Nonbenzenoid Aromatic Systems. 14.[1a] Buffered Acetolyses of Certain 2-, 3-, 4-, 5-, 6-, and 7-Substituted 2-(1-Azulyl)ethyl Tosylates

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Abstract: The kinetics of buffered acetolysis of 2-(1-azulyl)ethyl tosylate (**1**-OTs) and certain 2- (OCH_3, CH_3, Cl, Br, CN), 3- (OCH_3, CH_3, SCH_3, Br, $COCH_3$, CN, NO_2), 4- (CH_3), 5- (CH_3, Br, CN), 6- (OCH_3, CH_3, Br, CN), and 7-substituted (CH_3, Br, CN) derivatives of **1**-OTs are reported. Buffered acetolysis of specific side-chain deuterium labeled compounds demonstrates that **1**-OTs solvolyzes *completely* by the Fk_Δ pathway *without* ion-pair return ($F = 1.0$). Similar results with 3-NO_2-**1**-OTs show the presence of 2 ± 1% of the solvent assisted, k_s, pathway, and about 12% ion-pair return ($F \simeq 0.81$) after 1 solvolytic half-life. The kinetic secondary α-deuterium isotope effects were determined for **1**-OTs-α,α-d_2 and 3-NO_2-**1**-OTs-α,α-d_2 to be $k_H/k_D = 1.09$ and 1.08, respectively, per deuterium at 35 °C. The individual site substituent effects were found to be well correlated by σ_p° constants, and $\rho = -4.4$ calculated at the 2 position while ρ varied between −3.0 and −3.6 at the ring 3, 5, 6, and 7 positions. Using a Yukawa–Tsuno–Sawada linear free energy relationship a *single* correlation of the combined 3-, 5-, 6-, and 7-**X**-**1**-OTs (σ_p°) and the *m*- and *p*-X-neophyl brosylate acetolysis (σ_m° for *m*-X and $[\sigma_p^\circ + 0.69\ (\sigma_p^+ - \sigma_p^\circ)]$ for *p*-X) substituent effect data (k_X/k_H) was derived with $\rho = -3.20 \pm 0.14$. The reported para-substituent effects for the Fk_Δ process of 2-phenylethyl tosylate are also fitted by this correlation. Excellent correlation was found for ring substituent effects on the pK_a of 1-azuloic acid (H_2O–EtOH, 25 °C) and buffered acetolysis of **1**-OTs (25 °C) making the 1-azulyl ring a truly "Hammett-type" aromatic system. Of the conclusions reached in this paper, those of general significance include (1) a *single reaction constant* ($\rho = -3.2$) is found for β-arylethyl arenesulfonate acetolyses with relative aryl reactivities (X = H in each case) over a range of 10^5, thus we conclude that variations in ρ for a given reaction type *cannot* be interpreted as meaning late vs. early transition state structures, and (2) the lack of any significant change in secondary α-deuterium isotope effect for 2-arylethyl arenesulfonate solvolyses also eliminates use of this kinetic effect as a useful probe of early vs. late transition state structures in these systems. However, the α-deuterium effects may be useful in differentiating between types of participation, e.g., in 2-ferrocenylethyl tosylate acetolysis. It is suggested the ortho- and para-substituent constants in related benzene derivatives are given by the expression $\sigma_o^\circ = 1.4\sigma_p^\circ$ when steric effects are absent.

Several years ago, we began a program to evalute the nonbenzenoid aromatic azulene ring system compared to benzene in several different types of reactions. Our initial choices of reaction types were to examine the effects of these two aromatic rings as interactive substituents with an attached reaction center. To this end we have examined the pK_as of azuloic acids,[2] ring substituent effects on the pK_a of 1-azuloic acid,[3] and buffered acetolyses of 2-(2-,[4] 2-(4-,[5] and 2-(6-azulyl)ethyl arenesulfonates.[5] The processes involved in direct attack on the azulene ring by some nucleophilic anions to form Meisenheimer type species have also been published.[6]

We now wish to report our results of ring substituent effects on the buffered acetolysis of 2-(1-azulyl)ethyl tosylate (**1**-OTs). A number of these same substituents were examined in their effects on the pK_a of 1-azuloic acid.[3] While it is now generally agreed that aryl participation (k_Δ pathway) is a contributing or the sole reaction process in the solvolysis of derivatives of β-arylethanols,[7,8] it was felt that several questions could be addressed by such a study, some of which were specific to azulene chemistry while others would be of general interest in the area of linear free energy relationships (LFER). Such questions include (1) would ionization to or destruction of the intermediate be rate determining, (2) would ion-pair return be a major problem, (3) what σ constants would be appropriate at the variety of ring sites available in **1**-OTs, (4) what ρ value(s) would be calculated from these various substituent effects, and (5) how would this fit in with the idea of LFERs being useful in deciding early vs. late transition state structures in the same reaction type, (6) are secondary α-deuterium isotope effects useful in defining early vs. late transition states in the solvolysis of β-arylethyl arenesulfonates, and (7) would the azulene ring 3 position behave as a benzene meta position? Each of these questions will be dealt with in the discussion section.

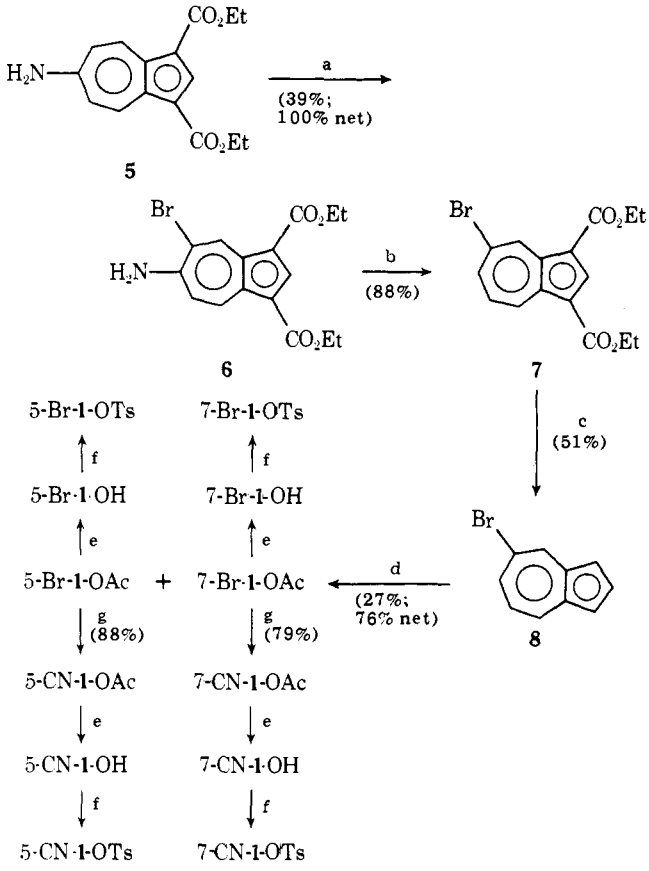
Substrate Synthesis. The syntheses of 2-, 3-, and 6-substituted derivatives of **1**-OH, **1**-OAc, and **1**-OTs, and of 5(7)-CH_3-**1**-OH,[10,11] have been reported. 4-CH_3-**1**-OH was prepared by Anderson's stepwise construction of the β-ethanol side chain (*N,N*-dimethylaminomethylation, quaternerization, $^-$CN displacement, hydrolysis, and diborane reduction).[12] *N,N*-Dimethylaminomethylation of 4-methylazulene gave 1-(*N,N*-dimethylaminomethyl)-4- (**2**, 49%) and -8-methylazulene (**3**, 5%), and 1,3-bis(*N,N*-dimethylaminomethyl)-4-methylazulene (**4**, 2%). Each was readily identified by the chemical shift of the ring CCH_3 group: **2**, τ 7.16; **3**, τ 6.77; **4**, τ 6.79. Direct β-hydroxyethylation[10] of 4-methylazulene gave a larger percentage of C_3 to C_1 substitution than did the above reaction, and we were unable to separate these isomers.

Synthesis of the individual 5- and 7-Br-**1**-OTs, and 5- and 7-CN-**1**-OTs began with diethyl 6-aminoazulene-1,3-dicarboxylate (**5**) available from the liquid ammonia amination of diethyl 6-bromoazulene-1,3-dicarboxylate.[9,14] *N*-Bromosuccinimide (NBS) bromination of **5** in chloroform solution led selectively to the 5-bromo derivative **6**. In dimethylformamide (DMF), reaction of **5** and NBS selectively produced the 2-bromo derivative, diethyl 6-amino-2-bromoazulene-1,3-dicarboxylate.

Initial attempts at protiodeamination of **6** were unsuccessful. To accomplish the **6** → **7** conversion, we developed a method of diazotization in the presence of *p*-hydroquinone to serve as an in situ reducing agent.[15] Using this method an 88% (100% net) yield of **7** was obtained.

With the hurdles of **5** → **6** → **7** in Scheme I overcome, the conversions of **7** → **8** → 5(7)-Br-**1**-OAc proceeded as expected. After chromatographic purification of the 5(7)-Br-**1**-OAc mixture, it was observed that 5-Br-**1**-OAc crystallized from carbon tetrachloride–hexane. Evaporation of the mother liquor (mainly 7-Br-**1**-OAc), base hydrolysis, and chromatography

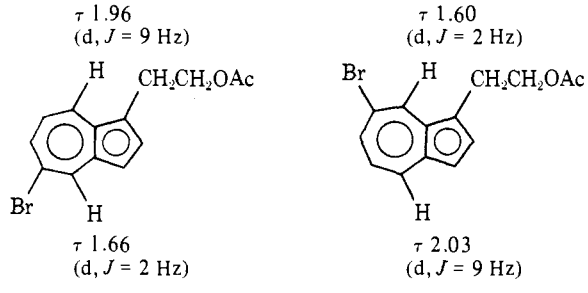
Scheme I



a, NBS, $CHCl_3$; b, *i*-AmONO, H_2SO_4, dioxane, *p*-hydroquinone; c, (1) KOH, EtOH–H_2O, (2) H^+, (3) 270°C (100 mm); d, (1) ethylene oxide, $AlCl_3$, CH_2Cl_2, 0°C(2) Ac_2O, pyridine; e, KOH, CH_3OH; f, TsCl, NaOH, THF, 0°C; g, CuCN, DMF, Δ.

followed by recrystallization of the product gave 7-Br-**1**-OH containing 5–10% of 5-Br-**1**-OH. The 5- and 7-Br-**1**-OAc isomers were separately treated with cuprous cyanide in DMF to give the 5- and 7-CN-**1**-OAc isomers, respectively. Standard procedures were then carried out for hydrolysis of the acetates to the alcohols which were then converted to their respective tosylate esters.

The assignment of structures to these 5- and 7-bromo isomers was based on their NMR spectra in the τ 1.5–2.1 region where the C_4 and C_8 H's absorb. This information is shown below with the chemical shifts measured from a mixture of the two isomers in carbon tetrachloride. Since we expect the bromine substituent effect of C_4 H and C_8 H, and C_8 H and C_4 H of 5-Br-**1**-OAc and 7-Br-**1**-OAc, respectively, to be the same within each pair of protons, the only difference in the two isomers is the peri-deshielding effect of the CH_2CH_2OAc group on the C_8 H.[19] This assignment was verified when we



found about 10% NOE enhancement of C_8 H (J = 9.2 Hz) in the cyano isomer (5-CN-**1**-OAc) derived from 5-Br-**1**-OAc when the β-CH_2 of the side chain was irradiated.

Results and Discussion

Buffered Acetolysis Kinetics. Buffered acetolysis conditions (1.2/1.0 equivalent ratio of KOAc/substrate) were used throughout this investigation since most azulenes are readily protonated by strong acids at their 1 or 3 positions. Partial ring protonation of **1**-OAc was observed in formic acid, with and without added formate buffer. The majority of kinetic runs were followed using the conductivity method previously described[1a,4,5,17] with about 1×10^{-3} M in substrate concentration. The rate constants and activation parameters for these derivatives of **1**-OTs are listed in Table I.

About one-half of the substituted X-**1**-OTs's listed in Table I were acetolyzed as their 1:1 1,3,5-trinitrobenzene (TNB) derivatives. This was done since these tosylate esters were obtained as oils or unstable solids, and formation of their TNB complexes led to crystalline solids with good stability. We felt that such complexes would be fully dissociated in the buffered acetolysis medium and offer no difficulty in the kinetic and preparative acetolysis studies. To check this point, an extra molar equivalent of TNB was added to a kinetic run of **1**-OTs·TNB. The average titrimetric rate constant, k_t, from two runs under these conditions was $(6.14 \pm 0.07) \times 10^{-5}$ s^{-1} at 25 °C, identical with that listed in Table I.

Infinity ($10t_{1/2}$) titers of the tosylate buffered acetolyses in Table I were 92–100% of the theoretical value. Preparative acetolyses for $10t_{1/2}$ followed by workup and chromatography gave 90–100% of the respective X-**1**-OAc. The single deviation from this behavior was observed with 3-SCN-**1**-OTs·TNB. With this tosylate ester the infinity titers were 77–80% of theory. The preparative acetolysis of 3-SCN-**1**-OTs·TNB gave 3-SCN-**1**-OAc in 77% yield along with an unknown yellow, water-soluble material. The yellow material was believed derived from the tosylate since 3-SCN-**1**-OAc was shown to be stable to the acetolysis conditions. Whatever the nature of this side reaction is, it did not influence the kinetics as evidenced by a linear rate plot using the infinity titer in the calculations (infinity points were used throughout this investigation).

Side-Chain Deuterium Scrambling Results. The substituent group effects and LFER correlation (discussed later) of the data in Table I point to the ionization step as being rate limiting. However, Grovenstein and Schmalstieg[18] showed that in the iodination of azulene destruction of the 1-iodoazulenium ion intermediate (k_2) was rate limiting. It was, therefore, considered essential to establish this point by specific side-chain deuterium labeling. These results would also allow us to determine the extent of return from the expected 1-ethyleneazulenium tosylate ion pair (**9**).

1-OTs-α,α-d_2 was prepared by perdeuteriodiborane reduction of 1-azulylacetic acid.[9] Nitration of **1**-OAc-α,α-d_2 gave 3-NO_2-**1**-OAc-α,α-d_2 which was converted to 3-NO_2-**1**-OTs-α,α-d_2. The scrambling results from these two labeled tosylate esters after 1 and 10 acetolysis half-lives are summarized in Table II.

The observations of complete methylene scrambling in **1**-OAc-d_2 while no methylene scrambling was evident in recovered **1**-OTs-α,α-d_2 after 1 acetolysis half-life requires that the ionization step (k_1) to ion pair **9** was rate limiting. (If k_2 were rate limiting some contribution of a k_{-1} step would have been

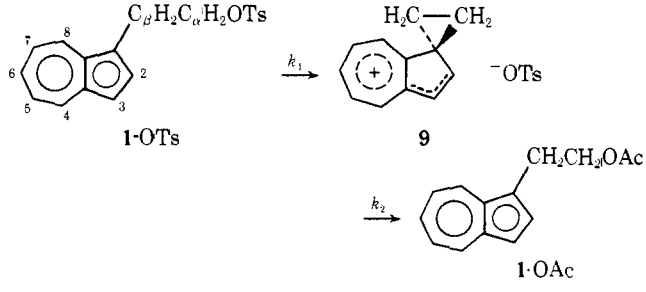


Table I. Buffered Acetolysis Data and Activation Parameters

Compd	Temp, °C	$10^5 k_t$, s^{-1} [a]	k_X/k_H (25 °C)	$\Delta H^{\ddagger}$, kcal/mol	$\Delta S^{\ddagger}$, eu
1-OTs[b,c]	25.0	6.09 ± 0.10	1.0	20.5	−9.2
	35.0	19.3 ± 0.02			
2-OCH_3-**1**-OTs[b]	25.0	27.10 ± 0.05	4.5	20.7	−5.3
	45.0	260 ± 1			
2-CH_3-**1**-OTs[b]	25.0	29.8 ± 0.6	4.9	20.5	−5.8
	45.0	281 ± 1			
2-Cl-**1**-OTs[b]	25.0	(0.407)[e]	0.067		
	50.0	9.02 ± 0.01		23.1	−5.7
	70.0	78.2 ± 0.1			
2-Br-**1**-OTs	25.0	(0.448)[e]	0.074		
	50.0	9.52 ± 0.01		22.8	−6.6
	70.0	80 ± 2			
2-CN-**1**-OTs	25.0	(0.0111)[e]	0.0018		
	90.0	20.92 ± 0.06		24.3	−8.8
	110.0	128.1 ± 0.4			
3-OCH_3-**1**-OTs[b]	25.0	14.3 ± 0.1	2.3	20.0	−9.0
	35.0	43.4 ± 0.1			
	45.0	127.8 ± 0.2			
3-CH_3-**1**-OTs[b]	25.0	11.8 ± 0.2	1.9	20.6	−7.4
	45.0	112 ± 2			
3-SCH_3-**1**-OTs[b,c]	25.0	1.95 ± 0.01	0.32	21.7	−7.4
	35.0	6.61 ± 0.06			
3-Br-**1**-OTs[b,c]	25.0	(0.417)[e]	0.068		
	35.0	1.58 ± 0.01		23.7	−3.6
	50.0	10.0 ± 0.1			
3-$COCH_3$-**1**-OTs[c]	25.0	(0.128)[e]	0.021		
	50.0	3.16 ± 0.07		24.0	−5.2
	70.0	29.5 ± 0.4			
3-CN-**1**-OTs	25.0	(0.0422)[e]	0.0069		
	85.0	30.9 ± 0.1		22.7	−11.6
	105.0	176 ± 5			
3-NO_2-**1**-OTs[c]	25.0	(0.00552)[e]	0.00091		
	70.0	1.36 ± 0.05		24.2	−10.4
	90.0	10.2 ± 0.1			
4-CH_3-**1**-OTs[b]	25.0	11.1 ± 0.1	1.8	20.9	−6.5
	45.0	109 ± 2			
5(7)-CH_3-**1**-OTs[b]	25.0	19.5 ± 0.3	3.2	21.2	−4.3
	45.0	198 ± 2			
5(7)-Br-**1**-OTs	25.0	(0.773)[e]	0.13		
	50.0	13.9 ± 0.1		21.5	−9.8
	70.0	104 ± 2			
5-Br-**1**-OTs	25.0	(0.821)[e]	0.13		
	45.0	8.7 ± 0.1		21.6	−9.2
	65.0	70 ± 1			
5-CN-**1**-OTs	25.0	(0.0288)[e]	0.0047		
	70.4	5.7 ± 0.1		23.1	−11.1
	90.2	38 ± 1			
6-OCH_3-**1**-OTs[b]	25.0	23.5 ± 0.6	3.9	20.0	−8.0
	45.0	210 ± 4			
6-CH_3-**1**-OTs[b]	25.0	12.4 ± 0.2	2.0	22.4	−1.3
	35.0	43.7 ± 0.6			
6-Br-**1**-OTs	25.0	(0.728)[e]	0.12		
	50.0	13.1 ± 0.4		21.5	−9.9
	70.0	98.1 ± 0.1			
6-CN-**1**-OTs	25.0	(0.0689)[e]	0.011		
	70.0	12.3 ± 0.1		22.8	−10.3
	90.0	82 ± 2			
7-Br-**1**-OTs[b]	65.0	50.3 ± 0.3			
7-CN-**1**-OTs	25.0	(0.0210)[e]	0.0034		
	70.3	4.25 ± 0.06		23.2	−11.2
	90.1	28.7 ± 0.3			
$C_6H_5CH_2CH_2OTs$[d] (**11**-OTs)	25.0	(9.0×10^{-5})[e]			
	110.0	0.987 ± 0.001		24.2	−18.8
	130.0	5.02 ± 0.01			
p-$CH_3OC_6H_4CH_2CH_2OTs$[d]	25.0	(5.0×10^{-3})[e]			
(**10**-OTs)	75.0	2.01 ± 0.02		24.1	−11.1
	95.0	14.1 ± 0.05			

[a] The values of k_t listed are averages of at least duplicate runs and the errors given are maximum deviations from this average value. Standard deviations of individual runs were uniformly small. [b] Solvolyzed as the 1,3,5-trinitrobenzene complex. [c] Titrimetric method used (0.010 M ROTs, 0.012 M KOAc). [d] Titrimetric method used (0.005 M ROTs, 0.006 M KOAc). [e] Extrapolated from data at other temperatures.

Table II. Methylene Scrambling in the Buffered Acetolysis of **1**-OTs-α,α-d_2 (35.0 °C) and 3-NO_2-**1**-OTs-α,α-d_2 (90.0 °C)[19]

Compd	Reaction time ($t_{1/2}$)	Deuterium content[a] C_α	Deuterium content[a] C_β	% proton content[a] C_α	% proton content[a] C_β
1-OTs-α,α-d_2	0	1.68	0.10[b]		
1-OTs-α,α-d_2	1	1.72	0.06		
1-$AzCH_2(D_2)CH_2(D_2)OAc$	1			51.1	48.9
1-$AzCH_2(D_2)CH_2(D_2)OAc$	10			51.5	48.5
3-NO_2-**1**-OTs-α,α-d_2	0	1.81	0.00		
3-NO_2-**1**-OTs-α,α-d_2	1	1.70	0.11		
3-NO_2-1-$AzCH_2(D_2)CH_2(D_2)OAc$	1			48.9	51.1
3-NO_2-1-$AzCH_2(D_2)CH_2(D_2)OAc$	10			49.3	50.7

[a] The results are the average of duplicate experiments. The errors are considered to be about ±1%. [b] This degree of scrambling occurred in preparation of the tosylate ester using the ether–KOH method.[21]

expected leading to methylene scrambling in the recovered tosylate ester.) Further these results establish that ion-pair return, $(1 - F)k_\Delta$, was *not* occurring from **9** and only contributes to about 12% of solvolysis processes from 3-NO_2-**9** for the first half-life. Analysis of the product acetates shows no variation in the results from the 1 and 10 half-life experiments.

The F values (fraction of ion pairs going to product) from **1**-OTs and 3-NO_2-**1**-OTs are calculated from the deuterium scrambling data in Table II to be 1.0 and 0.81, respectively, in buffered acetolysis after 1 half-life, assuming no secondary α-deuterium isotope effect in the reaction of 3-NO_2-**9**-d_2 with solvent. The F value for 3-NO_2-**1**-OTs was considered a minimum estimate since the concentration of the salt, KOAc, is constantly being depleted and replaced by the common ion salt, KOTs, as the reaction progresses. KOAc was probably functioning as a *special salt* in these systems.[22,23] Thus, we would expect the F value to decrease as the percent reaction increased under the buffered conditions employed.

$$F = \frac{\%\ \text{reaction}}{\%\ \text{reaction} + 2(\%\ \text{label scramble in recovered ROTs})}$$

This change in direction of the F value is opposite to that observed by Jenny and Winstein[24,25] in the acetolysis of 2-*p*-anisylethyl tosylate (**10**-OTs) in the presence of the nonconsumed special salt, $LiClO_4$. From their data we calculate that F increases (F = 0.26, 0.28, and 0.33) with increasing percent reaction (10, 13.7, and 38%, respectively). In their case, the increasing F value probably reflects the rapidly decreasing ratio $[R^{+-}OTs]/[LiClO_4]$ without substantially increasing the common anion concentration as a function of percent reaction.

Since the reactivities and activation parameters of 3-NO_2-**1**-OTs and 2-*p*-anisylethyl tosylate (**10**-OTs) under buffered acetolysis conditions are nearly the same (Table I), we would expect their F values to also be similar. However, Coke[26] has assigned $F = 0.466 \pm 0.017$ for the acetolysis of **10**-OTs compared to our value of F = 0.81 for buffered acetolysis of 3-NO_2-**1**-OTs. The reason for the apparent inconsistency was revealed by a study of the buffered acetolysis of **10**-α,α-d_2-OTs (0.010 M ROTs, 0.012 M KOAc) at 95.0 °C. The results showed 8 ± 1% label scramble in recovered tosylate and 0 ± 1% of the k_s (solvent displacement) pathway after 50% reaction; $F \sim 0.76$. Unbuffered acetolysis of **10**-α,α-d_2-OTs showed 35 ± 1% label scramble in recovered tosylate after 46% reaction at 75.0 °C ($F \sim 0.40$), and 35 ± 1% label scramble after 50% reaction at 95.0 °C.[25] Thus, the agreement of F values in buffered and unbuffered acetolysis was good with about the same F values for **10**-OTs and 3-NO_2-**1**-OTs under buffered acetolysis conditions. Here, as above, we attribute the differences observed in unbuffered vs. buffered acetolysis to a special salt effect by KOAc.

That this special salt effect explanation is probably an oversimplification in comparing derivatives of **1**-OTs and those of 2-phenylethyl tosylate (**11**-OTs) comes from our observations of the dependency of k_t on the absolute ROTs/KOAc concentration. For **1**-OTs, we find the same k_t in going from 0.010 M ROTs and 0.012 M KOAc (titrimetric) to 0.0010 M ROTs and 0.0012 M KOAc (conductometric).[27] The same change of method and concentrations with 3-NO_2-**1**-OTs leads to a 6–7% reduction in k_t at the lower concentrations used. With **10**-OTs a smaller concentration change (0.005 M ROTs and 0.006 M KOAc titrimetric) produced a larger, 19 ± 4%, reduction in k_t determined in the conductometric method compared to that from the titrimetric method. While the relative ratios of [ROTs]/[KOAc] and [intermediate ion pairs]/[KOAc] are held constant in these experiments (ignoring a small normal salt effect on the latter ratio), the major change is in the *absolute* [KOAc] present during solvolysis. One interpretation of these observations is that while KOAc is useful as a special salt in the acetolysis of **10**-OTs by decreasing the ion-pair return pathway, $(1 - F)k_\Delta$, the solvolysis of **1**-OTs proceeds without the requirement of such a special salt effect. The acetolysis of 3-NO_2-**1**-OTs shows an intermediate need for the special salt effect.[29]

Although the NMR integrated side-chain C_α and C_β proton contents of **1**-OAc-d_2 obtained from the 1 and 10 half-life experiments are probably the same within experimental error (Table II), their reproducibility from a number of runs suggests that these may be the result of a normal secondary α-deuterium isotope effect in the reaction of ion pair **9** to produce acetate product. Along the same lines, the values found for 3-NO_2-**1**-OAc-d_2 derived from 3-NO_2-**1**-OTs-α,α-d_2 suggest about 2 ± 1% of the k_s pathway present in this acetolysis. On the basis of 2% k_s, we calculate $k_s = 2 \times 10^{-6}\ s^{-1}$ (90 °C) under these conditions in good agreement with the value reported by Coke[26] of $k_s = (3.5 \pm 3.1) \times 10^{-6}\ s^{-1}$ for **10**-OTs at 90 °C. Since k_s has been shown to change little ($\rho \sim -1$) as a function of aryl ring substituent,[7,30] we conclude that the derivatives of **1**-OTs listed in Table I undergo buffered acetolysis exclusively by the k_Δ pathway (exceptions are 2% k_s for 3-NO_2-**1**-OTs and possibly ≤1% k_s in cyano derivatives) with little or no ion-pair return involved.

To see the magnitude of the kinetic effect of replacing phenyl by the 1-azulyl group, a simple comparison of their titrimetric rate constants from Table I, k_t (**1**-OTs)/k_t (**11**-OTs) = 23 000 at 90 °C, is of little value since k_t of **11**-OTs is composed of $Fk_\Delta + k_s$. Using Coke's[26] values (F = 0.32, $k_\Delta = 12 \times 10^{-7}\ s^{-1}$ at 90 °C) for **11**-OTs and the extrapolated rate constant for **1**-OTs to 90 °C ($3.6 \times 10^{-2}\ s^{-1}$), we find that k_{Fk_Δ}(**1**-OTs)/k_{Fk_Δ} (**11**-OTs) = 94 000.

Substituent Effects and Linear Free Energy Relationships. In the case of electrophilic attack at the 1 position of azulene, e.g., k_Δ ionization of **1**-OTs → **9**, canonical resonance contributing structures suggest that the ring 2 and 3 positions are related to ortho and meta positions in a related benzenium ion while the seven-ring 4 to 7 positions are long-range paralike positions. However, quantum mechanical modeling of this process using Pople's CNDO/2 method[32] suggested that the azulene 3 position should be more para- than metalike in its substituent effects since its Δq_r was about 50% of the largest Δq_r (5 and 7 positions) while the Δq_r at the meta position of the related phenyl derivatives was only 16% of the para Δq_r. This effect at the azulene 3 position is the result of electron density concentration at this site due to the dipolar character of the azulene ring (μ = 1.0 D)[33] which is more readily lost as cation **9** is generated.

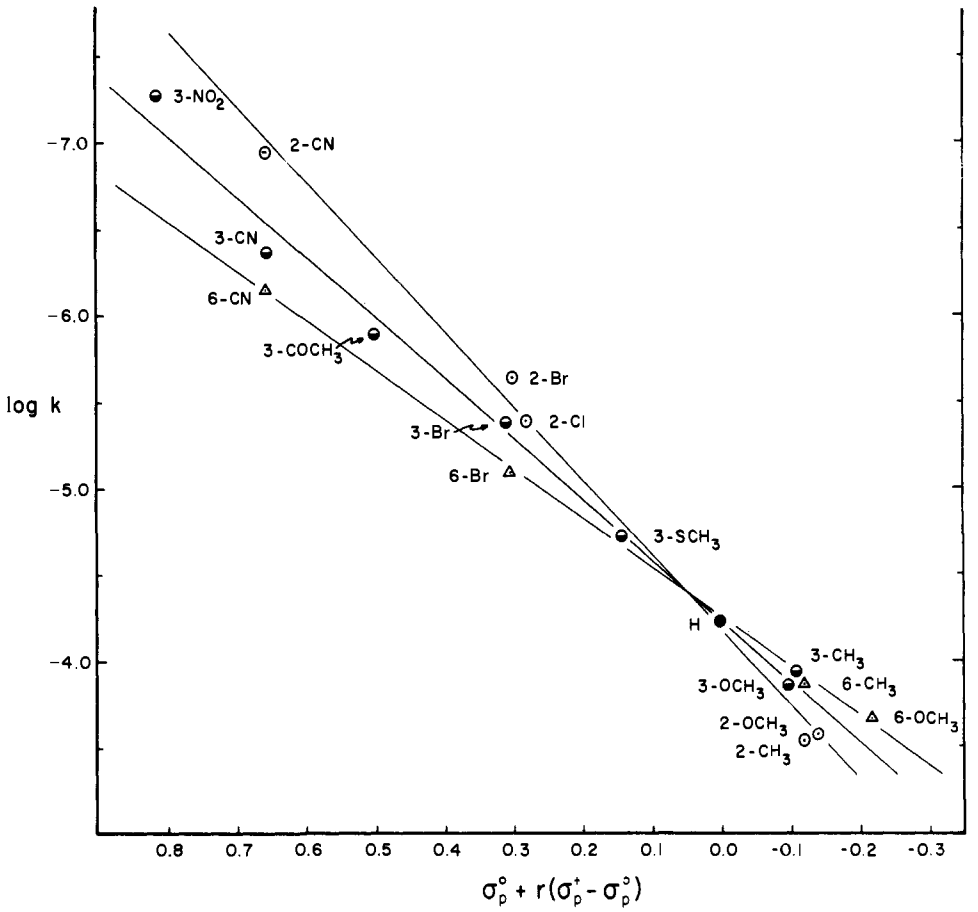


Figure 1. Plots of the 2- (⊙), 3- (◒), and 6-substituent (△) effect data vs. the YTS σ's calculated for these three positions (Table III).

Table III. Regression Analyses of Buffered Acetolysis Data for 2-, 3-, and 6-Substituted X-1-OTs at 25.0 °C[a]

LFER	Calcd parameters		CC[a]	s[b]	F[c]	No. of points[d]
		YTS[35a]				
2-X-1-OTs	$\rho = -4.41$	$r = -0.03$	0.997	0.13	285	6
3-X-1-OTs	$\rho = -3.54$	$r = -0.09$	0.996	0.13	339	8
6-X-1-OTs	$\rho = -2.91$	$r = +0.09$	0.999	0.06	506	5
		Swain-Lupton[36]				
2-X-1-OTs	$f = -2.64, r = -3.30, \%R = 44 \pm 2$		0.998	0.10	444	6
3-X-1-OTs	$f = -2.17, r = -2.46, \%R = 41 \pm 5$		0.994	0.17	193	8
6-X-1-OTs	$f = -1.69, r = -2.57, \%R = 49 \pm 3$		0.997	0.10	197	5
		$\sigma_p^\circ \rho$[35a]				
2-X-1-OTs	$\rho^\circ = -4.35 \pm 0.16$		0.997	0.11	721	6
3-X-1-OTs	$\rho^\circ = -3.39 \pm 0.14$		0.995	0.14	557	8
6-X-1-OTs	$\rho^\circ = -3.03 \pm 0.12$		0.997	0.08	589	5
3- and 6-X-1-OTs	$\rho^\circ = -3.31 \pm 0.14$		0.991	0.17	542	12
2-, 3-, and 6-X-1-OTs	$\rho^\circ = -3.56 \pm 0.17$		0.984	0.22	466	17

[a] Correlation coefficient. [b] Standard error of the estimate. [c] Critical value of the variance ratio test. [d] The data sets include all substituents listed in Table I at these positions plus H in each correlation.

From the k_X/k_H ratios at 25 °C in Table I for the CH_3O- (2, 3, and 6 positions) and CH_3-substituted derivatives (2 to 7 positions), where 4.5 and 4.9, respectively, represent the largest rate enhancements of 1-OTs, data correlations with σ_p^+ constants[34] were not to be expected. Our approach was to use the Yukawa-Tsuno-Sawada (YTS)[35] equation, $\log (k_X/k_H) = \rho[\sigma_p^\circ + r(\sigma_p^+ - \sigma_p^\circ)]$, to better define the larger sets of substituent effect data determined at the 2, 3, and 6 positions of 1-OTs. These results are given in Table III. The small values of r determined individually from these three ring positions showed that σ_p° constants would correlate these data sets (see the last correlation in Table III). Plots of these substituent effects ($\log k_t$'s) vs. the calculated YTS σ constants are shown in Figure 1.

The Swain-Lupton correlation[36] came to the same conclusions as did the YTS except that the field (f) and resonance (r) contributions from these three azulene ring positions are more clearly defined (Table III). These conclusions were also apparent from Taft correlations.[37] The decreasing field (2 > 3 > 6) and resonance (2 > 6 ≥ 3) are as expected from the above discussion of the resonance and quantum mechanical effects.

The divergent ρ's obtained at these three positions and the excellent statistical data suggest that indeed each of these three

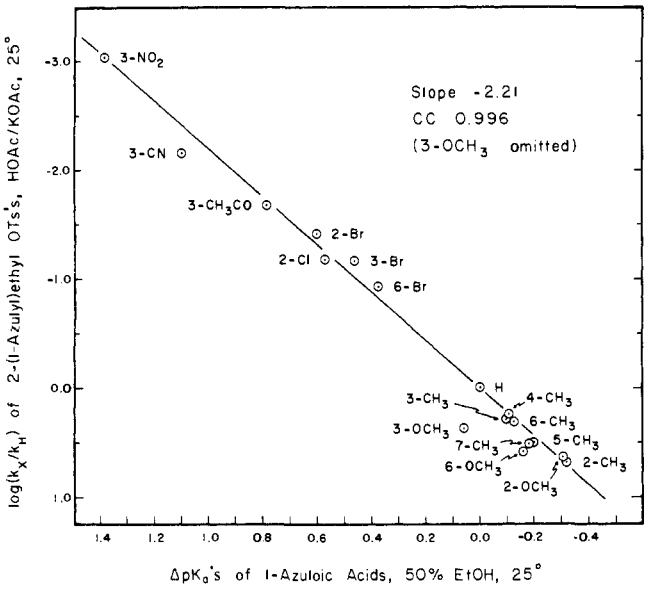


Figure 2. Plot of log (k_X/k_H) of X-**1**-OTs buffered acetolyses (25 °C) vs. ΔpK_as of X-1-azuloic acids in 50% ethanol (25 °C). The 3-OCH_3 data were omitted in the regression analysis.

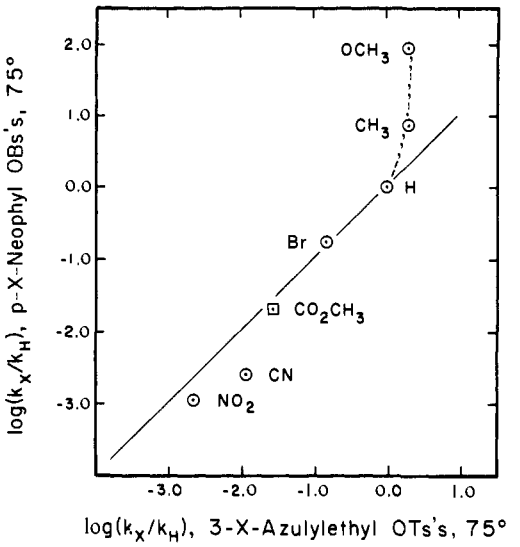


Figure 3. Plot of log (k_X/k_H)'s of *p*-X-neophyl brosylate acetolysis vs. 3-X-**1**-OTs buffered acetolysis. The point for 3-CO_2CH_3-**1**-OTs was estimated from its σ_p° value (0.464)[35a] and $\rho = -3.4$.

positions is more correctly treated as an individual substituent center. This statement appears to be most true when comparing the 2-X-**1**-OTs data set with the other two sets, but is debatable in the combining of the 3-X-**1**-OTs and 6-X-**1**-OTs sets. This division of the total substituent effect into components relative to the aromatic position has been observed in various systems and reaction types. Other examples include the pK_as of 1- and 2-naphthoic acids,[37] hydrolysis rates of methyl 1- and 2-naphthoates,[37] pK_as of 1- and 2-naphthylammonium,[37] pyridinium,[37] quinolinium,[37] and isoquinolinium cations,[37] and the solvolytic behavior of 1-(heteroaryl)-[38] and 1-(benzoheteroaryl)ethyl derivatives[39] bearing substituent groups at various ring positions.

It is of interest to point out that substituent effects on the pK_a of 1-azuloic acid showed very similar variations in ρ's at the 2, 3, and 6 positions[3] to those described above. Those substituent effects were also found to be well correlated with σ_p° [35a] constants. A plot of the substituent effects at these three positions in these two different reactions is shown in Figure 2. The calculated slope of this plot (omitting the 3-OCH_3 data) was −2.21 (CC 0.996) which is the $\rho_{acetolysis}/\rho_{pK_a}$ ratio at each of these three rings sites. On the basis of the data accumulated in these two very different reaction processes, we conclude that substituent effects on reactions occurring at the azulene 1 position will all be reasonably correlated by σ_p° constants. This makes the 1-azulyl group a truly "Hammett type" of aromatic ring system. Since steric inhibition of resonance was not found for the 2 substituents in the 1-azuloic acids pK_as,[3] we can exclude this effect from involvement in the 2-X-**1**-OTs acetolysis also.

A Single ρ Value in β-Arylethyl Derivative Solvolyses? In developing the FM[40] and FMMF[41] by Dewar and modified by Forsyth,[42] it was assumed that for a given reaction type ρ was to be that found in the phenyl series regardless of the aromatic substrate involved. This generalization appeared to conflict with a generally accepted interpretation of ρ that "the magnitude of ρ should therefore be a measure of the magnitude of the developing charge and of the extent to which it is able to interact with the substituents".[43] While the first portion of this quote has been adopted by numerous experimentalists (kinetically early vs. late transition state formation), the second part has even eluded the calculations of the theoretician. Johnson and Schofield[44] recently criticized the point of view that the magnitude of ρ was diagnostic of the extent of charge development in the transition state, i.e., the larger the magnitude of ρ, the later the transition state.[45]

In searching for a β-phenylalkyl arenesulfonate system with which to compare our results of **1**-OTs, we felt that the following criteria had to be met: (1) the leaving group should be attached to a primary carbon, and (2) a range of both electron-donating and -withdrawing substituent group effects must be available on the k_Δ acetolysis process. With these factors in mind, we were immediately led to consider the 2-phenyl-2-methyl-1-propyl (neophyl) system. To reduce the errors in extrapolation of the rate constants in these two systems an intermediate temperature, 75 °C, was chosen for this comparison. These rate constants are listed in Table IV.

The similarities of the electron-withdrawing substituents on the buffered acetolysis of 3-X-**1**-OTs and *p*-X-neophyl brosylate acetolysis are shown in Figure 3 where the log (k_X/k_H) ratios for these two systems are plotted against one another. The divergent behavior of the electron-donating substituent effects of CH_3 and especially OCH_3 are obvious here. This was expected since σ^+ constants are usually used to correlate the X-neophyl brosylate data[46-48] while σ_p° constants correlate the 3-X-**1**-OTs substituent effects.

It has been pointed out previously that σ^+ constants overestimate the rate constant of *p*-methoxyneophyl brosylate[35b,47,48] which was corrected using a YTS correlation with $r \sim 0.6$. Using this approach we have carried out regression analysis on the data in Table IV in the form of log (k_X/k_H) with σ_p° constants for the X-**1**-OTs sets, σ_m° for *m*-methylneophyl brosylate, and $[\sigma_p^\circ + 0.69(\sigma_p^+ - \sigma_p^\circ)]$[35] for the *p*-X-neophyl brosylates. The plot of this analysis is shown in Figure 4. When we consider that these data sets come from separate laboratories, the probable errors in certain of the temperature extrapolations, and the facts that for 3-NO_2-**1**-OTs $F \sim 0.8$ and that *p*-nitroneophyl brosylate acetolyzes with 72 and 25% aryl and methyl group rearrangement, respectively, we believe that this correlation is very good. Using the same YTS "σ" determined from the para-substituted neophyl brosylates and $\rho = -3.2$, good agreement is found between calculated log (k_X/k_H) ratios and those estimated for *p*-Cl, *p*-CH_3, and *p*-OCH_3 derivatives of 2-phenylethyl tosylate (**11**-OTs) Fk_Δ acetolysis from Coke's data at 75 °C.[26] Therefore, *we conclude that a single reaction constant, ρ, applies to aryl participation (Fk_Δ) in the acetolysis of β-arylethyl derivatives where the leaving group is attached to a primary carbon.*

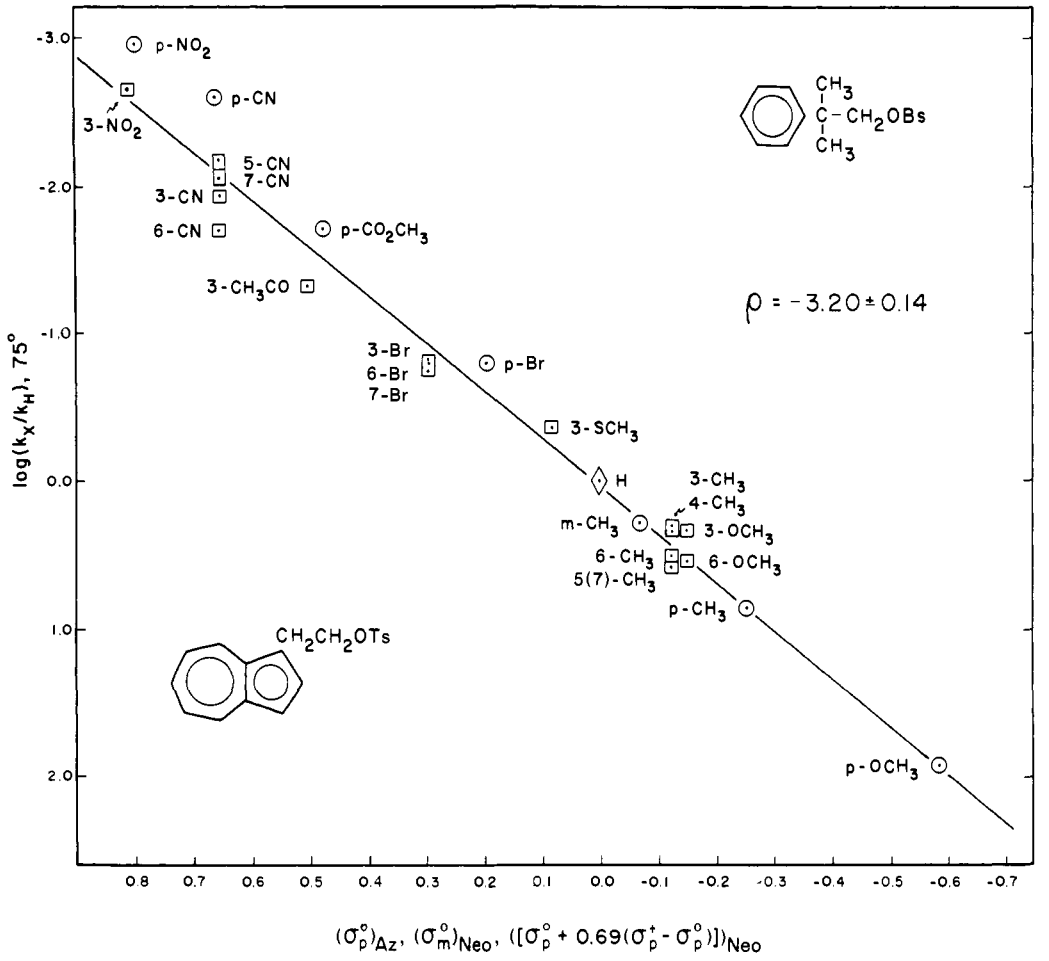


Figure 4. Modified Hammett plot of data from Table IV using σ's as given on the abscissa: ⊡ for X-**1**-OTs and ⊙ for X-neophyl points.

Table IV. Acetolysis and Buffered Acetolysis Rate Constants of Substituted Neophyl Brosylate and **1**-OTs, Respectively, at 75.0 °C

X-Neophyl OBs	k, s^{-1}	3-X-**1**-OTs	k, s^{-1}	Other X-**1**-OTs	k, s^{-1}
H[46]	6.8×10^{-5}	H	1.0×10^{-2}	4-CH_3	2.1×10^{-2}
p-OCH_3[a,46]	5.1×10^{-3}	OCH_3	2.1×10^{-2}	6-OCH_3	3.5×10^{-2}
p-CH_3[47]	5.0×10^{-4}	CH_3	2.0×10^{-2}	6-CH_3	3.3×10^{-2}
m-CH_3[47]	1.3×10^{-4}	SCH_3	4.4×10^{-3}	5(7)-CH_3	3.9×10^{-2}
p-Br[47]	1.1×10^{-5}	Br	1.5×10^{-3}	6-Br	1.6×10^{-3}
p-CO_2CH_3[47]	1.3×10^{-6}	$COCH_3$	5.0×10^{-4}	7-Br	1.8×10^{-3}
p-CN[48]	1.7×10^{-7}	CN	1.2×10^{-4}	5-CN	6.8×10^{-5}
p-NO_2[48]	7.7×10^{-8}	NO_2	2.3×10^{-5}	6-CN	2.0×10^{-4}
				7-CN	9.0×10^{-5}

[a] Value of ROTs multiplied by 3.0 to convert to ROBs.

This conclusion has more general implications when we consider the relative reactivity of **1**-OTs compared to **10**-OTs (150 at 75 °C) and **11**-OTs (94 000 at 90 °C for Fk_Δ). While it is not known if the 2,2-dimethylethylenebenzenium ion is a transition state or an intermediate in acetolysis of **10**-OTs,[7] certainly we would expect the solvolytic transition state to be formed earlier from **1**-OTs compared to that from **11**-OTs based on present theory. If this is true, *we must conclude that ρ obtained from substituent effect data cannot yield any information concerning early vs. late formed transition state structures.* However, if significantly different ρ values are obtained for the "same reaction type" as aryl groups are varied this could mean that σ constants were poorly chosen, the rate-limiting step had changed, and/or a number of different effects were being observed.

Until this point in the discussion we have largely ignored the 2-X-**1**-OTs substituent effect data except to point out the excellent correlation of this data set with σ_p° constants. A similar excellent correlation with σ_p° constants was seen with 2-X-1-azuloic acid pK_as[3] (Figure 2). This suggests that the relative mix of field and resonance effects by the 2 substituents on **1**-OTs buffered acetolysis and 1-azuloic acid ionization is about the same as that of the 3 and 6 substituents in these two reactions of azulene derivatives and that of *p*-phenyl substituents on those reactions used to define the σ_p° constants.[35,37] It is then possible to interrelate the σ° constants at ortho positions to those at the para position of benzene derivatives if we assume that the ρ derived from meta and para substituents is *the reaction constant* for the process. Using $\rho = -3.20$ and 1.45[3] as the reaction constants for 2-arylethyl arenesulfonate acetolysis and arylcarboxylic acid ionization in 50% ethanol, respectively, the ratio of the azulyl 2 substituents YTS ρ values for the corresponding 1-azulene derivative reactions is 4.41/3.20 = 1.38 for acetolysis and 2.15/1.45 = 1.48 for acid ionization.

Table V. Kinetics of Buffered Acetolysis of **1**-OTs-α,α-d_2 and 3-NO_2-**1**-OTs-α,α-d_2

Compd	Deuterium content, C_α	Temp, °C	10^5k, s^{-1} [a]	k_H/k_D [b]
1-$AzCH_2CH_2OTs$·TNB		35.0	19.43 ± 0.07	1.09
1-$AzCH_2CD_2OTs$·TNB	1.68 D	35.0	16.80 ± 0.04	
3-NO_2-1-$AzCH_2CH_2OTs$		90.0	9.53 ± 0.02	1.08
3-NO_2-1-$AzCH_2CD_2OTs$	1.87 D	90.0	8.46 ± 0.03	

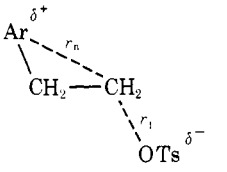
[a] These are averages of duplicate runs. The errors given are the maximum deviations from this average. [b] These k_H/k_D ratios are corrected to 35 °C and are per deuterium using the expression $\Delta(\Delta G^{\ddagger}) = (RT/n) \ln (k_H/k_D)$, when n is the number of deuterium atoms per molecule.

Thus, the ortho- and para-substituent constants appear to be related by the expression $\sigma_o^\circ \simeq 1.4\sigma_p^\circ$. It should be emphasized that the 2-substituent effects on 1-azuloic acid pK_a *do not* appear to show the steric problems as are seen with ortho substituents in o-$XC_6H_4CO_2H$ pK_as,[3] which negates the use of this expression in many reactions of ortho-substituted benzene derivatives.

Secondary α-Deuterium Isotope Effects on β-Arylethyl Arenesulfonate Solvolyses. With **1**-OTs-α,α-d_2 and 3-NO_2-**1**-OTs-α,α-d_2 available, their secondary α-deuterium isotope effects were determined conductometrically and are listed in Table V. Since it had been shown that there was no (or a minor) secondary β-deuterium isotope effect for solvolysis of several 2-arylethyl derivatives,[49] the smaller k_H/k_D for 3-NO_2-**1**-OTs-α,α-d_2 was expected as the result of partial methylene scrambling during ion-pair return (F = 0.81 for 3-NO_2-**1**-OTs) from 3-NO_2-**9**.

From a study of α-deuterium effects on several β-arylethyl arenesulfonates, Lee[50] concluded that k_H/k_D increased with increasing aryl participation, i.e., formation of the bridged transition state would be less developed with those substrates forming the more stable ethylenebenzenium ions producing less hindrance by the approaching aryl group on the out-of-plane CH and CD bending vibrations.[51] However, when the data are corrected for deuterium content and extrapolated to the same temperature (Table VI), the differences do not appear to be significant.[52] This suggestion appeared to be supported by the solvolysis of 2-ferrocenylethyl tosylate (**12**-OTs) with k_H/k_D = 1.13 per deuterium[53] at 35 °C since that gave a large rate ratio (3120) relative to **11**-OTs. However, with **1**-OTs in 2-arylethyl derivative solvolyses, we find k_H/k_D = 1.09 per deuterium at 35 °C. These and other α-deuterium effects are listed in Table VI.

Thus, it appears that *the kinetic secondary α-deuterium isotope effect for aryl participation in 2-arylethyl arenesulfonate solvolyses is k_H/k_D = 1.10 ± 0.01 per deuterium at 35 °C and is independent of the nature of the aryl group.* Since this covers a relative reactivity of 10^5, a comment on the lack of early vs. late transition states manifesting themselves in the α-deuterium effect is in order. The k_Δ solvolysis of β-arylethyl arenesulfonates is categorized as an intramolecular S_N2 process where the transition state structure can have varying r_n and r_l dimensions depending on the nature of the aryl group (**13**). Close proximity of either the entering aryl group or the



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leaving group to the α-methylene stiffens the C_α–H and C_α–D bonds and lowers the observed α-deuterium effect.[50-54] The constant α-deuterium effect as seen in Table VI means that as r_n increases r_l decreases in an early (vs. late) solvolytic transition state structure. These changes need not be exactly proportional since this will be accompanied by a smaller hydridization change at C_α thus influencing the resulting out-of-plane C_α–H and C_α–D bending force constants. Therefore, kinetic secondary α-deuterium isotope effects are not useful in probing the structures of these related solvolytic transition states. The single entry in Table VI which may be unique is that of 2-ferrocenylethyl tosylate (**12**-OTs) where Fe (not C) participation may be involved during ionization.

Conclusions Given by This Research. Returning to the original seven questions asked in the introductory section of this paper, the following answers are given. (1) Ionization of **1**-OTs to ion pair **9** was rate limiting under buffered acetolysis conditions. (2) Ion-pair return from **9** to **1**-OTs was of no importance except in the case with strongly electron-withdrawing substituents, e.g., 3-NO_2-**1**-OTs, where it was at a maximum of 12% after 1 solvolytic half-life. (3) σ_p° constants[35a] sufficed to effect LFER of substituent effects at the ring 2, 3, 5, 6, and 7 positions of **1**-OTs buffered acetolysis. (4) Substituent effects at the meta and para positions of neophyl brosylate acetolysis and the 3 and 6 positions of **1**-OTs buffered acetolysis were found to give the same correlation ($\rho = -3.2$) albeit with different substituent constants. (5) From the answer to question 4 and the fact that the known data on substituent effects on

Table VI. Kinetic Secondary α-Deuterium Isotope Effects in 2-Arylethyl Arenesulfonate Solvolyses

Compd	Solvolysis conditions	Atoms of D	k_H/k_D (obsd)	k_H/k_D per D at 35 °C [a,b]	Ref
$C_6H_5CH_2CH_2(D_2)OTs$ (**11**-OTs)	HOAc, 93.9 °C	1.83	1.03 [c]		49a
	HCO_2H, 75.3 °C	1.83	1.17	1.10	49a
p-$CH_3OC_6H_4CH_2CH_2(D_2)OTs$ (**10**-OTs)	HOAc–$LiClO_4$, 75 °C	2.00	1.18	1.10	49b
	HCO_2H, 50 °C	2.00	1.20	1.10	49b
$(C_6H_5)_2CHCH_2(D_2)OTs$	HOAc, 75 °C	2.00	1.21	1.11	49b
	HCO_2H, 75 °C	2.00	1.21	1.11	49b
2,4-$(CH_3O)_2C_6H_3CH_2CH_2(D_2)OBs$	HOAc, 50 °C	1.92	1.15 [c]	1.07 [c]	50
	HCO_2H, 25 °C	1.92	1.23	1.11	50
$FerCH_2CH_2(D_2)OTs$ (**12**-OTs)	Aq acetone, 30 °C	2.00	1.28	1.13	53
$AzCH_2CH_2(D_2)OTs$ (**1**-OTs)	HOAc–KOAc, 35 °C	1.68	1.16	1.09	This work

[a] Corrected using the equation $\Delta(\Delta G^{\ddagger}) = (RT/n) \ln (k_H/k_D)$ where n is the number of deuterium atoms per molecule. [b] Probable errors are about ±0.01. [c] These low k_H/k_D ratios are due to solvent displacement (k_s) and methylene scrambling from ion-pair return [$(1 - F)k_\Delta$] processes with the substrate under these conditions.

2-phenylethyl tosylate acetolysis were also correlated, we conclude that different ρ values *cannot* be interpreted as meaning early vs. late transition state structures for a given reaction type. (6) It was further concluded that kinetic secondary α-deuterium isotope effects were of *no* value in defining early vs. late transition state structures in 2-arylethyl arenesulfonate solvolyses. (7) Our answer to this final question of whether or not the azulene 3 position behaved as a benzene meta position in reactions at the 1 position was that it was variable and depends on the reaction type.

Experimental Section[55]

1-(*N,N*-Dimethylaminomethyl)-4-methylazulene (2). A mixture of 233 mg (2.28 mmol) of *N,N,N',N'*-tetramethyldiaminomethane, 60 mg (2.0 mmol) of paraformaldehyde, and 4 mL of acetic acid was heated until a clear solution was obtained. Then 2.7 mL of this solution was added to 200 mg (1.4 mmol) of 4-methylazulene in 20 mL of CH_2Cl_2 cooled to 0 °C. The mixture was swirled for 5 min and diluted with 20 mL of H_2O. The solution was washed with 5-mL portions of 10% hydrochloric acid until they were colorless. The CH_2Cl_2 layer was dried ($MgSO_4$) and chromatography over activity 2–3 alumina gave (elution with CCl_4) 57 mg (29%) of 4-methylazulene.

The acidic, aqueous layer was made basic with 10% aqueous NaOH (color changed from light blue to dark blue). The basic, aqueous solution was extracted with two 50-mL portions of ether which when dried (Na_2SO_4) and concentrated gave a blue oil. Chromatography over activity 2–3 alumina gave [elution with CH_2Cl_2–CCl_4 (1:3)] 14 mg (5%) of 1-(*N,N*-dimethylaminomethyl)-8-methylazulene as a blue oil: IR (neat film) 2920, 2790, 1550, 1255, and 1035 cm^{-1}; NMR (CCl_4, internal Me_4Si) τ 1.6–3.3 (m, Az H's, 6), 6.19 (s, CH_2, 2), 6.77 (s, CH_3, 3), and 7.80 (s, CH_3's, 6); vis-UV (cyclohexane) 691 nm (OD 0.243), 627 (0.644), 603 (0.683), 577 (0.760), 368 (0.058), 343 (0.104), 334 (0.068), 228 (0.967), 282 (0.956), and 243 (0.482).

Elution with CH_2Cl_2 gave 135 mg (50%) of 1-(*N,N*-dimethylaminomethyl)-4-methylazulene as a blue oil: IR (neat film) 2980, 2800, 1565, 1460, 1260, and 1035 cm^{-1}; NMR (CCl_4, internal Me_4Si) τ 1.4–3.2 (m, Az H's, 6), 6.18 (s, CH_2, 2), 7.16 (s, CH_3, 3), and 7.82 (s, CH_3's, 6); vis-UV (cyclohexane) 694 nm (log ϵ 2.23), 628 (2.56), 604 (2.58), 579 (2.63), 361 (3.59), 345 (3.78), 337 (3.69), 288 (4.70), 283 (4.71), and 342 (4.43). For elemental analysis, this compound was converted to the TNB complex. Recrystallization from EtOAc–petroleum ether gave brown needles, mp 122–128 °C dec.

Anal. Calcd for $C_{20}H_{20}N_4O_6$: C, 58.25; H, 4.89. Found: C, 58.30; H, 5.07.

Further elution with ether gave 5 mg (2%) of 1,3-bis(dimethylaminomethyl)-4-methylazulene as a blue oil: IR (neat film) 2980, 2780, 1560, 1260, and 1005 cm^{-1}; NMR (CCl_4, internal Me_4Si) τ 1.4–3.3 (m, Az H's, 5), 6.21 (s, CH_2, 4), 6.79 (s, CH_3, 3), and 7.80 (s, CH_3's, 12); vis-UV (cyclohexane) 702 nm (OD 0.219), 635 (0.610), 587 (0.744), 364 (0.039), 348 (0.046), 289 (0.316), 285 (0.313), and 243 (0.177).

4-Methyl-1-azulylacetonitrile. To a solution of 135 mg (0.68 mmol) of **2** in 5 mL of absolute EtOH was added 1 mL of CH_3I. Evaporation of the solvent gave 231 mg (100%) of the quaternary salt. The product crystallized from 95% ethanol as purple needles: mp >200 °C; IR (KBr) 2980, 1545, 1395, and 869 cm^{-1}; vis-UV (95% ethanol) 584 nm (sh), 544 (log ϵ 2.73), 353 (3.53), 338 (3.73), 286 (4.64), and 282 (4.64).

A solution of 348 mg (1.02 mmol) of the above salt and 199 mg (3.06 mmol) of KCN in 25 mL of absolute EtOH was heated under reflux for 40 min. The color changed from violet to blue. Ether (100 mL) was added and the solution was washed with two 100-mL portions of water and dried ($MgSO_4$). Chromatography over activity 2–3 alumina gave (elution with CCl_4–CH_2Cl_2, 4:1) 161 mg (87%) of the desired nitrile as a blue oil: IR (neat film) 2950 (C–H), 2260 (C≡N), and 1575 cm^{-1}; NMR (CCl_4, internal Me_4Si) τ 1.8–3.3 (m, Az H's, 6), 6.10 (s, CH_2, 2), and 7.22 (s, CH_3, 3).

The nitrile was converted to its TNB complex, and recrystallization from ethyl acetate–petroleum ether gave brown needles: mp 116–117 °C; vis-UV (CH_2Cl_2) 672 nm (sh), 605 (sh), 568 (log ϵ 2.67), 351 (3.46), 342 (3.70), 287 (4.68), and 282 (4.69).

Anal. Calcd for $C_{19}H_{14}N_4O_6$: C, 57.88; H, 3.58. Found: C, 57.66; H, 3.90.

4-Methyl-1-azulylacetic Acid. KOH (16 mL, 0.6 M) in 50% aqueous EtOH was heated under reflux with a nitrogen atmosphere for 3 h. To this solution was added 172 mg (0.95 mmol) of 4-methyl-1-azulylacetonitrile in 4 mL of THF. The solution was heated under reflux under a nitrogen atmosphere for 18 h. After cooling, 150 mL of water and 150 mL of ether were added. The basic layer was acidified with 10% HCl and extracted with three 100-mL portions of ether. The combined ether layers were dried ($MgSO_4$) and concentration of solvent gave 158 mg (83%) of blue solid which was recrystallized from CCl_4–petroleum ether to give blue needles of the acid: mp 107–109 °C; IR (KBr) 2900 (OH, broad) and 1700 cm^{-1} (C=O); NMR ($CDCl_3$, internal Me_4Si) τ −0.27 (s, CO_2H, 1), 1.5–3.2 (m, Az H's, 6), 5.89 (s, CH_2, 2), and 7.12 (s, CH_3, 3); vis-UV (CH_2Cl_2) 623 nm (sh), 547 (log ϵ 2.64), 358 (3.50), 340 (3.74), 288 (4.66), and 282 (4.66).

Anal. Calcd for $C_{13}H_{12}O_2$: C, 77.98; H, 6.04. Found: C, 78.04; H, 6.10.

The original ether layer was washed with three 100-mL portions of water and dried (Na_2SO_4). Chromatography over activity 2–3 alumina gave (elution with CH_2Cl_2) 10 mg of a dark blue oil assigned the structure of 4-methyl-1-azulylmethyl ethyl ether: IR (neat film) 2850 (C–H) and 1080 cm^{-1} (C–O); NMR (CCl_4, internal Me_4Si) τ 1.43–3.3 (m, Az H's, 6), 5.08 (s, CH_2, 2), 6.77 [q (J = 7 Hz), CH_2, 2], 7.11 (s, CH_3, 3), and 8.78 [t ill-defined due to impurity (J = 7 Hz), CH_3, 3].

Further elution with $CHCl_3$ gave a light blue oil assigned the structure of 4-methyl-1-azulylacetamide: IR (neat film) 3400 (N–H), 3300 (N–H), and 1670 cm^{-1} (C=O); NMR ($CDCl_3$, internal Me_4Si) τ 1.43–3.1 (m, Az H's, 6), 4.2 (broad singlet, NH_2, 2), 5.93 (s, CH_2, 2), and 7.08 (s, CH_3, 3).

2-(4-Methyl-1-azulyl)ethanol (4-CH_3-1-OH). Sodium borohydride (228 mg, 6.0 mmol) and 155 mg (0.78 mmol) of 4-methyl-1-azulylacetic acid were added under anhydrous conditions to 25 mL of dry THF. The mixture was stirred for 10 min and then cooled to 0 °C. To this solution was added dropwise 3 mL of BF_3·Et_2O in 20 mL of dry THF over a period of 10 min and the reaction mixture stirred at 0 °C for 15 min. After this time, 10 mL of 10% HCl and 100 mL of water were added and the mixture was then extracted with two 150-mL portions of ether. The combined ether extracts were washed with water, 5% $NaHCO_3$, and again with water, and dried (Na_2SO_4). Concentration gave a blue oil which was chromatographed over activity 2–3 alumina which gave (elution with CH_2Cl_2) 85 mg (59%) of 4-CH_3-**1**-OH as an oil: IR (neat film) 3300 (OH) and 1040 cm^{-1} (C–O); NMR (CCl_4, internal Me_4Si) τ 1.63–3.3 (m, Az H's, 6), 6.26 [t (J = 7 Hz), α-CH_2, 2], 6.85 [t (J = 7 Hz), β-CH_2, 2], 7.24 (s, CH_3, 3), and 7.48 (s, OH, 1).

A 1,3,5-trinitrobenzene complex was made and recrystallization from ethyl acetate–petroleum ether gave brown needles: mp 128–129 °C; vis-UV (CH_2Cl_2) 623 nm (sh), 582 (log ϵ 2.62), 361 (3.52), 346 (3.72), 289 (4.68), and 383 (4.69).

Anal. Calcd for $C_{19}H_{17}N_3O_7$: C, 57.14; H, 4.29. Found: C, 57.24; H, 4.40.

2-(4-Methylazulyl)ethyl Acetate (4-CH_3-1-OAc). To 10 mL of pyridine cooled to 0 °C was added 50 mg (0.27 mmol) of 4-CH_3-**1**-OH and 1 mL of Ac_2O. The solution was stirred at 0 °C for 2 h. CH_2Cl_2 (50 mL) was added and the organic layer was washed with 10% HCl and water and dried ($MgSO_4$). Concentration and chromatography on basic activity 3–4 alumina yielded (elution with CH_2Cl_2) 59 mg (95%) of a blue oil. The compound was converted to a TNB complex and crystallization from EtOAc–petroleum ether gave brown needles: mp 79–80 °C; IR (KBr) 1740 (C=O) and 1240 cm^{-1} (C–O); NMR ($CDCl_3$, internal Me_4Si) τ 0.71 (s, TNB H's, 3), 1.63–3.3 (m, Az H's, 6), 5.65 [t (J = 7 Hz), CH_2, 2], 6.62 [t (J = 7 Hz), CH_2, 2], 7.14 (s, CH_3, 3), and 7.97 (s, CH_3, 3); vis-UV (CH_2Cl_2) 620 nm (sh), 680 (log ϵ 2.50), 360 (3.22), 345 (3.56), 289 (4.55), and 283 (4.56).

Anal. Calcd for $C_{21}H_{19}N_3O_8$: C, 57.13; H, 4.35. Found: C, 57.41; H, 4.47.

2-(4-Methyl-1-azulyl)ethyl Tosylate (4-CH_3-1-OTs). To a solution of 80 mg (0.43 mmol) of 4-CH_3-**1**-OH dissolved in 5 mL of dry ether and cooled to 0 °C was added 82 mg (0.43 mmol) of sublimed tosyl chloride followed by 72 mg (1.29 mmol) of powdered KOH. The mixture was stirred at 0 °C for 12 h. To this mixture 100 mL of ether was added. The ether layer was washed with three 100-mL portions of water and dried (Na_2SO_4). Concentration gave a blue oil which was chromatographed on activity 2–3 alumina, where CH_2Cl_2 eluted the tosylate as an oil. The oil was heated in a sublimation apparatus (25 °C, 0.1 mm) to remove the excess tosyl chloride and gave 85 mg (56%) of tosylate. The tosylate was converted to the TNB complex

and recrystallization from ethyl acetate–petroleum ether gave brown needles: mp 96.0–96.8 °C; IR (KBr) 1545 ($C-NO_{2asym}$), 1340, and 1165 cm^{-1} ($S-O_{sym}$); NMR ($CDCl_3$, internal Me_4Si) τ 0.80 (s, TNB H's, 3), 1.6–3.3 (m, Az H's, 6), 5.60 [t (J = 7 Hz), α-CH_2, 2], 6.59 [t (J = 7 Hz), β-CH_2, 2], 7.14 (s, CH_3, 3), and 7.59 (s, CH_3, 3); vis-UV (CH_2Cl_2) 620 nm (sh), 578 (log ϵ 2.63), 359 (3.49), 345 (3.75), 288 (4.67), and 283 (4.69).

Anal. Calcd for $C_{26}H_{23}N_3O_9S$: C, 56.40; H, 4.19. Found: C, 56.53; H, 4.01.

Bromination of Diethyl 6-Aminoazulene-1,3-dicarboxylate (5). Method A. To 50 mg (0.174 mmol) of **5** in 10 mL of dry (distilled from BaO) DMF was added dropwise 31 mg of crude, commerical *N*-bromosuccinimide (NBS) in 10 mL of dry DMF. This mixture was stirred at room temperature for 2 h, diluted with 200 mL of water, and extracted with five 50-mL portions of ether. The combined ethereal extracts were washed with three 100-mL portions of 5% HCl and with two 100-mL portions of water. The extracts were dried (Na_2SO_4), the solvent volume reduced, and the residue chromatographed on alumina. $CHCl_3$ eluted a yellow band and EtOH eluted a narrow, gold-yellow band. The yellow band afforded ca. 20 mg (30%) of a compound identified on the basis of the NMR spectrum as diethyl 2-bromo-6-aminoazulene-1,3-dicarboxylate: NMR (Me_2SO-d_6, internal Me_4Si) τ 1.20 [d (J = 12 Hz), $C_{4,8}$ ring H's, 2], 1.73 (broad s, NH_2, 2), 3.03 [d (J = 12 Hz), $C_{5,7}$ ring H's, 2], 5.68 [q (J = 7 Hz), $CO_2CH_2CH_3$, 4], and 8.47 [t (J = 7 Hz), $CO_2CH_2CH_3$, 6].

Method B. To 115 mg (0.400 mmol) of **5** in 10 mL of dry (distilled from BaO) DMF was added dropwise 35 mg of crude, commercial NBS in 15 mL of dry DMF. This mixture was allowed to stir at room temperature for 2 h as the color changed to a dark yellow-brown. The mixture was diluted with 100 mL of water and extracted with three 50-mL portions of ether. The combined ethereal extracts were washed with four 100-mL portions of water and dried ($MgSO_4$), the solvent volume was reduced, and the residue was chromatographed on deactivated (6% water) alumina. A diffuse, yellow band was eluted with 1:1 C_6H_6–CH_2Cl_2 and CH_2Cl_2 eluted an orange-yellow band that afforded 127 mg (71%) of diethyl 2,5-dibromo-6-aminoazulene-1,3-dicarboxylate. Crystallization from CH_2Cl_2 yielded big, yellow plates: mp 191–193 °C; IR (KBr) 2.95 (s, N–H), 3.05 (s, N–H), 3.14 (s, N–H), 6.00 (s, C=O), and 9.50 μ (s, C–O); NMR (Me_2SO-d_6, internal Me_4Si) τ 0.42 (s, C_4 ring H, 1), 1.57 [d ($J_{7,8}$ = 12 Hz), C_8 ring H, 1], 1.67 (broad s, NH_2, 2), 2.78 [d ($J_{7,8}$ = 12 Hz), C_7 ring H, 1], 5.65 [q (J = 7 Hz), $CO_2CH_2CH_3$, 4], and 8.62 [t (J = 7 Hz), $CO_2CH_2CH_3$, 6]; λ_{max} (95% ethanol) 286 nm (log ϵ 4.21), 339 (4.84), 372 (4.19), 392 (4.09), and 430 (3.84) (sh).

Anal. Calcd for $C_{16}H_{15}O_4Br_2N$: C, 43.17; H, 3.40; N, 3.15. Found: C, 43.35; H, 3.60; N, 3.40.

Method C. To 165 mg (0.574 mmol) of **5** in 30 mL of $CHCl_3$ under a dry, oxygen-free nitrogen atmosphere was added 246 mg (ca. 1.38 mmol) of crude, commercial NBS. The color changed immediately from yellow to red. The mixture was stirred at room temperature for 5 h, the solvent volume reduced, and the residue chromatographed on basic alumina. CH_2Cl_2 eluted several narrow, diffuse, yellow bands and 1:1 ether–CH_2Cl_2 eluted a broad, yellow band. Ethanol eluted an orange band. The broad, yellow band afforded 110 mg (37%) of diethyl 2,5,7-tribromo-6-aminoazulene-1,3-dicarboxylate that crystallized from CH_2Cl_2 to yield red prisms: mp 196.5–197.0 °C; IR (KBr) 5.95 (s, C=O) and 9.69 μ (s, C–O); NMR ($CDCl_3$, internal Me_4Si) τ 0.18 (s, $C_{4,8}$ ring H's, 2), 3.50 (broad s, NH_2, 2), 5.57 [q (J = 7 Hz), $CO_2CH_2CH_3$, 4], and 8.53 [t (J = 7 Hz), $CO_2CH_2CH_3$, 6]; λ_{max} (95% ethanol) 286 nm (log ϵ 4.18), 343 (4.90), and 383 (4.23).

Anal. Calcd for $C_{16}H_{14}O_4Br_3N$: C, 36.67; H, 2.69; N, 2.67. Found: C, 36.37; H, 2.71; N, 2.38.

Method D. To 100 mg (0.35 mmol) of **5** in 30 mL of $CHCl_3$ under a continuous, oxygen-free, nitrogen sweep was added dropwise under stirring 125 mg (0.70 mmol) of recrystallized NBS in 10 mL of $CHCl_3$ over a 5–10-min period. After 15 min the color had changed from yellow to red, and after 5 additional min the color had changed to orange. Thirty minutes after the start of the initial mixing the color had returned to red. The mixture was then immediately diluted with 100 mL of ice-cold water, extracted with two 100-mL portions of CH_2Cl_2, and dried (Na_2SO_4), the solvent volume was reduced, and the residue was chromatographed on alumina. CH_2Cl_2 eluted a narrow, diffuse red band, 1:1 CH_2Cl_2–ether eluted a yellow band (band 1), and $CHCl_3$ eluted a second yellow band (band 2). Each yellow band was a mixture of two compounds, as determined by NMR. The red band was not examined owing to the small amount of material.

Band 1 was rechromatographed on alumina with CH_2Cl_2. A yellow band (band 1A) was followed closely by a second yellow band (band 1B). Band 1A afforded 25 mg (14%) of diethyl 2,5,7-tribromo-6-aminoazulene-1,3-dicarboxylate, identical with that identified from method C. Band 1B afforded 25 mg (16%) of diethyl 5,7-dibromo-6-aminoazulene-1,3-dicarboxylate. Crystallization from $CHCl_3$ yielded rhombic, orange crystals: mp 221–224 °C; IR (KBr) 5.92 (s, C=O) and 9.56 μ (s, C–O); NMR ($CDCl_3$, internal Me_4Si) τ −0.08 (s, $C_{4,8}$ ring H's, 2) 1.60 (s, C_2 ring H, 1), 3.42 (broad s, NH_2, 2), 5.62 [q (J = 7 Hz), $CO_2CH_2CH_3$, 4], and 8.52 [t (J = 7 Hz), $CO_2CH_2CH_3$, 6]; λ_{max} (95% ethanol) 276 nm (log ϵ 4.23) (sh), 287 (4.34), 307 (4.24), 346 (4.84), 369 (4.22) (sh), 380 (4.14) (sh), 395 (3.82], and 448 (3.31).

Band 2 was rechromatographed on deactivated (4.5% water) alumina with CH_2Cl_2. A yellow band (band 2A) was followed closely by a second yellow band (band 2B). Band 2B afforded 80 mg (51%) of diethyl 2,5-dibromo-6-aminoazulene-1,3-dicarboxylate, identical with that identified from method B. Band 2A yielded 30 mg (23%) of diethyl 5-bromo-6-aminoazulene-1,3-dicarboxylate (**6**). Crystallization from ethanol yielded yellow plates: mp 201–203 °C; IR (KBr) 2.96 (m, N–H), 3.08 (m, N–H), 3.18 (m, N–H), 6.02 (s, C=O), and 9.55 μ (s, C–O); NMR ($CDCl_3$, internal Me_4Si) τ −0.07 (s, C_4 ring H, 1), 0.67 [d ($J_{7,8}$ = 12 Hz), C_8 ring H, 1], 1.63 (s, C_2 ring H, 1), 2.95 [d ($J_{7,8}$ = 12 Hz), C_7 ring H, 1], 4.17 (broad s, NH_2, 2), 5.62 [q (J = 7 Hz), $CO_2CH_2CH_3$, 4], and 8.58 [(J = 7 Hz), $CO_2CH_2CH_3$, 6]; λ_{max} (95% ethanol) 274 nm (log ϵ 4.23) (sh), 286 (4.31), 340 (4.79), 374 (4.23), and 430 nm (3.69) (sh).

Method E. To 200 mg (0.70 mmol) of **5** in 60 mL of $CHCl_3$ under a continuous, dry, oxygen-free, nitrogen sweep was added dropwise 62 mg (0.35 mmol) of recrystallized NBS in 20 mL of $CHCl_3$ over a 60-min period. This mixture was stirred for an additional 20 min, diluted with 100 mL of water, and extracted with two 150-mL portions of chloroform. The combined, orange extracts were dried (Na_2SO_4), the solvent volume was reduced, and the residue was chromatographed on deactivated (3% water) alumina. CH_2Cl_2 eluted two yellow bands. The second yellow band yielded 120 mg of unreacted diethyl 6-aminoazulene-1,3-dicarboxylate, and the first yellow band afforded 100 mg (39%, 100% net) of diethyl 5-bromo-6-aminoazulene-1,3-dicarboxylate (**6**) identical with that obtained from method D.

Diethyl 5-Bromoazulene-1,3-dicarboxylate (7). To 404 mg (1.10 mmol) of **6** in 100 mL of dioxane were added 4 drops (ca. 130 mg) of concentrated H_2SO_4 and 120 mg (1.09 mmol) of H_2Q. In two addition funnels were placed separately 1.570 g (14.2 mmol) of H_2Q in 40 mL of dry dioxane and 1.69 g (14.4 mmol) of isoamyl nitrite in 40 mL of dry dioxane. The reaction was carried out and worked up as described above. Hexane was used to extract the product. It was dried (Na_2SO_4), the solvent volume reduced, and the residue chromatographed on alumina with CH_2Cl_2. A single, lavender band eluted that afforded 341 mg (88%) of the title compound. Crystallization from ether yielded violet, granular crystals: mp 115.0–115.5 °C (lit.[56] mp 125 °C); IR (KBr) 5.90 (s, C=O), 8.25 (s), and 9.55 μ (s, C–O); NMR ($CDCl_3$, internal Me_4Si) τ −0.05 [d ($J_{4,6}$ = 2 Hz), C_4 ring H, 1], 0.35 [d ($J_{7,8}$ = 10 Hz), C_8 ring H, 1], 1.20 (s, C_2 ring H, 1), 1.78 [broad d of d ($J_{6,7}$ = 10, $J_{4,6}$ = 2 Hz), C_6 ring H, 1], 2.58 [d of d ($J_{7,8}$ = 10, $J_{6,7}$ = 10 Hz), C_7 ring H, 1], 5.60 [q (J = 7 Hz). $CO_2CH_2CH_3$, 4], and 8.53 [t (J = 7 Hz), $CO_2CH_2CH_3$, 6]; λ_{max} (cyclohexane) 256 nm (log ϵ 4.42), 267 (4.46), 294 (4.57), 301 (4.62), 306 (4.69), 368 (4.07), 380 (4.10), 534 (2.69), 574 (2.64), and 629 (2.22).

Anal. Calcd for $C_{16}H_{15}O_4Br$: C, 54.72; H, 4.31. Found: C, 54.98; H, 4.40.

Three such reactions were carried out on 5–9-g scale of **6** and the yields of **6** were 75–79%. The other chromatographic fractions were combined and rechromatographed on alumina. C_6H_6–CH_2Cl_2 (9:1) eluted 323 mg of diethyl 2,5-dibromoazulene-1,3-dicarboxylate and 205 mg of tetraethyl 5,5′-dibromo-2,6′-biazulyl-1,1′,3,3′-tetracarboxylate (**14**) was eluted with 1:1 C_6H_6–CH_2Cl_2. **14** was tentatively identified from its NMR spectrum, which showed the characteristic singlet absorption for a C_2 H at τ 1.32 (1 H), and a doublet with further splitting at τ 1.72 characteristic of a C_6 H (1 H), along with two types of ethyl ester protons.

5-Bromoazulene (8). Method A. To 100 mg (0.284 mmol) of **7** in 3 mL of ethanol was added 300 mg (5.34 mmol) of KOH in 2.7 mL of water. This mixture was heated with stirring for 30 min at reflux, transferred to a centrifuge tube, and acidified with 6 M HCl. The resultant precipitate was collected by centrifugation, washed with six

25-mL portions of water, transferred with acetone into a large sublimation tube, and dried under an air stream.

This solid diacid was heated to 270 °C (100 Torr) and a blue sublimate formed on the condenser. The sublimate was removed with hexane and chromatographed on alumina. Hexane eluted a single, blue band that afforded 30 mg (51%) of 5-bromoazulene. Crystallization from 2:1 methanol–water gave blue plates: mp 46.0–47.0 °C (lit.[57] mp 48–50 °C); IR (CCl_4) no characteristic absorptions; NMR ($CDCl_3$, internal Me_4Si) τ 1.38 [d (J = 2 Hz), C_4 ring H, 1], 1.75 [d (J = 9.5 Hz), C_8 ring H, 1], 2.03 [d (J = 3.5 Hz), C_3 ring H, 1], 2.15 [d (J = 3.0 Hz), C_1 ring H, 1], 2.47–2.83 (m, $C_{2,6}$ ring H's, 2), and 3.08 [t (J = 9.5 Hz), C_7 ring H, 1]; λ_{max} (95% ethanol) 273 nm (log ϵ 4.56), 281 (4.57), 332 (3.43), 342 (3.58), 357 (3.28), 574 (2.27), 596 (2.33), 619 (2.30), 653 (2.26), 680 (2.00) (sh), and 723 (1.84).

Method B. 5-Bromoazulene-1,3-dicarboxylic acid (2.38 g, 8.1 mmol), obtained as in method A, and 23.0 g of LiBr in 150 mL of dry DMF were heated under reflux in a N_2 atmosphere for 5.3 h. The cooled reaction mixture was poured into aqueous $NaHCO_3$ and extracted three times with ether, and the combined ether extracts were dried (Na_2SO_4). Evaporation of the ether gave a blue residue which was dissolved in pentane and chromatographed on alumina. **8** was eluted by this solvent and evaporation gave 1.11 g of **8** as blue plates. Some di- and monocarboxylic acids were recovered from the basic extract. These were retreated as above producing 0.17 g of **8**. The total yield of **8** was 1.28 g (77%) identical in all respects with that from method A.

Anal. Calcd for $C_{10}H_7Br$: C, 58.00; H, 3.41. Found: C, 58.23; H, 3.63.

2-(5- and 2-(7-Bromo-1-azulyl)ethyl Acetates (5- and 7-Br-1-OAc). To an ice-cold solution of 1.46 g (7.1 mmol) of **8** in 80 mL of CH_2Cl_2 was added 1.86 g of $AlCl_3$ (blue to green) followed by 18 mL of a 0.75 M solution of ethylene oxide in CH_2Cl_2 (blue color returned). This mixture was poured into 600 mL of ice–10% HCl, the layers were separated, and the aqueous layer was extracted once with CH_2Cl_2 and twice with ether. The combined extracts were washed once with cold 10% HCl and twice with water, and dried (Na_2SO_4). The blue organic solution was passed down a column of alumina and 937 mg of **8** was recovered. CH_2Cl_2 and EtOH eluted the product alcohols. Evaporation of the solvent gave a residue which was dissolved in 10 mL of pyridine and 3 mL of Ac_2O. After standing overnight at 4 °C this mixture was diluted with ether, washed with cold 10% HCl, then water, and dried (Na_2SO_4). The solution was chromatographed on alumina where C_6H_6–CH_2Cl_2 (9:1) eluted a large blue band of 5(7)-Br-**1**-OAc (560 mg, 27%, 76% net) and C_6H_6–CH_2Cl_2 (7:3) eluted 47 mg of a compound believed to be 5-bromoazulyl-1,3-bis(hydroxyethyl)diacetate.[10] The NMR spectrum (CCl_4) of 5(7)-Br-**1**-OAc mixture was characterized by the doublets referred to in the synthesis section and indicated that we had a 55:45 mixture of these two isomers.

The combined yields of 5(7)-Br-**1**-OAc from three such reactions were recrystallized from CCl_4–hexane. Only the 5-Br-**1**-OAc crystallized which was further recrystallized from hexane: mp 80–81 °C; NMR (CCl_4, internal Me_4Si) τ 1.66 [d (J = 2 Hz), C_4 H, 1], 1.96 [d (J = 9 Hz), C_8 H, 1], 2.1–3.4 (m, 4), 5.8 [t (J = 7 Hz), C_α H_2, 2], and 6.75 [t (J = 7 Hz), C_β H_2, 2].

Anal. Calcd for $C_{14}H_{13}O_2Br$: C, 57.36; H, 4.47. Found: C, 57.37; H, 4.51.

2-(5-Bromo-1-azulyl)ethanol (5-Br-1-OH). A solution of 225 mg (0.77 mmol) of 5-Br-**1**-OAc and 1 g of KOH in 2 mL of water and 15 mL of EtOH was stirred for 2 h at ice-bath temperature. Ether and water were added, and the ether layer was separated and dried (Na_2SO_5). Evaporation of the solvent and chromatography of the residue on alumina with CH_2Cl_2–$CHCl_3$ (1:1) eluted a single blue band containing 170 mg (88%) of 5-Br-**1**-OH, which when recrystallized from CH_2Cl_2–hexane gave large blue plates: mp 94–96 °C dec; NMR ($CDCl_3$, internal Me_4Si) τ 1.57 [d (J = 2 Hz), C_4 H, 1], 1.87 [d (J = 10 Hz), C_8 H, 1], 2.05–3.45 (m, 4), 6.15 [t (J = 6 Hz), C_α H_2, 2], and 6.80 [t (J = 6 Hz), C_β H_2, 2]; the O–H was not defined.

Anal. Calcd for $C_{12}H_{11}OBr$: C, 57.39; H, 4.42. Found: C, 57.46; H, 4.44.

2-(5-Bromo-1-azulyl)ethyl Tosylate (5-Br-1-OTs). To a cold solution of 192 mg (0.77 mmol) of 5-Br-**1**-OH in 6 mL of THF were added 153 mg of tosyl chloride and 127 mg of powdered NaOH. After stirring in an ice bath for 8 h, the solvent was evaporated. The blue residue was dissolved in CH_2Cl_2 and this solution was passed down a column of alumina. Evaporation of the solvent from this blue eluate gave 252 mg (81%) of crystalline 5-Br-**1**-OTs which when recrystallized from CH_2Cl_2–hexane gave blue needles: mp 104–106 °C; NMR ($CDCl_3$, internal Me_4Si) τ 1.56 [d (J = 2 Hz), C_4 H, 1], 2.0 [d (J = 9 Hz), C_8 H, 1], 2.2–3.5 (m, 8), 5.7 [t (J = 8 Hz), C_α H_2, 2], 6.7 [t (J = 8 Hz), C_β H_2, 2], and 7.65 (s, CH_3, 3).

Anal. Calcd for $C_{19}H_{17}O_3SBr$: C, 56.30; H, 4.23. Found: C, 56.16; H, 4.22.

2-(7-Bromo-1-azulyl)ethanol (7-Br-1-OH). A solution of 540 mg (1.8 mmol) of 5(7)-Br-**1**-OAc (containing about 25% 5-Br-**1**-OAc by NMR) was hydrolyzed as above in the preparation of 5-Br-**1**-OH. Workup and alumina chromatography with CH_2Cl_2 gave three fractions: (1) 92% 7-Br-**1**-OH, 8% 5-Br-**1**-OH; (2) 87% 7-Br-**1**-OH, 13% 5-Br-**1**-OH; and (3) 76% 7-Br-**1**-OH, 24% 5-Br-**1**-OH. The total weight was 302 mg. A final fraction containing 57:43 7- and 5-Br-**1**-OH (144 mg) was also obtained. Rechromatography on alumina showed the first five fractions to be pure 7-Br-**1**-OH by NMR spectral analysis. Recrystallization produced clusters of green needles, mp 63–66 °C, of 7-Br-**1**-OH: NMR (CCl_4, internal Me_4Si) τ 1.60 [d (J = 2 Hz), C_8 H, 1], 2.0 [d (J = 9 Hz), C_4 H, 1], 2.15–3.5 (m, 4), 6.1 [t (J = 6 Hz), C_α H_2, 2], and 6.75 [t (J = 6 Hz), C_β H_2, 2]; the O–H was not defined.

Anal. Calcd for $C_{12}H_{11}OBr$: C, 57.39; H. 4.42. Found: C, 57.17; H, 4.41.

2-(7-Bromo-1-azulyl)ethyl Tosylate (7-Br-1-OTs). 7-Br-**1**-OH (55 mg, 0.22 mmol) was treated as in the preparation of 5-Br-**1**-OTs. Chromatographic separation gave a blue oil which was purified as its TNB complex. Recrystallization of this complex from EtOAc–hexane gave gold-brown needles: mp 87.8–88.1 °C; NMR ($CDCl_3$, internal Me_4Si) τ 1.76 [d (J = 2 Hz), C_8 H, 1], 1.98 [d (J = 9 Hz), C_4 H, 1], 2.1–3.4 (m, 4), 5.7 [t (J = 8 Hz), C_α H_2, 2], 6.7 [t (J = 8 Hz), C_β H_2, 2], and 7.65 (s, CH_3, 3).

Anal. Calcd for $C_{25}H_{20}O_9N_3SBr$: C, 48.55; H, 3.26. Found: C, 48.50; H, 3.30.

2-(5-Cyano-1-azulyl)ethanol (5-CN-1-OH). A solution of 250 mg (0.85 mmol) of 5-Br-**1**-OAc and 115 mg (1.3 mmol) of CuCN in 20 mL of dry DMF was heated under reflux and an N_2 atmosphere for 9 h. After cooling 75 mL of C_6H_6 was added. This mixture was washed with dilute aqueous NaCN and three times with water, and dried (Na_2SO_4). After solvent evaporation the blue, oily residue was chromatographed in alumina where C_6H_6–CH_2Cl_2 eluted a small blue band, CH_2Cl_2 eluted a large blue band, and CH_2Cl_2–EtOH (95:5) eluted a small green band followed by a small blue band. The first band yielded 20 mg of 5-Br-**1**-OAc. The large second band gave 160 mg (79%) of 5-CN-**1**-OAc which crystallized from CCl_4–hexane as dark blue needles: mp 89–89.5 °C; NMR ($CDCl_3$, internal Me_4Si) τ 1.5–3.1 (m, 6), 5.63 [t (J = 7 Hz), C_α H_2, 2], 6.6 [t (J = 7 Hz), C_β H_2, 2], and 8.0 (s, CH_3, 3).

Hydrolysis of 5-CN-**1**-OAc (200 mg) to 5-CN-**1**-OH was carried out above as in the preparation of 5-Br-**1**-OH. Chromatography on activity 2 alumina eluted a single large band with CH_2Cl_2–EtOH (99:1). From this eluent was obtained 150 mg (90%) of 5-CN-**1**-OH which when crystallized from CH_2Cl_2–CCl_4 gave greenish-blue plates: mp 104.7–105.2 °C; NMR ($CDCl_3$, internal Me_4Si) τ 1.5–3.2 (m, 6), 4.1 [t (J = 6 Hz), C_α H_2, 2], 4.7 [t (J = 6 Hz), C_β H_2, 2], and 8.1 (s, OH, 1).

Anal. Calcd for $C_{13}H_{11}NO$: C, 79.16; H, 5.62. Found, C, 78.96; H, 5.68.

2-(5-Cyano-1-azulyl)ethyl Tosylate (5-CN-1-OTs). 5-CN-**1**-OH (155 mg, 0.79 mmol) was converted to 5-CN-**1**-OTs as per the procedure for 5-Br-**1**-OTs. 5-CN-**1**-OTs was isolated in 89% yield along with 6% recovery of 5-CN-**1**-OH. The tosylate was recrystallized from CH_2Cl_2–hexane as blue plates: mp 106.3–107 °C; NMR ($CDCl_3$, internal Me_4Si) τ 1.6–3.2 (m, 10), 5.65 [t (J = 7 Hz), C_α H_2, 2], 6.6 [t (J = 7 Hz), C_β H_2, 2], and 7.6 (s, CH_3, 3).

Anal. Calcd for $C_{20}H_{17}NO_3S$: C, 68.35; H, 4.88. Found: C, 68.28; H, 4.91.

2-(7-Cyano-1-azulyl)ethyl Tosylate (7-CN-1-OTs). 7-Br-**1**-OAc (117 mg) was converted to 7-CN-**1**-OAc in 88% yield as in the preparation of 5-CN-**1**-OAc: NMR (CCl_4, internal Me_4Si) τ 1.6–3.2 (m, 6), 5.65 [t (J = 7 Hz), C_α H_2, 2], 6.65 [t (J = 7 Hz), C_β H_2, 2], and 8.0 (s, CH_3, 3). Hydrolysis of the acetate to 7-CH-**1**-OH as per the preparation of 5-CN-**1**-OH gave the alcohol in a quantitative yield which when recrystallized from CH_2Cl_2–hexane gave green needles, mp 61–64.5 °C. From 60 mg (0.31 mmol) of 7-CN-**1**-OH was obtained 50 mg (46%) of 7-CN-**1**-OTs as per the procedure for 5-

CN-**1**-OH → 5-CN-**1**-OTs. 7-CN-**1**-OTs was recrystallized from CCl_4 as clusters of green needles, mp 106.5–110 °C.

Anal. Calcd for $C_{20}H_{17}NO_3S$: C, 68.35; H, 4.88. Found: C, 68.55; H, 4.96.

Kinetics. The titrimetric (sealed ampule) and conductometric methods used were those previously discussed.[5,17]

Deuterated Compounds. **1**-OH-α,α-d_2 was prepared using $NaBD_4$ (Merck Sharp and Dohme, 98% D) in the B_2D_6 reduction of 1-azulylacetic acid.[9] 3-NO_2-**1**-OH-α,α-d_2 was prepared by mild nitration [$C(NO_2)_4$ in pyridine] of **1**-OH-α,α-d_2.[9] Both labeled alcohols were converted to their tosylate esters by the method given.[9]

Both alcohols were analyzed by mass spectrometry for total deuterium content. Average of multiple NMR integrations of these two methylene regions gave the total deuterium contents in excellent (±1%) agreement with the mass spectral analysis; the individual C_α and C_β deuterium contents from the NMR analyses are given in Table II. NMR analysis was used exclusively for the tosylates and acetates. Checks were determined using tosylate and acetate CH_3 groups as internal standards and agreement was always excellent (±1%).

Structures Used in CNDO/2 Calculations Listed in Table IV. The azulene ring geometry used in 1-ethylazulene and in the ethylene-1-azulenium ion (cation in ion pair **9**) was that employed in ab initio calculations[58] taken from x-ray crystallographic studies.[59] The geometry of the spiro three-membered ring was that found in spiro[2.4]-hepta-4,6-diene.[60] All C's in 1-ethylazulene and ethylbenzene were in the same plane. In 1-ethylazulene the side-chain C_α–C_β and ring C_1–C_2 bonds were syn, C_8–H bisected the H–C_α–H angle, and $C_\beta H_3$ was in a staggered conformation relative to $C_\alpha H_2$. Bond lengths of 1.505 Å for the Ar–C_α, 1.537 Å for the C_α–C_β, and 1.08 Å for the C–H bonds were used. These structures were not geometry minimized.

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