Synthesis of 1-Aminoheneicosane

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Received November 26, 1955

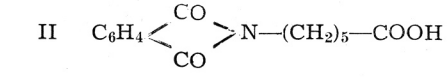
1-Aminoheneicosane [V] was prepared by the condensation of dibenzyl sodiotetradecylmalonate with ε-phthaloylaminocaproic acid chloride [III]. Following substances are described: 1. ε-Phthaloylaminocaproic acid [II], m. p. 107°; 2. ε-phthaloylaminocaproic acid chloride [III], b. p. 175—178° at 0.2 mm.; 3. 1-phthaloylamino-6-heneicosanone [IV], m. p. 83—84°; oxime, m. p. 59—60°; 4. 1-aminoheneicosane [V], m. p. 93—94°; oxalate, m. p. 170—172° (decomp.); 5. 1-benzoylamino-6-heneicosanone, m. p. 94—95°.

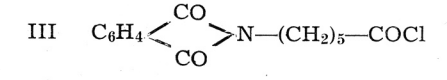
In an earlier communication from our laboratory it was reported that the Bowman ketone synthesis[1,2] could be generalyzed by the application of phthaloylamino acid chlorides for the acylation of the dibenzyl or ditetrahydropyranyl sodioalkylmalonates[3]. A method was proposed for the preparation of α-amino ketones, amines etc. An example was given in case of the preparation of 1-amino-4-phenylbutane.

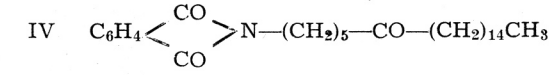
Further studies which we report in this paper have shown that the long-chain 1-aminoalcanes could also be obtained by this method. The readily available ε-phthaloylaminocaproic acid chloride [III] was condensed with dibenzyl sodiotetradecylmalonate. The resulting β-keto ester was easily converted into the 1-phthaloylamino-6-heneicosanone [IV] m. p. 83—84°, after hydrogenolysis and subsequent decarboxylation of the dicarboxylic acid. The Huang-Minlon reduction of the latter gave the desired 1-aminoheneicosane [V], m. p. 93—94°, as a crystalline compound which was characterized as the oxalate, m. p. 170—172° (decomp.).

When ε-benzoylaminocaproic acid chloride was used as a nitrogen containing component instead of the phthaloyl derivative, 1-benzoylamino-6-heneicosanone, m. p. 94—95°, was obtained in a very poor yield.

I $H_2N—(CH_2)_5—COOH$

II 

III 

IV 

V $CH_3(CH_2)_{20}—NH_2$

In spite of the fact that this synthesis does not compete in general with some other classical methods of preparation of 1-aminoalcanes, it might be, however, of interest in certain cases, for instance in cases when the long-chain starting material necessary in the older methods of preparation is not always readily accessible.

EXPERIMENTAL

The melting points are uncorrected.

ε-*Phthaloylaminocaproic acid* [II]

ε-Aminocaproic acid [I] (9 g., 68 mMoles, prepared according to Eck and Marvel[4]) and finely ground phthalic anhydride (18.18 g., 68 mMoles) were heated at 135—140° for 2 hr. with occassional stirring. The reaction product was dissolved in 800 ml. of boiling water. Upon cooling 14 g. colorless needles, m. p. 107°, was obtained (59.5% yield). For analysis the substance was recrystallized from water; m. p. 107°.

Anal. 8.405 mg. subst.: 19.83 mg. CO_2, 4.35 mg. H_2O
5.280 mg. subst.: 0.253 ml. N_2 (23.5°, 746 mm)
$C_{14}H_{15}O_4N$ (261.27) calc'd: C 64.35; H 5.79; N 5.36%
found: C 64.38; H 5.79; N 5.41%

ε-*Phthaloylaminocaproic acid chloride* [III]

A sample of [I] (2.52 g.) was refluxed with 10 ml. of thionyl chloride for 1 hr. The excess of thionyl chloride was then removed *in vacuo* leaving 3.73 g. of a slightly yellow oil which on distillation in vacuo gave 1.77 g. of an oily product, b. p. 175—178° at 0.2 mm. Hg; yield 52.3%. The chloride was used for the next step without further purification.

1-Phthaloylamino-6-heneicosanone [IV]

To a stirred suspension of 0.517 g. (22.5 mMoles) of powdered sodium in 50 ml. of absolute benzene, a solution of 10.83 g. (22.5 mMoles) of dibenzyl tetradecylmalonate in 50 ml. of absolute benzene was added. The reaction mixture was refluxed for 0.5 hr. ε-Phthaloylaminocaproic acid chloride [III] (6.3 g., 22.5 mMoles) was then added to the clear solution ot room temperature and stirring was continued for 5 hr. The yellow-colored reaction mixture was poured into 300 ml. of ice-water containing three drops of conc. sulphuric acid. The benzene layer was separated and the aqueous layer extracted three times with benzene. Combined benzene extracts were washed with water, dried with sodium sulphate and evaporated in vacuo at 40° to dryness. Thereby 15 g. yellow oil was obtained to which 50 ml. of 96% ethanol was added and the resulting emulsion hydrogenated in the presence of 2 g. of 10% palladium on barium sulphate catalyst at room temperature and at atmospheric pressure. The calculated amount of hydrogen was taken up in 20 hr. During the hydrogen absorption the content of the hydrogenation flask was crystallized. In order to dissolve the crystals 250 ml. of 96% ethanol was added and heated to the boiling point of ethanol for 5 min.. At the same time the β-keto acid was decarboxylated completely. After evaporation of the filtrate to dryness 2.03 g. (19.8% yield) of colorless plates, m. p. 80—81°, was obtained. For analysis the substance was recrystallized three times from methanol; m. p. 83—84°.

Anal. 8.850 mg. subst.: 24.56 mg. CO_2, 7.77 mg. H_2O
8.335 mg. subst.: 0.233 ml. N_2 (27°, 745 mm)
$C_{29}H_{45}O_3N$ (455.66) calc'd: C 76.44; H 9,91; N 3.07%
found: C 76.16; H 9.88; N 3.12%

Oxime. Obtained from [III] (250 mg.), hydroxylamine hydrochloride (100 mg.) and sodium acetate (150 mg.). Colorless crystals, m. p. 59—60°, from 96% ethanol.

Anal. 5.640 mg. subst.: 0.309 ml. N_2 (27.5°, 745 mm.)
$C_{29}H_{46}O_3N_2$ (468.67) calc'd: N 5.95%
found: N 6.10%

1-Aminoheneicosane [V]

Diethylene glycol (10 ml.), [III] (500 mg., 1.09 mMoles), hydrazine hydrate (1 ml.) and potassium hydroxide (1 g.) were heated at 140° for 1.5 hr. Heating was then continued at 230—240° for 2.5 hr. After cooling the flask content was poured into water and extracted three times with ether. After drying the ether extracts with potassium carbonate and evaporation of the solvent the resulting solid was crystallized from 2 ml. of 96% ethanol. Colorless leaflets (222 mg., 65.4% yield), m. p. 92—94°. For analysis the substance was recrystallized once more from ethanol; m. p. 93—94°.

Anal. 7.070 mg. subst.: 0.284 ml. N_2 (27.7°, 745 mm)
$C_{21}H_{45}N$ (311.58) calc'd: N 4.50%
found: N 4.47%

Oxalate. The acid salt was prepared in the usual manner. Three crystallizations from 96% ethanol gave colorless needles, m. p. 170—172° (decomp.).

Anal. 8.855 mg. subst.: 22.41 mg CO_2, 9.19 mg. H_2O
7.240 mg subst.: 0.226 ml. N_2 (26.5°, 750 mm)
$C_{23}H_{47}O_4N$ (401.61) calc'd: C 68.78; H 11.80; N 3.49%
found: C 69.06; H 11.61; N 3,51%

1-Benzoylamino-6-heneicosanone

ε-Benzoylaminocaproic acid chloride was prepared from 10 g. of the acid with oxalyl chloride in benzene solution. The crude, oily acid chloride was condensed with ditetrahydropyranyl sodiotetradecylmalonate prepared from 13.87 g. (165 mMoles) of dihydropyrane, 16.52 g. (55 mMoles) of tetradecylmalonic acid and 1.27 g. of powdered sodium. The reaction mixture was worked up in usual manner giving 23 g. of yellow oil which was dissolved in benzene and chromatographed on activated alumina. The benzene fractions (4.84 g.) were crystallized from 96% ethanol to give 580 mg. (2.7% yield) colorless prisms, m. p. 84—86°. Two more crystallizations from ethanol raised the m. p. to 94—95°.

Anal. 9.820 mg. subst.: 28.05 mg. CO_2, 9.97 mg. H_2O
7.995 mg. subst.: 0.214 ml. N_2 (21°, 752 mm)
$C_{28}H_{47}O_2N$ (429.66) calc'd: C 78.26; H 11.03; N 3,26%
found: C 77.95; H 11.36; N 3.08%

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

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IZVOD

Sinteza 1-amino-heneikosana

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1-Amino-heneikosan [V] je priređen kondenzacijom dibenzilnog estera tetradecil-malonske kiseline s kloridom ε-ftaloilamino-kapronske kiseline [III]. Opisane su ove tvari: 1. ε-Ftaloilamino-kapronska kiselina [II], t. t. 107°; 2. klorid ε-ftaloilamino-kapronske kiseline [III], t. v. 175—178°/0.2 mm.; 3. 1-ftaloilamino-6-heneikosanon [IV], t. t. 83—84°; oksim, t. t. 59—60°; 4. 1-amino-heneikosan [V], t. t. 93—94°; oksalat, t. t. 170—172° (rasp.); 5. 1-benzoilamino-6-heneikosanon, t. t. 94—95°.

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Primljeno 26. novembra 1955.