Room-Temperature Decarboxylative Alkynylation of Carboxylic Acids Using Photoredox Catalysis and EBX Reagents

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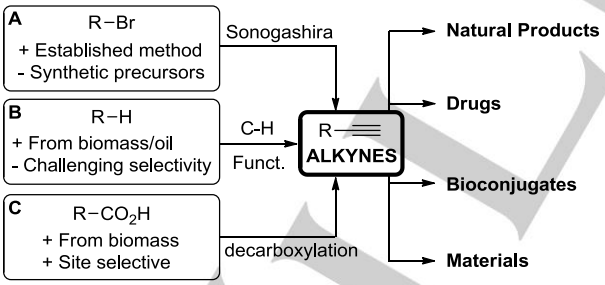
Dedication ((optional))

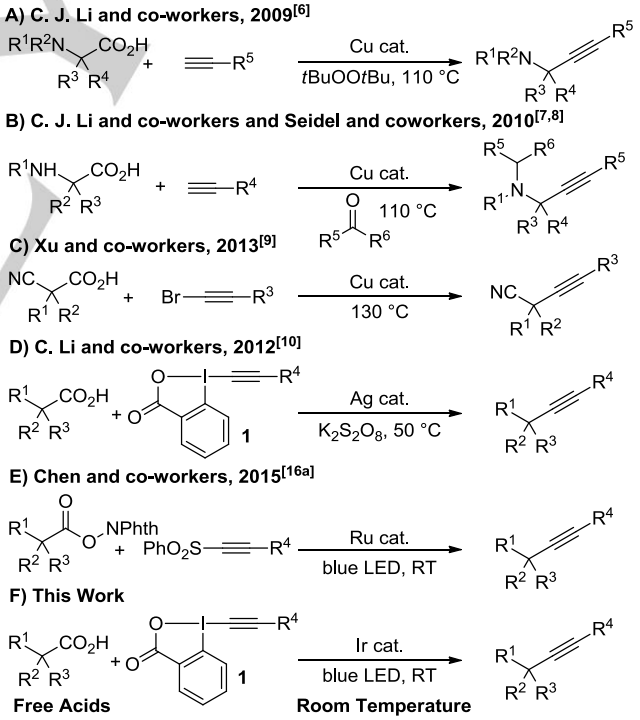
Abstract: Alkynes are used as building blocks in synthetic and medicinal chemistry, chemical biology and materials science. Therefore, efficient methods for their synthesis are the subject of intensive research. Herein, we report the synthesis of alkynes directly from broadly available carboxylic acids at room temperature under visible light irradiation. The combination of an iridium photocatalyst with EthynylBenziodoXolone (EBX) reagents allowed the decarboxylative alkynylation of carboxylic acids in good yields under mild conditions. The method could be applied to the transfer of silyl-, aryl- and alkyl- substituted alkynes. It was especially successful in the case of α-amino and α-oxo acids derived from the biomass.

Alkynes are among the most versatile functional groups in synthetic chemistry, as they are sufficiently stable, yet reactive enough to be easily modified. These properties made them ideally suited for applications not only in organic synthesis, but also in chemical biology and materials science (Scheme 1).[1] All potential applications remain tributary of an efficient synthesis of alkynes. In particular, the metal-catalyzed Sonogashira cross-coupling is now broadly applied to access acetylenes (Scheme 1, **A**).[2] However, the Sonogashira reaction requires starting materials functionalized with adequate leaving groups, which themselves need to be introduced into the molecules. New approaches are urgently needed to make the synthesis of structurally diverse alkynes more efficient. To meet this challenge, the direct alkynylation of SP^2[3] or SP^3[4] C-H bonds has been intensively investigated in the last decade (Scheme 1, **B**). Nevertheless, many of these methods still suffer from harsh conditions, limited scope and the need for directing groups or adjacent heteroatoms to control the selectivity in C-H functionalization.



Scheme 1. Synthesis and applications of alkynes.

As an alternative to classical cross-coupling or C-H functionalization, decarboxylative methods have recently attracted strong interest (Scheme 1, **C**).[5] Indeed, the required carboxylic acids starting materials are derived from the biomass, and are therefore often even cheaper than the corresponding C-H compounds. Furthermore, the carboxy group allows controlling the site of functionalization and only carbon dioxide is generated as waste. Despite these advantages, examples of decarboxylative alkynylation of aliphatic carboxylic acids are rare (Scheme 2). In 2009, Chao-Jun Li and co-workers reported the decarboxylative alkynylation of amino acids using a copper catalyst and di-*tert*-butyl peroxide as stoichiometric oxidant at 110 °C (Scheme 2, **A**).[6] In 2010, Seidel and co-workers[7] and Chao-Jun Li and co-workers[8] used the condensation of aldehydes or ketones instead of the peroxide oxidant (Scheme 2, **B**). The copper-catalyzed method was extended to α-cyano carboxylic acids by Xu and co-workers in 2013 using alkynyl bromides (Scheme 2, **C**).[9] Finally, in 2012, Chaozhong Li and co-workers reported a different approach based on the oxidative generation of radicals from carboxylic acids using a persulfate and a silver catalyst at 50 °C (Scheme 2, **D**).[10] Key for success was the use of ethynylbenziodoxolone (EBX, **1**) reagents, a class of reagents discovered by Ochiai and Zhdankin[11] and intensively investigated by our group[12] and others,[13] to intercept the formed radical. Nevertheless, the use of these methods remains limited by the higher temperatures needed and/or the use of strong stoichiometric oxidants.



Scheme 2. Synthesis of acetylenes via decarboxylative alkynylation.

In order to develop a decarboxylative alkynylation method under milder conditions, we envisaged the use of photoredox catalysis.[14] Indeed, this approach has been highly successful for the decarboxylative functionalization of carboxylic acids recently.[15] In 2015, Chen and co-workers reported a decarboxylative alkynylation method with alkynyl sulfones as reagents,[16] but in this case activation of the carboxylic acid as a N-hydroxy phthalimide ester was required,[17] which diminished the efficiency of the reaction (Scheme 2, **E**). Based on the exceptional reactivity of EBX reagents, we considered them to be well-suited for the development of a photoredox

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process starting directly from the free acids. Indeed, Chen and co-workers had demonstrated that EBX reagents were compatible with a photoredox process in the alkynylation or boronic acid esters.[13g] Herein, we report a method for the decarboxylative alkynylation of free carboxylic acids under photoredox conditions (Scheme 2, **F**). The reaction proceeds at room temperature for a broad range of acids, and allow the introduction of silyl, alkyl and aryl- substituted alkynes.

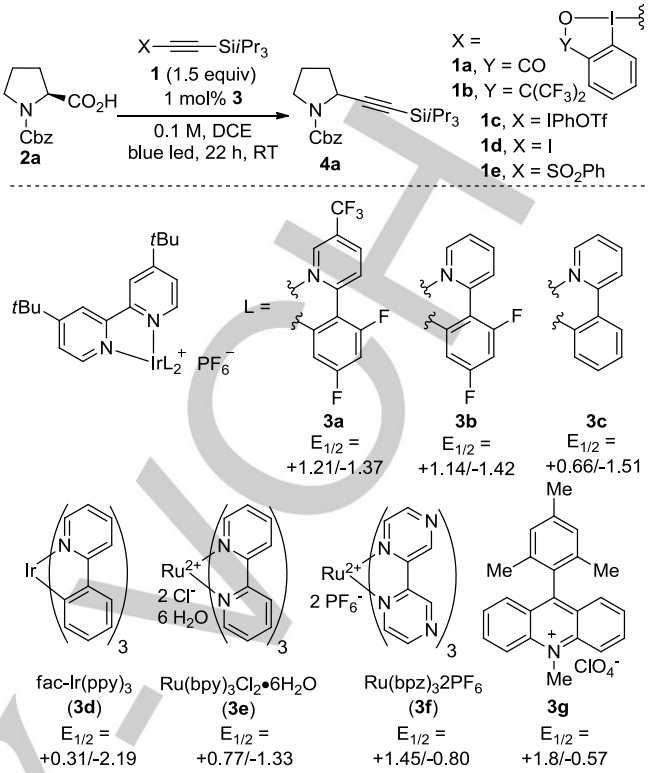
We started our investigations with Cbz-protected proline (**2a**) as substrate using iridium complex **3a** as photocatalyst and simple commercially available blue LED as light source (Table 1). Similar conditions had been highly successful in the work of MacMillan and co-workers.[15d-h] We decided to target specifically silylated alkynes as products, as they give easy access to the most versatile terminal acetylenes. Gratifyingly, using TIPS-EBX (**1a**) as reagent[18] and cesium acetate as base, the desired alkynylation product **4a** could be isolated in 31% yield (entry 1). Intensive investigation of the reaction conditions showed that both structure and amount of the base were essential to obtain a good yield.[19] With four equivalents of cesium acetate, the yield could be raised to 68% (entry 2). Other acetate salts such as potassium and sodium acetates were less efficient (entries 3-4). Cesium carbonate gave the desired product **4a** in 35% yield only (entry 5).[20] The best yield (74%) was finally obtained using cesium benzoate as base (entry 6). 68% yield of **4a** were also obtained with catalyst **3b**, whereas the use of other iridium (**3c** and **3d**) and ruthenium (**3e** and **3f**) complexes or organocatalyst **3g** did not lead to formation of the desired product (entries 7-12). A final optimization of base stoichiometry, concentration and reaction flask finally allowed to improve the yield to 92% using commercially available catalyst **3a** (entry 13).[21] As a final control, we then decided to examine other alkynylation reagents under the optimized reaction conditions (entries 14-17). With benziodoxole **1b**, 38% of **4a** was obtained (entry 14), whereas no product was formed with alkynyliodonium salt **1c**, (entry 15). Alkyne **4a** could be still obtained in 82% yield using simple alkynyl iodide **1d** (entry 16). Although the yield was lower than with EBX reagent **1a**, this result is noteworthy and well in line with the alkynylation of C-H bonds under photoredox conditions using alkynyl iodides recently developed by Hashmi and co-workers.[4d] No product was obtained when using alkynyl sulfone **1e** as reagent (entry 17).

With optimized conditions in hand we investigated the scope of the decarboxylative alkynylation (Scheme 3). We started with the examination of amino acids (Scheme 3, **A**). On preparative scale with only 0.5 mol% of catalyst **3a**, both Cbz- and Boc- protected proline derivatives **4a** and **4b** could be obtained in 90% yield. Piperidine **4c** could also be obtained in 66% yield. Tetrahydroquinoline **4d** was formed in 87% yield. This result is particularly interesting when considering that direct C-H alkynylation cannot be used to obtain this regioisomer, as the C-H bond adjacent to the benzene ring is more reactive. The reaction was not limited to cyclic amino acids: propargylic amine **4e** could also be isolated in 70% yield.

We then turned to the alkynylation of α-oxo acids (Scheme 3, **B**). Alkynylated tetrahydrofuran **4f** could be obtained in quantitative yield. The reaction also worked well in case of a pyran derivative (product **4g**) or simple acyclic substrates (product **4h** and **4i**). As an example of formation of an alkyne at a tertiary position, we attempted the more challenging functionalization of the drug fenofibric acid, which has been extensively used to treat hyperlipidemia and diabetes.[23] Gratifyingly, the desired product **4j** could still be obtained in 47% yield. Finally, carboxylic acids lacking the adjacent heteroatom were examined (Scheme 3, **C**). The desired products were obtained in moderate yields without further optimization for secondary (products **4k** and **4l**) and tertiary (product **4m**) carboxylic acids.

The scope of alkynes in the decarboxylative alkynylation reaction was examined next (Scheme 4). In the case of silyl alkynes, a bulky group was required: The TBDPS protected proline derivative **4n** was obtained in 78% yield, whereas no product could be isolated with TES or TMS groups (results not shown). This is probably due to the lower stability of these reagents under basic conditions. Aryl substituted EBX reagents worked very well in the alkynylation process giving products **4o-s** in 62-97% yield. In particular, the introduction of bromide-substituted benzene rings in **4r** and **4s** will allow easy further functionalization. Finally, EBX reagents bearing both primary and tertiary alkyl groups could also be used (products **4t** and **4u**).

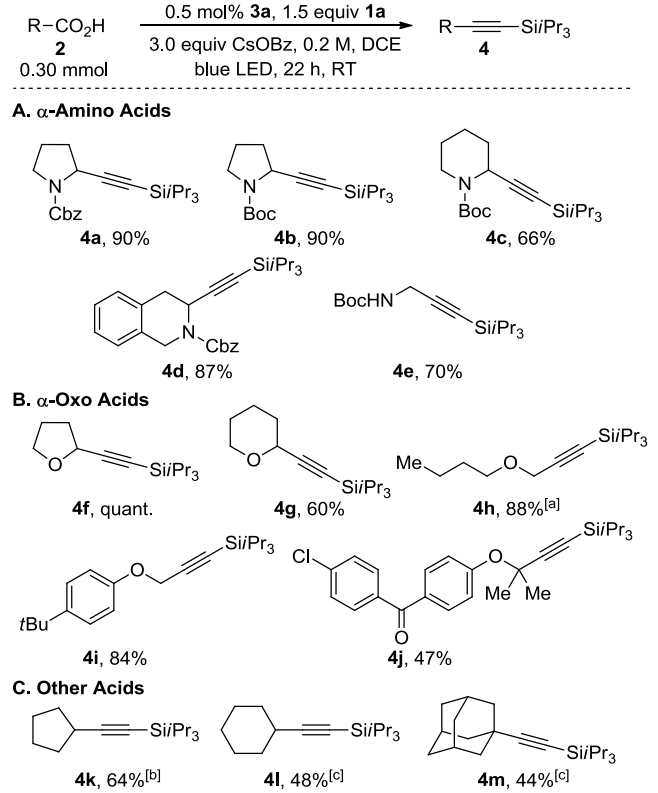
Table 1. Optimization of the decarboxylative alkynylation.



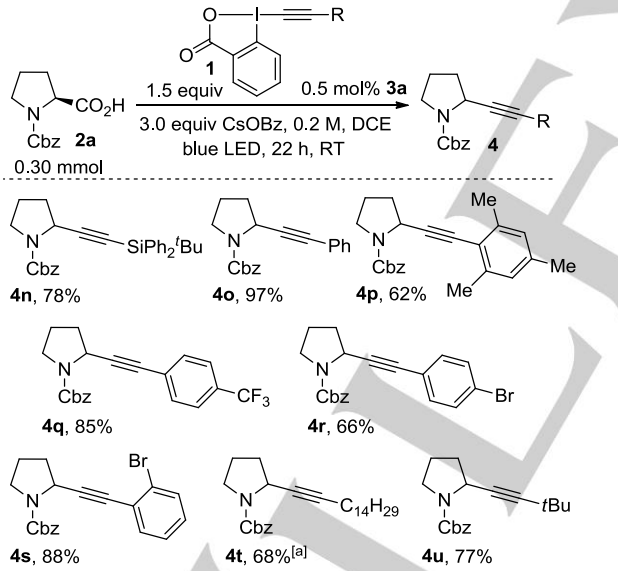
entry	catalyst	base	reagent	conversion[a]	yield[b]
1	**3a**	1.1 equiv CsOAc	**1a**	>95%	31%
2	**3a**	4.0 equiv CsOAc	**1a**	>95%	68%
3	**3a**	4.0 equiv KOAc	**1a**	<50%	9%
4	**3a**	4.0 equiv NaOAc	**1a**	<50%	22%
5	**3a**	4.0 equiv Cs_2CO_3	**1a**	>95%	35%
6	**3a**	4.0 equiv CsOBz	**1a**	>95%	74%
7	**3b**	4.0 equiv CsOBz	**1a**	>95%	68%
8	**3c**	4.0 equiv CsOBz	**1a**	<10%	<5%
9	**3d**	4.0 equiv CsOBz	**1a**	<10%	<5%
10	**3e**	4.0 equiv CsOBz	**1a**	<10%	<5%
11	**3f**	4.0 equiv CsOBz	**1a**	<10%	<5%
12	**3g**	4.0 equiv CsOBz	**1a**	<10%	<5%
13[c]	**3a**	3.0 equiv CsOBz	**1a**	> 95%	92%
14[c]	**3a**	3.0 equiv CsOBz	**1b**	>95%	38%
15[c]	**3a**	3.0 equiv CsOBz	**1c**	>95%	<5%
16[c]	**3a**	3.0 equiv CsOBz	**1d**	>95%	82%
17[c]	**3a**	3.0 equiv CsOBz	**1e**	> 95%	<5%

[a]Reaction conditions: Using 0.1 mmol **2a** (1 equiv), 0.15 mmol **1** (1.5 equiv), 1 μmol **3** (0.01 equiv) in DCE (1 mL) for 22 h at RT. The conversion of **2a** by NMR is given. The values for reduction potentials are given in volts for catalyst **3** in relation to SCE, except for **3b** which is reported relatively to ferrocene.[14f, 22] [b]Isolated yield after preparative TLC. [c] In 0.5 mL DCE.

We then wondered if the reaction could also be run using natural sun light. Indeed, product **4a** was obtained in 88% yield after only five hours at room temperature when the reaction flask was directly exposed to sun light (Scheme 5, **A**).[24] One of the main advantages of the alkynylation using TIPS-EBX (**1a**) is that the obtained products are easily deprotected to give the versatile terminal acetylenes. For example, proline derivative **4a** was obtained on the one mmol scale in 89% yield. Desilylation and [3+2] cycloaddition with benzyl azide gave then triazole **5** in 90% yield (Scheme 5, **B**).

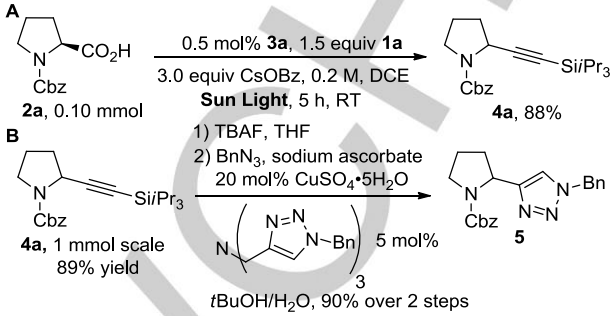


Scheme 3. Scope of carboxylic acids in the decarboxylative alkynylation. [a]NMR yield. [b]Using 1 mol% of catalyst **3a**. [c]Using 2 mol% of catalyst **3a**.



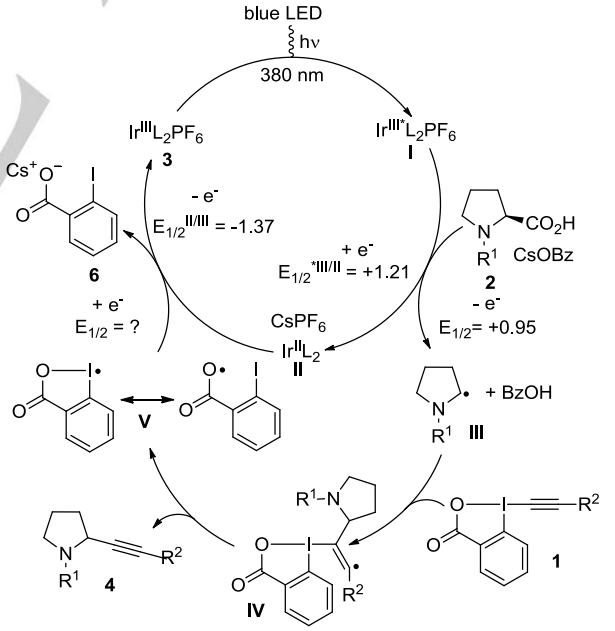
Scheme 4. Scope of alkynes in the decarboxylative alkynylation. [a]Using 1 mol% of catalyst **3a**.

In the future, in-depth investigations will be needed to gain a good understanding of the reaction mechanism. Nevertheless, based on the extensive research already done in the field of photoredox catalysis,[14,15] a tentative mechanism can be proposed (Scheme 6). The catalytic cycle would start with the activation of the iridium catalyst **3** by visible light, which occurs at 380 nm for **3a**. The obtained activated complex **I** has a reduction potential of +1.21 V and should be able to oxidize the cesium carboxylate of protected proline derivatives (reduction potential of +0.95 V for the Boc protected derivative **2b**).[15f] This would lead to reduced iridium complex **II** and α-amino radical **III**. Addition of **III** onto EBX reagent **1** in α position to the iodine could then lead to adduct **IV**, although addition on the β position followed by 1,2- shift or a concerted mechanism cannot be excluded at this stage. β-elimination of iodine radical **V** then would lead to alkynylation product **4**. A final key step of the catalytic cycle would be then reduction of radical **V** by iridium complex **II** to give cesium salt **6** and regenerate catalyst **3**. With **3a**, Ir^{II} complex **II** is an especially strong reductant, with a reduction potential of -1.37 V. This is higher than most of the tested catalysts, and could explain the exceptional performance of **3a**. A similar mechanism could be proposed with alkynyl iodide, as reduction of a potentially formed iodine radical is easy (reduction potential of +1.3 V).[25]



Scheme 5. Reaction with natural sun light (**A**) and derivatization of product **4a** (**B**).

In conclusion, we have reported the decarboxylative alkynylation of free carboxylic acids proceeding under photoredox catalysis. The process can be done at room temperature using visible light with only 0.5 mol% of an iridium photocatalyst. α-amino acids could be converted to the corresponding alkynes in good yields. The process was also successful in the case of α-oxo acids and simple aliphatic carboxylic acids and could be applied for the transfer of silyl-, aryl- and alkyl- substituted alkynes. The obtained products could be easily further functionalized. When considering the mild reaction conditions and broad functional group tolerance, the method is expected to become highly useful for the alkynylation of complex organic compounds and biomolecules in the future.



Scheme 6. Tentative mechanism for the decarboxylative alkynylation. The values for reduction potentials are given in volts for catalyst **3a** and substrate **2b**.

Acknowledgements

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acknowledged for the synthesis of reagents and starting materials and for the purification and characterization of compounds.

Keywords: Photocatalysis, Alkynes, Carboxylic Acids, Hypervalent Iodine, Amino Acids.

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[18] TIPS-EBX (**1a**) is commercially available. Alternatively, it can easily be synthesized in two steps from 2-iodobenzoic acid on 40 g scale: J. P. Brand, J. Waser, *Synthesis* **2012**, *44*, 1155.

[19] See Supporting Information for a full list of tested solvents and reaction conditions.

[20] The lower yield observed with this stronger base may be due to the sensitivity of silyl-EBX reagents to basic conditions leading to desilylation and decomposition. In fact, good yields were obtained also with cesium carbonate with aryl-substituted EBX reagents.

[21] See Supporting Information for details. No product was observed in the absence of either light or catalyst **3a**.

[22] a) A. Singh, K. Teegardin, M. Kelly, K. S. Prasad, S. Krishnan, J. D. Weaver, *J. Organomet. Chem.* **2015**, *776*, 51-59; b) D. J. Wilger, N. J. Gesmundo, D. A. Nicewicz, *Chem. Sci.* **2013**, *4*, 3160.

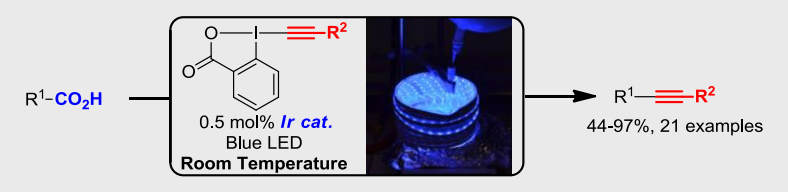
[23] a) J. A. Balfour, D. McTavish, R. C. Heel, *Drugs* **1990**, *40*, 260; b) A. Keech, R. J. Simes, P. Barter, J. Best, R. Scott, M. R. Taskinen, P. Forder, A. Pillai, T. Davis, P. Glasziou, P. Drury, Y. A. Kesaniemi, D. Sullivan, D. Hunt, P. Colman, M. d'Emden, M. Whiting, C. Ehnholm, M. Laakso, F. S. Investigators, *Lancet* **2005**, *366*, 1849; c) G. M. Keating, K. F. Croom, *Drugs* **2007**, *67*, 121.

[24] This experiment was performed in Lausanne (46°51' N, 6°57' E) on May 29, 2015 from 12:00 to 17:00 with a light intensity of 600-850 W/m^2 according to: http://www.meteolausanne.com/soleil-et-uv.html. See supporting information for a detailed irradiation spectrum.

[25] P. Wardman, *J. Phys. Chem. Ref. Data* **1989**, *18*, 1637. We prefer this mechanism over an alternative pathway involving alkynyl radicals, due to the very high energy of the later (see ref. 4d). Data for the reduction potential of radical intermediate **V** are currently not available and difficult to obtain due to its high instability.

Entry for the Table of Contents

COMMUNICATION



*Franck Le Vaillant, Thibaut Courant and Jerome Waser**

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Room-Temperature Decarboxylative Alkynylation of Carboxylic Acids Using Photoredox Catalysis and EBX Reagents

Alkynes are used as building blocks in synthetic and medicinal chemistry, chemical biology and materials science. Herein, we report the synthesis of alkynes directly from broadly available carboxylic acids proceeding at room temperature under visible light irradiation. The combination of an iridium photocatalyst with EthynylBenziodoXolone (EBX) reagents allowed the decarboxylative alkynylation of carboxylic acids in good yield under mild conditions.

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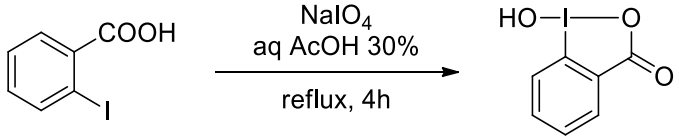
1. General method

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. All carboxylic acid starting materials were commercially available and used as received. 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, the latter was filled by water, in order to keep the temperature as constant as possible. On this flask were attached the blue LEDs (RUBAN LED 5MÈTRES - 60LED/M - 3528 BLEU - IP65 with Transformateur pour Ruban LED 24W/2A/12V, bought directly on RubanLED.com). The distance between the LEDs and the test tubes was approximatively 5 cm. Long irradiation resulted in temperature increasing up to 34°C during overnight reactions.

2. Preparation of Reagents and Catalysts

The synthesis of reagents **1a-1j** and **1n-1o** 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. Catalysts **3a** and **3c-g** are commercially available and were used as received. **3b** was synthesized as indicated below.

1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one (8)

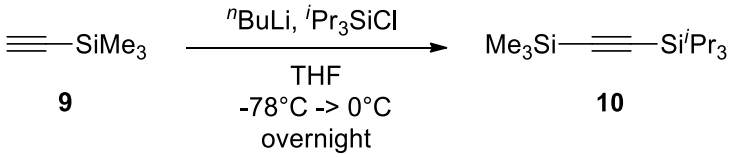


7 **8**

Following a reported procedure,[1] $NaIO_4$ (7.24 g, 33.8 mmol, 1.05 equiv) and 2-iodobenzoic acid (**7**) (8.00 g, 32.2 mmol, 1.00 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 **8** (8.3 g, 31 mmol, 98%) as a colorless solid.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) 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, $(CD_3)_2SO$) 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]

Tri*iso*propylsilyl trimethylsilylacetylene (10)



9 **10**

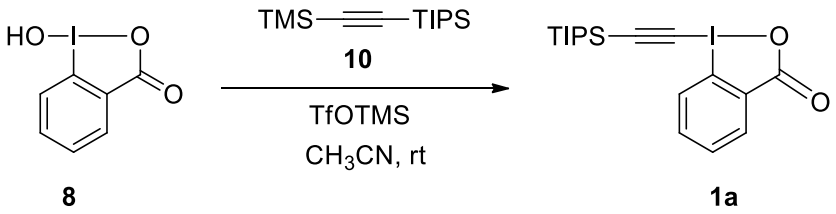
Following a reported procedure,[2] *n*-butyllithium (2.5 M in hexanes, 12.0 mL, 29.9 mmol, 0.98 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (**9**) (3.0 g, 30 mmol, 1.0 equiv) in THF (48 mL) at -78 °C. The mixture was then warmed to 0 °C and stirred for 5 min. The mixture was then cooled back to -78 °C and chlorotri*iso*propylsilane (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

[1].L. Kraszkiewicz, L. Skulski, *Arkivoc*. **2003**, *6*, 120.
[2] C J. Helal, P A. Magriotis, E J. Corey, *J. Am. Chem. Soc.* **1996**, *118*, 10938.

distillation (56-57°C/0.25 mmHg) to yield **10** (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 **10** corresponded to the literature values.[2]

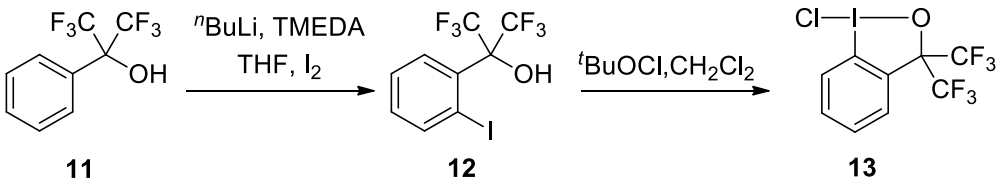
1-[(Tri*iso*-propylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (TIPS-EBX, 1a)



Following a reported procedure,[3] 2-iodosylbenzoic acid (**8**) (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 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)(tri*iso*propylsilyl)acetylene (**10**) (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 **1a** (30.1 g, 70.2 mmol, 86%) as colorless crystals.

Mp (Dec.) 170-176 °C. ^{1}H NMR (400 MHz, $CDCl_3$) 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, $CDCl_3$) 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 **1a** corresponded to the literature values.[3]

1-Chloro-1,3-dihydro-3,3-bis(trifluoromethyl)-1,2-benziodoxole (13)



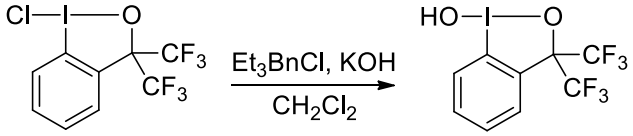
[3] J. P. Brand, J. Waser, *Angew. Chem., Int. Ed.* **2010**, *49*, 7304.

Following a reported procedure,[4] TMEDA (distilled over KOH) (1.26 mL, 8.20 mmol, 0.2 equiv) was added to a solution of ^{n}BuLi (2.5 M in hexanes, 36.6 mL, 91.6 mmol, 2.2 equiv). After 15 min, the cloudy solution was cooled to 0 °C and **11** (7.0 mL, 42 mmol, 1 equiv) in THF (6 mL) was added dropwise. The reaction was stirred 30 min at 0 °C and then at RT overnight. I_2 (11.2 g, 44.0 mmol, 1.06 equiv) was then added portion wise at 0 °C and the mixture stirred at 0 °C for 30 min and 4 h at RT. The reaction was quenched with saturated NH_4Cl. Et_2O (100 mL) was added and the layers were separated. The aqueous layer was then extracted twice with Et_2O (3 x 50 mL). The organic layers were combined, washed twice with saturated NaS_2O_3 (2 x 50 mL), dried over $MgSO_4$, filtered and reduced to afford 15.6 g of **12** as an brown oil which was used without further purification.

The crude oil was dissolved in wet CH_2Cl_2 (40 mL) in the dark under air. ^{t}BuOCl (5.2 mL, 44 mmol, 1.05 equiv) was then added dropwise at 0 °C. After 30 min, the resulting suspension was filtered to afford **13** (7.30 g, 18.1 mmol, 43%) as a yellow solid. The mother liquors were carefully reduced to one third and filtered to afford **13** (3.51 g, 8.71 mmol, 21%) as a yellow solid. Combined yield: 64%.

Mp 167 – 169 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, 1 H, *J* = 8.4 Hz, ArH), 7.85 (m, 1 H, ArH), 7.73 (m, 2 H, ArH). ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.8, 132.1, 131.6, 129.7, 128.5, 122.8 (q, 289 Hz), 113.4, 84.8. Consistent with reported values.[4]

1-Hydroxy-3,3-bis(trifluoromethyl)-3-(*1H*)-1,2-benziodoxole (14)

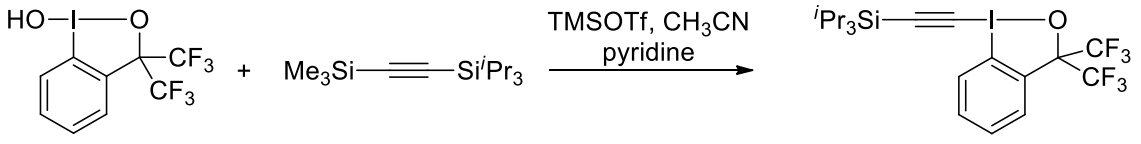


13 **14**

Following a preported procedure,[5] Et_3BnNCl (83 mg, 0.36 mmol, 0.05 equiv) was added to a stirring solution of **13** (10.7 g, 26.5 mmol, 1 equiv) in CH_2Cl_2 (150 mL) and KOH (1.48 g, 26.5 mmol, 1 equiv) in water (28 mL). The reaction was kept under air until TLC indicated that all starting material was consumed. The organic layer was separated and dried over $MgSO_4$. The resulting solid was purified over a silica plug eluting with EtOAc, then recristallized in EtOAC (30 mL) and washed with pentane to afford **14** (7.42 g, 19.2 mmol, 73%) as a white solid. ^{1}H NMR (400 MHz, DMSO) δ 7.96 (m, 2 H, ArH), 7.73 (m, 2 H, ArH). ^{13}C NMR (101 MHz, DMSO) δ 133.3, 131.0, 130.8, 128.9, 127.9, 123.4 (q, *J* = 290 Hz), 117.2, 83.7 (m). IR 1464 (w), 1435 (w), 1290 (w), 1263 (m), 1185 (s), 1139 (s), 1103 (m), 1041 (w), 1021 (w), 952 (s), 760 (m), 730 (m), 692 (m).

1-[(Tri*iso*propylsilyl)ethynyl]-3,3-bis(trifluoromethyl)-3(*1H*)-1,2-benziodoxole (1b)

[4] E. F. Perozzi, R. S. Michalak, G. D. Figuly, W. H. Stevenson, D. B. Dess, M. R. Ross, J. C. Martin, *J. Org. Chem.* **1981**, *46*, 1049.
[5] A. J. Blake, A. Novak, M. Davies, R. I. Robinson, S. Woodward, *Synth. Commun.* **2009,** *39*, 1065.

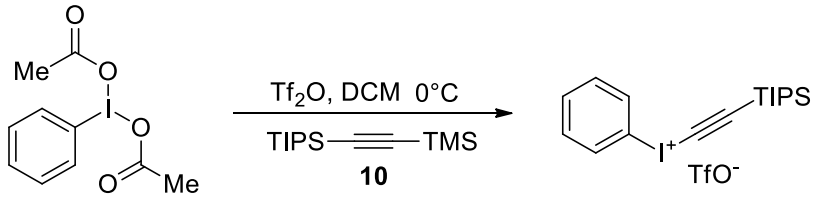


14 **10** **1b**

TMSOTf (3.80 g, 17.1 mmol, 1.1 equiv) was added to **14** (6.00 g, 15.5 mmol, 1.0 equiv) in CH_2Cl_2 (200 mL) at RT. After 20 min, the solution was concentrated at 0 °C under reduced pressure. After evaporation of the solvent, the reaction flask was directly filled with Ar, to prevent decomposition of the hygroscopic triflate intermediate. Then the resulting yellow solid was dissolved in CH_3CN (200 mL). (Trimethylsilyl)(tri*iso*-propylsilyl)acetylene (**10**) (5.14 g, 20.2 mmol, 1.3 equiv) was added and after 20 min several drops of pyridine were added. The reaction was then concentrated under vacuum, dissolved in Et_2O and filtered over a silica plug (eluant Et_2O). The resulting solid was recrystallized from pentane to afford **1b** (5.43 g, 9.87 mmol, 64%) as white crystals.

Rf (PET/Et_2O 95/5): 0.4. Mp 131 – 132 °C. ^{1}H NMR (400 MHz, $CDCl_3$) (*ca* 0.10 mmol/mL) δ 8.36 (dd, 1 H, *J* = 7.9, 1.7 Hz, ArH), 7.84 (d, 1 H, *J* = 6.7 Hz, ArH), 7.68 (m, 2H, ArH), 1.15 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.7, 131.1, 129.9, 129.9 (m), 128.2, 123.6 (q, 288 Hz), 112.1, 110.8, 81.4 (m), 69.7, 18.5, 11.2. Characterization data of **1b** corresponded to the literature values.[6]

Phenyl(tri*iso*propylsilyl)iodonium triflate (1c)



15 **1c**

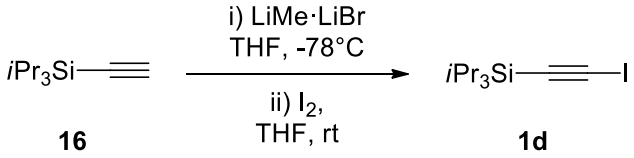
Following a slight modification of the reported procedure,[7] phenyliodonium diacetate (**15**) (2.53 g, 7.85 mmol, 1.00 equiv) was diluted with DCM (7 mL) and the mixture was stirred for 5 minutes. Tf_2O (0.60 mL, 3.9 mmol, 0.50 equiv.) was added dropwise at 0 °C and the resulting yellow mixture was stirred 30 min. (Trimethylsilyl)(tri*iso*propylsilyl)acetylene (**10**) (2.00 g, 7.86 mmol, 1.00 equiv) was added and the mixture was then stirred 2 h. Water was then added (30 mL) followed by extraction of the aqueous layer with DCM (2 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The resulting solid was triturated in hexane (10 mL). Filtration and removal of solvent *in vacuo* afforded phenyl(tri*iso*propylsilyl)iodonium triflate (**1c**) (2.90 g, 11.2 mmol, 70% yield) as a colorless solid.

Melting point: 109 – 114 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (m, 2 H, Ar*H*), 7.65 (m, 1 H, Ar*H*), 7.52 (m, 2 H, Ar*H*), 1.15-1.01 (m, 21 H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.7, 132.5, 132.4, 119.7, 117.6, 117.6, 44.9, 18.3, 11.1; IR ν 3288 (w), 3088 (m), 2949 (m), 2894

[6] Y. LI, J. Brand, J. Waser, *Angew. Chem., Int. Ed.* **2013**, *52*, 6743.
[7] T. Kitamura, M. Kotani, Y. Fujiwara, *Synthesis* **1998**, *10*, 1416.

(m), 2869 (w), 1563 (m), 1467 (w), 1451 (w), 1388 (w), 1281 (s), 1236 (s), 1221 (s), 1174 (s), 1068 (w), 1028 (s), 988 (m), 916 (m), 884 (m), 736 (s), 679 (m), 639 (s); HRMS (ESI) calcd for $C_{17}H_{26}ISi^+$ (M-OTf) 385.0843; found 385.0812; the reported values corresponded to the ones in literature.[3]

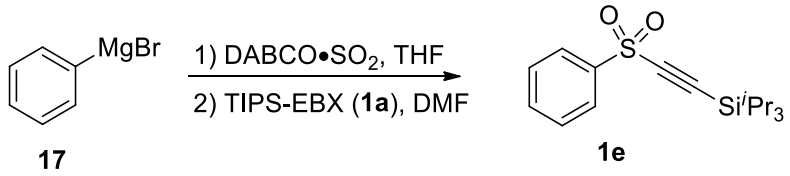
2-Iodo-1-tri*iso*propylsilyl acetylene (1d)



Following a reported procedure,[8] MeLi•LiBr (1.5 M in diethyl ether, 1.1.mL, 1.6 mmol, 1.0 equiv) was added to a stirred solution of tri*iso*propylsilylacetylene (**16**) (0.36 mL, 1.6 mmol, 1.0 equiv) in dry THF (1.8 mL), cooled at -78 °C, and the mixture was allowed to react for 1 h at that temperature. A solution of I_2 (457 mg, 1.80 mmol, 1.25 equiv) in dry THF (2.7 mL) was then added dropwise and the mixture was stirred for 1.5 h at -78°C. The mixture was then diluted with brine (6 mL) and the aqueous layer was extracted with ether (3 x 10 mL). The combined organic layers were washed with a saturated aqueous solution of $Na_2S_2O_3$ (3 x 20 mL), dried over $MgSO_4$ and concentrated under reduced pressure. Purification by column chromatography (SiO_2, hexane) afforded 2-iodo-1-tri*iso*propylsilyl acetylene (**1d**) (0.470 g, 1.52 mmol, 94% yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10-1.04 (m, 21 H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$) δ 100.8, 18.5, 11.4 (one acetylene carbon was not resolved); the reported values correspond to the ones in literature.[8]

Triisopropyl((phenylsulfonyl)ethynyl)silane (1e)



Following a reported procedure,[9] a stirring bar was placed in a 7.5 mL microwave tube with a cap (not sealed at this moment), and flamed dry under high vacuum. After cooling down to r.t. and filled with nitrogen, DABSO (48 mg, 0.20 mmol) was added in to the microwave tube. The tube was sealed, evacuated and filled with nitrogen four times. Anhydrous THF (0.65 mL) was added, and the tube was replaced in a -40 ^{0}C (MeCN + dry ice) bath for 10 min. Phenyl magnesium bromide (**17**) (0.20 mL, 0.20 mmol) was added, and

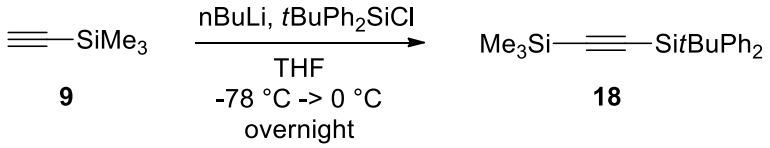
[8] López S.; Fernández-Trillo F.; Midón P.; Castedo L.; Saá *J. Org. Chem.* **2005**, *70*, 6346.
[9] C. C. Chen, J. Waser, *Org. Lett.* **2015**, *17*, 736.

the reaction mixture was stirred for 1 h. The cooling bath was then removed, and the resulting solution was stirred at r.t. for another 1 h.

The sealed cap was removed, and DMF 0.65 mL and TIPS-EBX (**1a**) (103 mg, 0.240 mmol) were subsequently added to the resulting solution and stirred for further 5 min. The reaction was quenched by adding 1 M HCl (2 mL). The resulting layers were separated and the aqueous layer was extracted with EtOAc (3x5 mL). All of the organic layers were combined, washed with (sat.) $NaHCO_3$, dried over $MgSO_4$, and filtrated. The organic solvent was removed under reduced pressure to give the crude product. The crude product was purified by column chromatography to afford the desired product **1e** as a colorless gel (55 mg, 0.17 mmol, 85% yield).

R*f* 0.5 (pentane/EtOAc 5/1, $KMnO_4$); pentane/EtOAc 5/1 was used as the eluting solvents for purification. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 8.07 – 7.97 (m, 2H, Ar-*H*), 7.70 – 7.61 (m, 1H, Ar-*H*), 7.57 (ddd, *J* = 8.2, 6.6, 1.3 Hz, 2H, Ar-*H*), 1.19 – 0.95 (m, 21H, Si*i*Pr$_3$). ^{13}C-NMR (101 MHz, $CDCl_3$) δ 142.1, 134.0, 129.2, 127.2, 100.9, 100.6, 18.3, 10.8. IR 4352(w), 3853(w), 3661(s), 3227(w), 2939(br), 2124(w), 1934(w), 1452(m), 1407(s), 1407(s), 1251(s), 1055(s), 893(s), 795(m).

***tert*Butyldiphenylsilyl trimethylsilylacetylene (18)**



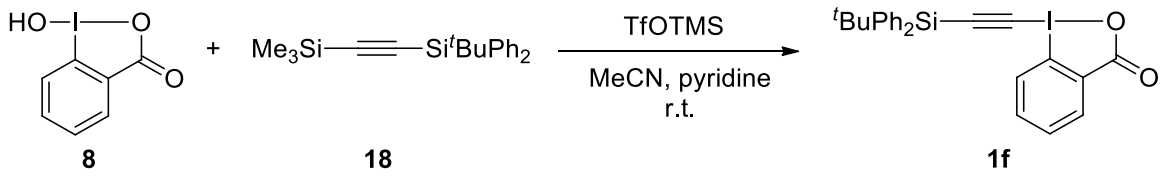
9 **18**

Following a reported procedure,[10] *n*-butyllithium (2.5 M in hexanes, 8.0 mL, 20 mmol, 0.98 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (**9**) (2.90 mL, 20.4 mmol, 1.0 equiv) in THF (30 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 *tert*-butylchlorodiphenylsilane (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 (30 mL) was added, and the reaction mixture was extracted with diethyl ether (2 x 50 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 (bp = 150°C, p = 0.25 mmHg) to yield **18** (2.95 g, 8.76 mmol, 44% yield) as a colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (m, 4H, ArH), 7.38 (m, 6H, ArH), 1.08 (s, 9H, *t*Bu), 0.27 (s, 9H, TMS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.6, 133.2, 129.5, 127.7, 119.0, 108.7, 27.0, 18.5, -0.0. The characterization data for compound **18** corresponded to the reported values.[10]

1-[(*tert*Butyldiphenylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (1f)

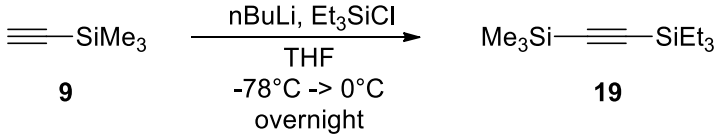
[10] P. Cuadrado, A.M. Gonzalez-Nogal, R. Valero, *Tetrahedron* **2002**, *58*, 4975.



Following a reported procedure,[11] trimethylsilyltriflate (1.58 mL, 8.70 mmol, 1.1 equiv, freshly distilled) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (**8**) (2.07 g, 7.90 mmol, 1.0 equiv) in acetonitrile (30 mL). Butyldiphenyl((trimethylsilyl)ethynyl)silane (**18**) (2.95 g, 3.70 mmol, 1.1 equiv) was then added dropwise, followed, after 15 min, by the addition of pyridine (710 μL, 3.70 mmol, 1.1 equiv). The mixture was stirred 10 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in dichloromethane. The organic layer was washed with 1 M HCl and the aqueous layer was extracted with CH_2Cl_2. The organic layers were combined, washed with a saturated solution of $NaHCO_3$, dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The resulting oil was stirred in hexane and ether and then reduced under vacuum to afford a colorless solid. Recrystallization from acetonitrile (*ca* 20 mL) afforded **1f** (2.77 g, 5.42 mmol, 69%) as a colorless solid.

^{1}H NMR (400 MHz, $CDCl_3$) (*ca* 0.12 mmol/mL) δ 8.43 (d, *J* = 6.5 Hz, 1H, ArH), 8.29 (d, *J* = 8.2 Hz, 1H, ArH), 7.82 (d, *J* = 6.6 Hz, 4H, ArH), 7.75 (t, *J* = 7.2 Hz, 1H, ArH), 7.66 (m, 1H, ArH), 7.53-7.41 (m, 6H, ArH), 1.21 (s, 9H, *t*Bu).^{13}C NMR (101 MHz, $CDCl_3$) δ 166.6, 135.5, 134.8, 132.4, 131.5, 131.3, 130.2, 128.1, 126.3, 116.0, 112.2, 68.5, 27.0, 18.7. One carbon was not resolved. IR ν_{max} 3072 (w), 2958 (w), 2932 (w), 2865 (w), 2860 (w), 2248 (w), 1649 (w), 1622 (m), 1561 (w), 1471 (w), 1430 (w), 1336 (w), 1297 (w), 1253 (w), 1113 (w), 1008 (w), 906 (s), 821 (w), 727 (s), 647 (m). The characterization data for compounds **1f** corresponded to the reported values.[11]

Triethyl trimethylsilylacetylene (19)



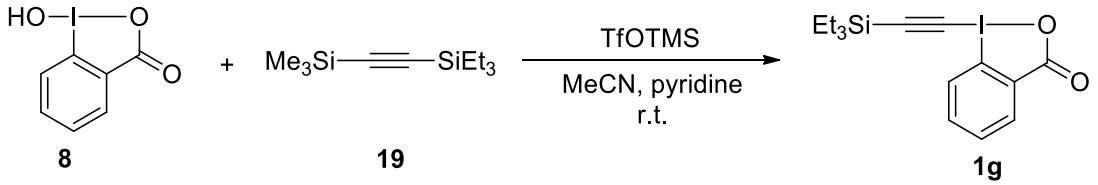
Following a reported procedure,[10] *n*-butyllithium (2.5 M in hexanes, 5.4 mL, 14 mmol, 1.0 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (**9**) (1.36 g, 13.8 mmol, 1.00 equiv) in THF (21 mL) at -78 °C. The mixture was then warmed to 0 °C and stirred for 5 min. The mixture was then cooled back to -78 °C and chlorotriethylsilane (2.3 mL, 14 mmol, 0.98 equiv) was added dropwise. The mixture was then allowed to warm to room temperature and stirred overnight. A saturated solution of ammonium chloride (20 mL) was added, and the reaction mixture was extracted with diethyl ether (2 x 20 mL). The organic layer was washed with water and brine, then dried over $MgSO_4$, filtered and

[11] J. P Brand, C. Chevalley, R. Scopelliti, J. Waser, *Chem. Eur. J.* **2012**, *18*, 5655.

concentrated under reduced pressure to obtain a colorless liquid which was further purified by Kugelrohr distillation to yield **19** (3.4 g, 11 mmol, 83% yield) as a colorless liquid.

^{1}H NMR (400 MHz, $CDCl_3$) δ 0.99 (t, *J* = 7.9 Hz, 9 H, $SiCH_2\mathit{CH_3}$), 0.59 (q, *J* = 7.9 Hz, 6 H, $Si\mathit{CH_2}CH_3$), 0.17 (s, 9 H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 115.4, 111.2, 7.4, 4.4, 0.0. IR ν 2958 (m), 2913 (m), 2879 (m), 1462 (w), 1414 (w), 1381 (w), 1250 (m), 1015 (m), 973 (w), 908 (w), 844 (s), 773 (s), 731 (s), 702 (sh), 679 (sh). Consistent with reported data.[12]

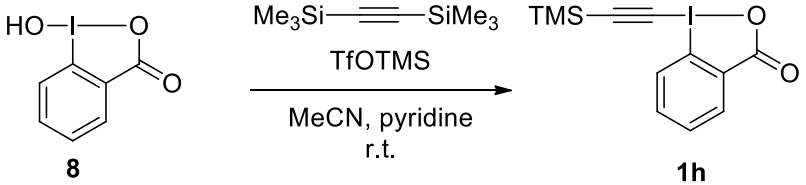
1-[(Triethylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (1g)



Trimethylsilyltriflate (2.78 mL, 15.4 mmol, 1.1 equiv, freshly distilled over CaH_2) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (**8**) (3.71 g, 14.0 mmol, 1.0 equiv) in acetonitrile (50 mL). After 15 min, (trimethylsilyl)(triethylsilyl)acetylene (**19**) (3.26 g, 15.4 mmol, 1.1 equiv) was then added dropwise. After 30 min pyridine (1.25 mL, 15.4 mmol, 1.1 equiv) was added and the mixture was stirred for an additional 15 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in dichloromethane (50 mL). The organic layer was washed with 1 M HCl (50 mL), and the aqueous layer was extracted with CH_2Cl_2 (50 mL). The organic layers were washed twice with saturated $NaHCO_3$ (75 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The resulting solid was recristalized twice in CH_3CN. The solid was washed with cold acetonitirile, hexanes and dried under high vacuum to afford **1g** (2.95 g, 7.64 mmol, 55% yield) as a slightly brown solid.

Mp (Dec.) 155 – 158 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.40 (m, 1 H, Ar*H*), 8.24 (m, 1 H, Ar*H*), 7.75 (m, 2 H, Ar*H*), 1.06 (t, *J* = 8.0 Hz, 9 H, $SiCH_2\mathit{CH_3}$), 0.73 (q, *J* = 8.0 Hz; 6H, $Si\mathit{CH_2}CH_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.5, 134.8, 132.5, 131.6, 131.3, 126.1, 115.5, 115.1, 64.6, 7.4, 4.1. IR ν 3064 (w), 3062 (m), 2957 (m), 2911 (m), 2877 (m), 1621 (s), 1587 (m), 1561 (m), 1460 (m), 1440 (m), 1415 (w), 1378 (w), 1336 (m), 1297 (m), 1237 (w), 1149 (w), 1113 (w), 1010 (m), 976 (w), 912 (w), 912 (w), 834 (m), 804 (w), 739 (s), 693 (m), 675 (m), 647 (w). Consistent with reported data. [12]

1-[(Trimethylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (1h)

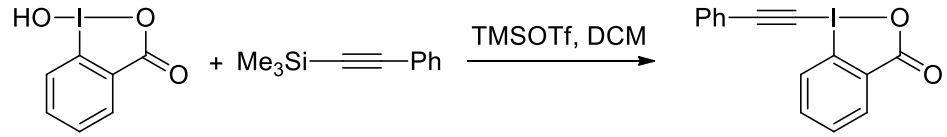


[12] Nicolai, S.; Piemontesi, C.; Waser, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 4680

Following a reported procedure,[13] trimethylsilyltriflate (2.8 mL, 15 mmol, 1.4 equiv, freshly distilled) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (**8**) (3.00 g, 11.4 mmol, 1.00 equiv) in acetonitrile (85 mL) until the mixture turned colorless. Bis(trimethylsilyl)acetylene (2.14 g, 12.5 mmol, 1.10 equiv) was then added dropwise, followed, after 20 min, by the addition of pyridine (1.2 mL, 15 mmol, 1.4 equiv). The mixture was stirred 30 min. The solvent was then removed under reduced pressure and the yellow crude oil was dissolved in dichloromethane (80 mL). The organic layer was washed with a large amount of water (130 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 x 65 mL). The organic layer was washed with brine (130 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (2.3 mL) afforded **1h** (2.35 g, 6.84 mmol, 60% yield) as a colorless solid.

Mp: 143-145 °C (dec); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.42 (dd, J = 6.4, 1.9 Hz, 1H, Ar*H*), 8.19 (m, 1H, Ar*H*), 7.78 (m, 2H, Ar*H*), 0.32 (s, 9H, *TMS*). ^{13}C NMR (100 MHz, $CDCl_3$) 166.4, 134.9, 132.6, 131.7, 131.4, 126.1, 117.2, 115.4, 64.2, -0.5. IR ν_{max} 3389 (w), 2967 (w), 1617 (s), 1609 (s), 1562 (m), 1440 (w), 1350 (m), 1304 (w), 1254 (w), 1246 (w), 1112 (w), 1008 (w), 852 (s), 746 (m), 698 (m), 639 (m). The characterization data for compounds **4c** corresponded to the reported values.[13]

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



8 **20** **1i**

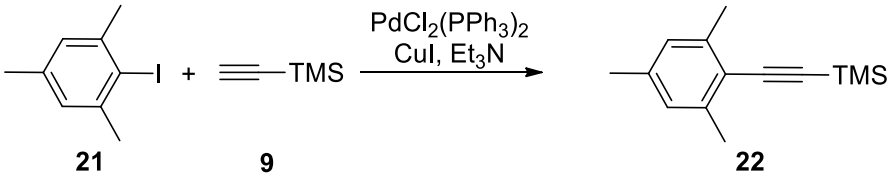
Following a reported procedure,[11] trimethylsilyltriflate (1.60 mL, 8.56 mmol, 1.1 eq.) was added dropwise to a stirred solution of 2-iodosylbenzoic Trimethylsilyl triflate (7.50 mL, 41.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**8**) (10.0 g, 37.7 mmol, 1 equiv) in CH_2Cl_2 (100 mL) at RT. The resulting yellow mixture was stirred for 1 h, followed by the dropwise addition of trimethyl(phenylethynyl)silane (**20**) (8.10 mL, 41.5 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 **1i** (6.08 g, 17.4 mmol, 46 %) as a colorless solid.

Mp (Dec.) 155 – 160 °C. ^{1}H NMR (400 MHz, $CDCl_3$) (*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

[13] V. V.Zhdankin , C. J Kuehl, A. P Krasutsky, J. T. Bolz, A. J. Simonsen, *J. Org. Chem.* **1996**, *61*, 6547.

NMR (101 MHz, $CDCl_3$) 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. [11]

(Mesitylethynyl)trimethylsilane (22)

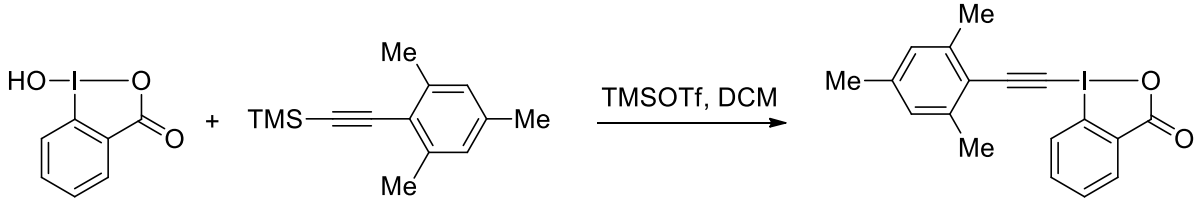


21 **9** **22**

Following a reported procedure,[11] Iodomesitylene (**21**) (1.05 g, 4.27 mmol, 1 equiv) was dissolved in Et_3N (10 mL) (without prior drying). After three freeze-thraw-pump cycle, $PdCl_2(PPh_3)_2$ (30 mg, 0.42 mmol, 0.1 equiv) and CuI (16 mg, 0.84 mmol, 0.2 equiv) were added under N_2. After the addition of trimethylsilylacetylene (**9**) (1.2 mL, 8.5 mmol, 2 equiv), the green suspension was stirred at RT for 1 h. The reaction mixture was reduced under vacuum, dissolved in CH_2Cl_2 (30 mL), washed with 5% EDTA solution (30 mL) and water (30 mL). The organic layers were them dried over $MgSO_4$, filtered and reduced under vacuum. The resulting oil was purified by column chromatography (PET) to afford **22** (526 mg, 2.43 mmol, 66%) along with 15% of starting material.

R_f 0.5 (PET). ^1H NMR (400 MHz, $CDCl_3$) δ 6.87 (s, 2 H, ArH), 2.41 (s, 6 H, CH_3), 2.29 (s, 3 H, CH_3), 0.28 (s, 9 H, TMS). Used without further purification.

1-[2,4,6-Trimethylphenylethynyl]-1,2-benziodoxol-3(1*H*)-one (Mes-EBX, 1j)



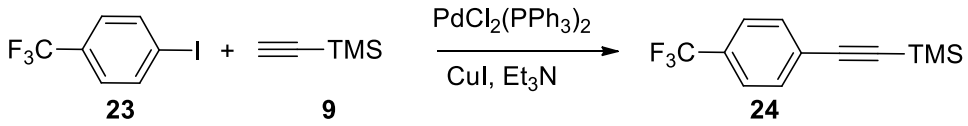
8 **22** **1j**

Following a reported procedure,[11] Trimethylsilyl triflate (212 μL, 1.15 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**8**) (1.00 g, 1.05 mmol, 1 equiv) in CH_2Cl_2 (4 mL) at RT. The resulting yellow mixture was stirred for 1 h, followed by the dropwise addition of (mesitylethynyl)trimethylsilane (**22**) (250 mg, 1.15 mmol, 1.1 equiv) dissolved in CH_2Cl_2 (1 mL). The resulting suspension was stirred for 6 h at RT. A saturated solution of $NaHCO_3$ (5 mL) was then added and the mixture was stirred vigorously. The layers were separated and the organic layer was washed with sat. $NaHCO_3$ (10 mL), dried over $MgSO_4$, filtered and evaporated under reduced pressure. The resulting solid was recrystallized in CH_3CN (ca 20 ml). The mother liquors were concentrated and and the obtained solid recrystallized in CH_3CN (4 mL). Both solids were combined, washed with pentane and dried under high vacuum to afford **1j** (120 mg, 0.307 mmol, 30%) as a tan solid.

Mp (Dec.) 171– 175 °C. ^1H NMR (400 MHz, $CDCl_3$) (*ca* 0.01 mmol/ml) δ 8.38 (m, 1 H, ArH), 8.28 (m, 1 H, ArH), 7.72 (m, 2 H, ArH), 6.92 (s, 2 H, MesH), 2.45 (s, 6 H, CH_3), 2.31

(s, 3 H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.7, 142.1, 140.5, 134.5, 132.2, 131.5, 131.3, 128.0, 126.2, 117.5, 116.5, 105.1, 55.6, 21.4, 21.0. IR 2979 (w), 2916 (w), 2247 (w), 2131 (w), 1650 (m), 1623 (m), 1562 (w), 1439 (w), 1333 (w), 1292 (w), 1212 (w), 1146 (w), 1008 (w), 906 (s), 855 (w), 833 (w), 729 (s), 647 (m). Consistent with reported data.[11]

Trimethyl((4-(trifluoromethyl)phenyl)ethynyl)silane (24)

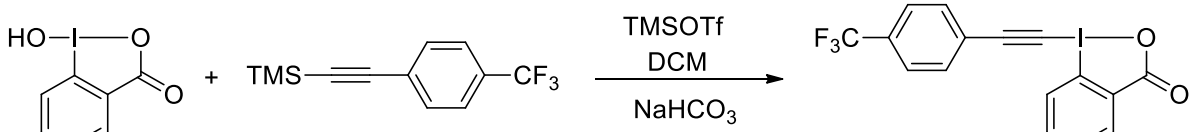


23 **9** **24**

Following a slight modification of the reported procedure,[14] a solution of trimethylsilyl acetylene (**9**) (2.13 mL, 15.0 mmol, 1.5 equiv) was added drop wise to a mixture of 1-iodo-4-(trifluoromethyl) benzene (**23**) (2.72 g, 10.0 mmol, 1 equiv), $Pd(PPh_3)_2C1_2$ (70 mg, 0.10 mmol, 0.01 equiv), and copper (I) iodide (38 mg, 0.20 mmol, 0.02 equiv) in triethylamine (30 mL). The reaction mixture was stirred at room temperature for 3 h, concentrated and purified by column chromatography (pure pentane) to afford the corresponding product **24** (1.60 g, 6.60 mmol, 66%) as a colorless oil.

R_f 0.8 (pentane). ^1H NMR (400 MHz, $CDCl_3$) δ 7.56 (s, 4 H, Ar*H*), 0.27 (s, 9 H, TMS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 132.2, 130.1 (q, *J* = 32.5 Hz), 126.9 (m), 125.1 (q, *J* = 3.8 Hz). 123.9 (q, *J* = 272.1 Hz), 103.6, 97.3, -0.04. The characterization data for compound **24** corresponded to the reported values.[15]

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



8 **24** **1k**

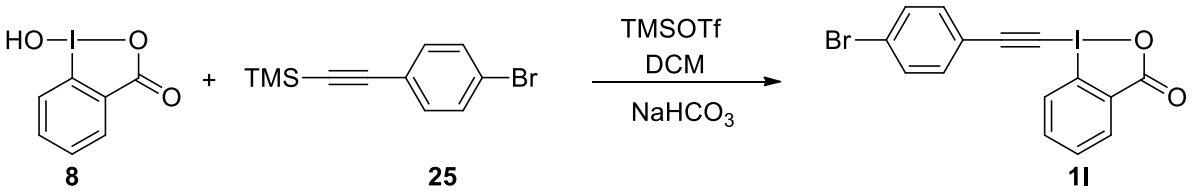
Following a reported procedure,[11] trimethylsilyl triflate (0.80 mL, 4.4 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**8**) (1.06 g, 4.00 mmol, 1 equiv) in CH_2Cl_2 (15 mL) at RT. The resulting yellow mixture was stirred for 1 h, followed by the dropwise addition of trimethyl((4-(trifluoromethyl)phenyl)ethynyl)silane (**24**) (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 **1k** (850 mg, 2.04 mmol, 51%) as a pale yellow solid.

^1H NMR (400 MHz, $CDCl_3$) 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, $CDCl_3$) δ 166.6, 135.0,

[14] H. Huang, G. Zhang, L. Gong, S. Zhang, Y. Chen, *J. Am. Chem. Soc.* **2014**, *136*, 2280.
[15] a) I. F. Dempsey Hyatt, D. J. Nasrallah, M. A. Maxwell, A. C. F. Hairston, M. M. Abdalhameed, M. P. Croatt, *Chem. Commun.* **2015**, *51*, 5287; b) O. Dumele, D. Wu, N. Trapp, N. Goroff, F. Diederich, *Org. Lett.* **2014**, *16*, 4722.

133.0, 132.6, 132.2 (q, J_{C-F} = 33.0 Hz), 131.7, 131.2, 126.3, 125.7 (q, J_{C-F} = 3.6 Hz), 124.4, 123.4 (q, J_{C-F} = 272.6 Hz), 116.1, 104.2, 53.7; Consistent with reported data.[16]

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

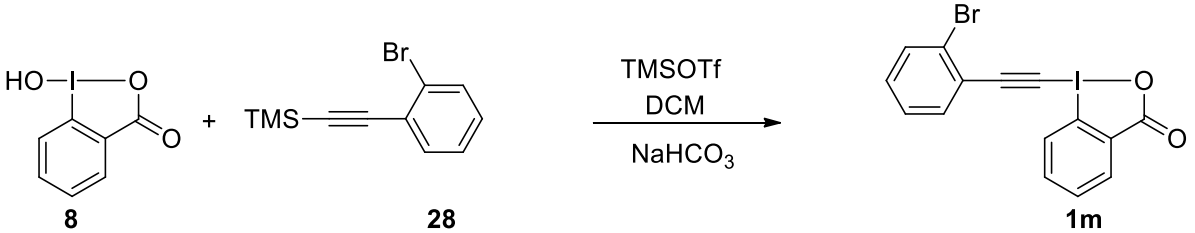


8 **25** **1l**

Following a reported procedure,[11] trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**8**) (1.32 g, 5.00 mmol, 1 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 (**25**) (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 **1l** (1.00 g, 2.34 mmol, 47%) as a pale yellow solid.

Mp 158-163 °C (decomposition). ^{1}H NMR (400 MHz, $CDCl_3$) 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, 2 H, *J* = 8.5 Hz, Ar*H*), 7.46 (d, 2 H, *J* = 8.5 Hz, Ar*H*).^{13}C NMR (101 MHz, $CDCl_3$) 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. IR ν 2155 (w), 1612 (s), 1559 (w), 1479 (w), 1445 (w), 1328 (m), 1297 (w), 1007 (w), 906 (w). HRMS (ESI) $C_{15}H_9BrIO_2^+$ $[M+H]^+$ calc. = 426.8825; $[M+H]^+$ obs. = 426.8830.

1-[2-Bromophenylethynyl]-1,2-benziodoxol-3(1H)-one (1m)



8 **28** **1m**

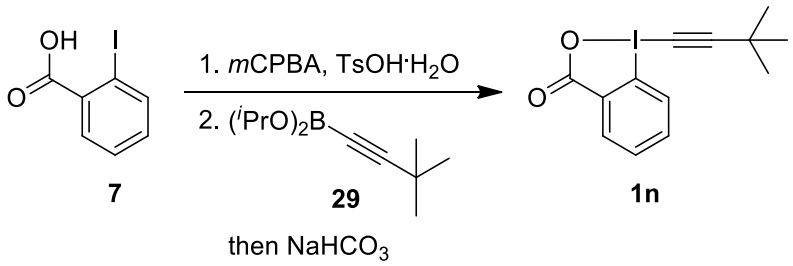
Following a reported procedure,[11] trimethylsilyl triflate (1.0 mL, 5.5 mmol, 1.1 equiv) was added to a suspension of 2-iodosylbenzoic acid (**8**) (1.32 g, 5.00 mmol, 1 equiv) in CH_2Cl_2 (15 mL) at RT. The resulting suspension was stirred for 3 h, followed by the drop wise addition of ((2-bromophenyl)ethynyl)trimethylsilane (**28**) (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

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

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 **1m** (1.50 g, 3.51 mmol, 70%) as a colorless solid.

Mp 174-177 °C (decomposition). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (td, 2 H, *J* = 7.3, 2.1 Hz, Ar*H*), 7.84 – 7.74 (m, 2 H, Ar*H*), 7.68 (d, 1 H, *J* = 1.1 Hz, Ar*H*), 7.61 (dd, 1 H, *J* = 7.6, 1.7 Hz, Ar*H*), 7.36 (dtd, 2 H, *J* = 22.4, 7.5, 1.5 Hz, Ar*H*).^{13}C NMR (101 MHz, $CDCl_3$)[17] 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. IR ν 2358 (w), 2155 (w), 1638 (s), 1616 (m), 1585 (w), 1466 (w), 1316 (m), 1147 (w). HRMS (ESI) $C_{15}H_9BrIO_2^+$ $[M+H]^+$ calc. = 426.8825; $[M+H]^+$ obs. = 426.8828.

3,3-Dimethylbutynyl-1,2-benziodoxol-3(1*H*)-one (1n)

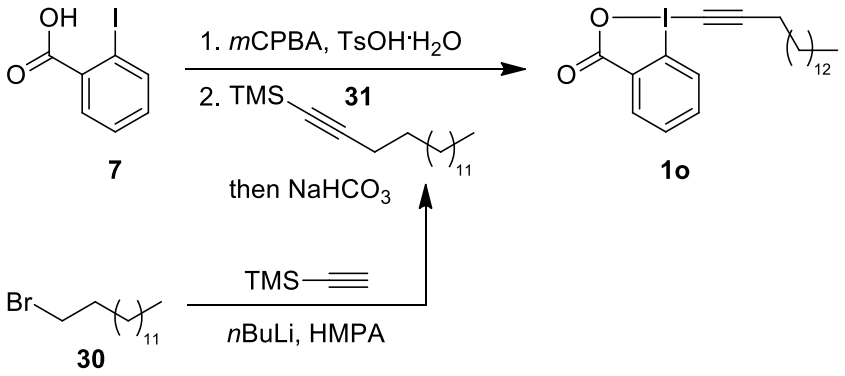


Following a slightly modified procedure,[18] 2-iodobenzoic acid (**7**) (1.64 g, 6.59 mmol, 1.00 eq.), *para*-toluenesulfonic acid monohydrate ($TsOH{\cdot}H_2O$, 1.25 g, 6.59 mmol, 1.00 eq.) and *meta*-chloroperoxybenzoic acid (*m*CPBA-70%, 1.79 g, 7.25 mmol, 1.10 eq.) were dissolved in dichloromethane (12 mL) and 2,2,2-trifluoroethanol (12 mL). The mixture was stirred at room temperature under nitrogen for 1 hour, after which diisopropyl (3,3-dimethylbut-1-yn-1-yl)boronate (**29**, 1.94 g, 9.23 mmol, 1.40 eq.) was added in one portion. The reaction mixture was stirred for 1 hour at room temperature, filtered and concentrated *in vacuo*. The resulting oil was dissolved in dichloromethane (120 mL) and under vigorous stirring, saturated aq. $NaHCO_3$ (120 mL) was added. The mixture was stirred for 60 minutes, the two layers were separated and the aqueous layer was extracted with additional portions of dichloromethane (3 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (ethyl acetate) to afford **1n** (2.06 g, 6.28 mmol, 95%) as a white solid.

R_f (EtOAc) = 0.36. Mp 189-192 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.39-8.33 (m, 1 H, Ar*H*), 8.13-8.07 (m, 1 H, Ar*H*), 7.78-7.66 (m, 2 H, Ar*H*), 1.34 (s, 9 H, *t*Bu). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.7, 134.7, 132.4, 131.6, 131.5, 126.0, 117.5, 115.7, 38.2, 30.6, 29.7. IR ν 3463 (w), 2971 (w), 2171 (w), 1646 (s), 1622 (s), 1440 (w), 1332 (m), 1248 (m), 913 (w), 832 (m), 745 (s). HRMS (ESI) $C_{13}H_{14}IO_2^+$ $[M+H]^+$ calc. = 329.0033; $[M+H]^+$ obs. = 329.0023.

Hexadecynyl-1,2-benziodoxol-3(1*H*)-one (1o)

[17] One carbon is not resolved.
[18] M. J. Bouma, B. Olofsson, *Chem. Eur. J.* **2012**, *18*, 14242.



Following a reported procedure,[19] To a mixture of trimethylsilylacetylene (8.33 g, 85.0 mmol, 1.20 eq.) and dry THF (46 mL) was added at -78 °C under nitrogen 2.5 M *n*BuLi in hexanes (33.9 mL, 85.0 mmol, 1.20 eq.) over a 10 minute time period. The resulting light yellow solution was stirred at -78 °C for 60 minutes, after which a mixture consisting of 1-bromotetradecane **30** (19.6 g, 70.7 mmol, 1.00 eq.), hexamethylphosphoramide (HMPA, 14.2 mL, 78.0 mmol, 1.10 eq.) and dry THF (23 mL) was slowly added *via* cannula over a 20 minute time period. The reaction mixture was stirred for 60 minutes at -78 °C, followed by 24 hours of stirring at room temperature. The reaction was quenched at 0 °C with saturated aq. NH_4Cl (50 mL) and diluted with water (10 mL) and EtOAc (50 mL). The two layers were separated and the aq. layer was extracted with additional portions of EtOAc (3 x 50 mL). The combined organic layers were washed with water (2 x 100 mL), brine (100 mL), dried over $MgSO_4$, filtered and concentrated *in vacuo*. The light brown crude liquid was finally pushed through a small plug of silica gel with pentane as eluent to afford pure hexadec-1-yn-1-yltrimethylsilane (**31**, 19.3 g, 65.5 mmol, 92.7% yield) as a colorless liquid. R_f (pentane) = 0.78.

^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.19 (t, 2 H, *J* = 7.1 Hz, CCC*H*$_2$), 1.54-1.44 (m, 2 H, CH_2), 1.42-1.18 (m, 22 H, CH_2), 0.87 (t, 3 H, *J* = 6.7 Hz, CH_2CH_3), 0.13 (s, 9 H, TMS). ^{13}C NMR ($CDCl_3$, 100 MHz):[20] δ 107.7, 84.3, 32.2, 29.9, 29.8, 29.7, 29.6, 29.3, 29.0, 28.9, 22.9, 20.0, 14.3, 0.3. IR ν 2924 (m), 2854 (m), 2175 (w), 1461 (w), 1249 (w), 910 (w), 841 (s), 761 (w), 736 (m). HRMS (ESI) $C_{19}H_{38}AgSi^+$ $[M+Ag]^+$ calc. = 401.1794; $[M+Ag]^+$ obs. = 401.1798.

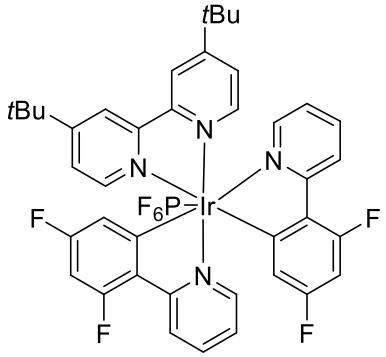
2-Iodobenzoic acid (**7**) (8.00 g, 32.2 mmol, 1.00 eq.), *para*-toluenesulfonic acid monohydrate ($TsOH·H_2O$, 6.13 g, 32.2 mmol, 1.00 eq.) and *meta*-chloroperoxybenzoic acid (*m*CPBA-70%, 8.74 g, 35.5 mmol, 1.10 eq.) were dissolved in dichloromethane (60 mL) and 2,2,2-trifluoroethanol (60 mL). The mixture was stirred at room temperature under nitrogen for 1 hour, after which hexadec-1-yn-1-yltrimethylsilane (**31**, 13.3 g, 45.1 mmol, 1.40 eq.) was added in one portion. The reaction mixture was stirred for 14 hours at room temperature, filtered and concentrated *in vacuo*. The resulting oil was dissolved in dichloromethane (400 mL) and under vigorous stirring, saturated aq. $NaHCO_3$ (400 mL) was added. The mixture was stirred for 60 minutes, the two layers were separated and the aqueous layer was extracted

[19] R. Frei, M. D. Wodrich, D. P. Hari, P. A. Borin, C. Chauvier, J. Waser, *J. Am. Chem. Soc.* **2014**, *136*, 16563.
[20] Some signals were not resolved at 100 MHz.

with additional portions of dichloromethane (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The crude product was purified by flash column chromatography (ethyl acetate) to afford **1o** (6.02 g, 12.9 mmol, 40%) as a white solid.

R_f (EtOAc) = 0.36. Mp 102.6-105.3 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 8.44-8.37 (m, 1 H, Ar*H*), 8.21-8.14 (m, 1 H, Ar*H*), 7.80-7.70 (m, 2 H, Ar*H*), 2.59 (t, 2 H, *J* = 7.1 Hz, CCC*H*$_2$), 1.65 (p, 2 H, *J* = 7.1 Hz, CCCH$_2$C*H*$_2$), 1.52-1.40 (m, 2 H), 1.39-1.19 (m, 20 H, CH_2), 0.86 (t, 3 H, *J* = 6.7 Hz, CH_2C*H*$_3$). ^{13}C NMR ($CDCl_3$, 100 MHz): δ 166.6, 134.7, 132.5, 131.7, 131.6, 126.2, 115.7, 109.9, 39.5, 32.1, 29.8, 29.7, 29.6, 29.5, 29.2, 29.1, 28.3, 22.8, 20.6, 14.3. IR ν 2924 (s), 2853 (m), 2166 (w), 1649 (m), 1623 (m), 1439 (w), 908 (m), 736 (s).

Iridium catalyst (3b)



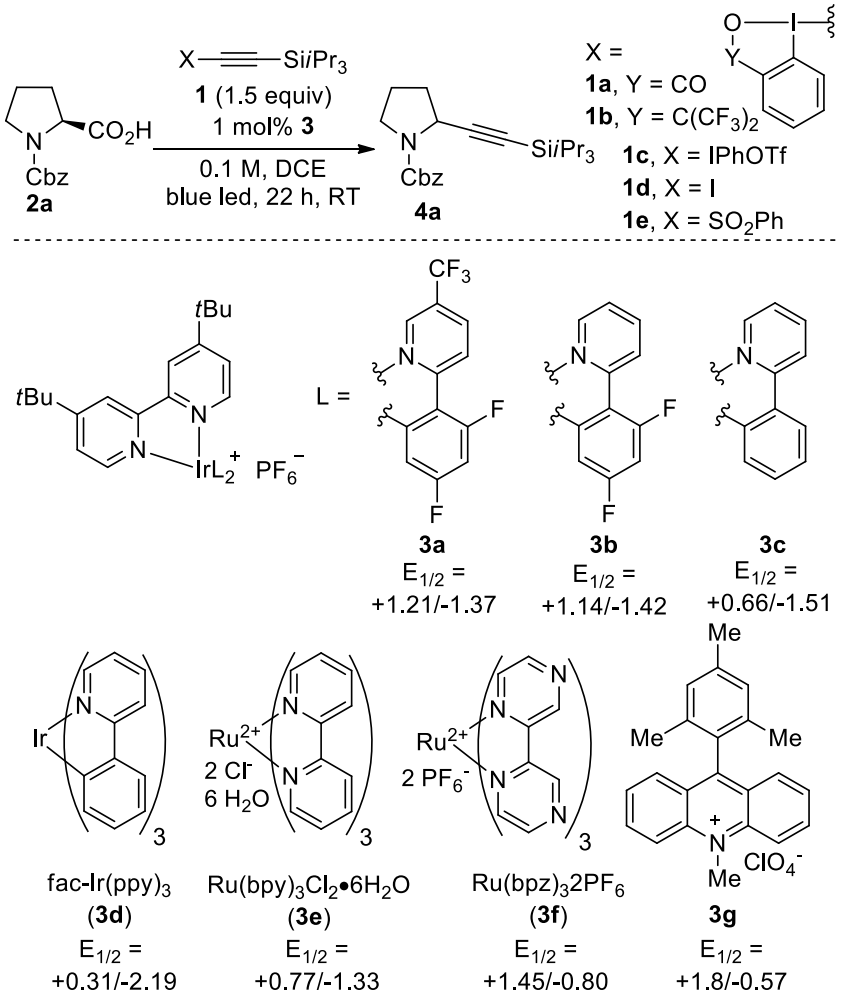
Following a reported procedure, [21]heteroleptic iridium **3b** was synthesized in two steps. First, the corresponding chloro-bridged dimer was synthesized by charging a two-necked reaction flask with magnetic stirring bar, iridium(III) chloride (366 mg, 1.16 mmol, 1 equiv), 2-(2,4-difluorophenyl)pyridine (0.50 g, 2.6 mmol, 2.3 equiv), and a 2:1 v:v mixture of 2-methoxyethanol (11 mL) /water (5.5 mL). After degassing the mixture with N_2 (via N_2 bubbling), the resulting solution was heated overnight under reflux at 120 °C. Then the reaction mixture was cooled to room temperature and filtered. The yellow precipitate was washed with water (3 x 10 mL), dried and directly used for the next step without further purification (620 mg of yellow powder, 0.510 mmol, 88% yield). In the second step, the chloro-bridged dimer (50 mg, 0.041 mmol, 1.0 equiv), 4,4'-ditertbutyl bipyridyl ligand (24 mg, 0.090 mmol, 2.2 equiv) and ethylene glycol (2.0 mL) were placed in a flame dried flask and then flushed with N_2. The mixture was heated at 150 °C for 7 h and then cooled before being washed with pentane (3 x 10 mL). Evaporation of pentane residues under vaccuo afforded a crude solution of catalyst in ethylene glycol. Addition of aqueous ammonium hexafluorophosphate (sat. solution) allowed the precipitation of the iridium-PF_6 salt, which was filtered, washed with diethylether, dried and recrystallized (acetone / ether) yielding the photocatalyst **3b** as a yellow solid (70 mg. 0.071 mmol, 86%). R_f (pentane) = 0.78. NMR matches the literature data. [21]

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

3. Decarboxylative alkynylation

Optimization of the reaction:

Dry degassed DCE (0.5 mL) was added in a flame dried 1.5 mL test tube containing a teflon coated stirring bar, the carboxylic acid **2** (0.10 mmol, 1.0 equiv), EBX reagent **1** (0.15 mmol, 1.5 equiv), CsOBz (0.30 mmol, 3.0 equiv) and $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ (**3a**) (0.001 mmol, 0.01 equiv) under N_2. The reaction mixture was again degassed by bubbling N_2 inside the test tube via syringe for 5 min before being irradiated using blue light LEDs for 22 h at rt.
The reaction mixture was filtered over celite, eluting with ethyl acetate, and evaporated under reduced pressure. The crude product was purified by preparative TLC (Heptane/Ethyl Acetate 8/2) directly without any further work-up.

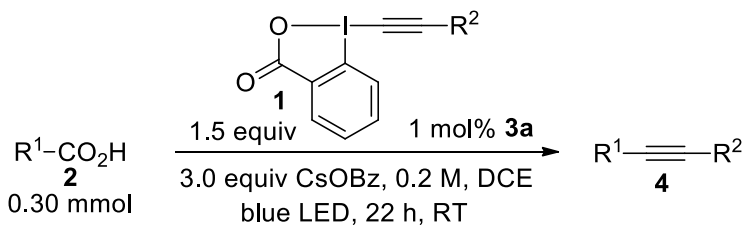


entry	catalyst	base	reagent	solvent	conversion[a]	yield[b]
1	**3a**	1.1 equiv CsOAc	**1a**	MeCN	NR	NR
2	**3a**	1.1 equiv CsOAc	**1a**	Toluene	-	28%
3	**3a**	1.1 equiv CsOAc	**1a**	THF	-	33%
4	**3a**	1.1 equiv CsOAc	**1a**	Water	NR	NR
5	**3a**	1.1 equiv CsOAc	**1a**	DMF	-	20%

6	**3a**	1.1 equiv CsOAc	**1a**	DMA	-	20%
7	**3a**	1.1 equiv CsOAc	**1a**	DMSO	-	20%
8	**3a**	1.1 equiv CsOAc	**1a**	DCE / DCM[c]	-	31%
9	**3a**	2.0 equiv CsOAc	**1a**	DCE	90	40%
10	**3a**	3.0 equiv CsOAc	**1a**	DCE	90	47%
11	**3a**	4.0 equiv CsOAc	**1a**	DCE	>95%	68%
12	**3a**	4.0 equiv KOAc	**1a**	DCE	<50%	9%
13	**3a**	4.0 equiv NaOAc	**1a**	DCE	<50%	22%
14	**3a**	4.0 equiv Cs_2CO_3	**1a**	DCE	>95%	35%
15	**3a**	4.0 equiv CsO(4-tBuBz)	**1a**	DCE	>95%	60%
16	**3a**	4.0 equiv CsOBz	**1a**	DCE	>95%	74%
17	**3b**	4.0 equiv CsOBz	**1a**	DCE	>95%	68%
18	**3c**	4.0 equiv CsOBz	**1a**	DCE	<10%	<5%
19	**3d**	4.0 equiv CsOBz	**1a**	DCE	<10%	<5%
20	**3e**	4.0 equiv CsOBz	**1a**	DCE	<10%	<5%
21	**3f**	4.0 equiv CsOBz	**1a**	DCE	<10%	<5%
22	**3g**	4.0 equiv CsOBz	**1a**	DCE	<10%	<5%
23[d]	**3a**	4.0 equiv CsOBz	**1a**	DCE	75%	38%
24[e]	**3a**	4.0 equiv CsOBz	**1a**	DCE	>95%	12%
25[f]	**3a**	3.0 equiv CsOBz	**1a**	DCE	> 95%	92%
26[f]	**3a**	3.0 equiv CsOBz	**1b**	DCE	>95%	38%
27[f]	**3a**	3.0 equiv CsOBz	**1c**	DCE	>95%	<5%
28[f]	**3a**	3.0 equiv CsOBz	**1d**	DCE	>95%	82%
29[f]	**3a**	3.0 equiv CsOBz	**1e**	DCE	> 95%	<5%

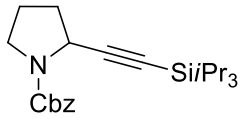
[a]Reaction conditions: Using 0.1 mmol **2a** (1 equiv), 0.15 mmol **1** (1.5 equiv), 1 μmol **3** (0.01 equiv) in DCE (1 mL) for 22 h at RT. The conversion of **2a** by NMR is given. The values for reduction potentials are given in volts for catalyst **3** in relation to SCE, except for **3b** which is reported relatively to ferrocene. [b]Isolated yield after preparative TLC. [c] DCE was preferred to avoid evaporation of the solvent during overnight reactions. [d]Using 1.1 equiv of EBX reagent. [e]Using 2.0 equiv of EBX reagent. [f] In 0.5 mL DCE.

General procedure for decarboxylative alkynylation.



Dry degassed DCE (1.5 mL) was added in a flame dried 4.0 mL test tube containing a teflon coated stirring bar, the carboxylic acid **2** (0.30 mmol, 1.0 equiv), EBX reagent **1** (0.45 mmol, 1.5 equiv), CsOBz (0.90 mmol, 3.0 equiv) and $Ir(dF(CF_3)ppy)_2(dtbbpy)PF_6$ (**3a**) (0.003 mmol, 0.01 equiv) under N_2. The reaction mixture was again degassed by bubbling N_2 inside the test tube via syringe for 5 min before being irradiated using blue light LEDs for 22h at rt.
The reaction mixture was filtered over celite, eluting with ethyl acetate, and evaporated under reduced pressure. The crude product was purified by column chromatography (Pentane/Ethyl Acetate) directly without any further work-up.

Benzyl 2-((triisopropylsilyl)ethynyl)pyrrolidine-1-carboxylate (4a)



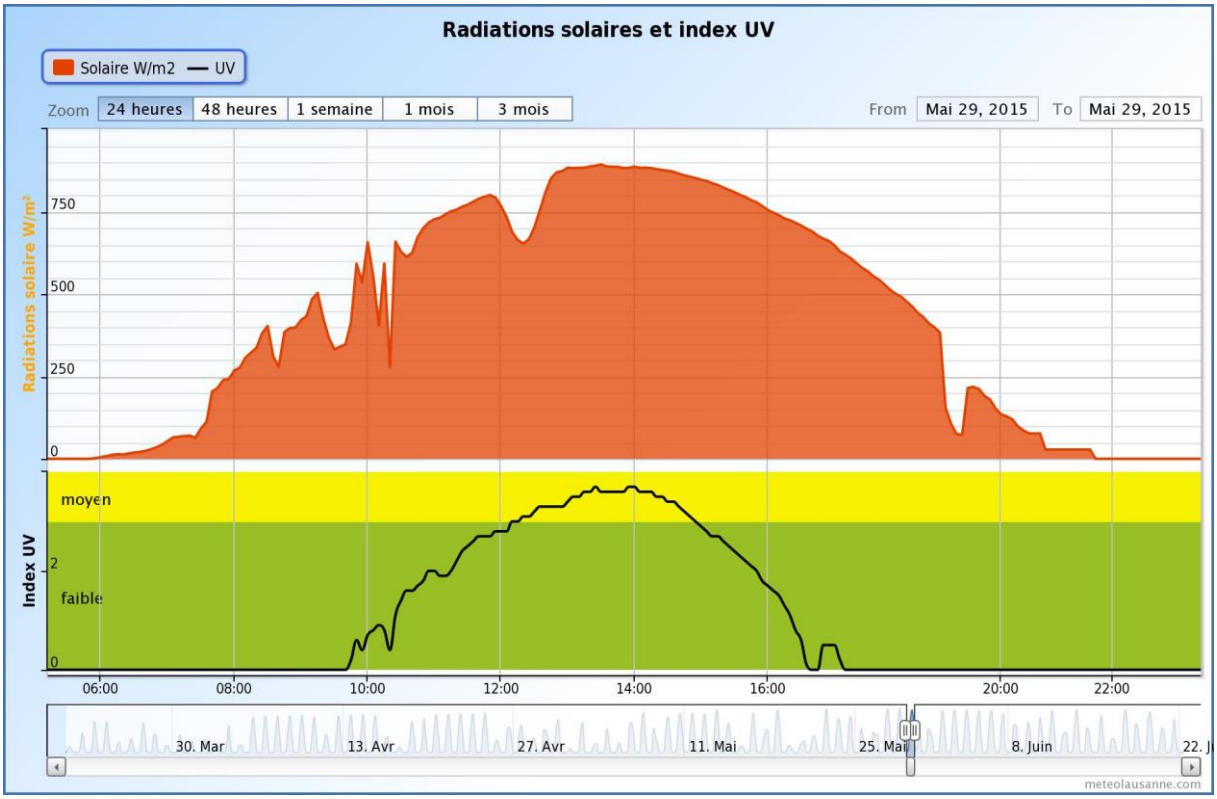
Scope scale: Starting from **2a** (75 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4a** as colorless oil (104 mg, 0.270 mmol, 90%).

1 mmol scale: Starting from **2a** (250 mg, 1.0 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4a** as colorless oil (344 mg, 0.892 mmol, 89%).

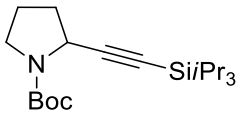
Sunlight experiment: Starting from **2a** (25 mg, 0.10 mmol), the reaction mixture was stirred for 5 h outdoors, under sunlight exposition instead of blue leds. The crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4a** as colorless oil (34 mg, 0.088 mmol, 88%).

R_f: 0.28 (Pentane/Ethyl Acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.46 – 7.27 (m, 5H, *Ph*), 5.16 (d, *J* = 3.2 Hz, 2H, C*H*$_2$-O), 4.67 – 4.51 (m, 1H, C*H*-C≡C), 3.64 – 3.49 (m, 1H, C*H*$_2$),

3.47 – 3.30 (m, 1H, CH_2), 2.21 – 1.98 (m, 3H, CH_2), 1.99 – 1.87 (m, 1H, CH_2), 1.11 – 0.93 (m, 21H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$)[22] δ 154.6, 136.9, 128.4, 127.8, 127.8, 127.6, 107.9, 82.6, 66.9, 66.7, 49.3, 48.8, 46.0, 45.5, 34.3, 33.4, 24.4, 23.6, 18.6, 11.1. IR 2943 (m), 2865 (m), 2170 (w), 1709 (s), 1464 (w), 1410 (s), 1356 (m), 1184 (m), 1119 (m), 1092 (m), 996 (w), 883 (m). HRMS (ESI) calcd for $C_{23}H_{35}NNaO_2Si^+$ $[M+Na]^+$ 408.2329; found 408.2334.
Sun spectra during experiment:[23]



***Tert*-butyl 2-((triisopropylsilyl)ethynyl)pyrrolidine-1-carboxylate (4b)**

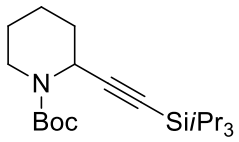


Starting from **2b** (65 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4b** as colorless oil (95 mg, 0.27 mmol, 90%).

R_f: 0.3 (Pentane/Ethyl Acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.52 – 4.35 (m, 1H, *CH*-C≡C), 3.55 – 3.41 (m, 1H, *NCH*$_2$), 3.36 – 3.19 (m, 1H, N*CH*$_2$), 2.14 – 1.94 (m, 3H, *CH*$_2$), 1.94 – 1.83 (m, 1H, *CH*$_2$), 1.46 (s, 9H, *tBu*), 1.12 – 0.87 (m, 21H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 108.5, 81.5, 79.5, 48.8, 45.4, 34.2, 28.4, 23.6, 18.6, 11.2. IR 2979 (w), 2974 (w), 2867 (w), 2173 (w), 1704 (s), 1392 (s), 1366 (m), 1332 (w), 1255 (w), 1170 (s), 1121 (m), 1092 (m), 955 (w), 882 (w). HRMS (ESI) calcd for $C_{20}H_{37}NNaO_2Si^+$ $[M+Na]^+$ 374.2486; found 374.2483.

[22] Mixture of two rotamers, which are not completely resolved.
[23] Taken from: http://www.meteolausanne.com/soleil-et-uv.html

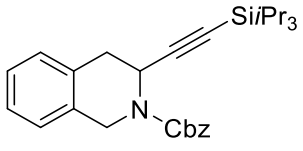
***Tert*-butyl 2-((triisopropylsilyl)ethynyl)piperidine-1-carboxylate (4c)**



Starting from **2c** (69 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4c** as colorless oil (72 mg, 0.20 mmol, 66%).

R_f: 0.45 (Pentane/Ethyl Acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.21 – 4.90 (m, 1H, *CH*-C≡C), 4.01 – 3.78 (m, 1H, *CH*$_2$-N), 3.15 – 2.91 (m, 1H, *CH*$_2$-N), 1.89 – 1.70 (m, 2H, *CH*$_2$), 1.71 – 1.52 (m, 4H, *CH*$_2$), 1.46 (s, 9H, *tBu*), 1.12 – 0.87 (m, 21H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.8, 106.1, 84.3, 79.8, 76.7, 30.6, 28.4, 25.3, 20.0, 18.6, 11.4, 11.2. IR 2941 (m), 2865 (m), 2166 (w), 1695 (m), 1464 (w), 1389 (m), 1367 (m), 1318 (m), 1271 (m), 1162 (s), 1007 (m), 924 (w), 884 (m). HRMS (ESI) calcd for $C_{21}H_{39}NNaO_2Si^+$ $[M+Na]^+$ 388.2642; found 388.2639.

Benzyl 3-((triisopropylsilyl)ethynyl)-3,4-dihydroisoquinoline-2(1H)-carboxylate (4d)

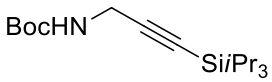


New compound

Starting from **2d** (93 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4d** as colorless oil (116 mg, 0.260 mmol, 87%).

R_f: 0.30 (Pentane/Ethyl Acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) [22] δ 7.50 – 7.30 (m, 5H, *Ph*), 7.25 – 6.99 (m, 4H, *Ar*H), 5.61 – 5.29 (m, 1H, *CH*-C≡C), 5.32 – 5.13 (m, 2H, *CH*$_2$), 4.94 (d, *J* = 16.6 Hz, 1H, *CH*$_2$-N), 4.57 (d, *J* = 16.7 Hz, 1H, *CH*$_2$-N), 3.21 (dd, *J* = 14.9, 4.9 Hz, 1H, *CH*$_2$), 3.02 – 2.78 (m, 1H, *CH*$_2$), 0.97 – 0.77 (m, 21H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$)[22] δ 155.0, 136.6, 132.3, 131.9, 129.3, 129.1, 128.5, 128.1, 127.9, 126.4, 125.8, 105.0, 84.7, 67.5, 43.3, 35.4, 18.3, 10.9. IR 2943 (w), 2865 (w), 2250 (w), 2171 (w), 1711 (w), 1464 (w), 1423 (w), 1319 (w), 1301 (w), 1243 (m), 1219 (m), 1118 (w), 998 (m), 909 (s), 883 (m). HRMS (ESI) calcd for $C_{28}H_{38}NO_2Si^+$ $[M+H]^+$ 448.2666; found 448.2661.

***Tert*-butyl (3-(triisopropylsilyl)prop-2-yn-1-yl)carbamate (4e)**

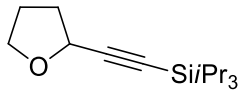


Starting from **2e** (53 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4e** as colorless oil (65 mg, 0.21 mmol, 70%).

R_f: 0.28 (Pentane/Ethyl Acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.74 – 4.58 (m, 1H, *NH*), 4.02 – 3.85 (m, 2H, *CH*$_2$), 1.44 (s, 9H, *tBu*), 1.15 – 0.92 (m, 21H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.2, 103.6, 84.1, 79.8, 31.6, 28.3, 18.5, 11.1. IR 3332 (w), 2943 (s), 2860

(s), 2178 (w), 1704 (s), 1502 (m), 1464 (m), 1367 (m), 1277 (m), 1249 (m), 1170 (s), 1049 (m), 1017 (s), 1002 (s), 918 (m), 884 (s). HRMS (ESI) calcd for $C_{17}H_{33}NNaO_2Si^+$ $[M+Na]^+$ 334.2173; found 334.2176.

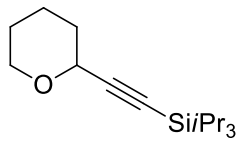
Triisopropyl((tetrahydrofuran-2-yl)ethynyl)silane (4f)



Starting from **2f** (35 mg, 0.30 mmol), the crude product was purified by column chromatography (100% Pentane) to afford **4f** as colorless oil (76 mg, 0.30 mmol, quantitative).

R_f: 0.8 (Pentane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.60 (dd, *J* = 7.2, 4.5 Hz, 1H, *CH*-*C*≡*C*), 3.97 – 3.90 (m, 1H, *CH*-*O*), 3.83 – 3.77 (m, 1H, *CH*-*O*), 2.20 – 1.80 (m, 4H, 2 x *CH*$_2$), 1.13 – 0.96 (m, 21H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 107.8, 85.0, 68.5, 67.5, 33.7, 25.1, 18.6, 11.1. IR 2943 (s), 2866 (s), 2168 (w), 1463 (s), 1329 (m), 1180 (w), 1055 (s), 996 (m), 919 (m), 883 (s).The data correspond to the reported values.[24]

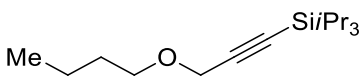
Triisopropyl((tetrahydro-2H-pyran-2-yl)ethynyl)silane (4g)



Starting from **2g** (39 mg, 0.30 mmol), the crude product was purified by column chromatography (100% Pentane) to afford **4g** as colorless oil (48 mg, 0.18 mmol, 60%)

R_f: 0.85 (Pentane). 4.40 (dd, *J* = 6.3, 3.0 Hz, 1H, *CH*-C≡C), 4.06 – 3.97 (m, 1H, C*H*$_2$O), 3.61 – 3.50 (m, 1H, C*H*$_2$O), 1.92 – 1.80 (m, 2H, C*H*$_2$), 1.75 – 1.65 (m, 1H, C*H*$_2$), 1.63 – 1.49 (m, 3H, C*H*$_2$), 1.11 – 0.99 (m, 21H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 106.4, 86.2, 67.0, 65.6, 32.2, 25.7, 21.1, 18.6, 11.2. IR 2941 (m), 2865 (m), 1726 (w), 1680 (m), 1620 (s), 1556 (m), 1464 (m), 1374 (m), 1334 (m), 1294 (w), 1265 (w), 1198 (s), 1158 (m), 1118 (w), 1085 (s), 1040 (s), 1021 (s), 1015 (m), 971 (m), 884 (s), 869 (s). HRMS (ESI) calcd for $C_{16}H_{30}NaOSi^+$ $[M+Na]^+$ 289.1958; found 289.1960.

(3-Butoxyprop-1-yn-1-yl)triisopropylsilane (4h)

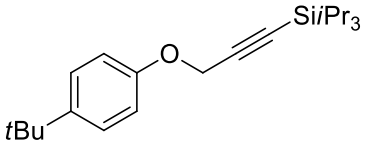


[24] R.-Y. Zhang, L.-Y. Xi, L. Zhang, S. Liang, S.-Y. Chen, X.-Q. Yu, *RSC Advances* **2014**, *4*, 54349.

Starting from **2h** (39 mg, 0.30 mmol), the crude product was analyzed directly by NMR using Trimethoxybenzene as internal standard. (11 mg, 0.21 equiv), which showed the formation of **4h** in 88% yield (71 mg, 0.26 mmol, 88% NMR yield).

R_f: 0.85 (Pentane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.17 (s, 2H, *CH*$_2$-C≡C), 3.54 (t, *J* = 6.6 Hz, 2H, *CH*$_2$O), 1.57 (dq, *J* = 8.3, 6.7 Hz, 2H, *CH*$_2$), 1.39 (dt, *J* = 14.8, 7.3 Hz, 2H, *CH*$_2$), 1.12 – 1.01 (m, 21H, *TIPS*), 0.92 (t, *J* = 7.4 Hz, 3H, *CH*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 103.8, 87.1, 69.4, 58.7, 31.6, 19.3, 18.6, 13.9, 11.2. IR 2942 (m), 2865 (m), 2248 (w), 2170 (w), 2094 (w), 1733 (s), 1680 (m), 1623 (m), 1510 (w), 1464 (m), 1437 (m), 1383 (s), 1294 (m), 1206 (m), 1152 (s), 997 (m), 884 (s). HRMS (ESI): calcd for $C_{16}H_{32}NaOSi^+$ $[M+Na]^+$ 291.2120; found 291.2112.

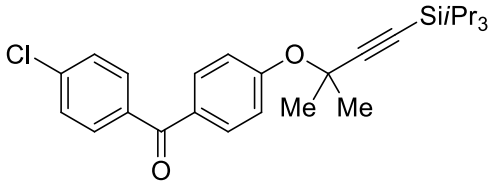
(3-(4-(*Tert*-butyl)phenoxy)prop-1-yn-1-yl)triisopropylsilane (4i)



Starting from **2i** (63 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane) affording the expected compound **4i** in 84% yield.

R_f: 0.85 (Pentane). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H, 2 x Ar*CH*), 6.96 – 6.90 (m, 2H, 2 x Ar*CH*), 4.71 (s, 2H, *CH*$_2$), 1.29 (s, 9H, *tBu*), 1.05 – 1.00 (m, 21H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$) δ ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.4, 144.1, 126.0, 115.0, 102.3, 100.8, 57.0, 34.1, 31.5, 18.5, 11.1. IR 3064 (w), 2835 (w), 2114 (w), 2081 (w), 1736 (w), 1622 (s), 1513 (s), 1440 (w), 1296 (w), 1224 (m), 1206 (m), 1205 (m), 1153 (s), 1041 (s), 985 (m), 830 (s). MS (EI): 344.2 (M^+).

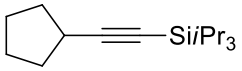
(4-Chlorophenyl)(4-((2-methyl-4-(triisopropylsilyl)but-3-yn-2-yl)oxy)phenyl)methanone (4j)



Starting from **2j** (96 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4j** as colorless oil (64 mg, 0.14 mmol, 47%)

R_f: 0.5 (Pentane/Ethyl Acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.72 (m, *J* = 8.6, 4.9 Hz, 4H, 4 x Ar*CH*), 7.45 (d, *J* = 8.5 Hz, 2H, 2 x Ar*CH*), 7.34 (d, *J* = 8.8 Hz, 2H, 2 x Ar*CH*), 1.73 (s, 6H, 2 x *CH*$_3$), 1.13 – 0.96 (m, 21H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 194.5, 160.2, 138.3, 136.5, 131.6, 131.2, 130.5, 128.5, 119.1, 108.7, 88.0, 73.0, 29.9, 18.6, 11.1. IR 2942 (m), 2865 (m), 1724 (w), 1658 (s), 1598 (s), 1505 (m), 1463 (m), 1383 (m), 1305 (m), 1285 (m), 1251 (m), 1136 (s), 1090 (m), 1016 (m), 928 (s), 884 (s). HRMS (ESI) calcd for $C_{27}H_{35}ClNaO_2Si^+$ $[M+Na]^+$ 477.1987; found 477.1999.

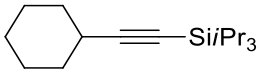
(Cyclopentylethynyl)triisopropylsilane (4k)



Starting from **2k** (34 mg, 32 µL, 0.30 mmol) and using 1 mol% of catalyst **3a**, the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4k** as colorless oil (48 mg, 0.19 mmol, 64%).

R_f: 0.9 (Pentane) ^{1}H NMR (400 MHz, $CDCl_3$)[25] δ 22.74 – 2.60 (m, 1H, *CH*-C≡C), 1.97 – 1.82 (m, 2H, *CH*$_2$), 1.81 – 1.46 (m, 6H, *CH*$_2$), 1.14 – 0.94 (m, 21H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 114.1, 79.0, 34.2, 31.2, 24.9, 18.6, 11.3. IR 2943 (m), 2865 (m), 2361 (w), 2159 (w), 2097 (m), 1777 (m), 1678 (m), 1642 (m), 1578 (w), 1512 (w), 1464 (w), 1383 (w), 1223 (m), 1138 (m), 996 (s), 919 (s), 883 (s). The data correspond to the reported values.[26]

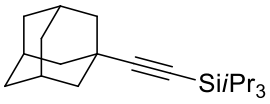
(Cyclohexylethynyl)triisopropylsilane (4l)



Starting from **2l** (39 mg, 0.30 mmol) and using 2 mol% of catalyst **3a**, the crude product was purified by column chromatography (100% Pentane) to afford **4l** as colorless oil (38 mg, 0.14 mmol, 48%).

R_f: 0.9 (Pentane). ^{1}H NMR (400 MHz, $CDCl_3$)[25] δ 2.49 – 2.41 (m, 1H, *CH*), 1.80 – 1.66 (m, 4H, 2 x *CH*$_2$), 1.54 – 1.41 (m, 3H, *CH*$_2$), 1.41 – 1.19 (m, 3H, *CH*$_2$), 1.13 – 0.96 (m, 21H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 113.6, 79.5, 32.7, 29.9, 26.0, 24.5, 18.5, 11.4. IR 2940 (s), 2865 (s), 2171 (w), 2098 (m), 1463 (m), 1384 (w), 1367 (w), 1235 (w), 1075 (w), 997 (m), 920 (m), 883 (s). The data correspond to the reported values.[26]

(Adamantan-1-ylethynyl)triisopropylsilane (4m)



Starting from **2m** (54 mg, 0.30 mmol) and using 2 mol% of catalyst **3a**, the crude product was purified by column chromatography (100% Pentane) to afford **4m** as colorless oil (42 mg, 0.13 mmol, 44%).

R_f: 0.85 (Pentane) ^{1}H NMR (400 MHz, $CDCl_3$) δ 1.96 – 1.91 (m, 3H, 3 x *CH*), 1.88 (dd, *J* = 3.1, 3.1 Hz, 6H, 3 x *CH*$_2$), 1.68 (dd, *J* = 3.1, 3.1 Hz, 6H, 3 x *CH*$_2$), 1.12 – 1.00 (m, 21H, *TIPS*). ^{13}C NMR (101 MHz, $CDCl_3$) δ 118.1, 77.3, 43.1, 36.4, 30.4, 28.0, 19.9, 18.5, 11.4. IR 2920 (s), 2865 (s), 2164 (w), 2098 (m), 1464 (m), 1383 (w), 1247 (w), 1155 (w), 1017 (w), 997 (m), 923 (m), 883 (s). The data correspond to the reported values.[27]

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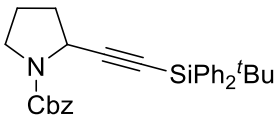
[24] Contains 5% of unseparable impurities (probably TIPS alkyne dimer).

[26] X. Liu, Z. Wang, X. Cheng, C. Li, *J. Am. Chem. Soc.* **2012**, *134*, 14330.

[27] R. H. Pouwer, J. B. Harper, K. Vyakaranam, J. Michl, C. M. Williams, C. H. Jessen, P. V. Bernhardt, *Eur. J. Org. Chem.* **2007**, *2007*, 241-248.

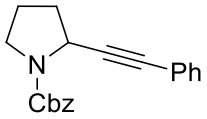
Benzyl 2-((tert-butyldiphenylsilyl)ethynyl)pyrrolidine-1-carboxylate (4n)



Starting from **2a** (46 mg, 0.20 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4n** as yellow oil (70 mg, 0.16 mmol, 78%).

R_f: 0.25 (Pentane/Ethyl Acetate = 9:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.88 – 7.70 (m, 4H, 4 x Ar*CH*), 7.45 – 7.29 (m, 9H, 9 x Ar*CH*), 7.29 – 7.19 (m, 2H, 2 x Ar*CH*), 5.29 – 5.12 (m, 2H, *CH*$_2$-*O*), 4.83 – 4.66 (m, 1H, *CH*-*C*≡*C*), 3.74 – 3.55 (m, 1H, *CH*-*N*), 3.54 – 3.35 (m, 1H, *CH*$_2$), 2.31 – 2.07 (m, *J* = 6.2 Hz, 3H, *CH* + *CH*$_2$), 2.04 – 1.89 (m, 1H, *CH*), 1.06 (s, 9H, 3 x *CH*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$)[22] δ 154.6, 154.4, 137.0, 136.7, 135.6, 135.6, 133.3, 133.3, 129.5, 128.5, 127.9, 127.8, 127.75, 127.70, 110.2, 82.0, 67.1, 66.9, 49.4, 49.0, 46.2, 45.7, 34.2, 33.2, 27.1, 24.7, 23.9, 18.6. IR 3070 (w), 3047 (w), 2955 (m), 2931 (m), 2891 (w), 2857 (m), 2173 (w), 1705 (s), 1428 (m), 1410 (s), 1356 (s), 1331 (m), 1265 (m), 1187 (s), 1111 (s), 996 (w), 912 (m), 822 (m). HRMS (ESI) calcd for $C_{30}H_{33}NNaO_2Si^+$ $[M+Na]^+$ 490.2173; found 490.2173.

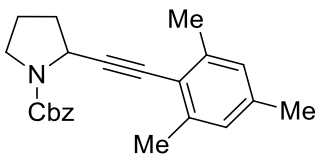
Benzyl 2-(phenylethynyl)pyrrolidine-1-carboxylate (4o)



Starting from **2a** (75 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4o** as yellow oil (89 mg, 0.29 mmol, 97%).

R_f: 0.25 (Pentane/Ethyl Acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.26 (m, 10H, 2 x *Ph*), 5.43 – 5.02 (m, 2H, *CH*$_2$Ph), 4.93 – 4.65 (m, 1H, *CH*-C≡C), 3.72 – 3.53 (m, 1H, N-*CH*$_2$), 3.53 – 3.29 (m, 1H, N-*CH*$_2$), 2.33 – 2.07 (m, 3H, *CH*$_2$), 2.03 – 1.86 (m, 1H, *CH*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$)[22] δ 154.5, 137.0, 131.8, 131.7, 128.4, 128.2, 128.1, 128.0, 127.7, 127.6, 123.0, 89.5, 82.2, 66.8, 49.2, 48.7, 46.2, 45.8, 34.0, 33.3, 24.5, 23.8. IR 3059 (w), 2988 (w), 1788 (w), 1721 (m), 1697 (m), 1491 (w), 1418 (s), 1358 (m), 1296 (m), 1266 (s), 1177 (s), 1116 (m), 1089 (m), 1023 (w), 915 (w). HRMS (ESI) calcd for $C_{20}H_{20}NO_2^+$ $[M+H]^+$ 306.1489; found 306.1490.

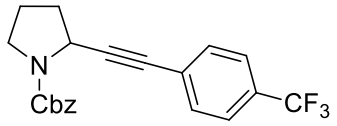
Benzyl 2-(mesitylethynyl)pyrrolidine-1-carboxylate (4p)



Starting from **2a** (60 mg, 0.24 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4p** as colorless oil (51.8 mg, 0.149 mmol, 62%).

R_f: 0.28 (Pentane/Ethyl Acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.20 (m, 5H, *Ph*), 6.83 (s, 2H, *Mesityl*), 5.20 (s, 2H, CH_2Ph), 5.02 – 4.77 (m, 1H, *CH*-C≡C), 3.74 – 3.54 (m, 1H, N-CH_2), 3.54 – 3.28 (m, 1H, N-CH_2), 2.46 – 2.22 (m, 9H, 3 x CH_3), 2.22 – 2.10 (m, 3H, CH_2), 2.03 – 1.93 (m, 1H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) [22] δ 154.6, 154.3, 140.1, 137.5, 137.4, 136.9, 136.8, 128.4, 127.8, 127.7, 127.5, 119.7, 119.6, 97.0, 96.8, 80.1, 66.9, 66.8, 60.4, 49.4, 49.1, 46.1, 45.6, 34.3, 33.5, 24.5, 23.7, 21.3, 20.8. IR 2984 (w), 1700 (m), 1481 (m), 1409 (m), 1357 (s), 1334 (s), 1271 (s), 1185 (s), 1109 (m), 1087 (m), 1031 (m), 912 (m), 852 (m). HRMS (ESI) calcd for $C_{23}H_{26}NO_2^+$ $[M+H]^+$ 348.1958; found 348.1952.

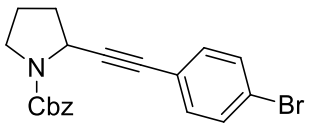
Benzyl 2-((4-(trifluoromethyl)phenyl)ethynyl)pyrrolidine-1-carboxylate (4q)



Starting from **2a** (75 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4q** as colorless oil (95 mg, 0.25 mmol, 85%).

R_f: 0.30 (Pentane/Ethyl Acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.44 – 6.84 (m, 9H, *Ph* + *Ar* H), 5.19 – 4.74 (m, 2H, CH_2O), 4.69 – 4.37 (m, 1H, *CH*-C≡C), 3.49 – 3.27 (m, 1H, NCH_2), 3.28 – 3.03 (m, 1H, NCH_2), 2.10 – 1.79 (m, 3H, CH_2), 1.79 – 1.60 (m, 1H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$)[22, 28] δ 154.5, 136.9 (m), 132.1, 131.9, 130.0, 128.4, 128.0, 127.8, 127.7, 126.8, 125.1, 123.9 (q, *J* = 272.0 *Hz*), 119.9, 92.0, 81.0, 76.7, 66.9, 49.1, 48.6, 46.3, 45.9, 33.8, 33.1, 29.7, 24.6, 23.8. IR 2991 (w), 2197 (w), 1705 (m), 1614 (w), 1410 (s), 1357 (m), 1323 (s), 1124 (s), 1067 (s), 968 (w), 911 (w), 844 (m). HRMS (ESI) calcd for $C_{21}H_{18}F_3NNaO_2^+$ $[M+Na]^+$ 396.1182; found 396.1181.

Benzyl 2-((4-bromophenyl)ethynyl)pyrrolidine-1-carboxylate (4r)



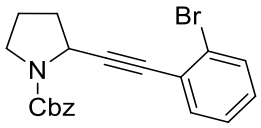
Starting from **2a** (75 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4r** as colorless oil (76 mg, 0.20 mmol, 66%).

R_f: 0.28 (Pentane/Ethyl Acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.08 (m, 9H, 2 x *Ar*), 5.43 – 5.03 (m, 2H, CH_2Ph), 4.92 – 4.65 (m, 1H, *CH*-C≡C), 3.70 – 3.52 (m, 1H, N- CH_2),

[28] Due to peaks overlap, not all C-F coupling constants could be resolved.

3.52 – 3.31 (m, 1H, N- *CH*$_2$), 2.29 – 2.03 (m, 3H, *CH*$_2$), 2.03 – 1.82 (m, 1H, *CH*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$)[22] δ 154.5, 136.9, 133.3, 133.1, 131.4, 130.1, 128.4, 128.4, 128.0, 127.8, 127.6, 122.3, 121.9, 90.7, 90.3, 81.2, 66.9, 53.5, 49.2, 48.7, 46.3, 45.9, 33.9, 33.2, 30.9, 29.7, 24.6, 23.8, 18.52 . IR 3032 (w), 2803 (w), 1699 (m), 1586 (w), 1487 (m), 1411 (w), 1344 (s), 1304 (s), 1185 (m), 1114 (m), 1088 (m), 1010 (s), 911 (m), 825 (s). HRMS (ESI) calcd for $C_{20}H_{18}BrNNaO_2^+$ $[M+Na]^+$ 406.0413; found 406.0423.

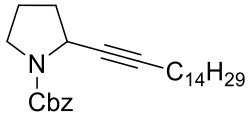
Benzyl 2-((2-bromophenyl)ethynyl)pyrrolidine-1-carboxylate (4s)



Starting from **2a** (75 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4s** as colorless oil (102 mg, 0.270 mmol, 88%).

R_f: 0.28 (Pentane/Ethyl Acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.0 Hz, 1H, C*H Bromophenyl*), 7.49 – 7.27 (m, 6H, 5 x C*H benzyl* + C*H Bromophenyl*), 7.22 (td, *J* = 7.6, 1.3 Hz, 1H, C*H Bromophenyl*), 7.14 (q, *J* = 6.9, 6.4 Hz, 1H, C*H Bromophenyl*), 5.36 – 5.10 (m, 2H, C*H*$_2$-O), 4.92 – 4.76 (m, 1H, C*H*-C≡C), 3.70 – 3.56 (m, 1H, N-*CH*$_2$), 3.52 – 3.36 (m, 1H, N-*CH*$_2$), 2.34 – 2.09 (m, 3H, C*H* + C*H*$_2$), 2.04 – 1.95 (m, 1H, C*H*). ^{13}C NMR (101 MHz, $CDCl_3$)[22] δ 154.5, 136.9, 133.5, 133.3, 132.3, 132.3, 129.4, 129.3, 128.4, 128.4, 128.0, 127.8, 127.7, 126.9, 125.9, 125.7, 125.1, 125.0, 94.2, 94.0, 81.0, 66.9, 49.3, 48.9, 46.2, 45.7, 33.9, 33.2, 29.7, 24.6, 23.8. IR 3064 (w), 3033 (w), 2982 (w), 2952 (w), 2881 (w), 1703 (s), 1469 (m), 1410 (s), 1356 (s), 1334 (m), 1268 (w), 1180 (m), 1116 (m), 1089 (m), 1027 (w), 915 (w). HRMS (ESI) calcd for $C_{20}H_{18}BrNNaO_2^+$ $[M+Na]^+$ 406.0413; found 406.0415.

Benzyl 2-(hexadec-1-yn-1-yl)pyrrolidine-1-carboxylate (4t)



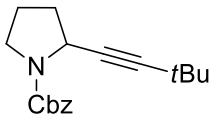
Starting from **2a** (75 mg, 0.30 mmol) and using 1 mol% of catalyst **3a**, the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4t** as colorless oil (87 mg, 0.204 mmol, 68%).

R_f: 0.20 (Pentane/Ethyl Acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$)[29] δ 7.48 – 7.27 (m, 5H, *Ph*), 5.31 – 5.08 (m, 2H, *CH*$_2$Ph), 4.63 – 4.48 (m, 1H, *CH*-C≡C), 3.61 – 3.46 (m, 1H, N-*CH*$_2$), 3.46 – 3.24 (m, 1H, N-*CH*$_2$), 2.24 – 1.77 (m, 4H, *CH*$_2$), 1.53 – 1.38 (m, 2H, *CH*$_2$), 1.38 – 1.18 (m, 24H, 12 x *CH*$_2$), 0.88 (t, *J* = 6.8 Hz, 3H, *CH*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$)[22] δ 154.6, 137.1, 133.2, 129.8, 129.7, 128.4, 128.4, 127.9, 127.7, 127.5, 82.6, 66.7, 62.8, 48.8, 48.4, 46.1, 45.7, 34.2, 33.5, 31.9, 29.72, 29.70, 29.68, 29.66, 29.6, 29.4, 29.1, 28.9, 28.7, 24.4, 23.6,

[29] About 95% pure by ^{1}H NMR.

22.7, 18.7, 14.1. IR 2925 (s), 2853 (s), 2359 (w), 1806 (w), 1766 (m), 1732 (m), 1715 (m), 1643 (w), 1511 (w), 1468 (m), 1343 (m), 1265 (s), 1195 (m), 1139 (m), 1104 (w), 929 (m), 902 (m). HRMS (ESI) calcd for $C_{28}H_{44}NO_2^+$ $[M+H]^+$ 426.3367; found 426.3361.

Benzyl 2-(3,3-dimethylbut-1-yn-1-yl)pyrrolidine-1-carboxylate (4u)

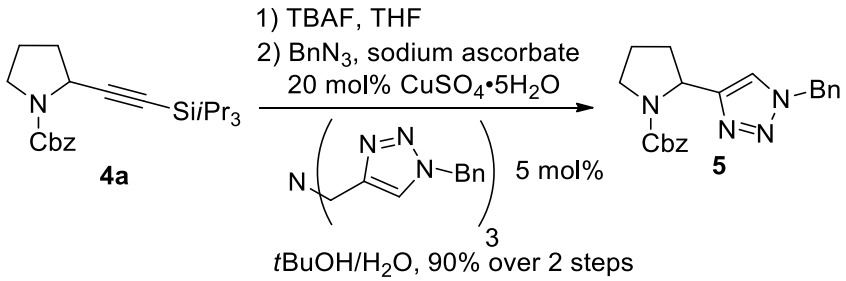


Starting from **2a** (75 mg, 0.30 mmol), the crude product was purified by column chromatography (Pentane/Ethyl Acetate = 9:1) to afford **4u** as colorless oil (66 mg, 0.23 mmol, 77%).

R_f: 0.28 (Pentane/Ethyl Acetate = 9:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.54 – 7.19 (m, 5H, *Ph*), 5.39 – 4.98 (m, 2H, *CH*$_2$Ph), 4.65 – 4.42 (m, 1H, *CH*-C≡C), 3.62 – 3.44 (m, 1H, N-*CH*$_2$), 3.44 – 3.21 (m, 1H, N-*CH*$_2$), 2.19 – 1.82 (m, 4H, *CH*$_2$), 1.16 (s, 9H, *tBu*). ^{13}C NMR (101 MHz, $CDCl_3$)[22] δ 154.6, 137.1, 129.8,128.4, 128.3, 127.8, 127.6, 127.4, 90.7, 78.5, 66.6, 48.8, 48.3, 46.1, 45.6, 34.3, 33.6, 31.0, 29.7, 27.2, 24.3, 23.6. IR 2970 (m), 2875 (w), 2236 (w), 1704 (s), 1410 (s), 1357 (s), 1335 (s), 1269 (s), 1183 (m), 1122 (m), 1095 (m), 1012 (w), 917 (w). HRMS (ESI) calcd for $C_{18}H_{23}NNaO_2^+$ $[M+Na]^+$ 308.1621; found 308.1620.

4. Further functionalization:

Benzyl 2-(1-benzyl-1H-1,2,3-triazol-4-yl)pyrrolidine-1-carboxylate (5)



Following a reported procedure,[30] **4a** (344 mg, 0.890 mmol, 1 equiv) was dissolved in dry THF (11 mL, 0.08 M) in a flame dried flask and the solution was cooled to 0 °C. Then TBAF (1.1 mL, 1.1 mmol, 1.2 equiv, 1.0 M in hexanes) was added dropwise and the reaction left stirring for 30 minutes. Then the reaction was quenched with sat NH_4Cl solution (20 mL). The aqueous and organic layers were separated and the aqueous layer was extracted with ether (3x10 mL). After drying over $MgSO_4$ and concentrating under vacuum, the crude product was immediately used in the next step. Rf: 0.30 (6:1 Pentane:EtOAc, $KMnO_4$).

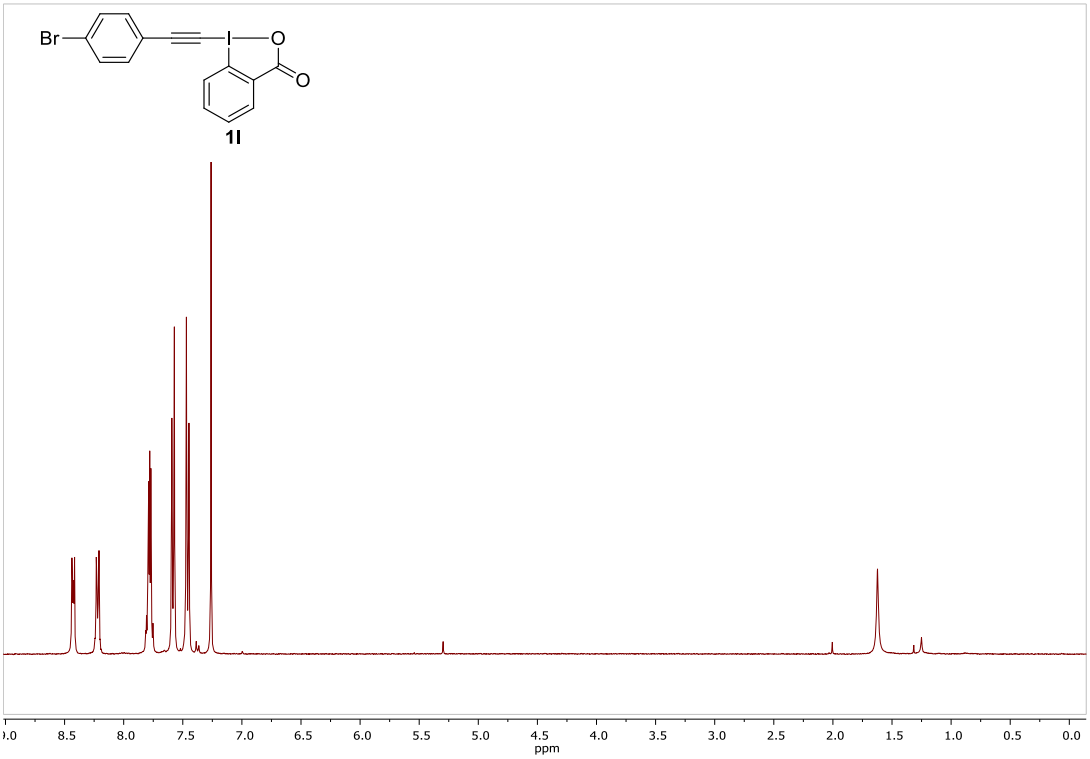
Following a reported,[31] benzyl 2-ethynylpyrrolidine-1-carboxylate (205 mg, 0.890 mmol, 1 equiv), (azidomethyl)benzene (134 µL, 1.10 mmol, 1.2 equiv), sodium ascorbate (71 mg, 0.36 mmol, 0.4 equiv), $CuSO_4$●$5H_2O$ (45 mg, 0.18 mmol, 0.20 equiv) and tris((1-benzyl-1H-1,2,3-triazol-4-yl)methyl)amine (24 mg, 0.045 mmol, 0.05 equiv) were dissolved a 2:1 mixture of ^tBuOH:H_2O (9 mL) in an open flask and left stirring for 2 h. Then the crude product was purified via flash chromatography on silica (from 4:1 to 2:1 Pentane:EtOAc) to afford **5** (292 mg, 0.810 mmol, 90% yield).

Rf: 0.20 (2:1 Pentane:EtOAc).^{1}H NMR (400 MHz, $CDCl_3$) δ 7.55 – 7.01 (m, 11H, 2 x *Ph* + *CHtriazole*), 5.60 – 5.34 (m, 2H, *CH*$_2$), 5.22 – 4.94 (m, 3H, C*H* and C*H*$_2$), 3.65 – 3.44 (m, 2H, *CH*$_2$), 2.57 – 1.87 (m, 4H, *CH*$_2$). ^{13}C NMR (101 MHz, $CDCl_3$)[22] δ 154.9, 154.7, 150.4, 149.3, 136.9, 136.6, 134.8, 134.7, 129.1, 128.7, 128.6, 128.4, 128.1, 127.9, 127.9, 127.8, 122.3, 121.3, 66.8, 54.0, 53.5, 46.9, 46.6, 32.6, 30.9, 24.5, 23.4. IR 3053 (w), 2986 (w), 1697 (s), 1590 (w), 1527 (w), 1498 (m), 1451 (m), 1414 (s), 1355 (m), 1268 (m), 1192 (m), 1176 (m), 1113 (m), 1051 (w), 913 (w). HRMS (ESI) calcd for $C_{21}H_{23}N_4O_2^+$ $[M+H]^+$ 363.1816; found 363.1811

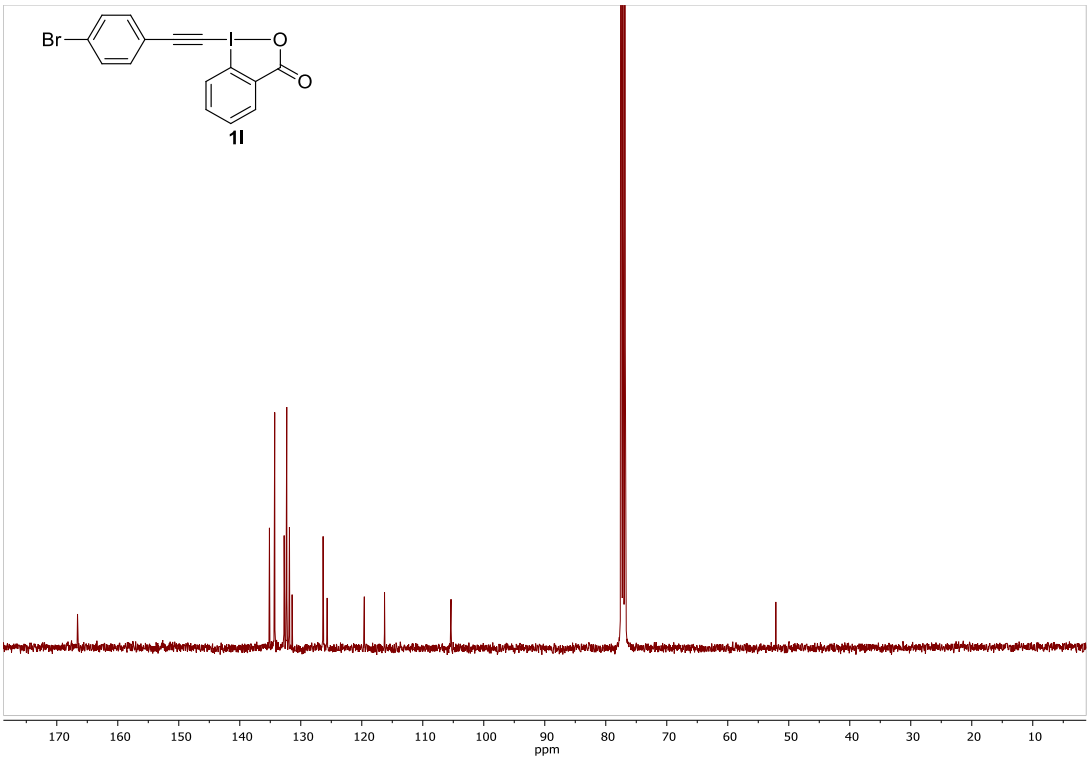
[30] Y. Li, J. Waser, *Angew. Chem., Int. Ed.* **2015**, *54*, 5438.
[31] Q.-H. Deng, T. Bleith, H. Wadepohl, L. H. Gade, *J. Am. Chem. Soc.* **2013**, *135*, 5356.

5. Spectra for new compounds

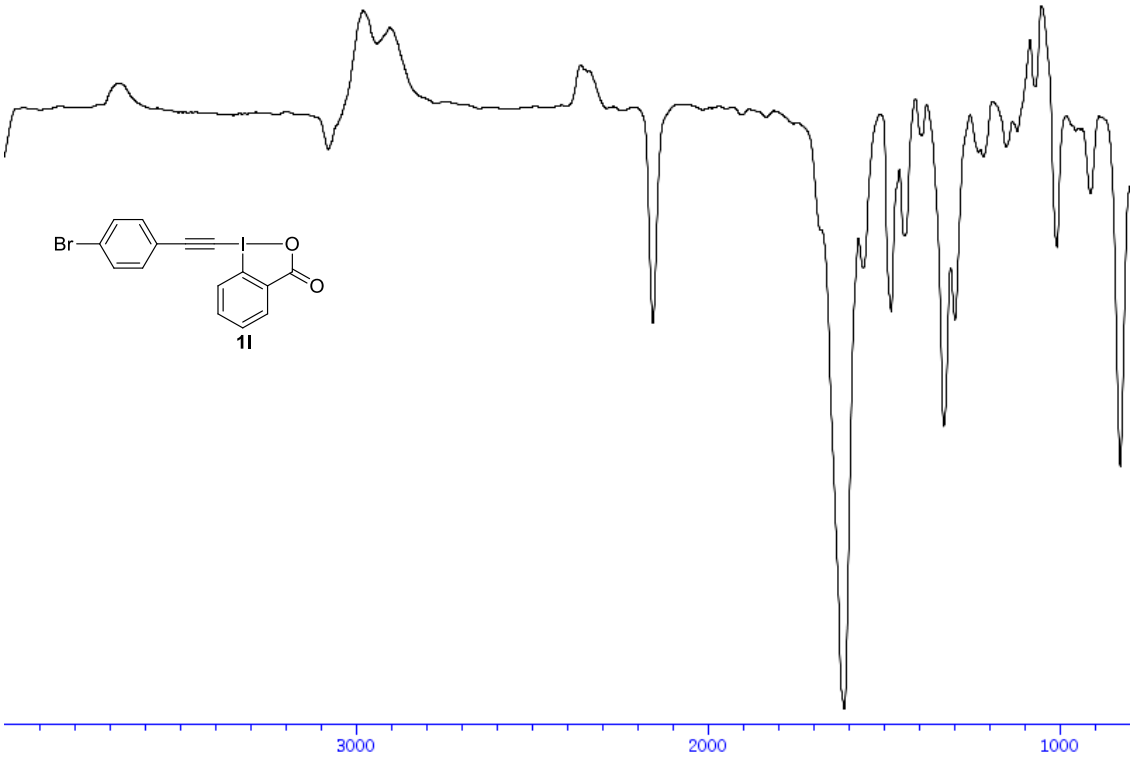
^{1}H-NMR (400 MHz, $CDCl_3$)



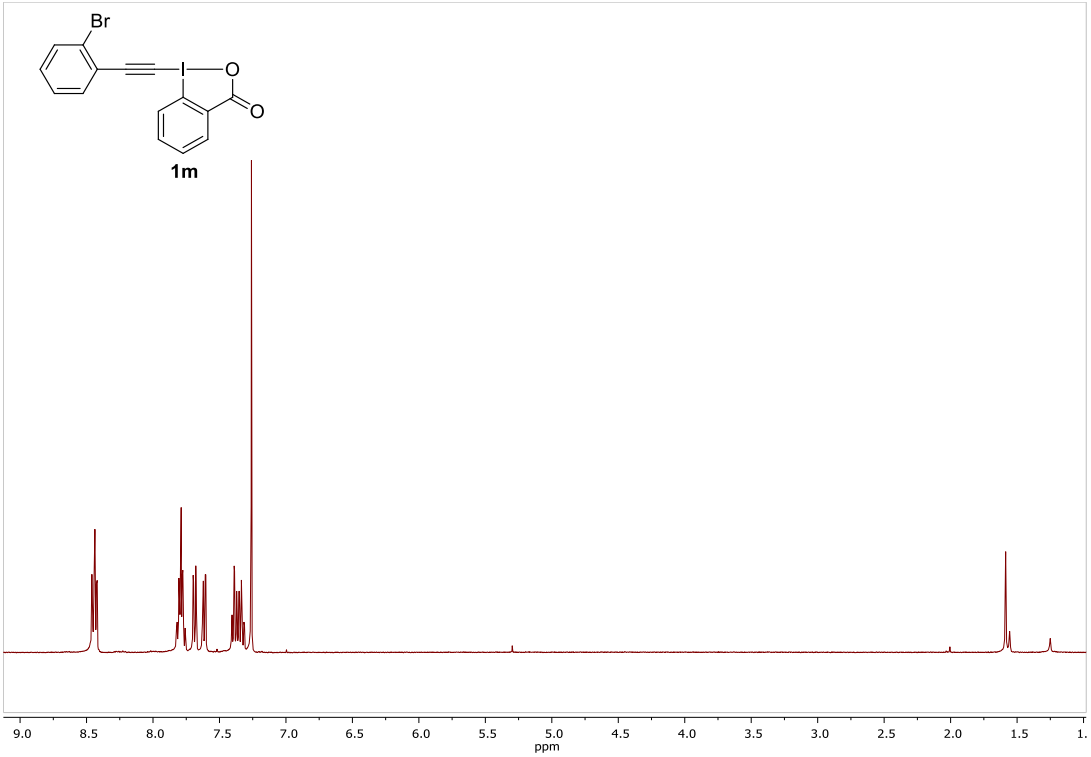
^{13}C-NMR (101 MHz, $CDCl_3$)



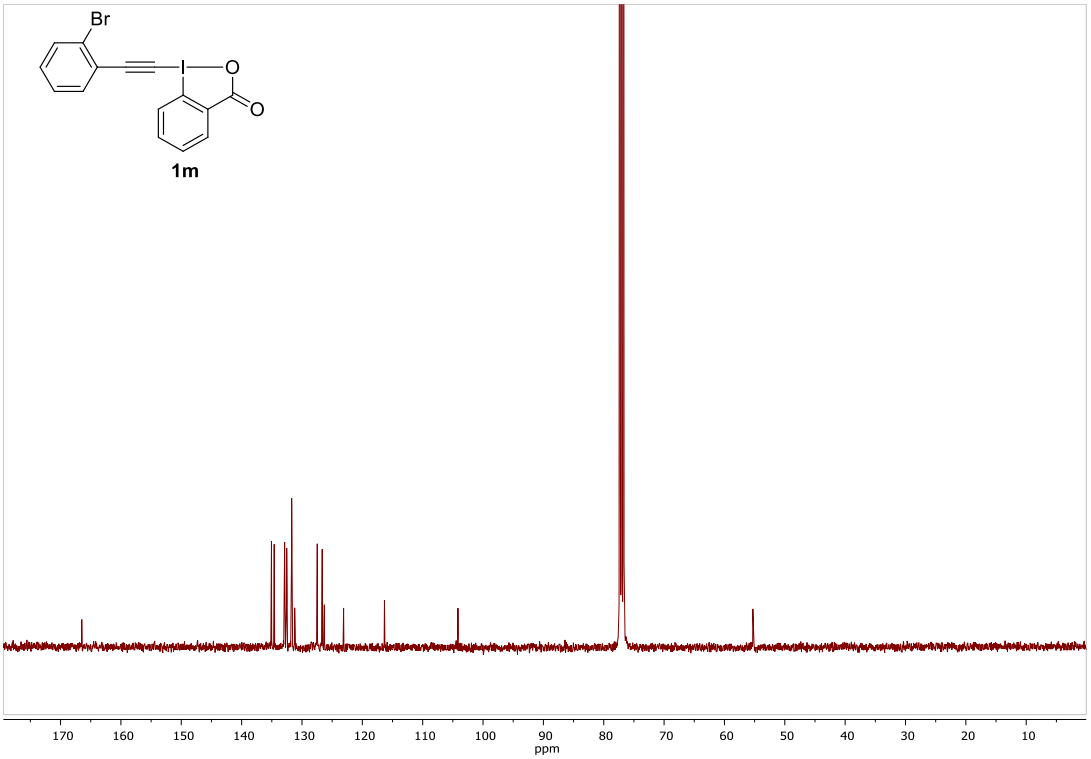
IR Spectra



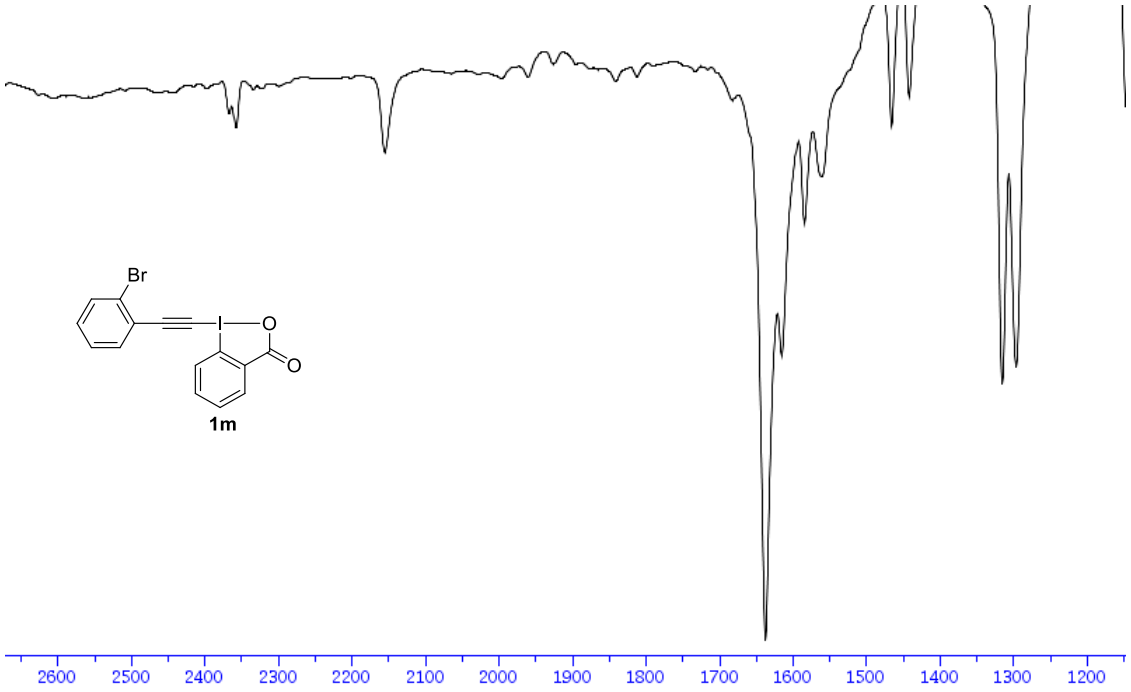
^{1}H-NMR (400 MHz, $CDCl_3$)



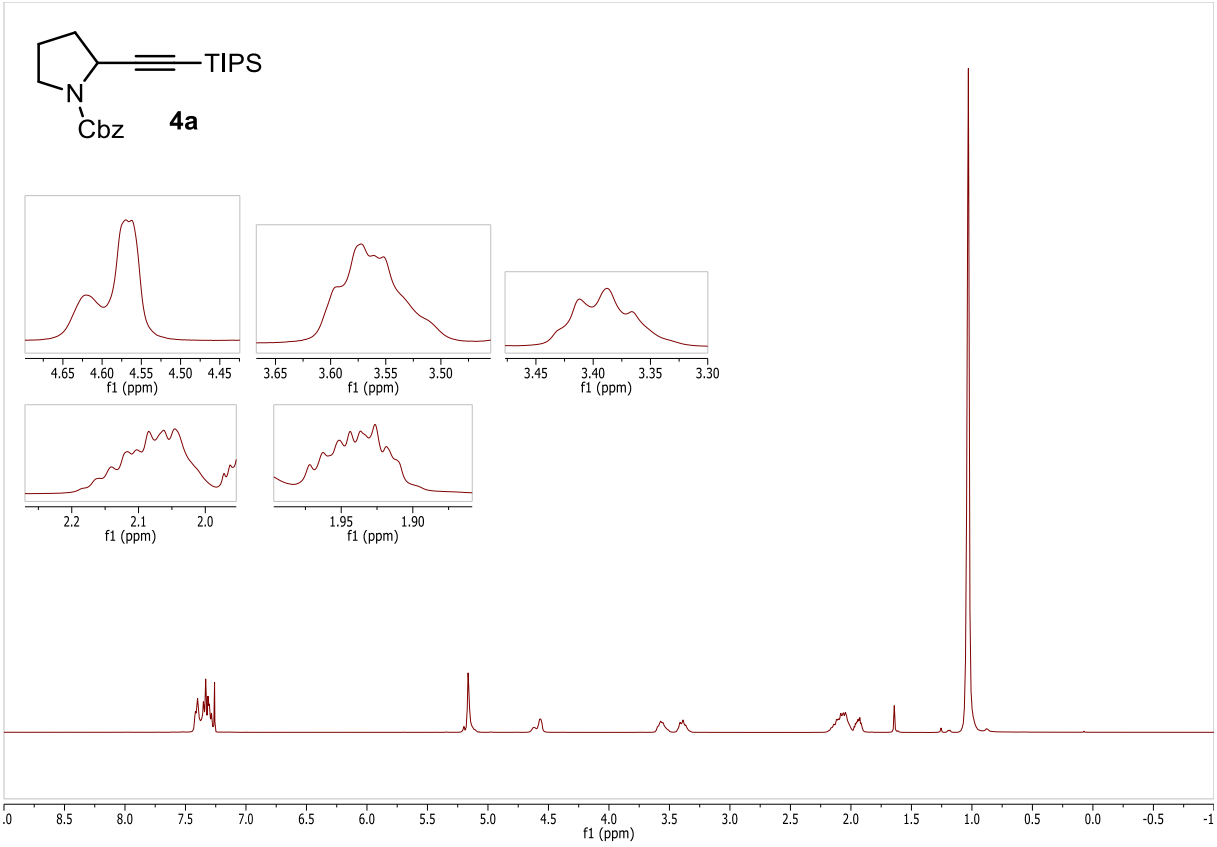
^{13}C-NMR (101 MHz, $CDCl_3$)



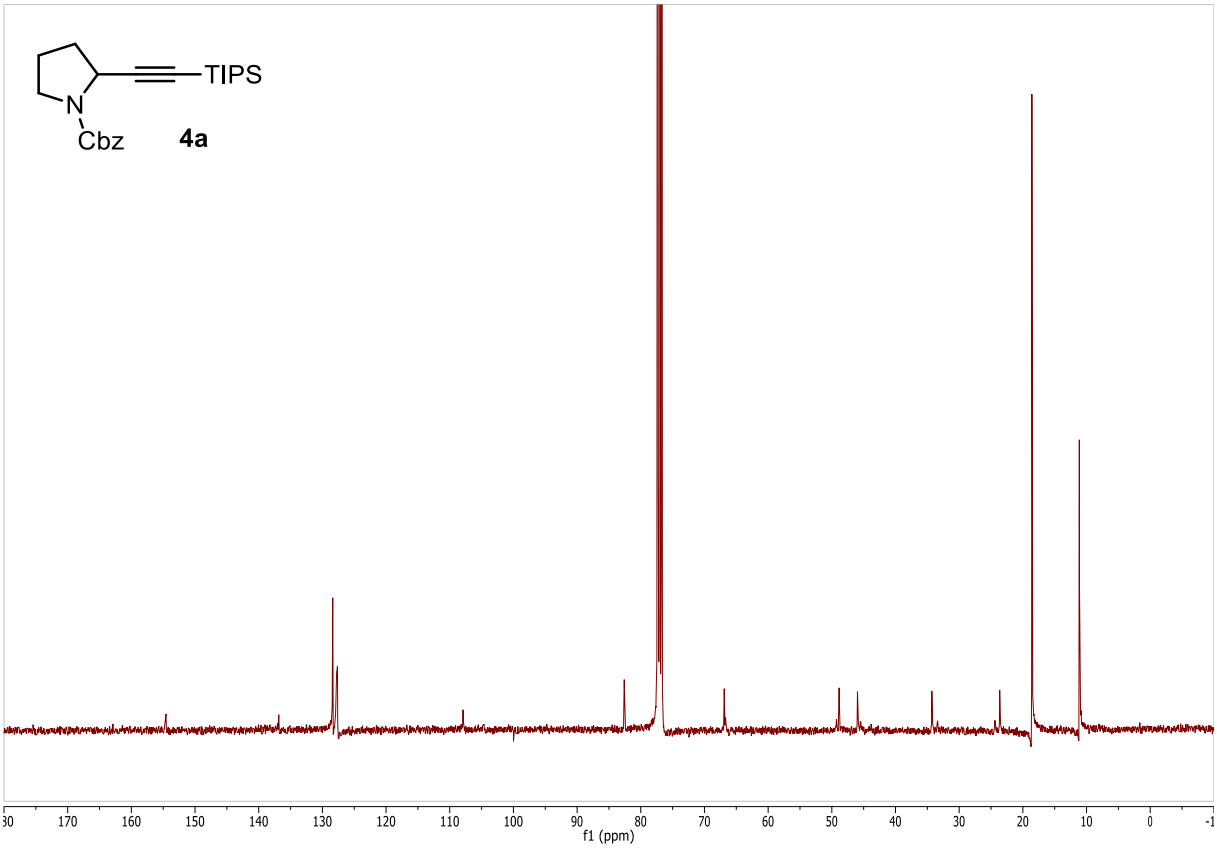
IR Spectra


Br
I
O
O
1m
2600
2500
2400
2300
2200
2100
2000
1900
1800
1700
1600
1500
1400
1300
1200

^{1}H-NMR (400 MHz, $CDCl_3$)



^{13}C-NMR (101 MHz, $CDCl_3$)



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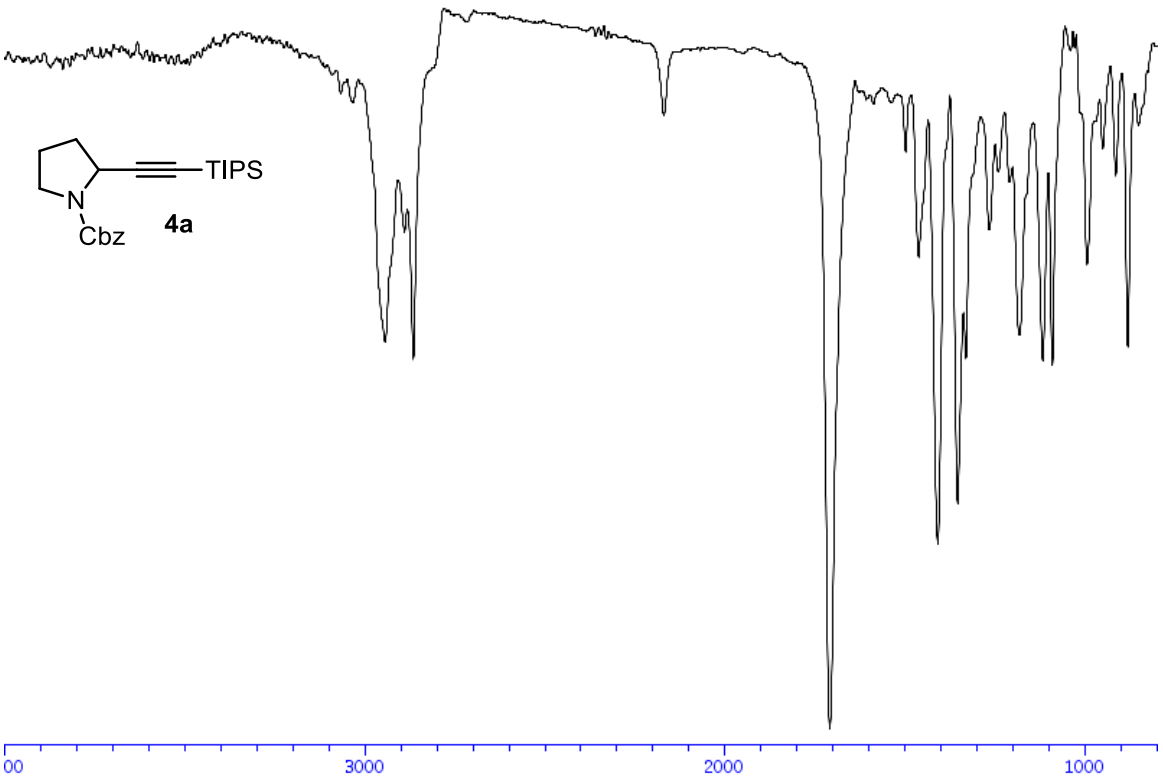
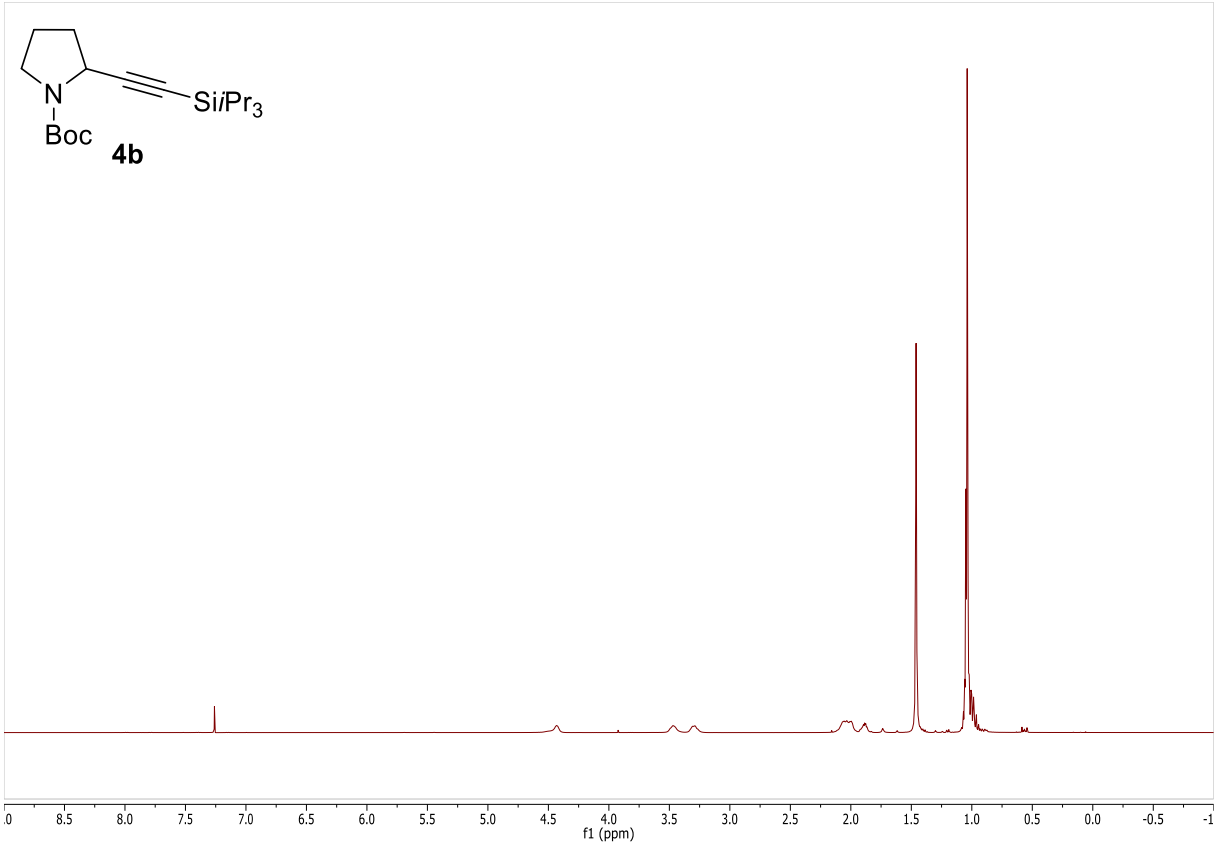
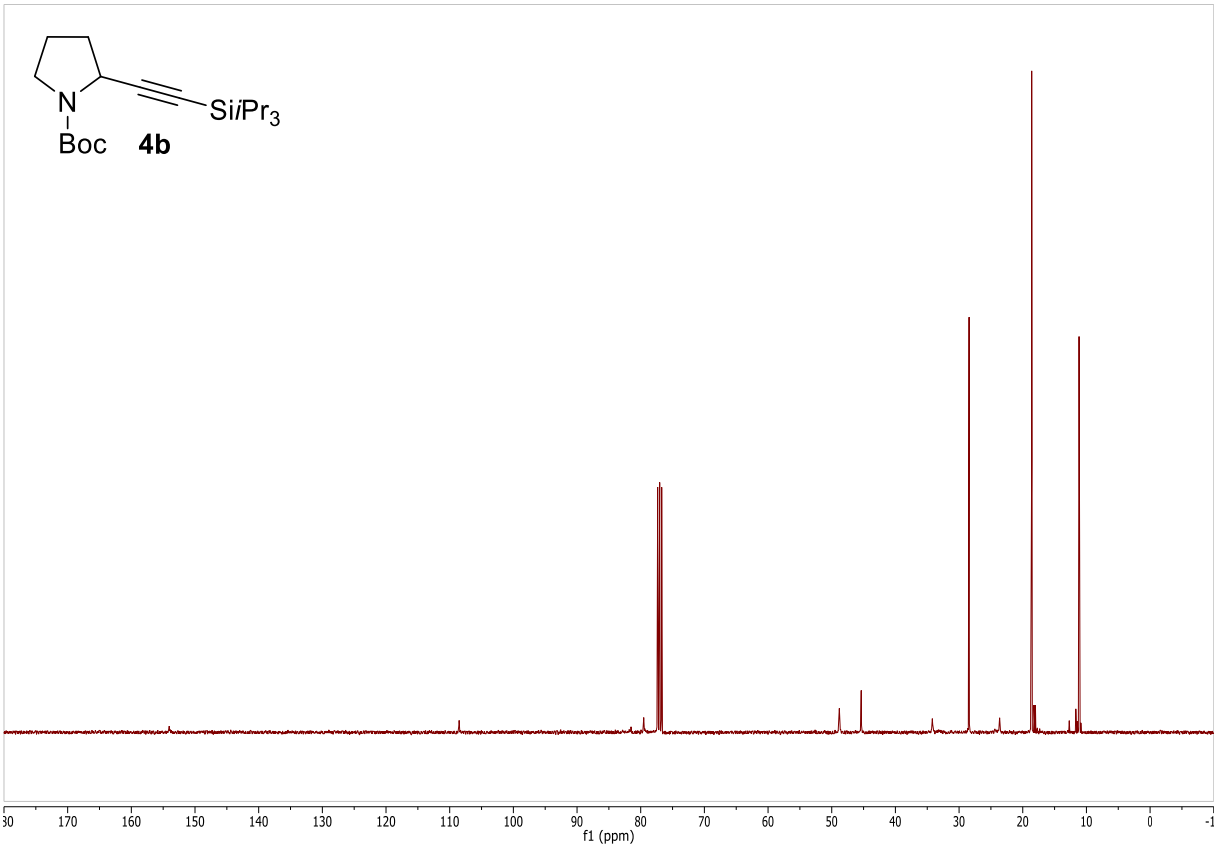


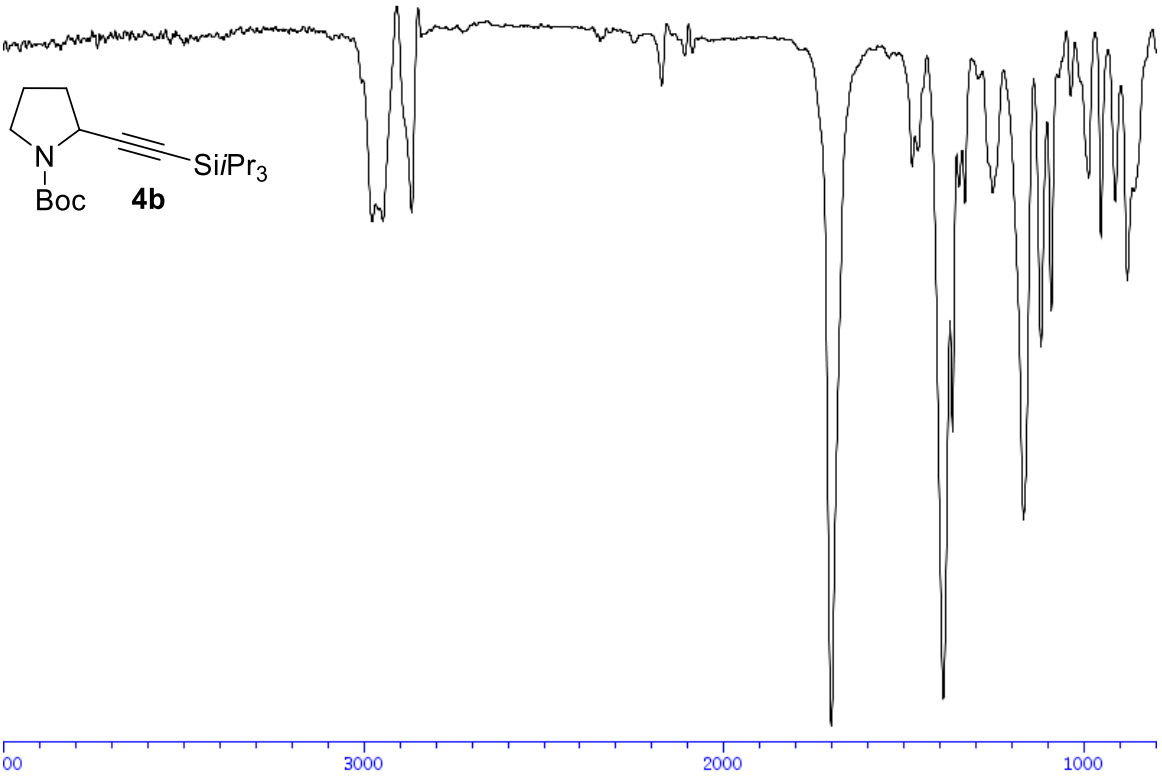
^{1}H-NMR (400 MHz, $CDCl_3$)



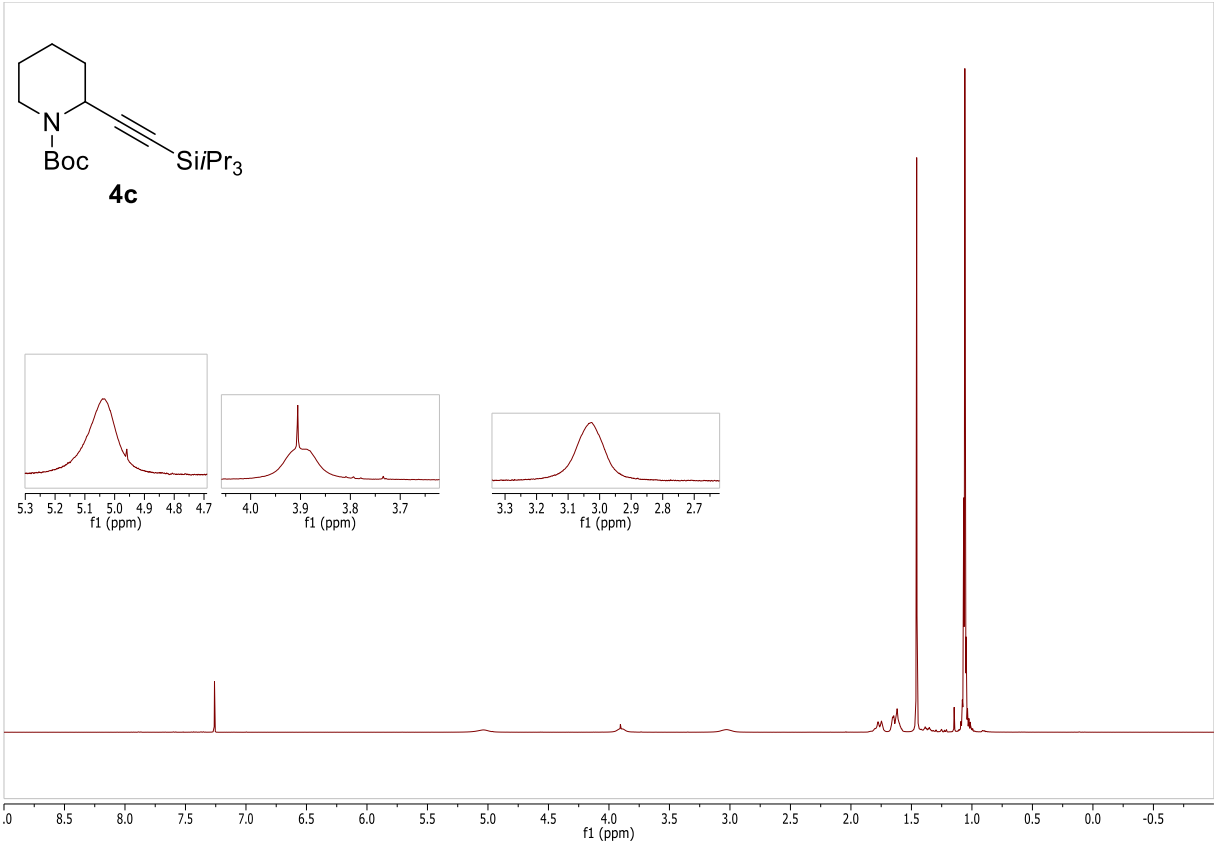
^{13}C-NMR (101 MHz, $CDCl_3$)



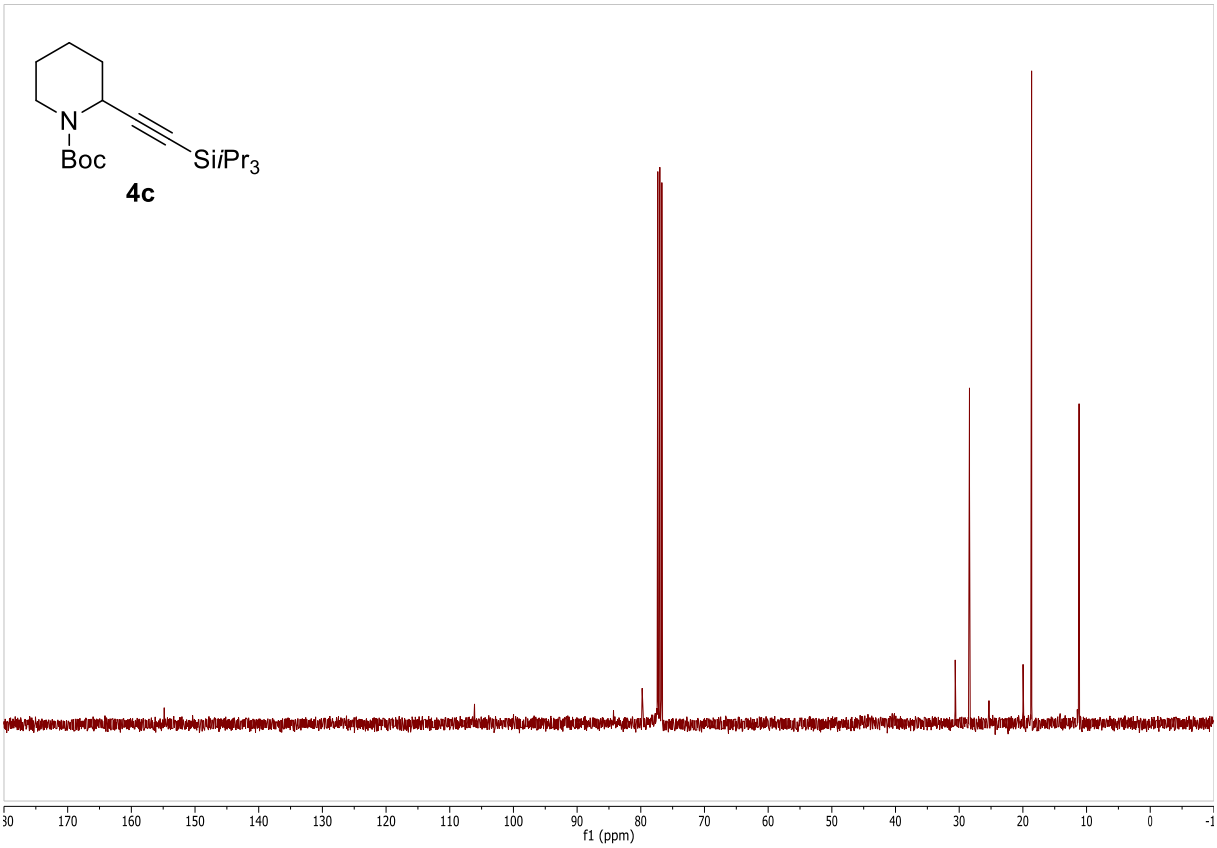
IR Spectra



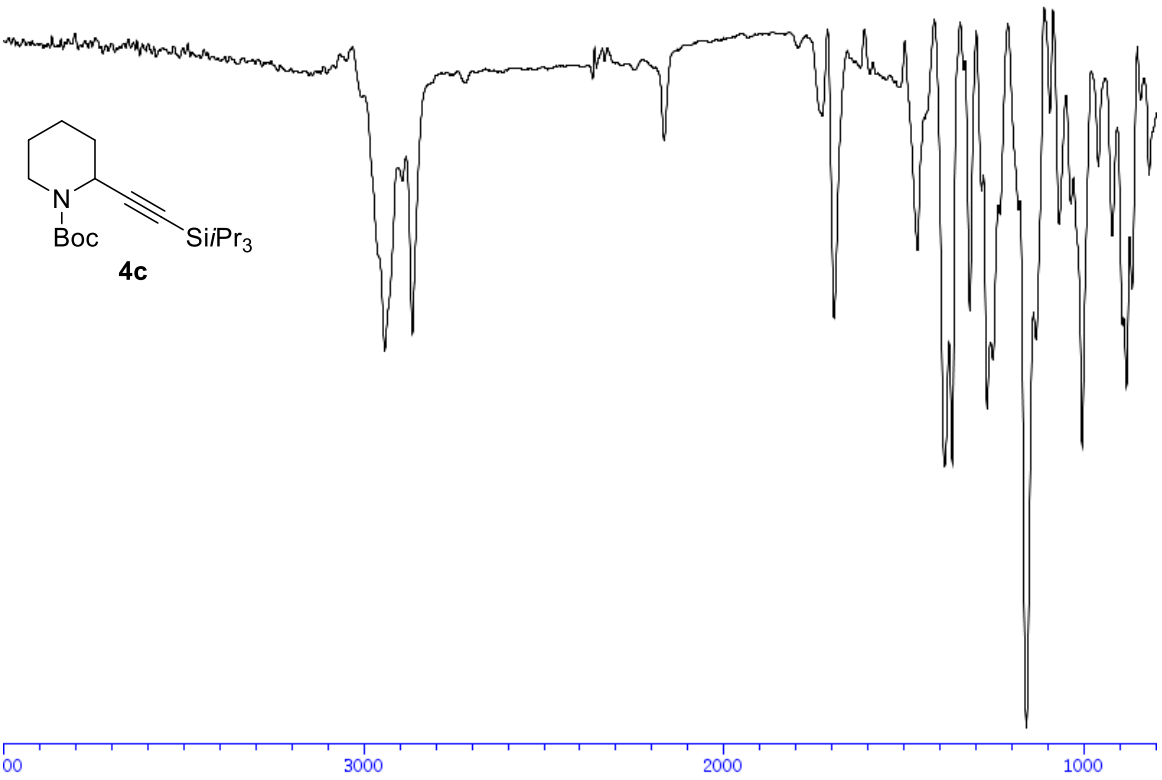
^{1}H-NMR (400 MHz, $CDCl_3$)



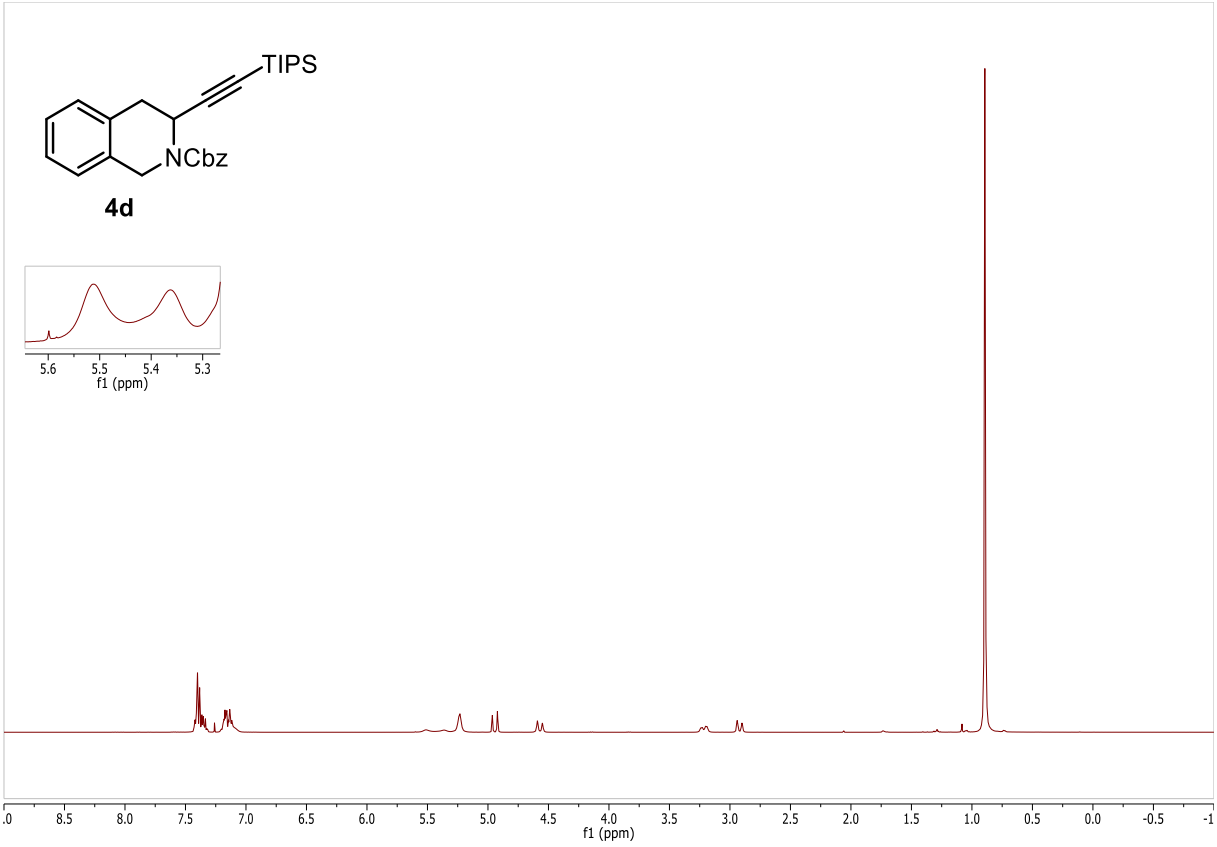
^{13}C-NMR (101 MHz, $CDCl_3$)



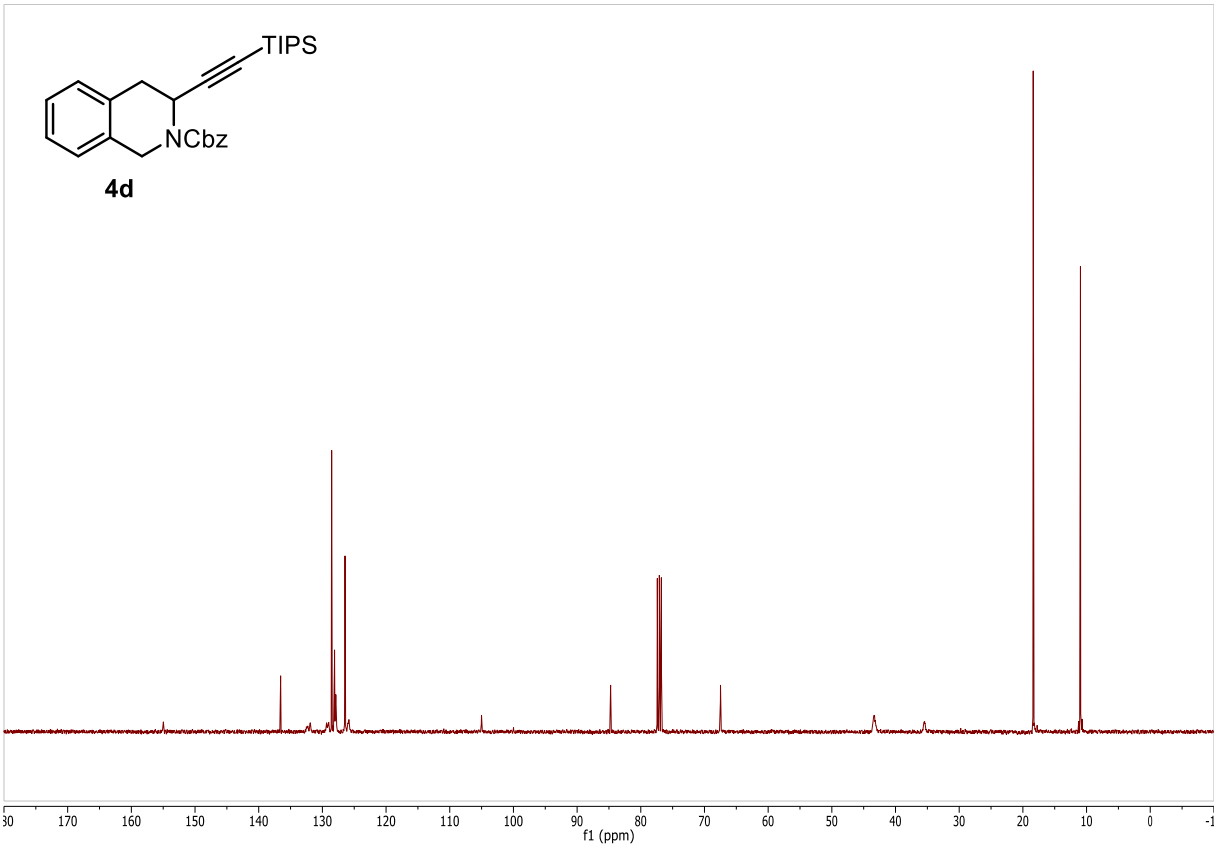
IR Spectra



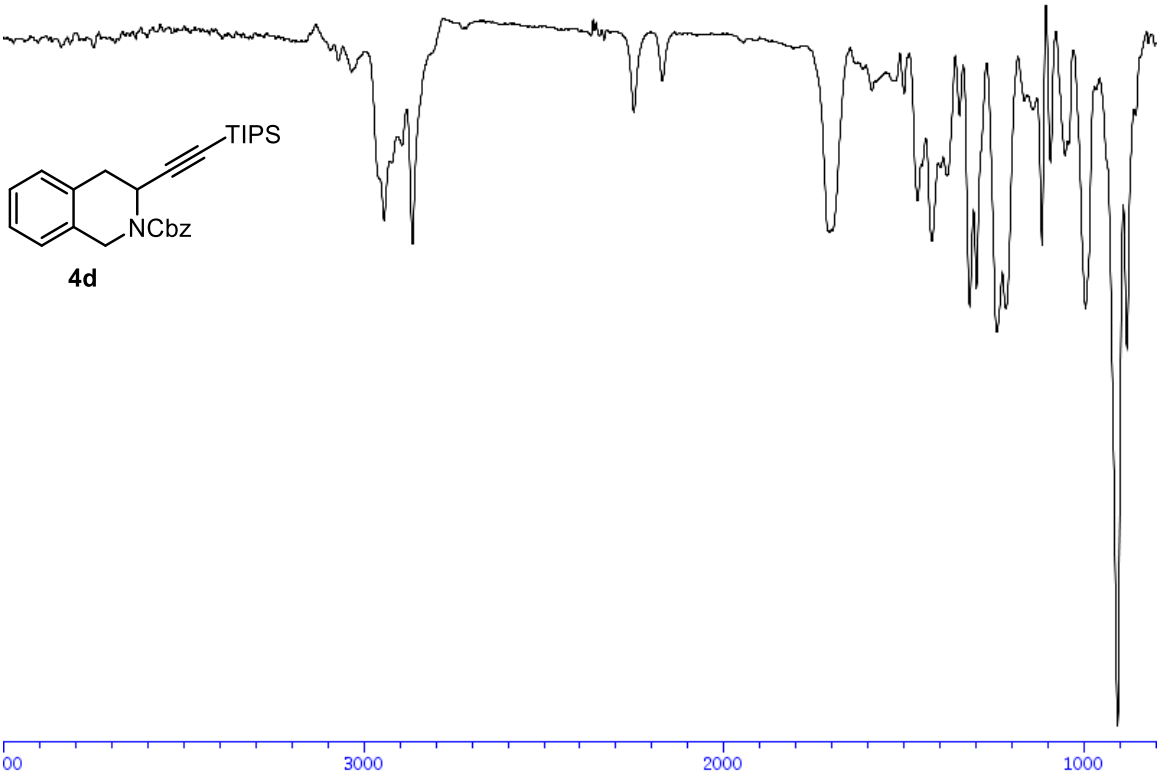
^{1}H-NMR (400 MHz, $CDCl_3$)



^{13}C-NMR (101 MHz, $CDCl_3$)



IR Spectra



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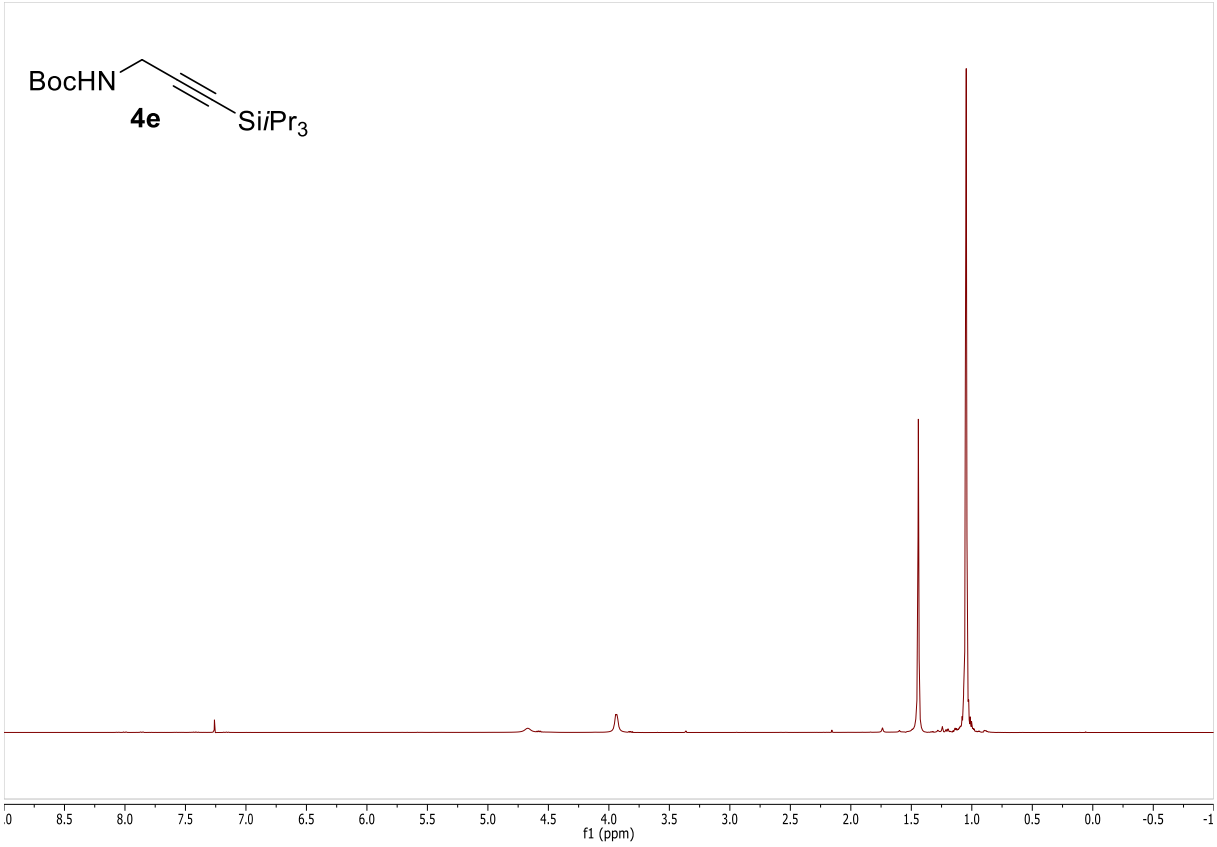
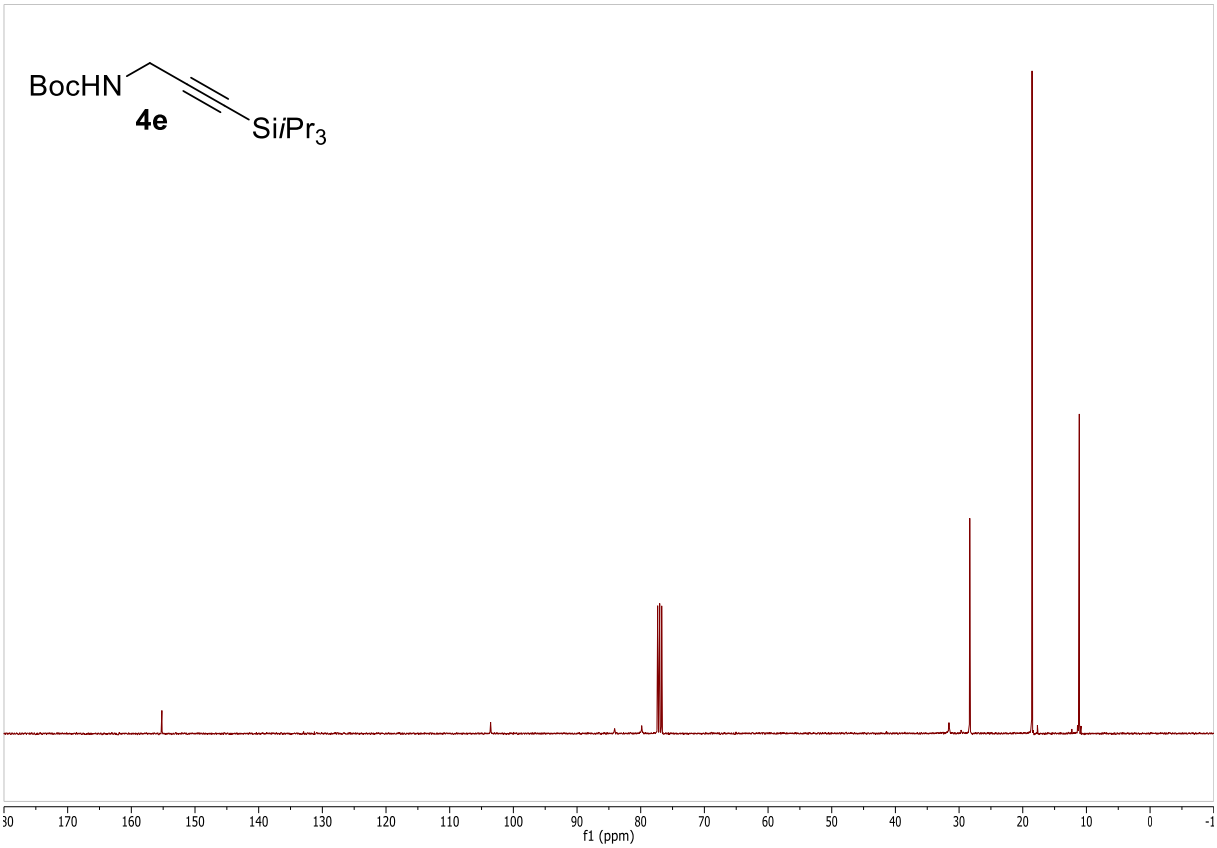
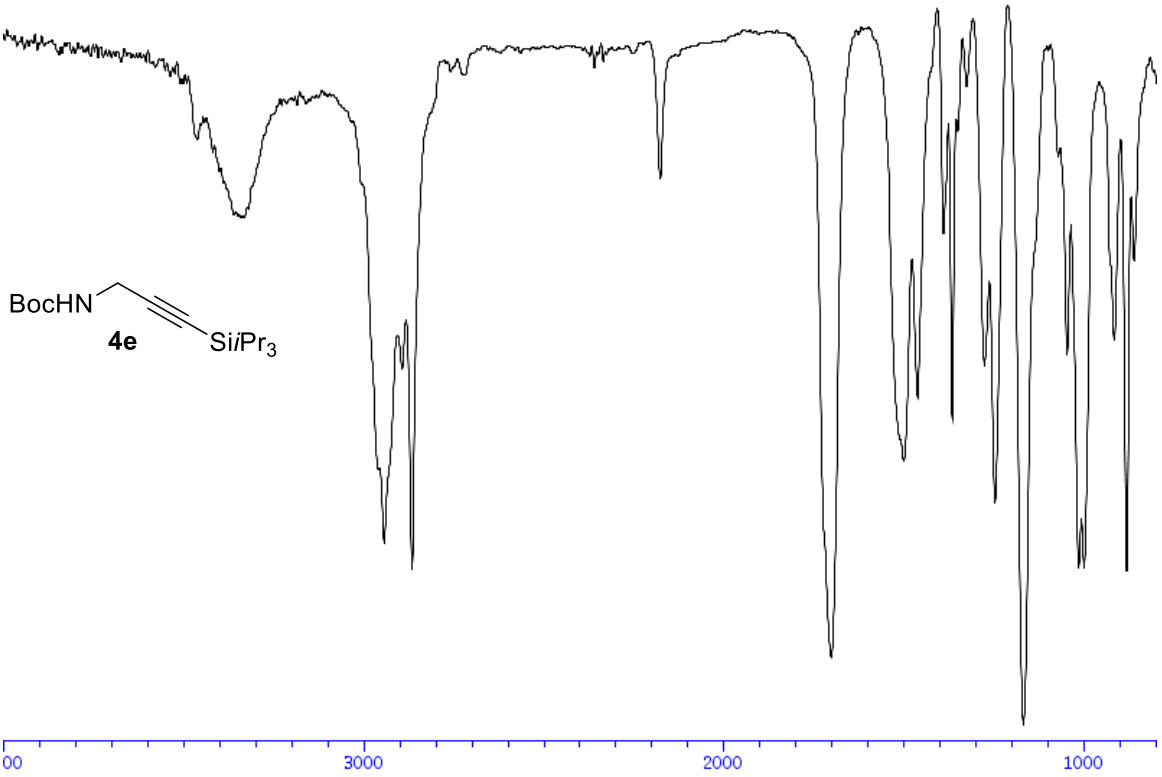


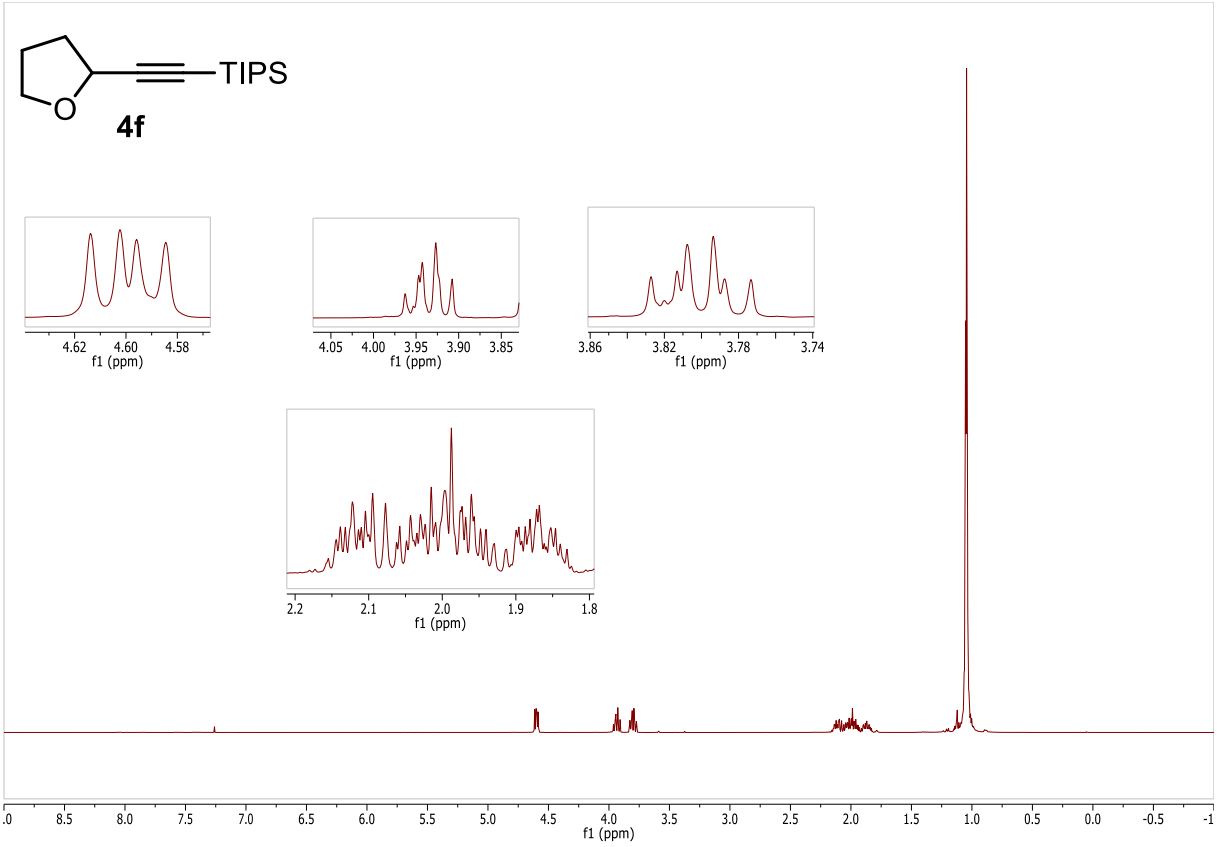
^{13}C-NMR (101 MHz, $CDCl_3$)



IR Spectra



^{1}H-NMR (400 MHz, $CDCl_3$)



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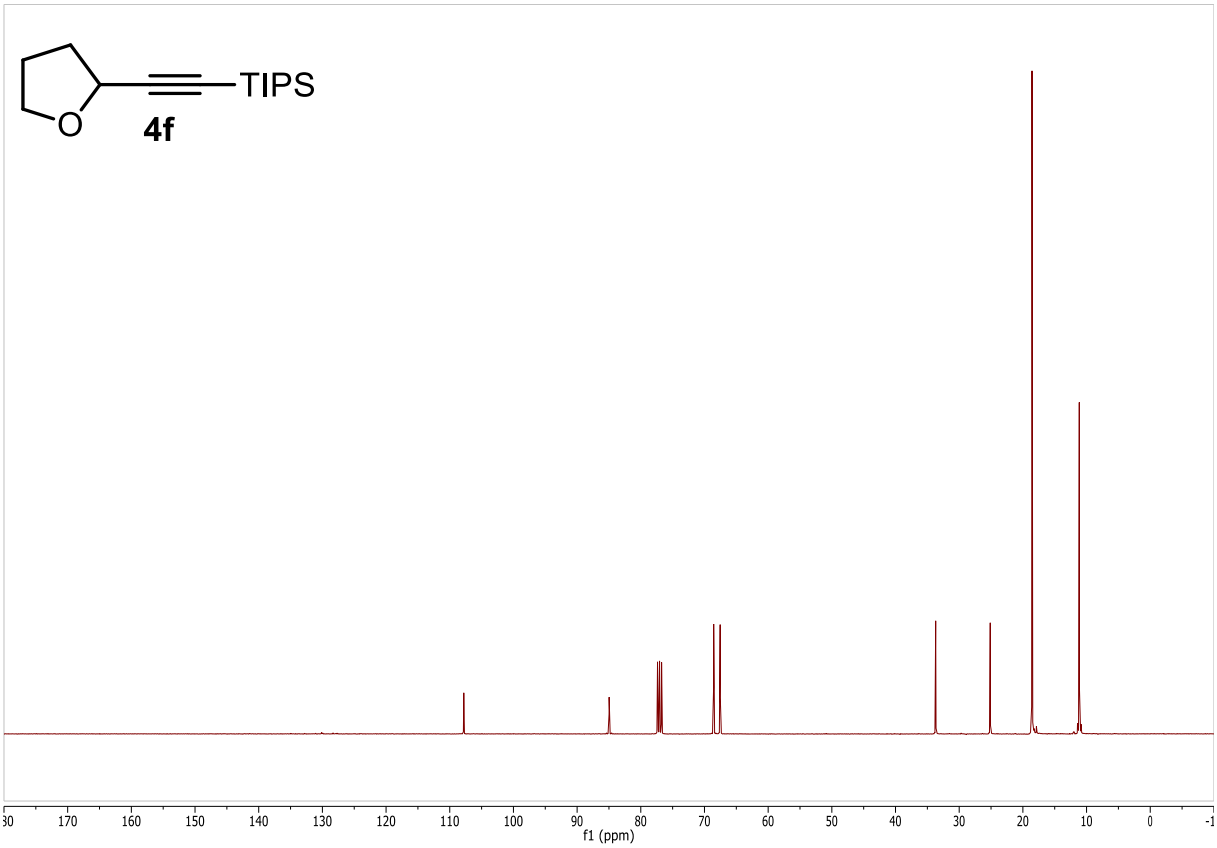

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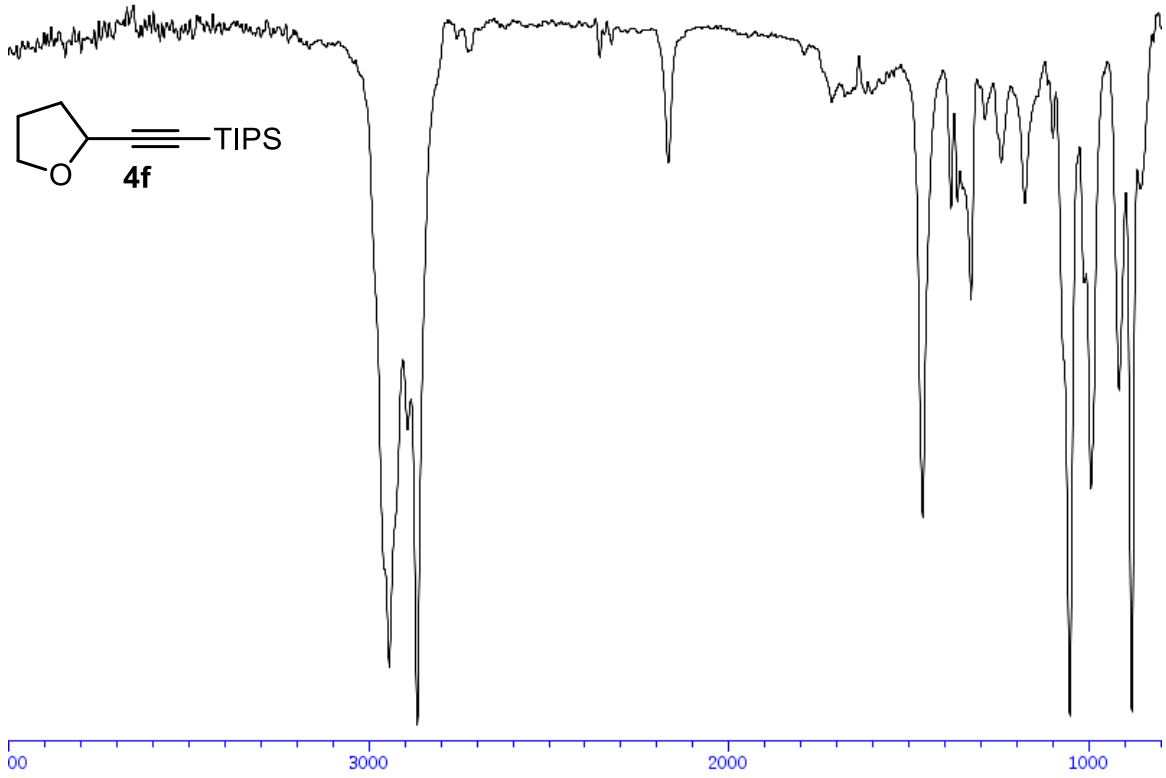
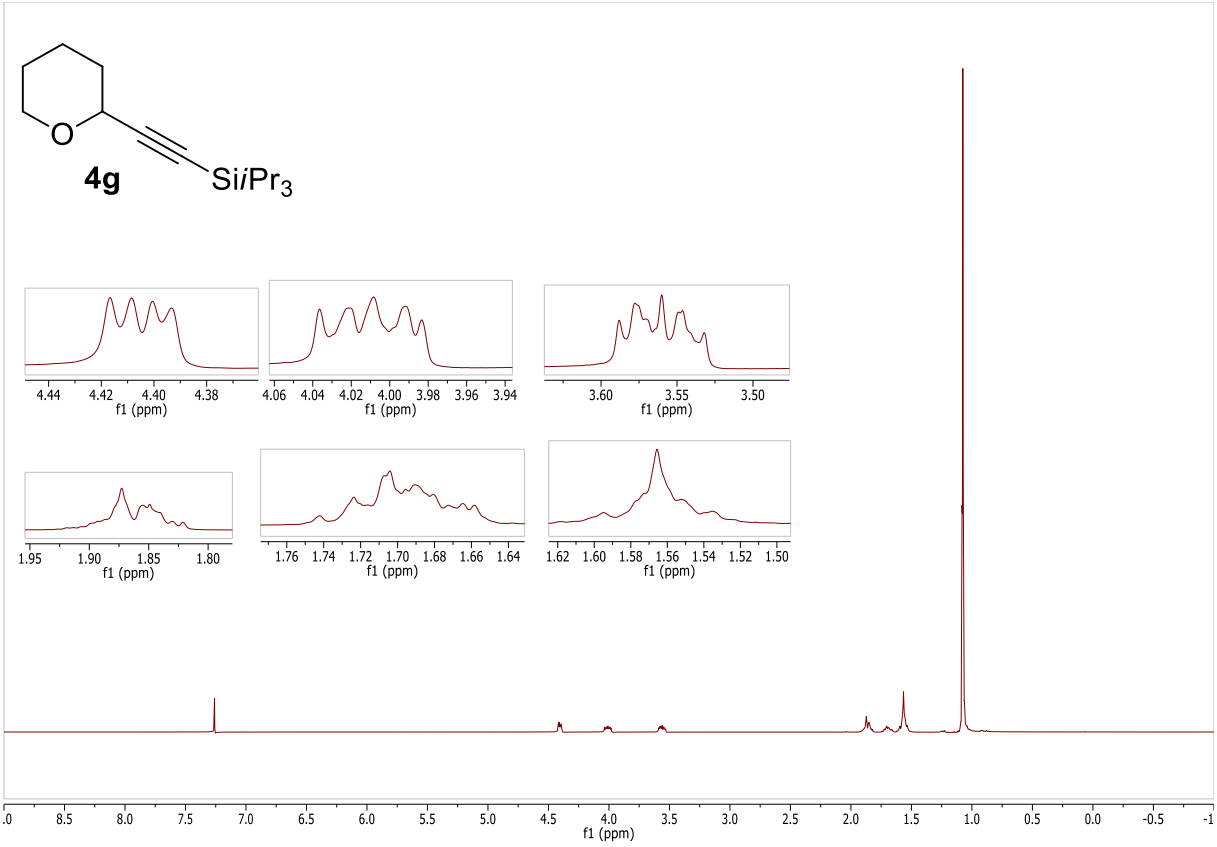
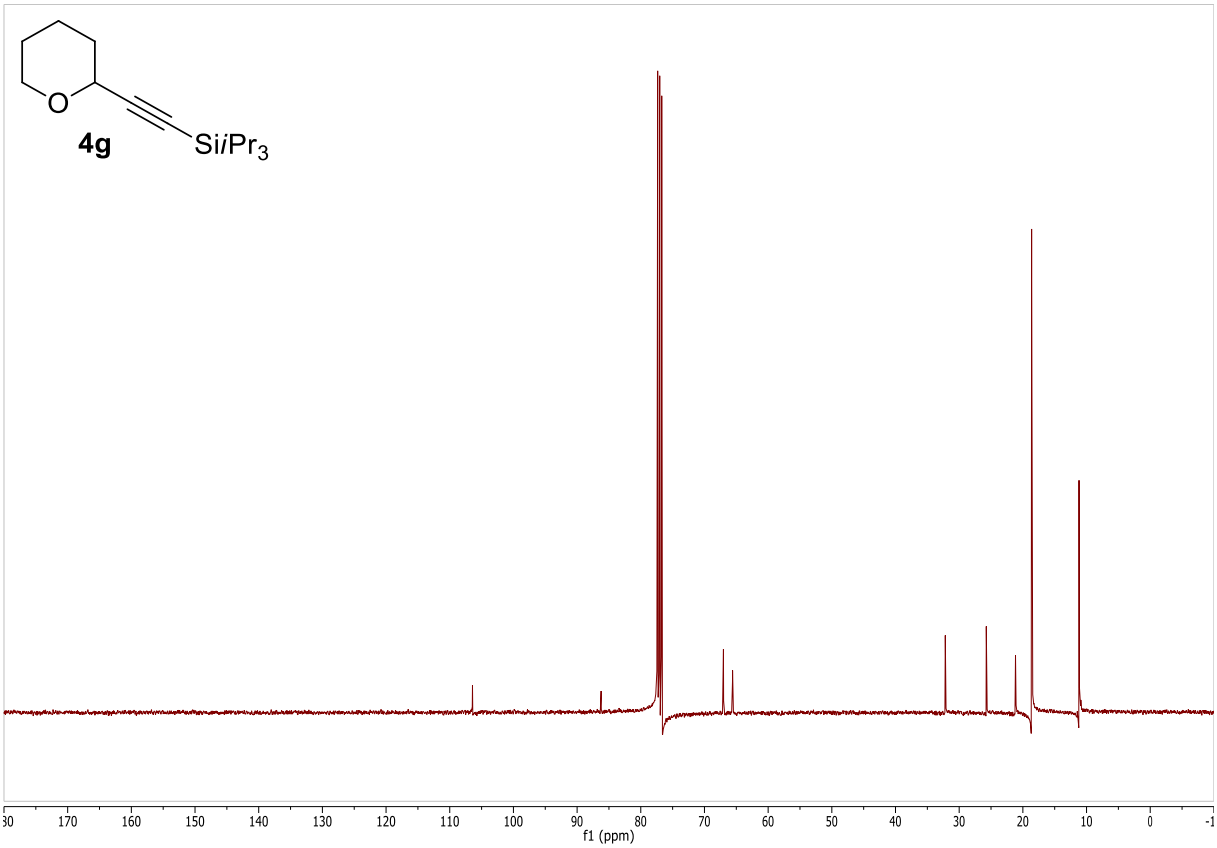


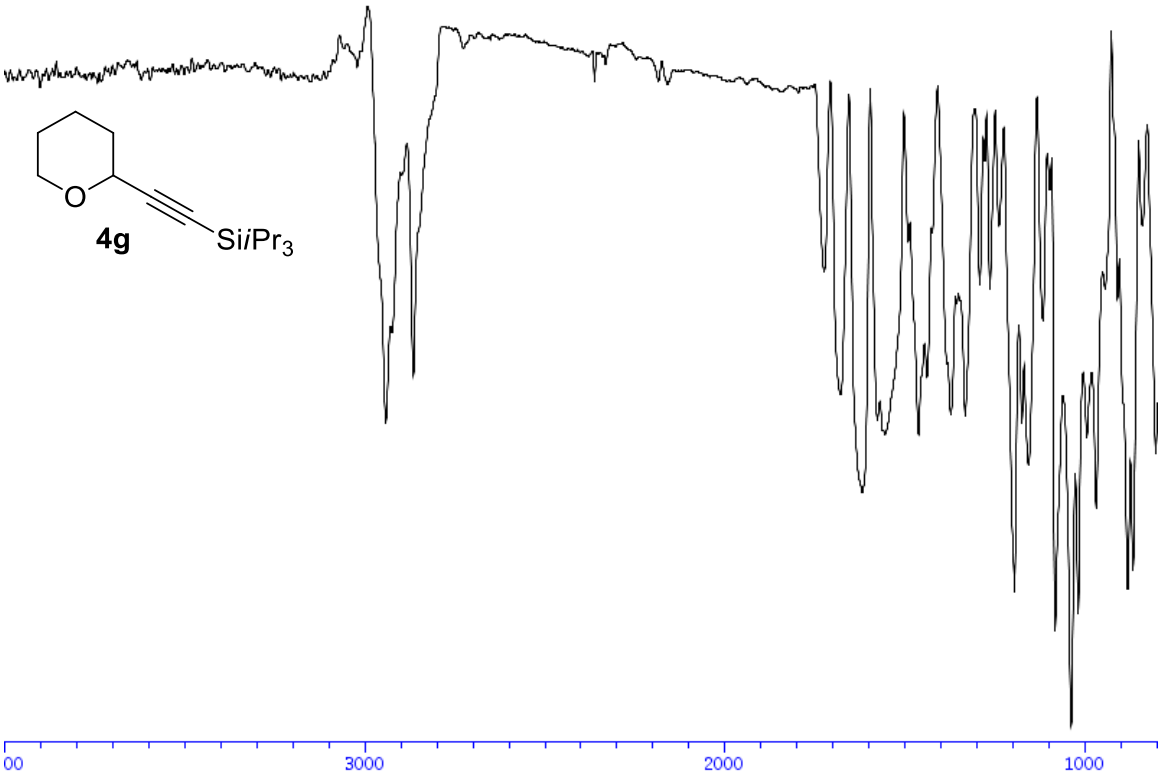
^{1}H-NMR (400 MHz, $CDCl_3$)



^{13}C-NMR (101 MHz, $CDCl_3$)



IR Spectra



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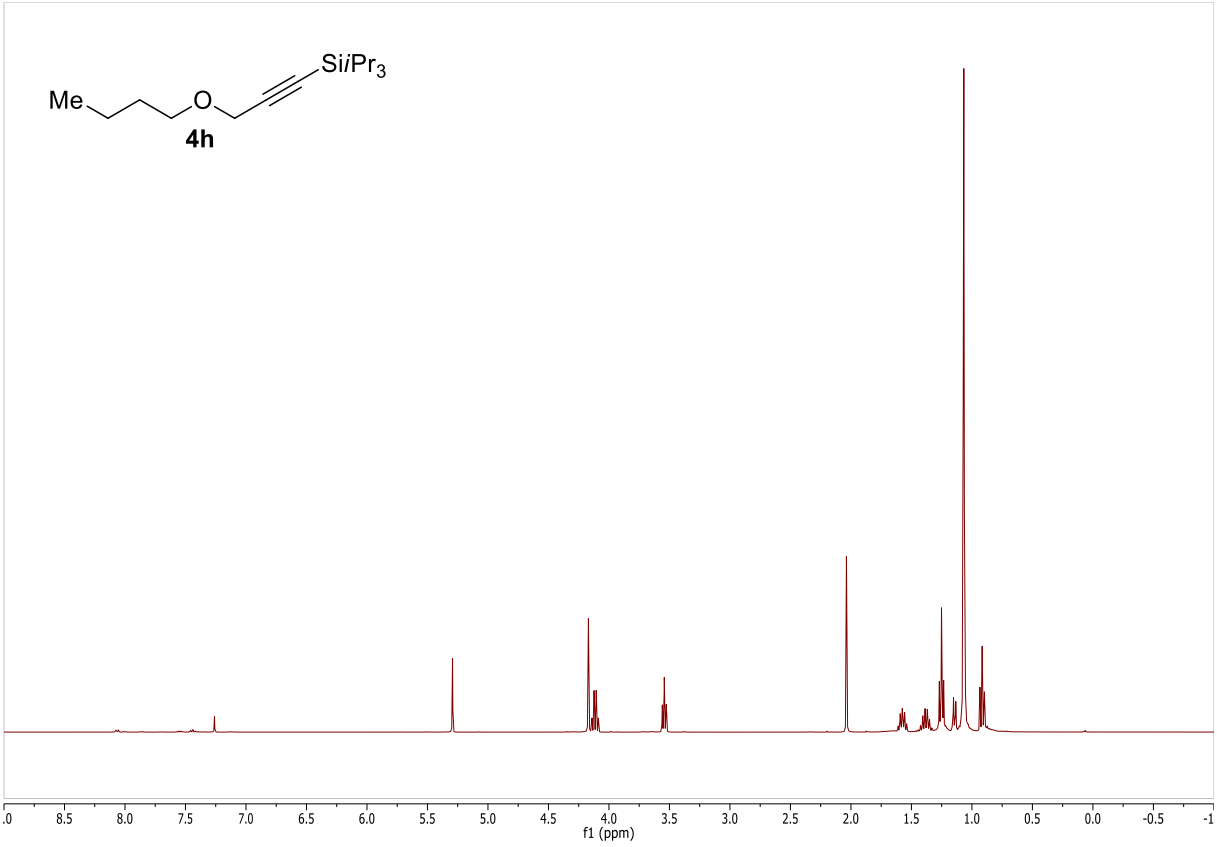

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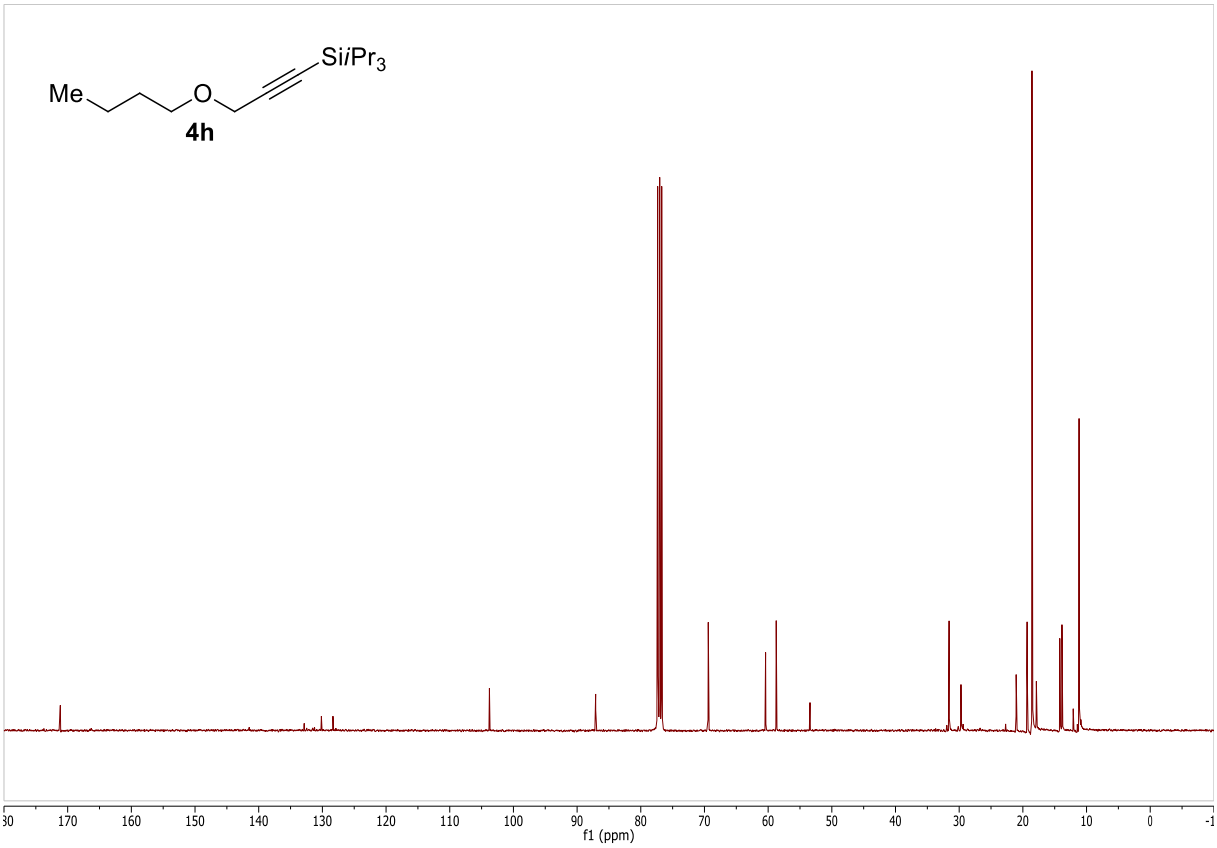
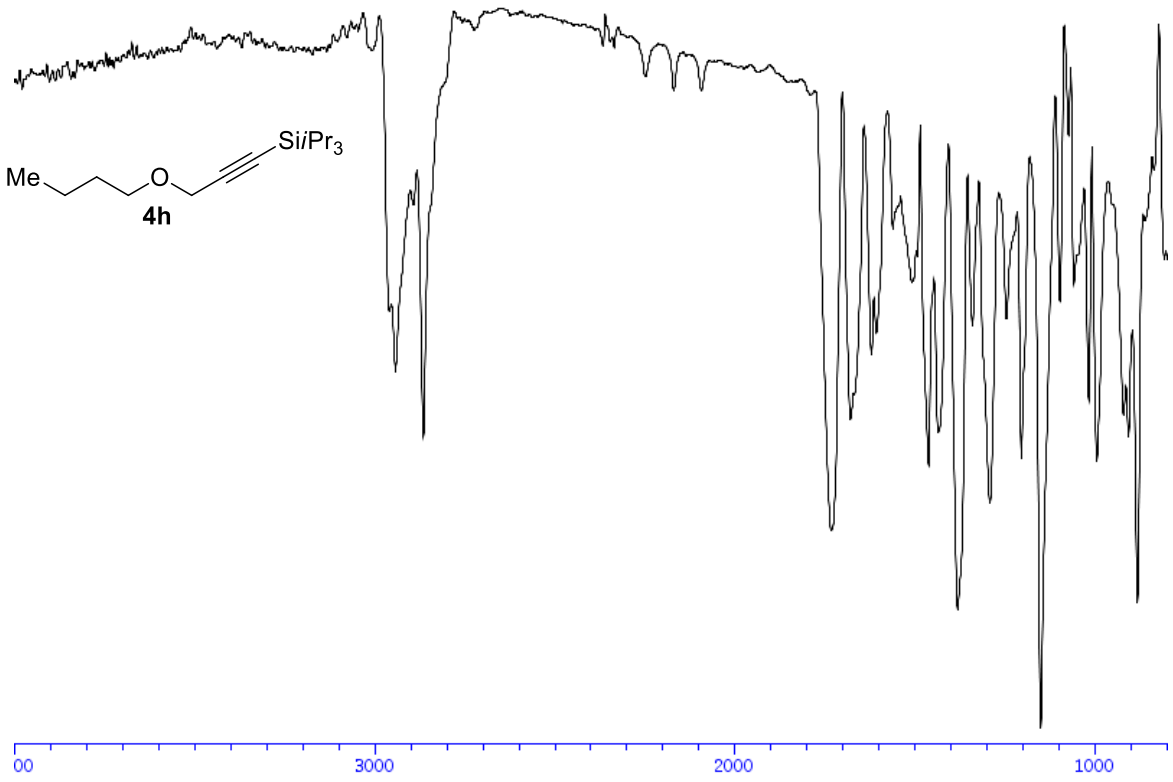
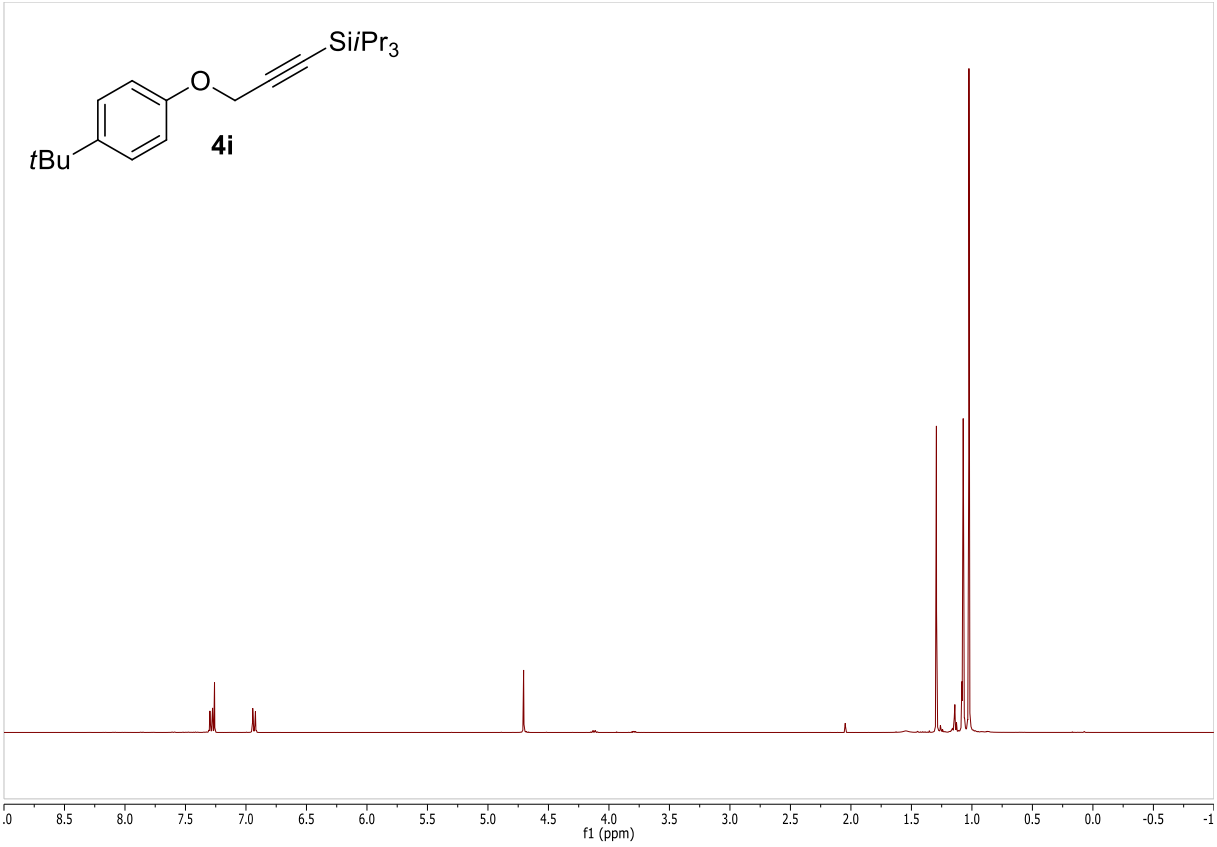


IR Spectra



^{1}H-NMR (400 MHz, $CDCl_3$)



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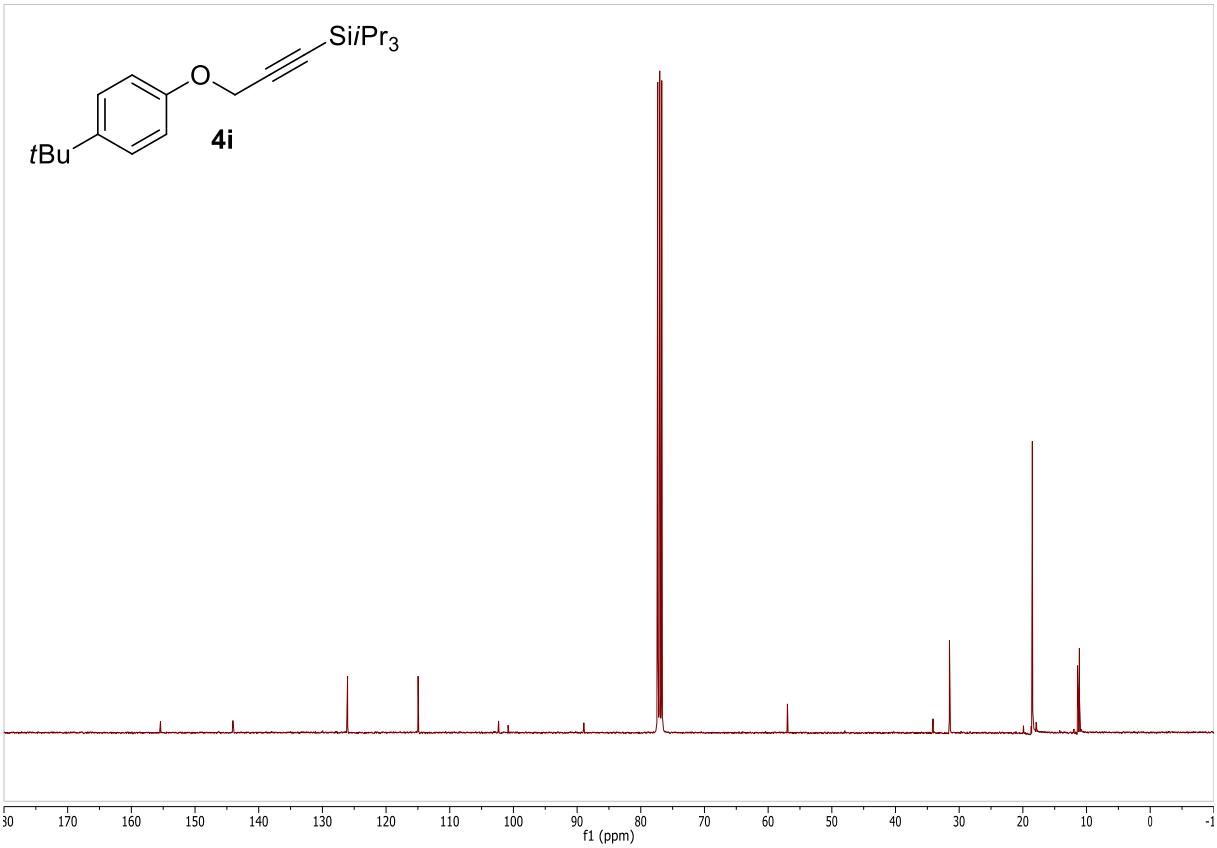
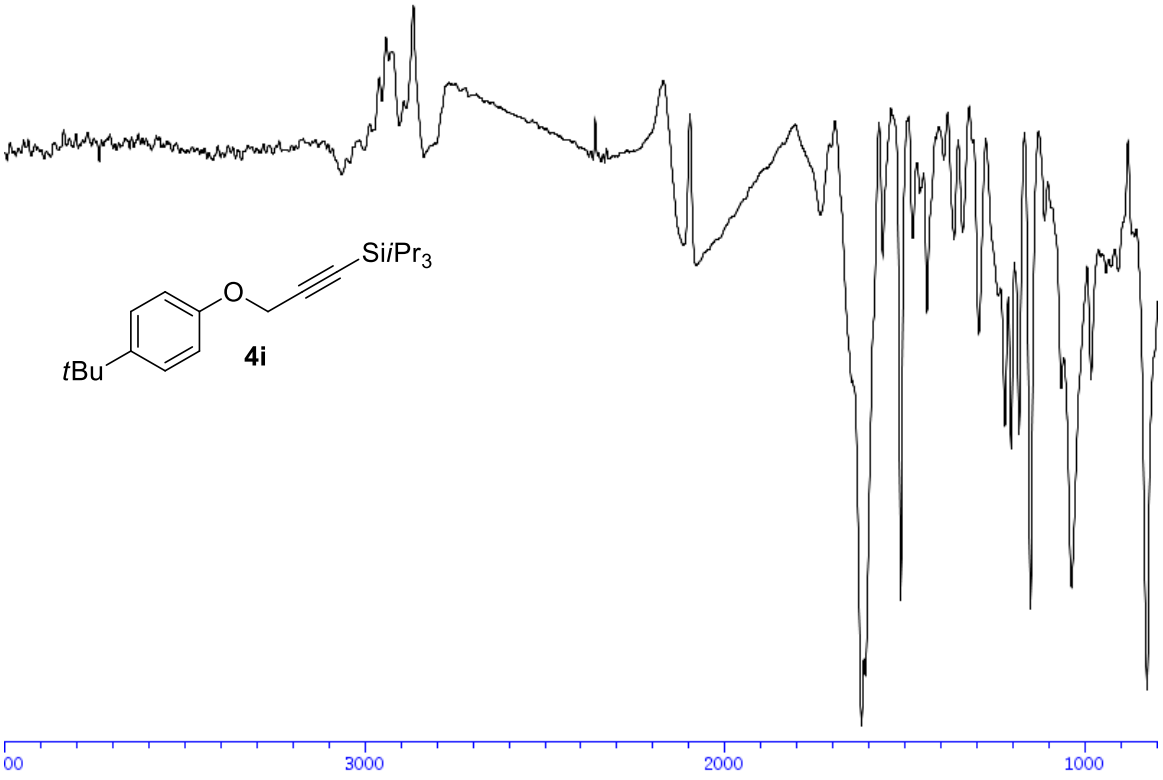


IR Spectra



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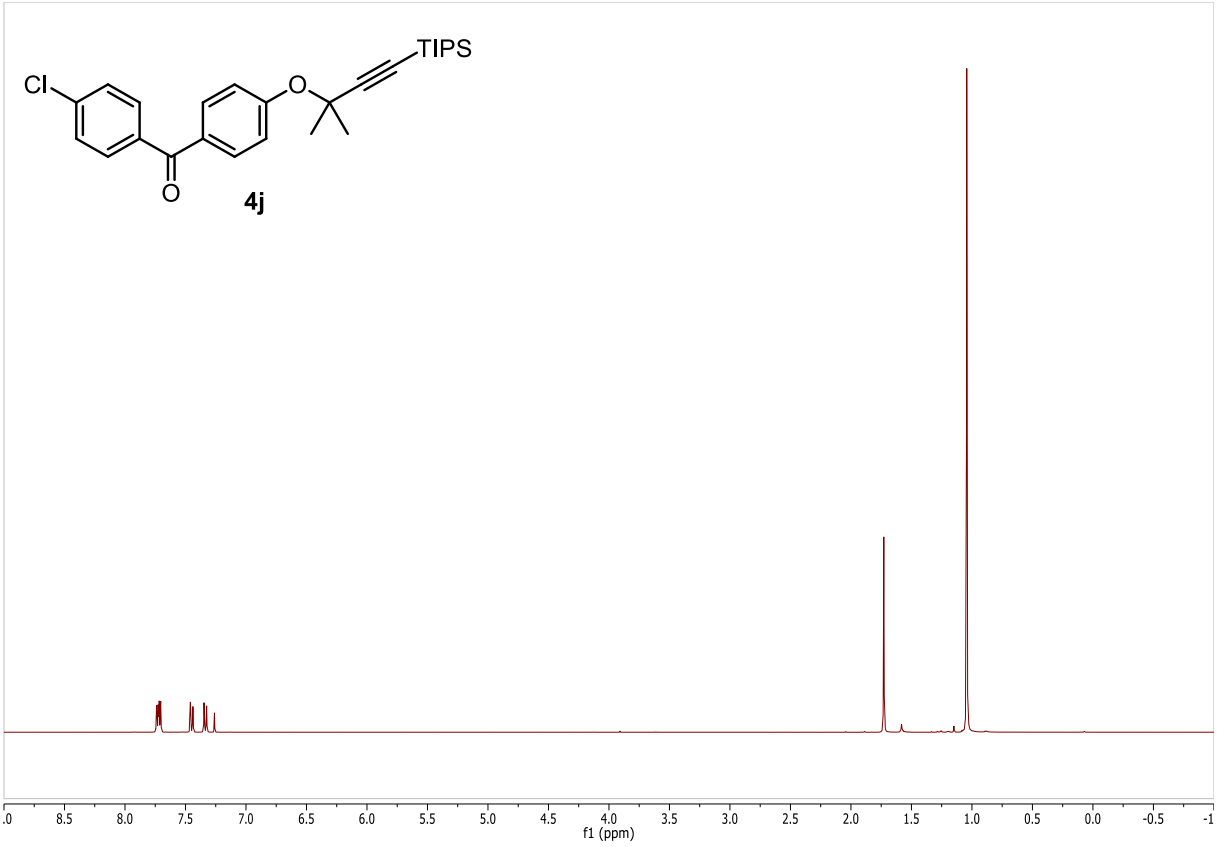

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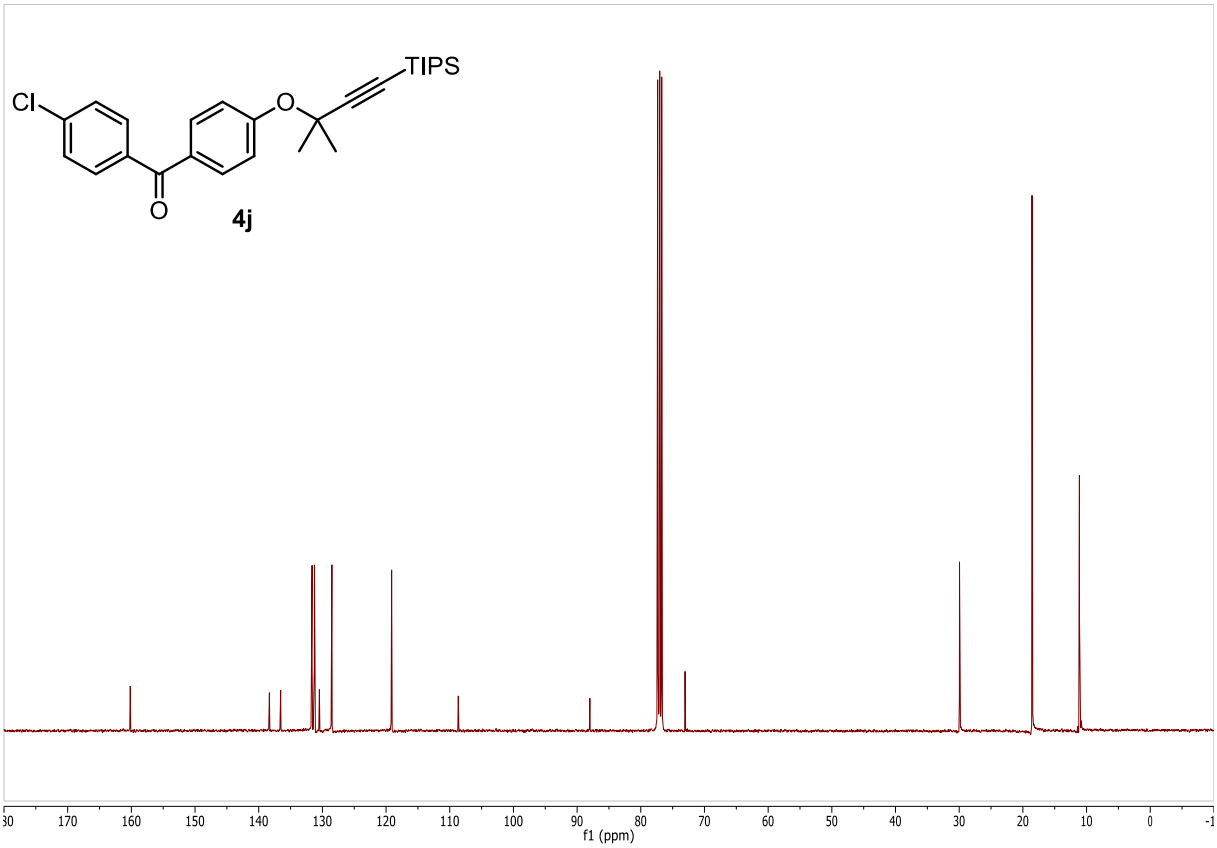
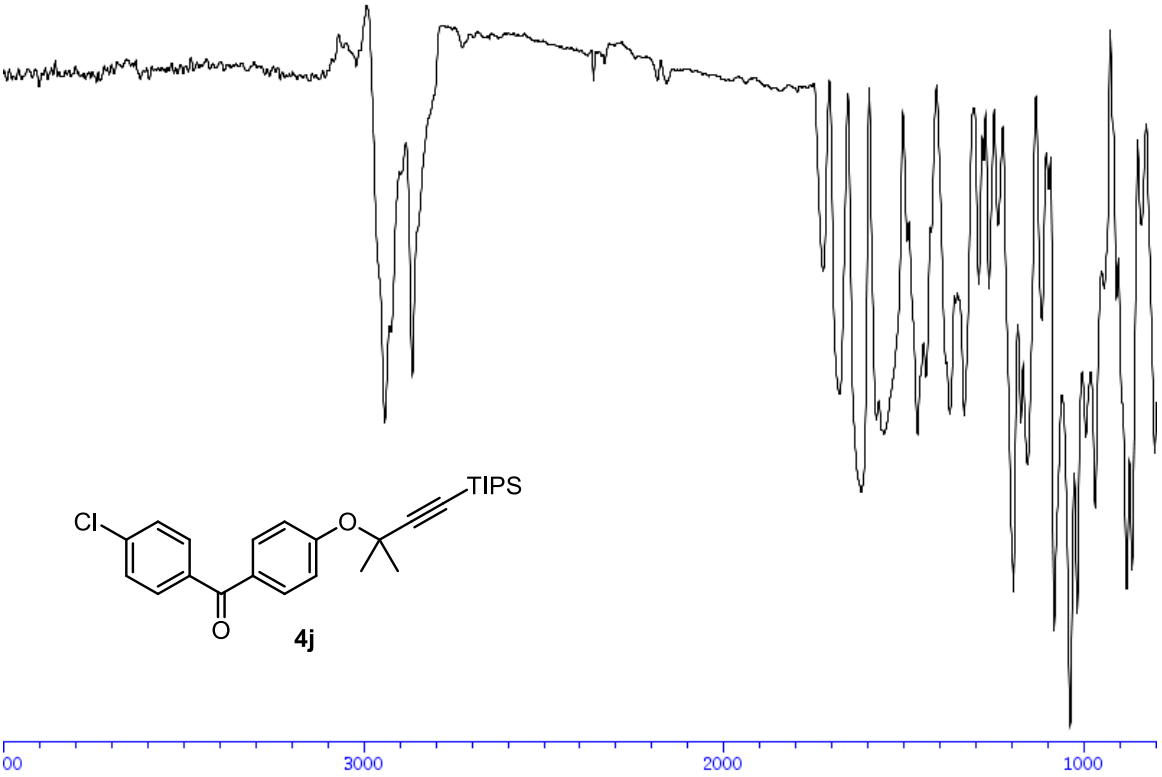


IR Spectra



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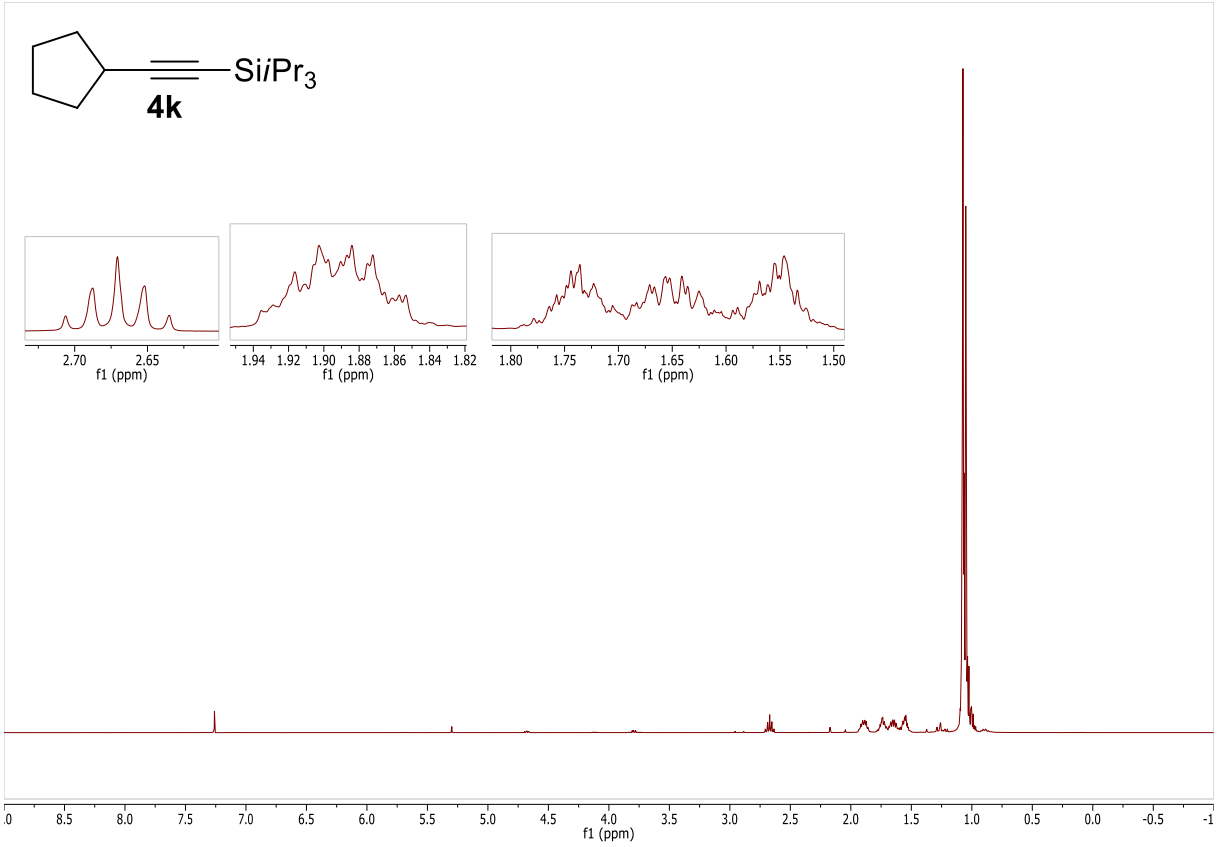

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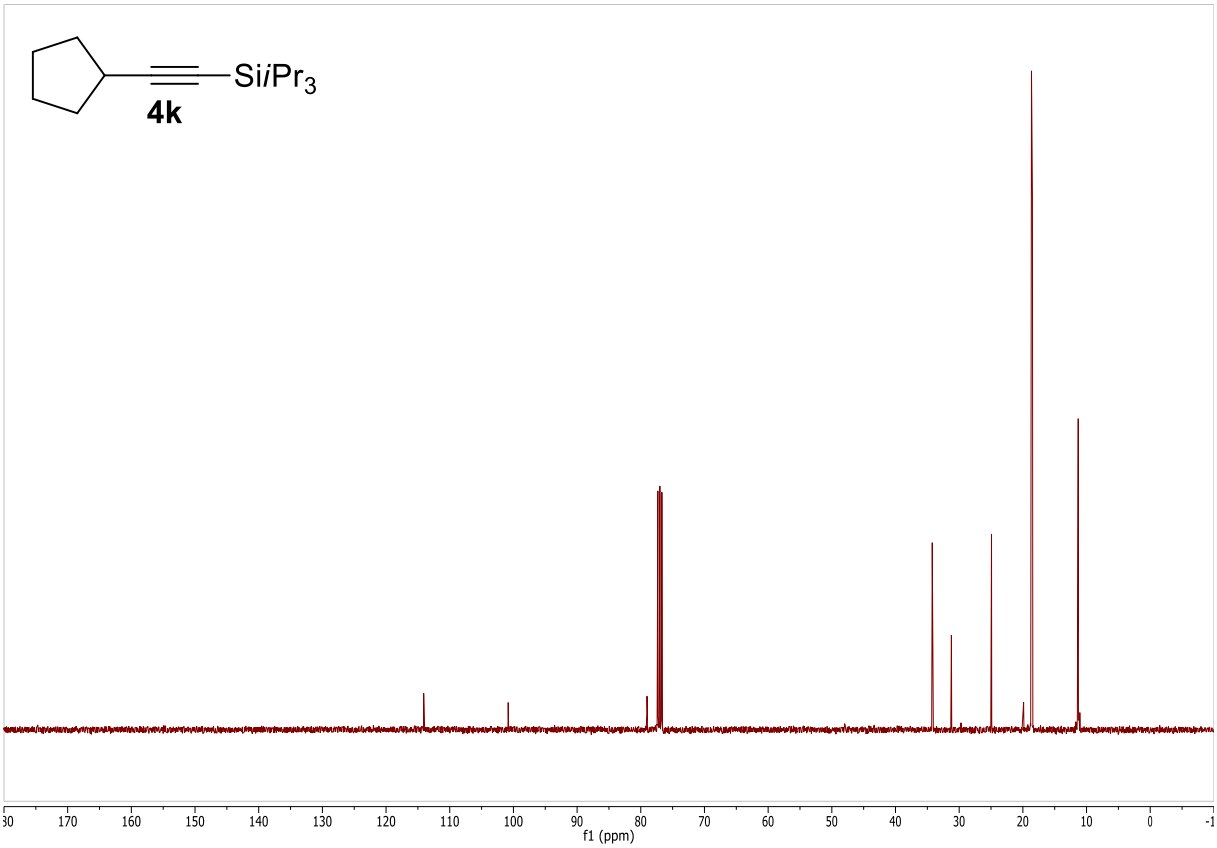

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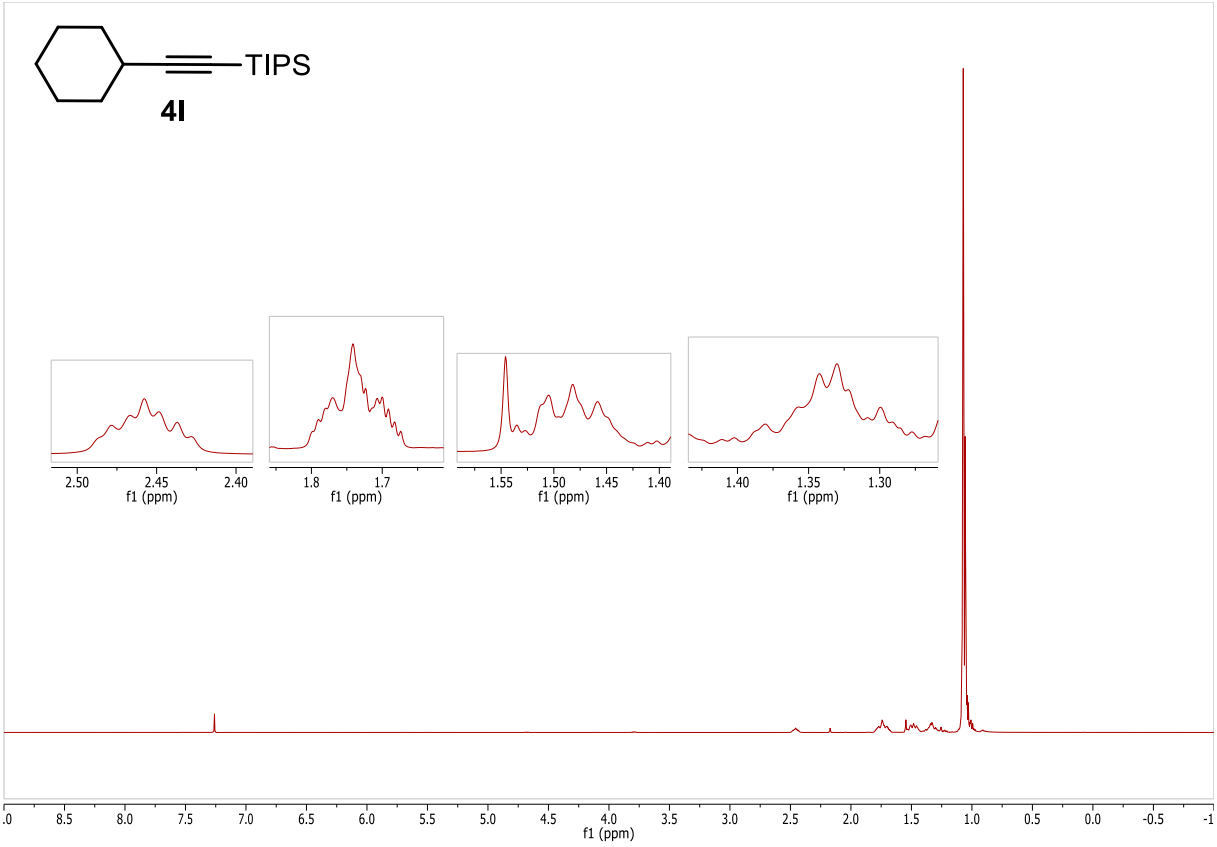

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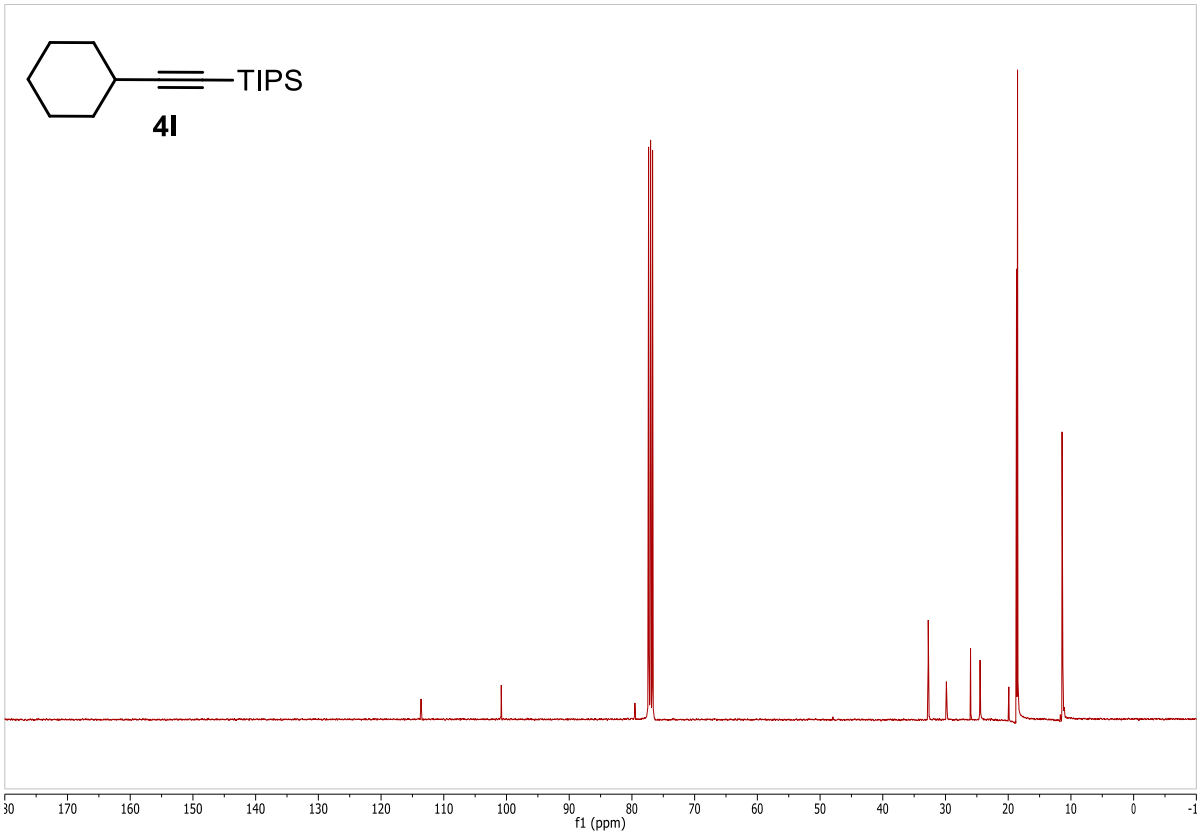
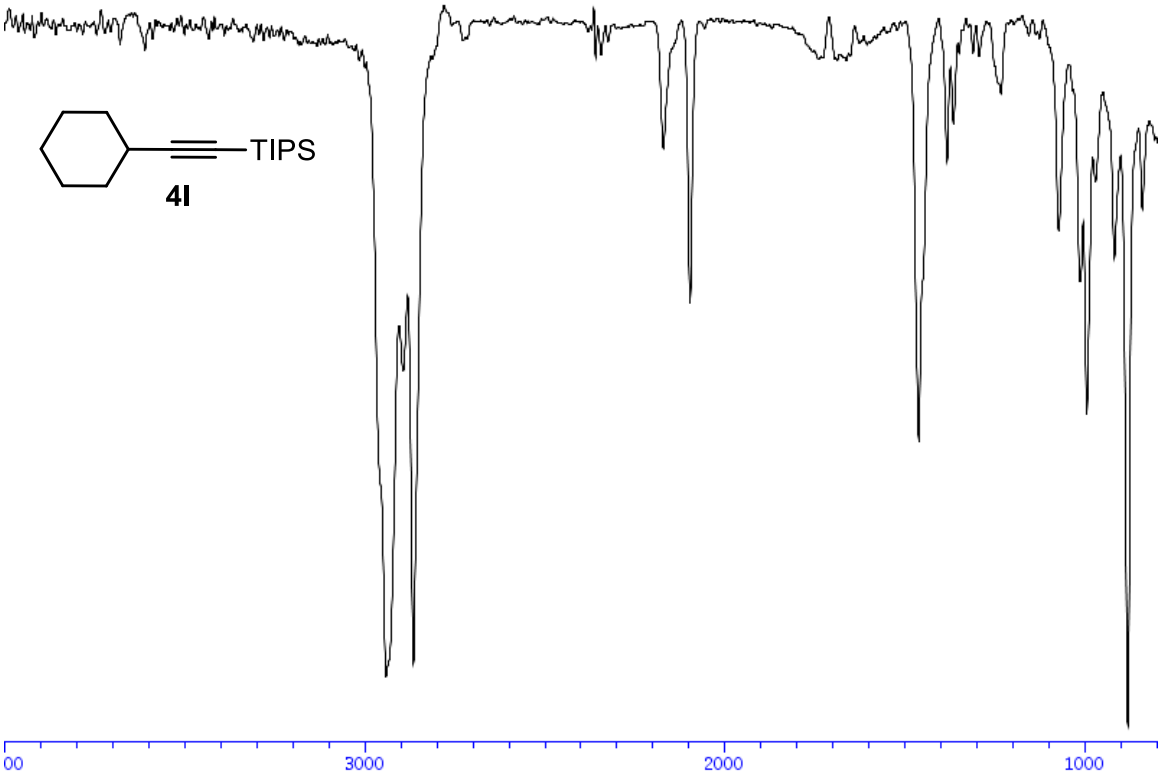


IR Spectra



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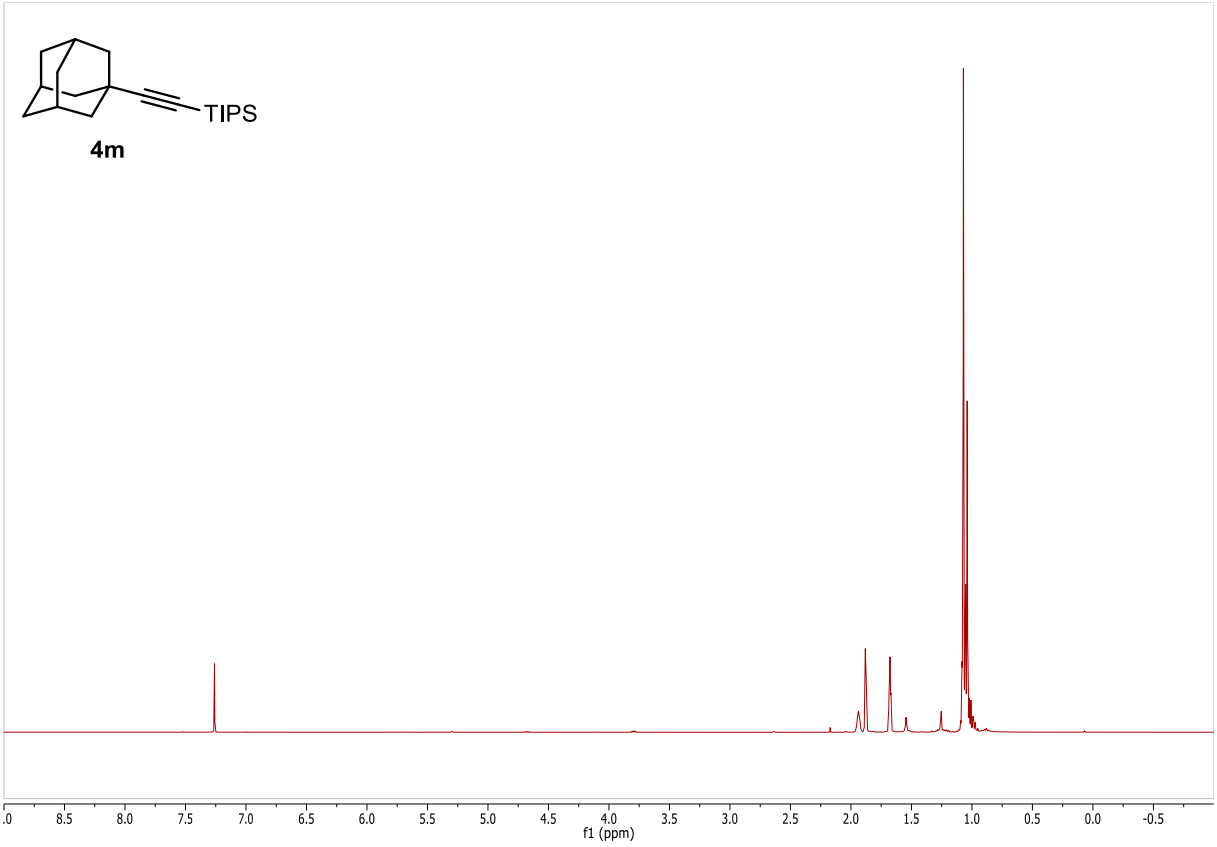

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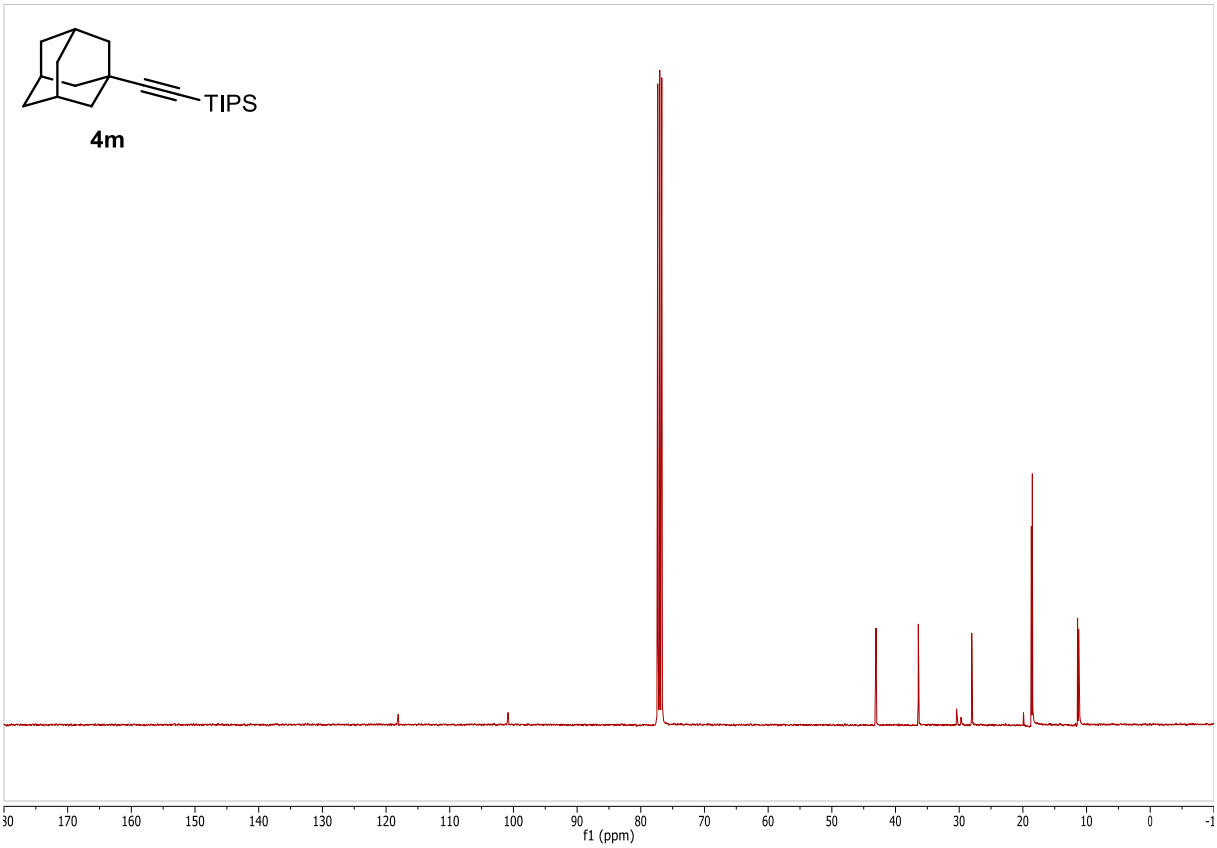
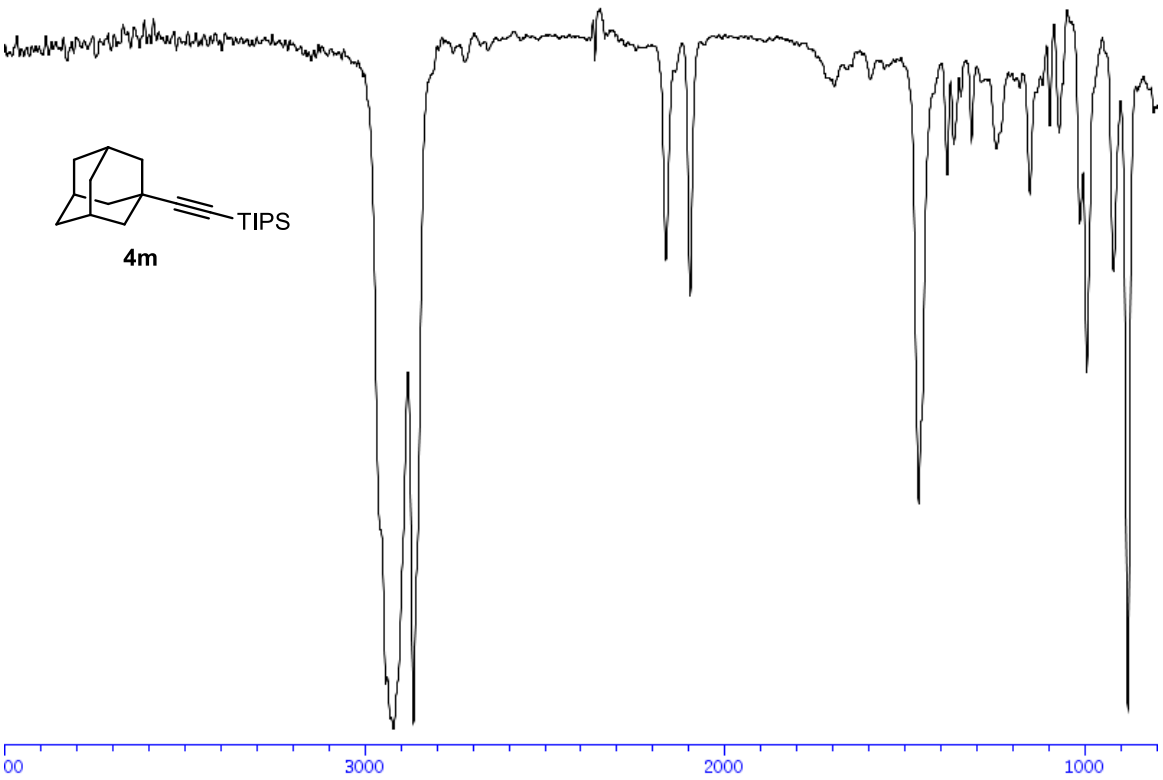


IR Spectra



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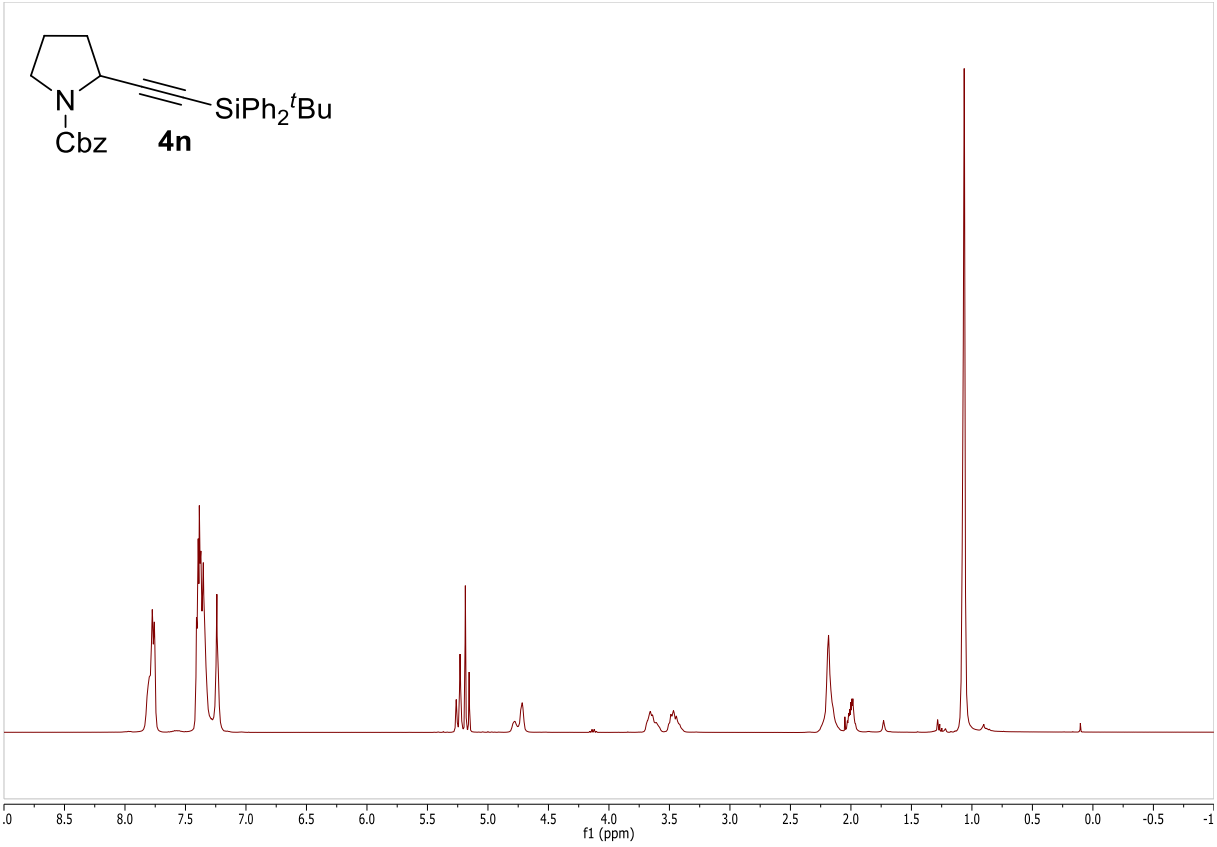

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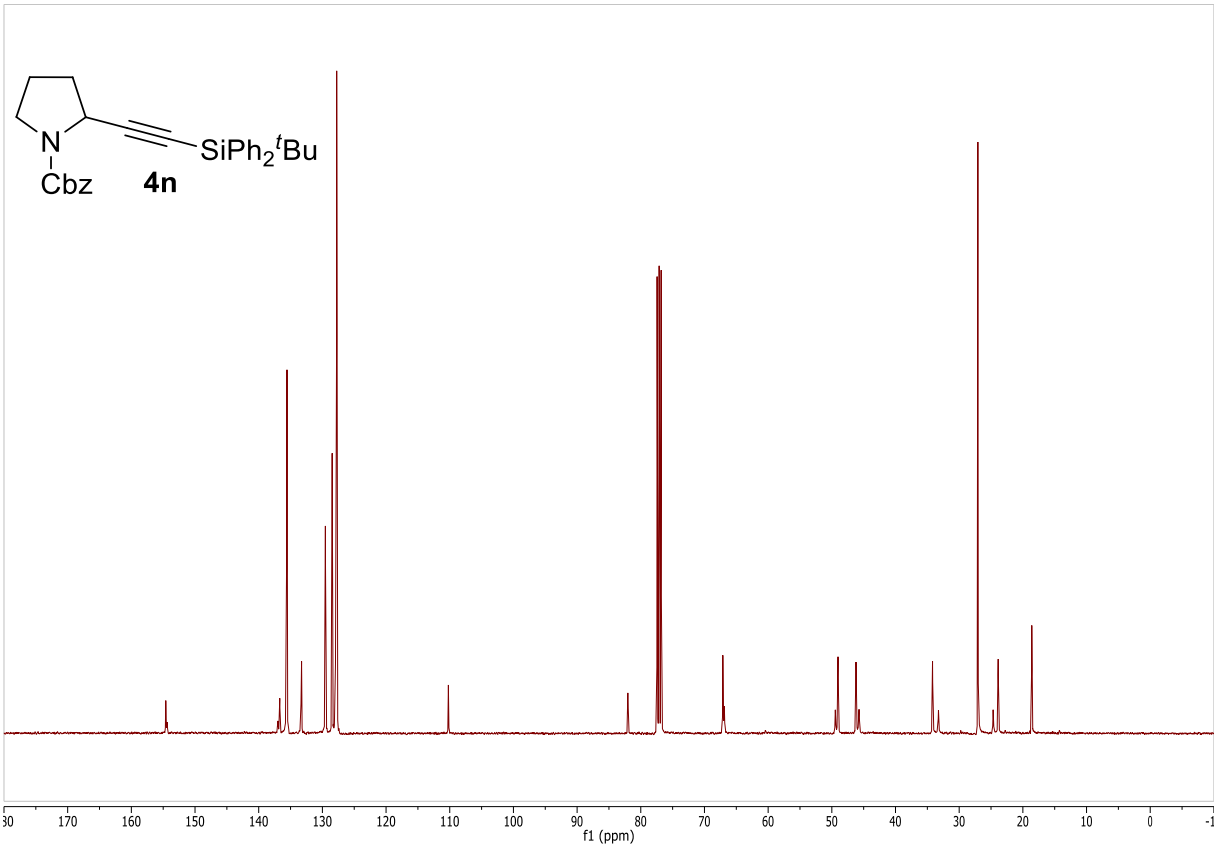
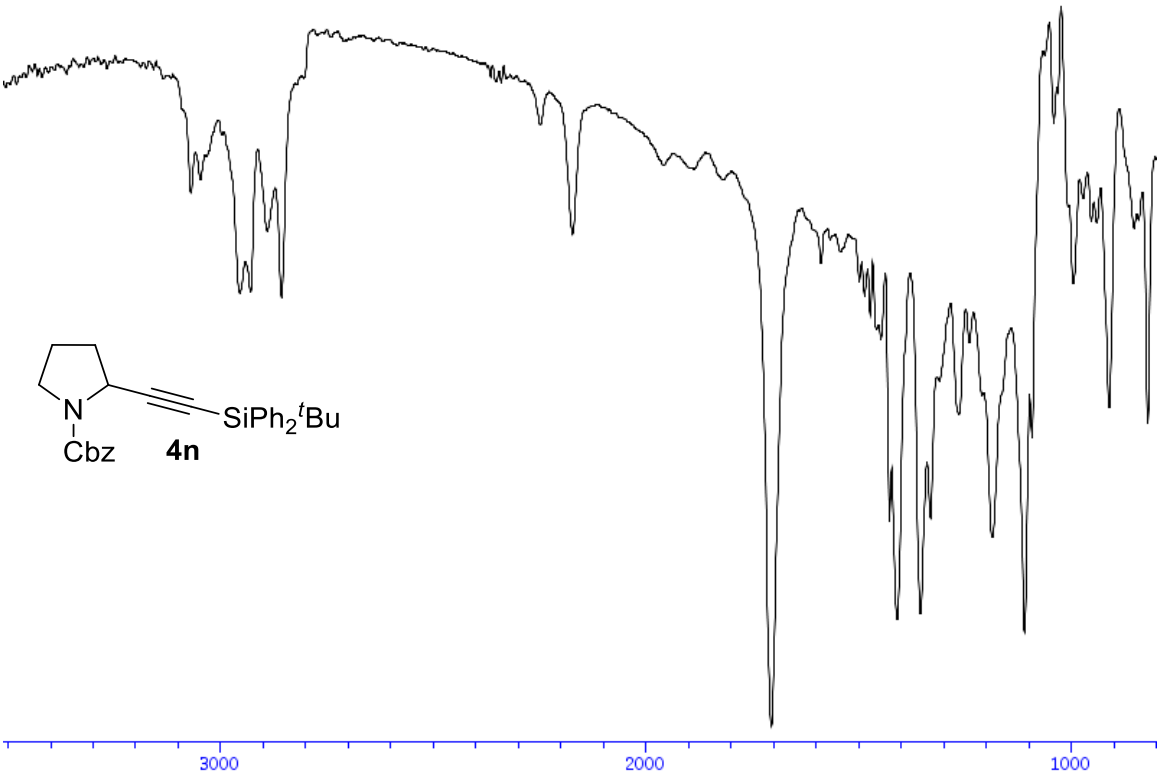


IR Spectra



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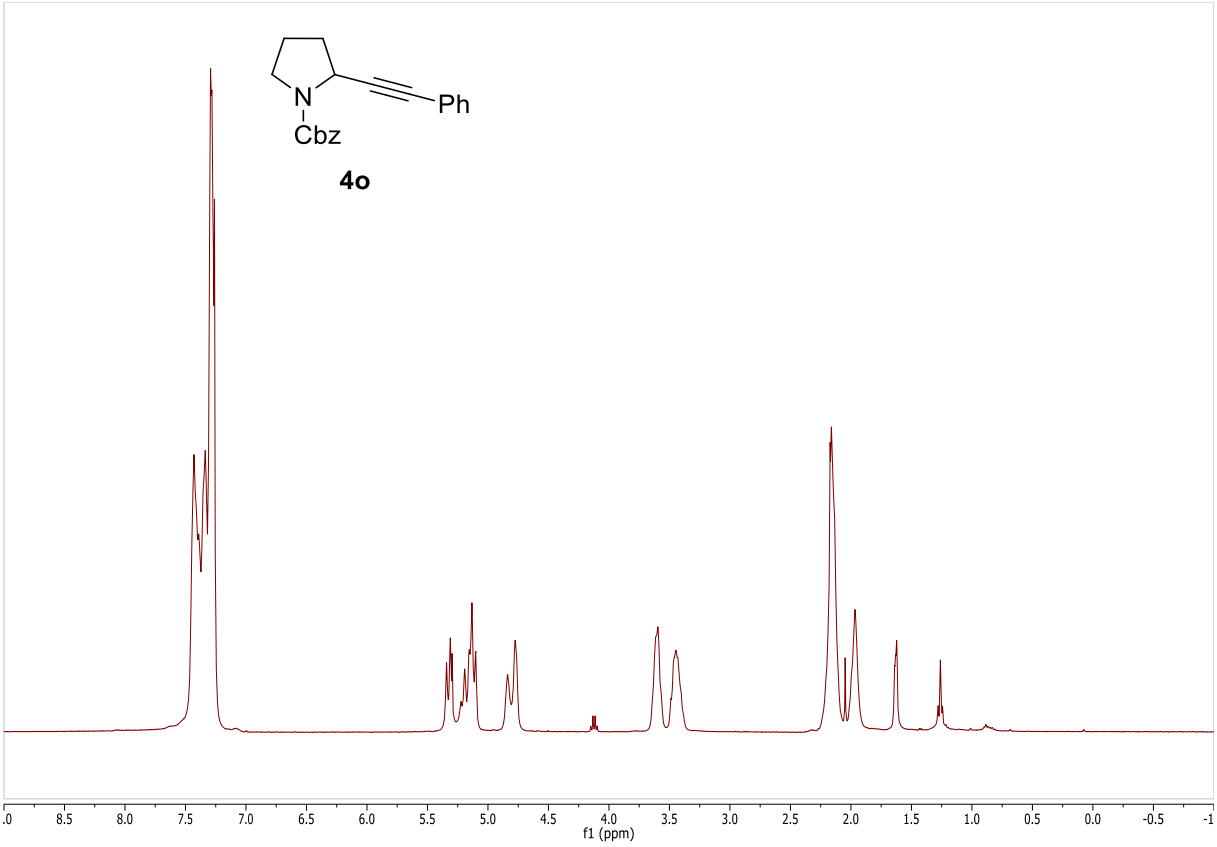

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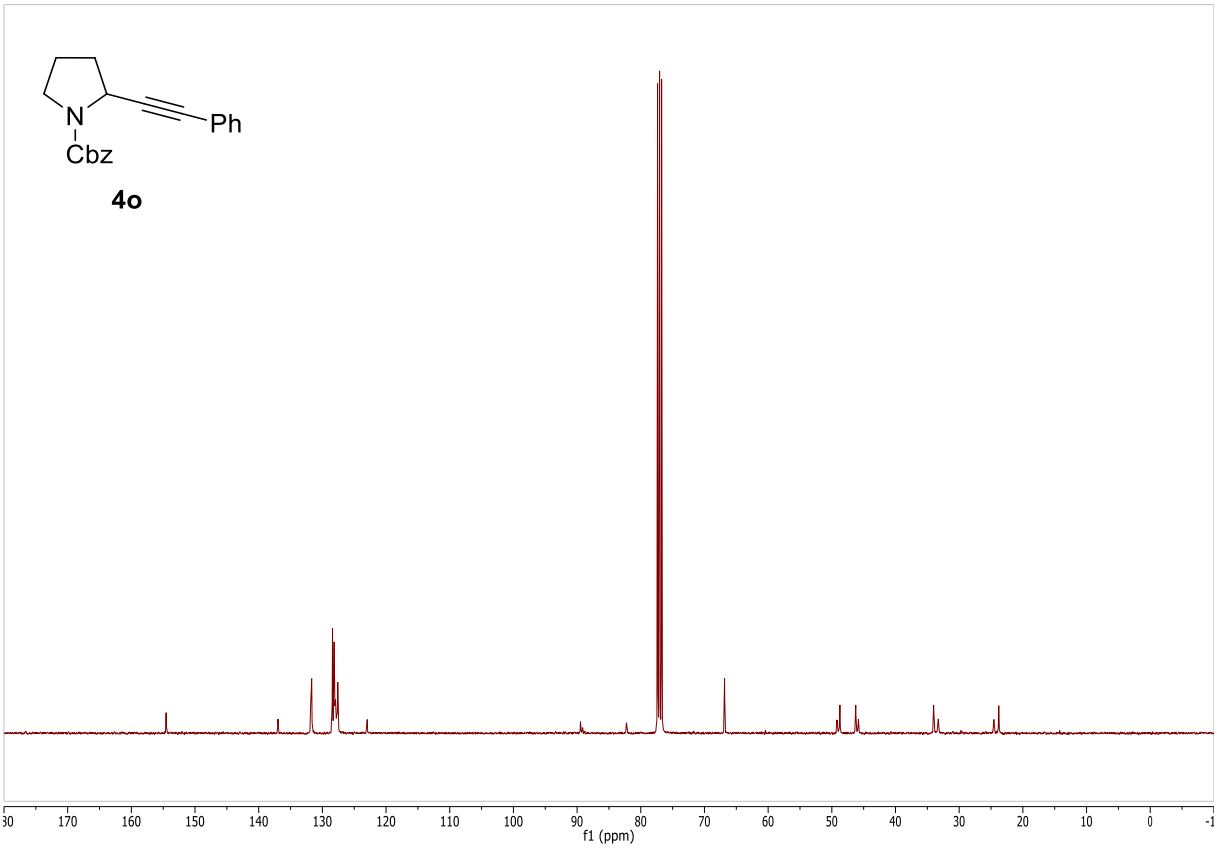
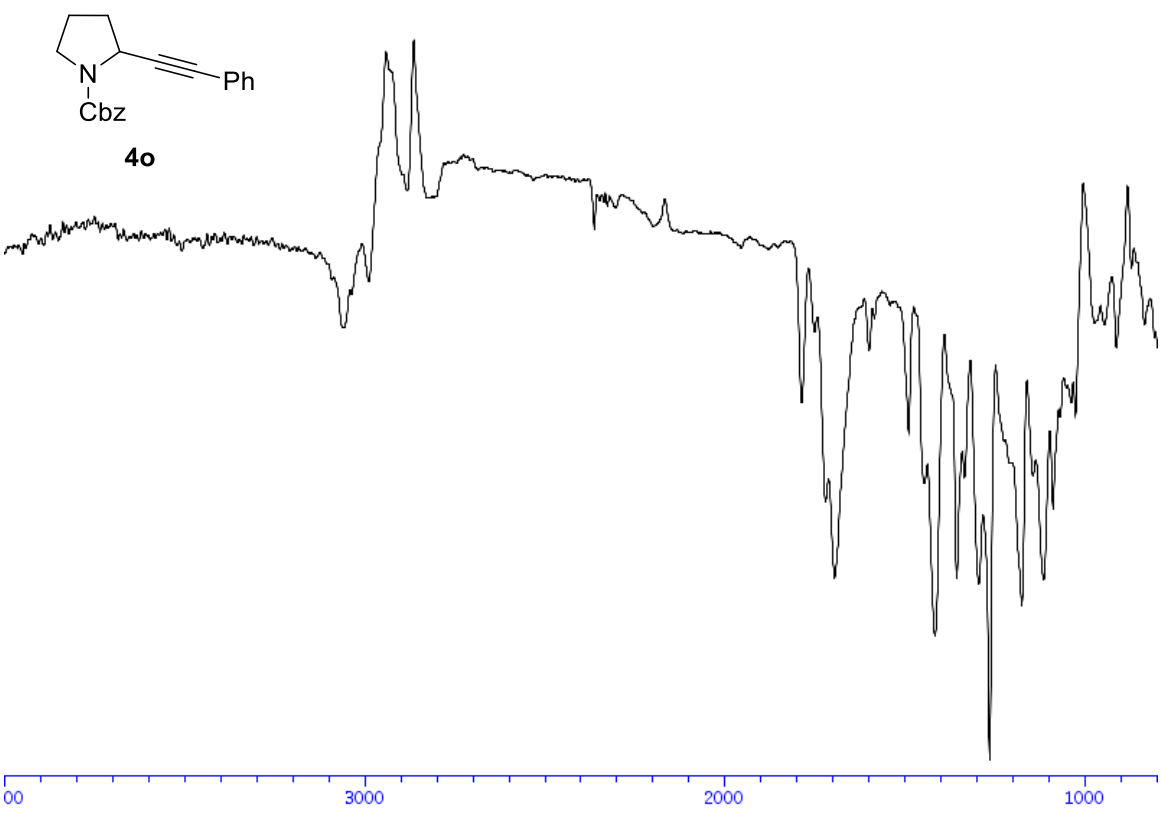


IR Spectra



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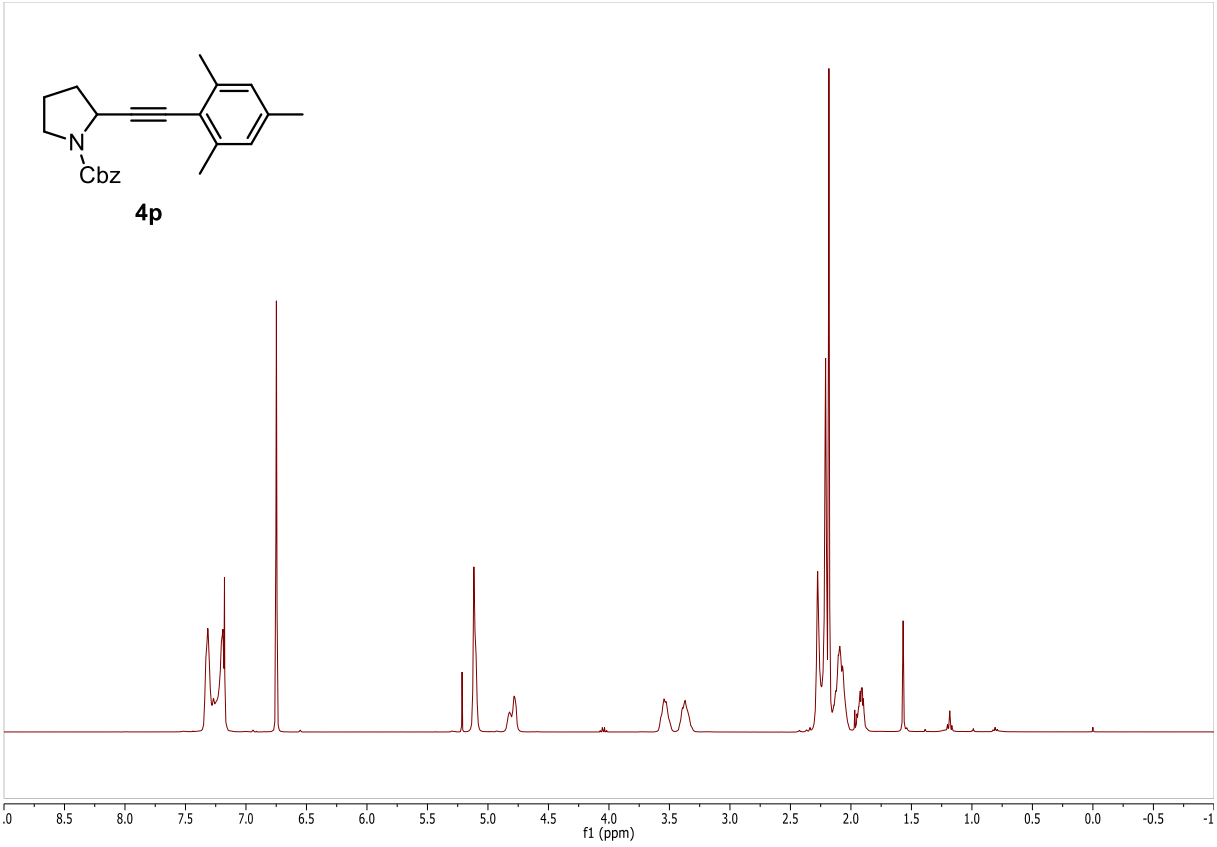

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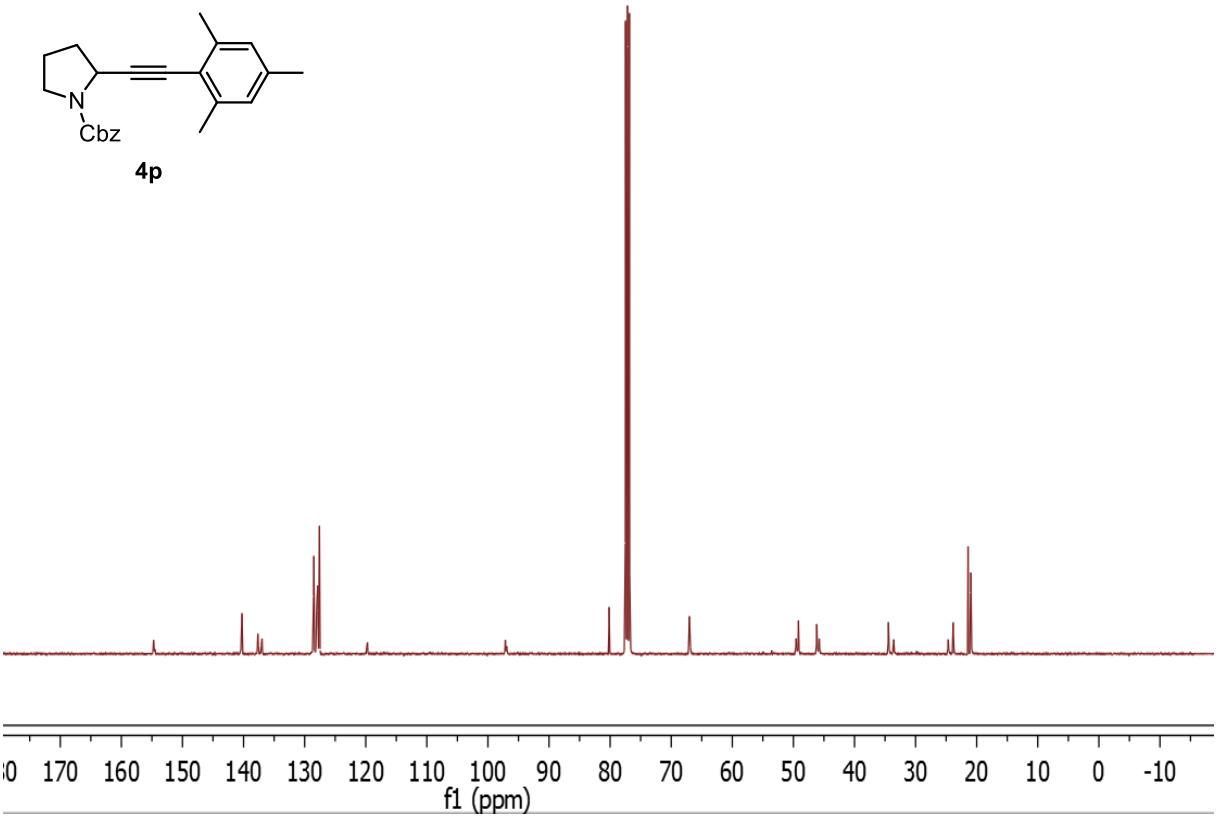
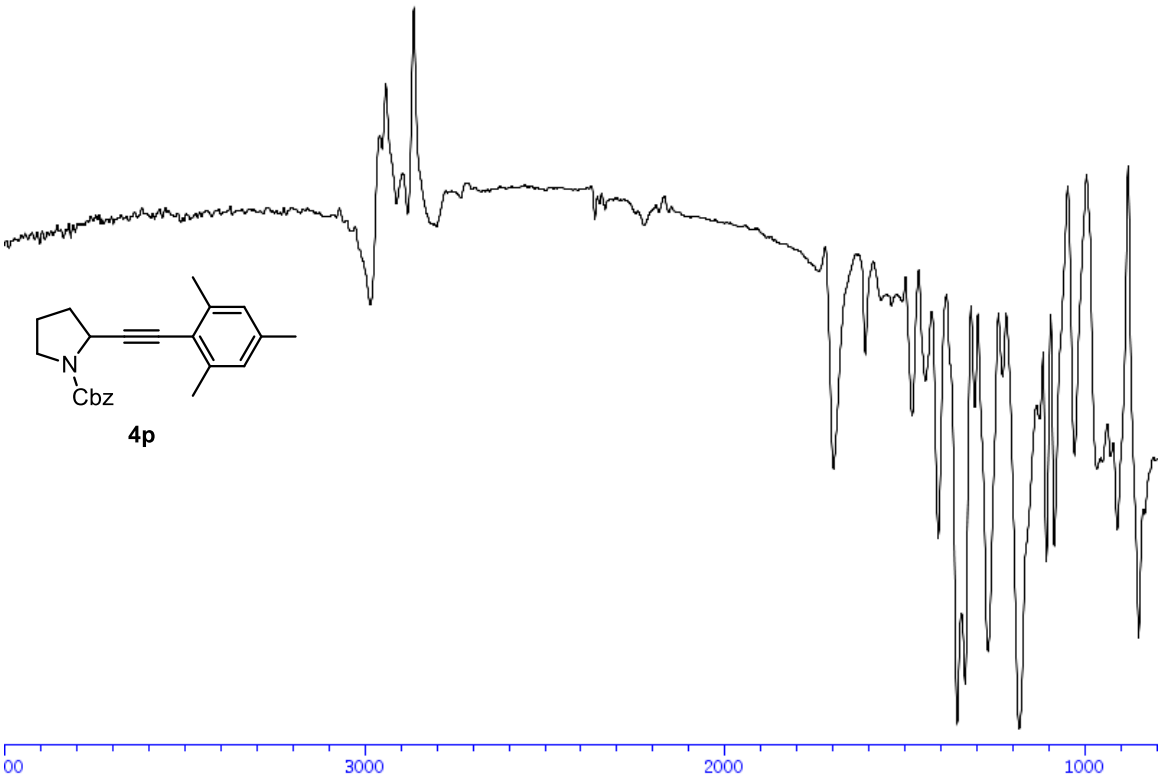


IR Spectra



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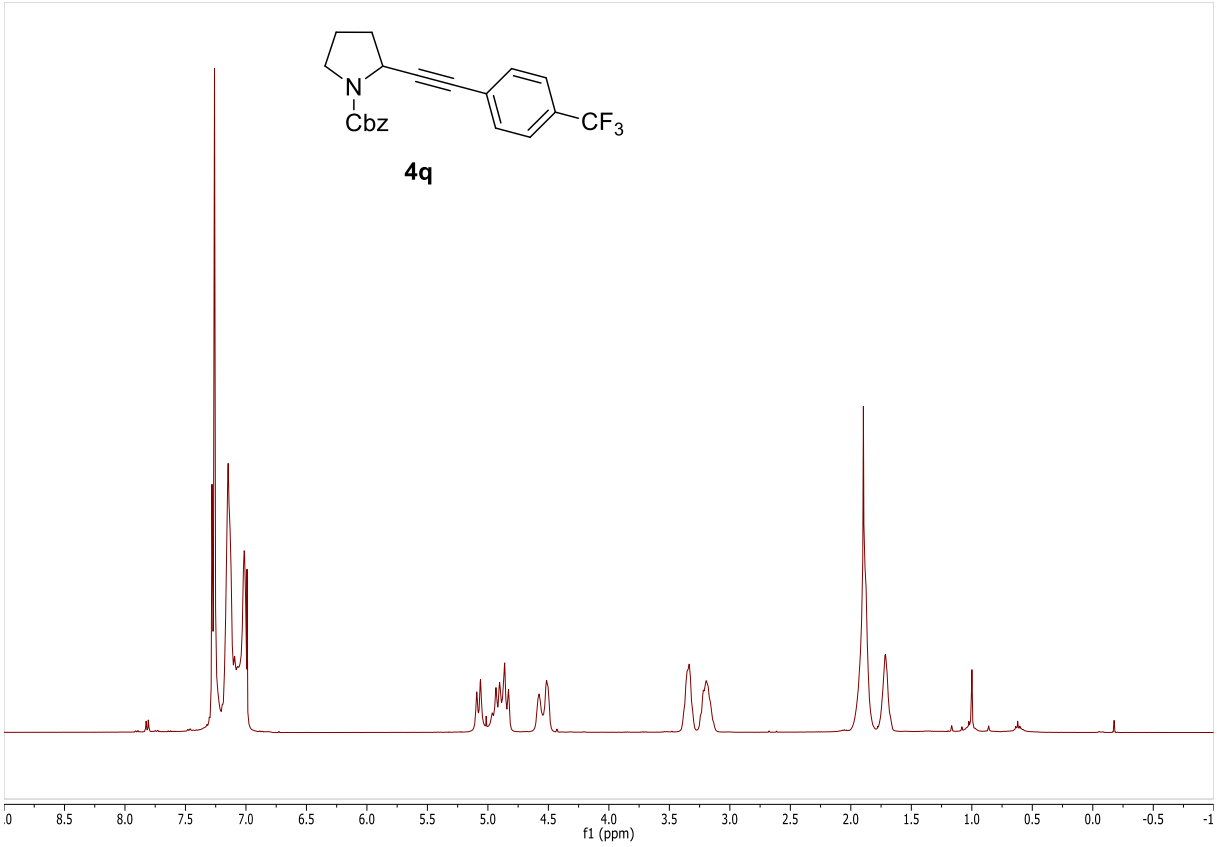

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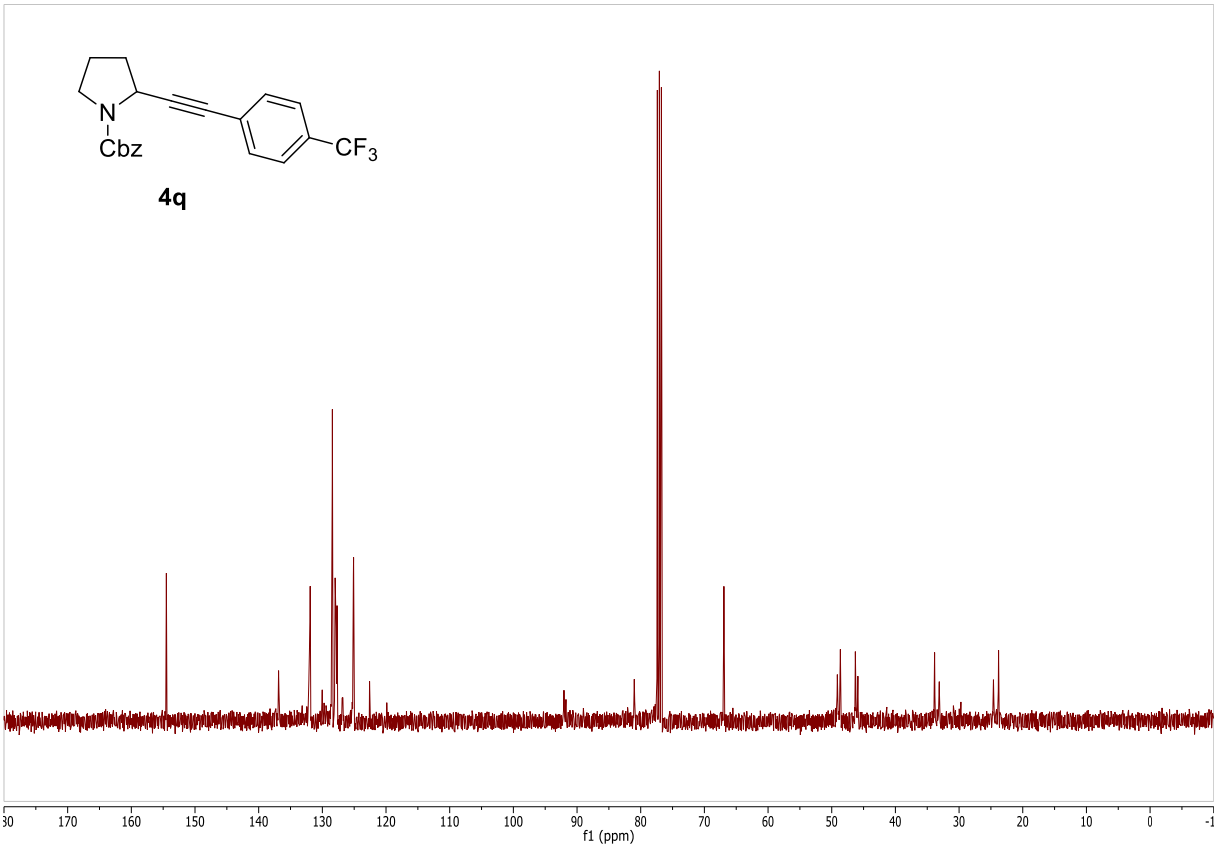

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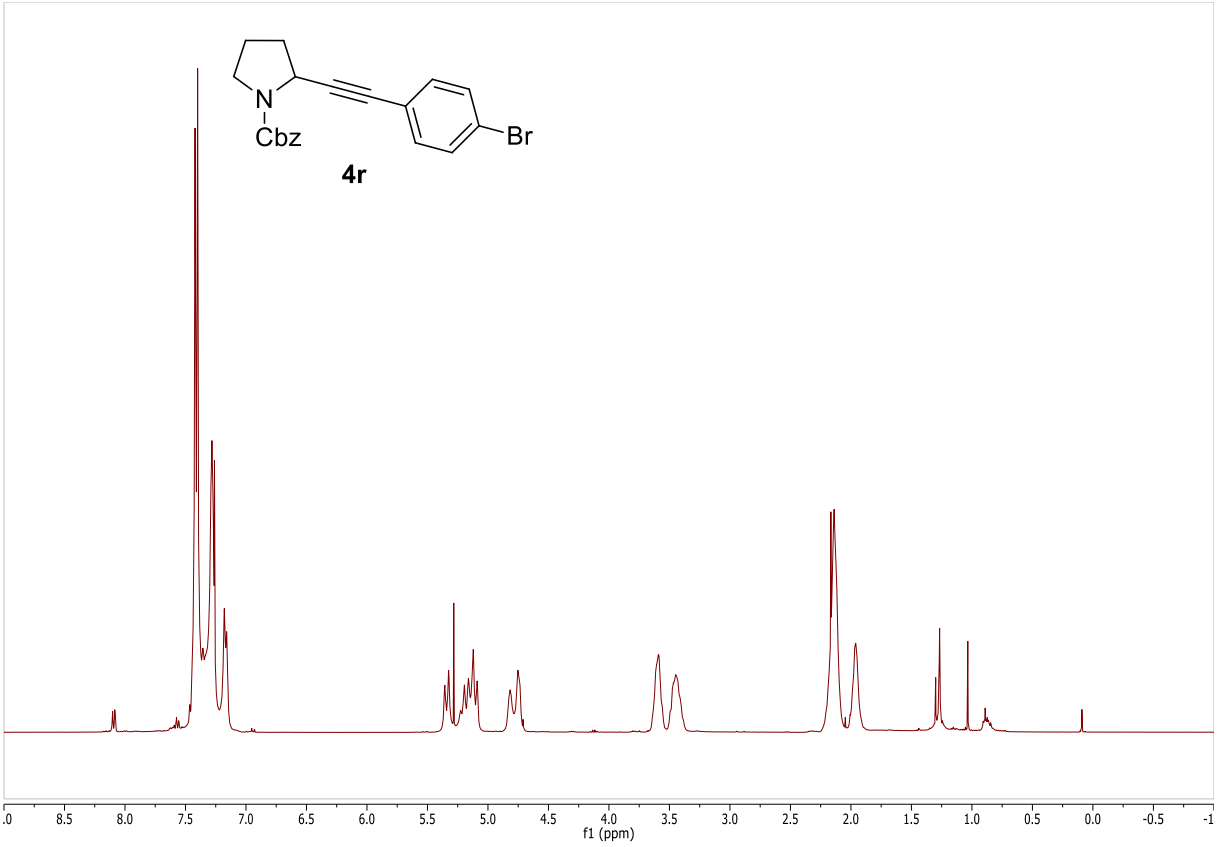

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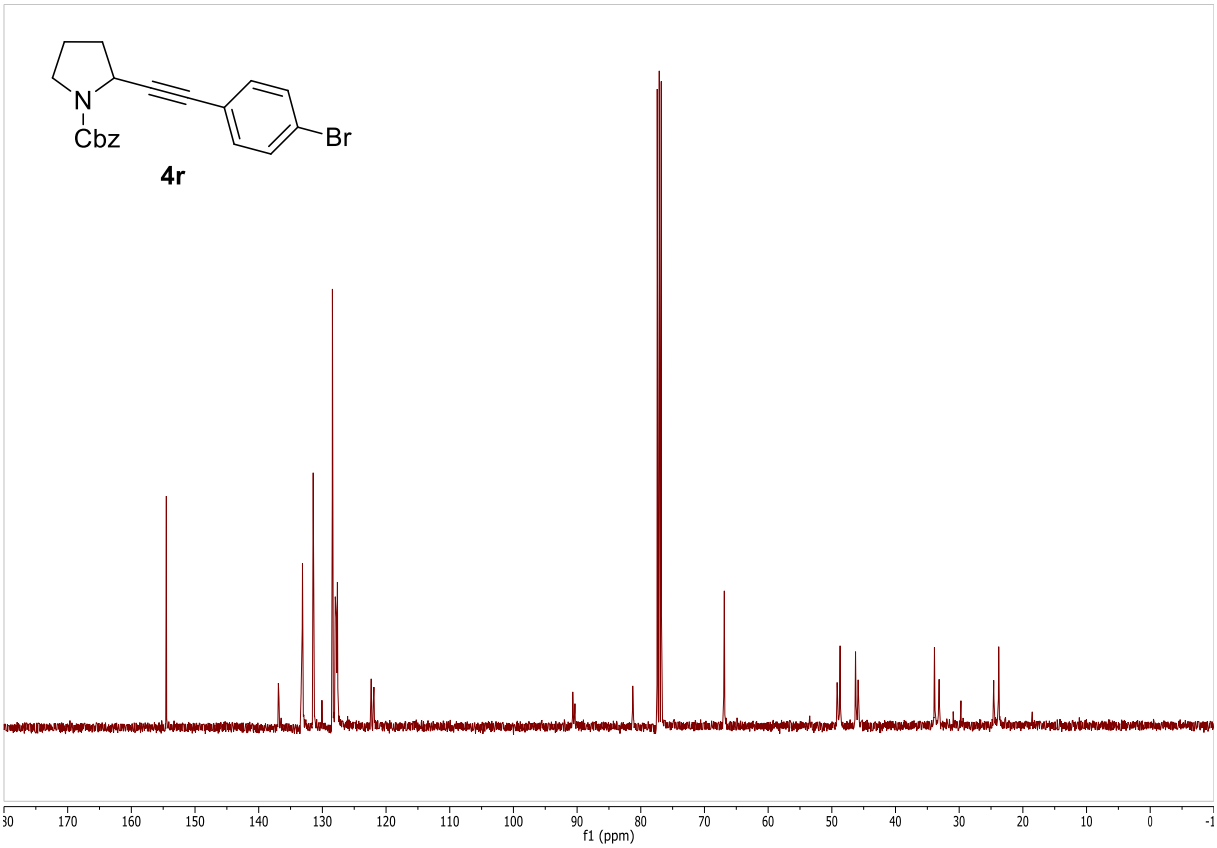
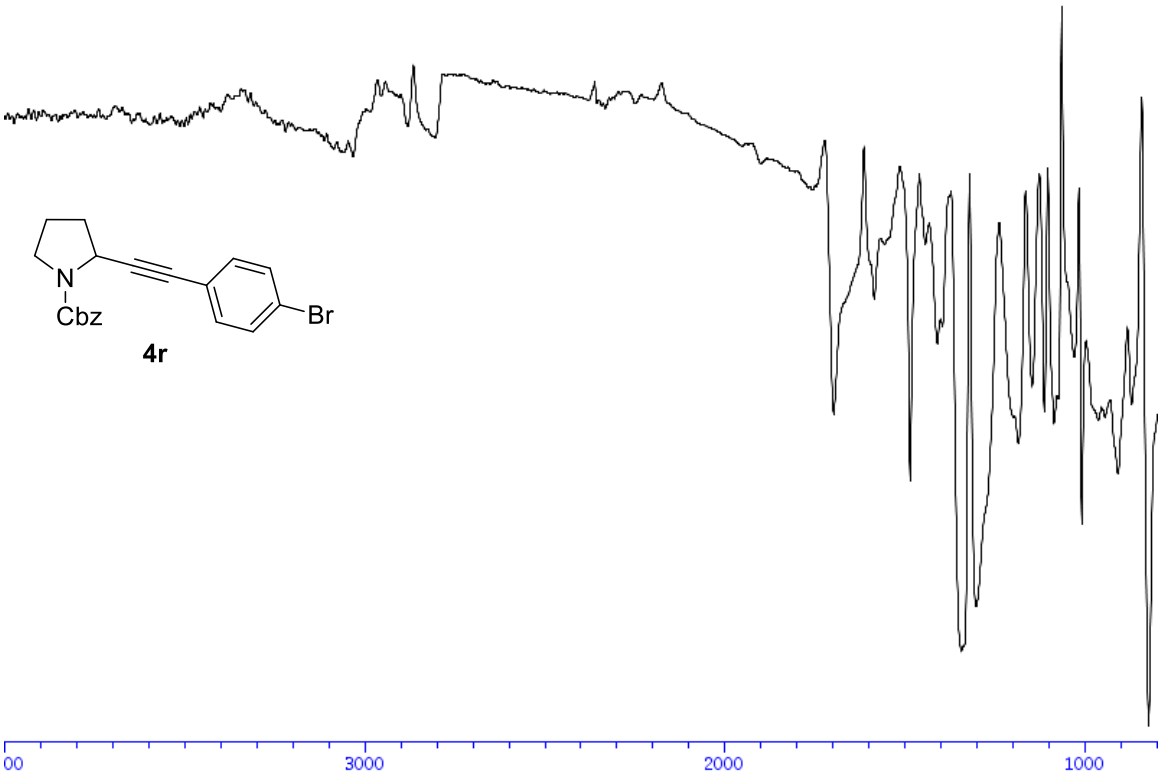


IR Spectra



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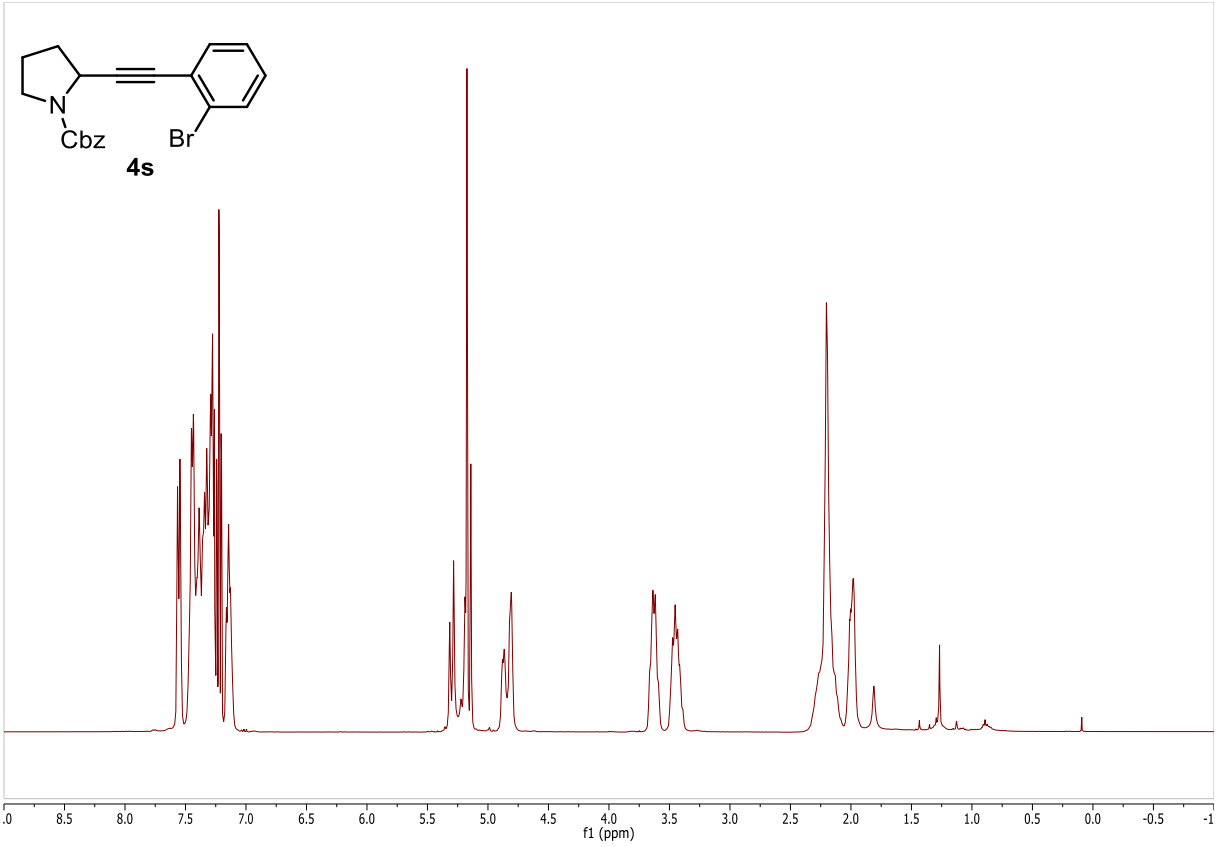

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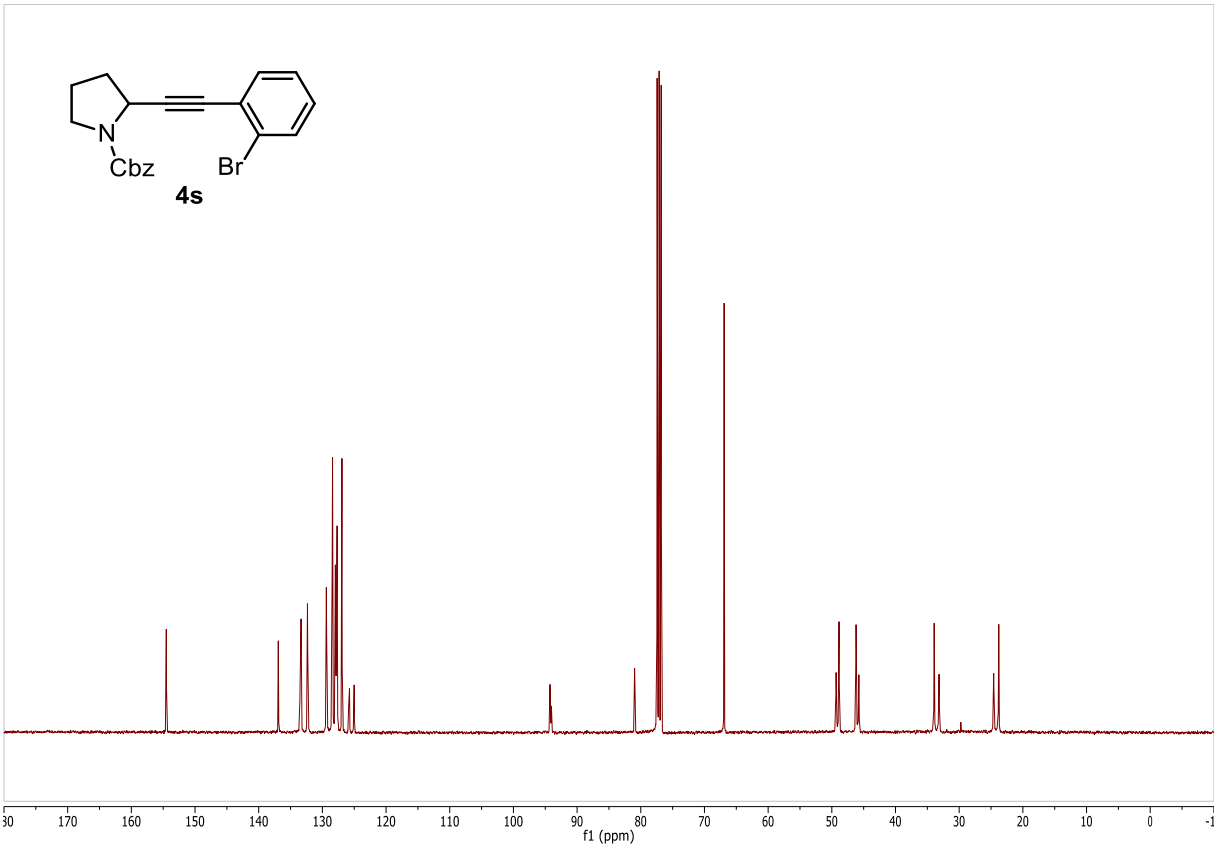
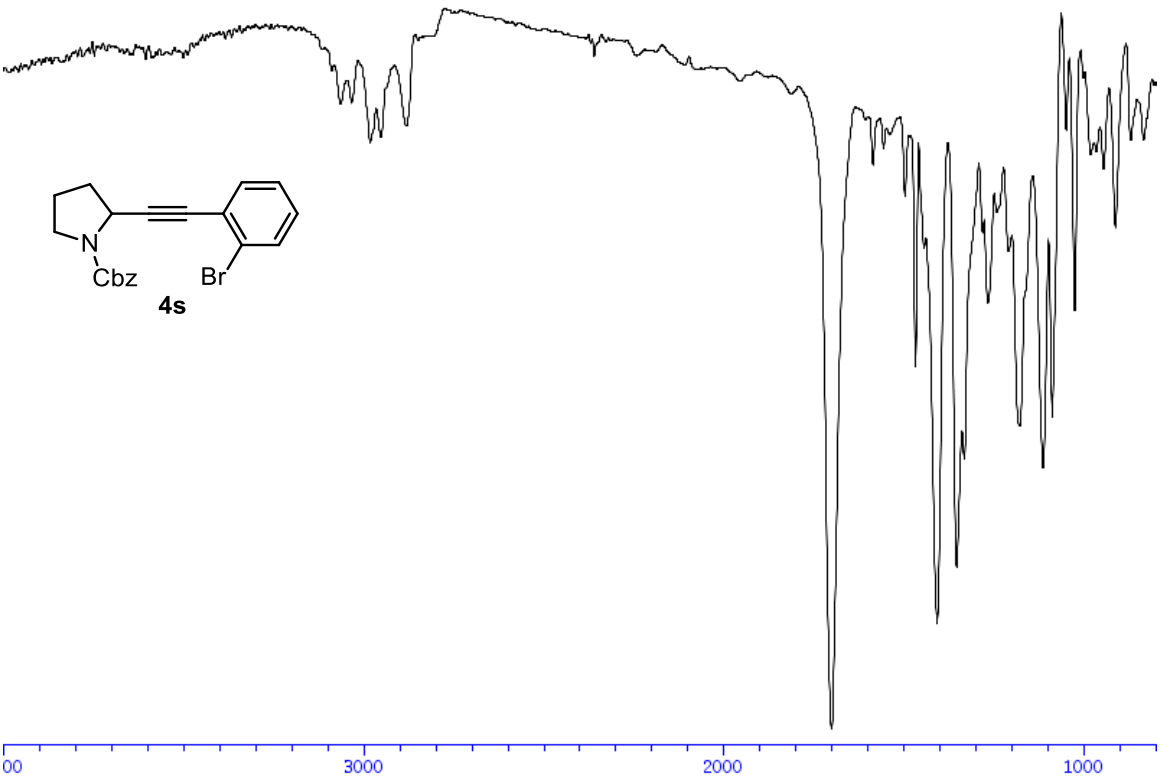
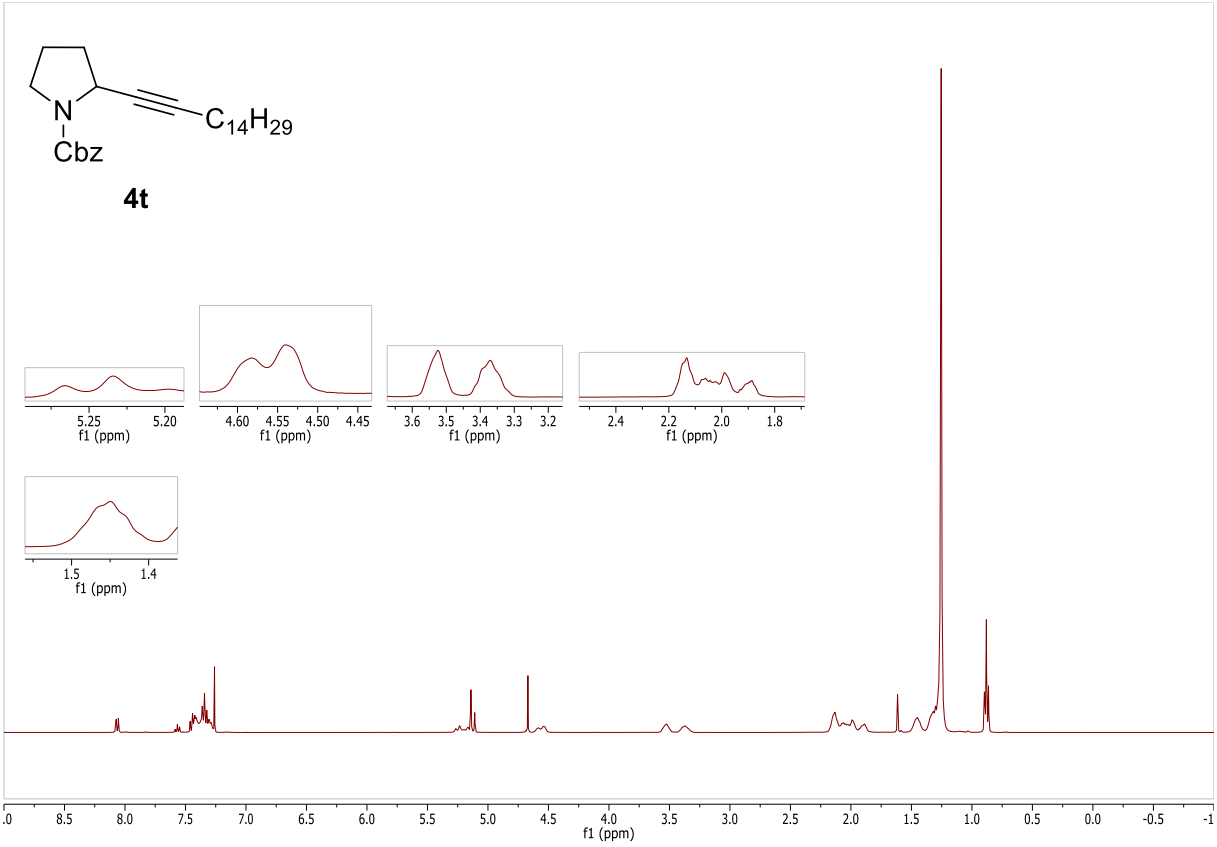


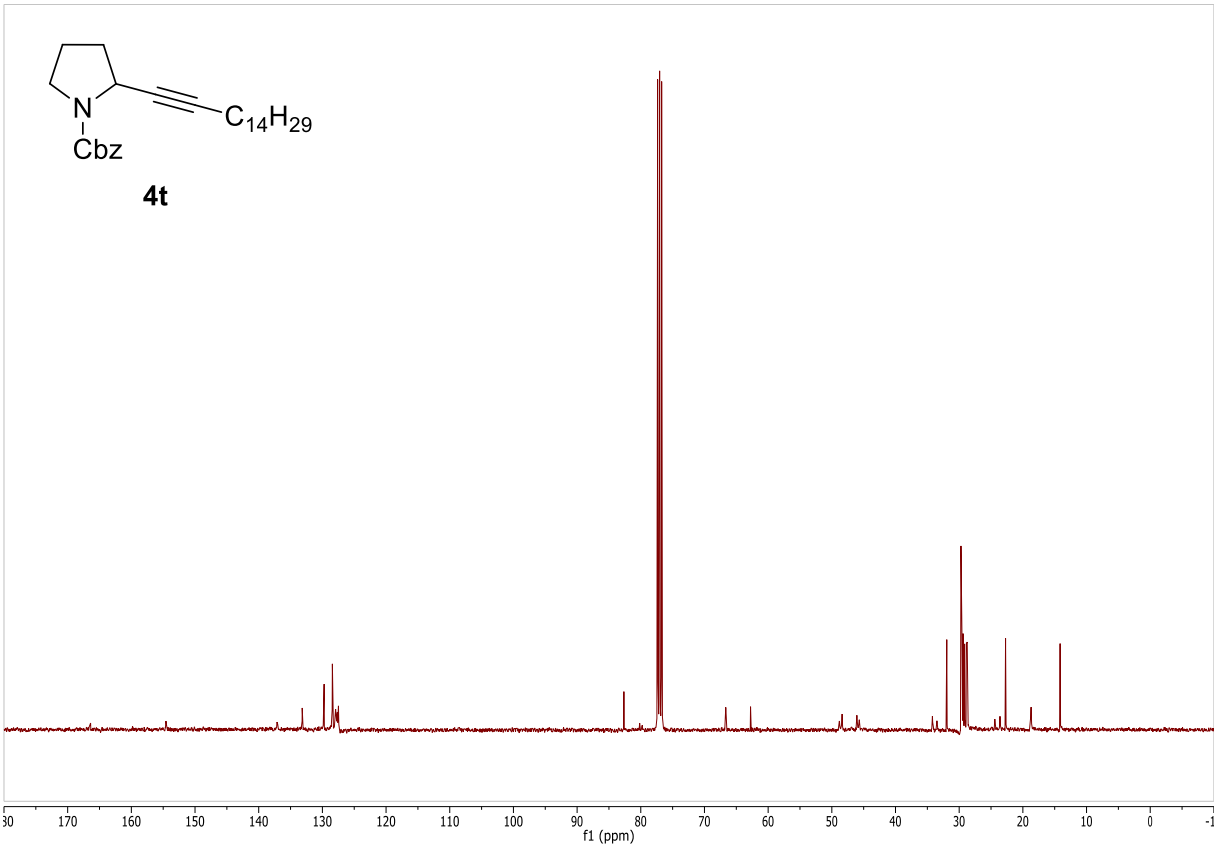
IR Spectra



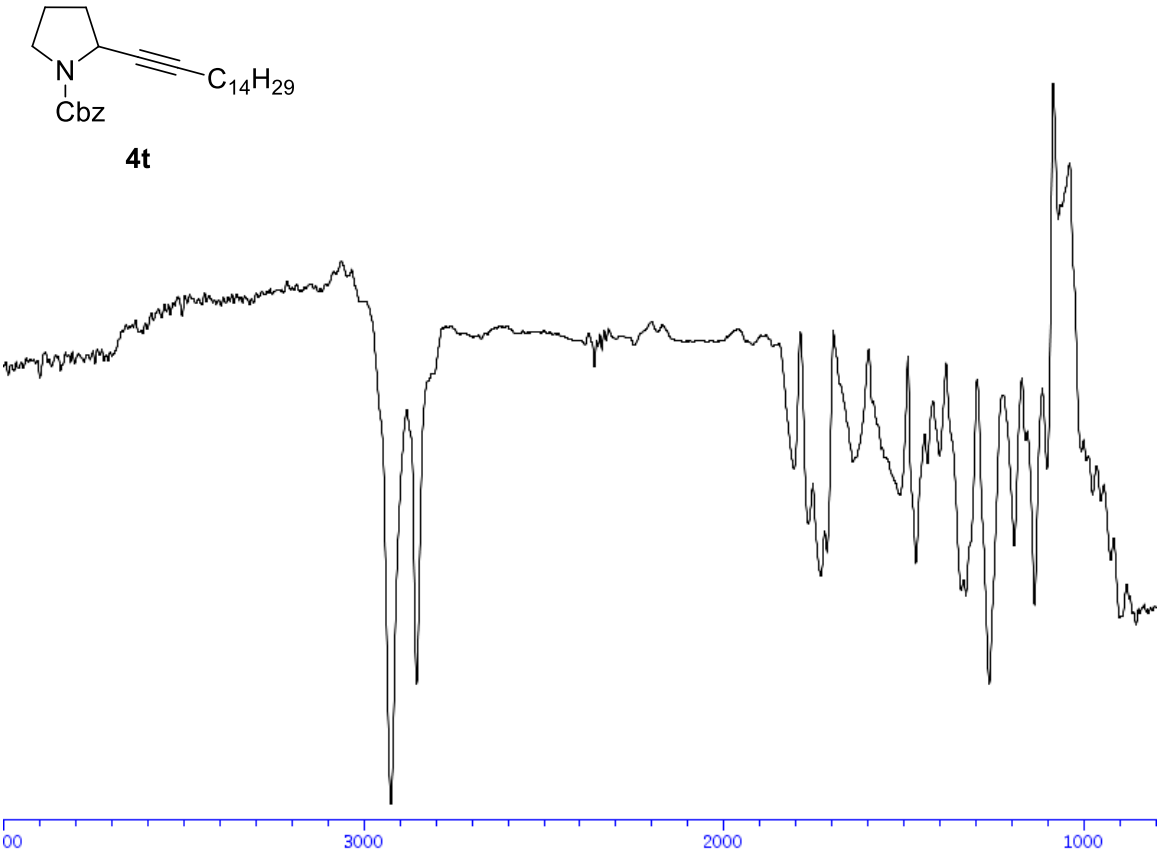
^{1}H-NMR (400 MHz, $CDCl_3$)



^{13}C-NMR (101 MHz, $CDCl_3$)



IR Spectra



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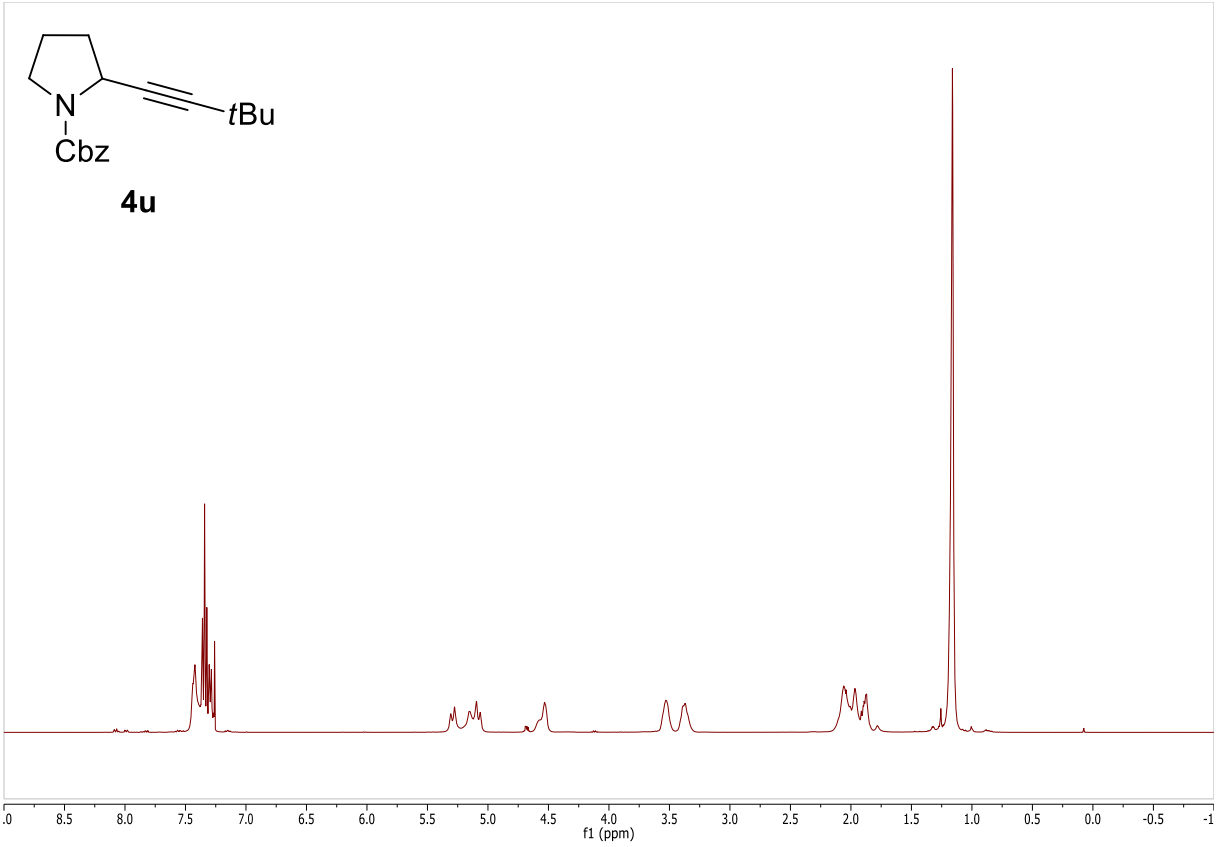

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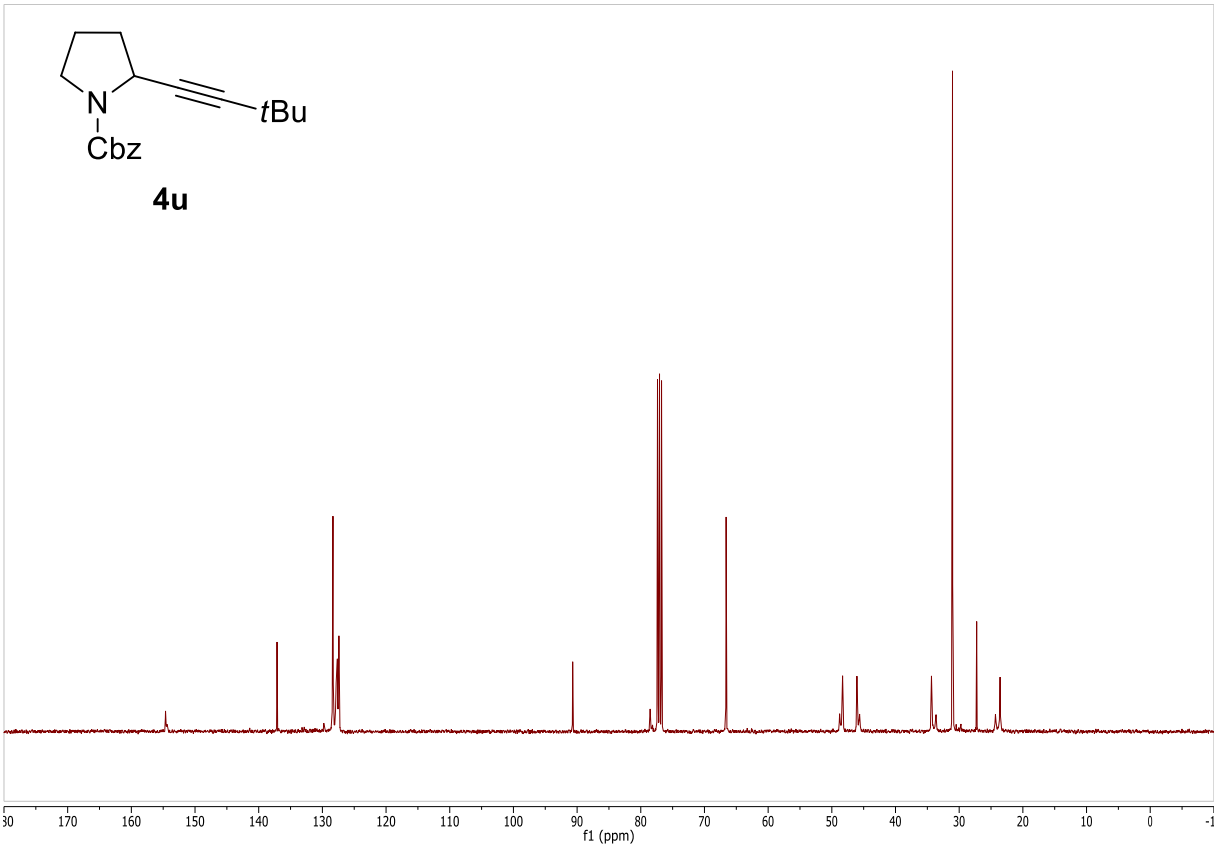

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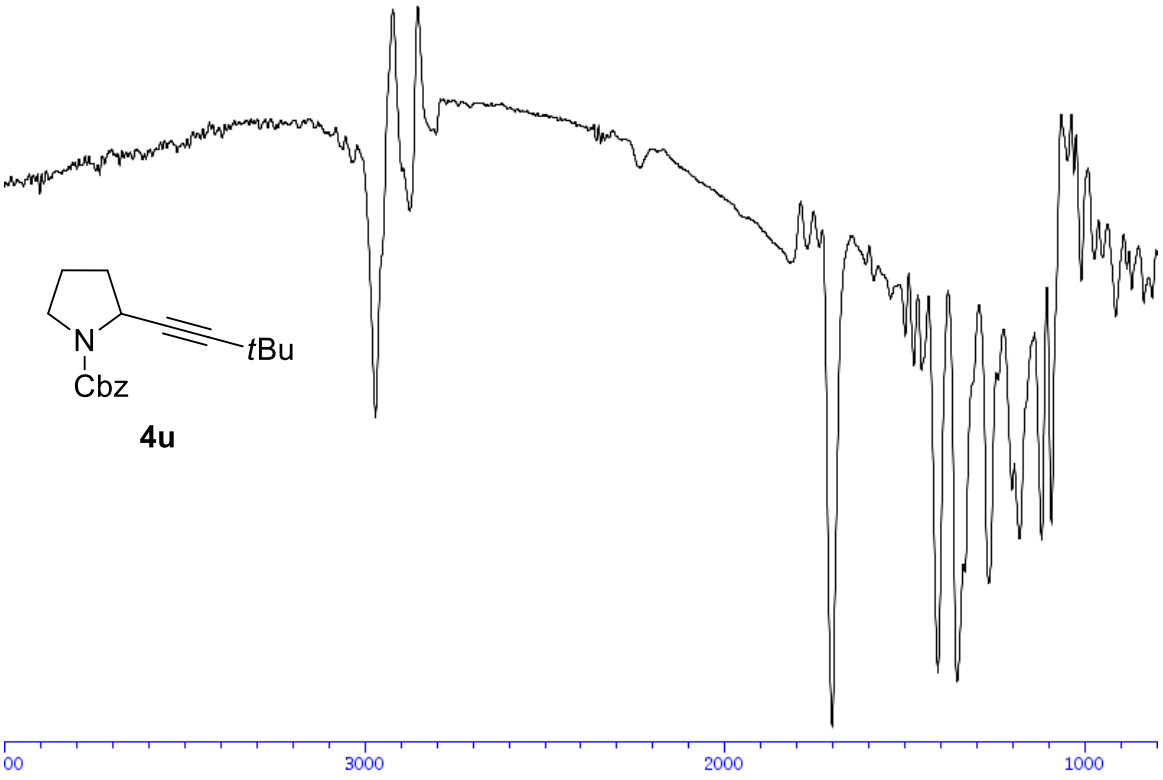

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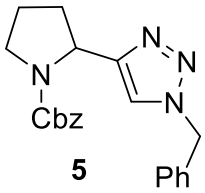

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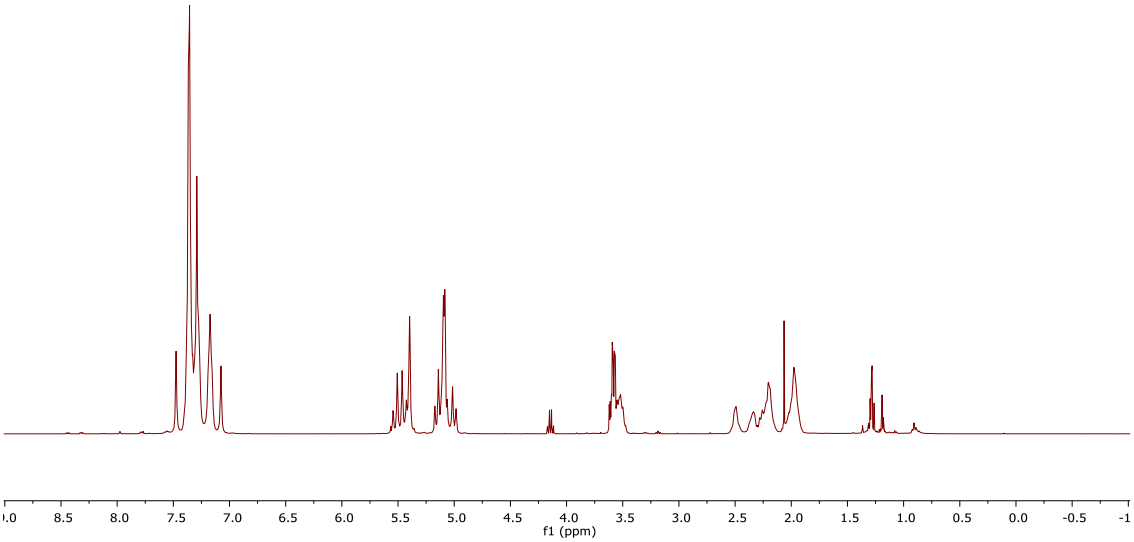

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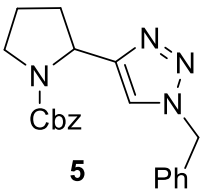

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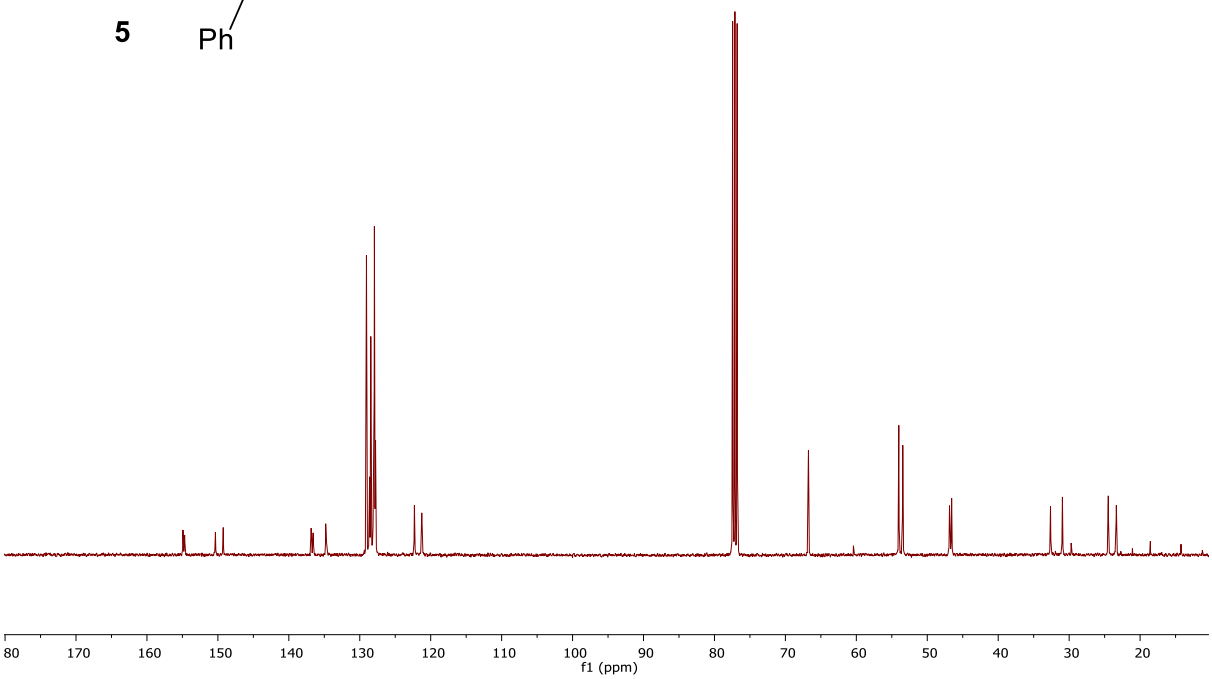

IR Spectra