[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Neighboring Carbon and Hydrogen. XXIV. Some Methoxyl-substituted 2-Aryl-1-alkyl Benzenesulfonates[1]

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RECEIVED MARCH 29, 1956

The present article reports the results of a study of several 2-aryl-1-alkyl benzenesulfonates of interest in connection with aryl participation in solvolysis. The aryl groups included phenyl, *p*-anisyl, *m*-anisyl and 3,5-, 3,4- and 2,4-dimethoxyphenyl. Rate and $\Delta S^{\ddagger}$ serve as criteria in deciding the proportions of anchimerically assisted and unassisted solvolytic processes for the different 2-aryl-1-ethyl esters. In the solvent sequence EtOH–AcOH–HCOOH, the 2-phenyl-1-ethyl system shifts from anchimerically unassisted to mainly assisted solvolysis between acetic and formic acid solvents, while 2-*p*-anisyl-1-ethyl does so between ethanol and acetic acid. As expected, the 2,4-dimethoxyphenyl group is powerfully rate-enhancing, the acetolysis of 2-(2,4-dimethoxyphenyl)-1-ethyl bromobenzenesulfonate being 1590 times as rapid as that of the 2-phenyl-1-ethyl ester at 75°. The 2,4-dimethoxylated ester solvolyzes by the aryl-assisted process in all three solvents mentioned above. The rates of acetolysis of the diastereomeric 1-phenyl-1-anisyl-2-propyl bromobenzenesulfonates differ by the small factor of 1.82 at 25°. An approximate dissection of the solvolysis of the 1,1-diphenyl-2-propyl ester into separate conformational contributions has been made. On this basis, the factor by which the *p*-methoxyl group accelerates the rate of phenyl-assisted ionization is 62 at 25°. This factor is similar to others obtained in the present and previous work. A *m*-methoxyl group is somewhat rate-retarding when present on a participating phenyl group. Also, in acetolysis, it is slightly rate-retarding when present on a non-participating phenyl group.

In the present article are reported the results of a study of several 2-aryl-1-alkyl benzenesulfonates of interest in connection with aryl participation in solvolysis. While the previous measurements[2] dealt with phenyl and *o*- and *p*-anisyl, the present measurements include *m*-anisyl, and 3,5-, 3,4- and 2,4-dimethoxyphenyl. The present results add to our knowledge of the effect of methoxyl substitution[2,3] in the β-aryl group. Also, they supply another comparison of relative reactivities of diastereomeric compounds.[4] Finally, they provide data for comparison purposes in other investigations.[5]

Results

The series of primary and secondary *p*-bromobenzenesulfonates or *p*-toluenesulfonates employed in the present study is shown in Table I, which summarizes the measured solvolysis rate constants. Unhindered primary arylsulfonates were prepared from the corresponding alcohols and the arylsulfonyl chloride in pyridine at −20°. The use of a short reaction time discouraged formation of alkyl chloride which can otherwise be quite troublesome. Neophyl type and secondary arylsulfonates were prepared by the usual method.[6]

The necessary primary alcohols were prepared by two methods. 2-*m*-Anisylethanol was derived from the reaction between *m*-anisylmagnesium bromide and ethylene oxide[7] while the other alcohols, 2-(3,5-dimethoxyphenyl)-ethanol, 2-(2,4-dimethoxyphenyl)-ethanol and *m*- and *p*-methoxyneophyl alcohols, were prepared in good yields by the reduction of the appropriate acid with lithium aluminum hydride.

Of the required acids, 3,5-dimethoxyphenylacetic acid was available from 3,5-dimethoxybenzoic acid by way of the corresponding benzyl alcohol, benzyl chloride[8] and nitrile.[8] 2,4-Dimethoxyphenylacetic acid was readily prepared by the azlactone method from 2,4-dimethoxybenzaldehyde.[9] Both *m*- and *p*-anisyldimethylacetic acids were prepared by the procedure of Heyningen,[10] which involves the methylation of *m*- or *p*-methoxybenzyl cyanide with the aid of sodium amide and methyl iodide in benzene, followed by hydrolysis at 140° in methanolic potassium hydroxide. The alkylation of *p*-methoxybenzyl cyanide was also attempted with two equivalents of sodium hydride and methyl iodide in ether, but only monoalkylated nitrile was obtained.

The secondary alcohol, 3,4-dimethoxybenzylmethylcarbinol, was obtained by the reduction of 3,4-dimethoxyphenylacetone. The two diastereomeric 1-phenyl-1-*p*-anisyl-2-propanols were kindly supplied by Dr. D. Y. Curtin[11] and A. Bradley.

Kinetic measurements in acetic acid were carried out in the conventional manner,[6] while measurements in formic acid were made by a simplified new method. In this new method, the potentiometric titration described previously[12] was avoided. Instead, formic acid solutions are diluted with four volumes of purified dioxane and titrated directly with acid or base in acetic acid.

All the compounds listed in Table I displayed good first-order kinetics in acetolysis and formolysis except 2-(2,4-dimethoxyphenyl)-ethyl *p*-bromobenzenesulfonate (I) in acetolysis. In acetolysis, this substance displayed a decreasing integrated first-order rate constant. This drift was clearly due to common ion rate depression, dealt with elsewhere.[13] As shown in Table I, inclusion of 0.0250 *M* sodium bromobenzenesulfonate depressed the rate constant to a constant value essentially equal to the one reported for 0.0300 *M*

(1) Research supported by the Office of Naval Research.

(2) *E.g.*, S. Winstein, C. R. Lindegren, H. Marshall and L. L. Ingraham, THIS JOURNAL, **75**, 147 (1953).

(3) (a) S. Winstein, M. Brown, K. C. Schreiber and A. H. Schlesinger, *ibid.*, **74**, 1140 (1952); (b) S. Winstein and K. C. Schreiber, *ibid.*, **74**, 2171 (1952).

(4) S. Winstein, B. K. Morse, E. Grunwald, K. C. Schreiber and J. Corse, *ibid.*, **74**, 1113 (1952).

(5) *E.g.*, S. Winstein, R. Heck, S. Lapporte and R. Baird, *Experientia*, **12**, 138 (1956)

(6) S. Winstein, E. Grunwald and L. L. Ingraham, THIS JOURNAL, **70**, 826 (1948)

(7) E. D. Bergmann and C. Weizmann, *J. Org. Chem.*, **4**, 266 (1939).

(8) R. Adams, S. MacKenzie, Jr., and S. Loewe, THIS JOURNAL, **70**, 666 (1948).

(9) R. Pschorr and G. Knoffler, *Ann.*, **382**, 55 (1911).

(10) E. Heyningen, THIS JOURNAL, **74**, 4862 (1952).

(11) D. Curtin, page 40 of Abstracts, 13th National Organic Symposium of the American Chemical Society, Ann Arbor, Mich., June 15–18, 1953.

(12) S. Winstein and H. Marshall, THIS JOURNAL, **74**, 1120 (1952)

(13) S. Winstein, E. Clippinger, A. H. Fainberg, R. Heck and G. C. Robinson, *ibid.*, **78**, 328 (1956).

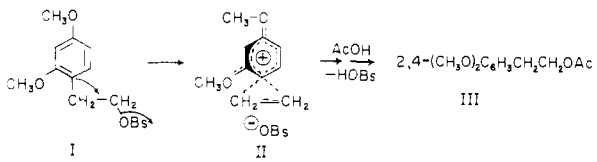
TABLE I

SUMMARY OF SOLVOLYSIS RATES

Compound	Solvent	Temp., °C.	Concn., *M*	Added salt, *M*	k (sec.$^{-1}$)	$\Delta H^{\pm}$, kcal./mole	$\Delta S^{\pm}$, e.u.
$C_6H_5CH_2CH_2OBs$	HOAc	75.00	0.0283		$(8.48 \pm 0.09) \times 10^{-7}$	24.9	−15.2
	HOAc	100.15	.0306		$(1.02 \pm 0.01) \times 10^{-5}$		
	HCOOH	50.00	.0302	0.0302 NaOCHO	$(6.48 \pm 0.06) \times 10^{-6}$		
	HCOOH	75.00	.0323	.0315 NaOCHO	$(1.01 \pm 0.01) \times 10^{-4}$	23.9	− 8.6
$C_6H_5CH_2CH_2OTs$	HCOOH	50.00	.0336	.0291 NaOCHO	$(2.54 \pm 0.05) \times 10^{-6}$		
	HCOOH	75.00	.0336	.0291 NaOCHO	$(4.10 \pm 0.04) \times 10^{-5}$	24.9	− 9.5
m-$CH_3OC_6H_4(CH_2)_2$ OBs	HOAc	75.00	.0261		$(8.11 \pm 0.15) \times 10^{-7}$		
3,5-$(CH_3O)_2C_6H_3$	HOAc	75.00	.0255		$(7.81 \pm 0.09) \times 10^{-7}$		
$(CH_2)_2OBs$	HCOOH	75.00	.0285	.0315 NaOCHO	$(2.82 \pm 0.08) \times 10^{-5}$	23.6	−11.8
	HCOOH	100.00	.0228	.0291 NaOCHO	$(2.97 \pm 0.07) \times 10^{-4}$		
2,4-$(CH_3O)_2C_6H_3$	HOAc	50.00	.0295		4.74×10^{-5}[a]		
CH_2CH_2OBs	HOAc	75.00	.0315		6.31×10^{-4}[a]	22.5	− 9.0
	HOAc	50.00	.0291	.0315 NaOAc	$(1.07 \pm 0.05) \times 10^{-4}$		
	HOAc	75.00	.0296	.0315 NaOAc	$(1.28 \pm 0.06) \times 10^{-3}$	22.2	−10.4
	HOAc	50.00	.0304	.0316 $LiClO_4$	$(1.49 \pm 0.01) \times 10^{-4}$		
	HOAc	50.20	.0281	.0250 NaOBs	$(3.64 \pm 0.03) \times 10^{-5}$		
	HCOOH	25.00	.0100		$(5.22 \pm 0.21) \times 10^{-4}$[b]		
	HCOOH	75.00			6.79×10^{-2}[c]		
$(CH_3)_2(p\text{-}CH_3OC_6H_4)$	HOAc	25.06	.0294		$(5.32 \pm 0.09) \times 10^{-6}$		
CCH_2OTs	HOAc	50.00	.0301		$(1.21 \pm 0.02) \times 10^{-4}$	23.2	− 4.4
	HOAc	75.00			1.77×10^{-3}[d]		
	HOAc	50.00	.0296	.0310 NaOAc	$(1.23 \pm 0.01) \times 10^{-4}$		
	HCOOH	25.00	.0273	.0302 NaOCHO	$(8.31 \pm 0.08) \times 10^{-4}$		
	HCOOH	50.00			1.53×10^{-2}[c]		
$(CH_3)_2(m\text{-}CH_3OC_6H_4)$	HOAc	75.00	.0342		$(1.39 \pm 0.01) \times 10^{-5}$	25.4	− 8.1
CCH_2OTs	HOAc	100.05	.0342		$(1.75 \pm 0.04) \times 10^{-4}$		
	HCOOH	50.00	.0302	.0302 NaOCHO	$(1.05 \pm 0.01) \times 10^{-4}$		
3,4-$(CH_3O)_2C_6H_3$	HOAc	50.02	.0366		$(1.15 \pm 0.02) \times 10^{-5}$		
$CH_2CH(OTs)CH_3$	HOAc	75.00	.0327		$(1.84 \pm 0.02) \times 10^{-4}$	24.1	− 6.6
$(p\text{-}CH_3OC_6H_4)(C_6H_5)$	HOAc	25.01	.0272		$(1.56 \pm 0.04) \times 10^{-5}$		
$CHCH(OBs)CH_3$ "B"	HOAc	50.02	.0185		$(3.64 \pm 0.05) \times 10^{-4}$	24.1	− 1.8
$(p\text{-}CH_3OC_6H_4)(C_6H_5)$	HOAc	25.00	.0213		$(8.56 \pm 0.13) \times 10^{-6}$		
$CHCH(OBs)CH_3$ "A"	HOAc	50.02	.0266		$(2.18 \pm 0.02) \times 10^{-4}$	24.1	− 0.8

[a] Extrapolated value from a plot of log [(ROBs)o/(ROBs)] *vs.* time. [b] Data of E. Clippinger, unpublished work. [c] Extrapolated from data at another temperature assuming $\Delta S^{\pm}$ is the same in formic acid as it is in acetic acid. [d] Extrapolated from data at another temperature.

lithium bromobenzenesulfonate.[13] Inclusion of lithium perchlorate gave rise to a special salt effect,[14-16] the rate constant being steady at the



proper level.[16] Similarly, the rate constant was almost completely steady at the special salt-enhanced level[16] when 0.0315 *M* sodium acetate was included. The product of acetolysis of 2,4-dimethoxyphenylethyl *p*-bromobenzene-sulfonate (I) proved to be simple unrearranged substitution product, 2,4-dimethoxyphenylethyl acetate (III). Treatment with lithium aluminum hydride gave rise to a high over-all yield of pure crystalline 2,4-dimethoxyphenylethanol.

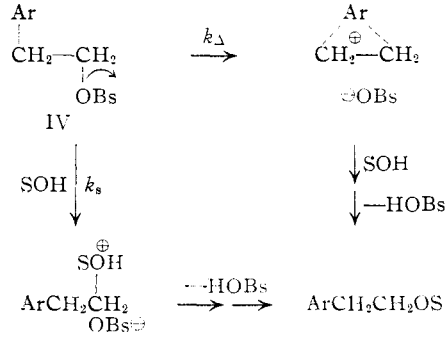
(14) (a) S. Winstein, E. Clippinger, A. H. Fainberg and G. C. Robinson, THIS JOURNAL, **76**, 2597 (1954); (b) *Chemistry and Industry*, 664 (1954).

(15) A. H. Fainberg and S. Winstein, THIS JOURNAL, **78**, 2763 (1956).

(16) S. Winstein and E. Clippinger, *ibid.*, **78**, 2784 (1956).

Discussion

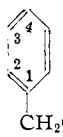
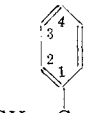
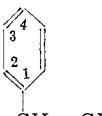
Primary Alkyl Benzenesulfonates.—In deciding the relative proportions of anchimerically assisted and unassisted solvolytic processes for the different 2-aryl-1-ethyl esters IV, we can employ two criteria. One criterion employed previously[2] is



rate. As the nature and degree of methoxy substitution of the neighboring phenyl group are varied, one can expect the following order of increasing values of k_Δ, the rate constant for aryl-assisted ionization

TABLE II

SUMMARY OF RATE COMPARISONS

Structure	Temp., °C.	Substituent	Rel. solvolysis rate AcOH	Rel. solvolysis rate HCOOH	$\Delta S^{\pm}$, e.u. EtOH	$\Delta S^{\pm}$, e.u. AcOH	$\Delta S^{\pm}$, e.u. HCOOH	Chief contributor to k AcOH	Chief contributor to k HCOOH
CH_3CH_2OTs[12]	75		2.68	0.48	−17.5	−16.7	−16.5	k_s	k_s
$C_6H_5CH_2CH_2OTs$	75		1.00[2]	1.00[2]	−20.2[15]	−17.3[2]	− 9.5	k_s	k_Δ
 CH_2CH_2OBs	75	H	1.00	1.00		−15.2	− 8.6	k_s	k_Δ
		3-MeO	0.96					k_s	
		3,5-$(MeO)_2$	0.92	0.34			−11.8	k_s	$k_\Delta + k_s$
		4-MeO[a]	81[b]	53[2]	−15.5[15]	− 8.8[2]	− 9.2[2]	k_Δ	k_Δ
		2-MeO[a]	71[b]	52[2]				k_Δ	k_Δ
		2,4-$(MeO)_2$	1590[d,c]	672	− 4.6[e]	− 9.0		k_Δ	k_Δ
 $CH_3—C(CH_3)(OCH_3)—CH_2OTs$	75	H[e]	1.00		− 7.5	− 5.5	− 6.3	k_Δ	
		3-MeO	0.70			− 8.1		k_Δ	
		4-MeO	88.5			− 4.4		k_Δ	
	50	H[e]	1.00	1.00				k_Δ	k_Δ
		3-MeO	0.74	0.45				k_Δ	k_Δ
		4-MeO	121.8	65.5				k_Δ	k_Δ
 $CH_2—CH(OTs)CH_3$	75	H[3,a]	1.00			− 6.4		k_Δ	
		3-MeO	0.94			− 6.6		k_Δ	
$(C_6H_5)_2CHCH(OBs)CH_3$	25	H[4]	1.00[d]			− 1.7		k_Δ	
		4-MeO "A"	22			− 0.8		k_Δ	
		4-MeO "B"	40			− 1.8		k_Δ	

[a] Three times rate constant for the toluenesulfonate. [b] Based on k°_{ext} from work of A. Fainberg.[15] [c] Based on k°_{ext} from work of E. Clippinger.[16] [d] Extrapolated from data of another temperature. [e] A. Fainberg, unpublished work.

$$m\text{-}CH_3OC_6H_4 \overset{1}{\cong} C_6H_5 \overset{2}{<} o\text{-}CH_3OC_6H_4 \overset{3}{\cong} p\text{-}CH_3OC_6H_4 \overset{4}{<} o,p\text{-}(CH_3O)_2C_6H_3$$

For k_s, the rate constant for aryl-unassisted solvolysis, one can anticipate roughly equal values from the various structures, except for possible steric retardation from the *ortho*-substituted structures. From the rate comparisons summarized in Table II, it is quite clear that k_Δ/k_s is quite large in both acetic and formic acid solvents for the *o*-CH_3O-, *p*-CH_3O- and *o,p*-$(CH_3O)_2$-substituted phenylethyl esters IV. In these cases the observed rate constant is almost exactly equal to k_Δ. The inequality 2 and the rough equality 3 in the sequence of k_Δ values was established in the previous[2] work. The present work demonstrates inequality 4, the 2,4-dimethoxyphenylethyl bromobenzenesulfonate (I) acetolyzing more rapidly than the phenylethyl analog by a factor of 1590 at 75°. The second methoxyl group enhances rate by a factor of *ca.* 20.

The other criterion is the entropy of activation observed in solvolysis, for there appears to be sufficient uniformity of behavior in formic acid, acetic acid and ethanol as solvents to warrant the use of $\Delta S^{\pm}$ in diagnosing mechanism. With the simple primary structures involved, apparently the anchimerically unassisted solvolyses tend to display a $\Delta S^{\pm}$ of *ca.* −18 ± 2 e.u. As summarized in Table II, this is true of ethyl toluenesulfonate in all three solvents. The anchimerically assisted solvolyses tend to be associated with a $\Delta S^{\pm}$ of *ca.* −7 ± 2 e.u. This is true of neophyl toluenesulfonate in all three solvents. Also, it is true of 2,4-dimethoxyphenylethyl bromobenzenesulfonate in acetic acid and even ethanol.

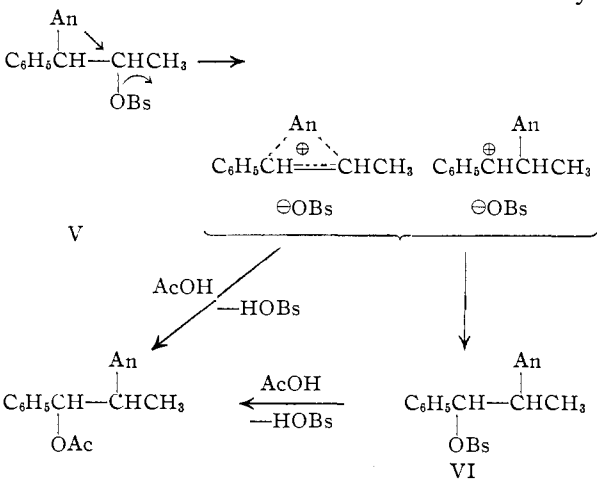
With some of the substances, the solvolysis apparently tends to shift from mainly anchimerically unassisted (rate constant k_s) to mainly anchimerically assisted (rate constant k_Δ) as solvent is changed from the more nucleophilic ethanol to acetic acid to formic acid. With the *p*-anisylethyl ester this change of mechanism apparently occurs between ethanol and acetic acid. With the phenylethyl ester, there is apparently a change between acetic and formic acid solvents, the $\Delta S^{\pm}$ being appropriate for a rate constant mainly k_s in acetic acid and mainly k_Δ in formic. Such an assignment is also suggested by rate comparisons,[2] the phenylethyl ester being substantially slower in acetic acid and more rapid in formic acid than the ethyl ester (Table II). That the change in mechanism should occur later and later in the solvent sequence as one proceeds from 2,4-$(MeO)_2C_6H_3CH_2CH_2OBs$ to 4-$MeOC_6H_4CH_2CH_2OBs$ to $C_6H_5CH_2CH_2OBs$ is to be expected.

The conclusions regarding which solvolytic process is the chief contributor to the rate constants for the different substances in acetic and formic acid solvents are summarized in Table II.

As expected, the newly investigated aryl group, 2,4-dimethoxyphenyl, has been found to be powerfully rate-enhancing. The nature of the participation responsible for the large rate increases in this case was verified by product isolation. Just as in the case of the anisylethyl analogs,[2] only unrearranged solvolysis product III was isolated, showing that rate enhancement is connected with

aryl participation. There are other indications[13,14,16] of a rather stable carbonium ion intermediate II in acetolysis of bromobenzenesulfonate I. The nature of the products rules out any appreciable fraction of solvolysis involving hydrogen participation.

Diastereomeric 1-Phenyl-1-anisyl-2-propyl Bromobenzenesulfonates.—The rates of acetolysis of the diastereomeric 1-phenyl-1-*p*-anisyl-2-propyl *p*-bromobenzenesulfonates (V) were measured because of the interest in the effects of both methoxyl

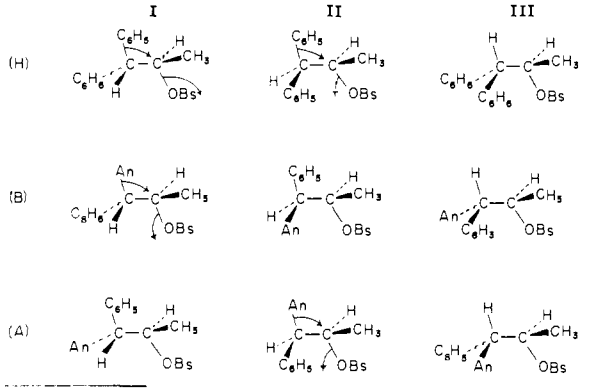


substitution in the benzene ring and also diastereomeric configuration on reactivity. The first-order rates of acetolysis were high, the diastereomers being 40 and 22 times as reactive as the parent compound, 1,1-diphenyl-2-propyl bromobenzenesulfonate.[4] Further, the $\Delta S^{\ddagger}$ values were equal to that for the parent substance. Good first-order kinetics of acetolysis were observed, so there was no indication of ion pair return to a new material attending the acetolysis. However, Curtin[11] has reported essentially exclusive anisyl migration in solvolysis of these materials. Therefore, any ion pair return would be expected to produce the α-phenylalkyl ester VI. The latter type of ester is so reactive in solvolysis,[17] that its formation would be undetected[3b] in the kinetics.

TABLE III

CONFORMATIONAL ANALYSIS OF ARYL-ASSISTED SOLVOLYSIS OF 1-PHENYL-1-ARYL-2-PROPYL *p*-BROMOBENZENESULFONATES

System/Conformation



(17) K. C. Schreiber, unpublished work.

The observed rates of the diastereomeric esters V are most clearly discussed in terms of our recent conformational discussion[18] of reactivity. In Table III are shown the three conformations, I, II and III, of the solvolyzing 1,1-diphenyl-2-propyl and diastereomeric 1-anisyl-1-phenyl-2-propyl bromobenzenesulfonates. These are labelled as systems H, B and A, respectively.

In the case of systems B and A, the solvolysis is essentially conformationally homogeneous. For B, the rate constant is $N_{\mathrm{I}}{}^{\mathrm{B}}k_{\mathrm{I}}{}^{\mathrm{B}}$, the product of the mole fraction of conformation I and the intrinsic rate constant for that conformation. For A, the rate constant is $N_{\mathrm{II}}{}^{\mathrm{A}}k_{\mathrm{II}}{}^{\mathrm{A}}$.

The solvolysis of 1,1-diphenyl-2-propyl bromobenzenesulfonate (H) involves quite predominantly anchimerically assisted ionization with phenyl participation, judging by rate[4] and products[17,19] of acetolysis. However, the ionization must be conformationally degenerate; two different conformations, I and II, shown in Table III, must enter into the ionization. The rate constant, k, in this case, is given by equation 1.

In order to estimate the effect of a methoxyl group on rate, it is necessary to dissect the solvolysis of the 1,1-diphenyl-2-propyl system (H) into the separate conformational contributions. This dissection was carried out with the aid of equation 2, the latter being based on the assumptions that: (i) $N_{\mathrm{I}}{}^{\mathrm{H}}/N_{\mathrm{II}}{}^{\mathrm{H}}$ equals $N_{\mathrm{I}}{}^{\mathrm{B}}/N_{\mathrm{II}}{}^{\mathrm{A}}$, or, in other words, that the conformational distribution is the same in

$$k = N_{\mathrm{I}}{}^{\mathrm{H}}k_{\mathrm{I}}{}^{\mathrm{H}} + N_{\mathrm{II}}{}^{\mathrm{H}}k_{\mathrm{II}}{}^{\mathrm{H}} \quad (1)$$

$$\frac{N_{\mathrm{I}}{}^{\mathrm{H}}k_{\mathrm{I}}{}^{\mathrm{H}}}{N_{\mathrm{II}}{}^{\mathrm{H}}k_{\mathrm{II}}{}^{\mathrm{H}}} = \frac{N_{\mathrm{I}}{}^{\mathrm{B}}k_{\mathrm{I}}{}^{\mathrm{B}}}{N_{\mathrm{II}}{}^{\mathrm{A}}k_{\mathrm{II}}{}^{\mathrm{A}}} \quad (2)$$

all three systems, H, B and A; (ii) $k_{\mathrm{I}}{}^{\mathrm{H}}/k_{\mathrm{II}}{}^{\mathrm{H}} = k_{\mathrm{I}}{}^{\mathrm{B}}/k_{\mathrm{II}}{}^{\mathrm{A}}$, or, in other words, steric effects due to eclipsing[4] methyl and aryl are the same whether phenyl or anisyl is participating.

The relationships in (i) and (ii) above are merely approximations, and it is not clear how exactly they are obeyed. For example, relationship (ii) may be somewhat upset because the degree of involvement of the participating anisyl, and therefore the *cis* effect[11] in the transition state may be different than when phenyl participates. Nevertheless, for lack of data on the question, the approximation of equation 2 seems preferable to the dissection of Cram and Abd Elhafez[19] who called $N_{\mathrm{I}}{}^{\mathrm{H}}.k_{\mathrm{I}}{}^{\mathrm{H}} >> N_{\mathrm{II}}{}^{\mathrm{H}}k_{\mathrm{II}}{}^{\mathrm{H}}$ because the ratio of diastereomeric rearranged products resembled more closely the ratio obtained from one diastereomeric 1,2-diphenyl-1-propyl ester than the other. The conformational dissection of the rate constant of H is summarized in Table IV, along with the factor of 62 by which it is estimated the *p*-CH_3O group accelerates rate of ionization at 25°.

In the same conformational terms employed above, the ratio of solvolysis rate constants of the two diastereomeric 1-phenyl-1-*p*-anisyl-2-propyl *p*-bromobenzenesulfonates, 1.82 at 25°, is given by equation 3. In this equation, the rate ratio is

$$\frac{k_{\mathrm{B}}}{k_{\mathrm{A}}} = \left(\frac{N_{\mathrm{I}}{}^{\mathrm{B}}}{N_{\mathrm{II}}{}^{\mathrm{A}}}\right)\left(\frac{k_{\mathrm{I}}{}^{\mathrm{B}}}{k_{\mathrm{II}}{}^{\mathrm{A}}}\right) \quad (3)$$

(18) S. Winstein and N. J. Holness, THIS JOURNAL, **77**, 5562 (1955).

(19) D. J. Cram and F. Abd Elhafez, *ibid.*, **76**, 28 (1954).

TABLE IV

ESTIMATED QUANTITATIVE CONFORMATIONAL ANALYSIS

System	Rel. rate 25°		N_{Ik}I 10^7 sec.$^{-1}$	N_{Ik}I Rel. value	N_{Ik}II 10^7 sec.$^{-1}$	N_{Ik}II Rel. value
H	1[a]		2.54	1	1.40	1
B	40	1.82	156	62		
A	22	1.00			85.6	62

[a] Total first-order rate constant of acetolysis extrapolated from data at other temperatures[4] is 3.94×10^{-7} sec.$^{-1}$ at 25.0°.

given as the product of two ratios; one deals with relative populations of the appropriate conformation of the ground state in the two diastereomers, and the other deals with the ratio of intrinsic rate constants pertaining to these conformations of each diastereomer. The ratio, 1.82, obviously quite small, is similar in magnitude to values observed with the 3-phenyl-2-butanols[4] (1.14 at 50°) and 3-anisyl-2-butanols[20] (1.73 at 25°). Further discussion of this matter is postponed until pertinent rate comparisons are reported on other systems, including some dealing with the pinacol rearrangement.

***m*- and *p*-Methoxyl Groups.**—In summarizing the effects of methoxyl substitution on rate we shall consider first the effect of methoxyl on a participating phenyl group. As is clear from Tables II and IV, the factor by which a *p*-methoxy group increases k_Δ is 62 (25°), 122 (50°) and >81 (75°) for 1,1-diphenyl-2-propyl, neophyl and phenylethyl esters, respectively, in acetic acid. The factors are of the order of magnitude observed with the 2-phenyl-1-propyl, benzylmethylcarbinyl and 3-phenyl-2-butyl systems.[3] There is some variation of the factor with structure. Also, they vary with solvent, the values tending to be smaller in formic than acetic acid (Table II). This is because the sensitivity of ionization rate to the solvent change tends to be less for the methoxylated than the parent structures. It will be more efficient to postpone further discussion of these variations of the magnitude of the methoxyl effect until the available data are more completely reported.

For the effect of a *m*-methoxy group on a participating phenyl group, one could anticipate either a small retardation or small acceleration[21] of rate, depending on what blend of inductive and resonance effects[22] applies to the example of electrophilic aromatic substitution[4] represented by the ionization of the arylsulfonate. In the present work, a slight retardation of rate of acetolysis is observed on introduction of a *m*-methoxy group into the neophyl and 1-*p*-anisyl-2-propyl systems (Table II). The effect on formolysis rate is larger, *m*-methoxyl in the neophyl system decreasing rate by a factor of 2. Two *m*-methoxyl groups in the 2-phenylethyl system decrease rate of formolysis by a factor of 3. Judging by the $\Delta S^\ddagger$ value for 3,5-$(MeO)_2C_6H_3CH_2CH_2OBs$, the formolysis rate is not so predominantly composed of k_Δ as in the case of the parent $C_6H_5CH_2CH_2OBs$ system. Because k_Δ is so much reduced, the contribution of k_s is now more serious.

Regarding the effect of *m*-methoxyl on a nonparticipating phenyl group, the present results show that very slight decreases in acetolysis rate are produced by one or two methoxyl groups in the phenylethyl system.

(20) A. H. Fainberg, G. C. Robinson and S. Winstein, THIS JOURNAL, **78**, 2777 (1956).

(21) P. B. D. de la Mare and C. A. Vernon, *J. Chem. Soc.*, 1764 (1951).

(22) P. B. D. de la Mare, *ibid.*, 4450 (1954).

Experimental Part

Arylsulfonates.—Unhindered primary esters were prepared in pyridine at low temperatures. In a typical preparation, 1 g. of the alcohol was dissolved in 10 ml. of anhydrous pyridine, and the solution, cooled to −20°, was treated with 1.5 equivalents of *p*-bromobenzenesulfonyl chloride in 5 ml. of pyridine. The mixture was allowed to warm up to 0° over a period of 10 or 15 minutes. The mixture was then poured into 100 ml. of water and extracted with ether. The extract was washed successively with water, cold dilute hydrochloric acid, water again, and finally with a saturated aqueous solution of sodium bicarbonate. After being dried, the ether solution was concentrated on a water-bath, the last traces of solvent being removed with a stream of air. The oils so obtained usually crystallized when they were triturated with pentane or pentane and ether at low temperatures. The crystalline products were ordinarily crystallized from a low boiling petroleum ether or a mixture of petroleum ether and ether. Yields were generally 40–60% of theory.

Analyses and melting points of the arylsulfonate preparations are summarized in Table V.

***m*-Anisylethyl *p*-Bromobenzenesulfonate.**—2-(*m*-Anisyl)-ethanol, $n^{25}D$ 1.5338, was prepared from *m*-anisylmagnesium bromide and ethylene oxide[7] and converted to the *p*-bromobenzenesulfonate by the low temperature method.

3,5-Dimethoxyphenylacetic Acid.—3,5-Dimethoxyphenyl acetonitrile[8] (34 g.) was refluxed for five hours with 15 g. of sodium hydroxide in 100 cc. of water and 50 cc. of ethanol. About 50 ml. of solvent was distilled off, and the remainder of the solution was poured onto ice and dilute hydrochloric acid. The acid was filtered off and recrystallized from aqueous ethanol. The yield of acid, m.p. 103.5–104.5° (reported[23] 99–100°), was 33 g.

2-(3,5-Dimethoxyphenyl)-ethanol.—A solution of 32 g. of 3,5-dimethoxyphenylacetic acid in 600 cc. of ether was added to a stirred solution of 6.3 g. of lithium aluminum hydride in 500 cc. of ether. After one hour of refluxing, the mixture was worked up as usual.[24] The alcohol, b.p. 140° (2 mm.), $n^{25}D$ 1.5387, weighed 26.8 g.

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 65.70; H, 7.78.

2-(2,4-Dimethoxyphenyl)-ethanol.—The reduction of 2,4-dimethoxyphenylacetic acid[9] with lithium aluminum hydride gave 2,4-dimethoxyphenylethanol in 70% yield. The alcohol formed long needles, m.p. 67–68° (reported[25] 67°), from petroleum ether (b.p. 60–80°).

Anal. Calcd. for $C_{10}H_{14}O_3$: C, 65.91; H, 7.74. Found: C, 66.21; H, 7.47.

α,α-Dimethyl-*p*-methoxybenzyl Cyanide.—This substance was prepared essentially by the method of Heyningen.[10] The use of *p*-methoxybenzyl cyanide, $n^{25}D$ 1.5304, prepared by the method of Rorig,[26] and the addition of 25% excess methyl iodide as rapidly as possible increased the yield of product, b.p. 110° (3 mm.), $n^{25}D$ 1.5143, to 53%.

Anal. Calcd. for $C_{11}H_{13}NO$: C, 75.40; H, 7.48. Found: C, 75.34; H, 7.22.

α-Methyl-*p*-methoxybenzyl Cyanide.—A mixture of 40 g. of *p*-methoxybenzyl cyanide and 16 g. of sodium hydride in 500 ml. of ether was stirred at room temperature for 20 hours. Then 90 g. of methyl iodide was added, and the mixture was stirred for two days. The mixture was treated with water, and the product was fractionated. The nitrile, b.p. 147.5–148.5° (12.5 mm.), weighed 25 g. This substance crystallized on cooling. When recrystallized from

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(25) B. Reicheot and W. Koch, *Arch. Pharm.*, **273**, 265 (1935); *Chem. Zentr.*, **106, II**, 686 (1935).

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TABLE V

PROPERTIES AND ANALYSES OF SOME ARYLSULFONATES

Compound	M.p., °C.	Formula	Analyses, % Carbon Calcd.	Carbon Found	Hydrogen Calcd.	Hydrogen Found
$C_6H_5CH_2CH_2OBs$	59–60	$C_{14}H_{13}O_3SBr$	49.28	49.26	3.84	3.77
m-$CH_3OC_6H_4CH_2CH_2OBs$	40.5–41.5	$C_{15}H_{13}O_4SBr$	48.53	48.39	4.07	4.24
3,5-$(CH_3O)_2C_6H_3CH_2CH_2OBs$	76.5–77.5	$C_{16}H_{18}O_5SBr$	47.89	47.58	4.27	4.21
2,4-$(CH_3O)_2C_6H_3CH_2CH_2OBs$	72–73	$C_{16}H_{18}O_5SBr$	47.89	48.17	4.27	4.23
$(CH_3)_2$(p-$CH_3OC_6H_4$)CCH_2OTs	44–46	$C_{18}H_{22}O_4S$	64.64	64.54	6.63	6.37
$(CH_3)_2$(m-$CH_3OC_6H_4$)CCH_2OTs	78–79	$C_{18}H_{22}O_4S$	64.64	64.80	6.63	6.49
3,4-$(CH_3O)_2C_6H_3CH_2CH(OTs)CH_3$	55–57	$C_{18}H_{22}O_5S$	61.69	61.54	6.33	6.62

petroleum ether, b.p. 60–80°, it formed colorless crystals, m.p. 37–38°.

Anal. Calcd. for $C_{10}H_{11}ON$: C, 74.50; H, 6.88. Found: C, 74.67; H, 6.94.

p-Anisyldimethylacetic Acid.—The hydrolysis of α,α-dimethyl-p-methoxybenzyl cyanide was carried out as described by Heyningen.[10] The acid, twice recrystallized from aqueous methanol, m.p. 88–89.5°, was obtained in 52% yield.

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26. Found: C, 68.27; H, 6.96.

p-Methoxyneophyl Alcohol.—Reduction of the above acid with lithium aluminum hydride produced p-methoxyneophyl alcohol, b.p. 110° (3 mm.), m.p. 45–46.5° after crystallization from petroleum ether (b.p. 60–80°), in 89% yield. Another crystallization raised the melting point to 46–47.5°.

Anal. Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.25; H, 8.86.

α,α-Dimethyl-m-methoxybenzyl Cyanide.—Alkylation of m-methoxybenzyl cyanide with sodium amide and methyl iodide, as described above for p-methoxybenzyl cyanide, yielded α,α-dimethyl-m-methoxybenzyl cyanide in 63% yield. It was necessary to fractionate the nitrile in order to purify it. The pure nitrile, $n^{25}D$ 1.5116, had the b.p. 139.5–144.5° (13.5 mm.).

Anal. Calcd. for $C_{11}H_{13}ON$: C, 75.40; H, 7.48. Found: C, 75.44; H, 7.47.

m-Anisyldimethylacetic Acid.—Hydrolysis of the above nitrile by the method used for the *para* isomer gave m-anisyldimethylacetic acid, m.p. 56–58°, in 43% yield.

Anal. Calcd. for $C_{11}H_{14}O_3$: C, 68.02; H, 7.26. Found: C, 68.30; H, 7.21.

3,4-Dimethoxybenzylmethylcarbinol.—The reduction of 3,4-dimethoxyphenylacetone[27] with lithium aluminum hydride afforded the pure carbinol in 62% yield. The crude product was first distilled, b.p. 137–140° (4 mm.), and then crystallized from a mixture of ether and petroleum ether. The alcohol formed colorless plates, m.p. 46–47.5°.

Anal. Calcd. for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.44; H, 8.22.

1-Phenyl-1-p-anisyl-2-propyl p-Bromobenzenesulfonate "B."—This substance, m.p. 71–72°, was prepared by the usual method[6] from the pure alcohol.

1-Phenyl-1-p-anisyl-2-propyl p-Bromobenzenesulfonate "A."—This compound, m.p. 75.5–76.5°, was also prepared by the usual method[6] from the pure alcohol.

(27) This material was obtained through the courtesy of Dr. E. Shepard of the Eli Lilly Co.

Acetolysis Products from 2-(2,4-Dimethoxyphenyl)-ethyl p-Bromobenzenesulfonate.—2-(2,4-Dimethoxyphenyl)-ethyl p-bromobenzenesulfonate (10.7 g.) was dissolved in 750 cc. of dry acetic acid and heated at 50° for 51 hours. After being cooled, the solution was poured into 4 liters of water, and the products were extracted with two 500-cc. portions of distilled petroleum ether. The extracts were washed, first with water and then with aqueous sodium bicarbonate. Evaporation of the petroleum ether through a short column left the crude product. After reduction with 1 g. of lithium aluminum hydride, an oil was obtained which was recrystallized from a mixture of Skellysolve B and ether. The first crop, 3.8 g., had m.p. 65–68.5° and mixed m.p. 66–68°. A second crop weighing 0.2 g. had m.p. 64.5–66°, and mixed m.p. 65–66.5°. The total yield was 4.0 g. or 82.4%.

Kinetic Measurements.—Acetolysis rate measurements were carried out in acetic acid containing about 0.01% of water in the manner described previously.[6]

For formolysis, solutions, *ca.* 0.03 M, of the compounds to be solvolyzed were made up at room temperature in a volumetric flask from a weighed portion of the material. Standard solutions of sodium formate in anhydrous formic acid, used as solvent in some of the formolyses, were prepared from J. T. Baker C.P. sodium formate. The concentration of these solutions was checked by the titration method described below, the agreement between calculated and observed concentrations being within 1%. The sealed ampoule technique was used for all rates above 25°. The decomposition of formic acid, however, limits the use of ampoules to about two days at 75° in weakly basic solutions, and to only a few hours at 75° in weakly acidic solutions. It was sometimes necessary in the case of slow rates to put samples for infinity titration in the thermostat in loosely stoppered flasks. Ampoules were removed from a thermostat controlled to ±0.02°, at suitable times and cooled in ice, the time of cooling being used in the rate calculations. From the cooled ampoule at 25°, a 5-cc. aliquot was removed with an automatic pipet and delivered into 20 ml. of purified dioxane. After addition of 20 drops of a saturated solution of brom cresol green in acetic acid as indicator, the solution was titrated with either sodium acetate in acetic acid or with perchloric acid in acetic acid. The indicator is yellow in the basic solution, colorless in the acid solution, and very pale yellow at the neutral point. Formolysis rates at 25° were measured similarly, except that the formolysis solution was placed in a glass-stoppered flask in the thermostat and the aliquots were removed directly. The time of dilution with dioxane was used in the rate calculation.

Using the new titration procedure, the formolysis rate of β-phenylethyl p-toluenesulfonate at 75.00° was found to be $(4.00 \pm 0.06) \times 10^{-5}$, in good agreement with the previous value of $(3.94 \pm 0.08) \times 10^{-5}$ obtained by the potentiometric method.[12]

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