AUTOCATALYTIC SOLVOLYTIC DEMERCURATION OF

4-METHOXYBENZYLMERCURIC CHLORIDE

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In general, solvolytic demercuration (DM) of organomercury salts (OMC) RHgX proceeds via a carbocationic mechanism [1-3], and is facile, especially if the R group corresponds to a reasonably stable carbocation, and if the anion X⁻ exhibits very low affinity for the organomercury cation (MC) RHg^+ (such as, for instance, $X^- = ClO_4^-$, $CF_3CO_2^-$, and OAc^-). When X = Hal, DM occurs significantly slower, as expected [1]. However, evidence has recently been obtained favoring the formation of radical particles R'. upon demercuration of secondarybenzylic type OMC in MeOH and MeNO₂ [4-6]. Although it is never possible to exclude completely the possibility that radicals are formed as a result of some type of side reaction, the large intensity of the signals in the EPR spectrum is indicative of radical character for the main DM process of secondary-benzylic compounds. We note also that recently the formation of alkyl radicals has been detected in a series of other reactions, in addition to DM, which previously had been assumed to be heterolytic in nature. For instance, in the hydrolysis of organoaluminum comounds [7], the decomposition of organocobalt compounds in acidic media [8], the hydrolysis of alkyl derivatives of Ti and V [9], as well as in alkyl ligand exchange in Zn, Cd, and Hg compounds [10], spin trapping and inhibitor methods have led to the detection of alkyl radicals, which appear in polar media at normal temperatures. In order to understand better the relationship between radical and ionic demercuration pathways of OMC, we have studied a series of substituted benzylmercuric halides, $Z-C_6H_4CH_2HgX_3$, containing both electron donating (4-OCH₃, 4-CH₃) and electron withdrawing (4-NO₂, 4-F, 3-OCH_a) substituents, in addition to unsubstituted benzylmercuric chloride. It was found that, of the compounds enumerated above, only p-methoxybenzylmercuric chloride (I) underwent facile DM upon heating in methanol, while the other OMC did not undergo reaction under these conditions. DM of (I) was carried out under anaerobic conditions in a vacuum-sealed ampul, since (I) is readily oxidized by oxygen in air to give $4-CH_3OC_6H_4CH0$, $4-CH_3OC_6H_4COOCH_3$, and Hg₂Cl₂ as the main reaction products. Solvolytic DM at 65°C in MeOH under these conditions gave metallic mercury and methyl p-methoxybenzyl ether in quantitative yields.

$$4-CH_{3}OC_{6}H_{4}CH_{2}HgCl \xrightarrow{\text{MeOH}} 4-CH_{3}OC_{6}H_{4}CH_{2}OCH_{3} + Hg(0) + HCl$$
(1)
(I)

Kinetic measurements revealed that the reaction was significantly accelerated with time (Fig. 1). Apparently, an autocatalytic process, in which one of the reaction products which is formed acts as a catalyst of the general reaction, is taking place. Autocatalysis similar to that reflected in Fig. 1 was also observed for DM in ethyl and tert-butyl alcohols. The total rate of the reaction process decreased in the series MeOH > EtOH > t-BuOH.

DM of (I) in MeOH at 65°C in the presence of a common ion (Cl⁻) salt (NaCl) was accomppanied by a substantial retardation of the entire process, particularly in the initial stages. For instance, after 90 min following onset of the reaction, the degree of conversion of (I) was 35% in the absence of salt, 1% in the presence of 0.168 M NaCl, and 72% in the presence of added 0.071 M Et₄NBF₄. These data can be explained within the framework of a mechanism involving reversible dissociation of the OMC at the Hg-Cl bond in the first stage of the reaction, and subsequent DM of the resulting MC according to Scheme 1.

Scheme 1

$$(I) \iff 4\text{-}CH_3OC_6H_4CH_2Hg^+ + Cl^-$$
(2)
4-CH_3OC_6H_4CH_2Hg^+ $\xrightarrow{} 4\text{-}CH_3OC_6H_4CH_2^+ + Hg (0)$ (3)

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Fig. 1. Application of a first-order equation to describe the kinetic data for demercuration of (I) $(1.4 \cdot 10^{-2} \text{ mole/liter})$ in MeOH at 65°C.

$$4 - CH_3OC_6H_4CH_2 + \frac{CI^- \text{ or } S_{OIV}}{\longrightarrow} \text{ Products}$$
(4)

A special series of experiments carried out with the addition of $AgNO_3$ to solutions of the substituted benzylmercuric halides revealed that $4-CH_3OC_6H_4CH_2Hg^+$ undergoes demercuration almost instantaneously, whereas in the presence of other substituents the reaction is either very slow (4-CH₃) or else does not occur at all (4-NO₂). This fact, coupled with the result mentioned previously, that of all the benzylmercuric halides examined, only (I) undergoes demercuration, substantiates the heterolytic reaction scheme shown in Scheme 1, in which a MC is formed as an intermediate.

In glacial acetic acid, however, demercuration of (I), which leads to p-methoxybenzyl acetate, does not appear to be autocatalytic; the rate of the reaction is described by a first-order equation. This difference leads to the conclusion that DM is catalyzed by acids, and that in alcohol solution autocatalysis is due to the presence of HCl which is liberated during the course of reaction (1). Acidic catalysis, in turn, may be associated with an increase in the concentration of MC as the acidity of the reaction medium is enhanced.

$$(I) + H^{+} \rightleftharpoons 4\text{-}CH_{3}OC_{6}H_{4}CH_{2}Hg^{+} + HCl$$
(5)

Similar catalysis (although by Lewis acids) has been observed for DM of cyclohexylmercuric acetates [11], but in the case of cyclohexylmercuric chloride, the reaction did not occur at 25°C even in the presence of acidic catalysis.

The mechanism depicted in Scheme 1 is very simple and describes very well all of the examples of DM reactions which have been studied up to this time [1-3]. Nevertheless, we have obtained data which indicate that the mechanism of DM may be more complex. First of all, it was always noted that the solutions of even rigorously purified samples of (I) contained very small amounts (ca. 0.5% of the weight of OMC) of HgCl₂. It is assumed that HgCl₂ is formed by symmetrization of RHgX, which occurs when the samples are dissolved in various solvents. Although the symmetrization equilibrium is shifted strongly to the left, the presence of trace amounts of HgCl₂ was always detected. Independent experiments with HgCl₂ as an additive demonstrated that it resulted in a significant increase in DM, but that in the presence of large amounts of HgCl₂ (>20%), the composition of reaction products was altered: in place of Hg, Hg₂Cl₂ was isolated. For these reasons, the presence of HgCl₂ impurities must be taken into account in constructing an overall reaction scheme.

It can be assumed that, in the presence of $HgCl_2$, an oxidative-reductive reaction is taking place [12, 13], as a result of which the initially formed cation-radical intermediate RHgX⁺ decomposes to give an R⁺ cation and HgCl· radical (pathway α in Scheme 2). This path is favored relative to path b in the case of (I), since the $4-CH_3OC_6H_4CH_2^+$ cation is quite stable. For benzylmercury salts containing other substituents instead of MeO, pathway b involving benzyl radicals may be more probable, and would lead to a degenerate reaction.



After all of the $HgCl_2$, either that added to the reaction mixture or that contained as impurity in the sample, has been consumed as a consequence of the oxidative-reductive process, the reaction continues, but with the formation of metallic mercury. In alcohols the acid which is liberated during solvolysis autocatalyzes DM, in accordance with Eq. (5).

Acting on the assumption that oxidation of (I) by mercuric chloride is rapid, and that acid formed during solvolysis catalyzes DM, we have analyzed the kinetic data (in alcohol solutions) using a kinetic scheme for an autocatalytic process [14], according to which the rate of DM is determined by reaction (5):

$$k_{2}t = \left\{\frac{1}{[A]_{0} - x}\right\} \ln\left\{\frac{[A]_{0}\left([P]_{0} + x\right)}{([A_{0}] - x)[P]_{0}}\right\} \equiv F(x)$$
(6)

for $A \rightarrow P$ with autocatalysis, where $dx/dt = k_2[A][P]$, and where k_2 is the rate constant for a second-order catalytic process, sec⁻¹; t is the time in sec; $[A]_0$ is the initial concentration of (I), mole/liter, $([A]_0 - x)$ is the running concentration of (I), mole/liter, $[P]_0$ is the initial concentration of HCl catalyst, mole/liter, and $([P]_0 + x)$ is the running concentration of catalyst, mole/liter.

For the calculations it was assumed that the initial concentration of HCl acid was equal to the concentration of HgCl₂ present either as impurity or as additive, i.e., $[P]_0 = [HgCl_2]_0$.

The amount of HgCl_2 present in (I) was determined polarographically based on the height of the two-electron reduction wave for HgCl_2 ($\text{E}_{1/2} = -0.11$ V relative to SCE). It was found that (I) prepared via the standard procedure [15] contained 1.5% HgCl_2 , and that specially purified material contained 0.4% HgCl_2 .

At $[P]_0 = 0.4\%$ (7·10⁻⁵ mole/liter) for the specially purified sample, and $[P]_0 = 1.5\%$ (2.8·10⁻⁴ mole/liter) for a standard sample, the kinetic data for DM in alcohol solutions give a straight line dependence of F(x) versus time (Fig. 2). Second-order rate constants k_2 were calculated by least squares and are summarized in Table 1.

Thermodynamic parameters for reaction (5) were determined based on the temperature dependence of the reaction rate in MeOH solution and have the following values: $E_a = 14.2 \text{ kcal/}$ mole, log A = 8.08, $\Delta S_{298}^{\pm} = -24.5 \text{ cal/K} \cdot \text{mole}$. The entropy of activation ΔS_{298}^{\pm} is characteristic of a bimolecular substitution reaction A+B - C \Rightarrow A - B + C (log A = 7-11; $\Delta S_{298}^{\pm} = -30 \text{ to } -10 \text{ cal/K} \cdot \text{mole}$ [16]).

DM is not autocatalytic in AcOH, so k_2 in this solvent was calculated using the dependence of k_{obs} on CH₃COOH concentration in acetic acid.

Addition of a common ion salt such as NaCl could have the following effects: a) deactivation of mercuric chloride in the initial oxidation reaction of RHgCl (since $HgCl_3^-$ is a worse electron acceptor than $HgCl_2$); b) deactivation of the acid catalyst; c) hinders the formation of MC (reaction (2)) due to the increase in Cl⁻ concentration in solution. For these reasons, there is no straight line correlation using Eq. (6) for the results obtained in MeOH containing NaCl.

The observation of a large positive salt effect upon the addition of Et_4NBF_4 , coupled with the fact that the calculated values of k_2 in four different protic solvents give good correlations with their Koppel-Pal'm polarity parameters (r = 0.987), suggests that the



Fig. 2. Application of a kinetic equation for an autocatalytic process to the kinetic data for DM of $4-CH_3OC_6H_4CH_2HgCl$ (1.4·10⁻² M) in the presence of HgCl₂ (2.8·10⁻⁴ M) in CH₃OH at 65°C.

TABLE 1. Second-Order Rate Constants k_2 for Reaction (5) Calculated Using Eq. (6) (HgCl₂ concentration 2.8·10⁻⁴ M: 1.5%; 9.3·10⁻⁵ M: 0.5%)

Solvent (con- centration of HgCl ₂ , %)	T, °C	k2, liter/mole• sec	Solvent (con- centration of 'HgCl ₂ , %)	Т, ℃	k2, liter/mole· sec
MeOH (0,4) MeOH (1,5) MeOH (1,5) MeOH (1,5)	65 65 60 55	$\begin{array}{c} 8,95\cdot 10^{-2} \\ 8,90\cdot 10^{-2} \\ 5,66\cdot 10^{-2} \\ 3,71\cdot 10^{-2} \end{array}$	EtOH (1,5) <i>t</i> -BuOH (1,5) AcOH (1,5)	65 65 65	$\begin{array}{c} 4.55 \cdot 10^{-2} \\ 2.54 \cdot 10^{-3} \\ 1.53 \cdot 10^{-6} \\ (k_1 \cdot 2.68 \cdot 10^{-5} \text{ sec}^{-1}) \end{array}$

transition state in catalytic DM is extremely polar (has a large amount of charge separation).

We have found that prolonged heating of (I) in aprotic solvents such as MeCN or $MeNO_2$ leads to 100% decomposition of OMC (practically pure mercury is formed at $HgCl_2$ equal to 0.4-1.5% by weight of OMC). In $MeNO_2$, $4-CH_3OC_6H_4CH_2Cl$ is obtained in 90% isolated yield. The reaction is sharply suppressed when the concentration of $HgCl_2$ in the sample is reduced. It is clear that $HgCl_2$ impurity plays a deciding role in this reaction as well. The reaction does continue, however, after all of the $HgCl_2$ has been consumed by oxidation of OMC. It is possible that the presence of very small amounts of water in these solvents* leads to the formation of catalytic quantities of HCl. In addition, we cannot exclude the possibility that small amounts of HgCl are generated constantly in solution as a result of self-symmetrization; this would guarantee the needed amount of $HgCl_2$, since DM occurs very slowly in aprotic solvents.

The results obtained herein are indicative of a complex heterolytic mechanism for DM of (I).

EXPERIMENTAL

Reaction mixtures were analyzed and the purity of organic compounds was estimated using GLC analysis (LKhM-8MD, model 5, chromatograph, 170°C, 2 m × 3 mm column with 3% SP 2100 on Chromaton H super, N₂ carrier gas, 30 ml/min, flame ionization detector, internal standard $C_{15}H_{32}$) and by chromatography/mass spectrometric analysis (Finnigan MAT 112-S chromatomass spectrometer, OV-101 (0.25%) column, 50 m × 0.25 mm, He carrier gas, 1 ml/min, 70-200°C, 6 deg/min, E = 80 eV).

The starting material, p-methoxybenzylmercuric chloride (I), was synthesized via a Grignard reaction, according to a known method [15]; mp 102-103°C (after multiple recrystallization from benzene) (cf. [15]).

*For example, MeCN which has been dried over CaH_2 and distilled over P_2O_5 contains ca. 0.03% water, according to Fischer titration. In absolute benzene, DM of p-methoxybenzylmercuric chloride is not observed even after heating for 100 h at 80°C.

<u>General Method for the Demercuration of OMC in Various Solvents</u>. An ampul fitted with a ground glass joint and stopcock was charged with the required weight of (I) in the appropriate solvent. The reaction mixture was degassed on a vacuum apparatus (fourfold freezethaw cycle) to a final pressure of $5 \cdot 10^{-3}$ mm Hg and the ampul was sealed. It was heated in a thermostat for the necessary period of time at the required temperature. The ampul was opened, the contents centrifuged, and the solution was decanted from the mercury precipitate. The metallic mercury was washed with acetone, dried, and weighed, and then mixed with NaOH in order to detect the presence of Hg_2Cl_2 within the finely dispersed mercury residue. The decanted solution was analyzed by TLC, GLC, and chromatomass spectrometry. If the solvent used contained a salt additive, a solution of the desired concentration in the solvent of choice was prepared. This solution was then placed in the ampul along with (I).

1) (I) in MeOH. The reaction was charged with 50 mg (0.1 mmole) (I) in 10 ml absolute MeOH. After 100 h heating in a thermostat at 65°C, the tube was broken. Isolated yields: 28.0 mg (99%) Hg (Hg₂Cl₂, traces), 20.7 mg 4-CH₃OC₆H₄CH₂OCH₃ (97%, traces of 4-CH₃OC₆H₄CH₃).

2) (I) in MeNO₂. The reaction was charged with 50 mg (0.1 mmole) (I) in 10 ml absolute MeNO₂. After heating for 50 h in a thermostat at 65°C for 50 h, 23.3 mg Hg (97%, small amount of Hg₂Cl₂ impurity) and 19.8 mg (90%) 4-CH₃OC₆H₄CH₂Cl were isolated.

CONCLUSION

1. The solvolytic demercuration reaction of 4-methoxybenzylmercuric chloride (I) was investigated. In alcohol solutions the reaction is autocatalytic in nature; the catalyst appears to be HCl which is formed during the course of the reaction with solvent.

2. The calculated second-order rate constants for the reaction of (I) were found to increase linearly as the polarity of the protic solvent increased (AcOH < t-BuOH < EtOH < MeOH).

3. Demercuration is initiated by the presence of traces of mercuric chloride, either from impurities or special additive. Initiation due to mercuric chloride is apparently associated with oxidation of the organomercury compound.

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