Halogen Bonding Organocatalysis Enhanced through Intramolecular Hydrogen Bonds

Asia Marie S. Riel, Daniel A. Decato, Jiyu Sun and Orion B. Berryman*

*Department of Chemistry and Biochemistry, University of Montana, 32 Campus Drive,
Missoula, Montana, United States, 59812

Table of Contents

General Methods

All reagents were obtained from commercial sources and were used without further purification unless otherwise noted. Thin layer chromatography (TLC) was performed using normal-phase silica gel glass-backed plates (0.25 mm, F-254, SiliCycle) and observed under UV light. Flash column chromatography was performed using normal-phase silica gel (230–400 mesh, SiliaFlash®P60, SiliCycle). Activated molecular sieves were used when anhydrous solvents were required. All compounds were dried in vacuo at room temperature as needed. High-resolution mass spectrometry was carried out using an Agilent 6520 Accurate-Mass Q-TOF LC/MS. Nuclear magnetic resonance (NMR) spectra were obtained with a VNMRS Varian 500 MHz or a Bruker Avance 400 MHz or an Agilent 400 MHz spectrometer. Chemical shifts are reported in parts per million (ppm) from high to low frequency using the residual solvent peak as the internal reference ($CHCl_3$= 7.26 ppm). For the ^{19}F NMR spectra hexafluorobenzene C_6F_6 (δ –164.9 ppm) was used as an internal standard. Signal splitting patterns are indicated as s, singlet; d, doublet; t, triplet; m, multiplet, b, broad. Coupling constants (J) are given in Hz. Catalyst **3** and **H3** were prepared as previously reported.[1]

Neutral scaffold synthesis of Catalyst 2

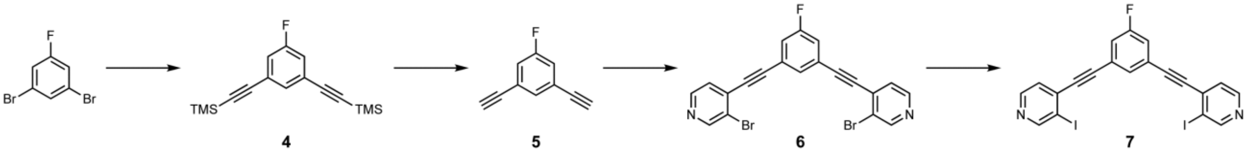


Figure S1. ChemDraw schematic of the neutral scaffold of catalyst **2**.

1-fluoro-3,5-bis((trimethylsilyl)ethynyl)benzene (4). An oven dried Schlenk flask was charged with bis(triphenylphosphine)palladium(II) dichloride (0.165 g, 0.236 mmol), vacuumed and backfilled with dry N_2 (3x). Copper (I) iodide (0.074 g, 0.393 mmol) was added, vacuumed, and backfilled with dry N_2 (3x). The dry reagents were dissolved in 60 mL dry dimethylformamide (DMF). 1,3-dibromo-5-fluorobenzene (0.495 mL, 3.93 mmol), N,N-diisopropylethylamine (3.48 mL, 20 mmol) and TMS-acetylene (1.59 mL, 9.84 mmol) were added to the DMF solution. The flask was carefully vacuumed and backfilled with dry N_2 (3x). The dark brown solution stirred overnight at room temperature. The reaction mixture was extracted with a mixture of 10% ethyl acetate/90% hexanes then washed with water to remove any excess salts and catalysts. Subsequent removal of ethyl acetate by rotary evaporation left a brown liquid **4** that was used directly in the next step with no purification. Molecule **4** spectra in accordance with previously reported.[2]

3,5-bisethynyl-1-fluorobenzene (5). 4 (1.1 g, 3.93 mmol) was dissolved in 50 mL methanol and 50 mL DCM in a 250 mL round bottom flask. Potassium carbonate (1.62 g, 11.8 mmol) was added to the organic mixture. The reaction stirred vigorously overnight at room temperature and reaction progress was monitored via TLC. Upon completion, water was added to quench the reaction. The crude product was extracted with ethyl acetate, dried over magnesium sulfate and gravity filtered. The organic mixture was reduced under vacuum and crude product remained a brown liquid (0.493 g, 87 % yield). Molecule **5** spectra in accordance with previously reported.[3]

3,5-bis(4-ethynyl-3-bromopyridinyl)-1-fluorobenzene (6). An oven dried Schlenk flask was charged with 3-bromo-4-iodopyridine (2.4 g, 8.55 mmol) then vacuumed and backfilled with dry N_2 gas (3x). Bis(triphenylphosphine)palladium (II) dichloride (0.143 g, 0.205 mmol) was added, vacuumed and backfilled with dry N_2 (3x). Copper (I) iodide (0.065 g, 0.342 mmol) was added, vacuumed and backfilled with dry N_2 (3x). The dry reagents were dissolved in 60 mL dry DMF. **5** (0.493 g, 3.42 mmol), N,N-diisopropylethylamine (3.0 mL, 17.1 mmol) were added to the DMF solution. The flask was carefully vacuumed and backfilled with dry N_2 (3x). The dark brown solution stirred overnight at room temperature. The reaction mixture was first run through a silica plug with a hexane/ethyl acetate solvent mixture (50:50) to remove any excess salts and catalysts. Subsequent removal of DMF, hexanes and ethyl acetate by roto-evaporation left and brown solid that was purified by column chromatography (gradient from 30% EtOAc/70% Hexanes to 50% EtOAc/50% Hexanes) to afford **6** (0.5897 g, 38%) as a dull yellow solid.

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.82 (s, 2H), 8.55-8.54 (d, J = 4.8 Hz, 2H), 7.62 (s, 1H), 7.45-7.44 (d, J = 4.8 Hz, 2H), 7.36-7.35 (d, J = 8.5 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 162.02 (d, J = 249.1 Hz), 151.62, 147.57, 132.41, 131.26, 126.62, 124.16 (d, J = 10.2 Hz), 123.16, 120.04 (d, J = 23.1 Hz), 95.85, 87.11.

^{19}F NMR (470 MHz, $CDCl_3$): δ (ppm) = –114.28 (t, J = 7.9 Hz, 1F).

HRMS (ESI pos) m/z for $C_{20}H_{10}Br_2FN_2^+$ [M+H]$^+$: calculated: 456.9169; found: 456.9114.

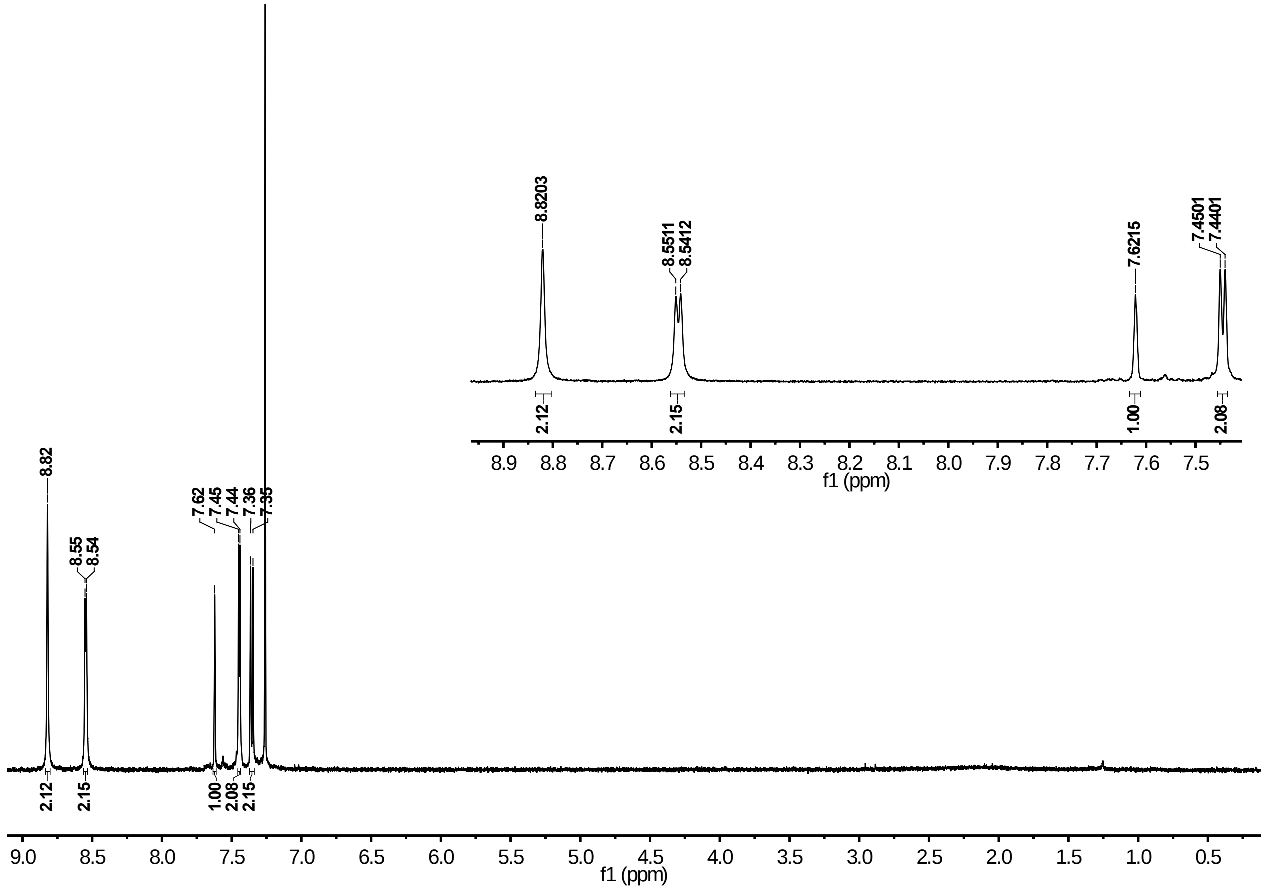


Figure S2. ^{1}H NMR of **6** (500 MHz, $CDCl_3$).

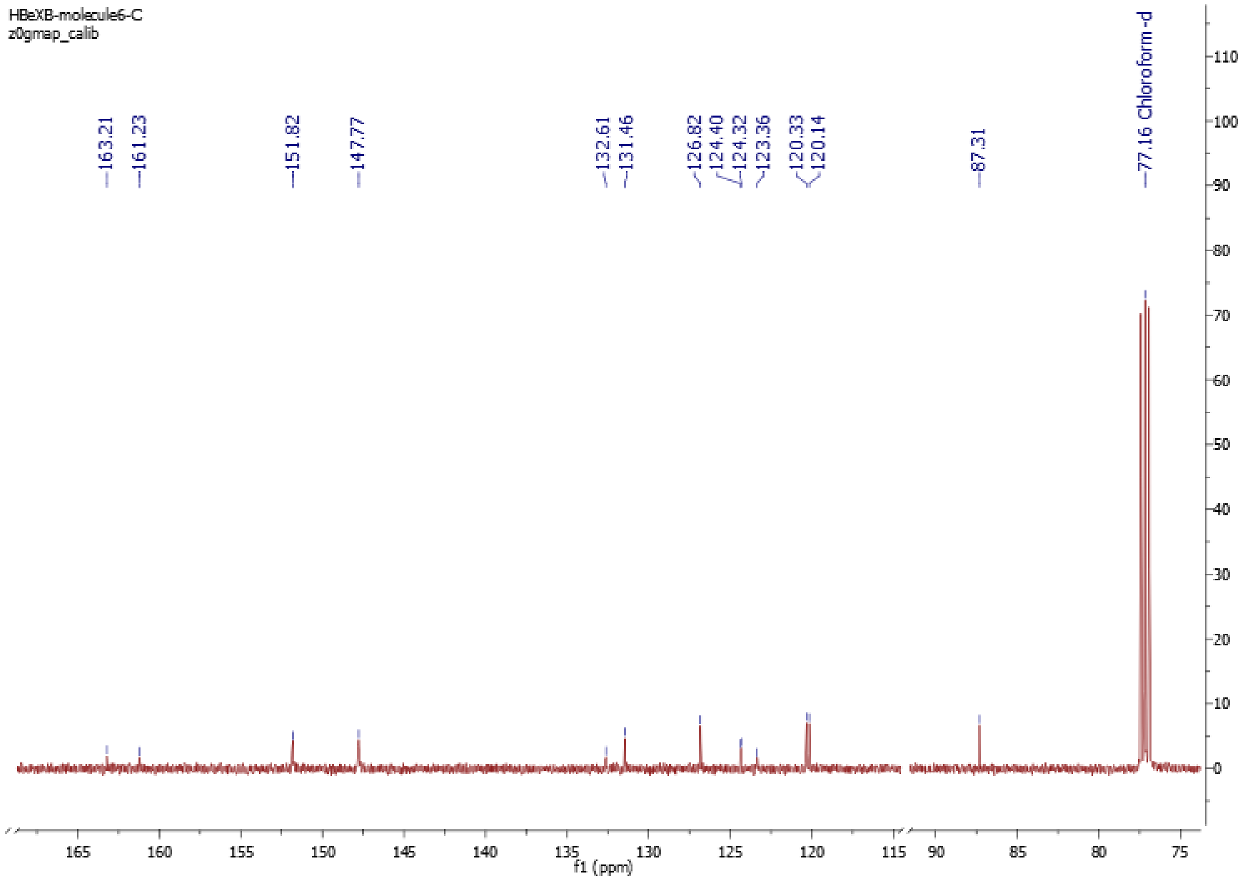


Figure S3. ^{13}C NMR of **6** (125 MHz, $CDCl_3$).

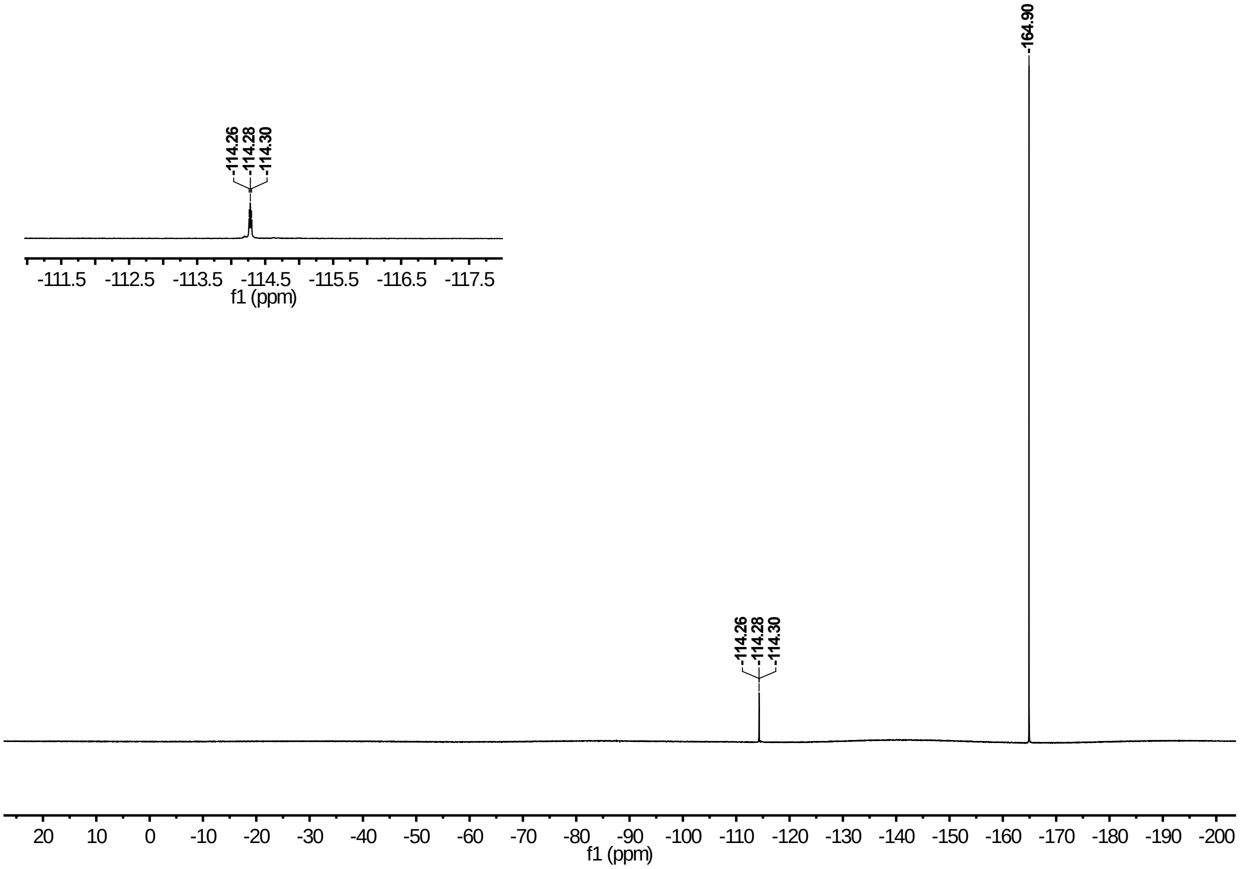


Figure S4. ^{19}F NMR of **6** (470 MHz, $CDCl_3$). Hexafluorobenzene (C_6F_6) internal reference.

3,5-bis(4-ethynyl-3-iodopyridinyl)-1-fluoroaniline (7). 6 (0.200 g, 0.439 mmol), copper iodide (0.008 g, 0.043 mmol), sodium iodide (0.263 g, 1.756 mmol) were added to a 10-20 mL microwave reaction vial containing a stir bar and dissolved in 13 mL 1,4-dioxane. To the vibrant yellow reaction mixture, trans-N,N'-dimethylcyclohexane-1,2-diamine (0.1 mL) was added. The microwave vial was sealed and placed in a Biotage Initiator+ microwave reactor for 8 hours at 150 ˚C. After cooling, the reaction was run through pipet silica plug with EtOAc to remove catalysts and salts. The EtOAc crude was then ran through GCMS in order to obtain % conversion of bromines to iodines. If the conversion from bromine to iodine was 99% or greater, then the reaction was concentrated. The beige/yellow product (0.194 g, 81%) was obtained after purified via column chromatography (gradient column 50% EtOAc/50% Hexanes to 75% EtOAc/25% Hexanes).

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 9.01 (s, 2H), 8.65-8.55 (d, J = 4.8 Hz, 2H), 7.65 (s, 1H), 7.43-7.42 (d, J = 5.1 Hz, 2H), 7.38-7.26 (d, J = 8.9 Hz, 2H).

^{13}C NMR (125 MHz, $CDCl_3$): δ (ppm) = 162.29 (d, J = 237.2 Hz), 157.01, 148.30, 136.94, 131.35, 131.33, 126.56, 124.40 (d, J = 10.3 Hz), 120.18 (d, J = 23.4 Hz), 99.50, 90.81.

^{19}F NMR (470 MHz, CDCl$_3$): δ (ppm) = –114.27 (t, J = 8.1 Hz, 1F).

HRMS (ESI pos) m/z for $C_{20}H_{10}I_2FN_2^+$ [M+H]$^+$: calculated: 550.8912; found: 550.8968.

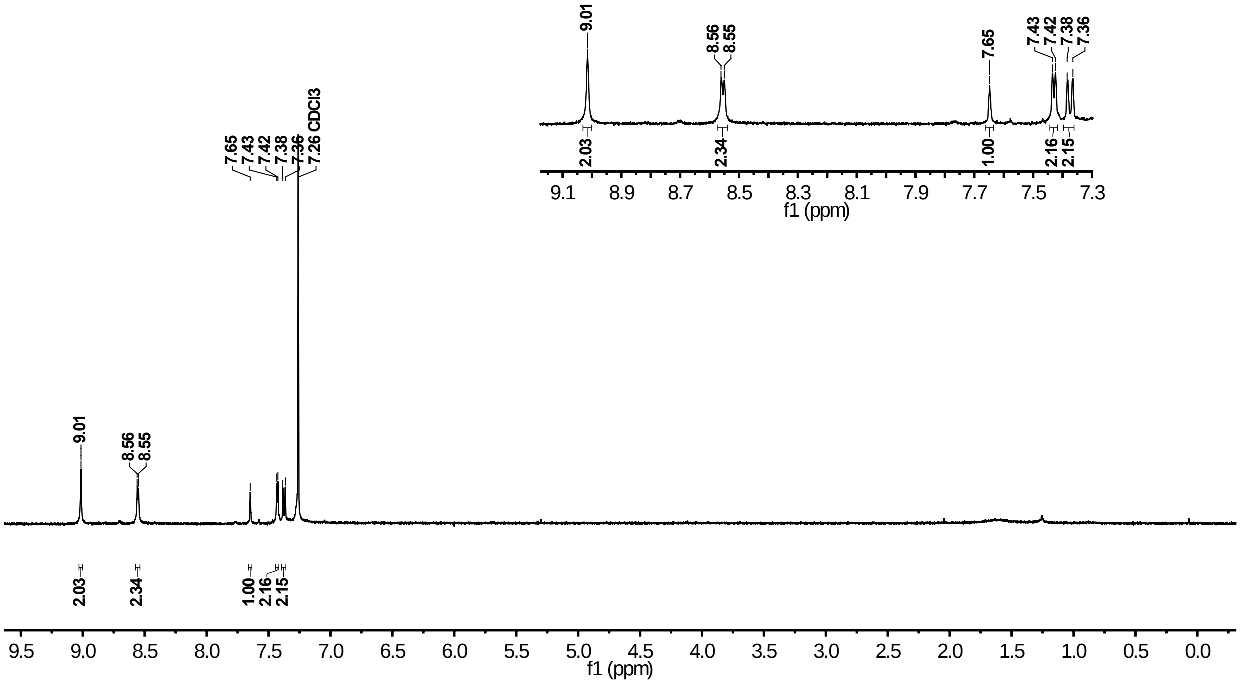


Figure S5. ^{1}H NMR of **7** (500 MHz, CDCl$_3$).

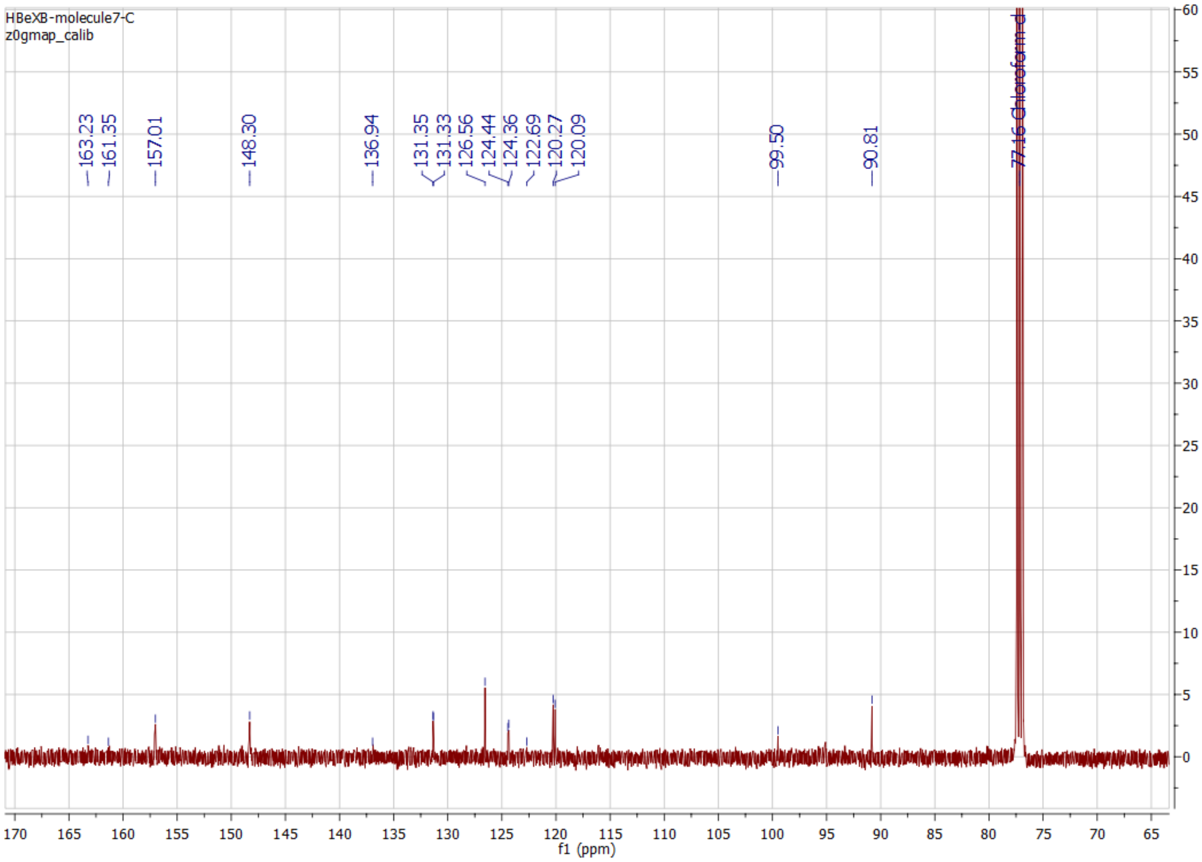


Figure S6. ^{13}C NMR of **7** (125 MHz, CDCl$_3$).

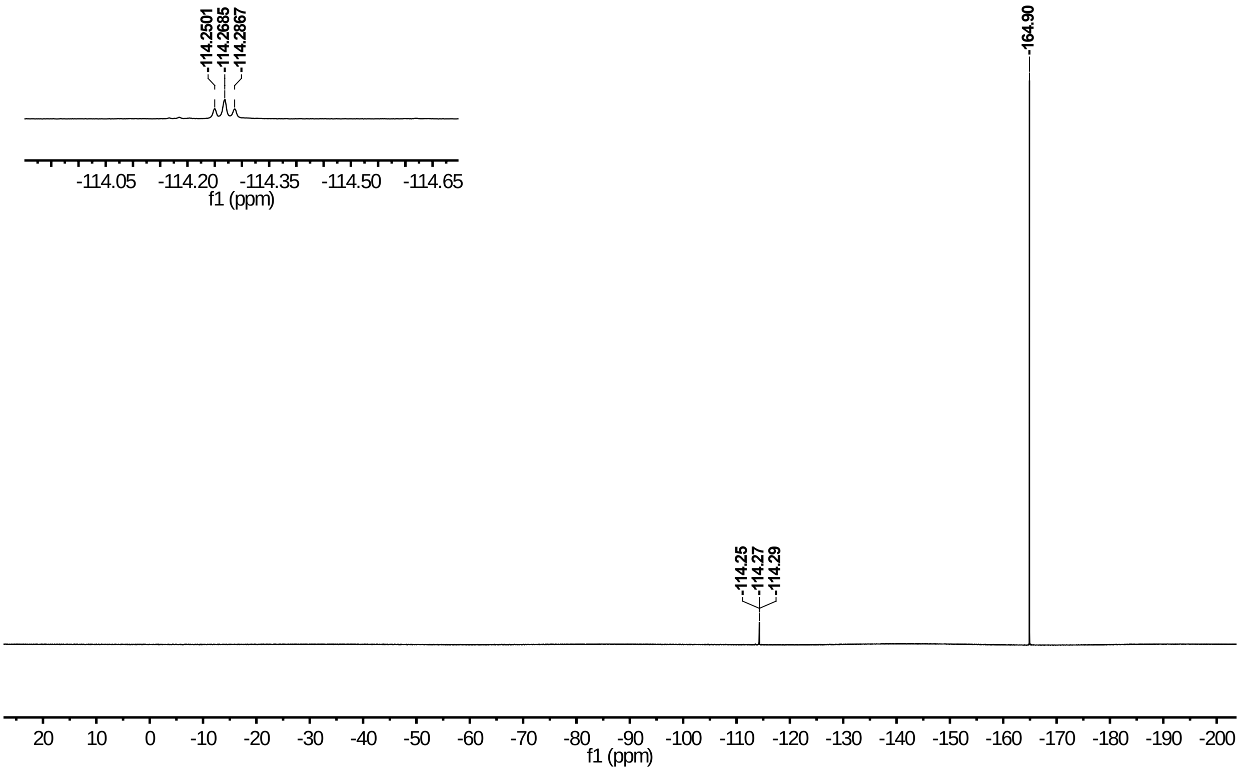


Figure S7. ^{19}F NMR of **7**(470 MHz, $CDCl_3$). Hexafluorobenzene (C_6F_6) internal reference.

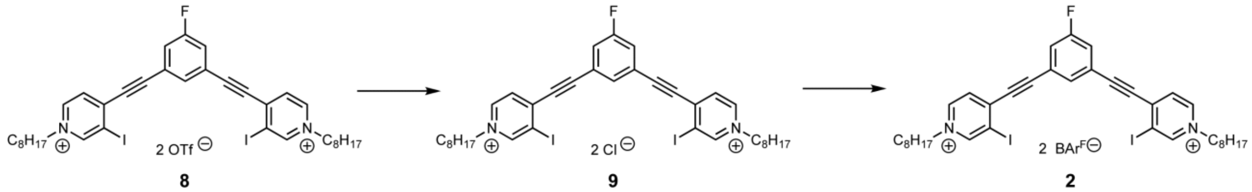


Figure S8. ChemDraw schematic of the alkylation and anion metathesis of catalyst 2.

Procedures for alkylation, anion metathesis and BArF metathesis were conducted as previously reported.[1, 4]

Molecule 2

^{1}H NMR (500 MHz, $CDCl_3$): δ (ppm) = 8.68 (s, 2H), 8.04-8.03 (d, J = 6.2, 2H), 7.80 (s, 1H), 7.70-7.66 (b, 17 H), 7.50-7.47 (b, 10H), 4.30-4.27 (t, J = 7.5, 4H), 1.96 (b, 4H), 1.35-1.26 (b, 20H), 0.87 (t, J = 6.7, 6H).

^{13}C NMR (125 MHz, CDCl$_3$): δ (ppm) = 161.83 (dd, J = 99.9, 49.8 Hz), 149.41, 147.43, 140.96, 134.93, 133.29, 132.84 (d, J = 2.9 Hz), 129.15, 129.10 (q, J = 33.1 Hz), 124.63 (q, J = 272.5 Hz), 123.11 (d, J = 23.4 Hz), 122.49 (d, J = 10.0 Hz), 117.67 (t, J = 4.2 Hz), 107.31 (d, J = 3.7 Hz), 100.84, 89.14, 62.98, 31.51, 31.45, 28.78, 28.66, 26.00, 22.51, 13.92.

^{19}F NMR (125 MHz, CDCl$_3$): δ (ppm) = –65.42 (s, 48F), –111.03 (t, J = 8.1 Hz, 1F).

HRMS (ESI pos) m/z for $C_{68}H_{55}BI_2F_{25}N_2^+$ [M–A]$^+$: calculated: 1639.2148; found: 1639.2128.
HRMS (ESI pos) m/z for $C_{36}H_{43}I_2FN_2^+$ [M–2A]$^{2+}$: calculated: 388.0744; found: 388.0745.

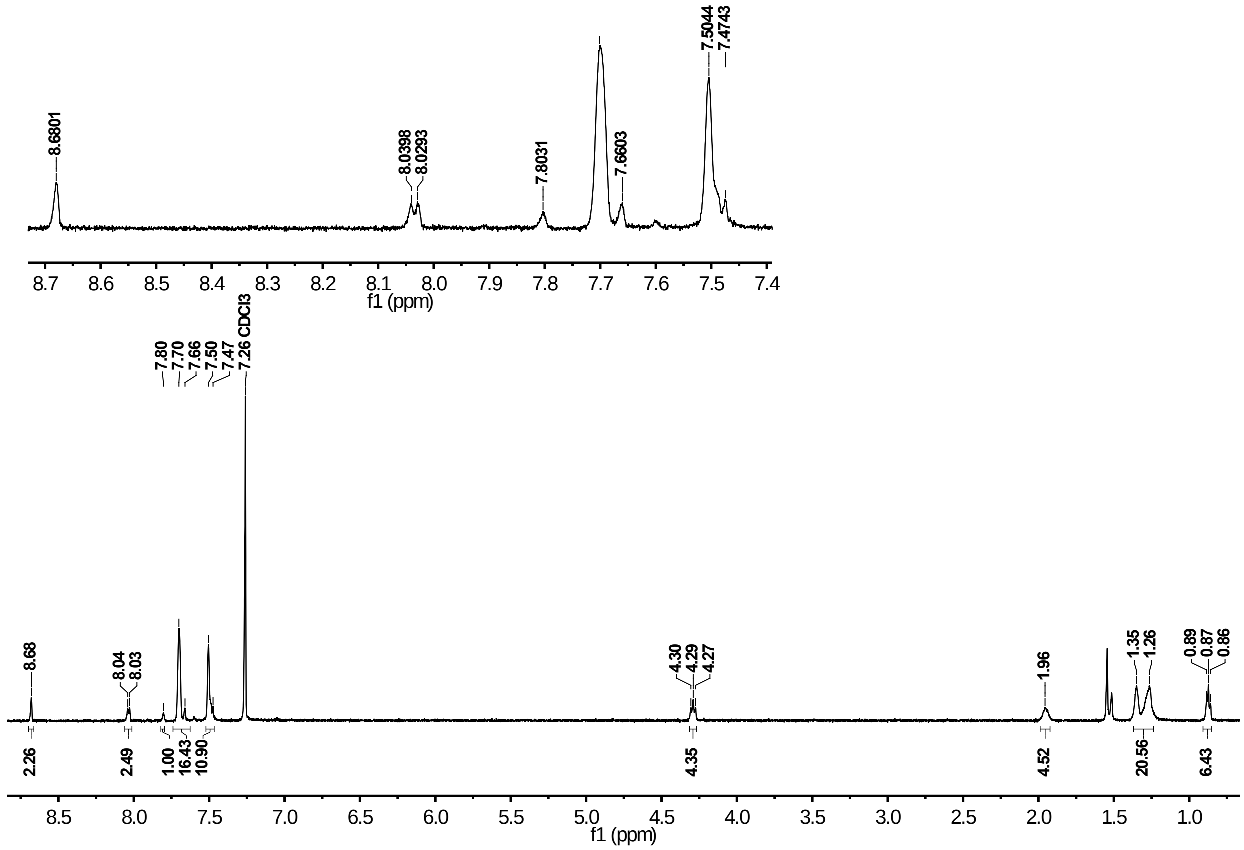


Figure S9. ^{1}H NMR of **2** (500 MHz, CDCl$_3$).

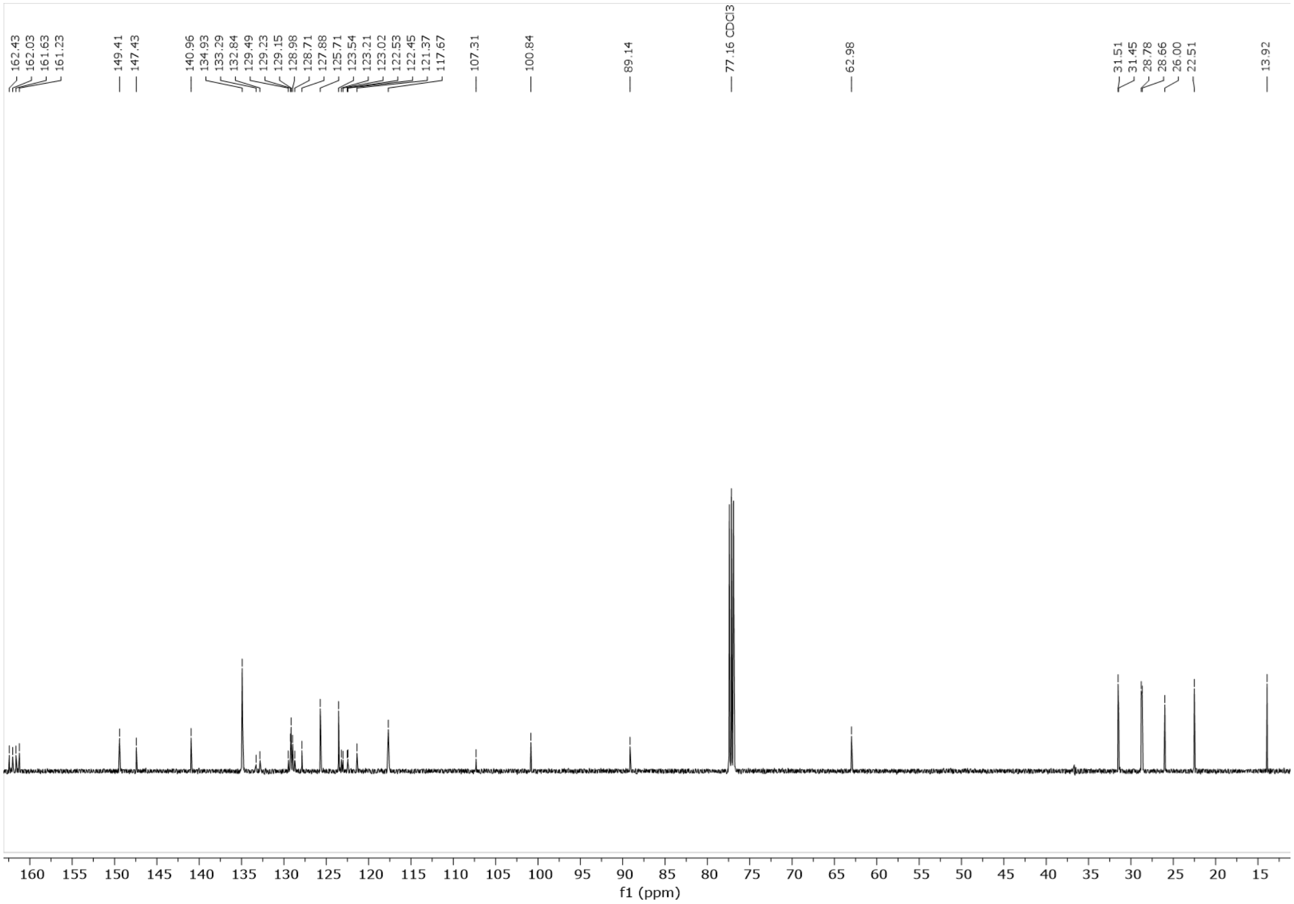


Figure S10. ^{13}C NMR of **2** (125 MHz, CDCl$_3$).

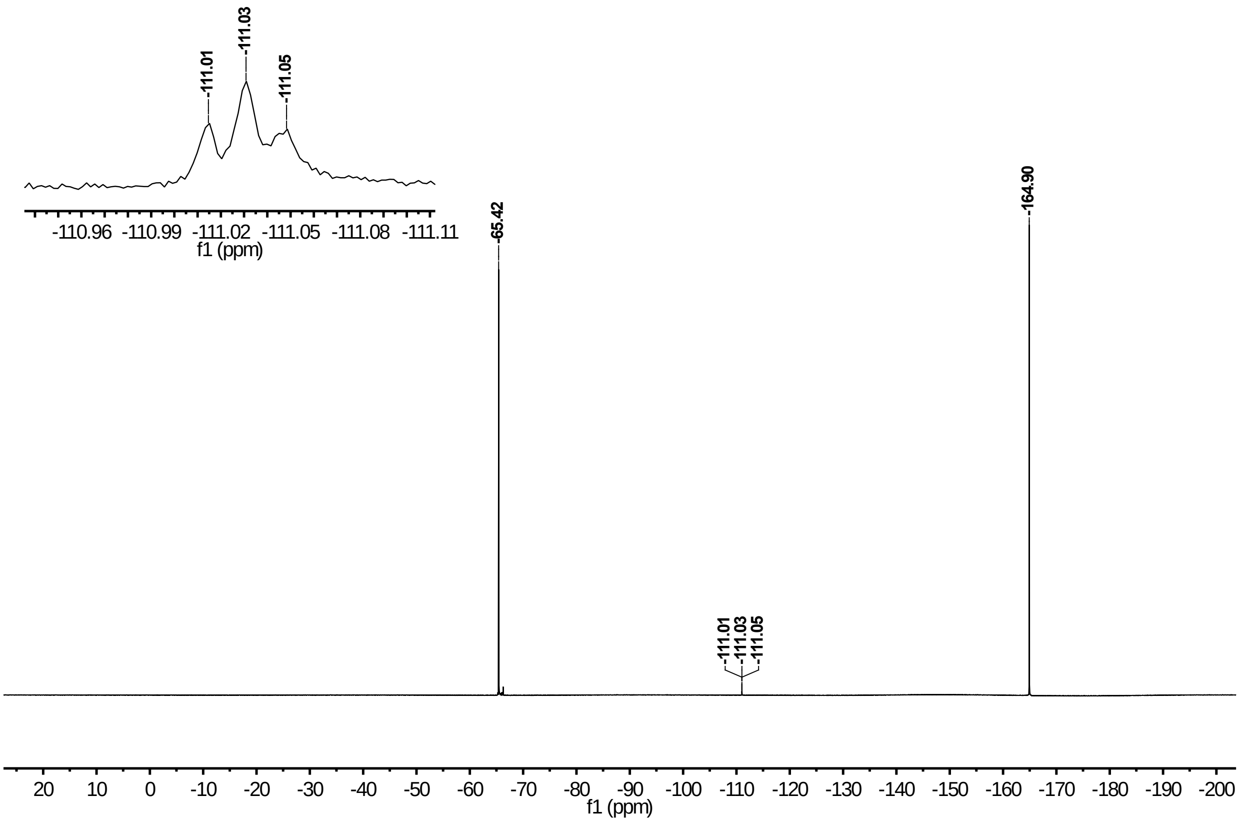


Figure S11. ^{19}F NMR of **2** (470 MHz, $CDCl_3$). Hexafluorobenzene (C_6F_6) internal reference.

General setup for halogen and hydrogen bond catalyzed reactions and determination of yield

$CDCl_3$ was dried over 3Å molecular sieves. This entire process was conducted in absence of light to avoid potential catalyst degradation. To a flame dried 4-dram vial that was cooled in a desiccator, 5.5 mg of benzhydryl bromide was dissolved in 2.2 mL of $CDCl_3$ resulting in a 10.12 mM solution. To this solution, 8.2 µL of N-methyl indole were added, resulting in 29.72 mM solution of N-methyl indole. 500 µL of this stock solution was added to a screw cap Norell™ NMR tube and 500 µL were added to each flame dried vial containing the catalyst of interest (**1**, **2**, **3**, or control molecules). Once the potential catalysts were dissolved, the resulting concentration of catalysts ranged from 1.99 to 2.03 mM (e.g. 20 mol% catalyst to bromodiphenylmethane) all the vials were then transferred to screw cap Norell™ NMR tubes. The reaction progress was monitored via ^{1}H-NMR spectroscopy. An error margin of 5% is assumed. All measurements with potential catalysts were reproduced in triplicate.

The yields were determined via the following procedure. The peak of benzhydryl bromide (s, 6.3 ppm) and the new peak forming from that same hydrogen with N-methyl indole (s, 5.7 ppm) were integrated and totaled to equal 1. The resulting value for the integration of product singlet dictated the percentage conversion.

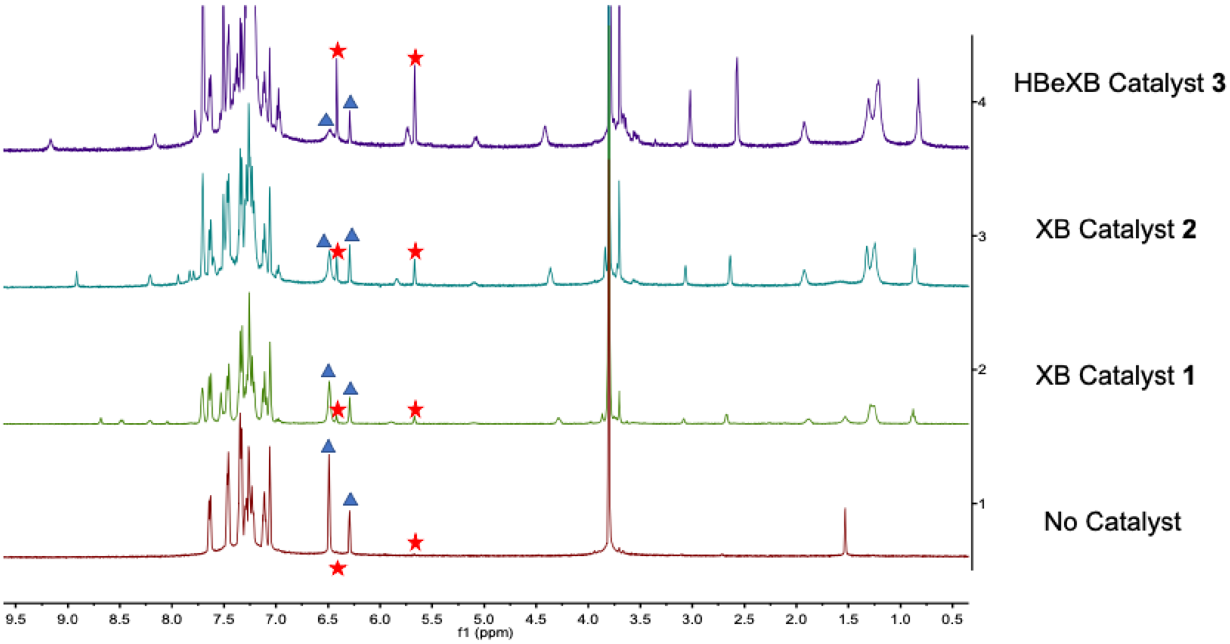


Figure S12. Stacked ^{1}H NMR spectra of all organocatalysts at 7.5 hours. Bromodiphenylmethane and N-methyl indole starting materials are highlighted with blue triangles. Product ^{1}H NMR signals are exhibited by red stars. HBeXB catalyst **3** (top spectrum) shows the most product conversion over 7.5 hours.

Determination of k_{rel}

For XB donors **1**-**3** and **H3** k_{rel} was determined. This was done by constructing a linear plot using the first two measurement points (approx. 7 mins and one hour) and setting the y-intercept to zero. The XB donor **1** was set to k_{rel} = 1.

Table S1. k_{rel} data

Catalyst	Slope	k_{rel}
1	0.14	1
2	0.28	2
3	0.65	4.6
H3	0.34	2.4

Halide Abstraction with Bases

As mentioned in the manuscript this reaction creates hydrobromic acid *in situ*, which leads to the dimerization of *N*-methyl indole but does not catalyze product formation of **A**. We tested this benchmark halide abstraction reaction with base (non-nucleophilic base to neutralize the HBr *in situ*).

We found that using a non-nucleophilic base to directly neutralize the acid and eliminate the *N*-methyl indole dimer formation was successful. However, some bases were ineffective to quench the acid (Cs_2CO_3, K_2CO_3), while others lead to decomposition of HBeXB catalyst **3** (Pyridine, TEA, DBU, Proton Sponge, 2,6-bis(tert-butyl)pyridine (BTBP)) and the XB catalyst **2** (Pyridine, TEA, Proton Sponge, DBU, DIPEA).

Unfortunately, due to decomposition of XB catalyst **2** or HBeXB catalyst **3**, two different non-nucleophilic bases had to be used to neutralize the HBr during the duration of the reaction. Diisopropylethylamine (DIPEA) was used with **3** while 2,6-bis(tert-butyl)pyridine (BTBP) was used with **2**. Control (no catalyst added) reactions were conducted to establish a baseline with each base. Product formation of 18 and 13% were observed with DIPEA and BTBP, respectively, which are similar yields to the control reaction without base (13 %). In both cases the presence of base improved the yield of the reaction by minimizing dimer formation. **3•**DIPEA resulted in a yield of 85% over 24 hours. In contrast, **2•**BTBP only showed a product yield of 37% over that same time period. The difference in product formation between catalysts **3•**DIPEA and **2•**BTBP was greater with base than without. Interestingly, Huber *et al.* (Chem. Commun., 2014, 50, 6281–6284) had observed BTBP coordinating to one of their XB catalysts, which may explain the greater difference in product formation between 3 and 2 when in the presence of the aforementioned bases. These results further demonstrate that the halide abstraction reaction is moderately acid insensitive. However, the necessity of using two different bases in order to quench the *in situ* acid formation with the catalysts was not followed up as it would make for a complicated discussion.

Table S2. Proto derivative of **3** (**H3**) catalyst data

Time average (mins)	% Product Formed Avg
7	11
74	24
127	31
184	35
259	40
327	45
429	49
1397	61

^{13}C Analysis

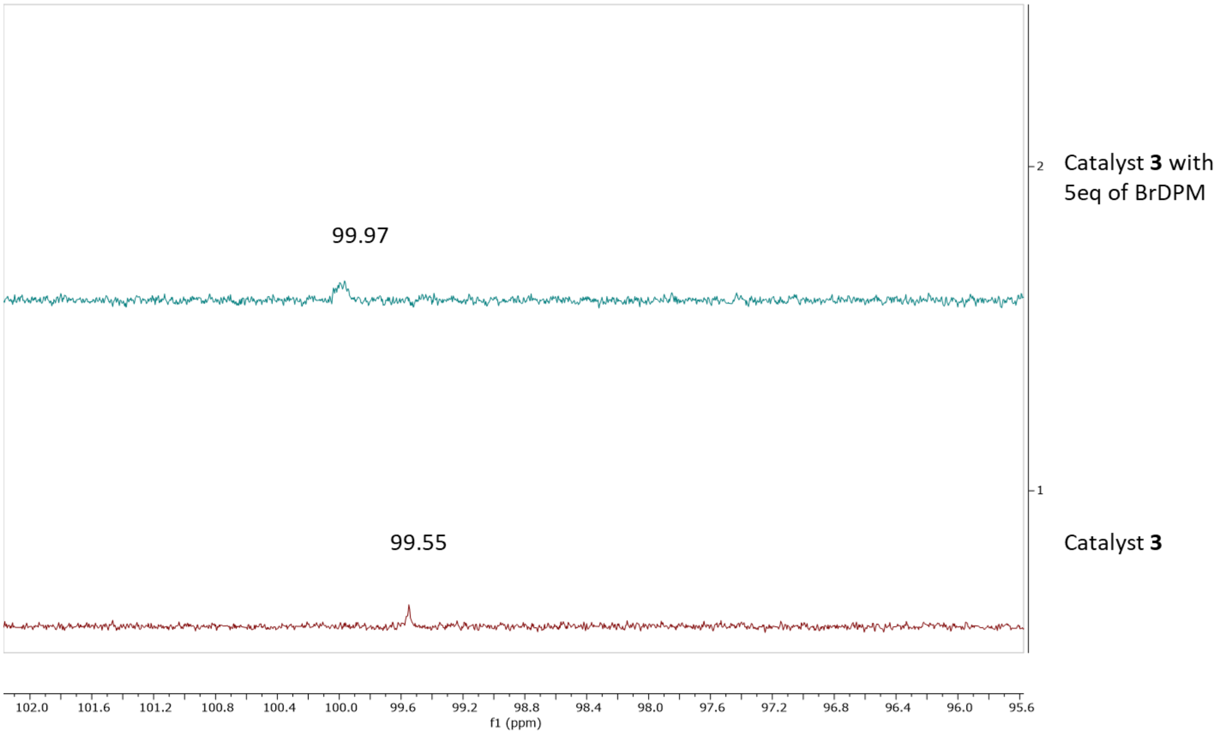


Figure S13. Selected region of ^{13}C spectra showing the shift of the ^{13}C signal that correlates to the carbon bound to the iodine atom of molecule 3. Upon addition of 5eq of BrDPM the signal shifts 0.42 ppm downfield indicative of halogen bonding.

Computations

Gas-phase density functional theory (DFT) calculations were performed with the B3LYP functional using the Gaussian 16 suite of programs. The M06-2X functional with the def2-TZVPP basis set for all atoms and the small-core energy-consistent relativistic effective core potential (def2-ECP) applied to iodine. The basis set was downloaded from the EMSL Basis Set Exchange.[5] Employing optimized geometries, frequency calculations were carried out confirm molecules and complexes were at local minima. The exception to this is the W conformation of **3Me** where two persistent small imaginary frequencies (≈ -42 and -32 cm^{-1}), corresponding to methyl rotations, remained despite our best efforts.

Binding energy (complexation energy) is the energy of the complex, minus the energy of the isolated monomers (host and guest) in their minima configuration. Binding energies were corrected for basis set superposition error (BSSE) by the counterpoise technique.[6]

Alkyne Driver Analysis

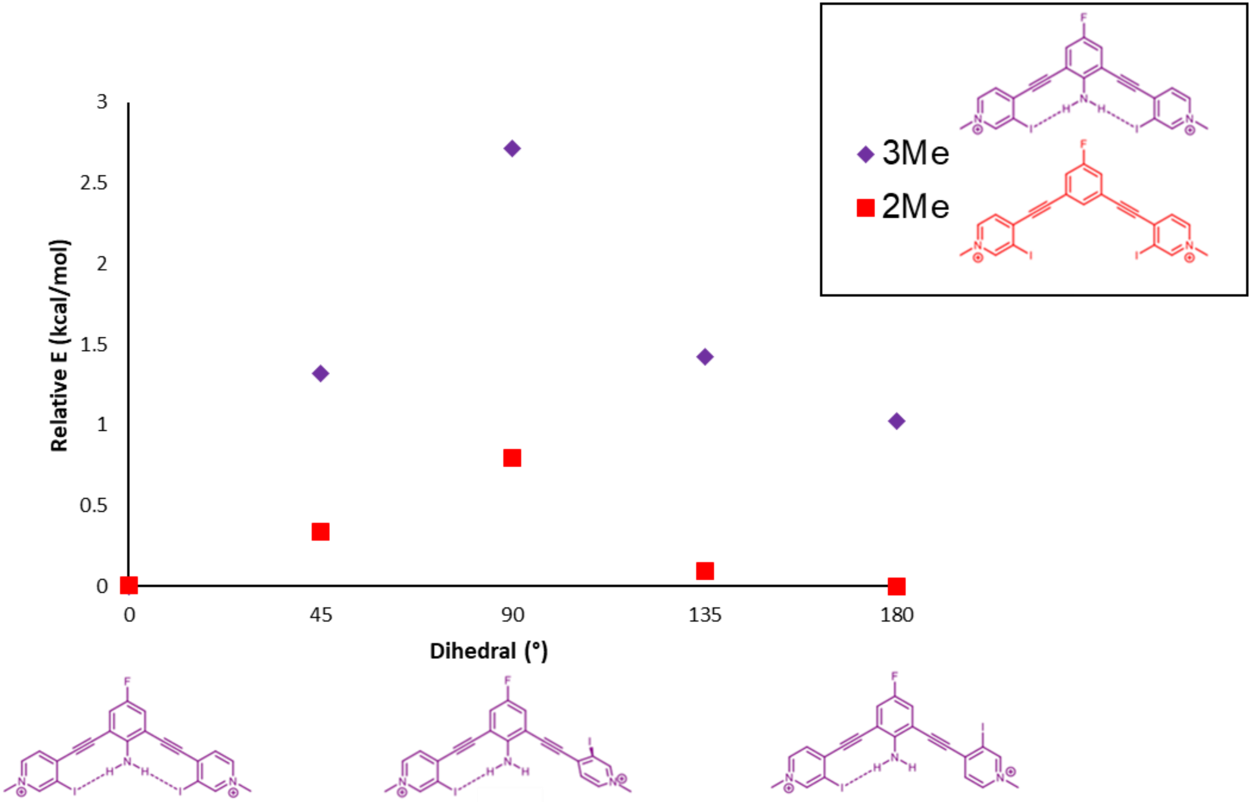
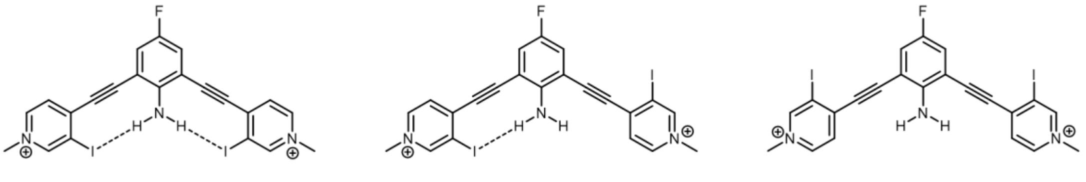


Figure S14. Dihedral driver energy plot highlighting relative energy at 45° intervals. **2Me** data is plotted as red squares while the and HBeXB **3Me** is plotted as purple diamonds. Figures below the x-axis depict the conformational change of the receptors going from bidentate conformation to the S conformation.

Single Point Energy Analysis



Bidentate S conformation W conformation

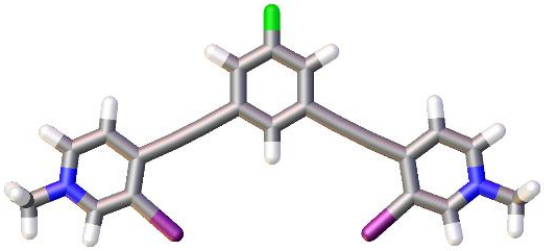
Figure S15. ChemDraw figures of **3Me** depicting the three planar conformations.

Table S3. Relative energies based on catalyst conformation. All values in kcal/mol.

Molecule	Bidentate	S	W

2Me	0.00	-0.40	-0.70
3Me	-1.44	-0.77	0.00

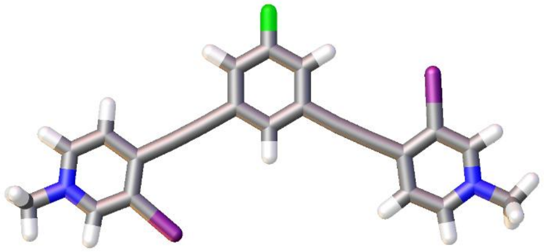
Optimized Atomic Coordinates



Bidentate conformation of 2Me

I	-3.48479300	-2.04057200	-0.01546600
I	3.48456400	-2.04034600	0.01523600
F	0.00000300	5.90679500	-0.00058800
N	-7.38747100	-0.32398300	0.00466800
H	0.00018500	0.73067400	0.00038600
N	7.38753000	-0.32433000	-0.00437500
C	-7.21112400	1.01112200	0.01199300
H	-8.10728800	1.61449300	0.01743900
C	-5.95267000	1.54877000	0.01220000
H	-5.83300900	2.62159600	0.01730400
C	-6.33293000	-1.15341800	-0.00209500
H	-6.55292600	-2.21063500	-0.00754900
C	-5.03819800	-0.67588000	-0.00251500
C	-4.82326700	0.71436800	0.00480200
C	-3.53134200	1.28802100	0.00379100
C	-2.45411000	1.82843300	0.00280900
C	-1.20396900	2.51503100	0.00149000
C	-1.20740600	3.91311700	0.00137100
H	-2.13068300	4.47409500	0.00241700
C	0.00005200	4.58152600	-0.00031600
C	1.20755500	3.91320200	-0.00172900
H	2.13079700	4.47423900	-0.00301600
C	0.00014200	1.81077400	0.00021400
C	1.20420900	2.51511800	-0.00132800
C	2.45438000	1.82857800	-0.00247700
C	3.53161300	1.28816800	-0.00333900
C	4.82347100	0.71437300	-0.00434100
C	5.95298300	1.54862000	-0.01153900
H	5.83347600	2.62146500	-0.01641800
C	7.21136300	1.01079700	-0.01142200
H	8.10760100	1.61406000	-0.01672800

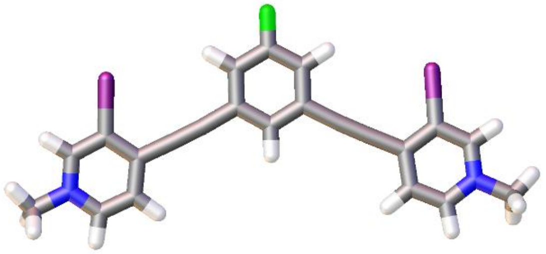
C	5.03821500	-0.67591800	0.00265100
C	6.33287700	-1.15362900	0.00217600
H	6.55273500	-2.21087600	0.00740100
C	-8.76262600	-0.86194800	0.01649300
H	-8.72133400	-1.94138900	-0.07731400
H	-9.31179500	-0.44027200	-0.82101100
H	-9.23978900	-0.58936500	0.95453500
C	8.76260300	-0.86249500	-0.01649200
H	9.23919200	-0.59105800	-0.95516300
H	8.72122800	-1.94182100	0.07860500
H	9.31237200	-0.43992500	0.82016000



S conformation of 2Me

I	-4.51765900	-2.16951000	0.01737300
I	5.88476400	1.30757600	0.06515900
F	0.61797600	4.81791500	-0.07240400
N	-7.96329800	0.34158000	0.02107400
H	-0.53952600	-0.22707600	-0.02554700
N	6.41917300	-2.92070200	-0.04060000
C	-7.50593000	1.60821200	0.00619500
H	-8.25268800	2.38894300	0.00481600
C	-6.16179100	1.86458500	-0.00626000
H	-5.81569800	2.88700600	-0.01808600
C	-7.11035700	-0.69400300	0.02387600
H	-7.55104800	-1.67985000	0.03596300
C	-5.74343500	-0.50425000	0.01181000
C	-5.23678100	0.80811400	-0.00366000
C	-3.85213200	1.09223900	-0.01615800
C	-2.68368700	1.38729200	-0.02626500
C	-1.31285700	1.78067500	-0.03762100
C	-1.00420900	3.14405100	-0.05047000
H	-1.77904400	3.89689500	-0.05281100
C	0.32225300	3.52588800	-0.06017100
C	1.34967500	2.60474600	-0.05719800
H	2.37632600	2.94161200	-0.06506200

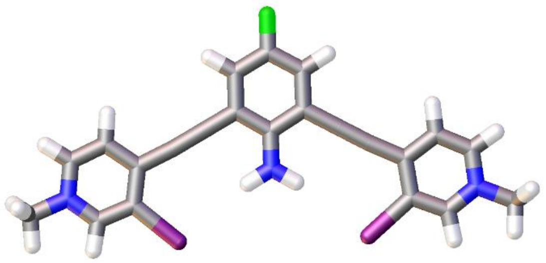
C	-0.29633900	0.82507300	-0.03533700
C	1.03399700	1.24266600	-0.04481500
C	2.10711400	0.30321600	-0.04159900
C	3.06459700	-0.42848000	-0.03864600
C	4.20818900	-1.25896600	-0.03672900
C	4.07497500	-2.65526300	-0.07593700
H	3.09436600	-3.10512100	-0.10726000
C	5.18464800	-3.45684500	-0.07710900
H	5.13033000	-4.53529400	-0.10703300
C	5.51109300	-0.72527500	0.00199400
C	6.58680300	-1.58985900	-0.00117200
H	7.60636700	-1.23456200	0.02781300
C	-9.42171100	0.11062000	0.03473900
H	-9.61115900	-0.95694200	0.04267900
H	-9.85684000	0.55640000	-0.85595100
H	-9.84189100	0.56706700	0.92721900
C	7.58967400	-3.82070000	-0.02427600
H	7.60965500	-4.35712700	0.92122700
H	8.49211100	-3.22945900	-0.13322200
H	7.50652500	-4.51981500	-0.85175100



W conformation of 2Me

I	5.92792500	1.49055300	-0.10481100
I	-5.92792200	1.49055300	0.10483200
F	0.00000000	3.76209800	-0.00008800
N	7.36761700	-2.51712300	0.09973000
H	-0.00000100	-1.41438200	0.00000000
N	-7.36761900	-2.51712200	-0.09968400
C	6.27887600	-3.30785200	0.14410700
H	6.45950100	-4.37154300	0.19671300
C	5.02153300	-2.76671200	0.12316200
H	4.16184300	-3.41838000	0.15893000
C	7.24246300	-1.18253500	0.03348100
H	8.16079700	-0.61489800	0.00145000
C	6.00488400	-0.57277800	0.00741100
C	4.84867600	-1.37600500	0.05488100

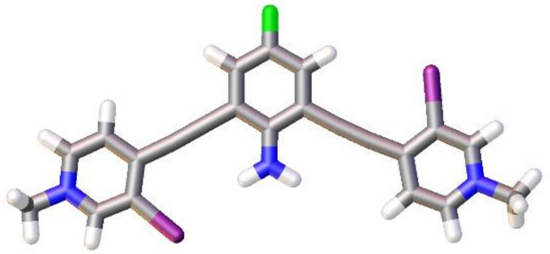
C	3.55194600	-0.81401200	0.03589700
C	2.45808400	-0.30859800	0.02398600
C	1.20360500	0.36981500	0.01107200
C	1.20734000	1.76784700	0.01037600
H	2.13284000	2.32546100	0.01886900
C	0.00000000	2.43635200	-0.00006500
C	-1.20734000	1.76784700	-0.01048400
H	-2.13283900	2.32546100	-0.01899500
C	0.00000000	-0.33461200	-0.00001800
C	-1.20360600	0.36981500	-0.01113200
C	-2.45808400	-0.30859800	-0.02402100
C	-3.55194600	-0.81401200	-0.03591300
C	-4.84867700	-1.37600500	-0.05487600
C	-5.02153600	-2.76671200	-0.12315200
H	-4.16184600	-3.41838000	-0.15893300
C	-6.27887900	-3.30785200	-0.14407700
H	-6.45950500	-4.37154300	-0.19667900
C	-6.00488500	-0.57277800	-0.00738900
C	-7.24246400	-1.18253500	-0.03343800
H	-8.16079700	-0.61489800	-0.00139400
C	8.70652700	-3.13757500	0.15119900
H	9.45340400	-2.38688900	-0.08243800
H	8.75026700	-3.93865900	-0.58118000
H	8.87555800	-3.53159100	1.15049400
C	-8.70653200	-3.13757100	-0.15113900
H	-8.87560200	-3.53152400	-1.15045300
H	-9.45339900	-2.38690000	0.08257600
H	-8.75024200	-3.93870100	0.58119000



Bidentate conformation of 3Me

I	-3.40720900	-2.03912300	-0.00429500
I	3.40714300	-2.03904800	0.00440400
F	0.00000800	5.95784600	0.00007200
N	-7.33690500	-0.38553900	-0.00183700
N	0.00004300	0.46955800	-0.00000300

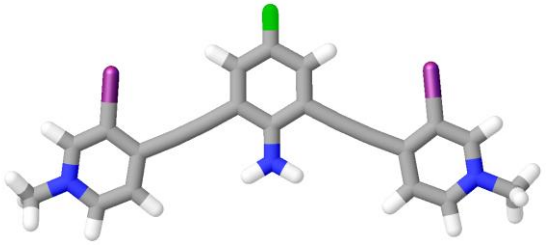
H	-0.86616400	-0.04200400	0.00011700
H	0.86625900	-0.04199100	-0.00013800
N	7.33691300	-0.38564900	0.00163000
C	-7.17959700	0.95323600	0.00052400
H	-8.08506300	1.54267200	0.00125900
C	-5.93197500	1.51172100	0.00174300
H	-5.83034300	2.58637700	0.00268300
C	-6.26795000	-1.19757900	-0.00238400
H	-6.47071300	-2.25829000	-0.00390800
C	-4.98381700	-0.69802800	-0.00142700
C	-4.78561800	0.69623900	0.00063800
C	-3.50855100	1.28755700	0.00065300
C	-2.44867800	1.86978100	0.00052900
C	-1.21215500	2.55255100	0.00033800
C	-1.19901200	3.94993500	0.00039800
H	-2.12681600	4.50420900	0.00066300
C	0.00001200	4.62761200	0.00005900
C	1.19905000	3.94995100	-0.00029500
H	2.12684100	4.50424800	-0.00054900
C	0.00003300	1.81623300	0.00002300
C	1.21221400	2.55257300	-0.00027200
C	2.44874900	1.86982000	-0.00049600
C	3.50864200	1.28763300	-0.00062900
C	4.78568000	0.69625400	-0.00068000
C	5.93207500	1.51167700	-0.00187400
H	5.83050100	2.58633900	-0.00282000
C	7.17967200	0.95312900	-0.00073500
H	8.08516500	1.54252300	-0.00154200
C	4.98380900	-0.69802600	0.00138900
C	6.26791600	-1.19763900	0.00226200
H	6.47063000	-2.25835900	0.00378600
C	-8.70309300	-0.94415000	0.01013100
H	-8.64559500	-2.02280800	-0.08485800
H	-9.25949100	-0.53087500	-0.82683500
H	-9.18488900	-0.68038400	0.94840500
C	8.70306900	-0.94433700	-0.01046700
H	9.18470600	-0.68081100	-0.94889100
H	8.64553100	-2.02297100	0.08478000
H	9.25964400	-0.53090300	0.82630100



S conformation of 3Me

I	-4.47947100	-2.14428400	0.02156600
I	5.82992300	1.33704300	-0.00827000
F	0.70454900	4.82150400	0.05482800
N	-7.93096500	0.35782100	-0.01923600
N	-0.62835900	-0.50311100	-0.02713600
H	-1.59168800	-0.78330900	-0.10340100
H	0.08325200	-1.20675400	-0.10698300
N	6.47700600	-2.87681000	-0.00881400
C	-7.47432900	1.62606700	-0.02962100
H	-8.22274000	2.40523100	-0.03983800
C	-6.13257900	1.88724200	-0.02754900
H	-5.78995200	2.91082500	-0.03643100
C	-7.07403400	-0.67529500	-0.00603800
H	-7.51195000	-1.66243900	0.00233100
C	-5.70998600	-0.47998900	-0.00307800
C	-5.20106300	0.83315100	-0.01448700
C	-3.82291100	1.11897200	-0.01247000
C	-2.65757100	1.44175000	-0.00741700
C	-1.29390400	1.81065400	-0.00002200
C	-0.94545700	3.16388300	0.02270600
H	-1.71246900	3.92517000	0.03302800
C	0.38156900	3.53097900	0.03292000
C	1.38068300	2.58278500	0.02142000
H	2.41621200	2.89270200	0.03082600
C	-0.29583600	0.80357700	-0.01447300
C	1.05721700	1.22351700	-0.00169700
C	2.11187200	0.28032500	-0.00948200
C	3.05931100	-0.47067300	-0.01272500
C	4.21674300	-1.27450900	-0.01029000
C	4.12578400	-2.67610400	-0.01169600
H	3.16021900	-3.15791200	-0.01490900
C	5.25690800	-3.44597300	-0.01072600
H	5.23056100	-4.52576600	-0.01144100
C	5.50870700	-0.70606500	-0.00751700
C	6.60616300	-1.53972500	-0.00618900
H	7.61582400	-1.15582300	-0.00373800

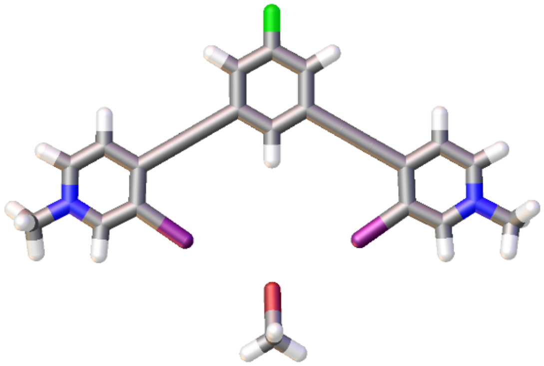
C	-9.38836800	0.12402500	-0.02136200
H	-9.57588400	-0.94396900	-0.01938100
H	-9.81602500	0.57171200	-0.91475900
H	-9.81947200	0.57585700	0.86833500
C	7.67559600	-3.73720300	0.02910100
H	7.80804000	-4.11854000	1.03900300
H	8.54046000	-3.15128800	-0.26267700
H	7.53978900	-4.55909500	-0.66761900



W conformation of 3Me

I	5.83462200	-1.56065900	0.08291700
I	-5.83617200	-1.55880200	-0.12135900
F	0.00176700	-3.74029900	0.09311300
N	7.43950200	2.38648700	-0.07239600
N	-0.00074700	1.75023700	-0.03644900
H	0.85866100	2.24972200	-0.18002700
H	-0.86116000	2.24906600	-0.17620600
N	-7.43823200	2.38616300	0.10543000
C	6.38455600	3.22135900	-0.11370900
H	6.60791400	4.27727000	-0.15326200
C	5.10573500	2.73373500	-0.10464600
H	4.27792400	3.42535400	-0.13488100
C	7.25576400	1.05636600	-0.02200700
H	8.14974100	0.45064600	0.00841300
C	5.99560100	0.49937200	-0.00882900
C	4.87019000	1.35050500	-0.05250500
C	3.55774300	0.83681400	-0.04122900
C	2.46083900	0.32894500	-0.02609600
C	1.21107800	-0.33477800	-0.00397300
C	1.19935900	-1.73180200	0.03419400
H	2.13005100	-2.28138000	0.04454700
C	0.00120800	-2.41005000	0.05786200

C	-1.19760800	-1.73250600	0.04703100
H	-2.12778300	-2.28264600	0.06908600
C	-0.00007300	0.39901400	-0.01853300
C	-1.21052100	-0.33549000	0.01148300
C	-2.46068400	0.32792400	0.01248500
C	-3.55754400	0.83595300	0.02066800
C	-4.86972000	1.35000100	0.04592700
C	-5.10414700	2.73225100	0.11992000
H	-4.27575600	3.42290900	0.15606200
C	-6.38277600	3.22008200	0.14836700
H	-6.60510200	4.27530200	0.20668800
C	-5.99582400	0.49971800	0.00063900
C	-7.25544700	1.05671900	0.03428700
H	-8.15003300	0.45183600	0.00436900
C	8.80694200	2.93923200	-0.12712000
H	9.49782000	2.21367300	0.28897500
H	8.83995300	3.85187500	0.45998300
H	9.06522100	3.14936100	-1.16260300
C	-8.80562800	2.93614700	0.18415500
H	-9.06398600	3.10093500	1.22781800
H	-9.49646800	2.22942800	-0.26347200
H	-8.83863900	3.87351300	-0.36239500

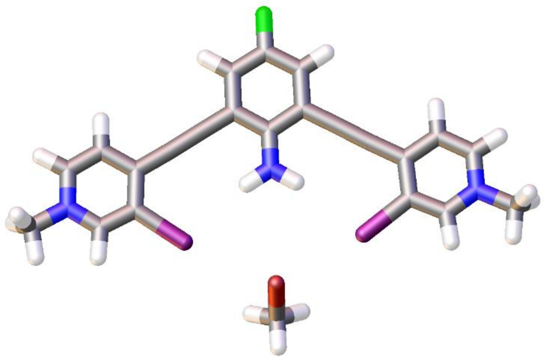


2Me•Bromomethane Complex

I	3.07814800	-1.36443600	-0.01332100

I	-3.07805100	-1.36423500	-0.01861400
F	0.00006600	6.62366400	0.10840600
N	7.15453700	-0.06957000	-0.04774000
H	-0.00005400	1.45081900	0.01473300
N	-7.15428400	-0.06935800	-0.06717700
C	7.11945500	1.27595400	-0.03291200
H	8.07348600	1.78251300	-0.03869000
C	5.92392600	1.94294100	-0.01196900
H	5.91727600	3.02236600	0.00150700
C	6.01770600	-0.78486600	-0.04312300
H	6.12863000	-1.85915400	-0.05739800
C	4.78021900	-0.17702700	-0.02127800
C	4.71561800	1.22987700	-0.00592500
C	3.48481900	1.92352700	0.01590400
C	2.44114900	2.52542100	0.03104900
C	1.20429700	3.23386600	0.04651000
C	1.20879400	4.63116400	0.07192900
H	2.13180500	5.19256200	0.08203500
C	0.00003500	5.29835600	0.08399100
C	-1.20875400	4.63124200	0.07066300
H	-2.13173800	5.19270200	0.07979600
C	-0.00002800	2.53102800	0.03388700
C	-1.20431900	3.23394500	0.04525700
C	-2.44119400	2.52556900	0.02851000
C	-3.48486900	1.92370900	0.01237900
C	-4.71563200	1.23003600	-0.01072800
C	-5.92390800	1.94309400	-0.02162400
H	-5.91726900	3.02255300	-0.01102100
C	-7.11931500	1.27613100	-0.04945700
H	-8.07330700	1.78269900	-0.05939800
C	-4.78014400	-0.17685800	-0.02755100
C	-6.01750700	-0.78467200	-0.05567600
H	-6.12835900	-1.85895200	-0.07101000
C	8.46113800	-0.75381400	-0.10708400
H	8.32814400	-1.79434900	0.16834600
H	9.14014100	-0.27449800	0.59193200
H	8.85305400	-0.68333800	-1.11911800
C	-8.46173800	-0.75452900	-0.06311900
H	-8.88344200	-0.70881200	0.93831100
H	-8.32017100	-1.78798600	-0.36010800
H	-9.12006600	-0.25808400	-0.76989400
Br	0.00006100	-3.13526800	-0.16809900
C	-0.00065200	-4.80293900	0.84341100
H	0.89330000	-5.34421400	0.56099800

H	-0.00086100	-4.54654300	1.89496300
H	-0.89474300	-5.34374500	0.56054200



3Me•Bromomethane Complex

I	3.15631000	-1.44821100	-0.11546100
I	-3.15631100	-1.44821200	-0.11544600
F	-0.00000200	6.52831900	0.25560000
N	7.20442800	-0.06588900	-0.17689600
N	-0.00000300	1.04335700	0.05216100
H	0.86425700	0.52734800	0.06683700
H	-0.86426400	0.52734900	0.06684300
N	-7.20442900	-0.06589500	-0.17689400
C	7.13499800	1.27836100	-0.10448600
H	8.07685700	1.80769400	-0.10808000
C	5.92742700	1.91523900	-0.03238500
H	5.89667700	2.99278700	0.02409300
C	6.08460000	-0.80790800	-0.17836900
H	6.21900300	-1.87779300	-0.23949700
C	4.83688500	-0.22980900	-0.10678700
C	4.73229400	1.17398300	-0.03287600
C	3.49118200	1.83323000	0.03470200
C	2.44492500	2.43790200	0.07970600
C	1.21262900	3.12572600	0.12205100
C	1.19930700	4.52186600	0.17540300
H	2.12714500	5.07586500	0.19306900
C	-0.00000200	5.19868000	0.20381000
C	-1.19931100	4.52186600	0.17540500
H	-2.12714900	5.07586600	0.19307300
C	-0.00000300	2.38837300	0.09993000
C	-1.21263300	3.12572700	0.12205300
C	-2.44492900	2.43790300	0.07970800
C	-3.49118600	1.83323000	0.03470400

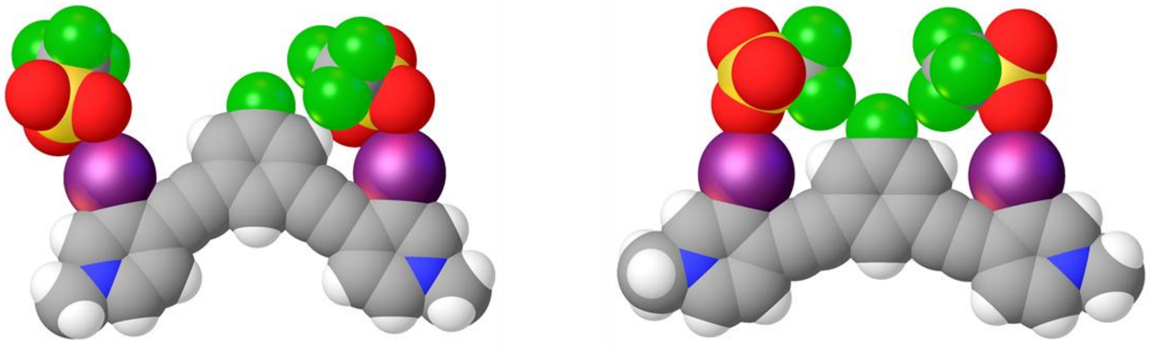
C	-4.73229700	1.17398100	-0.03287400
C	-5.92743100	1.91523600	-0.03238800
H	-5.89668300	2.99278300	0.02408500
C	-7.13500100	1.27835500	-0.10449000
H	-8.07686100	1.80768800	-0.10808800
C	-4.83688700	-0.22981100	-0.10678000
C	-6.08460100	-0.80791200	-0.17836200
H	-6.21900300	-1.87779800	-0.23948500
C	8.53019200	-0.70773000	-0.26316800
H	8.40307400	-1.78460900	-0.26341900
H	9.12409200	-0.40775100	0.59617800
H	9.01640800	-0.39344900	-1.18331400
C	-8.53019300	-0.70773700	-0.26317100
H	-9.12411100	-0.40772600	0.59615100
H	-8.40307600	-1.78461700	-0.26337900
H	-9.01638800	-0.39349000	-1.18333900
Br	0.00000400	-3.05106500	-0.00695600
C	0.00001700	-4.02746500	1.68254200
H	0.89489000	-3.74230700	2.22122300
H	-0.89493600	-3.74243700	2.22116000
H	0.00010100	-5.08131000	1.43518400

X-ray Diffraction Data

X-ray diffraction data for **2Me•2OTf⁻ (*Pbcn*)** and **2Me•2OTf⁻ (*P*-1)** were collected at 100 K on a Bruker D8 Venture using MoKα-radiation (λ=0.71073 Å). Data have been corrected for absorption using SADABS[7] area detector absorption correction program. Using Olex2[8], the structure was solved with the SHELXT[9] structure solution program using Direct Methods and refined with the SHELXL[10] refinement package using least squares minimization. All non-hydrogen atoms were refined with anisotropic thermal parameters. The hydrogen atoms of the investigated structure were located from difference Fourier maps but finally their positions were placed in geometrically calculated positions and refined using a riding model. Isotropic thermal parameters of the placed hydrogen atoms were fixed to 1.2 times the *U* value of the atoms they are linked to (1.5 times for methyl groups). Calculations and refinement of structures were carried out using APEX3[11], SHELXTL[12], and Olex2 software.

Crystallographic Data for **2Me•2OTf⁻ (*Pbcn*)** $C_{24}H_{15}F_7I_2N_2O_6S_2$ (M =878.30 g/mol): orthorhombic, space group *Pbcn* (no. 60), a = 22.3717(18) Å, b = 12.7201(10) Å, c = 10.8086(8) Å, V = 3075.8(4) Å^3, Z = 4, T = 100 K, μ(MoKα) = 2.263 mm^{-1}, $Dcalc$ = 1.897 g/cm^3, 2Θmax = 50.21°, 46254 reflections measured, 2735 unique (R_{int} = 0.0565, R_{sigma} = 0.0232) R_1 = 0.0389 (I > 2σ(I)), wR_2 = 0.0994 (all data).

Crystallographic Data for **2Me•2OTf⁻ (*P*-1)** $C_{24}H_{15}F_7I_2N_2O_6S_2$ (*M* =878.30 g/mol): triclinic, space group *P*-1 (no. 2), *a* = 7.8488(4) Å, *b* = 10.3020(6) Å, *c* = 18.2739(10) Å, *α* = 80.787(2)°, *β* = 85.112(2)°, *γ* = 86.769(2)°, *V* = 1451.86(14) Å^3, *Z* = 2, *T* = 100 K, μ(MoKα) = 2.397 mm^{-1}, *Dcalc* = 2.009 g/cm^3, 2Θmax = 52.842°, 56291 reflections measured, 5956 unique (R_{int} = 0.0502, R_{sigma} = 0.0263), R_1 = 0.0287 (I > 2σ(I)), wR_2 = 0.0685 (all data).



2Me•2OTf⁻ (*P*-1) **2Me•2OTf⁻ (*Pbcn*)**

Figure S16 Spacefill diagrams of 2Me•2OTf— both in the W conformation. Spheres drawn using default van der Waals radii in Olex2.

Table S4 Table of Crystallographic Data

Molecule	**2Me•2OTf⁻ (*P*-1)**	**2Me•2OTf⁻ (*Pbcn*)**
CCDC number	2036129	2036128
Empirical formula	$C_{24}H_{15}F_7I_2N_2O_6S_2$	$C_{24}H_{15}F_7I_2N_2O_6S_2$
Formula weight	878.30	878.30
Temperature (K)	100	100
Crystal system	triclinic	orthorhombic
Space group	*P*-1	*Pbcn*
a (Å)	7.8488(4)	22.3717(18)
b (Å)	10.3020(6)	12.7201(10)
c (Å)	18.2739(10)	10.8086(8)
α (°)	80.787(2)	90
β (°)	85.112(2)	90
γ (°)	86.769(2)	90
Volume (Å^3)	1451.86(14)	3075.8(4)
Z	2	4
ρ_{calc} (g/cm^3)	2.009	1.897
M (mm^{-1})	2.397	2.263
Crystal size (mm^3)	0.20 × 0.06 × 0.01	0.14 × 0.12 × 0.01

Reflections collected	56291	46254
Independent reflections	5956 [R_{int} = 0.0502, R_{sigma} = 0.0263]	2735 [R_{int} = 0.0565, R_{sigma} = 0.0232]
Data/restraints/parameters	5956/0/390	2735/9/197
Goodness-of-fit on F^2	1.069	1.127
Final R indexes [I>=2σ (I)]	R_1 = 0.0287, wR_2 = 0.0647	R_1 = 0.0389, wR_2 = 0.0911
Final R indexes [all data]	R_1 = 0.0401, wR_2 = 0.0685	R_1 = 0.0545, wR_2 = 0.0994
Largest diff. peak/hole / e $Å^{-3}$	1.12/-0.36	1.14/-0.41

References

1. Riel, Asia Marie S., et al., *Chem. Sci.,* **2018**, 9(26), 5828-5836.
2. Balasubramanian et al., *Chem –Eur. J.*, **2012**, 18(2), 554–564.
3. Jeong et al., *Chem. Commun*., **2016**, 52, 3406-3409.
4. Massena, Casey J., et al*., Chem. Commun*., **2015**, 51(8), 1417-1420.
5. Schuchardt, K. L.; Didier, B. T.; Elsethagen, T.; Sun, L.; Gurumoorthi, V.; Chase, J.; Li, J.; Windus, T. L. J. Chem. Inf. Model. 2007, 47 (3), 1045–1052.
6. Boys, S. F., Bernardi, F., *Mol. Phys*. **1970**, 19(4), 553–566.
7. Sheldrick, G. M. (**1996**). SADABS: Area Detector Absorption Correction; University of Göttingen, Germany.
8. Dolomanov, O.V.; Bourhis, L.J.; Gildea, R.J.; Howard, J.A.K.; Puschmann, H., *J. Appl. Cryst*., **2009**, 42, 339-341.
9. Sheldrick, G. M., *Acta Cryst. A71,* **2015**, 3-8.
10. Sheldrick, G. M., *Acta Cryst. C71*, **2015**, 3-8.
11. Bruker (**2016**). APEX3. Bruker AXS Inc., Madison, Wisconsin, USA.
12. Sheldrick, G.M., *Acta Cryst. A64*, **2008**, 112-122.