Reactions of Substituted Phenylnitromethane Carbanions with Aromatic Nitro Compounds in Methanol: Carbanion Reactivity, Kinetic, and Equilibrium Studies

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ABSTRACT: The feasibility of carrying out nucleophilic addition from electron-deficient heteroaromatics has been addressed through a detailed investigation of the interaction of a two 7-substituted-nitrobenzofurazan (R = OMe **2a**; R = Cl **2b**) with a series of substituted-nitroaryl anions (X = 4-NO_2 **1a**; X = 3-NO_2 **1b**; X = 4-CN **1c**; X = 4-Br **1d**), all reactions first lead to the quantitative formation of the σ-adducts **3a–d** and **4a–d** arising from covalent addition of the nucleophile to the C-5 carbon. The rate and equilibrium constants for the formation of σ-adducts **3a–d** and **4a–d** (k_5, K_5) together with the rate constants for their decomposition (k_{-5}) have been determined in methanol at 25°C, allowing a determination of intrinsic rate constants, $k_0 = 0.03$, the lower k_0 value reflects the very strong salvation by methanol of the negative charge on the nitro group. The discovery of a linear correlation between the E and pK_a^{MeOH} parameters allows a calibration of the electrophilicity power of **2a** and **2b**, $E = -11.67$ and -10.29, respectively. Applying the general approach to nucleophilicity/electrophilicity recently developed by Mayr et al. through the relationship $\log k = s(E + N)$, a successful ranking of our nitroaryl anions **1a–d** on the general nucleophilicity scale (N) has been carried out. The

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N values of **1a–d** are found to cover a range from 15.78 to 16.69. The results are compared with previously reported data in water and DMSO. © 2014 Wiley Periodicals, Inc. Int J Chem Kinet 46: 477–488, 2014

INTRODUCTION

There is much current interest in comparing nucleophilicities, particularly those of carbon nucleophiles [1–3]. The reactions of carbanions stabilized by ester, acyl, cyano, and nitro groups with a series of benzyl cations have been studied to assess nucleophilicities [4–6]. Although these studies provided useful relationships, they revealed that relative nucleophilicities may be strongly influenced by the solvent, e.g., water versus DMSO, and that often there is a poor correlation between the nucleophilic reactivity and the pK_a values of the corresponding carbon acids [4–6]. This also indicates that the nucleophilic reactivities of carbanions can be strongly affected by substituent variation in a methanol solution.

The nucleophilicities of many carbanions have been measured, and values for some nitroalkane anions have been assessed by measuring rate constants for their reactions with benzhydrylium cations and quinone methides in water [4], DMSO [4], and methanol–acetonitrile [6]. Conversely, the electrophilicities of some electrophiles and superelectrophiles, including, respectively, 1,3,5-trinitrobenzene (TNB) and 4,6-dinitrobenzofuroxan (DNBF), have been determined by measuring the rate constants for their reactions with some standard nucleophiles, including *N*-methylpyrrole and indole, in acetonitrile [7,8]. It is known that nitroalkane anions may react to form anionic σ-adducts [1], such as **1**, with DNBF [9,10] and TNB [11], and there is one report of the reaction of the 2-nitropropenide anion with 4-nitrobenzofurazan [12]. However, no rate constants have been reported for the reactions of nitroaryl anions with substituted (C-7) neutral electron-deficient heteroaromatic compounds and it is not known whether the relative product corresponds to a substitution product or σ-adduct formation.

Previous reports have largely concentrated on determining the structures of the adducts formed, although kinetic data are available for the reactions of nitroalkane anions with TNB in methanol [13] and with DNBF in water [9]. In a previous study, kinetic and equilibrium measurements of the reactions of carbanions derived from nitroalkane and benzyltriflone anions with nitrobenzofurazan derivatives in methanol were also investigated [14,15]

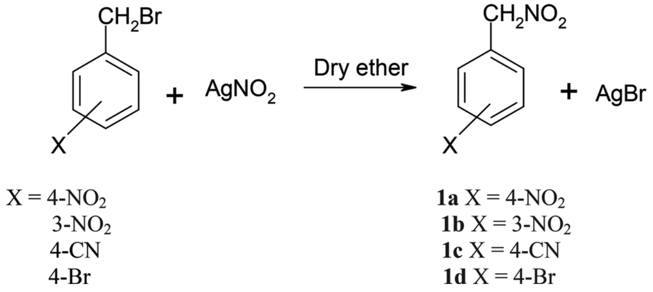
The present work is designed to extend our understanding of how nitro groups impact carbanion addition rates. To that end, the kinetics of the σ-adduct forming reactions of a series of nitro-substituted phenylnitromethane carbanions to 7-methoxy-4-nitrobenzofurazan **2a** and 7-chloro-4-nitrobenzofurazan **2b** have been probed via ^{1}H NMR studies in DMSO-d_6. In addition, kinetic measurements for the reactions of **2a** and **2b** with anions derived from 4-nitrophenylnitromethane **1a**, 3-nitrophenylnitromethane **1b**, 4-cyanophenylnitromethane **1c**, and 4-bromophenylnitromethane **1d** were obtained in methanol to allow comparison of the results with both the reactions of nitromethane anions with 4-nitrobenzofurazan derivatives [14] and the reactions of carbanions stabilized by trifluoromethylsulfonyl groups [15–18].

Our results additionally have relevance to studies of the nucleophilic substitution of hydrogen by the vicarious substitution mechanism [19], a process that allows the formation of neutral carbon–carbon bonded species. There is evidence that the first step in this pathway involves carbanion addition to give a σ-adduct [20,21], and the present work can provide insight into the factors governing the kinetics of this process.

EXPERIMENTAL

7-Chloro-4-nitrobenzofurazan **2b** (Sigma-Aldrich; 98%) and benzofurazan (Sigma-Aldrich; 97%) were the purest available commercial samples. 4-Nitrobenzofurazan was prepared by the nitration of benzofurazan using 1 equiv of nitric acid (Sigma-Aldrich; 70%) in 6 equiv of sulfuric acid 98% at 5°C: mp 92°C (lit. mp 93°C [22]).

7-Methoxy-4-nitrobenzofurazan **2a**, mp 113°C (lit. mp 115°C [23]), was prepared by the reaction of 7-chloro-4-nitrobenzofurazan with 1 equiv of sodium methoxide in methanol at 40°C for 1 h. Solutions of sodium methoxide were prepared by dissolving clean sodium in methanol under nitrogen. Cloudiness in the resulting solutions was removed by centrifugation. Other reagents, such as 4-nitrobenzyl bromide, 3-nitrobenzyl bromide, 4-cyanobenzyl bromide, 4-bromobenzyl bromide, silver nitrite, triethylamine, sodium methoxide, and diethyl ether (all Aldrich products), were available of the highest quality and were recrystallized or distilled before use whenever necessary. Methanol was used without further purification.



Scheme 1

NMR spectra of the parent compounds **2a** and **2b** were carried out in DMSO-d_6 in the absence of reagents, and then carried out in separate experiments by adding the reagents **1a–d** and following the spectral changes toward formation of σ-adducts **3a–d** and **4a–d**.

UV–vis spectra and kinetic measurements were made with a Shimadzu UV-2101 PC or SPECord® Analytik Jena spectrophotometer. First-order rate constants, precise to ±5%, were evaluated following the appearance of the σ-adduct **3a–d** $390 < \lambda < 410$ nm and **4a–d** $418 < \lambda < 430$ nm. All reactions in this study obeyed the pseudo–first-order kinetics under conditions of excess nitroaryl anions **5a–d**. Pseudo–first-order rate constants, k_{obs}, were obtained from the correlation $\ln(A_\infty - A_t)$ against time, where A_∞ refers to the absorbance of the product **3a–d** and **4a–d** at the completion of the reaction and A_t refers to the absorbance at time t.

The pseudo–first-order rate constants, k_{obs}, for all the reactions obeyed Eq. (1):

$$k_{\text{obs}} = k_5[5] + k_{-5} \tag{1}$$

From the slopes and intercepts of the plots $k_{\text{obs}} = k_5$ [**5**], the second-order rate constants k_5 and first-order rate constants k_{-5} were readily derived, respectively.

Preparation of 4-Nitrophenylnitromethane 1a and 3-Nitrophenylnitromethane 1b

The preparations of **1a** and **1b** were previously reported [24] (Scheme 1). An example procedure follows: To a mixture of silver nitrite (50 g, 0.325 mol) in dry diethyl ether (500 mL), a solution of 4-nitrobenzyl bromide (21.6 g, 0.1 mol) was added in dry diethyl ether (800 mL) over 1 h. The mixture was stirred at 0°C for 24 h. After filtration of the silver salts, the filtrate was evaporated via a rotary evaporator to afford a solid residue, which was recrystallized from ethanol. **1a**: mp 90–91°C. **1b**: mp 91–92°C.

Preparation of 4-Cyanophenylnitromethane 1c and 4-Bromophenylnitromethane 1d

The preparations of **1c** and **1d** were previously reported [25] (Scheme 1). An example procedure follows: 4-Cyanobenzyl bromide (12.5 g) and silver nitrite (9.0 g) were refluxed in dry diethyl ether for 2 h. Silver bromide was filtered, and the filtrate was concentrated. Recrystallization from ethanol gave crystals of **1c**, mp 46°C. Compound **1d** was prepared from 4-bromobenzyl bromide in a similar manner, mp 84°C.

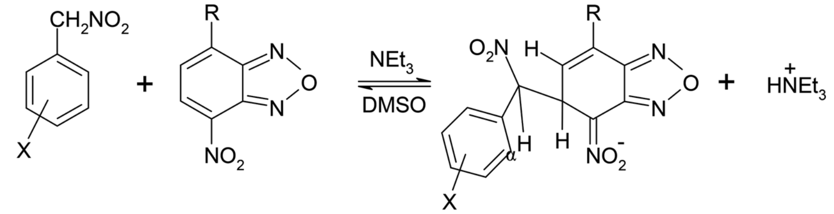
RESULTS AND DISCUSSION

^{1}H NMR Studies

^{1}H NMR measurements were performed in DMSO-d_6 to determine the structures of the intermediates and products produced in the reactions under investigation. These processes are summarized in Scheme 2. Spectral data for mixtures of the nitrobenzofurazan derivatives with two molecular equivalents each of the phenylnitromethane derivatives and triethylamine were recorded after mixing and the instantly formation of products **3a–d** and **4a–d**.

Spectra of 7-methoxy-4-nitrobenzofurazan **2a** (0.2 mol dm^{-3}), phenylnitromethane derivatives (0.7 mol dm^{-3}), and triethylamine (0.5 mol dm^{-3}) in DMSO-d_6 were obtained. Data for the parent molecules are listed in Table I, and chemical shifts of the σ–adducts are presented in Table II. The methoxy signal of 7-methoxy-4-nitrobenzofurazan **2a** appeared at δ 3.68 ppm.

The signals due to unreacted 7-methoxy-4-nitrobenzofurazan were seen at δ 8.76, 7.10, and 4.22 ppm. No change in the spectrum occurred after 24 h. With 7-chloro-4-nitrobenzofurazan **2b** (0.2 mol dm^{-3}), phenylnitromethane derivatives (0.5 mol dm^{-3}), and triethylamine (0.5 mol dm^{-3}) in DMSO-d_6 (Table II), the spectra indicate rapid and irreversible decomposition, thus no products could be positively identified.



1 **2**

1a X = 4-NO$_2$ **2a** R = OMe **3**
1b X = 3-NO$_2$ **2b** R = Cl **4**
1c X = 4-CN
1d X = 4-Br

Scheme 2

Table I ^{1}H NMR Data^a for Parent Molecules in DMSO-d_6

	δ, Chemical shift						
Compound	H_5	H_6	Me	CH_α	$J_{5,6}$		
7-Methoxy-4-nitrobenzofurazan, **2a**	8.75	7.06	4.21	-	8.6	-	-
7-Chloro-4-nitrobenzofurazan, **2b**	8.68	8.03	-	-	7.6	-	-
	$H_{2'}$	$H_{4'}$	$H_{5'}$	$H_{6'}$	CH_α	$J_{4',5'}$	$J_{5',6'}$
3-Nitrophenylnitromethane, **1b**	7.89	7.82	7.75	7.89	5.51	8.0	8.0
	H_5	H_6	Me	CH_α	$H_{2',6'}$	$H_{3',5'}$	$J_{2',3'}$
4-Nitrophenylnitromethane, **1a**	-	-	-	5.60	7.80	7.75	8.0
4-Cyanophenylnitromethane, **1c**	-	-	-	5.48	7.78	7.70	8.0
4-Bromophenylnitromethane, **1d**	-	-	-	5.30	7.45	7.69	8.0

^{a}Coupling constants are in hertz.

Table II ^{1}H NMR Data^a for σ-Adducts Formed with Phenylnitromethane Derivatives in DMSO-d_6

Compound	δ, Chemical shifts									
7-methoxy-4-nitrobenzofurazan, **2a**										
	δ H_5	δ H_6	CH_α	$H_{2',6'}$	$H_{3',5'}$	$J_{5,6}$	$J_{H_7H\alpha}$	$J_{H_6H_5}$	$J_{2',3'}$	
4-nitrophenylnitromethane, **1a**	5.01	5.80	6.40	7.77	7.74	6.2	1.2	0.8	8.8	
4-cyanophenylnitromethane, **1c**	4.90	5.70	6.25	7.74	7.70	6.2	1.2	0.8	8.8	
4-bromophenylnitromethane, **1d**	4.80	5.63	6.20	7.41	7.68	6.2	1.2	0.8	8.8	
	δ H_5	δ H_6	CH_α	$H_{2'}$	$H_{4'}$	$H_{5'}$	$H_{6'}$	$J_{5',6'}$	$J_{H_7H\alpha}$	$J_{H_6H_5}$
3-nitrophenylnitromethane, **1b**	4.99	5.75	6.35	7.91	7.84	7.77	7.90	8.2	1.2	0.8
7-chloro-4-nitrobenzofurazan, **2b**										
	δ H_5	δ H_6	CH_α	$H_{2',6'}$	$H_{3',5'}$	$J_{5,6}$	$J_{H_7H\alpha}$	$J_{H_6H_5}$	$J_{2',3'}$	
4-nitrophenylnitromethane, **1a**	5.90	6.86	6.80	7.79	7.76	6.0	1.1	0.8	8.8	
4-cyanophenylnitromethane, **1c**	5.03	6.50	6.40	7.76	7.73	6.0	1.1	0.8	8.8	
4-bromophenylnitromethane, **1d**	4.99	5.96	6.30	7.47	7.70	6.0	1.1	0.8	8.8	
	δ H_5	δ H_6	CH_α	$H_{2'}$	$H_{4'}$	$H_{5'}$	$H_{6'}$	$J_{5',6'}$	$J_{H_7H\alpha}$	$J_{H_6H_5}$
3-nitrophenylnitromethane, **1b**	4.51	5.77	6.39	7.94	7.88	7.79	7.93	8.2	1.1	0.8

^{a}Coupling constants are in hertz.

Generally, the recorded results indicate that, for the reactions of **2a** and **2b** with some selected nucleophiles, 5-adducts formation is kinetically favored.

This notice of the reactivity pattern has been recorded for some reactions with methoxide ions [23,28,30] in methanol, hydroxide ions [29] in water, sulfite ions [22] in water, and aliphatic amines [31] in DMSO. The brief explanation of this phenomenon is that the 5-adducts have fewer resonance forms available to delocalize negative charge than the 7-adducts, leading to smaller kinetic barriers and also the smaller thermodynamic stabilities [12,31]. It is interesting to cite that neither **2a** nor **2b** showed no evidence for nucleophilic attack at the substituted 7-position. This can be explained through the steric and electrostatic repulsion between the entering carbon base and the leaving group [23,29].

Kinetic and Equilibrium Measurements in Methanol

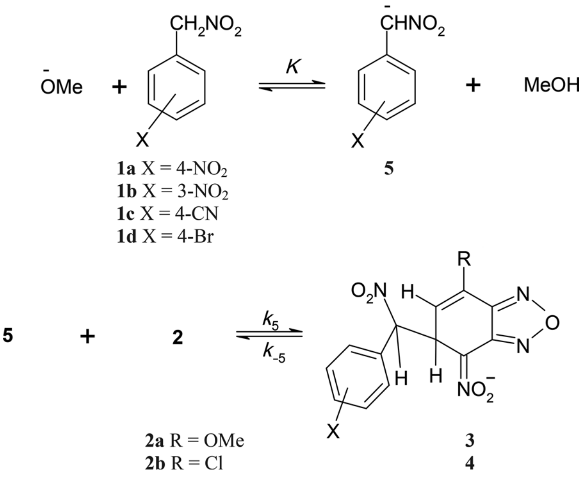
These measurements were made spectrophotometrically using phenylnitromethane anion derivatives, which were generated in situ from the parent phenylnitromethane derivatives and sodium methoxide. Owing to the known reactions of 4-nitrobenzofurazans with methoxide [20,22,27], it was necessary to reduce the concentration of free methoxide ions to low values; this was accomplished by working with [phenylnitromethane] ≥ [MeO$^-$] stoichiometries.

Kinetic measurements were made at 25°C, with concentrations of **1a–d** and methoxide in excess of the concentrations of **2a** and **2b**. Under these conditions, first-order kinetics were observed; the rate constant was designated as k_{obs}. These processes are interpreted in terms of Scheme 3. It is known that the first step, the equilibration of the phenylnitromethane derivatives with methoxide, is rapid [13]. In view of the ^{1}H NMR results and the known reactivity with other nucleophiles [22–29], the process that we observed was likely the formation of the 5-adduct. Therefore, Eq. (1) will apply:

$$k_{obs} = k_5[\mathbf{5}] + k_{-5} \qquad (1)$$

7-Methoxy-4-nitrobenzofurazan, 2a

The parent **2a** exhibited a UV maximum at 375 nm, $\varepsilon = 9.1 \times 10^3$ dm^3 mol^{-1} cm^{-1}. In the presence of the anions of **1a–d**, a process, k_{obs}, was observed in which the maximum shifted to 390 nm with increased absorbance. Kinetic measurements obtained for the reaction of **2a** (5×10^{-5} mol dm^{-3}) with 3-nitrophenyl compound **1b** (0.07 mol dm^{-3}) and methoxide in methanol are reported as specimen data in Table III. A linear plot of k_{obs} versus [**4**] gives a value for k_5. The plot, according to Eq. (1) and shown in Fig. 1, was linear, giving the values $k_5 = 3.50 \times 10^2$ dm^3 mol^{-1} s^{-1} and $k_{-5} = 1.10 \times 10^{-3}$ s^{-1}. Combining these values gave $K_5 = k_5/k_{-5}$. The reactions with **1a**, **1c**, and **1d** resulted in values for k_5 of 2.41×10^2, 5.31×10^2, and 8.35×10^2 dm^3 mol^{-1} s^{-1}, respectively. Values for k_5, k_{-5}, and K_5 are listed in Table IV. It should be noted that the equilibrium constant [28] for the formation of the 5-methoxy adduct was 22 dm^3 mol^{-1}; thus, at the equilibrium methoxide concentrations used here, there was no interference from this process. Methoxide may also be added at the 7-position to give a dimethoxy adduct. However, the rate constant, 14.5 dm^3 mol^{-1} s^{-1}, is sufficiently small that this process [23] cannot compete kinetically with carbanion addition at the 5-position. As found from the ^{1}H NMR spectra, there was no evidence for elimination from the 5-adducts to give alkene derivatives.



Scheme 3

Table III Kinetic Data for the Reaction of 7-Methoxy Substrate **2a**^{a} with **1b**^{a} and Methoxide in Methanol at 25°C

[NaOMe] (mol dm^{-3})	[MeO$^-$]$^b_{eq}$ (mol dm^{-3})	[3-nitro anion]^b (mol dm^{-3})	k_{obs}^{c} (s^{-1})
0.007	1.201×10^{-11}	6.99×10^{-3}	0.61×10^{-1}
0.010	1.720×10^{-11}	10.01×10^{-3}	0.35×10^{-1}
0.013	2.232×10^{-11}	11.30×10^{-3}	0.39×10^{-1}
0.017	2.920×10^{-11}	17.00×10^{-3}	0.59×10^{-1}

[a] [**2a**] = 5×10^{-5} mol dm^{-3a} and [**1b**] = 0.07 mol dm^{-3}. [b] Calculated using a value for K_{CH} of 8.32×10^9 dm^3 mol^{-1}. [c] Measured as a color-forming process at 418 nm.

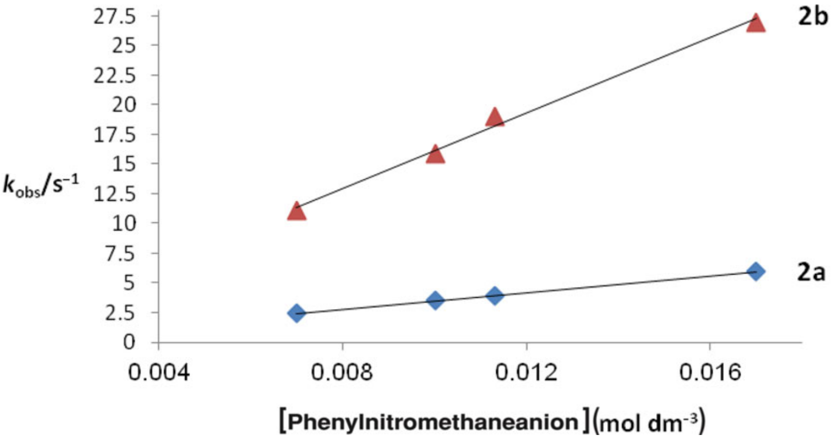


Figure 1 Plots according to Eq. (1), where $k_5 = 3.50 \times 10^2$ and 1.59×10^3, for the reactions of 7-methoxy-4-nitrobenzofurazan **2a** with 3-nitrophenylnitromethane anion **1b** and 7-chloro-4-nitrobenzofurazan **2b** with 4-nitrophenylnitromethane anion **1a**, respectively.

Table IV Comparison of Kinetic and Equilibrium Data for Reaction of 4-Nitrobenzofurazan Derivatives with Phenylnitromethane Anions in Methanol at 25°C

Phenylnitromethane Anion	k_5 (dm^3 mol^{-1} s^{-1})	k_{-5} (s^{-1})	K_5 (dm^3 mol^{-1})
		7-Methoxy-4-nitrobenzofurazan, **2a**	
4-Nitrophenylnitromethane, **1a**	2.41×10^2	1.30×10^{-3}	1.85×10^5
3-Nitrophenylnitromethane, **1b**	3.50×10^2	1.10×10^{-3}	3.18×10^5
4-Cyanophenylnitromethane, **1c**	5.31×10^2	0.90×10^{-3}	5.90×10^5
4-Bromophenylnitromethane, **1d**	8.35×10^2	0.80×10^{-3}	1.04×10^6
		7-Chloro-4-nitrobenzofurazan, **2b**	
4-Nitrophenylnitromethane, **1a**	1.59×10^3	3.98×10^{-3}	3.9×10^5
3-Nitrophenylnitromethane, **1b**	2.31×10^3	2.5×10^{-3}	9.2×10^5
4-Cyanophenylnitromethane, **1c**	3.46×10^3	-	-
4-Bromophenylnitromethane, **1d**	5.31×10^3	-	-

Table V Kinetic Data for the Reaction of 7-Chloro Substrate **2b**[a] with **1a**[a] and Methoxide in Methanol at 25°C

[NaOMe] (mol dm^{-3})	[MeO$^-$]$_{eq}$[b] (mol dm^{-3})	[4-nitro anion][b] (mol dm^{-3})	k_{obs}[c] (s^{-1})
0.007	1.20×10^{-12}	6.99×10^{-3}	1.11×10^1
0.010	1.72×10^{-12}	10.00×10^{-3}	1.59×10^1
0.013	2.23×10^{-12}	11.98×10^{-3}	1.90×10^1
0.017	2.92×10^{-12}	17.01×10^{-3}	2.70×10^1

[a] [2b] = 5×10^{-5} mol dm^{-3a} and [**1a**] = 0.07 mol dm^{-3}. [b] Calculated using a value for K_{CH} of 8.32×10^{10} dm^3 mol^{-1}. [c] Measured as a color-forming process at 430 nm.

7-Chloro-4-nitrobenzofurazan, 2b

7-Chloro-4-nitrobenzofurazan, **2b,** showed a UV absorption maximum at 337 nm, $\varepsilon = 1.0 \times 10^4$ dm^3 mol^{-1} cm^{-1}. A reaction with the four phenylnitromethane anions **1a–d** showed a rapid process, k_{obs}, giving an increase in the absorbance. Kinetic measurements were made in the range 418–430 nm, and values for the rate constants were independent of the wavelength of measurement.

Data for the reaction of **2b** (5×10^{-5} mol dm^{-3}) with **1a** (0.07 mol dm^{-3}) and methoxide in methanol are reported as specimen data in Table V. A linear plot of k_{obs} versus [**4**] gives the value for k_5. A plot

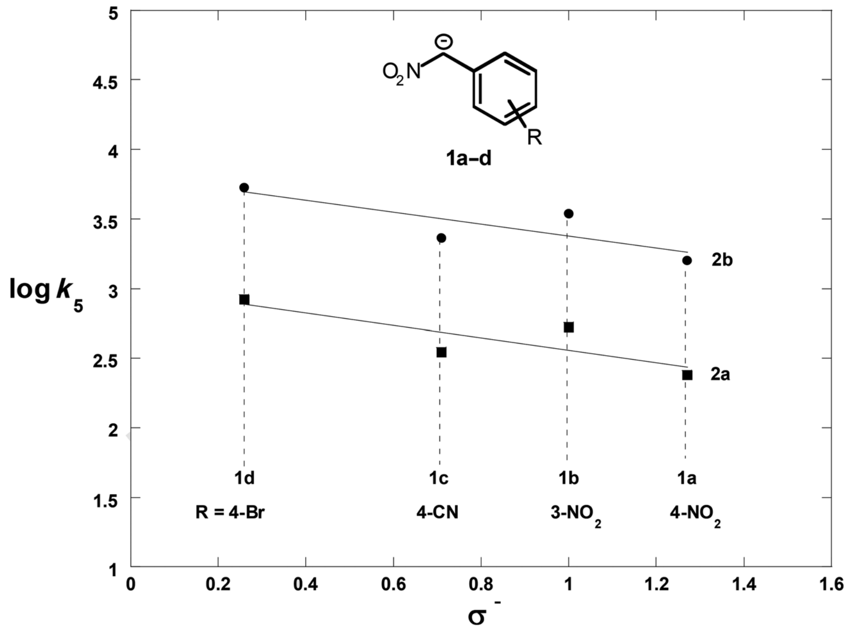


Figure 2 Correlations between log k_5 of the reactions of aryl-substituted nitronates **1a–d** with electrophiles **2a** and **2b** in MeOH and the corresponding σ^- values [30]. Correlation equations: (●) log $k_5 = -0.43\sigma^- + 3.80$ ($r^2 = 0.821$), (■) log $k_5 = -0.44\sigma^- + 3.00$ ($r^2 = 0.822$).

according to Eq. (1), shown in Fig. 1, was linear, giving the values $k_5 = 1.59 \times 10^3$ dm^3 mol^{-1} s^{-1} and $k_{-5} = 3.98 \times 10^{-3}$ s^{-1}. The combination of these values gave $K_5 = k_5/k_{-5}$. The reactions with **1b**, **1c**, and **1d** led to k_5 values of 2.31×10^3, 3.46×10^3, and 5.31×10^3 dm^3 mol^{-1} s^{-1}, respectively. Values for k_5, k_{-5}, and K_5 are listed in Table IV. It is worth noting that changes in the value of k_5 were much bigger than those in the value of k_{-5}, which probably indicates a product-like transition state for these reactions. Thus, the value of k_{-5} was too small to be accurately determined.

Hammett Correlations

Nucleophilic reactivities of phenolate and benzyl anions usually correlate with the Hammett–Brown parameter, σ^- (direct conjugation of the lone pair at the reaction center with the variable substituents) [30]. Accordingly, the reactions of carbanions **1a–d** with various electrophiles **2a–b** in MeOH follow the Hammett σ^- correlations with small negative reaction constants ($\rho \approx -0.5$), though with low correlation coefficients, indicating that only a small part of the negative charge in the carbanions is delocalized by the aromatic ring (Fig. 2).

Relative reactivities of aryl-substituted nitronates with benzhydrylium ions and quinone methides in DMSO and water also the reactivities of benzene and trifluoromethane sulfonyl–stabilized carbanions with quinone methides in DMSO have previously been investigated and showed the same trend [5,31]

Determination of Estimated Electrophilicity Parameters E of 4-Nitro-7-X-benzofurazan 2a–b

According to Mayr and co-workers' studies, it is possible to describe the rates of a large variety of electrophile–nucleophile combinations by the three parameter as shown in Eq. (2) [3,32,33] From this equation, it is clear that estimated E parameter expresses the strength of the electrophile, whereas the N and s parameters express the sensitivity to the nucleophile.

According Eq. (2), general electrophilicity (E) and nucleophilicity (N) scales have been identified. These scales have found to be interesting for predicting reactivity [3,32,33]:

$$\log k = s\,(N + E) \tag{2}$$

It has been found that the electrophilicity of the series of neutral electron-deficient nitroaromatics and heteroaromatics of widely different in terms of reactivity and the structure is appropriately described by Eq. (2). A most characteristic feature, however, was the finding that the measured estimated E values are

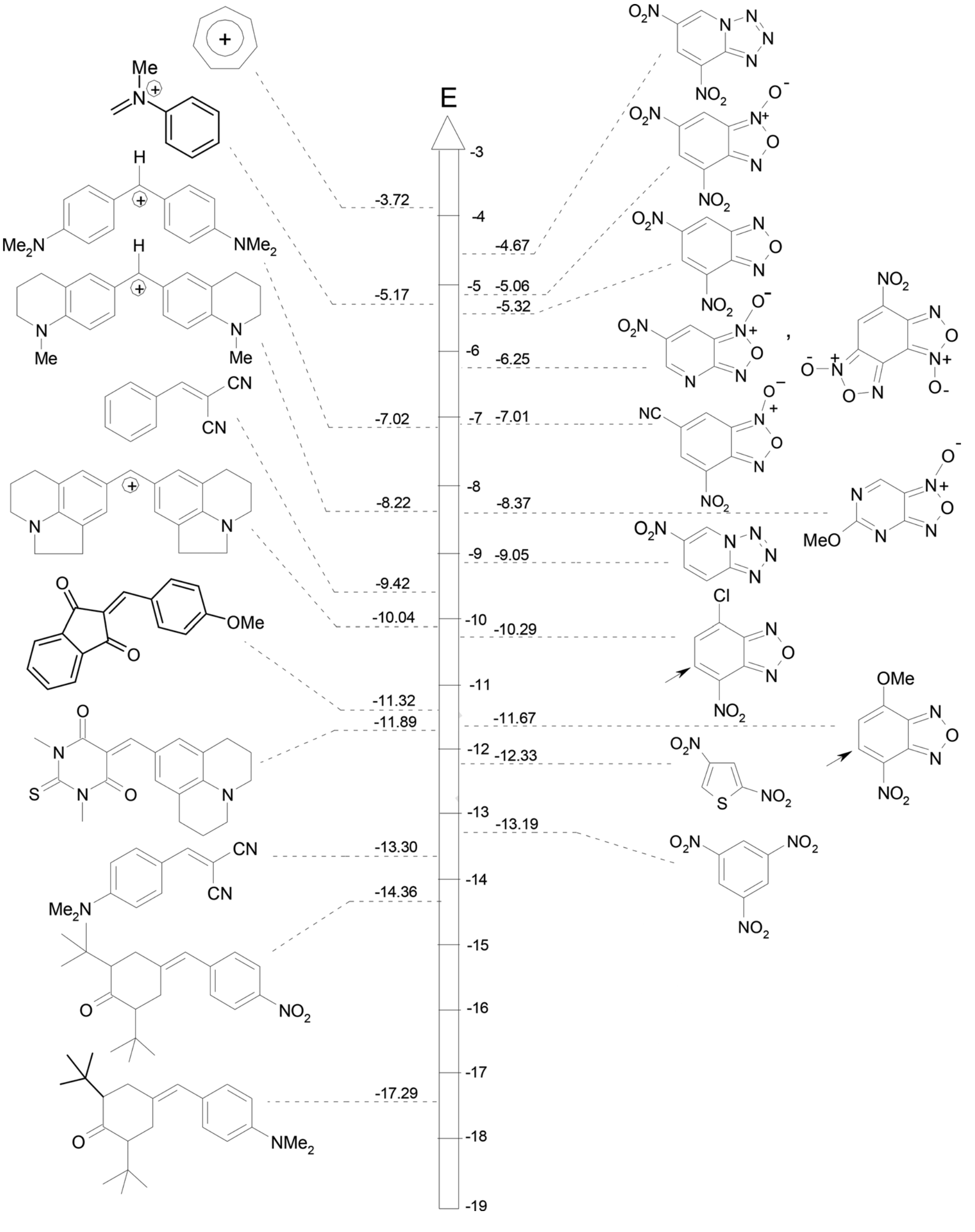


Figure 3 Ranking of 7-methoxy and 7-chloro-4-nitrobenzofurazan on the *E* scale, as defined by Mayr et al.

linearly related to the pK_α^{MeOH} values for covalent methoxylation of the Meisenheimer structures, defining a correlation as represented in Eq. (3) [34]:

$$E = -0.662\, pK_\alpha^{\text{MeOH}} - 1.53 \qquad (3)$$

Referring to methoxylation at an unsubstituted carbon C-5 to minimize steric effects, the following estimates of the *E* values (~ ±0.5 unit) for our 7-X-nitrobenzofurazan are obtained from Eq. (3): $E = -11.67$ for **2a** ($pK_\alpha^{\text{MeOH}} = 15.33$) and $E = -10.29$ for **2b** ($pK_\alpha^{\text{MeOH}} = 13.23$) [23]. This leads to their ranking on the Mayr electrophilicity scale, as shown in Fig. 3, making possible a comparison of their reactivity with that of representative structures previously calibrated by Mayr. Referring to the set of cationic and neutral electrophiles used to construct the *E* scale estimated, the finding of *E* ca. −10.29 for **2b** and −11.67 for **2a** indicates that these two 7-X-nitrobenzofurazans are two and three orders of magnitude, respectively, more electrophilic than the reference trinitro compound ($E = -13.19$ for TNB); the reactivity of **2b** is found to approach that of the most reactive neutral substrate studied by Mayr, namely, benzylidenemalonitrile ($E = -9.42$), however, considerably lower than that of DNTP ($E = -4.67$) and

DNBF ($E = -5.06$), the two most reactive Meisenheimer electrophiles known to date. Anchoring to carbocationic reactivity, the electrophilicity of **2b** is of the same order as that of a benzhydrylium cation ($E = -10.04$) but lower than that other positively charged species such as methyl(phenyl)methyleneammonium ($E = -5.17$) and the tropylium ion ($E = -3.72$).

Nucleophilicities Parameters of Carbanions 1a–d in Methanol

A more comprehensive comparison of nucleophilic reactivities can be based on Eq. (2), to determine the nucleophilicity parameters N and s of the nucleophiles **1a–d**, a plot of the rate constants ($\log k_5$) of the reactions of representative carbanions with reference electrophiles **2a** and **2b** in methanol against the corresponding estimated E parameters. Evaluation of the correlation lines according to Eq. (2) yields the N and s parameters for carbanions **1a–d** in methanol, as listed in Table VI.

As expected, electron-withdrawing groups at the paraposition of the aromatic ring decrease the nucleophilicities N of the carbanions **1a–d**. On the other hand, the solvent effects, as previously reported for the basicities of carbanions [35,36], have now been found for their nucleophilicities. Because the stabilization of most carbanions occurs to a large extent through hydrogen bonding, the basicities as well as the nucleophilicities of carbanions are usually smaller in protic than in aprotic solvents, in line with the observation that the nucleophilicities of carbanions **1a–d** are higher in DMSO than water and methanol. However, the decrease in nucleophilicity strongly depends on the nature of the carbanions. As a consequence, the carbanions **1a–d**, which are the stronger nucleophiles in DMSO, are the weaker nucleophiles in water. Mayr et al. have recently demonstrated that the solvent effect on the carbanions (aromatic nitronates) is much smaller ($\Delta N = 3$–6), It is thus indicated that the nucleophilicities parameters of our carbanions **1a–d** in methanol are generally within in this range, which is the case here (Fig. 4).

Table VI Comparison of the Reactivity Parameters N and s for Carbanions **1a–d** in Methanol, Water, and DMSO

	N/s		
Carbanion	Methanol[a]	Water[b]	DMSO[b]
1a	15.78/0.59	13.58/0.52	16.29/0.75
1b	15.95/0.59	14.25/0.46	18.06/0.71
1c	16.29/0.59	13.23/0.52	16.96/0.73
1d	16.69/0.58		

[a]This work. [b]From [5].

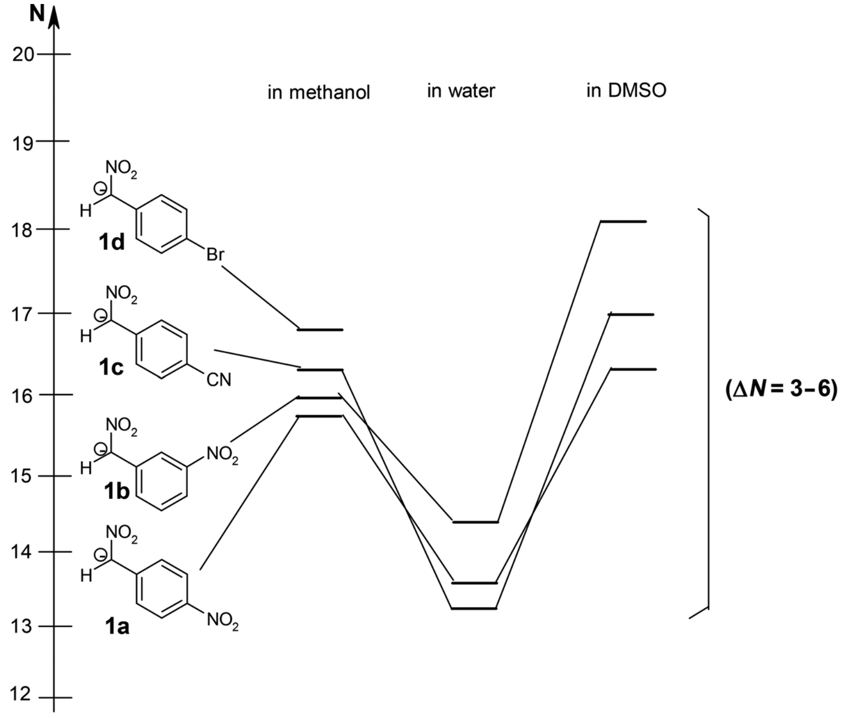


Figure 4 Comparison of the nucleophilicities of carbanions **1a–d** in methanol, water, and DMSO.

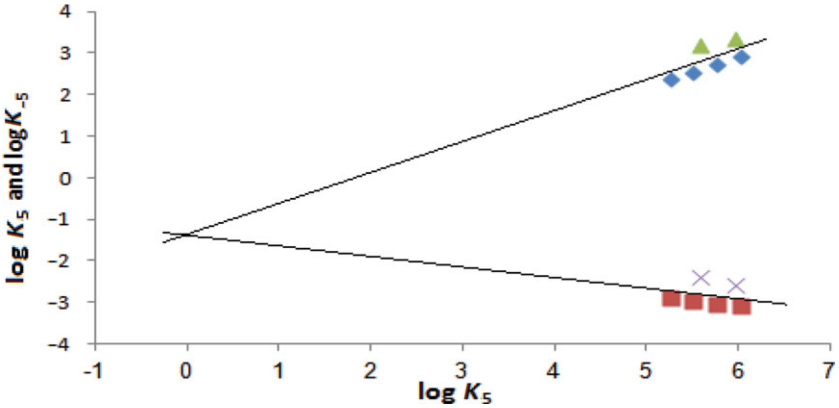


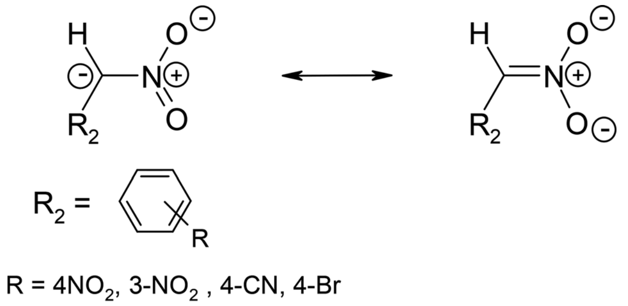
Figure 5 Logarithmic plots of the rate constants versus equilibrium constants for the reactions of phenylnitromethane anions at the 5-positions of 7-methoxy-4-nitrobenzofurazan **2a** (■ k_5 values and ■ k_{-5} values) and 7-chloro-4-nitrobenzofurazan **2b** (▲ k_5 values and × k_{-5} values).

From the kinetic studies and the NMR spectra for the reactions of nitrobenzofurazans **2a,b** with **1a–d**, the following comparisons and conclusions were inferred: The results in Table IV show that the reactivity order, in terms of k_5 values, for each of the phenylnitromethane anions was 7-chloro-4-nitrobenzofurazan, **2b** > 7-methoxy-4-nitrobenzofurazan, **2a**. The higher reactivity of the chloro derivative **2b** than the methoxy derivative **2a** was consistent with the inductive effect, σ_m 0.37, expected for chlorine meta to the reaction site at the 5-position [37]. The reduced electrophilicity of **2a** is attributed to resonance stabilization in the parent between the nitro and methoxy ring substituents [22] For **2b** and **2a**, the addition of carbanions occurred at the 5-position. There was no evidence for the displacement of chloride or methoxide by the carbon nucleophiles, presumably due to steric factors, as shown in Scheme 3. The usual behavior of 4-nitrobenzofurazan and its derivatives in reactions with nucleophiles is that 5-adducts are kinetically favored [1,38].

Although the data are limited, I thought it is worthwhile to estimate a value for the intrinsic rate constant k_0, in the Marcus [39] sense, was determined by suitable interpolation or extrapolation of the Bronsted plots; it has been recognized that there is commonly an inverse relationship between the intrinsic reactivity of a carbon acid and the extent of the structural and solvational reorganization, which is required to form the conjugate carbanion. The greater the resonance stabilization and therefore the sp^2-hybridized character of the resulting carbanion, the greater, in general, are the structural and solvation changes involved in the ionization process and the lower the intrinsic reactivity.

In practice, k_0 is obtained by interpolation or extrapolation of log k_5 and log k_{-5} versus log K_5 where log $K_5 = 0$ as shown schematically in Fig. 5. It is possible to estimate a value for the intrinsic rate constant for the carbon–carbon bond forming reaction between the phenylnitromethane derivatives anions with **2a** or **2b.** A plot of the values of log k_5 and log k_{-5} versus log K_5 gave $k = 0.03$, as shown in Fig. 5. The value of 0.03 can be compared with values of k_0, 0.20 and 0.05 found previously [13] for corresponding reactions of the nitroalkane anions with trinitrobenzene and nitrobenzofurazans, respectively. The values of the intrinsic rate coefficients are thought [40–44] to reflect the amount of electronic-structural reorganization and solvent reorganization accompanying a reaction; the more reorganization required, the lower the reactivity. The anions in methanol may be represented by Scheme 4 in which the negative charge is largely on the nitro group and will be strongly solvated. The lower k_0 value for the nitrobenzofurazan derivatives than trinitrobenzene and phenylnitromethane derivatives than nitroalkane anions may reflect the very strong solvation by methanol of the negative charge on the nitro groups. Bernasconi [40–44] has shown that the effects of a remote substituent, such as R in the benzyl cyanides, on values of intrinsic rate constants is expected to be small.

The value of k_5 for the reaction of 4-nitrophenylnitromethane **1a** was found to be lower than that for nitromethane [14], thus indicating considerably lower reactivity. These reaction results indicated that factors that affect the reactivities include the extent of charge delocalization and solvation by methanol, and the anions may be represented by Scheme 4 in which the negative charge is largely on the nitro group and will be strongly solvated: high in the case of phenylnitromethane, according to results with nitromethane



Scheme 4

[14] and low in the case of benzyltriflone derivatives (i.e., the negative charge is more localized on the carbon atom than in the nitroalkane anions) [15].

In agreement with this, it should be noted that Hibbert [45] found that little structural reorganization was involved in the ionization of disulfonyl carbon acids in water.

Through comparison of the rate constant k_5 values in Table IV with the previously reported 1 corresponding values for carbanion derivatives, it was concluded that the 4-bromophenylnitromethane **1d** was the most reactive carbanion whereas the 4-nitrophenylnitromethane **1a** was the least reactive. Therefore, the values of k_5 decreased with increasing electron withdrawal by the parasubstituent in the phenylnitromethane derivatives. The carbanions will be stabilized by the presence of Br, CN, and NO_2 groups.

CONCLUSION

In conclusion, the experimental studies of the kinetics of reaction of substituted-nitrobenzofurazan **2a–b** with substituted-phenylnitromethane **1a–d** fully support the consensus mechanism described in Scheme 2. The electrophilic reactivity of electron-deficient heteroaromatic structures **2a–b** is found to follow nicely the linear-free energy relationship defined by Mayr et al. This finding is of major interest for two reasons: It expands the applicability of Eq. (2) to σ-complexation processes involving neutral electrophiles, and it broadens considerably the range of coupling reactions that can be envisioned with nitrobenzofurazan and related heterocyclic structures. Nucleophilicity parameters N and s of carbanions in methanol are quantitatively described by Eq. (2) On the basis of the N and s parameters listed in Table VI we can now compare the reactivities of carbanions in methanol with their analogue in water and DMSO.

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