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LETTERS

4,5-Dehydrooctafluoro[2.2]paracyclophane: facile generation and extraordinary Diels–Alder reactivity

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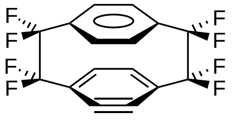
Abstract—Dehydroiodination of 4-iodo-1,1,2,2,9,9,10,10-octafluoro[2.2]paracyclophane by treatment with KO^{t}Bu in the presence of benzene, naphthalene, anthracene, or *t*-butylbenzene affords each of the corresponding Diels–Alder cycloadducts of the presumed aryne intermediate in high yield. The products were characterized by their NMR spectra, with one of them also being confirmed by X-ray crystallography. The extraordinary selectivity/reactivity of the aryne intermediate is discussed. © 2002 Published by Elsevier Science Ltd.

In the annals of aryne chemistry, following the elucidation of benzyne as a reactive intermediate,[1,2] perhaps the most striking feature of these dehydroaromatic intermediates is their dienophilic reactivity with other aromatic systems as diene partners. Depending on mode of generation and the nature of the aryne component, however, the yields in these Diels–Alder type reactions are often modest or poor.[3] For example, 75% is the best yield reported for benzyne addition to anthracene, considered one of the most reactive aromatic substrates in Diels–Alder reactions with arynes.[4,5] In that case, the benzyne was generated from benzenediazonium carboxylate, which is generally considered to be among the best methods for carrying out Diels–Alder chemistry with benzyne.[6] Benzene is a much poorer Diels–Alder substrate and it yielded only 9% Diels–Alder adduct in a similar reaction with benzyne,[7,8] although its reactions with tetrafluorobenzyne and tetrachlorobenzyne (among the more reactive arynes) yielded 33 and 62% of adduct, respectively.[9,10] In this letter we report the first generation of the novel aryne, 4,5-dehydrooctafluoro[2.2]paracyclophane, **1**, which has been found to exhibit the greatest Diels–Alder reactivity and selectivity of any aryne derivative yet reported.



1

Examples of 4,5-dehydro[2.2]paracyclophanes in the literature are rare. 4,5-Dehydro[2.2]paracyclophane itself appears to have been mentioned but once, in 1969 when Longone and Chipman reported its generation by potassium *t*-butoxide promoted dehydrobromination of 4-bromo[2.2]paracyclophane in *t*-butylbenzene in the presence of excess anthracene, with only a 15% yield of Diels–Alder adduct being obtained.[11–14] The low yield in this example is not surprising since the mode of generation of the benzyne intermediate is not an optimal one for diene trapping.

Nevertheless, we now report that under similar base and solvent conditions to the Longone report, dehydroiodination of 4-iodo-1,1,2,2,9,9,10,10-octafluoro[2.2]paracyclophane, **2**,[15,16] in refluxing benzene, or in refluxing *t*-butylbenzene in the presence of *stoichiometric* amounts of anthracene or naphthalene, affords the corresponding Diels–Alder adducts **3**, **4**, and **5**, respectively, each in greater than 80% yield.[17] The yields obtained with benzene and naphthalene are the largest yet reported for aryne reactions with these substrates.

The structural integrity of compounds **3**–**5**, as well as the stereochemistry of compound **4**, were demonstrated by NMR[18] as illustrated below for the representative adduct **5**. In the proton spectrum of **5**, the signals at 6.96, 7.32 and 7.27 ppm are the second order multiplets that are characteristic for an *ortho*-phenylene group. The proton at 7.65 has an extra coupling, most likely a

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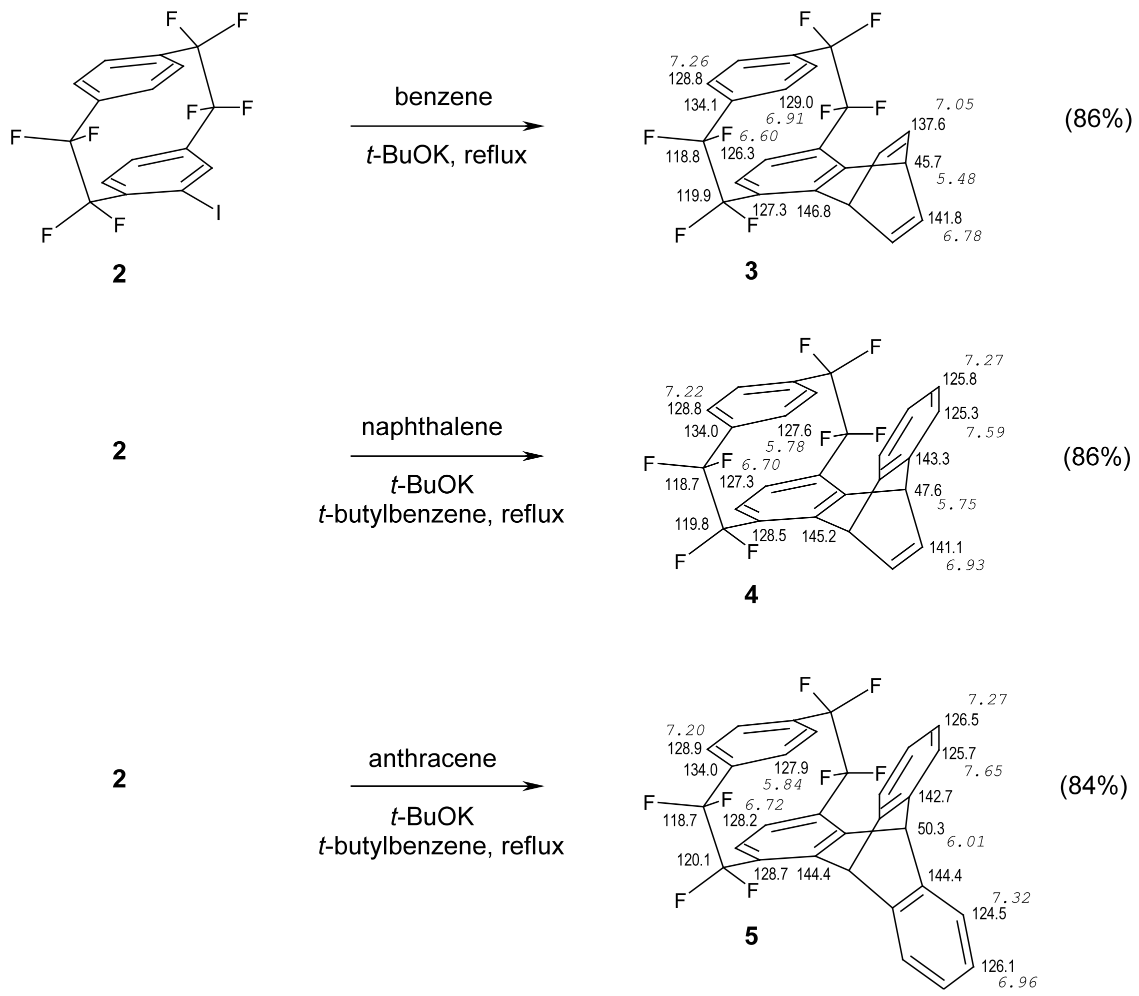


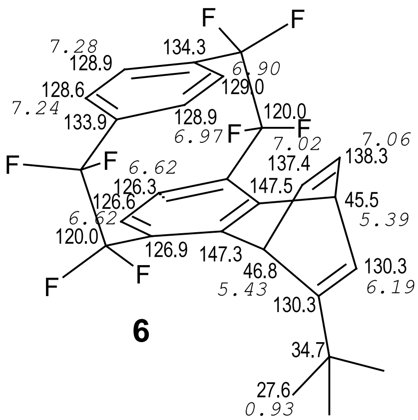
through-space coupling with fluorine. Of the three remaining aromatic CH's the two with protons at 7.20 and 5.84 are on the same aromatic ring as revealed by their mutual ^1H–^{13}C long-range couplings. The final aromatic proton, at 6.72, displays an NOE with the proton at 7.20, leaving the signal at 5.84 to be assigned as those facing the moiety originating from anthracene, and indeed the signal at 5.84 displays NOEs with the protons at 7.27 and 7.65, and no NOEs with those at 7.32 and 6.96. In a similar fashion, in compound **4**, the proton at 5.78 ppm displays NOEs with those at 7.27 and 7.59, and no NOE with the alkene proton at 6.93, proof for the *endo* stereochemistry. The upfield chemical shift of 5.78, which is comparable with the 5.84 signal in compound **5** and significantly smaller than the 7.16 signal of the parent cyclophane,[19] is diagnostic for its position above the plane of an aromatic ring. The chemical shift of the corresponding proton in compound **3**, 6.91 ppm, demonstrates that significantly less shielding is to be expected for a proton having a similar position above a double bond.

The stereoselectivity exhibited by **1** in its virtually exclusive formation of the *endo*-isomer (**4**) from naphthalene addition is remarkable, particularly since both molecular mechanics and AM1 calculations predict only a very slight thermodynamic preference for this isomer (0.75 and 0.02 kcal/mol, respectively).[20] We tentatively hypothesize that the *endo* transition state may be favored because of a stabilizing 'herringbone' H–π interaction[21] of the 5.78 protons that interact with the π cloud of the *endo* benzene ring of incipient **4**. This proposal is being tested both computationally and experimentally.

Another interesting aspect of this chemistry is that *no* products deriving from nucleophilic capture of the presumed aryne intermediate by the excess *t*-butoxide base are detected in any of these reactions. This is in contrast to Longone and Chipman's results,[11] as well as those of Cram and co-workers,[13] where *t*-butoxide adducts were found to be a major side product in each of their respective studies where this method of aryne generation was used.

Further to this point, when **2** was treated with *t*-butoxide in refluxing *t*-butylbenzene, with no additional substrate added, a similarly high yield (78%) of Diels–Alder adduct (**6**) *from addition of **1** to t-butylbenzene* was obtained, again with no indication of formation of the product of trapping of the aryne by *t*-butoxide!

The fact that NOEs are observed between the cyclophane protons that are pointed towards the for-



6

mer *tert*-butylbenzene (6.97 and 6.90) and the vinylic protons at 7.02 and 7.06 demonstrates that compound **6** is the *exo*-adduct.[22]

Based upon the above results, there can be no doubt that the reactive aryne intermediate, **1**, has been generated and is responsible for the chemistry observed in these reactions. Its relative ease of its generation (refluxing benzene) can be ascribed to an increase in acidity of the proton vicinal to the halogen, induced by the highly electronegative fluorinated bridges. The fluorinated bridges of **1** will also make it a highly *electrophilic* and therefore more reactive aryne (compared to the non-fluorinated dehydro[2.2]paracyclophane). However, such high electrophilicity should also lead to enhanced reactivity with nucleophiles, which is not observed. At this time, the only potential explanation we have for the selectivity exhibited by **1** is the possible electrostatic repulsion of the *t*-butoxide nucleophile by the fluorinated bridges of **1**. Further experiments are in progress to test this hypothesis.

Other characteristic reactions of benzynes, including ene reactions, additions of amines, sulfides and alcohols, as well as employment of other methods for generation of **1**, are currently under productive investigation.

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17. The structure of adduct **5** was confirmed by X-ray crystallography, whereas adducts **3**, **4**, and **6** were fully characterized by ^{1}H, ^{13}C and ^{19}F NMR, MS, and elemental analysis.
18. The NMR spectra were recorded on a Varian Inova 500 MHz, equipped with a 5 mm PFG indirect detection probe. The samples were run in chloroform-*d* at 25°C and the chemical shifts were referenced to TMS (0 ppm) for ^{1}H and to the solvent signal (77 ppm) for ^{13}C. The chemical shifts are indicated adjacent to each carbon on the individual product structures (in italics for ^{1}H).
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