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Generation and trapping of an unsymmetrical, caged pyramidalized alkene

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Abstract

Low-temperature reaction of 2,5-diiodopentacyclo[5.3.0.0^{2,5}.0^{3,9}.0^{4,8}]decane (**7**) with MeLi in dry THF results in elimination of I_2 with concomitant formation of the corresponding caged alkene, **8**. This highly strained pyramidalized alkene is trapped stereoselectively by 1,3-diphenylisobenzofuran (DPIBF) to afford a single [4+2] cycloadduct, **9b**. The corresponding reaction of **8** with 9-methoxyanthracene proceeds with relatively low regioselectivity. The origins of these phenomena have been investigated computationally. © 1999 Elsevier Science Ltd. All rights reserved.

1. Introduction

There is considerable current interest in the synthesis and chemistry of pyramidalized alkenes, which constitute a new class of theoretically interesting 'unnatural products'.[1] Many of the species of this type that have been synthesized and trapped in situ contain highly strained cyclopropene,[2] cyclobutene,[3] or cyclopentene[4] rings that are part of a more complex polycarbocyclic framework. The vast majority of polycyclic pyramidalized alkenes that have been synthesized possess a twofold $\pm x$ symmetry element (usually a mirror plane) that lies perpendicular to and bisects the C=C bond axis (as in, e.g. **1**,[2a,2b] **2**,[3a,3c] **3**,[2c] and **4**;[2d] the $\pm x$ mirror symmetry element is illustrated for **3** in Scheme 1). Some species of this type display higher symmetry and contain both $\pm x$ and $\pm y$ reflection symmetry elements [e.g., 'cubene' (**5**),[3b] Scheme 1). Herein, we describe the synthesis of an unsymmetrical, cage-annulated, highly pyramidalized alkene whose transient existence is inferred by the results of intermolecular trapping experiments that have been performed in situ by using various dienes.

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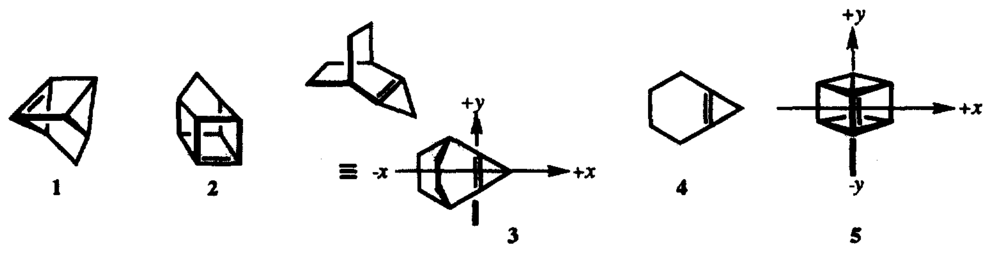
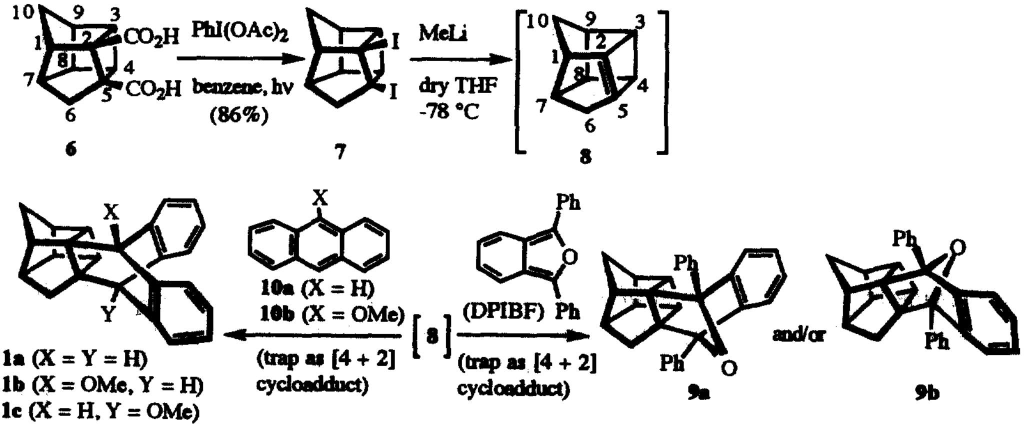


Scheme 1.

2. Experimental results

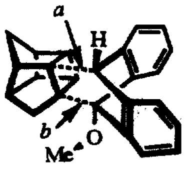
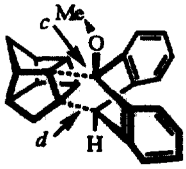
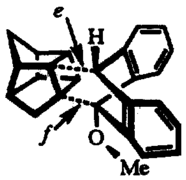
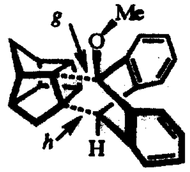
Pentacyclo[5.3.0.0^{2,5}.0^{3,9}.0^{4,8}]decane-2,5-dicarboxylic acid (**6**, Scheme 2)[5,6] was synthesized from 'Thiele's ester'.[7] Iododecarboxylation[8] of **6** afforded **7** in 86% yield. Subsequent reaction[3d,9] of **7** with MeLi in dry THF at −78°C resulted in the formation of the corresponding pentacyclo[5.3.0.0^{2,5}.0^{3,9}.0^{4,8}]dec-2(5)-ene, **8**. In the presence of DPIBF, caged alkene intermediate **8** was trapped as the corresponding Diels–Alder cycloadduct in 60% yield. This reaction conceivably could afford either (or both) of two stereoisomeric adducts (i.e., **9a** and/or **9b**). However, in our hands, only one Diels–Alder adduct was thereby obtained;[10] careful inspection of the ^{1}H and ^{13}C NMR spectra of the crude reaction product indicated the absence of a second [4+2] cycloadduct. The structure of the reaction product, **9b**, was established unequivocally via application of X-ray crystallographic methods.[11a]



Scheme 2.

The reaction of **8** with MeLi, when performed in the presence of anthracene (**10a**), afforded **11a** (Scheme 2) in 34% yield. The corresponding reaction of **8** with MeLi, when performed in the presence of 9-methoxyanthracene (**10b**), conceivably could afford either (or both) of two regioisomeric adducts (i.e., **11b** and/or **11c**). In our hands, *both* Diels–Alder cycloadducts were obtained in 45% yield (product ratio ca. 60:40). The structure of the minor product, **11b**, was established unequivocally via application of X-ray crystallographic methods.[11b]

Table 1
Results of ab initio transition state calculations for Diels–Alder cycloaddition of **8** to 9-methoxy-anthracene (**10b**)

	 **12a**	 **12b**	 **12c**	 **12d**
Relative energy (kcal-mol^{-1})	0.0	0.9,[i] 0.3[ii]	2.4,[i] 2.0[ii]	2.2,[i] 2.0[ii]
Bond lengths in transition state (Å)	*a*: 2.374 *b*: 2.768	*c*: 2.760 *d*: 2.377	*e*: 2.478 *f*: 2.583	*g*: 2.507 *h*: 2.551

Relative energy calculations: [i]HF/3-21G; [ii]B3LYP/6-31G*

3. Results of quantum chemical calculations[12–14]

3.1. Diels–Alder cycloaddition of 8 to DPIBF

The length of the C(2)=C(5) double bond in pyramidalized alkene **8** is calculated at the HF/6-31G* level of theory to be 1.345 Å. The results of these calculations also indicate that both sp^2-hybridized carbon atoms are strongly pyramidalized; the calculated pyramidalization angles at C(2) and C(5) are 45.7° and 46.4°, respectively. Next, ab initio transition states for Diels–Alder cycloaddition of **8** to two model dienes, i.e., furan and 2,5-dimethylfuran, were located at the HF/3-21G and HF/6-31G* levels of theory. The results thereby obtained indicate that these transition states proceed in concerted fashion but are slightly *asynchronous* in nature. The transition states which are analogous to that which leads to the formation of cycloadduct **9b** are favored energetically by 0.7 (3-21G) and 1.1 kcal mol^{-1} (6-31G*) for furan and by 1.3 (3-21G) and 1.9 kcal mol^{-1} (6-31G*) for 2,5-dimethylfuran, respectively.

In order to examine potential temperature effects, free energies of activation ($\Delta G^{\neq}$) have been calculated at the HF/3-21G level of theory for Diels–Alder cycloaddition of furan to **8** at different temperatures (i.e., 298 K, 273 K, and 195 K). The calculated $\Delta G^{\neq}$ values obtained at these temperatures suggest that the formation of the transition state that is analogous to that which leads to the formation of **9b** is favored by 0.7–0.8 kcal mol^{-1}.

3.2. Diels–Alder cycloaddition of 8 to 9-methoxyanthracene (10b)

Relevant Diels–Alder transition states for [4+2] cycloaddition of **8** to **10b** have been located at the HF/3-21G level of theory. In addition, single point calculations have been carried out at the B3LYP/6-31G* level of theory[14] by using HF/3-21G minimized geometries. The effect of reorientation of the OMe group in **10b** on transition state energetics, two possible C(9)–OMe rotational isomers have been considered for each of the two possible modes of [4+2] cycloaddition (see structures **12a–12d** in Table 1).

The results of HF/3-21G transition state calculations shown in Table 1 indicate that **12a** is preferred over the other transition states; indeed, this is one of the two transitions states considered in Table 1 (i.e., **12a** and **12c**) that leads to the formation of the observed major reaction product, **11c**. All four calculated transition states, **12a–12d**, are predicted to be concerted but asynchronous in nature. The orientation of the C(9)–OMe bond appears to have a significant effect upon the relative stabilities of the transition states. In the case of transition states **12a** and **12b** in which the C(9)–OMe bond is oriented *toward* the cage moiety, there appears to be a clear-cut energetic preference for **12a**. However, there is no clear corresponding preference for the case of transition states **12c** and **12d** in which the C(9)–OMe bond is oriented *away from* the cage moiety. Indeed, the energy differences between **12a** vs **12c** and **12b** vs **12d** are competitive with (or may even override) the observed ca. 60:40 regiochemical preference for Diels–Alder cycloaddition of **8** to **10b** which slightly favors formation of **11c** over **11b**.

4. Summary and conclusions

Low-temperature reaction of 2,5-diiodopentacyclo[5.3.0.0^{2,5}.0^{3,9}.0^{4,8}]decane (**8**) with MeLi in dry THF affords the corresponding caged alkene, **8**. When DPIBF is employed as diene to trap **8** in situ, the resulting [4+2] cycloadduct is formed stereoselectively. However, the corresponding reaction of **8** with 9-methoxyanthracene proceeds with relatively low regioselectivity to afford a mixture of two [4+2] cycloadducts, **11c** and **11b** (product ratio **11c**:**11b**=60:40). The results of ab initio molecular orbital calculations suggest that the Diels–Alder transition states are concerted but slightly asynchronous in nature; the computational results provide qualitative support for our experimental results.

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10. Formation of only one of two possible stereoisomeric [4+2] cycloadducts was also reported to result via in situ intermolecular trapping of **3**[2c] and **4**[2d] by DBIPF.

11. (a) Selected X-ray crystallographic data for **9b** ($C_{30}H_{24}O$): Space group: $P2_12_12_1$; a=11.25 (1) Å; b=17.59 (1) Å; c=10.69 (1) Å; V=2114 (3) Å^3; Z=4; μ=0.74 cm^{-1}; D_{calc}=1.26 gcm^{-3}; R=0.066; R_w=0.056. (b) Selected X-ray crystallographic data for **11b** ($C_{25}H_{22}O$): Space group: $P2_12_12_1$; a=9.984 (2) Å; b=24.190 (4) Å; c=6.270 (4) Å; V=1755.8 (7) Å^3; Z=4; μ=5.85 cm^{-1}; D_{calc}=1.28 gcm^{-3}; R=0.063; R_w=0.057. A complete description will be given in the full paper.
12. Ab initio calculations were performed by using Gaussian 94.[13] Diels–Alder transition states were generally located at the HF/3-21G level of theory. Whenever practical, calculations were repeated by using a larger basis set (HF/6-31G*). In addition, single-point calculations were performed at the B3LYP hybrid HF-DFT level of theory by using 3-21G basis sets.[14] Complete vibrational analyses were performed at the same levels of theory in order to characterize the transition states.
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