

and recrystallized from dilute ethanol. This pure anilide was a white crystalline compound; m. p. 176–177° (uncor.), yield 4.4 g. (67%).

Anal. Calcd. for $C_{14}H_{10}O_2Cl_3N$: N, 4.25. Found: N, 4.52.

2,4,6-Trichlorophenoxyacetanilide.—This compound was prepared according to the procedure described for 2,4,5-trichlorophenoxyacetanilide using 5 g. of the corresponding acyl chloride. This anilide was a white crystalline solid; m. p. 107–108° (uncor.), yield 4.1 g. (63%).

Anal. Calcd. for $C_{14}H_{10}O_2Cl_3N$: N, 4.25. Found: N, 4.20.

Phenyl Esters

Phenyl Phenoxyacetate.³—To 5 g. of phenoxyacetyl chloride in an erlenmeyer flask was added dropwise an alkaline solution containing an equivalent amount of phenol dissolved in 10% sodium hydroxide. The reaction mixture was heated over a steam-bath for thirty minutes and then cooled. The ester crystallized out and was purified by recrystallization from dilute ethanol. The white crystalline product melted at 56–57° (uncor.); yield 5.0 g. (73%), sapon. equiv. calcd. for $C_{14}H_{12}O_2$ 228.0, found 224.0.

Phenyl 2-Chlorophenoxyacetate.—This phenyl ester was prepared from the corresponding acyl chloride according to the procedure described for phenyl phenoxyacetate. Five grams of the acyl chloride gave 4.9 g. (80%) of phenyl 2-chlorophenoxyacetate, a white crystalline solid; m. p., 58–59° (uncor.); sapon. equiv. calcd. for $C_{14}H_{11}O_2Cl$, 262.7, found, 262.2.

Phenyl 4-Chlorophenoxyacetate.—Used 5 g. of 4-chlorophenoxyacetyl chloride. This phenyl ester melted at 73–74° (uncor.); yield, 4 g. (63.5%); sapon. equiv. calcd. for $C_{14}H_{11}O_2Cl$, 262.7, found, 276.0.

Phenyl 2,4-Dichlorophenoxyacetate.—This compound was prepared from 5 g. of 2,4-dichlorophenoxyacetyl chloride by the method described for phenyl phenoxyacetate. Recrystallization of the ester from dilute ethanol gave 5.1 g. (82%) of product; m. p., 100–101° (uncor.); sapon. equiv. calcd. for $C_{14}H_{10}O_2Cl_2$ 297.2, found 301.5.

Phenyl 2,4,5-Trichlorophenoxyacetate.—A solution of 5 g. of the acyl chloride and an equivalent amount of phenol dissolved in 10% sodium hydroxide was treated as described for the preparation of phenyl phenoxyacetate. Recrystallization from dilute ethanol gave 4 g. (70%) of white crystalline product; m. p., 116–117° (uncor.), sapon. equiv. calcd. for $C_{14}H_9O_2Cl_3$, 331.6, found 336.0.

Phenyl 2,4,6-Trichlorophenoxyacetate.—Five grams of 2,4,6-trichlorophenoxyacetyl chloride and an equivalent

amount of phenol were used in alkaline solution. The resulting phenyl ester was recrystallized from dilute ethanol. The yield of ester was 4.5 g. (75%); m. p. 84.5–85° (uncor.), sapon. equiv. found 332.0.

Determination of the saponification equivalents of the six phenyl esters presented several experimental difficulties. Because of the formation of phenol upon acidification of the hydrolytic mixture, certain experimental errors were introduced which rendered the usual procedure employed for determination of saponification equivalents inaccurate and unreliable.

Therefore, the following procedure was employed. An accurately weighed sample (0.2 to 0.5 g.) of the phenyl ester was introduced into an erlenmeyer flask and a measured excess of 0.25 *N* sodium hydroxide solution added. The flask was then attached to a water cooled condenser and the mixture refluxed for six to eight hours or until the ester disappeared. At the end of this time, the mixture was allowed to cool and a calculated excess of 0.25 *N* hydrochloric acid was added from a buret. At this point the total volume of the mixture was noted. The excess acid was then backtitrated with standard alkali to the end point of phenolphthalein as indicator.

The titration error due to the production of phenol was corrected by weighing out the theoretical amount of pure phenol as was present in the weighed sample of phenyl ester, and preparing an aqueous solution of the same molar concentration and volume as that of the saponification mixture after addition of the excess standard acid. The aqueous phenolic solution was then titrated with 0.25 *N* sodium hydroxide solution to the end point of phenolphthalein. The number of milliequivalents thus obtained was subtracted from the total number of milliequivalents of standard alkali used in saponification of the phenyl ester.

Summary

The preparation of 2,4,5- and 2,4,6-trichlorophenoxyacetyl chlorides from the corresponding acids has been reported. The reaction of these acyl chlorides with ammonia, aniline, ethanol and phenol has been investigated.

The phenyl esters chlorophenoxy-, 2-chlorophenoxy-, 4-chlorophenoxy-, 2,4-dichlorophenoxy-, 2,4,5-trichlorophenoxy- and 2,4,6-trichlorophenoxy acetate were prepared.

Several new compounds were prepared and identified.

NASHVILLE, TENNESSEE

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(3) Morel, *Bull. soc. chim.*, [3] 21, 967 (1899); m. p. 58°.

[CONTRIBUTION FROM THE G. W. CARVER FOUNDATION, TUSKEGEE INSTITUTE]

The Preparation and Properties of Some Branched-Chain Alkyl Bromomethyl Ethers

By HAROLD W. LUCIEN¹ AND CLARENCE T. MASON²

The importance of the halomethyl ethers as intermediates in synthesis, and the greater reactivity of the bromomethyl ethers³ make necessary the present investigation to extend the knowledge of the branched-chain bromomethyl ethers.

(1) A part of this article is taken from the thesis presented to the graduate faculty of Tuskegee Institute by Harold W. Lucien, in partial fulfillment of the requirement for the degree of Master of Science. Presented at the September, 1948, Meeting of the American Chemical Society, St. Louis, Mo.

(2) Director of Research, George W. Carver Foundation, Tuskegee Institute, Alabama.

(3) Hamonet, *Compt. rend.*, 138, 814 (1904).

The Henry synthesis and its modifications^{4–7} are carried out by saturating equimolar quantities of an alcohol-aldehyde mixture with a hydrogen halide. In the present work branched-chain bromoethers were prepared by the Henry synthesis,⁴ Wedekind's adaptation,⁷ and two new modifications of Henry's method. When pre-

(4) Henry, *Bull. acad. roy. Belg.*, [3] 25, 439 (1938).

(5) Karvonen, *Acad. sci. Fennicae*, 3A, 1 (1912); *C. A.*, 14, 2175 (1920).

(6) Blair and Henze, *THIS JOURNAL*, 54, 399 (1932).

(7) Wedekind, German patent 135,310, Aug. 31, 1901; *Chem. Zentr.*, 73, II, 1164 (1902).

TABLE I
PHYSICAL CONSTANTS OF SOME BRANCHED-CHAIN ALKYL ETHERS

Ether, 1-bromomethoxy	B. p. °C.	Mm.	Yield, %	Analyses Calcd.	Br, % Found	d_{25}^4	n_D^{25}	Molar Calcd.	Refraction Found	L_D cal./g.
-1-Methylethane	75-76	196	70(a), 85(c), 87(d)	52.15	52.21	1.3454	1.4251	30.080	30.849	68.7
-2-Methylpropane	52-53	30	79(a), 96(c), 98(d)	47.83	47.85	1.2350	1.4400	34.698	35.887	60.1
-3-Methylbutane	128-129	247	80(a), 96(c), 98(d)	44.13	44.21	1.2013	1.4489	39.316	40.769	56.9
-2-Methylbutane	67-68	16	79(a), 91(c), 98(d)	44.13	44.19	1.2291	1.4671	39.316	40.892	64.2
-1-Methylpropane	106-108	357	75(a), 97(d)	47.83	47.86	1.2550	1.4453	34.698	35.799	58.1
-1-Methylhexane	68-69	4	76(a), 92(c), 96(d)	38.22	38.39	1.1295	1.4537	48.552	50.109	58.4
-1-Methylheptane	71-72	3	77(a), 93(c)	35.82	35.91	1.1009	1.4562	53.170	54.894	75.4

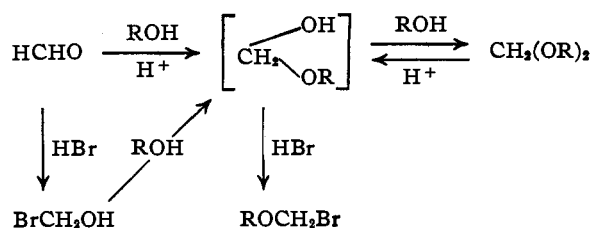
^a By Henry's synthesis. ^b By Wedekind's method modified by using calcium chloride during the preparation. ^c From molar quantities of bromomethanol and an alcohol with hydrogen bromide.

pared by known methods the yields reported for straight-chain ethers were not achieved, due, in part, to the easier formation of alkyl halides. A mixture composed of the bromomethyl ether, formals and alkyl halides was isolated from Henry's synthesis. Unless the amount of water was reduced during these preparations, an excess of hydrogen bromide was necessary to complete the reaction.

The use of molar quantities of calcium chloride in conjunction with the Wedekind modification of Henry's synthesis boosted yields by about 15%. From the reaction of the alcohol with bromoethanol, yields of the order of 97% were obtained. Contaminated bromomethyl tertiary alkyl ethers were isolated in small amounts by all of the methods employed, but their preparation in high yields does not appear imminent.

The ease of preparation, yield, boiling point, refractive index and stability of the bromoethers prepared increase with molecular weight; the density and heat of vaporization⁸ vary in an inverse manner. The exaltation increases with carbon content, being about 0.2 times the number of carbon atoms. These properties are summarized in Table I.

The formation of bromoethers from the reaction between an alcohol and bromomethanol appeared to take place by way of a hemiformal as an intermediate. It was not possible to isolate nor identify the compound suspected to be a hemiformal, due to the ease of formal formation. It was possible to obtain a bromoether from the reaction between a formal, paraformaldehyde, and hydrogen bromide.⁹ The reactions encountered suggest the mechanism



(8) Calculated by substituting ρ and T data in the Clapeyron-Clausius equation.

(9) $\text{ROCH}_2\text{OR} + 2\text{HBr} + \text{HCHO} \rightarrow 2\text{ROCH}_2\text{Br} + \text{H}_2\text{O}$.

Experimental

All alcohols and paraformaldehyde were obtained from Fisher Scientific Co. and were of the highest grade of purity. Bromomethanol was prepared according to Henry¹⁰ and di-isobutyl formal was prepared by the method of Favre.¹¹

Bromomethyl Alkyl Ethers. A. By the Henry Synthesis.⁴—Into a three-neck flask fitted with thermometer, stirrer and an inlet and outlet tube for hydrogen bromide, were placed one mole of the alcohol and 80 ml. of 37-38% formaldehyde solution. The flask was cooled to -5° and hydrogen bromide bubbled through the mixture until an excess of 1 mole accumulated in the flask. During the addition, the temperature was not allowed to rise above 25° . The crude bromoether was separated from the aqueous layer and dried for two hours over anhydrous calcium chloride. The products which resulted were amber in color, fumed on contact with air, and were lachrymatory. After drying, the crude bromoether was placed in an apparatus arranged for reduced pressure distillation, and the excess hydrogen bromide removed at 20 mm. pressure by bubbling nitrogen through the mixture. The product was distilled under reduced pressure.

B. By Wedekind's Modification⁷ of the Henry Synthesis.—Procedure A was modified by substituting 30.0 g. of paraformaldehyde for 80 ml. of a 37-38% formaldehyde solution.

C. By a Modification of the Wedekind Procedure.—Procedure B was modified by using molar quantities of calcium chloride to remove the water as it was formed, and using only 1 mole of hydrogen bromide to 1 mole of alcohol and 30 g. of paraformaldehyde. The resulting product was decanted from the solid material and the latter extracted three times with 25-ml. portions of isopropyl ether. After the removal of ether by distillation, the bromoether was combined with the extract and purified as in procedure A.

D. By the Reaction between Bromomethanol and an Alcohol.—Into a 500-ml. erlenmeyer flask containing 74.1 g. (1 mole) of isobutyl alcohol was placed 111.1 g. (1 mole) of bromomethanol. The temperature rose to 50° and after an hour the mixture had cooled and two water-insoluble layers remained. The bottom layer was more dense than water, the top layer was less dense than water, and constantly decomposed to the more dense product and an aqueous solution. The total water-insoluble portion was dried and purified as before and yielded 153.1 g. (91.6%) 1-bromomethoxy-2-methylpropane, b. p. $51-53^\circ$ at 30 mm., n_D^{25} 1.4402, d_{25}^4 1.2352.

Anal. Calcd. for $\text{C}_4\text{H}_{11}\text{BrO}$: Br, 47.83; *MR*, 34.698. Found: Br, 47.94; *MR*, 34.889.

Experiment D was repeated to find some indication of hemiformal formation in the top layer which was constantly changing to bromomethyl isobutyl ether, but all attempts to isolate a hemiformal from this layer resulted in the isolation of di-isobutyl formal, b. p. $164-166^\circ$,

(10) Henry, *Rec. trav. chim.*, **23**, 16 (1904).

(11) Favre, *Compt. rend.*, **119**, 285 (1894).

n_D^{25} 1.4003, d_4^{25} 0.8389. The product obtained also had a mixed boiling point with di-isobutyl formal (Favre,¹¹ b. p. 164.5°) of 164–166°.

The general procedure developed for the preparation of the bromoethers was similar to method D. Equimolar quantities of bromomethanol and an alcohol were intimately mixed and reduced pressure was applied to the flask containing the mixture. At the first indication of the formation of water, the use of reduced pressure was discontinued and the reaction was allowed to proceed of its own accord.

E. By the Reaction between a Formal, Paraformaldehyde and Hydrogen Bromide.—Into a 250-ml. round-bottom flask, cooled by running tap water and containing 50.6 g. (0.5 mole) of di-isobutyl formal, was placed 15 g. of paraformaldehyde. Hydrogen bromide was bubbled through the mixture until two layers separated, and thereafter for five minutes. The product of the reaction was isolated as in procedure A and yielded 76.8 g. (91.5%) of bromomethyl isobutyl ether, b. p. 40–42° at 23 mm., n_D^{25} 1.4401, d_4^{25} 1.2350.

Anal. Calcd. for $C_6H_{11}BrO$: Br, 47.83; *MR*, 34.698. Found: Br, 47.91; *MR*, 35.887.

The Identification of the Alkyl Portions of the Bromomethyl Alkyl Ethers.—A 10-g. sample of the purified bro-

moether was hydrolyzed by refluxing with 20 ml. of a 10% solution of sodium hydroxide for thirty minutes. The alcohol obtained was isolated and the 3,5-dinitrobenzoate prepared. The ester obtained was compared with that obtained from the known alcohol by melting point and mixed melting point determinations.

Acknowledgment.—The authors wish to express gratitude to the Research Corporation for a Frederick Gardner Cottrell grant which helped to support this investigation.

Summary

The bromomethyl ethers of seven branched-chain alcohols in the C_3 to C_1 range have been prepared. The physical constants determined include the boiling point, density, refractive index and the heat of vaporization. Evidence suggests the possibility that these bromomethyl alkyl ethers are formed in the Henry synthesis by way of a hemiformal as an intermediate.

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The Two-Step Reduction-Oxidation of Thiaxanthone-5-dioxide and Thiaxanthanol-5-dioxide¹

BY HANS HEYMANN

In connection with another investigation the synthesis of the acetate of thiaxanthanol-5-dioxide was required. The interesting color phenomena exhibited by this ester, by the related alcohol and by the corresponding ketone prompted the study reported here. Carl Graebe^{1a} had noted that thiaxanthone-5-dioxide gives blue solutions when heated with zinc and alkali or on heating with alcoholic potassium hydroxide; he observed that the color disappeared on continued heating with zinc and base. Ullmann and Glenck² found that the compound can be vatted with alkaline dithionite to give colored solutions. Recently Amstutz and his collaborators have again noted color phenomena akin to those seen by the earlier workers, and have voiced the suggestion that the colors appearing during the reduction of thiaxanthone-5-dioxides are due to semiquinone intermediates.³ The same thought had occurred to us and we wish to present substantiation of the hypothesis in the present paper.⁴

(1) A preliminary report of this work was presented to a meeting of the Oregon Academy of Science on Jan. 17, 1948, in Salem, Oregon.

(1a) Graebe and Schulthess, *Ann.*, **263**, 11 (1891).

(2) Ullmann and Glenck, *Ber.*, **49**, 2509 (1916).

(3) Amstutz, Fehnel and Hunsberger, *THIS JOURNAL*, **70**, 133 (1948).

(4) Our work had been in progress for over a year when Dr. Amstutz's publication appeared. In his friendly reply to our inquiry Dr. Amstutz informed us that he does not intend to investigate, at the present time, the oxidation-reduction properties of the thiaxanthone dioxides.

A. Preparative Part

The synthetic reactions are summarized in the accompanying flow sheet. The ketone I was obtained according to well-known procedures.^{1,2} Reduction to thiaxanthanol-5-dioxide was achieved smoothly by means of zinc dust in 80% acetic acid, conditions under which substituted sulfone-ketones like I may be reduced to the corresponding thiaxanthene-5-dioxides.³ The alcohol II melts sharply when heated relatively rapidly (*ca.* 0.5° per minute), but the behavior of a sample that is permitted to resolidify after melting indicates that a change accompanies protracted heating: the alcohol is transformed into the ether V, much as benzhydrol upon distillation goes to benzhydryl ether.

The carbinol II may be acetylated smoothly with acetic anhydride in pyridine to yield the acetate IV, and the same compound is conveniently prepared by reductive acetylation of I in the presence of little triethylamine. Larger amounts of base lead to the formation of small quantities of a yellow by-product of unknown nature. The acetate IV was also obtained by displacement with silver acetate of the bromine atom in 10-bromothiaxanthene-5-dioxide (VI), which was the sole product of the action of bromine in carbon tetrachloride on III. The correlation described confirms the assignment of the bromine atom to position 10.

The conditions of hydrolysis or displacement of