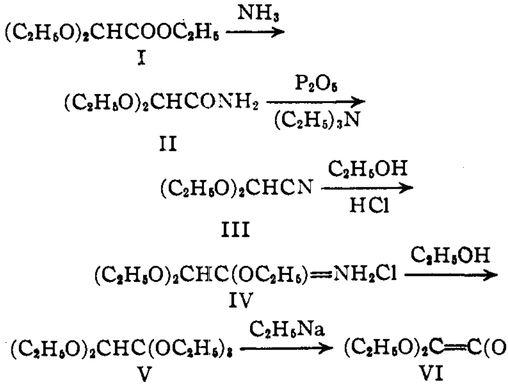
[CONTRIBUTION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

Ketene Acetals. XVIII. Pentaethoxyethane and Tetraethoxyethylene (Diethoxyketene Diethylacetal)

BY S. M. MCELVAIN AND ROBERT L. CLARKE[1]

Although the properties of the simple ketene acetals ($CH_2{=}C(OR)_2$) prepared in this Laboratory,[2] demonstrate beyond any doubt that the earlier claims of Scheibler and collaborators to have isolated such compounds from the reaction of sodium alkoxides with the corresponding alkyl acetates are spurious, it seemed desirable to prepare another ketene acetal, tetraethoxyethylene (VI), which has been reported by these German workers to dissociate spontaneously into a divalent carbon compound, carbon monoxide diethylacetal[3] ($C(OC_2H_5)_2$). The fact that this work was questioned[4] and could not be duplicated[5] gave added impetus to the development of an unequivocal synthesis of tetraethoxyethylene (VI).

An unsuccessful attempt to prepare this compound was reported in 1937.[6] The present paper reports the successful preparation of tetraethoxyethylene (VI) and its precursor pentaethoxyethane (V) by the following series of reactions



$$\underset{I}{(C_2H_5O)_2CHCOOC_2H_5} \xrightarrow{NH_3}$$

$$\underset{II}{(C_2H_5O)_2CHCONH_2} \xrightarrow[(C_2H_5)_3N]{P_2O_5}$$

$$\underset{III}{(C_2H_5O)_2CHCN} \xrightarrow[HCl]{C_2H_5OH}$$

$$\underset{IV}{(C_2H_5O)_2CHC(OC_2H_5){=}NH_2Cl} \xrightarrow{C_2H_5OH}$$

$$\underset{V}{(C_2H_5O)_2CHC(OC_2H_5)_3} \xrightarrow{C_2H_5Na} \underset{VI}{(C_2H_5O)_2C{=}C(OC_2H_5)_2}$$

The ester (I), prepared by the method of Cope[7] from ethyl dichloroacetate, was converted in 84% yield to the amide (II), which was dehydrated in 76–79% yields to the nitrile[8] (III). The conversion of the nitrile to the iminoester hydrochloride (IV) proceeded in 70% yield.

The alcoholysis of this salt to the desired orthoester (V) was accompanied by competitive reactions that limited the yield of V to only 12% of the theoretical. If the alcoholysis were allowed to proceed at room temperature to completion (four days) approximately 42% of the theoretical amount of ammonium chloride was obtained; the remainder of the nitrogen of IV was isolated in the form of the amide (II). However, none of the orthoester·(V) was obtained from this alcoholysis mixture; diethyl ether (small amount) and the ester I (26%) were the only volatile products isolated when the alcoholic solution was distilled. Further investigation of this alcoholysis, however, showed that if the isolation procedure was varied only by making the alcoholic solution strongly alkaline (to phenolphthalein) with sodium ethoxide after the insoluble ammonium chloride had been filtered off, and *before* any heat was applied, pentaethoxyethane (V) could be isolated in a 12% yield. Along with this product were obtained: I (8%), II (44%), and III (8%).

It is apparent from these results that the orthoester V is formed from the alcoholysis of IV, but is decomposed rapidly at the boiling point of the alcohol and to some extent at room temperature into diethyl ether and I by some catalyst present in the alcoholic solution. Further, it is apparent that this catalyst is destroyed by sodium ethoxide. Since the orthoester (V) was recovered unchanged when heated in refluxing alcohol with ammonium chloride for three hours, it is believed that the catalyst, which promotes the decomposition of V ino the ester I, is the iminoester salt (IV).[9]

Pentaethoxyethane (ethyl diethoxyorthoacetate) boils at 205–207° without decomposition[10]; indeed refluxing this compound for four hours produced negligible decomposition. The orthoester

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[2] Beyerstedt and McElvain, THIS JOURNAL, **58**, 529 (1936); Walters and McElvain, *ibid.*, **62**, 1482 (1940); **64**, 1059 (1942).

[3] A low yield (4%) of carbon monoxide acetal was reported to have been isolated from the action of sodium ethoxide on ethyl diethoxyacetate; a more successful method of preparation was claimed to start with sodium oxyethoxymethylene ($C(ONa)OC_2H_5$), which was obtained by the action of sodium ethoxide on ethyl formate (Scheibler, *Ber.*, **59**, 1022 (1926)).

[4] Adickes, *Ber.*, **60**, 272 (1927); **63**, 3012 (1930).

[5] Arbusow, *ibid.*, **64**, 698 (1931); Wood and Bergstrom, THIS JOURNAL, **55**, 3314 (1933).

[6] Beyerstedt and McElvain, THIS JOURNAL, **59**, 2266 (1937).

[7] Cope, THIS JOURNAL, **58**, 571 (1936).

[8] Scheibler, *et al.* (*Ber.*, **67**, 1513 (1934)) reported the preparation of this nitrile in 30% yield from the amide II with phosphorus pentoxide and quinoline. Mr. Bryce Tate, in this Laboratory, was unable to obtain the nitrile by this procedure, but did obtain a 45% yield using N-hexylpiperidine instead of quinoline. In the present work triethylamine was found to be uniquely efficient in the dehydration of this acid-sensitive amide as it was in the preparation of cyanoacetal (McElvain and Clarke, THIS JOURNAL, **69**, 2657 (1947)).

[9] The observation that the ester is concurrently formed with the orthester in the alcoholysis of ethyl iminovalerate hydrochloride was noted earlier by one of the present authors (R. L. C.) and reported in a paper by McElvain and Nelson, THIS JOURNAL. **64**, 1825 (1942).

[10] Scheibler, *et al.* (*J. prakt. Chem.*, **133**, 131 (1932)) reported the isolation of 0.7 g. of this orthoester, which presumably had formed from the addition of alcohol to some tetraethoxyethylene before it dissociated into carbon monoxide diethylacetal. The boiling point of the orthoester was listed as 170° (760 mm.), which, it should be noted, is 25° *lower* than that of the normal ester (I) and 35° lower than the boiling point found for V in the present work. As noted in the experimental part, approximately 50 g. of V now has been prepared.

was subjected to this treatment in the hope that it would pyrolyze into alcohol and tetraethoxyethylene (VI). Repetition of this heating in the presence of a trace of glacial phosphoric acid or sodium ethoxide also failed to cause any pyrolysis of V.

The orthoester was converted to tetraethoxyethylene (VI) in 39% yield by the action of sodium ethyl. This reagent causes more extensive alterations of V than are involved in the simple acid–base reaction to produce ethane and the salt, Va, and the subsequent decomposition of Va into VI and sodium ethoxide

$$\mathrm{V} + \overset{+}{\mathrm{N}}\mathrm{a}(\mathrm{C_2\overset{-}{H}_5}) \longrightarrow$$

$$\mathrm{C_2H_6} + \underset{\mathrm{Va}}{\mathrm{C_2H_5O)_2\overset{-}{C}{-}C(OC_2H_5)_3N\overset{+}{a}}} \longrightarrow \mathrm{VI} + \mathrm{C_2H_5ONa}$$

In addition to the 39% yield of VI, ethane and sodium ethoxide (determined as alcohol after hydrolysis) were formed in approximately 160 and 235% yields, respectively, calculated on the basis of the above reactions. These excessive yields indicate further reaction of V and VI with the excess of sodium ethyl and possibly with the sodium amalgam, which also is present in the reaction mixture, and account for the relatively low yield of VI as well as for the fact that no unchanged orthoester (V) was recovered.

Tetraethoxyethylene is a colorless liquid, which boils at 70–71° (5 mm.) and 195–196° (740 mm.) with no evidence of dissociation.[11] This ketene acetal was characterized by the addition of alcohol to regenerate the orthoester V and by its rapid absorption of bromine (I and V show no reaction with bromine) to form ethyl oxalate and, presumably, ethyl bromide. The latter compound was not isolated, but the ethyl oxalate was identified by conversion to oxamide and the dihydrazide of oxalic acid.

Experimental

Diethoxyacetamide.—In a 1-liter, round-bottom flask fitted with a stirrer was placed a mixture of 84 g. (0.48 mole) of ethyl diethoxyacetate and 475 ml. of concentrated ammonium hydroxide solution (7.1 moles of ammonia). The mixture was stirred for one hour during which time it became homogeneous. The water and ammonia were removed under reduced pressure while the mixture was heated by a bath at 50–60°. A residue of diethoxyacetamide was obtained which, after recrystallization from petroleum ether (60–68°), melted at 77–78°[12] and amounted to 59 g. or 84% of the theoretical quantity.

Diethoxyacetonitrile.—This nitrile was prepared from diethoxyacetamide by the procedure used for the preparation of cyanoacetal from β,β-diethoxypropionamide.[13] Diethoxyacetonitrile,[8] b. p. 68–70° (20 mm.); $n^{25}\mathrm{D}$. 1.3937, was obtained in yields of 76–79% of the theoretical amount.

Ethyl Diethoxyiminoacetate Hydrochloride.—This salt was prepared from diethoxyacetonitrile in yields of 66–71% of the theoretical using the method of McElvain and Nelson.[9] The chlorine content (18.4%) found for this salt was greater than the theoretical amount (16.8%) due to the presence of a small amount of ammonium chloride resulting from partial alcoholysis of the salt.

Ethyl Diethoxyiminoacetate.—To a solution of 30.6 g. (0.22 mole) of potassium carbonate in 40 ml. of water covered by 60 ml. of diethyl ether and chilled to −5° was quickly added 23.3 g. (0.11 mole) of ethyl diethoxyiminoacetate hydrochloride. The mixture was shaken vigorously for one minute and the ether layer was separated. After the aqueous layer was extracted with three 40-ml. portions of ether and the combined extracts were dried over potassium carbonate, the ether was removed on a steam-bath and the residue fractionated. Ethyl diethoxyiminoacetate was collected at 91–92° (20 mm.), $n^{25}\mathrm{D}$ 1.4147; $d^{25}{}_4$ 0.957. The yield was 15.4 g. or 80% of the theoretical amount.

Anal. Calcd. for $\mathrm{C_8H_{17}O_3N}$: N, 8.00; $\mathrm{C_2H_5O}$, 77.1. Found: N, 7.48; $\mathrm{C_2H_5O}$, 75.1.

The low nitrogen content was probably due to partial hydrolysis of the imino group to give some ethyl diethoxyacetate which boils at about the same temperature.

Pentaethoxyethane (Ethyl Orthodiethoxyacetate) (V).—A mixture of 47.5 g. (0.22 mole) of ethyl diethoxyiminoacetate hydrochloride and 104 g. (2.26 moles) of absolute alcohol was allowed to stand at room temperature for four days. (This alcoholysis reaction was found to proceed at too low a rate at 0° to be practical.) The precipitated ammonium chloride, removed by filtration, amounted to 5 g. (42%). The filtrate then was made alkaline to phenolphthalein by addition of sodium ethoxide in absolute alcohol, the alcohol removed under reduced pressure and the residue fractionated. There was obtained 2.3 g. (8%) of diethoxyacetonitrile, b. p. 48–50° (8 mm.), 10 g. of an intermediate fraction consisting of a mixture of ethyl diethoxyacetate and the orthoester (V), b. p. 74–85° (8 mm.), and 5.2 g. of ethyl orthodiethoxyacetate, b. p. 85–86° (8 mm.); $n^{25}\mathrm{D}$ 1.4072; $d^{25}{}_4$ 0.935; M_D 65.4 (calcd. 65.4). A residue of 14.5 g. (44%) of diethoxyacetamide remained from this distillation.

Anal. Calcd. for $\mathrm{C_{12}H_{26}O_5}$: C, 57.57; H, 10.47; $\mathrm{C_2H_5O}$, 90.0. Found: C, 57.10; H, 10.31; $\mathrm{C_2H_5O}$, 89.1.

To remove ethyl diethoxyacetate from the forerun of the orthoester, this fraction was stirred vigorously with 150 ml. of concentrated ammonia for one hour. The mixture was extracted with two 40-ml. portions of ether, the combined extracts dried over potassium carbonate, the ether removed by distillation and the residue fractionated. A low boiling fraction (3.3 g.) was collected at 70–85° (8 mm.) and 1.4 g. of the orthoester collected at 85–86° (8 mm.). The total yield of V amounted to 6.6 g. (12%). From the aqueous portion of this reaction mixture was isolated 2.5 g. of diethoxyacetamide which corresponds to 3.0 g. of ethyl diethoxyacetate.

A total of approximately 50 g. of pentaethoxyethane (V) was prepared in the present work by the above procedure.

Tetraethoxyethylene (Diethoxyketene Diethylacetal) (VI).—To a suspension of 0.08 mole of sodium ethyl prepared by the method of Whitmore and Zook[14] in petroleum ether (65–67°) under an atmosphere of nitrogen was added 4.7 g. (0.019 mole) of pentaethoxyethane dropwise and with stirring over a period of ten minutes at 20°. Ethane was evolved rapidly and approximately 700 ml. (S. T. P.) or 160% of the theoretical volume was collected. After addition of the pentaethoxyethane was complete, the mixture was stirred for two minutes, 50 ml. of petroleum ether was added, and the supernatant liquid decanted. The residue was washed with two 25-ml. portions of petroleum ether and the combined ether solutions were centrifuged to remove suspended matter present. After the petroleum ether was removed under reduced pressure, the residue was fractionated and tetraethoxyethylene collected at 70–71° (5 mm.); $n^{25}\mathrm{D}$ 1.4213; $d^{25}{}_4$ 0.949; M_R 54.5 (calcd. 54.5). The yield was 1.5 g. (39%). This ketene acetal boils at 195–196° (740 mm.).

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[11] Carbon monoxide diethylacetal, into which tetraethoxyethylene was said to dissociate (ref. 3) is reported as boiling at 78° (760 mm.).

[12] *Cf.* Beilstein, "Handbuch der organischen Chemie," 4th ed., Vol. 3, 603.

[13] McElvain and Clarke, This Journal, **69**, 2659 (1947).

[14] Whitmore and Zook, *ibid.*, **64**, 1783 (1942).

Anal. Calcd. for $C_{10}H_{20}O_4$: C_2H_5O, 88.2; C, 58.8; H, 9.87. Found: C_2H_5O, 85.8; C, 58.0; H, 9.70.

The petroleum ether insoluble portion of the reaction mixture was covered with toluene and treated with water to liberate ethyl alcohol from the sodium ethoxide produced in the reaction. The water layer was saturated with potassium carbonate and the organic layer was separated. The mixture of organic compounds was distilled and everything collected until pure toluene started to distil. The distillate, when treated with 3,5-dinitrobenzoyl chloride, yielded 10.7 g. of ethyl 3,5-dinitrobenzoate. This corresponds to a 235% yield of alcohol from the reaction between pentaethoxyethane and sodium ethyl to produce ethane, sodium ethoxide and VI.

Tetraethoxyethylene absorbs bromine rapidly with the formation of diethyl oxalate and, presumably, ethyl bromide. No attempt was made to isolate the latter compound. Treatment of the diethyl oxalate so produced with concentrated ammonia gave oxamide, a solid which decomposed without melting when heated to 340° for one minute in a sealed tube and melted with decomposition at 350° when placed in a copper block at that temperature. An authentic sample of oxamide, as well as a mixture of this sample with the amide derived from VI, showed the same behavior, which is in marked contrast to the melting point of 417–419° dec. reported[15] for oxamide in the literature. The diethyl oxalate from VI also was converted to oxalhydrazide by the procedure of Sah[16]; the m. p. of this product was 239–240° dec., as was that of a mixture of this product with an authentic sample of oxalhydrazide.

Summary

Diethoxyacetonitrile has been converted to pentaethoxyethane (ethyl diethoxyorthoacetate). This orthoester reacts with sodium ethyl to give tetraethoxyethylene (diethoxyketene diethylacetal), a colorless liquid, b. p. 195–196°, that shows no tendency to dissociate into carbon monoxide diethylacetal as has been reported by Scheibler and co-workers.

[15] Michael, *Ber.*, **28**, 1632 (1895).

[16] Sah, *Rec. trav. chim.*, **59**, 1036 (1940).

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Ester and Orthoester Formation in the Alcoholysis of Iminoester Hydrochlorides. A Proposed Mechanism

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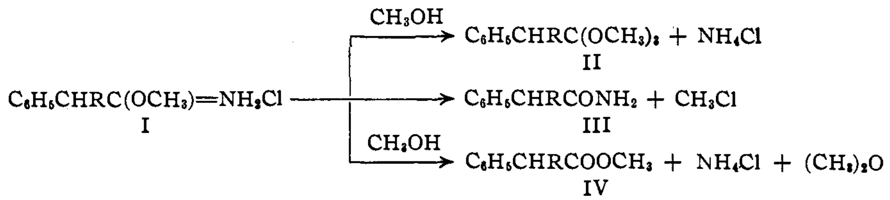
Orthoesters have been used extensively in this Laboratory as intermediates in the preparation of ketene acetals, $RCH{=}C(OR')_2$. When R is alkyl, these acetals are prepared by the action of sodium on the corresponding α-bromoorthoesters[2]; when R is phenyl, the ketene acetals result simply from the pyrolysis of the orthoesters.[3] Consequently, a further extension of the study of ketene acetals, particularly in the direction of the disubstituted compounds $R_2C{=}C(OR')_2$, necessitated the preparation of the corresponding orthoesters.

As previously indicated,[4] the concurrent formation of an amide and an alkyl chloride during the alcoholysis of an iminoester hydrochloride is the chief difficulty that has been encountered in the preparation of orthoesters by the Pinner procedure.[5] Attempts to eliminate or to minimize this undesired side reaction have been reasonably successful when the orthoester has a single α-substituent, but much less so if the orthoester has two α-substituents.[4]

The present paper reports a new complication that has been observed in the attempted preparation of certain α,α-disubstituted orthoesters: the reaction of the iminoester hydrochloride with alcohol to produce the ester, $R_2CHCOOR'$, and an ether, R'_2O. In an attempt to prepare methyl α-phenylorthobutyrate (II, R is C_2H_5) by the alcoholysis of the iminoester hydrochloride (I) derived from α-phenylbutyronitrile, none of the orthoester could be isolated, although the methoxyl content of the products indicated a small amount had been formed; the main products were the amide III together with the ester IV and dimethyl ether.



$$C_6H_5CHRC(OCH_3){=}NH_2Cl \ (I) \xrightarrow{CH_3OH} C_6H_5CHRC(OCH_3)_3 + NH_4Cl \ (II)$$

$$C_6H_5CHRC(OCH_3){=}NH_2Cl \ (I) \longrightarrow C_6H_5CHRCONH_2 + CH_3Cl \ (III)$$

$$C_6H_5CHRC(OCH_3){=}NH_2Cl \ (I) \xrightarrow{CH_3OH} C_6H_5CHRCOOCH_3 + NH_4Cl + (CH_3)_2O \ (IV)$$

However, the methanolysis of the iminoester hydrochloride (I, R is CH_3) derived from α-phenylpropionitrile gave the corresponding orthoester II in 21% yield; accompanying this product was 25% of the amide (III) and 28% of methyl α-phenylpropionate (IV). An intermediate fraction, consisting of approximately equal parts of II and IV, accounted for the remainder of the reaction products.

In the hope that the formation of amide could be prevented, and hence the yield of orthoester increased, the boron trifluoride coördination compound of methyl α-phenyliminopropionate (V)

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[2] McElvain, *et al.*, THIS JOURNAL, **62**, 1482 (1940); **64**, 1966 (1942).

[3] McElvain and Stevens, *ibid.*, **68**, 1917 (1946).

[4] McElvain and Fajardo-Pinzon, *ibid.*, **67**, 690 (1945).

[5] Pinner, *Ber.*, **16**, 356, 1644 (1883).