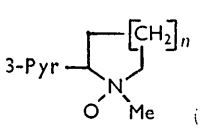
311. *Thermal Rearrangement of Nicotine 1′-Oxide and Related Compounds*

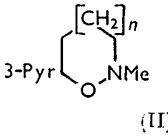
By W. Carruthers and R. A. W. Johnstone

Nicotine oxide, dihydronicotyrine oxide, 1′-methylanabasine oxide, and the oxide of 1-methyl-2-phenylhexahydroazepine (VI; R^1 = Ph, R^2 = H), on heating, rearrange to products in which the oxygen is contained in the ring. With the azepine oxide, an unsaturated hydroxylamine is also produced. The rearrangement of nicotine oxide takes place, to some extent at least, by an intramolecular concerted mechanism.

When nicotine 1′-oxide (I; $n = 1$) is heated at 200°, it rearranges to the tetrahydro-oxazine (II; $n = 1$),[1,2] and does not undergo Cope elimination [3] to form an unsaturated hydroxylamine. A number of other 2-aryl-1-methylpyrrolidine oxides behave similarly.[4] These reactions are analogous to the rearrangement of *N*-allyl- and *N*-benzyl-amine oxides to *O*-allyl- and *O*-benzyl-hydroxylamines, discovered by Meisenheimer [5] and studied by Cope and his collaborators [6] and by Wragg, Stevens, and Ostle.[7] These authors have shown that this rearrangement is an intramolecular process similar to the rearrangement of phenacylammonium salts. We have obtained evidence that the rearrangement of nicotine oxide also is probably intramolecular, and have found that similar rearrangement occurs with the analogous six- and seven-membered ring compound (I; $n = 2, 3$), and the oxide of (VI; R^1 = Ph, R^2 = H).

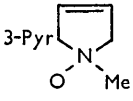


(I)

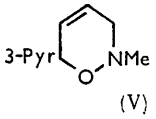


(II)

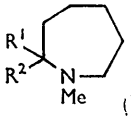
3-Pyr·CH(OH)·[CH$_2$]$_3$·NHMe (III)



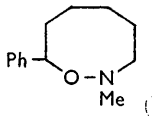
(IV)



(V)



(VI)

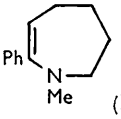


(VII)

Ph·CO·[CH$_2$]$_5$·NHMe (VIII)

Ph·CH=CH·[CH$_2$]$_4$·NMeOH (IX)

CH$_2$=CH·[CH$_2$]$_4$·NMeOH (X)



(XI)

[3-Pyr = 3-pyridyl]

Oxidation of *l*-nicotine with hydrogen peroxide afforded a crystalline dextrorotatory oxide (compare ref. 2) which, as reported,[1,2] formed the optically active oxazine (II; $n = 1$) when pyrolysed at 200°, as well as a small amount of nicotine. The oxazine, on reduction with zinc dust and acetic acid,[1,2] gave the lævorotatory amino-alcohol (III). [The optical activity of the oxazine and its conversion into the optically active alcohol (III) were reported [2] after the present work had been completed. The optical rotations of our products were significantly higher.] By treatment with thionyl chloride in pyridine, the alcohol (III) was reconverted into lævorotatory nicotine of about 25% optical purity, presumably by way of the chloride (III; Cl for OH). Reduction of the oxazine to the alcohol would not be expected to affect the asymmetric centre, but formation of chlorides

[1] C. H. Rayburn, W. R. Harlan, and H. R. Hanmer, *J. Amer. Chem. Soc.*, 1950, **72**, 1721.
[2] T. Kisaki, M. Ihida, and E. Tamaki, *Bull. Agric. Chem. Soc. Japan*, 1960, **24**, 719.
[3] Cf. A. C. Cope and E. R. Trumbull, *Org. Reactions*, 1960, **11**, 317.
[4] L. D. Quin and G. L. Roof, *J. Org. Chem.*, 1962, **27**, 4451.
[5] J. Meisenheimer, *Ber.*, 1919, **52**, 1667; J. Meisenheimer, H. Greeske, and A. Willmersdorf, *ibid.*, 1922, **55**, 513.
[6] R. F. Kleinschmidt and A. C. Cope, *J. Amer. Chem. Soc.*, 1944, **66**, 1929; A. C. Cope and P. H. Tewle, *ibid.*, 1949, **71**, 3423; A. C. Cope, T. T. Foster, and P. H. Towle, *ibid.*, 3929.
[7] A. H. Wragg, T. S. Stevens, and D. M. Ostle, *J.*, 1958, 4057.

from alcohols, under the conditions used, is known to proceed predominantly with inversion,[8] and it is reasonable to assume a second inversion during ring-closure of the intermediary chloride (III; Cl for OH) to nicotine. The sequence indicates, therefore, that the tetrahydro-oxazine (II; $n = 1$) has predominantly the same configuration as the nicotine from which it was derived. It is uncertain whether the loss of optical purity took place during formation of the oxazine from nicotine oxide, or in its subsequent reconversion to nicotine, but it may be significant that the rotation of the alcohol (III) is similar to that of the analogous series Ph·CHOH·R,[9] suggesting that the alcohol, and thus the oxazine, has a high degree of optical purity. Some loss of activity during formation of the chloride would not be unusual.[8] It is clear, however, that the rearrangement of the oxide to the oxazine takes place with at least 25% retention of configuration, and, to that extent at least, the reaction probably proceeds by a concerted intramolecular mechanism without inversion (S_Ni). In this, it resembles the Meisenheimer rearrangement,[6] the Stevens rearrangement of quaternary ammonium salts,[10] and other reactions (cf. ref. 8, p. 523, *et seq.*).

On further heating to 290°, the oxazine (II; $n = 1$) gives back optically inactive nicotine.[1] Preliminary experiments indicate a zero-order free-radical mechanism for this reaction.[11]

It has been suggested [12] that myosmine in tobacco smoke may be produced by pyrolysis of nicotine oxide in the tobacco. This view is not supported by the present work for myosmine was detected among the pyrolysis products of nicotine oxide.

It appears to be an important condition of the Meisenheimer rearrangement that the migrating group be able to delocalise electronic charge, as with the benzylic or allylic group [6,7] (see also ref. 4). In dihydronicotyrine 1′-oxide (IV), the α-carbon atom is both benzylic and allylic, and this compound rearranged easily to the dihydro-oxazine (V), even on attempted chromatography on alumina. The structure of the product (V) was confirmed by catalytic hydrogenation to the tetrahydro-oxazine (II; $n = 1$).

All the cyclic oxides which have been shown to undergo this rearrangement have been five-membered, and it seemed of interest to extend the reaction to the six- and seven-membered series. 1′-Methylanabasine 1′-oxide (I; $n = 2$), on pyrolysis under reduced pressure, behaved similarly to nicotine oxide, and gave a mixture from which 1′-methylanabasine and the tetrahydro-oxazepine (II; $n = 2$) were isolated by paper chromatography. The yield of the ring-enlarged product was somewhat lower than with nicotine oxide, and more tertiary base was recovered (see the Table).

Ratio of products formed in pyrolysis of oxides

Base	Nicotine	Dihydro-nicotyrine	1′-Methyl-anabasine	Azepine derivative (VI) *
Ring-enlarged product	92	87	71	38
Recovered base	8	13	29	62

* 24% of the product of this reaction was the unsaturated hydroxylamine derivative (IX).

The oxazepine (II; $n = 2$) was identified by reduction with zinc and acetic acid to an amino-alcohol which had a very similar infrared spectrum to that of the alcohol (III), and by the regeneration of 1′-methylanabasine on pyrolysis at 290—300°. Pyrolysis of 1-methylpiperidine oxide, or of 1,2-dimethylpiperidine oxide, did not afford [13] any ring-enlarged product analogous to (II; $n = 2$), in line with the view that only such groups as benzylic or allylic groups will migrate.

In the seven-membered series, we used the oxide of phenylhexahydroazepine (VI; $R^1 = Ph$, $R^2 = H$) because of the convenience of synthesis. Pyrolysis of the oxide

[8] Cf. C. K. Ingold, " Structure and Mechanism in Organic Chemistry," Bell, London, 1953, p. 392.
[9] R. H. Pickard and J. Kenyon, *J.*, 1911, 45.
[10] R. A. W. Johnstone and T. S. Stevens, *J.*, 1955, 4487.
[11] R. A. W. Johnstone and P. M. Quan, unpublished work.
[12] E. Wenkert, *Experientia*, 1954, **10**, 346.
[13] A. C. Cope and N. A. Le Bel, *J. Amer. Chem. Soc.*, 1960, **82**, 4656.

proceeded smoothly, and gave a mixture of three products which were separated by chromatography on alumina. The main fraction (see the Table) was the hexahydroazepine (VI; R^1 = Ph, R^2 = H), formed presumably by simple deoxygenation. Small amounts of tertiary amine are commonly recovered from pyrolysis of amine oxides (ref. 3, p. 370), but it is noteworthy that the extent of this reaction is considerably higher in the seven- than in the five- and six-membered series. The other two products, formed in approximately equal amounts, were isomeric with the oxide. One of them is regarded as the ring-enlarged compound (VII), for, on reduction with zinc and acetic acid, it gave an amino-alcohol identical with the product obtained from the ketone (VIII) with sodium borohydride. The infrared spectrum had no absorption in the 3000—4000 cm.$^{-1}$ region and no carbonyl absorption, but it did show a moderately strong peak at about 940 cm.$^{-1}$, absent in the reduction product, which, following Quin and Roof,[4] may be characteristic of the –N–O bond. The perhydro-oxazocine (VII), like the compounds (II; n = 1,2), loses its oxygen atom when heated at 290—300°, but in this case the product obtained was isomeric, but not identical, with the azepine (VI; R^1 = Ph, R^2 = H); because of scarcity of material, it has not yet been identified.

The third product of the reaction had a typical styrene-type ultraviolet spectrum, and is probably the unsaturated hydroxylamine (IX) formed by a straightforward Cope elimination reaction.[3] It showed infrared bands at 3300 (bonded OH) and at 960 cm.$^{-1}$ (*trans* double bond), and gave a red colour with alkaline triphenyltetrazolium chloride, a reaction reported to be specific for *N*-substituted hydroxylamines.[14] Pyrolysis of the oxide of 1-methylhexahydroazepine itself (VI; R^1 = R^2 = H) is reported [13] to give a high yield of the unsaturated hydroxylamine (X). With the oxide of the phenyl derivative (VI; R^1 = Ph, R^2 = H), the principal reaction is deoxygenation, and the seven-membered ring is apparently sufficiently flexible to allow attack of the oxygen on a β-hydrogen atom to compete effectively with the migration of the benzyl group from nitrogen to oxygen. The elimination reaction may be facilitated by conjugation of the incipient double bond in the transition state [3] with the benzene ring, and it is of interest in this connection that none of the alternative product, formed by attack of the oxide group on a hydrogen atom of the other β-carbon, was detected. Cope and Trumbull [3] have recorded a number of other instances where elimination reactions of *N*-oxides compete with migration of allyl or benzyl groups. In the five- and six-membered series, the elimination reaction is thought to be precluded by the geometrical difficulty of forming the necessary planar five-membered cyclic transition-state.[3,13]

For the preparation of the hexahydroazepine (VI; R^1 = Ph, R^2 = H), phenylmagnesium bromide was condensed with *N*-methylcaprolactam, and the mixture of ketone (VIII) and enamine (XI) obtained was converted wholly into the enamine with toluene-*p*-sulphonic acid in boiling xylene; the azepine was obtained by hydrogenation over palladium. A by-product of the Grignard reaction was the crystalline diphenylhexahydroazepine (VI; R^1 = R^2 = Ph), identified by means of its elemental analysis and ultraviolet spectrum, and by oxidation to benzophenone with chromium trioxide in acetic acid. Products of similar type were obtained by Lukeš and Smolek [15] from reaction of alkylmagnesium halides with *N*-methylcaprolactam and other lactams, but they were evidently mistaken in supposing that such products are not formed with aryl Grignard reagents.

Experimental

Melting points were determined on a Kofler hot-stage apparatus. Ultraviolet (u.v.) spectra refer to solutions in 95% ethanol. Light petroleum is the fraction of b. p. 60—80°, unless otherwise stated. Paper chromatography was by the descending technique, using Whatman No. 1 paper and butan-1-ol–water–acetic acid (4 : 5 : 1) as solvent.

[14] G. A. Snow, *J.*, 1954, 2588; M. A. T. Rogers, *ibid.*, 1955, 769.
[15] R. Lukeš and K. Smolek, *Coll. Czech. Chem. Comm.*, 1939, **11**, 506.

Pyrolysis of Nicotine 1'-Oxide.—Crystalline nicotine 1'-oxide, m. p. 183—184° (from benzene), $[\alpha]_D$ +73·4° (*c* 0·81 in ethanol) was obtained from nicotine and 10% hydrogen peroxide as described by Kisaki, Ihida, and Tamaki.[2] When the oxide was heated at 20 mm., a colourless liquid distilled at 155—160°. Heating was continued for 15 min.; there was only a small amount of residue. The oxazine was purified by crystallisation of its hydrochloride from ethanol [2] or by paper chromatography, and was obtained as a colourless oil, b. p. 120°/1·2 mm., $[\alpha]_D$ −29° (*c* 8·5 in ethanol). The nicotine produced, which ran more slowly in the chromatogram, was partly racemised, $[\alpha]_D$ −41° (lit.,[16] −169°). Refluxing the oxazine for 30 min. gave a high yield of (±)-nicotine, identified by its infrared (i.r.) spectrum and by mixed m. p. of the picrate.

Cyclisation of 1-(3'-Pyridyl)-1-hydroxy-4-methylaminobutane.—The above oxazine (800 mg.) was reduced with zinc dust (1 g.) in acetic acid (10%; 10 ml.), as described.[1,2] The amino-alcohol was obtained as an oil, b. p. 155—160°/2 mm., $[\alpha]_D$ −15° (*c* 5·5 in ethanol).

The amino-alcohol (600 mg.), thionyl chloride (600 mg.), and dry pyridine (2 c.c.) were mixed at 0° and allowed to stand at room temperature for 18 hr. The mixture was poured into water, made alkaline with sodium hydroxide, and extracted with ether. The ether was evaporated off, and the residue distilled to give nicotine $[\alpha]_D$ −51° (*c* 17·1 in ethanol), identified by its i.r. spectrum and by mixed m. p. of the picrate.

2-Methyl-7-(3'-pyridyl)perhydro-1,2-oxazepine (II; $n = 2$).—(−)-1'-Methylanabasine, $[\alpha]_D$ −41° (lit.,[16] −85°), was treated with hydrogen peroxide as for the preparation of nicotine 1'-oxide. The resulting viscous oil was extracted with chloroform and dried *in vacuo* over sulphuric acid. This crude oil, $[\alpha]_D$ +17° (*c* 19·9 in ethanol), was heated at 15 mm. to 190—200° (air-bath), when a vigorous reaction set in. The yellow distillate was separated by paper chromatography into (i) a colourless liquid, b. p. 90°/0·9 mm. (air-bath temp.), identified as 1'-methylanabasine by its i.r. spectrum and by the picrate, m. p. and mixed m. p. 244—246°, and (ii) the *oxazepine*, a colourless liquid, b. p. 115°/0·9 mm. (air-bath temp.) (Found: C, 69·1; H, 8·5; N, 14·3. $C_{11}H_{16}N_2O$ requires C, 68·7; H, 8·4; N, 14·6%); there was no observable rotation. For yields, see the Table. The *dipicrate* had m. p. 163—165° (from ethanol) (Found: C, 42·7; H, 3·7; N, 17·5. $C_{23}H_{22}N_8O_{15}$ requires C, 42·5; H, 3·4; N, 17·2%). On heating to 290—295° for 1½ hr., the oxazepine yielded 1'-methylanabasine, identified by its i.r. spectrum and mixed m. p. of the picrate.

1-(3'-Pyridyl)-1-hydroxy-5-methylaminopentane.—The foregoing perhydro-oxazepine (20 mg.) was dissolved in the minimum amount of dilute hydrochloride acid; 10% acetic acid (15 ml.) was added and then zinc dust (500 mg.), in portions, to the stirred solution. After 6 hr., the solution was made alkaline and extracted with ether. The *amino-alcohol* was obtained as a colourless oil, b. p. 175°/0·8 mm. (air-bath temp.) (Found: C, 68·4; H, 9·0; N, 14·2. $C_{11}H_{18}N_2O$ requires C, 68·0; H, 9·3; N, 14·4%).

Pyrolysis of Dihydronicotyrine Oxide.—The oxide was prepared by reaction of dihydronicotyrine with 6% hydrogen peroxide for 2 days, as described for nicotine oxide. The crude product was heated at 20 mm. At about 130°, a vigorous reaction set in, and the temperature of the bath was gradually raised to 170°. The distillate was purified by paper chromatography, and the *dihydro-oxazine* (V) was obtained as a colourless oil, b. p. 138°/12 mm. (air-bath temp.) (Found: C, 68·2; H, 6·8; N, 16·2. $C_{10}H_{12}N_2O$ requires C, 68·2; H, 6·9; N, 15·9%), $\lambda_{max.}$ (257), 262, (268) mμ [log ε (3·46), 3·5, (3·42)]. The *dipicrate* had m. p. 139—141° (from ethanol) (Found: C, 41·4; H, 2·9; N, 17·5. $C_{22}H_{18}N_8O_{15}$ requires C, 41·6; H, 2·8; N, 17·7%).

In another experiment, the crude semi-solid *N*-oxide was chromatographed on neutral alumina (Grade I). Elution with ether–light petroleum (b. p. 40—60°) (19 : 1) afforded a mobile oil having an i.r. spectrum identical with that of the dihydro-oxazine (V).

Hydrogenation of the dihydro-oxazine, in ethanol, with platinum led to uptake of 1 mol. hydrogen and formation of the tetrahydro-oxazine (II; $n = 1$), identified by its i.r. spectrum and the dipicrate, m. p. and mixed m. p. 192—193°.

Reaction of Phenylmagnesium Bromide with N-Methylcaprolactam.—In a typical experiment, a solution prepared from bromobenzene (25 g.) and magnesium (3·8 g.) in ether (200 ml.) was added to a stirred solution of *N*-methylcaprolactam (17 g.) in ether (100 ml.) at room temperature. The mixture was boiled for 2 hr., cooled, and decomposed with cold dilute hydrochloric acid. A solution of the recovered product (strong carbonyl absorption in i.r. spectrum) and toluene-*p*-sulphonic acid (0·5 g.) in xylene was boiled for 6 hr. with azeotropic removal of water.

[16] R. H. F. Manske and H. L. Holmes (ed.), "The Alkaloids," Academic Press Inc., New York, 1950, Vol. I, p. 235.

The *enamine* was obtained as a colourless oil, b. p. 150—160°/20 mm. (Found: C, 82·9; H, 9·1; N, 7·7. $C_{13}H_{17}N$ requires C, 83·4; H, 9·2; N, 7·5%), $\nu_{max.}$ 1680 cm.$^{-1}$. A later fraction, b. p. 200—210°/20 mm., crystallised in the receiver. After purification by chromatography on alumina, *1-methyl-2,2-diphenylperhydroazepine* (VI; $R^1 = R^2 = Ph$) was obtained as needles, m. p. 84—85° (from cyclohexane) (Found: C, 86·3; H, 8·8; N, 5·3. $C_{19}H_{23}N$ requires C, 86·0; H, 8·7; N, 5·3%), $\lambda_{max.}$ 250 mμ (log ε 3·45). The *picrate* formed yellow needles in ethanol, m. p. 151—152° (Found: C, 60·5; H, 5·3; N, 11·0. $C_{25}H_{26}N_4O_7$ requires C, 60·7; H, 5·3; N, 11·3%). Oxidation of the perhydroazepine (200 mg.) with chromium trioxide (300 mg.) in acetic acid (5 ml.) on the water-bath for 1 hr. gave benzophenone (40 mg.), m. p. and mixed m. p. 42—45° (2,4-dinitrophenylhydrazone, m. p. and mixed m. p. 235—237°, i.r. spectrum identical with that of the authentic compound).

An attempt to prepare the picrate of the enamine in ethanol led to hydrolysis with formation of the *picrate* of ω-benzoyl-*N*-methylpentylamine, yellow needles, m. p. 128—131° (from ethanol) (Found: C, 52·7; H, 4·8. $C_{19}H_{22}N_4O_8$ requires C, 52·5; H, 5·1%). The free base, recovered from the picrate, had b. p. 110°/0·2 mm., but the nuclear magnetic resonance spectrum and elemental analysis showed that distillation was accompanied by some dehydration.

Reduction of the benzoyl-*N*-methylpentylamine (600 mg.), prepared from the crude Grignard product and dilute hydrochloric acid on the water-bath, with sodium borohydride (600 mg.) in methanol for 1 hr., gave *6-hydroxy-6-phenyl-N-methylhexylamine* as a colourless oil, b. p. 130—140°/0·5 mm. (air-bath temp.) (Found: C, 74·7; H, 10·6; N, 7·0. $C_{13}H_{21}NO$ requires C, 75·3; H, 10·2; N, 6·8%), $\nu_{max.}$ 3300 cm.$^{-1}$ (broad).

1-Methyl-2-phenylperhydroazepine (VI; $R^1 = Ph$, $R^2 = H$).—The enamine described above (13·5 g.) was hydrogenated over palladised charcoal in methanol solution. Hydrogen was rapidly absorbed, and the product was purified by chromatography on alumina. Elution with light petroleum–benzene (4 : 1) gave the *perhydroazepine* (10·3 g.) as a colourless oil, b. p. 120°/6 mm. (Found: C, 82·4; H, 9·8; N, 7·7. $C_{13}H_{19}N$ requires C, 82·5; H, 10·1; N, 7·4%) Curiously, the compound showed no selective absorption in the u.v. region [log ε (220 mμ) 3·57; (230 mμ) 2·90]. Oxidation with 25% nitric acid at 160—170° for 16 hr. gave benzoic acid, m. p. and mixed m. p. 118—120°. The proton magnetic resonance spectrum of the perhydroazepine showed 5 aromatic protons (τ 2·5—2·9), 1 proton in the group Ar–CH–N (τ 6·67, triplet), 2 $-CH_2-N$ protons (τ 7·1), 3 protons in an $N-CH_3$ group (τ 7·8), and 8 $-CH_2$ protons (τ 7·95—8·65). The *picrate* formed yellow prisms, m. p. 143—145° (from methanol–benzene) (Found: C, 54·5; H, 5·3; N, 13·3. $C_{19}H_{22}N_4O_7$ requires C, 54·5; H, 5·3; N, 13·4%).

Pyrolysis of 1-Methyl-2-phenylperhydroazepine Oxide.—The oxide was prepared by stirring a mixture of the tertiary base (12·0 g.) and 30% hydrogen peroxide (50 ml.) for 3 days. The excess of peroxide was decomposed with manganese dioxide, and the mixture was diluted with water (50 ml.) and extracted with benzene to remove unchanged base (3·3 g.). The oxide was obtained as a brown syrup by concentration of the aqueous solution under reduced pressure, and azeotropic removal of final traces of water with benzene. The *picrate* gave yellow prisms in methanol, m. p. 147—152°, depressed to 120—140° when mixed with the picrate of the tertiary base (Found: C, 52·8; H, 4·8; N, 12·8. $C_{19}H_{22}N_4O_8$ requires C, 52·5; H, 5·1; N, 12·9%).

The syrupy oxide (4·0 g.) was heated at 0·6 mm. in an oil-bath. Colourless liquid began to distil from the black melt at about 110°; the temperature was gradually raised to 180°, when distillation had practically ceased. Gas–liquid-chromatographic analysis of the distillate (1·86 g.) showed the presence of three products in the proportions shown in the Table.

Chromatography on Woelm acid-washed alumina, and elution with light petroleum, gave the *hexahydro-oxazocine* (VII) (350 mg.) as a colourless oil, b. p. 110°/1 mm. (air-bath temp.) (Found: C, 76·2; H, 9·3; N, 7·1. $C_{13}H_{19}NO$ requires C, 76·1; H, 9·3; N, 6·8%), $\lambda_{max.}$ (250), 253, 259, 265 mμ [log ε (1·88), 2·09, 2·20, 2·03]. The picrate was oily. Continued elution gave mixtures, and then the perhydroazepine, identified by its gas–liquid chromatographic retention time and by its i.r. spectrum. The picrate, after one crystallisation, formed yellow prisms or needles, m. p. and mixed m. p. 146—147°. The third fraction was eluted from the column with ether, and a further quantity (240 mg.) was distilled from the residue of the original distillation, at 220°/1·5 mm. Redistillation at 150°/1 mm. (air-bath) gave the *hydroxylamine* (IX) as a pale yellow oil which rapidly became discoloured in the air (Found: C, 76·45; H, 8·9; N, 7·0. $C_{13}H_{19}NO$ requires C, 76·05; H, 9·3; N, 6·8%), $\lambda_{max.}$ 250, 284, 294 mμ [log ε 4·02, 3·31, 2·75].

Reduction and Pyrolysis of 2-Methyl-8-phenylhexahydro-oxazocine.—The oxazocine (60 mg.) was dissolved in acetic acid (10%; 3 ml.) containing a few drops of hydrochloric acid, and zinc

dust (150 mg.) was added gradually to the stirred solution. The *amino-alcohol* (43 mg.) was extracted from the basified solution with ether, and distilled at 150—160°/0·5 mm. (air-bath) (Found: C, 75·6; H, 10·2; N, 6·9. $C_{13}H_{21}NO$ requires C, 75·3; H, 10·2; N, 6·8%). The i.r. spectrum showed strong absorption in the 3000—3300 $cm.^{-1}$ region, and was superimposable on that of 6-hydroxy-6-phenyl-*N*-methylhexylamine described above.

The oxazocine (30 mg.) was heated at 290—300° in a sealed tube under nitrogen for 40 min. The crude product showed only one main peak on gas–liquid-chromatographic analysis, with retention time intermediate between those of the oxazocine and the azepine. It was distilled as a colourless oil, b. p. 130°/0·5 mm. (air-bath temp.) (Found: C, 82·6; H, 9·8; N, 7·5. Calc. for $C_{13}H_{19}N$: C, 82·5; H, 10·1; N, 7·4%), $\lambda_{max.}$ 250—255, (286), 294 mμ [log ε 2·97, (2·09), 1·91]. The i.r. spectrum was different from that of the azepine.

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