Tolyl Ethers of Choline[1]

The tolyl ethers of choline were prepared by a modification of the method used by Renshaw and Armstrong for the preparation of other aryl ethers.[3]

β-Cresoxy-ethyl Bromides.—One mole of the appropriate cresol and 2 moles of ethylene dibromide were suspended in water, stirred and heated to boiling. One mole of sodium hydroxide in 50% solution was added slowly and refluxing was continued for two hours. The lower oily layer was separated, washed free of alkali, dried and fractionated. The products so obtained are described in Table I.

TABLE I

β-CRESOXY-ETHYL BROMIDES

Compound	B. p., °C. (18 mm.)	Formula	Bromine, % Calcd.	Found	
Ortho	142.0–142.5	$C_9H_{11}OBr$	37.19	37.10	37.12
Meta	146.5–147.0	$C_9H_{11}OBr$	37.19	37.18	37.15
Para	136.0–138.0	$C_9H_{11}OBr$	37.19	37.00	37.19

Cresoxy-ethyl-trialkylammonium Bromides.—One mole of cresoxyethyl bromide in toluene solution and 1.2 moles of trimethylamine were mixed in a pressure bottle and heated to 40° for seventy-two hours. The precipitated solid was filtered and crystallized. The triethyl homologs were prepared similarly except that the time required for complete reaction was about one month at 60°. The products obtained are described in Table II.

TABLE II

CRESOXY-ETHYL-TRIALKYLAMMONIUM BROMIDES

$CH_3C_6H_4OCH_2CH_2NR_3^+Br^-$

R		M. p., °C.	Formula	Bromine, % Calcd.	Found	
CH_3	Ortho[a]	157.5	$C_{12}H_{20}NOBr$	29.20	29.30	29.19
	Meta[a]	145.4	$C_{12}H_{20}NOBr$	29.20	29.09	29.10
	Para[c]	144.0	$C_{12}H_{20}NOBr$	29.20	29.01	29.20
C_2H_5	Ortho[b]	152.0–152.5	$C_{15}H_{26}NOBr$	25.30	25.50	25.41
	Meta[b]	136.4	$C_{15}H_{26}NOBr$	25.30	25.31	25.40
	Para[d]	134.5	$C_{15}H_{26}NOBr$	25.30	25.23	25.41

[a] Purified by precipitation from ethyl acetate solution with amyl acetate. [b] Crystallized from acetone-ethyl acetate mixture. [c] Crystallized from acetone. [d] Crystallized from acetone–amyl acetate mixture.

---

[1] These compounds were prepared by A. R. Goldfarb[2] under the direction of the late Professor R. R. Renshaw.

[2] Present address Lawrence, Richard, Bruce, Inc., Stamford, Connecticut.

[3] Renshaw and Armstrong, *J. Biol. Chem.*, **103**, 187 (1933).

CHEMICAL LABORATORY
NEW YORK UNIVERSITY
NEW YORK, N. Y.
A. R. GOLDFARB

RECEIVED JUNE 9, 1941

Aryl and Alkyl Ethers of β-Methylcholine[1]

The syntheses of the intermediates and final products are reported.

1-Dialkylamino-propanol-2.—Dimethylamine from 50 g. of dimethylamine hydrochloride was passed through a mixture of 54 g. of propylene oxide and 50 cc. of methanol at 60°, under a reflux condenser. The addition of dimethylamine was regulated to last three hours. The mixture was fractionated twice through a fractionating column; 53 g. (70%) of product was obtained, b. p. 124.5–126.0° at 758 mm.

Anal. Calcd. for $C_5H_{13}ON$: N, 13.58. *Found:* N, 13.48, 13.52.

The diethyl homolog was prepared by a modification of the method described by Callsen and Hahl[3] in which methanol was used instead of water. In this case the yields were consistently 10% higher than those reported by Callsen and Hahl and obtained by this author using water; 72 g. of diethylamine was mixed with 59 g. of propylene oxide under reflux. No reaction occurred until the catalyst, 20 cc. of methanol, was added. After about five minutes, a strongly exothermic reaction set in, causing the reaction mixture to boil. After one hour the reflux subsided and the mixture was refluxed for one hour longer. The reaction product was fractionated twice, yielding 115 g. of product which boiled at 62.5–63.5° at 22 mm.

Anal. Calcd. for $C_7H_{17}ON$: N, 10.61. Found: N, 10.65, 10.70.

2-Chloropropyl-1-dialkylammonium Chlorides.—One-half mole of dialkylamino-propanol-2 in 100 cc. of dry chloroform was added slowly to a well-stirred solution of 60 cc. of thionyl chloride in 500 cc. of dry chloroform, cooled to −5 to 0°. The addition required two hours and the mixture was allowed to stand for two hours longer in the freezing mixture. At no time in this interval was the temperature of the reaction mixture permitted to rise above 0°. The chloroform was distilled off at a low temperature, alcohol was added and the alcohol was distilled *in vacuo* on a water-bath. The addition and distillation of alcohol was repeated until the distillate was free of the odor of sulfur dioxide. The solid was crystallized twice from an ethanol–ethyl acetate mixture. Yields consistently higher than 70% were obtained.

Anal. Calcd. for $C_5H_{13}NCl_2$: Cl, 22.44. Found: Cl, 22.48, 22.56. Calcd. for $C_7H_{17}NCl_2$: Cl, 19.05. Found: Cl, 19.18, 19.00.

Reaction of β-Chloropropyl-dialkylammonium Chlorides with Sodium Alcoholates and Arylates.—The β-chloropropyl-dialkylammonium chloride (one mole) was dissolved in the alcohol corresponding to the ether which was to be formed. A solution of 2.2 atoms of sodium metal, dissolved in the same alcohol, was added to the solution with stirring. The reaction mixture was heated on a water-bath for twenty-four hours and then filtered. The filtrate was fractionated through a one-foot column. The aryl ethers were prepared in the same manner, using anhydrous methyl alcohol as solvent, and the required phenol.

It was found necessary that the solvents be absolutely anhydrous, since small amounts of water hydrolyze the chloro compound rapidly. Average yields of 40–50% were obtained and the properties of the free amines are given in Table I. The amines were not analyzed but were converted directly to the quaternary ammonium salts.

Ethers of β-Methylcholine Iodide.—β-Aryloxy and β-alkoxy-propyl-dimethyl amines were treated with excess

---

[1] These compounds were prepared by A. R. Goldfarb[2] under the direction of the late Professor R. R. Renshaw.

[2] Present address: Lawrence, Richard, Bruce, Inc., Stamford, Connecticut.

[3] German Patent 430,960.

TABLE I

ALKYL AND ARYL ETHERS

Of 1-Dialkylamino-propanol-2, $CH_3CHOR'CH_2NR_2$				Of beta methyl choline, $CH_3CHORCH_2NR'_3I^-$				
		B. p.,				Iodine, %		
R	R′	°C.	Mm.	M. p., °C.	Formula	Calcd.	Found	
CH_3	CH_3	113–116	760	155.5–156.0[a]	$C_7H_{18}ONI$	48.99	48.99	49.12
	C_2H_5	133–135	760	144.5[b]	$C_8H_{20}ONI$	46.48	46.51	46.35
	i-C_3H_7	140–145	758	145.5[b]	$C_9H_{22}ONI$	44.21	44.00	44.10
	n-C_4H_9	55–58	18	156.5–157.0[c]	$C_{10}H_{24}ONI$	42.15	42.30	42.16
	C_6H_5	143–144	18	139.5–140.0[d]	$C_{12}H_{20}ONI$	39.53	39.41	39.45
	o-$C_6H_4CH_3$	132–135	18	141.0–142.0[d]	$C_{13}H_{22}ONI$	37.88	38.03	37.91
	m-$C_6H_4CH_3$	136–140	12	130.0–131.0[d]	$C_{13}H_{22}ONI$	37.88	37.82	37.91
	p-$C_6H_4CH_3$	140–143	15	140.0–141.0[d]	$C_{13}H_{22}ONI$	37.88	37.81	37.85
C_2H_5	CH_3	46–47	12	....	...	...	....	
	C_2H_5	70–72	18	....	...	...	....	
	i-C_3H_7	60–63	10	129.0–130.0[e]	$C_{12}H_{28}ONI$	38.60	38.80	38.83
	n-C_4H_9	63–65	10	....	...	...	....	
	C_6H_5	125–126	11	....	...	...	....	
	o-$C_6H_4CH_3$	141	12	128.0[b]	$C_{16}H_{28}ONI$	33.62	33.60	33.55
	m-$C_6H_4CH_3$	141–142	10	129.0–130.0[d]	$C_{16}H_{28}ONI$	33.62	33.50	33.52
	p-$C_6H_4CH_3$	144–146	14	138.0–139.0[c]	$C_{16}H_{28}ONI$	33.62	33.50	33.65

[a] Crystallized from chloroform–ethyl acetate solution. [b] Crystallized from amyl acetate–amyl alcohol solution. [c] Crystallized from amyl acetate. [d] Crystallized from ethyl acetate. [e] The oily product was dissolved in acetic anhydride and precipitated over a period of months by layering with dry ether.

methyl iodide in toluene solution. The reaction was vigorous and required cooling. The average yields were 65–80%.

β-Aryloxy and β-alkoxy-propyl-diethyl amines were treated with excess ethyl iodide in toluene solution. The mixture was heated on a water-bath under reflux for several hours. The yields obtained were 35–50%. Table I gives the properties of the substances prepared.

CHEMICAL LABORATORY
NEW YORK UNIVERSITY
NEW YORK, N. Y. A. R. GOLDFARB

RECEIVED JUNE 9, 1941

p-Bromophenacyl Esters

Three unreported *p*-bromophenacyl esters of acids have been prepared by the method outlined by Shriner and Fuson.[1] The melting points were taken with calibrated total immersion Anschütz thermometers.

***p*-Bromophenacyl Oxalate.**—The fine white plates from acetone, which were nearly insoluble in absolute alcohol, melted at 242° with decomposition.

Anal. Calcd. for $C_{18}H_{12}O_6Br_2$: C, 44.65; H, 2.50. Found: C, 44.50; H, 2.56.

Methyl *p*-Bromophenacyl Succinate.—Methyl hydrogen succinate was prepared by reaction of succinic anhydride with methanol, the product being recrystallized from carbon disulfide. The *p*-bromophenacyl ester formed white plates when recrystallized from dilute methyl alcohol, m. p. 104.6–104.8°.

Anal. Calcd. for $C_{13}H_{13}O_5Br$: C, 47.43; H, 3.98. Found: C, 47.45; H, 4.08.

Methyl *p*-Bromophenacyl Glutarate.—Sodium methylglutarate was prepared by a method analogous to that reported for sodium ethylglutarate.[2] White plates of the *p*-bromophenacyl ester are formed on recrystallization from dilute methyl alcohol, m. p. 46.6–46.8°.

Anal. Calcd. for $C_{14}H_{15}O_5Br$: C, 48.91; H, 4.41. Found: C, 48.96, 48.99; H, 4.53, 4.57.

DEPARTMENT OF CHEMISTRY
THE OHIO STATE UNIVERSITY DAVID T. MOWRY
COLUMBUS, OHIO WALLACE R. BRODE

RECEIVED JUNE 2, 1941

---

[1] Shriner and Fuson, "Identification of Organic Compounds," John Wiley and Sons, Inc., New York, N. Y., 1935, p. 144.

[2] Mol, *Rec. trav. chim.*, **26**, 379 (1907).