Neighboring Group Participation in Solvolysis. X. Dissection of Ar_1-5 and Ar_2-6 Pathways in Trifluoroacetolysis of 4-Arylbutyl 6-Methyl-2-naphthalenesulfonates[1]

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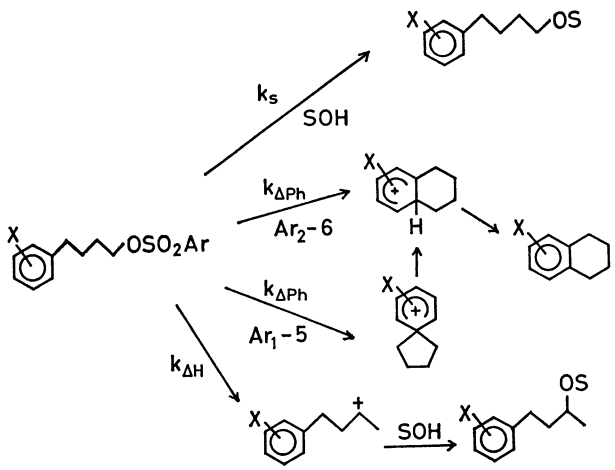
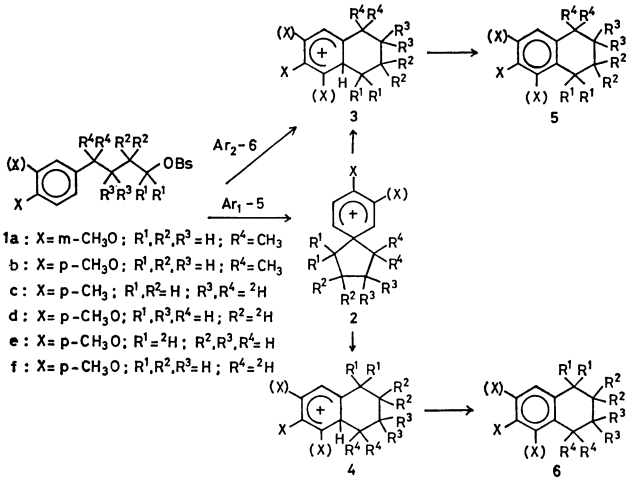
Trifluoroacetolysis rates and products were determined for eleven 4-(*m*- and *p*-substituted phenyl)butyl 6-methyl-2-naphthalenesulfonates. Most substrates solvolyze predominantly or even exclusively with aryl assisted (k_Δ) pathway. Dissection of k_Δ into Ar_1-5 and Ar_2-6 components was performed by means of quantitative ^{13}C NMR study of suitably labeled *p*-methyl and *p*-fluoro derivatives; the results were 32.4% Ar_1-5 and 67.6% Ar_2-6 for the former and 43.3% Ar_1-5 and 56.7% Ar_2-6 for the latter. For other substrates the dissection was carried out by postulating two independent linear free energy relationships (LFER) for the two pathways determined by the above four partial rates. Ar_2-6 is much prefered over Ar_1-5 through the series; for the unsubstituted derivative 90.6% Ar_2-6 *vs.* 9.4% Ar_1-5 was determined. A completely different approach by means of non-linear regression analysis of k_Δ as a sum of two independent LFER gave fairly different and rather unsettled results, limitations of such an approach being suggested. The characteristics of remote aryl participation are discussed based on the above data.

Recent study in this laboratory has shown that participation of a remote phenyl group is much more enhanced in a solvent of low nucleophilicity and high ionizing power such as trifluoroacetic acid than in an ordinary solvent.[2] 4-Phenylbutyl 6-methyl-2-naphthalenesulfonate (menasylate; Mns)[3] was found to solvolyze exclusively *via* the phenyl assisted pathway with 26.2 times rate enhancement relative to the standard, butyl menasylate. Heck and Winstein, who studied remote aryl participation in solvolysis systematically for the first time, proposed that δ-aryl participation proceeds with two possible modes; participation by the phenyl-1 (ipso) carbon forming a five-membered ring (Ar_1-5) and that by the phenyl-2 (ortho) carbon forming a six-membered ring (Ar_2-6) (Scheme 1).[4]



Scheme 1.

While anchimerically unassisted solvolysis gives a primary alkyl product, either mode of phenyl assisted solvolysis gives rise to 1,2,3,4-tetrahydronaphthalene (tetralin) as a final product. The rate constant of the former was designated k_s and that of the latter $k_{\Delta ph}$ as distinguished from $k_{\Delta H}$, the rate constant of neighboring hydrogen assisted solvolysis, which was found important in trifluoroacetic acid (Scheme 1, S= CF_3CO).[2,4] The identity of the products from the two modes of the $k_{\Delta ph}$ pathway makes its dissection difficult. The dissection is possible, however, by the double labeling technique, one lable on the phenyl ring and the other on the alkyl chain (Scheme 2).



Scheme 2.

Two differently substituted tetralins will be produced from a *p*-substituted substrate, and four from a *m*-substituted one. If we can accurately analyze the composition of tetralin isomers and also if we can reasonably estimate the migration ratio of CR^1R^1 and CR^4R^4 groups from the Ar_1-5 intermediate (**2**) to two types of protonated tetralins (**3** and **4**), then the two modes of $k_{\Delta ph}$ can be dissected quantitatively. Thus, Winstein and Heck studied the formolysis of 4-(*m*- and *p*-methoxyphenyl)butyl *p*-bromobenzenesulfonates (brosylates; Bs) utilizing methyl groups as a label on the alkyl chain (**1a** and **b**).[5] They postulated that only the $C(CH_3)_2$ group could migrate to the ortho position and the CH_2 group could not in the spiro intermediate **2**. Thus, the product ratio of **5** *vs.* **6** was considered to

be equal to the path ratio of Ar_2-6 *vs.* Ar_1-5. Introduction of two methyl groups on the chain, however, allows the intervention of a tertiary cation produced by ring opening of **2**, making the product analysis rather complicated. Furthermore, substitution with methyl groups is too large to be regarded as a perturbation. It is risky to estimate the behavior of the unperturbed substrate from the results of the dimethylated ones.

Jackman and Haddon,[6] and Gates and his coworkers[7] studied this dissection problem by use of deuterium as a label on the chain (**1c**—**f**). Although their analyses seem reasonable and substitution by deuterium is small enough a perturbation, the produced tetralins had to suffer rather drastic reaction such as oxidation or reduction before isotope analysis by means of mass spectroscopy was performed. These operations are tedious and may cause serious errors.

Carbon-13 NMR spectroscopy has become a familiar technique for organic chemists in recent years. Although quantitative application of FT NMR has so far been little exploited because of the widespread belief that the peak area does not give any information about the number of nuclei, it is actually quite useful in the quantitative and nondestructive analysis if enough precautions are taken. The large chemical shift range of ^{13}C NMR becomes one of the principal advantages in the quantitative analysis too. In this paper we report our study of the dissection of $k_{\Delta ph}$ in the trifluoroacetolysis of 4-(*p*-methyl- and *p*-fluorophenyl)butyl brosylates into Ar_1-5 and Ar_2-6 pathways by applying ^{13}C NMR to the analysis of the tetralins produced from suitably isotope-labeled substrates.

Although the double labeling technique with ^{13}C on the chain and a substituent on the ring is a sound method for evaluating the two reaction pathways, preparation of all the substituted phenylbutyl derivatives labeled with ^{13}C is laborious and expensive. Furthermore, the technique is not generally applicable because the quantitative analysis is only possible when tetralin isomers give a sufficient chemical shift difference. Among others $k_{\Delta ph}$ of the unsubstituted substrate can never be dissected by this method. On the other hand, if the two pathways are discrete and the partial rates of the both pathways follow individual LFER, a study of the substituent effects on the rate constants $k_{\Delta ph}$, when combined with the results of the double labeling technique, must give a possibility of a new and general approach to the dissection problem. Thus, $k_{\Delta ph}$ of substituted and unsubstituted substrates can reasonably be dissected to the two partial rates in such a manner as they follow two Hammett-type relationships, which have been determined by the data obtained from the double labeling method utilizing ^{13}C NMR spectroscopy. Two LFER thus obtained may give further information on the characteristics of remote aryl participation.

If the two independent LFER hold for the individual partial rates as postulated above, $k_{\Delta ph}$ can be described as a sum of them. Then, a completely different approach by means of non-linear regression analysis of substituent effects on $k_{\Delta ph}$ may become another possibility. It is a pure kinetic approach in contrast to the combination of the kinetic and product analyses described above. The results of this computer-programmed analysis are compared with those from the above combinational one, and the soundness of the two approaches is discussed.

Results

Trifluoroacetolysis rates of eleven 4-(*m*- and *p*-substituted phenyl)butyl menasylates (**7a**—**k**) were determined by the spectrophotometric method as described earlier.[2,3] The observed rate constants together with the corresponding activation parameters are given in Table 1, in which the data of butyl menasylate (**8**)[2] are also included. Each reported rate constant is the average value of duplicate to quadruplicate runs. The individual runs gave linear first-order rate plots over two half-lives for all the compounds with correlation coefficients greater than 0.9995.

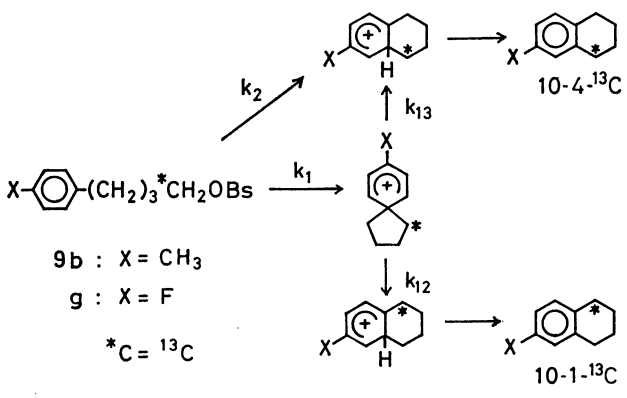
$X\text{-}C_6H_4(CH_2)_4OMns$ $CH_3(CH_2)_3OMns$

7a: X=*m*-CH_3 **g**: X=*p*-F **8**
b: X=*p*-CH_3 **h**: X=*m*-Cl
c: X=*m*-CH_3O **i**: X=*p*-Cl
d: X=*p*-CH_3O **j**: X=*p*-Br
e: X=H **k**: X=*m*-CF_3
f: X=*m*-F

Reaction products were analyzed by gas chromatography after more than six half-lives under the same conditions as those for the kinetic runs. Reaction solutions containing dodecane as an internal standard were injected directly into a gas chromatograph. The yields of the products corrected with their respective sensitivities are summarized in Table 2. Control experiments showed that typical tetralins (unsubstituted and 6-CH_3) and a primary trifluoroacetate (unsubstituted) were stable under the reaction conditions.[2]

In the trifluoroacetolysis of [1,1-$^2H_2$]-4-(*p*-methoxyphenyl)butyl menasylate (**7d**-1,1-$^2H_2$), no deuterium scrambling was detected in the recovered menasylate after one half-life. The same observation was already reported for **7e**-1,1-$^2H_2$.[2]

^{13}C NMR study was performed with 4-(*p*-methyl- and *p*-fluorophenyl)butyl brosylates (**9b** and **g**, respectively) instead of menasylates **7b** and **g**. Although the menasylate is an excellent leaving group for the rate study,



Scheme 3.

Table 1. Trifluoroacetolysis rates of 4-arylbutyl menasylates

Substituent	t/°C	$k_t \times 10^5$/s^{-1}	k_{rel}[a]	$\Delta H^{\neq}$/kcal mol^{-1} [b]	$\Delta S^{\neq}$/cal K^{-1} mol^{-1} [c]
m-CH_3 (**7a**)	50	4.19±0.02	117	19.9	−17.2
	65	17.3 ±0.1			
	70[d,e]	27.0			
p-CH_3 (**7b**)	50	3.64±0.03	106	20.3	−16.3
	60	9.58±0.03			
	70	24.3 ±0.1			
m-CH_3O (**7c**)	60	3.34±0.03	38.1	21.2	−15.5
	70	8.76±0.14			
p-CH_3O (**7d**)	60	2.93±0.02	34.2	22.1	−13.5
	70	7.86±0.04			
	80	20.6 ±0.1			
H (**7e**)[f]	70	7.46±0.02	32.4	21.2	−15.7
m-F (**7f**)	70[d]	1.02	4.43	21.3	−19.6
	85	3.95±0.02			
	105	20.3 ±0.1			
p-F (**7g**)	70[d]	1.24	5.39	21.3	−19.2
	85	4.79±0.06			
	105	24.6 ±0.3			
m-Cl (**7h**)	70[d]	0.832	3.62	21.5	−19.5
	90	4.98±0.02			
	110	24.8 ±0.1			
p-Cl (**7i**)	70[d]	0.615	2.67	22.5	−17.0
	90	3.98±0.01			
	100	9.65±0.03			
	110	21.4 ±0.1			
p-Br (**7j**)	70[d]	0.622	2.70	21.4	−20.2
	90	3.72±0.05			
	110	18.5 ±0.2			
m-CF_3 (**7k**)	70[d]	0.168	0.730	21.3	−23.2
	100	2.25±0.01			
	110	18.5 ±0.2			
$CH_3(CH_2)_3OMns$ (**8**)[f]	70[d]	0.230	1.00	23.1	−17.2

a) Relative rates to that of **8** at 70 °C. b) 1 kcal mol^{-1}=4.184 kJ mol^{-1}. c) 1 cal K^{-1} mol^{-1}=4.184 J K^{-1} mol^{-1}. d) Calculated from data at other temperatures. e) An observed rate constant of a single run was 27.4×10^{-5} s^{-1}. f) Ref. 2.

menasyl chloride is commercially unavailable. As the difference in the leaving group is reasonably expected to have no effect on the fractions of the two neighboring aryl assisted pathways, **9b** and **g** both labeled with 90% ^{13}C at 1-position as well as the unlabeled ones were prepared and solvolyzed. ^{13}C-Enriched and "natural abundance"[8] tetralins with a substituent on the 6-position (**10b** and **g**) were isolated from the reaction solutions after more than seven half-lives and then purified by column chromatography and molecular distillation (Scheme 3).

FT NMR spectra were taken with great care under the conditions adequate for quantitative analysis,[9,10] particularly with a long pulse interval and a small pulse flip angle (*cf.* Experimental Section). Under these conditions the peak area ratio of the two benzylic carbons, 1- to 4-position, of the 6-methyl "natural abundance" tetralin (**10b**) was 1/1.016, and that of the 6-fluorotetralin (**10g**) was 1/1.097. The inequality in the latter may be attributed to the peak splitting of the C_4 by the long-range coupling with the fluorine (1.6 Hz). The peak area ratio of the ^{13}C-enriched tetralin was 1/4.950 for the 6-CH_3 derivative and 1/3.817 for the 6-F one under the same conditions as above.

Discussion

Table 1 shows that the trifluoroacetolysis rates of 4-arylbutyl menasylates **7** vary more than 10^2 depending on the substituents of the phenyl ring. This large substituent effect of the aryl group remote from the reaction center clearly indicates the development of the direct interaction between these two groups in the transition state of the reaction. It is consistent with the fact that most substrates gave tetralins as principal products in the yields more than 90% (Table 2). Thus, it is concluded undoubtedly that the trifluoroacetolyses of most of 4-arylbutyl menasylates proceed predominantly or even exclusively with remote aryl group participation.

As being implied qualitatively in the above discussion, it is generally accepted that aryl assisted ($k_{\Delta ph}$) and aryl unassisted (k_s) reactions are discrete in 4-arylbutyl solvolysis just like as in 2-arylethyl solvo-

Table 2. Trifluoroacetolysis products of 4-arylbutyl menasylates[a]

Substituent	6-Tetralin[b]	5-Tetralin[c]	1-ROTFA[d]	2-R'OTFA[e]
m-CH_3 (**7a**)[f]	48.9	51.1	0	0
p-CH_3 (**7b**)	97.6	—	0	0
m-CH_3O (**7c**)[g]	56.6	24.6	0	0
H (**7e**)	99.8	—	0	0
m-F (**7f**)	91.2[h]		2.3	2.6
p-F (**7g**)	94.3	—	0.4	1.1
m-Cl (**7h**)	47.2	42.9	3.8	4.6
p-Cl (**7i**)	91.5	—	4.4	4.8
p-Br (**7j**)	91.1	—	4.5	5.4

a) Yields in %. No analysis was performed for the *p*-CH_3O derivative (**7d**). The *m*-CF_3 derivative (**7k**) did not give a clear-cut result. b) 6-Substituted tetralin. c) 5-Substituted tetralin. d) 4-Arylbutyl trifluoroacetate. e) 3-Aryl-1-methylpropyl trifluoroacetate. f) Only relative yields were determined, but methyltetralin was confirmed to be stable under the reaction conditions. g) An unknown compound (*ca.* 5%) was detected. h) The isomers could not be separated by gas chromatography. ^{13}C and ^{19}F NMR spectra showed that the mixture contained 75±1% 6-fluoro- and 25±1% 5-fluorotetralins.

lysis.[2,5,6,11] Thus, the yields of tetralins correspond to the fractions of $k_{\Delta ph}$ in k_t. Furthermore, the lack of deuterium scrambling in the samples of **7d-** and **e**-1,1-$^2H_2$ recovered from the reaction solutions revealed that ion-pair return from the spiro Ar_1-5 intermediate to the starting menasylate, either directly or *via* the Ar_2-6 intermediate, is prohibited. Friedlich and Winstein also reported their observation that ring expansion of the spiro Ar_1-5 intermediate was very much faster than ring opening or solvolysis.[12] These facts suggest that the two pathways of $k_{\Delta ph}$ are also discrete, and that the ratio of the two partial rate constants can be described as a function of the relative amounts of two isomeric tetralins. Thus, the two partial rate constants, k_1 and k_2 in Scheme 3, are able to be calculated from the combined data of the titrimetric rate constants k_t (Table 1), the yields of tetralins determined by gas chromatography (Table 2), and the fractions of the two pathways estimated quantitatively from the contents of isomeric tetralins.

From the two sets of the ^{13}C NMR data on **10b** and **g**, the ratio of the two pathways, k_1 *vs.* k_2, can be calculated for both **9b** and **g**. A "natural abundance" tetralin was obtained from **9** labeled with 1.1% each of 1-^{13}C and 4-^{13}C, and an enriched tetralin from **9** labeled with 90% 1-^{13}C and 1.1% 4-^{13}C. Since k_1/k_2 and k_{12}/k_{13} are common for each isotopic substrate, the rate ratio k_1/k_2 can be described as a function of k_{12}/k_{13} and the peak area ratios of the two benzylic carbons in the two types of tetralins, "natural abundance" and ^{13}C-enriched. By assuming no kinetic isotope effect at the migration step ($k_{12}/k_{13}=1.00$), the fractions of the two pathways were determined 32.4% Ar_1-5 and 67.6% Ar_2-6 for the *p*-CH_3 derivative and 43.3% Ar_1-5 and 56.7% Ar_2-6 for the *p*-F one. The isotope effect can reasonably be neglected because an effect of 5% ($k_{12}/k_{13}=1.05$) could alter the fractions of the pathways by only 0.3%. Then, by neglecting the difference in the leaving group, four partial rate constants, $k_1^{p\text{-}CH_3}$, $k_2^{p\text{-}CH_3}$, $k_1^{p\text{-}F}$, and $k_2^{p\text{-}F}$, in the trifluoroacetolysis of **7** can be obtained. The ^{13}C NMR measurement was repeated for **10g** with two other FT instruments and even with a CW one in order to confirm the above results. The fractions of the two pathways thus obtained agreed with each other within a range of ±1.0%.

It is interesting to compare the present results in the trifluoroacetolysis of **9b** with those in the formolysis of **1c** reported by Jackman and Haddon.[6] Their results, 30.6—33.6% Ar_1-5 and 69.4—66.4% Ar_2-6 varying with an assumed kinetic isotope effect in the migrating step of **2**, is in complete agreement with ours. It suggests the accuracy of their results in spite of the difficulty in their experiment as well as the absence of the solvent effect on the fractions of the two pathways. The latter conclusion is reasonable because the two pathways are both neighboring aryl assisted ones and the susceptibilities of the two transition states to the nature of the solvent must be similar. It is in contrast with the solvent effect on the ratio of k_Δ *vs.* k_s as we demonstrated already.[2]

It is well known that reactivities of *m*- and *p*-substituted benzene derivatives generally follow the Hammett-type LFER.[13] Substituent effects on the rates of the neighboring aryl assisted solvolysis of 2-arylethyl derivatives have also been treated successfully in this manner.[11] As a quite natural extension of 2-arylethyl solvolysis, the two pathways of remote aryl participation are expected to follow their individual LFER. The four partial rate constants of **7b** and **g** obtained above must give rise to two Hammett-type relationships for the two pathways, which then must hold for other substrates.[14] Thus, the rate constants $k_{\Delta ph}$ of other substrates can be divided into k_1 and k_2 in such a manner as their ratios hold the ones determined by the above two LFER.

Yukawa and Tsuno proposed the LArSR (linear aromatic substituent reactivity) relationship (Eq. 1)

$$\log k/k_0 = \rho(\sigma^0 + r\Delta\bar{\sigma}_R^+) \quad (1)$$

as a generalized equation of the extended Hammett relationship for reactions with nucleophilic character.[15] According to Tsuno, most k_Δ pathways of 2-arylethyl and related substrates have *r* values (resonance parameters) about 0.5.[16] Schadt, Lancelot, and Schleyer reported that the substituent constants obtained from the acetolysis of substituted neophyl brosylates, σ(neophyl), are effective for all other related solvolyses; σ(neophyl) correspond to the substituent constants with $r=0.58$ in the Yukawa-Tsuno treatment, Eq. 1.[11] Thus, we assumed that similar substituent constants, $\sigma^0+0.5\Delta\bar{\sigma}_R^+$ ($\equiv\sigma^\Delta$), are also effective for the two remote aryl participation reactions, and carried out the kinetic dissection using these σ^Δ.

Contrast to the Ar_1-5 pathway, in which *m*- and *p*-substituents behave naturally as *m*- and *p*-ones, respectively, in the Ar_2-6 pathway *m*-substituents affect the reaction center as *o*- or *p*-ones, and *p*-substituents as *m*-ones, respectively (Scheme 2). As σ_o has not been

well established as σ_p, only σ_p was used for the Ar_2-6 pathway of the *m*-CH_3 and *m*-Cl derivatives, for which the reactivities of the *o*- and *p*-positions were estimated similar from the relative yields of 5- and 6-substituted tetralins (Table 2). The dissection of $k_{\Delta ph}$ of the *m*-F derivative, in which the reactivity of the *o*-position is apparently lower than that of the *p*-one[17] (*cf.* footnote h of Table 2), was carried out by modifying the σ_p value in order to reflect this decreased reactivity. Since the substituent constants of a methoxyl group are not clear in trifluoroacetic acid, which is a strongly acidic solvent prone to form a hydrogen bond with the methoxyl oxygen, the dissection was unable to be performed. In fact, the rate enhancement in **7c** and **d** was much smaller than that expected for substrates with a strongly electron-donating substituent. Furthermore, the product study of **7c** revealed that an unknown compound other than methoxytetralins was detected in the reaction solution. Methoxytetralins may be unstable under the reaction conditions. The dissection was also impossible for the *m*-CF_3 derivative **7k**, because its product analysis did not give a clear-cut result. Thus, the dissection by means of the combination of the product and kinetic analyses was carried out for **7a**, **b**, **e**, **f**, **g**, **h**, **i**, and **j**. The results are summarized in Table 3.

Table 3. Dissection of $k_{\Delta Ph}$ into Ar_1-5 and Ar_2-6 pathways

Substituent	$k^{70}_{\Delta Ph}\times 10^5/s^{-1}$	$k_1\times 10^5/s^{-1}$	$k_2\times 10^5/s^{-1}$	% Ar_1-5	% Ar_2-6
m-CH_3 (**7a**)	27.0	1.0	26.0	3.7	96.3
p-CH_3 (**7b**)	23.7	7.7	16.0	32.4[a]	67.6[a]
H (**7e**)	7.45	0.70	6.75	9.4	90.6
m-F (**7f**)	0.930	0.009	0.921	1.0	99.0
p-F (**7g**)	1.17	0.51	0.66	43.3[a]	56.7[a]
m-Cl (**7h**)	0.750	0.009	0.741	1.2	98.8
p-Cl (**7i**)	0.563	0.132	0.431	23.4	76.6
p-Br (**7j**)	0.567	0.122	0.445	21.5	78.5

a) Determined by NMR analysis.

The four partial rate constants of **7b** and **g** gave ρ values of -4.07 for Ar_1-5 and -3.29 for Ar_2-6. After the dissection for the other substrates were performed, the linear regression of the calculated partial rate constants of all the substrates except **7f** gave the two LFER, Eqs. 2 and 3, in which k_1^X and k_2^X represent the rate constants of the Ar_1-5 and Ar_2-6 pathways, respectively, of the X-substituted **7**, and k^H ($=k_1^H+k_2^H$) denotes the overall rate constant of **7e**. The two LFER are plotted in Fig. 1.

$$\log k_1^X/k^H = -4.42\sigma^\Delta - 0.99 \quad \text{(correlation coeff: 0.985)} \quad (2)$$

$$\log k_2^X/k^H = -3.05\sigma^\Delta - 0.07 \quad \text{(correlation coeff: 0.978)} \quad (3)$$

The successful dissection of the rate constants of the neighboring aryl assisted reaction, $k_{\Delta ph}$, into k_1 and k_2, which are described by the two independent LFER, suggests a possibility of completely different approach. Since the two LFER are represented as Eqs. 4 and 5,

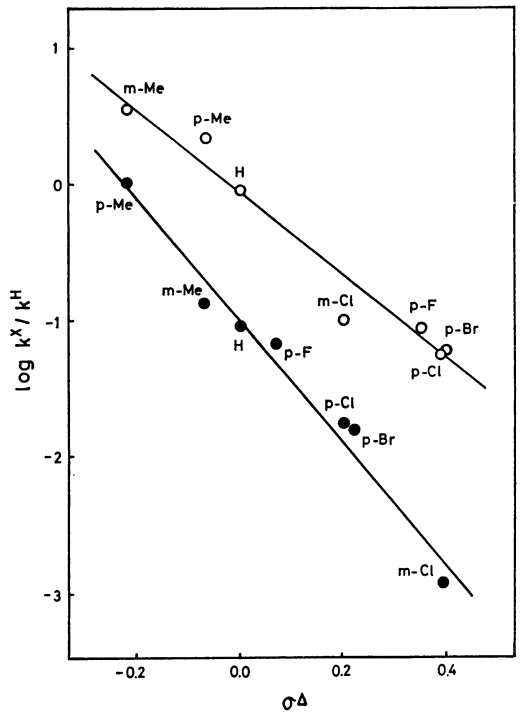


Fig. 1. LFER plots of dissected rate constants *vs.* σ^Δ.
●: k_1 (for Ar_1-5), ○: k_2 (for Ar_2-6).

the substituent effects on $k_{\Delta ph}$ ($\equiv k=k_1+k_2$) can be written as Eq. 6.

$$\log k_1^X/k_1^H = \rho_1\sigma_1^\Delta; \quad k_1^X = k_1^H\, 10^{\rho_1\sigma_1^\Delta} \quad (4)$$

$$\log k_2^X/k_2^H = \rho_2\sigma_2^\Delta; \quad k_2^X = k_2^H\, 10^{\rho_1\sigma_1^\Delta} \quad (5)$$

$$k^X/k^H = k_1^X/k^H + k_2^X/k^H = k_1^H\, 10^{\rho_1\sigma_1^\Delta}/k^H + k_2^H\, 10^{\rho_1\sigma_1^\Delta}/k^H \quad (6)$$

When the Ar_1-5 fraction of **7e**, k_1^H/k^H, is designated α, Eq. 6 can be substituted by Eq. 7.

$$k^X/k^H = \alpha 10^{\rho_1\sigma_1^\Delta} + (1-\alpha)10^{\rho_1\sigma_1^\Delta} \quad (7)$$

Non-linear regression analysis utilizing Eq. 7 was thus performed by putting in k^H and sets of k^X, σ_1^Δ, σ_2^Δ in order to determine the optimum values of α, ρ_1, and ρ_2. Computer-programmed calculations by means of the simplex[18] and Powell methods[19] gave a same answer, Eqs. 8 and 9.

$$\log k_1^X/k^H = -3.95\sigma^\Delta - 0.54 \quad \text{(correlation coeff: 0.996)} \quad (8)$$

$$\log k_2^X/k^H = -3.53\sigma^\Delta - 0.24 \quad \text{(correlation coeff: 0.997)} \quad (9)$$

Although the linearity of each LFER is excellent, fractions of the two pathways for all the substrates are quite different from those obtained by the combinational approach of product and kinetic analyses (Table 3). In particular, the calculated results for **7b** and **g**, 67% Ar_1-5 and 33% Ar_2-6 for **7b** and 83% Ar_1-5 and 17% Ar_2-6 for **7g**, did not coincide with the values determined directly by the NMR analysis at all.

Since the substituent constants are variable as shown in Eq. 1 and we are unaware how large the resonance parameter *r* should be in the two LFER, the non-linear regression analysis was extended to include the sets of

r_1 and r_2 both varied independently from 0 to 1 in Eq. 10.

$$k^X/k^H = \alpha 10^{\rho_1(\sigma_1^0 + r_1\Delta\bar{\sigma}_{R1}^+)} + (1-\alpha)10^{\rho_2(\sigma_2^0 + r_2\Delta\bar{\sigma}_{R2}^+)} \quad (10)$$

The results varied to a large extent depending on the r values used. However, any combination of r_1 and r_2 was unable to reproduce the observed data of the fractions of the two pathways for **7b** and **g** simultaneously. Furthermore, when the non-linear regression analysis by use of Eq. 10 was performed by treating r_1 and r_2 also as variables, it converged on an improbable point where r_1 was close to 0 and r_2 was larger than 1. The observed data for **7b** and **g** were again not reproduced at this point. Thus, the nonlinear regression analysis was unsuccessful in this case.

We do not regard the failure of the non-linear regression analysis in this case as the fundamental defect of the method. This type of analysis must be easier when the two reactions have different types of characters.[11,20,21] Unfortunately, ρ_1 and ρ_2 are both negative and similar in magnitude in this case. Strict accuracy of all the data used for the analysis, *i. e.*, $k_{\Delta ph}$ and σ, is an indispensable condition in such a case. However, $k_{\Delta ph}$ are estimated values from k_t and the product yields, and the identity of σ_o and σ_p was postulated in some cases. Such uncertainties in the data used, although they must be not large, may cause the analysis very difficult in the present case.

The idea of variable substituent constants (Eq. 10) is also applicable to the combinational approach of product and kinetic analyses. Calculations were thus performed using variable r values. Fractions of the two pathways obtained for each substrate certainly varied as expected according to the sets of the r values used. However, the extent of the variation was not so large as in the case of the non-linear regression analysis with variable r. The reason is obviously because the four partial rate constants were fixed to the experimental values throughout the calculations.

The above calculations with variable r revealed some characteristic features: (i) ρ_1 is always larger than ρ_2. (ii) The linearity of the two LFER is governed mostly by the value of r_2; the correlation coefficient becomes too small (<0.97) when r_2 larger than 0.5 is employed. (iii) There is a tendency that a better linearity is obtained when r_1 is larger than r_2. Further search for a point of best fit is apparently meaningless in the present case when the risk of statistical approach such as those encountered in the non-linear regression analysis is considered. We regard the results shown in Table 3 and Eqs. 2 and 3 as a reasonable answer to the dissection problem, although some uncertainties still remain.

It is apparent from Table 3 that the Ar_2-6 pathway is much favored than Ar_1-5. For the unsubstituted ester **7e** the former is 4.5 times more rapid than the latter after the statistical correction. Since the former pathway can be regarded as a kind of electrophilic aromatic substitution at the ortho position to the alkyl chain and the latter as the one at the ipso, the above result must reflect a difference in the reactivity of these positions toward a potential electrophile. A low π-electron density at the ipso position of toluene in comparison with the other positions was calculated by Libit and Hoffmann as an extended Hückel result.[22] Recently, *ab initio* STO-3G calculations of the relative energies of "late" and "early" transition state models for attack of a proton on benzene and the various positions of toluene were reported by Santiago *et al.*[23] The results show that the relative energies are para>ortho>H(benzene)>ipso for both the late and early transition state models. Our result indicating the unfavorable Ar_1-5 pathway is thus compatible with the theoretical calculations.

Santiago *et al.* also suggested that the ipso position is deactivated toward formation of an early transition state.[23] Thus, it is expected that the ipso substitution has a later transition state than the ortho substitution. Our conclusions that ρ_1 is larger than ρ_2 and, though not secured enough, r_1 may be larger than r_2 can be attributed to the development of a positive charge to a larger extent in the case of the ipso substitution, Ar_1-5. Another possible explanation that the lower electron density at the ipso position may cause a larger electron demand in the substitution reaction can also rationalize the larger substituent effect on Ar_1-5. A larger substituent effect on the chemical shifts of the ipso carbons in ^{13}C NMR spectra was reported in the case of *p*-substituted toluenes (**11**) compared with those of the para carbons of substituted benzenes (**12**).[24,25]

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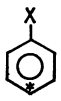

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The relative ease of remote aryl participation is affected by the ring size of the transition state other than the electronic effect. The ring size effect can be discussed in two aspects, *i.e.*, entropy and strain energy.

According to Page, the standard entropy loss on cyclization of terminal olefins is larger for a six-membered ring than for a five-membered one by *ca.* 8 cal K^{-1} mol^{-1} (=33 J K^{-1} mol^{-1}) at 298 K.[26] The corresponding difference in the ring-size corrections in Benson's thermochemical analysis[27] is also 8.5 cal K^{-1} mol^{-1}. Thus, the activation entropy must be in favor of the five-membered transition state. On the other hand, the strain energy of cyclopentane is 6 kcal mol^{-1} larger than that of cyclohexane.[28] Thus, the activation enthalpy must be in favor of the six-membered transition state. The preponderance of the Ar_2-6 pathway may be the outcome of the relative importance of the ethalpy term, but the firm conclusion is difficult because of the simultaneous operation of the electronic effect described above.

In connection with the above discussion, it is interesting to compare the activation parameters of the pairs of the substrates with same substituents at the *m*- and *p*-positions, namely **7a**, **c**, **f**, and **h** *vs.* **7b**, **d**, **g**, and **i**, respectively (Table 1). Throughout the series of these pairs, the *m*-substituted esters have smaller enthalpies

and smaller (more negative) entropies of activation than the corresponding *p*-substituted isomers. The activation enthalpy of **7f** must be raised slightly because of the peculiar deactivation at the ortho position of the fluorine substituent (*vide supra*).[17] It is apparent from Table 3 that the *m*-substituted esters solvolyze almost exclusively *via* the Ar_2-6 pathway. This must be also true for the *m*-CH_3O ester **7c**.[5] On the contrary, the solvolyses of the *p*-isomers proceed considerably *via* the Ar_1-5 pathway. Thus, the differences in the activation parameters are in perfect harmony with the differences in the reaction pathways. Furthermore, these observations secure our first assumption that the two modes of remote aryl participation are discrete.

Finally, the magnitude of the ρ values should be discussed briefly. The value for the Ar_1-5 pathway, *ca.* −4, is well in the range of the ρ values for the k_Δ pathway of 2-phenylethyl solvolysis (Ar_1-3).[11] Ouellette *et al.* reported that the ρ^+ values of the acetolyses decreased in the order benzyl>2-phenylethyl>4-phenylbutyl systems.[21] However, in their analysis of the acetolysis rates of 4-arylbutylmercury(II) perchlorates, they regarded all the k_Δ pathway as Ar_1-5. Since it is not the case as revealed in the present study, their ρ^+ value, −1.2, must be in serious error. Similar magnitudes of the ρ values for the Ar_1-5 and Ar_1-3 pathways rather indicate that the electronic natures of the aromatic rings in these through-space interactions with the potential electrophiles are almost identical independently of the ring size.

Experimental

General. All melting points were determined on a Yanagimoto MP-S2 hot stage melting point apparatus and not corrected. ^1H NMR spectra were obtained on a Hitachi R-20 or R-24 instrument at 60 MHz using tetramethylsilane as an internal standard.

Preparation of 4-Aryl-1-butanols. All the 4-(*p*-substituted phenyl)-1-butanols were prepared by the Friedel-Crafts reaction of substituted benzenes with succinic anhydride and aluminum chloride,[29] followed by the Wolff-Kishner reduction,[30] esterification, and lithium aluminum hydride reduction, successively. All the 4-(*m*-substituted phenyl)-1-butanols except the *m*-CH_3 derivative were prepared from the corresponding 3-(*m*-substituted phenyl)-1-propanols *via* chlorides,[31] cyanides,[32] acids, and esters, successively. The propanols were prepared by the Knoevenagel reaction of the corresponding *m*-substituted benzaldehydes with malonic acid,[33] followed by esterification and lithium aluminum hydride reduction.[34] 4-(*m*-Tolyl)-1-butanol was prepared by the hydroboration-oxidation[35] of 4-(*m*-tolyl)-1-butene, which was obtained by the coupling reaction of *m*-tolylmethylmagnesium chloride with allyl bromide.[36,37]

4-(m-Tolyl)-1-butanol: Bp 130.5 °C/7.5 Torr (1 Torr= 133.322 Pa). Found: C, 80.17; H, 9.99%. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82%.

4-(m-Fluorophenyl)-1-butanol: Bp 90—92 °C/5.5 Torr. Found: C, 71.12; H, 7.87%. Calcd for $C_{10}H_{13}FO$: C, 71.40; H, 7.79%.

4-(p-Fluorophenyl)-1-butanol: Bp 138.5—139.5 °C/15 Torr. Found: C, 71.17; H, 7.97%. Calcd for $C_{10}H_{13}FO$: C, 71.40; H, 7.79%.

4-(m-Chlorophenyl)-1-butanol: Bp 133 °C/5.0 Torr. Found: C, 64.89; H, 7.32; Cl, 19.02%. Calcd for $C_{10}H_{13}ClO$: C, 65.04; H, 7.10; Cl, 19.20%.

4-(p-Chlorophenyl)-1-butanol: Bp 140—148 °C/4.5 Torr. Found: C, 65.16; H, 7.21; Cl, 19.11%. Calcd for $C_{10}H_{13}ClO$: C, 65.04; H, 7.10; Cl, 19.20%.

4-(p-Bromophenyl)-1-butanol: Bp 157—158 °C/5.0 Torr. Found: C, 52.26; H, 5.75; Br, 34.58%. Calcd for $C_{10}H_{13}BrO$: C, 52.42; H, 5.72; Br, 34.88%.

4-(m-Trifluoromethylphenyl)-1-butanol: Bp 119—120 °C/40 Torr. Found: C, 60.25; H, 5.89; F, 25.78%. Calcd for $C_{11}H_{13}F_3O$: C, 60.55; H, 6.01; F, 26.12%.

Preparation of Labeled Alcohols. Both [1-^{13}C]-4-(*p*-tolyl)-1-butanol and [1-^{13}C]-4-(*p*-fluorophenyl)-1-butanol were prepared by carbonation of the corresponding Grignard reagents with $^{13}CO_2$ gas,[38] followed by esterification and reduction. [1,1-$^2H_2$]-4-(*p*-Methoxyphenyl)-1-butanol was prepared by the reduction of ethyl 4-(*p*-methoxyphenyl)-butanoate with lithium aluminum deuteride.

Table 4. Physical properties and analytical data of 4-(*m*- and *p*-substituted phenyl)butyl menasylates (**7**) and brosylates (**9**)

Ester	Subst	Mp/°C	Solv[a]	Carbon Found(Calcd)	Hydrogen Found(Calcd)	Sulfur Found(Calcd)	Other Found(Calcd)
7a	*m*-CH_3	64.0—64.3	P–B	71.82(71.71)	6.54(6.57)	8.87(8.70)	
7b	*p*-CH_3	131.2—131.7	L	71.56(71.71)	6.46(6.57)	8.85(8.70)	
7c	*m*-CH_3O	54.8—55.4	Pe–B	68.65(68.72)	6.21(6.29)	8.28(8.34)	
7d	*p*-CH_3O	95.5—96.5	H–B	68.54(68.72)	6.14(6.29)	8.08(8.34)	
7f	*m*-F	79.5—80.5	H–B	67.45(67.72)	5.52(5.68)	8.63(8.61)	
7g	*p*-F	97.8—98.5	H–B	67.99(67.72)	5.37(5.68)	8.79(8.61)	
7h	*m*-Cl	71.8—72.0	Pe–B	65.06(64.86)	5.42(5.44)	8.31(8.24)	(Cl) 9.33(9.11)
7i	*p*-Cl	122.3—123.4	C	64.86(64.86)	5.25(5.44)	8.43(8.24)	(Cl) 9.33(9.11)
7j	*p*-Br	125.2—125.7	C	58.08(58.20)	4.83(4.88)	7.49(7.40)	(Br) 18.28(18.44)
7k	*m*-CF_3	72.8—73.5	H	62.62(62.55)	5.02(5.01)	7.68(7.59)	(F) 13.22(13.49)
7d-1,1-$^2H_2$	*p*-CH_3O	95.7—96.2	H–B	68.27(68.30)	6.19(6.23)	8.33(8.29)	
9b	*p*-CH_3	46.0—46.5[c]	Pe–E	53.18(53.27)	4.88(5.00)	8.39(8.37)	(Br) 20.87(20.85)
9b-1-^{13}C[b]	*p*-CH_3	45.0—45.4	Pe–E	53.03(53.15)	4.99(4.98)	8.41(8.35)	(Br) 20.54(20.80)
9g-1-^{13}C[b]	*p*-F	liquid[d]	P	49.34(49.51)	3.98(4.15)	8.58(8.26)	(Br) 20.31(20.59)

a) Solvent used for recrystallization: B, benzene; C, carbon tetrachloride; E, ether; H, hexane; P, pentane; Pe, petroleum ether. b) Calculated values are for 90% ^{13}C enrichment. c) Lit,[6] 45.5—46.5 °C. d) Recrystallized from pentane at low temperature.

[*1*-^{13}C]-*4*-(p-*Tolyl*)-*1*-*butanol*: Bp 102—103 °C/3.5 Torr. ^{13}C Enrichment was 89.4% as measured by ^{1}H NMR.

[*1*-^{13}C]-*4*-(p-*Fluorophenyl*)-*1*-*butanol*: Bp 127—128 °C/10 Torr. ^{13}C Enrichment was 90.4% as measured by ^{1}H NMR.

[*1,1*-$^2H_2$]-*4*-(p-*Methoxyphenyl*)-*1*-*butanol*: Bp 151—152 °C/7.0 Torr. Deuterium content was better than 99% as measured by ^{1}H NMR.

Preparation of 4-Arylbutyl Arenesulfonates. The menasylates and brosylates were prepared by the standard procedures from alcohols with menasyl chloride and brosyl chloride, respectively, at 0 °C in pyridine as a solvent.[3,39] Physical properties and analytical data of these esters are summarized in Table 4.

Preparation of Solvolysis Products. *4-(*p-*Chlorophenyl)-butyl Trifluoroacetate*: Three molar equivalents of trifluoroacetic anhydride was added dropwise to 4-(*p*-chlorophenyl)-1-butanol under stirring at 0 °C. After stirring further 2 h at room temperature, the excess of the anhydride was removed under reduced pressure. Distillation of the residual oil gave the trifluoroacetate: bp 101—111 °C/5.0 Torr. Found: C, 51.27; H, 4.25%. Calcd for $C_{12}H_{12}ClF_3O_2$: C, 51.35; H, 4.31%.

*3-(*p-*Chlorophenyl)-1-methylpropyl Trifluoroacetate and 3-(*m-*Trifluoromethylphenyl)-1-methylpropyl Trifluoroacetate*: These secondary trifluoroacetates were prepared by heating 4-(*p*-chlorophenyl)-1-butene and 4-(*m*-trifluoromethylphenyl)-1-butene, respectively, in trifluoroacetic acid at 80 °C for 6 h.[37] After removing the excess of trifluoroacetic acid, these materials were used as the authentic samples for identification of solvolysis products by gas chromatography without further purification.

5-Methoxytetralin: The Wolff-Kishner reduction[30] of 25.0 g (0.142 mol) of 3,4-dihydro-5-methoxy-1(2*H*)-naphthalenone with 23.3 g of potassium hydroxide and 16.5 ml of 90% hydrazine hydrate in 200 ml of diethylene glycol gave 14.0 g of 5-methoxytetralin: bp 109.5 °C/10 Torr (lit,[40] 85—88 °C/3 Torr).

*6-Methyltetralin (**10b**)*: This material was isolated from the trifluoroacetolysis solution of **9b**. ^{13}C NMR (C_6D_6) δ (from external tetramethylsilane)=21.1 (Me), 23.8 (C_2 and C_3), 29.3 (C_1), 29.7 (C_4), 126.9 (C_7), 129.5 (C_8), 130.2 (C_5), 134.2 (C_6), 134.9 (C_9), and 137.0 (C_{10}); ^{1}H NMR ($CDCl_3$) δ=1.89 (4H, m, CH_2), 2.38 (3H, s, Me), 2.84 (4H, m, $ArCH_2$), and 7.04 (3H, br s, Ar). Found: C, 90.09; H, 9.52%. Calcd for $C_{11}H_{14}$: C, 90.35; H, 9.65%.

*6-Fluorotetralin (**10g**)*: This material was isolated from the trifluoroacetolysis solution of **7g**. ^{13}C NMR (C_6D_6) δ (from external tetramethylsilane)=23.1 (C_2 or C_3), 23.4 (C_3 or C_2), 28.9 (C_1), 29.6 (d, J_{CF}=1.6 Hz, C_4), 112.9 (d, J_{CF}=22.0 Hz, C_7), 115.7 (d, J_{CF}=20.7 Hz, C_5), 130.9 (d, J_{CF}=7.3 Hz, C_8), 132.8 (d, J_{CF}=3.6 Hz, C_9), 139.3 (d, J_{CF}=7.3 Hz, C_{10}), and 161.7 (d, J_{CF}=240.7 Hz, C_6); ^{1}H NMR ($CDCl_3$) δ=1.76 (4H, m, CH_2), 2.72 (4H, m, $ArCH_2$), and 6.67—7.05 (3H, m, Ar). Found: C, 79.72; H, 7.26%. Calcd for $C_{10}H_{11}F$: C, 79.97; H, 7.38%.

Trifluoroacetolysis Media. Trifluoroacetic acid containing 1 wt% of trifluoroacetic anhydride and 0.125 M (1M=1 mol dm^{-3}) of sodium trifluoroacetate was prepared according to the procedure described before.[3]

Kinetic Procedures. The usual ampule technique described before was employed.[3] Absorbance at about 326 nm was measured with a Hitachi Perkin-Elmer 139 or a Hitachi 100-30 UV-visible spectrophotometer. The absorbance after more than seven half-lives was used as that at "infinity."

Product Analyses. Reaction solutions containing 0.01 M of dodecane after more than six half-lives were directly injected into a Varian Aerograph Model 2850-30 gas chromatograph with a flame ionization detector and a Hewlett-Packard 3370B digital integrator. Columns packed with Silicone DC550 on Celite 545, Silicone OV-1 on Chromosorb W AW-DMCS, or PEG 20M on Chromosorb W NAW were used. Sensitivities were determined using authentic samples for tetralin, 6-methyltetralin, 5-methoxytetralin, and 4-(*p*-chlorophenyl)butyl trifluoroacetate. For other compounds sensitivities were calculated by the method described by Sternberg *et al.*[41] Accuracy of the calculated sensitivites were confirmed for the above authentic samples.

Trifluoroacetolyses of [*1*-^{13}C]-*4*-(p-*Tolyl and* p-*Fluorophenyl)-butyl Brosylates (**9b**-*1*-^{13}C and **9g**-*1*-^{13}C)* A reaction solution of 3.0 g **9b**-1-^{13}C in 100 ml of the same media as that for kinetic runs was heated at 70 °C for 14 h. The solvent was removed under reduced pressure, water being added to the residue. Extraction with ether gave a reaction product as an oil. Column chromatography through silica gel and molecular distillation gave 890 μl of a pure sample of [1,4-^{13}C]-6-methyltetralin (**10b**-1,4-^{13}C). Found: C, 89.82; H, 9.70%. Calcd for $C_{11}H_{14}$ containing 0.9 atom of ^{13}C: C, 89.80; H, 9.59 %. A similar reaction of **9g**-1-^{13}C at 85 °C for 22 h gave [1,4-^{13}C]-6-fluorotetralin (**10g**-1,4-^{13}C). Found: C, 79.28; H, 7.24% Calcd for $C_{10}H_{11}F$ containing 0.9 atom atom of ^{13}C: C, 79.50; H, 7.34%.

Trifluoroacetolysis of [*1,1*-$^2H_2$]-*4*-(p-*Methoxyphenyl)butyl Menasylate (**7d**-*1,1*-$^2H_2$)*. A solution of 970 mg of **7d**-1,1-$^2H_2$ in 50 ml of trifluoroacetic acid containg 1 wt% of trifluoroacetic anhydride was heated at 80 °C for 120 min. After the removal of the solvent under reduced pressure, the residue was poured into ice–water. Precipitates were recovered by filteration and purified by recrystallization. No scrambling of the deuterium in the recovered **7d**-1,1-$^2H_2$ was indicated by the absence of any signal due to the α-hydrogen.

Quantitative ^{13}C NMR Measurements. The measurements were performed on a JEOL JNM-FX 100 instrument at 25.05 MHz in normal FT mode. All spectra were run on 0.56 M (^{13}C-enriched) and 1.12 M (natural abundance) samples in perdeuteriobenzene solution contained in a 10-mm tube. The spectrometer was locked on the deuterium resonance of the solvent. Spectra were obtained at a spectral width of 1000 Hz with 16K data points using a normal pulse sequence (decoupling on at all the time). A pulse width was 4 μs, which corresponds to a flip angle of 30 °. A pulse repetition time was 25 s and an acquisition time was 8.192 s. Relaxation time of benzylic carbons is 5.1 s for both C_1 and C_4 of **10b**, and 5.4 and 5.5 s for C_1 and C_4, respectively, of **10g**. A longer pulse repetition time (60 s) did not alter the results. Number of pulses was 800 for the natural abundance samples and 100 for the ^{13}C-enriched ones. Relative peak areas integrated were described in the text.

Quantitative ^{13}C NMR spectra of **10g** were also obtained on another JEOL JNM-FX 100 instrument (25.05 MHz) and a Hitachi R22-FT one (22.633 MHz) both in FT mode, and on a Hitachi R20 instrument (15.085 MHz) in CW mode. Measurements were carried out using the same samples as above but in deuteriochloroform and under different conditions. All the results were identical to within a range of ±1.0%.

Non-linear Regression Analyses. The calculations were carried out using the ACOS 900 computer at the Computation Center of Osaka University.

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