The photo-Wallach rearrangement. Heavy-atom kinetic isotope effects and mechanism

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This paper is dedicated to Professor Arthur N. Bourns

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The photo-rearrangement of mixtures of azoxybenzene **4** and, successively, [^{15}N,^{15}N′]**4**, [^{18}O]**4**, and [2-^{14}C]**4** were carried out. Kinetic isotope effects (KIE) were calculated from measurements of isotopic ratios in both recovered **4** and the product, 2-hydroxyazobenzene (**6**). Analogous rearrangement of mixtures of 2,2′-azoxynaphthalene (**8**) with [^{15}N,^{15}N′]**8** and [1,1′-^{13}C$_2$]**8** were carried out and KIE were calculated from isotope ratios in the product. The results (particularly the lack of nitrogen KIE) collectively indicate that if an oxadiazole-like intermediate is involved in these rearrangements, an activation barrier exists in its formation rather than its decomposition.

HENRY J. SHINE, WITOLD SUBOTKOWSKI et EWA GRUSZECKA. Can. J. Chem. **64**, 1108 (1986).

On a réalisé des photo-transpositions sur des mélanges d'azoxybenzène (**4**) et successivement de composés **4** marqués au [^{15}N,^{15}N′], au [^{18}O] ou au [2-^{14}C]. On a calculé les effets isotopiques cinétiques (EIC) à partir de mesures des rapports isotopiques, tant dans le produit **4** qui était récupéré que dans le produit de la réaction, l'hydroxy-2 azobenzène (**6**). On a aussi réalisé des transpositions analogues sur des mélanges d'azoxynaphtalène-2,2′ (**8**) et de dérivés marqués au [^{15}N,^{15}N′] ou au [^{13}C$_2$-1,1′] et l'on a calculé les EIC en se basant sur les rapports isotopiques dans le produit. L'ensemble des résultats (et particulièrement le fait qu'il n'y a pas d'EIC de l'azote) indique que, si un intermédiaire ressemblant à un oxadiazole est impliqué dans ces transpositions, la barrière à l'activation existe plutôt dans sa formation que dans sa déomposition.

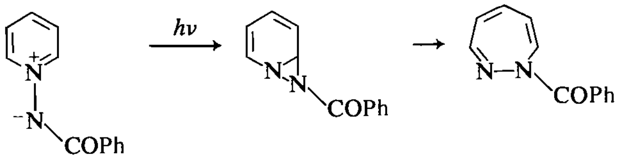
[Traduit par la revue]

Introduction

In recent years sporadic attempts have been made to detect intermediates in photochemical reactions in solution by measuring heavy-atom (other than hydrogen isotopes) kinetic isotope effects (KIE). The basis for this approach was expressed by Schutte and Havinga in 1967, who used the photo-Fries rearrangement to try to answer "the question that has been raised whether photochemical reactions after electron excitation pass through a transition state of appreciable energy of activation" (1). Schutte and Havinga used 4-methoxyphenyl-[^{14}C]acetate for measuring the carbon KIE in the photorearrangement of the ester into 2-acetyl-4-methoxyphenol, and found that within experimental error the rearrangement did not exhibit an isotope effect. They concluded, therefore, that rearrangement began in the electronically excited state (singlet) and proceeded very rapidly through vibrationally excited states in a process that required no thermal energy of activation.

The quest was later pursued by Kwart and co-workers (2), who sought evidence for a vibrationally excited ground state intermediate in the photochemical rearrangement of the ylide **1** into the diazepine **3**. In this case an inverse carbon KIE was found with the use of specifically labeled [^{13}C]**1**, and the result was attributed to the formation of the intermediate **2** in the pathway from excited **1** to product (**3**) (reaction [1]). To our knowledge this is the first time in which a heavy-atom KIE has been found in a photochemical rearrangement.

[1]



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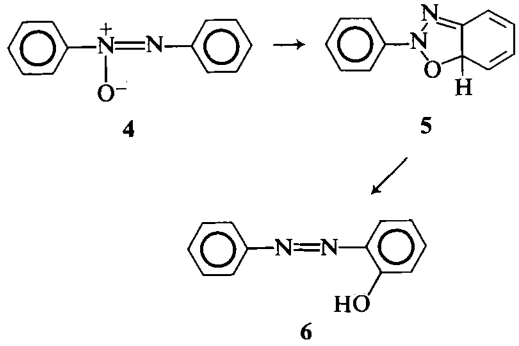
We have been attracted to the idea of using heavy-atom KIE measurements in seeking evidence for activation barriers in photochemical rearrangements in solution. Such a barrier can exist in the electronically excited state (3). If we accept Ullman's view (4) and Kwart's conclusion, an activation barrier may also exist in a vibrationally excited ground state, reached by internal conversion from an electronically excited state. Internal conversion of this kind is known from photophysics studies to occur in the gas phase (3), but there is considerable doubt, because of rapid collisional deactivation, that a vibrationally excited ground state intermediate could exist long enough for detection in reactions in solution (5, 6).

Nevertheless, we have thought it worthwhile to continue the search for heavy-atom KIE in photochemical reactions, and have chosen the photo-Wallach rearrangement for study.

The photo-Wallach rearrangement is the intramolecular converison of an azoxyarene into a hydroxyazoarene (7). It is a singlet-state reaction (8), and does not involve radical pairs. Hence, in the use of ^{13}C labeling, it is not subject to the magnetic isotope effects associated with radical-pair reactions (9).

The photo-Wallach rearrangement is exemplified by the conversion of azoxybenzene (**4**) into 2-hydroxyazobenzene (**6**). The hydroxy group is known, from studies of substituent effects and nitrogen and carbon labeling, to migrate to the distant ring

[2]



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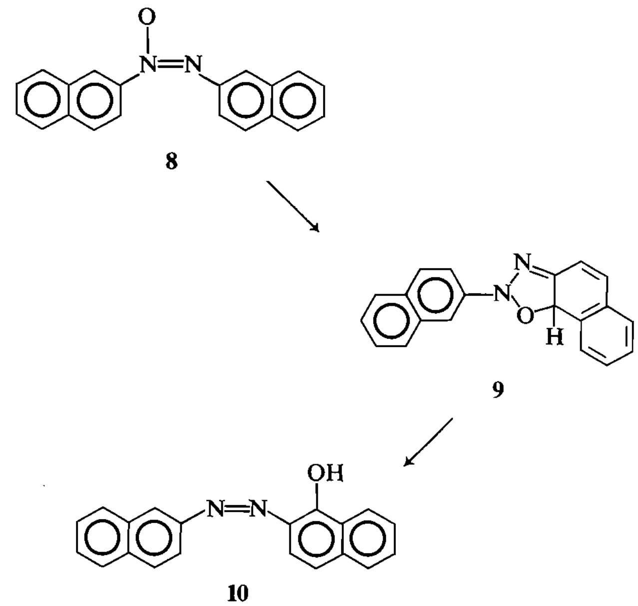
(7). It is now generally accepted that an intermediate is formed in the rearrangement, represented as **5** (eq. [2]) and attributed usually, but erroneously, to Badger and Buttery, in their finding and studies of the rearrangement's intramolecularity (10).[3]

Circumstantial evidence for the probable validity of **5** as an intermediate has been presented by Gegiou (13). That is, irradiation of 2,2′-azoxytoluene in solution at −70°C led to an absorption spectrum having a new band at approximately 436 nm. This was attributed to the dimethyl analog of **5** since it was thought to be the region in which an intermediate, similar to **5**, would absorb. This species was converted into the rearrangement product either by irradiation at 436 nm at −70°C or by warming the solution to room temperature without further irradiation. Although the corresponding band (i.e., for **5**) in the irradiation of **4** could not be detected, it was possible to irradiate **4** at temperatures in the range of −70 to −60°C and measure the rate of formation of **6** after irradiation was stopped. In this way an activation barrier for the formation of **6** of 12 kcal/mol was obtained and this was assigned to the decomposition of **5**. The several pieces of data when fitted together, then, showed that a ground-state intermediate is formed, consistent with the expectations for **5**, and that there is an activation barrier for its conversion into **6**. Noteworthy, also, is an additional report by the same authors that the formation of the ground-state intermediate appeared also to be temperature dependent; definitive supporting data for this report were not given, however (13).

The reports in the literature concerning rearrangement of **4** which we have briefly summarized suggested to us that we might be able to find heavy-atom KIE consistent with the formation and decay of an intermediate such as **5**. Our plan was to label **4** at its nitrogen, oxygen, and 2-carbon atoms and to measure the effects of labeling on the rate of rearrangement, seeking evidence thereby for bond-forming or bond-breaking steps in the conversion of **4** into **6**. Furthermore, because labeled precursors were available from earlier but unrelated work, we included the rearrangement of 2,2′-azoxynaphthalene (**8**) into 1-hydroxy-2,2′-azonaphthalene (**10**) in our plans, seeking evidence for the participation of the corresponding intermediate (**9**). The rearrangement of **8** into **10** had already been reported by Badger and Buttery (10).

[4]



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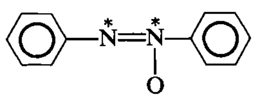
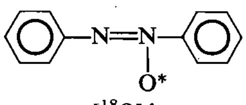
Results and discussion

Preparation of labeled substrates

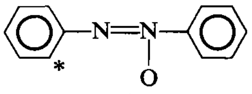
The labeled isomers of **4** which were prepared are designated as [^{15}N,^{15}N′]**4**, [^{18}O]**4**, and [2-^{14}C]**4**. Each of these was prepared by the reduction of the appropriately labeled nitrobenzene by heating with sodium hydroxide in methanol (14).



[^{15}N,^{15}N′]**4**



[^{18}O]**4**



[2-^{14}C]**4**

Labeled isomers of **4** have been prepared earlier in tracing the orientation and intramolecularity of the photorearrangement. The syntheses have been summarized by Dolenko and Buncel (15). These syntheses include singly labeled [^{15}N]**4** and [1-^{14}C]**4**. In our case we chose to use doubly labeled [^{15}N,^{15}N′]**4** and also [^{14}C]**4** which was a mixture of [2-^{14}C]**4** and [2′-^{14}C]**4**. The choice was made for convenience in preparation and also to avoid the raising of any question of ambiguity in our measurements from the possibility of isomerization of the azoxy group via an oxadiaziridine (16), prior to the photo-Wallach rearrangement. Such a possibility would appear to be ruled out by studies of orientation in the photo-Wallach rearrangement (10, 17), but isomerization of 4′- into 4-methoxyazoxybenzene has been reported, implicating the participation of an oxadiaziridine intermediate (17, 18), while the possible formation of diphenyloxadiaziridine as an initial side reaction in the photorearrangement of **4** has been proposed (19). Furthermore, Oae and co-workers found that a small amount of scrambling did, in fact, occur in the photo-rearrangement of [1-^{14}C]**4**. In that case the cause of the scrambling was attributed, however, to direct migrations to each *o*-position of **4** rather than to the initial involvement of a symmetrical oxadiaziridine ring (20).

[^{15}N,^{15}N′]**4** has been prepared earlier in our laboratory by the oxidation of [^{15}N,^{15}N′]azobenzene (21). In the present work it was more convenient to reduce [^{15}N]nitrobenzene containing 99 atom% of ^{15}N. In this way [^{15}N,^{15}N′]**4** was obtained containing

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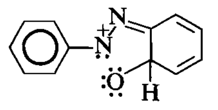
[3] It is curious that Badger and Buttery did not, in fact, claim that an intermediate with structure **5** was formed. Instead they concluded, from their studies with unsymmetrical azoxyarenes, that "an intramolecular mechanism is probably involved" and they represented this clearly as what we would now call a concerted process, as shown in reaction [3]

[3] **4** ⟶



⟶ **6**

7

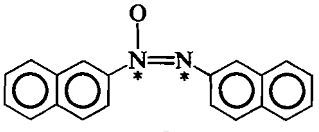
Structure **7** is described by Badger and Buttery as "the quinonoid transition state," but whether they really meant transition state in its modern sense rather than (as is more likely) an intermediate is not now known. Lewis and Reiss (11), as has been reported by Buncel (12), proposed in 1966 that **5** is the intermediate in the rearrangement. Spence, Taylor, and Buchardt (7) although reproducing the scheme of Lewis and Reiss, represent **5** as an intermediate in what they describe as a *reformation* of the mechanism of Badger and Buttery. It may be, in this way, that the mechanism first set out by Lewis and Reiss is now attributed to Badger and Buttery, in whose work, however, no suggestion of an oxadiazole-like intermediate is made at all.

approximately 98% of doubly labeled **4**. This was diluted with ordinary **4** to give 10 mol% of [^{15}N,^{15}N′]**4** for rearrangement.

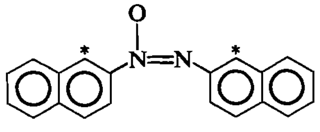
In the case of ^{14}C-labeling we began with [2-^{14}C]nitrobenzene which had been prepared earlier from 2-nitro-[1-^{14}C]aniline (22). This necessarily gave us a mixture of [2-^{14}C]**4** and [2′-^{14}C]**4**, which for convenience we designate here as solely [2-^{14}C]**4**. The final product had a radioactivity of approximately 16 mCi/mol.

In preparing [^{18}O]**4**, we found that the condensation of [^{18}O]phenylhydroxylamine with nitrosobenzene (23, 24), was inconvenient because of difficulties in preparing the labeled phenylhydroxylamine in reasonable yield and the loss of almost half of the initial ^{18}O content by this method. The method of choice, therefore, was by the reduction of [^{18}O]nitrobenzene (23) prepared by the nitration of benzene with [^{18}O]H_2O/NO_2BF_4 (25). After starting with [^{18}O]H_2O containing approximately 20 atom% of ^{18}O the **4** obtained had approximately 7 mol% of [^{18}O]**4**.

The compounds [^{15}N,^{15}N′]**8** and [1,1′-$^{13}C_2$]**8** were prepared from the corresponding 2,2′-azonaphthalene (26), by oxidation with *m*-chloroperbenzoic acid. Each labeled starting material contained approximately 10 mol% of the doubly labeled isomer.



[^{15}N,^{15}N′]**8**



[1,1′-$^{13}C_2$]**8**

Rearrangements and KIE measurements

Rearrangements were carried out by broad-band irradiation with 350-nm lamps in a Rayonet reactor. Solutions of **4** in 95% ethanol and, because of solubility problems, of **8** in dimethoxyethane (DME), contained in a cyclindrical quartz flask were irradiated for pre-determined times so as to bring about either partial (5–20%) or complete conversion into product. Times for these conversions were obtained by monitoring the rearrangement of unenriched azoxy compound, at 410 nm for **4** and 505 nm for **8**. However, the extents of conversion used in calculating KIE were measured also by separation and isolation of unrearranged azoxy compound and product. The two measures of conversion (uv and isolation) were in good agreement in the work with **4**. We found that the planned complete conversion of **4** was never quite complete. Small amounts of **4** remained and were isolated. The data on conversions are given in Tables 1 and 2. The data in Table 1 concern calculations of KIE from isotopic abundances in isolated product (**6**). Table 2 concerns calculations of KIE from isotopic abundances in the starting material (substrate). In that table, therefore, only data for high conversions are given, which, in the calculations, are related to the isotopic abundances in the starting substrate.

The separations of unconverted substrate from product by column chromatography in the rearrangements of **8** were not as sharp as those in the rearrangements of **4**. Eluted fractions containing small amounts of both **8** and **10** were always obtained. Therefore, the amount of product isolated at low conversions was always 1–2% less than anticipated from absorption spectroscopy. Because of this, the extent of low conversion (i.e., F) used in calculating KIE is the spectroscopic conversion. We have used the spectroscopic measure also for 100% conversion of **8**. In this case, also, the amount of product after chromatography and crystallization was only about 75–80% of the expected yield. Lengthy irradiation of **10** itself caused the formation of a small amount of another, unidentified substance. Therefore, the low, isolated yield of **10** is attributable, not only to losses on separation and crystallization but also to a small amount of photochemical loss.

We measured isotopic abundances in the product (**6**) for rearrangements of [^{18}O]**4** and [^{15}N,^{15}N′]**4**, and in the substrate (**4**) for rearrangements of [2-^{14}C]**4** and [^{15}N,^{15}N′]**4**. In the rearrangements of **8** isotopic abundances only in the product **10** were measured.

Calculations of the oxygen and nitrogen KIE from isotopic abundances in the product (**6**) were made in two ways, A and B. It is important in calculating KIE from isotope ratios in products to know that complete conversion is indeed complete. If the isotope ratio is measured in a product at less than complete conversion but with the impression that conversion was complete ($F = 1.0$) the KIE calculated (eq. [5]) (27) will be smaller than the true KIE. This is to say, KIE both greater than or smaller than 1.000 will appear deceptively to be closer to 1.000. In that case eq. [6] is used for calculating KIE. In these equations R_0, R_p, and R'_p are the ratios of normalized abundances $(M + 2)/M$ in the product at molar conversions 1.0, F, and F', while k_2/k_1 is the KIE (k_H/k_L) for the reaction. The method of calculating KIE from low and almost 100% conversions with the use of eq. [6] and an iteration procedure has been described earlier (27). The columns A and B in Table 1 list KIE (k_1/k_2) calculated (A) on the assumption that complete conversion reached 100% and (B) with the use of real conversions based on isolations of unused **4**. The results of the two methods do not differ greatly, but are important particularly insofar as the ^{18}O KIE is concerned. The ^{18}O KIE is seen to be, within experimental error, an inverse one. On the other hand, there does not appear to be a nitrogen KIE. These data (Table 1) are averaged and listed in Table 3.

$$[5] \quad R_p/R_0 = [1 - (1 - F)^{k_2/k_1}]/F$$

$$[6] \quad R_p/R'_p = \frac{F'[1 - (1 - F)^{k_2/k_1}]}{F[1 - (1 - F')^{k_2/k_1}]}$$

In Table 2 are listed ^{14}C and ^{15}N KIE (k_1/k_2) obtained with recovered substrate in the rearrangement of **4**. It was necessary for these determinations to hydrogenolyze the substrate to aniline first, and to prepare the trifluoroacetyl derivative for ^{14}C and ^{15}N analyses. In the case of ^{14}C, both **4** and **6** are themselves unsuitable for scintillation counting because, being colored, each causes quenching. Hydrogenolysis of **4** goes quantitatively to aniline, and the colorless trifluoroacetyl derivative, also obtained quantitatively, can be purified by repeated sublimation. In the case of ^{15}N, the substrate itself is unsuitable for whole-molecule mass spectrometry. The abundance of the parent ion is low and the fragmentation pattern is unsuitable for use. Therefore, hydrogenolysis and trifluoroacetylation are again most useful. The mass spectrum of the trifluoroacetyl derivative is highly suitable for whole-molecule mass spectrometry. The results are summarized in Table 2 and averaged in Table 3. They show, again, that there is no nitrogen KIE and that there is a small ^{14}C KIE, averaging 1.0145.

Kinetic isotope effects (k_1/k_2) for the rearrangement of **8** are listed in Table 4. These were calculated on the assumption that 100% conversion was reached, as indicated spectroscopically. In the event that, like the rearrangement of **4**, the final conversion was a few percent short of 100% the results in Table 4 are minima. Our conclusion is that the rearrangement of **8**, like that of **4**, does not exhibit a nitrogen KIE. On the other hand there is a small, positive carbon KIE, averaging 1.07%.

TABLE 1. KIE based on analyses of product in the photorearrangement of azoxybenzene (4) in ethanol

Run	Isotope[a]	Time of irradiation	Conversion (%)		KIE		σ
			Uv[b]	Isol.[c]	A[d]	B[e]	
1	^{18}O	15 m 40 h	10.3	10.0 97.2	0.9915	0.9905	0.0014
2	^{18}O	20 m 20 h	12.0	12.3 93.5	0.9935	0.9919	0.0007
3	^{18}O	30 m 20 h	16.9	17.4 94.5	0.9929	0.9913	0.0016
4	^{18}O	40 m 20 h	20.6	20.2 97.2	0.9954	0.9948	0.0008
5	^{15}N	10 m 30 h	6.5	6.5 96.8	1.0019	1.0021	0.0031
6	^{15}N	10 m 20 h	8.1	8.1 96.0	1.0024	1.0025	0.0046
7	^{15}N	30 m 40 h	16.8	16.6 97.0	1.0010	1.0012	0.0015

[a] ^{15}N means [^{15}N,^{15}N′]4.
[b] Based on change in absorption at 410 nm. Long irradiation (20–40 h) was assumed to have gone to 100% conversion. $[4]_0$ was 1×10^{-3} M in each run.
[c] Based on recovered 4.
[d] Assuming 100% conversion and calculated with eq. [5].
[e] Calculated with eq. [6], using % conversion based on recovered 4.

TABLE 2. KIE based on analyses of substrate in the photorearrangement of azoxybenzene (4) in ethanol

Run	Isotope[a]	Time of irradiation (h)	Conversion (%)		KIE[c]	σ
			Uv[b]	Isol.[c]		
8	^{14}C	12	70	68.4	1.0090	0.0010
9	^{14}C	12	70	69.5	1.0116	0.0034
10	^{14}C	12	70	70.0	1.0229	0.0027
11	^{15}N	10	75.7	74.2	1.0018	0.0014
12	^{15}N	10.3	81.5	81.3	1.0019	0.0030
13	^{15}N	15	86.6	85.8	0.9937	0.0029

[a] ^{15}N means [^{15}N,^{15}N′]4.
[b] Based on change in absorption at 410 nm. $[4]_0$ was 2.0×10^{-3} M for ^{14}C and 1.5×10^{-3} M for ^{15}N runs.
[c] Based on recovered 4.

TABLE 3. Summary of KIE in the photorearrangement of azoxybenzene (4)

Isotope	Basis	KIE[a]
^{18}O	Product	0.9921±0.0016
^{15}N	Product	1.0019±0.0006
^{15}N	Substrate	0.9991±0.0038
^{14}C	Substrate	1.0145±0.0060

[a] Average of data in Tables 1 and 2.

The meaning of the KIE

The absence of a nitrogen KIE in the rearrangements of both **4** and **8** indicates that if there is a step in the photo-Wallach rearrangement having a significant activation barrier, breaking of the N—O bond is not part of that step. The results are, then, not consistent with the barrier-less formation of an intermediate like **5** (and **9**) followed by its conversion over an activation barrier into product. The inverse oxygen KIE in the rearrangement of **4** and the positive, small carbon KIE in the formation of **6** and **10** suggest the surprising property of the rearrangement that it is in the formation of the intermediate that an activation barrier exists. The small size of the carbon KIE in the rearrangements of **4** and **8** is not inconsistent with the change in bonding which occurs at the aromatic position in a bond-forming reaction (27).

Bunce and co-workers (17) found that when an electron-donating group (CH_3) is placed in the ring which receives the migrating atom the quantum yield of rearrangement is greater than that when an electron-attracting group (CF_3) occupies the same position. For this reason it was proposed that the attack of the oxygen atom on the distant ring is an electrophilic rather than, as thought earlier, a nucleophilic reaction. This, in itself, suggests that the bonding of the oxygen atom with the ring is a ground-state reaction. Electrophilic attack was represented by Bunce and co-workers as in eq. [7]. This interesting proposal invites further analysis. Bunce noted that the photorearrangement involves an n,π^* singlet excitation, and proposed that excitation occurs from an n orbital on oxygen to an antibonding N—N orbital. If this is correct the oxygen atom has radical

TABLE 4. KIE[a] in the photo-rearrangement of 2,2′-azoxynaphthalene (**8**) in dimethoxyethane

Run	Isotope[b]	Conversion (%)[c]	KIE[d,g]	σ
14	^{15}N	4.0	0.9935[e]	
			1.0015[f]	0.0010
15	^{15}N	6.7	1.0060[e]	
			0.9999[f]	0.0006
16	^{15}N	6.7	1.0039[e]	0.0034
17	^{13}C	6.0	1.0090[e]	
			1.0071[f]	0.0005
18	^{13}C	6.0	1.0145[e]	
			1.0113[f]	0.0008
19	^{13}C	7.0	1.0115[e]	

[a] Based on analyses of product.

[b] $^{15}N,^{15}N'$ and $1,1'$-$^{13}C_2$ labeling.

[c] Based on the amount of product isolated at low conversions.

[d] Calculated with eq. [5], using the low conversions shown in the table and assuming that 100% conversion (by uv) was indeed 100%.

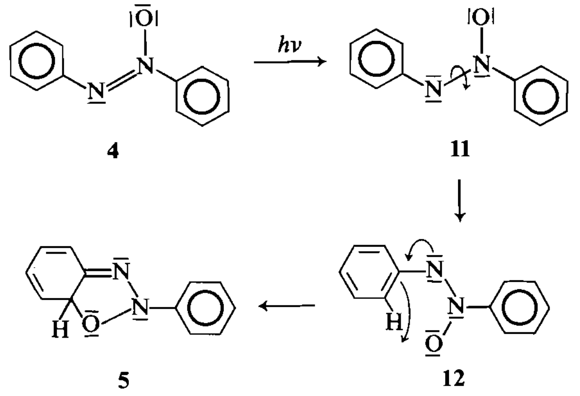
[e] Measured at Texas Tech University.

[f] Measured at Rutgers University.

[g] Average for [$^{15}N,^{15}N'$] **8**, 1.0010; average for [$1,1'$-$^{13}C_2$] **8**, 1.0107.

character rather than positive-charge character in the excited state, and only after electronic reorganization can the intermediate **11**, with its electron-deficient oxygen atom, be formed.[4] Again, this likelihood suggests that the formation of **5** is a ground state rather than an electronically excited state reaction, the intermediate **11** being formed by demotion from the electronically excited state to a ground excited state. Our KIE results are in harmony with this description. An inverse (here, for oxygen) or a small positive (here, for carbon) KIE is consistent with the forming of a new bond in the transition state (29). The result is, by coincidence, similar to that found by Kwart and co-workers in the photo-rearrangement of **1** (reaction [1]) (2).

[7]

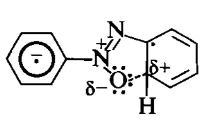


The photo-Wallach rearrangement then, appears to involve the formation, after excitation, of a ground-state intermediate in a step having an activation barrier. Collectively, the known information now indicates that this step is between ground-state intermediates.

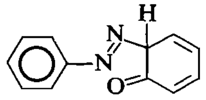
Among Bunce's results on the effect of substituents on quantum yields it is seen that the greatest relative increases in quantum yield occur not when the methyl groups are in the acceptor ring but when the CF_3 groups are in the ring nearer to the N—O bond (17). For example, the quantum yields for rearrangement of 4′-CH_3-**4** and 4′-CF_3-**4** were, respectively, 0.37 and 1.70; the values for 3′,5′-$(CH_3)_2$-**4** and 3′,5′-$(CF_3)_2$-**4** were, respectively, 0.80 and 2.5. These results show that electron-attracting CF_3 groups in the nearby ring enhance rearrangement, and suggest that the *n*,π* excitation may, in fact, be surprisingly from a nonbonding orbital on oxygen to a π* orbital of the nearby ring. Thereafter electron reorganization to an intermediate such as **11** would follow.

If these representations are incorrect, we are left with the alternative possibility that bonding to form an intermediate such as **5** may occur in the electronically excited state between the electrophilic oxygen radical and the electron-rich distant ring. In other words, the closure is a radical reaction, albeit with electrophilic character in the transition state. The transition state, in that case, might have the character of **13**.

We might now ask about the fate of **5**. Our results indicate that the conversion of **5** into **6** does not have an activation barrier large enough to show up in the KIE measurements. We would anticipate that, in spite of changes which occur in bond orders (e.g., a single bond is broken and a double one is formed at nitrogen), we should have found significant positive KIE for nitrogen and oxygen if opening of the heterocyclic ring in **5** was the rate-determining process in the sequence of ground-state reactions. If then, **5** is to proceed on toward the final product (**6**) without isotopic fractionation, the reverting of **5** to **4** must no longer be possible. That is, return of **5** to **4** must be an unfavorable process as compared with going on completely to **6**, and the low quantum yield (13) for forming **6** from **4** is decided in one of the paths toward forming **5**. The way in which formation of **6** from **5** occurs is not known, but some possibilities are open to conjecture. One of them is, simply, ring opening accompanying deprotonation by basic solvents, in the present cases of ethanol or DME (reaction [8]), such as was proposed in the early work of Lewis and Reiss (11).

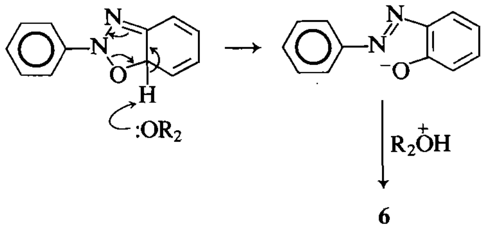


13



14

[8]



Another possibility arises as follows. Bunce has shown that diazonium ions are formed (and trapped by added 2-naphthol) during irradiations of **4** and other azoxyarenes in benzene solution. Diazonium ion formation was suppressed to very low amounts by the use of moderately basic solvents such as ethanol and diethyl ether (30). The origin of the diazonium ion was attributed by Bunce to an intermediate (**14**), obtained from **5** by

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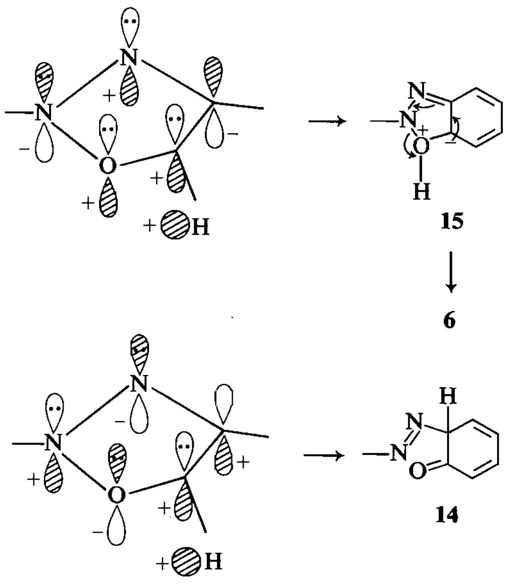
[4] An analogy can be drawn here with the electron distribution in an *n*,π*-excited carbonyl group. This has been represented by Zimmerman (28) as having in one of its two resonance structures a positively charged, electrophilic oxygen atom in which two single electrons remain in separate orbitals. *n*,π*-Excitation of the *N*-oxide group could be viewed similarly, that is as having positive charge character on the oxygen atom in the electronically excited state. But, we take structure **11** to represent a new, ground state, formed in Zimmerman's terminology, by electron demotion after excitation.



SCHEME 1

an intramolecular 1,2-hydrogen-atom shift, and undergoing either scission to give the diazonium ion or prototropy to form **6**. This proposal in itself could also account for the conversion of **5** into **6** in basic solvents. In connection with the intramolecularity of the H-migration, Bunce noted that *m*-cresol, obtained as the side product of irradiation of 2,2′-azoxytoluene in ethanol-*O*-*d*, contained no deuterium. We pose another possibility for intramolecular H-migration which may lead both to **6** and diazonium-ion formation, and this is a [1,5]-sigmatropic migration of hydrogen across the face of the heterocyclic ring, brought about by continuous broad-band irradiation. Suprafacial, solvent-dependent migration of the LUMO of the H atom across the HOMO of the excited eight-electron ring system could bring the H atom either to the *O*-terminus (**15**) or *C*-terminus (**14**), the former leading to **6** and the latter either to **6** by prototropy or diazonium ion by scission (Scheme 1). Perhaps these speculations may be related to the observations by Gegiou *et al.* that an intermediate was formed from 2,2′-azoxytoluene which, by continued irradiation (436 nm) at −70°C, went on to the rearrangement product (13).

Experimental

Preparation of labeled azoxybenzene (4)

Each labeled **4** was prepared from the reduction of the appropriately labeled nitrobenzene by heating with sodium hydroxide in methanol (14). Commercial (Merck, Sharpe and Dohme) [^{15}N]nitrobenzene, 99 atom% ^{15}N, was used for making [^{15}N,^{15}N′]**4**. [2-^{14}C]Nitrobenzene, previously prepared from 2-nitro-[1-^{14}C]aniline (22), was used for making [2-^{14}C]**4**. The product had an activity of approximately 16 mCi/mol. For making [^{18}O]**4** it was necessary first to prepare [^{18}O]nitrobenzene by the method of Høg (25) using $H_2{}^{18}O$ containing 20.3 atom% ^{18}O (Prochem BOC, Ltd.). The **4** finally obtained was found by mass spectrometry to contain approximately 7 mol% of [^{18}O]**4**. An example of the preparation of labeled **4** follows.

[^{15}N]Nitrobenzene (2.0 g, 16.3 mmol) was added during 50 min to a well-stirred solution of 3 g of sodium hydroxide in 8 mL of methanol at 75–80°C. The mixture was stirred at that temperature for 2.5 h and then diluted with crushed ice. After standing 12 h the yellow product was filtered, washed with water, and dried in air. The crude product was purified on a column of neutral alumina with benzene elution. Removal of the benzene left a liquid product (1.6 g, 8.0 mmol, 98%) which crystallized on standing overnight; mp 34.5°C. The solid was mixed with ordinary **4** and the mixture was crystallized from benzene, giving **4** containing 10 mol% of [^{15}N,^{15}N′]**4**.

Photo-rearrangements

Rearrangements were carried out in a Rayonet reactor with eight 350-nm U-tube lamps. Solutions to be irradiated were placed in a cylindrical quartz vessel and stirred gently during irradiation with a current of nitrogen. In order to specify particular extents of conversion, the disappearance of azoxy compound and the formation of product were first monitored spectroscopically with irradiations of unlabeled substrate. The formation of 2-hydroxyazobenzene (**6**) was monitored at 410 nm, while the formation of 1-hydroxy-2,2′-azonaphthalene (**10**) was monitored at 505 nm. Solvents for photo-rearrangement were 95% ethanol for **4** and 1,2-dimethoxyethane (DME) for **8**. Specific examples of rearrangement and workup follow.

Rearrangement of 4

(A) For product KIE measurement

A solution of 198 mg (1.0 mmol) of [^{18}O]**4** in 1.0 L of 95% ethanol was irradiated for 20 min. The solution was then divided into two parts. The larger part (750 mL) was evaporated at reduced pressure. The residue was dissolved in 20 mL of benzene and placed on a column of neutral alumina (Matheson, Coleman, Bell, AX0612-3, 80-200 mesh). Unrearranged **4** (130.2 mg 87.7%), mp 34.0–34.5°C, was eluted with benzene, while product, [^{18}O]**6**, was eluted with methanol. The crude product was dissolved in 80 mL of 10% aqueous sodium hydroxide, and the solution was acidified, after filtration, with hydrochloric acid. The product was then extracted with 3 × 50 mL of ether, giving 14.6 mg (9.6%) of [^{18}O]**6**. This was sublimed at low pressure to give [^{18}O]**6**, mp 81–82°C, for mass spectrometry.

The smaller part (250 mL) of the ethanol solution was irradiated again for 20 h to effect complete conversion of **4**. Workup as above then gave 3.2 mg (6.5%) of **4** and, for mass spectrometry, 41.4 mg (83.8%) of **6**. For the purpose of calculating KIE the extents of conversion of **4** were based on recovered **4**, namely 12% and 93.5% conversions.

Rearrangements of [^{15}N,^{15}N′]**4** designed for mass spectrometry of the product were carried out identically.

Results for all runs are listed in Table 1.

(B) For substrate KIE measurement

A solution of 297 mg (1.5 mmol) of [^{15}N,^{15}N′]**4** in 1 L of ethanol was irradiated for 12.2 h, the time calculated for 81% conversion. The solution was worked up as described above and gave 55.6 mg (18.7%) of recovered [^{15}N,^{15}N′]**4** and 226 mg (76.1%) of product. A portion (38.8 mg, 0.196 mmol) of recovered [^{15}N,^{15}N′]**4** was dissolved in 5 mL of absolute ethanol and was hydrogenolyzed over 5% Pd/charcoal at atmospheric pressure for 3 h. The ethanol solution was filtered and evaporated at 25°C, and the residue was dissolved in 15 mL of benzene. To this solution was added 2 mL of trifluoroacetic anhydride and the mixture was heated under reflux for 15 min. Evaporation gave crude product which was sublimed at low pressure to give 51.7 mg (0.27 mmol, 70%) of *N*-trifluoroacetyl[^{15}N]aniline, mp 87.5–88°C (lit. (31) mp 88.5–90°C). This was sublimed twice again for mass spectrometry.

A sample of unirradiated [^{15}N,^{15}N′]**4** was hydrogenolyzed and worked up in the same way to produce *N*-trifluoroacetyl[^{15}N]aniline for mass specrometry "at zero conversion".

Results are listed in Table 2.

(C) For scintillation counting and substrate KIE measurement

A solution of 400 mg (2.02 mmol) of [2-^{14}C]**4** in 1.0 L of ethanol was irradiated for 12 h, a time calculated for 70% conversion. Unrearranged substrate and product were separated on alumina as usual. The benzene eluate was evaporated at reduced pressure to give crystalline, unrearranged [2-^{14}C]**4**. This was again chromatographed on neutral alumina, crystallized, and hydrogenolyzed as described above, to give *N*-trifluoroacetyl-[2-^{14}C]aniline which was sublimed successively six times for scintillation counting. The final product had mp 87.6°C.

Preparation of labeled 2,2′-azoxynaphthalene (8)

Labeled **8** was prepared from [^{15}N,^{15}N′]- and [1,1′-^{13}C$_2$]-2,2′-azonaphthalene which had been synthesized earlier (26). Each of the azonaphthalenes contained approximately 10 mol% of the doubly labeled isomer.

A solution of 1.06 g (3.76 mmol) of labeled 2,2′-azonaphthalene in 190 mL of benzene was kept at 27°C in a thermostated bath. To this solution was added a freshly prepared solution of 3.24 g (18.8 mmol) of *m*-chloroperbenzoic acid in 55 mL of benzene. The mixture was kept at 27°C for 17 h, during which time the reaction was monitored periodically by TLC. After oxidation was complete the solution was washed with dilute sodium bicarbonate solution and water, and then was dried and evaporated. The residue was chromatographed on a column of silica gel, eluting with cyclohexane, and the product was crsytallized from ethanol giving 1.01 g (3.38 mmol, 90%) of labeled **8**, mp 167–168°C (lit. (10) mp 166°C).

Rearrangement of 8 for product KIE measurements

A solution of 149 mg (0.50 mmol) of **8** containing approximately 10 mol% of labeled **8** in 1.0 L of DME was irradiated for 40 min, a time calculated to result in approximately 8% conversion. The solvent was removed in a rotary evaporator and the residue was separated by flash chromatography on silica gel (E. T. Baker) into recovered **8** and product **10**. The eluent was a mixture of cyclohexane, benzene, and piperidine (91:5:4 by volume). The recovered **8** was crystallized from ethanol giving 121 mg (81%). The crude **10** was dissolved in a small amount of chloroform and streaked on preparative-scale TLC plates (EM silica gel). Development with a mixture of cyclohexane, benzene, and piperidine (80:15:5) separated **10** from a small amount of another, unidentified, substance. After removal from the plate material, **10** was crystallized from ethanol giving 10.5 mg (7%) of labeled **10** for mass spectrometry.

For complete conversion of **8** a solution of 75.5 mg (0.25 mmol) of labeled **8** in 50 mL of DME was irradiated for 32 h. Workup as described gave 54 mg (72.5%) of **10** for mass spectrometry and 3 mg (4.0%) of recovered **8**.

These experiments were repeated three times for each of the [^{15}N,^{15}N′]**8** and [1,1′-$^{13}C_2$]**8**, with similar results. It is seen that the total recovery of material from the low-conversion irradiation was 88%. Losses occurred in the flash chromatography in which some fractions containing both **8** and **10** were discarded. The amount of **10** recovered (7%) was pleasingly close to that anticipated. The total recovery of material from 100% conversion (76.5%) was rather low, particularly **10** itself. Irradiation of **10** (14.9 mg in 100 mL of DME) for 10 h showed, by TLC, that a very small amount of a new compound having lower R_f was formed. Possibly, therefore, the lengthy irradiations needed for complete conversion of **8** may have also caused loss of some of the product **10**. The lengthy irradiations are taken as having achieved 100% conversion. Results are listed in Table 4.

KIE measurements

(A) Whole-molecule – ion mass ratios were measured with Hewlett–Packard mass spectrometers, Model 5985B (Rutgers University)[5] and 5995 (Texas Tech University). In the latter case multiple scanning was carried out in the selected-ion-monitoring (SIM) mode and the data were analyzed in blocks (27) with the aid of a program kindly supplied by Professor San Filippo. The number of scans made with the Model 5995 instrument was in the order of 5000 per run. The handling of samples was as described earlier (27).

Ions monitored, at 50 ms/ion dwell times, were M and $(M + 2)$ in the products (**6** and **10**) of rearrangement of [^{15}N,^{15}N′]**4**, [^{18}O]**4**, [^{15}N,^{15}N′]**8**, and [1,1′-$^{13}C_2$]**8**. Ions monitored when substrate was recovered and hydrogenolyzed in the rearrangement of [^{15}N,^{15}N′]**4** were the M and $(M + 1)$ of *N*-trifluoroacetylaniline.

(B) Scintillation counting was carried out with a Beckman Model LS 7000 liquid scintillation counter. The sample (approximately 5 mg) was dissolved in 10 mL of cocktail (Parkard, S¢INT-0, No. 6103183) and counted ten times. Three separately weighed samples were counted for each conversion. Samples were weighed precisely (±0.001 mg) on a Cahn balance. Finally, the average of ten counts was expressed in counts per 1.000 mg and the results for the three samples were averaged for KIE calculations.

In making these calculations, it was assumed that equal amounts of [2-^{14}C]**4** and [2′-^{14}C]**4** were available for rearrangement. Therefore, in the labeled molecules, rearrangements to one labeled and three unlabeled *o*-position were possible, among which an intramolecular KIE existed and was assumed to have the same magnitude as the sought-after intermolecular KIE.

All KIE calculations were made as described earlier (27).

Acknowledgements

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[5] We thank Dr. J. San Filippo, Jr. and Mrs. Marilyn Brownawell for these measurements, Table 4. Information on the way of making measurements has been given (27).

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