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Reaction of an Aza[60]fullerene Radical with Diphenylmethanes and Fluorenes: A Mechanistic Approach

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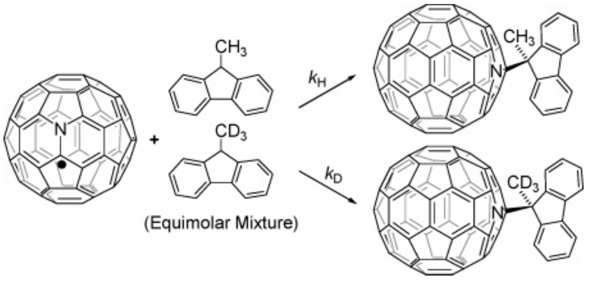

The mechanism of the reaction of azafullerene radical $C_{59}N^{\bullet}$ with diphenylmethane and 9-methyl-9*H*-fluorene has been investigated. The primary and secondary kinetic isotope effects provide strong evidence for a stepwise mechanism in which the hydrogen-atom abstraction is the rate-determining step.

A major target of scientists, who are involved with the chemistry of fullerenes, is the modification of the fullerene cage by introducing heteroatoms into the cage structure. This was achieved for the first time in 1995 by Wudl and co-workers via the isolation and characterization of aza[60]fullerene dimer $(C_{59}N)_2$ (**1**, Figure 1).[1] An alternative synthetic route to **1** was subsequently reported by Hirsch and co-workers.[2] Regarding the synthesis of azafullerene monoadducts, two basic procedures have been developed up to now.[3] The first one is based on the trapping of azafullerene radical $C_{59}N^{\bullet}$ (**2**, Figure 1), either by a hydrogen-atom donor such as hydroquinone, leading to hydroaza[60]fullerene $C_{59}HN$,[4] or by the diphenylmethane radical, leading to $C_{59}(CHPh_2)N$.[5] Alternatively, the trapping of azafullerenium carbocation $C_{59}N^+$ (**3**, Figure 1), which is thermally produced from the dimer $(C_{59}N)_2$ in the presence of air and excess toluene-*p*-sulfonic acid (*p*-TsOH), was elaborated by Hirsch. Electron-rich aromatics[6] and carbonyl compounds,[7] as well as alcohols and olefins,[8] may carry out the nucleophilic trapping of the cation. Moreover, monomeric **3** has been isolated in the form of its carborane anion salt by oxidation of the sp^3-sp^3 C−C bond of $(C_{59}N)_2$ with hexabromo(phenyl)carbazole.[9]

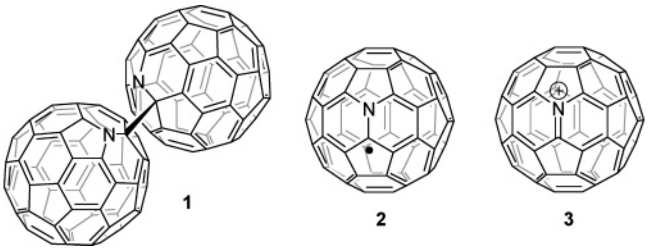

FIGURE 1. Azafullerene dimer $(C_{59}N)_2$, azafullerene radical $C_{59}N^{\bullet}$, and azafullerenium carbocation $C_{59}N^+$.

Following our continuous interest in fullerene chemistry,[10] we have recently revealed an unprecedented photochemical behavior of azafullerenium carbocation $C_{59}N^+$.[11] Hence, the photoinduced electron-transfer reaction between **3** and benzyltrimethylsilane affords aza[60]fullerene monoadduct **4** (Scheme 1). In the same study, we showed that $(C_{59}N)_2$ displays three different modes of reactivity toward benzyltrimethylsilane (namely, radical, electrophilic aromatic substitution, and photoinduced electron transfer), leading to novel aza[60]fullerene monoadducts. Furthermore, we have also reported a mechanistic study on the electrophilic aromatic substitution reaction between azafullerenium carbocation $C_{59}N^+$ and electron-rich aromatic compounds.[12] On the basis of kinetic isotope effect (KIEs) measurements, we propose that the arenium cation is formed by electrophilic attack of $C_{59}N^+$ on the aromatic ring in the first step, followed by hydrogen abstraction in a rate-determining second step.

The diphenylmethane[5] and 9-substituted fluorene[13] aza[60]fullerene monoadducts are the only aza[60]fullerene derivatives that have been isolated from the reaction of azafullerene radical $C_{59}N^{\bullet}$ (**2**) thus far;[4,5,13] however, apart from product isolation and characterization, little is known of their formation mechanism.

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[12] Vougioukalakis, G. C.; Chronakis, N.; Orfanopoulos, M. *Org. Lett.* **2003**, *5*, 4603−4606.

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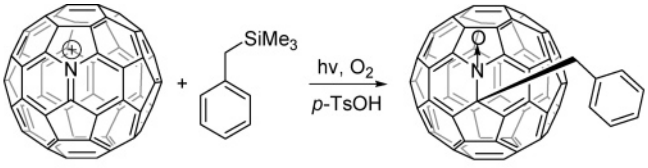
SCHEME 1. Photoinduced Electron-Transfer Reaction between $C_{59}N^+$ and Benzyltrimethylsilane



3 **4**

Building upon this work, we report herein a mechanistic study based on primary and secondary isotope effects in the reaction between **2** and the suitable deuterium-labeled diphenylmethanes and fluorenes. In general, deuterium isotope effects are a powerful tool to probe the transition state and provide valuable information on the extent of bond breaking and bond making.[14] The arylalkanes used for the present deuterium-based KIEs study are: diphenylmethane (**5-*d*$_0$**) and its deuterated analogues **5-*d*$_1$** and **5-*d*$_2$**, as well as 9-methyl-9*H*-fluorene (**6-*d*$_0$**) and its deuterated analogues **6-*d*$_3$** and **6-*d*$_4$** (Figure 2).[15]

All reactions between the aza[60]fullerene dimer and diphenylmethanes or methylfluorenes were carried out with a 100-fold molecular excess of the substrate in degassed HPLC grade *o*-dichlorobenzene (ODCB), under an argon atmosphere, and monitored by HPLC. To assess the extent of bond making and bond breaking in the transition state, we measured the intermolecular primary as well as the α- and *β*-secondary KIEs in the reactions of **2** with an equimolar mixture of **5-*d*$_0$** or **6-*d*$_0$** with their deuterated analogues **5-*d*$_2$**, **6-*d*$_3$**, and **6-*d*$_4$**, respectively, and **5-*d*$_1$** was used in the intramolecular (product) KIE experiments. In the case of 9-methylfluorenes, the reaction mixture was heated at 160 °C for 4 h,[13] whereas for diphenylmethanes, the temperature was kept at 180 °C for a period of 40 h.[5] Following the distillation of ODCB under reduced pressure, the crude mixtures were washed 4−6 times with acetonitrile and/or acetone to remove the remaining arylalkane. Chromatographic purification on SiO_2 afforded the desired azafullerene adducts. The isotope effects were measured from the ^1H NMR spectra by integrating the appropriate signals. For example, the *β*-secondary isotope effect, which is the result of the intermolecular isotopic competition between **6-*d*$_0$** and **6-*d*$_3$**, is proportional to the ratio of adducts **7-*d*$_0$**/**7-*d*$_3$**. A typical ^1H NMR spectrum of the reaction products **7-*d*$_0$** and **7-*d*$_3$** is shown in Figure 3 (methyl protons resonate at 2.95 ppm, and the four aromatic protons H_a, H_b, H_c, and H_d at 8.30, 7.96, 7.60, and 7.53 ppm, respectively). Integrations of the methyl signal of **7-*d*$_0$** at 2.95 ppm and the aromatic protons of both **7-*d*$_0$** and **7-*d*$_3$** determine the *β*-secondary KIE (**7-*d*$_0$**/**7-*d*$_3$** = k_H/k_D, Figure 3).

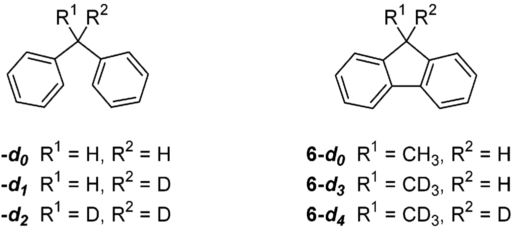
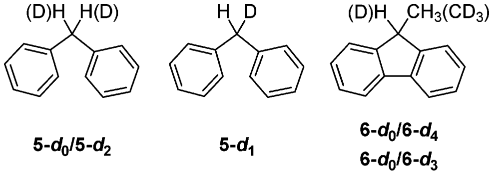


FIGURE 2. Deuterium-labeled diphenylmethanes and 9-methylfluorenes.

TABLE 1. KIEs for the Addition of $C_{59}N^{\bullet}$ to Diphenylmethane and 9-Methylfluorene[a]



competition	substrate	conversion (%)	$(k_H/k_D)_{obs}$
intermolecular	**5-*d*$_0$/5-*d*$_2$**	38	2.30 ± 0.07
intramolecular	**5-*d*$_1$**	37	2.00 ± 0.06
intermolecular	**6-*d*$_0$/6-*d*$_4$**	30	3.85 ± 0.12
intermolecular	**6-*d*$_0$/6-*d*$_3$**	31	1.06 ± 0.03

[a] The lower reaction rate of diphenylmethanes, compared to that of 9-methylfluorenes, is most probably correlated with its higher bond dissociation energy (ref 16).

The measured isotope effects for all inter- and intramolecular competitions are summarized in Table 1. For both substrates, a substantial primary KIE was determined. The values of the observed isotope effects may be rationalized as follows: The isotope effect for the intermolecular (kinetic) competition **5-*d*$_0$**/**5-*d*$_2$**, found to be $(k_H/k_D)_{obs} = 2.30 \pm 0.07$, is a combination of a primary and an α-secondary isotope effect. In general, α-secondary KIEs originate from the change of the hybridization at the α-carbon from the ground to the transition state.[14] The observed isotope effect may be fractionated into the primary $[(k_H/k_D)_{pr}]$ and α-secondary $[(k_H/k_D)_\alpha]$ isotope effects according to eq 1.

$$(k_H/k_D)_{obs} = (k_H/k_D)_{pr} \cdot (k_H/k_D)_\alpha = 2.30 \qquad (1)$$

Similarly, the observed intramolecular isotope effect for **5-*d*$_1$** is the summation of a primary and an α-secondary isotope effect. Nevertheless, in this case, the α-secondary KIE is in the opposite direction than the primary. Consequently, the $(k_H/k_D)_{obs}$ is expressed by eq 2. Assuming that the primary isotope effects for the inter- and intramolecular competition are equal and taking the ratio of eqs 1 and 2, we calculated the α-secondary isotope effect to be $(k_H/k_D)_\alpha = 1.07$ and the primary effect to be $(k_H/k_D)_{pr} = 2.14$.

$$(k_H/k_D)_{obs} = (k_H/k_D)_{pr} \cdot [(k_H/k_D)_\alpha]^{-1} = 2.00 \qquad (2)$$

Moreover, the observed isotope effect for the intermolecular competition **6-*d*$_0$**/**6-*d*$_3$** was found to be $(k_H/k_D)_{obs} = 1.06 \pm 0.03$. Therefore, the *β*-secondary isotope effect per deuterium is $(k_H/k_D)_\beta = (k_H/k_D)_{obs}{}^{-3} = 1.02$. Thus, the observed isotope effect for the intermolecular competition **6-*d*$_0$**/**6-*d*$_4$** may be written as:

$$(k_H/k_D)_{obs} = (k_H/k_D)_{pr} \cdot [(k_H/k_D)_\beta]^3 = 3.85 \qquad (3)$$

The neat primary isotope effect for the intermolecular competition **6-*d*$_0$**/**6-*d*$_4$** was consequently calculated to be $(k_H/k_D)_{pr} = 3.63$.

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(14) (a) Melander, L.; Saunders, W. H. *Reaction Rates of Isotopic Molecules*; Wiley-Interscience: New York, 1980. (b) Carpender, B. K. *Determination of Organic Reaction Mechanism*; John Willey: New York, 1984.

(15) Compounds **5-*d*$_0$**, **5-*d*$_1$**, and **5-*d*$_2$** were prepared by reduction of benzophenone with $LiAlH_4$ (or $LiAlD_4$ for **5-*d*$_2$** and **5-*d*$_1$**), followed by reduction of the produced alcohol by an etherated boron trifluoride−triethylsilane system (or triethylsilane-*d* for **5-*d*$_2$**). For a detailed experimental procedure, see: Orfanopoulos, M.; Smonou, I. *Synth. Commun.* **1988**, *18*, 833−839. Compounds **6-*d*$_0$**, **6-*d*$_3$**, and **6-*d*$_4$** were prepared from 9-fluorenone by addition of CH_3Li (or CD_3Li for **6-*d*$_3$** and **6-*d*$_4$**), followed by reduction of the produced alcohol by an etherated boron trifluoride−triethylsilane system (or triethylsilane-*d* for **6-*d*$_4$**).

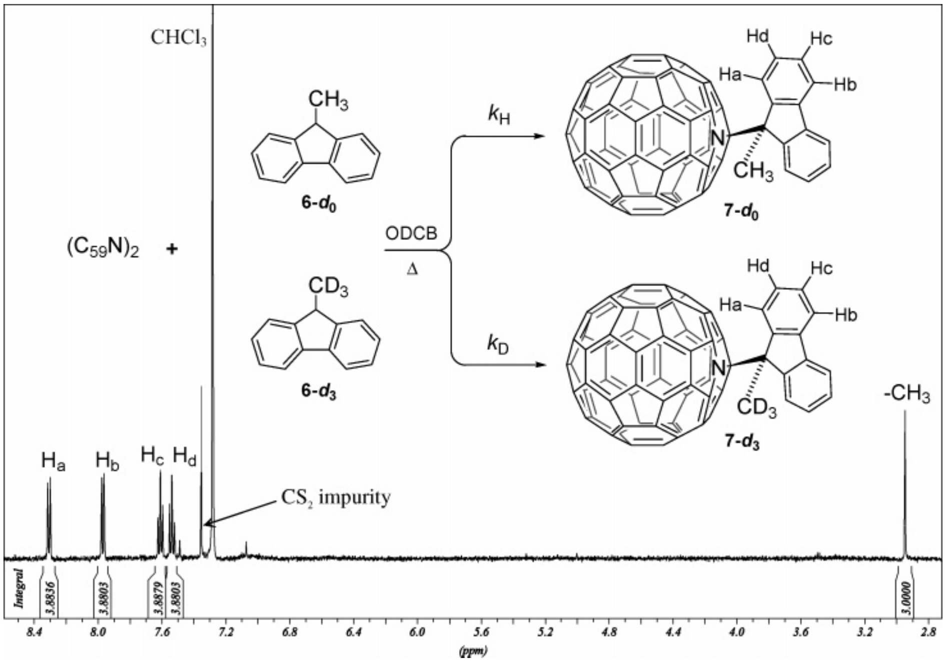


FIGURE 3. Determination of the β-secondary isotope effect for the intermolecular competition **6-d_0/6-d_3**.

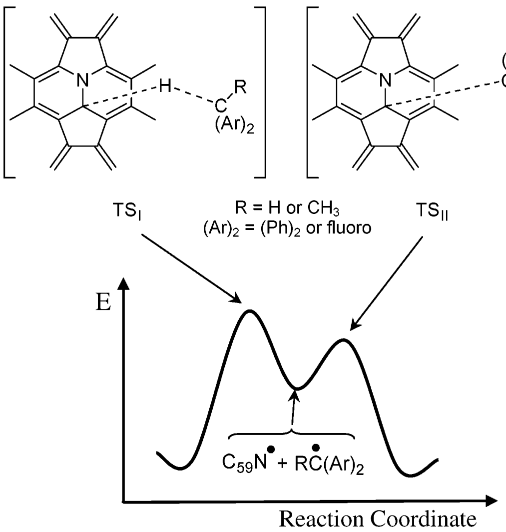
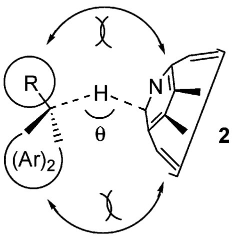


FIGURE 4. Proposed energy profile for the reaction of $C_{59}N^\bullet$ with diphenylmethanes and 9-methylfluorenes.



5 [$(Ar)_2 = (Ph)_2$, R = H]
6 [$(Ar)_2$ = Fluoro, R = CH_3]

FIGURE 5. Transition state of the hydrogen-atom transfer from diphenylmethane and 9-methylfluorene to $C_{59}N^\bullet$.

The substantial primary as well as the normal α-secondary KIEs support a mechanism where the hydrogen-atom abstraction occurs at the rate-determining step of the reaction, which is then followed by a fast coupling of the two radicals, as shown in Figure 4. If this had not been the case, all measured isotope effects would have been unity, or near unity.[14] Moreover, the larger primary isotope effect measured in the reaction of 9-methyl-9*H*-fluorene, compared to that for diphenylmethane (3.63 vs 2.14, respectively), could be rationalized on the basis of angle θ size during hydrogen transfer from the corresponding substrate to the aza[60]fullerene radical (Figure 5). Considering that the α-carbon of methylfluorene is tertiary, the nonbonded interactions between the methyl group and the aza[60]fullerene sphere (Figure 5) may very well impose an increased linearity in the corresponding transition state, compared to that for diphenylmethane where this interaction is absent. This differentiation is in good agreement with an extraordinary increase in the KIEs measured in hydride and proton-transfer reactions on going from nonsterically demanding systems[17] to the hydride-transfer reactions of triarylmethanes with triarylmethyl carbocations.[18] At this stereochemical extreme, the hydride-transfer transition state was proposed to be linear, affording large KIEs in the range of $k_H/k_D \approx 7-9$.[18] In an earlier work, the magnitude of the deuterium KIE had also been theoretically predicted to depend strongly on the θ value (Figure 5), reaching its highest value ($k_H/k_D = 7.9$) when $\theta = 180°$.[19]

In conclusion, the addition of the thermally produced azafullerene radical $C_{59}N^\bullet$ to diphenylmethane and methylfluorene occurs by a stepwise mechanism in which the rate-determining step is the hydrogen-atom abstraction, followed by

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a fast coupling of $C_{59}N^{\bullet}$ with the diphenylmethane or methylfluorene radical.

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Supporting Information Available: ^{1}H NMR spectra for all inter- and intramolecular competitions. This material is available free of charge via the Internet at http://pubs.acs.org.

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