The physical properties and yields of the 1,2-dialkoxyethanes prepared are given in Table I. The 1,2-dipropoxyethane has been identified by its physical constants, its stability to acids (showing it not to be an acetal) by cleavage with zinc chloride and acetic acid to give propyl acetate, and by carbon-hydrogen analyses.

Experimental

Halogenated Ethers.—The chloromethyl alkyl ethers prepared by the method of Henry[4] were dried over phosphorus pentoxide for 20 minutes and distilled immediately before using.

1,2-Dialkoxyethanes.—One mole of the chloromethyl alkyl ether was slowly dropped into 1.2 gram-atoms of sodium shot covered with sodium-dried ether, the rate of addition being such as to maintain a slow reflux. After the addition had been completed, the reaction mixture was stirred overnight, filtered, the solvent removed, and the product distilled. It is interesting to note that this reaction does not occur with 1-chloro-1-alkoxyethane. The results of this latter reaction will be reported later.

Acknowledgment.—This work was performed with the aid of U. S. Navy funds, and under a contract with the Office of Naval Research. We acknowledge also the help of Mr. Bennie Lacy, graduate chemistry student, in preparing some of the above compounds.

[4] L. Henry, *Bull. chim. soc. Belg.*, [2] **44**, 458 (1885).

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Acetyl Bromide as a Possible Intermediate in the Reaction of Acetaldehyde with Bromine in Aqueous Ethanol[1]

BY NORMAN N. LICHTIN AND FELIX GRANCHELLI

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Farkas, *et al.*,[2] have demonstrated that both acetic acid and ethyl acetate are formed when acetaldehyde, formed *in situ* by the oxidation of aqueous ethanol by bromine, is further oxidized by this reagent. They also proved that the ester does not result from esterification of acetic acid and postulated that it arises from oxidation of the hemiacetal of acetaldehyde while the acid is derived from the hydrate. An excellent analogy for this hypothesis is to be found in work of Isbell[3,4] who assembled compelling evidence that δ-lactones are produced directly on oxidation of several mono- and disaccharides by bromine in aqueous solution buffered with barium carbonate-carbon dioxide, and concluded that the pyranose hemiacetal sugars are the actual reactants. Very recently Mosher and Preiss[5] have demonstrated that with chromic acid as oxidant hemiacetals are more reactive than the corresponding free aldehydes and yield esters directly.

Both the products and the second-order kinetics which maintain[2,6] in the oxidation of acetaldehyde by bromine in aqueous ethanol are, however, consistent with an alternative possibility, namely, that acetaldehyde is converted in the rate-determining step to acetyl bromide which then rapidly undergoes solvolysis to a mixture of acid and ester. Acyl halides have been observed in reactions of aldehydes and bromine or chlorine. Thus, it has been reported that on treatment with dry chlorine in the absence of solvent, acetaldehyde[7] and benzaldehyde[8] yield the respective acid chlorides. The latter reacts[9] with bromine in the absence of solvent to yield α-bromobenzyl benzoate, a compound which was found to form rapidly from the reaction of benzoyl bromide with benzaldehyde.

A direct test of the hypothesis that acetyl bromide is an intermediate in the reaction of acetaldehyde in aqueous ethanol solution is made possible by the work of Farkas, *et al.*[2,10] These workers carried out the reaction at 25°, in the presence of bromate, in a solvent containing 41% by weight of ethanol. This reagent removes hydrogen bromide which otherwise catalyzes equilibration of acid and ester. Under these conditions they found that the molar ratio of ester to acid does not change significantly as the reaction proceeds and its value, approximately 2.3, is quite different from that at equilibrium, 0.87. If acetyl bromide is, in fact, an intermediate, its solvolysis in 41% aqueous ethanol at 25° must yield the former ratio provided that equilibration of esterification is slow compared to the rate of solvolysis.

Experimental

Acetyl bromide was distilled as needed from an all-glass rectifying column protected from moisture: b.p. 75.9° at 767 mm., $d^{23.2}$ 1.650. On titration with sodium hydroxide, 96.6% of the theoretical amount of acid was found. Solvolysis in aqueous ethanol (approx. 4:1) yielded 99.0% of theoretical bromide (Mohr titration).

Solvolysis Experiments.—Acetyl bromide was added dropwise with the aid of a dropping funnel protected by a drying tube into the stirred aqueous solvent containing 41% by weight of commercial absolute alcohol. The solvent had been equilibrated with a thermostat maintained at 25° and remained immersed therein during the addition. Enough solvent was used to give a solution 0.1 to 0.5 *M* in HBr prior to dilution. Slow addition (4 g. in 20 minutes) was necessitated by the strongly exothermic character of the reaction. Stirring was continued for several minutes after completion of addition. The solution was then made up to a standard volume and aliquots removed periodically for titration with standard base.

Results

Solvolysis in the absence of added reagents gave a solution which initially (40 minutes after addition was complete) contained 1.63 equivalents of acid per mole of acetyl bromide employed. The acidity slowly decreased so that two hours after addition was complete the ratio was 1.59, presumably because of esterification of acetic acid catalyzed by HBr. Solvolysis in the presence of slightly more than one mole of sodium acetate per mole of acetyl bromide yielded 1.61 equivalents of acid per

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[1] Based upon an A.M. Thesis submitted by Felix Granchelli to the Graduate School of Boston University, June, 1950.

[2] L. Farkas, B. Perlmutter and O. Schächter, THIS JOURNAL, **71**, 2829 (1949).

[3] H. S. Isbell, *J. Research Natl. Bureau of Standards*, **8**, 615 (1932).

[4] H. S. Isbell and W. W. Pigman, *ibid.*, **10**, 337 (1933).

[5] W. A. Mosher and D. M. Preiss, THIS JOURNAL, **75**, 5605 (1953).

[6] S. Burgarszky, *Z. physik. Chem.*, **48**, 74 (1904).

[7] A. Wurtz, *Ann.*, **102**, 93 (1857).

[8] F. Wöhler and J. Liebig, *ibid.*, **3**, 262 (1832).

[9] L. Claisen, *Ber.*, **14**, 2473 (1881).

[10] L. Farkas, B. Perlmutter and O. Schächter, THIS JOURNAL, **71**, 2833 (1949).

mole of acetyl bromide, the ratio remaining constant for 22 hours. This result corresponds to a product containing 0.64 mole of ethyl acetate per mole of acetic acid and differs sufficiently from the value of this ratio which was observed by Farkas, *et al.*,[2] to eliminate acetyl bromide as a possible intermediate in the oxidation reaction.

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The Synthesis of 2-Ethylhexanol-1-C^{14} and Esters[1]

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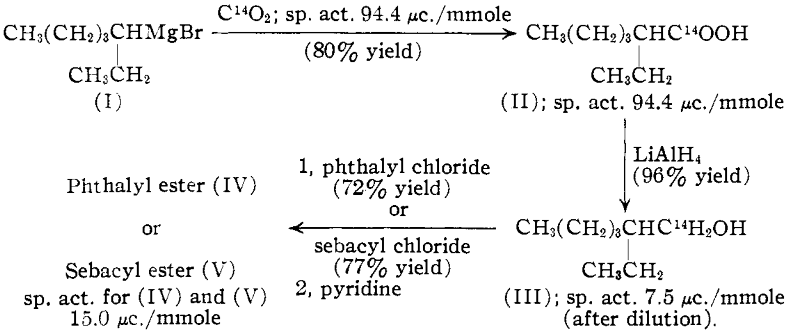
The sebacyl and phthalyl esters of 2-ethylhexanol-1-C^{14} were required at this Laboratory for the evaluation of primary plasticizers and synthetic lubricants using radioisotope-tracer techniques. These syntheses were accomplished by the radiocarbonation of 3-heptylmagnesium bromide (I), using a method similar to that of Dauben, Reid and Yankwich,[2] followed by lithium aluminum hydride reduction of the resulting 2-ethylcaproic acid-1-C^{14} (II). The 2-ethylhexanol-1-C^{14} (III) produced was esterified by the acid chloride–pyridine technique.



$$\underset{\text{(I)}}{\mathrm{CH_3(CH_2)_3\underset{\displaystyle CH_3CH_2}{\underset{|}{C}}HMgBr}} \xrightarrow[\text{(80\% yield)}]{\mathrm{C^{14}O_2};\ \text{sp. act. } 94.4\ \mu\text{c./mmole}} \mathrm{CH_3(CH_2)_3\underset{\displaystyle CH_3CH_2}{\underset{|}{C}}HC^{14}OOH}$$

(II); sp. act. 94.4 μc./mmole

$$\text{(II)} \xrightarrow[\text{(96\% yield)}]{\mathrm{LiAlH_4}} \mathrm{CH_3(CH_2)_3\underset{\displaystyle CH_3CH_2}{\underset{|}{C}}HC^{14}H_2OH}$$

(III); sp. act. 7.5 μc./mmole (after dilution).

$$\text{(III)} \xrightarrow[\text{2, pyridine}]{\text{1, phthalyl chloride (72\% yield) or sebacyl chloride (77\% yield)}} \text{Phthalyl ester (IV) or Sebacyl ester (V)}$$

sp. act. for (IV) and (V) 15.0 μc./mmole

The alcohol and esters so obtained were identical in physical properties (including infrared spectra) with the pure unlabeled compounds.[3]

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[1] The opinions or assertions herein are those of the authors, and are not to be construed as reflecting the views of the Navy Department or the Naval Service at large.

[2] (a) W. G. Dauben, J. C. Reid and P. E. Yankwich, *Anal. Chem.*, **19**, 828 (1947); (b) M. Calvin, C. Heidelberger, J. C. Reid, B. M. Tolbert and P. E. Yankwich, "Isotopic Carbon," John Wiley and Sons, Inc., New York, N. Y., 1948, p. 178.

[3] The full experimental details of the preparations described in this paper have been deposited as Document number 4229 with the ADI Auxiliary Publications Project, Photoduplication Service, Library of Congress, Washington 25, D. C. A copy may be secured by citing the Document number and by remitting in advance $1.25 for photoprints or $1.25 for 35 mm. microfilm, payable to Chief, Photoduplication Service, Library of Congress.

Pungents. Fatty Acid Amides[1]

BY LEONARD M. RICE, CHARLES H. GROGAN, BERNARD H. ARMBRECHT AND E. EMMET REID

RECEIVED FEBRUARY 22, 1954

Pungent principles or irritants have been discussed in recent reviews.[2,3] Although most of the pungents are amides, this is not always the case, as for example, gingerone and gingerol. In amides such as piperidine and chavicine the amine moiety is piperidine; in capsicin it is vanillylamine.

Staudinger, *et al.*,[4] studied the relationship of various acids with different amines with respect to pungency. They concluded that the amide linkage was necessary, since a salt did not give the same action. They prepared various amides of piperidine using fatty acids. With the lower or higher members of the fatty acid series they did not observe any peppers. Asano, *et al.*,[5] have expanded this work and found that the piperidides of the fatty acids were most pungent at pelargonic acid and that this pungency decreased in going up or down the series. It is interesting that furylvaleric piperidide has a strong taste. This acid, if split enzymatically, would approximate the C$_9$ length. Mitter and Ray[6] have found that with the acylated isobutylamines the highest degree of activity lies with the unsaturated fatty acids, 2-heptenoic and 2-nonenoic. Also when employing vanillylamine they found that the fatty acid moiety gave maximal pungency at the C$_9$-acid.

As part of our continuing study of various amides, we have found that the morpholides of fatty acids containing from seven to twelve carbon atoms are strong pungents. We have found in this series of morpholides that the greatest activity is produced when the fatty acid moiety is octanoic, nonanoic or decanoic. When the acid portion of the amide was either increased or decreased in length the activity was diminished. It was of interest to study the amine moiety in the most potent acid range in order to find out how essential the morpholine portion might be. When pelargonic acid was used, which exhibited maximum pungency in the morpholine series, and the heterocyclic part of the molecule was contracted to pyrrolidine or expanded to hexamethylenimine, the products obtained were almost devoid of pungency. In a like manner when diethylamine, dipropylamine or ethylpropylamine was substituted for morpholine, the resulting amides had very little pungency. It thus appears that the morpholides occupy a unique place in pungency not previously recognized. Indeed, the

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[1] Supported by a grant from the Geschickter Fund for Medical Research, Inc.

[2] M. B. Jacobs, *Am. Perfumer*, **48**, #7, 60 (1946).

[3] S. Takata, *Koryo*, #4, 6 (1948).

[4] (a) H. Staudinger and H. Schneider, *Ber.*, **56**, 699 (1923); (b) H. Staudinger and F. Muller, *ibid.*, **56**, 711 (1923).

[5] (a) M. Asano and F. Nakatomi, *J. Pharm. Soc. Japan*, **53**, 174 (1933); *C. A.*, **27**, 2672, 2703 (1933); (b) M. Asano and T. Kanematsu, *J. Pharm. Soc. Japan*, **531**, 375 (1926); *C. A.*, **20**, 2844 (1926).

[6] P. C. Mitter and S. C. Ray, *J. Indian Chem. Soc.*, **14**, 421 (1937).