

## Preparations and Reactions of Quaternary Salts of Bis(chloromethyl) Ether

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### Synopsis

The preparation of some novel quaternary salts of bis(chloromethyl) ether are described. The salts derived from trimethylamine are stable in alkali, whereas the ones containing pyridinium groups are unstable in alkali, and are formaldehyde donors and gelatin hardeners. A possible mechanism for the decomposition reaction is proposed.

Several years ago we became interested in preparing compounds to function as formaldehyde donors for the purpose of hardening polymers such as gelatin. Many types of such compounds are known and are commercially available.<sup>1</sup> Most of these compounds are either methylol compounds such as N-hydroxymethylpyrrolidone or the corresponding ethers or esters of these compounds. The free hydroxymethyl compounds in water are in equilibrium with formaldehyde. The ether derivatives usually require an acid catalyst to activate the donor. Our specific interest was in the creation of compounds which were stable in water but which would readily react with alkali to release formaldehyde. We decided to investigate the behavior of quaternary salts of bis(chloromethyl) ether (bis-CME) in the hope that they might be stable in water but decomposable in alkali to release formaldehyde.

At this time, we are publishing our novel but somewhat unfinished chemistry in this area because of the hazards involved in working with bis-CME and also chloromethyl methyl ether (CMME). The materials are both listed by OSHA as carcinogenic.<sup>2,3</sup> Although we plan no more work in this area, the reactions of these compounds with heterocyclic bases may be of interest to others.

The literature is somewhat confusing as to the properties of these materials. Many compounds, reported in the literature, were isolated as oils or pastes or perhaps as a picrate or gold chloride derivatives. However, the bis-(trimethylammonium methyl) ether dichloride salt was reported to be stable in aqueous alkali.<sup>4</sup>

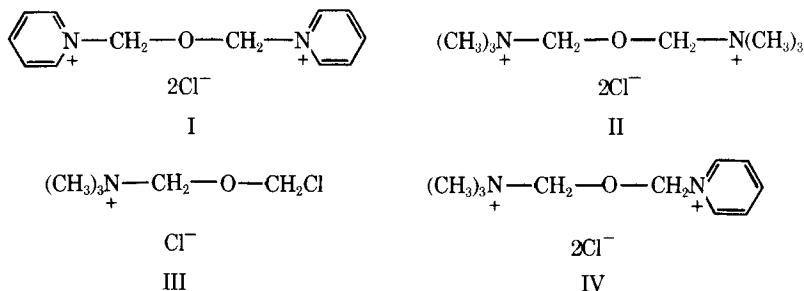
On the other hand, quaternary salts of bis-CME are reported to be somewhat unstable in terms of decomposition to formaldehyde.<sup>5</sup> Still another complication is that these materials are reported to be textile hardeners for applications such as forming permanent creases. This crosslinking reaction is reported to be an alkylation reaction with the base-catalyzed formation of

methylene ether crosslinks.<sup>5,6</sup> There exists patent literature also citing water-proofing cellulose with quaternary salts of octadecyl chloromethyl ether<sup>7</sup> and also how these compounds are not stable to alkali if the salts are derived from heterocyclic bases such as pyridine or quinoline.<sup>8</sup>

We first prepared the bis(pyridinium methyl) ether, I. It was stable in water as determined by NMR studies of a sample measured in water over a period of several months. It was an active gelatin hardener when treated with alkali. The presence of free formaldehyde was demonstrated by the formation of a methone derivative, and the odor of pyridine was evident.

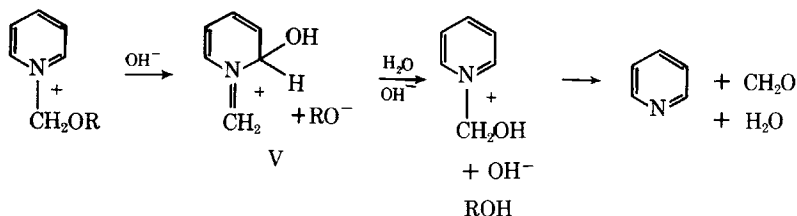
We then decided to prepare the bis(trimethylammonium methyl) ether dichloride, II, to see if this compound was indeed stable to alkali. We isolated in moderate yield a compound which hardened gelatin even without alkali and gave an extremely acid pH when dissolved in water. It proved to be the monoquaternary salt, III. Further reaction of III with trimethylamine produced the desired bisquaternary salt, II. It was unreactive to aqueous alkali, liberating neither trimethylamine nor formaldehyde.

Isolation of compound III enabled us to readily prepare unsymmetrical bisquaternary salts such as IV, which is part aliphatic nitrogen and part heterocyclic nitrogen:



Compound IV releases formaldehyde, pyridine, and trimethylamine when treated with alkali. It is stable in water and is a good base-catalyzed gelatin hardener. The presence of free formaldehyde was again confirmed by the isolation of a methone derivative.

Thus, we have several examples of the ease of reaction of pyridinium quaternary salts versus the extreme unreactivity of the aliphatic quaternary salts. It is apparent that the large difference in reactivity is more than some minor rate factor. We feel that the main mechanism of decomposition most likely involves addition of alkali to the 2-position of the pyridinium ring with expulsion of the alcoholate anion. Reactive intermediate V then reacts again with alkali and finally generates pyridine and formaldehyde:



## EXPERIMENTAL

**Bis(pyridinium Methyl) Ether Dichloride (I)**

A solution of 21 g (0.2 mole) dichloromethyl ether in 400 ml anhydrous acetone was placed into a three-necked, 1-liter flask equipped with stirrer, condenser, and drying tube. To this solution was added 32 g (0.4 mole) pyridine and refluxed for 1 hr. The solution was allowed to cool and the product was filtered. It was recrystallized from ethanol-acetone, mp 211°d. The product weighed 24 g, 48%.

ANAL. Calcd. for  $C_{12}H_{14}Cl_2N_2O$ : C, 52.8; H, 5.1; N, 10.3; Cl, 26.0. Found: C, 52.5; H, 5.4; N, 10.1; Cl, 25.8.

In a similar way was prepared bis(4-*t*-butylpyridinium methyl) ether dichloride, mp 239°d, 66%.

ANAL. Calcd. for  $C_{20}H_{30}N_2Cl_2O$ : C, 62.4; H, 7.8; N, 7.3; Cl, 18.4. Found: C, 62.5; H, 7.7; N, 7.5; Cl, 8.5.

**Trimethylammonium Methyl Chloromethyl Ether Chloride (III)**

In a manner similar to the preparation of I, a solution of 21 g (0.2 mole) in 400 ml dry acetone was saturated with gaseous trimethylamine. The product begins to form shortly after the initial introduction of trimethylamine. At saturation, the gas is shut off and the mixture is allowed to stir at reflux for 15 min. The product is filtered and washed with anhydrous acetone three times. It was vacuum dried at 40°C for a short time as this product decomposes under prolonged heat or vacuum. It is also hygroscopic and hydrolyzes to yield formaldehyde, trimethylamine hydrochloride, and hydrogen chloride; 10 g (33%) of analytically pure product, mp 143°d, was isolated.

ANAL. Calcd. for  $C_5H_{13}Cl_2NO$ : C, 34.4; H, 7.5; N, 8.1; Cl, 40.7. Found: C, 34.3; H, 7.7; N, 8.1; Cl, 40.3.

**Bis(trimethylammonium Methyl) Ether Dichloride (II)**

Into a solution of 17.4 g (0.1 mole) of II in 100 ml dimethylformamide was added gaseous trimethylamine. A crystalline salt was formed which was filtered and dried; 21 g (90%) was obtained, mp 201–202°d.

ANAL. Calcd. for  $C_8H_{22}Cl_2N_2O$ : C, 41.2; H, 9.5; N, 12.0; Cl, 30.4. Found: C, 41.1; H, 9.6; N, 12.0; Cl, 30.3.

**Pyridinium Methyl Trimethylammonium Methyl Ether (IV)**

Into a solution of 41 g (0.25 mole) of II in 100 ml hot dimethylformamide was added 39.5 g (0.5 mole) pyridine. The product was allowed to crystallize and was filtered and dried. 50 g (86%) of product was isolated, mp 185°d.

ANAL. Calcd. for  $C_{20}H_{30}N_2Cl_2O$ : C, 62.4; H, 7.8; N, 7.3; Cl, 18.4. Found: C, 62.5; H, 7.7; N, 7.5; Cl, 18.5.

Compound IV is very hygroscopic and on exposure to atmospheric moisture forms a complex hydrate, mp 65°d. This compound has both IR and

NMR spectra identical to product of melting 185°d. This complex seems to be of constant composition, and redrying will regenerate the original melting point. The hydrate has 1.75 moles of water.

ANAL. Calcd. for  $C_5H_{13}Cl_2NO$ : C, 34.4; H, 7.5; N, 8.1; Cl, 40.7. Found: C, 34.3; H, 7.7; N, 8.1; Cl, 40.3.

### Reactions of the Quaternary Salts

Compounds I and IV when added to a 5% gelatin solution do not harden the gelatin until treated with aqueous alkali, whereupon a rapid, irreversible gelation occurs. When aqueous solutions of compounds I and IV were mixed with methone in the presence of base, a white solid was obtained in both cases, mp 191°C. It is identical to that obtained from methone and formaldehyde in terms of melting point and infrared spectrum.<sup>9</sup> Compound II does not harden gelatin or produce a formaldehyde-methone derivative.

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