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MECHANISTIC ASPECTS OF ACID-CATALYZED REACTIONS OF 2,2,2-TRIFLUORODIAZOETHANE WITH ALCOHOLS

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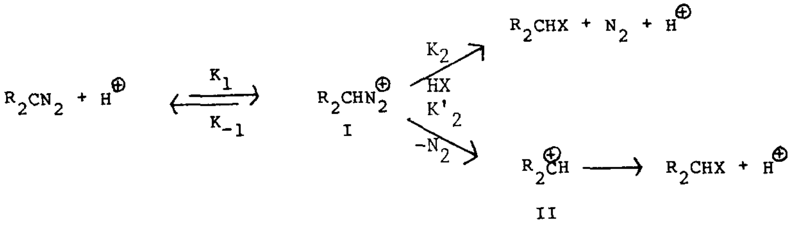
SUMMARY

This paper describes a mechanistic study of the acid-catalyzed reactions of various alcohols with 2,2,2-trifluorodiazoethane (TFD). Both specific and competitive reaction rates are reported for various oxygen nucleophiles (e.g., alcohols). In addition, evidence for a rapid pre-equilibrium proton transfer step was obtained using a deuterated alcohol and monitoring the products by ^{19}F NMR.

Numerous acid-catalyzed decomposition studies of diazo compounds have appeared in the literature [1-12] and various mechanistic schemes have been formulated (i.e., A-SE_2, A-1, or A-2). For the case of 2,2,2--trifluorodiazoethane (TFD), a deuterium isotope study by Dahn et al. [8] yielded a solvent (40% aqueous dioxane) isotope effect (K_D/K_H) of 0.6 ± 0.1. These results suggest that



(A-S_E2, K_1 slow; A-1, K'_2 slow; A-2, K_2 slow)

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the mechanism involves a rapid pre-equilibrium proton transfer step (i.e. A-1 or A-2). In addition, Mohrig and Keegstra [12] have observed the intermediate 2,2,2-trifluorodiazonium ion (corresponding to I) in a FSO_3H solution at -78°C utilizing NMR techniques. Warming the solution to -20°C led to vigorous evolution of N_2 and formation of 2,2,2-trifluoroethylsulfate.

In the present study, we have obtained additional evidence for a rapid pre-equilibrium proton transfer step (i.e., $K_{-1} > K_2$ or K'_2). Specifically, addition of TFD (0.21 mmole) in methylene chloride to a d-chloroform solution containing an excess of CD_3OD (99.5% deuterium, 4.0 mmoles) and $DBF_4 \cdot OEt_2$ (0.05 mmole) at 25°C initiates a rapid reaction with evolution of N_2. The reaction product trifluoroethyl methyl ether contains over 85% of the completely deuterated product (CF_3CD_2-O-CD_3). This is clearly evident in Figure 1 which is the ^{19}F NMR spectrum for this reaction mixture*. The remaining product (~15%) is the product (CF_3CHD-O-CD_3). Additional experiments with a weaker nucleophile (d_3-trifluoroethanol) have provided similar results. Furthermore, control experiments indicate that the product (CF_3CD_2-O-CD_3) does not exchange protons with the solvent over an extended time period (~1 hr.).

The next question is whether the diazonium ion decomposes in unimolecular fashion (A-1) yielding carbonium ion II or loses nitrogen with attack of a nucleophile in a bimolecular step (A-2). At first glance, the existence of II requires loss of a neutral, highly stable molecule of nitrogen. In addition, solvation of the departing nitrogen is not required. These considerations make the activation energy for its decomposition very small which can result in an exothermic process. [13] We have measured the reaction rate of TFD with various alcohols in CH_2Cl_2 and 1,2-dimethoxyethane (85:15) under pseudo-first order kinetic conditions at 25°C. Specifically, the disappearance of TFD was monitored using a UV spectrometer (Hitachi Model 100-60) at 403 nm. At low concentrations of alcohol (e.g., methanol) the rate is first order with respect to nucleophile. Using the slopes at low nucleophile concentration, pseudo first order rate constants can be estimated (MeOH≈EtOH≈n-PrOH≈80 $l^2 mole^{-2}$-min^{-1}; CF_3CH_2OH = 5.0 $l^2 mole^{-2}$-min^{-1}).

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[*] The quintet in Fig. 1 exhibits a fluorine-deuterium coupling constant ($^3J_{DF}$) of 1.3 Hz for the completely deuterated product ($CF_3CD_2OCD_3$). In addition, a deuterium isotope shift (0.06 ppm, increasing shielding) is clearly evident between the center of the ^{19}F signals for the quintet and the doublet of triplets ($^3J_{HF}$ = 8.9 Hz, $^3J_{DF}$ = 1.3 Hz) for CF_3CHD-OCD_3.

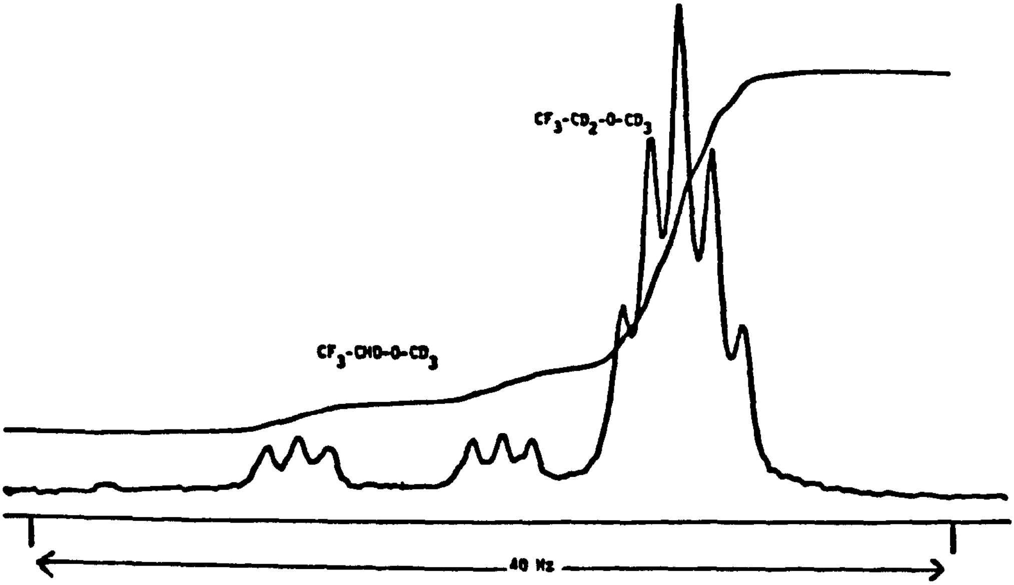

Fig. 1. 188 MHz ^{19}F NMR Spectrum for the Products of the Reaction of 2,2,2-Trifluorodiazoethane with CD_3OD.

In addition to the kinetic experiments described above, competitive rates for various oxygen nucleophiles were determined (Table 1). Specifically, two or three alcohol nucleophiles in a solution containing the acid catalyst ($HBF_4 \cdot H_2O$) were allowed to compete for a limited amount of TFD added to this mixture. The relative amounts of products were determined by ^{19}F NMR integration in these competitive rate studies. An order of reactivity can be established for the reactions involving TFD which might suggest nucleophilic assistance in the rate determining step.

R-CH_2-OH >	Sec-butyl >	t-butyl alcohol >	trichloroethanol >
25-16	6.7	3.3	2.7
trifluoroethanol >>	p-nitrophenol		
1.0	< 0.01		

This series appears to parallel decreasing basicity with increasing nucleophilicity [13-14]. However, the sensitivity of TFD to steric

TABLE 1

Competitive Reaction Rates of Oxygen Nucleophiles with 2,2,2-Trifluorodiazoethane[a]

Competing Nucleophiles	Relative Rates
CF_3CH_2OH/CH_3CH_2OH	1/23
$CF_3CH_2OH/CH_3CH_2CH_2CH_2OH$[c]	1/16
$CF_3CH_2OH/CCl_3CH_2OH/CH_3CH_2OH$	1/2.7/22
$CF_3CH_2OH/\phi\text{-}OH$	1/1.5
$\phi\text{-}OH/p\text{-}NO_2\text{-}\phi\text{-}OH$[b]	1/<0.01
$\phi CH_2OH/CH_3OH$	1/1.3
$\phi CH_2OH/CH_3CH_2OH$	1/1.3
$\phi CH_2OH/CH_3CH_2CH_2OH$	1/1.3
$CH_3CH_2CH_2CH_2OH/H_2O$[b,c]	1/1.3
$CH_3CH(OH)CH_2CH_3/CH_3CH_2CH_2CH_2OH$	1/2.4
$(CH_3)_3COH/CH_3CH_2CH_2CH_2OH$	1/4.8

[a] All competitive experiments were conducted at 25°C in $CDCl_3$ with 0.18 mmole of TFD and 0.19 mmole of $HBF_4 \cdot OEt_2$. In all cases the nucleophile concentrations were 5-50 times larger than the TFD concentrations. All values were obtained from ^{19}F-NMR integrations and represent the average of at least 2-4 independent determinations.

[b] 1 determination

[c] A slightly modified procedure was employed in these cases with the TFD in methylene chloride added to a $CDCl_3$ solution containing the respective nucleophiles.

constraints is also illustrated from our studies. For example, a slightly greater steric selectivity is found with TFD (n:sec:tert, 4.8:3.4:1.0) when compared to that reported for diazomethane (n:sec:tert, 2.2:1.3:1.0) [15]. In addition, it is also probable that a modified mechanism model is operational in the reaction of secondary and tertiary alcohols with TFD. Nevertheless, the mechanistic model which emerges from the results obtained is consistent with an A-2 mechanism for the acid-catalyzed reaction of TFD with primary alcohols in methylene chloride.

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