Electronic Supplementary Material (ESI) for CrystEngComm.

"A family of powerful halogen-bond donors: A structural and theoretical analysis of triply activated 3-iodo-1-phenylprop-2-yn-1-ones"

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Supplementary information

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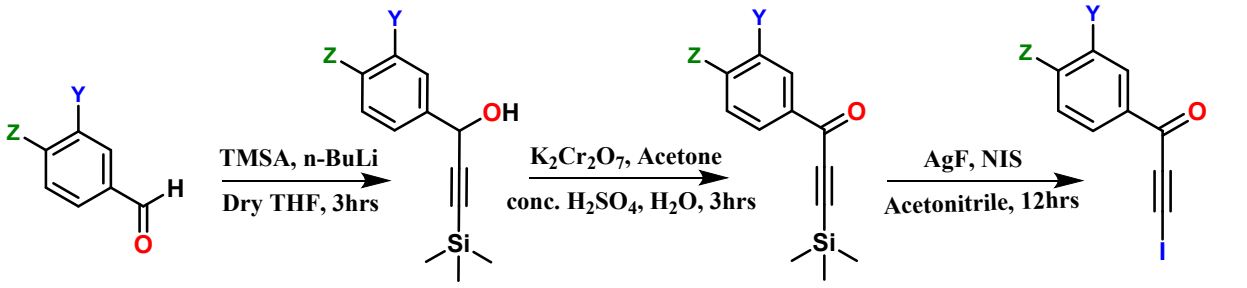
1 General Remarks

Commercial reagents were purchased as reagent–grade and used without further purification. All solvents utilized in this study were purchased commercially as technical grade and used as is without further purification. Targets were synthesized by modified versions of previously reported synthetic routes as described next. Melting points were measured using a TA Instruments DSC Q20 differential scanning calorimeter. Nuclear magnetic resonance (NMR) data were collected using either a Bruker Ascend 400 MHz spectrometer. The residual solvent peak was used as the internal reference for ^{1}H and ^{13}C NMR ($CDCl_3$: δH=7.26ppm, δC=77.16ppm). For the ^{19}F NMR spectra, the fluorine peak was referenced against the residual solvent peak in its corresponding ^{1}H spectrum (δH=7.26ppm). Target signals have been picked and labeled in all spectra, and have been integrated in ^{1}H spectra. IR stretches were obtained using a Nicolet 380 FT-IR spectrometer using an attenuated total reflection (ATR) technique and ZnSe as the crystal. Single crystal X-ray diffraction data were collected either using a Rigaku XtaLAB Synergy-S[1] (**4CN**, **3N**, **4N**) or Bruker Kappa APEX-II CCD[2] (**US**, **4F**, **3CN**) diffractometer. The structure was solved using Olex2[3] with the SHELXT[4] structure solution program using Intrinsic Phasing and refined with the SHELXL[5] refinement package using Least Squares minimization. Computational calculations were carried out using Spartan '14 software package. The σ-hole potentials were determined from the optimized geometries at B3LYP/6-311++G** level of theory with iso=0.002 e/au. To determine the interactions energies, the target-ammonia dimer geometries were first optimized at MP2/6-311++G** level of theory, following which a single-point energy calculation was carried out at the same level of theory to determine the counterpoise corrected interaction energies (ΔE) defined as ΔE = E(dimer complex) – [E(target) + E(ammonia)].

2 Synthetic procedures



US-I1	Y=H,	Z=H	US-I2	Y=H,	Z=H	US	Y=H,	Z=H
4F-I1	Y=H,	Z=F	4F-I2	Y=H,	Z=F	4F	Y=H,	Z=F
3CN-I1	Y=CN,	Z=H	3CN-I2	Y=CN,	Z=H	3CN	Y=CN,	Z=H
4CN-I1	Y=H,	Z=CN	4CN-I2	Y=H,	Z=CN	4CN	Y=H,	Z=CN
3N-I1	$Y=NO_2$,	Z=H	3N-I2	$Y=NO_2$,	Z=H	3N	$Y=NO_2$,	Z=H
4N-I1	Y=H,	$Z=NO_2$	4N-I2	Y=H,	$Z=NO_2$	4N	Y=H,	$Z=NO_2$

Scheme 1: Schematic showing the pathway used to synthesize the targets explored in this study

General synthetic procedure

Targets were synthesized using modified versions of previously reported synthetic procedures.[6-8]

Anhydrous THF (120ml) was added to an evacuated round bottom (RB) flask and cooled to −78°C in a dry ice/acetone bath under N_2 flow, to which trimethylsilylacetylene (TMSA, 1.5 Eq, 15mmol, 2.25ml) was added followed by slow dropwise addition of n-BuLi (1.5 Eq, 15mmol, 6ml of 2.5M in Hexanes). The mixture was stirred for 15 minutes, following which the corresponding aldehyde (10mmol) was slowly added dropwise, after which the mixture was continued stirring at −78°C for 3 hours to form the first intermediate, correspondingly substituted 1-phenyl-3-(trimethylsilyl)prop-2-yn-1-ols **(-I1).**

Since this intermediate was unstable, the subsequent Jones oxidation was carried out in-situ without isolating first intermediate. To the previous mixture still in cooling bath, acetone (60ml) was first added followed by $K_2Cr_2O_7$ (1.8 Eq, 12mmol, 3.530g), conc. H_2SO_4 (2ml) and water (60ml). After complete addition, RB is removed from the cooling bath and stirred at RT under N_2 flow for 3 hours to form the product. The crude mixture was first evaporated under reduced pressure to remove organic solvents, and the resulting aqueous mixture was extracted with chloroform (6X25ml), combined organic fractions dried with $MgSO_4$ and evaporated, and resulting residue was purified by column chromatography (Using hexanes, eluted with 5% EtOAc in Hexanes) to the give purified second intermediate, correspondingly substituted 1-phenyl-3-(trimethylsilyl)prop-2-yn-1-ones **(-I2)** in 73-82% yield.

Intermediate **-I2** from the previous reaction was dissolved in acetonitrile (50ml) in a RB covered in aluminum foil, to which silver(I)fluoride (AgF, 10mmol, 1.2687g) and N-iodosuccinimide (NIS, 10mmol, 2.250g) was added and the mixture stirred under N_2 flow for 12 hours to form the product. The crude mixture was evaporated under reduced pressure and the residue purified by column chromatography (Using dichloromethane, eluted with 100% dichloromethane). The appropriate fraction was collected and washed with water (4X25ml), aqueous sodium thiosulfate (1X25ml), brine (1X25ml) and dried with $MgSO_4$ and evaporated to yield purified final targets, correspondingly substituted 3-iodo-1-phenylprop-2-yn-1-ones in 60-84% yield.

2.1 1-phenyl-3-(trimethylsilyl)prop-2-yn-1-one (US-I2)

Yield: 77.7%. Bp: 128-130°C. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.14 (d, J = 7.4 Hz, 2H), 7.68 – 7.54 (m, 1H), 7.48 (t, J = 7.0 Hz, 2H), 0.32 (s, 9H). ^{13}C NMR (101 MHz, CDCl3) δ 177.80, 136.52, 134.29, 129.73, 128.67, 100.90, 100.69, -0.60. FTIR (cm^{-1}, ZnSe crystal): 2153 (C≡C).

2.2 3-iodo-1-phenylprop-2-yn-1-one (US)

Yield: 71.9%. Mp:143-145°C. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.12 (d, J = 7.7 Hz, 2H), 7.62 (t, J = 7.6 Hz, 1H), 7.48 (t, J = 7.7 Hz, 2H). ^{13}C NMR (101 MHz, CDCl3) δ 176.52, 136.15, 134.57, 129.90, 128.78, 94.01, 20.62. FTIR (cm^{-1}, ZnSe crystal): 2144 (C≡C)

2.3 1-(4-fluorophenyl)-3-(trimethylsilyl)prop-2-yn-1-one (4F-I2)

Yield: 73.1%. Bp: 143-145°C. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.15 – 8.12 (m, 2H), 7.13 (dd, J = 9.5, 7.7 Hz, 2H), 0.29 (s, 9H). ^{13}C NMR (101 MHz, CDCl3) δ 176.06, 167.82, 165.27, 133.06, 132.43, 132.33, 115.99, 115.77, 100.95, 100.57, -0.66. ^{19}F NMR (376 MHz, CDCl3) δ -103.09. FTIR (cm^{-1}, ZnSe crystal): 2153 (C≡C).

2.4 1-(4-fluorophenyl)-3-iodoprop-2-yn-1-one (4F)

Yield: 83.7%. Mp: 96-98°C. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.14 (ddd, J = 7.9, 5.4, 2.1 Hz, 2H), 7.16 (td, J = 8.7, 2.0 Hz, 2H). ^{13}C NMR (101 MHz, CDCl3) δ 174.88, 168.03, 165.47, 132.67, 132.58, 116.21, 115.99, 93.75, 20.82. ^{19}F NMR (376 MHz, CDCl3) δ -102.30. FTIR (cm^{-1}, ZnSe crystal): 2145 (C≡C).

2.5 3-(3-(trimethylsilyl)propioloyl)benzonitrile (3CN-I2)

Yield: 80.0%. Mp: 47-49.0°C. ^{1}H NMR (400 MHz, CDCl3) δ 8.35 (s, 1H), 8.31 (d, J = 7.9 Hz, 1H), 7.86 (d, J = 7.7 Hz, 1H), 7.62 (t, J = 7.8 Hz, 1H), 0.30 (s, 9H). ^{13}C NMR (101 MHz, CDCl3) δppm 175.26, 137.05, 136.89, 133.26, 133.15, 129.75, 117.73, 113.17, 103.02, 99.80, -0.79. FTIR (cm^{-1}, ZnSe crystal): 2152 (C≡C), 2230 (C≡N).

2.6 3-(3-iodopropioloyl)benzonitrile (3CN)

Yield: 72.5%. Mp: 126-128°C. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.36 (s, 1H), 8.31 (d, J = 8.0 Hz, 1H), 7.88 (d, J = 8.1 Hz, 1H), 7.64 (t, J = 7.8 Hz, 1H). ^{13}C NMR (101 MHz, CDCl3) δ 174.12, 137.14, 136.80, 133.42, 133.38, 129.88, 117.66, 113.27, 93.15, 24.16. FTIR (cm^{-1}, ZnSe crystal): 2146 (C≡C), 2239 (C≡N).

2.7 4-(3-(trimethylsilyl)propioloyl)benzonitrile (4CN-I2)

Yield: 80.1%. Mp: 75-77°C. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.18 (d, J = 7.4 Hz, 2H), 7.76 (d, J = 7.7 Hz, 2H), 0.29 (s, 8H). ^{13}C NMR (101 MHz, CDCl3) δ 175.82, 139.09, 132.45, 129.84, 117.80, 117.18, 103.04, 100.02, -0.82. FTIR (cm^{-1}, ZnSe crystal): 2154 (C≡C), 2229 (C≡N).

2.8 4-(3-iodopropioloyl)benzonitrile (4CN)

Yield: 66.9%. Decomp: 176-178°C. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.21 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 8.1 Hz, 1H). ^{13}C NMR (101 MHz, CDCl3) δ 174.73, 138.93, 132.62, 130.11, 117.82, 117.53, 93.49, 23.71. FTIR (cm^{-1}, ZnSe crystal): 2147 (C≡C), 2231 (C≡N).

2.9 1-(3-nitrophenyl)-3-(trimethylsilyl)prop-2-yn-1-one (3N-I2)

Yield: 81.5%. Mp: 55-57°C. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.94 (s, 1H), 8.44 (t, J = 7.3 Hz, 1H), 7.71 (t, J = 8.0 Hz, 1H), 0.34 (s, 9H). ^{13}C NMR (101 MHz, CDCl3) δ 175.22, 148.49,

137.74, 134.79, 130.03, 128.33, 124.65, 103.59, 99.93, -0.71. FTIR (cm^{-1}, ZnSe crystal): 2148 (C≡C), 1531 (-NO_2).

2.10 3-iodo-1-(3-nitrophenyl)prop-2-yn-1-one (**3N**)

Yield: 60.0%. Mp: 106-108°C. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.88 (s, 1H), 8.44 (dd, J = 12.3, 8.0 Hz, 2H), 7.72 (t, J = 8.0 Hz, 1H). ^{13}C NMR (101 MHz, CDCl3) δ 173.99, 148.50, 137.39, 135.08, 130.17, 128.58, 124.53, 93.31, 23.99. FTIR (cm^{-1}, ZnSe crystal): 2142 (C≡C), 1527 (-NO_2).

2.11 1-(4-nitrophenyl)-3-(trimethylsilyl)prop-2-yn-1-one (**4N-I2**)

Yield: 73.6%. Mp: 96-98°C. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.30 (q, J = 8.9 Hz, 4H), 0.33 (s, 7H). ^{13}C NMR (101 MHz, CDCl3) δ 175.68, 150.99, 140.60, 130.62, 123.91, 103.60, 100.19, 83.02, -0.70. FTIR (cm^{-1}, ZnSe crystal): 2154 (C≡C), 1523 (-NO_2).

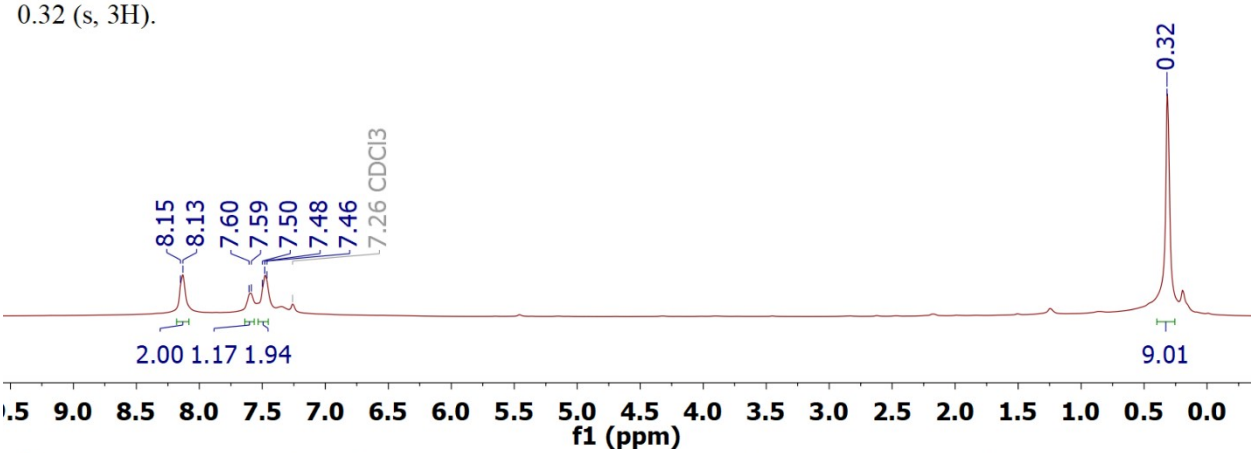
2.12 3-iodo-1-(4-nitrophenyl)prop-2-yn-1-one (**4N**)

Yield: 63.6%. Decomp: 189-191°C. ^{1}H NMR (400 MHz, Chloroform-d) δ 8.37 – 8.25 (m, 4H). ^{13}C NMR (101 MHz, CDCl3) δ 174.46, 151.16, 140.34, 130.82, 124.04, 93.65, 23.78. FTIR (cm^{-1}, ZnSe crystal): 2146 (C≡C), 1506 (-NO_2).

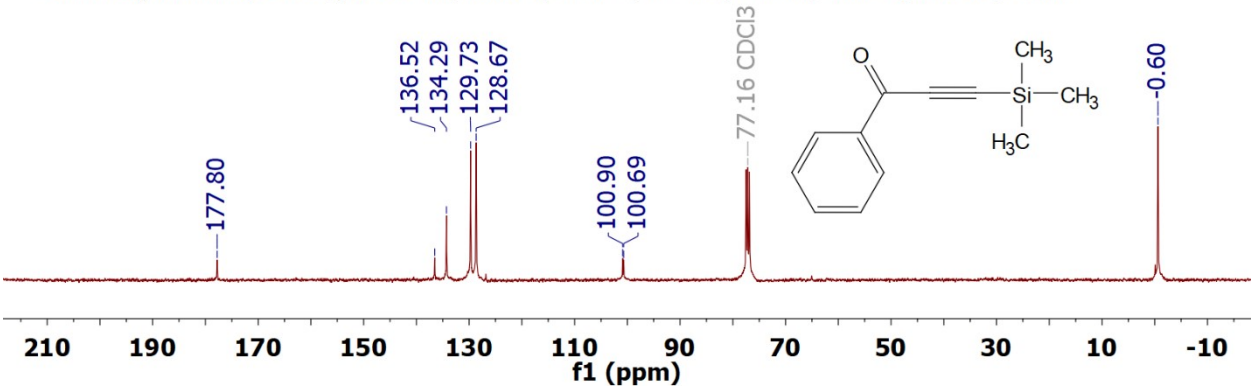
3 Spectral data

3.1 1-phenyl-3-(trimethylsilyl)prop-2-yn-1-one (US-I2)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 7.4 Hz, 1H), 7.68 – 7.54 (m, 1H), 7.48 (t, *J* = 7.0 Hz, 1H), 0.32 (s, 3H).

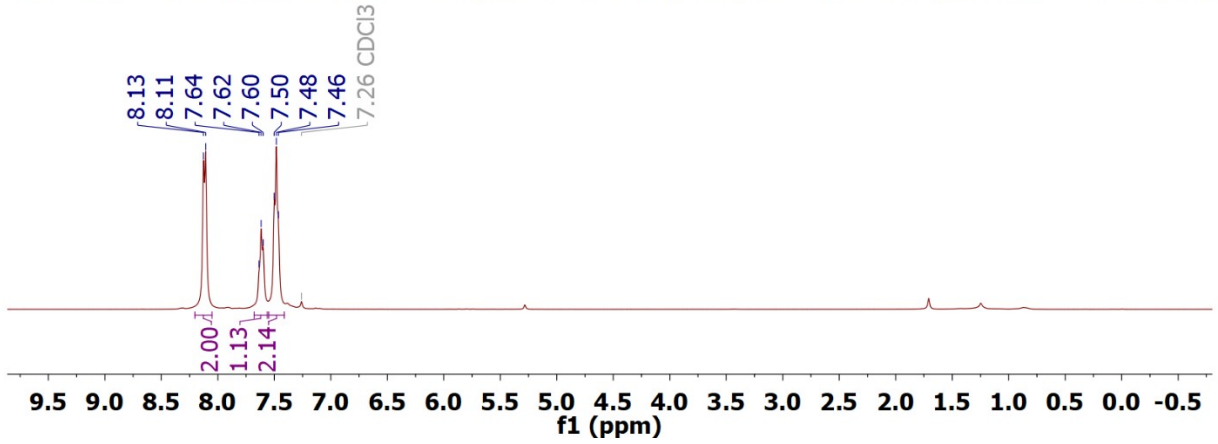


^{13}C NMR (101 MHz, $CDCl_3$) δ 177.80, 136.52, 134.29, 129.73, 128.67, 100.90, 100.69, -0.60.

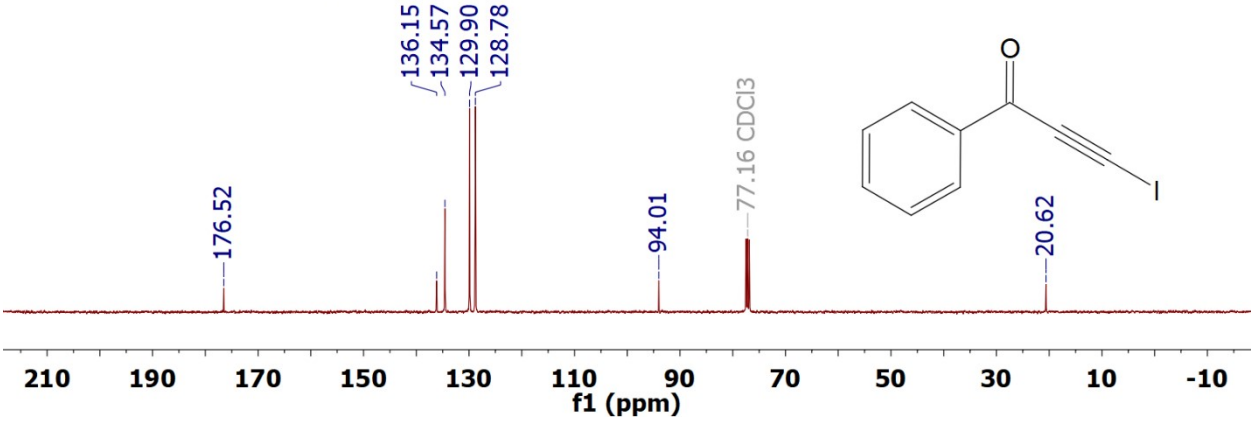


3.2 3-iodo-1-phenylprop-2-yn-1-one (US)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.12 (d, *J* = 7.7 Hz, 2H), 7.62 (t, *J* = 7.6 Hz, 1H), 7.48 (t, *J* = 7.7 Hz, 2H).

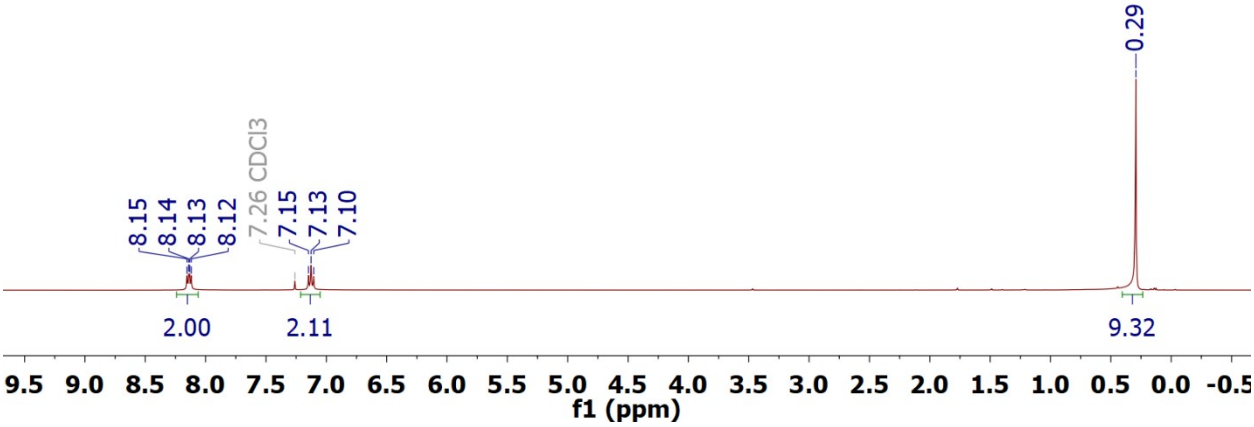


^{13}C NMR (101 MHz, $CDCl_3$) δ 176.52, 136.15, 134.57, 129.90, 128.78, 94.01, 20.62.

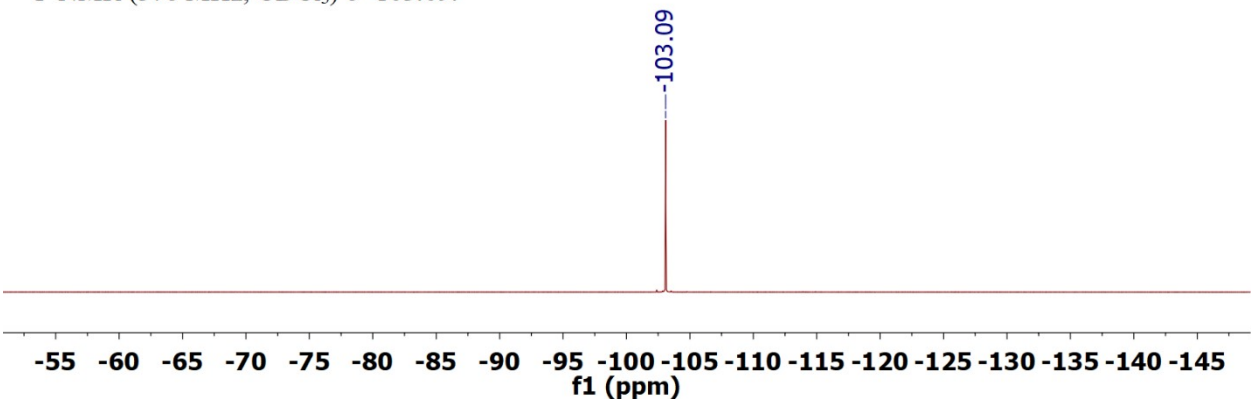


3.3 1-(4-fluorophenyl)-3-(trimethylsilyl)prop-2-yn-1-one (4F-I2)

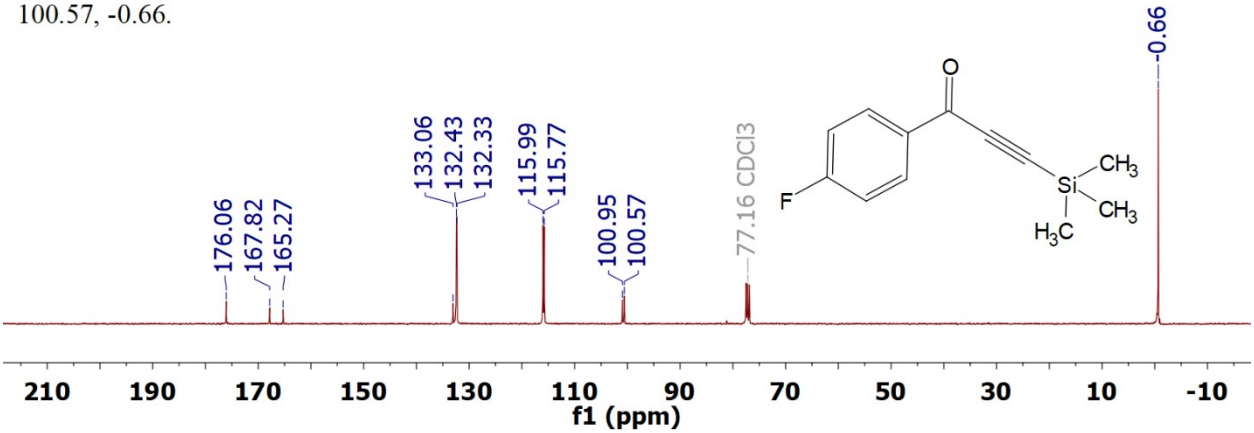
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 – 8.12 (m, 2H), 7.13 (dd, *J* = 9.5, 7.7 Hz, 2H), 0.29 (s, 9H).



^{19}F NMR (376 MHz, $CDCl_3$) δ -103.09.

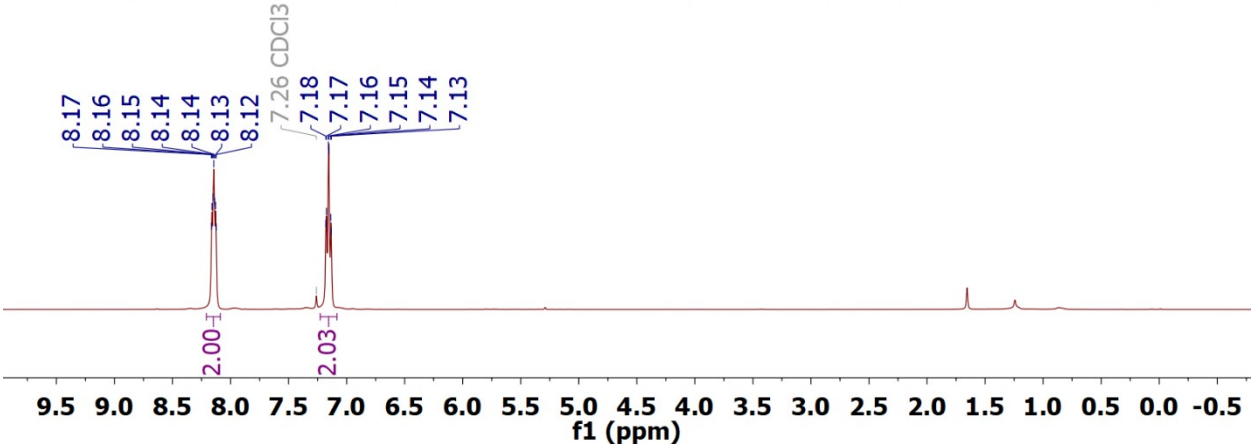


^{13}C NMR (101 MHz, $CDCl_3$) δ 176.06, 167.82, 165.27, 133.06, 132.43, 132.33, 115.99, 115.77, 100.95, 100.57, -0.66.

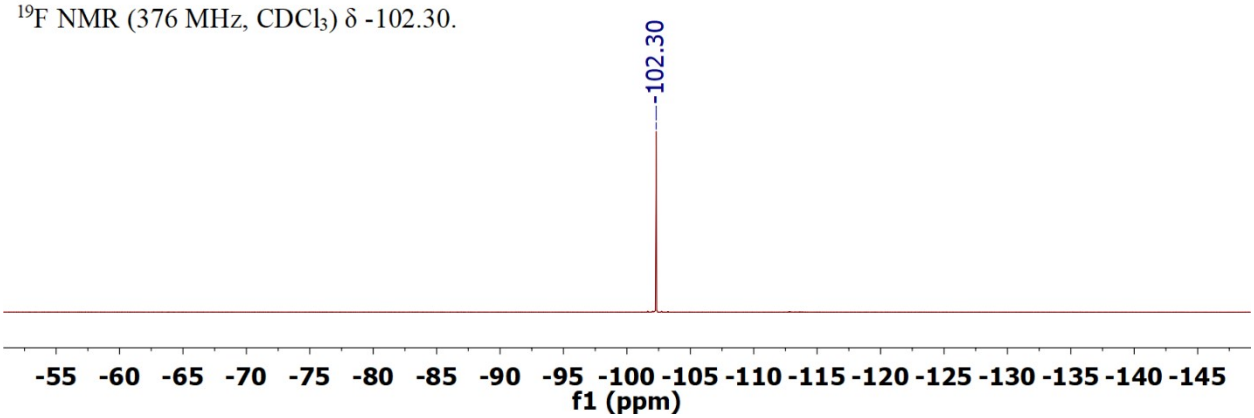


3.4 1-(4-fluorophenyl)-3-iodoprop-2-yn-1-one (**4F**)

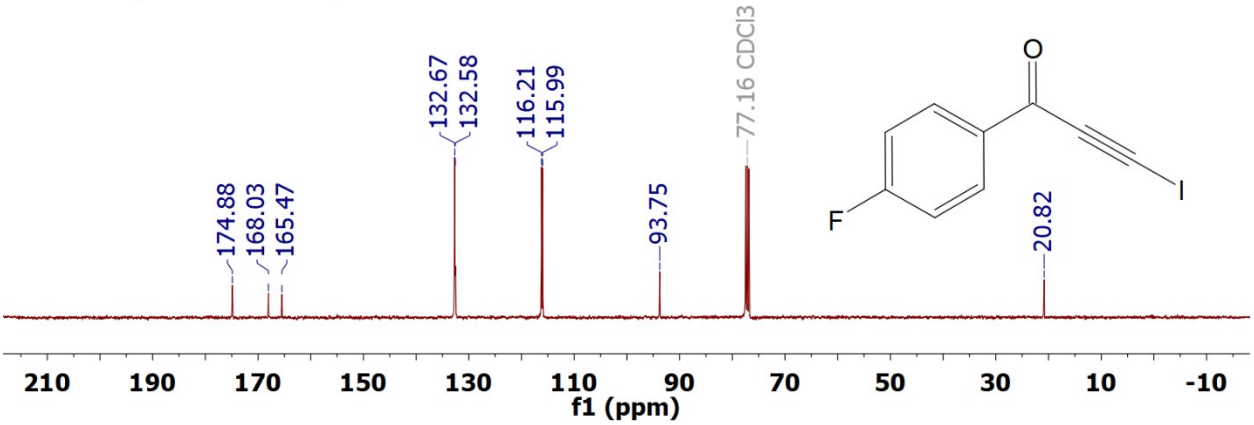
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (ddd, *J* = 7.9, 5.4, 2.1 Hz, 2H), 7.16 (td, *J* = 8.7, 2.0 Hz, 2H).



^{19}F NMR (376 MHz, $CDCl_3$) δ -102.30.

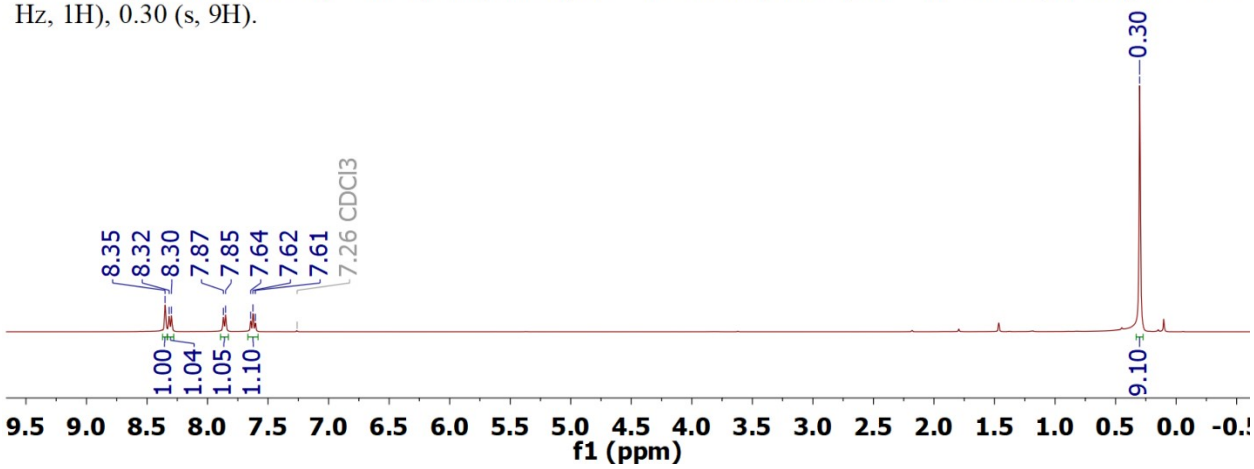


^{13}C NMR (101 MHz, $CDCl_3$) δ 174.88, 168.03, 165.47, 132.67, 132.58, 116.21, 115.99, 93.75, 20.82.

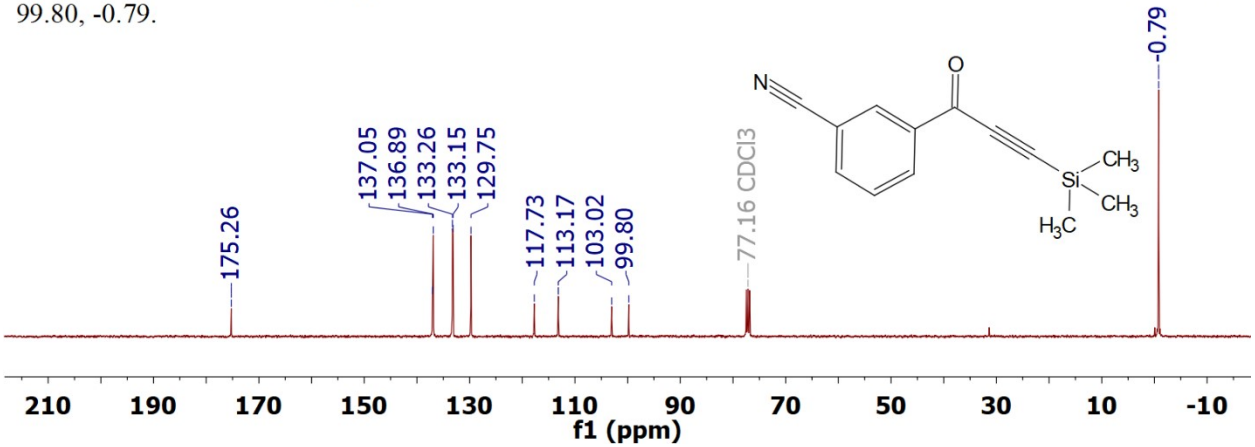


3.5 3-(3-(trimethylsilyl)propioloyl)benzonitrile (3CN-I2)

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.35 (s, 1H), 8.31 (d, J = 7.9 Hz, 1H), 7.86 (d, J = 7.7 Hz, 1H), 7.62 (t, J = 7.8 Hz, 1H), 0.30 (s, 9H).

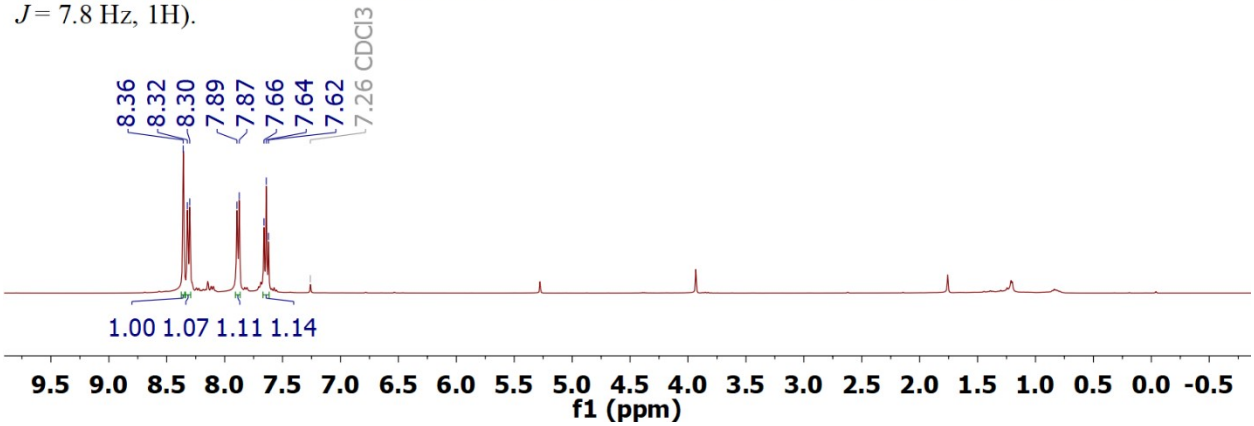


^{13}C NMR (101 MHz, $CDCl_3$) δppm 175.26, 137.05, 136.89, 133.26, 133.15, 129.75, 117.73, 113.17, 103.02, 99.80, -0.79.

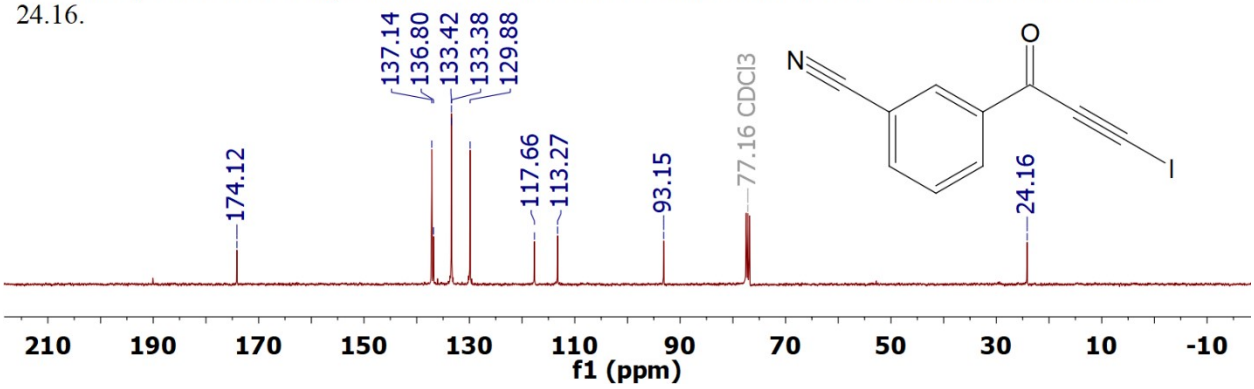


3.6 3-(3-iodopropioloyl)benzonitrile (3CN)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.36 (s, 1H), 8.31 (d, *J* = 8.0 Hz, 1H), 7.88 (d, *J* = 8.1 Hz, 1H), 7.64 (t, *J* = 7.8 Hz, 1H).

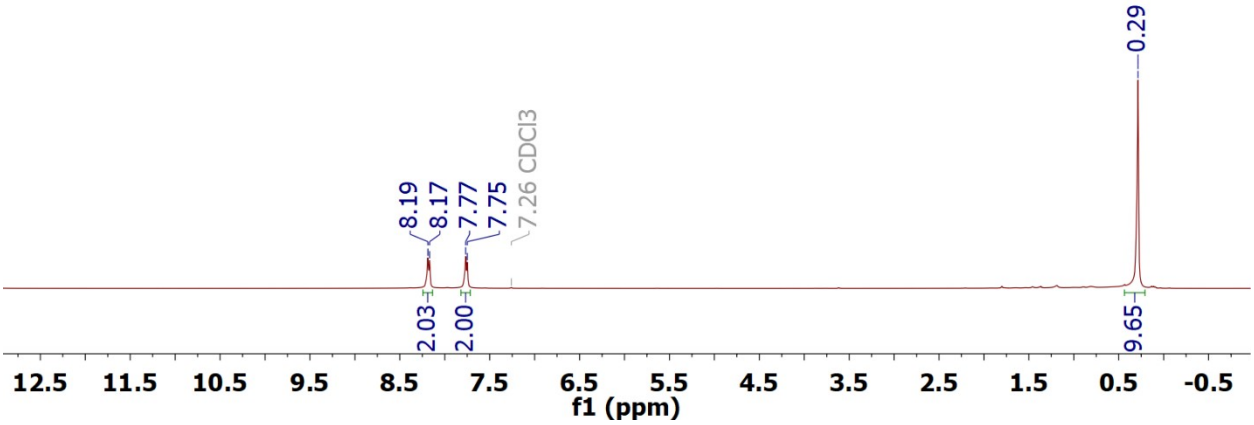


^{13}C NMR (101 MHz, $CDCl_3$) δ 174.12, 137.14, 136.80, 133.42, 133.38, 129.88, 117.66, 113.27, 93.15, 24.16.

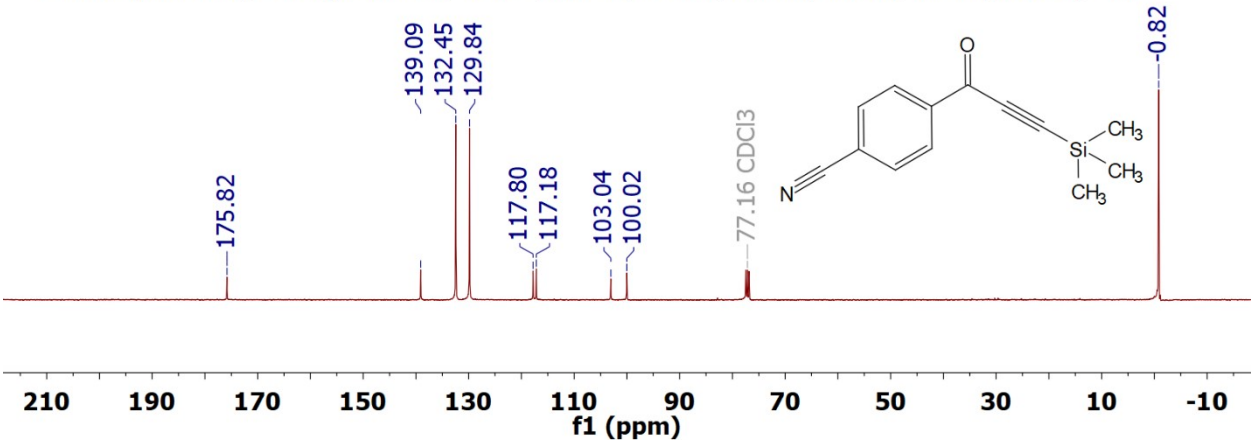


3.7 4-(3-(trimethylsilyl)propioloyl)benzonitrile (4CN-I2)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.18 (d, *J* = 7.4 Hz, 2H), 7.76 (d, *J* = 7.7 Hz, 2H), 0.29 (s, 8H).

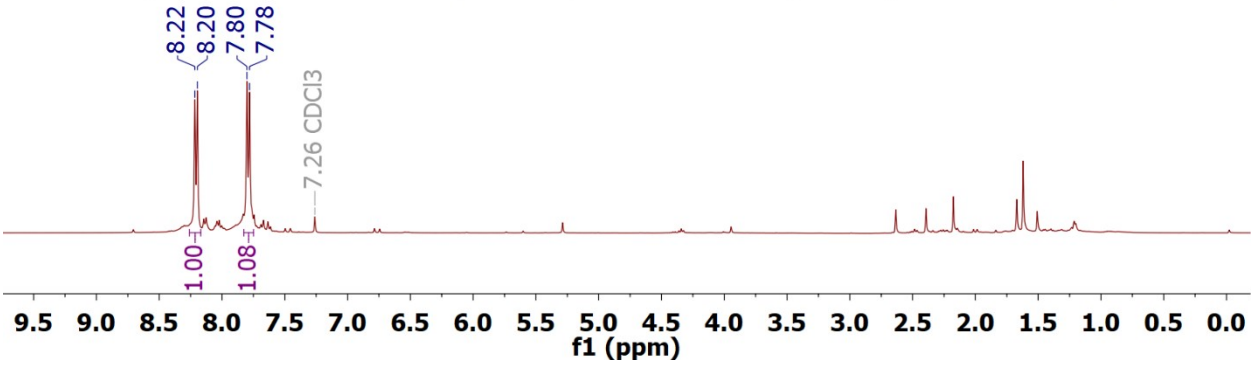


^{13}C NMR (101 MHz, $CDCl_3$) δ 175.82, 139.09, 132.45, 129.84, 117.80, 117.18, 103.04, 100.02, -0.82.

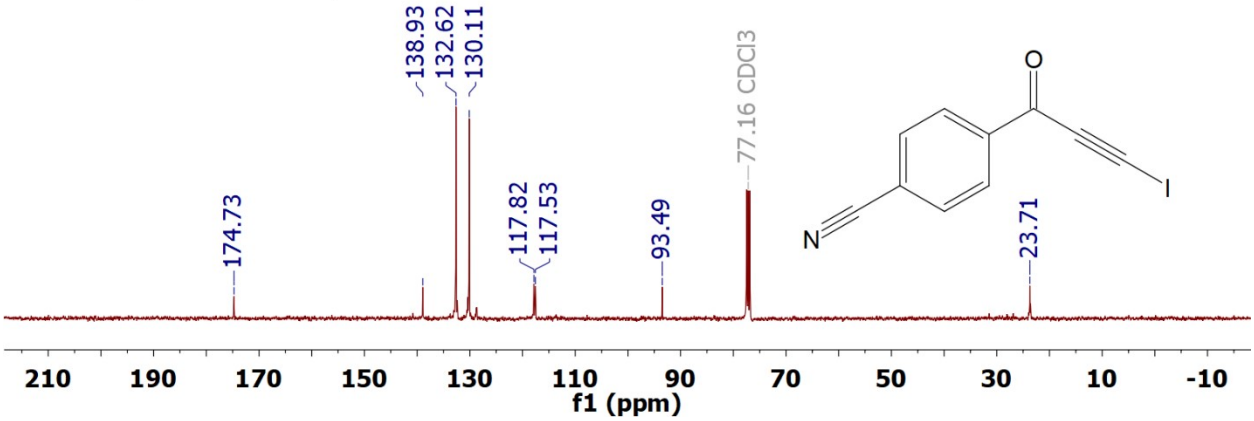


3.8 4-(3-iodopropioloyl)benzonitrile (4CN)

1H NMR (400 MHz, Chloroform-*d*) δ 8.21 (d, *J* = 8.0 Hz, 1H), 7.79 (d, *J* = 8.1 Hz, 1H).

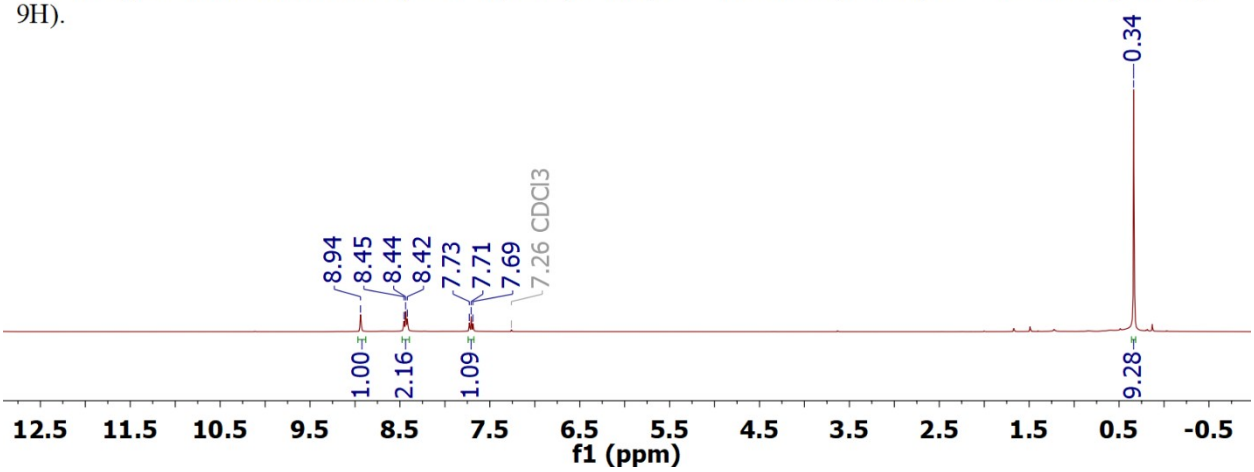


^{13}C NMR (101 MHz, $CDCl_3$) δ 174.73, 138.93, 132.62, 130.11, 117.82, 117.53, 93.49, 23.71.

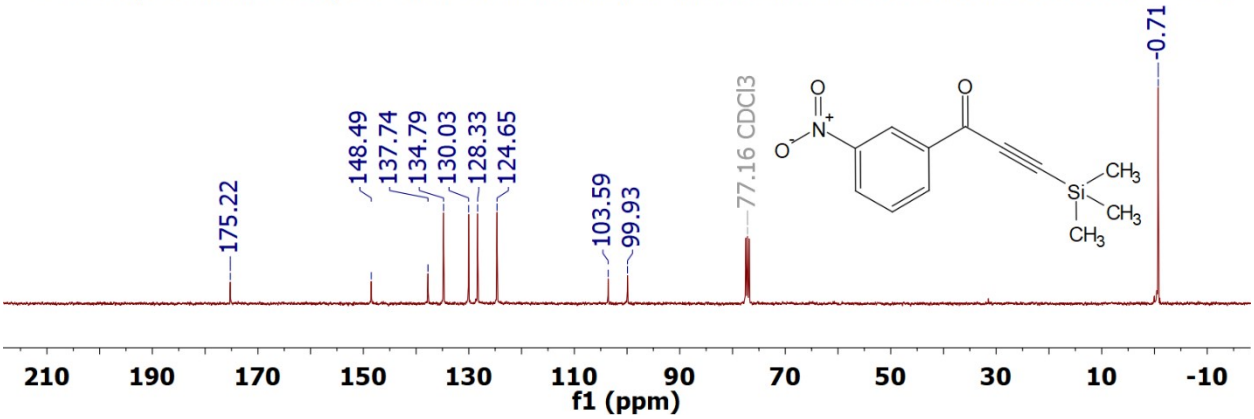


3.9 1-(3-nitrophenyl)-3-(trimethylsilyl)prop-2-yn-1-one (3N-I2)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.94 (s, 1H), 8.44 (t, *J* = 7.3 Hz, 1H), 7.71 (t, *J* = 8.0 Hz, 1H), 0.34 (s, 9H).

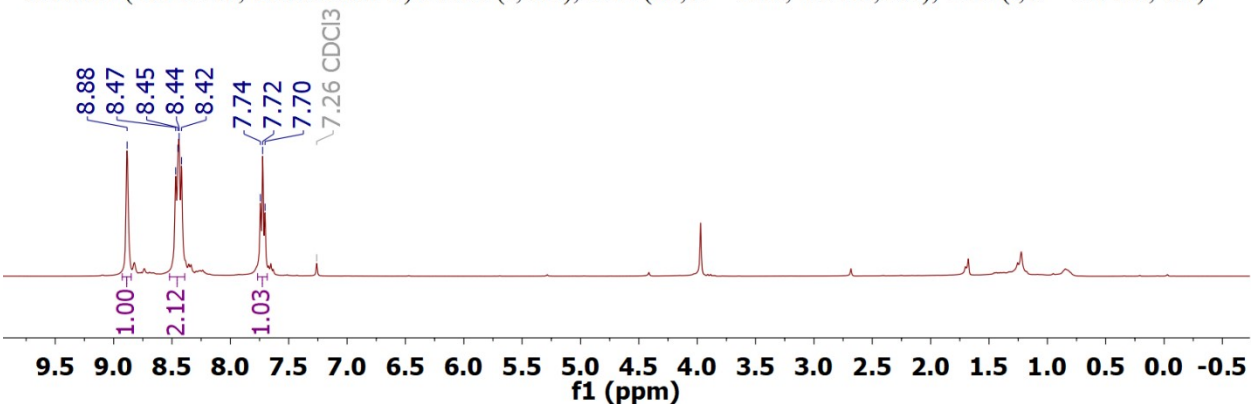


^{13}C NMR (101 MHz, $CDCl_3$) δ 175.22, 148.49, 137.74, 134.79, 130.03, 128.33, 124.65, 103.59, 99.93, -0.71.

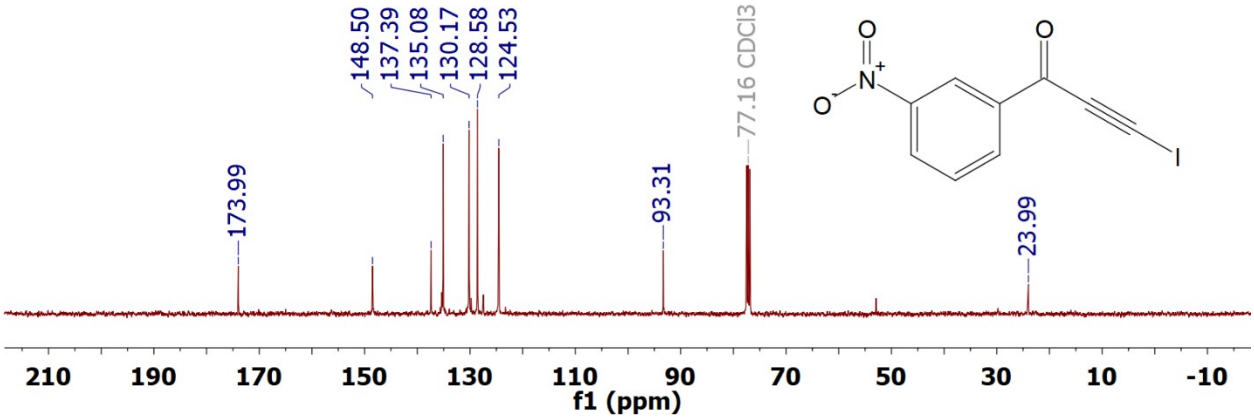


3.10 3-iodo-1-(3-nitrophenyl)prop-2-yn-1-one (3N)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.88 (s, 1H), 8.44 (dd, *J* = 12.3, 8.0 Hz, 2H), 7.72 (t, *J* = 8.0 Hz, 1H).

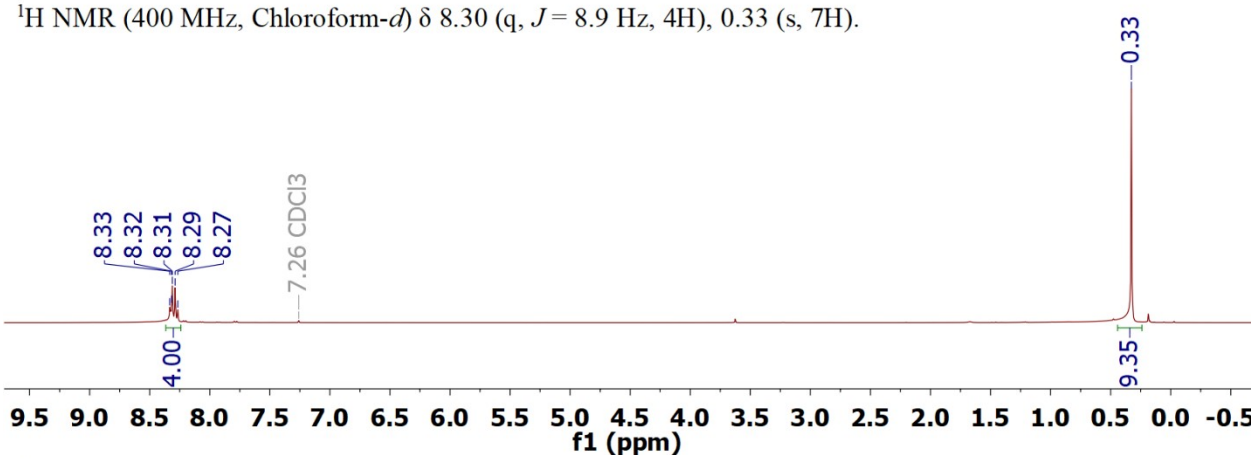


^{13}C NMR (101 MHz, $CDCl_3$) δ 173.99, 148.50, 137.39, 135.08, 130.17, 128.58, 124.53, 93.31, 23.99.

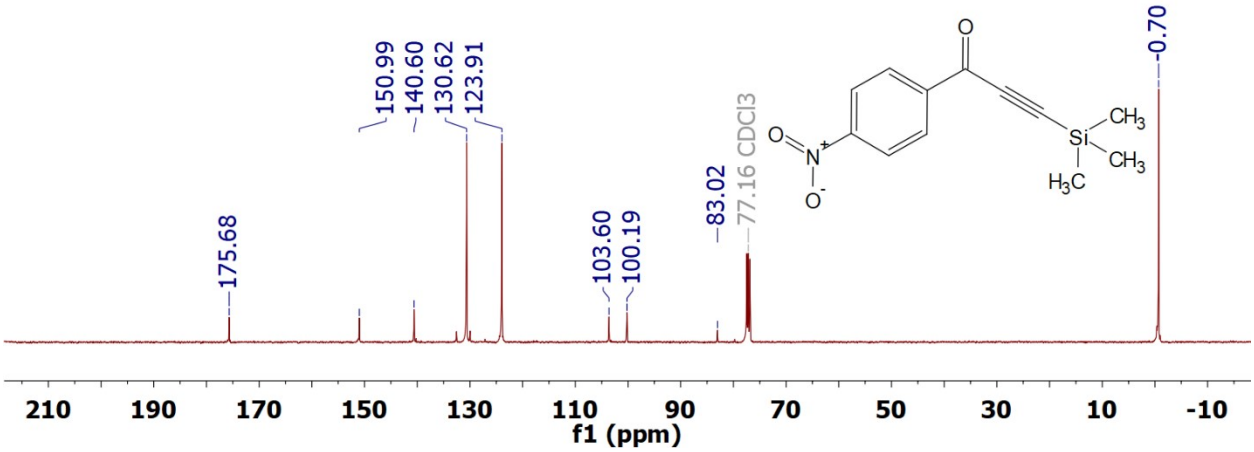


3.11 1-(4-nitrophenyl)-3-(trimethylsilyl)prop-2-yn-1-one (4N-I2)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.30 (q, *J* = 8.9 Hz, 4H), 0.33 (s, 7H).

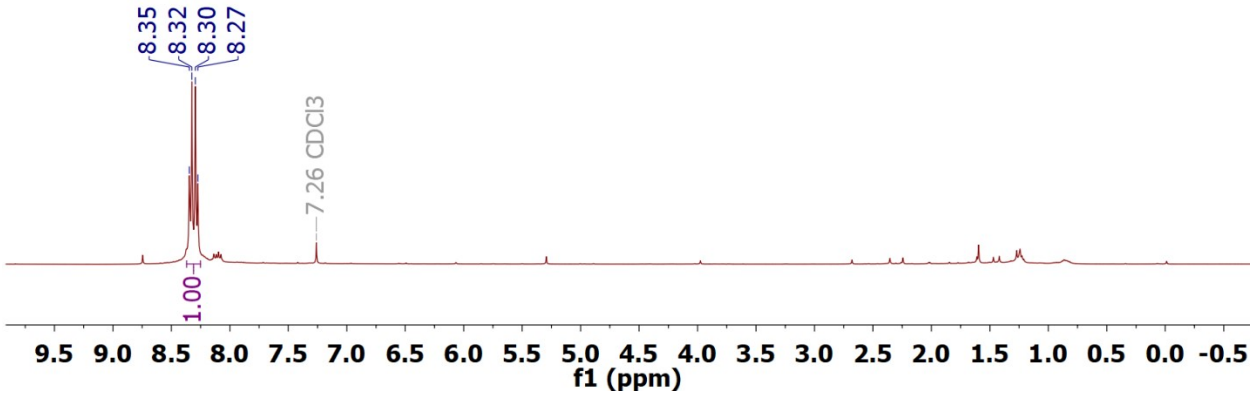


^{13}C NMR (101 MHz, $CDCl_3$) δ 175.68, 150.99, 140.60, 130.62, 123.91, 103.60, 100.19, 83.02, -0.70.

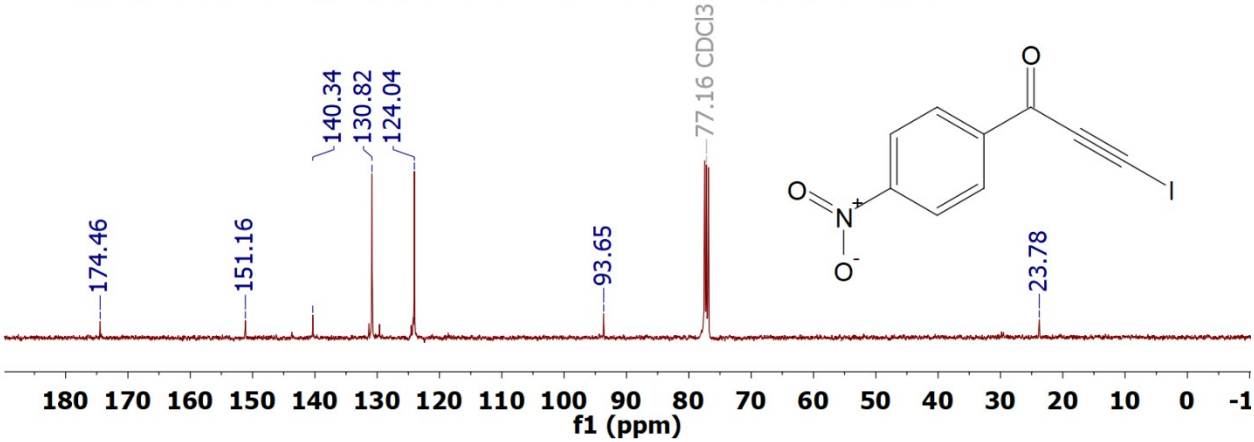


3.12 3-iodo-1-(4-nitrophenyl)prop-2-yn-1-one (**4N**)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.37 – 8.25 (m, 4H).



^{13}C NMR (101 MHz, $CDCl_3$) δ 174.46, 151.16, 140.34, 130.82, 124.04, 93.65, 23.78.



4 Crystallographic information

Table S1. Crystallographic information of targets explored in this study

Target code	**US**	**4F**	**3CN**	**4CN**	**3N**	**4N**
CCDC Number	2110111	2110113	2110114	2110094	2110098	2110093
Systematic name	3-iodo-1-phenylprop-2-yn-1-one	1-(4-fluorophenyl)-3-iodoprop-2-yn-1-one	1-(3-cyanophenyl)-3-iodoprop-2-yn-1-one	1-(4-cyanophenyl)-3-iodoprop-2-yn-1-one	1-(3-nitrophenyl)-3-iodoprop-2-yn-1-one	1-(4-nitrophenyl)-3-iodoprop-2-yn-1-one
Formula moiety	C_9H_5IO	C_9H_4FIO	$C_{10}H_4INO$	$C_{10}H_4INO$	$C_9H_4INO_3$	$C_9H_4INO_3$
Empirical formula	C_9H_5IO	C_9H_4FIO	$C_{10}H_4INO$	$C_{10}H_4INO$	$C_9H_4INO_3$	$C_9H_4INO_3$
Molecular weight	256.04	274.03	281.04	281.04	301.04	301.04

Solvent used for crystallization	Dioxane	Dioxane	Dioxane	Dioxane	THF	Dioxane
Color, Habit	Colorless, Chunk	Colorless, Block	Colorless, Thin plate	Colorless, Plate	Clear pale colorless, Block	Clear light colorless, Plate
Crystal system	Monoclinic	Tetragonal	Tetragonal	Monoclinic	Triclinic	Monoclinic
Space group, Z	$P2_1/c$, 4	I-4, 8	P -1, 2	$P2_1/c$, 4	P -1, 4	$P2_1/c$, 4
a, Å	10.0763(2)	19.4398(5)	5.6138(3)	4.06532(16)	6.8676(9)	4.0639(1)
b, Å	11.2448(2)	19.4398(5)	7.8625(4)	24.0246(11)	11.0423(10)	23.333(1)
c, Å	7.2619(2)	5.05770(10)	11.1133(5)	9.7176(4)	13.0715(11)	10.0221(4)
α, º	90	90	104.330(2)	90	82.581(7)	90
β, º	91.0130(10)	90	96.117(2)	96.002(4)	74.932(9)	93.341(3)
γ, º	90	90	94.399(3)	90	77.837(9)	90
Volume, Å^3	822.69(3)	1911.33(11)	469.84(4)	943.89(7)	932.79(18)	948.71(6)
Density, g/cm^3	2.067	1.905	1.987	1.978	2.144	2.108
T, ºK	200.(2)	200.(2)	200.(2)	100.02(19)	100.15	170.01(10)
Crystal size, min x mid x max	0.065 × 0.055 × 0.04	0.11 × 0.1 × 0.1	0.030 x 0.080 x 0.135	0.036 X 0.127 X 0.153	0.09 X 0.11 X 0.12	0.069 X 0.129 X 0.151
X-ray wavelength, Å	1.54178	1.54184	1.54184	1.54184	0.71073	0.71073
μ, mm^{-1}	30.056	26.082	26.425	26.308	3.410	3.353
Trans min / max	0.25 / 0.38	0.16 / 0.18	0.13 / 0.50	0.43858 / 1.00	0.647 / 1.00	0.41985 / 1.00
θ_{min}, º	4.39	4.55	4.14	3.680	2.586	2.21
θ_{max}, º	69.83	70.32	70.02	72.120	26.369	33.58
Reflections						
collected	5730	4548	6165	2731	10762	11750
independent	1501	1611	1643	2731	3815	3206
observed	1416	1557	1566	2644	3414	2656
R_{int}	0.0270	0.0538	0.0491	0.095	0.0415	0.0262
Threshold expression	> 2$\sigma(I)$	> 2$\sigma(I)$	> 2$\sigma(I)$	> 2$\sigma(I)$	> 2$\sigma(I)$	> 2$\sigma(I)$
No. parameters	100	111	118	119	489	128
No. restraints	0	0	0	0	478	0
R_1 (observed)	0.0265	0.0390	0.0392	0.0429	0.0539	0.0345
wR_2 (all)	0.0687	0.1006	0.1053	0.1271	0.1193	0.0835
Goodness of fit (all)	1.061	1.028	1.041	1.105	1.106	1.0409
ρ_{max}, ρ_{min}, e Å^{-3}	1.04/-1.19	1.19/-1.26	1.144, -0.992	1.532, -0.717	1.485, -1.378	1.8023, -1.3657
Completeness to 2θ limit	0.963	0.967	0.922	0.997	0.995	0.8529

5 References:

1. We acknowledge the NSF-MRI grant CHE-2018414, which was used to purchase the single-crystal X-ray diffractometer and associated software employed in this study.
2. We acknowledge the NSF-MRI grant CHE-0923449, which was used to purchase the single-crystal X-ray diffractometer and associated software employed in this study
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