Nitrogen Isotope Effects in the Hydrolysis of Benzenediazonium Salts[1]

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Abstract: The α-nitrogen kinetic isotope effect, k_{14}/k_{15}, in dediazoniation of 0.1 M benzenediazonium (I) fluoborate in 1% H_2SO_4 solution at 25° is 1.0384 ± 0.0010, as deduced from the β-nitrogen isotope effect of 1.0106 ± 0.0003 for I-β-^{15}N BF_4^- and the overall nitrogen isotope effect of 1.0245 ± 0.0005 for normal I. Use of an independent method of analysis for the nitrogens in benzenediazonium ion confirms the conclusion of Lewis, Insole, and Holliday that its rearrangement is a minor reaction (1.6% relative to dediazoniation) under these conditions. These isotope effects strongly indicate rate-determining formation of phenyl cation.

As part of our mechanistic study of reactions of benzenediazonium salts in solution,[2-4] we undertook to measure separately the α- and β-nitrogen kinetic isotope effects in the solvolysis of benzenediazonium ion (I) to give phenol in aqueous 1% H_2SO_4 solution at 25°.

Several previous studies of nitrogen isotope effects have been published. Lewis and Insole reported a k_{14}/k_{15} of 1.019 ± 0.004 from comparison of separate dediazoniation rates of p-toluenediazonium and p-toluenediazonium-α-^{15}N fluoborates in 0.02 M HCl at 49°.[5] Brown and Drury[6] used a competition experiment by measuring $^{28}N_2/^{29}N_2$ both before 5% reaction and after complete decomposition, using natural abundance ^{15}N in I and isotope ratio mass spectrometry. They found 1.022 ± 0.002 for the initial ratio of these ratios. The value is relatively insensitive to substituents (H, o-CH_3, m-CH_3, p-CH_3, m-Cl) and temperature (7-68°). By assuming the simplest two-atom (^{12}C-^{15}N) model, *i.e.*, *no* isotope effect for the β-N, they inferred that the α-N isotope effect is about 1.045. Our latest measurements (by K.G.H.) of the initial ratio of $^{28}N_2/^{29}N_2$ ratios average 1.0245 ± 0.0005 for I in 1% H_2SO_4 (and 1.0232 in 80% H_2SO_4) at 25°, in fair agreement with the values observed by Brown and Drury.[6,7] However, we were unwilling to assume that the isotope effect of the β-N is zero. Because the N≡N bond is so strong, it seemed just as reasonable to treat the N≡N leaving group as a rigid unit of mass 28 or 29,[12] *i.e.*, to assume the *same* isotope effect for α- and β-N, which yields an isotope effect of "2.2-2.4%" (1.022-1.024) for each, rather than "4.5-4.9%" for the α nitrogen only. To find where the truth lies between these two extremes, we undertook also the measurement of N isotope effects on specifically labeled I as well as on normal I, in order to obtain experimentally the separate α-N and β-N isotope effects, instead of only the average N isotope effect obtained previously.

Although the α- and β-N were shown previously by ^{15}N labeling to be substantially nonequivalent,[13] Lewis and Insole did observe 2% exchange of α- and β-N in the remaining I after 80% decomposition at 35 or 50°.[5] In order to account for this exchange, a mechanism was proposed[5] involving formation of a diazonium intermediate in which the α carbon is sp^3 hybridized and a spirodiazirine intermediate. However, the large average N isotope effect in dediazoniation seems inconsistent with rate-determining formation of either of these proposed intermediates because insufficient C-N bond weakening would be involved. There is no compelling evidence that this minor rearrangement involves any intermediate in common with the dediazoniation reaction;[14] and it seems possible that this rearrangement may be simply a 1,2-phenide shift to the slightly electron-deficient β-N, involving no intermediate (free-energy minimum) at all between I and rearranged I. The percentage of this rearrangement is doubled by a p-methyl substituent and increased even more by p-methoxy but less by p-chloro,[14] as expected for a 1,2-aride shift but contrary to expectation for recapture by any intermediate of a detached but not yet departed N_2 leaving group.

Since any rearrangement during dediazoniation might affect our determination of the separate α- and β-N isotope effects, we first reinvestigated this minor rearrangement, using a method different from that of previous investigators. Our method involved coupling remaining I-β-^{15}N with 2-naphthol-3,6-disulfonate ion, reduction by $Na_2S_2O_4$ to aniline, separation of the aniline, Kjeldahl reduction to ammonia, oxidation by NaOBr to N_2, and mass spectrometric assay of ^{15}N in this N_2, all steps being essentially quantitative. Our results (Table I) confirm those of Lewis, Insole, and Holliday. The extent of this rearrangement is 1.6% relative to dediazoniation and independent of the extent of reaction or of the concentration of I.[15]

The β-N isotope effect in the dediazoniation of 0.1 M I-β-^{15}N BF_4^- in 1% H_2SO_4 at 25° was determined by isotopic analyses of both the N_2 formed and the α-N of recovered I by the degradation above. Its average value is 1.0106 ± 0.0003 (Table II).

A α-N isotope effect was determined as 1.0384 ± 0.0010 from the β effect above and the average effect determined as 1.0245 ± 0.0005 using normal I under the same conditions (Table III).

This very large α-N isotope effect (1.038) indicates that the C-N bond has greatly reduced vibrational energy at the transition state I*, corresponding to almost complete formation of phenyl cation. The much smaller β-N isotope effect (1.011) indicates that the N≡N leaving group cannot be considered as a rigid unit of 28 or 29 amu, because that would predict *equal* isotope effects for α and β nitrogens. The much smaller value for the β-N suggests that the reaction coordinate motion may increase the N-N bond order above that in the reactant I, the bond order of which is already almost as high as in the product N_2 (infrared 2298 cm^{-1} in I *vs.* 2331 cm^{-1} in N_2).[16]

We conclude that the transition state has an almost completely broken C-N bond and lower force constants for the ortho C-H bonds (from aromatic hydrogen isotope effects),[3] and fairly closely resembles the phenyl cation that is the immediate product of the rate-determining step. The phenyl cation intermediate is formed in its lowest electronic singlet state and reacts rapidly in that electronic state to give the observed products.[2]

Experimental Section

I-β-^{15}N BF_4^- was prepared as was I BF_4^-,[3] except from a mix-

Table I. Isotopic Exchange of 0.1 *M* I-β-^{15}N BF_4^- in 1% H_2SO_4 at 25°

% reaction	$10^6[29]/([29]+[28])_\alpha$	$[^{15}N]_\alpha$, % enriched	$[^{15}N]_\alpha$,[a] % normal	% exchange[b]	k_{rearr}/k_{hyd}
0	7,482	0.3755	0.3755		
0[c]	7,527	0.3776		0.008	
16.9	9,218	0.4530	0.3785	0.291	0.0159
32.0	10,698	0.5376	0.3825	0.604	0.0159
54.6	14,021	0.7060	0.3874	1.231	0.0158
79.7	20,969	1.0594	0.3993	2.513	0.0162
79.7[d]	20,894	1.0556	0.3993	2.499	0.0160
100[e]	261,461	25.879[f]			

[a] Isotopic composition of α-N from normal compound multiplied by 1.0051. [b] Corrected for α-isotope effect on exchanged N. [c] Coupled with phenol instead of R salt. [d] 0.025 *M* solution. [e] Total N_2; average of two values. [f] Isotopic composition of β-N.

Table II. β-Nitrogen Isotope Effect on Dediazoniation of I BF_4^- in 1% H_2SO_4 at 25°

Series	Sample	*N*	$10^6[29]/([29]+[28])^a$	$[^{15}N]$, %	$(k_{14}/k_{15})_\beta{}^a$
I	100%	2	113258 ± 22	11.0285	
	10%	1	112210	10.9341	1.0100
	α	1	7467	0.3748[b]	
II	100%	1	63267	5.9810	
	5%	1	62404	5.9210	1.0110
IIIa[c]	100%	4	83751 ± 89	8.0455	
	10%	3	82851 ± 39	7.9672	1.0110 ± 0.0013
IIIb[c]	100%	3	83821 ± 77	8.0525	
	5%	2	82938 ± 34	7.9761	1.0106 ± 0.0012
IIIc[d]	100%	4	83941 ± 14	8.0645	
	10%	3	83064 ± 30	7.9884	1.0107 ± 0.0003
	5%	2	83050 ± 34	7.9874	1.0106 ± 0.0005
	α	2	7831 ± 6	0.3931[b]	
				Av:	1.0106 ± 0.0003

[a] Error limits are standard deviations. [b] Isotopic composition of α-N. [c] Not corrected for drift of background. [d] Corrected for drift of background; see Experimental Section.

Table III. Average Nitrogen Isotope Effect on Dediazoniation of I BF_4^- in 1% H_2SO_4 at 25°

Sample	*N*	$10^6[29]/[28]^a$	$[^{15}N]_\alpha$, %[b]	$(k_{14}/k_{15})_{av}$	$(k_{14}/k_{15})_\alpha$
100%	1	7428	0.3707		
4%	1	7253	0.3572	1.0246	1.0386
α	1	7443	0.3707		
100%	6	7400 ± 3	0.3672		
α	5	7371 ± 2	0.3672		
β	1	7425	0.3699[c]		
10%	4	7231 ± 2	0.3542	1.0246 ± 0.0005	1.0386 ± 0.0010
5%	4	7229 ± 4	0.3541	1.0243 ± 0.0006	1.0380 ± 0.0013
				Av: 1.0245 ± 0.0005	1.0384 ± 0.0010

[a] Error limits are standard deviations of the average for several samples. [b] Isotopic composition of α-N calculated using the β-N isotope effect. [c] Isotopic composition of β-N.

ture of enriched $Na^{15}NO_2$ (Volk Radiochemical Co. or Isomet Corp.) and normal $NaNO_2$. The last few per cent of diazotization was performed with normal $NaNO_2$. The salt was washed with cold, dilute HBF_4 and stored at 0° or on Dry Ice.

Degradation of I BF_4^-. The α-N of I was isolated as follows. To a cold solution containing 0.20–0.25 mmol of I was added 10 ml of 0.1 *M* 2-naphthol-3,6-disulfonic acid disodium salt (R salt). The solution was slowly neutralized with NaOH and allowed to warm to 25°. The resulting azo compound was reduced with 0.52 g of $Na_2S_2O_4$. The solution was made 2 *M* in NaOH and half was distilled into HCl acid. The distillate was neutralized and extracted thrice with an equal volume of Et_2O; the Et_2O layers were each extracted twice with 1 *M* HCl. The acidic extracts were subjected to Kjeldahl digestion with 5 ml of H_2SO_4, 2 g of $KHSO_4$, and a Hengar selenized boiling granule. The NH_3 produced was isolated by neutralization of the digests with NaOH and distilled into dilute HCl. For analysis, the NH_3 was oxidized to N_2 as described below.

In several cases, the β-N was isolated by subjecting the solution remaining after distillation of aniline to Kjeldahl digestion. The isotopic ratio of the β-N was in reasonable agreement with the value calculated from the isotopic ratios of the α-N and of the N_2 obtained from complete hydrolysis of I. Control experiments demonstrated that the C_6H_5OH produced in the reaction causes no difficulties since when C_6H_5OH is substituted for R salt in the above procedure, the N_2 is not appreciably contaminated by the β-N. There was 0.36% contamination by normal N compounds in the reagents. The very slight enrichment of the α-N from the labeled compound with respect to that from I prepared with normal $NaNO_2$ is accountable in terms of 0.5–1% hydrolysis during preparation, isolation, and dissolution of the I BF_4^- and indicates that the degradation is effective.

Mass Spectrometric Measurements. NH_4^+ ion isolated from α- and β-N of I was converted to N_2 by oxidation with NaOBr.[17] In a cell fitted with a hollow-bore stopcock was placed 0.2–0.4 mmol of NH_4Cl solution; in a side arm was placed 5 ml of *ca.* 0.5 *M* NaOBr in 10% NaOH. The solutions were degassed by evacuation and vigorous shaking on the high-vacuum rack below 10^{-4} mm (after the trap); *ca.* 1–2 ml of solution was distilled in the degassing procedure. The cell was closed, the solutions were mixed, and the cell was chilled in a Dry Ice-EtOH bath. The N_2 formed was pumped *via* a Toepler pump through a trap cooled in liquid N_2 into a previously evacuated storage vessel. The isotopic composition of the N_2 obtained by oxidation of NH_3 or from decomposition of I was determined using a CEC Model 21-201 dual-collector isotope ratio mass spectrometer. In general, measurements reported are averages of five determinations of the isotopic ratio. For N_2 of normal isotopic composition, the standard deviation of a single reading was about 0.000002. Isotopic ratios of *m/e* 29 *vs.* *m/e* 28 were corrected for minor air contamination and for the relative sensitivities of the two amplifiers. Isotopic compositions were calculated assuming that the distribution of ^{15}N between *m/e* 29 and *m/e* 30 is statistical.

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Isotopic Exchange. A 0.1 *M* solution of I-β-^{15}N BF_4^- (26% ^{15}N) in 1% H_2SO_4 at 0° was prepared. Samples of the solution were partially hydrolyzed in a 25.0° bath for effective times between 68 min (16.9% reaction) and 584 min (79.7%). The percentage of reaction was calculated using a rate constant of 4.55×10^{-4} sec^{-1}. The samples were chilled, and the unreacted I was degraded as above; I not subjected to hydrolysis was also degraded. Two samples of the solution were degassed as below and decomposed completely at 50° to determine the initial isotopic composition. The isotopic compositions of the α-N from the samples were measured as above; a correction was applied for contamination from the reagents. Normal I BF_4^- was subjected to the same series of reactions as the enriched compound. The initial isotopic ratio of the α-N of the enriched compound was 0.51% above that of the normal compound. To correct for the appreciable α-N isotope effect, the isotopic compositions for the normal compound were multiplied by 1.0051 and subtracted from the corresponding isotopic composition of the enriched series. A small additional correction was applied for the α-N isotope effect on the rearranged N.

β-Nitrogen Isotope Effect. Samples of I-β-^{15}N BF_4^- were placed in the side arm of a 100-ml cell fitted with a hollow-bore stopcock and joint. Dilute H_2SO_4 was placed in the cell and was degassed on the high-vacuum rack below 10^{-4} mm. The cell was closed and placed in the 25.0° bath. After at least 10 min, the salt was dissolved, and the solution was maintained in the bath for 18.8 (5% reaction) or 38.5 min (10% reaction). The cell was shaken vigorously and frozen in a Dry Ice-EtOH bath. The N_2 was pumped *via* a Toepler pump through a trap chilled in liquid N_2 into a storage vessel in order to remove H_2O and C_6H_5OH vapors. Total decomposition points, prepared and degassed as above, were heated in a 50° bath for at least 2 hr (16 half-lives), then the N_2 was transferred to the storage vessels. The isotopic composition of the α-N was determined by degradation of the I BF_4^-. The *m/e* 29 to *m/e* 28 ratio of the N_2 was measured. Corrections for the α-N isotope effect were made using the data for normal I; a small correction for the α-N isotope effect upon the rearranged N was also made. For measurements of isotopic ratios appreciably different from natural abundance, it is important to correct for the N_2 background on the mass spectrum. Although the background at *m/e* 28 with the inlet system evacuated is only 0.1–0.2% of the 28 peak at typical sample pressures, the background is increased by a factor of 5 when there is a sample in the inlet system. In order to reduce the effect of the background in the first experiments, for which the background was low, the mass spectrometer was equilibrated for a period of several hours with enriched N_2 of the same isotopic composition as the samples. In the last series, for which the background was high, the mass spectrometer was equilibrated for 45 min with an infinity point sample, then series of infinity point and one or two partial reaction samples were measured alternately. An upward drift of 0.5% in the 29/28 ratio of the infinity point samples was observed during the 4-hr period in which measurements were made. On the basis of a graph of isotopic ratio *vs.* time for the infinity point samples, a correction of 0.000106/hr was applied to the *m/e* 29 to *m/e* 28 ratios to compensate for drift of the background. This correction gives isotope effects in close agreement with values calculated using the average of the readings, but the calculated precision is more realistic.

Average Nitrogen Isotope Effect. Samples of I BF_4^- of normal isotopic composition were decomposed in 1% H_2SO_4 as in the determination of the β-N isotope effect. The isotopic ratios of the starting aniline and the α-N of I were found to be identical. The isotopic ratio of the β-N was in agreement with the value calculated from the isotopic ratios of the α-N and of the N_2 obtained from complete decomposition of I. The α-N isotope effect was calculated using a correction for the β-N isotope effect based on the composition of the α-N and on the β-N isotope effect determined above. At least one extra digit beyond significance was retained throughout the calculations.

References and Notes

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(7) These experimentally observed average N kinetic isotope effects are comparable to the observed isotope effects for decomposition of 1′,1′,1′-benzeneazotriphenylmethane in toluene, $k_{14}/k_{15} = 1.02017 \pm 0.00016$ at 40.25°, 1.02178 ± 0.00018 at 25°, and 1.02339 ± 0.00020 at 0°,[8] and base-catalyzed cleavage of benzyl nitrate at 30°,

$$C_6H_5CH_2ONO_2 + C_2H_5O^- \longrightarrow C_6H_5CHO + C_2H_5OH + NO_2^-$$

$k_{14}/k_{15} = 1.0196 \pm 0.0007$,[9] reactions that involve extensive C–N bond breakage at the transition state. They are larger than the effect, $k_{14}/k_{15} = 1.009 \pm 0.001$, observed for thermal decomposition at 220° of NH_4NO_3 labeled in the NH_4^+ ion[10] or the 1.0094 ± 0.0004, 1.0117 ± 0.0007, 1.0154 ± 0.0004, and 1.0173 ± 0.0001 values for E2 reaction of $NaOC_2H_5$ in ethanol with $C_6H_5CH_2CH_2(CH_3)_3NBr$ at 60 and 40° and with $C_2H_5(CH_3)_3NI$ at 95 and 60°, respectively.[11] Henderson[8] found that the N isotope effect for 4-NO_2, 3-NO_2, 3-Cl, and unsubstituted 1′,1′,1′-triphenylbenzeneazomethane at 40.25° varied from $k_{14}/k_{15} = 1.01787 \pm 0.00013$ for 4-NO_2 through 1.01810 ± 0.00021 for 3-NO_2 and 1.01903 ± 0.00011 for 3-Cl to 1.02017 ± 0.00016 for the unsubstituted compound, in good correlation with the Hammett σ. Although all of the substituted diazonium ions gave the same isotope effect within experimental error,[6] the experimental error was sufficiently higher for the diazonium salts to mask a substituent effect of the magnitude observed by Henderson.

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