

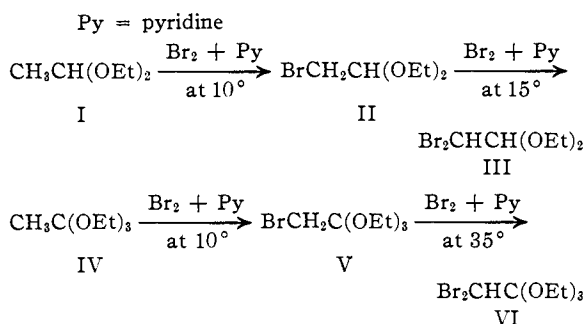
[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

The Preparation and Properties of Certain Polyethoxyethanes and their Bromo Derivatives

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The original object of most of the work that is described in this paper was the preparation of triethoxyethylene (ethoxyketene diethylacetal) in order that its properties might be recorded with those of the other ketene acetals recently reported¹ from this Laboratory. To date, however, all attempts to prepare this particular ketene acetal have been consistently unsuccessful, but the preparation and properties of the various ethoxyethanes and their bromo derivatives that have been used in these attempts seem to be of sufficient interest to record.

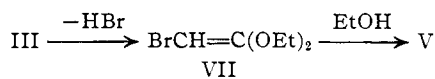
The unsymmetrical diethoxyethane, acetal (I), in the presence of pyridine is brominated readily (at 10–15°) and in fair yields (25–30%) to the mono- and dibromo derivatives II and III.² The unsymmetrical triethoxyethane, ethyl orthoacetate (IV), brominates in good yields (55–75%) in the presence of pyridine, but at slightly higher temperatures (10–35°) to the bromo derivatives V and VI, thus



However, the corresponding symmetrically substituted compounds, ethylene glycoldiethyl ether and ethoxyacetal, $\text{EtOCH}_2\text{CH}(\text{OEt})_2$, not only require a decidedly higher reaction temperature (65°) to cause one equivalent of bromine and pyridine to react with each of them, but yield a variety of cleavage products instead of mono-bromo derivatives. In all of the above mentioned brominations higher reaction temperatures are required if pyridine is not used, and under

these conditions the bromination is not smooth but is accompanied by cleavage of ethoxyl groups by the hydrogen bromide produced in the reaction.

The differences in the behavior of the bromo compounds II, III, V and VI toward sodium or potassium alkoxides are interesting. As previously reported³ bromoacetal (II) yields mainly ethoxyacetal when treated with an alcoholic solution of sodium ethoxide, but with potassium *t*-butoxide in *t*-butyl alcohol it is converted into ketene acetal.⁴ Dibromoacetal (III) reacts readily with one equivalent of potassium ethoxide but is very resistant to further action of this reagent. It was first thought⁵ that the product of the reaction of one equivalent of potassium ethoxide with III was bromoethoxyacetal, $\text{EtOCHBrCH}(\text{OEt})_2$, together with a small amount of bromoketene acetal (VII), which added a molecule of alcohol to give the orthobromoester (V) that was always isolated as one of the reaction products. With potassium *t*-butoxide in *t*-butyl alcohol the dibromoacetal (III) was smoothly transformed with the loss of hydrogen bromide, into VII.



It is now found that the earlier observation was in error and that the reaction of III with potassium ethoxide in ethyl alcohol solution does not yield any detectable quantities of the bromoethoxyacetal by direct replacement of a bromine by ethoxy but instead gives bromoketene acetal (VII) by the elimination of hydrogen bromide from III. Indeed, if the reaction mixture is worked up within a few hours after the reaction is finished, yields of VII as high as those obtained in *t*-butyl alcohol may be isolated. As previously reported⁵ ethyl orthobromoacetate (V) is always present as a reaction product; in fact, it is the only product if the reaction mixture is allowed to stand too long before working up. It appears from these results that bromoketene acetal reacts sufficiently slowly with alkaline alcohol to allow

(1) McElvain and Walters, *THIS JOURNAL*, **64**, 1059 (1942).

(2) This method of preparation, however, is not as satisfactory for II as is the bromination of vinyl acetate [Filachione, *ibid.*, **61**, 1705 (1939)] nor for III as is the bromination of II in the presence of calcium carbonate [Beyerstedt and McElvain, *ibid.*, **59**, 2267 (1937)].

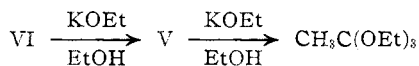
(3) Beyerstedt and McElvain, *ibid.*, **58**, 529 (1936).

(4) Johnson, Barnes and McElvain, *ibid.*, **62**, 968 (1940).

(5) Beyerstedt and McElvain, *ibid.*, **59**, 2266 (1937).

it to be formed in and isolated from this medium.⁶ This behavior is in a marked contrast to the instantaneous reaction of this ketene acetal with alcohol, containing a trace of acid, to produce the ortho-ester V.

Since it was not possible to obtain the bromoethoxyacetal $\text{EtOCHBrCH}(\text{OEt})_2$ from III due to the ease with which this latter compound lost hydrogen bromide, the preparation of ethyl orthobromoethoxyacetate, $\text{EtOCHBrC}(\text{OEt})_3$, from the orthodibromoester (VI) was undertaken. If this bromoethoxyorthoester were available it should be readily convertible into the desired triethoxyethylene by the action of sodium.⁷ Although the dibromo-orthoester (VI) cannot lose hydrogen bromide it failed to give the expected bromoethoxyorthoester when treated with one equivalent of potassium ethoxide in alcohol solution. Instead the monobromo-orthoester (V) was the reaction product. This latter orthoester was found to react similarly with alcoholic potassium ethoxide with the formation of ethyl orthoacetate, thus



The positive character of the bromine in the orthoesters V and VI is striking. It is well known⁸ that an increase in the number of negative (electron attracting) groups on a carbon carrying a halogen increases the tendency of that halogen to be replaced, through hydrolytic cleavage, by hydrogen (instead of hydroxyl) as, for example, in the hydrolysis of carbon tetrabromide to bromoform and bromomalonic ester to malonic ester. In the cases of the orthoesters, V and VI, however, it is seen that the effect of the three ethoxy groups is sufficiently great to render positive in its reaction a bromine one carbon removed from the carbon carrying the ethoxy groups.

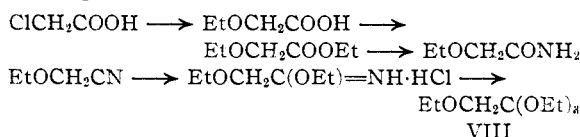
The failure of the dibromo-orthoester VI to yield the bromoethoxyorthoester led to the

(6) Dichloroacetal shows a similar behavior with alcoholic potassium ethoxide and yields 60% of the theoretical amount of chloroketene acetal even after the reaction mixture is allowed to stand overnight before it is worked up. In this connection it is interesting to note that Pinner (*Ber.*, **5**, 151 (1872)) reported the preparation of the symmetrical tetraethoxyethane, glyoxal-tetraethylacetal, from the reaction of sodium ethoxide with dichloroacetal. He reported no yields or analyses, but did remark that he could not obtain a completely chlorine-free product. In the light of the present work it would seem that Pinner did not have the glyoxal-acetal but ethyl orthochloroacetate (from the addition of alcohol to chloroketene acetal) probably mixed with ethyl orthoacetate (from the reaction of sodium ethoxide with the orthochloroester).

(7) Walters and McElvain, *THIS JOURNAL*, **62**, 1482 (1940).

(8) Cf. Schmidt, *et al.*, *Ber.*, **59**, 1876 (1926).

attempt to prepare this latter compound by the bromination of ethyl orthoethoxyacetate (VIII). This latter ester was obtained through the following sequence of reactions



The orthoester VIII shows a resistance to bromination similar to that of ethylene glycol diethyl ether and ethoxyacetal mentioned above. It did react with bromine in the presence of pyridine at 80° to yield pyridine hydrobromide, but the ester was transformed in the process into a tar from which nothing could be distilled.

Experimental

Ethyl Orthobromoacetate.—This bromo-orthoester was prepared by the bromination of ethyl orthoacetate in pyridine employing the method of Beyerstedt and McElvain.⁹

Ethyl Orthodibromoacetate.—To a stirred mixture of 162 g. (1 mole) of ethyl orthoacetate and 158 g. (2 moles) of pyridine was added dropwise 320 g. (2 moles) of bromine over a period of two hours. The reaction mixture was cooled to about 30° until one-half of the bromine had been added, whereupon the temperature was allowed to rise to 60–70° for the remainder of the bromine addition. The reaction mixture was stirred for an additional two hours. The brominated ester then was separated from the precipitated pyridine hydrobromide and this salt thoroughly washed with anhydrous ether. These washings were combined with the dibromoester and distilled. The yield of ethyl orthodibromoacetate was 170 g. (53%); b. p. 102–104° (8 mm.); n_D^{25} 1.4691; d_4^{25} 1.5272.

This compound has been previously isolated and identified as a by-product of the monobromination of ethyl orthoacetate.⁹

Bromination of Acetal in Pyridine.—Diethyl acetal was brominated in pyridine by the above method at a somewhat lower temperature (10–15°) to monobromoacetal (23%) and dibromoacetal (29%).

Bromination of Ethoxyacetal and Ethylene Glycol Diethylether.—Bromination of ethoxyacetal¹⁰ in pyridine at 65° failed to give the expected monobromination product, bromoethoxyacetal, but resulted in a variety of cleavage products. The only clean-cut fraction obtained on fractionation was a 15% yield of a material boiling at 79° (12 mm.); n_D^{25} 1.4175. This material gave a positive Fehling test and yielded a sodium bisulfite addition product, reactions which the original ethoxyacetal failed to show. These two tests and the ethoxyl analysis would indicate this fraction to be diethoxyacetaldehyde.

Anal. Calcd. for $\text{C}_6\text{H}_{12}\text{O}_3$: $\text{C}_2\text{H}_5\text{O}$, 68.1. Found: $\text{C}_2\text{H}_5\text{O}$, 68.3.

This compound has been reported previously by Fischer

(9) Beyerstedt and McElvain, *THIS JOURNAL*, **59**, 1274 (1937).

(10) Späth, *Monatsh.*, **36**, 4 (1915).

and Baer¹¹ who prepared it by the lead tetraacetate oxidation of glyceraldehyde acetal. However, they reported a considerably lower boiling point for their product than was obtained in the present work.

Bromination of ethoxyacetal in the absence of a solvent at 80° yielded a number of cleavage products. From one mole of acetal, there was obtained 0.48 mole of ethyl bromide, b. p. 38–40°; 0.97 mole of water, b. p. 98–100°; 0.75 mole of ethyl alcohol, b. p. 76–80°; and 0.275 mole of dibromoacetal, b. p. 95–97° (12 mm.); n_D^{25} 1.4788; C_2H_5O , 32.6% (calcd. 32.6%).

Bromination of ethylene glycol diethylether in pyridine at 65° and bromination in the absence of a solvent at a somewhat higher temperature (80°), resulted in a variety of cleavage products instead of monobromo derivatives.

The Reaction of Alcoholic Potassium Ethoxide with Ethyl Orthobromoacetate and with Ethyl Orthodibromoacetate.—To a stirred solution of 30 g. (0.77 atom) of potassium in 400 ml. of absolute alcohol was added 80 g. (0.25 mole) of ethyl orthodibromoacetate and the resulting mixture gently refluxed for thirty-six hours. The excess alcohol then was removed carefully by atmospheric distillation, and the orthoesters separated from the precipitated potassium bromide by extracting the residue several times with anhydrous ether. The ether extracts were combined and distilled. Twenty-one grams (52%) of ethyl orthoacetate, b. p. 68–70° (50 mm.), and 25 g. (42%) of ethyl orthobromoacetate, b. p. 78–80° (10 mm.), were obtained.

In a similar experiment employing equimolar quantities of potassium ethoxide and dibromo ester, there was obtained 30 g. (50%) of ethyl orthobromoacetate and 12 g. (15%) of unchanged ethyl orthodibromoacetate. Repetition of this experiment with ethyl orthobromoacetate as the starting material gave ethyl orthoacetate as the reaction product.

Reaction of Dibromo- and Dichloroacetal with Alcoholic Potassium Ethoxide.—To a stirred mixture of 138 g. (0.5 mole) of dibromoacetal and 100 ml. of absolute alcohol in a 1-liter three-necked flask, fitted with a dropping funnel and reflux condenser was added slowly a solution of 20 g. (0.5 atom) of potassium in 300 ml. of absolute alcohol. The flask was heated on a steam-bath during the addition and for two hours after the last of the alcoholic alkali had been added. The condenser then was set for downward distillation and 300 ml. of alcohol removed from the reaction mixture, after which the precipitated potassium bromide was filtered off. The filtered salt was washed thoroughly with anhydrous ether and the washings combined with the filtrate, and distilled. The yield of bromoacetene acetal was 61 g. (62.5%); b. p. 72–3° (11 mm.); n_D^{25} 1.4610; d_4^{25} , 1.319; C_2H_5O , 45.7% (calcd. 46.1%).

In a similar experiment employing dichloroacetal instead of dibromoacetal there was obtained 45 g. (60%) of chloroacetene acetal, b. p. 57–58° (10 mm.); n_D^{25} 1.4378; d_4^{25} , 1.052; C_2H_5O , 59.4% (calcd. 59.8%).

In each of the above preparations the product should be worked up as rapidly as possible to ensure the optimum yields of the respective ketene acetals.

(11) Fischer and Baer, *Helv. Chim. Acta*, **18**, 514 (1935).

Ethoxyacetonitrile.—Ethoxyacetamide, b. p. 225–230°, m. p. 82–83°, was obtained in 85% yields by the action of aqueous ammonia on ethyl ethoxyacetate.¹² A mixture of 103 g. of this amide and 142 g. of phosphorus pentoxide in a 1-l. distilling flask was heated in an oil-bath at 150–180° as long as the ethoxyacetonitrile distilled over. The crude distillate was redistilled from 5 g. of fresh phosphorus pentoxide. The yield of nitrile boiling at 133–134°, n_D^{25} 1.3888,¹³ amounted to 51 g. (60%).

Ethyl Orthoethoxyacetate.—This orthoester was prepared by the method of McElvain and Nelson.¹⁴ The iminoester hydrochloride precipitated in 88% yield when the procedure described for the preparation of the hydrochloride from chloroacetonitrile was followed. A 47% yield of the orthoester was obtained when 1 mole of the hydrochloride was alcoholysed in a refluxing mixture of 290 ml. of absolute alcohol and 340 ml. of absolute ether over a period of three hours. Ethyl orthoethoxyacetate boils at 69–70° (10 mm.) or 180–181° (740 mm.); n_D^{25} 1.4055; d_4^{25} , 0.921.

Anal. Calcd. for $C_{10}H_{22}O_4$: C, 58.2; H, 10.8; C_2H_5O , 87.4. Found: C, 58.4; H, 10.7; C_2H_5O , 86.5.

Bromination of Ethyl Orthoethoxyacetate.—To a stirred mixture of 20.6 g. (0.1 mole) of ethyl orthoethoxyacetate and 7.7 g. (0.098 mole) of pyridine was added dropwise 16.0 g. (0.1 mole) of bromine over a period of thirty minutes. The reaction mixture was heated at a temperature of 80° during the bromine addition with no apparent reaction occurring until the bromine addition was practically completed. Then a vigorous reaction occurred which had to be controlled by the application of a cold water-bath. After the initial reaction had subsided, the reaction flask was heated for an additional hour at 80°. The precipitated pyridine hydrobromide (88%) was removed by filtration and thoroughly extracted with anhydrous ether. These washings were combined with the filtrate and distilled.

From none of the several brominations carried out could any bromination product be isolated and identified. The products obtained were mainly low-boiling liquids and a non-distillable, carbonaceous residue.

Summary

The behavior of acetal, ethyl orthoacetate, ethylene glycol diethyl ether, ethoxyacetal, and ethyl orthoethoxyacetate toward bromination is compared.

Dibromoacetal is shown to give only bromoacetene acetal with alcoholic potassium ethoxide, and not bromoethoxyacetal as was reported previously. Both ethyl orthobromoacetate and ethyl orthodibromoacetate have their bromine replaced by hydrogen instead of ethoxyl with this reagent.

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(12) "Organic Syntheses," **13**, 42 (1933).

(13) *Cf. Henry, Ber.*, **6**, 260 (1873).

(14) McElvain and Nelson, *THIS JOURNAL*, **64**, 1825 (1942).