CCA-30 547.415.1

Necrosamine Series. II.* Synthesis of Racemic 4,5-Diaminoeicosane and of 2-Methyl-3,4-diaminononadecane

P. Alaupović and M. Proštenik

Department of Chemistry, Medical Faculty, University of Zagreb
and
Department of Biochemistry, Institute »Ruđer Bošković«, Zagreb, Croatia, Yugoslavia

Received September 19, 1956

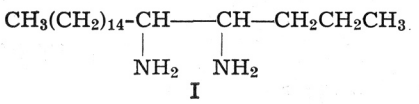
Racemic 4,5-diaminoeicosane (I) and 2-methyl-3,4-diaminononadecane (II) were obtained by reaction of dibenzyl sodiotetradecylmalonate (III) with *N*-phthaloyl-DL-norvalinoyl chloride (IVa) and *N*-phthaloyl-DL-valinoyl chloride (IVb). Following compounds were prepared: Dibenzyl tetradecylmalonate (III), m. p. 42—42.5°; *N*-phthaloyl-DL-norvaline, m. p. 102—103°; *N*-phthaloyl-DL-norvalinoyl chloride (IVa), b. p. 158°/1 mm; 4-phthalimido-5-eicosanone (VIa), m. p. 38—38.5°; 4-(*o*-carboxybenzamido)-5-eicosanone (VIIa), m. p. 111—112°; 4-amino-5-eicosanone hydrobromide (VIIIa), m. p. 95—96°; 4-amino-5-eicosane oxime (IXa), m. p. 114—115°; 4,5-diaminoeicosane dihydrochloride (Xa), m. p. 265—267°; 4,5-diacetylaminoeicosane (XIa), m. p. 122—123°; 2-methyl-3-phthalimido-4-nonadecanone (VIb), m. p. 52—53°; 2-methyl-3-(*o*-carboxybenzamido-)4-nonadecanone (VIIb), m. p. 118—119°; 2-methyl-3-amino-4-nonadecanone hydrobromide (VIIIb), m. p. 127—128°; 2-methyl-3-amino-4-nonadecane oxime (IXb), m. p. 108—108.5°; 2-methyl-3,4-diaminononadecane dihydrochloride (Xb), m. p. 225—226°; 2-methyl-3,4-diacetylaminononadecane (XIb), m. p. 136—138°.

The synthesis of (I) and (II) represents at the same time a general method for the preparation of aliphatic α-diamines. The application of this procedure to some stereochemical questions is discussed.

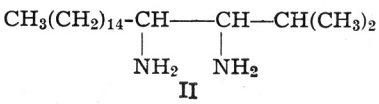
It has been reported that an agent which is synthesized by *Escherichia coli*[2–5] and other bacteria[6–8] produces an intense tumor hemorrhage in mice bearing sarcoma 180. The agent was found to be a complex polysaccharide containing both a peptide and a phospholipide component[8–10]. The hydrolysis of the carbohydrate component gave D-glucose, D-galactose and D-glucosamine. The acid hydrolysis of the phospholipid moiety gave lauric, myristic, palmitic and D-β-hydroxymyristic acid as well as nitrogen-containing components. When the nitrogeneous fraction — insoluble both in water and in ether — was treated with aqueous sodium hydroxide, a base was isolated which was characterized *inter alia* as a crystalline dihydrochloride. The base which has been named necrosamine appears to be one of the isomers of 4,5-diaminoeico-

* Paper I, see reference[1].

sane (I) or of 2-methyl-3,4-diaminononadecane (II). It has not yet been definitively established which of these two structures is correct.



I



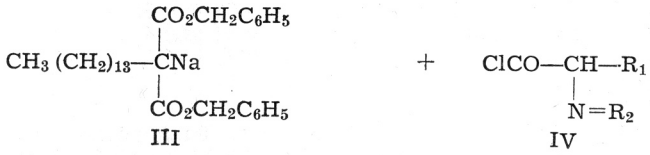
II

Despite of the fact that necrosamine possesses two asymmetric carbon atoms no measurable optical activity was observed. It is likely that the *erythro*-configuration about the asymmetric centers might be assigned.

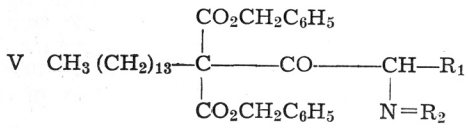
Some work towards synthesis of necrosamine has been also done. Ikawa and Niemann[11] prepared 4,5-diaminoeicosane and 2-methyl-3,4-diaminononadecane by means of the acyloin condensation of methyl palmitate with methyl butyrate and methyl isobutyrate respectively. The oxidation of the acyloins gave the diketones which were converted into the diamines via the oximes. Each diamine dihydrochloride could be separated into the ether-soluble and ether-insoluble salt. Both salts were suggested to be diastereoisomeric dihydrochlorides. Unfortunately no melting points of the synthetic dihydrochlorides were given.

It is the purpose of this communication to report on the new synthesis of racemic 4,5-diaminoeicosane and of 2-methyl-3,4-diaminononadecane. A new synthetic route was examined with DL-α-amino acids as starting materials. We prepared each of these two diamines by virtue of the Bowman reaction[12], i. e. its extension to amino acids as acylating components[13–16]. Thus, dibenzyl (III) and ditetrahydropyranyl sodiomalonates were condensed with *N*-phthaloyl-DL-norvalinoyl chloride (IVa) and *N*-phthaloyl-DL-valinoyl chloride (IVb) respectively. It was found that the reaction via the dibenzyl esters was more convenient in respect to the purity and yields of the intermediate ketones thus obtained. The yields of α-phthalimido ketones (VIa) and (VIb) in the best experiments were as high as 38 per cent and 43 per cent r[illegible]

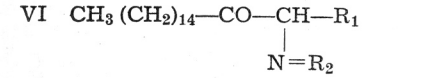
stereospecific synthesis of α-diamines from natural, optically active α-amino acids. Thus, natural amino acids which belong configurationally to the L-series should yield optically active diamines and the formation of two active diastereoisomers is expected. In this way, by applying L-valine and L-norvaline as the acylating components and the stereospecific induction of the second amino group into the molecule some evidence of the configuration about the asymmetric centers of necrosamine might be given. This problem is under investigation in our laboratories.



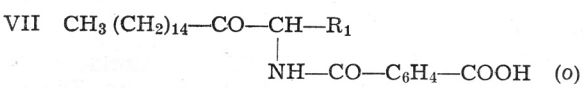
III IV



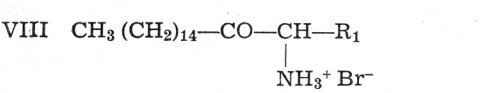
V



VI

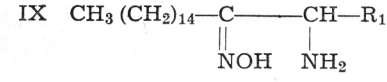


VII

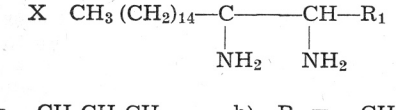


(o)

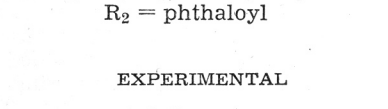
VIII



IX



X



a) $R_1 = -CH_2CH_2CH_3$, b) $R_1 = -CH(CH_3)_2$
R_2 = phthaloyl

EXPERIMENTAL

The melting points are uncorrected.

Tetradecylmalonic Acid

The acid was prepared following the procedures of Sunko and Prošteník[14] for the preparation of pentadecylmalonic acid and of Floyd and Miller[17] for the preparation of hexadecymalonic acid. Crystallization from acetic acid gave colorless leaflets, m. p. 118—120°. Hell and Jordanoff[18] give m. p. 117—118°.

Dibenzyl tetradecylmalonate (III)

A mixture of 40 g. (0.133 mole) of tetradecylmalonic acid, 40 g. (0.370 mole) of benzyl alcohol and 2 g. of *p*-toluenesulphonic acid in 200 ml. of benzene was refluxed for 10 hrs. using water separator. The calculated amount of water (2.4 ml.) was collected. The reaction mixture was washed successively with saturated solution of sodium hydrogen carbonate and water. Benzene was removed by distillation and the residual yellow oil dried *in vacuo* for 30 minutes at 100°. After addition of 40 ml. of ethanol and cooling in an ice-box the oil crystallized. There was obtained 63.2 g. (98.9%) colorless crystals, m. p. 40—42°. The sample for analysis was recrystallized three times from absolute ethanol; m. p. 42—42.5°.

Anal. 8.940 mg. subst.: 25.44 mg. CO_2, 7.56 mg. H_2O
$C_{31}H_{44}O_4$ (480.66) calc'd: C 77.46; H 9.22%
found: C 77.66; H 9.46%

N-*Phthaloyl*-DL-*norvaline*

A finely ground mixture of DL-norvaline (15 g., 0.128 mole) and phthalic anhydride (18.95 g.) was heated with occassional stirring in an oil bath at 150—160° for 2 hr. The yellow melt was dissolved in 60 ml. of carbon tetrachloride and decolorized with activated carbon. Petroleum ether (50—70°, 60 ml.) was added to the hot, colorless solution and allowed to stand at room temperature overnight. Thereby 28.8 g. (91.2%) colorless crystals were obtained, m. p. 102—103°. The melting point was unchanged after two crystallizations from the mixture of carbon tetrachloride-petroleum ether.

Anal.: 8.760 mg. subst.: 20.14 mg. CO_2, 4.05 mg. H_2O
7.420 mg. subst.: 0.381 ml. N_2 (23.4°, 743 mm)
$C_{13}H_{13}O_4N$ (247.24) calc'd: C 63.15; H 5.30; N 5.67%
found: C 62.74; H 5.17; N 5.78%

N-*Phthaloyl*-DL-*norvalinoyl Chloride* (IVa)

A solution of II (12.36 g., 0.05 mole) in thionyl chloride was left to stand at room temperature overnight and then refluxed for 1 hr. The excess of thionyl chloride was distilled off *in vacuo* and to the residual pale yellow oil benzene was added (30 ml.) and evaporated *in vacuo* in order to remove the thionyl chloride completely. The crude acid chloride was distilled *in vacuo*. Pale, yellow oil (12.3 g., 92.5%), b. p. 158° at 1 mm. was obtained.

Anal.: 17.700 mg. subst.: 0.845 ml. N_2 (23.7°, 750 mm)
$C_{13}H_{12}O_3NCl$ (265.69) calc'd: N 5.27%
found: N 5.42%

4-Phthalimido-5-eicosanone (VIa)

Method A. — Tetradecylmalonic acid (14.98 g., 0.0498 mole) was added in portions with stirring in the course of 30 minutes to the mixture of dihydropyrane (11 g.), benzene (150 ml.) and concentrated sulphuric acid (4 drops). The temperature was kept below 30°. Stirring was continued for 1 hr. Anhydrous potassium carbonate (3 g.) was added to the almost clear solution and stirring continued for additional 30 minutes. The solution was filtered from inorganic material and benzene and excess of dihydropyrane removed *in vacuo* below 30°. The residual oil (11 g., 47.1%) was dissolved in benzene (150 ml.) and the solution added to a stirred suspension of powdered sodium (0.57 g.) in benzene (100 ml.). Stirring was continued for 2 hr. and the solution decanted from some unreacted sodium. The solution of the acid chloride IVa (6.11 g., 0.0249 mole) in benzene (100 ml.) was then added dropwise at room temperature. During the addition the color of the solution was turned from dark yellow to pale yellow and finally the reaction mixture became viscous and turbid. Stirring was continued for 24 hrs. The mixture was acidified with acetic acid (5 ml.) and refluxed for 2 hr. The cooled mixture was washed with water and the solvent evaporated to dryness. The residual oil (12 g.) was dissolved in 30 ml. of benzene and chromatographed over activated alumina (120 g., Riedel-de Haën). From

the benzene eluates 1.211 g. of a pale yellow oil was obtained, which was dissolved in 5 ml. of 96% ethanol. On cooling collorless crystals m. p. 35—37° were obtained, yield 10% based on the acid chloride. Five crystallizations from absolute ethanol gave colorless prisms, m. p. 38—38.5°.

Anal.: 8.580 mg. subst. 23.99 mg. CO_2, 7.70 mg. H_2O
5.180 mg. subst: 0.157 ml. N_2 (23.5°, 748 mm)
$C_{28}H_{43}O_3N$ (441.63) calc'd: C 76.15; H 9.81; N 3.17%
found: C 76.30; H 10.04; N 3.43%

Method B. — To 1.15 g. of sodium powder in benzene (150 ml.) was added all at once a solution of 24.03 g. (0.05 mole) of dibenzyl tetradecymalonate (III) in benzene (150 ml.). The mixture was stirred at room temperature for 1—2 hr. until all sodium was dissolved. A solution of IVa (13.28 g., 0.05 mole) in benzene (100 ml.) was then added with continuous stirring. The reaction mixture — which became viscous and turbid — was stirred for 12 hrs. and poured into the ice water containing a few drops of concentrated sulphuric acid. The benzene layer was washed with water and the solvent evaporated *in vacuo* at 40—45° (bath temperature) to give 31.9—35.5 g. (90—98%) of a pale yellow oil. It was dissolved in 96% ethanol (200 ml.) and hydrogenated in the presence of 3—4 g. of palladium on barium sulphate catalyst at room temperature and at atmospheric pressure. The hydrogen uptake was 1900—2170 ml. (85—97%). The catalyst was filtered off and the filtrate refluxed for 2 hr. After removal of the solvent the resulting oil was heated for additional 30 minutes at 100° *in vacuo*. The oily residue was taken into 50 ml. of benzene. After standing at room temperature 2.5—4 g. of tetradecylmalonic acid (m. p. 115—118°) was separated. The filtrate was chromatographed on activated alumina (Riedel-de Haën). From benzene eluates 12.5—14.5 g. of slightly yellow oil was obtained, which was dissolved in 30 ml. of absolute ethanol and crystallized in a refrigerator overnight. A crop of 7.16—9.62 g. (31.8—42.7%) colorless crystals melting at 37—38° was obtained. One crystallization from absolute ethanol raised the m. p. to 38—38.5°. No melting point depression was observed in admixture with 4-phthalimido-5-eicosanone obtained by the method A.

4-(o-Carboxybenzamido-)5-eicosanone (VIIa)

A sample of VIa (0.5 g., 1.1 mMole) was mixed with 96% ethanol (10 ml.) and 17% ethanolic potassium hydroxide (5 ml.) and allowed to stand at room temperature for 24 hrs. The mixture was then poured into 2*N* sulphuric acid (15 ml.), the resulting precipitate filtered and washed with water. Crystallization from 96% ethanol gave 0.46 g. (90%) colorless crystals, m. p. 100—102°. The analytical sample was recrystallized five times from absolute ethanol; m. p. 111—112°.

Anal.: 8.245 mg. subst.: 22.27 mg. CO_2, 7.23 mg. H_2O
$C_{28}H_{45}O_4N$ (459.65) calc'd: C 73.16; H 9.86%
found: C 73.71; H 9.81%

4-Amino-5-eicosanone hydrobromide (VIIIa)

A. By hydrolysis of VIa. — The ketone VIa (2 g., 4.5 mMole) was refluxed with glacial acetic acid (15 ml.) and 66% hydrobromic acid (10 ml.) for 20 hrs. The reaction mixture was then evaporated *in vacuo* to dryness. Chloroform (20 ml.) was added to the dry residue and heated for a few minutes on the water bath. The undissolved phthalic acid (0.68 g., 90%, m. p. 196—197°) was filtered off and the mother liquid evaporated *in vacuo* to dryness. After one crystallization from ethyl acetate 1.1 g. (88.7%) colorless crystals, m. p. 92—94° were obtained. The analytical sample was recrystallized three times from the same solvent; m. p. 95—96°.

Anal.: 7.885 mg. subst.: 17.65 mg. CO_2, 7.28 mg. H_2O
$C_{20}H_{42}ONBr$ (392.46) calc'd: C 61.25; H 10.78%
found: C 61.08; H 10.33%

B. By hydrolysis of VIIa. — The substance (0.82 g., 1.8 mMole) was refluxed with glacial acetic acid (7 ml.) and 66% hydrobromic acid (5 ml.) and worked up as

described above. The yield on phthalic acid was 0.26 g. (88%) and 0.59 g. (85%) on the ketone hydrobromide, m. p. 92—94°. After one crystallization from ethyl acetate the substance melted at 95—96° and gave no depression of melting point when mixed with the compound described under A.

4-Amino-5-eicosane oxime (IXa)

The amino ketone hydrobromide VIIIa (0.65 g., 1.6 mMole) was refluxed for 3 hrs. with a solution of hydroxylamine acetate prepared from hydroxylamine hydrochloride (0.7 g.), sodium acetate (1.4 g.) and absolute ethanol (30 ml.). Ethanol was then distilled off, water (10 ml.) was added to the residue and extracted with ether. After washing with water and drying with sodium sulphate the ether extracts gave an oil which crystallized on standing. Recrystallization from ethyl acetate gave 0.41 g. (72.5%) colorless crystals, m. p. 109—111°. Three additional crystallizations raised the m. p. to 114—115°, but the oxime was not pure enough to give the correct analysis.

4,5-Diaminoeicosane dihydrochloride (Xa)

A solution of IXa (0.55 g., 1.7 mMole) in absolute ethanol (100 ml.) was hydrogenated in the presence of 0.2 g. of Adams platinum catalyst and 0.5 ml. of concentrated hydrochloric acid at room temperature and at atmospheric pressure. After 7 hrs. the calculated amount of hydrogen was absorbed, the catalyst was filtered off and the solvent removed by distillation. An oil was obtained which was treated with the saturated solution of sodium carbonate (15 ml.) and extracted with ether (60 ml.). The ether extract was dried with sodium sulphate and saturated with dry hydrogen chloride. The separated crystals were filtered by suction (0.23 g., 35.8%, m. p. 265° [sint. from 175°]). Three crystallizations from water gave colorless, glistening leaflets, m. p. 265—267° (sint. from 185°).

Anal.: 8.700 mg. subst.: 19.95 mg. CO_2, 9.12 mg. H_2O
5.445 mg. subst.: 0.370 ml. N_2 (25.5°, 743 mm)
$C_{20}H_{46}O_2N_2$ (385.5) calc'd: C 62.31; H 12.03; N 7.26%
found: C 62.58; H 11.73; N 7.60%

The mother liquid gave after evaporation of the ether an oil which was crystallized from ethyl acetate. Colorless crystals (80 mg., 12.3%); m. p. 180—210°.

4,5-Diacetylaminoeicosane (XIa)

Fifty miligrams of Xa was heated with acetic anhydride (1 ml.) and pyridine (2 ml.) at 100° for 1 hr. After cooling the reaction mixture was poured into 2*N* sulphuric acid (60 ml.), the resulting suspension extracted with ether, the extracts washed with water, dried with sodium sulphate and the solvent distilled off. The oily residue was crystallized twice from acetonitrile; m. p. 122—123°.

Anal.: 3.790 mg. subst.: 0.221 ml. N_2 (21.5°, 749 mm)
$C_{24}H_{48}O_2N_2$ (396.59) calc'd: N 7.06%
found: N 6.66%

2-Methyl-3-phthalimido-4-nonadecanone (VIb)

The substance was prepared following exactly the same procedure as described for VIa.

Method A. — Starting from tetradecylmalonic acid (24 g., 0.08 mole), dihydropyrane (16.5 g.), sodium powder (1.84 g.) and *N*-phthaloyl-DL-valinoyl chloride (IVb) (21.2 g., 0.08 mole) 5.0 g. (13.8%) colorless crystals melting at 51—52° were obtained. The sample for analysis was recrystallized from absolute ethanol and melted at 52—53°.

Anal.: 8.285 mg. subst.: 23.14 mg. CO_2, 7.40 mg. H_2O
8.470 mg. subst.: 0.257 ml. N_2 (25.8°, 741 mm)
$C_{28}H_{43}O_3N$ (441.63) calc'd: C 76.15; H 9.81; N 3.17%
found: C 76.22; H 10.00; N 3.38%

Method B. — Starting from dibenzyl tetradecylmalonate (23.5 g., 0.0489 mole), sodium powder (1.12 g.) and *N*-phthaloyl-DL-valinoyl chloride (IVb) (13 g., 0.0489 mole) 6.9—8.3 g. (31.4—38.4%) colorless crystals, m. p. 49—49.5° were obtained. Crystallization from absolute ethanol gave a product melting at 51—52° identical with the ketone obtained by the method A.

2-Methyl-3-(o-carboxybenzamido-)4-nonadecanone (VIIb)

From 0.5 g. (1.1 mMole) of VIb in 10 ml. of 96% ethanol and 5 ml. of 17% ethanolic potassium hydroxide, 0.48 g. (96%) colorless crystals, m. p. 118—119°, were obtained. Two crystallizations from absolute ethanol did not change the melting point.

Anal.: 8.635 mg. subst.: 23.16 mg. CO_2, 7.65 mg. H_2O
$C_{28}H_{45}O_4N$ (459.65) calc'd: C 73.16; H 9.86%
found: C 73.19; H 9.91%

2-Methyl-3-amino-4-nonadecanone hydrobromide (VIIIb)

A. — By hydrolysis of VIb. — One gram (2.2 mMole) of VIb was refluxed with glacial acetic acid (7 ml.) and 66% hydrobromic acid (5 ml.) for 17 hrs. By working up the reaction mixture as described above 0.62 g. (70%) colorless crystals from ethyl acetate, m. p. 127—127.5°, were obtained.

Anal.: 8.480 mg. subst.: 19.02 mg. CO_2, 8.20 mg. H_2O
6.370 mg. subst.: 0.230 ml. N_2 (21°, 750 mm)
$C_{20}H_{42}ONBr$ (392.46) calc'd: C 61.25; H 10.78; N 3.56%
found: C 61.21; H 10.82; N 4.14%

B. By hydrolysis of VIIb. — A sample of VIIb (0.82 g., 1.8 mMole) treated with a mixture of glacial acetic acid (7 ml.) and 66% hydrobromic acid (5 ml.) gave 0.55 g. (78.9%) of the hydrobromide melting at 127—128°.

2-Methyl-3-amino-4-nonadecanone oxime (IXb)

The oxime was prepared in the usual manner from 0.95 g. (2.4 mMole) of VIIIb, 1 g. of hydroxylamine hydrochloride and 2 g. of sodium acetate in 60 ml. of absolute ethanol. Thus, 0.56 g. (70.8%) colorless crystals from ethyl acetate m. p. 108—108.5° were obtained. The sample for analysis could not be purified completely.

Anal.: 5.990 mg. subst.: 0.402 ml. N_2 (21°, 752 mm)
$C_{20}H_{42}ON_2$ (326.55) calc'd: N 8.57%
found: N 7.71%

2-Methyl-3,4-diaminononadecane dihydrochloride (Xb)

The oxime IXb (0.34 g., 1 mMole) in absolute ethanol (50 ml.) was hydrogenated in the presence of 0.2 g. of Adams platinum catalyst and 0.3 ml. of concentrated hydrochloric acid and worked up as described for Xa. Colorless crystals (0.25 g., 62.5%), m.p. 195—197°. Two crystallization from absolute ethanol gave 0.18 g. (45%) colorless leaflets, m.p. 225—226° (sint. from 195°).

Anal.: 3.295 mg. subst.: 7.60 mg. CO_2, 3.43 mg. H_2O
$C_{20}H_{46}N_2Cl_2$ (385.5) calc'd: C 62.31; H 12.03%
found: C 62.94; H 11.65%

From the ether mother liquid 40 mg. colorless crystals, m. p. 100—101° (crystallized from ethyl acetate) were obtained.

2-Methyl-3,4-diacetylaminononadecane (XIb)

The diacetyl derivative was prepared in the usual manner and crystallized from acetonitrile; m. p. 136—138° (sint. from 125°).

Anal.: 7.810 mg. subst.: 20.87 mg. CO_2, 8.16 mg. H_2O
3.700 mg. subst.: 0.245 ml. N_2 (24°, 744 mm)
$C_{24}H_{48}O_2N_2$ (396.59) calc'd: C 72.68; H 12.19; N 7.06%
found: C 72.92; H 11.69; N 7.45%

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

REFERENCES

1. M. Prošteník and P. Alaupović, *Naturwiss.* **43** (1956) 349.
2. A. Gratia and R. Linz, *Compt. rend. Soc. biol.* **108** (1931) 427.
3. M. J. Shear and H. B. Andervont, *Proc. Soc. Exptl. Biol. Med.* **34** (1936) 323.
4. M. Shear, *Proc. Soc. Exptl. Biol. Med.* **34** (1936) 325.
5. M. Ikawa, J. B. Koepfli, S. G. Mudd, and C. Niemann, *J. Nat. Cancer Inst.* **13** (1952) 157.
6. G. Shwartzman and N. Michailovsky, *Proc. Soc. Exptl. Biol. Med.* **29** (1932) 737.
7. M. J. Shear and F. C. Turner, *J. Nat. Cancer Inst.* **4** (1943) 81.
8. J. L. Hartwell, M. J. Shear, and J. R. Adams Jr., *J. Nat. Cancer Inst.* **4** (1943) 107.
9. M. Ikawa, J. B. Koepfli, S. G. Mudd, and C. Niemann, *J. Am. Chem. Soc.* **74** (1952) 5219; **75** (1953) 1035.
10. For other references about lipopolysaccharides see an excellent review by O. Westphal and O. Lüderitz, *Angew. Chem.* **66** (1954) 407.
11. M. Ikawa and C. Niemann, *J. Am. Chem. Soc.* **75** (1953) 6314.
12. R. E. Bowman, *J. Chem. Soc.* **1950**, 325; R. E. Bowman and W. D. Fordham, *J. Chem. Soc.* **1951**, 2753.
13. R. E. Bowman and W. D. Fordham, *J. Chem. Soc.* **1952**, 3945.
14. D. E. Sunko and M. Prošteník, *Arhiv kem.* **26** (1954) 7.
15. M. Prošteník and N. Ž. Stanaćev, *Arhiv kem.* **27** (1955) 197.
16. M. Prošteník, M. Munk-Weinert, and D. E. Sunko, *J. Org. Chem.* **21** (1956) 406.
17. D. E. Floyd and S. E. Miller, *Org. Syntheses, Vol.* **34** (1954) 13.
18. C. Hell and Ch. Jordanoff, *Ber.* **24** (1891) 990.
19. R. Adams, V. Voorhees, and R. L. Shriner, *Org. Syntheses,* Coll. Vol. I, 2nd ed. (1941) 463.

IZVOD

Nekrozamin. II.

Sinteza racemičkog 4,5-diamino-eikosana i 2-metil-3,4-diamino-nonadekana

P. Alaupović i M. Prošteník

Pripravljeni su racemički 4,5-diamino-eikosan (I) i 2-metil-3,4-diamino-nonadekan (II) u reakciji dibenzilnog estera natrium-tetradecil-malonske kiseline (III) s kloridom *N*-ftaloil-DL-norvalina (IVa) i s klorídom *N*-ftaloil-DL-valina (IVb). Pripravljeni su i opisani ovi spojevi: dibenzilni ester tetradecil-malonske kiseline (III), t. t. 42—42.5°; *N*-ftaloil-DL-norvalin, t. t. 102—103°; klorid *N*-ftaloil-DL-norvalina (IVa), t. v. 158°/1 mm; 4-ftalimido-5-eikosanon (VIa), t. t. 111—112°; 4-amino-5-eikosanon hidrobromid (VIIIa), t. t. 95—96°; 4-amino-5-eikosan oksim (IXa), t. t. 114—115°; 4,5-diamino-eikosan dihidroklorid (Xa), t. t. 265—267°; 4,5-diacetilamino-eikosan (XIa), t. t. 122—123°; 2-metil-3-ftalimido-4-nonadekanon (VIb), t. t. 52—53°; 2-metil-3-(o-karboksi-benzamido-)4-nonadekanon (VIIb), t. t. 118—119°; 2-metil-3-amino-4-nonadekanon hidrobromid (VIIIb), t. t. 127—128°; 2-metil-3-amino-4-nonadekan oksim (IXb), t. t. 108—108.5°; 2-metil-3,4-diamino-nonadekan dihidroklorid (Xb), t. t. 225—226°; 2-metil-3,4-diacetilamino-nonadekan (XIb), t. t. 136—138°.

Sintezu (I) i (II) smatramo općom metodom za pripravljanje alifatskih α-diamina. Istaknuta je mogućnost primjene toga postupka za rješavanje nekih stereokemijskih problema, osobito u vezi s nekrozaminom.

MEDICINSKI FAKULTET
ZAVOD ZA KEMIJU
I
INSTITUT »RUĐER BOŠKOVIĆ«
BIOKEMIJSKI ODJEL
ZAGREB

Primljeno 19. rujna 1956.