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Notes

Base-Catalyzed Solvolysis of 1,1,1-Trihaloacetones in the Presence of Ammonia Buffer. Analogy with Substitution at Silicon and Tin

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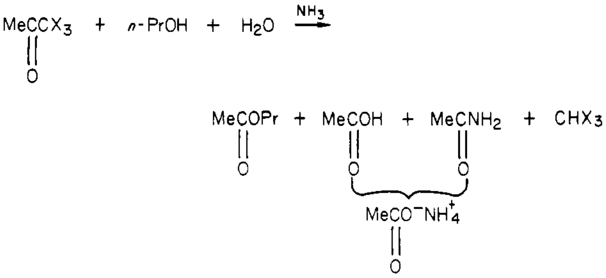
The cleavage of the carbon–carbon bond (C–Y) in carbonyl compounds RCOY, such as in hydrolyses of acetyl- and acetylethylmalonates, acyl cyanides, acetylacetone, and chloral, has been reviewed by Jencks.[1] The ease of such a cleavage depends on the ability of the group Y to sustain a negative charge. The well-known haloform reaction for cleaving methyl ketones is driven by the accumulation of negative charge on the trihalomethyl group. Although the haloform reaction is a useful method for preparing acids,[2] its mechanism has been studied only for the halogenation phase.[3] The subsequent alkali-promoted cleavage has been postulated to proceed through an addition intermediate.[4] We report here the results of a kinetic study of the ammonia-promoted solvolysis of 1,1,1-trichloroacetone and 1,1,1-tribromoacetone in aquenous *n*-propanol and compare the results with those previously reported for the ammonia-promoted solvolytic cleavage of polyhalomethyl groups from silicon[5] and tin.[6]

Results and Discussion

Solvolysis of 1,1,1-Trihaloacetones. Solvolyses of CH_3COCX_3 (X = Cl, Br) were carried out in *n*-propanol–water (8:2 v/v) in the presence of ammonia buffer.[3] The kinetics were determined by GC determination of the halo ketone and the haloform released in the reaction. The ionic strength was maintained at 0.4 by addition of LiCl.

Acetic acid and acetamide were formed during the reaction (eq 1), consuming the ammonia catalyst. For this reason the first-order rate constants were determined by the initial-rate method.



$$\mathrm{MeC(O)CX_3} + n\text{-}\mathrm{PrOH} + \mathrm{H_2O} \xrightarrow{\mathrm{NH_3}} \mathrm{MeC(O)OPr} + \underbrace{\mathrm{MeC(O)OH} + \mathrm{MeC(O)NH_2}}_{\mathrm{MeC(O)O^-NH_4^+}} + \mathrm{CHX_3} \qquad (1)$$

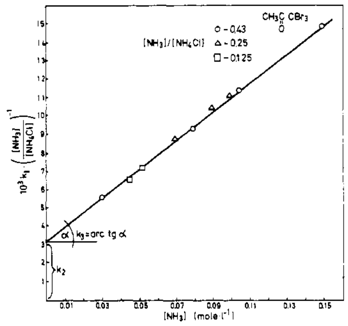


Figure 1. Dependence of the observed first-order rate constant on the ammonia and buffer concentrations for the cleavage of $MeC(O)CBr_3$ in *n*-PrOH–H_2O (8:2 v/v) at 25 °C.

Table I. Kinetic Data for Solvolysis of $MeC(O)CCX_3$ in *n*-PrOH–H_2O (8:2 v/v; t = 25 °C; μ = 0.4)

compd (concn, M)	$[NH_3]$, mol/L	$[NH_3]/[NH_4Cl]$	$10^5 k_I$, s^{-1}	catalytic constants k_2, s^{-1}, and k_3, L $mol^{-1} s^{-1}$
$MeC(O)CCl_3$ (0.15)	0.092	11.5	24	$k_2 = 1.5 \times 10^{-5}$
	0.3	11.5	42	$k_3 = 7.0 \times 10^{-5}$
	0.46	11.5	57	
	0.7	11.5	75	
	0.92	11.5	91	
	0.084	5.25	11	
	0.274	5.25	18	
	0.639	5.25	32	
	0.84	5.25	38	
	0.068	2.12	4.2	
	0.68	2.12	13	
$MeC(O)CBr_3$ (0.15)	0.03	0.43	239	$k_2 = 3.1 \times 10^{-3}$
	0.08	0.43	395	$k_3 = 7.8 \times 10^{-2}$
	0.105	0.43	488	
	0.15	0.43	639	
	0.07	0.25	217	
	0.09	0.25	257	
	0.10	0.25	275	
	0.045	0.125	81.2	
	0.052	0.125	89.7	

Analysis of the kinetics determined at different ammonia concentrations and buffer ratios indicated that two catalytic reactions were occurring in the system, as shown in eq 2. The rate constants k_2 and k_3 were determined from

$$-\frac{d[\mathrm{MeC(O)CX_3}]}{dt} = \frac{d[\mathrm{CHX_3}]}{dt} = \left(k_2 \frac{[\mathrm{NH_3}]}{[\mathrm{NH_4Cl}]} + k_3[\mathrm{NH_3}]\frac{[\mathrm{NH_3}]}{[\mathrm{NH_4Cl}]} \right)[\mathrm{CH_3C(O)CX_3}] = k_I[\mathrm{CH_3C(O)CX_3}] \qquad (2)$$

the dependence of the first-order rate constant k_I on $[NH_3]$ (Figure 1) and are shown in Table I.

Both of the processes occurring in this system lead to carbon–carbon bond cleavage. The rate of one, k_2, is proportional to the concentration of the ketone and that

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Table II. Comparison of Kinetics of Solvolytic Cleavage of the Polyhalomethyl Group from Silicon, Tin, and Carbonyl Carbon (8:2 v/v n-PrOH-H_2O or NH_3-NH_4Cl, 25 °C): Catalytic Constants for Simple Solvent Conjugate Base Catalysis (k_2), Complex Solvent Conjugate Base-Ammonia Nucleophile Catalysis (k_3), and Ammonia General-Base Catalysis (k_1)

compd	$10^7 k_2$, s^{-1}	$10^7 k_3$, L mol^{-1} s^{-1}	k_3/k_2	$10^7 k_1$, L mol^{-1} s^{-1}	ref
$Me_3SiCHCl_2$	0.92	6.99	7.59		20
$Me_3SiCHBr_2$	107	169	1.58		
Me_3SiCHI_2	226	343	1.52		
$Me_3SnCHCl_2$	0.43	0.3	0.7	4.15	6a
$Me_3SnCHBr_2$	4.37	5.12	1.17	60.5	
$MeC(O)CCl_3$	150	700	4.67		this work
$MeC(O)CBr_3$	31500	779000	24.73		

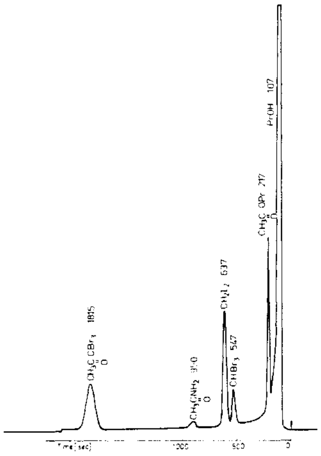


Figure 2. Gas chromatogram of the reaction system at 10% conversion; $[CH_3C(O)CBr_3]_0 = 0.15$ mol/L.

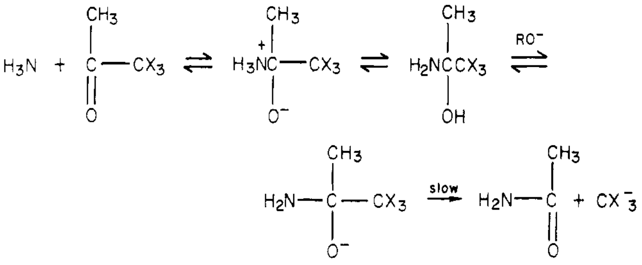
of the solvent conjugate base n-$C_3H_7O^-$ or HO^-,[7] thus showing the characteristics of specific base catalysis. The rate of the other process, k_3, also depends on the concentration of the weak base ammonia. The role of ammonia can be considered in terms of nucleophile catalysis, since acetamide was found to be the intermediate product of the cleavage (see Figure 2) which then undergoes solvolysis by n-propanol or water.

We observed a substantial increase in reaction rate on changing the leaving group from CCl_3 to CBr_3. This order of reactivity is in accord with the order $HCCl_3 < HCBr_3 < HCI_3$ reported for base-catalyzed D-H exchange.[8] These orders of reactivity reflect the negative charge stability on the CX_3 group and point to C-C bond cleavage as the rate-limiting step in our solvolysis reaction.

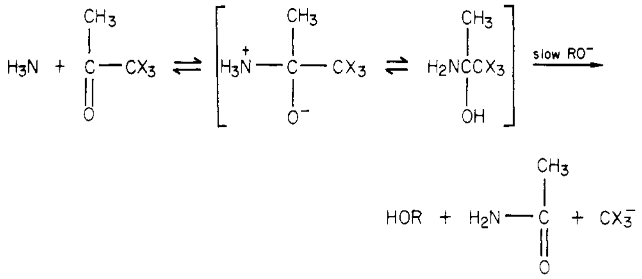
The mechanism of the base-catalyzed ammonolysis of the trihaloacetones should not proceed by any route involving ammonia as a conjugate base because amide ion is not likely to appear in the system in a kinetically significant concentration.[9] There are three possible pathways that can be considered for the catalyzed solvolysis, and these are shown in Schemes I-III.

Scheme I is a stepwise mechanism that involves specific base catalysis by lyate ion RO^-. It includes a series of fast preequilibria that lead to formation of the conjugate base of the ammonia-substrate complex. The accumulation of negative charge provides the driving force for C-C bond cleavage in the subsequent rate-limiting step. Scheme III is a concerted mechanism that involves formation of the bond with the approaching nucleophile, breaking the bond to the leaving group, and proton transfer from ammonia to the lyate ion. In Scheme II an intermediate complex between ammonia and the ketone is formed in the preequilibrium step. This complex then undergoes general-base-catalyzed decomposition with C-C bond rupture, making this mechanism similar to that of Scheme III.

Scheme I



Scheme II



Kinetic data do not suffice to distinguish among these three mechanisms. Tetrahedral intermediates have been established in reactions of carbonyl compounds,[10] and stepwise mechanisms analogous to Scheme I have been proposed for hydrolysis and aminolysis of esters,[10,11] transimination reactions,[12] and hydrolysis of chloral.[13] This last reaction most closely resembles the solvolysis of trihalo ketones, but its catalysis differs in requiring two molecules of the strong base HO^- to split off the CCl_3 group. A process analogous to the simple base-catalyzed solvolysis of 1,1,1-trihaloacetones has also been observed with chloral, but it proceeds much more slowly. This observation probably reflects the destabilization of a tetrahedral intermediate by CH_3 compared with H.

The possibility that the mechanism corresponds to Scheme II is supported by the fact that general-base catalysis is commonly observed in the aminolysis of carbonyl compounds. However, the concerted mechanism of Scheme III cannot be excluded.

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(7) The buffer ratio $[NH_3]/[NH_4Cl]$ was taken as the measure of the solvent conjugate base concentration.

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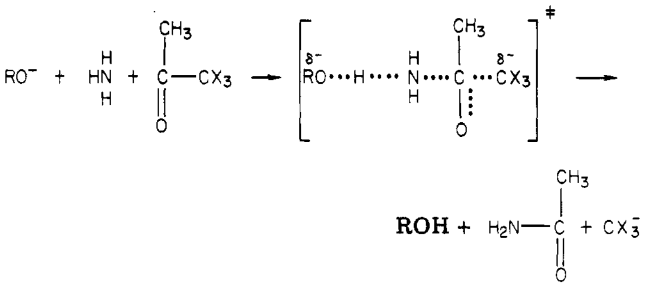
Scheme III



The kinetics of the solvolytic cleavage of the C_{sp^2}–C_{sp^3} bond in these trihaloacetones resemble those of the cleavages of Si–C_{sp^3} and Sn–C_{sp^3} bonds studied in similar systems.[5,6,14] All of these reactions involve competition between direct base solvolysis and base-catalyzed ammonolysis. Similar mechanisms have been proposed for all, although the kinetic data do not distinguish among them. The general expression for the observed first-order rate constant is shown in eq 3.

$$k_\mathrm{I} = k_1[\mathrm{NH_3}] + k_2\frac{[\mathrm{NH_3}]}{[\mathrm{NH_4Cl}]} + k_3\frac{[\mathrm{NH_3}]}{[\mathrm{NH_4Cl}]}[\mathrm{NH_3}] = k_1'[\mathrm{NH_3}] + k_2'[\mathrm{RO^-}] + k_3'[\mathrm{RO^-}][\mathrm{NH_3}] \quad (3)$$

Catalysis by the weak base ammonia (k_1) is the predominant reaction in the solvolysis of Sn–C bonds, whereas only simple base (k_2) and base–nucleophile (k_3) catalyses are observed in the solvolysis of Si–C and C–C bonds.[15] The catalytic rate constants for solvolysis of these three bond types are shown in Table II.

Experimental Section

All solvents were carefully dried and purified by standard techniques.[16] Kinetic analyses were performed with a GCHF 18.3 Willy Giede gas chromatograph equipped with a Takeda Riken TR 2215 A integrator.

1,1,1-Trichloroacetone was prepared from acetic anhydride and sodium trichloroacetate in 1,2-dimethoxyethane;[17] NMR (CCl_4) δ 2.89 (s, 3 H, CH_3).

1,1,1-Tribromoacetone was obtained by bromination of bromoacetone[18] with *N*-bromosuccinimide in CCl_4. It was separated from the reaction mixture and purified by preparative GLC using a column packed with SE-30 on Chromosorb W (45/60 mesh); NMR (CCl_4) δ 2.77 (s, 3 H, CH_3) (lit.[19] NMR δ 2.73).

Kinetic measurements were carried out in thermostated flasks, sealed with silicone rubber membranes, at 25 °C. Samples (0.3 μL) were taken at predetermined intervals with a 1-μL gas-tight Hamilton syringe and analyzed by GLC (see Figure 2) using a double FID system. The haloforms were determined with the aid of internal standards: *n*-octane for $CHCl_3$ and CH_2I_2 for $CHBr_3$.

Registry No. MeC(O)CCl_3, 918-00-3; MeC(O)CBr_3, 3770-98-7.

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[15] The role of catalysis by weak base in the Si–C bond cleavage was disclosed by studies of the cleavage of (trihalomethyl)trimethylsilanes cleavage in the presence of pyridine–pyridine hydrochloride buffer. In this system, catalytic reactions involving the solvent conjugate base were not able to compete with spontaneous solvolysis and with the reaction catalyzed by pyridine acting as a general base.[3]

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Conformational Studies by Dynamic Nuclear Magnetic Resonance. 22.[1] Torsional Barriers in Some (Dimethylamino)nitrothiophens

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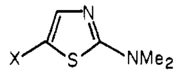
Evidence for restricted rotation about the C–N bond in a number of amino-substituted aromatic derivatives has been obtained by dynamic nuclear magnetic resonance spectroscopy.[2-9] The same effect has recently been observed in some 5-substituted 2-(dimethylamino)thiazoles (**1**; X = H, Br, NO_2).[8] We now report the results of a similar study of some 5-substituted 2-(dimethylamino)-3-nitrothiophenes (**2a**–**h**).



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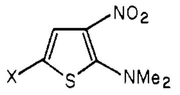

2a, X = H
b, X = Br
c, X = $CONH_2$
d, X = CO_2Me
e, X = COMe
f, X = SO_2Me
g, X = CN
h, X = NO_2

The interaction of the dimethylamino group with the aromatic ring and the consequent double bond character of the C–N linkage are determined by two factors: the conjugative effect and the steric effect. The hyperortho relation[10] between substituents linked to the 2- and 3-

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