155. *The Electrolytic Reduction of Vasicine.*

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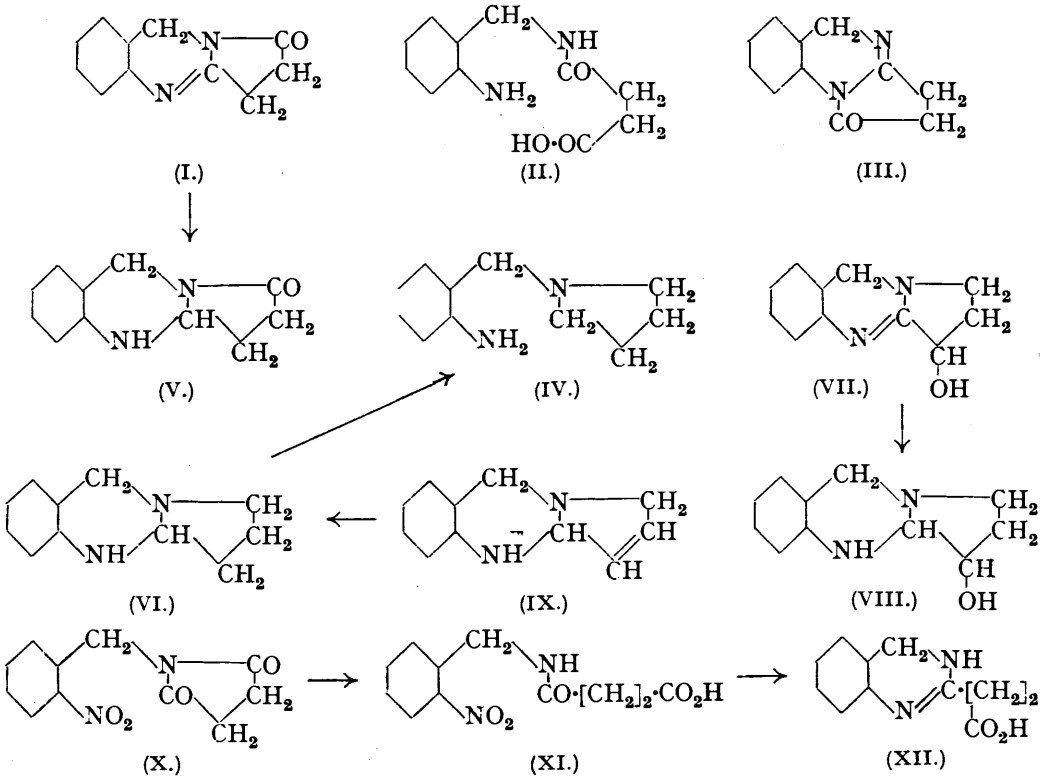
SPÄTH and PLATZER (*Ber.*, **1936**, **69**, 387) have been unable to support the following results and conclusions reached by Juneja and us (J., 1935, 1277):

(*a*) (I) on electrolytic reduction gave a base $C_{11}H_{16}N_2$, instead of $C_{11}H_{14}N_2$ found by us, which they consider to be 1-*o*-aminobenzylpyrrolidine (IV), m. p. 30—31°. Therefore the conclusion of Juneja, Narang, and Ray that vasicine (VII) has a linear cyclic formula is considered to be based on unsound experimental evidence.

(*b*) Juneja, Narang, and Ray obtained a substance (III) by the ring closure of the substance (II), whereas Späth and Platzer find that the substance (I) is formed, because a mixture of the two substances shows no lowering in m. p.



We have reinvestigated (*a*) and find that the electrolytic reduction of vasicine (VII) proceeds through four distinct stages: (1) reduction of N=C in the middle ring (V from I and VIII from VII); (2) formation of an unsaturated substance by the loss of water from the oxygenated part in the third ring (IX from VIII); (3) reduction of the unsaturation temporarily created in (2) to (VI); (4) disruption of the middle ring (IV).

In an experiment on the reduction of (I) as described (J., 1935, 1277), the time of reduction was diminished to 5 hours. After isolation in the usual manner the *base* (V), was obtained, m. p. 115° after crystallisation from light petroleum (Found: C, 70·2; H, 6·4. $C_{11}H_{12}ON_2$ requires C, 70·2; H, 6·4%). It contained no amino-group (shown by the diazo-reaction). Vasicine was similarly reduced for five hours and the *picrolonate* of the reduction product (VIII) was isolated; purified by recrystallisation from hot alcohol, it formed parallelepiped plates, m. p. 165—168° (decomp.) (Found: N, 19·6. $C_{11}H_{14}ON_2,2C_{10}H_8O_5N_4$ requires N, 19·5%). This substance also contained no diazotisable amino-group. Therefore, whether vasicine or (I) is reduced, the first addition of hydrogen takes place at N=C in the middle ring. Again, reduction of a sample of vasicine was continued for 8 hours and then interrupted for ½ hour; the current was re-established for 15 minutes, but inadvertently the poles were reversed. This error was rectified, and reduction carried on for another 2 hours. The *base* (IX) isolated was converted into its *picrolonate*, which formed needles, m. p. 224—228° (decomp.) after crystallisation from alcohol (Found: C, 57·7; H, 4·7; N, 19·0. $C_{11}H_{12}N_2,C_{10}H_8O_5N_4$ requires C, 57·8; H, 4·5; N, 19·2%). The base isolated from the picrolonate had m. p. 92° and crystallised from ligroin in needles (about 1 cm. long) (Found: N, 15·8. $C_{11}H_{12}N_2$ requires N, 16·2%); the available material was insufficient for recrystallisation.

The base from the picrolonate of (VI) (J., 1935, 1279) was isolated; it melted at *ca.* 65° without crystallisation [Spath and Platzer give m. p. 30—31° for the base (IV)]. After being submitted to the process of diazotisation it did not give an azo-colour with alkaline β-naphthol solution. The base was not sufficient in amount for recrystallisation and analysis. We considered it hardly necessary to analyse the base, as the full analysis of its picrolonate has already been recorded.

Lastly, in an experiment in which vasicine was reduced for 21 hours, we got a base which gave an unmistakable diazo-reaction but could not be satisfactorily purified. This was 1-*o*-aminobenzylpyrrolidine (IV) formed by disruption of the middle ring and probably is the substance isolated by Späth and Platzer. From the mother-liquor of the crystallisation of the picrolonate of (VI), there was occasionally deposited a small amount of a second substance of approximately the same m. p. (204—207°) but differing in crystalline form. This substance markedly depressed the m. p. of the picrolonate of (VI) and the base from it gave a diazo-reaction. A space model reveals some strain in the middle ring and it is conceivable that this opens during vigorous reduction.

The reduction of vasicine therefore proceeds through (VII) ⟶ (VIII) ⟶ (IX) ⟶ (VI) ⟶ (IV). We have now demonstrated the stages (VIII) and (IX). Späth and Platzer have shown the stage (IV). Therefore the reduction must have passed through the stage (VI), which we have already described and no purpose would be served in recapitulating the details. In all the experiments the reduction was carried out continuously for 8 hours, stopped for 12 hours, and then resumed for the requisite time. In the reduction of vasicine or (I), 15—16 hours was sufficient for the stage (VI). Lastly, by a different method from ours, Späth and Platzer prepared a picrolonate of (VI) for which they give m. p. 195—197°; we recorded m. p. 202°, but we now find that the m. p. depends on the rate of heating and is 195—197° with slow heating in a vacuum. This is sufficient confirmation of our statement that the product we described is (VI). The structure is not disproved because a further product is obtainable on more vigorous reduction. Thus the objection (*a*) is answered.

(*b*) We have again taken a mixed m. p. of our substance (III) and the substance (I) and find a depression of more than 60°; the mixture melts at 125—135°. The two products differ in solubility and in crystalline form, the one crystallising in long prismatic rods and the other in stellate clusters of minute needles. Moreover, the picrolonates of the electrolytic reduction product of (I) and of the reduction product of (III) crystallise in well-defined

rectangular plates and thick prisms respectively and a mixture of the two shows a considerable depression in m. p. We are certain that heating of *o*-aminobenzylsuccinamic acid (II) with sodium acetate results in the production of the angular cyclic product (III), as this is a strainless structure. Späth and Platzer have found that *o*-nitrobenzylsuccinamic acid on heating is converted into succino-*o*-nitrobenzylimide: this is no proof of the linear structure also being formed in the case of ring closure of (II).

A possible reason for Späth and Platzer's (I) and (III) being identical is this: since they isolate 3 : 4-dihydroquinazoline-2-β-propionic acid (XII) as a by-product, it is clear that this substance has been formed by ring-opening during reduction. The intermediate (XI) may undergo reduction to (II) and thence to (III), or (XII) itself may give (III) owing to the mobility of the amidine system. In this case the same product would be formed as in the ring closure of (II). The isolation of (XII) suggests that in the reduction Späth and Platzer may not have followed our conditions. We do not say that in every experiment this has happened, because their isolation of 1-*o*-aminobenzylpyrrolidine (IV) by electrolytic reduction indicates that the sample in that experiment at least had the linear structure (I), unless of course (I) in that case was prepared by their alternative method of cyclisation of succino-*o*-aminobenzylimide.

If it is admitted that the substance (I) is different from (III) in the manner we suggest, then one and the same product cannot be obtained from (III) and (I) by electrolytic reduction. Even if the ring opens in the case of (I) as Späth and Platzer find, to form 1-*o*-aminobenzylpyrrolidine (IV), it is difficult to see how this substance can be formed from (III) by ring opening. Therefore the whole of the argument of Späth and Platzer falls and no further comments on our part become necessary.

Späth and Platzer found the following discrepancies in melting points (ours are in parentheses): (1) succino-*o*-nitrobenzylimide, m. p. 133° (after two distillations in a high vacuum) (130°); (2) *o*-nitrobenzylsuccinamic acid, m. p. 123—124° (116°); (3) the substance (I), m.p. 191° (186°). In our hands, (1) gave the same m. p. as before, but (2) should be 126° instead of 116°. As regards (3), the substance which Späth and Platzer consider to be (I) is in reality (III), for which we get the m. p. 192°. The m.p.'s recorded by us are uncorrected.

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