ligand rate-limiting step rather than the usual rapid stepwise water loss or diffusion-controlled encounter. A plausible explanation is that the metal ion be required to lose a majority of its solvation shell, prior to formation of an exclusive complex. Such a process would be energetically unfavorable and so reflected in ΔH_1 and ΔS_1. A full accounting of the unsually slow complexation rates would require monitoring several other ions as well as the larger cryptands and the monocyclic cryptands (e.g., 220).

Finally this study raises the exciting applications of monitoring an intrinsic reaction parameter, such as heat, in revealing the overall dynamical processes of molecules on the stopped-flow time scale. Another area of particular application would be protein–protein interactions, most specifically *lac* repressor–operator interactions.[11]

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(10) G. W. Liesegang and E. M. Eyring, "Synthetic Multidentate Macrocyclic Compounds", R. M. Izatt and J. J. Christensen, Eds., Academic Press, New York, 1978, Chapter 5.

(11) A. D. Riggs, S. Bourgeois, and M. Cohn, *J. Mol. Biol.*, **51**, 303 (1970).

Mechanism of the Benzidine Rearrangement. Kinetic Isotope Effects and Transition States. Evidence for Concerted Rearrangement[1,2]

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The name "benzidine rearrangement" refers to a class of rearrangements of hydrazo aromatics, among which are the benzidine rearrangement itself (i.e., the rearrangement of hydrazobenzene), and the diphenyline, *o*-semidine, *p*-semidine, and *o*-benzidine rearrangements. These names describe the types of product given by rearrangement of particular hydrazo aromatics. Although an extraordinarily large amount of work has been devoted to these rearrangements and their products and kinetics have been described in ample detail,[3] a decisive answer to one question has always been elusive: namely, how do the rearrangements occur? Concerning this question, three major theories have been proposed in recent years. One of these, calling for a rate-determining ring protonation,[4] was shown subsequently to be inconsistent with the kinetic nitrogen isotope effect in the rearrangement of hydrazobenzene.[2] The two remaining ones are the polar-transition-state theory, which says in essence that the benzidine rearrangements are concerted and go through polar transition states,[3a] and the π-complex theory, which says that the rearrangements go through π-complex intermediates, and, in essence, are not concerted.[5] The major remaining unanswered question about the benzidine rearrangements may thus be stated quite simply: are they or are they not concerted? More specifically, does the transition state of a rearrangement involve concerted bond breaking and bond making? We are now able to answer that question as it applies to the rearrangement of hydrazobenzene to benzidine. We hope, in time, to answer the question as it applies to the several types of benzidine rearrangement.

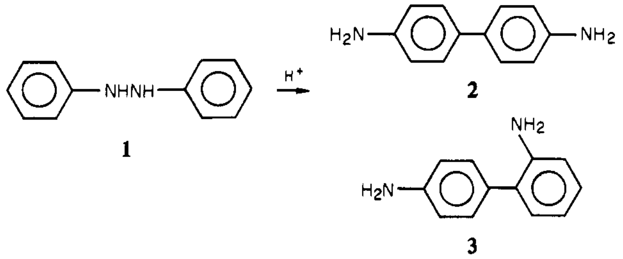
Table I. Experimental and Calculated Kinetic Isotope Effects for the Benzidine and Diphenyline Rearrangements

		kinetic isotope effect, $k_{\text{light}}/k_{\text{heavy}}$		
			calcd (model)	
rearrangement	isotope	obsd	concerted	dissociative
benzidine	$^{14}N^{15}N$	1.0222[a]	1.025	1.055
diphenyline	$^{14}N^{15}N$	1.063[b]	1.027	1.055
benzidine/ diphenyline	H/D	0.962[c]	<1.0	>1.0[e]
benzidine	$^{12}C^{14}C$	1.050[d]	1.0367	

[a] Mean value for 5% (1.0229 ± 0.0009), 10% (1.0222 ± 0.0034), and 15% (1.0214 ± 0.0001) conversions. [b] Mean value for 5% (1.0634 ± 0.0037), 10% (1.0630 ± 0.0009), and 15% (1.0635 ± 0.0007) conversions. [c] Mean value for 40% (0.9618), 50% (0.962), 60% (0.962), 70% (0.961), 80% (0.962), and 95% (0.062) conversions, all data equal to or better than 0.004 deviation. [d] Mean value for four runs, 5% (1.042), 5% (1.054), 5% (1.050), and 10% (1.055) conversions. [e] A hyperconjugative effect of deuterium at the 4,4′ positions for the charged structures formed in the dissociative mechanism would give rise to $k_H/k_D > 1.0$.[17–19]

The rearrangement of hydrazobenzene is second order in acid. We shall assume for the sake of simplicity that the second proton is fully transferred to nitrogen in the transition state, although this has been questioned,[2,6] and confine ourselves to the question of whether N–N bond breaking and C–C bond making are concerted.

When hydrazobenzene (**1**) rearranges in acid solution, two major products are formed: benzidine (**2**) and diphenyline (**3**).



The question of concertedness should, therefore, be asked for each product. Concerted rearrangement should result in a kinetic nitrogen isotope effect for bond breaking and a kinetic carbon isotope effect for bond making. Rate-determining C–C bonding should also result in a secondary deuterium isotope effect.

That N–N bond breaking is part of the transition state was, in fact, shown a few years ago by using ordinary **1** and isotope-ratio mass spectrometry after converting the products to N_2.[2] We have repeated the determination, but this time by using an enrichment with doubly labeled **1** and by measuring the relative abundances of the products, i.e., of masses 184 and 186. Also, the measurements were made for both of the separated products, **2** and **3**. The results are given in Table I. They show that the transition state for forming each product involves N–N bond breaking but

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[§] Supported by the National Science Foundation, Grant 79-11110.

(1) Benzidine Rearrangements, 15.

(2) Part 14: Shine, H. J.; Henderson, G. N.; Cu, A.; Schmid, P. *J. Am. Chem. Soc.* **1977**, *99*, 3719.

(3) (a) Banthorpe, D. V.; Hughes, E. D.; Ingold, C. K. *J. Chem. Soc.* **1964**, 2864. (b) Shine, H. J. "Aromatic Rearrangements", Elsevier: New York, 1967; pp 126–179. (c) Shine, H. J. *MTP Int. Rev. Sci.: Org. Chem., Ser. 1* **1973**, *3*, 79–84. (d) *MTP Int. Rev. Sci.: Org. Chem., Ser. 2* **1976**, *3*, 100–110. (e) Cox, R. A.; Buncel, E. *Chem. Hydrazo, Azo, Azoxy Groups* **1975**, *2*, 777–805 and references therein.

(4) Olah, G. A.; Dunne, K.; Kelly, D. P.; Mo, Y. K. *J. Am. Chem. Soc.* **1972**, *94*, 7438.

(5) (a) Dewar, M. J. S. In "Molecular Rearrangements"; de Mayo, P., Ed.; Interscience: New York, 1963; Vol. 1, pp 323–343. (b) Dewar, M. J. S.; Marchand, A. P. *Annu. Rev. Phys. Chem.* **1965**, *16*, 338.

(6) Bunton, C. A.; Rubin, R. J. *Tetrahedron Lett.* **1975**, 59; *J. Am. Chem. Soc.* **1976**, *98*, 4236.

0002-7863/81/1503-955$01.25/0

the transition states seem to be quite different from each other.

We have measured also the secondary deuterium isotope effect for 4,4′-dideuteriohydrazobenzene (**1**-d_2). To do this, a mixture of **1** and **1**-d_2 was used, and the hydrazo compound remaining at particular conversions was oxidized to azobenzene. The relative abundances of masses 182 and 184 were measured and converted into ratios of rate constants for the disappearance of **1** and **1**-d_2. The results (Table I) show that there is a 4% inverse isotope effect (2% for each D atom) and are consistent with concerted rearrangement but cannot distinguish between the formation of the two products. The consistency in k_H/k_D (Table I) over the range of conversions of 40–95% indicates that exchange of aromatic deuterium with the solvent medium was not taking place during the time of rearrangement.

In harmony with these results we have also measured a kinetic carbon isotope effect for the formation of **2**, using **1**-*4*-^{14}*C*. Our data (Table I) lack the precision of the mass spectrometric data but nevertheless leave no doubt that there is a carbon isotope effect for the formation of **2**. We have not yet been able to separate enough of **3** for satisfactory combustion measurements of the ^{14}C content.

It is possible to calculate[7] the nitrogen and carbon isotope effects for concerted and dissociative transition states for the formation of benzidine. We have done this by assuming that these transition states have the geometries shown in Figure 1. We have assumed also that the transition states are diprotonated, the force constants in the concerted transition states are half those in the ground states, and the critical bond in the dissociative transition state is fully broken.[11] The calculated results are also given in Table I.

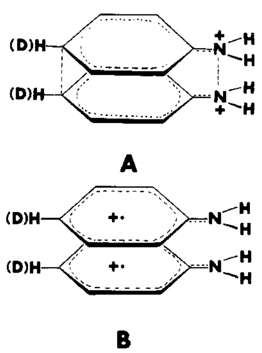

Figure 1. Transition state models for the benzidine rearrangement. (A) Concerted rearrangement, (B) dissociative, cation-radical pair.

These calculations are in excellent agreement with the experimental results for the concerted formation of **2**. They suggest also that formation of **3** is, in fact, a dissociative process. As has been pointed out before,[3d] the concerted formation of **2** is an allowed sigmatropic suprafacial [5,5] process, while the concerted formation of **3** would be a forbidden suprafacial [3,5] process. The isotope data for the formation of **3** indicate that it is indeed quite different from formation of **2**. The nitrogen isotope data suggest that C–C bonding should not be part of the transition state for **3**, and we hope to be able to check that directly by carbon isotope measurements.

The conditions for rearrangement were like those described earlier.[2] Sufficiently large-scale runs were carried out so that sampling at low conversions (for products) and high conversions (for reactant) would give enough material for isolation and purification. Thus, most runs involved 2.208 g of **1** in 1200 mL of solution.[2] The whole of this solution was quenched with base at the appropriate calculated time. Unrearranged **1** was oxidized with air to azobenzene, and the solution was worked up as earlier.[2] Products (**2** and **3**) were isolated as mixed hydrochlorides and converted into **2** and **3**, and these were separated by preparative-scale TLC. Product **2** was recrystallized from water, while **3** was reprecipitated as the hydrochloride, again converted with base into **3**, and isolated as an oil. Sufficient quantities of ^{14}C-labeled **3** have not yet been isolated for combustion ^{14}C analyses.[13] The method of measuring the relative abundances of whole molecule masses has been described earlier.[14]

4,4′-Dideuterioazobenzene was made from 4′-deuterionitrobenzene, which in turn was made from *p*-nitrobenzenediazonium tetrafluoroborate and D_3PO_2 using a standard method.[15] Mass spectrometric analysis showed the dideuterioazobenzene to be 97% d_2 and 3% d_1.[16] Azobenzene was reduced to **1** with zinc powder and NH_4Cl.[2] Nitrobenzene-*4*-^{14}*C* was made[15] from 4-nitroaniline-*1*-^{14}*C* which was prepared commercially in a standard sequence and shown to be a unique isomer and free of 2-nitro- and 3-nitroaniline-*1*-^{14}*C* by tracer/GC analysis. ^{14}C-labeled-**1** was then prepared by standard methods.

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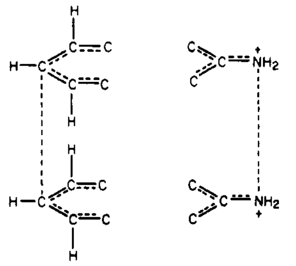
(7) By omitting, in a cutoff approximation, parts of the molecule more than two bonds removed from the position of isotopic substitution[8] and applying the Bigeleisen equation,[9] modified according to Slater[10] to include the reduced masses of the appropriate portions of the light and heavy transition states, we find in the present case,

$$k_L/k_H = (m_H^{\ddagger}/m_L^{\ddagger})^{1/2}[1 + (u_{14} - u_{15})G(u_{15}) - (u_{14}^{\ddagger} - u_{15}^{\ddagger})G(u_{15}^{\ddagger})]$$

in which $m_H^{\ddagger}$ and $m_L^{\ddagger}$ are the reduced masses in the transition states and the other terms have their designated meanings.[9] For example, using the cutoff approximation, the parts of the molecule which are considered in the transition state for concerted rearrangement to benzidine would be as shown.



In this case the so-called temperature independent term, $(m_H^{\ddagger}/m_L^{\ddagger})^{1/2}$, would read $[106 \times 230/104 \times 232]^{1/2}$, while the vibrational frequencies needed for calculating the second term of the Bigeleisen equation would be obtained as described below.[11] In calculating the isotope effect for the dissociative transition state only the nitrogen containing fragments are used, and $(m_H^{\ddagger}/m_L^{\ddagger})^{1/2}$ becomes $(106/104)^{1/2}$.

(8) Stern, M. J.; Wolfsberg, M., *J. Chem. Phys.* **1966**, *45*, 4105.

(9) Bigeleisen, J.; Wolfsberg, M. *Adv. Chem. Phys.* **1958**, *1*, 15. See also: Fry, A. In "Isotope Effects in Chemical Reactions"; Collins, C. J., Bowman, N. S., Eds.; Van Nostrand Rheinhold, NY, 1970; p 364.

(10) Slater, N. B. *Proc. R. Soc. London, Ser. A* **1948**, *194*, 112.

(11) The ^{14}N–^{14}N bond stretch in hydrazobenzene (methanol solution) was found by Raman spectroscopy to be at 996 cm^{-1}. The bathochromic shift in going from hydrazine to diprotonated hydrazine was 120 cm^{-1} so that the ^{14}N–^{14}N stretching frequency for our diprotonated ground-state model is taken as 876 cm^{-1}. By calculating the force constant for this frequency and applying it to the ^{15}N–^{15}N masses, the stretching frequency of the ^{15}N–^{15}N bond is calculated to be 846 cm^{-1} in the diprotonated ground state. The ground state for C–C bonding in the product should be the quinonoid-like diprotonated product, prior to its rapid deprotonations. However, in order to obtain a C–C bond frequency we have used 4,4′-biphenyls as the model, in which Raman data for the central C–C bond average at 1286 cm^{-1}.[12] The frequency for a ^{12}C–^{14}C bond in a biphenyl was then calculated to be 1239 cm^{-1}.

(12) Michelsen, H.; Klaeboe, P.; Hagen, G.; Stroyer-Hansen, T. *Acta Chem. Scand.* **1972**, *26*, 1576.

(13) (a) Raen, V. F.; Collins, C. J. *Pure Appl. Chem.* **1964**, *8*, 347. (b) Raen, V. F.; Dunham, T. K.; Thompson, D. D.; Collins, C. J. *J. Am. Chem. Soc.* **1963**, *85*, 3497. (c) Raen, V. F.; Tsiomis, A. K.; Collins, C. J. *Ibid.* **1960**, *82*, 5502.

(14) (a) Kwart, H.; Stanulonis, J. L. *J. Am. Chem. Soc.* **1976**, *98*, 4009. (b) Kwart, H.; Barnette, W. E. *Ibid.* **1977**, *99*, 614. (c) Kwart, H.; George, T. J. *Ibid.* **1977**, *99*, 5214. (d) Kwart, H.; George, T. J.; Louw, R.; Ultree, W. *Ibid.* **1978**, *100*, 3927. (e) Kwart, H.; Streith, J.; Benko, D. A.; Harris, D. J.; Schuppiser, J. L. *Ibid.* **1978**, *100*, 6501. (f) Kwart, H.; Benko, D. A.; Bromberg, M. E. *Ibid.* **1978**, *100*, 7093. (g) Kwart, H.; George, T. J. *J. Org. Chem.* **1979**, *44*, 162. (h) Kwart, H.; Benko, D. A. *J. Am. Chem. Soc.* **1979**, *101*, 1277.

(15) Korzeniowski, S. H.; Blum, L.; Gokel, G. W. *J. Org. Chem.* **1977**, *42*, 1469.

(16) We are grateful to Mr. James Hudson, University of Texas Mass Spectrometry Laboratory, for these measurements.

(17) Shiner, V. J., Jr.; Humphrey, J. S., Jr. *J. Am. Chem. Soc.* **1963**, *85*, 2416.

(18) Halevy, E. A. *Prog. Phys. Org. Chem.* **1963**, *1*, 109.

(19) Swain, C. G.; Sheats, J. E.; Gorenstein, D. G.; Harbison, K. G. *J. Am. Chem. Soc.* **1975**, *97*, 791.