

Addition of Electron-Rich Aromatics to Azafullerenium Carbocation. A Stepwise Electrophilic Substitution Mechanism

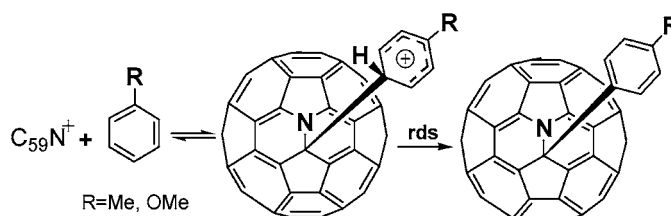
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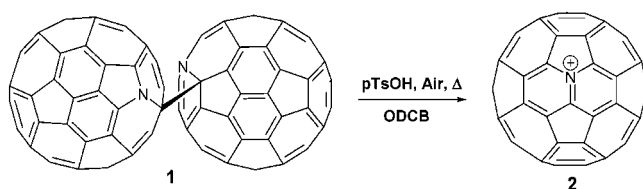
ABSTRACT



The reaction between the $C_{59}N^+$ carbocation and the electron-rich aromatic compounds toluene and anisole has been mechanistically studied. The measured intermolecular kinetic isotope effects are consistent with an electrophilic aromatic substitution mechanism in which the arenium cation is formed by electrophilic attack of $C_{59}N^+$ on the aromatic ring in the first step of the reaction, followed by hydrogen abstraction in a rate-determining second step.

Since the synthesis and isolation of the aza[60]fullerene dimer ($C_{59}N$)₂ (**1**) in 1995 by the research groups of Wudl¹ and Hirsch,² attention has been paid to synthetic procedures for the preparation of monomeric aza[60]fullerene adducts.³ So far, two basic strategies have been developed. The first is based on the trapping of the aza[60]fullerene radical $C_{59}N^{\cdot}$.^{4,5} The second, and most popular, has been elaborated by Hirsch and co-workers and is based on the trapping of the azafullerenium carbocation $C_{59}N^+$ (**2**) by a number of nucleophiles (Scheme 1). Carbocation **2**, which is isoelec-

Scheme 1



tronic to [60]fullerene, is produced and reacted in situ by thermal treatment of dimer **1** in the presence of oxygen,

toluene-*p*-sulfonic acid, and the nucleophile.^{6–8} Moreover, the monomeric $C_{59}N^+$ cation has been recently isolated as the carborane anion salt by oxidation of the sp^3 – sp^3 C–C bond of **1** with hexabromo(phenyl)carbazole.⁹

Although the addition of electron-rich aromatics and other nucleophiles to $C_{59}N^+$ has received considerable recent attention, no mechanistic details on this reaction have been reported. Following our continuous interest on [60]fullerene chemistry,¹⁰ we present here a deuterium isotope effect study

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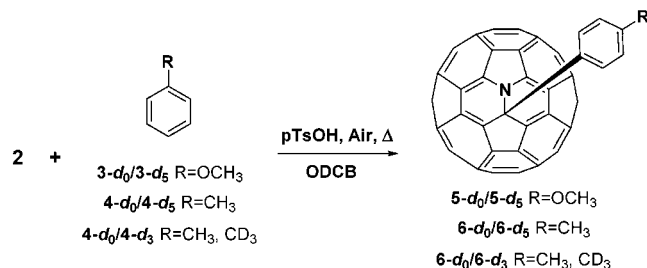
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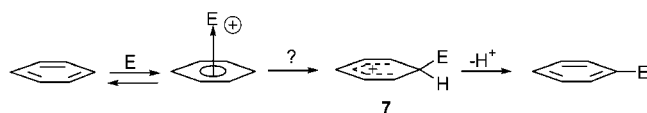
and discuss the mechanism of the title reaction. To measure the primary and the secondary isotope effects in the electrophilic substitution addition we used anisole (**3-d₀**) and its deuterated analogue **3-d₅**, as well as toluene (**4-d₀**) and its deuterated analogues **4-d₃** and **4-d₅** (Scheme 2).

Scheme 2. Electrophilic Aromatic Substitution between Azafullerenium Ion **2** and the Equimolar Mixtures **3-d₀/3-d₅**, **4-d₀/4-d₅**, and **4-d₀/4-d₃**



In most electrophilic aromatic substitution reactions the electrophilic attack, leading to the formation of the intermediate arenium ion (**7**), is the rate-determining step.¹¹ The second step, which is usually a fast loss of a proton or a leaving group such as Br⁻, H₂O, or OTs⁻, leads to the products by restoring the aromatic sextet. Primary isotope effects are expected for a rate-determining deprotonation. Substantial primary isotope effects have been observed in the past for acylation, sulfonation, and nitrosation reactions.¹² It also has been established that in some cases a π or charge transfer complex is formed, but it is still not clear whether this complex lies on the main reaction coordinate or is simply a bystander (Scheme 3).¹³ Recently, a unified mechanistic

Scheme 3



proposal, involving three discrete intermediates in the electrophilic aromatic nitration, also has been reported.¹⁴ Apart from the isolation of arenium ion intermediates, deuterium

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kinetic isotope effects have been applied to study the mechanism of the electrophilic aromatic substitution.

Substrates **3-d₀**, **4-d₀**, **4-d₃**, and **4-d₅** are all commercially available. The **3-d₅** was prepared by deprotonation of phenol **d₆** with sodium hydride, followed by trapping of the formed phenoxy anion with methyl iodide. To determine the primary intermolecular isotope effects a mixture of (C₅₉N)₂ and a 100-fold excess of the equimolar quantities **3-d₀** and **3-d₅**, as well as **4-d₀** and **4-d₅**, in separate experiments, was dissolved in 1,2-dichlorobenzene, together with a 20-fold excess of toluene-*p*-sulfonic acid. The reaction mixture was then heated at 130 °C, while a constant air stream was maintained over the solution, for about 1 h. After the reaction was cooled to room temperature, a 100-fold excess of triethylamine was added and 1,2-dichlorobenzene was distilled from the reaction mixture. The remaining crude product was washed and centrifuged with acetonitrile. The isotope effects were determined by the integration of the appropriate product proton signals. In the case of the intermolecular competition **3-d₀/3-d₅** the primary isotope effect is proportional to the ratio of **5-d₀/5-d₅** (Figure 1). Integration of the ortho (Ha) or the meta (Hb) phenyl hydrogens of **5-d₀**, at 7.78 or 7.41 ppm, respectively, as well as the methoxy hydrogens of both **5-d₀** and **5-d₅**, at 4.08 ppm, determines the isotope effect k_H/k_D (**5-d₀/5-d₅** = k_H/k_D , Figure 1). The isotope effects measured from the intermolecular competitions **3-d₀/3-d₅** and **4-d₀/4-d₅** were found to be $k_H/k_D = 1.52 \pm 0.05$ and 1.18 ± 0.04 , respectively, as presented in Table 1.

Table 1. Primary Intermolecular Isotope Effects for the Reaction of Azafullerenium Ion **2** with Equimolar Mixtures **3-d₀/3-d₅** and **4-d₀/4-d₅**

| substrate | k_H/k_D^a |
|--|-----------------|
| 3-d₀/3-d₅ | 1.18 ± 0.04 |
| 4-d₀/4-d₅ | 1.52 ± 0.05 |

^a The isotope effects were determined by ¹H NMR integration of the proper hydrogen absorptions. The error was $\pm 3\%$. Each value is the average of three consecutive measurements.

Unlike most electrophilic aromatic substitution reactions reported earlier, the primary isotope effects found ($k_H/k_D = 1.18–1.52$) in the intermolecular competition of **3-d₀** vs **3-d₅** and **4-d₀** vs **4-d₅** with **2** indicate a substantial carbon–hydrogen bond breaking, leading to the rearomatization, in the transition state TS₁ of the reaction (Scheme 4). These results exclude a mechanism where the formation of an intermediate arenium ion is the rate-determining step. Had this been the case, no intermolecular kinetic isotope effect would have been expected. It is interesting to note here that the relatively small primary isotope effect measured in this reaction ($k_H/k_D = 1.18–1.52$) may be attributed either to a bent transition state (i.e. nonlinear proton transfer) or to an early transition state in which C–H bond breaking is not

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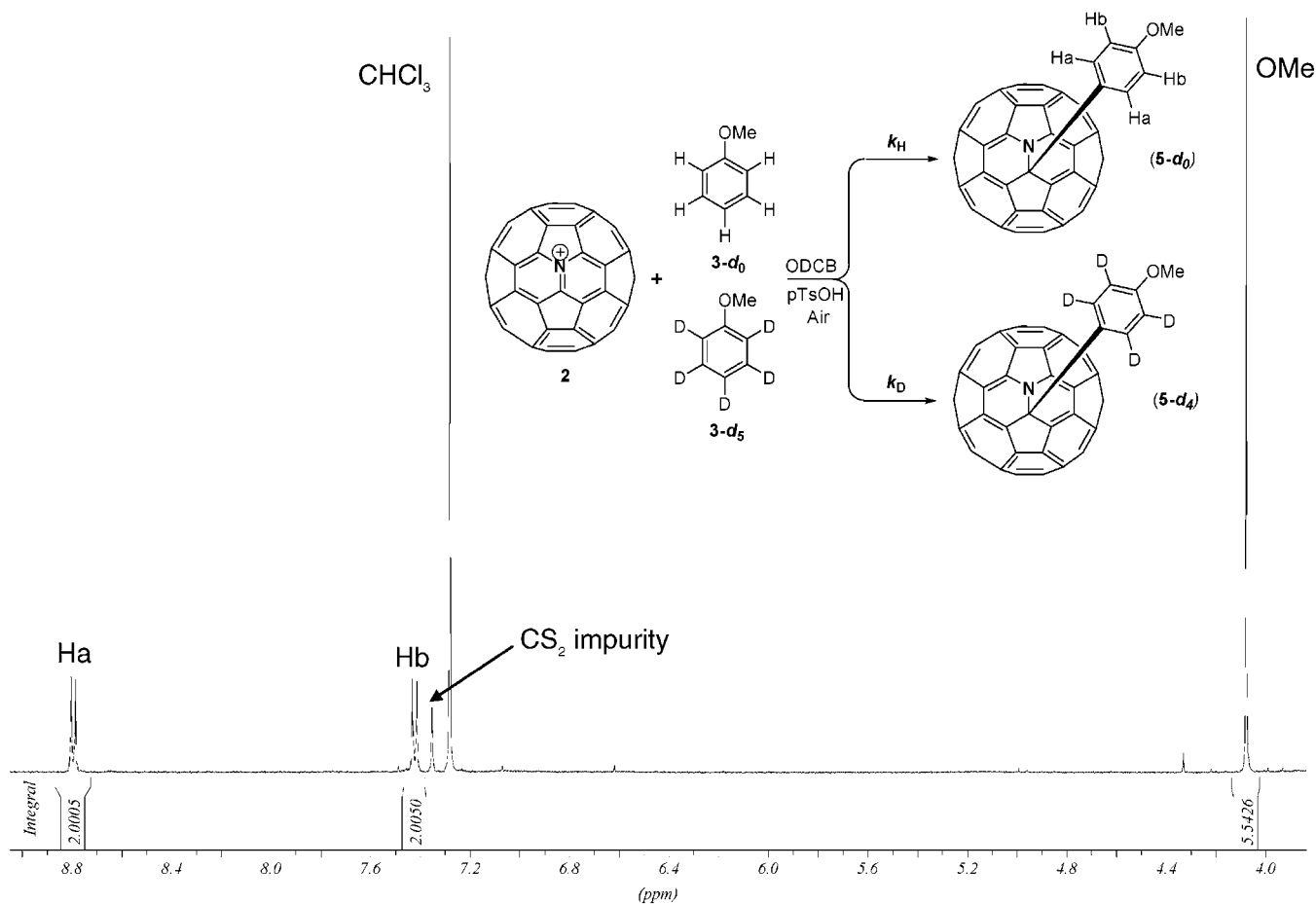
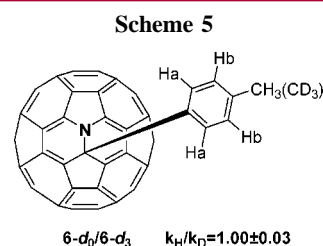
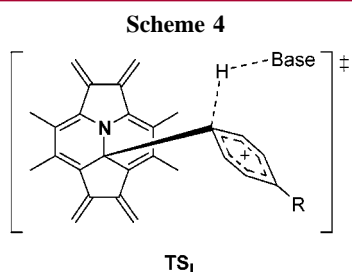
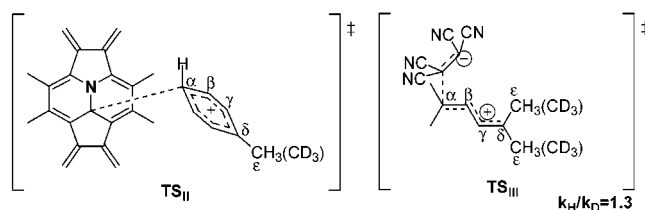


Figure 1. Determination of the primary isotope effect k_H/k_D by integration of the proper ^1H NMR signals of the products **5- d_0** and **5- d_4** .



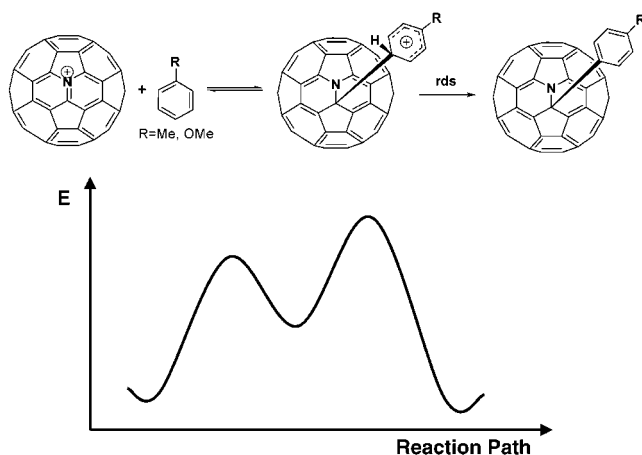
extensively developed. We would also like to point out that the reaction of **2** with the electron-rich anisole is faster and gives a better yield than that with toluene. Therefore, the smaller value of the primary isotope effect measured for the reaction of azafullerenium cation **2** with the more nucleophilic pair **3- d_0 /3- d_5** , compared to that with **4- d_0 /4- d_5** , may be rationalized in terms of an earlier transition state for the reaction of **2** with anisole than with toluene.

To assess further the extent of bond making and bond breaking in the transition state, we measured the intermolecular remote ϵ -secondary isotope effect for the reaction of **2** with an equimolar mixture of toluene (**4- d_0**) and its methyl-deuterated analogue toluene- d_3 (**4- d_3**). The product ratio **6- d_0** /



6- d_3 is proportional to the isotope effect k_H/k_D . Therefore, the secondary isotope effect k_H/k_D was determined by the ^1H NMR integration of the Ha or the Hb hydrogens of both **6- d_0** and **6- d_3** at 8.76 or 7.71 ppm, and the methyl hydrogens of **6- d_0** at 2.70 ppm (Scheme 5).

Scheme 6



The absence of a secondary kinetic isotope effect ($k_{\text{H}}/k_{\text{D}} = 1.00 \pm 0.03$) found in this reaction excludes the formation of the positively charged transition state (TS_{II}, Scheme 5) at the rate-determining step. In transition state TS_{II} the hyperconjugative effects¹⁵ involving the three hydrogens in **4**-*d*₀ versus the three deuterium atoms in **4**-*d*₃ are expected to give a normal remote ϵ -secondary isotope effect ($k_{\text{H}}/k_{\text{D}} = 1.05$ –

1.10 per deuterium), as found previously in the cycloaddition of TCNE to 2,4-hexadiene (TS_{III}, Scheme 5).¹⁶

The primary and secondary isotope effects measured for the electrophilic aromatic substitution reaction between the azafullerenium cation C₅₉N⁺ and electron-rich aromatic compounds toluene and anisole are consistent with a rate-limiting hydrogen abstraction during the second, re-aromatization step of the reaction. The proposed energy profile is presented in Scheme 6.

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Supporting Information Available: Detailed experimental procedures and ¹H NMR spectra. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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