CCXXXII.—*Strychnine and Brucine. Part XI. Note on Dihydrobrucine and Some Derivatives.*

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Skita and Franck (*Ber.*, 1911, **44**, 2863) studied the catalytic reduction of brucine, but it appears from their memoir that only one-half of the volume of hydrogen theoretically required was absorbed and the product can scarcely have been homogeneous—a conclusion confirmed by the description of dihydrobrucine as a substance that crystallises from ethyl acetate in small spherical clusters, m. p. 115°.

Wieland and Münster (*Annalen*, 1930, **480**, 39; footnote by Gumlich) have just published a further account of the hydrogenation of brucine in the presence of platinum oxide, and we therefore take the earliest opportunity to record our experiments in this field of work.

Dihydrobrucine, prepared with the aid of palladinised charcoal, crystallises from water with $4H_2O$ and from ethyl acetate with $1\cdot5CH_3\cdot CO_2Et$; it also exhibits a tendency to combine with and to retain other solvents, *e.g.*, methyl alcohol, benzene, and chloroform. This behaviour characterises many reduced brucine and brucidine derivatives, and is the frequent cause of difficulties in connexion with the analyses. Catalytic reduction of brucidine yielded *dihydrobrucidine*, and *hexahydrobrucine* has similarly been obtained from tetrahydrobrucine.

EXPERIMENTAL.

Dihydrobrucine, $C_{22}H_{28}O_3N(\dot{:}N{\cdot}CO{\cdot})$.—The conditions followed those employed for the reduction of strychnine (Part VI; J., 1927, 2393). A solution of palladous chloride (2 g.) in water (200 c.c.) and a few drops of hydrochloric acid was mixed with norite (25 g.), previously strongly heated and stirred with hydrogen until no more of the gas was absorbed; brucine (30 g.), dissolved in 50% acetic acid (120 c.c.), was then introduced and the rapid stirring continued.

Absorption ceased after 5 hours (1720 c.c. at 16° and 770 mm.) and the filtered liquid was then treated at 0° with an excess of 40% aqueous sodium hydroxide, giving a pale yellow gum which set to a hard cake. This was dissolved in boiling water and, on cooling, the solution deposited rhombs of the *tetrahydrate* (27 g.) (Found: C, 59·3; H, 7·7; N, 6·5; loss at 105° in a vacuum, 15·2. $C_{23}H_{28}O_4N_2,4H_2O$ requires C, 59·0; H, 7·7; N, 6·0; H_2O, 15·4%). The palladinised charcoal was reactivated by exposure to the air and was used eight times without serious loss of catalytic efficiency. In this experiment, the pressure of the hydrogen was maintained at 1·2 atms., but the ordinary pressures have also been used with equal success. An alternative isolation process depends on extraction of the solution, saturated with potassium carbonate, with chloroform. The substance also separates from aqueous methyl alcohol in large hard prisms of the tetrahydrate (Found: loss at 130°, 15·3%. Found in anhydrous material: C, 69·8; H, 7·4. $C_{23}H_{28}O_4N_2$ requires C, 69·7; H, 7·2%). The tetrahydrate melts at 70—72° and, on further heating, the anhydrous base crystallises at 130—140° and melts again at 179—181°. The base crystallises from ethyl acetate in very large, rhombic prisms, m. p. 48—50°, which effloresce rapidly in a vacuum and cannot be entirely freed from the mother-liquor by washing with ether or light petroleum without losing some of their transparency (Found: loss at 105° in a vacuum, 26·0. $C_{23}H_{28}O_4N_2,1{\cdot}5CH_3{\cdot}CO_2Et$ requires $CH_3{\cdot}CO_2Et$, 25·0%). *Dihydrobrucine* is readily soluble in most organic solvents, but it is sparingly soluble in benzene and in light petroleum; its colour reactions closely resemble those of brucine and it possesses an intensely bitter taste. Unlike brucine, it is not attacked by potassium permanganate in acetone solution.

The hydriodide crystallised from water in rods, softening at 250° and melting at 260—262°.

The *methosulphate* was obtained by ready combination of the components in benzene or methyl alcohol; it separated from water in colourless hexagonal tablets, m. p. 242—244° after sintering at 215° (Found in material dried over sulphuric acid: C, 53·9;

H, 7·1; N, 4·9. $C_{23}H_{28}O_4N_2,Me_2SO_4,2H_2O$ requires C, 53·8; H, 6·8; N, 5·0%).

The *methiodide*, prepared by the addition of sodium iodide to an aqueous solution of the methosulphate, crystallised from water in colourless double pyramids exhibiting a curious twinning tendency (Found in material dried over sulphuric acid: C, 51·7; H, 5·8; N, 4·8. $C_{24}H_{31}O_4N_2I,H_2O$ requires C, 51·8; H, 5·9; N, 5·0%). This specimen sintered at 245° and melted at 283—285° to a dark brown froth.

Direct combination of dihydrobrucine and methyl iodide gave a salt which crystallised from methyl alcohol in colourless needles, m. p. 242—245° (decomp.) (Found: C, 53·5; H, 5·9. $C_{24}H_{31}O_4N_2I$ requires C, 53·5; H, 5·8%). It is probable that a trace of impurity in one of these two specimens, the latter of which was examined some three years later than the former and in a different laboratory, accounts for the divergence in the melting points, but it should be noted that there is a theoretical possibility of stereoisomerism.

The picrate crystallised from alcohol in orange tablets and exploded on heating.

Bisapomethyldihydrobrucine was prepared from dihydrobrucine by following the method of Leuchs and Anderson (*Ber.*, 1911, **44**, 2136) for bisapomethylbrucine. The hydrochloride crystallised in pale yellow, rectangular prisms, and the base obtained by the action of potassium bicarbonate in aqueous solution separated as a colourless crystalline powder which did not melt at 320° (Found: N, 7·4. $C_{21}H_{24}O_4N_2$ requires N, 7·6%). The reactions of the substance resembled those of bisapomethylbrucine.

Dihydrobrucidine, $C_{22}H_{28}O_3N(\vdots N\cdot CH_2\cdot)$.—Brucidine (9 g.) was reduced in the manner described for brucine in 50% acetic acid solution, palladous chloride (1 g.) and activated norite (10 g.) being used; 600 c.c. of hydrogen at 20° and 759 mm. were absorbed (theoretical, 570 c.c.). Under atmospheric pressure, the reduction was very slow, but an 86% yield resulted when the base (5 g.) in dilute acetic acid (80 c.c. of 20%) was added to a catalyst suspension prepared from palladous chloride (0·3 g.), norite (1 g.), and water (250 c.c.) and agitated at 60—65° in hydrogen for 10 hours. In either case, the filtered solution was rendered strongly alkaline and extracted with chloroform, and the *dihydrobrucidine* was ultimately crystallised from acetone, forming pale yellow rods, pyramidal at one end, m. p. 172—172·5° (Found in material dried at 105° in a vacuum: C, 71·2; H, 7·6. $C_{23}H_{30}O_3N_2,C_3H_6O$ requires C, 70·9; H, 8·0%. Found in material dried at 130°: C, 72·6; H, 7·9. $C_{23}H_{32}O_3N_2$ requires C, 72·3; H, 7·8%). Even after crystallisation from light petroleum, the base, having once been in contact with acetone, retained this solvent tenaciously.

Addition of ferric chloride to a solution in very dilute hydrochloric acid produced the characteristic brucidine reaction, a coloration green in thick layers and pink in thin layers by transmitted light. Sodium nitrite added to an acid solution gave a deep green coloration, changing in less than a second to yellow; addition of sodium carbonate then produced a wine-red colour which was completely removed by extraction with chloroform.

The picrate crystallised from alcohol in long old-gold needles that exploded on heating. The hydriodide crystallised from water in stellate aggregates of diamond-shaped plates which softened at 230° and decomposed at 235—240°.

The *dimethosulphate*, prepared from the components in dry benzene solution on the steam-bath, crystallised from acetone (with 5% methyl alcohol) in colourless rods, m. p. 270° (Found in material dried at 105° in a vacuum: C, 50·8; H, 6·8; N, 4·0. $C_{23}H_{30}O_3N_2,2Me_2SO_4$ requires C, 51·1; H, 6·6; N, 4·4%).

Hexahydrobrucine, $C_{22}H_{28}O_3N(NH)(CH_2{\cdot}OH)$.—Tetrahydrobrucine (15 g.) in 50% acetic acid (100 c.c.) absorbed 900 c.c. of hydrogen (theoretical, 885 c.c.) in the presence of a catalyst prepared in the usual manner from palladous chloride (2 g.) and norite (25 g.). The colourless filtrate was rendered strongly alkaline by means of sodium hydroxide, and the precipitated base (13 g.) extracted in a Soxhlet apparatus with a mixture of benzene and light petroleum; it separated in the flask in a micro-crystalline condition, m. p. 131—133° (Found: loss at 120° in a vacuum, 3·0; C, 66·6; H, 8·0; N, 6·5. $C_{23}H_{32}O_4N_2$ with 3% of H_2O requires C, 67·0; H, 8·0; N, 6·8%). Further crystallisation did not affect the melting point. The ferric chloride reaction in faintly acid solution was green (not pink in thin layers), fading to yellow.

Electrolytic Reduction of Dihydrobrucine.—Dihydrobrucine (5 g.), dissolved in 20% sulphuric acid (150 c.c.), was reduced in the usual manner (compare Part II, J., 1924, **125**, 1798) at a lead cathode for 20 hours by a current of 5 amps. The solution was basified with ammonia (no precipitate), mixed with an excess of potassium carbonate, and extracted with chloroform. The gum thus isolated was dissolved in acetone and ultimately crystals, m. p. 170—172°, alone or mixed with dihydrobrucidine from the catalytic reduction of brucidine, were obtained (yield, 2 g.) (Found: C, 71·0; H, 7·7. $C_{23}H_{30}O_3N_2,C_3H_6O$ requires C, 70·9; H, 8·1%). The hexahydrobrucine doubtless formed in this experiment could not be purified.

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