Reactions of Carbonyl Compounds in Basic Solutions. Part V.[1] The Mechanism of the Alkaline Hydrolysis of Methyl 8-(3- or 4-Substituted Benzoyl)-, 8-Formyl-, and 8-Pivaloyl-1-naphthoates and Methyl 5-Formylphenanthrene-4-carboxylate. Neighbouring-group Participation by Carbonyl Groups

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Rate coefficients have been measured for the alkaline hydrolysis of methyl 8-formyl-, 8-(3- or 4-substituted benzoyl)-, and 8-pivaloyl-1-naphthoates and methyl 5-formylphenanthrene-4-carboxylate in 70% (v/v) dioxan–water at several temperatures. The entropies and enthalpies of activation have been evaluated. The effect of a series of 8-substituents on the alkaline hydrolysis of methyl 1-naphthoate has been examined. The relative rates of hydrolysis, activation parameters, substituent effects, and solvent isotope effects have been used to demonstrate the occurrence of neighbouring-group participation by the formyl- or benzoyl-carbonyl groups in the alkaline hydrolysis. The importance of proximity, orientation, and steric strain factors are discussed.

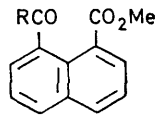
In Parts II to IV,[1-3] the extent and importance of intramolecular catalysis in the alkaline hydrolysis of 2-acylbenzoates and *cis*-3-benzoylacrylates was assessed. A number of possible criteria were evaluated for these systems, which include relative rates, activation parameters, substituent (*both* polar and steric), solvent isotope, and solvent effects. Several other studies[4] have also indicated participation by suitably orientated acyl-carbonyl groups in ester hydrolysis.

In this study, we have investigated the alkaline hydrolysis of methyl 8-formyl-, 8-pivaloyl-, and 8-(3- or 4-substituted benzoyl)-1-naphthoates, as well as of methyl 5-formylphenanthrene-4-carboxylate. These particular systems were selected to enable the more precise delineation of the importance of, in particular, proximity, orientation, and steric strain factors. The relative rates, the activation parameters, substituent, solvent isotope, and other effects are discussed.

RESULTS AND DISCUSSION

The alkaline hydrolysis of the methyl 8-(3- or 4-substituted benzoyl)-, 8-formyl-, and 8-pivaloyl-1-naphthoates, as well as of methyl 5-formylphenanthrene-4-carboxylate, are of first order both in ester and in hydroxide anion. The products of these alkaline hydrolyses are the anions of the corresponding acids. Rate coefficients for the hydrolysis of the esters in 70% (v/v) dioxan–water at several temperatures are shown in Table 1.

Relative Rates.—It has been shown previously that significant rate enhancements are usually observed when



(I)

TABLE 1

Rate coefficients for the alkaline hydrolysis of methyl 8-acyl-1-naphthoates and related esters in 70% (v/v) dioxan–water *

Substnt. [R in (I)]	10^3k_2/l mol^{-1} s^{-1}				
	20·0 °C	30·0 °C	40·0 °C	50·0 °C	60·0 °C
H	35,500	57,300	82,000	132,000	
Bu^t					0·478
Ph		1·33	3·60	7·61	16·6
Methyl 5-formylphenanthrene-4-carboxylate	7,470	11,200	19,500	31,500	46,800
Methyl 1-naphthoate		6·88	13·7	27·6	51·4
Methyl phenanthrene-4-carboxylate			0·120		

* Rate coefficients were reproducible to within ±3%.

[1] Part IV, K. Bowden and M. P. Henry, *J. Chem. Soc.* (*B*), 1971, 156. For a preliminary account of part of this study see *Chem. Comm.*, 1970, 1315.

[2] K. Bowden and G. R. Taylor, *J. Chem. Soc.* (*B*), 1971, 145.

[3] K. Bowden and G. R. Taylor, *J. Chem. Soc.* (*B*), 1971, 149.

[4] (*a*) M. S. Newman and S. Hishida, *J. Amer. Chem. Soc.*, 1962, **84**, 3582; M. S. Newman and A. L. Leegwater, *ibid.*, 1968, **90**, 4410; Y. Shalitin and S. A. Bernhard, *ibid.*, 1964, **86**, 2292; H. G. O. Becker, J. Schneider, and H. D. Steinleitner, *Tetrahedron Letters*, 1965, 3761; L. Holleck, G. A. Melkonian, and S. B. Rao, *Naturwiss.*, 1958, **45**, 438; H. D. Burrows and R. M. Topping, *Chem. Comm.*, 1969, 904, *J. Chem. Soc.* (*B*), 1970, 1323; K. C. Kemp and M. L. Mieth, *Chem. Comm.*, 1969, 1260; (*b*) M. L. Bender and M. S. Silver, *J. Amer. Chem. Soc.*, 1962, **84**, 4589; M. L. Bender, J. A. Reinstein, M. S. Silver, and R. Mikulak, *ibid.*, 1965, **87**, 4545.

intramolecular nucleophilic catalysis occurs by participation of a neighbouring acyl carbonyl group.[1,3,4] Therefore it is necessary to estimate the ' expected ' rate ratios, relative to the parent unsubstituted ester, if the alkaline hydrolysis occurred by the normal direct hydrolytic path. Previously only isolated studies of the alkaline hydrolyses of alkyl 8-substituted 1-naphthoates have been made.[5,6] Fischer *et al.*[5] have shown that ethyl 8-nitro-1-naphthoate hydrolysed at a slower rate than the unsubstituted ester; while it has been shown that 8-methyl-1-naphthoate is *very* resistant to alkaline hydrolysis.[6] We have therefore investigated the hydrolysis of several methyl 8-substituted 1-naphthoates, as shown in Table 2. Only upper limits for the rate coefficients of the 8-bromo and 8-methyl esters could be estimated. All the 8-substituents shown in Table 2

TABLE 2

Rate coefficients for the alkaline hydrolysis of methyl 8-substituted 1-naphthoates in 70% (v/v) dioxan–water at 60·0 °C *

8-Substnt.	10^3k_2/l mol^{-1} s^{-1}
H	51·4
NO_2	1·09
Cl	0·277
OMe	0·041 (±0·004)
Br,Me	<0·02 †

* See Table 1. † Rates were too slow to measure. An estimated upper limit for the hydrolysis of these substrates is given.

powerfully retard the rate of hydrolysis. The polar effect of the *peri*-substituents can be expected to be very greatly reduced or even reversed.[7-9] All the 8-substituents cause the carboxylate group to be completely or very extensively deconjugated with the naphthalene ring. However, the steric ' bulk ' effect of the substituents is of paramount importance. This severely destabilises the transition state for alkaline hydrolysis, as the reaction site has a much greater steric requirement than the initial state. In selecting a model upon which to base an estimate of the normal direct rate of hydrolysis of the three 8-acyl-1-naphthoates, both the steric and polar factors [10] of the 8-acyl substituent must be considered. Thus while the polar effect of a formyl group is somewhat less than that of a nitro-group, the more important steric factors are in the reverse order and we would therefore expect the 8-formyl and -nitro esters to have comparable rates of hydrolysis.

It is important to note that we are considering here mainly the lateral ' bulk ' of the substituent groups, as opposed to the maximum Van der Waals' radii for the substituent, *cf.* refs. 9, 11, and 12. Estimates based on these considerations are given in Table 3 for the 8-acyl-1-naphthoates as ' expected ' relative rate ratios for alkaline

TABLE 3

Relative rate ratios for the alkaline hydrolysis of methyl 8-acyl-1-naphthoates and related ester in 70% (v/v) dioxan–water

Substnt. [R in (I)]		k/k_0 Observed	' Expected '	* Enhancement
H	(30 °C)	8330	0·02	400,000
Bu^t	(60 °C)	0·00930	≪0·01	†
Ph	(30 °C)	0·193	<0·01	>20
Methyl 5-formylphenanthrene-4-carboxylate	(40 °C)	162,000	<0·01	>20,000,000

* Ratios are the maximum that could reasonably be expected. † Uncertain.

hydrolysis reaction. The estimate for the phenanthrene-carboxylate ester is even more difficult. The only relevant measurements have been made on methyl phenanthrene-4-carboxylate itself, *i.e.* Table 1 and ref. 13. The latter ester is not a realistic model for the 5-formyl ester because of the proximity of the substituent to the reaction site. First, the formyl substituent causes excessive steric ' bulk ' interactions, possibly even distorting the planar aromatic ring.[14] Second, the normally activating polar effect of the formyl group would be expected to be absent or even reversed because of its stereochemical relation to the reaction site, *cf.* references 7—9. While difficult to estimate, these two factors should result, compared to the unsubstituted phenanthrene-4-carboxylate, in a retardation by at least a factor of 10^2, but very probably even more. The latter estimate was made from a consideration of the steric and polar effects in the 1,8-naphthalene system discussed above and the 1,2-benzene system [15] in the alkaline hydrolysis reaction.

The rate enhancements noted in Table 3 clearly indicate that the two formyl esters hydrolyse with intramolecular catalysis. For the latter esters and the corresponding benzoate,[3] this path is very favourable. The 8-benzoyl ester has a much smaller rate enhancement, but it would appear sufficient, *i.e.* $k/k_0 > 10$, to indicate the operation of intramolecular catalysis. The consideration of the 8-pivaloyl ester is more difficult, particularly because of the difficulty in estimating the ' expected ' rate ratio. The steric ' bulk ' of the t-butyl group would appear to inhibit attack at *both* the keto- and ester-carbonyl

[5] A. Fischer, J. D. Murdoch, J. Packer, R. D. Topsom, and J. Vaughan, *J. Chem. Soc.*, 1957, 4358.
[6] G. J. Karabatsos, G. C. Sonnichsen, C. G. Papaioannou, S. E. Scheppele, and R. J. Shone, *J. Amer. Chem. Soc.*, 1967, **89**, 463; G. J. Karabatsos and C. G. Papaioannou, *Tetrahedron Letters*, 1968, 2629.
[7] K. Bowden and D. C. Parkin, *Chem. Comm.*, 1968, 75; *Canad. J. Chem.*, 1969, **47**, 185.
[8] M. Hojo, K. Katsurakawa, and Z. Yoshida, *Tetrahedron Letters*, 1968, 1497.
[9] K. Bowden, M. J. Price, and G. R. Taylor, *J. Chem. Soc.* (*B*), 1970, 1022.
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[12] M. Charton, *Progr. Phys. Org. Chem.*, 1971, **8**, 235; and references therein.
[13] J. F. Corbett, A. Feinstein, P. H. Gore, G. J. Reed, and E. C. Vignes, *J. Chem. Soc.* (*B*), 1969, 974.
[14] M. S. Newman and A. S. Hussey, *J. Amer. Chem. Soc.*, 1947, **69**, 3023; M. S. Newman and H. S. Whitehouse, *ibid.*, 1949, **71**, 3664.
[15] N. B. Chapman, J. Shorter, and J. H. P. Utley, *J. Chem. Soc.*, 1963, 1291; D. P. Evans, J. J. Gordon, and H. B. Watson, *ibid.*, 1937, 1430; Y. Iskander, R. Tewfik, and S. Wasif, *ibid.*, (*B*), 1966, 424.

groups. However, it seems probable that the observed rate, compared to the other 8-substituents shown in Table 2, is sufficiently rapid to indicate the likelihood of intramolecular catalysis.

Substituent Effects at the Neighbouring Carbonyl Group.—The order of the 8-substituent effect on the rate coefficients, *i.e.* reactivity of H $\gg$ Ph > Bu^t, is in accord with the steric and resonance effects [11] of these substituents progressively inhibiting attack at the keto-carbonyl group.

The effect of 3- or 4-substituents in the 8-benzoyl group is very informative and is shown in Table 4. This

TABLE 4

Rate coefficients for the alkaline hydrolysis of methyl 8-(3- and 4-substituted benzoyl)-1-naphthoates in 70% (v/v) dioxan–water at 60·0 °C *

Substnt.	10^3k_2/ l mol^{-1} s^{-1}
H	16·6
4-Me	8·86
4-OMe	4·12
3-Me	12·7
4-Cl	36·2
3-Cl	59·8
4-Br	36·1
3-CF_3	88·2

* See Table 1.

TABLE 5

Hammett reaction constants for the alkaline hydrolysis of the methyl 8-(3- or 4-substituted benzoyl)-1-naphthoates in 70% (v/v) dioxan–water at 60·0 °C *

	ρ	log k_0	r	s	n
(*a*)	1·727	−1·822	0·992	0·087	8
(*b*)	1·857	−1·886	0·952	0·244	8

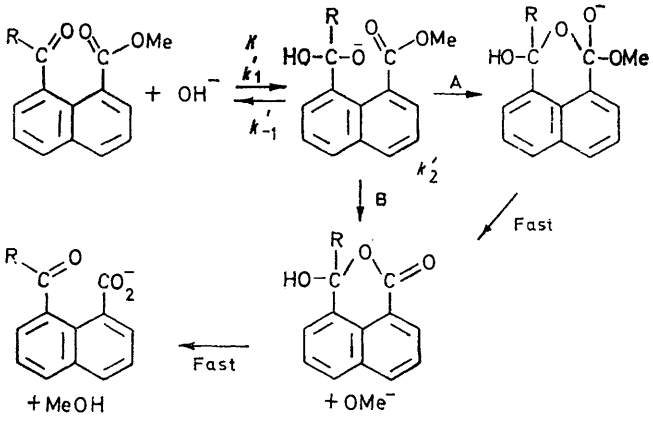
* r Is the correlation coefficient, s is the standard deviation, and n is the number of substituents used. Correlations (*a*) are these using σ and (*b*) those using σ^n.

series has been successfully correlated by the Hammett equation (1), by use of the substituent parameters σ [16]

$$\log (k/k_0) = \rho\sigma \qquad (1)$$

and σ^n.[17] The correlations are shown in Table 5. Bowden and Taylor [2] found the reaction constant for the alkaline hydrolysis of methyl 2-benzoylbenzoates in 70% (v/v) dioxan–water at 30 °C to be 2·07, while Bowden and Henry [1] found ρ equal to 2·56 and 2·10 for two different series of methyl *cis*-3-benzoylacrylates in the same medium at 1 °C. The reaction constant for the alkaline hydrolysis of methyl benzoates in the same medium at 30 °C was found to be 2·20.[2] We must now estimate ρ for the hydrolysis of the 8-benzoyl system by *both* the neighbouring group and the normal direct hydrolysis paths. The former can be confidently estimated from our previous studies [1,2] as *ca.* 1·7 to 2·1 in this medium at 60 °C. This is in excellent agreement with the reaction constant found in the 8-benzoyl system in Table 5. The estimate of ρ for the normal direct path is much more difficult. The reaction constant ratio, ρ/ρ_0, where ρ_0 is the reaction constant for the hydrolysis of methyl benzoates under identical conditions, for the 8-benzoyl system can be calculated [18] to be *ca.* 0·1 to 0·2, *if* we only consider inductive transmission of the substituent polar effect to occur. This estimate is very unrealistic as the transmission is known to have a *major* direct field component.[18,19] Consideration of molecular models suggests that the methyl phenylacetate system is both a good stereochemical (geometrical) model for the methyl 8-benzoyl-1-naphthoates and has a similar transmissive cavity. The reaction constant ratio would then be estimated as 0·5(±0·1).[18] The ionisation of 8-(substituted benzoyl)-1-naphthoic acids should provide an excellent method of computing this ratio. Unfortunately, this approach is complicated by the presence of ring-chain tautomerism in this system.[20] The reaction constant for the true pK_a^T values of the 8-(substituted benzoyl)-1-naphthoic acids in 80% (v/v) 2-methoxyethanol–water at 25 °C is 0·68,[20] but the correlation coefficient is only 0·94. This gives a reaction constant ratio of 0·4, as ρ for benzoic acids under the same conditions is 1·68.[2] The observed value of ρ/ρ_0 for the alkaline hydrolysis of methyl 8-benzoyl-1-naphthoates is 0·9, so that all these estimates confirm that the hydrolysis cannot be occurring by the normal direct hydrolysis path.

The mechanism proposed for the hydrolysis of the methyl 8-acyl-1-naphthoates studied here, as well as for methyl 5-formylphenanthrene-4-carboxylate, is shown below and closely resembles those previously suggested for related systems.[1-4] The product can be formed either



by route A [3,21] through a cyclic intermediate or by a direct displacement mechanism, route B. The rate-determining step, k_{obs} could be equal to the rate of hydroxide anion addition, k_1', or the product of the pre-equilibrium involving addition and the rate of intramolecular step, Kk_2'. A likely alternative to the stepwise path

[16] D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 420.
[17] H. van Bekkum, P. E. Verkade, and B. M. Wepster, *Rec. Trav. chim.*, 1959, **78**, 815.
[18] K. Bowden, *Canad. J. Chem.*, 1963, **41**, 2781.
[19] J. D. Roberts and W. T. Moreland, *J. Amer. Chem. Soc.*, 1953, **75**, 2167; R. Golden and L. M. Stock, *ibid.*, 1966, **88**, 5928; K. Bowden and D. C. Parkin, *Canad. J. Chem.*, 1969, **47**, 177; H. D. Holtz and L. M. Stock, *J. Amer. Chem. Soc.*, 1964, **86**, 5188; F. W. Baker, R. C. Parish, and L. M. Stock, *ibid.*, 1967, **89**, 5677.
[20] K. Bowden and A. M. Last, *J.C.S. Perkin II*, in the press.
[21] K. Bowden and G. R. Taylor, *Chem. Comm.*, 1967, 1112.

above is a concerted process in which the cyclic intermediates are formed directly. These possibilities are discussed in detail below.

Activation Parameters.—The activation parameters for the alkaline hydrolysis of the esters in 70% (v/v) aqueous dioxan are shown in Table 6. The enthalpies of activation of the two formyl esters are exceptionally small and

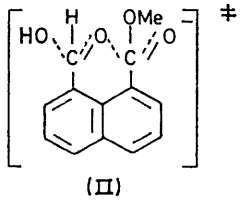
TABLE 6

Activation parameters for the alkaline hydrolysis of methyl 8-acyl-1-naphthoates and related esters in 70% (v/v) dioxan–water at 30·0 °C *

Substnt. [R in (I)]	$\Delta H^{\ddagger}$/cal mol^{-1}	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1}
H	7480	−26
Ph	16,100	−19
Methyl 5-formylphenanthrene-4-carboxylate	8460	−26
Methyl 1-naphthoate	12,900	−26

* Values of $\Delta H^{\ddagger}$ are accurate to within ±500 cal mol^{-1} and $\Delta S^{\ddagger}$ to within ±2 cal mol^{-1} K^{-1}.

clearly indicate an energetically highly favourable path with very small enthalpy requirements, as for the corresponding methyl 2-formylbenzoate.[3] However, the entropies of activation for the former two esters are comparable to those for normal ester hydrolysis,[3,13] unlike those for the methyl 2-acylbenzoates and related systems which are often considerably more negative.[3] The latter had been interpreted tentatively as arising from a transition state involving the intramolecular step or a concerted process, both requiring high degrees of orientation. However, for the 8-acyl-1-naphthoates and the 5-formylphenanthrene-4-carboxylate this orientation is 'built-in' to the systems. Consideration of molecular models of these esters, and that of methyl 2-formylbenzoate, clearly indicate the more favourable juxtaposition of the formyl groups in the naphthoate (*peri*-substituted) and phenanthrenecarboxylate. The internal nucleophile, generated by addition of the hydroxide anion to the acyl-carbonyl group, has the close proximity and orientation of the two substituents already within the methyl 8-formyl-1-naphthoate and 5-formylphenanthrene-4-carboxylate. This enables an immediate interaction between this developing anion and the electrophilic centre of the ester-carbonyl group. The resulting transition states would have similar entropy requirements to that for normal ester hydrolysis. Therefore it is tentatively suggested that the hydrolysis of the two formyl esters studied here proceeds by a rate-determining step with concerted attack at the formyl carbonyl-carbon synchronised with intramolecular attack at the ester carbonyl-carbon, *e.g.* (II).



(II)

The enthalpy of activation for the 8-benzoyl ester is much larger than that for both the formyl esters and methyl 1-naphthoate itself. This is not unexpected because of the steric 'bulk' of the phenyl group and the conjugation of the keto-carbonyl group with the phenyl ring. In all the 8-acyl systems, both the acyl-carbonyl and the ester-carbonyl groups are completely or *very* extensively deconjugated with the naphthalene ring. While the 8-benzoyl ester carbonyl group is almost completely deconjugated with the naphthalene ring, it is still fully conjugated with the phenyl group. Both the resonance and steric 'bulk' interactions in the 8-benzoyl ester will cause an increase in the enthalpy of activation. The entropy of activation for this ester is less negative than for the other systems. These factors can be tentatively ascribed to an 'early' transition state involving addition of the hydroxide anion to the benzoyl-carbonyl group, as previously suggested for methyl 2-benzoylbenzoate.[3]

It can be concluded from our studies of activation parameters that they can be used as a positive criterion for intramolecular catalysis, *e.g.* methyl 2-formylbenzoate,[3] methyl 8-formyl-1-naphthoate (this study), methyl *cis*-3-benzoylacrylate.[1] However, these parameters may not be used to rule out such participation when it is indicated and confirmed by other criteria, *e.g.* methyl 2-benzoylbenzoate [3] and methyl 8-benzoyl-1-naphthoate (this study).

Oxygen-18-Exchange.—The results of the ^{18}O-enriched water hydrolysis of methyl 8-benzoyl-1-naphthoate are shown in Table 7. The considerations here are the same

TABLE 7

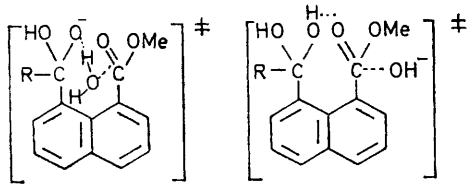
^{18}O-Enriched water hydrolyses at 50·0 °C

Methyl ester or control acid	Enrichment/atom % * $M + 2/M$	$(M\text{-}CO_2) + 2/M\text{-}CO_2$	$(M\text{-PhCO}) + 2/(M\text{-PhCO})$
8-Benzoyl-1-naphthoic acid	1·8(±0·1)	$1{\cdot}5(\pm 0{\cdot}2_5)$	None
Methyl 8-benzoyl-1-naphthoate	$1{\cdot}7_5(\pm 0{\cdot}0_5)$	$1{\cdot}4(\pm 0{\cdot}1_5)$	None

* Solvent enrichment $1{\cdot}9_9$ atoms %.

as those discussed by Bowden and Taylor [3] in the study of the hydrolysis of methyl 2-benzoylbenzoate. The single enrichment observed and its position, identified by the mass spectral breakdown, at the keto-carbonyl group exclude any significant hydrolysis by the normal direct ester hydrolysis path. The only possible paths for hydrolysis involve intramolecular catalysis involving either addition of hydroxide anion to the keto-carbonyl, followed by intramolecular attack at the ester-carbonyl, or a concerted process with attack at the keto-carbonyl synchronised with the intramolecular attack at the ester-carbonyl. The fairly rapid exchange of the keto-carbonyl group in the control (see Experimental section and Table 7) and lack of either significant concurrent oxygen exchange at the ester carbonyl group or scrambling of oxygens in the mass spectral ion have been confirmed as before.[3] This result also excludes the possibilities of a general-base or general-acid mechanism in which addition to the keto-carbonyl catalyses substitu-

tion at the ester-carbonyl by a water molecule (III) or hydroxide anion (IV).[4b] Both of these possibilities



(III) (IV)

would require double enrichment under the conditions of our experiments.

[These results appear to favour a synchronous path, rather than distinct addition and cyclisation steps, as in (II). However, the process could occur by addition/cyclisation if proton-transfer in the addition intermediate was slow.]

Solvent Effects.—The effect of varied aqueous dioxan mixtures on alkaline hydrolysis reactions was not found to be a useful criterion in our previous studies[3] and this was confirmed for the esters in this study. However, the effect of varied aqueous dimethyl sulphoxide (DMSO) mixtures on the ester hydrolysis was examined as shown in Table 8. The moderate rate enhancements observed

TABLE 8

Rate coefficients for the alkaline hydrolysis of methyl 8-acyl-1-naphthoate in aqueous DMSO *

Substnt. [R in (I)]		10^3k_2/l mol^{-1} s^{-1} in mol % aqueous DMSO				
		14·5	20·3	27·3	37·2	50·4
H	(12·7 °C)	66,900	87,900	110,000	131,000	223,000
Ph	(60·0 °C)	43·7	53·7	76·8	122	206

* See Table 1.

with increasing DMSO content are similar to those observed for normal direct ester-hydrolysis.[22,23] This is in contrast to our studies of carbon acid participation described in Part VI.[24] The kinetic solvent isotope

TABLE 9

Solvent isotope effects on the alkaline hydrolysis of methyl 8-acyl-1-naphthoates *

Substnt. [R in (I)]		10^3k_2/l mol^{-1} s^{-1}		
		In 70% (v/v) dioxan–water	In 70% (v/v) dioxan–deuterium oxide	k_{H_2O}/k_{D_2O}
H	(25·0 °C)	44,100	48,800	0·90
Ph	(60·0 °C)	16·6	18·9	0·88

* See Table 1.

effects are shown in Table 9. In both cases, rate enhancement in the deuterium oxide solvent was observed and these are similar to values found for related hydrolyses.[3] This can be attributed to greater nucleophilicity of the deuterioxide than the hydroxide anion and confirms the exclusion of the intramolecular general-base (III) and general-acid hydroxide anion (IV) paths, which would very probably require k_{H_2O}/k_{D_2O} values equal to or greater than unity.[3] As above our present results are in contrast to those described in Part VI [24] for carbon acid participation.

Proposed Mechanism.—The alkaline hydrolysis of methyl 8-formyl- and 8-(substituted benzoyl)-1-naphthoates, as well as of methyl 5-formylphenanthrene-4-carboxylate, has been shown to proceed by a mechanism having initial hydroxide-anion attack at the acyl-carbonyl of these esters by various criteria. The two formyl esters appear to proceed by a rate-determining concerted process, while the hydrolysis of the 8-benzoyl ester probably has a rate-determining addition at the keto-carbonyl. The most significant finding is that, even for acyl esters where attack at both the acyl- and ester-carbonyl group is severely inhibited by steric 'bulk' interactions, the intramolecular-catalytic path provides a favourable route for hydrolysis. This is made possible by two factors. First, it is facilitated by the proximity and orientation of the internal nucleophile once formed. Second, the steric 'crowding' induced by the 'primary' addition process is relieved as the 'secondary' intramolecular attack proceeds. These factors create a drive for the intramolecular catalysis.[25] As we pass along the series, 2-substituted benzoate, 8-substituted 1-naphthoate, and 5-substituted phenanthrene-4-carboxylate, we observe the intramolecular route becoming increasingly favourable compared with the normal direct hydrolytic path, *cf.* Table 3 and ref. 3. This appears to arise from the greater proximity, more favourable orientation and increased induced steric strain derived from the 'primary' addition process as we traverse this series.

EXPERIMENTAL

Methyl 1-naphthoate, 8-nitro-, 8-chloro-, 8-bromo-, and 8-methyl-1-napthoate, and methyl phenanthrene-4-carboxylate were prepared by Fischer–Speier esterification of the corresponding acid in methanol.[3] The four 8-substituted naphthoates were prepared by Mr. B. Abercrombie.[9] A sample of methyl 8-methoxy-1-naphthoate was kindly supplied by Mr. D. Law. The esterification of the corresponding acids [20] with diazomethane in dry ether gave methyl 8-(substituted benzoyl)-, 8-formyl- and 8-pivaloyl-1-naphthoate and methyl 5-formylphenanthrene-4-carboxylate, according to Lansbury and Bieron's method.[26] After recrystallisation or distillation, and drying in a desiccator (P_2O_5), the esters had either m.p.s in good agreement with literature values,[13,27-31] or, if previously unreported, satisfactory elemental analyses. The physical constants of the

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[26] P. T. Lansbury and J. F. Bieron, *J. Org. Chem.*, 1963, **28**, 3564.
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TABLE 10

Physical constants of methyl 8-substituted-1-naphthoates and related compounds

8-Substnt.	M.p. (*t*/°C)	Lit. m.p. (*t*/°C)	Ref.	λ/nm
H	B.p. 105—107° at 0·7 mmHg	B.p. 167—167° at 20 mmHg	27	303
COH	73—74		*a*	305
$COBu^t$	67—69		*b*	325
NO_2	95—96	97—98	27 [b]	300
Cl	B.p. 208° at 0·1 mmHg		*c*	292
OMe	51·5—52	51—52	28 [d]	302
Br	B.p. 218° at 0·1 mmHg	33	29 [e]	295
Me	B.p. 170—171° at 15 mmHg			302
Methyl 5-formylphenanthrene-4-carboxylate	108—110	113—114	30 [e]	339
Methyl 4-phenanthroate	84—85	84—85	13 [f]	335

[a] Pale yellow prisms from methanol. [b] Colourless prisms from light petroleum (b.p. 60—80°). [c] Colourless crystalline solids with low m.p.s. [d] Colourless plates from light petroleum (b.p. 60—80°). [e] Colourless needles from methanol. [f] Colourless plates from methanol.

TABLE 11

Physical constants of methyl 8-(3- or 4-substituted benzoyl)-1-naphthoates

Substnt.	M.p. (*t*/°C)	Lit. m.p. (*t*/°C)	Ref.	λ/nm
H	144 [a]	144—145	31	300
4-Me	150—151 [a]	149—150	31	300
3-Me	128 [a]			300
4-OMe	175 [b]			300
4-Br	148 [a]			300
4-Cl	159 [a]			300
3-Cl	122 [b]			300
$3\text{-}CF_3$	101—102 [b]			303

[a] From benzene–light petroleum (b.p. 60—80°). [b] From methanol.

esters are listed in Tables 10 and 11, together with their appearance and recrystallisation solvent, and the elemental analyses of the previously unreported esters are given in Table 12. The λ-values quoted in Tables 10 and 11 are those used in the kinetic measurements (and not the $\lambda_{max.}$ values for the esters). The ^1H n.m.r. and i.r. spectra confirmed the structures and purity of the esters. Solvents were purified as previously described.[22]

Kinetic Procedure.—Rate coefficients for the alkaline hydrolysis of the esters were determined spectrophotometrically by use of an SP 800 spectrophotometer. The cell temperature was controlled to ±0·05 °C by means of a Churchill thermocirculator. The reactions were followed at suitable wavelengths, as shown in Tables 10 and 11, which were normally those having the greatest difference between the substrate and product. The procedure then followed was that described previously [22] using a Beckmann 1005 chart recorder. At least a ten-fold excess of base (5×10^{-4} to 5×10^{-2}M) over substrate (5×10^{-5} to 1×10^{-4}M) concentrations was used. The final optical density was assumed to be that measured after 10 ' half-lives ' for all except the five following esters which had the slowest hydrolyses. For methyl 8-pivaloyl-, 8-methoxy-, 8-nitro-, and 8-chloro-1-naphthoate, as well as methyl phenanthrene-4-carboxylate, Guggenheim's method [32] was used. The reactions were found to be first-order in both the substrate and hydroxide anion. The products of the reactions were found to be the anion of the corresponding acids in quantitative yield in all cases, and were further confirmed spectrophotometrically by comparison of the spectrum of the acid in base with that of the reaction product. The rates of hydrolysis of methyl 8-bromo- and 8-methyl-1-naphthoate were too slow to measure at 60·0 °C and, at higher temperatures for long reaction times, the solvent-base solution was not stable. However, these esters did hydrolyse very slowly at 60·0 °C and an estimate of the upper limit for these rates is given in Table 2.

^{18}O-*Exchange Studies.*—The alkaline hydrolyses were studied by use of ^{18}O-enriched water (1·5$_9$ atoms %, Yeda R and D Co.). Hydrolyses were conducted under normal conditions for *ca.* 10 ' half-lives ' of the ester. After neutralisation and removal of the solvent, the acid was isolated and purified. The mass spectrum of each sample and controls (using *both* ester with ordinary water and acid with enriched water) was recorded on an A.E.I. MS9 spectrometer. Repeated scans of the spectra were made. The hydrolysis of methyl 8-benzoyl-1-naphthoate resulted in single enrichment. The hydrolysis of corresponding pseudo-ester results in double enrichment.[33] The oxygen-18 exchange of methyl 8-formyl-1-naphthoate (and the corresponding pseudo-ester) could not be investigated by this particular mass spectrometric method as traces of 8-hydroxy-

TABLE 12

Elemental analyses of previously unreported methyl 8-substituted 1-naphthoates

8-Substnt.	Molecular Formula	Calc. % C	Calc. % H	Calc. % O	Calc. % Other	Found % C	Found % H	Found % O	Found % Other
COH	$C_{13}H_{10}O_3$	72·9	4·7	22·4		73·0	4·7	22·5	
$COBu^t$	$C_{17}H_{18}O_3$	75·5	6·7	17·8		75·8	6·7	17·9	
Cl	$C_{12}H_9ClO_2$	65·3	4·1	16·1	14·5 (Cl)	65·4	4·2	16·2	14·3 (Cl)
Me	$C_{13}H_{12}O_2$	78·0	6·0	16·0		77·9	6·1	16·1	
8-Benzoyl Substnt.									
3-Me	$C_{20}H_{16}O_3$	78·9	5·3	15·8		78·8	5·2	15·9	
4-OMe	$C_{20}H_{16}O_4$	75·0	5·0	20·0		74·9	5·1	20·0	
4-Br	$C_{19}H_{13}BrO_3$	61·5	3·6	13·0	21·6 (Br)	61·7	3·7	13·1	21·4 (Br)
4-Cl	$C_{19}H_{13}ClO_3$	70·3	4·0	14·8	10·9 (Cl)	70·1	4·1	14·9	10·7 (Cl)
3-Cl	$C_{19}H_{13}ClO_3$	70·3	4·0	14·8	10·9 (Cl)	70·4	4·0	14·9	10·8 (Cl)
$3\text{-}CF_3$	$C_{20}H_{13}F_3O_3$	67·0	3·7	13·4	15·9 (F)	67·2	3·8		16·1 (F)

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methyl-1-naphthoic acid occur in the product. The impurity apparently results from a slow Cannizzaro side-reaction of the product of the hydrolysis, the anion of 8-formyl-1-naphthoic acid. This impurity interferes with the mass spectroscopic analysis of the $M + 2$ peak.

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