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and in the region δ 1.18–1.38, which could not be assigned.

Fraction III.2: $R_f = 0.39$; 65 mg; slightly yellow solid, which was impure according to its ^1H NMR spectrum. Recrystallization from acid-free methylene chloride (stored over Na_2CO_3) and *n*-hexane gave pure **12**: yield 15 mg (2.1%); white solid; ^1H NMR (270 MHz, C_6D_6) δ 0.10 (m, 12 H), 0.58 (m, 12 H); ^{13}C NMR (67.93 MHz, [d_2]methylene chloride, broad-band decoupling and DEPT) δ 13.15 (–), 17.09 (ϕ), 63.15 (ϕ), 81.50 (ϕ); IR (KBr pellet) 3100, 3020, 2245, 2160 (s), 2125 (w), 2082 (w), 1630 (br), 1425, 1310, 1182 (s), 1062, 1038, 1028, 978 (s), 940, 84 cm^{-1}; UV (methanol) λ_{max} (10 g ϵ) 226.8 nm (3.53), 239.5 (3.60), 252.6 (3.64), 267.5 (3.46); MS (70 eV) *m/z* 384 (9.8, M^+), 367 (15), 353 (40), 339 (73), 324 (100), 300 (60), 287 (34), 276 (23), 263 (20), 250 (16), 226 (16), 213 (13), 162 (15), 150 (17), 135 (16), 123 (16), 111 (18), 99 (23), 87 (33), 75 (35), 63 (39), 51 (35), 39 (43); HRMS exact mass for $C_{30}H_{24}$, calcd 384.1878, found 384.1876.

1,4-Dicyclopropylbutadiyne (4-H_2). To a solution of anhydrous copper(Il) acetate (6.0 g, 33.1 mmol) in dry methanol/pyridine (1:1 v/v) (80 mL) was added ethynylcyclopropane (**3-H_2**) (1.0 g, 15.1 mmol) in dry methanol (1.0 mL), and the mixture was stirred at ambient temperature for 3 days. The reaction mixture was then poured into ice-cold 18 N sulfuric acid (100 mL) and extracted with two portions of diethyl ether (30 mL each). The combined organic layers were dried over $MgSO_4$, the solvents were distilled over a 40-cm packed column, and the residue was purified by Kugelrohr distillation (100 °C (0.1 Torr)): yield 560 mg (57%); **4-H_2**; colorless liquid; ^1H NMR (270 MHz, $CDCl_3$) δ 0.63–0.81 (m, 8 H), 1.19–1.30 (m, 2 H); ^{13}C NMR (67.93 MHz, $CDCl_3$, broad-band decoupling) δ 0.07, 8.56, 61.08, 79.92; IR (film) 3090, 3020, 2240, 2190, 2160 cm^{-1}; UV (methanol) λ_{max} (log ϵ) 228.4 nm (2.91), 240.0 (3.10), 253.2 (3.18), 268 (3.00); MS (70 eV) *m/z* 130 (M^+), 128 ($M - H_2$), 115 ($M - CH_3$), 102 ($M - C_2H_4$).

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Supplementary Material Available: Crystallographic data on **12**, a stereoscopic view of the unit cell, tables of atomic coordinates, bond lengths and angles, and anisotropic thermal parameters as well as UV spectra of **12** and 1,4-dicyclopropylbuta-1,3-diyne (10 pages); a table of observed and calculated structure factors for **12** (9 pages). Ordering information is given on any current masthead page.

Concerted Mechanism for Alcoholysis of Esters: An Examination of the Requirements

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Abstract: The application of an extension of Marcus theory to exchange reactions of carboxylic esters leads to results in agreement with the conclusions, based on structure reactivity studies, reported by Williams and co-workers (*J. Am. Chem. Soc.* **1989**, *111*, 2647), namely, that, for strongly acidic phenols (p*K*a < 1), exchange will proceed by a limiting mechanism involving an acylium ion in a very "exploded" transition state and, for weakly acidic phenols (p*K*a > 11), exchange will proceed by the tetrahedral intermediate mechanism, while for p*K*a values between these limits the reaction will be concerted, with no intermediate and simultaneous formation of the bond to the nucleophile and breaking of the bond to the leaving group. Further we conclude that, in essentially all reactions of aryl acetates, the reactions have no intermediates of significant lifetimes because of the very small intrinsic barriers for making or breaking a bond to aryl oxide ion. For alkoxide ions, the intrinsic barriers are higher but p*K*a-dependent so that we can predict a concerted reaction for alcohols of low p*K*a, if such could be devised. Hydroxide ion has a uniquely high intrinsic barrier for attack on carbonyl.

Introduction

Several mechanisms have been found for base-catalyzed ester alcoholysis or hydrolysis, depending on the structure of the ester and the reaction conditions. The overwhelming majority of mechanistic studies have been interpreted in terms of the tetrahedral intermediate mechanisms described in the IUPAC system[1] as SuAC following an $A_N + D_N$ mechanism, although other mechanisms are known in special cases: elimination addition mechanisms,[2] $D_HA_H + D_N + A_N + D_HA_H$; S_N2 at the alkyl carbon of the ester,[3] SuAL following an A_ND_N mechanism; S_N1 with alkyl oxygen cleavage is known, although normally only in acid solution,[4] SuAL following a $D_N + A_N$ mechanism; S_N1 with acyl oxygen cleavage is also known, but for esters is only encountered in acid,[5] although for acid chlorides it has been proposed for uncatalyzed reactions,[6–13] SuAC following a $D_N + A_N$ mechanism. Recently there has been considerable interest in the question of whether ester alcoholyses can be concerted,[14–20] i.e., whether an SuAC reaction can follow an A_ND_N pathway. Williams has proposed[17] a theory predicting when ester alcoholysis will be concerted and when it will go by the limiting stepwise reactions, either $D_N + A_N$ through an acylium ion or $A_N + D_N$ through a tetrahedral intermediate. We thought it would be of interest to see what

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Table I. Equilibrium for Ester Formation as a Function of p*K*a of ArOH or ROH[a]

X in ArOH	p*K*a[b]	ΔG° [b,c]
p-NO_2	7.14	9.43
m-NO_2	8.35	8.55
p-Cl	9.38	7.59
H	9.99	7.39
p-Me	10.19	6.89
p-MeO	10.2	6.59
R in ROH	**p*K*a[b]**	**ΔG° [b,c]**
CF_3CH_2	12.43	4.97
$ClCH_2CH_2$	14.31	2.84
$MeOCH_2CH_2$	14.87	2.18
Et	15.83	1.66

[a] All in aqueous solution at 25 °C. [b] Reference 22. [c] ΔG° for ester formation, expressed in terms of neutral species; $a_{H_2O} = 1$.

predictions emerged from our extended Marcus theory approach,[14,21] and we present the results of this analysis.

Results

We have previously analyzed the exchange reactions of *p*-nitrophenyl acetate with *p*-nitrophenoxide and of 2,4-dinitrophenyl acetate with 2,4-dinitrophenoxide[14] and shown that the observed free energy of activation was less than the free energy level of either the acylium ion or anionic tetrahedral intermediate. This was interpreted in terms of a concerted mechanism resulting from the low intrinsic barrier for aryl oxide ion attack on a carbonyl. We will now undertake a more detailed and more extensive analysis of exchange reactions of carboxylic esters.

We will be examining the reactions of esters over a wide range of reactivity, and not all measurements will be available for all esters of interest. We start by developing some linear free energy relations that can be used to estimate rate and equilibrium constants that we will need.

Literature data for the equilibrium constant for acetate ester formation[22] lead to a linear free energy relation between ΔG° for ester formation (neutral species in aqueous solution) and the pK_a of the alcohol or phenol reacting with acetate.[22] The data are shown in Table I: The correlation line is

$$\Delta G^\circ = 16.33 \pm 0.23 - (0.934 \pm 0.026)\mathrm{p}K\mathrm{a} \qquad (1)$$

with the correlation coefficient $r^2 = 0.994$. This line is based on six phenols and four alcohols.

The rate constants for hydroxide ion catalyzed hydrolysis of aryl acetates are linearly correlated with the p*K*a of the leaving group.[18] The data are found in Table II: The correlation line is

$$\log k_{OH} = 2.95 \pm 0.13 - (0.281 \pm 0.023)\mathrm{p}K\mathrm{a} \qquad (2)$$

with the correlation coefficient $r^2 = 0.968$. This line is based on seven aryl acetates. Data are also available for five alkyl acetates (see Table II), and for the alkyl esters a slightly different correlation line is obtained:

$$\log k_{OH} = 5.07 \pm 0.07 - (0.39 \pm 0.03)\mathrm{p}K\mathrm{a} \qquad (3)$$

with the correlation coefficient $r^2 = 0.987$.

We need to estimate the free energy levels of the possible intermediates in the exchange reactions $RO^- + CH_3COOR \rightleftharpoons CH_3COOR + RO^-$. In order to do this, we follow the procedure that we previously employed[14] and begin by estimating the equilibrium constant for hydration of the various esters, using the Marcus relation (eq 4), which we previously reported for hydroxide ion attack on esters.[23]

$$HO^- + S \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} HO^-,S \overset{k_2}{\rightleftharpoons} T^- \rightarrow \text{product} \qquad (4)$$

$$k_1 = 1.7 \times 10^9\ M^{-1}\ s^{-1} \qquad k_{-1} = 1 \times 10^{11}\ s^{-1}$$

$$\log k_2 = 13.0 - b(1 - \log K_2/4b)^2 \qquad b = 8.99$$

Table II. Rates of Alkaline Hydrolysis of Esters as a Function of p*K*a of ArOH or ROH[a]

X in ArOAc	p*K*a	k_{OH}[b] ($M^{-1}\ min^{-1}$)	log *k* ($M^{-1}\ s^{-1}$)
2,4-$(NO_2)_2$	4.02	3220	1.73
p-NO_2	7.14	570	0.98
m-NO_2	8.35	412	0.84
p-Cl	9.38	132	0.34
H	9.95	76	0.10
p-Me	10.19	59	−0.01
p-MeO	10.2	63	0.02
ROAc	**p*K*a**	**k_{OH}[b] ($M^{-1}\ min^{-1}$)**	**log *k* ($M^{-1}\ s^{-1}$)**
EtOAc	15.83	4.5	−1.12
MeOEtOAc	14.87	8.9	−0.83
ClEtOAc	14.31	17	−0.55
$HCCCH_2OAc$	13.50	28	−0.33
CF_3CH_2OAc	12.43	102	0.23

[a] All in aqueous solution at 25 °C. [b] Data from ref 41.

In eq 4, *b* is the intrinsic barrier, expressed in log *k* units.[24] These calculations are summarized in Table III. From log k_{OH}, using experimental values where they are available and values calculated from eq 2 where necessary, we obtain log K_{OH}, the equilibrium constant for addition of hydroxide ion to the ester. Then by estimating the p*K*a of the tetrahedral intermediate using eq 5 as previously described,[25] we can obtain log

$$\mathrm{p}K\mathrm{a} = 17.03 - 1.32\sum\sigma^* \qquad (5)$$

K_{H_2O}, the equilibrium constant for the addition of water to the ester; this calculation requires σ^* values for the OAr groups, which were estimated where necessary either by the use of the p*K*a for $ArOCH_2COOH$[26] and the equation for the p*K*a of XCH_2COOH[27] or from the p*K*a of the phenol, which can be used to estimate an effective $\sum\sigma$ for the substituent(s) on the phenol, which in combination with equations for the p*K*a of XCH_2COOH[27] and $XPhOCH_2COOH$[26] leads to σ^* for the OAr group.

The next step is to estimate the equilibrium constant for addition of RO^- to CH_3COOR. This can be done by estimating the equilibrium constant for the hypothetical reaction in which one OH in the ester hydrate is replaced by OR. The linear free energy relation permitting this is derived for each ester as was done for *p*-nitrophenyl acetate.[14] In effect, we obtain the free energy relation from two hypothetical exchange processes. One is based on

$$CH_3C(OH)_3 + HOAr \rightleftharpoons CH_3C(OH)_2(OAr) + H_2O$$

and the other is based on

$$CH_3C(OH)_2(Im) + HOAr \rightleftharpoons CH_3C(OH)(Im)(OAr) + H_2O$$

The free energies of $CH_3C(OH)_2(Im)$ and $CH_3C(OH)(Im)(OAr)$ are derived as described in ref 14. Imidazolyl (Im) is used as the high σ^* substituent for which data permitting these calculations are available. The net result is that we can determine the relationship (eq 6) between the free energy change for replacement

$$\Delta G_{OH>OAr} = a + b\sum\sigma^* \qquad (6)$$

of OH by OAr and the sum of Taft σ^* values for the three remaining substituents on the central carbon. It is then possible to use the thermodynamic cycle

$$\begin{tikzcd}
CH_3COOAr + H_2O + HOAr \arrow[r, shift left, harpoon] \arrow[dr, shift left, harpoon] & CH_3C(OH)_2(OAr) + HOAr \arrow[l, shift left, harpoon] \arrow[d, shift left, harpoon] \\
 & CH_3C(OH)(OAr) + H_2O \arrow[ul, shift left, harpoon] \arrow[u, shift left, harpoon]
\end{tikzcd}$$

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Table III. Free Energies of Covalent Hydration of Esters[a]

ArOH	p*K*a[b]	$-\Delta G_{hydrol}$[c]	log k_{OH}[d]	log K_{OH}[e]	σ^*_{OAr}[f]	log K_{H_2O}[g]	$\Delta G°_{hydrat}$[h]
4-Cl-2-NO_2	6.46	10.29	1.13	-3.92	3.19	-7.94	10.85
4-NO_2	7.14	9.65	0.94	-4.28	2.78	-7.69	10.50
4-CHO	7.66	9.17	0.80[k]	-4.55	2.9	-8.20	11.20
3-NO_2	8.35	8.52	0.60	-4.91	2.95	-7.83	10.70
H	9.86	7.10	0.18	-5.68	2.37	-8.76	11.97
3-Cl	9.02	7.89	0.42[k]	-5.25	2.52	-8.62	11.77
4-CN	7.95	8.89	0.72[k]	-4.70	2.72	-7.66	10.47
2,3,5-Cl_3	6.43	10.32	1.14	-3.90	3.16	-7.88	10.77
2,4,5-Cl_3	6.72	10.05	1.06	-4.06	3.12	-7.98	10.91
i	1.00	15.40	2.67	-0.91	4.16	-6.21	8.48
i	2.00	14.47	2.39	-1.48	3.96	-6.52	8.90
i	3.00	13.53	2.10	-2.04	3.76	-6.81	9.31
i	4.00	12.60	1.82	-2.59	3.56	-7.10	9.70
i	5.00	11.66	1.54	-3.14	3.36	-7.38	10.08
i	6.00	10.73	1.26	-3.67	3.16	-7.66	10.46
i	7.00	9.80	0.98	-4.20	2.96	-7.92	10.82
i	8.00	8.86	0.70	-4.73	2.76	-8.18	11.17
i	9.00	7.93	0.42	-5.24	2.56	-8.43	11.52
i	10.00	6.99	0.14	-5.75	2.36	-8.67	11.85
i	11.00	6.06	-0.14	-6.25	2.16	-8.91	12.18
i	12.00	5.13	-0.42	-6.75	1.96	-9.15	12.49
i	13.00	4.19	-0.70	-7.24	1.76	-9.37	12.80
ROH	p*K*a[b]	$-\Delta G_{hydrol}$[c]	log k_{OH}[d]	log K_{OH}[e]	σ^*_{OAr}[f]	log K_{H_2O}[g]	$\Delta G°_{hydrat}$[h]
EtOH	15.83	1.66	-1.12	-7.96	1.68	-9.99	13.64
MeOH	15.54	1.7	-0.82	-7.44	1.81	-9.64	13.17
$HCCCH_2OH$	13.50	3.67	-0.33	-6.59	2.13	-9.21	12.58
CF_3CH_2OH	12.43	4.97	0.23	-5.59	2.16	-8.25	11.27
j	14.00	3.26	-0.45	-6.79	1.95	-9.18	12.53
j	13.00	4.19	-0.05	-6.09	2.09	-8.66	11.83
j	12.00	5.13	0.34	-5.38	2.23	-8.14	11.12
j	11.00	6.06	0.74	-4.66	2.37	-7.60	10.38
j	10.00	6.99	1.13	-3.92	2.51	-7.05	9.63
j	9.00	7.93	1.52	-3.17	2.65	-6.48	8.85
j	8.00	8.86	1.92	-2.41	2.79	-5.90	8.06
j	7.00	9.80	2.31	-1.62	2.93	-5.30	7.24

[a] All in aqueous solution at 25 °C. The standard state for all species except water is the ideal 1 M solution with an infinitely dilute reference state; for water, the standard state is the pure liquid with unit activity. [b] p*K*a of ArOH or ROH. [c] Free energy of hydrolysis of the esters, either experimental (Table I) or calculated with use of eq 1. [d] Rate constants for hydroxide ion catalyzed hydrolysis of the ester, either experimental value (Table II) or calculated with use of eq 2 or 3 unless otherwise noted. [e] Equilibrium constant for hydroxide ion addition, calculated with use of eq 4. [f] Taft σ^* values calculated as described in the text. [g] Equilibrium constant for addition of water to the ester, calculated from the equilibrium constant for hydroxide ion addition and a p*K*a for the tetrahedral intermediate estimated with use of eq 5. [h] Free energy for covalent hydration. [i] Hypothetical phenol of indicated p*K*a. [j] Hypothetical alcohol of indicated p*K*a. [k] Calculated from data in ref 42.

to calculate the desired free energy change for the addition of HOAr to CH_3COAr. Finally, estimation of the p*K*a of the tetrahedral adduct $CH_3C(OH)(OAr)_2$ allows us to calculate the free energy change for the process $ArO^- + CH_3COOAr \rightleftharpoons CH_3C(O^-)(OAr)_2$. These calculations are described in Table IV.

We also need to calculate the free energy level of the acylium ion: This is based on the equilibrium measurements of Deno and co-workers,[28] which we extrapolated to aqueous solution.[14] This procedure is based on the thermodynamic cycle

$$\begin{tikzcd}
CH_3COOAr + H_2O \arrow[r, shift left] \arrow[d, shift left] & CH_3COOH + HOAr \arrow[l, shift left] \arrow[d, shift left] \\
CH_3C{\equiv}O^+ + {}^-OAr + H_2O \arrow[u, shift left] \arrow[r, shift left] & CH_3COOH + H^+ + {}^-OAr \arrow[l, shift left] \arrow[u, shift left]
\end{tikzcd}$$

These calculations are summarized in Table V.

In order to assess the degree of concertedness of the reactions of various esters, we must attempt to estimate the various work terms involved in the application of Marcus theory. In the present case, this means the energies involved in forming the initial encounter complex RO^-,CH_3COOR and the triple ion $RO^-,CH_3C{\equiv}O^+,RO^-$. In order to be able to treat a wide range of nucleophiles, we take explicit account of the need for desolvation of RO^- in order to have nucleophlic attack at the carbonyl carbon. The need for such desolvation has been proposed to explain nonlinearities in structure reactivity correlations.[18-20] This treatment is more elaborate than we have previously used[14,23] but will allow us to present a unified treatment for a wide range of reactivities. The energy cost of desolvating RO^- by loss of one of the solvating waters hydrogen bonded to O^- is estimated[21] from the change in p*K*a on transfer from water to DMSO, for which we have reported a linear correlation between $\Delta pKa/n_{hb}$, the change in p*K*a per hydrogen bond, and pKa_{DMSO}:

$$\Delta pKa/n_{hb} = -0.222 \pm 0.100 + (0.161 \pm 0.005)pKa_{DMSO} \quad (7)$$

The free energy for ion pair formation from the free ions in solution is assumed to be the same as for *tert*-butyl cation and chloride,[29] namely, 0.1 kcal/mol. This represents the sum of the attractive electrostatic interaction and the entropic cost of bringing species together, together with any desolvation cost. For the case of chloride and *tert*-butyl cation, we assume negligible desolvation cost. The entropic cost is calculated after Hine[24] assuming an equilibrium constant for encounter complex formation, in the absence of any attractive or repulsive interactions, of 0.0085*n*, where *n* is the number of equivalent sites that could be occupied by the basic atom encountering the Lewis acid. In the case of *tert*-butyl cation and chloride, the free energy of encounter complex formation, in the absence of electrostatic stabilization, is calculated to be +2.42 kcal/mol. Consequently the free energy of electrostatic interaction is -2.32 kcal/mol. We will use the same electrostatic interaction in estimating free energies for ion pair and ion triplet formation. In the case of the ion triplet $ArO^-,CH_3C{\equiv}O^+,ArO^-$, the geometry implied by the concerted mechanism (vide infra) has an orthogonal arrangement, with the two

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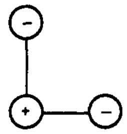
Table IV. Free Energies of Formation of Tetrahedral Intermediates[a]

ArOH	p*K*a[b]	ΔG^c (OH > OAr)	ΔG^d (OH > OAr/Im)	*b*[e]	*a*[f]	$\Delta G_{\mathrm{addn}}{}^g$ (HOAr, AcOAr)	log $k_{ii}{}^h$
4-Cl-2-NO_2	6.46	9.21	14.07	3.77	-0.90	27.03	-1.98
4-NO_2	7.14	8.23	12.01	2.93	0.36	22.95	-1.93
4-CHO	7.66	8.44	12.54	3.18	-0.08	24.60	-1.96
3-NO_2	8.35	7.76	11.99	3.28	-1.03	24.21	-1.69
H	9.86	7.15	9.86	2.10	1.53	21.28	-0.82
3-Cl	9.02	7.74	10.84	2.40	1.29	22.34	-1.22
4-CN	7.95	7.44	11.07	2.81	-0.10	21.79	-2.08
2,3,5-Cl_3	6.43	9.16	13.94	3.71	-0.78	26.68	-1.91
2,4,5-Cl_3	6.72	9.02	13.70	3.63	-0.70	26.39	-1.88
i	1.00	11.94	19.36	5.75	-3.46	36.63	
i	2.00	11.43	18.31	5.34	-2.89	34.32	
i	3.00	10.90	17.26	4.93	-2.32	32.14	
i	4.00	10.36	16.20	4.52	-1.77	30.10	
i	5.00	9.81	15.12	4.12	-1.23	28.21	
i	6.00	9.25	14.03	3.71	-0.69	26.46	
i	7.00	8.68	12.93	3.30	-0.17	24.84	
i	8.00	8.09	11.83	2.89	0.34	23.38	
i	9.00	7.50	10.71	2.49	0.84	22.05	
i	10.00	6.90	9.59	2.08	1.33	20.87	
i	11.00	6.30	8.45	1.67	1.82	19.84	
i	12.00	5.68	7.31	1.26	2.29	18.95	
i	13.00	5.05	6.16	0.86	2.76	18.21	

ROH	p*K*a[b]	ΔG^c (OH > OR)	ΔG^d (OH > OR/Im)	*b*[e]	*a*[f]	$\Delta G_{\mathrm{addn}}{}^g$ (HOR, AcOR)
EtOH	15.83	3.36	4.25	0.69	1.51	17.35
MeOH	15.54	2.43	3.67	0.96	-0.13	
$HCCCH_2OH$	13.50	3.81	5.88	1.61	-0.51	
CF_3CH_2OH	12.43	3.78	5.93	1.67	-0.70	
j	14.00	3.85	5.46	1.24	0.52	17.14
j	13.00	4.09	6.06	1.53	-0.01	17.07
j	12.00	4.30	6.64	1.81	-0.56	17.03
j	11.00	4.50	7.21	2.10	-1.12	17.04
j	10.00	4.68	7.76	2.38	-1.71	17.10
j	9.00	4.84	8.29	2.67	-2.31	17.19
j	8.00	4.98	8.79	2.95	-2.94	17.33
j	7.00	5.10	9.28	3.24	-3.59	17.49

[a] All in aqueous solution at 25 °C. The standard state for all species except water is the ideal 1 M solution with an infinitely dilute reference state; for water, the standard state is the pure liquid with unit activity. [b] p*K*a of ArOH or ROH. [c] Free energy change for the reaction $CH_3C(OH)_3 + HOAr \rightleftharpoons CH_3C(OH)_2(OAr) + H_2O$. [d] Free energy change for the reaction $CH_3C(OH)_2(Im) + HOAr \rightleftharpoons CH_3C(OH)(Im)(OAr) + H_2O$; Im is 1-imidazolyl. [e] Slope for eq 6. [f] Intercept for eq 6. [g] Free energy change for the reaction $CH_3COOAr + HOAr \rightleftharpoons CH_3C(OH)(OAr)_2$, calculated as described in the text. [h] Rate constant for the exchange reaction.[17] [i] Hypothetical phenol of indicated p*K*a. [j] Hypothetical alcohol of indicated p*K*a.

anions at the same distance from the cationic center and disposed at right angles to each other.



For this arrangement of point charges, a simple electrostatic calculation shows that the interaction energy will be proportional to $[(1 - 2(2)^{1/2}/2^{1/2}](1/r)$, while that for a simple ion pair with the same separation distance will be proportional to $(-1/r)$. Thus, the ion triplet will have an electrostatic interaction 1.29 times as large as the ion pair, or the electrostatic stabilization when a second anion is brought up to an ion pair, with the orthogonal geometry described above, would only be 0.29 times that for the original ion pair.

We will take a stepwise approach to formation of the ion triplet in order to estimate the energy of ion triplet formation from the three separate ions in solution. For both steps of the process, we assume

$$\Delta G = \Delta G_{\mathrm{encounter}} + \Delta G_{\mathrm{electrostatic}} + \Delta G_{\mathrm{desolvation}}$$

For the first step

$$CH_3C{\equiv}O^+ + {}^-OAr \rightleftharpoons CH_3C{\equiv}O^+,{}^-OAr$$

we assume that *n* is 4 for the cylindrically symmetrical acylium ion interacting with an oxyanion. The desolvation energy depends on the p*K*a of the phenol, and the values estimated as described above are found in Table V. For the second step

$$CH_3C{\equiv}O^+,{}^-OAr + {}^-OAr \rightleftharpoons {}^-OAr,CH_3C{\equiv}O^+,{}^-OAr$$

we assume that *n* is 2, since there are two equivalent orthogonal positions relative to the first aryl oxide ion. The desolvation energy is the same as for the first step, and the electrostatic energy is 0.29 times the ion pair electrostatic energy.

Thus, by the sequence of reactions

$$CH_3COOAr,{}^-OAr \rightleftharpoons CH_3COOAr + {}^-OAr$$

$$CH_3COOAr \rightleftharpoons CH_3C{\equiv}O^+ + {}^-OAr$$

$$CH_3C{\equiv}O^+ + {}^-OAr \rightleftharpoons CH_3C{\equiv}O^+,{}^-OAr$$

$$CH_3C{\equiv}O^+,{}^-OAr + {}^-OAr \rightleftharpoons {}^-OAr,CH_3C{\equiv}O^+,{}^-OAr$$

for each of which we have now described a method for estimating the free energy change, we can calculate the free energy change for the overall process of interest

$$CH_3COOAr,{}^-OAr \rightleftharpoons {}^-OAr,CH_3C{\equiv}O^+,{}^-OAr$$

For several of the phenols of interest here, p*K*a values in DMSO have been measured,[30] so the calculation of desolvation energies via eq 7 is straightforward. For the other phenols, we calculated

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(30) Bordwell, F. G.; McCallum, R. J.; Olmstead, W. N. *J. Org. Chem.* **1984**, *49*, 1424.

Table V. Free Energies of Acylium Ion and Ion Triplet Formation[4]a

ArOH	p*K*a[b]	$-\Delta G_{\text{hydrol}}$[c]	$\Delta G_{\text{acylium}}$[d]	σ[e]	p*K*a$_{\text{DMSO}}$[f]	Δp*K*a/n_{hb}[g]	$\Delta G_{\text{acylium}}$[h]
4-Cl-2-NO_2	6.46	10.30	22.09	1.48	10.16	1.41	23.04
4-NO_2	7.14	9.67	23.65	1.24	10.40	1.45	24.66
4-CHO	7.66	9.18	24.85	1.03	12.54	1.80	26.32
3-NO_2	8.35	8.54	26.43	0.74	14.39	2.09	28.32
H	9.86	7.13	29.91	0.00	18.03	2.68	32.59
3-Cl	9.02	7.91	27.98	0.37	15.83	2.33	30.17
4-CN	7.95	8.91	25.51	0.88	13.34	1.93	27.16
2,3,5-Cl_3	6.43	10.33	22.02	1.42	10.47	1.46	23.04
2,4,5-Cl_3	6.72	10.06	22.69	1.29	11.16	1.58	23.86
i	1.00	15.40	9.53	4.00	−3.20	−0.74	7.54
i	2.00	14.47	11.83	3.55	−0.81	−0.35	10.37
i	3.00	13.53	14.13	3.10	1.55	0.03	13.19
i	4.00	12.60	16.43	2.65	3.93	0.41	16.01
i	5.00	11.66	18.73	2.21	6.31	0.79	18.83
i	6.00	10.73	21.03	1.76	8.68	1.18	21.66
i	7.00	9.80	23.33	1.31	11.06	1.56	24.48
i	8.00	8.86	25.63	0.86	13.44	1.94	27.30
i	9.00	7.93	27.93	0.41	15.81	2.32	30.12
i	10.00	6.99	30.23	−0.04	18.19	2.71	32.95
i	11.00	6.06	32.53	−0.48	20.57	3.09	35.77
i	12.00	5.13	34.83	−0.93	22.94	3.47	38.59
i	13.00	4.19	37.13	−1.38	25.32	3.85	41.41

ROH	p*K*a[b]	$-\Delta G_{\text{hydrol}}$[c]	σ[e]	p*K*a$_{\text{DMSO}}$[f]	Δp*K*a/n_{hb}[g]	$\Delta G_{\text{acylium}}$[h]
EtOH	15.83	1.55	43.64	29.00	4.45	48.62
j	14.00	3.26	39.43		4.77	44.96
j	13.00	4.19	37.13		4.44	42.22
j	12.00	5.13	34.83		4.12	39.48
j	11.00	6.06	32.53		3.80	36.73
j	10.00	6.99	30.23		3.47	33.99
j	9.00	7.93	27.93		3.15	31.25
j	8.00	8.86	25.63		2.82	28.51
j	7.00	9.80	23.33		2.50	25.77

[a] All in aqueous solution at 25 °C. The standard state for all species except water is the ideal 1 M solution with an infinitely dilute reference state; for water, the standard state is the pure liquid with unit activity. [b] p*K*a of ArOH or ROH. [c] Free energy of hydrolysis of the ester. [d] Free energy of heterolysis of the ester: $CH_3COOAr \rightleftharpoons CH_3C{\equiv}O^+ + {}^-OAr$. [e] Hammett σ value for the substituent[32] or effective $\sum\sigma$. [f] p*K*a value in DMSO; experimental value[43] or value calculated from eq 8.[43] [g] The change in p*K*a from H_2O to DMSO divided by the number of hydrogen bonds, used as a measure of the energy cost of losing a hydrogen bond. [h] Free energy of heterolysis of the encounter complex of aryl oxide ion or alkoxide ion and ester to the ion triplet: $ArO^-,CH_3COOAr \rightleftharpoons ArO^-,CH_3C{\equiv}O^+,{}^-OAr$. [i] Hypothetical phenol of indicated p*K*a. [j] Hypothetical alcohol of indicated p*K*a.

the p*K*a in DMSO from the linear free energy relation between p*K*a and Hammett σ[30] with use of

$$\mathrm{p}K\mathrm{a}_{\mathrm{DMSO}} = 18.0 - 5.3\sigma \tag{8}$$

Where necessary, we used an effective σ calculated from the p*K*a of the phenol in water[31] and the relation[32]

$$\mathrm{p}K\mathrm{a}_{\mathrm{H_2O}} = 9.92 - 2.23\textstyle\sum\sigma \tag{9}$$

For alcohols, we note that, for methanol and trifluoromethanol, for which p*K*a values in DMSO are available,[33] the data fit eq 7. We assume that Δp*K*a/n_{hb} is also linear in p*K*a$_{\mathrm{H_2O}}$ for the alcohols, so we estimate values of desolvation energies for other alcohols.

Calculations of the energies of the kinetically significant species, the ion triplet $[ArO^-,CH_3C{\equiv}O^+,{}^-OAr_2]$, and the anionic tetrahedral intermediate $[CH_3C(O^-)(OAr)_2]$ relative to the encounter complex of aryl oxide ion and ester $[CH_3COOAr,{}^-OAr]$ are summarized in Table VI.

Now that we have energies for the corners of the diagram, we can turn to calculating the energy at every point within the diagram. We note that, in general, for the exchange reactions of aryl acetates the free energies of activation based on rate constants interpolated by Williams[17] are less than the estimated free energies of the corner intermediates, implying that the reactions must be concerted. We will base this calculation upon the quartic approximation to the reaction coordinate,[21] i.e.

$$G = a_1x^2 + a_2y^2 + a_3x^3 + a_4y^3 + a_5x^4 + a_6y^4 + a_7x^2y^3 + a_8x^3y^2 + a_9x^3y^3 + a_{10}x^2y^2 \tag{10}$$

$$a_1 = 16\tilde{G}_x + 3(G_{10} - G_{00}) \qquad a_2 = 16\tilde{G}_y + 3(G_{01} - G_{00})$$

$$a_3 = -32\tilde{G}_x - 2(G_{10} - G_{00}) \qquad a_4 = -32\tilde{G}_y - 2(G_{01} - G_{00})$$

$$a_5 = 16\tilde{G}_x \qquad a_6 = 16\tilde{G}_y$$

$$a_7 = a_8 = -6(G_{11} - G_{10} - G_{01} + G_{00})$$

$$a_9 = 4(G_{11} - G_{10} - G_{01} + G_{00})$$

$$a_{10} = 9(G_{11} - G_{10} - G_{01} + G_{00})$$

where $\tilde{G}_x$ and $\tilde{G}_y$ are the intrinsic barriers for the two orthogonal coordinates and G_{xy} is the free energy of the indicated corners. The quartic approximation has the correct shape along the reaction coordinate: the initial and final points, at each of which it is approximately an upward opening parabola, and the transition state where it is approximately a downward opening parabola. Thus, we expect it to be better for points far from the transition state than the more commonly used quadratic approximation, which has the correct shape only at the transition state and is quite unrealistic at the initial and final points.

For the special case of an exchange reaction, $\tilde{G}_x = \tilde{G}_y$ and the transition state must fall on the line $x = 1 - y$ if the reaction is concerted. Along this perpendicular diagonal, where $y = 1 - x$, substitution and collection of terms leads to

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(31) Jencks, W. P.; Regenstein, J. Physical and Chemical Data. In *Handbook of Biochemistry and Molecular Biology*, 3rd ed.; Fasman, G., Ed.; Chemical Rubber Company: Cleveland, 1976; Vol. 1.

(32) Perrin, D. D.; Dempsey, B.; Serjeant, E. P. *pKa Prediction for Organic Acids and Bases*; Chapman and Hall: London, 1981.

(33) Bordwell, F. G. *Acc. Chem. Res.* **1988**, *21*, 456.

$$
\begin{aligned}
G = {} & a_2 + a_4 + a_6 \\
& - (2a_2 + 3a_4 + 4a_6)x \\
& + (a_1 + a_2 + 3a_4 + 6a_6 + a_7 + a_{10})x^2 \\
& + (a_3 - a_4 - 4a_6 - 3a_7 + a_8 + a_9 - 2a_{10})x^3 \\
& + (a_5 + a_6 + 3a_7 - 2a_8 - 3a_9 + a_{10})x^4 \\
& - (a_7 - a_8 - 3a_9)x^5 \\
& - a_9x^6
\end{aligned}
$$

It is advantageous to replace a_1–a_{10} by the free energies, leading to

$$
\begin{aligned}
G = {} & (G_{01} - G_{00}) \\
& + (32\tilde{G} + 3(G_{10} - G_{01}) + 3(G_{11} - G_{10} - G_{01} + G_{00}))x^2 \\
& + (-64\tilde{G} - 2(G_{10} - G_{01}) - 2(G_{11} - G_{10} - G_{01} + G_{00}))x^3 \\
& + (32\tilde{G} - 9(G_{11} - G_{10} - G_{01} + G_{00}))x^4 \\
& + 12(G_{11} - G_{10} - G_{01} + G_{00})x^5 \\
& - 4(G_{11} - G_{10} - G_{01} + G_{00})x^6
\end{aligned}
$$

The condition for a minimum (or maximum) is $dG/dx = 0$, and after simplification this leads to

$$
\begin{aligned}
0 = {} & 2(32\tilde{G} + 3(G_{10} - G_{01}) + 3(G_{11} - G_{10} - G_{01} + G_{00})) \\
& + 3(-64\tilde{G} - 2(G_{10} - G_{01}) - 2(G_{11} - G_{10} - G_{01} + G_{00}))x \\
& + 4(32\tilde{G} - 9(G_{11} - G_{10} - G_{01} + G_{00}))x^2 \\
& + 60(G_{11} - G_{10} - G_{01} + G_{00})x^3 \\
& - 24(G_{11} - G_{10} - G_{01} + G_{00})x^4
\end{aligned}
$$

It turns out that $x = 1$ is a root, so the condition for the other three roots is

$$
\begin{aligned}
0 = {} & 64\tilde{G} + 6(G_{10} - G_{01}) + 6(G_{11} - G_{10} - G_{01} + G_{00})) \\
& -(128\tilde{G})x \\
& - 36(G_{11} - G_{10} - G_{01} + G_{00})x^2 \\
& + 24(G_{11} - G_{10} - G_{01} + G_{00})x^3
\end{aligned}
$$

These equations are intractable toward algebraic solution but can be solved numerically for $\tilde{G}$ and x^*. The results are slightly different from those obtained with the analytical equation for the quadratic surface[14] but are clearly similar. $\tilde{G}$ values calculated with use of both the quadratic and the quartic approximations are given in Table VI. When this is done, we obtain the intrinsic barriers shown in Table VI. These are uniformly low for the aryl oxide ions.

The intrinsic barrier shows no systematic variation with phenol p*K*a for the range of compounds for which there are data. The two points for phenols of highest p*K*a deviate from the average, but we hesitate to construct an interpretation of this. These values ultimately derive from rate constants for exchange obtained by extrapolation rather than interpolation[17] and hence are subject to greater uncertainty. A constant intrinsic barrier means that we may examine the question of when the aryl oxide ion/aryl acetate reaction will proceed by one of the limiting mechanisms, i.e., when the reaction path will pass through one or the other of the corner intermediates. This can be done by estimating the energies for the corner species for a series of hypothetical strongly or weakly acidic phenols, by using the procedures outlined above and assuming that the intrinsic barrier remains effectively constant at the average value of 1.41. In discussing the degree of concertedness of a reaction, it is common to use the parameter τ, the tightness parameters.[34,35] This measures distance along the diagonal joining the two possible intermediates and runs from 0 at one corner to 2 at the other. For symmetrical exchange reactions, the transition state necessarily falls on the tightness diagonal and $\tau = 2x^*$. In order to have τ run from 0 to 2, the distance along the diagonal must be multiplied by a factor of $2^{1/2}$. Thus $\tau = 2^{1/2}((1 - y^*)^2 + x^{*2})^{1/2} = 2x^*$. When we do this (Table VI), we obtain the values of τ as a function of phenol p*K*a shown in Figure 1. Clearly for strongly acidic phenols of p*K*a < 1, we predict a limiting reaction passing through or near an acylium ion, while for weakly acidic phenols of pKa > 16 we predict a limiting reaction passing through a tetrahedral species, if the intrinsic barrier is the same for all phenols. If weakly acidic phenols behave like alcohols, which we consider more likely, then we predict a transition to a stepwise reaction by the tetrahedral intermediate mechanism for phenols of p*K*a > 11. In both cases, because the intrinsic barriers are small and the intermediates are unstable, there is no effective barrier to breakdown of the "intermediates" to starting materials or products. Thus, although in one sense the limiting reactions are not concerted, because the reaction proceeds along the edges of the square diagram, in another sense they are concerted, because there is no intermediate with a finite lifetime. The nature of the reaction surfaces for three illustrative cases (for phenols of p*K*a = 1 (reacting via an acylium ion), 7 (reacting via the fully concerted path), and 12 (reacting via a tetrahedral intermediate)) are shown by the contour diagrams in Figure 2. These are "state" diagrams including solvent and not just the reactants explicitly shown.

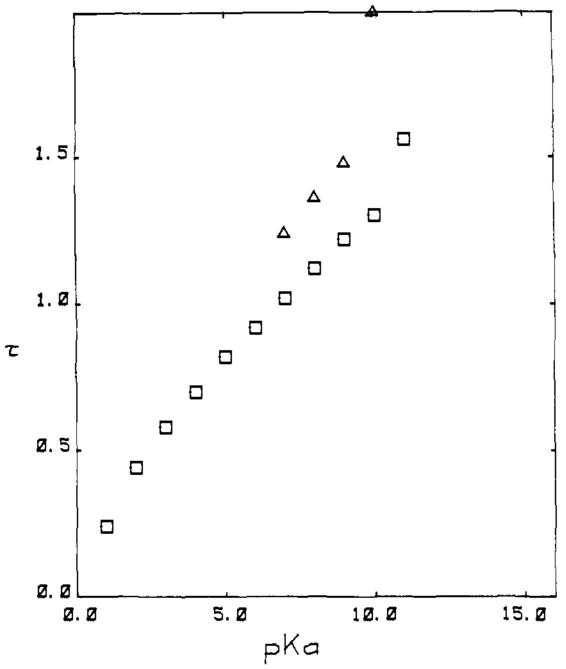

Figure 1. Position of the transition states along the diagonal from the acylium ion ($\tau = 0$) to the tetrahedral intermediate ($\tau = 2$) as a function of p*K*a for phenols (□) and alcohols (△).

We turn now to estimating intrinsic barriers for alkoxide ion addition to esters. The data that provide a starting point are the rates of transesterification from aryl acetates reported by Jencks and Gilchrist.[37] As we did to estimate the free energies of $CH_3C(OH)(OAr)_2$, we next estimate the free energy of $CH_3C(OH)_2(OAr)$ from the rate of hydroxide ion catalyzed hydrolysis of CH_3COOAr and a linear energy relation for replacement of OH by OR. This allows us to calculate the free energy of $CH_3C(OH)(OR)OAr)$ from the free energy of $CH_3C(OH)_2(OAr)$. With the free energy of $CH_3C(OH)(OR)(OAr)$ in hand and hence, by p*K*a estimation, the free energy of $CH_3C(O^-)(OR)(OAr)$, we can derive an intrinsic barrier for the attack of RO^- on CH_3COOAr. In these reactions, it turns out that the tetrahedral intermediate is at lower energy than the observed transition state for transesterification, leading to the presumption that the mechanism is stepwise. These calculations, which are summarized in Table VII, lead to intrinsic barriers for RO^- attack on an ester, which are larger than for ArO^- but distinctly smaller than for HO^-.

Now we must examine further implications of this treatment of the reactions because it is known that hydrolyses of alkyl esters

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(34) Albery, W. J.; Kreevoy, M. M. *Adv. Phys. Org. Chem.* **1978**, *16*, 87.
(35) Kreevoy, M. M.; Lee, I. S. H. *J. Am. Chem. Soc.* **1984**, *106*, 2550.
(36) Olmstead, W. N.; Margolin, Z.; Bordwell, F. G. *J. Org. Chem.* **1980**, *45*, 3295.
(37) Jencks, W. P.; Gilchrist, M. *J. Am. Chem. Soc.* **1962**, *84*, 2910.

Table VI. Free Energies for Concertedness Calculations

ArOH	p*K*a[b]	$\Delta G_{\mathrm{acylium}}$[c] (corrected)	ΔG_{ti}[d] (corrected)	$\Delta G^{\ddagger}$[e] (corrected)	$\tilde{G}$[f] (quad)	$\tilde{G}$[g,j] (quartic)
4-Cl-2-NO_2	6.46	23.04	25.61	15.81	1.85	1.85
4-NO_2	7.14	24.66	22.03	15.68	2.03	2.00
4-CHO	7.66	26.32	22.07	15.25	1.64	1.60
3-NO_2	8.35	28.32	18.57	14.48	1.74	1.18
H	9.86	32.59	16.44	12.49	0.89	0.12
3-Cl	9.02	30.17	18.60	13.52	1.08	0.66
4-CN	7.95	27.16	19.33	15.24	2.07	1.82
2,3,5-Cl_3	6.43	23.04	25.34	15.64	1.79	1.80
2,4,5-Cl_3	6.72	23.86	24.65	15.45	1.66	1.69
h	1.00	7.54	13.50	8.29		
h	2.00	10.37	13.65	10.05		
h	3.00	13.19	11.59	7.48		
h	4.00	16.01	9.69	4.44		
h	5.00	18.83	42.11	10.22		
h	6.00	21.66	38.63	12.29		
h	7.00	24.48	35.29	13.90		
h	8.00	27.30	32.08	15.04		
h	9.00	30.12	29.02	15.72		
h	10.00	32.95	26.10	15.94		
h	11.00	35.77	23.32	15.69		
h	12.00	38.59	20.69	14.98		
h	13.00	41.41	18.20	13.80		

ROH	Δp*K*a[b]	$\Delta G_{\mathrm{acylium}}$[c] (corrected)	ΔG_{ti}[d] (corrected)	$\Delta G^{\ddagger}$[e] (corrected)
EtOH	15.83	48.73	4.43	11.7
i	14.00	44.96	5.32	
i	13.00	42.22	6.54	
i	12.00	39.48	7.81	
i	11.00	36.73	9.13	
i	10.00	33.99	10.49	
i	9.00	31.25	11.88	
i	8.00	28.51	13.32	
i	7.00	25.77	14.79	

[a] All in aqueous solution at 25 °C. The standard state for all species except water is the ideal 1 M solution with an infinitely dilute reference state; for water, the standard state is the pure liquid with unit activity. [b] p*K*a of ArOH or ROH. [c] Free energy of heterolysis of the encounter complex of aryl oxide ion or alkoxide ion and ester to the ion triplet: $ArO^-,CH_3COOAr \rightleftharpoons ArO^-,CH_3C{\equiv}O^+,{}^-OAr$. [d] Free energy change for conversion of the encounter complex of aryl oxide ion or alkoxide ion and ester to the anionic tetrahedral intermediate. [e] Free energy of activation, calculated for reaction from the encounter complex of aryl oxide or alkoxide ion and ester. [f] Intrinsic barrier calculated with use of the quadratic model.[14] [g] Intrinsic barrier calculated with use of the quartic model, as described in the text. [h] Hypothetical phenol of indicated p*K*a. [i] Hypothetical alcohol of indicated p*K*a. [j] Average 1.41.

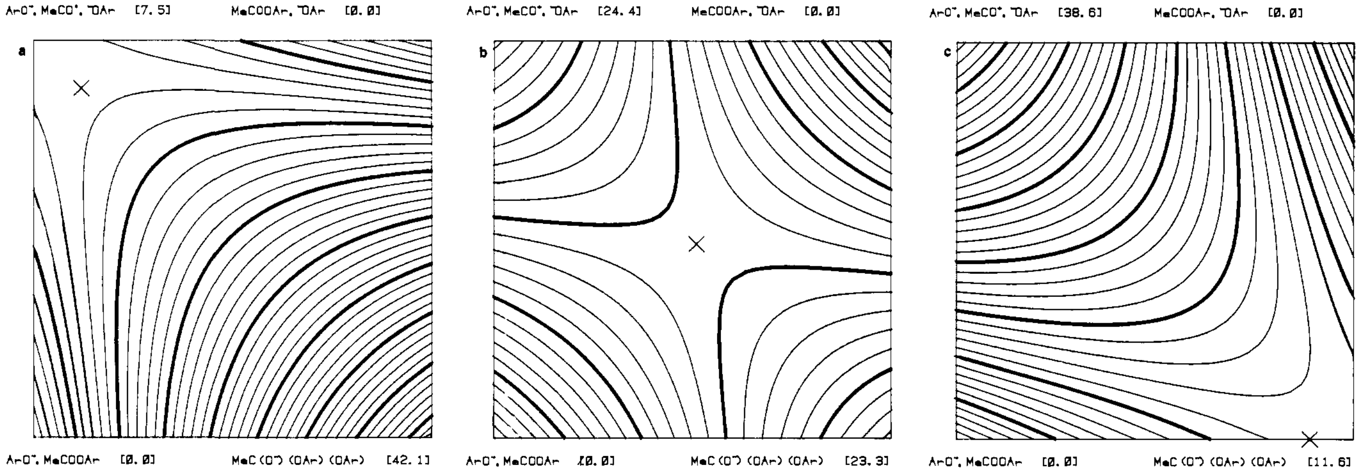

Figure 2. Contour diagrams for three illustrative cases of the symmetrical exchange reaction $ArO^- + CH_3COOAr \rightleftharpoons ArOOCCH_3 + {}^-OAr$. (a) p*K*a of ArOH is 1. (b) p*K*a of ArOH is 7. (c) p*K*a of ArOh is 12. Contours are drawn every 1 kcal, with heavier lines every 5 kcal.

proceed by tetrahedral intermediates with finite lifetimes.[38]

In Figure 3, we plot the intrinsic barrier as a function of p*K*a of ROH, including aryl oxide ions, alkoxide ions, and hydroxide ion. The value for hydroxide ion has been calculated, from rate and equilibrium data for the esters for which we have determined the free energies of the tetrahedral intermediates by our thermochemical method,[23] for reaction starting from the encounter complex of ester and desolvated hydroxide ion. The energy of desolvation for hydroxide ion was calculated from the p*K*a in DMSO[36] as was done for alkoxide ions.

For the aryl oxide ions, as discussed above, the values of the intrinsic barrier show scatter but no clear tendency. We have used an average value, indicated by the horizontal line in Figure 3. For the alkoxide ions, there is a suggestion of a linear relation between $\tilde{G}$ and p*K*a; this line passes through the cluster of points for aryl oxide ions. The value for hydroxide ion is uniquely higher, a point to which we will return. We can now ask when the mechanism

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(38) Johnson, S. L. *Adv. Phys. Org. Chem.* **1967**, *5*, 237.

Table VII. Intrinsic Barrier for the Addition of Trifluoroethoxide, Propargyl oxide, and Methoxide to Esters[a]

ArOH[b]	σ^* (OAr)[c]	ΔG_{hydrat}[d]	ΔG_{addn}[e]	ΔG_{ti}[f] (corrected)	log k[g]	ΔG^{*}[h] (corrected)	$\bar{G}$[i,k]
			CF_3CH_2OH, $\Delta G_{\text{desolv}} = 5.63$[j]				
PhOH	2.37	11.97	17.47	7.53	0.83	8.26	3.48
p-NPOH	2.91	10.73	17.13	6.22	1.81	6.94	3.02
DNPOH	3.32	9.52	16.60	4.96	2.60	5.85	2.83
			$HC{\equiv}CCH_2OH$, $\Delta G_{\text{desolv}} = 6.52$[j]				
PhOH	2.37	11.97	17.44	6.61	1.37	7.53	3.34
p-NPOH	2.91	10.73	17.06	5.27	2.26	6.32	3.14
DNPOH	3.32	9.52	16.51	3.98	3.05	5.23	2.90
			CH_3OH, $\Delta G_{\text{desolv}} = 6.15$[j]				
PhOH	2.37	11.97	15.39	4.94	1.94	6.76	3.90
p-NPOH	2.91	10.73	14.67	3.24	2.68	5.74	3.95
DNPOH	3.32	9.52	13.85	1.68	3.51	4.62	3.73

[a] All in aqueous solution at 25 °C. The standard state for all species except water is the ideal 1 M solution with an infinitely dilute reference state; for water, the standard state is the pure liquid with unit activity. [b] p*K*a of ArOH or ROH. [c] Taft σ^* value for OAr, calculated as described in the text. [d] Free energy change for covalent hydration of CH_3COOAr. [e] Free energy change for the exchange reaction $CH_3C(OH)_2(OAr) + HOR \rightleftharpoons CH_3C(OH)(OR)(OAr) + H_2O$, calculated as described in the text, with parameters for eq 6 from Table IV. [f] Free energy change for conversion of the encounter complex $[RO^-,CH_3COOAr]$ to the anionic tetrahedral intermediate $[CH_3C(O^-)(OR)(OAr)]$. [g] Logarithm of the observed rate constant ($M^{-1}\ s^{-1}$) for reaction of RO^- with CH_3COOAr.[37] [h] Free energy of activation, calculated for reaction starting at the encounter complex, $[RO^-,CH_3\text{-}COOAr]$. [i] Intrinsic barrier for addition of RO^-. [j] Free energy of desolvation, estimated as described in the text. [k] Average $\bar{G}$ values: CF_3CH_2OH, 3.11; $HC{\equiv}CCH_2OH$, 3.15; CH_3OH, 3.86.

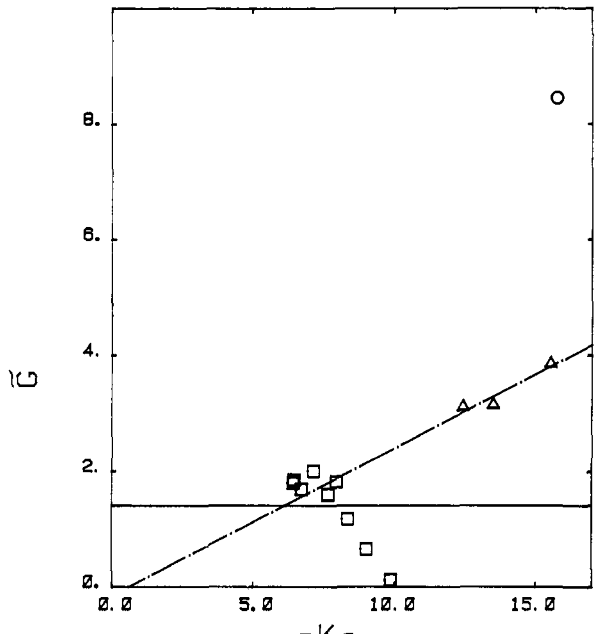

Figure 3. Intrinsic barrier as a function of p*K*a for aryl oxide ions (□), alkoxide ions (△), and hydroxide ion (○).

of exchange reaction of alkyl esters would change from one with a transition state resembling a tetrahedral intermediate to one with a tetrahedral intermediate with a finite lifetime. When we do this (Table VI), we find that the changeover happens at a p*K*a of 10. Thus, we predict that, for an alcohol of p*K*a 7 or 8, exchange should be a concerted process, with a rate constant of $10^{0.4}$ (p*K*a 7) or $10^{0.2}$ (p*K*a 8). This process would be observable since the exchange would be studied at a pH near the p*K*a value of the alcohol, where the hydroxide ion catalyzed hydrolysis, with a rate constant of $10^{2.3}$ (p*K*a 7) or $10^{2.0}$ (p*K*a 8), would not be a serious problem. The difficulty is to devise a suitable alcohol with such a low p*K*a. Tris(trifluoromethyl)carbinol has a p*K*a of 5.4[31] and so should react by a concerted pathway except that it would be expected to show severe rate retardation because of steric hindrance in the transition state for exchange. Bis(trifluoromethyl)carbinol has a p*K*a of 9.3[31] so that it would be expected to be close to the transition between concerted and stepwise mechanisms. Other powerful electron-withdrawing groups are likely to give alcohols unstable to breakdown in basic solutions. Our prediction will likely be difficult to test.

Discussion

There can be no doubt that the calculations reported above are only a rough approximation to the actual energetics of ester exchange reactions. Numerous extrapolations have been used, and error cumulation is bound to have serious effects. The question is not whether we have constructed a precisely accurate picture of these reactions but whether we have been led to useful insights. It is striking that our thermodynamic calculations have led to exactly the same conclusions concerning the nature of the exchange reactions of aryl acetates with aryl oxide ions as Williams and co-workers were led to by structure reactivity studies.[17] These conclusions have not been universally accepted.[39] The present research has shown that, as a logical consequence of the low intrinsic barriers that make a concerted mechanism favored for the aryl oxide ions studied by Williams and co-workers, all ester exchanges of aryl acetates and all hydrolyses of aryl acetates proceed by mechanisms with no intermediates of significant lifetimes, even when the mechanism is one of the limiting ones via acylium ion or tetrahedral species. The only exceptions to this might be for phenols of p*K*a greater than 11 for which, if the intrinsic barrier is similar to that for alcohols, there might be a tetrahedral intermediate of very short lifetime. Since there are few phenols with such high p*K*a values (Jencks and Regenstein[31] list only one phenol with a p*K*a above 11, although second p*K*a's of poly(hydroxyphenols) should be in this range), this is not a major limit to the generality of our conclusion. In addition, we can predict that concerted mechanisms should be seen for alcohols with sufficiently low p*K*a values, we and can predict the approximate rate constants to be expected for this path, although conveniently useable alcohols of such low p*K*a are as unlikely as conveniently useable phenols of very high p*K*a.

Although our qualitative conclusions concerning the nature of the transition states for the exchange reactions of aryl acetate/aryl oxide ion pairs are in good agreement with those of Williams and co-workers,[17] there are some differences in detail. We predict that the limiting acylium ion mechanism will only be attained for phenols of p*K*a < 1, where Williams and co-workers predicted this limiting mechanism for p*K*a < 2.0. We predict that (assuming phenols behave similarly to alcohols) the switch to a tetrahedral intermediate mechanism will occur in the p*K*a range 11–12, which is coincidentally very close to the prediction of Williams and co-workers, i.e., p*K*a = 11.7. In our analysis, the switch in mechanism occurs because the increasing intrinsic barrier because a shift to a stepwise mechanism, although this mechanism has no intermediate with a finite lifetime. If the intrinsic barrier for

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(39) Buncel, E.; Um, I. H.; Hoz, S. *J. Am. Chem. Soc.* **1989**, *111*, 971.

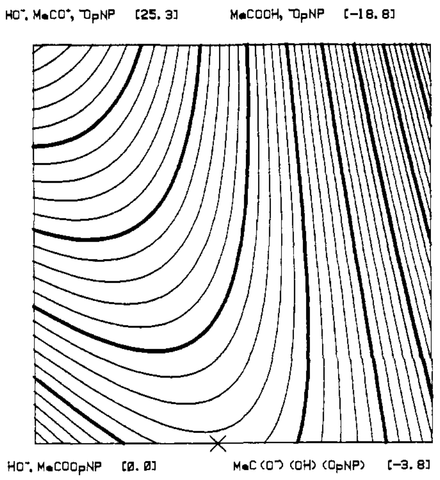

Figure 4. Contour diagram for the hydroxide ion catalyzed hydrolysis of *p*-nitrophenyl acetate, showing that the transition state is along the edge, corresponding to simple addition of hydroxide ion to give a tetrahedral intermediate, even though the tetrahedral intermediate need not be on the reaction coordinate because it is not in an energy well. Contours are drawn every 1 kcal, with heavier lines every 5 kcal.

phenoxide addition does not change with increasing p*K*a, then the transition state would not reach the tetrahedral intermediate limit until a p*K*a of about 15.

Implicit in the analysis represented above in the conclusion that the reaction that we use to estimate the free energy of the tetrahedral intermediate $CH_3C(O^-)(OH)(OAr)$, namely, hydroxide ion catalyzed hydrolysis of CH_3COOAr, is one in which there is no intermediate of significant lifetime because of the very low barrier for expulsion of ArO^-. We must ask whether the procedure is logically defensible. We believe that there is no inconsistency, because calculation of the energy surface (Figure 4) shows that the reaction follows the edge reaction leading toward the tetrahedral intermediate until after the transition state for this process. Thereafter there is no reason for the reaction path to include the point representing the tetrahedral intermediate, and there is no energy well at this point to impose a lifetime of this species. Thus, we have the situation that the free energy level of the tetrahedral intermediate determines the energy of the transition state, even though it need not be on the reaction path. We suspect that this will prove to be a common situation for reactions where there is a significant intrinsic barrier to formation of an intermediate along one coordinate and only a small intrinsic barrier to breakdown along the other, provided that the energy of the other corner intermediate is high enough to enforce an edge reaction.

The examination of ester exchange reactions has shown that, in ordinary discourse, physical organic chemists use "concerted" in two senses: One implies that two (or more) bond making/breaking processes occur synchronously as a reaction proceeds through the transition state; the other implies that there is no intermediate with a finite lifetime along the reaction coordinate. Although a reaction concerted in the first sense is concerted in the second sense, the converse does not follow, and in fact we are led to predict the most aryl ester hydrolyses will have no intermediate of finite lifetime on the reaction path.

Williams and co-workers[17] reported an equation relating k_{ii}, the rate constant for a symmetrical exchange reaction of aryl acetate and aryl oxide ion, to the pKa of the phenol. Using this equation to extrapolate leads to a prediction of very high rate constants for exchange involving a phenol of p*K*a = 15, which (if ethanol can be used as an approximation to a phenol of pKa = 15) is false to fact. The reason for this discrepancy is the implicit assumption that the intrinsic barrier is independent of phenol p*K*a, which as we have seen is correct for the range of phenols studied by Williams and co-workers but is not correct for alcohols of higher p*K*a.

Our treatment of the transition from the acylium ion mechanism through various concerted paths to the tetrahedral intermediate mechanism is based on the assumption that there can be a smooth transition between these mechanisms. This in turn has geometrical implications. If the nucleophile and leaving group are both partially bonded to the central carbon, they must either be interacting in the S_N2 sense with opposite lobes of a single orbital, implying a linear transition state, or with two distinct orbitals (sp^3 at the tetrahedral intermediate extreme and two p orbitals at the acylium ion extreme). S_N2-type mechanisms may be feasible for concerted pathways and could smoothly merge into acylium ion mechanisms, but there are severe difficulties in merging smoothly into a tetrahedral intermediate mechanism. If the reaction involves two p orbitals at the acylium ion extreme, then it is simple for there to be a smooth merging through concerted reaction to a tetrahedral intermediate.

Our analysis of intrinsic barriers shows that hydroxide ion has a uniquely high value, quite out of line with alkoxide ions of similar p*K*a. This unusually low reactivity of hydroxide ion has been commented upon.[18-20] Demonstrating that this phenomenon results from the intrinsic barriers and not the energetics of the addition reactions helps focus attention on the unique behavior of hydroxide ion. While we do not claim to have a convincing explanation, we offer two possible rationales.

(1) Studies of gas-phase p*K*a values of small molecules show that solvation is uniquely important for very small ions, while large ions are able to provide internal solvation by various mechanisms of charge delocalization.[40] This means that solvation will be uniquely important for hydroxide ion and that reorganization of solvation during chemical reactions will be more important and thus will contribute to a larger intrinsic barrier for hydroxide ion than for alkoxide ions of similar p*K*a.

(2) In addition, hydroxide ion has a unique property because of the nature of its R group (hydrogen). This hydrogen is essentially unsolvated in the initial state because it is very weakly acidic and hence unlikely to be hydrogen bonded to water. It will require a normal hydrogen bond in the product where it becomes a normally acidic alcohol; the second p*K*a of a tetrahedral intermediate will be around 15. Although the energy of this new hydrogen bond will be only a few kilocalories per mole, the need to have solvent reorganization to provide it during the reaction will contribute to the intrinsic barrier.

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