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THE REACTION OF 2-SUBSTITUTED-9-(ORTHO-SUBSTITUTED PHENYLMETHYL)FLUOREN-9-YLTRIMETHYLAMMONIUM IONS IN CHLOROFORM. ALKENE FORMATION VIA A CARBOCATION.

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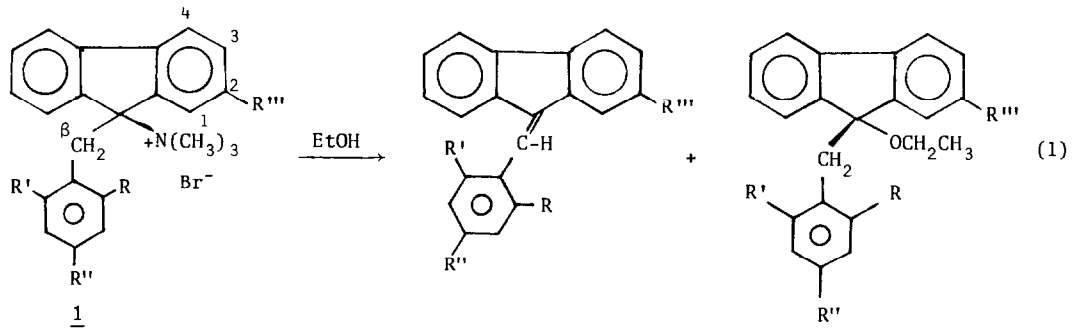
Abstract: The reaction of several quaternary ammonium salts in chloroform is found to give exclusively the alkene product by the E1 mechanism.

Quaternary ammonium salts usually require strong base like ethoxide in ethanol in order to promote 1,2-elimination. To our knowledge there has been only two examples of quaternary ammonium salts reacting in a polar protic solvent to give the alkene via the E1 mechanism (1,2). Hughes and Wilby (1) investigated the reaction of menthyltrimethyl- and neomenthyltrimethylammonium ions in water and found that the 2- and 3-menthenes were formed in a first order process. Pradhan and Smith (2) studied the reaction of 9-(ortho-substituted phenylmethyl)-fluoren-9-yltrimethylammonium ions, 1, in ethanol. It was found that when the ortho-positions did not bear substituents (R=R'=H) that the substrates 1 were stable in ethanol. However, when one ortho-position carried a substituent (R=H,R'=CH_3) then the quaternary ammonium salts decomposed in a first order process to give both the alkene and ether products, equation 1. The addition of a second ortho substituent caused a significant increase in the rate of reaction and a corresponding decrease in the percent alkene formed. It was proposed (2) that the loss of trimethylamine, a poor leaving group, is favoured by a relief of steric interactions between the ortho- substituents and the onium group.



1 (1)

Recent studies (3,4) have been carried out on the reaction of quaternary ammonium salts in the relatively non polar solvent chloroform. It was found that 1-phenylethyldimethyl-phenylammonium bromide gave exclusively the substitution product, 1-phenylethyl bromide, when dissolved in chloroform. It was concluded from a kinetic study (3) that a triple ion (5) decomposed via a transition state where there is a partial positive charge on the central carbon atom with some covalent bonding to halide ion. As well, on the basis of both secondary α- and β- hydrogen-deuterium isotope effect measurements for reaction of the ammonium ion with both bromide and iodide it was also considered (4) that the reaction proceeded via the S_N2 mechanism within the triple ion complex.

Since it has been established that 1 reacts in EtOH to give both alkene and ether products via a carbocation intermediate (2) and that 1-phenylethyldimethylphenylammonium bromide reacts only in chloroform to give only the substitution product at the benzylic carbon by the S_N2 mechanism, it was decided to investigate the reaction of 1 in the relatively non polar aprotic solvent chloroform in order to determine the products and mechanism for this reaction.

Several phenyl- and fluorenyl-ring substituted derivatives of 1 and their β-d_2 analogues were prepared and the reaction was studied in chloroform at 50.6°C by monitoring the formation of the alkene product using U.V. spectroscopy. As well, the reaction of several substrates in chloroform was followed using n.m.r. spectroscopy at 50°C. The n.m.r. samples were placed in the temperature controlled probe and the change in intensity of several hydrogen signals with time was monitored. The various substrates, along with the β-dideuterated analogues, are shown in Table 1 together with the first order rate constants for reaction in chloroform and the observed hydrogen-deuterium kinetic isotope effects.

Table 1. Rate constants and observed hydrogen-deuterium isotope effects for reaction of 2-substituted-9-(ortho-substituted phenylmethyl)fluoren-9-yltrimethylammonium bromides and their β-d_2 analogues in chloroform.

Ring substituents on 1	Temp. (°C)	k x 10^5(sec^{-1})	k^H/k^D
R=R'=Me; R''=R'''=H 2	50.6	128 ± 3[a]	1.47 ± 0.04
β-d_2 analogue	"	87.2 ± 1.3[a]	
R=R'=Me; R''=H; R'''=Br 3	"	16.6 ± 0.2[a]	
R=R'=Me; R''=R'''=H 2	50	88.9 ± 3.4[b]	1.88 ± 0.12
β-d_2 analogue	"	47.2 ± 2.2[b]	
R=R'=R''=Me; R'''=H 4	"	108 ± 2[b]	1.55 ± 0.03
β-d_2 analogue	"	68.6 ± 1.3[b]	
R=Me; R'=R''=R'''=H 5	"	0.760[b]	

[a] Determined using u.v. spectroscopic methods.

[b] Determined using n.m.r. methods.

The reaction of the para-methyl derivative of 1, R=R'=R'''=H; R''=methyl, did not proceed at a measurable rate at 50°C in chloroform while the reaction of the ortho-methyl derivative, 5, R=R''=R'''=H; R'=methyl, reacted slowly to give the alkene product in 100 percent yield, k=0.760 x 10^{-5}(sec^{-1}). The other substrates shown in Table 1, where both ortho positions

carry a methyl group, are very much more reactive, i.e. when R=R'=Me and R''=R'''=H, 2, $k = 128 \times 10^{-5}(sec^{-1})$. In all cases the alkene is formed in 100 ± 5 per cent yield in contrast to the earlier studies (3,4) on reaction of quaternary ammonium bromides in chloroform where only the substitution product was formed.

The failure of the para-methyl substrate to react in chloroform at 50°C and the increased reactivity of the substrates when both ortho positions contain a methyl group suggests that reaction is facilitated by a relief of steric interaction between the ortho substituents and the onium group and/or the 1,8 hydrogens on the fluorenyl ring. The presence of a para methyl group, when both ortho positions contain methyl groups, has very little effect on the rate of reaction (see rate constants for reaction of 2 and 4).

It is of interest to consider the mechanism of the elimination reaction of 1 in the relatively non polar solvent chloroform. Possible mechanisms include the E2 and Elcb processes with bromide acting as the abstracting base. Significant primary hydrogen-deuterium kinetic isotope effects, $k^H/k^D > 2$, would be expected for reaction proceeding either by the concerted one-step process or the two step reaction where the formation of the carbanion is rate determining. As well, a positive rho value would be expected for reaction of α-aryl substituted quaternary ammonium salts with base proceeding either by the E2 mechanism (6) or the Elcb mechanism where the rate of decomposition of the carbanion intermediate is fast relative to its return to starting material (7).

The other possible mechanism for elimination in chloroform is the E1 mechanism. Rate determining formation of the carbocation intermediate would give rise to only a secondary β-deuterium kinetic isotope effect, k^H/k^D = 1.1-1.2 per β-D, (8) while loss of the β- proton in the rate-determining step would give a value of k^H/k^D greater than 2 (9). The reaction of an α-aryl substituted substrate proceeding via a carbocation intermediate is facilitated by electron donating groups on the phenyl ring and, hence, negative values for rho are observed (10).

It is unlikely that the ortho substituted compounds, 1, react in chloroform by way of either the E2 or Elcb processes since the para-substituted compounds (where R=R'=H) are unreactive in this solvent. The bromide promoted reaction should be more favourable for steric reasons when the phenyl ring does not carry ortho substituents. The observation of the large negative Hammett rho value of -2.28 (a measure of the charge development at C_α) which can be calculated from the rate constants obtained for the reaction of 2 and 3 in chloroform at 50.6°C, lends support to this suggestion since reaction by way of either the E2 or Elcb mechanisms would lead to the observation of a positive value for rho.

The observed hydrogen-deuterium isotope effects, k^H/k^D = 1.46-1.88, appear to be too small to be primary effects at 50°C. Consequently, it can be concluded that the loss of the β-hydrogen does not occur at the transition state of the slow rate-determining step as required for either the E2 mechanism or the Elcb process, where the formation of the carbanion is rate determining.

The experimental results are in complete accord with the proposal that reaction of the substrates 1 proceeds by way of a carbocation intermediate in chloroform solvent. The large negative rho value found indicates considerable positive charge buildup at C_α in the transi-

tion state. As well, the observed isotope effects are of the order of magnitude expected for secondary β-deuterium isotope effects for rate-determining carbocation formation, i.e. $(k^H/k^D)_{per\ D}$ = 1.21 - 1.37. It appears, from a consideration of Dreiding models, that the β-hydrogens are sterically favourable for hyperconjugative release to the positive centre (8).

A suggested mechanism for the reaction of 1 in chloroform is shown in equation 2. It is considered that the formation of the carbocation is not reversible. Tentatively, it is

$$\text{Substrates } \underline{1} \xrightarrow[\text{slow}]{k_1} \text{carbocation, } Br^-, \text{ intimate ion pair} \xrightarrow{k_E} \text{alkene + HBr} \qquad (2)$$

proposed that bromide, which would be a strong base in chloroform, acts as the abstracting base in the intimate ion pair to give the alkene product. It is concluded that reaction of the ortho-substituted compounds, 2-5, in chloroform proceeds by way of the E1 mechanism with the major driving force for the loss of the poor leaving group being the relief of steric interactions between the leaving group and the ortho-substituents.

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