1628 BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 44, 1628—1632 (1971) [Vol. 44, No. 6

Elimination Reactions Promoted by Fluoride Ion in Acetonitrile. Elimination Reaction from 2-Arylethyl Derivatives[1]

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(Received September 21, 1970)

Rates of bimolecular elimination have been determined for the reaction of 2-arylethyl bromides, chlorides, and tosylates with anhydrous tetraethylammonium fluoride in acetonitrile. The rates of elimination reactions in this new base system were much faster than those in conventional base systems (alkoxide-alcohol). The Hammett ρ values were found to be $\rho=2.033$ (X=Cl) at 25.0°C and $\rho=1.879$ (X=Br) at 5.0°C for p-Y-$C_6H_4CH_2$-CH_2X. Kinetic deuterium isotope effects were determined using 2-phenylethyl-2,2-d_2 bromide and chloride to be $k_H/k_D=3.99$ (X=Cl) and 5.03 (X=Br). These data and the low k_{OTs}/k_{Br} ratio suggest that fluoride-ion-promoted elimination reaction proceeds through a very tight transition state where β-proton is less than half transferred to the base.

Recent works on the transition state of the bimolecular elimination invoked interesting problems. Bunnett proposed the theory of the variable E2 transition state—a continuous spectrum between pane-carbonium extreme through central to pane-carbanion extreme of the transition state.[3] Parker and co-workers proposed the theory of a variable transition state in the spectrum between E2C—E2H extreme with the concept of variable "looseness" or "tightness".[4] Hoffmann's view[5] may be in close agreement with the latter interpretation.

Some examples of the halide ion promoted bimolecular elimination reactions were explored to establish a criterion of the theory. Halide ion, especially the halide ion in a dipolar aprotic solvent, is a weak hydrogen but a strong carbon nucleophile. A study of the bimolecular elimination in a dipolar aprotic solvent promoted by a strong hydrogen nucleophile might be of use in order to establish a better understanding of the reaction.

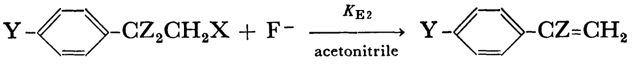
In previous papers[6] the authors reported that tetraethylammonium fluoride behaves as a strong base and that styrene was produced in an excellent yield in the reaction of 2-phenylethyl bromide. Under similar conditions tetraethylammonium chloride and bromide underwent solely the substitution reaction.

Substitution reactions and elimination reactions by chloride, bromide, and iodide ion are well-known and the mechanism of these reactions have been studied extensively.[4] However, there are few reports on fluoride ion promoted bimolecular reactions, and no quantitative kinetic data are available.[7] This may be due to the difficulty in finding the electrolyte soluble in pure dipolar aprotic solvents to secure fluoride anion in a homogeneous reaction system. This difficulty has been overcome by use of tetraethylammonium fluoride in a dipolar aprotic solvent.

In the present communication the authors report the characteristics of the elimination reaction from 2-phenylethyl derivatives promoted by the new base system and suggest a structure for the transition state.

Results and Discussion

Kinetic measurements of the elimination reactions of the series of the para-substituted 2-phenylethyl bromide and chloride were undertaken using the base system of tetraethylammonium fluoride in acetonitrile. Similar experiments with several of the para-substituted 2-phenylethyl tosylates were undertaken. The general formula is as follows.



$Y=CH_3O, CH_3, H, Cl$ (1)
$Z=H, D$
$X=Cl, Br, OTs$

Reaction rates were determined by following the appearance of styrene or substituted styrenes spectrophotometrically. With a large excess of the base, first order (pseudo-first-order) kinetics held for every run. A typical example is given in Table 5. Second order rate constants were calculated by dividing the pseudo-first-order rate coefficients by the pertinent tetraethylammonium fluoride concentrations. The concentration of the fluoride ion was determined by titration with thorium nitrate.[8] The results are given in Table 1. The olefin-forming elimination was accompanied by the bimolecular substitution to some extent,[6] and olefin was obtained in the yield of 75% for the elimination from tosylates. In other cases olefin was obtained almost quantitatively as is shown in Table 1 (see Experimental).

A four-fold variation in base concentration caused no

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1) Presented at the 22nd Annual Meeting of the Chemical Society of Japan, Tokyo, April 1969.

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3) a) J. F. Bunnett, *Angew. Chem.*, **74**, 731 (1962). b) J. F. Bunnett, *Surv. Prog. Chem.*, Vol. 5, Academic Press, New York, N. Y. (1969), p. 53. c) D. J. McLennan, *Quart. Revs.*, **21**, 490 (1967). d) Z. Rappoport, *Tetrahedron Lett.*, **1968**, 3601.

4) a) A. J. Parker, M. Raune, G. Biale, and S. Winstein, *ibid.*, **1968**, 2113. b) D. J. Lloyd and A. J. Parker, *ibid.*, **1968**, 5183. c) R. Alexander, E. F. C. Ko, A. J. Parker, and T. J. Broxton, *J. Amer. Chem. Soc.*, **90**, 5049 (1968). d) E. F. C. Ko and A. J. Parker, *ibid.*, **90**, 6447 (1968). e) G. Biale, A. J. Parker, I. D. R. Stevens, and S. Winstein, *ibid.*, **92**, 115 (1970).

5) G. M. Fraser and H. M. R. Hoffmann, *J. Chem. Soc., B*, **1967**, 265.

6) a) J. Hayami, N. Ono, and A. Kaji, *Tetrahedron Lett.*, **1968**, 1385. b) J. Hayami, N. Ono, and A. Kaji, *Nippon Kagaku Zasshi*, **92**, 87 (1971).

7) a) L. Rand and M. J. Albinak, *J. Org. Chem.*, **25**, 1837, (1960). b) J. T. Maynard, *ibid.*, **28**, 112 (1963). c) J. F. Normant and H. Deshayes, *Bull. Soc. Chim. Fr.*, **1967**, 2455.

8) W. Selig, *Analyst*, **93**, 118 (1968).

TABLE 1. RATE CONSTANTS FOR ELIMINATIONS FROM p-Y-$C_6H_4CZ_2CH_2X$ WITH Et_4NF IN CH_3CN

Y	Z	X	Temp.[a] (°C)	$[F^-]\times10^2$ (mol/l)	$k_{E2}\times10^3$ [b] (l/mol sec)	Olefin yield[c] (%)
Cl	H	Cl	35	2.12	29.7	100
Cl	H	Cl	25	1.26	11.0	100
Cl	H	Cl	15	2.56	3.48	100
H	H	Cl	35	2.12	10.7	100
H	H	Cl	25	2.16	3.89	100
H	H	Cl	15	2.02	1.26	100
CH_3	H	Cl	35	2.12	5.57	100
CH_3	H	Cl	25	2.50	1.75	100
CH_3	H	Cl	25	5.00	1.78	100
CH_3	H	Cl	25	10.00	1.80	100
CH_3O	H	Cl	35	2.12	3.55	100
CH_3O	H	Cl	25	2.16	1.06	100
H	H	Br	5	2.05	29.9	100
CH_3	H	Br	15	2.38	38.7	100
CH_3	H	Br	5	2.05	15.4	100
CH_3O	H	Br	15	2.56	26.3	100
CH_3O	H	Br	5	2.05	9.30	100
CH_3	H	OTs	15	2.09	1.04	75
CH_3O	H	OTs	15	2.09	0.710	75
H	D	Cl	35	1.84	2.68	100
H	D	Cl	25	1.84	0.888	100
H	D	Br	5	2.09	5.94	100

a) Bath temperature was controlled to ±0.1°C or better.

b) Pseudo-first-order rate constants were determined spectrophotometrically and converted to second-order rate constants. Usual conditions were [substrate]=*ca.* 1.0×10^{-3} mol/l, [base]=*ca.* 2×10^{-2} mol/l.

c) The olefin yields were determined spectrophotometrically from the values of A_∞ for rate determinations. The values contain errors of 1—2%.

significant change in the second order rate constants. Thus the elimination reactions promoted by fluoride ion should follow the second-order rate law, first order in the substrate and also first order in the fluoride. The rate data were fitted to log k_{E2} *vs.* $1/T$ plots and enthalpies and entropies of activation were calculated. These values are shown in Table 2.

TABLE 2. ACTIVATION PARAMETERS FOR ELIMINATIONS FROM p-Y-$C_6H_4CH_2CH_2Cl$ WITH Et_4NF IN CH_3CN

Y	$\Delta H^{\neq}$ [a] (kcal/mol)	$\Delta S^{\neq}$ [a] (e. u.)
Cl	17.7	−7.4
H	19.0	−7.1
CH_3	21.3	−2.2
CH_3O	22.4	−0.2

a) $\Delta H^{\neq}$, $\Delta S^{\neq}$: at 25°C

The Hammett ρ-values were derived by the least-squares procedure of Jaffé[9] from the rate constants of the 2-phenylethyl derivatives with para substituents, methoxy, methyl, hydrogen and chlorine. These calculations together with results of elimination reactions in ethanol and *t*-butyl alcohol are summarized in Table 3. The kinetic deuterium isotope effects with 2-phenylethyl-2,2-d_2 bromide and chloride were determined, the results are also given.

Kinetic data show that tetraethylammonium fluoride in acetonitrile is about 800 times as effective as sodium ethoxide in ethanol in promoting the E2 reaction from 2-phenylethyl chloride, k_{E2} being 3.89×10^{-3} and 4.5×10^{-6} l/mol sec at 25°C.[10] The activation parameters in Table 2 fall in a reasonable range for typical E2 reactions.

Second order kinetics and the activation parameters show that the E1 mechanism can be excluded for the present cases. Of the two mechanisms E2 and E1cB, compatible with the kinetics, E1cB should be excluded since the ρ-values and the k_H/k_D ratios, both obtained in the present communication, are against criteria for E1cB.

Recently, McLennan[3c] and also Rappoport[3d] reviewed the criteia for E1cB. They suggested that E1cB should show a very high positive value of ρ (which should be greater than 3.7 obtained in the E2 reaction of 2-arylethyl-trimethylammonium salt) and the k_H/k_D ratio of unity. In certain cases of "Type II" E1cB, E1cB with negative ρ-values are suggested.

In the present cases, the ρ-values are positive but the values in the neighborhood of 2 seem to be too small and the k_H/k_D ratios of more than 3 are too high for the

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[9] H. H. Jaffé, *Chem. Revs.*, **53**, 191 (1953).

[10] The value for sodium ethoxide was calculated by extrapolation from other temperatures, using the experimental data of DePuy *et al.*[11] They have reported that k_{E2} is 24.1×10^{-5} at 60°C and 185×10^{-5} at 80°C.

[11] C. H. DePuy and C. A. Bishop, *J. Amer. Chem. Soc.*, **82**, 2535, (1960).

TABLE 3. HAMMETT CORRELATIONS AND DEUTERIUM ISOTOPE EFFECTS FOR ELIMINATIONS FROM p-Y-$C_6H_4CZ_2CH_2X$

X	Temp. °C	Base	Solvent	ρ[a]	r[b]	k_H/k_D
Cl	35	F^-	CH_3CN	1.851	0.999	3.99
Cl	25	F^-	CH_3CN	2.033	0.998	4.38
Br	5	F^-	CH_3CN	1.879[c]	0.986	5.03
Cl	30	EtO^-	EtOH	2.61[d]		
Br	30	EtO^-	EtOH	2.154[e]	0.987	7.11[f]
Br	30	t-BuO^-	t-BuOH	2.08[g]	0.999	7.89[f]
Br	30	t-BuO^-	t-BuOH	2.529[h]	0.999	8.16[h]
Cl	60	$^{36}Cl^-$	CH_3CN	0.57[i]	0.991	

a) Calculated by the method of least squares. b) Correlation coefficient.
c) Based on p-MeO, p-Me and H only (p-Cl; rate was too high to be measured).
d) Ref. 11 e) Ref. 12 f) Ref. 13 g) Ref. 14 h) Ref. 15 i) ρ-value for substitution reaction. (Ref. 18)

E1cB mechanism to be operative (Table 3).

Interesting features of the fluoride promoted elimination from substituted 2-phenylethyl derivatives can be characterized by the small ρ values, low k_H/k_D ratios and very diminished ratios of k_{OTs}/k_{Br} although they are not at all out of the range of the expected magnitude for the E2 reaction.

As is shown in Table 3, the k_H/k_D ratio of 5 for 2-phenylethyl bromide at 5°C is smaller than the k_H/k_D ratios for the same compound with a conventional base, which gives the k_H/k_D ratios sometimes exceeding 7. The k_H/k_D ratios for the E2 reaction generally decrease with the increase in reaction temperature. An example can be found in reports by Saunders[13,15] as well as in Table 3. This implies that the k_H/k_D ratio for the 2-phenylethyl bromide might decrease to a certain amount and more diminished ratios would be anticipated at higher temperatures. Smaller k_H/k_D ratios were also obtained for 2-phenylethyl chloride.

The positive ρ value with k_H/k_D less than the theoretical maxima (*ca.* 7)[16] may suggest the pane-carbanion transition state in which the proton is more than half transferred.

The other characteristics of the fluoride promoted E2 reaction, however, are strongly against the pane-carbanion interpretation. According to Hoffmann,[5] the small value of the leaving group selectivity coefficient, the rate ratio k_{OTs}/k_{Br}, is a good criterion for the little C-X (C_α-leaving group) bond-breaking together with the little C–H (C_β-hydrogen) bond-breaking in the bimolecular reaction. The k_{OTs}/k_{Br} ratio of 0.027 obtained is one of the smallest values (Table 4).[17] Rho (ρ) value of 1.8 or less (anticipated at higher temperatures) for the 2-arylethyl bromide seems too low for a pane-carbanion transition state but may be compatible with the "central" synchronous process.

TABLE 4. RATIOS k_{OTs}/k_{Br} FOR ELIMINATIONS FROM p-Y-$C_6H_4CH_2CH_2X$

Y	Base	Solvent	k_{OTs}/k_{Br}
CH_3	F^-	CH_3CN	0.027
CH_3O	F^-	CH_3CN	0.027
CH_3O	EtO^-	EtOH	0.1[a]
CH_3O	t-BuO^-	t-BuOH	0.15[a]
H	EtO^-	EtOH	0.1[a]
NO_2	t-BuO^-	t-BuOH	1.57[a]

a) Ref. 5.

Taking into account the very low k_{OTs}/k_{Br} ratio and the diminished Hammett ρ value, the present authors suggest that in the fluoride promoted E2 reaction, β-proton is less than half transferred in the transition state. In other words, a very tight and reactant-like transition state should be ascribed to this E2 reaction where both the C–H and C–X bond-breaking are not far advanced.

It might be interesting to discuss a plausible mechanism in the light of E2C—E2H spectrum. As Parker[4] has pointed out, the tight transition state such as proposed in the present study is against the E2C mechanism. Another kinetic result in authors' laboratory[18] is also against the E2C mechanism. The E2C transition state should be much like an SN2 transition state, and the ρ value for the E2C reaction of 2-arylethyl chloride may be expected to be similar or slightly higher than the ρ value for the SN2 reaction of the same compounds. The ρ value (*ca.* 2) obtained in the present study is substantially higher than the ρ value found in the SN2 reaction of 2-arylethyl chloride with radioactive chloride ion in acetonitrile ($\rho=0.57$)[18] and is in a reasonable range for normal E2H reactions. This conclusion is consistent with the "principle of hard and soft acids and bases" which predicts that hard fluoride ion is liable to attack a hard proton while the soft halide ion (Cl^-, Br^-, or I^-) can attack relatively soft carbon.[19]

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[12] W. H. Saunders, Jr., and R. A. Williams, *J. Amer. Chem. Soc.*, **79**, 3712, (1957).

[13] W. H. Saunders, Jr., and D. H. Edison, *ibid.*, **82**, 138 (1960).

[14] C. H. DePuy and C. A. Bishop, *ibid.*, **82**, 2532 (1960).

[15] A. F. Cockerill, S. Rottschaefer, and W. H. Saunders, Jr., *ibid.*, **89**, 901 (1967).

[16] F. H. Westheimer, *Chem. Revs.*, **61**, 265 (1961).

[17] The smaller k_{OTs}/k_{Br} for the reaction in acetonitrile compared to the one in the protic solvent may be rationalized in terms of the lack of the solvation stabilization of the leaving group (anion) in a dipolar aprotic solvent. In a protic solvent, assistance by the solvation may give rise to a relatively looser transition state that reflects upon slightly enhanced k_{OTs}/k_{Br} ratios.

[18] J. Hayami, N. Tanaka, S. Kurabayashi, Y. Kotani, and A. Kaji, Abstracts of Papers, III-1323, 23rd Annual Meeting of Chemical Society of Japan, Tokyo, April 1970.

[19] R. G. Pearson and J. Songstad, *J. Amer. Chem. Soc.*, **89**, 1827 (1967).

The idea of the tight transition state is not incompatible with the Swain-Thornton rule,[20] which postulates a more reactant-like transition state for a more reactive base. The tight transition state in the fluoride promoted elimination can be rationalized in terms of the very small steric requirement of the fluoride ion in a dipolar aprotic solvent and the high proton affinity of the fluoride which is the reflection of the intrinsically high electronegativity of fluorine.

The results clearly show that the fluoride promoted elimination from 2-arylethyl derivatives is a typical E2 reaction, and the characteristics of the reaction suggest features of the tight transition state. Utility of the fluoride ion in a dipolar aprotic solvent is promising. Features of the elimination reaction including the orientation rule in the olefin-formation from secondary alkyl derivatives were given in a previous paper.[21]

Experimental[22]

Materials. 2-Arylethyl *p*-toluenesulfonates were prepared in the usual way from the corresponding 2-arylethanols and were recrystallized from ethanol.

2-Phenylethyl tosylate, mp 38.5—39.0°C (lit,[23] 38.5—39.0°C); 2-*p*-chlorophenylethyl tosylate, mp 79.0—79.3°C (lit,[24] 79.5—80.1°C); *p*-tolylethyl tosylate, mp 68.0—69.0°C (lit,[24] 68.6—69.3°C); *p*-anisylethyl tosylate, mp 58.5—59.0°C (lit,[24] 58.3—59. °C); 2-phenylethyl-2,2-d_2 tosylate, mp 38.5—39. °C (lit,[13] 37.4—38.0°C).

2-Arylethyl Chlorides: 2-Arylethyl chlorides were prepared by heating to reflux arylethyl tosylates with excess of tetraethylammonium chloride in acetonitrile. In a typical example, 2-phenylethyl-2,2-d_2 tosylate (12.0 g, 0.044 mol) and tetraethylammonium chloride (16.5 g, 0.1 mol) were dissolved in 100 m*l* of acetonitrile and the solution was heated under gentle reflux for 24 hr. The solution was cooled and poured into 100 m*l* of water and the organic layer was taken out with pentane. After washing and drying the extracts, pentane was carefully removed and the product was distilled to give 4.8 g (86%) of 2-phenylethyl-2,2-d_2 chloride, bp 84.0°C/16 mmHg. On the NMR spectra of the deuterated compound, the signal due to β hydrogen (7.1 τ) completely vanished. Boiling points of the chlorides are as follows; 2-phenylethyl chloride, bp 90°C/25 mmHg;[11] 2-*p*-chlorophenylethyl chloride, bp 84°C/4 mmHg[11]; 2-*p*-anisylethyl chloride, bp 95°C/4 mmHg; 2-*p*-tolylethyl chloride, bp 67°C/4 mmHg.

2-Arylethyl Bromide: 2-Arylethyl bromides were prepared in a procedure analogous to that for the preparation of the 2-arylethyl chlorides using sufficient acetonitrile to dissolve tetraethylammonium bromide at a reflux temperature. Boiling points of the bromides are as follows: 2-phenylethyl bromide, bp 90°C/11 mmHg[12]; 2-phenylethyl-2,2-d_2 bromide, bp 95°C/16 mmHg[13]; 2-*p*-anisylethyl bromide, bp 124°C/4 mmHg[12]; 2-*p*-tolylethyl bromide, bp 101°C/10 mmHg.

Solvent and Base. Acetonitrile was purified as previously reported.[25] Preparation of tetraethylammonium fluoride was reported.[6] Fluoride reagent should be prepared freshly before use, as it is very hygroscopic and liable to decompose slowly to form triethylamine and ethylene even at room temperature. Hydrogen fluoride evolved seemed to deteriorate the specimen by forming tetraethylammonium acid fluoride. Tetraethylammonium fluoride stored for a month in a vacuum desiccator showed a greatly diminished rate of elimination reactions, sometimes about one hundredth of a fresh specimen.

Determination of Amount of Substitution Reactions. The amount of 2-arylethyl fluorides arising from substitution reactions of 2-arylethyl chlorides, bromides, and tosylates with fluoride in acetonitrile was determined by glc analysis. A solution in acetonitrile containing 0.2 M of tetraethylammonium fluoride and 0.1 M of a 2-phenylethyl derivative was allowed to react to completion. The resulting solution was poured into water and extracted with pentane. The extracts were dried and concentrated by careful fractionation of pentane. The concentrate was analyzed on a column of TG-3000 on Celite 545 at 110°C. Glc analysis showed that the fluorides were formed from the corresponding halides in 4% yield while the tosylates gave fluorides in 25% yield.

Kinetic Measurements. The reactions in acetonitrile were carried out in a thermostat kept within ±0.1°C of the stated temperature. Reaction rates were followed by analysis of styrene or substituted styrene spectrophotometrically. The reaction mixture was placed in a 50 m*l* volumetric flask, and after an appropriate time 1 m*l* aliquots of the solution were withdrawn at intervals and the reaction was quenched by the addition of 0.05 N nitric acid. The time of the first withdrawal was taken as "time-zero". Thus $\log A_\infty/(A_\infty - A_t)$ *vs.* t plot gave a good straight line with a negative time intercept. About 20-fold excess of fluoride was used and pseudo-first-order rate constants were determined from the slope of a plot of $\log A_\infty(A_\infty - A_t)$ against time, where A_t is the absorbance at time t and A_∞ is the absorbance after at least ten half-lives. The last values, A_∞, showed that the olefins were produced essentially in quantitative yield except for tosylates where a fair amount of the substitution was accompanied by elimination. The absorbance was meas-

Table 5. Reaction of 2-(p-chlorophenyl)ethyl chloride with Et_4NF in CH_3CN at 25.0°C

Time (min)	A_t	$\log A_\infty/(A_\infty - A_t)$	$k_1 \times 10^3$ [a] (min^{-1})
5	0.180	0.04386	
10	0.250	0.05928	8.36
15	0.320	0.08027	8.80
20	0.378	0.09621	8.43
25	0.450	0.1173	8.41
30	0.504	0.1339	8.50
	1.900		Av. 8.50[b]

$[ArCH_2CH_2Cl]_0 = 1.02 \times 10^{-3}$ mol/l, $[F^-] = 1.26 \times 10^{-2}$ mol/l.

a) Corrected for zero intercept of $[\log A_\infty/(A_\infty - A_t)]_0 = 0.023$.

b) From the slope of the best fit straight line.

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20) C. G. Swain and E. R. Thornton, *ibid.*, **84**, 817 (1962).

21) N. Ono, This Bulletin, **44**, 1393 (1971). Part of the work was published in a preliminary form: J. Hayami, N. Ono, and A. Kaji, *Tetrahedron Lett.*, **1970**, 2727.

22) Melting points were determined on a Yanagimoto hot stage apparatus and were uncorrected. NMR spectra were determined with a Jeolco 3H-60 spectrometer using tetramethylsilane as an internal standard, and UV spectra with a Hitachi Perkin-Elmer 139 spectrophotometer. Glc analyses were performed with a Yanagimoto GCG-5DH gas-chromatograph.

23) C. H. DePuy and D. H. Froemsdorf, *J. Amer. Chem. Soc.*, **79**, 3710 (1957).

24) W. H. Saunders, Jr., D. G. Bushman, and A. F. Cockerill, *ibid.*, **90**, 1775 (1968).

25) R. U. Lemieux and J. Hayami, *Can. J. Chem.*, **43**, 2162 (1965).

ured at the absorption maximum of styrene or substituted styrene. Molar extinction coefficients are as follows: styrene λ_{max}, 248 mμ ($\varepsilon = 1.46\times10^4$); p-chlorostyrene λ_{max}, 253 mμ ($\varepsilon = 1.86\times10^4$); p-methylstyrene λ_{max}, 252 mμ ($\varepsilon = 1.69\times10^4$); p-methoxystyrene λ_{max}, 259 mμ, ($\varepsilon = 1.69\times10^4$). Initial concentration in the reaction mixture was 2×10^{-2} mol/l in fluoride and 1×10^{-3} mol/l in 2-arylethyl compounds unless otherwise stated. A typical example is shown in Table 5.