portions of ice-cold petroleum ether and dried, yield 0.065 g. The data of White and Brown[31] on the effect of oleic acid on the yield of cold petroleum ether insoluble tetrabromostearic acid obtained from linoleic acid under these conditions permit the calculation of a 28% content of linoleic acid in this crude semi-hydrogenation product. The crude bromination product, after recrystallization from ethylene chloride, melted at 113.2–113.8°; after mixing with an approximately equal amount of authentic linoleic acid tetrabromide[32] (m.p. 114.4–115.2°), the mixture melted at 113.8–115.3°.

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Tris-(hydroxymethyl)-aminomethane Derivatives. II. Alkylation Products[1,2]

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Tris - (hydroxymethyl) - aminomethane, $(HOCH_2)_3CNH_2$, (I) by reason of the plurality of functional groups, presents interesting possibilities as an intermediate for synthetic work. In a previous publication from this Laboratory,[4] highly water-soluble aliphatic polyhydroxyamines derived from I were described.

We now wish to report the preparation of the N-alkyl and N-arylalkyl derivatives listed in Table I.

TABLE I

ALKYL- AND ARYLALKYLTRIS-(HYDROXYMETHYL)-METHYLAMINE HYDROBROMIDES AND HYDROCHLORIDES[a] $RNHC(CH_2OH)_3 \cdot HX$

R	Empirical formula	M.p., °C. (uncor.)	Halogen,[b] % Calcd.	Found
C_2H_5	$C_6H_{16}O_3BrN$	90–92	34.73	35.28
n-C_4H_9	$C_8H_{20}O_3BrN$	93–94	30.96	31.07
n-C_6H_{13}	$C_{10}H_{24}O_3BrN$	99–100.5	27.92	28.55
$CH_2{=}CHCH_2$	$C_7H_{16}O_3BrN$	Sirup	33.01	32.54
$CH_2BrCHBrCH_2$[5,c]	$C_7H_{16}O_3Br_3N$	118–120	19.88[d]	19.92
n-$C_5H_{11}OCOCH_2$	$C_{11}H_{24}O_5ClN$	Sirup	12.41	12.77
$HOOCCH_2$	$C_6H_{14}O_5ClN$	Sirup	16.44	16.56
p-$O_2NC_6H_4CH_2$	$C_{11}H_{17}O_5ClN_2$	160–162	12.11	12.06
p-$H_2NC_6H_4CH_2$[5,e]	$C_{11}H_{20}O_3Cl_2N_2$[f]	171–172	23.70	23.31[g]

[a] Acknowledgment is made to Dr. R. S. Murphey for assistance in the preparation of some of these compounds. [b] Acknowledgment is made to E. E. Bowden for most of the analyses and to R. L. Kersey and W. E. Reid, Jr., for a few of the analyses. [c] Prepared in 92% yield by bromination of allyltris-(hydroxymethyl)-methylamine hydrobromide, in chloroform solution. Purified by solution in methanol, precipitation with ether and recrystallization from acetone and benzene. [d] Ionizable halogen. [e] Prepared by reduction of p-nitrobenzyltris-(hydroxymethyl)-methylamine with hydrogen gas with Raney nickel as catalyst and conversion of the free base to the dihydrochloride. [f] In this case type formula is $RNHC(CH_2OH)_3 \cdot 2HX$. [g] The chloride analysis was made after decomposition of this compound in a Parr bomb. Volhard titration could not be carried out because of the unexpected solubilizing action of this substance on silver chloride.

Experimental

General Alkylation Procedure.—N-Alkylation of I was carried out in alcohol solution, usually in glass tubes at approximately 110° for 12 to 15 hours, with the alkyl halide and I in equimolar quantities. By this method I was alkylated with ethyl, n-propyl, n-butyl, n-amyl and n-hexyl bromides, with p-nitrobenzyl chloride and amyl chloroacetate.

In the isolation and purification of n-hexyltris-(hydroxymethyl)-methylamine hydrobromide, excess hydrobromic acid was added to the reaction mixture, the mixture was evaporated to a sirup and extracted with acetone. The product was precipitated from the acetone solution with ether and recrystallized three times from nitromethane and three times from acetone and dry ether. By the same general method, except for the use of nitromethane, ethyl- and n-butyltris-(hydroxymethyl)-methylamine hydrobromides were obtained in crystalline form but the n-propyl and n-amyl derivatives were obtained as sirups with bromine analyses distinctly high. On similar treatment, except vacuum evaporation of the solvent, n-amyl tris-(hydroxymethyl)-methylaminoacetate hydrochloride was obtained as a sirup. On hydrolysis of this compound, evaporation of the solvent and drying in a desiccator, tris-(hydroxymethyl)-methylaminoacetic acid hydrochloride was obtained as a sirup.

Allyltris-(hydroxymethyl)-methylamine Hydrobromide, $CH_2{=}CHCH_2NHC(CH_2OH)_3 \cdot HBr$.—A mixture of 48.4 g. of (I) (0.4 mole), 24.2 g. of allyl bromide (0.2 mole) and 200 ml. of absolute ethanol was refluxed for 72 hours. Excess (I)·HBr was removed by filtering, concentrating the filtrate and filtering, treatment of the filtrate with anhydrous hydrogen bromide until it was acidic and filtering. The total recovery of (I)·HBr was 46.5 g. (0.23 mole). This indicated a reaction of 0.17 mole or 85% of theory. On evaporation of the filtrate and drying the residue in a vacuum oven there was obtained 41.9 g. (86.4%) of crude allyltris-(hydroxymethyl)-methylamine hydrobromide, a viscous red oil.

p-Nitrobenzyltris-(hydroxymethyl)-methylamine, p-$O_2NC_6H_4CH_2NHC(CH_2OH)_3$.[5]—The reaction mixture of p-nitrobenzyl chloride and (I), in alcohol, was acidified with hydrochloric acid and diluted with water to form a 25% aqueous alcohol solution. The solution was extracted with toluene, made basic with sodium hydroxide and extracted immediately with ether. A precipitate started to form in the lower, light yellow layer within a few minutes. This precipitate of p-nitrobenzyltris-(hydroxymethyl)-methylamine and others obtained by concentration of the mother liquor, were purified by recrystallization from alcohol and water; m.p. 137–138°. *Anal.* Calcd. for $C_{11}H_{16}O_5N_2$: N, 10.94. Found: N, 10.78.

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[3] Taken in part from a thesis submitted by John Wotiz in partial fulfillment of the requirements for the degree of Master of Science.

[4] J. S. Pierce and John Wotiz, THIS JOURNAL, **66**, 879–881 (1944).

[5] Reported by H. E. Thompson, C. P. Swanson and A. G. Norman, *Bot. Gazette*, **107**, 476 (1946), but no m.p. or analysis is given.