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Necrosamine Series. IV.* Preparation of 2-Methyl-3-hexahydrophthalimido-4-aminononadecane

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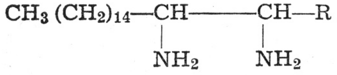
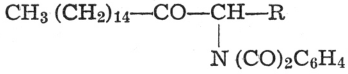
In a recent paper[1] we have described the synthesis of racemic 2-methyl-3, 4-diaminononadecane (Ia) and of 4,5-diaminoeicosane (Ib), where also a survey of the literature on necrosamine is to be found. The reaction has been effected with 2-methyl-3-phthalimido-4-nonadecanone (IIa) and 4-phthalimido-5-eicosanone (IIb) as intermediate components. In the course of our investigation we have applied several different routes in endeavor to convert both ketones into the diamines. In fact, the route described in this paper did not lead to the expected bases, but the compounds which were obtained can be regarded as derivatives of them.

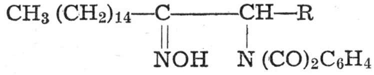
The introduction of the second nitrogen atom into the molecule has been accomplished by oximation of the ketones IIa and IIb. The readily available oximes IIIa and IIIb were hydrogenated in the presence of Raney-Nickel catalyst W4 at 80° and 100 at. in order to reduce the oximino group. It is to be

I 

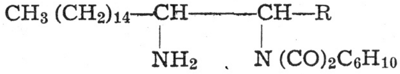
$CH_3(CH_2)_{14}-\underset{|\atop NH_2}{CH}-\underset{|\atop NH_2}{CH}-R$

II 

$CH_3(CH_2)_{14}-CO-\underset{|\atop N(CO)_2C_6H_4}{CH}-R$

III 

$CH_3(CH_2)_{14}-\underset{\|\atop NOH}{C}-\underset{|\atop N(CO)_2C_6H_4}{CH}-R$

IV 

$CH_3(CH_2)_{14}-\underset{|\atop NH_2}{CH}-\underset{|\atop N(CO)_2C_6H_{10}}{CH}-R$

a) $R = -CH(CH_3)_2$
b) $R = -CH_2CH_2CH_3$

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* Paper III, P. Alaupović and M. Proštenik, Croat. Chem. Acta, **28** (1956) 219.

pointed out that the aromatic ring was reduced simultaneously with the formation of 2-methyl-3-hexahydrophtalimido-4-aminononadecane (IVa) and of 4-hexahydrophthalimido-5-aminoeicosane (IVb). The bases could not be obtained in a pure condition, but IVa gave a well crystalline oxalate.

EXPERIMENTAL

The melting points are uncorrected.

2-Methyl-3-phthalimido-4-nonadecane oxime (IIIa)

2-Methyl-3-phthalimido-4-nonadecanone (IIa)[1] (4 g.) and the solution of hydroxylamine acetate, prepared from hydroxylamine hydrochloride (4 g.), anhydrous sodium acetate (8 g.) and absolute ethanol (60 ml.) was refluxed for 3 hrs. Ethanol was then distilled off, water (30 ml.) was added to the oil thus obtained and the mixture extracted with ether. The combined ether extracts were washed with water, dried with anhydrous sodium sulphate and the solvent removed. The oxime crystallized on standing in the refrigerator. Colorless crystals (2.1 g., 50.7%), m. p. 70—71°. The sample for analysis was recrystallized three times from petroleum ether; m. p. 75—76°.

Anal. 6.700 mg. subst.: 18.07 mg. CO_2, 5.87 mg. H_2O
6.475 mg. subst.: 0.363 ml. N_2 (25.6°, 749 mm)
$C_{28}H_{44}O_3N_2$ (456.65) calc'd: C 73.61; H 9.71; N 6.14%
found: C 73.60; H 9.80; N 6.32%

2-Methyl-3-hexahydrophthalimido-4-aminononadecane (IVa)

The oxime IIIa (2 g., 0.0044 mMole) was dissolved in absolute ethanol (100 ml.) and hydrogenated in the presence of Raney-Nickel W4 catalyst (5 ml.)[2] at 80° and 100 at. for 6 hrs. The catalyst was then removed by filtration and the solvent distilled off. There was obtained 1.8 g. (91.8%) of a pale, yellow oil which could not be induced to crystallization. Oily products were also obtained by precipitation with Reinecke-Salt, picrolonic and hydrochloric acid. The acid oxalate was formed by mixing the ethanolic solutions of oxalic acid and of the crude base. The salt was recrystallized twice from absolute ethanol; colorless prisms, m. p. 135—136°.

Anal. 3.605 mg. subst.: 8.85 mg. CO_2, 3.30 mg. H_2O
5.320 mg. subst.: 0.245 ml. N_2 (25°, 747 mm)
$C_{30}H_{54}O_6N_2$ (538.75) calc'd: C 66.87; H 10.10; N 5.20%
found: C 66.99; H 10.24; N 5.19%

Attempts to split off the hexahydrophthaloyl group from the crude base by refluxing its ethyl cellosolve solution with hydrazine hydrate in the course of 14 hrs. failed. The reaction product was an oil which could not be identified as a diamine. When the experiment was repeated by refluxing the solution only for 2 hr. the unreacted base isolated as the oxalate, m. p. and mixed m. p. 132—134°, was obtained.

4-Phthalimido-5-eicosane oxime (IIIb)

The oxime was prepared in the usual manner from 2 g. (0.0045 mole) of 4-phthalimido-5-eicosanone (IIb)[1], hydroxylamine hydrochloride (2 g.), anhydrous sodium acetate (4 g.) and absolute ethanol (30 ml.). The yield was 1.23 g. (59.7%). Colorless crystals, m. p. 66—68°, which were recrystallized three times from petroleum ether; m. p. 72.5—73°.

Anal. 5.635 mg. subst.: 15.14 mg. CO_2, 4,94 mg. H_2O
6.650 mg. subst.: 0.352 ml. N_2 (23°, 749 mm)
$C_{28}H_{44}O_3N_2$ (456.65) calc'd: C 73.61; H 9.71; N 6.14%
found: C 73.32; H 9.81; N 6.02%

4-Hexahydrophthalimido-5-aminoeicosane (IVb)

A. The reduction of the oxime was carried out under the same conditions as described for IVa. The crude, oily base could not be induced to crystallization. The oxalate, hydrochloride, sulphate and picrate separated also as oils.

The crude base when refluxed either with 10% ethanolic sulphuric acid or with hydrazine hydrate in ethyl cellosolve yielded only unidentified oils.

B. The oxime IIIb (0.5 g.) was dissolved in 96% ethanol (50 ml.) to which 0.1 ml. of concentrated hydrochloric acid was added and hydrogenated in the presence of Adams platinum catalyst (0.2 g.). The hydrogen uptake was 134 ml. at 20° and 750 mm. An oily base (0.46 g.) was obtained, which did not crystallize. The picrate, picrolonate, hydrochloride and oxalate were also oils.

We are indebted to Mrs. M. Munk-Weinert from our microanalytical laboratory for the microanalyses.

REFERENCES

1. P. Alaupović and M. Proštenik, *Croat. Chem. Acta,* **28** (1956) 211.
2. A. A. Pavlic and H. Adkins, *J. Am. Chem. Soc.* **68** (1946) 1471; H. Adkins and A. A. Pavlic, *J. Am. Chem. Soc.* **69** (1947) 3039.

IZVOD

Nekrozamin. IV.
Pripravljanje 2-metil-3-heksahidro-ftalimido-4-amino-nonadekana

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Derivati racemičkog nekrozamina (Ia ili Ib) 2-metil-3-heksahidro-ftalimido-4-amino-nonadekan (IVa), oksalat t. t. 135—136°, i 4-heksahidro-ftalimido-5-amino-eikosan (IVb), pripravljeni su redukcijom oksima 2-metil-3-ftalimido-4-nonadekanona (IIIa), t. t. 75—76°, i oksima 4-ftalimido-5-eikosanona (IIIb), t. t. 72.5—73° uz katalizator Raney-nikalj W4 kod 80° i 100 at.

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