an intense ^{31}P NMR resonance at −41.8 ppm which replaced almost entirely the downfield resonance previously observed. The solution was stripped of solvent and the residue recrystallized from ethyl acetate to yield phosphorane **3** as large colorless prisms: mp 155–170 °C.

Anal. Calcd for $C_{28}H_{19}Cl_4O_8P$: C, 51.24; H, 2.92; Cl, 21.61; P, 4.72. Found: C, 50.36; H, 2.73; Cl, 21.95; P, 4.94.

2-Hydroxy-2′,4,4′-trimethoxybenzophenone. A mixture of 50.0 g (0.182 mol) of 2,2′-dihydroxy-4,4′-dimethoxybenzophenone, 25.8 g (0.182 mol) of methyl iodide, and 2.29 g (0.182 mol) of potassium carbonate in 250 mL of acetone was heated for 6 h at reflux. The reaction product obtained was determined to be a 1:1 mixture of starting material and 2-hydroxy-2′,4,4′-trimethoxybenzophenone by TLC and ^{1}H NMR. The mixture was heated at reflux for another 6 h in acetone with an additional 25.8 g (0.182 mol) of methyl iodide and 2.29 g (0.182 mol) of potassium carbonate. Addition of 100 mL of water caused yellow solids to precipitate. Recrystallization of the precipitated solids from methanol/acetone, following treatment with decolorizing carbon and hot filtration, yielded 36.0 g (68.6%) of 2-hydroxy-2′,4,4′-trimethoxybenzophenone as very pale yellow prisms: mp 110–111.5 °C (lit.[15] 104–105 °C); ^{1}H NMR ($CDCl_3$) δ 3.60 (s, 3 H, OMe), 3.70 (s, 3 H, OMe), 3.72 (s, 3 H, OMe), 6.10–6.47 (m, 4 H, Ar–H), 7.02–7.20 (m, 2 H, Ar–H), 12.67 (s, 1 H, Ar–OH, exchanges with D_2O); IR (KBr) 1610 cm^{-1} (C=O); mass spectrum (70 eV), *m/e* (rel intensity, >20) 288 (M$^+$, 22), 257 (100), 138 (84).

Anal. Calcd for $C_{16}H_{16}O_5$: C, 66.66; H, 5.60. Found: C, 66.87; H, 5.74.

An additional 6.7 g (81.4% total) of 2-hydroxy-2′,4,4′-trimethoxybenzophenone was isolated by concentration and recrystallization of the filtrate from methanol/acetone.

3,4:8,9-Bis(4′-methoxybenzo)-5,7-bis(2′,4′-dimethoxyphenyl)-1-phenyl-2,6,10,11-tetraoxa-1-phospha(V)tricyclo[5.3.1.0^{1,5}]undecane (5). A solution of 0.68 mL (1.31 g, 0.005 mol) of phenylphosphonous dichloride in 15 mL of THF was added dropwise to a stirred solution of 2.88 g (0.01 mol) of 2-hydroxy-2′,4,4′-trimethoxybenzophenone and 1.39 mL (1.01 g, 0.01 mol) of triethylamine in 60 mL of THF at −78 °C. The cold bath was removed 15 min after addition was completed and the cloudy yellow reaction mixture warmed slowly to 25 °C overnight. The precipitated triethylamine hydrochloride (1.37 g) was collected by filtration under N_2 and identified by ^{1}H NMR.

The clear yellow filtrate was evaporated and the residue was dissolved in ethyl acetate. Removal of solvent under reduced pressure caused colorless solids to precipitate. Following the addition of 10 mL of ether, 2.86 g (83.9%) of phosphorane **5** (mp 138–140 °C, with decomposition) was collected by filtration under N_2.

Purification was accomplished by recrystallization from ethyl acetate to yield small, colorless, slightly hygroscopic crystals: mp 143–145.5 °C, with decomposition; ^{1}H NMR (C_6D_6) δ 2.67 (s, 3 H, OMe), 3.07 (s, 3 H, OMe), 3.18 (s, 3 H, OMe), 3.28 (s, 6 H, OMe), 3.40 (s, 3 H, OMe), 3.62 (s, 3 H, OMe), 5.90–7.78 (m, Ar–H), 8.30–8.67 (m, 2 H, Ar–H ortho to P); ^{31}P NMR (C_6D_6) −18.6; mass spectrum (10 eV), *m/e* (rel intensity, >20) 682 (M$^+$, 3), 396 (34), 271 (25), 257 (100), 138 (86).

Anal. Calcd for $C_{38}H_{35}O_{10}P$: C, 66.86; H, 5.17; P, 4.54. Found: C, 67.04; H, 5.10; P, 4.49.

Acknowledgment is made to the National Science Foundation (NSF CHE 78-14-7720862 and CHE-8104980) for its support of this work. This work was also supported in part by the University of Illinois NSF Regional Instrumentation Facility, Grant No. NSF CHE 79-16100.

Registry No. **1a**, 75589-80-9; **1e**, 81044-38-4; **1f**, 81044-39-5; **2a**, 77086-07-8; **2c**, 77086-08-9; **2d**, 81044-40-8; **3**, 81044-41-9; **5**, 81095-44-5; phenylphosphonous dichloride, 644-97-3; salicylaldehyde, 90-02-8; salicylaldehyde monosodium salt, 3116-83-4; 2-hydroxybenzophenone, 117-99-7; 2-hydroxy-2′,3′,5′,6′-tetramethylbenzophenone, 46954-49-8; 2-trifluoroacetylphenol, 25666-51-7; methyl salicylate, 119-36-8; 2-(*N*-methylformimidoyl)phenol, 3117-65-5; tetrachloro-*o*-benzoquinone, 2435-53-2; 2-hydroxy-2′,4,4′-trimethoxybenzophenone, 4142-51-2; 2,2′-dihydroxy-4,4′-dimethoxybenzophenone, 131-54-4; **8**, 81044-42-0.

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(15) Kurosawa, K.; Sasaki, Y.; Ikeda, M. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1498–1501.

Benzidine Rearrangements. 16. The Use of Heavy-Atom Kinetic Isotope Effects in Solving the Mechanism of the Acid-Catalyzed Rearrangement of Hydrazobenzene. The Concerted Pathway to Benzidine and the Nonconcerted Pathway to Diphenyline[1]

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Contribution from the Departments of Chemistry, Texas Tech University, Lubbock, Texas 79409, and University of Delaware, Newark, Delaware 19711. *Received July 30, 1981*

Abstract: Kinetic isotope effects (KIE) in the acid-catalyzed rearrangement of hydrazobenzene (**1**) to benzidine (**2**) and diphenyline (**3**) have been measured. Nitrogen KIE were determined by whole-molecule mass spectrometry on each of the products obtained at low and 100% conversions from mixtures of **1** and [^{15}N,^{15}N′]**1**. The results were $k(^{14}\mathrm{N})/k(^{15}\mathrm{N}) = 1.0222$ for **2** and 1.0633 for **3**. Carbon KIE were determined with both ^{14}C and ^{13}C labeling, using counting techniques for the former and whole-molecule mass spectrometry for the latter. Again measurements were made on both products isolated from low and 100% conversions. Use of mixtures of **1** and [4-^{14}C]**1** gave $k(^{12}\mathrm{C})/k(^{14}\mathrm{C}) = 1.0284$ for **2** and 1.0011 for **3**. Use of mixtures of **1** and [4,4′-$^{13}C_2$]**1** gave $k(^{12}\mathrm{C})/k(^{13}\mathrm{C}) = 1.0209$ for **2** and 1.000 for **3**. The results show that the formation of **2** is a concerted process while the formation of **3** is a dissociative process involving the formation of an intermediate (possibly a π complex or pair of caged radical ions) in the rate-determining step. Calculations of the KIE were made on simplified models of transition states for concerted and dissociative processes and were found to be in reasonable agreement with the experimental results. In harmony with the concerted formation of **2** (the major product) we found also by whole-molecule mass spectrometry and with the use of mixtures of **1** and [4,4′-$^2H_2$]**1** that the disappearance of **1** has an inverse secondary deuterium KIE, $k(^1\mathrm{H})/k(^2\mathrm{H}) = 0.962$.

The acid-catalyzed rearrangements of hydrazoaromatics, described collectively as the benzidine rearrangement, have been known for over 100 years.[4] The rearrangements were long known to be intramolecular, and in the early years of mechanistic interest

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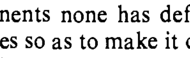
attempts were made to explain the course of rearrangement on the basis of this rather limited knowledge.[16-18] In 1950, however, Hammond and Shine reported that the rearrangement of hydrazobenzene was kinetically second order in hydrogen ion rather than first order as had been thought somewhat earlier.[19] In the 30 or so years which have since passed, a wealth of information has been gathered by various groups of workers on the kinetics and products of rearrangements and on the effects that solvent, medium, and substituents have on them In broad detail the rearrangements were shown to be first order in hydrazoaromatic and either first or second order in acid, depending on the hydrazoaromatic and, in some cases, the concentration of acid. The objective of this period of research was to discover the mechanism or mechanisms of the rearrangements, and it is fair to say that until now the objective has not really been reached. Writing about this in 1975 Cox and Buncel said: "this fascinating reaction has been a fruitful source for mechanistic speculation over the years".[15] Cox and Buncel list and discuss five theories of the rearrangement. One of these, originating with Lukashevich, appears to be inconsistent with kinetic data and needs no further discussion. Of the other four theories, none has been universally accepted, and each has, in one way or another, been heavily criticized.[15] We shall reconsider these theories in the light of our new results with kinetic isotope effects. The theories may be grouped in a way that is appropriate for our presentation, as follows. The polar transition state (PTS) theory of Ingold, Hughes, and Banthorpe[10] treats all rearrangements, regardless of their order in acid and the types of product which are formed, as being concerted and as going through polar transition states. That is, protonation is considered to be fast and reversible at the nitrogen atom(s) and to cause the rate-determining heterolytic scission of the N–N bond, thus leading into a polar transition state. Bond making, whether C–C or C–N, is regarded as coinciding with N–N bond breaking. The essence of the theory which distinguishes it from others is its requirement of concertedness. A second theory, which has elicited a great deal of interest and support, is Dewar's π-complex one.[8,9] The essence of this theory is that rearrangements are not concerted, and again, this applies to all rearrangements regardless of their kinetic and product form. The idea is that a mono- or diprotonated hydrazoarene forms a π-complex intermediate in a rate-determining step, and that after adopting an appropriate configuration with respect to each other the two halves of the π complex rapidly combine to give a product. The π-complex theory provides for heterolytic scission of the N–N bond in the protonated hydrazoarene and in this respect can also be looked upon as having a polar transition state. The major difference in these two theories then becomes the matter of concertedness. A third theory is the caged-radical theory. The theory calls for the homolysis of the N–N bond and the formation of either a solvent-caged radical and cation radical pair (in one-proton rearrangements) or pair of cation radicals (in two-proton rearrangements). The theory has never been given much credence, mainly, because evidence for odd-electron intermediates has never been found in the usual repertoire of rearrangements. For our purpose however, the key point of this theory is again in the matter of concertedness. According to this theory all rearrangements go through a caged-radical intermediate and are not concerted. In this, the caged-radical theory is no different from the π-complex intermediate theory.

The fourth theory is the ring protonation theory. It is unlike the first three theories in that it is concerned more with the site of protonation than with the course of reaction following protonation. The ring-protonation theory calls for protonation at a ring carbon atom adjacent to the hydrazo group. We will discuss the theory in more detail later, but point out now that among its proponents none has defined the timing of rearrangement sequences so as to make it clear to us whether rearrangements are thought to be concerted or not.

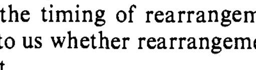
Some years ago one of us wrote that "no firm evidence exists, however, to *demand* the interposition of intermediates (π complex or otherwise) in the reaction paths. The settling of this point is the remaining major task in the mechanism of the benzidine rearrangement."[12] By that it was meant indirectly that it was necessary to settle whether or not the rearrangements were concerted. This is what we have now set out to settle and we shall show that a decision can now be made in the rearrangement of hydrazobenzene with our data on kinetic isotope effects. The same writer also wrote that "if it is felt that the acid-catalyzed benzidine rearrangements should follow the Woodward–Hoffman rules we must conclude that some rearrangements may be concerted while others must go through an intermediate of some sort".[14a] We hope to show that this rather vague presentiment has turned out to be true.

Results and Discussion

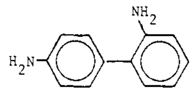
We have chosen to work with the prototype of the benzidine rearrangements, the rearrangement of hydrazobenzene (**1**) itself. This, in aqueous ethanol or aqueous dioxane solutions, under the usual conditions of rearrangement gives two products, benzidine (**2**) in 70% and diphenyline (**3**) in 30% yields. It has also been reported that trace amounts of other rearrangement products (e.g., the semidines) can be found by chromatographic techniques.[20] However, we have not noticed, but really not sought such products, but have confined ourselves to the major (if not the only) products, **2** and **3**. It can be seen that **2** is formed from bonding of the 4,4′-carbon atoms and **3** is formed from bonding of the 2,4′-carbon atoms of **1**. We have set out to find, therefore, whether these bondings occur along with or after the breaking of the N–N bond. To do this we have used ^{15}N,^{15}N′, 4-^{14}C, 4,4′-^{13}C$_2$, and 4,4′-^{2}H$_2$ labeling of **1**.



1



2



3

The rearrangement of **1** is second order in acid. It is generally agreed that the first protonation occurs at nitrogen and is reversible (eq 1). However, general agreement on the site (nitrogen or

$$C_6H_5NHNHC_6H_5 + H_3O^+ \rightleftarrows C_6H_5N^+H_2NHC_6H_5 + H_2O \quad (1)$$

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(1) Part 15. Shine, H. J.; Zmuda, H.; Park, K. H.; Kwart, H.; Horgan, A. G.; Collins, C.; Maxwell, B. E. *J. Am. Chem. Soc.* **1981**, *103*, 955.

(2) (a) Supported by the Robert A. Welch Foundation, Grant No. D-028 and the National Science Foundation, Grant No. CHE 78-00813. (b) Supported by the National Science Foundation, Grant No. 79-11110.

(3) (a) Texas Tech University. (b) University of Delaware.

(4) The rearrangements have been documented and reviewed in much detail during the last 60 years.[5-15]

(5) Jacobson, P. *Justus Liebigs Ann. Chem.* **1922**, *428*, 76.

(6) Hughes, E. D.; Ingold, C. K. *Q. Rev., Chem. Soc.* **1952**, *6*, 34.

(7) Vecera, M. *Chem. Listy.* **1958**, *52*, 1373.

(8) Dewar, M. J. S. In "Molecular Rearrangements"; de Mayo, P., Ed.; Interscience: New York, 1963; Vol. 1, pp 323–343.

(9) Dewar, M. J. S.; Marchand, A. P. *Annu. Rev. Phys. Chem.* **1965**, *16*, 338.

(10) Banthorpe, D. V.; Hughes, E. D.; Ingold, C. K. *J. Chem. Soc.* **1964**, 2864.

(11) Shine, H. J. "Aromatic Rearrangements"; Elsevier: New York, 1967; pp 126–179.

(12) Shine, H. J. In "Mechanisms of Molecular Migration"; Thyagarajan, B. S., Ed.; Interscience: New York, 1969; Vol. 2, pp 191–247.

(13) Banthorpe, D. V. *Top. Carbocycl. Chem.* **1969**, *1*, 1.

(14) (a) Shine, H. J. *MTP Int. Rev. Sci.: Org. Chem., Ser. One* **1973**, *3*, 79–84. (b) *MTP Int. Rev. Sci. Org. Chem., Ser. Two* **1976**, *4*, 100–110.

(15) Cox, R. A.; Buncel, E. In "The Chemistry of the Hydrazo, Azo, and Azoxy Groups"; Patai, S., Ed.; Wiley: New York, 1975; pp 775–859.

(16) Hughes, E. D.; Ingold, C. K. *J. Chem. Soc.* **1941**, 606.

(17) Robinson, R. *J. Chem. Soc.* **1941**, 220.

(18) Hammick, D. Ll.; Mason, S. F. *J. Chem. Soc.* **1946**, 638.

(19) Hammond, G. S.; Shine, H. J. *J. Am. Chem. Soc.* **1950**, *72*, 220.

(20) Gasparic, J.; Petranek, J.; Vecera, M. *Mikrochim. Acta* **1955**, 1026.

$$C_6H_5N^+H_2NHC_6H_5 + H_3O^+ \rightleftarrows C_6H_5N^+H_2N^+H_2C_6H_5 + H_2O \quad (2)$$

$$C_6H_5N^+H_2N^+H_2C_6H_5 \xrightarrow{\text{rds}} \text{products}^{2+} \quad (3)$$

$$\text{products}^{2+} \xrightarrow[\text{fast}]{H_2O} \text{products} + 2H_3O^+ \quad (4)$$

carbon) and the timing of the second protonation does not prevail. We shall discuss the question of the site later, but in the meantime we will represent it as occurring at the second nitrogen atom (eq 2). As to the question of timing, Bunton and Rubin[21] have proposed that the second protonation is part of the rate-determining process if it occurs at nitrogen. But, in dealing with the question of concertedness of the rearrangement it does not matter if the second protonation at nitrogen is or is not reversible. Therefore, for the sake of simplicity we will represent it as being fast and reversible, and discuss further implications later. In this representation, then, the question we wish to answer concerns the rate-determining step, eq 3: is this a concerted process or not; and we must answer it for both of the products, **2** and **3**.

Preparation of Labeled Hydrazobenzenes. The objective in each case was to prepare a labeled azobenzene (**4**) and to recrystallize this with an appropriate amount of unlabeled **4**. The mixture was then reduced to give the required mixture of labeled and unlabeled **1**.

[^{15}N,^{15}N′]**4** was prepared by oxidation of commercially-available [^{15}N]aniline with manganese dioxide.

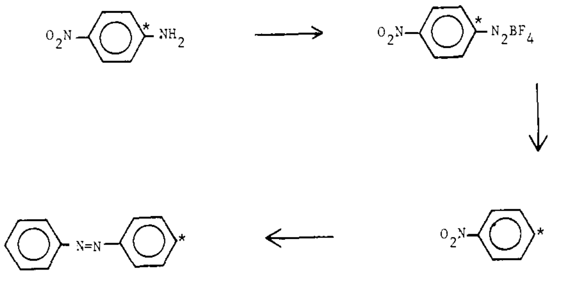
[4-^{14}C]**4** was prepared from commercially available 4-nitro-[1-^{14}C]aniline (Scheme I). Dilutions with ordinary 4-nitroaniline, nitrobenzene, and finally **4** itself were made so as to end with a product having close to 5 mCi/mol of radioactivity.[22]

[4,4′-^{13}C$_2$]**4** was prepared as shown in Scheme II. Our reasons for turning to ^{13}C labeling and for using the route shown were threefold. The 4-nitro[1-^{14}C]aniline which we used successfully for measuring the carbon KIE (see later) had been prepared commercially[23] by well-known sequences of reactions,[24,25] one step of which was dehydrogenation of 1-methyl[1-^{14}C]cyclohexene to [1-^{14}C]toluene. Marshall and co-workers, however, have shown that when 1-methyl[1-^{13}C]cyclohexene was dehydrogenated in this way "a considerable amount of scrambling" occurred in the ring by methyl group migrations.[26] We do not know if some scrambling had occurred also in the preparation of the toluene precursor for our 4-nitro[1-^{14}C]aniline. It turns out, in fact, that, had this occurred, it would not have affected our results. Nevertheless, we were uneasy about relying on the ^{14}C results only. Second, in the event that small amounts of radioactive impurities had intruded into our products for ^{14}C KIE measurements, the magnitudes of our results might have been questionable. The mass spectrometric technique adopted for the ^{13}C KIE measurements is not affected by the presence of small amounts of impurities, provided of course that they do not have the same mass as the product being assayed. Last, the multiscan mass spectrometric measurements have very low errors and promised to give much more precise measurements of the carbon KIE than obtained with [^{14}C]**1**.

The preparation of 4-nitro[1-^{13}C]phenol from labeled acetone has been described by Swartz and Gulick,[27] who converted the phenol into 4-nitro[1-^{13}C]aniline by pyrolysis of a quinazolinyl ether. On the other hand, Musliner and Gates have shown that phenols can be deoxygenated by hydrogenolysis of their 1-phenyltetrazolyl 5-ethers, and this was the technique we adopted. Musliner and Gates obtained aniline from the 5-*p*-aminophenyl ether. We found that hydrogenolysis of the ether **5** gave a mixture of aniline and phenylhydroxylamine and that the mixture could be oxidized to azobenzene without isolating the components. In this way the use of acetone with 91% 2-^{13}C gave azobenzene which was 83% [4,4′-^{13}C$_2$]**4**.

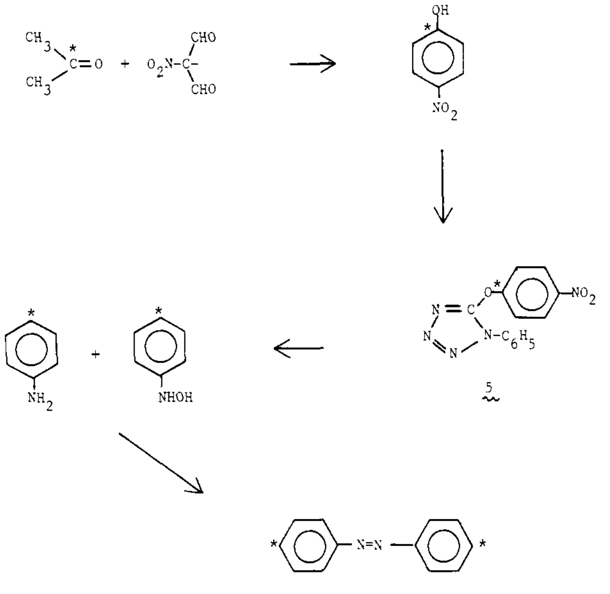
In making [4,4′-^{2}H$_2$]**4** we first set out to use [4-^{2}H]aniline made by lithiation of *p*-bromoaniline and reaction of *p*-lithioaniline with D$_2$O as described by Swain et al.[28] However, the azobenzene obtained by oxidation of the expected [4-^{2}H]aniline was found by mass spectrometry to contain also [^{2}H]- and [^{2}H$_3$]azobenzene, so the method was abandoned. Use of the diazonium tetrafluoroborate method described by Gokel and co-workers[29] worked

Scheme I



[4′-^{14}C]**4**

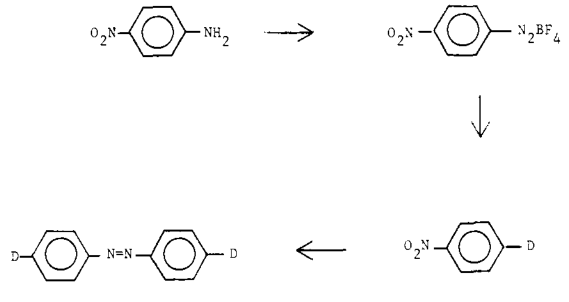
Scheme II



5

[4,4′-^{13}C$_2$]**4**

Scheme III



[4,4′-^{2}H$_2$]**4**

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(21) Bunton, C. A.; Rubin, R. J. *J. Am. Chem. Soc.* **1976**, *98*, 4236.

(22) We thank Dr. Clair Collins, Oak Ridge National Laboratory, for the ^{14}C combustion assays which allowed us to adjust the radioactivity content of **4** to be close to 5 mCi/mol and for the assays in the first measurement of a carbon KIE for the formation of **2**.

(23) American Hoechst Co., Frankfurt-am-Main, Germany.

(24) We are grateful to Dr. Herok of American Hoechst (Frankfurt) for sending us a complete scheme of the synthetic route used.

(25) Murray, A., III; Williams, D. L. "Organic Synthesis with Isotopes", Part 1; Interscience: New York, 1958; pp 102-322.

(26) Marshall, J. L.; Miller, D. E.; Ihrig, A. M. *Tetrahedron Lett.* **1973**, 3491.

(27) Swartz, G. L.; Gulick, W. M., Jr. *J. Labelled Compd.* **1975**, *11*, 525.

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

Table I. Nitrogen Kinetic Isotope Effects for the Formation of Benzidine (2) and Diphenyline (3) from the Acid-Catalyzed Rearrangement of Hydrazobenzene (1) and [^{15}N,^{15}N′]1

	$k(^{14}N)/k(^{15}N)$	
conversion, %	2	3
5	1.0229 ± 0.0009	1.0634 ± 0.0037
10	1.0222 ± 0.0034	1.0630 ± 0.0009
15	1.0214 ± 0.0001	1.0635 ± 0.0007

Table II. Carbon-14 Kinetic Isotope Effects for the Formation of Benzidine (2) and Diphenyline (3) from the Acid-Catalyzed Rearrangement of Hydrazobenzene (1) and [4-^{14}C]1

	$k(^{12}C)/k(^{14}C)$		
conversion, %	2		3^a
5	1.021^b		
5	1.043^b	1.0297^a	
5	1.020^b	1.0294^a	
10	1.028^b	1.0266^a	
5			1.002, 1.004
10			1.002, 1.000, 0.9984
10		1.0278^a	1.000

[a] By scintillation counting. [b] By combustion analysis.[22]

very well. Banthorpe and Hughes[30] had used a diazonium procedure earlier to make nitro[4-^{2}H]benzene, but the procedure was more elaborate than the more modern one,[29] which finally gave azobenzene with 97% d_2 content (Scheme III).

Nitrogen Kinetic Isotope Effects. A few years ago the nitrogen KIE for the benzidine rearrangement was determined by isotope ratio mass spectrometry after converting rearrangement products to N_2 gas. A value of 1.0203 was obtained for the formation of mixtures of **2** and **3**, while a value of 1.0205 was obtained for the formation of **2** only. At that time it was not possible to separate enough of **3** at low conversions to provide for Kjeldahl digestion and isotope ratio mass spectrometry.[31]

We have now repeated the measurement of the nitrogen KIE by whole-molecule mass spectrometry on both of the separated products **2** and **3**. The results are given in Table I. The $k(^{14}N)/k(^{15}N)$ for forming **2** is 1.0222 while for forming **3** it is much larger, 1.063. That there is a substantial isotope effect in each case shows that the breaking of the N–N bond is part of the rate-determining transition state in each case, but the large difference in the magnitude of the isotope effects suggests that the two processes, formation of **2** and **3**, have quite different transition states. This is made more clear from the carbon KIE.

Carbon Kinetic Isotope Effects. These have been measured for both **2** and **3**. Initially, when [1-^{14}C]-4-nitroaniline was commercially available, we set out to measure $k(^{12}C)/k(^{14}C)$ after the products were converted to CO_2. This was carried out successfully for the formation of **2**, but combustions of samples of diphenyline, obtained as an oil, gave unreliable and unreproducible results.[22] The value of $k(^{12}C)/k(^{14}C)$ for formation of **2** was obtained, furthermore, by comparing the ^{14}C content of **2** with that of the original azobenzene (**4**) from which **1** had been made. Combustions of **4** were also difficult to control. A value of $k(^{12}C)/k(^{14}C)$ of 1.050 was reported.[1] Subsequently, KIE measurements were made for both **2** and **3** by scintillation counting, the measurements being made this time by comparing products at low conversion with products at 100% conversion, rather than with the original **4**. The results are given in Table II, along with results for **2** obtained by the combustion technique, but these data are from comparing **2** from low with **2** from 100% conversions.

The finding of a sizeable KIE leaves no doubt again[1] that C–C bond formation occurs as part of the rate-determining transition state for the formation of **2**. In contrast however, from the fact that no KIE is observed it can be concluded that C–C bond formation is not part of the transition state for formation of **3**. Thus, in the case of **3** the significantly higher nitrogen KIE (1.063) and the absence of a carbon KIE describes a transition state in which N–N bond rupture and C–C bond formation are not concerted.

Table III. Carbon-13 Kinetic Isotope Effects for the Formation of Benzidine (2) and Diphenyline (3) from the Acid-Catalyzed Rearrangement of Hydrazobenzene (1) and [4,4′-$^{13}C_2$]1

	$k(^{12}C)/k(^{13}C)$	
conversion, %	2	3
5	1.0201	1.0010
10	1.0206	1.0003
10	1.0220	1.0004

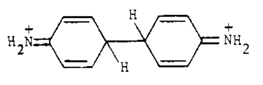
Bearing in mind that each theory of the benzidine rearrangement has assumed that all products are formed by the same processes, the difference now revealed in formation of **2** and **3** was startling. Therefore, the carbon KIE were redetermined but, this time, with the use of [4,4′-$^{13}C_2$]**1** and whole-molecule mass spectrometry. In essence, rearrangement of **1** (mass 184) containing 5 mol% of [4,4′-$^{13}C_2$]**1** (mass 186) was carried out and the ratio of masses 184/186 was determined for separated **2** and **3** at low and 100% conversions. The results are given in Table III. Again, the presence of a large KIE for **2** and the absence of one for **3** confirm the conclusions drawn from the ^{15}N and ^{14}C data, namely, that formation of benzidine is a concerted process but formation of diphenyline is not.

Calculations of the relationship of rate constants for isotope pairs[32a,b] show that the KIE for ^{13}C and ^{14}C should have the relationship

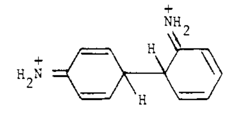
$$r = \log (k(^{12}C)/k(^{14}C))/\log (k(^{12}C)/k(^{13}C)) \simeq 1.9 \quad (5)$$

Our measurement of $k(^{12}C)/k(^{13}C)$ was made with doubly labeled **I** and calculated from mass ratios of 184/186. On the other hand, our measurement of $k(^{12}C)/k(^{14}C)$ is for singly labeled **1** (Scheme I). We have calculated r (eq 5), therefore, by using the square root of our ^{13}C KIE (Table V), namely, $k(^{12}C)/k(^{13}C) = 1.0104$,[32c] and obtain the ratio $r = 1.98$. We feel that this is in reasonable agreement with the prediction.

Deuterium Isotope Effects. The initial products of rearrangement of **1** are, in fact, the quinoidal intermediates **2a** and **3a**. The deprotonation of these intermediates to give **2** and **3**, respectively, was shown 20 years ago not to be rate limiting. That is, primary kinetic deuterium isotope effects were found to be absent in studies with [4,4′-$^2H_2$]**1** and [2,2′,3,3′,5,5′,6,6′-$^2H_8$]**1**.[30]



2a



3a

However, if C–C bond formation were part of the rate-limiting process, we should expect to find an *inverse* secondary deuterium isotope effect when using, say, [4,4′-$^2H_2$]**1**. The method of measuring rates of rearrangement (the use of Bindschedler's Green in a titration procedure) used earlier[30] was too imprecise to detect very small differences between rates of labeled and unlabeled hydrazobenzene. Banthorpe and Hughes report, for example, rate constants ($10^{-3}k$, s^{-1}) of 0.113 and 0.111 for **1** and 0.112 and 0.116 for [4,4′-$^2H_2$]**1**, the rates having been measured on the two substrates separately.

We have now measured relative rates of rearrangement of **1** and [4,4′-$^2H_2$]**1** in a competitive way by whole-molecule mass

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[29] Korzeniowski, S. H.; Blum, L.; Gokel, G. W. *J. Org. Chem.* **1977**, *42*, 1469.

[30] Banthorpe, D. V.; Hughes, E. D. *J. Chem. Soc.* **1962**, 3308.

[31] Shine, H. J.; Henderson, G. N.; Cu, A.; Schmid, P. *J. Am. Chem. Soc.* **1977**, *99*, 3719.

[32] (a) Swain, C. G.; Stivers, E. C.; Reuwer, J. F., Jr.; Schaad, L. J. *J. Am. Chem. Soc.* **1958**, *80*, 5885. (b) Melander, L.; Saunders, W. H., Jr. "Reaction Rates of Isotopic Molecules"; Wiley-Interscience: New York, 1980; pp 52, 228. (c) Melander, L.; Saunders, W. H., Jr. *Ibid.* p 275.

Table IV. Secondary Deuterium Kinetic Isotope Effects for the Acid-Catalyzed Rearrangement of Hydrazobenzene (1) and [4,4'-$^2H_2$]1

conversion, %	$k(^1H)/k(^2H)$	conversion, %	$k(^1H)/k(^2H)$
40	0.9618	70	0.961
50	0.962	80	0.961
60	0.962	95	0.962

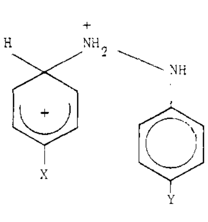
spectrometry. A 1:1 mixture of **1** and [4,4'-$^2H_2$]**1** was allowed to rearrange to specific conversions, and the unrearranged substrate was oxidized back to azobenzene (**4**). The relative amounts of unlabeled **4** (mass 182) and [4,4'-$^2H_2$]**4** (mass 184) present in the recovered azobenzene were measured at large and zero conversions and used to compute values of $k(^1H)/k(^2H)$ at each partial conversion. The results are given in Table IV. They show that there is indeed an inverse secondary deuterium isotope effect of 3.8%. This originates from the change of sp^2 hybridization of C-4 in **1** to sp^3 hybridization in the transition state leading to the intermediate **2a**.[33] The data cannot distinguish between forming **2** and **3** but concern only the disappearance of substrate. However, the data are clearly consistent with the involvement of a concerted process in this disappearance.

A further comment is needed, however, about the *substituent* effect of the 4,4'-deuterium atoms. Ring deuteration increases the basicity of aniline.[34] Therefore, one might expect by analogy that [4,4'-$^2H_2$]**1** would be protonated a little more extensively than **1** itself and hence rearrange a little faster than **1**. This effect would then be in the same direction as our measured secondary deuterium KIE. However, the effect of deuteration on the basicity is felt mainly in the ortho positions and only very little or not at all in the para positions, as was demonstrated, in fact, with 2,6-[4-^{2}H]xylidine.[34] Therefore, we believe that our $k(^1H)/k(^2H)$ result is a true secondary deuterium KIE rather than a substituent effect on basicity and therefore that the deuterium isotope effect results add support to the conclusions drawn from the carbon isotope effect results.

Summary of KIE. All of our data are consistent with the concerted formation of **2** and the nonconcerted formation of **3**. Our data show, then, that none of the three theories of rearrangement (the PTS, π complex, and caged-radical ones) is correct as a whole. It is now apparent that the concerted feature of the PTS describes the formation of **2**, while the other theories could describe the formation of **3**. The nature of the intermediate in the pathway to **3** is not definable any further, but we prefer to call it a π complex and to designate its formation via a polar transition state. The formation of **2**, furthermore, can be classified as an allowed [5 + 5] sigmatropic rearrangement, while the formation of **3** can be likened to a [3 + 5] sigmatropic rearrangement, forbidden by orbital symmetry restrictions from being suprafacially concerted. It is to be expected that other benzidine rearrangements will also be found to follow the rules of symmetry conservation, and, in fact, we have preliminary data in this regard for the rearrangements of 4-methoxy- and 2,2'-dimethoxyhydrazobenzene.[35] It is also anticipated that the uncertainties regarding the mechanism of the disproportionation reaction, which often accompanies rearrangements,[11-15] will also be resolved.[35]

The Ring Protonation Theory. This theory calls for protonation of hydrazoarenes at a carbon atom which is attached to the hydrazo group, that is the ipso position. Ipso protonation is an attractive idea for two reasons which were first enunciated to our knowledge by Lupes.[36,37] These reasons are illustrated with two-proton rearrangements, to which the ipso-protonation theory is best suited. It is generally accepted that in two-proton rearrangements the first proton adds to one of the hydrazino nitrogen atoms (eq 1). Ipso protonation calls for the bonding of the second proton at a ring carbon atom and in this way avoids the placing of the second proton on the second nitrogen atom, creating thereby adjacent positive charges (eq 2). Ipso protonation, in fact, puts the second positive charge in one of the aryl rings, far away from the first positively charged nitrogen atom, and this is considered to be a telling factor in favor of ipso protonation by its advocates. The second reason for the attractiveness of ipso protonation is that it is thought to place the protonated aryl ring in a configuration stereochemically suited to bonding with the other aryl ring.

When first advocated, ipso protonation was represented as occurring at the carbon atom adjacent to the positively charged nitrogen atom (**6**, X = Y = H).[37] This formulation was also proposed by Allan who devised the bent conformation (**7**) in order to explain, particularly, how the intramolecular *p*-semidine rearrangement could occur.[38] Heesing and Schinke have also adopted this mode of protonation for rearrangements of 4-chlorohydrazobenzene and have represented the *o*-semidine as originating from **6** (X = Cl, Y = H) and *p*-semidine from **7** (X = H, Y = Cl).[39]



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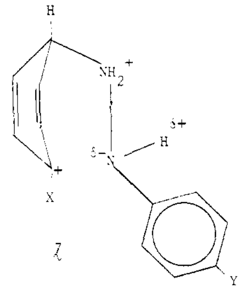

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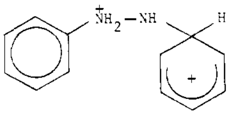

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On the other hand, Olah and co-workers[40] have represented ipso protonation as occurring in the more remote ring (**8**). An arenium ion is thereby created which is regarded as well suited for 4,4' (benzidine) and 2,4' coupling (diphenyline). The concept was expanded by Olah to account for the various other types of benzidine rearrangements and the effects of ring substituents on them.

It is not completely clear from the presentations how the advocates of ipso protonation regard the timing of the second proton's addition. Olah and co-workers say that "in the benzidine rearrangement diprotonation is considered to be rate determining", but it is not clear if they mean that all other steps are fast or if, perhaps, they are concerted with protonation. If the former is meant the concept is not in accord with what we now know, at least in the rearrangement of hydrazobenzene itself, that the N–N bond is being broken in the transition state. Heesing and Schinke represent intramolecular bonding, in each case from carbon to nitrogen, as occurring after ipso protonation but make no commitment as to the timing of the several steps that lead eventually to products.

It is possible in two-proton rearrangements that the second protonation is concerted with rearrangement in a rate-determining way. This view has been advocated most recently by Bunton and Rubin,[21] who suggest that substrates containing strongly electron-donating groups may undergo rate-limiting protonation at carbon while those not containing such groups may undergo the second protonation on nitrogen. Concerted rate-determining protonation on carbon has also been suggested as a possibility by Allan but in the sense that the approach of the proton is concerted

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

(34) Bernasconi, C.; Koch, W.; Zollinger, H. *Helv. Chim. Acta* **1963**, *46*, 1184.

(35) Unpublished work.

(36) Lupes, M. E., letters to H. J. Shine in 1969.

(37) Lupes, M. E. *Rev. Roum. Chim.* **1972**, *17*, 1253.

(38) Allan, Z. J. *Tetrahedron Lett.* **1971**, 4225.

(39) Heesing, A.; Schinke, U. *Chem. Ber.* **1977**, *110*, 3319.

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

not with the breaking of the N–N bond but with the bonding of the approaching positions. This is next followed by breaking of the N–N bond.[41]

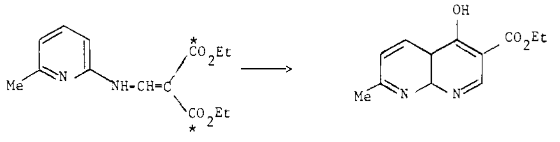
There is a fault in proposals for concerted processes initiated by ipso protonations, however, at least as they pertain to what we now know about the formation of benzidine from hydrazobenzene. The concerted rearrangement requires a continuum of conjugation among π orbitals. An ipso proton interrupts this continuum. Therefore, in calling for a concerted rate-determining ipso protonation, we ask the proton to initiate the very process which, by its position, it must interrupt. Clearly, ipso protonation is not consistent with a concerted rearrangement.

We pose also a second argument against ipso protonation. It is our view, and the view of others,[42,43] that if ring protonation is to occur it should occur not only at the ipso position but (preferentially) also at the ortho and para positions of the ring. Lupes acknowledges that such ring protonations may occur but concludes that since they cannot lead to rearrangement they must be reversible.[37]

One would anticipate from protonation of other ring positions that ring deuteration should occur if rearrangement were carried out in deuterium solvent and acid. Olah has tested this corollary with hydrazobenzene and found by NMR spectroscopy that deuterium was not present in the rings of the product (benzidine); it was concluded that deuterium exchange at the 2- and 3-positions of the hydrazobenzene could not have occurred.[40] The possibility that exchange at the 4-position occurs cannot be checked by examining the product benzidine. In connection with the rearrangement of *N*-acetylhydrazobenzene Cox and Dunn[42] also found, but by mass spectrometry, that the product did not contain ring deuterium after rearrangement in D_3O^+ and they consider the ring-protonation theory to be inconsistent with this result. It seems to us that all of the accrued evidence is weighted indirectly against ipso protonation.

To settle further the question of ring protonation, we have resorted to the more precise multiscan mass spectrometry and have examined not the product but the reactant remaining from incomplete conversion. We have carried out rearrangement of 0.01 M hydrazobenzene in 75% EtOD/D_2O which was 0.1 M in DCl. Rearrangement was allowed to proceed to 50% conversion and was then stopped by adding sodium hydroxide. The unrearranged hydrazobenzene was oxidized to azobenzene and separated for mass spectrometric assay. A search for ring deuteration was made by measuring the ratio of masses 182/183 in the recovered and initial azobenzene. Two separate runs were made. The ratios, 182/183 were as follows: for the starting material 6.652 ± 0.03 (20 000 scans) and for the isolated azobenzene 6.665 ± 0.02 (20 000 scans) and 6.645 ± 0.04 (10 000 scans). It is evident that *under conditions of rearrangement* exchange of ring protons for solvent deuterium has not occurred. This result indicates to us that although one cannot test directly for ipso protonation it, too, does not occur. The collective results tell us that the second protonation of **1** occurs at nitrogen. Whether or not this is an equilibrium process (i.e., eq 2) or is concerted with rearrangement would best be settled by direct but difficult measurement of specific- vs. general-acid catalysis.

Transition States and Calculated KIE. In the rearrangements of **1** into **2** and **3** we are confronted with a bond-breaking isotope effect (N–N) and a less common bond-forming isotope effect (C–C). The magnitudes of bond-forming KIE have been discussed briefly by Fry.[44] Some examples which are analogous to our work are to be found in the literature. The addition of *N*,α-diphenylnitrone to styrene has been shown to be a concerted 1,3-dipolar addition, with carbon KIE ranging from 1.012 to 1.068 depending on which carbon atom was labeled.[47] The [2 + 2] cycloaddition of diphenylketene to styrene also has carbon KIE in the range of 1.0055–1.08.[46] A carbon KIE of 1.05 was found for the polymerization of [β-^{14}C]styrene at 40 °C.[47] Finally, in the intramolecular rearrangement of the alkylidene malonic ester (**9**) into **10** a carbon KIE of 1.044 was obtained.[48]



9 10

In all of these cases, as in ours, a new C–C bond is formed while a bonding change (unsaturated to saturated) also occurs at the site of labeling in the original molecule. The new bond formation and change in the old bonding are part of the transition state of the rate-determining process. It is necessary to try to represent how this transition state is developed in the rearrangement of **1** to **2**.

Presumably, the lowest energy conformation of hydrazobenzene in solution is the staggered one **11**. For rearrangement, however, the two rings must be eclipsed. What is it that holds the rings in the required configuration? We presume this to be an attraction of one ring for the other in a polarized state of the monoprotonated molecule **12**. Rearrangement is initiated by the second protonation either in an equilibrium process or in a step concerted with the rearrangement. If the second protonation is an equilibrium one, we should represent the initial attractive conformation as in **13**. We have earlier represented the transition states for concerted and nonconcerted rearrangement as in **14** and **15**.

We visualize covalent bonding at the 4,4′-positions as beginning with the ground-state conformation as in **12** or **13** and ending with the quinonoid structure **2a**. In order to make our simplistic calculations of KIE, we have had to derive vibrational frequencies for the N–N bond and the C–C bond in the transition state and to do that we have assumed that the force constants are half of those in the ground state.

Of course, nothing is known about the vibrational frequencies or force constants of the ground state, since the diprotonated molecule cannot even be isolated. We made some assumptions, therefore, about the ground state. One of these was that the vibrational frequency of the N–N bond would be the same as that in diprotonated hydrazine with an allowance of adding the two phenyl groups.[1] The second of these concerned C–C bonding. There is no formal C–C bond in the ground state. There is an ill-defined attraction between rings, and when rearrangement begins, this attraction changes into a progressive bonding at the 4,4′-positions, ending finally in **2a**. Therefore, we have assumed that in the transition state the force constant for the C–C bond reaches half of that in **2a**. Once again, though, the C–C frequency in a dicyclohexadienyl structure such as **2a** is unknown to us, so we have made yet one more assumption that the C–C frequency will not be far away from that of a biphenyl. Consequently, we finally derive the force constant for the C–C bond in the transition state from that in a biphenyl. The assumptions are unquestionably imaginative, yet they serve reasonably well in distinguishing between the concerted and nonconcerted processes. Further details have been given earlier.[1]

The representations **14** and **15** were used to calculate approximate KIE for the nitrogen-15 and carbon-14 cases.[49] We have also used the concerted-state representation to calculate the KIE for carbon-13. The assembled data are given in Table V, along with a summary of the measured mean KIE. It can be seen that the experimental and calculated results are in reasonable agreement. We emphasize that the models chosen, and the simplistic method of calculation, serve mainly to compare concerted

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(41) Allan, Z. J. *Justus Liebigs Ann. Chem.* **1978**, 705.

(42) Cox, J. R., Jr.; Dunn, M. F. *J. Org. Chem.* **1972**, *37*, 4415.

(43) Banthorpe, D. V. *Tetrahedron Lett.* **1972**, 2707.

(44) Fry, A. In "Isotope Effects in Chemical Reactions"; Collins, C. J., Bowman, N. S., Eds.; ACS Monograph 167, Van Nostrand Reinhold Co.: New York, 1971, Chapter 6.

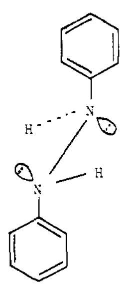
(45) Benjamin, B. M.; Collins, C. J. *J. Am. Chem. Soc.* **1973**, *95*, 6145.

(46) Collins, C. J.; Benjamin, B. M.; Kabalka, G. W. *J. Am. Chem. Soc.* **1978**, *100*, 2570.

(47) Barson, C. A.; Blanplain, C. M. *Eur. Polym. J.* **1974**, *10*, 705.

(48) Volford, J.; Meszaros, Z.; Kovacs, G. *J. Labelled Compd.* **1973**, *9*, 231.

(49) The details of the calculations are given in ref 1.



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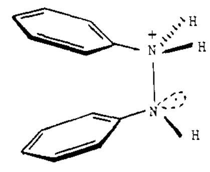

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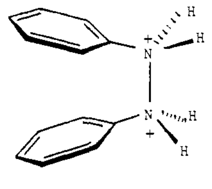

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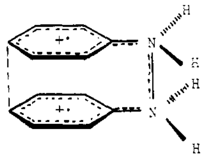

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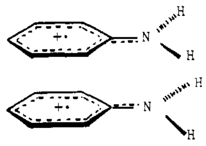

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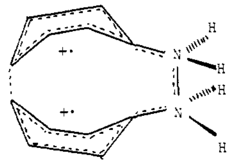

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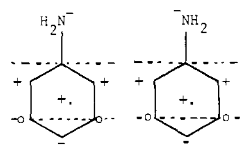

17

vs. nonconcerted KIE. It is more likely that the geometry of rings in the transition state for the concerted rearrangement should be bent and somewhat cyclohexadienyl-like rather than flat, i.e., as in **16**. This is discussed further below. We hope to be able to delineate the real geometry of the concerted transition state by more sophisticated calculations.

Symmetry-Allowed and -Forbidden Rearrangements. The rearrangement of hydrazobenzene is an overall 14-electron sigmatropic process. This can be treated by the frontier-orbital method, and the two halves of the molecule can be designated as a HOMO–LUMO pair or, as is convenient here, with two SOMO's (**17**). The nodal properties of these halves then correspond with those of the benzyl radical. It can be seen that the [5,5] rearrangement to benzidine is symmetry allowed while that to diphenyline, a [3,5], is not.

Another feature is also seen. One would expect that a symmetry-allowed [3,3] rearrangement should occur to give a 2,2′-diaminobiphenyl, the *o*-benzidine-type product. However, this does not occur; or, if it occurs at all, it does so in the present conditions in trace quantities only.[50–52]

The Claisen rearrangements are to some extent analogous to the benzidine rearrangement in orbital designations. The rearrangement of allyl phenyl ether to *p*-allylphenol goes through two successive [3 + 3] sigmatropic shifts. The rearrangement of pentadienyl phenyl ether to *p*-pentadienylphenol has two pathways, one being a direct [5 + 5] shift and the other being two successive [3 + 3] shifts.[54] Nothing like that appears to happen in the rearrangement of **1**. We can suggest two possible explanations for this but do not know if either can be verified.

Table V. Calculated and Experimental Nitrogen and Carbon Kinetic Isotope Effects for the Formation of Benzidine and Diphenyline

		KIE, $k_{\text{light}}/k_{\text{heavy}}$		
			calcd (model)	
product	isotope	obsd	concerted	non-concerted
2	$^{14}N^{15}N^{a}$	1.0222^{b}	1.025	1.055
3	$^{14}N^{15}N^{a}$	1.0633^{b}	1.027	1.055
2	$^{12}C^{13}C^{a}$	1.0209^{b}	1.0401	
3	$^{12}C^{13}C^{a}$	1.0006^{b}	1.000	
2	$^{12}C^{14}C$	1.0284^{c}	1.0367	
3	$^{12}C^{14}C$	1.0011^{c}	1.000	

[a] Measured and calculated values of KIE are for doubly labeled 1. [b] By mass spectrometry. [c] By scintillation counting.

Although we treat the configuration of the rings in the transition states as being planar for our calculations of KIE, they may really be bent, as in **16**. In that case the ortho positions are displaced far enough away from each other to inhibit bonding, and the path of least motion brings the para positions close enough for bonding. Moderately bent or "dished" rings would still retain sufficient p-orbital overlap for concerted rearrangement.[55]

A second view is that the bonding of para positions occurs because these are the positions of highest charge and electron density. This is most easily represented as unpaired electron density in the SOMO's of **17**. Ring–proton coupling constants in the ESR spectrum of the aniline cation radical show that the para position has by far the largest ring spin density.[62] We expect this to be true for the SOMO representation (**17**), too, and hence be in accord with preferred 5,5 bonding. This view might also accommodate 3,5 bonding (diphenyline), forbidden by orbital symmetry from being concerted but promoted by charge or spin density controls in the dissociated pathway.

Experimental Section

General Procedures for Rearrangement. Rearrangements of **1** were carried out at 0 °C in 75% aqueous ethanol (i.e., 225 mL of 95% ethanol and 75 mL of water) so as to reproduce the kinetic conditions and rate constants of earlier work.[19,31] After having made **4** containing the appropriate concentration of labeled **4**, the mixture was reduced to **1** with zinc and ammonium chloride in aqueous acetone. The **1** was precipitated by filtration into degassed ammonium hydroxide solution, filtered, washed, and dried under vacuum for use. Freshly prepared **1** was used for each experiment.

Rearrangements were stopped by adding 40% sodium hydroxide solution quickly to the cold acidic solution of **1**. The times over which rearrangement was allowed to continue were determined from the rate constant previously reported[19] which was checked once again by the Bindschedler's Green titration method. Solutions in which rearrangement

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(50) Vecera, M.; Petranek, J.; Gasparic, C. *Collect. Czech. Chem. Commun.* **1957**, *22*, 1603, identified the formation of all of the possible products in the rearrangement of **1**, including the *o*-benzidine, by using paper chromatography.

(51) Banthorpe, D. V.; Hughes, E. D.,[30] reported that they were not able to confirm the observations of Vecera et al.[50]

(52) Remarkably, when **1** is mixed with dry sand and treated with dry hydrogen chloride, almost equal amounts of **2**, **3**, the *o*-benzidine, and *p*-semidine are obtained.[53]

(53) Vecera, M.; Gasparic, J.; Petranek, J. *Collect. Czech. Chem. Commun.* **1958**, *23*, 249.

(54) Frater, G.; Schmid, H. *Helv. Chim. Acta* **1970**, *53*, 269.

(55) For example, the retention of aromatic character in strained, nonplanar rings such as the *p*-cyclophanes[56–58] and bridged annulenes[59–61] is well documented.

(56) Vollhardt, K. P. C. *Pure Appl. Chem.* **1980**, *52*, 1645.

(57) Smith, B. H. "Bridged Aromatic Compounds"; Academic Press: New York, 1964.

(58) Greenberg, A.; Liebman, J. F. "Strained Organic Molecules"; Academic Press: New York, 1978.

(59) Destro, R.; Simonetta, M.; Vogel, E. *J. Am. Chem. Soc.* **1981**, *103*, 2863.

(60) Simonetta, M. *Pure Appl. Chem.* **1980**, *52*, 1597.

(61) Vogel, E. *Isr. J. Chem.* **1980**, *20*, 215.

(62) Neugebauer, F. A.; Bamberger, S.; Groh, W. R. *Chem. Ber.* **1975**, *108*, 2406.

was to go to completion were allowed to stand for at least 10 half-lives.

A typical procedure for 10% conversions and recovery of product was as follows. To a solution of 1.104 g (6.0 mmol) of **1** in 225 mL of 95% ethanol and 75 mL of water at 0 °C was quickly added a solution of 7.71 g (0.182 mol) of lithium chloride in 225 mL of 95% ethanol and 75 mL of water which was 0.06 M in HCl. This solution was also cooled to 0 °C before the mixing. The rearrangement was allowed to run under oxygen-free argon for 890 seconds at 0 °C and stopped by adding 30 mL of 40% sodium hydroxide solution. Air was bubbled through the solution overnight to oxidize the unrearranged **1** to **4**. The solution was then concentrated to a smaller volume on a rotary evaporator at room temperature, and to it was added 35 mL of concentrated hydrochloric acid. The **4** was extracted with ether, and the amine products were liberated with sodium hydroxide and extracted with ether. After the solution was dried over sodium sulfate and the ether was evaporated, 122 mg of the crude mixture of products **2** and **3** was obtained. The mixture was applied to thick-layer chromatography plates (E. Merck, 20 × 20 cm, 2 mm, silica gel, 60 F254) as streaks of a solution in acetone. The benzidine and diphenyline bands were separated readily by hexane–ether–acetone, 43:47:10 by volume. The bands were removed from the plates, and each product was extracted with ether. Workup gave 70 mg of **2** and 29 mg of **3**. Product **2** was crystallized with water, giving 50 mg, mp 127 °C. Product **3** was an oil and was again dissolved in dry ether, precipitated as the hydrochloride, and regenerated with sodium hydroxide. Workup gave an oil in the ^{15}N and ^{14}C work. In the ^{13}C work, however, it was found that the **3** could be crystallized by placing a solution in petroleum ether in the freezer.

For 5% conversions the scale was doubled and the rearrangement was stopped after 432 s. For 100% conversions the scale was halved.

The procedure adopted for recovery of substrate rather than products was much the same, except that the ether solution of **4** (obtained by air oxidation of unrearranged **1**) was worked up. In this case also, rearrangement was allowed to proceed toward completion, sampling being carried out at 40%, 50%, 60%, 70%, 80%, and 95% conversions.

In a typical experiment, 1.104 g of **1**, which had been prepared from a 1:1 mixture of **4** and [4,4′-^{2}H$_2$]**4**, was used as above and was allowed to rearrange for 98 min for 50% conversion. After the treatment with sodium hydroxide and air, the ethanol was removed from the reaction mixture on a rotary evaporator and the organic materials were extracted with ether. Rearrangement products were removed with 4 N hydrochloric acid, and the washed and dried ether solution was evaporated to give 520 mg of crude **4**. This was purified by preparative-scale TLC to give 380 mg of **4** which was next crystallized from aqueous ethanol, giving 346 mg, mp 67–67.5 °C. This was then analyzed for the ratio of masses 182/184. The times of rearrangement for other conversions were as follows: for 60%, 129 min; for 70%, 170 min; for 80%, 227 min; 95%, 422 min; 100%, 24 h. It was necessary to be sure that the **4** which was isolated in this way was not being formed to a large extent by either disproportionation of **1** or adventitious oxidation of **1** by air in the system. Therefore, rearrangement was allowed to go to completion, and the **4** present was isolated (omitting the treatment with air). From 2.208 g of a mixture of **1** and [^{2}H$_2$]**1** we obtained 11.4 mg of **4**, which is small in comparison with the **4** obtainable from partial rearrangements of **1**. In fact, the amount of **4** which we obtained after complete rearrangement of 2.208 g of **1** (11.4 mg) corresponds with only 10% of the amount of **4** (about 55 mg) anticipatable from the 95% conversion run. Furthermore, the 182/184 mass ratio of the 11.4 mg was 1.1588 as compared with 1.1594 for the original **4** used. Therefore, we feel assured that the **4** isolated from air oxidation of unrearranged **1** in our partial rearrangement runs truly represents unrearranged **1**.

[4-^{14}C]Azobenzene ([4-^{14}C]4). This was prepared from nitro[4-^{14}C]benzene. A mixture of 60 mg of commercial, highly radioactive, 4-nitro[1-^{14}C]aniline[23] (known from radiochromatography to be free of other isomers and radioactive impurities) and 6.74 g of ordinary 4-nitroaniline (a total of 49.3 mmol) was dissolved in a small volume of ethanol, and the solution was evaporated to dryness. The residue was suspended in 22 mL of 50% fluoroboric acid, stirred magnetically in an ice bath, and diazotized with 3.4 g (49.2 mmol) of sodium nitrite in 7 mL of cold water. The resulting fluoroborate salt was filtered and washed with 6 mL of cold fluoroboric acid, 95% ethanol (twice), and ether (10 times).[63] The diazonium salt was next suspended in 350 mL of chloroform cooled in ice, and to this suspension was added 350 mg of Cu$_2$O and, dropwise, 26 mL of 50% aqueous hypophosphorous acid. The mixture was stirred for 2 h, and anhydrous sodium carbonate was added until the pH reached 8–9. The chloroform layer was removed, washed three times with water, and dried over anhydrous magnesium sulfate. Evaporation of the solvent and distillation of the residue gave 6 g (48.8 mmol, 99%) of nitro[4-^{14}C]benzene, approximately 130 mCi/mol.

The nitrobenzene was mixed with 18 g of unlabeled nitrobenzene in 240 mL of methanol. To this solution was added 27 g of zinc dust and 31 g of sodium hydroxide dissolved in 72 mL of water. The mixture was stirred under reflux for 8 h. Workup of the hot suspension gave azobenzene (**4**) which was heated and stirred with 50 mL of 2% hydrochloric acid to remove zinc salts. The cooled, solidified **4** was filtered, washed well with water, and recrystallized from aqueous ethanol to give 15 g (85%) of [4-^{14}C]**4**, mp 68 °C, approximately 32.5 mCi/mol. For KIE work this was again diluted with ordinary **4** and crystallized to give approximately 8 mCi/mol.

[^{15}N,^{15}N′]Azobenzene ([^{15}N$_2$]4). A solution of 2 g (21.3 mmol) of aniline (99% ^{15}N, Stohler Isotope Chemicals) in 150 mL of benzene was oxidized under reflux with 10.3 g of MnO$_2$ for 6 h, the water being removed as it was formed with a Dean–Stark separator. Concentration of the solution and chromatography on a column of silica gel (Woelm) with benzene gave 1.82 g (10 mmol, 94%) of [^{15}N$_2$]**4**, mp 68 °C. For the KIE work this was mixed with ordinary **4** and crystallized from aqueous ethanol so as to give a 5 mol % content of labeled **4**.

4-Nitro[1-^{13}C]phenol was prepared in 72% yield from [2-^{13}C]acetone and sodium nitromalonaldehyde as described by Swartz and Gulick.[27] Bromomucic acid for making sodium nitromalonaldehyde was from Aldrich Chemical Co., while the acetone (90% ^{13}C) was obtained from several sources (Stohler Isotope Chemicals, Prochem, and Merck Isotopes). A sample of the labeled 4-nitrophenol was converted into bromopicrin by reaction with bromine and calcium hydroxide,[64] and the bromopicrin was found by mass spectrometry to be identical with bromopicrin obtained similarly from ordinary 4-nitrophenol. Thus, there was not an enrichment of ^{13}C in positions other than C-1 of the labeled 4-nitrophenol.

5-(4-Nitro[1-^{13}C]phenoxy)-1-phenyl-1*H*-tetrazole. A solution of 4.5 g (32.1 mmol) of 4-nitro[1-^{13}C]phenol and 6.2 g (34.3 mmol) of 5-chloro-1-phenyl-1*H*-tetrazole (Aldrich Chemical Co.) in 250 mL of dry acetone was refluxed with 9.8 g of anhydrous potassium carbonate for 24 h. The mixture was poured onto 250 g of crushed ice and filtered. Crystallization from benzene gave 8.3 g (29.2 mmol, 91% based on 4-nitrophenol) of product.

A sample of this compound made from unlabeled *p*-nitrophenol was crystallized twice from 95% ethanol and had a melting point of 117–117.5 °C. Anal. Calcd for C$_{13}$H$_9$N$_5$O$_3$: C, 55.13; H, 3.20; N, 24.73. Found: C, 55.20; H, 3.04; N, 24.71.

[4,4′-^{13}C$_2$]Azobenzene ([^{13}C$_2$]4). A solution of 8 g (28.2 mmol) of 5-(4-nitro[1-^{13}C]phenoxy)-1-phenyl-1*H*-tetrazole in 250 mL of benzene at 40 °C was hydrogenated over 0.8 g of 10% Pd/carbon at atmospheric pressure for 48 h. The mixture was filtered, and the solution plus benzene washings was extracted with 10% hydrochloric acid. The acid solution was made basic with 40% sodium hydroxide solution, and the free aniline (see below) was extracted with benzene. The benzene solution was oxidized with 15 g of MnO$_2$ in the usual way for 8 h. Workup gave 1.8 g (9.78 mmol, 69%) of [^{13}C$_2$]**4**. Mass spectrometry showed this to contain 83.6% of [^{13}C$_2$]**4**, 15.6% of [^{13}C$_1$]**4**, and 0.87% of [^{13}C$_0$]**4**. Also present was a small amount of the correspondingly labeled azoxybenzenes.[65] For KIE work the labeled **4** was mixed with ordinary **4** and crystallized so as to give an estimated 5 mol % of [^{13}C$_2$]**4**. The small amount of azoxybenzene was not removed from the **4** prior to its reduction to **1** for KIE work, since azoxybenzene is itself reduced to **1** by NH$_4$Cl/Zn. To be certain that reduction of the unpurified 5 mol % [^{13}C$_2$]**4** would give only **1**, a portion was reduced to 5 mol % [^{13}C$_2$]**1** and reoxidized with air to **4**. Mass spectrometry[65] and also TLC before and after this treatment showed that the azoxybenzene had been removed.

We found in trial experiments with unlabeled 4-nitrophenol that our hydrogenolysis of the 4-nitrophenyl tetrazolyl ether gave not only aniline but, as shown by TLC, some phenylhydroxylamine. Oxidation of phenylhydroxylamine alone with MnO$_2$ gives nitrosobenzene.[66] We checked this in benzene and found nitrosobenzene to be the only product by TLC, but our attempted recovery gave us mainly nitrobenzene. However, oxidation of a mixture of aniline and phenylhydroxylamine, even in a 1:1 ratio, in benzene gave only azobenzene.

A second factor that might have been inimical to our procedure was the possibility of acid-catalyzed Bamberger rearrangements of the phenylhydroxylamine, to give some *p*-aminophenol or *p*-chloroaniline[67] even under the mild conditions of extraction with 10% hydrochloric acid.

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(63) This procedure is described by Starkey, E. B. "Organic Syntheses"; Wiley: New York, 1943; Coll. Vol. 2, p 225.

(64) Baddiley, J.; Ehrensvärd, G.; Klein, E.; Reio, L.; Saluste, E. *J. Biol. Chem.* **1950**, *183*, 777.

(65) Midwest Center for Mass Spectrometry, Department of Chemistry, University of Nebraska, Lincoln, NE.

(66) Papadopoulos, E. P.; Jarrar, A.; Issidorides, C. H. *J. Org. Chem.* **1966**, *31*, 615; oxidized in water.

(67) Reference 11, pp 182–190.

Therefore, authentic phenylhydroxylamine was extracted from benzene in the same way and recovered again, after neutralizing the acid, as a solution in benzene. Workup gave a concentrated solution which by TLC was found to contain only phenylhydroxylamine. The phenylhydroxylamine used in these experiments was made from nitrobenzene.[68] Our procedure for preparing [4,4'-$^{13}C_2$]**4**, therefore, was conveniently shortened by our not having to isolate and separate the [4-^{13}C]aniline and [4-^{13}C]phenylhydroxylamine before oxidation with MnO_2.

4,4'-Dideuterioazobenzene. To a stirred suspension of 10.7 g (45 mmol) of 4-nitrobenzenediazonium tetrafluoroborate[63] in 100 mL of $CDCl_3$ (99.6% D) cooled in ice was added 14.4 mL of D_3PO_2 (50% solution in D_2O, 99% D) and 100 mg of Cu_2O. The mixture was stirred for 5 min, and to it was added enough sodium carbonate to neutralize the acid. The chloroform layer was washed with D_2O and dried over sodium sulfate. Removal of the chloroform and distillation of the residue under vacuum gave 4.8 g (86.7%) of 4-deuterionitrobenzene with a satisfactory ^{1}H NMR spectrum. Earlier workers obtained a 99% yield (by GLC) of ordinary nitrobenzene.[29] The nitro[4-^{2}H]benzene was converted into [4,4'-$^2H_2$]**4** by reduction with zinc in aqueous methanolic sodium hydroxide solution,[69] in 64% yield.

Crystallization from aqueous ethanol gave a melting point of 67–67.5 °C. The product had an acceptable ^{1}H NMR spectrum and was found by mass spectrometry to contain 94% [$^2H_2$]-, 5.8% [$^2H_1$]-, and 0.1% [$^2H_0$]**4**. This product was mixed with an equal weight of ordinary **4** and recrystallized for use in determining the secondary deuterium isotope effect.

Search for Ring-Deuterium Exchange during Rearrangement of 1. Two solutions were prepared and cooled to 0 °C before mixing. The first contained 105 mg (0.571 mmol) of ordinary **1** in 20 mL of 95% [O^{2}H]ethanol (EtOD) and 6.7 mL of D_2O. The second was 26.7 mL of 0.2 N DCl in 75% EtOD in D_2O, containing 686 mg of lithium chloride. The mixture was allowed to stand for 97 min (50% conversion of **1**) and then treated with sodium hydroxide and air as described above. Workup gave 54.4 mg of **4** for mass spectrometric analysis. Two runs were made. The ratio of masses 182/183 were 6.665 ± 0.02 and 6.645 ± 0.04, as compared with 6.652 ± 0.03 for the original **4**.

Mass Spectrometric KIE. The mass spectra of all compounds were obtained on a Hewlett-Packard instrument, Model 5930A, equipped with a data system, Model 5932. Introduction of a sample was effected with a direct insertion probe. The temperatures of the source and filter were adjusted for each compound so as to obtain sufficient volatility. An ionizing energy of 70 eV and ionizing current of 25 mA were used. The high-precision, isotope ratio measurement procedure used was as originally described by Kwart and Stanulonis[70] and as most recently applied by Reimschussel and Paneth.[71] Parent peaks of unlabeled or labeled substrate and/or product were scanned 20 000 times per sample to yield a mean ratio with a standard deviation of less than or equal to 0.2%.

The procedure which was used measured the relative change in isotope ratio in the samples as the reaction proceeded as compared with the ratio in the starting material or final product. For calculating k_H/k_L the data were treated according to the Bigeleisen equation[72]

$$(k_H/k_L - 1)\ln[1 - f(x/y)] = \ln\left[1 + \frac{R_{A0} - R_{Af}}{R_{A0}}\,\frac{f(x/y)}{1 - f(x/y)}\right]$$

in which H and L designate the heavy and light isotope respectively, f = extent of reaction, R_{A0} = the AMU mass ratio at 100% reaction, R_{Af} = AMU mass ratio at f extent of reaction, $x = (1 + R_{A0})$, and $y = (1 + R_{Af})$.

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Registry No. 1, 122-66-7; **2**, 92-87-5; **3**, 492-17-1; [4-^{14}C]**4**, 81141-91-5; [4,4'-$^{13}C_2$]**4**, 81141-92-6; [4,4'-$^2H_2$]**4**, 35427-74-8; [$^{15}N_2$]**4**, 35427-75-9; **5**, 81141-93-7; unlabeled **5**, 81141-94-8; 4-nitro[1-^{14}C]aniline, 81141-95-9; nitro[4-^{14}C]benzene, 81141-96-0; 4-nitro[1-^{13}C]phenol, 3881-07-0; 4-deuterionitrobenzene, 13122-36-6; [^{15}N]aniline, 7022-92-6; 5-chloro-1-phenyl-1*H*-tetrazole, 14210-25-4.

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(68) Vogel, A. I. "Textbook of Practical Organic Chemistry", 4th ed.; Longman: London, 1978; p 722.

(69) Bigelow, H. E.; Robinson, D. B. "Organic Syntheses"; Wiley: New York, 1955, Coll. Vol. 3, p 103.

(70) Kwart, H.; Stannulonis, J. J. *J. Am. Chem. Soc.* **1976**, *98*, 4009.

(71) Reimschussel, W.; Paneth, P. *Org. Mass Spectrom.* **1980**, *15*, 302.

(72) Bigeleisen, J. "Advances in Chemical Physics"; Prigogine, I., Ed.; Interscience: New York, 1958; Vol. 1.

Photohydration of Aromatic Alkenes and Alkynes[1]

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Abstract: The photohydrations of aromatic alkenes and alkynes **2–12** have been studied in aqueous sulfuric acid. For the nonnitro-substituted substrates **2–8**, the products are the compounds obtained via Markovnikov addition of water to the alkene or alkyne moiety. Nitro-substituted styrenes **11** and **12** and phenylacetylenes **9** and **10** gave anti-Markovnikov addition products. Product quantum yields (Φ_{pdt}) generally show a strongly sigmoidal dependence on the acidity of the medium, with the exception of the nitrostyrenes, where no such dependence was observed. For compounds **2–8**, quenching of fluorescence with increasing acidity was observed, and the proposed photohydration mechanism involves a rate-limiting protonation step on the first excited singlet state (S_1), while for the nitrostyrenes, a rate-limiting attack of water on T_1 is consistent with the available data. A mechanism involving a concerted addition of H_3O^+ to T_1 is proposed for the photohydration of (nitrophenyl)acetylenes **9** and **10**. The solvent isotope effect on the product quantum yield (Φ_H/Φ_D) is consistent with these proposals. Photoprotonation rate constants (k_H) have been obtained—via transient and steady-state measurements—for substrates **2**, **4–6**, and **8**. Alkenes are approximately one order of magnitude less reactive than alkynes to photoprotonation, both of which are 10^{11}–10^{14} times more reactive than the corresponding ground-state molecules.

The acid-catalyzed hydration of phenylacetylenes and styrenes in the ground state has been studied extensively.[3] The products are, respectively, the acetophenones and 1-phenylethanols, both of which arise from Markovnikov addition of a proton in the rate-limiting step, followed by attack of water.[3]

At room temperature, these hydrations are very slow in the 0–25% (w/w) range of sulfuric acid concentrations, with half-lives of several hours or even days. A means by which the observed rate can be enhanced is by increasing the "basicity" of the substrate, thus making the protonation step more facile. This can, in principle, be achieved via photochemical excitation to the singlet or triplet excited states, since the enhanced basicity of numerous aromatic chromophores upon excitation is well-known.[4]

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[1] Part of this work was presented at the 64th Chemical Conference of the Chemical Institute of Canada, June, 1981, Halifax, Nova Scotia, Canada.

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[3] (a) Phenylacetylenes: Noyce, D. S.; Schiavelli, M. D. *J. Am. Chem. Soc.* **1968**, *90*, 1020. (b) Styrenes: Schubert, W. M.; Keefe, J. R. *Ibid.* **1972**, *94*, 559 and references therein.

[4] For reviews, see: (a) Ireland, J. F.; Wyatt, P. A. H. *Adv. Phys. Org. Chem.* **1976**, *12*, 131. (b) Lahiri, S. C. *J. Sci. Ind. Res.* **1979**, *38*, 492.