

642. *The Melting Point and Structure of Tryptamine*

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TRYPTAMINE (I) has been accorded three different melting points in the literature: 145° ;¹ 101° ;² and by most authors a melting point in the range 114 — 118° .³⁻⁸ We now present evidence that the correct melting point is 118° , that the product of m. p. 145° is probably *N*-isopropylidenetryptamine, and that the product of m. p. 101° is probably impure tryptamine.

The product of m. p. 145° (hydrochloride m. p. 246° , picrate m. p. 242°) was obtained

¹ A. Ewins, *J.*, 1911, **99**, 270.

² G. R. Clemo, *J.*, 1936, 1695.

³ R. H. F. Manske, *Canad. J. Res.*, 1931, **5**, 592.

⁴ R. Majima and T. Hoshimo, *Ber.*, 1925, **58**, 2042.

⁵ J. Thesing and F. Schülde, *Chem. Ber.*, 1952, **85**, 324.

⁶ D. A. Lyttle and D. I. Weisblat, *J. Amer. Chem. Soc.*, 1955, **77**, 5747.

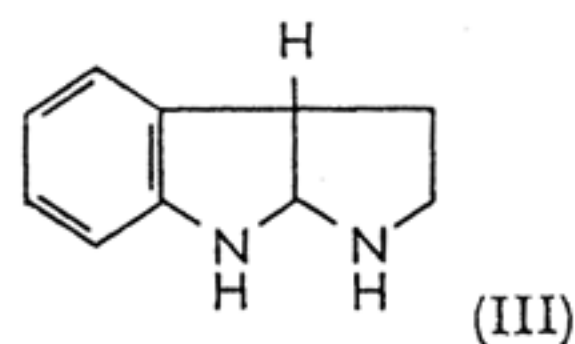
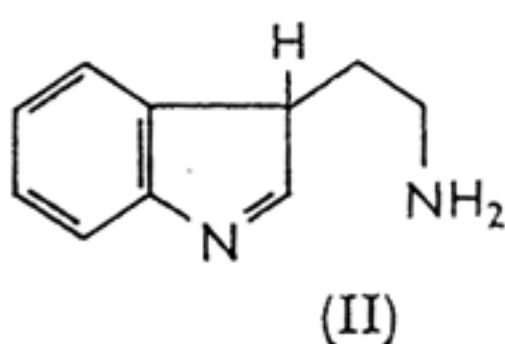
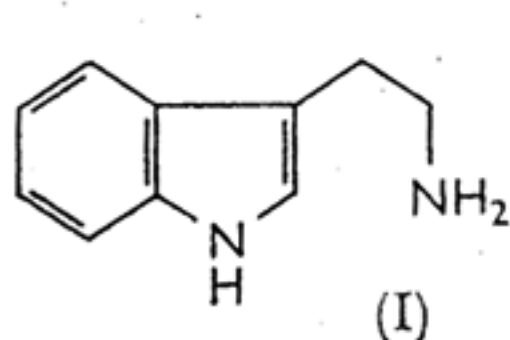
⁷ E. H. P. Young, *J.*, 1958, 3493.

⁸ M. E. Speeter and W. C. Anthony, *J. Amer. Chem. Soc.*, 1954, **76**, 6208.

by Ewins¹ in the earliest recorded synthesis of tryptamine, although when Manske³ later used the same method his product had m. p. 118° (hydrochloride m. p. 246°, picrate m. p. 242°).

In connection with other work,⁹ we have prepared tryptamine by two different methods,^{7,8} and our products had m. p. 118° after recrystallisation from light petroleum (b. p. 60—80°); however, if the products were recrystallised from acetone a substance of m. p. 146° was obtained. The infrared spectrum of this material was considerably different from that of the base with m. p. 118°, and in particular exhibited an intense peak at 6.02 μ (C=N) which suggested that it was *N*-isopropylidene-tryptamine. This was confirmed by elemental analysis and by its proton magnetic resonance spectrum. The hydrochloride (m. p. 248°) and the picrate (m. p. 244°) obtained from the latter were identical with the hydrochloride and picrate obtained from tryptamine, thus showing that the isopropylidene-tryptamine is readily hydrolysed as well as readily formed. In view of the closeness of the melting points we conclude that Ewin's product¹ was probably *N*-isopropylidene-tryptamine, and may have arisen from impurity in his solvents, or from attempts to recrystallise it from acetone; he reported crystallising his product of m. p. 145° from benzene, and also from ethanol, both of which we found satisfactory for *N*-isopropylidene-tryptamine but unsuitable for tryptamine, m. p. 118°, on account of its greater solubility.

The product of m. p. 101°² was obtained as an alkaline degradation product from strychnine, and was isolated initially as its red picrate "m. p. 253—254° (decomp.), after darkening from 245°." The base "(C)"² was prepared by regeneration from this picrate, and on crystallisation from ether gave "faintly brown prisms, m. p. 100—101°," or, after sublimation in a high vacuum at 180°, "colourless prisms, m. p. 101—102°." Metcalfe (see ref. 2) repeated Majima and Hoshimo's preparation⁴ of tryptamine and obtained, "after three recrystallisations from ether, a faintly brown poorly crystalline solid, m. p. 114°," mixed m. p. with the base (C) obtained from strychnine, 102—112°. The picrate of the base of m. p. 114° had the same crystalline form and decomposition point as the picrate of the base (C), and "furthermore, the base regenerated from the picrate formed prisms (from ether), m. p. 101°, unchanged by admixture with (C), and gives well-formed prisms, m. p. 101°, on sublimation."



Clemo suggested² that the base (C) might be the tautomeric indolenine form (II) of tryptamine. However, this now seems very unlikely as it would be expected to cyclise immediately to the tricyclic indoline (III) by analogy with similar cyclisations in the physostyminine series.¹⁰ In addition, spectroscopic studies^{9,11} (u.v. and p.m.r.) have shown that tryptamine exists entirely in the indolic form (I) in neutral solution, and that there is no evidence of the existence of any tautomeric forms.

We therefore reinvestigated formation of the picrate of tryptamine, and regeneration of the free base with alkali as described by Clemo. However, our picrate had m. p. 242°, in accord with all other authors' results,³⁻⁸ and on regeneration the free base had m. p. 110° (from ether). The infrared and ultraviolet spectra of this product were identical with those of the original tryptamine, m. p. 118°, and on recrystallisation from light petroleum the melting point was raised to 118°. We therefore conclude that Clemo's product, m. p.

⁹ A. H. Jackson and A. E. Smith, *J.*, 1964, 5510.

¹⁰ "Heterocyclic Compounds," Vol. III, ch. 1, ed. R. C. Elderfield, Wiley, New York.

¹¹ L. A. Cohen, J. W. Daly, H. King, and B. Witkop, *J. Amer. Chem. Soc.*, 1960, 82, 2184.

101°, was probably impure tryptamine, the low melting point being due to the use of a solvent (ether) which we have found is not satisfactory for the recrystallisation of tryptamine.

Experimental.—Tryptamine was prepared by reduction of 3-(2-nitrovinyl)indole,⁷ or 3-indolyglyoxylamide,⁸ and crystallised from light petroleum (b. p. 60—80°) to give needles, m. p. 118°. (It crystallised from ether as buff coloured prisms, m. p. 114°.) λ_{max} (ethanol) 222, 282, 290 m μ ; log ϵ 4.56, 3.78, 3.71. The hydrochloride formed minute needles, m. p. 248° (from ethanol-ethyl acetate), and the picrate crystallised from ethanol as red needles, m. p. 242° (unchanged even after prolonged heating in boiling ethanol). Treatment of this picrate with alkali as described by Clemo, gave a gum which was crystallised from ether and sublimed at 180°/0.01 mm., to give a product, m. p. 110°. The latter had ultraviolet and infrared spectra identical with those of the original tryptamine, and on recrystallisation from light petroleum (b. p. 60—80°) the m. p. was raised to 118°.

N-Isopropylidenetryptamine. Tryptamine (m. p. 118°) was recrystallised from acetone and gave *N-isopropylidenetryptamine* as rosettes of needles, m. p. 145—146° (Found: C, 77.9; H, 8.2; N, 13.2. $\text{C}_{13}\text{H}_{16}\text{N}_2$ requires C, 78.0; H, 8.1; N, 14.0%.) λ_{max} (m μ) (log ϵ) in ethanol: 222 (4.57), 282 (3.79), and 289 (3.71); ν_{max} (CHCl_3): 6.02 μ . The hydrochloride, m. p. 248°, and the picrate, m. p. 242°, prepared in ethanol were shown by mixed m. p. comparisons to be identical with the hydrochloride and picrate of tryptamine.
