g), mp 161.5–162 °C. Anal. Calcd for $C_{25}H_{26}N_2O_7S$: C, 60.24; H, 5.26; N, 5.62; S, 6.43. Found: C, 59.92; H, 5.21; N, 5.58; S, 6.56.

p-Methoxybenzyl 2β-Methoxy-3-methyl-7-(phenoxyacetamido)-3-cephem-4-carboxylate (6a). A 58/42 mixture of **6a** and **7a** (0.500 g), prepared through the sequence described above from the mixture of **2a** and **3a** obtained in the bromination of **1a** in CCl_4 at 0 °C, was subjected to preparative TLC, a 7:3 mixture of ethyl acetate and hexane being used as the eluent. Elution was repeated three times. Extraction of the two bands (the faster moving band contains **7a**) yielded **7a** (0.070 g), mp 161.5–162 °C, and pure **6a** as an oil (0.110 g). Anal. Calcd for $C_{25}H_{26}N_2O_7S$: C, 60.24; H, 5.26; N, 5.62; S, 6.43. Found: C, 59.90; H, 5.18; N, 5.30; S, 6.33.

p-Nitrobenzyl 2β-Methoxy- (6b) and p-Nitrobenzyl 2α-Methoxy-3-methyl-7-(phenoxyacetamido)-3-cephem-4-carboxylate (7b). A mixture of **2b** and **3b** (2.50 g) obtained from the bromination of **1b** (2.0 g) in CH_2Cl_2 at 0 °C as described above for **1a** was transformed into a mixture of **4b** and **5b** (2.05 g) and then into a mixture of **6b** and **7b** (1.45 g) through a sequence similar to that used above for the transformation of **2a** and **3a** into **6a** and **7a**. Two crystallizations of the crude mixture of **6b** and **7b** from acetone–hexane gave pure **7b** (0.300 g), mp 172–173 °C, identical with a sample prepared according to the method of Spry[6] (lit.[6] mp 171.5–172 °C). The mother liquors were subjected to TLC on silica gel, using a 7:3 mixture of ethyl acetate and hexane as the eluent. Elution was repeated twice. Extraction of the two bands (the faster moving band contains **7b**) yielded **7b** (0.110 g), mp 172–173 °C, and pure **6b** (0.220 g), as an oil. Anal. Calcd for $C_{24}H_{23}N_3O_8S$: C, 56.13; H, 4.51; S, 6.24. Found: C, 56.51; H, 4.45; S, 6.11.

2β-Methoxy-3-methyl-7-(phenoxyacetamido)-3-cephem-4-carboxylic Acid (6, R = H). A. A solution of **6a** (0.510 g) and anisole (0.36 ml) in anhydrous benzene (45 ml) was treated with trifluoroacetic acid (1.71 ml). After stirring for 2 h at room temperature the reaction mixture was evaporated, taken up in ethyl acetate, and extracted three times with 3% aqueous $NaHCO_3$. The aqueous extracts were washed with ethyl acetate, then layered with ethyl acetate and acidified to pH 3. Evaporation of the organic solvent gave a residue consisting of **6** (R = H) (0.250 g), which crystallized from 2-propanol to yield pure **6** (R = H) (0.090 g): mp 140–141 °C; uv λ_{max} 269 nm (ϵ 4650). Anal. Calcd for $C_{17}H_{18}N_2O_6S$: C, 53.96; H, 4.79; N, 7.40; S, 8.47. Found: C, 53.96; H, 4.86; N, 7.14; S, 8.43.

B. A suspension of **6b** (0.500 g) in a mixture of methanol (25 ml) and water (6 ml) was shaken under hydrogen at room temperature for 4 h in the presence of 5% Pd on carbon (0.150 g). The catalyst was then separated by filtration and the solvent evaporated. The residue was dissolved in ethyl acetate and extracted three times with 5% aqueous $NaHCO_3$. The aqueous extracts were washed with ethyl acetate, then layered with ethyl acetate, and acidified at pH 3. Evaporation of the organic solvent afforded an oil (0.220 g) which crystallized from 2-propanol to yield pure **6** (R = H) (0.110 g), mp 140–141 °C.

2α-Methoxy-3-methyl-7-(phenoxyacetamido)-3-cephem-4-carboxylic Acid (7, R = H). A suspension of **7b** (0.300 g) in methanol (20 ml) and water (4 ml) was hydrogenated as described above for the preparation of **6**, R = H, in B. Workup yielded crude **7**, R = H (0.120 g), as an oil which crystallized from acetone–hexane to give pure **7**, R = H (0.075 g), mp 141–145 °C. Anal. Calcd for $C_{17}H_{18}N_2O_6S$: C, 53.96; H, 4.79; N, 7.40; S, 8.47. Found: C, 53.65; H, 4.48; N, 7.38; S, 8.52. Spry[6] reports the formation of **7**, R = H, from **7b**, but no experimental value has been given.

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Registry No.—**1a**, 58800-52-5; **1b**, 24647-43-6; **2a**, 58747-39-0; **2b**, 58747-40-3; **3a**, 58747-41-4; **3b**, 58747-42-5; **4a**, 58747-43-6; **4b**, 58747-44-7; **5a**, 58747-45-8; **5b**, 58747-46-9; **6a**, 58747-47-0; **6b**, 58800-53-6; 6 (R = H), 58800-54-7; **7a**, 58747-48-1; **7b**, 37901-26-1; 7 (R = H), 58800-55-8.

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On the Role of Electronic and Steric Factors upon the Formation of Meisenheimer-Type Adducts

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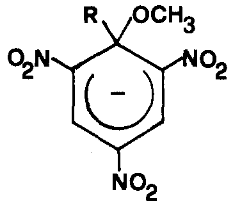
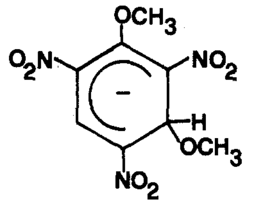
The rate and equilibrium constants for the formation of Meisenheimer adducts from 4-cyano-2-nitrothiophene, 3-cyano-2-methoxy-5-nitrothiophene, and 5-cyano-2-methoxy-3-nitrothiophene have been determined in methanol at 25 °C. The comparison of these data with those for the formation of adducts from dinitrothiophene, trinitrobenzene, and cyanodinitrobenzene derivatives provides a reliable indication of the role of steric and electronic factors on the formation of the adducts.

A major factor in the formation of Meisenheimer adducts is the electron delocalization ability of electron-withdrawing substituents. However, other factors may more subtly modify the stability and the rate of formation of these adducts. In the reaction of 2,4,6-trinitroanisole (TNA) with methoxide ion in methanol solution the equilibrium is more shifted toward the 1,1 adduct 1 (K_1, 25 °C, = 1.7×10^4 l. mol^{-1}) than toward the 1,3 adduct 2 (K_2, 25 °C, = 2.71 l. mol^{-1}).[1] It is commonly accepted that a larger steric relief[2] is at least partially responsible for the larger stabilization of adduct 1 with respect to adduct 2. Also, the equilibrium constant, K_3, 25 °C, = 23.1 l. mol^{-1},[1] for the formation of adduct 3, which is obtained from



1 R = OCH_3

3 R = H



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1,3,5-trinitrobenzene (TNB), is closer to that of 2 than to that of 1. Another stabilizing effect for adduct 1 is attributed to the presence of the geminal alkoxy groups.[3]

Steric hindrance on the approach of the reagent (F-strain) has been held responsible for the rate decrease observed for the formation of 1 relative to the formation of either 2 or 3.[2] However, according to Bernasconi[3] the observed reactivity pattern could be better accounted for by ground-state stabilization of TNA due to through-conjugation effects from methoxy to nitro groups.

The replacement of a nitro group in TNA and TNB by another electron-withdrawing group having smaller steric requirements is expected to provide a deeper insight into the controversial role of the steric effects involved in the reaction. A comparison of this kind concerning the effect of a cyano group relative to a nitro group in the formation of adducts from benzene and methoxybenzene derivatives has been carried out by Fendler[4] and Terrier.[5] These authors observed that the replacement of a nitro group by a cyano group brings about a decrease in the equilibrium constant because of the smaller electron-withdrawing power of the latter group. Kinetic and equilibrium data were reported for the formation of adducts from cyanonitroanisoles. However, the equilibrium constants for the reactions of nitrocyanobenzenes are very small[4] and have been obtained in methanol only for the reaction of 3,5-dinitrobenzonitrile; moreover, kinetic data for the formation of adducts are not available. Therefore, a complete assessment of the role of the cyano group at present appears to be difficult to obtain.

Since thiophene derivatives show a relatively higher tendency than benzene derivatives to undergo nucleophilic addition,[6] we expected that suitable nitrocyano thiophene derivatives could provide the required kinetic and equilibrium data in a reliable manner for the formation of adducts resulting from nucleophilic addition to methoxy-bearing and hydrogen-bearing positions.

Nitrocyanothiophenes are not devoid of complications, however. At the beginning of this work we ran into an interesting solvent effect, whereby methoxide ion in methanol adds to the cyano group of 2-cyano-4-nitrothiophene rather than to the ring.[7] The expected adducts in this solvent are observed for the remaining group of cyanonitro derivatives of the original plan, i.e., 4-cyano-2-nitrothiophene (4), 5-cyano-2-methoxy-3-nitrothiophene (5), and 3-cyano-2-methoxy-5-nitrothiophene (6).

In this paper we wish to report a full account of the behavior of compounds 4, 5, and 6, leading to a step forward in the interpretation of the factors involved in the formation of Meisenheimer adducts.

Experimental Section

Melting points are uncorrected. The NMR spectra were obtained on a JEOL C-60 HL apparatus, at 24 °C, usually at a sweep width of 540 Hz; chemical shifts are reported in τ and are approximate to ± 0.03; coupling constants are accurate to ± 0.4 Hz. Mass spectra were obtained on an AEI MS 12 mass spectrometer. Ir spectra were determined in KBr disks on a Perkin-Elmer 257 spectrophotometer. The electronic spectra were obtained on a Beckman DB-GT spectrophotometer.

Kinetic and equilibrium determinations were obtained by spectrophotometric measurements in a constant-temperature housing, kept at 25.0 ± 0.1 °C. Fast reactions were run in two-compartment cells (optical length 0.875 cm), where the solutions of the reagents were separately thermostatted before mixing. The absorbance changes were followed at the high-wavelength maximum of each adduct on a W + W 1100 Kontron recorder. In each case the concentration of the substrate was in the range of $3\text{–}5 \times 10^{-5}$ M. In the case of the reaction of 5 and 6, the absorbance maximum reached its highest value at approximately 4×10^{-3} and 6×10^{-2} M sodium methoxide, respectively, and remained constant at higher concentrations; a similar behavior was observed in the case of the reaction of 4 only beyond 6×10^{-1} M sodium methoxide. Under the experimental conditions, the observed first-order rate constant k_{obsd} is related to the second-order rate constant for the formation of the adduct and to the equilibrium constant by the equation

$$k_{\text{obsd}} = k_1([CH_3O^-] + K^{-1})$$

Methanol and sodium methoxide were purified, prepared, and standardized as previously described.[8]

4-Cyano-2-nitrothiophene (4) was prepared in 30% yield by nitrating 3-cyanothiophene[9] according to the procedure reported[10] for the nitration of 2-cyanothiophene: crystals from ethanol, mp 122–122.5 °C; ν (CN) at 2240 cm^{-1}, ν (NO_2) at 1335 and 1505 cm^{-1}; M^+ at *m/e* 154; τ (see Table I).

2-Cyano-5-methoxythiophene was prepared from 2-formyl-5-methoxythiophene,[11] through the formation of the oxime (mp 109–111 °C) and subsequent dehydration in refluxing acetic anhydride: $n^{25}\text{D}$ 1.561 (lit.[12] $n^{18}\text{D}$ 1.5681); ν (CN) at 2210 cm^{-1}; τ (in CCl_4) at 2.74 (d, 1 H, J = 4.5 Hz), 3.80 (d, 1 H, J = 4.5 Hz), and 3.94 (s, 3 H).

5-Cyano-2-methoxy-3-nitrothiophene (5). Nitric acid (1 ml, *d* 1.5) was slowly added under efficient stirring to a solution of 1 g of 2-cyano-5-methoxythiophene in 10 ml of acetic anhydride, at 0 °C. The reaction mixture was stirred for 3 h at a temperature lower than 15 °C, and was poured into ice. Upon standing for 12 h at 0 °C, a yellow precipitate (0.3 g, 25% yield) was formed. It was collected and recrystallized from hexane: mp 130–131 °C; ν (CN) at 2220 cm^{-1}, ν (NO_2) at 1385 and 1545 cm^{-1}; M^+ at *m/e* 184; τ (see Table I).

2-Bromo-3-cyano-5-nitrothiophene. The preparation of this compound was essentially the same as that recently reported by Spinelli,[13] mp 119–120 °C (lit.[13] 123 °C).

3-Cyano-2-methoxy-5-nitrothiophene (6). A preliminary NMR study of the reaction of 2-bromo-3-cyano-5-nitrothiophene with 1 equiv of sodium methoxide showed that only nearly one-half of the bromo derivative reacts very rapidly to yield a new species, that was then identified as the dimethoxy adduct 9. On standing, the reaction mixture changes slowly to give the expected cyanomethoxynitro derivative as the main product. Therefore, we found it convenient to convert quantitatively the bromo derivative into the adduct and to decompose the latter with an acid. 2-Bromo-3-cyano-5-nitrothiophene (0.2 g) was dissolved in 2 ml of methanol and 2 equiv of sodium methoxide in 2 ml of methanol was added rapidly to this solution. After a few minutes, 1 equiv of acetic acid was added. Salts were precipitated by adding ether and removed by filtration. The residue of the evaporation of the solvent was purified through a small column of silica gel (benzene–hexane, 4:1, as eluent) and recrystallized from hexane (25% yield): mp 147.5–148 °C; ν (CN) at 2240 cm^{-1}, ν (NO_2) at 1310 and 1485 cm^{-1}; M^+ at *m/e* 184; τ (see Table I).

Results and Discussion

The spectrophotometric study of the reactions of 4, 5, and 6 with methoxide ion in methanol shows that in each case, on addition of the nucleophile, the electronic spectrum of the substrate disappears while a new species, displaying two maxima of absorption, is formed (see Table I). The high-wavelength maxima of the species formed in the three examined cases fall in the region of 400 nm, in accordance with the view that they all belong to the same type of electronic

Table I. NMR and Spectrophotometric Data for Substrates 4, 5, and 6 and the Corresponding Adducts

		τ (H_α)	τ (H_β)	τ (OCH_3)	J, Hz	λ_1, nm	ϵ_1, l. mol^{-1} cm^{-1}	λ_2, nm	ϵ_2, l. mol^{-1} cm^{-1}
4	CH_3OH	1.48	1.73		1.8	273	6.3×10^3	298	5.6×10^3
	Me_2SO	1.10	1.39		1.8				
7	CH_3OH	3.80	2.54		0.1	260	1.0×10^4	398	1.8×10^4
	Me_2SO	3.82	2.60	6.79	0.1				
5	CH_3OH		1.80	5.75[a]		278	8.8×10^3	313	5.3×10^3
	Me_2SO		1.63	5.74					
8	CH_3OH		2.97			290	4.9×10^3	399	1.7×10^4
	Me_2SO		2.89	6.78[b]					
6	CH_3OH		1.95	5.75[a]		241	8.7×10^3	350	9.3×10^3
	Me_2SO		1.48	5.71					
9	CH_3OH		2.45			258	7.7×10^3	402	1.9×10^4
	Me_2SO		2.56	6.75[b]					

[a] In CD_3OD. [b] Observed by dissolving the isolated adduct in Me_2SO-d_6 (see text).

structure. The bathochromic shifts are smaller than those observed in the formation of Meisenheimer adducts from 2,4-dinitrothiophene[14] and 2,4-dinitro-5-methoxythiophene,[6] but much larger than that observed under similar reaction conditions in the case of 2-cyano-4-nitrothiophene,[7] where addition occurs predominantly at the cyano group rather than at a ring carbon atom. Thus, the observed spectral changes are in reasonable accordance with the formation of Meisenheimer adducts.

More direct evidence for the formation of adducts is given by NMR spectra (see Table I). Addition of 1 equiv of methoxide ion to a methanol or Me_2SO-d_6 solution of **4**, **5**, and **6** causes the disappearance of the signals of the substrates and the appearance of new signals at higher field. The addition of less than 1 equiv of methoxide ion allows the detection of the signals of both the unreacted substrate and the reaction product at the same time. In the case of the reaction of 4-cyano-2-nitrothiophene (**4**) the determination of the structure of the adduct was reported by Terrier.[15] In agreement with this report we found that in tetradeuteriomethanol both the substrate and the corresponding adduct undergo a base-catalyzed hydrogen/deuterium exchange, as shown by the decrease of intensity of the signals at τ 1.48 of **4** and at τ 3.80 of the adduct.

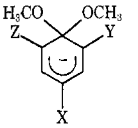
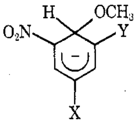
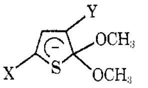
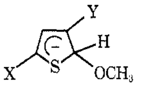
The structure of the products of the reaction of **4**, **5**, and **6** is conclusively established by the NMR spectra of the Me_2SO-d_6 solutions of the solid residues as obtained upon evaporation of the related reaction mixtures made up with equivalent amounts of sodium methoxide and the substrate in methanol solution. For the reaction of **4**, the spectrum displays also a signal at τ 6.79, which is three times as intense as the signal at τ 3.82, and is therefore attributed to the methoxy group bound to the ring. The detection in the reactions of **5** and **6** of a singlet at about τ 7.8, six times as intense as the low-field signal (see Table I), indicates the presence of two equivalent methoxy groups.

In the reaction of **4**, **5**, and **6** with methoxide ion, the hydrogen atoms at the β position undergo relatively small upfield shifts, that are comparable to those observed in the formation of Meisenheimer adducts from the dinitrothiophene derivatives.[6,14]

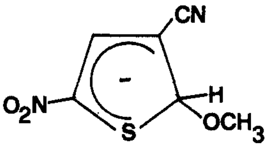
The chemical shifts observed at low field for the Me_2SO-d_6 solutions of the solids are coincident with those observed when the reactions are performed in situ in the same solvent. Moreover, the positions of the signals are not significantly different from those observed when the reactions are run in methanol. We wish to emphasize the fact that with each of the compounds **4**, **5**, and **6** the same adduct appears to be formed in either solvent; in contrast, 2-cyano-4-nitrothiophene was found to exhibit a solvent-dependent behavior toward methoxide ion.[7] The observed NMR patterns are consistent with the formation of adducts **7**, **8**, and **9**, respectively.

In Table II we have collected equilibrium and rate data for the formation of adducts **7**, **8**, and **9**, in methanol, at 25 °C, together with similar data for the formation of adducts from the parent thiophene compounds and the related benzene derivatives. In accordance with our initial hypothesis, a reliable indication of the role of cyano group in adduct formation is indeed more accessible in the thiophene series than in the benzene series.

Table II. Rate and Equilibrium Constants for the Formation of Meisenheimer Adducts in Methanol at 25 °C

	(No.)	X	Y	Z	k, l. mol^{-1} s^{-1}	K, l. mol^{-1}	Ref
	(1)	NO_2	NO_2	NO_2	17.3	1.7×10^4	4a
	(10)	CN	NO_2	NO_2	6.1	2.8×10^2	4a
	(11)	NO_2	CN	NO_2	18.8	2.6×10^3	4a
		NO_2	CN	CN	12.0	34	4b
	(3)	NO_2	NO_2		7.05×10^3	2.31×10	1
		CN	NO_2				4d
		NO_2	CN			1.5	4d
		NO_2	NO_2		3.6×10	$>4 \times 10^5$	6
						3.6×10^{5a}	*b*
	(8)	CN	NO_2		2.14	1.53×10^3	7
	(9)	NO_2	CN		4.85	2.5×10^4	*c*
		NO_2	NO_2		1.5×10	8×10^2	14
	(7)	NO_2	CN		7.8×10^{-1}	1.5×10^2	7
		CN	NO_2			<3	7

[a] At 20° C. [b] F. Terrier, A. P. Chatrousse, C. Paulmier, and R. Schaal, *J. Org. Chem.*, **40**, 2911 (1975). [c] This work.



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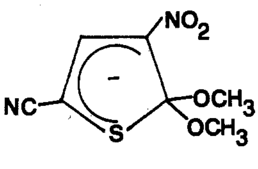

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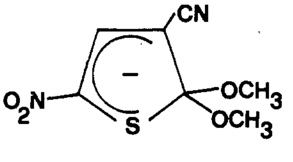

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Both in benzene and thiophene series, the replacement of a nitro group with the less electron-withdrawing cyano group results in a decrease of the equilibrium constant. In the benzene series, this destabilizing effect is stronger with a group para to the reaction center than with a group located at a position ortho.[4a] A similar effect is also observed in the thiophene series, the replacement of a nitro group by a cyano group being more effective from the 5 position (paralike) than from the 3 position (ortholike), the reaction center being at the 2 position. The effect is confirmed by the apparently very low tendency to adduct formation of 2-cyano-4-nitrothiophene in methanol.[7] The K_9/K_8 ratio is found to be 16, and compares well with the K_{11}/K_{10} ratio (9.3) for the adducts obtained from 2-cyano-4,6-dinitroanisole and 4-cyano-2,6-dinitroanisole. The observed stability order suggests that, as in the benzene series,[4a] the negative charge in the thiophene adducts is predominantly delocalized toward the paralike substituent. It is worth noting that the present results are consistent with the fact that nucleophilic substitutions with anionic nucleophiles occur more rapidly in 2-bromo-5-nitrothiophene than in 2-bromo-3-nitrothiophene.[16]

Starting from similarly activated thiophenes, the equilibrium constant for adduct formation at a methoxyl-bearing position is at least three orders of magnitude larger than the equilibrium constant for the addition at a hydrogen-bearing position. This effect is also observed for the formation of adducts from benzene derivatives.

It has been shown that in the reactions of the five-membered thiophene ring steric factors usually play a less significant role than in reactions of the benzene ring;[17] moreover, unlike the benzene derivatives used for the present comparison, the thiophene substrates have one, rather than two, substituent flanking the reaction center. Therefore, in the thiophene series major factors responsible for the relative stabilization of the adducts should involve the charge delocalization ability of the electron-withdrawing substrate and, for the more stable dimethoxy adducts, the geminal alkoxy substitution at an sp^3 carbon atom.[3] The same conclusion may probably apply to the benzene adducts, because in both rings a given modification of the substrate, such as the introduction of a methoxyl at the reaction center and the replacement of a nitro group with a less electron-withdrawing substituent, have similar effects on the equilibrium constant. Therefore, steric factors, as compared with other structural factors, do not seem to play a significant role in determining the stability of Meisenheimer adducts.

We now wish to analyze how the rate of formation of a thiophene adduct is affected by the replacement of a nitro group with a cyano group. A decrease in rate is generally observed. It is more marked for the replacement of an α-nitro group, which is in a paralike position relative to the reaction center. It must be noted that changes in the equilibrium constants for the formation of thiophene adducts are dependent to a good extent on the changes of k_1. This is in contrast with what is found in the benzene series, where the equilibrium constants correlate poorly with the forward rate constants. For example, in TNA the replacement of a nitro group ortho to the methoxyl results in a slight increase in k_1, even if the corresponding change in equilibrium constant is by one order of magnitude less than K_1.

Furthermore, in striking contrast with what is found in the benzene series, the rate of addition to a methoxyl-bearing position (**9**) is higher than that to a hydrogen-bearing position (**7**), a result which fully confirms our previous findings with the dinitro-activated substrates.[14]

The failure of the rate of formation to correlate with the stability of the adducts thus seems to be limited to the benzene systems.

Let us now consider the perturbing influence of a methoxy group whenever this is present as a substituent in the initial substrate.

A purely polar effect on the rate of addition cannot be held responsible for the different behavior between the thiophene and benzene substrates because it would possibly cause different selectivities, but not an inverted trend of reactivity.

Through-conjugation of the methoxyl with the electron-withdrawing substituents is expected to enhance the stabilization of the initial substrates and could in principle be responsible for the low reactivity of the position 1 of TNA.[3] However, the relatively high rates of reaction of the methoxy thiophenes can hardly be rationalized by this view; in fact, an even stronger rate-depressing effect than in the benzene series is anticipated on the ground of a substantially lower steric inhibition of resonance effect.

The decrease in reactivity observed in going from 2,4-dinitro-5-methoxythiophene to the cyanonitromethoxythiophenes, and from 2,4-dinitrothiophene to 4-cyano-2-nitrothiophene, can be safely attributed to the lower electron-attracting properties of the cyano group. Surprisingly, no large rate decrease is observed in going from TNA to 2-cyano-4,6-dinitroanisole and to 2,6-dicyano-4-nitroanisole (Table II). The change in polar effect is clearly offset here by some other factor. We propose that a major factor for the observed difference in the two systems is the different geometry of the five- and six-membered rings. In benzene derivatives an ortho-substituted bulky group is expectedly more subject to steric inhibition of resonance than in thiophene compounds. In particular, in TNA the steric interaction between the methoxyl and the flanking nitro groups will prevent the attainment of full coplanarity of these groups with the ring.[18] Furthermore, rotation of one or more groups out of the ring plane may increase the F-strain on the approach of the nucleophile to the methoxyl-bearing reaction center. This effect seems to be even more important than that of steric inhibition of resonance, since the attack to the position 3 of TNA (k, at 25 °C, in CH_3OH = 950 l. mol^{-1} s^{-1})[1] is only nearly one order of magnitude slower than the formation rate of **3**. Steric hindrance is probably relieved in the adduct, owing to the change in hybridization of the carbon atom at the reaction center. A transition state not too closely resembling the product may be envisaged in order to allow for the different steric requirements of adduct 1 and the transition state leading to it. The substitution of a nitro group with a less bulky, linear cyano group brings about a decrease of steric hindrance at the reaction center, keeping the reactivity of position 1 of 2-cyano-4,6-dinitroanisole at a level comparable to that of position 1 of TNA, in spite of the smaller electron-withdrawing power of one of the substituents.

Registry No.—**4**, 42137-23-5; **5**, 49620-82-8; **6**, 58703-24-5; **7**, 42133-96-0; **8**, 49796-96-5; **9**, 58702-90-2; 3-cyanothiophene, 1641-09-4; 2-cyano-5-methoxythiophene, 58703-25-6; 2-formyl-5-methoxythiophene, 35087-46-8; nitric acid, 7697-37-2; 2-bromo-3-cyano-5-nitrothiophene, 58703-24-5.

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Elucidation of the Role of *syn*- and *anti*-Arylazo Alkyl Ethers in the Dediazoniation of Aryldiazonium Salts in Basic Alcoholic Solvents

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From kinetic studies of ionization rates of *anti*-arylazo alkyl ethers in methanol and ethanol and of dediazoniation rates in both solvents, it is concluded that when an aryldiazonium ion is dissolved in basic methanol a partitioning between *syn*- (k_{1S}) and *anti*- (k_{1A}) arylazo methyl ether occurs (k_{1S}/k_{1A} = 120 for Ar = 4-NO_2Ph) and subsequent protection of the diazonio function (i.e., conversion of *syn*- into *anti*-arylazo ether) occurs via an ionization–recombination pathway ($k_{-1S} \rightarrow k_{1A}$). Decomposition of *p*-nitrobenzenediazonium ion occurs from the *syn*-arylazo ether ($k_{1S} \rightarrow k_{1D}$) presumably by the electron transfer mechanism of Bunnett. Dediazoniation of the anti *p*-nitrophenylazo ether also occurs from the *syn*-arylazo ether which is formed via prior ionization of the anti ether ($k_{-1A} \rightarrow k_{1S} \rightarrow k_D$). Steric acceleration was observed for some reactions of the 2-chlorobenzenediazonium system (k_{-1A} and k_{-1S}).

The decomposition of aryldiazonium salts (ArN_2^+) in methanolic solution was studied by DeTar and co-workers almost 20 years ago.[1,2] It was found that in neutral or acidic methanol the major product was the corresponding anisole ($ArOCH_3$) presumably formed via a carbonium ion intermediate. In weakly basic solution (sodium acetate) the yield of anisole was much less and the major products were reduction products (ArH) and biaryls (Ar–Ar). Since the reaction in basic solution was affected by the presence of oxygen it was concluded that the dediazoniation ($ArN_2^+ \rightarrow ArH$) reaction was free radical in nature.

Bunnett subsequently looked at reactions of aryldiazonium salts in more strongly basic solution (MeO^-/MeOH) and found that dediazoniation yields were high enough to be of