Reactions of Carbonyl Compounds in Basic Solutions. Part VI.[1] The Mechanism of the Alkaline Hydrolysis of Methyl 8-Acetyl-, 8-Propionyl-, and 8-Isobutyryl-1-naphthoate. Neighbouring-group Participation by Carbon Acids

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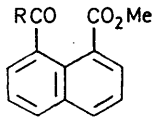
Rate coefficients have been measured for the alkaline hydrolysis of methyl 8-acetyl-, 8-propionyl-, and 8-isobutyryl-1-naphthoate, as well as the 8-[$^2H_3$]acetyl ester, in 70% (v/v) dioxan–water at several temperatures. The immediate products of these reactions are the corresponding phenalene-1,3-diones and the rate-determining step for this cyclisation was found to be the base-catalysed ionisation process. Thus the kinetic isotope effect, k^H/k^D, observed for the 8-acetyl ester was *ca.* 5 to 6. All the diones eventually hydrolyse to give the anions of the corresponding 8-acyl-1-naphthoic acids. Whereas 2,3-dihydrophenalene-1,3-dione and 2-methyl-2,3-dihydrophenalene-1,3-dione ionise in base and are relatively stable in this anionic form, 2,2-dimethyl-2,3-dihydrophenalene-1,3-dione hydrolyses relatively rapidly. The rates of ring fission for the latter dione have been measured in 70% (v/v) dioxan–water at several temperatures. The entropies and enthalpies of activation for the cyclisation and fission processes are evaluated. Solvent (aqueous dimethyl sulphoxide) and solvent isotope effects have been studied for the 8-acetyl ester. The hydrolysis rates of this and related esters are correlated with an acidity function. The evidence indicates a mechanism of ester hydrolysis with neighbouring-group participation by carbon acid for these three 8-acyl esters. The implications of the results are discussed.

INTRAMOLECULAR nucleophilic catalysis by neighbouring groups of ester hydrolysis has been shown to occur widely and by means of a variety of participating groups.[2,3] Our previous studies[1,4–6] have been concerned with neighbouring keto- and formyl-groups. We have evaluated a number of possible criteria and attempted a delineation of the extent and importance of this intramolecular path. These systems are particularly useful in simulating the nucleophilic hydroxy-groups in enzymes.[7] Our model for this nucleophilic group is generated in these systems by addition of the hydroxide anion to neighbouring carbonyl groups. In extending these studies, we were fortunate to investigate a system in which a switch of the neighbouring-group action can be observed. Keto-groups, which have α-hydrogens, can react with a basic nucleophile in two ways. These are, first, by addition to the carbonyl group and, second, by abstraction of the relatively acidic α-hydrogen.[8] The first results in a tetrahedral intermediate, while the second gives rise to an enolate anion. Both are, in principle, effective nucleophiles and could act as intramolecular catalysts. A study of such a system is reported here, the alkaline hydrolysis of methyl 8-acetyl-, 8-propionyl-, and 8-isobutyryl-1-naphthoates. A series of mechanistic probes have been employed, which include kinetic studies, intermediate isolation, isotope, and solvent effects. The mechanism of these reactions are



(I) a; R = Me
b; R = CH_2Me
c; R = $CHMe_2$

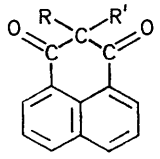
elucidated and the implications of the results are discussed.

RESULTS AND DISCUSSION

When excess of base (aqueous sodium hydroxide) was added to the methyl 8-acetyl-, 8-propionyl-, and 8-isobutyryl-1-naphthoates in 70% (v/v) dioxan–water, a yellow colour rapidly developed. As the sodium salt of the corresponding carboxylic acids at the concentrations of the kinetic study appear colourless, it was immediately apparent that the rapid reaction observed was not the anticipated hydrolysis. For the 8-isobutyryl ester, the yellow colour disappeared completely after several hours. The hydrolysis of the three esters was monitored

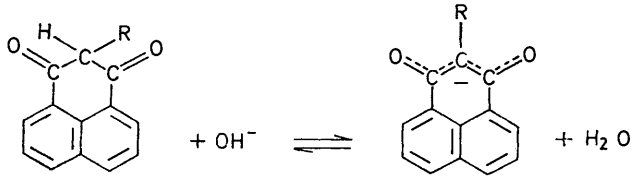
[1] Part V, K. Bowden and A. M. Last, preceding paper. For a preliminary account of part of this study see *Chem. Comm.*, 1970, 1315.
[2] B. Capon, *Quart. Rev.*, 1964, **18**, 45.
[3] T. C. Bruice and S. J. Benkovic, 'Bioorganic Mechanisms,' vol. 1, W. A. Benjamin, Inc., New York, 1966.
[4] K. Bowden and G. R. Taylor, *J. Chem. Soc.* (*B*), 1971, 145.
[5] K. Bowden and G. R. Taylor, *J. Chem. Soc.* (*B*), 1971, 149.
[6] K. Bowden and M. P. Henry, *J. Chem. Soc.* (*B*), 1971, 156.
[7] K. Bowden and A. M. Last, *Canad. J. Chem.*, 1971, **49**, 3887.
[8] C. D. Gutsche, 'The Chemistry of Carbonyl Compounds.' Prentice-Hall, Inc., Englewood Cliffs, New Jersey, 1967.

by u.v. spectrophotometry. The 8-acetyl and 8-propionyl esters rapidly formed a relatively stable intermediate. Similarly the 8-isobutyryl ester gave an intermediate, which reacted further to yield a product whose u.v. spectrum was identical to that of the anion of the corresponding acid. Intermediate and product analyses were carried out. The intermediates were identified as the corresponding phenalene-1,3-diones (IIa,b,c). The



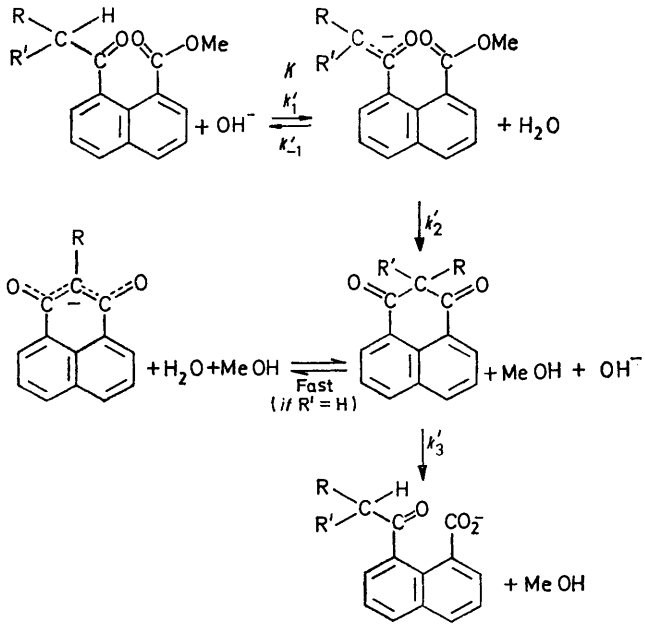
(II) a; R = R' = H
b; R = Me, R' = H
c; R = R' = Me

phenalene-1,3-diones, produced from the reactions of the 8-acetyl and 8-propionyl esters, ionise in base. These relatively stable anionic forms (IIIa,b) are predominant in these alkaline solutions and hydrolyse very slowly to



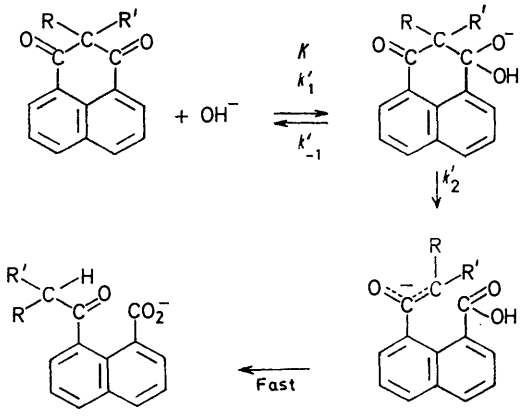
(II) (III) a; R = H
b; R = Me

the final product of the overall hydrolysis, the anion of the corresponding 8-acyl-1-naphthoic acid. However, the dione (IIc), which is formed in the reaction of the 8-isobutyryl ester with base and cannot ionise, hydrolyses relatively rapidly to the final product. The above



SCHEME 1

evidence indicates that all the three 8-acyl esters studied here undergo alkaline hydrolysis by the mechanism shown in Scheme 1. The first step is an ionisation, followed by an intramolecular cyclisation. If the phenalene-1,3-dione can ionise in base, hydrolysis to the overall product of the reaction, the anion of the corresponding 8-acyl-1-naphthoic acid, is very slow. If the dione cannot ionise, the hydrolysis proceeds to completion by ring fission. The rate-determining step of the cyclisation reaction could either be the initial abstraction of a proton from the acyl-group or the intramolecular attack by the ' internal ' carbanion. Likewise the ring fission can have as the rate-determining step either addition of hydroxide anion to one of the dione-carbonyl groups or the ring cleavage of this intermediate shown Scheme 2.



SCHEME 2

Cyclisation of the Esters to the Phenalene-1,3-diones.— The cyclisation is of first-order in ester and hydroxide anion. The rate coefficients for the cyclisation of the three methyl 8-acyl-1-naphthoates to the corresponding phenalene-1,3-diones in 70% (v/v) dioxan–water have been determined at several temperatures and are shown in Table 1. Substitution of the α-carbon with

TABLE 1

Rate coefficients for the base-catalysed cyclisation of methyl 8-acyl-1-naphthoates to phenalene-1,3-diones 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
Me	533	1040	1860	3370	
	(533)	(1070)	(1800)	(3470)	
CD_3 †	90·5	172	354	652	
	(94·0)	(190)	(384)	(670)	
CH_2Me	98·3	202	484	915	
$CHMe_2$ ‡ (*a*)		30·9	60·3	120	236
(*b*)		26·6	57·7	120	222

* Rate coefficients were reproducible to within ±3% and are for the appearance of the dione. Those in parentheses are for the disappearance of the ester (see Discussion and Experimental sections). † Methyl 8-[$^2H_3$]acetyl-1-naphthoate. ‡ Calculated by (*a*) ' initial rate ' and (*b*) ' theoretical infinity ' methods (see Experimental section).

methyl groups progressively decreases the rate of cyclisation, *i.e.* at 40 °C, the first methyl substitution reduces

the rate by a factor of *ca.* 4 and the second further by a factor of *ca.* 8. This order closely compares with that found for the base-catalysed exchange of α-substituted toluenes exchanging at the α-position,[9-11] as shown in Table 2, despite the varied solvent and base systems used.

TABLE 2

Relative rates for the isotopic exchange of PhR at the α-position

	k/k_0			k/k_0 for the cyclisation of the esters, 70% (v/v) dioxan–water at 40 °C (this study)
R	KND_2/liquid ND_3 at 10 °C [9]	$KOBu^t$/DMSO at 40 °C [10]	$LiNHC_6H_{11}$/$C_6H_{11}NH_2$ * at 50 °C [11]	
Me	1·0	1·0	1·0	1·0
CH_2Me	0·14	0·22	0·12	0·26
$CHMe_2$	0·03	0·023	0·008	0·032

* C_6H_{11} = cyclohexyl

The probable explanation of the order of reactivity for the esters is that the acidity of the α-hydrogen decreases as the number of α-methyl groups increases. This arises from the 'inductive' electron-releasing effect of the methyl group.[12]

Kinetic Isotope Effect.—The rate coefficients for the cyclisation of methyl 8-[$^2H_3$]acetyl-1-naphthoate are also shown in Table 1 and the kinetic isotope effect, k^H/k^D, has been evaluated for the 8-acetyl ester as shown in Table 3. The values of k^H/k^D are in the range $5{\cdot}1_5$

TABLE 3

Kinetic isotope effect on the rate coefficients for cyclisation of methyl 8-acetyl-1-naphthoate in 70% (v/v) dioxan–water at several temperatures *

k^H/k^D			
20·0 °C	30·0 °C	40·0 °C	50·0 °C
5·9	$6{\cdot}0_5$	$5{\cdot}2_5$	$5{\cdot}1_5$

* Rate ratios were reproducible to ±0·2.

to $6{\cdot}0_5$. This magnitude of kinetic isotope effect clearly indicates that the ionisation step is rate-determining. Thus, the ionisation of acetophenone in water catalysed by hydroxide anion has been studied by Jones *et al.*,[13] with k^H/k^T at 25 °C approximately equal to 15. This corresponds to k^H/k^D of *ca.* 6·5, using Swain's relation.[14] Bell and Cox[15] have investigated the base-catalysed rate of inversion of (—)-menthone in 0 to 75 mol % aqueous dimethyl sulphoxide (DMSO) and found k^H/k^D to be in the range 5·5 to $6{\cdot}4_5$ (with the maximum at 35 mol % DMSO). These results were interpreted as indicating a rate-determining step with the proton approximately half-transferred in the transition state.

While a number of treatments[16] have related the extent of hydrogen transfer to the primary hydrogen isotope effect, others[17] have recently concluded either that k^H/k^D is relatively insensitive to the symmetry of the transition state or that the symmetry does not change over wide ranges of difference in pK_a between substrate or base. However, we can be certain that the transition state is comparatively 'advanced' and comprises a developed carbanion.

Activation Parameters.—The activation parameters for the cyclisation of the three esters are shown in Table 4.

TABLE 4

Activation parameters for the base-catalysed cyclisation of methyl 8-acyl-1-naphthoates and cleavage of 2,2-dimethyl-2,3-dihydrophenalene in 70% (v/v) dioxan–water at 30·0 °C *

Substnt. [R in (I)]	$\Delta H^‡$/cal mol^{-1}	$\Delta S^‡$/cal mol^{-1} K^{-1}
Me	10,900	−22
CD_3 †	11,700	−22
CH_2Me	13,600	−17
$CHMe_2$	13,300	−22
2,2-Dimethyl-2,3-dihydrophenalene	14,000	−24

* Values of $\Delta H^‡$ are accurate to within ±500 (cyclisation) and ±800 (cleavage) cal mol^{-1} and $\Delta S^‡$ to within ±2 (cyclisation) and ±3 (cleavage) cal mol^{-1} K^{-1}. † See Table 1.

Our results for the 8-acetyl ester are similar to those for the base-catalysed ionisation of acetophenone in water,[13] *i.e.* for the latter reaction $\Delta H^‡$ and $\Delta S^‡$ at 30·0 °C are $12{\cdot}2_5$ kcal mol^{-1} and −18 cal mol^{-1} K^{-1}, respectively. The effect of α-methyl substitution for the 8-acyl esters is not large, but appears mainly to affect the enthalpy of activation term. The increase observed appears to arise from the unfavourable polar and, possibly, steric effects of the α-methyl groups.

Possibility of Second Hydrolytic Path.—Both the rate of disappearance of the ester and the appearance of the dione for the 8-acetyl and 8-[$^2H_3$]acetyl esters (see Experimental section) could be measured under identical conditions as shown in Table 1. For the 8-acetyl ester the rate coefficients were identical within the experimental reproducibility. However, for the 8-[$^2H_3$]acetyl ester there does appear to be a minor reaction *not* proceeding *via* the dione. Although this minor reaction does not appear to be a very significant contribution to the total hydrolysis, this ester is the most likely substrate for such an observation as this particular acyl group has both a comparatively slow ionisation and a small steric 'bulk'. The minor hydrolysis reaction would have a rather uncertain rate of about 2×10^{-2} l mol^{-1} s^{-1} at 30 °C. This would represent a rate ratio of *ca.* 3 compared to methyl 1-naphthoate at this temperature,[1] in comparison to an estimated 'expected' rate ratio for

[9] A. I. Shatenshstein, *Adv. Phys. Org. Chem.*, 1963, **1**, 155, and references therein.
[10] J. E. Hoffmann, R. J. Muller, and A. Schriesheim, *J. Amer. Chem. Soc.*, 1963, **85**, 3002.
[11] A. Streitwieser, jun., and D. E. van Sickle, *J. Amer. Chem. Soc.*, 1962, **84**, 249.
[12] A. Streitwieser, jun., and J. H. Hammons, *Progr. Phys. Org. Chem.*, 1965, **3**, 41.
[13] J. R. Jones, R. E. Marks, and S. C. Subba Rao, *Trans. Faraday Soc.*, 1967, **63**, 111, 993.
[14] C. G. Swain, E. C. Stivers, J. F. Reuwer, and L. J. Schaad, *J. Amer. Chem. Soc.*, 1958, **80**, 5885.
[15] R. P. Bell and B. G. Cox, *J. Chem. Soc.* (*B*), 1970, 194.
[16] F. H. Westheimer, *Chem. Rev.*, 1961, **61**, 265; R. P. Bell, W. H. Sachs, and R. L. Tranter, *Trans. Faraday Soc.*, 1971, **67**, 1995, and references therein.
[17] F. G. Bordwell and W. J. Boyle, *J. Amer. Chem. Soc.*, 1971, **93**, 512, and references therein.

a direct hydrolysis mechanism of *ca.* 0·01 (see ref. 1 for details of estimate). If the minor hydrolysis *not* proceeding *via* the dione is real, the minor hydrolysis path would be occurring with carbonyl group participation as described for other 8-acyl esters in Part V.[1]

Solvent Effects.—The rate coefficients for the base-catalysed cyclisation of methyl 8-acetyl-1-naphthoate in aqueous DMSO at 25 °C have been determined and are shown in Table 5. Like many other substrates reacting

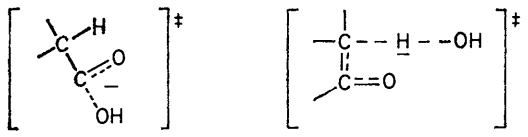
TABLE 5

Rate coefficients for the base-catalysed cyclisation of methyl 8-acetyl-1-naphthoate to the phenalene-1,3-dione in aqueous DMSO at 25·0 °C *

Mole % DMSO	14·5	20·3	27·6	37·2	50·4
H_- [18]	13·74	14·53	15·28	16·23	17·51
$H_- + \log a_w$ [19]	13·65	14·32	15·01	15·83	16·89
$10^2 k_2$/l mol^{-1} s^{-1}	121	207	433	1270	6030

* See Table 1.

with base,[19,20] the reaction shows enhanced rates with increasing DMSO content. Linear relations [19] between log k_2 and $H_- + \log a_w$ exist for the cyclisation of the 8-acetyl ester, as well as for the hydrolysis of methyl 8-benzoyl- and 8-formyl-1-naphthoate studied in Part V,[1] and are shown in Table 6. The slopes of these correlations, and those for relations with H_-, have been considered in some detail in previous studies.[19,20] These accelerations arise from the differential effects of the two solvents. In aqueous DMSO containing hydroxide anion, an increase in the DMSO content increases the activity of the hydroxide anion. For systems with comparable initial states, *e.g.* hydroxide anion and ester, a reaction in which protic solvation is less important would respond more effectively to an increase in DMSO than those in which protic solvation of the transition state is more important. Protic solvation is more important for transition states which have a localised-charge structure, especially where the localisation is on electronegative atoms, than for those in which the charge is delocalised. Thus reactions which involve attack by hydroxide anion at a carbonyl group, *e.g.* (IV), require more protic solvation for the ' alkoxide-like ' transition state than reactions which proceed by abstraction of a proton by hydroxide anion from a carbon acid, *e.g.* (V), having a delocalised ' enolate-like ' transition state. Two important points must be made before considering these and similar results. First, if the correlations compared are for rates measured at different



(IV) (V)

TABLE 6

Regression analysis for equation, $\log k_2 = l\,(H_- + \log a_w) + c$, correlating the base-catalysed reactions of methyl 8-acyl-1-naphthoates in aqueous DMSO *

Substnt. [R in (I)]	Temp. (t/°C)	l	c	r	s	n
H	12·7	0·153	−0·269	0·991	0·012	5
Me	25·0	0·529	1·224	0·994	0·034	5
Ph	60·0	0·214	−2·311	0·997	0·010	5

* r Is the correlation coefficient, s the standard deviation, and n the number of points used.

temperatures, it must be remembered that the slope, l, will vary with temperature and tend to decrease with increasing temperature. Second, those correlations with $H_- + \log a_w$ and those with H_- are not directly comparable. Those correlations with the former acidity function will tend to have greater slopes than those with the latter. However, it is clear from the results shown in Table 6 and those in previous studies [19] that reactions proceeding by carbon acid ionisation (8-acetyl ester) have a significantly higher slope than those reacting by carbonyl-addition paths (8-benzoyl and 8-formyl ester, as well as methyl benzoate). Furthermore, the result found here for the cyclisation of the 8-acetyl ester at 25 °C compares closely with that for the detritiation of 2′-[^{3}H]acetophenone in aqueous DMSO at 25 °C studied by Jones and Stewart.[21] Similar results have been found for the base-catalysed rate of inversion of (—)-menthone in aqueous DMSO [15] and of the ionisation of phenylmethylacetophenone in aqueous DMSO.[22] It would appear that, in this particular situation, the acidity function correlation can be used as a criterion to differentiate between carbon acid and carbonyl addition mechanisms.

Kinetic Solvent Isotope Effect.—The kinetic deuterium solvent isotope effect was examined for the cyclisation of methyl 8-acetyl-1-naphthoate at 30·0 °C in 70% aqueous dioxan as shown in Table 7. A rate enhancement in the deuterium oxide solvent was observed which arises from the greater basicity of the deuterioxide anion in deuterium oxide than hydroxide anion in water.[23] The value of k_{H_2O}/k_{D_2O} obtained in this study (0·69) appears to be significantly less than those for the alkaline hydrolyses of methyl 8-formyl- and 8-benzoyl-1-naphthoate,[1] as well as for the corresponding methyl pseudo-8-acyl-1-naphthoates [24] and methyl benzoate [5] (0·80 to

TABLE 7

Solvent isotope effects on the base-catalysed cyclisation of methyl 8-acetyl-1-naphthoate at 30·0 °C *

$10^3 k_2$/l mol^{-1} s^{-1}		
In 70% (v/v) dioxan–water	In 70% (v/v) dioxan–deuterium oxide	k_{H_2O}/k_{D_2O}
1040	1510	0·69

* See Table 1.

[18] D. Dolman and R. Stewart, *Canad. J. Chem.*, 1967, **45**, 911.
[19] K. Bowden and R. S. Cook, *J. Chem. Soc.* (*B*), 1971, 1765, 1771, and references therein.
[20] K. Bowden and M. J. Price, *J. Chem. Soc.* (*B*), 1971, 1748.
[21] J. R. Jones and R. Stewart, *J. Chem. Soc.* (*B*), 1967, 1173.
[22] D. W. Earls, J. R. Jones, and T. G. Rumney, *J.C.S. Faraday I*, 1972, **68**, 925.
[23] K. B. Wiberg, *Chem. Rev.*, 1955, **55**, 713.
[24] K. Bowden and A. M. Last, following paper.

0·90). All the latter ester hydrolyses proceed by addition of hydroxide anion to a carbonyl group. However, the value of k_{H_2O}/k_{D_2O} for the alkaline hydrolysis of methyl 2-acetylbenzoate at 20 °C in 70% aqueous dioxan has been found to be only 0·68;[5] whereas this ester hydrolyses with neighbouring-group participation by the carbonyl group.

Calculations based on the method of Bunton and Shiner[25] indicate that, for the transition state (V), k_{H_2O}/k_{D_2O} at 30 °C equals 0·78 (' electrostatic ' or ' free-proton ' model) and 0·43 (' covalent ' model),[26] assuming no further protic solvation at the carbonyl oxygen. Our value corresponds closely to that of k_{H_2O}/k_{D_2O} of 0·68 found by Pocker[27] for the hydroxide anion-catalysed enolisation of acetone in water at 30 °C. While the reduced value of the ratio cannot be used as a criterion for such a process because of the exception noted above, it would appear to indicate both little charge delocalisation onto the carbonyl oxygen and small protic solvation requirements in the transition state.

Base-catalysed Cleavage of 2,2-Dimethyl-2,3-dihydrophenalene-1,3-dione.—The cleavage is of first-order in dione and in hydroxide anion. The rate coefficients for the alkaline cleavage of 2,2-dimethyl-2,3-dihydrophenalene-1,3-dione in 70% (v/v) dioxan–water at various temperatures were determined and are shown in Table 8.

TABLE 8

Rate coefficients for the base-catalysed cleavage of 2,2-dimethyl-2,3-dihydrophenalene in 70% (v/v) dioxan–water *

10^3k_2/l mol^{-1} s^{-1}			
30·0 °C	40·0 °C	50·0 °C	60·0 °C
2·37	4·34	10·1	20·4

* See Table 1.

The activation parameters for the cleavage are shown in Table 4. The product of this reaction has been found previously to be the anion of 8-isobutyryl-1-naphthoic acid.[28,29] The dimethyl dione would be expected to hydrolyse more rapidly than 2,3-dihydrophenalene-1,3-dione and 2-methyl-2,3-dihydrophenalene-1,3-dione as the latter two diones ionise in base. The anions of β-diketones are known to be resistant to hydrolysis.[30] In the alkaline solution, both of the latter two diones are predominantly ionised and can only hydrolyse easily *via* the un-ionised diones themselves.

The cleavage reaction proceeds *via* the monoanionic intermediate, as shown in Scheme 2, in a similar manner to 3,3-dimethylacetylacetone.[30,31] Other related cleavages often involve a dianionic intermediate in addition to the monoanionic pathway.[32] The rate-determining step for the dione in this study could be the addition process, k_1', or the ring fission step, where k_{obs} would equal Kk_2'. The ring-fission step involves the expulsion of a carbanion from the intermediate and the nature of the rate-determining step will depend on the relative leaving-group abilities of the hydroxide anion and the carbanion, *i.e.* the enolate anion. The leaving-group ability appears to depend in general on the basicity of the group[33] and thus hydroxide anion (pK_a of water, the conjugate acid, is 15·7)[34] would appear to be a better leaving-group than the enolate anion (pK_a of acetophenone, which approximates to the conjugate acid, is about 19).[35] Steric factors could also well contribute. Thus the hydroxide anion loss would be accompanied by release of ' crowding ' interactions in the tetrahedral intermediate, while the fission process would release any ' ring-strain '. It appears likely that the rate-determining process for the cleavage is the fission of the intermediate expelling the enolate anion. The activation parameters obtained for the cleavage in this study (Table 4) appear to be quite consistent with this discussion.

Proposed Mechanism.—When methyl 8-acetyl-, 8-propionyl-, and 8-isobutyryl-1-naphthoates are treated with an excess of base in aqueous dioxan, the immediate product is the corresponding phenalene-1,3-dione. The diones produced from the two former esters can ionise in base and are relatively stable in this anionic form, which predominates in the alkaline solution. These hydrolyse very slowly to give the final product, the anion of the corresponding 8-acyl-1-naphthoic acid. However, 2,2-dimethyl-2,3-dihydrophenalene-1,3-dione, produced from methyl 8-isobutyryl-1-naphthoate, cannot ionise in base and the base-catalysed ring-fission proceeds relatively rapidly to produce the anion of 8-isobutyryl-1-naphthoic acid.

It is apparent that steric and stereochemical control of mechanism operates in the alkaline hydrolysis of methyl 8-acyl-1-naphthoates. The steric ' bulk ' of the 8-substituent inhibits normal direct hydrolysis. The proximity and favourable orientation of the carbonyl group at the 8-position facilitates intramolecular catalysis from this group.[1] The proximity of the ' internal ' nucleophile and the relief of steric interactions further developed in the addition intermediate are the driving forces for this process.[36] However, the formation of the tetrahedral intermediate at the 8-acyl carbonyl group has distinct spatial requirements. When the acyl group is comparatively acidic (pK_a of about 19),[34] as in methyl 8-acetyl-, 8-propionyl-, and 8-isobutyryl-1-naphthoates, a more favourable process is the ionisation of this weak

[25] C. A. Bunton and V. J. Shiner, jun., *J. Amer. Chem. Soc.*, 1961, **83**, 3207, 3214.
[26] K. Bowden and R. S. Cook, *J.C.S. Perkin II*, 1972, 1407.
[27] Y. Pocker, *Chem. and Ind.*, 1959, 1383.
[28] M. Freund and K. Fleischer, *Annalen*, 1913, **399**, 182.
[29] D. Cohen, B. Hankinson, and I. T. Millar, *J. Chem. Soc.* (*C*), 1968, 2428.
[30] R. G. Pearson and E. A. Mayerle, *J. Amer. Chem. Soc.*, 1951, **73**, 926.
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carbon acid. This ionisation produces a very strong 'internal' nucleophile which very rapidly attacks the ester carbonyl-carbon intramolecularly. This process is again assisted by the release of steric interactions in going from the carbon acid to the cyclic product. Methyl 2-acetylbenzoate and related esters evidently lack both the severe steric 'crowding', which drives the intramolecular attack by the carbanion, and the favourable orientation for attack of the carbanion on the ester group. Therefore the latter esters hydrolyse with neighbouring-group participation by the carbonyl group,[5] although the acidity of the acyl groups in the latter 2-acylbenzoates would be expected to be very similar to those of the 8-acyl-1-naphthoates. The control of the type of neighbouring participation arising from the orientation and environment of the participating group is demonstrated by the change in reaction paths employed by the two acetyl esters.[7]

EXPERIMENTAL

The methyl 8-acyl-1-naphthoates were prepared by the esterification of the corresponding acids [36] with diazomethane in dry ether according to Lansbury and Bieron's method.[37] 2,3-Dihydrophenalene-1,3-dione was prepared by the reaction of naphthalene-1,8-dicarboxylic anhydride and diethyl malonate, in the presence of zinc chloride.[38] The latter dione was methylated by methyl iodide in ethanol containing sodium ethoxide at 94 °C for 30 h in an autoclave at 11 atm to give 2-methyl-2,3-dihydrophenalene-1,3-dione. The yield was lower than that of Cohen *et al.*,[29] who employed a pressure of 18 atm. Further methylation of the monomethyl dione by methyl iodide in anhydrous acetone containing sodium methoxide gave 2,2-dimethyl-2,3-dihydrophenalene-1,3-dione.[38] After repeated recrystallisation to constant m.p. and drying in a vacuum desiccator (P_2O_5), the compounds had either m.p.s in good agreement with literature values [28,37,38] or, if previously unreported, satisfactory elemental analyses. The ^1H n.m.r. and i.r. spectra of these compounds confirmed their structures and indicated them to be pure. The physical constants of the methyl 8-acyl-1-naphthoates and related compounds are given in Table 9, together with their appearance and recrystallisation solvents. The λ-values quoted in Table 9 are those used in the kinetic measurements (and not the $\lambda_{max.}$ values for the esters). The elemental analyses of the previously unreported esters are given in Table 10. Solvents were purified as previously described.[19,20]

Kinetic Procedure.—Rate coefficients for the alkaline hydrolysis of the esters (cyclisation and cleavage) were determined spectrophotometrically by use of an SP 800 spectrophotometer, as described previously.[1,20] The reactions were followed at a suitable wavelength, as shown in Table 9, which was normally that having greatest difference between the substrate and product. When the three 8-acyl esters studied here were treated with sodium hydroxide in aqueous dioxan, the initial product of reaction was the corresponding phenalene-1,3-dione (see Product Analysis below). 2,3-Dihydrophenalene-1,3-dione and 2-methyl-2,3-dihydrophenalene-1,3-dione, produced from methyl 8-acetyl-1-naphthoate and 8-propionyl-1-naphthoate, respectively, exist in the alkaline solutions predominantly as the anions (III) and react very slowly with base to give the anions of the corresponding 8-acyl-1-naphthoic acid. As the disappearance of the diones was very slow compared to their formation in these two cases, it was possible to follow their formation at the wavelength shown in Table 9 and the maximum optical density observed was equivalent to the final optical density (*i.e.* that normally measured after 10 'half-lives'). At least a 10-fold excess of base (2×10^{-3} to 1×10^{-2}M) over substrate (5×10^{-5} to 1×10^{-4}M) concentration was used. The reactions were found to be first-order in both the substrate and hydroxide anion. The observed first-order rate coefficient, k_1, was converted to the second-order rate coefficient, k_2, by relation (1).

$$k_2 = k_1/[OH^-] \quad (1)$$

However, 2,2-dimethyl-2,3-dihydrophenalene-1,3-dione, produced from methyl 8-isobutyryl-1-naphthoate, cannot ionise in base; but reacts with base readily to form the anion of 8-isobutyryl-1-naphthoic acid. If the reaction was followed at an absorption maximum for the intermediate (336 nm), the optical density first rose rapidly to a maximum and then decreased less rapidly. The two consecutive reactions were sufficiently close in rates to require a separation treatment. The reaction scheme is essentially that of two consecutive first-order rate processes as shown below (2) (studied in *excess* base), where A, B, and C are the substrate ester, intermediate dione, and product carboxylate

$$A \xrightarrow{k_1^A} B \xrightarrow{k_1^B} C \quad (2)$$

TABLE 9

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

Substnt.	M.p. (*t*/°C)	Lit m.p. (*t*/°C)	Ref.	λ/nm
Me	93	92—93	37 [a]	336(297)
CD_3 *	90—90·5		*a*	336(297)
CH_2Me	83·5—84		*b*	339
$CHMe_2$	109—110		*c*	336
2,2-Dimethyl-2,3-dihydrophenalene-1,3-dione	99—100·5	100—101	28 [d]	336
2,3-Dihydrophenalene-1,3-dione	248—250 (d)	247 (d)	38 [e]	
2-Methyl-2,3-dihydrophenalene-1,3-dione	183	183—185	38 [f]	

* Methyl 8-[$^2H_3$]acetyl-1-naphthoate.

[a] Yellow needles from light petroleum (b.p. 60—80°). [b] Colourless needles from light petroleum (b.p. 60—80°). [c] Pale yellow prisms from light petroleum (b.p. 60—80°). [d] Pale yellow needles from light petroleum (b.p. 80—100°). [e] Dark yellow crystalline solid from acetic acid. [f] Orange-yellow crystalline solid from ethanol.

TABLE 10

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

Substnt.	Molecular formula	Calc. % C	Calc. % H	Calc. % O	Found % C	Found % H	Found % O
CD_3 *	$C_{14}{}^1H_9{}^2H_3O_3$	72·7	6·5 †	20·8	72·7	6·7 †	20·6
CH_2Me	$C_{15}H_{14}O_3$	74·4	5·8	19·9	74·1	5·7	19·8
$CHMe_2$	$C_{16}H_{16}O_3$	75·0	6·3	18·7	74·8	6·1	18·9

* See Table 9. † % is for $^1H + {}^2H$.

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anion, respectively. As before, at least a 10-fold excess of base (1×10^{-3} to 1×10^{-2}M) over substrate (5×10^{-5} to 1×10^{-4}M) concentration was used so that the reactions were approximated to first order in the substrate alone. A determination of k_1^B was relatively simple as the hydrolysis of the dione intermediate, prepared directly (see Experimental above), could be studied separately. The cleavage reaction was found to be first order in both the substrate and hydroxide anion, allowing the evaluation of first- and second-order rate coefficients for this process. Three methods were then available for the calculation of k_1^A. First, the kinetics of two consecutive first-order rate processes have been considered in detail [39] and the expression (3) obtained, where β equals $[B]/[A]_0$, τ equals $k_1^A t$, and κ equals k_1^B/k_2^A. Thus β as a function of time, t,

$$\beta = \frac{1}{\kappa - 1}(e^{-\tau} - e^{\kappa\tau}) \qquad (3)$$

passes through a maximum, equal to $\beta_{min.}$. The value of $\beta_{max.}$ depends only upon κ. In our study, it was not possible to use these treatments [39] to obtain both k_1^A and k_1^B directly. However, from a plot of $\beta_{max.}$ against κ [39] and as k_1^B was separately determined, it was possible to determine k_1^A. Second, an ' initial rate ' method can be used. The initial rate of disappearance of A, the ester, is equal to formation of B, the dione, and is given by (4). From the

$$-\left(\frac{d[A]}{dt}\right)_0 = \left(\frac{d[B]}{dt}\right)_0 = k_1^A[A]_0 \qquad (4)$$

tangent to the curve at zero time for the plot of [B] against time, t, k_1^A can be obtained. Third, in the early stages of the reaction, very little of the intermediate will have reacted to form the final product. Therefore a ' theoretical infinity ' method can be used, where the optical density of the intermediate dione was measured for the same concentration as the initial concentration of ester. This optical density was then used as the final value to construct a normal first-order plot and the linear portion over the early stage of the reaction was used to calculate the first-order rate coefficient. This reaction was also found to be first-order in ester and hydroxide anion. The results from the second and third methods were very reproducible, *i.e.* $\pm 3\%$, and were consistent with each other as shown in Table 1. The rate coefficients obtained from the first method were not either as reproducible as the second and third methods or very consistent with the results from these two methods. This very probably resulted from two factors. First, the ratio of k_1^B/k_1^A was not close to unity and therefore minor inaccuracies were greatly magnified. Second, for the first method it is very important to measure $\beta_{max.}$ accurately and this depends on accurate measurements of both the optical density and concentration of the intermediate. Unfortunately the ester and final product present in the kinetic hydrolysis runs have absorptions which do affect to some extent the spectral measurements of the intermediate.

While the main reaction of methyl 8-acetyl-1-naphthoate with base was the cyclisation process, it was considered important to determine if any hydrolysis of this ester occurred directly to the final product, albeit to a minor extent. It was found possible to measure the disappearance of ester at 297 nm, independent of the appearance of the dione, as shown in Table 1. For the 8-acetyl ester, the rate coefficients are identical within their experimental reproducibility. For the 8-[$^2H_3$]-acetyl ester, the differences remain small, but appear significant (see Results and Discussion). The rate coefficients for the cyclisation of the 8-[$^2H_3$]acetyl and 8-acetyl esters, as well as for the determination of the kinetic solvent isotope effects, were measured simultaneously under identical conditions to minimise the errors in determining the rate ratios.

Product Analysis.—The u.v.–visible spectrum of the initial product of the reaction of methyl 8-acetyl-1-naphthoate and 8-propionyl-1-naphthoate with base was almost identical with that of 2,3-dihydrophenalene-1,3-dione and 2-methyl-2,3-dihydrophenalene-1,3-dione in base, respectively. After several days, the spectrum of the products had changed and was now almost identical with that of the corresponding 8-acyl-1-naphthoic acids in base. Both the corresponding phenalene-1,3-diones and 8-acyl-1-naphthoic acids were isolated by quenching preparative-scale reactions with dilute aqueous hydrochloric acid at the appropriate times. The products were identical with authentic compounds synthesised directly (see Experimental above) and were in almost quantitative yield. The u.v.–visible spectrum of the intermediate from the reaction of methyl 8-isobutyryl-1-naphthoate with base approximated closely to that of 2,2-dimethyl-2,3-dihydrophenalene-1,3-dione. The spectrum of this reaction after some time and of the product of the base-catalysed fission of the latter dione was almost identical with that of 8-isobutyryl-1-naphthoic acid in base. Quenching the preparative scale reactions of the latter hydrolysis and fission reactions at final completion gave 8-isobutyryl-1-naphthoic acid in almost quantitative yield. However, it was only possible to isolate an impure sample of 2,2-dimethyl-2,3-dihydrophenalene-1,3-dione by quenching the hydrolysis reaction when the intermediate was at its maximum concentration. The latter sample was shown to be mainly 2,2-dimethyl-2,3-dihydrophenalene-1,3-dione by its i.r. and ^1H n.m.r. spectra.

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