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OXIDATION STUDIES OF SYMMETRICAL AND UNSYMMETRICAL ETHERS

COMPARISON OF TRICHLOROISOCYANURIC ACID AND HYPOCHLOROUS ACID REAGENT

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Abstract—The study of the oxidation of symmetrical and unsymmetrical ethers in the direct conversions of ethers to esters by trichloroisocyanuric acid is reported. Initial work indicates that there is a selectivity in the oxidation of unsymmetrical ethers and that Newman's "rule of six" may be an important factor in this selectivity. Hypochlorous acid which is a simpler positive halogenating agent and which could actually be the functioning oxidizing agent generated by hydrolysis of trichloroisocyanuric acid is not effective as a general oxidizing agent or substitute for trichloroisocyanuric acid. although it does oxidize diethyl ether and tetrahydrofuran.

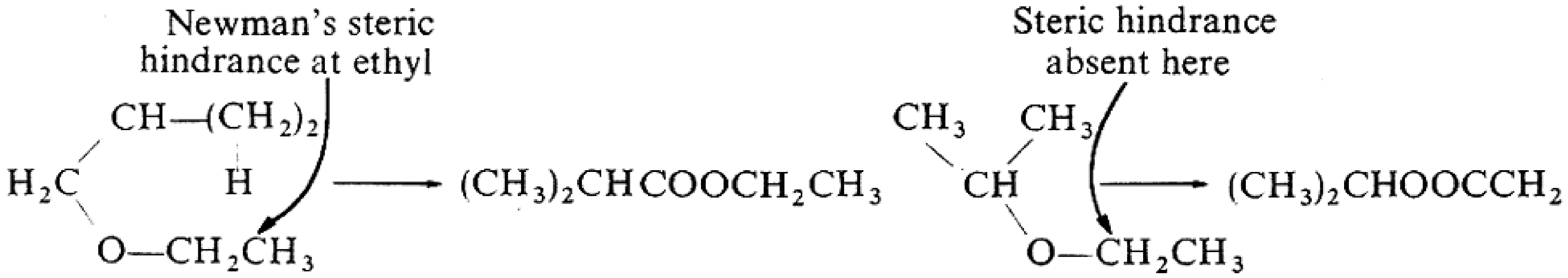
THE first simple convenient laboratory method for conversion of ethers to esters by use of the inexpensive reagent. aqueous trichloroisocyanuric acid. has been reported in a previous paper.[1] Good yields are obtained with quantitative precipitation of insoluble and easily removable cyanuric acid. Various modifications of procedure may be employed.

With various reagents oxidation occurs fairly readily in the case of certain ethers such as tetrahydrofuran[2] and benzyl ethers;[3] although in the latter case, cleavage of the ether linkage may occur.[4] Thus, tetrahydrofuran has been converted to γ-butyrolactone by aqueous bromine[4] or air oxidation.[2] Trichloroisocyanuric acid has been found to give similar results for conversion of tetrahydrofuran to γ-butyrolactone[5] and cleavage of benzyl ethers to benzaldehyde.[1] t-Butyl benzyl ether has been converted to t-Butyl benzoate through ozonization by Erickson *et al.*[6]

Attempted photooxidation by Stenberg *et al.*[7] of diethyl ether to ethyl acetate in the liquid phase by oxygen has given only a 3% yield of ester. Moreover, ozone has failed to yield ethyl acetate by reaction with diethyl ether. This ozonization has been examined to exclude it as a possible explanation for ester formation in the above reaction with oxygen.[7] The rather expensive ruthenium tetroxide, however, has been found to serve successfully for conversion of ethers to esters, although its selectivity in the oxidation of unsymmetrical ethers was not investigated.[8]

Symmetrical ethers are converted to a single ester product. Initial study of unsymmetrical ethers presented here indicates that the product is selectively determined by steric effect. namely Newman's "rule of six". Thus. ethyl isobutyl ether yielded ethyl isobutyrate while ethyl isopropyl ether yielded isopropyl acetate.

At first sight it would appear likely that oxidation would occur at the opposite organic groups because of stabilization of likely intermediates (free radical or carbonium



ion) through hyperconjugation afforded by methyl substituents. The resulting product from ethyl isobutyl ether may be explained by Newman's steric hindrance, that is, the whiplike hindrance at the methylene part of the ethyl group by the terminal hydrogens of the methyls in the isobutyl group. The product from ethyl isopropyl ether may be explained by the lack of Newman's steric hindrance and by the fact that the trichloroisocyanuric acid molecule is a fairly large one and subject to steric hindrance at the larger isopropyl group. Thus, the acetate was obtained instead of acetone which would be expected on oxidation of the isopropyl group. Oxidation of diisopropyl ether did yield acetone on oxidation by trichloroisocyanuric acid in the presence of water.

OXIDATION OF ETHERS TO ESTERS

TO[a]	Add	Temp	Period of addition	Prod.	Yield (%)
Et_2O and H_2O	TCIA	0–10°	45 min	Et acetate	49
TCIA and H_2O	Bu_2O	0–10°	1 hr	Bu butyrate	50
i-BuOEt and H_2O	TCIA	0–10°	45 min	Et i-butyrate	83
i-PrOEt and H_2O	TCIA	0–10°	45 min	i-Pr acetate	55
$(i\text{-}Pr)_2O$ and H_2O	TCIA	0–10°	1 hr	acetone	39
OOEt and H_2O	TCIA	0–10°	45 min	OCHO	53
Et_2O and H_2O	Cl_2	0–10°	1 hr	Et acetate	29[c]
THF[b] and H_2O	Cl_2 & Cl_2	0–10° 40°	15 min 2 hr	γ-butyrolactone	5[c]

[a] TCIA is added slowly with initial reaction at 0–10°. The possibility of reversing the addition is illustrated by the Bu_2O oxidation.

[b] THF also reacts with TCIA and H_2O to yield ester.[1] Caution—adding THF directly to excess TCIA once[2] resulted in an explosion.

[c] Amount of Cl_2 consumed was not measured and no attempt was made to optimize yields.

Since it is known that upon hydrolysis, trichloroisocyanuric acid yields hypochlorous acid,[9] attempts were made to oxidize several ethers with hypochlorous acid (chlorine-water). Limited investigation indicates that hypochlorous acid is not effective as a general substitute for trichloroisocyanuric acid. Chlorine-water was effective for conversion of diethyl ether and tetrahydrofuran to ethyl acetate and butyrolactone, respectively. An ether with a longer alkyl chain was studied in order to check the generality of the chlorine-water oxidation. Dibutyl ether was more difficult to oxidize. Reaction of this ether with trichloroisocyanuric acid gave about 50% yield of ester and the reaction with hypochlorous acid failed. Repeated attempts to convert dibutyl ether to butyl butyrate by hypochlorous acid oxidation were unsuccessful. Butyl butyrate was not obtainable by distillation of, or evident from, gas chromatographic analysis of reaction products. Evidence of polymerization often appeared during distillation and traces of butyraldehyde were found in some of the reaction products. Even though attempted under a great variety of conditions, the reaction failed. Free radical conditions such as irradiation by ultraviolet light or catalysis by benzoyl peroxide at 60° were fruitless and ferric chloride also failed to catalyze the reaction. Prohibiting the interference of HCl in the isolation of butyl butyrate by addition of t-butyl alcohol (as a scavenger) also failed to give the ester.

A sample taken of the mixture from the chlorine water-diethyl ether run was subjected to a series of IR analyses. It was noted from these spectra that the CO peak (1710 cm^{-1}) increased with time as the OH peak (3100 cm^{-1}) decreased. At room temperature this sample evolved hydrogen chloride; however, no hydrogen chloride evolution occurred at 0°. This data would suggest the presence of a temperature unstable intermediate such as a 1,1-halohydrin which could be stabilized as a H-bonded dimer in the low molecule weight ether. Higher molecular weight ethers might yield, on the other hand, simple alpha chloro-ethers which are known to dehydrohalogenate to give vinyl ethers and ultimate polymerization. Such formation of vinyl ethers is observed in the chlorination of ethers in the absence of water.[10] These observations may account for the fact that hypochlorous does not serve as a general substitute for trichloroisocyanuric acid in direct conversion of ethers to esters.

EXPERIMENTAL

Diethyl ether and trichloroisocyanuric acid. To anhyd. ether (35·5 g) and distilled water (3·6 g) stirred at 0–10° was added over 45 min TCIA (7·06 g). The mixture was stirred 2 hr at 0° and then 10 min at room temp. Cyanuric acid precipitated, was removed by filtration, and the filtrate was shaken with saturated $NaHCO_3$. The ethereal layer was decanted and dried over $MgSO_4$. Distillation yielded EtOAc (1·89 g, 49%), b.p. 76°. The IR spectrum was consistent with that of an authentic sample of EtOAc.

Dibutyl ether and trichloroisocyanuric acid. To water (50 g) stirred at 0–10° was added over 20 min TCIA (11·62 g) followed by addition of dibutyl ether (100 ml, 77 g) over 1 hr at the same temp. The mixture was then stirred at 10° for 11 hr and at 27° for 8 hr. The cyanuric acid which precipitated was removed by filtration, and the organic and aq layers were separated. The organic layer was shaken with saturated $NaHCO_3$ and dried over anhyd. $MgSO_4$. Distillation of the organic layer yielded butyl butyrate (10·8 g, 50·5%), b.p. 78°/23 mm. The IR spectrum of the product was consistent with that found in Sadtler's Index.

Ethyl isobutyl ether and trichlorocyanuric acid. The procedure followed was the same as that for diethyl ether in the previous experiment. Ethyl isobutyl ether (15·3 g), TCIA (34·6 g), and water (9 g) were used. Ethyl isobutyrate (14·4 g, 83%), b.p. 23°/20 mm was obtained with an IR spectrum identical to that in Sadtler's Index.

Ethyl isopropyl ether and trichloroisocyanuric acid. Again the procedure used paralleled that used with diethyl ether. Ethyl isopropyl ether (72 g), TCIA (19·6 g), and water (4 g) were used. Isopropyl acetate (55%), b.p. 23° 20 mm was product. The IR spectrum of the product was consistent with that of an authentic sample of the ester.

Diisopropyl ether and trichloroisocyanuric acid. Diisopropyl ether (21·43 g, 0·223 mole) and water (100 g, 5.55 mole) were chilled to 0–10° and TCIA (56·4 g, 0·244 mole) was added following the procedure used for diethyl ether. The mixture was stirred at 0–10° for 6 hr and at room temp for 3½ hr. The cyanuric acid precipitated, was removed by filtration, and the entire filtrate neutralized with solid $NaHCO_3$. Distillation yielded acetone (6·65 g, 39·4%) b.p. 56·1°, but no isopropanol. The IR spectrum of the product was identical to that found for acetone in Sadtler's Index.

Diethyl ether and chlorine water. An excess of diethyl ether (106·5 g) and distilled water (5 g) were stirred rapidly at 0–10°, and chlorine was passed over the mixture for 1 hr followed by additional stirring for 3 hr. The mixture separated into an upper layer of 30 ml and a lower layer of 83 ml.

The upper layer was neutralized with solid K_2CO_3 and dried over $CaSO_4$. Examination of this layer by IR spectroscopy indicated increase of the C=O peak at the expense of the O—H peak and the C—Cl peak with time. After removal of the solvent by distillation, a residue of ethyl acetate (3·6 g) was obtained.

The lower layer was extracted several times with small quantities of water and dried over $CaSO_4$. The water extracts were combined, neutralized with solid K_2CO_3, and extracted three times with 20 ml portions of diethyl ether. The combined diethyl ether extracts together with the lower layer were distilled. Removal of solvent by distillation left EtAc (3·6 g).

The IR spectra of products obtained from the upper and lower layers were identical with that of an authentic spectrum of EtAc. The total yield was (7·2 g, 29·6%), b.p. 74°.

Tetrahydrofuran and chlorine water. A slow stream of Cl gas was allowed to flow over a slowly stirred mixture of THF (55 g, 0·77 mole) and water (8 g, 0·44 mole) cooled to 0°. After introducing Cl_2 for 15 min, the temp increased to 40°. After 2 hr Cl_2 was discontinued, and the mixture was allowed to stir overnight. The mixture separated into 2 layers, 15 ml of upper aq layer and 60 ml of ethereal layer. The combined layers were mixed with 60 ml of diethyl ether and extracted 4 times with 5% $NaHCO_3$. The ethereal layer was discarded, and the water layer was neutralized to a pH of approximately 5 with solid $NaHCO_3$. Precipitated NaCl was removed by filtration. Benzene (20 ml) was added to the filtrate, and H_2O, HCl, and THF were removed by azeotropic distillation with benzene for 48 hr. The benzene was then removed by distillation leaving a slurry of NaCl. The slurry was extracted several times with diethyl ether. The combined ether extract yielded after distillation γ-butyrolactone (3·16 g, yield depending on the amount of Cl_2 introduced was not calculated), b.p. 67°/3 mm. IR analysis indicated the product was γ-butyrolactone.

Ethyl benzyl ether and trichloroisocyanuric acid. The procedure followed was the same as that given for diethyl ether oxidation by TCIA. The reactants employed were ethyl benzyl ether (57·0 g, 0·42 mole), water (6g, 0·33 mole), and TCIA (23·5 g, 0·10 mole). The presence of Cl_2 was observed after $\frac{1}{3}$ of TCIA was added. After addition stirring was continued for 14 hr at 3°. The cyanuric acid was removed by filtration, and the ether layer was washed with water and neutralized with $NaHCO_3$ aq. The ether layer was dried and a volatile fraction was removed through a 10 cm Vigreux column, yielding a 15·3 ml fraction, b.p. 75–77°/12 mm.

The residue from the distillation (1 ml) was identified as ethyl benzoate by its IR spectrum. A portion of this distillate was converted to the 2,4-dinitrophenylhydrazone of benzaldehyde, m.p. 237–238°, (2·86 g, corresponding to 0·01 mole benzaldehyde). Redistillation of the benzaldehyde fraction with a spinning band column gave benzaldehyde (6·93 g, 0·07 mole), b.p. 92–95°/38 mm identified by IR spectrum. The combined yield of benzaldehyde (0·08 mole) represents a 53·3% yield.

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