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Solvolysis of 2-Aryl-3,3-dimethyl-2-butyl p-Nitrobenzoates. β-Deuterium Kinetic Isotope Effects and the Linear Free Energy Relationships

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Abstract: Solvolysis of 2-aryl-3,3-dimethyl-2-butyl p-nitrobenzoates (4a-4d) and the 1,1,1-trideuterio derivatives (5a, 5b, 5c) in HFIP exhibited a high kinetic isotope effect, $k(CH_3)/k(CD_3)$ = 1.90 at 60°C for the deactivating substrates 4c vs 5c. This effect decreased significantly with increasing electron releasing of the substituent on the aryl ring. Hammett-Brown treatment of the rate data for 4 yielded excellent linear relationships (r = 0.999) with ρ^+ = -3.48. It is evident that the contribution of the α-methyl group to the stabilization of the cationic transition state is not constant. The approximation in the linear free energy relationship is discussed.

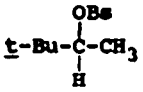
The pinacolyl, 3,3-dimethyl-2-butyl, derivatives have been a useful system for mechanistic study in organic chemistry. For instance, the secondary 3,3-dimethyl-2-butyl arenesulfonates have been employed as a model for the study of internal ion-pair returns,[1] and the solvolytic reactivity of the corresponding tertiary 2-phenyl[2] and 2-alkyl[3] p-nitrobenzoates have been correlated with steric strains. Moreover, a negligible γ-d_9 kinetic isotope effect, 1.003-1.011, for the solvolysis of 3,3-dimethyl-2-butyl p-bromobenzenesulfonate (1) has been observed.[1a]

Recently it was noticed that in the solvolysis of 2-aryl-1,1,1-trifluoro-2-propyl p-toluenesulfonates (2) and of 2-aryl-2-propyl p-nitrobenzoates (3) the β-deuterium kinetic isotope effects increased with increasing electron attracting of the substituent on the aromatic ring. It was rationalized by a variable contribution of the α-methyl group in stabilizing the cationic reaction center in the transition state.[4] The tertiary benzylic esters, 2-aryl-3,3-dimethyl-2-butyl p-nitrobenzoates (4) and the 1,1,1-tri-deuterio derivatives (5), were likely to be appropriate for testing this proposal, since the effect of the other α-alkyl group, t-butyl, on the reaction rates would be constant. The results of our kinetic studies on 4 and 5 will be discussed herein.

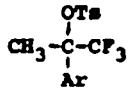
Results

2-Aryl-3,3-dimethyl-2-butyl p-nitrobenzoates (4a-4d) were prepared from 3,3-dimethyl-2-butanone with suitable aryllithium reagents, and followed by adding p-nitrobenzoyl chloride in a one-pot procedure.[5] By using the same method, their 1,1,1-trideuterio derivatives (5a-5c) could be made from Grignard reaction of trideuteriomethyl magnesium iodide with pivalyl

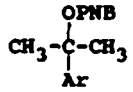
chloride in the presence of copper powder and copper(I) chloride.[6] The rate of solvolysis of 3,3-dimethyl-2-phenyl-2-butyl p-nitrobenzoate (4b) in 90% aqueous acetone is very slow and has been measured at 160°C.[2] Then the kinetic study on the less reactive 4c and 4d should be done at even higher temperature. It is undesirable to measure the isotope effect at such high temperatures because of the relatively uncertainty in measurement. This difficulty could be circumvented by carrying out the reaction in a more ionizing solvent. In the binary water-acetone or water-ethanol mixture containing more than 50% water, however, these p-nitrobenzoates were found insoluble. Hence, the highly ionizing 97% hexafluoroisopropanol(HFIP) was employed as the medium in our solvolytic studies.



(1)



(2)



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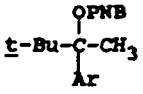

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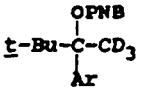
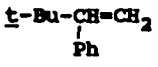
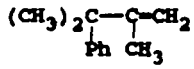


(5)

a: Ar = 4'-$CH_3C_6H_4$
b: Ar = H
c: Ar = 3'-$CF_3C_6H_4$
d: Ar = 4'-$CF_3C_6H_4$
e: Ar = 3'-ClC_6H_4



(6)



(7)

The reaction kinetics were monitored titrimetrically in 97% HFIP up to about two half-lives at appropriate temperatures. The kinetic isotope effect was measured by running the reactions side by side in the same constant temperature bath. The deviation of the rate constant was less than 2% in two independent experiments, and excellent linear regression (r = 0.995-0.999) for 8-11 points was obtained in each case. The results are shown in Table 1. Direct proton n.m.r. analysis of the reaction product from 4b indicated that in the first 15% of the solvolysis at 75°C the olefinic proton was essentially absent. About 35% of a mixture of olefins, 3,3-dimethyl-2-phenyl-1-butene (6) (olefinic protons at δ 5.16 and 4.87) (Lit δ 5.2 and 4.8)[7] and 2,3-dimethyl-3-phenyl-1-butene (7) (olefinic protons at δ 4.97 and 4.69)(Lit δ 4.9 and 4.5)[7] was found at the completion of solvolysis. Moreover, the corresponding tertiary alcohols were the major products.

The ρ values in Hammett-Brown plots[8], $\log(k/k_o) = \rho\sigma^+$, were -3.48 for 4 and -3.91 for 5. The correlation coefficients in both cases were 0.999.

Discussion

Secondary deuterium isotope effects have successfully been employed

Table 1. Rates of solvolysis of p-nitrobenzoates 4 and 5

Substrate	k/s^{-1}(°C)	$\Delta H^{\ddagger}$ kcal mol^{-1}	$\Delta S^{\ddagger}$ cal $K^{-1}mol^{-1}$
(4a)	1.68×10^{-4}(60)		
	5.63×10^{-5}(50)	22.8	-7.6
(4b)	1.87×10^{-4}(90)		
	5.59×10^{-5}(75)		
	1.50×10^{-5}(60)[b]	19.6	-21.9
(4c)	6.46×10^{-5}(125)		
	1.98×10^{-5}(110)		
	1.78×10^{-7}(60)[b]	23.3	-19.7
(4d)	4.52×10^{-5}(125)		
	1.38×10^{-5}(110)		
	1.23×10^{-7}(60)[b]	23.4	-20.2
(4e)	6.11×10^{-7}(60)[c]		
(5a)	1.61×10^{-4}(60)		
	5.31×10^{-5}(50)	23.1	-6.7
(5b)	1.63×10^{-4}(90)		
	4.74×10^{-5}(75)		
	1.23×10^{-5}(60)[b]	20.1	-20.9
(5c)	6.09×10^{-5}(125)		
	1.66×10^{-5}(110)		
	9.36×10^{-8}(60)[b]	25.6	-13.9
(5e)	3.38×10^{-7}(60)[c]		

[a] In 97% HFIP.

[b] Extrapolate from rates at higher temperature.

[c] Estimated from Hammett-Brown plot.

to investigate the rate-determining step of chemical ractions,[9] especially solvolysis.[11] On the other hand, the kinetic outcome can also be used to understand the origin of the isotope effect.[12] In a recent communication[4] we have demonstrated the hyperconjugative stabilization of the cationic transition state in the solvolysis of tertiary benzylic substrates 2 and 3. Thus, at 60°C the β-deuterium isotope effect increases from 1.04 to 2.13 for 2 and from 1.02 to 1.40 for 3 as the substituent on the aryl ring changes from the electron-releasing p-methylphenyl to the electron-attracting m-chlorophenyl.

In the present study the isotope effect was determined in 97% HFIP, since the p-nitrobenzoates 4 and 5 were very unreactive and were almost insoluble in aqueous acetone or aqueous ethanol. The solvent influence on the deuterium isotope effect for 1,1,1-trifluoro-2-phenyl-2-propyl tosylate(2b) has been studied by Tidwell and coworkers.[13] At 25°C, the

magnitude of this effect revealed only a small variation, 1.34 in 97% trifluoroethanol (TFE) and 1.28 in trifluoroacetic acid (TFA), in solvents of large difference in ionizing power, $\underline{Y}$ = 1.80 for 97% TFE and $\underline{Y}$ = 4.57 for TFA.[14]. Owing to the use of the highly electrophilic but poorly nucleophilic solvent HFIP($\underline{Y}$ = 3.79)[14,15] the solvent assitance to ionization can be ruled out. Table 1 showed that the β-deuterium kinetic isotope effect increased from 1.04 for 4a/5a and 1.22 for 4b/5b and to 1.90 for 4c/5c. The possibility of the intervention of rate-determining elimination or hydride-shift[16] in this weakly nucleophilic medium could also be excluded from the product analysis by n.m.r. (vide supra). These results are compatible with the previous finding that the effect decreases with decreasing electron demand of the α-aryl ring. Moreover, the comparison of the secondary isotope effects observed for 2, 3, and 4 (Table 2) revealed the influence of the other α-groups. As the α-group is changing from the more electron-releasing methyl to the less electron-releasing t-butyl and to the electon-attracting trifluoromethyl, the isotope effect increases and the variation becomes larger. Obviously, it strongly supports the proposal of the electron-releasing hyperconjugative origin of the isotope effect.

In considering the structure-reactivity relationships, we found that both 4 and 5 exhibited linear correlation from Hammett-Brown treatment of the rate data. These values are less negative than those calculated for systems having similar structures, e.g. 3 (ρ = -4.72) and 2-aryl-3-methyl-2-butyl p-nitrobenzoates (ρ = -4.76),[17] but are more negative than that observerd for 1-aryl-1-phenyl-1-ethyl p-nitrobenzoates (ρ = -3.23).[18] It has been pointed out that in solvolysis ρ values are essentially insensitive to solvent composition.[19] Furthermore, a normal order of reactivity, $\underline{k}$(p-CF_3)/$\underline{k}$(m-CF_3) = 0.681,[20] was realized. Thus, the less negative ρ value and the low solvolytic reactivity for 4 suggest a rate-retarding steric hindrance to resonance stabilization in the transition state.[2]

The significant increase of β-deuterium isotope effect with the increasing eletron demand of the aryl group has a remarkable mechanistic implication. The correlations of reactivities with σ^+ constants by Hammett-Brown treatment[8] have been widely employed in studying the mechanism of reactions involving the development of cationic transition states α to aryl rings.[8, 21, 22] From the previous[4] and the present studies it is evident that in the solvolysis of 2-4 the α-methyl group shows more profound influence to stabilize the cationic transition state if the latter is more electron deficient. Therefore, the Hammett-Brown treatment is unsensitive to the variation of the contribution of α-methyl group. The lack of response to the small, but definite, stabilization effect due to α-methyl groups in benzylic substrates is then an indication that there is an inherent inaccuracy in this treatment to describe the resonance effect of

Table 2. β-Deuterium isotope effects for substrates 2, 3, and 4

	$k(CH_3)/k(CD_3)$, 60°C			σ^+ [a]
	2[b]	3[b]	4[c]	
Ar = 4'-$CH_3C_6H_4$	1.04	1.02	1.04	-0.311
= H	1.38	1.18	1.22	0
=3'-ClC_6H_4	2.13	1.40	1.81[d]	0.399
=3'-$CF_3C_6H_4$			1.90	0.52

[a] Reference 8. [b] Reference 4. [c] This work.
[d] Estimated from Hammett-Brown plot.

the aryl group in the solvolytic transition state.

We have already shown the deficiency of both Hammett-Brown and Yukawa-Tsuno[20] treatments of rate data in detecting the absence of resonance interaction in the transition state.[21] Although we do not have enough data to comment the dual-parameter treatment, the present results gives further evidence that the single-parameter Hammett-Brown treatment of linear free energy relationship in solvolysis is only an approximation, and should be used with caution. Further study in this aspect is in progress.

Experimental

Capillary melting points were uncorrected. Infrared spectra(KBr) were recorded with a Perkin-Elmer Model 983G spectrometer. Proton n.m.r spectra were taken with a Varian Model EM390 or a Bruker Model AM300 instrument. Mass spectral analysis were obtained with a JOEL Model MSD-300 spectrometer at National Taiwan Normal University. Elemental analyses were performed in the Elemental Analysis Laboratory of this department.

Materials.--Reagent grade chemicals for the preparative purpose were obtained from commercial sources, and were used without purification. Solvents for the rate studies were purified according to standard methods.[24]

1,1,1-Trideuterio-3,3-dimethyl-2-butanone--Methyl-d_3-magnesium iodide was made from methyl-d_3 iodide (99% D minimum from E. Merck) and magnesium granules in anhydrous diethyl ether by conventionl method. It was then transferred through a Teflon tubing into a flask containing equivalent amount of copper powder, copper(I) chloride and trimethylacetyl chloride in ether at 0°C. After being stirred for two hours at this temperature, it was allowed to raise to room temperature and the stirring was continued for six hours. Water was added and the reddish brown solution was washed with 10% sodium hydroxide to become neutral. The ethereal solution was dried($MgSO_4$) and was distilled. The yield was 50% (bp 98-99°C) from a reaction with 50-

mmole scale of the starting materials.

Preparation of benzylic esters--The p-nitrobenzoates 4a-4d, and 5a-5c were prepared from 3,3-dimethyl-2-butanone and from 1,1,1-trideuterio-3,3-dimethyl-2-butanone, respectively, with appropriate aryllithium reagents and followed by the addition of p-nitrobenzoyl chloride as was described in a one-pot procedure.[5] Characteristic infrared absorptions for nitro and ester functions are present in all p-nitrobenzoates. The yield, melting point, pertinent 90 MHz proton n.m.r. and mass spectral data, and the analytical data of these compounds are listed as follows.

3,3-Dimethyl-2-(4'-methylphenyl)-2-butyl p-nitrobenzoate (4a): yield 41%; m.p. 170-171°C; proton n.m.r.(CCl_4) δ 1.03(s, 9, t-Bu), 2.01(s, 3, Me), 2.32 (s, 3, Me), 6.93(br s, 4, C_6H_4), 8.13 and 8.19(d, 4, C_6H_4); M.s.(20eV): m/z 341(M^+), 338($M^{+\cdot}$ - t-Bu), 150($NO_2C_6H_4CO^+$, 100%).Anal. Found:C,70.29; H,6.74; N,4.30 ($C_{20}H_{23}NO_4$ requires C,70.38; H,6.74; N,4.11%).

3,3-Dimethyl-2-phenyl-2-butyl p-nitrobenzoate (4b): yield 46%; m.p. 105-106°C (Lit 95-96°C)[2]; proton n.m.r.(CCl_4)δ 1.06(s, 9, t-Bu), 2.04(s, 3, Me), 7.18(s, 5, Ph), 8.20 and 8.23(d, 4, C_6H_4); M.s.(20eV):m/z 270($M^{+\cdot}$ - t-Bu), 150($NO_2C_6H_4CO^+$, 100%)

3,3-Dimethyl-2-(3'-trifluoromethylphenyl)-2-butyl p-nitrobenzoate (4c): yield 52%; m.p. 153.5-154°C; proton n.m.r.(CCl_4)δ 1.07(s, 9, t-Bu), 2.08 (s, 3, Me), 7.38-7.50(m, 4, C_6H_4), 8.23 and 8.28(s, 4, C_6H_4); M.s.(20 eV):m/z 395(M^+), 338($M^{+\cdot}$ - t-Bu), 150($NO_2C_6H_4CO^+$, 100%) Anal. Found:C,60.76; H,5.07; N,3.52 ($C_{20}H_{20}NO_4F_3$ requires C,60.76, H,5.06; N,3.54%).

3,3-dimethyl-2-(4'-trifluoromethylphenyl)-2-butyl p-nitrobenzoate (4d): yield 39%; m.p. 163-164°C; proton n.m.r.(CCl_4) δ 1.07(s, 9, t-Bu) 2.06 (s, 3, Me), 7.18, 7,28, 7.46 and 7.56(dd, 4, C_6H_4), 8.21 and 8.27(d, 4, C_6H_4); M.s.(20 eV)m/z 395(M$^{\cdot}$), 150($NO_2C_6H_4\dot{C}O^{\cdot}$, 100%). Anal. Found: C,60.76; H,5.07; N,3.48 ($C_{20}H_{20}NO_4F_3$ requires C,60.76; H,5.06; N,3.54%).

1,1,1-Trideuterio-3,3-dimethyl-2-(4'-methylphenyl)-2-butyl p-nitrobenzoate (5a): yield 37%; m.p. 173-173.5°C; proton n.m.r.(CCl_4) δ 1.03(s, 9, t-Bu), 2.30(s, 3, Me), 6.96(br s, 4, C_6H_4), 8.21 and 8.24(d, 4, C_6H_4); M.s.(20 eV)m/z 344(M^+), 150($NO_2C_6H_4CO^+$, 100%).

1,1,1-Trideuterio-3,3-dimethyl-2-phenyl-2-butyl p-nitrobenzoate (5b): yield 22%; m.p. 103-103.5°C; proton n.m.r.(CCl_4)δ1.03(s, 9, t-Bu), 7.18 (br s, 5, Ph), 8.23 and 8.26(d, 4, C_6H_4); M.s. (20 eV)m/z 273($M^{+\cdot}$ - t-Bu), 150($NO_2C_6H_4CO^+$, 100%).

1,1,1-Trideuterio-3,3-dimethyl-2-(3'-trifluoromethylphenyl)-2-butyl p-nitrobenzoate (5c): yield 35%; m.p. 153-153.5°C; proton n.m.r.(CCl_4)δ 1.03(s, 9, t-Bu),7.28-7.53(m, 4, C_6H_4), 8.18 and 8.23(d, 4, C_6H_4); M.s.(20 eV)m/z 398(M^+), 341($M^{+\cdot}$ - t-Bu), 150($NO_2C_6H_4CO^+$, 100%).

Kinetic procedure--A 0.01M solution of the substrate in 97%HFIP (w/w) was prepared at room temperature and aliquots of 2 ml were sealed in KIMAX tubes under nitrogen. The ampules were placed in a well circulated

thermostat with the actual temperature measured by NBS certified thermometers of appropriate range and the variation of temperature was within 0.05°C. Eight to eleven of them were successively removed after certain time intervals, and was immediately quenched . The solution was titrated with 0.01M NaOH using bromocresol green as indicator. All rates were followed to about two half-lives, and the kinetic data were calculated using least-squares regression method. For measuring the isotope effect the solvolysis of the isotopic pairs were run side by side in the same constant temperature bath. The deviation of rate constant was smaller than 2% in two independent experiments. The mean values of the rate data are reported in Table 1.

Product analysis--A solution of 4b in 97% HFIP-D_2O was sealed in an n.m.r. tube and the composition was examined by using 300MHz proton n.m.r..

Acknowledgement

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