After thermal decomposition of this salt at 150° vpc analysis showed one peak (on 6-ft 20% SE-30 columns), which was shown to be 1-iodonaphthalene by the peak enhancement method with an authentic sample.

Di-2-naphthyliodonium iodide, mp 151–154° dec (lit.[24] mp 147°), was prepared similarly.

Anal. Calcd for $C_{20}H_{14}I_2$: C, 47.08; H, 2.77. Found: C, 47.09; H, 2.91.

Again thermal decomposition at 200° showed one peak on vpc analysis; this was shown to be 2-iodonaphthalene by the peak-enhancement method with an authentic sample.

Diphenyliodonium Trichloromercurate(II).—To 5.6 g (10 mmol) of phenyl(*trans*-chlorovinyl)iodonium trichloromercurate-(II)[8c] suspended in 80 ml of toluene at Dry Ice–acetone temperature under an argon atmosphere, 10 mmol of phenyllithium solution was added slowly with stirring; the ice bath was allowed to "melt." After 1 day at room temperature the precipitate was collected and recrystallized from 300 ml of water. The white crystalline diphenyliodonium trichloromercurate(II) was collected and dried to give 4.3 g (73%), mp 177–180° (lit. mp 168–170°,[8a] 172–175°[18]).

Phenyl(1-naphthyl)iodonium Chloride.—To 440 mg (1.5 mmol) of phenyl(*trans*-chlorovinyl)iodonium chloride suspended in 30 ml of toluene at Dry Ice–acetone temperatures under an argon atmosphere, 1.5 mmol of 1-naphthyllithium solution was slowly added with stirring, thereafter allowing the ice bath to "melt." After 3 days at room temperature the solid was collected, suspended in 25 ml of cold water for 3 hr, recollected, washed with acetone and ether, and dried under vacuum to give 151 mg (27.5%) of phenyl(1-naphthyl)iodonium chloride, mp 170–171° (lit.[25] mp 168°).

Registry No.—**1,** 18964-25-5; di-9-anthryliodonium bromide, 18963-90-1; di-1-naphthyliodonium chloride, 18963-91-2; di-2-naphthyliodonium perchlorate, 18963-92-3; di-1-naphthyliodonium iodide, 18963-93-4.

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(24) C. Willgerodt and M. Auerbach, Dissertation, Freiburg, 1900.

(25) C. Willgerodt and P. Schlösser, *Ber.*, **33,** 692 (1900).

Intermediates in Nucleophilic Aromatic Substitution. VI.[1] Formation of Meisenheimer Complexes of the Isomeric 2,4,6-Cyanodinitroanisoles

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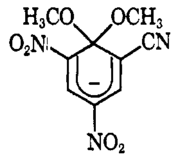
The rate constants for the formation and decomposition of the 1,1-dimethoxy Meisenheimer complexes **3** and **5** formed by the reaction of methoxide ion with 2-cyano-4,6-dinitroanisole (**1**) and 2,4,6-trinitroanisole (**6**), respectively, in methanolic solution have been determined at three different temperatures, allowing a determination of K, k_1, and k_2 and the energies and entropies of activation for the reactions. A similar study of the 1,1-dimethoxy complex **4** formed from 4-cyano-2,6-dinitroanisole (**2**) has been carried out. These data indicate that the relative order of stabilities of the complexes is **5** > **3** > **4** and that the replacement of a *p*-nitro group by a cyano group has a much more serious effect on the stability of the complex than the corresponding replacement of an *o*-nitro group, *i.e.*, $K_5/K_3 = 6.5$, $K_5/K_4 = 60$. Both the forward and reverse reactions for these complexes are dependent to a greater extent on changes in the entropies than in the enthalpies of activation. The entropy of activation for the formation of **3** is *ca.* 15 eu higher than that for either **4** or **5**, implying a much less extensively solvated transition state for the formation of **3**. The rate of decomposition of complex **3** in H_2O and D_2O has been determined over the pH range 5.27–10.80 at 25.00°. The lesser stability of **3** relative to **5** is further demonstrated by its higher rate of decomposition (k_2^0 for **3** = $15k_2^0$ for **5**); a significant deuterium isotope effect on the entropy of this reaction is observed. The formation and decomposition of **3** was also followed in CH_3OD and the solvent isotope effect on the equilibrium constant (K^H/K^D) was found to be 0.45, an apparently typical value for nucleophilic aromatic substitution reactions. The structures of complexes **3**, **4**, and **5** have been substantiated by studies of the pmr spectra of both the isolated and *in situ* generated complexes. In the *in situ* generation of **3** and **4** by the reaction of methanolic methoxide ion with **1** and **2** in DMSO-d_6 solution, the formation of unstable transients is observed. The initial attack of methoxide ion is at an unsubstituted ring position to yield 1,3-dimethoxy complexes, *i.e.*, 1,3-dimethoxy-2-cyano-4,6-dinitrocyclohexadienylide (**10**) from **1** and 1,3-dimethoxy-4-cyano-2,6-dinitrocyclohexadienylide (**12**) from **2**. The lifetimes of the transient complexes **10** and **12** are dependent on methanol concentration.

The formation of complexes by the addition of methanolic sodium methoxide to solutions of 2-cyano-4,6-dinitroanisole (**1**) and 4-cyano-2,6-dinitroanisole (**2**) has been observed and the electronic spectra of the complexes have been reported.[3] More recently, the proton magnetic resonance (pmr) spectra of the solid complexes of **1**, potassium 1,1-dimethoxy-2-cyano-4,6-dinitrocyclohexadienylide (**3**),[4] and **2**, potassium 1,1-dimethoxy-4-cyano-2,6-dinitrocyclohexadienylide (**4**),[5]



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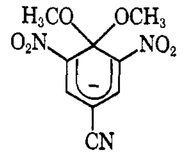

4

in DMSO-d_6 solution have been obtained. The observed electronic and pmr spectra of complexes **3**[4] and **4**,[5] generated *in situ*, suggested that these complexes

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(1) Part V: E. J. Fendler, J. H. Fendler, and C. E. Griffin, *Tetrahedron Lett.*, 5631 (1969).

(2) NASA Postdoctoral Fellow, 1966–1968.

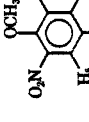
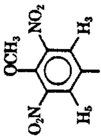
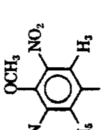
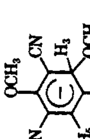
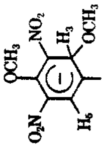
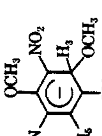
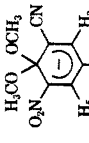
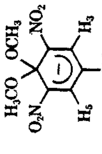
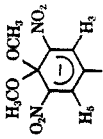
(3) R. J. Pollitt and B. C. Saunders, *J. Chem. Soc.*, 1132 (1964).

(4) P. Caveng, P. B. Fischer, E. Heilbronner, A. L. Miller, and H. Zollinger, *Helv. Chim. Acta*, **50,** 848 (1967).

(5) J. E. Dickenson, L. K. Dyall, and V. A. Pickles, *Aust. J. Chem.*, **21,** 1267 (1968).

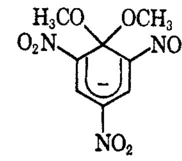
Table I

Pmr Spectra of Cyanodinitro- and Trinitroanisoles and the Corresponding 1,3- and 1,1-Dimethoxycyclohexadienylides[a]

	 1	 2	 6	 10[b]	 12[b]	 11[b]	 3	 4	 5
τ_1-OCH$_3$	5.73 (5.73)[c]	5.97 (5.95)[d]	5.92 (5.87)[e]	6.23	6.22	6.53 (6.55)[e]	7.03 (6.99)[c]	7.02 (6.98)[d]	6.92 (6.94)[e]
τ_3-OCH$_3$				6.92	6.92	6.82 (6.80)[e]			
τ_3	0.93 (0.97)[c]	1.33 (1.15)[d]	0.95 (0.93)[e]	4.50	4.52	3.83 (3.83)[e]	2.10 (1.71)[c]	1.98 (1.97)[d]	1.35 (1.33)[e]
τ_5	0.93 (0.97)[c]	1.33 (1.15)[d]	0.95 (0.93)[e]	1.47	2.25	1.59 (1.58)[e]	1.28 (1.26)[c]	1.98 (1.97)[d]	1.35 (1.33)[e]
J_{35}				2-3		2-3 (2-3)[e]	2.8 (2.8)[c]		

[a] Except where noted, spectra were determined in DMSO-d_6 solution at 25°. Details of method are given in Experimental Section. Literature values are given in parentheses. [b] Spectra were determined in MeOH–DMSO-d_6 solution. [c] Values were taken from ref 4. [d] Spectra were recorded at 43°; values were taken from ref 5. [e] Values were taken from ref 14.

were less stable than their picryl analog, potassium 1,1-dimethyoxy-2,4,6-trinitrocyclohexadienylide (**5**). Indeed, under their experimental conditions, Zollinger[4] and Dyall[5] and their coworkers were unable to follow the attainment of equilibrium for **3** and **4** in dilute methanolic solutions of **1** and **2** utilizing the electronic spectra of the systems. However, Dyall and coworkers[5] were able to estimate the equilibrium constant for the formation of **4** from **2** in more concentrated solutions by the use of pmr techniques. The equilibrium constant obtained for the formation of **4** (K = 2.46 ± 0.07 l. mol^{-1}) is significantly less than that previously reported[6] for **5** (K = 7700 l. mol^{-1}).[7]



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As a continuation of our studies of the structures and reactivities of Meisenheimer complexes, we have prepared and isolated **3**, **4**, and **5** as crystalline potassium salts and have studied the effects of replacing a nitro group by a cyano group on the structures of complexes from nitroanisoles and on the kinetics and thermodynamics of their formation and decomposition. We also wish to report the formation of transient 1,3-dimethoxy complexes as intermediates in the *in situ* generation of **3** and **4**, as well as solvent isotope effects, in CH$_3$OD, on the rate of formation and decomposition of **3** and, consequently, on its equilibrium constant.

Experimental Section

The solvents and reagents were prepared, purified, and standardized as previously described.[8] Methanol-O-*d* (>99%, Merck) was dried by and stored over Linde Type 4A Molecular Sieve. 2,4,6-Trinitroanisole (**6**) (Eastman) was recrystallized from aqueous methanol and dried *in vacuo:* mp 68°.

Compounds **1** and **2** were prepared by a modification of the procedure of Blanksma.[9] **2-Cyano-4,6-dinitroanisole** (**1**) was prepared by the addition of 3.0 g (17 mmol) of 2-cyano-4-nitroanisole[10] to 50 ml of fuming nitric acid at 2–3°. The reaction mixture was stirred at 60–70° for 50 min and at room temperature for 16 hr, cooled, and poured onto 150 g of ice. The flocculent white crystals which formed slowly were filtered, washed with distilled water, and dried *in vacuo:* mp 73° (lit.[11] mp 72°).

The same procedure was used to prepare **4-cyano-2,6-dinitroanisole** (**2**) from 5.0 g (28 mmol) of 4-cyano-2-nitroanisole[12] and 50 ml of fuming nitric acid with the exception that the reaction mixture was stirred at 60–70° for 1.5 hr. After drying *in vacuo*, the white crystals melted at 113–113.5° (lit.[5,9] mp 114°). The structures of **1** and **2** were verified by their pmr spectra (Table I); these parameters were in good agreement with the reported[4,5] values for these compounds.

Potassium 1,1-dimethoxy-2-cyano-4,6-dinitrocyclohexadienylide (**3**) was prepared by the addition of 0.371 ml (2.13 mmol)

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(6) V. Gold and C. H. Rochester, *J. Chem. Soc.*, 1687 (1964).

(7) A direct comparison of these equilibrium constants is only qualitatively indicative of the relative stabilities of **4** and **5**, since the two equilibrium constants were determined for drastically different concentration ranges. See Table VII of this study for the determination of K for **4** under conditions comparable with those for **5** by Gold and Rochester.[6]

(8) W. E. Byrne, E. J. Fendler, J. H. Fendler, and C. E. Griffin, *J. Org. Chem.*, **32**, 2506 (1967).

(9) J. J. Blanksma and C. H. Witte, *Rec. Trav. Chim.*, **60**, 811 (1941).

(10) H. P. Baudet, *ibid.*, **43**, 707 (1924).

(11) J. J. Blanksma, *ibid.*, **20**, 411 (1901).

(12) J. F. Mattaar, *ibid.*, **41**, 24 (1922).

of 5.73 M potassium methoxide in methanol to a solution of 0.449 g (2.16 mmol) of **1** in a mixture of 0.5 ml of methanol and 1 ml of dioxane. The red crystals which formed immediately were removed by filtration under dry nitrogen and washed with dry benzene and anhydrous ether. The product decomposed at 180° (lit.[4] dec pt 164–166°). The pmr spectrum of **3** in DMSO-d_6 (Table I) was essentially identical with that reported[4] with the exception of a higher field chemical shift for H-5. In addition, our sample of **3** contained approximately 0.3 mol of dioxane of crystallization (by pmr integration of dioxane singlet, τ 6.43 ppm[8]).

The same procedure and reactant quantities were used to prepare **potassium 1,1-dimethoxy-4-cyano-2,6-dinitrocyclohexadienylide (4)** from **2**; after washing and drying, **4** decomposed at 210°. The pmr spectrum of **4** in DMSO-d_6 (Table I) was essentially identical with that reported[5] with the exception of the presence of approximately 0.3 mol of dioxane of crystallization (by pmr integration of dioxane singlet).

Anal.[13] Calcd for $C_9H_8N_3O_6K$: C, 36.9; H, 2.75; N, 14.3; K, 13.3. Calcd for $C_9H_8N_3O_6K \cdot 0.25C_4H_8O_2$: C, 38.1; H, 3.20; N, 13.3; K, 12.4. Found: C, 37.04; H, 3.04; N, 13.31; K, 12.14.

Potassium 1,1-dimethoxy-2,4,6-trinitrocyclohexadienylide (5) was prepared by the addition of 0.842 ml (4.25 mmol) of 5.05 M potassium methoxide in methanol to a solution of 0.884 g (4.32 mmol) of **6** in 1 ml of dry dioxane. The reaction mixture was allowed to stand at room temperature under dry nitrogen for 15 min. The red crystals were removed by filtration under dry nitrogen and washed with dry benzene and anhydrous ether. After drying over phosphorus pentoxide, the complex decomposed at 200°. With the exception of a singlet due to the presence of 1 mol of dioxane of crystallization, the pmr spectrum of **5** in DMSO-d_6 was identical with that reported by Servis[14] for the *in situ* generated complex.

The attainment of equilibrium for the formation of complexes **3**, **4**, and **5** from **1**, **2**, and **6** (Table II) in dilute methanolic sodium methoxide solutions was followed at 470[3,4] (**1**), 520[3] (**2**), and 410[6] and 495 (**6**) mμ in the thermostated cell compartment of a Beckman DU-2 spectrophotometer using Teflon-stoppered 1-cm cells. An energy recording adaptor (ERA) was used in conjunction with a Hewlett-Packard recorder. The cell compartment was equipped with a set of dual thermospacers; the temperature was measured inside the cells and maintained within ±0.02°. Runs were started by injecting the appropriate methanolic solution of **1**, **2**, or **6** into the cell which contained the sodium methoxide solution. A thermostated Hamilton syringe was used and the solution was injected through a small bore in the Teflon stopper. The mixing time was established to be 0.1 sec by the neutralization reaction of 0.01 M sodium hydroxide by 0.01 M hydrochloric acid using p-nitrophenol as the indicator.[15]

The decomposition of the solid complexes in methanol and in aqueous buffers was followed by dissolving the appropriate solid complexes in the thermostated solution. The pH of the buffer solutions used for the studies of the decomposition of **3** was measured at 25.00° by an Orion Model 801 digital pH meter. The pD value was obtained from the relationship, pD = meter pH + 0.4.[16]

Pmr spectra (60 MHz) were obtained with a Varian Associates A-60 spectrometer at 25° (probe temperature maintained with a V6040 variable-temperature controller). Unless otherwise noted, all spectra were determined on solutions in DMSO-d_6 using tetramethylsilane (TMS) as an internal standard; chemical shifts are given on the τ scale in parts per million (ppm) relative to TMS (τ 10.00 ppm) and are accurate to ±0.03 ppm. Chemical-shift data were taken from spectra determined at a sweep width of 500 Hz. The reported coupling constant for **3** is the average of three determinations at 50-Hz sweep widths and is accurate to ±0.2 Hz. Owing to the instability and low concentration of the complex, the coupling constant reported for 1,3-dimethoxy-2-cyano-4,6-dinitrocyclohexadienylide (**10**) was estimated from 500-Hz sweep width spectra. The *in situ* reaction of methoxide ion with **1** and **2** was followed by examining the pmr spectra of solutions resulting from the dropwise addition of 5.05 M potassium methoxide in methanol to *ca.* 10% solutions of **1** and **2** in DMSO-d_6. The spectrum of each solution was determined immediately after the addition of methoxide ion and the spectrum was scanned repeatedly until no further changes were observed. The process was repeated until sufficient methoxide ion had been added to consume all of the starting **1** or **2**. The half-life of the transient species formed from **1** was sufficiently great so that its formation and conversion into **3** could be followed by recording 500-Hz sweep width (τ *ca.* 0–8 ppm) spectra at 250-sec sweep times. However, the transient species formed from **2** was sufficiently short-lived so that its formation and conversion into **4** could only be followed accurately by recording the spectra of the ring proton (τ *ca.* 1–4.7 ppm) and alkoxyl (τ 6–7.5 ppm) regions in separate runs at 250-sec sweep rates.

TABLE II

INTERACTION OF 2,4,6-TRINITROANISOLE [(3.4–5.0) × 10^{-5} M] WITH METHANOLIC SODIUM METHOXIDE[a]

10^3[NaOCH$_3$], M	10^3k_{obsd}	k_1, l. mol^{-1} sec^{-1} [b]
	At 5.75°	
1.09	2.34	
2.18	8.05	
3.27	15.5	
4.60	16.6	
5.45	21.0	
10.5	49.5	3.7[c]
	At 14.60°	
0.00	0.288[d,e]	
1.09	8.65	7.65
2.18	20.7	9.36
3.27	28.5	8.63
4.36	36.8	8.37
5.45	54.1	9.87
10.5	137.1	13.0
	At 25.00°	
0.00	1.04[d,e]	
0.00	1.0[f]	
0.00	0.5[g]	
0.00	2.01[h]	
0.246	1.21[g]	2.88[i,j]
0.410	2.38[g]	4.59[i,k]
1.05	17.48[d]	15.69[l]
1.05	20.0	18.09[l]
2.10	31.5[d]	14.52[l]
2.10	37.2	17.23[l]
3.15	59.9	18.69[l]
4.20	75.4	17.71[l]
4.20	77.0	18.09[l]
5.25	85.3[d]	16.06[l]
5.25	88.5	16.66[l]
5.45	109.4	19.88[l]

[a] Followed spectrophotometrically at 410 mμ unless stated otherwise. [b] Calculated from $k_1 = k_{obsd} - k_2/[\mathrm{NaOCH_3}]$ unless otherwise stated. [c] Slope of k_{obsd} *vs.* [NaOCH$_3$]. [d] Followed at 495 mμ. [e] Mean of five runs (each within ±3%) obtained by following the decomposition of the solid methoxyl complex (**5**) of 2,4,6-trinitroanisole in methanol: 10^3K_2 sec^{-1}. [f] Twice the value obtained by the use of eq 4,[19] since k_1 in eq 4 was defined in ref 19 as being equal to half of k_1 as defined in the present paper. [g] Determined by Gold and Rochester.[6] [h] Determined by Abe, Kumai, and Arai.[18] [i] Using $k_2 = 0.5 \times 10^{-3}$ sec^{-1}. [j] K = 5760 l. mol^{-1}. [k] K = 9180 l. mol^{-1}. [l] K = (17,000 ± 400) l. mol^{-1}.

Results

Using the fast mixing technique described in the Experimental Section, it was possible to follow the rate

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[13] The analysis was performed by Galbraith Laboratories, Inc., Knoxville, Tenn.

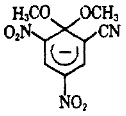
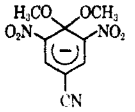
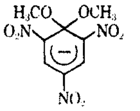
[14] K. L. Servis, *J. Amer. Chem. Soc.*, **89**, 1508 (1967).

[15] F. J. W. Roughton in "Techniques of Organic Chemistry," S. L. Friess, E. S. Lewis, and A. Weissberger, Ed., Vol. VIII, 2nd ed, Interscience Publishers, New York, N. Y., 1963, p 704.

[16] P. K. Glasoe and F. A. Long, *J. Phys. Chem.*, **64**, 188 (1960).

TABLE III

KINETIC AND THERMODYNAMIC PARAMETERS FOR THE FORMATION AND DECOMPOSITION OF CYANODINITRO- AND TRINITRO-SUBSTITUTED MEISENHEIMER COMPLEXES IN METHANOL AT 25.00°

	 3	 4	 5
k_1, l. mol^{-1} sec^{-1}	18.8 30.4[a]	6.1	17.3
10^3k_2, sec^{-1}	7.20 5.3[a]	22.0	1.04
K, l. mol^{-1}	2600 5736[a]	280	17,000
E_1,[b] kcal mol^{-1}	17.8 ± 0.8 17.1 ± 0.8[a]	13.9 ± 0.8	13.5 ± 1.0
$\Delta S_1^\ddagger$, eu	+5.0 ± 2.0 +3.8 ± 2.0[a]	−10.4 ± 2.0	−9.4 ± 2.0
E_2,[b] kcal mol^{-1}	14.4 ± 0.8 15.6 ± 0.8[a]	9.6 ± 0.8	19.0 ± 1.0
$\Delta S_2^\ddagger$, eu	−20 ± 2.0 −14 ± 2.0[a]	−32.0 ± 2.0	−4.8 ± 2.0

[a] Obtained in CH_3OD. [b] Arrhenius activation energy.

of equilibrium attainment for complexes **3**, **4**, and **5** at methoxide ion concentrations of $10^{-3} - 10^{-2}M$ by measuring the increase in absorbance at the appropriate wavelength.[17] Since the concentrations of the aromatic ethers **1**, **2**, and **6** were usually a hundredfold smaller than that of the methoxide ion, pseudo-first-order relationships were obtained in all cases. Such first-order plots for typical runs are given in Figure 1. Under the experimental conditions, the observed first-order rate constant for equilibrium attainment, k_{obsd}, is expressed by eq 1, where k_1 is the second-order rate

$$k_{obsd} = k_1[NaOCH_3] + k_2 \qquad (1)$$

constant for the formation of complexes **3**, **4**, and **5** and k_2 is the first-order rate constant for their decomposition. Using eq 1, plots of k_{obsd} against sodium methoxide concentration for all compounds at all temperatures within the range of methoxide ion concentrations used gave good straight lines whose slopes are k_1 and intercepts k_2. The first-order rate constants, k_2, for the decomposition of the solid complexes in methanol agreed very well with those values obtained from the intercepts. Figure 2 illustrates such plots for the reactions of **2** in methanol and methanol-O-*d* at 25.00°.

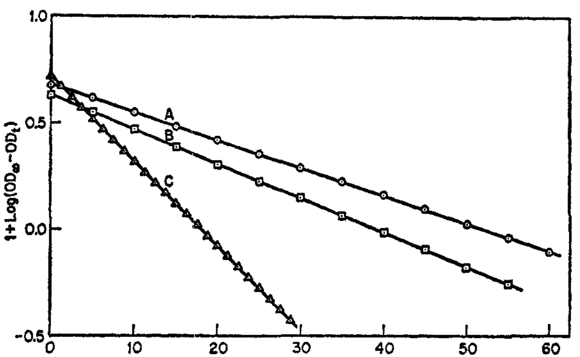


Figure 1.—Plot of 1 + log ($OD_\infty - OD_t$) against time for the attainment of equilibrium at 25.00° in MeOH: A, [4-cyano-2,6-dinitroanisole] = 5.44 × 10^{-5} M, [$NaOCH_3$] = 6.00 × 10^{-3} M; B, [2,4,6-trinitroanisole] = 4.41 × 10^{-5} M, [$NaOCH_3$] = 2.10 × 10^{-3} M; C, [2-cyano-4,6-dinitroanisole] = 3.26 × 10^{-5} M, [$NaOCH_3$] = 4.85 × 10^{-3} M.

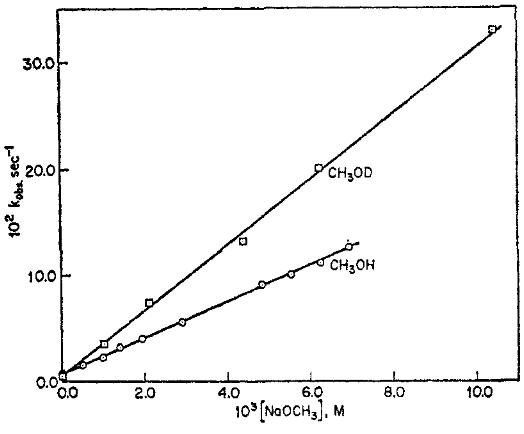


Figure 2.—Plot of 10^2k_{obsd} against $NaOCH_3$ concentration in CH_3OH and CH_3OD for the attainment of equilibrium for the methoxyl complex (**3**) of 2-cyano-4,6-dinitroanisole at 25.00°.

Although kinetic data for complex **5** have been previously obtained by other workers,[6,18] these data have been redetermined in the present study as a continuation of earlier work by one of us.[19] It was desired to determine the data for **5** under conditions comparable with those used for **3** and **4** and other recently examined Meisenheimer complexes.[8,20,21] The mean equilibrium constant (1.7 × 10^4 l. mol.$^{-1}$) for **5** at 25.00° is greater than that obtained (*e.g.*, 7.7 × 10^3 l. mol^{-1})[6] by previous workers,[6,18] possibly because their

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[17] Zollinger[4] and Dyall[5] and their coworkers reported that they were unable to follow the rate of equilibrium attainment for complexes **3** and **4**; erratic results were obtained using conventional mixing techniques. This difficulty was overcome in the present study by the use of rapid mixing techniques.

[18] T. Abe, T. Kumai, and H. Arai, *Bull. Chem. Soc. Jap.*, **38**, 1526 (1965).

[19] J. H. Fendler, *J. Amer. Chem. Soc.*, **88**, 1237 (1966).

[20] J. H. Fendler, E. J. Fendler, W. E. Byrne, and C. E. Griffin, *J. Org. Chem.*, **33**, 977 (1968).

[21] E. J. Fendler, J. H. Fendler, W. E. Byrne, and C. E. Griffin, unpublished results.

data were obtained at lower concentrations of sodium methoxide. However, values for k_2, E_2, and $\Delta S_2^\ddagger$ obtained in this work spectrophotometrically (see Table III) agreed extremely well with those previously obtained by carbon-14 exchange techniques.[19] When the concentrations of methoxide ion exceeded approximately $10^{-2} M$, both k_1 and K increased, presumably owing to specific salt effects and/or ion pairing.[22]

The kinetic data for the formation and decomposition of **3** in methanol and in methanol-O-*d* are presented in Tables IV and V. Table VI contains kinetic and thermodynamic data on the decomposition of **3** in H_2O and in D_2O. The rate constants for the formation and decomposition of **4** together with the corresponding equilibrium constants are collected in Table VII. A comparison of the kinetic and thermodynamic data for complexes **3**, **4**, and **5** is given in Table III. Allowing an over-all 5% error in the individual rate constants, at the temperature interval used, the statistical error in the activation energies is ±0.8 kcal mol^{-1} and in the activation entropies is ±2.0 eu.[25]

TABLE IV

INTERACTION OF 2-CYANO-4,6-DINITROANISOLE ($3.26 \times 10^{-5} M$) WITH METHANOLIC SODIUM METHOXIDE

$10^3[NaOCH_3]$, M	10^3k_{obsd}, sec^{-1}		
	6.70°[a]	14.30°[b]	25.00°[c]
0.00[d]	1.43	3.10	7.20
0.49			15.2
0.97	4.03	8.70	23.2
1.39			32.0
1.94	6.21	16.0	40.0
2.76		22.0	
2.91	9.70		56.8
3.88	11.3		
4.85	15.2	34.5	91.1
5.55			99.0
6.25			111.0
6.95			126.0
7.80		54.0	
9.70	27.3	66.7	
12.11	34.5		

[a] $k_1 = 2.68$ l. mol^{-1} sec^{-1}; $10^3k_2 = 1.43$ sec^{-1}; $K = 1870$ l. mol^{-1}. [b] $k_1 = 6.54$ l. mol^{-1} sec^{-1}; $10^3k_2 = 3.10$ sec^{-1}; $K = 2100$ l. mol^{-1}. [c] $k_1 = 18.8$ l. mol^{-1} sec^{-1}; $10^3k_2 = 7.20$ sec^{-1}; $K = 2600$ l. mol^{-1}. [d] Decomposition of the solid methoxyl complex (**3**) of 2-cyano-4,6-dinitroanisole in methanol; mean of five runs (each with a ±3% error).

TABLE V

INTERACTION OF 2-CYANO-4,6-DINITROANISOLE ($4.4 \times 10^{-5} M$) WITH SODIUM METHOXIDE IN METHANOL-O-*d*

$10^3[NaOCH_3]$, M	10^2k_{obsd}, sec^{-1}	
	14.6°[a]	25.00°[b]
0.00[c]	0.213	0.53, 1.41[d]
1.03	1.23	3.60
2.08	2.44	7.36
4.16		13.2
6.18	7.51	
6.24		20.0
8.32	10.12	
10.4	12.88	32.9

[a] $k_1 = 12.2$ l. mol^{-1} sec^{-1}; $10^3k_2 = 2.13$ sec^{-1}; $K = 5730$ l. mol^{-1}. [b] $k_1 = 30.4$ l. mol^{-1} sec^{-1}; $10^3k_2 = 5.3$ sec^{-1}; $K = 5736$ l. mol^{-1}. [c] Decomposition of the solid methoxyl complex (**3**) of 2-cyano-4,6-dinitroanisole in methanol-O-*d*; mean of five runs (each with a 3% error). [d] At 35.00°.

TABLE VI

DECOMPOSITION OF THE METHOXYL COMPLEX (**3**) OF 2-CYANO-4,6-DINITROANISOLE IN WATER AND IN DEUTERIUM OXIDE

$E(_{H^0} = 16.8 \pm 0.8$ kcal mol^{-};[a] $\Delta S^\ddagger_{H^0} = -15 \pm 2$ eu;[a,b]
$E_{D^0} = 18.5 \pm 1.0$ kcal mol^{-1};[c] $\Delta S^\ddagger_{D^0} = -9 \pm 3$ eu.[b,c])

pH[d]	10^3k_2, sec^{-1}	10^{-4} $k_2^{H^+}$, l. mol^{-1} sec^{-1} [e]
5.27	100	1.74
5.40	77.0	1.73
5.59	52.0	1.71
5.75	38.2	1.70
5.95	25.8	1.75
6.31	14.3	
6.67	9.89	
7.00[f]	9.43	
8.00[g]	8.00	
8.00[g,h]	1.62	
8.00[g,i]	3.64	
8.30[j,k]	5.52	
8.30[j,l]	1.46	
10.00[g]	8.05	
10.80[m]	7.95	

[a] Calculated from runs at 6.70, 14.30°, and at 25.00°. [b] Calculated at 25.00°. [c] Calculated from runs at 12.80 and at 25.00°. [d] Aqueous $KHC_8H_4O_4$ buffer (0.01 M) at 25.00° unless stated otherwise. [e] $k_2^{H^+} = k_2(\text{measured}) - k_2^0/[H^+]$, where $k_2^0 = 8.00 \times 10^{-3}$ sec^{-1}. [f] Aqueous KH_2PO_4 buffer (0.01 M). [g] Aqueous $Na_2B_4O_7$ buffer (0.01 M). [h] Mean of three runs at 6.70°. [i] Mean of three runs at 14.30°. [j] pD = 8.30 adjusted by 0.01 M $Na_2B_4O_7$ + NaOD. [k] Mean of three runs at 25.00°. [l] Mean of three runs at 12.80°. [m] Aqueous K_2HPO_4 buffer (0.01 M).

TABLE VII

INTERACTION OF 4-CYANO-2,6-DINITROANISOLE ($5.44 \times 10^{-5} M$) WITH METHANOLIC SODIUM METHOXIDE

$10^3[NaOCH_3]$, M	10^3k_{obsd}, sec^{-1}		
	14.60°[a]	25.00°[b]	35.00°[c]
0.00[d]	8.85	22.0	45.0
0.95			59.0
1.50		32.0	
1.90			73.0
3.00	14.0	41.0	86.0
4.10	15.6		
4.50		51.0	
4.85			120.0
5.02	17.5		
5.55			134.0
6.00		60.0	
6.95			151.0
7.50		69.5	
10.5	24.0		
15.0	33.7		

[a] $k_1 = 1.35$ l. mol^{-1} sec^{-1}; $10^3k_2 = 8.85$ sec^{-1}; $K = 153$ l. mol^{-1}. [b] $k_1 = 6.10$ l. mol^{-1} sec^{-1}; $10^3k_2 = 22.0$ sec^{-1}; $K = 280$ l. mol^{-1}. [c] $k_1 = 15.6$ l. mol^{-1} sec^{-1}; $10^3k_2 = 45.0$ sec^{-1}; $K = 345$ l. mol^{-1}. [d] Decomposition of the solid methoxyl complex (**4**) of 4-cyano-2,4-dinitroanisole in methanol; mean of four runs (each with a ±3% error).

The pmr spectra of the isolated complexes **3**, **4**, and **5** were in complete accord with the postulated structures

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(22) A similar situation has been noted for the interaction of methoxide ion with 2,4-dinitroanisole[23] and 2,4-dicyanoanisole.[24]

(23) C. F. Bernasconi, *J. Amer. Chem. Soc.*, **90**, 4982 (1968).

(24) J. H. Fendler, W. G. Ernsberger, E. J. Fendler, and C. E. Griffin, unpublished results.

(25) L. L. Schaleger and F. A. Long, *Advan. Phys. Org. Chem.*, **1**, 1 (1963).

and were essentially identical, as previously noted, with the spectra reported for these complexes by other workers.[4,5,14] The *in situ* generation of complexes **3** and **4** from **1** and **2** in DMSO-d_6 solution was also examined. Addition of methanolic potassium methoxide to a solution of **1** in DMSO-d_6 resulted in an immediate reduction in the intensity of the signals (0.93 and 5.73 ppm) attributable to **1** and the development of methoxyl singlets at τ 6.23, 6.92, and 7.03 ppm. A somewhat slower development of weak doublets at τ 1.47 and 4.50 ppm (J = 2–3 Hz) occurred. With time, the intensities of the 1.47-, 4.50-, 6.23-, and 6.92-ppm signals decreased and ultimately disappeared, while the intensity of the 7.03-ppm signal increased and doublets developed at 1.28 and 2.10 ppm (J = 2.8 Hz). With the addition of further methoxide ion, the transient signals were again observed and then decreased with a further increase in the intensity of the 1.28-, 2.10-, and 7.03-ppm signals. After the addition of 1 equiv of methoxide ion was completed, the stable spectrum consisted only of the signals associated with complex **3**, *i.e.*, 1.28, 2.10, and 7.03 ppm. Representative spectra for the *in situ* generation of **3** are shown in Figure 3. The rate of disappearance of the transient signals increased with the increase in methanol content of the system.[26]

Similar observations were made in the examination of the *in situ* generation of complex **4** by the addition of methanolic potassium methoxide to **2**. In this case, the transient singlets were observed at τ 2.25, 6.22, and 6.92 ppm.[27] The ultimate stable spectrum was that of **4** (Table I). The transient signals could also be observed if 0.75–1.0 equiv of methoxide ion was added in an instantaneous, rather than dropwise, fashion. However, the intensities of these signals were very weak and their lifetimes were quite short (<4 min) under these conditions.[28] Furthermore, the addition of base in this manner led to isotopic exchange of the ring protons of both intermediates and **3** and **4** with solvent deuterium.[29] No such exchange was noted for solutions of **3** and **4** in DMSO-d_6 in the absence of added methoxide ion. The *in situ* generation of **5** by the addition of methanolic potassium methoxide to a solution of **6** in DMSO-d_6 was reinvestigated following the general procedure of Servis.[14] The results of this study confirmed the previous observations of Servis and good agreement was obtained with the published[14] parameters for **5**, **6**, and the transient species (see Table I).

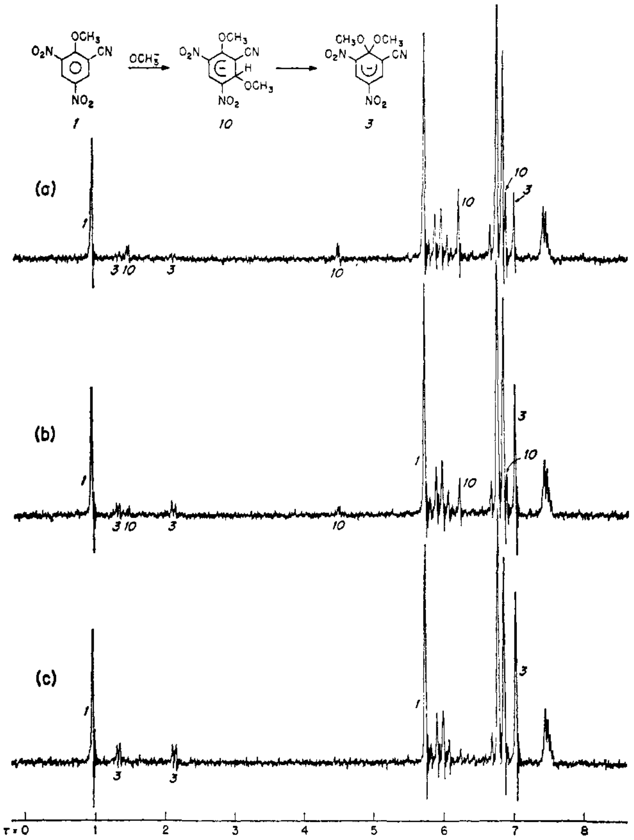

Figure 3.—Pmr spectra of the *in situ* generation of 1,1-dimethoxy-2-cyano-4,6-dinitrocyclohexadienylide (**3**) by the addition of 5.05 M methanolic potassium methoxide to 2-cyano-4,6-dinitroanisole (**1**) in DMSO-d_6 (a) 15, (b) 45, and (c) 105 min after the addition of the second drop of methoxide solution. Resonances are identified by structure numbers. Other resonances follow: τ 5.94 (q) and 6.83 (d), CH_3OH; 6.70 (s), H_2O impurity; 7.50 (m), DMSO-d_5 (s, singlet; d, doublet; q, quartet; m, multiplet).

Discussion

The ease of nucleophilic aromatic substitution and, hence, the stability of Meisenheimer complexes depends on the extent of the delocalization of the negative charge in the complex. Other factors remaining constant, the electron density at C-1, the point of attack, is decreased for benzenoid derivatives by substitutents in the order $N_2^+ > NO_2 > CN$.[30] The relative stabilities of the Meisenheimer complexes investigated in the present work, **5** > **3** > **4**, parallels the electron-withdrawing power and charge delocalization of these substituents and is best demonstrated by their respective equilibrium constant ratios. Replacing one nitro group by a cyano group in positions 2 and 4 causes, respectively, a 6.5- and a 60-fold decrease in the equilibrium constant for the formation of these complexes; *i.e.*, K_5/K_3 = 6.5, K_5/K_4 = 60 (Table III). Since the activating power of the nitro group for methoxydehalogenation is greater in the *para* than in the *ortho* position,[31] it is not surprising that replacement of the *p*-nitro group by a substituent with a weaker electron-withdrawing power causes a more dramatic change in the K values than the corresponding replacement in the *ortho* position. The generality of this effect is supported by the recent observation that the equilibrium constant (10 l. mol^{-1}) for the formation of the methoxyl complex (**7**) of 2,4-dicyano-6-nitroanisole in methanol at 25.00° is smaller than that observed for the formation of the

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[26] The addition of 4 drops of 5.05 M methanolic potassium methoxide to a ~10% solution of **1** was required for the complete consumption of **1**. The apparent half-life of the intermediate decreased from 60 min for the first drop to 15 min for the fourth drop.

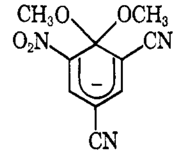
[27] The apparent half-lives for this intermediate are approximately one-half those observed[26] for the intermediate formed from **1**.

[28] Dyall and coworkers[5] have also examined the *in situ* generation of **4**, but failed to observe the transient signals cited above. However, their experimental conditions would probably preclude any such observation; base was added in one aliquot; and the solution was allowed to reach temperature (43°) equilibrium in the probe before measurements were made.

[29] A similar exchange process has been observed for the ring protons of the 1,1-dialkoxy complexes of 1-alkoxy-2,4-dinitronaphthalenes.[20]

[30] J. F. Bunnett and R. E. Zahler, *Chem. Rev.*, **49**, 273 (1951), and references cited therein.

[31] J. F. Bunnett and R. J. Morath, *J. Amer. Chem. Soc.*, **77**, 5051 (1955); W. Greizerstein and J. A. Brieux, *ibid.*, **84**, 1032 (1962).



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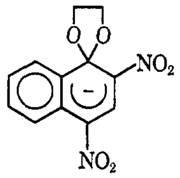
methoxyl complex of 2,6-dicyano-4-nitroanisole (K = 34 l. mol^{-1}).[21] Both Zollinger[4] and Dyall[5] and their coworkers have previously commented on the greater stabilizing effect of nitro groups in the *para* rather than in the *ortho* positions of Meisenheimer complexes, specifically **3**, **4**, and **5**. Molecular models of these complexes suggest the existence of a steric interaction between the geminal methoxyls and the nitro groups in the 2 and 6 positions, resulting in a twisting of the nitro groups from the plane of the ring.[5] The Hückel molecular orbital (HMO) calculations carried out by Zollinger and coworkers[4] were made for various angles of nitro group twist in **3** and showed the *para* substituent must carry the bulk of the negative charge.

The changes in the equilibrium constants for complexes **3**, **4**, and **5** are dependent to a larger extent on the changes in k_2 than those in k_1 (Table III). A similar situation has been encountered in comparing the rate constants for the formation and decomposition of the methoxyl complex (**8**) of 1-methoxy-2,4-dinitronaphthalene[20] and the methoxyl complex of 2,4-dinitroanisole.[23]

Comparing the energies of activation, changes in E_2 for complexes **3**, **4**, and **5** are also a better measure of the stabilities of these complexes than changes in E_1. Changes in structure in these complexes and their parent ethers **1**, **2**, and **6** are represented by the differences in the entropies of activation. Indeed, both the forward and reverse reactions for these complexes are dependent to a greater degree on changes in the entropies rather than in the enthalpies of activation. Entropy changes were also found to predominate over enthalpy changes in comparing the activation parameters for the formation and decomposition of **5** or **8** with those of the spiro complex (**9**) of 1-(β-hydroxyethoxy)-2,4-dinitronaphthalene.[32] The cyclic structure of **9** increases the orderliness of the system which is manifested by the large negative $\Delta S^‡$ value (−20 eu).[32] A different situation exists for structurally similar complexes in which case the driving force for the equilibrium is more enthalpy than entropy dependent. Indeed, changes in $\Delta H^‡$ rather than in $\Delta S^‡$ have been the rule for most nucleophilic aromatic substitutions,[33] presumably because the substrates were similar, generally activated only by nitro groups. The entropy of activation for the formation of **3** is some 15 eu higher than that for either **4** or **5** indicating that, other factors remaining constant, the transition state for the formation of **3** is less extensively solvated than that for **4** or **5**.



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The lesser stability of **3** relative to its picryl analog **5** is further demonstrated by its rate of decomposition in water (k_2^0 in Table VI) which is some 15-fold faster than that for **5**.[34] This reaction, like the analogous reactions for **5**[34] and **8**,[20] is strongly catalyzed by acids. The rate constant for the acid-catalyzed decomposition of **3** (1.73×10^4 l. mol^{-1} sec^{-1}, Table VI) is somewhat greater than that for **5**[34] (1.2×10^4 l. mol^{-1} sec^{-1}) or **8**[20] (1.5×10^4 l. mol^{-1} sec^{-1}). The variation in the acid-catalyzed rate constants, however, is somewhat less significant than that in k_2^0. The decomposition of **3** in water (k_2^0) is faster than in D_2O; k_2^0 in H_2O/k_2^0 in D_2O = 1.45 (Table VI). More significantly, the entropy of activation for this reaction is some 6 eu more positive in D_2O than in H_2O. Since deuterium oxide has a higher structural order than water,[35] the solvation requirements for the transition state in going from the complexes to the parent ethers is less in the former than in the latter case resulting in an increase in $\Delta S^‡$ in D_2O relative to H_2O.

The rate constant for the formation of **3** at 25.00° was considerably enhanced when CH_3OD was used as the solvent: $k_1^H/k_1^D = 0.6$ (Tables V and VI and Figure 2). The decomposition of **3**, however, was somewhat slower in the deuterated solvent than in methanol: $k_2^H/k_2^D = 1.36$. The solvent isotope effect on the equilibrium constant, K^H/K^D, is therefore 0.45. Bernasconi[23] recently observed a solvent isotope effect of 0.38 on the equilibrium constant for the formation and decomposition of potassium 1,1-dimethoxy-2,4-dinitrocyclohexadienylide ($K^H/K^D = 0.38$). Using the simple model of Bunton and Shiner,[36] Bernasconi calculated the theoretical solvent isotope effect for this equilibrium to be 0.47 and interpreted the observed result as a secondary solvent isotope effect.[23] A solvent isotope effect of $K_{EtOH}/K_{EtOD} = 0.54$ has recently been reported for the ethoxydechlorination of 2,4-dinitrochlorobenzene at 25.00°.[37] Assuming a covalently bound transition state, the calculated isotope effect agreed very well with the experimental value. The values for the solvent isotope effects reported in the present work agree extremely well with the other two reported isotope effect ratios,[23,37] the only such data available for kinetic solvent deuterium isotope effects for nucleophilic aromatic substitutions, and suggest that their magnitudes are typical for these reactions. The entropy of activation for the decomposition of **3** is some 6 eu more positive in CH_3OD than in CH_3OH ($\Delta S_2^‡$ values in Table III). This effect can be rationalized in a similar manner to that advanced for the relatively higher $\Delta S^‡$ values for the decomposition of **3** in D_2O (*vide supra*).

The pmr spectra (Table I) of solutions of the isolated complexes **3** and **4** in DMSO-d_6 were in full accord with their postulated structures and the observed parameters were consistent with those reported by other workers[4,5] for these complexes. However, pmr studies of the *in situ* generation of these complexes[1] yielded results not

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(32) W. E. Byrne, E. J. Fendler, J. H. Fendler, and C. E. Griffin, *J. Org. Chem.*, submitted for publication.

(33) D. L. Hill, K. C. Ho and J. Miller, *J. Chem. Soc., B*, 299 (1966).

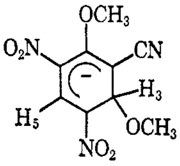
(34) J. Murto and J. Vainionpää, *Suomen Kem.*, **B39**, 133 (1966).

(35) G. Nemethy and H. A. Scheraga, *J. Chem. Phys.*, **41**, 680 (1964), and references cited therein.

(36) C. A. Bunton and V. J. Shiner, *J. Amer. Chem. Soc.*, **83**, 3207 (1961).

(37) I. R. Bellobono, P. Beltrame, M. G. Cattania, and M. Simonetta, *Tetrahedron Lett.*, 2673 (1968).

observed in earlier studies.[4,5] Addition of methanolic potassium methoxide to a solution of **1** in DMSO-d_6 (Figure 3) resulted in the formation of a set of transient signals at the expense of the signals originating from **1**.[38] With time, the intensities of these transient signals decreased and this decrease was accompanied by the formation of the signals due to the 1,1 complex **3**. These transient signals consisted of a two-proton AX system (τ = 1.47 and 4.50 ppm, J_{AX} = 2–3 Hz) and two methoxyl singlets at τ = 6.23 and 6.92 ppm, assignable as H-5, H-3, and the C-1 and C-3 methoxyls, respectively, of 1,3-dimethoxy-2-cyano-4,6-dinitrocyclohexadienylide (**10**). These assignments are made on the basis of the chemical shifts previously reported by Servis[14] for the analogous 1,3 complex **11** and for the 1,3 complex **12** (Table I) formed by the reaction of methoxide ion with **2** (*vide infra*). Servis has shown that the reaction of methoxide ion with 2,4,6-trinitroanisole (**6**) results in the initial formation of **11** followed by the appearance of 1,1 complex **5**.[14] The reported (Table I) chemical shifts for **11** follow: H-3, τ (ppm) 3.83; H-5, 1.58; C-1 OCH$_3$, 6.55; and C-3 OCH$_3$, 6.80.[14] The chemical shift of the higher field (6.92 ppm) methoxyl singlet of **10** is consistent with the attachment of that group to an sp^3-hydridized carbon, *e.g.*, 7.03 and 7.02 ppm for the C-1 methoxyls of **3** and **4** and 6.80 ppm for the C-3 methoxyl of **11**. The chemical shift of the lower field (6.23 ppm) methoxyl singlet of **10** indicates it to be attached to an sp^2-hybridized carbon, *e.g.*, 5.73, and 6.55 ppm for the C-1 methoxyls of **1** and **11**, respectively. These observed chemical shifts clearly establish complex **10** to be a 1,*x*- and not a 1,1-dimethoxycyclohexadienylide, but do not establish unequivocally the positional relationship of the two methoxyl groups,[39] although arguments can be made in support of the 1,3 relationship.



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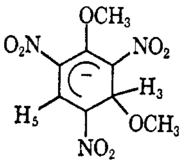

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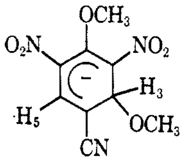

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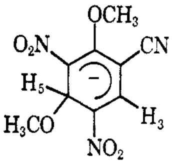
However, the positional relationship of the methoxyl groups and the structure of **10** is unequivocally established by a consideration of the ring-proton chemical shifts. The high field shift (4.50 ppm) observed for H-3 of **10** is consistent with an sp^3-hybrid environment for that proton; the chemical shift of H-3 of **11** is similarily to high field (3.83 ppm).[14] If the methoxyl group in **10** were attached to one of the substituted positions (2, 4, or 6), both of the ring protons would be expected to be in an sp^2 hybrid and would possess chemical shifts in the ranges reported (*ca.* 1–3 ppm) for similar ring protons in other Meisenheimer complexes (*e.g.*, **3** and **4**, Table I).[41] The chemical shift of H-5 of **10** (1.47 ppm) is typical for such protons and is quite similar to that observed for H-5 of **11** (1.58 ppm). Thus, the pmr parameters of **10** are consistent with the postulated structure.

It must be noted that **1** is unsymmetrical with respect to attack of methoxide ion at the unsubstituted ring positions and two isomeric complexes **10** and **13** could be formed. The 1,5 complex **13** would be expected to yield a spectrum of grossly similar appearance to that of **10**, but a consideration of chemical shifts indicates the observed intermediate to possess structure **10**. In complex **13**, the environment of H-5 is essentially identical with that of H-3 in **11**, *i.e.*, an sp^3-hybrid proton with two *o*-nitro groups, and the chemical shifts of the two protons would be expected to be quite similar. However, as noted above, the high field proton observed in **10** is more strongly shielded (0.67 ppm) than H-5 of **11**. H-3 of **10** has one *o*-nitro and one *o*-cyano group and, since the cyano group has been shown to be less strongly deshielding than the nitro group,[4,5] the resonance position of this proton would be expected to be to higher fields than those of H-3 of **11** and H-5 of **13**. In support of this argument, the chemical shift (4.52 ppm) of H-3 of **12** is essentially identical with that of H-3 of **10** (4.50 ppm); the environments of the two



13

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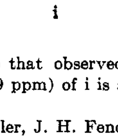
[38] Throughout this paper we have referred to the 1,3 complexes **10**, **11**, and **12** as transient intermediates in the formation of the 1,1 complexes **3**, **4**, and **5**. However, by the use of this terminology we do not intend to imply that the 1,3 complexes are direct precursors of the 1,1 complexes. Indeed, it is more probable that concurrent equilibria exist and that the 1,1 complexes are formed *via* the aromatic ethers **1**, **2**, and **6**, or similar ion-paired species, formed by the dissociation of the 1,3 complexes.

[39] A recent observation[40] of the pmr spectrum of 1,2-dimethoxy-2,4-dinitrocyclohexadienylide (i) has shown a similar chemical-shift relationship for the methoxyl resonances. The chemical shift (7.07 ppm) of the C-2 OCH$_3$ resonance of i is quite similar to that observed for the C-3 methoxyl of **10**, although the C-1 resonance (6.79 ppm) of i is at higher field than the corresponding resonance of **10**.



i

[40] W. E. Byrne, E. J. Fendler, J. H. Fendler, and C. E. Griffin, *J. Org. Chem.*, submitted for publication.

[41] The chemical shifts of H-3 and H-5 of i[39] are 1.35 and 2.15 ppm, respectively.[40]

protons are effectively identical. Similar conclusions regarding the structure of **10** can be drawn from a consideration of the chemical shift of the second (sp^2 hydrid) ring proton. In **10**, this proton (H-5) has two *o*-nitro substituents and, consequently, has the same environment as H-5 of **11**. As expected, the two protons have nearly identical chemical shifts (**10**, 1.47; **11**, 1.58 ppm). In **13**, the sp^2-hybrid proton (H-3) is flanked by one cyano and one nitro group and would be expected to be shifted to higher field, *e.g.*, H-5 of **12**. These conclusions are further supported, though less unequivocally, by a comparison of the methoxyl chemical shifts of **10**, **11**, and **12**. Apparently, attack of methoxide ion on **1** is specific at H-3 to yield **10**. If the isomeric complex **13** is formed, its concentration is too low to allow detection.

Similar observations were made in the study of the *in situ* generation of complex **4**. The reaction of methoxide ion with **2** results in a decrease in the intensities of the resonances of **2** and the development of transient signals ascribable to the 1,3 complex **12**: two proton AX system[42] (τ_3 4.52, τ_5 2.25 ppm) and two methoxyl singlets at τ 6.22 (C-1) and 6.92 (C-3) ppm. The observed spectrum is only consistent with structure **12**. Substitution of the methoxyl group at positions other than C-3 can be eliminated by arguments analogous to those advanced in the case of **10**. With time, the signals of **12** decrease and those attributable to **4** develop.

The only previous report of the formation of 1,3 complexes from the reactions of alkoxide ions with nitroaryl ethers is that of Servis,[14] who observed the initial formation of **11** in the *in situ* generation of **5** from the reaction of methoxide ion with 2,4,6-trinitroanisole (**6**). This observation has been considered to be unique in the literature of Meisenheimer complex chemistry.[43] Studies of the *in situ* reactions of 2,4-[8,43] and 2,6-dinitrophenyl[43] and 2,4-dinitronaphthyl[20] ethers with alkoxide ions have failed to yield evidence for the formation of complexes analogous to **10**, **11**, or **12**. In each of these cases, the attack of alkoxide ion is either specific at the C-1 position to yield the 1,1-dialkoxy complexes or the 1,3 complexes, if formed by attack at C-3, rearrange too rapidly to be detected.[28]

In an attempt to provide a rationale for the results obtained by Servis,[14] Crampton and Gold[44] have suggested that the 1,1 complex **5** is a less strained structure than the initial reactant **6**, but that the transition state leading to its formation is more strained. Consequently, the initial attack of methoxide ion occurs at C-3 to yield the thermodynamically less stable **11**, which rearranges to **5**. Strain considerations would be less important in the transition state leading to the formation of **11** than in the formation of **5**. On this basis, the observation of the formation of 1,3 complexes in the reactions of methoxide ion with **1** and **2** is expected since the steric situation for these ethers is similar to that for **6**. Also, the failure to observe the formation of 1,3 complexes in reactions of alkoxide ions with 2,4-dinitrophenyl ethers[8,43] supports the steric rationalization since, in these ethers, the transition states leading to the formation of the 1,3 complexes would be expected to be more strained than those leading to the formation of the observed 1,1 complexes. However, the failure to observe 1,3 complexes as intermediates in reactions leading to the formation of the 2,6-dinitrophenyl[43] and 2,4-dinitronaphthyl[20] analogs of **5** is unexpected and inconsistent with the steric argument. In the 2,6-dinitrophenyl case, the transition state leading to the formation of the 1,3 complex would be expected to be quite strongly favored by steric factors at the expense of the transition state leading to the 1,1 complex. Consequently, the over-all free energies of systems consisting of aryl ether, 1,3 and 1,1 complexes must be delicately balanced between the relative abilities of the ring substituents to carry the negative charge and specific solvent and steric requirements. From the results observed in this study, it appears that a possible correlation exists between the stabilities of the various complexes in methanol and the equilibrium between 1,1 and 1,3 complexes. The formation of 1,3 complexes is observed in reactions leading to the more stable 1,1 complexes **5**, **3**, and **4** (K = 17,000, 2600, and 280, respectively, Table III). In the *in situ* generation of the less stable 1,1-dimethoxy complexes from 1-methoxy-2,4-dinitronaphthalene (**8**, K = 230),[20] 2,4-dinitroanisole ($K = 2.53 \times 10^{-5}$),[23] and 2,6-dinitroanisole ($K = 9.85 \times 10^{-20}$),[45] 1,3-complex formation is not observed.[46] However, it is apparent that neither complex stability nor steric considerations can provide a full rationalization for the occurrence of kinetic *vs.* thermodynamic control in reactions leading to the formation of 1,3 complexes. Although the above results indicate complex stability to be an important determinant, it has been shown recently[1] that 1,3-complex formation is observed for a system in which the 1,1 complex is less stable than **8**. Thus, the reaction of methanolic potassium methoxide with a solution of 2,4-dicyano-6-nitroanisole in DMSO-d_6 results in the formation of 1,3-dimethoxy-2,4-dicyano-6-nitrocyclohexadienylide (**14**); on standing, **14** rearranges to the 1,1 complex **7**.[1,37] The stability of **7** (K in CH_3OH at 25.00° = 10)[21] has been shown to be less than that of **8**. A full understanding of the factors promoting the formation of the presumably less thermodynamically stable 1,3 complexes as transients in the formation of 1,1 complexes must await more extensive studies of these systems. However, it is highly probable that specific solvation effects play an important role in the observation of kinetic control in these reactions. The utilization of equilibrium constants determined in dilute methanolic solutions as indicators of complex stabilities for comparison with the observation of kinetic control in more concentrated solutions in DMSO may not be valid.

The selectivity observed in the reaction of methoxide ion with **1** to yield the 1,3 complex **10** rather than the

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(42) The coupling of these protons was not resolved, but, from a consideration of the line widths of the resonances, was apparently of the same order (2–3 Hz) as the analogous couplings in **10** and **11**.

(43) R. Foster and C. A. Fyfe, *Rev. Pure Appl. Chem.*, **16,** 61 (1966).

(44) M. R. Crampton and V. Gold, *J. Chem. Soc.*, *B*, 893 (1966).

(45) F. Terrier, P. Pastour, and R. Schall, *Compt. Rend.*, **260,** 5783 (1965).

(46) Because of the similarity in the stabilities of **4** and **8** in methanol, the reaction of methanolic potassium methoxide with 1-methoxy-2,4-dinitronaphthalene was reinvestigated in this study using the experimental conditions employed for the detection of intermediate **12**. However, no evidence for the formation of a 1,3 complex was obtained, confirming the results of the earlier study[20] of this reaction.

isomeric **13** is a further reflection of the relative stabilizing effects of nitro and cyano groups on Meisenheimer complexes (*vide supra*). In **10**, the entering methoxyl group is situated *para* to the nitro substituent, while in the presumably less stable **13** an *ortho* relationship is present. This selectivity in substitution is paralleled by the relative stabilities of complexes **3** and **4**. In the former complex, the entering methoxyl group is *para* to a nitro function and the complex is more stable by an order of magnitude than **4**, a complex for which only *ortho* relationships between the entering methoxyl and nitrogroups are present. Similarly, in the reaction of methoxide ion with 2,4-dicyano-6-nitroanisole, attack of methoxide ion is specific at the position *para* to the nitro substituent to yield **14**; no evidence was obtained for attack of methoxide at the position *ortho* to the nitro group.[1] It is thus apparent that the same factors which determine the relative stabilities of the cyanodinitro complexes **3** and **4** and the dicyanonitro complex **7** also determine the position of attack in the formation of the 1,3 complexes **10** and **14**.

Registry No.—**1**, 19019-04-6; **2**, 19018-96-3; **3**, 12247-59-5; **4**, 12321-51-6; **5**, 1270-28-6; **6**, 606-35-9; **10**, 12321-50-5; **12**, 12321-49-2; sodium methoxide, 124-41-4;.

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The Chemistry of Cyclic Enamino Ketones. IV. Factors Affecting C and O Alkylation[1]

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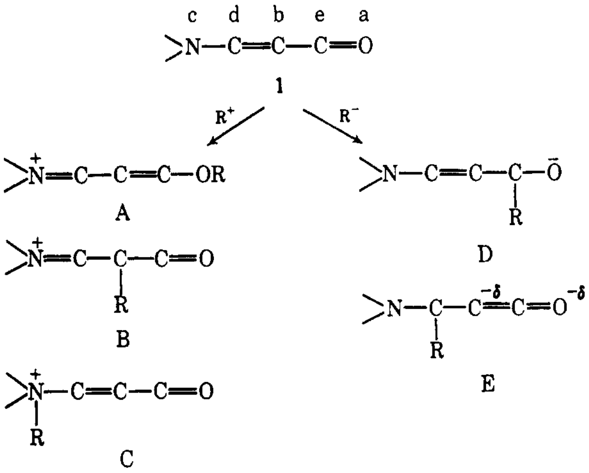
The reaction of *cis*- and *trans*-enamino ketones with alkyl halides has been investigated with emphasis upon solvent and steric effects. For *cis*-enamino ketones, aprotic solvents produced mixtures of the C- and O-alkyl salts, whereas protic solvents yielded mixtures of the O-alkyl and O-protonated salts. Possible mechanisms leading to the latter products are discussed. Alkylation on nitrogen was never observed in any of the cases examined. The results of this study clearly demonstrate the ability of the solvent to decide the course of an enamino ketone alkylation reaction. With data from enamino ketones having six-, seven-, and eight-membered fused rings now available, the effect of ring size on the site of alkylation is summarized as well as the influence of the alkyl halides. The reactions of *trans*-enamino ketones with alkyl iodide are essentially insensitive to solvent and gave exclusively O-alkyl derivatives.

The enamino ketone (β-amino-α,β-unsaturated carbonyl) moiety, **1**, represents an area of considerable synthetic scope when one considers that there are present in this group three nucleophilic sites (a, b, and c) and two electrophilic sites (d and e) available for reaction. Thus, electrophilic addition could lead to adducts A, B, and C while nucleophilic addition could provide D and E (Scheme I). If the factors affecting the sites of addition can be understood and brought under control, there would be available a synthetic pathway to a variety of substances inaccessible by other means. We have previously demonstrated, in brief reports,[3,4] that the enamino ketone group is indeed versatile and capable of reacting with electrophilic and nucleophilic agents under varying sets of conditions. The problem of the site of alkylation on systems such as **1** (leading to A, B, and C) appeared to be sufficiently complex, however, that further studies were obviously necessary. A search of the literature revealed that Leonard and Adamcik[5] had made the only systematic attempt to determine sites of alkylation in acyclic enamino ketones, **2**, and monocyclic *trans*-enamino ketones, **3**. The reaction conditions were limited to prolonged heating of the substrate with an excess of alkyl halide.

Scheme I



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[1] This study supported by the National Institutes of Health (RG-06248-08).

[2] Taken from the Ph.D. Dissertation of A. H. Reine, June 1968. Financial support (to A. H. Reine) by the Eli Lilly Co., Indianapolis, Ind., is gratefully acknowledged.

[3] A. I. Meyers, A. H. Reine, and R. Gault, *Tetrahedron Lett.*, No. 41, 4049 (1967).

[4] A. I. Meyers and S. Singh, *ibid.*, No. 52, 5319 (1967).

[5] N. J. Leonard and J. A. Adamcik, *J. Amer. Chem. Soc.*, **81**, 595 (1959), and previous references cited therein.