REACTION OF AMINO ALCOHOLS WITH CARBON DISULPHIDE

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ABSTRACT

 ω -Amino alcohols possessing five or more methylene units between the amino and hydroxyl groups on condensation with carbon disulphide gave good yields of 1,3-di-(ω -hydroxyalkyl) thioureas. These symmetrically disubstituted thioureas on oxidation gave the corresponding 1,3-di-(ω -hydroxyalkyl) ureas.

The investigation of the reaction of carbon disulphide with amino alcohols (1) has been extended to the longer chain ω -amino alcohols. The ω -amino alcohols having five or more methylene units between the amino and hydroxy groups combine with carbon disulphide to give 1,3-di-(ω -hydroxyalkyl) thioureas (II). A series of these symmetrical thiourea derivatives II have been prepared and their properties are listed in Table I. 1,3-Di-(5-hydroxypentyl)-thiourea (II, n = 5) was isolated as an oil and it was converted directly into the corresponding urea without further purification. The 1,3-di-(5-hydroxy-



pentyl)-, 1,3-di-(6-hydroxyhexyl)-, and 1,3-di-(7-hydroxyheptyl)-thioureas were oxidized in alkaline solution with hydrogen peroxide into the corresponding symmetrical urea derivatives III. 1,3-Di-(11-hydroxyundecyl)-thiourea was not oxidized under the same conditions but it was converted into 1,3-di-(11-hydroxyundecyl)-urea by refluxing with ethanolic silver nitrate solution (2).

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$HO(CH_2)_n NHCNH(CH_2)_n OH$												
		V:.1.1			C		H		N		s	
x	n	<i>%</i>	M.p., ° C.	Formula	Calc.	Found	Calc.	Found	Calc.	Found	Calc.	Found
0 \$ 0 \$ 0 \$ 0 \$ 0	$5 \\ 6 \\ 7 \\ 7 \\ 11 \\ 11$	$\begin{array}{c} 73.2\\ 81.5\\ 68.9\\ 69.0\\ 60.9\\ 69.3\\ 88.3 \end{array}$	$\begin{array}{c} 106.5 - 108.5 \\ 79.5 - 80.5 \\ 117 - 118 \\ 82.5 - 83 \\ 122.5 \\ 97 - 98.5 \\ 134.5 - 136 \end{array}$	$\begin{array}{c} C_{11}H_{24}N_2O_3\\ C_{13}H_{25}N_2O_2S\\ C_{13}H_{25}N_2O_3\\ C_{15}H_{32}N_2O_3S\\ C_{15}H_{32}N_2O_3\\ C_{23}H_{45}N_2O_2S\\ C_{23}H_{45}N_2O_3\\ \end{array}$	56.87 56.48 59.95 59.18 62.48 66.28 68.95	57.06 56.49 59.75 59.55 62.58 66.45 68.80	$10.41 \\ 10.21 \\ 10.84 \\ 10.59 \\ 11.19 \\ 11.61 \\ 12.08$	$10.14 \\ 10.23 \\ 10.83 \\ 10.35 \\ 11.00 \\ 11.81 \\ 12.11$	$\begin{array}{c} 12.06 \\ 10.14 \\ 10.76 \\ 9.20 \\ 9.72 \\ 6.72 \\ 6.99 \end{array}$	$11.96 \\ 10.21 \\ 10.96 \\ 8.96 \\ 9.71 \\ 6.74 \\ 6.78$	11.60 10.53 7.69	11.42 9.98 7.81

¹Manuscript received September 19, 1957.

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> Contribution from the L. G. Ryan Research Laboratories of Monsanto Canada Limited, Ville LaSalle, Quebec. Can. J. Chem. Vol. 36 (1958)

Other urea derivatives prepared for characterizing the amino alcohols were $1-(\alpha - naphthyl)-3-(6-hydroxyhexyl)$ -urea, 1-phenyl-3-(7-hydroxyheptyl)-urea, and $1-(\alpha - naphthyl)-3-(11-hydroxyundecyl)$ -urea.

EXPERIMENTAL²

5-Aminopentanol-1

5-Aminopentanol-1 (b.p. 119–120° C. at 17 mm.; m.p. 26–28° C.; n_D^{16} 1.4608) was prepared in 45.5% yield by the method of Putokhin (3). The previously reported (3) physical constants are m.p. 26° C., d_4^{17} 0.9488, and n_D^{17} 1.4618.

6-Aminohexanol-1

6-Aminohexanol-1 was prepared by a modification of Wallach's method (4). Metallic sodium (150 g., 6.52 moles) was added to a refluxing solution of caprolactam (30 g., 0.26 mole) in freshly distilled absolute ethanol (1500 cc.) at a sufficient rate to maintain vigorous reflux. The reaction was complete in $1\frac{1}{2}$ hours. The reaction mixture was steam distilled and the distillates were collected in 1 liter fractions. These fractions were acidified with hydrochloric acid and then evaporated to dryness. The first two fractions gave an impure hydrochloride melting at 215-235° C., yield 5.85 g. (16.25%). These crystals were considered to be impure hexamethylenimine hydrochloride, which Wallach reported (4) to melt at 236-237° C. The remaining distillate fractions gave a vellowish colored hydrochloride melting at 63-64° C., yield 28.91 g. (70.9%). This crude material (23.63 g., 0.15 mole) in absolute methanol (500 cc.) was passed through IRA-400 resin (1000 cc. of resin in the hydroxyl form previously washed with methanol) at a rate of 5 cc. per minute. The column of resin was washed with methanol (2500 cc.) and the eluate and washings were taken to dryness in vacuo under nitrogen. The product was distilled in vacuo under nitrogen. A crystalline product (b.p. 137-139° C. at 20 mm.) was obtained, yield 13.10 g. (42.1%). This crystalline product appeared to be dimorphous with one form melting at 57-58° C. and the other at 75-78° C. Wallach (4) reported a melting point of 55-56° C. Both forms gave one spot with a R_f value of 0.54 when chromatographed on Whatman No. 1 paper with butanol: acetic acid: water (4:1:5) solvent.

A sample (0.15 g., 0.001 mole) of 6-aminohexanol-1 was treated with α -naphthylisocyanate (0.218 g., 0.001 mole) in dry benzene (10 cc.). This suspension was refluxed for 1 hour. The gummy precipitate of 1- α -naphthyl-3-(6-hydroxyhexyl)-urea was removed by filtration and then crystallized from boiling acetone (5 cc.). A crop of colorless needles (m.p. 140–141° C.) was obtained, yield 0.265 g. (71.8%). The melting point was not changed by further crystallization. Anal. Calc. for C₁₇H₂₂N₂O₂: C, 71.30; H, 7.69; N, 9.78%. Found: C, 71.39; H, 7.83; N, 9.97%.

7-Aminoheptanol-1

Cycloheptanone oxime (b.p. $129-130^{\circ}$ C. at 23 mm.) was prepared in 94.4% yield by the method of Pearson and Bruton (5). It was then converted into enantholactam (b.p. $148-150^{\circ}$ C. at 10 mm.) in 82% yield by the method of Eck and Marvel (6).

Enantholactam (75.95 g., 0.6 mole) was converted into 7-aminoheptanol-1 hydrochloride by the method described above for the preparation of 6-aminohexanol-1. The first two distillates yielded a brownish oil (20 g.), which is probably impure heptamethylenimine hydrochloride. The residue from distillate fractions 3–7 was obtained as

²All melting points are uncorrected. Microanalyses were performed by Micro Tech Laboratories, Skokie, Illinois.

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brownish needles melting at $67-75^{\circ}$ C., yield 25.06 g. This crude 7-aminoheptanol-1 hydrochloride was dissolved in water (500 cc.) and the solution passed through a column of IRA-400 resin (600 cc. of resin in the hydroxyl form) at a rate of 5 cc. per minute. The column was washed with water (3500 cc.) and the eluate and washings were evaporated to dryness *in vacuo* under nitrogen. A crystalline distillate (b.p. 123° C. at 5 mm.; m.p. 48–53° C.) was obtained from the residue, yield 23.5 g. (29.9%). Wallach (4) reported a melting point of 48–50° C. for 7-aminoheptanol-1. A sample of the 7-aminoheptanol-1 (0.67 g., 0.0051 mole) in dry benzene (10 cc.) was treated with phenylisocyanate (0.61 g., 0.0051 mole). The product (m.p. 79.5–83° C.) was recovered by filtration, yield 1.25 g. (97%). One crystallization from acetone raised the melting point to 87–88° C. Anal. Calc. for C₁₄H₂₂N₂O₂: C, 67.16; H, 8.86; N, 11.20%. Found: C, 67.03; H, 8.71; N, 11.22%.

11-Bromoundecanoic Acid

11-Bromoundecanoic acid (m.p. 48° C.) was prepared in 69.9% yield from 11-undecanoic acid by the method of Ashton and Smith (7). The reported (7) melting point is 49.25° C.

11-Aminoundecanoic Acid

The patent procedure (8) for the preparation of 11-aminoundecanoic acid from 11bromoundecanoic acid gave a 78.4% yield of product melting at 182–185° C. The reported (9) melting point of 11-aminoundecanoic acid is 186–187° C.

11-Aminoundecanoic acid (47 g., 0.23 mole) in 3.5 N methanolic hydrogen chloride solution was allowed to stand at room temperature for 16 hours. After most of the methanol was removed *in vacuo*, the crude methyl ester hydrochloride (m.p. 158–161° C.) was recovered by filtration, yield 51.1 g. (86.8%). One crystallization from methanol raised the melting point to 159.5–160.5° C. Anal. Calc. for $C_{12}H_{26}CINO_2$: C, 57.24; H, 10.14; Cl, 14.09; N, 5.56%. Found: C, 57.33; H, 10.25; Cl, 14.35; N, 5.50%.

11-Aminoundecanol-1

Methyl 11-aminoundecanoate hydrochloride (m.p. 158–161° C.) (22.2 g., 0.088 mole) in methanol (400 cc.) was passed through a column of IRA-400 (OH) resin (400 cc. of resin previously washed with methanol) at a rate of 5–7 cc. per minute. The eluates and washings were evaporated to dryness *in vacuo* under nitrogen. The residue of crude methyl 11-aminoundecanoate melted at 70–85° C., yield 16.2 g. (85.3%). Pellets of metallic sodium (28 g., 1.2 moles) were added to the crude methyl ester (16.2 g., 0.075 mole) in absolute ethanol (500 cc.) at a rate to maintain the alcoholic solution at gentle reflux. After the solution cooled it was diluted with water (250 cc.) to decompose the excess sodium ethoxide. The methanol was removed *in vacuo* under nitrogen and the residual aqueous solution was extracted with chloroform. The chloroform extract was dried over anhydrous sodium sulphate and evaporated to dryness. A residue (m.p. 74–78° C.) of yellowish crystals was obtained, yield 4.0 g. (28.3%). This crude 11-aminodecanol-1 was purified by solution in warm methanol (13.5 cc./g.), and filtration and dilution of the filtrate with water (10 cc.). The final product melted at 71–73° C.

A sample (0.187 g., 0.001 mole) of 11-aminoundecanol-1 in dry benzene on treatment with α -naphthylisocyanate (0.169 g., 0.001 mole) gave 0.286 g. (80.2%) of crude 1- α -naphthyl-3-(11-hydroxyundecyl)-urea (m.p. 126–130° C.). Crystallization from acetone-benzene solution raised the melting point to 131° C. Anal. Calc. for C₂₂H₃₂N₂O₂: C, 74.11; H, 9.05; N, 7.86%. Found: C, 73.73; H, 9.05; N, 7.84%.

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The aqueous filtrate from the chloroform extraction gave 16.5 g. of material melting at 197-205° C. This is considered to be the crude sodium salt of 11-aminoundecanoic acid. On treatment with concentrated hydrochloric acid solution it gave 11-aminoundecanoic acid hydrochloride (m.p. 148-149° C.). The latter material did not depress the melting point of a known sample of 11-aminoundecanoic acid hydrochloride (m.p. 148-149° C.).

Reaction of Amino Alcohols with Carbon Disulphide

The amino alcohol (0.05 mole) in absolute alcohol (25 cc). was added dropwise over a period of 20 minutes to a stirred solution of carbon disulphide (0.025 mole) at 5° C.

After the reaction mixture had remained at room temperature for several hours, it was refluxed for 9 to 15 hours. The colored alcoholic solution was treated with Norite A and filtered. The product was recovered by evaporating the filtrate to dryness in vacuo under nitrogen. The crystals were purified by crystallizing from a suitable solvent such as ethyl acetate. The properties of the symmetrical 1,3-di-(ω -hydroxyalkyl) thioureas prepared in this manner are given in Table I.

$1,3-Di-(\omega-hydroxyalkyl)$ Ureas

Method A

The 1,3-di-(ω -hydroxyalkyl) ureas with the exception of 1,3-di-(11-hydroxyundecyl)urea were prepared in the manner described below for 1,3-di-(7-hydroxyheptyl)-urea.

To 1,3-di-(7-hydroxyheptyl)-thiourea (3.04 g., 0.01 mole) in alcoholic sodium hydroxide solution (34 cc. containing 0.8 g. of sodium hydroxide) hydrogen peroxide (5.08 cc. of 7.6 molar solution; 0.03 mole) was added dropwise at a temperature of 25–28° C. After the solution had been left at room temperature for 4 hours, it was diluted with water (250 cc.). The crystals (m.p. 121-122° C.) were recovered by filtration and dried, yield 2.77 g. (86.3%). One crystallization from absolute ethanol raised the melting point to 122-122.5° C.

Method B

1,3-Di-(11-hydroxyundecyl)-thiourea was converted in 88.3% yield into 1,3-di-(11hydroxyundecyl)-urea (m.p. 128-129° C.) by the method of Kjaer et al. (2). Two crystallizations from ethyl acetate - ethanol (1:1) solution along with one treatment with Norite A raised the melting point to 134.5–136° C.

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