

INFLUENCE OF DIMETHYL SULFOXIDE
ON REACTIVITY OF SUBSTITUTED 2-NITROCHLOROBENZENES
AND 3-NITRO-4-CHLOROAZOBENZENES

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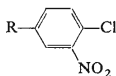
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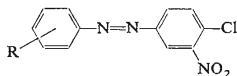
Reactions of substituted 2-nitrochlorobenzenes *I-IX* and 3-nitro-4-chloroazobenzenes *X-XXI* with piperidine in dimethyl sulfoxide have been studied kinetically. The rate constants have been correlated with substituent σ constants. The ρ constants found have been compared with those found in benzene. The value ρ (4.02 ± 0.4) is the same in the both solvents for 2-nitrochlorobenzenes, whereas for the azobenzenes there is a difference, the ρ values being 1.2 ± 0.2 and 1.8 ± 0.2 in dimethyl sulfoxide and benzene respectively. Reasons of these differences are discussed also from the point of view of their influence on the transmission coefficient of phenylazo group π .

Influence of solvent on nucleophilic aromatic substitution is considerable. Solvent influences strongly the reaction rate¹ and, sometimes, causes also a change of reaction mechanism by its catalytic properties².

The aim of the present work is to determine the extent of solvent influence on the substituent effects in reaction of substituted 2-nitrochlorobenzenes and 3-nitro-4-chloroazobenzenes with piperidine. We have followed the change of reaction constant ρ in the Hammett equation caused by polarity of solvent. Further we were interested in to what extent the influence of polarity of medium would make itself felt in the value of the π coefficient of phenylazo group in the reaction type studied. We found in our previous work³ studying another type of reaction (acidobasic equilibria) that π of phenylazo group is dependent on the polarity of medium. The purpose of the present work was to verify the change in π caused by medium polarity in the case of a reaction having a higher ρ value. For our study we have chosen a series of substituted 2-nitrochlorobenzenes *I-IX* and azobenzenes *X-XXI* as model substances and dimethyl sulfoxide as solvent.



- I*, R = H
II, R = CH₃
III, R = OCH₃
IV, R = Cl
V, R = SO₂CH₃
VI, R = CN
VII, R = NO₂
VIII, R = COCH₃
IX, R = CO₂CH₃



- X*, R = H
XI, R = 4'-OCH₃
XII, R = 4'-CH₃
XIII, R = 4'-F
XIV, R = 3'-NHCOCH₃
XV, R = 4'-Cl
XVI, R = 3'-Cl
XVII, R = 3'-F
XVIII, R = 3'-CO₂CH₃
XIX, R = 4'-CO₂CH₃
XX, R = 3'-NO₂
XXI, R = 4'-NO₂

EXPERIMENTAL

Reagents

Preparation of chloronitro derivatives *X*, *XII*, *XIII*, *XV*, *XVII*, *XIX*, and *XXI* was described in a previous report⁴. Derivatives *I*–*IV* and *VI*–*IX* were prepared according to known methods⁵.

4-Methylsulfonyl-2-nitrochlorobenzene (*V*) was prepared by nitration of *p*-methylsulfonylchlorobenzene⁵. Crystallization from methanol gave white needles, m.p. 122.5–124°C. For C₇H₆ClNO₄S (235.6) calculated: 35.68% C, 2.57% H; found: 35.94% C, 2.86% H.

4-Methoxy-4-chloro-3-nitroazobenzene (*XI*), 0.5 g 4'-Hydroxy-4-chloro-3-nitroazobenzene⁴ was dissolved in 0.1M-NaOH, 0.5 ml freshly distilled dimethylsulphate was added, and the mixture was heated on water bath half an hour. After cooling and acidifying with hydrochloric acid the precipitate was filtered, dried, and purified chromatographically on an alumina column (Brockmann II) with benzene as eluent. 0.3 g (60%) orange needles were obtained after crystallization from ethanol, m.p. 133–135°C. For C₁₃H₁₀ClN₃O₃ (291.7) calculated: 53.53% C, 3.46% H; found: 53.33% C, 3.50% H.

The following new substances were prepared by condensation of substituted nitrosobenzenes with 3-nitro-4-chloroaniline⁴:

3,3'-Dinitro-4-chloroazobenzene (*XX*), m.p. 135–137°C. For C₁₂H₇ClN₄O₄ (306.7) calculated: 47.00% C, 2.30% H; found: 47.30% C, 2.38% H.

3',4-Dichloro-3-nitroazobenzene (*XVI*), m.p. 97–99°C. For C₁₂H₇Cl₂N₃O₂ (296.2) calculated: 48.67% C, 2.38% H; found: 48.78% C, 3.32% H.

3'-Methoxycarbonyl-3-nitro-4-chloroazobenzene (*XVIII*), m.p. 110–111°C. For C₁₄H₁₀ClN₃O₄ (319.7) calculated: 52.59% C, 3.15% H; found: 52.84% C, 3.10% H.

3'-Acetylamino-3-nitro-4-chloroazobenzene (*XIV*), m.p. 86–89°C. For C₁₄H₁₁ClN₄O₃ (318.7) calculated: 52.76% C, 3.48% H; found: 53.01% C, 3.44% H.

Piperidyl derivatives whose properties and analyses are given in Tables I and II were prepared by heating piperidine with substituted chloronitrobenzenes according to known method^{6,7}.

Dimethyl sulfoxide (Lachema, Brno) was dried with calcium oxide powder and molecular sieve Linde A4 and distilled *in vacuo* (b.p. 86–87°C/25 Torr). Piperidine (Sojuzchimexport, Moscow) was twice distilled, b.p. 106–106.5°C.

Kinetic Measurements

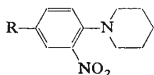
2–2.5 ml Solution containing suitable concentration of the chloro derivative studied (see Table III) was placed in sample cell which was located in thermostated cell holder ($\pm 0.2^\circ\text{C}$) of spectrophotometer Unicam SP 800. To this thermostated solution such an amount of piperidine was added from a micropipette that its concentration was 10–100 \times greater than that of the chloro-derivative. The micropipette was rinsed with the reaction mixture several times so that the amount measured was transferred in the cell completely and, at the same time, the content of the cell was mixed. At definite time intervals, extinction was measured at the λ_{anal} of the respective piperidyl derivative (see Tables I and II). At the same λ_{anal} the validity of the Lambert-Beer law was verified for the experimental condition chosen, and calibration lines were obtained for individual substances (Table III). From these lines concentration of piperidyl derivative could be read because starting chloro derivatives and piperidine absorbed only to a negligible extent at the wavelength chosen and, therefore, did not interfere. The reaction was followed until 40–90% conversion (according to the reactivity of chloro derivative). As the measurements were carried out with an excess of piperidine (Table III), equation (1) could be used for computing the rate constant,

$$kt = -2.3(1/b) \log(a - x) + \text{const.} \quad (1)$$

where a is the initial concentration of the chloro derivative, x is its decrease at a time t , and b stands for the initial piperidine concentration.

TABLE I

4-Substituted 2-Nitro-N-piperidylbenzenes and Photometric Characteristics of their Solutions in Dimethyl Sulfoxide



R	M.p., $^\circ\text{C}$	% C		% H		λ_{anal} nm	$\log \epsilon_{\text{anal}}$
		calc./found	calc./found	calc./found	calc./found		
H	76–77 ^a	—	—	—	—	450	3.06
CH ₃	24–27	65.43	64.98	7.32	7.37	450	2.96
CH ₃ O	39–41	61.01	60.80	6.82	7.02	450	2.93
Cl	46–48	54.72	54.34	5.44	5.59	440	3.16
CH ₃ SO ₂	120–122	50.69	50.52	5.68	5.82	420	3.41
CN	110–112	62.32	62.47	5.66	5.67	420	3.39
NO ₂	91–93 ^b	—	—	—	—	400	4.15
CH ₃ CO	45–47	62.88	62.49	6.49	6.53	420	3.38
CH ₃ OCO	44–47	59.10	59.97	6.10	6.21	430	3.38
C ₆ H ₅ N ₂	63–64 ^c	—	—	—	—	410	4.17

^a Ref.¹⁹ 80–81 $^\circ\text{C}$; ^b ref.¹⁹ 92 $^\circ\text{C}$; ^c ref.⁴ 64 $^\circ\text{C}$.

RESULTS AND DISCUSSION

Reactions (A) and (B) were kinetically followed in dimethyl sulfoxide.

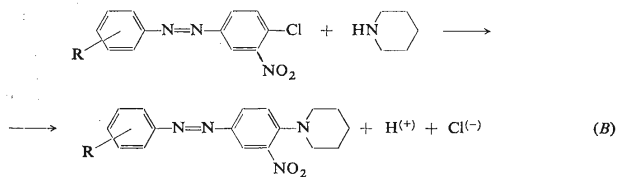
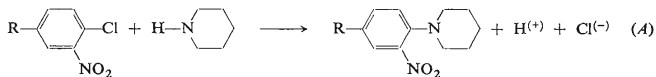
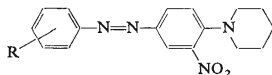


TABLE II

3'-and 4'-Substituted 3-Nitro-4-N-piperidylazobenzenes and Photometric Characteristics of their Solutions in Dimethyl Sulfoxide



R	M.p., °C	% N		λ_{anal} nm	log ϵ_{anal}
		calc./found			
H	63–64 ^a	—	—	410	4.17
4'-CH ₃	105–106 ^a	—	—	393	4.20
4'-F	82–83 ^a	—	—	395	4.24
3'-NHCOCH ₃	157–160	19.06	18.88	400	4.15
4'-Cl	97–98 ^a	—	—	405	4.25
3'-Cl	94–96	16.25	16.47	405	4.23
3'-F	85–86 ^a	—	—	405	4.22
3'-COOCH ₃	81–83	15.21	15.18	405	4.20
4'-COOCH ₃	128–130	15.21	14.91	420	4.33
3'-NO ₂	139–141	19.71	19.89	415	4.20
4'-NO ₂	144–145 ^a	—	—	450	4.33
4'-CH ₃ O	85–86	16.46	16.50	410	4.28

^a Melting points agree with ref.⁴.

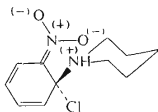
^a Calculated from the equation (I) (see Experimental); error in calculation of a rate constant from 3–5 independent experiments was 4–6%.

TABLE III
Rate Constants of Reactions (A) and (B) Calculated According to Equation (1)

Experiment No	Compound	Conc. of chloro derivative 10^4 mol/l	Conc. of piperidine 10^3 mol/l	k^a l/mol . s	Temperature $^{\circ}\text{C}$	E kcal/mol
1	<i>I</i>	98.8	1 680	$0.56 \cdot 10^{-5}$	20	12.9 ± 0.5
2	<i>I</i>	98.8	960	$1.4 \cdot 10^{-5}$	30	
3	<i>I</i>	91.8	920	$3.2 \cdot 10^{-5}$	45	
4	<i>I</i>	91.8	1 920	$3.3 \cdot 10^{-5}$	45	13.1 ± 1
5	<i>II</i>	18.4	0.92	$6.5 \cdot 10^{-6}$	45	
6	<i>III</i>	820	1 318	$1.8 \cdot 10^{-7}$	20	
7	<i>III</i>	805	1 163	$3.7 \cdot 10^{-7}$	30	
8	<i>III</i>	827	919	$10.9 \cdot 10^{-7}$	45	
9	<i>III</i>	829	16.2	$10.5 \cdot 10^{-7}$	45	
10	<i>IV</i>	14	919	$3.6 \cdot 10^{-4}$	45	
11	<i>V</i>	9.4	4.6	0.18	45	
12	<i>VI</i>	9.1	4.6	0.25	45	
13	<i>VII</i>	2.2	7.4	1.1	20	
14	<i>VII</i>	1.3	7.4	1.3	20	
15	<i>VII</i>	1.2	21.1	1.3	20	7.8 ± 0.5
16	<i>VII</i>	1.3	4.8	2.1	30	
17	<i>VII</i>	1.3	3.5	3.6	45	
18	<i>VIII</i>	8.7	27	$4.9 \cdot 10^{-2}$	45	
19	<i>IX</i>	9.2	27	$5.0 \cdot 10^{-2}$	45	
20	<i>X</i>	1.1	240	$1.5 \cdot 10^{-2}$	20	
21	<i>X</i>	1.0	350	$2.3 \cdot 10^{-2}$	30	
22	<i>X</i>	1.0	61	$3.5 \cdot 10^{-3}$	45	
23	<i>X</i>	1.1	325	$3.7 \cdot 10^{-3}$	45	
24	<i>XI</i>	1.0	480	$2.04 \cdot 10^{-3}$	20	
25	<i>XI</i>	1.0	980	$2.1 \cdot 10^{-3}$	20	
26	<i>XI</i>	0.9	480	$4.5 \cdot 10^{-2}$	30	9.2 ± 0.5
27	<i>XI</i>	1.1	246	$9.9 \cdot 10^{-2}$	45	
28	<i>XII</i>	0.63	91.9	$2.1 \cdot 10^{-2}$	45	
29	<i>XIII</i>	0.89	91.9	$3.1 \cdot 10^{-2}$	45	
30	<i>XIV</i>	0.81	298	$3.4 \cdot 10^{-2}$	45	
31	<i>XV</i>	0.90	91.9	$6.4 \cdot 10^{-2}$	45	
32	<i>XVI</i>	0.82	91.9	$8.5 \cdot 10^{-2}$	45	
33	<i>XVII</i>	0.98	91.9	$7.3 \cdot 10^{-2}$	45	
34	<i>XVIII</i>	0.91	27.5	$6.8 \cdot 10^{-2}$	45	
35	<i>XIX</i>	0.80	91.9	$8.9 \cdot 10^{-2}$	45	
36	<i>XX</i>	0.81	2.7	$1.83 \cdot 10^{-1}$	45	9.2 ± 0.5
37	<i>XXI</i>	0.9	14	$0.7 \cdot 10^{-1}$	20	
38	<i>XXI</i>	0.9	39	$0.65 \cdot 10^{-1}$	20	
39	<i>XXI</i>	0.9	16	$1.2 \cdot 10^{-1}$	30	
40	<i>XXI</i>	0.9	21	$2.2 \cdot 10^{-1}$	45	

We ascertained earlier^{4,5} that these reactions in benzene are of 2. order. Results of measurements of derivatives *I*, *III*, *VII*, *X*, *XI* and *XXI* ($R = H, 4-OCH_3, 4-NO_2$) (experiments No 1–4, 6–9, 13–17, 20–27, and 37–40 in Table III) show that the rate of reaction (*A*) and (*B*) in dimethyl sulfoxide depends on the first power of piperidine and chloro derivative concentrations.

The same series (*I*, *III*, *VII*, *X*, *XI*, and *XXI*) has been measured at 20, 30, and 45°C wherefrom the Arrhenius activation energy has been computed (Table III). Its values are lower than the respective values for the reaction in benzene^{4,5} by 1–2 kcal which is not significant with respect to experimental error. A dependence of activation energy on structure was observed only in the case of reaction (*A*) (Table III). The influence of solvent on the value of entropic term is negligible. The entropy change for the reaction of substance *I* has a value $\Delta S = -38$ e.u. and is practically identical with the value found in benzene ($\Delta S = -40$ e.u.)⁵. A relatively small acceleration of reaction caused by solvent change was remarkable. The reaction of substance *I* proceeds 7.5 times faster in dimethyl sulfoxide than in benzene^{2,5}. A 400 fold acceleration was found for analogous reaction of 4-nitrochlorobenzene and piperidine¹ in the same pair of solvents under the same reaction conditions (50°C). This fact can be explained on the basis of the following pieces of knowledge. Substitution of chlorine is generally faster in 2-nitro- than in 4-nitrochlorobenzene as far as their reactions with secondary amines are concerned^{8,9}. This difference in reactivity is explained by so called intramolecular solvation¹⁰. Addition of piperidine to 2-nitrochlorobenzene gives an adduct having character of inner salt of the type *A* the polarity of which is lower than that of 4-nitro derivative, and, therefore, the polarity of solvent influences the reaction rate less too.



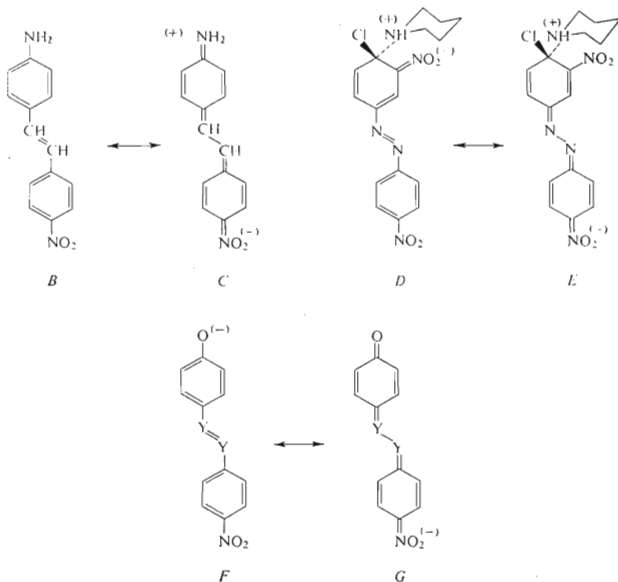
A

The influence of dimethyl sulfoxide on the reaction of 4-nitrochlorobenzene with piperidine is more pronounced because the activated complex is strongly polar, and the reaction is, therefore, accelerated by increased solvent polarity. Dependence between logarithms of the rate constants k_A and k_B measured at 20–45°C (experiments 1, 3, 6, 8, 15, 17, 20, 22, 25, 27, 37, and 40) is linear which verifies the validity of the so called isokinetic relation¹¹ for the both reactions (*A*) and (*B*). Therefore the Hammett equation¹² could be used for correlation of reactivities and structure in the both series of chloro derivatives (experiments 4, 5, 9–12, 17–19, 22, 27–36, and 40). As in the case of benzene solutions^{4,5}, exalted σ^- constants^{13,14} had to be

chosen in this case too for the reaction (A) (Fig. 1). On the other hand, a good correlation of rate constants with σ substituent constants could be found in the case of reaction (B) (Fig. 2). A similar phenomenon was encountered also in the case of acid-base equilibria of 4'-nitro-4-aminostilbene¹⁵ (structures B and C) which can be compared with the transition state of the compound XXI in the reaction (B) (Structures D and E).

Mesomeric influence of the nitro group in 4 position expressed by structures C, E is apparently much weaker than that expressed by G (Y = CH, N) because the former results in a disadvantageous charge distribution whereas the latter in an advantageous charge dispersion^{15,16}.

A value $\rho_A = 4.02 \pm 0.4$ was found for the reaction (A) (Fig. 1) (the error given in this and other data refers to 95% probability range), and correlation coefficient $r = 0.989$; the ρ constant has practically the same value as that found for the analogous reaction in benzene ($\rho_A = 4.08$)⁵. Value $\rho_B = 1.2 \pm 0.2$ was found for reaction (B) (Fig. 2), correlation coefficient $r = 0.980$; the ρ constant is lower than that for the reaction in benzene ($\rho_B = 1.8 \pm 0.2$)⁴.



There are different points of view as to the influence of solvent on the value of ρ constant. Some authors state that the ρ value which represents a measure of sensitivity of a reaction towards polar effects depends *inter alia* on the solvent used^{13,17}. Others do not ascribe any substantial influence on the change of this constant to solvent especially in the case of nucleophilic aromatic substitution¹⁸. An unambiguous answer to this question will apparently need still further experimental results. The coefficient of weakening of electronic effects of substituents, π , for phenylazo group in dimethyl sulfoxide calculated from the ratio ρ_B/ρ_A has a value of 0.30. This is lower than that found for benzene solution (0.45) (ref.⁴). In order to be able to ascribe a statistical meaning to the change of π with solvent, we carried out a correlation of $\log k$ belonging to analogously substituted derivatives in reactions (A) and (B). A value $\pi = 0.38 \pm 0.12$ was calculated from literature data^{4,5} for seven substituents in benzene solution. Only an approximate value of $\pi = 0.32 \pm 0.11$ was obtained for dimethyl sulfoxide owing to small number (four) of identical substituents in the both series.

So far, the weakening effect of phenylazo group in the case of dissociation equilibria of N, N-dimethylaniline¹³ ($\pi = 0.13$) and phenol¹⁶ ($\pi = 0.25$ and 0.24 (ref.³) in 50 and 20% ethanol respectively) has been studied. Comparison of these data with those of aromatic nucleophilic substitution disagree with the opinion that transmission coefficient does not depend on the type of reaction¹³. The above-mentioned results show that the π value depends much more on the type of reaction than on the reaction medium.

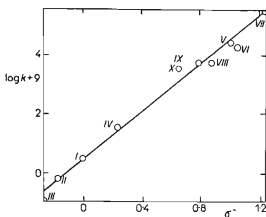


FIG. 1
Influence of Structure of 4-Substituted 2-Nitrochlorobenzenes I—X on Rate Constants of their Reaction with Piperidine in Dimethyl Sulfoxide at 45°C

For numbers see text.

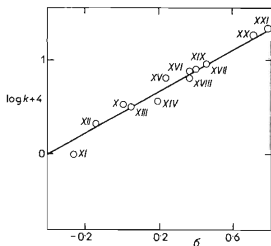


FIG. 2

Influence of Structure of 3'- or 4'-Substituted 3-Nitro-4-chloroazobenzenes X and XI—XX on Rate Constants of their Reaction with Piperidine in Dimethyl Sulfoxide at 45°C

For numbers see text.

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