Transmission of Polar Effects. Part 20.[1] Ionisation and Esterification, with Diazodiphenylmethane, of a Series of 8-(2-Substituted Phenyl)-1-naphthoic and 2- and 4-(8-Substituted 1-Naphthyl)benzoic Acids

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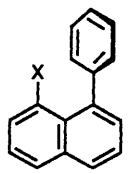
The pK_a-values of a series of 8-(2-substituted phenyl)-1-naphthoic and 2- and 4-(8-substituted 1-naphthyl)benzoic acids have been determined in 80% (w/w) 2-methoxyethanol–water at 25 °C. The rate coefficients for the esterification of these acids with diazodiphenylmethane have been measured in 2-methoxyethanol at 30 °C. For the reactivity of the 2- and 4-(8-bromo-1-naphthyl)benzoic acids, reversed dipolar substituent effects were observed in both reactions. The reactivities are quantitatively accounted for by either comparison with the results for the 2- and 4-bromobenzoic acids or Kirkwood–Westheimer calculations. For the reactivity of the 8-(2-substituted phenyl)-1-naphthoic acids, both normal and reversed dipolar substituent effects were observed in the ionisation reaction; whereas, for the esterfication reaction, only normal effects were shown.

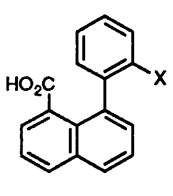
In studies [1–3] of polar substituent effects in the diphenyl system, the stereochemical uncertainties are a distinct disadvantage in the interpretation of experimental data. The coaxial twisting in the biphenyl system itself will modify resonance interaction and can be expected to vary considerably with the nature of any 2- or 2′-substituent.[1] Furthermore, the 2-carboxy and 2′-substituent groups, such as nitro, carbonyl, *etc.*, will also be affected by steric 'bulk' interactions and will be partially deconjugated with the aryl ring. A better model for such systems was required. The 1-phenylnaphthalene system was selected as, in the presence of an 8-substituent, it would be 'locked' in a fixed conformation with the two aryl groups almost orthogonal,[4] as in structure (**1**). This situation has the advantages of both (i) fixing any



(**1**)

substituents in space and (ii) full deconjugation of the aryl groups and, if relevant, the 8-substituent and naphthalene ring.

In the present study we have prepared three novel systems; the 8-(2-substituted phenyl)-1-naphthoic (**2**) and the 2- or 4-(8-substituted 1-naphthyl)benzoic acids (**3**) and (**4**). The reactivity



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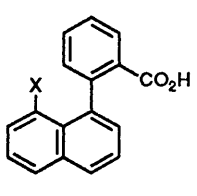

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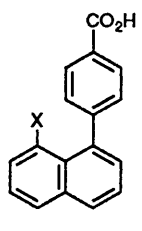


(**4**)

of the acids has been assessed by measurements of their pK_a-values and their rates of esterification with diazodiphenylmethane (DDM).

Results and Discussion

pK_a Values.—The pK_a values of the acids were measured in 80% (w/w) 2-methoxyethanol–water at 25 °C (Table 1).

The first model to be considered is the 4-(8-substituted 1-naphthyl)benzoic acid system (**4**).[4] The pK_a value of the parent acid of this series, 6.60, is very close to those of benzoic and 4-phenylbenzoic acids in this medium, *i.e.* 6.63 and 6.61, respectively. The 8-bromo acid of this series is an almost completely reversed model of a 4-bromobenzoic acid. Any direct steric effect of the 8-bromo group in compounds (**4**) on the reaction site is most unlikely because of the lack of proximity. The value of ΔpK_a, 0.53,[6] for the 4-bromobenzoic acid system is in quantitative agreement with a complete reversal of the result for the 8-bromo acid system, with ΔpK_a −0.49. The latter result is a clear and unequivocal reversed dipolar substituent effect. Thus, an 'inductive' effect transmitted *via* the bonds has no significant importance.

The second model to be considered is the 2-(8-substituted 1-naphthyl)benzoic acid system (**3**). The pK_a value of the parent acid of this series is *ca.* 0.4 pK_a units stronger than that of benzoic acid in this medium, *i.e.* 6.63,[6] and *ca.* 0.2 pK_a units stronger than that of 2-phenylbenzoic acid, *i.e.* 6.47.[1] The 'bulky' *ortho*-substituent in the 2-(1-naphthyl)benzoic acid causes partial deconjugation of *both* the naphthyl-phenyl groups *and* the phenyl-carboxylic acid groups. The latter effect results in acid strengthening.[7] The 8-bromo acid of this series can be considered to be a 'reversed' model of 2-bromobenzoic acid; but it is not ideal. The steric 'environment' of the carboxylic acid group in the 8-bromo acid in model (**3**) is different from that in the simple *ortho*-bromobenzoic acid. The result for the latter acid system, with ΔpK_a equal to 1.01, requires correction before comparison with the result for model (**3**). The parent acid of the latter model has an *ortho*-substituent, unlike benzoic acid itself. Previous studies[8] suggest that a value of ΔpK_a of 0.35 in this medium should be deducted from the value for 2-bromobenzoic acid to compensate for the specific effect of *ortho*-substitution. Thus, the observed ΔpK_a of −0.46 for the 8-bromo acid system (**3**) compares with the corrected ΔpK_a of 0.66 for the 2-bromobenzoic acid system. Thus, this comparison can be considered to give qualitative and roughly quantitative agreement.

The 8-(2-substituted phenyl)-1-naphthoic acids (**2**) are the third model to be considered. The pK_a value of the parent acid of this series is *ca.* 0.42 pK_a units weaker than that of

Table 1. pK_a Values of 8-(2-substituted phenyl)-1-naphthoic and 2- or 4-(8-substituted 1-naphthyl)benzoic acids in 80% (w/w) 2-methoxyethanol–water at 25 °C, and rate coefficients (k_2) for esterification of the acids with DDM in 2-methoxyethanol at 30 °C.[a]

Substituent	pK_a	k_2/dm^3 mol^{-1} min^{-1}
8-(2-Substituted phenyl)-1-naphthoic		
H	6.82	1.16
Br	7.08	1.32
Cl	6.89	1.27
Me	7.20	1.10
OMe	7.29	0.895
NO_2	6.64	1.43
2-(8-Substituted 1-naphthyl)benzoic		
H	6.24	2.14
Br	6.70	1.20
4-(8-Substituted 1-naphthyl)benzoic		
H	6.60	0.659
Br	7.09	0.330
4-Phenylbenzoic	6.61	0.646
4-Bromobenzoic		1.26[b]

[a] The measurements are the mean of at least two determinations. The pK_a values are reproducible to within ±0.02 units and the rate coefficients to ±3%. [b] k_2-Value for benzoic acid is 0.640 dm^3 mol^{-1} min^{-1}.[5]

Table 2. Kirkwood–Westheimer calculations of ΔpK_a for certain acids in 80% (w/w) 2-methoxyethanol–water at 25 °C.

Acid	pK_a Calc.[a]	pK_a Found
4-(8-Bromo-1-naphthyl)benzoic	−0.39	−0.49
4-Bromobenzoic	0.44	0.53[b]
2-(8-Bromo-1-naphthyl)benzoic	−0.50	−0.46
2-Bromobenzoic	0.60	0.66[b,c]
8-(2-Bromophenyl)-1-naphthoic	0.04	−0.26
8-(2-Nitrophenyl)-1-naphthoic	0.44[d]	0.18

[a] Spherical, point-charge model (see the text). [b] Ref. 5. [c] Corrected for specific *ortho*-effect (see the text). [d] Positive end of dipole considered to be on the nitrogen atom.

1-naphthoic acid in this medium, *i.e.* 6.40.[9] However, the true reference acid for model (**2**) should be an almost completely deconjugated 1-naphthoic acid which has been estimated to have a pK_a value of *ca.* 5.9;[10] *cf.* the pK_a value of 8-methyl-1-naphthoic acid (5.99).[9] Thus, 8-phenyl-1-naphthoic acid is considerably weaker than might be expected, *i.e.* $\Delta pK_a \approx 0.9$. Inspection of models indicates that steric interactions would cause the naphthalene group to be almost completely deconjugated from *both* the phenyl and carboxylic groups. However, one face of the carboxylic group is completely shielded by the 8-phenyl group and solvation will be completely denied from this face. The carboxylate anion requires significant protic solvation and a strong acid-weakening will result from steric inhibition of solvation,[11] as is observed. For the 2-substituents the electron-withdrawing groups, Br and Cl, which would be 'expected' to increase acidity, are now acid weakening. However, the 2-NO_2 group, as 'expected', is acid strengthening. Thus, in this model system both reversed and normal dipolar substituent effects are observed. It would appear that model (**2**) is of 'borderline' stereochemistry. This has been previously observed for *cis-ortho*-substituted cinnamic acids.[12] The exact stereochemistry and type of the dipolar substituent will determine which effect is observed. Calculations confirm the reality of this interpretation (see later). The strong acid-weakening effect of the 2-OMe group is not unexpected. The electron-releasing resonance effect of this group will be almost completely absent because of deconjugation and the reversal of the dipolar substituent effect can now be dominant. The effect of the 2-Me group is perplexing. As in other systems,[1,12,13] a powerful acid-weakening effect is observed, when a reversed dipolar substituent effect would have been expected to result in weak acid strengthening. This observation has no obvious and simple explanation.

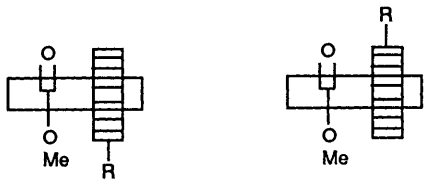
Kirkwood–Westheimer Calculations for the Acids.—In Table 2 are shown the results of Kirkwood–Westheimer calculations for all the bromo-substituted acids studied here, as well as 2- and 4-bromobenzoic and 8-(2-nitrophenyl)-1-naphthoic acids. The agreement between the calculated and found ΔpK_a values, shown in Table 2, is both qualitative and quantitative for *all* the benzoic acids with both reversed and normal dipolar substituent effects. For the 8-phenyl-1-naphthoic acids, the calculations do represent the trends observed, *i.e.* the 2-nitro acid is more acidic than the 2-bromo acid. For model compounds (**2**), the situation is a 'borderline' one between normal and reversed effected, which is highly sensitive to the type of dipolar substituent and the exact stereochemistry involved. These results do confirm and establish the source of the polar substituent effects here to be an electrostatic field effect.

Esterification with Diazodiphenylmethane (DDM).—The rate coefficients for the esterification of the acids with DDM in 2-methoxyethanol at 30 °C are shown in Table 1.

The first model system (**4**), the 4-(8-bromo-1-naphthyl)-benzoic acid, shows a strong reversed dipolar substituent effect, with $\Delta \log k$ −0.300. The value of $\Delta \log k$ for 4-bromobenzoic acid is 0.294 and is therefore in very good agreement with a quantitative reversal of the substituent effect. The second model system (**3**), the 2-(8-bromo-1-naphthyl)benzoic acid, also shows a strong reversed dipolar substituent effect, with $\Delta \log k$ −0.251. The value of $\Delta \log k$ for 2-bromobenzoic acid is 0.681;[14] but this requires correction for the specific rate-enhancing effect of *ortho*-substitution.[8,14] This can be estimated to be *ca.* 0.4 log *k* units for this reaction system, which reduces the observed $\Delta \log k$ to *ca.* 0.3. This is in reasonable quantitative agreement with that observed for the reversed effect.

The third model system, (**2**), the 8-(2-substituted phenyl)-1-naphthoic acids, shows normal substituent effects in the esterification reaction, in contrast with the reversal noted for several substituents in their ionisation reaction. This type of behaviour has been previously noted for other systems.[9,15] The geometric disposition of substituent groups in such systems is such that the 'negative' end of the substituent dipole can interact significantly with both incipient negative and positive charges in the transition state for the esterification with DDM. In equilibria ionisation the final state is anionic alone.

Carbonyl Stretching Frequencies of the Methyl 8-(2-Substituted Phenyl)naphthoates.—The carbonyl stretching frequencies of the methyl 8-(2-substituted phenyl)naphthoates are shown in Table 3. All the 2-substituted esters show only one absorption, unlike the methyl 8-(3- or 4-substituted benzoyl)naphthoates which have two absorptions corresponding to two isomers, '*trans*' and '*cis*'.[16] This arises from the 'locked' stereochemistry in the 1,8-disubstituted naphthalene. Such a situation must also exist for esters in this study having 2-substituents and would give rise to the two isomers (**5**) and (**6**). This present series of methyl esters must consist either of one isomer or of both



isomers, if both have identical or close frequencies with unresolved absorptions.

Experimental

Materials.—The acids were prepared by use of the Ullman reaction, followed by hydrolysis of the corresponding methyl esters.

General.—All products had IR, ^{1}H, and ^{13}C NMR, and mass spectra in accord with the stated structures. The m.p.s, recrystallisation solvents, and elemental analyses of the esters and acids are shown in Table 4.

Table 3. Carbonyl stretching frequencies, ν_{max}, of the methyl 8-(2-substituted phenyl)-1-naphthoates in tetrachloromethane.[a]

Substituent	ν_{max}/cm^{-1}
H	1 726 (1 733)[b]
Br	1 728
Cl	1 729
Me	1 730
OMe	1 727
NO_2	1 729

[a] Measurements reproducible to ±1 cm^{-1}. [b] Shoulder.

Methyl 8-Phenyl-1-naphthoate.—The methyl ester was prepared by the method of Craig *et al.*[17]

Methyl 8-(2-Bromo-, 2-chloro-, 2-nitro-, 2-methyl-, and 2-methoxy-phenyl)-1-naphthoates.—These *esters* were synthesized by the method of Craig *et al.*[17,18] from the relevant 2-substituted iodobenzenes.

8-Phenyl-1-naphthoic Acid and 8-(2-Methyl- and 2-methoxy-phenyl)-1-naphthoic Acids.—The corresponding *esters* were hydrolysed to the *acids* by the method of Cooke and Harris[21] using alcoholic potassium hydroxide.

8-(2-Bromo-, 2-chloro-, and 2-nitro-phenyl)-1-naphthoic Acids.—The corresponding *esters* were hydrolysed to the *acids* by the method of Olah *et al.*[22] using chlorotrimethylsilane–sodium iodide.

2-(1-Naphthyl)benzoic Acid.—The methyl ester of this acid was prepared by the method of Baddar and Warren.[23] The ester was hydrolysed to the acid by the method of Cooke and Harris.[21]

2-(8-Bromo-1-naphthyl)benzoic Acid.—8-Bromo-1-iodonaphthalene[24] (5.6 g, 0.024 mol) and methyl 2-iodobenzoate (10.4 g, 0.038 mol) were stirred together at 150 °C, while copper-bronze (12 g, 0.19 mol) was added in small portions at 20 min intervals. The reaction mixture was then held at 170 °C for a further 8 h. After addition of further methyl 2-iodobenzoate (5.2 g, 0.019 mol) and copper-bronze (6 g, 0.095 mol) in small portions, the reaction mixture was held at 170 °C for a further

Table 4. Physical constants of the acids and esters.

Substituent	M.p./ °C	Lit. m.p./ °C	Formula	Found (%) C	H	Other	Requires (%) C	H	Other	Recrystallisation solvent
8-(2-Substituted phenyl)-1-naphthoic acids										
H	223–224		$C_{17}H_{12}O_2$	82.7	4.9		82.3	4.9		EtOH–acetone
Br	218–219		$C_{17}H_{11}BrO_2$	62.4	3.4	23.6 (Br)	62.4	3.4	24.4 (Br)	EtOH
Cl	209–210		$C_{17}H_{11}ClO_2$	71.9	4.3	12.3 (Cl)	72.2	3.9	12.5 (Cl)	EtOH
Me	232–233		$C_{18}H_{14}O_2$	82.6	5.3		82.4	5.4		light petroleum (b.p. 40–60 °C)–acetone
OMe	221–222		$C_{18}H_{14}O_3$	76.0	5.1		76.7	5.1		acetone–benzene
NO_2	247–248		$C_{17}H_{11}NO_4$	69.9	3.6	4.7 (N)	69.6	3.8	4.8 (N)	acetone–benzene
Methyl 8-(2-substituted phenyl)-1-naphthoates										
H	113–115	113–114[a]								EtOH–toluene
Br	149–150		$C_{18}H_{13}BrO_2$	62.6	3.8	23.6 (Br)	63.4	3.8	23.4 (Br)	EtOH–benzene
Cl	126–128		$C_{18}H_{13}ClO_2$	72.2	4.3	11.9 (Cl)	72.8	4.4	11.9 (Cl)	benzene
Me	98–100	99–100[a]								toluene
OMe	80–82		$C_{19}H_{16}O_3$	77.9	5.6		78.0	5.5		EtOH–toluene
NO_2	198–199	199–200[b]								toluene
2-(8-Substituted 1-naphthyl)benzoic acids										
H	161–162	159.5–161[c]								aq.EtOH
Br	185–186		$C_{17}H_{11}BrO_2$	62.6	3.4	23.9 (Br)	62.4	3.4	24.4 (Br)	EtOH
4-(8-Substituted 1-naphthyl)benzoic acids										
H	239–241	229[d]	$C_{17}H_{12}O_2$	82.5	5.0		82.3	4.9		EtOH
Br	250–251		$C_{17}H_{11}BrO_2$	62.3	3.5	23.8 (Br)	62.4	3.4	24.4 (Br)	EtOH
4-Phenylbenzoic acid	223–225	222–224[e]								

[a] Ref. 17. [b] Ref. 18. [c] Ref. 19. [d] Ref. 20. [e] Ref. 13.

12 h. After extraction of the cooled product with boiling toluene ($4 \times 50\ cm^3$), evaporation of the extract afforded a dark yellow solid, which was subjected to column chromatography on alumina with benzene as the eluant. The second fraction gave the required *ester* as a pale yellow solid. The latter was hydrolysed by the method of Olah *et al.*[22] using chlorotrimethylsilane–sodium iodide to give the acid, m.p. 185–186 °C (0.1 g, 2%).

4-(1-*Naphthyl*)*benzoic Acid*.—The methyl *ester* of this *acid* was prepared and then hydrolysed to the acid by a similar method to that used for the synthesis of 3-isomer by Hall *et al.*[19]

4-(8-*Bromo*-1-*naphthyl*)*benzoic Acid*.—The methyl *ester* and this *acid* were prepared from methyl 4-iodobenzoate as described above for the 2-isomer. The hydrolysis of the ester to the acid (0.3 g, 5%) was completed by the method of Hall *et al.*[19] employed for 3-(1-naphthyl)benzoic acid. The solvents and DDM were prepared as previously described.[25]

Measurements.—The pK_a values and the rate coefficients for esterification with DDM were determined as described previously,[24,26] as were the IR spectra of the methyl esters.[16]

Kirkwood and Westheimer Calculations.—These calculations were carried out for a spherical, point-charge model[27] for all bromo acids studied here, as well as 2- and 4-bromobenzoic and 8-(2-nitrophenyl)-1-naphthoic acids. In general, the calculations were carried out as before.[10,15] However, in the present model, the embedding distance suggested by Ehrenson[28] and the embedded dipole moments suggested by Orttung[29] have been used.

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