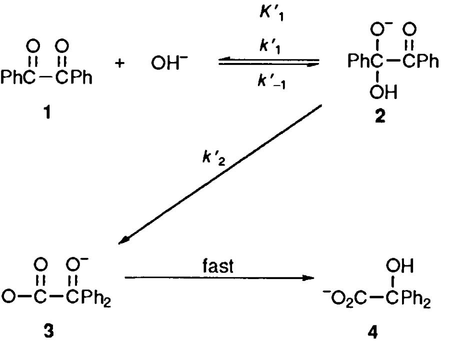
Reactions of Carbonyl Compounds in Basic Solutions. Part 20.[1] Mechanism of the Base-catalysed Rearrangement of Symmetrically Substituted Benzils

Keith Bowden* and Karl D. Williams
Department of Chemistry and Biological Chemistry, University of Essex, Wivenhoe Park, Colchester, Essex, UK CO4 3SQ

Rate coefficients have been measured for the base-catalysed rearrangement of a series of symmetrically 2,2′-, 3,3′- and 4,4′-disubstituted benzils at 30.0 and 60.0 °C in 70% (v/v) aqueous dimethyl sulfoxide (DMSO), as well as at 40.0 and 50.0 °C for benzil itself. The enthalpies and entropies of activation have been evaluated. For benzil itself, rate coefficients have been measured at 60.0 °C in a series of aqueous DMSO and dioxane mixtures. The effects of *meta*/*para*-substitution have been assessed by means of the Hammett equation to give, using σ (and not 2σ), a ρ value of about 5.7. The role of these effects for the migrating and non-migrating phenyl groups have been separated. The steric effects from *ortho*-substitution have been evaluated. The limiting conditions for the observation of the base-catalysed rearrangement and two types of fission for benzils are delineated. The results are discussed in terms of mechanistic paths for the rearrangement and fission processes and the structures of the transition states.

The benzilic acid rearrangement was discovered by Liebig in 1838 and there now exists an extensive range of data for this reaction covering virtually all the applicable physical organic techniques.[2-4] Scheme 1 shown below represents the accepted pathway. The kinetics of the reaction have been found to be second-order, first-order both in benzil and hydroxide anion. The second step, k'_2, appears to be rate determining. The overall k'_{obs} thus equals $K'_1k'_2$. The overall transition state has been considered to resemble more closely the intermediate **2**.[2,3] Thus the 1,2-aryl shift appears to have only just started to proceed in this transition state.



Scheme 1

In symmetrically disubstituted benzils, electron-attracting substituents accelerate and electron-releasing substituents retard the rearrangement, whereas the rearrangement is retarded by steric 'bulk' effects. Unfortunately, these results are derived from diverse sources.[5-7] For *meta*- and *para*-mono-substituted benzils labelled with ^{14}C at the carbon atom adjacent to the unsubstituted phenyl, the actual phenyl group undergoing migration can be determined. A plot of the logarithm of the migration ratios against the respective Hammett σ value yields a reaction constant, ρ, of about 1.43.[3]

There are a number of base-catalysed rearrangements which are closely related to the benzilic acid rearrangement.[2,3] However, it is also possible to find base-catalysed fission of substituted benzils and related compounds in which the fission can occur between either the carbonyl-carbons or the carbonyl-carbon and aryl group, *cf.* refs. 7 and 8. A recent theoretical treatment[9] of the benzilic acid and related rearrangements has considered alternative classical anionic and single electron transfer (SET) pathways[10] and the effects of substituents on these.

The present studies were prompted by the need to establish clearly the dependence of the benzilic acid rearrangement on substituent and solvent effects to enable the elucidation of related reactions.[11] We describe here the base-catalysed benzilic rearrangement of a series of symmetrically 2,2′-, 3,3′- or 4,4′-disubstituted benzils in aqueous dimethyl sulfoxide (DMSO). The effects of substitution, solvent composition and the activation parameters are discussed. More extreme examples of substituent effects have been re-examined and the factors controlling the boundaries of the benzilic acid rearrangement are discussed.

Experimental and Results

Materials.—Benzil and benzilic acids were available commercially. The substituted benzils were prepared by oxidation of the corresponding benzoins by published procedures.[12,13] The corresponding benzilic acids were isolated by the base-catalysed rearrangement of the benzils.[14] After recrystallisation from suitable solvents and drying under reduced pressure (P_2O_5), the m.p.s of the benzils and benzilic acids were in good agreement with literature values.[7,12-16] The methyl esters of the benzilic acids were prepared by treatment of the acids with diazomethane in diethyl ether, *cf.* ref. 17. The products of the rearrangement/fission of 3,3′-dinitro- and 5,5′-dibromo-2,2′-dihydroxy-benzil were isolated as has been previously described by others.[7,8] The possible fission products of the benzils which apparently only rearranged were available commercially and the corresponding benzoic acids were esterified using diazomethane to give the methyl esters as described above.

The solvents for the kinetic studies were prepared as previously described.[18]

Measurements.—Rate coefficients for the base-catalysed rearrangement of the benzils to the benzilic acid anions were determined spectrophotometrically by use of a Perkin-Elmer lambda 5 UV–VIS spectrometer. The reactions were followed at the wavelengths shown in Table 1. The procedure used was that described previously.[19] The products of the reactions, except for the 3,3′-dinitro- and 5,5′-dibromo-2,2′-dihydroxy-benzils, were found to be the anions of the corresponding benzilic acids in

Table 1 Rate coefficients (10^3k_2/dm^3 mol^{-1} s^{-1}) for the base-catalysed rearrangement of symmetrically substituted benzils in 70% (v/v) aqueous DMSO[a]

	10^3k_2/dm^3 mol^{-1} s^{-1}		
Substituents	T = 30.0 °C	T = 60.0 °C	λ/nm[b]
H,H	4.60 (9.31)[c] (17.8)[d]	35.7	280,[c] 295[d]
2,2′-$(CH_3)_2$	0.301	2.84	290, 315
3,3′-$(CH_3)_2$	1.73_5	16.3_5	285, 315
4,4′-$(CH_3)_2$	0.682	5.04_5	300, 300
2,2′-$(OCH_3)_2$	0.0220	0.146	320, 320
4,4′-$(OCH_3)_2$	0.148	1.22_5	310, 310
2,2′-$(Cl)_2$	22.0	215	270, 280
3,3′-$(Cl)_2$	1140	8490	285, 280
4,4′-$(Cl)_2$	45.3	$375._5$	280, 280

[a] Rate coefficients were reproducible to ±5%. [b] Wavelength used to monitor the reaction at 30.0 and 60.0 °C, respectively. [c] At 40.0 °C. [d] At 50.0 °C.

Table 2 Activation parameters for the base-catalysed rearrangement of symmetrically substituted benzils in 70% (v/v) aqueous DMSO[a]

Substituents	$\Delta H^{\ddagger}$/kcal mol^{-1} [b]	$\Delta S^{\ddagger}$/cal mol^{-1} K^{-1} [b]
H,H	13.0	−26
2,2′-$(CH_3)_2$	14.4	−27
3,3′-$(CH_3)_2$	14.4	−24
4,4′-$(CH_3)_2$	12.8	−31
2,2′-$(OCH_3)_2$	12.1	−40
4,4′-$(OCH_3)_2$	13.5	−31
2,2′-$(Cl)_2$	14.7	−18
3,3′-$(Cl)_2$	12.8	−16
4,4′-$(Cl)_2$	13.5	−20

[a] Values of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ are considered accurate to within ±300 cal mol^{-1} and ±2 cal mol^{-1} K^{-1}, respectively. [b] 1 cal = 4.184 J.

Table 3 Rate coefficients (10^3k_2/dm^{-3} mol s^{-1}) for the base-catalysed rearrangement of benzil in aqueous DMSO and dioxane at 60.0 °C[a]

Volume (%) non-aqueous solvent	DMSO	Dioxane
10	0.791	—
30	1.36	0.343
40	—	0.317
50	3.58	0.311
60	—	0.364
70	35.7	0.474
80	115	0.758
90	409	—

[a] See footnote to Table 1.

Table 4 Hammett reaction constants (ρ) for the base-catalysed rearrangement of symmetrically disubstituted benzils in 70% (v/v) aqueous DMSO[a]

T/°C	ρ	$\log k_0$	r	s	n
30	5.696	−2.318	0.991	0.393	7
60	5.656	−1.413	0.992	0.360	7

[a] s is the standard deviation, r the correlation coefficient and n the number of substituents studied. The correlations are obtained using σ and not 2σ.

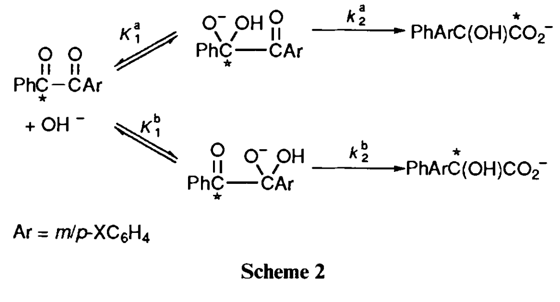
quantitative yield and were confirmed spectrophotometrically by comparison of the spectrum of the acid in base with that of the reaction product. The products of the kinetic runs were isolated by acidification with concentrated hydrochloric acid and extraction with dichloromethane. The extracts were treated with diazomethane in diethyl ether and subjected to analysis using an F17 Perkin-Elmer gas chromatograph. Except as discussed below, no products of fission (*i.e.* < 2%) were detected. The rate of the reaction of the 5,5′-dibromo-2,2′-dihydroxybenzil was very slow, compared to the benzils undergoing rearrangement. The products of reaction were confirmed to be the corresponding benzilic acid, as the main product, with *para*-bromophenol and 2-(5-bromo-2-hydroxyphenyl)-2-oxoethanoic acid, as the minor product. The reaction of 3,3′-dinitrobenzil was found to be relatively rapid, compared to the benzils undergoing rearrangement, and the products were confirmed as a mixture of 3-nitrobenzoic acid and azoxybenzene-3,3′-dicarboxylic acid.[8]

The benzilic acid rearrangement was found to be first order both in the benzil and hydroxide anion as found previously.[2] Rate coefficients in 70% (v/v) aqueous DMSO at 30.0 and 60.0 °C, as well as at 40.0 and 50.0 °C for benzil itself, are shown in Table 1. The activation parameters are shown in Table 2. The rate coefficients for the rearrangement of benzil in aqueous DMSO and dioxane at 60.0 °C are shown in Table 3. The rearrangement fission of 5,5′-dibromo-2,2′-dihydroxybenzil was too slow to measure under the conditions described above. No simple kinetic measurements were found possible for the fission of 3,3′-dinitrobenzil, which appears to have complex kinetics.

Discussion

Substituent Effects in the Symmetrically Substituted Benzils.—The effect of *meta*- and *para*-substituents in both phenyl rings of the symmetrically disubstituted benzils has been assessed using the Hammett equation with *meta*/*para* σ values,[20], as shown in Table 4. The ρ values in 70% (v/v) aqueous DMSO, obtained using σ (and not 2 σ) as the substituent effect, are 5.696 and 5.656 at 30 and 60 °C, respectively. The results of the migration of the *meta*- and *para*-monosubstituted benzils yielded a Hammett reaction constant, ρ_m, of about 1.43 in about 33% aqueous ethanol at room temperature when the logarithms of the migration ratios (corrected for an isotope effect) were correlated with σ.[21] The latter ρ_m requires correction for the differences in solvent and temperature before comparison with the former ρ value at 30 °C in 70% aqueous DMSO. Hojo *et al.*[22] have studied ρ values for the alkaline hydrolysis of ethyl benzoates in a range of aqueous ethanol and DMSO compositions, as well as water itself, at 25 °C. Furthermore, ρ appears to vary with $1/T$ for the alkaline hydrolysis of esters and similar reactions.[23] Application of these two considerations results in an estimate for ρ_m for the migration of about 2.0 in 70% aqueous DMSO at 39.0 °C.

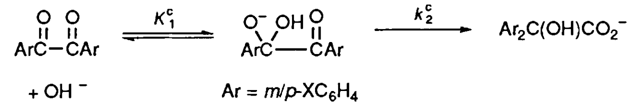
The overall rate processes for the migration of the monosubstituted labelled benzils[21] is shown in Scheme 2. Using Wegscheider's principle[24] for concurrent reactions of the same order, Exner[25] has related the amount of both products to the observed rate coefficients, $K^a{}_1k^a{}_2$ and $K^b{}_1k^b{}_2$, and hence to the reactions constants, ρ_b and ρ_a, for the relevant overall processes in Scheme 2, as shown in eqn. (1) below. Thus, the



Scheme 2

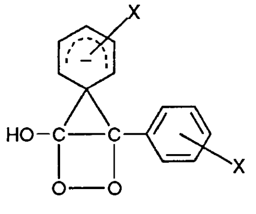
$$\log (x_b/x_a) = \rho_b - \rho_a \qquad (1)$$

observed value of ρ_m for the migration of the monosubstituted benzil is equal to $\rho_b - \rho_a$. Furthermore, the overall rate process for the reaction of the symmetrically disubstituted benzils is shown below in Scheme 3. Such commulative effects



Scheme 3

have also been considered by Exner.[26] An example relevant to this study is the base-catalysed hydrolysis of phenyl benzoates[27] which are substituted in both the aryl and aroyl groups and give additive ρ values. In the present study, as shown in Scheme 3, one of the substituted phenyl groups migrates, while the other does not. Thus, the overall value of ρ_c is the sum of that resulting from migration, ρ_b, and non-migration, ρ_a, *i.e.* ρ_c is equal to $\rho_a + \rho_b$. This simple additive behaviour appears to be common as has been shown by Johnson[28] in his analysis of the reactivity–selectivity principle. These considerations allow the separation of the observed overall reaction constants into those for the overall migration, with ρ equal to 3.8_5, and non-migration, with ρ equal to 1.8_5. Estimates of these two reaction constants can be made for the extreme structures for the transition state, the intermediates **2** and **3**, as about 2.1(±0.2) and 4.7(±0.6), respectively, for ρ for non-migration, and as about 4.7(±0.6) for both **2** and **3** for ρ migration. These estimates are based on the equilibria addition of hydroxide anion to substituted benzaldehydes[29] in water at 30 °C for which ρ is about 2.5(±0.3), together with a reduction for the transmission of polar effects *via* the carbonyl group[30] when required. The estimated ρ values have been corrected for the difference in solvent from water to 70% aqueous DMSO using the results of Hojo *et al.*[22] for the alkaline hydrolysis of ethyl benzoates at 25 °C. However, the migration process has been compared also to a nucleophilic aromatic process.[31] An extreme structure for an intermediate or transition state for the latter can be 'represented' as **5** below. An estimate of the ρ for formation of **5** is more difficult. However, estimated ρ values of about 6.1, for migration, and 0.7, for non-migration, can be derived from the reaction constants for the reaction of hydroxide with 4-substituted 1-methoxy-2-nitrobenzene with ρ equal to about 6.1,[32] and 1-(3- or 4-substituted phenoxy)-2,4-dinitrobenzene, with ρ equal to about 0.7, in aqueous DMSO at 30 °C.[33]



5

The reaction constants ρ_a and ρ_b separated above can be used to characterise the transition state in terms of charge development, employing the model reactions described above. Thus ρ for non-migration would indicate very little development of charge on the oxygen bonded to the carbon bonded to the carbon receiving migration; while ρ for migration would indicate little dispersal of charge onto the migrating phenyl.

The polar effects of 2,2′-substituents are likely to be accompanied by steric effects arising mainly from the proximity of the reaction site and 2-substituent migrating. A crude estimate of the steric effect can be made from the ratio of the rates for the 2,2′- to the 4,4′-disubstituted substrates. This assumes that the polar effects cancel each other out, which is easier to justify for the more 'distant' substituent in the non-migrating phenyl group. The ratios are 0.44, 0.15 and 0.49 at 30 °C for the methyl-, methoxy- and chloro-substituents, respectively. These factors, converted to logarithms, correlate with the Taft steric substituent constants, E_s, for *ortho*-substituents.[34] This result indicates significant crowding in the transition state, relative to the initial state, causing rate retardation for 'bulky' 2-substituents.

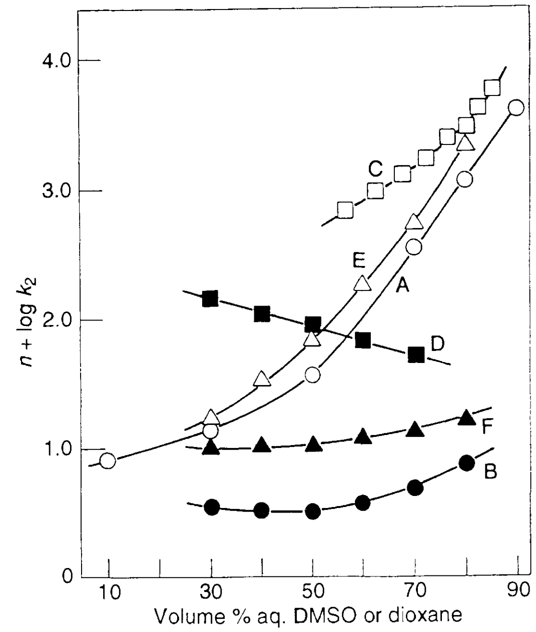
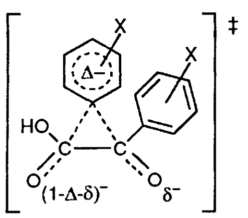


Fig. 1 Relation between $\log k_2$ for base-catalysed reactions for several substrates and the composition of aqueous DMSO or dioxane mixtures; benzil, A (DMSO), B (dioxane); methyl benzoate, C (DMSO), D (dioxane); 1-methoxy-2,4-dinitrobenzene, E (DMSO), F (dioxane) (*n* equals 4 for A and B at 60 °C and for C at 25 °C, 3 for D, E and F at 50 °C)

The activation parameters shown in Table 2 can be compared to those observed in the alkaline hydrolysis of substituted methyl benzoates,[35] *e.g.* electron-withdrawing substituents decrease and electron-releasing increase $\Delta H^{\ddagger}$. The trends in the present results are, in general, similar to those in the latter study; but the effects are not as decided.

Solvent Effects.—The effects of solvent on the rates of rearrangement of benzil itself are shown in Table 3. In Fig. 1 a comparison is shown between the present results and the effects of solvent composition on the alkaline hydrolysis of methyl benzoate and 1-methoxy-2,4-dinitrobenzene.[36,37] The rates of reaction increase markedly with increasing DMSO content as has been noted for several other reactions involving hydroxide anions.[33,37,38] This is considered to arise mainly from the increased activity of hydroxide. DMSO is also known to stabilise extended charge-delocalised structures.[38] However, the effect of increasing dioxane content on the rates of similar reactions has been found to be comparatively minor, but discriminating, with both increases and decreases in rates observed.[36] The results shown in Fig. 1 indicate that the effect of solvents on the initial to transition state stabilities for the reaction of benzil is closer to that of the alkaline hydrolysis of 1-methoxy-2,4-dinitrobenzene than for the same reaction of methyl benzoate. The reduced requirement for protic solvation, compared to the alkaline hydrolysis of methyl benzoate, is observed in both aqueous DMSO and dioxane. The evidence from the effect of solvent on the rates appears to favour some charge-delocalisation on the phenyl ring in the rearrangement of benzil.

Thus the transition state for the benzilic acid rearrangement is close to **2**, but has minor charge delocalisation as shown in **6** below.

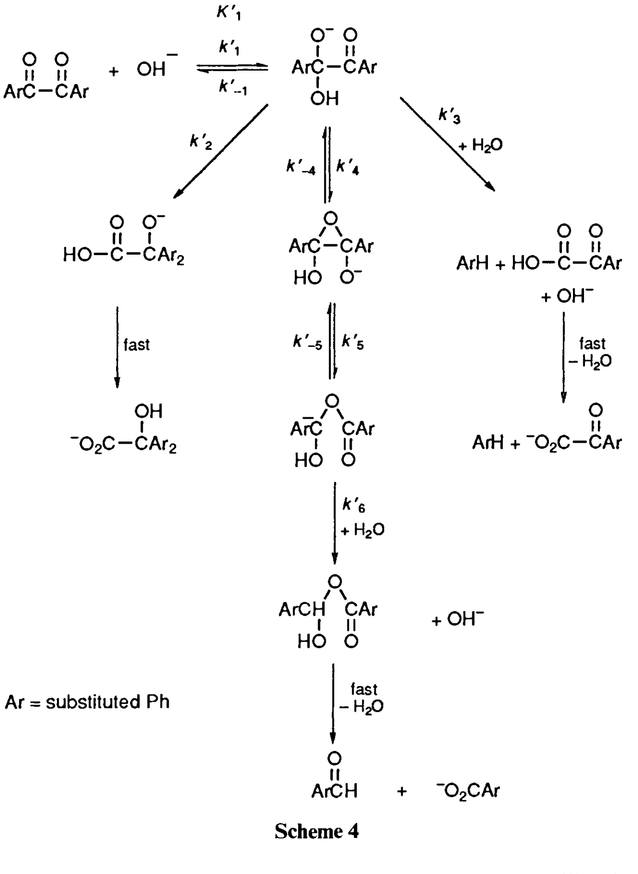


6

Reaction Pathways.—Benzils react in three ways with base, *i.e.* (i) rearrangement to form a benzilic acid anion, (ii) aryl–carbonyl fission and (iii) carbonyl–carbonyl fission.

The benzilic acid rearrangement, case (i), occurs for benzils with ring substituents that are 'moderately' either electron-withdrawing or electron-releasing. As discussed above, the rate determining step appears to be k'_2 in Scheme 4 below, with a transition state shown as **6** above.

The reactions (iii) and (ii) appear to arise when the ring substituents are either strongly electron-withdrawing or *ortho* and strongly electron-releasing, respectively. In case (iii), the formation of the adduct is relatively very favourable. This is followed by intramolecular nucleophilic attack and formation of the carbanion, as shown in Scheme 4. Both the latter are strongly assisted by the electron-withdrawing substituent effect. The formation of the carbanion is analogous to the formation of a similar carbanion in the reaction of benzil with cyanide anion.[39] For 3,3′-dinitrobenzil, the primary products of the base-catalysed fission would appear to be 3-nitrobenzoic acid and 3-nitrobenzaldehyde. 3-Nitrobenzaldehyde undergoes a Cannizzaro reaction to give the expected products of disproportionation under carefully controlled conditions of base concentration and temperature.[40] However, stronger base and higher temperatures results in a more complex product mixture including azobenzenecarboxylic acids.[40] This accounts for the result observed for the reaction here of 3,3′-dinitrobenzil. In case (ii), the formation of the adduct is relatively very unfavourable. However, the benzil–benzilic aryl migration is also very unfavourable. The formation of a phenyl carbanion by fission is not itself favoured, as well as not being favoured by such electron-releasing substituents. The aryl fission of benzil with such substituents could be concerted with proton capture, as shown in Scheme 4. However, the fission reaction becomes now competitive with rearrangement. Such a fission reaction is likely to be assisted by *ortho*-substitution as it is closely analogous to that of 2,6-dihalo- and dinitro-benzaldehydes, as well as 2,4-dinitrobenzaldehyde, with base in which the 1,3-disubstituted benzene and formate anion is formed *via* a phenyl carbanion.[41]



Scheme 4

A complete pathway for the base-catalysed rearrangement/fission of substituted benzils is shown in Scheme 4. The rate determining steps for the three cases (i), (ii) and (iii) are k'_2, k'_3 and, probably, k'_6, respectively.

References

1 Part 19. K. Bowden and C. S. Manning, *J. Chem. Res.*, 1994, in the press.
2 S. Selman and J. F. Eastham, *Quart. Rev.*, 1960, **14**, 221.
3 C. J. Collins and J. F. Eastham, *Chemistry of the Carbonyl Group*, ed. S. Patai, Wiley, London, 1966, ch. 15.
4 T. S. Stevens and W. E. Watts, *Selected Molecular Rearrangements*, Van Nostrand Reinhold, London, 1973.
5 M. L. Black, Ph.D. Thesis, University of Tennessee, 1949 (see ref. 2).
6 J. H. Blanksma and W. H. Zaayer, *Rec. Trav. Chim. Pays-Bas.*, 1938, **67**, 883.
7 E. Pfeil, G. Geisler, W. Jacquemin and F. Lomker, *Chem. Ber.*, 1951, **84**, 229.
8 M. L. Black and H. A. Smith, *J. Org. Chem.*, 1952, **17**, 1315.
9 I. Rajyaguru and H. S. Rzepa, *J. Chem. Soc., Perkin Trans. 2*, 1987, 1819.
10 C. G. Screttas, M. Micha-Screttas and C. T. Cazianis, *Tetrahedron Lett.*, 1983, 3287.
11 A. Al-Najjar, K. Bowden and M. V. Horrie, unpublished studies.
12 C. W. N. Cumper and A. P. Thurston, *J. Chem. Soc., Perkin Trans. 2*, 1972, 106.
13 P. Girard and H. B. Kagen, *Tetrahedron Lett.*, 1975, 4513.
14 A. H. Ford-Moore, *J. Chem. Soc.*, 1947, 952.
15 J. C. Irvine and A. M. Moodie, *J. Chem. Soc.*, 1907, 536; F. D. Chattaway and E. A. Coulson, *J. Chem. Soc.*, 1926, 1070; A. A. Boon and H. B. Nisbet, *J. Chem. Soc.*, 1929, 1901.
16 W. Voeghi and P. Langer, *Helv. Chim. Acta*, 1955, **38**, 46; H. L. Haller, P. D. Bartlett, N. L. Drake, M. S. Newman, S. J. Cristol, C. M. Eaker, R. A. Hayes, G. W. Kilmer, B. Magerlein, G. P. Mueller, A. Schneider and W. Wheatley, *J. Am. Chem. Soc.*, 1945, **67**, 1591; R. C. Fuson and A. I. Rachlin, *J. Am. Chem. Soc.*, 1946, **68**, 343; S. Selman and J. F. Eastham, *J. Org. Chem.*, 1965, **30**, 3804.
17 J. G. Cannon, *J. Org. Chem.*, 1960, **25**, 959.
18 K. Bowden and G. R. Taylor, *J. Chem. Soc. B*, 1971, 145; K. Bowden and R. S. Cook, *J. Chem. Soc. B*, 1968, 1529.
19 K. Bowden and A. M. Last, *J. Chem. Soc., Perkin Trans. 2*, 1973, 345.
20 D. H. McDaniel and H. C. Brown, *J. Org. Chem.*, 1958, **23**, 420.
21 M. T. Clark, E. C. Hendley and O. K. Newton, *J. Am. Chem. Soc.*, 1955, **77**, 3280.
22 M. Hojo, M. Utaka and Z. Yoshida, *Tetrahedron Lett.*, 1966, **19**, 25.
23 H. H. Jaffé, *Chem. Rev.*, 1953, **53**, 191.
24 R. Wegscheider, *Z. Phys. Chem.*, 1899, **30**, 593.
25 O. Exner, *Collect. Czech. Chem. Commun.*, 1961, **26**, 1.
26 O. Exner, *Collect. Czech. Chem. Commun.*, 1976, **41**, 1516.
27 J. F. Kirsch, W. Clewell and A. Simon, *J. Org. Chem.*, 1968, **33**, 127.

28 C. D. Johnson, *Chem. Rev.*, 1975, **75**, 755.
29 P. Greenzaid, *J. Org. Chem.*, 1973, **38**, 3164; W. J. Bover and P. Zuman, *J. Chem. Soc., Perkin Trans. 2*, 1973, 786.
30 K. Bowden, *Can. J. Chem.*, 1963, **41**, 2781.
31 J. D. Roberts, footnote as ref. 26 in ref. 21 above.
32 K. Bowden and R. S. Cook, *J. Chem. Soc. B*, 1971, 1765.
33 K. Bowden and R. S. Cook, *J. Chem. Soc. B*, 1971, 1771.
34 R. W. Taft, in *Steric Effects in Organic Chemistry*, ed. M. S. Newman, Wiley, New York, 1956, ch. 13.
35 N. B. Chapman, J. Shorter and J. H. P. Utley, *J. Chem. Soc.*, 1963, 1291.
36 K. Bowden, R. S. Cook and M. J. Price, *J. Chem. Soc. B*, 1971, 1778; K. Bowden and M. J. Price, *J. Chem. Soc. B*, 1971, 1784.
37 D. D. Roberts, *J. Org. Chem.*, 1966, **31**, 4037.
38 K. Bowden and R. S. Cook, *J. Chem. Soc., Perkin Trans. 2*, 1972, 1407; K. Bowden and S. Prasannan, *J. Chem. Soc., Perkin Trans. 2*, 1987, 185 and refs. therein.
39 J. P. Kuebrich and R. L. Schowen, *J. Am. Chem. Soc.*, 1971, **93**, 1220 and refs. therein.
40 T. A. Geissman, *Org. React.*, 1944, **2**, 94.
41 J. F. Bunnett, J. H. Miles and K. H. Nahabedian, *J. Am. Chem. Soc.*, 1961, **83**, 2512.

Paper 3/05399G
Received 8*th September* 1993
Accepted 28*th September* 1993