# Transmission of Polar Effects. Part 19.[1] Ionisation and Esterification with Diazodiphenylmethane of a Series of 2'- and 4'-Substituted-biphenyl-2-carboxylic Acids

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The pK_a values of a series of 2'- and 4'-substituted-biphenyl-2-carboxylic 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. The transmission of polar effects from the 4'-position is normal and the transmission coefficient is ca. 0.4. However, for the normally electron-withdrawing substituents at the 2'-position, reversed dipolar substituent effects are observed in both reactions. The reactivity studies indicate that the conformation of the 2,2'-disubstituted-biphenyl system appears to be close to that having orthogonal aryl groups.

The transmission of polar effects in biphenylcarboxylic acids has been studied by several groups.[2-7] An early study[2] of the 3'- or 4'-substituted-biphenyl-4-carboxylic acids (1) in their
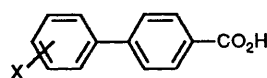
(1)

ionisation showed the 'normal' behaviour of these substituents and gave good correlations by use of the Hammett equation. A more extensive study of the system[3] confirmed these findings. The former results and those for the reactivity of such acids with diazodiphenylmethane (DDM)[4] allowed estimates of the transmission of polar effects to be obtained.[8] However, a study by Gray et al.[5] of the 2'-substituted-biphenyl-4-carboxylic acids (2) showed that the usually strongly acid-strengthening
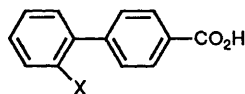
(2)

dipolar substituents exert either small acid-strengthening or acid-weakening effects. Their explanation of the results was that the 'normal' electronic effects were modified by steric effects and a repulsion of π-electron system by the dipolar substituent resulted.[5] Bowden and Parkin[9] have re-interpreted these results in terms of a reversed dipolar substituent effect. All 2'-substituents cause significant coaxial twisting in the biphenyl system so that the end of the substituent dipole embedded in the molecule no longer has a favourably positioned low dielectric cavity for transmission. The latter is then effectively opposed by the 'negative' end of the dipole which results in a diminished or reversed substituent effect. Drapala[6,7] has studied the effect of substituents on the ionisation of a limited series of 2'-, 3'-, and 4'-substituted biphenyl-2-carboxylic acids. The 'unexpected' results for the 2'-substituents were initially attributed to an intramolecular hydrogen bond; but the latter could not be demonstrated for the acids in carbon tetrachloride by IR spectroscopy.[6]

Table 1. pK_a Values of 2'- and 4'-substituted-biphenyl-2-carboxylic acids in 80% (w/w) 2-methoxyethanol–water at 25 °C.[a]

Substituent	pK_a 2'	4'
H	6.47	6.47
Me	6.89	6.54
Cl	6.86	6.19
Br	6.92	6.19
I	6.95	6.20
CN	6.52	5.95
NH₂	—	6.57
NO₂	6.81	5.85
OH	—	6.50
OMe	7.12	6.42
CO₂Me	7.02	—
CO₂H	4.88 (5.18)[b]	—
CO₂⁻	8.73 (8.43)[b]	—
CONH₂	5.65	—

[a] The measurements are the mean of at least two determinations. The pK_a values are reproducible to within ±0.02 units. [b] Statistically corrected.

In the present study we have prepared a comprehensive series of both 2'- and 4'-substituted biphenyl-2-carboxylic acids. The reactivity 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 pK_a of the parent acid of these series is about 0.2 pK_a unit stronger than that of benzoic acid in this medium, i.e. 6.63.[10] The 'bulky' ortho-substituent in the benzoic acid causes partial deconjugation of both the aryl–aryl groups and the aryl–carboxylic groups. The latter effect results in the acid-strengthening.[11]

The effects of substitution at 4'-position can be assessed by means of the Hammett equation using σ or σⁿ values.[12,13] The resulting correlations are shown in Table 2. Both correlations

Table 2. Hammett reaction constants for the reactivity of the 4'-substituted-biphenyl-2-carboxylic acids.[a]

| Reaction		ρ	$\log K_0$	s	r	n
Ionisation	(a)	0.598	6.34	0.069	0.959	9
	(b)	0.698	6.40	0.046	0.985	9
Esterification	(a)	0.328	0.245	0.031	0.970	9
with DDM	(b)	0.380	0.214	0.020	0.991	9

[a] s Is the standard deviation, r the correlation coefficient and n the number of substituents studied. Correlation (a) with σ and (b) with σ^n. The 4'-amino is excluded from the correlations because of excessive deviation.

Table 3. Rate coefficients (k_2) for esterification of 2'- and 4'-substituted biphenyl-2-carboxylic acids with DDM in 2-methoxyethanol at 30 °C.[a]

	$k_2/\text{dm}^3\text{ mol}^{-1}\text{ min}^{-1}$	
Substituent	2'	4'
H	1.55	1.55
Me	0.969	1.44
Cl	0.971	2.04
Br	0.955	2.15
I	0.952	2.30
CN	1.47	2.88
NH_2	—	1.11
NO_2	1.43	3.13
OH	—	1.37
OMe	0.526	1.51
CO_2Me	0.948	—
CO_2H	3.04 (1.52)[b]	—
$CONH_2$	4.33	—

[a] The measurements are the mean of at least two determinations. The rate coefficients are reproducible to within 3%. [b] Statistically corrected.

are satisfactory, but the use of σ^n is more successful, as would be expected for an insulated system. The transmissive efficiency, ρ/ρ_0, of the system,[8] by use of the ionisation of benzoic acids in the same system as the reference reaction (1.66),[14] is 0.42. The 4'-substituted biphenyl-2-carboxylic acid system (3) is closely comparable to *para*-substituted-(Z)-cinnamic acid system (4), both in terms of the transmissive route
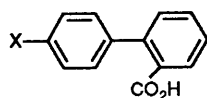
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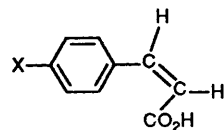
(4)

and environment of the reactive site. Thus, ρ/ρ_0 for the (Z)-cinnamic system is 0.52.[15] These results contrast with ρ/ρ_0 of 0.26 for the 4'-substituted-biphenyl-4-carboxylic acids (2). The present result could be accommodated by transmission *via* either an inductive or a direct field effect.

The effects of substitution at the 2'-position are more complex. The effects of 2-substitution on the stereochemistry of biphenyl has been investigated.[16] The conformation of each member of the series studied here is variable and would

not be either of the coplanar forms, *i.e.* s-*cis* (5) or s-*trans* (6); but will be a compromise conformation which involves partial deconjugation of both the aryl–aryl and aryl–carboxylic groups, as well as the aryl–substituent groups (if applicable). The actual conformation will probably be closer to that having orthogonal aryl groups. The 2'-substituent effects, shown in Table 1, indicate that the normally electron-withdrawing groups, CN, NO_2, CO_2Me, Cl, Br, and I, which would be 'expected' to increase acidity, are now acid-weakening. In the system under study, the stereochemistry causes the end of the substituent dipole embedded in the molecule to no longer have a favourable position for transmission and is effectively opposed by the other end of the dipole, which results in a reversal of the 'normal' effect. It is difficult to conduct Kirkwood–Westheimer calculations to confirm our conclusions on these systems because the exact stereochemistry is not known. However, the calculations have been made for the coplanar s-*cis* and s-*trans* conformations (5) and (6) of the 2'-bromo acid, both conformations being extreme cases and unlikely. The values of $\Delta p K_a$ are then 0.45 (found), 0.93 (calculated s-*cis*), and -0.37 (calculated s-*trans*). Thus, these results indicate that a conformation occurs which has significant twisting and is closer to orthogonal than to either extreme conformations (5) and (6). The acid-strengthening observed
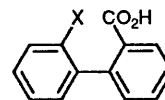
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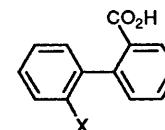
(6)

for the 2'-CO_2H and $CONH_2$ substituents appears to arise from an intramolecular hydrogen bond in the mono-anion, similar to that in many related sytems.[17] Likewise, this effect will cause acid-weakening for the 2'-CO_2^- substituent, as is observed. The strong acid-weakening effect of the 2'-OMe substituent is not unexpected. The overall electron-releasing effect of the methoxy group arises from the dominant resonance effect.[18] The 4'-OMe group (see Table 1) is only slightly acid-strengthening, presumably because of the partial deconjugation in the biphenyl-2-carboxylic acid system. For the 2'-OMe acid, the reversal of the dipolar field effect is now the dominant feature, which is reinforced by any residual resonance effect and results in significant acid-weakening. An intramolecular hydrogen bond would not be expected in the 2'-OMe acid as it would require an eight-membered ring structure and has, in any case, unfavourable steric interactions.[19] Drapala[6] found no evidence for such an effect in a study of the IR spectra of the 2'-OMe acid in carbon tetrachloride.

The result for the 2'-Me acid is perplexing. A small reversal in the opposite direction to those observed for the electron-withdrawing substituents might be expected. However, the significant acid-weakening effect observed is consistent with the effects of the 2'-Me, Et, and Pr^i groups in the ionisation of the biphenyl-4-carboxylic acid system.[5] No obvious explanation of the observed effect is apparent.

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 3. This reaction

has been used widely in the study of polar substituent effects,[20] and the rate-determining step of the esterification being the transfer of a proton from the acid to DDM. The Hammett equation can be used again to assess the effects of substitution at the 4'-position by use of σ or σ^n values.[12,13] Satisfactory correlations have been obtained and are shown in Table 2. The use of σ^n is again more successful and the transmissive coefficient, ρ/ρ_o, of this system can be calculated to be ca. 0.32, by use of the reaction of benzoic acids under the same conditions as the reference reaction (1.18).[21] The latter transmission again appears to be significantly greater than that found for the 4'-substituted-biphenyl-4-carboxylic acid system where ρ/ρ_o is ca. 0.24.[4] This confirms our conclusions from the study of the ionisation reaction discussed earlier. Again, all the normally electron-withdrawing 2'-substituents show rate retardations and this parallels the results for the ionisation reaction. Previously, the results for the esterification with DDM for similar systems[9,22–24] showed diminished reversals or even unreversed results, compared with the ionisation reaction. However, in the system under present study, the reversals observed in the DDM esterification are decided. The stereochemical situation in the system under study is thus more ideal for the observation of reversed dipolar substituent effects.

Experimental

Materials.—Biphenyl-2-carboxylic acid and its 2'- and 4'-methyl, -chloro, -bromo, -cyano, -nitro, and -methoxy and 4'-amino, -iodo, and -hydroxy derivatives, as well as diphenic and diphenamic acids, were prepared by previously reported methods.[6,25–34] The compounds had m.p.s in good agreement with literature values.

2'-Iodobiphenyl-2-carboxylic Acid.—This acid was prepared by a modification of the preparative method employed for the synthesis of 2'-bromo acid.[26] The acid was recrystallised from aqueous ethanol as pale pink plates, m.p. 150–151 °C (Found: C, 48.4; H, 2.8; I, 38.9; O, 9.9. $C_{13}H_9IO_2$ requires C, 48.2; H, 2.8; I, 39.1; O, 9.9%).

The solvents and DDM were prepared as described previously.[34]

Measurements.—The pK_a values and the rate coefficients were determined as described previously.[35]

Kirkwood and Westheimer calculations.—These calculations for a spherical model were carried out for 2'-bromo acid as described previously.[22]

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