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Microwave-Assisted Synthesis of Tricarbonyl Rhenacarboranes: Steric and Electronic Effects on the 1,2 → 1,7 Carborane Cage Isomerization

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A series of tricarbonyl rhenacarboranes {[M][Re(CO)$_3$(RR′C$_2$B$_9$H$_9$)]} (M = Na, K) were synthesized in water using microwave radiation with reaction times of less than 15 min. The novel complexes were isolated in good yields (57–94%) as either 3,1,2-(R = H: R′ = CH_2Pyr **6**; R′ = CH_2Cy, **20**) or 2,1,8-(R = H: R′ = H, **4**; R′ = CH_2PyrMe **12**; R′ = CH_2PyrH, **13**; R′ = Pyr, **15**; R′ = Ph, **17**; R = R′ = Bn, **19**) metallacarboranes and characterized by multinuclear (^{1}H, ^{11}B, ^{13}C) and NOE NMR spectroscopy, IR spectroscopy, mass spectrometry, and X-ray crystallography in the case of compounds **12** and **13**. Carborane cage isomerization from the original 1,2 configuration to the 1,7 orientation occurred in cases where significant steric crowding was present at the metal center. Incorporation of a methylene spacer between the carborane cage and the six-membered ring as in **7** and **20** decreased steric strain such that the 3,1,2 configuration was maintained. Conversion of the 3,1,2 complex **6** to the 2,1,8 isomers **12** and **13** takes place at room temperature upon methylation or protonation of the pyridyl ring, indicating that electronic effects also play a significant role in the isomerization process.

Introduction

The synthesis of *ortho-closo*-dicarbadodecaborane $C_2B_{10}H_{12}$ from acetylene and decaborane was first reported in 1963.[1] The same year, the thermally induced conversion of this molecule from the *ortho* isomer to *meta* carborane at ca. 500 °C was described;[2] further heating (615 °C) yielded the *para* isomer.[3] Numerous transition metal complexes of substituted *ortho* carboranes have since been prepared[4] where it has been observed that the introduction of sterically demanding substituents on the carborane carbon atoms decreases the barrier to isomerization so that the more thermally stable 2,1,8-metallacarboranes are obtained at much lower temperatures.[5]

Despite substantial documentation of their occurrence, little remains known regarding the mechanism of these carborane cage isomerization reactions. Two widely disseminated pathways are the diamond−square−diamond[6] and triangular face rotation[7] "mechanisms", but these are best considered schematic representations of the process rather than true reaction mechanisms. Furthermore, the 1,2 → 1,7 isomerization process appears to vary from system to system. For example, in situ NMR studies have shown that the platinacarborane [1-Ph-3,3-(PMe_2Ph)$_2$-3,1,2-*closo*-$PtC_2B_9H_{10}$] is converted directly from the 3,1,2 species to its 2,1,8 isomers (Scheme 1).[8] In this instance, no intermediate is observed, and migration of either carborane C atom can occur. In contrast, an analogous isomerization to yield the rhodium complex [2,2-(2,3,8-η^3):(5,6-η^2)-$C_7H_7CH_2$)-1,8-(4′-MeC_6H_4)$_2$-

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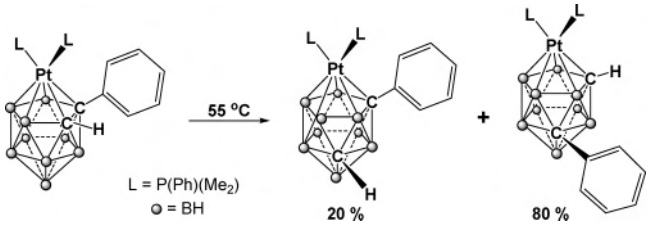
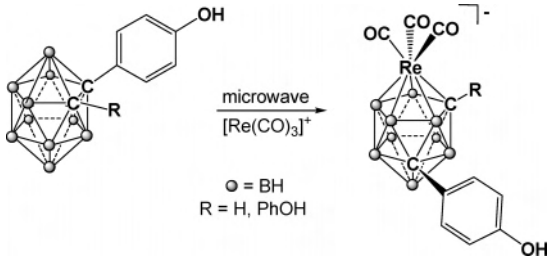
Scheme 1. Carborane Cage Isomerization of a Platinacarborane Complex[8]



Scheme 2. Microwave-Assisted Formation of {[Na][2,2,2-$(CO)_3$-8-PhOH-1-R-2,1,8-*closo*-$ReC_2B_9H_9$]} (R = H, PhOH)[13]



2,1,8-*closo*-$RhC_2B_9H_9$] proceeds via a stable pseudo-*closo* intermediate; X-ray crystallography revealed that the two carborane C atoms of this species remain adjacent but not bonded to one another ($dC\cdots C$ = 2.539(7) Å).[9]

Our research interests involve the synthesis of $[Re(CO)_3]-$carborane complexes and their radioactive ^{99m}Tc counterparts as synthons for preparing molecular imaging and therapy agents. Preparative scale syntheses are done with rhenium in order to develop a synthetic methodology for reactions with technetium, which does not possess a non-radioactive isotope. The rhenium congeners also serve as characterization (HPLC) standards for tracer level work with ^{99m}Tc. We have recently reported[10,11] the aqueous synthesis of rhenacarboranes and their ^{99m}Tc congeners which is a significant advance over the traditional anhydrous reaction conditions that were formerly thought to be required for the synthesis of these complexes. However, the long reaction times of 18 h to 7 days are not suitable for ^{99m}Tc syntheses due to the relatively short half-life ($t_{1/2}$ = 6.02 h) of that isotope.

As microwave heating is capable of decreasing reaction times significantly,[12] we investigated its use in the preparation of metallacarborane complexes and demonstrated that it results in decreased reaction times of ca. 15 min, as well as substantial improvements in product yields.[13] Over the course of this work, it was observed that the reaction of $[Re(CO)_3(H_2O)_3]$Br with mono- or bis-phenol-carborane resulted in the exclusive formation of the 2,1,8 isomers {[Na][2,2,2-$(CO)_3$-8-PhOH-1-R-2,1,8-*closo*-$ReC_2B_9H_9$]} (R = H, PhOH, Scheme 2), as the high pressure (20 atm) and temperature (200 °C) attained in the microwave reactor provide sufficient energy to overcome the activation energy barrier to afford isomerization. Notably, the incorporation of a methylene spacer between the carborane cage and the phenyl ring decreased steric strain at the bonding face of the carborane ligand such that the mono-benzyl species {[K][3,3,3-$(CO)_3$-1-Bn-3,1,2-*closo*-$ReC_2B_9H_{10}$]} (Bn = $CH_2C_6H_5$) displayed the expected 3,1,2 conformation, with the two carborane C atoms adjacent to one another on the C_2B_3 bonding face of the cage. Prior to this, carborane cage isomerization had not been reported for rhenacarborane complexes.

This microwave-assisted methodology has proven amenable to working with ^{99m}Tc at the tracer level;[13] however, in the synthesis of clinically relevant species, it is imperative to be able to accurately predict which isomer of a given carborane complex will form. The vast majority of the metallacarboranes known to undergo 1,2 → 1,7 carborane cage isomerization contain either phenyl or *p*-tolyl substituents on the carborane C atoms:[5] no investigation of the amount of steric bulk required to induce isomerization has yet been conducted. An additional factor which may affect the isomerization barrier is the electronic character of the substituent(s) on the carborane cage. In order to further our understanding of the isomerization process of these complexes, we report here the synthesis of a series of tricarbonyl rhenium carboranes, wherein the carborane cage has been mono- or disubstituted with a variety of moieties. For simplicity, the structures discussed here are compiled in Chart 1.

Experimental

Reagents and General Procedures. Decaborane and *closo-ortho*-carborane **1** were purchased from Katchem Ltd.; ^{n}BuLi (2.5 M, 1.6 M solutions in hexanes), 3-cyclohexyl-1-propyne, KF, $MeSO_3CF_3$, and HSO_3CF_3 were purchased from Sigma-Aldrich and used without further purification. Benzyl chloride (Baker) and NaF (EM Science) were also purchased. Compounds prepared according to literature procedures were $[Re(CO)_3(H_2O)_3]$Br,[14] [1-$CH_2C_5H_4N$-*closo*-$C_2B_{10}H_{11}$] (**8**),[15] [1-C_5H_4N-*closo*-$C_2B_{10}H_{11}$] (**14**),[16] and [1-Ph-*closo*-$C_2B_{10}H_{11}$].[1] Solvents were purchased from Caledon, dried over calcium hydride (CH_2Cl_2, CH_3CN, and toluene) or Na/benzophenone (Et_2O), and freshly distilled prior to use.

Instrumentation. Multi-NMR spectra were recorded on a Bruker DRX-500 spectrometer with chemical shifts reported in ppm relative to the residual proton signal of the deuterated solvent (^{1}H NMR) or the carbon signal of the solvent (^{13}C NMR). Boron-11 NMR spectra were referenced externally to $BF_3\cdot Et_2O$. Proton NOE experiments were conducted on a Bruker AV-600 NMR spectrometer. Infrared spectra were acquired using a BioRad FTS-40 FT-IR spectrometer. All spectra were recorded at 22 °C. A Biotage Initiator Sixty Microwave Reactor was employed for reactions requiring microwave radiation. Thin layer chromatograms (Merck F_{254} silica gel on aluminum plates) were visualized using 0.1% $PdCl_2$ in 3 M $HCl_{(aq)}$ and/or UV light. Purification of all products was effected

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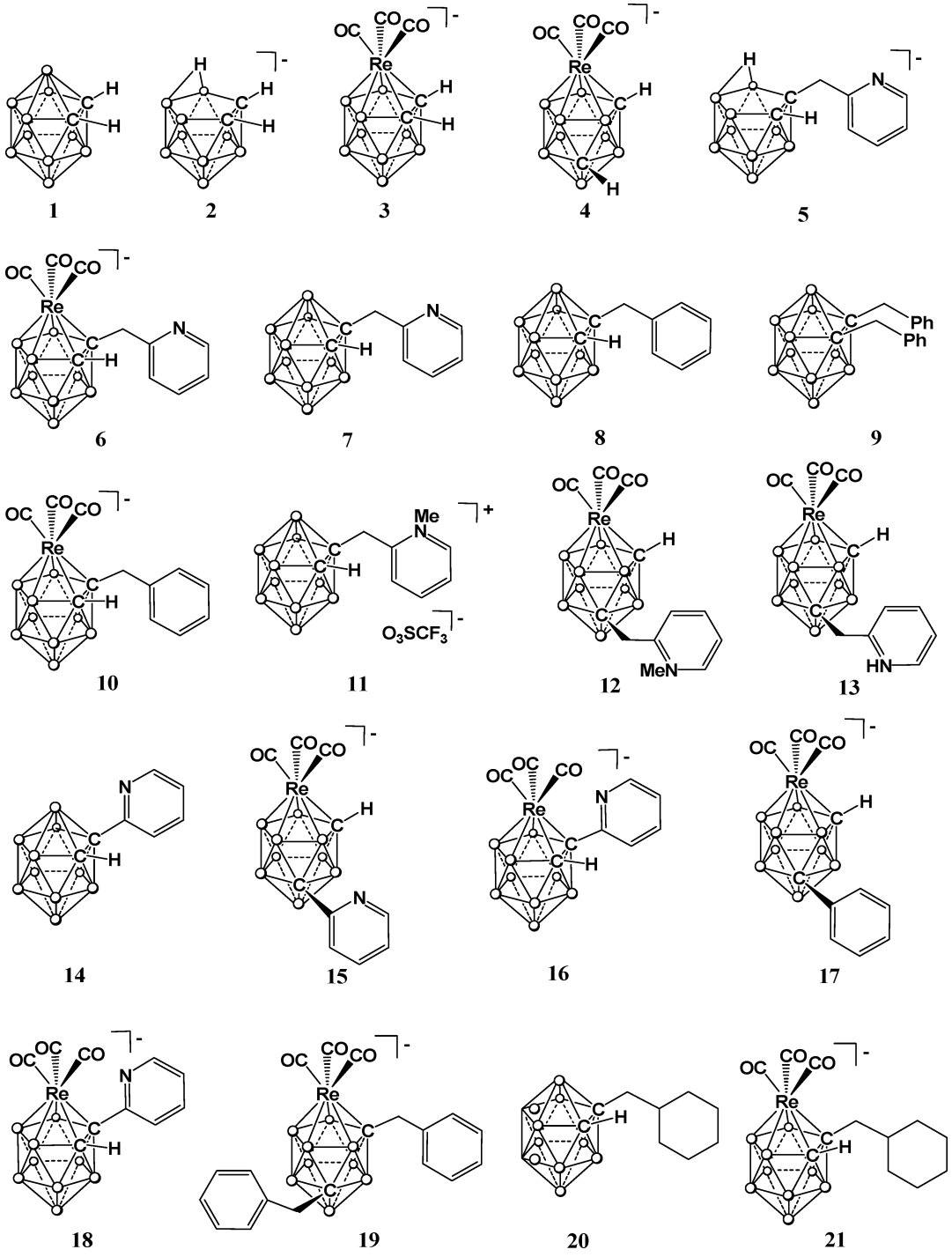
Chart 1. Structures of Compounds Discussed (Shaded Circle Represents BH)



either by flash chromatography using Ultrapure Silica Gel from Silicycle (70−230 mesh), or by using a Biotage SP1 autopurification system. Low-resolution mass spectra were obtained on a Waters/micromass GCT-ToF spectrometer using electron impact ionization or a Waters/Micromass Quattro Ultima spectrometer using electrospray ionization. High-resolution mass spectra were obtained on a Waters/Micromass Q-ToF Ultima Global spectrometer.

Preparation of {[K][2,2,2-(CO)$_3$-2,1,8-*closo*-ReC$_2$B$_9$H$_{11}$]} (4). The potassium salt of [7,8-*nido*-H$_2$C$_2$B$_9$H$_{10}$] (**2**) (0.0636 g, 0.369 mmol) and [Re(CO)$_3$(H$_2$O)$_3$]Br (0.1765 g, 0.437 mmol) were weighed into a microwave vial (5 mL) and dissolved in aqueous ethanol (10%, 4 mL). The vial was crimp-sealed, and the opaque reaction mixture was heated in a microwave reactor at 200 °C for 20 min. An additional portion of [Re(CO)$_3$(H$_2$O)$_3$]Br (0.0605 g, 0.150 mmol) was added, and the reaction mixture was heated at 200 °C for 40 min, resulting in a clear yellow solution with a small amount of black precipitate. The solvent was removed by rotary evaporation; the product was isolated as a tan semisolid (0.1429 g, 0.323 mmol, 87%) by silica gel chromatography using an automated purification system and a solvent gradient of 3−30% MeOH in CH_2Cl_2. ^{1}H NMR (d_4-methanol, δ): 2.12 (br, 1 H, CH), 1.58 (br, 1 H, CH). ^{11}B{^{1}H} NMR (d_4-methanol, δ): −7.4, −8.1, −10.7, −11.2, −11.6, −14.7, −18.8, −20.2, −21.6 (all resonances equal in intensity). ^{13}C{^{1}H} NMR (d_4-methanol, δ): 200.58 (C═O), 37.13 (br, CH), 29.12 (br, CH). IR (neat): 2555 (br, ν_{B-H}) 2001 ($\nu_{C=O}$), 1894 cm^{-1} (br, $\nu_{C=O}$). TLC (20% MeOH/CH_2Cl_2): R_f = 0.37.

HRMS (ES^-) *m/z* for $C_5H_{11}O_3B_9Re_1$: calcd 402.1163, observed 402.1146 [M^-].

Preparation of {[Na][3,3,3-(CO)$_3$-1-CH$_2$C$_5$H$_4$N-3,1,2-*closo*-ReC$_2$B$_9$H$_{10}$]} (6). Method A. The *closo*-carborane **7** (19.1 mg, 0.0812 mmol) was combined with KF (44.9 mg, 0.773 mmol) in a microwave vial (5 mL) and mixed with aqueous ethanol (10%, 4 mL); the vial was crimp-sealed. The resulting suspension was heated in a microwave reactor at 195 °C for 12 min to form the *nido*-carborane **5** in situ. [Re(CO)$_3$(H$_2$O)$_3$]Br (42.9 mg, 0.106 mmol) was added, and the reaction mixture heated for 15 min at 190 °C. The solvent was removed by rotary evaporation, and the product isolated (36.5 mg, 0.0685 mmol, 84%) via silica gel chromatography using an automated purification system with a gradient of 3−30% MeOH in CH_2Cl_2.

Method B. The potassium salt of **5** (23.8 mg, 0.101 mmol) was combined with KF (40.6 mg, mmol) and [Re(CO)$_3$(H$_2$O)$_3$]Br (51.7 mg, 0.128 mmol) in a microwave vial (5 mL). Aqueous ethanol (10%, 4 mL) was added, the vial crimp-sealed, and the reaction mixture was heated at 190 °C for 15 min in a microwave reactor. The solvent was removed by rotary evaporation, and the product isolated (37.5 mg, 0.0704 mmol, 87%) via silica gel chromatography using an automated purification system with a gradient of 3−30% MeOH in CH_2Cl_2. Spectroscopic data were consistent with those reported previously.[11a]

Preparation of [1-Bn-*closo*-C$_2$B$_{10}$H$_{11}$] (8) and [1,2-Bn$_2$-*closo*-C$_2$B$_{10}$H$_{10}$] (9). *Closo-ortho*-carborane **1** (1.0865 g, 7.544 mmol) was dissolved in Et_2O (40 mL) and cooled to −78 °C under an inert (nitrogen) atmosphere. ^{n}BuLi (9.4 mL, 15.0 mmol) was added, and the resulting white slurry was stirred for 50 min prior to addition of benzyl chloride (1.3 mL, 1.43 g, 11.3 mmol). After 3 h, the reaction mixture was warmed slowly to 22 °C; stirring was continued for an additional 18 h. The yellow slurry was washed with water (3 × 20 mL), then dried over Na_2SO_4 prior to removal of the solvent by rotary evaporation. The two products were separated by silica gel chromatography using an automated purification system with a gradient of 2−20% CH_2Cl_2 in hexanes.

[1-Bn-*closo*-C$_2$B$_{10}$H$_{11}$] (8). Colorless crystals (0.2484 g, 1.06 mmol). ^{1}H NMR (d_6-acetone, δ): 7.37 (m, 3 H, CH_{Ar}), 7.28 (m, 2 H, CH_{Ar}), 4.49 (br, 1 H, $CH_{carborane}$), 3.69 (s, 2 H, CH_2). ^{11}B{^{1}H} NMR (d_6-acetone, δ): −1.6 (1 B), −4.8 (1 B), −8.4 (2 B), −10.1 (2 B), −10.9 (2 B), −11.8 (2 B). ^{13}C{^{1}H} NMR (d_6-acetone, δ): 136.47, 131.02, 129.54, 128.93 (C_{Ar}), 77.15 (br, $C_{carborane}$), 62.76 (br, $CH_{carborane}$), 43.92 (CH_2). IR (neat): 3066 (ν_{C-H}), 2594 cm^{-1} (br, ν_{B-H}). TLC (10% CH_2Cl_2/hexanes): R_f = 0.27. HRMS (EI^+) *m/z* for $C_9H_{18}B_{10}$: calcd 234.2416, observed 234.2412 [M^+].

[1,2-Bn$_2$-*closo*-C$_2$B$_{10}$H$_{10}$] (9). White powder (0.2153 g, 0.660 mmol). ^{1}H NMR ($CDCl_3$, δ): 7.37 (m, 3 H, CH_{Ar}), 7.23 (m, 2 H, CH_{Ar}), 3.64 (s, 2 H, CH_2). ^{11}B{^{1}H} NMR ($CDCl_3$, δ): −3.9 (2 B), −9.5 (4 B), −10.2 (4 B). ^{13}C{^{1}H} NMR ($CDCl_3$, δ): 135.18, 130.59, 128.80, 128.29 (C_{Ar}), 79.57 (br, $C_{carborane}$), 41.59 (CH_2). IR (neat): 3070 (ν_{C-H}), 3030 (ν_{C-H}), 2583 cm^{-1} (br, ν_{B-H}). TLC (10% CH_2Cl_2/hexanes): R_f = 0.18. HRMS (EI^+) *m/z* for $C_{16}H_{24}B_{10}$: calcd 326.2809, observed 326.2810 [M^+].

Preparation of {[1-(*N*-Me)CH$_2$C$_5$H$_4$N-*closo*-C$_2$B$_{10}$H$_{11}$][O$_3$SCF$_3$]} (11). The *closo*-carborane **7** (96.2 mg, 0.409 mmol) was dissolved in CH_2Cl_2 (15 mL) under an inert (nitrogen) atmosphere, yielding a clear colorless solution. A freshly prepared solution of $MeSO_3CF_3$ in CH_2Cl_2 (5% v/v, 0.92 mL, 0.406 mmol) was added to the reaction mixture. After 18 h, the solvent was removed from the clear pale yellow solution leaving **11** as a yellow oil which solidified to a fine yellow powder (0.1301 g, 0.326 mmol, 80%) upon standing for 12 h. ^{1}H NMR (d_6-acetone, δ): 9.21 (d, 1 H, CH_{Ar}), 8.77 (t, 1 H, CH_{Ar}), 8.34 (d, 1 H, CH_{Ar}), 8.24 (t, 1 H, CH_{Ar}), 5.18 (br, 1 H, $CH_{carborane}$), 4.67 (s, 3 H, CH_3), 4.57 (s, 2 H, CH_2). ^{11}B{^{1}H} NMR (d_6-acetone, δ): −2.2 (1 B), −4.5 (1 B), −8.7 (2 B), −11.4 (3 B), −12.1 (3 B). ^{13}C{^{1}H} NMR (d_6-acetone, δ): 152.38, 149.19, 147.15, 133.36, 128.91 (C_{Ar}), 72.40 ($C_{carborane}$), 64.79 ($CH_{carborane}$), 47.92 (CH_2), 39.15 (CH_3). IR(neat): 3047 (ν_{C-H}), 2594 (br, ν_{B-H}), 1262 cm^{-1} (ν_{S-O}). HRMS (ES^+) *m/z* for $C_9H_{20}NB_{10}$: calcd 250.2604, observed 250.2625 [M^+].

Preparation of {2,2,2-(CO)$_3$-8-[(*N*-Me)CH$_2$C$_5$H$_4$N]-2,1,8-*closo*-ReC$_2$B$_9$H$_{10}$} (12). Method A. The *closo*-carborane **11** (47.0 mg, 0.118 mmol) was combined with NaF (32.3 mg, 0.767 mmol) and aqueous ethanol (10%, 3 mL) in a crimp-sealed microwave vial (5 mL). The resulting suspension was heated for 8 min at 195 °C in a microwave reactor, resulting in a clear solution with a dense white precipitate. A solution of [Re(CO)$_3$(H$_2$O)$_3$]Br (54.6 mg, 0.135 mmol) in aqueous ethanol (10%, 1 mL) was added, and the reaction mixture was heated for 15 min at 190 °C; a second aliquot of [Re(CO)$_3$(H$_2$O)$_3$]Br (27.3 mg, 0.067 mmol) in $EtOH_{(aq)}$ (10%, 0.5 mL) was added, and the reaction mixture was heated for an additional 5 min at 190 °C. The solvent was removed via rotary evaporation, and the product **12** isolated as a yellow oil (56.2 mg, 0.110 mmol, 93%) by silica gel chromatography using an automated purification system and a gradient of 2−20% MeOH in CH_2Cl_2.

Method B. The potassium salt of **6** (37.5 mg, 0.0704 mmol) was dissolved in CH_2Cl_2 (10 mL) under an inert (nitrogen) atmosphere. A freshly prepared solution of $MeSO_3CF_3$ in CH_2Cl_2 (5% v/v, 0.16 mL, 0.0707 mmol) was added to the reaction mixture, which was stirred for 18 h. The reaction mixture was washed with water (3 × 8 mL), then dried over Na_2SO_4 prior to removal of the solvent by rotary evaporation, leaving the product **12** as a pale yellow solid (28.0 mg, 0.0548 mmol, 78%). X-ray quality crystals were grown from CH_2Cl_2/hexanes (ca. 1:2). ^{1}H NMR (d_6-acetone, δ): 9.04 (d, 1 H, Pyr), 8.64 (t, 1 H, Pyr), 8.11 (t, 1 H, Pyr), 8.04 (d, 1 H, Pyr), 4.55 (s, 3 H, CH_3), 3.82 [AA′, 2 H, CH_2, $\Delta\delta$ AA′ = 46.0 Hz, ^2J (^{1}H−^{1}H) = 15 Hz], 1.84 (br, s, 1 H, $CH_{carborane}$). ^{11}B-{^{1}H} NMR (d_6-acetone, δ): −5.4 (1 B), −8.5 (2 B), −9.0 (1 B), −11.0 (1 B), −11.7 (1 B), −18.0 (1 B), −19.7 (1 B), −20.0 (1 B). ^{13}C{^{1}H} NMR (d_6-acetone, δ): 199.58 (C═O), 156.10, 147.50, 145.84, 133.10, 127.59 (C_{Ar}), 49.36 ($C_{carborane}$), 47.51 (CH_2), 42.85 (CH_3). IR (neat): 2549 (br, ν_{B-H}), 2000 ($\nu_{C=O}$), 1890 cm^{-1} (br, $\nu_{C=O}$). TLC (10% MeOH in CH_2Cl_2): R_f = 0.41.

Preparation of {2,2,2-(CO)$_3$-8-[(*N*-H)CH$_2$C$_5$H$_4$N]-2,1,8-*closo*-ReC$_2$B$_9$H$_{10}$} (13). The sodium salt of compound **6** (57.7 mg, 0.112 mmol) was combined with CH_2Cl_2 (15 mL) under an inert (nitrogen) atmosphere, resulting in a cloudy light yellow liquid. A freshly prepared solution of HSO_3CF_3 in CH_2Cl_2 (5% v/v, 0.20 mL, 0.113 mmol) was added to the reaction mixture. After 15 min, a white solid had formed while the supernatant liquid was now clear. After 13 h, the reaction mixture was washed with water (3 × 10 mL) to remove the dense white solid. The organic phase was dried over Na_2SO_4 prior to removal of the solvent by rotary evaporation, leaving the product **13** as a pale yellow solid (44.8 mg, 0.0909 mmol, 81%). X-ray quality crystals were grown from MeOH/CH_2Cl_2/hexanes (ca. 1:5:10). ^{1}H NMR (d_6-acetone, δ): 11.6 (br, NH), 9.03 (d, 1 H, Pyr), 8.77 (t of d, 1 H, Pyr), 8.20 (t, 1 H, Pyr), 8.10 (d, 1 H, Pyr), 3.71 [AA′, 2 H, CH_2, $\Delta\delta$ AA' = 59.3 Hz, ^2J (^{1}H−^{1}H) = 14.8 Hz], 1.80 (br, s, 1 H, $CH_{carborane}$). ^{11}B{^{1}H} NMR (d_6-acetone, δ): −5.72 (1 B), −8.38 (2 B), −9.35 (1 B), −11.2 (1 B), −11.86 (1 B), −18.06 (1 B), −19.61 (1 B), −19.93 (1 B). ^{13}C{^{1}H} NMR (d_6-acetone, δ): 199.82 (C═O), 154.83, 146.84, 142.88, 130.11, 126.53 (C_{Ar}), 50.38 ($C_{carborane}$), 44.77 (CH_2), 29.21 ($CH_{carborane}$). IR (neat): 2545 (br, ν_{B-H}), 2001 ($\nu_{C=O}$), 1902 cm^{-1} (br, $\nu_{C=O}$). TLC (20% MeOH in CH_2Cl_2): R_f = 0.25. HRMS (ES^-) *m/z* for $C_{11}H_{16}B_9O_3NRe$: calcd 494.1581, observed 494.1591 [M^-].

Preparation of {[K][2,2,2-(CO)$_3$-8-C$_5$H$_4$N-2,1,8-*closo*-ReC$_2$B$_9$H$_{10}$]} (15). [1-C$_5$H$_4$N-*closo*-C$_2$B$_{10}$H$_{11}$] **14** (18.0 mg, 0.0813 mmol) was combined with KF (51.2 mg, 0.881 mmol) and [Re(CO)$_3$(H$_2$O)$_3$]Br (38.0 mg, 0.0941 mmol) in a microwave vial (5 mL). Aqueous ethanol (10%, 4 mL) was added to the crimp-sealed vial, and the resulting suspension was heated for 15 min at 200 °C in a microwave reactor. A second portion of [Re(CO)$_3$(H$_2$O)$_3$]Br (31.0 mg, 0.0767 mmol) was added, and the reaction mixture was heated for an additional 10 min at 190 °C. The solvent was removed via rotary evaporation, and the product isolated (39.7 mg, 0.0764 mmol, 94%) by silica gel chromatography using an automated purification system and a gradient of 3−30% MeOH in CH_2Cl_2. ^{1}H NMR (d_4-methanol, δ): 8.28 (d, 1 H, Pyr), 7.64 (t of d, 1 H, Pyr), 7.57 (d, 1 H, Pyr), 7.19 (t, 1 H, Pyr), 1.81 (br, s, 1 H, CH$_{carborane}$). ^{11}B{^{1}H} NMR (d_4-methanol, δ): −4.2 (1 B), −6.4 (1 B), −7.0 (2 B), −10.8 (1 B), −11.6 (1 B), −17.4 (1 B), −18.7 (2 B). ^{13}C{^{1}H} NMR (d_4-methanol, δ): 200.14 (C═O), 161.41, 148.03, 138.11, 124.72, 123.09 (C$_{Ar}$), 57.73 (C$_{carborane}$), 28.82 (CH$_{carborane}$). IR (neat): 2555 (br, ν_{B-H}), 2011 ($\nu_{C=O}$), 1904 cm^{-1} (br, $\nu_{C=O}$). TLC (15% MeOH in CH_2Cl_2): R_f = 0.09. HRMS (ES$^-$) m/z for C$_{12}$H$_{23}$B$_9$O$_3$NRe: calcd 480.1425, observed 480.1413 [M$^-$].

Preparation of {[K][2,2,2-(CO)$_3$-1,8-Bn$_2$-2,1,8-*closo*-ReC$_2$B$_9$H$_9$]} (19). [1,2-Bn$_2$-*closo*-C$_2$B$_{10}$H$_{10}$] **9** (24.9 mg, 0.0767 mmol) was combined with KF (51.1 mg, 0.879 mmol) and [Re(CO)$_3$(H$_2$O)$_3$]-Br (35.7 mg, 0.0883 mmol) in aqueous ethanol (10%, 4 mL) in a microwave vial (5 mL). The reaction mixture was sealed and heated at 200 °C for 15 min in a microwave reactor. A second portion of [Re(CO)$_3$(H$_2$O)$_3$]Br (15.0 mg, 0.0371 mmol) was added, and the reaction mixture was heated at 200 °C for 10 min; a third (10 min) and fourth (15 min) heating with additional [Re(CO)$_3$(H$_2$O)$_3$]Br (15.0 mg, 0.0371 mmol; 34.4 mg, 0.0851 mmol) was required for complete consumption (by ^{11}B NMR) of the carborane ligand. The solvent was removed via rotary evaporator, and the product **19** was isolated (27.2 mg, 0.0437 mmol, 57%) using an automated purification system and a gradient of 3−30% MeOH in CH_2Cl_2. ^{1}H NMR (d_4-methanol, δ): 7.24−6.98 overlapping (m, 10 H, CH$_{Ar}$), 3.05 [AA′, 2 H, CH_2, $\Delta\delta$ AA′ = 26.0 Hz, ^2J (^{1}H−^{1}H) = 14 Hz], 2.93 [AA′, 2 H, CH_2, ^2J (^{1}H−^{1}H) = 15 Hz]. ^{11}B{^{1}H} NMR (d_4-methanol, δ): −5.5 (2 B), −8.1 (2 B), −9.1 (1 B), −11.8 (1 B), −15.7 (1 B), −17.5 (2 B). ^{13}C{^{1}H} NMR (d_4-methanol, δ): 201.07 (CO), 142.41, 140.92, 131.28, 131.26, 128.46, 128.20, 127.18, 126.90 (C$_{Ar}$), 60.15 (br, C$_{carborane}$), 57.01 (br, C$_{carborane}$), 51.11 (CH$_2$), 48.08 (CH$_2$). IR (neat): 2534 (υ_{B-H}), 1999 ($\upsilon_{C=O}$), 1904 ($\upsilon_{C=O}$), 1870 cm^{-1} ($\upsilon_{C=O}$). HRMS (ES$^-$) m/z for C$_{19}$H$_{23}$B$_9$O$_3$Re: calcd 583.2101, observed 583.2098 [M$^-$].

Preparation of [1-CH$_2$Cy-*closo*-C$_2$B$_{10}$H$_{11}$] (20). Decaborane (0.6545 g, 5.355 mmol) was dissolved in a mixture of acetonitrile (5.5 mL) and toluene (25 mL) and brought to reflux under an inert (nitrogen) atmosphere. After 1 h, 3-cyclohexyl-1-propyne (0.85 mL, 0.72 g, 5.9 mmol) was added, and the reaction mixture was heated at reflux for an additional 15 h. The solvent was removed by rotary evaporation; the product **19** was isolated by silica gel chromatography (10% CH_2Cl_2 in hexanes) as a colorless semisolid (0.7512 g, 3.125 mmol, 58%). ^{1}H NMR ($CDCl_3$, δ): 3.54 (br, CH), 2.09 [d, 2 H, C$_{carborane}$−CH_2, ^3J(^{1}H−^{1}H) = 6 Hz], 1.78 (br, d, 2 H, Cy), 1.64 (m, 2 H, Cy), 1.48 (m, 1 H, Cy), 1.24 (m, 2 H, Cy), 1.15 (m, 2 H, Cy), 0.92 (m, 2 H, Cy). ^{11}B{^{1}H} NMR ($CDCl_3$, δ): −1.82 (1 B), −5.22 (1 B), −8.91 (2 B), −10.78 (2 B), −11.35 (2 B), −12.68 (2 B). ^{13}C{^{1}H} NMR ($CDCl_3$, δ): 75.33 (C$_{carborane}$−CH$_2$), 62.00 (CH$_2$−CH), 45.93 (CH$_2$), 37.93 (Cy), 34.06 (Cy), 30.98 (CH$_{carborane}$), 26.00 (Cy). IR (neat): 2930 (ν_{C-H}), 2857 (ν_{C-H}), 2590 cm^{-1} (br, ν_{B-H}). TLC (10% CH_2Cl_2/hexanes): R_f = 0.41. HRMS (EI$^+$) m/z for C$_9$H$_{24}$B$_{10}$: calcd 242.2809, observed 242.2804 [M$^+$].

Table 1. Crystallographic Data

parameter	11	12	13
formula	$C_{10}H_{20}NO_3SF_3B_9$	$ReC_{12}H_{19}NO_3B_9$	$ReC_{12}H_{21}NB_9O_4$
fw	388.63	508.79	526.79
space group	*P*2(1)	*P*2(1)/*c*	*P*2(1)/*n*
a, Å	6.8158(6)	7.4000(2)	9.4919(2)
b, Å	10.9599(9)	15.4930(4)	12.8949(3)
c, Å	12.8039(10)	15.3055(4)	15.9481(4)
α, deg	90	90	90
β, deg	95.531(5)	92.328(2)	96.7330(10)
γ, deg	90	90	90
V, Å^3	952.00(14)	1753.30(8)	1938.54(8)
Z	2	4	4
T, K	173(2)	173(2)	173(2)
λ, Å	1.54178	0.71073	0.71073
d_{calcd}, g cm^{-3}	1.356	1.928	1.805
μ, mm^{-1}	1.685	6.942	6.285
F(*000*)	408	968	1008
R^a	0.0417	0.0265	0.0463
$R_w{}^b$	0.1121	0.0477	0.0586

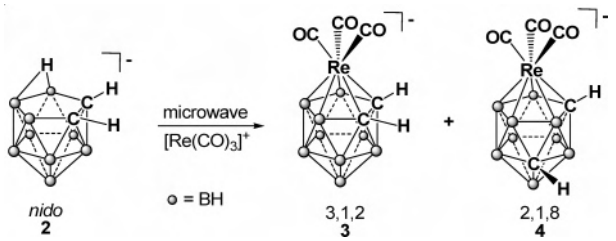
^{a} $R = [\sum||F_o| - |F_c||]/[\sum|F_o|]$ for reflections with $I > 2.00\sigma(I)$. ^{b} $R_w = \{[\sum w(F_o^2 - F_c^2)^2]/[\sum w(F_o^2)^2]\}^{1/2}$ for all reflections.

Preparation of {[K][3,3,3-(CO)$_3$-1-CH$_2$Cy)-*closo*-ReC$_2$B$_9$H$_{10}$]} (21). [1-CH$_2$Cy-*closo*-C$_2$B$_{10}$H$_{11}$] **20** (20.1 mg, 0.0832 mmol) was combined with KF (47.6 mg, 0.819 mmol) and [Re(CO)$_3$(H$_2$O)$_3$]-Br (40.9 mg, 0.101 mmol) in aqueous ethanol (10%, 4 mL) in a microwave vial (5 mL). The reaction mixture was crimp-sealed and heated at 200 °C for 15 min in a microwave reactor. A second portion of [Re(CO)$_3$(H$_2$O)$_3$]Br (34.8 mg, 0.0861 mmol) was added, and the reaction mixture was heated at 200 °C for 10 min. The resulting colorless solution was evaporated to dryness under a stream of $N_{2(g)}$. The product **21** was isolated as a light brown oil (31.4 mg, 0.0583 mmol, 70%) by silica gel chromatography using an automated purification system and a gradient of 3−30% MeOH in CH_2Cl_2. ^{1}H NMR (d_4-methanol, δ): 1.78 (br, t, 2 H, Cy), 1.67 (t, 2 H, C$_{carborane}$−CH_2, ^3J = 5.5 Hz], 1.63 (br, s, 1 H, C$H_{carborane}$), 1.61 (m, 2 H, Cy), 1.38 (m, 2 H, Cy), 1.26 (m, 2 H, Cy), 1.12 (m, 2 H, Cy), 0.77 (br, q, 2 H, Cy). ^{11}B{^{1}H} NMR (d_4-methanol, δ): −5.2 (1 B), −7.7 (2 B), −10.4 (1 B), −11.9 (2 B), −14.8 (1 B), −20.0 (2 B). ^{13}C{^{1}H} NMR (d_4-methanol, δ): 200.89 (CO), 55.11 (br, $C_{carborane}$), 39.12 (C$_{carborane}$−CH$_2$), 35.64 (Cy), 29.42 (br, CH$_{carborane}$), 27.51 (Cy), 27.35 (Cy), 27.32 (Cy). IR (neat): 2531 (br, ν_{B-H}), 1996 ($\nu_{C=O}$), 1884 cm^{-1} (br, $\nu_{C=O}$). TLC (15% MeOH in CH_2Cl_2): R_f = 0.13. HRMS (ES$^-$) m/z for C$_{12}$H$_{23}$B$_9$O$_3$Re: calcd 499.2099, observed 499.2091 [M$^-$].

X-ray Analyses. Colorless crystals of **11** and **12** and a pale yellow crystal of **13** were mounted on glass fibers. Measurements of **11** were made on a Bruker D8 diffractometer with a SMART6000 CCD detector using Cu Kα radiation rendered monochromatic via cross-coupled parallel focusing mirrors. Data for **12** and **13** were collected on a Bruker P4 diffractometer with a SMART1K CCD detector using graphite-monochromated Mo Kα radiation. The program SMART[17] was used for data collection; data processing was carried out by use of the program SAINT;[18] the data were scaled using SADABS.[19] Data were corrected for absorption using the multiscan method. Crystallographic data are summarized in Table 1. The structures were solved by direct methods and refined by full matrix least-squares using SHELXL-97.[20] For **11** and **12**,

(17) Sheldrick, G. M. *SMART, Release 6.45*; Siemens Energy and Automation Inc.: Madison, WI, 2003.
(18) Sheldrick, G. M. *SAINT, Release 6.45*; Siemens Energy and Automation Inc.: Madison, WI, 2003.
(19) Sheldrick, G. M. *SADABS (Siemens Area Detector Absorption Corrections)*; Siemens Energy and Automation Inc.: Madison, WI, 2003.

Scheme 3. Microwave-Assisted Formation of 3,1,2- and 2,1,8-[*closo*-$Re(CO)_3(C_2B_9H_{11})]^-$



some hydrogen atoms were located from a difference map, while the remainder were included at geometrically idealized positions; for **13**, all hydrogen atoms were included at geometrically idealized positions. Non-hydrogen atoms were refined anisotropically. Compound **13** crystallized with a molecule of MeOH in the lattice. Thermal ellipsoid plots were created using Mercury 1.4.1.[21]

Discussion

Generation of 3 and 4. *Closo-ortho*-carboranes are known to undergo fluoride-mediated deboronation reactions in water heated to reflux;[22] similarly, heating aqueous *closo-ortho*-carborane $C_2B_{10}H_{12}$ (**1**) in a microwave reactor at ≥190 °C in the presence of excess MF (M = Na, K) results in quantitative conversion of **1** to the corresponding alkali metal salt [M][7,8-*nido*-$C_2B_9H_{12}$] (**2**) in less than 10 min. The *nido*-carborane **2** is readily differentiated from the starting material by ^{11}B NMR spectroscopy, as it produces a total of five resonances, two of which are at significantly higher field (−33.3, −38.1 ppm) than those of **1** (δ range: −2.0 to −13.2 ppm).

In order to develop a viable set of experimental conditions for the microwave-assisted synthesis of rhenacarboranes, a series of reactions was conducted between the unsubstituted *nido*-carborane **2** and $[Re(CO)_3(H_2O)_3]Br$ in aqueous ethanol. The reaction time was fixed at 10 min, while temperatures of 100, 120, 140, 160, 180, and 200 °C were employed. The crude reaction mixtures were then dissolved in d_4-methanol and analyzed by ^{1}H and ^{11}B NMR spectroscopy. The reactions conducted at 100 and 120 °C were found to contain only unreacted **2**, which is consistent with our observation that only ca. 5% conversion of **2** to the 3,1,2 rhenacarborane **3** (Scheme 3) can be accomplished by refluxing in water for 18 h. When the reaction temperature was increased to 140 °C, however, an additional albeit minor ^{1}H NMR resonance emerged downfield (2.92 ppm) of that of the starting material **2** (1.74 ppm). At 180 °C, this second species constituted nearly 40% of the material detected by NMR spectroscopy; an additional set of resonances was now readily distinguished in the ^{11}B NMR spectrum (Figure 1), though without the two high-field peaks (ca. −33 and −38 ppm) that are characteristic of *nido-ortho*-carboranes. These additional resonances were attributed to the formation of the 3,1,2-rhenacarborane **3** as the ^{1}H NMR signal was in agreement with the literature value.[23] Though the ^{11}B{^{1}H} NMR spectrum of **3** was recorded when it was originally synthesized,[23] the chemical shifts were not reported; however, the chemical shift range observed was consistent with those of other *closo*-(tricarbonyl)-rhenacarboranes.[11a]

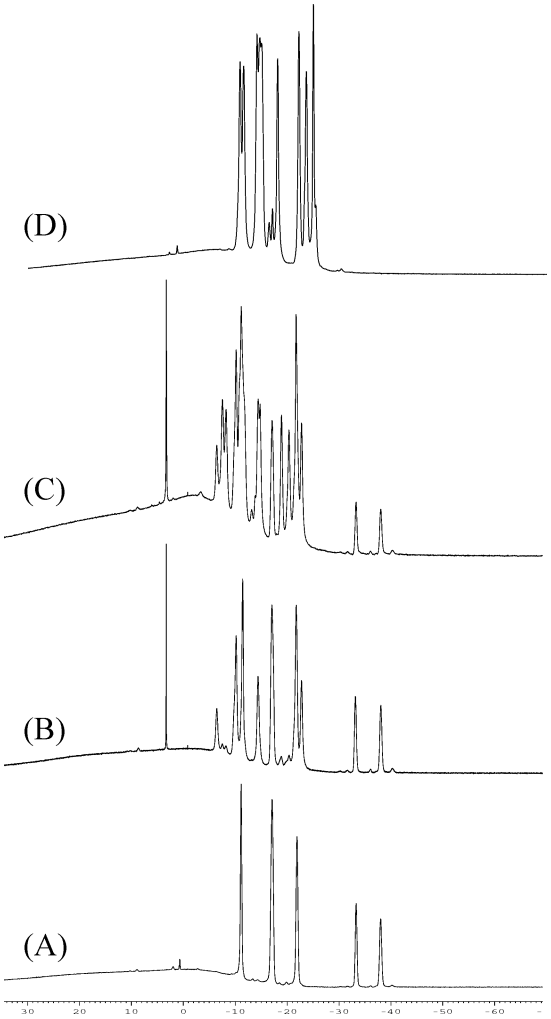
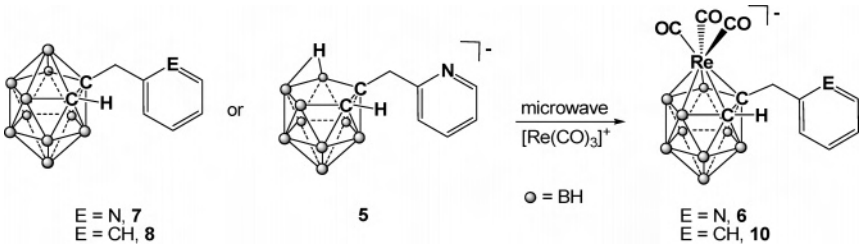


Figure 1. ^{11}B{^{1}H} NMR spectra of the microwave-assisted reaction of **2** with $[Re(CO)_3(H_2O)_3]Br$ at (A) 120, (B) 180, (C) 200 °C, and (D) purified **4**.

The reaction conducted at 200 °C was expected to contain a mixture of **2** and **3**, with a greater proportion of **3**. In actuality, the ^{1}H NMR spectrum indicated a 1:1:2 mixture of **2** and **3** and a third compound, which gave rise to two broad ^{1}H NMR signals (2.21, 1.58 ppm) of equal intensities, and several additional ^{11}B NMR resonances. The reaction mixture was also analyzed by electrospray mass spectrometry, which revealed that the only anionic species present were **2** and a peak corresponding to the tricarbonyl rhenium complex **3**, both of which exhibit diagnostic isotope patterns due to the presence of boron (^{10}B, 19.9%; ^{11}B, 80.1%) and rhenium (^{185}Re, 37.4%; ^{187}Re, 62.6%). Taken in concert, these data suggested that the majority of the 3,1,2-rhenacarborane **3** had been converted to the more thermodynamically stable 2,1,8 isomer **4**, which cannot be differentiated from **3** by mass spectrometry, and displays C_1 symmetry such

(20) Sheldrick, G. M. *SHELXTL, Release 6.14*; Siemens Crystallographic Research Systems: Madison, WI, 2000.
(21) *Mercury 1.4.1*; CCDC: Cambridge, UK, 2001−2005.
(22) Fox, M. A.; MacBride, J. A. H.; Wade. K. *Polyhedron* **1997**, *16*, 2499−2507.
(23) Hawthorne, M. F.; Andrews, T. D. *J. Am. Chem. Soc.* **1965**, *87*, 2496−2496.

Scheme 4. Microwave-Assisted Synthesis of 3,1,2-Rhenacarboranes **6** and **10**



that two carborane C*H* resonances are expected in its ^{1}H NMR spectrum.

In order to confirm these assignments, efforts were made to isolate each of the two isomers **3** and **4** by adjusting the microwave reaction conditions. While it proved possible to obtain **3** as the major species (ca. 80%), it was not formed exclusively under any conditions, nor was it possible to separate **2**, **3**, and **4** chromatographically. Experiments directed at preparing the purported 2,1,8 isomer **4** were far more successful. Starting either with the crude 3,1,2 isomer **3** prepared as outlined above, or from pure **2** and $[Re(CO)_3(H_2O)_3]Br$, heating in a microwave reactor at 200 °C for 1 h was found to yield exclusively the 2,1,8 complex **4**, which was isolated by silica gel chromatography and characterized spectroscopically. The ^{13}C NMR spectrum of **4** contained two resonances (37.13, 29.12 ppm) corresponding to the two inequivalent CH units observed in the ^{1}H NMR spectrum, as well as a signal at 200.58 ppm due to the three CO ligands. The presence of these CO units was also confirmed by infrared spectroscopy, with two broad absorptions centered at 2001 and 1894 cm^{-1} in addition to the B−H stretching vibrations (2555 cm^{-1}). A total of nine signals are readily distinguished in the ^{11}B NMR spectrum due to the decrease in symmetry of the C_2B_9 cage upon isomerization. High-resolution electrospray mass spectrometry was used to confirm the identity of the product, with a characteristic isotope distribution centered at 402.1146 *m*/*z* corresponding to the molecular anion.

Deriving from these and other experiments a set of conditions that would be generally applicable to the synthesis of tricarbonyl rhenacarboranes was challenging, as the temperature at which complexation of a *nido*-carborane to the $[Re(CO)_3]^+$ core occurs is highly dependent upon the identity of the substituent(s) attached to the carborane cage. For example, complexation of the pyridyl-derivatized *nido*-carborane **5** with $[Re(CO)_3(H_2O)_3]Br$ is 90% complete after 20 min at 140 °C; conversely, only 8% conversion of *nido*-phenyl carborane to a rhenacarborane is observed under identical conditions. Ultimately, reaction conditions of 15 min at 200 °C were selected as a starting point for the synthesis of compounds of the type $[M][Re(CO)_3(RR'C_2B_9H_9)]$, as they appear to be more than sufficient for effecting the majority of the desired complexation reactions.

Pyridyl-Bearing Rhenacarboranes: Electronic Contributions to Isomerization. We are not aware of any studies done to date that have examined the impact of altering the electron-donating properties of the carborane substituent on the barrier to cage isomerization and decided to explore this area by revisiting the synthesis of the 3,1,2-rhenacarborane **6**. The potassium salt of this anion has been synthesized previously by combining the corresponding *nido*-carborane **5** with $[Re(CO)_3]^+$ in boiling water over 24 h.[11a] The spectroscopic data obtained for the product of the analogous microwave-assisted reaction (Scheme 4), including the ^{11}B NMR spectrum, were consistent with those reported for **6**, indicating that the same isomer formed in both cases.[11a]

In order to definitively establish the configuration of the carborane cage of **6**, a NOE ^{1}H NMR experiment was done wherein the carborane C*H* resonance frequency was irradiated in order to enhance the signals due to neighboring protons. A significant enhancement of the signal due to the diastereotopic methylene protons (3.38 ppm) was observed (see Supporting Information), indicating close proximity to the carborane CH. An identical experiment was performed using the *closo*-carborane precursor **7**, and a similar enhancement in the methylene proton signal was observed. This indicated that the distance between the carborane CH and CH_2 unit of **7** is comparable to that in the rhenacarborane **6**, and confirmed that the 3,1,2 isomer had indeed been isolated.

In order to examine what impact, if any, altering the electron-withdrawing properties of the carborane substituent on the carborane cage would have on the isomerization process, it was decided to prepare the benzyl (Bn, $CH_2-C_6H_5$) analogue of **6**. This was done by treating *closo-ortho*-carborane **1** with 1.5 equiv of ^{n}BuLi at −78 °C, followed by addition of an excess of benzyl chloride or bromide: this reaction produces a mixture of *closo*-benzyl carborane **8** and *closo*-dibenzyl carborane **9**, which can be separated by silica gel chromatography. Further reaction of **8** with $[Re(CO)_3(H_2O)_3]Br$ in the presence of sodium fluoride yielded the 3,1,2 tricarbonyl rhenium complex **10** (Scheme 4), as described in a preliminary communication.[13] The $^{11}B\{^1H\}$ NMR spectrum of **10** is essentially identical to that of **6**, displaying six signals in the 1:2:1:2:1:2 pattern that we have found to be characteristic of monosubstituted 3,1,2 rhenacarboranes including the previously reported species $\{[Na][3,3,3\text{-}(CO)_3\text{-}1\text{-}R\text{-}3,1,2\text{-}closo\text{-}ReC_2B_9H_{10}]\}$ (R = CH_2CH_2COOH, glucose).[11a] This pattern arises due to incidental equivalences in the ^{11}B NMR signals of three cage boron atoms, since the molecular point group of these 3,1,2-rhenacarboranes is C_1.

Both the 3,1,2 complexes **6** and **10** were subjected to prolonged heating in the microwave reactor: ^{1}H and ^{11}B NMR spectra were recorded afterward, but were found not to undergo carborane cage isomerization despite the harsh conditions (200 °C, 20 bar). This finding was slightly

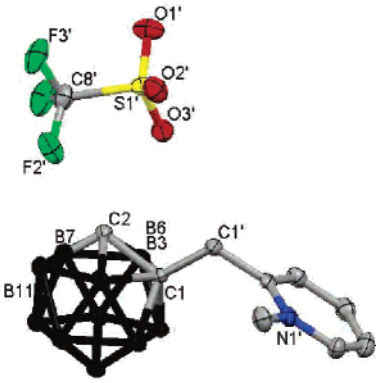


Figure 2. Thermal ellipsoid plot of **11** (30% probability ellipsoids); H atoms omitted.

Table 2. Selected Bond Lengths (Å) and Angles (deg) for **11**

C(1)−C(2)	1.649(4)	C(1)−C(1′)	1.527(4)
C(1)−B(3)	1.723(4)	C(1)−B(4)	1.720(4)
C(1)−B(5)	1.711(4)	C(1)−B(6)	1.736(4)
C(2′)-N(1′)	1.374(4)	C(7′)−N(1′)	1.482(4)
B(7)−B(12)	1.783(5)	B(10)−B(12)	1.785(5)
C(2)−C(1)−B(3)	115.7(2)	B(3)−C(1)−B(5)	113.9(2)
B(4)−C(1)−B(6)	113.4(2)	B(3)−C(1)−B(6)	113.6(2)
C(2)−B(3)−B(4)	104.7(2)	B(3)−B(4)−B(5)	108.0(2)
B(4)−B(5)−B(6)	108.4(2)	B(5)−B(6)−C(2)	103.8(2)
B(7)−B(12)−B(9)	107.6(2)	B(8)−B(12)−B(10)	108.4(2)

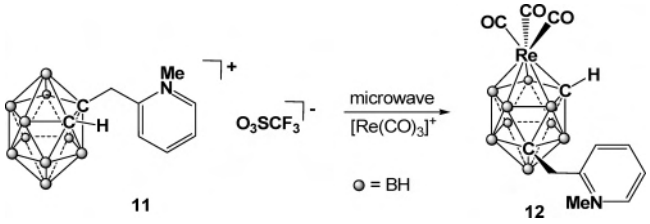
surprising in light of the results described for the unsubstituted complex **3**/**4**, where isomerization was observed even at 170 °C. Though in all three cases (**3**, **6**, and **10**) the 2,1,8 isomer is more thermodynamically stable, the activation energy barrier for a process involving the movement of a benzyl or CH_2−pyridyl substituent is rationalized to be much larger than the corresponding process involving a cage CH unit: thus, compound **3** isomerizes to **4**, but compounds **6** and **10** remain unchanged.

To further alter the electronic nature of the carborane substituent, methylation of the pyridyl ring of **7** was effected using methyl triflate, yielding the *closo*-carborane **11**, which was characterized both spectroscopically and by X-ray crystallography. The ^{1}H NMR spectrum of **11** in d_6-acetone contained four resonances in the aromatic region as well as sharp singlets at 4.67 and 4.57 ppm due to the CH_3 and CH_2 moieties, respectively; the carborane CH appeared as a broad peak at 5.18 ppm, which is typical for a monosubstituted *closo*-carborane. The ^{13}C NMR spectrum was consistent with this, though the anticipated quartet due to the $[CF_3SO_3]^-$ carbon atom remained unresolved; the ^{11}B NMR spectrum of **11** was virtually unchanged from that of **7**.

The product was definitively identified by high-resolution electrospray mass spectrometry ([M^+] 251.2587 *m*/*z*) and X-ray crystallography. A thermal ellipsoid plot of **11**, which crystallizes in the $P2_1$ space group, is shown in Figure 2; crystallographic data and pertinent metrical parameters are summarized in Tables 1 and 2, respectively. The solid-state structure of **7** has been determined previously;[24] as expected, the most significant difference between the structures of **7**

(24) Alekseyeva, E. S.; Batsanov, A. S.; Boyd, L. A.; Fox, M. A.; Hibbert, T. G.; Howard, J. A. K.; MacBride, J. A. H.; Mackinnon, A.; Wade, K. *Dalton Trans.* **2003**, 475−482.

Scheme 5. Microwave-Assisted Synthesis of the 2,1,8-Rhenacarborane **12**



and **11** is the average C−N bond distance within the pyridyl ring, which increased from 1.331(4) to 1.428(4) Å upon methylation. The carborane cage C−C bond length of **11** [1.649(4) Å] is also slightly longer than that of **7** [1.622(4) Å] due to the inductive electron-withdrawing effect of the methylated pyridyl ring. The B−B distances in **11** range from 1.755(5) to 1.783(5) Å.

The *closo*-carborane **11** was converted to its *nido* analogue in situ by combining it with sodium fluoride and heating under microwave irradiation at 195 °C (Scheme 5) prior to addition of the rhenium reagent $[Re(CO)_3(H_2O)_3]Br$; the product **12** was isolated by silica gel chromatography. The ^{1}H NMR spectrum of **12** in d_6-acetone displayed the expected four resonances in the aromatic region, as well as a sharp singlet at 4.55 ppm due to the methyl group, an AA′ pattern at 3.82 ppm due to the diastereotopic protons of the methylene unit, and a broad resonance attributed to the carborane CH vertex (1.84 ppm). The corresponding signals were observed in the ^{13}C NMR spectrum, as well as a resonance at 199.58 ppm, assigned to the three CO ligands. Curiously, the ^{11}B NMR spectrum of the product did not display the 1:2:1:2:1:2 pattern that we have found to be characteristic of 3,1,2-rhenacarboranes: a total of eight distinct signals could be resolved, indicating that the carborane cage of this product had lower symmetry than those of **6** and **10**.

In order to assess whether compound **12** was in the 3,1,2 or 2,1,8 configuration, ^{1}H NMR NOE experiments were conducted on both the *closo*-carborane **11** and the rhenacarborane **12** (see Supporting Information). Irradiation of the carborane CH vertex of **11** resulted in a distinct enhancement in the methylene signal, and to a lesser extent, of one aromatic proton and the methyl resonance. However, when the CH resonance frequency of the rhenacarborane **12** was irradiated, no enhancement was observed in methylene signal, presumably due to an increase in the distance between those two moieties, suggesting that the 2,1,8 isomer had been obtained.

Following recrystallization of the product, confirmation of this hypothesis was obtained by single-crystal X-ray diffraction. As shown in Figure 3, complex **12** consists of a 1,7 carborane ligand that is coordinated to the $[Re(CO)_3]^+$ core through a CB_4 bonding face. The carborane cage C atom that is directly bonded to the CH_2−pyridyl substituent has migrated out of the bonding face of the ligand. The average Re−B bond length (see Table 3) in **12** is 2.317(4) Å, while the Re−C distance is slightly shorter at 2.301(3) Å, consistent with the smaller size of carbon as compared to boron. A greater range of B−B distances [1.744−1.814(5) Å] is seen

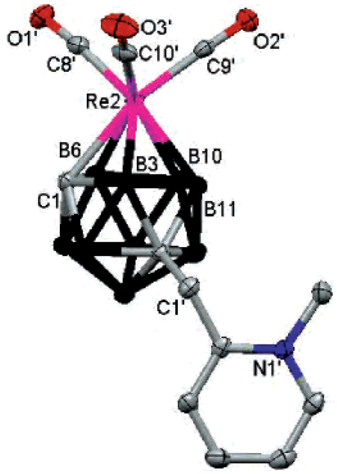


Figure 3. Thermal ellipsoid plot of **12** (50% probability ellipsoids); H atoms omitted.

Table 3. Selected Bond Lengths (Å) and Angles (deg) for **12**

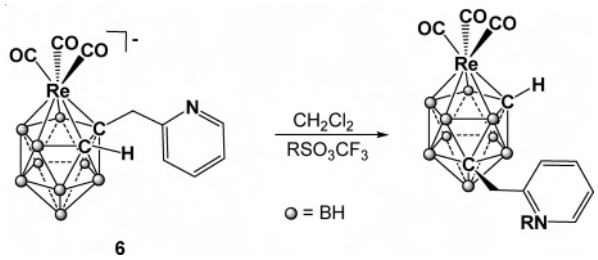
B(3)−Re(2)	2.268(3)	B(6)−Re(2)	2.312(4)
B(10)−Re(2)	2.353(4)	B(11)−Re(2)	2.333(4)
Re(2)-C(8′)	1.924(4)	C(1)−Re(2)	2.301(3)
C(1)−B(3)	1.721(5)	C(1)−B(6)	1.755(5)
B(3)−B(11)	1.791(5)	B(6)−B(10)	1.790(6)
B(10)−B(11)	1.814(5)	C(1)−B(5)	1.714(5)
B(5)−B(6)	1.787(5)		
C(1)−Re(2)−B(10)	75.29(13)	C(1)−Re(2)−B(3)	44.25(12)
B(3)−Re(2)−B(11)	45.80(13)	B(3)−Re(2)−B(6)	77.56(13)
C(1)−B(3)−B(11)	107.6(2)	B(3)−C(1)−B(6)	111.3(3)
B(6)−B(10)−B(11)	107.3(3)	C(1)−B(6)−B(10)	106.6(3)

for **12** than for **11** due to the significantly different electronic environments of the boron atoms on the bonding face of the carborane versus those in the rest of the cluster.

We were curious regarding the temperature required to induce this isomerization process compared to that of **3**/**4**, as the energetic cost associated with movement of the methylated pyridyl unit was expected to be much larger than the CH unit of **3**/**4**. This could potentially be determined by preparing the 3,1,2 isomer of **12**, and monitoring its behavior as a function of temperature. To that end, the synthesis of the 3,1,2 isomer of **12** was undertaken via the reaction of **6** with an equivalent of methyl triflate. The reaction mixture was stirred at 22 °C in dichloromethane, and the product characterized by multinuclear NMR spectroscopy. Surprisingly, the spectra obtained for this supposed 3,1,2 isomer were identical to those obtained of **12**, indicating that the 3,1,2 rhenacarborane undergoes isomerization at room temperature upon methylation (Scheme 6). This result clearly demonstrates that the electronic nature of the substituent on the carborane cage is as influential as steric consideration in determining the activation energy barrier to carborane cage isomerization.

To confirm that formation of the 2,1,8 isomer was indeed caused by the introduction of a positively charged unit onto the carborane substituent, rather than a result of the increased size of the substituent upon methylation, we sought to prepare the protyl analogue of **12** by reacting **6** with an equivalent of triflic acid rather than methyl triflate. Notably, the ^{11}B NMR spectrum of this reaction product **13** was not consistent with that of **6** as expected for two isostructural compounds.

Scheme 6. Room-Temperature Isomerization of **6** to **12** (R = Me) and **13** (R = H)



A ^{1}H NMR NOE experiment was then conducted in which the carborane CH resonance of **13** was irradiated. Contrary to what was seen for **6**, no enhancement of the methylene signal of **13** occurred, indicating that the distance between the CH_2 unit and the carborane CH vertex was greater in **13** than in **6**. Final confirmation that isomerization of the carborane cage had occurred upon protonation of **6** to yield **13** (Scheme 6) was obtained in the form of an X-ray crystal structure (not shown) which revealed that **13** is isostructural with **6**, with the carborane cage bonded to the rhenium center through a CB_4 bonding face, and the substituted carborane C vertex removed from the bonding face. Corresponding metrical parameters for **12** and **13** were in close agreement with one another (see Supporting Information).

Steric Contributions to Isomerization. As the formation of the 2,1,8 isomers **12** and **13** was evidently an electronic effect, we explored the possibility of inducing a similar process by increasing the steric crowding on the bonding face of the carborane ligand: this can be done by eliminating the methylene unit between the pyridyl ring and the carborane cage. *Closo*-pyridyl carborane **14** was prepared according to the literature procedure,[16] then reacted with $[Re(CO)_3(H_2O)_3]Br$ in a microwave reactor at 200 °C. Following purification by silica gel chromatography, the rhenacarborane **15** was characterized spectroscopically.

The ^{1}H NMR spectrum of **15** in d_4-methanol contained four resonances of equal intensities in the aromatic region, as well as a broad singlet at 1.81 ppm. Incidentally, the carborane CH of the closely related phenyl-bearing 3,1,2-rhenacarborane **16** resonates at 3.95 ppm, while isomerization to its 2,1,8 analogue **17** is accompanied by a decrease in chemical shift to 1.75 ppm. This observation, combined with the ^{11}B NMR spectrum of **15**, which did not display the pattern typical of a 3,1,2 rhenacarborane, suggested that the 2,1,8 isomer had in fact been prepared. This was confirmed by a ^{1}H NMR NOE experiment, in which irradiation of the carborane CH proton failed to result in any enhancement of the signals of the pyridyl ring.

For comparison with the variable-temperature experiment conducted for the complexation of **2** with the rhenium tricarbonyl core, a similar reaction series was done with the *nido*-pyridyl carborane, generated by fluoride-mediated deboronation of **14**. All reaction times were 10 min, while temperatures of 100, 120, 140, 160, 180, and 200 °C were employed. Analysis of the crude reaction mixtures by ^{1}H and ^{11}B NMR spectroscopy revealed complete consumption

of the carborane ligand to form the 2,1,8 complex **15** at temperatures of 160 °C and above. This was somewhat surprising, given that the corresponding reaction of **2** is not complete even after 15 min at 200 °C, and the pyridyl ring at the ligand bonding face would be expected to provide enough steric hindrance to slow this reaction considerably relative to that of **2**. The reaction conducted at 100 °C was subjected to high-resolution electrospray mass spectrometry, which confirmed the presence of the *nido*-carborane and suggested the second species to be the rhenacarborane **15**. However, the ^{1}H NMR spectrum of the reaction indicated that it contained a 1:1 mixture of unreacted *nido*-pyridyl carborane and a second species which was inconsistent with the ^{1}H NMR spectrum obtained previously for **15**. Most notably, a broad singlet attributable to a carborane CH vertex was observed at 4.21 ppm, rather than the expected resonance seen at 1.81 ppm in compound **15**. The ^{11}B NMR spectrum, though complicated by the presence of two species with several overlapping signals, did not exhibit the characteristic peaks of **15**. Bearing in mind that isomerization of the closely related phenyl-bearing 3,1,2-rhenacarborane **16** to its 2,1,8 isomer **17** is accompanied by a decrease in the ^{1}H NMR chemical shift of the carborane CH from 4.1 to 1.76 ppm, the data as a whole suggest that the second species present in this reaction is the 3,1,2 analogue of **15**, i.e., {[Na][3,3,3-$(CO)_3$-1-C_5H_4N-3,1,2-*closo*-$ReC_2B_9H_{10}$]} (**18**).

The reaction conducted at 120 °C contained a 1:3:5 mixture (by ^{1}H NMR integration) of **15**, *nido*-pyridyl carborane, and the species identified as **18**, indicating that this slight increase in reaction temperature was sufficient to overcome the activation energy barrier to isomerization such that a small amount of **18** had been converted to the more thermodynamically stable product **15**. As expected, when the reaction temperature was increased to 140 °C, the same three compounds were present but in a 5:1:3 ratio, based on ^{1}H NMR integrations: that is, the majority of the material present had isomerized to yield **15**.

An analogous variable-temperature study of the reaction of *nido*-phenyl carborane with $[Re(CO)_3(H_2O)_3]$Br yielded no evidence for the initial formation of the 3,1,2 isomer: the only species present in the reaction mixtures were *nido*-phenyl carborane and **17**, indicating that complexation of the carborane ligand to the $[Re(CO)_3]^+$ core and isomerization of the carborane cage occur simultaneously. Also, in contrast to the experiments done with **14**, no complex formation could be detected at temperatures less than 160 °C, while only 50% conversion of the *nido*-carborane to **17** was observed at 200 °C. By analogy with the pyridyl−carborane complexes **15** and **18**, this temperature is well in excess of that which is expected to be required for isomerization of the 3,1,2 metallacarborane **16** to occur and explains why only the 2,1,8 isomer **17** is observed from microwave-assisted reactions. What remains unclear is the reason for the drastic difference in the minimum temperature required for formation of the two isosteric rhenacarboranes **16** and **18** at a constant reaction time of 10 min. A possible explanation is that the basic pyridyl functionality assists in removing the bridging hydrogen atom of the *nido*-carborane cage, thus assisting in the formation of the η^5-complex.

To further probe the amount of steric crowding required to induce carborane cage isomerization, reactions between dibenzyl carborane **9** and $[Re(CO)_3(H_2O)_3]$Br were undertaken. We have demonstrated that the presence of one benzyl unit was not sufficient to effect isomerization: the presence of a second benzyl substituent will increase steric crowding at the ligand bonding face considerably, though not nearly as much as for bis-phenol carborane (Scheme 2) due to the flexibility provided by the methylene spacers. The reagents were combined with potassium fluoride and heated in the microwave at 200 °C; the product **19** was isolated by silica gel chromatography and identified by mass spectrometry (583.2098 *m*/*z* [M$^-$]) and multinuclear NMR spectroscopy. Both the ^{1}H and ^{13}C NMR spectra clearly indicated the presence of two inequivalent benzyl substituents: two distinct signals (60.15, 57.01 ppm) were also detected in the carbon-13 spectrum due to inequivalent carborane cage C atoms. Thus, the dibenzyl rhenacarborane **19** was determined to be in the 2,1,8 configuration that was observed for the sterically crowded monosubstituted carboranes **15** and **17**.

A final compound of interest for the purposes of this study was one with an intermediate amount of steric bulk between the 3,1,2 complexes **6**, **10**, **12**, and **13**, and the 2,1,8 species **15** and **17**. A logical target molecule was one that retains the methylene spacer of the 3,1,2 complexes between the carborane cage and the six-membered ring but possesses a bulkier, e.g., cyclohexyl, ring after that unit. To that end, the novel *closo*-carborane **20** was synthesized via an alkyne insertion into the boron cage of decaborane and isolated in modest yield (58%) via silica gel chromatography. Compound **20** was then reacted with $[Re(CO)_3(H_2O)_3]$Br at 200 °C; following purification by silica gel chromatography, the rhenacarborane **21** was recovered in good yield (70%) and characterized spectroscopically. The ^{1}H and ^{13}C NMR spectrum of **21** in d_4-methanol contained the expected resonances due to the CH_2−Cy (Cy = C_6H_{11}, cyclohexyl) unit and carborane CH, but gave little indication of the configuration of the carborane cage. A ^{11}B NMR spectrum was subsequently obtained and found to display six resonances in a 1:2:1:2:1:2 pattern, indicating that the original ortho geometry of the carborane cage had been retained. Unfortunately, attempts to confirm this utilizing a ^{1}H NMR NOE experiment were not successful due to significant overlap of the BH, CH, and cyclohexyl resonances, rendering it impossible to discern whether enhancement of the cyclohexyl signals occurred upon irradiation of the carborane CH resonance frequency. The identity of the novel rhenacarborane **21** was confirmed by high-resolution electrospray mass spectrometry (499.2091 *m*/*z* [M$^-$]).

Conclusion

The use of a microwave reactor has facilitated an investigation of 1,2 → 1,7 carborane cage isomerization in rhenacarborane complexes. For the unsubstituted carborane **2**, cage isomerization occurs upon heating at ∼170 °C; introduction of a CH_2−R (R = Ph, Pyr, Cy) unit increases

the isomerization energy barrier such that the 3,1,2 configuration is retained. Removal of the methylene spacer increases steric crowding at the metal center: relief of this steric strain provides sufficient energy to overcome this activation energy barrier, and the 2,1,8 complexes are obtained. Though the mechanism of this process remains unknown, our observation that the presence of a positively charged substituent lowers the isomerization energy barrier significantly may provide a starting point for further empirically or computationally based investigations into this phenomenon.

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Supporting Information Available: ^{1}H NMR and ^{1}H NMR NOE spectra for **11** and **12**; crystallographic cif files for **11**−**13**. This material is available free of charge via the Internet at http://pubs.acs.org.

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