Pergamon

Tetrahedron Letters 41 (2000) 8691–8694

TETRAHEDRON
LETTERS

Hydrogen abstraction on photolysis of a naphthocarborane

Alexander Z. Bradley,[a] A. James Link,[a] Kaustav Biswas,[a] Daniel Kahne,[a]
Jeffrey Schwartz,[a] Maitland Jones Jr.,[a,*] Zhendong Zhu[b] and Matthew S. Platz[b]

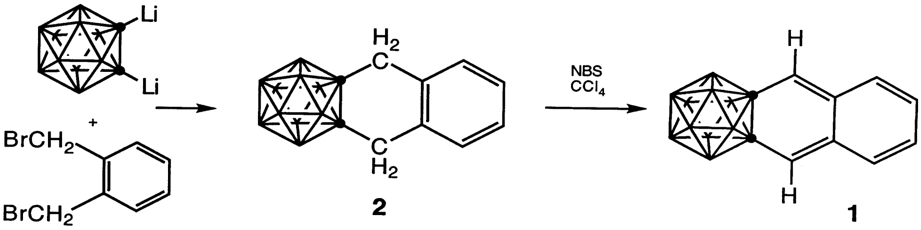
[a] *Department of Chemistry, Princeton University, Princeton, NJ 08544, USA*
[b] *Department of Chemistry, The Ohio State University, Columbus, OH 43210, USA*

Received 13 June 2000; revised 11 September 2000; accepted 12 September 2000

Abstract

Photolysis of 'naphtho-*o*-carborane' in the presence of excellent hydrogen donors such as 1,4-cyclohexadiene leads to quantitative double hydrogen abstraction. Other molecules, including supercoiled DNA, similarly act as hydrogen atom donors towards photolyzed naphtho-*o*-carborane. A diradical intermediate is proposed. © 2000 Elsevier Science Ltd. All rights reserved.

In 1970, Matteson and Davis reported the synthesis of 'naphthocarborane' **1**.[1] They were interested in the question of whether **1** could be called aromatic—was there sufficient orbital connection across the carborane carbon–carbon bond to close the cycle? Since Matteson and Davis' pioneering efforts, they and others have answered this question in the negative, as was suspected from the beginning.[1,2] In this paper we revisit compound **1**, describe some of its photochemical reactions, and suggest a mechanism for the hydrogen abstraction observed. At the end, we point to future developments in the practical application of the photochemistry of **1**. Matteson's exquisitely simple synthesis is shown below. We have slightly modified the original synthesis to eliminate isolation of an intermediate dibromide.



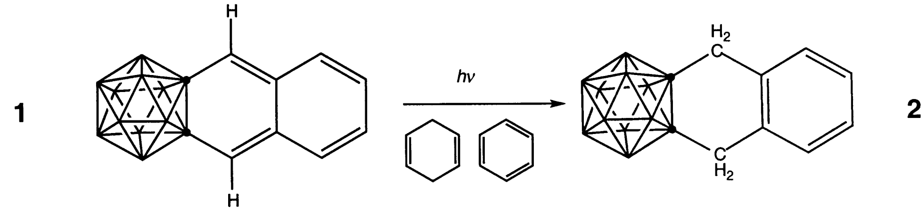
Photolysis of **1** with a medium pressure Hanovia mercury arc through either quartz or Pyrex in relatively poor sources of hydrogen such as THF and pentane leads to modest amounts of **2**,

---

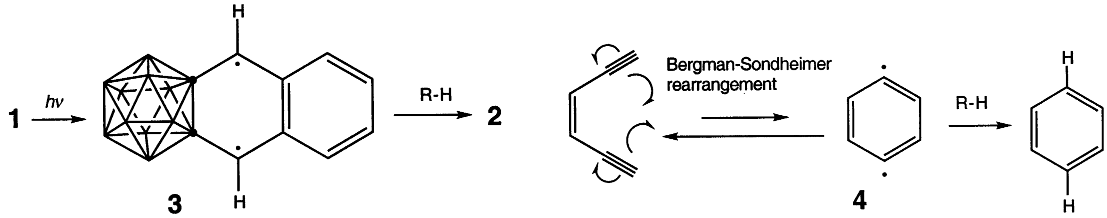
* Corresponding author.

PII: S0040-4039(00)01578-1

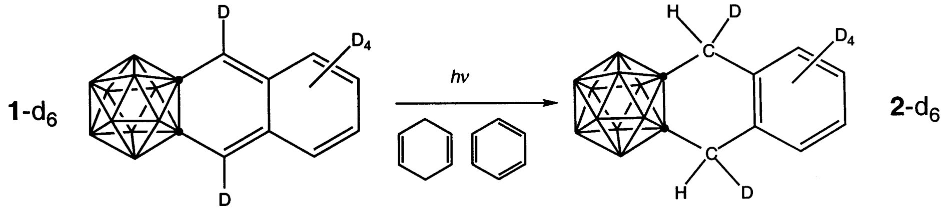
the product of abstraction of two hydrogen atoms. Much intractable solid is also formed, and this material is the sole 'product' when photolysis is carried out in an even worse hydrogen donor such as benzene. We were intrigued despite the poor yield, and pursued photolysis in the presence of an excellent hydrogen donor, 1,4-cyclohexadiene. The yield as measured by ^{1}H NMR spectroscopy is now quantitative, and **2** can be isolated by preparative thick layer chromatography in ca. 80% yield.



The question naturally arises as to the structure of the abstracting species, and the diradical **3** seems a likely intermediate. The relationship of **3** to the diradical **4** formed from enediynes[3] in the Bergman/Sondheimer[4] rearrangement is obvious. Activity remains high in the chemistry of related 1,4-diradicals. For example, Sander, Herges, and their collaborators have recently described the matrix isolation of **5**, a diradical closely related to **4** and superficially much like **3**.[5] However, diradicals **4** and **5** and all their relations are sigma diradicals, whereas **3** is likely a pi diradical. Moreover, there are two offending hydrogens in **3** that are not present in **4** or **5**, and the steric demands of the species may be very different.



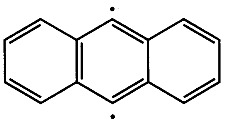
A labeling experiment using hexadeuterio-**1** reveals that the new hydrogens appear in the expected positions, assuming **3** to be the reactive ingredient in the abstraction process. Analysis by ^{1}H NMR spectroscopy shows a 1:1:1 triplet at δ 3.83 ($J=2.5$ Hz) ppm.

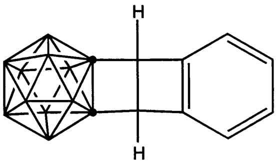


In further support of the intermediacy of **3**, we find that laser flash photolysis of **1** (308 nm, XeCl eximer laser, 17 ns) produces a transient species that absorbs broadly between 350 and 450 nm. The transient decays exponentially at ambient temperature with lifetimes of 250, 320, and 778 ns in methanol, pentane, and cyclohexane respectively. The lifetime (τ) in cyclohexane-d_{12} is 1754 ns ($\tau D/\tau H=2.44$), demonstrating that the transient reacts with the C–H bonds of the solvent. This notion is consistent with the finding that $\tau=2360$ ns in $CF_2ClCFCl_2$, a solvent devoid of hydrogens. The lifetime of the transient is reduced to 1770 ns in aerated $CF_2ClCFCl_2$.

The relative insensitivity of τ to oxygen demonstrates that the carrier of the transient absorption is not a radical species. It is also likely not a triplet, although we must qualify that surmise until we know more about the steric shielding afforded the radical center by the carborane cage, and in particular the 3,6 pair of hydrogens, which overhang the reactive center. Further, although we see diradical **3** as the most likely source of the transient, and as the active ingredient in the double hydrogen abstraction, we cannot entirely eliminate the closed species **6** at this point. We hope to report on the resolution of this problem in short order.[6]

5





6

The practical opportunities of the photo-induced hydrogen abstraction are obvious, especially given the potential therapeutic utility of molecules such as calicheamicin and the synthetic enediynes. Accordingly, we next investigated the photochemical reaction in supercoiled cyclic DNA (PBR322). Irradiation of a solution of **1** in a TE buffer (40 mM Tris, 4 nM EDTA, pH 7.5) with 10% vol./vol. DMSO with a Rayonet Reactor (350 nm) for 1 h at 37°C led to efficient single strand cleavage.[7] Cleavage of DNA on photolysis of **1** is as efficient as that by any of a host of synthetic enediyne mimics.[8,9] Matteson's synthesis is exceptionally simple, and starts from quite cheap starting materials. The triggering procedure does not depend upon heating or some chemical event, and the abstraction process can be induced at 37°C. Moreover, the reaction is light-initiated, and therefore it seems possible that substantial selectivity in activating this agent should be possible.[10]

It is also important to note that the carborane cage is far from an innocent bystander. Even though it is not directly involved in the chemistry of hydrogen abstraction, it enables diradical character to be expressed by the *o*-quinodimethane portion of **1**. In fact, had **1** been deliberately designed to do what it does (in truth, it was not), much could be made of the cleverness of incorporating the carborane. In **1**, the boron–carbon cage eliminates all of the normal escape routes for *o*-quinodimethanes. Were the carborane not present, **1** would be a simple *o*-xylylene, and would surely close to a benzocyclobutene[11] or possibly dimerize. The long carbon–carbon bond in the cage (1.63 Å in the parent compound,[12]) apparently prevents closure. If the cage carbon–carbon bond were replaced with a normal carbon–carbon bond, a Cope rearrangement would seem certain to ensue.[13] Again, the cage makes the escape route impossible. That cage carbon–carbon bond is no normal two-electron bond, but a participant in the web of three-center, two-electron bonding making up the cage. Although it looks like a normal bond, it is not, and cannot participate in the array of pericyclic reactions available to normal bonds.[14]

Acknowledgements

This work was supported by the National Science Foundation through grant CHE-97-02823. AZB thanks the Council on Science and Technology of Princeton University and the Camille and Henry Dreyfus Foundation Special Grants Program for financial support.

References

1. Matteson, D. S.; Davis, R. A. *Chem. Commun.* **1970**, 669. Matteson, D. S.; Davis, R. A. *Inorg. Chem.* **1974**, *13*, 859. The name is a poor one, as it implies an aromaticity not present in the pendant carbon polyene framework. Nonetheless, the usage does have a history, and we use this name as a tribute to Matteson and Davis, who began the study of such molecules.
2. Wu, S.-H.; Jones Jr., M. *Inorg. Chem.* **1986**, *25*, 4802. Hota, N. K.; Matteson, D. S. *J. Am. Chem. Soc.* **1968**, *90*, 3570.
3. Grissom, J. W.; Gunawardena, G. U.; Klingberg, D.; Huang, D. *Tetrahedron* **1996**, *52*, 6453. Wang, K. K. *Chem. Rev.* **1996**, *96*, 207.
4. Jones, R. R.; Bergman, R. G. *J. Am. Chem. Soc.* **1972**, *94*, 660. Mayer, J.; Sondheimer, F. *J. Am. Chem. Soc.* **1966**, *88*, 603.
5. Kötting, C.; Sander, W.; Kammermeier, S.; Herges, R. *Eur. J. Org. Chem.* **1998**, 799. Sander, W. *Acc. Chem. Res.* **1999**, *32*, 669.
6. We are actively pursuing a synthesis of **6**. Jones, A.; Bradley, A. Z.; Jones Jr., M., unpublished work.
7. Povirk, L. F.; Subker, W.; Johnlein, W.; Hutchinson, F. *Nucleic Acids Res.* **1977**, *4*, 3573. Lloyd, R. S.; Haidle, C. W.; Robberson, D. L. *Biochemistry* **1978**, *17*, 1890.
8. Drak, J.; Iwasawa, N.; Danishefsky, S.; Crothers, D. M. *Proc. Natl. Acad. Sci. USA* **1991**, *88*, 7464.
9. Hirama, M.; Gomobuti, T.; Fujiwara, K. *J. Am. Chem. Soc.* **1991**, *113*, 9851. Nicolaou, K. C.; Schreiner, E. P.; Iwabuchi, Y.; Suzuki, T. *Angew. Chem., Int. Ed. Engl.* **1992**, *31*, 340. Boger, D. L.; Zhou, J. *J. Org. Chem.* **1993**, *58*, 3018. Tokuda, M.; Fujiwara, K.; Gomibuti, T.; Hirama, M.; Uesugi, M.; Suguira, Y. *Tetrahedron Lett.* **1993**, *34*, 669. Semmelhack, M. F.; Gallagher, J. J.; Ding, W.-D.; Krishnamurthy, G.; Babine, R.; Ellestad, G. A. *J. Org. Chem.* **1994**, *59*, 4357. Wittman, M. D.; Kandow, J. F.; Langeley, R. D.; Wyas, D. M.; Rose, W. C.; Solomon, W.; Zein, N. *Bioorg. Med. Chem. Lett.* **1995**, *5*, 1049. Toshima, K.; Ohta, T.; Ohashi, A.; Nakamura, T.; Nakata, M.; Tatsuta, K.; Matsumura, S. *J. Am. Chem. Soc.* **1995**, *117*, 4822. Myers, A. G.; Hammond, M.; Wu, Y.; Xiang, J.-N.; Harrington, P. M.; Kuo, E. Y. *J. Am. Chem. Soc.* **1996**, *118*. 10006. Takahashi, T.; Tanaka, H.; Yamada, H.; Matsumoto, T.; Suguira, Y. *Angew. Chem., Int. Ed. Engl.* **1997**, *36*, 1524. Takahashi, T.; Tanaka, H.; Matsuda, A.; Doi, T.; Yamada, H.; Matsumoto, T.; Sasaki, D.; Sugiura, Y. *Bioorg. Med. Chem. Lett.* **1998**, *8*, 3303. Takahashi, T.; Tanaka, H.; Doi, T.; Yamada, H. *J. Syn. Org. Chem. Jpn.* **1998**, *56*, 987. Dai, W. M.; Fong, K. C.; Lau, C. W.; Zhou, L.; Hamaguchi, W.; Nishimoto, S. *J. Org. Chem.* **1999**, *64*, 682.
10. For a discussion of light-induced therapeutic agents see: *The Economist*, February 13, 1999, p 77, Science and Technology, 'Medical Light-swords.'
11. Roth, W. R.; Biermann, M.; Dekker, H.; Jochems, R.; Mosselman, C.; Hermann, H. *Chem. Ber.* **1978**, *111*, 3892.
12. Ott, J. J.; Gimarc, B. M. *J. Comput. Chem.* **1986**, *7*, 673.
13. For a closely related example, see: DeCamp, M. R.; Levin, R. H.; Jones Jr., M. *Tetrahedron Lett.* **1974**, 3575.
14. Chiang, S.-H.; Chari, S. have made many unpublished attempts to induce such reactions. In one example, heating 1,2-dimethylene-*o*-carborane in the presence of dieneophiles fails to give the slightest amount of cycloaddition product.