74. *Studies in Relation to Biosynthesis. Part IX.* The Structure of Spherophysine.*

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N-*iso*Pent-2-enyltetramethylenediamine (II) has been synthesised. Oxidation with permanganate in acid solution followed by the action of hot dilute acid gives 3-methyl-2-oxobutyraldehyde (III). On the basis of these and published[3] results the structure (IV) is proposed for the alkaloid spherophysine.

The suggestion was made[1] that *iso*pentenyl groups are introduced as units into certain natural aromatic compounds during biosynthesis. Such introductions are formally analogous to the introductions of methyl groups into the skeletons of some natural acylphloroglucinol and chromone derivatives,[1, 2] and the mechanism may be similar. The widespread natural occurrence of both methyl and *iso*pentenyl groups attached to carbon and to oxygen, and of methyl groups attached to nitrogen, would lead to the expectation, if this hypothesis is correct, that some examples of natural substances with *iso*pentenyl groups attached to nitrogen would be found. The only natural substance reported to contain such a structure is the alkaloid galegine, $Me_2C{:}CH{\cdot}CH_2{\cdot}NH{\cdot}C({:}NH){\cdot}NH_2$.

Spherophysine, $C_{10}H_{22}N_4$, from *Sphaerophysa salsula* can be hydrogenated to a dihydro-derivative, and on alkaline hydrolysis the alkaloid and its dihydro-derivative give urea and amines $C_9H_{20}N_2$ and $C_9H_{22}N_2$ respectively. The last of these was shown[3] to be *iso*pentyltetramethylenediamine, $Me_2CH{\cdot}CH_2{\cdot}CH_2{\cdot}NH{\cdot}[CH_2]_4{\cdot}NH_2$, and the former must contain this skeleton with a double bond: structures (I) and (II) are the most likely alternatives. Rubinstein and Menshikov[3] considered that formula (I) was supported by oxidation with

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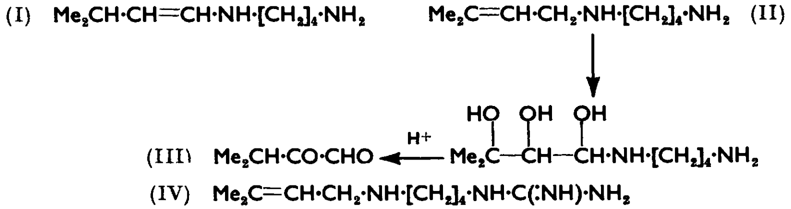
* Part VIII, *J.*, 1956, 3717.

[1] Birch, Elliott, and Penfold, *Austral. J. Chem.*, 1954, **7**, 169.

[2] Birch and Elliott, *ibid.*, 1956, **9**, 95; Jain and Seshadri, *Quart. Rev.*, 1956, **10**, 169.

[3] Rubinstein and Menshikov, *Zhur. obshchei Khim. S.S.S.R.*, 1944, **14**, 161.

permanganate in acidic solution to the aldehyde (III). However, an alternative route to this substance from the base (II) appeared to us more likely, the intermediate stage being as shown. There were two grounds for this belief: that the keto-aldehyde is only obtainable after *heating* in acid solution [3] and that neither spherophysine nor its hydrolysis product shows the acid-instability characteristic of vinylamines. They give rise, for example, to stable picrates and hydrochlorides. We have accordingly synthesised compound (II) by the action of *iso*pentenyl bromide on tetramethylenediamine (putrescine).



(I) $Me_2CH{\cdot}CH{=}CH{\cdot}NH{\cdot}[CH_2]_4{\cdot}NH_2$

(II) $Me_2C{=}CH{\cdot}CH_2{\cdot}NH{\cdot}[CH_2]_4{\cdot}NH_2$

$$Me_2C(OH){-}CH(OH){-}CH(OH){\cdot}NH{\cdot}[CH_2]_4{\cdot}NH_2 \xrightarrow{H^+} Me_2CH{\cdot}CO{\cdot}CHO \text{ (III)}$$

(IV) $Me_2C{=}CH{\cdot}CH_2{\cdot}NH{\cdot}[CH_2]_4{\cdot}NH{\cdot}C({:}NH){\cdot}NH_2$

	*iso*Pentenyltetramethylenediamine	Hydrolysis product
B. p.:	117—120° (bath)/13 mm.	105—106°/10 mm.
Picrate:	M. p. 174—178° *	M. p. 180—181°
Dihydrochloride:	M. p. 254—256° *	M. p. 262° (decomp.)

* The Russian authors do not state whether their m. p. are corrected; ours are not.

We were not able to procure authentic natural specimens for comparison, but the only real evidence which appeared to support structure (I) rather than (II) was destroyed by showing that the synthetic product (II), on oxidation under the described conditions, gave rise to the α-keto-aldehyde (III). The postulated oxidation α to the nitrogen which is necessary to explain this result is known with tertiary amines [4] and there seems no reason why it should not also occur with secondary amines. Spherophysine is therefore represented by (IV).

The alkaloid smirnovine from *Smirnovia turkestana* [5] is a malonamide derivative of spherophysine. These two substances are further members of the natural *iso*pentenylamine series, and are probably derived by substitution and decarboxylation of ornithine. The natural occurrence of three compounds containing such a group gives some support to the original biosynthetic hypothesis.

EXPERIMENTAL

N-iso*Pent-2-enyltetramethylenediamine.*—A mixture of *iso*pent-2-enyl bromide (5·9 g.) and tetramethylenediamine (3·5 g.) in methanol (40 ml.) was left for 12 hr., refluxed for 2 hr., and then acidified with dilute hydrochloric acid. Most of the solvent was removed and the residue taken up in a little water. 40% Aqueous potassium hydroxide in considerable excess was added and the product extracted several times with ether. Several distillations gave some tetramethylenediamine, followed by N-iso*pent-2-enyltetramethylenediamine* (0·42 g.), b. p. 117—120°/13 mm. The *picrate* had m. p. 174—178° (from ethanol) (Found: C, 41·2; H, 4·65. $C_{15}H_{23}O_6N_5$ requires C, 41·0; H, 4·2%), and the *dihydrochloride* m. p. 254—256° after crystallisation from ethanol (Found: N, 12·8; Cl, 31·4. $C_9H_{22}N_2Cl_2$ requires N, 12·2; Cl, 31·0%).

Oxidation [3] and steam-distillation of the acid solution and saturation of the distillate with ammonium sulphate gave colourless needles. This material was taken up in a little ether and sublimed in the form of very long needles, m. p. 94—96° alone or mixed with 3-methyl-2-oxobutyraldehyde,[6] m. p. 94—96°.

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[4] Wenkert, *Experientia*, 1954, **10**, 346.

[5] Ryabinia and Ilina, *Doklady Akad. Nauk S.S.S.R.*, 1951, **76**, 851.

[6] Dakin and Dudley, *J.*, 1914, **105**, 2458.