Heterocyclic Meisenheimer Complexes: Kinetic and Equilibrium Data for Methoxide Ion Attack on Various Disubstituted 2,4-Y,Z-Thiophenes and -Selenophenes in Methanol

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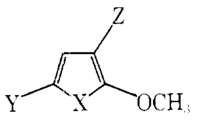
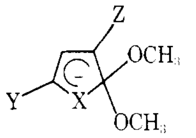
The rate and equilibrium constants for the formation and decomposition of the monomethoxyl Meisenheimer complexes **6a–f** derived from 2,4-dinitro-, 2-nitro-4-cyano-, and 2-cyano-4-nitrothiophenes (**5a, 5b, 5c**) and -selenophenes (**5d, 5e, 5f**) have been determined at different temperatures in methanol. The stability of the selenophenic adducts is two orders of magnitude greater than that of the thiophenic analogues, essentially because of their much slower decomposition. In each series, the relative order of stabilities of the complexes is 2,4-dinitro > 2-nitro-4-cyano > 2-cyano-4-nitro, showing that, as in the benzene series, the replacement of a nitro group by a cyano group in the para position of the sp^3 carbon has a much more important effect on the stability of the complex than has a similar replacement in the ortho position. In contrast, quite different trends are unexpectedly observed when comparing the rates of formation and decomposition (k_1, k_{-1}) as well as the kinetic and thermodynamic parameters ($\Delta H°$, $\Delta S°$, $\Delta H^{\ddagger}_1$, $\Delta H^{\ddagger}_{-1}$, $\Delta S^{\ddagger}_1$, $\Delta S^{\ddagger}_{-1}$) associated with the reactions. It thus appears that strong differences exist between the reactions of methoxide ion with 2,4-dinitro- as well as 2-cyano-4-nitrothiophenes and -selenophenes to give **6a, 6c, 6d,** and **6f** and the reactions of methoxide ion with 2-nitro-4-cyanothiophene and -selenophene to give **6b** and **6e**. These differences show that, in the thiophene and selenophene series, an ortho-like nitro group may have more influence on the course of a nucleophilic substitution reaction than a para-like nitro group.

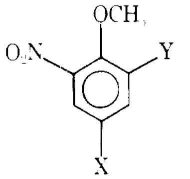
Dinitro- and nitro-activated methoxythiophenes and -selenophenes of the general structure **1a** have been shown to react with methoxide ion in methanolic solution to give the very stable *gem*-dimethoxyl Meisenheimer-type complexes **2**.[2,3] The pK_a values for the formation of the dinitro complexes **2a** and **2d** are 11.36 and 10.07, respectively, at 20 °C.[3b] In comparison, the pK_a values for the formation of the complexes **4a** and **4b**, which are the most stable benzene adducts known to date, are 10.90 and 12.58, respectively.[4,5] As revealed by NMR spectroscopy in Me_2SO-d_6 and methanol, thiophene and selenophene derivatives not bearing a methoxyl group (general structure **5**) also react with methoxide ion to give the monomethoxyl complexes **6**.[2c,6,7] In this paper, we report a comprehensive kinetic and thermodynamic analysis of the formation and decomposition of several adducts of this type in methanol, namely, the adducts **6a–f** derived from the parent 2,4-dinitro-, 2-nitro-4-cyano-, and 2-cyano-4-nitrothiophenes (**5a, 5b, 5c**) and -selenophenes (**5d, 5e, 5f**). Whereas they confirm some of the conclusions reached in comparing the *gem*-dimethoxyl adducts **2a** and **2d**, our results also reveal some new interesting features. In particular, we observe some striking differences between the kinetic and thermodynamic parameters for the formation and decomposition of the adducts **6b** and **6e** on the one hand and those for the formation and decomposition of the adducts **6a, 6c, 6d,** and **6f** on the other hand. These differences show that, in the thiophene and selenophene series, the effect of an ortho-like nitro group may predominate over that of a para-like nitro group.



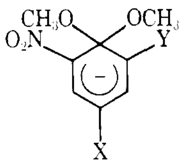
1a, X = S; Y = Z = NO_2
b, X = S; Y = NO_2; Z = CN
c, X = S; Y = CN; Z = NO_2
d, X = Se; Y = Z = NO_2



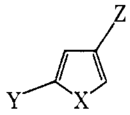
2a
b
c
d



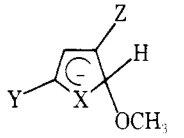
3a, X = SO_2CF_3; Y = NO_2
b, X = Y = NO_2
c, X = NO_2; Y = CN
d, X = CN; Y = NO_2



4a
b
c
d



5a, X = S; Y = Z = NO_2
b, X = S; Y = NO_2; Z = CN
c, X = S; Y = CN; Z = NO_2
d, X = Se; Y = Z = NO_2
e, X = Se; Y = NO_2; Z = CN
f, X = Se; Y = CN; Z = NO_2



6a
b
c
d
e
f

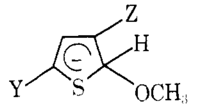
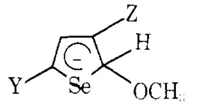
Indeed, at the same time as our preliminary communication,[6a] a report by Illuminati et al. appeared describing a similar study of the thiophene derivatives **5a** and **5b**.[2c,7b] Although we are in agreement with their results, our study provides additional data regarding the temperature dependence of the reactions. We also report the first observation of the adduct **6c** derived from 2-cyano-4-nitrothiophene (**5c**) in methanol.

Results

The kinetics of the formation and decomposition of adducts **6** were studied spectrophotometrically by using the stopped-flow method as well as conventional methods. In all runs, the concentrations of base or buffer components were in large excess over the substrate concentration, assuring pseudo-first-order kinetics throughout.

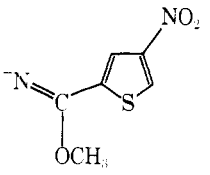
2,4-Dinitro-, 2-Nitro-4-cyano-, and 2-Cyano-4-nitrothiophenes (5a, 5b, 5c). Addition of dilute potassium methoxide to a colorless solution of **5a** and **5b** results in the immediate formation of the adducts **6a** [λ_{max} 530 nm (ϵ 16 000 M^{-1} cm^{-1})] and **6b** [λ_{max} 400 nm (ϵ 14 000 M^{-1} cm^{-1})]. In contrast, as noted and discussed by Illuminati et al.,[7b] methoxide ion attacks the CN group of **5c** *in methanol to give* methyl 4-nitro-2-thiophenecarboximidate (**7**) (λ_{max} 245 nm). At methoxide ion concentrations greater than 5×10^{-2} M, the

Table I. Rate and Equilibrium Constants for the Formation and Decomposition of Thiophenic and Selenophenic Meisenheimer Complexes 6a–f in Methanol at Different Temperatures

							
	t, °C	**6a** Y = NO_2 Z = NO_2	**6b** Y = NO_2 Z = CN	**6c** Y = CN Z = NO_2	**6d** Y = NO_2 Z = NO_2	**6e** Y = NO_2 Z = CN	**6f** Y = CN Z = NO_2
k_1, $M^{-1}\,s^{-1}$	10	4.75		0.54			0.59
	20	10.3	0.415	1.48	18.2	0.83	1.52
	30	21.3	0.94	3.72	47^a	2.85^a	4.08^a
	40		2.16		91.5	6.18^b	9.78^b
k_{-1}, s^{-1}	10	6.5×10^{-3}		0.113			$8 \times 10^{-4\,c}$
	20	1.25×10^{-2}	3×10^{-3}	0.24	2.85×10^{-4}	4.7×10^{-5}	3.02×10^{-3}
	30	2.50×10^{-2}	7.25×10^{-3}	0.535	8.05×10^{-4}	1.86×10^{-4}	9.49×10^{-3}
	40		2×10^{-2}		2.37×10^{-3}	6.1×10^{-4}	2.7×10^{-2}
K_1, M^{-1}	10	730		4.80			730
	20	825	138	6.15	6.4×10^4	1.77×10^4	505
	30	851	130	7	5.85×10^4	1.53×10^4	430
	40		108		3.86×10^4	1.01×10^4	360

[a] t = 31 °C. [b] t = 41 °C. [c] t = 9 °C.

oscilloscope pictures revealed, however, that the appearance of **7** is preceded by the much faster formation of the yellow-colored adduct **6c**. The visible spectrum taken in the stopped-flow apparatus (not shown) has a maximum at 400 nm (ϵ 13 500 $M^{-1}\,cm^{-1}$) and is very similar to the spectrum of **6c** in situ generated in Me_2SO and previously identified by NMR.[6a]



7

Equation 1 describes the formation of the three adducts from the respective parent thiophenes, and the observed first-order rate constant k_{obsd} for the approach to equilibrium is given by eq 2. Plots of k_{obsd} against the methoxide ion concentration (not shown) are linear at the various temperatures studied. The k_1 and k_{-1} values obtained from slopes and intercepts are given in Table I, together with the values of the equilibrium constant K_1 calculated from $K_1 = k_1/k_{-1}$.

$$\mathbf{5a\ (b,c)} + CH_3O^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathbf{6a\ (b,c)} \tag{1}$$

$$k_{obsd} = k_{-1} + k_1[CH_3O^-] \tag{2}$$

2,4-Dinitro-, 2-Nitro-4-cyano-, and 2-Cyano-4-nitroselenophenes (5d, 5e, 5f). The adducts **6d, 6e,** and **6f** with visible spectra showing a maximum at 530 nm (ϵ 16 000 $M^{-1}\,cm^{-1}$), 400 (15 000), and 400 (14 000), respectively, are rapidly formed when methoxide ions react with the parent selenophenes **5d, 5e,** and **5f** in methanol. We note that the behavior of **5f** contrasts strongly with that of its thiophene analogue **5c** since no competing methoxide ion attack on the CN group of **5f** could be detected. Due to the relatively high stability of the three adducts, some of our experiments were performed at relatively low pH, which made it necessary to work in buffered solutions. The buffered solutions were prepared from the same AH-type acids as those used in the study of the methoxyl derivatives **1a** and **1d**.[3b] The same ionic strength of 0.01 M was also chosen, allowing the calculation of the mean activity coefficient $\gamma_\pm$ by using the simplified Debye–Hückel type equation $\log \gamma_\pm = -Bz^2\sqrt{\mu}$ with B = 1.8[8] and therefore the calculation of the hydrogen ion concentration [H^+] of the solutions from the measured activity a_{H^+} of the solvated proton: $[H^+] = a_{H^+}/\gamma_\pm = 10^{-pH}/\gamma_\pm$.

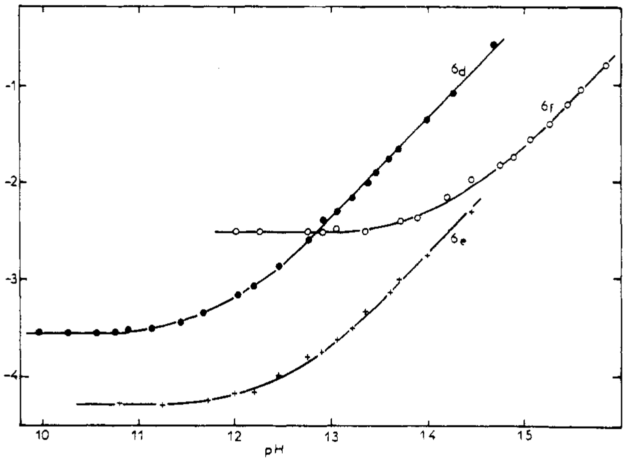
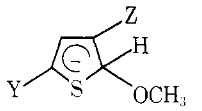


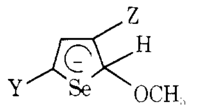
Figure 1. pH dependence of k_{obsd} (s^{-1}) for the formation and decomposition of the selenophenic adducts **6d, 6e,** and **6f** in methanol: 20 °C, μ = 0.01 M.

The pH dependence of the observed first-order rate constant k_{obsd} for the combined formation and decomposition of **6d, 6e,** and **6f** is shown in Figure 1 (t = 20 °C). Note that the pH values > 13.50 correspond to dilute potassium methoxide solutions (5×10^{-4}–10^{-2} M). In the pH range 10 to 13.50, variation of buffer concentration at constant pH did not change the value of k_{obsd} within experimental error, indicating the absence of buffer catalysis, at least at the low concentrations used. The pH–rate profiles of Figure 1 are consistent with a formation of the adducts according to eq 3, and the expression for k_{obsd} is given by eq 4, where K_s is the autoprotolysis constant of methanol (pK_s = 16.86 at 20 °C). The k_{-1} and k_1 values were thus easily determined from the plateaus ($\log k_{obsd} = \log k_{-1}$) and the straight lines of slope +1 ($\log k_{obsd} = \log k_1 - pK_s + pH - \log \gamma_\pm$) observed at low and high pH, respectively, in Figure 1. The rate coefficients for the various complexes are collected in Table I, which also gives the values of k_1 and k_{-1} determined at 10, 30, and 40 °C.

$$\mathbf{5d\ (e,f)} + CH_3O^- \underset{k_{-1}}{\overset{k_1}{\rightleftharpoons}} \mathbf{6d\ (e,f)} \tag{3}$$

Table II. Kinetic and Thermodynamic Parameters for the Formation and Decomposition of Thiophenic and Selenophenic Meisenheimer Complexes in Methanol at 25 °C





	6a Y = NO_2 Z = NO_2	**6b** Y = NO_2 Z = CN	**6c** Y = CN Z = NO_2	**6d** Y = NO_2 Z = NO_2	**6e** Y = NO_2 Z = CN	**6f** Y = CN Z = NO_2
k_1, $M^{-1}\ s^{-1}$	14.9–15[a]	0.63–0.78[a]	2.38	27.7	1.37	2.62
k_{-1}, s^{-1}	1.75×10^{-2} 1.87×10^{-2} [a]	5×10^{-3} 5.2×10^{-3} [a]	0.35	4.8×10^{-4}	9.55×10^{-5}	5.37×10^{-3}
K_1, M^{-1}	850–800[a]	126–150[a]	6.8	5.78×10^4	1.43×10^4	490
$\Delta H^{\ddagger}{}_1$, kcal mol^{-1}	12.40 ± 0.6	14.05 ± 0.6	15.85 ± 0.8	14.05 ± 0.4	16.85 ± 0.6	15.85 ± 0.6
$\Delta S^{\ddagger}{}_1$, cal deg^{-1} mol^{-1}	−11.55 ± 2.3	−12.25 ± 2.3	−3.50 ± 2.7	−4.70 ± 1.4	−0.80 ± 2.3	−3.80 ± 2.3
$\Delta H^{\ddagger}{}_{-1}$, kcal mol^{-1}	11.10 ± 0.6	16.95 ± 0.6	12.75 ± 0.8	18.95 ± 0.6	22.9 ± 0.6	19.4 ± 0.4
$\Delta S^{\ddagger}{}_{-1}$, cal deg^{-1} mol^{-1}	−29.20 ± 2.3	−12.15 ± 2.3	−17.65 ± 2.7	−10 ± 2.3	0.15 ± 2.3	−3.9 ± 1.4
$\Delta H°$, kcal mol^{-1}	1.3 ± 1.2	−2.90 ± 1.2	3.10 ± 1.6	−4.90 ± 1	−6.05 ± 1.2	−3.55 ± 1
$\Delta S°$, cal deg^{-1} mol^{-1}	17.65 ± 4.6	−0.1 ± 4.6	14.15 ± 5.4	5.3 ± 3.7	−1 ± 4.6	0 ± 3.7
$\Delta G°$, kcal mol^{-1}	−3.95 ± 2.5	−2.90 ± 2.5	−1.10 ± 3.20	−6.5 ± 2.1	−5.75 ± 2.6	−3.55 ± 2.1

[a] Reference 2c.

$$k_{obsd} = k_{-1} + k_1[CH_3O^-] = k_{-1} + k_1K_s/a_{H^+}\gamma_{\pm} \quad (4)$$

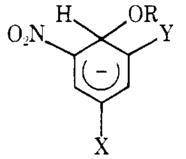
From the temperature dependence of k_1 and k_{-1}, activation and thermodynamic parameters for the formation and decomposition of adducts **6a–f** were calculated. They are summarized in Table II.

Discussion

Thiophene and Selenophene Complex Formation. The interaction of methoxide ion with 2,4-Y,Z-disubstituted thiophenes **5a**, **5b**, and **5c** resembles qualitatively that with the selenophene analogues **6a**, **6b**, and **6c**. Thus, both complexes **6a** and **6d** have similar UV–vis absorption spectra, and the same is true for complexes **6b**, **6e** or **6c**, **6f**. Interesting differences exist, however, between the rate and equilibrium constants for formation and decomposition of complexes in both series. Table II reveals that the thermodynamic stability of the selenophene adducts is about two orders of magnitude greater than that of the similarly substituted thiophene adducts; the ratios $K_1{}^{6d}/K_1{}^{6a}$, $K_1{}^{6e}/K_1{}^{6b}$, and $K_1{}^{6f}/K_1{}^{6c}$ are equal to 68, 113, and 72, respectively. We note that these stability differences are appreciably greater than that previously found between the *gem*-dimethoxyl complexes **2a** and **2d** resulting from the reaction of methoxide ion with 2,4-dinitro-5-methoxythiophene (**1a**) and -selenophene (**1d**); the ratio $K_2{}^{2d}/K_1{}^{2a}$ was found to be equal to about 20.[3b]

The higher stability of **6d**, **6e**, and **6f** compared with that of **6a**, **6b**, and **6c**, respectively, derives mainly from a large decrease in the rates of decomposition; the ratios $k_{-1}{}^{6a}/k_{-1}{}^{6d}$, $k_{-1}{}^{6b}/k_{-1}{}^{6e}$, and $k_{-1}{}^{6c}/k_{-1}{}^{6f}$ are equal to 36, 52, and 65, respectively. Here, the much higher values of the enthalpies of activation $\Delta H^{\ddagger}{}_{-1}$ for **6d**, **6e**, and **6f** relative to those for **6a**, **6b**, and **6c** must be noted even though they are largely compensated by corresponding higher entropies of activation: for example, $\Delta H^{\ddagger}{}_{-1}{}^{6d} - \Delta H^{\ddagger}{}_{-1}{}^{6a} = 7.85$ kcal mol^{-1}; $\Delta S^{\ddagger}{}_{-1}{}^{6d} - \Delta S^{\ddagger}{}_{-1}{}^{6a} = 19.20$ eu. On the other hand, the ratios $k_1{}^{6d}/k_1{}^{6a}$, $k_1{}^{6e}/k_1{}^{6b}$, and $k_1{}^{6f}/k_1{}^{6c}$ for methoxide ion attack are small and equal to 1.8, 2.1, and 1.1, respectively. Nevertheless, they confirm the somewhat lower reactivity of thiophene substrates toward nucleophilic reagents.[9,10] A noteworthy feature is also that the enthalpies of activation for the formation of **6a** and **6b** are appreciably lower than those for the formation of **6d** and **6e**: $\Delta H^{\ddagger}{}_1{}^{6d} - \Delta H^{\ddagger}{}_1{}^{6a} = 1.65$ kcal mol^{-1}; $\Delta H^{\ddagger}{}_1{}^{6e} - \Delta H^{\ddagger}{}_1{}^{6b} = 2.8$ kcal mol^{-1}. As a consequence, **6d** and **6e** are formed faster only because the entropies of activation for their formation are significantly higher than those associated with the formation of **6a** and **6b**. A similar predominance of the entropy changes was found to be responsible for the faster formation of **2d** compared with that of **2a**. This may indicate that the transition states for the formation of the selenophene adducts are less solvated than those for the formation of the thiophene analogues.

Because of their high stability, the dinitrothiophene adduct **6a** and the three selenophenes adducts **6d**, **6e**, and **6f** could be isolated as stable potassium crystalline salts by adding an equimolar amount of methanolic potassium methoxide to solutions of the parent molecules in methanol and eliminating the solvent. Good elemental analyses have been obtained for these solids, which are very explosive and also have NMR spectra identical with those previously recorded by studying the reactions in situ.[6a] The isolation of these monomethoxyl adducts is of interest in that it emphasizes their much higher stability compared with that of the monomethoxylbenzene adducts. Thus, **6a** and **6d** are 37- and 2500-fold more stable than the monomethoxyl adduct **8a** derived from the reaction of methoxide ion with trinitrobenzene (see data for **8a** in Table III). As previously mentioned, these stability differences are certainly the result of the geometrical differences between five- and six-membered rings.[2c]

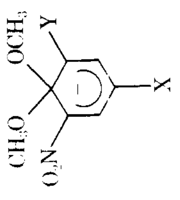
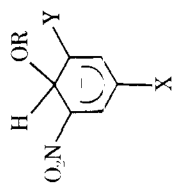
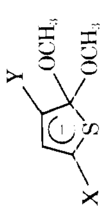


8a, X = NO_2; Y = NO_2; R = CH_3
b, X = NO_2; Y = CN; R = CH_3
c, X = CN; Y = NO_2; R = CH_3
d, X = NO_2; Y = NO_2; R = H
e, X = NO_2; Y = CN; R = H
f, X = CN; Y = NO_2; R = H

Because of the stabilizing influence of the two methoxyl groups at the sp^3 carbon, the thiophene and selenophene *gem*-dimethoxyl adducts are much more stable than their monomethoxyl analogues; for example, the ratios $K_1{}^{2d}/K_1{}^{6d}$ and $K_1{}^{2a}/K_1{}^{6a}$ for the dinitro derivatives are equal to about 100 and 400, respectively. This situation, which compares well with the one observed in the benzene series, has been extensively discussed by Illuminati et al.[2c]

Influence of the Nitro and Cyano Groups. The order of stability of the complexes is the same in the two series: 2,4-

Table III. Influence of Ortho and Para Nitro and Cyano Groups on the Rate and Equilibrium Constants for the Formation and Decomposition of Meisenheimer Complexes

												
	4b[a] X = NO_2 Y = NO_2	**4c**[a] X = NO_2 Y = CN	**4d**[a] X = CN Y = NO_2	**8a**[b] X = NO_2 Y = NO_2 R = CH_3	**8b**[c] X = NO_2 Y = CN R = CH_3	**8c**[c] X = CN Y = NO_2 R = CH_3	**8d**[d] X = NO_2 Y = NO_2 R = H	**8e**[e] X = NO_2 Y = CN R = H	**8f**[e] X = CN Y = NO_2 R = H	**2a** X = NO_2 Y = NO_2	**2b**[h] X = NO_2 Y = CN	**2c**[h] X = CN Y = NO_2
k_1, M^{-1} s^{-1}	17.3	18.8	6.1	7050	19 300	40 000	547	112	272	40.7,[f] 28.2[g]	4.85	2.14
k_{-1}, s^{-1}	1.04×10^{-3}	7.20×10^{-3}	2.2×10^{-2}	305	4.5	118	0.145	0.3	7.70	7.8×10^{-5} [g]	1.95×10^{-4}	1.4×10^{-3}
K_1, M^{-1}	1.7×10^4	2600	280	23.1	4300	340	3770	372	35	3.62×10^5 [g]	2.5×10^4	1.530

[a] Reference 5a; in methanol at 25 °C. [b] Reference 5b; in methanol at 25 °C. [c] Reference 12; in 50% Me_2SO–50% methanol at 20 °C. [d] Reference 21; in 50% Me_2SO–50% water at 20 °C. [e] Reference 12; in 50% Me_2SO–50% water at 20 °C. [f] Reference 3b; in methanol at 25 °C. [g] Reference 3b; in methanol at 20 °C. [h] Reference 2c; in methanol at 25 °C.

dinitro > 2-nitro-4-cyano > 2-cyano-4-nitro. The ratios K_1^{6a}/K_1^{6b} and K_1^{6a}/K_1^{6c} are equal to 6.7 and 125, respectively, whereas the ratios K_1^{6d}/K_1^{6e} and K_1^{6d}/K_1^{6f} are equal to 4 and 118, respectively. Thus, as found for the *gem*-dimethoxylthiophene adducts[3b] and in agreement with what was always found in the benzene series for the *gem*-dimethoxyl[11] as well as the monomethoxyl or hydroxyl adducts,[12] the replacement of a nitro group by a cyano group in the para-like 2 position of the sp^3 carbon has a much more important effect on the stability of the adducts **6** than a similar replacement in the ortho-like 4 position. This suggests that, as in the benzene series,[13-15] the negative charge in the thiophene and selenophene adducts is predominantly delocalized through the para-like substituent, particularly when this substituent is a nitro group.

Despite this similarity with previous results in the field, a careful examination of kinetic and thermodynamic data associated with the formation and decomposition of adducts **6** reveals some new features. First, we note that the rate of methoxide ion attack on compounds **5** is much more affected by the substitution of a nitro group by a cyano group in the ortho than in the para position to the reaction center; both the ratios k_1^{6a}/k_1^{6b} and k_1^{6d}/k_1^{6e} are of about 20, whereas the ratios k_1^{6a}/k_1^{6c} and k_1^{6d}/k_1^{6f} are equal to 6.2 and 10, respectively. In other words, the ortho-like 4-NO_2 group has a greater effect on the reactivity of the 5 position of compounds **5** than the para-like 2-nitro group. Such a result evidently contrasts with what was generally observed in nucleophilic aromatic substitution reactions involving benzene substrates bearing ortho and para nitro and/or cyano groups,[16,17] and in particular with the data obtained for methoxide ion attack on anisoles of general formula **3**[5a,11b,18] to give the 1,1-complexes **4**. This also contrasts with what was observed for the methoxide ion attack on 2,4-disubstituted-5-methoxylthiophenes **1a**, **1b**, and **1c**.[2c] However, we note that our results are in agreement with the recent work of Spinelli et al. on the piperidino debromination of 2,4-disubstituted-5-bromothiophenes in methanol.[19,20] In fact, these authors report that this reaction occurs faster with substituted 2-X-4-nitro-5-bromo derivatives[20] than with the corresponding substituted 2-NO_2-4-X-5-bromo derivatives:[19] for example, the rate constants for the piperidino debromination of 2,4-dinitro-, 2-nitro-4-cyano-, and 2-cyano-4-nitro-5-bromothiophenes are equal to 1.99, 3.78 × 10^{-2}, and 0.127 M^{-1} s^{-1}, respectively. Our results are also in agreement with the recent observation that methoxide and hydroxide ion attacks occur more rapidly at the carbon 4 than at the carbon 2 of 3,5-dinitro-1-cyanobenzene[12] (compare the rate constants for formation of complexes **8b**, **8c** and **8e**, **8f** in Table III).[25] It thus appears that the ortho substituents may be, in some cases, more efficient than para substituents in activating nucleophilic aromatic substitution reactions. The absence of unfavorable steric effects in the parent substrates is evidently of major importance for the observation of this behavior. The fact that the double-bond character is weaker between the β than the α positions of thiophene and selenophene[19,20] also favors in the present case the transmission of the effect of the ortho-like 4 substituent to the 5 position.

The rate constants for the decomposition of the adducts **6b** and **6e** are lower than those for the decomposition of the dinitro analogues **6a** and **6d**; the ratios k_{-1}^{6a}/k_{-1}^{6b} and k_{-1}^{6d}/k_{-1}^{6e} are equal to 3.5 and 5, respectively. This is an unexpected result since it has never been observed previously that a nitrocyano adduct decomposes less rapidly than a dinitro adduct (see data of Table III for comparison). Table II reveals, indeed, considerable differences in both the enthalpies and entropies of activation ($\Delta H^{\ddagger}_{-1}$, $\Delta S^{\ddagger}_{-1}$) for the decomposition of the corresponding adducts. The much higher values of $\Delta H^{\ddagger}_{-1}$ for **6b** and **6e** compared with those for **6a** and **6d** ($\Delta H^{\ddagger}_{-1}{}^{6b}$ − $\Delta H^{\ddagger}_{-1}{}^{6a}$ = 5.85 kcal mol^{-1}; $\Delta H^{\ddagger}_{-1}{}^{6e}$ −

$\Delta H^{\ddagger}{}_{-1}{}^{6d} = 3.95$ kcal mol^{-1}) are, in particular, responsible for the large differences observed in the enthalpy changes $\Delta H°$ associated with the equilibrium formation of these adducts in eq 1 and 3. Thus, we see that the formation of **6b** is exothermic, whereas that of **6a**, as well as that of **6c**, is endothermic; on the other hand, the formation of **6e** is more exothermic than that of **6d** and **6f**. All of these results point out that strong differences exist between the reactions of methoxide ion with **5b** and **5e**, which do not have a nitro group at their 4 position, and those with **5a**, **5c**, **5d**, and **5f**, which have a nitro group in this position. From this one may reasonably conclude that the presence of such an ortho-like nitro group is of great importance in determining the relative energy levels of intial states, adducts, and transition states in these reactions. This interpretation agrees with the previous findings of Spinelli, that in five-membered ring derivatives a change in an ortho-like 3 substituent causes more variation in the structure of the transition states for various reactions occuring at the 2 carbon than does a change in a para-like 5 substituent.[19b,20b]

Experimental Section

Materials. 2,4-Dinitrothiophene (**5a**) (K & K) was purified by chromatography and recrystallized from chloroform, mp 57 °C. 2,4-Dinitroselenophene (**5d**) was prepared by direct nitration of selenophene[22] and separated from the mononitro derivatives by chromatography; after recrystallization, **5d** had mp 78 °C (lit.[22] 76 °C). 2-Nitro-4-cyano and 2-cyano-4-nitro derivatives **5b**, **5c** and **5e**, **5f** were prepared from the corresponding nitrothiophene- and selenophenecarboxaldehydes; these latter compounds were obtained by a method similar to that described by Yurev and Zaitseva,[23] converted into oximes, and dehydrated according to standard methods. Recrystallization in chloroform gave the following: **5b**, mp 120 °C (lit.[2c,24] 122 °C); **5c**, mp 102 °C; **5e**, mp 148 °C; **5f**, mp 146 °C.

The potassium salts of adducts **6a**, **6d**, **6e**, and **6f** were prepared by addition of nearly 1 equiv of 1 M methanolic potassium methoxide to a solution of the parent molecules **5a**, **5d**, **5e**, and **5f** (100 mg) in a minimum amount of methanol. The reaction mixture turned immediately reddish purple or yellow and was allowed to stand at room temperature for 15 min. Then, the solvent was removed under vacuum and the residues, collected as red or yellow solids, were washed with anhydrous ether and dried under vacuum to eliminate any associated solvent. Good elemental analyses were obtained for the solids, which explode upon heating.

Anal. Calcd for $C_5H_5N_2KO_5S$ (**6a**): C, 24.58; H, 2.06; N, 11.47. Found: C, 24.50; H, 2.13; N, 11.38. Anal. Calcd for $C_5H_5N_2KO_5Se$ (**6d**): C, 20.62; H, 1.73; N, 9.62. Found: C, 20.83; H, 1.84; N, 9.48. Anal. Calcd for $C_6H_5N_2KO_3Se$ (**6e** and **6f**): C, 26.57; H, 1.86; N, 10.33. Found for **6e**: C, 26.45; H, 1.81; N, 10.54. Found for **6f**: C, 26.38; H, 1.93; N, 10.24.

Methanol and methanolic potassium methoxide solutions were prepared as previously described.[3b,4] The various buffers used for the rate measurements were purified according to classical methods.

Rate and pH Measurements. Stopped-flow determinations were performed on a Durrum stopped-flow spectrophotometer, the cell compartment of which was maintained at 20 ± 0.5 °C.

Other kinetic measurements were made using a Beckman spectrophotometer. All kinetic runs were carried out under pseudo-first-order conditions with a substrate concentration of about 3×10^{-5} M. Rate constants are accurate to ±3%.

The pH of buffered solutions and dilute potassium methoxide solutions has been measured according to a method previously reported by using a hydrogen electrode.[8] The pH values so obtained are relative to the standard state in methanol.

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Registry No.—**5a**, 5347-12-6; **5b**, 42137-23-5; **5c**, 42137-24-6; **5d**, 42137-19-9; **5e**, 42137-20-2; **5f**, 42137-21-3; **6a**, 69225-00-9; **6a** potassium salt, 69225-01-0; **6b**, 42133-96-0; **6c**, 42133-97-1; **6d**, 42045-48-7; **6d** potassium salt, 69225-02-1; **6e**, 42045-49-8; **6e** potassium salt, 69225-03-2; **6f**, 42045-50-1; **6f** potassium salt, 69225-04-3; **7**, 69225-81-6.

References and Notes

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(25) Due to the low thermodynamic stability of the methoxyl adducts **8b** and **8c** in methanol and the hydroxyl adducts **8e** and **8f** in water, the observation that methoxide and hydroxide ions attack more rapidly the carbon 4 than the carbon 2 of 3,5-dinitro-1-cyanobenzene has been made in 50% Me_2SO–50% methanol and 50% Me_2SO–50% water mixtures, respectively.[12] However, the effect of Me_2SO on the rate and equilibrium constants for formation and decomposition of benzenic Meisenheimer adducts has been shown to be practically independent of the number and type of substituents on the aromatic nucleus.[4,26] As a consequence, the ratios $k_1{}^{8c}/k_1{}^{8b}$ and $k_1{}^{8f}/k_1{}^{8e}$ for formation of the methoxyl and hydroxyl adducts, respectively, would be about the same in methanol and water than in the corresponding Me_2SO–solvent mixtures. In other words, the Me_2SO cosolvent is not expected to significantly affect the relative influence of the ortho- and para-like nitro groups on the formation of the adducts **8b, 8c** and **8e, 8f.**

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