2-Azidoazobenzenes. 3. Kinetics of the Thermal Decomposition to Give 2-Arylbenzotriazoles

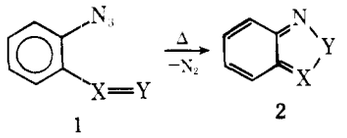
J. Herbert Hall* and Francis W. Dolan

Department of Chemistry and Biochemistry, Southern Illinois University, Carbondale, Illinois 62901

Received March 20, 1978

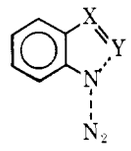
A series of 2-azido-4′-R-azobenzenes has been prepared and the rate of their thermal decomposition to give 2-(4-R-phenyl)benzotriazoles has been determined in anisole. The effect of substituents was small, showing a slight acceleration by electron withdrawing groups. The reaction exhibited an isokinetic region at 77 ± 20 °C. In several cases, rates were observed on each side of the isokinetic temperature. The enthalpy of activation varied from 18.2 to 22.9 kcal mol^{-1} and the entropy of activation from −5.7 to −18.4 cal deg^{-1} mol^{-1}. Acceleration of the rate is observed when a methyl group is placed ortho to the azo linkage on the ring bearing the azido group, but the rate is retarded by methyl ortho to the azido group. These results are rationalized by the postulation of the formation of an intermediate pentazole by intramolecular 1,3-dipolar addition of the azido group to the azo group.

The enhancement of the rate of thermal decomposition of phenyl azides by the presence of ortho substituents with α,β unsaturation (1) is well known. Dyall and Kemp[1] reported



1 2

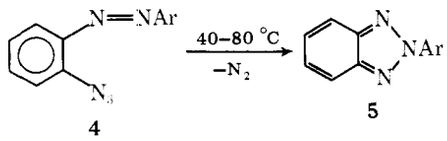
that ortho substituents increase the rate of decomposition in the order H < C_6H_5CO < CH_3CO < NO_2 < $C_6H_5N{=}N$ (relative rate in decalin: 1:45.1:254:537:6680). In the 1-substituted-2-naphthyl azides[2] the order was: H < $C_6H_5N{=}N$ < NO_2 (relative rate in nitrobenzene: 1:211:1730). This rate enhancement has generally been explained by assuming some anchimeric assistance in the transition state (3).



3

In order to secure more information about these reactions, a kinetic study of the cyclization of 4′-R-2-azidoazobenzenes to give 2-phenylbenzotriazoles was undertaken. Formation of benzotriazoles from 2-azidoazobenzenes is an old reaction. The earliest reports were by Zincke and co-workers.[3,4] More recent work was reported by Carboni and co-workers[5,6] and by workers in this laboratory.[7,8]

The needed 4′-R-2-azidoazobenzenes were prepared by condensation of 2-azidoaniline[9,10] with 4-substituted nitrosobenzenes in glacial acetic acid,[7] except 4′-dimethylamino-2-azidoazobenzene which was prepared as reported previously.[8] The isolated yields are given in Table I. All of these compounds decomposed to give the benzotriazole before melting. Five of them were sufficiently stable to obtain elemental analyses. The elemental analyses of the remaining compounds showed the correct C/H ratio, but the nitrogen analyses were low by 2–3% indicating that decomposition had occurred. Because of the instability, the compounds were purified immediately before use and stored in a freezer.



4 5

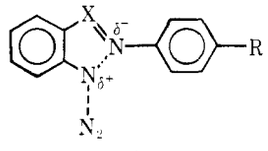
Thermal decomposition of the 2-azidoazobenzenes in refluxing hexane or tetrahydrofuran gave the corresponding benzotriazole in high yield. The new compounds are listed in Table II.

The kinetic study was carried out in anisole as the solvent. The rate was determined by following the rate of nitrogen evolution. First-order plots were linear over 4 half-lives. The first-order rate constants were calculated using a linear least-squares computer program. Each constant is the average of two or three determinations. The constants are given in Table III. The enthalpies and entropies of activation were calculated and are listed in Table IV.

As seen in Table III, the reaction is accelerated slightly by electron-withdrawing groups and retarded by electron-donating substituents at 60.0 °C. As shown in Figure 1, the enthalpy of activation varies linearly with the entropy of activation. The slope of this plot indicates an isokinetic temperature region of 77 ± 20 °C. As can be seen in Table III, the kinetic measurements were made at the lower end of the region. In fact if the data in Table III are examined carefully, several isokinetic inversions can be seen. For example, the 4′-methyl compound decomposes faster at 50 °C than the 4′-acetamido compound, but at 70 °C, the 4′-acetamido compound is the fastest. At 50 °C the sulfonamido compound is slower than either the nitro or cyano compounds, but at 70 °C it is considerably faster than the cyano and slightly faster than nitro. At 50 °C the cyano group accelerates the reaction more than the acetyl group, but at 70 °C the rates are identical. These examples appear to be one of the few cases where it has been possible to make kinetic measurements on both sides of the isokinetic temperature. Similar results were observed in the cyclization of 2-azidobenzophenones to 3-phenylanthranils[11] and in the cyclization of benzylidine-2-azidoanilines to 2-phenylindazoles.[12]

In spite of these inversions the Hammett plots shown in Figure 2 exhibit reasonably linear plots. As expected from theory, ρ decreases as the isokinetic temperature is approached—temperature (°C), ρ, root mean square of residuals: 49.3, 0.374, 0.035; 60.1, 0.334, 0.035; 71.6, 0.294, 0.057. As might be expected, the scatter increases as the isokinetic temperature is approached.

If the rapid rate of these reactions is due to anchimeric assistance in the transition state as shown in structure 6, one



6

might expect that the reaction would be accelerated by electron-donating groups since the azide nitrogen attached to the ring would be expected to be nitrene-like, i.e., electron defi-

0022-3263/78/1943-4608$01.00/0

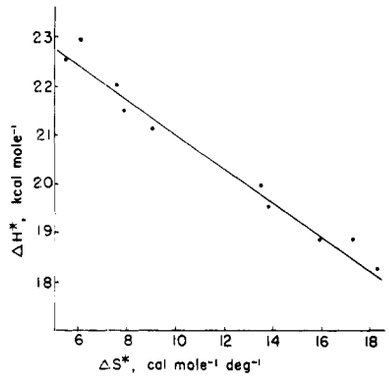


Figure 1. Entropy of activation vs. enthalpy of activation.

Table I. 4′-R-2-Azidoazobenzenes

compd[a]	R[b]	registry no.	isolated yield, %	formula
I	H	17277-44-0	37	$C_{12}H_9N_5$
II	CO_2CH_3	67661-43-2	77	$C_{14}H_{11}N_5O_2$
III	$COCH_3$	67661-44-3	78	$C_{14}H_{11}N_5O$
IV	NO_2	67661-45-4	45	$C_{12}H_8N_6O_2$
V	SO_2NH_2	67661-46-5	65	$C_{12}H_{10}N_6O_2S$
VI	$NHCOCH_3$	67661-47-6	20	
VII	CH_3	67661-48-7	35	
VIII	Cl	67661-49-8	47	
IX	CN	67661-50-1	81	

[a] IR (cm^{-1}): I, 2120; II, 2120, 2095, 1730, 1280; III, 2110, 1681; IV, 2120, 1530, 1345; V, 3325, 3250, 2110, 1330, 1155; VI, 3320, 3420, 2090, 2110, 1659, 1590, 1300; VII, 2130; VIII, 2110; IX, 2220, 2100. [b] Satisfactory analytical data (±0.4 for C,H,N) were reported for compounds I–V.

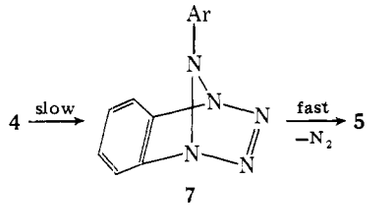
Table II. 2-(4′-R-Phenyl)benzotriazoles

R[a]	registry no.	isolated yield, %	mp, °C	formula
CN	67661-51-2	97	230.0–230.5	$C_{13}H_8N_4$
$COCH_3$	67661-52-3	92	178.5–79.5	$C_{14}H_{11}N_3O$
CO_2CH_3	67661-53-4	93	200	$C_{14}H_{11}N_3O_2$
CH_3	3682-80-2	97	122[b]	$C_{13}H_{11}N_3$
$NHCOCH_3$	1916-66-1	62	194–195	$C_{14}H_{12}N_4O$
SO_2NH_2	67661-54-5	99	300	$C_{12}H_{10}N_4O_2S$[d]
NO_2	51776-70-6	73	286.5–287.5[c]	$C_{12}H_8N_4O_2$

[a] Satisfactory analytical data (±0.3 for C,H,N,S) were reported for all compounds in the table. [b] Reported 114 °C, ref 20. [c] Reported 275 °C, ref 21. [d] Calcd S 11.66; found 11.54.

cient. As seen in Table III there is a small acceleration by electron-withdrawing groups which seems to argue against this mechanism.

Another possibility is that these reactions are actually 1,3-dipolar cycloaddition reactions involving rate-determining formation of a pentazole, which subsequently loses nitrogen in a fast step to give product. A similar type mechanism has



7

been postulated in the decomposition of 2-azidobenzophenones.[11] Pentazole formation could account for the substituent effect if one assumes a transition state as pictured in structure **8** in which bond formation between N-1 and N-5 is ahead of bond formation between N-2 and N-3 or alternatively as in **9** with bond formation between N-2 or N-3 ahead of bond formation between N-1 and N-5. Structures **8** and **9** differ only in the dipolar structure written for the azide. The transition state as depicted has a high degree of symmetry. This would account for the small effect of substituents and also for the

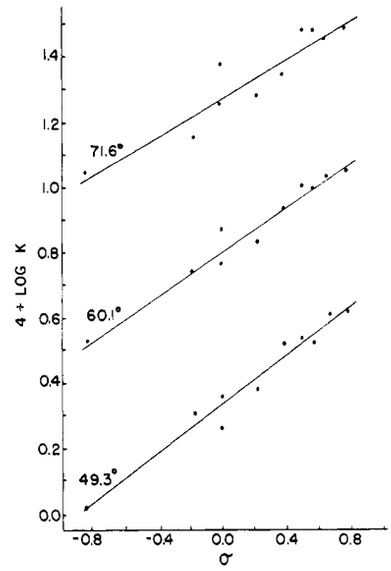


Figure 2. Hammett plots as a function of temperature.

Table III. Rate of Decomposition of 4′-R-2-Azidoazobenzenes[a]

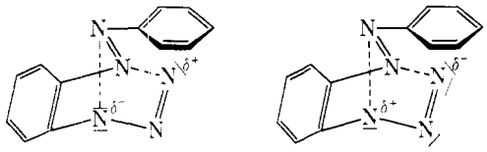
R	temp, °C	$k \times 10^2$,[d] min^{-1}	rel rate at 60.0 °C
$N(CH_3)_2$	46.87	0.44 ± 0.06	0.432
	50.05	0.67[b]	
	65.82	3.66 ± 0.12	
	81.00	16.4 ± 0.7	
$NHCOCH_3$	50.00	1.14 ± 0.01	0.748
	60.05	3.40 ± 0.05	
	70.02	8.80 ± 0.10	
CH_3	46.80	0.89 ± 0.02	0.720
	59.95	3.30 ± 0.10	
	76.78	12.4 ± 0.5	
H	46.92	0.99 ± 0.02	1.00
	49.88	1.44 ± 0.02	
	59.95	4.58 ± 0.14	
Cl	46.74	1.05 ± 0.07	0.853
	59.60	3.82 ± 0.09	
	76.88	15.8 ± 0.7	
CO_2CH_3	46.82	1.41 ± 0.01	1.19
	59.98	5.45 ± 0.10	
	76.84	17.1 ± 0.1	
$COCH_3$	50.00	2.08 ± 0.01	1.33
	59.95	6.08 ± 0.11	
	70.08	14.8 ± 0.8	
SO_2NH_2[c]	49.90	2.08 ± 0.04	1.27
	59.98	5.82 ± 0.12	
	70.18	15.7 ± 0.3	
CN	49.98	2.50 ± 0.06	1.39
	59.88	6.37 ± 0.01	
	70.18	14.8 ± 0.2	
NO_2	49.98	2.35 ± 0.10	1.45
	60.02	6.66 ± 0.26	
	70.40	15.6 ± 0.4	

[a] Solvent was anisole. [b] Single run. [c] The azide was only partially soluble in the anisole. [d] Errors are standard deviations.

Table IV. Activation Parameters for 4'-R-2-Azidoazobenzenes in Anisole[a]

R	ΔH^*, kcal mol^{-1}	ΔS^*, cal deg^{-1} mol^{-1}, at 60.0 °C
CO_2CH_3	18.2 ± 1.1	−18.4 ± 3.3
CH_3	18.8 ± 0.7	−17.4 ± 2.1
CN	18.8 ± 0.4	−16.0 ± 1.2
NO_2	19.5 ± 0.7	−13.9 ± 2.1
Cl	19.9 ± 0.4	−13.6 ± 1.2
$COCH_3$	21.1 ± 0.6	−9.2 ± 1.8
SO_2NH_2	21.5 ± 0.2	−8.0 ± 0.6
$NHCOCH_3$	22.5 ± 0.4	−7.7 ± 1.2
H	22.5 ± 0.9	−5.7 ± 2.7
$N(CH_3)_2$	22.9 ± 0.2	−6.3 ± 0.6

[a] Errors were estimated from the extreme slopes of the log k/T vs. $1/T$ plots.



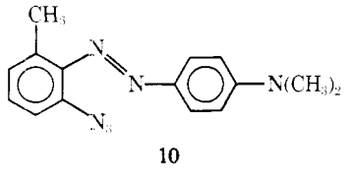
8 9

decreasing effect of substituents at higher temperature as the isokinetic temperature is approached; i.e., the transition state more closely resembles the symmetric pentazole structure, bond formation between N-1 and N-5 and between N-2 and N-3 being essentially simultaneous at the higher temperature.

The observed entropy of activation for an intermolecular 1,3-dipolar addition reaction usually falls in the range of −30 to −45 cal mol^{-1} deg^{-1}. Since the usual difference between an intermolecular and an intramolecular cycloaddition reaction is of the order of 25 cal mol^{-1} deg^{-1}, the expected range for an intramolecular 1,3-dipolar cycloaddition would be −5 to −20 cal mol^{-1} deg^{-1}, consistent with the data in Table IV. Also it should be noted in Table IV that the changes in the entropy of activation with the substituent are quite large. The changes in entropy of activation have almost as much effect on the rate as do the changes in enthalpy of activation.

One objection that could be raised to the postulation of the 1,3-dipolar cycloaddition could be the fact that phenyl azide does not undergo intermolecular 1,3-dipolar cycloaddition to azobenzene.[13] However, if one assumes that both the intermolecular and intramolecular processes have about the same energy of activation (Table IV), the higher negative entropy of activation for the intermolecular process could prevent it from occurring at an appreciable rate.

The transition state pictured in **8** or **9** requires that the phenylazo group be twisted out of the plane of the ring to which the azido group is attached. It was reasoned that if properly selected substituents were introduced ortho to the phenylazo group, it would be forced into a more favorable conformation for reaction, and steric acceleration should be observed. In order to test this idea, an attempt was made to prepare 2-azido-6-methyl-4'-dimethylaminoazobenzene (**10**). Attempts to isolate and purify the compound gave only the corresponding benzotriazole due to its rapid decomposition. In order to at least get some semiquantitative information on the compound, it was prepared and extracted directly from

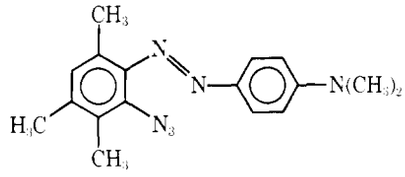


10

the reaction mixture. The extracts were then added directly to the anisole without further purification. A rate constant of 0.67×10^{-2} min^{-1} at 50 °C was obtained. Comparison of this value with the value of the unmethylated compound in Table III indicates a steric acceleration by a factor of 30.

Dyall and Kemp[1] reported that the methyl group in 2-nitro-3-methylphenyl azide decreased the rate of cyclization to the benzfuroxan by a factor of 0.0885 compared to the increase noted above. This result suggests that the steric requirements in the two reactions are radically different. One obvious explanation is that cyclization to the nitro group requires a planer transition state[1] analogous to **6**, whereas the 2-azidoazo compounds require the nonplaner conformation of **8** or **9**.

Dyall and Kemp[1] also reported that the methyl group in 2-nitro-6-methylphenyl azide retarded the cyclization to the benzofuroxan by a factor of 0.0130. Attempts to prepare the analogous compound in the 2-azidoazobenzene series were unsuccessful, but a few milligrams of compound **11** was pre-



11

pared. A single kinetic run at 50 °C gave a rate constant of 0.082×10^{-2} min^{-1}, indicating a retardation of the rate by a factor of 0.12. The retardation of the rate by a lone methyl adjacent to the azido group would be expected to be much larger than 0.12, because acceleration of the rate by the methyl adjacent to the azo group in **11** should accelerate the rate by a factor of 30 as given above; i.e., the net effect of the methyl adjacent to the azido group would be a retardation by a factor of 0.004.

The retardation of the rate caused by the methyl in 2-nitro-6-methylphenyl azide was interpreted as meaning that the azido group had to be coplanar with the ring as in transition state **3**. This may be correct in that case, but there is an alternate explanation for retardation of the rate in **11**. Since the methyl groups in **11** would be expected to force both the azido and azo groups out of the plane of the benzene ring, **11** would be expected to exist in syn and anti conformers. However, only the anti conformer could lead to transition states **8** or **9**. There is no steric reason for expecting either the syn or anti conformation to be more stable, but the syn isomer does have the possibility of π bonding between the azido group and the azo group, an effect that could lead to stabilization of the syn conformer and retardation of the rate. The existence of stable conformers is indicated by the fact that the NMR (60 MHz) of **11** exhibited two peaks for the dimethylamino group at 182 and 219 Hz. The two peaks are equally intense indicating equal population of the two conformers.

Experimental Section

All melting points are uncorrected. The NMR spectra were recorded on a 60-MHz instrument. The 4'-R-azidoazobenzenes were prepared by condensation of the appropriately substituted nitrosobenzene with 2-azidoaniline in glacial acetic acid[7] except 4'-dimethylamino-2-azidoazobenzene whose preparation has been reported.[8] The 2-azidoaniline preparation used was that reported previously.[9,10] Several methods of preparing the substituted nitrosobenzenes were investigated, but the one that worked best with a variety of substituents was patterned after the procedure of Nutting, Jewell, and Rapoport.[14]

General Preparation of 4-Substituted Nitrosobenzenes. To a solution of 0.210 mol of the corresponding 4-substituted nitrobenzene in 560 mL of 2-methoxyethanol was added 17.0 g (0.317 mol) of

ammonium chloride in 135 mL of water. Nitrogen was bubbled through the solution for a few minutes and then the solution was stirred vigorously under nitrogen, while 36.0 g (0.550 mol) of zinc dust was added over a 30-min period. During the addition the temperature was maintained at 33–36 °C by applications of hot or cold water baths. After an additional 30 min of stirring, the residues were filtered and washed once with 30 mL of 2-methoxyethanol. The filtrate was kept under nitrogen and added dropwise over a period of 1.5–3.0 h to a stirred solution of 140 g (0.52 mol) of ferric chloride hexahydrate in 240 mL of ethanol and 900 mL of water. The mixture was kept at −5 to −15 °C with a methanol–ice bath. After an additional 30 min of stirring, the mixture was diluted to 4000 mL with ice water to give the crude nitroso compound. Substituent, purification method, and yield were as follows: 4-CO_2CH_3, steam distillation, 60%; 4-CH_3, steam distillation, and recrystallization from ethanol at −10 °C, 35%; 4-CN, steam distillation and recrystallization from ethanol at −10 °C, 50%; 4-SO_2NH_2, recrystallization from ethanol, 60%; 4-$NHCOCH_3$, recrystallization from 50% ethanol, 69% (in this case 700 mL of methoxethanol was used in the preparation); 4-$COCH_3$, recrystallized from ethanol, 36%. The melting points all agreed with literature values. 4-Nitrosoacetophenone, mp 111 °C, is a new compound.

Anal. Calcd for $C_8N_7NO_2$: C, 64.42; H, 4.73; N, 9.39. Found: C, 64.31; H, 4.74; N, 9.40.

4-Nitronitrosobenzene.[15] Potassium persulfate (100 g, 0.37 mol) was added with stirring to 100 mL of concentrated sulfuric acid. After 1 h, this slurry was poured on 2000 g of ice and neutralized with 5 M potassium carbonate solution. The suspension was stirred at room temperature while 100 mL of dioxane containing 9.0 g (0.065 mol) of *p*-nitroaniline was added dropwise. The mixture was extracted with two 250-mL portions of methoxyethanol. The extracts were diluted with water to give 8.2 g of solid material. Steam distillation gave 2.9 g (30%) of the nitroso compound, mp 117–121 °C (lit.[16] 118–118.5 °C).

4-Chloronitrosobenzene. The procedure of Barrow and Thorneycraft[17] was used except the material was not steam distilled; it was repeatedly recrystallized from ethanol, mp 89–90 °C (lit.[17] mp 90 °C).

General Procedure for 4′-R-2-Azidoazobenzenes. In 80 mL of glacial acetic acid was dissolved 5.36 g (0.04 mol) of 2-azidoaniline and 0.04 mol of the 4-substituted nitrosobenzene. The reaction mixture was stirred at a temperature below 20 °C, but above the freezing point of the mixture for 5–12 h. The mixture was poured onto ice and made basic with 2 N sodium hydroxide. The mixture was extracted with an appropriate solvent (pentane for R = H, CH_3; chloroform for R = Cl, CO_2CH_3, $NHCOCH_3$; ether for R = $COCH_3$, NO_2, CN). The solution was extracted with dilute hydrochloric acid to remove any remaining amine. The solution was dried over magnesium sulfate and the solvent removed. The 4-nitro compound was purified by recrystallization from ethanol at −10 °C. The remaining compounds were dissolved in an appropriate solvent and passed quickly through a short alumina column. The solvents used were: chloroform, R = Cl, CO_2CH_3; ether, R = CO_2CH_3, CN; ether–petroleum ether (1:7), R = H; pentane–ether (1:1), R = CH_3; chloroform–ether (1:2), R = $NHCOCH_3$. The red azo compound emerges first leaving most impurities behind. After removal of the solvent the azidoazo compound was recrystallized from ethanol (hexane for R = H) at −10 °C. Some of the compounds were stable enough to obtain satisfactory analyses and these are listed in Table I. The remaining compounds were unstable and had lost nitrogen by the time they could be analyzed. The yields are listed in Table I along with IR data. No melting points could be obtained as the compounds were transformed into benzotriazoles before melting.

4′-Sulfonamido-2-azidoazobenzene. The reaction was carried out as described above. The acetic acid solution was poured on ice and neutralized with sodium bicarbonate solution. The solid was filtered and then slurried with dilute hydrochloric acid to remove amines. The solid was filtered, dried, and dissolved in acetone (1.2 L). The solution was poured into ten times its volume of pentane. The precipitated solid was filtered to give 7.8 g (65%) of the pure azidoazo compound.

Preparation of 2-(4-R-Phenyl)benzotriazoles. The corresponding 4′-R-2-azidoazobenzene was refluxed 2–5 h in hexane or tetrahydrofuran. The solvent was removed and the residue recrystallized from hexane or ethanol (95%). 2-(4-Sulfonamidophenyl)-benzotriazole was recrystallized from acetone.

***N*-(2-Nitro-3,4,6-trimethylphenyl)phthalimide.** 2-Nitro-3,4,6-trimethylaniline[18] (27.0 g, 0.150 mol) and phthalic anhydride (23.0 g, 0.155 mol) were melted together and heated to 180 °C where evolution of water began. The temperature was slowly raised to 240 °C over a period of 30 min, by which time evolution of water had ceased. The mixture was cooled and allowed to solidify. Recrystallization from 4 L of ethanol gave 34 g (73%), mp 239.5–240.5 °C.

Anal. Calcd for $C_{17}H_{14}N_2O_4$: C, 65.81; H, 4.55; N, 9.04. Found: C, 65.67; H, 4.58; N, 9.10.

***N*-(2-Amino-3,4,6-trimethylphenyl)phthalimide.** The nitro compound (32.5 g, 0.105 mol) was placed in 900 mL of hot acetone and stirred rapidly. To this slurry was added 90 mL of acetic acid and 90 mL of water. Powdered iron (70 g, 1.2 mol) was added in small portions over a period of 2 h. After refluxing and stirring for 2 days, the hot solution was filtered and the inorganic residues washed with 500 mL of hot acetone. The acetone solution was neutralized by the addition of a concentrated sodium bicarbonate solution. The acetone layer was separated, concentrated to 1 L, and poured into 2.5 L of ice water. Filtration of the solid, followed by recrystallization from 1.2 L of 95% ethanol, gave 20.5 g (70%): mp 214–215 °C; IR (Nujol) 3490, 3410 (NH_2), 1783, 1760, 1710 cm^{-1} (C=O); NMR ($CDCl_3$) Hz 119, 122, 133 (CH_3's); 205 (NH_2), 393 (1 H), 467 ($A'_2B'_2$), 119 (s, 3 H), 122 (s, 3 H), 133 (s, 3 H), 205 (bs, 2 H), 393 (s, 1 H), and 467 ($A'_2B'_2$, 4 H).

Anal. Calcd for $C_{17}H_{16}N_2O_2$: C, 72.84; H, 5.77; N, 10.11. Found: C, 72.73; H, 5.71; N, 9.87.

***N*-(2-Azido-3,4,6-trimethylphenyl)phthalimide.** The finely powdered amino compound (19.6 g, 0.07 mol) was stirred rapidly with 500 mL of water. Concentrated hydrochloric acid (80 mL) was added all at once, followed by addition of ice. The amine was diazotized with 5.4 g (0.078 mol) of sodium nitrite in 30 mL of water. The mixture was stirred for 2 h at 5 °C. The cold mixture was filtered and to the filtrate was slowly added 6.0 g (0.092 mol) of sodium azide in 25 mL of water at 5 °C. Small amounts of ether were added from time to time, just enough to control the foaming. After 1.5 h the azide was filtered and dried in the dark to give 20.6 g (96%), mp 152–3 °C dec. After recrystallization from ethanol it decomposed sharply at 159 °C: IR (Nujol) 2120 (N_3), 1788, 1770, 1724 cm^{-1} (C=O); NMR ($CDCl_3$) Hz 126 (s, 3 H), 136 (s, 6 H), 418 (s, 1 H), and 471 ($A'_2B'_2$, 4 H).

Anal. Calcd for $C_{17}H_{14}N_4O_2$: C, 66.65; H, 4.62; N, 18.29. Found: C, 66.75; H, 4.67; N, 1814.

2-Azido-3,4,6-trimethylaniline. The above phthalimide (19.6 g, 0.064 mol) was slurried in 250 mL of methanol and 25 mL of anhydrous hydrazine added all at once. The phthalimide dissolved after 10 min, and after 20 min more a solid precipitated. After 1.5 h of additional stirring the solid was filtered and washed with two portions of methanol. The methanol filtrates were poured into water to precipitate the amine. The amine was filtered and recrystallized from hexane to give 2.8 g (27%): mp 56.5–57 °C; IR ($CHCl_3$) 3472, 3390 (NH_2), 2120 cm^{-1} (N_3); NMR ($CDCl_3$) Hz 123 (s, 3 H), 127 (s, 3 H), 132 (s, 3 H), 219 (bs, 2 H), 400 (s, 1 H).

2-Azido-3,4,6-trimethyl-4′-dimethylaminoazobenzene. To 1.76 g (10 mmol) of the above amine was added 20 mL of water and 2 mL of concentrated hydrochloric acid. It was diazotized at 0 °C with 0.82 g (12 mmol) of sodium nitrite in 10 mL of water. After 30 min, the solution was filtered and the filtrate was added to 1.22 g (10 mmol) of *N,N*-dimethylaniline in 1 mL of concentrated hydrochloric acid. Sodium acetate was added to raise the pH to 5, followed by enough sodium bicarbonate to raise the pH to 6. The mixture was stirred at 3 °C for 26 h. The red solution was extracted with 300 mL of benzene. The benzene was dried over magnesium sulfate and the resulting solution passed through a short water cooled alumina column. The red band that came off first was collected. The solvent was removed under vacuum and the residue recrystallized from 95% ethanol at −10 °C: IR ($CHCl_3$) 3012, 2950, 2793, 2100, 1600, 1488, 1458, 1361, 1328, 1211, 816 cm^{-1}; NMR ($CDCl_3$) Hz 132 (s, 6 H), 136 (s, 3 H), 182 (s), 219 (s, 6 H), 425 (m, 5 H).

Anal. Calcd for $C_{17}H_{20}N_6$: C, 66.21, H, 6.49; N, 27.25. Found: C, 66.08; H, 6.23; N, 27.51.

Attempted Preparation of 2-Azido-6-methyl-4′-dimethylaminoazobenzene. 2-Azido-6-methylaniline[19] (2.96 g, 20 mmol) was diazotized and reacted with *N,N*-dimethylaniline as described in the preceding preparation. After stirring at 0 °C for 1 day the precipitated solid was filtered and dissolved in cold benzene and the solution passed through a short alumina column at 10 °C. The benzene containing the red band was frozen and the solid benzene evaporated under vacuum. During the evaporation the red color disappeared, leaving a light yellow residue. Recrystallization from alcohol gave 1.25 g (52%), mp 129.5–130.5 °C, of a compound identified as 4-methyl-2-(4′-dimethylaminophenyl)benzotriazole: NMR ($CDCl_3$) Hz 160 (s, 3 H), 175 (s, 6 H), 446 (m, 7 H).

Anal. Calcd for $C_{15}H_{16}N_4$: C, 71.40; H, 6.39; N, 22.21; mol wt 252. Found: C, 71.61; H, 6.52; N, 22.38; mol wt 260 (cryoscopic).

Acknowledgment. The authors would like to acknowledge the work of Charles Hearn, who prepared the 4′-dimethyl-

amino-2-azidoazobenzene and ran some of the kinetics on this compound.

Registry No.—11 isomer 1, 67661-60-3; 11 isomer 2, 67661-61-4; 4'-dimethylamino-2-azidoazobenzene, 16675-41-5; nitrosobenzene, 586-96-9; 4-methoxycarbonylnitrosobenzene, 13170-28-0; 4-acetylnitrosobenzene, 31125-05-0; 4-nitrosobenzene, 4485-08-9; 4-nitrosobenzenesulfonamide, 2990-12-7; 4-acetamidonitrosobenzene, 67661-55-6; 4-methylnitrosobenzene, 623-11-0; 4-chloronitrosobenzene, 932-98-9; 4-cyanonitrosobenzene, 31125-07-2; 2-azidoaniline, 1005-07-8; methyl 4-nitrobenzoate, 619-50-1; 4-methylnitrobenzene, 99-99-0; 4-nitrobenzonitrile, 619-72-7; 4-nitrobenzenesulfonamide, 6325-93-5; *N*-(4-nitrophenyl)acetamide, 104-04-1; 4-nitroacetophenone, 100-19-6; *p*-nitroaniline, 100-01-6; *N*-(2-nitro-3,4,6-trimethylphenyl)phthalimide, 67661-56-7; 2-nitro-3,4,6-trimethylaniline, 41571-53-3; phthalic anhydride, 85-449; *N*-(2-amino-3,4,6-trimethylphenyl)phthalimide, 67661-57-8; *N*-(2-azido-3,4,6-trimethylphenyl)phthalimide, 67661-58-9; 2-azido-3,4,6-trimethylaniline, 67661-59-0; *N*,*N*-dimethylaniline, 121-69-7; 2-azido-6-methylaniline, 17537-14-3; 4-methyl-2-(4'-dimethylaminophenyl)benzotriazole, 67661-62-5.

References and Notes

(1) L. K. Dyall and J. E. Kemp, *J. Chem. Soc., Part B*, 976–9 (1968).
(2) G. Boshev, L. K. Dyall, and P. R. Sadler, *Aust. J. Chem.*, **25**, 599 (1971).
(3) T. Zincke and A. T. Lawson, *Chem. Ber.*, **20**, 1176 (1887).
(4) T. Zincke and H. Jaenke, *Chem. Ber.*, **21**, 540 (1888).
(5) R. A. Carboni and J. E. Castle, *J. Am. Chem. Soc.*, **84**, 2453 (1962).
(6) R. A. Carboni, J. C. Kauer, J. E. Castle, and H. E. Simmons, *J. Am. Chem. Soc.*, **89**, 2618 (1967).
(7) J. H. Hall, J. G. Stephanie, and D. Nordstrom, *J. Org. Chem.*, **33**, 2951 (1968).
(8) J. H. Hall, *J. Org. Chem.*, **33**, 2954 (1968).
(9) P. A. S. Smith, J. H. Hall, and R. O. Kan, *J. Am. Chem. Soc.*, **84**, 485 (1962).
(10) J. H. Hall and D. R. Kamm, *J. Org. Chem.*, **30**, 202 (1965).
(11) J. H. Hall, F. Behr, and R. L. Reed, *J. Am. Chem. Soc.*, **94**, 4952 (1972).
(12) J. H. Hall, unpublished results.
(13) The rate of decomposition of phenyl azide in decalin is unaffected by the addition of azobenzene; J. H. Hall, unpublished work.
(14) W. H. Nutting, R. A. Jewell, and H. Rapoport, *J. Org. Chem.*, **35**, 505 (1970).
(15) J. McIntyre and J. C. E. Simpson, *J. Chem. Soc.*, 2606 (1952).
(16) E. Bamberger and R. Hübner, *Chem. Ber.*, **36**, 3809 (1903).
(17) F. Barrow and F. J. Thorneycraft, *J. Chem. Soc.*, 774 (1939).
(18) G. VanKleef, *Recl. Trav. Chim. Pays-Bas*, **55**, 765 (1936).
(19) J. H. Hall and E. Patterson, *J. Am. Chem. Soc.*, **89**, 5856 (1967).
(20) H. Willgerodt and H. Klein, *J. Pract. Chem.*, **60** (2), 97 (1899).
(21) L. Gatterman and G. W. Wichmann, *Chem. Ber.*, **21**, 1633 (1888).

Kinetics and Mechanism of Aliphatic Transnitrosation

Sandra S. Singer

NCI Frederick Cancer Research Center, Frederick, Maryland 21701

Received June 16, 1978

The kinetics and mechanism of nucleophile-catalyzed transnitrosation by alicyclic nitrosamines are discussed. Transnitrosating agents used included 4-methyl-1-nitrosopiperazine, 2,6-dimethyldinitrosopiperazine, 3,5-dimethyl-1-nitrosopiperazine, and 3-methyl-4-nitroso-2-phenylmorpholine (nitrosophenmetrazine). In all cases morpholine was the recipient amine and thiocyanate ion the nucleophilic catalyst. The transnitrosation reaction was found to be first order in donor nitrosamine and thiocyanate ion, and to be acid dependent. The recipient amine entered into the kinetic rate equation only at low concentrations.

Transnitrosation, which we will define as the transfer of a nitroso group from a nitrosamine to another amine, is a well-known characteristic reaction of aromatic nitrosamines such as diphenylnitrosamine,[1] nitrosocarbazole,[2] and *N*-nitroso-*N*-methylaniline.[3,4] Challis suggested that transnitrosation might be a reaction of aliphatic nitrosamines,[5] but it was only recently demonstrated that certain aliphatic nitrosamines are in fact capable of facile transnitrosation under appropriate conditons,[6] i.e., the presence of a nucleophilic catalyst and appropriate hydrogen ion concentration.

Nitrosation[7] and transnitrosation[6] generally are reversible reactions, but nitrosotransfer to a compound which then decomposes to gaseous products provides an uncomplicated method for studying the kinetics of nitrosotransfer. Challis studied this form of transnitrosation with aromatic nitrosamines and nitrosomorpholine.[3,5] Williams also used this type of reaction in connection with his studies of the Fischer–Hepp rearrangement.[4,8,9] Challis[5] and Boyland[10] found that denitrosations are catalyzed by nucleophiles such as chloride, bromide, and thiocyanate in the same manner that nitrosations are catalyzed by these species.[11,12]

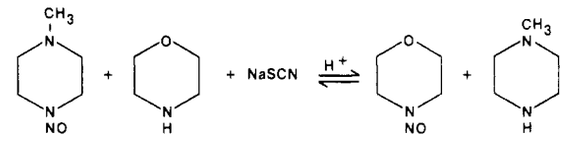
We recently reported the first examples of facile transnitrosation by alicyclic nitrosamines in which both donor and recipient amines were aliphatic.[6,13] We now report the detailed kinetics and mechanism of this reaction.

Results

The thiocyanate-catalyzed reaction between alicyclic nitrosamines and morpholine was chosen for study because of its importance to related in vivo carcinogenicity studies and because of the relative ease of analyzing for the principal products.

The kinetic reaction order of each reactant was determined by observing the change in the pseudo-first-order rate constant for appearance of product nitrosamine caused by varying the concentration of one reactant (the isolation method). The concentration of the reactant being studied was varied while all other reagents were kept at a constant, higher level. For a given set of reactions, the pH was held constant, in the range 1.5–1.8. This relatively low concentration of H^+ was necessary to retard the reaction rates for convenient study.

The reaction of *N*-nitroso-4-methylpiperazine with morpholine was found to be first order in thiocyanate. The results are given in Table I. The reaction was zero order in morpholine at high concentrations but approached first order at lower



(1)

concentrations (Table II). The pH dependence of the reaction shown in eq 1 was determined by one-point kinetics at 10 different pH's. The pH profile is shown in Figure 1.

The pH dependence of the rate of transnitrosation by nitrosophenmetrazine at three pH's was determined. In all cases good first-order plots were obtained, and the rate constants reflect a dependence on $[H^+]$. These reactions are run in 50%

0022-3263/78/1943-4612$01.00/0