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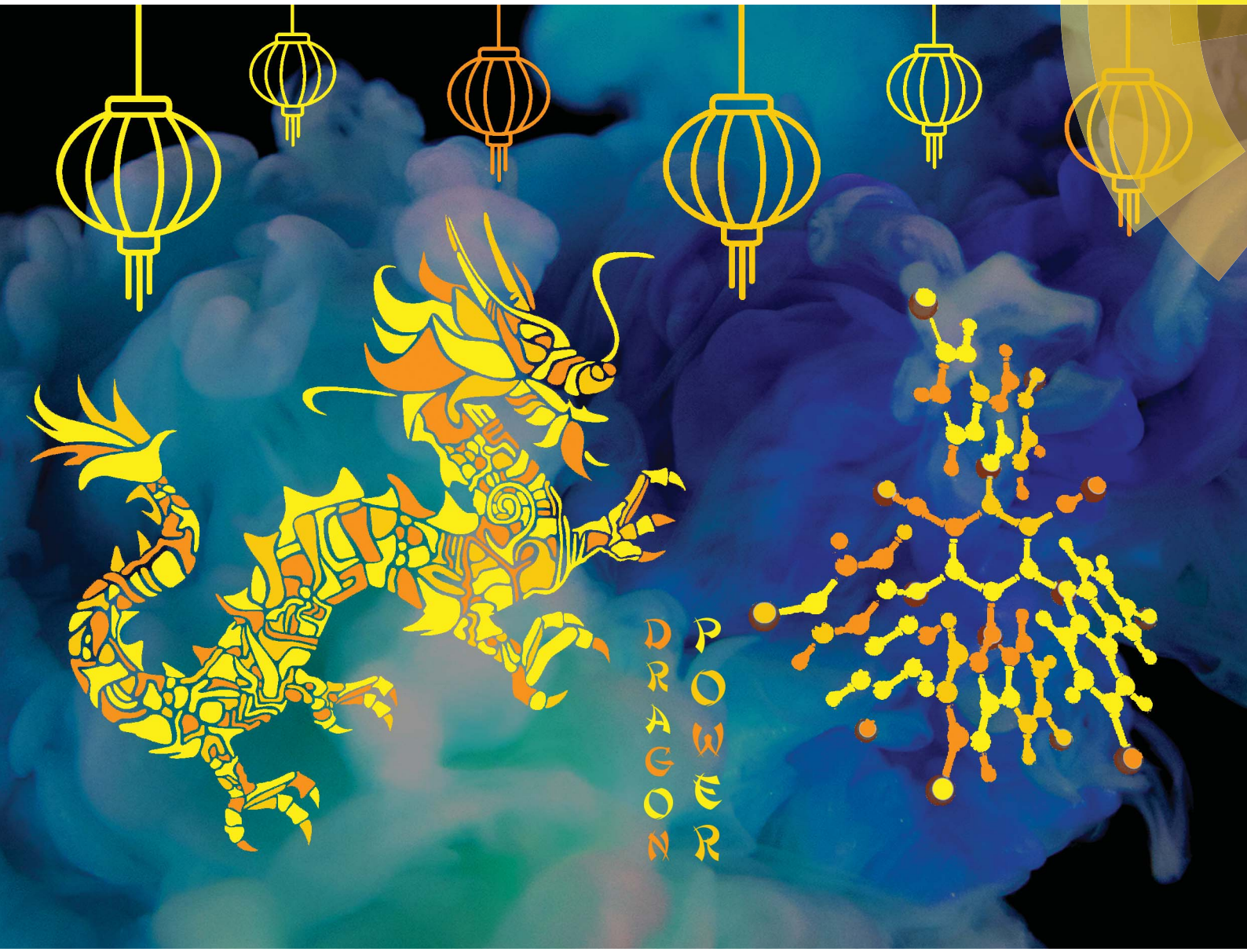

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Fine-tuned organic photoredox catalysts for fragmentation-alkynylation cascades of cyclic oxime ethers†

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Fine-tuned organic photoredox catalysts are introduced for the metal-free alkynylation of alkylnitrile radicals generated *via* oxidative ring opening of cyclic alkylketone oxime ethers. The redox properties of the dyes were determined by both cyclic voltammetry and computation and covered an existing gap in the oxidation potential of photoredox organocatalysts.

1. Introduction

Cascade reactions leading to several bond forming/bond breaking events are important tools to access efficiently the complex carbon skeleton of organic compounds.[1] Single electron chemistry is well suited for cascade transformations due to the high reactivity of radical intermediates combined with neutral reaction conditions.[2] However, many radical-based cascade reactions still require the stoichiometric use of toxic reagents, such as tin hydrides and/or harsh reaction conditions. In the last decade, visible light driven photoredox catalysis has emerged as a general method for radical generation under mild oxidative or reductive conditions without the need for toxic reagents.[3] First successes were met with metal complexes as catalysts.[4] More recently organic dyes have been introduced, as they are often cheap, non-toxic and easy to modify.[5]

In the case of reductive quenching cycles for the generation of radical by oxidation, the reduction potential of the photoactivated catalyst is an essential parameter (Fig. 1). The reduction potential of the most often used iridium catalyst ($Ir[dF(CF_3)ppy]_2(dtbbpy))PF_6$ (**1**) (+1.21 V *vs.* SCE in MeCN)[6] is lower than frequently used organic dyes, such as Fukuzumi dye (**2**) and dicyanoanthracene (**3**) (+2.06 V *vs.* SCE in MeCN).[5,7] To enrich the range of transformations available to organic catalysts, using dyes with lower oxidation values would be highly desirable.

In this context, 2,4,5,6-tetra(9*H*-carbazol-9-yl)isophthalonitrile (4CzIPN, **4a**) has emerged as an alternative organic dye with a lower reduction potential (+1.35 V *vs.* SCE in MeCN).[8] Nevertheless, there is a need for further catalysts with reduction

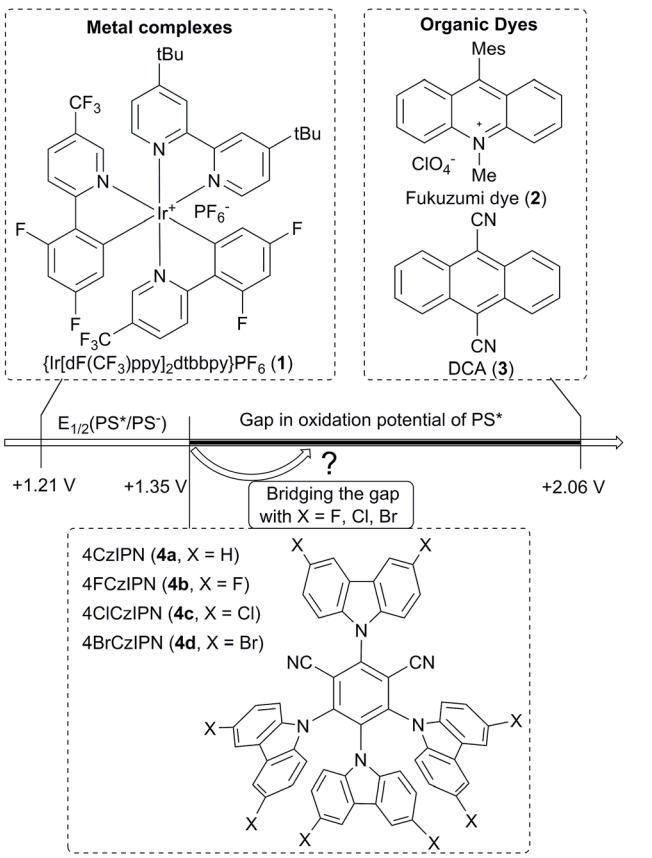

Fig. 1 Bridging the gap in the reduction potential of activated organic photocatalysts.

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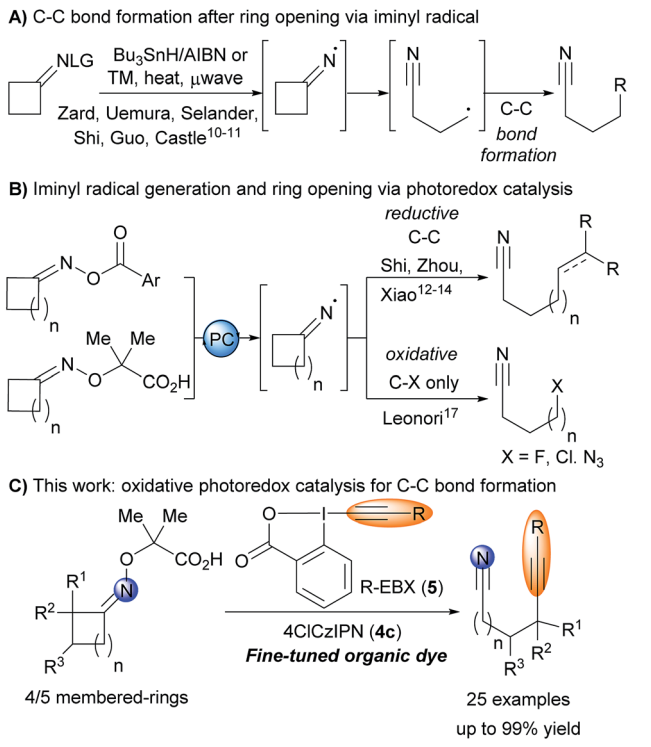
potentials between +1.4 V and + 2.0 V to allow challenging transformations asking for efficient oxidation.

In this context, heteroatom centered radicals initiated transpositions have found widespread applications in synthetic chemistry.[9] Zard and coworkers developed iminyl radical initiated cascades using tin reagents and electrophilic olefins to trap the generated intermediate (Scheme 1A).[10] Transition metal catalysis (Pd, Ir, Fe) and/or heating at temperature higher than 90 °C were later reported to avoid the use of tin reagents.[11] In 2017, Shi and co-workers described one single example of a Heck-like coupling at room temperature under photoredox conditions (Scheme 1B).[12] After Shi's pioneering example, Xiao and coworkers developed in 2018 a general method for C–C bond formation after reductive cleavage of cycloalkyloxime esters for the introduction of both alkanes and alkenes.[13] Zhou and coworkers reported a multicomponent alkylation etherification of alkenes using a similar strategy.[14] These breakthroughs greatly enhanced the synthetic potential of fragmentation cascades, but the exclusive use of reductive conditions limited the types of bond formations possible.

Recently, Studer and coworkers[15] and Leonori and coworkers[16] independently reported a new approach for the generation of iminyl radicals based on an oxidative quenching cycle starting from carboxylic acid derived oxime ethers. In 2018, this activation strategy was used by Leonori to develop the fluorination, chlorination and azidation of alkylnitrile radicals generated by fragmentation of iminyl radicals (Scheme 1B).[17]



Scheme 1 Existing methods for C–C bonds formation after iminyl radical initiated ring opening (A and B) and our work based on oxidative photoredox catalysis (C) (PC = photoredox catalysis, EBX = ethynyl benziodoxolone).

However, no example of C–C bond formation was reported. In this respect, our group and others have shown that ethynylbenziodoxolones (EBX) reagents **5** allowed the alkynylation of radicals generated through oxidative photoredox cycles.[18] We therefore envisioned that EBX reagents would be ideally suited to overcome these limitations and deliver remotely-functionalized alkynyl nitrile through an oxidative fragmentation C–C bond formation sequence. Such a transformation has never been reported under photoredox conditions.[19] However, preliminary results showed that only low yields could be obtained in this reaction using established photoredox catalysts **1**–**3** (see Results and Discussions).

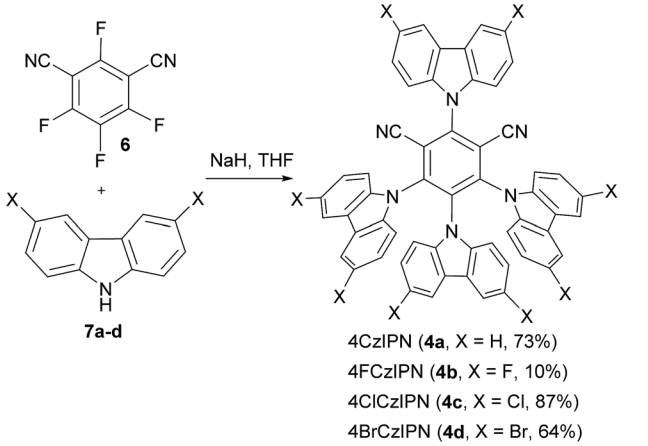
Herein, we report for the first time the use of the modified 4XCzIPN dyes **4b–d** in photoredox catalysis. In particular, 4ClCzIPN dye **4c** led to a highly efficient fragmentation alkynylation process. Both theory and experiment showed that **4c** has an increased reduction potential compared to **4a**, leading to the efficient fragmentation of both four- and five-membered cyclic oxime ethers to give compounds containing versatile alkyne and nitrile functionalities in good yield under mild conditions.

2. Results and Discussions

Dye synthesis and properties

The catalysts **4a–d** were easily synthesized from commercially available 2,4,5,6-tetrafluoroisophthalonitrile (**6**) and the corresponding carbazoles **7a–d** *via* nucleophilic aromatic substitution (Scheme 2).[20] Good yields were obtained, except for fluoro-substituted dye **4b**.

The redox properties of catalysts **4a–d** were then determined (Table 1). Ground state reduction and oxidation potentials of −1.21 V and +1.52 V for catalyst **4a** in acetonitrile have been reported based on cyclic voltammetry.[8a] These values combined with the difference in absorbance and emission signals of the dye allowed to estimate the potentials in the excited state: +1.35 V and −1.04 V for reduction and oxidation, respectively (entry 1). In our hand, slightly different values were obtained (entry 2). In particular, a higher reduction potential of +1.59 V



Scheme 2 Synthesis of 4XCzIPN dyes **4a–d**.

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Table 1 Literature (lit), measured (mes) and computed (comp) values for reduction potentials of dyes **4a–d**[a]

Entry	Catalyst	Solvent	$E_{1/2}(P/P^-)$	$E_{1/2}(P^+/P)$	E_{0-0}	$E_{1/2}(P^*/P^-)$	$E_{1/2}(P^+/P^*)$
1	**4a**(lit)	CH_3CN	−1.21	+1.52	2.56	+1.35	−1.04
2	**4a**(mes)	CH_3CN	−1.05	+1.68	2.64	+1.59	−0.96
3	**4c**(mes)	CH_3CN	−0.97	+2.05	2.68	+1.71	−0.63
4	**4a**(comp)	CH_3CN	−1.29	+1.56	2.64[b]	+1.35	−1.08
5	**4b**(comp)	CH_3CN	−1.18	+1.67	—	—	—
6	**4c**(comp)	CH_3CN	−1.10	+1.76	2.68[b]	+1.58	−0.92
7	**4d**(comp)	CH_3CN	−0.83	+1.89	2.65[b]	+1.82	−0.76
8	**4a**(comp)	CH_2Cl_2	−1.29	+1.67	2.59[b]	+1.30	−0.92
9	**4b**(comp)	CH_2Cl_2	−1.18	+1.79	2.60[b]	+1.42	−0.81
10	**4c**(comp)	CH_2Cl_2	−1.10	+1.87	2.59[b]	+1.49	−0.72
11	**4d**(comp)	CH_2Cl_2	−0.85	+1.98	2.58[b]	+1.73	−0.60

[a] Potentials in V *vs.* SCE. The excitation energy E_{0-0} was estimated by the point of intersection of the normalized absorbance and emission signals. $E_{1/2}(P^+/P^*) = E_{1/2}(P^+/P) - E_{0-0}$ and $E_{1/2}(P^*/P^-) = E_{0-0} + E_{1/2}(P/P^-)$. See ESI for details. [b] Experimental values of E_{0-0} were used.

was observed in the excited state. We then turned to halogenated dyes. With catalyst **4c**, both the cationic and anodic shifts were measured, with reduction and oxidation potentials of −0.97 V and +2.05 V (entry 3). This resulted in an increased reduction potential of +1.71 V of the photoexcited dye. Unfortunately, the cyclic voltammograms of dyes **4b** and **4d** could not be determined in acetonitrile due to their limited solubility. Only the absorption/emission spectra of dye **4d** could be measured. We therefore turned to theory to have a more reproducible and expanded access to redox potential values. At the PCM-UAKS/PBE0-D3BJ/def2-SVP level, the ground state reduction potentials decrease and the oxidation potentials increase in the order of **4a**, **4b**, **4c**, **4d** (entries 4–7).[21] This leads to a higher reduction potential in the excited state for catalyst **4c** and **4d** compared to **4a** (+1.58 V and + 1.82 V respectively compared to + 1.35 V). Therefore, both measurement and computation confirmed the increased potential for **4c**. The same trends but with lower reduction potentials were obtained in dichloromethane as solvent (entries 8–11). In this case, absorption and emission spectra could be measured for all dyes, but no good quality cyclic voltammograms could be acquired. Values in the ground state were therefore again obtained by computation.

The trend in reduction potentials increasing in the order of **4a** < **4b** < **4c** < **4d** (substituents on catalyst **4**: H < F < Cl < Br) can be rationalized as follows. Upon reduction, an electron is added to the lowest unoccupied molecular orbital (LUMO), located mostly on the central isophthalonitrile ring (Fig. 2). However, the LUMO also involves the carbazole moieties in the 4 and 6 positions of the isophthalonitrile ring and is potentially stabilized by them to a greater extent in the case of Cl and Br substituents (resonance donors) compared to H and F. We also note that while molecules **4a** and **4b** are fairly symmetric, systems **4c** and **4d** feature noticeable distortion of the 4-carbazole (Fig. 2). This peculiar structure, observed both in the gas-phase optimized geometries, obtained at several dispersion-corrected DFT levels, and experimental crystal structures,[22] is due to strong Cl···Cl and Br···Br contacts in **4c** and **4d**, respectively.[23]

Optimization of the fragmentation cascade

Our investigations began with the gram scale synthesis of hydroxylamine **10** (Scheme 3, eqn (1)).[24] Nucleophilic substitution of commercially available *N*-hydroxyphthalimide (**8**) and ethyl 2-bromo-2-methylpropanoate (**9**), followed by acidic hydrolysis of the phthalimide, gave 5.8 g of **10** in 86% yield over 2 steps. Condensation of **10** with cyclobutanone (**11**) led to oxime ether **12a** in 90% yield as a crystalline solid (Scheme 3, eqn (2)).

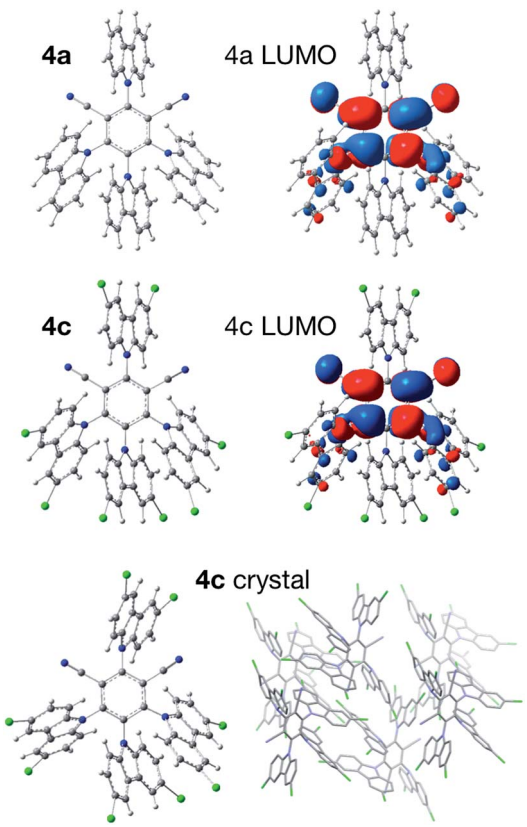

Fig. 2 Optimized structures and LUMO plots (isovalue 0.02) of the dyes **4a** and **4c** at the PBE0/def2-SVP level, as well as the crystal structure of **4c**. See the SI for the plots of **4b** and **4d**.

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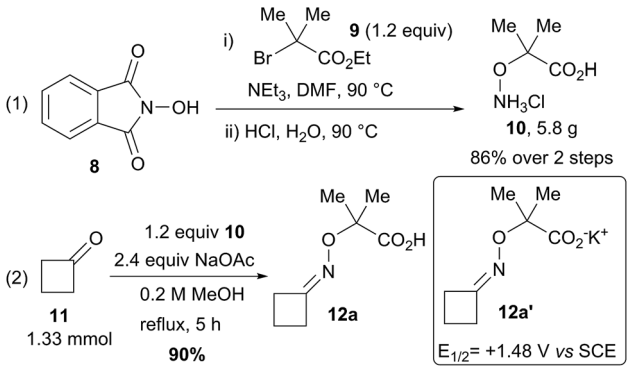
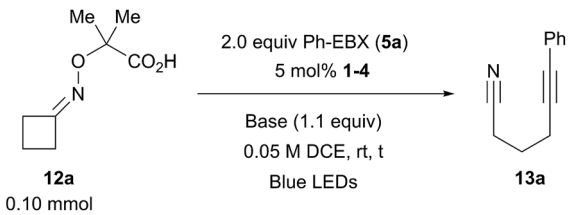


Scheme 3 Gram scale synthesis of 1-carboxy-1-methylethoxyammonium chloride (**10**), and condensation with cyclobutanone (**11**) to give model substrate **12a**.

A cyclic voltammetry measurement on the corresponding potassium carboxylate **12a′** showed a clear oxidation peak at +1.48 V *vs.* SCE in DMF. We decided then to first test the best catalysts reported by Studer:[15] $(Ir[dF(CF_3)ppy]_2(dtbbpy))PF_6$ (**1**) and Leonori:[16,17] Fukuzumi's catalyst **2** (Table 2). Based on our previous studies on photoredox catalysis using EBX reagents,[18a,b] we used DCE as solvent and an excess of Ph-EBX reagent **5a** (2.0 equiv.). With 1 mol% of **1a**, full conversion and 55% NMR yield of alkyne **13a** were reached after 2 h, whereas only 50% conversion and 20% NMR yield was obtained with **2** (Table 2, entries 1–2). In both cases, significant side products formation was observed. DiCyanoAnthracene (DCA, **3**) gave only 5% NMR yield of **13a** (entry 3). With 4CzIPN (**4a**) we were pleased to observe 60% conversion of **12a** and 50% NMR yield of **13a** after 2 h (entry 4).

Increasing reaction time (6 h) and/or temperature (50 °C) was not successful to improve conversion. Speculating that stronger oxidizing dyes could lead to better results, catalyst **4c** was then examined. Full conversion of **12a** was observed and 70% of **13a** could be isolated (entry 5). K_2CO_3 was found to be slightly better than Cs_2CO_3 as a base (entry 6), allowing us to reduce the reaction time to 1 h (entry 7). The other new photocatalysts **4b** and **4d** were then tested, and provided similar photocatalytic activity as **4c** (entries 8–9). Due to its better solubility and ease of synthesis, **4c** was selected as photocatalyst to continue the study. Decreasing the number of equivalents of **5a** to 1.5 resulted in lower yield and more side reactions (entry 10). Interestingly, the catalyst loading could be decreased to 3 mol% (entry 11) or the reaction time reduced to only 30 min (entry 12) without any effect on the yield. Finally, control experiments showed that photocatalyst, base and light were all required for the reaction to proceed (entries 13–15).

Table 2 Optimization of the reaction conditions



Entry	Catalyst	Base	Time	Conversion[a]	Yield[b]
1[c,d]	**1**	Cs_2CO_3	2 h	>95%	55%
2[d]	**2**	Cs_2CO_3	2 h	50%	20%
3[d]	**3**	Cs_2CO_3	2 h	90%	5%
4	**4a**	Cs_2CO_3	2 h–6 h	60%	50%
5	**4c**	Cs_2CO_3	2 h	>95%	70%
6	**4c**	K_2CO_3	2 h	>95%	75%
7	**4c**	K_2CO_3	1 h	>95%	80%
8	**4d**	K_2CO_3	1 h	>95%	75%
9	**4b**	K_2CO_3	1 h	>95%	75%
10[e]	**4c**	K_2CO_3	1 h	>95%	70%
11[f]	**4c**	K_2CO_3	1 h	>95%	80%
12	**4c**	K_2CO_3	0.5 h	>95%	80%
13	—	K_2CO_3	1 h	NR	NR
14	**4c**	—	1 h	<10%	5%
15[g]	**4c**	K_2CO_3	1 h	NR	NR

[a] Reaction conditions: using 0.1 mmol **12a** (1 equiv.), 0.2 mmol **5a** (2.0 equiv.), 5 mol% **1–4** (0.05 equiv.) in DCE (2.0 mL) for 2 h at RT. The conversion of **12a** by NMR is given. NR = no reactivity. [b] NMR yield using dibromomethane as internal standard. [c] Using 1 mol% of **1**. [d] Using 1.0 equiv. of base. [e] Using 1.5 equiv. of **5a**. [f] Using 3.0 mol% of organic dye **4c**. [g] Without irradiation.

Scope of the fragmentation cascade

We then investigated the scope of oximes at 0.30 mmol scale using 3 mol% of **4c** (Scheme 4A). Oxime **12a** afforded **13a** in 79% isolated yield. Phenyl, alkyl and protected amines were tolerated at the β-position (**13b–d**, 41–80% yield). Benzocyclobutenone oxime **12e** afforded propargylic benzocarbonitrile **13e** in 40% yield. Bicyclic compound **13f** was obtained in 65% yield and excellent diastereoselectivity. Oxetanone and azetidinones oximes ethers were also excellent substrates (**13g–i**). Cyclopentanones derivatives were also successful. Using a *gem*-dimethyl substituent for the generation of a δ-tertiary alkylnitrile radical allowed the isolation of **13j** in 77% yield. In the work of Leonori and coworkers, a benzylic position was used to promote ring opening.[17] In our case, an α-heteroatom was exploited. With an oxygen linker, product **13k** was obtained in 65% yield, whereas a nitrogen group led to a modest yield (30%) of **13l**. In addition, compounds **13a** and **13h** were obtained in similar yields using sunlight instead of LEDs.

We then turned our attention to the scope of the reagents (Scheme 4B). The conversion of azetidinone oxime ether **12h** into α-α′-cyanoalkynylamines was achieved in good yields, tolerating electron-withdrawing groups (**13m–o**) and electron-donating groups (**13p**) in *para* position of the benzene ring.[25] Good yields were also obtained with a fluorine in *meta* or a bromine in *ortho* positions (**13q** and **13r**). Cyclobutanone oxime **12a** could also be used with fluorinated arene substituents on the EBX (**13s–t**). Products **13u** and **13v** bearing a trifluoromethyl and bromine at the *para*-position were obtained in moderate yields from cyclopentanone oxime **12j**. Alkynyl nitriles are important building blocks combining two highly useful

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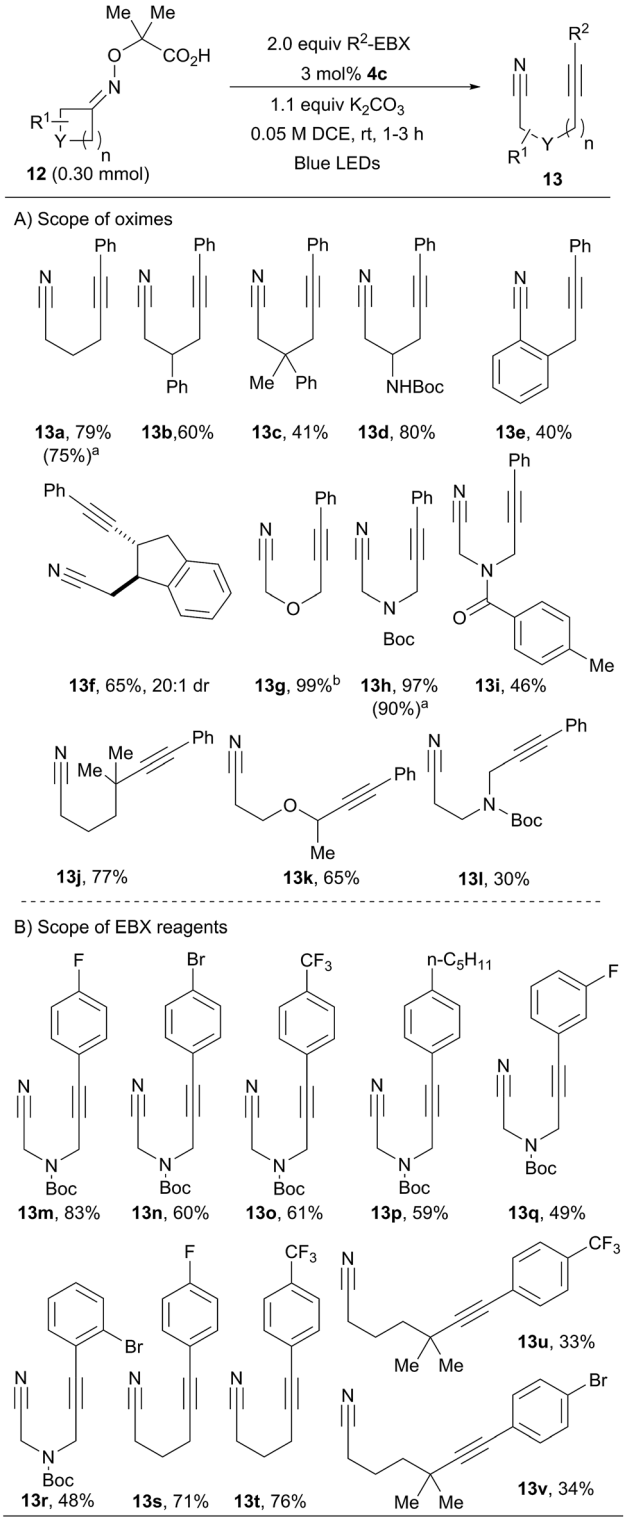
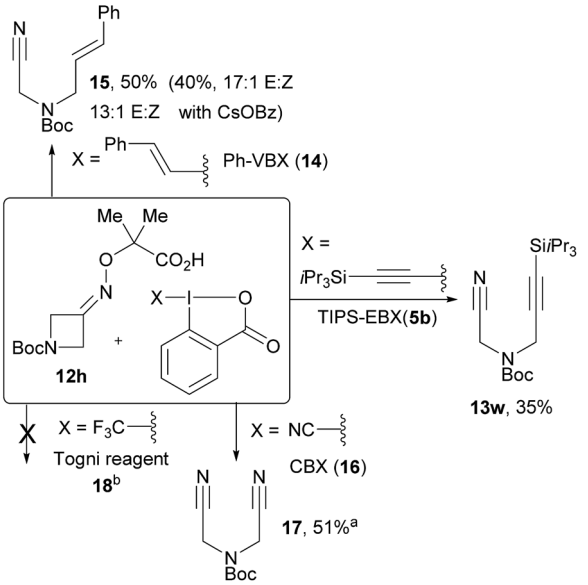


Scheme 4 Scope of the reaction. Using oximes **12** (1.0 equiv.), photocatalyst **4c** (3 mol%), EBX **5** (2 equiv.) and K_2CO_3 (1.1 equiv.) in DCE (0.05 M) at rt, 1–3 h. [a]Using sunlight instead of blue LEDs. NMR yield is given. [b]On 0.10 mmol scale.

functional groups.[26] For example, compounds such as **13a** have been used in cyclization reactions with alkynes,[26a–c] vinyl iodonium salts,[26d] or benzyne equivalents.[26e]



Scheme 5 Extension to other C–C bond forming reactions. Reaction conditions: 5 mol% **4c**, K_2CO_3 (1.1 equiv.), 0.05 M DCE, blue LEDs, rt, 1 h. [a]Reaction run of reagent **16** (2 equiv.) for 14 h. NMR yield is given (isolated yield: 31%) [b]reaction run of reagent **18** (2 equiv.) for 24 h.

Preliminary investigations were then conducted for other types of C–C bond formation (Scheme 5). A silyl EBX reagent gave a lower yield of product **13w** and alkyl EBX could not be used. Preliminary results for an alkenylation cascade were also obtained using Phenyl Vinyl BenziodoXolone (PhVBX, **14**), recently introduced by Olofsson and co-workers.[27] Under the optimized reaction conditions, alkene **15** was isolated in 50% yield with a 12 : 1 *E*/*Z* selectivity.[28] Changing the base from K_2CO_3 to CsOBz afforded lower yield (40%), but with enhanced selectivity (17 : 1 *E*/*Z*). Using two equivalents of cyanobenziodoxolone (CBX, **16**),[18b] bisnitrile **17** was obtained in 51% yield. With Togni reagent **18**,[29] no desired product was formed.

A one-pot protocol starting directly from the ketones was then developed (Scheme 6A). After condensation of cyclobutanone (**11**) with hydroxylamine **10**, addition of two equivalents of Ph-EBX (**5a**) and 5 mol% of the organic dye followed by one hour of irradiation delivered alkyne **13a** in 71% yield. A frequent drawback of organic dyes is their limited stability, leading often to low turnover numbers. Nevertheless, 66% of **13h** could still be isolated when using only 1 mol% of **4c** at a 1.0 mmol scale (Scheme 6B).

According to previous studies on EBX reagents,[18a,b] and the redox potential of dye **4c**, we assume that the reaction starts with the oxidation of the potassium carboxylate **12a′** ($E_{1/2}$ = +1.48 V *vs.* SCE in DMF) by the excited state PS* of the organic dye to generate carboxyl radical **I** and the reduced state PS^- (Scheme 7). Fast decarboxylation releases the α-oxy radical **II**, which can either lead to iminyl radical **III** after acetone extrusion, or can be directly trapped by EBX reagents forming **19**. Although **19** was not detected, its hydrated form **20** was observed by ^{1}H NMR. The iminyl radical **III** then fragments into a nucleophilic alkyl nitrile radical **IV**, which reacts with EBX **5**.

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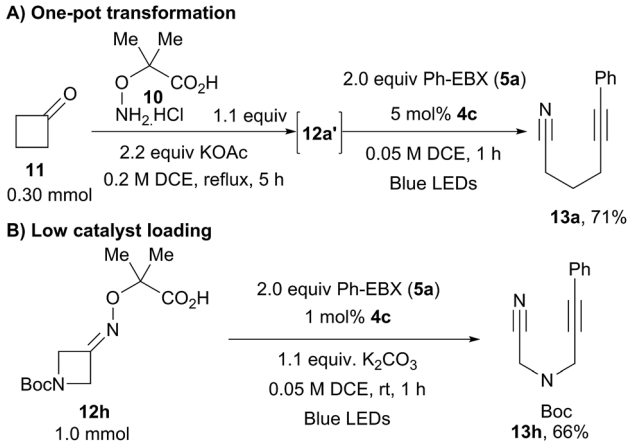
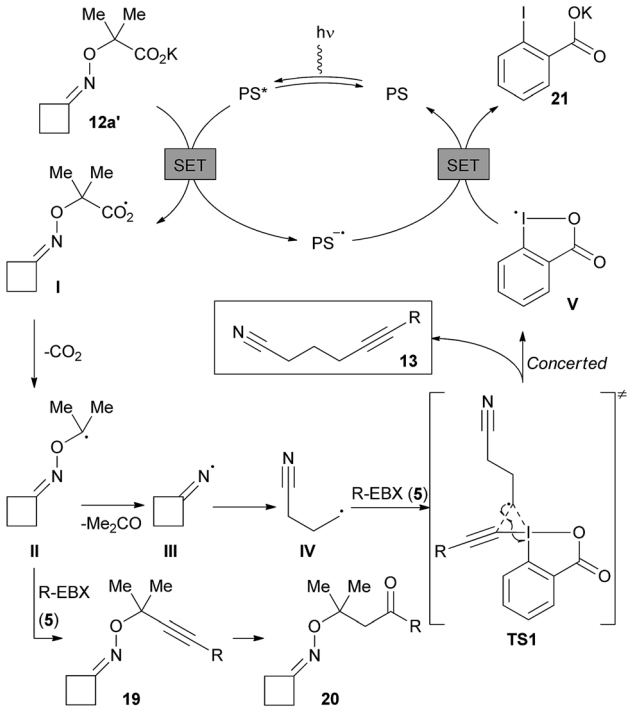


Scheme 6 One-pot protocol and low catalyst loading.



Scheme 7 Speculative reaction mechanism.

For this step, a concerted mechanism *via* transition state TS1 can be envisioned according to our previous studies[18b] to afford the desired alkynylnitrile and radical **V**. A β-addition followed by a 1,2 shift of the EBX substituent could also be considered depending on the migratory aptitude.[18b] Final reduction of **V** allows the regeneration of the ground state photocatalyst PS and generates carboxylate **21**.

3. Conclusions

In summary, we have described the fine-tuning of organic dyes for the synthesis of alkynyl nitriles based on the alkynylation of alkylnitrile radicals generated after a visible light-driven oxidative ring fragmentation reaction involving an iminyl radical as intermediate. Preliminary results for the corresponding alkenylation and cyanation were also achieved. High yields were obtained in a short reaction time with low catalyst loading. We envision a bright future for these new dyes and further applications of cascade approaches in challenging C–C bond forming reactions.

Conflicts of interest

There are no conflicts to declare.

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Table of Contents

1. General Methods	S2
2. Preparation of Reagents	S3
3. Library of organic dyes: 4CzIPN derivatives	S13
4. Physical measurement	S18
5. Synthesis of the Activating reagents for carbonyl substrates	S29
6. Synthesis of oxime starting materials	S32
7. Decarboxylative ring opening / alkynylation cascade	S43
8. Computational details	S62
9. Spectra	S79

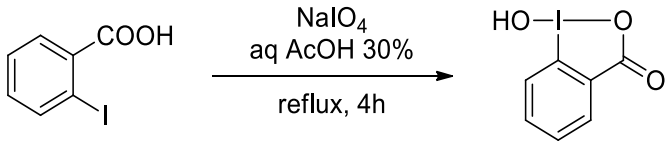
1. General methods

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et_2O, CH_3CN, toluene, hexane and CH_2Cl_2 were dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 10 ppm, *Karl-Fischer* titration). NEt_3 and pyridine were distilled under nitrogen from KOH. The solvents were degassed by Freeze-Pump-Thaw method when mentioned. All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Aplichem or Merck and used as such unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure.TLC was performed on Merck silica gel 60 F_{254} TLC glass plates or aluminium plates and visualized with UV light, permanganate stain, CAN stain or Anisaldehyde stain. Melting points were measured on a Büchi B-540 melting point apparatus using open glass capillaries, the data is uncorrected. ^{1}H-NMR spectra were recorded on a Brucker DPX-400 400 MHz spectrometer in chloroform-d, DMSO-d_6 or CD_3OD, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm, the internal DMSO signal at 2.50 ppm or the internal methanol signal at 3.30 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation).^{13}C-NMR spectra were recorded with ^{1}H-decoupling on a Brucker DPX-400 100 MHz spectrometer in chloroform-d, DMSO-d_6 or CD_3OD, all signals are reported in ppm with the internal chloroform signal at 77.0 ppm, the internal DMSO signal at 39.5 ppm or the internal methanol signal at 49.0 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm^{-1} (w = weak, m = medium, s = strong, br = broad). High-resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. Reactions were performed in test tubes (1.0 to 10 mL) which were hold using a rack for test tubes placed at the center of a crystallization flask. On this flask were attached the blue LEDs (Ruban LED avec câble à extrémités ouvertes Barthelme Y51516414 182405 24 V 502 cm bleu 1 pc(s), bought directly on www.conrad.ch/fr). The distance between the LEDs and the test tubes was approximatively 3 to 4 cm. Long irradiation for more than 2 h resulted in temperature increasing up to 34 °C. UV/Vis spectroscopy was performed on an Agilent Cary 60 UV-Vis and steady-state luminescence spectroscopy was recorded on a Varian Cary Eclipse spectrophotometer.

2. Preparation of Reagents

The synthesis of reagents **2a**, **2b, 2i and 16** had already been described before by our group. The procedures are taken from the indicated publications to facilitate reproduction of the results by having all data in the same file. Unless specified, the silyl alkynes are commercially available and used directly as received. Togni reagent I (**18**) is commercially available and has been used as received (stabilized with 60% of diatomaceous earth).

1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one (23)



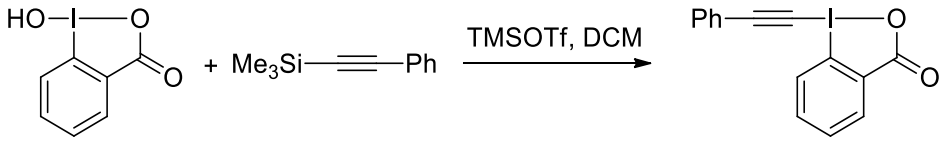
22 **23**

Following a reported procedure,[1] $NaIO_4$ (7.24 g, 33.8 mmol, 1.05 equiv) and 2-iodobenzoic acid (**22**) (8.00 g, 32.2 mmol, 1.0 equiv) were suspended in 30% (v:v) aq. AcOH (48 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (180 mL) and allowed to cool to rt, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 20 mL) and acetone (3 x 20 mL), and air-dried in the dark to give the pure product **23** (8.3 g, 31 mmol, 98%) as a colorless solid.

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.02 (dd, 1 H, J = 7.7, 1.4 Hz, Ar*H*), 7.97 (m, 1 H, Ar*H*), 7.85 (dd, 1 H, J = 8.2, 0.7 Hz, Ar*H*), 7.71 (td, 1 H, J = 7.6, 1.2 Hz, Ar*H*); ^{13}C NMR (100 MHz, DMSO-d_6) δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4; IR ν 3083 (w), 3060 (w), 2867 (w), 2402 (w), 1601 (m), 1585 (m), 1564 (m), 1440 (m), 1338 (s), 1302 (m), 1148 (m), 1018 (w), 834 (m), 798 (w), 740 (s), 694 (s), 674 (m), 649 (m); the reported values correspond to the ones in literature.[1]

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.08 (m, 21 H, TIPS), 0.18 (s, 9 H, TMS). IR ν 2959 (m), 2944 (m), 2896 (w), 2867 (m), 1464 (w), 1385 (w), 1250 (m), 996 (w), 842 (s), 764 (s), 675 (m), 660 (m). Characterization data of **23** corresponded to the literature values.[2]

1-[Phenylethynyl]-1,2-benziodoxol-3(1*H*)-one (Ph-EBX, 5a)



23 **24** **5a**

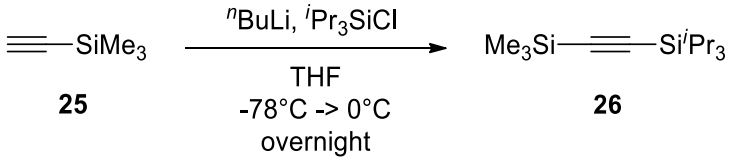
Following a reported procedure,[2] trimethylsilyltriflate (1.60 mL, 8.56 mmol, 1.1 equiv) was added dropwise to a stirred solution of 2-iodosylbenzoic Trimethylsilyl triflate (7.50 mL, 41.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**23**) (10.0 g, 37.7 mmol, 1.0 equiv) in CH_2Cl_2 (100 mL) at RT. The resulting yellow mixture was stirred for 1 h, followed by the dropwise addition of trimethyl(phenylethynyl)silane (**24**) (8.10 mL, 41.5

[1] L. Kraszkiewicz, L. Skulski, *Arkivoc*. **2003**, *6*, 120.
[2] J. P Brand, C. Chevalley, R. Scopelliti, J. Waser, *Chem. Eur. J.* **2012**, *18*, 5655.

mmol, 1.1 equiv) (slightly exothermic). The resulting suspension was stirred for 6 h at RT, during this time a white solid was formed. A saturated solution of $NaHCO_3$ (100 mL) was then added and the mixture was stirred vigorously. The resulting suspension was filtered on a glass filter of porosity 4. The two layers of the mother liquors were separated and the organic layer was washed with sat. $NaHCO_3$ (100 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting mixture was combined with the solid obtained by filtration and boiled in CH_3CN (300 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **5a** (6.08 g, 17.4 mmol, 46 %) as a colorless solid.

Mp (Dec.) 155 – 160 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) (*ca* 0.03 mmol/ml) δ 8.46 (m, 1 H, ArH), 8.28 (m, 1 H, ArH), 7.80 (m, 2 H, ArH), 7.63 (m, 2 H, ArH), 7.48 (m, 3 H, ArH). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.9, 134.9, 132.9, 132.5, 131.6, 131.3. 130.8, 128.8, 126.2, 120.5, 116.2, 106.6, 50.2. Consistent with reported data.[4]

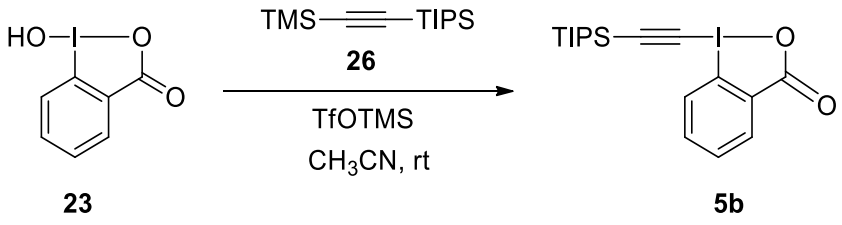
Triisopropylsilyl trimethylsilylacetylene (26)



Following a reported procedure,[3] *n*-butyllithium (2.5 M in hexanes, 12.0 mL, 29.9 mmol, 0.98 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (**25**) (3.0 g, 30 mmol, 1.0 equiv) in THF (48 mL) at -78 °C. The mixture was then warmed to 0 °C and stirred for 5 min. The mixture was then cooled back to -78 °C and chlorotriisopropylsilane (6.4 mL, 30 mmol, 1.0 equiv) was added dropwise. The mixture was then allowed to warm to room temperature and stirred overnight. A saturated solution of ammonium chloride (40 mL) was added, and the reaction mixture was extracted with diethyl ether (2 x 60 mL). The organic layer was washed with water and brine, then dried over $MgSO_4$, filtered and concentrated under reduced pressure to obtain a colorless liquid which was further purified by Kugelrohr distillation (56-57°C/0.25 mmHg) to yield **26** (7.16 g, 28.0 mmol, 92% yield) as a colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) *δ* 1.08 (m, 21 H, TIPS), 0.18 (s, 9 H, TMS). IR ν 2959 (m), 2944 (m), 2896 (w), 2867 (m), 1464 (w), 1385 (w), 1250 (m), 996 (w), 842 (s), 764 (s), 675 (m), 660 (m). Characterization data of **26** corresponded to the literature values.[3]

1-[(Triiso-propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (TIPS-EBX, 5b)



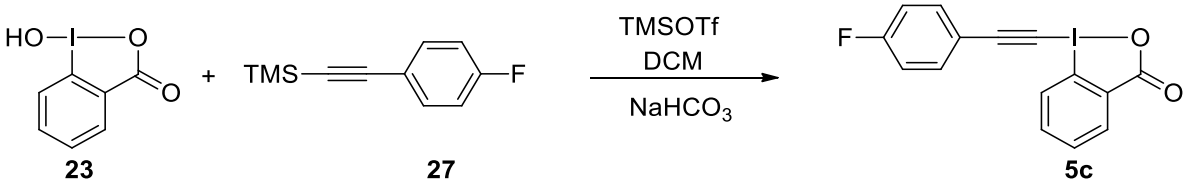
Following a reported procedure,[4] 2-iodosylbenzoic acid (**23**) (21.7 g, 82.0 mmol, 1.0 equiv) was charged in oven-dried three-neck 1L flask equipped with a magnetic stirrer. After 3

[3] C J. Helal, P A. Magriotis, E J. Corey, *J. Am. Chem. Soc.* **1996***, 118*, 10938.
[4] J. P. Brand, J. Waser, *Angew. Chem., Int. Ed.* **2010**, *49*, 7304.

vacuum/nitrogen cycles, anhydrous acetonitrile (500 mL) was added via canula and cooled to 0 °C. Trimethylsilyltriflate (16.4 mL, 90.0 mmol, 1.1 equiv) was added dropwise via a dropping funnel over 30 min (no temperature increase was observed). After 15 min, (trimethylsilyl)(triisopropylsilyl)acetylene (**26**) (23.0 g, 90.0 mmol, 1.1 equiv) was added via canula over 15 min (no temperature increase was observed). After 30 min, the suspension became an orange solution. After 10 min, pyridine (7.0 mL, 90 mmol, 1.1 equiv) was added via syringe. After 15 min, the reaction mixture was transferred in a one-neck 1L flask and reduced under vacuum until a solid was obtained. The solid was dissolved in DCM (200 mL) and transferred in a 1L separatory funnel. The organic layer was added and washed with 1 M HCl (200 mL) and the aqueous layer was extracted with CH_2Cl_2 (200 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (2 x 200 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 120 mL) afforded **5b** (30.1 g, 70.2 mmol, 86%) as colorless crystals.

M.p. (Dec.) 170-176 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.44 (m, 1 H, Ar*H*), 8.29 (m, 1 H, Ar*H*), 7.77 (m, 2 H, Ar*H*), 1.16 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, Chloroform-*d*) δ 166.4, 134.6, 132.3, 131.4, 131.4, 126.1, 115.6, 114.1, 64.6, 18.4, 11.1. IR ν 2943 (m), 2865 (m), 1716 (m), 1618 (m), 1604 (s), 1584 (m), 1557 (m), 1465 (m), 1439 (w), 1349 (m), 1291 (m), 1270 (w), 1244 (m), 1140 (m), 1016 (m), 999 (m), 883 (m), 833 (m), 742 (m), 702 (s), 636 (m); Characterization data of **5b** corresponded to the literature values.[4]

1-[4-Fluorophenylethynyl]-1,2-benziodoxol-3(1*H*)-one (5c)



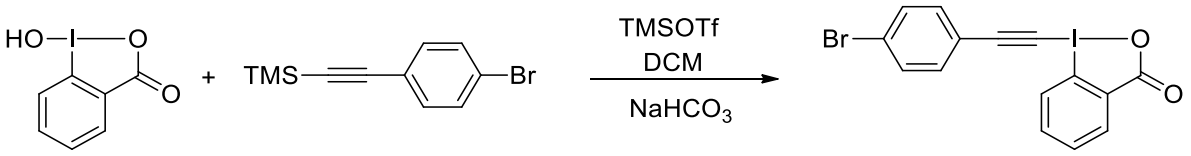
23 **27** **5c**

Following a reported procedure,[5] trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**23**) (1.32 g, 5.00 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) at RT. The resulting suspension was stirred for 1 h, followed by the drop wise addition of ((4-fluorophenyl)ethynyl)trimethylsilane (**27**) (1.1 mL, 5.5 mmol, 1.1 equiv), which was dissolved in CH_2Cl_2 (1 mL). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with sat. $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was boiled in CH_3CN (20 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **5c** (750 mg, 2.05 mmol, 41%) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.48 – 8.34 (m, 1H, Ar*H*), 8.29 – 8.16 (m, 1H, Ar*H*), 7.85 – 7.69 (m, 2H, Ar*H*), 7.68 – 7.53 (m, 2H, Ar*H*), 7.17 – 7.05 (m, 2H, Ar*H*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.8, 164.0 (d, *J* = 253.9 Hz), 135.2 (d, *J* = 8.8 Hz), 135.0, 132.6, 131.7, 131.50, 126.4, 116.9 (d, *J* = 3.6 Hz), 116.4 (d, *J* = 22.4 Hz), 116.3, 105.5, 50.5. Consistent with reported data.[6]

1-[4-Bromophenylethynyl]-1,2-benziodoxol-3(1H)-one (5d)

[5] K. Jia, F. Zhang, H. Huang, Y. Chen, *J. Am. Chem. Soc.* **2016**, *138*, 1514−1517.
[6] F. Le Vaillant, T. Courant, J. Waser, *Angew. Chem. Int. Ed.* **2015**, *54*, 11200–11204.

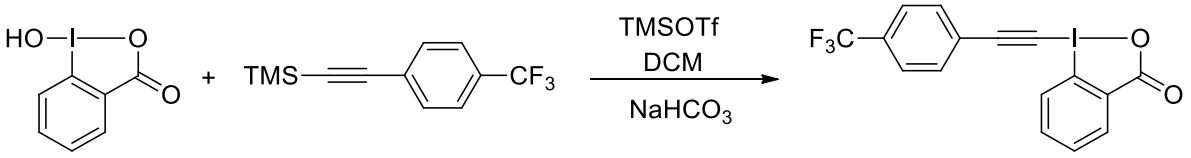


23 **28** **5d**

Following a reported procedure,[5] trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**23**) (1.32 g, 5.00 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) at RT. The resulting suspension was stirred for 3 h, followed by the drop wise addition of ((4-bromophenyl)ethynyl)trimethylsilane (**27**) (1.17 g, 5.50 mmol, 1.1 equiv), which was dissolved in CH_2Cl_2 (1 mL). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with sat. $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was boiled in CH_3CN (20 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **5d** (1.0 g, 2.3 mmol, 47%) as a pale yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.51 – 8.30 (m, 1 H, Ar*H*), 8.30 – 8.13 (m, 1 H, Ar*H*), 7.84 – 7.72 (m, 2 H, Ar*H*), 7.58 (d, *J* = 8.5 Hz, 2 H, Ar*H*), 7.46 (d, *J* = 8.5 Hz, 2 H, Ar*H*).^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.6, 135.1, 134.3, 132.7, 132.3, 131.9, 131.4, 126.3, 125.7, 119.6, 116.3, 105.4, 52.1. Consistent with reported data.[6]

1-[4-Trifluoromethylphenylethynyl]-1,2-benziodoxol-3(1*H*)-one (5e)



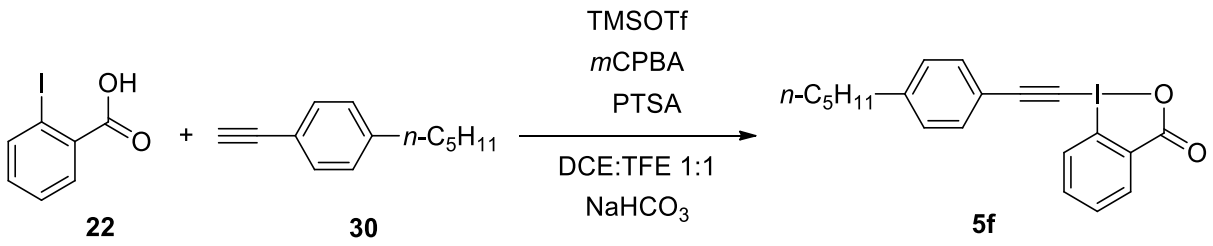
23 **29** **5e**

Following a reported procedure,[5] trimethylsilyl triflate (0.80 mL, 4.4 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**23**) (1.06 g, 4.00 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) at RT. The resulting yellow mixture was stirred for 1 h, followed by the dropwise addition of trimethyl((4-(trifluoromethyl)phenyl)ethynyl)silane (**29**) (1.07 g, 4.40 mmol, 1.1 equiv). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with sat. $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was recrystallized in CH_3CN (ca 20 mL) to afford **5e** (850 mg, 2.04 mmol, 51%) as a pale yellow solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.46 – 8.38 (m, 1 H, Ar*H*), 8.28 – 8.19 (m, 1 H, Ar*H*), 7.84 – 7.74 (m, 2 H, Ar*H*), 7.74 – 7.65 (m, 4 H, Ar*H*).^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.6, 135.0, 133.0, 132.6, 132.2 (q, $J_{C\text{-}F}$ = 33.0 Hz), 131.7, 131.2, 126.3, 125.7 (q, $J_{C\text{-}F}$ = 3.6 Hz), 124.4, 123.4 (q, $J_{C\text{-}F}$ = 272.6 Hz), 116.1, 104.2, 53.7; Consistent with reported data.[7]

1-((4-Pentylphenyl)ethynyl)-1,2-benziodoxol-3(1H)-one (5f)

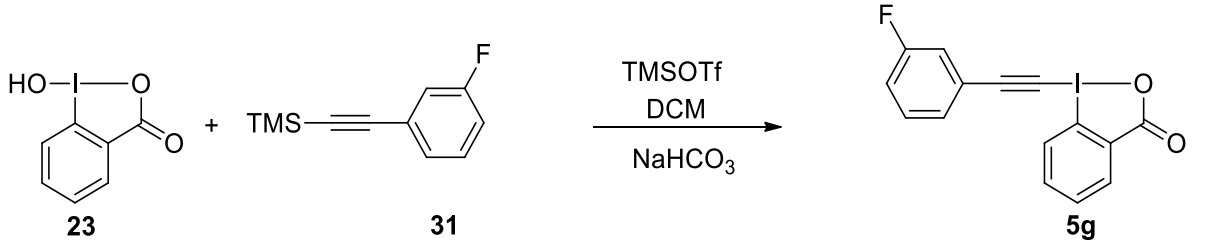
[7] B. Lu, J. Wu, N. Yoshikai, *J. Am. Chem. Soc.* **2014**, *136*, 11598.



Following a slightly modified procedure,[8] in a sealed tube, 2-iodobenzoic acid (**22**) (1.00 g, 4.03 mmol, 1.0 equiv), 4-methylbenzenesulfonic acid (775 mg, 4.03 mmol, 1.0 equiv) and mCPBA (994 mg, 4.44 mmol, 1.1 equiv) were suspended in DCE:TFE 1:1 (12 mL) and stirred for 1 h at 55 °C. After 1 h, 1-ethynyl-4-pentylbenzene (**30**) (1.1 mL, 5.6 mmol, 1.4 equiv) was added and the reaction was stirred at 55 °C for 24 h. After 24 h, the solvent was evaporated and the residue was redissolved in CH_2Cl_2 (20 mL) and stirred vigorously with $NaHCO_3$ sat. (30 mL). After 1 h, the reaction mixture was transferred into a separating funnel and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (2x50 mL). The combined organic layers were washed with sat. $NaHCO_3$, dried over $MgSO_4$, filtered and concentrated under vacuum. The resulting solid was boiled in MeCN (20 mL), then filtered and the collected solid was further purified by column chromatography using pure ethyl acetate. Trituration in pentane afforded **5f** (191 mg, 0.457 mmol, 11%) as a pale yellow solid.

M.p. (Dec.) 104-107 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.45 – 8.40 (m, 1H, Ar*H*), 8.28 – 8.21 (m, 1H, Ar*H*), 7.79 – 7.74 (m, 2H, Ar*H*), 7.56 – 7.48 (m, 2H, Ar*H*), 7.26 – 7.23 (m, 2H, Ar*H*), 2.71 – 2.60 (m, 2H, ArCH_2), 1.69 – 1.54 (m, 2H, ArCH$_2$CH_2), 1.40 – 1.27 (m, 4H, CH_2CH_2CH$_3$), 0.90 (t, *J* = 6.8 Hz, 3H, CH$_2$CH_3). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 166.6, 146.7, 135.0, 133.0, 132.6, 131.7, 131.5, 129.0, 126.3, 117.7, 116.4, 107.4, 49.4, 36.2, 31.5, 31.0, 22.6, 14.1. IR ν 3446 (m), 3359 (w), 2349 (w), 1644 (s), 1482 (m), 1327 (m), 1214 (m), 1121 (m), 1034 (m), 840 (s), 753 (m). HRMS (ESI) calcd for $C_{20}H_{20}IO_2^+$ $[M+H]^+$ 419.0503; found 419.0496.

1-[3-Fluorophenylethynyl]-1,2-benziodoxol-3(1H)-one (5g)



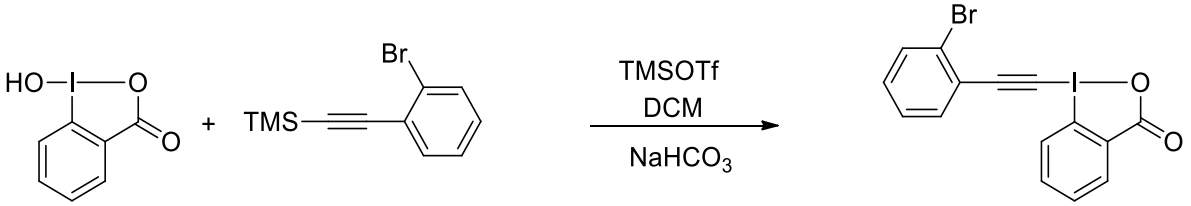
Following a reported procedure,[5] trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**23**) (1.32 g, 5.00 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) at RT. The resulting suspension was stirred for 1 h, followed by the drop wise addition of ((3-fluorophenyl)ethynyl)trimethylsilane (**31**) (1.1 mL, 5.5 mmol, 1.1 equiv). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with sat. $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was boiled in CH_3CN (20

[8] M. J. Bouma, B. Olofsson, *Chem. Eur. J.* **2012**, *18*, 14242 – 14245.

mL). The mixture was cooled down, filtered and the collected solid was dried under high vacuum to afford **5g** (787 mg, 2.15 mmol, 43%) as a colorless solid.

M.p. (Dec.) 160-164 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.33 (dd, J = 8.2, 0.8 Hz, 1H, Ar*H*), 8.13 (dd, J = 7.4, 1.7 Hz, 1H, Ar*H*), 7.91 (ddd, J = 8.2, 7.2, 1.7 Hz, 1H, Ar*H*), 7.81 (td, J = 7.3, 0.9 Hz, 1H, Ar*H*), 7.64 – 7.59 (m, 1H, Ar*H*), 7.58 – 7.53 (m, 2H, Ar*H*), 7.47 – 7.37 (m, 1H, Ar*H*). ^{13}C NMR (101 MHz, DMSO-d_6)[9] 166.3, 161.8 (d, J = 245.6 Hz), 135.3, 131.9, 131.3, 131.2 (d, J = 8.7 Hz), 129.0 (d, J = 2.9 Hz), 127.7, 122.4 (d, J = 9.6 Hz), 119.2 (d, J = 23.4 Hz), 118.1 (d, J = 21.1 Hz), 116.4, 102.5 (d, J = 3.3 Hz), 53.8. ^{19}F NMR (376 MHz, $(CD_3)_2SO$) δ -111.7. IR ν 3477 (w), 3334 (w), 2380 (w), 1644 (s), 1457 (m), 1339 (w), 1252 (w), 1146 (m), 946 (w), 840 (w), 753 (m), 2143 (w). HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calcd for $C_{15}H_9FIO_2^+$ 366.9626; Found 366.9625.

1-[2-Bromophenylethynyl]-1,2-benziodoxol-3(1*H*)-one (5h)

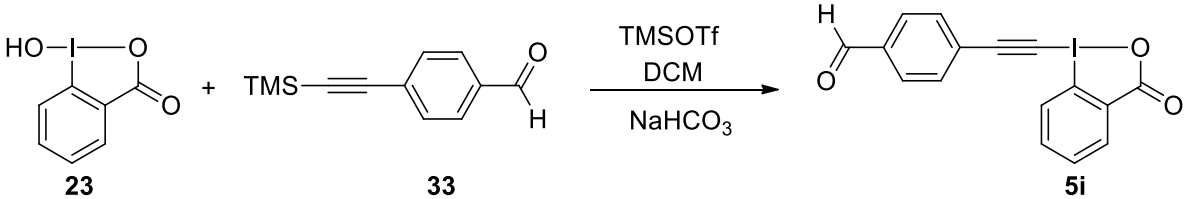


23 **32** **5h**

Following a reported procedure,[6] trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**23**) (1.32 g, 5.00 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) at RT. The resulting suspension was stirred for 3 h, followed by the drop wise addition of ((2-bromophenyl)ethynyl)trimethylsilane (**32**) (1.17 g, 5.50 mmol, 1.1 equiv). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with sat. $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was boiled in CH_3CN (20 mL). The mixture was cooled down, filtered and the collected solid was dried under high vacuum to afford **5h** (1.50 g, 3.51 mmol, 70%) as a colorless solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.44 (td, J = 7.3, 2.1 Hz, 2 H, Ar*H*), 7.84 – 7.74 (m, 2 H, Ar*H*), 7.68 (d, J = 1.1 Hz, 1 H, Ar*H*), 7.61 (dd, J = 7.6, 1.7 Hz, 1 H,Ar*H*), 7.36 (m, 2 H, Ar*H*).^{13}C NMR (101 MHz, Chloroform-*d*)[9] δ 166.6, 135.2, 134.7, 133.0, 132.7 , 131.8, 131.3, 127.6, 126.8, 126.4, 123.2, 116.5, 104.3, 55.4. Consistent with reported data.[6]

1-((4-Formylphenyl)ethynyl)-1,2-benziodoxol-3(1*H*)-one (5i)



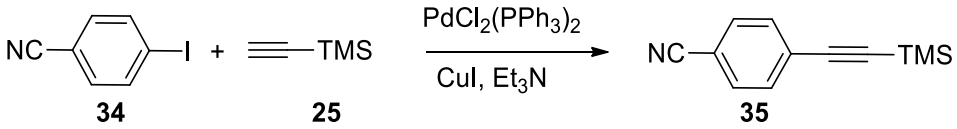
23 **33** **5i**

[9] One carbon is not resolved.

Following a reported procedure,[10] trimethylsilyl triflate (0.89 mL, 4.9 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**23**) (1.19 g, 4.49 mmol, 1.0 equiv) in CH_2Cl_2 (15 mL) at RT. The resulting suspension was stirred for 1 h, followed by the drop wise addition of ((4-formylphenyl)ethynyl)trimethylsilane (**33**) (1.00 g, 4.94 mmol, 1.1 equiv), which was dissolved in CH_2Cl_2 (1 mL). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with sat. $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was boiled in CH_3CN (20 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **5i** (0.80 g, 2.1 mmol, 41%) as a yellow solid.

^{1}H NMR (400 MHz, DMSO-d_6) δ 10.08 (s, 1H, C*H*O), 8.35 (d, *J* = 9.1 Hz, 1H, Ar*H*), 8.14 (dd, *J* = 7.4, 1.7 Hz, 1H, Ar*H*), 8.02 (d, *J* = 8.5 Hz, 2H, Ar*H*), 7.96 – 7.88 (m, 3H, Ar*H*), 7.82 (t, *J* = 7.3 Hz, 1H, Ar*H*). ^{13}C NMR (101 MHz, DMSO-d_6) δ 192.6, 166.3, 136.7, 135.3, 133.2, 131.9, 131.4, 129.8, 127.7, 126.1, 116.4, 102.9, 56.6. Consistent with reported data.[7]

Trimethyl((4-cyanophenyl)ethynyl)silane (35)

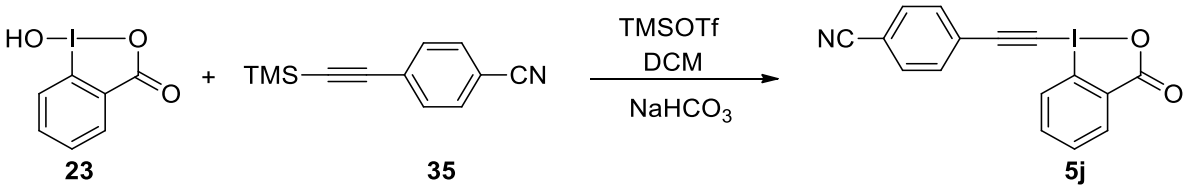


34 **25** **35**

Following a slight modification of the reported procedure,[11] 4-iodobenzonitrile (**34**) (1.00 g, 4.37 mmol, 1.0 equiv) was dissolved in triethylamine (10 mL) (without prior drying). After three freeze-thraw-pump cycles, $PdCl_2(PPh_3)_2$ (92 mg, 0.13 mmol, 3 mol%) and copper iodide (42 mg, 0.22 mmol, 5 mol%) were added under N_2. After the addition of ethynyltrimethylsilane (**25**) (1.2 mL, 8.7 mmol, 2 equiv) the green suspension was stirred at RT for 3 h. The reaction mixture was concentrated under vacuum, dissolved in CH_2Cl_2 (30 mL), washed with a saturated ammonium chloride solution (30 mL) and water (30 mL). The organic layers were then dried over $MgSO_4$, filtered and concentrated under vacuum. The resulting oil was purified by column chromatography (pentane/ethyl acetate 25:1) to afford 4-((trimethylsilyl)ethynyl)benzonitrile (**35**) (847 mg, 4.25 mmol, 97%) as a white solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.53 (d, *J* = 8.8 Hz, 2H, Ar*H*), 0.26 (s, 9H, SiC*H*$_3$). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 132.6, 132.1, 128.1, 118.6, 111.9, 103.1, 99.7, -0.12. Consistent with reported data.[12]

1-[4-Cyanophenylethynyl]-1,2-benziodoxol-3(1*H*)-one (5j)



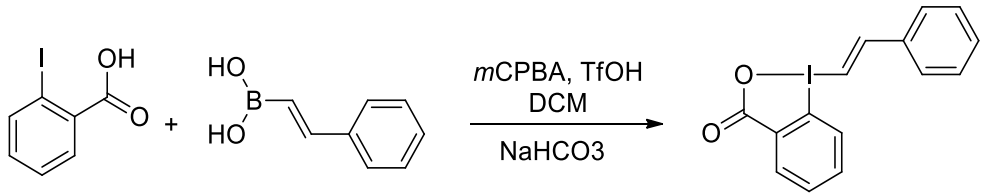
23 **35** **5j**

[10] H. Huang, G. Zhang, L. Gong, S. Zhang, Y. Chen, *J. Am. Chem. Soc.* **2014**, *136*, 2280-2283.
[11] Y. Feng, C. Xie, W.-L. Qiao, and H.-J. Xu, *Org. Lett.* **2013**, *15*, 936-939.
[12] R. Rahaim and J. Shaw, *J. Org. Chem.* **2008**, *73*, 2912–2915.

Following a reported procedure,[5] trimethylsilyl triflate (0.73 mL, 4.0 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**23**) (963 mg, 3.65 mmol, 1.0 equiv) in CH_2Cl_2 (12 mL) at RT. The resulting suspension was stirred for 1 h, followed by the drop wise addition of ((4-cyanophenyl)ethynyl)trimethylsilane (**35**) (800 mg, 4.01 mmol, 1.1 equiv), which was dissolved in CH_2Cl_2 (1 mL). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (20 mL) was then added and the mixture was stirred vigorously for 30 minutes, the two layers were separated and the organic layer was washed with sat. $NaHCO_3$ (20 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was boiled in CH_3CN (20 mL). The mixture was cooled down, filtered and dried under high vacuum to afford **5j** (865 mg, 2.32 mmol, 64%) as a pale brown solid.

^{1}H NMR (400 MHz, DMSO-d_6) δ 8.34 (d, J = 8.2 Hz, 1H, Ar*H*), 8.13 (dd, J = 7.4, 1.7 Hz, 1H, Ar*H*), 7.99 (d, J = 8.6 Hz, 2H, Ar*H*), 7.90 (d, J = 8.6 Hz, 3H, Ar*H*), 7.81 (t, J = 7.3 Hz, 1H, Ar*H*). ^{13}C NMR (101 MHz, DMSO-d_6) δ 166.3, 135.3, 133.3, 132.8, 131.9, 131.4, 131.4, 127.8, 125.3, 118.2, 116.4, 112.7, 102.0, 57.4. Consistent with reported data.[5]

PhVBX (14)



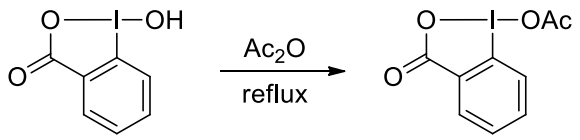
22 **36** **14**

Following a reported procedure,[13] *m*CPBA (1.25 g, 5.50 mmol, 1.1 equiv) was added to a solution of 2-iodobenzoic acid (**22**) (1.25 g, 5.00 mmol, 1.0 equiv) in CH_2Cl_2 (25 mL). The reaction mixture was cooled to 0 ˚C and trifluoromethanesulfonic acid (0.66 mL, 7.5 mmol, 1.5 equiv) was added at this temperature before being stirred at r.t for 15 min. The reaction mixture was again cooled to 0 ºC over 10 min and (*E*)-styrylboronic acid (**36**) (1.0 g, 7.0 mmol, 1.4 equiv) and the mixture was stirred at r.t for 1 h. A saturated $NaHCO_3$ solution (25 mL) was added and the mixture was stirred for 1 h. The mixture was diluted with CH_2Cl_2 (25 mL) and H_2O (25 mL) and the layers were separated. The aqueous layer was extracted with CH_2Cl_2 (3 x 50 mL) and the combined organic layers were washed with brine, dried (Mg_2SO_4) and filtered. The solvent was removed under reduced pressure. The crude mixture contained a lot of impurities, so purification by column chromatography over silica gel (DCM with 2 to 10% Acetone) afforded 500 mg of pure Ph-VBX **14** as off white crystalline solid (29%).

^{1}H NMR (400 MHz, Methanol-d_4) δ 8.28 (dd, J = 5.8, 3.4 Hz, 1H, Ar*H*), 7.96 (d, J = 15.4 Hz, 1H, Ar*H*), 7.74 (dd, J = 5.9, 3.5 Hz, 1H, Ar*H*), 7.70 (dd, J = 7.5, 3.5 Hz, 4H, Ar*H*), 7.66 (d, J = 8.7 Hz, 1H, Ar*H*), 7.49 (dd, J = 5.1, 2.0 Hz, 3H, Ar*H*). The NMR shifts match the literature data.[12]

[13] E. Stridfeldt, A. Seemann, M. J. Bouma, C. Dey, A. Ertan and B. Olofsson, *Chem. Eur. J.* **2016**, *18*, 16066-16070.

1-Acetoxy-1,2-benziodoxol-3-(1*H*)-one (37)

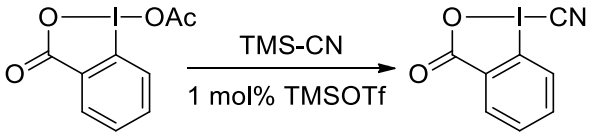


23 **37**

Following a reported procedure,[14] 1-hydroxy-1,2-benziodoxol-3-(1*H*)-one (**23**, 10.3 g, 39.1 mmol, 1.00 equiv.) was suspended in acetic anhydride (35 mL) and heated to reflux for 30 minutes. The resulting clear, slightly yellow solution was slowly let to warm up to room temperature and then cooled to 0 °C for 30 minutes. The white suspension was filtered and the filtrate was again cooled to 0 °C for 30 minutes. The suspension was once again filtered and the combined two batches of solid product were washed with hexane (2 x 20 mL) and dried *in vacuo* affording **37** (10.8 g, 35.3 mmol, 90%) as a white solid.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.24 (dd, 1 H, *J* = 7.6, 1.6 Hz, Ar*H*), 8.00 (dd, 1 H, *J* = 8.3, 1.0 Hz, Ar*H*), 7.92 (ddd, 1 H, *J* = 8.4, 7.2, 1.6 Hz, Ar*H*), 7.71 (td, 1 H, *J* = 7.3, 1.1 Hz, Ar*H*), 2.25 (s, 3 H, COC*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 176.5, 168.2, 136.2, 133.3, 131.4, 129.4, 129.1, 118.4, 20.4. The values of the NMR spectra are in accordance with reported literature data.[14]

1-Cyano-1,2-benziodoxol-3-(1*H*)-one (16)



37 **17**

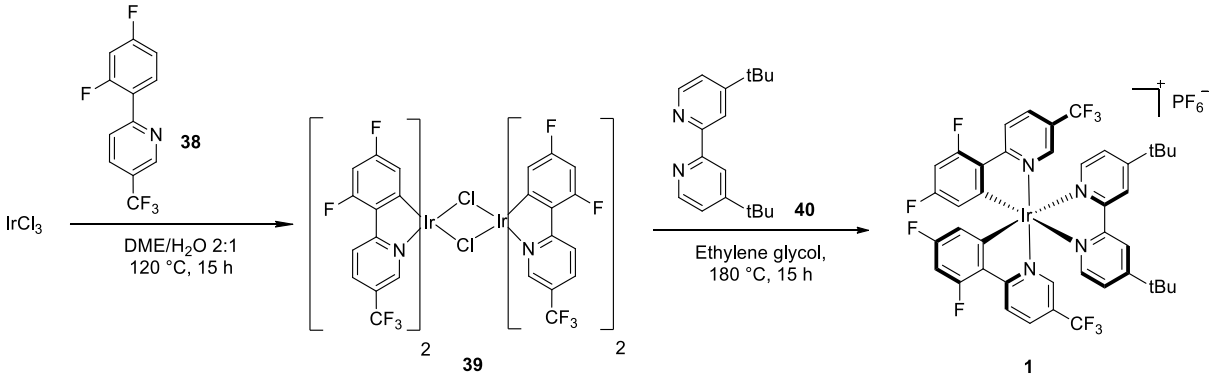
Following a reported procedure,[15] 1-acetoxy-1,2-benziodoxol-3-(1*H*)-one (**37**, 11.8 g, 38.6 mmol, 1.00 eq.) was dissolved under nitrogen in dry dichloromethane (200 mL). Trimethylsilyl cyanide (TMS-CN, 10 mL, 77 mmol, 2.00 eq.) was added *via* syringe to the clear colorless solution over a five minute time period, followed by trimethylsilyl trifluoromethanesulfonate (TMS-OTf, 70 µL, 0.39 mmol, 0.01 equiv.). Precipitation occurred within 5 min and the reaction mixture was stirred at room temperature and under nitrogen for 30 min to ensure the completion of the reaction. The resulting thick white suspension was diluted with hexane (5 mL) before being filtered and the solid was washed with hexane (3 x 20 mL) and dried *in vacuo* affording **17** (10.3 g, 37.7 mmol, 98 %) as a white solid.

[14] P. Eisenberger, S. Gischig, A. Togni, *Chem. Eur. J.* **2006**, *12*, 2579.

[15] M. Chen, Z. T. Huang, Q. Y. Zheng, *Org. Biomol. Chem*. **2015**, *13*, 8812.

^{1}H NMR (DMSO-d_6, 400 MHz): δ 8.29 (d, J = 8.3 Hz, 1 H, Ar*H*), 8.13 (dd, J = 7.4, 1.7 Hz, 1 H, Ar*H*), 8.06-7.97 (m, 1 H, Ar*H*), 7.88 (t, J = 7.3 Hz, 1 H, Ar*H*). ^{13}C NMR (DMSO-d_6, 100 MHz): δ 166.7, 136.5, 132.0, 131.9, 130.2, 127.8, 117.5, 87.9. IR ν 3157 (w), 3093 (w), 2160 (w), 1629 (s), 1562 (m), 1439 (m), 1321 (s), 1298 (s), 1148 (m), 839 (m), 747 (s). The characterization data is in accordance with reported literature values.[15]

[Ir{dF(CF$_3$)ppy}$_2$(dtbpy)]PF$_6$ (1)



Following a reported procedure,[16] heteroleptic iridium **1** was synthesized in two steps.

In a 25 mL tube were placed iridium(III) chloride (170 mg, 0.540 mmol, 1.0 equiv) and 2-(2,4-difluorophenyl)-5-(trifluoromethyl)pyridine (**38**) (315 mg, 1.20 mmol, 2.26 equiv) in a 2:1 v:v mixture of 2-methoxyethanol/water (12 mL) to give a dark purple solution. The mixture was degassed with Ar (Ar bubbling for 10 min) and heated at 120 °C overnight to afford an orange suspension. The reaction mixture was cooled down and filtered. The precipitate was washed with water (3 x 10 mL) and dried under vacuum to afford (**39**) as a yellow solid (246 mg, 0.170 mmol, 62%), which was directly used for the next step without further purification.

In a 25 mL tube were added the chloro-bridged dimer (**39**) (100 mg, 0.670 mmol, 1.0 equiv) and 4,4'-di-*tert*-butyl-2,2'-bipyridine (**40**) (39.7 mg, 0,148 mmol, 2.2 equiv) in ethylene glycol (4 mL) to give a yellow suspension. The mixture was heated at 150 °C overnight. The mixture was cooled and washed with hexane (3 x 40 mL) and the ethylene glycol layer was heated to 85 °C for 5 min to remove residual hexane. An aqueous saturated ammonium hexafluorophosphate solution was added, causing the iridium-PF_6 salt to precipitate, which was filtered, dried and recrystallized (acetone/ether), affording **1** (117 mg, 0.104 mmol, 78%) as a yellow solid.

^{1}H NMR (400 MHz, Acetone-d_6) δ 9.01 (d, J = 7.6 Hz, 2H, Ar*H*), 8.64 (dd, J = 8.8, 2.5 Hz, 2H, Ar*H*), 8.47–8.38 (m, 4H, Ar*H*), 8.31 (d, J = 5.3 Hz, 2H, Ar*H*), 8.00 (s, 2H, Ar*H*), 7.81 (t, J = 8 Hz, 2H, Ar*H*), 6.87 (ddd, J = 12.7, 9.3, 2.3 Hz, 2H, Ar*H*), 5.98 (dd, J = 8.5, 2.3 Hz, 2H, Ar*H*). ^{1}H NMR matches the literature data.[16]

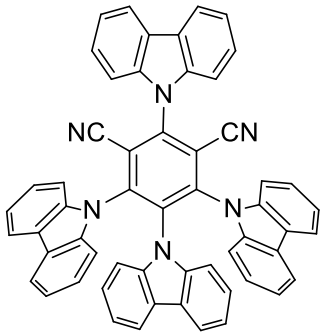
[16] A. Singh, K. Teegardin, M. Kelly, K. S. Prasad, S. Krishnan, J. D. Weaver, *J. Organomet. Chem.* **2015**, *776*, 51–59

3. Library of organic dyes: 4CzIPN derivatives

General procedure 1:

Sodium hydride (60% suspension in mineral oil, 8.0 equiv) was added slowly to a stirred solution of substituted-carbazole **7a-d** (5.0 equiv) in dry THF (0.05 M) under a nitrogen atmosphere at room temperature. After 30 min, 2,4,5,6-tetrafluoroisophthalonitrile **6** (0.179 g, 0.895 mmol, 1.0 equiv) was added. After stirring at room temperature for 15 h, 2 mL water was added to the reaction mixture to quench the excess of NaH. The resulting mixture was then concentrated under reduced pressure. The crude product was purified by recrystallization from hexane/CH_2Cl_2 then filtered. The brown liquid filtrate was concentrated and recrystallized as before. The combined solid were then purified by column chromatography on silica gel with DCM/Hexane.

2,4,5,6-Tetra(9*H*-carbazol-9-yl)isophthalonitrile (4CzIPN, 4a)



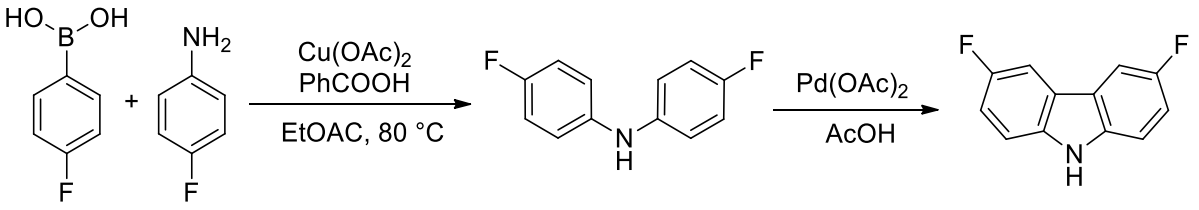
4a

Following the general procedure 1 and starting from 9H-carbazole **7a** (1.67 g, 10.0 mmol, 5.0 equiv), sodium hydride (0.60 g, 15 mmol, 7.5 equiv) and 2,4,5,6-tetrafluoroisophthalonitrile **6** (0.40 g, 2.0 mmol) in 40 mL of THF. Recrystallization (Hexanes/CH_2Cl_2 (1:1, 90 mL)) afforded the crude product as a yellow powder. Column chromatography afforded 2,4,5,6-tetra(9H-carbazol-9-yl)isophthalonitrile (**4a**) was obtained as a bright yellow crystalline solid (1.14 g, 1.45 mmol, 73 % yield).

Rf (Hexane/DCM 1/1) = 0.29. (yellow spot on TLC). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.2 (d, *J* = 7.7 Hz, 2H, Ar*H*), 7.8 – 7.6 (m, 8H, Ar*H*), 7.5 (ddd, *J* = 8.0, 6.6, 1.6 Hz, 2H, Ar*H*), 7.3 (d, *J* = 7.5 Hz, 2H, Ar*H*), 7.2 (dd, *J* = 8.4, 1.5 Hz, 4H, Ar*H*), 7.2 – 7.0 (m, 8H, Ar*H*), 6.8 (t, *J* = 7.8 Hz, 4H, Ar*H*), 6.6 (td, *J* = 7.6, 1.2 Hz, 2H, Ar*H*).^{13}C NMR (101 MHz, Chloroform-*d*) δ 145.2, 144.6, 140.0, 138.2, 136.9, 134.7, 127.0, 125.8, 124.9, 124.7, 124.5, 123.8, 122.4, 121.9, 121.4, 121.0, 120.4, 119.6, 116.3, 111.6, 109.9, 109.5, 109.4. ^{1}H NMR shift in $CDCl_3$ are consistent with reported data.[17]

3,6-Difluoro-9*H*-carbazole (7b)

[17] H. Uoyama, K. Goushi, K. Shizu, H. Nomura, C. Adachi, *Nature* **2012**, *492*, 234–238.



41 **42** **43** **7b**

Following a reported procedure,[18] a mixture of anhydrous $Cu(OAc)_2$ (182 mg, 1.00 mmol, 0.2 equiv), benzoic acid (611 mg, 5.00 mmol, 1.0 equiv), 4-fluoroaniline (**42**) (556 mg, 5.00 mmol, 1.0 equiv), 4-fluorophenylboronic acid (**41**) (2.10 g, 15.0 mmol, 3.0 equiv) and K_2CO_3 (61 mg, 5.0 mmol, 1.0 equiv) in ethyl acetate (15 mL) was heated at 80 °C for 4 hours. The crude mixture was concentrated under vacuum and purified by column chromatography (pentane/ethyl acetate 1:1) to afford bis(4-fluorophenyl)amine (**43**) (184 mg, 0.897 mmol, 18%) as a sticky black oil.

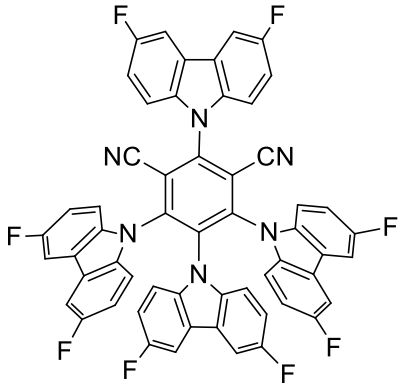
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.03 – 6.89 (m, 8H, Ar*H*), 5.46 (bs, 1H, N*H*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.9 (d, *J* = 239.9 Hz), 139.6, 119.5 (d, *J* = 7.7 Hz), 116.0 (d, *J* = 22.4 Hz). NMR matches the literature data.[18]

A mixture of bis(4-fluorophenyl)amine (**43**) (159 mg, 0.775 mmol, 1.0 equiv), $Pd(OAc)_2$ (174 mg, 0.775 mmol, 1.0 equiv) in glacial acetic acid (14 mL) was heated at reflux for 30 minutes. The reaction mixture was filtered through celite, which was subsequently washed with sodium bicarbonate (3 X 40 mL) and ethyl acetate (3 X 40 mL). The filtrate was concentrated under vacuum and purified by column chromatography (pentane/ethyl acetate 5:1) to afford 3,6-difluoro-9H-carbazole (**7b**) (115 mg, 5.66 mmol, 73%) as a pale brown solid.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98 (s, 1H, N*H*), 7.66 (dd, *J* = 8.9, 2.5 Hz, 2H, Ar*H*), 7.35 (dd, *J* = 8.8, 4.3 Hz, 2H, Ar*H*), 7.18 (td, *J* = 9.0, 2.5 Hz, 2H, Ar*H*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.3 (d, *J* = 235.9 Hz), 136.8, 123.5 (dd, *J* = 9.5, 4.3 Hz), 114.4 (d, *J* = 25.7 Hz), 111.5 (d, *J* = 8.9 Hz), 106.1 (d, *J* = 23.8 Hz). NMR matches the literature data.[18]

[18] K. L. Woon, Z. N. Nadiah, Z. A. Hasan, A. Ariffin, S.-A. Chen. *Dyes and Pigments,* **2016**, *132*, 1-6.

(2r,4s,5r)-2,4,5,6-Tetrakis(3,6-difluoro-9*H*-carbazol-9-yl)isophthalonitrile (4FCzIPN, 4b)

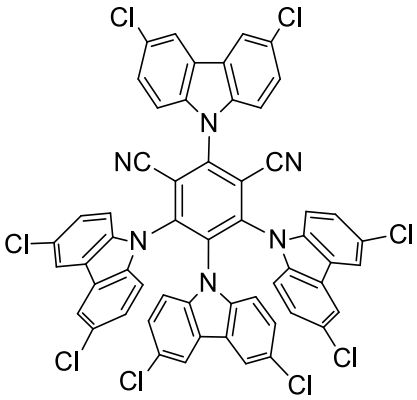


4b

Following the general procedure 1 and starting from 3,6-difluoro-9H-carbazole (**7b**) (105 mg, 0.517 mmol, 5.0 equiv), sodium hydride (33 mg, 0.83 mmol, 8.0 equiv) and 2,4,5,6-tetrafluoroisophthalonitrile **6** (20.7 mg, 0.103 mmol) in 2 mL of THF, (2r,4s,5r)-2,4,5,6-tetrakis(3,6-difluoro-9H-carbazol-9-yl)isophthalonitrile (**4b**) was obtained as a bright yellow crystalline solid (10 mg, 11 μmol, 10 % yield) after recrystallization in acetone (5 mL) and column chromatography using pure dichloromethane.

Rf (Hexane/DCM 1/1) = 0.23. (yellow spot on TLC). ^{1}H NMR (400 MHz, DMSO-d^{6}) δ 8.34 – 8.27 (m, 2H, Ar*H*), 8.09 (dd, *J* = 9.0, 4.2 Hz, 2H, Ar*H*), 7.81 (dd, *J* = 9.0, 2.6 Hz, 3H, Ar*H*), 7.72 – 7.61 (m, 6H, Ar*H*), 7.45 (dd, *J* = 8.9, 2.6 Hz, 2H), 7.36 (dd, *J* = 9.1, 4.2 Hz, 2H, Ar*H*), 7.15 – 7.05 (m, 4H, Ar*H*), 6.73 – 6.63 (m, 3H, Ar*H*).
^{13}C NMR not enough material for recording a clean spectra.
^{19}F NMR (376 MHz, DMSO-d_6) δ -120.6 (s, 2F), -120.8 (s, 4F), -121.5 (s, 2F). IR (ν_{max}, cm^{-1}) 3670 (w), 2985 (s), 2897 (s), 2367 (w), 2330 (w), 1725 (w), 1464 (m), 1395 (m), 1233 (m), 1183 (m), 1071 (s), 859 (m), 753 (w). HRMS (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{56}H_{24}F_8N_6^+$ 932.1929; Found 932.1955.

(2r,4s,5r)-2,4,5,6-Tetrakis(3,6-dichloro-9*H*-carbazol-9-yl)isophthalonitrile (4ClCzIPN, 4c)



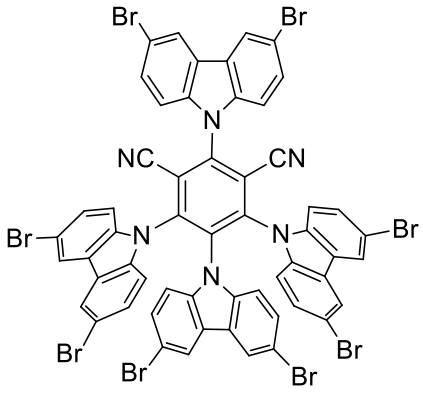
4c

Following the general procedure 1 and starting from 3,6-dichloro-9H-carbazole **7c** (1.10 g, 4.47 mmol, 5.0 equiv), sodium hydride (0.286 g, 7.16 mmol, 8.0 equiv) and 2,4,5,6-tetrafluoroisophthalonitrile **6** (0.179 g, 0.895 mmol) in 18 mL of THF. Recrystallization

(Hexanes/CH_2Cl_2 (1:2, 80 mL)) gave 900 mg of yellow powder, then second recrystallization gave 325 mg of brown powder. Column chromatography of the combined solid afforded (2r,4s,5r)-2,4,5,6-tetrakis(3,6-dichloro-9H-carbazol-9-yl)isophthalonitrile (**4c**) was obtained as a bright yellow crystalline solid (830 mg, 0.780 mmol, 87 % yield).

Rf (Hexane/DCM 1/1) = 0.25. (yellow spot on TLC). Mp: >240°C, turned dark yellow, decomp.
^{1}H NMR (400 MHz, DMSO-d_6) δ 8.60 (d, *J* = 2.1 Hz, 2H, Ar*H*), 8.15 (d, *J* = 2.1 Hz, 4H, Ar*H*), 8.08 (d, *J* = 8.8 Hz, 2H, Ar*H*), 7.87 (dd, *J* = 8.8, 2.1 Hz, 2H, Ar*H*), 7.80 (d, *J* = 2.2 Hz, 2H, Ar*H*), 7.69 (d, *J* = 8.8 Hz, 4H, Ar*H*), 7.46 (d, *J* = 8.8 Hz, 2H, Ar*H*), 7.32 (dd, *J* = 8.8, 2.2 Hz, 4H, Ar*H*), 6.93 (dd, *J* = 8.8, 2.2 Hz, 2H, Ar*H*). ^{13}C NMR (101 MHz, DMSO-d_6) δ 145.0, 144.5, 138.5, 137.4, 136.5, 135.8, 134.5, 127.8, 127.0, 126.4, 125.7, 125.3, 124.2, 123.8, 123.3, 121.6, 120.9, 120.3, 116.8, 112.6, 112.5, 112.3, 111.7. HRMS (ESI) calcd for $C_{56}H_{24}Cl_8N_6$ [M+] 1059.9565; found 1059.9573.
^{1}H NMR shift in $CDCl_3$ are consistent with reported data.[19] However, for better solubility and better resolution new ^{1}H and ^{13}C spectra were recorded in DMSO-d_6.

(2r,4s,5r)-2,4,5,6-Tetrakis(3,6-dibromo-9*H*-carbazol-9-yl)isophthalonitrile (4BrCzIPN, 4d)



4d

Following the general procedure 1 and starting from 3,6-dibromo-9H-carbazole **7d** (1.00 g, 3.08 mmol, 5.0 equiv), sodium hydride (0.197 g, 4.92 mmol, 8.0 equiv) and 2,4,5,6-tetrafluoroisophthalonitrile **6** (0.123 g, 0.615 mmol) in 12 mL of THF, (2r,4s,5r)-2,4,5,6-tetrakis(3,6-dibromo-9*H*-carbazol-9-yl)isophthalonitrile (**4d**) was obtained as a bright yellow crystalline solid (562 mg, 0.396 mmol, 64 % yield) after recrystallization in acetone (15 mL) and column chromatography using pure dichloromethane.

Rf (Hexane/DCM 1/1) = 0.43. (yellow spot on TLC). ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.74 (d, *J* = 1.8 Hz, 2H, Ar*H*), 8.30 (d, *J* = 2.0 Hz, 4H, Ar*H*), 8.04 – 7.99 (m, 4H, Ar*H*), 7.96 (dd, *J* = 8.6, 1.9 Hz, 2H, Ar*H*), 7.64 (d, *J* = 8.8 Hz, 4H, Ar*H*), 7.47 – 7.35 (m, 6H, Ar*H*), 7.05 (dd, *J* = 8.8, 2.0 Hz, 2H, Ar*H*). ^{13}C NMR (101 MHz, DMSO-d_6) δ 145.0, 144.5, 138.6, 137.7, 136.8, 135.9, 130.4, 129.1, 128.0, 124.7, 124.2, 123.9, 123.8, 116.8, 115.0, 114.4, 113.6, 112.9, 112.7, 111.7. NMR matches the literature data.[19]

[19] A. Kretzschmar, C. Patze, S. T. Schwaebel, and U. H. F. Bunz *J. Org. Chem*. **2015**, *80*, 9126−9131.

4. Physical measurement

Spectroscopic characterization

4CzIPN derivatives were studied at 10 µmol.L^{-1} in acetonitrile and dichloromethane. Absorbance was recorded between 200 and 800 nm. The excitation wavelength for fluorescence was 360 nm.

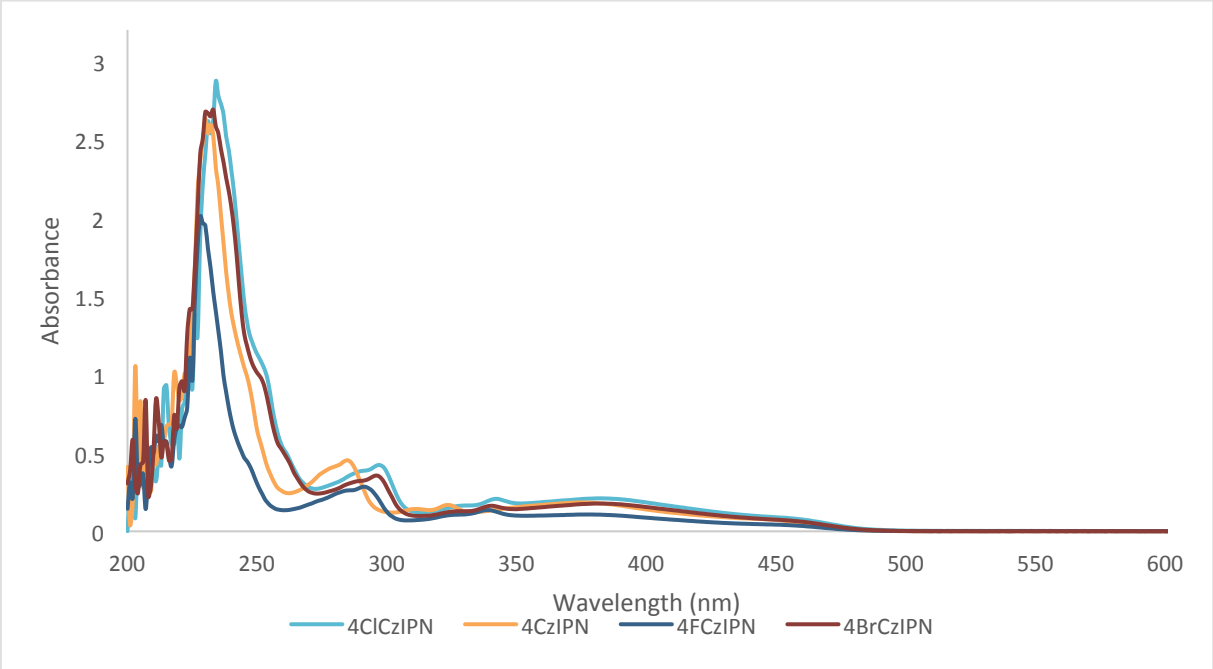


Figure 1: UV-Vis spectra of 4CzIPN derivatives in DCM.

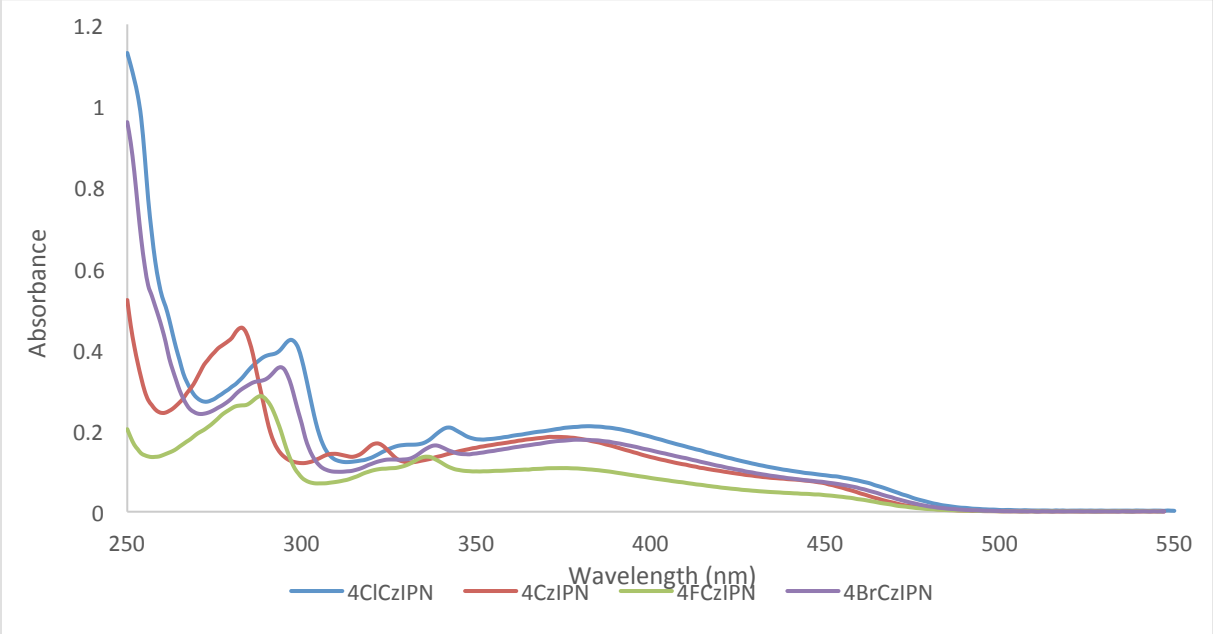


Figure 2. Zoom on the 250-550 nm region of the UV-Vis spectra of 4CzIPN derivatives in DCM.

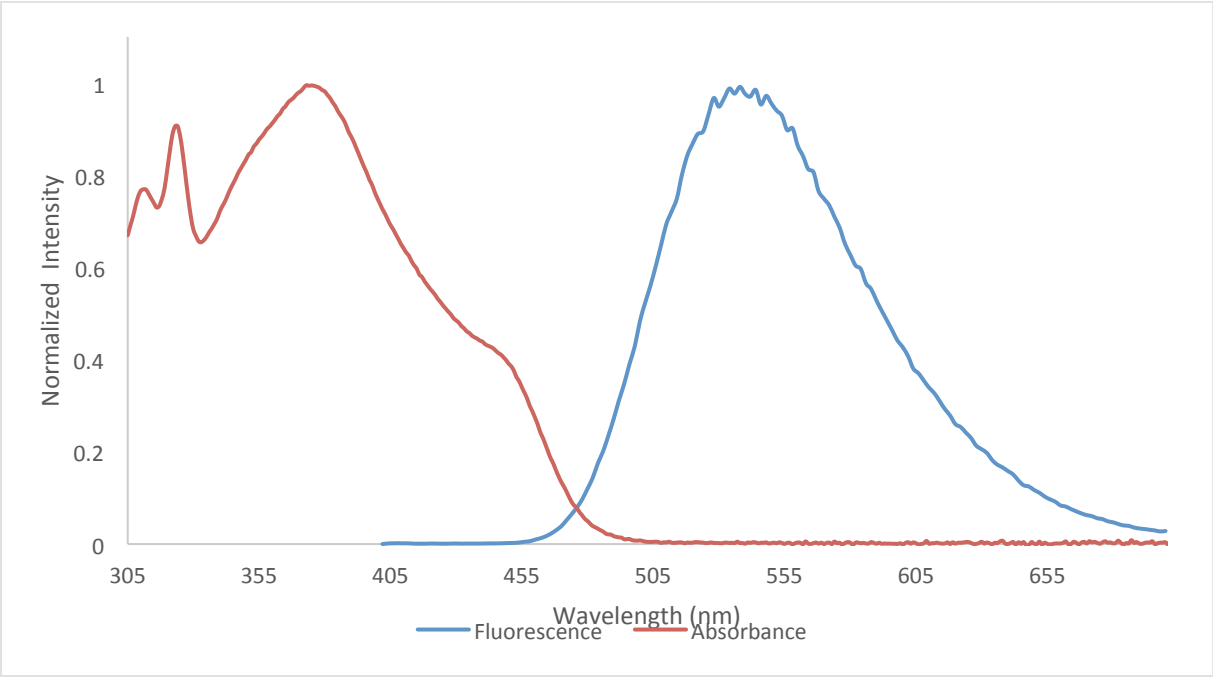


Figure 3. Absorbance and emission of 4CzIPN at 10 µmol.L^{-1} in DCM.

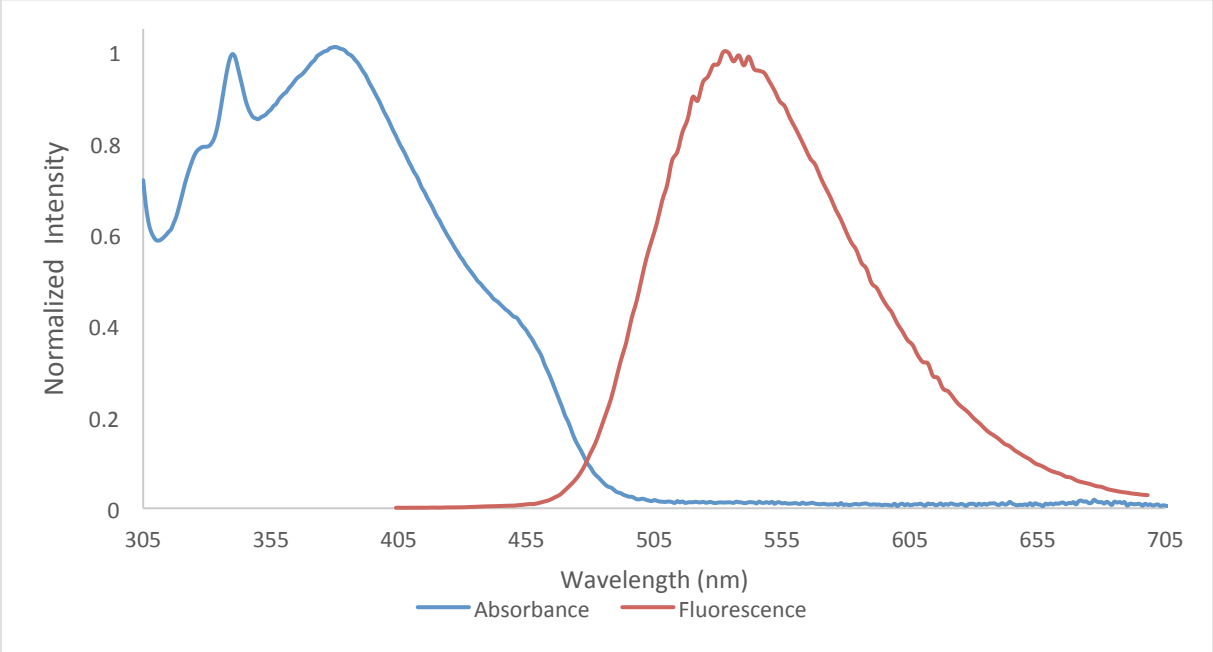


Figure 4. Absorbance and emission of 4ClCzIPN at 10 µmol.L^{-1} in DCM.

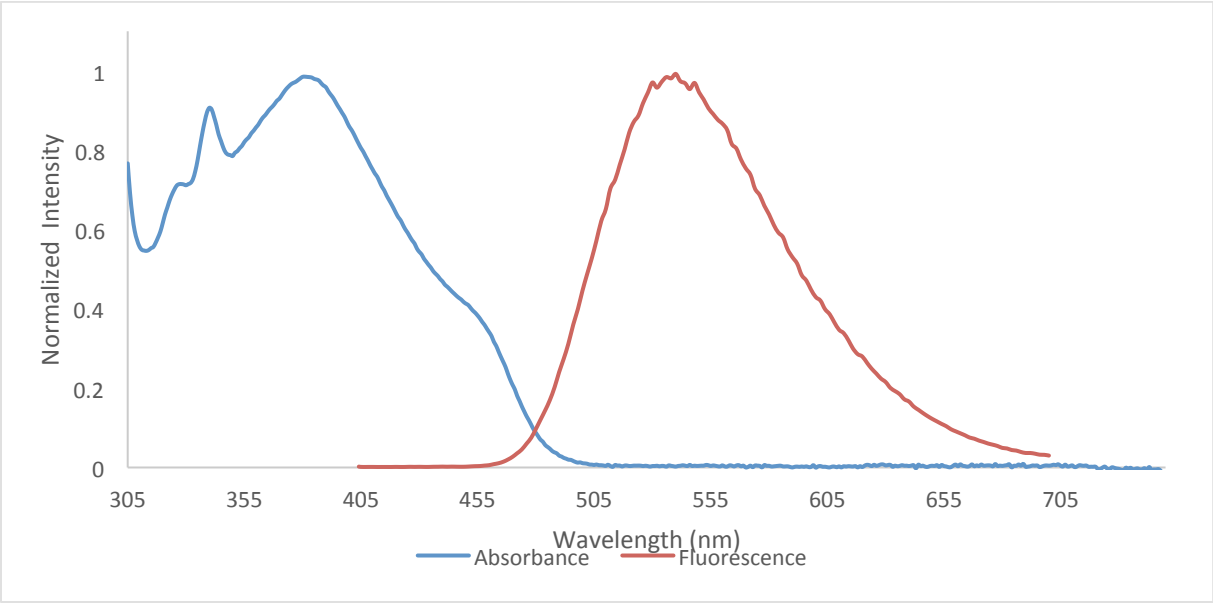


Figure 5. Absorbance and emission of 4BrCzIPN at 10 µmol.L^{-1} in DCM.

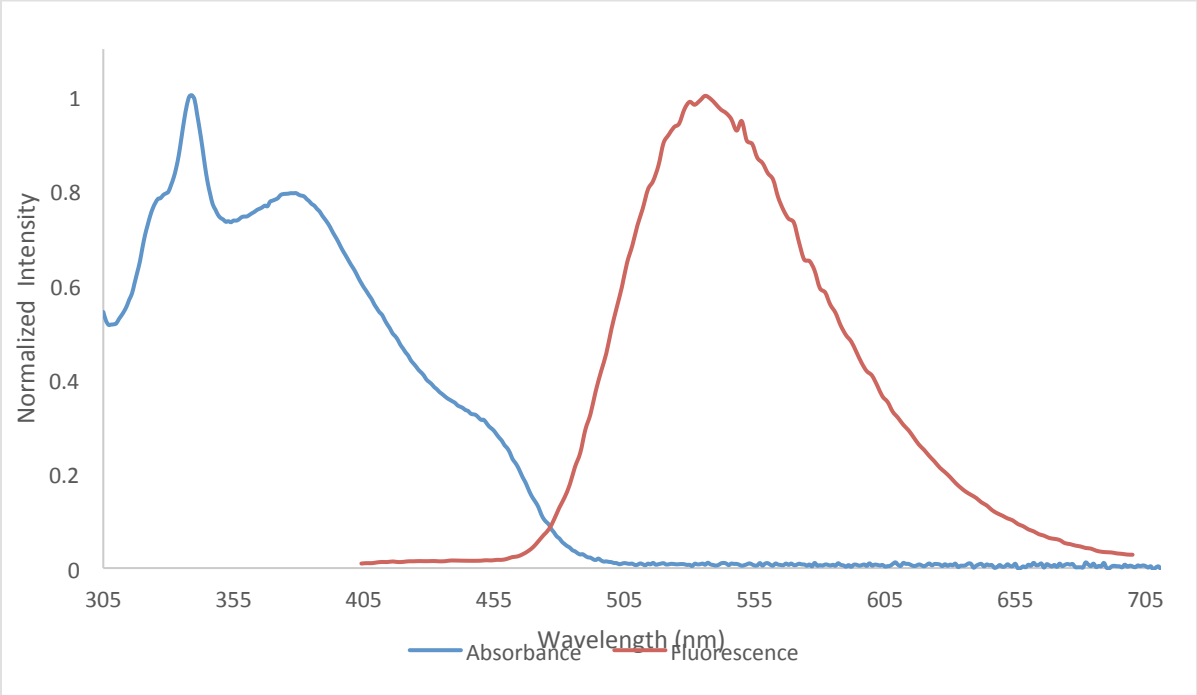


Figure 6. Absorbance and emission of 4FCzIPN at 10 µmol.L^{-1} in DCM.

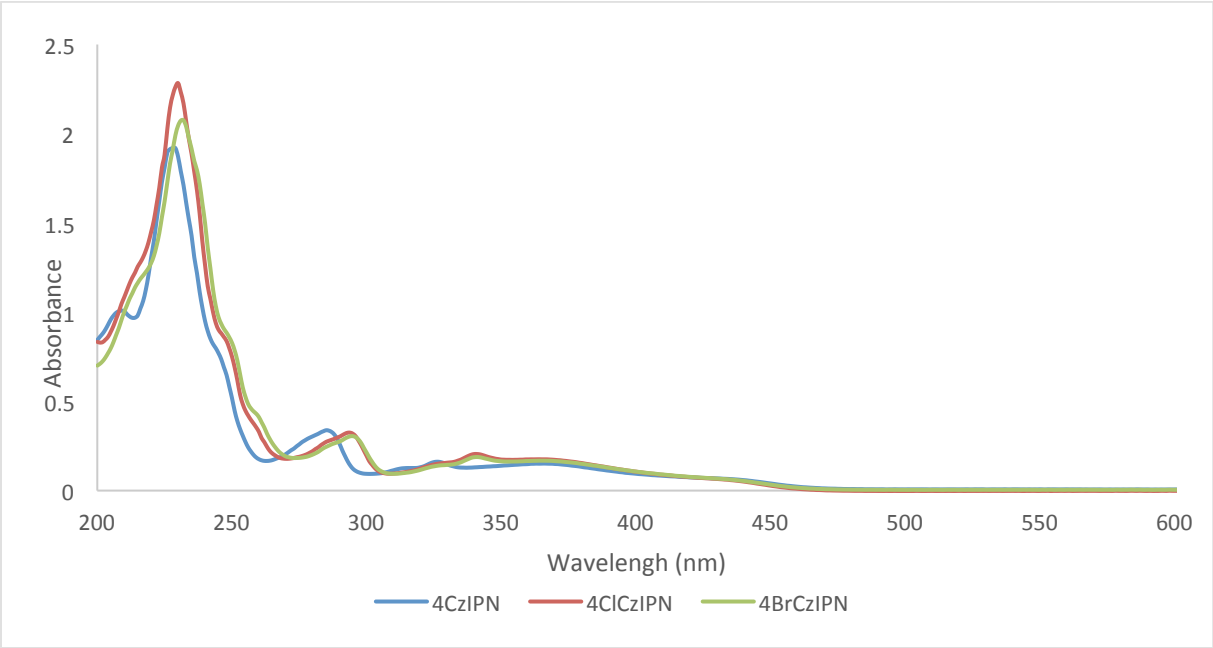


Figure 7. UV-Vis spectra of 4CzIPN derivatives in acetonitrile.

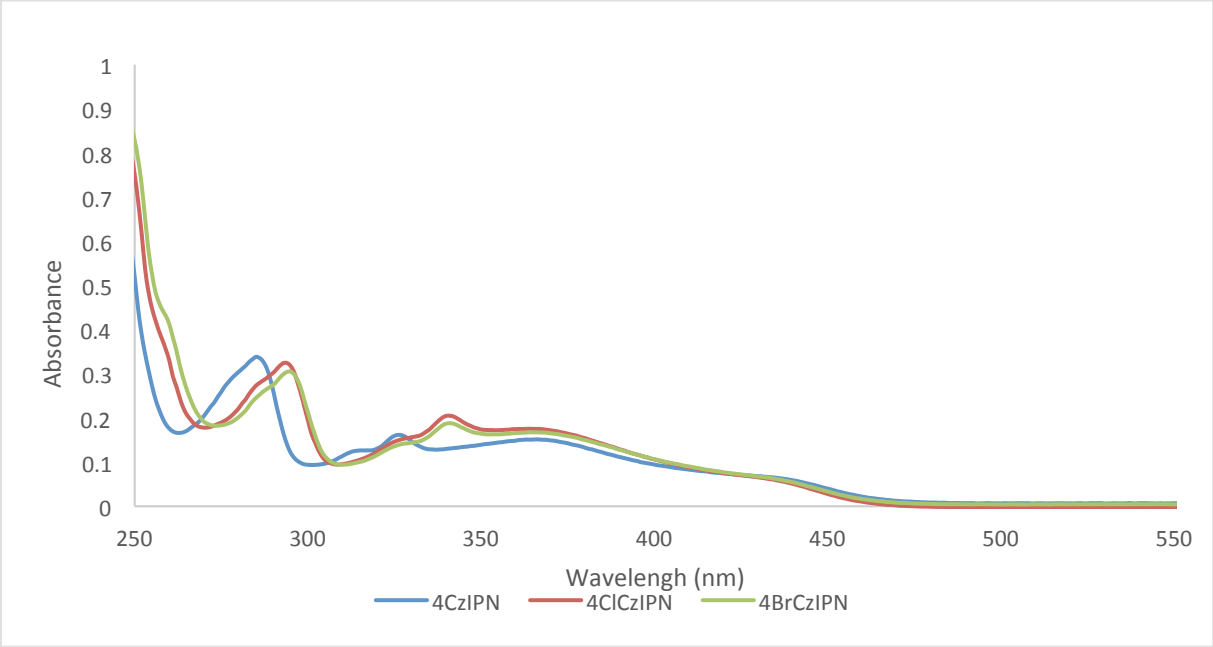


Figure 8. Zoom on the 250-550 nm region of the UV-Vis spectra of 4CzIPN derivatives in acetonitrile.

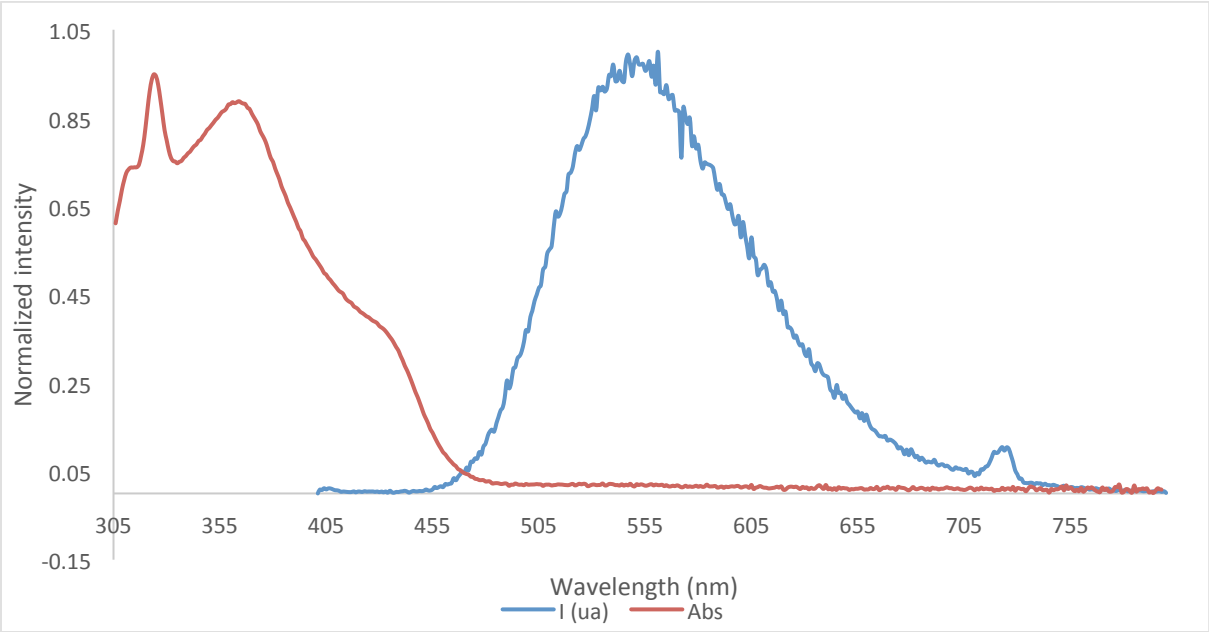


Figure 9. Absorbance and emission of 4CzIPN at 10 µmol.L^{-1} in acetonitrile.

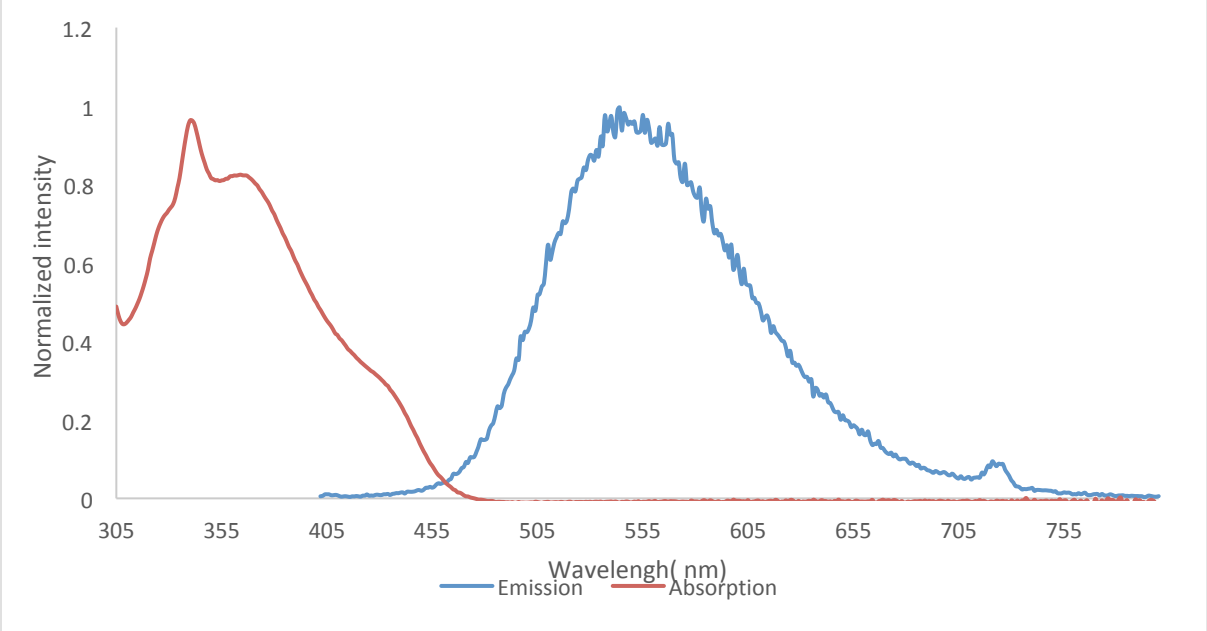


Figure 10. Absorbance and emission of 4ClCzIPN at 10 µmol.L^{-1} in acetonitrile.

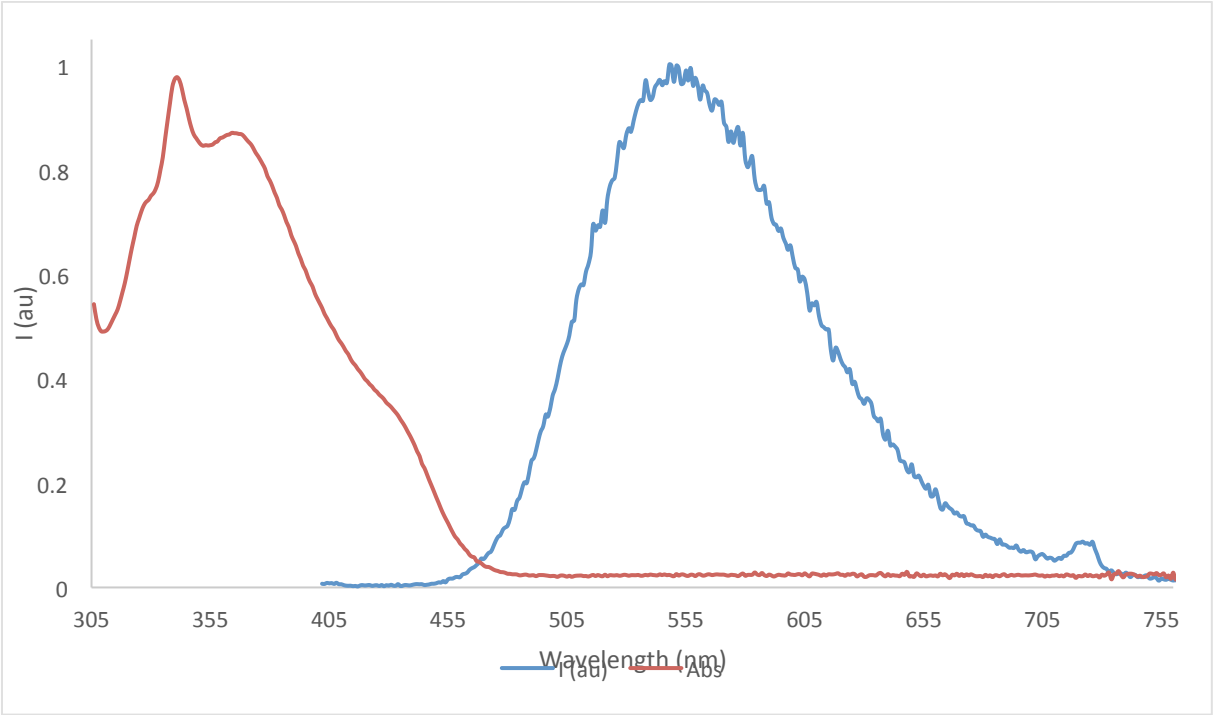


Figure 11. Absorbance and emission of 4BrCzIPN at 10 µmol.L^{-1} in acetonitrile.

Electrochemical measurements

Cyclic Voltammetry (CV) was performed using an Autolab Potentiostat, with a three-electrode cell configuration: a glassy carbon electrode as the working electrode, Pt wire as a counter electrode and an Ag/AgCl (KCl, 3M) electrode as the reference electrode. Bu_4NPF_6 was employed as the electrolyte (0.1 M) and ferrocene was added as the internal standard.

For comparison, 4ClCzIPN (**7e**) was studied in the same conditions as previous reports on 4CzIPN, at 1mM in degassed acetonitrile.[20,19] All 4CzIPN derivatives were studied in 1 mM solutions in degassed DCM at a scan rate of 0.1 V/s, to ensure solubility. Measures on 4FCzIPN were performed on a 0.5 mM solution due to the quantity of available material.

5 mM solutions of the oximes were prepared in degassed DMF to ensure solubility. The influence of the solvent on the redox properties of similar substrates has been studied by Leonori and coworkers.[21] Voltammograms were recorded at 4 different scan rates from 0.1 V/s to 1V/s. In the absence of reversible behaviour, the formal oxidation or reduction potentials were estimated with the $E_p$max, introducing a ~50 mV approximation. In the case of the oximes, determination of the potentials was achieved at 1 V/s, the highest scan rate.

[20] R. Ishimatsu, S. Matsunami, T. Kasahara, J. Mizuno, T. Edura, C. Adachi, K.Nakano and T. Imato, *Angew, Chem, Int. Ed.* **2014**, *53*, 6993-6996.
[21] J. Davies, N. S. Sheikh and D. Leonori, *Angew. Chem. Int. Ed.* **2017**, *56*, 13361–13365.

Photocatalyst	$E_{1/2}(P/P^-)$	$E_{1/2}(P^+/P)$	E_{0-0}	$E_{1/2}(P^+/P^*)$	$E_{1/2}(P^*/P^-)$
4CzIPN[22]	-1.21	+1.52	2.56	-1.04	+1.35
$4CzIPN_{exp}$	-1.05	+1.68	2.64	-0.96	+1.59
4ClCzIPN	-0.97	+2.05	2.68	-0.63	+1.71

Table 1. Redox potentials of 4CzIPN derivatives in acetonitrile[a]

Photocatalyst	$E_{1/2}(P/P^-)$	$E_{1/2}(P^+/P)$	E_{0-0}	$E_{1/2}(P^+/P^*)$	$E_{1/2}(P^*/P^-)$
4CzIPN	-1.16	+1.61	2.59	-0.98	+1.43
4ClCzIPN	-1.11	+1.73	2.59	-0.86	+1.48
4BrCzIPN	-1.06	+1.76	2.58	-0.82	+1.52
4FCzIPN	-1.08	+1.45	2.60	-1.15	+1.52

Table 2. Redox potentials of 4CzIPN derivatives in DCM[a]

[a]Potentials in V *vs* SCE, wavelength in nanometers. The excitation energy E_{0-0} was estimated by the point of intersection of the normalized absorbance and emission signals. $E_{1/2}(P^+/P^*) = E_{1/2}(P^+/P) - E_{0-0}$ and $E_{1/2}(P^*/P^-) = E_{0-0} + E_{1/2}(P/P^-)$.

It worth to be noted that measured values were significantly different from previous reports, both in cyclic voltammetry and in the estimation of E_{0-0}, likely due to difference of approximation methods (Table 1). However, in the conditions of this study, an anodic and cathodic shift were measured for 4ClCzIPN in acetonitrile in comparison to 4CzIPN. This confirmed our hypothesis regarding the influence of electron-withdrawing substituents on the carbazole moieties. Results in DCM were in alignment, with anodic and cathodic shifts measured for 4BrCzIPN and 4FCzIPN.

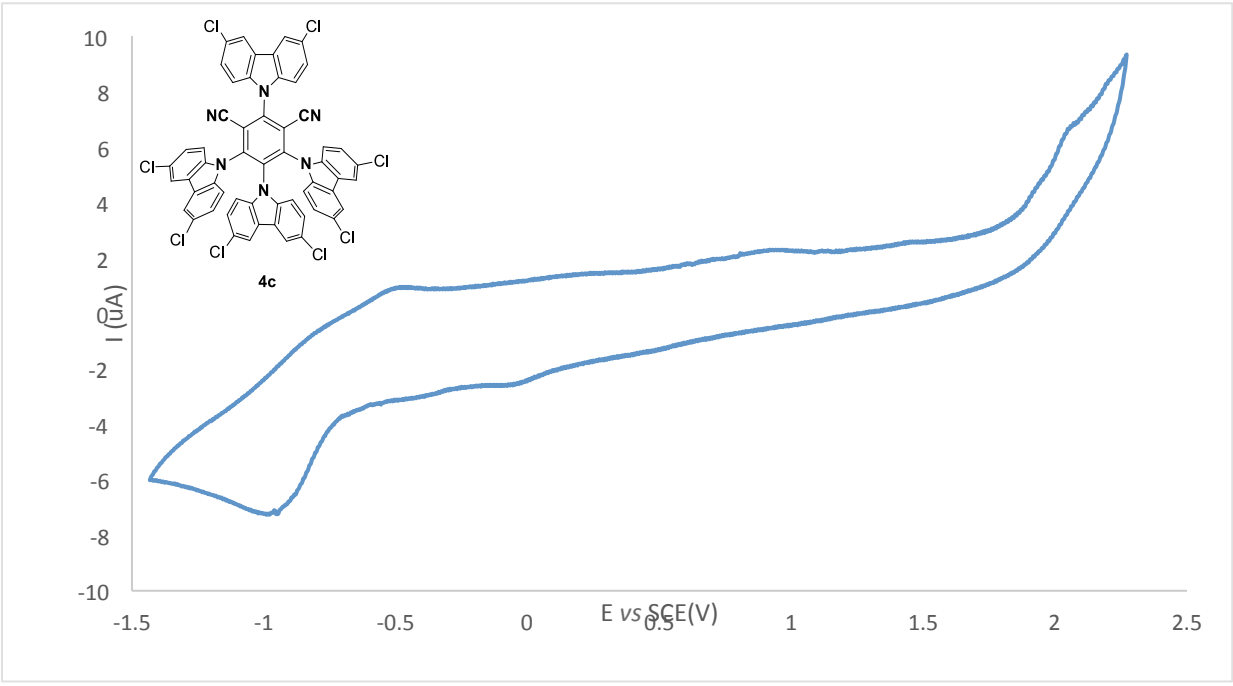


Figure 12. Cyclic Voltammetry of 4ClCzIPN in acetonitrile.

[22] J. Luo and J. Zhang, *ACS Catal.* **2016**, *6*, 873–877.

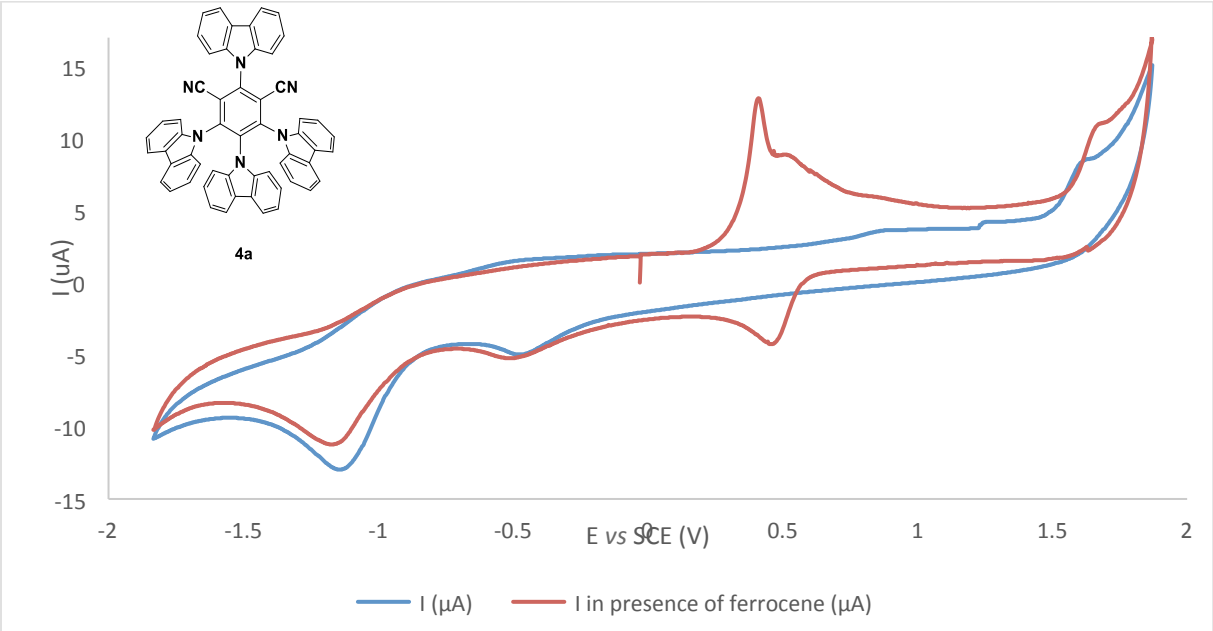


Figure 13. Cyclic Voltammetry of 4CzIPN in DCM.

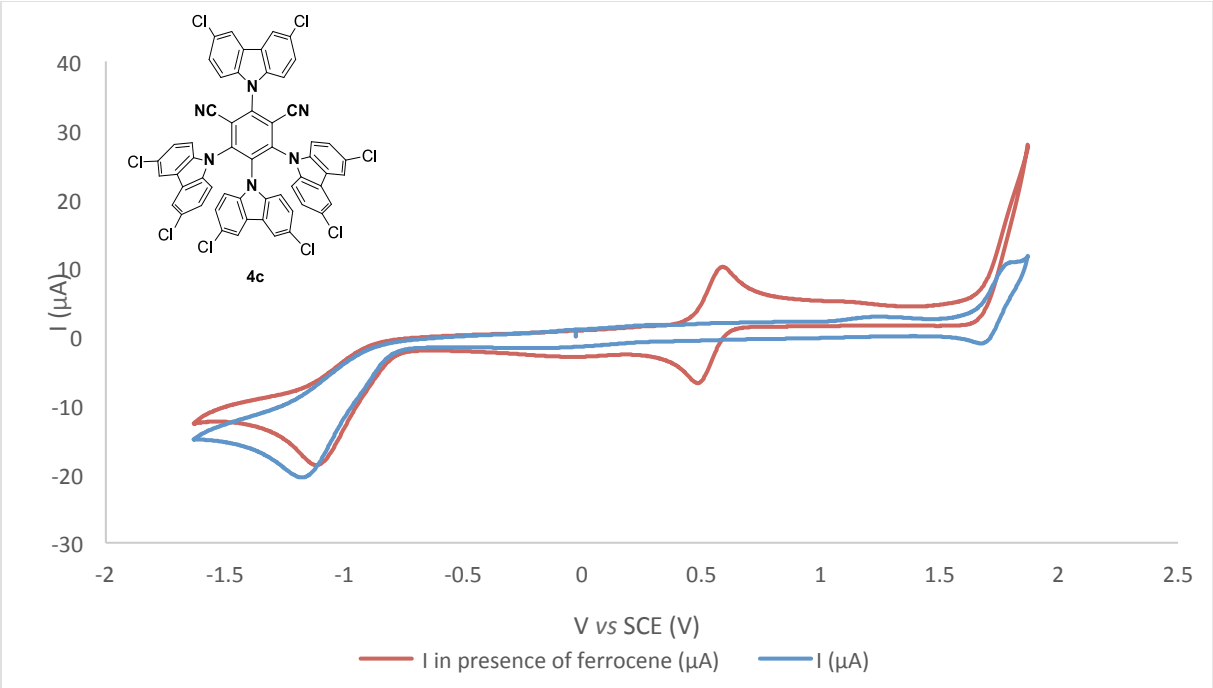


Figure 14. Cyclic Voltammetry of 4ClCzIPN in DCM.

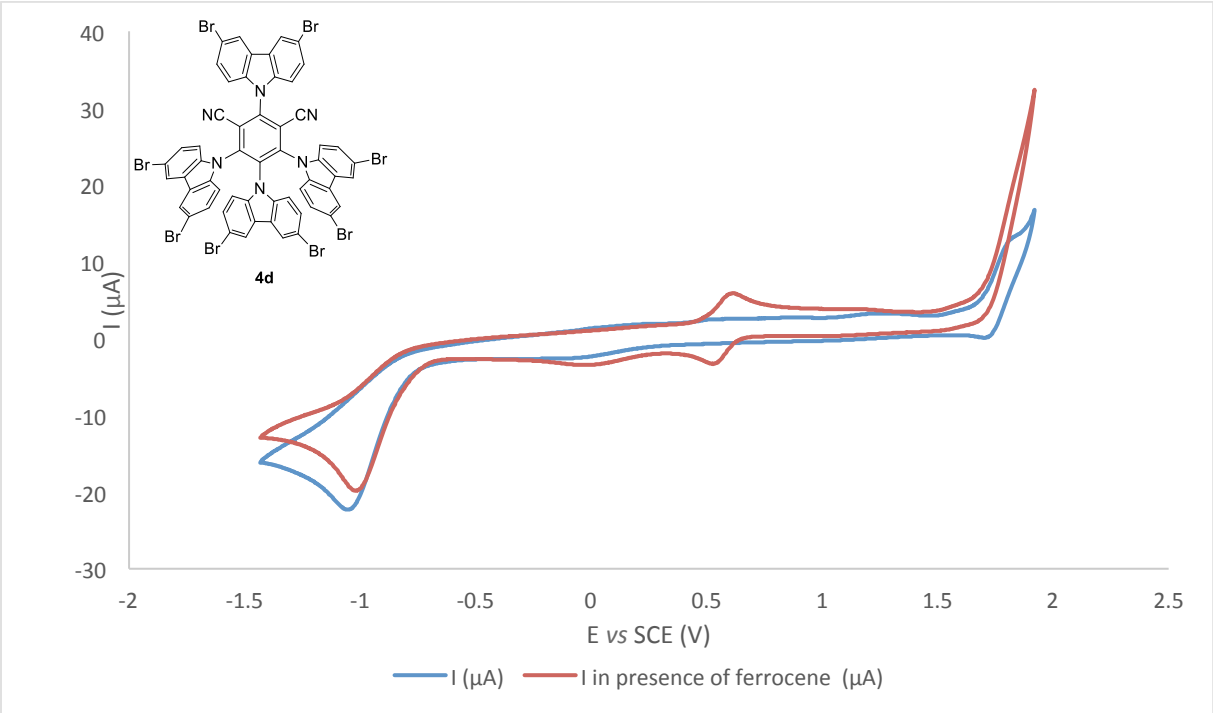


Figure 15. Cyclic Voltammetry of 4BrCzIPN in DCM.

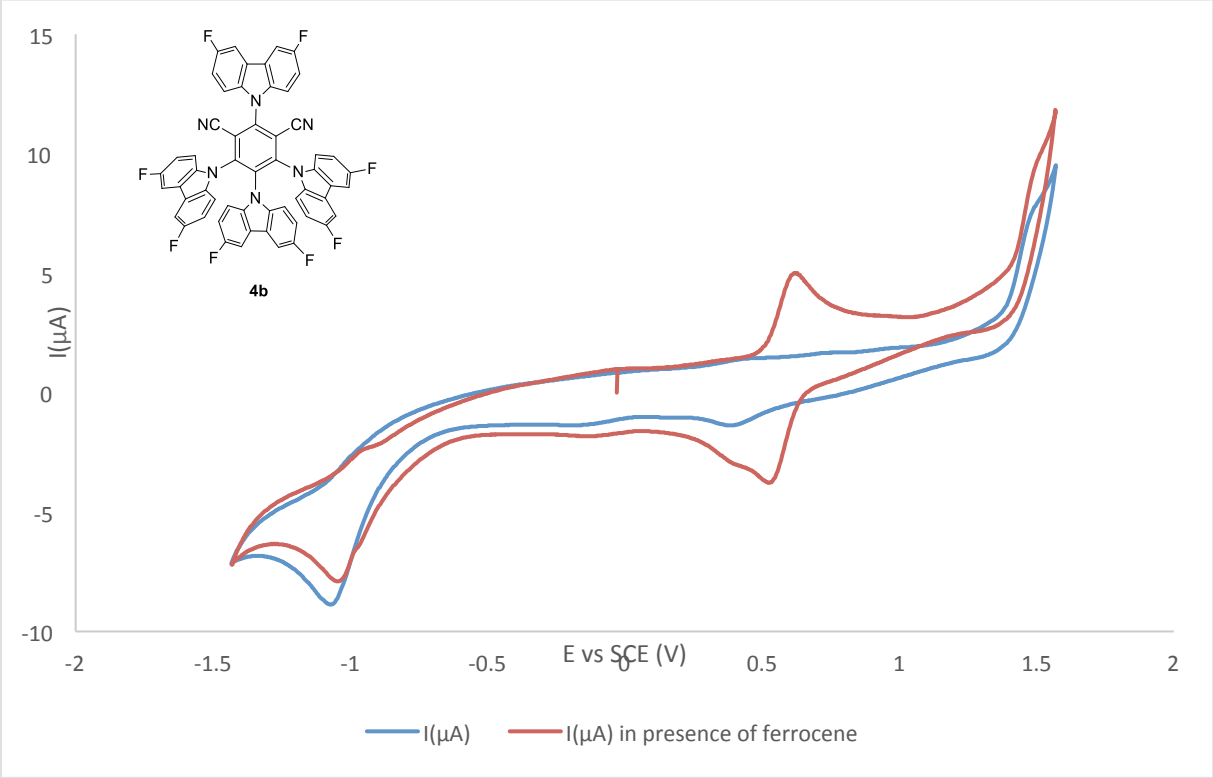


Figure 16. Cyclic Voltammetry of 4FCzIPN in DCM.

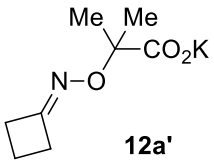
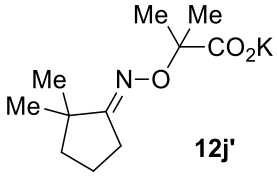
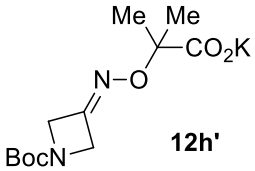
Oxime	$E_{1/2}^{ox}$ (V vs SCE)
 **12a'**	+1.48
 **12j'**	+1.50
 **12h'**	+1.59

Table 3. Electrochemical potentials of the oximes in DMF.[23]

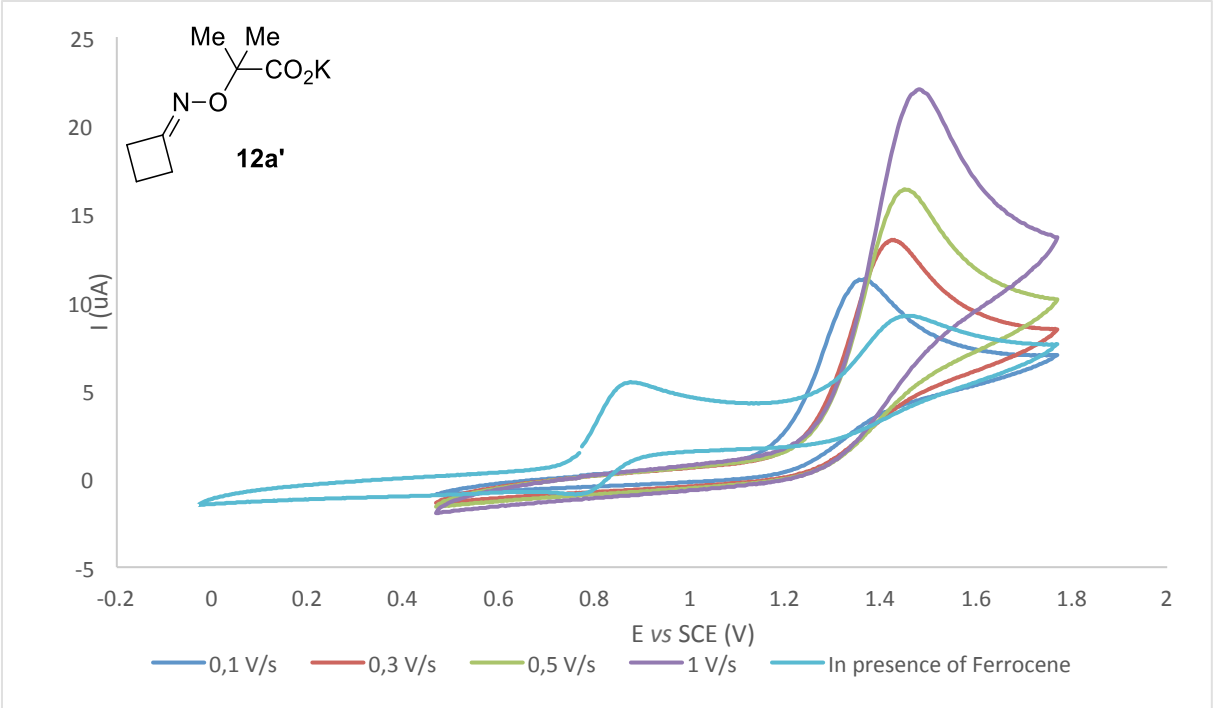


Figure 17. Cyclic Voltammetry of **12a'** in DMF.

[23] The potassium carboxylate salts were prepared by treatment of the corresponding acids with 1 equivalent of ^{t}BuOK in ethanol for 2h, followed by concentration under vacuum.

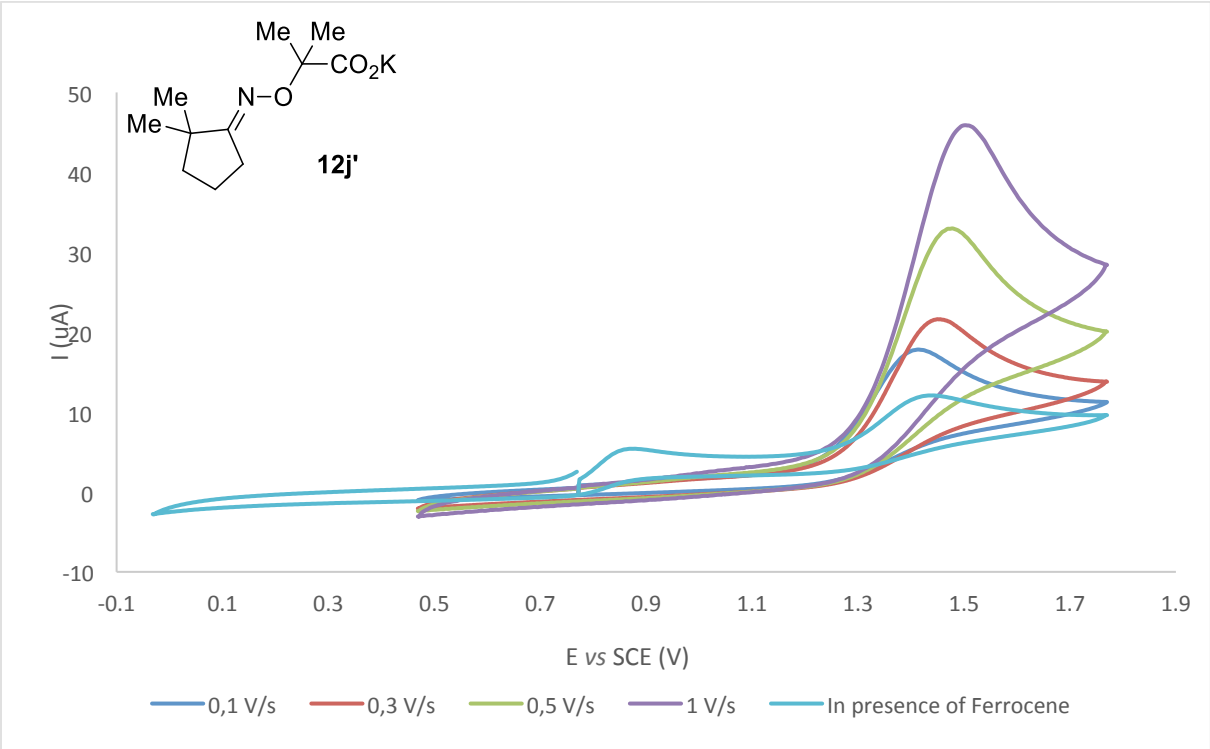


Figure 18. Cyclic Voltammetry of **12j'** in DMF.

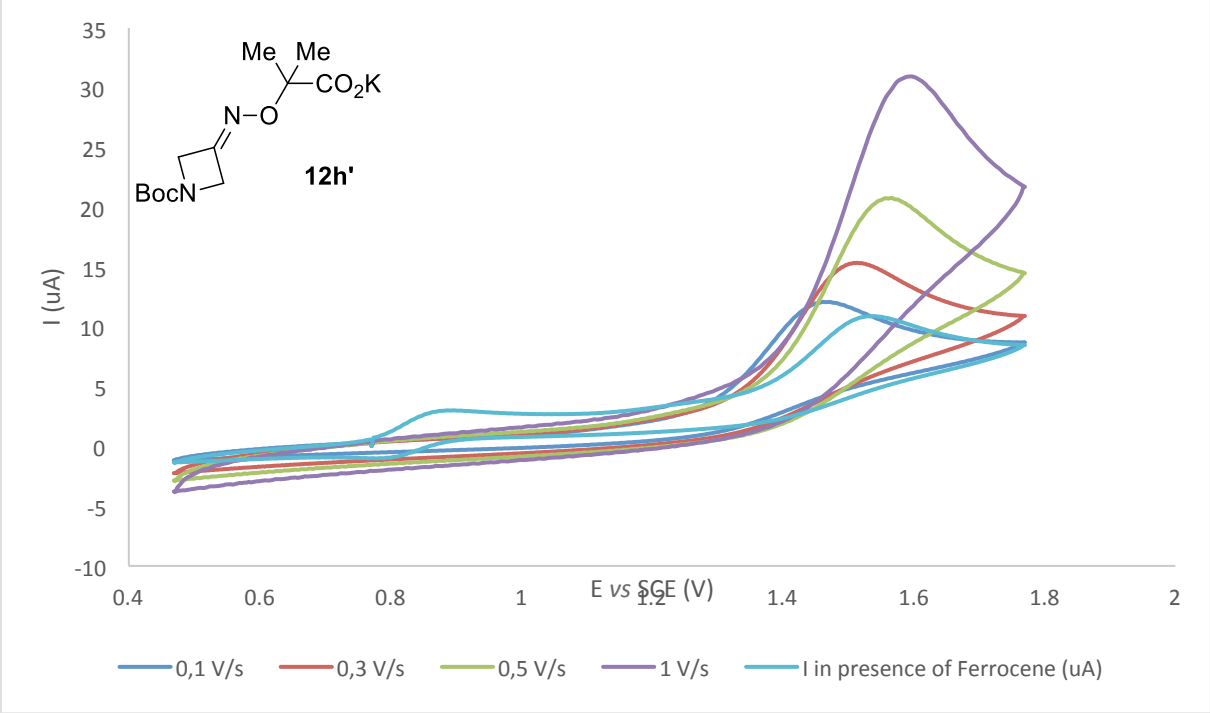
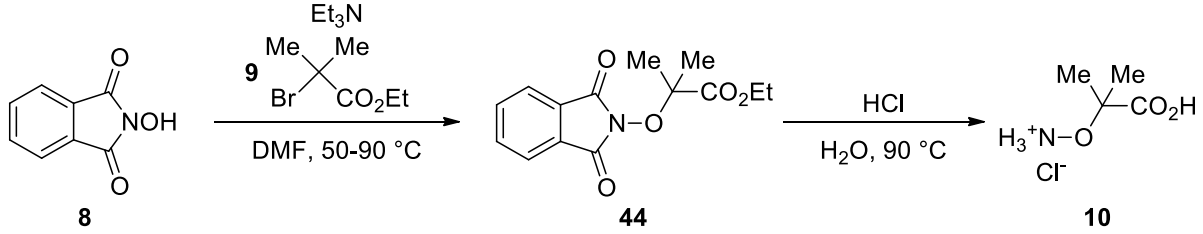


Figure 19. Cyclic Voltammetry of **12h'** in DMF.

5. Synthesis of the activating reagents for carbonyl substrates

2-(Aminooxy)-2-methylpropanoic acid hydrochloride (10)



8 **44** **10**

Following a reported procedure,[24] N-hydroxyphthalimide (**8**) (9.00 g, 55.2 mmol, 1.0 equiv) was suspended in DMF (21.6 mL). The suspension was heated to 50 °C, leading to the complete dissolution of the solid to provide a clear bright yellow solution. Ethyl 2-bromo-2-methylpropanoate **9** (9.4 mL, 66 mmol, 1.2 equiv) was then added, followed by triethylamine (10.9 mL, 78.0 mmol, 1.42 equiv). The addition of triethylamine resulted in the darkening of the solution from yellow-green to dark red. The mixture was then stirred at 90 °C. After 45 minutes, the formation of a solid and the decoloration of the mixture to orange-red was noticed. After 5 hours since the beginning of the reaction, heating was stopped and the brown mixture was allowed to cool down to room temperature. The mixture was then poured onto ice (150 g) in a 500 mL becher and stirred until the ice had melted completely. The bright red liquid was then filtered off to furnish a solid, which was washed with two portions of water (50 mL each) and dried under high vacuum for 5 hours. Ethyl 2-((1,3-dioxoisoindolin-2-yl)oxy)-2-methylpropanoate (**44**) (14.1 g, 50.8 mmol, 92% yield) was obtained as a pale brown-colored solid.

^{1}H NMR (400 MHz, DMSO-d_6) δ 7.88 (s, 4H; Ar*H*), 4.13 (q, *J* = 7.1 Hz, 2H; O*CH*$_2$CH$_3$), 1.51 (s, 6H, C(*CH*$_3$)$_2$), 1.22 (t, *J* = 7.1 Hz, 3H; OCH$_2$*CH*$_3$). ^{13}C NMR (101 MHz, DMSO-d_6) δ 170.0, 164.4, 135.1, 128.6, 123.5, 86.1, 61.4, 22.7, 13.8. IR (νmax, cm-1) 2992 (w), 2943 (w), 2899 (w), 1796 (m), 1735 (s), 1611 (w), 1371 (m), 1470 (m), 1451 (w), 1353 (m), 1297 (m), 706 (s), 1137 (m), 1183 (s), 1240 (w), 1082 (w), 1024 (m), 974 (m), 876 (m), 789 (w), 765 (w), 943 (w), 859 (w).

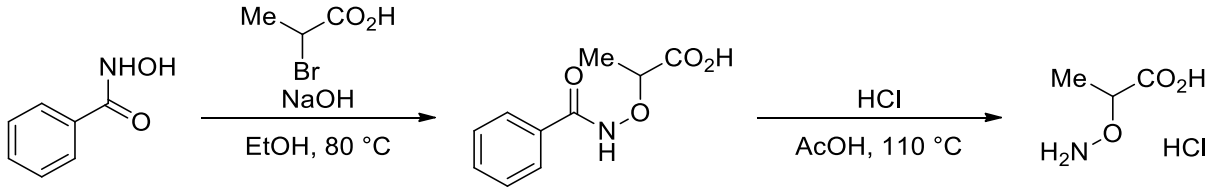
Ethyl 2-((1,3-dioxoisoindolin-2-yl)oxy)-2-methylpropanoate (**44**) (11.95 g, 43.10 mmol, 1.0 equiv) was suspended in aq. HCl (6.0 N; 71.8 mL, 431 mmol, 10.0 equiv). The pale brown suspension was stirred, while being heated to 90 °C. The solids were initially almost completely dissolved; after 2-3 hours, an off-white solid started to precipitate. After 4 hours, heating was stopped and the mixture was allowed to cool down to room temperature. The reaction flask was stored at 4 °C overnight. After 16 hours, the solids were filtered off, washed with water, and dried in the air. Side product phthalic acid (7.04 g, 42.4 mmol, 98% yield) was collected as pale brown solid.
The collected pale yellow clear aqueous solution was concentrated under reduced pressure. The resulting pale yellow solid was further dried at 65 °C under vacuum for 3 hours. It was then suspended in EtOAc (41 mL) and EtOH (1.8 mL) and the mixture was stirred at reflux for 20 minutes. It was then allowed to slowly cool down to room temperature and then further to -20 °C for 20 hours. This led to the precipitation of a crystalline colorless solid that was collected by filtration and washed with EtOAc/Pentane (30/10 mL) and pentane (20 mL). 2-

[24] L. Jiang, J. Yang, Z. Shumin, *Synthesis of Oxoamino-Aliphatic Carboxylic Acids*, **1991**, CN1051170 (A).

(Aminooxy)-2-methylpropanoic acid hydrochloride **10** (6.32 g, 40.6 mmol, 94%) was obtained as a colorless solid.

^{1}H NMR (400 MHz, DMSO-d_6; the signals corresponding to carboxylic and amine ^{1}Hs were not resolved) δ 1.46 (s, 6H, CH_3). ^{13}C NMR (101 MHz, DMSO-d_6) δ 173.6, 82.5, 23.2. IR (ν_{max}, cm^{-1}) 3440 (m), 2972 (m), 2897 (m), 2648 (w), 2299 (w), 1719 (s), 1757 (m), 1152 (s), 747 (m), 847 (m), 940 (m), 996 (m), 1052 (m), 1252 (m), 1202 (m), 1401 (w), 1507 (w), 1339 (w). The NMR spectra match the ones obtained from a commercially available batch: 1 g supplied by ABCR, cat. number AB456479 (lot 1371225).

2-(Aminooxy)propanoic acid hydrochloride (43)



45 **46** **47**

Following a reported procedure,[25] N-hydroxybenzamide **45** (6.08 g, 44.3 mmol, 1.0 equiv) and finely ground NaOH (5.32 g, 133 mmol, 3.0 equiv) were suspended in absolute EtOH (66 mL). To the resulting thick, off-white suspension, 2-bromopropanoic acid (4.1 mL, 44 mmol, 1.0 equiv) was added slowly via syringe under stirring. This resulted in the conversion of the homogeneous suspension into a pale brown solution, which was then heated to 80 °C. Once this temperature was reached, the mixture looked again as a homogeneous, off-white suspension, which was stirred overnight. The mixture was then concentrated under reduced pressure to provide a solid residue, which was dissolved in water (90 mL). The resulting aqueous solution was washed once with diethyl ether (100 mL) and then acidified by careful addition of aq. HCl (37 % w/w) until pH = 1. It was then extracted with EtOAc (3 x 100 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under vacuum to provide an off-white solid. Recrystallization from hexane (50 mL) and EtOAc (100 mL) afforded 2-(benzamidooxy)propanoic acid (**46)** (7.08 g, 33.9 mmol, 76% yield) as a colorless solid.

^{1}H NMR (400 MHz, DMSO-d_6) δ 12.98 (s, 1H, CO_2H or CON*H*), 11.91 (s, 1H, CO_2H or CON*H*), 7.76 (d, J = 7.6 Hz, 2H, Ph*H*), 7.54 (t, J = 7.4 Hz, 1H, Ph*H*), 7.45 (t, J = 7.6 Hz, 2H, Ph*H*), 4.53 (q, J = 6.9 Hz, 1H, *CH*CH$_3$), 1.40 (d, J = 6.9 Hz, 3H, CH_3). ^{13}C NMR (101 MHz, DMSO-d_6) δ 188.2, 173.0, 165.3, 131.9, 128.5, 127.4, 78.8, 16.6.

2-(Benzamidooxy)propanoic acid (**46**) (7.08 g, 33.8 mmol, 1.0 equiv) was suspended in acetic acid (20.5 mL). Aq. HCl (5.0 M; 68 mL, 34 mmol, 10 equiv) was then added and the mixture was heated to reflux (110 °C), which resulted in the formation of a pale yellow, clear solution. The latter was refluxed for 18 hours. It was then allowed to cool down to room temperature. This led to the precipitation of a crystalline solid (benzoic acid), which was filtered off. The resulting solution was stored at 4 °C overnight, which permitted the precipitation of a further amount of benzoic acid. Upon removal of the latter (4.13 g, 33.8 mmol, 100% yield) through filtration, the so-obtained clear solution was concentrated under vacuum. The resulting wet solid was further dried under vacuum at 60 °C for 3 hours. It was then refluxed in a mixture of

[25] H. Jiang, A. Studer, *Angew. Chem. Int. Ed.* **2017**, *56*, 12273–12276.

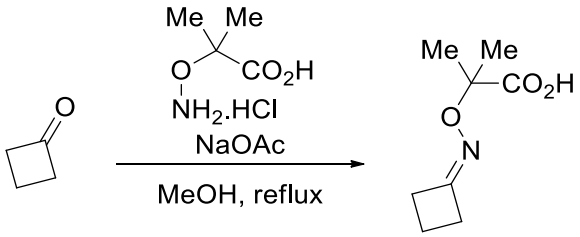
EtOAc (30 mL) and EtOH (1.5 mL) for 20 minutes, filtered, washed with pentane, and dried in the air. 2-(Aminooxy)propanoic acid hydrochloride (**47**) was obtained as a colorless solid (4.15 g, 29.3 mmol, 87% yield).

^{1}H NMR (400 MHz, Deuterium Oxide) δ 4.70 (q, J = 6.9 Hz, 1H, *CH*CH_3), 1.46 (t, J = 6.9 Hz, 3H, CH*CH*$_3$). ^{13}C NMR (101 MHz, DMSO-d_6) δ 171.8, 77.1, 16.4. The values for the ^{1}H-NMR spectrum are in roughly agreement with the data reported in the literature (small differences are likely due to concentration effects).[25]

6. Synthesis of oxime starting materials

General Procedure 2 (GP2)
Following a reported procedure,[26] a solution of ketone (1.0 equiv) in MeOH (0.20 M) was treated with 2-(aminooxy)-2-methylpropanoic acid hydrochloride (**10**) (1.2 equiv), sodium acetate (2.4 equiv) and heated to reflux until complete by TLC analysis (4.5 – 6.0 hours). The mixture was then allowed to cool to room temperature and aq. Na_2CO_3 (2.0 M) was added. In some cases, the addition of a small volume of water was necessary to achieve the complete dissolution of the solids. The resulting aqueous solution was extracted once with Et_2O and the organic layer was washed with aq. Na_2CO_3 (2.0 M; 2 x). The combined aqueous extracts were then acidified by careful addition of aq. HCl solution (30% v/v) until pH < 2, and extracted with DCM (3 x). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under vacuum to provide the pure product.

2-((Cyclobutylideneamino)oxy)-2-methylpropanoic acid (12a)

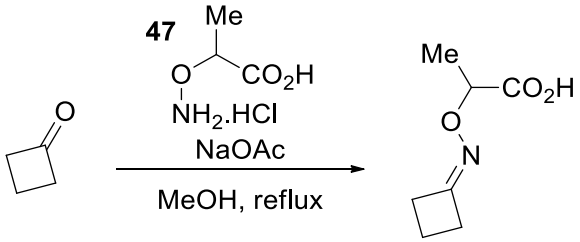


11 **12a**

Starting from commercially available cyclobutanone (**11**) (0.0930 mg, 0.100 mL, 1.33 mmol), 2-methyl-2-(((3-phenylcyclobutylidene)amino)oxy)propanoic acid (**12a**) was obtained as a pale yellow solid (0.202 g, 1.18 mmol, 90% yield), upon following the GP2.

M.p. 103.6-105.9°C ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.26 (s, 1H, CO_2H), 3.02 – 2.81 (m, 4H, $CH_2CH_2CH_2C$=N), 2.02 (p, J = 8.1 Hz, 2H, $CH_2CH_2CH_2$), 1.50 (s, 6H, Me_2). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.5, 161.5, 80.7, 31.8, 31.3, 24.1, 14.5. NMR shifts consistent with literature data.[26]

2-((Cyclobutylideneamino)oxy)propanoic acid (48)



11 **48**

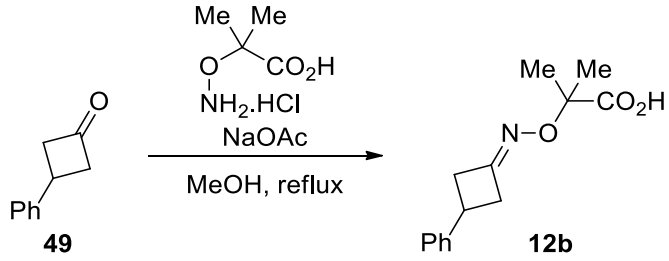
Starting from commercially available cyclobutanone (**11**) (0.0930 mg, 0.100 mL, 1.33 mmol), using **47** as activating reagent (226 mg, 1.60 mmol, 1.2 equiv), 2-methyl-2-(((3-

[26] E. M. Dauncey, S. P. Morcillo, J. J. Douglas, N. S. Sheikh, D. Leonori, *Angew. Chem. Int. Ed.* **2018**, *57*, 744–748.

phenylcyclobutylidene)amino)oxy)propanoic acid (**48**) was obtained as a pale yellow solid (0.150 g, 0.954 mmol, 72% yield), upon following the GP2.

M.p. 55.6-57.2°C ^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.51 (s, 1H, CO_2H), 4.63 (q, *J* = 7.1 Hz, 1H, OC*H*), 3.09 – 2.77 (m, 4H, $CH_2CH_2CH_2C$=N), 2.00 (p, *J* = 8.4 Hz, 2H, $CH_2CH_2CH_2$), 1.47 (d, *J* = 7.1 Hz, 3H, *Me*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.7, 161.4, 76.5, 31.6, 31.3, 16.8, 14.5. IR (ν_{max}, cm^{-1}) 2995 (m), 2934 (m), 2559 (w), 1727 (s), 1689 (m), 1455 (m), 1403 (w), 1330 (m), 1229 (m), 1189 (m), 1131 (s), 1099 (s), 1044 (m), 972 (m), 943 (m), 911 (m), 873 (s), 736 (m). HRMS (ESI) calcd for $C_7H_{10}NO_3$ [M+H-1] 156.0661; found 156.0659.

2-Methyl-2-(((3-phenylcyclobutylidene)amino)oxy)propanoic acid (12b)

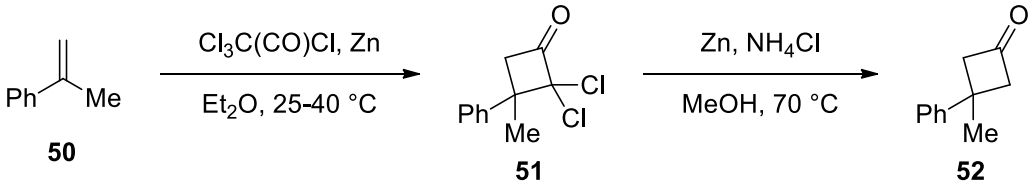


49 **12b**

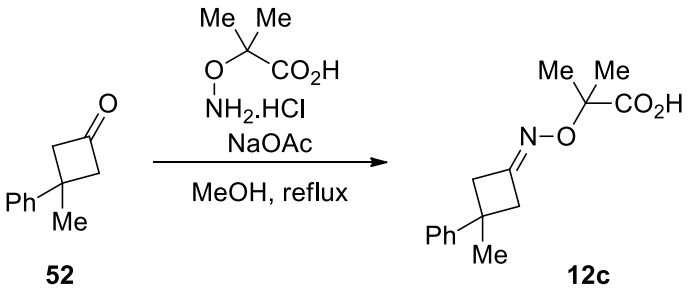
Starting from commercially available 3-phenylcyclobutanone (**49**) (0.200 g, 1.30 mmol), 2-methyl-2-(((3-phenylcyclobutylidene)amino)oxy)propanoic acid (**12b**) was obtained as a pale yellow solid (0.295 g, 1.19 mmol, 92% yield), upon following the GP2.

M.p. 90-93.5 °C. Rf (Pentane/EtOAc 5/1) 0.31. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.33 (br s, 1H, CO_2H), 7.38 - 7.32 (m, 2H, Ph*H*), 7.29 - 7.25 (m, 3H, Ph*H*), 3.64 (p, *J* = 8.4 Hz, 1H, Ph*CH*), 3.50-3.35 (m, 2H, CH_2), 3.10 (m, 1H, CH_2), 3.06 (ddd, *J* = 7.7, 4.9, 3.4 Hz, 1H, CH_2), 1.54 (s, 6H, CH_3). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.7, 158.9, 143.6, 128.7, 126.7, 126.4, 81.1, 39.7, 38.9, 32.9, 24.2, 24.2. IR (νmax, cm-1) 1694 (w), 1582 (w), 1482 (w), 1420 (w), 1333 (w), 1270 (m), 1214 (w), 1127 (m), 1071 (w), 1009 (m), 940 (m), 909 (m), 834 (m), 747 (s), 2835 (w), 2754 (w), 3115 (w), 3739 (w), 3651 (w), 3552 (w), 3365 (w), 3253 (w). HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{14}H_{17}NNaO_3^+$ 270.1101; Found 270.1109.

2-Methyl-2-(((3-methyl-3-phenylcyclobutylidene)amino)oxy)propanoic acid (12c)



50 **51** **52**



52 **12c**

Following a modified version of a reported procedure,[27] zinc powder (1.61 g, 24.6 mmol, 4.0 equiv) was suspended in diethyl ether (32 mL) under inert atmosphere. After the addition of alpha-methylstyrene (**50**) (0.80 mL, 6.1 mmol, 1.0 equiv), a solution of trichloroacetyl chloride (1.4 mL, 12 mmol, 2.0 equiv) in diethyl ether (16 mL) was also added drop-wise over a period of 40-45 minutes. During this time, the mixture was irradiated with ultrasound, while being maintained at a temperature < 25 °C by using a water bath and adding ice when necessary. Once the addition was completed, the mixture was kept under sonication for another 4 hours. The reaction then started suddenly: the reaction mixture became darker, from colorless to yellow and then to orange-brown. Consumption of zinc powder also became evident. Ultrasound irradiation was continued for another hour. At this point, TLC analysis (elution with only heptane) showed the (almost) complete conversion of the starting material and the formation of a major product. The reaction was therefore stopped and the mixture diluted with diethyl ether (20 mL) and the solids were filtered off through a plug of celite and washed with diethyl ether. The filtrate was then washed with water (2 x 20 mL), sat. aq. $NaHCO_3$ (4 x 20 mL), and brine; it was then dried over $MgSO_4$, filtered and concentrated under vacuum. Column chromatography (25 g SiO_2; EtOAc in Pentane 2 to 10%) furnished 2,2-dichloro-3-methyl-3-phenylcyclobutanone (**51**) (1.41 g - 85% pure, 5.23 mmol, 85% yield) as pale orange oil.

Rf (pentane/EtOAc 9/1) 0.70. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 (m, 2H, Ph*H*), 7.35 (m, 1H, Ph*H*), 7.29 (m, 2H, Ph*H*), 4.00 (dd, *J* = 16.3, 1.0 Hz, 1H, (CO)*CH*$_2$), 3.09 (d, *J* = 16.4 Hz, 1H, (CO)*CH*$_2$), 1.67 (d, *J* = 0.9 Hz, 3H, *CH*$_3$). The values for the ^{1}H-NMR spectrum are in roughly agreement with the data reported in the literature.[28]

Following a reported procedure,[29] zinc powder (2.00 g, 30.6 mmol, 5.0 equiv) and ammonium chloride (0.817 g, 15.3 mmol, 2.5 equiv) were suspended in MeOH (8.7 mL). A solution of 2,2-dichloro-3-methyl-3-phenylcyclobutanone (**51**) (1.40 g, 6.11 mmol, 1.0 equiv) in MeOH (8.7 mL) was added to the suspension under stirring, at such a rate to prevent it from refluxing (ca 15 minutes). Once the addition was finished, the mixture was stirred at 70 °C for 3 hours. After this time, TLC analysis (pentane/EtOAc 9/1) showed that full conversion was achieved, with formation of a major product. The mixture was then allowed to cool down to room temperature and the solids were filtered off through a pad of celite. The filtrate was concentrated under reduced pressure, diluted with aq. HCl (1.0 M; 15 mL) and extracted with diethyl ether (3 x 15 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The resulting crude oil was submitted to column chromatography (40 g SiO_2; EtOAc in pentane 1 to 20%) to afford 3-methyl-3-phenylcyclobutanone (**52**) (0.438 g, 2.73 mmol, 45% yield) as colorless oil.

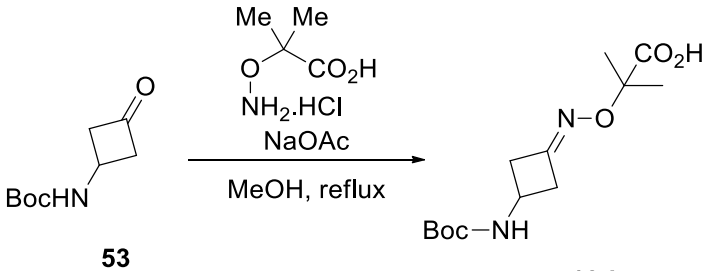
Rf (Pentane/EtOAc 9/1) 0.70. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 (dd, *J* = 8.1, 6.9 Hz, 2H, Ph*H*), 7.33 (m, 2H, Ph*H*), 7.27 (m, 1H, Ph*H*), 3.49 (d, *J* = 19.2 Hz, 2H, (CO)*CH*$_2$), 3.13 (d, *J* = 19.3 Hz, 2H, (CO)*CH*$_2$), 1.62 (s, 3H, *CH*$_3$). The values for the ^{1}H-NMR spectrum are in roughly agreement with the data reported in the literature [30]

[27] J. Boivin, E. Fouquet, S. Z. Zard, *Tetrahedron* **1994**, *50*, 1757–1768.
[28] W. Cao, I. Erden, R. H. Grow, J. R. Keeffe, J. Song, M. B. Trudell, T. L. Wadsworth, F.-P. Xu, J.-B. Zheng, *Can. J. Chem.* **1999**, *77*, 1009–1034.
[29] B. D. Johnston, K. N. Slessor, A. C. Oehlschlager, *J. Org. Chem* **1985**, *50*, 114-117.
[30] H.-J. Xu, F.-F. Zhu, Y.-Y. Shen, X. Wan, Y.-S. Feng, *Tetrahedron* **2012**, *68*, 4145–4151.

Starting from 3-methyl-3-phenylcyclobutanone (**52**) (0.438 g, 2.73 mmol), 2-methyl-2-(((3-methyl-3-phenylcyclobutylidene)amino)oxy)propanoic acid (**12c**) was obtained as a colorless solid (0.440 g, 1.68 mmol, 62% yield), upon following the GP2.

M.p. 112.6-114.6 °C. Rf (Pentane/EtOAc 4/1) 0.43. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.04 (s, 1H, CO_2H), 7.38 - 7.32 (m, 2H, Ph*H*), 7.28 - 7.20 (m, 3H, Ph*H*), 3.30 (dd, *J* = 9.9, 3.0 Hz, 1H, CH_2), 3.26 (dd, *J* = 10.6, 2.9 Hz, 1H, CH_2), 3.10 (dt, *J* = 16.7, 3.2 Hz, 1H, CH_2), 3.00 (dt, *J* = 16.1, 3.2 Hz, 1H, CH_2), 1.54 (s, 3H, CH_3), 1.53 (s, 3H, CH_3), 1.52 (s, 3H, CH_3). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 179.0, 157.1, 148.6, 128.5, 126.1, 125.2, 80.8, 44.8, 44.2, 38.0, 30.9, 24.1, 24.1. IR (ν_{max}, cm^{-1}) 3608 (w), 2986 (m), 2930 (m), 2567 (w), 2684 (w), 1716 (s), 1593 (m), 1488 (m), 1168 (s), 971 (s), 1297 (m), 1408 (m), 1248 (w), 1371 (m), 730 (s), 872 (m), 909 (s), 699 (s), 749 (m). HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{20}NO_3^+$ 262.1438; Found 262.1442.

2-(((3-((*tert*-Butoxycarbonyl)amino)cyclobutylidene)amino)oxy)-2-methylpropanoic acid (12d)

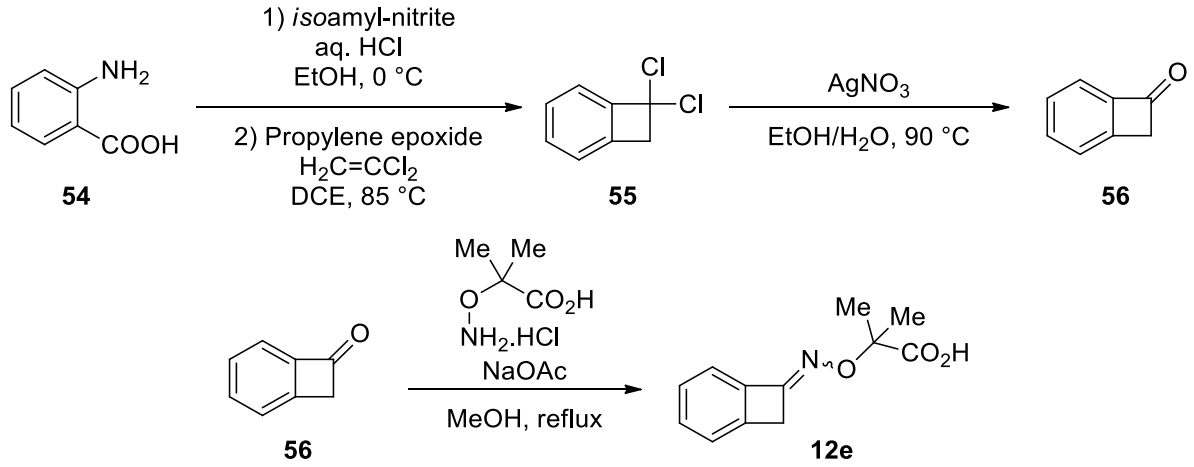


53 **12d**

Starting from tert-butyl (3-oxocyclobutyl)carbamate (**53**) (0.25 g, 1.28 mmol) the product **12d** was obtained as a white solid (0.360 g, 1.23 mmol, 98%), upon following the GP2.

M.p. 171.6-175.5°C (decomp). ^{1}H NMR (400 MHz, DMSO-d_6) δ 12.40 (s, 1H, CO_2H), 7.38 (d, *J* = 7.4 Hz, 1H, N*H*), 4.03 (q, *J* = 7.4 Hz, 1H, C*H*NHBoc), 3.19 – 2.98 (m, 2H, CH_2), 2.83 – 2.66 (m, 2H, CH_2), 1.39 (s, 9H, N*Boc*), 1.36 (s, 3H, CMe_2)., 1.35 (s, 3H, CMe_2). ^{13}C NMR (101 MHz, DMSO-d_6) δ 175.0, 154.7, 153.3, 80.1, 78.0, 38.8, 28.2, 24.0 (2C). IR (ν_{max}, cm^{-1}) 3361 (w), 2986 (m), 2936 (w), 1715 (s), 1693 (s), 1524 (m), 1457 (w), 1395 (m), 1368 (m), 1278 (m), 1254 (m), 1163 (s), 1070 (w), 1006 (w), 968 (m), 915 (m), 873 (m), 824 (w), 782 (w), 738 (m). HRMS (ESI) calcd for $C_{13}H_{22}N_2NaO_5^+$ $[M+Na]^+$ 309.1421; found 309.1424.

2-((Bicyclo[4.2.0]octa-1,3,5-trien-7-ylideneamino)oxy)-2-methylpropanoic acid (12e)



Following a reported procedure,[31] anthranylic acid (**54**) (0.75 g, 5.5 mmol, 1.0 equiv) was dissolved in absolute EtOH (8.2 mL). Under stirring, the solution was cooled to 0 °C (ice-water bath). Aq. HCl (37% v/v; 0.45 mL, 5.5 mmol, 1.0 equiv) was added via pipette (the reaction mixture darkened from yellowish to brown), followed by ice-cold *iso*pentyl nitrite (1.25 mL, 9.30 mmol, 1.7 equiv). Stirring was continued at 0 °C for 10 minutes. During this time, the mixture converted into a pink-yellow suspension. Diethyl ether (8.2 mL) was then added and stirring was continued at the same temperature for another 5 minutes. The formed solid was then collected by filtration and washed with ether (2 x 8.0 mL) (behind an anti-blast shield: the dry product is reported explosive!). The obtained pale yellow solid was immediately suspended in DCE (12.1 mL). Propylene oxide (0.77 mL, 11 mmol, 2.0 equiv) and 1,1-dichloroethene (3.6 mL, 45 mmol, 8.2 equiv) were then added by syringe. The mixture was then heated to reflux over a period of 20 hours: during this time, the suspension turned from pale yellow to dark orange-brown, and a gentle release of gas was observed. It was then allowed to cool down to room temperature and a brown solid was removed through filtration over a pad of celite, which was washed with several portions of DCM. The filtrate was concentrated under reduced pressure to give an orange-brown crude oil, which was used directly in the following step, without further purification.

Following a reported procedure,[32] the crude oil obtained from the previous step was diluted with EtOH (9.3 mL) and water (2.3 mL). Silver nitrate (1.91 g, 11.2 mmol, 2.05 equiv) was then added in small portions. The resulting suspension was heated at 90 °C under stirring for 4 hours: this resulted in the mixture darkening to grey-black. The solids were then removed by filtration through a pad of celite, which was washed with several portions of EtOH. The filtrate was concentrated under reduced pressure, diluted with water (15 mL), and extracted with diethyl ether (3 x 30 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered and concentrated under vacuum. The resulting crude oil was submitted to column chromatography (25 g SiO_2; DCM in Pentane 6 to 50%) to furnish bicyclo[4.2.0]octa-1,3,5-trien-7-one (**56**) (0.458 g, 3.88 mmol, 71% yield) as a colorless solid.

Rf (Pentane/DCM 3/1) 0.38. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 - 7.47 (m, 2H, Ar*H*), 7.38 (t, *J* = 7.5 Hz, 1H, Ar*H*), 7.32 (dd, *J* = 7.6, 1.0 Hz, 1H, Ar*H*), 4.00 - 3.92 (m, 2H, Ar*CH*$_2$). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 188.7, 151.3, 147.9, 135.2, 128.7, 123.7, 120.6, 52.3.

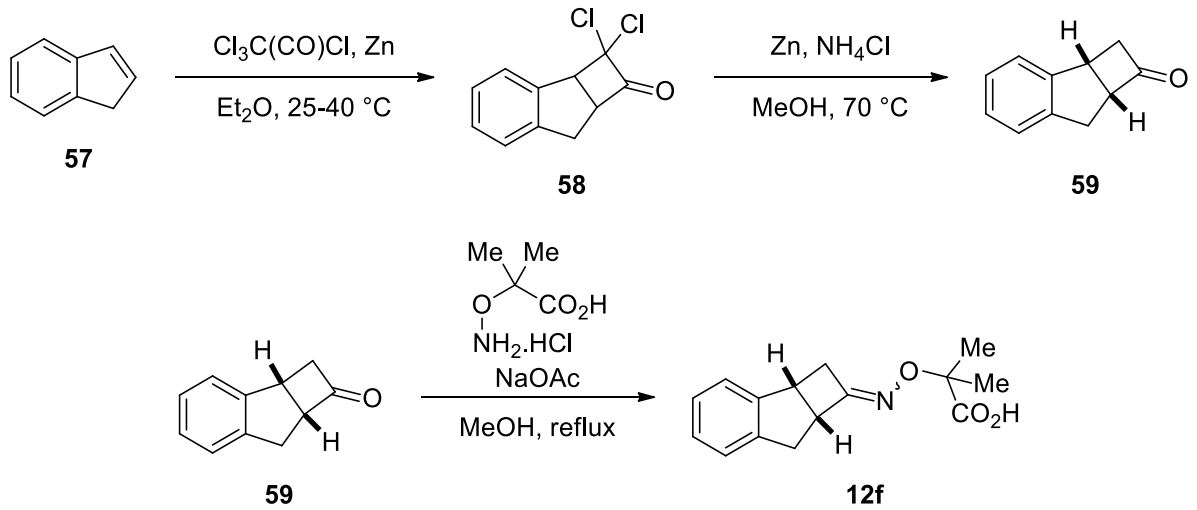
[31] M. S. South, L. S. Liebeskind, *J. Org. Chem.* **1982**, *47*, 3815–3821.
[32] O. Abou-Teim, M. C. Goodland, J. F. W. McOmie, *J. Chem. Soc. Perkin Trans. 1* **1983**, 2659–2662.

The values for the ^{1}H-NMR spectrum are in roughly agreement with the data reported in the literature.[33]

Starting from bicyclo[4.2.0]octa-1,3,5-trien-7-one (**56**) (0.200 g, 1.69 mmol), 2-((bicyclo[4.2.0]octa-1,3,5-trien-7-ylideneamino)oxy)-2-methylpropanoic acid (**12e**) was obtained as a colorless solid (mixture of E and Z isomers; 0.195 g, 0.889 mmol, 52% yield), upon following the GP2.

M.p. 120-125.2 °C. Rf (pentane/EtOAc 4/1) 0.38. ^{1}H NMR (400 MHz, Chloroform-*d*; the signals corresponding to the minor isomer are reported in *italics*) δ 10.73 (br s, 1 H, CO_2H), 7.42 (dd, J = 13.2, 7.3 Hz, 2H, Ar*H*), 7.32 (q, J = 9.7, 8.7 Hz, 2H, Ar*H*), *3.91* (s, 2H, ArCH_2), 3.89 (s, 2H, ArCH_2), 1.63 (s, 6H, CH_3), *1.59* (s, 6H, CH_3). ^{13}C NMR (101 MHz, Chloroform-*d*) δ *178.3*, 178.2, *154.7*, 152.2, 145.6, *144.6*, *140.7*, 139.3, 132.2, *131.7*, *128.3*, 128.2, 123.3, *123.2*, 123.0, *120.0*, 81.5, *81.4*, 39.6, *39.4*, 24.2, *24.2*. IR (ν_{max}, cm^{-1}) 3009 (m), 2922 (m), 2816 (m), 2660 (m), 2548 (w), 1713 (s), 1595 (w), 1557 (w), 1476 (w), 1364 (w), 1302 (m), 1177 (s), 965 (s), 915 (s), 828 (m), 766 (s). HRMS (ESI/QTOF) m/z: $[M + H-1]^+$ Calcd for $C_{12}H_{12}NO_3^+$ 218.0817; Found 218.0817.

2-Methyl-2-(((2,2a,7,7a-tetrahydro-1*H*-cyclobuta[a]inden-1-ylidene)amino)oxy)propanoic (12f)



Following a modified version of a reported procedure,[27] zinc powder (1.00 g, 15.3 mmol, 2.0 equiv) was suspended in diethyl ether (40 mL) under inert atmosphere. After the addition of indene (**57**) (0.90 mL, 0.89 mmol, 1.0 equiv), a solution of trichloroacetyl chloride (1.3 mL, 11 mmol, 1.5 equiv) in diethyl ether (20 mL) was also added drop-wise over a period of 40-45 minutes. During this time, the mixture was irradiated with ultrasound, while being maintained at a temperature < 25 °C by using a water bath and adding ice when necessary. Once the addition was completed, ultrasound irradiation was continued for one additional hour. Suddenly, an exothermal process started leading the grey suspension to rapidly turn to brown. After another 15 minutes, TLC analysis (pentane/EtOAc 8/1) showed the complete conversion of the starting material. The reaction was therefore stopped, the mixture diluted with diethyl ether (20 mL), and the solids were filtered off through a pad of celite, and washed with diethyl ether. The filtrate was then washed with water (2 x 20 mL), sat. aq. $NaHCO_3$ (4 x

[33] K. Nishikawa, H. Fukuda, M. Abe, K. Nakanishi, Y. Tazawa, C. Yamaguchi, S. Hiradate, Y. Fujii, K. Okuda, M. Shindo, *Phytochemistry* **2013**, *96*, 223–234.

20 mL), and brine; it was then dried over $MgSO_4$, filtered and concentrated under vacuum. Column chromatography (50 g SiO_2; EtOAc in pentane 1 to 25%) furnished 2,2-dichloro-2,2a,7,7a-tetrahydro-1*H*-cyclobuta[a]inden-1-one as an off-white solid (**58**) (0.832 g, 3.66 mmol, 48% yield).

Rf (pentane/EtOAc 9/1) 0.71. ^{1}H NMR (400 MHz, Chloroform-*d*) δ = 7.44 (m, 1H, Ar*H*), 7.34 – 7.30 (m, 2H, Ar*H*), 7.27 (m, 1H, Ar*H*), 4.50 (dd, *J* = 8.0, 1.5, 2H, Ar*CH*$_2$), 3.40 (dd, *J* = 16.9, 1.4, 1H, *CH*), 3.20 (dd, *J* = 16.7, 8.0, 1H, *CH*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 197.6, 143.5, 137.6, 129.3, 128.7, 127.5, 125.5, 88.3, 59.3, 58.9, 34.4. HRMS (LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{11}H_8Cl_2O^+$ 225.9947; Found 225.9951.

Following a reported procedure,[29] zinc powder (1.01 g, 15.4 mmol, 5.0 equiv) and ammonium chloride (0.412 g, 7.71 mmol, 2.5 equiv) were suspended in MeOH (4.0 mL). A solution of 2,2-dichloro-2,2a,7,7a-tetrahydro-1*H*-cyclobuta[a]inden-1-one (0.700 g, 3.08 mmol, 1.0 equiv) in MeOH (10 mL) was added to the suspension under stirring, at such a rate to prevent it from refluxing (ca. 15 minutes). Once the addition was finished, the mixture was stirred at 70 °C for 3 hours. After this time, TLC analysis (pentane/EtOAc 9.5/0.5) showed that full conversion was achieved. The mixture was then allowed to cool down to room temperature and the solids were filtered off through a pad of celite. The filtrate was concentrated under reduced pressure, diluted with aq. HCl (1.0 M; 20 mL) and extracted with diethyl ether (3 x 20 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The resulting crude oil was submitted to column chromatography (25 g SiO_2; EtOAc in pentane 2 to 20%) to provide 2,2a,7,7a-tetrahydro-1*H*-cyclobuta[a]inden-1-one (**59**) (0.330 g, 2.09 mmol, 68% yield) as colorless oil.

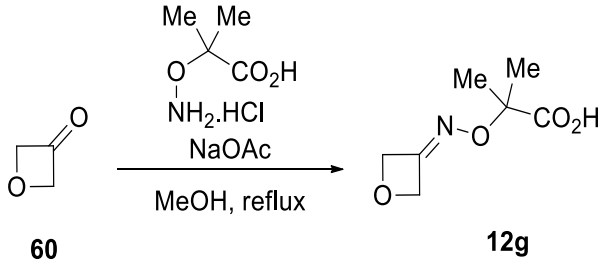
Rf (Pentane/EtOAc 9/1) 0.52. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.30 (m, 1H, Ar*H*), 7.25 - 7.20 (m, 3H, Ar*H*), 4.07 (m, 1H, (CO)*CH*), 4.05 (d, *J* = 1.3 Hz, 1H, Ar*CH*), 3.61 (m, 1H, *CH*$_2$), 3.31 (dt, *J* = 16.9, 1.4 Hz, 1H, *CH*$_2$), 3.12 (m, 1H, *CH*$_2$), 2.89 (m, 1H, *CH*$_2$). ^{13}C NMR (101 MHz, Chloroform-*d*; the signal for one aromatic carbon is not resolved) δ 212.3, 144.5, 143.0, 127.4, 125.4, 125.0, 62.8, 55.6, 36.6, 34.0. The reported values are in agreement with the characterization data reported in the literature.[34]

Starting from 2,2a,7,7a-tetrahydro-1*H*-cyclobuta[a]inden-1-one (**59**) (0.330 g, 2.09 mmol), 2-methyl-2-(((2,2a,7,7a-tetrahydro-1H-cyclobuta[a]inden-1-ylidene)amino)oxy)propanoic (**12f**) was obtained as a crystalline, colorless solid (inseparable mixture of E and Z isomers; 0.160 g, 0.617 mmol, 30% yield), upon following the GP2.

Rf (Pentane/EtOAc 7/1) 0.25. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.71 (s, 1H, CO_2H), 7.34 - 7.21 (m, 4H, Ar*H*), 4.09 - 3.88 (m, 1.6H, CH or CH_2), 3.57 (ddd, *J* = 17.3, 2.2, 1.1 Hz, 0.4H, CH or CH_2), 3.48 - 3.35 (m, 1H CH or CH_2), 3.33 - 3.21 (m, 1.6H, CH or CH_2), 2.86 (dt, *J* = 17.2, 3.1 Hz, 0.6H, *CH*), 2.74 (dt, *J* = 16.8, 3.4 Hz, 0.4H, *CH*), 1.59 (s, 1.2H, *CH*$_3$), 1.56 (s, 1.2H *CH*$_3$), 1.51 (s, 1.8H, *CH*$_3$), 1.50 (s, 1.8H, *CH*$_3$). ^{13}C NMR (101 MHz, Chloroform-*d;* the signals corresponding to the minor isomer are reported in *italics*) δ *179.9*, 179.8, 163.0, *161.6*, 144.8, *144.7*, *143.4*, 143.3, *127.1*, 127.1, 127.1, *127.0*, 125.1, *124.9*, 124.8, *124.7*, 80.6, *80.6*, 47.5, *47.2*, 40.6, *39.7*, *39.7*, 39.5, 37.1, *34.8*, 24.2, *24.1*, *23.9*, 23.6. The reported values are in agreement with the characterization data reported in the literature.[26]

[34] M. D. Lawlor, T. W. Lee, and R. L. Danheiser, *J. Org. Chem.*, **2000**, *65*, 4375–4384.

2-Methyl-2-((oxetan-3-ylideneamino)oxy)propanoic acid (12g)

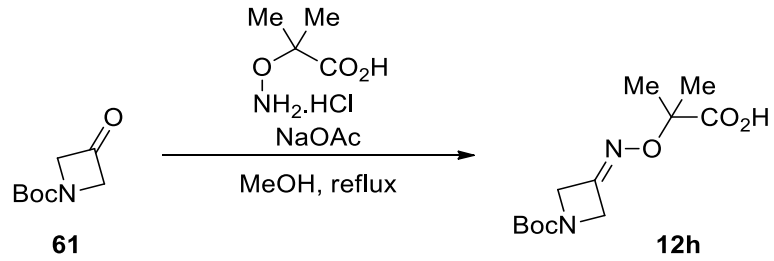


60 **12g**

Starting from oxetanone (**60**) (85 μL, 1.3 mmol. 1.0 equiv), 2-Methyl-2-((oxetan-3-ylideneamino)oxy)propanoic acid **12g** was obtained as a colorless solid (55 mg, 0.32 mmol, 24%), upon following the GP2.

M.p. 86.2-89.8 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.77 (s, 1H, CO_2H), 5.33 (dd, *J* = 3.7, 2.3 Hz, 2H, CH_2OCH_2), 5.29 (dd, *J* = 3.2, 2.1 Hz, 2H, CH_2OCH_2), 1.51 (s, 6H, Me_2). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 179.3, 153.8, 81.4, 79.1, 78.9, 23.8. IR (ν_{max}, cm^{-1}) 2989 (m), 2944 (w), 2664 (w), 2559 (w), 1741 (s), 1469 (w), 1383 (w), 1366 (w), 1294 (w), 1278 (w), 1227 (m), 1189 (s), 1157 (s), 1074 (w), 1050 (w), 984 (s), 957 (s), 861 (m), 788 (w), 740 (m). HRMS (ESI) calcd for $C_{18}H_{15}NNa^{+}$ $[M+Na]^{+}$ 268.1097; found 268.1100.

2-(((1-(*tert*-Butoxycarbonyl)azetidin-3-ylidene)amino)oxy)-2-methylpropanoic acid (12h)

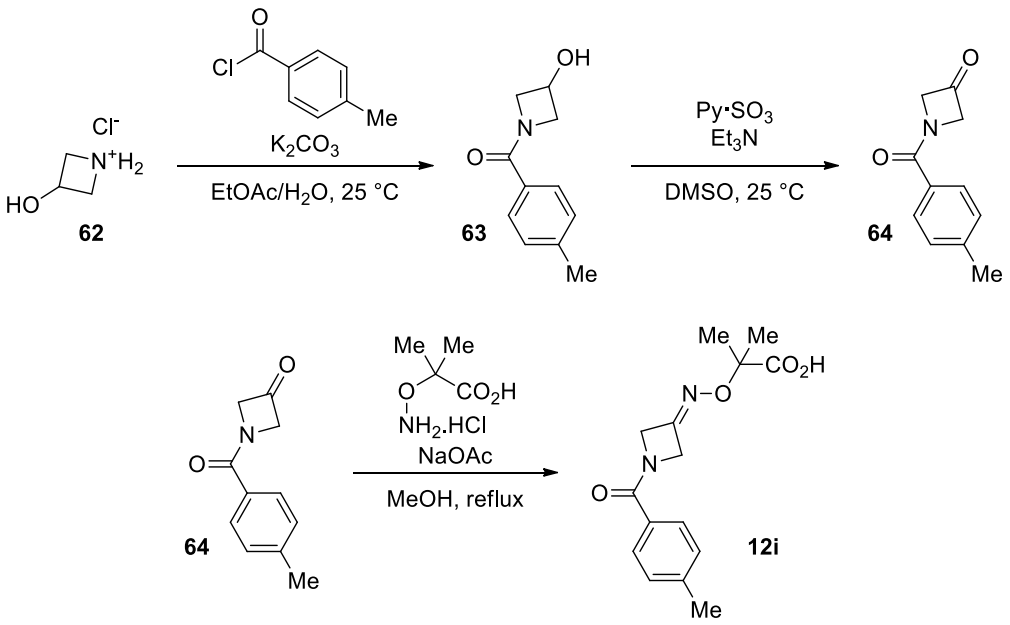


61 **12h**

Starting from commercially available *tert*-butyl 3-oxoazetidine-1-carboxylate (**61**) (0.275 g, 1.61 mmol), 2-(((1-(*tert*-butoxycarbonyl)azetidin-3-ylidene)amino)oxy)-2-methylpropanoic acid (**12h**) was obtained as a colorless solid (0.404 g, 1.48 mmol, 92% yield), upon following the GP2.

M.p. 145.8-148.6 °C. Rf (Pentane/EtOAc 5/1) 0.26 ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.42 (br s, 1H, CO_2H), 4.64 (d, *J* = 3.3 Hz, 3H, NCH_2), 4.62 (d, *J* = 2.8 Hz, 2H, NCH_2), 1.52 (s, 6H, CH_3), 1.46 (s, 9H, CH_3 in Boc). ^{13}C NMR (101 MHz, Chloroform-*d; The signals correspondings to the carbons in α to the nitrogen are not fully resolved.*) δ 178.6, 156.3, 149.3, 81.5, 80.7, 58.3, 28.3, 23.9. IR (νmax, cm-1) 2991 (w), 2928 (w), 2554 (w), 1694 (s), 1464 (w), 1414 (s), 1370 (m), 1302 (m), 1171 (s), 1127 (s), 965 (s), 871 (m), 766 (m). HRMS (ESI/QTOF) m/z: $[M + Na]^{+}$ Calcd for $C_{12}H_{20}N_2NaO_5^{+}$ 295.1264; Found 295.1261.

2-Methyl-2-(((1-(4-methylbenzoyl)azetidin-3-ylidene)amino)oxy)propanoic acid (12i)



Following a reported procedure,[35] 3-hydroxyazetidine hydrochloride (**62**) (1.72 g, 15.7 mmol, 1.0 equiv) and 4-methylbenzoyl chloride (2.1 mL, 16 mmol, 1.0 equiv) were dissolved in a 3:2 mixture of water and ethyl acetate (86 mL). Potassium carbonate (10.9 g, 79.0 mmol, 5.0 equiv) was added at room temperature and the resulting heterogeneous mixture was stirred vigorously for 18 hours. The organic layer was the separated and concentrated under reduced pressure. The resulting residue was dissolved in a 2:1 mixture of THF and methanol (27 mL) and stirred with aq. sodium hydroxide (1.0 M; 7.0 mL) at room temperature. After 1 hour, the reaction mixture was concentrated under reduced pressure, and the resulting residue was partitioned between EtOAc and water. The organic layer was separated, washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure to provide (3-hydroxyazetidin-1-yl)(*p*-tolyl)methanone (**63**) (96% pure; 2.54 g, 12.7 mmol, 81% yield) as a colorless solid.

M.p. 117.9-121.3 °C. Rf (Pentane/EtOAc 9/1) 0.71. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.19 (d, *J* = 7.9 Hz, 2H, Ar*H*), 4.75 (s, 1H, O*H*), 4.63 (t, *J* = 6.0 Hz, 1H, *CH*OH), 4.44 - 4.34 (m, 2H, NCH_2), 4.18 (dd, *J* = 9.9, 4.4 Hz, 1H, NCH_2), 4.02 (dd, *J* = 11.2, 4.6 Hz, 1H, NCH_2), 2.38 (s, 3H, ArCH_3). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 170.4, 141.5, 129.9, 129.0, 127.8, 61.4, 51.9, 21.4. IR (νmax, cm-1) 3251 (w), 2949 (w), 1722 (s), 1605 (m), 1556 (m), 1439 (m), 1279 (s), 1180 (m), 1106 (m), 1038 (w), 971 (w), 847 (m), 755 (s), 743 (m). HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{11}H_{13}NNaO_2^+$ 214.0838; Found 214.0841.

(3-Hydroxyazetidin-1-yl)(*p*-tolyl)methanone (**63**) (1.70 g, 8.89 mmol, 1.0 equiv) was dissolved in DMSO (34.2 mL). Triethylamine (10.2 mL, 73.8 mmol, 8.3 equiv) was then added at room temperature, followed by solution of pyridine- sulfur trioxide-complex (10.1 g, 62.2 mmol, 7.0 equiv) in DMSO (34.2 mL). The resulting mixture was stirred at room temperature for 1.5 hours, slowly turning from colorless to pale orange. The mixture was poured into iced water (120 mL) and extracted with ethyl acetate (3 x 70 mL). The combined

[35] S. Kasai, T. Kaku, M. Kamaura, *Heterocyclic Compound as Blood RBP4 Lowering Agent*, **2010**, EP2202223 (A1).

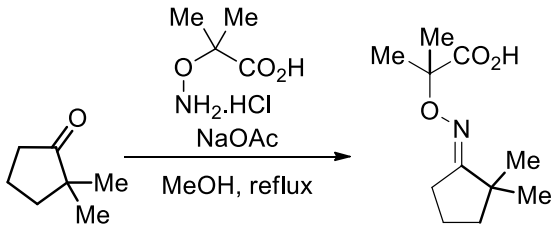
organic layers were washed with brine, dried over $MgSO_4$, filtered, and concentrated under vacuum. The resulting yellow crude solid was submitted to column chromatography (25 g SiO_2; EtOAc in DCM, 3 to 30%) to afford 1-(4-methylbenzoyl)azetidin-3-one (**64**) (0.836 g, 4.42 mmol, 50% yield) as a pale yellow solid.

M.p. 130.3-134.0 °C. Rf (DCM/EtOAc 9/1) 0.45. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.25 (m, 2H, Ar*H*), 4.95 (s, 4H, N*(CH)$_2$*CO), 2.40 (s, 3H, *CH$_3$*). ^{13}C NMR (101 MHz, Chloroform-*d*; the signal reported in italics is barely resolved due to the existence of the compound as a mixture of two rotamers) δ 196.0, 171.2, 142.4, 129.6, 129.3, 128.2, *72.4*, 21.5. IR (νmax, cm-1) 3054 (m), 1833 (m), 1655 (w), 1550 (w), 1494 (w), 1420 (w), 1383 (w), 1605 (w), 1266 (m), 1205 (w), 1125 (w), 1057 (m), 1008 (m), 909 (w), 940 (w), 736 (s). HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{12}NO_2^+$ 190.0863; Found 190.0863.

Starting from 1-(4-methylbenzoyl)azetidin-3-one (**64**) (0.500 g, 2.64 mmol), 2-methyl-2-(((1-(4-methylbenzoyl)azetidin-3-ylidene)amino)oxy)propanoic acid (**12i**) was obtained as a colorless solid (95% pure; mixture of rotamers; 0.606 g, 2.09 mmol, 79% yield), upon following the GP2.

M.p. 158.7-163.0 °C. Rf (DCM/EtOAc 9/1) 0.16. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.63 (br s, 1H, CO_2*H*), 7.55 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.23 (d, *J* = 7.9 Hz, 2H, Ar*H*), 4.93 (s, 2H, N*CH$_2$*), 4.90 (m, 2H, N*CH$_2$*), 2.39 (s, 3H, Ar*CH$_3$*), 1.52 (s, 6H, *CH$_3$*). ^{13}C NMR (101 MHz, Chloroform-*d*; in italics are reported the signals corresponding to the same C in either rotamers) δ *178.5*, *178.3*, 171.1, 148.5, 142.2, 129.5, 129.2, 128.0, 81.7, *61.5*, *58.1*, 23.9, 21.5. IR (νmax, cm-1) 3054 (w), 1735 (w), 1562 (w), 1531 (w), 1433 (w), 1371 (w), 1266 (m), 1162 (w), 1094 (w), 1026 (w), 866 (w), 736 (s). HRMS (ESI/QTOF) m/z: $[M + H-1]^+$ Calcd for $C_{15}H_{17}N_2O_4^+$ 289.1188; Found 289.1186.

(E)-2-(((2,2-Dimethylcyclopentylidene)amino)oxy)-2-methylpropanoic acid (12j)

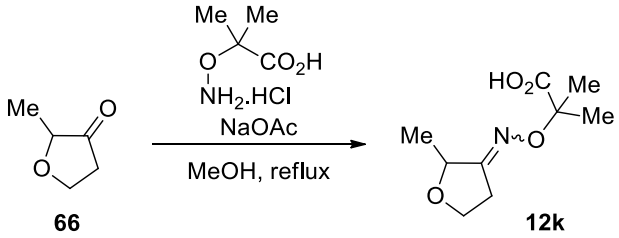


65 **12j**

Starting from 2,2-dimethylcyclopentanone (**65**) (0.243 g, 2.16 mmol), (E)-2-(((2,2-dimethylcyclopentylidene)amino)oxy)-2-methylpropanoic acid (**12j**) was obtained as a colorless solid (0.455 g, 2.13 mmol, 99% yield), upon following the GP2.

M.p. 53.4 - 55.5°C ^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.14 (s, 1H, CO_2*H*), 2.55 (t, *J* = 7.5 Hz, 2H, C*H$_2$*C=N), 1.80 (p, *J* = 7.1 Hz, 2H, C*H$_2$*CH$_2$*C=N), 1.65 (t, *J* = 6.8 Hz, 2H, C*H$_2$*CH$_2$*CH$_2$*C=N), 1.49 (s, 6H, C*Me$_2$*COOH), 1.16 (s, 6H, C*Me$_2$*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 176.0, 175.5, 81.2, 42.8, 40.7, 27.8, 26.4, 24.4, 20.8. NMR shifts consistent with literature data.[26]

2-Methyl-2-(((2-methyldihydrofuran-3(2*H*)-ylidene)amino)oxy)propanoic acid (12k)

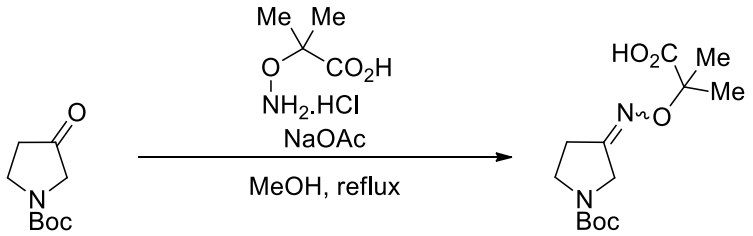


66 **12k**

Starting from 2-methyldihydrofuran-3(2*H*)-one (**66**) (129 µL, 1.33 mmol), 2-methyl-2-(((2-methyldihydrofuran-3(2*H*)-ylidene)amino)oxy)propanoic acid (**12k**) was obtained as a colorless oil (inseparable mixture of E and Z isomers in 8:2 ratio; 0.227 g, 1.13 mmol, 85% yield), upon following the GP2.

Rf (DCM/EtOAc 9/1) 0.29. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 11.10 (bs, 1H, CO_2H), 4.70 (q, *J* = 6.6 Hz, 0.2H, CH_3CHO), 4.33 (q, *J* = 6.3 Hz, 0.8H, CH_3CHO), 4.14 (td, *J* = 8.6, 4.0 Hz, 0.8H, OCH_2), 4.08 (dd, *J* = 8.3, 5.3 Hz, 0.2H, OCH_2), 3.94 – 3.77 (m, 1H, OCH_2), 2.84 – 2.59 (m, 2H, NCCH_2), 1.53 (s, 6H, CH_3), 1.41 (d, *J* = 6.7 Hz, 0.6H, CH_3), 1.35 (d, *J* = 6.4 Hz, 2.4H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$; the signals corresponding to the minor isomer are reported in *italics*) δ *178.6*, 178.4, *166.6*, 165.6, 81.3, *80.8*, 74.5, *73.2*, 65.9, *65.7*, *30.5*, 28.5, 24.3, 23.9, *22.1*, 18.1, *17.0*, *15.9*. IR (ν_{max}, cm^{-1}) 2986 (m), 2887 (m), 2363 (w), 1722 (s), 1470 (w), 1371 (m), 1285 (w), 1174 (s), 1069 (m), 977 (m), 853 (m), 743 (w). HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + Na]^+$ Calcd for $C_9H_{15}NNaO_4^+$ 224.0893; Found 224.0892.

2-(((1-(*tert*-Butoxycarbonyl)pyrrolidin-3-ylidene)amino)oxy)-2-methylpropanoic acid (12l)



67 **12l**

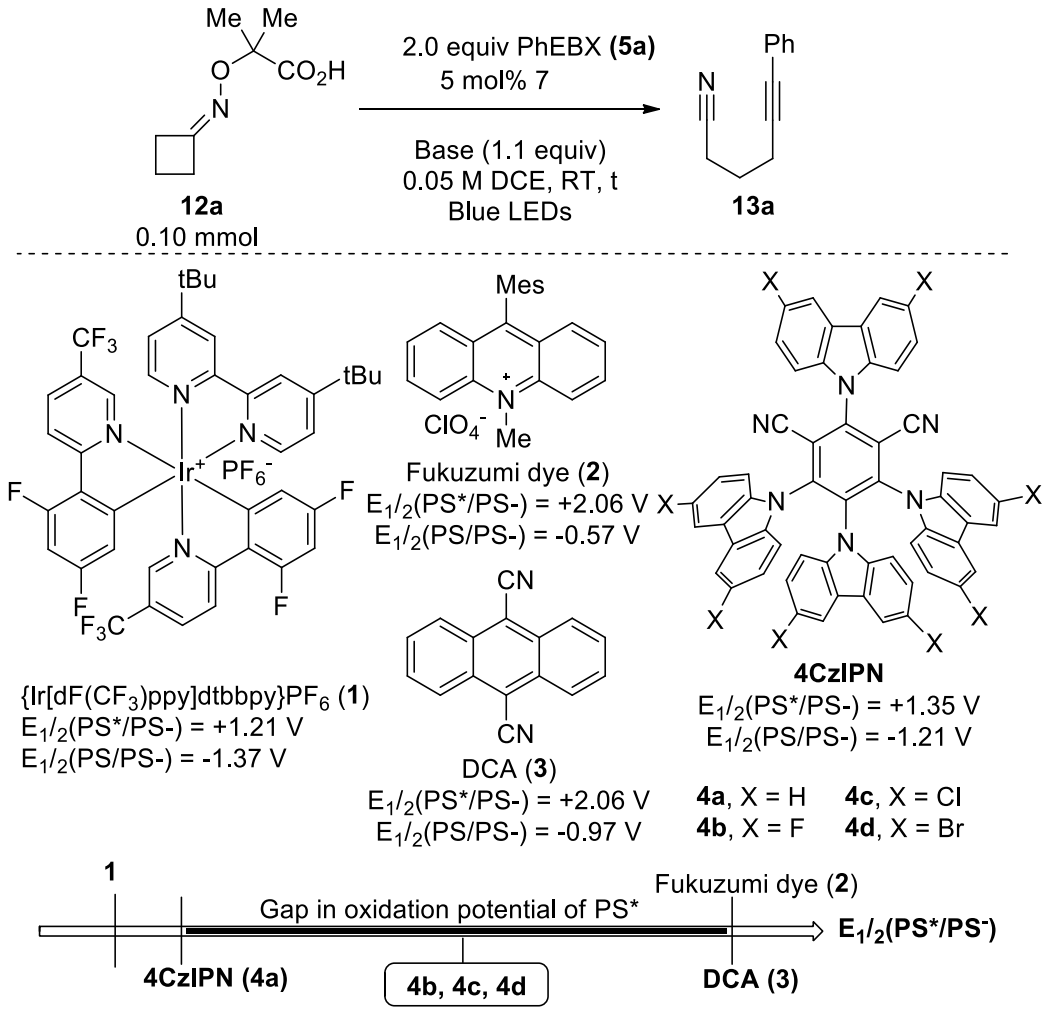
Starting from *tert*-butyl 3-oxopyrrolidine-1-carboxylate (**67**) (0.246 g, 1.33 mmol), 2-(((1-(*tert*-butoxycarbonyl)pyrrolidin-3-ylidene)amino)oxy)-2-methylpropanoic acid (**12l**) was obtained as a colorless solid (inseparable mixture of rotamers of E and Z isomers in 8:2 ratio; 0.247 g, 0.863 mmol, 65% yield), upon following the GP2.

M.p. 90.4-103.2 °C. Rf (DCM/MeOH 9.5/0.5) 0.39. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 9.93 (s, 1H, CO_2H), 4.11 (s, 1.6H, NCH_2), 4.06 (s, 0.4H, NCH_2), 3.59 (m, 1.6H, NCH_2CH_2), 3.38 (dd, *J* = 10.6, 6.0 Hz, 0.4H, NCH_2CH_2), 2.79 (t, *J* = 7.8 Hz, 0.6H, NCH_2CH_2), 2.71 (t, *J* = 7.5 Hz, 1H, NCH_2CH_2), 2.58 (dd, *J* = 8.3, 3.7 Hz, 0.4H, NCH_2CH_2), 1.53 – 1.45 (m, 15H, CH_3). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 178.5, 177.4, 161.1, 158.0, 154.4, 154.3, 81.3, 80.8, 80.1, 46.1, 28.4, 28.4, 28.4, 24.3, 24.1, 22.1, 15.9. IR (ν_{max}, cm^{-1}) 2992 (w), 2943 (w), 1704 (s), 1427 (m), 1168 (s), 977 (m), 897 (m), 767 (w). HRMS (ESI/QTOF) m/z: $[M + H-1]^+$ Calcd for $C_{13}H_{21}N_2O_5^+$ 285.1450; Found 285.1453.

7. Decarboxylative ring opening / alkynylation cascade

Optimization of the reaction:

Dry DCE was freeze-dried before using (3 cycles) and kept under argon. Dry degassed DCE (2.0 mL, 0.05 M) was added in a flame dried 5.0 mL test tube containing a teflon coated stirring bar, the oxime **12** (0.10 mmol, 1.0 equiv), EBX reagent **5** (0.20 mmol, 2.0 equiv), K_2CO_3 (0.11 mmol, 1.1 equiv) and organic dye (**4**) (0.05 mmol, 0.05 equiv) under N_2. The reaction mixture was irradiated using blue light LEDs for 1 h at rt. The reaction mixture was filtered over celite, eluting with pentane/DCM (2:1), and evaporated under reduced pressure. 6 µL of CH_2Br_2 was added as internal standard for NMR yield. Purification was performed only under optimized conditions to obtain isolated yield. The crude product was purified by preparative TLC (Heptane/Ethyl Acetate 85/15) directly without any further work-up affording 6-phenylhex-5-ynenitrile as a yellowish oil in two cases (entry 8, average of two experiments, 87%, and entry 19, 82%).



entry	catalyst	base	concentration	solvent	time	conversion[a]	yield[b]
1[c]	**1**	1.0 equiv Cs_2CO_3	0.05	DCE	2 h	>95%	50%
2	**2**	1.0 equiv Cs_2CO_3	0.05	DCE	2 h	50%	20%
3	**3**	1.0 equiv Cs_2CO_3	0.05	DCE	2 h	>95%	5%
4	**4a**	1.0 equiv Cs_2CO_3	0.05	DCE	2 h – 6 h	60%	50%
5	**4a**	1.0 equiv Cs_2CO_3	0.10	DCE	2 h	60%	40%
6	**4c**	1.0 equiv Cs_2CO_3	0.05	DCE	2 h	>95%	70%
7	**4c**	1.1 equiv K_2CO_3	0.05	DCE	2 h	>95%	75%
8	**4c**	1.1 equiv K_2CO_3	0.05	DCE	1 h	>95%	80%
9	**4b**	1.1 equiv K_2CO_3	0.05	DCE	1 h	90%	75%
10	**4d**	1.1 equiv K_2CO_3	0.05	DCE	1 h	90%	75%
11	**4c**	1.1 equiv $KHPO_4$	0.05	DCE	1 h	<10%	<10%
12	**4c**	1.1 equiv KOAc	0.05	DCE	1 h	>95%	70%
13	**4c**	1.1 equiv K_2CO_3	0.05	DCM	1 h	>95%	80%
14	**4c**	1.1 equiv K_2CO_3	0.025	DCM	1 h	>95%	45%
15	**4c**	1.1 equiv K_2CO_3	0.05	THF	1 h	>95%	25%
16	**4c**	1.1 equiv K_2CO_3	0.05	DMF	1 h	>95%	55%
17[e]	**4c**	1.1 equiv K_2CO_3	0.05	DCE	1 h	>95%	70%
18	**4c**	1.1 equiv K_2CO_3	0.05	DCE	30 min	>95%	80%
19[f]	**4c**	1.1 equiv K_2CO_3	0.05	DCE	1 h	>95%	80%
20[g]	**4c**	1.1 equiv K_2CO_3	0.05	DCE	1 h	>95%	80%

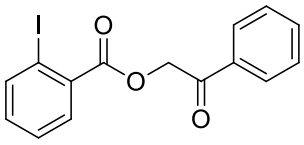
Table 4: PS: photosensitizer. [a]Reaction conditions: Using 0.1 mmol **12a** (1 equiv), 0.2 mmol **5a** (2.0 equiv), 5 mol% **4** (0.05 equiv) in DCE (2.0 mL) for 2 h at RT. The conversion of **12a** by NMR is given. The values for reduction potentials are given in volts for catalyst **4** in relation to SCE, in MeCN. [b]NMR yield using dibromomethane as internal standard. [c] Using 1 mol% of **1**. [e] Using 1.5 equiv. of **5a**. [f] Using 3.0 mol% of organic dye **4c**. [g] Using oxime **48**.

Control experiments without light or catalyst showed no reactivity, whereas only 5% were observed in the crude NMR when no base was added in the reaction mixture.

2-Oxo-2-phenylethyl 2-iodobenzoate (68)

A side product was identified as 2-oxo-2-phenylethyl 2-iodobenzoate. It seems to be formed via a decomposition pathway of Ph-EBX in presence of either water or oxygen, possibly catalyzed by photoredox, however the mechanism is still unclear. The NMR shifts match the literature data.[36]

[36] B. Lu, J. Wu, N. Yoshikai, *J. Am. Chem. Soc.* **2014**, *136*, 11598−11601.



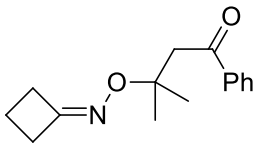
68

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.07 (dd, *J* = 7.8, 1.7 Hz, 1H, Ar*H*), 8.03 (dd, *J* = 7.9, 1.1 Hz, 1H, Ar*H*), 7.97 (d, *J* = 7.1 Hz, 2H, Ar*H*), 7.67 – 7.59 (m, 1H, Ar*H*), 7.52 (t, *J* = 7.7 Hz, 2H, Ar*H*), 7.46 (td, *J* = 7.6, 1.2 Hz, 1H, Ar*H*), 7.20 (td, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 5.60 (s, 2H, OCH_2COAr). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 191.7, 165.7, 141.4, 134.1, 134.0, 133.9, 133.1, 131.7, 128.9, 128.0, 127.8, 94.5, 66.7. HRMS (ESI) calcd for $C_{15}H_{11}IO_3$ [M+] 365.9747; found 365.9752.

Sunlight experiments

Reaction performed on 21st December, 2017

Starting from **12a** (17.1 mg, 0.10 mmol, 1.0 equiv), the reaction mixture was stirred for 2 h outdoors (12:15 – 14:15), under sunlight exposition. The crude product was purified by preparative TLC (pentane/Ethyl acetate 9:1) to afford **13a** (5.6 mg, 0.033 mmol, 33%, (45% NMR yield)) as a pale yellow oil. The conversion was low, around 50%. Interestingly, the formation of **69** was observed by NMR, in greater amount than usual. Its structure is assumed according to ^{1}H NMR. This product could arise from direct alkynylation, before fragmentation of acetone, followed by hydration of the alkyne moiety. We hypothesize that the fragmentation alkynylation reaction is temperature dependent as the outside temperature was around 4 °C at the time of the experiment. It is noteworthy that variable amounts of this side-product were observed in most of the reactions, albeit in low yield (<10%).



69

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.96 – 7.86 (m, 2H, Ar*H*), 7.66 – 7.56 (m, 1H, Ar*H*), 7.49 (dt, *J* = 8.7, 6.8 Hz, 3H, Ar*H*), 5.38 (s, 2H, CH_2CO), 2.94 (dt, *J* = 16.8, 7.9 Hz, 4H), 1.99 (p, *J* = 8.1 Hz, 2H), 1.60 (s, 6H, CH_3).

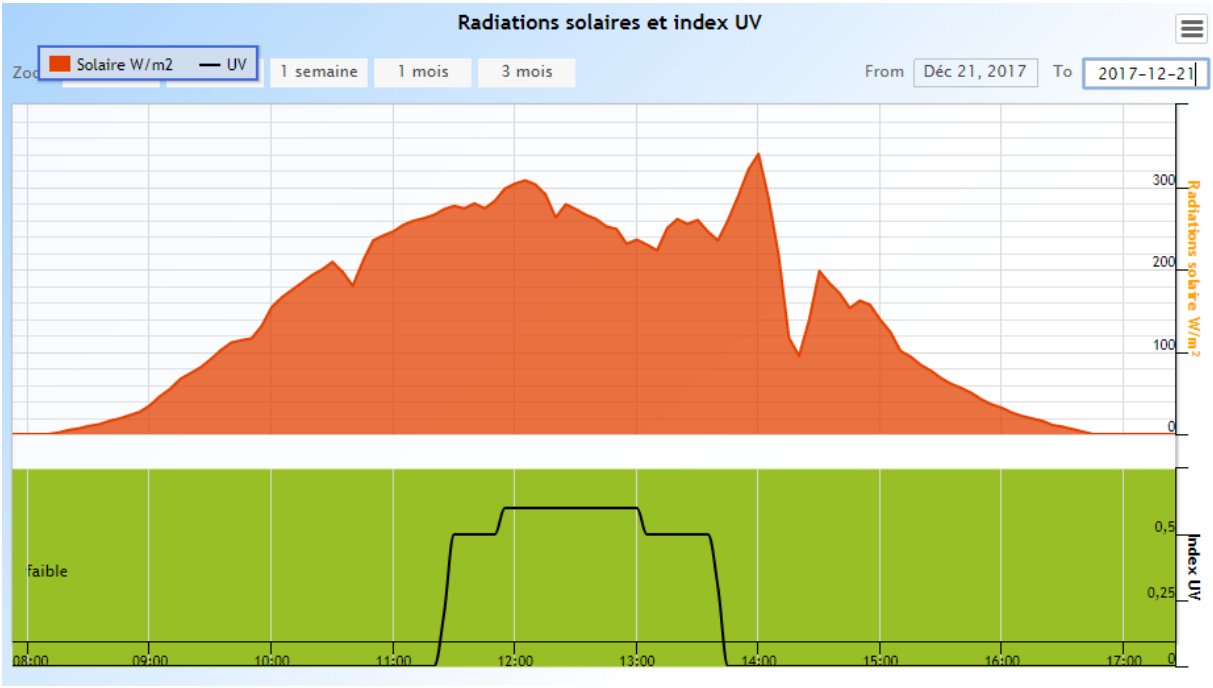


Figure 20. Sun spectra during experiment[37]

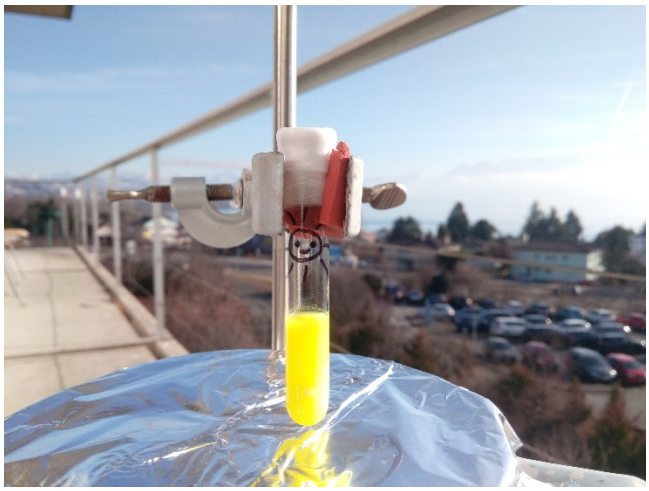


Figure 21. Set-up of the sunlight experiment, December 21st 2017.

Reactions performed on 17th May, 2018

Starting from **12a** (17 mg, 0.10 mmol, 1.0 equiv), the reaction mixture was stirred for 1 h outdoors (15:30 – 16:30, 25-26°C), under sunlight exposition. The crude product was analyzed by NMR, using 6 µL of CH_2Br_2 as internal standard. (**13a,** 55% NMR yield, 20% remaining starting material **12a**). Detection of **69** possible by NMR.

Starting from **12h** (24 mg, 0.10 mmol, 1.0 equiv), the reaction mixture was stirred for 2 h30 outdoors (15:30 – 18:00, 25-26°C), under sunlight exposition, the conversion was followed by TLC control (DCM/MeOH 9/1). The crude product was analyzed by NMR, using 6 µL of CH_2Br_2 as internal standard. (**13h,** 90% NMR yield, <10% remaining starting material **12h**). Clean reaction profile.

[37] Capture form http://www.meteolausanne.com/soleil-et-uv.html

Reaction performed on 18th May, 2018

Starting from **12a** (17 mg, 0.10 mmol, 1.0 equiv), the reaction mixture was stirred for 2 h outdoors (15:30 – 17:30, 25-26°C), under sunlight exposition. The crude product was analyzed by NMR, using 6 µL of CH_2Br_2 as internal standard. (**13a,** 75% NMR yield, <5% remaining starting material **12a**). Detection of **69** possible by NMR. Clean reaction profile.

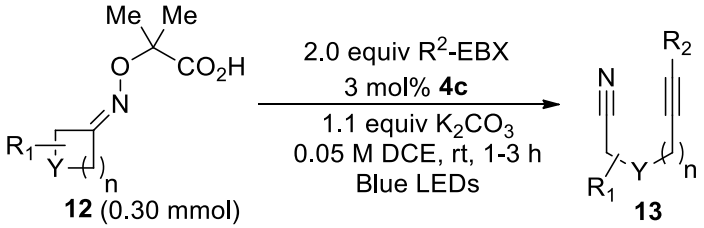
Figure 22. Set-up of the sunlight experiment, May 18th 2018.

One-pot procedure:

A solution of cyclobutanone **11** (23 µl, 0.30 mmol) in DCE (Volume: 1.5 ml) was treated with 2-(aminooxy)-2-methylpropanoic acid hydrochloride **10** (51 mg, 0.33 mmol, 1.1 equiv.), anhydrous potassium acetate (65 mg, 0.66 mmol, 2.2 equiv.) and heated to reflux until complete by TLC analysis (6 h). The mixture was allowed to cool to room temperature and (2r,4s,5r)-2,4,5,6-tetrakis(3,6-dichloro-9H-carbazol-9-yl)isophthalonitrile **4c** (16 mg, 0.015 mmol, 0.05 equiv.) and PhEBX **5a** (209 mg, 0.600 mmol, 2.0 equiv.) were added, along with 4 mL of DCE. The reaction mixture was then stirred for 1h under irradiation with Blue LEDs without water or cooling system.

After 1h, the mixture was diluted with 5mL of pentane/DCM (2:1) and filtered over celite, using pentane/DCM (2:1, 50mL) to wash. The yellow solution was then concentrated under reduced pressure. 18 µL of CH_2Br_2 was added as internal standard. (72% NMR yield). The crude NMR Isolation of pure compound **13a** was possible by column chromatography starting from full pentane then 20:1 pentane/EA (Rf 0.40), with 71% isolated yield.

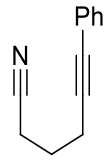
General procedure for the oxidative ring opening / alkynylation cascade



Dry DCE was freeze-dried (3 cycles) before using and kept under argon. Dry degassed DCE (6.0 mL) was added in a flame dried 14.0 mL test tube containing a teflon coated stirring bar, the oxime (0.30 mmol, 1.0 equiv), EBX reagent **5** (0.60 mmol, 2.0 equiv), K_2CO_3 (0.33 mmol, 1.1 equiv) and organic dye (**4c**) (0.009 mmol, 0.03 equiv) under N_2. The reaction mixture was irradiated using blue light LEDs for 1 h at rt. The reaction mixture was filtered over celite, eluting with pentane/DCM (2:1), and evaporated under reduced pressure. The crude product was purified by column chromatography directly without any further work-up.

Note: α-α-aminoalkynylnitriles were obtained as mixtures of non-resolved rotamers.

6-Phenylhex-5-ynenitrile (13a)



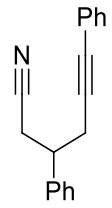
13a

Starting from **12a** (51 mg, 0.30 mmol, 1.0 equiv) and Ph-EBX (**5a**) (0.21 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 20:1) to afford **13a** as light yellow oil (40 mg, 0.24 mmol, 79%).

Rf (Heptane/Ethyl Acetate = 85:15) 0.40. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (dtd, *J* = 5.5, 4.1, 2.4 Hz, 2H, Ar*H*), 7.32 – 7.27 (m, 3H, Ar*H*), 2.60 (t, *J* = 6.8 Hz, 2H, *CH₂*), 2.56 (t, *J* = 7.2 Hz, 2H, *CH₂*), 1.96 (p, *J* = 7.0 Hz, 2H, C*H₂*CH₂C≡C). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 131.5, 128.3, 128.0, 123.2, 119.2, 86.9, 82.4, 24.6, 18.5, 16.2. The reported values are in agreement with the characterization data reported in the literature.[38]

3,6-Diphenylhex-5-ynenitrile (13b)

[38] L.-G. Xie, S. Shaaban, X. Chen, N. Maulide, *Angew.Chem. Int. Ed.* **2016**, *55*, 12864 –12867.

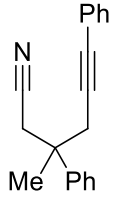


13b

Starting from **12b** (74 mg, 0.30 mmol, 1.0 equiv) and Ph-EBX (**5a**) (0.21 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 20:1) to afford **13b** as colorless solid (44 mg, 0.18 mmol, 60%).

Rf (Pentane/Ethyl Acetate = 9:1) 0.40. Mp: 49.2 – 51.5 °C. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.35 (m, 4H, Ar*H*), 7.35 – 7.28 (m, 6H, Ar*H*), 3.31 (tt, *J* = 7.7, 6.1 Hz, 1H, C*H*Ph), 2.96 (dd, *J* = 16.8, 6.2 Hz, 1H, *CH*$_2$), 2.89 (dd, *J* = 6.9, 3.2 Hz, 2H, *CH*$_2$), 2.83 (dd, *J* = 16.7, 7.7 Hz, 1H, *CH*$_2$C≡C). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 140.4, 131.5, 128.9, 128.3, 128.1, 127.8, 127.0, 123.0, 118.2, 85.9, 83.5, 41.2, 25.8, 23.2. IR (ν_{max}, cm^{-1}) 3065 (w), 3031 (w), 2920 (w), 2251 (w), 1735 (w), 1691 (w), 1600 (w), 1493 (m), 1451 (w), 1427 (w), 1381 (w), 1326 (m), 1225 (w), 1107 (w), 1072 (w), 1030 (w), 915 (w), 847 (w), 758 (s). HRMS (ESI) calcd for $C_{18}H_{15}NNa^{+}$ $[M+Na]^{+}$ 268.1097; found 268.1100.

3-Methyl-3,6-diphenylhex-5-ynenitrile (13c)

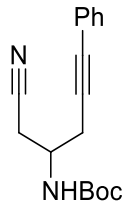


13c

Starting from **12c** (78 mg, 0.30 mmol, 1.0 equiv) and Ph-EBX (**5a**) (0.21 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 20:1) to afford **13c** as pale yellow oil colorless oil (31.9 mg, 0.123 mmol, 41%).

Rf (Pentane/EtOAc 9/1) 0.48. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 - 7.37 (m, 4H, Ph*H*), 7.37 - 7.32 (m, 2H, Ph*H*), 7.31 - 7.27 (m, 4H, Ph*H*), 2.93 (d, *J* = 16.7 Hz, 1H, *CH*$_2$), 2.91 (m, 2H, *CH*$_2$), 2.86 (d, *J* = 16.9 Hz, 1H, *CH*$_2$), 1.68 (s, 3H, *CH*$_3$). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 143.4, 131.5, 128.7, 128.2, 128.1, 127.3, 125.6, 123.1, 117.9, 85.5, 84.1, 40.4, 32.5, 29.7, 25.6. IR (νmax, cm-1) 3054 (w), 2986 (w), 2912 (w), 2844 (w), 2252 (w), 1957 (w), 1883 (w), 1747 (w), 1698 (w), 1599 (w), 1494 (m), 1445 (m), 1383 (w), 1328 (w), 1266 (w), 1131 (w), 1069 (w), 1026 (w), 958 (w), 909 (m), 847 (w), 755 (s). HRMS (APPI/LTQ-Orbitrap) m/z: $[M + H]^{+}$ Calcd for $C_{19}H_{18}N^{+}$ 260.1434; Found 260.1436.

***tert*-Butyl (1-cyano-5-phenylpent-4-yn-2-yl)carbamate (13d)**

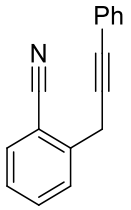


13d

Starting from **12d** (86 mg, 0.30 mmol, 1.0 equiv) and Ph-EBX (**5a**) (0.21 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography ((Pentane/Ethyl Acetate = 15:1 to 8:2) to afford **13d** as light yellow oil (68 mg, 0.24 mmol, 80%).

Rf (Pentane/Ethyl Acetate = 8:2) 0.25. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.30 (m, 2H, Ar*H*), 7.30 – 7.20 (m, 3H, Ar*H*), 4.90 (d, *J* = 8.5 Hz, 1H, N*H*), 4.06 (ddd, *J* = 10.3, 7.9, 4.3 Hz, 1H, BocHNC*H*), 2.84 – 2.62 (m, 4H, N≡CC*H*$_2$CHC*H*$_2$), 1.39 (s, 9H, *Boc*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.7, 131.6, 128.4, 128.3, 122.5, 116.9, 84.3, 83.3, 80.5, 46.3, 28.2, 24.5, 22.5. IR (ν_{max}, cm^{-1}) 3341 (m), 2978 (m), 2251 (w), 1693 (s), 1516 (s), 1499 (s), 1423 (w), 1368 (m), 1254 (m), 1163 (s), 1050 (m), 1024 (m), 915 (m), 867 (w), 758 (s), 734 (s). HRMS (ESI) calcd for $C_{17}H_{20}N_2NaO_2^+$ $[M+Na]^+$ 307.1417; found 307.1422.

2-(3-Phenylprop-2-yn-1-yl)benzonitrile (13e)



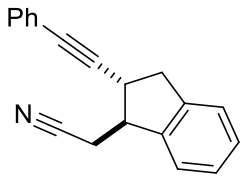
13e

Starting from **12e** (66 mg, 0.30 mmol, 1.0 equiv) and Ph-EBX (**5a**) (0.21 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 20:1) to afford **13e** as light yellow oil (26 mg, 0.12 mmol, 40%).

Rf (Heptane/Ethyl Acetate = 85:15) 0.33. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.81 – 7.73 (m, 1H, Ar*H*), 7.66 (dd, *J* = 7.7, 1.3 Hz, 1H, Ar*H*), 7.61 (td, *J* = 7.7, 1.4 Hz, 1H, Ar*H*), 7.47 (ddt, *J* = 5.4, 2.9, 1.6 Hz, 2H, Ar*H*), 7.42 – 7.34 (m, 1H, Ar*H*), 7.34 – 7.29 (m, 3H, Ar*H*), 4.06 (s, 2H, C*H*$_2$Ar). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 140.5, 133.1, 132.7, 131.7, 129.1, 128.3, 128.2, 127.3, 123.0, 117.4, 111.9, 84.8, 84.0, 24.6. IR (ν_{max}, cm^{-1}) 3061 (w), 2366 (w), 2225 (m), 1600 (w), 1489 (m), 1447 (w), 1415 (w), 1332 (w), 1284 (w), 1211 (w), 1171 (w), 1094 (w), 1068 (w), 1030 (w), 961 (w), 913 (w), 760 (s), 734 (w). The reported values are in agreement with the characterization data reported in the literature.[39]

2-(*trans*-2-(Phenylethynyl)-2,3-dihydro-1*H*-inden-1-yl)acetonitrile (13f)

[39] X. Zhang, X. X. and Y. Liu, *Chem. Sci.*, **2016**, *7*, 5815-5820.

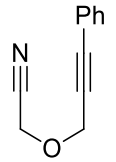


(+/-) 13f

Starting from **12f** (78 mg, 0.30 mmol, 1.0 equiv) and Ph-EBX (**5a**) (0.21 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 20:1) to afford **13f** as light yellow oil (50 mg, 0.19 mmol, 65%).

Rf (Pentane/Ethyl Acetate = 10:1) 0.3. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 – 7.40 (m, 2H, Ar*H*), 7.38 – 7.21 (m, 7H, Ar*H*), 3.56 (dtt, *J* = 7.7, 5.1, 1.2 Hz, 1H, C*H*CH$_2$CN), 3.43 – 3.27 (m, 1H, C*H*C≡CPh), 3.23 – 3.06 (m, 2H, ArC*H*$_2$), 2.97 (dd, *J* = 17.0, 5.1 Hz, 1H, C*H*$_2$CN), 2.86 (dd, *J* = 17.0, 6.5 Hz, 1H, C*H*$_2$CN). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 141.5, 141.2, 131.6, 128.3, 128.1, 128.0, 127.2, 124.7, 123.0, 118.0, 89.5, 82.5, 48.0, 38.6, 37.5, 20.5. IR (ν_{max}, cm^{-1}) 3045 (w), 2918 (w), 2247 (w), 1598 (w), 1489 (m), 1461 (w), 1443 (w), 1423 (w), 1348 (w), 1320 (w), 1233 (w), 1207 (w), 1070 (w), 1022 (w), 913 (w), 754 (s). HRMS (ESI) calcd for $C_{19}H_{15}NNa^{+}$ $[M+Na]^{+}$ 280.1097; found 280.1098. By analogy with compounds isolated from the work of Zard (with methyl acrylate)[24] and Leonori (with fluorine),[23] the major diastereoisomer is the *trans* compound.

2-((3-Phenylprop-2-yn-1-yl)oxy)acetonitrile (13g)

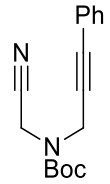


13g

Starting from **12g** (17 mg, 0.10 mmol, 1.0 equiv) and Ph-EBX (**5a**) (70 mg, 0.20 mmol, 2.0 equiv), the crude product was purified by preparative TLC (Pentane/Ethyl Acetate = 9:1) to afford **13g** as colorless oil (17 mg, 0.99 mmol, 99%).

Rf (Pentane/Ethyl Acetate = 9:1) 0.38. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.51 – 7.43 (m, 2H, ArH), 7.40 – 7.29 (m, 3H, ArH), 4.56 (s, 2H, OC*H*$_2$CN), 4.45 (s, 2H, OC*H*$_2$C≡CPh). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 131.8, 129.0, 128.4, 121.7, 115.6, 88.6, 82.0, 58.9, 54.1. The reported values are in agreement with the characterization data reported in the literature.[35]

***tert*-Butyl (cyanomethyl)(3-phenylprop-2-yn-1-yl)carbamate (13h)**



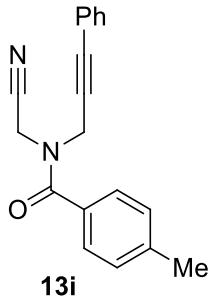
13h

0.30 mmol scale: Starting from **12h** (82 mg, 0.30 mmol, 1.0 equiv) and Ph-EBX (**5a**) (0.21 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 20:1 to 9:1) to afford **13h** as yellow oil (82 mg, 0.29 mmol, 97%, 96% purity).

1 mmol scale: Starting from **12h** (272 mg, 1.00 mmol) and using 1 mol % of **4c** (10.6 mg, 10.0 μmol), the crude product was purified by column chromatography (pentane/DCM/EtOAc 7/3/0 to 4/6/0 to 3/7/0.5) to afford **13h** as yellow, viscous oil (0.178 g, 0.658 mmol, 66% yield).

Rf (pentane/DCM 1/1) 0.28. ^{1}H NMR (400 MHz, Acetonitrile-d_3) δ 7.46 (m, 2H, Ph*H*), 7.37 (m, 3H, Ph*H*), 4.34 (s, 2H, CH_2), 4.27 (s, 2H, CH_2), 1.49 (s, 9H, CH_3 in Boc). ^{13}C NMR (101 MHz, Acetonitrile-d_3) δ 155.0, 132.4, 129.7, 129.5, 123.3, 117.6, 85.1, 84.5, 82.7, 38.7, 36.1, 28.3. IR (νmax, cm-1) 2986 (w), 1704 (s), 1476 (w), 1451 (m), 1402 (s), 1371 (m), 1248 (s), 1162 (s), 1131 (m), 971 (w), 872 (m), 761 (m), 1026 (w). HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{16}H_{18}N_2NaO_2^+$ 293.1260; Found 293.1263

N-(Cyanomethyl)-4-methyl-N-(3-phenylprop-2-yn-1-yl)benzamide (13i)

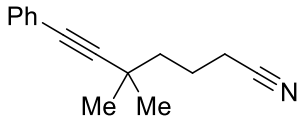


13i

Starting from **12i** (87 mg, 0.30 mmol, 1.0 equiv) and Ph-EBX (**5a**) (0.21 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/DCM/EtOAc 3/7/0 to 2/8/1) to afford **13i** as yellow solid (39.4 mg, 0.137 mmol, 46%).

M.p. 54.0-57.0 °C (it melts to form a viscous oil). Rf (DCM/EtOAc 96/4) 0.54. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.51 - 7.44 (m, 2H, Ph*H*), 7.39 - 7.32 (m, 3H, Ph*H*), 7.28 (d, *J* = 7.9 Hz, 2H, Ar*H*), 4.57 (br s, 2H, CH_2), 4.50 (br s, 2H, CH_2), 2.41 (s, 3H, PhCH_3). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.2, 141.6, 131.8, 130.3, 129.4, 129.0, 128.4, 127.5, 121.7, 115.3, 86.3, 81.8, 40.3, 33.5, 21.5. IR (νmax, cm-1) 2986 (w), 3060 (w), 1741 (w), 1661 (w), 1451 (w), 1396 (w), 1260 (w), 1143 (w), 909 (s), 730 (s), 1001 (w). HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{16}N_2NaO^+$ 311.1155; Found 311.1155.

5,5-Dimethyl-7-phenylhept-6-ynenitrile (13j)

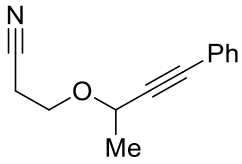


13j

Starting from **12j** (64 mg, 0.30 mmol, 1.0 equiv) and Ph-EBX (**5a**) (0.21 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 20:1) to afford **13j** as light yellow oil (49 mg, 0.23 mmol, 77%).

Rf (Pentane/Ethyl Acetate = 9:1) 0.33. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.34 (m, 2H, Ar*H*), 7.32 – 7.20 (m, 3H, Ar*H*), 2.41 (t, *J* = 7.1 Hz, 2H, CH_2C≡N), 1.99 – 1.79 (m, 2H, CH_2CH$_2$C≡N), 1.71 – 1.54 (m, 2H, CH_2CH$_2$CH$_2$C≡N), 1.32 (s, 6H, CMe_2). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 131.5, 128.1, 127.6, 123.5, 119.6, 95.8, 81.1, 42.2, 31.4, 29.2, 21.8, 17.5. IR (ν_{max}, cm^{-1}) 2970 (m), 2922 (m), 2872 (w), 2247 (w), 1739 (w), 1687 (w), 1598 (w), 1491 (m), 1467 (m), 1427 (w), 1383 (w), 1368 (w), 1316 (m), 1276 (w), 1205 (m), 1141 (w), 1072 (w), 917 (w), 754 (s). HRMS (ESI) calcd for $C_{15}H_{17}NNa^+$ $[M+Na]^+$ 234.1253; found 234.1247.

3-((4-Phenylbut-3-yn-2-yl)oxy)propanenitrile (13k)

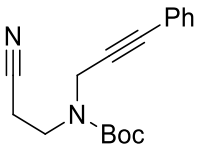


13k

Starting from **12k** (60 mg, 0.30 mmol, 1.0 equiv) and Ph-EBX (**5a**) (0.21 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Chloroform/Pentane = 8:2 then 9:1) to afford **13k** as light yellow oil (39 mg, 0.20 mmol, 65%).

Rf (Chloroform/Pentane = 9:1) 0.35. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 – 7.38 (m, 2H, Ar*H*), 7.38 – 7.27 (m, 3H, Ar*H*), 4.47 (q, *J* = 6.6 Hz, 1H, OC*H*CH$_3$), 4.14 – 3.90 (m, 1H OCH_2CH$_2$), 3.85 – 3.58 (m, 1H, OCH_2CH$_2$), 2.66 (t, *J* = 6.4 Hz, 2H, OCH$_2$CH_2), 1.59 – 1.43 (m, 3H, *Me*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 131.7, 128.5, 128.3, 122.2, 117.8, 87.8, 85.7, 66.3, 63.1, 22.0, 18.9. IR (ν_{max}, cm^{-1}) 3057 (w), 2991 (w), 2936 (w), 2878 (w), 2251 (w), 1731 (w), 1598 (w), 1491 (w), 1445 (w), 1415 (w), 1375 (w), 1330 (m), 1258 (w), 1223 (w), 1107 (s), 1070 (m), 1038 (w), 941 (w), 917 (w), 760 (s). HRMS (ESI) calcd for $C_{13}H_{13}NNaO^+$ $[M+Na]^+$ 222.0889; found 222.0885.

***tert*-Butyl (2-cyanoethyl)(3-phenylprop-2-yn-1-yl)carbamate (13l)**

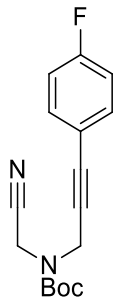


13l

Starting from **12l** (86 mg, 0.30 mmol, 1.0 equiv) and Ph-EBX (**5a**) (0.21 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1 then 8:2) to afford **13l** as light yellow oil (26 mg, 0.090 mmol, 30%).

Rf (Pentane/Ethyl Acetate = 8:2) 0.33. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 – 7.38 (m, 2H, Ar*H*), 7.32 (dd, *J* = 5.3, 2.0 Hz, 3H, Ar*H*), 4.36 (m, NC*H*$_2$C≡C), 3.78 – 3.58 (m, 2H, NC*H*$_2$CH$_2$), 2.72 (m, 2H, NCH$_2$C*H*$_2$), 1.51 (s, 9H, *Boc*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.6, 131.7, 128.6, 128.4, 122.4, 118.1, 99.8, 84.0, 81.5, 43.3, 38.6, 28.3, 17.0. IR (ν_{max}, cm^{-1}) 3660 (w), 2980 (m), 2904 (w), 2364 (w), 1703 (s), 1582 (w), 1459 (w), 1409 (m), 1369 (m), 1326 (w), 1250 (m), 1165 (s), 1127 (m), 1068 (m), 961 (w), 913 (m), 867 (w), 760 (m), 736 (w). HRMS (ESI) calcd for $C_{17}H_{21}N_2O_2^+$ $[M+H]^+$ 285.1598; found 285.1595.

***tert*-Butyl (cyanomethyl)(3-(4-fluorophenyl)prop-2-yn-1-yl)carbamate (13m)**

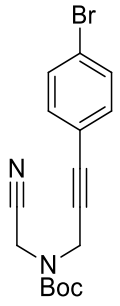


13m

Starting from **12h** (82 mg, 0.30 mmol, 1.0 equiv) and *p*F-Ph-EBX (**5c**) (0.22 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 15:1 to 9:1) to afford **13m** as light yellow oil (72 mg, 0.25 mmol, 83%).

Rf (Pentane/Ethyl Acetate = 9:1) 0.38. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 (dd, *J* = 8.7, 5.5 Hz, 2H, Ar*H*), 7.01 (t, *J* = 8.7 Hz, 2H, Ar*H*), 4.34 (m, 4H, C*H*$_2$NC*H*$_2$), 1.51 (s, 9H, *Boc*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.7 (d, *J* = 250.0 Hz), 153.4 (br s), 133.7 (d, *J* = 8.5 Hz), 118.1 (d, *J* = 3.5 Hz), 115.7, 115.64 (d, *J* = 22.2 Hz), 84.4, 82.6, 82.1, 37.1, 34.6, 28.1. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -110.1. IR (ν_{max}, cm^{-1}) 3672 (w), 2984 (m), 2940 (w), 2904 (w), 2360 (w), 1705 (s), 1602 (m), 1508 (s), 1479 (w), 1449 (m), 1397 (m), 1368 (m), 1340 (w), 1248 (s), 1159 (s), 1129 (m), 1052 (w), 966 (w), 909 (w), 865 (m), 839 (s), 816 (w), 774 (w), 740 (w). HRMS (ESI) calcd for $C_{16}H_{17}FN_2NaO_2^+$ $[M+Na]^+$ 311.1166; found 311.1169.

***tert*-Butyl (3-(4-bromophenyl)prop-2-yn-1-yl)(cyanomethyl)carbamate (13n)**

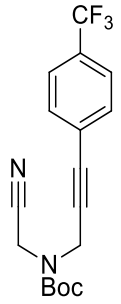


13n

Starting from **12h** (82 mg, 0.30 mmol, 1.0 equiv) and *p*Br-PhEBX (**5d**) (0.26 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 15:1 to 9:1) to afford **13n** as light yellow oil (63 mg, 0.18 mmol, 60%).

Rf (Pentane/Ethyl Acetate = 9:1) 0.34. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 (d, *J* = 8.5 Hz, 2H, Ar*H*), 7.30 (d, *J* = 8.5 Hz, 2H, Ar*H*), 4.34 (m, C*H*$_2$NC*H*$_2$), 1.52 (s, 9H, Boc). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.2 (br), 133.2, 131.7, 123.7, 121.0, 115.7, 84.4 (br), 83.6, 82.7, 37.2, 34.7, 28.2. IR (ν_{max}, cm^{-1}) 2980 (m), 2940 (w), 2906 (w), 2362 (w), 1749 (m), 1703 (s), 1588 (w), 1485 (m), 1451 (w), 1397 (m), 1368 (m), 1338 (w), 1248 (s), 1159 (s), 1072 (m), 1012 (m), 963 (w), 909 (w), 863 (m), 828 (m), 770 (m), 740 (m). HRMS (ESI) calcd for $C_{16}H_{17}{}^{79}BrN_2NaO_2^+$ $[M+Na]^+$ 371.0366; found 371.0362.

***tert*-Butyl (cyanomethyl)(3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-yl)carbamate (13o)**

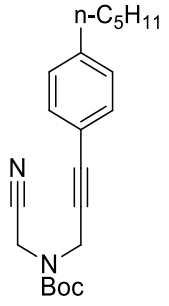


13o

Starting from **12h** (82 mg, 0.30 mmol, 1.0 equiv) and *p*CF$_3$-Ph-EBX (**5e**) (0.25 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 15:1 to 9:1) to afford **13o** as light yellow oil (62 mg, 0.18 mmol, 61%).

Rf (Pentane/Ethyl Acetate = 9:1) 0.38. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.65 – 7.48 (m, 4H, Ar*H*), 4.52 – 4.16 (m, 4H, C*H*$_2$NC*H*$_2$), 1.52 (s, 9H, *Boc*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.4, 132.0, 130.4 (q, *J* = 32.7 Hz), 125.9 (app s), 125.3 (q, *J* = 3.9 Hz), 123.8 (q, *J* = 272.2 Hz), 115.6, 85.0, 84.0, 82.8, 37.2, 34.6, 28.1. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.9. IR (ν_{max}, cm^{-1}) 2984 (w), 2362 (w), 1707 (s), 1616 (w), 1479 (w), 1449 (m), 1401 (m), 1368 (w), 1324 (s), 1248 (s), 1163 (s), 1127 (s), 1068 (s), 1018 (w), 968 (w), 941 (w), 901 (w), 865 (m), 845 (s), 770 (w), 720 (w). HRMS (ESI) calcd for $C_{17}H_{17}F_3N_2NaO_2^+$ $[M+Na]^+$ 361.1134; found 361.1136.

***tert*-Butyl (cyanomethyl)(3-(4-pentylphenyl)prop-2-yn-1-yl)carbamate (13p)**

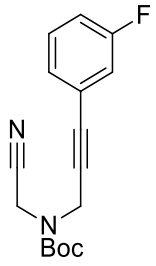


8p

Starting from **12h** (24 mg, 0.10 mmol, 1.0 equiv) and *p*C_5H_{11}-Ph-EBX (**5f**) (84 mg, 0.20 mmol, 2.0 equiv), the crude product was purified by preparative TLC (Pentane/Ethyl Acetate = 85:15) to afford **13p** as light yellow oil (20 mg, 0.060 mmol, 59%).

Rf 0.50 (Pentane/Ethyl Acetate = 85:15). ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.27 (m, 2H, Ar*H*), 7.17 – 7.04 (m, 2H, Ar*H*), 4.35 (m, 4H, CH_2NCH_2), 2.59 (t, *J* = 7.8 Hz, 2H, CH_2Ph), 1.67 – 1.54 (m, 2H, CH_2CH$_2$Ph), 1.52 (s, 9H, *Boc*), 1.30 (m, 4H, CH_2CH_2(CH$_2$)$_2$Ph), 0.88 (t, *J* = 6.9 Hz, 3H, *Me*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.6, 144.0, 131.7, 128.5, 119.2, 115.7, 85.7, 82.5, 81.6, 37.1, 35.8, 34.4, 31.4, 30.9, 28.2, 22.5, 14.0. IR (ν_{max}, cm^{-1}) 3670 (w), 2970 (m), 2930 (m), 2870 (w), 2364 (w), 1709 (s), 1510 (w), 1447 (m), 1399 (m), 1368 (w), 1248 (s), 1163 (s), 1127 (m), 1062 (w), 966 (w), 943 (w), 911 (w), 865 (w), 770 (w), 736 (w). HRMS (ESI) calcd for $C_{21}H_{28}N_2NaO_2^+$ $[M+Na]^+$ 363.2043; found 363.2042.

tert-Butyl (cyanomethyl)(3-(3-fluorophenyl)prop-2-yn-1-yl)carbamate (13q)

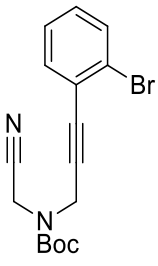


13q

Starting from **12h** (82 mg, 0.30 mmol, 1.0 equiv) and *m*F-Ph-EBX (**5g**) (0.22 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 15:1 to 9:1) to afford **13q** as light yellow oil (42 mg, 0.15 mmol, 49%).

Rf (Pentane/Ethyl Acetate = 9:1) 0.38. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.27 (m, 1H, Ar*H*), 7.25 (dd, *J* = 7.7, 1.5 Hz, 1H, Ar*H*), 7.16 (dd, *J* = 9.3, 2.1 Hz, 1H, Ar*H*), 7.07 (td, *J* = 8.4, 2.4 Hz, 1H, Ar*H*), 4.74 – 4.18 (m, 4H, CH_2NCH_2), 1.54 (s, 8H, *Boc*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.2 (d, *J* = 246.8 Hz), 153.3, 130.0 (d, *J* = 8.6 Hz), 127.6 (d, *J* = 3.1 Hz), 123.9 (d, *J* = 9.5 Hz), 118.5 (d, *J* = 22.9 Hz), 116.1 (d, *J* = 21.2 Hz), 115.6, 84.2, 83.4, 82.7, 37.1, 34.6, 28.1. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -112.6. IR (ν_{max}, cm^{-1}) 2980 (m), 2936 (w), 2906 (w), 1707 (s), 1610 (m), 1582 (m), 1483 (m), 1445 (m), 1399 (s), 1368 (m), 1248 (s), 1165 (s), 1127 (m), 1080 (w), 1004 (w), 964 (w), 945 (w), 907 (w), 867 (m), 788 (m), 732 (w). HRMS (ESI) calcd for $C_{16}H_{17}FN_2NaO_2^+$ $[M+Na]^+$ 311.1166; found 311.1162.

tert-Butyl (3-(2-bromophenyl)prop-2-yn-1-yl)(cyanomethyl)carbamate (13r)

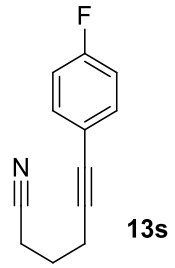


13r

Starting from **12h** (82 mg, 0.30 mmol, 1.0 equiv) and *o*Br-Ph-EBX (**5h**) (0.26 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **13r** as light yellow oil (50 mg, 0.14 mmol, 48%).

Rf (Pentane/Ethyl Acetate = 9:1) 0.25. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.63 – 7.54 (m, 1H, Ar*H*), 7.47 (dd, *J* = 7.7, 1.7 Hz, 1H, Ar*H*), 7.30 – 7.24 (m, 1H, Ar*H*), 7.19 (td, *J* = 7.8, 1.7 Hz, 1H, Ar*H)*, 4.52 – 4.32 (m, 4H, C*H*$_2$NC*H*$_2$), 1.52 (s, 9H, *Boc*). ^{13}C NMR (101 MHz, Chloroform-*d*; one carbon signal is not resolved) δ 153.7, 133.5, 132.4, 130.0, 127.2, 125.6, 124.3, 115.7, 87.1, 82.7, 37.0, 34.5, 28.2, 28.1, 28.0, 27.9. IR (ν_{max}, cm^{-1}) 2980 (m), 2934 (w), 1705 (s), 1473 (m), 1445 (m), 1397 (s), 1368 (m), 1248 (s), 1159 (s), 1129 (m), 1054 (w), 1026 (w), 968 (w), 943 (w), 911 (w), 865 (m), 758 (s). HRMS (ESI) calcd for $C_{16}H_{17}{}^{79}BrN_2NaO_2^+$ $[M+Na]^+$ 371.0366; found 371.0363.

6-(4-Fluorophenyl)hex-5-ynenitrile (13s)

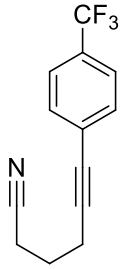


13s

Starting from **12a** (51 mg, 0.30 mmol, 1.0 equiv) and *p*F-Ph-EBX (**5c**) (0.22 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 20:1) to afford **13s** as light yellow oil (50.1 mg, 0.214 mmol, 71%, 80% purity). NMR analysis identified **64** as the impurity. A sample was purified by preparative TLC (DCM/toluene 1:1) for characterization.

Rf (DCM/toluene 1/1) 0.43. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.34 (m, 2H, Ar*H*), 7.04 – 6.94 (m, 2H, Ar*H*), 2.59 (t, *J* = 6.9 Hz, 2H), 2.56 (t, *J* = 7.2 Hz, 2H) 1.96 (p, *J* = 7.0 Hz, 2H, $CH_2CH_2CH_2$). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.3 (d, *J* = 240 Hz), 133.4 (d, *J* = 8.4 Hz), 119.3, 119.1, 115.5 (d, *J* = 22.0 Hz), 86.6, 81.4, 24.6, 18.5, 16.3. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -111.4. IR (ν_{max}, cm^{-1}) 2980 (m), 2906 (w), 2363 (w), 2252 (w), 1741 (w), 1704 (w), 1599 (w), 1507 (s), 1433 (w), 1223 (m), 1069 (m), 841 (s), 749 (w). HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{12}H_{11}FN^+$ 188.0870; Found 188.0863.

6-(4-(Trifluoromethyl)phenyl)hex-5-ynenitrile (13t)

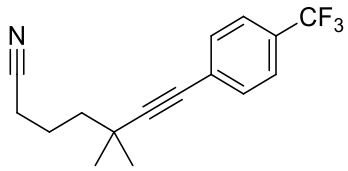


13t

Starting from **12a** (51 mg, 0.30 mmol, 1.0 equiv) and *p*CF_3-Ph-EBX (**5e**) (0.25 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 20:1) to afford **13u** as light yellow oil (54 mg, 0.23 mmol, 76%).

Rf (Chloroform/Pentane = 9:1) 0.40. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.56 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.49 (d, *J* = 8.2 Hz, 2H, Ar*H*), 2.63 (t, *J* = 6.8 Hz, 2H, CH_2CC), 2.56 (t, *J* = 7.1 Hz, 2H, CH_2CN), 1.98 (p, *J* = 6.9 Hz, 2H, CH_2CH_2CN). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 131.8, 129.8 (q, *J* = 32.6 Hz), 127.0 (q, *J* = 1.2 Hz), 125.2 (q, *J* = 3.8 Hz), 123.9 (q, *J* = 272.1 Hz), 119.0, 89.6, 81.2, 24.4, 18.5, 16.3. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.79. IR (ν_{max}, cm^{-1}) 2946 (w), 2251 (w), 1616 (w), 1431 (w), 1409 (w), 1324 (s), 1167 (m), 1125 (s), 1068 (m), 1018 (w), 915 (w), 845 (m), 760 (w), 738 (w). Consistent with reported data.[40]

5,5-Dimethyl-7-(4-(trifluoromethyl)phenyl)hept-6-ynenitrile (13u)

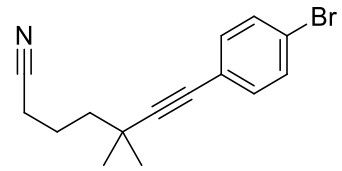


13u

Starting from **12j** (64 mg, 0.30 mmol, 1.0 equiv) and *p*CF_3-Ph-EBX (**5e**) (0.25 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 20:1) to afford **13u** as light yellow oil (28 mg, 0.10 mmol, 33%).

Rf (Chloroform/Pentane = 9:1) 0.42. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.53 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.47 (d, *J* = 8.0 Hz, 2H, Ar*H*), 2.42 (td, *J* = 7.1, 1.4 Hz, 2H, CH_2CN), 1.89 (ddd, *J* = 14.5, 8.3, 4.3 Hz, 2H, CH_2CH_2CN), 1.72 – 1.58 (m, 2H, CH_2CMe_2), 1.32 (s, 6H, CMe_2). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 131.8, 129.4 (q, *J* = 32.7 Hz), 127.4, 125.1 (q, *J* = 3.9 Hz), 123.9 (q, *J* = 272.1 Hz), 119.6, 98.6, 80.0, 42.0, 31.5, 29.0, 21.8, 17.5. ^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.72. IR (ν_{max}, cm^{-1}) 2974 (m), 2918 (w), 2876 (w), 2358 (w), 2245 (w), 1713 (w), 1616 (w), 1455 (w), 1405 (w), 1326 (s), 1246 (w), 1169 (m), 1127 (s), 1109 (m), 1068 (m), 1018 (w), 845 (m), 740 (w). HRMS (ESI) calcd for $C_{16}H_{16}F_3N$ [M+] 279.1235; found 279.1234.

7-(4-Bromophenyl)-5,5-dimethylhept-6-ynenitrile (13v)



13v

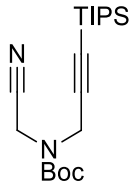
Starting from **12j** (64 mg, 0.30 mmol, 1.0 equiv) and *p*Br-Ph-EBX (**5d**) (0.26 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 20:1) to afford **13v** as light yellow oil (30 mg, 0.10 mmol, 34%).

Rf (Pentane/Ethyl Acetate = 9:1) 0.35. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.37 (m, 2H, Ar*H*), 7.25 – 7.19 (m, 2H, Ar*H*), 2.41 (t, *J* = 7.0 Hz, 2H, CH_2CN), 2.05 – 1.77 (m, 2H, CH_2CH_2CN), 1.65 – 1.57 (m, 2H, CH_2(CH_2)$_2$CN), 1.30 (s, 6H, CMe_2). ^{13}C NMR (101 MHz,

[40] L. Melzig, J. Stemper, P. Knochel *Synthesis*, **2010,** *12*, 2085–2091.

Chloroform-*d*) δ 133.0, 131.4, 122.5, 121.8, 119.6, 97.1, 80.1, 42.1, 31.4, 29.1, 21.8, 17.5. IR (ν_{max}, cm^{-1}) 2970 (s), 2918 (m), 2874 (m), 2354 (w), 2247 (w), 1741 (m), 1677 (w), 1588 (w), 1487 (s), 1465 (m), 1427 (w), 1391 (w), 1368 (w), 1318 (w), 1276 (w), 1227 (m), 1205 (m), 1141 (w), 1072 (s), 1012 (m), 915 (w), 828 (s), 740 (m). HRMS (ESI) calcd for $C_{15}H_{16}{}^{79}BrNNa^+$ $[M+Na]^+$ 312.0358; found 312.0358.

***tert*-Butyl (cyanomethyl)(3-(triisopropylsilyl)prop-2-yn-1-yl)carbamate (13w)**

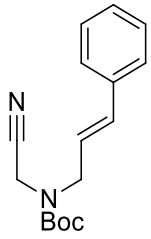


13w

Starting from **12h** (82 mg, 0.30 mmol, 1.0 equiv) and TIPS-EBX (**5b**) (0.26 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 20:1 to 10:1) to afford **13w** as light yellow oil (37 mg, 0.11 mmol, 35%).

Rf (Heptane/Ethyl Acetate = 85:15) 0.4. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.48 – 3.80 (m, 4H, C*H*$_2$NC*H*$_2$), 1.50 (s, 9H, *Boc*), 1.07 (s, 21H, *TIPS*). ^{13}C NMR (101 MHz, Chloroform-*d, mixture of not fully resolved rotamers (M=major, m=minor*) δ 153.7 (br s), 153.3 (br s), 115.5, 100.4, 87.6 (br s), 87.0 (br s), 82.4, 37.6 (br s), 37.2 (br s), 34.0 (br s), 29.7 (m), 28.1 (M), 18.5 (M), 17.7 (m), 12.3 (m), 11.0 (M). IR (ν_{max}, cm^{-1}) 3668 (w), 2944 (s), 2896 (s), 2866 (s), 2362 (w), 2177 (w), 1461 (m), 1395 (s), 1368 (m), 1248 (s), 1165 (s), 1129 (w), 1074 (m), 1012 (s), 917 (w), 883 (m), 865 (m), 826 (w), 772 (w), 738 (w). HRMS (ESI) calcd for $C_{19}H_{34}N_2NaO_2Si^+$ $[M+Na]^+$ 373.2282; found 373.2287.

***tert*-Butyl cinnamyl(cyanomethyl)carbamate (15)**



15

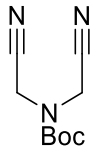
Starting from **12h** (27 mg, 0.10 mmol, 1.0 equiv) and Ph-VBX (**14**) (70 mg, 0.20 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 20:1 to 10:1) to afford **15** as light yellow oil (14 mg, 0.051 mmol, 51%).

Rf (Heptane/Ethyl Acetate = 85:15) 0.4. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.20 (m, 5H, Ar*H*), 6.77 – 6.68 (m, 0.05H, HC=C*H*Ar, Z isomer), 6.58 (d, *J* = 15.8 Hz, 1H, HC=C*H*Ar, E isomer), 6.11 (dt, *J* = 15.8, 6.6 Hz, 1H, *H*C=CHAr, E isomer), 5.65 (dt, *J* = 11.6, 6.5 Hz, 0.05H, Z isomer, *H*C=CHAr, Z isomer), 4.30 – 3.79 (m, 4H, CH_2), 1.52 (s, 9H, *Boc*). ^{13}C NMR (101 MHz, Chloroform-*d*)[41] δ 154.0, 136.0, 134.4, 128.6, 128.4 (Z), 128.1,

[41] 13:1 E:Z mixture, in which the peaks of the Z isomer in ^{1}H and ^{13}C NMR are not fully resolved.

127.5 (Z), 126.5, 123.2, 116.0, 82.0, 49.2, 34.4, 28.2. IR (ν_{max}, cm^{-1}) 2982 (m), 2934 (w), 1830 (w), 1705 (s), 1481 (m), 1455 (m), 1401 (m), 1369 (m), 1252 (s), 1165 (s), 1066 (w), 966 (w), 913 (m), 875 (w), 772 (w), 742 (m). HRMS (ESI) calcd for $C_{16}H_{20}N_2NaO_2^+$ $[M+Na]^+$ 295.1417; found 295.1421.

***tert*-Butyl bis(cyanomethyl)carbamate (17)**

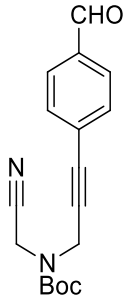


17

Starting from **12h** (27 mg, 0.10 mmol, 1.0 equiv) and CBX (**16**) (55 mg, 0.20 mmol, 2.0 equiv), irradiation for 14 h, the crude product was analyzed by NMR using 6 μL of CH_2Br_2 as internal standard. Integration of peak at 4.42-4.18 ppm (m, 4H, C*H*$_2$CN) revealed 51% NMR yield. The crude was then purified by preparative TLC (Heptane/Ethyl Acetate = 7:3) to afford **17** as light yellow oil (6.1 mg, 0.031 mmol, 31%).

Rf (Heptane/Ethyl Acetate = 70:30) 0.45. ^{1}H NMR (400 MHz, Chloroform-*d*)[42] δ 4.42-4.18 (m, 4H, C*H*$_2$CN), 1.52 (s, 9H, *Boc*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 152.6, 114.4, 84.5, 35.5 (brs, non-resolved rotamers), 28.0. IR (ν_{max}, cm^{-1}) 2988 (w), 2933 (w), 2255 (w), 1829 (w), 1712 (s), 1454 (m), 1398 (s), 1373 (m), 1256 (s), 1164 (s), 1139 (m), 942 (m), 911 (m), 868 (m), 776 (m), 739 (m). HRMS (ESI) calcd for $C_9H_{13}N_3NaO_2^+$ $[M+Na]^+$ 218.0900; found 218.0892.

***tert*-Butyl (cyanomethyl)(3-(4-formylphenyl)prop-2-yn-1-yl)carbamate (70)**



70

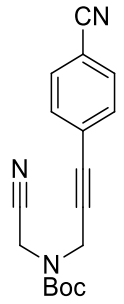
Starting from **12h** (82 mg, 0.30 mmol, 1.0 equiv) and *p*CHO-Ph-EBX (**5i**) (0.23 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 15:1 to 9:1) to afford **70** as light yellow oil (25 mg, 0.080 mmol, 27%, 95% purity).

Rf (Chloroform/Pentane = 9:1) 0.20. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.01 (s, 1H, C*H*O), 7.84 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.60 (d, *J* = 8.3 Hz, 2H, Ar*H*), 4.37 (m, 4H, C*H*$_2$NC*H*$_2$), 1.52 (s, 9H, *Boc*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 191.4, 153.3 (br s), 135.8, 132.3, 129.6, 128.3, 115.6, 86.5, 84.5, 82.8, 37.3, 34.7, 28.2. IR (ν_{max}, cm^{-1}) 3670 (w), 2982 (m), 2902 (w), 2733 (w), 1703 (s), 1604 (m), 1562 (w), 1447 (w), 1399 (m), 1368 (w), 1302 (w), 1250 (m), 1207 (w), 1163 (m), 1131 (w), 1074 (w), 1052 (w), 1014 (w), 964 (w), 911 (w),

[42] Mixture of non-resolved rotamers.

865 (w), 835 (m), 774 (w), 738 (w). HRMS (ESI) calcd for $C_{17}H_{19}N_2O_3^+$ $[M+H]^+$ 299.1390; found 299.1395.

***tert*-Butyl (cyanomethyl)(3-(4-cyanophenyl)prop-2-yn-1-yl)carbamate (71)**



71

Starting from **12h** (82 mg, 0.30 mmol, 1.0 equiv) and *p*CN-Ph-EBX (**5j**) (0.22 g, 0.60 mmol, 2.0 equiv), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 15:1 to 9:1) to afford **71** as light yellow oil (31 mg, 0.11 mmol, 35%).

Rf (Chloroform/Pentane = 9:1) 0.15. ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.53 (d, *J* = 8.4 Hz, 2H, Ar*H*), 4.35 (m, 4H, C*H*$_2$NC*H*$_2$), 1.52 (s, 9H, *Boc*). ^{13}C NMR (101 MHz, Chloroform-*d*) δ 153.4 (br s), 132.3, 132.1, 127.0, 118.3, 115.6, 112.1, 87.0, 83.8, 82.9, 37.3, 35.0, 28.2. IR (ν_{max}, cm^{-1}) 2982 (m), 2908 (m), 2366 (w), 2230 (m), 1706 (s), 1608 (w), 1503 (w), 1449 (m), 1399 (m), 1368 (m), 1250 (s), 1161 (s), 1129 (m), 1052 (m), 911 (w), 845 (m), 770 (w), 738 (m). HRMS (ESI) calcd for $C_{17}H_{18}N_3O_2^+$ $[M+H]^+$ 296.1394; found 296.1384.

8. Computational details

Geometries of all species were optimized using several different DFT methods and dispersion corrections. All methods give comparable results indicating that, compared to rather symmetric species **4a** and **4b**, molecules **4c** and **4d** feature noticeable distortion of the carbazole moiety in the 4th position of the central ring (Figure 23). This distortion is equally observed in the gas-phase optimized geometries and in the experimental crystal structures.[43] The likely cause of this feature is the halogen…halogen bonding between the halogen atoms of the neighbor carbazole moieties, absent/insignificant in **4a** and **4b** but increasingly pronounced in **4c** and **4d**, as exemplified by the corresponding interatomic distances. Similar intermolecular interaction also causes distortion of the 1-carbazole ring in the crystal of **4c**. This hypothesis is supported by the fact (*i*) that distortion is almost entirely lifted in solution and (*ii*) is absent in the optimized structures of dyes, analogous to **4c** and **4d**, but with halogens selectively removed from the carbazole moieties in either the 4th and or the 3rd and 5th positions of the central ring.

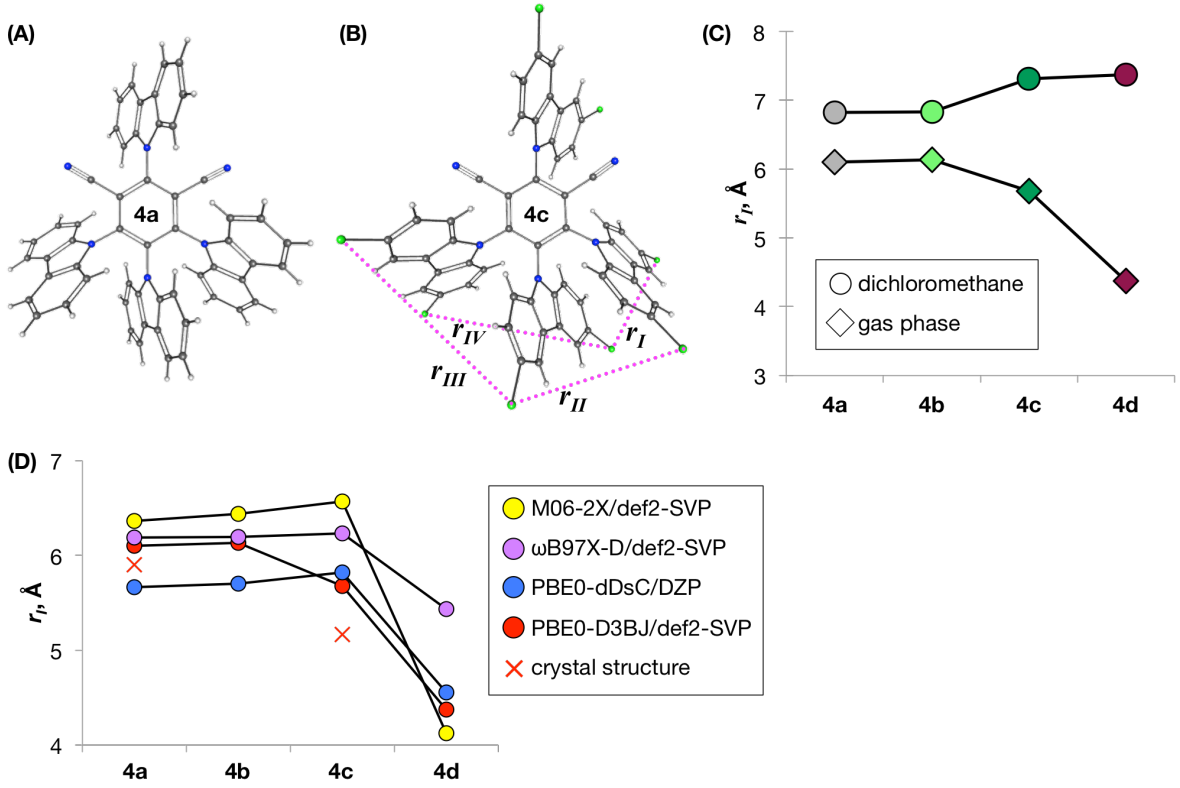


Figure 23. X-ray structures of dyes **4a** (A) and **4c** (B). Interhalogen distances in **4c** are labelled as r_I-r_{IV} (dotted pink lines). (C) Interhalogen distance r_I in the optimized geometries of the studied dyes in the gas phase (PBE0-D3BJ/def2-SVP) and dichloromethane solution (PCM-UAKS/PBE0/6-31G(d)). (D) Shortest interhalogen distances r_I in the optimized geometries for several different dispersion-corrected DFT methods and experimental crystal structures.

[43] a) Crystal structure of **4a** is deposit to CCDC under number 1052646 (YUGDOV), see S. Wang, Y. Zhang, W. Chen, J. Wei, Y. Liu and Y. Wang, *Chem. Commun*., 2015, **51**, 11972. b) Crystal structure of **4c** is available at CCDC under number 1838186.

Electronic energies of the studied molecules were computed at the PBE0-D3BJ/def2-SVP level using Gaussian 09 software[44] and including LANL2DZ effective core potential for bromine atoms. Using the *stable=opt* keyword ensured stability of the wavefunction for all species. Gas-phase vertical and adiabatic ionization potentials and electron affinities were computed as follows:

Ionization potential $IP = E_{P^+} - E_P$ and

Electron affinity $EA = E_P - E_{P^-}$,

where E_P is the electronic energy of the neutral (parent) compound, E_{P+} is the electronic energy of its radical cation and E_{P-} – of its radical anion, in eV.

Gas-phase entropies and thermal corrections at 25°C were computed at the PBE0-D3BJ/def2-SVP level under the harmonic oscillator approximation in conjunction with the optimized geometries and scaled[45] frequencies. Gas-phase Gibbs free energies at 25°C were computed using Gibbs fundamental equation. Gibbs free energies of solvation in acetonitrile (MeCN) and dichloromethane (DCM) were computed in conjunction with geometries, relaxed in solution, using the polarizable continuum model with scaled UAKS radii[46] at the PBE0/6-31G(d) level of theory. These computations include the solvent-solute dispersion and repulsion interaction energies and the solute cavitation energy. Free energies of each species in solution were computed as the sum of the corresponding gas-phase free energy and the free energy of solvation. The phase change correction term cancels out in the computation of redox potentials.

RedOx potentials of the investigated systems in their ground states relative to the saturated calomel electrode (SCE) in a given solvent were computed as follows:

Oxidation potential $E_{1/2}(P^+/P) = \frac{G_{electron} + G_{P+}^{soln} - G_P^{soln}}{F} - E_{SCE}$ and

Reduction potential $E_{1/2}\left(P/P^-\right) = \frac{G_{electron} + G_P^{soln} - G_{P-}^{soln}}{F} - E_{SCE}$,

[44] Gaussian 09, Revision D.01, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Mennucci, B.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Li, X.; Hratchian, H. P.; Izmaylov, A. F.; Bloino, J.; Zheng, G.; Sonnenberg, J. L.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Rega, N.; Millam, J. M.; Klene, M.; Knox, J. E.; Cross, J. B.; Bakken, V.; Adamo, C.; Jaramillo, R.; Gomperts, R.; Stratmann, R. E.; Yazyev, J.; Austin, A. J.; Cammi, R.; Pomelli, C.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Zakrzewski, V. G.; Voth, G. A.; Salvador, P.; Dannenberg, J. J.; Dapprich, S.; Daniels, A. D. Farkas, Ö.; Foresman, J. B.; Ortiz, J. V.; Cioslowski, J.; Fox, D. J. Gaussian, Inc., Wallingford CT, 2009.

[45] Merrick, J. P.; Moran, D.; Radom, L. An Evaluation of Harmonic Vibrational Frequency Scale Factor. *J. Phys. Chem. A* **2007,** *111,* 11683-11700 (PBE0/6-311+G(d,p) scaling factors were adopted).

[46] (a) Scaling factor α=1.45 is used for MeCN, see Gryn'ova, G.; Barakat, J. M.; Blinco, J. P.; Bottle, S. E.; Coote, M. L. Computational Design of Cyclic Nitroxides as Efficient Redox Mediators for Dye-Sensitized Solar Cells. *Chem. Eur. J.* **2012**, *18*, 7582-7593. (b) Scaling factor α=1.30 is used for DCM, see Luque, F. J.; Zhang, Y.; Alemán, C.; Bachs, M.; Gao, J.; Orozco, M. *J. Phys. Chem.* **1996**, *100*, 4269-4276.

where $G_{electron}$ is the gas-phase Gibbs free energy of an electron, equal under Fermi-Dirac statistics to –3.632 kJ mol^{-1},[47] G^{soln} are the Gibbs free energies of the neutral compound (P), its cation radical (P^+) and anion radical (P^-) in solution, F is the Faraday constant equal to 96.485 kJ V^{-1}, E_{SCE} is the absolute potential of SCE in a given solvent (4.429 eV in acetonitrile[48] and 4.462 eV in dichloromethane[49]).

Results. Computed redox energetics (Figure 24) indicate that one-electron removal becomes harder (higher $E_{1/2}(P^+/P)$) and one-electron addition becomes easier (higher $E_{1/2}(P/P^-)$) in the order of **4a** < **4b** < **4c** < **4d**, *i.e.* H < F < Cl < Br substituents in the 3' and 6' (*i.e.*, *para*-) positions in carbazole rings. A possible explanation of the observed trends is as follows:

- Upon oxidation/ionization, an electron is removed from the peripheral carbazole moieties (Figure 25), in which the stronger resonance donors, such as Cl and Br, stabilize the formed radical cation better. This is reflected in the average Hirshfeld spin densities of the hydrogen and halogen atoms in the 3' and 6' positions in the carbazole rings: 0.002 on H-atoms in **4a**, 0.010 on F in **4b**, 0.019 on Cl in **4c** and 0.023 on Br in **4e**.

- Upon reduction, an electron is added to the lowest unoccupied molecular orbital (LUMO), located mostly on the central isophthalonitrile ring (Figure 25). It also involves the carbazole moieties in the 4 and 6 positions of the isophthalonitrile ring and is potentially stabilized by them to a greater extent in the case of Cl and Br substituents (resonance donors) compared to H and F.

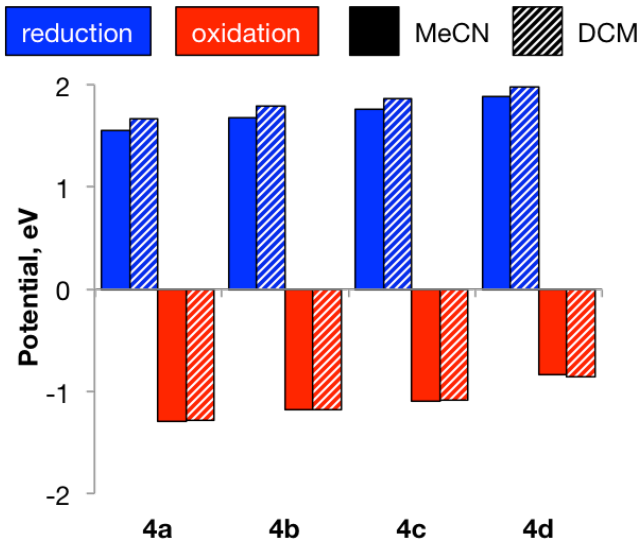


Figure 24. Computed oxidation and reduction potentials *vs.* SCE at 25 °C in acetonitrile and dichloromethane.

[47] Ho, J.; Coote, M. L.; Cramer, C. J.; Truhlar, D. G. Theoretical Calculation of Reduction Potentials. In *Organic Electrochemistry: Revised and Expanded*, 5th Edition; Hammerich, O.; Speiser, B., Eds.; CRC Press, Taylor and Francis Group: Boca Raton, **2015**; Chapter 6, pp 231-261.

[48] Isse, A. A.; Gennaro, A. Absolute Potential of the Standard Hydrogen Electrode and the Problem of Interconversion of Potentials in Different Solvents. *J. Phys. Chem. B* **2010,** *114,* 7894-7899 .

[49] Derived from the 4.927 eV absolute potential of Fc^+/Fc couple in 1,2-dichloroethane (Namazian, M.; Lin, C. Y.; Coote, M. L. *J. Chem. Theory Comput.* **2010**, *6*, 2721–2725) and the 0.465 eV correction to SCE in dichloromethane (Palmer, J. H. *Iridium corroles: synthesis, properties, and electronic structure.* 2011, Dissertation (Ph.D.), California Institute of Technology).

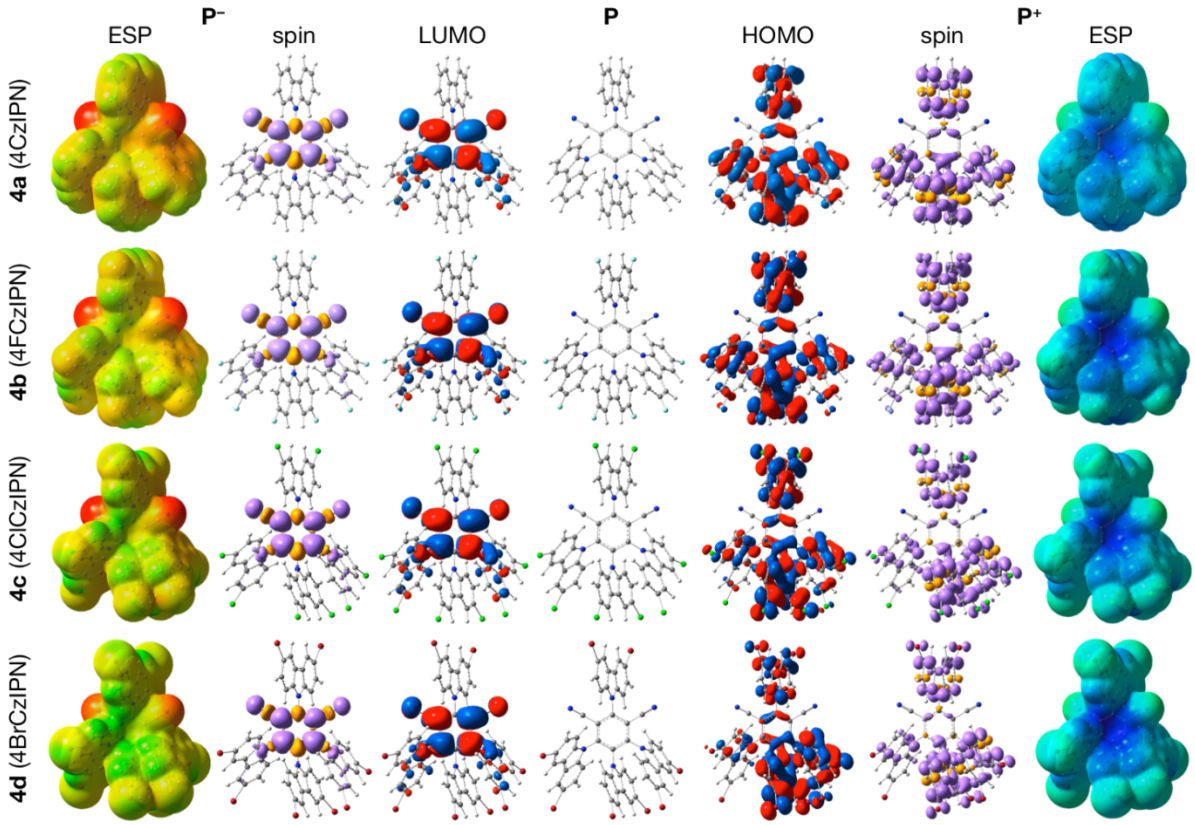


Figure 25. Molecular structures of the parent dyes (P) and their HOMO and LUMO plots (isovalue 0.02), as well as the spin densities and electrostatic potential maps (isovalue 0.001) of the products of one-electron addition (P^-) and removal (P^+), all at the PBE0/def2-SVP level.

	MeCN		DCM	
	$E_{1/2}(P^+/P)$	$E_{1/2}(P/P^-)$	$E_{1/2}(P^+/P)$	$E_{1/2}(P/P^-)$
4a	1.56	-1.29	1.67	-1.29
4b	1.67	-1.18	1.79	-1.18
4c	1.76	-1.10	1.87	-1.09
4d	1.89	-0.83	1.98	-0.85

Table 5. Computed oxidation and reduction potentials in acetonitrile, *N,N*-dimethylformamide and dichloromethane *vs.* SCE at 25 °C (based on PBE0-D3BJ/def2-SVP gas-phase Gibbs free energies and PCM-UAKS/PBE0/6-31G(d) Gibbs free energies of solvation). All values are in eV.

	Oxidation			Reduction		
	gas phase	MeCN	DCM	gas phase	MeCN	DCM
4a	7.00	5.99	6.02	1.89	3.14	3.06
4b	7.30	6.10	6.14	2.27	3.25	3.17
4c	7.37	6.19	6.22	2.50	3.33	3.26
4d	7.46	6.32	6.33	2.78	3.60	3.50

Table 6. Computed Gibbs free energies (PBE0-D3BJ/def2-SVP) of oxidation and reduction at 25 °C in the gas phase and solution (PCM-UAKS/PBE0/6-31G(d)). All values are in eV.

	I	II	III	IV	I	II	III	IV
	gas phase				X-ray			
4a	6.099	6.186	6.215	6.301	5.900	6.609	6.611	7.266
4b	6.134	6.216	6.420	6.320				
4c	5.678	5.700	6.863	7.142	5.164	6.558	8.326	9.150
4d	4.371	4.396	7.655	8.133				
	DCM				MeCN			
4a	6.823	6.833	6.833	6.823	6.362	6.405	6.467	6.380
4b	6.831	6.946	6.945	6.829	6.403	6.496	6.800	6.576
4c	7.310	7.377	7.456	7.419	6.871	6.981	6.988	6.883
4d	7.372	7.409	7.629	7.757	7.079	7.168	7.169	7.081

Table 7. Interatomic distances in the optimized geometries and crystal structures of the studied dyes, in Å.

		gas phase				MeCN	DCM
	geometry / state	S^{298}, J mol^{-1} K^{-1}	TC^{298}, kJ mol^{-1}	$ZPVE$, kJ mol^{-1}	E, Hartree	ΔG^{298}_{solv}, kcal mol^{-1}	
4a	0 1 / 0 1	1118.5401	121.3468	1888.9644	-2477.41341	23.53	5.00
	0 1 / 1 2				-2477.15623		
	1 2 / 1 2	1083.3725	119.3373	1884.9387	-2477.15769	0.93	-16.79
	0 1 / -1 2				-2477.47126		
	-1 2 / -1 2	1130.1518	122.5092	1879.1700	-2477.47829	-6.13	-22.91
4b	0 1 / 0 1	1264.5510	140.0826	1718.2348	-3269.96854	25.73	5.02
	0 1 / 1 2				-3269.70054		
	1 2 / 1 2	1226.5210	137.8545	1715.1549	-3269.70244	-1.09	-20.84
	0 1 / -1 2				-3270.04226		
	-1 2 / -1 2	1250.3950	139.0590	1708.9503	-3270.04947	2.23	-16.74
4c	0 1 / 0 1	1361.7109	148.6806	1687.7816	-6151.89172	31.19	8.21
	0 1 / 1 2				-6151.62241		
	1 2 / 1 2	1309.0876	146.1016	1684.2253	-6151.62444	4.73	-17.56
	0 1 / -1 2				-6151.97211		
	-1 2 / -1 2	1368.2332	149.6635	1679.3511	-6151.97992	11.10	-10.32
4d	0 1 / 0 1	1399.6969	152.0885	1675.4331	-2576.77867	30.75	6.12
	0 1 / 1 2				-2576.50149		
	1 2 / 1 2	1398.6982	152.0594	1672.1752	-2576.50320	5.14	-19.08
	0 1 / -1 2				-2576.86906		
	-1 2 / -1 2	1420.3436	153.2410	1667.5107	-2576.87601	11.12	-11.19

Table 8. Computed gas-phase entropies, thermal corrections, zero-point vibrational energies and electronic energies (PBE0-D3BJ/def2-SVP) and Gibbs free energies of solvation (PCM-UAKS/PBE0/6-31G(d)) for all studied species.

Geometries

PBE0-D3BJ/def2-SVP optimized geometries of all species in the form of Gaussian archive entries.

4a

```
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953197\H,0.6349946028,0.5126322843,-2.9914249126\H,-3.6716327383,0.900
1562556,0.5586616629\H,-2.5032783371,-1.7095814676,0.2154814838\H,3.52
08151501,1.2587561602,0.7609657913\H,-0.4862218126,-2.5225936561,1.745
8642893\H,0.863240312,7.117368691,3.8451471112\H,5.7650579046,-3.23417
26127,0.7645636149\H,3.7836995012,-5.1058459738,1.2261384177\H,-1.0005
211283,-5.4059458349,-2.8269998015\H,-3.2981428001,-1.5455078481,-5.33
08630381\H,-5.4344328355,-1.3170153694,-3.589372797\H,-1.7497759188,6.
5019814086,4.564642343\H,-6.9271231543,-0.8682511405,-1.6476235604\H,-
6.0481586874,0.219048036,0.3966060078\H,-1.0584580748,-1.4907679713,-6
.4178621899\H,0.8779436698,-0.4595793127,-5.2655826257\H,-4.025348706,
-3.5850805118,-0.3386504759\H,-3.2931827507,-5.4050951105,-1.854956673
1\H,-0.4789938194,-5.0023919239,1.8909373995\H,1.6259309678,-6.2831402
639,1.6223368202\H,7.0750192471,-1.1523492625,0.3769809179\H,5.9590729
554,1.0587846816,0.3695953029\H,3.1676314036,7.1125389203,2.9034869011
\H,3.9392228758,5.2590620994,1.4563740146\H,-3.9853199111,5.4438793449
,4.8474397558\H,-4.4914070448,3.2576876905,3.803506706\C,3.379341501,-
1.9929615805,-2.6481127628\C,3.1028827866,-3.241172893,-3.2160795334\H
,2.6395010762,-0.343402322,-1.464842955\H,1.6364879719,-4.8070235776,-
3.525861701\H,4.3505998652,-1.5231127551,-2.8130564148\H,3.8654755209,
-3.7367099187,-3.8199477812\\Version=ES64L-G09RevD.01\HF=-2477.1577432
\S2=0.761223\S2-1=0.\S2A=0.750127\RMSD=7.934e-09\RMSF=3.059e-06\Dipole
=0.0846467,-1.7521867,-1.1087699\Quadrupole=12.3496978,12.4080739,-24.

7577717,6.6890391,-12.8964389,35.7003711\PG=C01 [X(C56H32N6)]\\@

4a.ar_opt

1\1\GINC-R05-NODE53\FOpt\UPBE1PBE\Gen\C56H32N6(1-,2)\GRYNOVA\30-Mar-20
18\0\\#PBE1PBE/gen SCF=Tight INT(grid=finegrid) OPT IOP(2/17=4) Empiri
calDispersion=GD3BJ Nosymm\\7d.ar_opt.pbe0.freq\\-1,2\C,-0.9737363676,
1.8248584848,0.1320625738\C,-0.9332416466,0.5649520609,-0.5920076821\C
,0.0267699684,-0.3959041928,-0.2411736038\C,0.9098992423,-0.1925583104
,0.829940644\C,0.7901018714,1.0162057514,1.628725514\C,-0.1292607488,1
.9985410115,1.2365076734\C,-1.7979602888,2.8832079191,-0.3123127791\N,
-2.4933333272,3.7439928108,-0.6785707939\C,1.5355644143,1.1683251663,2
.81946586\N,2.1670334451,1.2909252934,3.7915456874\N,-0.2078079767,3.1
972849217,1.975500068\C,0.793210186,4.1513340544,2.0752819518\C,-1.301
4217958,3.6152108402,2.718432633\N,-1.8469120845,0.3383177769,-1.63858
90227\C,-1.5258402439,-0.0169947703,-2.9423519083\C,-3.219454194,0.197
1250241,-1.474119406\N,0.1069724154,-1.5938698913,-0.9849056134\C,1.21
51617375,-2.0285807276,-1.6992758565\C,-0.9018448965,-2.5392964847,-1.
1108700918\N,1.9031184073,-1.1377861797,1.1497031061\C,3.2700734481,-0
.9208111136,1.0212498698\C,1.6979382696,-2.4911493077,1.3863350473\C,-
1.0026647828,4.8652526617,3.3140951543\C,0.3388568399,5.2103866973,2.8
993106213\C,3.9542330469,-2.1543456632,1.1481901155\C,2.9447930917,-3.
1637239137,1.3748157741\C,-0.4392957927,-3.60211263,-1.9243756316\C,0.
9203587244,-3.2794158514,-2.2933447631\C,-2.7006531398,-0.426750287,-3
.6197495598\C,-3.7888154455,-0.2823886559,-2.6792596833\C,2.0550596911
,4.170652167,1.4823367853\C,-2.521797287,2.9740825977,2.9272401969\C,-
0.2834307901,-0.0076278284,-3.5744062742\C,-3.9932853814,0.4143600403,
-0.3337500971\C,2.4382560774,-1.3929528628,-1.9039306095\C,-2.16939118
49,-2.561181323,-0.5318881177\C,3.9481629115,0.2687696378,0.7539205428
\C,0.5025103208,-3.1731706085,1.6086593182\C,1.1777804397,6.3025960099
,3.1382127818\C,5.343155161,-2.1891098083,1.0030143656\C,2.9821261448,
-4.549196055,1.5547703651\C,-1.2826884063,-4.6838102284,-2.1890318233\
C,1.890338017,-3.9177894468,-3.0700709051\C,-2.6145385567,-0.863981710
8,-4.944647706\C,-5.1593475919,-0.5470402681,-2.7350328551\C,-1.957329
5355,5.483826768,4.1264532919\C,-5.9365438659,-0.3338583117,-1.6012057
327\C,-5.3547273085,0.1427848255,-0.4151937298\C,-1.3725668483,-0.8852
636179,-5.5694637354\C,-0.2217689621,-0.4550428042,-4.8883770236\C,-2.
9933481168,-3.6440732369,-0.8168766521\C,-2.561185232,-4.6943659888,-1
.6416633018\C,0.5642135789,-4.5512013145,1.7756583168\C,1.7891056303,-
5.2379821858,1.743570964\C,6.0252631236,-1.0070141167,0.7342361705\C,5
.3302671655,0.2072356192,0.6125020718\C,2.4407102396,6.3242393361,2.55
71587529\C,2.8693543953,5.2680031598,1.7367003278\C,-3.1797111022,4.85
40368327,4.3322477895\C,-3.4534858308,3.6110735856,3.7383983864\H,2.38
5125738,3.3485853349,0.8460894862\H,-2.7313869023,2.0092537127,2.46380
93447\H,0.609617237,0.3297353041,-3.0492970169\H,-3.5410446375,0.78840
80333,0.5853371878\H,-2.5070635647,-1.755626288,0.1187254803\H,3.40762
86179,1.2114688986,0.6634222178\H,-0.4483534359,-2.6419641719,1.637511
9191\H,0.8416175844,7.1270086219,3.7718695917\H,5.8823499441,-3.135722
4127,1.0897462587\H,3.9367405049,-5.0809696733,1.5404126569\H,-0.93799
4755,-5.5087630413,-2.8172218919\H,-3.5119312375,-1.1895614639,-5.4766
006562\H,-5.6099086906,-0.9255315578,-3.6559403757\H,-1.7418040015,6.4
483335022,4.592790905\H,-7.0098419083,-0.535617873,-1.63138651\H,-5.98
34442873,0.3107687022,0.4626073073\H,-1.288274845,-1.2370568069,-6.600
3202829\H,0.7461943861,-0.4765304284,-5.3945405203\H,-3.9993010764,-3.
6668041223,-0.3914712232\H,-3.2349401739,-5.5289033472,-1.8492904781\H
,-0.3640836288,-5.107129218,1.926651832\H,1.8017260687,-6.3228705936,1
.8715251819\H,7.1116363718,-1.0196660071,0.6192201981\H,5.8848635049,1
.1264761449,0.4088405645\H,3.10797662,7.1700986595,2.737960299\H,3.865
6733222,5.3052035617,1.2896529884\H,-3.936256838,5.3278564722,4.961968
8836\H,-4.4205564923,3.1334461,3.9132164541\C,3.3904396973,-2.05148097
61,-2.6734075383\C,3.1262627041,-3.3049440278,-3.247247062\H,2.6455846
128,-0.4155299065,-1.4705910765\H,1.6762793294,-4.8851375256,-3.530944
8477\H,4.3644574583,-1.580086201,-2.8234348394\H,3.8976134996,-3.79836
87637,-3.8431022007\\Version=ES64L-G09RevD.01\HF=-2477.478192\S2=0.767
387\S2-1=0.\S2A=0.750211\RMSD=4.811e-09\RMSF=2.242e-06\Dipole=0.145804
,-2.1297179,-1.3162405\Quadrupole=11.6009494,-5.0786305,-6.522319,14.8
92257,-22.28218,-2.0937666\PG=C01 [X(C56H32N6)]\\@

4b

1\1\GINC-R02-NODE38\FOpt\RPBE1PBE\Gen\C56H24F8N6\GRYNOVA\29-Mar-2018\0
\\#PBE1PBE/gen SCF=Tight INT(grid=finegrid) OPT IOP(2/17=4) EmpiricalD
ispersion=GD3BJ Nosymm\\7g.pbe0.freq\\0,1\C,-0.9953756294,1.8140187687
,0.1687445317\C,-0.9443841409,0.6071760137,-0.5598448135\C,0.029154266
4,-0.3664532075,-0.2372458081\C,0.9229931066,-0.1349251345,0.834581185
2\C,0.8178575073,1.0519322617,1.5894227834\C,-0.1288333474,2.034219321
4,1.2525888076\C,-1.855479451,2.867138876,-0.2660792675\N,-2.543257511
1,3.7280439597,-0.6237134233\C,1.5999443222,1.2088633041,2.7733426482\
N,2.2247966226,1.335069013,3.7406801899\N,-0.2092409169,3.2148026373,1
.9868474639\C,0.8058912146,4.1658537472,2.1158285792\C,-1.3219931148,3
.6460427574,2.7133913865\N,-1.8396625402,0.4070438034,-1.6102329044\C,
-1.5029806127,-0.0794135726,-2.8800295397\C,-3.2295827649,0.2741508758
,-1.4454524089\N,0.1069887254,-1.548719578,-0.9721996983\C,1.235741475
4,-2.0099706763,-1.6534490913\C,-0.9177372811,-2.4862887606,-1.1238473
623\N,1.8914670189,-1.0775133439,1.1803220911\C,3.2759447362,-0.862998
249,1.0573684418\C,1.6730880159,-2.457114514,1.2878407469\C,-1.0169453
679,4.8875684946,3.3151670828\C,0.3385011315,5.2190922795,2.9338517448
\C,3.9304632177,-2.1150288683,1.0532185375\C,2.9097280989,-3.129725503
4,1.1956047144\C,-0.4415952483,-3.5566272265,-1.9141806261\C,0.9364010
953,-3.2610998308,-2.2371859116\C,-2.6685411923,-0.556047609,-3.515907
1243\C,-3.7681237053,-0.3283296366,-2.6044043535\C,2.0732388994,4.1916
712113,1.5395199056\C,-2.5464632304,3.0144498314,2.9147728986\C,-0.265
1243871,-0.0965125887,-3.5152474847\C,-4.0260255739,0.5627699726,-0.34
03894622\C,2.4670035187,-1.3903363139,-1.8469675369\C,-2.1944616362,-2
.5011128104,-0.5692980529\C,3.978573209,0.3241383262,0.8685241011\C,0.
4806524276,-3.1439914964,1.4932472965\C,1.1670379958,6.3112802429,3.20
32404292\C,5.3129928594,-2.1832564841,0.8751444869\C,2.9518174559,-4.5
245347892,1.2465198564\C,-1.2785059602,-4.6361377784,-2.2042674452\C,1
.9104881116,-3.9369272067,-2.975024096\C,-2.5886422623,-1.1183007696,-
4.7917446053\C,-5.12914778,-0.6303715753,-2.6699612471\C,-1.9680830278
,5.5249580934,4.1158545591\C,-5.9106697161,-0.3283393198,-1.5662108662
\C,-5.3812354517,0.2555680058,-0.4121676227\C,-1.3395204554,-1.1796374
553,-5.3885018284\C,-0.188826917,-0.6697200083,-4.7786060653\C,-3.0234
873402,-3.5767240438,-0.867130927\C,-2.5623745955,-4.6143038549,-1.683
0941316\C,0.5263442205,-4.5322417888,1.5279012988\C,1.7489987084,-5.19
74334701,1.3920170792\C,5.9996233231,-0.9929365835,0.6964506366\C,5.35
61579062,0.2476905675,0.6879184275\C,2.4328303659,6.3137431911,2.64056
85194\C,2.891041678,5.2811299916,1.8157890565\C,-3.1897788242,4.895589
1985,4.2900351954\C,-3.487231676,3.6578749759,3.7103022745\H,2.4200652
807,3.3909608392,0.8846586603\H,-2.7675378208,2.0415433818,2.473353828
2\H,0.6266524095,0.3149314,-3.0436654165\H,-3.6191653883,1.0192473562,
0.5615081621\H,-2.5498096692,-1.7038259805,0.0824948306\H,3.4823203423
,1.2942804212,0.8623989829\H,-0.4677446339,-2.6211954154,1.6132742038\
H,0.8465110082,7.145999835,3.8280531536\H,5.8511325931,-3.1319417088,0
.8582773283\H,3.8851953447,-5.0840241635,1.1730553888\H,-0.9508591191,
-5.4801579164,-2.8126203853\H,-3.4639811046,-1.5033923591,-5.316216333
5\H,-5.5789814331,-1.100695031,-3.5453543941\H,-1.7743841314,6.4828586
258,4.6003993553\F,-7.2128808967,-0.6062706376,-1.5971213318\H,-6.0512
80325,0.4721810608,0.4210356019\F,-1.2260379021,-1.7271369604,-6.59750
6919\H,0.7613450134,-0.7308906279,-5.3110932316\H,-4.0400508018,-3.626
217491,-0.4743176507\F,-3.3885486052,-5.6248958399,-1.9518923397\H,-0.
3826772257,-5.1208179054,1.6594969999\F,1.7523996325,-6.5291399501,1.4
237850528\F,7.3195400728,-1.0247059735,0.5207928534\H,5.9552200043,1.1
485131963,0.5473924774\F,3.2478024967,7.3398924342,2.8813937113\H,3.89
60209541,5.3529723039,1.3974301881\F,-4.1187968858,5.4801137436,5.0452
693294\H,-4.4658113257,3.2139009201,3.898606169\C,3.4338841717,-2.0721
493749,-2.5767839668\C,3.1492938003,-3.331251773,-3.1140327427\H,2.684
5166861,-0.4020809221,-1.4434103605\H,1.7225976027,-4.9067044924,-3.43
7632215\H,4.4229237785,-1.6407260061,-2.7375210489\F,4.1040365008,-3.9
58530663,-3.8004911927\\Version=ES64L-G09RevD.01\HF=-3269.9685005\RMSD
=7.416e-09\RMSF=2.864e-06\Dipole=0.0432976,-0.6677445,-0.4188723\Quadr
upole=5.3335757,-3.01749,-2.3160857,7.8542901,-11.6049653,-2.3840731\P
G=C01 [X(C56H24F8N6)]\\@

4b.cr_opt

1\1\GINC-R03-NODE57\FOpt\UPBE1PBE\Gen\C56H24F8N6(1+,2)\GRYNOVA\30-Mar-
2018\0\\#PBE1PBE/gen SCF=Tight INT(grid=finegrid) OPT IOP(2/17=4) Empi
ricalDispersion=GD3BJ Nosymm\\7g.cr_opt.pbe0.freq\\1,2\C,-1.0363379165

,1.806482638,0.210846802\C,-0.9728329684,0.6076199303,-0.524726866\C,0
.0234345478,-0.3487140167,-0.2170732941\C,0.9426748143,-0.1084706983,0
.8315511115\C,0.8510873029,1.0830979355,1.5761228891\C,-0.1320157702,2
.0456640538,1.2662161742\C,-1.9242775914,2.839092604,-0.2136577847\N,-
2.6429544876,3.675154691,-0.5690287167\C,1.6626031824,1.2441193655,2.7
382123954\N,2.3199027627,1.365075817,3.6843169951\N,-0.2086406348,3.22
38572052,1.9951748188\C,0.8226804784,4.1568034753,2.1440400778\C,-1.33
16423247,3.6733481926,2.6974468273\N,-1.8509010179,0.3886380803,-1.582
8081925\C,-1.4751725373,-0.0691493169,-2.856912532\C,-3.2343451581,0.2
043906859,-1.4390807607\N,0.0996738788,-1.5298874324,-0.9496197758\C,1
.2227580698,-1.9815622628,-1.6415445188\C,-0.9297998165,-2.4582950056,
-1.1012719596\N,1.9007702719,-1.0641174071,1.1587151698\C,3.2838664279
,-0.8790882344,1.0092325177\C,1.652304535,-2.4401424778,1.2948192833\C
,-1.0175229437,4.910142615,3.3051121961\C,0.3558596644,5.2189892983,2.
951283146\C,3.9110698792,-2.1472534663,0.9983385054\C,2.8710385069,-3.
1395750205,1.1792689754\C,-0.4648798923,-3.5224109271,-1.9089507072\C,
0.9162938536,-3.2249402497,-2.241525111\C,-2.6091625777,-0.5968829894,
-3.5073537837\C,-3.730649768,-0.4223492183,-2.6066551851\C,2.095581873
,4.1670734017,1.5759139775\C,-2.5643538594,3.0508294683,2.8870707296\C
,-0.234755955,-0.0024941099,-3.484200226\C,-4.0575509726,0.4633222466,
-0.3433149336\C,2.4454469983,-1.3448702255,-1.8539425846\C,-2.19333064
72,-2.4825216488,-0.5107639992\C,4.0069436456,0.2945845865,0.796654882
1\C,0.4531704462,-3.0953250369,1.5589073153\C,1.188393912,6.2978367039
,3.2294522987\C,5.2843468781,-2.2474413888,0.7894294619\C,2.8883267935
,-4.5311332124,1.2620933012\C,-1.3020960784,-4.5927047027,-2.197009472
5\C,1.8742044929,-3.8835079752,-3.0018418528\C,-2.4923788213,-1.134815
7596,-4.7883339578\C,-5.0735781504,-0.7815677505,-2.6911920909\C,-1.96
53461398,5.5593454402,4.0890458833\C,-5.8830219748,-0.5102278241,-1.59
56138343\C,-5.3950861705,0.0985859707,-0.4327823083\C,-1.23532376,-1.1
172894124,-5.3799197955\C,-0.1190713504,-0.5505109914,-4.7569826843\C,
-3.0302300233,-3.5516625119,-0.8071443582\C,-2.5854546259,-4.573195640
2,-1.6511617868\C,0.4717581298,-4.4840164858,1.6270598867\C,1.67516241
84,-5.1774468761,1.4652651789\C,5.9925448751,-1.0699153203,0.586968304
\C,5.3757470681,0.1872438988,0.5845768262\C,2.468793586,6.2810950828,2
.682367367\C,2.9248671936,5.2439769846,1.8615196521\C,-3.2043141827,4.
9429600228,4.2444785795\C,-3.5093073172,3.7062062616,3.6658200558\H,2.
4384420657,3.3665073731,0.9194878577\H,-2.7893919971,2.0765811972,2.45
16667062\H,0.6252304715,0.4673346097,-3.0066021736\H,-3.6836143435,0.9
427949726,0.5609907995\H,-2.5259146004,-1.7043559496,0.1749084698\H,3.
5320074781,1.2753417539,0.800055687\H,-0.4769635603,-2.5486440502,1.71
51136089\H,0.8715863135,7.1422335176,3.8430619582\H,5.8046793598,-3.20
59533546,0.7686582461\H,3.8075308234,-5.1126479616,1.1798841717\H,-0.9
88677683,-5.4359637624,-2.8139891885\H,-3.342467025,-1.5530646407,-5.3
288980586\H,-5.4944864057,-1.2694677366,-3.5713584642\H,-1.7679866895,
6.5124001814,4.5816042458\F,-7.1629738155,-0.8423703179,-1.6430084694\
H,-6.0882922803,0.2889218573,0.3877897734\F,-1.0873374983,-1.637681643
3,-6.5895860598\H,0.8316109462,-0.5380873977,-5.2919788238\H,-4.035135
4561,-3.6136702117,-0.3873593669\F,-3.4057109083,-5.5733884633,-1.9204
365182\H,-0.4404852063,-5.0511293036,1.8177598238\F,1.6552427962,-6.50
08403783,1.5292925833\F,7.2982203857,-1.1311192722,0.3812460316\H,5.99
3620532,1.0722159763,0.426063512\F,3.2835837646,7.2906031182,2.9339096
462\H,3.9344044143,5.306280231,1.4532540887\F,-4.126211708,5.539552581
7,4.9795975893\H,-4.494619736,3.2741772179,3.8454277917\C,3.4039821797
,-2.0106370784,-2.6083133617\C,3.1159211854,-3.2658501926,-3.151572318
1\H,2.6558399121,-0.3519333604,-1.4589071772\H,1.6852787473,-4.8434148
55,-3.4843714246\H,4.3843535791,-1.5685469449,-2.7909521259\F,4.049122
9059,-3.878778773,-3.8581075722\\Version=ES64L-G09RevD.01\HF=-3269.702
4267\S2=0.759945\S2-1=0.\S2A=0.750097\RMSD=4.748e-09\RMSF=1.902e-06\Di
pole=0.0170982,-0.3266919,-0.1952875\Quadrupole=4.8257543,9.8987292,-1
4.7244835,4.7939198,-9.8689303,23.0664102\PG=C01 [X(C56H24F8N6)]\\@

4b.ar_opt

```
1\1\GINC-R04-NODE04\FOpt\UPBE1PBE\Gen\C56H24F8N6(1-,2)\GRYNOVA\30-Mar-
2018\0\\#PBE1PBE/gen SCF=Tight INT(grid=finegrid) OPT IOP(2/17=4) Empi
ricalDispersion=GD3BJ Nosymm\\7g.ar_opt.pbe0.freq\\-1,2\C,-0.986654514
4,1.8400931536,0.152381176\C,-0.9401608985,0.5838322202,-0.5776005281\
C,0.024899791,-0.3735774594,-0.2318326378\C,0.9118051972,-0.1697836299
,0.8368559753\C,0.7963720374,1.041030263,1.6327157028\C,-0.1328584037,
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2.0181734743,1.249664332\C,-1.8241070597,2.8916138885,-0.2825106528\N,
-2.5346774439,3.7441152797,-0.6386686104\C,1.5571072549,1.1985817889,2
.8128493566\N,2.2060568374,1.3269393587,3.7724767338\N,-0.211588877,3.
2152951023,1.9891634516\C,0.791272843,4.1673481192,2.0976330056\C,-1.3
083669996,3.639761307,2.7248223536\N,-1.8480514165,0.3584795839,-1.629
1159466\C,-1.5185274777,-0.0118298956,-2.9268865668\C,-3.2203792446,0.
2014210045,-1.4716630596\N,0.106260385,-1.5692506008,-0.977252827\C,1.
2199845515,-2.0096585747,-1.6795591525\C,-0.8962209016,-2.5222885908,-
1.0986150552\N,1.898322055,-1.1209216996,1.1597936685\C,3.2670436813,-
0.9226612352,1.0110207991\C,1.6814533697,-2.4773273151,1.3697353319\C,
-1.0089143494,4.8885399322,3.3219996988\C,0.3346394106,5.2277221441,2.
9181038339\C,3.9350065804,-2.1686799944,1.0950832944\C,2.917175386,-3.
1673435769,1.3155658512\C,-0.42280145,-3.5936829657,-1.894430205\C,0.9
362070941,-3.2707437427,-2.2566219063\C,-2.6840943682,-0.447433368,-3.
6035506919\C,-3.7770669114,-0.3028172409,-2.6725995112\C,2.0580355781,
4.1883635971,1.515054415\C,-2.5340749655,3.0074146067,2.9299182457\C,-
0.2753942539,0.0033867033,-3.5579941948\C,-4.00677964,0.421312379,-0.3
405209687\C,2.4410134805,-1.3720888253,-1.8918312128\C,-2.16655554,-2.
5500901688,-0.5254744258\C,3.9614621223,0.259816601,0.7551038221\C,0.4
831356585,-3.1516249881,1.6009158038\C,1.1670883871,6.323553429,3.1696
270089\C,5.3209162527,-2.23224866,0.9219067761\C,2.9485587103,-4.55872
85969,1.4579352249\C,-1.2499954655,-4.6904081997,-2.1542840957\C,1.909
3273785,-3.9253925521,-3.017827219\C,-2.5973110066,-0.9049857793,-4.92
29803993\C,-5.143941756,-0.5886571752,-2.7433426737\C,-1.9595301866,5.
5208788031,4.1304797101\C,-5.9079884351,-0.3654106087,-1.6111242427\C,
-5.3635983444,0.1310135348,-0.4214840133\C,-1.3494406368,-0.9114939595
,-5.5202911198\C,-0.1979123875,-0.4609690044,-4.8641333594\C,-2.983312
3044,-3.6411434354,-0.7951404141\C,-2.5204153215,-4.6831992589,-1.6052
740033\C,0.5231631025,-4.5332745952,1.7316250574\C,1.7444057354,-5.212
3641401,1.6502484539\C,5.992581715,-1.0496272276,0.6657538315\C,5.3383
483577,0.1844623853,0.5808503149\C,2.4236667715,6.3227740037,2.5909808
28\C,2.8753325149,5.2814862303,1.772339306\C,-3.1732250289,4.883140723
6,4.3153513435\C,-3.4698208024,3.6451562391,3.7340311583\H,2.395560262
6,3.3692689779,0.8794178668\H,-2.750196723,2.0428780039,2.4696425143\H
,0.6128953294,0.3622844341,-3.0395033105\H,-3.570426021,0.813932557,0.
5781474041\H,-2.5159684093,-1.7427037749,0.1162177308\H,3.4393693215,1
.2150196309,0.6966025175\H,-0.4605841916,-2.6113875376,1.667213867\H,0
.8541682832,7.1609152345,3.795198778\H,5.8712767254,-3.173180842,0.970
0280574\H,3.8783721282,-5.1279356987,1.4146808749\H,-0.9225743583,-5.5
342025053,-2.7633863986\H,-3.4699654093,-1.2545102392,-5.4767960156\H,
-5.6098894839,-0.9850448877,-3.6468630391\H,-1.7691342504,6.4825413536
,4.6094112285\F,-7.2210912633,-0.6318352505,-1.6470461691\H,-6.0261940
104,0.2920344963,0.4304652943\F,-1.2313131012,-1.3566588137,-6.7790230
26\H,0.75516277,-0.4872771651,-5.3948085127\H,-3.9935557439,-3.6979422
345,-0.3868437528\F,-3.3395955028,-5.7157849566,-1.8447803852\H,-0.390
2185711,-5.1085097208,1.8911779883\F,1.7397322667,-6.5468558082,1.7749
332534\F,7.3212731226,-1.0781011308,0.4917572173\H,5.9316552126,1.0793
600774,0.3859973367\F,3.2452693751,7.3576428198,2.814173464\H,3.878587
5752,5.3473071521,1.3482654492\F,-4.1052683011,5.4643947495,5.08295367
53\H,-4.4477159548,3.1994828644,3.9232546215\C,3.4041064624,-2.0334398
011,-2.6432948494\C,3.1302109855,-3.2945463093,-3.1828663508\H,2.64276
9373,-0.3853660879,-1.4777689305\H,1.7314758959,-4.8996289385,-3.47543
42902\H,4.3839805853,-1.5857070412,-2.8160472961\F,4.0863097728,-3.902
9923991,-3.8972129841\\Version=ES64L-G09RevD.01\HF=-3270.0495101\S2=0.
767349\S2-1=0.\S2A=0.750212\RMSD=6.764e-09\RMSF=2.682e-06\Dipole=0.105
092,-1.5068355,-0.9208502\Quadrupole=4.0559236,-9.3811647,5.3252411,13
.5475761,-19.0182082,-17.3027345\PG=C01 [X(C56H24F8N6)]\\@

4c

1\1\GINC-R03-NODE52\FOpt\RPBE1PBE\Gen\C56H24Cl8N6\GRYNOVA\29-Mar-2018\
0\\#PBE1PBE/gen SCF=Tight INT(grid=finegrid) OPT IOP(2/17=4) Empirical
Dispersion=GD3BJ Nosymm\\7e.pbe0.freq\\0,1\C,-1.0119548129,1.847041863
4,0.1760975468\C,-0.9569077813,0.6453653636,-0.5602363471\C,0.01469822
37,-0.3289120402,-0.241988213\C,0.8932115893,-0.1141393703,0.847671826
3\C,0.7879561428,1.0688668146,1.6062163759\C,-0.149710367,2.0583584869
,1.2644924748\C,-1.8745957748,2.9006752187,-0.2526028938\N,-2.56535147
13,3.7610682104,-0.6053981975\C,1.5675637383,1.2189775826,2.7928363869
\N,2.1931474486,1.3403208721,3.7602260598\N,-0.222988784,3.2396236287,

2.0000767411\C,0.7986155839,4.1828788956,2.124438606\C,-1.3304066501,3
.6772898062,2.728892209\N,-1.8507646604,0.445823914,-1.6132363596\C,-1
.5110597156,-0.0266564434,-2.8864075911\C,-3.2375255388,0.2993624976,-
1.4458810599\N,0.1055699918,-1.4984565815,-0.9984014927\C,1.2672510687
,-1.9563436199,-1.6217089618\C,-0.8783116119,-2.4847533846,-1.11161411
28\N,1.849494612,-1.0695008455,1.2041498878\C,3.2347261912,-0.88466122
97,1.0389321254\C,1.6022388029,-2.4465383171,1.2685065454\C,-1.0161452
079,4.9168955795,3.3288079817\C,0.3415183458,5.2396533481,2.9427585953
\C,3.8555586767,-2.1506296756,0.9569359828\C,2.8132866978,-3.146350884
8,1.0898390945\C,-0.3331589638,-3.5911038408,-1.8013904354\C,1.0418535
56,-3.2619505554,-2.109017928\C,-2.6730515553,-0.5063265618,-3.5252477
369\C,-3.7735990928,-0.2980751783,-2.6080759934\C,2.0643918892,4.19854
91319,1.5452308798\C,-2.5586242968,3.0546831533,2.9324962591\C,-0.2732
161068,-0.0336175141,-3.5209774048\C,-4.0325853074,0.568970075,-0.3353
654401\C,2.4758400677,-1.2983647719,-1.8278617925\C,-2.1677054851,-2.5
171022528,-0.5896419289\C,3.9590687101,0.2908262458,0.8649005621\C,0.3
995754689,-3.1093731854,1.4857550952\C,1.1788601491,6.3246231887,3.207
7157807\C,5.2215078322,-2.2459250318,0.6959634718\C,2.8089270255,-4.54
00190434,1.0294581861\C,-1.1037302162,-4.7352003154,-2.0061388159\C,2.
0778586374,-3.9594652265,-2.7302028588\C,-2.588609093,-1.058326171,-4.
8042366185\C,-5.129522289,-0.6185494467,-2.6678039154\C,-1.9612095551,
5.5595806124,4.1302942196\C,-5.920658652,-0.3409316802,-1.5582785723\C
,-5.3835821823,0.2448948317,-0.403327316\C,-1.3391376827,-1.1133709712
,-5.4116166686\C,-0.1928730612,-0.5974618732,-4.7876355325\C,-2.932638
2651,-3.6573903146,-0.8065100724\C,-2.4037541202,-4.7479309222,-1.5125
848957\C,0.3987983495,-4.4966904107,1.4151908065\C,1.5887099267,-5.194
7933145,1.1625204565\C,5.939298405,-1.0686197424,0.5169419787\C,5.3215
138858,0.1871804753,0.6031300587\C,2.4498179784,6.3263533055,2.6444805
962\C,2.8911733012,5.2814953906,1.8182754431\C,-3.1942331515,4.9443493
663,4.3140518854\C,-3.4934142888,3.7043869301,3.7291614971\H,2.4047685
67,3.3950437331,0.8901355879\H,-2.788809379,2.0835962255,2.4915523069\
H,0.6172575212,0.3774681091,-3.04634359\H,-3.6281547757,1.0220760347,0
.5694571706\H,-2.5811847764,-1.6890689284,-0.0153790756\H,3.4911170207
,1.2731949134,0.9263022601\H,-0.5258644512,-2.5668878763,1.6782492209\
H,0.8536786002,7.1560517118,3.8343048632\H,5.7168925099,-3.2131165999,
0.6036973614\H,3.7244532539,-5.1080603519,0.86147931\H,-0.7024960196,-
5.6067879549,-2.5245128398\H,-3.4690543829,-1.4440315911,-5.319402014\
H,-5.5643561332,-1.0893981264,-3.550312374\H,-1.7474593109,6.516691758
4,4.607625441\Cl,-7.606702437,-0.7320835221,-1.5940134612\H,-6.0403167
403,0.4491474092,0.4430200048\Cl,-1.1885740033,-1.8199997456,-6.984839
1769\H,0.7645254594,-0.6442095673,-5.3078107914\H,-3.9533982359,-3.712
1041599,-0.426084993\Cl,-3.3937152364,-6.1478502058,-1.7565817535\H,-0
.5317881888,-5.0524224024,1.5362104753\Cl,1.5282342042,-6.9188983474,1
.0129041625\Cl,7.6330669556,-1.1482570465,0.1673243632\H,5.9242542636,
1.0857164287,0.4660868811\Cl,3.5178471861,7.6533518061,2.9569595397\H,
3.8931136647,5.3319179144,1.3904874031\Cl,-4.3930694507,5.7163397468,5
.2969358895\H,-4.4706333651,3.2554531447,3.9105353831\C,3.5035616463,-
1.9992003712,-2.4467933305\C,3.3071470581,-3.322695723,-2.8672046879\H
,2.6348571488,-0.2705238997,-1.5022399313\H,1.9418754967,-4.9787630567
,-3.09329227\H,4.476738734,-1.5299584588,-2.5955915502\Cl,4.633101041,
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\RMSD=7.916e-09\RMSF=3.369e-06\Dipole=0.02181,-0.5642622,-0.3817545\Qu
adrupole=5.917381,-3.2476726,-2.6697085,8.0943238,-11.9230946,-2.33270
96\PG=C01 [X(C56H24Cl8N6)]\\@

4c.cr_opt

1\1\GINC-R05-NODE47\FOpt\UPBE1PBE\Gen\C56H24Cl8N6(1+,2)\GRYNOVA\30-Mar
-2018\0\\#PBE1PBE/gen SCF=Tight INT(grid=finegrid) OPT IOP(2/17=4) Emp
iricalDispersion=GD3BJ Nosymm\\7e.cr_opt.pbe0.freq\\1,2\C,-1.067432131
4,1.8513633817,0.2006925785\C,-0.9847203248,0.6724550075,-0.5696075881
\C,0.0306999904,-0.2623169593,-0.2900596589\C,0.8864694549,-0.06876254
32,0.8165323059\C,0.7929277903,1.1007459954,1.5857109733\C,-0.17508860
97,2.0781204097,1.2679619584\C,-1.978172628,2.874512165,-0.1996367749\
N,-2.7135202268,3.7021393862,-0.5397341369\C,1.6100628283,1.2352301503
,2.747498782\N,2.2873188759,1.328670209,3.6825008824\N,-0.2424208709,3
.253608627,2.0033586505\C,0.8027626474,4.1713587336,2.1523202722\C,-1.
3596975877,3.7207335627,2.7023649467\N,-1.8848510935,0.44425422,-1.604
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26005108,-1.4148660046\N,0.1968552256,-1.4050014324,-1.0826269708\C,1.
4082139409,-1.7465182528,-1.6737695476\C,-0.6514804784,-2.5145438428,-
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.0803549763,0.8875021652\C,1.3717812639,-2.4223319841,1.3385104578\C,-
1.0286981642,4.9541869466,3.3063802319\C,0.3499400597,5.2421723188,2.9
544209738\C,3.5973929263,-2.4179304277,0.7782594303\C,2.463224384,-3.2
751472262,1.071409487\C,0.064841388,-3.60811954,-1.6574565214\C,1.3808
778938,-3.1151441159,-2.0249638222\C,-2.7075389304,-0.4227275402,-3.55
54399432\C,-3.793626402,-0.3287542024,-2.5991179037\C,2.0786565872,4.1
594596496,1.592961944\C,-2.6038172667,3.1218097102,2.8878559151\C,-0.3
389483923,0.1901899233,-3.5854653279\C,-4.0345675871,0.3992586341,-0.2
714526714\C,2.5087348186,-0.9346347476,-1.9535655065\C,-1.946815083,-2
.656554765,-0.6223991419\C,3.9880051581,0.0031957296,0.6438526959\C,0.
1255581609,-2.9170552613,1.7150969396\C,1.1988665421,6.3087708562,3.23
09867019\C,4.8951501585,-2.677661191,0.3561277906\C,2.2859331281,-4.65
59307758,1.0948576917\C,-0.5065809805,-4.8728641816,-1.6706164388\C,2.
5069820866,-3.706218028,-2.5834713726\C,-2.638599106,-0.8592660979,-4.
8779095307\C,-5.1361599387,-0.6971759328,-2.6494345738\C,-1.9700174314
,5.620675946,4.0836207203\C,-5.9144500181,-0.5115274505,-1.508753023\C
,-5.3724566283,0.027615924,-0.3307524982\C,-1.4103265926,-0.7861191934
,-5.5307641709\C,-0.2737683724,-0.2567360643,-4.8994684522\C,-2.521899
9471,-3.9218297575,-0.6633277618\C,-1.8029341152,-5.0168542362,-1.1626
576838\C,-0.0448372704,-4.2956259504,1.7403889094\C,1.0147234924,-5.14
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6552877,-0.2654385965,0.2337353683\C,2.4874489333,6.2819513617,2.69337
23721\C,2.9225422665,5.2249831275,1.8782878361\C,-3.2271568527,5.03380
2374,4.2435563334\C,-3.5405548281,3.7958538383,3.6600250143\H,2.416492
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13\H,0.5385515217,0.6295835877,-3.1115113388\H,-3.6260689328,0.8180310
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072\H,0.8783038726,7.1529704198,3.842711402\H,5.260619327,-3.695488956
2,0.2147947124\H,3.1014651676,-5.3438057126,0.8679857603\H,0.036238998
8,-5.7461621291,-2.0340287029\H,-3.5152152602,-1.244942136,-5.39984573
67\H,-5.5754887157,-1.1308241347,-3.5486976879\H,-1.7448815238,6.57279
84251,4.5656710147\Cl,-7.5778401488,-0.9587023454,-1.5340717283\H,-6.0
191726904,0.1580245047,0.5376631823\Cl,-1.2814133757,-1.3363865714,-7.
1598600744\H,0.660699031,-0.1897086554,-5.4578948476\H,-3.5345160318,-
4.0764443597,-0.2887144366\Cl,-2.5157218915,-6.5791476749,-1.124967398
5\H,-1.0091817013,-4.7286047617,2.0074002371\Cl,0.7285594636,-6.846443
2367,1.3382666304\Cl,7.312320592,-1.8804317778,-0.521284707\H,5.981979
3091,0.5501799115,0.0281090783\Cl,3.565378877,7.5809749787,3.023207773
5\H,3.9328256417,5.2547588213,1.4689173702\Cl,-4.417579771,5.836956195
8,5.1896211296\H,-4.5304713201,3.3692453446,3.8247765018\C,3.626008636
1,-1.5265000894,-2.5250764046\C,3.6336343892,-2.9031212384,-2.79920344
32\H,2.5026076059,0.132536481,-1.7296660842\H,2.5322654467,-4.76512653
38,-2.8439081559\H,4.516257913,-0.9365464345,-2.7438137836\Cl,5.071520
6501,-3.6185465131,-3.4109608519\\Version=ES64L-G09RevD.01\HF=-6151.62
44985\S2=0.7581\S2-1=0.\S2A=0.750066\RMSD=5.639e-09\RMSF=3.229e-06\Dip
ole=0.6000222,-0.5841405,-0.0332361\Quadrupole=7.6779123,13.0273837,-2
0.7052959,2.7303431,-14.2922603,22.5539184\PG=C01 [X(C56H24Cl8N6)]\\@

4c.ar_opt

1\1\GINC-R05-NODE56\FOpt\UPBE1PBE\Gen\C56H24Cl8N6(1-,2)\GRYNOVA\30-Mar
-2018\0\\#PBE1PBE/gen SCF=Tight INT(grid=finegrid) OPT IOP(2/17=4) Emp
iricalDispersion=GD3BJ Nosymm\\7e.ar_opt.pbe0.freq\\-1,2\C,-1.02662888
76,1.8750019852,0.1326588217\C,-0.9432344946,0.6392009692,-0.631663899
6\C,0.0264169492,-0.3071129857,-0.3021452524\C,0.8779992938,-0.1350233
551,0.8074245197\C,0.7529191683,1.0644204982,1.6127326969\C,-0.1777991
498,2.0405956161,1.2395647403\C,-1.8811653597,2.9181445064,-0.28459158
53\N,-2.6065547576,3.7636014161,-0.6284909288\C,1.5347837392,1.2184516
317,2.7809320645\N,2.2025608796,1.3397590113,3.7276576414\N,-0.2605256
011,3.2309970008,1.9907739703\C,0.7428654844,4.1805565106,2.1083795214
\C,-1.361001009,3.6521435196,2.7211840076\N,-1.8529909383,0.4132482733
,-1.6816037149\C,-1.5467294731,0.168698516,-3.0115789487\C,-3.21847312
54,0.2392080723,-1.5095076296\N,0.156447267,-1.479469207,-1.0880071795
\C,1.3506317248,-1.8735340693,-1.6800504536\C,-0.6829983015,-2.5863325
768,-1.0223725934\N,1.8100911949,-1.1334562634,1.1652632803\C,3.167553

5201,-1.0848286065,0.8653867878\C,1.4720298713,-2.4641100754,1.3891306
574\C,-1.0633255993,4.896297484,3.3278555935\C,0.2840575082,5.23664336
04,2.9322782337\C,3.6910535018,-2.4000509675,0.8264933658\C,2.59828863
81,-3.2878730578,1.1550375614\C,0.0003494854,-3.7169319097,-1.53425937
13\C,1.3043930614,-3.2589503181,-1.9560301242\C,-2.7281200524,-0.19016
20873,-3.7064393738\C,-3.8027106321,-0.1417190112,-2.7419109019\C,2.01
29355567,4.2023193164,1.5336434812\C,-2.59009301,3.0228564038,2.912645
4974\C,-0.3160106432,0.2403087332,-3.6619668369\C,-3.9787162784,0.3506
726562,-0.3449273903\C,2.4703986321,-1.1053709479,-1.9947340493\C,-1.9
699030918,-2.6895425603,-0.4990258771\C,3.9568602249,0.0249163673,0.57
0884859\C,0.2421698593,-3.0019427408,1.7646972691\C,1.1156670103,6.328
4001523,3.1935657978\C,5.0127095023,-2.6115163442,0.4298850438\C,2.467
682916,-4.67805324,1.2136082082\C,-0.597354,-4.9768380013,-1.482047639
8\C,2.4256361843,-3.8999030432,-2.488937973\C,-2.6707683839,-0.5009864
36,-5.0675186388\C,-5.1716682601,-0.4096985955,-2.8102207572\C,-2.0160
410024,5.5240968955,4.1340771154\C,-5.9208334433,-0.2938386187,-1.6461
839997\C,-5.3390210913,0.0812464562,-0.4249650109\C,-1.4359743781,-0.4
449398555,-5.6998433611\C,-0.2684592157,-0.0751592153,-5.0125185697\C,
-2.5603819061,-3.9461717104,-0.4633103963\C,-1.8707511581,-5.072973525
1,-0.9365029414\C,0.1220008327,-4.3826892844,1.8279638389\C,1.22004228
58,-5.2026730933,1.5239300848\C,5.7809016323,-1.5019019384,0.102477571
1\C,5.2732901956,-0.1954613684,0.1867953019\C,2.3814897021,6.337176248
8,2.6234093087\C,2.8305567426,5.2920007928,1.8007063414\C,-3.239340180
9,4.8925261221,4.3135285549\C,-3.5293508399,3.6563167334,3.7148031067\
H,2.3553612979,3.3851139356,0.8979016254\H,-2.809814354,2.0648765314,2
.4407710179\H,0.5860239002,0.5326350078,-3.1263091781\H,-3.5192874229,
0.6471692907,0.5986691332\H,-2.4959316461,-1.8193861621,-0.108326661\H
,3.5473010197,1.0342822684,0.6275969559\H,-0.6089844563,-2.3534661884,
1.9730578135\H,0.7884172131,7.1566372696,3.8235871827\H,5.4295576121,-
3.6154416394,0.3403765616\H,3.3068414619,-5.3397192226,0.9946623499\H,
-0.0755141258,-5.8710625328,-1.8244614684\H,-3.5640909552,-0.783209932
1,-5.6264560013\H,-5.6480322754,-0.7113578029,-3.7441156439\H,-1.81392
88604,6.482244783,4.6147758929\Cl,-7.6288049607,-0.6231910929,-1.69476
53649\H,-5.9710184967,0.1641633794,0.4601945123\Cl,-1.3247257941,-0.83
85894979,-7.3912688775\H,0.6792009265,-0.0420173013,-5.5516262263\H,-3
.5653813749,-4.0685925922,-0.057236515\Cl,-2.6298718262,-6.6323102135,
-0.8149270115\H,-0.8336335125,-4.8444598883,2.0778520383\Cl,0.98987294
76,-6.9270852061,1.5073195886\Cl,7.4160592717,-1.7293881675,-0.4457241
852\H,5.9255690554,0.6433610852,-0.0603210768\Cl,3.4460546942,7.679171
5503,2.9297543828\H,3.8339730331,5.3453605105,1.376410516\Cl,-4.451196
4192,5.6467409157,5.3087565879\H,-4.5059678253,3.2013026349,3.88464521
81\C,3.5779663509,-1.7472683476,-2.5305758905\C,3.5545124135,-3.133395
4681,-2.746634039\H,2.4939861706,-0.0355814643,-1.7865783396\H,2.43215
12248,-4.974280583,-2.6769508784\H,4.4880660708,-1.1889161237,-2.75120
45011\Cl,4.9993313418,-3.9085199755,-3.3256089645\\Version=ES64L-G09Re
vD.01\HF=-6151.979874\S2=0.767575\S2-1=0.\S2A=0.750219\RMSD=7.128e-09\
RMSF=4.256e-06\Dipole=0.2153552,-1.5497361,-0.8827777\Quadrupole=4.335
4309,-11.535436,7.2000051,14.9557599,-17.0726744,-18.0516664\PG=C01 [X
(C56H24Cl8N6)]\\@

4d

1\1\GINC-R08-NODE07\FOpt\RPBE1PBE\Gen\C56H24Br8N6\GRYNOVA\30-Mar-2018\
0\\#PBE1PBE/gen SCF=Tight INT(grid=finegrid) OPT IOP(2/17=4) Empirical
Dispersion=GD3BJ pseudo=read Nosymm\\7f.pbe0.freq\\0,1\C,-1.0460453376
,1.862909102,0.1737836128\C,-0.9739461744,0.6740272243,-0.5826059837\C
,0.0102655539,-0.2872123607,-0.2831515758\C,0.852214038,-0.0997829243,
0.839194809\C,0.7496391724,1.0753630195,1.6045717565\C,-0.1825083455,2
.0717523613,1.2620250403\C,-1.9335153293,2.9030185698,-0.2375505035\N,
-2.6473834924,3.7491415347,-0.5782268894\C,1.5407570818,1.2143459705,2
.7851909895\N,2.184490513,1.3266355764,3.7415458903\N,-0.2444989301,3.
2541439224,1.9970757794\C,0.7934473812,4.1798925909,2.1211308406\C,-1.
346525816,3.7125942968,2.7213412763\N,-1.8753933243,0.4687089489,-1.62
86971638\C,-1.5463936279,0.0743051744,-2.9290880033\C,-3.2500503208,0.
2700546275,-1.4395399508\N,0.159279857,-1.4249745346,-1.0845600235\C,1
.3730603961,-1.7961647609,-1.6667797286\C,-0.7047677474,-2.5240110239,
-1.1234973785\N,1.7612924777,-1.0959967053,1.2232484249\C,3.1406758556
,-1.0301164835,0.9655313371\C,1.4065226801,-2.4469923146,1.3317730665\
C,-1.0119581303,4.9487955519,3.3175829373\C,0.3518604751,5.2472269871,

2.9339914349\C,3.6464977034,-2.3442387863,0.84804004\C,2.5389979792,-3
.2484614462,1.0799874531\C,-0.012492154,-3.6229717182,-1.6828435372\C,
1.3143161618,-3.158306397,-2.0278125497\C,-2.7101974184,-0.3960771239,
-3.5733151784\C,-3.7957803215,-0.2752364441,-2.6229823956\C,2.06149606
65,4.1690618027,1.5466149328\C,-2.5860884645,3.1120299538,2.9223859178
\C,-0.3213763166,0.1384109235,-3.5853556036\C,-4.0243496089,0.45915214
72,-0.2979401403\C,2.5004448795,-1.0182449552,-1.915730777\C,-2.005331
6167,-2.6456803335,-0.6445700891\C,3.9449074909,0.0853529598,0.7568475
881\C,0.1712107671,-2.9998627081,1.6534789519\C,1.2069178384,6.3187301
778,3.1971966125\C,4.9728401922,-2.549389228,0.4695363862\C,2.41054809
96,-4.6378788021,1.0461253646\C,-0.6210266122,-4.8768504083,-1.7346865
89\C,2.443693129,-3.7819824372,-2.561001724\C,-2.6400503017,-0.8567267
915,-4.8892364058\C,-5.145649004,-0.6236893063,-2.671682218\C,-1.94735
93581,5.6108181718,4.1144889793\C,-5.9147399285,-0.4245425966,-1.53083
09877\C,-5.3693565424,0.1087399003,-0.3552617648\C,-1.4039941917,-0.83
04714024,-5.5233034952\C,-0.2553664179,-0.3327245737,-4.8902890142\C,-
2.6088116986,-3.8962184574,-0.7121247859\C,-1.9138680897,-4.9944036656
,-1.2388307034\C,0.0488541702,-4.3834291525,1.6235716982\C,1.152611544
6,-5.178980673,1.2863560684\C,5.7615188195,-1.4308271261,0.2287726635\
C,5.2678527863,-0.1276778679,0.3840617507\C,2.4781618072,6.2927615286,
2.6366668456\C,2.9069561886,5.2383139476,1.817630167\C,-3.1897781771,5
.0152658368,4.2950587439\C,-3.5121984932,3.7802507105,3.7142572936\H,2
.3919740087,3.3551299479,0.8994431554\H,-2.8341563154,2.1456597604,2.4
813595707\H,0.5688466705,0.5390814186,-3.101909268\H,-3.6068861388,0.8
694258878,0.6216099774\H,-2.542647993,-1.8057518603,-0.2055744232\H,3.
5618855063,1.100425959,0.8673522184\H,-0.6872975022,-2.3731954249,1.89
70395171\H,0.8896493709,7.1560868975,3.8201973157\H,5.3730766534,-3.55
40774835,0.3277257679\H,3.2597498887,-5.2807283793,0.8109678352\H,-0.0
926422474,-5.7478001997,-2.1241191676\H,-3.5245951376,-1.229203414,-5.
4074960837\H,-5.585801897,-1.0542682061,-3.5722314324\H,-1.7131057854,
6.5657424422,4.586952867\Br,-7.7523074449,-0.8975115096,-1.5553548943\
H,-6.0073033284,0.2512828546,0.5178960801\Br,-1.2616855629,-1.47245618
25,-7.3034923816\H,0.6932485153,-0.314538218,-5.428409858\H,-3.6272572
27,-4.0286561023,-0.3442617169\Br,-2.759794299,-6.6925695014,-1.249958
5513\H,-0.9130166783,-4.8537919483,1.829961352\Br,0.8987150833,-7.0516
40154,1.1151258637\Br,7.5512222874,-1.6670554736,-0.3545499315\H,5.928
7245554,0.7217777739,0.2065177272\Br,3.6717704323,7.7289965343,2.97749
32904\H,3.9106538352,5.2631589447,1.3914662331\Br,-4.4898803324,5.8888
946203,5.3674035228\H,-4.4967081841,3.3447388141,3.8896038329\C,3.6180
888185,-1.6408239344,-2.4567290384\C,3.5887537581,-3.0140052441,-2.738
8389435\H,2.5291186177,0.0433321556,-1.6678671558\H,2.439143548,-4.843
4373224,-2.8122868926\H,4.5316841504,-1.0720986232,-2.6329263306\Br,5.
1818005591,-3.8465748389,-3.3477695507\\Version=ES64L-G09RevD.01\HF=-2
576.7787164\RMSD=3.411e-09\RMSF=3.761e-06\Dipole=-0.0525069,-0.1498629
,-0.2085434\Quadrupole=4.420551,-4.6488058,0.2282548,8.2778991,-11.174
5657,-5.8325233\PG=C01 [X(C56H24Br8N6)]\\@

4d.cr_opt

1\1\GINC-R03-NODE39\FOpt\UPBE1PBE\Gen\C56H24Br8N6(1+,2)\GRYNOVA\30-Mar
-2018\0\\#PBE1PBE/gen SCF=Tight INT(grid=finegrid) OPT IOP(2/17=4) Emp
iricalDispersion=GD3BJ pseudo=read Nosymm\\7f.cr_opt.pbe0.freq\\1,2\C,
-1.0630476349,1.8728919291,0.1991275053\C,-0.980181865,0.6954860456,-0
.5724661008\C,0.0261338735,-0.2462273119,-0.2844434916\C,0.8760384982,
-0.0587711083,0.827013873\C,0.7828718474,1.1100809639,1.5972464576\C,-
0.1778263499,2.0921959004,1.2736767497\C,-1.9704470202,2.8990483672,-0
.2013414531\N,-2.7043020873,3.7285791092,-0.5398505234\C,1.5964633144,
1.2426997853,2.7617834728\N,2.2710482103,1.3354308507,3.6987189167\N,-
0.244770197,3.267477255,2.0111876803\C,0.8006643073,4.1841821981,2.160
5469993\C,-1.3611366174,3.7325691604,2.7120744783\N,-1.8736002559,0.47
20220017,-1.6164576409\C,-1.5252737102,0.0823644421,-2.918066211\C,-3.
24252988,0.2288871288,-1.4308844361\N,0.190942487,-1.3905221919,-1.076
3447707\C,1.3994438739,-1.7326448713,-1.6720727985\C,-0.6630945141,-2.
4943002883,-1.1149204388\N,1.7644285801,-1.0854801974,1.1899602752\C,3
.1314374685,-1.0766158646,0.8996119529\C,1.3537701326,-2.4159657654,1.
344081507\C,-1.0293587636,4.9649924836,3.3179205633\C,0.348772541,5.25
34199572,2.9653170947\C,3.5801208229,-2.4152164382,0.7864144947\C,2.44
31739261,-3.2703015667,1.0735922588\C,0.0452197622,-3.5868402774,-1.67
06958536\C,1.3640373038,-3.0983924384,-2.0342915522\C,-2.6652022332,-0

.4477739162,-3.555681555\C,-3.7588187988,-0.3599202475,-2.6077495359\C
,2.0763707989,4.1702458934,1.6011585376\C,-2.6049022209,3.1325397903,2
.89555076\C,-0.3085511417,0.2130995748,-3.5793056166\C,-4.0291336713,0
.4069551758,-0.2947743535\C,2.5034242067,-0.9234285662,-1.9450024105\C
,-1.9583329097,-2.6313034162,-0.6209619749\C,3.9764625432,0.0065543472
,0.661702389\C,0.1054029227,-2.907958077,1.7162055244\C,1.1998260703,6
.3183594716,3.2439484364\C,4.8783751422,-2.6766424593,0.366285304\C,2.
2603327735,-4.6506905296,1.0846656977\C,-0.5367579299,-4.8468300094,-1
.6985614164\C,2.4886965757,-3.691294588,-2.5943285131\C,-2.5746592754,
-0.9149959006,-4.866728514\C,-5.0910671246,-0.7657361606,-2.6557992397
\C,-1.9710476546,5.6297010788,4.0969543565\C,-5.8752408653,-0.58101110
46,-1.5201288236\C,-5.3566965804,-0.0018755711,-0.3515926998\C,-1.3411
25891,-0.8326089009,-5.5066872261\C,-0.2210399104,-0.2645756493,-4.881
6488008\C,-2.5447683895,-3.8910592454,-0.6776105216\C,-1.834301928,-4.
9835225474,-1.192599742\C,-0.0709905169,-4.2868189005,1.7302474797\C,0
.986481144,-5.1380065503,1.3819367591\C,5.7085834341,-1.5889055054,0.0
858364754\C,5.2763929949,-0.2634866108,0.2528357098\C,2.4868511999,6.2
884334054,2.7049486701\C,2.9224797518,5.234068106,1.8884761597\C,-3.22
62334758,5.0401356448,4.2550034313\C,-3.5420778921,3.8046532659,3.6697
711356\H,2.4128370509,3.3605468145,0.9522348334\H,-2.8488304036,2.1642
781551,2.4569359392\H,0.5546500348,0.682169418,-3.107376514\H,-3.63679
27472,0.8563403146,0.6175551269\H,-2.5040002594,-1.7976700114,-0.18058
09991\H,3.6393280575,1.0365115371,0.7847092393\H,-0.7146628478,-2.2403
837414,1.9836811678\H,0.8758864015,7.1591706071,3.8590083426\H,5.23766
17558,-3.697121226,0.2261119914\H,3.0766905248,-5.3357432235,0.8513310
501\H,0.0023544617,-5.7168521332,-2.0760724308\H,-3.4410252186,-1.3318
84752,-5.3821885057\H,-5.5097902631,-1.2285234763,-3.55070091\H,-1.740
96908,6.5812767659,4.5783581697\Br,-7.6820364124,-1.1331161677,-1.5413
975936\H,-6.0061124488,0.1312454161,0.514705534\Br,-1.1703026079,-1.48
33965216,-7.2744269961\H,0.7201284213,-0.1899801283,-5.4282301617\H,-3
.5586045443,-4.036063675,-0.3017933934\Br,-2.6293116091,-6.6897746674,
-1.1728804381\H,-1.0398163915,-4.7126215651,1.9936328895\Br,0.66520500
8,-6.9975978942,1.2933813149\Br,7.4473766572,-1.9108910406,-0.56268894
54\H,5.9687055389,0.5555029759,0.0529002153\Br,3.6707316499,7.71086952
89,3.0704851769\H,3.9320193411,5.2575178657,1.4763574973\Br,-4.5300120
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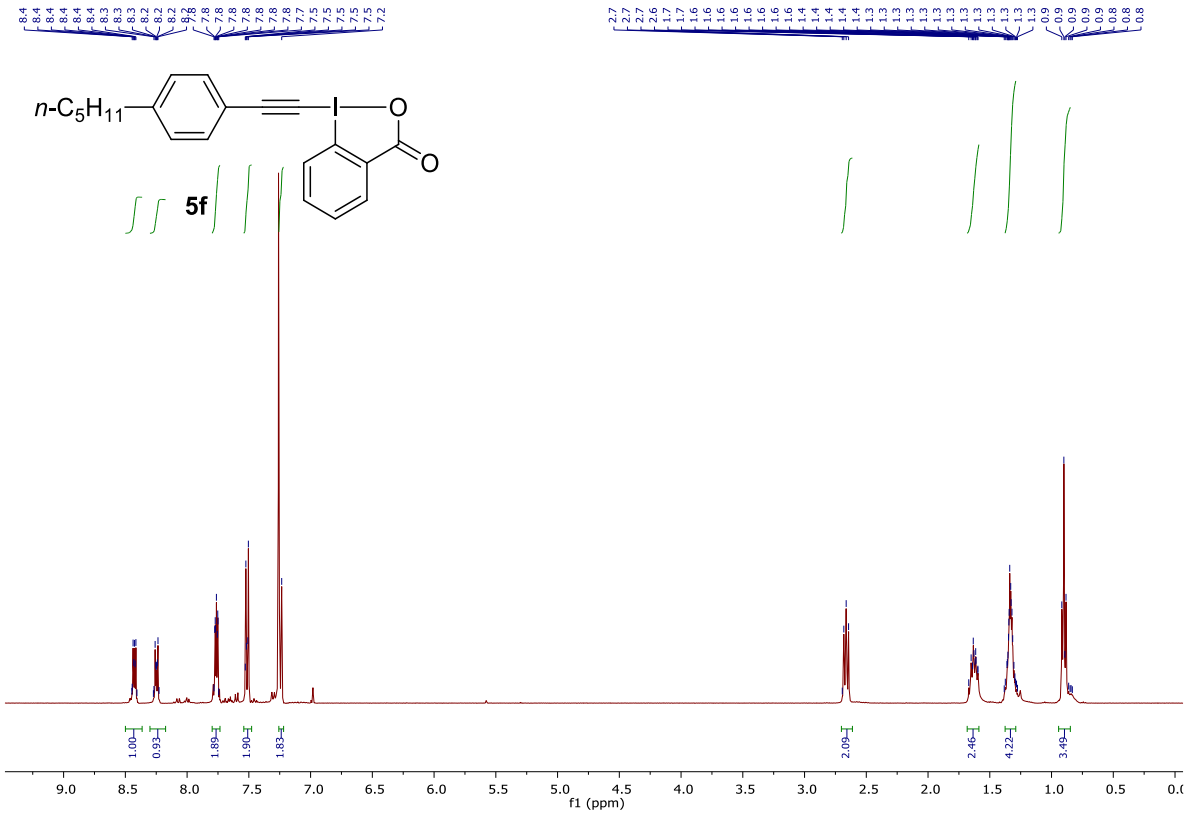
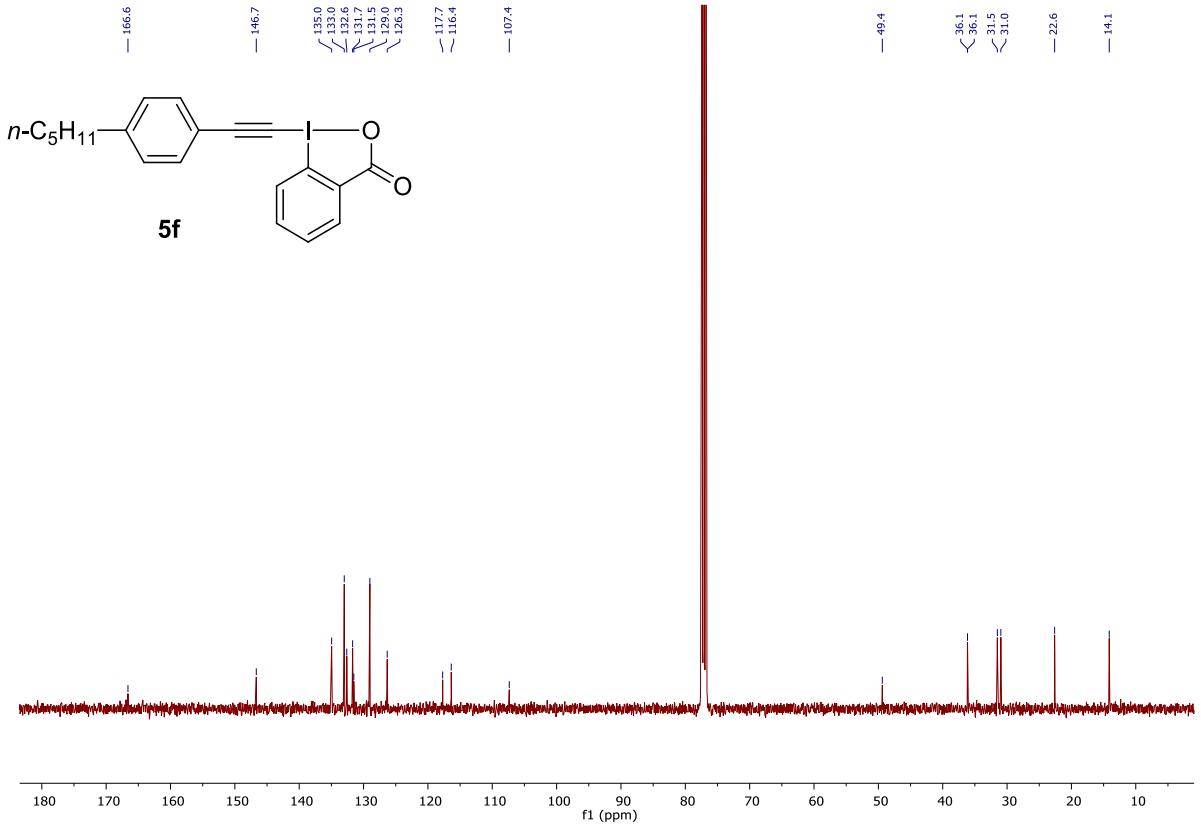
9. Spectra for new compounds

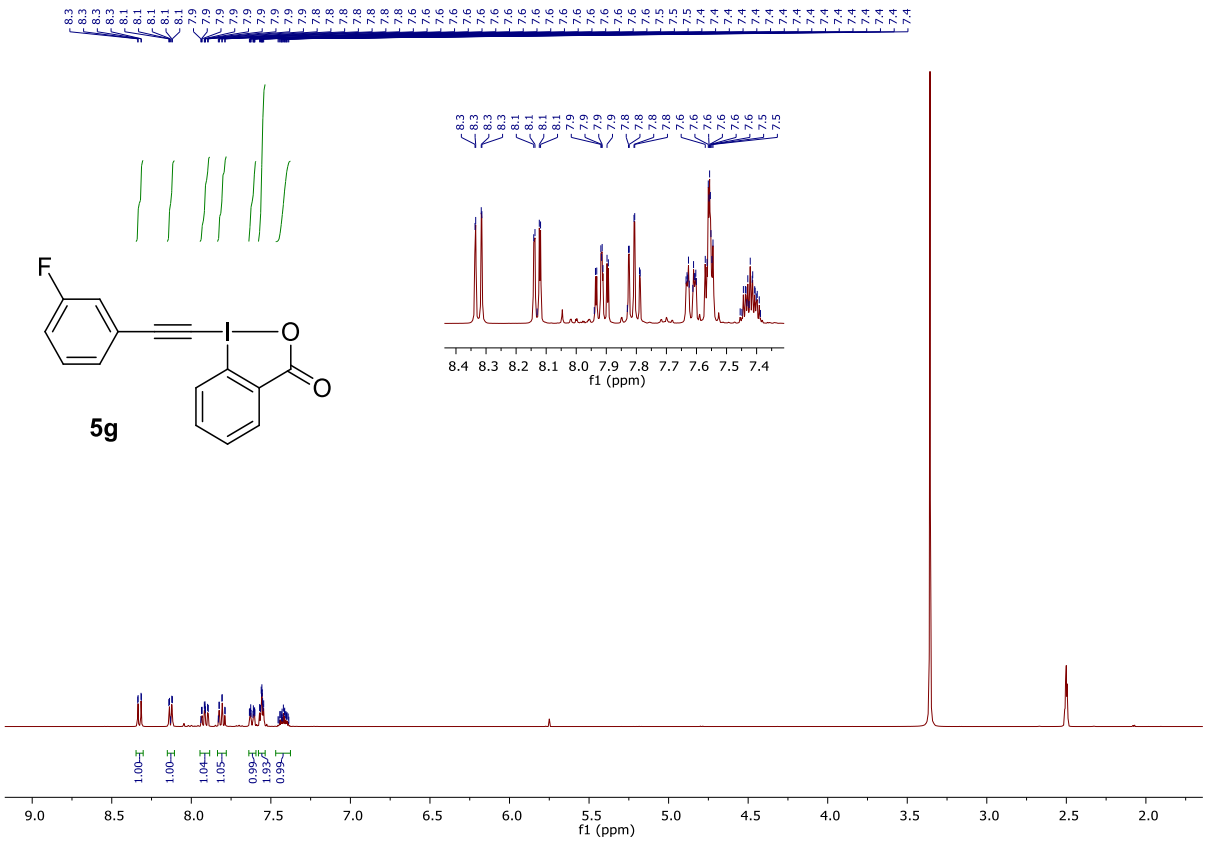
^{1}H-NMR (400 MHz, Chloroform-*d*)



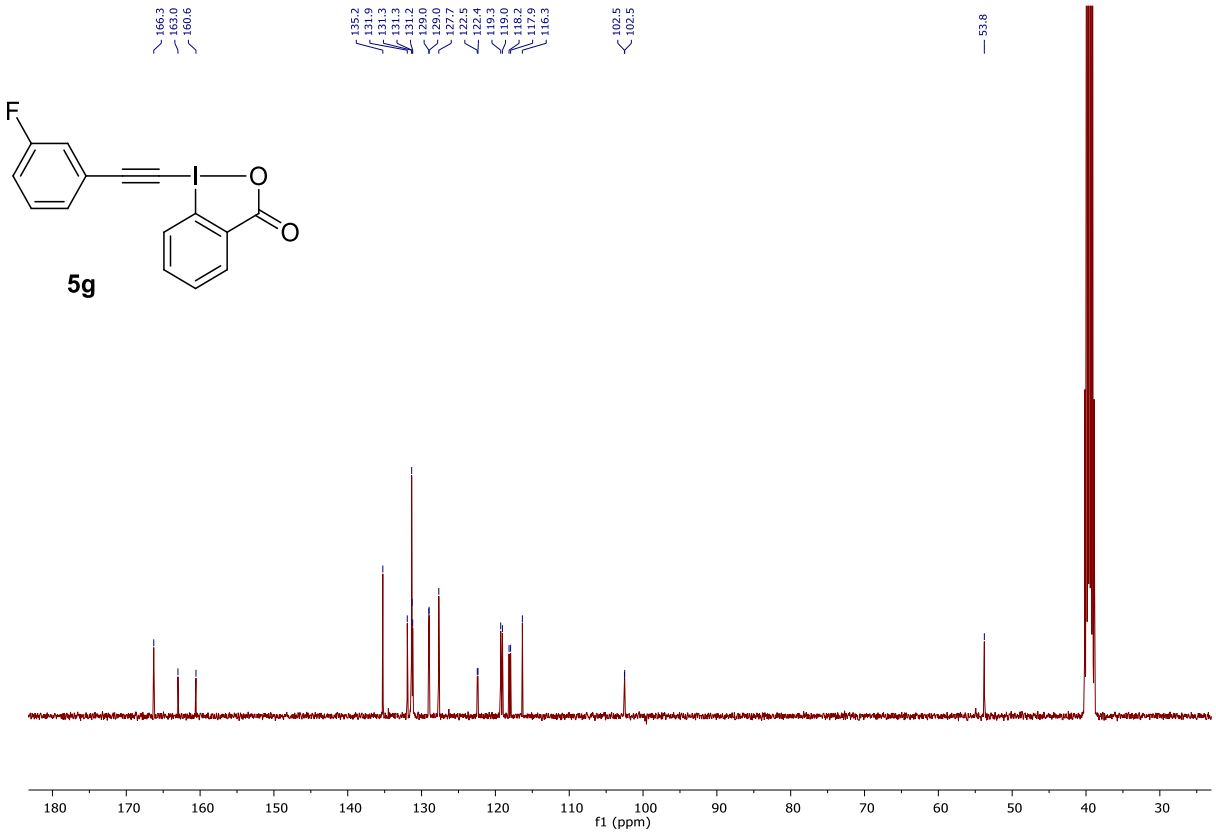
^{13}C-NMR (101 MHz, Chloroform-*d*)



^{1}H-NMR (400 MHz, DMSO-d_6)

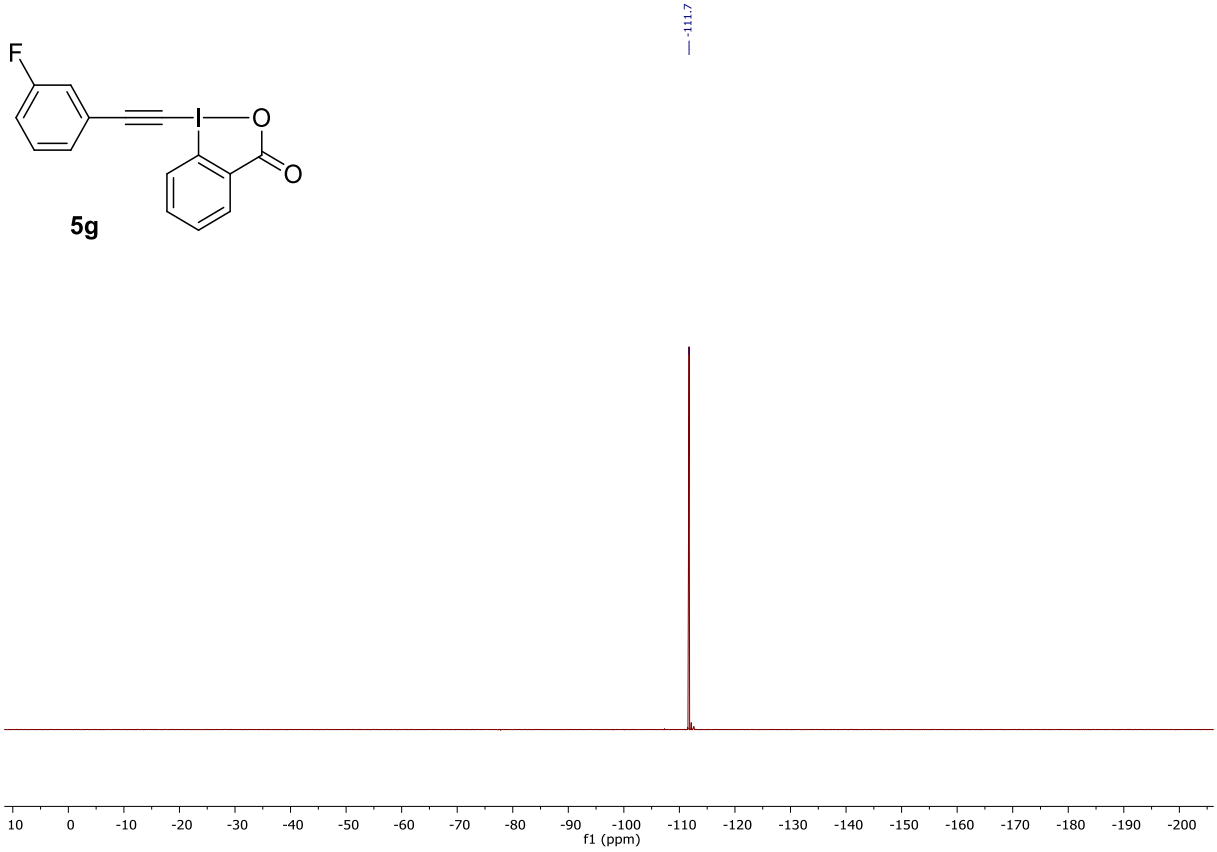


^{13}C-NMR (101 MHz, DMSO-d_6)

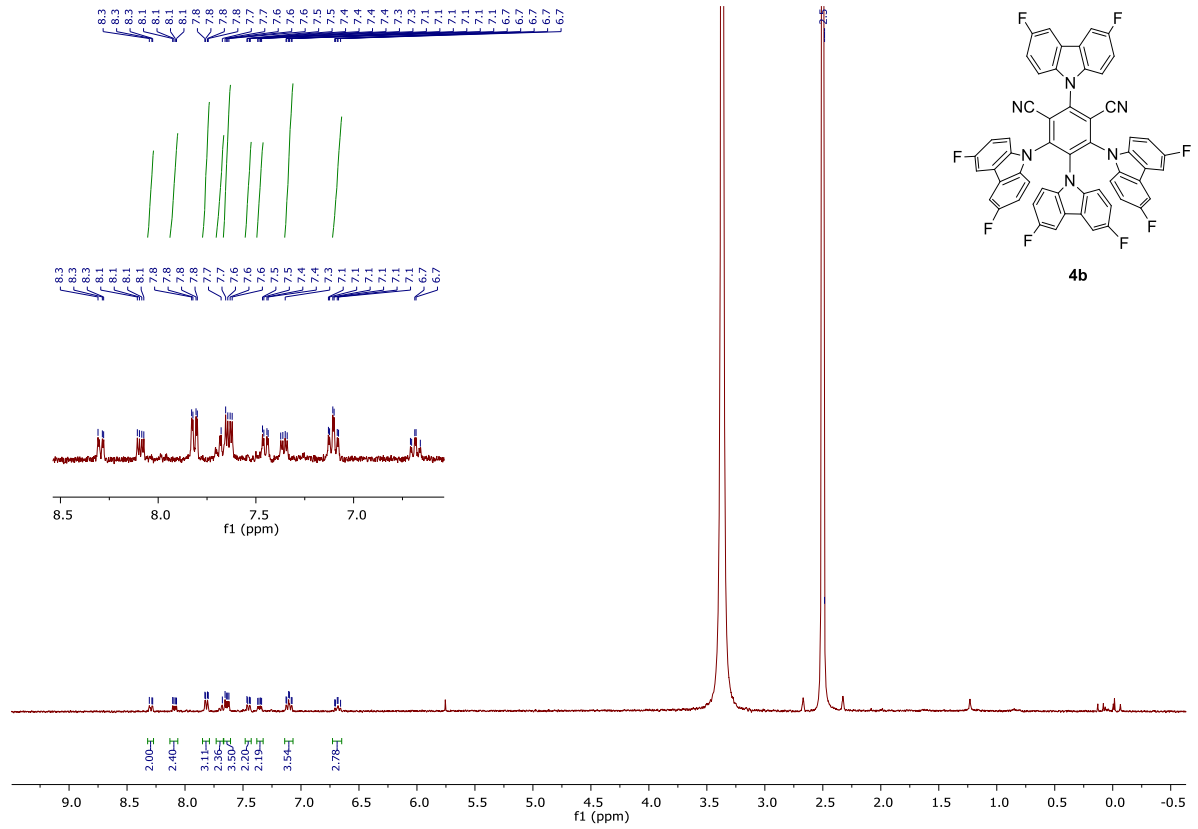


^{19}F NMR (376 MHz, DMSO-*d*$_6$)

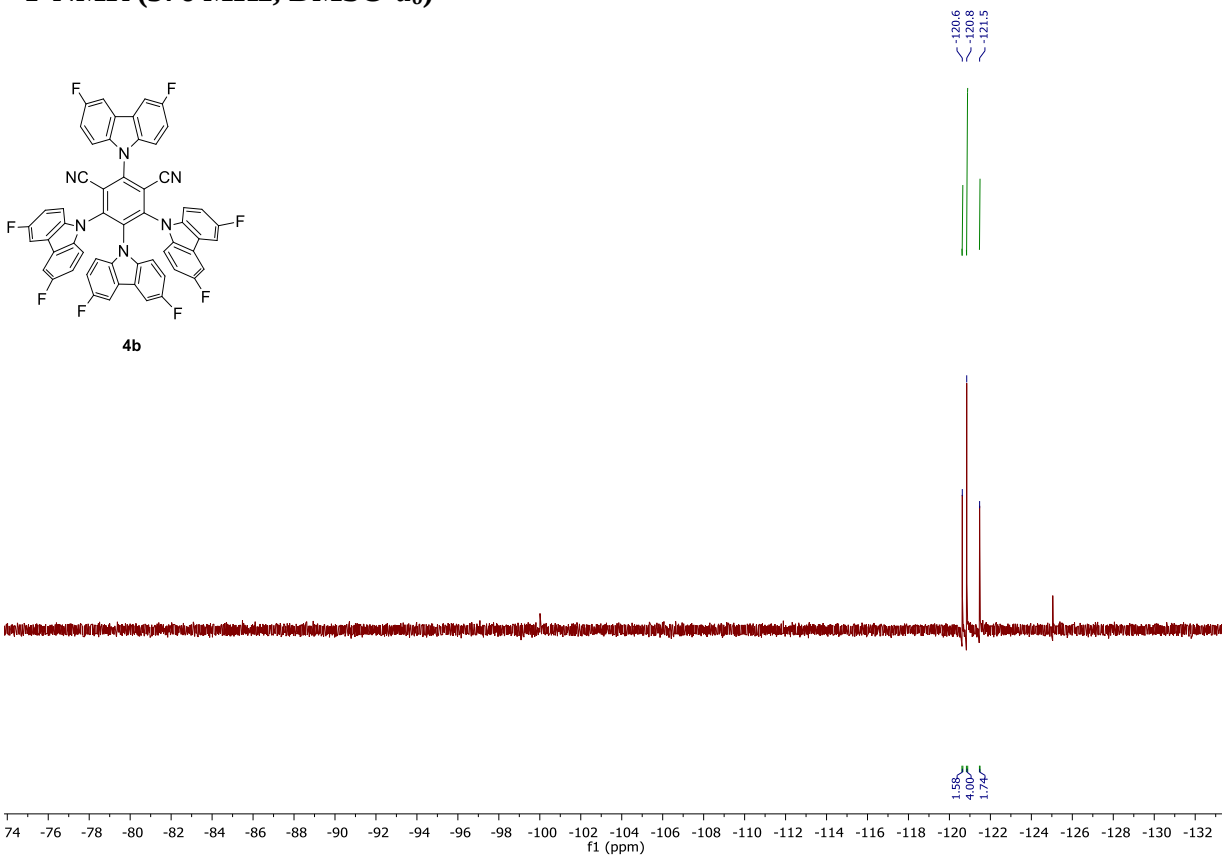
5g



^{1}H-NMR (400 MHz, DMSO-d_6)



^{19}F NMR (376 MHz, DMSO-d_6)



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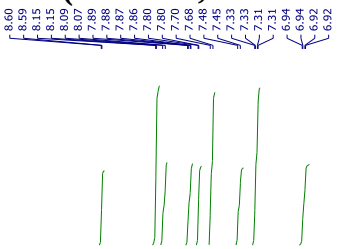
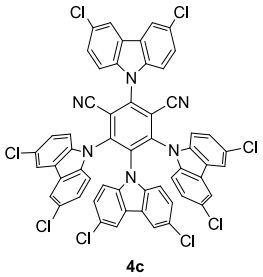
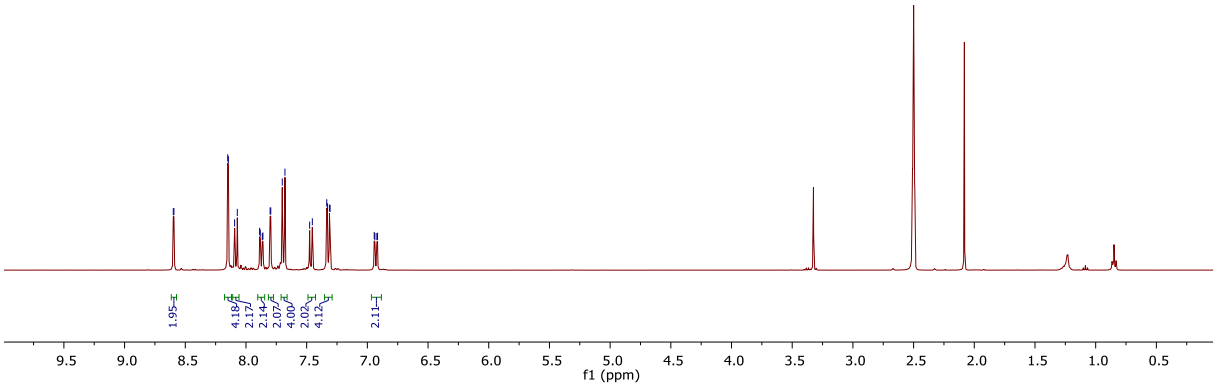
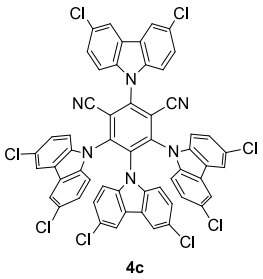




4c



^{13}C-NMR (101 MHz, DMSO-d^{6})



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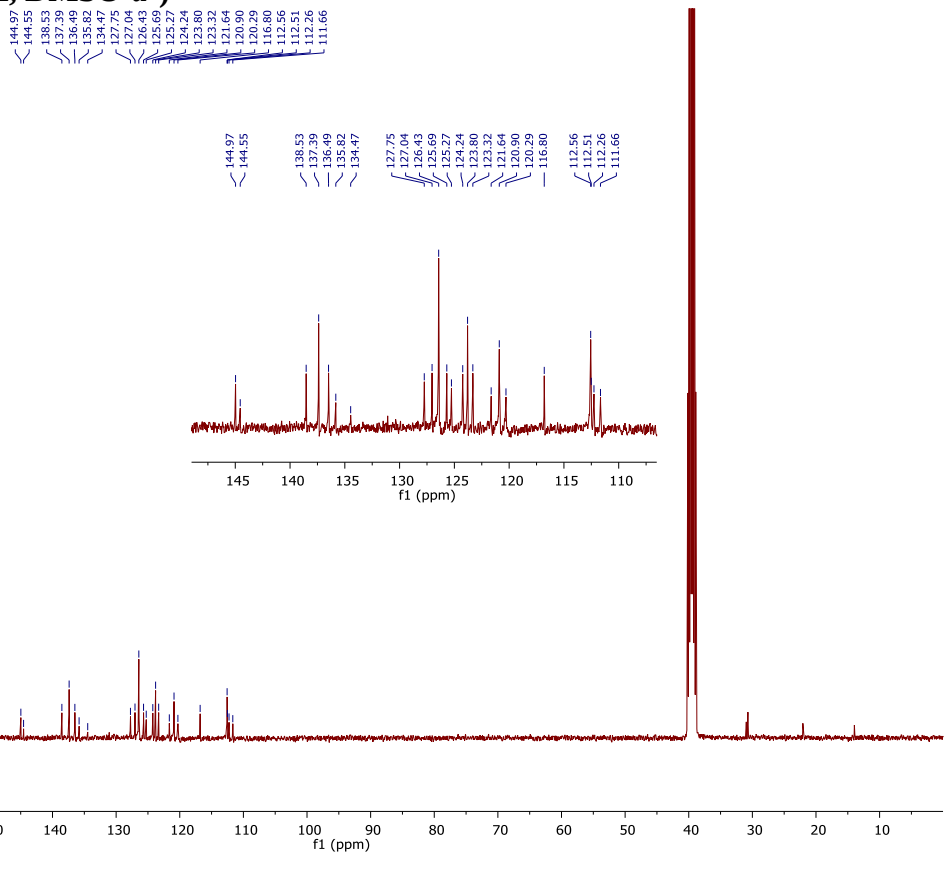
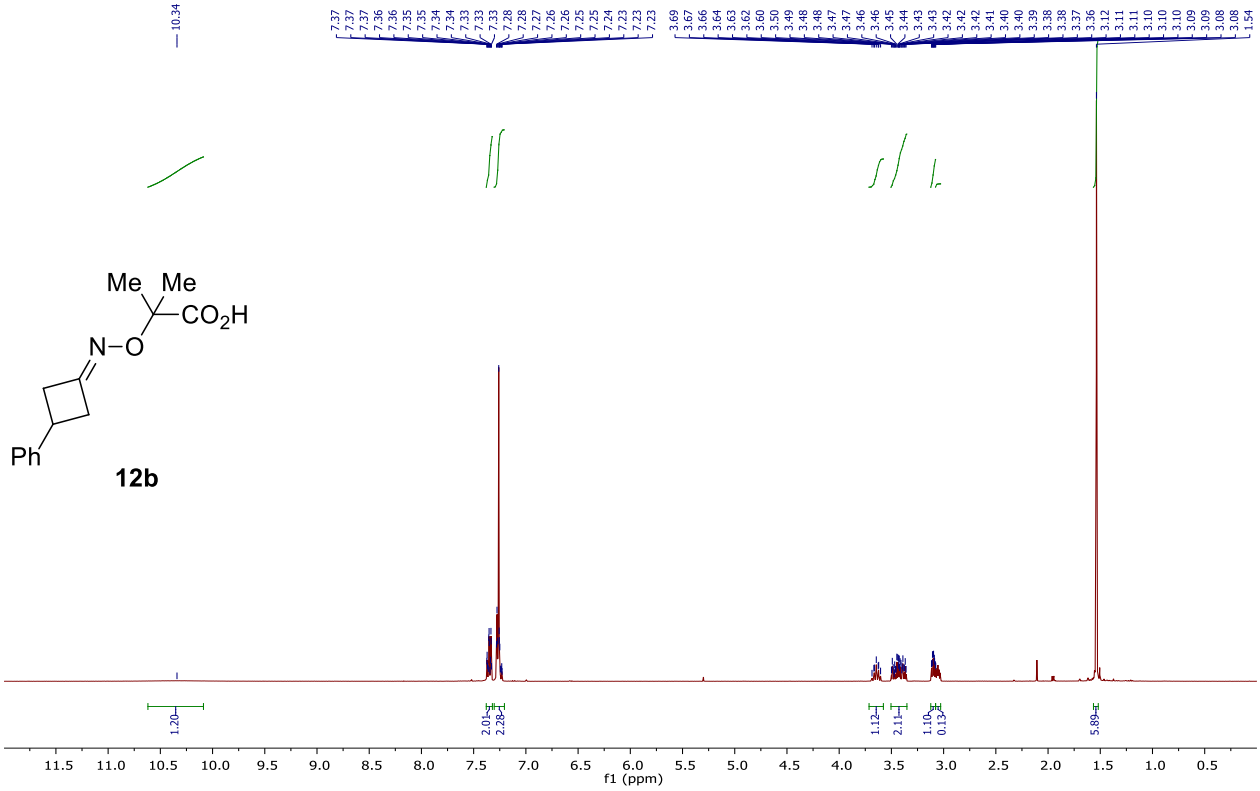
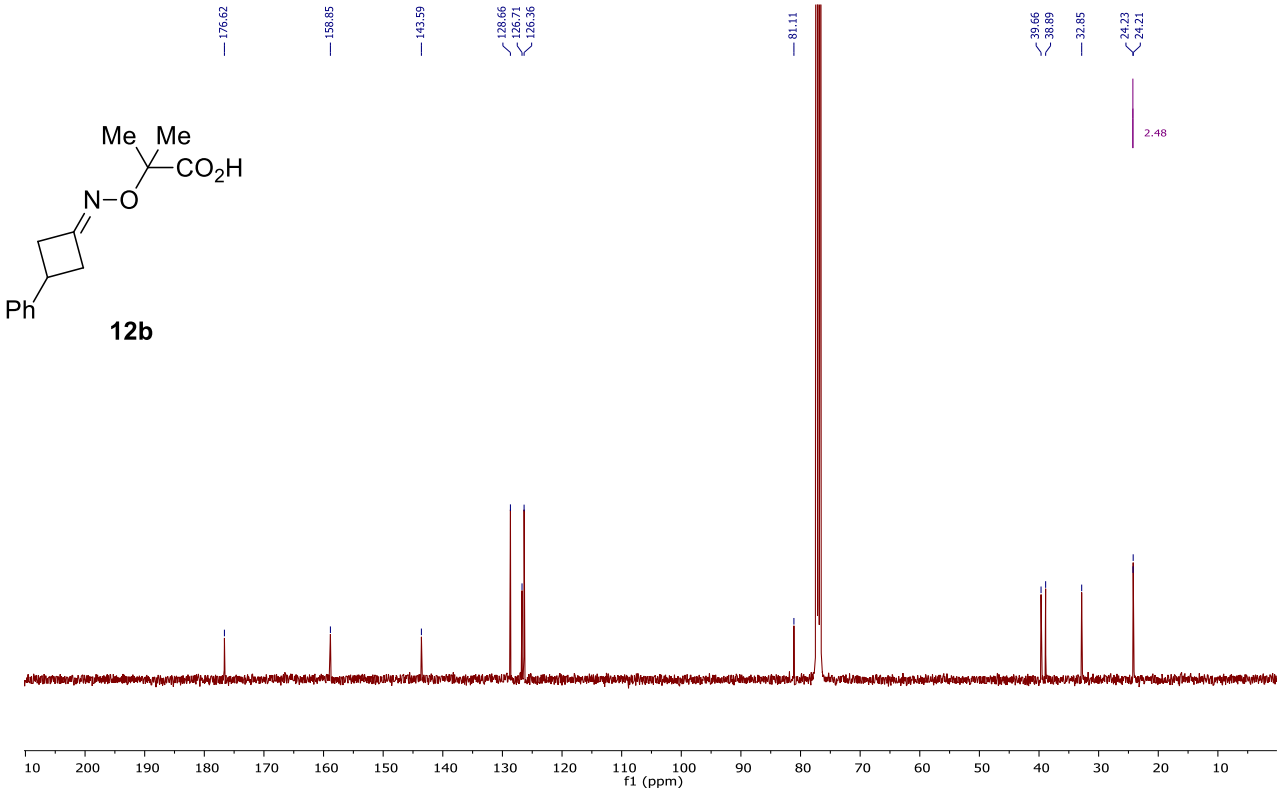


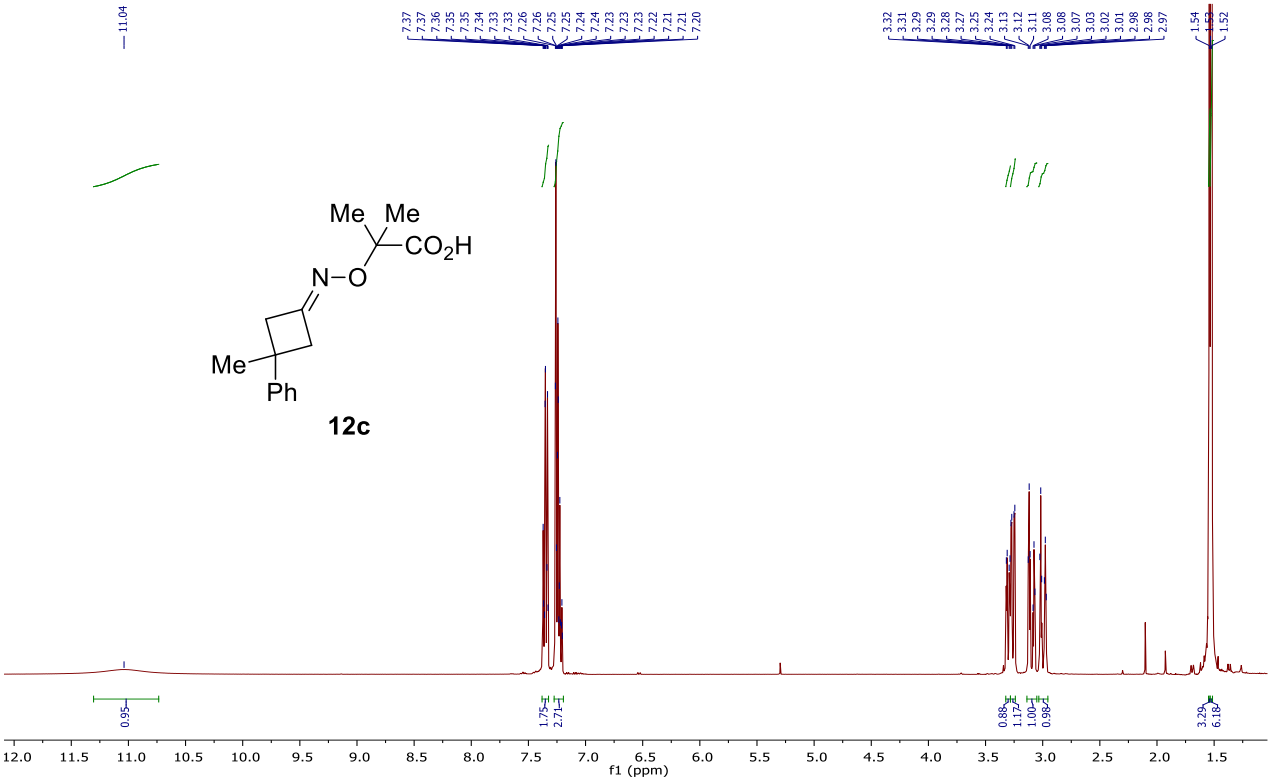
^{1}H-NMR (400 MHz, Chloroform-*d*)



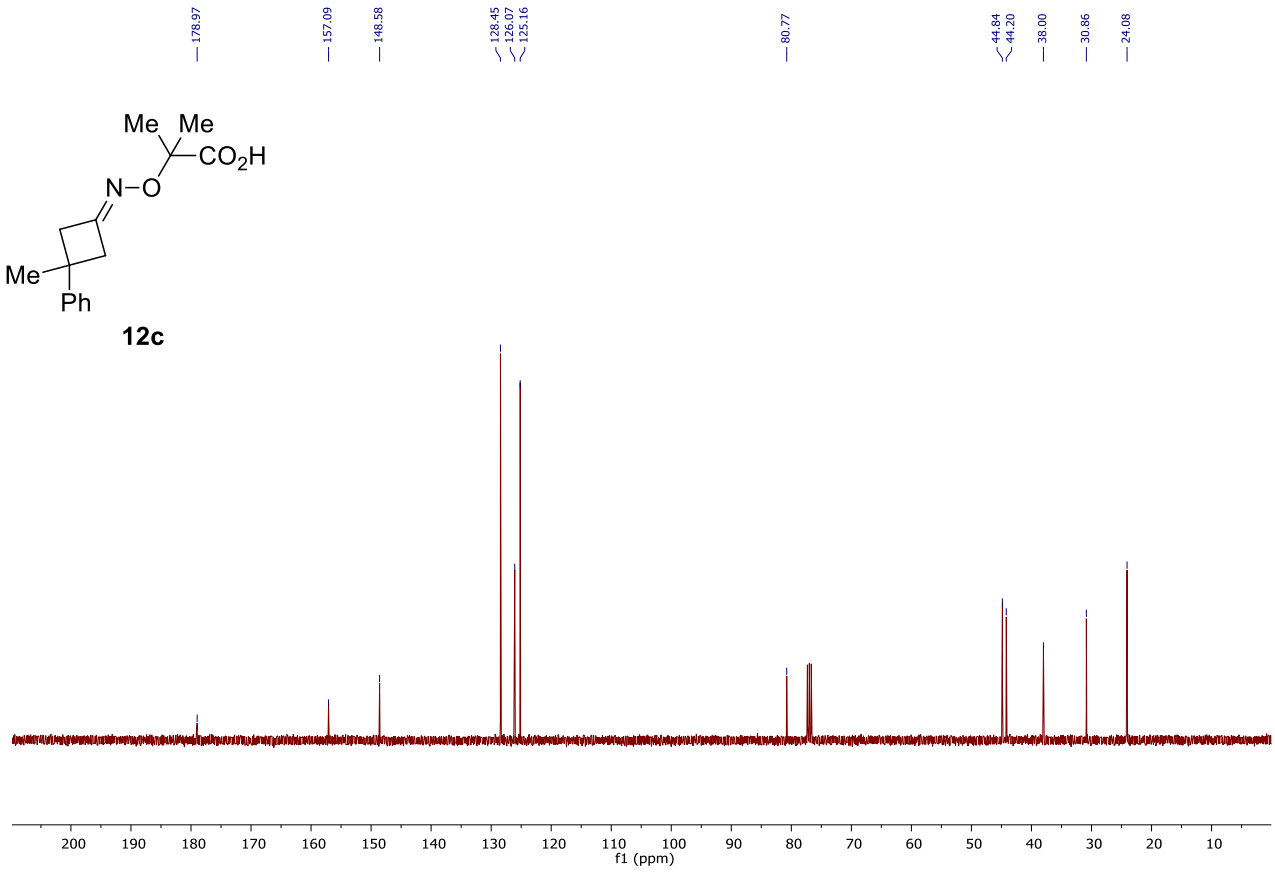
^{13}C-NMR (101 MHz, Chloroform-*d*)



^{1}H-NMR (400 MHz, Chloroform-*d*)



^{13}C-NMR (101 MHz, Chloroform-*d*)



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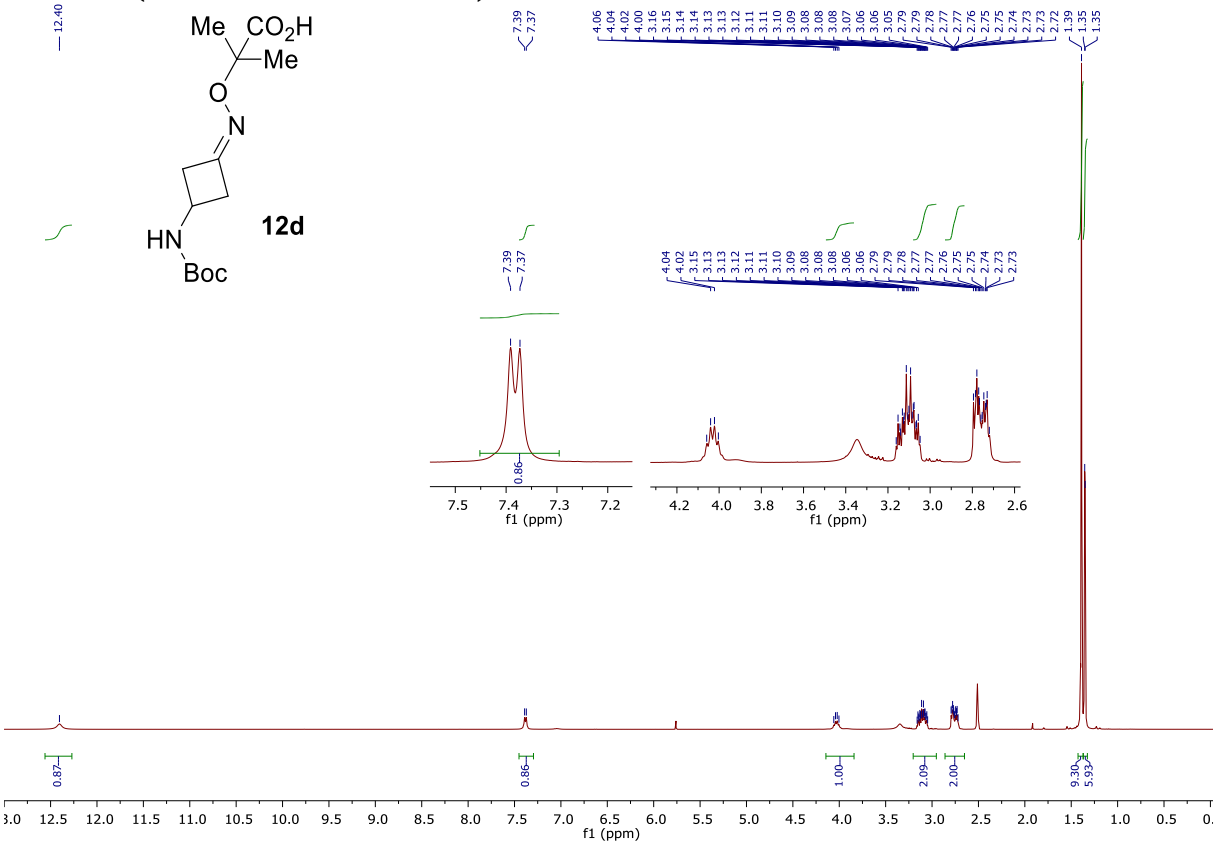
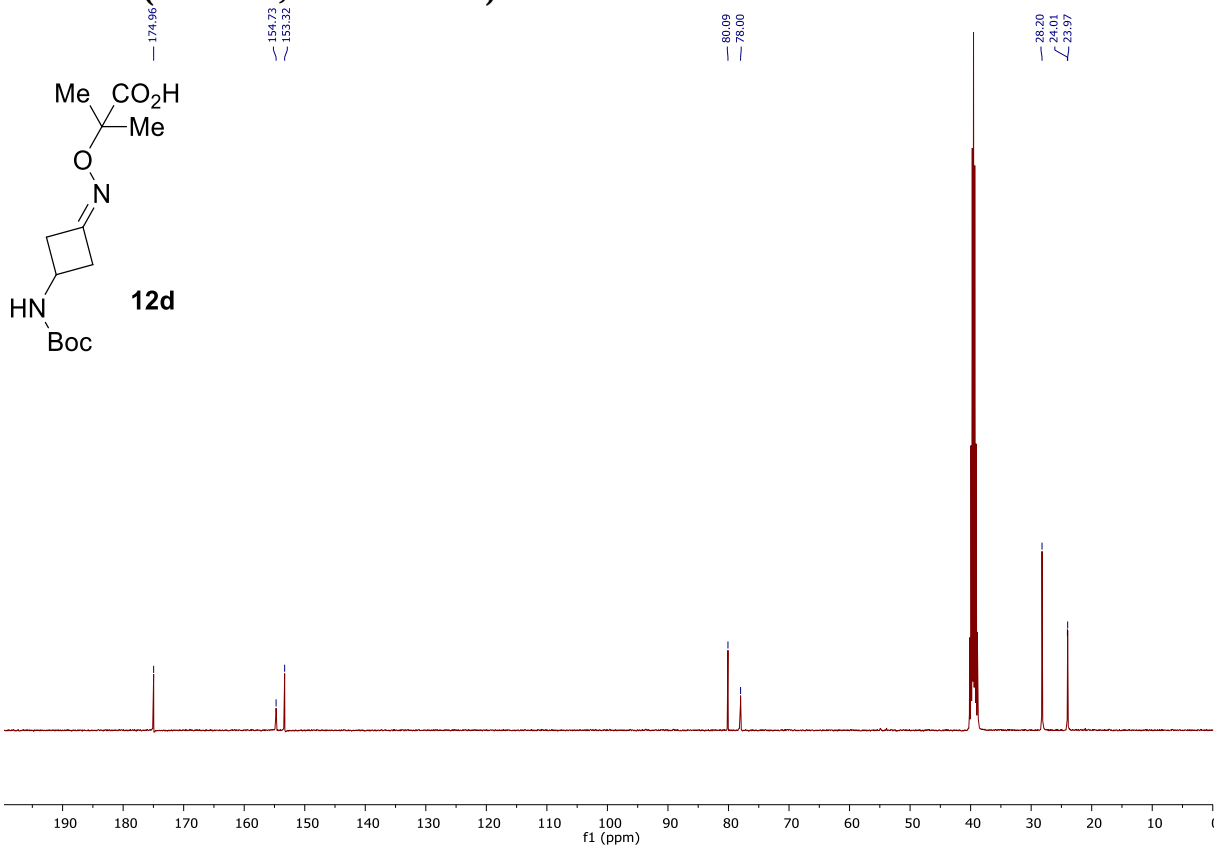


^{13}C-NMR (101 MHz, Chloroform-*d*)



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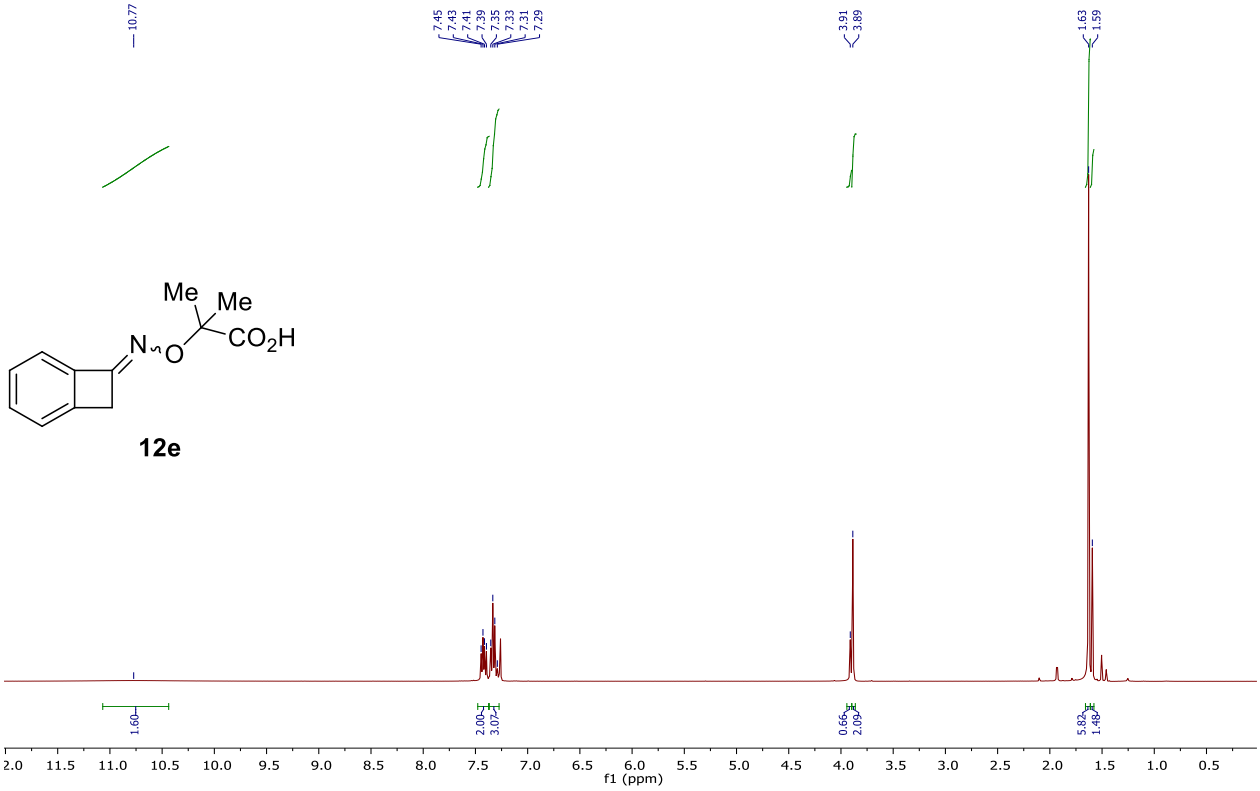

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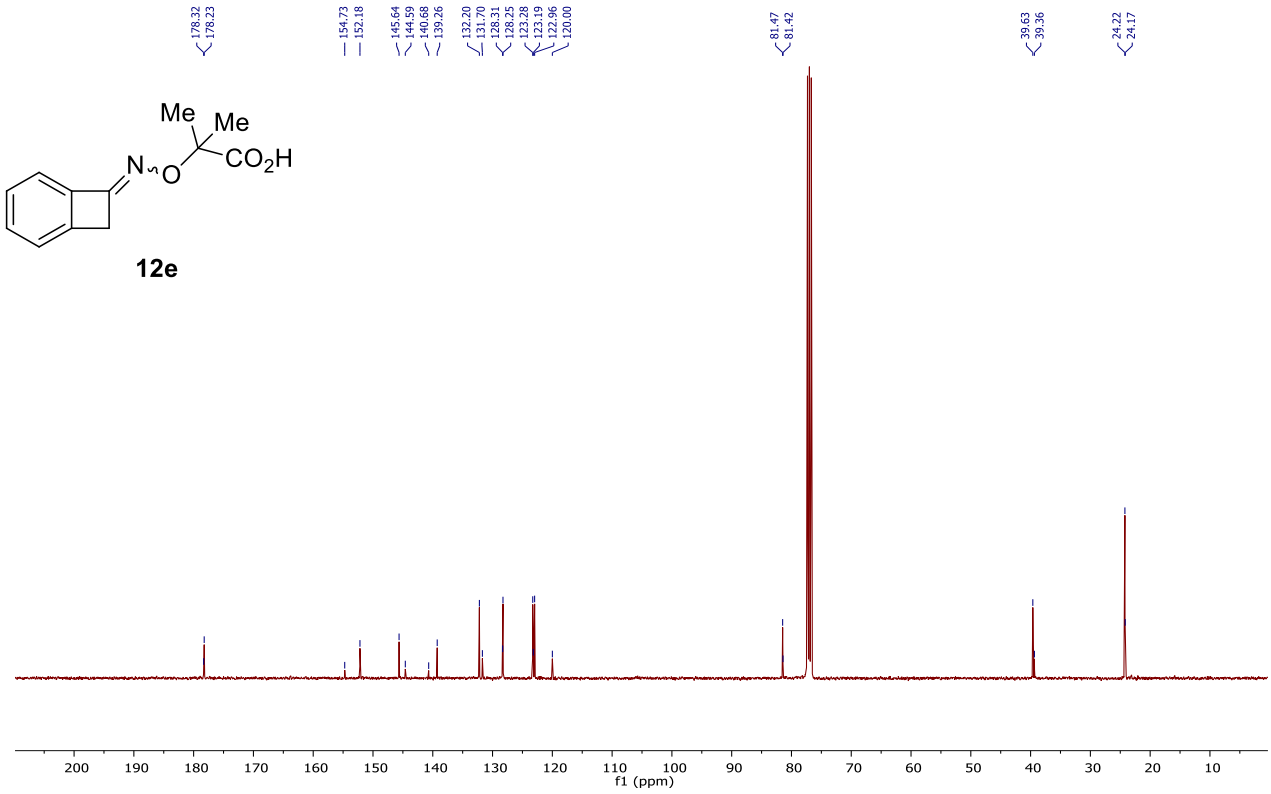
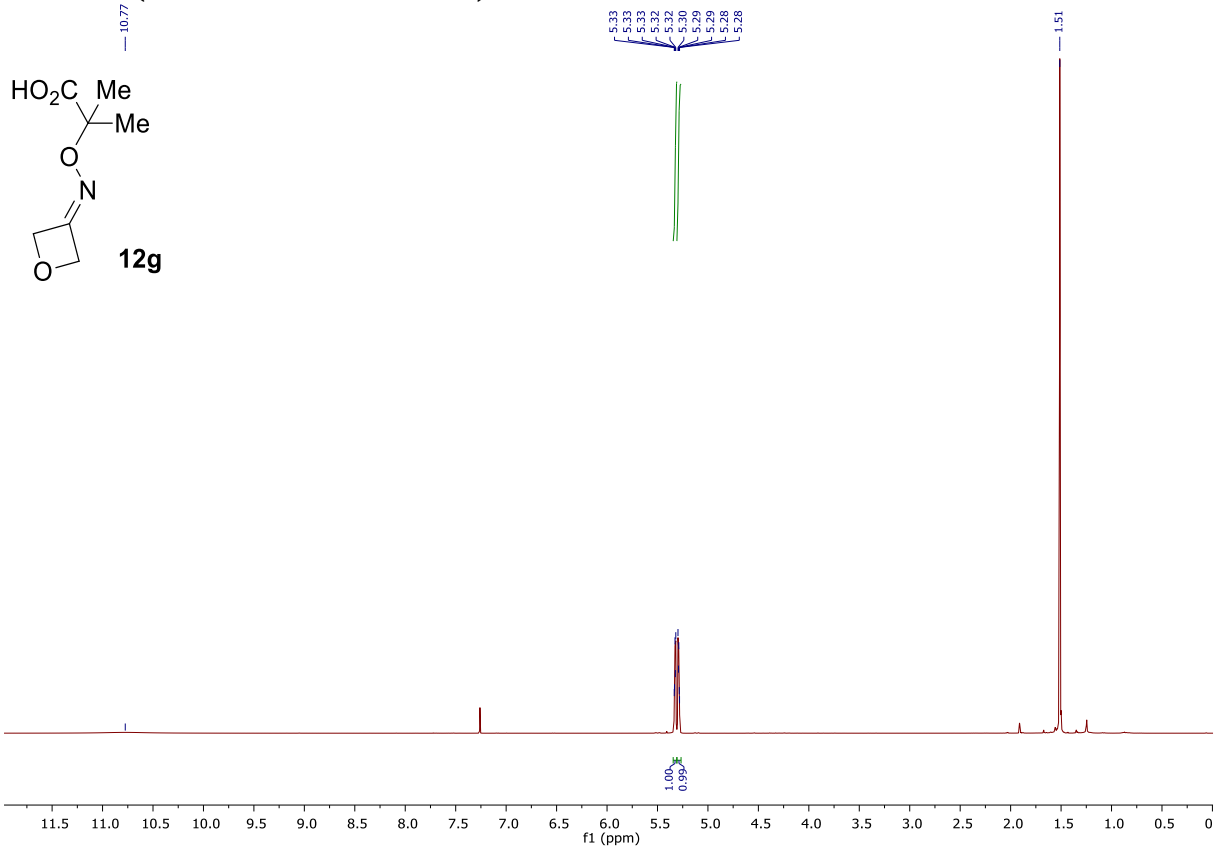


^{1}H-NMR (400 MHz, Chloroform-*d*)



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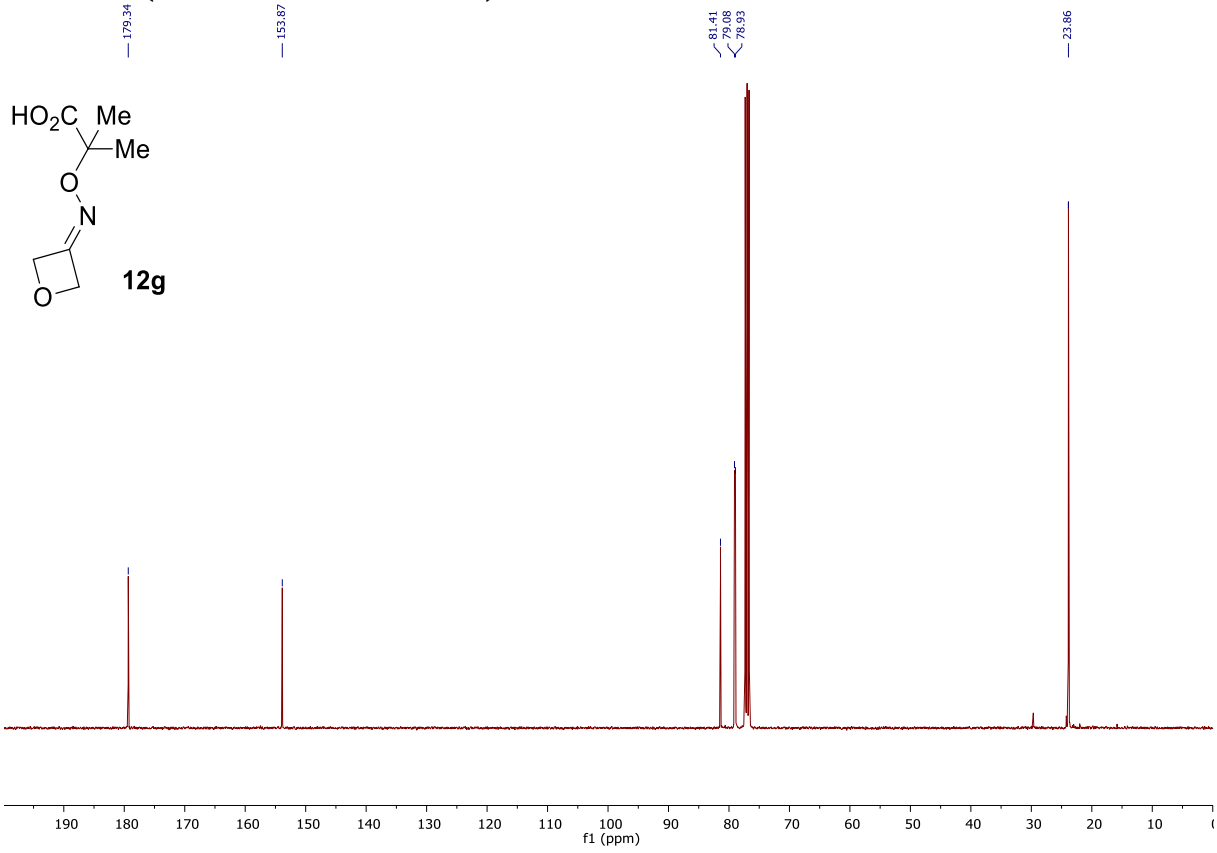

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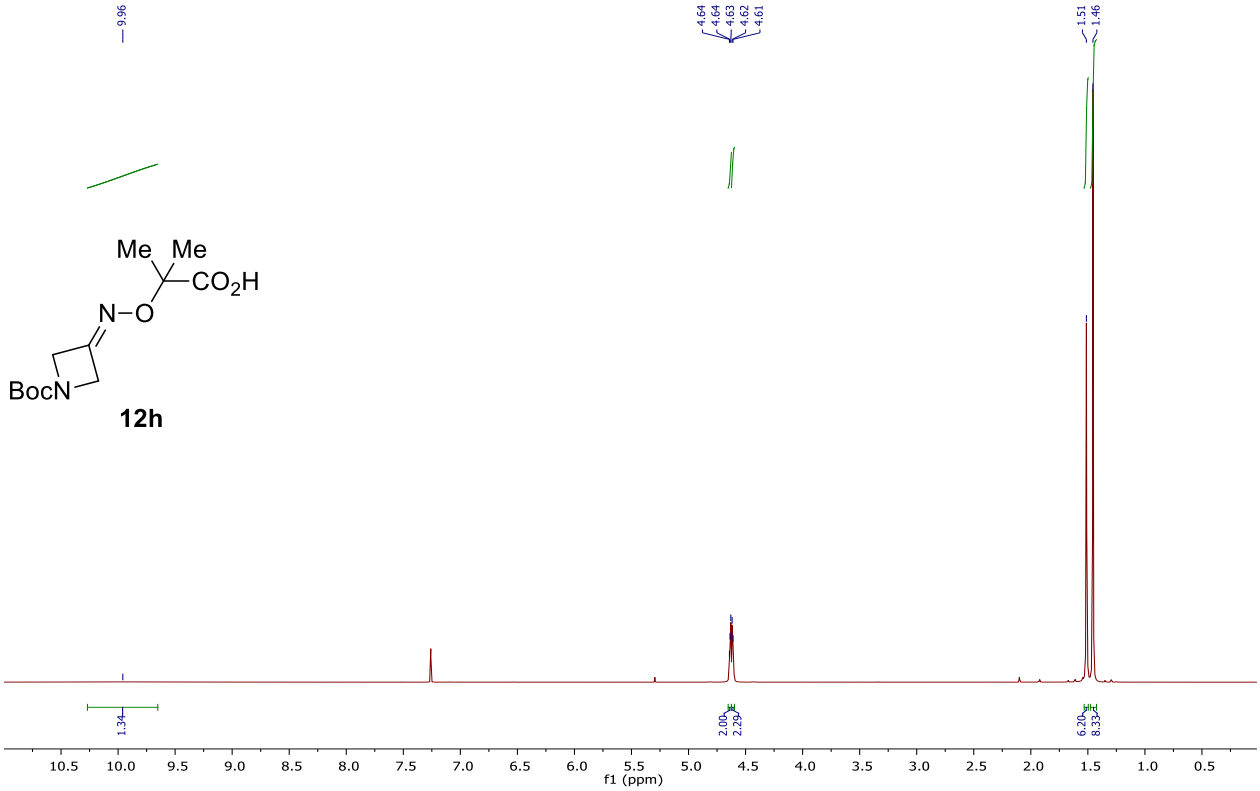

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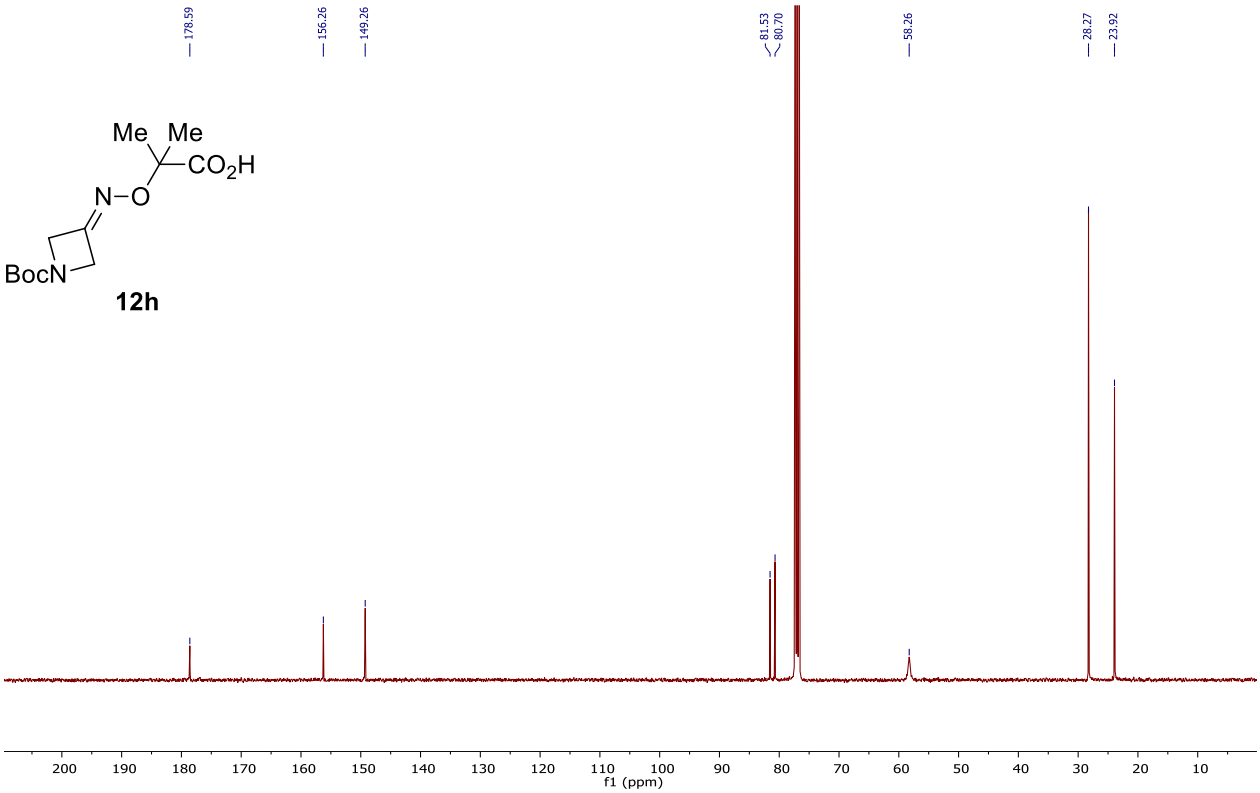

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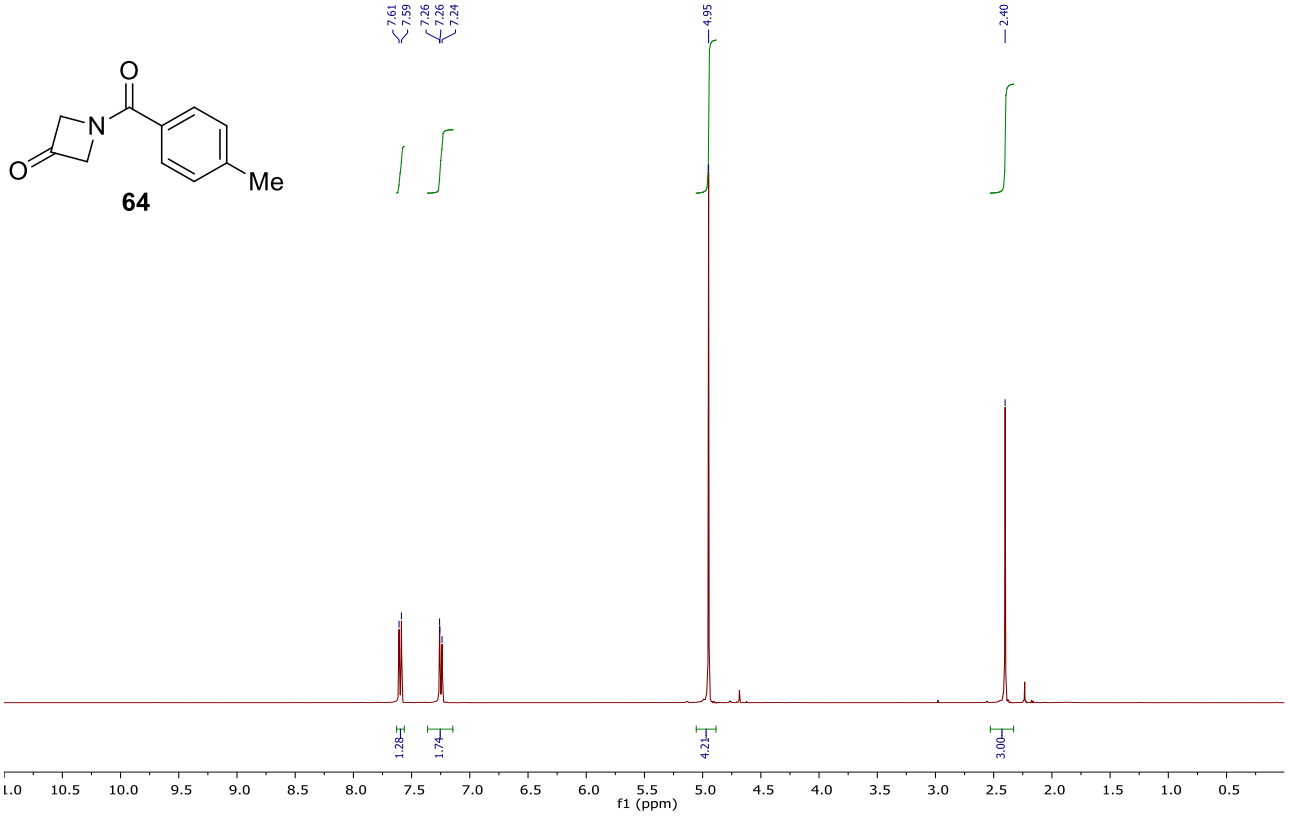
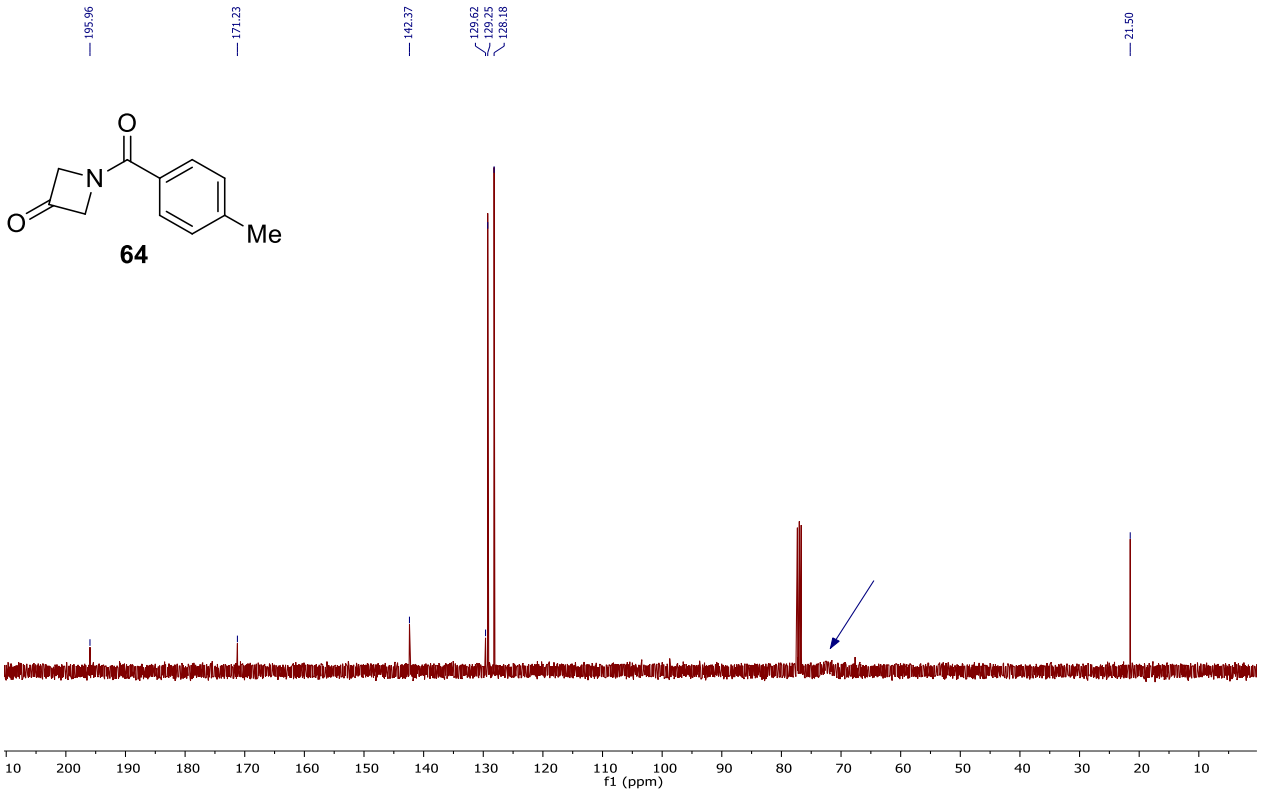


^{13}C-NMR (101 MHz, Chloroform-*d*)



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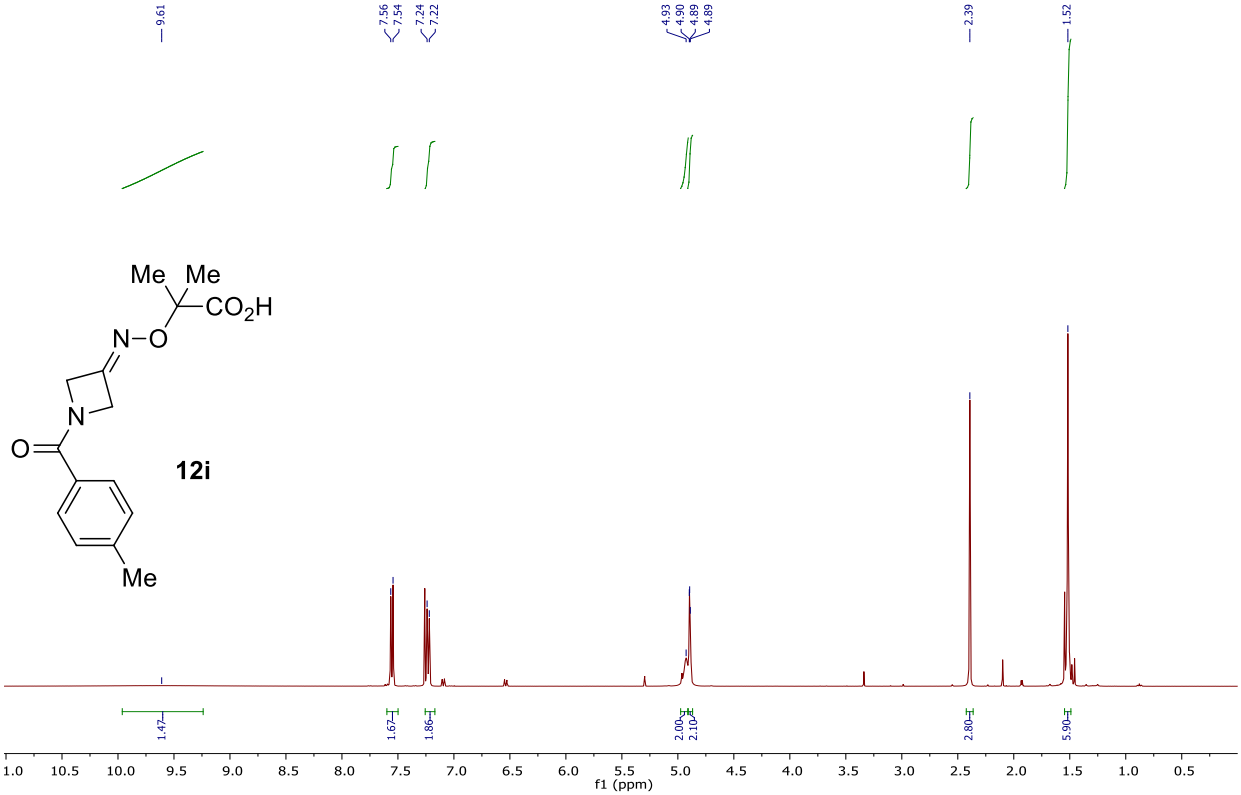

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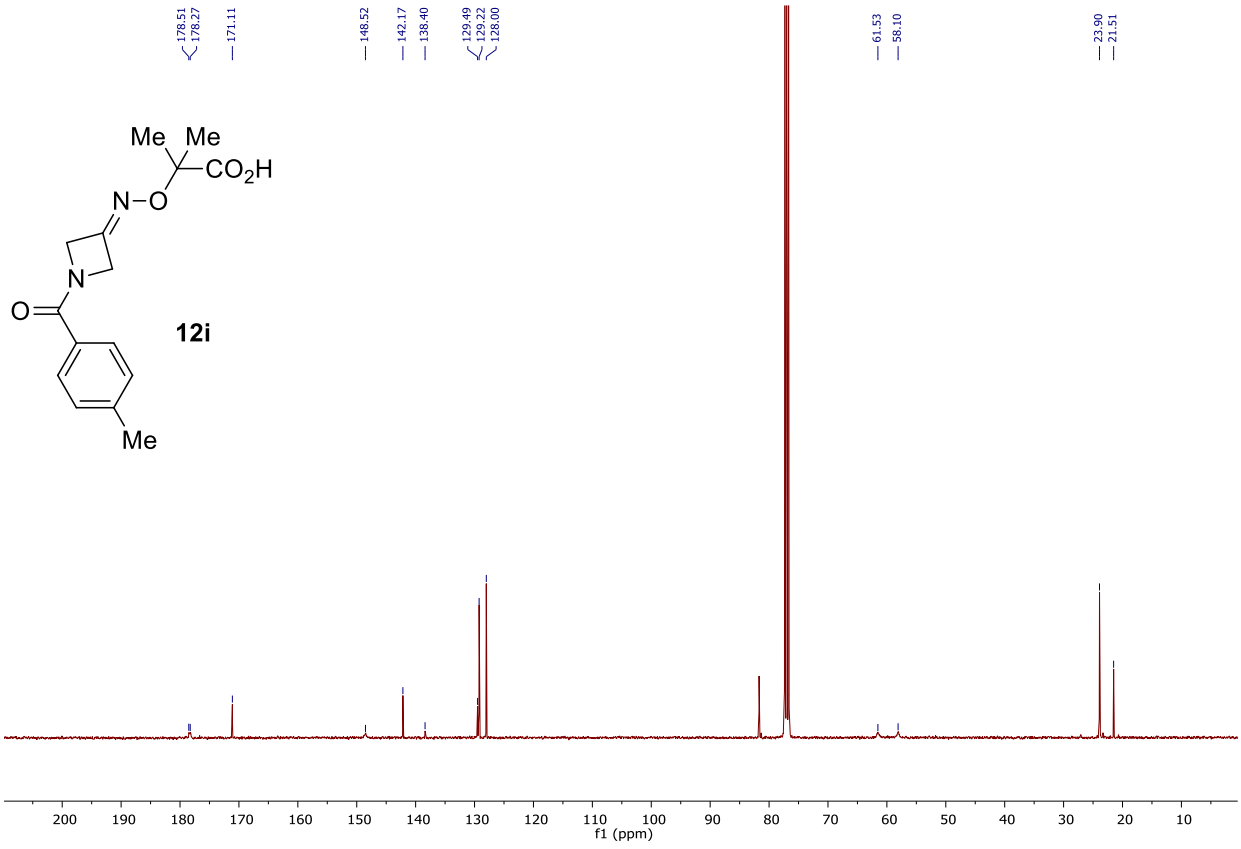

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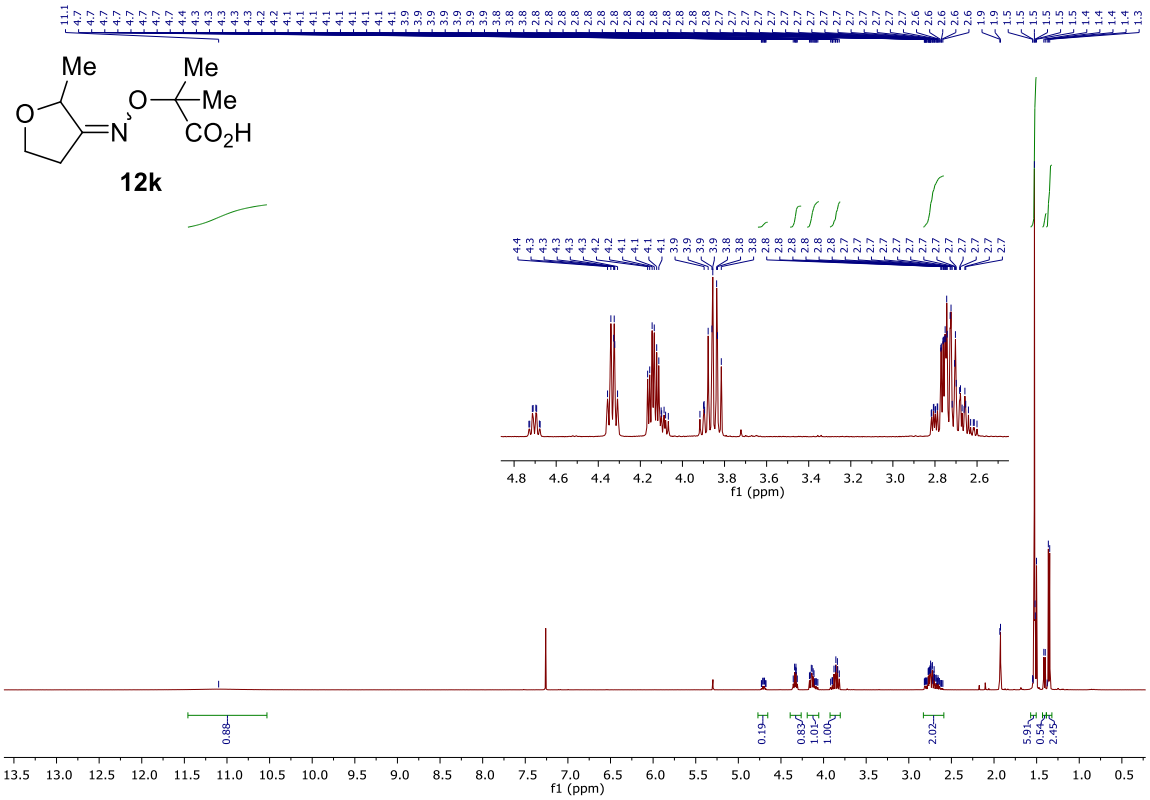

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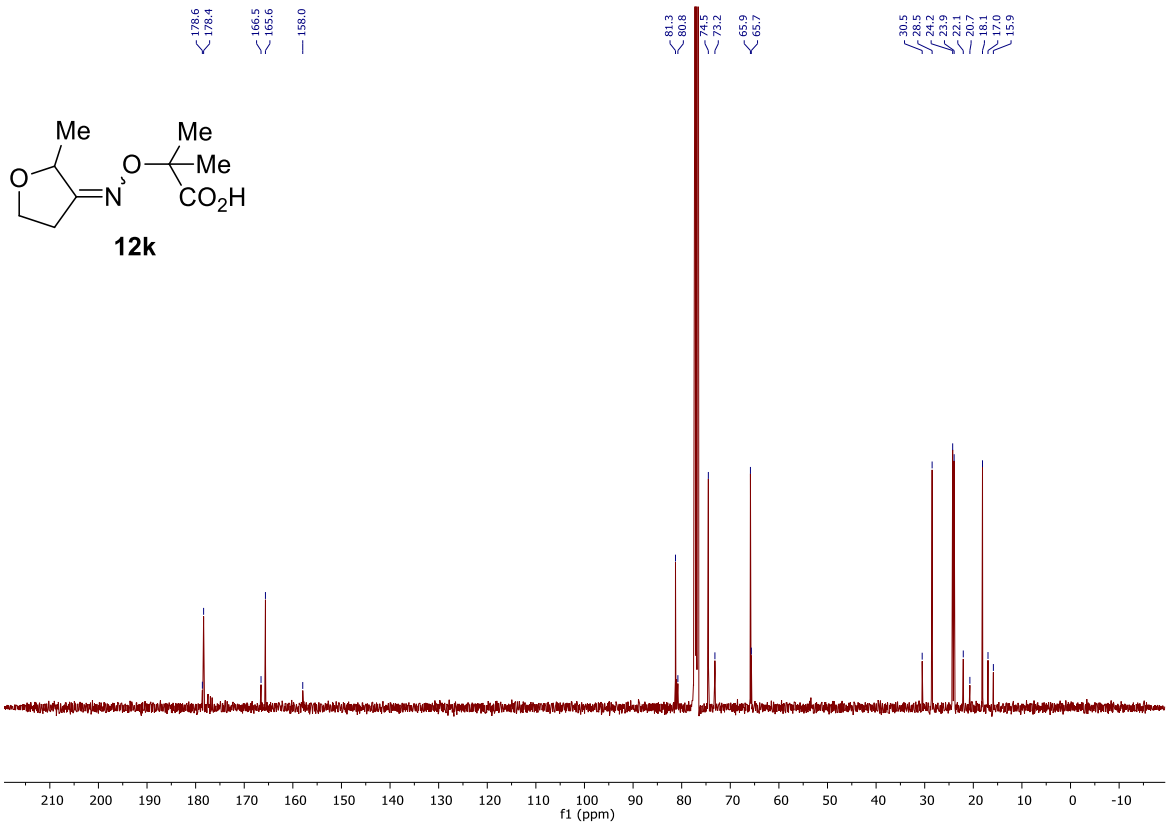

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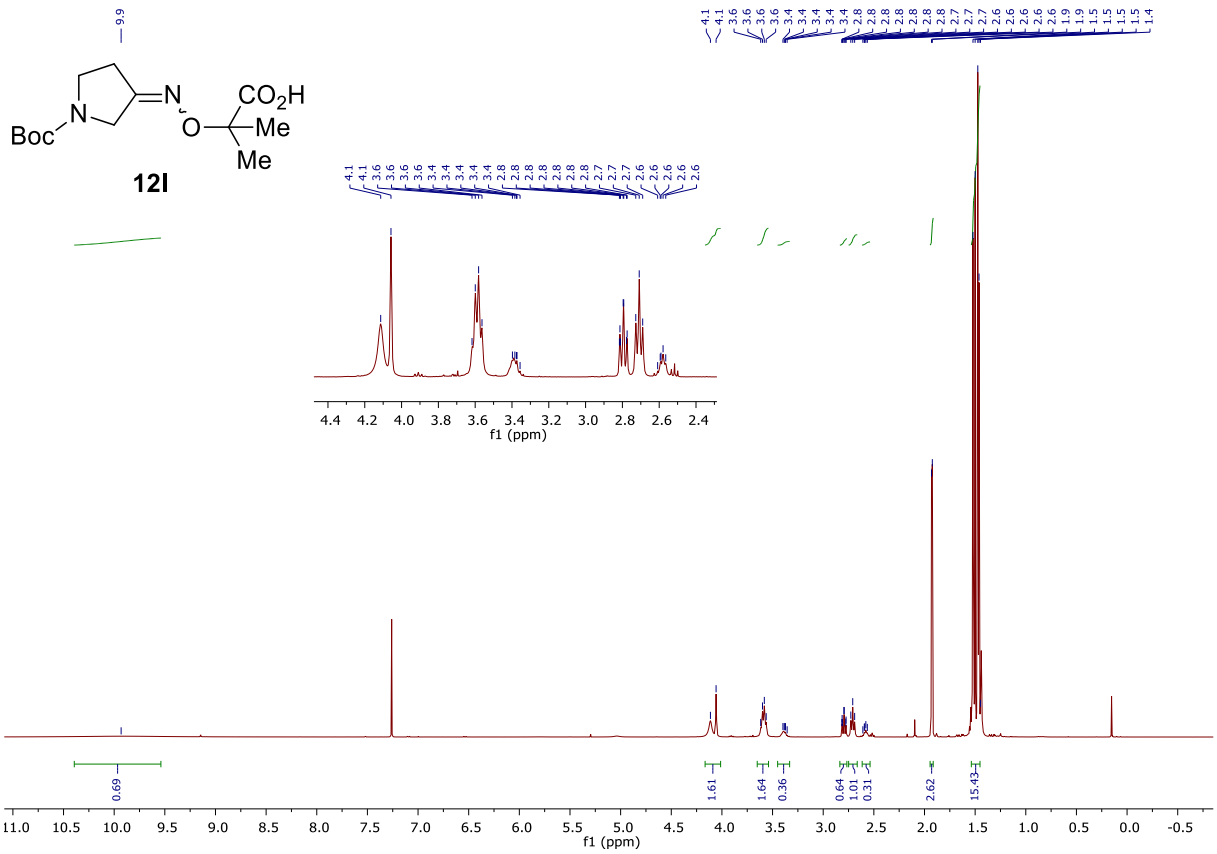

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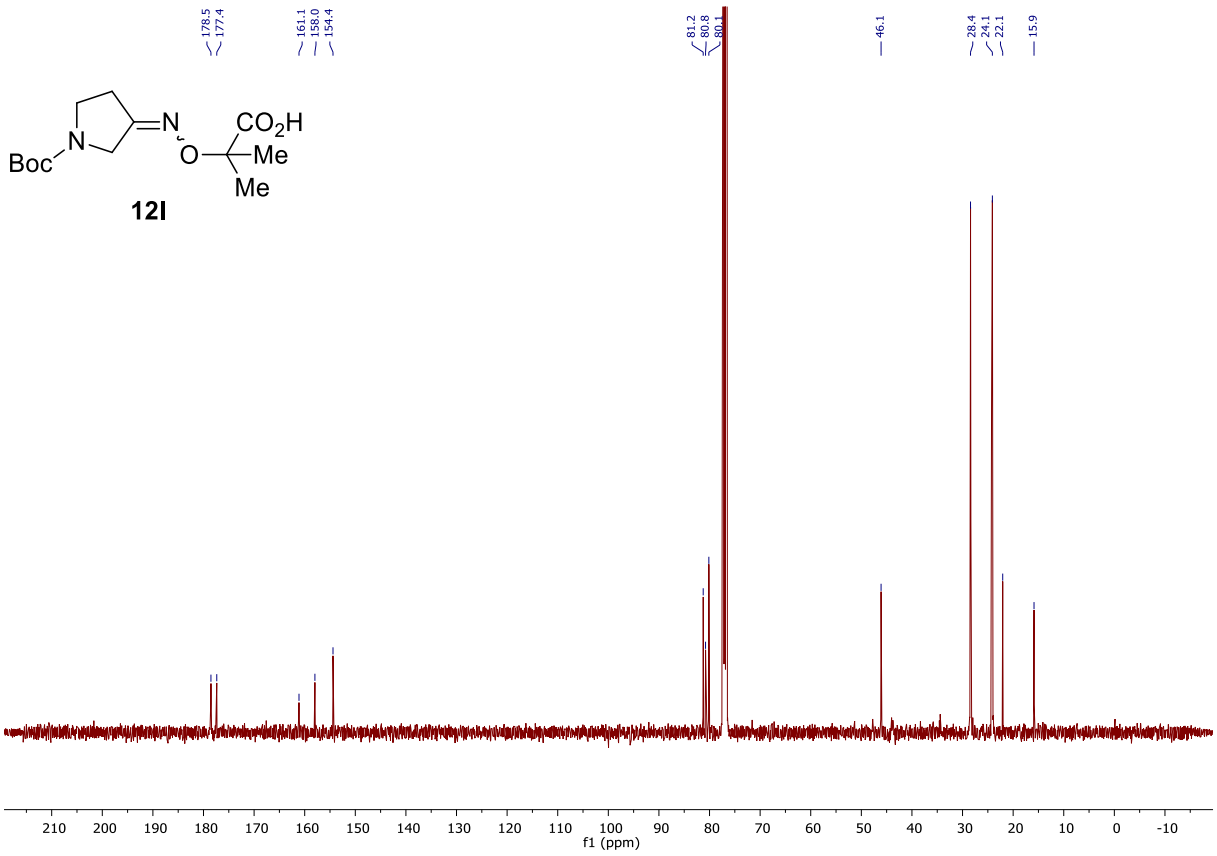
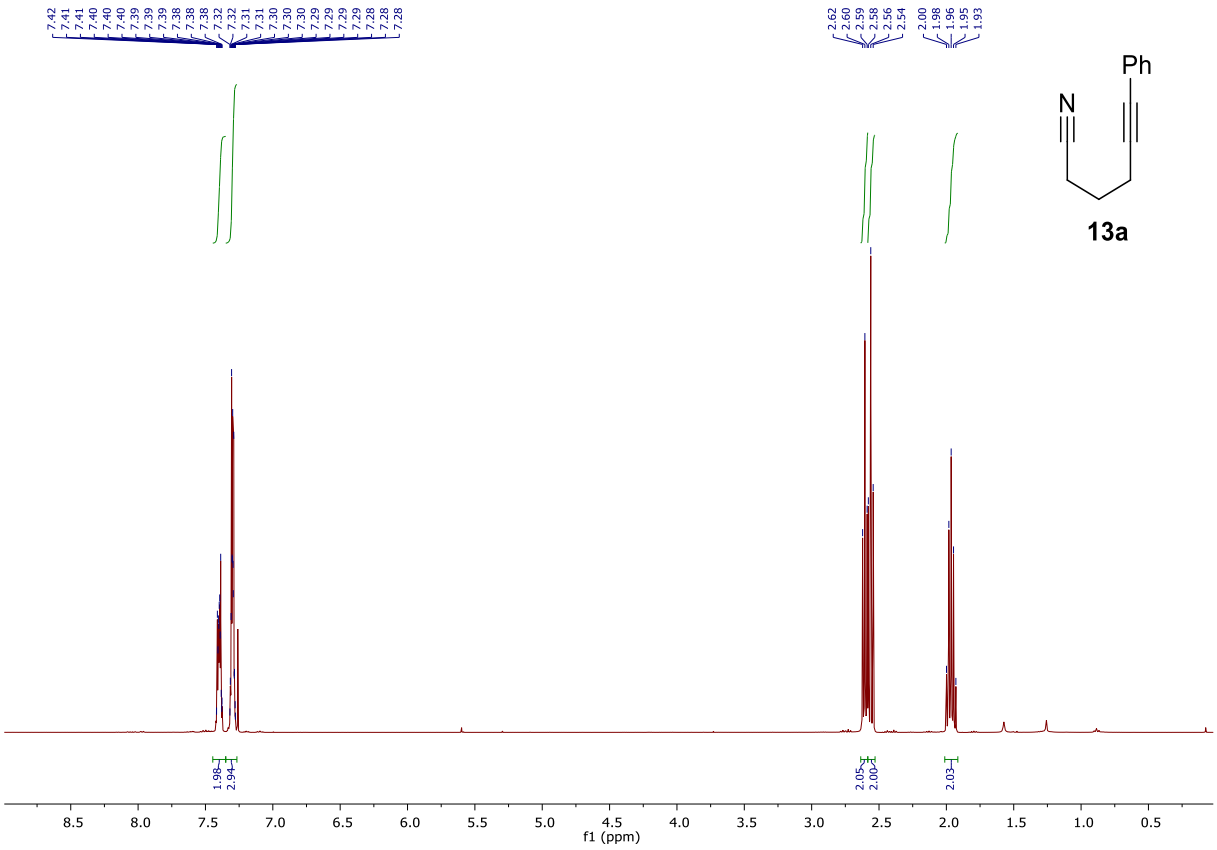
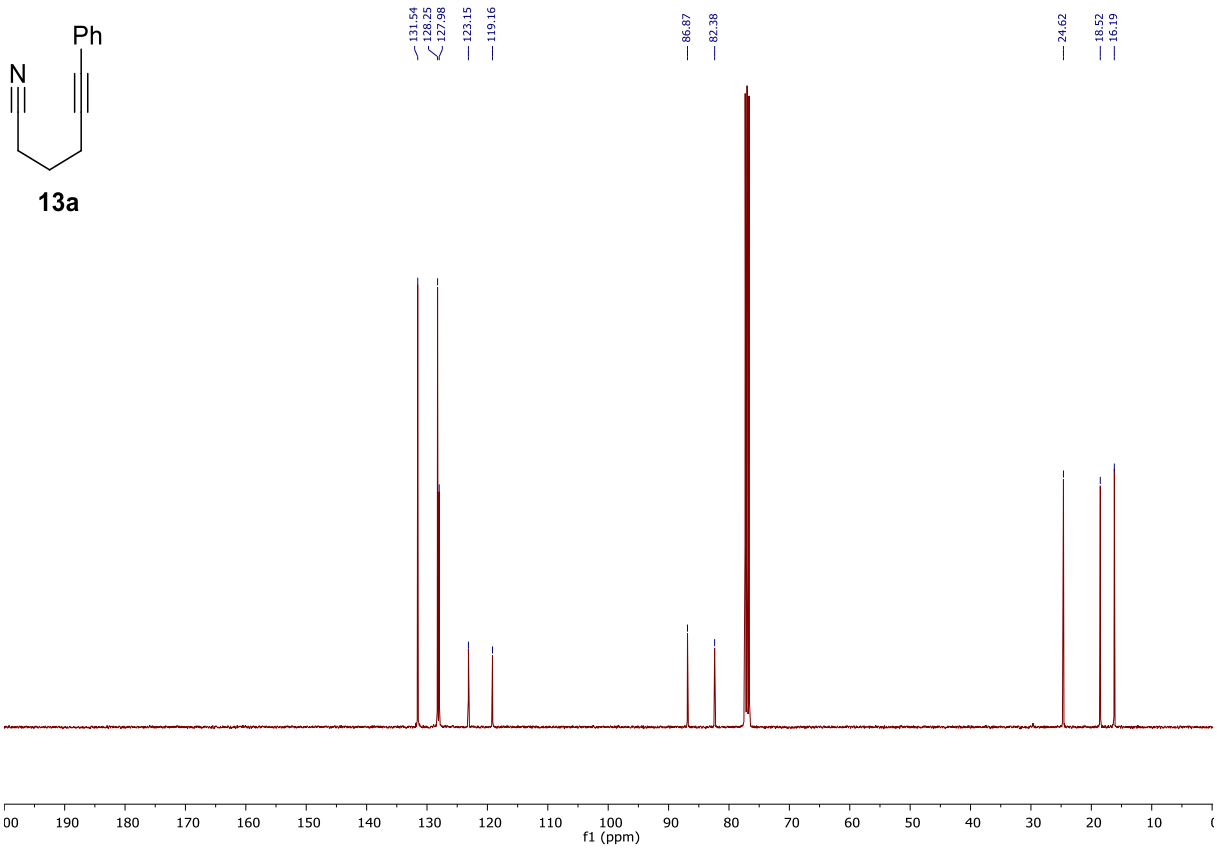


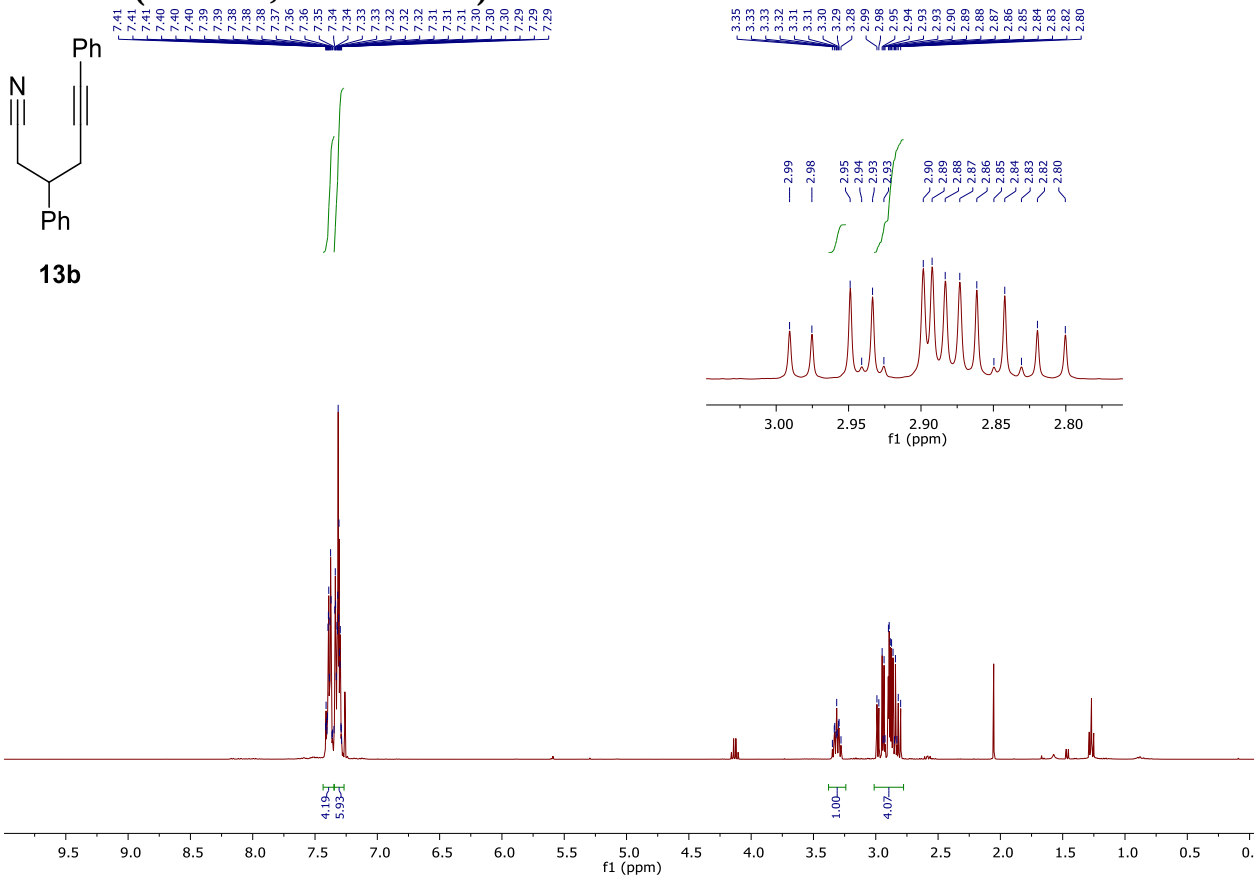
^{1}H-NMR (400 MHz, Chloroform-*d*)



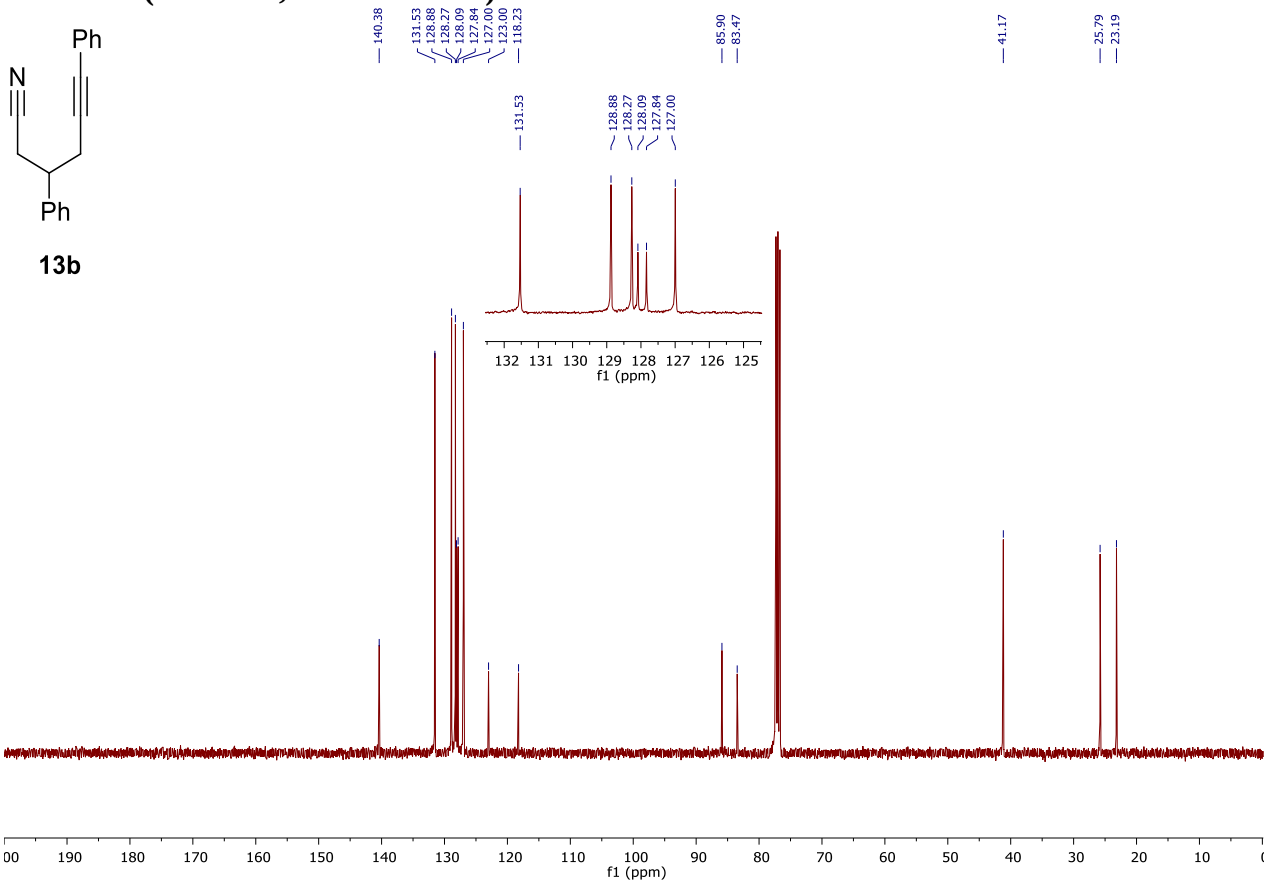
^{13}C-NMR (101 MHz, Chloroform-*d*)



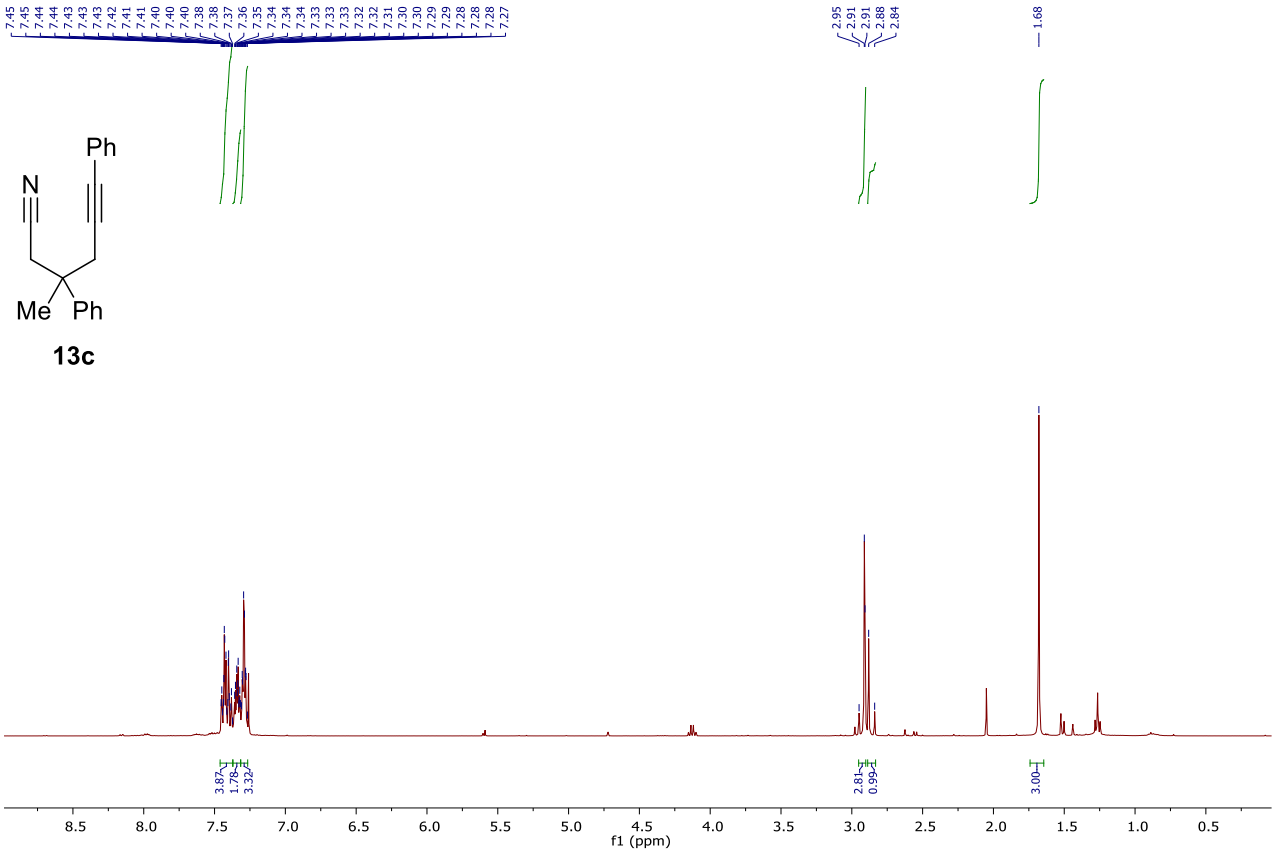
^{1}H-NMR (400 MHz, Chloroform-*d*)



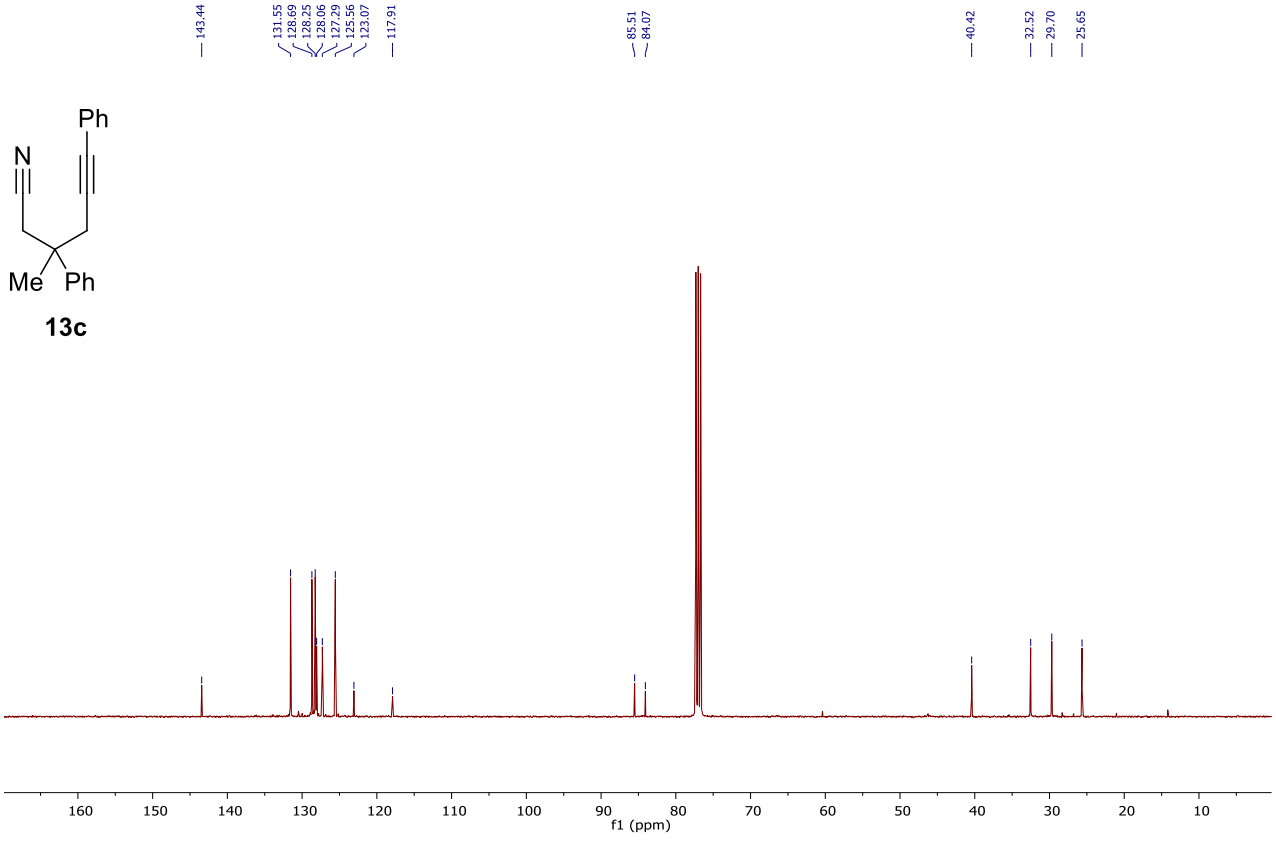
^{13}C-NMR (101 MHz, Chloroform-*d*)



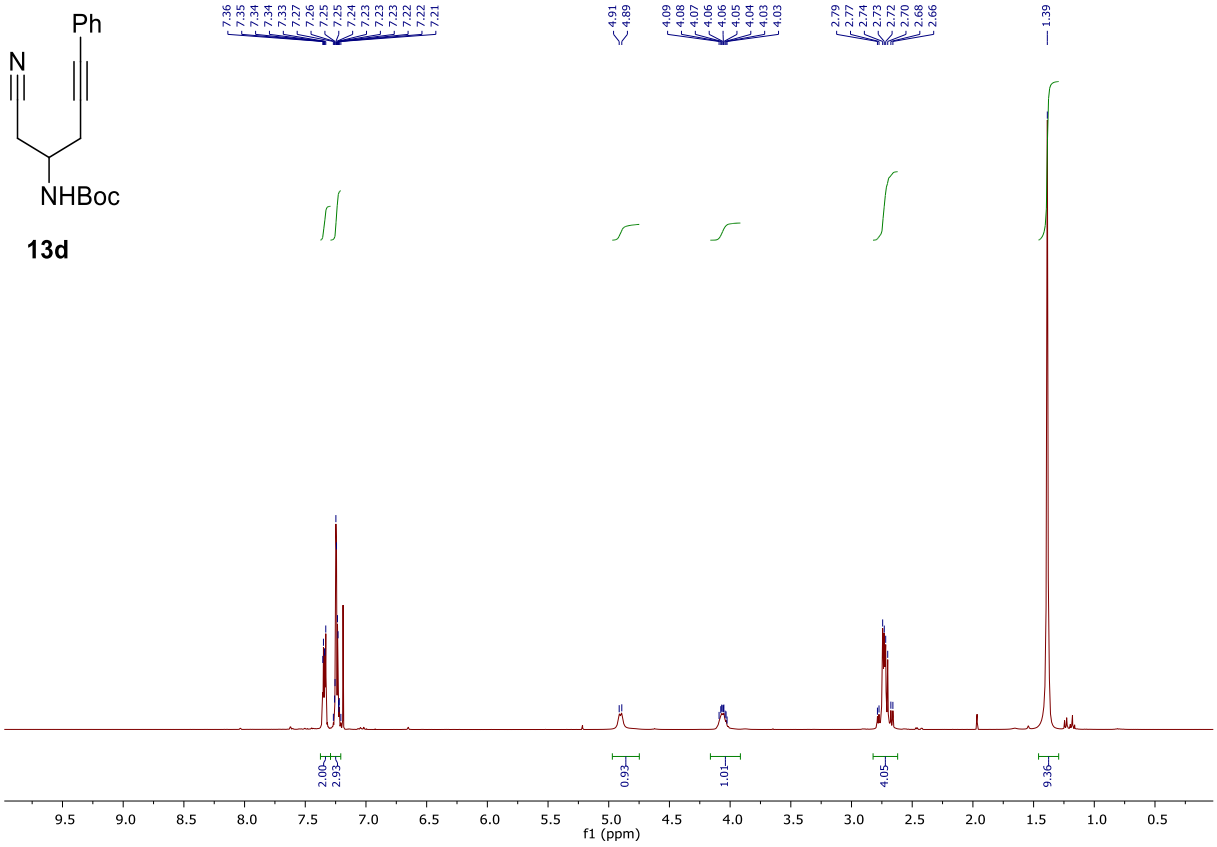
^{1}H-NMR (400 MHz, Chloroform-*d*)



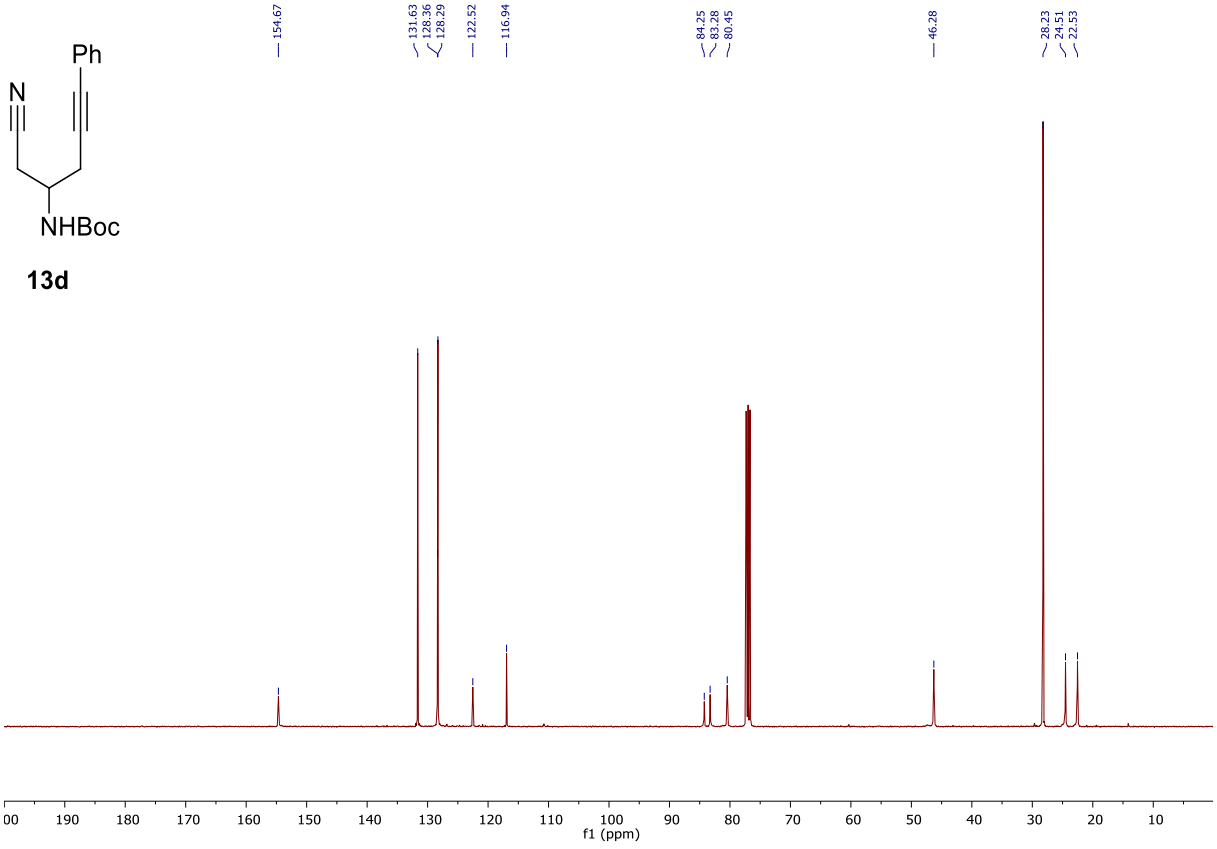
^{13}C-NMR (101 MHz, Chloroform-*d*)



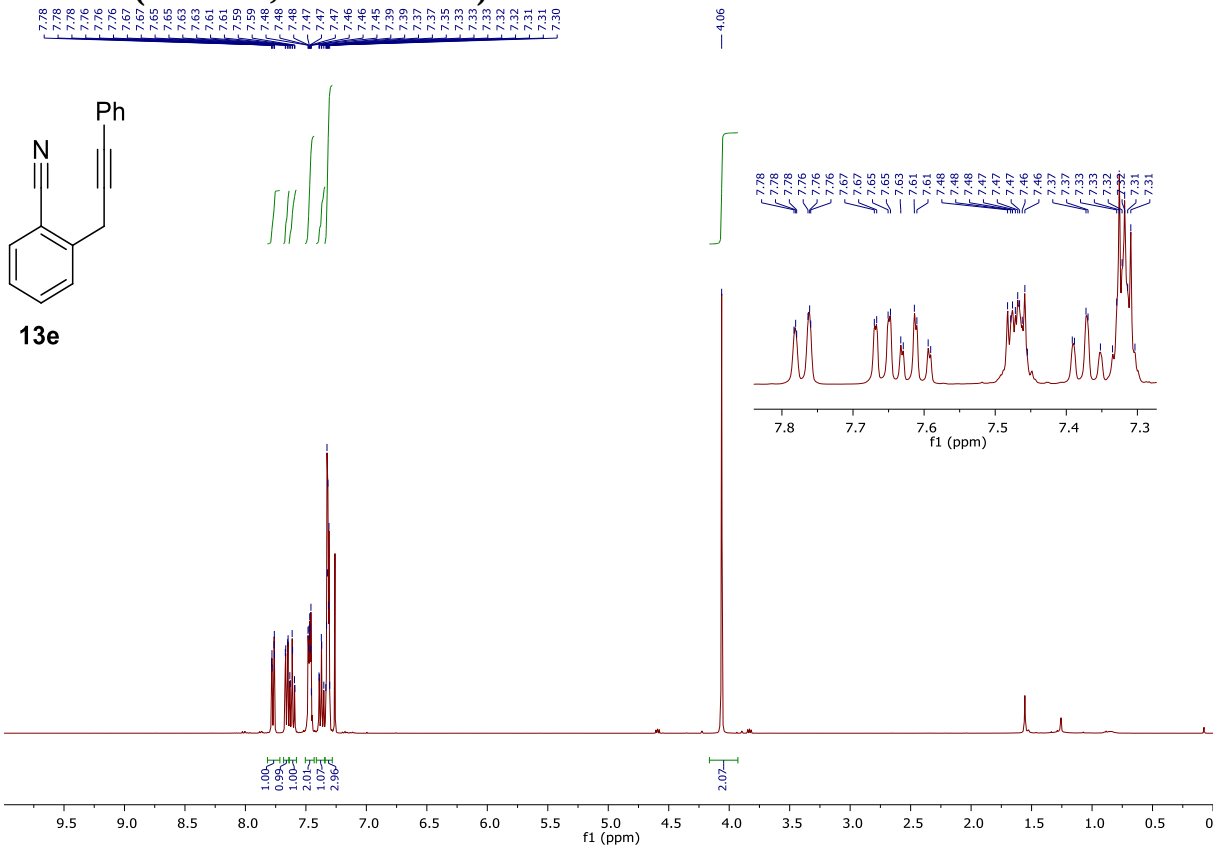
^{1}H-NMR (400 MHz, Chloroform-*d*)



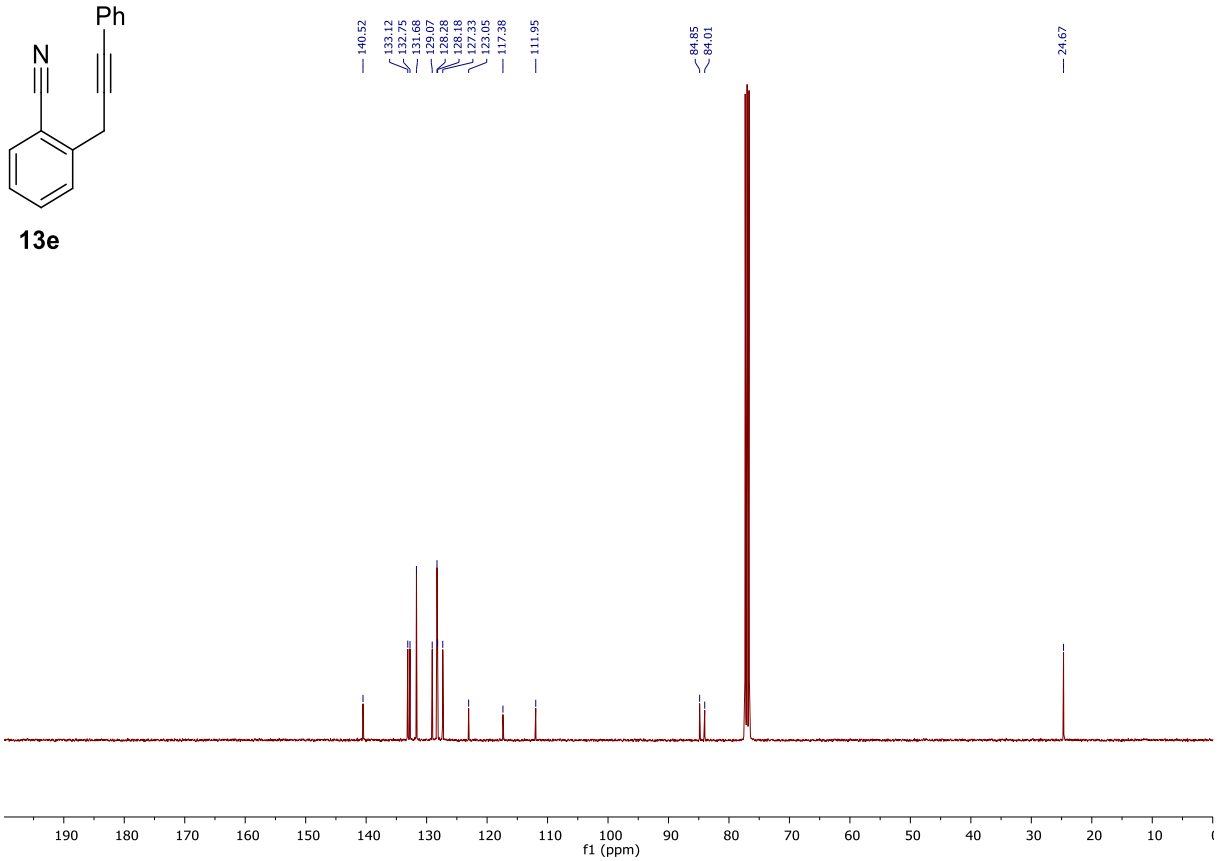
^{13}C-NMR (101 MHz, Chloroform-*d*)



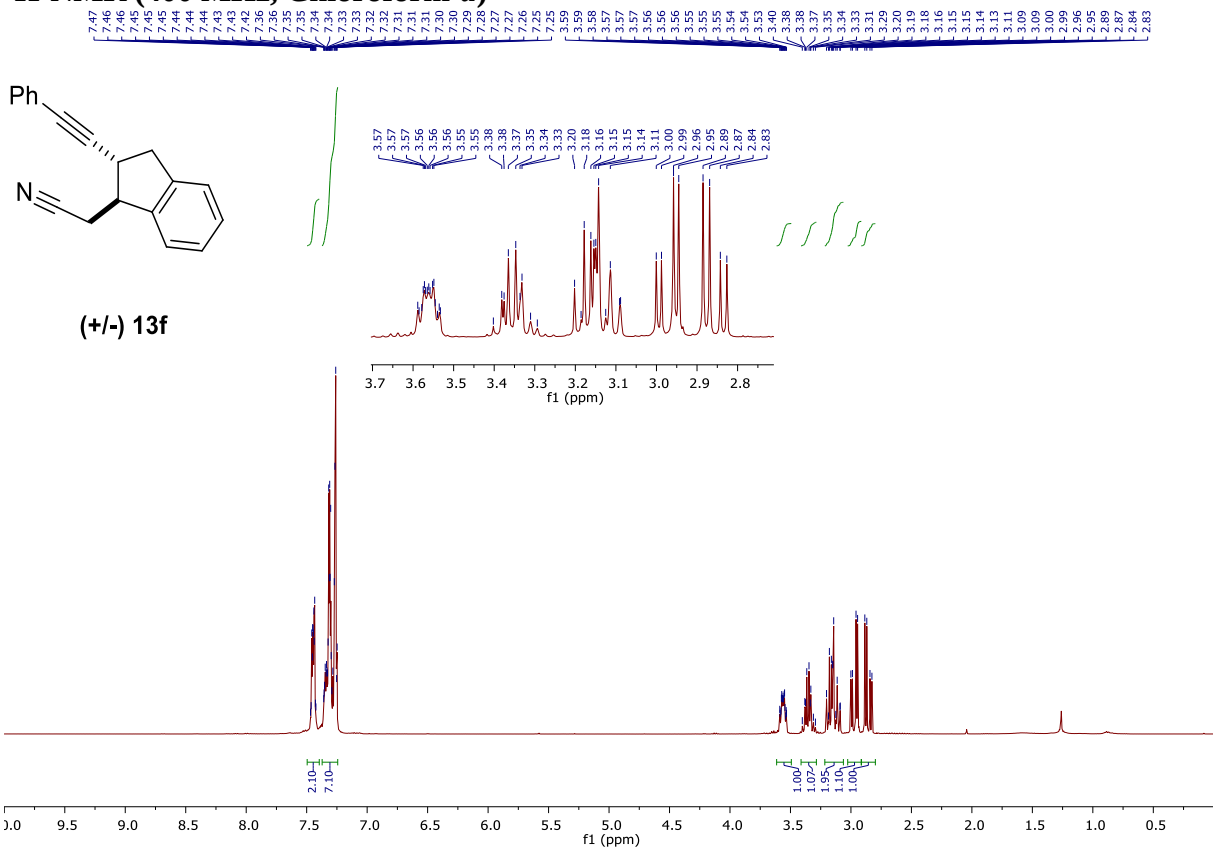
^{1}H-NMR (400 MHz, Chloroform-*d*)



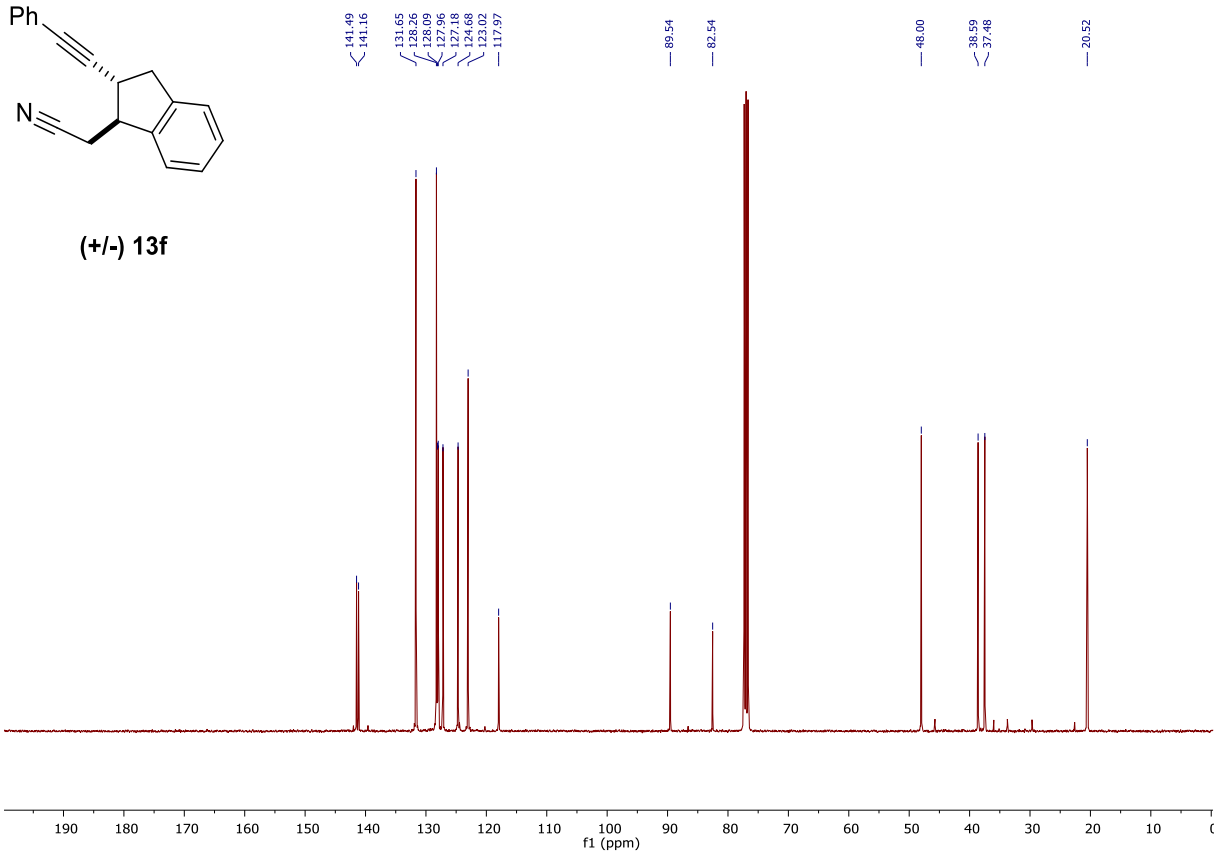
^{13}C-NMR (101 MHz, Chloroform-*d*)



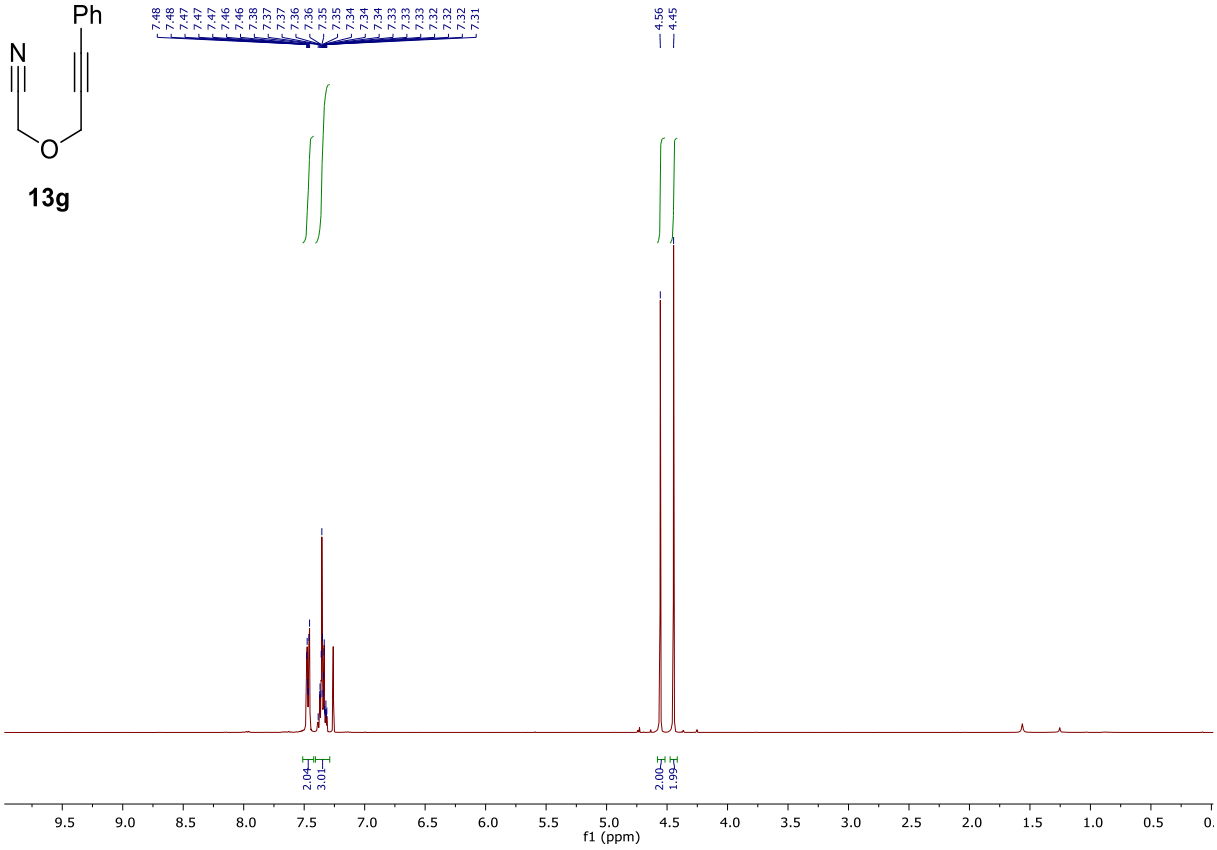
^{1}H-NMR (400 MHz, Chloroform-*d*)



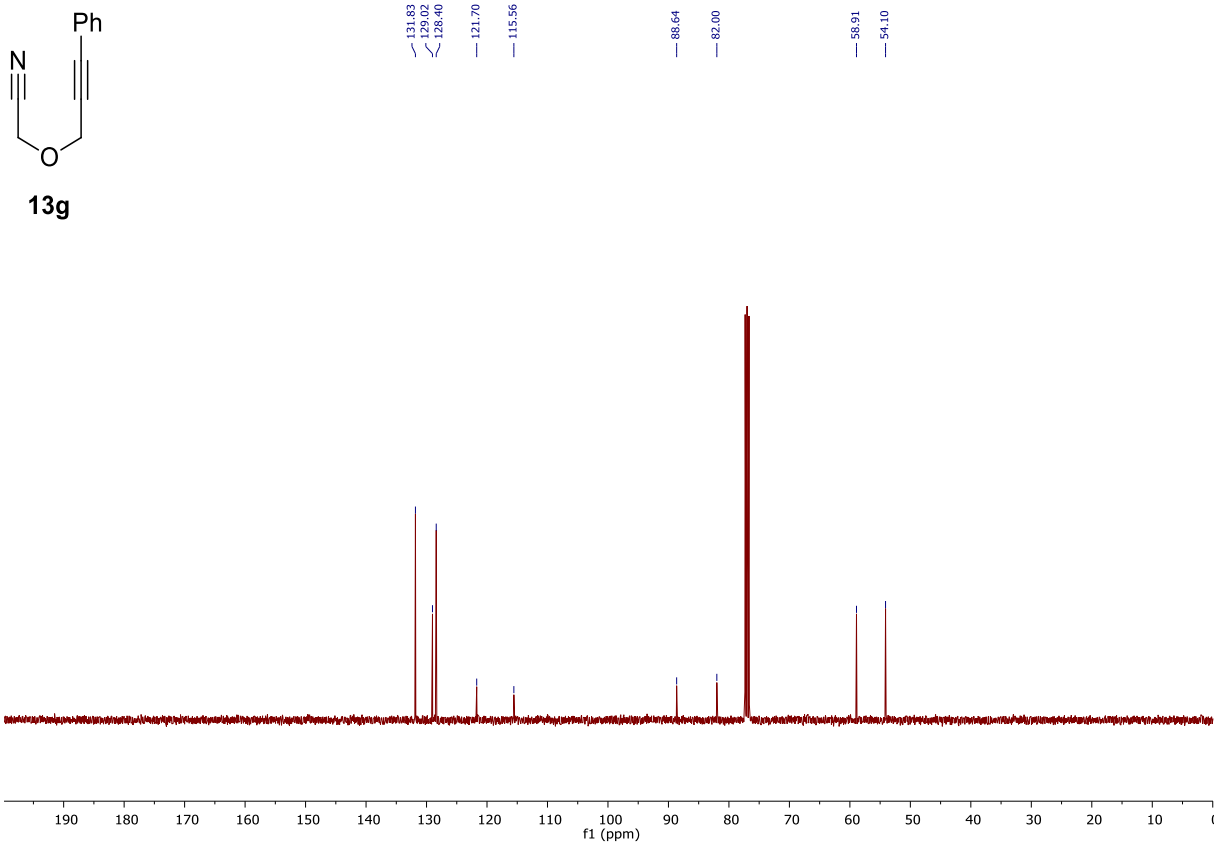
^{13}C-NMR (101 MHz, Chloroform-*d*)



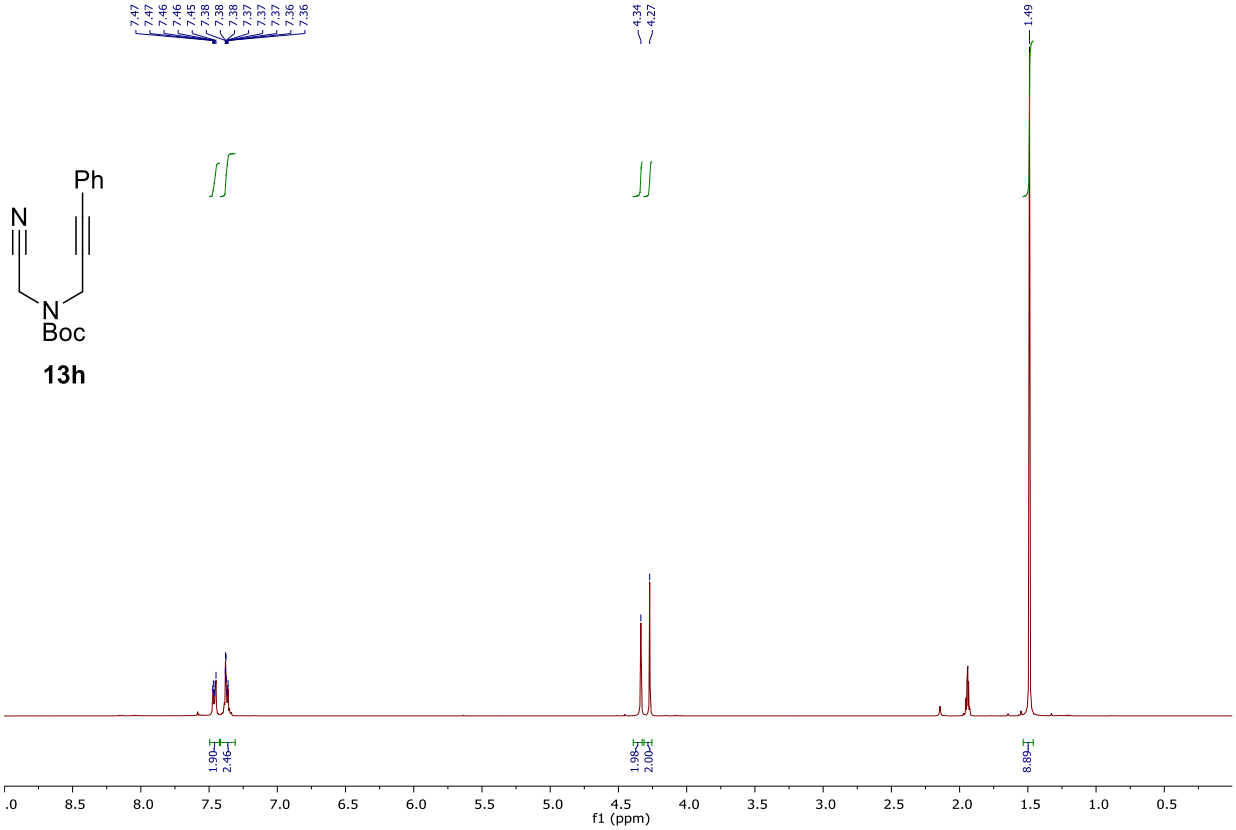
^{1}H-NMR (400 MHz, Chloroform-*d*)



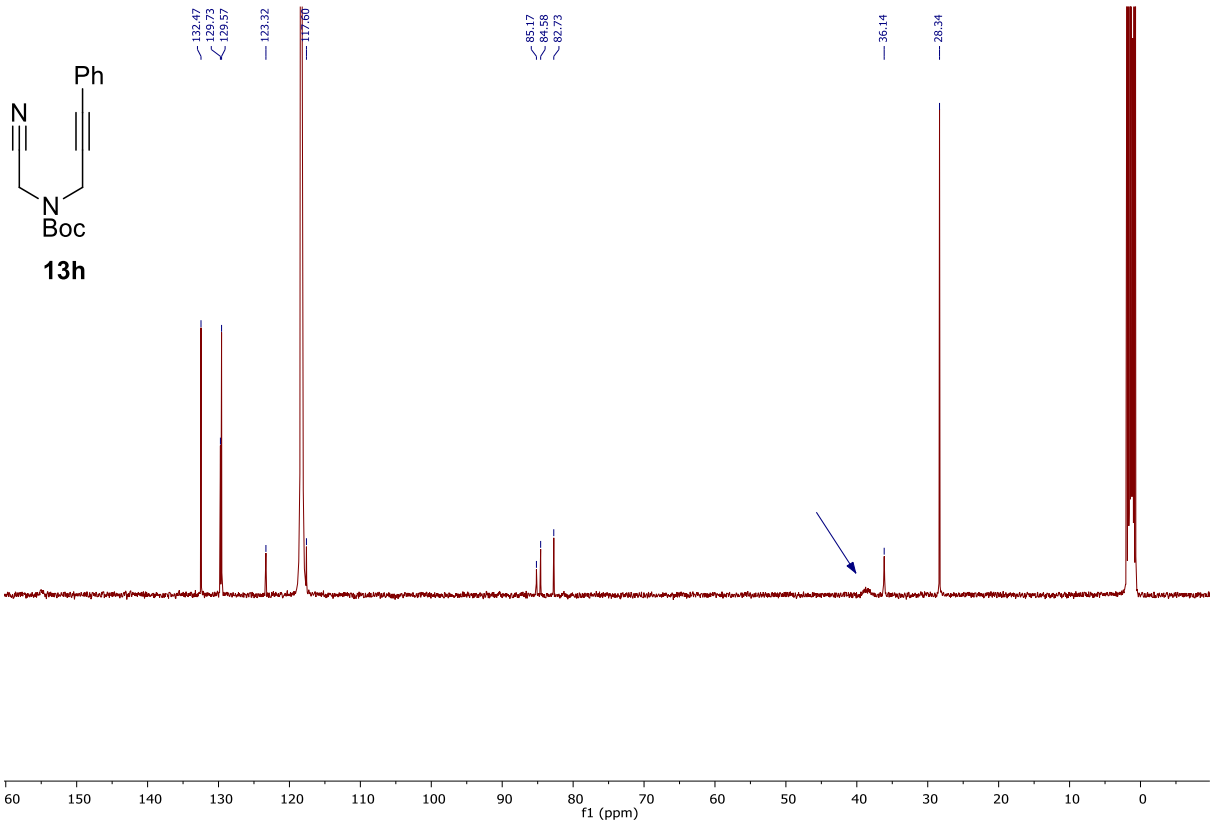
^{13}C-NMR (101 MHz, Chloroform-*d*)



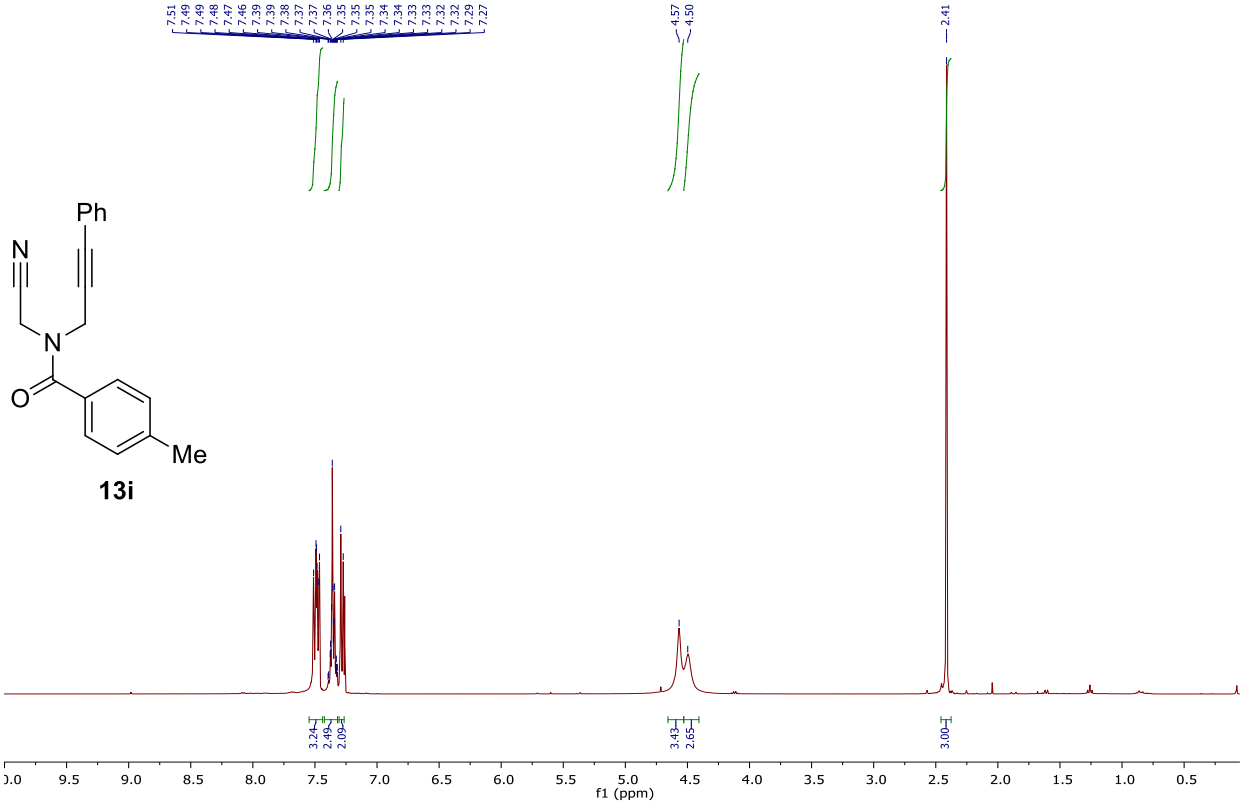
^{1}H-NMR (400 MHz, Acetonitrile-d_6)



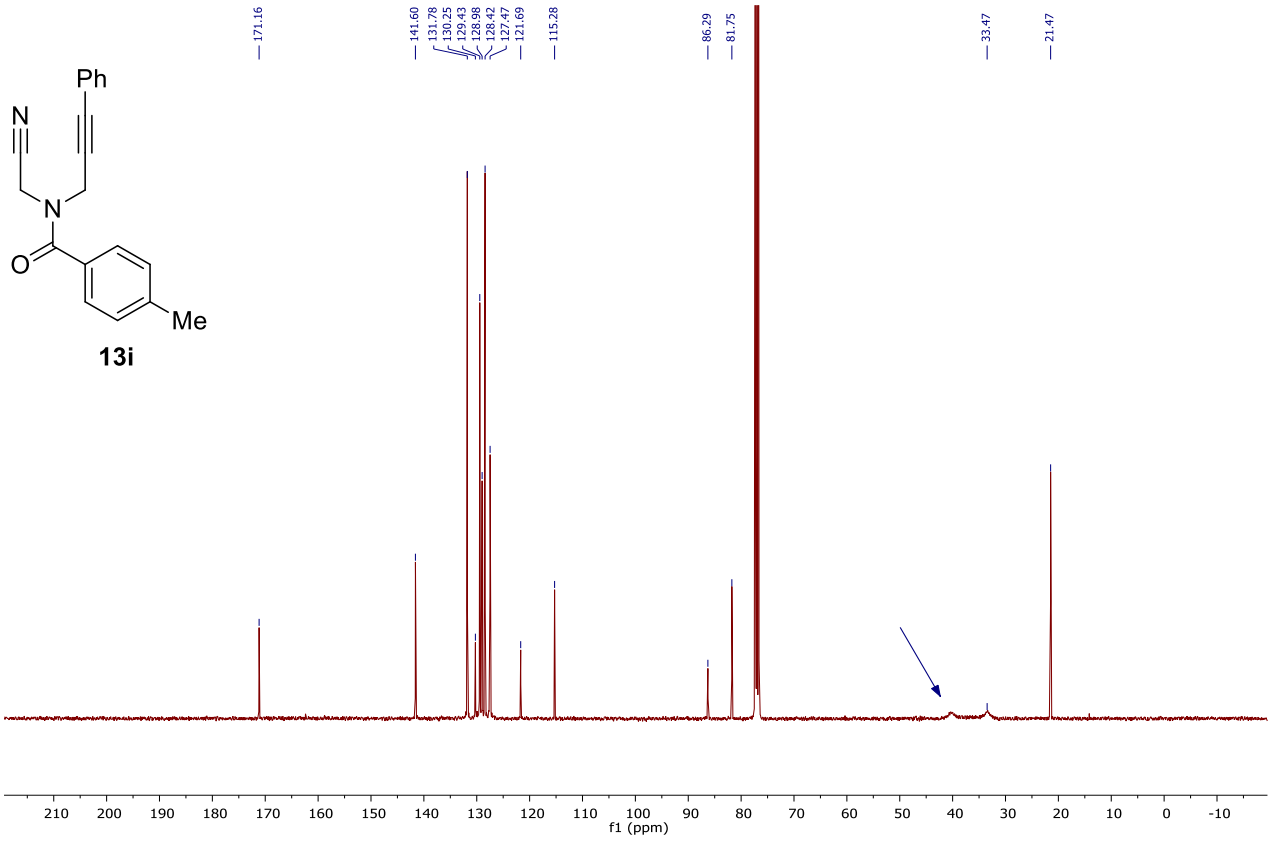
^{13}C-NMR (101 MHz, Acetonitrile-d_6)



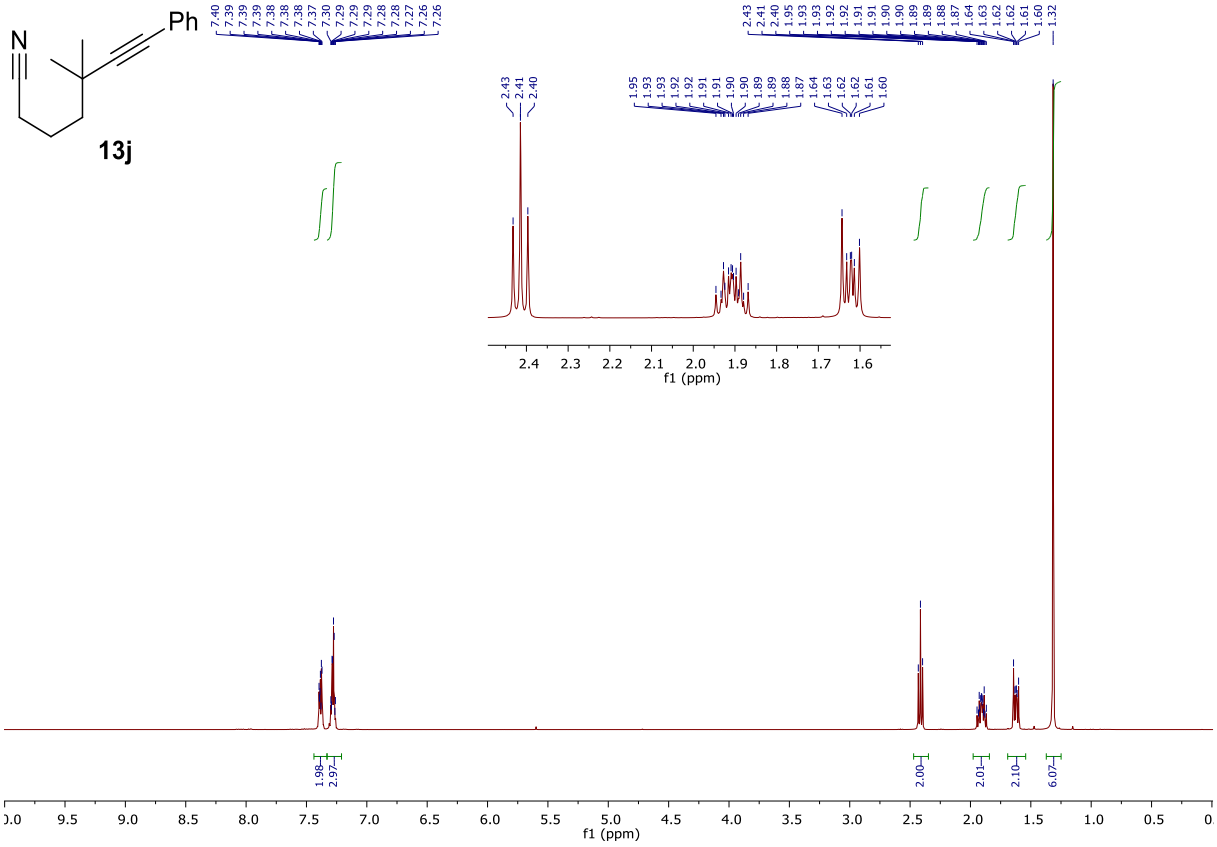
^{1}H-NMR (400 MHz, Chloroform-*d*)



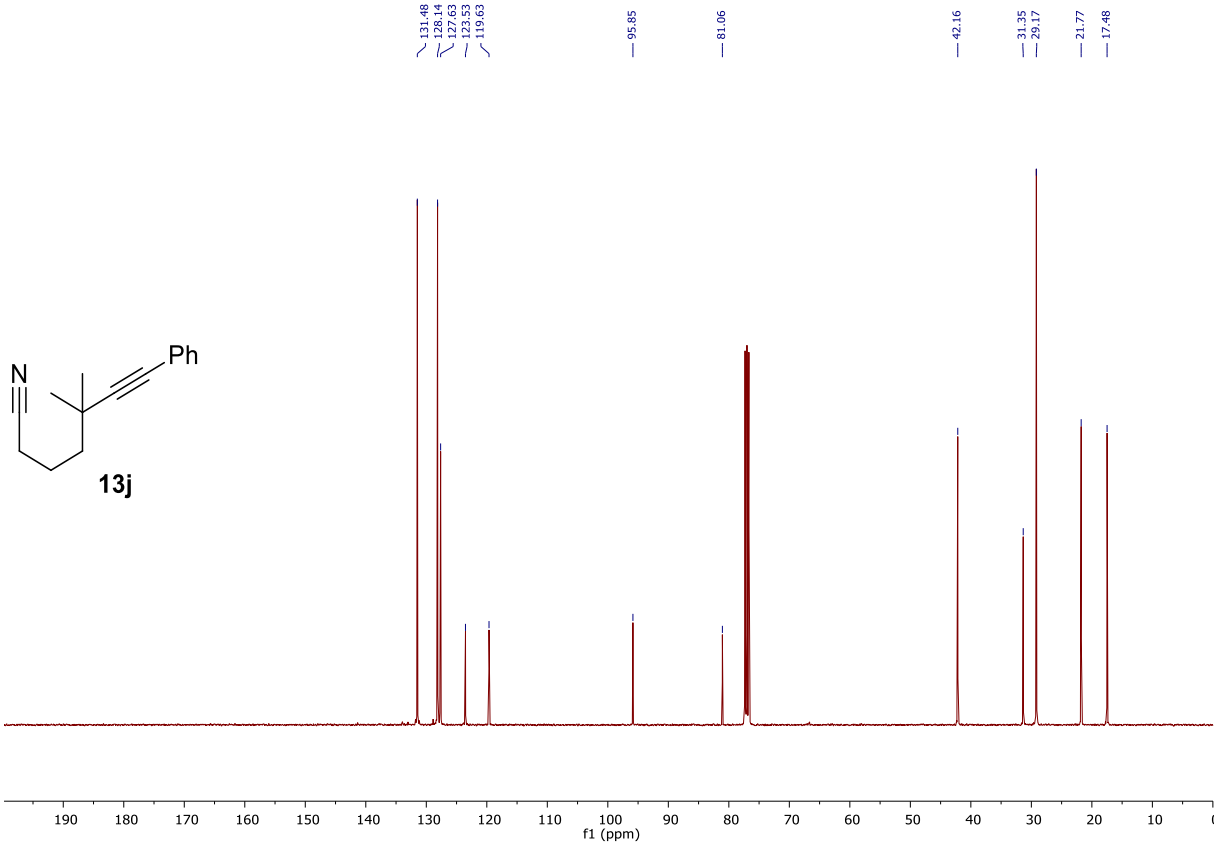
^{13}C-NMR (101 MHz, Chloroform-*d*)



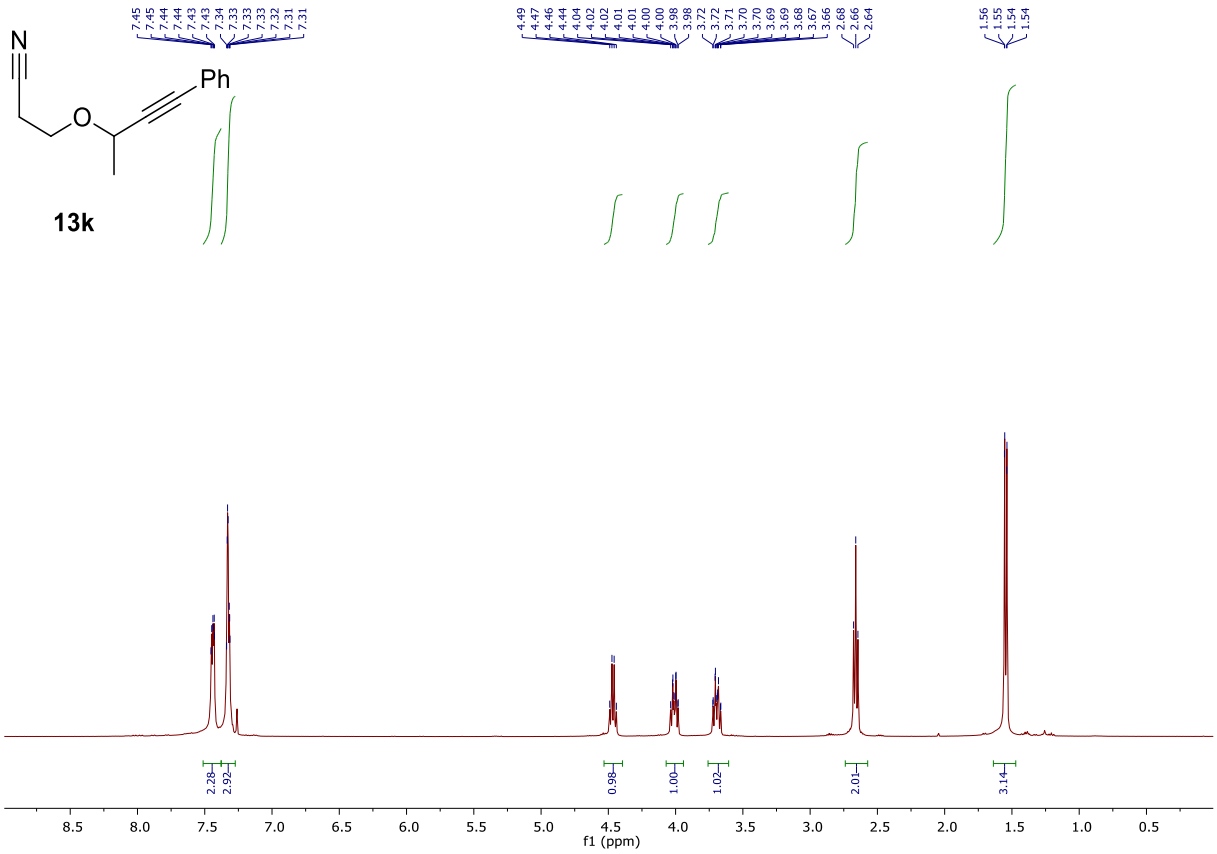
^{1}H-NMR (400 MHz, Chloroform-*d*)



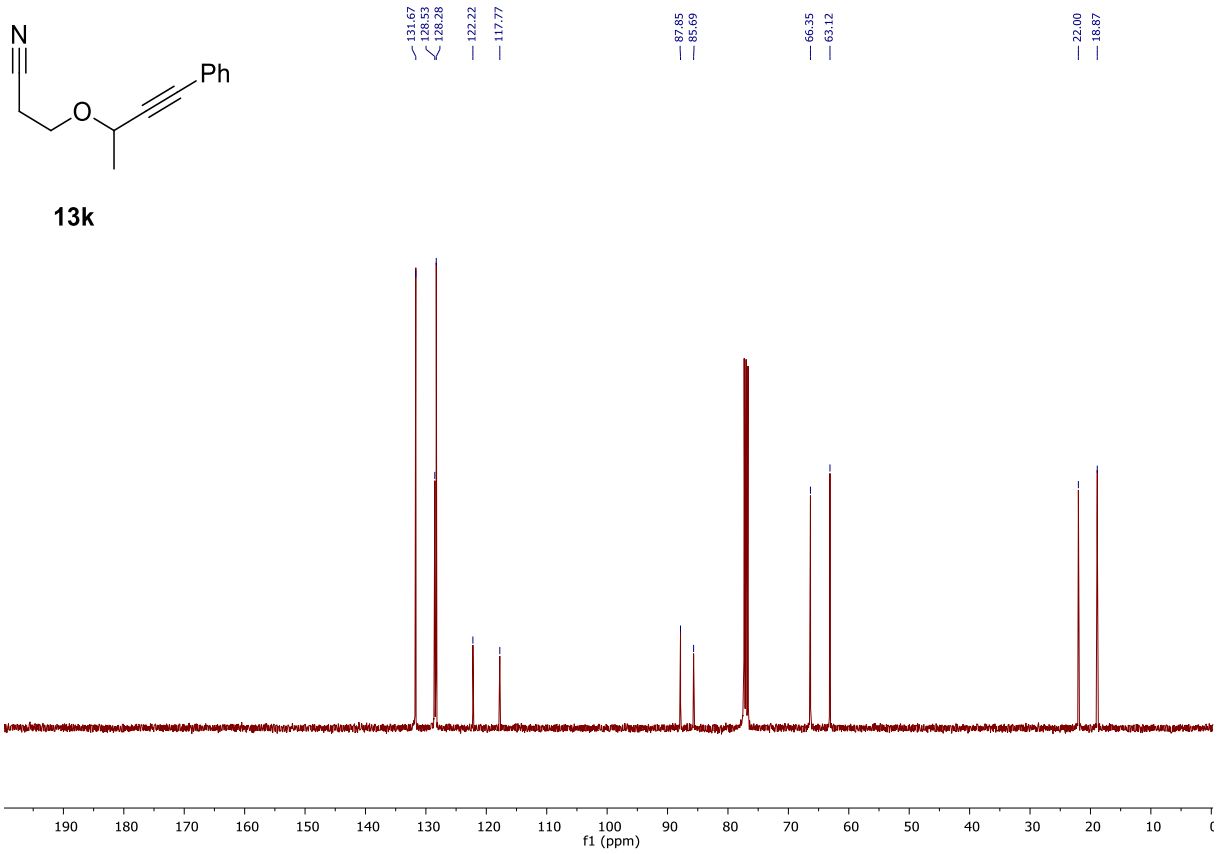
^{13}C-NMR (101 MHz, Chloroform-*d*)



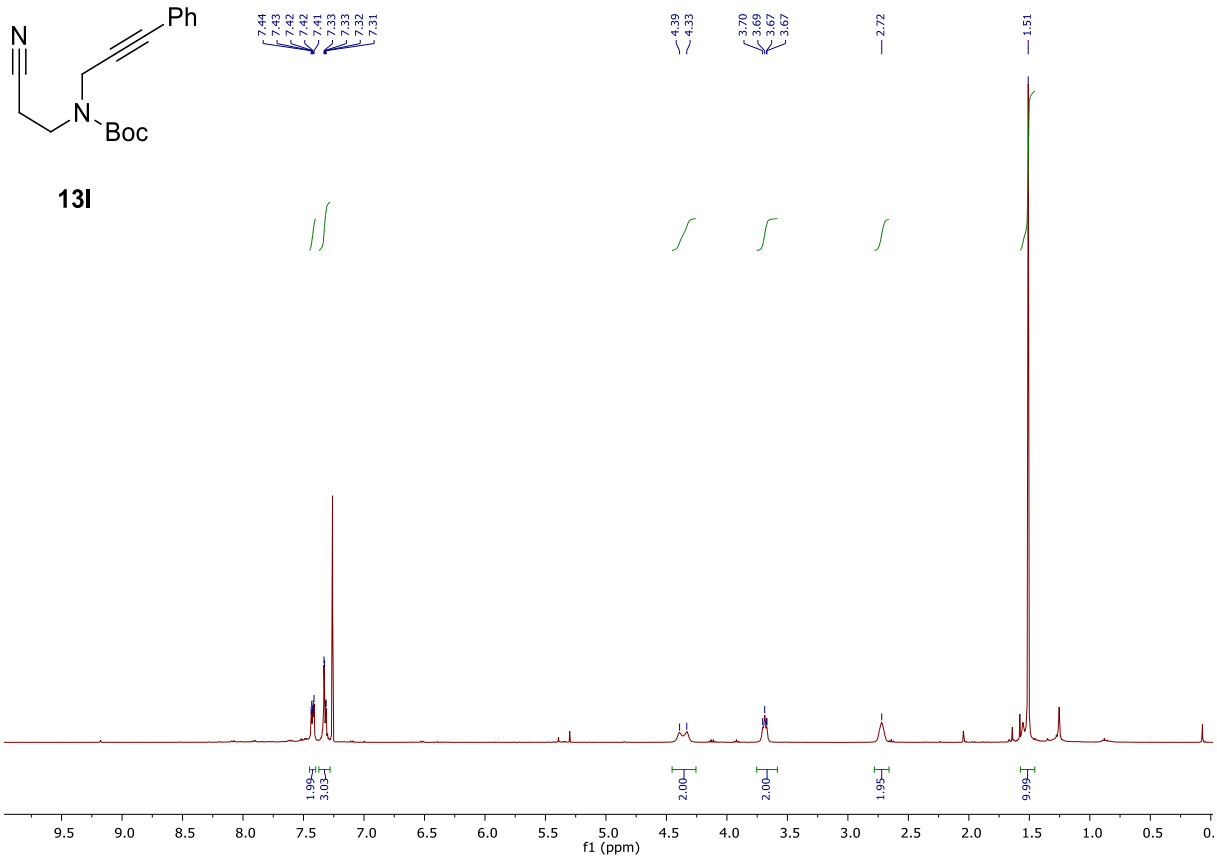
^{1}H-NMR (400 MHz, Chloroform-*d*)



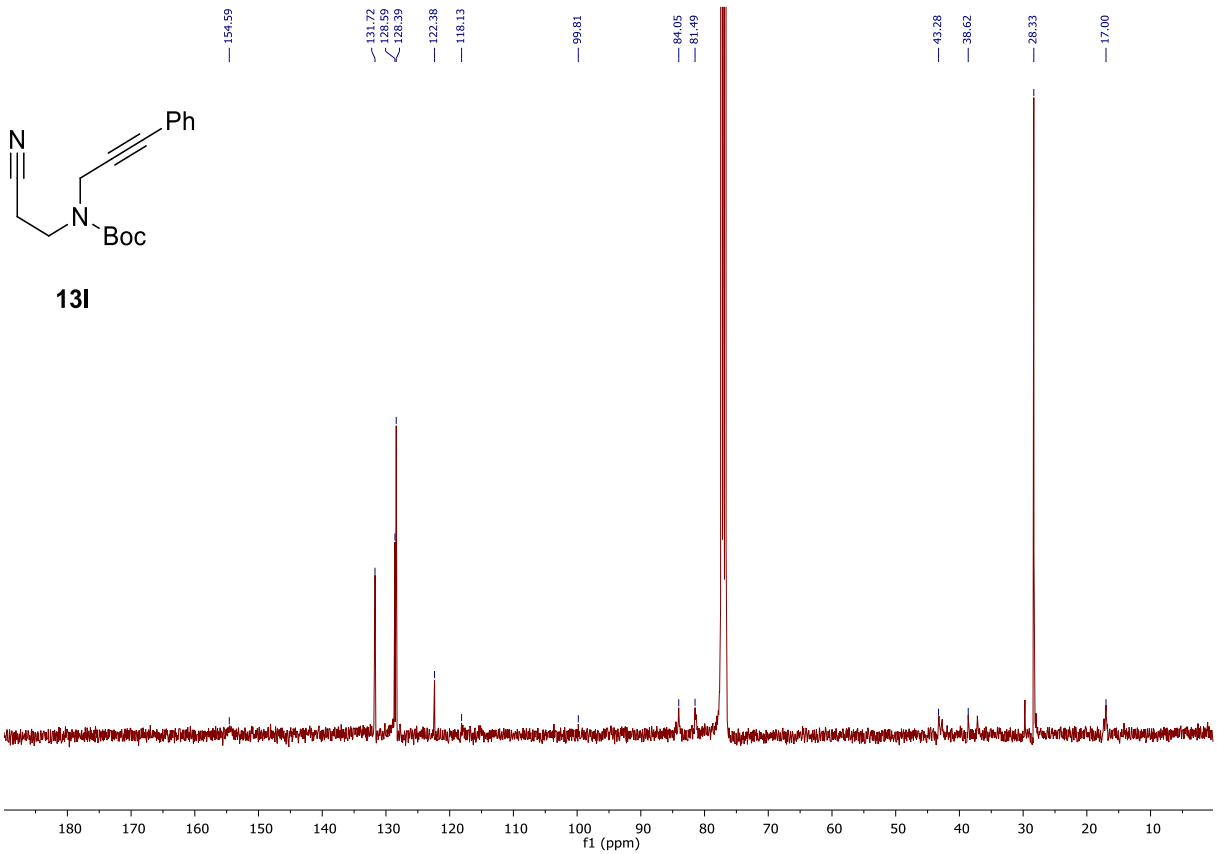
^{13}C-NMR (101 MHz, Chloroform-*d*)



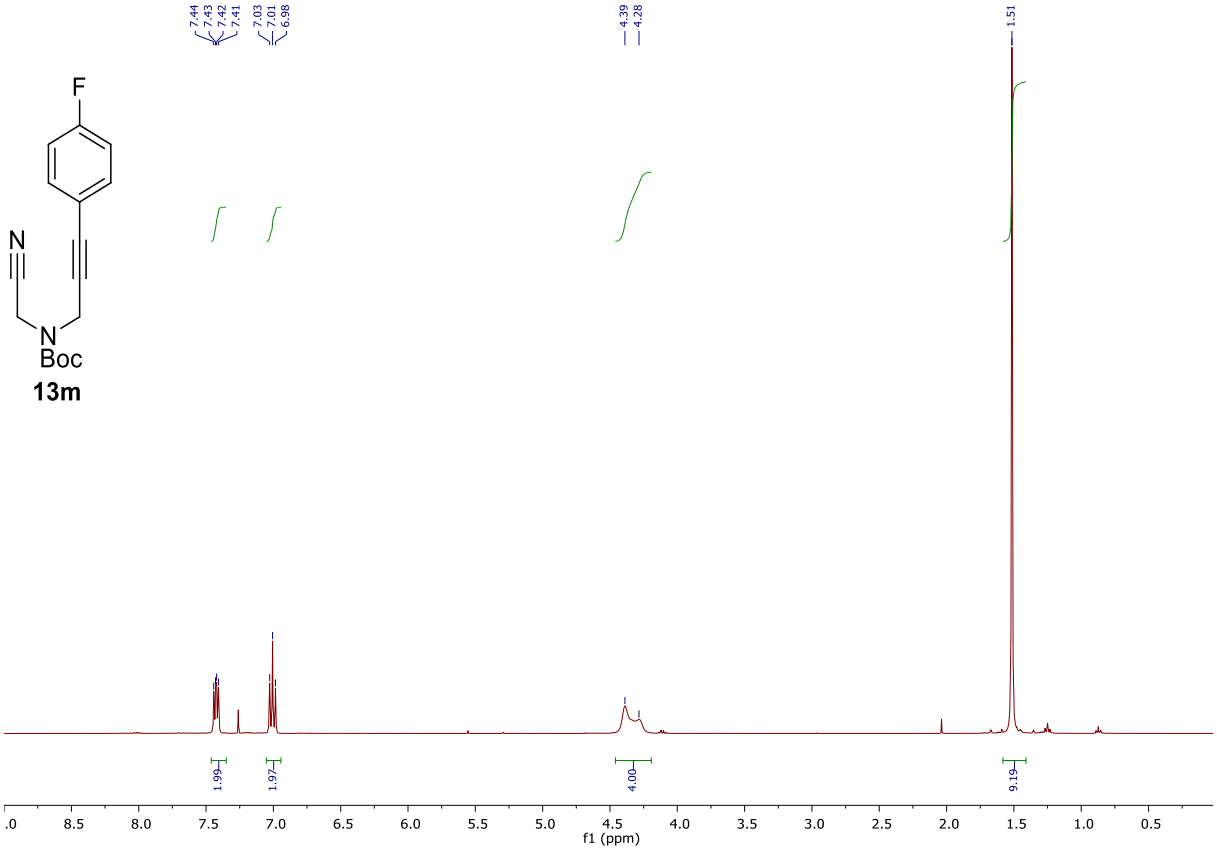
^{1}H-NMR (400 MHz, Chloroform-*d*)



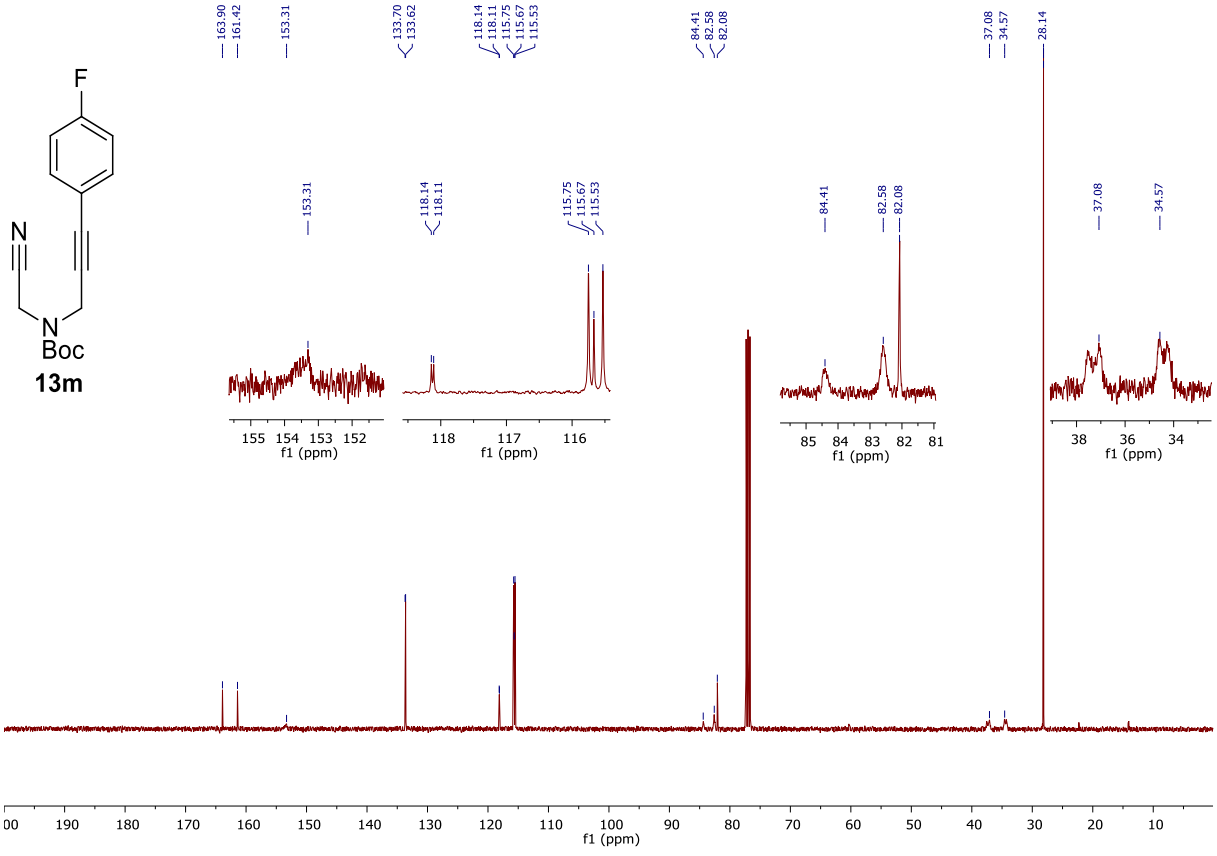
^{13}C-NMR (101 MHz, Chloroform-*d*)



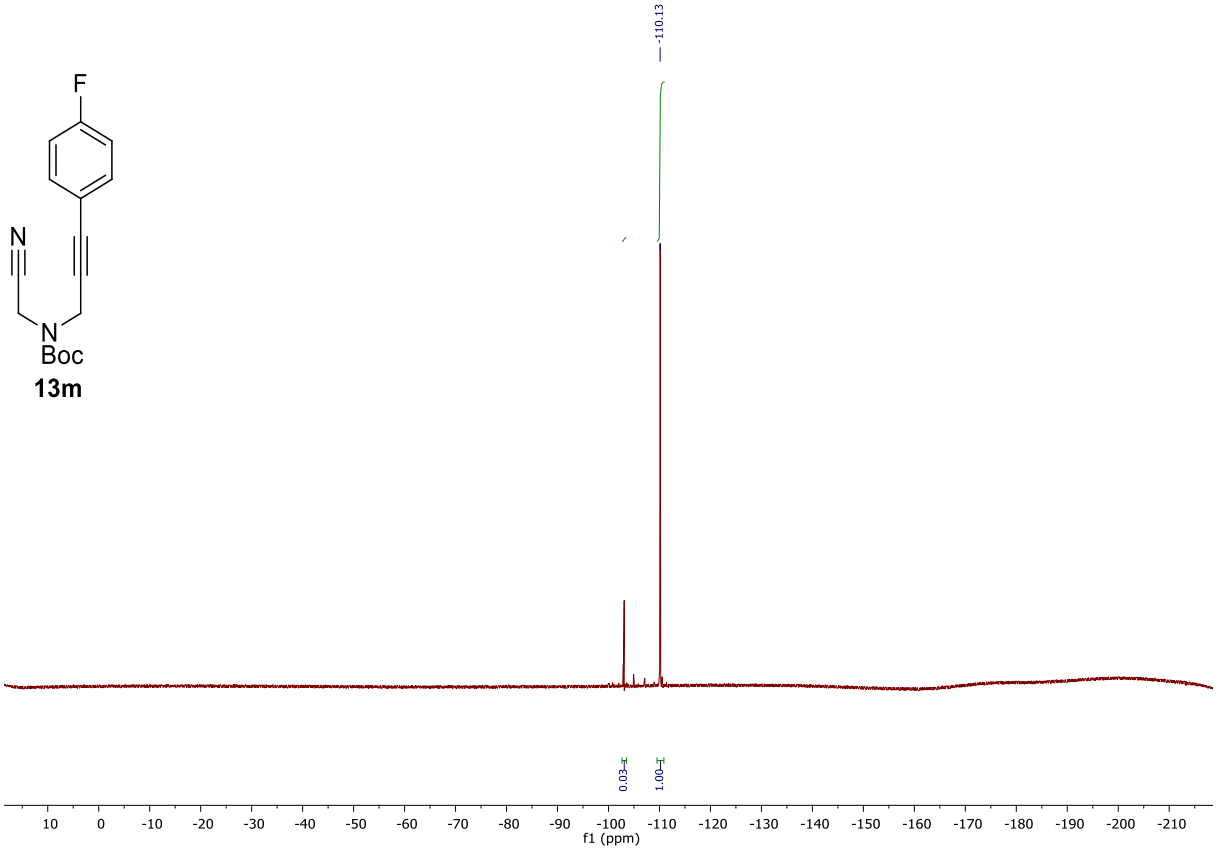
^{1}H-NMR (400 MHz, Chloroform-*d*)



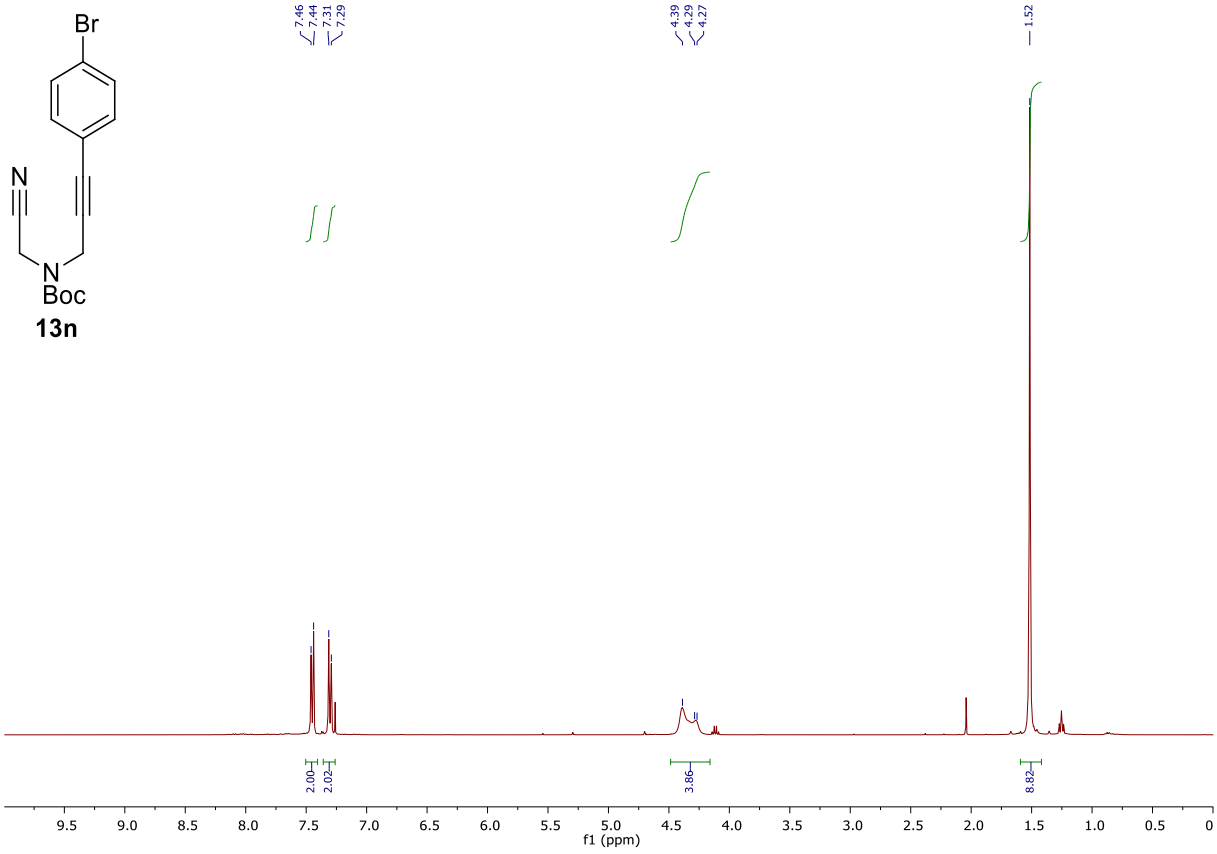
^{13}C-NMR (101 MHz, Chloroform-*d*)



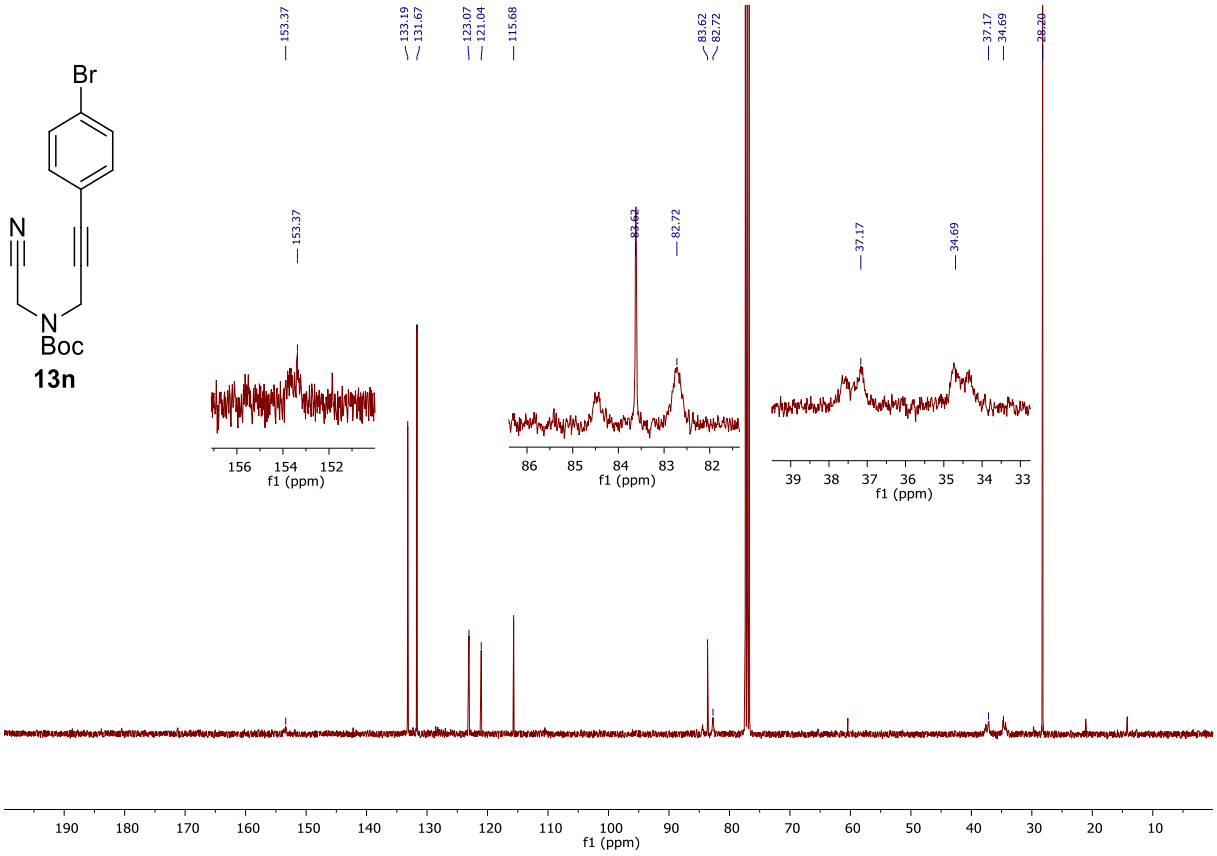
^{19}F-NMR (376 MHz, Chloroform-*d*)



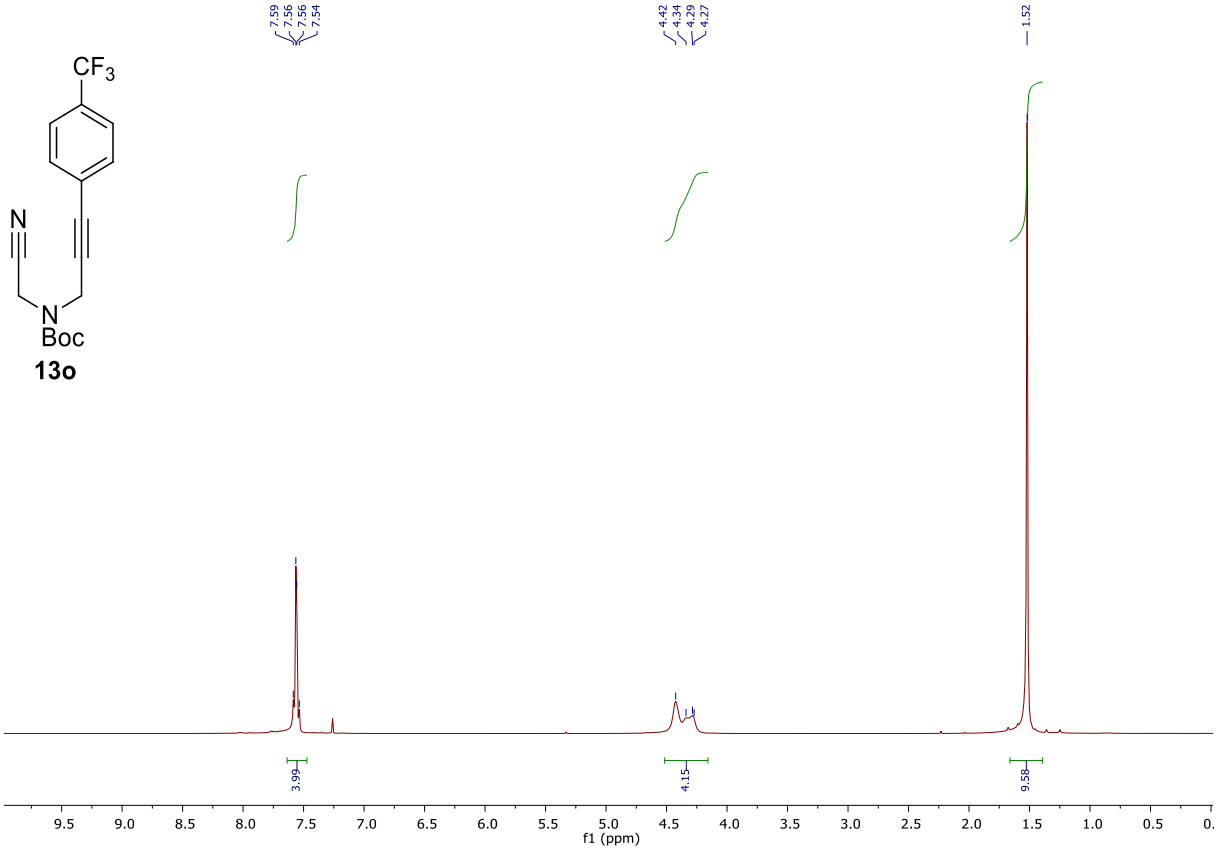
^{1}H-NMR (400 MHz, Chloroform-*d*)



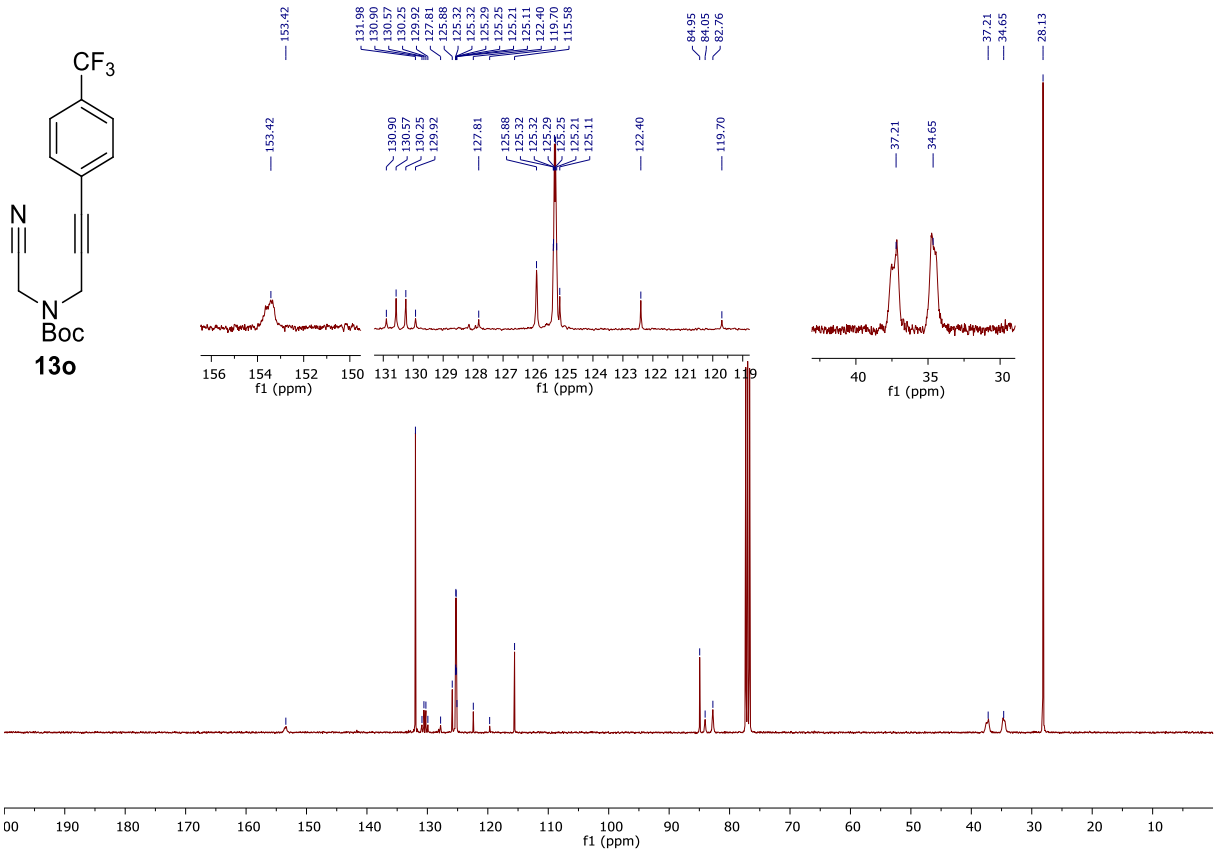
^{13}C-NMR (101 MHz, Chloroform-*d*)



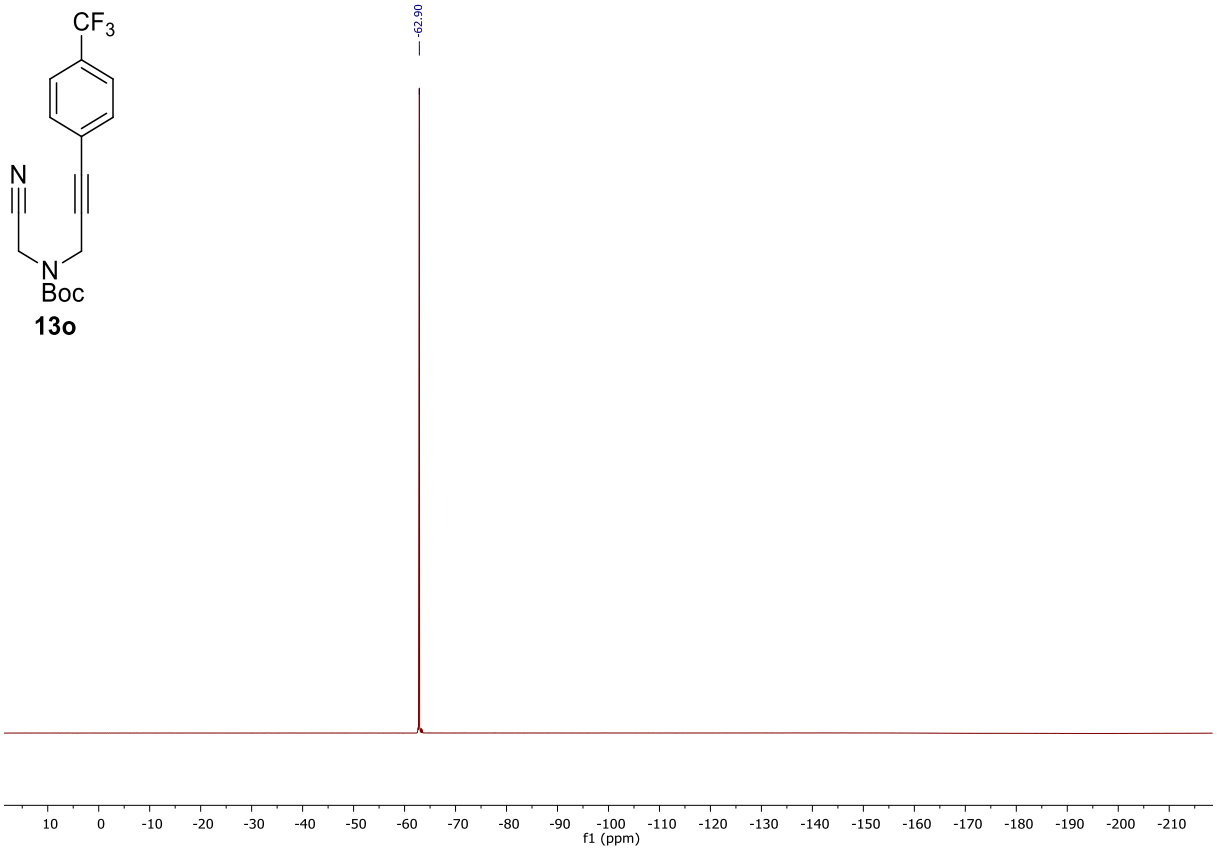
^{1}H-NMR (400 MHz, Chloroform-*d*)



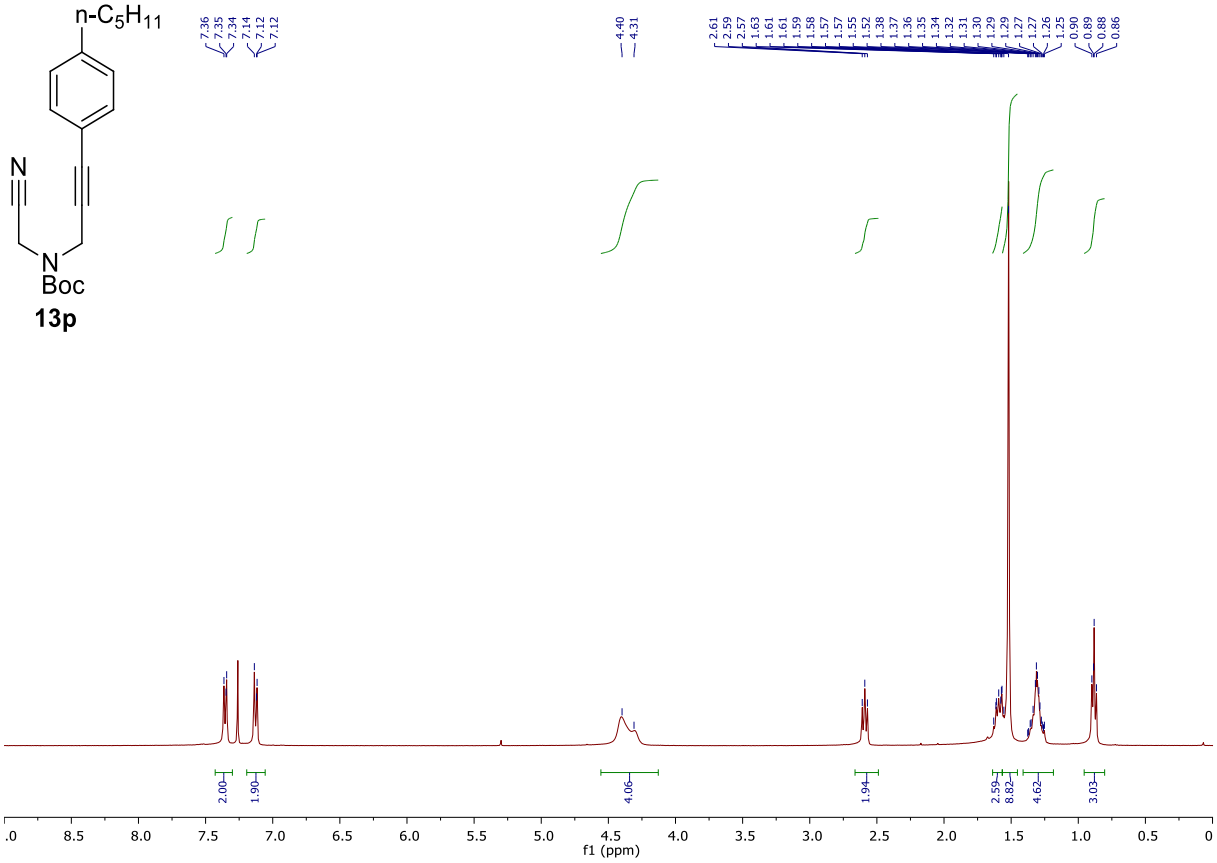
^{13}C-NMR (101 MHz, Chloroform-*d*)



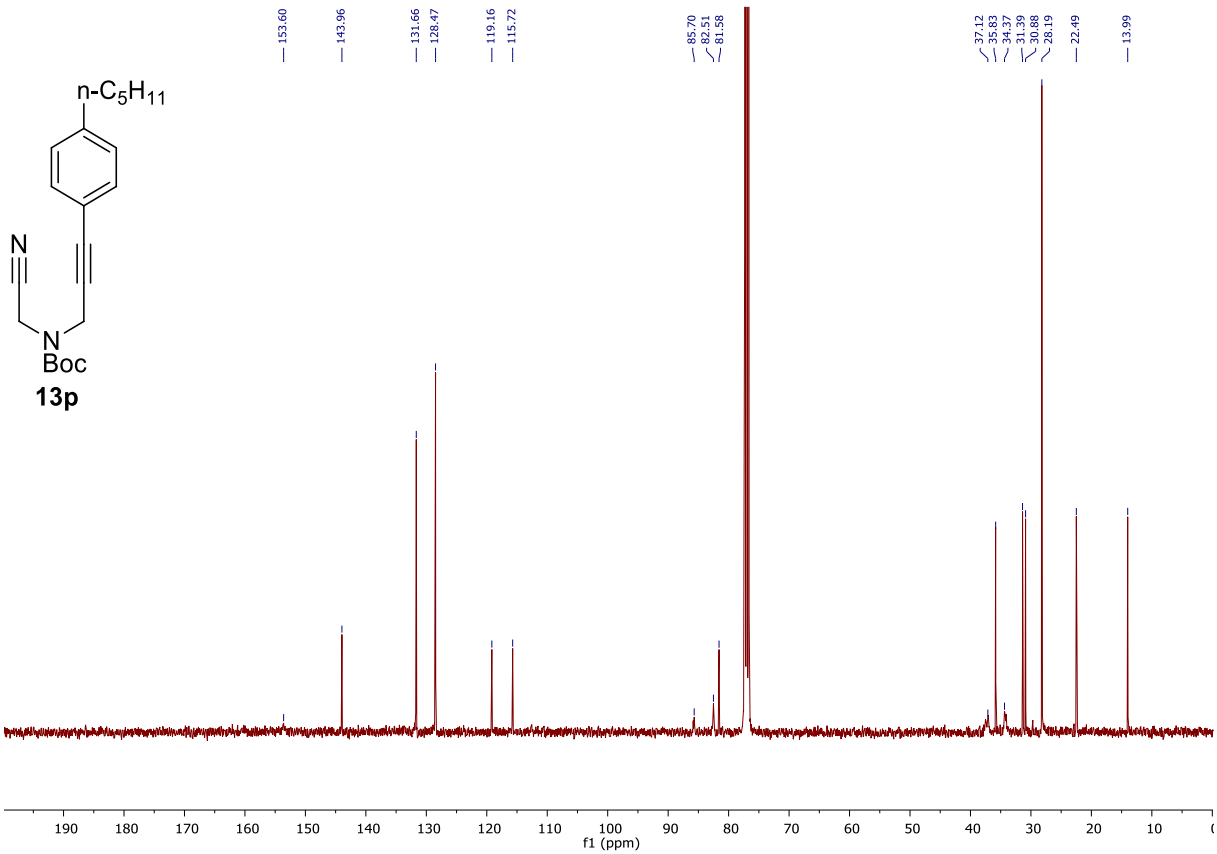
^{19}F-NMR (376 MHz, Chloroform-*d*)



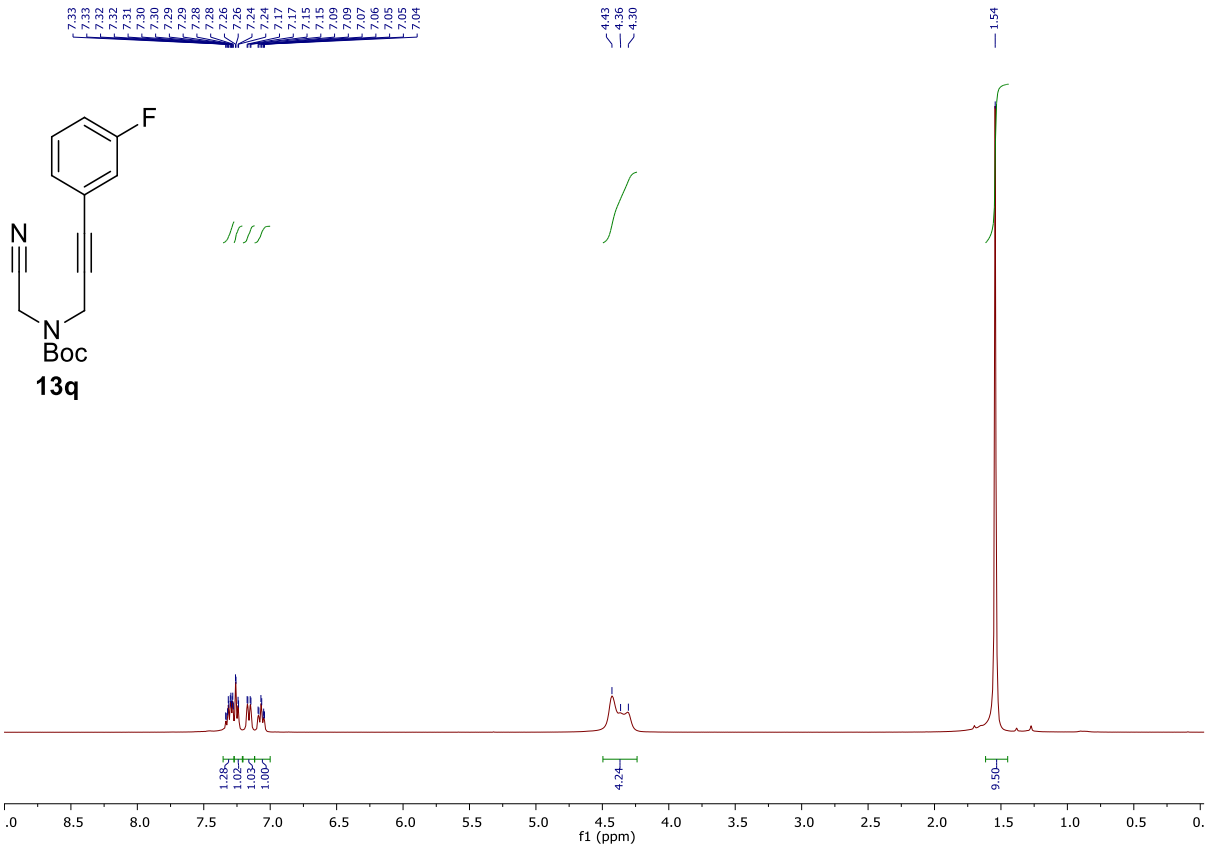
^{1}H-NMR (400 MHz, Chloroform-*d*)



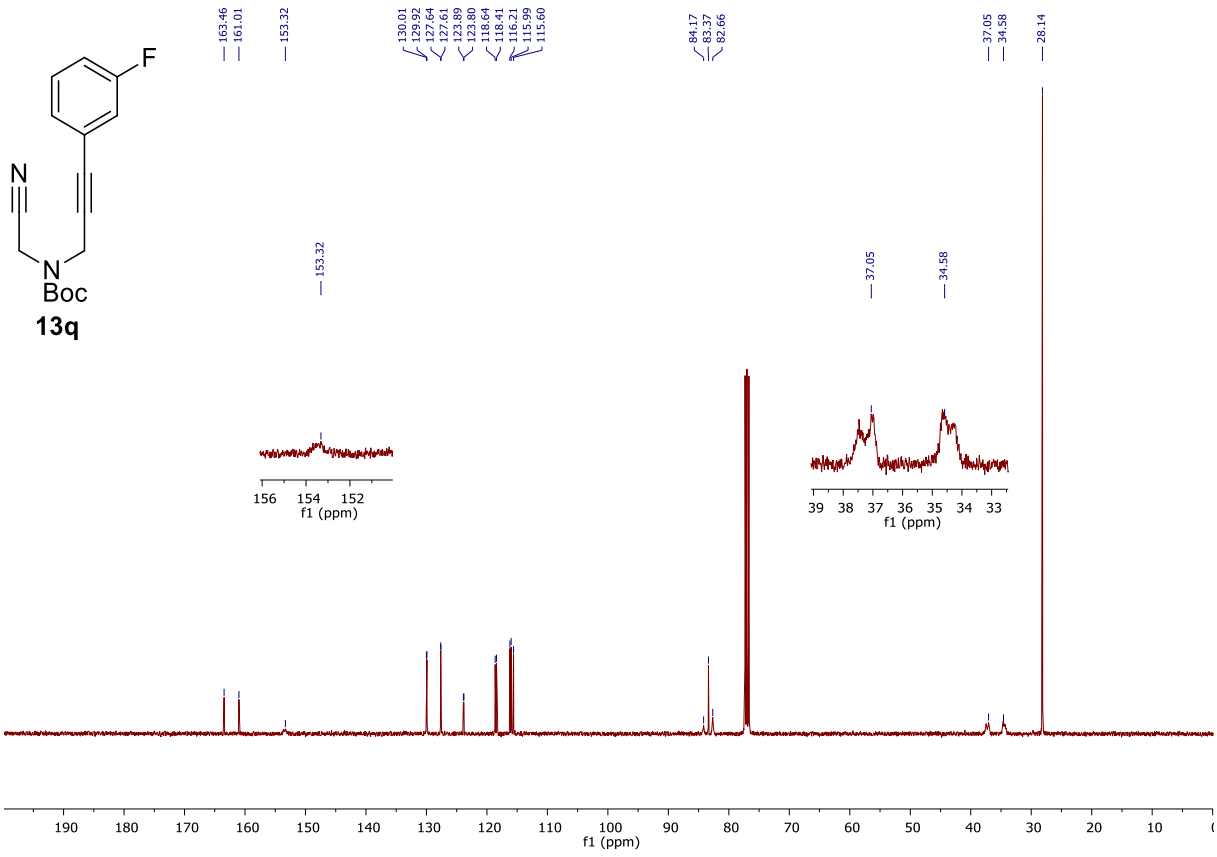
^{13}C-NMR (101 MHz, Chloroform-*d*)



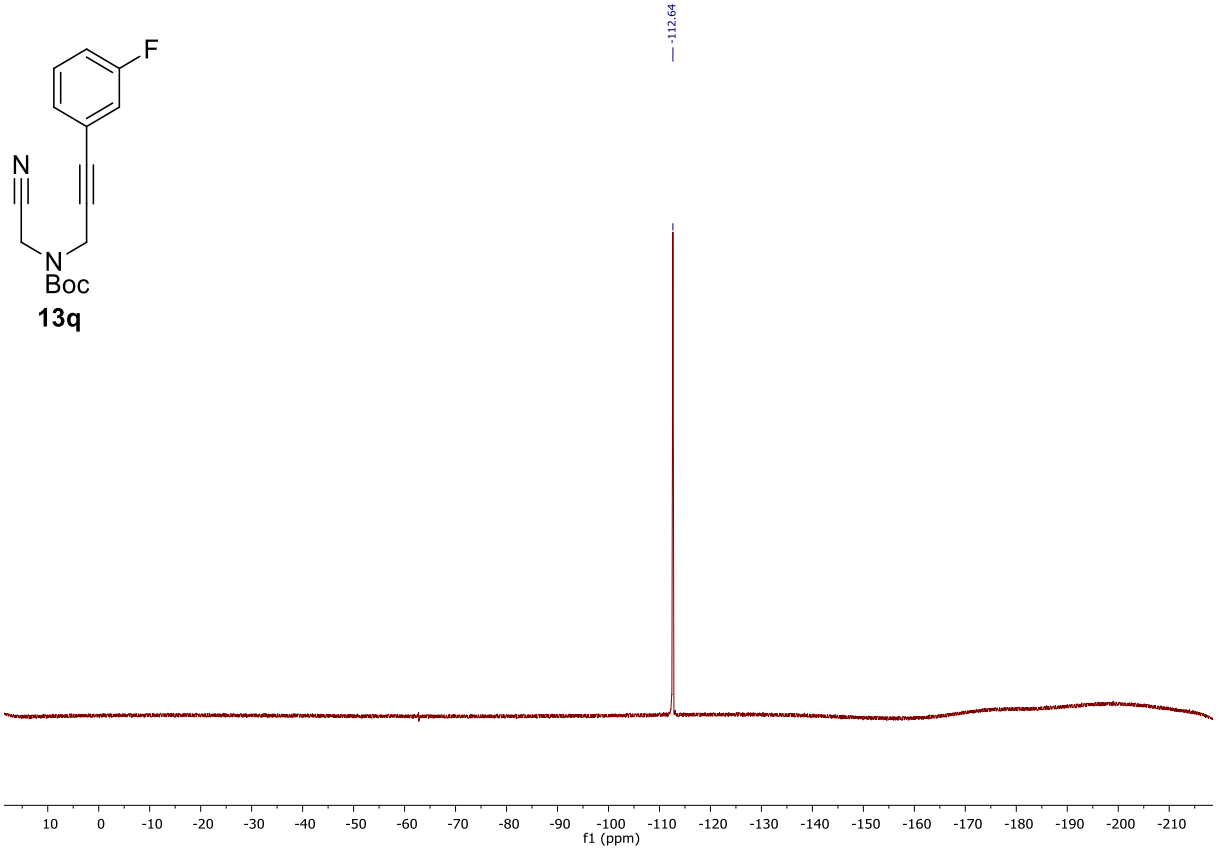
^{1}H-NMR (400 MHz, Chloroform-*d*)



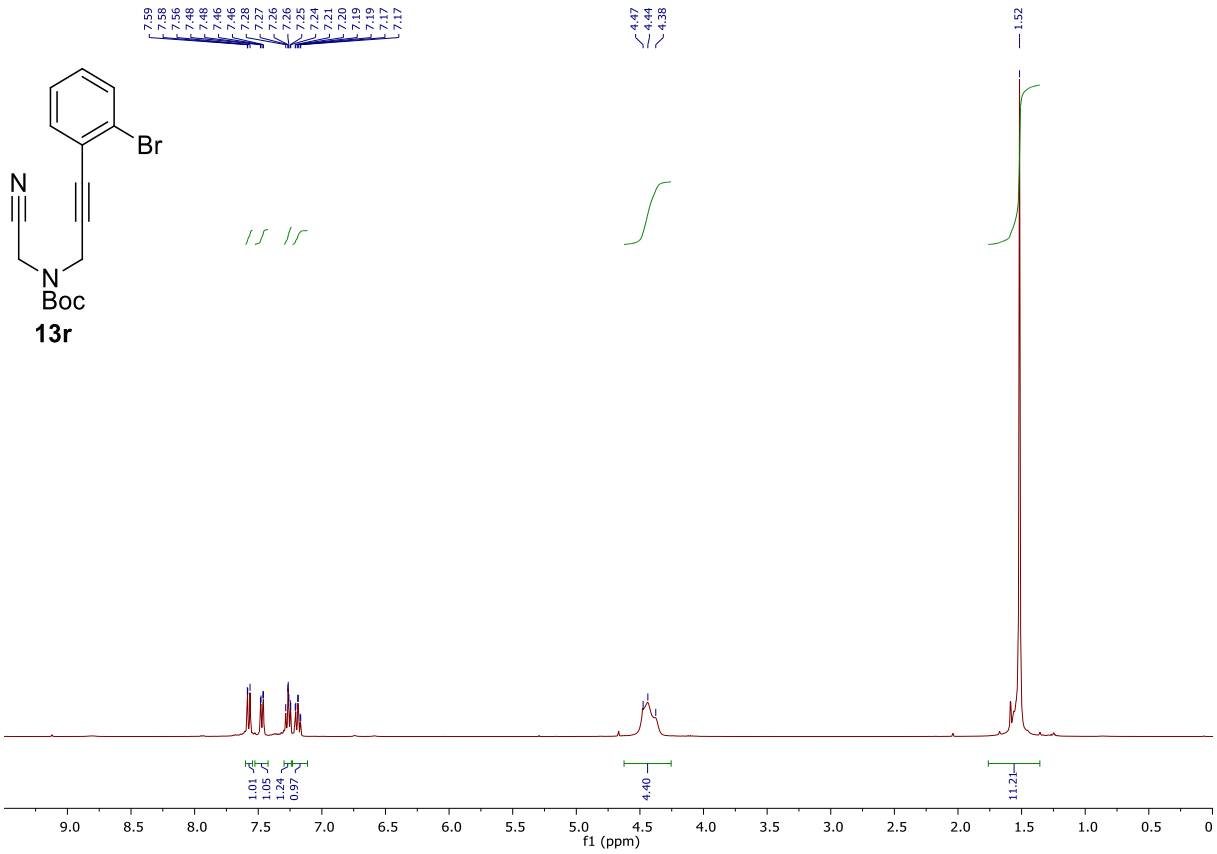
^{13}C-NMR (101 MHz, Chloroform-*d*)



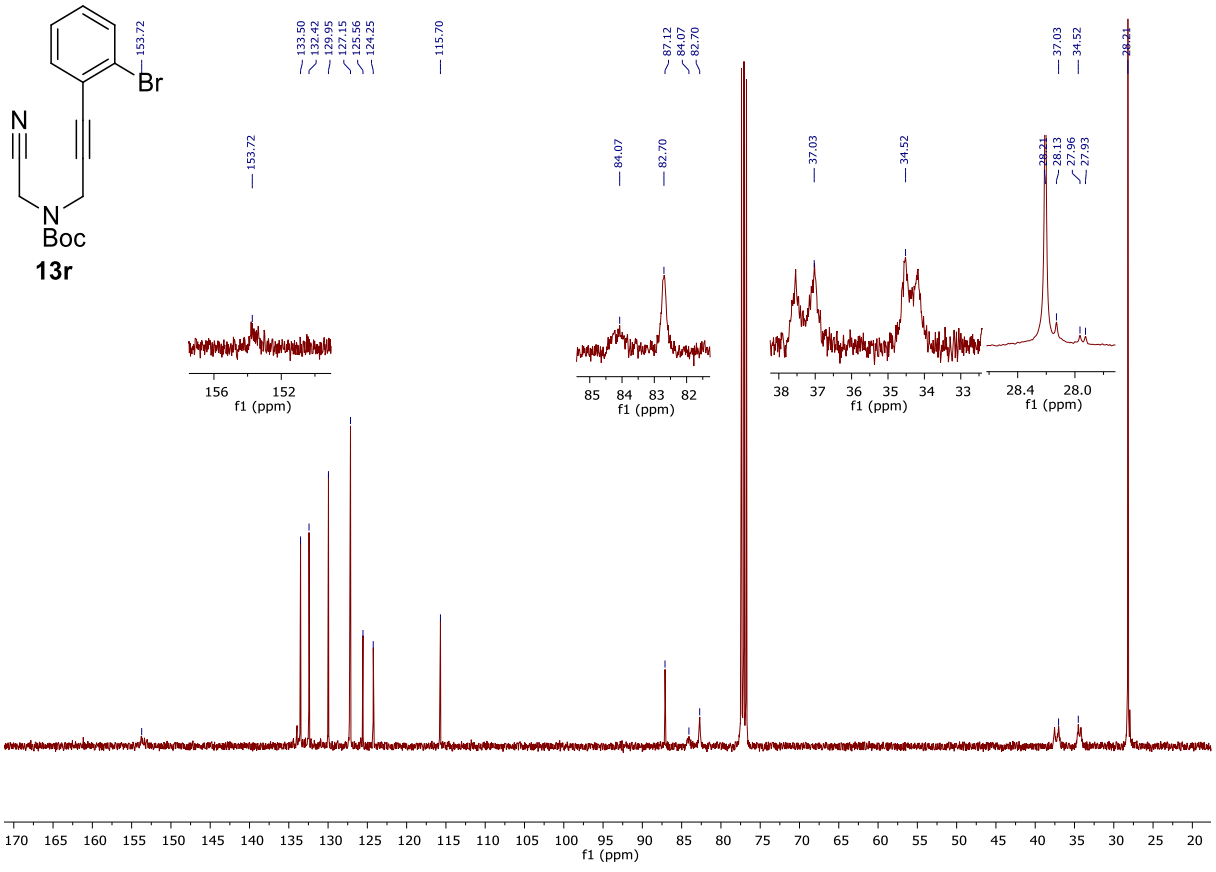
^{19}F-NMR (376 MHz, Chloroform-*d*)



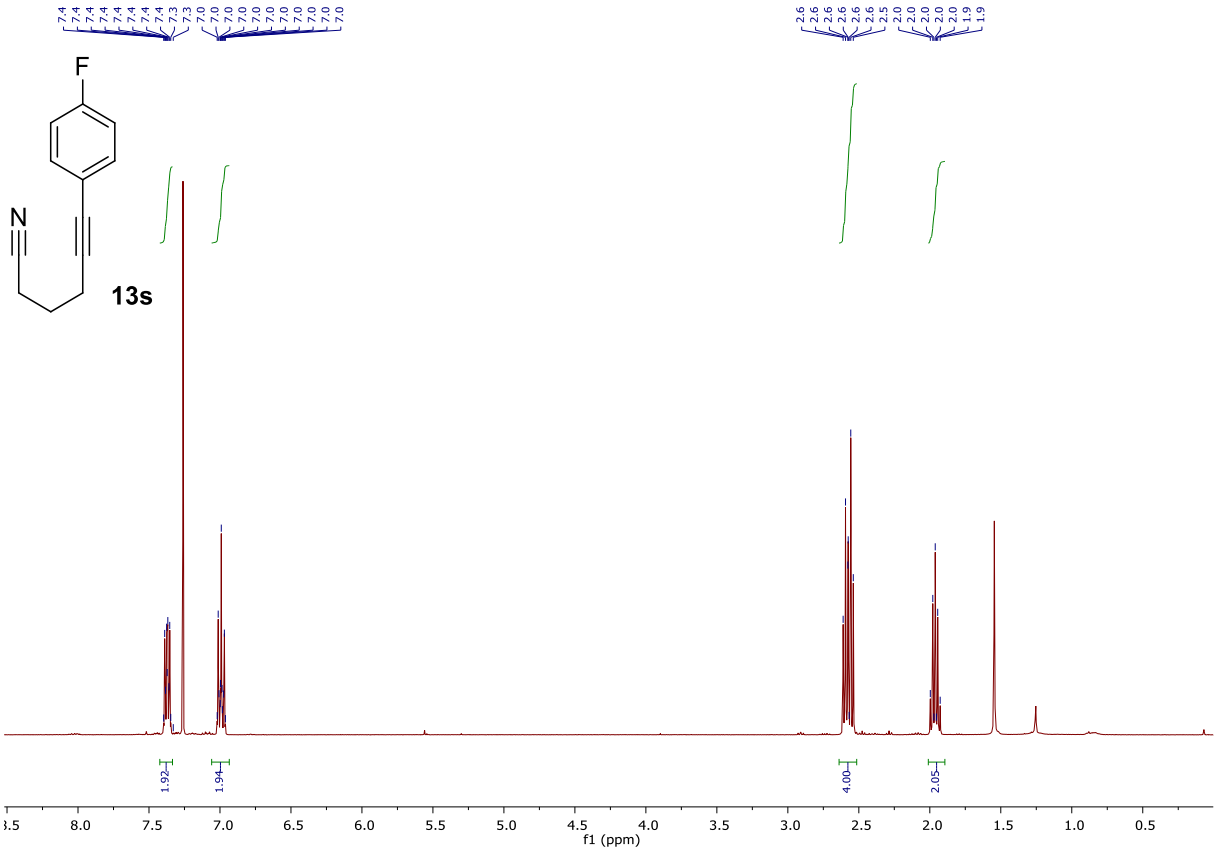
^{1}H-NMR (400 MHz, Chloroform-*d*)



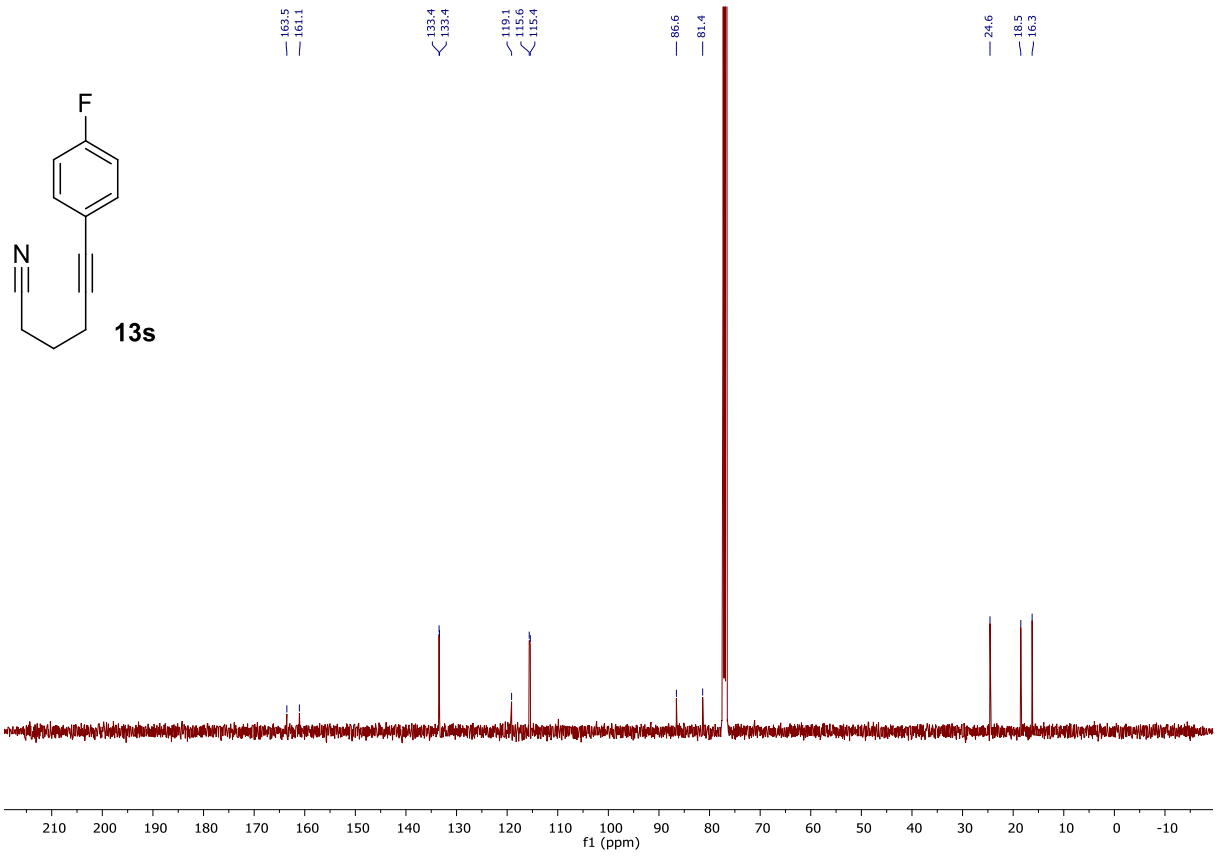
^{13}C-NMR (101 MHz, Chloroform-*d*)



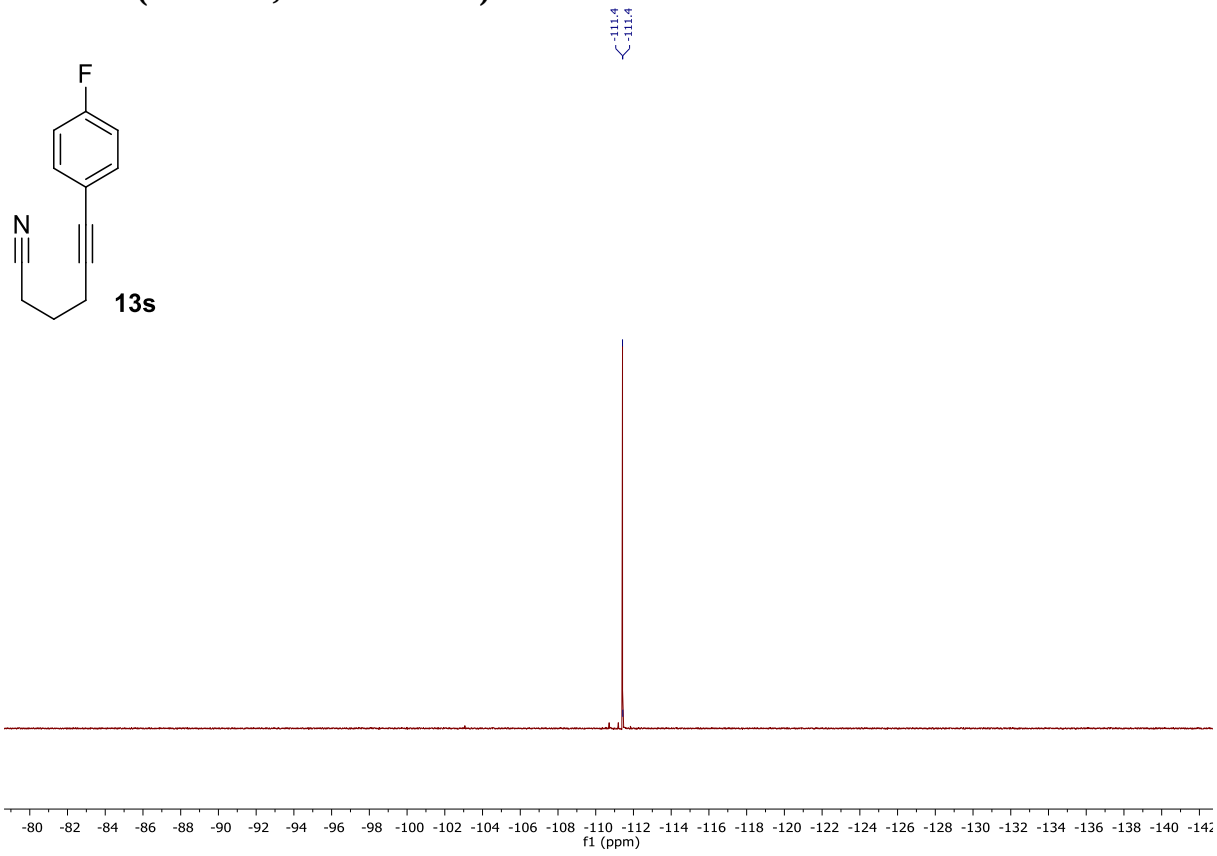
^{1}H-NMR (400 MHz, Chloroform-*d*)



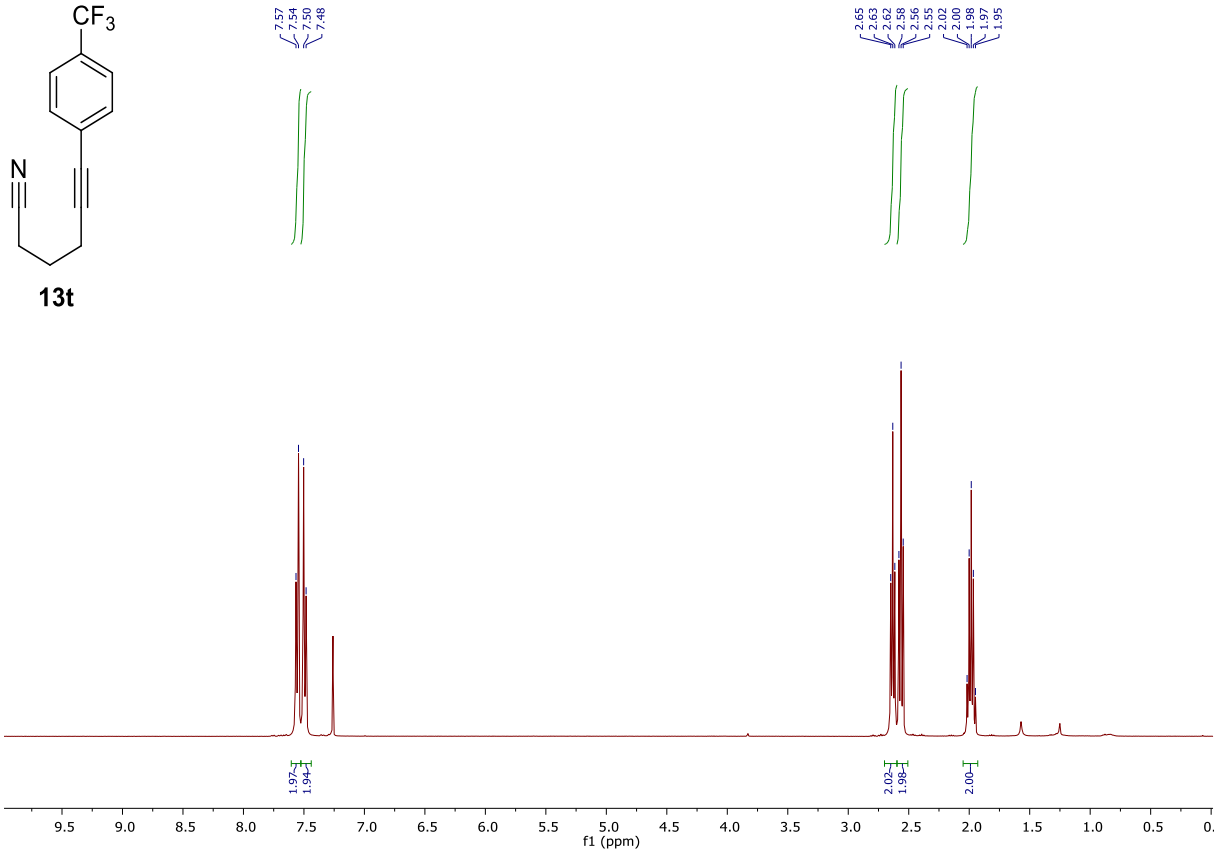
^{13}C-NMR (101 MHz, Chloroform-*d*)



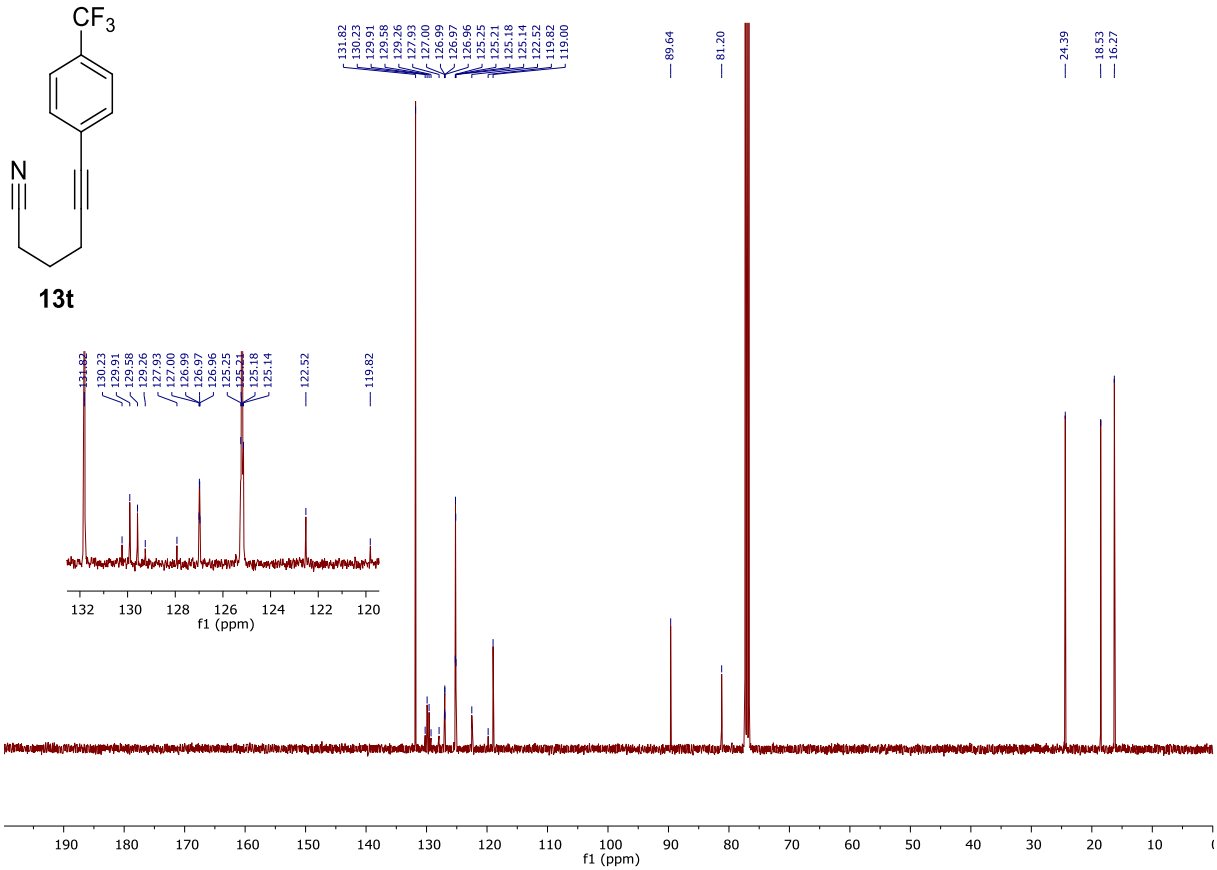
^{19}F NMR (376 MHz, Chloroform-*d*)



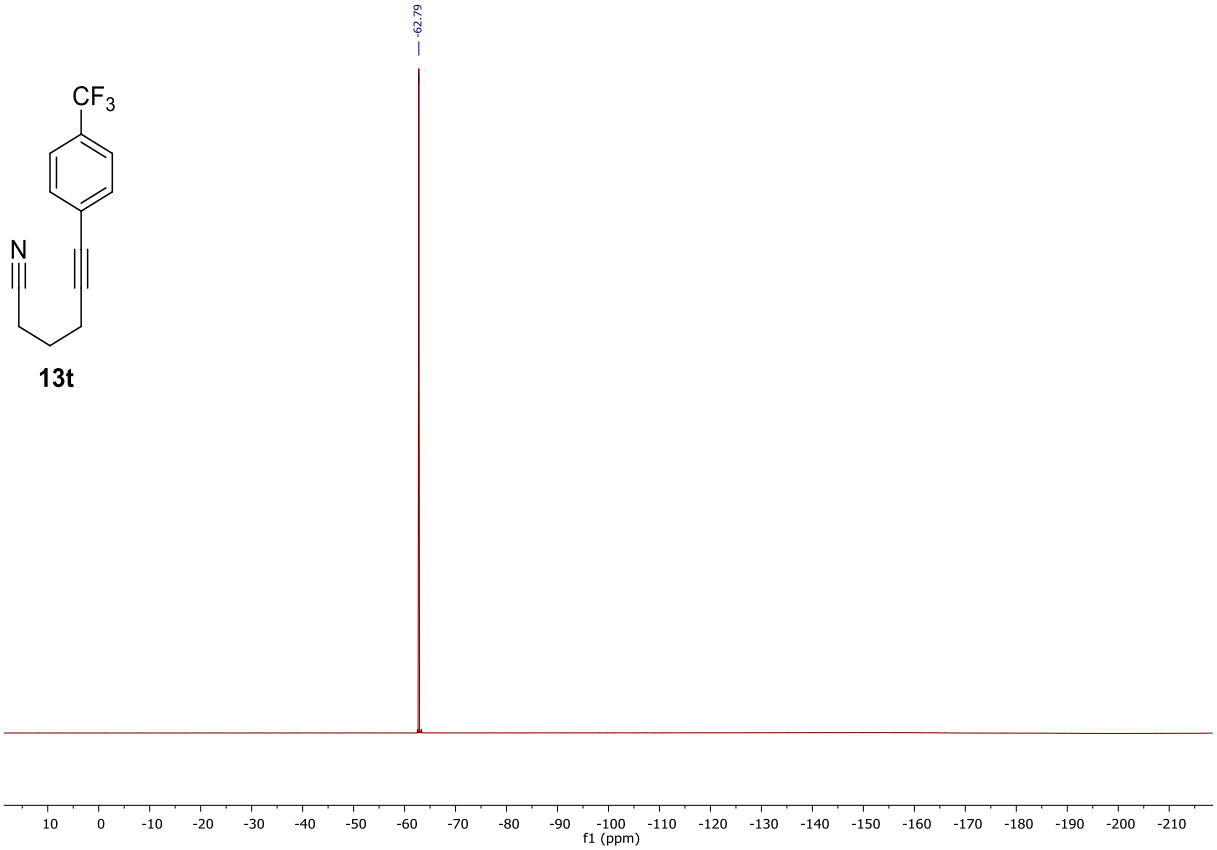
^{1}H-NMR (400 MHz, Chloroform-*d*)



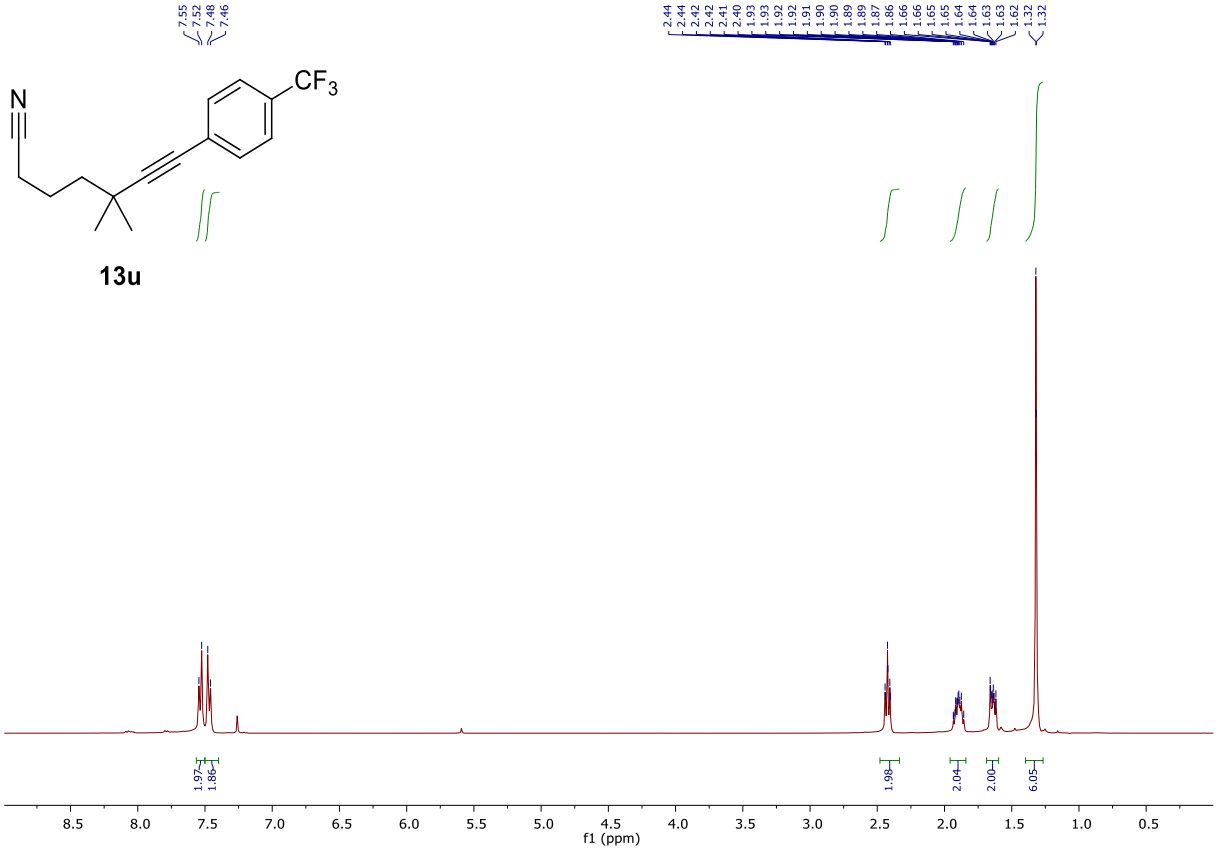
^{13}C-NMR (101 MHz, Chloroform-*d*)



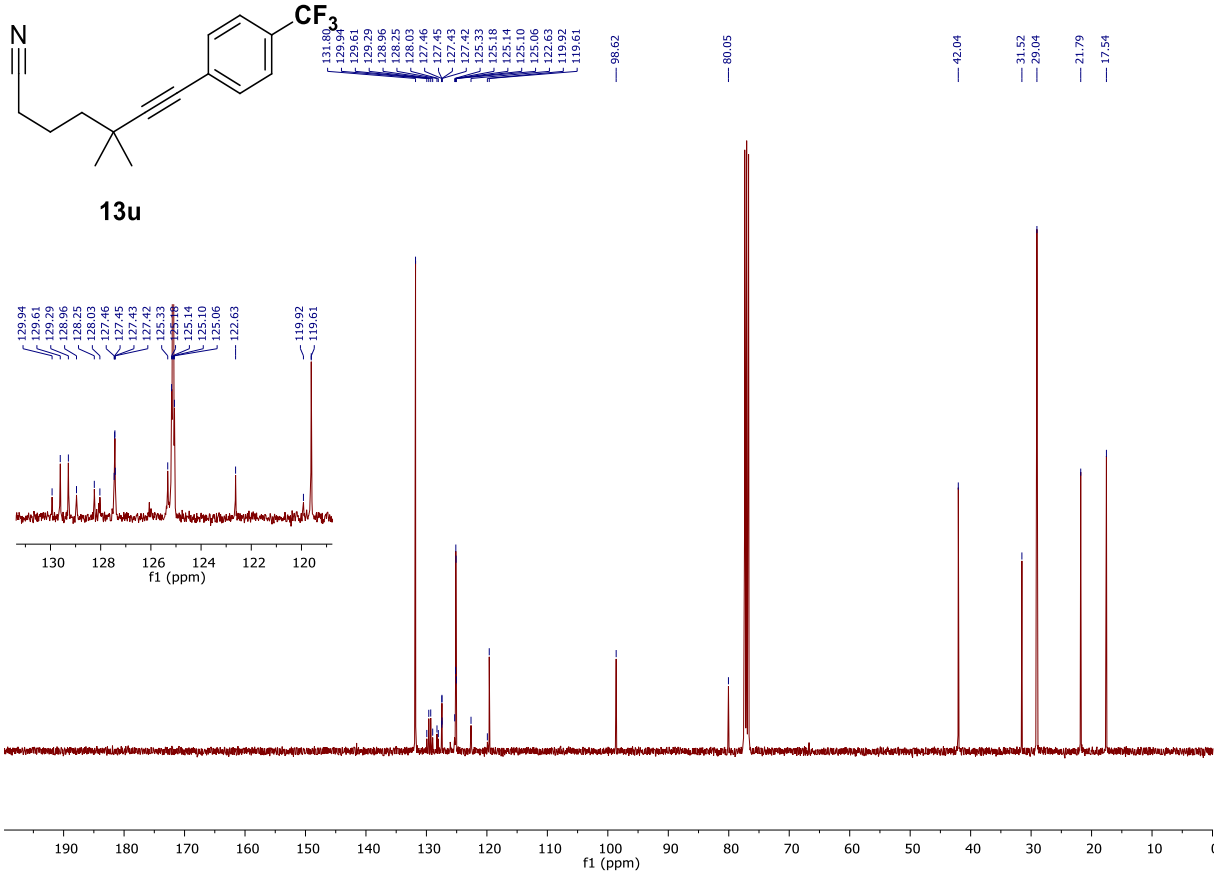
^{19}F-NMR (376 MHz, Chloroform-*d*)



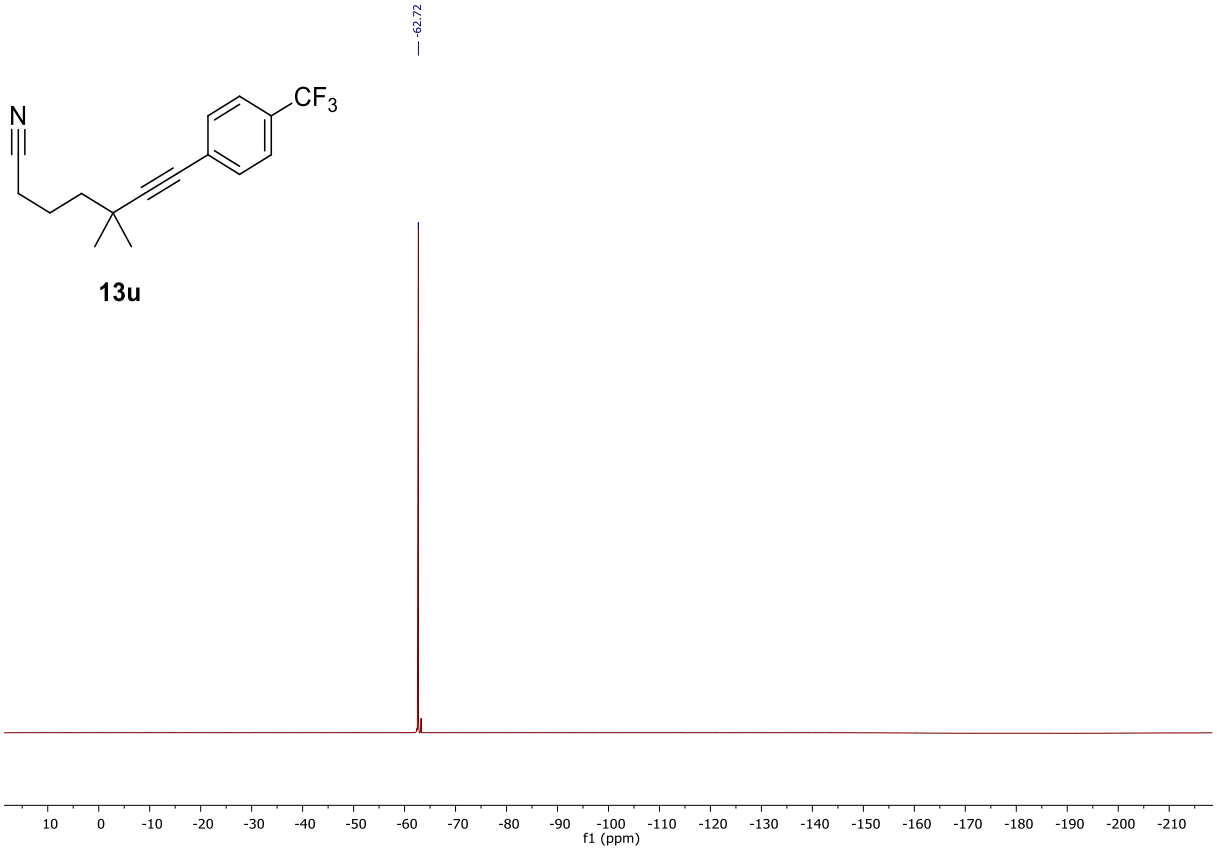
^{1}H-NMR (400 MHz, Chloroform-*d*)



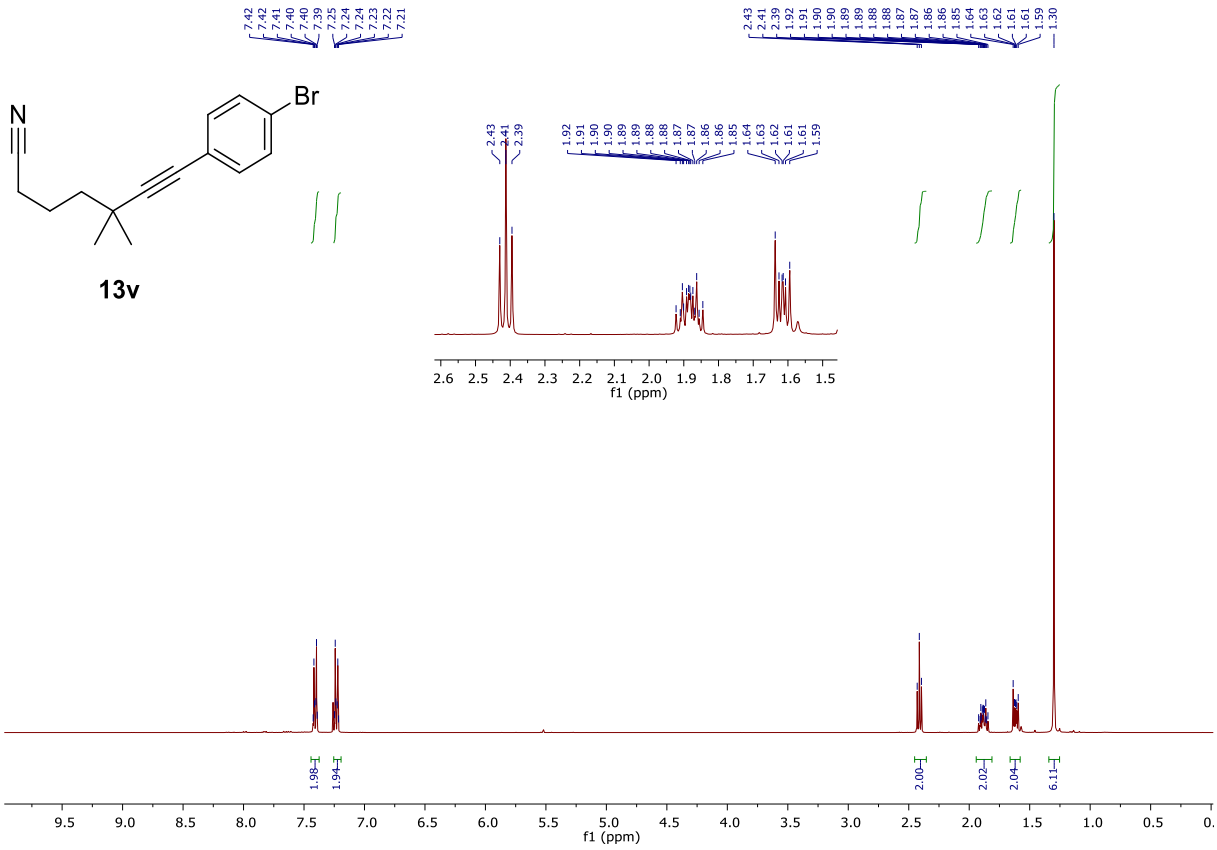
^{13}C-NMR (101 MHz, Chloroform-*d*)



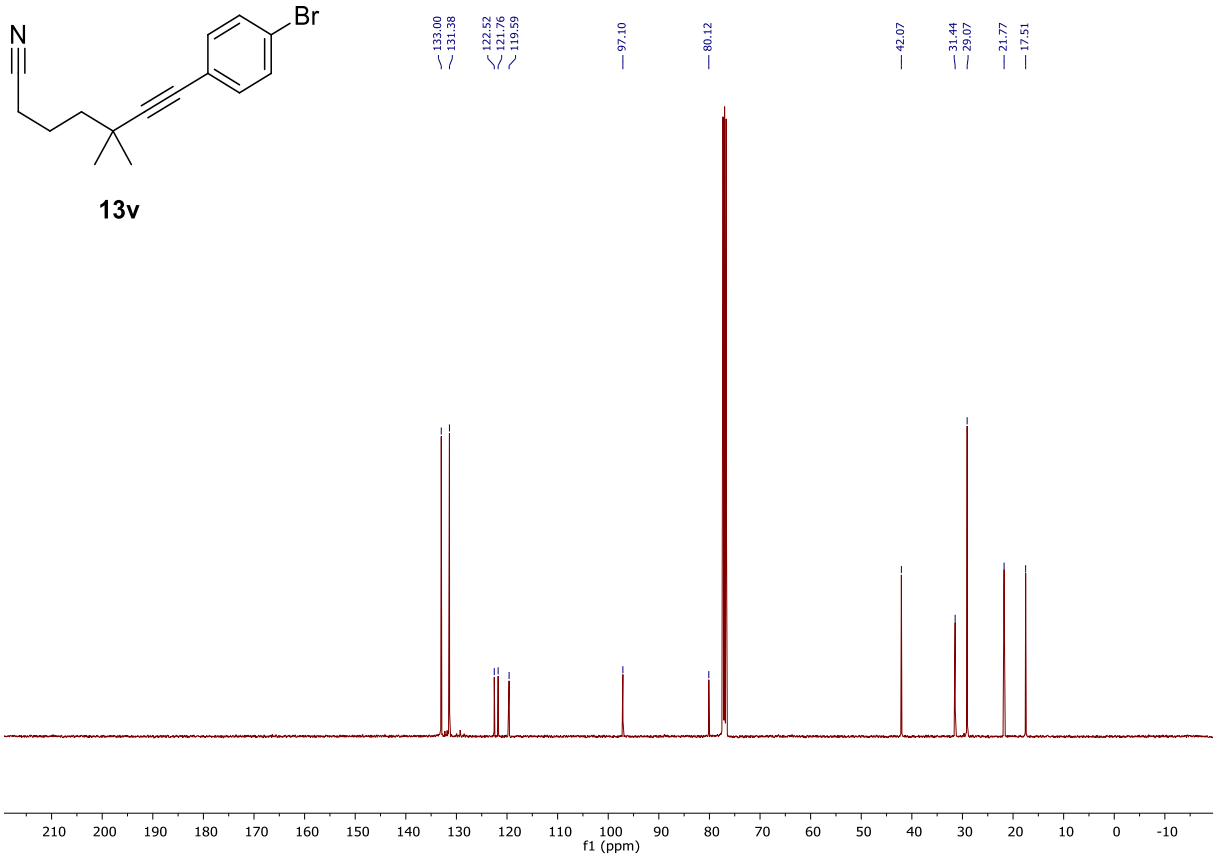
^{19}F-NMR (376 MHz, Chloroform-*d*)



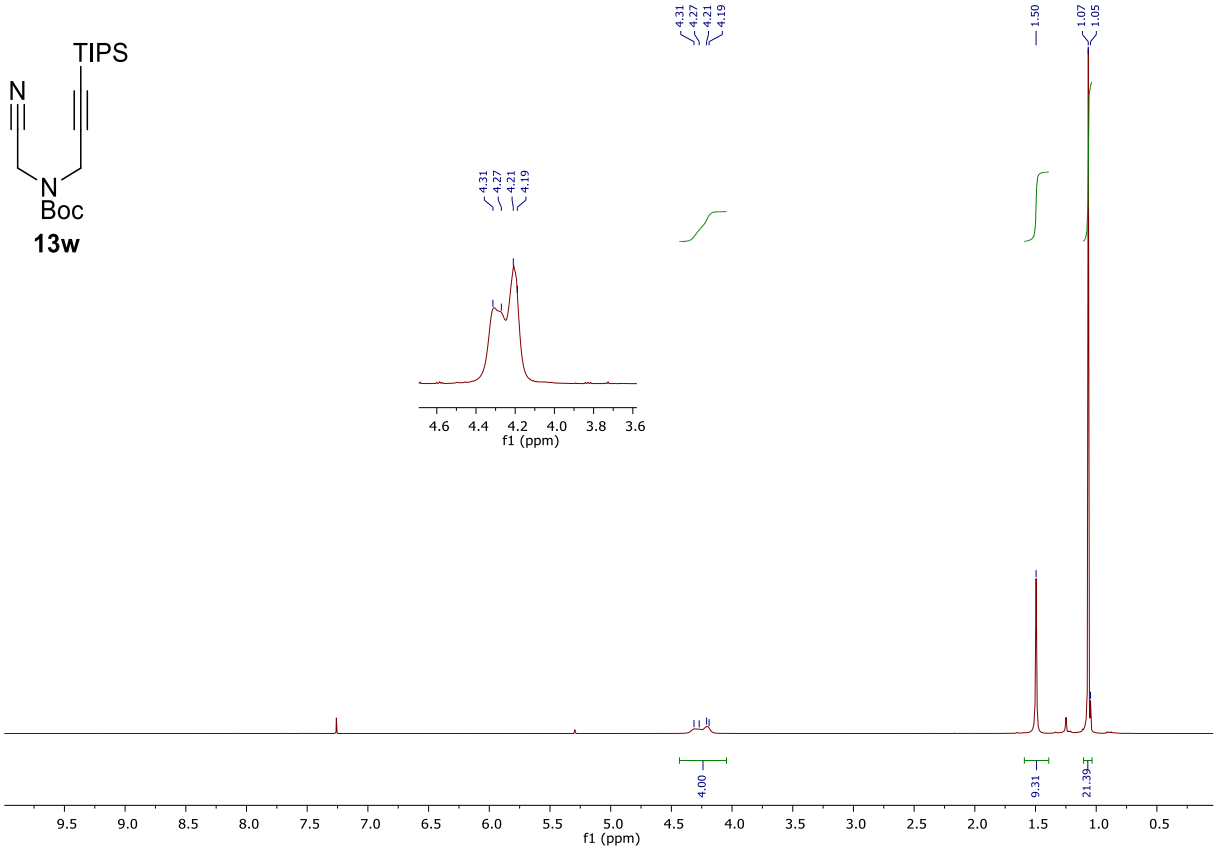
^{1}H-NMR (400 MHz, Chloroform-*d*)



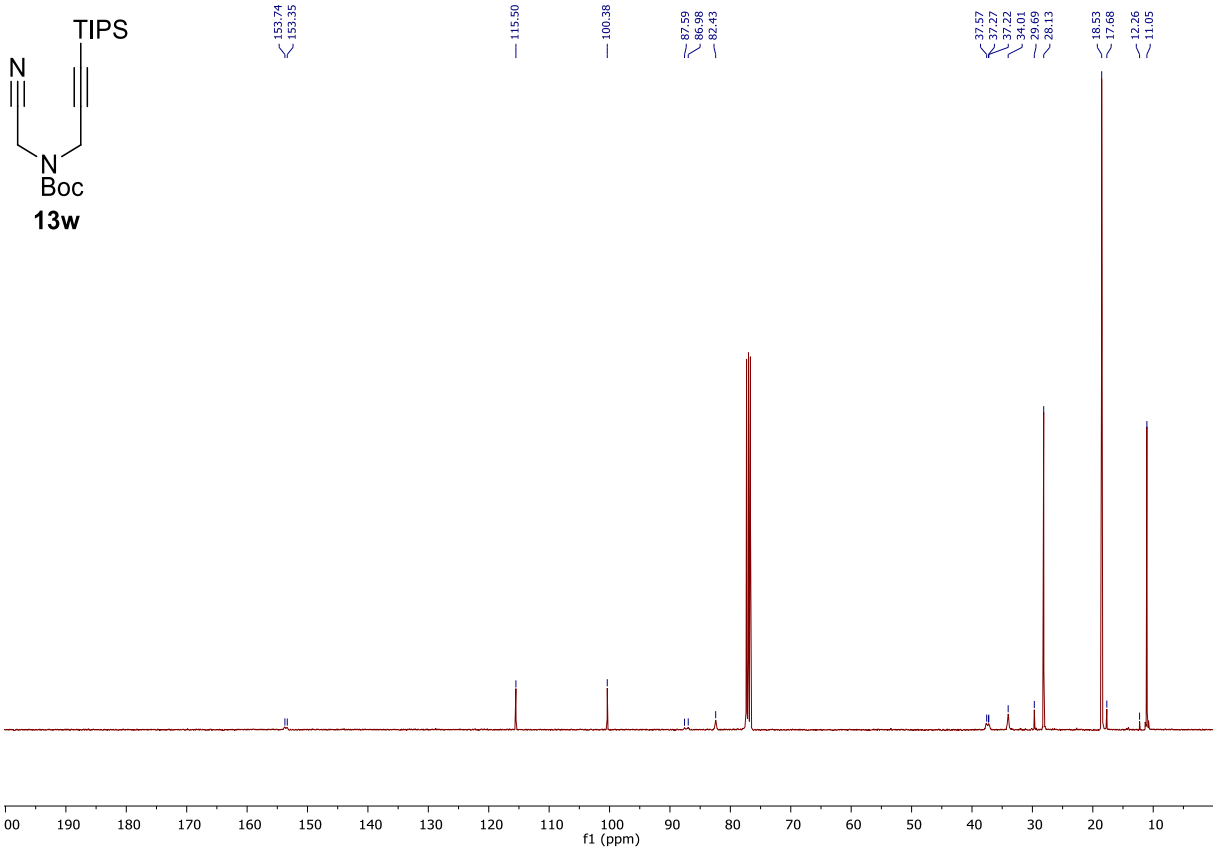
^{13}C-NMR (101 MHz, Chloroform-*d*)



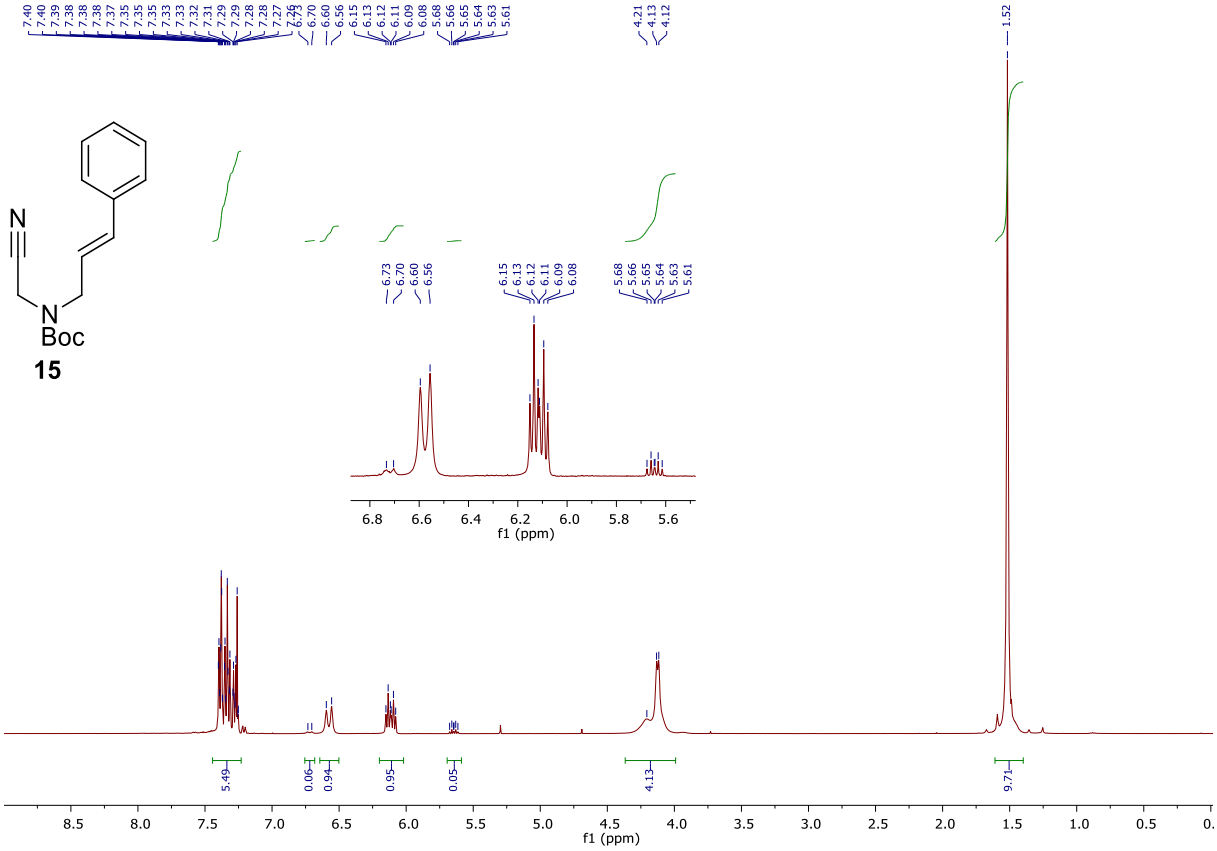
^{1}H-NMR (400 MHz, Chloroform-*d*)



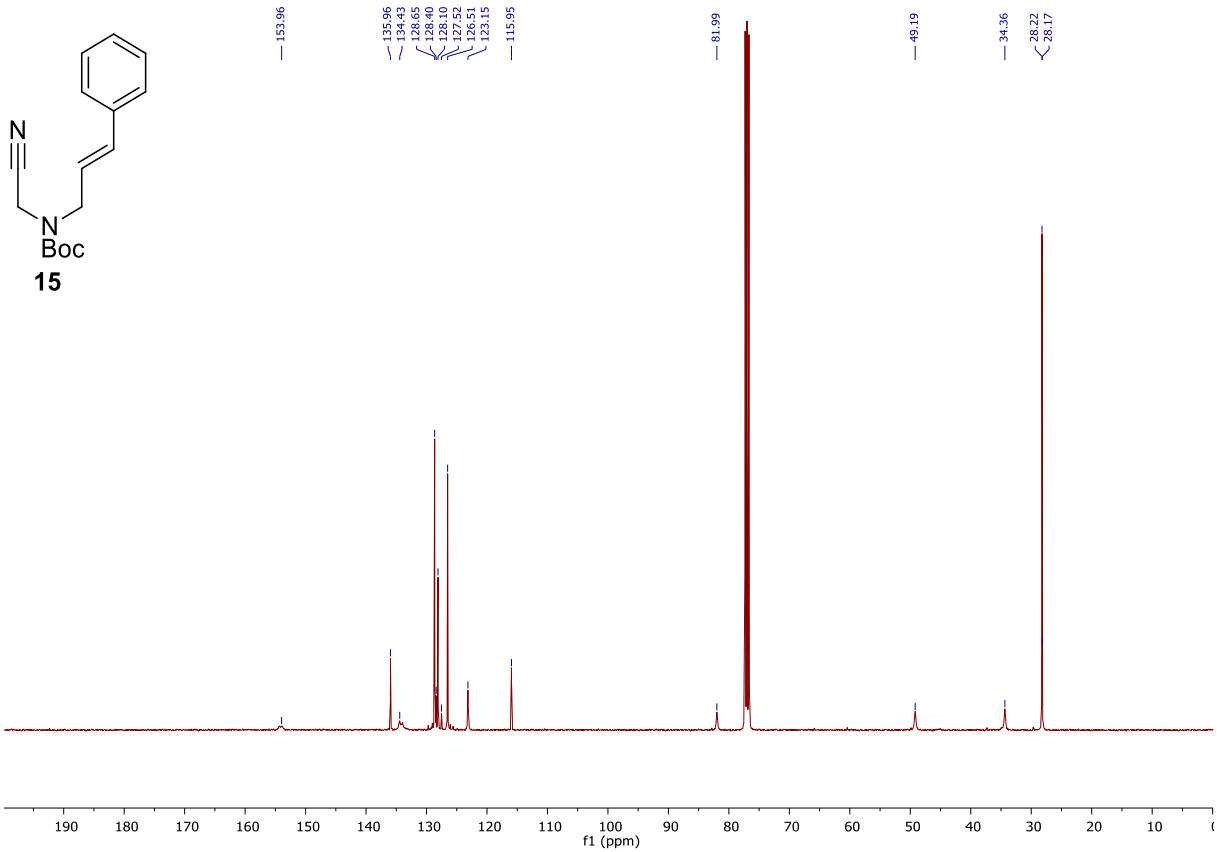
^{13}C-NMR (101 MHz, Chloroform-*d*)



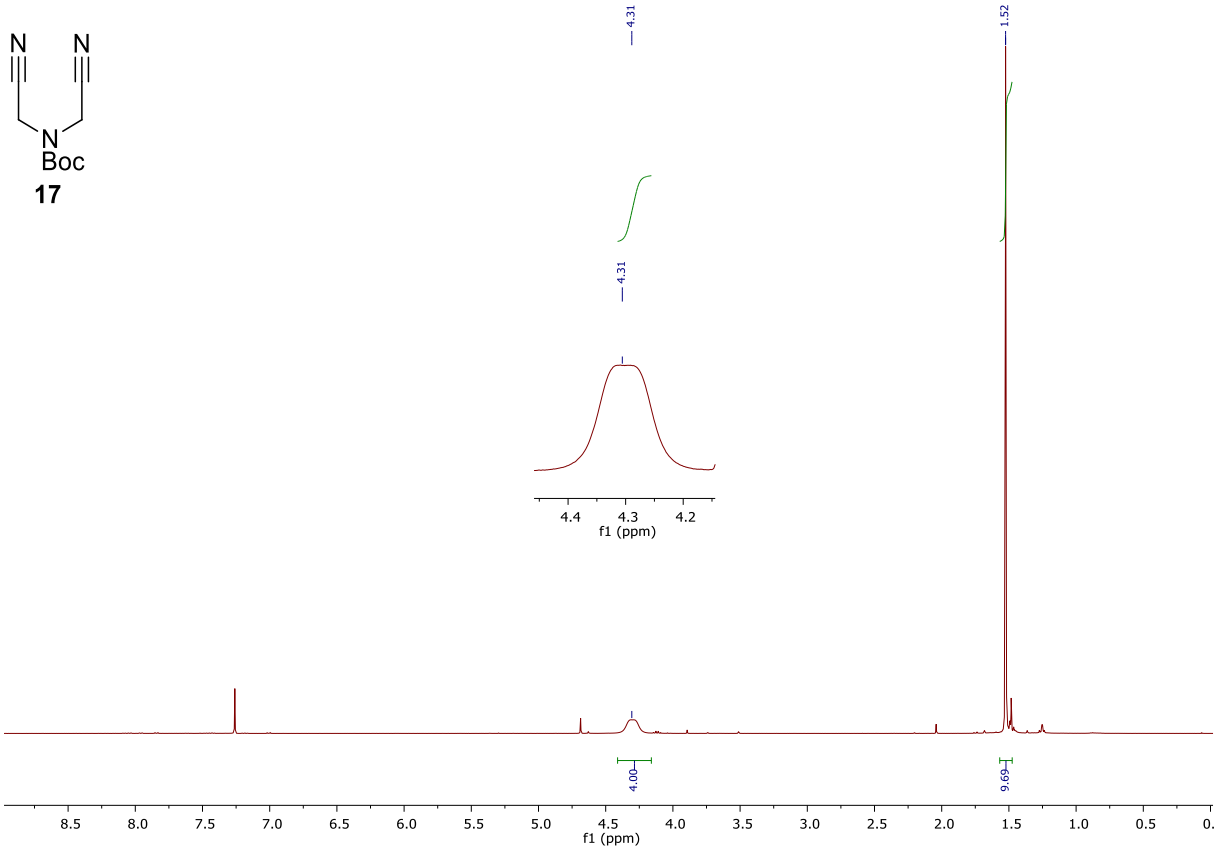
^{1}H-NMR (400 MHz, Chloroform-*d*)



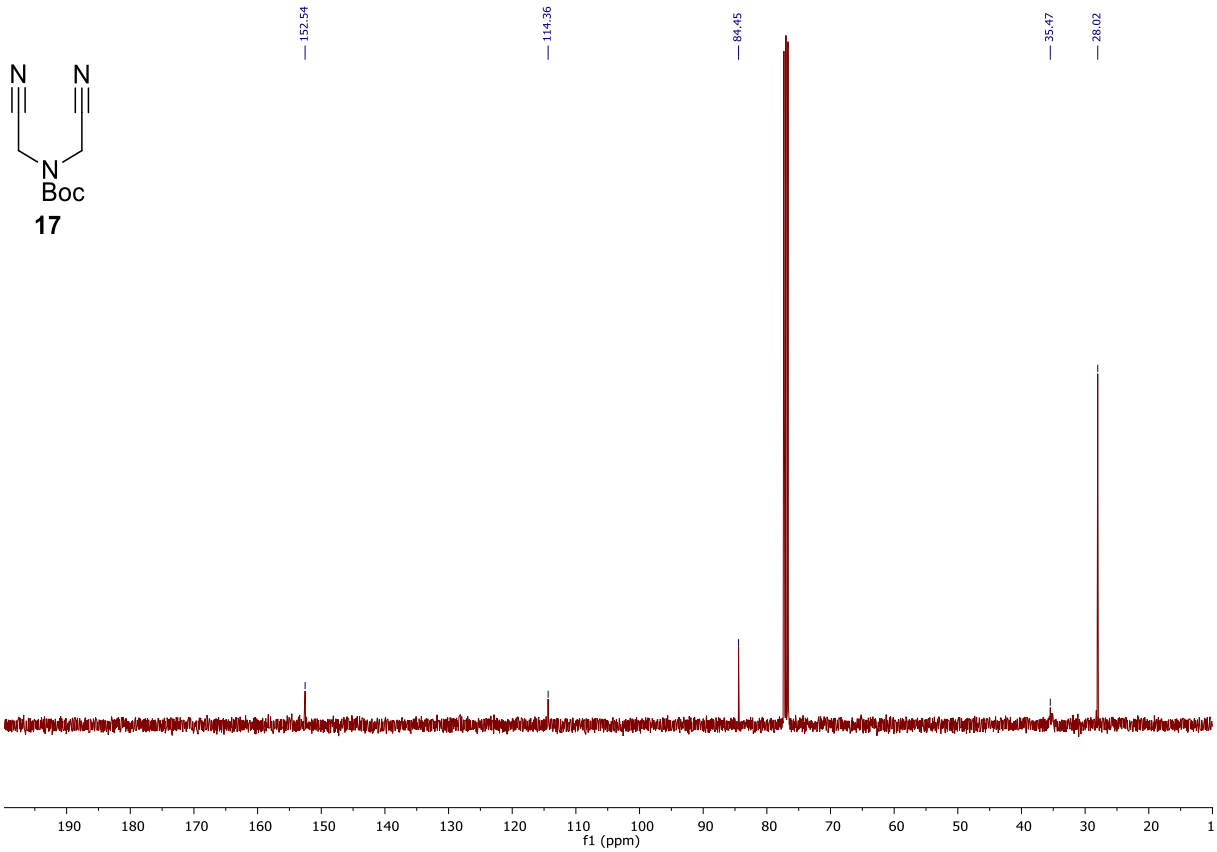
^{13}C-NMR (101 MHz, Chloroform-*d*)



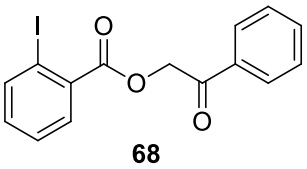
^{1}H-NMR (400 MHz, Chloroform-*d*)



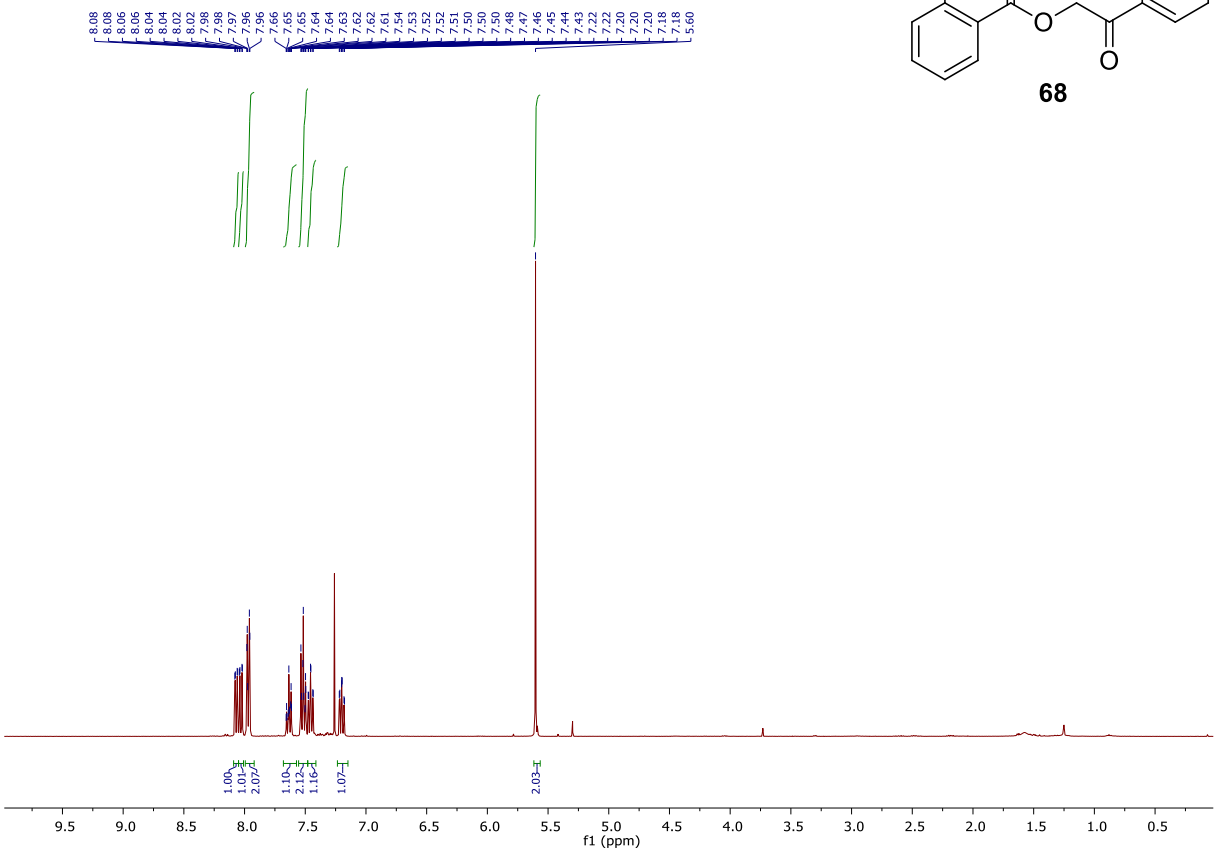
^{13}C-NMR (101 MHz, Chloroform-*d*)



^{1}H-NMR (400 MHz, Chloroform-*d*)



68



^{13}C-NMR (101 MHz, Chloroform-*d*)

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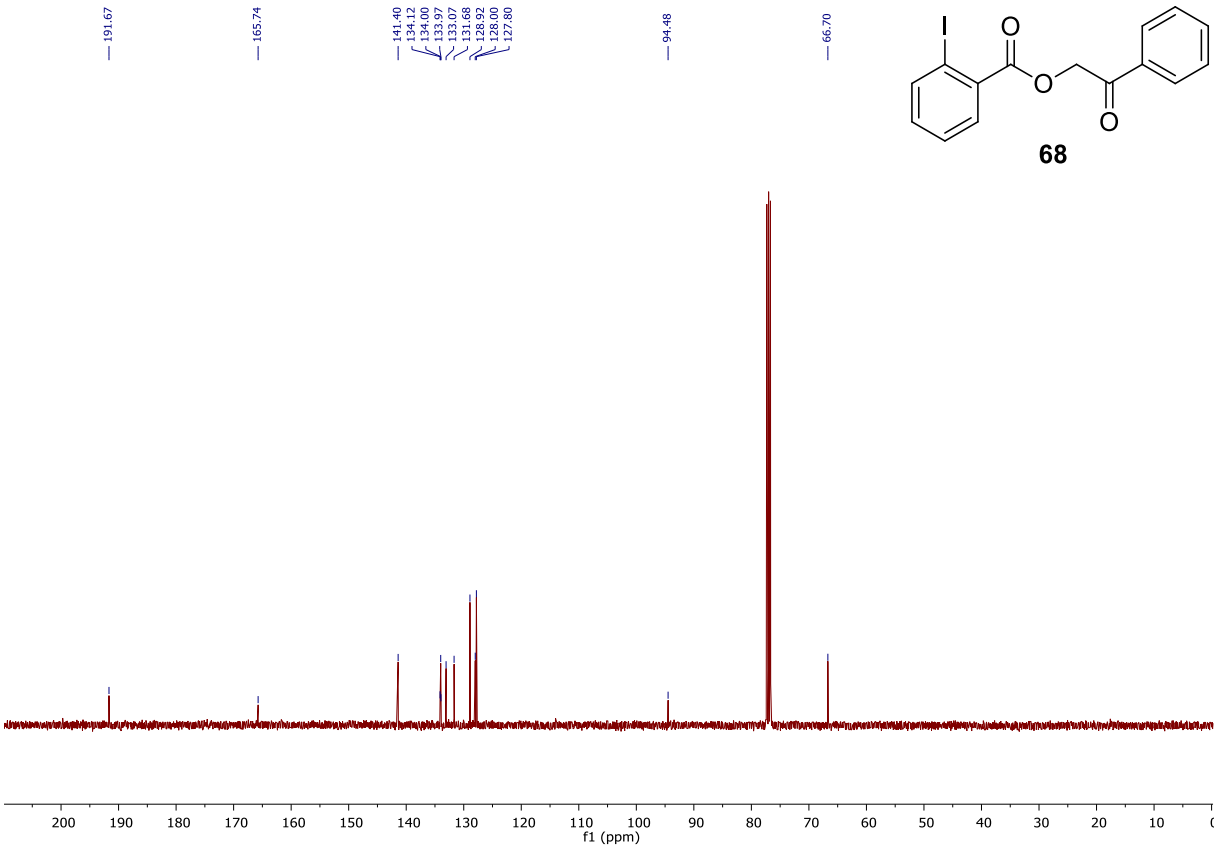
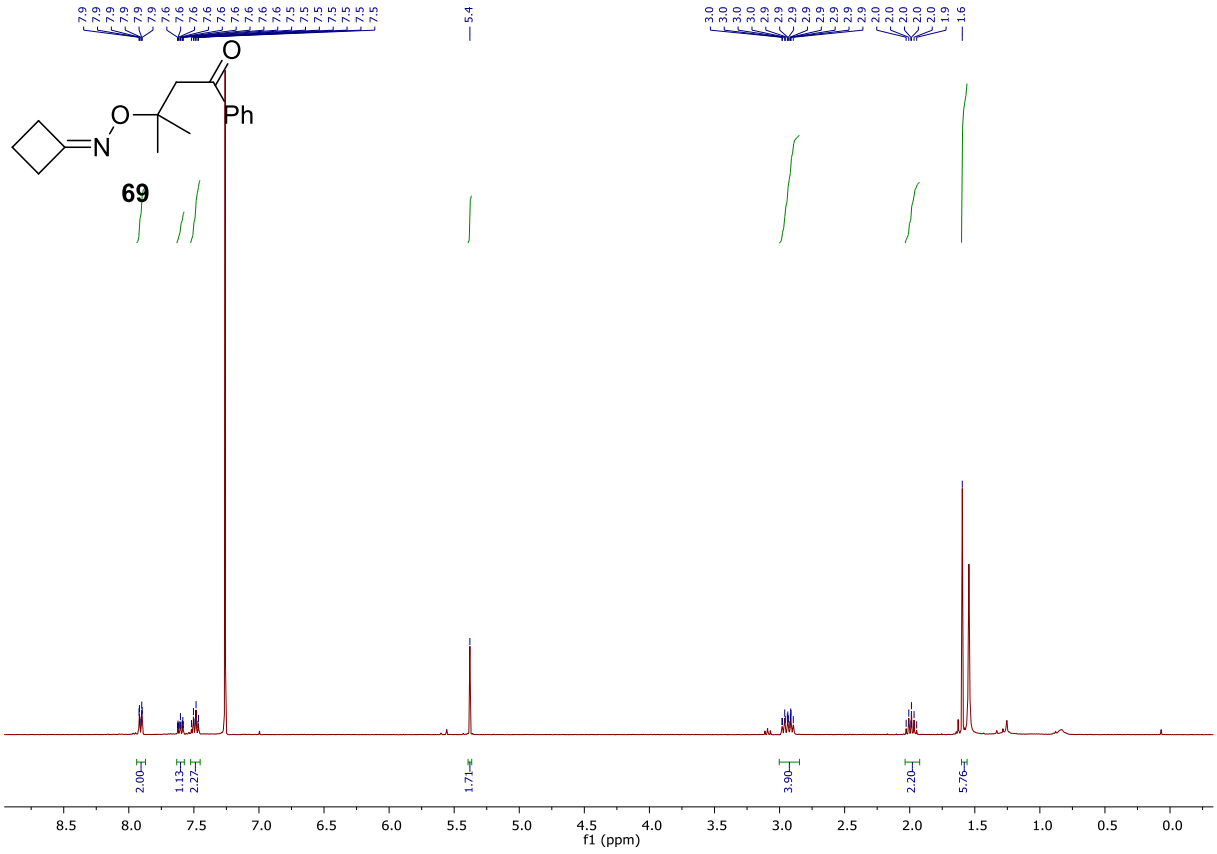
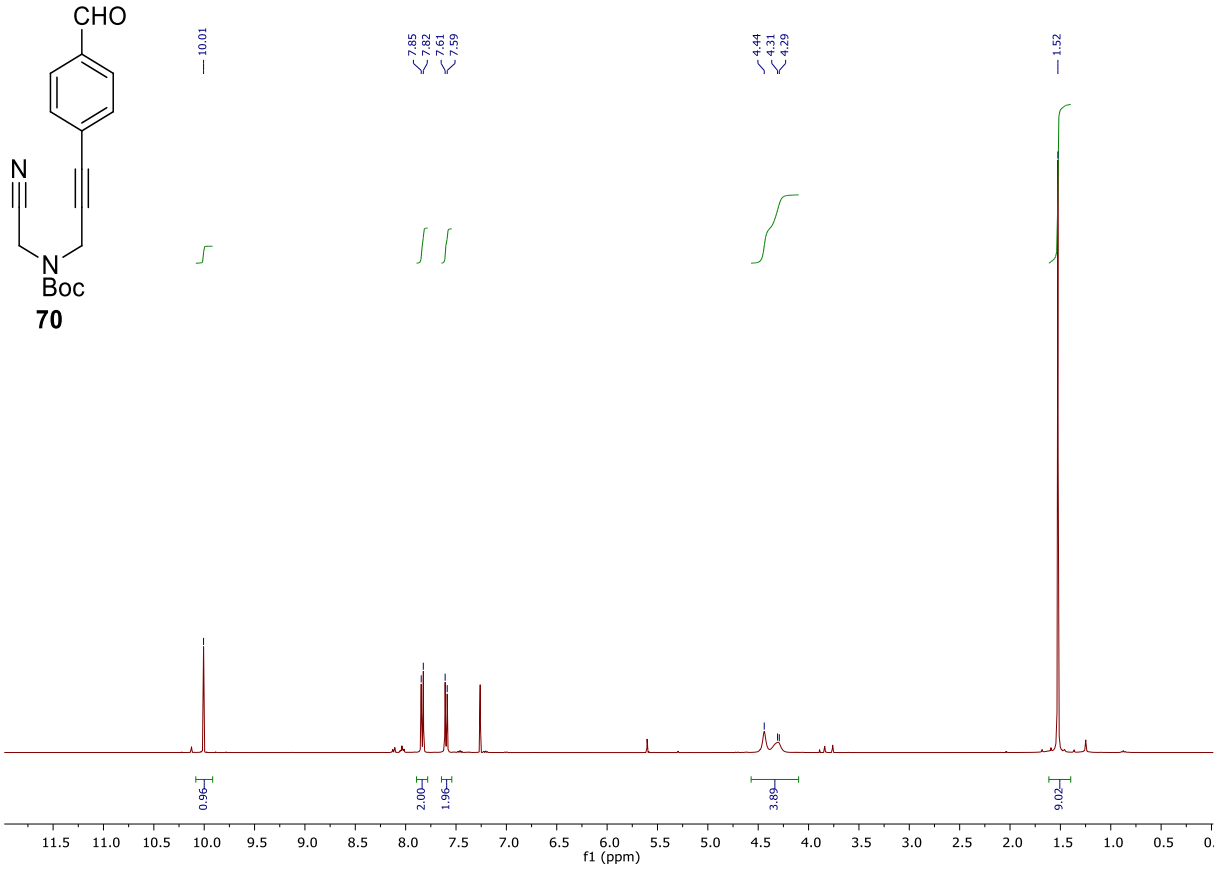


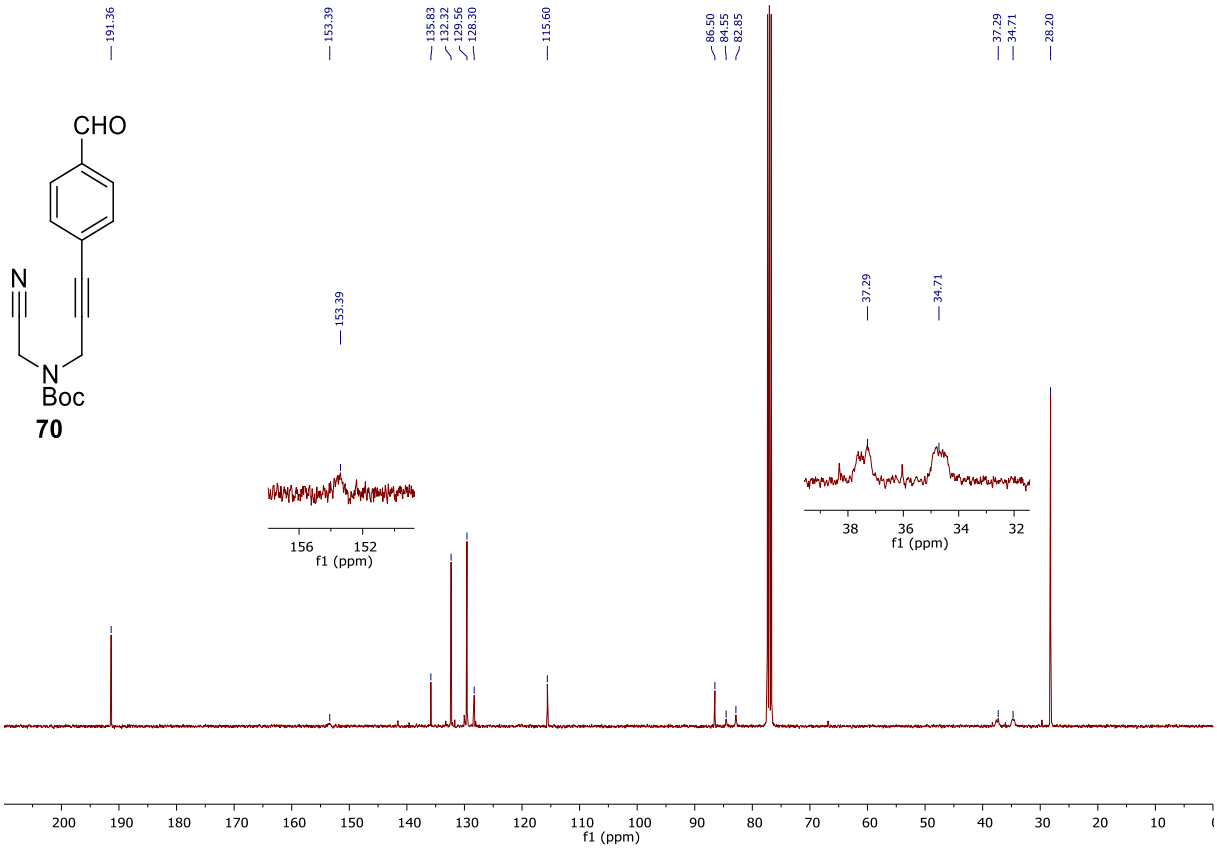
^{1}H-NMR (400 MHz, Chloroform-*d*)



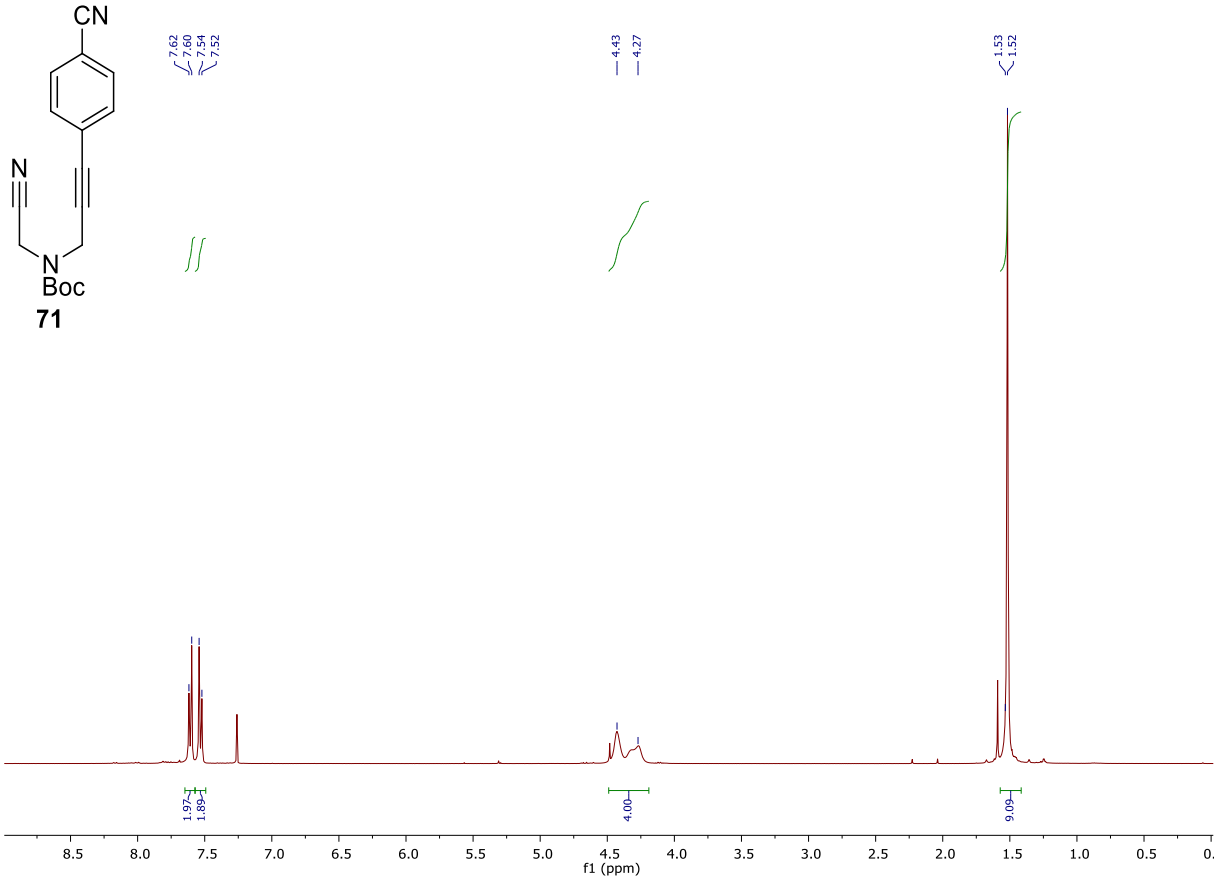
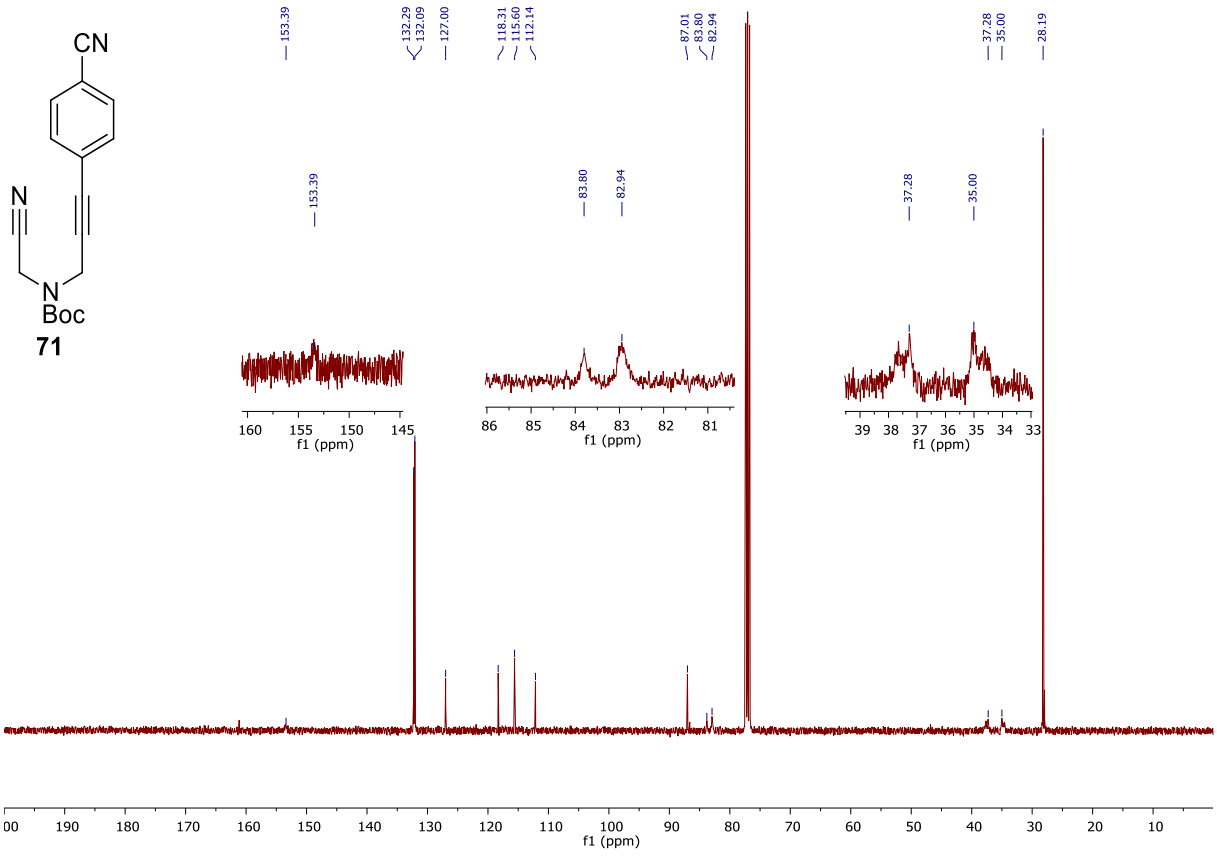
^{1}H-NMR (400 MHz, Chloroform-*d*)



^{13}C-NMR (101 MHz, Chloroform-*d*)



^{1}H-NMR (400 MHz, Chloroform-*d*)



^{13}C-NMR (101 MHz, Chloroform-*d*)