Supporting Information

for

Carborane guests for cucurbit[7]uril facilitate strong binding and on demand removal

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Supporting Figures

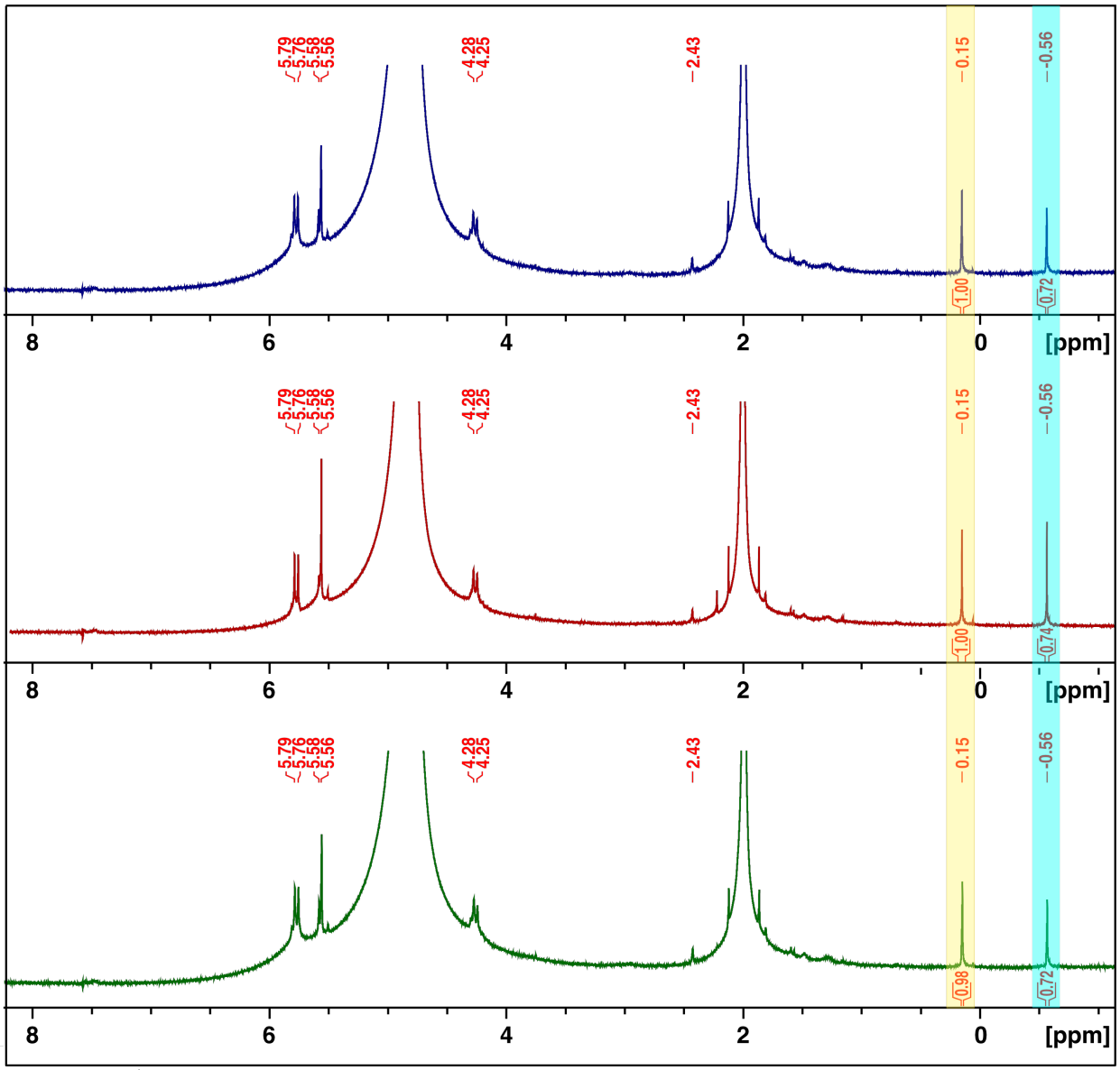


Figure S1: ^{1}H NMR spectra of competition experiment to determine binding affinity of 9-amino-*ortho*-carborane (**4**). Each spectrum (blue, green, red) represents each of three replicate experiments. In short, 1.5 equivalents of (trimethylsilyl)methylamine (0.5049 mM), and 1 equivalent of **4** (0.3366 mM) were added to a limited amount of CB[7] (0.2806 mM) in 50 mM deuterated sodium acetate buffer. A relative binding affinity (K_{rel}) was calculated based on the relative integration values of (trimethylsilyl)methylamine **bound** to CB[7] (-0.56 ppm, highlighted blue) or **free** (0.15 ppm, highlighted yellow). K_{rel} was used to determine the K_a based on the known K_a of (trimethylsilyl)methylamine (K_a = 8.88 x 10^8 M^{-1}) and according to equations and error analysis presented by Isaacs and coworkers in 2005.[1]

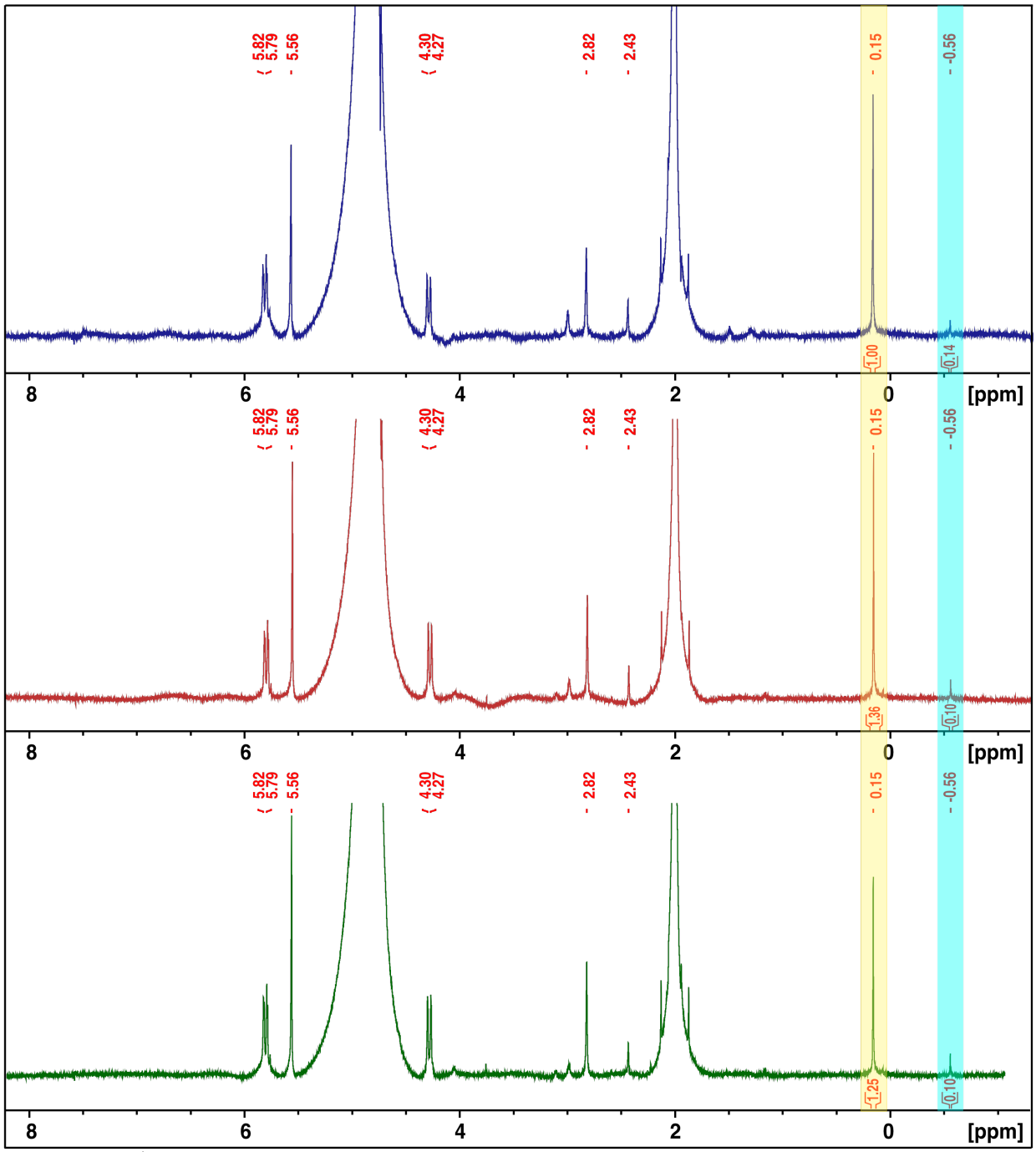


Figure S2: ^{1}H NMR spectra of competition experiment to determine binding affinity of 9-trimethylammonium-*ortho*-carborane (**5**). Each spectrum (blue, green, red) represents each of three replicate experiments. In short, 1.5 equivalents of (trimethylsilyl)methylamine (0.5049 mM), and 1 equivalent of **5** (0.3366 mM) were added to a limited amount of CB[7] (0.2806 mM) in 50 mM deuterated sodium acetate buffer. A relative binding affinity (K_{rel}) was calculated based on the relative integration values of (trimethylsilyl)methylamine **bound** to CB[7] (-0.56 ppm, highlighted blue) or **free** (0.15 ppm, highlighted yellow). K_{rel} was used to determine the K_a based on the known K_a of (trimethylsilyl)methylamine (K_a = 8.88x10^{8} M^{-1}) and according to equations and error analysis presented by Isaacs and coworkers in 2005.[1]

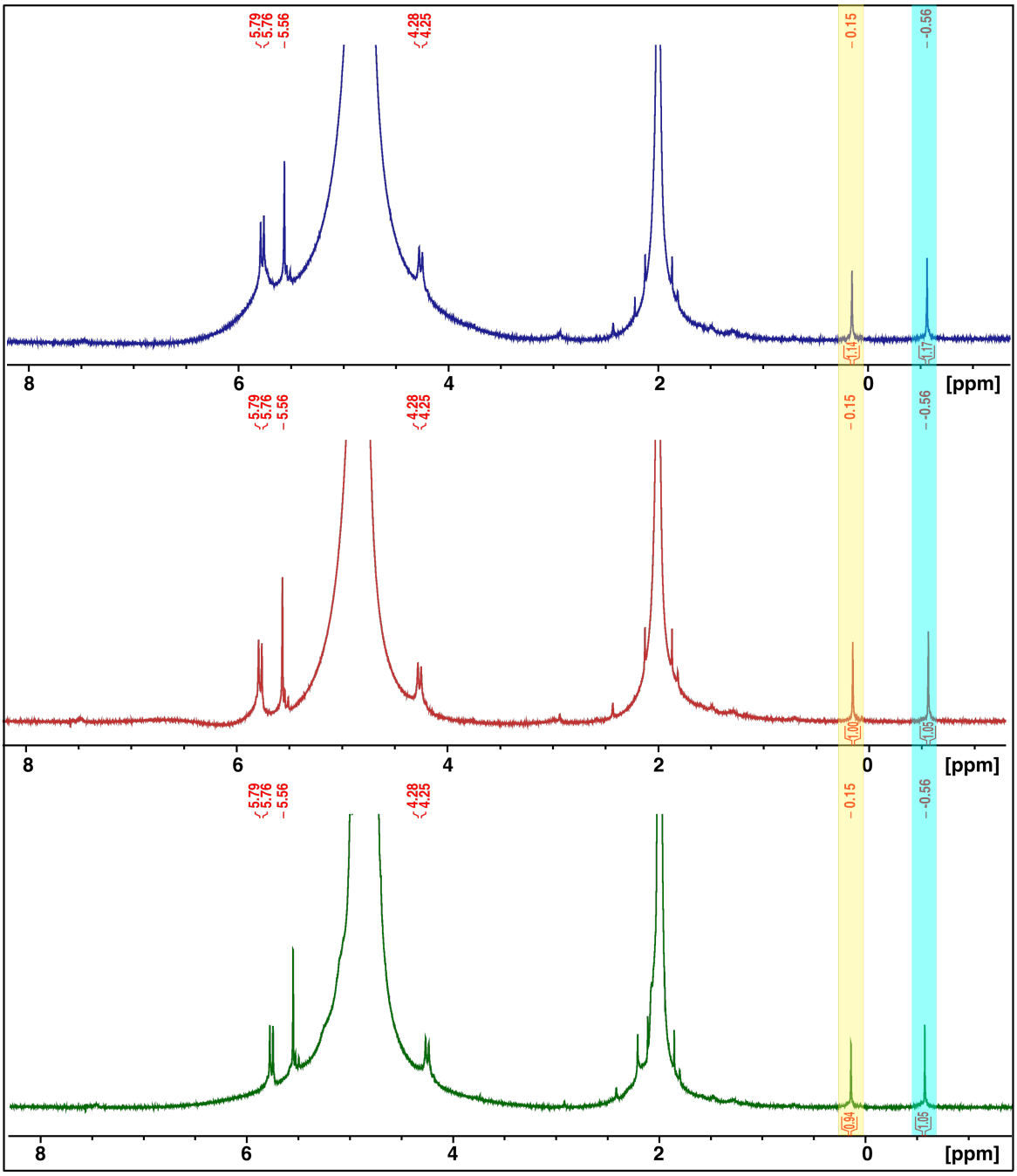


Figure S3: ^{1}H NMR spectra of competition experiment to determine binding affinity of 9-trimethylammonium-*meta*-carborane (**7**). Each spectrum (blue, green, red) represents each of three replicate experiments. In short, 1.5 equivalents of (trimethylsilyl)methylamine (0.5049 mM), and 1 equivalent of **7** (0.3366 mM) were added to a limited amount of CB[7] (0.2806 mM) in 50 mM deuterated sodium acetate buffer. A relative binding affinity (K_{rel}) was calculated based on the relative integration values of (trimethylsilyl)methylamine **bound** to CB[7] (-0.56 ppm, highlighted blue) or **free** (0.15 ppm, highlighted yellow). K_{rel} was used to determine the K_a based on the known K_a of (trimethylsilyl)methylamine (K_a = 8.88x10^{8} M^{-1}) and according to equations and error analysis presented by Isaacs and coworkers in 2005.[1]

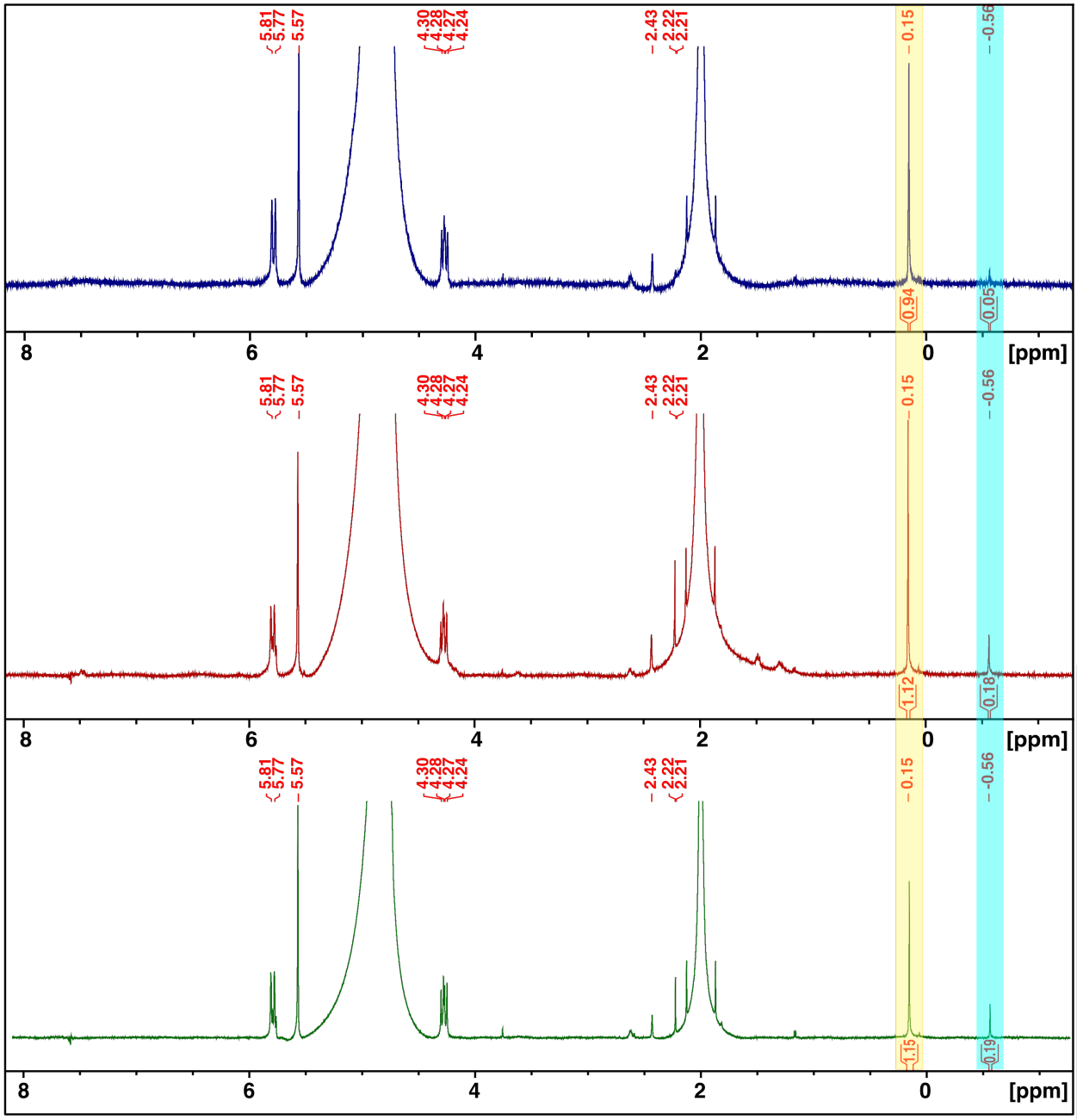


Figure S4: ^{1}H NMR spectra of competition experiment to determine binding affinity of 9-amino-*meta*-carborane (**8**). Each spectrum (blue, green, red) represents each of three replicate experiments. In short, 1.5 equivalents of (trimethylsilyl)methylamine (0.5049 mM), and 1 equivalent of **8** (0.3366 mM) were added to a limited amount of CB[7] (0.2806 mM) in 50 mM deuterated sodium acetate buffer. A relative binding affinity (K_{rel}) was calculated based on the relative integration values of (trimethylsilyl)methylamine **bound** to CB[7] (-0.56 ppm, highlighted blue) or **free** (0.15 ppm, highlighted yellow). K_{rel} was used to determine the K_a based on the known K_a of (trimethylsilyl)methylamine (K_a = 8.88x10^{8} M^{-1}) and according to equations and error analysis presented by Isaacs and coworkers in 2005.[1]

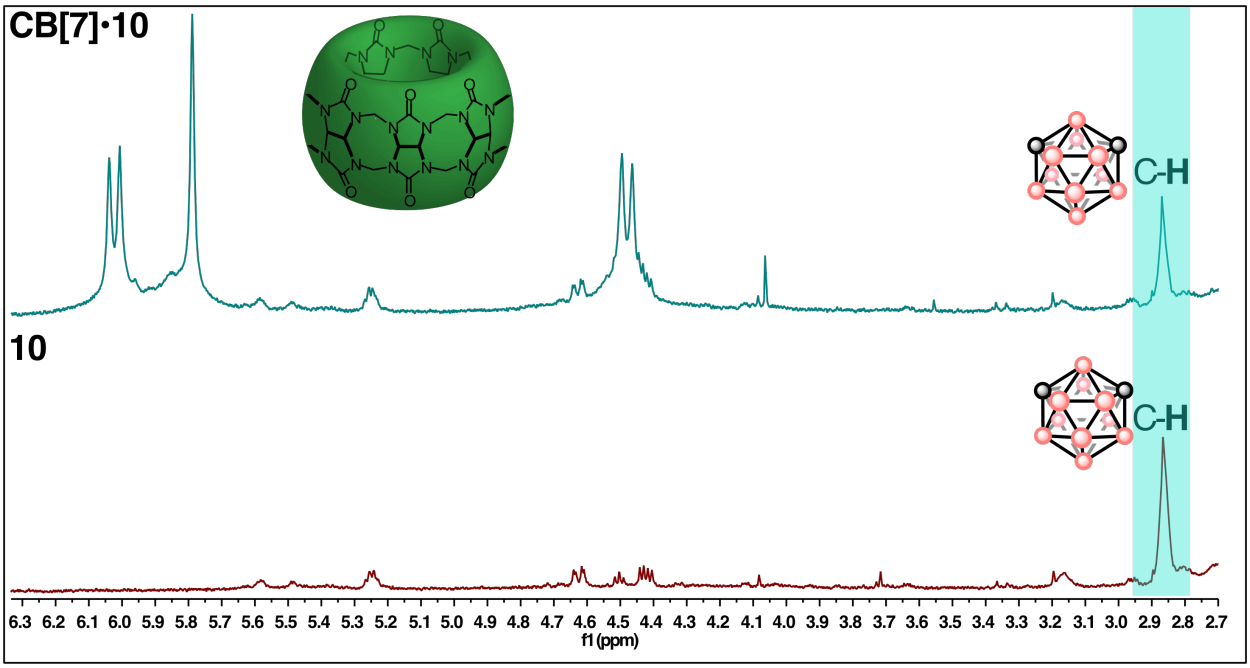


Figure S5: ^{1}H NMR spectra of **10** in the presence (top, blue) and absence (bottom, red) of CB[7]. Spectra taken in TFA-d_1 show no shift in the carborane C-H proton when **10** is incubated with CB[7] in 100% TFA (top, blue spectrum).

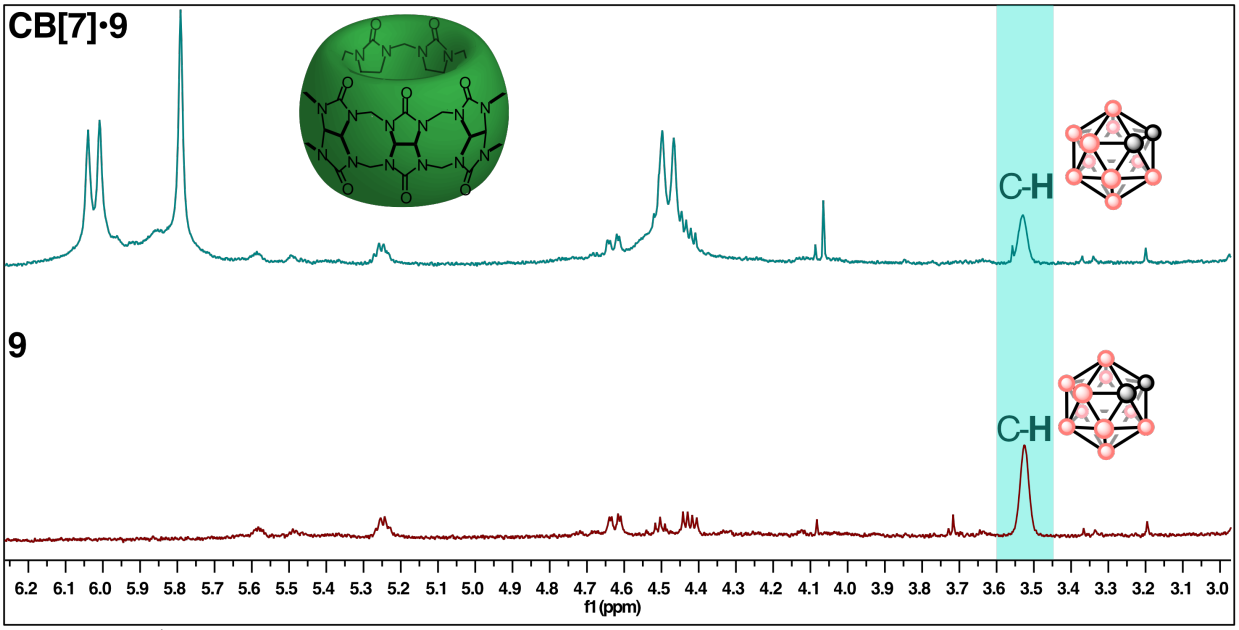


Figure S6: ^{1}H NMR spectra of **9** in the presence (top, blue) and absence (bottom, red) of CB[7]. Spectra taken in TFA-d_1 show no shift in the carborane C-H proton when **9** is incubated with CB[7] in 100% TFA (top, blue spectrum).

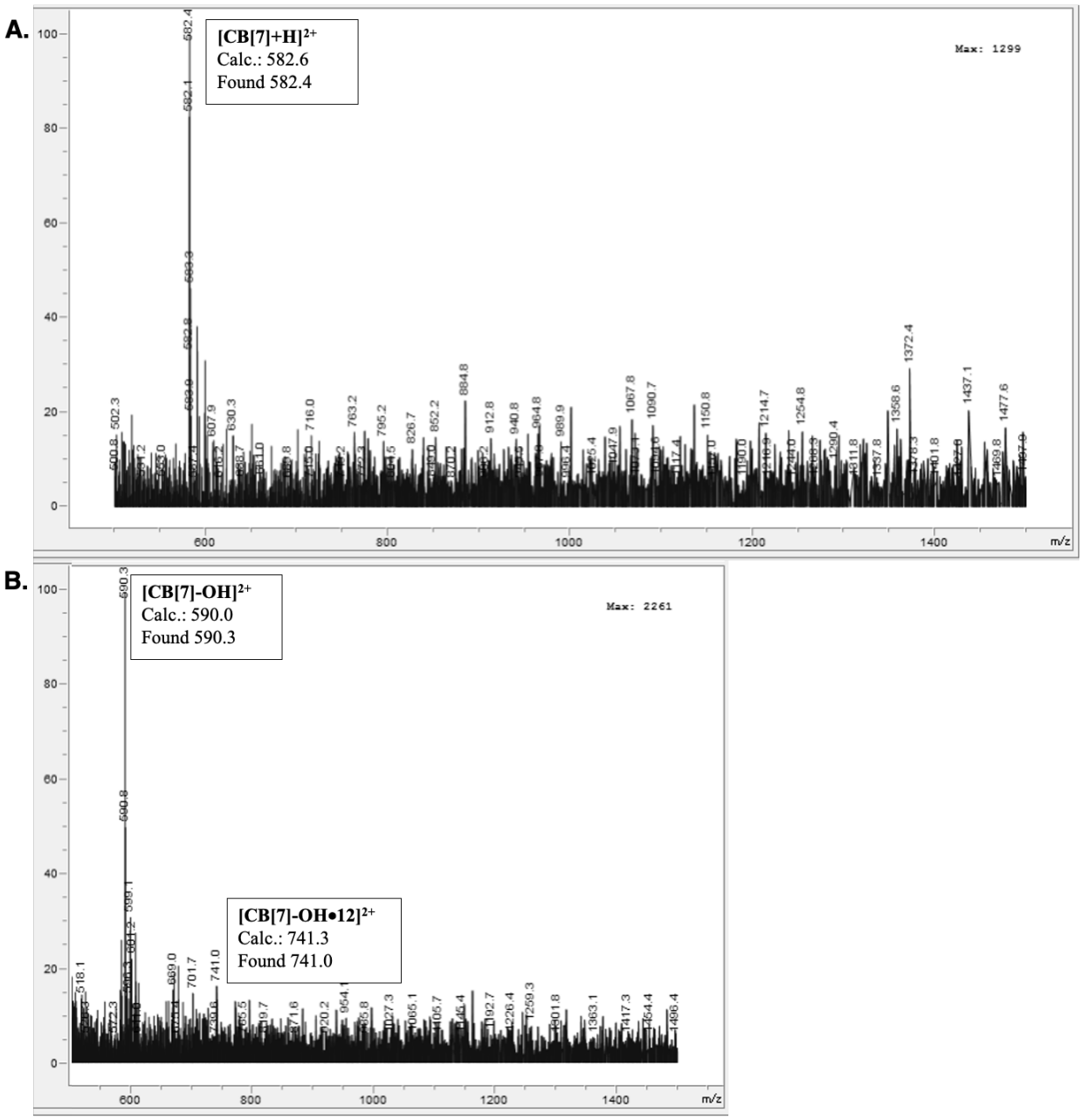


Figure S7: (A) Mass spectrum (ESI) of **CB[7]•9** formed in TFA and isolated by MeOH precipitation and DCM wash. The isolated complex was analyzed in H_2O. (**B**) **CB[7]-OH•10** isolated after addition of **10** (1.7 mg, 11 μmol, 10 eq.) in a solution of **CB[7]-OH•12** (1.9 mg, 1 μmol, 1 eq.) in TFA (1.5 mL) and brief sonication. The **CB[7]-OH•10** complex was isolated by precipitation with MeOH and **12** and excess **10** were washed away with DCM. Note: We have not been able to observe **CB[7]•9** and **CB[7]•10** masses, despite confirming complexation by NMR. Instead the spectra show a single mass for **CB[7]** or **CB[7]-OH**. CB[7] alone appears as a collection of m/z in ESI due to association with Na^+, K^+, and other positively charged ions. Hence, we found that single CB[7] mass when analyzing **CB[7]•9** and **CB[7]•10** particularly interesting and we hypothesize that carboranes bound to CB[7] degrade or sublime during ionization.

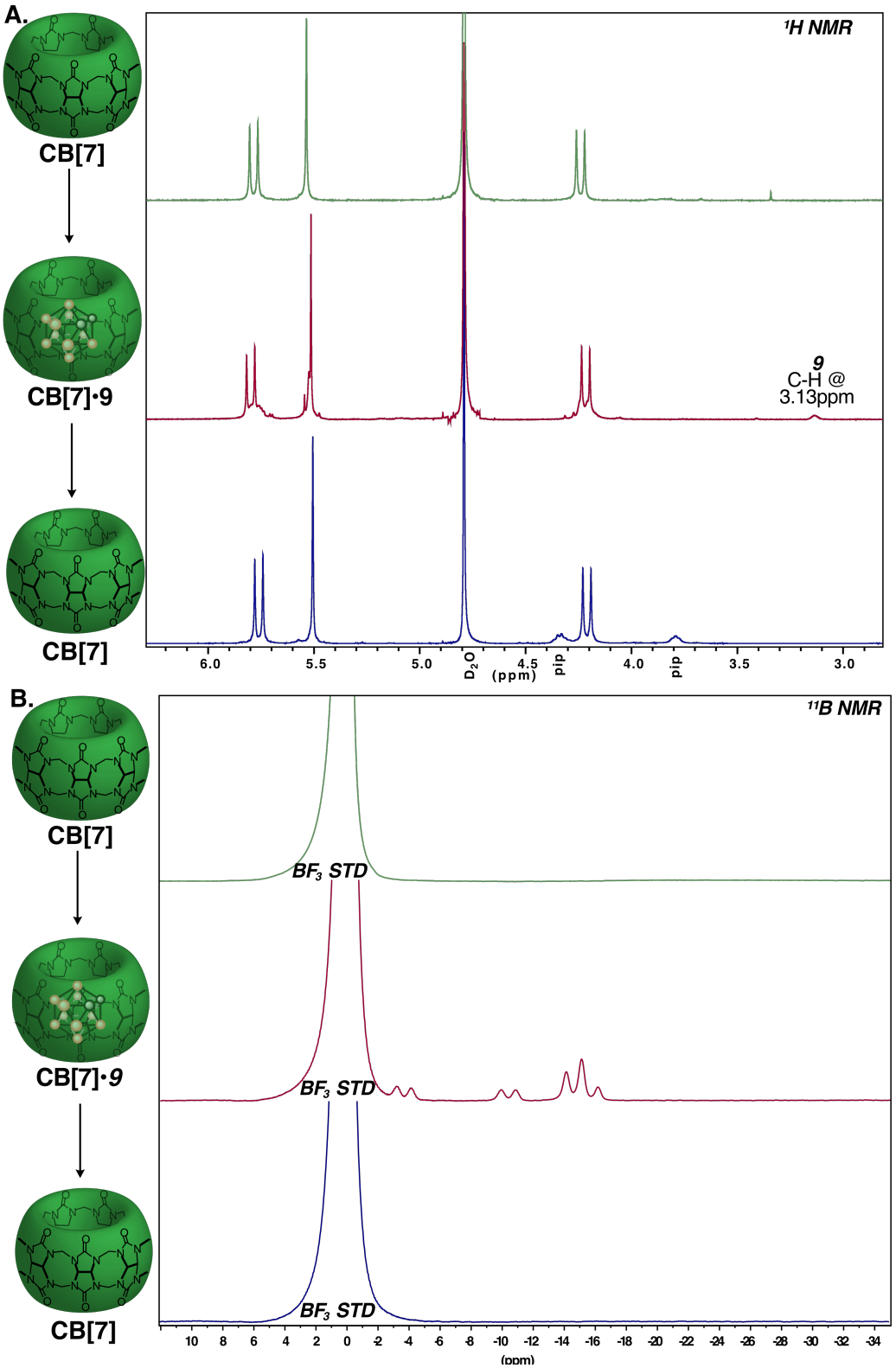


Figure S8: (A) ^{1}H NMR spectra and (**B**) ^{11}B NMR of CB[7]•**9** complexation and decomplexation by deboronation resulting in guest-free CB[7]. STD = standard. *Note: These spectra were taken without washing excess piperidine (abbreviated pip) after deboronation reaction, hence some piperidine is visible in ^{1}H-NMR (blue, bottom left).*

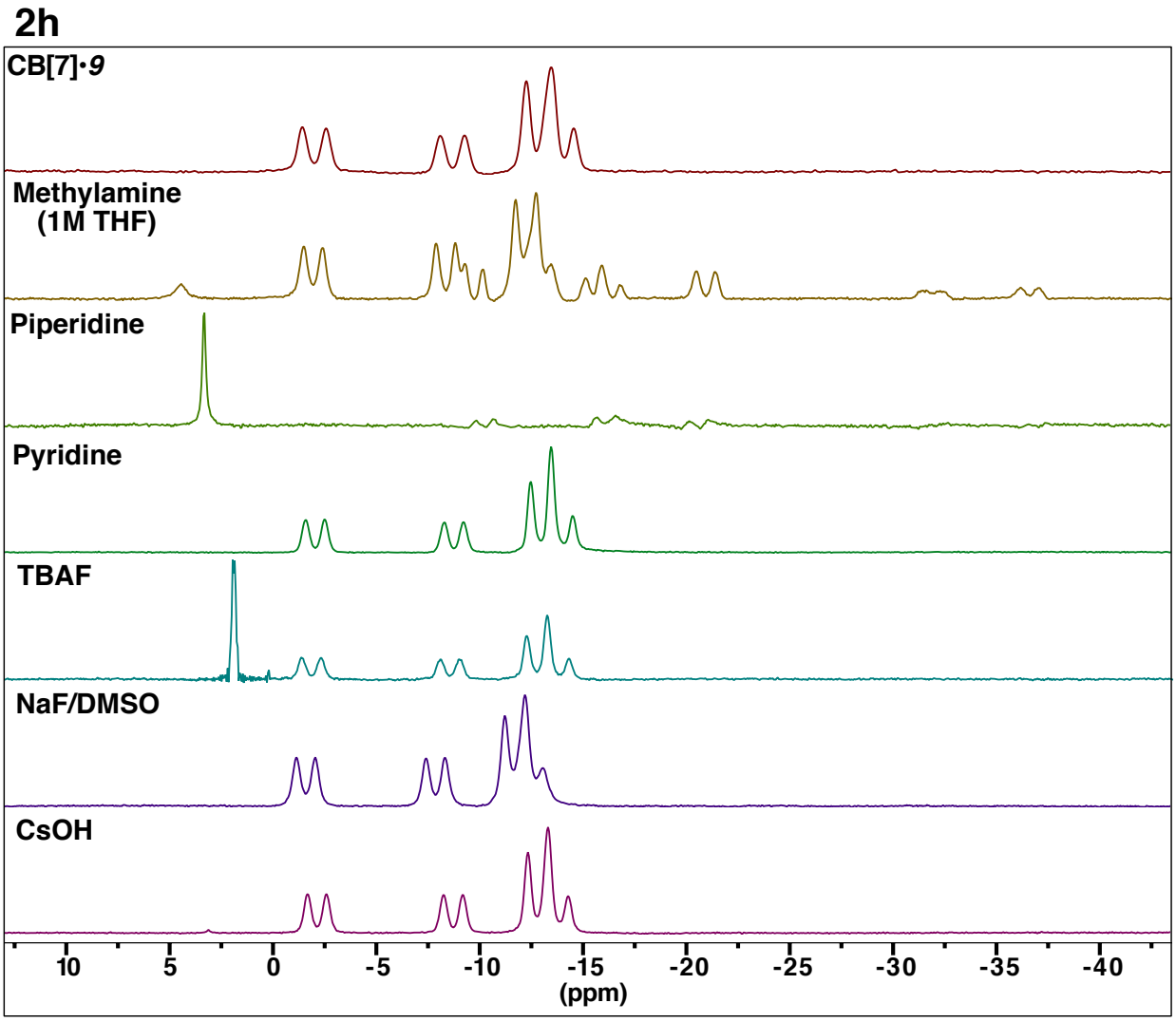


Figure S9: ^{11}B NMR spectra of **CB[7]•9** complex undergoing deboronation after 2h of subjection to a series of Lewis bases. ^{11}B NMR spectra **9** (0.03 mmol) and the corresponding base (1.6 mmol) were dissolved or suspended in H_2O to a total volume of 2 mL, stirred at 60 °C, and monitored by ^{11}B NMR spectroscopy. Note: These spectra are not calibrated since only relative integration values were necessary to calculate the degree of deboronation. Singlet peaks present are boric acid and borate side-products which we hypothesize are a result of extensive incubation in deboronation conditions that cause further degradation of *ortho*-carborane.

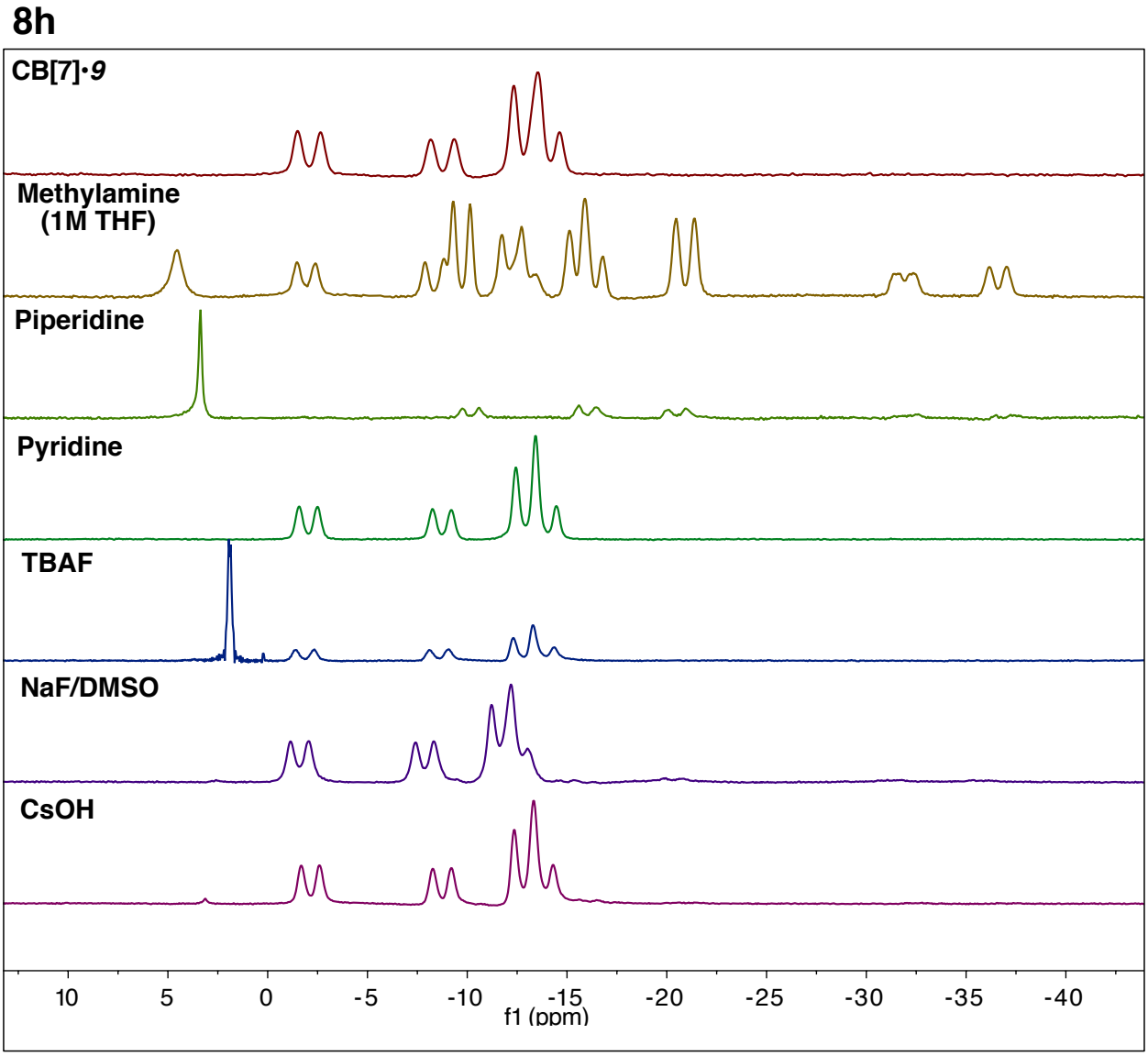


Figure S10: ^{11}B NMR spectra of **CB[7]•9** complex undergoing deboronation after 8 h of subjection to a series of Lewis bases. ^{11}B NMR spectra **9** (0.03 mmol) and the corresponding base (1.6 mmol) were dissolved or suspended in H_2O to a total volume of 2 mL, stirred at 60 °C, and monitored by ^{11}B NMR spectroscopy. Note: These spectra are not calibrated since only relative integration values were necessary to calculate the degree of deboronation. Singlet peaks present are boric acid and borate side-products which we hypothesize are a result of extensive incubation in deboronation conditions that cause further degradation of *ortho*-carborane.

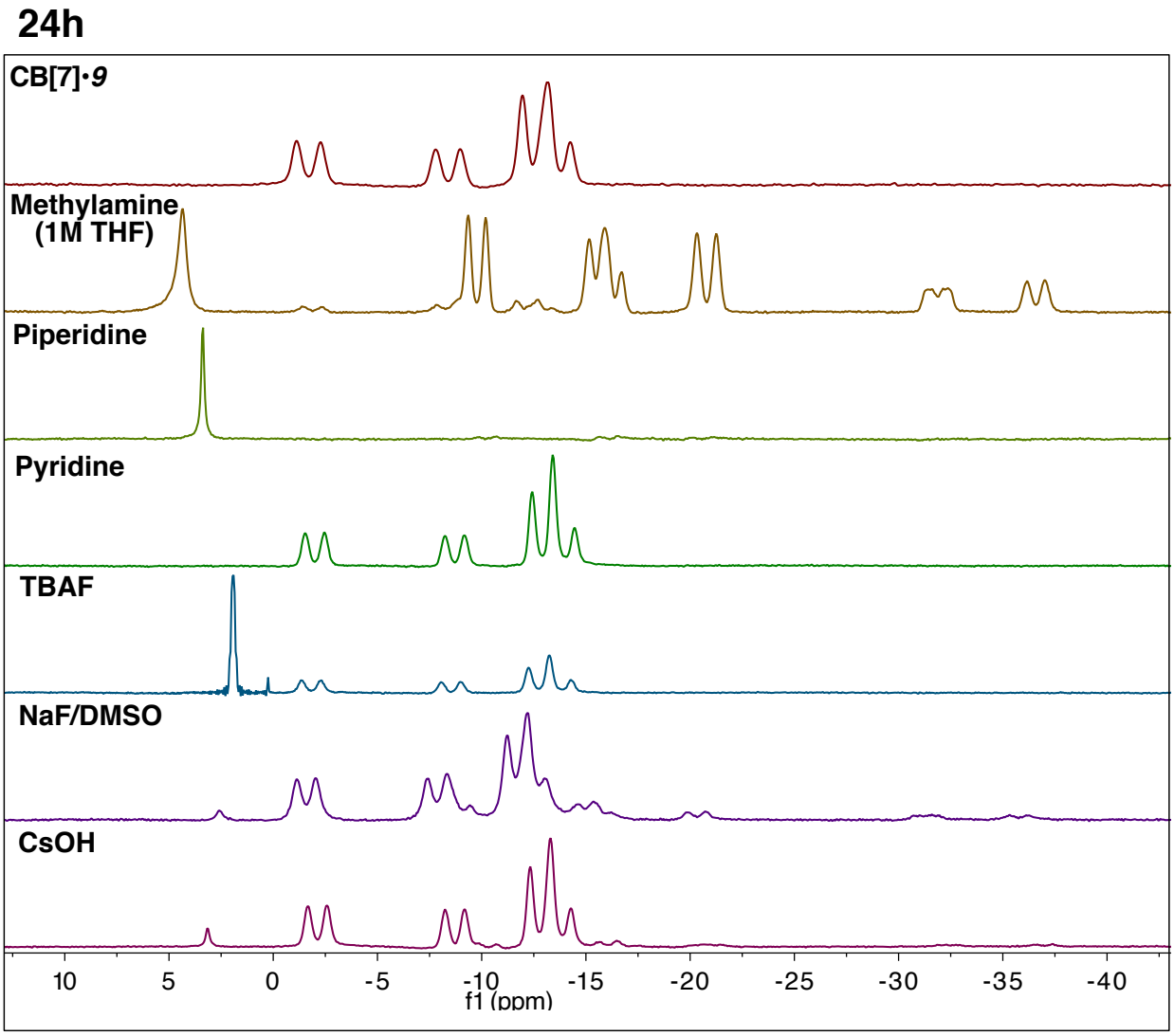


Figure S11: ^{11}B NMR spectra of **CB[7]•9** complex undergoing deboronation after 24 h of subjection to a series of Lewis bases. ^{11}B NMR spectra **9** (0.03mmol) and the corresponding base (1.6 mmol) were dissolved or suspended in H_2O to a total volume of 2 mL, stirred at 60 ^{o}C, and monitored by ^{11}B NMR spectroscopy. Note: These spectra are not calibrated since only relative integration values were necessary to calculate the degree of deboronation. Singlet peaks present are boric acid and borate side-products which we hypothesize are a result of extensive incubation in deboronation conditions that cause further degradation of *ortho*-carborane.

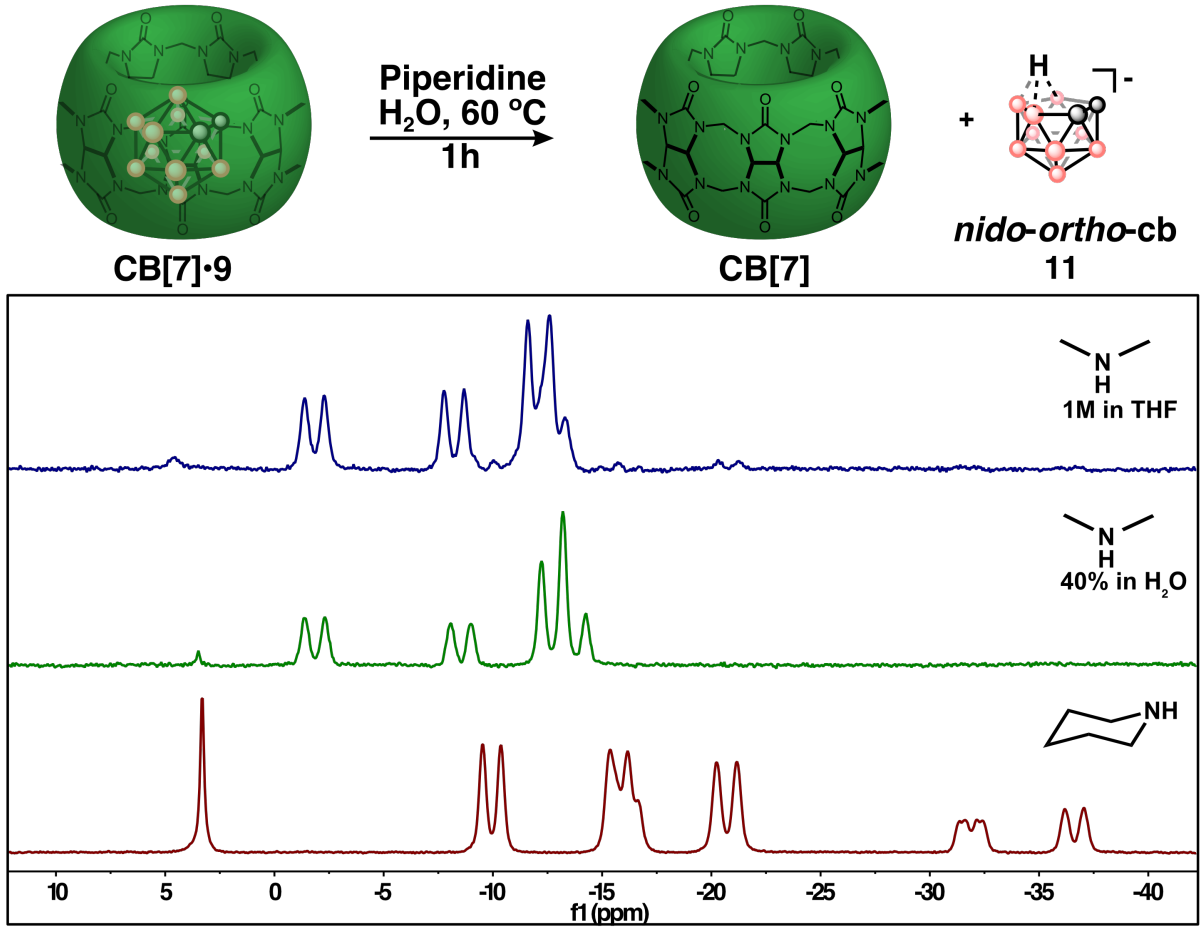


Figure S12: ^{11}B NMR spectra of **CB[7]•9** complex (190 mg, 0.29 mmol) 1 h after subjection to dimethylamine (1M in THF, 1.6 mmol), dimethylamine (40% in H_2O, 1.6 mmol), piperidine (1.6 mmol).

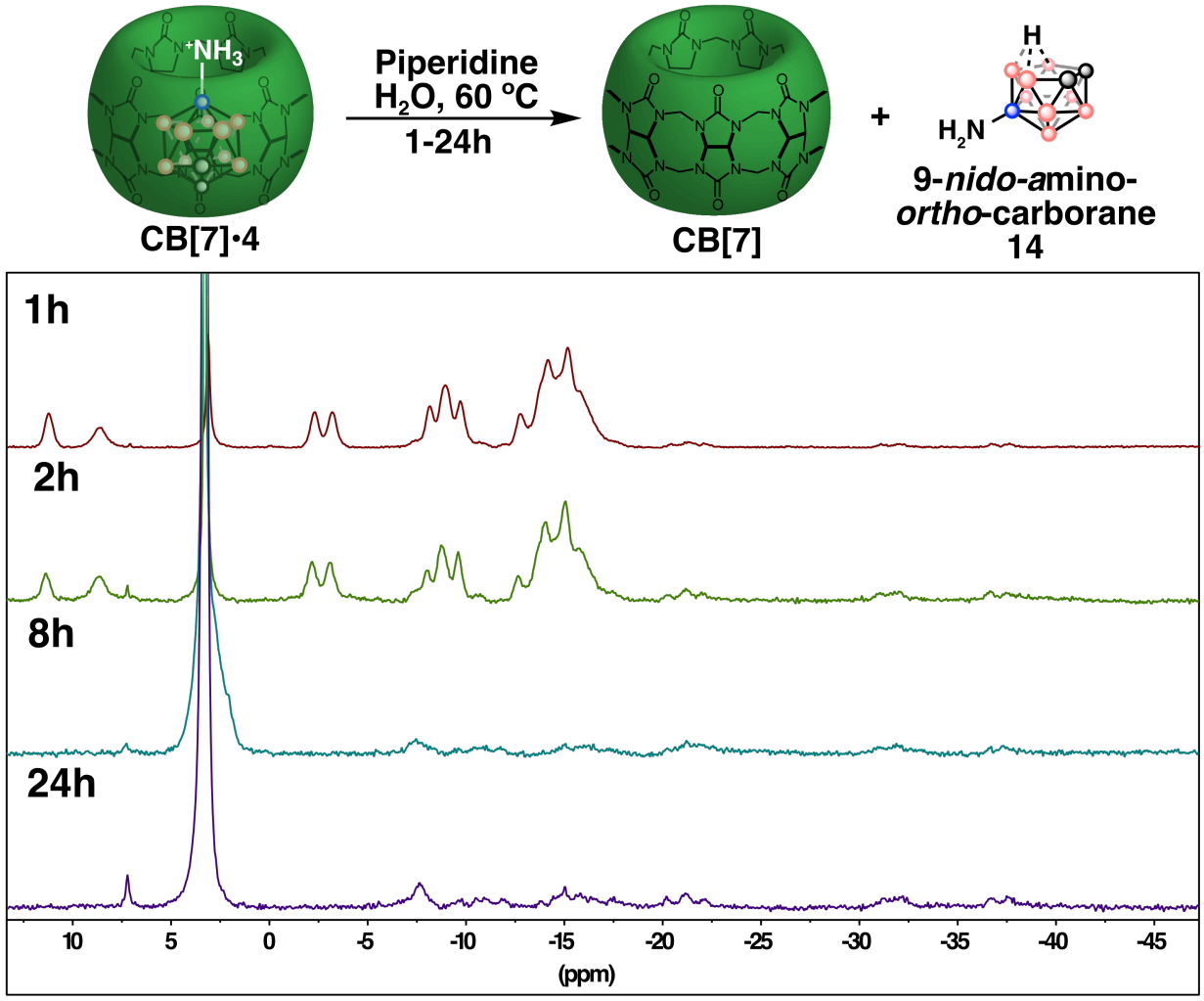


Figure S13: ^{11}B NMR spectra taken 1, 2, 8, 24 h after subjection of **CB[7]•4** complex to equimolar amounts (1.6 mmol) of piperidine in H_2O at 60 °C. **CB[7]•4** complex is susceptible to deboronation similarly to unfunctionalized *ortho*-carborane. While the *nido*- product appears insoluble in the reaction solvents, completion by 8 h of reaction time is seen by the disappearance of the doublet at -2.5 ppm. We hypothesize that deboronation appears slower due to differential solubilities between **4** and *ortho*-carborane (**9**).

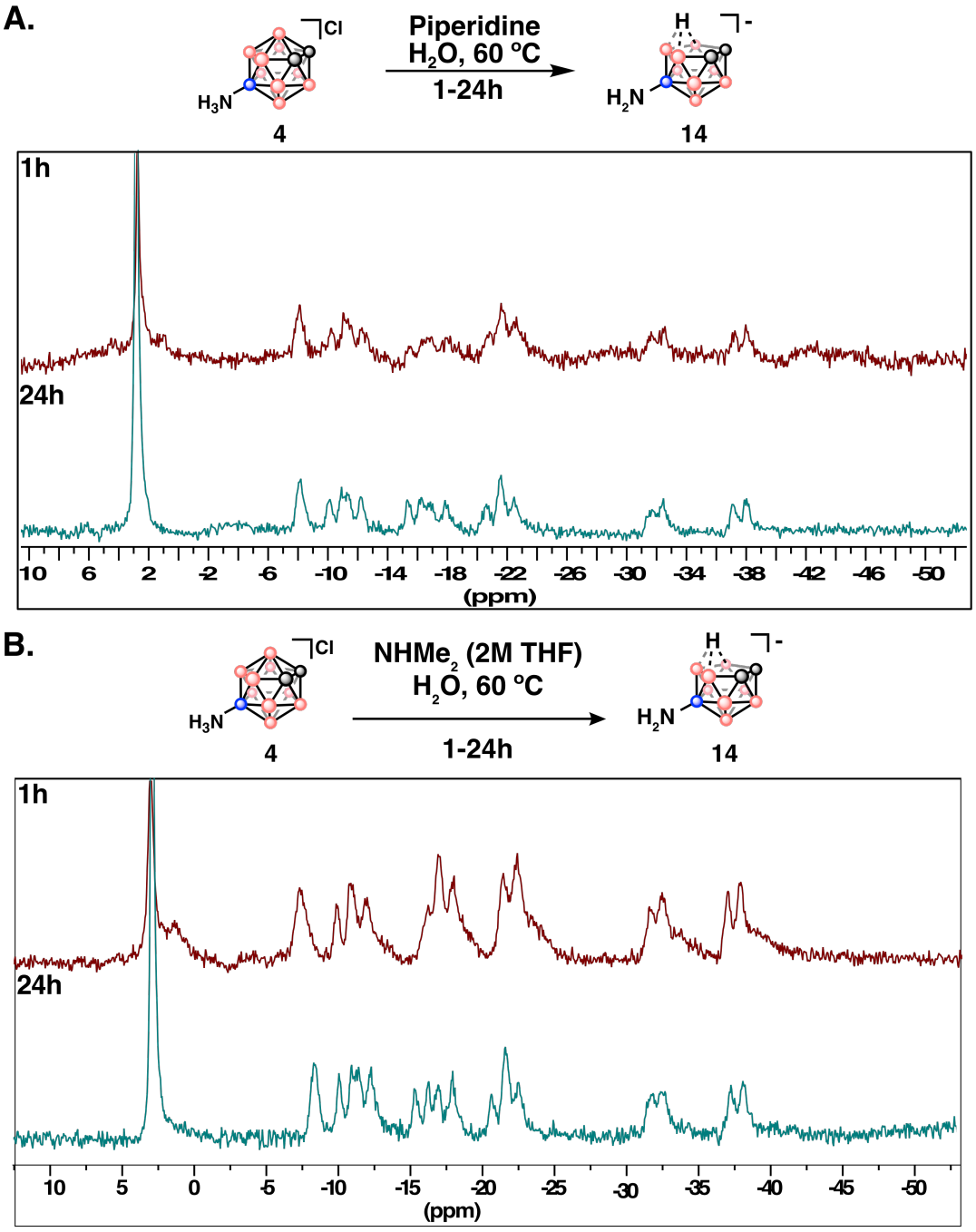


Figure S14: ^{11}B NMR spectra taken 1, 24 h after subjection of (**A**) piperidine (0.16 mmol) and (**B**) dimethylamine (2M in THF) (0.16 mmol) in H_2O at 60 °C. Complex **4** is susceptible to deboronation at a faster rate than when encapsulated in CB[7] (see Figure S14). The reaction has reached completion within 1 h, as noted by the disappearance of the doublet at -2.5 ppm and the presence of the characteristic *nido*-carborane peaks at -31.5ppm and -37.5ppm. The increased solubility of the free *ortho*-9-aminocarborane (**4**) results in fast deboronation by both piperidine and dimethylamine, in contrast to slow deboronation rates observed with the **CB[7]•4** complex (Figure S13).

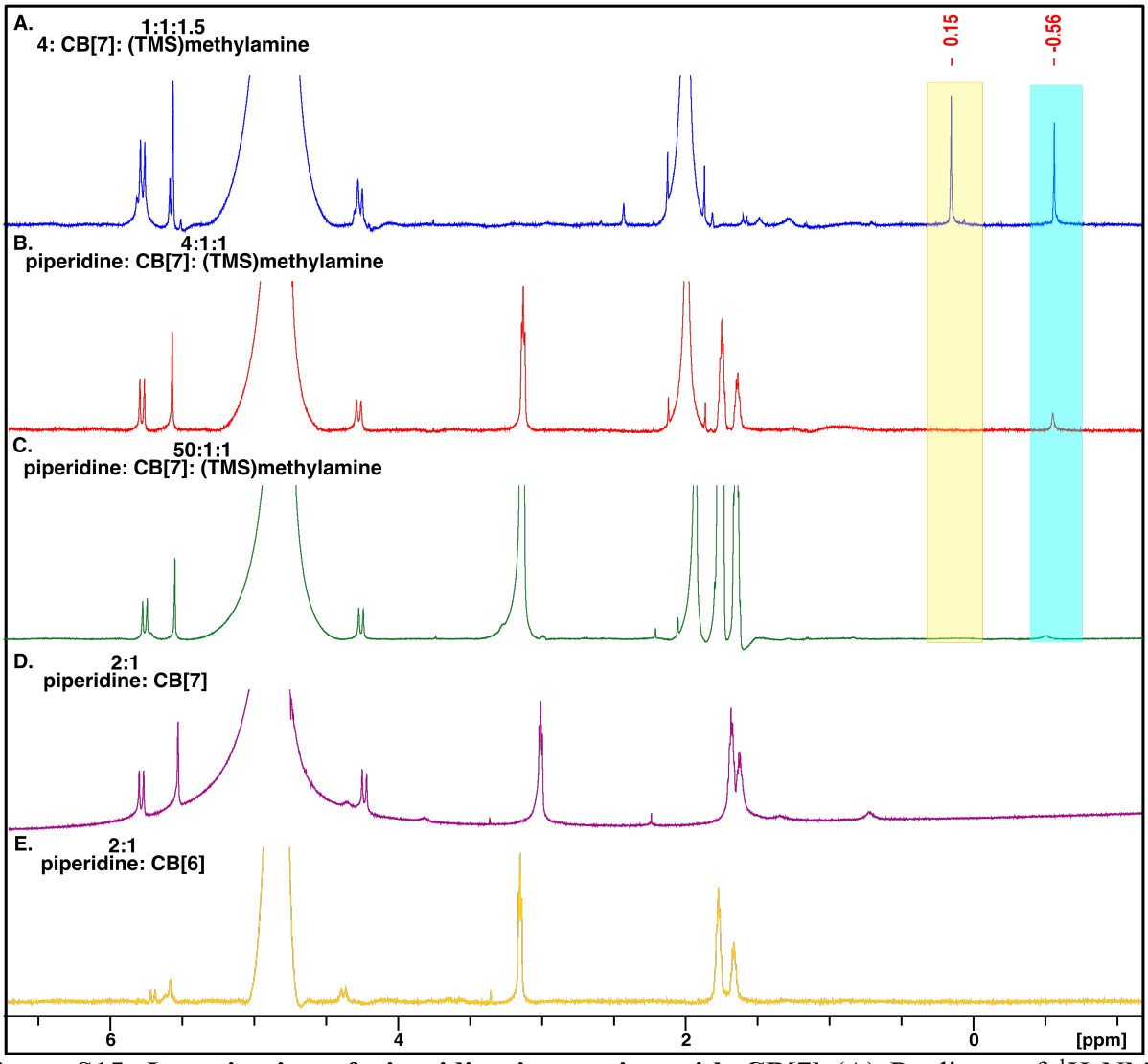


Figure S15: Investigation of piperidine interaction with CB[7] (**A**) Replicate of ^{1}H NMR spectrum (500 MHz, 50mM *d*-NaOAc buffer, pH 4.75) of competition experiment to determine binding affinity of **4** (0.3366 mM, 1 eq.) with CB[7] (0.261 mM) by competition with (trimethylsilyl)methylamine (0.5049 mM, 1.5 eq.). (**B**) ^{1}H NMR spectrum (500 MHz, 50 mM *d*-NaOAc buffer, pH 4.75) of competition experiment to determine binding affinity of piperidine (13.02 mM, 50 eq.) with CB[7] (0.261mM) by competition with (trimethylsilyl)methylamine (0.261 mM, 1 eq.). (**C**) ^{1}H NMR spectrum (500 MHz, 50mM *d*-NaOAc buffer, pH 4.75) of competition experiment to determine binding affinity of piperidine (1.043 mM, 4eq.) with CB[7] (0.261 mM) by competition with (trimethylsilyl)methylamine (0.261 mM, 1 eq.). (**D**) ^{1}H NMR (500 MHz, D_2O) spectrum of CB[7] (0.261 mM) with piperidine (0.522 mM, 2 eq.) showing a splitting pattern which we hypothesize indicates interaction with CB carbonyl portals. (**E**) ^{1}H NMR (500 MHz, D_2O) spectrum of CB[6] (0.261 mM) with piperidine (0.522 mM, 2 eq.) showing a splitting pattern which we hypothesize indicates interaction with CB carbonyl portals. Note: Despite observing the same splitting pattern as when CB[7] is incubated with piperidine alone, the (trimethylsilyl)methylamine peaks remained all in the "bound" state (-0.56 ppm, highlighted blue) and no "free" peaks were observed (0.16 ppm, highlighted yellow) leading us to conclude that piperidine is not encapsulated by CB[7] with a relevant binding affinity.

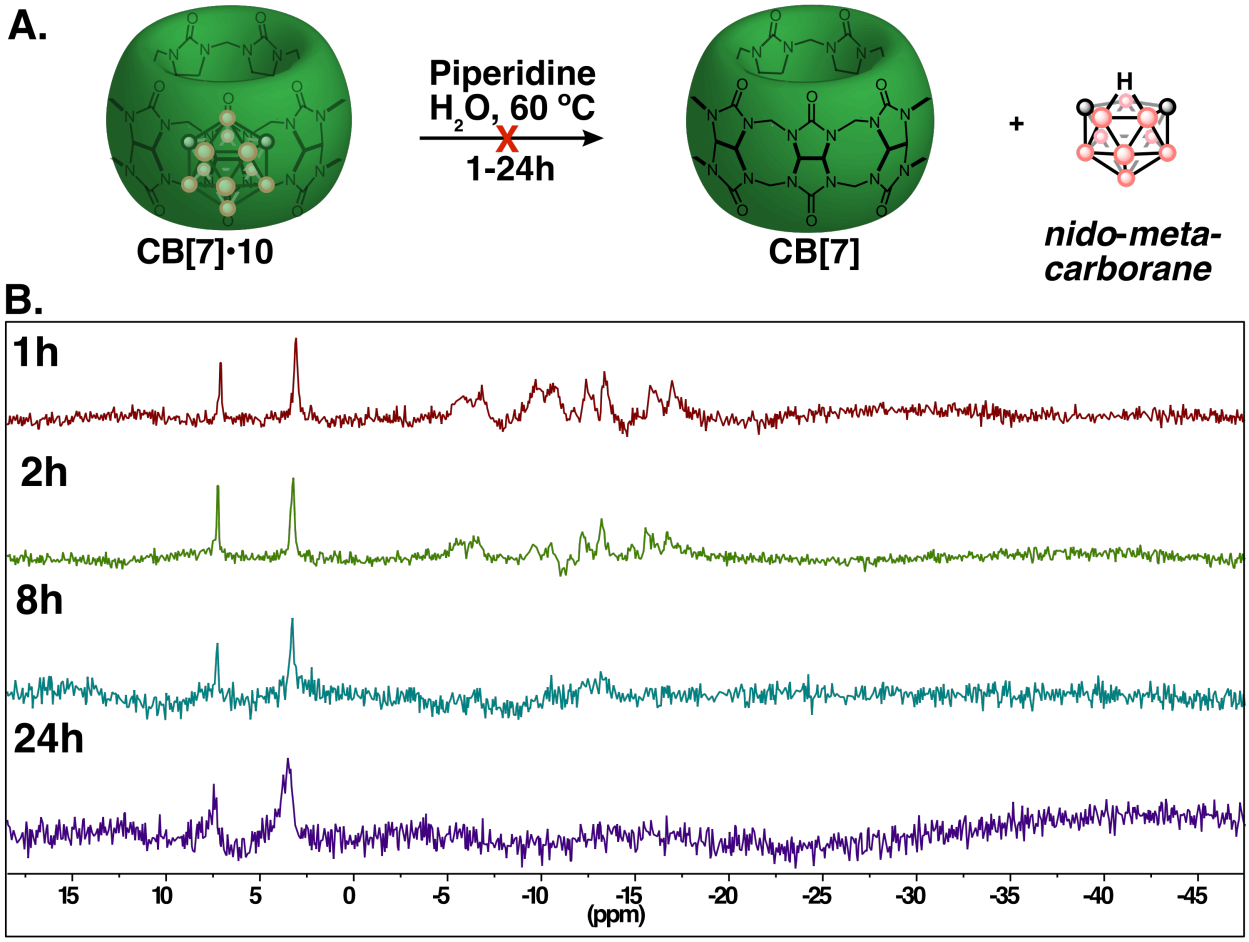


Figure S16: ^{11}B NMR spectra taken 1, 2, 8, 24 h after subjection of **CB[7]•10** complex to equimolar amounts (1.6 mmol) of piperidine in H_2O at 60 °C. The spectral changes despite loss of signal due to insolubility of the complex, show no deboronation of **10** as the characteristic *nido*-carborane peaks usually present as -30 – -40 ppm are absent. Thus, we conclude that *meta*-carborane (**10**) is an orthogonal guest to *ortho*-carborane (**9**).

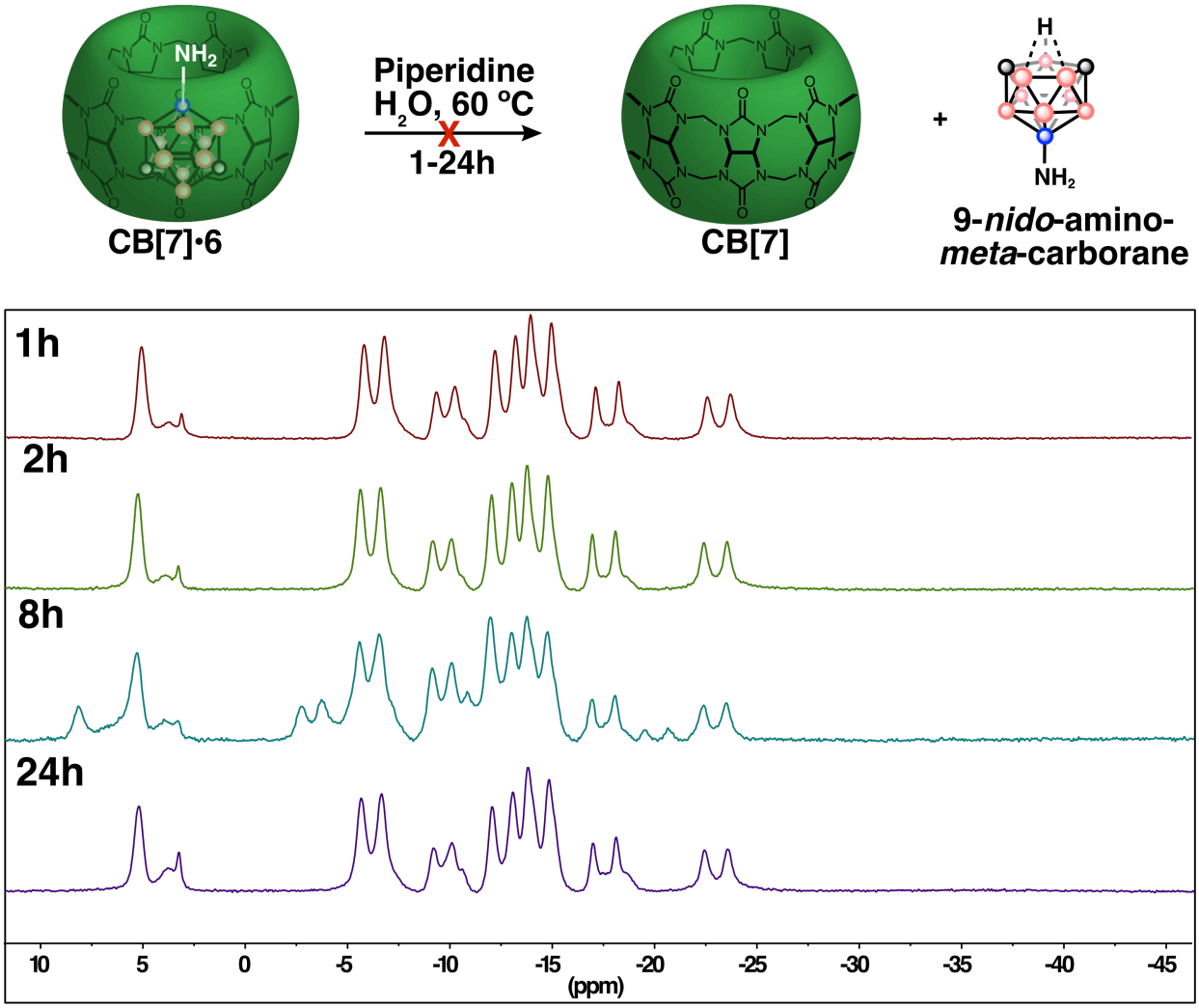


Figure S17: ^{11}B NMR spectra taken 1, 2, 8, 24 h after subjection of **CB[7]•6** complex to equimolar amounts (1.6 mmol) of piperidine in H_2O at 60 °C. **CB[7]•6** complex remains stable under deboronation conditions (50% aqueous piperidine, 60 °C).

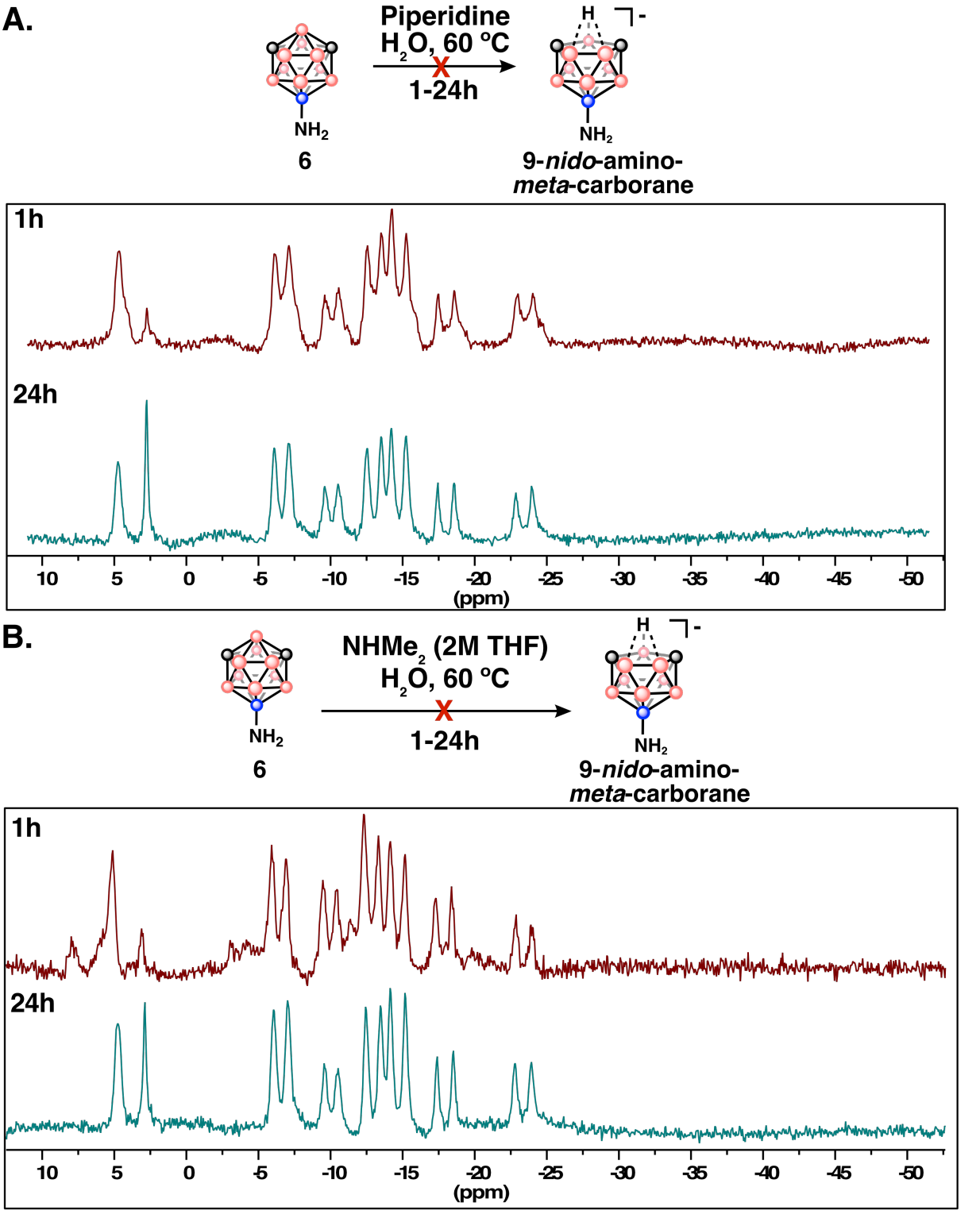


Figure S18: ^{11}B NMR spectra taken 1, 24 h after subjection of **6** to (**A**) piperidine (0.16 mmol) and (**B**) dimethylamine (2M in THF) (0.16 mmol) in H_2O at 60 °C. *Meta*-carborane **6** remains stable to deboronation similarly to complex **CB[7]•6** (Figure S17).

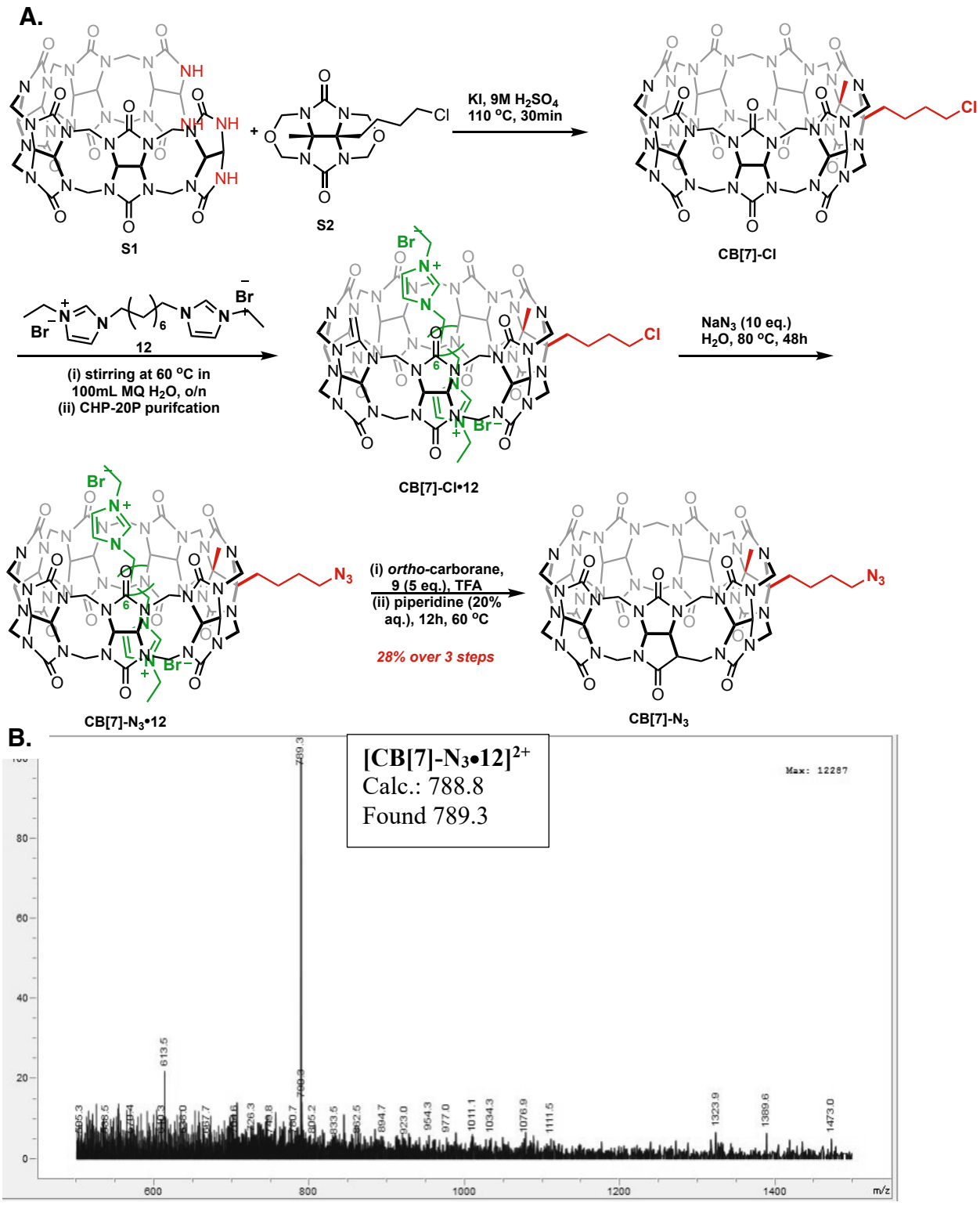


Figure S19: Preparation of guest-free CB[7]-N_3 using decomplexation method (**A**) Synthetic scheme of CB[7]-N_3 preparation adapted from synthetic procedure reported by Isaacs and coworkers.[2] (**B**) LCMS spectrum of isolated, guest-free CB[7]-N_3 complexed to **12** for characterization.

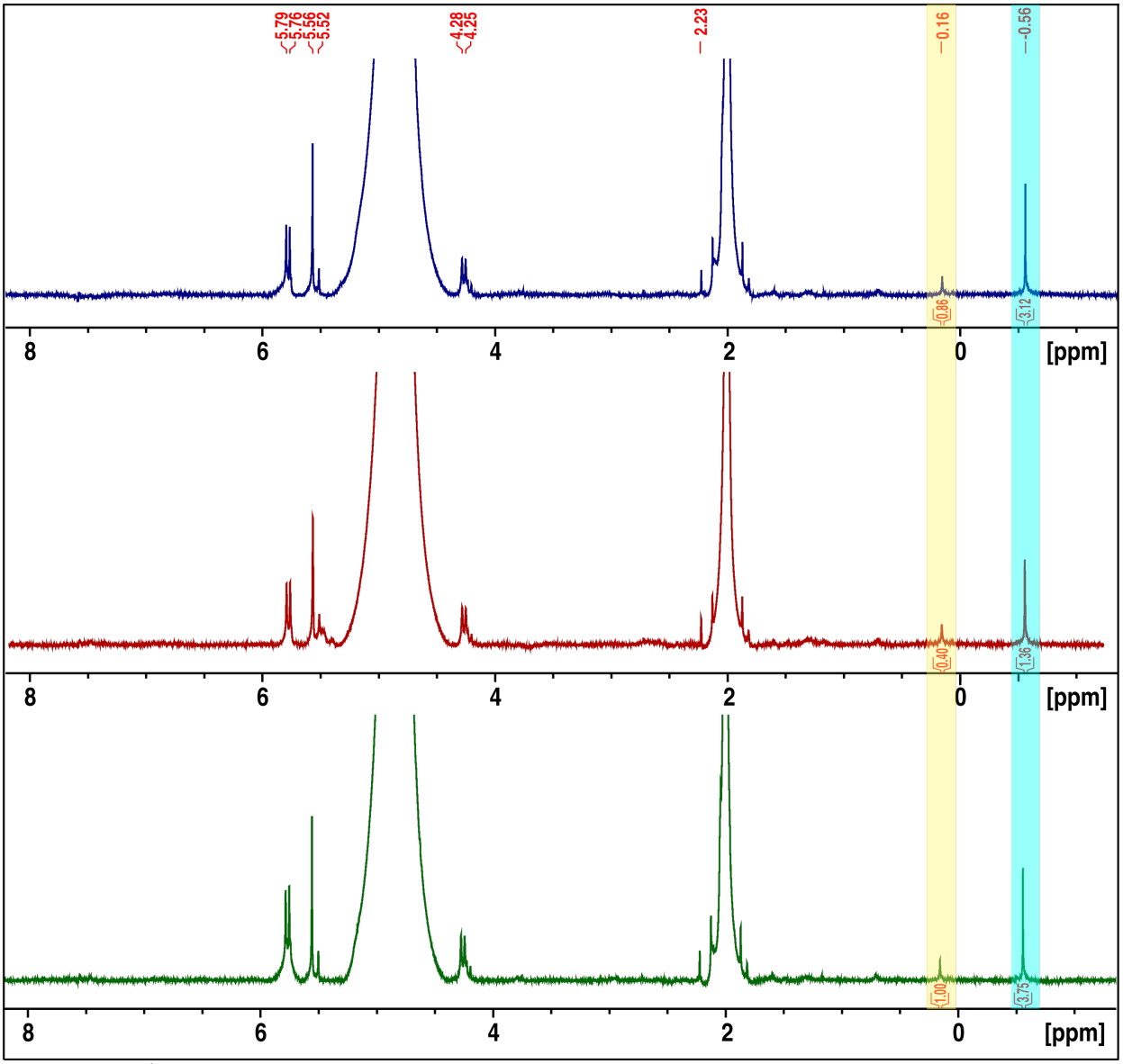


Figure S20: [1]H NMR spectra of competition experiment to determine binding affinity of Ad-FITC (**13**). Each spectrum (blue, green, red) represents each of three replicate experiments. In short, 1.5 equivalents of (trimethylsilyl)methylamine (0.337 mM), and 1 equivalent of **4** (0.337 mM) were added to a limited amount of CB[7] (0.281 mM) in 50 mM deuterated sodium acetate buffer. A relative binding affinity (K_{rel}) was calculated based on the relative integration values of (trimethylsilyl)methylamine **bound** to CB[7] (-0.56 ppm, highlighted blue) or **free** (0.15 ppm, highlighted yellow). K_{rel} was used to determine the K_a based on the known K_a of (trimethylsilyl)methylamine (K_a = 8.88x10^8 M^{-1}) and according to equations and error analysis presented by Isaacs and coworkers in 2005.[1]

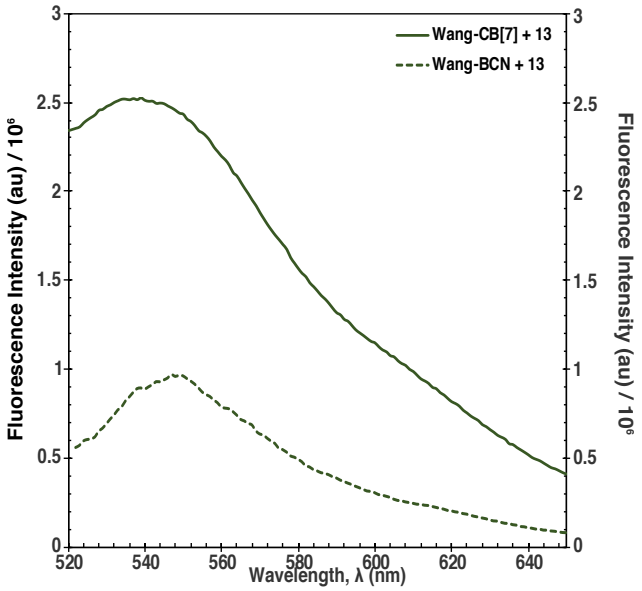


Figure S21: Confirmation of attachment of CB[7] onto the Wang resin. Briefly, **13** (5 µmol) was added to BCN-Wang resin (10 mg, 5 µmol) and CB[7]-Wang resin (13 mg, 5 µmol) samples and incubated at room temp. for 5 minutes. Samples were washed by centrifugation (2,818 x *g*, 1 min) with DMF (3x1 mL). Fluorescence spectra were taken in DMF (λ_{exc} = 495nm, 10 nm em. slit widths, 5 nm exc. slit widths).

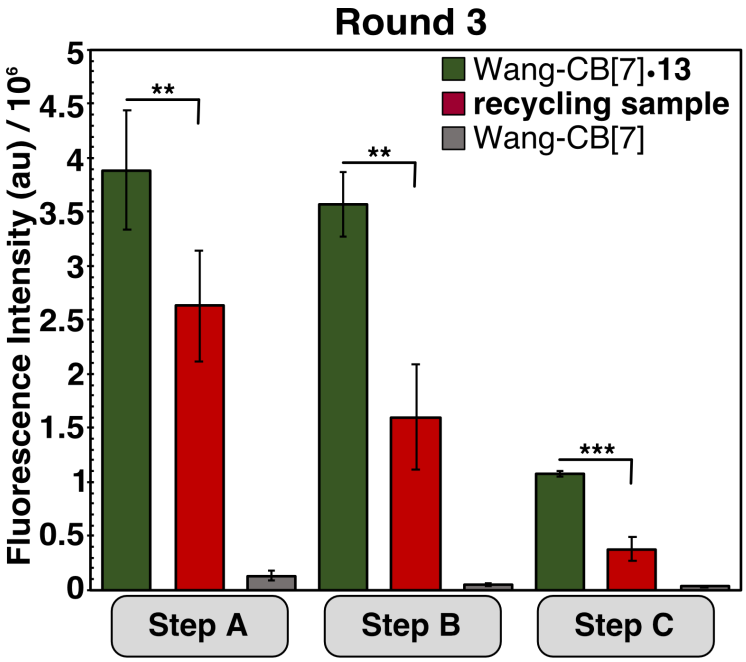


Figure S22: (**A**) Round three of recycling Wang-CB[7] resin using the decomplexation method. Due to significant loss of resin in the washing steps during round 3, these data were not included in the main text. See main text **Figure 6** for first two rounds of recycling and Figure Experimental Procedures for experimental details.

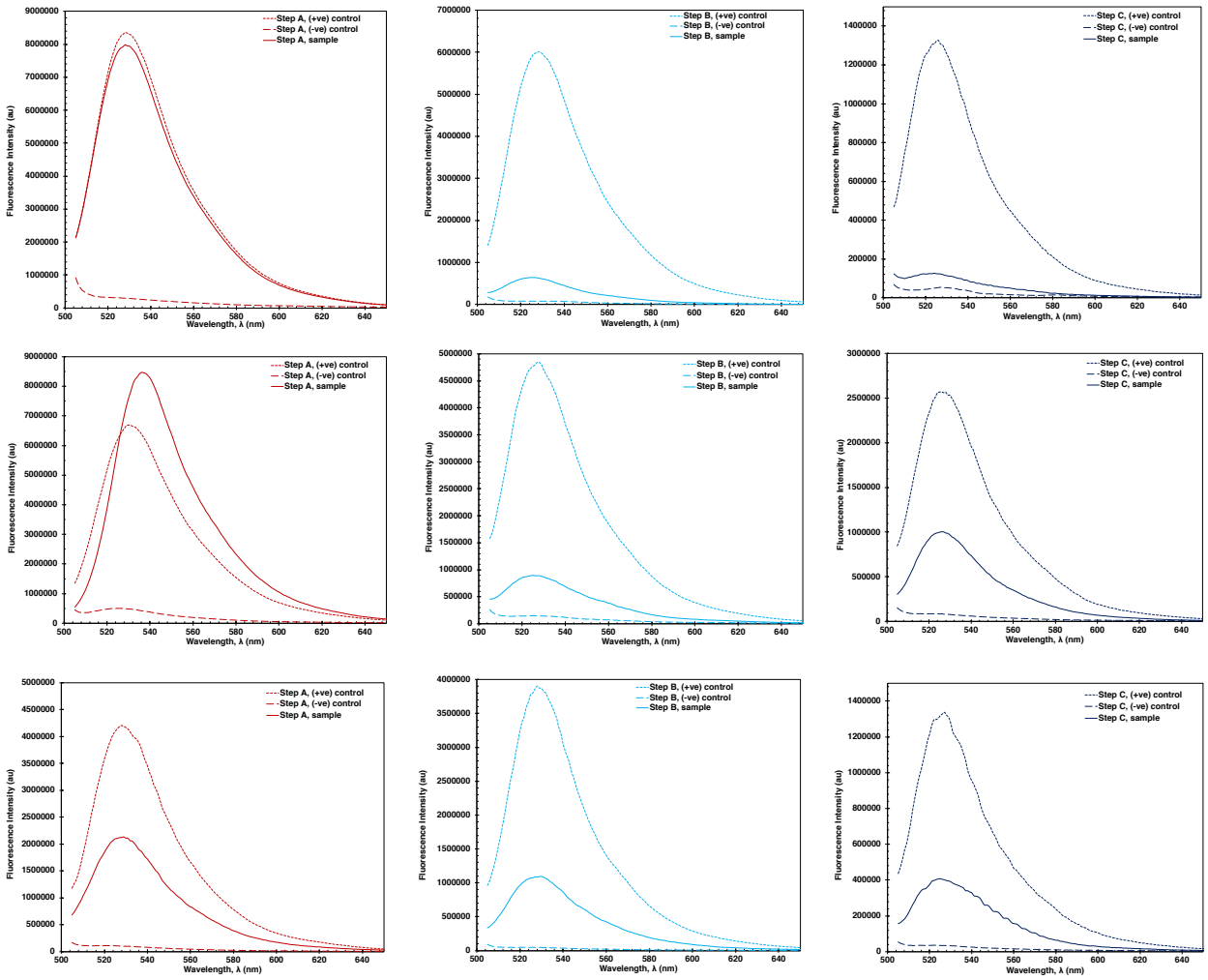


Figure S23: (**A**) Representative raw data from recycling experiment, round 1, (**B**) Representative raw data from recycling experiment, round 2, (**C**) Representative raw data from recycling experiment, round 3.

Sample: Step A: **Wang-CB[7]•13,** Step B: Addition of **4** to make **Wang-CB[7]•4**, Step C: Incubation with 20% piperidine to produce **Wang-CB[7]**. These samples are represented by the solid lines.

Controls:

(+ve) control (**Wang-CB[7]•13**) –"always" fluorescent samples where **13** was added in Step A but no **4** was added in Step B. These samples are represented by the dashed lines.

(-ve) control (**Wang-CB[7]**)–"always" non-fluorescent samples that underwent the same washes and incubations without addition of **13** or **4**. These samples are represented by the dotted lines.

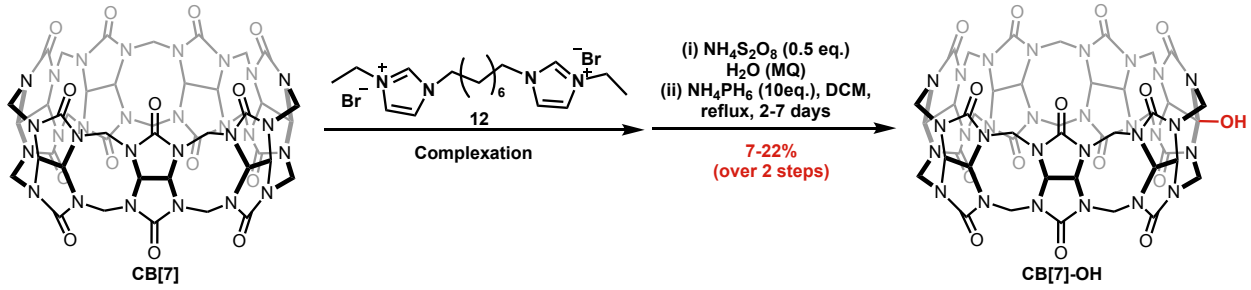
Supporting table

Table S1: Generation of *nido*-carborane (**11**) from **CB[7]•9** calculated by relative integration of baseline corrected ^{11}B NMR spectra (see Figure S9-S11 for spectra and ^{11}B NMR section, pS54-S56 for Entry 2 integrated spectra). **CB[7]•9** and the corresponding base (5 equiv.) were dissolved or suspended in H_2O, stirred at 60 ^{o}C, and monitored by ^{11}B NMR spectroscopy.

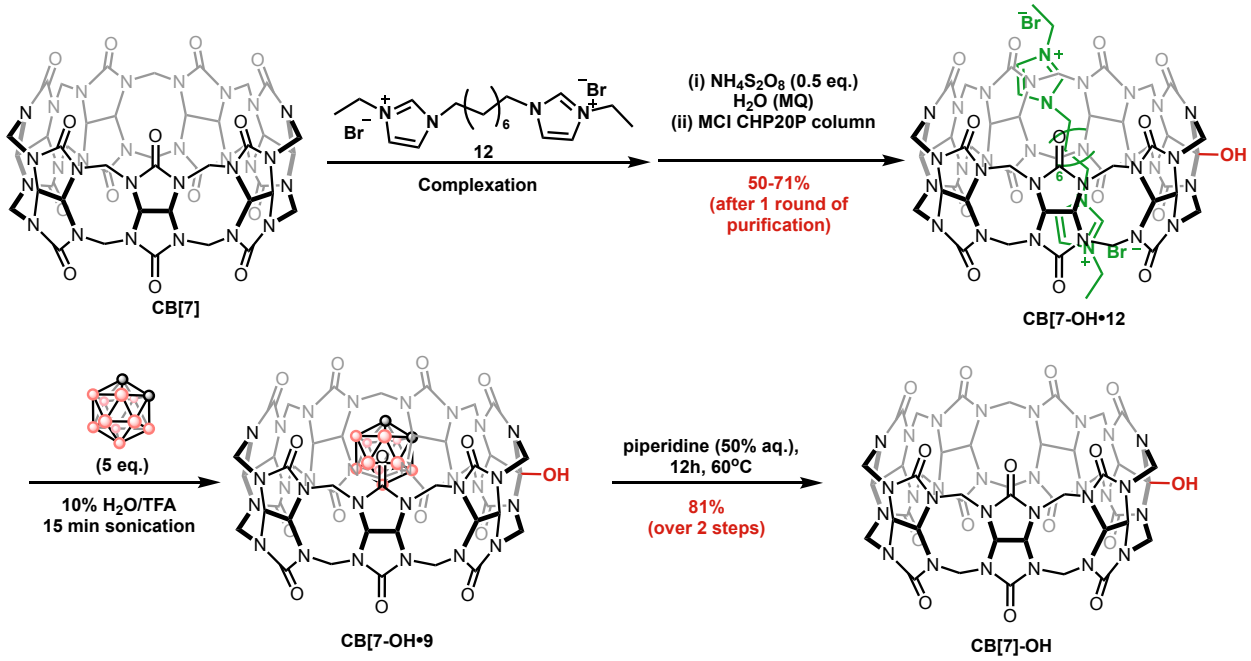
Entry	*Carborane*	Base	1h	2h	8h	24h
1	**9**	$HNMe_2$ (1M THF)	9%	17%	45%	86%
2	**9**	$HNMe_2$ (40% in H_2O)	<5%	<5%	<5%	<5%
3	**9**	Pyridine	<5%	<5%	<5%	<5%
4	**9**	KOMe	-	-	<5%	<5%
5	**9**	TBAF	<5%	<5%	<5%	<5%
6	**9**	DMSO/H_2O	<5%	<5%	-	<5%
7	**9**	NaF/DMSO	<5%	<5%	7%	12%
8	**9**	CsOH	<5%	<5%	<5%	7%
9	**9**	**Piperidine**	**>95%**	**>95%**	**>95%**	**>95%**
10	**4**	**Piperidine**	**8%**	**19%**	**>95%**	**>95%**
11	**10**	Piperidine	<5%	<5%	<5%	<5%
12	**6**	Piperidine	<5%	<5%	<5%	<5%

Supporting schemes

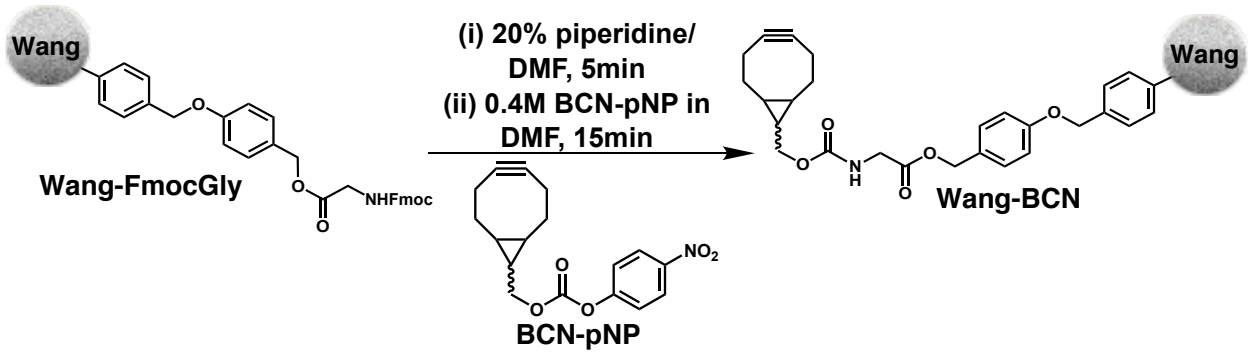
Scheme S1: Synthesis of monofunctionalized CB[7] by complexation and decomplexation using methods described by Scherman, O. and coworkers.[3,4]



Scheme S2: Synthesis of monofunctionalized CB[7], **CB[7]-OH** by complexation and decomplexation using *ortho*-carborane (**9**). See Figure 5 experimental procedure for details.



Scheme S3: Preparation of Wang-BCN beads in a solid-phase peptide synthesis setup. FmocGly-Wang (1.00 g, 0.372 mmol/g FmocGly) was swollen in DMF (5 min), washed with 20% piperidine/DMF (3x) and incubated in 20% piperidine/DMF for 5 min (until Kaiser test showed complete deprotection). BCN-pNP[5] (0.14 g, 0.45 mmol, 1.2 equiv.) was added in DMF (0.4 M) and reacted for 15 min (Kaiser test to confirm coupling was successful). The resin was washed with DMF (5x20 mL) and dried under N_2 overnight. The resin was stored under inert atmosphere at 4 °C.



General experimental procedures:

Materials: Chemical reagents were purchased from Sigma-Aldrich, Fisher Scientific, TCI America or Acros Organics and used without purification unless noted otherwise. *Meta*-$C_2B_{10}H_{12}$ (KatChem) and *ortho*-$C_2B_{10}H_{12}$ (Boron Specialties) were sublimed prior to use. 1,2-dimethoxyethane (Sigma Aldrich) was dried over sodium metal, distilled, and stored over activated molecular sieves in a nitrogen-filled glovebox. Anhydrous K_3PO_4 (Sigma-Aldrich, anhydrous, free-flowing, Redi-Dri, reagent grade, >98%) was stored in a nitrogen-filled glovebox. Methyl iodide (Alfa Aesar), K_2CO_3 (Amresco), SPhos-Pd-G3, SPhos, PMe_3 (Sigma Aldrich), were used as received. Wang-GlyFmoc resin was purchased from ChemImpex and used as received. Anhydrous dimethylsulfoxide (DMSO) was obtained from a Sure-Seal^{TM} bottle (Aldrich) that after opening was stored in a Schlenk-bomb flask over 4Å molecular sieves. Anhydrous and deoxygenated solvents dimethylformamide (DMF), methanol (MeOH), tetrahydrofuran (THF) and dichloromethane (DCM) were dispensed from a Grubb's-type Phoenix Solvent Drying System constructed by JC Meyer. $CDCl_3$ and D_2O were purchased from Cambridge Isotope Laboratories and used as received. Thin layer chromatography was performed using Silica Gel 60 F254 (EMD Millipore) plates. Flash chromatography was executed with technical grade silica gel with 60 Å pores and 40 – 63 μm mesh particle size (Sorbtech Technologies). Cross-coupling reactions were performed in 13x125mm or 16x125mm oven-dried culture tubes (Fisher) with a PTFE-lined magnetic stir bar and a PTFE-lined septum cap.

Instrumentation: Masses for analytical measurements were taken on a Sartorius MSE6.6S-000-DM or MSA6.6S-000-DM Cubis Micro Balance. Centrifugation was performed on a Thermo Scientific Sorvall ST 16 Centrifuge. All sonication was done in a Branson M-Series Model 3800 120V bath sonicator. Solvent was removed under reduced pressure with a Büchi Rotovapor with a Welch self-cleaning dry vacuum pump and further dried with a Welch DuoSeal pump. Bath sonication was performed using a Branson 3800 ultrasonic cleaner. ^{1}H, $^{13}C\{^{1}H\}$, ^{11}B, $^{11}B\{^{1}H\}$, and ^{31}P NMR spectra were acquired on a Bruker AV 500, DRX 500 or DRX 400 spectrometer. ^{1}H and $^{13}C\{^{1}H\}$ NMR spectra were referenced to residual solvent resonances in deuterated solvents ($CDCl_3$: ^{1}H, 7.26 ppm; ^{13}C, 77.16 ppm, Note: due to high humidity H_2O resonances are often present; D_2O: ^{1}H, 4.79 ppm) and are reported relative to tetramethylsilane ($\delta = 0$ ppm). ^{11}B and $^{11}B\{^{1}H\}$ NMR spectra were referenced to $Et_2O{\cdot}BF_3$ in a sealed capillary ($\delta = 0$ ppm). ^{31}P NMR spectra were referenced to an external H_3PO_4 (85%) standard ($\delta = 0$ ppm). Spectra were processed with MestReNova or TopSpin (K_a integrations) software. All deuterated solvents were referenced according to Nudelman and coworkers.[6] Mass spectra were taken using an Agilent 1260 series HPLC-tandem MS or an ultraflex MALDI-TOF instrument. Photoluminescence spectra were obtained on a Horiba Instruments PTI QuantaMaster Series fluorometer. Quartz cuvettes (10 mm, 3 mm and 2 mm) were used for photoluminescence measurements. Gas Chromatography Mass Spectrometry (GC-MS) data were collected on an Agilent 6890-5975 GC-MS equipped with an Agilent J&W HP-5 column with He carrier gas.

Abbreviations:
CB[7] : Cucurbit[7]uril
BCN: Bicyclononyne
DCM: Dichloromethane
MeOH: Methanol
MeCN: Acetonitrile
THF: Tetrahydrofuran
DMF: Dimethylformamide
DMSO: Dimethylsulfoxide
TFA: Trifluoroacetic acid
FITC: Fluorescein isothiocyanate isomer I
LCMS: Liquid-chromatography tandem mass-spectroscopy
NMR: Nuclear Magnetic Resonance
MALDI-TOF: Matrix-assisted laser desorption/ionization – time of flight
PTFE: Polytetrafluoroethylene
pNP: *para*-nitrophenol
Ad: 1-Adamantylamine

Figure experimental procedures

Figure 2: CB[7] complexation with *ortho*-carborane and decomplexation
CB[7] (0.50 g, 0.43 mmol) was suspended in H_2O (5 mL) and added to a suspension of *ortho*-carborane in trifluoroacetic acid (TFA) (10 mL). The solution was sonicated for 1 h to solubilize *ortho*-carborane. Excess solvents were evaporated and the product was washed with DCM (3 x 10 mL) and methanol (10 mL). The resulting solid was air-dried to give product as a white solid (0.3815 g, 0.2917 mmol, 67%).

Isolated **CB[7]•9** (190 mg, 0.14 mmol, 1 eq.) was dissolved in H_2O (10 mL). To the slightly opaque solution was added piperidine (1.6 mL, 16 mmol) and the reaction was heated to 60 °C and stirred vigorously. Within minutes, the solution became clear and full conversion was observed within one hour (as monitored by ^{11}B NMR). The excess solvents were evaporated and later lyophilized to dryness. The crude product was washed with DCM (3 x 10mL) to give the desired product as a white solid (0.15 g, 0.13 mmol, 87%).

Figure 3: Procedure for K_a determination of aminocarboranes (4,5,7,8) by a competition experiment with (trimethylsilyl)methylamine:

Triplicates of stock solutions of CB[7] (1.043 mM), (trimethylsilyl)methylamine (2.693 mM), and 9-aminocarboranes **4, 5, 7, 8** (0.673 mM) in 50 mM deuterated sodium acetate buffer (pH 4.75) were prepared. To each NMR sample was added the following stock solutions: 100 µL of CB[7], 75 µL (trimethylsilyl)methylamine and 200µL of 9-aminocarborane (**4, 5, 7, 8**) and 25µL of 50 mM *d*-NaOAc buffer to give final concentrations of CB[7] (0.261 mM), (trimethylsilyl)methylamine (0.505 mM), and 9-aminocarboranes **4, 5, 7, 8** (0.337 mM). In order to check the equilibrium both ways, we prepared the replicate solutions in two distinct ways. Two samples were prepared by adding a (trimethylsilyl)methylamine stock solution to a solution of CB[7] and 9-aminocarborane, while the third replicate was prepared by adding the 9-aminocarboranes to a previously prepared solution of CB[7] and (trimethylsilyl)methylamine. We used slight excess of (trimethylsilyl)lmethylamine (1.5 eq.) to be able to accurately integrate both "free" and "bound" peaks while also maintaining similar concentrations of the two competing guests. The solutions were allowed to equilibrate overnight before ^1H NMR (500Hz) spectra were taken. NMR acquisition was taken with a delay time (D1) >5x T_1 to eliminate systematic errors arising from differential relaxation times.
The ratio between "bound" and "free" (trimethylsilyl)methylamine was determined by integration (region 0 to -1 ppm) (Figure S1-S4) which correspond to the concentrations of free guest and the host-guest complexes. This allowed for determination of a K_{rel} value for each 9-aminocarborane relative to (trimethylsilyl)methylamine. The equations and error analysis used to determine the binding affinities based on K_{rel} was described by Isaacs and coworkers in 2005 and 2014.[1,7]

Figure 4: Straightforward isolation of guest-free CB[7]-OH can be accomplished by guest exchange with *ortho*-carborane and subsequent decomplexation with piperidine that can be conveniently monitored by ^{11}B NMR in H_2O. We have performed this procedure on up to 200 mg (0.12 mmol) of CB[7]-OH.

Ortho-carborane (**9**) (0.086 g, 0.60mmol, 5 eq.) was dissolved in trifluoroacetic acid (TFA) (20 mL) by sonication (about 10 min). Isolated **CB[7]-OH•12** (0.192 g, 0.117 mmol, 1 eq.) was dissolved in H_2O (2 mL) and added to the TFA solution (solution was clear but still heterogenous due to some remaining insoluble *ortho*-carborane). The solution was sonicated for 1 h, filtered and the excess TFA was evaporated *in vacuo*. The product was washed with DCM (2 x 40 mL) and methanol (2 x 40 mL). The isolated white solid was dissolved in H_2O (20 mL) and to the solution was added piperidine (20 mL, 0.2mol, >300 eq.). The solution was heated to 60 °C and was stirred overnight. Excess solvents were evaporated to give the crude product as a pale yellow solid. The crude product was washed with DCM (3 x 40 mL) and methanol (3 x 40 mL) to give the desired product as a white solid (0.12 g, 0.10 mmol, 80%). Spectral data are consistent with the literature[8]: ^{1}H NMR (500 MHz, D_2O): δ 5.85 (d, J = 15.2 Hz, 2H), 5.78 (d, J = 15.4 Hz, 10H), 5.59 (s, 1H), 5.53 (s, 12H), 5.46 (d, J = 9 Hz, 1H), 5.30 (s, 1H), 4.53 (d, J = 15.5 Hz, 2H), 4.32 (s, 5H), 4.29 (s, 2H), 4.27-4.18 (m, 12H).

Figure 5: Facile synthesis of guest-free monofunctionalized CB[7], CB[7]-OH, by complexation and decomplexation using *ortho*-carborane (**9**). Bisimidazolium **12** in **CB[7]-OH•12** (0.345g, 0.210 mmol, 1 eq.) was displaced by *ortho*-carborane (**9**) (0.151g, 1.05 mmol, 5 eq.) in 10% H_2O/TFA (20mL) solution by sonication. The **CB[7]•9** (121 mg, 0.914 mmol, 1eq.) complex was disassociated chemically using aqueous piperidine (10 mL piperidine:15 mL H_2O) and incubating at 60 °C for 1 hour. **CB[7]-OH** was isolated after wash by centrifugation (2,818 x *g*, 3 min) with DCM (1 x 40mL), MeOH (1 x 15mL).

Figure 6: Recycling of Wang-CB[7] and isolation of a fluorescent payload.
(A) Attachment of CB[7]-N_3 on Wang-BCN through copper-free click chemistry
To a scintillation vial was added CB[7]-N_3 (61 mg, 0.048 mmol, 1.3 eq.) and dissolved in a 1:1 mixture of DMF:DMSO (6 mL) after sonication for 5 minutes. Wang-BCN resin (0.10 g, 0.037 mmol BCN, 1 eq.) were suspended in DMF (1 mL) and added to the vial. The suspension was vigorously stirred at room temperature for 24 h. The reaction was transferred to a 15 mL Falcon tube and washed by centrifugation (2818 x g, 3min) with DMF (5 x 6 mL). The resin was dried under vacuum and stored at 4 °C under inert atmosphere. Attachment of CB[7] to the resin was confirmed by introduction of Ad-FITC **(13)** and fluorescent analysis (see Figure S16).

(B,C) Recycling of Wang-CB[7] after isolating fluorescent payload from cell lysate
The experimental procedure described below was repeated three times. No additional resin was added in between rounds to showcase the recycling properties that decomplexation offers. Controls:
(+ve) control (**Wang-CB[7]•13**) –"always" fluorescent samples where **13** was added in Step A but no **4** was added in Step B
(-ve) control (**Wang-CB[7]**)–"always" non-fluorescent samples that underwent the same washes and incubations without addition of **13** or **4**.
Each sample was prepared and tested in triplicate.
Step A – For each (+ve) control, recycling and (-ve) control samples: Ad-FITC (**13**) (0.3 mg, 2 μmol) was dissolved in DMF (0.3 mL) and added to an Eppendorf tube containing Jurkat lysate (0.2mL, 2 mg/mL). The solution was adjusted to 50% DMF/H_2O (1 mL total) to ensure adequate solubility of all components. Wang-CB[7] (3.0 mg, 1.3 μmol) was added as a solid. The samples were rocked at room temp. for 5 minutes before being washed by centrifugation (17,108 x *g*, 1

min) with DMF (2 x 1mL) and H_2O (2 x 1mL). Fluorescence spectra were taken in H_2O (λ_{exc} = 495 nm, using a NE10B-B neutral density filter (Thorlabs), 3 nm emission slit widths, 5 nm excitation slit widths.
Step B – Recycling samples were resuspended in H_2O (0.5 mL) and 9-amino-*ortho*-carborane (**4**) (0.5 mg, 3 μmol) was added in DMF (0.5 mL) to result in a 1:1 DMF:H_2O solution.
(+ve) and (-ve) control samples were resuspended in 1:1 DMF:H_2O solution (1 mL). All samples were rocked at rt for 1h before being washed by centrifugation (17,108 x *g*, 1 min) with 1:1 DMF:H_2O (1 x 1 mL) and H_2O (2 x 1 mL). Fluorescence spectra were taken in H_2O (λ_{exc} = 495 nm, using a NE10B-B neutral density filter (Thorlabs), 3 nm emission slit widths, 5 nm excitation slit widths.
Step C – For (+ve) control, recycling and (-ve) control samples: Samples were resuspended in 20% piperidine/DMF (0.5 mL) and incubated at 60 ºC for 45 min (vortexed every 10 min). After decomplexation, the samples were washed by centrifugation (17,108 x *g*, 1 min) with 1:1 DMF:H_2O (1 x 1 mL) and H_2O (2 x 1 mL). Fluorescence spectra were taken in H_2O (λ_{exc} = 495 nm, using a NE10B-B neutral density filter emission filter (Thorlabs), 3nm emission slit widths, 5nm excitation slit widths.

Procedure for K_a determination of Ad-FITC (13) by a competition experiment with (trimethylsilyl)methylamine:

Triplicates of stock solutions of CB[7] (1.043 mM), (trimethylsilyl)methylamine (2.693 mM), and Ad-FITC (**13)** (0.673 mM) in 50 mM deuterated sodium acetate buffer (pH 4.75) were prepared. To each NMR sample was added the following stock solutions: 100 μL of CB[7], 50 μL (trimethylsilyl)methylamine and 200 μL of Ad-FITC **(13**) and 50 μL of 50 mM *d*-NaOAc buffer to give final concentrations of CB[7] (0.261 mM), (trimethylsilyl)methylamine (0.337 mM), and Ad-FITC **(13**) (0.337 mM). In order to check the equilibrium both ways, we prepared the replicate solutions in two distinct ways. Two samples were prepared by adding a (trimethylsilyl)methylamine stock solution to a solution of CB[7] and 9-aminocarborane, while the third replicate was prepared by adding the 9-aminocarboranes to a previously prepared solution of CB[7] and (trimethylsilyl)methylamine. The solutions were allowed to equilibrate overnight before ^{1}H NMR (500Hz) spectra were taken. NMR acquisition was taken with a delay time (D1) >5x T_1 to eliminate systematic errors arising from differential relaxation times.
The ratio between bound and free (trimethylsilyl)methylamine was determined by integration (region 0 to -1 ppm) which correspond to the concentrations of free guest and the host-guest complex. This allowed for determination of a K_{rel} value for Ad-FITC relative to (trimethylsilyl)methylamine. The equations and error analysis used to determine the binding affinities based on K_{rel} was described by Isaacs and coworkers in 2005 and 2014.[1,7]

Table experimental procedures

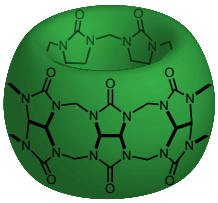
Table S1: Base screen to determine most efficient generation of *nido*-carborane (**11**) from **CB[7]•9**

Sample preparation: CB[7]•carborane complex and base (5 equiv.) were combined in H_2O (total volume of 2 mL), stirred at 60 °C, Interestingly, only the samples with piperidine formed clear, pale yellow solutions, with the rest of the bases forming dilute suspensions. Aliquots (0.2 mL) from each sample were taken at 1 h, 2 h, 8 h, and 24 h timepoints and diluted with H_2O.

^{11}B NMR acquisition and processing:
^{11}B NMR spectra were acquired in H_2O with standard acquisition parameters. The raw spectra where phased and baseline corrected to allow for accurate integrations. We chose to determine deboronation by integrating a *closo*-carborane characteristic doublet at -2 ppm with one of the *nido*-carborane unique doublets at -31ppm. This allow for an easy and reliable way to obtain relative deboronation rates. Note: Entry 2 integrated spectra can be found at ^{11}B NMR spectra section (p S54-S56).
In the case of piperidine, within 1 h deboronation was complete and we believe further degradation of the *ortho*-carboranes resulted in the formation of borate side-products which is exhibited as a singlet at about 5 ppm (spectra were not referenced with a standard).

Synthetic procedures:

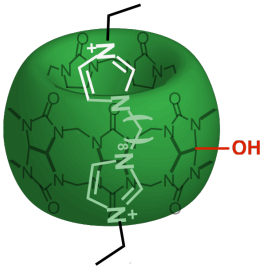
Cucurbit[7]uril: The synthesis and isolation of CB[7] was performed according to Bardelang and coworkers.[9] A slightly modified procedure is outlined below:



Glycoluril (100 g, 0.7 mol, 1 eq.) was dissolved in 12M HCl to form a pale orange mixture. Paraformaldehyde (42.6 g, 1.41 mol, 2 eq.) was added portionwise over 35 minutes. The mixture slowly starts thickening and heat is released. The viscous mixture (becomes a gel in smaller scales) was stirred at room temperature for an additional 30 minutes until it became very thick—almost gel-like at which point it was heated to 100 °C and refluxed for 17.5 h. The orange solution was slowly cooled down to room temperature and cooled to 0 °C overnight (CB[6] precipitates as well-formed pale yellow crystals). After 24 h, the mixture was filtered through vacuum to isolate the CB[6] crystals and the dark orange filtrate was concentrated *in vacuo* to produce a dark orange sticky solid. A solution of 45% aqueous formic acid (90 mL FA in 110 mL H_2O) was slowly added until all the solid was dissolved or had formed a white precipitate (CB[8]). The mixture was stirred at room temperature for 1 h to ensure all CB[8] had precipitated out and then was filtered to isolate crude CB[8]. The filtrate was concentrated *in vacuo* to produce an orange gel. In order to precipitate out CB[6], distilled H_2O (400 mL) was added and the mixture was sonicated (6 h) in order to transform the orange gel into a white precipitate (starts forming immediately) and a yellow solution. The mixture was stirred at room temperature overnight, then filtered and washed with H_2O (400 mL). The orange filtrate was concentrated *in vacuo* to about 100 mL and methanol (750 mL) was added to immediately form a white precipitate. The resulting mixture was stirred at room temperature overnight and then filtered through vacuum and washed with copious amount of methanol. A pale yellow solid was recovered and was redissolved in water (400 mL) and sonicated for 40 h. The mixture was centrifuged (2,818 x *g*, 3 min)(8 x 50 mL), cooled to 4 °C overnight and centrifuged again to get a clear yellow solution that was concentrated *in vacuo* to produce a yellow solid (mostly CB[7] with some CB[6] and CB[5] seen by ^{1}H NMR in D_2O). The crude product was dissolved in 20% glycerol solution and stirred at room temperature overnight, then it was heated to 90 °C and stirred for 4 h (clear yellow solution). Excess methanol (400 mL) was added to the solution and the resulting mixture was stirred at room temperature for 1 h (to precipitate out all CB[7]) and then filtered. The solid was washed extensively with methanol and air-dried to give a white solid (turns yellow when left out too long). ^{1}H NMR in D_2O showed 15% of CB[6] still present so the solid was redissolved in water (150 mL) and sonicated for 6 h (until the mixture was hot) to give a yellow solution with a white precipitate that was collected through centrifugation. To the supernatant was added methanol (400 mL) and the white precipitate was collected through filtration. The white solid was air-dried and ^{1}H NMR in D_2O showed >95% pure CB[7] (12.3 g, 0.106 mol, 15%). ^{1}H NMR (500 MHz, D_2O): δ 5.78 (d, J = 15.4 Hz, 14H), 5.51 (s, 14H), 4.21 (d, J = 15.4 Hz, 14H). ^{13}C NMR (500 MHz, D_2O): δ 71.22, 52.21.

Notes: CB[7] was synthesized and purified from 0.1 g to 100 g scales. The isolation from the rest of the ring sizes is greatly facilitated by the addition of 20% aqueous glycerol, however, the glycerol tends to stick to the product so it should be used with caution (extensive washing and sonication in methanol is required to remove the glycerol). In smaller scale, centrifugation (2,818 x *g*, 3-5 min) was determined to be superior to filtration at all steps of the purification process. CB[7] is a white powder but it tends to turn yellow/orange when wet.

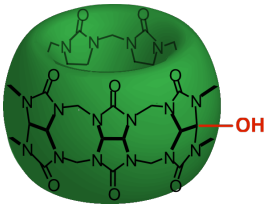
Monohydroxylated cucurbit[7]uril complexed with bisimidazolium (12), CB[7]-OH•12: The synthesis and purification of **CB[7]** was based on literature procedures[2,8,10] with slight modifications.



CB[7] (1.0 g, 0.09 mmol, 1 eq) and 3,3'-(octane-1,8-diyl)bis(1-ethyl-imidazolium) bromide[2] **12** (0.399 g, 0.859 mmol, 1 eq.) were dissolved in milli-Q water (100 mL) and purged with nitrogen gas for 15 min at 60 °C to make complexed CB[7] (**CB[7]•12**). Ammonium persulfate (0.0588 g, 0.258 mmol, 0.3 eq.) was added and the resulting clear solution was heated to 85 °C and stirred overnight under N_2. The reaction was quenched by immersing it in liquid N_2. The solution was concentrated *in vacuo* to 20 mL and filtered. The filtrate was concentrated *in vacuo* to about 3 mL and purified on a reverse-phase resin (MCI Gel CHP20P). The column (100 g of resin) was eluted with milli-Q water and 10 mL fractions were collected. The monohydroxylated product starting eluting at fraction 30 with usually 2-5 mixed fractions, then clean **CB[7]-OH•12** was eluted. The fractions were analyzed by LCMS (bypass method in H_2O). The pure fractions were collected and evaporated *in vacuo* to yield the desired product, **CB[7]-OH•12** (1 g, 0.06 mmol, 71%). Spectral data was consistent with the literature[8]: ^{1}H NMR (500 MHz, D_2O): δ 8.78 (s, 3H, **12**), 7.55 (s, 3H, **12**), 7.49 (s, 3H, **12**), 5.85 (d, J = 15.2 Hz, 2H), 5.78 (d, J = 15.4 Hz, 10H), 5.59 (s, 1H), 5.53 (s, 12H), 5.46 (d, J = 9 Hz, 1H), 5.30 (s, 1H), 4.53 (d, J = 15.5 Hz, 2H), 4.32 (s, 5H), 4.29 (s, 2H), 4.27-4.18 (m, 12H).

Notes: The amount of ammonium persulfate can be varied up to 3 equivalents depending on the desired conversion. The reaction can be easily monitored by LCMS or other ESI+ mass spec with 1 mg/mL samples. The yield of the monohydroxylated product varied depending on conversion and purification with a range of 22–71%.

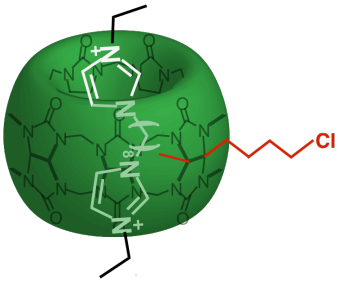
Monohydroxylated cucurbit[7]uril, CB[7]-OH via reported NH_4PF_6 treatment: Isolated



CB[7]-OH•12 (250 mg, 0.15 mmol, 1 eq.) was dispersed in DCM (50 mL) in the presence of excess NH_4PF_6 (240 mg, 1.5 mmol, 10 eq.). The mixture was refluxed (34 °C) for 48h. Centrifugation (2,818 x *g*, 5 min) and washing with methanol (3 x 50 mL) to give a white solid. The product was dried *in vacuo* overnight (0.104 g, 0.08 mmol, 53%). Spectral data consistent with the literature[8]: ^{1}H NMR (500 MHz, D_2O): δ 5.85 (d, J = 15.2 Hz, 2H), 5.78 (d, J = 15.4 Hz, 10H), 5.59 (s, 1H), 5.53 (s, 12H), 5.46 (d, J = 9 Hz, 1H), 5.30 (s, 1H), 4.53 (d, J = 15.5 Hz, 2H), 4.32 (s, 5H), 4.29 (s, 2H), 4.27-4.18 (m, 12H).

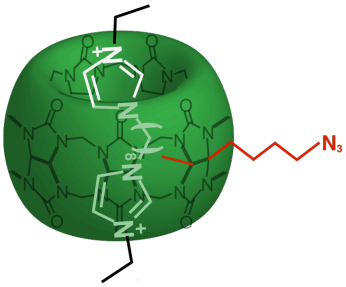
Notes: Complete isolation of CB[7]-OH from excess NH_4PF_6 was unsuccessful, hence yield determination was not possible. Upon scale-up of decomplexation to 500 mg or more the procedure required at least 7 days to reach completion and excess NH_4PF_6 could not be completely removed from the product.

Monochlorinated cucurbit[7]uril complexed with bisimidazolium 12, CB[7]-Cl•12:



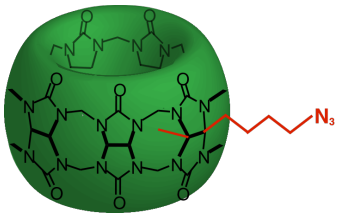
Glycoluril hexamer (**S1**)[11] (1.00 g, 1.03 mmol, 1 eq.) and potassium iodide (0.230 g, 1.35 mmol, 1.3 eq.) were added in a scintillation vial and dissolved in 9M H_2SO_4 after sonication and stirring for about 5 minutes. To the dark orange solution was added the monochlorinated glycoluril monomer (**S2**)[12] that was slowly dissolved after vigorous stirring. The reaction was heated to 110 °C and stirred for 35 min. The brown mixture was poured into MeOH (25 mL) in a 50 mL Falcon tube and centrifuged (2,818 x *g*, 3 min) to give a gray solid. The solid was washed by centrifugation with MeOH (3x40 mL). The pellet was suspended in H_2O (25 mL) containing **12** (0.55 g, 1.2 mmol) and diluted to 200 mL. The mixture was stirred at 80 °C overnight and concentrated to 40 mL for purification using a CHP-20P resin: 500 mL H_2O, 400 mL 5% MeCN/H_2O, 400 mL 10% MeCN/H_2O, 20% MeCN/H_2O, 50% MeCN/H_2O and 400 mL MeCN. Fraction purity was determined by LCMS analysis and **CB[7]-Cl•12** came out between 20%-50% MeCN/H_2O. The appropriate fractions were combined, excess MeCN was concentrated *in vacuo* and the sample was lyophilized to dryness to produce **CB[7]-Cl•12** (0.405 g, 0.257 mmol, 25%). The compound was used without further purification.

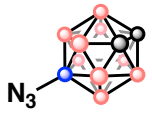
Azido-cucurbit[7]uril complexed with bisimidazolium 12:



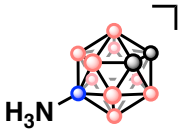
CB[7]-N_3•12: CB[7]-Cl (0.405 g, 0.257 mmol) was suspended in H_2O (8 mL) and sodium azide was added while vigorously stirring. The mixture was heated to 80 °C and stirred for 48 h (it becomes a clear orange solution after a few hours). The reaction was diluted with H_2O (to 30 mL total volume) and the product was precipitated with MeOH (40 mL). The crude product was washed by centrifugation (2,818 x *g*, 3min) with MeOH (3 x 40 mL) to give the product, **CB[7]-N_3•12**, as an orange solid (0.274 g, 0.173 mmol, 65%).

Azido-cucurbit[7]uril, CB[7]-N_3: In a 50mL Falcon tube, *ortho*-carborane (**9**) (0.254 g, 1.76 mmol, 10 eq.) was dissolved in TFA (10 mL) by sonication for 30 min. **CB[7]-N_3•12** (0.274 g, 0.173 mmol) was dissolved in 1:5 TFA/H_2O (10mL) mixture and added to the TFA solution of **9**. The resulting orange solution was sonicated for 1h until precipitate formed. The solvents were evaporated *in vacuo* and the remaining solid was washed by centrifugation (2,818 x *g*, 3min) with DCM (1 x 40 mL) and MeOH (2 x 40 mL). The orange solid was dissolved in 20% aqueous piperidine (50 mL), heated to 60 °C and stirred overnight. The resulting mixture was evaporated *in vacuo* and washed by centrifugation (2,818 x *g*, 3min) with MeOH (3 x 15mL). The pellet was dissolved in 5% MeCN/H_2O and lyophilized to dryness to yield the desired product as an off-white solid (0.22 g, 0.17 mmol, >95%). The product was characterized by LCMS (see Figure S7), ^{1}H and ^{11}B NMR to confirm decomplexation (see spectra below). All spectral data were consistent with the literature:[12] ^{1}H NMR (500 MHz, 2:1 D_2O/CD_3CN): δ 5.93 (m, 14H), 5.70 (m, 14H), 4.45 (m, 14H), 3.34 (m, 3H), 2.05 (m, 2H), 1.86 (m, 4H), 1.76 (m, 2H).



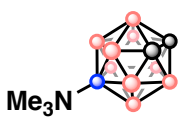


9-N_3-*o*-$C_2B_{10}H_{11}$ (2). 9-Br-*o*-$C_2B_{10}H_{11}$ (350 mg, 1.53 mmol) was charged to an 8 mL reaction tube with NaN_3 (153 mg, 2.35 mmol, 1.5 eq.), SPhosPdG3 (61 mg, 0.078 mmol, 0.05 eq.), SPhos (32 mg, 0.078 mmol, 0.05 eq.). The solids were dissolved in 1,2-dimethoxyethane (3 mL) and the resulting mixture was heated in an oil bath at 80 ˚C for 2h. Full conversion was confirmed by GC-MS and the resulting mixture was allowed to cool, diluted with EtOAc (20 mL) and flushed through a pad of silica gel. The filtrate was concentrated under vacuum to give a red oil. The oil was diluted in DCM (5 mL) and treated with Celite to give a damp solid mass. The solid purified by sublimation at 80 ˚C for 12 h. (Note: carbazole also sublimes under these conditions but the following reaction(s) can be carried out with the minor carbazole impurity, if desired). The white sublimate was then subjected to column chromatography in 1:1 Hexanes/Et_2O to afford **2** (179 mg, 1.02 mmol, 67%) of the desired product. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.52 (br s, 1H, carborane C – H), 3.44 (br s, 1H, carborane C – H), 3.0 – 1.6 (m, 10H, carborane B – H region); ^{13}C NMR: 51, 44; ^{11}B NMR: 7.78 (s, 1B, B – N_3), -3.78 (d, 1B), -10.29 (2B, d), -14.7 – -17.4 (m, 6B). (Note: A delay time of 5 sec was necessary for collecting ^{11}B NMR spectra for accurate integration values). IR (cm^{-1}) 3071, 2622, 2596, 2579, 2562, 2121, 1323, 1311, 1203, 1152, 1086, 1070, 1020, 994, 976, 926, 847, 742, 730, 692, 632.



[9-NH_3-*o*-$C_2B_{10}H_{11}$]Cl (4). 9-N_3-$C_2B_{10}H_{11}$ (150 mg, 0.810 mmol, 1 eq.) was charged to an 8 mL reaction tube and the atmosphere was removed under vacuum and backfilled with nitrogen. Dry MeCN (4 mL) was added under positive nitrogen pressure, followed by PMe_3 (668 µL, 6.48 mmol, 8 eq.). The resulting solution was placed in a 60 ˚C oil bath and was stirred for 12 h. Conversion to the desired product was verified by ^{1}H NMR. The solvent was removed under vacuum to afford a white solid. The corresponding 9-N=PMe_3-*o*-$C_2B_{10}H_{11}$ (**3**) was used directly without further purification (see below for representative NMR spectra of the intermediate iminophosphorane product). HRMS (GC, m/z) calc. for $N_3C_2B_{10}H_{11}[M]^+$: 234.2124; found: 234.1761.

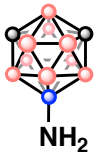
The solid was suspended in MeOH (1 mL), after which concentrated aqueous HCl (1 mL) was added dropwise. The mixture was stirred for 1h with conversion being monitored by mass spectrometry and ^{11}B NMR. After 1 h, the solvent was removed *in vacuo*. The white residue was suspended in acetone (~5 mL) and was stirred vigorously at room temperature for 30 min, after which time the solid was isolated by filtration and washed with acetone. Additional rounds of stirring and filtering may be necessary to completely remove the O=PMe_3 byproduct. The solid was dried *in vacuo* to afford the desired product (91 mg, 0.58 mmol, 72%). ^{1}H NMR (500 MHz, D_2O): δ 4.45 (br s, 1H, carborane C – H), 4.40 (br s, 1H, carborane C – H), 2.9 – 1.8 (m, 10H, carborane B – H region); ^{11}B NMR (delay time (d1) = 5s): 3.86 (s, 1B, B – NH_3), -2.21 (d, 1B), -8.66 (2B, d), -12.3 – -14.3 (m, 6B). HRMS (GC, m/z) calc. for $C_2B_{10}H_{14}N$ $[M\text{-}HCl]^+$: 160.2493; found: 160.1830.



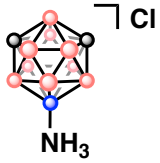
[9-NMe_3-*o*-$C_2B_{10}H_{11}$]I (5). [9-NH_3-*o*-$C_2B_{10}H_{11}$]Cl (30 mg, 0.155 mmol, 1eq.) was charged to an 8 mL reaction tube with a stir bar and K_3PO4 (106 mg, 0.767 mmol, 5 eq.) and a septum cap. The atmosphere was removed under vacuum and backfilled with nitrogen. MeCN (600 µL) and MeI (286 µL, 4.60 mmol, 30 eq.) were added in sequence, and the reaction was stirred for 2 h at room temperature. The mixture was diluted with MeOH (5 mL) and filtered through Celite. The filtrate was dried *in vacuo* to afford the desired product (37 mg, 0.11 mmol, 73%). ^{1}H NMR (500 MHz, D_2O): δ 4.57 (br s,

2H, carborane C – H), 2.97 (br s, 9H, N*Me*$_3$, 3.5 – 1.5 (m, 10H, carborane B – H region); ^{11}B NMR (delay time (d1) = 5s): 10.58 (s, 1B, B – NH$_3$), -3.16 (d, 1B), -9.77 (2B, d), -13.3 – -14.4 (m, 6B). HRMS (GC, m/z) calc. for $C_5B_{10}H_{20}N$ [M-I]$^+$: 202.3290; found: 202.2088.

9-NH$_2$-*m*-C$_2$B$_{10}$H$_{11}$ (6) was synthesized according to literature procedures (Dziedzic, R. M.; Saleh, L. M. A.; Axtell J. C.; Martin, J. L.; Stevens, S. L.; Royappa, A. T.; Rheingold, A. L.; Spokoyny, A. M. *J. Am. Chem. Soc.* **2016**, *138*, 9081 – 9084.)

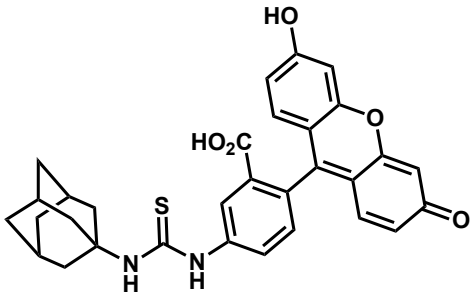


[9-NMe$_3$-*m*-C$_2$B$_{10}$H$_{11}$]I (7). [9-NH$_2$-*m*-C$_2$B$_{10}$H$_{11}$]Cl (62 mg, 0.389 mmol, 1 eq.) was charged to an 8 mL reaction tube with a stir bar and K$_3$PO$_4$ (269 mg, 1.95 mmol, 5 eq.) and a septum cap. The atmosphere was removed under vacuum and backfilled with nitrogen. MeCN (2 mL) and MeI (727 µL, 11.7 mmol, 30 eq.) were added in sequence, and the reaction was stirred for 2h at room temperature. The mixture was diluted with MeOH (5 mL) and filtered through Celite. The filtrate was dried *in vacuo* and was dissolved in water. The mixture was passed through a syringe filter and the filtrate was lyophilized to afford the desired product (120 mg, 0.365 mmol, 94%). ^{1}H NMR (500 MHz, D$_2$O): δ 3.72 (br s, 2H, carborane C – H), 3.72 (br s, 9H, N*Me*$_3$), 2.4 – 16 (m, 10H, carborane B – H region); ^{11}B NMR (delay time (d1) = 5s): 5.91 (s, 1B, B – NH$_3$), -5.85 (d, 1B), -10.36 – -18.23 (7B, m). HRMS (GC, m/z) calc. for $C_5B_{10}H_{20}N$ [M-I]$^+$: 202.3290; found: 202.2100.



[9-NH$_3$-*m*-C$_2$B$_{10}$H$_{11}$]Cl (8). 9-NH$_2$-*m*-C$_2$B$_{10}$H$_{11}$ (45 mg, 0.283 mmol, 1eq.) was dissolved in Et$_2$O (10 mL). HCl gas (generated from the addition of H$_2$SO$_4$ to NaCl in a separate round-bottom) was bubbled into the ethereal solution *via* cannula until a white precipitate formed. The suspension was stirred for 10 min at room temperature, after which the solid was isolated on a fritted funnel and washed with Et$_2$O (10mL). The product solid (28 mg, 0.14 mmol, 51%) was dried *in vacuo*. ^{1}H NMR (500 MHz, D$_2$O): δ 3.61 (br s, 2H, carborane C – H), 3.5 – 1.5 (m, 10H, carborane B – H region); ^{11}B NMR (delay time (d1) = 5s): -2.46 (s, 1B, B – NH$_3$), -6.16 (d, 2B), -10.02 (1B, d), -12.86 (d, 4B), -16.45 (d, 1B), -18.81 (d, 1B). HRMS (GC, m/z) calc. for $C_2B_{10}H_{14}N$ [M]$^+$: 160.2493; found: 160.1894.

5-(3-((1s,3s)-adamantan-1-yl)thioureido)-2-(6-hydroxy-3-oxo-3H-xanthen-9-yl)benzoic acid (AdFITC, 13): In an oven-dried scintillation vial was added fluorescein isothiocyanate isomer 1 (0.105 g, 0.270 mmol, 1 eq.), 1-adamantylamine.HCl (0.100 g, 0.533 mmol, 2 eq.) and triethylamine (74 µL, 0.53 mmol, 2 eq.) under high N$_2$ flow. Anhydrous MeOH (2 mL) was used to dissolve the solids and form a dark orange solution after 1 h. The reaction was stirred at room temp. under N$_2$ atmosphere for 12 h. The solvents were evaporated and the crude reaction mixture was analyzed by LCMS to determine approximately 50% conversion to the product. The crude product was purified by silica column chromatography (0-5% MeOH/DCM + 0.5% AcOH) to give the desired product (**13**) as a dark orange solid after extensive drying *in vacuo* (76 mg, 0.14 mmol, 52%). All spectral data were consistent with literature.[13,14]



Supplementary Notes

SI Note 1: Summary of existing literature regarding stimuli-responsive removal of guests from CB[7]

Removing guests from the CB[7] cavity–even guests with relatively lower binding affinities (e.g. **12**, $K_a \approx 10^6$ M^{-1})– has been a formidable challenge. To put our work in context, we have summarized the existing literature below.

Organic solvent extraction, Jiao, D.; et al *Chem. Commun.* **2010**, *46*, 2007-2009
In their report[4], Scherman and coworkers (*Chem. Commun.* **2010**, *46*, 2007) used 100% organic solvent (dichloromethane), elevated temperatures and long reactions time (48 h) to remove the 1-alkyl-3-ethylimidazolium (**12**) guests. Note that in our hands, the same method required even higher temperatures and double the reaction time to remove **12** (as shown in Schemes S1-S2 within this manuscript).

Basic treatment, Lucas, D., et al *J. Am. Chem. Soc.* **2011**, *133*, 17966-17976
Isaacs and coworkers in their report of synthesizing monofunctionalized CB[7] compounds[11] removed *para*-xylylenediamine ($K_a = 10^{10}$ M^{-1}) from the cavity of a hexamer by treatment with 5M aq. NaOH. However, this approach has not been successful for isolating guest-free CB[7].

pH change, Vásquez, J.; et al *Chem. Commun.,* **2016**, *52*, 6245-6248
Another example of polyamines being removed from the CB[7] cavity was presented in 2016 by Pischel and coworkers.[15] The work exploits a photo-induced pH jump from 8 to 5, and is combined with the pH-dependent switching of the competitive capacity of a guest-dye. While the approach is elegant utilizing light as a mild trigger, it has not been optimized to yield a guest-free CB[7] cavity.

Redox and pH change, Fox, M.; et al *Langmuir* **2012**, *28*, 15075-15079
Significant reduction in binding affinities of ferrocene and viologen guests with CB[6] and CB[7] has been reported in relation to changes in pH and oxidation state.[16] However, despite substantial reduction in binding affinity (up to 2 orders of magnitude), complete decomplexation was not exhibited and it was stated to still require organic solvents and excessive salt treatment.

Use of organic solvent, Wang, W.; Kaifer, A. E. *Supramol. Chem.* **2010**, *22*, 710-716
Kaifer and coworkers have exhibited dramatic reductions in binding affinity (up to 8 orders of magnitude) of ferrocenyl guests that are transferred from aqueous media to organic solvents (DMSO, MeCN).[17] On the contrary, methylviologen guests that form slightly weaker complexes with CB[7] in water retain much of their binding affinity in organic solvent. This investigation provides a potential solution of isolating empty CB[7] in some cases (depending on the guest bound), although complete removal of guests from the cavity was not reported.

Salt treatment, Ong, W.; Kaifer, A. E. *J. Org. Chem*. **2004**, *69*, 1383-1385
Kaifer and coworkers have investigated the effect of salt treatment in the isolation of CB[7]-methyl viologen complexes.[18] They found that salt concentrations up to 0.2M reduce the binding affinity by two orders of magnitude. Combined with additional methods to lower binding affinity, low

concentration salt treatment could lead to decomplexation. However, excessive amounts of salt and multiple round are necessary to remove high affinity guests from the CB[7] cavity.[19]

SI Note 2: Discussion of the role of piperidine in deboronation

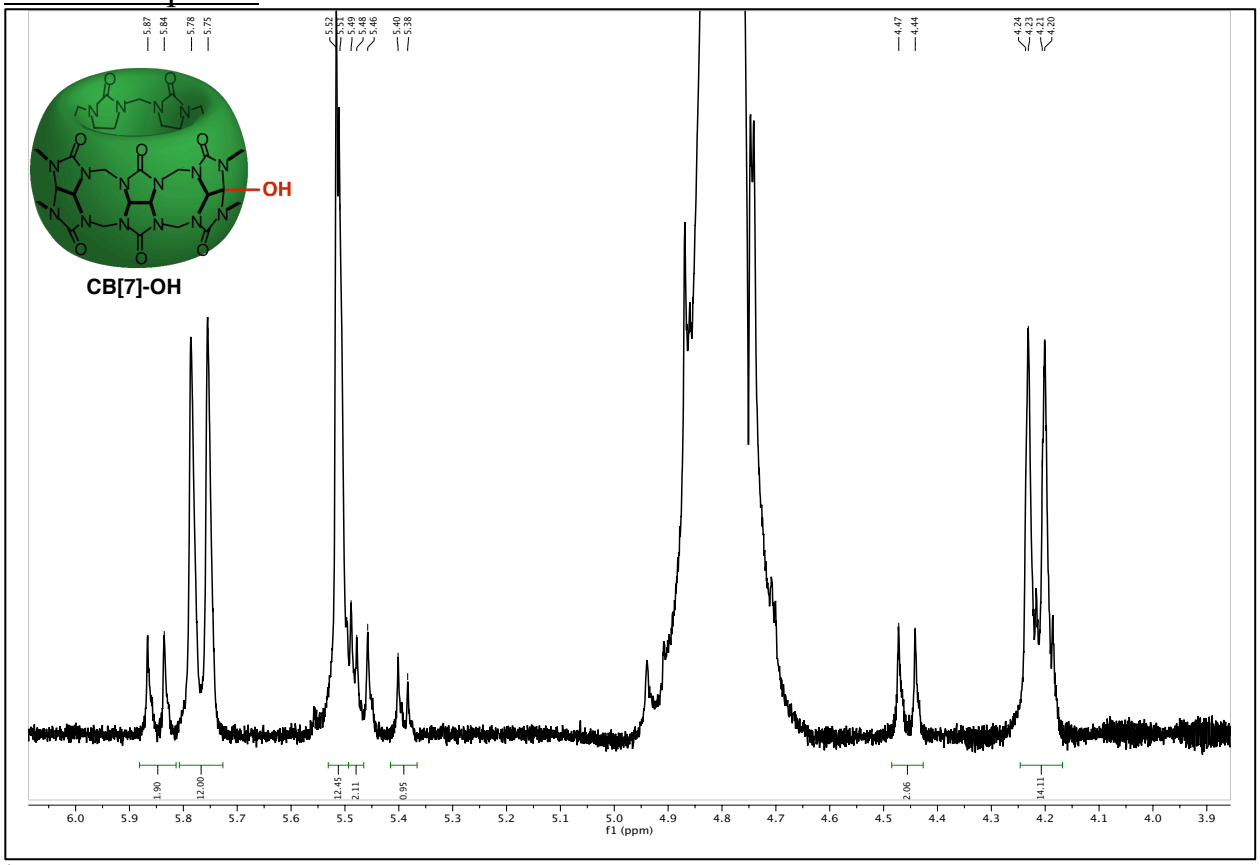
Piperidine seems to be a privileged base for deboronation of **4** and **6** bound to CB[7] as we observe that without CB[7] present the deboronation of **4** and **6** proceeds at similar rates with piperidine and dimethylamine (Figure S14, S18).

To explore the difference between piperidine and dimethylamine, we first investigated if the piperidine was able to displace **4** from CB[7]. Due to the ability for **4** to be deboronated by piperidine, we could not perform a direct competition experiment and instead employed (trimethylsilyl)methylamine displacement as a comparative metric. While 58% displacement of (trimethylsilyl)methylamine is observed using a 1.5:1 ratio of (trimethylsilyl)methylamine:**4** (Figure S15A), indicating **4** is a stronger binder than (trimethylsilyl)methylamine, no displacement is observed when piperidine is added to a solution of (trimehylsilyl)methylamine and CB[7] at all concentrations tested (up to 50 equivalents of piperidine, Figure S15B,C)). These data support that the K_a of piperidine with CB[7] is well below that of **4** and the privileged nature of piperidine is not due to its ability to displace the *ortho*-carborane from CB[7].

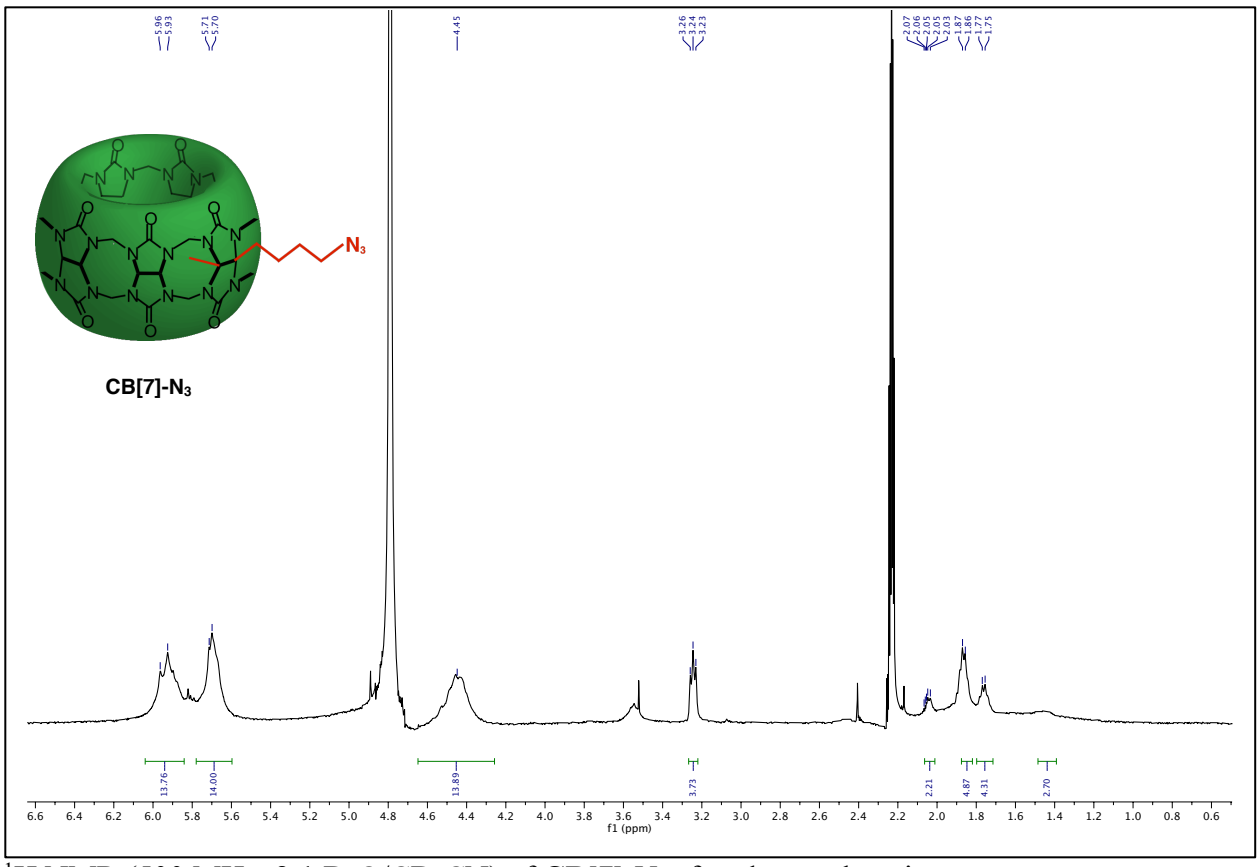
While displacement of the (trimethylsilyl)methylamine guest was not observed when piperidine was added, careful analysis of the NMR spectra did show a new piperidine species present at 2.7ppm (Figure S15B). This piperidine species was also observed in the presence of CB[7] and the smaller CB[6] (Figures S15D-E). We attribute these new piperdine resonances to be from interaction of the piperidine with the carbonyl portals of the CB[n]s but encapsulation inside the host. These type of interactions have been observed with positively charged rhodamine dyes (*J. Am. Chem. Soc.,* **2016**, *138*, 16549-16552*)* and cations such as Na^+ (*J. Am. Chem. Soc.,* **2011**, *133*, 20623-20633).

Experimentally, we observe that the reaction mixture for deboronation of CB[7]•**4** with piperidine is a transparent yellowish solution while reaction mixtures with all other bases tested formed dilute suspensions. We hypothesize that the interaction of the piperidine with the portals of the CB[7] help solubilize the complex and that the solubility is crucial for efficient deboronation as complete deboronation requires two molecules of base.[20–22] It is also possible that the piperidine assists in the removal of the *nido*-carboranes from CB[7].

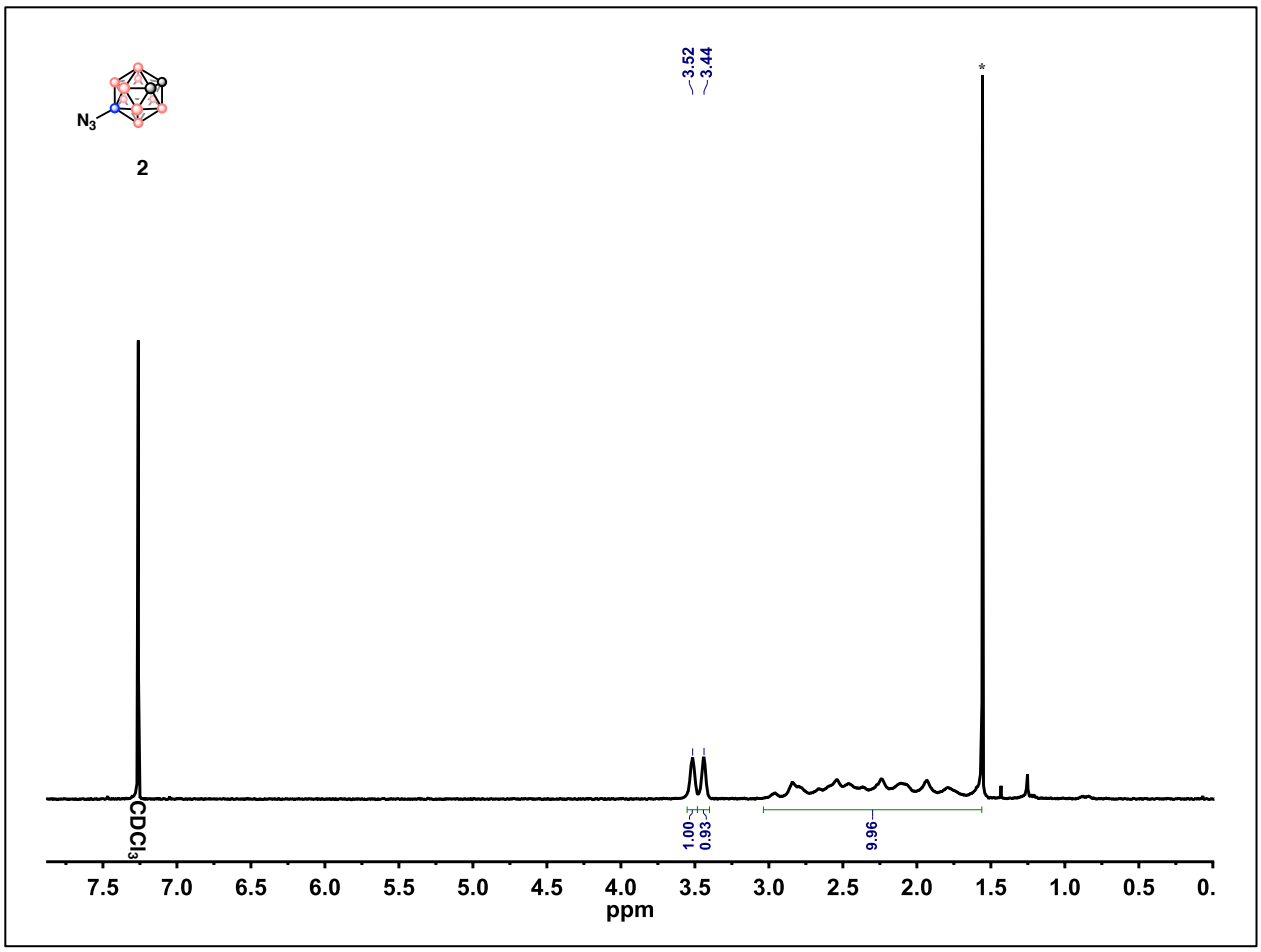
^{1}H NMR Spectra



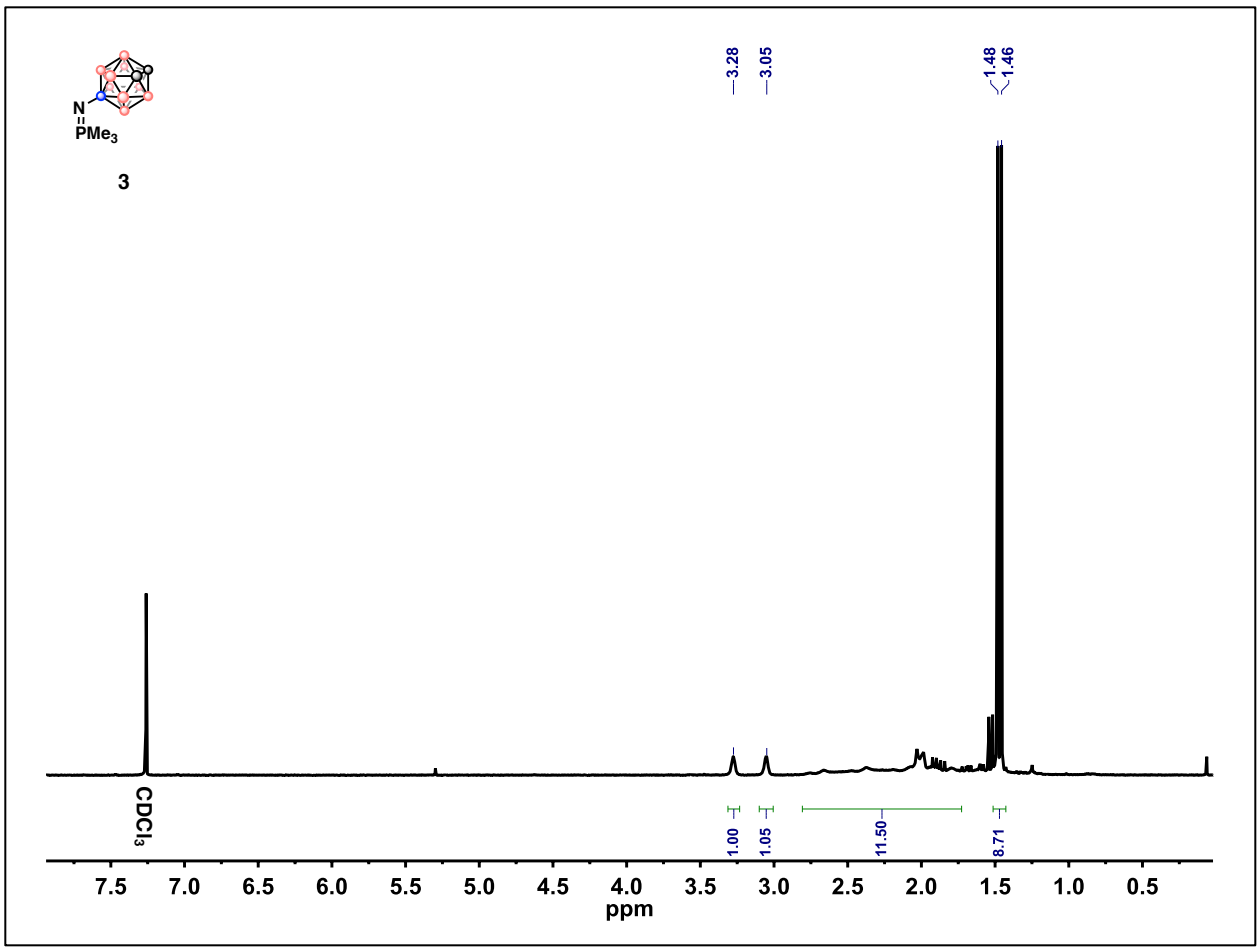
^{1}H NMR (500 MHz, D_2O) of **CB[7]-OH** after decomplexation.



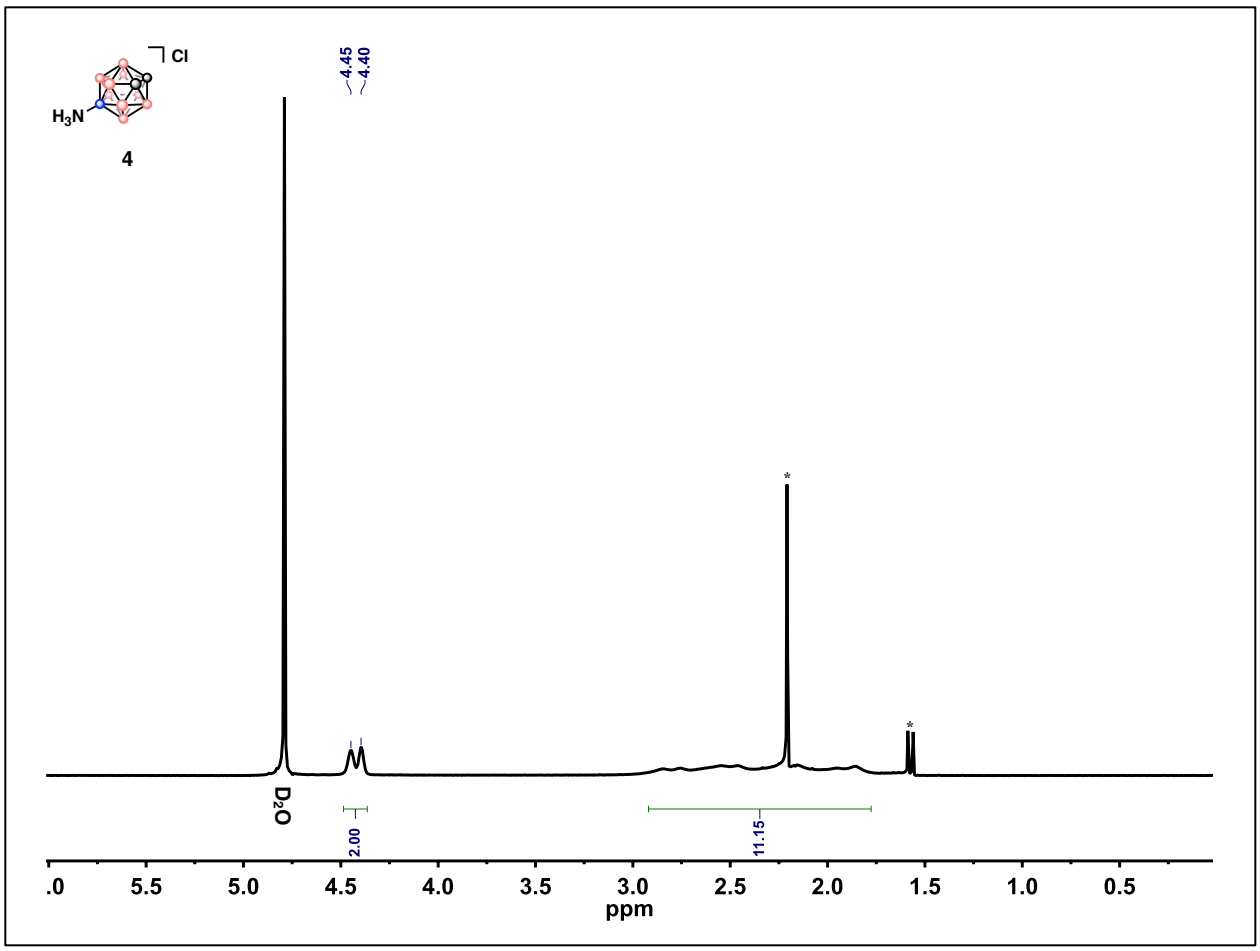
^{1}H NMR (500 MHz, 2:1 D_2O/CD_3CN) of **CB[7]-N_3** after decomplexation.



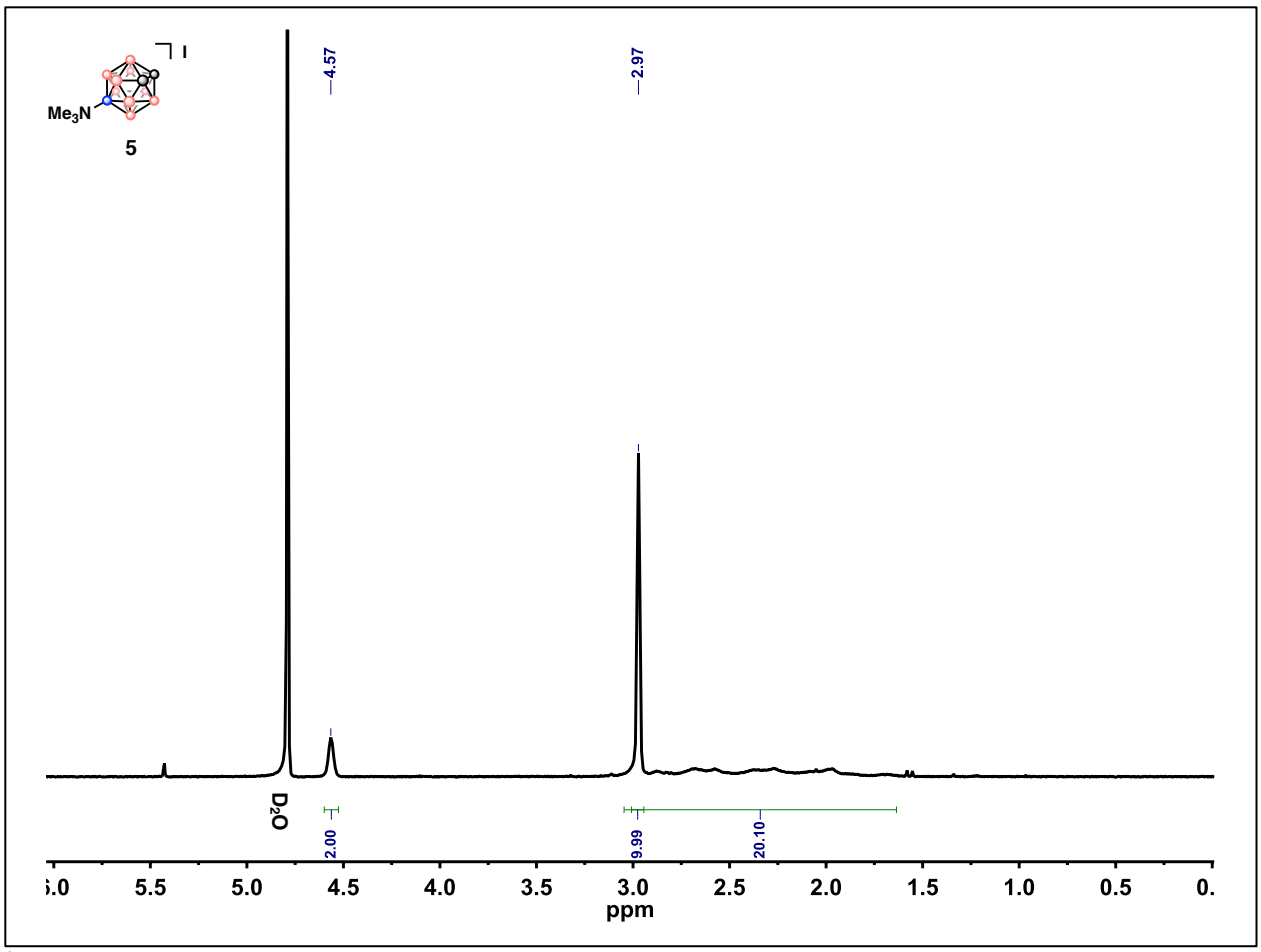
^{1}H NMR Compound **2**



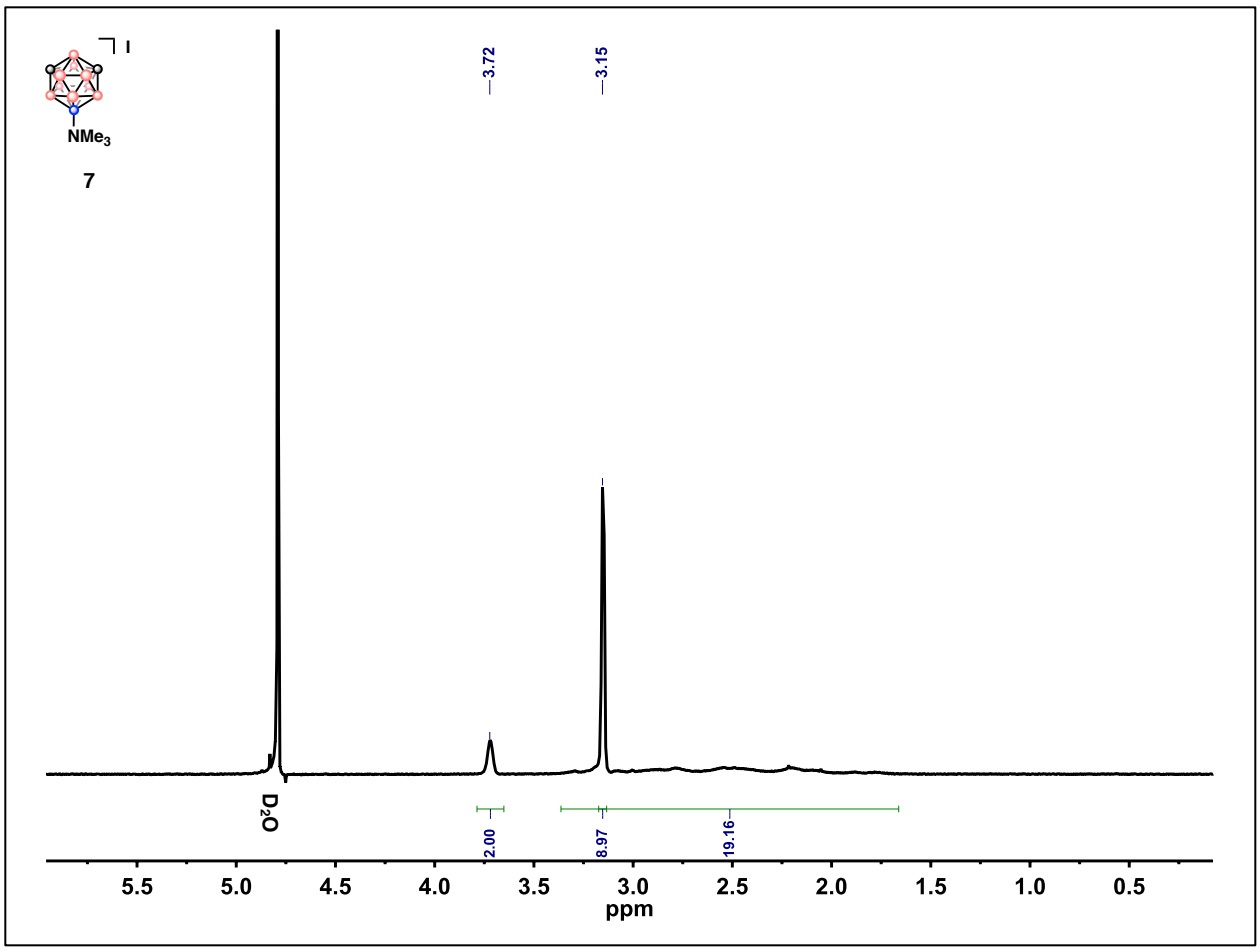
^{1}H NMR Compound **3**



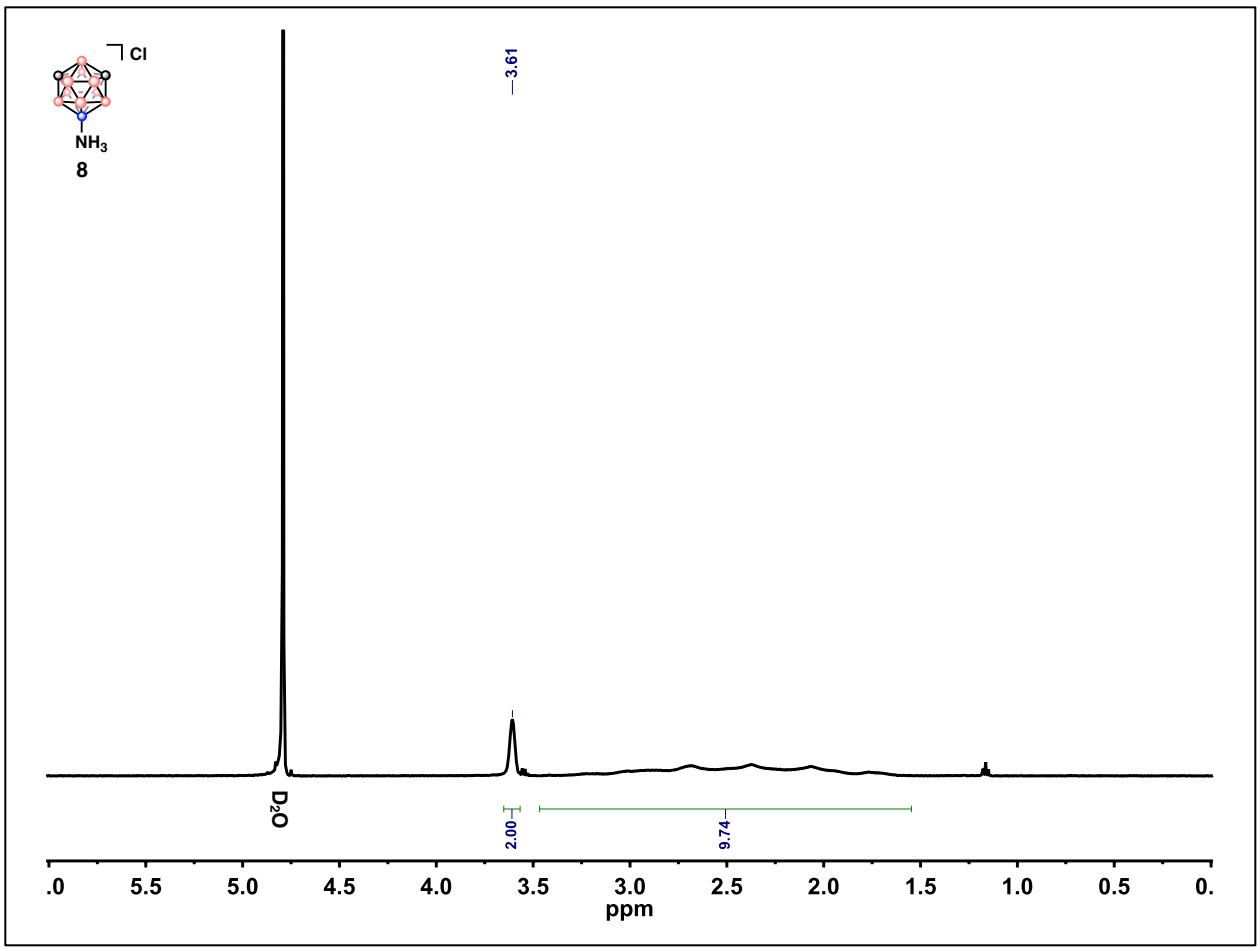
^{1}H NMR Compound **4**



^{1}H NMR Compound **5**



^{1}H NMR Compound **7**

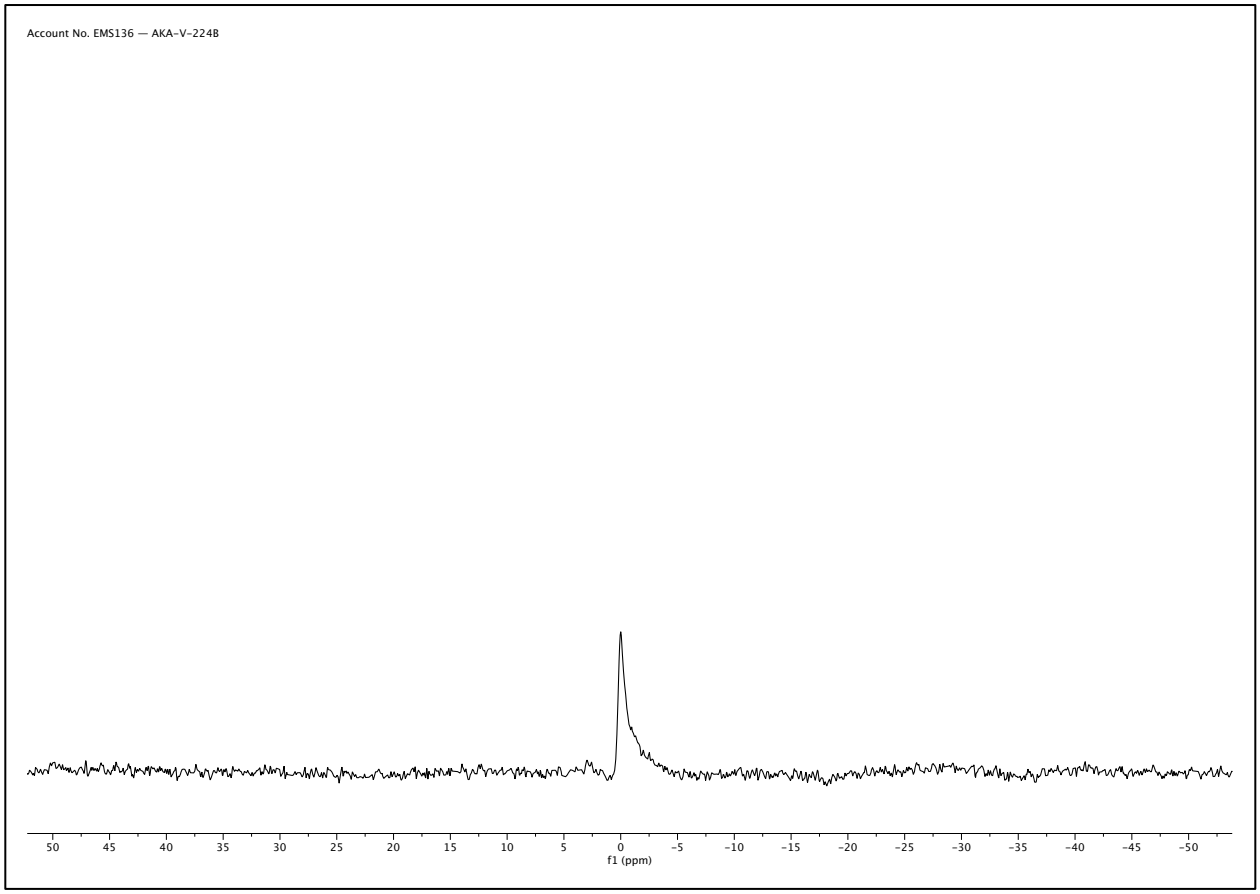


^{1}H NMR Compound **8**

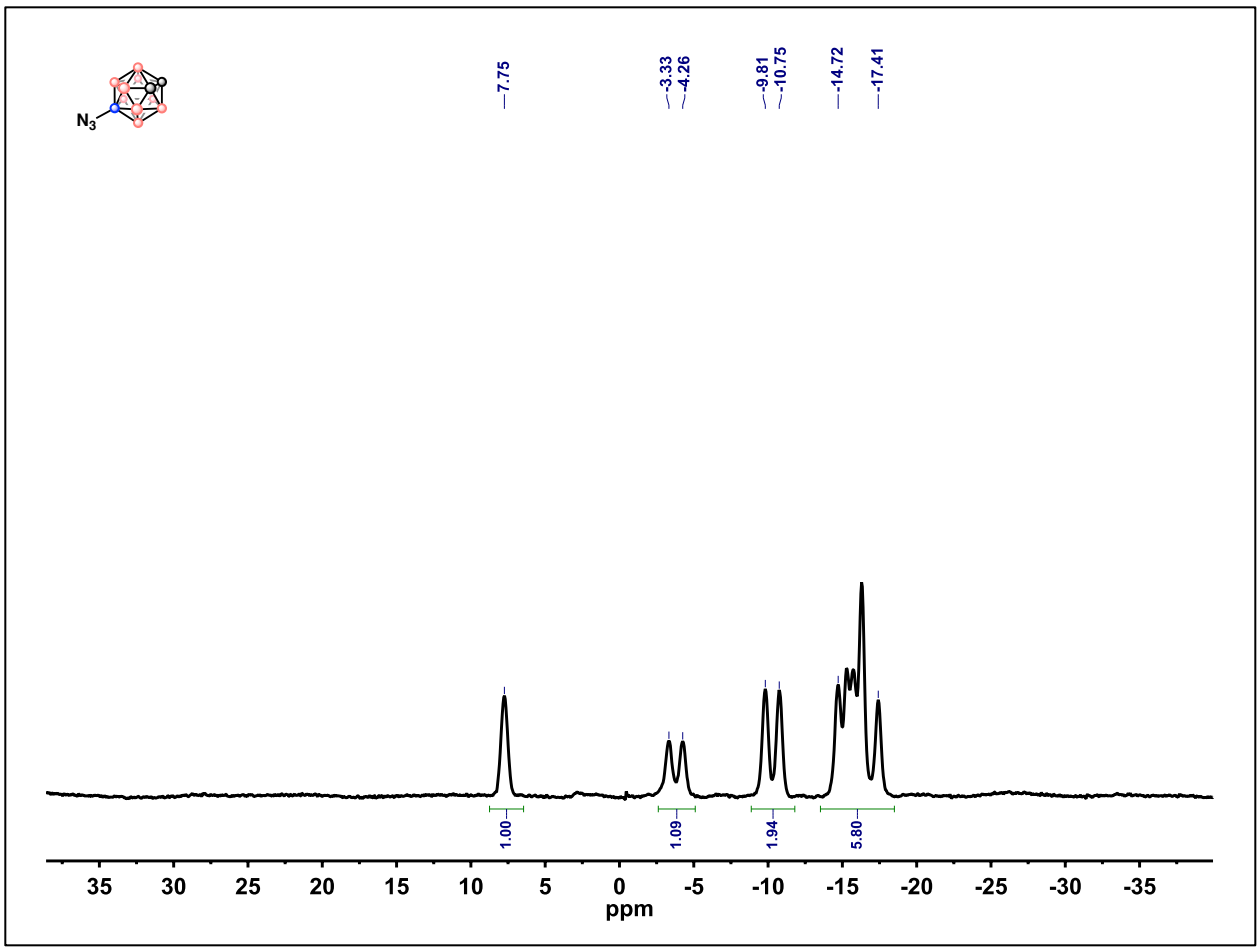
^{11}B NMR Spectra

Baseline corrected spectra were necessary for accurate integration. For compounds **2-8** a delay time of 5 sec for collecting the spectra.

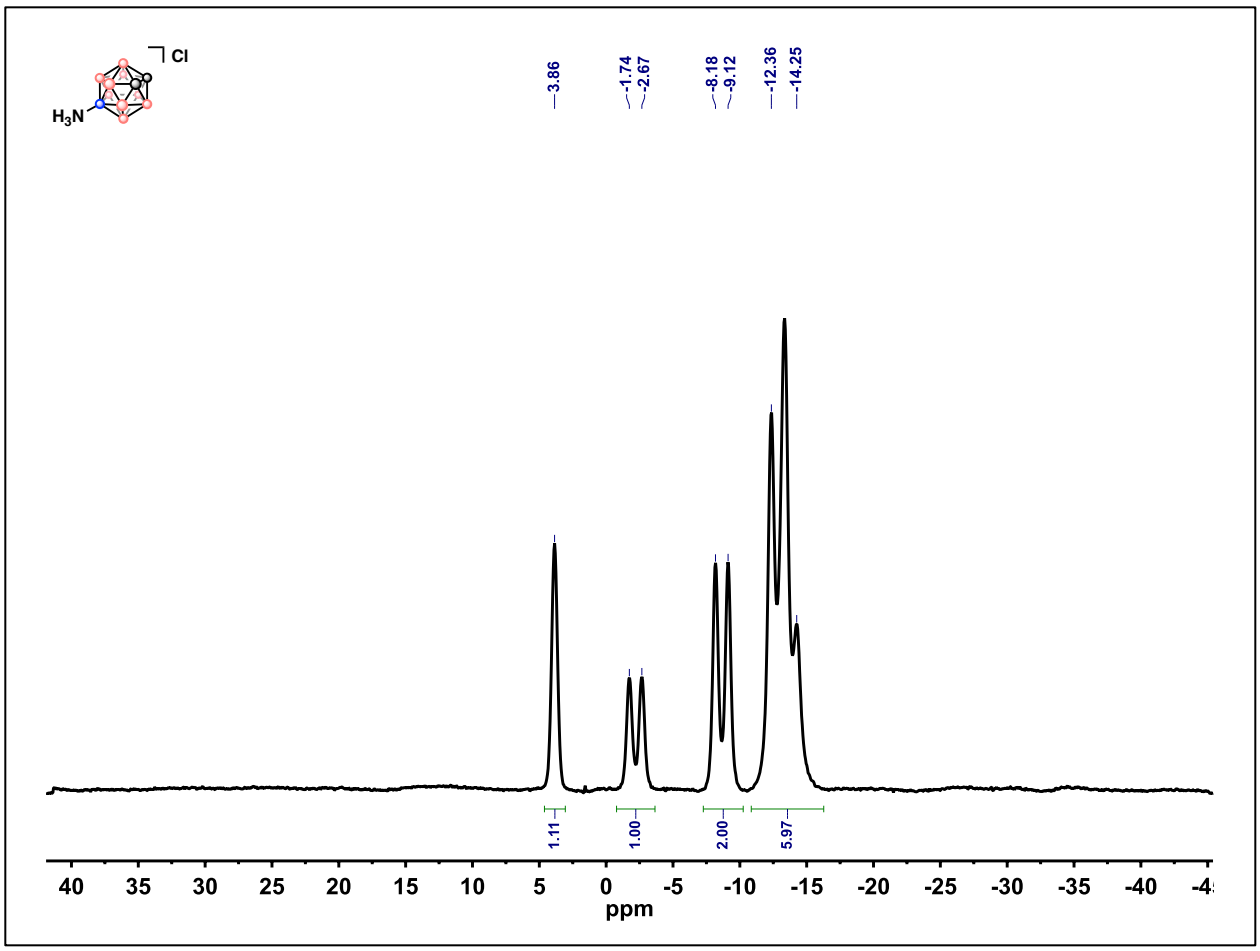
Baseline-corrected Spectra



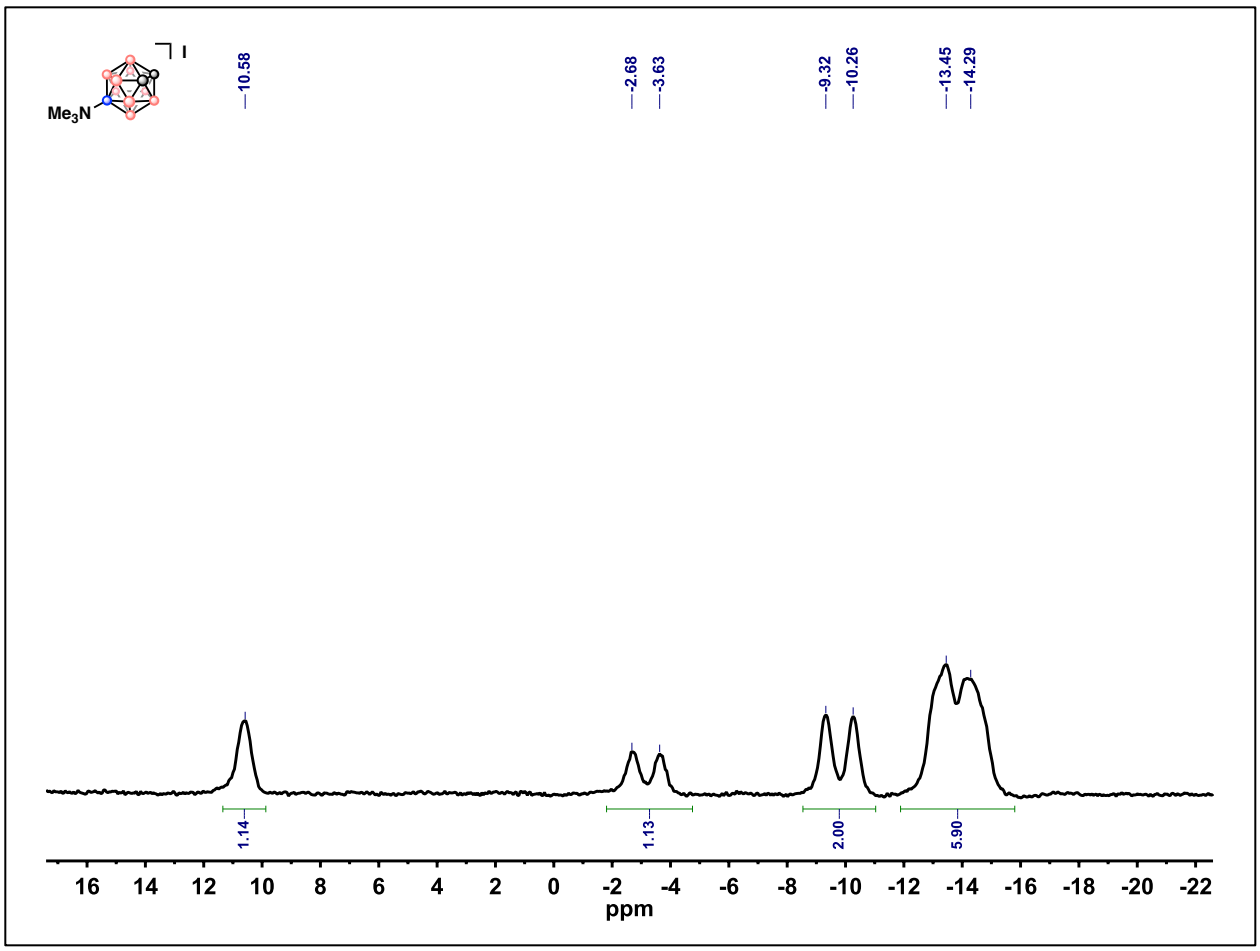
^{11}B NMR (500 MHz, 2:1 D_2O/CD_3CN) (baseline corrected) CB[7]-N_3 after decomplexation. Only $BF_3.OEt_2$ standard is present showcasing complete removal of **9** from cavity.



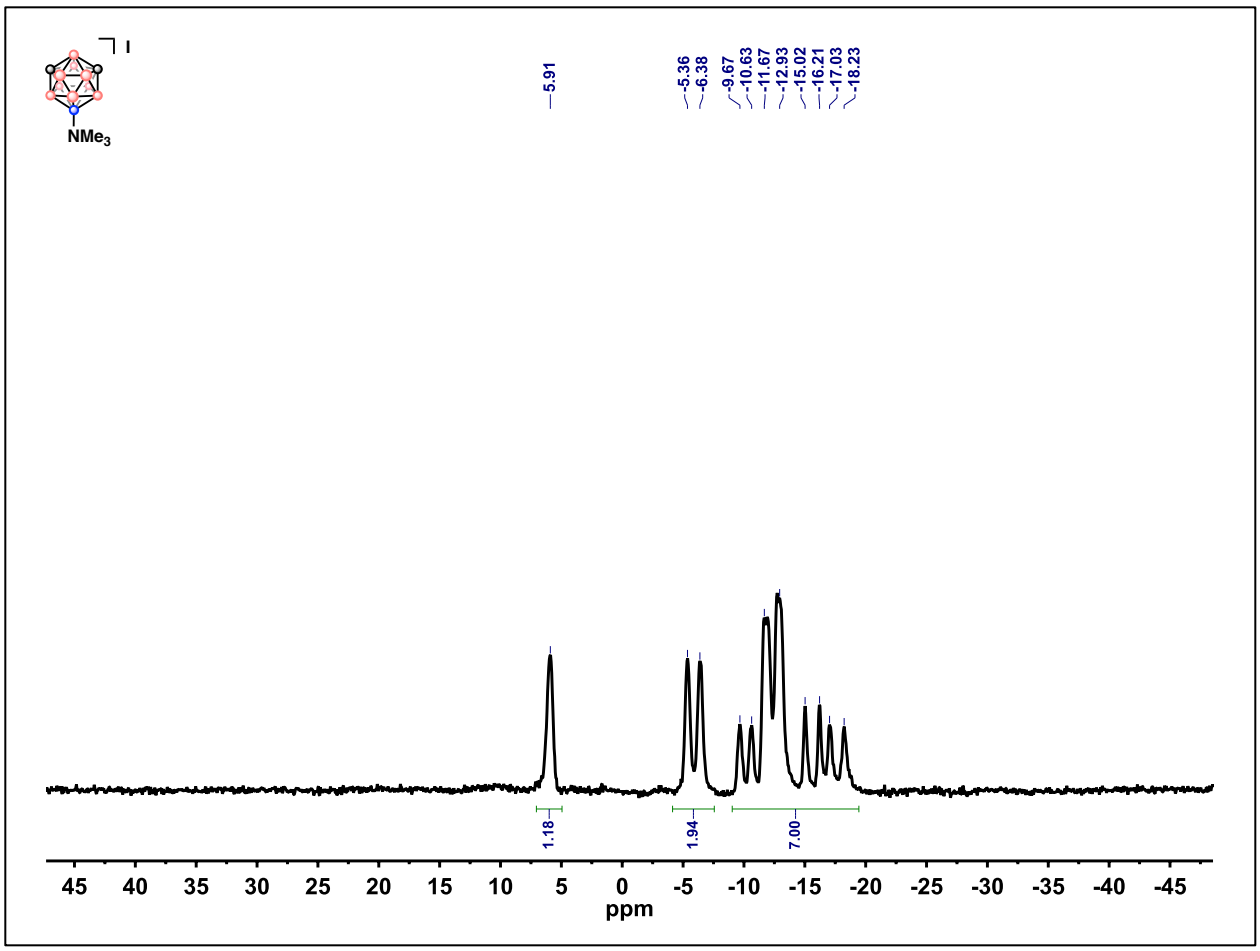
^{11}B NMR Compound **2** (baseline corrected)



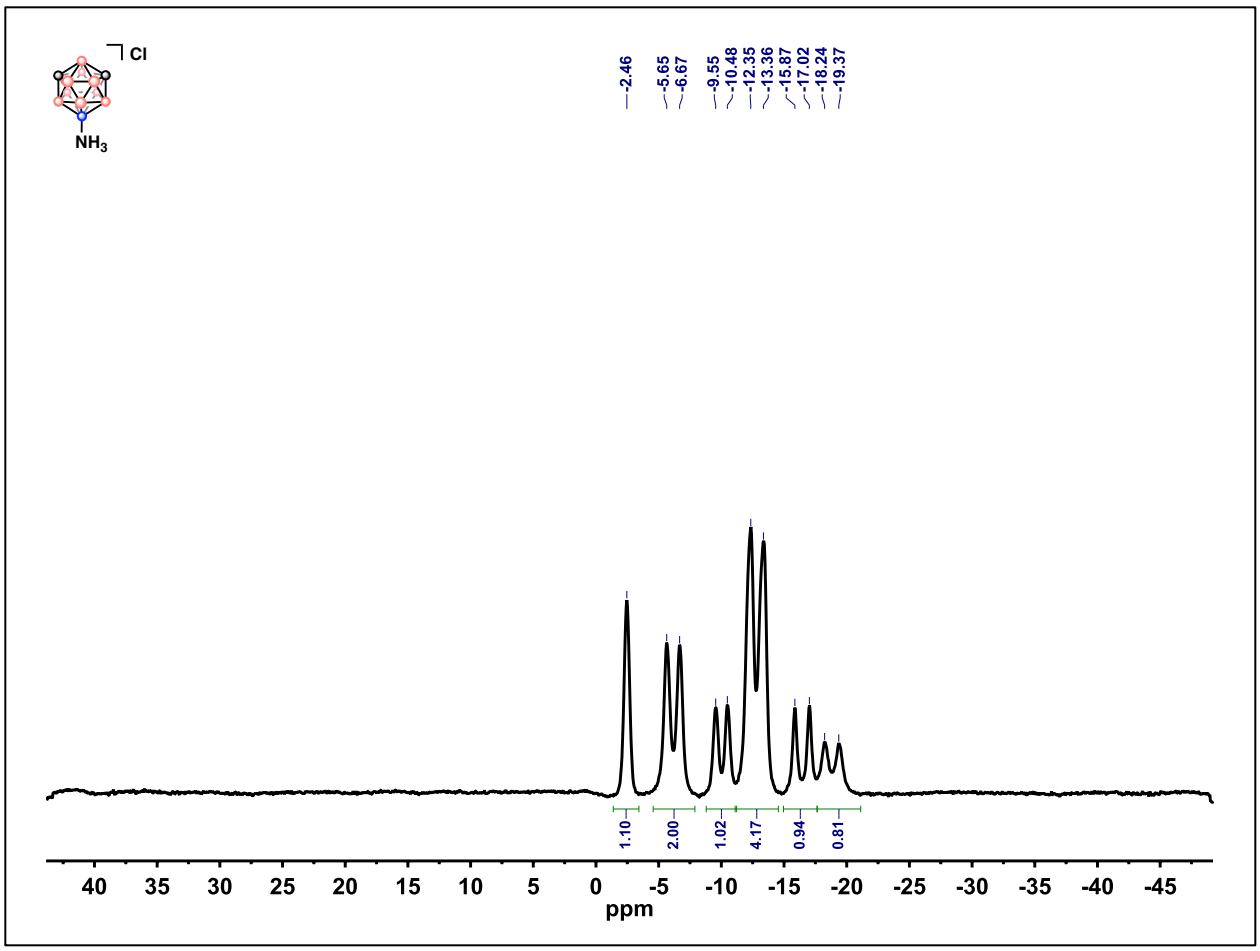
^{11}B NMR Compound **4** (baseline corrected)



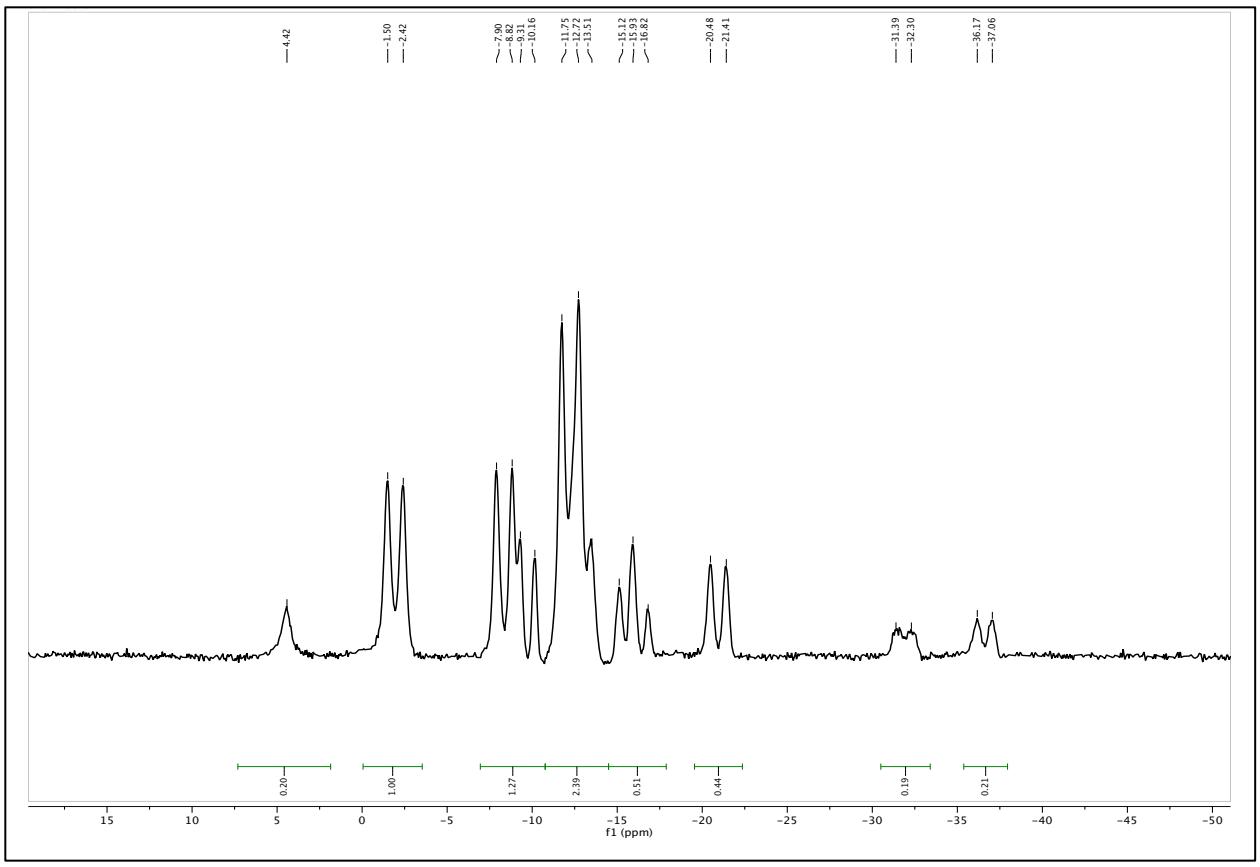
^{11}B NMR Compound **5** (baseline corrected)



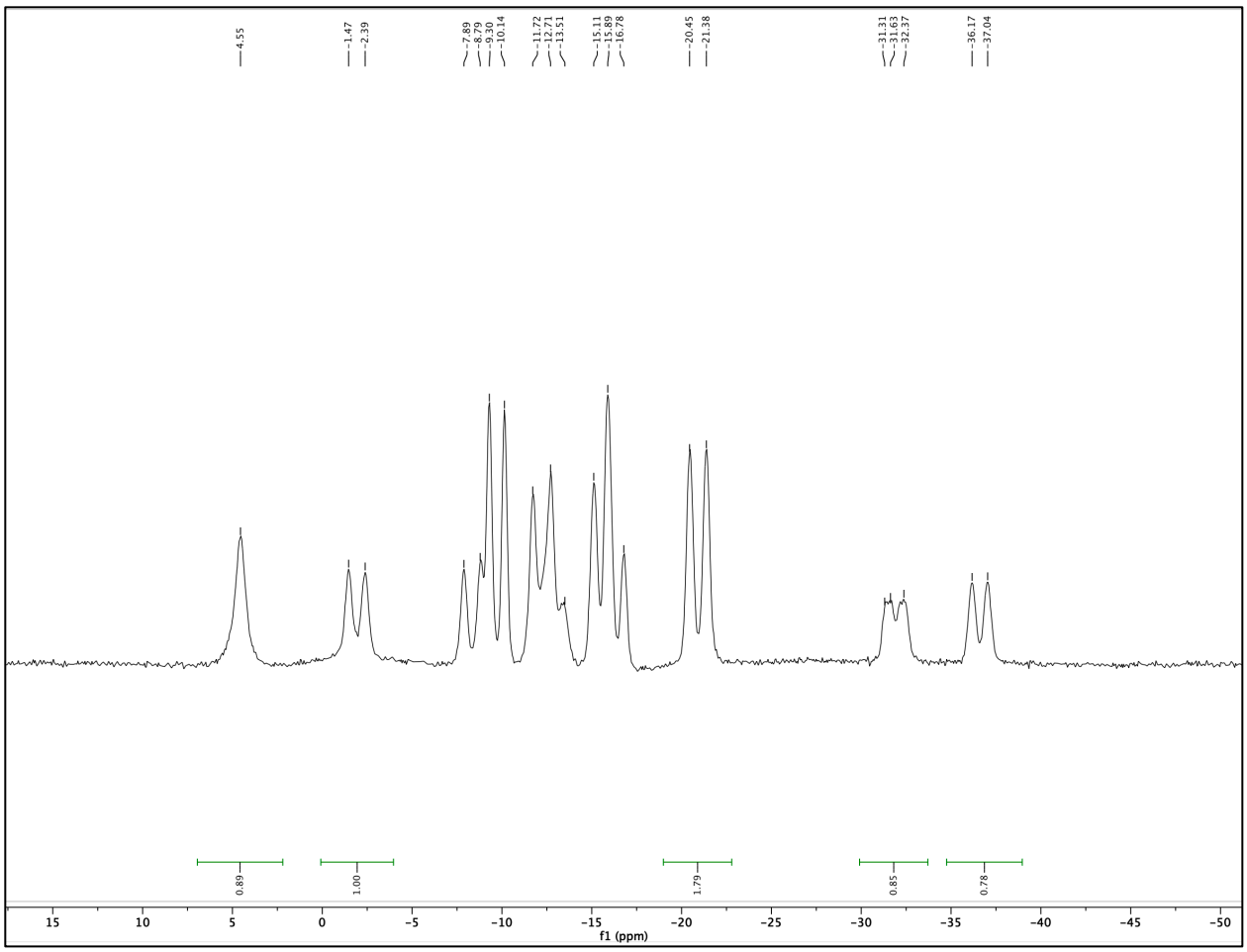
^{11}B NMR Compound **7** (baseline corrected)



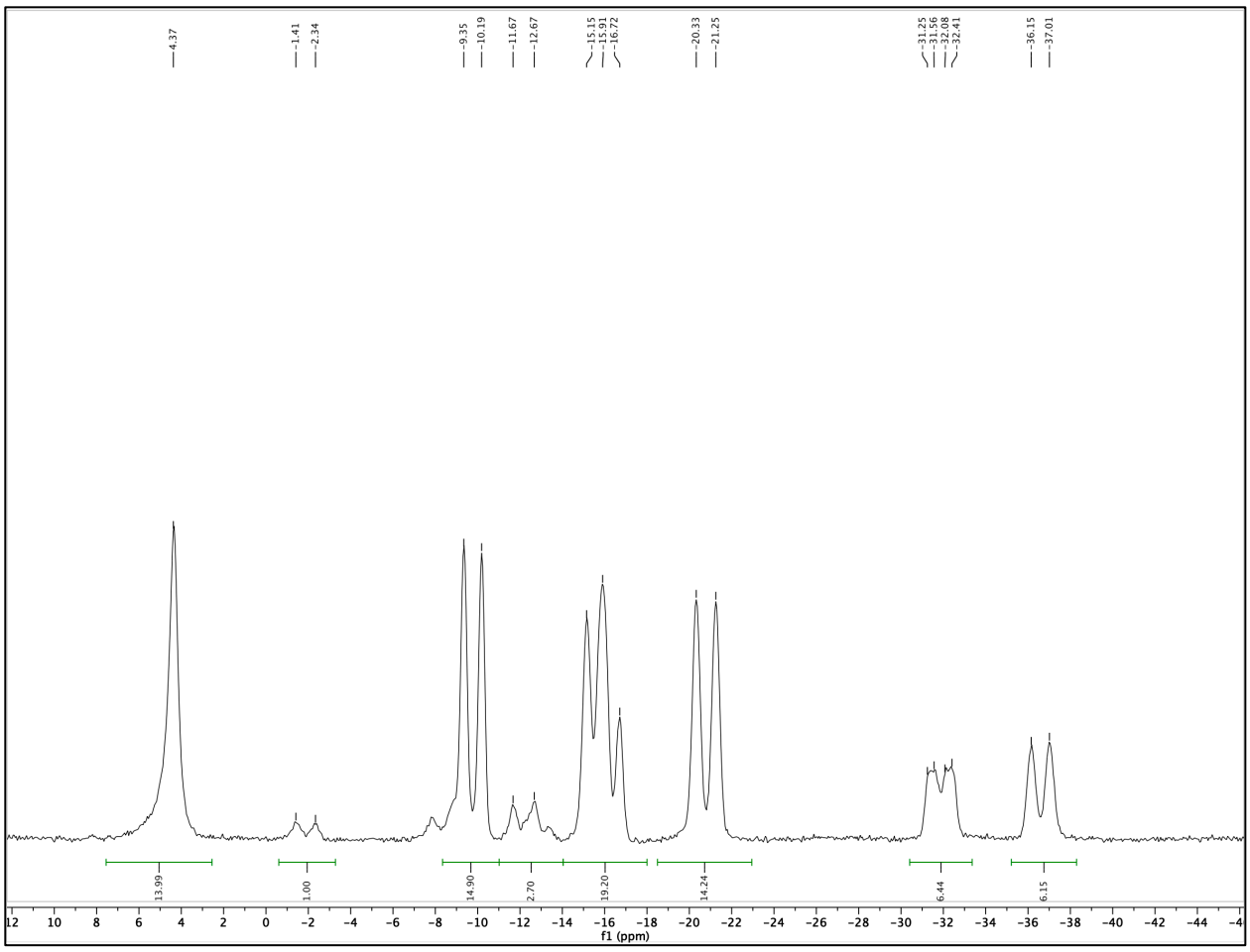
^{11}B NMR Compound **8** (baseline corrected)



^{11}B NMR spectra of **CB[7]•9** after 2h incubation at 60 ^{o}C with methylamine (1M THF)

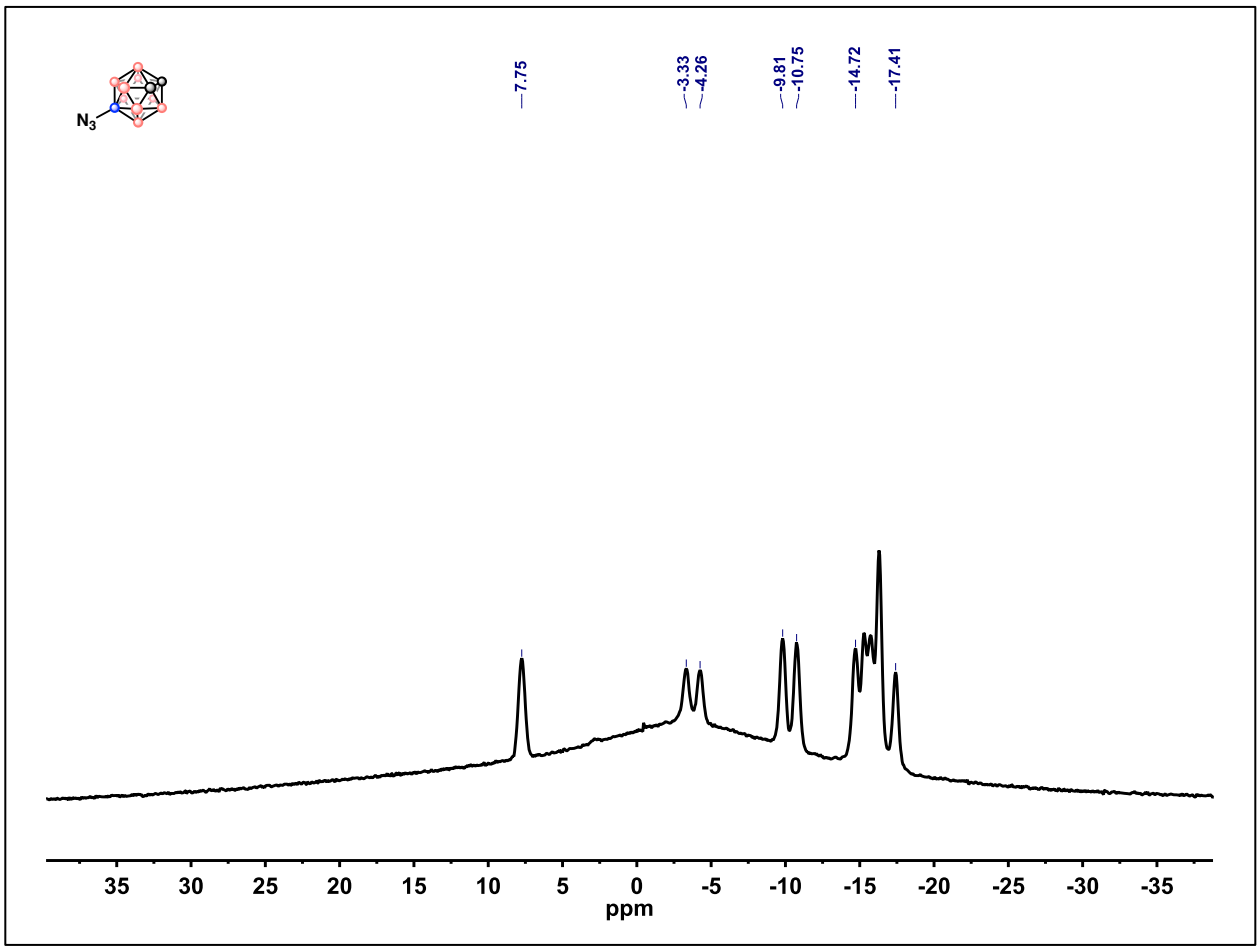


^{11}B NMR spectra of **CB[7]•9** after 8h incubation at 60 ^{o}C with methylamine (1M THF)

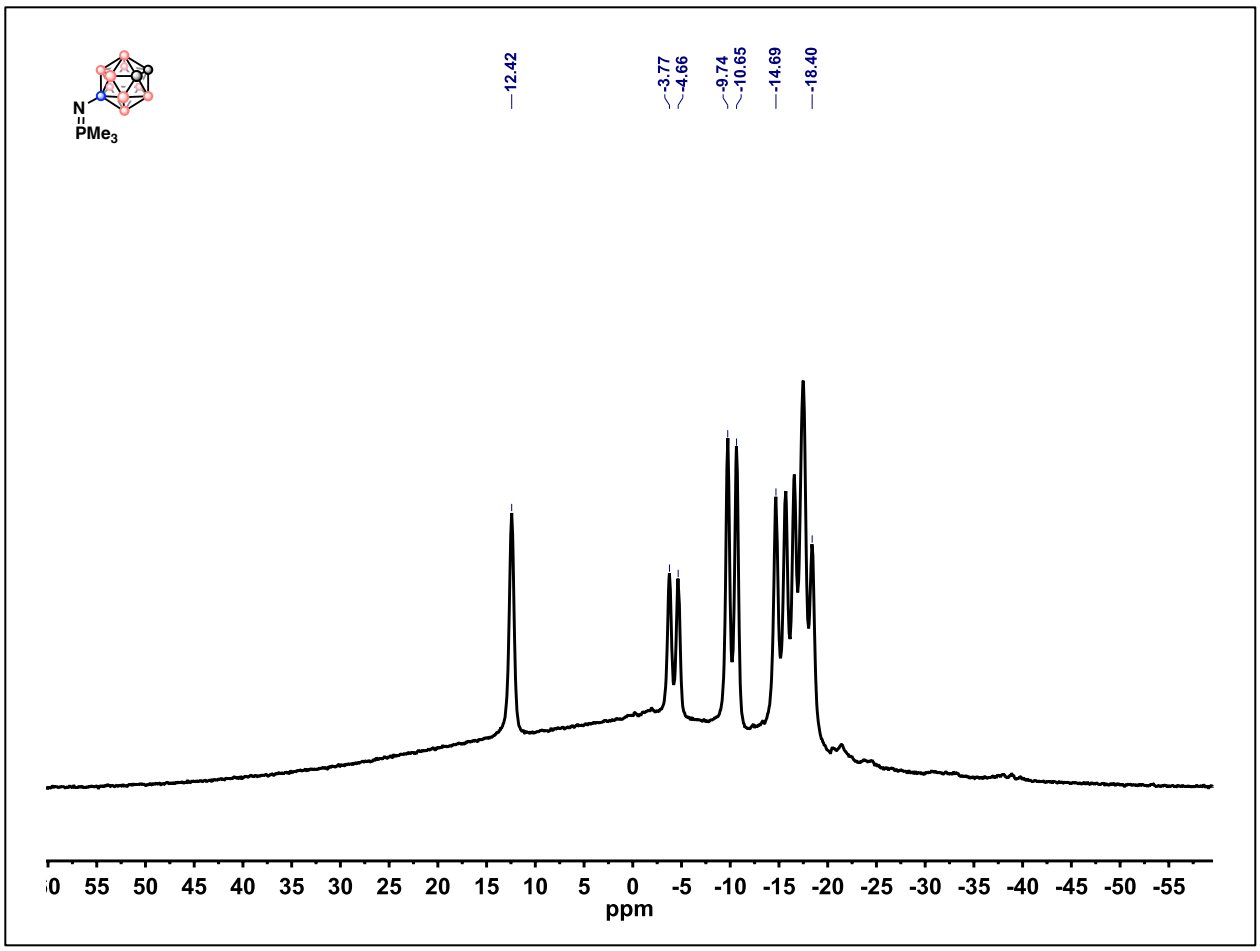


^{11}B NMR spectra of **CB[7]•9** after 24h incubation at 60 ºC with methylamine (1M THF)

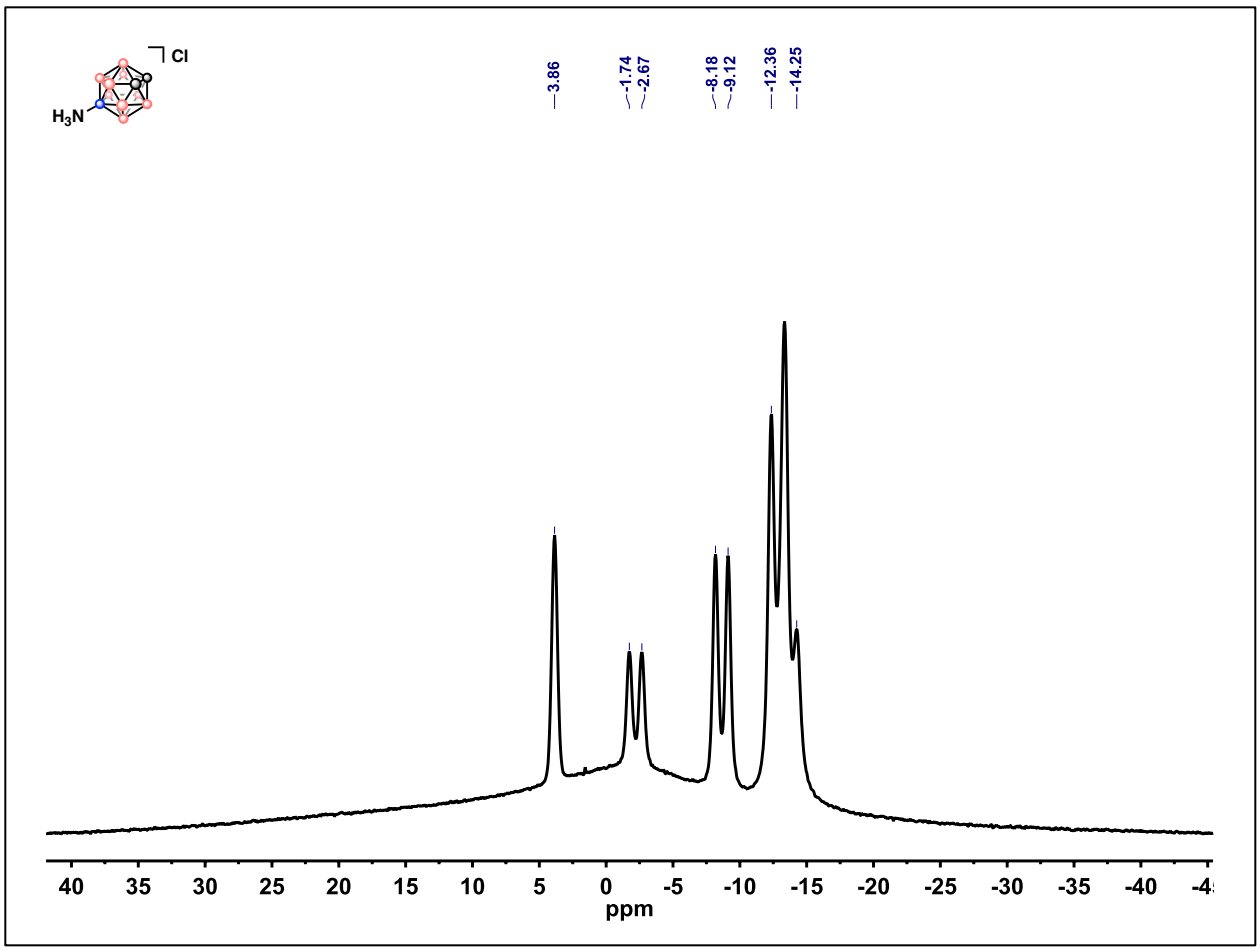
Raw Spectra



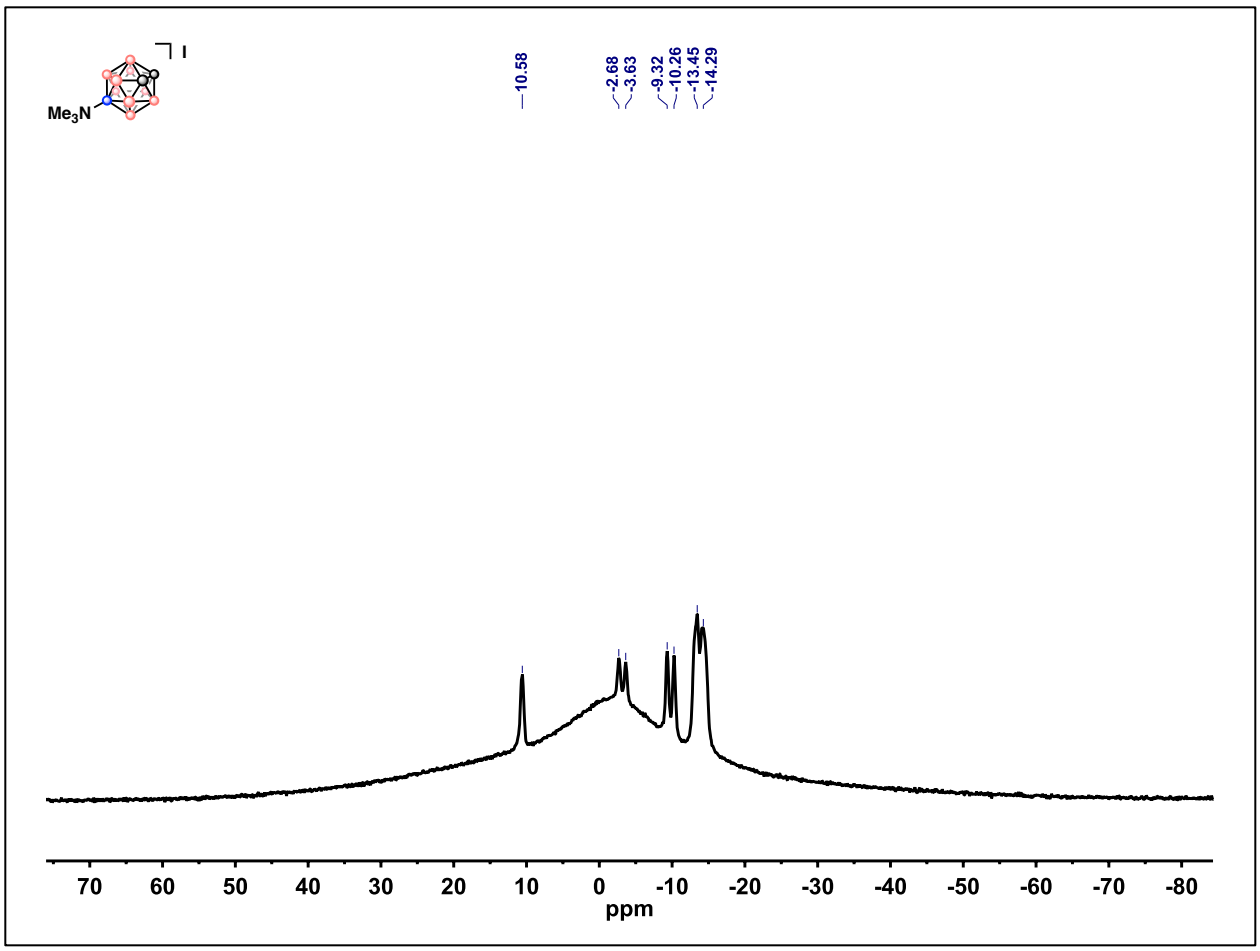
^{11}B NMR Compound **2**



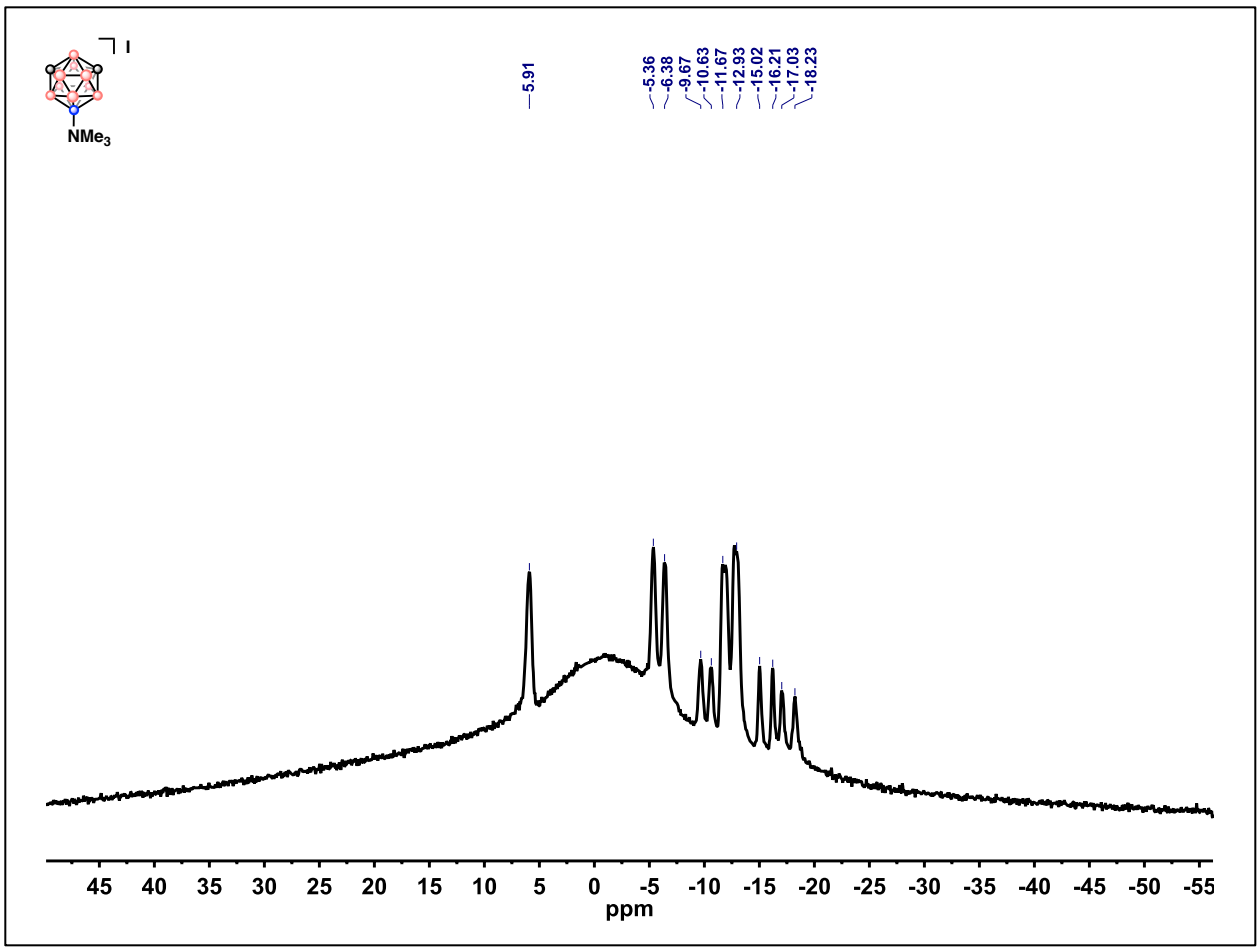
^{11}B NMR Compound **3**



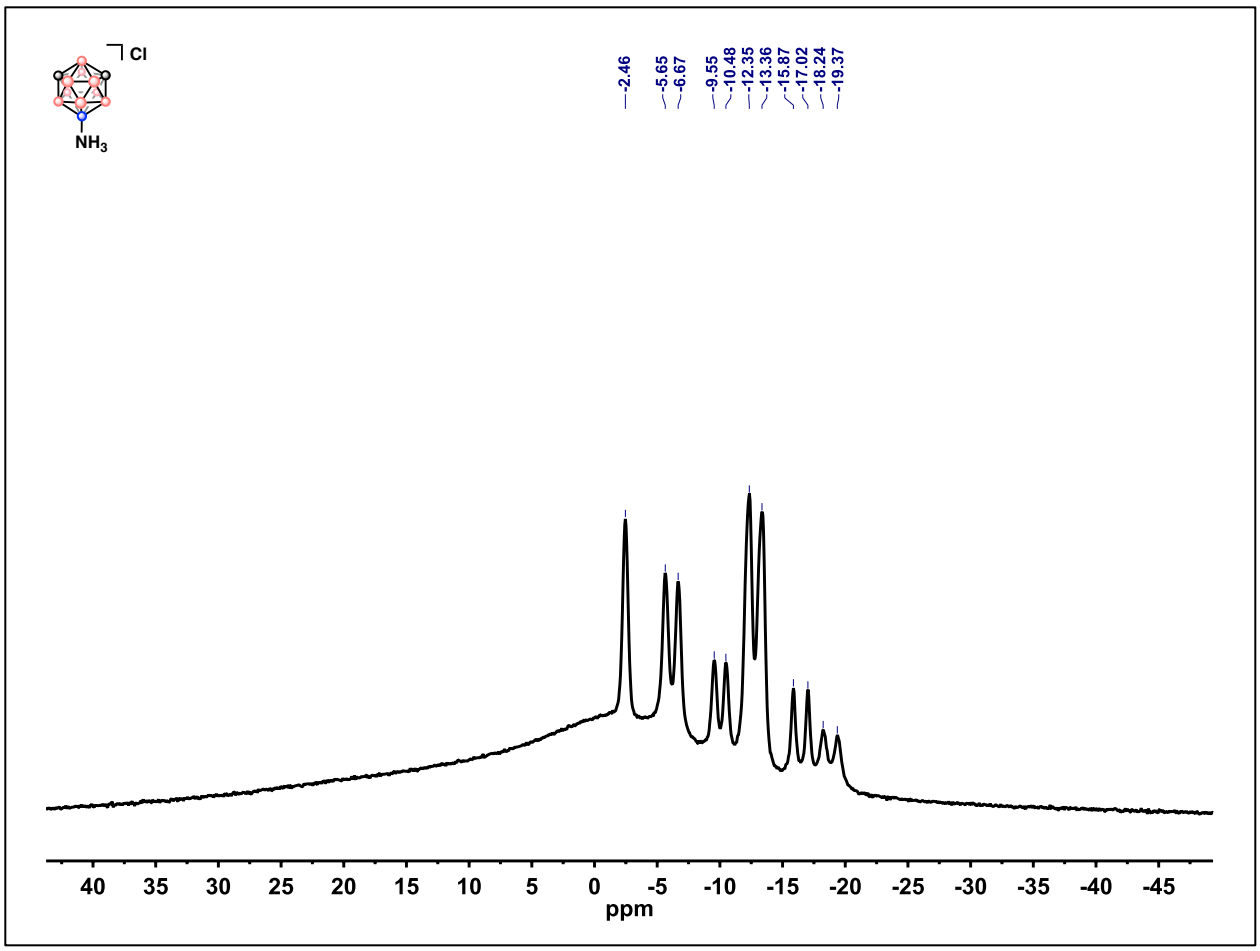
^{11}B NMR Compound **4**



^{11}B NMR Compound **5**

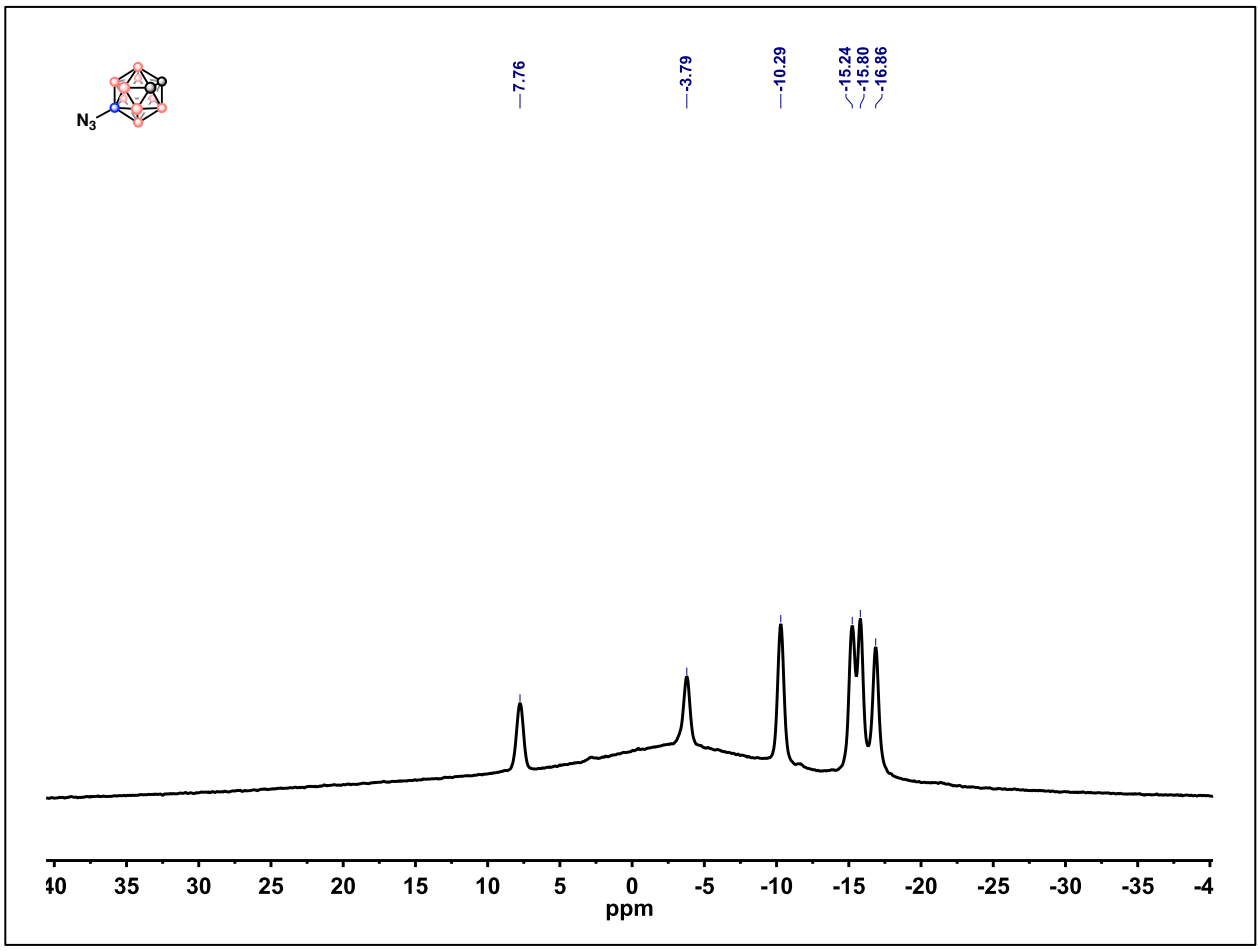


^{11}B NMR Compound **7**

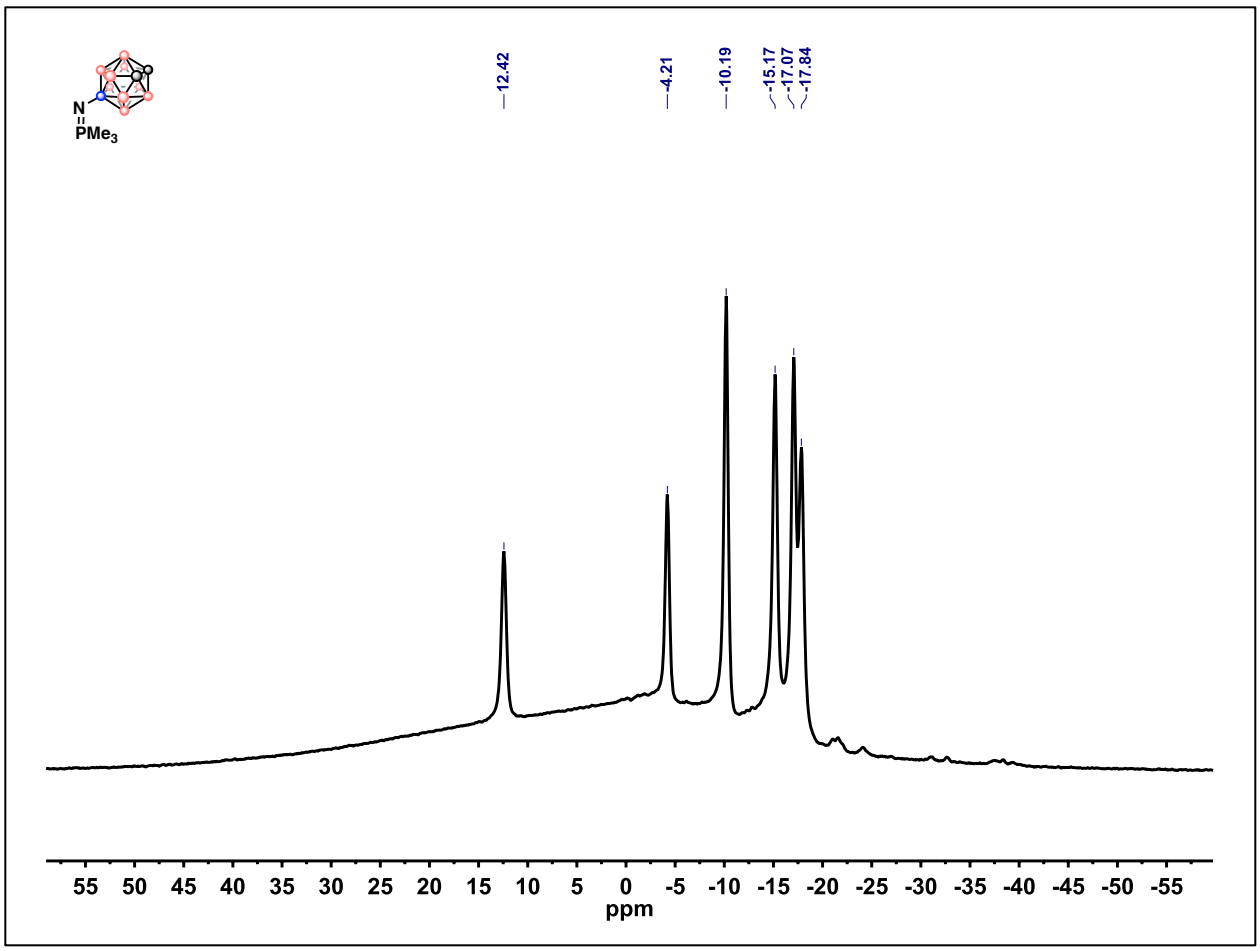


^{11}B NMR Compound **8**

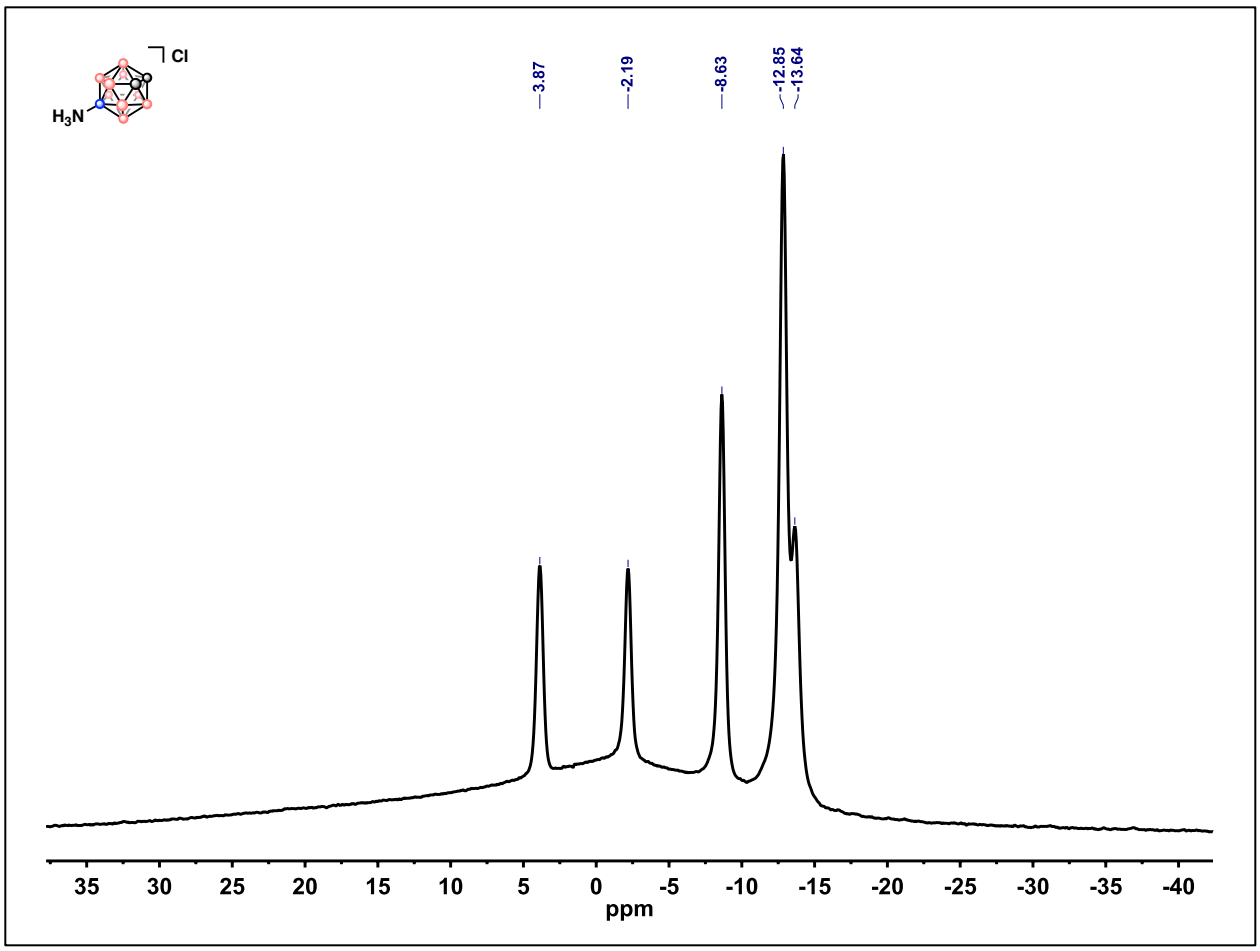
Raw Spectra. Without 5 sec delay



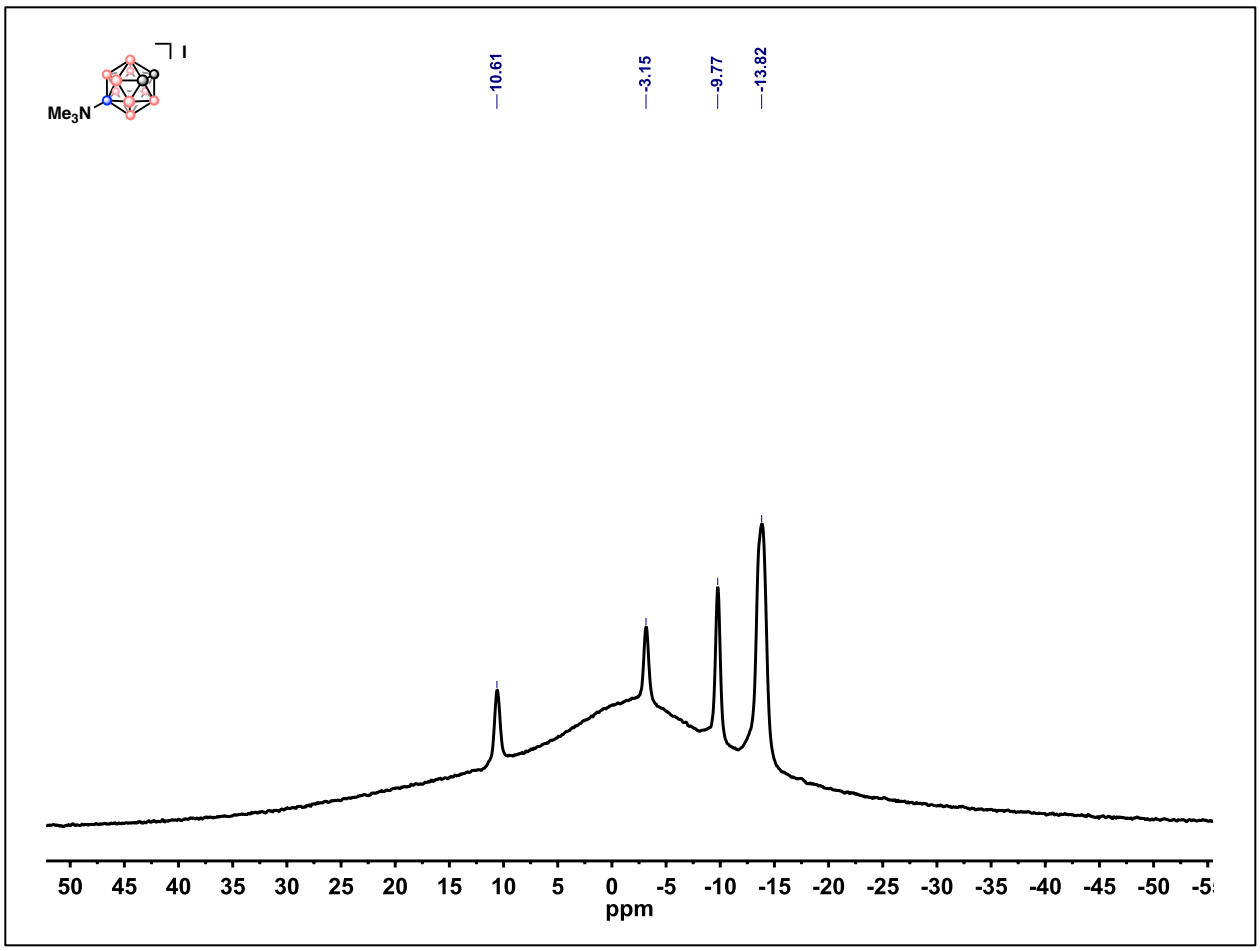
^{11}B NMR Compound **2** (without 5 sec delay)



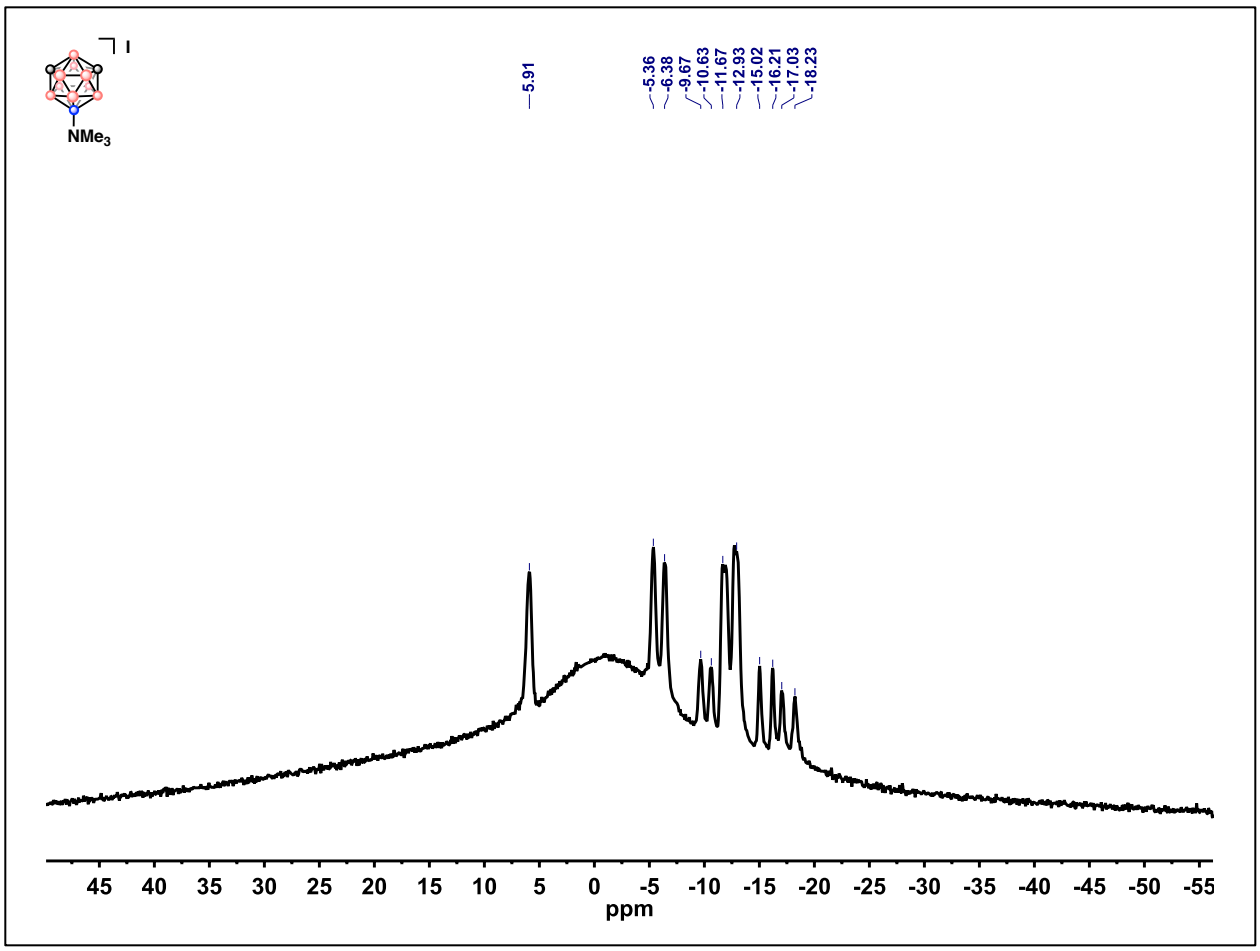
^{11}B NMR Compound **3** (without 5 sec delay)



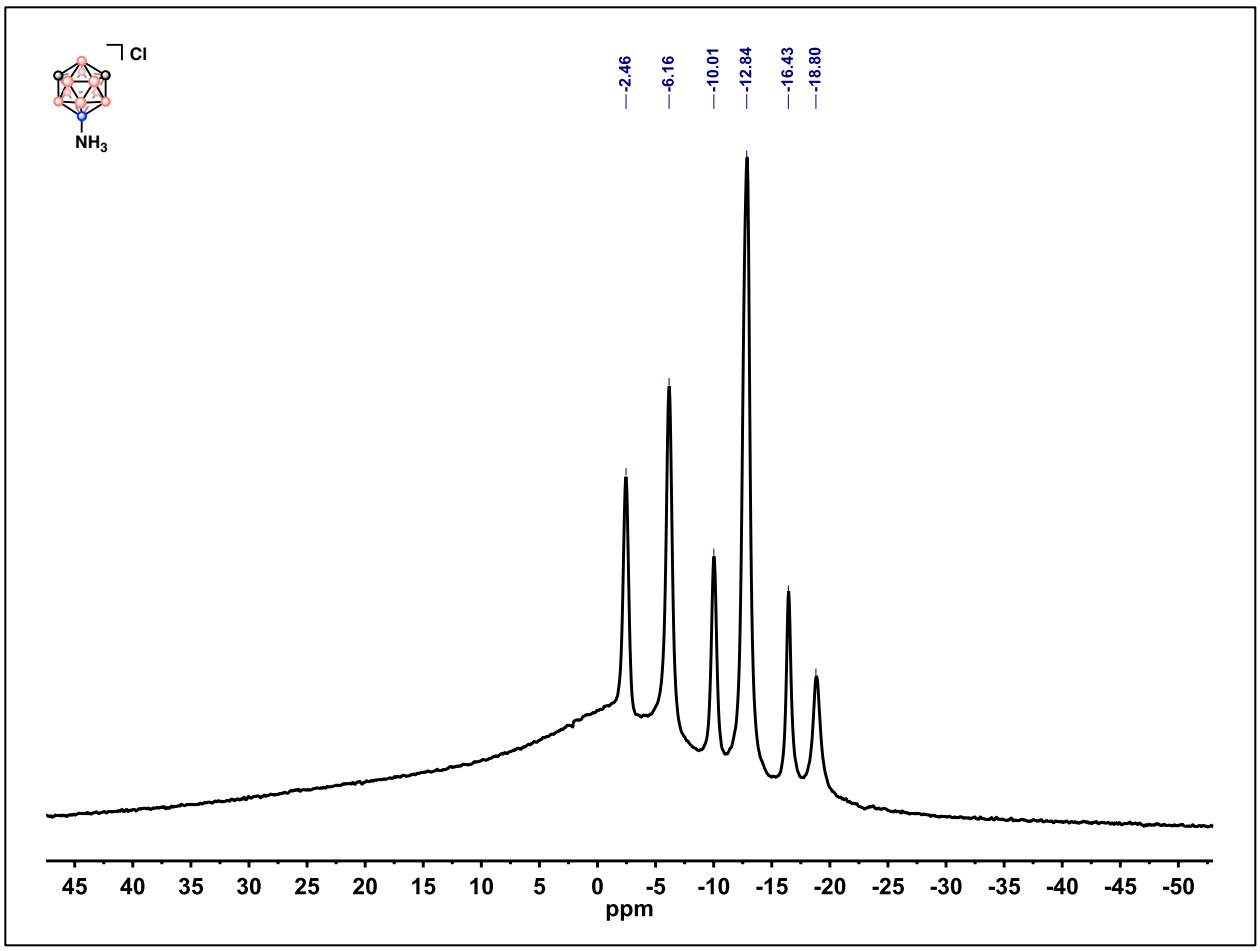
^{11}B NMR Compound **4** (without 5 sec delay)



^{11}B NMR Compound **5** (without 5 sec delay)

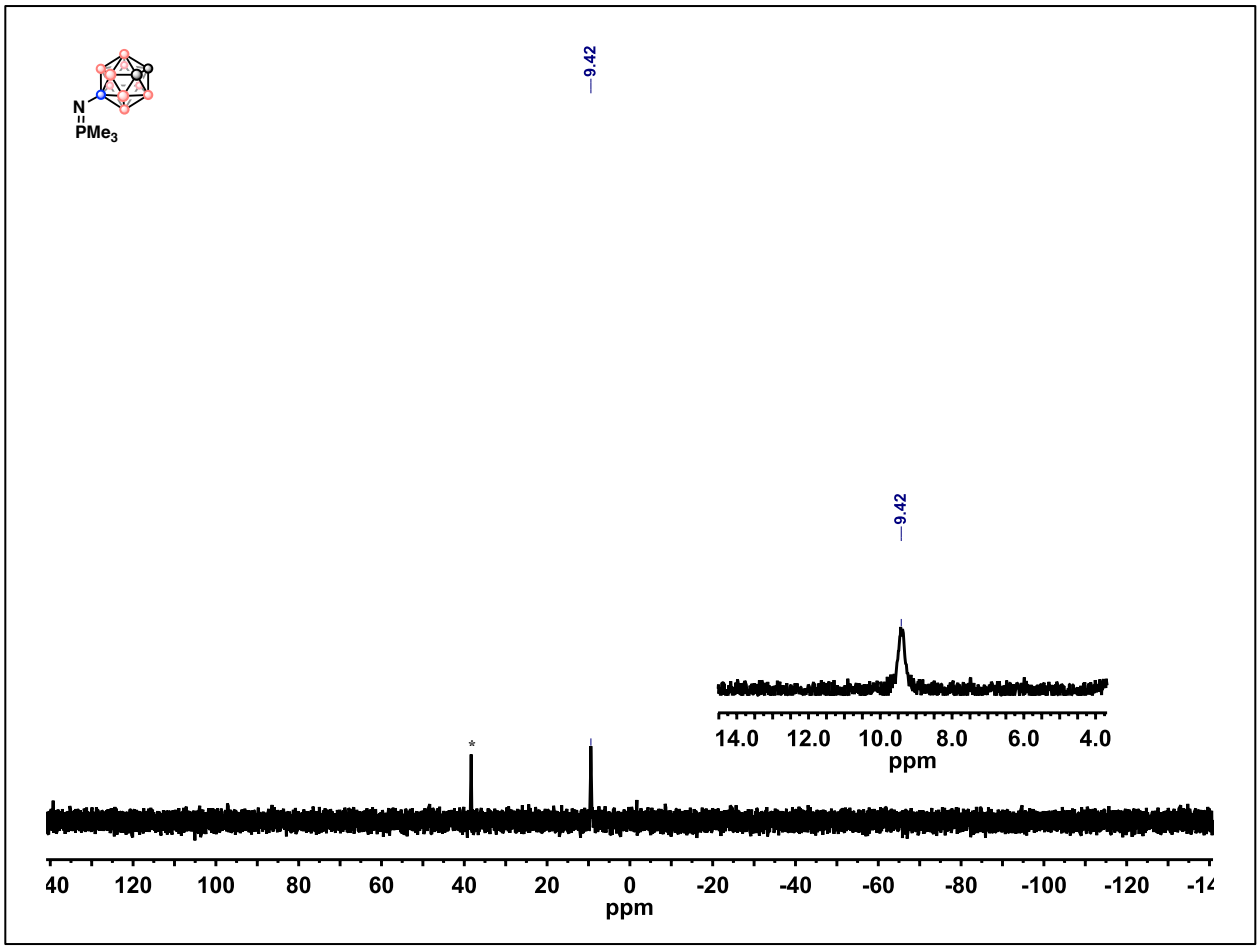


^{11}B NMR Compound **7** (without 5 sec delay)



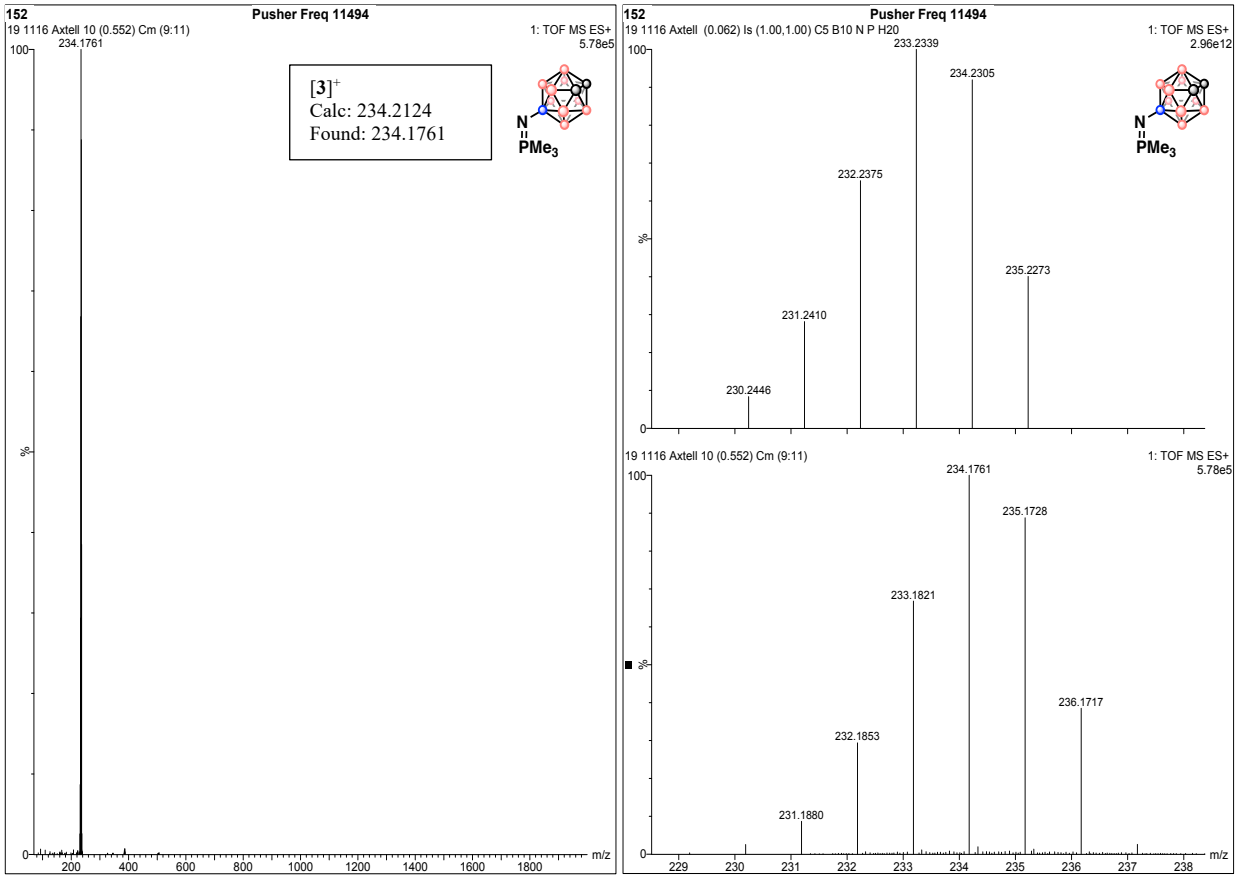
^{11}B NMR Compound **8** (without 5 sec delay)

^{31}P NMR Spectra

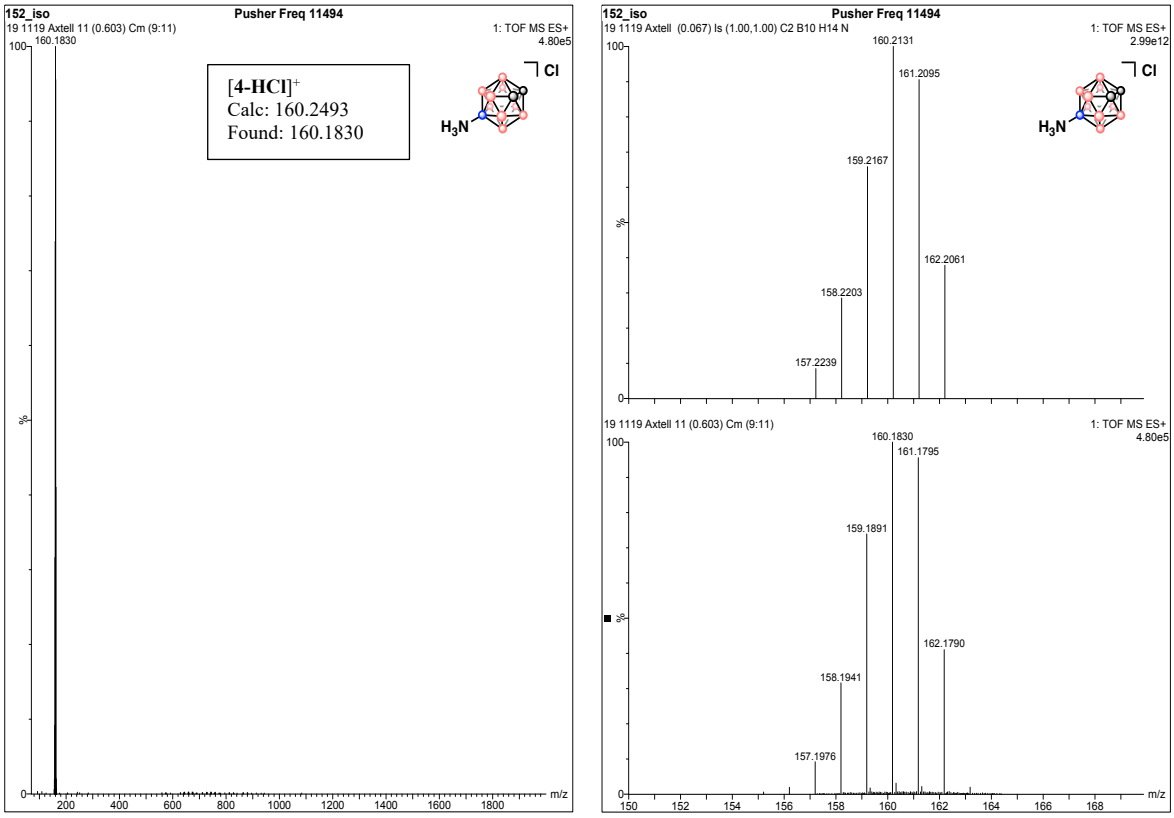


^{31}P NMR Compound **3:** Unidentified peak at 40ppm that is hypothesized to be an oxidized side-product of the reaction that upon reduction to the amine to produce **4** is removed by acetone washes.

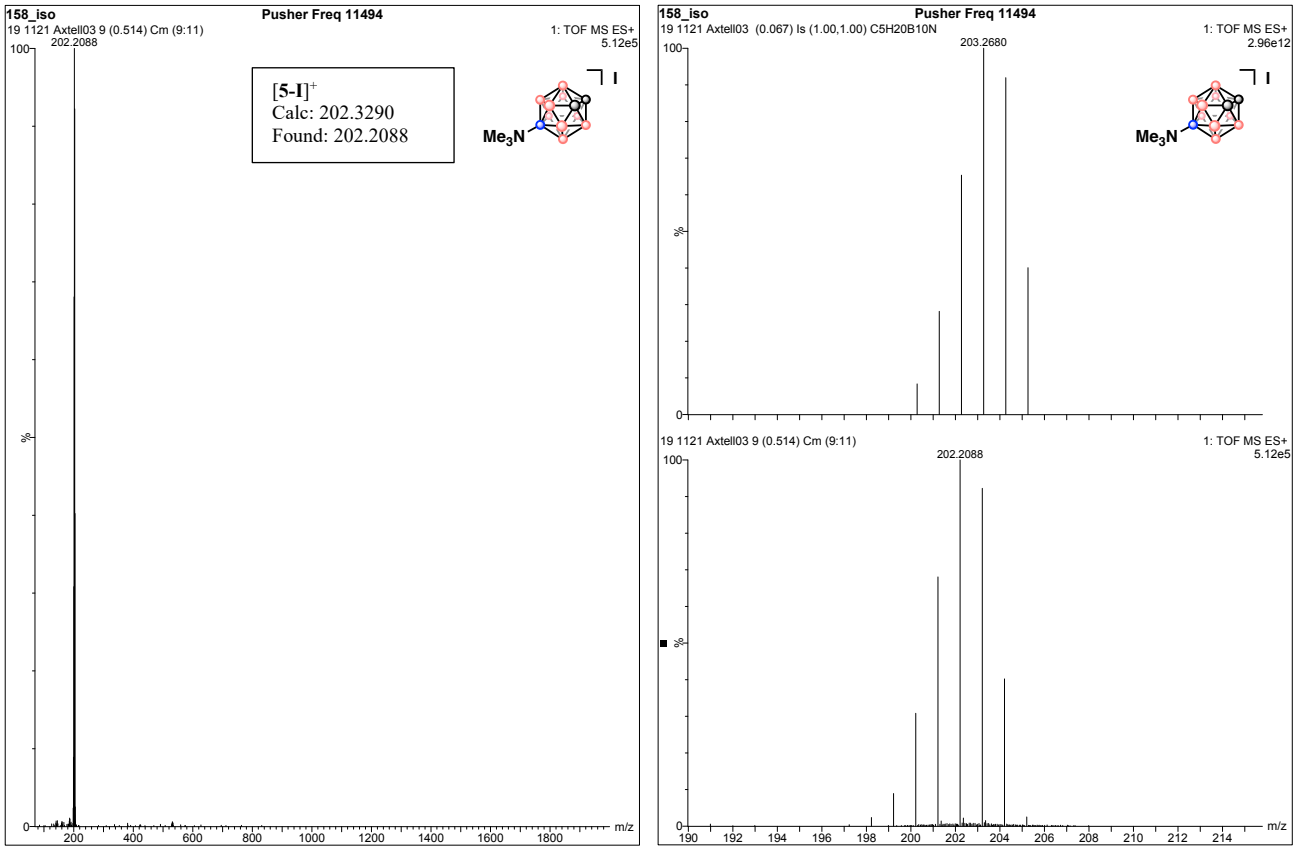
Mass Spectra (High Res GCMS)



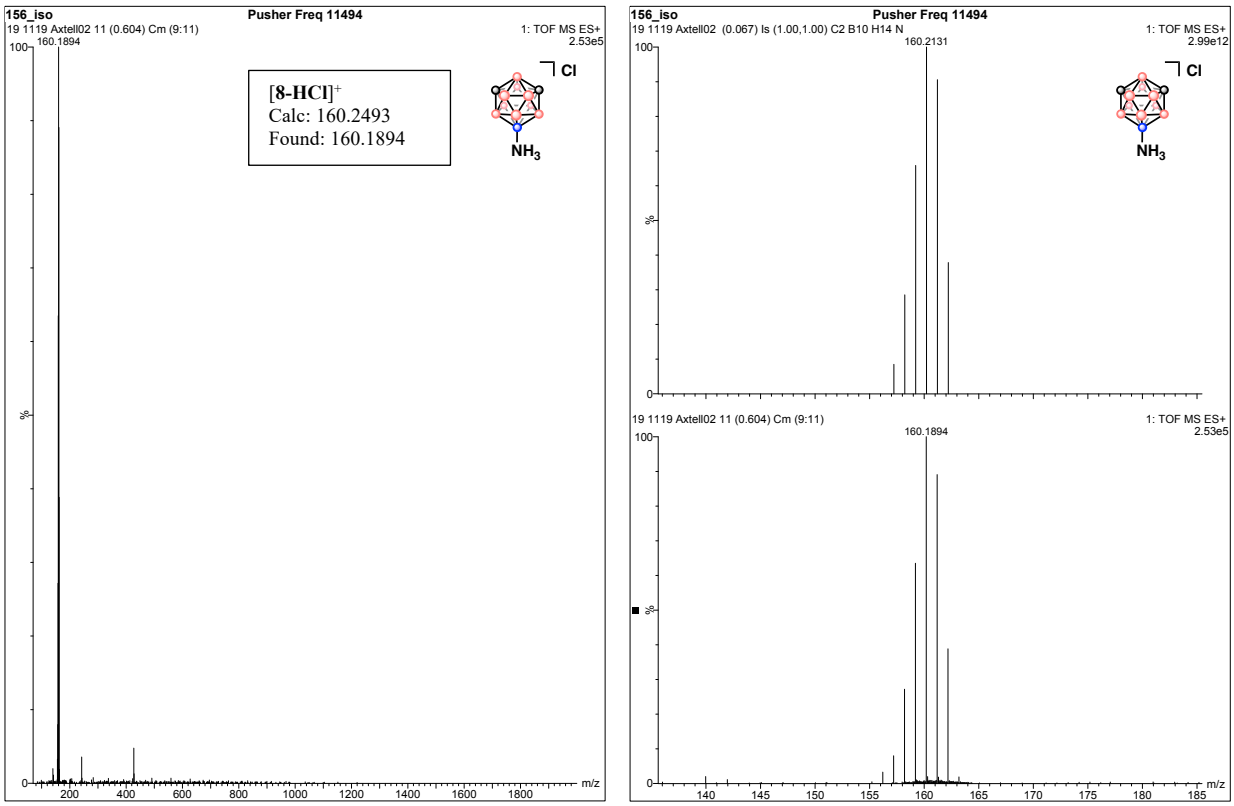
GCMS (EI) of compound **3**



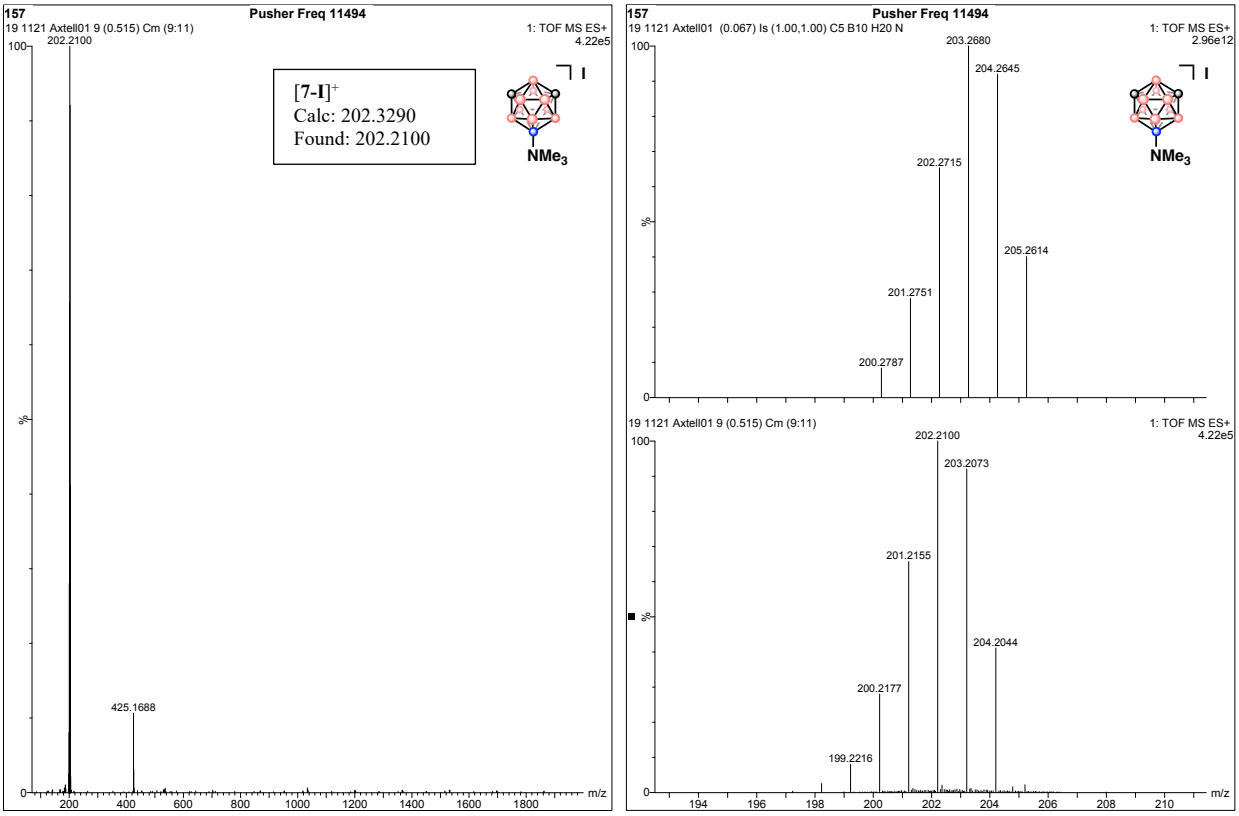
GCMS (EI) of compound **4**



GCMS (EI) of compound **5**

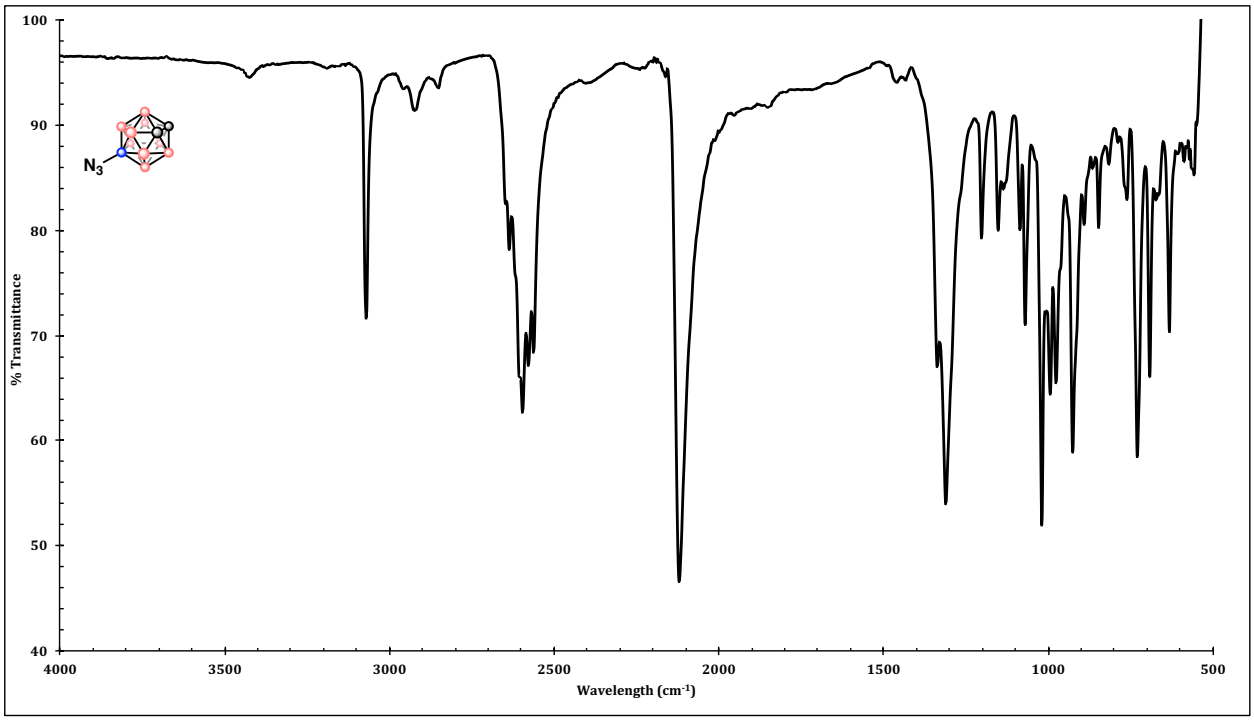


GCMS (EI) of compound **8**



GCMS (EI) of compound **7**

IR Spectra



IR spectrum Compound **2**

X-ray Crystallographic Data

The single crystal X-ray diffraction studies were carried out on a Bruker SMART APEX II CCD diffractometer equipped with Cu K_α radiation (λ = 1.54178). Crystals of the subject compound were used as received (grown from acetone). A 0.300 x 0.130 x 0.050 mm colorless plate crystal was mounted on a Cryoloop with Paratone-N oil.

Data were collected in a nitrogen gas stream at 100(2) K using ω and φ scans. Crystal-to-detector distance was 40 mm using exposure times of 2, 13, 14 and 30 seconds (depending on the 2θ position) with a scan width of 1.40°. Data collection was 100.0 % complete to 67.679° in θ. A total of 60118 reflections were collected. 7424 reflections were found to be symmetry independent, with an R_{int} of 0.0446. Indexing and unit cell refinement indicated a **Primitive Monoclinic** lattice. The space group was found to be ***P2$_1$/n***. The data were integrated using the Bruker SAINT Software program and scaled using the SADABS software program. Solution by direct methods (SHELXT) produced a complete phasing model consistent with the proposed structure.

All non-hydrogen atoms were refined anisotropically by full-matrix least-squares (SHELXL-2014). The positions for all C-**H** and B-**H** hydrogen atoms were located in the electron density map. The C-**H** and B-**H** distances were restrained to 1.00 Å using the DFIX command in SHELXL-2014. The B-**H** and C-**H** hydrogen atom isotropic displacement parameters were fixed to ride at 1.2X the equivalent value for their parent atoms. The N-**H** hydrogen atoms were placed in calculated positions using a riding model (AFIX 137).

Notes: Excellent data and refinement. In the initial refinement electron density from disordered acetone solvent molecules and a weaker unidentified peak (most likely from disordered water) were found. Platon Squeeze was used in the final refinement to remove the disordered solvent (125 e^-/unit cell) and to obtain a better model. The asymmetric unit from the final refinement consists of three independent carborane molecules and 3 Cl^- counterions. The figure below shows one cation of the asymmetric unit.

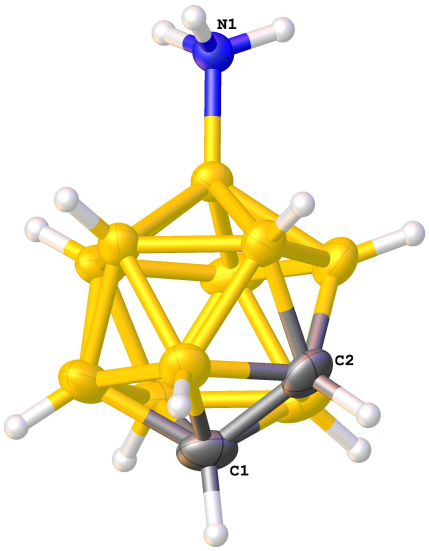


Table 1. Crystal data and structure refinement for **4**.

CDCC Deposition #	2026553
Report date	2019-11-21

Identification code	Spok148_sq	
Empirical formula	C2 H14 B10 Cl N	
Formula weight	195.69	
Temperature	100.0 K	
Wavelength	1.54178 Å	
Crystal system	Monoclinic	
Space group	P 1 21/n 1	
Unit cell dimensions	a = 13.1320(3) Å	α = 90°.
	b = 13.0203(3) Å	β = 90.227(2)°.
	c = 22.5419(6) Å	γ = 90°.
Volume	3854.24(16) $Å^3$	
Z	12	
Density (calculated)	1.012 Mg/m^3	
Absorption coefficient	2.185 mm^{-1}	
F(000)	1200	
Crystal size	0.3 x 0.13 x 0.05 mm^3	
Theta range for data collection	3.889 to 71.214°.	
Index ranges	-16<=h<=16, -15<=k<=15, -27<=l<=27	
Reflections collected	60118	
Independent reflections	7424 [R(int) = 0.0446]	
Completeness to theta = 67.679°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7535 and 0.5966	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	7424 / 33 / 482	
Goodness-of-fit on F^2	1.096	
Final R indices [I>2sigma(I)]	R1 = 0.0447, wR2 = 0.1106	
R indices (all data)	R1 = 0.0487, wR2 = 0.1133	
Extinction coefficient	n/a	
Largest diff. peak and hole	0.511 and -0.227 $e.Å^{-3}$	

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for Spok148_sq. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
Cl(1)	2672(1)	4083(1)	5253(1)	29(1)
Cl(2)	6064(1)	2906(1)	3977(1)	25(1)
Cl(3)	5878(1)	3887(1)	6360(1)	28(1)
N(1)	3803(1)	3757(1)	4022(1)	24(1)
C(1)	1781(2)	1771(2)	2724(1)	45(1)
C(2)	2620(2)	2561(2)	2481(1)	40(1)
B(1)	3143(2)	3122(2)	3600(1)	26(1)
B(2)	2720(2)	3621(2)	2915(1)	39(1)
B(3)	3655(2)	2632(2)	2933(1)	32(1)
B(4)	3364(2)	1775(2)	3520(1)	32(1)
B(5)	2238(2)	2240(2)	3870(1)	37(1)
B(6)	1834(2)	3388(2)	3503(1)	43(1)
B(7)	3047(2)	1443(2)	2786(1)	39(1)
B(8)	2162(2)	1210(2)	3361(1)	44(1)
B(9)	1222(2)	2197(3)	3351(1)	49(1)
B(10)	1516(2)	3055(3)	2761(1)	51(1)
N(1")	3655(1)	4794(1)	6477(1)	24(1)
C(1")	2133(2)	4419(2)	8366(1)	32(1)
C(2")	2253(2)	3469(2)	7912(1)	34(1)
B(1")	3169(2)	4674(2)	7090(1)	22(1)
B(2")	2137(2)	3829(2)	7199(1)	42(1)
B(3")	3339(2)	3542(2)	7517(1)	31(1)
B(4")	3916(2)	4690(2)	7755(1)	31(1)
B(5")	3070(2)	5711(2)	7588(1)	41(1)
B(6")	1955(2)	5186(3)	7240(1)	48(1)
B(7")	3312(2)	3887(2)	8274(1)	32(1)
B(8")	3135(2)	5221(2)	8318(1)	42(1)
B(9")	1941(3)	5532(2)	8002(1)	56(1)
B(10")	1352(2)	4376(3)	7758(1)	54(1)
N(1')	7120(1)	3573(1)	5172(1)	27(1)
C(1')	10385(2)	2207(2)	5586(1)	39(1)

C(2')	10196(2)	3128(2)	5118(1)	33(1)
B(1')	8156(2)	3092(2)	5311(1)	25(1)
B(2')	9089(2)	2997(2)	4745(1)	28(1)
B(3')	9239(2)	3898(2)	5338(1)	30(1)
B(4')	8777(2)	3332(2)	6002(1)	31(1)
B(5')	8345(2)	2072(2)	5823(1)	34(1)
B(6')	8528(2)	1859(2)	5043(1)	34(1)
B(7')	10098(2)	3399(2)	5863(1)	39(1)
B(8')	9558(2)	2262(2)	6160(1)	41(1)
B(9')	9409(2)	1355(2)	5576(1)	42(1)
B(10')	9852(2)	1908(2)	4905(1)	35(1)

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