).

Some explanation of this remarkable differentiation of β-naphthylamine from the



(II.) (I.) (III.) (IV.)

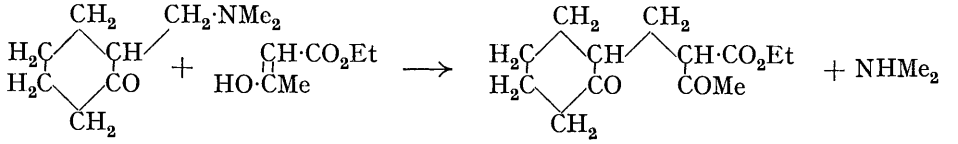
aromatic bases previously employed was revealed by a study of the reaction between the methylol*cyclo*hexanone and ethyl β-aminocrotonate. Besides ethyl dihydrolutidinedicarboxylate, doubtless arising from partial decomposition of the methylol into formaldehyde and *cyclo*hexanone, a basic product was isolated and readily characterised by its *picrate* and its *picrolonate*. The formation of quinaldine on dehydrogenation indicated that the base was *ethyl hexahydroquinaldine-3-carboxylate* (V), and this was confirmed by its hydrolysis and simultaneous oxidation by hydrochloric acid (cf. the similar behaviour of ethyl dihydrolutidinedicarboxylate) to tetrahydrobenzoquinaldine-3-carboxylic acid (VI) (Basu, *Annalen*, 1934, **512**, 131), from which tetrahydrobenzoquinaldine (VII) itself was obtained.



(V.) (VII.) (VI.)

This little-known base, which had previously been obtained in very small yield by the reduction of quinaldine and certain of its derivatives (v. Braun, Gmelin, and Schultheiss,

Ber., 1923, **56**, 1344; Tröger and Pahle, *J. pr. Chem.*, 1926, **112**, 221; Tröger and Ungar, *ibid.*, p. 243), has been conveniently prepared by the condensation of ethyl aminocrotonate with 2-hydroxymethylene*cyclo*hexanone (Basu, *loc. cit.*). This reaction is akin to that now described, as is also that of ethyl sodioacetoacetate with 2-dimethylamino*cyclo*hexanone (Mannich, Koch, and Borkowsky, *Ber.*, 1937, **70**, 355) :



It would appear from these results that β-naphthylamine is intermediate in character between the various aromatic amines already studied and ethyl aminocrotonate. This conclusion obviously invites correlation with the views expressed by Mills and Nixon (J., 1930, 2580) and later workers, but before proceeding to this it is desirable to see what results are afforded by other amines when submitted to condensation with methylol*cyclo*hexanone.

Experimental.

Bases from β-Naphthylamine.—A mixture of picrates (19 g.) from 2-methylol*cyclo*hexanone (12·8 g.) and corresponding amounts of the other reactants (cf. Kenner, Ritchie, and Statham, *loc. cit.*) was obtained from the unacetylated portion of the basic products, b. p. 220—400°/20 mm. Extraction with boiling alcohol (2250 c.c.) for ¾ hour left 7·1 g. of almost pure, sparingly soluble *picrate*, m. p. 253—254° after crystallisation from a very large volume of alcohol (Found : N, 12·2. $C_{17}H_{15}N,C_6H_3O_7N_3$ requires N, 12·1%), from which the *tetrahydronaphthacridine*, m. p. 94—94·5° (Found : C, 87·4; H, 6·6; N, 6·0. $C_{17}H_{15}N$ requires C, 87·5; H, 6·4; N, 6·0%), dehydrogenated *base*, m. p. 106° (Found : C, 88·6; H, 4·8; N, 6·2. $C_{17}H_{11}N$ requires C, 89·1; H, 4·8; N, 6·1%), and its *picrate*, m. p. 247—248° (decomp.) (Found : N, 12·3. $C_{17}H_{11}N,C_6H_3O_7N_3$ requires N, 12·2%), were derived. The more soluble *picrate* (9·9 g.), m. p. 218—219° (decomp.) (Found : N, 12·2%), yielded a *tetrahydro-base*, m. p. 114—115° (Found : C, 87·4; H, 6·4; N, 6·0%), a dehydrogenated *base*, m. p. 127° (Found : C, 89·0; H, 4·9; N, 6·2%), and its *picrate*, m. p. 266—267° (decomp.) (Found : N, 12·3%). From a similar experiment with 1-bromo-β-naphthylamine, the methylol (12·8 g.) yielded a mixture (6·0 g.) from which bromine-free picrates, m. p.'s 246—249° (decomp.) (4·3 g.) and 213—215° (decomp.) (0·9 g.), and tetrahydro-bases, m. p.'s 94—95° and 111—113°, were prepared, and identified by direct comparison with those just described.

3-Bromo-β-naphthylamine.—The following series of compounds was very briefly described by Wynne (P., 1914, **30**, 204), but without experimental details or analyses. Doubtless it is for this reason that the relevant data have not been included in Beilstein's Handbuch.

A hot solution of 2-amino-3-naphthoic acid, m. p. 219—220° (22·4 g.), in hydrobromic acid (*d* 1·48; 36 c.c.) and water (150 c.c.) was rapidly cooled, and treated during 1 hour at 2—3° dropwise with a solution of sodium nitrite (8·4 g.) in water (20 c.c.). After 2 hours the solid diazonium salt was collected in an ice funnel, and added to a cold solution of cuprous bromide [from copper sulphate, 21·6 g.; potassium bromide, 10·8 g.; and hydrobromic acid (*d* 1·48), 36 c.c.]. The mixture, after being shaken and diluted with water, was heated at 100° to complete the reaction. Yield 28·2 g., m. p. 213—215°. For analysis, the brownish-red *2-bromo-3-naphthoic acid* was decolorised in glacial acetic acid solution by sulphurous acid and a trace of zinc dust, and then crystallised successively from formic acid and from alcohol; needles, m. p. 219—220° (Wynne, 220°) (Found : Br, 31·9; equiv., 250. $C_{10}H_6Br\cdot CO_2H$ requires Br, 31·9%; equiv., 251). The *methyl* ester was most conveniently prepared by treating a solution of the crude acid (6·3 g.) in methanol (25 c.c.) and dry ether (100 c.c.) with diazomethane, generated by slowly adding nitroso-β-methylamino*iso*butyl methyl ketone (8 c.c.) to a 3% solution of sodium benzyloxide in benzyl alcohol (10 c.c.) at 70° under 400 mm. pressure. After 12 hours, methyl alcohol and ether were removed from the solution under reduced pressure, and the ester removed by repeated extraction with light petroleum (b. p. 40—60°); lustrous needles, m. p. 66·5° (Wynne 67°) (Found : C, 54·3; H, 3·5. $C_{12}H_9O_2Br$ requires C, 54·4; H, 3·4%). A solution of the ester (4·6 g.) in methyl alcohol (25 c.c.), and hydrazine hydrate (6 g.) at 35° for 17 hours yielded the *hydrazide* (4·1 g.), m. p. 222° after recrystallisation from alcohol (Wynne 218°) (Found : C, 49·6; H, 3·5; N, 10·8. $C_{11}H_9ON_2Br$ requires C, 49·8; H, 3·4; N, 10·6%).

3-*Bromo*-2-*naphthylurethane* was formed when ethyl nitrite (1 g.) was added to a mixture of the suspended hydrazide (2·65 g.) in alcohol (25 c.c.) with a solution of hydrogen chloride (0·5 g.) in alcohol (5 c.c.), and the resulting solution was boiled under reflux; yield 2·2 g.; needles, m. p. 114° (Wynne, 114°) (Found: C, 52·9; H, 4·2; N, 5·0. $C_{13}H_{12}O_2NBr$ requires C, 53·1; H, 4·1; N, 4·8%). When the urethane (20 g.) was boiled with hydrobromic acid (*d* 1·48; 100 c.c.) under reflux, the oil gradually gave place to the crystalline hydrobromide of 3-*bromo*-β-*naphthylamine*, and by extracting this crude salt with ether (Soxhlet) any unchanged urethane was recovered. The base separated from alcohol in plates, m. p. 168—169° (Wynne 168°) (Found: C, 53·9; H, 3·8; N, 6·5. $C_{10}H_8NBr$ requires C, 54·1; H, 3·6; N, 6·3%). 2 : 3-*Dibromonaphthalene*, from the base under conditions similar to those applied to 2-amino-3-naphthoic acid, crystallised from light petroleum (b. p. 60—80°) in lustrous, rectangular plates, m. p. 140° (Wynne 140°) (Found: C, 41·8; H, 2·2. $C_{10}H_6Br_2$ requires C, 42·0; H, 2·1%).

The basic product from methylol*cyclo*hexanone (4·3 g.), 3-bromo-β-naphthylamine (13·4 g.), its hydrochloride (8·6 g.), hydrated stannic chloride (13·2 g.), and alcohol (25 c.c.) was extracted thrice with hot hydrobromic acid (25 c.c.; *d* 1·48) and the residue was then no longer sticky. The base from the liquors yielded 3·3 g. of picrate, from which two salts were separated by crystallisation from alcohol. The less soluble *picrate*, m. p. 206° (decomp.) (Found: N, 10·5. $C_{17}H_{14}NBr,C_6H_3O_7N_3$ requires N, 10·4%), yielded a *base*, m. p. 133° (Found: N, 4·5. $C_{17}H_{14}NBr$ requires N, 4·5%), whilst the more soluble *picrate*, m. p. 156—157° (decomp.) (Found: N, 10·3%), furnished a *base*, m. p. 145° (Found: N, 4·5%). The amount of material available was too small for further work, but the results establish the formation of two isomeric bromo-tetrahydro-bases in the reaction.

Interaction of Ethyl β-*Aminocrotonate with* 2-*Methylol*cyclo*hexanone*.—After the ester (400 g.) and the methylol (400 g.) had been heated together at 100° for 48 hours, ethyl dihydrolutidinedicarboxylate (202 g.; m. p. 182—184° from alcohol) was collected [Found: N, 6·0; *M* (Rast), 242. Calc. for $C_{13}H_{19}O_4N$: N, 5·5%; *M*, 253], and identified by conversion into ethyl lutidinedicarboxylate, m. p. 72°, with nitrous acid, and into 2 : 6-lutidine (picrate, m. p. 160—162°) by dehydrogenation with selenium at 340° for 12 hours. Each substance was identified by direct comparison with an authentic specimen. Ether extraction of a solution of the oily portion of the product in dilute sulphuric acid yielded a further small quantity (4 g.) of the above ester. The basic material recovered from the acid solution yielded a main fraction (141 g.), b. p. 187—192°/25 mm., and 78 g., b. p. 192—240°/25 mm. No definite substance was isolated from the latter, but the main fraction, b. p. 171—174·5°/18 mm. after further fractionation, was readily characterised by its *picrolonate*, light yellow needles from alcohol, m. p. 212—214° (Found: C, 56·7; H, 5·6; N, 14·4. $C_{13}H_{19}O_2N,C_{10}H_8O_5N_4$ requires C, 56·9; H, 5·6; N, 14·4%). The base was identified as *ethyl hexahydroquinaldine*-3-*carboxylate* by its conversion after 18 hours at 320° by selenium into quinaldine, b. p. 235—242°, picrate, m. p. 187—188·5°, methiodide, m. p. 194—195°, *picrolonate*, m. p. 231—232·5° (Found: N, 17·4. $C_{10}H_{19}N,C_{10}H_8O_5N_4$ requires N, 17·5%). Although unattacked by boiling aqueous or alcoholic potassium hydroxide solution (by contrast with ethyl tetrahydrobenzoquinaldinecarboxylate; Basu, *loc. cit.*), the hexahydrobase (15 g.) underwent hydrolysis by boiling hydrochloric acid (*d* 1·17; 200 c.c.) during 20 hours. The cooled, filtered solution was evaporated, and the aqueous solution of the residue rendered neutral to Congo-red paper. Evaporation to dryness, followed by extraction with alcohol, and concentration of the alcoholic solution, furnished tetrahydrobenzoquinaldinecarboxylic acid (9·5 g.), m. p. 230—231° (decomp.) (Found: N, 7·3. Calc. for $C_{11}H_{13}O_2N$: N, 7·3%), which did not express the m. p. of a sample of the acid prepared by Basu's method (*loc. cit.*). By distillation with 10 times its weight of soda lime, the acid was converted into tetrahydrobenzoquinaldine, b. p. 224—225°, picrate, m. p. 152—156° (Found: N, 14·9. Calc.: N, 14·9%) (Basu, *loc. cit.*, gives m. p. 157°), *picrolonate*, yellow prisms, m. p. 220° (Found: N, 16·9. $C_{10}H_{13}N,C_{10}H_8O_5N_4$ requires N, 17·0%). In a repetition of Basu's preparation of the carboxylic ester, no tarry product was formed if freshly prepared hydroxymethylene*cyclo*hexanone was employed, and the yield was 40%.

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