Reactivity in S_NAr Reactions of 2-(4-Chloro-3-nitrophenyl)-1,3-diphenyl-1,3,4-triazol-1-ium-5-thiolate with some Anionic and Neutral Nucleophiles

Aurea Echevarria
Universidade Federal Rural do Rio de Janeiro, Departamento de Química, 23.851 Itaguaí RJ, Brasil
Joseph Miller *
Faculdade de Filosofia, Ciências e Letras de Robeiraõ Preto, 14.049 Ribeirão Preto SP and Instituto de Química, 05508 São Paulo SP, Brasil

The S_NAr reactions in methanol of the title compound with a selected range of anionic and neutral nucleophiles, *viz.*, azide, benzenethiolate, and methoxide ions, and with the amines *N,N*-diethylethane-1,2-diamine, guanidine, morpholine, pyrrolidine and piperidine have been studied. We have also studied the reaction with azide ion in *N,N*-dimethylformamide (DMF). As far as possible we have compared these reactions with those of the nucleophiles with the convenient reference substrate, 1-chloro-2,4-dinitrobenzene.

With all the nucleophiles we verified large differences in the Arrhenius parameters by comparing the mesoionic with reference substrates. For the former, values of log B and of $\Delta E^{\ddagger}$ were always much higher. This has been ascribed to the betaine character of the mesoionic substrate with well-separated positive and negative regions and the marked effects of this on solvation energy and solvation entropy.

We have also verified significant changes in relative reactivities of azide and benzenethiolate ions, the former being better and the latter poorer than that of 1-chloro-2,4-dinitrobenzene. The rationale involves the high polarity of the covalently bound azido group and its distance from the main region of negative charge in the σ-complex (and rate-limiting transition state), and adverse steric interactions in the reactions of benzenethiolate ion.

Comparing DMF and MeOH as solvents in the azide-ion reactions, we found an increase in reactivity in DMF similar to the well known solvent effects with typical S_NAr substrates.

We have recently reported [1] the exceptional kinetic parameters observed in the reaction of the title compound with methoxide ion in methanol, compared with those observed for 1-chloro-2,4-dinitrobenzene as the main reference compound, and with a range of 1-chloro-2-nitro-4-XY-benzenes.

We included in that study an estimate of the activating power of the mesoionic moiety compared with that of a nitro group in the 4-position with reference to the nucleofugal group (chloro). We found that this corresponded to a σ^- value at 50 °C = 0.724: the σ^- value of a p-NO_2 group is universally accepted as 1.27. This substantial inferiority of the mesoionic moiety is remarkably similar to that observed in our early work [2] with the mesoionic 1,2,3-oxadiazolium-5-olate system.

We have now extended the S_NAr reactions of the title compound to include a selected group of anionic and neutral nucleophiles, again making comparisons with reactions of 1-chloro-2,4-dinitrobenzene. We have studied the reactions of the title compound in methanol with azide and benzenethiolate ions, with methoxide ion and with the amines *N,N*-diethylethane-1,2-diamine, guanidine, morpholine, piperidine, and pyrrolidine. We have confirmed both the similarities and the modifications.

We thought it likely that we would again observe similar large differences in the kinetic parameters, but with some significant and important modifications, and this has been confirmed.

Experimental

Preparation of the Hydrochloride of 2-(4-*Chloro*-3-*nitrophenyl*)-1,3-*diphenyl*-1,3,4-*triazol*-1-*ium*-5-*thiolate*.—A solution of 4-chloro-3-nitrobenzoyl chloride (42 mmol) in 1,4-dioxane (20 cm^3) was added at ambient temperature to a suspension of 1,4-diphenylsemicarbazide in 1,4-dioxane (20 cm^3). The mixture clarified and was allowed to stand overnight. Fine crystals formed and were filtered at the pump. These were extremely insoluble and were not recrystallized. Yield 97%, m.p. 262–263 °C (Found: C, 53.9; H, 3.35; N, 12.9. Calc. for $C_{20}H_{14}N_4O_2SCl$: C, 53.94; H, 3.16; N, 12.58%); m/z 408 (M^+, free mesoionic compound) 408; ν_{max}(KBr) 1 530 (NO_2 superimposed on C=C and C=N stretching bands), and 1 330 cm^{-1} (C–S, characteristic of mesoionic thiolates [3]); δ(CF_3CO_2H) 7.0–8.10 (m, 13 H, aromatic) and 4.0 (s, SH).

Kinetic Procedure.—Solutions of the conjugate acid of the mesoionic substrate (0.0125 mol dm^{-3}) in methanol were allowed to react with 2 equiv. of the anionic nucleophiles sodium azide, sodium benzenethiolate (but see below), and sodium methoxide or with 3 equiv. of the neutral nucleophiles *N,N*-diethylethane-1,2-diamine, morpholine, piperidine, and pyrrolidine. In the first case, in general, 1 equiv. of reagent was used to liberate the free mesoionic compound, the other as the nucleophile. In the second case the extra equivalent of reagent was used to remove a proton from the initially formed product. In the specific case of the reaction with sodium benzenethiolate, 1 equiv. of sodium methoxide was used to liberate the free mesoionic compound and 1 equiv. of sodium benzenethiolate was used as nucleophile. Furthermore, the reactions were carried out under nitrogen.

From the thermostatted reaction mixture in a thermostat, aliquots (2 cm^3) were removed at convenient intervals and the reaction stopped with sufficient 0.005 mol dm^{-3} aqueous HNO_3. The amounts of chloride ion were determined by potentiometric titration against standardised aqueous $AgNO_3$. The rate

Table 1. Rate coefficients (k_2) for the reactions in MeOH of the title compound with various nucleophiles.

Nucleophile	T/°C	$k_2/10^3$ dm^3 mol^{-1} s^{-1}	Correlation coefficient
CH_3O^-	55.30	4.20	0.9968
	55.35	4.60	0.9804
	63.55	15.0	0.9854
	69.45	29.2	0.9849
	69.55	29.0	0.9953
	75.50	60.6	0.9853
N_3^-	45.35	4.20	0.9972
	45.35	3.60	0.9939
	60.10	15.4	0.9932
	60.10	16.6	0.9905
	75.00	85.8	0.9935
	75.00	88.6	0.9876
$C_6H_5S^-$	10.00	0.75	0.9973
	10.00	0.75	0.9889
	26.40	5.30	0.9965
	26.50	5.80	0.9903
	35.65	15.40	0.9947
	35.85	15.30	0.9936
$(C_2H_5)_2NCH_2CH_2NH_2$	35.50	0.521	0.9884
	35.50	0.516	0.9932
	50.00	2.03	0.9924
	50.00	1.85	0.9814
	50.00	1.91	0.9867
	57.70	3.55	0.9847
	65.10	5.75	0.9980
	65.10	5.82	0.9970
$(NH_2)_2C{=}NH$	75.10	2.16	0.9958
	75.50	2.63	0.9761
	60.00	0.53	0.9919
	60.00	0.51	0.9864
	45.30	0.13	0.9924
	45.30	0.13	0.9993
$HNCH_2CH_2OCH_2CH_2$	60.05	1.5	0.9903
	69.50	4.8	0.9939
	75.35	6.5	0.9977
	79.90	11.9	0.9923
	89.85	27.0	0.9982
	89.95	21.6	0.9905
$HN(CH_2)_5$	59.95	1.6	0.9944
	59.95	1.5	0.9904
	75.00	5.6	0.9924
	75.25	7.6	0.9887
	89.90	23.7	0.9956
	89.90	22.3	0.9965
$HN(CH_2)_4$	54.60	2.1	0.9850
	60.00	4.2	0.9975
	60.00	4.3	0.9985
	67.55	8.9	0.9982
	75.00	14.6	0.9887
	75.00	17.7	0.9896

Table 2. Rate coefficients (k_2) for the reaction of sodium azide in DMF with the title compouund.

T/°C	$k_2/10^{-2}$ dm^3 mol^{-1} s^{-1}	Correlation coefficient
−30.00	0.24	0.9874
−30.00	0.24	0.9904
−20.00	0.55	0.9837
−21.00	0.64	0.9962
0.05	3.01	0.9951
0.05	3.67	0.9876

coefficients (k_2) were obtained by usual kinetic analysis and using a linear regression of the points obtained. The potentiometer, coupled to a burette, was a Metrohm–Herisau Dosimatic model.

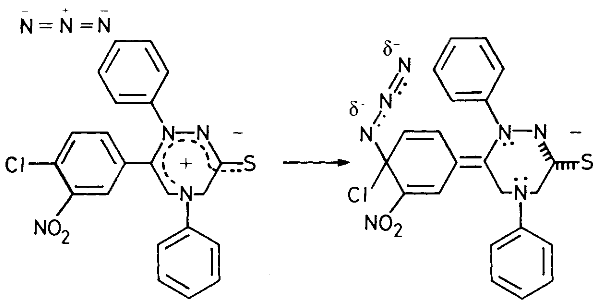


Figure 1. Initial state and σ-complex (as canonical forms) for the reaction of azide ion with 2-(4-chloro-3-nitrophenyl)-1,3-diphenyl-1,3,4-triazol-1-ium-5-thiolate.

Results and Discussion

In Tables 1 and 2 we present experimental kinetic data. In Table 3 we present the values of the bimolecular coefficients (k_2) calculated at 25 and 50 °C (convenient temperatures for comparison) plus derived kinetic parameters for the reactions in methanol of eight nucleophiles with the title compound. We also include data for the reaction of azide ion in DMF. In Table 4 we present data available in the literature for the corresponding reactions with 1-chloro-2,4-dinitrobenzene. These are regettably incomplete as (*a*) there are no data for the reaction with *N*,*N*-diethylethane-1,2-diamine although we are sure that its reactivity is of the same order as that of the secondary amines; and (*b*) the data for reactions of morpholine and pyrrolidine are limited to the rate-coefficients at 25 °C and in ethanol, not methanol. We are confident that the difference between these two alcohols as solvent has but a small effect.

It is convenient first to summarise the marked differences between the Arrhenius parameters of the title mesoionic substrate and 1-chloro-2,4-dinitrobenzene in their reactions with methoxide ion in methanol. For the mesoionic compound $\Delta E^{\ddagger}$ is 50.9 kJ mol^{-1} higher (123.9–73.0), while log B is 6.1 (B in dm^3 mol^{-1} s^{-1}) higher (17.35–11.25). The rate-coefficient ratios (1-chloro-2,4-dinitrobenzene:mesoionic compound) at 25 and 50 °C are 675 and 135, respectively. With azide ion in methanol, although $\Delta E^{\ddagger}$ and B values are again high we note that $\Delta E^{\ddagger}$ for the mesoionic substrate is only 22.6 kJ mol^{-1} higher and log B only 3.7 units higher. The corresponding rate-coefficient ratios at 25 and 50 °C are decreased to only 1.81 and 0.87 respectively.

It is clear that with the mesoionic compound, azide ion is improved to a marked degree relative to methoxide ion. We ascribe this combination of differences to a single cause, *viz*., the markedly polar character of the covalently bound azido group, $-\overset{\delta-}{N}=\overset{+}{N}=\overset{\delta-}{N}$ and its distance from the main region of negative charge in the σ-complex (and rate-limiting transition state). There is thus a smaller loss of solvation energy on proceeding from the initial state to the rate-limiting transition state and σ-complex for the azide ion reaction, in comparison with the methoxide ion reaction, and this is accompanied by a smaller increase in entropy due to liberation of solvent molecules. Figure 1 shows the initial state and σ-complex, as canonical forms, for the reaction of azide ion with the mesoionic substrate.

With benzenethiolate ion in methanol values of $\Delta E^{\ddagger}$ and log B are again high for the reaction with the title mesoionic substrate with values of $\Delta E^{\ddagger}$ and log B = 50.5 kJ mol^{-1} and 5.25 log units, respectively. These are similar to the values encountered with methoxide ion in methanol.

Calculation of the rate-coefficient ratios, however, indicates a mild reduction in the relative reactivity of benzenethiolate ion in the reactions with the title mesoionic substrate. The rate-coefficient ratios at 0, 25, and 50 °C for PhS^- : MeO^- are 344, 112, and 43.8, respectively, whereas the corresponding ratios

Table 3. Derived kinetic data for reactions of mesoionic 2-(4-chloro-3-nitrophenyl)-1,3-diphenyl-1,3,4-triazol-1-ium-5-thiolate in MeOH with various nucleophiles.

Nucleophile	k_2 (25 °C) ($dm^3 mol^{-1} s^{-1}$)	k_2 (50 °C) ($dm^3 mol^{-1} s^{-1}$)	log B (B/$dm^3 mol s^{-1}$)	ΔE^+/ kJ mol^{-1}	$\Delta S^\ddagger$/ J mol^{-1} K	$\Delta G^\ddagger$/ kJ mol^{-1}	$\Delta H^\ddagger$/ kJ mol^{-1}
OCH_3^-	4.47×10^{-5}	2.13×10^{-3}	17.3_5	123.9	78.94	97.85	121.4
$HNCH_2CH_2OCH_2CH_2$	4.04×10^{-5}	5.64×10^{-4}	11.9_5	91.05	−21.4	98.35	91.57
$HN(CH_2)_5$	3.36×10^{-5}	5.68×10^{-4}	11.4_0	90.61	−31.98	98.56	88.13
$HN(CH_2)_4$	8.31×10^{-5}	1.45×10^{-3}	11.9_5	91.51	−24.45	96.32	89.03
N_3^-	3.03×10^{-4}	6.16×10^{-3}	13.3_9	96.55	3.2	93.11	94.07
$(NH_2)_2C=NH$	1.23×10^{-4}	2.05×10^{-3}	11.8_6	90.00	−26.2	95.33	87.52
$C_6H_5S^-$	5.02×10^{-3}	9.33×10^{-2}	14.1_0	93.61	16.71	86.15	91.13
$(C_2H_5)_2NCH_2$-CH_2NH_2	2.02×10^{-4}	1.86×10^{-3}	8.7_5	71.04	−85.70	94.11	68.56
N_3^-/DMF	1.98×10^{-1}	8.91×10^{-1}	7.7_6	48.30	−96.40	77.04	45.82

Table 4. Derived kinetic data for reactions of 1-chloro-2,4-dinitrobenzene with various nucleophiles in CH_3OH or C_2H_5OH.

Nucleophile	k_2 (25 °C)/ $dm^3 mol^{-1} s^{-1}$	k_2 (50 °C)/ $dm^3 mol^{-1} s^{-1}$	log (B/dm^3 $mol^{-1} s^{-1}$)	$\Delta E^\ddagger$/ kJ mol^{-1}	$\Delta S^\ddagger$/ J mol^{-1} K	$\Delta G^\ddagger$/ kJ mol^{-1}	Solvent
OCH_3^{-} [a]	(2.00×10^{-3} at 0 °C) 2.88×10^{-2}	2.88×10^{-1}	11.2_5	73.0	−38.5	82.7	CH_3OH
$HNCH_2CH_2OCH_2CH_2$	4.2×10^{-3}	—	—	—	—	—	C_2H_5OH
$HN(CH_2)_5$	1.0×10^{-2}	(4.85×10^{-2})	6.7	49.5_8	—	—	CH_3OH
$HN(CH_2)_4$	4.6×10^{-2}	—	—	—	—	—	C_2H_5OH
N_3^- [b]	5.49×10^{-4}	5.36×10^{-3}	9.7	73.95	−68.1	93.4	CH_3OH
$(NH_2)_2C=NH$ [c]	2.30×10^{-2}	1.18×10^{-1}	7.5_1	52.2	−101	79.9	C_2H_5OH
$C_6H_5S^-$ [d]	3.89 at 0 °C 1.89×10^1	(7.32×10^1)	(8.8_3)	43.1	−83.7	—	CH_3OH

[a–d] Refs. 1, 9, 6, and 10, respectively.

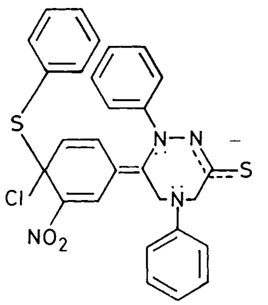


Figure 2. Representation of the σ-complex for the reaction of benzenethiolate ion with 2-(4-chloro-3-nitrophenyl)-1,3-diphenyl-1,3,4-triazol-1-ium-5-thiolate (in MeOH).

with 1-chloro-2,4-dinitrobenzene are 1 945, 656, and 254, *i.e.* an approximately six-fold reduction occurred. This mild effect is clearly entropic in character since the $\Delta E^\ddagger$ values are virtually identical. We ascribe the effect to mildly adverse non-bonded interactions in the rate-limiting transition-state and σ-complex between the phenyl group of the bound phenylthio group and a phenyl group joined to ring (position 3) nitrogen. This is illustrated in Figure 2. There is no corresponding interference in the reaction with 1-chloro-2,4-dinitrobenzene.

For a discussion of the five amines, it is necessary to mention that detailed comparisons are available only for guanidine and piperidine[4–6] and it seems convenient therefore to discuss the amines as a group.

Rate-coefficients at 25 °C are also available for reactions with 1-chloro-2,4-dinitrobenzene for all of the amines, except for *N*,*N*-diethylethane-1,2-diamine. The rate-coefficient ratios at 25 °C, 1-chloro-2,4-dinitrobenzene: mesoionic compound, are 187, 104, 298, and 524 for guanidine, morpholine, piperidine, and pyrrolidine, respectively. These ratios are of the same order of magnitude, though slightly lower than that encountered for methoxide ion, *viz.*, 674. At 50 °C ratio-coefficient ratios are available only for guanidine and piperidine. At 57.6 and 85.4, respectively, these are also of the same order of magnitude, again slightly less than that encountered with methoxide ion, *viz.*, 135.

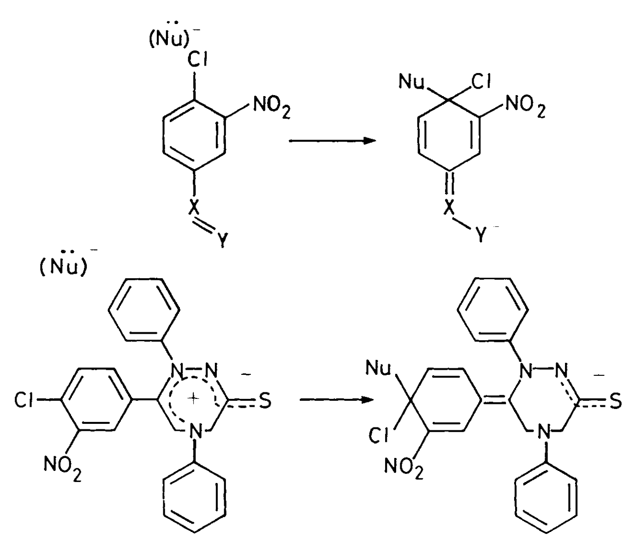
While no ratio can be attributed to the reactions of *N*,*N*-diethylethane-1,2-diamine it is worth noting that the rate-coefficients at 25 and 50 °C are very similar to those of the other four amines, so that there is no reason to suggest that there is anything exceptional about this reagent.

With guanidine and piperidine we can estimate values of Δlog B and of $\Delta\Delta E^\ddagger$ (values for the mesoionic compound minus those for 1-chloro-2,4-dinitrobenzene), *viz.*, Δlog B = 4.35 and 4.7 (B in $dm^3 mol^{-1} s^{-1}$) and $\Delta\Delta E^\ddagger$ = 37.8 and 41.0 kJ mol^{-1}, for guanidine and piperidine, respectively. This is important since it indicates that, with the mesoionic substrate, the characteristic differences betwen the Arrhenius parameters are maintained in reactions of anionic and neutral nucleophiles. This is well known with typical S_NAr substrates and is represented by 1-chloro-2,4-dinitrobenzene.

To illustrate this we quote firstly the values for methoxide ion and piperidine in their reactions with 1-chloro-2,4-dinitrobenzene, *viz.*, log B = 11, 25, and 6.7 (B in $dm^3 mol^{-1} s^{-1}$) and $\Delta E^\ddagger$ 73.0 and 49.6 kJ mol^{-1}, respectively. The values of Δlog B and $\Delta\Delta E^\ddagger$ are thus 4.55 (B in $dm^3 mol^{-1} s^{-1}$) and 23.4 kJ mol^{-1}.

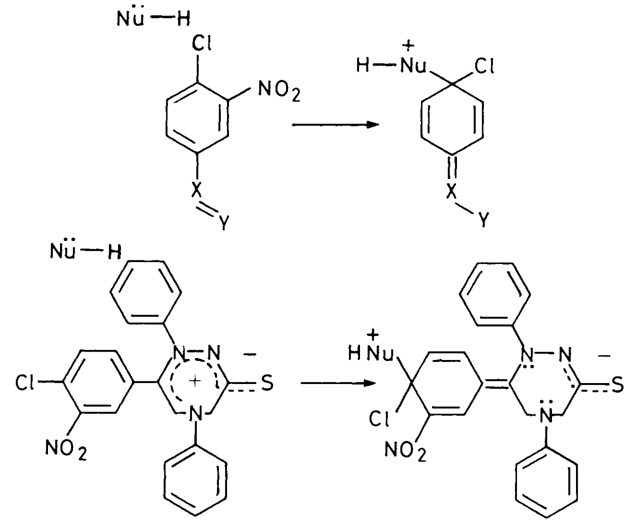
Our data enable us to present corresponding values with the mesoionic substrate. These are 17.35 and 11.4 for log B and 123.9 and 90.6 kJ mol^{-1} for $\Delta E^\ddagger$, leading to Δlog B and $\Delta\Delta E^\ddagger$ values 4.95 units and 33.3 kJ mol^{-1}. These are slightly larger values but clearly present the same characteristics as the typical substrates.

It may therefore be concluded that with both anionic and neutral nucleophiles there is a substantial relative loss of solvation energy and gain in solvation entropy, on proceeding



Initial state (equivalent to three ions) σ-complex (equivalent to one ion)

Figure 3. Initial state and σ-complex, represented as a canonical form in the reaction of methoxide ion with 2-(4-chloro-3-nitrophenyl)-1,3-diphenyl-1,3,4-triazol-1-ium-5-thiolate (in MeOH).



Initial state (equivalent to two ions) σ-complex (equivalent to two ions)

Figure 4. Initial state and σ-complex, represented as a canonical form in the reaction of piperidine with 2-(4-chloro-3-nitrophenyl)-1,3-diphenyl-1,3,4-triazol-1-ium-5-thiolate (in MeOH).

from the initial state to the rate-limiting transition state and σ-complex. Indeed it is interesting to note that the values of log *B* and $\Delta E^{\ddagger}$ for the neutral nucleophiles in their reactions with the mesoionic substrate are of a magnitude similar to those observed with anionic reagents in their reactions with typical substrates. We conclude that it is necessary to superimpose on the marked divergence in the Arrhenius parameters, comparing 1-chloro-2,4-dinitrobenzene and the mesoionic substrate, a nearly standard difference between those of anionic and neutral nucleophiles.

The marked differences with methoxide ion are discussed in ref. 1, but we present here a relevant representation (Figure 3) of anionic nucleophiles and another (Figure 4) for neutral nucleophiles.

For the reactions of azide ion with the mesoionic substrate, it should be recalled that we suggested[7,8] some considerable time ago that the polar aprotic solvent DMF is less able to solvate anions than is MeOH, except for very large anions. We suggest, however, that DMF is better able to solvate cations.

We conclude therefore that in DMF there is a smaller loss of solvation energy and a smaller increase in solvation entropy on proceeding from the initial state and rate-limiting transition state and σ-complex than in MeOH. This is analogous to conclusions reached with typical substrates.[7,8] In both cases the result is a substantial increase in reactivity of the anionic nucleophile in DMF.

The relevant data for the reaction of the azide ion with the mesoionic substrate is as follows: k_2 at 25 °C 1.98×10^{-1} and 3.03×10^{-4} $dm^3 mol^{-1} s^{-1}$, in DMF and MeOH respectively, giving a rate-coefficient ratio (DMF:MeOH) = 654. At 50 °C the values are 8.91×10^{-1} and 6.16×10^{-3} $dm^3 mol^{-1} s^{-1}$ giving a rate-coefficient ratio of 145. The values of log *B* and $\Delta E^{\ddagger}$ for the reactions in MeOH and DMF are 13.4 and 7.75 for log *B* (*B* in $dm^3 mol^{-1} s^{-1}$) and 96.55 and 48.3 kJ mol^{-1} for $\Delta E^{\ddagger}$, respectively. The values of Δlog *B* and $\Delta\Delta E^{\ddagger}$ are thus 5.65 and 48.25 kJ mol^{-1}, respectively.

We do not have the corresponding available data for 1-chloro-2,4-dinitrobenzene, but in ref. 4 there are data available for other typical S_NAr substrates and the values encountered there are in fact similar to those now reported by us.

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