Kinetics and mechanism of aminolysis of phenyl acetates and phenyl trimethylacetates in dimethyl sulfoxide

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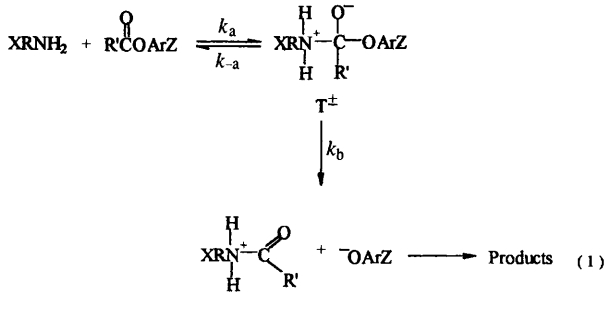
Kinetic studies have been carried out on the reactions of phenyl acetates and phenyl trimethylacetates in dimethyl sulfoxide. The rate ratios between the two acyl compounds, and the positive sign and large magnitude of the cross-interaction constants, ρ_{XZ}, between substituents X in the nucleophile and Z in the leaving group are considered to favour the rate-limiting expulsion of aryl oxide from the tetrahedral intermediate $T^{\pm}$. The aprotic solvent used makes the proposed mechanism with a cyclic transition state more attractive especially in view of the greater charge dispersion and assistance to leaving group departure provided in such a structure.

Introduction

The aminolysis of acyl compounds can occur through a stepwise mechanism, with a tetrahedral addition intermediate that has a significant lifetime,[1] or through a concerted, single step mechanism with a tetrahedral transition state (TS) and no addition intermediate.[2] The aminolysis reactions of acetate and benzoate esters,[1b,c] anhydrides,[3] methyl chloroformate,[1d] and acetyl chloride[4] exhibit a nonlinear structure–reactivity correlation of log k with the pK_a of the attacking amines showing a break from a large [$\beta_X(\beta_{nuc}) = 0.8 \sim 1.0$] to a low ($\beta_X = 0.1 \sim 0.3$) slope as the basicity of amine nucleophile increases. This behaviour has been interpreted as evidence for a change in rate determining step of a multistep reaction, from rate-limiting breakdown, k_b in eqn. (1), to formation, k_a in eqn. (1), of the intermediate. The rate-limiting step is determined



by the relative rates of expulsion of the amine nucleophile, $XRNH_2$ in eqn. (1), and leaving group, ^-OArZ in eqn. (1), from a tetrahedral addition intermediate, $T^{\pm}$, k_{-a}/k_b; the step involving the poorer leaving group (LG) is rate determining. It has often been assumed that at the breaking point where the mechanistic change occurs the pK_a values of the two groups are equal, pK_a(amine) = pK_a(LG) with $\Delta pK_a \cong 0$. However, the relative leaving ability of the two groups is not only determined by their pK_a values because of different bond strengths to carbon for different leaving atoms, steric effects, and solvent effects.[5,6] In addition, the relative rate of expulsion also depends on the push provided by the acyl group, R′ in eqn. (1), that remain behind as well as the pull provided by the group that leaves.[7]

In this work, in order to gain further information as to the effects of solvent and of the acyl group, R′, on the aminolysis mechanism, we carried out kinetic studies of the reactions of benzylamines, R = $C_6H_4CH_2$ in eqn. (1), with phenyl acetates, R′ = CH_3 and phenyl trimethylacetates, R′ = $(CH_3)_3C$, in dimethyl sulfoxide (DMSO) solvent. We varied substituents X in the nucleophile and Z in the leaving group to probe the structure of transition state (TS) through structure–reactivity correlation analysis involving the cross-interaction constants ρ_{XZ}[8] in eqn. (2). Previous work in our laboratory suggested that

$$\log (k_{XZ}/k_{HH}) = \rho_X\sigma_X + \rho_Z\sigma_Z + \rho_{XZ}\sigma_X\sigma_Z \qquad (2)$$

the sign and magnitude of ρ_{XZ} provide valuable information for the TS structure and its variation with substituents.[8]

Results and discussion

Second-order rate constants, k_2 ($dm^3\ mol^{-1}\ s^{-1}$), observed for the reactions of benzylamines with phenyl acetates at 25.0 °C and phenyl trimethylacetates at 55.0 °C in DMSO are summarized in Tables 1 and 2, respectively. The rates for the phenyl trimethylacetates are much lower, due most probably to steric effects, than those for the acetates so that the reaction temperature was raised by 30.0 °C to 55.0 °C. In general the rates are faster with a stronger nucleophile (X = p-CH_3O) as well as with a better leaving group (Z = p-NO_2) as expected from a typical nucleophilic substitution reaction. However, close examination of Tables 1 and 2 reveals that there is a large increase in the rate ratio, $r = k_2(R' = Me, 25\ °C)/k_2(R' = Bu^t, 55\ °C)$ for a poorer leaving group (Z = p-Cl) compared to that for a stronger nucleofuge (Z = p-NO_2): for X = H, r = 330 *versus* r = 12, respectively. In contrast the rate ratio changes little as the nucleophile is varied from X = p-CH_3O to X = p-Cl, *e.g.* when Z = p-Cl, r = 372 and 339 and when Z = p-NO_2, r = 12 and 13 for X = p-CH_3O and p-Cl, respectively. Similarly, comparison of the rate ratios, r, at a common temperature of 35.0 °C gave $r \cong 3.0$ and $r \cong 0.11$ for Z = p-Cl and Z = p-CN, respectively with both X = p-CH_3 and p-Cl.

This large rate decrease for phenyl trimethylacetates relative to the corresponding acetates as the leaving group is changed from Z = p-NO_2 to Z = p-Cl should indicate that steric retardation due to the *tert*-butyl group in phenyl trimethylacetates becomes important, (i) when the nucleophile is bonded to the carbonyl carbon as in the tetrahedral adduct, $T^{\pm}$, or (ii) when the nucleophile approaches closer to the carbonyl carbon in the tetrahedral TS. This conclusion can be derived from the sign (positive)[8] and magnitude (large)[8] of ρ_{XZ} (ρ_{XZ} = 0.62 and 0.69 for R = methyl and *tert*-butyl, respectively, *vide infra*). It has been shown that if ρ_{XZ} is positive, a weaker nucleofuge, $\delta\sigma_Z < 0$ (*e.g.* Z = p-Cl), leads to a tighter bond formation of the

nucleophile, $\delta\rho_X < 0$ (ρ_X is more negative), in accordance with the definition of ρ_{XZ},[8] eqns. (2) and (3). A tighter bond formation

$$\rho_{XZ} = \frac{\partial^2 \log k_{XZ}}{\partial\sigma_X\partial\sigma_Z} = \frac{\partial\rho_X}{\partial\sigma_Z} = \frac{\partial\rho_Z}{\partial\sigma_X} > 0 \qquad (3)$$

should lead to a greater steric effect. On the other hand, a large ρ_{XZ} value is an indication that the distance between the two substituents, X and Z, is shorter and hence they interact strongly in the TS as in the rate-limiting breakdown of $T^{\pm}$ in the stepwise mechanism **I**;[8] the interaction will be stronger in the breakdown step than in the concerted bond formation and bond cleavage in the single step mechanism, **II**, so that a large positive ρ_{XZ} value is in favour of the rate-limiting breakdown mechanism with TS **I**. In the tetrahedral intermediate, $T^{\pm}$, a stronger electron-withdrawing substituent in the leaving group, $\delta\sigma_Z > 0$, is known to favour the expulsion of amine and aryl oxide by destabilizing the intermediate in general but the sensitivity to polar substituents is larger for substituents on oxygen than on nitrogen, ($|\rho_X| < |\rho_Z|$).[1h,7] This relative magnitude of ρ_X and ρ_Z is indeed borne out in our results, as shown in Tables 1 and 2. Since a stronger electron-withdrawing substituent destabilizes the intermediate $T^{\pm}$ more the steric effect within $T^{\pm}$ should be relatively smaller if such a stronger electron-withdrawing group is present in the LG. On the other hand, the relatively small difference in rate ratio, r, with the variation of nucleophile ($\delta\sigma_X > 0$) is an indication that large differences in the degree of bond cleavage [$\delta\rho_Z$ is greatly positive since ρ_{XZ} is greatly positive, eqn. (3)] has little effect on the degree of bond making.[8]

The β_X and β_Z values listed in Tables 1 and 2 are considered to be less reliable since the pK_a values used are not those determined in DMSO but those determined in water. Moreover the pK_a value for X = *p*-CH_3O is excluded from the correlation so that the β_X values are obtained only with three pK_a values. Thus the β_X and β_Z values given in Tables 1 and 2 are considered to indicate only the trends of changes with substituents. The magnitude of ρ_X is well within the range of the ρ_X values for typical nucleophilic substitution reactions. The magnitude of ρ_Z is, however, somewhat larger, especially for the phenyl trimethylacetates, than those for a typical concerted process.

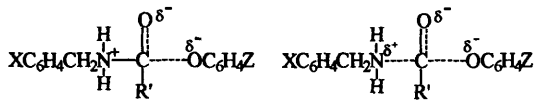
Relatively large ρ_Z (ρ_{lg}) values observed in aprotic solvent has been considered to favour the rate-limiting breakdown of $T^{\pm}$ since an electron-withdrawing substituent in the leaving group of the ester shifts the equilibrium in eqn. (1) to the right and accelerates the second step.[9] In contrast, simultaneous bond cleavage and bond formation of the carbonyl carbon in **II** should result in small ρ_Z values (1 ~ 2).[9b] Compared to protic solvents, aprotic solvents favour expulsion of amine from $T^{\pm}$ leading to rate-limiting expulsion of aryl oxide leaving group, since an aprotic solvent, *e.g.* DMSO, stabilizes the TS, **III**, for the breakdown of $T^{\pm}$ to form uncharged products relative to that for the formation of aryl oxide anion and cationic amide, **I**.[9]

The rate constants, k_2, in Tables 1 and 2 were subjected to multiple regression analysis using eqn. (2).[8] The results are given by eqns. (4*a*) and (4*b*) for phenyl acetates and phenyl

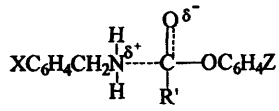
$$\log (k_{XZ}/k_{HH}) = -1.21\sigma_X + 1.72\sigma_Z^- + 0.62\sigma_X\sigma_Z^- \qquad (4a)$$

$$\log (k_{XZ}/k_{HH}) = -0.98\sigma_X + 2.81\sigma_Z^- + 0.69\sigma_X\sigma_Z^- \qquad (4b)$$

trimethylacetates respectively. The ρ_{XZ} values (0.62 and 0.69) are positive and relatively large. The definition of ρ_{XZ},[8] eqn. (3), requires an earlier TS for a stronger nucleophile and/or a stronger nucleofuge, *i.e.* a less positive ρ_Z value for a more negative σ_X [eqn. (5*a*)] and a more positive (or a less negative) ρ_X for a more positive σ_Z [eqn. (5*b*)]. Variations of ρ_X with respect



I **II**



III

$$\rho_{XZ} = \frac{\partial\rho_Z}{\partial\sigma_X} = \frac{(-)}{(-)} > 0 \qquad (5a)$$

$$\rho_{XZ} = \frac{\partial\rho_X}{\partial\sigma_Z} = \frac{(+)}{(+)} > 0 \qquad (5b)$$

to σ_Z and of ρ_Z with respect to σ_X in Tables 1 and 2 confirm that these expectations [eqns. (5*a*) and (5*b*)] are fulfilled. The magnitude of ρ_{XZ} has been shown to be inversely proportional to the distance between the two substituents.[8d] Thus, as discussed above, the relatively large magnitude (considering an intervening methylene group in benzylamine which is known to reduce the magnitude by a factor of approximately 2.8)[8a,b] observed in the present work favours the rate-limiting expulsion of an aryl oxide leaving group from $T^{\pm}$ in the stepwise mechanism relative to a concerted nucleophilic substitution. For S_N2 processes, the ρ_{XZ} values were typically *ca.* 0.1 ~ 0.3 under similar reaction conditions (including the intervening non-conjugate group).[8]

Secondary kinetic isotope effects involving deuteriated benzylamine nucleophiles[8c] are summarized in Tables 3 and 4. Benzylamines have two mobile protons so that in a general base-catalysed nucleophilic attack in S_N2 type concerted processes one of the mobile hydrogens on the N atom will cause an inverse isotope effect due to steric hindrance to N–H bending vibration. Thus, in such cases, the k_H/k_D values are either less than unity (inverse effect) or marginally greater than unity (normal effect) due to cancellation of the primary kinetic effect of deprotonation process.[8c] The k_H/k_D values observed in Tables 3 and 4 are all greater than 1.0.

Similarly, if the reactions proceed by a stepwise mechanism with rate-limiting breakdown of $T^{\pm}$ the H–N–H moiety will be sterically relieved in the TS as the LG departs from $T^{\pm}$, **I**. This will cause a decrease in the N–H vibration frequencies and the k_H/k_D values will be greater than 1.0. Thus, the normal k_H/k_D values ($k_H/k_D > 1.0$) alone do not allow us to predict the correct mechanism. Previously we have noted that the k_H/k_D values are close to 1.0 in the rate-limiting breakdown of $T^{\pm}$.[10] The values in Tables 3 and 4 are somewhat larger than those values for such a mechanism. This can be rationalized by a cyclic TS of the types shown as **IV** and **V**, respectively, for the stepwise and concerted mechanism.

The cyclic TSs are often suggested for reactions in solutions of low relative permittivity since the cyclic TSs minimize charge creation, or separation, and have an energetic advantage.[9b] In such cyclic proton transfer, leaving group departure is facilitated in addition to charge dispersion. The assistance to bond cleavage of the LG is especially important in aprotic solvents since the solvent cannot assist by hydrogen bonding. It is difficult to choose one from the two cyclic TSs, but as noted above the relatively large ρ_{XZ} values observed favour **IV** rather than **V**; in the two structures, **IV** and **V**, interaction between substituents X and Z will be strong since X and Z can interact

Table 1 Second-order rate constants, k_2/dm^3 mol^{-1} s^{-1} for the reactions of Z-phenyl acetates with X-benzylamines in DMSO at 25.0 °C

X or Z	*p*-Cl	*m*-CN	*p*-CH_3CO	*p*-CN	*p*-NO_2	ρ_Z^{-} [a]	β_Z [b]
p-CH_3O	0.129	0.398	1.14	2.00	5.27	1.55	−0.74
p-CH_3	0.045[c]			0.905[c]			
	0.102	0.316	0.932	1.65	4.78	1.61	−0.76
	0.210[d]			3.01[d]			
H	0.0676	0.224	0.759	1.40	4.01	1.72	−0.82
p-Cl	0.188[c]			0.66[c]			
	0.0390	0.137	0.534	1.03	3.17	1.85	−0.88
	0.0810[d]			1.88[d]			
ρ_X [e]	−1.05	−0.93	−0.66	−0.56	−0.44		
β_X [f]	1.04	0.91	0.61	0.52	0.44		

[a] Correlation coefficients were better than 0.998 in all cases. [b] Correlation coefficients were better than 0.988 in all cases. [c] At 15.0 °C. [d] At 35.0 °C. [e] Correlation coefficients were better than 0.997 in all cases. [f] Correlation coefficients were better than 0.998 in all cases. X = *p*-CH_3O is excluded from the Brønsted plot for β_X(benzylamine) due to unreliable pK_a values listed.

Table 2 Second-order rate constants, $k_2/10^{-3}$ dm^3 mol^{-1} s^{-1} for the reactions of Z-phenyl trimethylacetates with X-benzylamines in DMSO at 55.0 °C

X or Z	*p*-Cl	*m*-CN	*p*-CH_3CO	*p*-CN	*p*-NO_2	ρ_Z^{-} [a]	β_Z [b]
p-CH_3O	0.347	4.17	30.2	98.1	457	3.02	−1.43
p-CH_3	0.0680[c]			25.3[c]			
	0.140[d]			46.3[d]			
	0.288	3.16	26.3	85.1	407	3.06	−1.45
H	0.204	2.40	18.6	67.2	321	3.10	−1.47
p-Cl	0.0266[c]			17.3[c]			
	0.0553[d]			25.0[d]			
	0.115	1.58	13.0	45.6	242	3.20	−1.53
ρ_X [e]	−0.96	−0.82	−0.76	−0.67	−0.56		
β_X [f]	1.00	0.75	0.76	0.68	0.56		

[a] Correlation coefficients were better than 0.998 in all cases. [b] Correlation coefficients were better than 0.985 in all cases. [c] At 35.0 °C. [d] At 45.0 °C. [e] Correlation coefficients were better than 0.996 in all cases. [f] Correlation coefficients were better than 0.998 in all cases. X = *p*-CH_3O is excluded from the Brønsted plot for β_X(benzylamine) due to unreliable pK_a values listed.

Table 3 Kinetic isotope effects for the reactions of Z-phenyl acetates with deuteriated X-benzylamines in DMSO at 25.0 °C

X	Z	k_H/dm^3 mol^{-1} s^{-1}	k_D/dm^3 mol^{-1} s^{-1}	k_H/k_D
H	*p*-NO_2	4.01 ± 0.05[a]	3.23 ± 0.07	1.24 ± 0.007[b]
	p-CN	1.40 ± 0.02	1.16 ± 0.03	1.20 ± 0.008
	p-CH_3CO	0.759 ± 0.006	0.644 ± 0.008	1.18 ± 0.01
	m-CN	0.224 ± 0.006	0.191 ± 0.007	1.17 ± 0.01
	p-Cl	0.0676 ± 0.0007	0.0585 ± 0.0008	1.16 ± 0.02
Z	X	$k_H/10^{-1}$ dm^3 mol^{-1} s^{-1}	$k_D/10^{-1}$ dm^3 mol^{-1} s^{-1}	k_H/k_D
p-Cl	*p*-CH_3O	1.29 ± 0.02[a]	1.20 ± 0.02	1.07 ± 0.007[b]
	p-CH_3	1.02 ± 0.02	0.899 ± 0.01	1.14 ± 0.008
	H	0.676 ± 0.007	0.585 ± 0.008	1.16 ± 0.02
	p-Cl	0.390 ± 0.004	0.325 ± 0.006	1.20 ± 0.01

[a] Standard deviation. [b] Standard error.

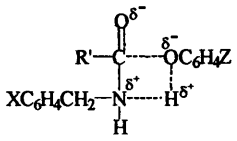
Table 4 Kinetic isotope effects for the reactions of Z-phenyl trimethylacetates with deuteriated X-benzylamines in DMSO at 55.0 °C

X	Z	$k_H/10^{-3}$ dm^3 mol^{-1} s^{-1}	$k_D/10^{-3}$ dm^3 mol^{-1} s^{-1}	k_H/k_D
H	*p*-NO_2	321 ± 6[a]	270 ± 5	1.19 ± 0.007[b]
	p-CN	67.2 ± 0.8	57.9 ± 0.8	1.16 ± 0.008
	p-CH_3CO	18.6 ± 0.3	16.6 ± 0.4	1.12 ± 0.01
	m-CN	2.40 ± 0.05	2.18 ± 0.06	1.10 ± 0.01
	p-Cl	0.204 ± 0.004	0.191 ± 0.005	1.07 ± 0.02
Z	X	$k_H/10^{-4}$ dm^3 mol^{-1} s^{-1}	$k_D/10^{-4}$ dm^3 mol^{-1} s^{-1}	k_H/k_D
p-Cl	*p*-CH_3O	3.47 ± 0.06[a]	3.31 ± 0.04	1.05 ± 0.007[b]
	p-CH_3	2.88 ± 0.04	2.72 ± 0.05	1.06 ± 0.008
	H	2.04 ± 0.04	1.91 ± 0.05	1.07 ± 0.02
	p-Cl	1.15 ± 0.02	1.02 ± 0.03	1.13 ± 0.01

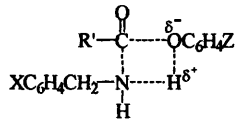
[a] Standard devation. [b] Standard error.

via two routes (an additional one is provided by the hydrogen-bonded bridge);[8c,11] however, a shorter route, therefore a stronger interaction with a larger ρ_{XZ} value, is provided in **IV**.

The k_H/k_D values observed with pyrrolidine, which has only one mobile proton, are somewhat greater (Table 5) than those corresponding values with benzylamine. The smaller k_H/k_D



IV



V

Table 5 Kinetic isotope effects for the reactions of Z-phenyl trimethylacetates with deuteriated pyrrolidine in DMSO at 55.0 °C

Z	k_H/dm^3 mol^{-1} s^{-1}	k_D/dm^3 mol^{-1} s^{-1}	k_H/k_D
p-Cl	0.408 ± 0.005[a]	0.320 ± 0.006	1.23 ± 0.007[b]
m-CN	4.80 ± 0.07	4.01 ± 0.08	1.20 ± 0.008

[a] Standard deviation. [b] Standard error.

values with benzylamine could be due to the cumulative sum of an inverse effect (k_H/k_D < 1.0) provided by the other hydrogen that is not transferred.[10]

We have determined activation parameters, $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, with the k_2 values at three temperatures as shown in Table 6. The magnitude of both parameters are within the range of values expected for normal nucleophilic substitution processes.

In summary, the magnitude of ρ_X and ρ_Z values and activation parameters are compatible with both a stepwise and concerted mechanism. However, the large ρ_{XZ} value and the relatively large secondary kinetic isotope effect involving the deuteriated benzylamine nucleophile favour a stepwise mechanism in which the cyclic TS, **IV**, is involved. The suggested stepwise mechanism is, however, somewhat surprising in view of the electron-donating nature of the acyl groups, R′ = methyl and *tert*-butyl.

High level *ab initio* MO calculations predict that an electron-donor acyl group, R′, favours a triple-well energy profile in the gas phase (which corresponds to a concerted mechanism in solution) if the leaving ability of the nucleofuge is not too poor. In contrast, for the strong nucleophile or weak nucleofuge, a single-well energy profile in the gas phase (which corresponds to a stepwise mechanism in solution) is obtained even for the electron-donating acyl group, R′.[12] On the other hand, the aminolysis reactions of benzoyl fluoride have been reported to proceed by the concerted mechanism in protic solvents;[13] in contrast, however, the mechanism of the reaction changes to a rate-limiting breakdown of $T^{\pm}$ in aprotic solvent.[9b] This is in line with the rate increase observed for the reactions involving polarizable and charge dispersed TS in such aprotic and highly polarizable solvents as DMSO or DMF.[14] In this respect, DMSO is the most likely candidate in which acyl transfer reactions proceed by the stepwise mechanism, especially because there can be no assistance to LG departure by hydrogen bonding. Moreover, the cyclic TS, **IV**, suggested will make it more attractive in DMSO, since in such a structure not only is further charge dispersion provided, but also leaving group departure is assisted.

Experimental

Materials

Merck GR DMSO was used after three distillations. The benzylamine nucleophiles, Aldrich GR, were used without further purification. Preparations of deuteriated benzylamines and pyrrolidine were as described previously.[10,11] The analysis (NMR and GC mass spectroscopy) of the deuteriated amines showed more than 99% deuterium content, so that no corrections to kinetic isotope effects for incomplete deuteriation were made. Phenyl acetates were prepared by dissolving the corresponding phenols in excess pyridine, adding excess acetic anhydride, and stirring the resulting reaction mixtures for at least 10 h, followed by cold aqueous work-up and simple distillation or recrystallization from hexane. The melting points or boiling point agreed with literature values.[15] Phenyl trimethylacetates were prepared by reacting phenols with pivaloyl chloride. These were purified by a similar method, as above. The substrates synthesized were confirmed by spectral analyses as follows.

Table 6 Activation parameters for the reactions of Z-phenyl acetates and Z-phenyl trimethylacetates with X-benzylamines in DMSO at 25.0 °C

	$\Delta H^{\ddagger}$/kcal mol^{-1} [a]	$-\Delta S^{\ddagger}$/cal mol^{-1} K^{-1} [b]
Phenyl acetates		
X = *p*-CH_3, Z = *p*-Cl	12.6	21
X = *p*-CH_3, Z = *p*-CN	10.9	23
X = *p*-Cl, Z = *p*-Cl	12.5	23
X = *p*-Cl, Z = *p*-CN	10.4	24
Phenyl trimethylacetates		
X = *p*-CH_3, Z = *p*-Cl	13.5	29
X = *p*-CH_3, Z = *p*-CN	11.2	30
X = *p*-Cl, Z = *p*-Cl	14.6	32
X = *p*-Cl, Z = *p*-CN	11.7	31

[a] Probable errors are ±0.5 kcal mol^{-1}. [b] Probable errors are ±1.0 cal mol^{-1} K^{-1}.

$CH_3C(O)OC_6H_4$-(*p*)-Cl. Liquid, $\delta_H(CDCl_3)$, 6.7–7.3 (4 H, m, phenyl), 2.2 (3 H, s, CH_3), ν_{max}(neat), 2800 (CH, aromatic), 1750 (C=O) (Calc. for $C_8H_7O_2Cl$: C, 56.5; H, 4.1. Found: C, 56.4; H, 4.2%). *m/z* 170 (M^+).

$CH_3C(O)OC_6H_4$-(*m*)-CN. Mp 59–60 °C, $\delta_H(CDCl_3)$, 7.1–7.8 (4 H, m, phenyl), 2.3 (3 H, s, CH_3), ν_{max}(KBr), 2800 (CH, aromatic), 2250 (CN), 1750 (C=O) (Calc. for $C_9H_7NO_2$: C, 67.1; H, 4.3. Found: C, 67.0; H, 4.4%). *m/z* 161 (M^+).

$CH_3C(O)OC_6H_4$-(*p*)-$COCH_3$. Mp 45–46 °C, $\delta_H(CDCl_3)$, 7.1–7.7 (4 H, m, phenyl), 2.7 [3 H, s, $COCH_3$(acetyl)], 2.3 (3 H, s, CH_3), ν_{max}(KBr), 2800 (CH, aromatic), 1730 (C=O) (Calc. for $C_{10}H_{10}O_3$: C, 67.4; H, 5.6. Found: C, 67.3; H, 5.7%). *m/z* 178 (M^+).

$CH_3C(O)OC_6H_4$-(*p*)-CN. Mp 56–57 °C, $\delta_H(CDCl_3)$, 7.1–7.8 (4 H, m, phenyl), 2.3 (3 H, s, CH_3), ν_{max}(KBr), 2800 (CH, aromatic), 2250 (CN), 1750 (C=O) (Calc. for $C_9H_7NO_2$: C, 67.1; H, 4.3. Found: C, 67.0; H, 4.4%). *m/z* 161 (M^+).

$CH_3C(O)OC_6H_4$-(*p*)-NO_2. Mp 77–79 °C, $\delta_H(CDCl_3)$, 7.1–7.8 (4 H, m, phenyl), 2.2 (3 H, s, CH_3), ν_{max}(KBr), 2800 (CH, aromatic), 1750 (C=O) (Calc. for $C_8H_7NO_4$: C, 53.0; H, 3.9. Found: C, 53.1; H, 3.8%). *m/z* 181 (M^+).

$(CH_3)_3CC(O)OC_6H_4$-(*p*)-Cl. Liquid, $\delta_H(CDCl_3)$, 7.2–7.8 (4 H, m, phenyl), 1.3 [9 H, s, $(CH_3)_3$], ν_{max}(neat), 2800 (CH, aromatic), 1750 (C=O) (Calc. for $C_{11}H_{13}O_2Cl$: C, 62.6; H, 6.1. Found: C, 62.6; H, 6.1%). *m/z* 212 (M^+).

$(CH_3)_3CC(O)OC_6H_4$-(*m*)-CN. Mp 33–34 °C, $\delta_H(CDCl_3)$, 7.1–7.6 (4 H, m, phenyl), 1.3 [9 H, s, $(CH_3)_3$], ν_{max}(KBr), 2800 (CH, aromatic), 2350 (CN), 1750 (C=O) (Calc. for $C_{12}H_{13}NO_2$: C, 70.9; H, 6.4. Found: C, 70.8; H, 6.5%). *m/z* 203 (M^+).

$(CH_3)_3CC(O)OC_6H_4$-(*p*)-$COCH_3$. Mp 48–49 °C, $\delta_H(CDCl_3)$, 7.1–7.6 (4 H, m, phenyl), 2.2 [3 H, s, $COCH_3$(acetyl)], 1.3 [9 H, s, $(CH_3)_3$], ν_{max}(KBr), 2800 (CH, aromatic), 1750 (C=O) (Calc. for $C_{13}H_{17}O_3$: C, 70.6; H, 7.7. Found: C, 70.7; H, 7.6%). *m/z* 221 (M^+).

$(CH_3)_3CC(O)OC_6H_4$-(*p*)-CN. Mp 32–33 °C, $\delta_H(CDCl_3)$, 7.1–7.6 (4 H, m, phenyl), 1.3 [9 H, s, $(CH_3)_3$], ν_{max}(KBr), 2800 (CH, aromatic), 2350 (CN), 1750 (C=O) (Calc. for $C_{12}H_{13}NO_2$: C, 70.9; H, 6.4. Found: C, 70.8; H, 6.5%). *m/z* 203 (M^+).

$(CH_3)_3CC(O)OC_6H_4$-(*p*)-NO_2. Mp 92–94 °C, $\delta_H(CDCl_3)$, 7.3–8.3 (4 H, m, phenyl), 1.3 [9 H, s, $(CH_3)_3$], ν_{max}(KBr), 2800 (CH, aromatic), 1750 (C=O) (Calc. for $C_{11}H_{13}NO_4$: C, 59.2; H, 5.8. Found: C, 59.1; H, 5.9%). *m/z* 223 (M^+).

Kinetic procedures

Rates were measured conductimetrically in DMSO. The conductivity bridge used in this work was a self-made computer automatic A/D converter conductivity bridge. Pseudo-first-order rate constants, k_{obs}, were determined by the Guggenheim method[16] with a large excess of benzylamine; [phenyl acetate] = 4.0×10^{-4} mol dm^{-3} and [benzylamine] = 0.04–0.40 mol dm^{-3}. Second-order rate constants, k_2, were obtained from the slope of a plot of k_{obs} *vs.* [benzylamine] with more than four concentrations of benzylamine, eqn. (6), where $k_1 = 0$ in

$$k_{obs} = k_1 + k_2[\text{benzylamine}] \quad (6)$$

DMSO. The k_2 values in Tables 1 and 2 are the averages of more than triplicate runs and were reproducible to within ± 3%.

Product analysis

p-Nitrophenyl acetate was treated with excess *p*-methylbenzylamine with stirring for more than 15 half-lives at 25.0 °C in DMSO, and the products were isolated by evaporating the solvent under reduced pressure. The product mixture was treated with column chromatography (silica gel, 20% ethyl acetate–hexane). The same method was used for the other product. Analysis of the products gave the following results.

$CH_3C(O)NHCH_2C_6H_4CH_3$. Mp 224–226 °C, $\delta_H(CDCl_3)$, 6.9–7.2 (4 H, m, phenyl), 5.8 (1 H, broad, NH), 4.3 (2 H, d, CH_2), 2.3 (3 H, s, $COCH_3$), 2.0 (3 H, s, CH_3), ν_{max}(KBr), 3300 (NH), 1660 (C=O) (Calc. for $C_{10}H_{13}NO$: C, 73.6; H, 8.0. Found: C, 73.5; H, 8.1%). *m/z* 163 (M^+).

$(CH_3)_3CC(O)NHCH_2C_6H_4CH_3$. Mp 226–228 °C, $\delta_H(CDCl_3)$, 6.6–7.3 (4 H, m, phenyl), 5.3 (1 H, broad, NH), 4.3 (2 H, d, CH_2), 2.3 (3 H, s, CH_3), 1.2 (9 H, s, $(CH_3)_3$), ν_{max}(KBr), 3300 (NH), 1660 (C=O) (Calc. for $C_{13}H_{19}NO$: C, 76.1; H, 9.3. Found: C, 76.2; H, 9.2%). *m/z* 205 (M^+).

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References

1 (*a*) M. L. Bender, *Chem. Rev.*, 1960, **60**, 53; (*b*) W. P. Jencks and M. Gilchrist, *J. Am. Chem. Soc.*, 1968, **90**, 2622; (*c*) E. A. Castro and C. L. Santander, *J. Org. Chem.*, 1985, **50**, 3595; (*d*) P. M. Bond, E. A. Castro and R. B. Moodie, *J. Chem. Soc., Perkin Trans. 2*, 1976, 68; (*e*) E. A. Castro and M. Freudenberg, *J. Org. Chem.*, 1980, **45**, 906; (*f*) E. A. Castro and C. Ureta, *J. Org. Chem.*, 1990, **55**, 1676; (*g*) E. A. Castro, F. Ibanez, A. M. Saitua and J. G. Santos, *J. Chem. Res.*, 1993, (*S*) 56, (*M*) 0317–0327; (*h*) M. J. Gresser and W. P. Jencks, *J. Am. Chem. Soc.*, 1977, **99**, 6963; (*i*) D. J. Hupe and W. P. Jencks, *J. Am. Chem. Soc.*, 1977, **99**, 453.
2 A. Williams, *Chem. Soc. Rev.*, 1994, **23**, 93.
3 (*a*) E. A. Castro, M. T. Borquez and P. M. Parada, *J. Org. Chem.*, 1986, **51**, 5072; (*b*) C. Castro and E. A. Castro, *J. Org. Chem.*, 1981, **46**, 2939.
4 D. J. Palling and W. P. Jencks, *J. Am. Chem. Soc.*, 1984, **106**, 4869.
5 W. P. Jencks, S. R. Brant, J. R. Gandler, G. Fendrich and C. Nakamura, *J. Am. Chem. Soc.*, 1982, **104**, 7045.
6 D. Stefanidis, S. Cho, S. Dhe-Paganon and W. P. Jencks, *J. Am. Chem. Soc.*, 1993, **115**, 1650.
7 M. J. Gresser and W. P. Jencks, *J. Am. Chem. Soc.*, 1977, **99**, 6970.
8 (*a*) I. Lee, *Chem. Soc. Rev.*, 1990, **19**, 317; (*b*) I. Lee, *Adv. Phys. Org. Chem.*, 1992, **27**, 57; (*c*) I. Lee, *Chem. Soc. Rev.*, 1995, **24**, 223; (*d*) I. Lee, *J. Phys. Org. Chem.*, 1992, **5**, 736.
9 (*a*) F. M. Menger and J. H. Smith, *J. Am. Chem. Soc.*, 1972, **94**, 3824; (*b*) M. Jedrzejczak, R. E. Motie, D. P. N. Satchell, R. S. Satchell and W. N. Wassef, *J. Chem. Soc., Perkin Trans. 2*, 1994, 1471.
10 (*a*) T. H. Kim, C. Huh, B.-S. Lee and I. Lee, *J. Chem. Soc., Perkin Trans. 2*, 1995, 2257; (*b*) H. K. Oh, C. H. Shin and I. Lee, *J. Chem. Soc., Perkin Trans. 2*, 1995, 1169; (*c*) H. J. Koh, H. C. Lee, H. W. Lee and I. Lee, *Bull. Korean Chem. Soc.*, 1995, **16**, 839.
11 (*a*) I. Lee, H. Y. Kim, H. K. Kang and H. W. Lee, *J. Org. Chem.*, 1988, **53**, 2678; (*b*) I. Lee, C. S. Shim, H. W. Lee and B.-S. Lee, *Bull. Korean Chem. Soc.*, 1991, **12**, 255; (*c*) I. Lee, H. J. Koh and H. W. Lee, *J. Chem. Res.*, 1990, (*S*) 282, (*M*) 2177–2194.
12 I. Lee, D. Lee and C. K. Kim, submitted for publication.
13 B. D. Song and W. P. Jencks, *J. Am. Chem. Soc.*, 1989, **111**, 8479.
14 C. Reichardt, *Solvents and Solvent Effects in Organic Chemistry* VCH, Weinheim, 1988, p. 218.
15 (*a*) R. L. Van Etten, J. F. Sebastian, G. A. Clowes and M. L. Bender, *J. Am. Chem. Soc.*, 1967, **89**, 3242; (*b*) T. Nishioka, T. Fugita, K. Kitamura and M. Nakajima, *J. Org. Chem.*, 1975, **40**, 2520; (*c*) J. C. Hogan and R. D. Gandour, *J. Org. Chem.*, 1991, **56**, 2821.
16 E. A. Guggenheim, *Phil. Magn.*, 1926, **2**, 538.

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