JACS
JOURNAL OF THE AMERICAN CHEMICAL SOCIETY
Communication
pubs.acs.org/JACS

Reactivity of a σ,σ,σ,σ-Tetraradical: The 2,4,6-Tridehydropyridine Radical Cation

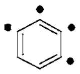
Vanessa A. Gallardo,[‡] Bartłomiej J. Jankiewicz,[†,‡] Nelson R. Vinueza,[‡] John J. Nash,[‡] and Hilkka I. Kenttämaa*,[‡]

[‡]Department of Chemistry, Purdue University, West Lafayette, Indiana 47907, United States

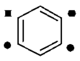
Supporting Information

ABSTRACT: The 2,4,6-tridehydropyridine radical cation, an analogue of the elusive 1,2,3,5-tetradehydrobenzene, was generated in the gas phase and its reactivity examined. Surprisingly, the tetraradical was found not to undergo radical reactions. This behavior is rationalized by resonance structures hindering fast radical reactions. This makes the cation highly electrophilic, and it rapidly reacts with many nucleophiles by quenching the N−C *ortho*-benzyne moiety, thereby generating a relatively unreactive *meta*-benzyne analogue.

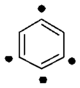
Aromatic carbon-centered σ,σ,σ,σ-tetraradicals are fascinating due to their complex electronic structures, yet they are extremely difficult to study experimentally. The first attempts to generate these species were reported in 1966 by Meyerson.[1] Pyrolysis of 1,2,3,4- and 1,2,4,5-benzenetetracarboxylic dianhydrides was found to yield products that were thought to be derived from the benzdiynes **1** and **2**. About 25 years later, McNaughton detected triacetylene **4**, a possible ring-opening product of benzdiyne **2**, by IR spectroscopy after gas-phase flash vacuum photolysis of 1,2,4,5-benzenetetracarboxylic dianhydride.[2] Photolysis of the same dianhydride in a low-temperature argon matrix was reported by Yabe et al. in 1995 to generate an acyclic reactive species with the molecular formula of C_6H_2, possibly carbene **5**.[3] This carbene was later proposed to form via ring-opening of the benzdiyne **2** and to be the precursor of the final product, **4**.[4]



1

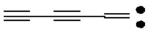


2



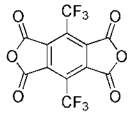
3

4

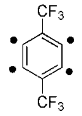


5

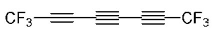
Yabe et al. reported several attempts to generate benzdiynes by photolysis of unsubstituted and substituted benzenetetracarboxylic anhydrides.[4,5] Via IR and UV−Vis spectroscopies, they detected two substituted benzdiynes in 2002.[5a,c] They found that the photolyses of **6** and **9** yielded benzdiynes **7** and **10**, respectively, which upon further irradiation underwent rearrangement to **8** and **11**, respectively. On the basis of these results, they proposed that benzdiyne **2** cannot be observed due to its rearrangement via hydrogen atom migration,[5a] and that substituting the hydrogen atoms with CF_3 groups or F atoms prevents the isomerization. No further information was obtained about their properties.



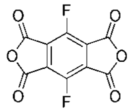
6



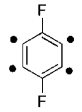
7



8



9



10

11

The first theoretical study on isomeric tetradehydrobenzenes was published shortly after the first attempts to generate these species: in 1969, Hoffman reported on the electronic structures of **1**−**3**, which were examined using extended Hückel theory.[6] Fifteen years later, other computational studies started to appear.[7] In 1986, Radom et al. used *ab initio* molecular orbital theory (CASSCF/3-21G and UHF/6-31G) to study both didehydro- and tetradehydroaromatic systems, among them benzdiynes **1** and **2**.[7d]

Eight years later, Hobza et al. reported MP2/6-31G(d) calculations on the relative stabilities of several strained unsaturated molecules, including **1** and **2**, and noted the possibility of isomerization of **1** to **2**.[7f] In 1999, Yabe et al. calculated the relative stabilities of **1**−**3** by using the CCSD(T)/6-31G(d,p)//CASSCF(4,4)/6-31G(d,p) level of theory. These calculations showed not only that **3** is the most stable isomer but also that **1**−**3** may be able to interconvert under certain conditions.[4] The same year, Schleyer, Schaefer, and collaborators studied the energies and structures of **1**−**3** and **7** by using both *ab initio* methods (e.g., CCSD(T)/TZ2P//CCSD/DZP) and density functional theory.[7c] The following year, Sattelmeyer and Stanton studied nine isomers of C_6H_2, including **1**−**3**, by using high-level *ab initio* methods (e.g., CCSD(T)/cc-pVTZ).[7e] A year later, Yabe and co-workers used both *ab initio* and DFT methods to determine the heats of formation of the three isomeric tetradehydrobenzenes.[7a]

Based on the above studies, **3** is the most stable of the tetradehydrobenzenes, lying 14 kcal/mol below **2** and 7.8 kcal/mol below **1** (G2 level of theory).[7a] The singlet−triplet (S-T) splittings for **1**−**3** were calculated to be 26.3, 18.3, and 37.5 kcal/mol,

Received: September 26, 2011
Published: January 2, 2012

respectively (at the CCSD(T)/TZ2P//CCSD/DZP level of theory).[7c]

In spite of the above extensive research, the chemical properties of tetradehydrobenzenes, or more broadly, any organic σ-type polyradical, are entirely unknown. We report here the first such study on the 2,4,6-tridehydropyridine radical cation, **12**, calculated to have a singlet ($^1A_1$) electronic ground state, with S-T ($^1A_1$−$^3B_2$) and singlet−quintet ($^1A_1$−$^5B_2$) gaps of 31.2 and 109.2 kcal/mol (RHF-UCCSD(T)/cc-pVTZ//UBPW91/cc-pVDZ), respectively, and a vertical electron affinity (EA) of 6.50 eV (UBLYP/aug-cc-pVDZ//UBLYP/cc-pVDZ level of theory). The calculated tetraradical stabilization energies (RHF-UCCSD(T)/cc-pVTZ//UBPW91/cc-pVDZ; Figure 1) indicate that the radical site on C2 strongly destabilizes the system.

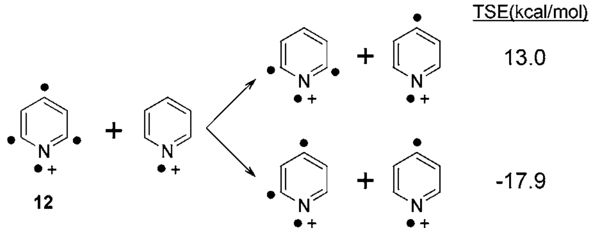
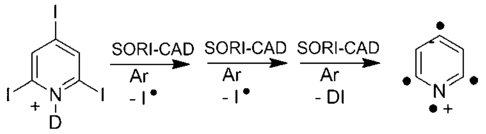


Figure 1. Calculated tetraradical stabilization energies for the ground ($^1A_1$) state of **12**.

Tetraradical **12** was generated by introducing synthesized[8] 2,4,6-triiodopyridine in a heated probe into a dual-cell Fourier-transform ion cyclotron resonance (FT-ICR) mass spectrometer.[9] Chemical ionization with deuterated acetone was used to transfer a deuteron to the molecule to form **13**. Sustained off-resonance irradiation collision-activated dissociation[10] (SORI-CAD) was used to cleave two C−I bonds in the precursor ion in a consecutive manner (Scheme 1). During the third SORI-CAD, loss of an iodine atom (to form the 2,4,6-tridehydropyridinium cation studied previously[8]) and loss of DI were observed. The latter reaction forms tetraradical **12**. **12** was isolated by ejecting all unwanted ions from the cell and allowed to react with several reagents for varying periods of time to determine its reaction products, second-order reaction rate constants (k_{exp}), and reaction efficiencies ($k_{exp}/k_{collision}$, Table 1), as described previously.[11]

Scheme 1. Generation of Tetraradical 12



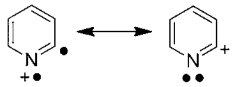
13 **12**

The structure of tetraradical **12** was confirmed by using structurally diagnostic ion−molecule reactions.[8,9] For example, the number of hydrogen atoms abstracted from cyclohexane has been shown to indicate the number of radical sites for related bi- and triradicals.[8] Tetraradical **12** abstracts four hydrogen atoms (Table 1), which supports the presence of four radical sites.

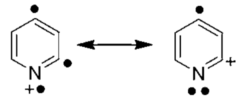
In this paper, the gas-phase reactivity of the tetraradical is compared to those of related, previously unreported biradicals, the 2-dehydropyridine radical cation **14** and the 4-dehydropyridine radical cation **15**, as well as related, previously unreported σ,σ,σ-triradicals, the 2,4-didehydropyridine radical cation **16** and the 2,6-didehydropyridine radical cation **17** (Table 1). The structures of all previously unreported species were confirmed by using structurally diagnostic ion-molecule reactions.[8,9] Based on the reactivity data for **15** (Table 1), about half of the initially formed biradicals undergo a retro-Bergman-type rearrangement to produce an unreactive enediyne during generation. The relatively small calculated activation enthalpy for this reaction (17.8 kcal/mol; UBPW91/cc-pVTZ//UBPW91/cc-pVDZ) supports this hypothesis.

The identities of the radical sites in tetraradical **12** that react first with cyclohexane were probed by examining the reactivity of biradicals **14** and **15**. These biradicals react with cyclohexane by abstraction of a hydride and two hydrogen atoms at similar efficiencies of 70% and 62%, respectively (Table 1). A similar product distribution and reaction efficiency (64%) were also measured for **12**, thus providing no unambiguous information for the sites of initial bond formation. However, when the biradical formed after abstraction of two hydrogen atoms by **12** was isolated and allowed to react with cyclohexane, different reactivity was observed. This product ion abstracts two hydrogen atoms at a low reaction efficiency of 0.02%, reactivity that is essentially identical to that of the 2,4-didehydropyridinium cation (this biradical abstracts[8] two hydrogen atoms from cyclohexane at an efficiency of 0.03%). The other isomers that could be formed upon abstraction of two hydrogen atoms by **12**, biradicals **14** and **15** (Table 1), and the 2,6-didehydropyridinium cation[8] (predominant abstraction of two hydrogen atoms at 39% efficiency), react quite differently. These findings demonstrate that the first two hydrogen atoms abstracted by **12** involve radical sites C2 and N. Hence, **12** behaves like an *ortho*-benzyne. After the first two hydrogen atom abstractions, two additional hydrogen atoms are slowly abstracted by the remaining two radical sites of the *meta*-benzyne moiety.

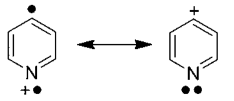
All the radicals discussed above behave differently toward allyl iodide than cyclohexane. Surprisingly, the typical radical reaction observed for allyl iodide, iodine atom abstraction,[8] is slow or not observed at all. For example, biradicals **14** and **15** react with allyl iodide by a fast iodide ion abstraction (Table 1). Slow HI abstraction was also observed. This reaction has been proposed to occur via a nonradical mechanism for related biradicals.[12] The reactivity of **14** and **15** can be understood on the basis of the resonance structures **14a** and **15a** that do not contain radical sites. These resonance structures suggest electrophilic, carbocation-like reactivity, which was observed (iodide ion abstraction). However, for the triradicals **16** and **17**, a radical reaction, iodine atom abstraction, was also observed due to the presence of a (formally) unpaired electron in all resonance structures, including **16a** and **17a**.



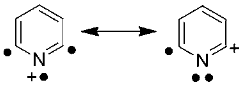
14 **14a**



16 **16a**



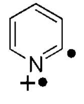
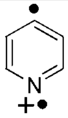
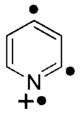
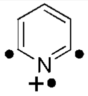
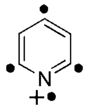
15 **15a**



17 **17a**

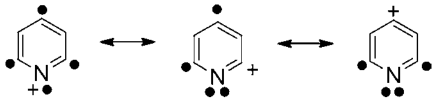
Tetraradical **12** shows no radical reactions with allyl iodide. This may be explained by resonance structures **18** and **19**, which are related to the resonance structures discussed above for the bi- and triradicals. The coupling of the radical sites in the *meta*-

Table 1. Reaction Efficiencies[a] and Product Branching Ratios[b]

radical	cyclohexane	allyl iodide	dimethyl disulfide
 **14** **EA**[c] = 6.80 eV **S/T gap**[d] = -58.0 kcal/mol	H^- abs **52%** 2 x H abs **48%** **I**[e] **23% (8%)** **Efficiency = 70%**	I^- abs **55%** *(2°) H^+ trns* C_3H_4 abs **27%** HI abs **18%** **Efficiency = 65%**	$HSCH_3$ abs **83%** SCH_2 abs **14%** SCH_3 abs **3%** **Efficiency = 100%**
 **15** **EA** = 7.57 eV **S/T gap** = -23.5 kcal/mol	H^- abs **83%** 2 x H abs **17%** **UI**[f] ***47%*** **Efficiency = 62%**	I^- abs **81%** *(2°) H^+ trns* C_3H_4 abs **10%** HI abs **9%** **I**[e] **58% (4%)** **Efficiency = 61%**	e^- abs **51%** *(2°) SCH_3 abs* $HSCH_3$ abs **18%** SCH_3 abs **12%** *(2°) $SSCH_3$ abs* $SSCH_3$ abs **10%** SCH_2 abs **9%** **I**[e] **55% (4%)** **Efficiency = 80%**
 **16** **EA** = 8.13 eV **D/Q gap** = -56.4 kcal/mol	H^- abs **76%** 2 x H abs **24%** *(2°) H abs* **Efficiency = 71%**	C_3H_4 abs **35%** CH_2 abs **24%** *(2°) C_3H_4 abs* I abs **23%** *(2°) C_3H_4 abs* *(2°) HI abs* I^- abs **12%** C_3H_5 abs **6%** **Efficiency = 81%**	e^-abs **52%** SCH_3 abs **32%** *(2°) SCH_2 abs* *(2°) $HSCH_3$ abs* $HSCH_3$ abs **16%** *(2°) SCH_3 abs* **Efficiency = 95%**
 **17** **EA** = 7.49 eV **D/Q gap** = -69.4 kcal/mol	H^- abs **53%** H abs **24%** 2 x H abs **23%** **UI**[f] ***81%*** **Efficiency = 85%**	C_3H_5 abs **72%** CH_2 abs **11%** *(2°) C_3H_4 abs* I abs **10%** *(2°) HI abs* e^- abs **7%** **Efficiency = 47%**	e^- abs **97%** *(2°) SCH_3 abs* SCH_3 abs **3%** **Efficiency = 100%**
 **12** **EA** = 6.50 eV **S/T gap** = -31.2 kcal/mol	H^-abs **87%** 2 x H abs **13%** *(2°) 2 x H abs* **I**[e] ***27%*** **(18%)** **Efficiency = 64%**	CH_2 abs **48%** *(2°) I abs* *(2°) CH_2 + H abs* *(2°) C_3H_5 abs* C_3H_4 abs **20%** *(2°) I abs (3°) I abs* *(2°) C_3H_4 abs* *(2°) C_3H_5 abs* I^- abs **21%** *(2°) H^+ trns* CH_2 + H abs **11%** *(2°) CH_2 + H abs* **Efficiency = 67%**	e^- abs **69%** *(2°) SCH_3 abs* SCH_3 abs **10%** SCH_2 abs **8%** $SSCH_3$ abs **3%** Unknown **10%** (m/z 97) **Efficiency = 96%**

[a] Reaction efficiency[9,11d] (% of collisions leading to reaction) = $k_{\text{reaction}}/k_{\text{collision}} \times 100$; precision ±10%; accuracy ±50%. [b] abs = abstraction; trans = transfer; branching ratios in bold, precision ±10%; secondary (2°) and tertiary (3°) products in italics under the reaction(s) that produce them. [c] Electron affinities calculated at the UBLYP/aug-cc-pVDZ//UBLYP/cc-pVDZ level of theory. Note that we are calculating the EA of the radical sites, not the EA of the molecules. [d] S-T and D-Q gaps calculated at the RHF-UCCSD(T)/cc-pVTZ//UBPW91/cc-pVDZ level of theory. A negative value means that the singlet (doublet) state lies below the triplet (quartet) state. [e] I = isomer; relative abundance in italics, reaction efficiency in parentheses. [f] UI = unreactive isomer; relative abundance in italics.

benzyne moieties in these resonance structures is expected to hinder fast radical reactions.

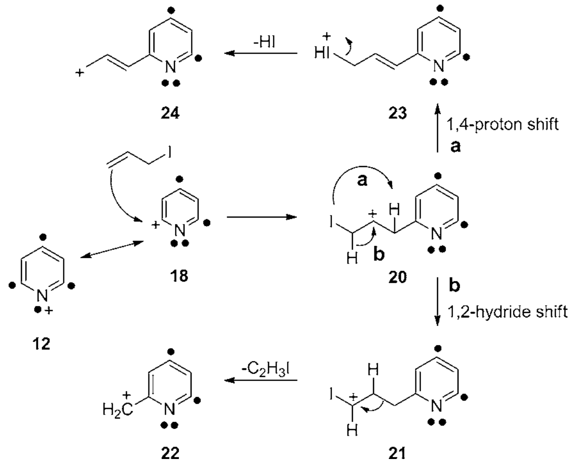


12 **18** **19**

Unexpectedly, CH_2 abstraction is the major reaction (48%) for **12** with allyl iodide (Table 1). A possible mechanism is shown in Scheme 2. Nucleophilic attack by the carbon−carbon double bond of allyl iodide at the most electron-deficient carbon atom in **18** yields the adduct **20**. A subsequent 1,2-hydride shift produces **21**, which loses vinyl iodide to yield the CH_2 abstraction product. This reaction occurs faster than elimination of HI, which likely occurs via a 1,4-proton transfer to yield **23**, which then loses HI to form **24** (the allene (C_3H_4) abstraction product).

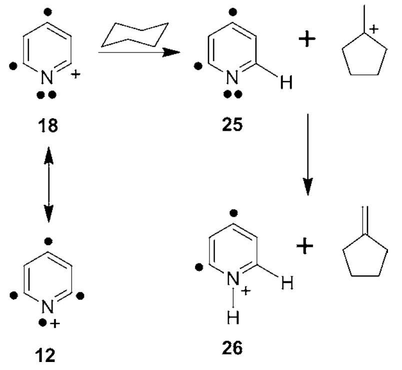
The third reagent examined, dimethyl disulfide, has a relatively low ionization energy (8.2 eV).[13] Hence, electron abstraction by the radicals dominates for most reactions. In addition, all the radicals react by CH_3S abstraction, as expected.[12] The CH_3S abstraction is the only reaction observed for the tetraradical that involves a homolytic bond cleavage in the initially formed adduct. The weakness of the S−S bond explains this observation.

Scheme 2. Major Reactions of Tetraradical 12 with Allyl Iodide



The above results inspired us to take a second look at the reactions of **12** with cyclohexane. The initial assumption of two hydrogen atom abstractions by **12** from cyclohexane is likely not correct since **12** does not react with allyl iodide by iodine atom abstraction. Further, hydride abstraction is the major reaction for **12** upon interaction with cyclohexane (as well as for **14**−**17**; Table 1). Instead, the formal abstraction of two hydrogen atoms likely occurs by hydride abstraction by C2 of **12** to yield **25** (Scheme 3), followed by proton transfer from the methylcyclopentyl cation, a rearrangement product of the initially formed cyclohexyl cation.[14]

Scheme 3. Reaction of Tetraradical 12 with Cyclohexane



In conclusion, the 2,4,6-tridehydropyridine radical cation **12** was successfully generated. The first bond formation in **12** occurs at C2 via nucleophilic addition, which quenches the C−N *ortho*-benzyne moiety. This reactivity can be explained by considering resonance structures of **12** that hinder radical reactions.

Experimental Details. The 2- and 4-iodopyridine precursors for **14** and **15** were purchased from Sigma-Aldrich and used as received. The diiodo precursors for **16**[15] and **17**[16] and the triiodo precursor for **12**[12] were synthesized using reported methods. The experiments were carried out in an FT-ICR mass spectrometer as reported earlier.[9] SORI-CAD[10] was used to cleave iodine atoms or H(D)I from protonated/deuterated radical precursors. Molecular orbital calculations were carried out with the Gaussian 98[17] and Molpro[18] electronic structure program suites.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

Cartesian coordinates, electronic and zero-point vibrational energies, 298 K thermal contributions and derived enthalpies, and complete refs 17 and 18. This material is available free of charge via the Internet at http://pubs.acs.org.

■ AUTHOR INFORMATION

Corresponding Author

hilkka@purdue.edu

Present Address

†Institute of Optoelectronics, Military University of Technology, Ul. Gen. Sylwestra Kaliskiego, 2, 00-908 Warsaw, Poland

■ ACKNOWLEDGMENTS

This material is based upon work supported by the National Science Foundation under Grant No. 103762.

■ REFERENCES

(1) Fields, E. K.; Meyerson, S. *J. Org. Chem.* **1966**, *31*, 3307−3309.

(2) McNaughton, D.; Bruget, D. N. *J. Mol. Spectrosc.* **1991**, *150*, 620−634.

(3) Moriyama, M.; Ohana, T.; Yabe, A. *Chem. Lett.* **1995**, *24*, 557−558.

(4) Moriyama, M.; Sato, T.; Uchimaru, T.; Yabe, A. *Phys. Chem. Chem. Phys.* **1999**, *1*, 2267−2274.

(5) (a) Moriyama, M.; Ohana, T.; Yabe, A. *J. Am. Chem. Soc.* **1997**, *119*, 10229−10230. (b) Moriyama, M.; Yabe, A. *Chem. Lett.* **1998**, *27*, 337−338. (c) Sato, T.; Arulmozhiraja, S.; Niino, H.; Sasaki, S.; Matsuura, T.; Yabe, A. *J. Am. Chem. Soc.* **2002**, *124*, 4512−4521. (d) Sato, T.; Niino, H.; Yabe, A. *J. Am. Chem. Soc.* **2003**, *125*, 11936−11941.

(6) Adam, W.; Grimison, A.; Hoffmann, R. *J. Am. Chem. Soc.* **1969**, *91*, 2590−2599.

(7) (a) Arulmozhiraja, S.; Sato, T.; Yabe, A. *J. Comput. Chem.* **2001**, *22*, 923−930. (b) Arulmozhiraja, S.; Sato, T.; Yabe, A. *J. Org. Chem.* **2003**, *68*, 5084−5090. (c) Bettinger, H. F.; Scheleyer, P. v. R.; Schaefer, I. H. F. *J. Am. Chem. Soc.* **1999**, *121*, 2829−2835. (d) Radom, L.; Nobes, R. H.; Underwood, D. J.; Li, W.-K. *Pure Appl. Chem.* **1986**, *58*, 75−78. (e) Sattelmeyer, K. W.; Stanton, J. F. *J. Am. Chem. Soc.* **2000**, *122*, 8220−8227. (f) Zahradnik, R.; Hobza, P.; Burcl, R.; Hess, J. B. A.; Radziszewski, J. G. *J. Mol. Struct. (Theochem)* **1994**, *313*, 335−349.

(8) Jankiewicz, B. J.; Adeuya, A.; Yurkovich, M. J.; Vinueza, N. R.; Gardner, S. J. III; Zhou, M.; Nash, J. J.; Kenttämaa, H. I. *Angew. Chem., Int. Ed.* **2007**, *46*, 9198−9201.

(9) (a) Price, J. M.; Kenttämaa, H. I. *J. Phys. Chem.* **2003**, *107*, 8985−8995. (b) Thoen, K. K.; Kenttämaa, H. I. *J. Am. Chem. Soc.* **1999**, *121*, 800−805.

(10) Gauthier, J. W.; Trautman, T. R.; Jacobson, D. B. *Anal. Chim. Acta* **1991**, *246*, 211−225.

(11) (a) Amegayibor, F. S.; Nash, J. J.; Lee, A. S.; Thoen, J.; Petzold, C.; Kenttämaa, H. I. *J. Am. Chem. Soc.* **2002**, *124*, 12066−12067. (b) Nash, J. J.; Kenttämaa, H. I.; Cramer, C. J. *J. Phys. Chem. A* **2006**, *110*, 10309−10315. (c) Nelson, E. D.; Li, R.; Kenttämaa, H. I. *Int. J. Mass Spectrom.* **1999**, *185*−*187*, 91−96. (d) Su, T.; Chesnavich, W. J. *J. Chem. Phys.* **1982**, *76*, 5183−5185.

(12) Jankiewicz, B. J.; Reece, J. N.; Vinueza, N. R.; Nash, J. J.; Kenttämaa, H. I. *Angew. Chem., Int. Ed.* **2008**, *47*, 9860−9865.

(13) Leeck, D. T.; Kenttämaa, H. I. *Org. Mass Spectrom.* **1994**, *29*, 106−107.

(14) Wesdemiotis, C.; Wolfschutz, R.; Schwarz, H. *Tetrahedron* **1979**, *36*, 275−278.

(15) Yutaka, Y.; Akihiko, Y. *Chem. Pharm. Bull.* **1982**, *30*, 1731−1737.

(16) Newkome, G. R.; Moorfield, C. N.; Sabbaghian, B. *J. Org. Chem.* **1986**, *51*, 953−954.

(17) Frisch, M. J.; et al. *Gaussian 03*, revision D.01; Gaussian, Inc.: Pittsburgh, PA, 2003.

(18) Werner, H. J.; et al. *MOLPRO*, version 2008.1, a package of ab initio programs.