the positive charge may be placed on a secondary carbon either γ or δ to the carboxyl function.

Experimental

β,γ-Butenoic Acid.—The substance was obtained by the acid hydrolysis[8] of the corresponding nitrile, which was in turn produced by the reaction[9] of allyl bromide with cuprous cyanide.

β,γ-Pentenoic Acid.—Crotyl bromide[10] was converted to crotononitrile by treatment with cuprous cyanide[11]; hydrolysis of the nitrile, which was separated from the isomeric methallyl cyanide by fractionation, was carried out according to the directions of Lane, *et al.*[12]

Δ^1-Cyclohexeneacetic Acid.—Cyclohexanone was subjected to a Reformatsky reaction,[13] and the resulting β-hydroxyester was dehydrated[14] with dry hydrogen chloride and subsequently hydrolyzed[2] under acidic conditions.

γ,δ-Pentenoic Acid.—The material was obtained by the hydrolysis and decarboxylation of diethyl allylmalonate.[15]

Δ^2-Cyclohexeneacetic Acid.—Sodium diethyl malonate was alkylated with 3-bromocyclohexene[16,17]; the resulting diester was hydrolyzed and decarboxylated.

δ,ϵ-Hexenoic Acid.—Allyl bromide, after conversion to the Grignard reagent, was treated with gaseous formaldehyde[18]; the resulting 3-butenol was transformed into butenyl bromide, which was in turn used to alkylate sodium diethyl malonate. Hydrolysis and decarboxylation of the substituted product led to the desired acid.

ϵ,ζ-Heptenoic Acid.—The procedure used for δ,ϵ-hexenoic acid was modified[19,20] by using ethylene oxide instead of formaldehyde.

Preparation of Iodolactones.—A solution of 5 mmoles of the acid in 30 cc. of 0.5 *N* sodium bicarbonate and a solution of 10 mmoles of iodine and 30 mmoles of potassium iodide in 15 cc. of water were mixed and allowed to stand in the dark for 24 hours. The dark precipitate which had separated was washed with water and then shaken with chloroform and aqueous thiosulfate until two almost colorless phases were obtained. The aqueous layer was extracted with chloroform, and the combined extracts were washed successively with aqueous bicarbonate and with water and finally dried over anhydrous sodium sulfate. The oil remaining after evaporation of the solvent was dried *in vacuo* for several hours, and the product (*ca.* 40% yield) was then analyzed.[21] In case the product solidified, it was recrystallized from ethanol–petroleum ether. Iodolactones are unstable, and therefore every attempt was made to purify, analyze and obtain the infrared spectrum of the lactone as soon as possible after the preparation was complete. The infrared spectra were obtained using matched sodium chloride cells with the lactone dissolved in chloroform. A Baird Automatic Infrared Spectrophotometer with a sodium chloride prism was used for the determination.

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MADISON, WISCONSIN

[CONTRIBUTION FROM THE COLLEGE OF PHARMACY, UNIVERSITY OF MICHIGAN]

The Preparation of Basic Alcohols and Basic Alkyl Chlorides which Contain a 1-Hexa-, 1-Hepta- or 1-Octamethylenimino Radical

BY F. F. BLICKE AND N. J. DOORENBOS[1,2]

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The preparation of eighteen basic alcohols and eighteen basic alkyl chlorides which contain a 1-hexamethylenimino, 2-methyl-1-hexamethylenimino, 4-methyl-1-hexamethylenimino, 1-heptamethylenimino or a 1-octamethylenimino radical has been described.

Basic alcohols and basic alkyl chlorides, which contain dialkylamino as well as polymethylenimino radicals (pyrrolidino and piperidino) as the basic substituents, have been used extensively for the preparation of such synthetic drugs as local anesthetics, antispasmodics, antihistaminics, analgesics and antimalarials. It seemed desirable to extend the series of basic alcohols and chlorides which contain polymethylenimino groups to include compounds which contain seven-, eight- and nine-membered rings, *i. e.*, hexa-, hepta- and octamethylenimino radicals. This project became feasible only after methods had been found by means of which hepta- and octamethylenimine could be obtained readily in relatively large amounts.

The five cyclic imines, used as intermediates, were synthesized by reduction of the required lactam with lithium aluminum hydride. Thus, ϵ-caprolactam yielded hexamethylenimine. 2-Methyl- and 4-methylcyclohexanone, treated with sodium azide and hydrochloric acid, produced 2-methyl-7-keto- and 4-methyl-2-ketohexamethylenimine, respectively, and these keto compounds yielded 2-methyl- and 4-methylhexamethylenimine. Cycloheptanone, sodium azide and hydrochloric acid produced 2-ketoheptamethylenimine which was reduced to heptamethylenimine. Cyclooctanone was treated with sodium azide and hydrochloric acid to produce 2-ketoöctamethylenimine which was reduced to octamethylenimine.

Incidentally, the N-formyl and methyl derivatives of heptamethyleimine was prepared and hexa-, hepta- and octamethylenimines were allowed to react with carbon disulfide to form polymethylenammonium polymethylenedithiocarbamates. Mannich reactions were carried out with the hydrochlorides of hepta- and octamethylenimine.

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[1] This paper represents part of a dissertation submitted by N. J. Doorenbos in partial fulfillment of the requirements for the Ph.D. degree in the University of Michigan, 1953.

[2] Michigan Chemical Corporation Fellow.

The basic alcohols were obtained by interaction of the required imine with ethylene (A), trimethylene (A) or propylene bromohydrin (B), or by interaction of a polymethylenimine with ethyl α-bromopropionate and reduction of the ethyl α-(1-polymethylenimino)-propionate produced with lithium aluminum hydride (C). Thionyl chloride converted the alcohols into the chloride hydrochlorides. In those instances in which the hydrochlorides were hygroscopic, the chlorides were characterized as picrates or methiodides.

$$\text{(A)}\quad \mathrm{RH} \xrightarrow{\mathrm{Br(CH_2)_xOH}} \mathrm{R(CH_2)_xOH} \xrightarrow{\mathrm{SOCl_2}}$$
$$\mathrm{R(CH_2)_xCl\cdot HCl} \quad \mathrm{R} = \text{1-polymethylenimino}, \; x = 2 \text{ or } 3$$

$$\text{(B)}\quad \mathrm{RH} \xrightarrow{\mathrm{BrCH_2C(CH_3)HOH}}$$
$$\mathrm{RCH_2C(CH_3)HOH} \xrightarrow{\mathrm{SOCl_2}} \mathrm{RCH_2C(CH_3)\cdot HCl}$$

$$\text{(C)}\quad \mathrm{RH} \xrightarrow{\mathrm{BrCH(CH_3)COOC_2H_5}}$$
$$\mathrm{RCH(CH_3)COOC_2H_5} \xrightarrow{\mathrm{LiAlH_4}}$$
$$\mathrm{RCH(CH_3)CH_2OH} \xrightarrow{\mathrm{SOCl_2}} \mathrm{RCH(CH_3)CH_2Cl\cdot HCl}$$

Some of the alcohols were converted into *p*-nitro- and *p*-aminobenzoates.

When a solution of 2-(1-heptamethylenimino)-ethyl chloride in isopropyl alcohol was refluxed for 24–48 hours, a high-melting compound, undoubtedly N,N,N′,N′-diheptamethylenepiperazinium dichloride, precipitated. 2-(1-Octamethylenimino)-ethyl and 2-(2-methyl-1-hexamethylenimino)-ethyl chloride behaved in a similar manner.

It was observed that when some of the basic chloride hydrochlorides and picrates were heated to a temperature which was a few degrees higher than that of their melting points and maintained at that temperature for a short time, the molten material would solidify; the solidified material exhibited a higher melting point than the original substance. This behavior was found to be due to the conversion of the salt of the chloride into the salt of an isomeric chloride. For example, 2-methyl-2-(1-hexamethylenimino)-ethyl chloride picrate was isomerized to 1-methyl-2-(1-hexamethylenimino)-ethyl chloride picrate. This type of isomerization has been reported[3] for other basic chlorides.

$$\mathrm{CH_3CH(X)CH_2Cl} \xrightarrow{\text{heat}} \mathrm{CH_3CH(Cl)CH_2X}$$

X = 1-hexamethylenimino (picrate), (2-methyl-1-hexamethylenimino) (picrate), (4-methyl-1-hexamethylenimino) (hydrochloride), 1-heptamethylenimino (hydrochloride) or 1-octamethylenimino (hydrochloride).

Experimental

Hexamethylenimine.[4]—Lithium aluminum hydride (100 g.) and 2 liters of ether were put into a 5-liter, 3-necked flask equipped with two modified[5] Soxhlet extractors. The extractors were charged with a total of 240 g. of ε-caprolactam and the ether was refluxed for 30 hours. The extractors were removed and the flask was fitted with a stirrer, dropping funnel and a condenser. Water (100 cc.) was added cautiously from the dropping funnel to the stirred mixture which was maintained at 0°. After filtration, the filter cake was washed with ether. From the dried ether solution 170.7 g. (81%) of the imine was obtained; b.p. 136–137°, $n^{20}\mathrm{D}$ 1.4658.

2-Methyl-7-ketohexamethylenimine.—A mixture of 250 cc. of concd. hydrochloric acid and 56 g. (0.5 mole) of 2-methylcyclohexanone was stirred, cooled in an ice-bath and 50 g. (0.77 mole) of sodium azide was added as rapidly as the evolution of nitrogen would permit. The mixture was stirred for 4 hours, sodium carbonate was added until the mixture was slightly alkaline, water was added to dissolve the inorganic salts, and the yellow oil which had separated was extracted with chloroform. The extract was dried over anhydrous sodium sulfate, the solvent was removed and the residue was distilled; b.p. 153–158° (20 mm.), m.p. 91–92°,[6] yield 45 g. (71%).

2-Methylhexamethylenimine.—The required lactam (157 g., 1.2 moles), dissolved in 2 liters of ether, was reduced with 70 g. (1.8 moles) of lithium aluminum hydride dissolved in 1 liter of ether. The yield of the imine was 126 g. (88%)[7,8]; b.p. 148–150° (747 mm.), $n^{20}\mathrm{D}$ 1.4588.

The hydrochloride melted at 202–203°[9] after recrystallization from isopropyl alcohol–ether.

Anal. Calcd. for $C_7H_{16}NCl$: N, 9.36; Cl, 23.69. Found: N, 9.34; Cl, 23.84.

4-Methylhexamethylenimine.—In order to obtain the required lactam, a mixture of 112.2 g. (1.0 mole) of 4-methylcyclohexanone and 500 cc. of concd. hydrochloric acid was treated with 97.5 g. (1.5 moles) of sodium azide in the manner described above. After the removal of the chloroform, the residue (the crude lactam) was dissolved in 1 liter of ether and added to a stirred suspension of 49.4 g. (1.3 moles) of lithium aluminum hydride in 500 cc. of ether. After the mixture had been stirred and refluxed for 36 hours, 60 cc. of water was added. The mixture was filtered, and the filtrate treated in the usual manner; b.p. 153–156° (748 mm.).[10]

2-Ketoheptamethylenimine. (A).—A mixture of 22.4 g. of cycloheptanone[11] and 100 cc. of concd. hydrochloric acid was treated with 20.0 g. of sodium azide in the manner which has been described. The yield of imine was 22.1 g. (87%); b.p. 147–150° (10 mm.).[12]

(B).—Concentrated sulfuric acid (100 cc.) was stirred and heated to 100°; 92 g. of cycloheptanone oxime[12] was added, dropwise, at such a rate that the temperature of the mixture could be maintained at 100–105°. The mixture was allowed to cool to room temperature, it was poured onto 500 g. of ice and the mixture was made alkaline with sodium hydroxide solution while the temperature was kept below 5°. The mixture was extracted with five 100-cc. portions of chloroform. The extract was dried over anhydrous magnesium sulfate, the solvent was removed and the product was distilled; b.p. 157–160° (18 mm.).

Heptamethylenimine.[4]—2-Ketoheptamethylenimine (100 g.), dissolved in 1 liter of ether, was reduced with 37 g. of lithium aluminum hydride suspended in 500 cc. of ether. There was obtained 70 g. (79%) of imine; b.p. 57–60° (17 mm.),[13] $n^{20}\mathrm{D}$ 1.4721.

The hydrochloride melted at 176–177° after recrystallization from acetone.[14]

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[3] E. M. Schultz and J. M. Sprague, THIS JOURNAL, **70**, 48 (1948).

[4] This method has been used previously by L. Ruzicka, M. Kobelt, O. Häfliger and V. Prelog (*Helv. Chim. Acta*, **32**, 544 (1949)). Presumably, they reduced only a small amount of the lactam, and they did not report the experimental details.

[5] See L. F. Fieser, "Experiments in Organic Chemistry," 2nd Ed., D. C. Heath and Co., New York, N. Y., p. 41.

[6] H. Schechter (THIS JOURNAL, **73**, 3087 (1951)) obtained this lactam in 70% yield with the use of sulfuric instead of hydrochloric acid; m.p. 90.5–91.5°. He showed that the isomeric compound, 6-methyl-7-ketohexamethylenimine is not formed in the reaction.

[7] A. Müller and P. Krauss (*Monatsh.*, **61**, 218 (1932)) obtained the imine in 8.6% yield by reduction of the lactam with sodium and alcohol.

[8] G. R. Clemo, R. Raper and H. J. Vipond (*J. Chem. Soc.*, 2095 (1949)) reduced the lactam with lithium aluminum hydride and isolated the imine in 44% yield.

[9] Ref. 7, m.p. 200°; ref. 8, m.p. 156°; S. Gabriel (*Ber.*, **42**, 1259 (1909)), m.p. 196°.

[10] G. R. Toy, Dissertation, University of Michigan, 1951, b.p. 154–156°.

[11] F. F. Blicke, N. J. Doorenbos and R. H. Cox, THIS JOURNAL, **74**, 2924 (1952).

[12] L. Ruzicka, M. Kobelt, O. Häfliger and V. Prelog, *Helv. Chim. Acta*, **32**, 544 (1949), b.p. 162–164° (22 mm.).

[13] Ref. 12, b.p. 75–77° (30 mm.), $n^{21}\mathrm{D}$ 1.4740.

[14] A. Müller, E. Srepel, E. Funder-Fritzsche and F. Dicher (*Monatsh.*, **83**, 386 (1952)) described the hydrochloride as hygroscopic; the melting point was not reported.

Anal. Calcd. for $C_7H_{16}NCl$: N, 9.36; Cl, 23.69. Found: N, 9.36; Cl, 23.55.

N-Formylheptamethylenimine.—Heptamethylenimine (11.3 g., 0.1 mole), dissolved in 50 cc. of chloroform, was placed in a 200-cc. three-necked flask fitted with a stirrer, dropping funnel and a condenser to which a calcium chloride tube was attached. The solution was stirred, cooled in an ice-bath and 14.7 g. (0.1 mole) of chloral,[15] dissolved in 50 cc. of chloroform, was added, dropwise. The solution was refluxed for 2 hours and then distilled; yield 13.2 g. (94%), b.p. 120–123° (11 mm.).

Anal. Calcd. for $C_8H_{15}ON$: N, 9.92. Found: N, 9.91.

N-Methylheptamethylenimine Hydrochloride.—The formyl derivative (12.0 g.), dissolved in 50 cc. of ether, was reduced with 5.0 g. of lithium aluminum hydride, suspended in 75 cc. of ether. After treatment in the usual manner, hydrogen chloride was passed into the ethereal solution of the N-methyl derivative. The precipitated hydrochloride weighed 12.6 g. (91%); m.p. 163–164° after recrystallization from methyl ethyl ketone.[16]

Anal. Calcd. for $C_8H_{18}NCl$: N, 8.56; Cl, 21.66. Found: N, 8.56; Cl, 21.49.

2-Ketoöctamethylenimine.[17]—This compound was obtained in the manner which has been described from 42.0 g. of cycloöctanone,[18] 167 cc. of concd. hydrochloric acid and 33.8 g. of sodium azide; yield 41.0 g. (88%), m.p. 69–71°.[19]

Octamethylenimine.[4]—2-Ketoöctamethylenimine (41.0 g.), dissolved in 200 cc. of ether, was reduced with 14.5 g. of lithium aluminum hydride dissolved in 200 cc. of ether. There was obtained 31.7 g. (86%) of the imine; b.p. 71–74° (11 mm.),[20] $n^{20}\mathrm{D}$ 1.4771.

The picrate melted at 150–151°[21] after recrystallization from ethanol.

The hydrochloride melted at 163–164° after recrystallization from acetone.

Anal. Calcd. for $C_8H_{18}NCl$: N, 8.56; Cl, 21.66. Found: N, 8.51; Cl, 21.41.

Hexamethylenammonium Hexamethylenedithiocarbamate.[22]—Carbon disulfide (5 cc.) was added to an ice-cold solution of 5.0 g. of hexamethylenimine in 200 cc. of absolute ether. The precipitate, which formed almost immediately, was filtered and washed with ether; yield 6.4 g. (91%), m.p. 141–142°.

Anal. Calcd. for $C_{13}H_{26}N_2S_2$: N, 10.21; S, 23.36. Found: N, 10.20; S, 23.71.

Heptamethylenammonium Heptamethylenedithiocarbamate.—Prepared in the manner described above, 5.0 g. of heptamethylenimine yielded 5.0 g. (75%) of the salt; m.p. 134–135°.

Anal. Calcd. for $C_{15}H_{30}N_2S_2$: N, 9.26; S, 21.20. Found: N, 9.27; S, 21.51.

Octamethylenammonium Octamethylenedithiocarbamate.—From 5.0 g. of octamethylenimine there was obtained 3.2 g. (50%) of the salt; m.p. 118–119°.

Anal. Calcd. for $C_{17}H_{34}N_2S_2$: N, 8.48; S, 19.40. Found: N, 8.44; S, 19.68.

Phenyl β-(1-Heptamethylenimino)-ethyl Ketone Hydrochloride.—A mixture of 7.5 g. of heptamethylenimine hydrochloride, 6.0 g. of acetophenone, 2.3 g. of paraformaldehyde, 3 drops of concd. hydrochloric acid and 15 cc. of absolute ethanol was refluxed for 1 hour. An additional 1.5 g. of paraformaldehyde was added and the material was refluxed for 2 hours. Boiling acetone (125 cc.) was added to the hot solution and the mixture was placed in a refrigerator. The precipitate was filtered and washed with ether; yield 8.4 g. (56%). The hydrochloride melted at 150–151° after recrystallization from ethanol–acetone.

Anal. Calcd. for $C_{16}H_{24}ONCl$: C, 68.19; H, 8.58; N, 4.97; Cl, 12.58. Found: C, 68.08; H, 8.69; N, 4.94; Cl, 12.41.

Phenyl β-(1-Octamethylenimino)-ethyl Ketone Hydrochloride.—From 5.7 g. of octamethylenimine hydrochloride, 4.3 g. of acetophenone, 3.2 g. of paraformaldehyde, 2 drops of concd. hydrochloric acid and 12 cc. of absolute ethanol there was obtained 4.9 g. (47%) of the hydrochloride; m.p. 145–146°.

Anal. Calcd. for $C_{17}H_{26}ONCl$: C, 69.02; H, 8.86; N, 4.73; Cl, 11.98. Found: C, 69.25; H, 9.12; N, 4.72; Cl, 11.96.

When 2-methylhexamethylenimine hydrochloride was treated with acetophenone and paraformaldehyde, in the manner described above, the imine hydrochloride was recovered unchanged.

Basic Alcohols and Salts (Tables III and IV).—Alcohols 1, 2 and 3 were prepared by the general process illustrated below. Compounds 4–13 were obtained by a similar procedure except that ethylene bromohydrin was replaced by trimethylene bromohydrin for compounds 4–8 and by propylene bromohydrin for compounds 9–13. Compound 4 was prepared also from allyl alcohol by the process described below.

2-(1-Heptamethylenimino)-ethanol (2).—Heptamethylenimine (28.0 g., 0.25 mole) was stirred and 15.6 g. (0.12 mole) of ethylene bromohydrin was added slowly. After the mixture had been stirred and heated for 14 hours on a steam-bath, it was cooled in an ice-bath and 6 g. of sodium hydroxide, dissolved in 60 cc. of water, was added. The organic layer was separated and the aqueous layer was extracted with ether. The combined organic layer and the extract were dried and distilled. The excess imine was recovered.

3-(1-Hexamethylenimino)-propanol (4).—Sodium (1.4 g. 0.061 mole) was added to 10.0 g. (0.17 mole) of allyl alcohol. After the sodium had dissolved, 6.0 g. (0.061 mole) of hexamethylenimine was added, the mixture was heated on a steam-bath for 90 hours, cooled and acidified with 20% hydrochloric acid. The mixture was extracted with ether and the extract was discarded. The solution was made basic with 20% sodium hydroxide solution, extracted with ether and the extract dried and distilled; yield 5.5 g. (58%), b.p. 115–117° (12 mm.). The hydrochloride melted at 153–154° after recrystallization from isopropyl alcohol–ether.

Alcohols 14–18 were prepared by reduction of ethyl α-(1-polymethylenimino)-propionate (Table I) with lithium aluminum hydride. The synthesis of the propionates and the manner in which they were reduced is illustrated below.

TABLE I

ETHYL α-(1-POLYMETHYLENIMINO)-PROPIONATES

$CH_3CH(R)COOC_2H_5$

	R	B.p., °C.	Mm.	Yield, %	$n^{20}\mathrm{D}$
1	1-Hexamethylenimino	118–120	16	92	1.4584
2	(2-Methyl-1-hexamethylenimino)	111–113	7	78	1.4591
3	(4-Methyl-1-hexamethylenimino)	117–119	10	68	1.4574
4	1-Heptamethylenimino	116–118	10	89	1.4630
5	1-Octamethylenimino	125–128	10	80	1.4682

TABLE II

ETHYL α-(1-POLYMETHYLENIMINO)-PROPIONATE SALTS

	Salt	M.p., °C.	Formula	Analyses, % Nitrogen Calcd.	Found	Halogen Calcd.	Found
1	HCl	137–138	$C_{11}H_{22}O_2NCl$	5.95	5.87	15.10	15.02
2	HCl	127–128	$C_{12}H_{24}O_2NCl$	5.62	5.58	14.22	14.16
3	HBr	104–105	$C_{12}H_{24}O_2NBr$	4.76	4.75	27.17	27.29
4	HCl	118–119	$C_{12}H_{24}O_2NCl$	5.62	5.59	14.22	14.14
5	HCl	102–103	$C_{13}H_{26}O_2NCl$	5.31	5.31	13.44	13.38

Compounds 1, 2 and 4 were recrystallized from isopropyl alcohol–ether and compounds 3 and 5 from methyl ethyl ketone.

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(15) F. F. Blicke and Chi-Jung Lu, THIS JOURNAL, **74**, 3933 (1952).

(16) It has been stated (ref. 14) that the hydrochloride is hygroscopic.

(17) L. Ruzicka, M. W. Goldberg, M. Hürbin and H. A. Boekenoogen (*Helv. Chim. Acta*, **16**, 1323 (1933)) obtained this substance in 70% yield from cycloöctanone, sulfuric acid and sodium azide.

(18) F. F. Blicke, J. Azuara, N. J. Doorenbos and E. B. Hotelling, THIS JOURNAL, **75**, 5418 (1953).

(19) Ref. 12, m.p. 72–73°.

(20) Ref. 12, b.p. 90–92° (24 mm.), $n^{21}\mathrm{D}$ 1.4777.

(21) Ref. 12, m.p. 135–136°; ref. 17, m.p. 148–149°.

(22) It was stated by A. M. Neal and B. M. Sturgis (U. S. patent 2,208,935; *C. A.*, **35**, 140 (1941)) that this dithiocarbamate was formed when hexamethylenimine, in aqueous solution, was treated with carbon disulfide.

TABLE III

BASIC ALCOHOLS

	R	B.p. °C.	Mm.	Yield, %	n^{22}_D
	RCH_2CH_2OH				
1	(2-Methyl-1-hexamethylenimino)	94–97	7	67	1.4790
2	1-Heptamethylenimino	109–112	14	87	1.4829
3	1-Octamethylenimino	112–116	9	72	1.4860
	$RCH_2CH_2CH_2OH$				
4	1-Hexamethylenimino	112–114	9	89	1.4825
5	(2-Methyl-1-hexamethylenimino)	119–122	7	74	1.4809
6	(4-Methyl-1-hexamethylenimino)	123–127	12	66	1.4780
7	1-Heptamethylenimino	121–124	9	79	1.4847
8	1-Octamethylenimino	144–148	15	58	1.4880
	$RCH_2CH(CH_3)OH$				
9	1-Hexamethylenimino	97–100	11	63	1.4680
10	(2-Methyl-1-hexamethylenimino)	96–98	7	59	1.4670
11	(4-Methyl-1-hexamethylenimino)	101–104	12	71	1.4643
12	1-Heptamethylenimino	109–112	11	84	1.4743
13	1-Octamethylenimino	127–129	15	47	1.4800
	$RCH(CH_3)CH_2OH$				
14	1-Hexamethylenimino	110–112	17	97	1.4748
15	(2-Methyl-1-hexamethylenimino)	113–116	11	94	1.4745
16	(4-Methyl-1-hexamethylenimino)	111–113	11	86	1.4705
17	1-Heptamethylenimino	109–112	10	70	1.4800
18	1-Octamethylenimino	134–138	16	92	1.4851

TABLE IV

SALTS OF BASIC ALCOHOLS

Compounds 1 and 15 were recrystallized from diisopropyl ketone, 2, 12 and 17 from ethanol–ether, 3, 10 and 16 from methyl ethyl ketone, 4, 5, 6, 9, 11 and 14 from isopropyl alcohol–ether, 7 from acetone–ether, 8, 13 and 18 from methyl ethyl ketone–ether.

				Analyses, %			
				Nitrogen		Halogen	
	Salt	M.p., °C.	Formula	Calcd.	Found	Calcd.	Found
1	Methiodide	213–215	$C_{10}H_{22}ONI$	4.68	4.69	42.41	42.22
2	Hydrochloride	76–77	$C_9H_{20}ONCl$	7.23	7.24	18.34	18.22
3	Hydrochloride	83–84	$C_{10}H_{22}ONCl$	6.75	6.78	17.11	17.01
4	Hydrochloride	153–154	$C_9H_{20}ONCl$	7.23	7.31	18.34	18.22
5	Hydrochloride	114–115	$C_{10}H_{22}ONCl$	6.75	6.72	17.11	17.16
6	Hydrochloride	115–116	$C_{10}H_{22}ONCl$	6.75	6.69	17.11	17.22
7	Hydrochloride	102–103	$C_{10}H_{22}ONCl$	6.75	6.71	17.11	17.04
8	Picrate	88–89	$C_{17}H_{26}O_8N_4$	13.52	13.47[a]		
9	Hydrochloride	131–132	$C_9H_{20}ONCl$	7.23	7.19	18.34	18.31
10	Methiodide	180–181	$C_{11}H_{24}ONI$	4.47	4.49	40.52	40.44
11	Hydrochloride	105–106	$C_{10}H_{22}ONCl$	6.75	6.83	17.11	17.08
12	Hydrochloride	110–111	$C_{10}H_{22}ONCl$	6.75	6.73	17.11	17.15
13	Picrate	137–138	$C_{17}H_{26}O_8N_4$	13.52	13.80[b]		
14	Hydrochloride	111–112	$C_9H_{20}ONCl$	7.23	7.16	18.34	18.20
15	Hydrochloride	121–122	$C_{10}H_{22}ONCl$	6.75	6.75	17.11	17.10
16	Methiodide	77–78	$C_{11}H_{24}ONI$	4.47	4.47	40.52	40.30
17	Hydrochloride	78–79	$C_{10}H_{22}ONCl$	6.75	6.72	17.11	17.18
18	Picrate	110–111	$C_{17}H_{26}O_8N_4$	13.52	13.62[c]		

[a] *Anal.* Calcd.: C, 49.27; H, 6.33. Found: C, 49.51; H, 6.61. [b] *Anal.* Calcd.: C, 49.27; H, 6.33. Found: C, 49.26; H, 6.95. [c] *Anal.* Calcd.: C, 49.27; H, 6.33. Found: C, 49.18; H, 6.38.

Ethyl α-(1-Hexamethylenimino)-propionate (1).—Hexamethylenimine (79.2 g., 0.8 mole) was stirred and 72.4 g. (0.4 mole) of ethyl α-bromopropionate was added, dropwise. The mixture was stirred and heated for 12 hours on a steam-bath, cooled in an ice-bath and 20 g. of sodium hydroxide, dissolved in 150 cc. of water, was added. The organic layer was separated and the aqueous portion extracted with ether. The organic layer and the extract were combined, dried over anhydrous magnesium sulfate, and distilled. The excess imine was recovered.

2-Methyl-2-(1-hexamethylenimino)-ethanol (14).—Lithium aluminum hydride (5.0 g., 0.13 mole) and 300 cc. of ether were placed in a 500-cc., three-necked flask fitted with a stirrer, dropping funnel and a condenser to which a soda-lime tube was attached. The flask was cooled in an ice-bath, the mixture was stirred and 19.0 g. (0.095 mole) of ethyl α-(1-hexamethylenimino)-propionate, dissolved in 70 cc. of ether, was added, dropwise. The mixture was stirred and refluxed for 12 hours. The flask was cooled in an ice-bath, the mixture was stirred rapidly and 7 cc. of water was added, dropwise. After the material had been stirred for one-half hour at room temperature, it was filtered through a sintered-glass funnel, and the inorganic material was washed with ether. The ether solution was dried, the solvent removed and the product was distilled.

The hydrochlorides of the *p*-nitrobenzoates (Table V) and of the *p*-aminobenzoates (Table VI) were obtained in the manner illustrated below.

2-(1-Hexamethylenimino)-ethyl *p*-Nitrobenzoate Hydrochloride.—*p*-Nitrobenzoyl chloride (6.9 g., 0.037 mole), dissolved in 100 cc. of dry benzene, was added slowly to a mixture of 4.9 g. (0.034 mole) of 2-(1-hexamethylenimino)-ethanol and 25 cc. of benzene The solvent refluxed during the addition and a precipitate formed. The mixture was stirred for 2 hours and the product was then filtered and washed with benzene.

2-(1-Hexamethylenimino)-ethyl *p*-Aminobenzoate Hydrochloride.—A solution of 8.5 g. (0.026 mole) of 2-(1-hexamethylenimino)-ethyl *p*-nitrobenzoate hydrochloride in 100 cc. of absolute ethanol was hydrogenated in the presence of 0.15 g. of platinum oxide catalyst under an initial pressure of 50 pounds. The hydrogenation was continued for about one hour after the calculated amount of hydrogen had been absorbed (total time about 1.5 hours). The mixture was warmed to dissolve the product which had precipitated, filtered and the solvent removed from the filtrate under reduced pressure. The semi-solid was covered with dry ether and placed in a refrigerator whereupon the product became crystalline.

Salts of Basic Chlorides (Table VII).—The basic chloride hydrochlorides were prepared in the manner illustrated be-

TABLE V

HYDROCHLORIDES OF *p*-NITROBENZOATES: p-$O_2NC_6H_4COOR \cdot HCl$

Compounds 1, 2, 4, 5 and 7 were recrystallized from isopropyl alcohol, 6 from ethanol and 3 from acetone.

					Analyses, %			
					Nitrogen		Chlorine	
	R	Yield, %	M.p., °C.	Formula	Calcd.	Found	Calcd.	Found
1	2-(1-Hexamethylenimino)-ethyl	92	176–177	$C_{15}H_{21}O_4N_2Cl$	8.52	8.49	10.79	10.81
2	2-(1-Heptamethylenimino)-ethyl	96	163–164	$C_{16}H_{23}O_4N_2Cl$	8.18	8.13	10.34	10.42
3	2-(1-Octamethylenimino)-ethyl	92	182–183	$C_{17}H_{25}O_4N_2Cl$	7.85	7.79	9.94	10.06
4	3-(1-Hexamethylenimino)-propyl	96	192–193	$C_{16}H_{23}O_4N_2Cl$	8.18	8.17	10.34	10.40
5	1-Methyl-2-(1-hexamethylenimino)-ethyl	92	157–158	$C_{16}H_{23}O_4N_2Cl$	8.18	8.21	10.34	10.26
6	2-Methyl-2-(1-hexamethylenimino)-ethyl	96	174–175	$C_{16}H_{23}O_4N_2Cl$	8.18	8.15	10.34	10.26
7	2-Methyl-2-(1-heptamethylenimino)-ethyl	85	165–166	$C_{17}H_{25}O_4N_2Cl$	7.85	7.77	9.94	9.89

TABLE VI

HYDROCHLORIDES OF *p*-AMINOBENZOATES: p-$H_2NC_6H_4COOR \cdot HCl$

Compounds 1, 3, 4 and 5 were recrystallized from methanol and 2 and 6 from ethanol.

					Analyses, %			
					Nitrogen		Chlorine	
	R	Yield, %	M.p., °C.	Formula	Calcd.	Found	Calcd.	Found
1	2-(1-Hexamethylenimino)-ethyl	96	207–208	$C_{15}H_{23}O_2N_2Cl$	9.38	9.38	11.87	11.81
2	2-(1-Heptamethylenimino)-ethyl	95	193–194	$C_{16}H_{25}O_2N_2Cl$	8.96	8.95	11.33	11.40
3	2-(1-Octamethylenimino)-ethyl	96	182–183	$C_{17}H_{27}O_2N_2Cl$	8.57	8.53	10.85	10.68
4	3-(1-Hexamethylenimino)-propyl	88	262–263	$C_{16}H_{25}O_2N_2Cl$	8.96	8.94	11.33	11.21
5	2-Methyl-2-(1-hexamethylenimino)-ethyl	96	192–193	$C_{16}H_{25}O_2N_2Cl$	8.96	8.93	11.33	11.34
6	2-Methyl-2-(1-heptamethylenimino)-ethyl	94	190–191	$C_{17}H_{27}O_2N_2Cl$	8.57	8.55	10.85	10.71

TABLE VII

SALTS OF BASIC CHLORIDES

Compounds 1, 9', 10, 14' and 15 were recrystallized from methyl ethyl ketone–heptane, 2, 4, 6, 9, 11, 12, 14 and 16 from isopropyl alcohol–ether, 3 from acetone and 5, 7, 8, 12, 17 and 18 from methanol–ether.

						Analyses, %			
						Nitrogen		Chlorine	
	R	Salt	M.p., °C.	Yield, %	Formula	Calcd.	Found	Calcd.	Found
			RCH_2CH_2Cl						
1	(2-Methyl-1-hexamethylenimino)	Picrate	127–128	80	$C_{15}H_{21}O_7N_4Cl$	13.84	13.75	8.76	8.75
2	1-Heptamethylenimino	HCl	193–194	92	$C_9H_{19}NCl_2$	6.60	6.56	33.44	33.41
3	1-Octamethylenimino	HCl	205–207	90	$C_{10}H_{21}NCl_2$	6.20	6.17	31.38	31.43
			$RCH_2CH_2CH_2Cl$						
4	1-Hexamethylenimino	HCl	208–209	79	$C_9H_{19}NCl_2$	6.60	6.65	33.44	33.27
5	(2-Methyl-1-hexamethylenimino)	HCl	113–114	89	$C_{10}H_{21}NCl_2$	6.20	6.15	31.38	31.43
6	(4-Methyl-1-hexamethylenimino)	HCl	158–159	79	$C_{10}H_{21}NCl_2$	6.20	6.23	31.38	31.21
7	1-Heptamethylenimino	HCl	164–165	80	$C_{10}H_{21}NCl_2$	6.20	6.18	31.38	31.38
8	1-Octamethylenimino	HCl	147–148	67	$C_{11}H_{23}NCl_2$	5.83	5.78	29.52	29.55
			$RCH_2CH(CH_3)Cl$						
9	1-Hexamethylenimino	HCl	198–199	74	$C_9H_{19}NCl_2$	6.60	6.56	33.44	33.33
9'	1-Hexamethylenimino	Picrate	127–128		$C_{15}H_{21}O_7N_4Cl$	13.84	13.76	8.76	8.79
10	(2-Methyl-1-hexamethylenimino)	Picrate	102–103	88	$C_{16}H_{23}O_7N_4Cl$	13.38	13.25	8.47	8.42
11	(4-Methyl-1-hexamethylenimino)	HCl	176–177	75	$C_{10}H_{21}NCl_2$	6.20	6.19	31.38	31.47
12	1-Heptamethylenimino	HCl	158–159	85	$C_{10}H_{21}NCl_2$	6.20	6.23	31.38	31.46
13	1-Octamethylenimino	HCl	127–128	62	$C_{11}H_{23}NCl_2$	5.83	5.80	29.52	29.57
			$RCH(CH_3)CH_2Cl$						
14	1-Hexamethylenimino	HCl	198–199	88	$C_9H_{19}NCl_2$	6.60	6.48	33.44	33.46
14'	1-Hexamethylenimino	Picrate	117–118	..	$C_{15}H_{21}O_7N_4Cl$	13.84	13.68	8.76	8.75
15	(2-Methyl-1-hexamethylenimino)	Picrate	89–90	57	$C_{16}H_{23}O_7N_4Cl$	13.38	13.48	8.47	8.40
16	(4-Methyl-1-hexamethylenimino)	HCl	158–159	74	$C_{10}H_{21}NCl_2$	6.20	6.23	31.38	31.27
17	1-Heptamethylenimino	HCl	132–133	67	$C_{10}H_{21}NCl_2$	6.20	6.21	31.38	31.34
18	1-Octamethylenimino	HCl	115–117	65	$C_{11}H_{23}NCl_2$	5.83	5.83	29.52	29.37

low. Since the hydrochlorides of compounds 10 and 15 (Table VII) could not be obtained in pure form, the crude hydrochlorides, in aqueous solution, were treated with picric acid whereupon the picrates precipitated.

3-(1-Heptamethylenimino)-propyl Chloride Hydrochloride (7).—3-(1-Heptamethylenimino)-propanol (3.4 g., 0.020 mole), dissolved in 50 cc. of benzene, was added, dropwise, to a stirred solution of 2.6 g. (0.022 mole) of thionyl chloride in 75 cc. of benzene. The mixture was stirred and refluxed for 2 hours, and the benzene was then removed. The dark, semi-solid residue was dissolved in methanol, the solution was treated with Norite and filtered. Dry ether was added to the hot filtrate until it became turbid, and the mixture was then place in a refrigerator whereupon the product precipitated gradually in crystalline form.

N,N,N',N'-Diheptamethylenepiperazinium Dichloride.—A solution of 2-(1-heptamethylenimino)-ethyl chloride (obtained from 1.0 g. of the hydrochloride) in 25 cc. of isopropyl alcohol was refluxed for 26 hours. The precipitated product was filtered and washed with ether; yield 0.36 g. (41%), m.p. 285–286° dec.

Anal. Calcd. for $C_{18}H_{36}N_2Cl_2$: N, 7.98; Cl^-, 20.18. Found: N, 7.94; Cl^-, 19.92.

N,N,N′,N′-Dioctamethylenepiperazinium Dichloride.—The base, obtained from 2.4 g. of the hydrochloride, was treated in the manner described above; yield 0.37 g. (20%), m.p. 275–276° dec.

Anal. Calcd. for $C_{20}H_{40}N_2Cl_2$: N, 7.38; Cl^-, 18.66. Found: N, 7.37; Cl^-, 18.62.

N,N,N′,N′-Di-(1-methylhexamethylene)-piperazinium Dichloride.—The base was isolated from 3.0 g. of the required hydrochloride, and treated as described above. The product weighed 1.2 g. (49%); m.p. 276–277° dec.

Anal. Calcd. for $C_{18}H_{36}N_2Cl_2$: N, 7.98; Cl^-, 20.18. Found: N, 7.93; Cl^-, 20.14.

Isomerization.—It was found that the hydrochlorides of the two isomeric compounds, 2-methyl-2-(1-hexamethylenimino)-ethyl chloride (14) and 1-methyl-2-(1-hexamethylenimino)-ethyl chloride (9), melted at the same temperature (m.p. 198–199°, mixed m.p. 198–199°). When each of these hydrochlorides was converted into a picrate, one picrate (14′) melted at 117–118°, the other (9′) at 127–128°. We believe that during the melting point determination, the one hydrochloride (14) was converted into the isomeric hydrochloride (9).

2-Methyl-2-(1-hexamethylenimino)-ethyl chloride picrate, m.p. 117–118°, was heated at 130° for 4 minutes. The material was then crystallized from methyl ethyl ketone-heptane, and it proved to be 1-methyl-2-(1-hexamethylenimino)-ethyl chloride picrate; mixed m.p. 127–128°.

Four other compounds (Table VII, 15, 16, 17 and 18) behaved in a similar manner and yielded the four isomers (Tables VII, 1, 11, 12 and 13).

$$\text{Cpd. 15 (m.p. 89–90°)} \xrightarrow{105°} \text{cpd. 10 (mixed m.p. 102–103°)}$$

$$\text{Cpd. 16 (m.p. 158–159°)} \xrightarrow{162–165°} \text{cpd. 11 (mixed m.p. 176–177°)}$$

$$\text{Cpd. 17 (m.p. 132–133°)} \xrightarrow{140°} \text{cpd. 12 (mixed m.p. 158–159°)}$$

$$\text{Cpd. 18 (m.p. 115–117°)} \xrightarrow{125°} \text{cpd. 13 (mixed m.p. 127–128°)}$$

The free bases of 14, 16, 17 and 18 (Table VII) did not isomerize, in ether solution, during a two-hour period at room temperature.

During distillation, the base of 17 isomerized to the base of 12.

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[Contribution from the Department of Chemistry, Massachusetts Institute of Technology]

Organic Peroxides. XIX. α-Hydroperoxyethers and Related Peroxides

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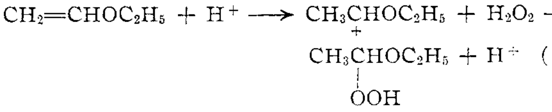
Several α-hydroperoxyethers have been synthesized by the controlled addition of hydrogen peroxide to the corresponding vinyl ethers. Some of the reactions of these hydroperoxides which have a bearing on their structure have been studied and elucidated. Some of these reactions include spontaneous or thermal decomposition or decomposition in the presence of ferrous ions.

It has been known for some time[2–4] that ethers form peroxides when exposed to air or oxygen. Although the initial peroxides are assumed to be α-hydroperoxyethers very few instances are known in which peroxides of this structure have been isolated in the pure state. With the single exception of 2-hydroperoxytetrahydrofuran[5,6] the peroxides isolated are secondary products which belong to the highly explosive alkylidene peroxide group.[7] For example, from ethyl and diisopropyl ethers only the polymeric ethylidene peroxide[4] and the trimeric isopropylidene (acetone) peroxide[8,9] were isolated, respectively.

Rieche and Meister[4] attempted the synthesis of α-hydroperoxyethyl ether by the dehydration of a mixture of α-hydroxyethyl hydroperoxide and ethanol with phosphorus pentoxide but they obtained a highly explosive viscous oil which behaved more like ethylidene peroxide than α-hydroperoxyethyl ether. We now wish to report a successful synthesis of this and other α-hydroperoxyethers by the modification of a method originally published from this Laboratory.[10] α-Hydroperoxyethyl ether was synthesized by allowing hydrogen peroxide to add to ethyl vinyl ether in the presence of a trace of sulfuric acid as a catalyst.



$$CH_2{=}CHOC_2H_5 + H^+ \longrightarrow CH_3\overset{}{\underset{+}{C}}HOC_2H_5 + H_2O_2 \longrightarrow \underset{\displaystyle\mathrm{OOH}}{CH_3\underset{|}{C}HOC_2H_5} + H^+ \quad (1)$$

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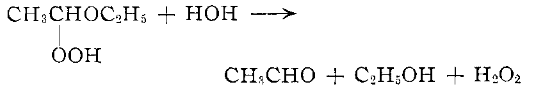
This peroxide was easily purified by distillation and was found to have the correct analysis for the formula assigned to it. Furthermore, a Zerewitinoff determination indicated the presence of one active hydrogen and an infrared spectrum showed a prominent band at 11.92 μ due to the hydroperoxy group, a broadened band at 3 μ due to the hydroxyl group of the hydroperoxy radical and a strong ether band at 9 μ. Upon heating with water, it decomposed quantitatively in accordance with equation 2. When treated with ferrous ions at 0 to 5° it gave mainly ethyl acetate. This reaction



$$\underset{\displaystyle\mathrm{OOH}}{CH_3\underset{|}{C}HOC_2H_5} + HOH \longrightarrow CH_3CHO + C_2H_5OH + H_2O_2 \quad (2)$$

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