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Mercuracarborand-catalyzed Diels–Alder reactions of a thionoester with cyclopentadiene

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Abstract

The multidentate Lewis acids *B*-octamethyl [12]-mercuracarborand-4 (**1**) and *B*-hexamethyl [9]-mercuracarborand-3 (**2**) catalyze the Diels–Alder reaction of a thionoester **4** with cyclopentadiene. The reaction proceeds more rapidly when catalyzed with **1** and **2** than with monodentate bis(*closo*-9,12-dimethyl-1,2-carboran-1-yl)mercury (**3**). Mercury-199 NMR studies demonstrated the formation of a 1:1 complex of **1** with **4** in which the thio function of **4** is coordinated to the Hg(II) centers of **1**, while the **2**·**4** and **3**·**4** complexes are not observed by NMR.

Keywords: carboranes; catalysis; thiocarbonyl compounds; mercury.

Catalyzed Diels–Alder reactions, involving electronic activation of a conjugated carbonyl group of the dienophile by certain Lewis acids, are known to exhibit enhanced reaction rates as well as regio-, and stereochemical selectivities.[1] The recent emergence of multidentate Lewis acids which may concertedly coordinate to a conjugated carbonyl oxygen center[2,3] can further enhance reactivity and selectivity.[2–4] In contrast to these observations, the involvement of conjugated thiocarbonyl group complexation is limited[5,6] and reports of Lewis acid-catalyzed thiocarbonyl mediated Diels–Alder reactions are scarce.[7] We have previously reported a novel class of macrocyclic so-called mercuracarborands composed of *ortho*-carborane modules linked by electrophilic Hg(II) centers[8,9] that readily complex anions such as Cl^-, Br^-, I^-, and *closo*-$B_{10}H_{10}^{2-}$ as well as a variety of uncharged nucleophilic species.[9] While multidentate Lewis acidic hosts have attracted significant attention due to their potential to recognize, bind, and chemically activate complementary electron rich guests,[2–4,10] the insolubility of mercuracarborands in noncoordinating solvents has limited their use as homogenous catalysts. However, the recently reported synthesis of the *B*-octamethyl [12]-mercuracarborand-4 (**1**) and *B*-hexamethyl [9]-mercuracarborand-3 (**2**) (Fig. 1), has overcome this obstacle.[11] We report herein our initial results obtained using **1** and **2** as multidentate Lewis acids which catalytically activate an unsaturated thionoester for Diels–Alder reactions.

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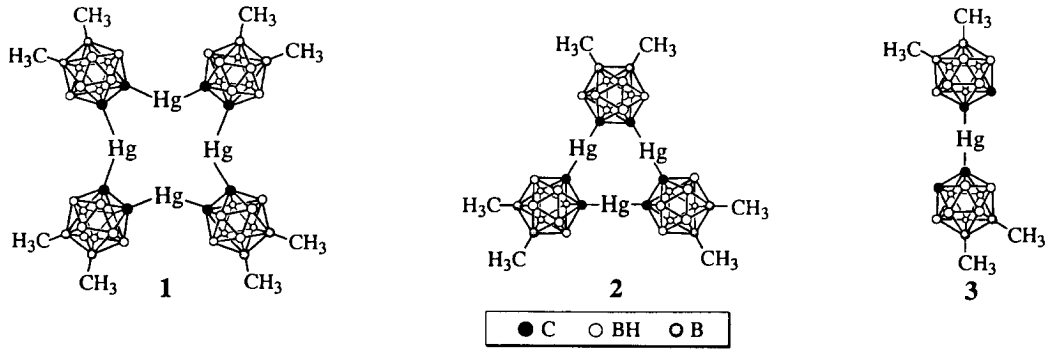
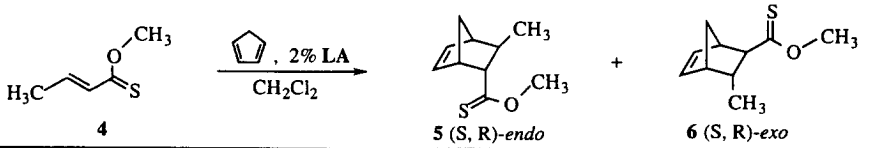


Figure 1. Representation of *B*-octamethyl [12]-mercuracarborand-4 (**1**), *B*-hexamethyl [9]-mercuracarborand-3 (**2**), and bis(*closo*-9,12-dimethyl-1,2-carboran-1-yl)mercury, (**3**)

Table 1
Diels–Alder reactions of a thionoester and cyclopentadiene



4 → **5** (S, R)-*endo* + **6** (S, R)-*exo*

Lewis acid (**LA**)	conditions (°C, d)	yield[a], % (*endo*:*exo*)[b]	Lewis acid (**LA**)	conditions (°C, d)	yield[a], % (*endo*:*exo*)[b]
1	(0, 2.5)	75 (60:40)	HgI_2	(0, 8)	—
2	(0, 7.5)	83 (99:1)	$Hg(OAc)_2$	(0, 8)	—
3	(0, 11)	65 (99:1)	none	(25, 8)	—

[a] Isolated yields. [b] Determined by 400 MHz ^{1}H NMR analysis.

The reaction of a 1 M methylene chloride solution of *O*-methyl *trans*-2-butenethioate (**4**)[12] with 1.5 mol equiv. of cyclopentadiene and 0.02 equiv. of **1**,[13] after 2.5 days at 0°C yields racemic mixtures of *endo* (**5**)[14] and *exo* (**6**)[15] products. An *endo*:*exo* ratio of 60:40 is observed, based upon integrated ^{1}H NMR spectra, with an 89% total yield based on ^{1}H NMR spectroscopy (75% recovered yield). Under similar conditions, a 1 M methylene chloride solution of **4** with 1.5 mol equiv. of cyclopentadiene and 0.02 equiv. of **2** led almost exclusively to the *endo* isomer (99:1) with a 94% ^{1}H NMR yield (83% recovered) after 7.5 days at 0°C. For comparison, the use of 0.02 equiv. of monodentate bis(*closo*-9,12-dimethyl-1,2-carboran-1-yl)mercury (**3**)[16] required 11 days to predominantly form the *endo* isomer (99:1) in 65% isolated yield. These and other examples are listed in Table 1. All reactions were carried out under nitrogen and monitored by ^{1}H NMR. The ^{11}B NMR spectra of the completed reaction mixtures confirmed that structures **1–3** remained intact.[17] No product formed when **1–3** were excluded from the reaction mixture and the use of HgI_2 and $Hg(OAc)_2$ did not lead to Diels–Alder products.

The complexation of **1–3** with **4** was studied by ^{199}Hg NMR spectroscopy, a technique that is very sensitive to changes in the immediate environment surrounding the mercury centers.[18] Due to similar ^{1}H, ^{13}C, and ^{11}B NMR spectra of both complexed and uncomplexed mercuracarborands,[9] ^{199}Hg NMR serves as the most useful probe for observing host/guest interactions. The ^{199}Hg NMR resonance of a 0.02 M CH_2Cl_2 solution of **1** (concentration is equiv. to that used in the catalyzed Diels–Alder reactions) was observed at −1204 ppm.[19] The addition of a 0.5 mol equiv. of **4** to the CH_2Cl_2 solution of **1** resulted in two resonances which corresponded to a complex species at −997 ppm and a broad peak

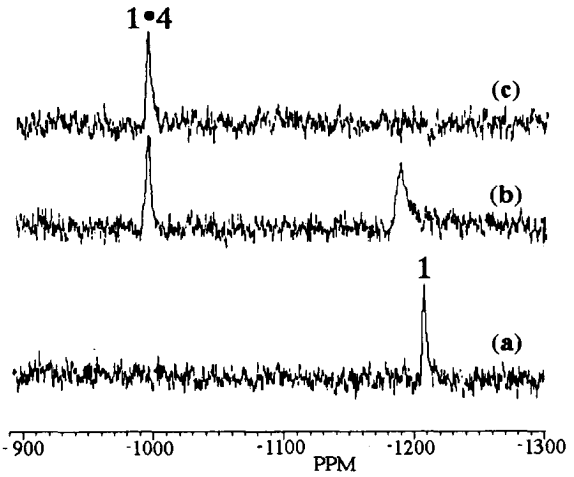


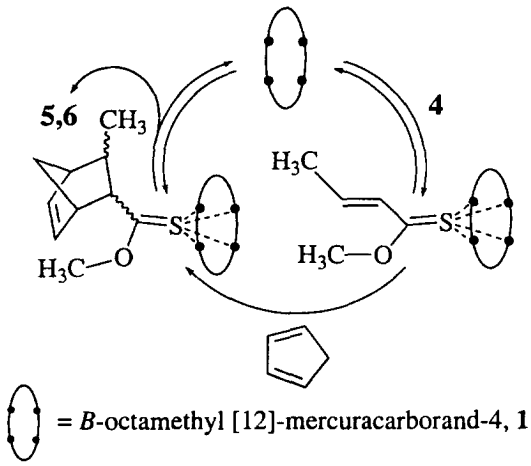
Figure 2. A ^{199}Hg NMR study on the addition of **4** to a 0.02 M CH_2Cl_2 solution of **1** with **4**:**1** ratios of: (a) 0.0; (b) 0.5; and (c) 1.0

at −1190 which was shifted 14 ppm downfield from **1** (Fig. 2).[20] The direction of the ^{199}Hg shift was consistent with the previously reported complexation by bis(trifluoroacetato)-1,2-phenylenedimercury and a thiobenzophenone.[5] Upon addition of 1 equiv. of **4** to **1**, only a sharp resonance at −997 ppm was observed. When more than 1 equiv. was added, no further change in the spectrum was observed. The sharp resonance at −997 ppm is presumed to arise from the **1·4** complex. The **1·5** and **1·6** complexes both have resonances at −997 ppm. The broadened resonance at −1190 ppm accompanied by the downfield shift of 14 ppm from that of **1**, is tentatively explained by weak indeterminate interactions between **1** and the **1·4** complex, resulting in a rapid (fast on NMR timescale) and reversible process.[9] Similar experiments involving the incremental addition of **4** to **2** and **3**, respectively, showed no apparent change in peak broadness or chemical shift. The observation of Diels–Alder catalysis with both **2** and **3** and the absence of a ^{199}Hg NMR chemical shift difference when **2** and **3** are in the presence of **4** suggests that the postulated **2·4** and **3·4** precursor complexes are present in very low concentrations in contrast to the efficient complexation of **1** and **4**, assuming that all of these processes proceed by similar mechanisms.

A general mechanism illustrating Diels–Alder reactions catalyzed by **1** is depicted in Scheme 1. The first step in the proposed catalytic cycle involves a rapid (slow on NMR time scale) and reversible coordination of the mercuracarborand and **4**, thereby converting essentially all available **1** to a discrete **1·4** thionoester complex. The activated thionoester in complex **1·4** subsequently undergoes Diels–Alder reactions with cyclopentadiene leading to the isomeric **5** and **6** adducts. Dissociation of **5** and **6** from their mercuracarborand complexes completes the catalytic cycle.

The ^{199}Hg NMR studies demonstrate that complex **1·4** is more stable than the corresponding **2·4** and **3·4** complexes. The enchanced stability of **1·4** may explain the formation of both *endo* and *exo* cycloaddition products through a late transition state, while the less stable **2·4** and **3·4** precursors lead to the kinetically preferred *endo* isomer.[21] The observed relative reactivity of the catalytically active species is **1>2>3**. The enhanced reactivity observed with **1** compared with **2** and monodentate **3**, may indicate that only **1** is capable of multiple mercury coordination to the C=S group of **4**.

X-Ray crystallography has demonstrated coordination of the oxygen of an amide function and a mercury-based multidentate Lewis acid.[3] Similarly, X-ray crystallography of **1** crystallized in acetone, shows eight acetone molecules with each carbonyl group simultaneously coordinating two adjacent mercury atoms of **1**.[22] However, the attempted reaction of **1–3** with methyl crotonate (**7**) and cyclopentadiene



Scheme 1.

at room temperature for 8 days, resulted in no product formation. No evidence of complexation of **7** with **1** and **2** was observed by ^{199}Hg NMR spectroscopy in agreement with the suggestion that **1** and **2** are soft Lewis acids and more tightly bound to the soft sulfur atom of **4** in contrast to the harder carbonyl oxygen of **7**. Studies of **1–3** and related catalysts in other processes are in progress.

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13. $AgBF_4$ instead of AgOAc was used to form empty host **1**.
14. (a) (*S,R*)-*O*-methyl *endo*-bicyclo[2.2.1]hept-5-ene-2-thionocarboxylate-3-methyl (**5**). (b) Separated by HPLC using a silica column with a mixture of acetonitrile and pentane. (c) Spectroscopic data for compound **5**: ^1H NMR [400 MHz, $CDCl_3$]: δ 6.23 (dd, 1H, *J*=5.7, 3.1 Hz), 5.93 (dd, 1H, *J*=5.7, 2.8 Hz), 4.01 (s, 3H), 3.20 (br s, 1H), 2.71 (dd, 1H, *J*=4.5, 3.6 Hz), 2.43 (br s, 1H), 2.05–1.98 (m, 1H), 1.58–1.56 (m, 1H), 1.41 (ddd, 1H, *J*=8.6, 3.5, 1.8 Hz), 1.18 (d, 3H, *J*=7.0 Hz); $^{13}C\{^1H\}$ NMR [90 MHz, $CDCl_3$]: δ 226.4 (C=S), 138.3, 133.0 (C=C), 63.6 (C2), 58.8 (OCH_3), 49.1 (C4), 48.4 (C1), 46.3 (C7), 40.6 (C3), 20.9 (CH_3); HRMS (EI) for $C_{10}H_{14}OS$ (*m/z*) calcd: 182.0765; found: 182.0765 (M^+).
15. (a) (*S,R*)-*O*-methyl *exo*-bicyclo[2.2.1]hept-5-ene-2-thionocarboxylate-3-methyl (**6**). (b) Separated by HPLC using a silica column with a mixture of acetonitrile and pentane. (c) Spectroscopic data for compound **6**: ^1H NMR [400 MHz, $CDCl_3$]: δ 6.24 (dd, 1H, 5.8, *J*=3.2 Hz), 6.10 (dd, 1H, 5.7, *J*=3.1 Hz), 4.08 (s, 3H), 2.95 (br s, 1H), 2.68 (br s, 1H), 2.43 (br s, 1H), 2.08 (dd, 1H, 5.2, *J*=1.5 Hz), 2.04–1.98 (m, 1H), 1.87–1.85 (m, 1H), 0.91 (d, 3H, *J*=6.9 Hz); $^{13}C\{^1H\}$ NMR [90 MHz, $CDCl_3$]: δ 228.1 (C=S), 137.2, 135.9 (C=C), 62.8 (C2), 59.0 (OCH_3), 49.7 (C7), 47.8, 47.6 (C1, C4), 42.3 (C3), 19.2 (CH_3); HRMS (EI) for $C_{10}H_{14}OS$ (*m/z*) calcd: 182.0765; found: 182.0768 (M^+).
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