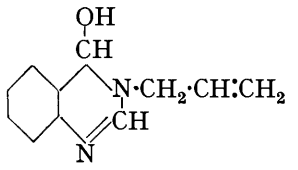
304. *The Constitution of Vasicine.*

By Hari R. Juneja, Kartar S. Narang, and Jnanendra N. Rây.

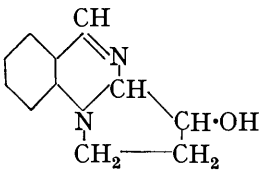
Narang and Rây (*Current Sci.*, 1934, **2**, 388; *Chem. and Ind.*, 1934, **53**, 698) gave reasons for the failure of Späth and Nikawitz's formula (*Ber.*, 1934, **67**, 45) for vasicine (I), and proposed a cyclic and an open-chain alternative. Of these, they preferred the latter, chiefly on account of the formation of 4-quinazolone by oxidation, although they realised (J., 1932, 2740) that this did not necessarily fix the position of the oxygen atom of vasicine. It has now become evident that an open-chain formula is untenable, and hence vasicine can be either (II) or (III).

The formation of 4-quinazolone-3-acetic acid (Späth and Nikawitz, *loc. cit.*) does not necessarily depend on the existence of the alcoholic hydroxyl group on the carbon atom β to the nitrogen atom. A compound of structure (II) is incapable of furnishing 4-quin-

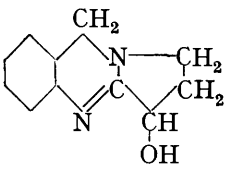
azolone-3-acetic acid, but in view of the fact that we isolated 4-quinazolone only by oxidation, we could not entirely rule it out.



(I.)

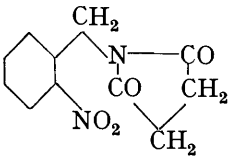


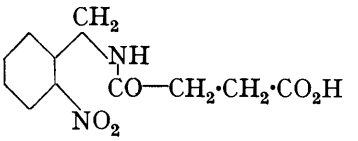
(II.)



(III.)

(IV.)

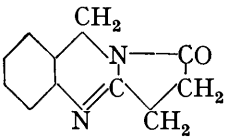


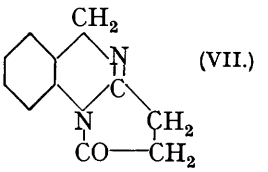


(V.)

In order to decide between formulæ (II) and (III) the *substances* (IV) and (V) were prepared. The former was obtained by the condensation of *o*-nitrobenzyl chloride with potassium succinimide, and the latter by the addition of succinic anhydride to *o*-nitrobenzylamine. On reduction, these compounds gave respectively (VI) and (VII).

(VI.)





(VII.)

Electrolytic reduction of (VI), (VII), and natural vasicine furnished three bases, of which the *picrolonates* of those derived from (VI) and natural vasicine were identical. Therefore, there is no doubt that vasicine has the structure (III). These results have been already outlined (*Current Sci.*, 1935, **3**, 352), and we were engaged in synthesising vasicine by condensing ω-bromoacetoacetic ester with *o*-nitrobenzylamine and closing the ring in the product by reduction of the keto-group to a secondary alcohol when we were forestalled by the publication of an almost identical synthesis (*Ber.*, 1935, **68**, 699).

Experimental.

The base from 2 g. of *o*-nitrobenzylamine hydrochloride in benzene (50 c.c.) was heated under reflux with succinic anhydride (1·0 g.) for 1 hr., and the crystalline deposit (1·7 g.) collected; *o-nitrobenzylsuccinamic acid* (V) crystallised from toluene in needles, m. p. 116° (Found: C, 52·4; H, 4·85. $C_{11}H_{12}O_5N_2$ requires C, 52·4; H, 4·8%).

o-Aminobenzylsuccinamic Acid.—The foregoing amic acid (1 g.) in aqueous ammonia (*d* 0·84; 10 c.c.) was reduced with ferrous sulphate (10 g.) in water (20 c.c.) at 100°. The filtrate was concentrated, acidified with acetic acid, and extracted with ethyl acetate (100 c.c.). The residue obtained from the ethyl acetate was crystallised from xylene; m. p. 145° (0·6 g.) (Found: C, 59·7; H, 6·3. $C_{11}H_{14}O_3N_2$ requires C, 59·9; H, 6·3%). The presence of a free amino-group was proved by diazotisation and coupling with alkaline β-naphthol.

This *substance* (1 g.) was mixed with freshly-fused sodium acetate (5·0 g.) and heated in dry hydrogen at 140—150° for 1 hr. The *product* (VII), after treatment with cold water, was crystallised from water; m. p. 192° (Found, in substance dried at 125°: C, 71·0; H, 5·3. $C_{11}H_{10}ON_2$ requires C, 71·0; H, 5·3%).

Succino-o-nitrobenzylimide (IV).—A mixture of *o*-nitrobenzyl chloride (1·37 g.), potassium succinimide (1·72 g.), and sodium chloride (4·5 g.) was stirred at 120—130° for 45 minutes. After treatment with water, the residue was crystallised from dilute alcohol; m. p. 130° (Found: N, 12·2. $C_{11}H_{10}O_4N_2$ requires N, 12·0%).

The foregoing *substance* (1 g.) was added in small quantities to a solution of stannous chloride (5·0 g.) in hydrochloric acid (*d* 1·16; 5 c.c.), kept at 70—80° for 1 hr. The double tin compound was collected and decomposed by alkali and the *base* (VI) was extracted in chloroform (100 c.c.)

and crystallised from water; m. p. 186°, mixed m. p. with (VII) 125—150° (Found, after drying at 100° in a high vacuum: C, 70·8; H, 5·3. $C_{11}H_{10}ON_2$ requires C, 71·0; H, 5·4%).

Electrolytic Reduction.—The substances (VI), (VII), and natural vasicine were each reduced at a lead cathode (9 cm. × 5 cm.) on which electrolytic lead had been freshly deposited. The anode was a strip of lead. The concentration of sulphuric acid was 10—15% in the anodic compartment and 20—25% in the cathodic. The current strength was 5—6 amps. The temperature of the cathodic compartment was kept at 20—30° by a circulating water device. The average temperature of the anodic compartment was 30—40°.

(*a*) 0·7 G. of (VII), dissolved in 20% sulphuric acid (20 c.c.), was reduced for 18 hrs. The product was isolated with ether after basification. The residue obtained from the ether was treated with picrolonic acid in alcoholic solution. The *picrolonate* crystallised from alcohol in thick well-defined prisms, m. p. 203—210° (decomp.) (195—197° in a vacuum) (Found: C, 52·9; H, 4·4; N, 19·1. $C_{31}H_{30}O_{10}N_{10}$ requires C, 53·0; H, 4·3; N, 19·9%). The percentage of nitrogen was low on account of traces of unreduced oxides of nitrogen.

(*b*) Vasicine (0·7 g.), in sulphuric acid (20%), was reduced for 18 hrs. The product was isolated as before and converted into a *picrolonate*, which crystallised from alcohol in well-defined rectangular plates, m. p. 207—213° (decomp.) (202—205° in a vacuum) (Found: C, 52·5; H, 4·3; N, 19·2%). This picrolonate differed in solubility and crystalline form from the preceding picrolonate and depressed its m. p.

(*c*) The substance (VI) on reduction furnished a base which gave a picrolonate, crystallising from alcohol in thick well-defined rectangular plates, indistinguishable from the picrolonate of reduced vasicine, m. p. and mixed m. p. 207—213° (decomp.) (202—205° in a vacuum) (Found: C, 52·6; H, 4·7. $C_{31}H_{30}O_{10}N_{10}$ requires C, 53·0; H, 4·3%).

THE UNIVERSITY, LAHORE.

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