n Participation and Secondary Deuterium Isotope Effects in Solvolysis of 1-Aryl-4-methoxy-1-butyl Chlorides. Are There Two Distinct k_Δ Pathways?

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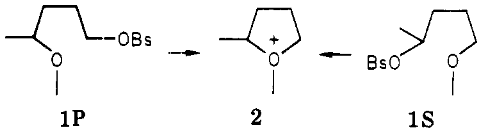
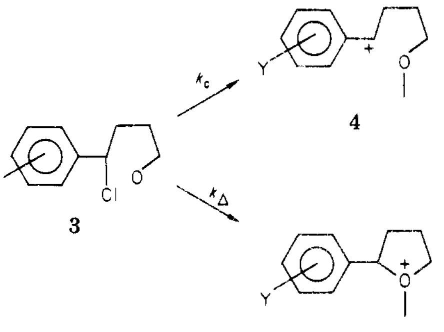
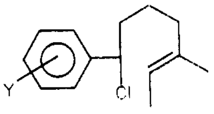
A series of 1-aryl-4-methoxy-1-butyl chlorides (**3**) and their *1-d* and *2,2-d_2* analogues were prepared and the solvolysis rates measured. All compounds show rate accelerations relative to the corresponding 1-aryl-1-alkyl chlorides. The results indicate that k_Δ is the main pathway, except possibly for the *p*-anisyl derivative. α-Deuterium isotope effects increase from $k_H/k_D = 0.97$ to 1.10 with decreasing σ^+ of the phenyl substituent and/or with increasing ionizing power of the solvent. Such results are indicative of a change in mechanism and can best be accommodated by assuming two distinct k_Δ pathways. The first, operative in cases when an α-deuterium effect of about unity is observed, is the internal direct displacement of the chloride by the methoxy group, yielding an oxonium ion intermediate (**5**). The other k_Δ pathway involves a rate-determining ionization into an intimate ion pair (**10**) which is then converted into **5** in a fast process. With the *p*-anisyl derivative the **10** to **5** conversion becomes rate determining, competing with further ionization of **10** into a solvent-separated ion pair (k_c process). The observed small β-deuterium isotope effects are consistent with such a mechanism except that they appear to be about 3–4% too low for a rate-determining ionization to **10**. This observation can be explained if it is assumed that there is an interaction between the aliphatic methoxyl and the carbenium ion center in **10**, restricting the motions of the side chain and forcing C_2–H(D) bonding orbitals into a geometry unfavorable to hyperconjugative electron release. The main defect of the proposed mechanism is a lack of analogy to the corresponding π participation. A mechanistic alternative is a single k_Δ process involving a rate-determining transformation of **3** into **5** throughout the series, but with a variable magnitude of bridging in the transition state. The observed trend in the α-deuterium effects can be explained as being due to a nonlinear dependence of k_H/k_D upon the sum of the reacting bond orders. The data do not allow a clear distinction between the two mechanisms. Solvolysis rates, which do not include that for the *p*-anisyl derivative, are well correlated with σ^+ constants even in 95% ethanol where isotope effects indicate a change in the structure of the transition states. Thus, secondary deuterium isotope effects are shown to be far more sensitive to change in mechanistic detail than are substituent effects. It can be shown in an indirect manner that the rate of the *p*-anisyl derivative must be significantly faster than calculated on the basis of ρ^+ in 95% ethanol at 50 °C. A break in the correlation line is consistent with a change in mechanism from k_Δ to k_c.

It has been reported[2] that in the solvolysis of brosylates **1P** and **1S** participation by the methoxy group competes with direct displacement by the solvent. Even in the very nucleophilic 100% ethanol, the reaction is essentially completely controlled by k_Δ. Secondary deuterium isotope effects indicate that the solvolysis mechanism of these compounds is best described as an internal displacement reaction, the transition states resembling closely the intermediate **2**.[3] In view of these results, it seemed of interest to investigate if 5-methoxyl participation can compete against an efficient k_c process. In solvolysis of **3**, k_Δ is pited against an ionization process, producing a resonance-stabilized α-arylalkyl cation. If the participating group is a substituted carbon–carbon double bond as in **6**, it has been shown that the contribution of k_Δ can be varied by changing the σ^+ value of the substituent Y. Is n participation in reactions of **3** similar to π participation in reactions of **6**? In order to compare the solvolyses of **3** and **6**, we prepared three series of 1-aryl-4-methoxy-1-butyl chlorides **3** and deuterated analogues **3**-*1-d* and **3**-*2,2-d_2* and measured their solvolysis rates.







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Results

Chlorides **3** and their deuterated analogues were prepared as shown in Scheme I and are described in detail in the Experimental Section.

Solvolysis rates were followed by continuous titration of the liberated acid by means of a pH stat. Typically, 0.05

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[1] "Pliva" Pharmaceutical and Chemical Works. Taken in part from the M.S. thesis of I.M., University of Zagreb, 1973, and in part from the M.S. thesis of J.Š., University of Zagreb, 1976. (b) Faculty of Pharmacy, University of Zagreb.

[2] S. Winstein, E. Allred, R. Heck, and R. Glick, *Tetrahedron*, 3, 1 (1958); E. L. Allred and S. Winstein, *J. Am. Chem. Soc.*, **89**, 3991 (1967); **89**, 3398 (1967).

[3] R. Eliason, S. Borčić and D. E. Sunko, *Croat. Chem. Acta*, **51**, 203 (1978).

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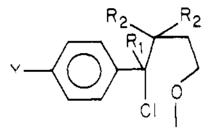
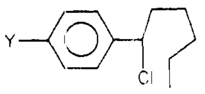


3, $R_1 = R_2 = H$
3-*1-d*, $R_1 = D$; $R_2 = H$
3-*2,2-d*$_2$, $R_1 = H$; $R_2 = D$

a, $Y = OCH_3$; b, $Y = CH_3$; c, Y = F; d, Y = H; e, Y = Cl; f, Y = Br

mmol of the chloride was dissolved in 25 mL of the solvent thermostated at ±0.05 °C and the liberated acid titrated with a 0.02 N solution of sodium alkoxide conjugate to the solvent. Each measurement was repeated at least once and five or six times when isotope effects had to be measured. In all cases the first-order rate law was obeyed up to at least 80% reaction completion. The first-order rate constants were calculated from points between 15–80% reaction by using a nonlinear least-squares program. The results are shown in Table I.

In order to estimate the contribution of k_Δ, it is necessary to compare the rates of **3** to a reference compound solvolyzing by way of carbenium ions resembling **4** as closely as possible. Chlorides **7**, **8**, and **9** seemed the most appropriate candidates.[4] In fact, **7** resembles **3** the most, but since the rates of **8** and **9** were shown[4] to differ very little from those of the corresponding chloride **7**, they are used to estimate k_c whenever the data for **7** are not available.[5] These rate constants are shown in the last column of Table I. Using the equation $k_t = k_c + k_\Delta$, we calculated the contribution of k_Δ, and the result is shown as percent participation in Table II. Secondary deuterium isotope effects were calculated from the data in Table I and are shown in Table II.



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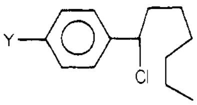

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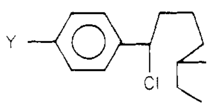

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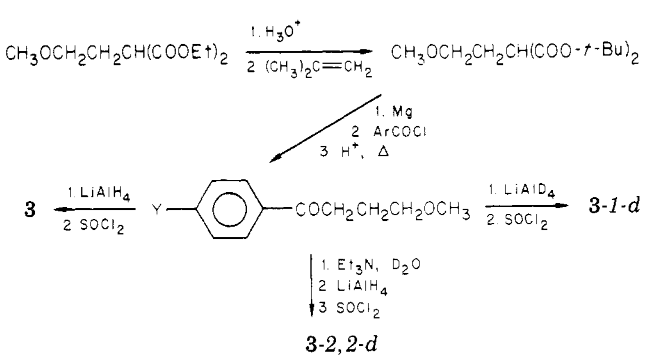
1-(*p*-Anisyl)hexyl chlorides (**7**; $Y = OCH_3$) deuterated either in the α-position or in the β-position (two deuteriums) were also prepared and their solvolysis rates measured in 93% acetone at 25 °C. The rate constants are shown in Table I and the calculated isotope effects in Table II. Since isotope effects in solvolysis of 1-(*p*-anisyl)ethyl chloride are available for the same solvent and temperature,[5] it is possible to estimate the isotope effects for the k_c process in solvolysis of **3** from Shiner's[5] extensive data for solvolysis of 1-arylethyl chlorides. The α-deuterium effect on the k_c process with **3** is thus found to be 1.15 for the whole series and in all solvents, while the β-effect varies from 1.09 to 1.17 (for two deuteriums) as shown in Table II.

Discussion

The data in Table I show that solvolysis rates of all chlorides **3** are enhanced relative to those of series **7**, **8**, and

Scheme I



9. However, an examination of data in Table II reveals two inconsistencies. Although there might be some difficulty in estimating "percent participation"[6] values to the desirable degree of accuracy from the data, it could be expected that an increase in the electron-donating power of the substituent on the phenyl ring would favor k_c over k_Δ. In the analogous case of π participation with a compound structurally related to **8** and having a double bond between carbons 5 and 6, the percent participation at 25 °C drops from 84% for the *p*-Br derivative (97 wt % trifluoroethanol) to 30% for the *p*-tolyl derivative (80% ethanol).[4] The corresponding numbers for **3** with the same substituents, solvents, and temperature are 87 and 82%, respectively (Table II).

Another inconsistency is found when measured isotope effects with the *p*-anisyl derivative of **3** are compared with the calculated percent participation. From the data in Table II it can be inferred that the k_Δ part of the solvolysis of **3a** should be associated with an α-deuterium effect of 1.10 and the k_C part with an effect of 1.15. If the reaction proceeds halfway by k_c, the α-deuterium effect should be 1.125, which is higher than the measured value by more than the experimental error. In the same manner, the measured β-effect can be shown to be about 2% too low for the assumed relative contribution of k_c and k_Δ.

Both inconsistencies can be removed if it is assumed that solvolysis rates of **7**, **8**, and **9** do not accurately reflect k_c for the reaction of **3**. The methoxyl of the aliphatic chain in **3** has an electron-withdrawing inductive effect which could decrease k_c relative to **7**, **8**, and **9**. This rate-retarding inductive effect can roughly be estimated. The σ^* value for the CH_2OCH_3 is known to be + 0.52.[7] By use of the usual attenuation factor of 2.8 per intervening CH_2 group,[7] a σ^* for $CH_2CH_2CH_2OCH_3$ can be calculated as 0.066. A conservative estimate for ρ^* would be −6, which is the calculated ρ^+ for series **8** and **9**.[4] Therefore, k_c in solvolysis of **3** should be about 2.5 times smaller than that in the reaction of chlorides with a saturated aliphatic side chain. Dividing the rate constants of the reference compounds by 2.5 yields a corrected set of percent participation values in parentheses in Table II. Thus it appears that k_Δ is practically the sole reaction pathway throughout the series except for **3a** where one-fifth of the reaction proceeds by way of k_c. Isotope effects for **3a** calculated by using relative contributions of k_c and k_Δ fall within the experimental errors of the measured values.

It has been reported[4] that **6**, $Y = p\text{-}OCH_3$, solvolyzes exclusively by way of k_c. Thus, the *p*-anisyl group is powerful enough in stabilizing an adjacent carbenium ion cen-

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Table I. Solvolysis Rates of 1-Aryl-4-methoxy-1-butyl Chlorides and of Their Deuterated Analogues

$Y^{a,k}$	solvent[b]	T, °C	10^5k_H,[c] s^{-1}	$10^5\alpha$-k_D,[c,d] s^{-1}	$10^5\beta$-k_D,[c,e] s^{-1}	10^5k,[c] s^{-1} (for 1-arylalkyl)
OCH_3	95E	5	678 (7)			289[f] (9)
	93A	25	148 (1)	135 (1)	141 (1)	71.1[f] (6)
CH_3	95E	50	111 (1)			16.2[f] (7)
		40	40.0 (3)	36.4 (3)	38.5 (2)	5.56[g]
	80E	25	67.7 (7)	61.3 (7)	64.3 (2)	12.2[g] (2)
	97T	25	3870 (40)			
F	95E	50	12.8 (1)	11.6 (1)	12.1 (1)	
	80E	40	38.0 (1)	34.8 (2)	35.7 (1)	
	97T	25	446 (4)			
		20	255 (1)	231 (1)	250 (3)	
H	95E	50	8.64 (7)			
		40	2.42 (1)			
	80E	50	63.9 (2)			3.55[g] (2)
		25	4.43 (2)	4.03 (2)	4.30 (3)	0.214[g]
	97T	25	278 (3)			48.8[i] (12)
		20	159 (1)			
Cl	95E	50	3.46 (4)	3.36 (3)	3.36 (3)	
	80E	50	23.9 (2)	23.1 (3)	23.4 (1)	
	97T	25	92.9 (8)	85.6 (8)	92.3 (8)	
Br	95E	50	2.86 (3)	2.85 (3)	2.95 (2)	
	80E	50	16.7 (1)	17.2 (1)	16.7 (1)	0.79[h]
	97T	25	67.5 (7)	60.2 (2)	64.7 (6)	8.45[g] (5)
7-*p*-OCH_3[i]	93A	25	71.1 (6)	61.8 (6)	65.2 (6)	
j	93A	25	70.51	61.46	62.21	

[a] *p*-Substituent on the phenyl ring. [b] 95E, 80E, and 93A are vol % aqueous ethanol and acetone, respectively. 97T is 97 wt % aqueous 2,2,2-trifluoroethanol. [c] Numbers in parentheses are uncertainties of the last reported figure, i.e., 67.7 (7) = 67.7 ± 0.7. Uncertainties are standard deviations of the means. [d] Rate of **3**-*1*-*d*. [e] Rate of **3**-*2,2*-d_2. [f] Rate of 1-aryl-1-hexyl chlorides. [g] Rate of 1-aryl-1-heptyl chlorides. [h] Rate of 1-aryl-5-methyl-1-heptyl chloride. [i] 1-(*p*-Methoxyphenyl)-1-hexyl chloride. [j] 1-(*p*-Methoxyphenyl)ethyl chloride. Reference 5. β-k_d for three deuteriums. [k] Satisfactory elemental C and H analyses (±0.3%) for all parent ketones of the new compounds listed in the table were reported.

Table II. Contribution of k_Δ and Secondary Deuterium Isotope Effects

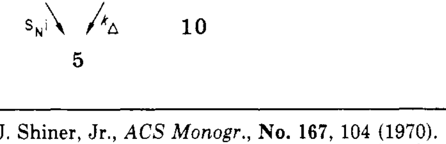
Y^a	solvent[b]	T, °C	% participn[c]	α-$k_H/k_D{}^d$	β-$k_H/k_D{}^{d,e}$	β-$k_H/k_D{}^{e,f,i}$
OCH_3	95E	5	58 (83)			
	93A	25	52 (81)	1.10	1.05	1.09
CH_3	95E	50	85 (94)			
		40	86 (94)	1.10	1.04	1.15
	80E	25	82 (93)	1.10	1.05	1.15
F	95E	50		1.10	1.06	
	80E	40		1.09	1.06	1.17
	97T	20		1.10	1.02	
H	80E	50	91 (96)			
		25	95 (98)	1.10	1.03	1.17
	97T	25	82 (93)			
Cl	95E	50		1.03	1.03	
	80E	50		1.03	1.02	1.17
	97T	25		1.09	1.01	
Br	95E	50		1.00	0.97	
	80E	50	95 (98)	0.97	1.00	1.17
	97T	25	87 (95)	1.12	1.04	
7-*p*-OCH_3[g]	93A	25		1.15	1.09	
h	93A	25		1.147	1.133	

[a] Para substituents on the phenyl ring. [b] 95E, 80E, and 93A are 95, 80, and 93 vol % aqueous ethanol and acetone, respectively, and 97T is 97 wt % aqueous 2,2,2-trifluoroethanol. [c] Calculated as $100k_\Delta/(k_c + k_\Delta)$, k_c being the rate constant of the 1-aryl-1-alkyl chloride. In parentheses are values corrected for the inductive effect of OMe on k_c. [d] The standard deviation of the mean for all isotope effects is ±0.01. The values are corrected to 25 °C, assuming normal temperature dependence. In no case was the correction larger than 0.01. [e] For two deuteriums. [f] Calculated from data in ref 5 corrected for two deuteriums by using the values given in the last two rows. [g] 1-(*p*-Methoxyphenyl)-1-hexyl chloride. [h] 1-(*p*-Methoxyphenyl)ethyl chloride. From ref 5. β effect is for three deuteriums. [i] Isotopic effect on k_c.

ter and promoting the k_c process to make 5,6 π participation ineffective. In 5-MeO n participation, this is not the case. This difference between n and π participation is consistent with the difference in nucleophilicities of the two neighboring groups.

α-Deuterium Isotope Effects. All α-deuterium effects in solvolyses of **3**-*1*-*d* are reduced in magnitude as compared to the limiting effect of 1.15 measured for a pure k_c process with chloride as a leaving group.[5,8] This is quite consistent with participation, since bridging would tend to hinder the C_1–H(D) bending motions. A decrease in the frequency of these vibrations during the ionization process is thought to be the cause of the α-deuterium effect in the solvolyses.[9]

An interesting feature of our results is the increasing trend of the α-deuterium effect as the electron-donating power of the aryl substituent or the ionizing power of the solvent is increased, but only until $k_H/k_D = 1.10$ is reached. The α-deuterium effect remains constant after it reaches two-thirds of the limiting maximum value (1.15). Such results could indicate a shift in the reaction mechanism. Since k_Δ is in command of the reactions throughout the series, this would mean that there are two distinct and different k_Δ pathways. A possible rationalization is in terms of analogy to the usual mechanistic scheme for solvolysis reaction.[8,10,11] Thus **3** could yield **5** directly, in a



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reaction which can properly be called an internal direct displacement reaction (S_Ni). This pathway would be preferred when Y is electron withdrawing and in solvents of relatively low ionizing power. Increasing the electron-donating ability of the aryl substituent and/or the ionizing power of the solvent increases k_1 relative to the S_Ni process, and the reaction switches to the **3** → **10** → **5** pathway, k_1 being rate determining, followed by a fast k_Δ process. Decreasing σ^+ still further increases k_1 and decreases k_Δ so that k_Δ and/or the conversion of the internal ion pair **10** to a solvent-separated ion pair (k_2) becomes rate determining. Such a mechanism has several appealing features. Thus, if the solvolysis of 1-arylethyl chlorides is taken as a model,[5] the k_c process should proceed by way of **10**, with k_2 being rate determining. Therefore, it seems plausible that, at least in some cases, 5-OMe participation (k_Δ) would be able to compete successfully with further ionization (k_2) for the intimate ion pair **10**. It is interesting that Shiner[10] has estimated for trifluoroacetolysis of 1-phenylethyl chloride that internal return (k_{-1}) is 6 times faster than further solvolysis (k_2). If neighboring-group participation in the analogous reaction of **3d** has the effect of cutting out internal return and making k_1 rate determining, then Shiner's data give 87% for the percent participation which is very close to the value obtained in this work.

The observed trend in α-deuterium isotope effects can also be well understood in terms of such mechanism. The *p*-Br derivative solvolyzes in 95 and 80% ethanol by an S_Ni mechanism, and α-deuterium effects should be typical for such a process. Compounds **3b–f** in trifluoroethanol and **3b–d** in all other solvents solvolyze with k_1 being rate determining and should give α-deuterium effects of corresponding magnitudes. The observed rate increases with these compounds should then be due only indirectly to internal displacement which, moreover, could not affect the magnitude of the α-deuterium effect since it occurs only after the rate-determining step. The reaction of the *p*-Cl derivative in 95 and 80% ethanol represents a transition between the two mechanisms, k_1 competing with the S_Ni process, giving rise to α-deuterium effects of intermediate magnitudes.

It has been shown[3] that **1S** reacts in 95% ethanol by an S_Ni mechanism with an α-deuterium effect of 1.06. Since the limiting effect for a brosylate (1.22)[8] is higher than the one for a chloride (1.15)[5,8] it can be calculated[13] that a direct internal displacement on the secondary chloride **3f** should proceed with an α-deuterium effect of 1.00, which is very close to the measured value in less ionizing solvents.

The solvolysis of 3,3-dimethyl-2-butyl (pinacolyl) brosylates seems to proceed via the rate-determining formation of the intimate ion pair, followed by a fast rearrangement to the tertiary carbenium ion, from which the products are formed.[14] The measured α-deuterium effects are 1.153–1.159 which corresponds to 1.104–1.108 for the chlorides, again very close to the measured values with **3** where k_1 is supposed to be rate determining. Moreover, the effects with pinacolyl brosylate are practically solvent independent,[14] which is observed in this work for relevant cases. The proposed mechanism also provides an alternative explanation for inconsistencies in the results discussed previously and ascribed to the inductive effect of aliphatic methoxyl. If the proposed mechanism is valid, then "percent participation" as it is calculated is equal to $100/[1 + k_2/k_{-1}]$ for all cases where k_1 is rate determining. Since it is possible that the partitioning of the intimate ion pair **10** between further ionization (k_2) and internal return (k_{-1}) is not very sensitive to the σ^+ value of the aryl substituent, the percent participation could remain approximately constant. With the *p*-OCH_3 derivative, there should be a switch in mechanism from k_1 being rate determining to a mixture of k_2 and k_Δ being rate determining. By use of the uncorrected values for the percent participation, the measured k_H/k_D, and $k_H/k_D = 1.15$ for the unassisted route, an α-deuterium effect of 1.05 is calculated for the assisted pathway, which is quite a reasonable value if bridging is part of the rate-determining step.[15]

β-Deuterium Isotope Effects. Are the measured β effects consistent with the proposed mechanism? The methylene-d_2 β effect is unfortunately not available for the solvolysis of the secondary substrate **1S**, but there are indications that it might be slightly larger than 0.96 which was measured with primary isomer **1P**.[3] Thus the β effect obtained with the secondary substrate **3** in cases where internal displacement is thought to be rate determining is of the expected magnitude.

What should the β *effects* be with **3** when k_1 is rate determining? Again the analogy to pinacolyl brosylate[14] seems appropriate. The effect for a β-CD_3 group under conditions which give rise to the quoted α effects is 1.188–1.205.[14] On the other hand, trifluoroacetolysis of isopropyl brosylate is associated with the limiting maximum α-deuterium effect of 1.22[12] and a β-CD_3 group effect of 1.46.[12] Thus the β effect for k_1 being rate determining is about 41–45% of that when k_2 is rate determining. Hence, in solvolysis of **3**, when the formation of **10** is rate determining, it is calculated that β effects should be 1.07–1.08, which is higher than the average measured value of 1.04. This small difference could be due to some electrostatic interactions between the 5-OMe group and the reaction center in **10**, restricting the motions of the aliphatic side chain. The preferred conformation would then be such that the C–D bonding orbitals and the empty p orbital at the reaction center make a dihedral angle of about 60°, which is unfavorable to hyperconjugative electron release and should result in reduced isotope effects.[16] Corroborating evidence for such "internal solvation" of the carbenium ion center in **10** is found in the activation parameters. The $\Delta H^\ddagger$ and $\Delta S^\ddagger$ for solvolysis of **3d** in 80% ethanol are 16.8 kcal/mol and –24.4 eu, respectively, and for the corresponding derivative **8** are 21.5 kcal/mol and –14.5 eu.[4] Although these numbers are not very accurate, the more negative entropy of activation for the reaction of **3d** is consistent with a restricted rotational freedom of the aliphatic side chain[4] in the transition state leading to **10**. Such an electrostatic interaction would probably increase k_1 and also slightly enhance k_c which is equal to k_1k_2/k_{-1}, compensating for the rate-retarding inductive effect of the methoxyl group and making a correction in the percent participation unnecessary.

Thus both the observed rate enhancements and the isotope effects are quite consistent with the proposed mechanism. A difficulty with this interpretation arises,

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(12) A. Streitwieser, Jr., and A. Dafforn, *Tetrahedron Lett.*, 1263 (1969).

(13) Assuming complete rupture of the old bond and complete formation of the new bond in the reaction transition state, the α-deuterium effect measured with **1P**[3] ($k_H/k_D = 0.98$ per deuterium) can be considered to be the product of a bond-breaking isotope effect of 1.22 and a bond-making isotope effect of 1/1.24. Replacing brosylate by chloride should then reduce the bond-breaking isotope effect to 1.15 and produce a composite effect of 1.15/1.24 = 0.93. **1S** reacts with an α-detuerium effect (1.06) which is higher than that measured with **1P** by one-third of the possible range (0.98–1.22). Since the analogous range for chloride is 0.93–1.15, a α-deuterium effect of 1.06 for **1S** corresponds to 1.00 for the related chloride.

(14) V. J. Shiner, Jr., R. D. Fisher, and W. Dowd, *J. Am. Chem. Soc.*, **91**, 7748 (1969).

(15) D. E. Sunko and S. Borčić, ref 8, Chapter 3.

(16) V. J. Shiner, Jr., and G. Meier, *J. Org. Chem.*, 31, 137 (1966).

Table III. Free-Energy Correlations[a]

solvent	T, °C	ρ^+	r^b	s^c	ψ^d
97T	25	−3.83	0.999	0.03	0.04
95E	50	−3.48	0.997	0.05	0.09

[a] From five data points. Includes all compounds of series **3** except the *p*-anisyl derivative. [b] Correlation coefficient. [c] Standard deviation of regression line. [d] Statistical test,[23] $\psi = [n(1 - r^2)/(n - 2)]^{1/2}$ where n = number of data points. The correlation is satisfactory if $\psi \leqslant 0.10$.

however, when the data obtained with **3** are compared to those measured with **6**: the solvolysis of **6** is also anchimerically assisted but cannot possibly proceed by an analogous mechanism.[4,17] The direct involvement of the aliphatic double bond in the rate-determining step of the k_Δ process in solvolysis of all chlorides of series **6** has been unequivocally demonstrated.[4,17]

An alternative mechanism for the solvolysis of series **3**, which is more in accord with results obtained with **6**, is that k_Δ for all compounds involves a rate-determining transformation of **3** directly into **5** with varying degrees of bridging in the transition state and possibly also in the intermediate **5**. An apparent difficulty arises then with respect to the trend observed with α-deuterium effects. However, it has been pointed out[13,18] that α-deuterium effects are a sensitive measure of the amount of bridging in the transition state only if the sum of the reacting bond orders (Σ_{ts}) approaches unity. Such should be the case with **3e** and **3f** in less ionizing solvents. As σ^+ decreases, bridging also decreases. On the other hand, increasing the electron-donating power of the aryl substituent enhances the reaction rates, with the effect that transition states move further away from **5** along their respective reaction pathways.[19] In other words, decreasing σ^+ will decrease bridging but also increase the bond order to the leaving group in the reaction transition state. If Σ_{ts} is not large, small $\Delta\Sigma_{ts}$ values due to a change in σ^+ are not expected to produce significant changes in the α-deuterium effect.[18]

In our opinion, a clear-cut distinction between the two possible mechanisms is not possible on the basis of the present data. This conclusion is reached on the following grounds. (a) There is too much uncertainty in estimating k_c for the reaction of **3** and thus also in the percent participation values. (b) By analogy to the 1-phenylethyl system, some intrusion of the k_s process (direct displacement by the solvent) is possible in the reaction of the less reactive chlorides of the series **7**, **8**, and **9** in solvents of low ionizing power. In the present treatment of data this k_s component is included in the k_c values although the expected isotope effects for the two processes are different. (c) The isotope-effect data are not accurate enough to distinguish between a process in which k_1 is completely rate determining and another in which a mixture of k_1 and k_Δ is rate determining.

Free-Energy Correlations. Solvolysis rates of **3b–f** are quite well correlated by σ^+ values as shown in Table III. The value of ρ^+ at 25 °C of −3.83 is very close to −3.93 which was calculated for series **6**,[4] demonstrating that benzylic resonance stabilization of the transition states is considerable and about equal for both n and π participation. The corresponding ρ^+ for solvolysis of 1-arylalkyl chlorides is about −6.2.[4] It is interesting that a good correlation is obtained also in 95% ethanol although α-deuterium effects suggest a shift in the structure of the transition state with decreasing σ^+.

The reaction constants for the two solvents seem to be very similar in magnitude, especially if the difference in the temperatures is taken into account. The relative insensitivity of ρ^+ to solvent changes has been used by Schleyer[20] as a criterion for suggesting that the kinetically significant magnitude of aryl bridging in the transition state of the assisted solvolysis of phenylethyl tosylate is invariant with the solvent. The α-deuterium effects observed with **3e** and **3f** demonstrate that it is possible to change the magnitude of bridging in the transition state by changing the ionizing power of the solvent without significantly affecting ρ^+. Thus secondary deuterium isotope effects are demonstrated to be much more sensitive tools for detecting details in mechanistic changes than substituents effects.

Another point seems worth mentioning. By use of the ρ^+ value obtained from all other chlorides of the series **3** at 50 °C in 95% ethanol, the rate of **3** is calculated to be 4.4×10^{-2} s^{-1}, which is only 6.4 times faster than the rate measured at 5 °C. Such a small rate enhancement for a 45 °C temperature difference yields quite unrealistic activation parameters which suggests that the rate of **3a** at 50 °C is not well correlated by ρ^+ value used. This is not surprising since k_c is an important process with **3a** even at 5 °C and since a temperature increase is expected to increase the k_c/k_Δ ratio due to the different activation parameters of the two processes.

Experimental Section

All melting and boiling points are uncorrected. Deuterium content of deuterated compounds was determined by mass spectroscopy and was found to be over 95% in all cases.

Di-*tert*-butyl (2-Methoxyethyl)malonate.[21] To a stirred solution of 100 g (1.8 mol) of KOH in 100 mL of water was added 100.4 g (0.46 mol) of diethyl (2-methoxyethyl)malonate and the reaction mixture refluxed for 2 h. Another 100 mL of water was then added and the ethanol distilled off. The reaction mixture was then cooled and acidified with concentrated sulfuric acid, and the product was continuously extracted with ether. The ether extract was dried with $CaSO_4$, the solvent evaporated under reduced pressure, and the crude substituted malonic acid dried in vacuo. The yield was 68.1 g (92%).

A mixture of 27 g (0.17 mol) of (2-methoxyethyl)malonic acid, 42.3 mL (0.53 mol) of liquid isobutene, 35 mL of ether, and 1.8 mL of concentrated sulfuric acid was shaken for 36 h. The reaction mixture was then added to 100 mL of a 27% solution of NaOH and 100 g of ice and the product extracted several times with ether. The ether extract was dried with $CaSO_4$, the solvent evaported under reduced pressure, and the residue subjected to fractional distillation. The boiling point of the product was 134–136 °C (10 mmHg). The product gave a satisfactory elemental C and H analysis and spectra (IR, NMR) consistent with its structure.

1-Aryl-4-methoxy-1-butanones.[22] The title compounds were all prepared by the procedure which is described for the *p*-bromophenyl compound. To a stirred mixture of magnesium (1.22 g, 0.05 g-atom), anhydrous ethanol (1 mL), carbon tetrachloride (0.1 mL), and ether (15 mL) was added dropwise a solution of 13.7 g (0.05 mol) of di-*tert*-butyl (2-methoxyethyl)malonate in 4.8 mL of anhydrous ethanol and 5.0 mL of ether and the reaction

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[17] E. Polla, S. Borčić, and D. E. Sunko, *J. Org. Chem.*, following paper in this issue.

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[23] O. Exner, *Collect. Czech. Chem. Commun.*, **31**, 65, 3222 (1966).

mixture refluxed until complete solution of magnesium. A solution of 10.97 g (0.05 mol) of *p*-bromobenzoyl chloride in 10 mL of ether was then added and the reaction mixture refluxed for an additional 30 min. After the mixture was cooled and acidified with dilute sulfuric acid, the product was extracted several times with ether. The extract was dried with $CaSO_4$, the solvent evaporated, the residue dissolved in 100 mL of toluene, 0.43 g of *p*-toluenesulfonic acid added, and the mixture refluxed until the evolution of CO_2 ceased. The toluene solution was then washed with a 20% solution of potassium carbonate and several times with water and dried over $CaSO_4$, the solvent evaporated, and the residue distilled in vacuo. The product was recrystallized from methanol and redistilled at 1 mmHg. The yield was 48% (6.2 g) and ranged between 45–55% for the other title compounds. Melting points were as follows: *p*-Br, 54–56 °C; *p*-Cl, 49–51 °C; *p*-F, 26–28 °C; *p*-OCH_3, 42–44 °C. Boiling points were as follows: H, 140–145 °C (14 mmHg); *p*-CH_3, 116–118 °C (14 mmHg). All compounds gave satisfactory elemental C and H analyses and spectra (IR, NMR) consistent with their structures.

1-Aryl-*2,2-d*$_2$-4-methoxy-1-butanones. The title compounds were all prepared by the procedure described for the *p*-bromophenyl compound. 1-(*p*-Bromophenyl)-4-methoxy-1-pentanone (2 g, 7.8 mmol) was dissolved in 3.5 mL of dioxane containing 1 mL of D_2O and 0.05 mL of redistilled triethylamine and the mixture refluxed overnight. The solvent was then evaporated and the residue dissolved in the same amount of fresh solvent. After four exchanges, the product was distilled at 1 mmHg. The yield was 89% (1.8 g); mp 54–56 °C.

1-Aryl-4-methoxy-1-butanols. The title compounds were prepared by reduction of the corresponding ketones with either $LiAlH_4$ or $LiAlD_4$ in ether and conversion of the resulting carbinol into the chloride with thionyl chloride. Both reactions were carried out in the usual way. The products were distilled twice on a vacuum line and gave 96–99% of the theoretical amount of HCl upon solvolysis. The yields based on ketones were 78–85%. The spectra (IR, NMR) of the chlorides were consistent with their structures.

1-(*p*-Methoxyphenyl)-1-hexyl Chloride and Deuterated Analogues. Chlorides were prepared from carbinols with thionyl chloride in the usual way. Carbinols were prepared from the corresponding *p*-methoxybenzaldehyde and a Grignard reagent of *n*-hexyl bromide.[4] The preparation of deuterated reagents was completely analogous to that described in the synthesis of *trans*-1-chloro-5-methyl-1-aryl-5-heptenes.[17]

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Registry No. 3a ($R_1 = R_2 = H$), 71433-84-6; **3a**-*1-d* ($R_1 = D$; $R_2 = H$), 71433-85-7; **3a**-*2-d* ($R_1 = H$; $R_2 = D$), 71433-86-8; **3b** ($R_1 = R_2 = H$), 71433-87-9; **3b**-*1-d* ($R_1 = D$; $R_2 = H$), 71433-88-0; **3b**-*2-d* ($R_1 = H$, $R_2 = D$), 71433-89-1; **3c** ($R_1 = R_2 = H$), 71433-90-4; **3c**-*1-d* ($R_1 = D$; $R_2 = H$), 71433-91-5; **3d**-*2-d* ($R_1 = H$; $R_2 = D$), 71433-92-6; **3d** ($R_1 = R_2 = H$), 71433-93-7; **3d**-*1-d* ($R_1 = D$; $R_2 = H$), 71433-94-8; **3d**-*2-d* ($R_1 = H$; $R_2 = D$), 71433-95-9; **3e** ($R_1 = R_2 = H$), 71433-96-0; **3e**-*1-d* ($R_1 = D$; $R_2 = H$), 71433-97-1; **3e**-*2-d* ($R_1 = H$; $R_2 = D$), 71433-98-2; **3f** ($R_1 = R_2 = H$), 71433-99-3; **3f**-*1-d* ($R_1 = D$; $R_2 = H$), 71434-00-9; **3f**-*2-d* ($R_1 = H$; $R_2 = D$), 71434-01-0; **7**, 71434-02-1; **7**-*1-d*, 71434-03-2; **7**-*2-d*, 71434-04-3; di-*tert*-butyl (2-methoxyethyl)malonate, 71434-05-4; diethyl (2-methoxyethyl)malonate, 6335-02-0; (2-methoxyethyl)malonic acid, 35841-35-1; isobutene, 115-11-7; *p*-methoxybenzoyl chloride, 100-07-2; *p*-methylbenzoyl chloride, 874-60-2; *p*-fluorobenzoyl chloride, 403-43-0; benzoyl chloride, 98-88-4; *p*-chlorobenzoyl chloride, 122-01-0; *p*-bromobenzoyl chloride, 586-75-4; 1-*p*-anisyl-4-methoxy-1-butanone, 71434-06-5; 1-*p*-tolyl-4-methoxy-1-butanone, 71434-07-6; 1-(*p*-fluorophenyl)-4-methoxy-1-butanone, 71434-08-7; 1-phenyl-4-methoxy-1-butanone, 34904-87-5; 1-(*p*-chlorophenyl)-4-methoxy-1-butanone, 64413-31-6; 1-(*p*-bromophenyl)-4-methoxy-1-butanone, 71434-09-8; 1-*p*-anisyl-*2,2-d*$_2$-4-methoxy-1-butanone, 71434-10-1; 1-*p*-tolyl-*2,2-d*$_2$-4-methoxy-1-butanone, 71434-11-2; 1-(*p*-fluorophenyl-*2,2-d*$_2$)-4-methoxy-1-butanone, 71434-12-3; 1-phenyl-*2,2-d*$_2$-4-methoxy-1-butanone, 71434-13-4; 1-(*p*-chlorophenyl-*2,2-d*$_2$)-4-methoxy-1-butanone, 71434-14-5; 1-(*p*-bromophenyl-*2,2-d*$_2$)-4-methoxy-1-butanone, 71434-15-6; *p*-methoxybenzaldehyde, 123-11-5; *n*-hexyl bromide, 111-25-1.

Secondary Deuterium Isotope Effects in Solvolysis of 1-Aryl-5-methyl-5-hepten-1-yl Chlorides. Comparison of π and n Participation Mechanisms

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Three series of deuterated compounds related to **1** were prepared and their solvolysis rates measured. Since the relative contribution of k_c and k_Δ to the observed solvolysis rates of **1** are known and since the isotope effects on the k_c route can be estimated, it is possible to extract from the data secondary deuterium isotope effects associated with the k_Δ process. In all cases, the α-deuterium isotope effects on k_Δ are reduced in magnitude as compared to those in the k_c process, which is consistent with bridging. β-Deuterium isotope effects on k_Δ are essentially nil which can be explained as being due to both conformational restrictions to hyperconjugative electron release from the C–D bonding orbitals caused by bridging and to charge delocalization away from the reaction center. Deuteration of the aliphatic double bond produces inverse isotope effects in all cases where anchimeric assistance is operative. The latter observation clearly demonstrates the direct involvement of the aliphatic double bond in the rate-determining step of the k_Δ process. A direct comparison of rates show that 1-aryl-4-methoxy-1-butyl chlorides **3** solvolyze slightly faster than the corresponding chlorides of the series **1**. The rate factors are, however, too small to confirm the possibility that n and π participations proceed by different mechanisms. If the aliphatic methoxyl group is directly involved in the rate-determining step of the k_Δ process throughout the series **3**, then measured isotope effects reflect transition-state structures with a variable amount of bridging, depending upon the solvent and/or the nature of the aromatic substituent.

It has been shown[2] that **1** solvolyzes, depending upon the nature of the substituent Y, from 0 to 98% by way of k_Δ. The anchimerically assisted route seems to proceed via charge-delocalized carbonium ions **2** rather than car-