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THEORETICAL STUDIES ON THE REACTIONS OF SUBSTITUTED PHENOLATE ANIONS WITH FORMATE ESTERS*

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Semiempirical MO (PM3) studies are reported on the reactions of 18 substituted phenolate anions with *m*-(MNPF), *p*-(PNPF) and 3,4-dinitrophenyl formates (DNPF). The mechanistic change from rate-limiting formation to breakdown of the anionic intermediate (T^-) can occur in the gas phase, especially for MNPF, at approximately an equal proton affinity (*PA*) of the nucleophile and leaving group phenolates, i.e. $\Delta PA = 0$ as the *PA* of the phenolate anion is decreased. In solution, however, owing to the low stability of T^- and a greater stabilization by solvation of the transition state for the breakdown step (TS2), all three formate esters are predicted to proceed by a concerted mechanism, which is in agreement with the experimental results. The low stability of T^- can be ascribed to the relatively high electron affinity of the phenolate anions.

INTRODUCTION

Nucleophilic displacement reactions at carbonyl centers are one of the fundamental class of reactions that have been extensively studied both in solution and in the gas phase. Early experimental results of the hydrolysis of esters suggested that acyl-transfer reactions occur through a stepwise mechanism involving a tetrahedral addition intermediate. Subsequent studies, however, indicated that the reaction can also occur through a concerted, one-step mechanism with a single transition state (TS) and no addition intermediate.[2] The mechanistic change from a stepwise to a concerted or from rate-limiting breakdown to formation of the intermediate depends primarily on relative basicities of the nucleophile (nucleophilicity) and nucleofuge (nucleofugicity).

The mechanistic change-over has been shown to manifest as a non-linear Brønsted-type plots showing a break from a large ($\beta \approx 0{\cdot}8$–$1{\cdot}0$) to a small ($\beta \approx 0{\cdot}1$–$0{\cdot}3$) rate dependence on basicity of the nucleophile as the basicity of nucleophile increases.[3]

Williams and co-workers[4] have shown that the reactions of substituted phenolate anions with *p*-nitrophenyl acetate proceed concertedly with no indication of a break in the Brønsted plot at pK_0, where $\Delta pK_a = 0$ for the attacking and leaving phenolate anions, that would be expected for a stepwise mechanism when the rate-limiting step changes from formation to breakdown of the tetrahedral addition intermediate for attacking phenolate ions that are less basic than the nucleofuge. Recently Jencks and co-workers[5] reported a concerted mechanism for both acetyl- and formyl-transfer reactions involving substituted phenolate anions with *m*-nitrophenyl, *p*-nitrophenyl, and 3,4-dinitrophenyl formates (MNPF, PNPF and DNPF) and acetates (MNPA, PNPA, and DNPA). They noted non-linear Brønsted-type correlations that might be taken as evidence for a mechanistic change-over, but the correlation is shown to represent two different Brønsted lines that are defined by *meta-* and *para*-substituted phenolate and by *meta-* and *para*-substituted *o*-chlorophenolate anions.

The mechanisms of gas-phase carbonyl addition–elimination reactions are less clear. Asubiojo and Brauman[6] proposed a double-well potential energy surface (PES) (Figure 1) to explain their results of the gas-phase displacement reactions at carbonyl centres.

In this model, the two minima of the PES are unsymmetrical complexes in which the ionic species is electrostatically bound by the dipole of the neutral

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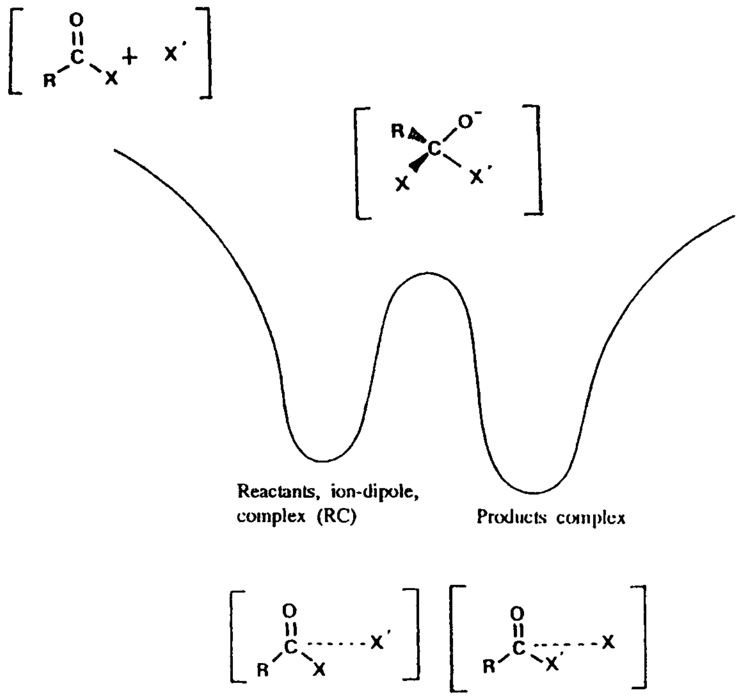


Figure 1. Double-well potential energy surface

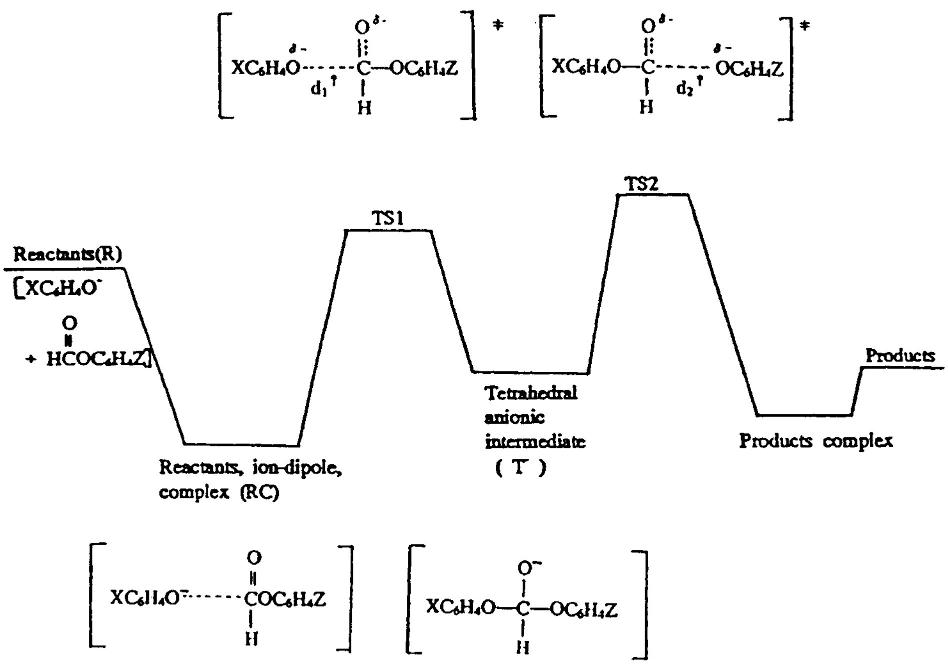


Figure 2. Energy profile scheme

molecule. The tetrahedral adduct in between the two 'ion-dipole' complexes is a transition state (TS). For most carbonyl addition–elimination reactions, the binding energy is known to be relatively constant, between 12 and 20 kcal mol^{-1} (1 kcal = 4·184 kJ).[7]

For a nucleophile with a very low electron affinity (e.g. H^-, CH_3^-) the tetrahedral adduct can be very stable and form an anionic tetrahedral intermediate, T^-, with a triple-well PES[8] (Figure 2). On the other hand, if the nucleophile has a very high electron affinity (e.g. Cl^-, CN^-) the tetrahedral adduct becomes relatively unstable.[9] Such differences in the stability of the tetrahedral adduct, T^-, have been experimentally verified in the gas phase.[8,9]

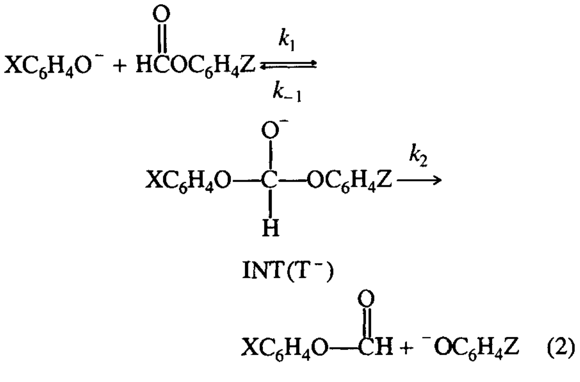
Ab initio studies on the tetrahedral adducts formed by anion nucleophiles with various neutral molecules predicted in general an ion–dipole complex on the reaction coordinate for the anion nucleophiles of relatively high electron affinity (e.g. F^-, Cl^-, CN^-, HS^-).[10]

Our recent high-level *ab initio* studies (MP2/6–31 ++G**//MP2/6–31 ++G**) on the thermoneutral S_N2' reactions of the allylic system:

$$X^- + CH_2{=}CH{-}CH_2X \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} [XCH_2{-}CH{-}CH_2X]^- \xrightarrow{k_2} XCH_2{-}CH{=}CH_2 + X^- \qquad (1)$$

with the nucleophiles $X = H^-$, F^- and Cl^-, have indicated a similar trend with a stable tetrahedral intermediate formation for $X = H^-$ but ion–dipole formation with no such intermediate for $X = F^-$ and Cl^-.[11]

In this work, we examine theoretically the reactions of a series of substituted phenolate anions with MNPF, PNPF and DNPF, [equation (2)] in order to shed light on a more detailed understanding of the factors that determine the mechanism and mechanistic change-over.



$$XC_6H_4O^- + HC({=}O)OC_6H_4Z \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \underset{\text{INT}(T^-)}{XC_6H_4O{-}C(O^-)(H){-}OC_6H_4Z} \xrightarrow{k_2} XC_6H_4O{-}C({=}O)H + {}^-OC_6H_4Z \qquad (2)$$

X = 18 substituents in the nucleophile (Table 1)

Z = m-NO_2, p-NO_2 and 3,4-$(NO_2)_2$

The anionic nucleophiles used in this work have a relatively wide range of electron affinity or conversely proton affinity (or experimentally the pK_a scale); the pK_a values of the phenolate anion nucleophiles range from 10.13 (X = 2-CH_3) to 5·41 (X = 2,3,5,6-F_4).

CALCULATIONS

In this work, a semiempirical method, PM3,[12] was used in the calculations due to the complex reaction systems. We have tested performance of the AM1[13] and PM3 methods by computing the proton affinities (*PA*) of phenolate anions. The correlations of the computed *PA* versus experimental pK_a values gave linear correlations with $r = 0·934$ and 0·948 for the AM1 and PM3 methods, respectively, the latter method being slightly better owing to an improved parameterization for hydrogen-bond energy calculation. The PM3 *PA* values are listed in Table 1 together with the experimental pK_a values.

All equilibrium structures including TSs were fully optimized and were characterized by force calculation and identifying positive or negative eigenvalues in the Hessian matrix.[14] Various equilibrium states along the reaction coordinate are schematically presented in Figure 2. The distance between phenoxy oxygen of the nucleophile and carbonyl carbon was taken as the reaction coordinate. Ground states (GS) were optimized by the use of the EF option. Transition States (TS) were located by the reaction coordinate (RC) method and refined by the use of NLLSQ or TS option.

Table 1. Proton affinities (*PA*, in kcal mol^{-1}) calculated by PM3 method

Substituent in the nucleophile	pK_a[a]	*PA*
2-CH_3	10·13	330·4
4-CH_3	10·09	330·7
H	9·81	331·2
4-Cl	9·26	324·9
3-Cl	8·87	325·0
2-F	8·48	324·4
3,4-Cl_2	8·44	320·2
2-Cl	8·32	324·9
3,5-Cl_2	8·03	319·6
4-CN	7·80	314·8
2,4-Cl_2	7·75	319·2
3,4,5-Cl_3	7·69	316·0
2,3-F_2	7·68	317·8
2,3-Cl_2	7·51	320·2
2,6-F_2	7·12	318·8
2,4,5-Cl_3	6·88	315·0
2,3,5-Cl_3	6·58	315·2
2,3,5,6-F_4	5·41	306·0

[a] Determined in aqueous solution at 25 °C and ionic strength 1·0 M; taken from Ref. 5.

RESULTS AND DISCUSSION

The calculated heats of formation, ΔH_f in kcal mol^{-1}, for the reactions of MNPF, PNPF and DNPF with phenolate anion nucleophiles are summarized in Tables 2, 3 and 4, respectively.

Reaction of *meta*-nitrophenyl formate (MNPF)

In this reaction, the pK_a value (8·19) of the nucleofuge [or leaving group (LG)] $3\text{-}NO_2\text{-}C_6H_4O^-$, is relatively high. The binding energies, $\delta\Delta H_f$ in kcal mol^{-1} in Table 2, of the reactants ion–dipole complexes (RC) are between 19 and 27 kcal mol^{-1}, whereas the stabilities of the intermediate (T^-) are between 8 kcal mol^{-1} (above the reactants level) and −12 kcal mol^{-1} (below the reactants level). The rate-determining step corresponds to the highest point on the energy profile. Thus, when the level of TS2 is higher than that of TS1, the breakdown of the intermediate is rate limiting, whereas when TS1 is higher than TS2 the formation of the intermediate is rate determining. We note that for the phenolate nucleophiles with the relatively high pK_a values (for entries 1–8), the TS2 level is lower than the TS1 level, indicating that the rate-limiting step is formation of T^-. In contrast, for the nucleophiles with the lower pK_a values (for entries 9–18), the level of TS2 is higher than that of TS1, leading to rate-limiting breakdown of T^-. This shows that for the gas-phase reactions of MNPF the mechanistic change occurs at $pK_a \approx 8\cdot0\text{–}8\cdot3$, which is in agreement with pK_0 [where $\Delta pK_a = pK_a(X) - pK_a(Z) = 0$] at which the mechanistic change-over is expected to take place. Admittedly the differences in the two TS levels are small for most of the nucleophiles, but the general trend of the mechanistic change exhibited is rather remarkable. Based on this mechanistic change, the rate-limiting TS levels, $\Delta H_f(TS^{\ne})$, in the gas phase are satisfactorily correlated with the experimental log k_2 values in solution with $r = 0\cdot960$. The two critical bond lengths, $d_1^{\ne}$ and $d_2^{\ne}$ i.e. the partial bonds between C-α and O in TS1 and TS2, respectively (Figure 2), are summarized in Table 5. The data in Table 5 reveal that reversal in the relative length of the two bonds takes place at pK_0 ($\Delta pK_a = 0$ of the nucleophile,[3] i.e. for entries 1–8, $d_1^{\ne}$ is greater than $d_2^{\ne}$, while for entries 9–18 the opposite is true, $d_1^{\ne} < d_2^{\ne}$. This means that at pK_0, the two become approximately equal, $d_1^{\ne} \approx d_2^{\ne}$, indicating that the rate-determining step is characterized by a TS formed with the partial bond of a phenolate anion of a higher pK_a and a longer $d^{\ne}$. This is in agreement with the well known [Bell–Evans–Polanyi (BEP]) principle[15] that a stronger nucleophile (with a higher pK_a) leads to an earlier TS along the reaction coordinate, and the (intrinsic) barrier height increases with a greater deformation or bond stretching required in the TS. This corresponds to a breakdown of T^- in the direction of producing a phenolate anion of lower pK_a in equation (2), i.e. for $pK_a(X) > pK_a(Z)$ k_2 is greater than k_{-1}, whereas for $pK_a(X) < pK_a(Z)$ the opposite holds, $k_2 < k_{-1}$. Thus, the

Table 2. Heats of formation (ΔH_f, in kcal mol^{-1}) of various states[a,b] for the reactions of *m*-nitrophenyl formate (MNPF) with phenolate anion nucleophiles

Entry	Substituent in the nucleophile	ΔH_f(R)	$\delta\Delta H_f$(RC)	$\delta\Delta H_f$(TS1)	$\delta\Delta H_f$(T^-)	$\delta\Delta H_f$(TS2)
1	$2\text{-}CH_3$	−111·6	−26·2	−5·0	−10·9	−8·5
2	$4\text{-}CH_3$	−112·5	−26·3	−5·2	−11·3	−8·9
3	H	−102·9	−26·7	−5·6	−11·8	−10·0
4	4-Cl	−115·9	−24·5	−3·3	−7·8	−5·0
5	3-Cl	−115·7	−24·4	−3·3	−7·7	−4·9
6	2-F	−151·6	−24·9	−2·8	−6·7	−3·8
7	$3,4\text{-}Cl_2$	−126·0	−22·8	−1·3	−4·7	−1·4
8	2-Cl	−114·4	−24·2	−2·7	−6·7	−3·8
9	$3,5\text{-}Cl_2$	−127·6	−22·4	−1·0	−4·1	−0·7
10	4-CN	−84·5	−21·1	+0·8	−1·7	+2·0
11	$2,4\text{-}Cl_2$	−126·6	−22·2	−0·3	−3·1	+0·2
12	$3,4,5\text{-}Cl_3$	−135·7	−21·1	+0·7	−1·8	+1·9
13	$2,3\text{-}F_2$	−201·1	−22·9	−0·4	−2·9	+0·7
14	$2,3\text{-}Cl_2$	−124·7	−22·4	−0·7	−3·7	−0·4
15	$2,6\text{-}F_2$	−199·6	−22·6	+2·2	+1·0	+4·3
16	$2,4,5\text{-}Cl_3$	−136·3	−20·7	+1·6	−0·3	+3·5
17	$2,3,5\text{-}Cl_3$	−136·1	−20·7	+1·6	−0·4	+3·4
18	$2,3,5,6\text{-}F_4$	−296·8	−19·1	+8·0	+8·0	+12·9

[a] R = reactants; RC = reactant (ion–dipole) complex; TS1 and 2 = transition states for the formation and breakdown steps of the intermediate, respectively; T^- = Tetrahedral anionic intermediate.

[b] $\delta\Delta H_f(Y) = \Delta H_f(Y) - \Delta H_f(R)$.

Table 3. Heats of formation (ΔH_f, in kcal mol^{-1}) of various states[a,b] for the reactions of *p*-nitrophenyl formate (PNPF) with phenolate anion nucleophiles

Entry	Substituent in the nucleophile	ΔH_f(R)	$\delta\Delta H_f$(RC)	$\delta\Delta H_f$(TS1)	$\delta\Delta H_f$(T$^-$)	$\delta\Delta H_f$(TS2)
1	2-CH_3	-112·7	-30	-8	-15	-15
2	4-CH_3	-113·6	-30	-8	-16	-15
3	H	-104·0	-31	-9	-16	-16
4	4-Cl	-117·0	-29	-6	-12	-12
5	3-Cl	-116·8	-29	-6	-12	-11
6	2-F	-152·7	-29	-6	-11	-10
7	3,4-Cl_2	-127·1	-27	-4	-9	-8
8	2-Cl	-115·5	-29	-6	-11	-10
9	3,5-Cl_2	-128·7	-27	-4	-8	-7
10	4-CN	-85·6	-25	-2	-6	-5
11	2,4-Cl_2	-127·7	-26	-4	-7	-6
12	3,4,5-Cl_3	-136·7	-25	-2	-6	-5
13	2,3-F_2	-202·2	-27	-4	-7	-6
14	2,3-Cl_2	-125·8	-27	-4	-8	-7
15	2,6-F_2	-200·7	-25	-1	-3	-3
16	2,4,5-Cl_3	-137·3	-25	-2	-5	-3
17	2,3,5-Cl_3	-137·2	-25	-2	-5	-3
18	2,3,5,6-F_4	-297·9	-23·5	+4·4	+4·0	+6·1

[a,b] See Table 2.

Table 4. Heats of formation (ΔH_f, in kcal mol^{-1}) of various states[a,b] for the reactions of *m,p*-dinitrophenyl formate (DNPF) with phenolate anion nucleophiles

Entry	Substituent in the nucleophile	ΔH_f(R)	$\delta\Delta H_f$(RC)	$\delta\Delta H_f$(TS1)	$\delta\Delta H_f$(T$^-$)	$\delta\Delta H_f$(TS2)
1	2-CH_3	-110·6	-35	-15	-	-
2	4-CH_3	-111·5	-35	-15	-	-
3	H	-101·9	-35	-15	-	-
4	4-Cl	-114·9	-33	-13	-22	-
5	3-Cl	-114·7	-33	-13	-22	-
6	2-F	-150·6	-33	-13	-20	-
7	3,4-Cl_2	-125·0	-31	-11	-18	-
8	2-Cl	-113·4	-33	-13	-21	-
9	3,5-Cl_2	-126·6	-30	-11	-17	-17
10	4-CN	-83·5	-29	-9	-15	-15
11	2,4-Cl_2	-125·6	-30	-10	-17	-16
12	3,4,5-Cl_3	-134·7	-29	-9	-15	-15
13	2,3-F_2	-200·1	-31	-10	-16	-16
14	2,3-Cl_2	-123·7	-31	-11	-17	-17
15	2,6-F_2	-198·6	-31	-9	-13	-13
16	2,4,5-Cl_3	-135·3	-29	-9	-13	-13
17	2,3,5-Cl_3	-135·1	-29	-9	-13	-13
18	2,3,5,6-F_4	-295·8	-27	-3	-4	-4

[a,b] See Table 2.

gas-phase reactions of MNPF with substituted phenolates are expected to proceed through an anionic intermediate, T$^-$, with mechanistic change-over at pK_0, i.e. the pK_a of the LG, (where $d_1^{\neq} \approx d_2^{\neq}$) from rate-limiting formation to breakdown of T$^-$ as the nucleophile is varied to a less basic phenolate anion. This is, however, in striking contrast to the concerted mechanism found for all the phenolate nucleophiles in solution.[5] In order to investigate the effect of solvent, H_2O, on the mechanism, we have carried out calculations of heats of mono-hydration to RC, TS1 and TS2. The results are presented in Table 6. It is interesting to note

Table 5. Bond lengths (Å) of the partial bonds between $C_{-\alpha}$ and O in TS1 ($d_1^{\ne}$) and TS2 ($d_2^{\ne}$) (Figure 1)

	m-NO_2		p-NO_2		m,p-(NO_2)	
	$d_1^{\ne}$	$d_2^{\ne}$	$d_1^{\ne}$	$d_2^{\ne}$	$d_1^{\ne}$	$d_2^{\ne}$
2-CH_3	1·928	1·779	1·977	1·662	2·090	—
4-CH_3	1·954 (1·820)[a]	1·778 (1·576)[a]	1·995	1·659	2·109	—
H	1·954	1·665	2·004	1·659	2·122	—
4-Cl	1·870	1·797	1·917	1·680	2·023	—
3-Cl	1·861 (1·757)	1·797 (1·628)	1·911	1·681	2·017	—
2-F	1·861	1·797	1·894	1·683	1·997	—
3,4-Cl_2	1·813	1·811	1·854	1·697	1·946	—
2-Cl	1·850 (1·757)	1·7944 (1·628)	1·893	1·680	1·997	—
3,5-Cl_2	1·807	1·816	1·845	1·699	1·936	1·619
4-CN	1·770	1·829	1·811	1·712	1·891	1·636
2,4-Cl_2	1·791 (1·718)	1·812 (1·660)	1·831	1·697	1·916	1·621
3,4,5-Cl_3	1·772	1·829	1·789	1·711	1·889	1·633
2,3-F_2	1·786	1·814	1·824	1·702	1·909	1·627
2,3-Cl_2	1·800 (1·718)	1·808 (1·659)	1·840	1·694	1·932	1·617
2,6-F_2	1·694	1·802	1·724	1·690	1·786	1·608
2,4,5-Cl_3	1·749	1·830	1·783	1·714	1·858	1·638
2,3,5-Cl_3	1·749 (1·667)	1·828 (1·659)	1·785	1·713	1·862	1·637
2,3,5,6-F_4	1·607	1·850	1·632	1·734	1·689	1·664

[a] Values in parentheses are those for the mono-hydrated TS.

Table 6. Heats of formation (ΔH_f in kcal mol^{-1}) of various monohydrated states[a,b] the reactions of *m*-nitrophenyl formate (MNPF) with phenolate anion nucleophiles

Substituent in the nucleophile	ΔH_f(R)	$\delta\Delta H_f$(RC)	$\delta\Delta H_f$(TS1)	$\delta\Delta H_f$(TS2)	$\delta\Delta H_f$(TS2) − $\delta\Delta H_f$(TS1)[d]	
					Gas phase	Mono-hydrated
4-CH_3	165·9	−32·1(−5·8)[c]	−13·2(−8·0)[c]	−17·2(−8·3)[c]	−4	−4
2-CH_3	169·1	−30·1(−5·7)	−10·4(−7·1)	−13·2(−8·3)	−2	−3
2-Cl	167·8	−30·0(−5·6)	−10·4(−7·7)	−12·0(−8·2)	−1	−2
2,4-Cl_2	180·0	−28·0(−5·8)	−7·3(−7·0)	−8·1(−8·3)	0	−1
2,3-Cl_2	178·1	−28·4(−6·0)	−7·8(−7·1)	−8·8(−8·4)	+1	−1
2,3,5-Cl_3	189·5	−26·5(−5·8)	−4·8(−6·4)	−4·9(−8·3)	+2	0

[a,b] See Table 2.

[c] Hydrogen bond energy = $\Delta H_f(H_2O) - \Delta H_f$(gas-phase).

[d] Relative levels of the two TSs.

that the stabilization afforded by mono-hydration increases successively on proceeding stepwise along the reaction coordinate, RC → TS1 → TS2, by *ca* 1 kcal mol^{-1} in each step. As a result, the level of TS2 is depressed more relative to that of TS1 and the rate-limiting step shifts from k_2 (TS2) to k_1 (TS1) for the last three entries in Table 6. A greater lowering of TS2 in solution should lead to a lowering of the barrier to breakdown of the intermediate and the process should then corresponds to an enforced concerted mechanism,[16] in agreement with the mechanism proposed in solution. In line with this mechanistic change, $d_2^{\ne}$ becomes shorter than $d_1^{\ne}$ in all cases in Table 5 as a result of mono-hydration, although the difference between the two, $\Delta d^{\ne} = d_1^{\ne} - d_2^{\ne}$, narrows to a very small value for the least basic nucleophile studied, X = 2,3,5,6-F_4.

Reaction of *p*-nitrophenyl formate (PNPF)

The pK_a value (7·15) of the LG, $4\text{-}NO_2C_6H_4O^-$, is lower by *ca* 1·0 unit than that of the MNPF, and hence the levels of RC and T^- (Table 3) are accordingly lower by *ca* 4 kcal mol^{-1} uniformly than those for the corresponding reactions of MNPF. In this case, the levels of TS2 are lower than those of TS1 for all phenolate nucleophiles except for the least basic nucleophile, $X = 2,3,5,6\text{-}F_4$. This means that the reactions of PNPF proceed by rate-limiting formation of the intermediate, except for the 2,3,5,6-fluorophenolate anion, which reacts by the rate-limiting breakdown of T^-. We would have expected the mechanistic change to occur at pK_0 [where $\Delta pK = pK_a(X) - pK_a(Z) = 0$], i.e. $pK_a(X) \approx 7{\cdot}15$, which corresponds to $X = 2,6\text{-}F_2$, but the mechanistic change occurred at much lower basicity of the nucleophile, $pK_a(X) \approx 5{\cdot}4\text{–}6{\cdot}6$. This discrepancy is, however, a result of differences in the calculated *PA*, i.e. the *PA* for $4\text{-}NO_2C_6H_4O^-$ and $2,6\text{-}F_2C_6H_3O^-$ are 303·7 and 318·8 kcal mol^{-1}, respectively, so that even though their pK_a values in water are similar (7·15 and 7·12) the calculated *PA* values differ substantially. Since the energetics in Tables 2–4 are those for the gas-phase reactions, we should really use the gas-phase *PA* values and not the pK_a values (in water). If we compare the *PA* values, the mechanistic change in the gas phase observed here falls in approximately the right place; *PA* for $4\text{-}NO_2C_6H_4O^-$ and $2,3,5,6\text{-}F_4C_6HO^-$ are 303·7 and 306·0 kcal mol^{-1}, respectively. There is a reversal of the relative order in $d^{\neq}$ from $d_1^{\neq} > d_2^{\neq}$ to $d_1^{\neq} < d_2^{\neq}$ in Table 5, supporting the mechanistic change. For the case of MNPF, the pK_a (8·19 versus 8·03) and *PA* 314·8 versus 319·6) values agreed approximately to give the right phenolate nucleophile, i.e. $3,5\text{-}Cl_2C_6H_3O^-$, at which the mechanistic change-over occurs.

Here again, the differences between the levels of the two TSs are small, but there is a distinct trend of change in the mechanism. The depth of the intermediate, T^-, is too shallow and almost indistinguishable from TS2. T^- has a property of transient equilibrium point on the potential energy surface so that passage through the intermediate should experience a negligible barrier to decomposition thus the process becomes an enforced *concerted* mechanism.[16] If we take the solvent effect into account, the levels of TS2 will be depressed more relative to those of the corresponding TS1, leading to the concerted mechanism for all the nucleophiles studied including the last entry in Table 3, $X = 2,3,5,6\text{-}F_4$, which is in agreement with that observed experimentally in water.

Reactions of 3,4-dinitrophenyl formate (DNPF)

Reference to Table 4 reveals that the levels of TS2 are all lower than those of the corresponding TS1 and the tetrahedral anionic intermediates, T^-, are of transient equilibrium point type;[16] the reactions of DNPF with all the phenolate nucleophiles will therefore proceed concertedly in the gas phase, in agreement with the proposal based on the experimental results in solution. The $d_1^{\neq}$ values are all greater than the $d_2^{\neq}$ values in Table 5, which is again consistent with a single mechanism for all the nucleophiles. The transient equilibrium point[16] (or unstable intermediate) after the TS1 level should not have any kinetic effect experimentally and hence the reactions become a concerted, single-step processes. However, in this case $d_2^{\neq}$ is not exactly the same as that of the corresponding bond length in TS1, the TS for the concerted process.

In summary, the gas-phase reactions of MNPF show a mechanistic change for rate-limiting formation to breakdown of the tetrahedral intermediate (T^-) at approximately pK_0 (also $\Delta PA \approx 0$) as the basicity of the phenolate nucleophile is decreased. For PNPF, all phenolate anions except the weakest nucleophile, $2,3,5,6,\text{-}F_4C_6HO^-$, react concertedly, whereas for DNPF all phenolate anions react concertedly. This indicates that as the leaving group basicity is decreased from $3\text{-}NO_2$- to $4\text{-}NO_2$- and to $3,4\text{-}(NO_2)_2$-phenolates, the single-step mechanism becomes successively more favoured and the enforced concerted mechanism starts at phenolate nucleophiles of successively lower basicity.

Examination of Tables 2–4 reveals that as the leaving group basicity is decreased stepwise, MNPF → PNPF → DNPF →, the levels of TS1, T^- and TS2 are depressed uniformly by *ca* 5, 6 and 8 kcal mol^{-1}, respectively, in each step. Thus the depression of the TS2 level is greater by *ca* 3 kcal mol^{-1} than that of TS1, thereby shifting the rate-determining step more and more to TS1, i.e. the reaction tends to proceed more and more by a single-step, concerted mechanism. The successively greater lowering of the TS2 level relative to TS1 is shown schematically in Figure 3.

Conversely, the level changes due to a decrease in the basicity of the phenolate nucleophile with a constant leaving group, e.g. MNPF, can be considered in a similar manner. In this case, the depression of TS1 should become greater than that of TS2 and the mechanistic change from rate-limiting formation to breakdown of T^- can be envisaged as shown schematically in Figure 4.

The results of these two energy scheme analyses in Figures 3 and 4 suggest that whichever phenolate anion has the lower basicity, the TS level involving partial bond of that lower basicity phenolate gives the lower TS. For example, in Figure 3, the pK_a of $2,3,5,6\text{-}F_4$-phenolate anion (5·41) is lower than that of both $3\text{-}NO_2$-(8·19) and $4\text{-}NO_2$-(7·15) phenolate anions but is higher than that of $3,4\text{-}(NO_2)_2$-phenolate anion (5·28), so that the level of TS2 are higher than that of TS1 for

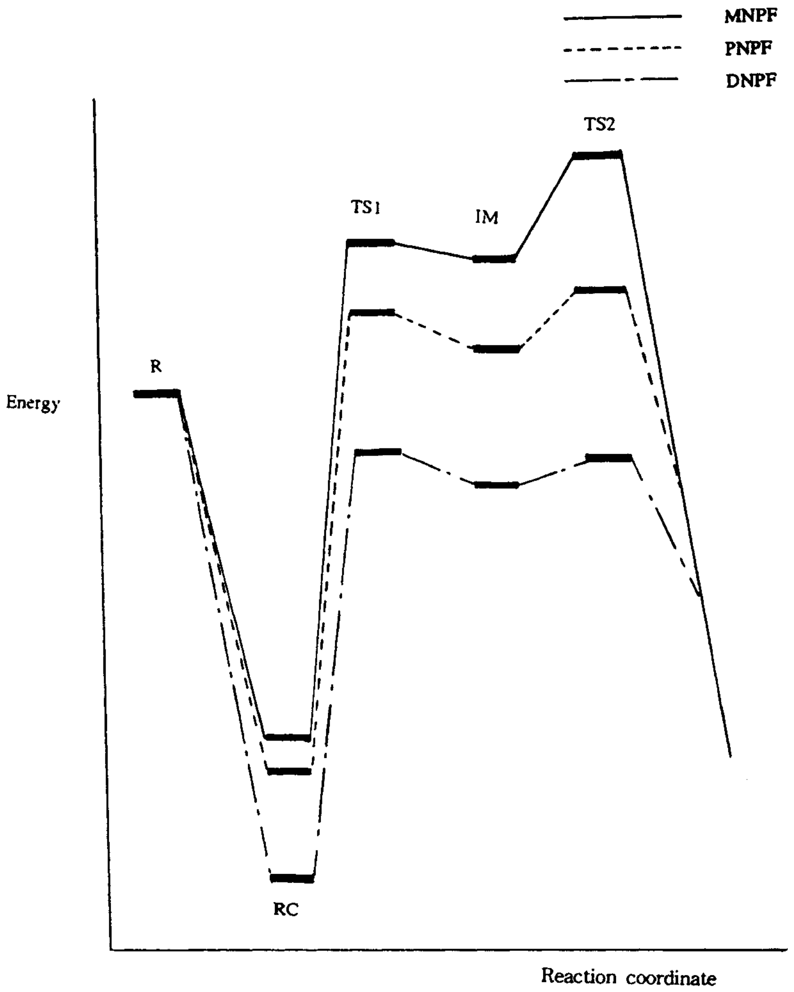
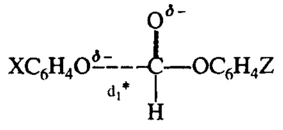


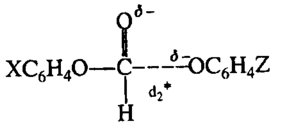
Figure 3. Energy level depression due to a decrease in the basicity of the leaving group phenolate anion, 3-NO_2-(8·19)→4-NO_2-(7·15)→3,4-$(NO_2)_2$-phenolate (5·28). The relative levels and level changes correspond roughly to that of 2,3,5,6-F_4-phenolate anion

the former two but is lower for the latter. Similarly in Figure 4, the level of TS1 is higher than that of TS2 for 4-CH_3- ($pK_a = 10·09$) and 3-Cl-phenolate anion ($pKa = 8·87$) but is lower for 2,6-F_2-phenolate ($pK_a = 7·12$) since the *m*-nitrophenolate anion has a pK_a of 8·19.



$XC_6H_4O^{\delta-}\cdots\overset{O^{\delta-}}{\underset{H}{C}}-OC_6H_4Z$ (d_1^*)

TS1



$XC_6H_4O-\overset{O^{\delta-}}{\underset{H}{C}}\cdots{}^{\delta-}OC_6H_4Z$ (d_2^*)

TS2

For the type of reactions studied in this work, i.e. the acyl transfer between two phenolate anions, the stability of any TS seems to depend largely on how efficiently the anionic charge is delocalized. Thus when the substituent(s) X in the nucleophile is a stronger electron-withdrawing group(s) than the substituent(s) Z in the nucleofuge, i.e. σ_x (or $\Sigma\sigma_x$) $> \sigma_z$ (or $\Sigma\sigma_z$), which is tantamount to $pK_a(X) < pK_a(Z)$, the anionic charge is more efficiently delocalized in TS1 rather than in TS2 so that the level of TS1 becomes lower than that of TS2 and also bond length d_1^* becomes shorter than d_2^*. The opposite will be true when σ_x (or $\Sigma\sigma_x$) $< \sigma_z$ (or $\Sigma\delta_z$) which is tantamount to

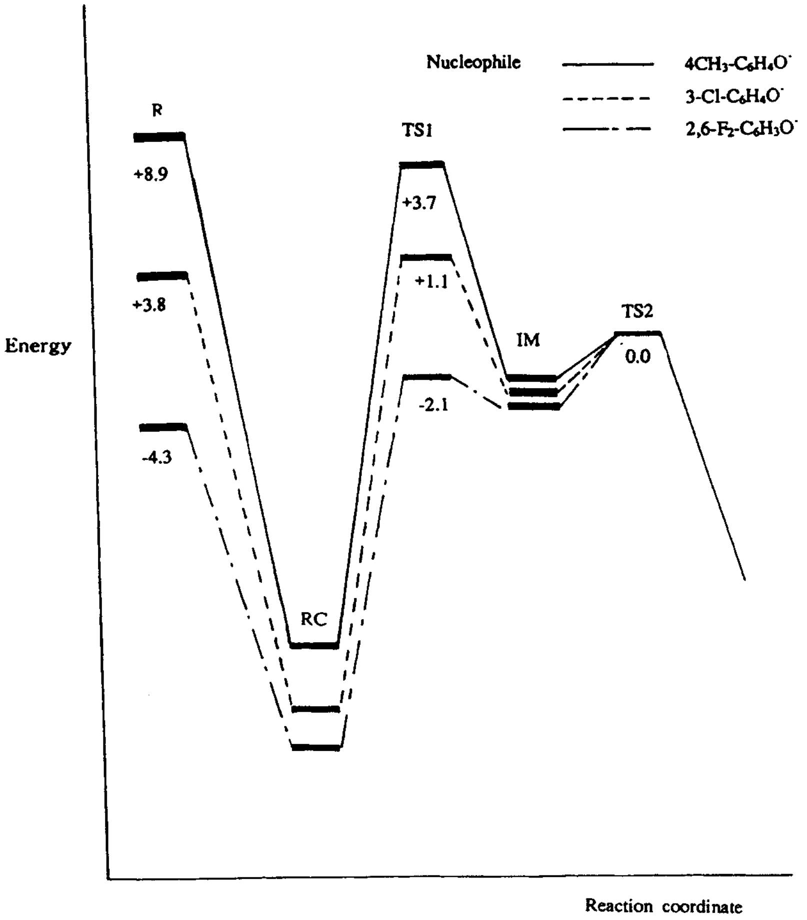


Figure 4. Energy level depression due to a decrease in the basicity of the phenolate nucleophiles, e.g. 4-CH_3-(10·09)→3-Cl (8·87)→2,6-F_2-phenolate (7·12). The relative levels for TS2 correspond to that of MNPF

$pK_a(X) > pK_a(Z)$. The higher is the pK_a of a phenolate anion, the stronger is the nucleophilicity but the weaker is the nucleofugicity.

The relative bond length changes in Table 5 reveal that a stronger nucleophile (with a higher pK_a value) leads to an earlier TS, i.e. the bond length $d_1^{\neq}$ is longer in TS1 (compare, for example, the $d_1^{\neq}$ values of X = 4-CH_3 and X = 2,6-F_2) and a stronger nucleofuge (with a lower pK_a value) also leads to an earlier TS, i.e. the bond length $d_2^{\neq}$ is shorter in TS2 [compare, for example, the $d_2^{\neq}$ values of Z = 3-NO_2 and Z = 3,4-$(NO_2)_2$).

We conclude that for the reactions of substituted phenolate anions with formate esters the mechanistic change can occur in the gas phase at $\Delta PA = 0$ (or pK_0), but in solution, owing to the relatively low stability of the anionic intermediate, T^-, and a greater degree of depression of the second barrier, TS2, by solvation than the first barrier, TS1, the reaction is expected to proceed by a single-step mechanism, as observed experimentally. The low stability of T^- can be ascribed to the relatively high electron affinity of the phenolate anion nucleophiles due to relatively strong electron delocalization within the phenolate rings. In contrast, the zwitterionic tetrahedral intermediate, $T^{\pm}$, in the aminolysis of the carbonyl compounds can be very stable, especially in hydrogen-bonding solvents, allowing the observation of mechanistic change-over in solution.

SUPPLEMENTARY MATERIAL

Bond angles (in degrees) and imaginary frequencies (in cm^{-1}) of TSs are available as supplementary material.

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