Meisenheimer-type Adducts from Thiophene Derivatives. Part 7.[1] Interdependence of ^{13}C NMR, Thermodynamic and Kinetic Data

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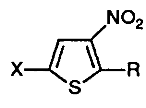
A ^{13}C NMR study has been carried out in $(CD_3)_2SO$ on the thiophene derivatives **5** and **7** and the related Meisenheimer adducts **6** and **8**. The data obtained, and in particular the sums of the chemical-shift changes ($\Sigma\Delta\delta$) at C-3, C-4 and C-5, accompanying the formation of the adducts, are compared with the corresponding data previously obtained for analogous substrates **1** and **3** and adducts **2** and **4**. The four series of $\Sigma\Delta\delta$ values are then examined in the light of the already reported thermodynamic (K_e) and kinetic (k_1) constants for the formation of the adducts. For a given X-substituent, $\log K_e$ values increase linearly as the corresponding absolute $\Sigma\Delta\delta$ values decrease. On these grounds, the smaller π-electron-density rearrangement accompanying the formation of *gem*-dimethoxy adducts emerges as an important factor, contributing to the larger observed K_e values. A further outcome is that, within a single series of adducts, a linear relationship of either $\log K_e$ or $\log k_1$ with $\Sigma\Delta\delta$ holds only when excluding the terms with X = Ac or NO_2. Such findings are interpreted on the basis of the two-component nature of the substituent −R effects: while for the nitro and the acetyl substituents the π-electron acceptor component is prevalent, the stabilizing effect of the other substituents is due mainly to a charge–dipole interaction. The analysis of some literature data for the benzene series fits the above conclusions.

^{13}C NMR studies[2] on 2,4,6-trinitroanisole and 1,1-dimethoxy-2,4,6-trinitrocyclohexadienyl anion have shown an excellent correlation between chemical-shift differences at those carbon atoms retaining the sp^2 configuration and MNDO-SCF-MO charge-density variations on the same carbons in going from the substrate to the adduct. On the other hand, attempts[3,4] to correlate ^{13}C chemical-shift variations of aromatic carbons with the thermodynamic stabilities of other Meisenheimer adducts in the benzene series gave unsatisfactory results. The data obtained in our previous ^{13}C NMR investigations on the adducts **2** and **4**, formed from 2-methoxy-3-nitro-5-X-thiophenes **1a–g**[5] and 2-methoxy-5-nitro-3-X-thiophenes **3b–f**[6] with sodium methoxide in methanol or methanol–$(CD_3)_2SO$ mixtures, suggested[5,6] that such a lack of correlation could arise mainly from the multiform nature of the stabilizing effect of the various X-substituents. Comparison of the kinetic and thermodynamic data obtained for the formation of **2** and **4** with those relevant to adducts **6** and **8**, from 4-nitro-2-X-thiophenes **5c–g**[1] and 2-nitro-4-X-thiophenes **7b–g**,[1] showed stability constants for adducts **6** and **8** much lower than those for the corresponding adducts **2** and **4** respectively. Moreover the stability of the various adducts appeared to be more sensitive to the change of substituent at C-5 (as in adducts **2** and **6**) than at C-3 (as in adducts **4** and **8**).

The herein reported ^{13}C NMR study of compounds **5** and **7** and of their adducts **6** and **8** has been carried out in order to complete the picture of Meisenheimer-type adducts in the thiophene series and to contribute to a better definition of the relationship between the ^{13}C NMR chemical-shift changes accompanying the formation of the same adducts and relevant thermodynamic and kinetic constants.



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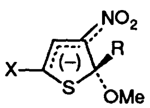
5 R = H



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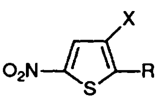
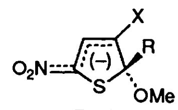
6 R = H



3 R = MeO
7 R = H



4 R = MeO
8 R = H

a X = H
b X = $CONH_2$
c X = CO_2Me
d X = Ac
e X = SO_2Me
f X = CN
g X = NO_2

Experimental

Compounds **5a**,[7] **5b**,[8] **5c**,[9] **5d**,[10] **5e**,[11] **5f**,[12] **5g** (identical with **7g**),[13] **7a**,[7] **7b**,[1] **7c**,[14] **7d**,[15] **7e**[16] and **7f**[17] were pure samples from our laboratories prepared and/or purified according to literature methods.

^{13}C NMR spectra were recorded in $(CD_3)_2SO$ on a Varian XL-200 spectrometer operating at 50 MHz and chemical shifts are given relative to an internal $SiMe_4$ standard.

Results and Discussion

^{13}C NMR chemical shifts of substrates **5** and **7** [0.3 mol dm^{-3} in $(CD_3)_2SO$] are reported in Table 1. For **5a** and **7a** assignments followed those reported[18] for these compounds in $(CD_3)_2CO$ solutions. For the other terms unambiguous assignments could be obtained on the basis of fully coupled spectra and known[18] substituent effects in the thiophene series.

^{13}C NMR chemical shifts of adducts **6** and **8**, formed from the corresponding substrates [0.3 mol dm^{-3} in $(CD_3)_2SO$] upon addition of 1 equiv. of 5 mol dm^{-3} MeONa in MeOH are reported in Table 2. The ^{13}C NMR signals of **6d** and **8d** could not be recorded, possibly because of their short lifetime. For **6a**,[19] **8b** and **8e** coupled spectra of reasonable quality were obtained and signals could be assigned according to their multiplicity. For the other adducts, assignments were made by comparison with **6a**, **8b** and **8e** and on the basis of the relative intensities of the signals.

In Table 3 are reported consistent ^{13}C NMR chemical-shift

Table 1 ^{13}C NMR chemical shifts[a] of substrates **5** and **7** in $(CD_3)_2SO$

		δ				δ_X	
Compound	X	C-2	C-3	C-4	C-5	C-α	Me
5a[b]	H	129.76	148.01	122.15	128.90	—	—
5b	$CONH_2$	133.08	147.10	122.48	141.50	161.32	—
5c	CO_2Me	135.00	147.26	126.90	133.92	160.53	52.89
5d	Ac	135.87	147.52	127.12	144.34	190.81	26.36
5e	SO_2Me	135.17	146.89	127.18	143.42	—	44.43
5f	CN	136.26	146.92	133.44	110.69	112.77	—
5g	NO_2	134.71	145.05	123.16	150.63	—	—
7a	H	135.32	127.72	129.79	151.51	—	—
7b	$CONH_2$	136.82	136.67	128.08	151.14	161.81	—
7c	CO_2Me	140.04	131.54	128.26	151.64	161.03	52.39
7d	Ac	139.46	140.37	127.76	151.59	191.51	27.23
7e	SO_2Me	138.14	140.39	126.91	152.50	—	43.23
7f	CN	144.15	109.30	130.78	152.18	113.60	—
7g[c]	NO_2	134.71	145.05	123.16	150.63	—	—

[a] δ(ppm) with respect to Me_4Si. [b] Data from ref. 19. [c] Identical with **5g**.

Table 2 ^{13}C NMR chemical shifts[a] of adducts **6** and **8**

		δ				δ_X		
Adduct	X	C-2	C-3	C-4	C-5	C-α	Me	MeO
6a[b]	H	86.52	122.97	119.37	114.50	—	—	51.84
6b	$CONH_2$	86.46	124.27	124.03	121.51	165.16	—	51.88
6c	CO_2Me	87.49	123.61	129.76	109.98	163.52	51.16	51.59
6e	SO_2Me	90.10	121.36	129.17	116.46	—	43.51	51.73
6f	CN	88.56	122.44	133.66	84.11	117.87	—	52.03
6g	NO_2	87.70	128.69	129.17	122.84	—	—	52.49
8a	H	92.95	122.85	128.39	120.56	—	—	52.58
8b	$CONH_2$	90.32	125.15	132.31	119.03	165.87	—	52.13
8c	CO_2Me	90.33	116.90	135.48	119.15	164.75	50.74	52.25
8e	SO_2Me	89.50	122.86	135.65	116.75	—	45.04	52.32
8f	CN	90.81	93.28	137.91	117.95	118.79	—	51.57
8g[c]	NO_2	87.70	128.69	129.17	122.84	—	—	52.49

[a,b] Refer to corresponding footnotes of Table 1. [c] Identical with **6g**.

Table 3 Differences between the ^{13}C NMR chemical shifts of Meisenheimer complexes **6** and **8** and those of the corresponding substrates **5** and **7**

		$\Delta\delta$				$\Delta\delta_X$	
	X	C-2	C-3	C-4	C-5	C-α	Me
6a–5a[a]	H	−43.24	−25.04	−2.78	−14.40	—	—
6b–5b	$CONH_2$	−46.62	−22.83	1.55	−19.99	3.84	—
6c–5c	CO_2Me	−47.51	−23.65	2.86	−23.94	2.99	−1.73
6e–5e	SO_2Me	−45.07	−25.53	1.99	−26.96	—	−0.92
6f–5f	CN	−47.70	−24.48	0.22	−26.58	5.10	—
6g–5g	NO_2	−47.01	−16.36	6.01	−27.79	—	—
8a–7a	H	−42.37	−4.87	−1.40	−30.95	—	—
8b–7b	$CONH_2$	−46.50	−11.52	4.23	−32.11	4.06	—
8c–7c	CO_2Me	−49.71	−14.64	7.22	−32.49	3.72	−1.65
8e–7e	SO_2Me	−48.64	−17.53	8.74	−35.75	—	1.81
8f–7f	CN	−53.34	−16.02	7.13	−34.23	5.19	—
8g–7g[b]	NO_2	−47.01	−16.36	6.01	−27.79	—	—

[a] Data from ref. 19. [b] Identical with **6g–5g**.

differences (Δδ) between Meisenheimer adducts **6** and **8** and the corresponding substrates **5** and **7**. While the larger figures obtained for C-2 are mainly a consequence of the hybridization change at this atom, the values exhibited by the other carbons are possible indicators of the π-electron-density changes accompanying the formation of the adducts. Accordingly, the expectation that a significant part of the adduct negative charge is essentially distributed on C-3 and C-5 is supported by the larger additional shielding of the same nuclei in the adducts. For the pairs **5a–6a** and **7a–8a** such additional shielding is much more marked for the nitrated carbon (C-3 and C-5 respectively) than for the unsubstituted one (C-5 and C-3 respectively), but the introduction of electron-withdrawing X-substituents in positions 5 or 3 of the adducts (pairs **5b–6b** to **5g–6g** and **7b–8b**

Table 4 Differences between the ^{13}C NMR chemical shifts of Meisenheimer complexes **2** and **4** and those of the corresponding substrates **1** and **3**[a]

		Δδ				$\Delta\delta_X$	
	X	C-2	C-3	C-4	C-5	C-α	Me
2a–1a	H	−42.2	−11.42	−1.11	−0.31	—	—
2b–1b	$CONH_2$	−44.8	−10.16	2.29	−8.83	3.31	—
2c–1c	CO_2Me	−44.3	−10.47	2.69	−9.31	2.78	−1.53
2d–1d	Ac	−47.6	−9.06	3.22	−8.91	−2.00	−0.78
2e–1e	SO_2Me	−40.8	−12.23	1.35	−11.38	—	−1.51
2f–1f	CN	−42.5	−11.34	−0.34	−12.26	4.75	—
2g–1g	NO_2	−44.9	−9.95	4.91	−13.88	—	—
4b–3b	$CONH_2$	−44.5	−2.8	3.0	−13.4	3.2	—
4c–3c	CO_2Me	−47.2	1.7	6.1	−19.8	3.0	−1.3
4d–3d	Ac	−46.7	1.2	5.3	−19.0	0.7	−3.1
4e–3e	SO_2Me	−45.7	−1.7	7.9	−22.8	—	2.2
4f–3f	CN	−51.4	1.1	5.8	−21.9	5.7	—
4g–3g[b]	NO_2	−44.9	−9.95	4.91	−13.88	—	—

[a] Data from refs. 5 and 6. [b] Identical with **2g–1g**.

Table 5 Sums of the chemical-shift changes (ΣΔδ)[a] at C(3)–C(5) accompanying the formation of adducts **6**, **8**, **2** and **4** in $(CD_3)_2SO$ together with thermodynamic[b] and kinetic[c] constants for their formation at 25 °C in CH_3OH

		6			**8**			**2**			**4**		
Series	X	ΣΔδ	K_e[d]	k_1[d]	ΣΔδ	K_e[d]	k_1[d]	ΣΔδ[e]	K_e[e]	k_1[e]	ΣΔδ[f]	K_e[f]	k_1[f,g]
a	H	−42.2[h]	—[i]	—[i]	−37.2	—[i]	—[i]	−12.8	6	0.0013	—[j]	—[i]	—[i]
b	$CONH_2$	−41.3	—[i]	—[i]	−39.4	0.29	0.010	−16.7	34.2	0.0278	−13.2	2 500	0.257
c	CO_2Me	−44.7	0.17	0.114	−39.9	2.5	0.045	−17.1	109	0.116	−12.0	2 580	0.209
d	Ac	—[j]	0.21	0.146	—[j]	7.5	0.900	−14.8	152	0.301	−12.5	3 300	0.489
e	SO_2Me	−50.5	2.6	0.63	−44.5	213	0.310	−22.3	3 130	0.769	−16.6	17 300	0.573
f	CN	−50.8	6.8[k]	2.38[k]	−43.1	126[k]	0.630[k]	−23.9	7 650	1.30	−15.0	72 700	2.90
g	NO_2	−38.1	850[k]	14.9[k]	−38.1	850[k]	14.9[k]	−18.9	350 000[l]	27.2[l]	−18.9	350 000[l]	27.2[l]

[a] ppm. [b] $dm^3\ mol^{-1}$. [c] $dm^3\ mol^{-1}\ s^{-1}$. [d] Data from ref. 1. [e] Data from ref. 5. [f] Data from ref. 6. [g] At 20 °C. [h] Data from ref. 19. [i] In CH_3OH this adduct could not be detected. [j] In $(CD_3)_2SO$ this adduct could not be detected. [k] Data from ref. 31. [l] Data from ref. 32.

to **7g**–**8g**) causes an increasing negative charge to be localized on the X-substituted ring carbons. Moreover, as evidence that substituent effects on π-electron-density changes at the X-substituted carbons are quite similar in **6** and **8**, a good linear correlation ($r = 0.983$, $n = 6$, intercept $= 7.2 \pm 2.0$), with a slope (0.89 ± 0.08) close to unity, is obtained by plotting the $\Delta\delta_{C\text{-}3}$ values accompanying the formation of **8** *vs.* the corresponding $\Delta\delta_{C\text{-}5}$ values accompanying the formation of **6**. Conversely, an analogous linear correlation does not seem to hold ($r = 0.649$) when comparing the $\Delta\delta_{C\text{-}3}$ and $\Delta\delta_{C\text{-}5}$ values (Table 4) previously measured[5,6] for the formation of **4** and **2**. In our opinion the above results should hinge upon different proximity effects deriving from the substitution of the hydrogen at C-2 for a methoxy group in going from the pair **7**–**8** to **3**–**4**. The possible influence of such proximity effects is further emphasized by the scattering of points observed on attempting to correlate the $\Delta\delta_{C\text{-}3}$ values for series **4** and **8**, contrasting with the linear relationship ($r = 0.959$, $n = 6$, slope 0.89 ± 0.13, intercept $= 11.3 \pm 3.1$) of $\Delta\delta_{C\text{-}5}$ values for series **2** *vs.* **6**.

As a further observation on the data of Table 3, it can be noted that, unlike the C-3 and C-5 ring carbons, the α-carbons of the $CONH_2$, COOMe and CN groups are less shielded in adducts **6b**, **c**, **f** and **8b**, **c**, **f** than in the parent substrates. These last findings, qualitatively analogous to those previously observed[5,6] for the formation of adducts **2b**, **c**, **f** and **4b**, **c**, **f** (see Table 4), appear to confirm our hypothesis that the $CONH_2$, COOMe and CN substituents stabilize the corresponding adducts not so much by conjugation with the ring as by stabilizing a larger negative charge on the X-substituted carbon by an enhancement of their polarity.[5,6]

In Table 5 are reported the overall chemical-shift changes (ΣΔδ) at the sp^2 ring carbons C-3, C-4 and C-5 accompanying the formation of adducts **6** and **8**, relevant thermodynamic and kinetic constants for their formation in methanol at 25 °C and the corresponding data[5,6] for adducts **2** and **4**. Analysis of the data of Table 5 shows that: (i) the previously mentioned greater dependence of the stability constant on the change of the X substituent at C-5 in **2** and **6** than at C-3 in **4** and **8** seems to be somehow related to the ΣΔδ values which show changes for substituents at C-5 larger than those induced by the same substituents at C-3 (*cf.* series **2** *vs.* **4** and **6** *vs.* **8**); (ii) in all the series the adduct-stabilizing effect of the various X-groups also appears to be related to their capacity for favouring negative charge delocalization on the ring carbons; (iii) as for the formation of Meisenheimer complexes in the benzene series,[3,4] no evident correlation between ΣΔδ and either equilibrium or kinetic constants for series **2**, **4**, **6** and **8** appears to hold; (iv) while ΣΔδ values are more negative for series **6** and **8**, the equilibrium constants are greater for the *gem*-dimethoxy adducts **2** and **4**.

If ΣΔδ values actually reflect the overall π-electron-density variations on the sp^2 ring carbons following adduct formation, point (iv) above suggests that, other factors being equal, the lower the electron-density variation the larger the corresponding stability constant. As a matter of fact, a good linear correlation ($r = 0.995$, slope $= 0.11 \pm 0.01$) is obtained by plotting log K_e *vs.* ΣΔδ values for adducts **2h**, **4h**, **6h** and **8h** (X = CN). The analogous correlations for X = SO_2CH_3 or $COOCH_3$ are less satisfactory ($r = 0.941$ and 0.972), possibly because of the previously mentioned proximity effects when bulky groups are bonded at C-3; however, the obtained slope values (0.09 ± 0.02 and 0.11 ± 0.02), being not significantly different from

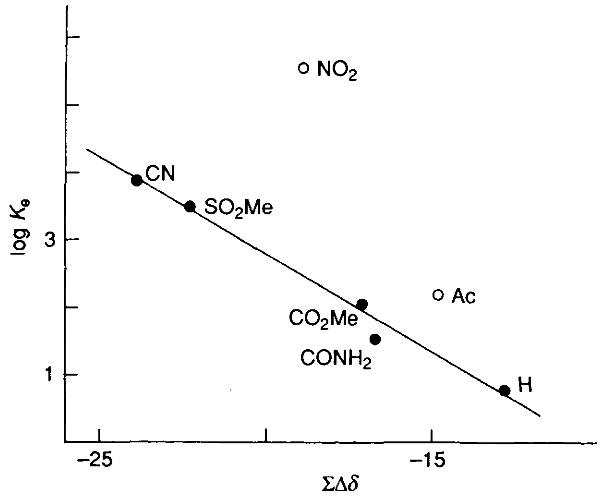
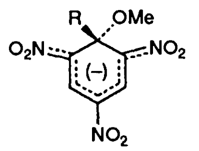


Fig. 1 Plot of log K_e *vs.* the sum of the chemical-shift changes at C(3)–C(5) relevant to the formation of adducts **2**. The points X = Ac and NO_2 are excluded from the least-squares regression analysis (see the text).

that calculated for X = CN, suggest analogous free-energy relationships for the three substituents examined. Even if no significative conclusion in this sense can be drawn for the carbamoyl-, acetyl- and nitro-substituted adducts, because of the insufficient data available, the dependence of the $\Sigma\Delta\delta$ values on log K_e indicates a trend consistent with that shown by the other X substituents. The positive slope values confirm that, substituents being the same, and independent of their positon with respect to C-2, the stability constants increase as the corresponding $\Sigma\Delta\delta$ absolute values decrease. On these grounds the larger stability constants of *gem*-dimethoxy adducts appear to be related to the smaller π-electron rearrangement accompanying adduct formation.[*] A hint that the above-mentioned relation between thermodynamic constants and the extent of $\Sigma\Delta\delta$ variations could be more general comes from the analysis of literature data[3,20] concerning Meisenheimer adducts in the benzene series. Consistently, the formation of **9** from 2,4,6-trinitroanisole in $(CD_3)_2SO$ causes an overall shielding of sp^2 ring carbons ($\Sigma\Delta\delta$ −44.2 ppm) lower than the formation of **10** from 1,3,5-trinitrobenzene ($\Sigma\Delta\delta$ −57.5 ppm),[3] the equilibrium constant in methanol being larger in the former case (K_e = 17 000 and 23.1 dm^3 mol^{-1} respectively).[20]



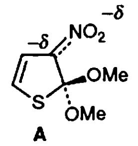
9 R = MeO
10 R = H

With regard to the kinetic constants for the formation of adducts, in going from **2** to **4**, **6** and **8** for a given substituent, no firm dependence of log k_1 on $\Sigma\Delta\delta$ values is observed and this can be possibly ascribed to different extents of bond-formation in the relevant transition states.

The above-mentioned relation between log K_e and $\Sigma\Delta\delta$ values also suggests that within each series of adducts such parameters should not be independent of each other, as a superficial glance at the data would indicate [see point (iii) above]. Actually a deeper analysis of the experimental data relevant to series **2** (for which a larger set of parameters is available) reveals an excellent linear correlation [eqn. (1) and

$$\log K_e = -0.29(\pm 0.02)\Sigma\Delta\delta - 3.03(\pm 0.39) \quad (n = 5, r = 0.993) \qquad (1)$$

Fig. 1] provided that the terms X = Ac and NO_2 are excluded. The negative slope value of eqn. (1) and the data of Table 5 confirm that, within a single series of adducts and for the five substituents considered, the equilibrium constants increase as both the additional shielding of sp^2 ring carbons accompanying the formation of adducts and the electron-withdrawing power of X increase. Therefore such K_e variations appear to depend mainly on the different ability of the various substituents to favour delocalization of the increased electron density among the sp^2 ring carbons of the adducts. Such findings, including the correlation expressed in eqn. (1) and the scattering of the points corresponding to X = Ac and NO_2 can be rationalized by considering the multiform nature of the substituent stabilizing effect. In previous ^{13}C NMR studies on the real nature of the resonance (−*R*) effect of some electron-withdrawing groups in aromatic derivatives (acetophenones, benzonitriles and methyl benzoates,[21] benzamides[22] and analogous 2-thienyl derivatives[8]) we concluded that the conjugative component of the −*R* effect, dominant in the case of the acetyl group, is of negligible importance for the cyano, methoxycarbonyl and carbamoyl groups. In the last three cases the main component of the resonance effect appears to be the π-polarization of the group itself, induced by the charge density on the X-substituted carbon. On these grounds, as the π-electron-acceptor effect of the methylsulphonyl group can be neglected,[11,23] while that of the nitro group can be important at least in the adducts,[5] the present results find a straightforward rationale: while in **2a** the negative charge is essentially distributed on C-3 and the nitro group (structure **A**), the introduction at C-5 of a substituent such as CN, $CONH_2$, COOMe or SO_2Me causes an increase in both the adduct stability and the absolute $\Sigma\Delta\delta$ value through a delocalization of the negative charge onto C-5 (structure **B**). The negative charge on C-5, which increases with the electron-withdrawing power of X, is related to the substituent ability to stabilize it by a charge–dipole interaction[24] as, *e.g.* for X = CN, in the limit resonance structure **C**. Consistent with this, the marked contribution of charge-induced polarization to the stabilization of adducts **2b**, **2c** and **2f** is evidenced by the increased shielding of C-5, and by the concomitant significant deshielding of the C-α of the X substituents, accompanying the formation of the adducts. Conversely, in the cases of **2d** and **2g** the X-substituent appears to stabilize the corresponding adduct by delocalizing part of the negative charge through a true conjugative interaction. This is in agreement with the observed increased shielding of the C-α of the acetyl group (see Table 3) and with the finding that, for both **2d** and **2g**, the $\Sigma\Delta\delta$ values are less negative than expected (Fig. 1): in this line, the differences observed between the $\Sigma\Delta\delta$ values calculated by eqn. (1) and the experimental ones can give a rough estimate of the fractional charge on the X substituent.



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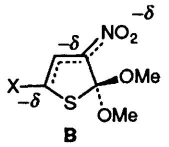
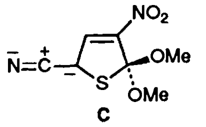


B



C

Another significant result has been obtained by plotting

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[*] As expected, on going from substrates **5** to **1** and from **7** to **3**, the introduction of a methoxy group at C-2 causes an overall shielding of the other ring carbons, mainly determined by the marked shielding (15–20 ppm) of the conjugated carbons C-3 and C-5.

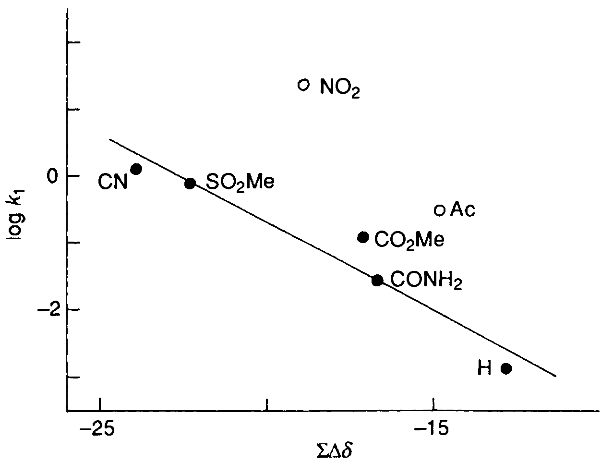


Fig. 2 Plot of log k_1 *vs.* the sum of the chemical-shift changes at C(3)–C(5) relevant to the formation of adducts **2**. The points X = Ac and NO_2 are excluded from the least-squares regression analysis (see text).

Table 6 Sums of the chemical-shift changes (ΣΔδ)[a] at C(2)–C(6) accompanying the formation of adducts **11** in $(CD_3)_2SO$ together with thermodynamic[b] and kinetic[c] constants for their formation at 20 °C in CH_3OH

X	ΣΔδ[d]	K_e[e]	k_1[e]
CF_3	−57.6	5	0.4
COPh	−48.3	45	
SO_2Me	−58.5	101	1.75
CN	−60.9	168	2.82
NO_2	−45.9	19 500	11.8
SO_2CF_3	−65.3	1.2 × 10^6	141

[a] ppm. [b] $dm^3\ mol^{-1}$. [c] $dm^3\ mol^{-1}\ s^{-1}$. [d] Data from ref. 4. [e] Data from ref. 25.

log k_1 *vs.* the ΣΔδ values for adducts **2** (Fig. 2). Provided that adducts with substituents of similar stabilizing effect are considered (and therefore excluding the terms **2d** and **2g** for which, in this case also, ΣΔδ values are less negative than expected) a reasonable linear correlation is observed [eqn. (2)].

$$\log k_1 = -0.26(\pm 0.04)\Sigma\Delta\delta - 5.89(\pm 0.79) \qquad (n = 5, r = 0.964) \qquad (2)$$

This result indicates that the rates of adduct formation increase with the possibility of charge-delocalization on the sp^2 ring carbons. Interestingly, the calculated slope value, being very similar to that of eqn. (1), suggests a marked extent of bond-formation in the relevant transition states.

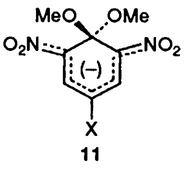
An analogous rationale can be applied to the electronic effect of X substituents on the dependence of K_e and k_1 on the ΣΔδ values for adducts **4**, **6** and **8**, even if the more restricted set of experimental data for each of these series and the possible involvement of proximity effects for **4** and **8** prevents a more detailed analysis.

Further support for the interpretation given comes from the comparison with literature values of ΣΔδ,[4] K_e[4] and k_1[25] for adducts **11**, structurally similar to **2** (Table 6). On plotting log K_e or log k_1 values *vs.* the corresponding ΣΔδ, satisfactory linear correlations [eqns (3) and (4)] are obtained when

$$\log K_e = -0.65(\pm 0.12)\Sigma\Delta\delta - 36.75(\pm 7.14) \qquad (n = 4, r = 0.969) \qquad (3)$$

$$\log k_1 = -0.31(\pm 0.05)\Sigma\Delta\delta - 18.08(\pm 2.85) \qquad (n = 4, r = 0.978) \qquad (4)$$

excluding the terms with X = NO_2 and COPh, an outcome which can be given an interpretation analogous to that of **2d** and **2g**. The larger difference between the slope values of eqns. (3) and (4) than between those of eqns. (1) and (2) may be indicative of a different extent of bond-forming in the relevant transition states.



11

Conclusions

The present study reveals unprecedented close relationships between ^{13}C NMR chemical-shift variations accompanying the formation of Meisenheimer adducts and the relevant thermodynamic and/or kinetic constants. Such relationships hold only if substituents of similar stabilizing effect (π-polarization) are considered, in agreement with the two-component nature of the −*R* substituent effect.

The results obtained, moreover, allow us to obtain a clearer picture of the factors contributing to the observed differences in the stability constants of *gem*-dimethoxy and non-*gem*-Meisenheimer adducts. Such factors are commonly[26–28] considered to be: (i) the steric interaction between the methoxy group and an *ortho* substituent, which destabilizes the substrate with respect to the adduct; (ii) the conjugation of the methoxy group with the aromatic system in the substrate, which would disfavour the formation of *gem*-dimethoxy adducts; (iii) the electron-withdrawing effect of the methoxy group favouring attack of the methoxide ion by lowering the electron density at the reaction centre; (iv) the F-strain, which is larger in *gem*-dimethoxy adduct formation; (v) the stabilizing effect of geminal substitution by oxygen atoms at the same carbon atom (double bond–no bond resonance).

In our opinion the results of the present ^{13}C NMR study point out the importance of a factor which has been previously suggested[29] but not considered further, namely the extent of electronic reorganization on going from the starting materials to the transition states or to the σ-adducts. We think that, in determining the higher stability constants of *gem*-dimethoxy with respect to non-*gem*-adducts, the conjugation between the methoxy group and the aromatic moiety in the starting compounds is a factor of relevance. According to point (ii) above, such conjugation would increase the activation energy on going to the transition state and to the σ-adduct.[27] On the contrary, we believe that this effect induces in the substrate an electronic distribution which decreases the energy barrier for adduct formation by lowering the extent of electron rearrangement necessary. Such an effect could also decrease the energy content of the adduct with respect to the parent compound. The relative stability of the former is further enhanced by the *gem*-dimethoxy substitution effect, which lowers the rate of the reverse reaction.

As a final comment, it is interesting to note that this effect could also contribute to favour the formation of five-membered-ring *gem*-dimethoxy adducts with respect to six-membered-ring analogues (compare, for example, the K_e values of adducts **2** and **11** of Tables 5 and 6). As a matter of fact, because of the different geometries of the aromatic rings, in *ortho*-substituted nitrothiophenes **1** the steric inhibition to coplanarity of the nitro group is much lower than in 2,6-dinitro-4-X-anisoles.[30] Consequently, the higher through-conjugation between the methoxy group and the *ortho*-nitro group in **1**, by lowering the demand of electron reorganization, may help to decrease the activation energy for the formation of adducts **2**.

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