

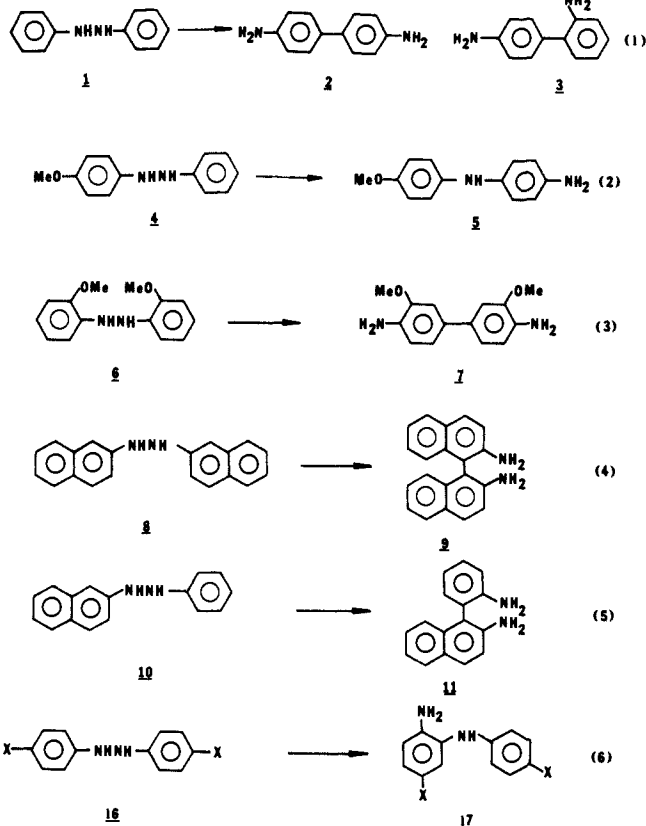
Heavy-Atom Kinetic Isotope Effects and Mechanism of the Acid-Catalyzed *o*-Semidine and *p*-Semidine Rearrangements and Disproportionation of 4,4'-Dichlorohydrazobenzene

Eun Sook Rhee and Henry J. Shine*

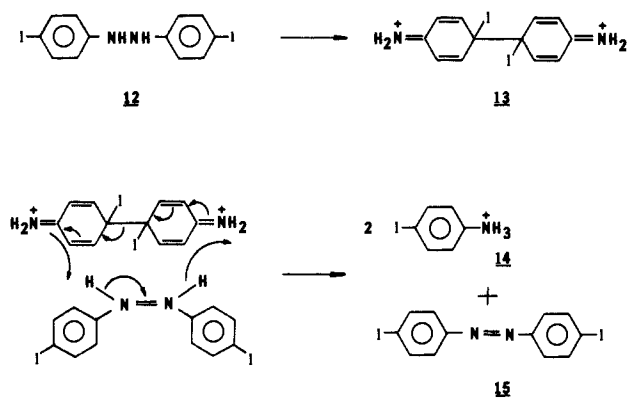
Contribution from the Department of Chemistry, Texas Tech University, Lubbock, Texas 79409-4260. Received September 24, 1985

Abstract: In acidic 60% aqueous dioxane solution at 0 °C, 4,4'-dichlorohydrazobenzene (**18**) undergoes concurrent disproportionation, to *p*-chloroaniline (**19**) and 4,4'-dichloroazobenzene (**20**), and *o*- (**21**) and *p*-semidine (**22**) rearrangement. In the *p*-semidine rearrangement one of the chlorine atoms of **18** is displaced, in essence, as Cl⁺. This requires participation of a second molecule of **18** in a redox reaction. The overall fate of **18**, therefore, is to give 11% *o*- and 12% *p*-semidine rearrangement (along with 12% of **20**) and 60% disproportionation, accounting for 95% of the **18**. Nitrogen and carbon kinetic isotope effects (KIE) have been determined for each of these reactions, using [¹⁵N,¹⁵N']**18**, [2-¹⁴C]**18**, [4-¹⁴C]**18**, and [4,4'-¹³C₂]**18**. Isotope ratios were obtained, measured on the trifluoroacetyl derivatives of **19**, **21**, and **22**, with a combination of scintillation counting, whole-molecule-ion mass spectrometry (WMIMS), and isotope-ratio mass spectrometry (IRMS). Nitrogen KIE were obtained by WMIMS for two ¹⁵N atoms in disproportionation (1.0260) and *p*-semidine rearrangement (1.0282) and by IRMS for one (naturally abundant) ¹⁵N atom in disproportionation (1.0141) and *o*- (1.0155) and *p*-semidine (1.0162) rearrangement. ¹³C (IRMS) and ¹⁴C KIE were measured for all reactions, but in no case was a KIE other than, effectively, unity obtained. These results show that *o*-semidine formation from **18** complies with expectations of sigmatropic shifts; that is, that this 1,3-sigmatropic shift is not a concerted process. The results suggest that, although a concerted 1,5-sigmatropic shift is possible, the *p*-semidine rearrangement of **18** is not characterized by one. In this case, however, a firm decision is not possible. Finally, the results indicate that disproportionation involves one (or both) of the two semidine rearrangement intermediates. The most likely one is that of the *p*-semidine. Rapid redox reaction of this intermediate (**26**), formed in the rate-determining step, with a second molecule of **18** can then lead to the *p*-semidine by removal of Cl⁺ and to disproportionation by scission of the central C-C bond of the intermediate. These paths account for the distribution of the products formed and the KIE of their formation.

Recent measurements of heavy-atom kinetic isotope effects (KIE) in benzidine rearrangements have indicated that these intramolecular rearrangements conform with the rules for sigmatropic rearrangements. For example, the two-proton, acid-catalyzed rearrangement of hydrazobenzene (**1**) into benzidine (**2**) was found, with the use of [¹⁵N,¹⁵N']**1**, [4-¹⁴C]**1**, and [4,4'-¹³C₂]**1**, to be a [5,5]-sigmatropic rearrangement, whereas concomitant rearrangement of **1** into diphenylene (**3**) was found not to be a concerted process.¹ Further, the acid-catalyzed rear-



Scheme I



angement of 4-methoxyhydrazobenzene (**4**) into the *p*-semidine (**5**) was found with the use of [¹⁵N,¹⁵N']**4** and [4-¹⁴C]**4** to be a concerted [1,5]-sigmatropic shift.² A [5,5]-sigmatropic rearrangement was also deduced in the one-proton, acid-catalyzed rearrangement of 2,2'-dimethoxyhydrazobenzene (**6**) into 3,3'-dimethoxybenzidine (**7**). In that case [¹⁵N,¹⁵N']**6** and [4,4'-¹³C₂]**6** were used for heavy-atom KIE measurements.³ Latterly, it was established with ¹⁵N, ¹⁴C, and ¹³C labeling that the acid-catalyzed and thermal rearrangements of 2,2'-hydrazonaphthalene (**8**) into 2,2'-diamino-1,1'-binaphthyl (**9**)⁴ and the acid-catalyzed rearrangement of *N*-2-naphthyl-*N'*-phenylhydrazine (**10**) into the diamine (**11**)⁵ are [3,3]-sigmatropic processes. Last, with the use of [2,2',6,6'-¹³C₄]**1** the nonconcerted nature of the rearrangement of **1** into **3** was confirmed.⁶

(1) Shine, H. J.; Zmuda, H.; Park, K. H.; Kwart, H.; Horgan, A. G.; Brechbiel, M. *J. Am. Chem. Soc.* **1982**, *104*, 2501.

(2) Shine, H. J.; Zmuda, H.; Kwart, H.; Horgan, A. G.; Brechbiel, M. *J. Am. Chem. Soc.* **1982**, *104*, 5181.

(3) Shine, H. J.; Park, K. H.; Brownawell, M.; San Filippo, J., Jr. *J. Am. Chem. Soc.* **1984**, *106*, 7077.

(4) Shine, H. J.; Gruszecka, E.; Subotkowski, W.; Brownawell, M.; San Filippo, J., Jr. *J. Am. Chem. Soc.* **1985**, *107*, 3218.

(5) Shine, H. J.; Kupczyk-Subotkowska, L.; Subotkowski, W. *J. Am. Chem. Soc.* **1985**, *107*, 6674.

These investigations covered, then, most of the major types in the family of benzidine rearrangements, namely, those designated as 4,4', 2,4', 2,2', and *N*,4',⁷ finding them, in summary, to correspond with [5,5]-, [3,5]-, [3,3]-, and [1,5]-sigmatropic shifts, respectively.

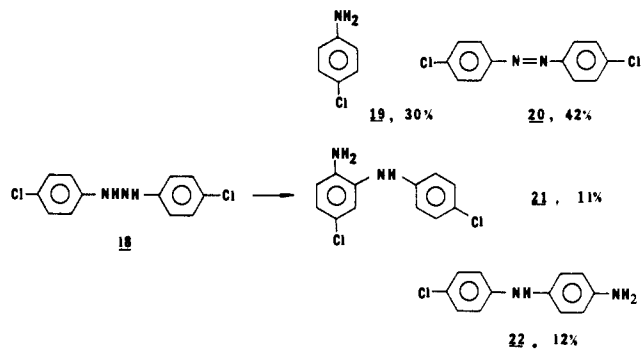
Another reaction, disproportionation, accompanies most (perhaps, all) acid-catalyzed benzidine rearrangements. The mechanism of this reaction, whose kinetic characteristics are always the same as those of the rearrangement it accompanies, was a puzzle for many years. Banthorpe, Cooper, and Ingold proposed in 1967⁸ that a *p*-quinoidal-type intermediate (**13**, Scheme I), formed in a rate-determining step, may be involved in the disproportionation reaction. We were able to substantiate this proposal with ¹⁵N, ¹⁴C, and ¹³C labeling of 4,4'-diiodohydrazobenzene (**12**) and heavy-atom KIE measurements.⁹

In the family of types of benzidine rearrangement, therefore, only one eventually remained untested, namely, the *o*-semidine rearrangement (eq 6). According to the rules of pericyclic reactions the *o*-semidine rearrangement, a [1,3]-sigmatropic shift, should not be concerted. Our investigation of this point with the acid-catalyzed reactions of 4,4'-dichlorohydrazobenzene (**18**) is the subject of this report.

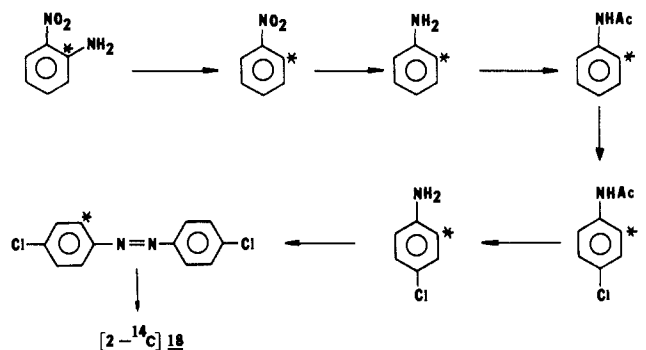
Ideally, the substrate needed for testing an *o*-semidine rearrangement is a 4,4'-disubstituted hydrazobenzene whose kinetics and products of rearrangement have been proven, and which can be labeled conveniently in the nitrogen and ortho- and para-carbon atoms. Not many candidates are available for choice. Suitable substrates with known kinetics and products of rearrangement have been listed by Cox and Buncl.⁷ They comprise **16** in which X = Me, Ph, *t*-Bu, F, Cl, and Br. We would have preferred to have used **16** in which group X was alkyl or phenyl, but labeling such a substrate in its ortho- and para-carbon atoms was not an attractive proposition. At first sight, *p*-hydrazotoluene (**16**, X = Me) would be the substrate of choice, because not only is it reported to undergo *o*-semidine rearrangement and disproportionation, and in the ratio 40:60, but also, in principle, labeling at the ortho- and para-carbon atoms could be achieved with labeled *p*-toluidines, obtainable from Reilly-Hickinbottom and Hofmann-Martius rearrangements of *N*-methylaniline. However, contrary to reports of the successes of these rearrangements^{10,11} we were unable to carry them out cleanly ourselves.¹² Consequently, we chose to work with 4,4'-dichlorohydrazobenzene, in spite of the expected complexity that the chlorine isotopes would give to the mass spectrometry measurements in some of our KIE determinations.

The kinetics of reaction of 4,4'-dichlorohydrazobenzene in acidic 60% aqueous dioxane solution have been reported by Banthorpe and Cooper.¹³ Rearrangement and concomitant disproportionation are second order in acid and, of course, first order in 4,4'-dichlorohydrazobenzene. The products of reaction under kinetic conditions were given as 22% *o*-semidine, 75% disproportionation (*p*-chloroaniline and 4,4'-dichloroazobenzene), and a trace of *p*-semidine (4-amino-4'-chlorodiphenylamine).¹³ These product distributions, initially attractive to us, had been determined spectroscopically after separations by paper chromatography and, unfortunately, turned out to be misleading. The products of reaction of 4,4'-dichlorohydrazobenzene in acidic ethanol have been reported also by Vecera and Petranek.¹⁴ The same products, along with traces of benzidine itself, were identified by paper

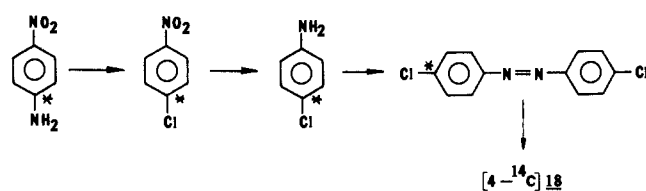
Scheme II



Scheme III



Scheme IV



chromatography, while the *p*-semidine was isolated in 7% yield from reaction in approx 2.7 M acid solution. The only other product isolated was 4,4'-dichloroazobenzene, corresponding with 34% of disproportionation.

In setting out to measure KIE for the *o*-semidine rearrangement, therefore, it became necessary for us to establish and separate the products of reaction of 4,4'-dichlorohydrazobenzene (**18**) quantitatively under kinetic conditions. This has been accomplished, and the results are listed in Scheme II. Separation of products allowed us to measure also KIE for *p*-semidine formation and for disproportionation. KIE measurements were achieved with the synthesis and use of [¹⁵N,¹⁵N']**18**, [2-¹⁴C]**18**, [4-¹⁴C]**18**, and [4,4'-¹³C₂]**18**, and with a combination of scintillation counting, whole-molecule-ion mass spectrometry (WMIMS) and isotope-ratio mass spectrometry (IRMS).

Results and Discussion

Syntheses of Labeled Substrates. The synthesis of the azoarene precursor to [¹⁵N,¹⁵N']**18**, containing 99.1% ¹⁵N₂, and to [4,4'-¹³C₂]**18**, containing 95.4% ¹³C₂, has been described earlier.¹⁵ Synthesis of [2-¹⁴C]**18** was carried out as shown in Scheme III. Radioactivity, measured at the colorless *p*-chloroaniline stage, was 16.7 mCi/mol, and dilution was carried out so that after oxidation to [2-¹⁴C]**20** the product would have approximately 7.5 mCi/mol radioactivity. Synthesis of [4-¹⁴C]**18** was carried out as in Scheme IV, and the radioactivity of the product, based on *p*-chloroaniline, was calculated to be 8.0 mCi/mol.

Products of Reaction. Although **18** has been reported correctly to undergo disproportionation into **19** and **20**, the quantitative

(6) Shine, H. J.; Zygmunt, J.; Subotkowski, W., unpublished work.

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

(8) Banthorpe, D. V.; Cooper, A.; Ingold, C. K. *Nature (London)* **1967**, *216*, 232.

(9) Shine, H. J.; Habdas, J.; Kwart, H.; Brechbiel, M.; Horgan, A. G.; San Filippo, J., Jr. *J. Am. Chem. Soc.* **1983**, *105*, 2823.

(10) Hickinbottom, W. J. *J. Chem. Soc.* **1934**, 1700. Reilly, J.; Hickinbottom, W. J. *J. Chem. Soc.* **1920**, 117, 103.

(11) Beckmann, E.; Correns, E. *Chem. Ber.* **1922**, *55*, 852.

(12) Unpublished work.

(13) Banthorpe, D. B.; Cooper, A. *J. Chem. Soc. B* **1968**, 618.

(14) Vecera, M.; Petranek, J. *Collect. Czech. Chem. Commun.* **1960**, *25*, 2005.

(15) Shine, H. J.; Rhee, E. S. *J. Labelled Compd. Radiopharm.* **1984**, *21*, 569.

Table I. Yields^a of Products in the Acid-Catalyzed Reaction of 4,4'-Dichlorohydrazobenzene (**18**)

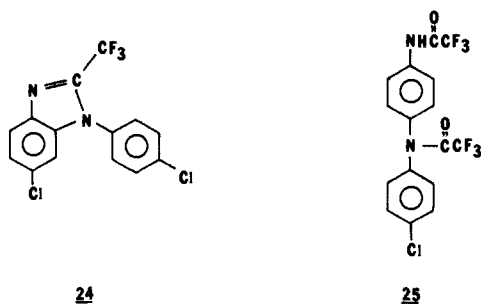
run	isotope enrich ^b	% conv		% 23	% 24	% 25	% 20		20(C) × 100/ (23 + 25)	total recov, %
		A ^c	B ^d				C ^e	D ^f		
1	¹⁵ N	22.2	18.0	6.1	2.3	1.8	7.8	77.8		95.8
2	¹⁵ N	100	88.8	30.3	10.9	9.2	38.4		97.2	88.8
		22.5	19.2	5.9	2.9	1.9	8.5	77.5		96.7
3	¹⁵ N	100	95.2	30.2	10.0	13.4	41.6		95.4	95.2
		20.0	16.4	5.8	1.9	1.9	6.8	80.0		96.4
4	¹³ C	100	92.0	28.3	10.2	13.4	40.1		96.2	92.0
		20.0	18.1	5.8	2.5	1.3	8.5	80.0		98.1
5	¹³ C	100	96.2	29.9	11.0	13.0	42.3		98.6	96.2
		24.3	20.9	7.4	2.9	2.4	8.2	75.7		96.6
6	¹³ C	100	95.8	30.8	10.0	13.3	41.7		94.5	95.8
		14.7	13.1	4.2	1.8	1.0	6.1	85.3		98.4
13 ^g	none	100	96.7	30.7	10.8	12.7	42.5		97.9	96.7
		100	93.5	26.3	14.8	12.1	40.3		104.9	93.5

^a Expressed as percent of **18** converted into product. ^b Two atoms. ^c Based on the amount of **20** recovered after air oxidation of unreacted **18**. ^d Sum of yields of **20**(C), **23**, **24**, and **25**. ^e Filtered from acid solution. ^f Recovered after air oxidation of unreacted **18**. ^g Assays by HPLC. All other runs by FC.

descriptions that were given are quite wrong.^{13,14} We have re-determined product distributions therefore, in two ways: by HPLC and flash chromatography (FC). Rather than measure the distribution of amine products, **19**, **21**, and **22**, directly, however, we found it better to convert them into trifluoroacetyl derivatives, not only for quantitative analysis but, more to the point, for isotopic assays. Quantitative analysis was carried out by HPLC once on products of reaction of unenriched **18** and by FC 12 times (all runs) on products of reaction of [¹⁵N, ¹⁵N']**18** and [4,4'-¹³C₂]**18**. The data are given in Table I. The initial concentrations of **18** which were used were in the range 0.02–0.03 M, and the concentration of HClO₄ was always 0.5 M. To comply with Banthorpe's kinetic condition, the solutions were also 0.5 M in LiClO₄. Reactions were carried out at 0 °C in 60% aqueous dioxane. In these conditions almost all of the azo compound **20** which had been formed, either at low or 100% conversion of **18**, precipitated from the solution. This, then, was filtered first from the cold solution and the filtrate was received into NaOH solution to quench further reaction. This filtered portion of **20** was a critical point in our material balances and understanding of the reaction, as is discussed below. When reactions were carried to 100% conversion, separation and analysis of the dissolved, small amount of **20** and of products (**19**, **21**, and **22**) proceeded next, after trifluoroacetylation. When reactions were carried to low conversions, the solution which had been quenched with NaOH now contained unreacted **18**, and this was oxidized into **20** by air bubbling. The newly formed **20** was removed and the amine products were then trifluoroacetylated for separation and analysis.

Consequently, our presentation of data in Table I for reactions to low conversions lists the amount of **20** in two ways: that which was formed as a result of reaction of **18** with acid and that formed by air oxidation of unreacted **18**. Necessarily, only one listing for the amount of **20** is given for reactions of **18** which were carried to completion.

Trifluoroacetylation of the mixture of amine products converted **19** into *N*-(trifluoroacetyl)-*p*-chloroaniline (**23**), **21** (the *o*-semidine) into the diazole **24**, and **22** (the *p*-semidine) into the bis-trifluoroacetyl derivative **25**. Therefore, the analysis of products



was, finally, an analysis of the amounts of **20** and **23–25** that were formed, and these are given in Table I. In our discussions,

however, we shall refer to amine products in their original sense, namely **19**, **21**, and **22**.

The data in Table I are a reasonably accurate documentation of what happens to **18** under the conditions used. We see that *o*-semidine formation is not the only major rearrangement product, but that the *o*- and *p*-semidines are formed in comparable amounts. Another feature is striking. The yields of **19** and **20** which are formed from **18** by disproportionation must be identical (Scheme I). However, the amount of **20** which was filtered from the cold reaction solution both at low and 100% conversions was always larger than the assayed amount of **19**. On the other hand, the yield of **20** was always equatable to the sum of the yields of **19** and **22**. This is shown for 100% conversion in the last column of Table I as the ratio **20**/(**19** + **22**), always close to 1.00. It is evident that **20** is formed not only by acid-catalyzed disproportionation of **18** but also in the pathway of the *p*-anisidine rearrangement. In the *p*-semidine rearrangement, Cl⁺ must in essence be ejected from the one of the para positions of rearranging, diprotonated **18**. This means that a reducing partner is needed for that rearrangement, and this role is served by a second molecule of **18** itself. This consequence not only affects the material balance in the reaction (Table I) but has a role in accounting for KIE in the disproportionation reaction, too, as is shown later.

The acid-catalyzed reactions of **18**, therefore gave approx 11% *o*-semidine, 12% *p*-semidine, and 60% disproportionation, accounting in total for 95% of the **18**. We shall argue below, also, that the route to the *p*-semidine rearrangement may be far more extensive and important in the reactions of **18** than can be seen by the product distributions alone.

Low Conversions (Percent). Table I lists the extents of low conversion of **18** in two ways, A and B. The times for low conversions were determined from the pseudo-first-order rate constant ($k = 7.33 \times 10^{-5} \text{ s}^{-1}$) reported by Banthorpe and Cooper.¹³ However, the times were used only as a guide. A more realistic measure of the extent of low conversion was taken to be the amount **18** remaining after low conversion and this was measured as **20** obtained by air oxidation of the filtered, quenched reaction solution. The results are given in column A. In principle, the low conversion measured in this way should be the same as that obtained from the sum (listed in column B) of the yields of isolated products, namely, **20** filtered from the cold, acid solution plus **23–25**. This is seen (Table I) to be only approx true although the two results are, pleasingly, not too dissimilar. The percent low conversion is used (as *F*) in calculating KIE. Because of errors in assays of small amounts of products we have used the conversions listed under column A for calculating KIE.

KIE Measurements. Isotopic ratios in the products **23–25** were measured in three ways: scintillation counting for ¹⁴C labeling, whole-molecule-ion mass spectrometry (WMIMS), and isotope-ratio mass spectrometry (IRMS) for ¹⁵N and ¹³C labeling. WMIMS was carried out with a Hewlett-Packard quadrupole mass spectrometer. Reasonably reproducible results could be

Table II. Kinetic Isotope Effects (KIE) in the Acid-Catalyzed Disproportionation of 4,4'-Dichlorohydrazobenzene (**18**)^a

run	isotope	method	% conv ^b	KIE
1	¹⁵ N, ¹⁵ N'	WMIMS ^c	22.2	1.024 ± 0.0075
2	¹⁵ N, ¹⁵ N'	WMIMS ^c	22.5	1.024 ± 0.0005
3	¹⁵ N, ¹⁵ N'	WMIMS ^c	20.0	1.030 ± 0.0086
5	¹⁵ N ^d	IRMS ^e	24.3	1.0126
6	¹⁵ N ^d	IRMS ^e	14.7	1.0155
5	4,4'- ¹³ C	IRMS ^e	24.3	0.9997
6	4,4'- ¹³ C	IRMS ^e	14.7	1.0039
7	4- ¹⁴ C	scint	18.0	1.0000 ± 0.0017
8	4- ¹⁴ C	scint	23.0	0.9956 ± 0.0020
9	4- ¹⁴ C	scint	17.0	0.9966 ± 0.0024
10	2- ¹⁴ C	scint	22.0	1.0019 ± 0.0016
11	2- ¹⁴ C	scint	26.0	1.0003 ± 0.0018
12	2- ¹⁴ C	scint	18.0	0.9987 ± 0.0027

^a Obtained from isotope ratios in product **23**. ^b Based on **20** assayed after air oxidation of unreacted **18**. ^c Whole-molecule-ion mass spectrometry. ^d Naturally abundant ¹⁵N. ^e Isotope-ratio mass spectrometry.

obtained only in measuring mass ratios in products **23** and **25** (representing disproportionation and *p*-semidine formation respectively) from rearrangements of [¹⁵N,¹⁵N']**18**. Reproducible results could not be obtained by WMIMS for compound [¹⁵N,¹⁵N']**24** and for any of the products obtained from reactions of [4,4'-¹³C]**18**. Failure to obtain reproducible WMIMS results with [¹⁵N,¹⁵N']**24** is attributable to the volatile nature of **24** and difficulties in controlling a steady concentration of **24** in the mass spectrometer. This led to further problems with the electron multiplier, and hence WMIMS on **24** was abandoned. Failure to obtain reproducible results with all ¹³C-labeled samples derived, as was found later, from there being no carbon KIE in the reactions of **18**. This led to WMIMS measurements of ¹³C KIE close to 1.00, but which was scattered too widely around the error limits of the instrumentation to be considered reliable. As a result, WMIMS was abandoned for ¹³C measurements in favor of the more precise IRMS.

Measurements of isotopic abundances in samples of [¹⁵N]**23** were complicated by two features. Volatility of **23** made repetitive mass measurements in the customary direct, solid inlet probe (DIP) impossible. Consequently a DIP was used in which samples of **23** were placed in an attached external glass tube, and **23** was metered into the mass spectrometer through needle valves of the DIP under controlled external heating of the glass tube, valves, and probe. In this way controllable, steady, low concentrations of **23** could be maintained in the mass spectrometer. The second complication lay in the effect of the chlorine isotopes on measuring (M + 1)/M ratios. Our preference was to measure the abundance of ¹⁵N in [³⁵Cl]**23**, namely, the ratio of masses 224/223. However, although the abundance of an (M - 1) ion in the mass spectrum of **23** is quite low, its contribution from [³⁷Cl]**23** (namely, mass 224) was enough to complicate the measurements of the ratio 224/223. Therefore, we settled for measuring the abundances of ¹⁵N in [³⁷Cl]**23**, namely, the mass ratio (M + 3)/(M + 2) = 226/225, in which the effect of (M - 1) contributions to mass 225 were very small.

Measurement of isotopic abundances in samples of [¹⁵N,¹⁵N']**25** were carried out with the normal DIP. Because mass ratio measurements were for (M + 2)/M ions, contributions from small (M - 1) abundances were not important and the ratio of masses 412/410 was used. Precision in a particular run was reasonably good but the KIE results themselves from run to run were scattered. For this reason two sets of measurements were made in each run, totaling six in all (Table IV).

Samples used for ¹³C measurements by IRMS were **23**–**25** obtained from reactions of [4,4'-¹³C]**18**. The atom percent enrichment of ¹³C in these samples was quite low and suitable, therefore, for IRMS. That is, although a mixture of 5 mol % of [4,4'-¹³C]**18** in **18** was used for reaction, the atom percent enrichment in the samples was much lower, amounting in the cases of **23**, **24**, and **25** samples to approx 0.63, 0.72, and 0.63 atom % above the normal abundance of ¹³C, respectively. These en-

Table III. Kinetic Isotope Effects (KIE) in the Acid-Catalyzed *o*-Semidine Rearrangement of 4,4'-Dichlorohydrazobenzene (**18**)^{a,b}

run	isotope	method	% conv	KIE
5	¹⁵ N	IRMS	24.3	1.0157
6	¹⁵ N	IRMS	14.7	1.0152
5	4,4'- ¹³ C	IRMS	24.3	1.0002
6	4,4'- ¹³ C	IRMS	14.7	0.9984
7	4- ¹⁴ C	scint	18.0	1.0050 ± 0.0024
8	4- ¹⁴ C	scint	23.0	1.0055 ± 0.0081
9	4- ¹⁴ C	scint	17.0	0.9975 ± 0.0031
10	2- ¹⁴ C	scint	22.0	0.9978 ± 0.0010
11	2- ¹⁴ C	scint	26.0	1.0029 ± 0.0028
12	2- ¹⁴ C	scint	18.0	0.9984 ± 0.0032

^a Obtained from isotope ratios in product **24**. ^b See footnotes, Table II.

Table IV. Kinetic Isotope Effects (KIE) in the Acid-Catalyzed *p*-Semidine Rearrangement of 4,4'-Dichlorohydrazobenzene (**18**)^{a,b}

run	isotope	method	% conv	KIE
1 ^c	¹⁵ N, ¹⁵ N'	WMIMS	22.2	1.0187 ± 0.0027
	¹⁵ N, ¹⁵ N'	WMIMS		1.0221 ± 0.0075
2 ^c	¹⁵ N, ¹⁵ N'	WMIMS	22.5	1.0344 ± 0.0025
	¹⁵ N, ¹⁵ N'	WMIMS		1.0310 ± 0.0041
3 ^c	¹⁵ N, ¹⁵ N'	WMIMS	20.0	1.0380 ± 0.0042
	¹⁵ N, ¹⁵ N'	WMIMS		1.0251 ± 0.0037
5	¹⁵ N	IRMS	24.3	1.0157
6	¹⁵ N	IRMS	14.7	1.0166
5	4,4'- ¹³ C	IRMS	24.3	0.9945
6	4,4'- ¹³ C	IRMS	14.7	0.9995
7	4- ¹⁴ C	scint	18.0	1.0058 ± 0.0020
8	4- ¹⁴ C	scint	23.0	0.9981 ± 0.0020
9	4- ¹⁴ C	scint	17.0	1.0004 ± 0.0025

^a Obtained from isotope ratios in product **25**. ^b See footnotes, Table II. ^c Duplicate assays of mass ratios were made in each run.

Table V. Summary of Averaged Nitrogen Kinetic Isotope Effects (KIE) in Acid-Catalyzed Reactions of 4,4'-Dichlorohydrazobenzene (**18**)

reaction	KIE and basis		
	¹⁵ N, ¹⁵ N' ^a	¹⁵ N ^b	(¹⁵ N) ²
disproportionation	1.0260 ± 0.0028	1.0141 ± 0.0015	1.0284
<i>o</i> -semidine rearr		1.0155 ± 0.0003	
<i>p</i> -semidine rearr	1.0282 ± 0.0068	1.0162 ± 0.0005	1.0327

^a WMIMS. ^b IRMS.

Table VI. Summary of Averaged Carbon Kinetic Isotope Effects (KIE) in Acid-Catalyzed Reactions of 4,4'-Dichlorohydrazobenzene (**18**)

reaction	KIE and basis		
	2- ¹⁴ C	4- ¹⁴ C	4,4'- ¹³ C ₂ ^a
disproportionation	1.0003 ± 0.0013	0.9974 ± 0.0019	1.0018 ± 0.0021
<i>o</i> -semidine rearr	0.9997 ± 0.0023	1.0027 ± 0.0037	0.9993 ± 0.0009
<i>p</i> -semidine rearr		1.0014 ± 0.0032	0.9970 ± 0.0025

^a IRMS.

richments were amenable to measurements of the ratio ¹³CO₂/¹²CO₂.

The ¹³C-enriched samples contained no enrichment in ¹⁵N. Therefore, they were also suitable for measuring nitrogen mass ratios by IRMS. The ratio ²⁹N₂/²⁸N₂ was measured, and in these measurements changes were sought in the natural abundance of ¹⁵N which might have been brought about by reactions of **18**. Thus, both ¹³C and ¹⁵N KIE were measured with the same samples by IRMS.

Detailed results of KIE measurements are given in Table II (disproportionation), Table III (*o*-semidine formation), and Table IV (*p*-semidine formation). The results are presented as averages for nitrogen KIE in all reactions (Table V) and carbon KIE for all reactions (Table VI).

Meaning of the KIE: Nitrogen KIE. Each of the reactions, disproportionation and rearrangements to the *o*- and *p*-semidine, exhibits a small, positive nitrogen KIE. The KIE are hardly distinguishable from each other and thereby give no indication of substantial differences in transition states of the three concurrent processes. The size of the KIE for double labeling in disproportionation and the *p*-semidine rearrangement are close to the square of the KIE for the corresponding single labeling in these reactions. Concordance of the results for single and double labeling gives us confidence in their validity. Had we been able to measure the KIE for double labeling in the *o*-semidine rearrangement the result would have been, we feel, also close to 1.03. The KIE data tell us that the N-N bond in diprotonated **18** is weakened in the transition state for each of the three processes.

An *o*-semidine rearrangement cannot, by the principles of orbital symmetry, be suprafacially concerted. The nitrogen KIE, therefore, is that for a two-step process. A *p*-semidine rearrangement can be suprafacially concerted. In such a concerted rearrangement the N-N bond dissociates while the *p*-C-N bond is being formed, so that the nitrogen KIE reflects the sum of these bond changes. The fact that the nitrogen KIE for the *o*- and *p*-semidine rearrangements are almost the same (1.0155 and 1.0162) suggests that the transition states should be the same, that is, both dissociative. The carbon KIE (below) also lead to this conclusion; but we are not really able to make this commitment with certainty for the *p*-semidine rearrangement, as is discussed further, below.

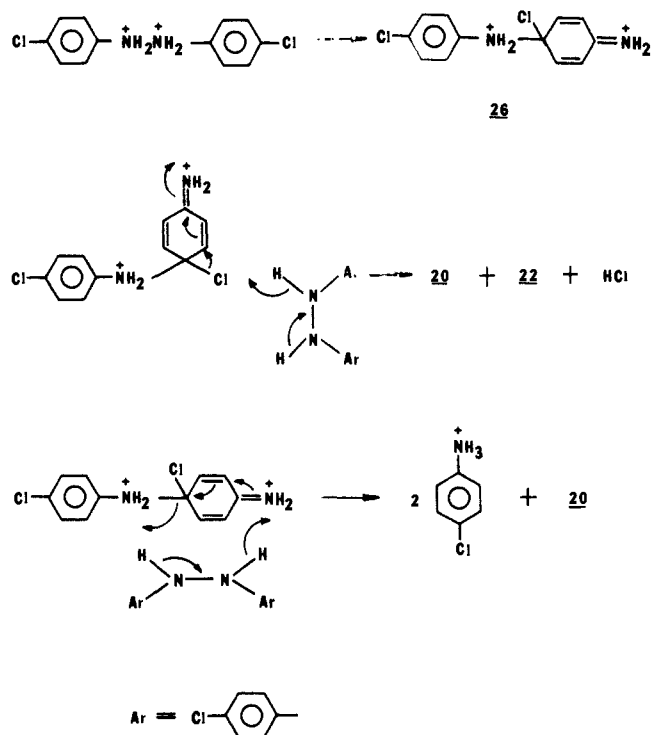
Carbon KIE. There is no carbon KIE for any of the three reactions. We shall discuss each in succession.

***o*-Semidine Rearrangement.** In principle, there should not be a carbon KIE for this 1,3-sigmatropic rearrangement. Two of our carbon results have a direct bearing on this point, namely, from [2-¹⁴C]**18** and [4,4'-¹³C₂]**18**. The 2-¹⁴C KIE (0.9997) is considered to be unity. It is supported, insofar as confidence in the experimental procedure is concerned, by the ¹⁴C KIE for *o*-semidine formation from [4-¹⁴C]**18**. That, of course, cannot be anything but unity, and our result (1.0027) gives a measure of our precision and confidence in the result. The same confidence can be placed, therefore, on the result (0.9997) from direct labeling in [2-¹⁴C]**18**. The ¹³C KIE (0.9993) was measured with [4,4'-¹³C₂]**18**, that is, **18** which had ¹³C enrichments in its two para positions. Since these positions aren't involved in *o*-semidine formation the ¹³C KIE for the *o*-semidine derives from naturally abundant ¹³C in the ortho positions. The specific labeling in the para positions represents only a net unchanging ¹³C content, just as is represented by the natural abundance of all of the other carbon atoms in the molecule (**24**) which was assayed by IRMS. Therefore, the KIE reported (0.9993) is a true measure for this rearrangement, albeit from the natural abundance, and is also considered to be unity.

Had we found a carbon KIE meaningfully less or greater than unity for *o*-semidine formation, that, along with the nitrogen KIE, would have meant that the *o*-semidine rearrangement, a 1,3-sigmatropic shift, was a concerted process. This would have been somewhat of a dilemma since a concerted 1,3-sigmatropic shift contravenes orbital-symmetry requirements. The reason for our having set out with **18** was, in fact, to verify this part of our understanding of the family of benzidine rearrangements. Our result, then, is in accordance with a nonconcerted process.

***p*-Semidine Rearrangement.** The ¹⁴C KIE (1.0014) is sufficiently close to 1.000 as to be considered unity. Since only one *p*-position of **18** is involved in *p*-semidine formation the ¹³C KIE (0.9970) measured with [4,4'-¹³C₂]**18** is for only one enriched position and we consider that result, too, to be unity. We were surprised with these results. The *p*-semidine rearrangement is a 1,5-sigmatropic shift. In principle, then, it can be a concerted shift and give a carbon KIE. Earlier, it was found, indeed, that the *p*-semidine rearrangement of 4-methoxyhydrazobenzene (**4**) is a concerted one, exhibiting both substantial nitrogen and carbon KIE, and we had anticipated finding the same result in the present work. However, although the two *p*-semidine rearrangements are the same in form, they differ considerably in character. Rear-

Scheme V



angement of **4** is first order in acid, and a proton is displaced from its para position. Rearrangement of **18** is second order in acid and Cl⁺ is displaced. We do not know if these differences lead to the difference in transition states in the *p*-semidine rearrangements of **4** and **18**, which is suggested by the difference in KIE results. The carbon and nitrogen results with **18** suggest that its *p*-semidine rearrangement is not a concerted process. In reality, we cannot say if that is correct or not. We are dealing here with a bond-forming reaction for which the KIE may be smaller than, greater than, or fortuitously equal to 1.000. Thus, the presence of a carbon KIE here could be used as evidence for concertedness, but in the absence of a carbon KIE the nonconcertedness cannot be assumed. An intermediate (**26**) is certainly formed, but we cannot define well the pathway to it.

There is a subtle difference in the meaning of the KIE results for the *o*- and *p*-semidine rearrangements of **18**. The *o*-semidine result validates our understanding of sigmatropic rearrangements. Perhaps we are preconditioned for that result. The *p*-semidine result cannot substantiate a concerted rearrangement, but is not necessarily contradictory of one.

p-Semidine formation requires the loss of the chlorine atom from the *p*-position of **18** at which the new C-N bond has been made. The chlorine atom must leave effectively as Cl⁺, and our proposal for the way in which this happens is linked to the disproportionation reaction shown in Scheme V.

Disproportionation. Disproportionation reactions have the same kinetic characteristics of the rearrangements they accompany. In this case, disproportionation is first order in **18** and second order in acid. The kinetic character and stoichiometry of disproportionation require, then, that an intermediate is formed from one molecule of **18** in the rate-determining step and next undergoes a rapid redox reaction with a second molecule of **18**. In analogy with earlier work on the disproportionation of 4,4'-diiodohydrazobenzene,⁹ we had anticipated that disproportionation of **18** would involve also a 4,4'-quinonoid intermediate analogous to **13** (Scheme I) and that the formation of this intermediate would be disclosed by our carbon KIE measurements. The carbon KIE data (Table VI) reveal, however, that, probably the intermediate in this case is instead the quinonoid of either the *o*- or *p*-semidine, since these are formed without exhibiting carbon KIE. Our feeling is that the *p*-semidine quinonoid intermediate (**26**) is the most likely candidate for the disproportionation reaction. Thereby, reaction of **26** with a second molecule of **18** can occur in two ways:

by C-C scission for disproportionation and by Cl^+ abstraction for *p*-semidine (**22**) formation. The latter route provides the azo compound (**20**) in excess of that from the disproportionation reaction, as is documented in Table I.

Experimental Section

Dioxane (Aldrich) was distilled over LiAlH_4 prior to use. Perchloric acid (MCB) was assayed after 100-fold dilution and was found to be 11.68 N. 4,4'-Dichlorohydrazobenzene (**18**) was prepared immediately before its use from 4,4'-dichloroazobenzene (**20**). Typically, 6.0 g of **20** in 120 mL of acetone was stirred with 8.0 g of zinc dust. A saturated solution of aqueous NH_4Cl was added until the yellow color of **20** had disappeared completely. The colorless solution was filtered through fritted glass into 400 mL of 10% ammonium hydroxide solution which had been degassed. The suspension of **18** was stirred for coagulation under aspirator vacuum for 30 min. The colorless **18** was filtered, washed with water, and dried under vacuum, giving 5.9 g (98%), mp 125–126 °C, lit. mp 120 °C.¹³

Syntheses of Labeled 18. The syntheses of [$^{15}\text{N},^{15}\text{N}$]**20** and [4,4'- $^{13}\text{C}_2$]**20** have been described earlier. In these cases the ^{15}N label was introduced with $^{15}\text{NH}_4\text{Cl}$ in the preparation of 4-chloro[^{15}N]aniline, and the ^{13}C label was introduced with [2- ^{13}C]acetone in the preparation of [1- ^{13}C]-4-nitrophenol.¹⁵ A mixture of [$^{15}\text{N},^{15}\text{N}$]**20** and unenriched **20** was crystallized from CHCl_3 so as to give **20** containing 5 mol % of the labeled isomer. Analogously, a 5 mol % mixture of [4,4'- $^{13}\text{C}_2$]**20** was prepared. These mixtures were used for reduction to labeled **18**.

[2- ^{14}C]**18.** A solution of 140 mg (4.42 mCi) of [1- ^{14}C]-2-nitroaniline (Hoechst) and 14.85 g (108 mmol) of 2-nitroaniline in 73 mL of 50% H_3PO_2 containing a small amount of Cu_2O was stirred at 0 °C while a solution of 9.4 g (140 mmol) of NaNO_2 in 20 mL of water was added dropwise during 1 h. The solution was made alkaline with 40% NaOH and extracted with 4 × 200 mL of ether. Workup of the dried ether solution gave dark brown [2- ^{14}C]nitrobenzene, which was distilled under reduced pressure. The product was diluted by adding nitrobenzene to the residue in the distillation flask and distilling through the same apparatus. Finally 20.7 g (65.7%, based on *o*-nitroaniline used) of [2- ^{14}C]nitrobenzene was obtained. Assay by scintillation counting showed this to have an activity of 15.7 mCi/mol.

A mixture of 14.8 g (120 mmol) of [2- ^{14}C]nitrobenzene, 51.4 g (508 mmol) of triethylamine, and 300 mg of 10% Pd/C was stirred at 90 °C while 21.1 g (463 mmol) of formic acid was added dropwise. This mixture was heated under reflux for 5 h, cooled, diluted with 250 mL of CH_2Cl_2 , and filtered. The filtrate was dried over MgSO_4 and evaporated to give crude [2- ^{14}C]aniline, which was acetylated by standing at room temperature in a solution of Ac_2O (20 mL) and AcOH (15 mL) for 24 h. Precipitation by pouring into ice water gave 10.6 g (79 mmol, 66% based on nitrobenzene) of [2- ^{14}C]acetanilide, mp 112–114 °C.

[2- ^{14}C]-4-Chloroacetanilide was prepared from [2- ^{14}C]acetanilide by some modification of the method of Orton and Jones.¹⁶ Chlorox (5% NaOCl , 120 mL, 85 mmol) was slowly run into a solution of 10.6 g (79 mmol) of [2- ^{14}C]acetanilide in 105 mL of AcOH . After stirring the mixture for 2 days at room temperature the colorless precipitate was collected, giving 5.6 g (33 mmol, 42%) of [2- ^{14}C]-4-chloroacetanilide, mp 179–180 °C. The product was shown by GC to be free of the ortho isomer. The filtrate was diluted with 540 mL of water, giving 980 mg of a tan mixture of labeled *o*- and *p*-chloroacetanilide. This was heated at 75–80 °C under atmospheric pressure to remove the ortho isomer by sublimation. The residue was triturated with 25 mL of benzene and crystallized from aqueous AcOH , giving 450 mg of [2- ^{14}C]-4-chloroacetanilide: mp 179–180 °C, total yield 606 mg (45%); lit. mp 179 °C.¹⁶

Hydrolysis of this product was carried out by boiling with 320 mL of 15% H_2SO_4 for 5 h. Neutralization by slow addition of 98 g of Na_2CO_3 and extraction with 9 × 100 mL of ether gave 4.18 g (33 mmol, 92%) of [2- ^{14}C]-4-chloroaniline, mp 68–69 °C. Assay by scintillation counting showed this to have an activity of 16.7 mCi/mol. This product was mixed with 14.0 g of *p*-chloroaniline to give a calculated activity of 3.8 mCi/mol. The mixture was oxidized with MnO_2 to give 16.1 g (90%) of [2- ^{14}C]**20**. Crystallization from CHCl_3 gave mp 188–189 °C.

[4- ^{14}C]**18.** A mixture of 37 mg (1.55 mCi) of [1- ^{14}C]-4-nitroaniline (Hoechst) and 3.47 g (25 mmol) of *p*-nitroaniline was dissolved in 7.0 mL of concentrated HCl and 7.0 mL of water and cooled to 0 °C. To this was added slowly a precooled solution of 1.9 g (28 mmol) of NaNO_2 in 4.0 mL of water. The mixture was stirred vigorously for complete solution of solids and poured slowly into a precooled solution of 3.5 g (35 mmol) of Cu_2Cl_2 in 14 mL of concentrated HCl . This mixture was allowed to warm to room temperature and stirred until N_2 evolution ceased. Steam distillation gave 3.6 g (23 mmol, 90%) of [4- ^{14}C]-4-

chloronitrobenzene, mp 81–82.5 °C. This product was reduced with $\text{SnCl}_2 \cdot 2\text{H}_2\text{O}$ and hydrochloric acid to [4- ^{14}C]-4-chloroaniline in 91% yield. Assay showed the product to have an activity of 60 mCi/mol. Of this, 2.66 g was diluted with *p*-chloroaniline and crystallized so that the final product, [4- ^{14}C]-4-chloroaniline had an activity of 4.2 mCi/mol. Oxidation with MnO_2 gave [4- ^{14}C]**20**, mp 188–189 °C (from CHCl_3).

2'-Amino-4,5'-dichlorodiphenylamine (o-Semidine, 21). Following the method of Kottenhahn et al.¹⁷ a solution of 20.3 g (0.10 mol) of 1-chloro-3,4-dinitrobenzene (Aldrich) and 41.5 g (0.30 mol) of *p*-chloroaniline in 150 mL of ethanol was kept at 40–50 °C for 12 h. The orange product formed on cooling the solution was filtered and washed with cold ethanol and 3 N HCl , giving 13.7 g (48 mmol, 48%) of 4,5'-dichloro-2'-nitrodiphenylamine, mp 157–158 °C, lit. mp 158–158.5 °C.¹⁷

One gram (3.5 mmol) of this product was reduced to **21** by boiling with 5 mL of ethanol, 9 mL of concentrated HCl , and 2.7 g of Sn shot for 2 h. The cooled solution deposited the hydrochloride of **21**. Dilution of the filtrate with 40 mL of ice water gave a second crop. Treatment of the salt in 20 mL of ethanol with 20 mL of 40% NaOH and extraction with 3 × 300 mL of ether gave 430 mg (1.7 mmol, 49%) of **21**, mp 89–91 °C, after crystallizing from aqueous ethanol, lit. mp 90 °C.¹³

Trifluoroacetylation of 21. Formation of 24. Reaction of **21** with trifluoroacetic anhydride (TFA) failed to give the trifluoroacetyl derivative even when carried out at –6 °C. The product always contained some **24**. Therefore, the formation of **24** alone was sought and achieved by boiling a solution of 93 mg (0.37 mmol) of **21** in 5 mL of benzene containing 0.20 mL (1.33 mmol) of TFA for 3 h. Evaporation of solvent gave 120 mg (0.36 mmol, 98%) of **24**, mp 95–96 °C (petroleum ether, bp 30–60 °C): $^1\text{H NMR}$ ($\text{Me}_2\text{CO}-d_6$) δ 7.32–7.97 (m); there were no peaks in the NH region of the infrared (KBr); high-resolution MS, M^+ (46.5%) 329.9955,¹⁸ calcd for $\text{C}_{14}\text{H}_7\text{N}_2\text{F}_3\text{Cl}$ 330.0021.

Bis(trifluoroacetyl) Derivative of the p-Semidine (25). Attempts to prepare the authentic *p*-semidine were not successful. Therefore, the identity of **25** was established after isolation from workup in the rearrangement of unenriched **18**. Product **25** had mp 121–122 °C and M^+ 410. Trifluoroacetylation of the mixture of amine products was carried out so as to ensure that none of the monotrifluoroacetyl derivative of the *p*-semidine remained. A monotrifluoroacetyl derivative was obtained from partial trifluoroacetylation and had mp 178–179 °C and M^+ 314.0438; calcd for $\text{C}_{14}\text{H}_{10}\text{N}_2\text{OF}_3\text{Cl}$ 314.0521. That the diarylamino secondary position could be trifluoroacetylated was validated by reaction of TFA with diphenylamine, which gave the trifluoroacetyl derivative, mp 70–71 °C and M^+ 265.

Rearrangements of 4,4'-Dichlorohydrazobenzene (18). An example of the technique is illustrated with [$^{15}\text{N},^{15}\text{N}$]**18**. A solution of 5.06 g (20 mmol) of [$^{15}\text{N},^{15}\text{N}$]**18** containing 5 mol % of the labeled isomer in 300 mL of dioxane and 200 mL of water was cooled to 0 °C. A second solution, also cooled to 0 °C was made by dissolving 42.8 mL (0.50 mol) of standardized 72% HClO_4 and 80.2 g (0.50 mol) of $\text{LiClO}_4 \cdot 3\text{H}_2\text{O}$ in 300 mL of dioxane and making up to 500 mL with water. The precooled solutions were flushed with argon, mixed quickly, and kept under argon. After 5 min a 200-mL aliquot was pumped out under argon pressure and kept in the refrigerator under argon for 48 h.

(a) **Low Conversion.** After 30 min from mixing the remaining cold solution (800 mL) was filtered by suction through sintered glass into a flask containing 17 g (0.425 mol) of NaOH in 50 mL of water. The acid solution was kept cold during filtration, which took 6 min. The filtered solid was washed with 60% aqueous dioxane and dried, giving 290 mg (1.16 mmol, 7.2%) of 4,4'-dichloroazobenzene (**20**). Air was bubbled into the alkaline solution gently for 36 h, after which **20** (3.1 g, 12.4 mmol, 77.5%) was again recovered. The filtrate was extracted with 9 × 100 mL portions of ether, the ether solution was dried, and most of the solvent was evaporated. To the residue was added 2 mL of benzene and 1 mL of TFA. The mixture was refluxed for 2 h, and allowed to stand for 24 h. Next, 20 mL of benzene was added and the solution was washed twice with 20 mL of saturated NaHCO_3 solution and twice with water and then dried over Na_2SO_4 . Evaporation gave 930 mg of mixed derivatives which were separated into the following components by flash column chromatography using benzene elution and collecting 20-mL aliquots: 54 mg (0.22 mmol, 1.3%) of **20** (fractions 1–4); 109 mg (0.33 mmol, 2.1%) of **24** (fractions 8–11); 380 mg (1.70 mmol, 5.3%) of **23**, the trifluoroacetyl derivative of *p*-chloroaniline (fractions 14–24); 84 mg (approx 1.5%) of a mixture of **23** and **24**. Finally, elution with CH_2Cl_2 gave 122 mg (0.30 mmol, 1.9%) of **25** the bis(trifluoroacetyl) derivative of the *p*-semidine (fractions 27–29). Each product was recrystallized 3 times for mass spectrometry, giving the following: **23** (benzene) 156 mg, mp

(17) Kottenhahn, A. P.; Seo, E. T.; Stone, H. W. *J. Org. Chem.* **1963**, *28*, 3114.

(18) Midwest Center for Mass Spectrometry, an NSF Facility, Department of Chemistry, University of Nebraska, Lincoln, NE.

123–124 °C; **24** (petroleum ether), 13.5 mg, mp 95–96 °C; **25** (petroleum ether-CH₂Cl₂) 50 mg, mp 121–122 °C.

(b) **100% Conversion.** After standing 24 h the 200-mL aliquot was filtered, as earlier, into a solution of 4.5 g (0.114 mol) of NaOH in 15 mL of water, giving 400 mg (1.59 mmol, 39.7%) of **20**. The filtrate was worked up exactly as before but without prior air bubbling. Flash chromatography gave 19 mg (0.08 mmol, 1.8%) of **20** (fractions 1–4), 92 mg (0.28 mmol, 6.8%) of **24** (fractions 8–10), 500 mg (2.24 mmol, 27.3%) of **23** (fractions 13–27), and 83 mg (approximately 5.6%) of a mixture of **23** and **24**. Elution with CH₂Cl₂ gave 221 mg (0.54 mmol, 13.1%) of **25** (fractions 33–40). Crystallization followed as above.

This experiment was repeated 3 times in all. Product distributions are summarized in Table I.

Rearrangements of [4,4-¹³C]**18** were carried out in the same way. Times for low conversions were 24, 32, and 38 min, while [18]₀ was, correspondingly, 0.028, 0.02, and 0.02 M. Product distributions are summarized in Table I.

Rearrangements of [2-¹⁴C]**18** and [4-¹⁴C]**18** were carried out in the same way, except that initial concentrations were 0.019 M [2-¹⁴C]**18** and 0.026 M [4-¹⁴C]**18**. Each trifluoroacetylated product was sublimed once after three crystallizations and prior to scintillation counting. Only **23** and **24** were isolated in rearrangements of [2-¹⁴C]**18**.

KIE Measurements. Whole-molecule-ion mass spectrometry (WMIMS) was carried out successfully in measuring isotopic abundances only in products **23** and **25** from rearrangements of [¹⁵N, ¹⁵N]**18**. Reproducible results could not be obtained by WMIMS for [¹⁵N, ¹⁵N]**24** and also for any of the derivatives of the ¹³C-labeled products. Failure to obtain reproducible results with samples of **24** derived from the difficulty in controlling a steady concentration of **24** in the mass spectrometer, and this led to problems with the electron multiplier. Failure to obtain reproducible results with any ¹³C-labeled sample derived, as was found later, from the absence of carbon KIE in the rearrangements, resulting in WMIMS measurements that were scattered widely around the error limits of the instrumentation.

WMIMS measurements were made with a Hewlett-Packard quadrupole mass spectrometer, Model 5995, operated in the selected-ion-monitoring mode. Samples were introduced via a direct insertion probe (DIP) and the source pressure was maintained at 3×10^{-7} torr by controlled

heating of the sample. Samples of **23** were heated externally in a specially designed probe and bled into the source via needle valves. A total of 10 000–29 000 scans of relative abundances was made per sample and were analyzed statistically in 25 blocks; that is, for example, when 10 000 scans were made each block of 400 scans was averaged and the 25 results were treated statistically. The method has been described earlier.^{3,4}

Isotope-ratio mass spectrometry was carried out in the laboratory of the Krueger Geochron Co. Samples were converted directly into N₂ and CO₂ by Sofer's method,¹⁹ and the gases were analyzed for ²⁹N₂/²⁸N₂ and ⁴⁵CO₂/⁴⁴CO₂ ratios in a triple-collector instrument after cryogenic separation. The method and treatment of the "del" data have been described earlier.⁵

KIE were calculated with eq 7, in which *F* is the extent of low conversion and *R_p* and *R₀* the isotopic ratios at low and 100% conversion, respectively.²⁰

$$k_L/k_H = \ln(1 - F) / \ln(1 - R_p F / R_0) \quad (7)$$

Scintillation counting was carried out with a Beckman Model LS7000 liquid scintillation counter. Four separate 5-mg samples of each derivative, weighed precisely on a Cahn balance to ±0.001 mg, were counted 7–11 times each. The average of counts per 1.000 mg was used in KIE calculations.

HPLC analysis: The mixture of the trifluoroacetyl derivatives of the products of rearrangement of unenriched **18** was dissolved in acetonitrile. Acetonitrile was used as an internal standard. The flow solvent was 38% aqueous acetonitrile. Quantitative assays were made with a Varian integrating computer, Model CDS111, using response factors established with authentic samples. In the assay of **23** a calibration curve was also used as a check on response-factor data. Results are given in run 13, Table I.

Acknowledgment. This work was supported by the Robert A. Welch Foundation, Grant D-028, and the National Science Foundation, Grant CHE 8314947.

(19) Sofer, Z. *Anal. Chem.* **1980**, *52*, 1389.

(20) Melander, L.; Saunders, W. H., Jr. "Reaction Rates of Isotopic Molecules"; Wiley-Interscience: New York, 1980; p 100.

Photochemical Trans ⇌ Cis Isomerization of 1,2-Bis(heteroaryl)ethylenes: 1,2-Bis(pyrazinyl)ethylene

Pill-Hoon Bong,[†] Hyeong Jin Kim,[†] Kyu Ho Chae,^{††} Sang Chul Shim,^{*†} Nobuaki Nakashima,[‡] and Keitaro Yoshihara[‡]

Contribution from the Department of Chemistry, Korea Advanced Institute of Science and Technology, Cheongyangni, Seoul 131, Korea, and the Institute for Molecular Science, Myodaiji, Okazaki 444, Japan. Received December 13, 1984

Abstract: The direct and sensitized trans ⇌ cis photoisomerization of 1,2-bis(pyrazinyl)ethylene is investigated in various conditions. Quantum yields of the direct trans → cis photoisomerization increase with increasing solvent polarity because of the proximity of the lowest ¹(n,π*) and ¹(π,π*) states. Azulene quenches the direct and sensitized photoisomerization, giving the same Stern–Volmer constant indicating that the triplet state is the reactive state in both cases. The directly measured triplet lifetime of *trans*-1,2-bis(pyrazinyl)ethylene by laser spectroscopy is the same as the lifetime calculated from the azulene quenching studies. Laser spectroscopy also indicates efficient intersystem crossing following direct irradiation. From these results, it is concluded that the direct photoisomerization of 1,2-bis(pyrazinyl)ethylene proceeds through the triplet manifold in contrast to stilbene which undergoes direct trans ⇌ cis photoisomerization through the singlet manifold.

The photochemical behavior of stilbene has been studied extensively, and the photoreaction mechanism is well-understood.^{1–3} Experimental observations have established that the unsubstituted stilbene isomerizes in the singlet manifold.^{1,4} The photochemical

reactions and spectroscopy of nitrogen heterocyclic compounds have also been the subject of considerable investigation and

(1) Salties, J.; D'Agostino, J.; Megarity, E. D.; Metts, L.; Neuberger, K. R.; Wrighton, M.; Zafriou, O. C. *Org. Photochem.* **1973**, *3*, 1 and references therein.

(2) (a) Orlandi, G.; Siebrand, W. *Chem. Phys. Lett.* **1975**, *30*, 352. (b) Orlandi, G.; Palmieri, P.; Poggi, G. *J. Am. Chem. Soc.* **1979**, *101*, 3492. (c) Orlandi, G.; Marconi, G. *Nuovo Cimento* **1981**, *63B*, 332.

[†] Korea Advanced Institute of Science and Technology.

^{††} Department of Polymer Engineering, College of Engineering, Chonnam National University, Kwang Ju 505, Korea.

[‡] Institute for Molecular Science.