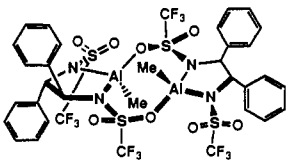

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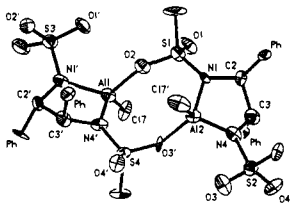
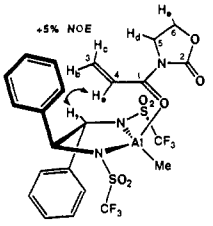


5 (TELP plot)

structure **5**, the monomeric subunits are joined by Lewis acid-base association of a sulfonyl oxygen with aluminum to form an 8-membered ring consisting of two Al-N-S-O sequences joined head to tail. The S(1)-O(2) and S(4)-O(3′) bond lengths (ca. 1.46 Å) indicate extensive double-bond character for the S-O bonds in the 8-membered ring. The nitrogen atoms have sp^2 geometry. The ^1H NMR spectrum of a solution of the catalyst in CD_2Cl_2 at 23 °C is also consistent with the dimeric structure **5**; two $AlCH_3$ peaks appear at δ −0.32 and −0.54, and four benzylic C-H peaks appear at δ 4.82, 4.85, 4.88, and 5.24. The ^{13}C NMR spectrum in CD_2Cl_2 provides further support for the dimeric structure of **5** with benzylic carbon peaks at δ 72.2, 67.7, and 66.9 and four peaks for the attached aromatic (ipso) carbons at δ 138.5, 139.9, 140.4, and 140.8, as well as four different overlapping CF_3 quartets. As indicated below, the addition of 1 equiv of dienophile **2** to the catalyst results in the total conversion to a new species as shown by the appearance of new NMR peaks due to a 1:1 complex of dienophile **2** and monomeric catalyst **3**, the structure of which is indicated by the NMR data.

The dienophile **2** is monocoordinated to aluminum in the 1:1 complex at the *acryloyl oxygen*, as depicted in **6** and as revealed clearly by the ^1H and ^{13}C NMR data listed (for CD_2Cl_2 solution at 23 °C). Especially noteworthy are the downfield shifts on complexation for C_1 and C_3 and for H_b and H_c and the lack of the same for the oxazolidinone moiety.[5]

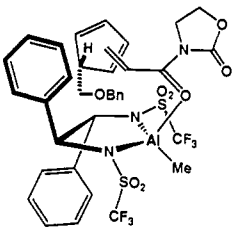


6

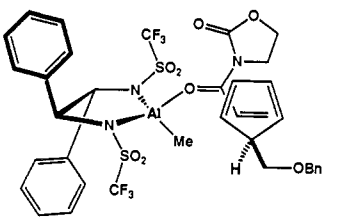
	^1H NMR (δ; Hz)		^{13}C NMR (δ)	
	2	6	2	6
	H_a 7.45	H_a 7.74	C_1 165.1	C_1 172.8
	H_b 5.87	H_b 6.60	C_2 153.8	C_2 150.7
	H_C 6.49	H_C 7.15	C_3 131.4	C_3 144.3
	J_{ab} =8.6	J_{ab} =13.6	C_4 127.5	C_4 127.4
	J_{ac} = 15.2	J_{ac} = 21.3	C_5 42.9	C_5 44.3
	J_{bc} = 1.8	J_{bc} < 1	C_6 62.7	C_6 63.7
	H_d 4.03	H_d 4.25		
	H_e 4.40	H_e 4.38		

In the ^1H NMR spectrum of the 1:1 complex (CD_2Cl_2, 23 °C) there is a single $AlCH_3$ peak at δ −0.19 and two benzylic CH peaks at δ 5.13 and 4.76. In addition, there is a 5% positive NOE enhancement between the benzylic H_f (δ = 4.76) and H_a of the acryloyl subunit. These data support the geometry shown in **6** for the 1:1 complex of **2** and **3**, which presumably is the reactive species in the catalyzed Diels-Alder process. The ^{13}C NMR data for the diazaaluminolidine moiety of the complex are consistent with this formulation; there are two benzylic carbon peaks (δ 68.7 and 67.6), two peaks due to the attached aromatic carbons (δ 141.6 and 140.9), and two overlapping quartets due to the CF_3 carbons (center at δ 120).

Expression **6** for the complex of catalyst and activated dienophile strongly suggests that the transition-state assembly for the formation of Diels-Alder adduct **4** is that shown in **7**, which is uniquely consistent with the X-ray and NMR results and also the absolute configuration of the reaction product. Although the three-dimensional assembly **8** which was suggested earlier[1] cannot be ruled out, it is out of harmony with the ^1H NOE data for **6**. In structure **7** it is necessary that the two O_2S-CF_3 bonds project away from the same face of the diazaaluminolidine ring to make room for the approaching diene. One of the phenyl substituents then plays the crucial role of shielding one face of the *s-trans*-acryloyl subunit from attack by the diene. A structure analogous to **7** is capable of explaining the enantioselective Diels-Alder addition of cyclopentadiene to menthyl acrylate under catalysis by **3**.[1,6]



7



8

(5) The carbonyl carbons in the 1:1 complex were assigned using coupled ^1H-^{13}C NMR measurements. The acryloyl carbonyl (C_1) was identified by long-range couplings to the vinylic protons.

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Boron Analogs of Cyclopropenium Cation: $B_3H_6^+$, the First Three-Membered Nonplanar 2π Aromatic

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The nonplanar structure of cyclobutadiene dication came as a revelation to chemists; 2π aromaticity no longer requires planarity.[1] The neutral boron analog, 1,3-diborocyclobutadiene, has been structurally characterized.[2] The isoelectronic boron analogs of the cyclopropenyl cation, the smallest 2π aromatic ring, **1**,[3] are C_2BH_3 (**2**, C_{2v}),[4] CB_2H_4 (**3**, C_{2v}),[5] B_3H_5 (**4**, C_{2v}),[6] and $B_3H_6^+$ (**5**, D_{3h}). We present here theoretical results to show that **2**-**4** are indeed planar and aromatic but **5** represents a transition state. A nonplanar aromatic structure (**6**, C_{3v}) is found to be a minimum. There are interesting implications to this observation in areas as different as polylithium compounds and metallaboranes. Isomers of **1**-**5** which lie close in energy are also studied here.

Ab initio MO theory at the 6-31G*,[7] MP2/6-31G*,[8] and QCISD(T)/6-31G*[9] levels is used in this study.[10] Unless oth-

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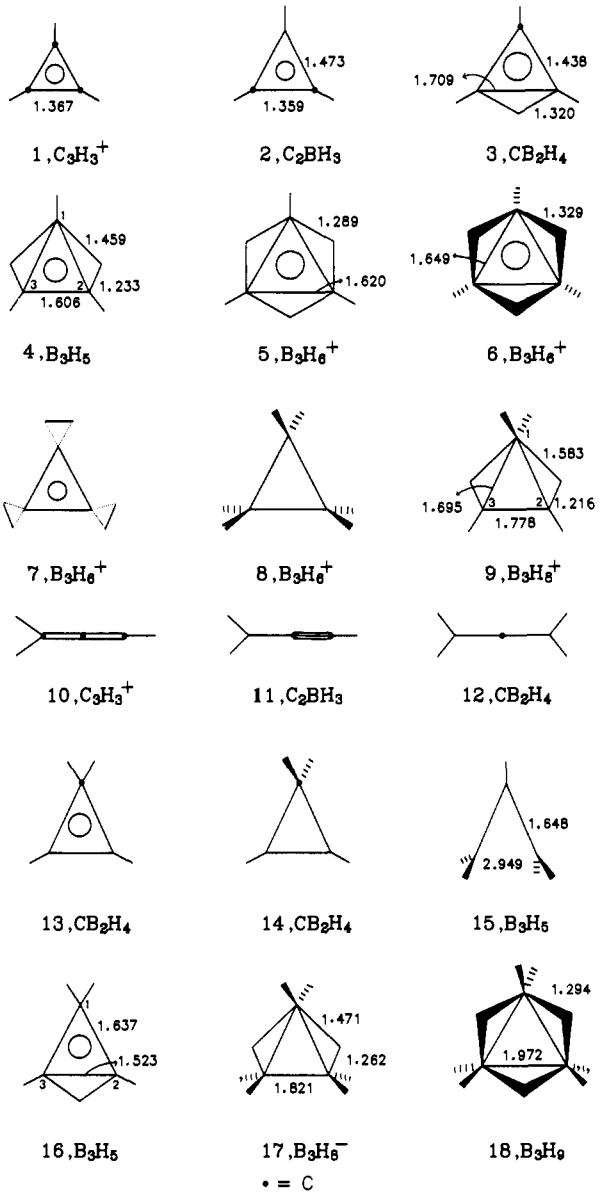

erwise stated, all structures and energy comparisons are made at the MP2/6-31G* level. Structures **1–5** were optimized initially at the 6-31G* level. A frequency analysis showed **1–4** to be true minima and **5** to be a transition state. Optimization along the distortion coordinate of **5** led to **6**, calculated to be a minimum, 61.7 kcal/mol below **5** at the 6-31G* level (42.0 and 44.7 kcal/mol at MP2/6-31G* and QCISD(T)/6-31G* levels). The bridging hydrogens are 0.678 Å above the B_3 plane and the terminal hydrogens 0.385 Å below the B_3 plane. The nearest D_{3h} minimum of the $B_3H_6^+$ isomers corresponds to the interaction of B_3^+ with three H_2 molecules, **7** (D_{3h}), 124.5 kcal/mol higher in energy than **6**. Two other structures, **8** and **9**, with three and one negative frequencies at the 6-31G* level were not considered further. These results are in direct contrast to the structures and energies of isomers of **1–4**.

The cyclic isomers **1–4** are calculated to be more stable than their acyclic counterparts **10–12** and **15** (Table I). Among these, the results on isomers of **4** alone are contrary to previous studies.[6] One of the criteria used in judging the degree of aromaticity is the shortening and lengthening of bonds in comparison to standard single- and double-bond lengths.[11b] Structures **1–4** are aromatic according to this criterion. For example, the C–B distance as well as the bridged B–B distance in **3** is considerably shorter than that found in **17**.[11-13] The anti-van't Hoff 2π aromatic structure **13** and the van't Hoff structure[5b] **14** are not minima. A description of the bonding in **5** is familiar in terms of the Walsh orbitals of B_3H_3 and the MOs of H_3^+.[14] The degenerate MOs of the H_3^+ find a profitable three-orbital interaction. The totally symmetric MO of H_3^+ has only two choices to interact on the B_3H_3 side. The first one corresponds mainly to the symmetric combination of the BH bond orbitals and is not effective in its interaction with H_3^+. The second one arises as the symmetric combination of the three B–B bonds and leads to a moderately stable bonding combination with the H_3^+ orbital. The corresponding antibonding combination is the LUMO in **5**. The HOMO is the expected π MO. Under the C_{3v} symmetry the HOMO and LUMO mix, resulting in a dramatic stabilization of the HOMO (3.0 eV). There is enhanced π delocalization (six-orbital ribbon; three from B_3 π and three from the all-bonding combination of the three hydrogens) in **6**.

A more general way of looking at the preference of **6** over **5** involves the steric congestion brought about by the third bridging hydrogen. The formally nonbonding H_t–H_b distances in **3** (2.026 Å) and **4** (2.013 Å) are decreased to 1.882 Å in **5**. This is an unusually short H–H nonbonded distance.[15] Structure **6** is an attempt to increase this distance to 2.093 Å. Similar distortions should be seen in the 4π and 6π ligands, B_4H_8 and $B_5H_{10}^-$.[16] **6**

Table I. Total Energies (hartrees) and Relative Energies (kcal/mol) for the Structures Studied

structure no. (symmetry)	total energy HF/6-31G*// HF/6-31G*	total energy MP2/6-31G*// MP2/6-31G*	rel energy[a] MP2/6-31G* (QCISD(T)/6-31G*)
1 (D_{3h})[b]	−115.007 02	−115.363 65	0.0
10 (C_{2v})[b]	114.951 10	−115.311 30	31.2
2 (C_{2v})	−102.102 40	−102.435 39	0.0
11 (C_{2v})	−102.089 07	−102.420 45	7.4
3 (C_{2v})	−89.511 86	−89.814 81	0.0
12 (D_{2h})	−89.473 81	−89.741 48	42.8
13 (C_{2v})	−89.452 25	−89.759 73	33.3
14 (C_{2v})	−89.447 87	−89.729 83	50.8
4 (C_{2v})	−76.865 11	−77.148 40	0.0 (0.0)[c]
15 (C_{2v})	−76.882 21	−77.109 84	21.9 (16.7)
16 (C_{2v})	−76.867 27	−77.146 94	1.3 (0.5)
6 (C_{3v})	−77.193 51	−77.459 69	0.0 (0.0)[d]
5 (D_{3h})	−77.092 89	−77.390 40	42.0 (44.7)
7 (D_{3h})	−76.945 39	−77.254 64	124.5
8 (D_{3h})	−77.095 79		
9 (C_{2v})	−77.168 65	−77.412 22	26.6
18 (C_{3v})	−79.183 52	−79.485 13	
C_3H_6 (D_{3h})	−117.058 53[e]	−117.462 85	
B_2H_6 (D_{2h})	−52.812 40[e]	−53.002 28[f]	
B_2H_2 ($D_{\infty h}$)	−50.384 11[e]	−50.507 33	

[a] Including zero-point vibrational energy correction after scaling by 0.89. [b] Reference 3. [c] Corresponding total energy is −77.178 40 au. [d] Corresponding total energy is −77.494 83 au. [e] Reference 20. [f] Reference 12a.

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should prove to be a versatile 2π ligand. An isolobal analog, $[(CO)_3Fe]_3(\mu\text{-}H)_3CR$, is well-known.[17] Other instances where a planar skeleton distorts under the strain of bridging groups must exist. Recently Schaefer and Xie had suggested a hexabridged D_{6h} structure for C_6Li_6.[18] It is unlikely that higher analogs of these would prefer D_{nh} structures.[19]

The $B_3H_6^+$ (**6**) is a highly favored ion. Equations 1 and 2 compare the extra stability of **6** against the cyclopropenium ion, **1**. It should be possible to observe $B_3H_6^+$ experimentally.

$$2B_3H_6^+ + 2C_3H_6 \rightarrow 2C_3H_3^+ + 3B_2H_6 \qquad \Delta E = 58.70 \text{ kcal/mol} \quad (1)$$

$$B_3H_6^+ + C_3H_6 \rightarrow C_3H_3^+ + B_3H_9 \qquad \Delta E = 41.59 \text{ kcal/mol} \quad (2)$$

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Supplementary Material Available: Table of geometric parameters of structures **1-18** at the HF/6-31G*, MP2/6-31G*, and QCISD(T)/6-31G* levels (3 pages). This supplementary material is provided in the archival edition of the journal, which is available in many libraries. Alternatively, ordering information is given on any current masthead page.

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Cylindrospermopsin: A Potent Hepatotoxin from the Blue-Green Alga *Cylindrospermopsis raciborskii*

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Hepatoenteritis in humans caused by toxic cyanobacterial blooms in domestic water supplies that have become eutrophic is a growing concern. *Microcystis aeruginosa* is the most frequently implicated blue-green alga in these poisonings,[1] and the hepatotoxins associated with this cyanophyte are cyclic heptapeptides known as microcystins.[2] Circumstantial evidence is slowly emerging linking toxic *Microcystis* blooms with a higher incidence of liver cancer among populations in Third World countries such as China that depend on surface drinking water.[3] In 1979, however, an outbreak of hepatoenteritis on Palm Island in northern Queensland, Australia, was traced to a different cyanobacterium, *Cylindrospermopsis raciborskii* (Woloszynska) Seenaya and Subba Raju, a species that had not been previously found to be toxic.[4] We report here the isolation and gross structure determination of an unusual alkaloid, cylindrospermopsin, which is hepatotoxic with symptoms indistinguishable from those originally described for the cyanobacterial extract.[4,5]

C. raciborskii was grown in culture as previously described.[4] An aqueous extract (0.9% NaCl) of the ultrasonicated, freeze-dried alga (0.7 g) was fractionated (bioassay-guided) by successive gel filtration on Toyopearl HW40F with 1:1 MeOH/H_2O and reversed-phase HPLC on C18 with 5% MeOH in H_2O to give white microcrystals of cylindrospermopsin (**1**, $C_{15}H_{21}N_5O_7S$; positive ion HRFABMS, glycerol matrix: MH^+ m/z 416.1236, Δ = 0.4 mmu), in 0.5% yield, $[\alpha]_D$ -31° (H_2O, *c* 0.1), as the only detectable hepatotoxin. The intense negative ion FABMS ($M - H^-$ m/z 414) and UV spectrum in H_2O [λ_{max} 262 (ϵ 5800), sh 290 nm (2100)] was consistent with **1** being a substituted uracil. Comparison of the ^{13}C chemical shifts in both D_2O and H_2O (Figure 1) and $^1J_{CH}$ for C-5 (175 Hz) with values reported for uracil[6] indicated that the substitution was on C-6. The toxin appeared to be a sulfate ester since the air CIDMS of the MH^+ ion (FAB mode) showed fragment ions at m/z 336.1688 ($C_{15}H_{22}N_5O_4$, Δ = -1.6 mmu), 318, 274 [MH - (hydroxymethyl)uracil]$^+$, 194, and 176 for the loss of SO_3 and H_2SO_4 from the MH^+ and [MH - (hydroxymethyl)uracil]$^+$ ions.

Detailed analysis of the 500-MHz ^1H and 125-MHz ^{13}C NMR spectra in D_2O, aided by two-dimensional COSY, HMQC, and HMBC experiments, enabled us to assign all of the ^1H and ^{13}C signals and to propose the structure shown in Figure 1. Chemical shifts suggested that nitrogen was attached to the carbons resonating at 45.0 (C-10), 48.3 (C-15), 53.6 (C-8), and 57.9 (C-14) ppm whereas oxygen was present on the carbons absorbing at 70.7 (C-7) and 78.2 (C-12) ppm. Isotope shifts for the C-7, C-8, and C-15 signals in H_2O (see $\Delta\delta_C$ values in Figure 1) established that NH's were on C-8 and C-15 and an OH group was on C-7. The sulfate group was therefore attached to C-12, and its placement here was supported by the CIDMS data. The coupling constants (J_{trans} = 11.1-11.8 Hz, J_{cis} = 2.0-3.9 Hz, and J_{gem} = -13.9 ± 0.5 Hz) associated with the signals for the protons on C-8, C-9 (28.5 ppm), C-10, C-11 (36.3 ppm), C-12, C-13 (39.8 ppm), and C-14 showed that these nuclei were located in six-membered rings which required that (1) the same nitrogen be connected to C-10 and C-14, (2) the sulfate ester group on C-12 be oriented axially, and (3) the methyl substituent on C-13 be equatorially disposed. The proton on C-8 (3.87 ppm) and one of the protons on C-15 (3.84 ppm) were coupled (HMBC cross peaks) to a guanidino carbon resonating at 156.5 ppm, and this meant that the toxin was a

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