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XXV.—The Oxidation of Aconitine.

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A PROMISING step towards the elucidation of the constitution of aconitine was made by Carr (T., 1912, 101, 2241), who described a product of oxidation, for which he suggested the formula C₂₃H₂₉O₉N and the name oxonitin. Brady (T., 1913, 103, 1821) obtained a very similar product, to which he gave the formula $C_{24}H_{29}O_9N$. The price of aconitine makes the yield a matter of importance; Brady obtained only 3 per cent. by oxidation in acid solution and 10-15 per cent. in (at first) neutral solution. Carr's yields were much higher, but variable; his process demands considerable attention to detail. Aconitine permanganate is prepared at 0°, and decomposed by 15 per cent. sulphuric acid at 20-40° in the course of a week or longer. Using Carr's method we generally obtained an amount of oxonitin corresponding with 65-70 per cent. of the theory, although Carr in one or two experiments obtained more than 90 per cent. We have now worked out a simple process by which the yield consistently approaches to the theoretical. The loss in the older experiments was partly due to hydrolysis, by the sulphuric acid employed, and we therefore oxidise by potassium permanganate in acetone solution, a method applied with great success by Leuchs to the oxidation of strychnine (Ber., 1908, 41, 1711), and also used by one of us in the case of carpaine (T., 1910, 97, 470). Since aconitine is, however, oxidised only very slowly in acetone solution, we add glacial acetic acid as the oxidation proceeds. The process then is as follows:

Five grams of aconitine are dissolved in 250 c.c. of pure acetone by warming on the water-bath. After cooling, 11 grams of very finely powdered potassium permanganate and 12.5 c.c. of glacial acetic acid are added in the course of five to seven days, each day about one-fifth of both reagents. The acetic acid may be conveniently diluted with acetone to a known volume. The oxidation proceeds at room temperature, and the oxonitin for the most part separates in large crystals on the sides of the flask. When all the permanganate has been reduced, the oxonitin and manganese dioxide are filtered off, washed with acetone, and suspended in water. On passing a current of sulphur dioxide an amount of oxonitin corresponding with 65 per cent. of the theory remains behind in a practically pure condition (melting at 274° without recrystallisation). The rest is obtained in a slightly impure condition by evaporating the acetone and adding water, and after recrystallisation yields an additional 25 per cent.; the total is therefore 90 per cent. of the

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theoretical. In order to purify the oxonitin for analysis it can be recrystallised (a) by dissolving in fuming hydrochloric acid and diluting with water, (b) by dissolving in a mixture of methyl alcohol and chloroform, and adding dry ether, and (c) by dissolving in boiling glacial acetic acid and adding acetone; we prefer the third method. The substance then separates in well-formed, stout prisms, melting at $276-277^{\circ}$ (bath previously heated to 260°).

Five specimens were analysed. I was prepared by Carr's method and recrystallised by method (c) above. The others were prepared by oxidation in acetone solution, III and IV being recrystallised from glacial acetic acid, II by method (b) and V by method (a). Specimen IV was prepared from japaconitine, and the identity of the oxidation product with that from aconitine itself, which identity had been established by Carr by means of the melting point and specific rotation, is now confirmed by analysis. (We found that IV melted at 277-278°):

I. 0.1270 gave 0.2821 CO₂ and 0.0746 H_2O . C=60.57; H=6.53. C = 60.48; H = 6.54. II. 0·1488 $0.33\overline{0}0 \text{ CO}_2$, $0.0874 \text{ H}_2\text{O}$. ,, 0.3038 CO_2 , $0.0844 \text{ H}_2\text{O}$. III. 0·1370 C = 60.48; H = 6.84. ,, 0.2662 CO_2 , $0.0728 \text{ H}_2\text{O}$. C = 60.50; H = 6.74.IV. 0.1200 ,, V. 0.1390 0.3108 CO_2 , $0.0794 \text{ H}_2\text{O}$. C = 61.0; H = 6.35. ,,

The mean of these results is C=60.60, H=6.60, or, excluding V, where the aberrant results may be due to recrystallisation from fuming hydrochloric acid, C=60.51, H=6.66. These figures agree fairly closely with those obtained by Brady (C=60.7; H=6.55), but not with those of Carr, who found considerably less carbon. On this account Brady considered his substance to be different from Carr's oxonitin. Our analysis for the oxidation product prepared by Carr's method (specimen I) is, however, in close agreement with the other analyses, and the rather characteristic melting point is identical in whatever way the substance is prepared. We consider, therefore, that the oxidation product is the same in all cases, and Mr. Carr has recently expressed to us his agreement with this view.

The determination of the methoxy-groups gave the following results:

0.2370 gave 0.3265 AgI. MeO=18.2. 0.1574 , 0.2256 AgI. MeO=18.8. (Brady found 18.2, Carr 19.3.)

The following formulæ may be considered:

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Of these the first is that of Brady, which does not agree perfectly as regards hydrogen; the second not as regards carbon; the other two not with respect to methoxyl; the third and fourth, moreover, do not agree well with Carr's determination of the acetyl and benzoyl groups, but cannot perhaps be wholly excluded at present.

On heating with fuming nitric acid, oxonitin yields the same oxidation product as aconitine itself, namely, the nitrosocarboxylic acid described by Brady. Of the various methods of degradation which we have tried, we consider the most hopeful to be that of heating with hydriodic acid and phosphorus. This would set free five hydroxyl groups and reduce some of them. 0.3 Gram of oxonitin was heated for five hours with 4 c.c. of hydriodic acid (D 1.96) and 0.3 gram of red phosphorus to 285°. The reaction mixture was diluted with water, treated with sulphur dioxide, and extracted with chloroform. On evaporation of the latter a liquid remained which crystallised on keeping. On recrystallisation from boiling alcohol prisms were obtained, melting at 121-122°, and boiling at about 200°/15 mm. The substance is reprecipitated from alcoholic solution by water, and the suspension is insoluble in acids or alkalis. We have not yet obtained enough for analysis, but the substance must be a relatively simple one.

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