Substituent and pH Effects on the Hydrolysis Modes of 9-(Dinitromethyl)-9-alkoxylfluorenes

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The hydrolysis of 9-(dinitromethyl)-9-alkoxyfluorene [alkoxy = i-PrO (2-Pr), EtO (2-Et), MeO (2-Me), and CF_3CH_2O (2-Tf)] was studied in aqueous solution over the pH range 3-12. Under acidic conditions, the reactions proceed via the fluorenyl oxocarbonium ion in analogy with ketal hydrolysis reactions. Rate constants for the neutral adducts decrease in the order 2-Pr > 2-Et > 2-Me \gg 2-Tf. This order of reactivity indicates that substituent electronic effects dominate, whereas steric affects are only of secondary importance. Comparison with literature data for ketal hydrolysis reactions indicates the general validity of this conclusion for the above class of reactions. Out of the four substrates only 2-Tf undergoes hydrolysis under basis conditions by an E1cB mechanism. The other three adducts are practically inert under basic conditions (pH >9). The pK_a 's of the four substrates range from 6.3 to 6.7, indicating again a small or constant sensitivity to the steric size of the substituent.

A nucleophilic attack on an activated double bond usually results in the formation of an adduct which according to the pH of the medium and the nature of the activating groups may appear either in its ionized or neutral forms (eq 1).

$$N^{\bar{}} + > C = C < \underbrace{\stackrel{*_{t}}{\underset{N}{\longrightarrow}}}_{N} > C - \bar{C} < \underbrace{\longrightarrow}_{N} < C = N + \bar{C} < \underbrace{\stackrel{H}{\underset{N}{\longrightarrow}}}_{N} (1)$$

This adduct might revert to the starting olefin by expelling the nucleophile in an E1cB mechanism (k_r) , or in cases where the nucleophile contains an extra pair of electrons (in addition to the pair utilized for bond formation) it may expel the carbon bearing the activating groups (k_{ex}) . The latter process is mainly encountered in hydrolytic reactions where the attacking nucleophile is hydroxide anion.¹ Examples of cleavage reactions with other nucleophiles are rarely found, and the factors affecting the predominance of one pathway over the other are not clearly identified. An example which effectively demonstrates the complexity of these reactions is the reaction of 1,1-dinitro-2,2-diphenylethene with alkoxides.² With methoxide the reaction yielded benzophenone dimethyl ketal, with ethoxide the starting olefin was the sole product isolated, and with trifluoroethoxide² a stable adduct was obtained. Bernasconi³ has recently reported a detailed kinetic analysis for the reactons of amines with several olefins including 1,1-dinitro-2,2-diphenylethene. Although the amino adducts obtained are capable of reacting in both directions $(k_r \text{ and } k_{ex})$, the preferred pathway depends primarily on protonation of the nitrogen. It is only the quaternary ammonium ion that can serve as a nucleofuge in the E1cB mode, and only the free lone pair on the neutral nitrogen can expel the carbon bearing the activating groups. These adducts, neutral or protonated, are short-lived intermediates rather than stable, isolatable compounds.

In the course of our studies of nucleophilic reactions with activated double bonds,⁴ we found that relatively stable adducts can be obtained from the reactions of 9-(dinitro-

Table I. First-Order Rate Constants for Solvolysis Reactions of 2-Pr

pH	$10^{5}k_{1}, s^{-1}$	pН	$10^{5}k_{1}, s^{-1}$
2.91	338 ± 22	6.62	174 ± 11
3.91	324 ± 19	6.9	122 ± 5
4.97	335 ± 23	7.21	74.1 ± 2
5.59	397 ± 20	7.53	41.2 ± 2.8
6.23	268 ± 4	7.89	28.0 ± 1.5
6.48	204 ± 18	8.68	4.64 ± 0.18

 Table II.
 First-Order Rate Constants for the Solvolysis Reactions of 2-Et

pH	$10^{5}k_{1}, s^{-1}$	pH	$10^{5}k_{1}, s^{-1}$
2.92	264 ± 26	6.62	105.2 ± 4.1
3.35	273 ± 2.4	6.9	67.8 ± 1.2
3.89	284 ± 10	7.18	53.1 ± 3.6
4.96	280 ± 9.5	7.53	23.6 ± 0.8
6.23	232 ± 20	7.89	11.5 ± 0.3
6.46	192 ± 3.8		

methylene)fluorene (1) and various alcohols. We report here the kinetics and mechanism of the reactions of these adducts in the pH range 3-12.

Results

The hydrolysis reactions of the adducts of 1 with the alcohols MeOH, EtOH, *i*-PrOH, and CF₃CH₂OH (2-Me, 2-Et, 2-Pr, and 2-Tf, respectively, eq 2) were carried out in aqueous dioxane (10% dioxane v/v) at pH's ranging from 3 to 12 at 25 °C.



The reactions were followed spectrophotometrically at $\lambda = 259$ nm (λ_{max} of fluorenone). Repetitive scanning spectra between 220 and 450 nm was performed on each of the substrates prior to kinetic measurements at each pH under exactly the same conditions of the kinetic experiment. These scanning spectroscopy experiments revealed (a) that the reactons go to completion to give fluorenone and dinitromethane (confirmed also by TLC), (b) that while fluorenone is a stable product, dinitromethane (which at certain pH's appears as its conjugated base)

⁽¹⁾ Patai, S.; Rappoport, Z. J. Chem. Soc. 1962, 392 and references cited therein. Bernasconi, C. F.; Leonarduzzi, G. D. J. Am. Chem. Soc. 1980, 102, 1361.

⁽²⁾ Albeck, M.; Hoz, S.; Rappoport, Z. J. Chem. Soc., Perkin Trans. 2 1975, 628.

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 Table III.
 First-Order Rate Constants for the Solvolysis Reactions of 2-Me

 pH	$10^{5}k_{1}, s^{-1}$	pH	$10^{5}k_{1}, s^{-1}$	
 2.88	106 ± 10	6.62	30 ± 1.6	
3.89	103 ± 6	6.9	19 ± 5	
4.97	89 ± 5.6	7.17	10.2 ± 0.9	
5.59	89 ± 9.1	7.54	4.9 ± 0.2	
6.23	60 ± 2.6	7.89	2.67 ± 0.11	
6.45	49 ± 3.6			

Table IV. First-Order Rate Constants for the Solvolysis Reactions of 2-Tf

pН	$10^{5}k_{1}, s^{-1}$	pH	$10^{5}k_{1}, s^{-1}$
3.54	1.91 ± 0.13	7.06	8.1 ± 1.3
5.26	1.93 ± 0.06	8.62	11.4 ± 0.27
6.23	6.2 ± 0.3	9.67	11.2 ± 0.23
6.62	7.54 ± 0.02	10.33	10.7 ± 0.44
6.9	7.9 ± 1.4	11.6	10.3 ± 0.17

decomposes to some extent under the reaction conditions, (c) that in all cases clear isobestic points were found, indicating the absence of any accumulative intermediates in the course of the reaction, and (d) that 9-(dinitromethylene)fluorene was not formed during the reactions. At each pH, at least three different buffer concentrations (0.01-0.05 M) were used. The results were independent (within the limit of error) of the buffer concentrations, eliminating the possibility of general catalysis.

In Table I-IV the first-order reaction-rate constants are given for the four substrates at various pH's. The reactions of 2-Tf exhibits in the pH range 6.2-9.7 an initial (maximum up to 3% reaction) "S" shape in the graph of absorbance vs. time. In these cases, the rate constants were calculated after discarding these data points.

With 2-Et, an oxocarbonium trapping experiment was performed. The reaction was carried out in a sulfite buffer and was monitored by repetitive scanning spectroscopy. At the first stage, a buildup of the fluorenone peak at 259 nm was observed. During this stage, the isobestic point which appears under "normal" conditions at 244 nm was not seen. After the absorbance of fluorenone reached a constant value, 15 μ L of 30% H₂O₂ was added to the UV cell, and an additional fast increase in the absorbance due to fluorenone was observed.

Discussion

Examination of the kinetic data clearly indicates that 2-Tf differs from the other three adducts by being capable of reacting under basic conditions faster than in acidic solutions whereas 2-Me, 2-Et, and 2-Pr are practically inert at a pH higher than 10. This inertness at high pH and the gradual increase in the reaction rate toward the plateau as the pH goes down is typical of a substrate existing in equilibrium between basic and acidic forms where only the acidic one is reactive. The detailed rate expression is thus

$$k_{\rm obsd} = k_{\rm p}[{\rm H}^+] / ([{\rm H}^+] + K_{\rm s})$$
 (3)

where k_p is the first-order rate constant at the plateau where 2 is completely neutralized and K_a is its eqilibrium acidity constant. k_p and K_a in Table V are the values that give a best fit on applying a nonlinear regression procedure for the data and using eq 3 (eq 4 for 2-Tf). The good fit between the theoretical line obtained this way and the experimental data (full curve and points, respectively, in Figure 1) suggests the mechanism in path a of Scheme I.

In this mechanism the oxocarbonium ion is a key intermediate. In order to establish its existence along the reaction coordinate, we have carried out a trapping experiment with sulfite dianion which was shown recently

Table V. pK_a 's and Plateau Rate Constants for the Adducts 2-Pr, 2-Et, 2-Me and 2-Tf

			compd	
parameter	2-Pr	2-Et	2-Me	2-Tf
pK_{a} 10 ⁵ k_{p} , s ⁻¹	6.68 325	6.57 279	6.32 92	6.27 1.92 (10.6) ^a

^a Value in parantheses denotes $k_{p'}$.



Figure 1. Plot of the first-order rate constants for the hydrolysis of 2-Pr (\Box) , 2-Et (Δ) , and 2-Me (O) vs. pH. The plot for 2-Tf is given in the insert.

by Jencks et al.⁵ to be an effective agent in trapping oxocarbonium ions produced in the hydrolysis of certain acetals.

⁽⁵⁾ Jencks, W. P.; Young, P. R. J. Am. Chem. Soc. 1977, 99, 8238.

In this method, SO_3^{2-} competes with water molecules for the oxocarbonium intermediate to give α -alkoxy sulfonic acid and the corresponding ketone. Addition of H_2O_2 to the reaction mixture induces a second phase where the sulfonic acid is irreversibly converted to the ketone.⁵ The biphasic behavior observed in the trapping experiment performed on 2-Et indicates the intermediacy of the oxocarbonium in these reactions.

The results obtained in this work cannot pinpoint the exact rate-determining step. However, on the basis of the plateau in the lower acidic region, the possibility of acid catalysis for the expulsion of dinitromethane either from the covalent substrate or from any of the ion pairs possibly involved prior to the rate-determining step can be safely excluded. By analogy to the solvolysis of other tertiary substrates where it is generally assumed that the transfer from intimate to solvent-separated ion pairs comprises the rate-determining step,⁶ one can assume that 2, being a tertiary system, will follow this pattern as well. Recently, Jencks^{5,7} has introduced a variant to the general Winstein⁸ scheme of solvolysis reactions called the "Preassociation Mechanism". In this mechanism a water molecule moves into a reactive position before the transition state takes place. It was shown by a microscopic reversibility argument to be valid for the hydrolysis of acetals of formaldehyde where the derived oxocarbonium ion is highly unstable and has a very short lifetime. The preassociation mechanism is, however, less likely to occur in our system due to the following reasons.

(a) Steric crowdedness around the C-9 of the fluorenyl is likely to prohibit the approach of a water molecule to the reaction center before a major reorganization takes place.

(b) Although the fluorenyl oxocarbonium ion has some antiaromatic character, it is probably much more stable than the oxocarbonium derived from formaldehyde. This can be inferred irom the relative ease of preparation of cations of fluorenyl derivatives⁹ as opposed to CH_3^+ and from the ability of 9-fluorenyl derivative to undergo solvolysis reactions¹⁰ whereas methyl derivatives react only via an S_N^2 mechanism. Further assessment more directly related to the oxocarbonium can be gained from the relative rates of the ketal hydrolysis. The rate constant for the hydrolysis of fluorenone diethyl ketal is $(5.2 \text{ M}^{-1} \text{ s}^{-1})$ four orders of magnitude larger than that of formaldehyde dimethyl ketal ($2.2 \times 10^{-4} \text{ M}^{-1} \text{ s}^{-1}$),¹¹ indicating a higher stability of the fluorenyl oxocarbonium ion. Hence its tendency to react with the solvent is much smaller than that of the analogous methyl oxocarbonium ion which largely eliminates the possibility of the preassociation mechanism.

Compound 2-Tf reacts in both pH regions, and unlike the other substrates (2-Me, -Et, and -Pr), it reacts faster under basic conditions. The mechanism of its basic hydrolysis is very likely to be the E1cB mechanism (path b, Scheme I). Equation 4 describes its kinetic behavior over

$$k = \frac{k_{\rm p}[{\rm H}^+]}{[{\rm H}^+] + K_{\rm a}} + \frac{k_{\rm p}'K_{\rm a}}{[{\rm H}^+] + K_{\rm a}} = \frac{k_{\rm p}'K_{\rm a} + k_{\rm p}[{\rm H}^+]}{[{\rm H}^+] + K_{\rm a}} \quad (4)$$

the whole pH range. $(k_p'$ denotes the first-order rate constant at the plateau in the basic region). Again the good fit obtained between the theoretical line obtained by nonlinear regression and the experimental points (Figure 1) supports the suggested mechanism.

It is noteworthy that in a previously studied analogous case, the elimination of trifluoroethoxide from its adduct with the 2,2-dinitro-1,1-diphenylethylene, general acid caatalysis was observed in acetonitrile giving rise to an E2cB mechanism.² No such catalysis was observed over the whole range for the anionic elimination of trifluoroethoxide from 2-Tf. This is likely to be the result of the transfer from acetonitrile to water which caused a change in the basicity of trifluoroethoxide, rendering the general-acid catalysis energetically unprofitable.

Substituent Effects

Since all four substrates react at a measurable rate in the lower pH region, information about the substituent effect on the dissociative mechanism of the neutral adduct can be obtained. The first three alkyl substituents (Me, Et, *i*-Pr) differ from each other mainly in their steric bulkiness, whereas their electronic efffects are quite close to each other.¹² Since there is only a factor of 3 between the rate constant of the fastest substrate (2-Pr) to that of the slowest one (2-Me), the conclusion must be that, along this series, steric effects are either small or constant. Thus, steric compression, if it exists, is probably determined by the first atom of the substituent, namely, oxygen, which, being the common atom for the whole series, gives rise to essentially similar steric effects.

On the basis of steric effects, 2-Tf should react with a rate constant of about 300 s⁻¹, since sterically, trifluoroethoxy has an intermediate size between that of the isopropoxy and the ethoxy groups. However, the observed rate constant is only 1/150th of the expected value, which indicates the predominance of the electronic effects over steric ones. A similar conclusion is obtained from analysis of the results reported by Salomaa¹³ for the analogous hydrolysis of formaldehyde acetals. Applying the general Taft equation,¹⁴ we obtained s = -0.64 and $\rho^* = -5.3$, which support the idea again that the rate constants are governed mainly by electronic effects. This lack of sensitivity to the steric size of the substituent seems to be a rather general phenomenon for ketal hydrolysis and related reactions. The enthalpies of hydrolysis of ketals of the formula RC- $(OCH_3)_2CH_3$ remain almost constant (within 0.25 kcal/ mol) for R = Me, Et, and *i*-Pr. (It decreases to ca. 4 kcal/mol for R = 4-Bu).¹⁵ In light of the fact that the enthalpies measured entail differences between the carbonyl compounds and their derived ketals and not between the ketals and their transition states, and that ΔH varies only slightly inspite of the direct bonding between the substituent and the reaction center without the intermediacy of an oxygen atom, the assumption that the hydrolvsis reactions of substrates similar to those studied here are primarily subjected to electronic but not to steric substituent effects is largely supported.

Another point of interest is the substituent effect on the acidity of the substrates. The pK_{a} of dinitromethane is ca. 3.6,¹⁶ and the pK_a of compounds 2 is higher by about $3 \, pK_a$ units. This is to be expected as it is well-known that

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Table VI. Experimental Data for $9-(Dinitromethyl)-9-alkoxyfluorenes (2)^a$

	yield,		
compd	%	mp, ^b °C	NMR ^c (CDCl ₃), δ
2-Me	68	92	2.84 (3 H, s), 6.82 (1 H, s),
			7.2-7.7 (8 H, m)
$2\text{-}\mathrm{Et}$	46	113	1.02 (3 H, t), 2.96 (2 H, q),
			6.86 (1 H, s), 7.2-7.7 (8 H, m)
2- Pr	6.5	94	0.9 (6 H, dd), 3.2 (1 H, m),
			6.9 (1 H, s), 7.4 (8 H, m)
2- Tf	43	84-85	3.26 (2 H, q), 6.9 (1 H, s),
			7.5 (8 H, m)

^a All four compounds gave satisfactory C, H, N, and F analyses. ^b Uncorrected, taken on Fischer-Johns apparatus. ^c Taken on Varian HA-100. The internal standard was Me₄Si.

branching of the alkyl chain leads to decreased acidity probably because of steric inhibition of reasonance by forcing the nitro groups out of the plane.¹⁷ However, in spite of the large difference in the steric size of the substituents, the pK_a values of the four substrates fall into a narrow range. Since the demand for planarity in the carbanion renders it more sensitive to steric effects when compared to the neutral molecule, it is unlikely that the observed lack of sensitivity to steric effects results from a mutual cancellation of identical effects exerted on the acid and its conjugated base. This is consistent with our previous assumption that the dinitromethide moiety is sterically affected mainly by the first atom of the added nucleophile. The observed pK_a 's of the substrates 2 can be correlated with the electronic effects of the substituents.

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Experimental Section

Materials. 9-Alkoxy-9-(dinitromethyl)fluorenes (2-Me, -Et, -Pr, and -Tf). All four compounds were prepared by the addition of the alkoxide (4.5 mmol) in 30 mL of the parent alcohol to 9-(dinitromethylene)fluorene (1.86 mmol). After gentle heating for 10 min, during which the solid is dissolved, the reaction mixture is cooled by adding ice directly to the reaction vessel and is gently acidified by cold diluted HCl. Extraction with ether, drying over Na₂SO₄, and evaporation of the solvent yielded a white solid which was recrystallized from petroleum ether. The experimental data are given in Table VI.

The solutions for the kinetic experiments were composed of 90% doubly distilled water and 10% dioxane (by volume) purified according to a published procedure.¹⁸ The buffering agents (starting from low to high pH's) were chloroacetic acid, phthalic acid, formic acid, acetic acid, dihydrogen phosphate, borax, and sodium hydroxide.

Kinetics. The hydrolysis of 2 was followed spectroscopically. In each of the buffers used, the reaction was first monitored with each of the substates by repetitive scanning in the UV-vis region (Perkin-Elmer 402 spectrophotometer), and the actual kinetics were observed by following the increase in the absorbance of fluorenone at 259 nm with a Gilford 2400 spectrophotometer. The spectrophotometer was attached to a PDP 11/40 minicomputer for data handling. The buffered solutions were preincubated (ca. 0.5 h) in the cell compartment which was thermostated to $25 \pm$ 0.1 °C. The substrates were injected (10 μ L) into the UV cell as a concentrated dioxane solution, and the monitoring started immediately after a rapid mixing. Each data point in the tables is an average of four to seven different experiments.

Registry No. 2 (R = i-Pr), 82615-41-6; 2 (R = Et), 82615-42-7; 2 (R = Me), 82615-43-8; 2 (R = Tf), 82615-44-9; 9-(dinitro-methylene)fluorene, 25945-85-1.

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Cyclopropanation of α,β-Unsaturated Carbonyl Compounds and Nitriles with Diazo Compounds. The Nature of the Involvement of Transition-Metal Promoters

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In the presence of molybdenum hexacarbonyl or molybdenum(II) acetate, ethyl diazoacetate and α -diazoacetophenone react with α,β -unsaturated carbonyl compounds and nitriles to form derivative cyclopropane and vinyl CH insertion products. In the absence of these promoters or in the presence of catalytic amounts of pyridine, 2-pyrazolines are the major or sole reaction products. Kinetic investigations for reactions between ethyl diazoacetate and α,β -unsaturated esters and nitriles in the presence of $M_0(CO)_6$, $M_{02}(OAc)_4$, or pyridine demonstrate the absence of any significant influence by these molybdenum promoters or pyridine on the rates and activation parameters for ethyl diazoacetate decomposition. Representative 1-pyrazolines have been synthesized and observed to undergo dinitrogen extrusion without apparent influence by molybdenum promoters. The composite results suggest that these molybdenum promoted reactions occur by dipolar cycloaddition of diazocarbonyl compounds to α,β -unsaturated systems and that the derivative 1-pyrazoline intermediates undergo dinitrogen extrusion to form the observed cyclopropane and vinyl CH insertion products. Molybdenum promoters function to inhibit competitive tautomerization of the initially formed cycloaddition products. The relative effectiveness of a broad selection of transition-metal compounds in directing reactions between ethyl diazoacetate and $\alpha_{j}\beta$ -unsaturated esters and nitriles to cyclopropane products is described. The cycloaddition/dinitrogen extrusion pathway is presented as a viable mechanism for cyclopropanation of α,β -unsaturated systems by diazo compounds, even for reactions performed in the presence of traditional cyclopropanation catalysts.

Diazo compounds readily undergo 1,3-dipolar addition to α,β -unsaturated carbonyl compounds and nitriles.¹⁻³

The resulting 1-pyrazoline, if formed from an activated olefin or a diazocarbonyl compound that possesses an α