Hyperconjugative Antiaromaticity Activates 4*H*-Pyrazoles as Inverse-Electron Demand Diels–Alder Dienes

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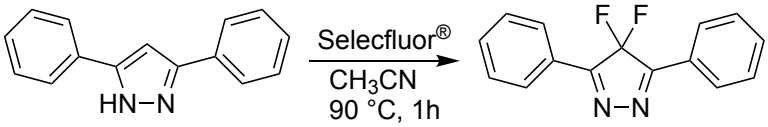
Computational Methods

Computations were performed using Gaussian09 Rev D.01[2] on the Hoffman2 cluster of the Institute for Digital Research and Education (IDRE) at UCLA and the Extreme Science and Engineering Discovery Environment (XSEDE). Geometry optimizations were performed with the M06-2X[3] density functional and the 6-31G(d) basis set in the gas phase. Conformational searches were performed using Maestro from the Schrödinger suite. Single-point calculations were performed at the 6-311++G(d,p) level of theory with the SMD[4] solvation model. Stationary points were verified with frequency analyses. Local minima showed no imaginary frequencies and transition states showed one imaginary frequency. A Quasiharmonic correction was applied by setting all frequencies that fell below 100 cm^{-1} to 100 cm^{-1}. Thermodynamic data were obtained at the standard state of 1 atm and 298.15 K. NICS calculations were carried out using the NMR keyword with the 6-31G(d) basis set. Dummy atoms denoted Bq were placed at the center of the ring for NICS(0) calculations and 0.5 Å and 1.0 Å above the center of the ring for NICS(0.5) and NICS(1) calculations, respectively. Molecular orbital calculations were done at the M06-2X/6-31G(d)//M06-2X/6-311++G(d,p) level of theory.

Materials

General. All chemicals were from commercial sources and used without further purification. NMR spectra were acquired on Bruker spectrometers operating at 500 mHz in the MIT Department of Chemistry Instrumentation Facility. The melting point of DFP was determined with a Stanford Research Systems Optimelt automated melting point system and a temperature increase of 0.2 °C/min. Mass spectra were acquired with a Jeol AccuTOF dart spectrometer in the MIT Department of Chemistry Instrumentation Facility using positive ionization. UV-vis experiments were carried out with an Agilent Cary 60 UV-vis spectrometer with measurements every 0.1 s for kinetic experiments and absorbance scans for stability studies.



Synthesis of DFP. DFP was synthesized by procedures reported previously.[1] 3,5-Diphenylpyrazole (210 mg, 0.95 mmol) and 1-chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis(tetrafluoroborate) (760 mg, 2.1 mmol) were added to an oven-dried flask, along with activated 3-Å molecular sieves. The flask was purged with N_2(g), and 3 mL of dry acetonitrile was added. The reaction mixture was heated to 90 °C and allowed to react for 1 h. Following reaction, the solution was diluted with ethyl acetate (5 mL) and filtered. Solvent was evaporated, and the product was purified by silica chromatography (0–10% v/v ethyl acetate in hexanes) to give 226 mg of DFP (93%) as a light yellow solid with mp 87.8–90.3 °C. **^{1}H NMR** (500 MHz, $CDCl_3$, δ): 8.15 (d, 4H, J = 8.2 Hz), 7.73–7.44 (m, 6H). **^{13}C NMR** (126 MHz, $CDCl_3$, δ): 162.40 (t, J = 23.1 Hz), 133.09, 129.26, 128.27, 126.03, 125.67. **^{19}F NMR** (471 MHz, $CDCl_3$, δ): –116.35. $[M + H]^+$ calcd for $C_{15}H_{11}F_2N_2$, 257.08848; found, 257.08725.

Characterization of Diels–Alder Product. DFP (4.1 mg, 0.024 mmol) and BCN (6.2 mg, 0.027 mmol) were dissolved in 1 mL of $CDCl_3$, and the resulting solution was incubated for 30 min. Following incubation, the product was characterized by NMR spectroscopy and mass spectrometry. **^{1}H NMR** (500 MHz, $CDCl_3$, δ): 7.52–7.47 (m, 3H), 7.44 (dd, 3H, J = 8.5, 6.8 Hz),

7.39–7.34 (m, 2H), 3.83 (d, 2H, J = 7.2 Hz), 2.90 (ddd, 2H, J = 13.7, 8.6, 4.4 Hz), 2.46 (dd, 2H, J = 13.8, 6.7 Hz), 2.32 (ddt, 2H, J = 13.4, 8.9, 4.2 Hz), 1.59–1.37 (m, 3H), 1.33–1.10 (m, 3H). **^{13}C NMR** (126 MHz, $CDCl_3$, δ): 146.46, 133.54, 131.87, 128.46, 128.42, 127.84, 127.55, 59.62, 24.86, 21.88, 21.46, 19.83. **^{19}F NMR** (471 MHz, $CDCl_3$, δ): –122.88 – –125.15 (m). $[M + H]^+$ calcd for $C_{25}H_{25}F_2O$, 378.17897; found, 378.18034.

Reaction of DMP with BCN. DMP (2.3 mg, 0.0093 mmol) and BCN (1.3 mg, 0.0087 mmol) were dissolved in 1 mL of $CDCl_3$ and the resulting solution was mixed for 2 h. An ^{1}H NMR spectrum did not reveal the formation of a new species.

UV-vis Kinetics

DFP and BCN. Stock solutions of DFP (200 μM) and BCN (20 mM, 10 mM, and 2 mM) were prepared in 9:1 MeOH/H_2O. A 0.5-mL aliquot of the DFP stock solution was mixed with 0.5 mL of each concentration of BCN, and the absorbance at 355 nm was monitored until no DFP remained. Each reaction was carried out in triplicate. Absorbance data were plotted as ln(absorbance) versus time, and the slope of each line was used as k_{obs}. These values were plotted with respect to the BCN concentration, allowing for the calculation of a second-order rate constant of 5.2 $M^{-1}s^{-1}$.

Tz and BCN. Stock solutions of Tz (200 μM) and BCN (20 mM, 10 mM, and 2 mM) were prepared in 9:1 MeOH/H_2O. A 0.5-mL aliquot of the Tz stock solution was mixed with 0.5 mL of each concentration of BCN, and the absorbance at 295 nm was monitored until no Tz remained. Each reaction was carried out in triplicate. Absorbance data were plotted as ln(absorbance) versus time, and the slope of each line was used as k_{obs}. These values were plotted with respect to the BCN concentration, allowing for calculation of a second-order rate constant of 3.2 $M^{-1}s^{-1}$.

Compound Stability Studies

DFP Stability. A solution of DFP (0.1 mM) was prepared in phosphate-buffered saline with fetal bovine serum (10% v/v) and DMSO (2% v/v). Absorbance was measured at 355 nm with the baseline corrected to the solution without DFP. The solution was then incubated at 37 °C for 8 h before another absorbance reading was taken to determine the amount of DFP remaining. The average amount of DFP from 3 trials was 42% after 8 h (Figure S1).

DMP Stability. A solution of DMP (0.1 mM) was prepared in phosphate-buffered saline containing fetal bovine serum (10% v/v) and DMSO (2% v/v). Absorbance was measured at 306 nm with the baseline corrected to the solution without DMP. The solution was then incubated at 37 °C for 8 h before another absorbance reading was taken to determine the amount of DMP remaining. The average amount of DMP from 3 trials was 98% after 8 h (Figure S1).

DFP–BCN Cycloadduct Stability. A solution of DFP–BCN cycloadduct (0.1 mM) was prepared in phosphate-buffered saline containing fetal bovine serum (10% v/v) and DMSO (2% v/v). Absorbance was measured at 350 nm with the baseline corrected to the solution without the cycloadduct. The solution was then incubated at 37 °C for 8 h before another absorbance reading was taken to determine the amount of cycloadduct remaining. The average amount of cycloadduct from 3 trials was 100% after 8 h (Figure S1).

References

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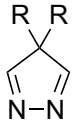
(4) Marenich, A. V.; Cramer, C. J.; Truhlar, D. G. Universal Solvation Model Based on Solute Electron Density and on a Continuum Model of the Solvent Defined by the Bulk Dielectric Constant and Atomic Surface Tensions. *J. Phys. Chem. B* **2009**, *113*, 6378–6396.

Table S1. Calculated NICS(n) and NICS(n)zz Values for 4*H*-Pyrazoles (R = F, H, SiH_3)



	R		
	F	H	Si
NICS(0)	6.2	0.5	–3.3
NICS(0.5)	1.4	–4.3	–8.2
NICS(1)	–2.4	–6.9	–9.9
NICS(0)zz	25.8	12.5	0.2
NICS(0.5)zz	15.2	–1.0	–14.1
NICS(1)zz	0.9	–13.6	–23.7

Table S2. Calculated Energies[a]

Compound	E_{Water}	E_{MeOH}	E_{Gas}	qG_{Water}	f
BCN	–350.015553	–350.023487	–350.010847	–349.858916	None
DMP	–766.797437	–766.80461	–766.780848	–766.547159	None
TS DMP–BCN	–1116.799891	–1116.812252	–1116.781486	–1116.366528	–353.75
DFP	–886.656413	–886.663007	–886.645173	–886.47816	None
TS DFP–BCN	–1236.669932	–1236.682488	–1236.654306	–1236.310026	–297.27
Tz	–758.341107	–758.345768	–758.329168	–758.163703	None
TS Tz–BCN	–1108.354517	–1108.36306	–1108.336769	–1107.995349	–343.23
DFP–BCN adduct	–1236.744578			–1236.379449	None
DMP–BCN adduct	–1116.865274			–1116.42851	None
Tz–BCN adduct	–766.797437			–766.547159	None

[a]*E*: Single point energies at 6-311++G(d,p) level of theory in Hartrees; *qG*: Gibbs free energies of activation in Hartrees; *f*: Imaginary frequencies in cm^{-1}.

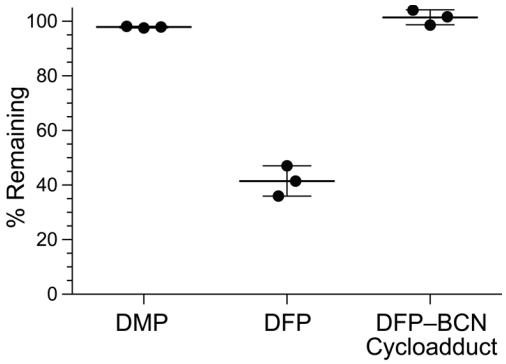
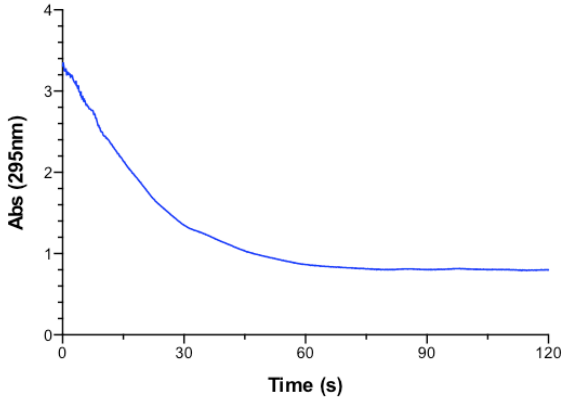


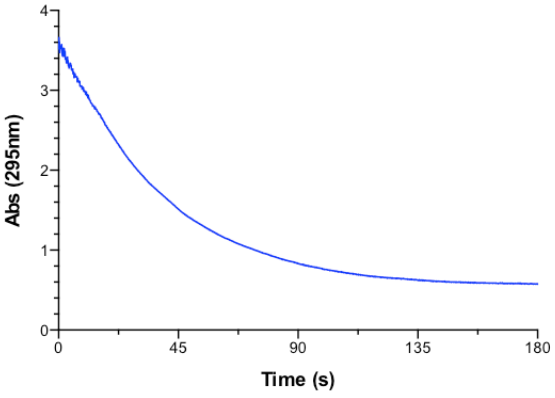
Figure S1. Bar graph of DMP, DFP, and DFP–BCN adduct stability after 8 h in PBS containing FBS (10% v/v), as assessed by UV-vis spectroscopy.

Representative Absorbance Traces for Kinetic Experiments

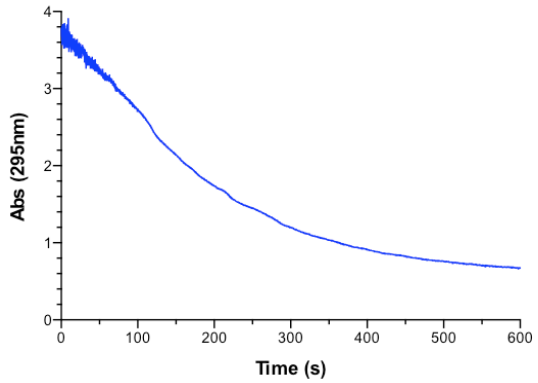
Reaction of 0.1 mM Tz with 10 mM BCN



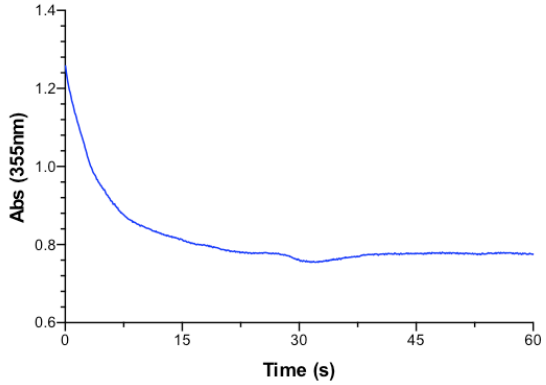
Reaction of 0.1 mM Tz with 5 mM BCN



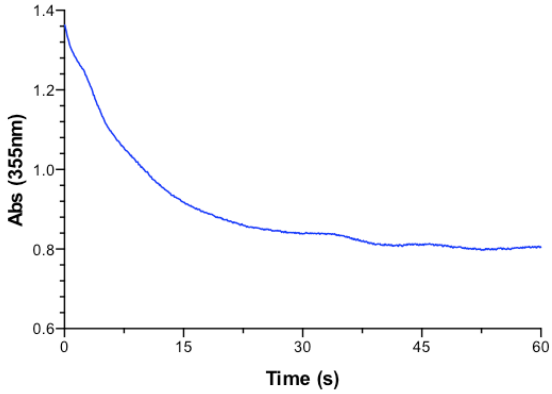
Reaction of 0.1 mM Tz with 1 mM BCN



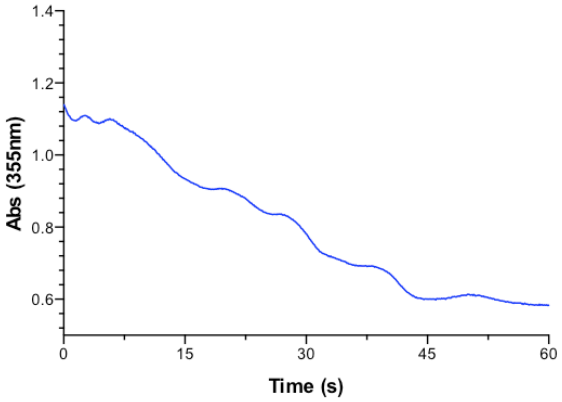
Reaction of 0.1 mM DFP with 10 mM BCN



Reaction of 0.1 mM DFP with 5 mM BCN



Reaction of 0.1 mM DFP with 1 mM BCN



M06-2X/6-31G(d) Optimized Coordinates

DMP

C	1.13695800	-0.47461200	0.00000700
C	-1.13695800	-0.47461200	0.00000300
C	0.00000000	0.52912600	0.00000200
N	-0.70159500	-1.68990800	0.00001200
N	0.70159500	-1.68990800	0.00001400
C	2.58738000	-0.20449000	0.00000300
C	3.12383400	1.08799000	0.00001700
C	3.46877300	-1.29747600	-0.00001800
C	4.50275500	1.28430600	0.00001300
H	2.47476000	1.95572600	0.00003300
C	4.84096900	-1.09886300	-0.00002200
H	3.04887600	-2.29745600	-0.00003100
C	5.36522000	0.19416200	-0.00000700
H	4.89955600	2.29476500	0.00002500
H	5.50716200	-1.95601500	-0.00003800
H	6.43982700	0.34856800	-0.00001100
C	-2.58738000	-0.20449000	-0.00000100
C	-3.12383400	1.08799000	-0.00001300
C	-3.46877300	-1.29747600	0.00000800
C	-4.50275500	1.28430600	-0.00001700
H	-2.47476000	1.95572600	-0.00002000
C	-4.84096900	-1.09886300	0.00000400
H	-3.04887700	-2.29745600	0.00001800
C	-5.36522000	0.19416200	-0.00000800
H	-4.89955600	2.29476500	-0.00002700
H	-5.50716200	-1.95601500	0.00001100
H	-6.43982700	0.34856800	-0.00001100
C	-0.00000700	1.36971300	1.29061000

H	0.88451500	2.00833300	1.34451400
H	-0.88454000	2.00831800	1.34451300
H	-0.00000200	0.71534400	2.16705700
C	0.00000600	1.36971500	-1.29060400
H	0.88453900	2.00832000	-1.34450600
H	0.00000100	0.71534800	-2.16705200
H	-0.88451600	2.00833500	-1.34450700

DFP

C	-1.15852000	0.63486000	0.00023500
C	1.15852000	0.63486000	0.00023500
C	0.00000000	-0.34962600	0.00020300
N	0.72149400	1.83892500	0.00051300
N	-0.72149400	1.83892500	0.00051300
C	-2.56736600	0.25002700	0.00002000
C	-2.92825400	-1.10180500	0.00010800
C	-3.55973100	1.23896000	-0.00030600
C	-4.27266800	-1.45883600	-0.00011000
H	-2.16259800	-1.87103900	0.00038200
C	-4.89774000	0.87484000	-0.00052600
H	-3.25845400	2.28161100	-0.00036700
C	-5.25627400	-0.47431800	-0.00044200
H	-4.55123700	-2.50776800	-0.00003800
H	-5.66613000	1.64160600	-0.00079900
H	-6.30479800	-0.75605900	-0.00062000
C	2.56736600	0.25002700	0.00002000
C	2.92825400	-1.10180500	0.00010900
C	3.55973100	1.23896000	-0.00030700
C	4.27266800	-1.45883600	-0.00010900
H	2.16259800	-1.87103900	0.00038400
C	4.89774000	0.87484000	-0.00052700
H	3.25845400	2.28161100	-0.00037000
C	5.25627400	-0.47431800	-0.00044100
H	4.55123700	-2.50776800	-0.00003600
H	5.66613000	1.64160600	-0.00080200
H	6.30479800	-0.75605900	-0.00062000
F	0.00000000	-1.15517200	-1.08856500
F	0.00000000	-1.15467500	1.08931300

Tz

C	1.28738000	0.00001800	-0.00000800
C	-1.28738200	-0.00002300	0.00001700
C	2.76401400	0.00002300	0.00000300
C	3.46485500	-1.21061700	-0.00004400

C	4.85437400	-1.20642600	-0.00003200
H	2.91153600	-2.14307400	-0.00010600
C	4.85439500	1.20640600	0.00003100
C	5.55136800	-0.00001800	0.00000000
H	5.39517200	-2.14752900	-0.00008500
H	5.39520700	2.14751000	0.00007600
H	6.63709900	-0.00003100	0.00000200
C	-2.76401300	-0.00002500	0.00000700
C	-3.46484900	1.21061600	-0.00058900
C	-4.85439700	-1.20640200	0.00060100
C	-4.85436900	1.20642900	-0.00060800
H	-2.91152800	2.14307100	-0.00102100
C	-5.55136700	0.00002400	0.00000000
H	-5.39520800	-2.14750600	0.00115400
H	-5.39515900	2.14753700	-0.00115100
H	-6.63709800	0.00003900	0.00000400
N	-0.65170800	-1.18314400	-0.00087100
N	0.65174300	-1.18312900	-0.00062600
N	0.65170200	1.18314000	0.00060900
N	-0.65174600	1.18312600	0.00086600
C	-3.46489800	-1.21063600	0.00059800
H	-2.91164500	-2.14313900	0.00097900
C	3.46489600	1.21063700	0.00005700
H	2.91164100	2.14313700	0.00011100

TS DMP–BCN

C	1.11656600	-1.17814700	-0.41927600
C	-0.61932500	1.00835500	-0.51884900
C	0.61931600	1.00835400	-0.51885600
C	-1.89501400	1.74664900	-0.47439100
H	-2.52724500	1.47691800	-1.32850700
H	-2.46377300	1.46505200	0.42290500
C	1.89501000	1.74664200	-0.47446800
H	2.52718600	1.47691200	-1.32862500
H	2.46382300	1.46503500	0.42279200
C	1.60683000	3.25920900	-0.46844800
H	2.56013100	3.80205500	-0.44078400
H	1.11846500	3.53057300	-1.41147500
C	0.75551100	3.69560700	0.70543500
C	-1.60682300	3.25921500	-0.46839500
H	-2.56011700	3.80206900	-0.44070700
H	-1.11848400	3.53056600	-1.41144000
C	-0.75546300	3.69561100	0.70545900
H	1.19829100	3.44597800	1.66923800

H	-1.19821400	3.44598600	1.66927600
C	0.00002700	4.99568500	0.66531500
H	0.00001600	5.52880800	-0.28260600
C	-1.11657200	-1.17814300	-0.41927500
H	0.00004200	5.63807800	1.53943100
N	0.66224300	-1.41580800	-1.65853200
N	-0.66225100	-1.41580800	-1.65853100
C	-0.00000200	-1.42288500	0.58100100
C	2.56546200	-1.27319700	-0.15985400
C	3.45444200	-1.18041500	-1.24163700
C	3.08702200	-1.43716100	1.12878800
C	4.82505900	-1.24592700	-1.03609700
H	3.04077600	-1.06488000	-2.23840200
C	4.46397800	-1.50514100	1.33064700
H	2.42171900	-1.52294100	1.98178500
C	5.33636100	-1.40613300	0.25232000
H	5.50034900	-1.17501200	-1.88343900
H	4.85310200	-1.63735900	2.33559700
H	6.40903100	-1.45650500	0.41204700
C	-2.56546900	-1.27318900	-0.15985600
C	-3.45444500	-1.18034400	-1.24163800
C	-3.08703600	-1.43721100	1.12877700
C	-4.82506300	-1.24584900	-1.03610600
H	-3.04077400	-1.06476800	-2.23839500
C	-4.46399400	-1.50518300	1.33062700
H	-2.42173800	-1.52304700	1.98177100
C	-5.33637200	-1.40610900	0.25230200
H	-5.50035100	-1.17488700	-1.88344600
H	-4.85312300	-1.63744500	2.33556900
H	-6.40904300	-1.45647500	0.41202400
C	-0.00000600	-2.94405100	0.89740500
H	0.00000100	-3.53543400	-0.02118300
H	0.88779000	-3.20649000	1.48085600
H	-0.88781000	-3.20649300	1.48084300
C	0.00000200	-0.59445000	1.88176400
H	-0.87511500	0.05629500	1.94367500
H	0.00012300	-1.24850200	2.76093100
H	0.87499500	0.05647100	1.94355900

TS DFP–BCN

C	-1.14126800	-1.08030000	0.57549800
C	-0.61590800	1.05624300	-0.11865300
C	0.61632200	1.05624700	-0.11820000
C	-1.90786000	1.74686300	-0.25395800

H	-2.54590700	1.25206700	-0.99531600
H	-2.44895500	1.71032500	0.70052100
C	1.90833700	1.74695500	-0.25251700
H	2.54695400	1.25227900	-0.99346100
H	2.44872400	1.71033200	0.70236500
C	1.62299200	3.20502400	-0.66733300
H	2.57749000	3.73487400	-0.77772500
H	1.14751500	3.20192200	-1.65520700
C	0.75651400	3.95003800	0.32714400
C	-1.62225700	3.20491000	-0.66868200
H	-2.57668300	3.73471300	-0.77991200
H	-1.14594300	3.20175400	-1.65615100
C	-0.75664900	3.94999700	0.32649800
H	1.19128600	3.98633400	1.32498800
H	-1.19227000	3.98629700	1.32397400
C	0.00007400	5.18284400	-0.08547600
H	0.00053000	5.41942300	-1.14717400
C	1.14114000	-1.08035600	0.57541900
H	-0.00023000	6.05090300	0.56504300
N	0.67906900	-0.91341500	1.79939100
N	-0.67910700	-0.91337900	1.79942500
C	-0.00009500	-1.58584000	-0.29578900
F	-0.00011100	-2.94892200	-0.28573500
F	-0.00010600	-1.23959300	-1.60336300
C	2.56454500	-1.26597900	0.28122500
C	3.52009700	-1.01174900	1.27354600
C	2.97870500	-1.67039700	-0.99274200
C	4.87059800	-1.16486200	0.99168800
H	3.17975300	-0.70304300	2.25698800
C	4.33421900	-1.82616800	-1.26637100
H	2.24116100	-1.86127900	-1.76564600
C	5.28118800	-1.57223200	-0.27815000
H	5.60826500	-0.97122900	1.76434400
H	4.65036300	-2.14599700	-2.25432800
H	6.33828000	-1.69264800	-0.49455200
C	-2.56471000	-1.26576400	0.28137800
C	-3.52017000	-1.01165700	1.27382200
C	-2.97900700	-1.66997700	-0.99261200
C	-4.87070100	-1.16469500	0.99206500
H	-3.17973900	-0.70312200	2.25728600
C	-4.33455100	-1.82566100	-1.26614400
H	-2.24153400	-1.86075600	-1.76560800
C	-5.28142300	-1.57186000	-0.27779600
H	-5.60829200	-0.97115100	1.76481600

H	-4.65078800	-2.14532500	-2.25412400
H	-6.33853900	-1.69221100	-0.49411900

TS Tz–BCN

C	1.25160900	-1.38956600	0.08150600
N	0.63730300	-1.55091500	1.30221400
N	-0.63735300	-1.55090700	1.30221500
C	-1.25165700	-1.38955400	0.08150700
N	-0.63717100	-1.91403700	-1.03251400
N	0.63711700	-1.91404000	-1.03251600
C	5.52089300	-1.22058400	0.05099000
C	4.82454400	-1.06638000	1.24776200
C	3.43531100	-1.13099100	1.26277200
C	2.73315800	-1.35216000	0.07477100
C	4.82206100	-1.44478100	-1.13333400
H	6.60533700	-1.16839100	0.04158600
H	5.36461500	-0.89657000	2.17413000
H	2.88206200	-1.01927800	2.18972200
H	5.36017200	-1.57157000	-2.06768400
C	-5.52093000	-1.22049000	0.05088500
C	-4.82461400	-1.06629700	1.24767600
C	-2.73320100	-1.35212400	0.07475600
C	-3.43292000	-1.51035600	-1.12476500
C	-4.82206800	-1.44470800	-1.13342000
H	-6.60537300	-1.16827300	0.04144700
H	-5.36470900	-0.89646900	2.17402700
H	-2.87796700	-1.69096900	-2.03955600
H	-5.36015300	-1.57149300	-2.06778500
C	0.61977300	0.72067600	-0.24006700
C	-0.61982500	0.72070100	-0.23998300
C	1.88818800	1.47661500	-0.32048100
C	1.59371600	2.95918900	-0.60628000
H	1.10263500	3.04435600	-1.58219100
H	2.55055900	3.48941600	-0.69078800
C	0.75517600	3.61844900	0.46590900
C	-0.75489500	3.61849000	0.46608000
C	-1.59371500	2.95928800	-0.60592500
H	-1.10285000	3.04444300	-1.58194500
H	-2.55054700	3.48957200	-0.69020900
C	-1.88821500	1.47672500	-0.32009200
H	-2.53817600	1.06134800	-1.09764300
H	-2.43827000	1.37348700	0.62360400
H	2.43847000	1.37336600	0.62308000
H	2.53792300	1.06116300	-1.09818100

C	0.00014300	4.88577300	0.17451000
H	1.20123700	3.55743100	1.45741700
H	-1.20073600	3.55749600	1.45768900
H	0.00025000	5.68404200	0.90887900
H	0.00003400	5.22691700	-0.85824500
C	-3.43538200	-1.13093600	1.26273100
H	-2.88216100	-1.01922300	2.18969600
C	3.43291000	-1.51039800	-1.12472600
H	2.87800000	-1.69098300	-2.03954700

DFP-BCN adduct

C	-1.11267400	-0.73169400	-0.40532600
C	1.11267000	-0.73170000	-0.40533000
C	-0.00000200	-1.31455900	0.48687800
C	0.67507000	0.74335000	-0.41084400
F	0.00000300	-0.85851100	1.76078200
F	-0.00000500	-2.65561400	0.56911600
C	-0.67507000	0.74335300	-0.41083200
C	-5.20010100	-1.72277400	0.46132800
C	-4.33997200	-1.33083000	1.48447600
C	-3.01572800	-1.01401600	1.20089900
C	-2.53789400	-1.09112100	-0.11104000
C	-3.40203300	-1.48577500	-1.13372000
C	-4.72821300	-1.79837200	-0.84579300
H	-6.23389600	-1.96927200	0.68331700
H	-4.70007200	-1.27243000	2.50704300
H	-2.34601400	-0.71001900	1.99991500
H	-3.02497500	-1.55718800	-2.14830200
H	-5.39271000	-2.10611000	-1.64742200
C	5.20009300	-1.72278600	0.46133500
C	4.33996600	-1.33082100	1.48447700
C	3.01572500	-1.01400600	1.20089600
C	2.53788900	-1.09112900	-0.11104100
C	3.40202400	-1.48580400	-1.13371600
C	4.72820400	-1.79840300	-0.84578400
H	6.23388700	-1.96928600	0.68332700
H	4.70006800	-1.27240700	2.50704300
H	2.34601200	-0.70999300	1.99990800
H	3.02496600	-1.55723100	-2.14829600
H	5.39269900	-2.10615700	-1.64740900
C	-1.80155800	1.73821200	-0.48840800
C	1.80156000	1.73820400	-0.48844100
C	1.51640900	3.23225000	-0.59150500
H	2.42961200	1.43371700	-1.33826800
H	2.43715800	1.56653200	0.39222000
C	-1.51640500	3.23225700	-0.59147500
H	-2.42962700	1.43372800	-1.33822400
H	-2.43714100	1.56654000	0.39226500

C	-0.75164200	3.77667800	0.58976600
H	-2.48347700	3.74559400	-0.65960100
H	-0.99408400	3.45557000	-1.52663200
C	0.75167200	3.77667500	0.58975100
H	1.22577200	3.58566700	1.55078300
C	0.00001700	5.07290600	0.47015100
H	0.99407000	3.45556400	-1.52665200
H	2.48348200	3.74558400	-0.65965100
H	-1.22572400	3.58567200	1.55080700
H	0.00000800	5.55815000	-0.50306900
H	0.00002600	5.75637500	1.31221200
N	-0.61544200	-1.31227800	-1.72461700
N	0.61543300	-1.31230200	-1.72461000

DMP-BCN adduct

C	-1.16986500	-0.64434300	-0.37903300
C	1.03491900	-0.71898600	-0.42545600
C	-0.07038500	-1.30551900	0.51326100
C	0.65393200	0.76220800	-0.47676200
C	-0.01617300	-0.80699900	1.95397800
C	-0.12492900	-2.83329000	0.55537500
C	-0.69223100	0.79997200	-0.45846100
C	-5.25051400	-1.55218600	0.63844400
C	-4.51193200	-0.66273300	1.41522900
C	-3.19972300	-0.35920100	1.06761900
C	-2.60552900	-0.93825100	-0.05971300
C	-3.35274500	-1.83218000	-0.83095300
C	-4.66726000	-2.13373500	-0.48338600
H	-6.27565300	-1.78949700	0.90610200
H	-4.95796800	-0.20355100	2.29227700
H	-2.62543200	0.33501100	1.67672800
H	-2.89873200	-2.28126700	-1.70760100
H	-5.23803400	-2.82683900	-1.09418100
C	5.05449900	-2.00386700	0.42250600
C	4.44792300	-1.02570400	1.20606600
C	3.15698400	-0.59994800	0.91117400
C	2.45083700	-1.14143000	-0.16893100
C	3.06717500	-2.12476600	-0.94789000
C	4.36021500	-2.54989400	-0.65316100
H	6.06282700	-2.33685500	0.64876100
H	4.97968700	-0.59023900	2.04672900
H	2.68888100	0.16536800	1.52483200
H	2.53002400	-2.54685800	-1.79043700
H	4.82650700	-3.31261400	-1.26968700
C	-1.67660900	1.89152000	-0.75695400
C	1.68297200	1.85007400	-0.63926700
C	1.80273100	2.75823000	0.59595100
H	1.49750100	2.45179900	-1.53427000
H	2.65543200	1.37593400	-0.80150200

C	-1.08453200	3.25198500	-1.11440600
H	-2.37754000	2.01078700	0.08014600
H	-2.29606900	1.53164500	-1.59238100
C	-0.56281900	4.03519800	0.07123800
H	-1.87582100	3.85805700	-1.57236900
H	-0.31967600	3.13669800	-1.88648300
C	0.73833100	3.82216700	0.81326500
H	0.65241100	4.08767900	1.86496400
C	0.57398900	5.00173400	-0.10472300
H	2.77820800	3.26009400	0.56646300
H	1.81843700	2.11563000	1.48450900
H	-1.36812600	4.37646800	0.72050500
H	1.09237500	4.95162300	-1.06046000
H	0.51369700	5.99897300	0.31851100
H	-1.01520100	-3.14979100	1.10934700
H	-0.15776100	-3.29457900	-0.43292400
H	0.75562500	-3.21607700	1.08235400
H	-0.89301100	-1.16922100	2.50143800
H	0.86983200	-1.21967400	2.44888800
H	0.01631000	0.28246000	2.02662900
N	-0.73092400	-1.23924900	-1.73958500
N	0.49174000	-1.28096500	-1.76712200

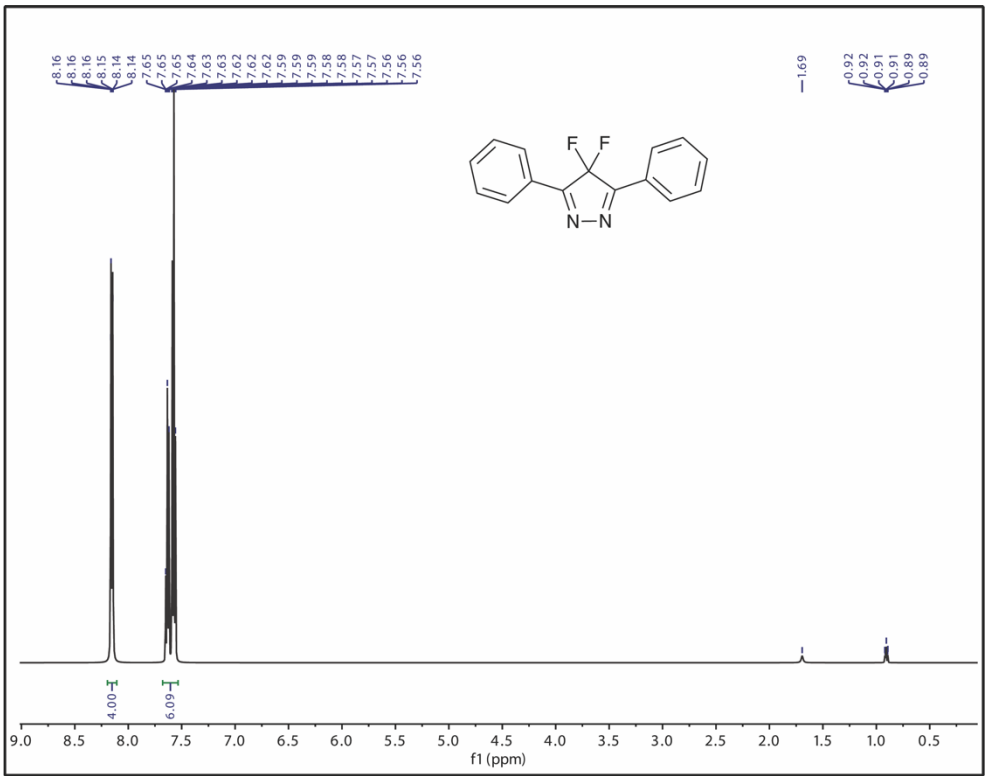
Tz-BCN adduct

C	0.86534300	2.70573700	0.57429800
C	-0.60024700	2.90719700	0.28367300
C	-1.12645200	2.75503600	-1.12463400
C	-1.56851200	1.30312700	-1.43196900
C	-0.70989100	0.24411200	-0.78084900
C	0.62898800	0.19093900	-0.78574900
C	1.53636500	1.18881900	-1.43934300
C	1.87440000	2.40388100	-0.52533600
H	-1.27590100	2.52741300	1.05020000
C	0.24977400	4.07562400	0.68996400
H	-1.98737000	3.41572100	-1.28107900
H	-0.35989400	3.08794600	-1.83281100
H	-2.59860900	1.17199500	-1.08958900
H	-1.59076800	1.14847900	-2.51858700
H	1.04499400	1.53761800	-2.35298800
H	2.46679000	0.70469900	-1.75143800
H	2.84547900	2.22752000	-0.05090800
H	2.00878200	3.28353200	-1.16518200
C	1.16230900	-0.91378900	0.08103800
N	0.54773000	-0.70285800	1.46308600
N	0.50242500	-2.19051100	-0.39196700
C	-1.30177000	-0.83879500	0.08452900
N	-0.71708500	-2.15302800	-0.39165100
N	-0.66839300	-0.66560800	1.46429100
C	-5.58263400	-0.99971700	0.30048700
C	-4.86524000	-0.27307200	1.24700300

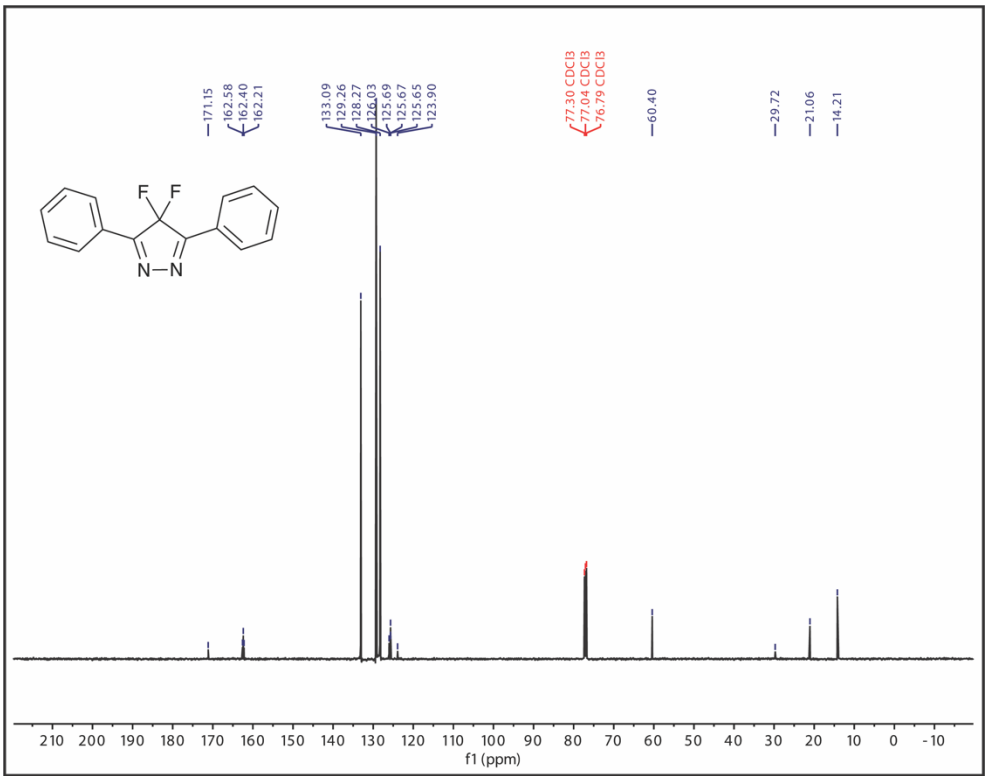
C	-3.47471800	-0.23638300	1.19433600
C	-2.79493400	-0.92810300	0.19098600
C	-3.51512700	-1.65477800	-0.75765900
C	-4.90497800	-1.69065700	-0.70118200
H	-6.66706600	-1.02909200	0.34415600
H	-5.38810000	0.26369700	2.03255900
H	-2.90974600	0.31800200	1.93719000
H	-2.98049600	-2.19721400	-1.53134600
H	-5.45925700	-2.26070400	-1.44041900
C	5.43614500	-1.22620100	0.25776200
C	4.72158400	-1.96586000	-0.68128900
C	3.33267600	-1.88580600	-0.72612300
C	2.65132500	-1.06387600	0.17209300
C	3.36842200	-0.32623500	1.11488300
C	4.75731900	-0.40719900	1.15617900
H	6.51942300	-1.29058800	0.29129600
H	5.24628400	-2.60907300	-1.38108700
H	2.76931400	-2.46534000	-1.45080200
H	2.83157600	0.29889100	1.82277700
H	5.30865800	0.16615200	1.89505200
H	1.06710600	2.19618400	1.51480200
H	0.10287100	4.50768600	1.67403600
H	0.51232000	4.79651600	-0.08073500
H	5.24628400	-2.60907300	-1.38108700
H	2.76931400	-2.46534000	-1.45080200
H	2.83157600	0.29889100	1.82277700
H	5.30865800	0.16615200	1.89505200
H	1.06710600	2.19618400	1.51480200

NMR Spectra

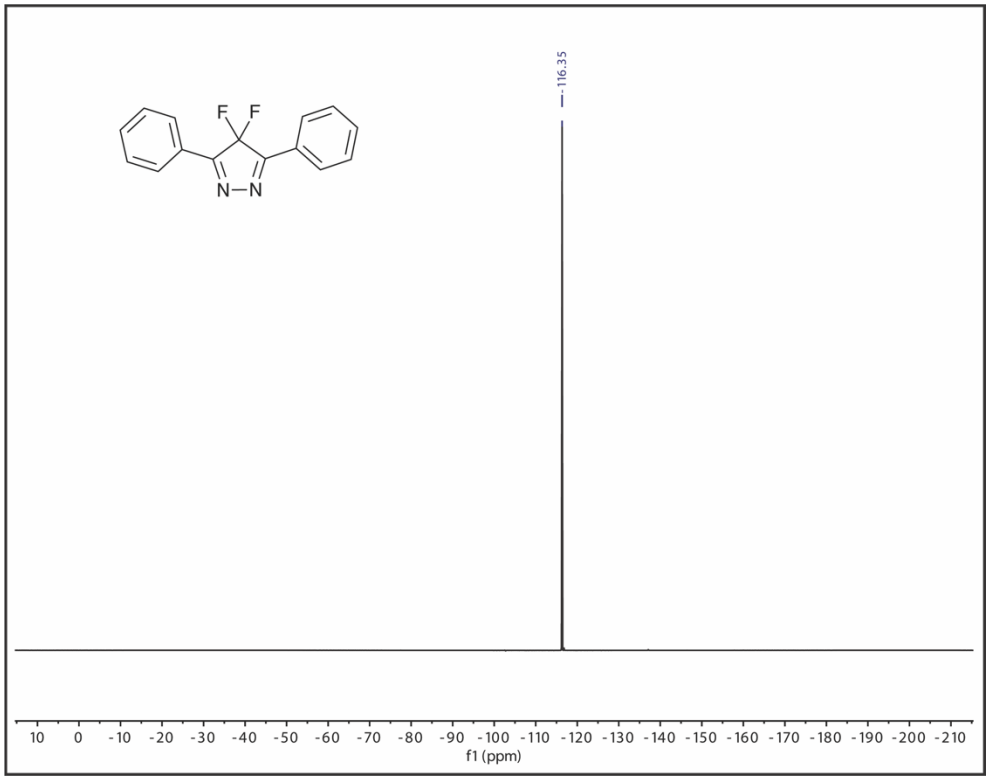
^{1}H NMR Spectrum of **DFP** in $CDCl_3$



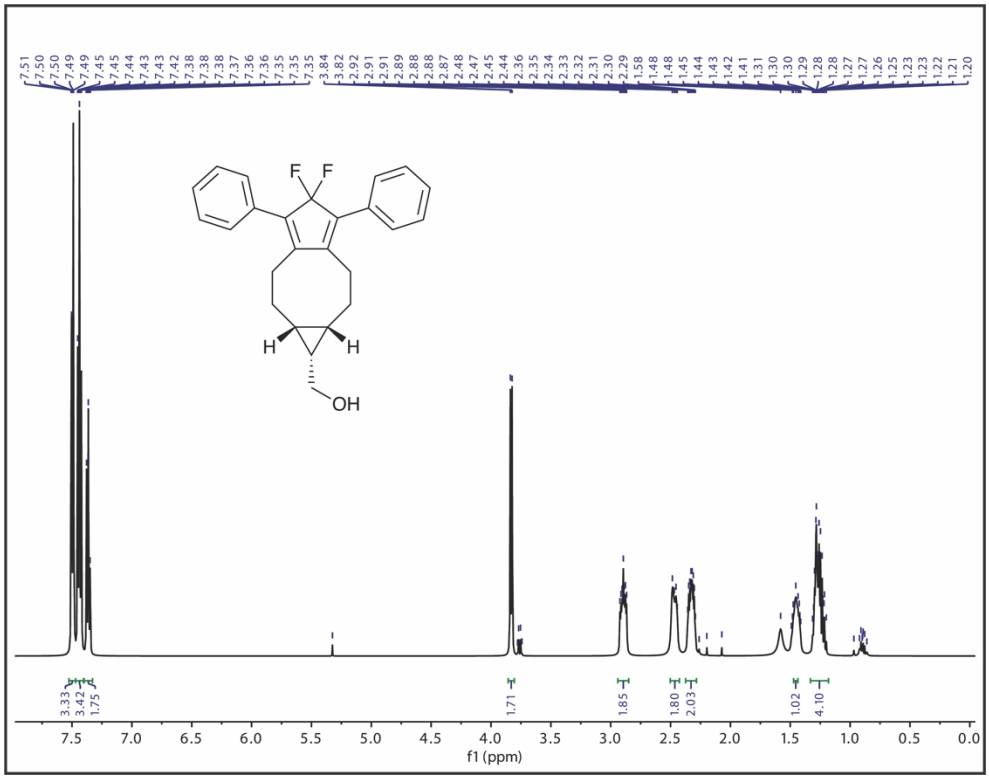
^{13}C NMR Spectrum of **DFP** in $CDCl_3$



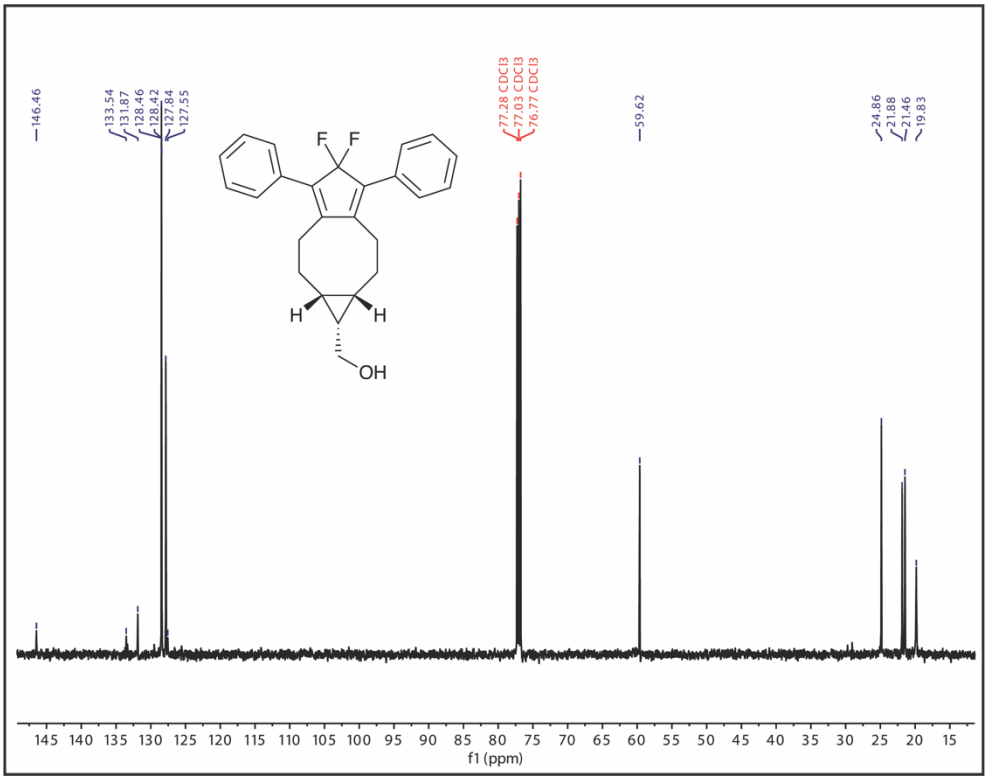
^{19}F NMR Spectrum of **DFP** in $CDCl_3$



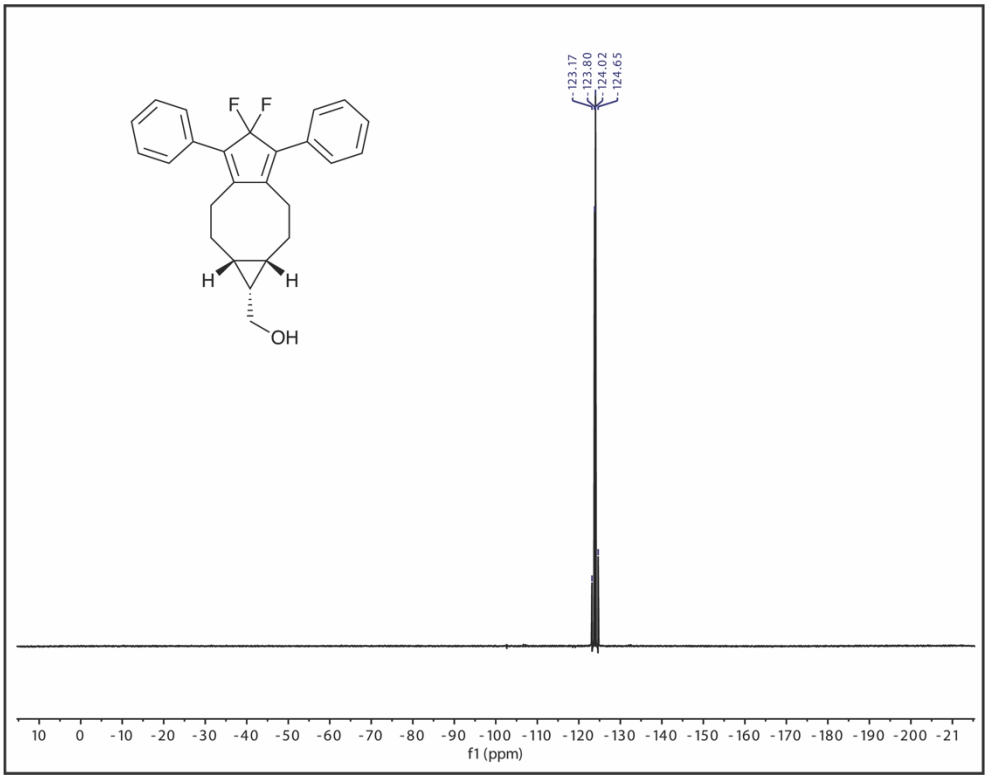
^{1}H NMR Spectrum of Diels–Alder Product in $CDCl_3$



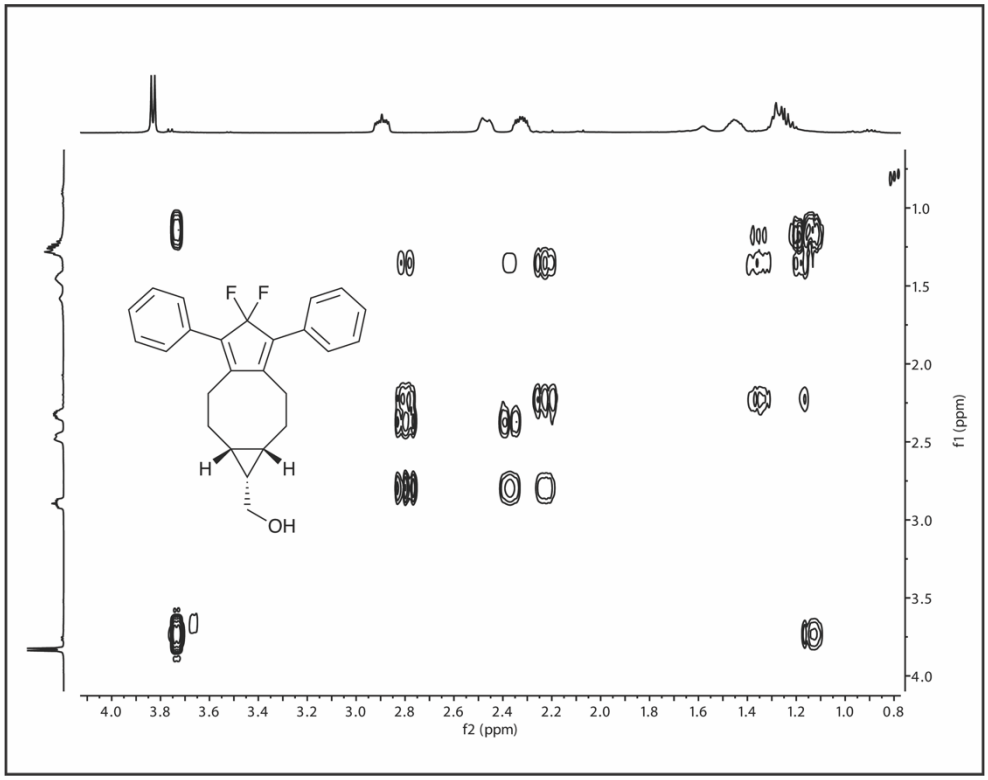
^{13}C NMR Spectrum of Diels–Alder Product in $CDCl_3$



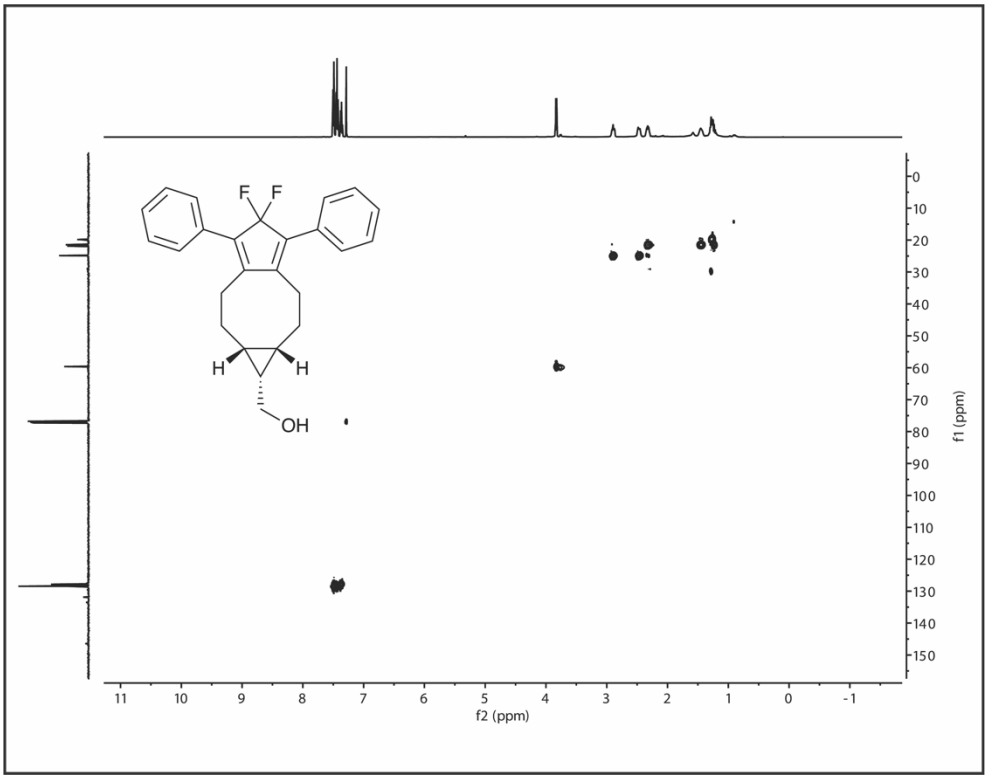
^{19}F NMR Spectrum of Diels–Alder Product in $CDCl_3$



COSY NMR Spectrum of Diels–Alder Product in $CDCl_3$



^{13}C–^{1}H HSQC NMR Spectrum of Diels–Alder Product in $CDCl_3$



^{1}H NMR Spectra of DMP, BCN and DMP + BCN After a 2-h Reaction