Pd-Catalyzed Intramolecular Oxyalkynylation of Alkenes with Hypervalent Iodine

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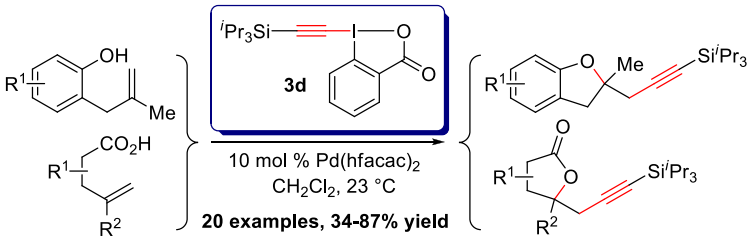
ABSTRACT



The first example of intramolecular oxyalkynylation of non-activated alkenes using oxidative Pd chemistry is reported. Both phenol and aromatic or aliphatic acid derivatives could be used under operator friendly conditions (room temperature, technical solvents, under air). The discovery of the superiority of benziodoxolone-derived hypervalent iodine reagent 3d as alkyne transfer reagent further expands the rapidly increasing utility of hypervalent iodine reagents in catalysis and is expected to have important implications for other similar processes.

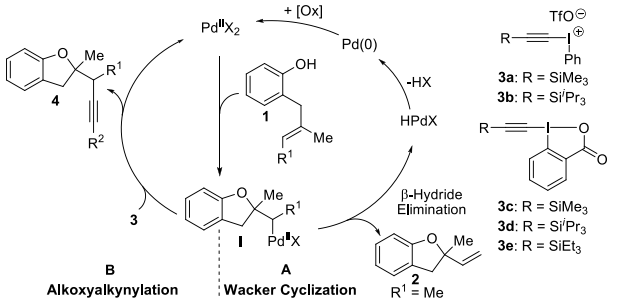
Cyclic structures are ubiquitous in natural products and other bioactive substances.[1] Consequently, the efficient synthesis of carbo- and hetero-cycles is an important field of research in organic chemistry. Metal-catalyzed cyclization reactions, especially when involving multiple C-C or C-X bond formations, constitute an efficient pathway to heterocycles.[2] One such method is the Wacker cyclization, which is the Pd catalyzed cyclization of nucleophiles on double bonds (Scheme 1, **A**).[2c,3] In place of β-hydride elimination, further C-C,[2c,4] C-O,[5] C-N[6] and C-Cl[7] bond formation together with cyclization have been reported.[8]

In particular, C-O and C-N bond formations have profited tremendously from the use of hypervalent iodine reagents as oxidants.[5,6] In contrast, C-C bond formation has been limited to SP^2 hybridized vinyl, carbonyl and aryl groups; none of these methods reported the use of hypervalent iodine reagents.[2c,4] It was recently demonstrated that oxidation of Pd(II) intermediates with aryliodonium salts was much slower than with $PhI(OAc)_2$, which would make C-C bond formation unable to compete with other side reactions.[8b] Herein, we report a Pd-catalyzed Wacker cyclization-alkynylation domino process using a benziodoxolone-derived reagent **3d** (Scheme 1, **B**).

Acetylenes have broad utility in organic chemistry, biological chemistry and material sciences.[9] Furthermore, the direct addition of acetylenes to non-activated olefins is challenging, and has been successful only for strained olefins[10] or using radical methods.[11] The Pd-catalyzed C-C bond formation between a SP^3 and a SP center is also a difficult process, which was successful only in rare cases.[12] Our report constitutes the first example of intramolecular oxyalkynylation of non-activated alkenes, which represents an important breakthrough in the area of oxidative Pd chemistry. The discovery of the unique

superiority of benziodoxolone derived reagents **3c**-**3e** for alkynyl transfer when compared with established alkynyliodonium salts (**3a**, **3b**) constitutes an important advance in the burgeoning field of hypervalent iodine chemistry[13] and opens new perspective for the development of more efficient reagents in Pd-mediated C-C bond formation and other acetylene transfer processes. Indeed, we recently discovered in our group that benziodoxolone derivatives were also unique acetylene-transfer reagents in a completely different process, namely the Au-catalyzed alkynylation of heterocycles.[14]

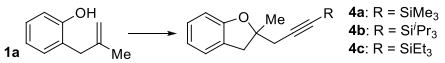
Scheme 1. Wacker Cyclization and Alkoxyalkynylation Reaction



Alkynyliodonium salts are known as oxidative/electrophilic alkynylation reagents,[13c-f] but they have been used only rarely for the metal-mediated introduction of acetylene groups.[15] Preliminary results using Stoltz' conditions[3g] with phenol **1a** and alkynyliodonium salts **3a** were disappointing, leading mostly to acetylene dimerization and low conversion (Table 1, Entry 1). However, using neutral benziodoxolone reagents **3c** and **3d**, which have been largely ignored as acetylene transfer reagents, a 19% yield of the desired product was obtained with **3d** (Entries 2-3).[16] Bases were not required and CH_2Cl_2 was the best solvent (Entry 4).[17] At this point, full conversion was obtained, but a non-identified decomposition pathway consumed the starting material.[18] A catalyst screen (Entries 4-6) identified $Pd(hfacac)_2$[19] as the most efficient Pd source for preventing the decomposition of the substrates (73% yield, Entry 6). To the best of our knowledge, the use of this complex has not been reported yet for oxidative Pd catalysis.

A sterically hindered silyl group is important to obtain good yields, (Entries 6-8), but it is the benziodoxolone structure which is essential for success, as the use of alkynyliodonium salts **3a** or **3b** or simple iodoacetylenes under the optimized conditions were not successful (results not shown). On a 0.40 mmol scale with 10 mol % catalyst, 71% of **4b** was isolated after purification (Entry 9). Using technical grade CH_2Cl_2 in a flask open to air, 73% of product was obtained, demonstrating the tolerance of the reaction to air and moisture (Entry 10). On a 2.4 mmol scale, 68% of product was isolated and 65% of 2-iodobenzoic acid was recovered through basic extraction. This acid can then be recycled to prepare reagent **3d** in 2 steps and 76% overall yield.

Table 1. Optimization of the Alkoxyalkynylation Reaction.



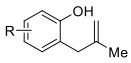
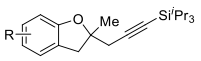
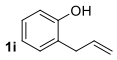
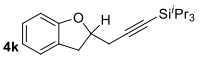
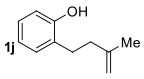
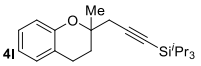
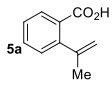
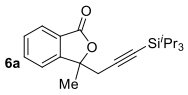
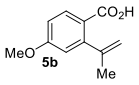
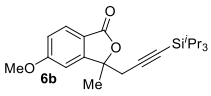
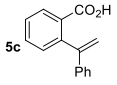
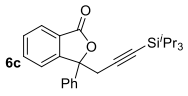
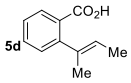
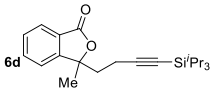
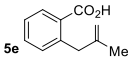
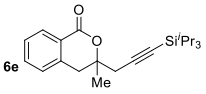
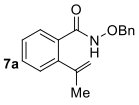
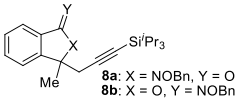
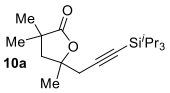
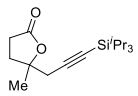
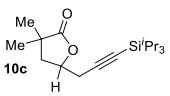
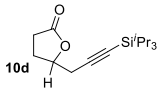
entry	catalyst	reagent	solvent/additive	yield[a]
1	$PdCl_2(CH_3CN)_2$	**3a**	Toluene, base[b]	6% (<20%)
2	$PdCl_2(CH_3CN)_2$	**3c**	Toluene, base[b]	traces (<20%)
3	$Pd(TFA)_2$	**3d**	Toluene, base[b]	19% (73%)
4	$Pd(TFA)_2$	**3d**	CH_2Cl_2	17% (100%)
5	$PdCl_2(CH_3CN)_2$	**3d**	CH_2Cl_2	40% (93%)
6	$Pd(hfacac)_2$	**3d**	CH_2Cl_2	73% (100%)
7	$Pd(hfacac)_2$	**3c**	CH_2Cl_2	20% (84%)
8	$Pd(hfacac)_2$	**3e**	CH_2Cl_2	43%[c] (>90%)
9	$Pd(hfacac)_2$	**3d**	CH_2Cl_2	71%[c]
10	$Pd(hfacac)_2$	**3d**	CH_2Cl_2	73%[c,d]

[a]Reaction conditions: 0.069 mmol **1a**, 0.014 mmol catalyst, 0.083 mmol reagent in 5 mL dry solvent under N_2 at 23 °C for 12-16 h. Yield was determined via GC-MS. Conversion is given in parenthesis. [b]2 equiv K_2CO_3 and 0.20 equiv pyridine were used as base. [c]Isolated yield using 0.40 mmol **1a**, 0.48 mmol **3d** and 0.040 mmol catalyst in 10 mL CH_2Cl_2. [d]As Entry 9, but using technical solvent under air.

The scope of the reaction with phenols was examined next (Table 2, Entries 1-10). A 4-methyl group led to a lower yield (Entry 2) and more electron-rich derivatives could not be used.[20] Apart from this limitation, the reaction displayed good functional group tolerance, including bromo, cyano, nitro and ketone groups (Entries 3-6). The bromo tolerance makes the method orthogonal to Pd(0) chemistry. The reaction was also successful for 5-Br and 6-Br substituted substrates (Entries 7 and 8). Promising preliminary results were obtained for allyl phenol **1i** (Entry 9) and for the formation of 6-membered rings (Entry 10). The former result demonstrates that alkynylation can be efficient even in the presence of a β-hydrogen atom. Although full conversion was observed, no compound was isolated in significant amount beside the desired product and optimization of the reaction conditions was not successful to improve the yield.

As we hypothesized, the limitation of the scope observed with phenols was due to the sensibility of the substrate under oxidative conditions, we thus decided to examine benzoic acid derivatives next (Table 1, Entries 11-15).

Table 2. Scope of the Oxyalkynylation reaction.

entry	substrate	product	isolated yield[a]
			
1	**1a**: R=H	**4b**	71%
2	**1b**: R=4-Me	**4d**	34%
3	**1c**: R=4-Br	**4e**	68%
4	**1d**: R=4-CN	**4f**	76%
5	**1e**: R=4-NO_2	**4g**	72%
6	**1f**: R=4-Ac	**4h**	87%
7	**1g**: R=5-Br	**4i**	66%
8	**1h**: R=6-Br	**4j**	52%
9			43%[b]
10			46%[c]
11			83%
12			80%
13			70%
14			56%
15			80%
16		 **8a**: X = NOBn, Y = O **8b**: X = O, Y = NOBn	69% **8a**:**8b** = 1.5:1
17			70%[d]
18			72%[d]
19			76%[d]
20			82%[d]

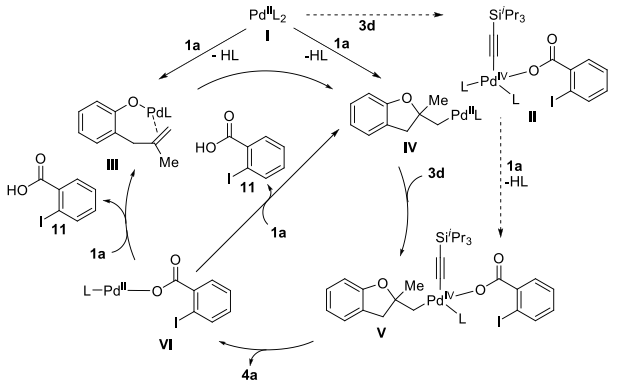
[a]Reaction conditions: 0.40 mmol substrate, 0.48 mmol reagent and 0.040 mmol $Pd(hfacac)_2$ in 10 mL CH_2Cl_2 at 23 °C for 12 h. [b]In 10 mL $CHCl_3$. [c]No full conversion was observed. [d] Reaction time was 3 h.

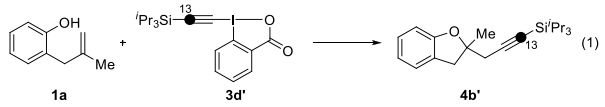
Indeed, excellent results were obtained and an electron-donating group on the benzene ring (Entry 12) or a diaryl olefin (Entry 13) were now tolerated in the reaction. Even a trisubstituted olefin could be used (Entry 14). In this case the 1,3 addition product was obtained, probably via isomerization of the formed Pd-alkyl intermediate. Formation of a 6-membered ring was also possible in 80% yield (Entry 15). A single example of nitrogen nucleophile gave a useful amount of product, but further control of the chemoselectivity will be needed (Entry 16).

Although aliphatic alcohols could not be used (not shown), aliphatic acids worked well in the reaction and full conversion and good yields were obtained after 3 h (Entries 17-20). In this case, the presence of β-hydrogen on the double bond was not deleterious to the yield (Entries 19-20) and even simple commercially available 4-pentenoic acid could be cyclized in good yield (Entry 20). The obtained γ-lactones bearing an acetylene group are important building blocks for the synthesis of bioactive compounds.[21]

As the oxyalkynylation process involves several bond forming steps, understanding the mechanism is challenging. Nucleophilic attack on alkynyliodonium salts proceeds via β-addition followed by 1,2 shift.[13d] However, when a ^{13}C-label was introduced next to Si in **3d**, no shift was observed (eq 1), eliminating the possibility of this pathway. At least two mechanisms could still be envisaged (Scheme 2): (1) oxidative addition of **3d** to Pd^{II} to form a Pd^{IV} intermediate **II**,[22] followed by oxy-palladation to form **V** and reductive elimination to give **4a** or (2) initial oxy-palladation to give **IV**, either via phenolate complex **III** or directly from **1a**; oxidative reaction with **3d** to form **V** and reductive elimination. Currently, we tend to favor the latter, as oxidation to form a Pd^{IV} from Pd^{II}-alkyl intermediate should be easier, electron-deficient catalysts worked best and the intramolecular oxy-palladation of olefins with Pd^{II} catalysts is well-precedented.[3g] Furthermore, a fast reaction was not observed when mixing the reagent and the catalyst.

Scheme 2. Speculative Mechanism.





Finally, we think that the basicity of the 2-iodo benzoate formed in the reaction could be important to promote reaction turnover by accelerating proton transfer from **1a** in the oxy-palladation step (conversion of **VI** to **III** or **IV** in Scheme 2). The generation of a basic carboxylate upon reaction is again specific to the benziodoxolone derivative **3d**, and could further contribute to the exceptional performance of this reagent when compared with more often used alkynyliodonium salts.

In summary, we have reported a novel oxyalkynylation reaction of olefins. Our work represents the first example of acetylene incorporation to olefins using oxidative Pd chemistry. It is operatively simple and was successful both in the case of phenol and acid derivatives. With phenols, good yields were obtained only for substrates with a geminally disubstituted double bond and electron-donating groups on the benzene ring were not tolerated. With acids, the scope was more general, and good yields were obtained, even for the monosubstituted double bond and in the case of aliphatic substrates. The unprecedented use of benziodoxolone-derived hypervalent iodine was essential for success. Further work on the reaction mechanism, an asymmetric method and the use of hypervalent iodine reagents in other catalytic alkynylation reactions is currently ongoing in our group.

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Supporting Information Available Experimental details and characterization data. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) (a) Shirakura, M.; Suginome, M. *J. Am. Chem. Soc.* **2008**, *130*, 5410. (b) Shirakura, M.; Suginome, M. *J. Am. Chem. Soc.* **2009**, *131*, 5060. (c) Kohno, K.; Nakagawa, K.; Yahagi, T.; Choi, J. C.; Yasuda, H.; Sakakura, T. *J. Am. Chem. Soc.* **2009**, *131*, 2784.
(11) (a) Gong, J. C.; Fuchs, P. L. *J. Am. Chem. Soc.* **1996**, *118*, 4486. (b) Schaffner, A. P.; Darmency, V.; Renaud, P. *Angew. Chem., Int. Ed.* **2006**, *45*, 5847.
(12) Altenhoff, G.; Wurtz, S.; Glorius, F. *Tetrahedron Lett.* **2006**, *47*, 2925.
(13) (a) Wirth, T. *Hypervalent iodine chemistry: modern developments in organic synthesis*, Vol. 224, Springer, New York, 2003. (b) Zhdankin, V. V.; Stang, P. J. *Chem. Rev.* **2008**, *108*, 5299. (c) Beringer, F. M.; Galton, S. A. *J. Org. Chem.* **1965**, *30*, 1930. (d) Ochiai, M.; Ito, T.; Takaoka, Y.; Masaki, Y.; Kunishima, M.; Tani, S.; Nagao, Y. *J. Chem. Soc. Chem. Commun.* **1990**, 118. (e) Stang, P. J.; Arif, A. M.; Crittell, C. M. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 287. (f) Zhdankin, V. V.; Stang, P. J. *Tetrahedron* **1998**, *54*, 10927. (g) Ochiai, M.; Masaki, Y.; Shiro, M. *J. Org. Chem.* **1991**, *56*, 5511. (h) Zhdankin, V. V.; Kuehl, C. J.; Krasutsky, A. P.; Bolz, J. T.; Simonsen, A. J. *J. Org. Chem.* **1996**, *61*, 6547.
(14) Brand, J. B.; Charpentier, J.; Waser, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 9346.
(15) (a) Kang, S. K.; Lee, H. W.; Jang, S. B.; Ho, P. S. *J. Org. Chem.* **1996**, *61*, 4720. (b) Huang, X. A.; Zhong, P. *J. Chem. Soc. Perkin Trans. 1* **1999**, 1543. (c) Yu, C. M.; Kweon, J. H.; Ho, P. S.; Kang, S. C.; Lee, G. Y. *Synlett* **2005**, 2631. (d) Canty, A. J.; Rodemann, T.; Skelton, B. W.; White, A. H. *Organometallics* **2006**, *25*, 3996. (e) Canty, A. J.; Gardiner, M. G.; Jones, R. C.; Rodemann, T.; Sharma, M. *J. Am. Chem. Soc.* **2009**, *131*, 7236. (f) Chaudhuri, P. D.; Guo, R.; Malinakova, H. C. *J. Organomet. Chem.* **2008**, *693*, 567.
(16) Previous to our work, the only report of benziodoxolone reagents for C-C bond formation concerned CF_3-transfer: (a) Eisenberger, P.; Gischig, S.; Togni, A. *Chem. Eur. J.* **2006**, *12*, 2579. (b) Kieltsch, I.; Eisenberger, P.; Togni, A. *Angew. Chem., Int. Ed.* **2007**, *46*, 754. (c) Koller, R.; Stanek, K.; Stolz, D.; Aardoom, R.; Niedermann, K.; Togni, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 4332.
(17) See Supporting Information for a complete list of tested reaction conditions and catalysts.
(18) Beside the desired product, no low-molecular weight compound was isolated from the reaction mixture. That would indicate that the main pathway for decomposition is polymerization, either via the alkene, or via the aromatic nucleus, for example through hypervalent iodine mediated oxidation.
(19) hfacac = hexafluoroacetonate.
(20) Excepted when stated otherwise, full conversion was observed for all substrates in table 2. In case of electron-rich substrates, decomposition was observed and no defined low-molecular weight product could be isolated. We speculate that this class of substrates is not compatible with the oxidative conditions of the reaction.
(21) (a) Jones, E. R. H.; Jones, J. B.; Skattebol, L.; Whiting, M. C. *J. Chem. Soc.* **1960**, 3489. (b) Doad, G. J. S.; Barltrop, J. A.; Petty, C. M.; Owen, T. C. *Tetrahedron Lett.* **1989**, *30*, 1597. (c) Braukmuller, S.; Bruckner, R. *Eur. J. Org. Chem.* **2006**, 2110. (d) Habel, A.; Boland, W. *Org. Biomol. Chem.* **2008**, *6*, 1601.
(22) See reference 15d for an example of Pd^{IV}-acetylene complex.

Supporting information

Pd-Catalyzed Intramolecular Oxyalkynylation of Alkenes with Hypervalent Iodine

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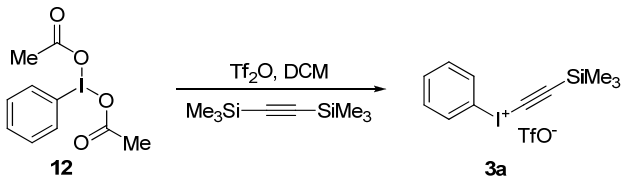
1. General Methods

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et_2O, CH_3CN, toluene, hexane and CH_2Cl_2 were dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 30 ppm, *Karl-Fischer* titration). NEt_3 and pyridine were distilled under nitrogen from KOH. All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Aplichem or Merck and used as such unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F254 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, CD_2Cl_2 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, the internal CD_2Cl_2 signal at 5.31 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, b = broad signal, 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, CD_2Cl_2 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, the internal CD_2Cl_2 signal at 53.5 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, sh = shoulder). Gas chromatographic and low resolution mass spectrometric measurements were performed on a Perkin-Elmer Clarus 600 gas chromatographer and mass spectrometer using a Perkin-Elmer Elite fused silica column (length: 30 m, diameter: 0.32 mm) and Helium as carrier gas. 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. HPLC measurement were done on a JASCO HPLC system with an AS2055 Autosampler, a PU 2089 Pump, a UV 2075 detector and a SEDEX 85 (SEDERE) detector using a CHIRALPAK IC column from DAICEL Chemical Industries Ltd. HPLC grade solvents from Sigma-Aldrich were used.

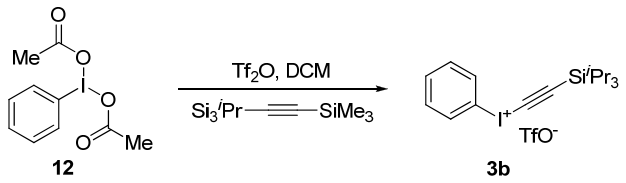
2. Preparation of Reagents

Phenyl(trimethylsilylethynyl)iodonium triflate (3a).



Following a reported procedure,[1] phenyliodonium diacetate (**12**) (3.22 g, 10.0 mmol, 1.00 equiv) was diluted with CH_2Cl_2 (10 mL) and the mixture was stirred for 5 minutes. Tf_2O (0.67 mL, 5.0 mmol, 0.50 equiv.) was added dropwise at 0 °C and the resulting yellow mixture was stirred 30 min. Bis(trimethylsilyl)acetylene (2.28 mL, 10.0 mmol, 1.00 equiv) was added. The mixture was then stirred 2 h and diethyl ether was added to precipitate the product. Filtration afforded **3a** (2.11 g, 4.67 mmol, 47% yield) as a colorless solid. Mp (Dec.) 139-145°C; Lit.: [1] 143-146°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, J = 8.3 Hz, 2 H, ArH), 7.66 (s, 1 H, ArH), 7.55 (m, 2 H, ArH), 0.24 (s, 9 H, TMS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 133.9, 132.4, 132.2, 119.7 (q, J = 319 Hz), 119.1, 116.2, 43.3, -1.1. IR ν 1448 (w), 1286 (m), 1253 (m), 1236 (s), 1222 (s), 1161 (m), 1026 (s), 988 (w), 863 (m), 847 (s), 742 (w), 714 (m), 678 (w), 637 (s). Characterization data of **3a** correspond to the literature values.[1]

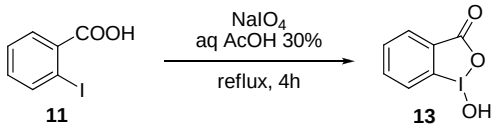
Phenyl(tri*iso*propylsilyl)iodonium triflate (3b)



Following a slight modification of the reported procedure,[1] phenyliodonium diacetate (**12**) (2.53 g, 7.85 mmol, 1.00 equiv) was diluted with CH_2Cl_2 (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 (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 CH_2Cl_2 (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 (**3b**) (2.90 g, 11.2 mmol, 70% yield) as a colorless solid. Mp 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 (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.

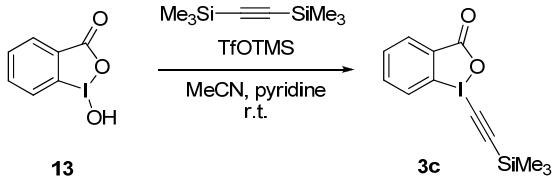
1-Hydroxy-1,2-benziodoxol-3(1*H*)-one (13)

(1) Kitamura, T.; Kotani, M.; Fujiwara, Y. *Synthesis* **1998**, 1416.



Following a reported procedure,[2] $NaIO_4$ (6.7 g, 31 mmol; 1.0 equiv) and 2-iodobenzoic acid (**11**) (7.4 g, 30 mmol, 1.0 equiv) were suspended in 30% (v:v) aq. AcOH (45 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (120 mL) and allowed to cool to room temperature, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 30 mL) and acetone (3 x 30 mL), and air-dried in the dark to give the pure product **13** (7.3 g, 19 mmol, 92% yield) as a colorless solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.02 (dd, *J* = 7.7, 1.4 Hz, 1 H, Ar*H*), 7.97 (m, 1 H, Ar*H*), 7.85 (dd, *J* = 8.2, 0.7 Hz, 1 H, Ar*H*), 7.71 (td, *J* = 7.6, 1.2 Hz, 1 H, 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 characterization data for compounds **13** correspond to the reported values.[2]

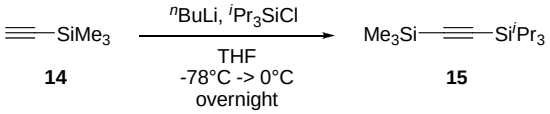
1-[(Trimethylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (3c)



Following a reported procedure,[3] trimethylsiyltriflate (2.8 mL, 15 mmol, 1.4 equiv, freshly distilled) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (**13**) (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 **3c** (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, 1 H, Ar*H*), 8.19 (m, 1 H, Ar*H*), 7.78 (m, 2 H, Ar*H*), 0.32 (s, 9 H, 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 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 **3c** corresponded to the reported values.[3]

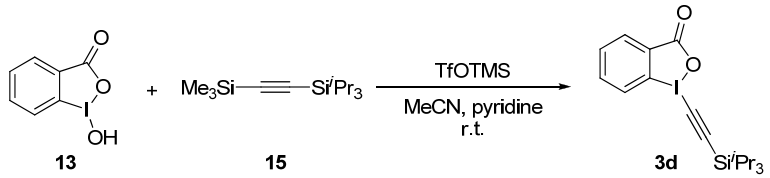
(2) Kraszkiewicz, L.; Skulski, L. *Arkivoc*, **2003**, *6*, 120.
(3) Zhdankin, V. V.; Kuehl, C. J.; Krasutsky, A. P.; Bolz, J. T.; Simonsen, A. J. *J. Org. Chem.* **1996**, *61*, 6547.

Tri*iso*propylsilyl trimethylsilylacetylene (15)



Following a reported procedure,[4] *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 (**14**) (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 distillation (56-57°C/0.25 mmHg) to yield **15** (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 **15** correspond to the literature values.[4]

1-[(Tri*iso*propyllsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (3d)

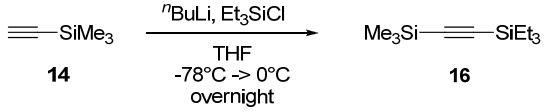


Following a reported procedure,[3] trimethylsilyltriflate (3.6 mL, 20 mmol, 1.1 equiv, freshly distilled) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (**13**) (4.7 g, 18 mmol, 1.0 equiv) in acetonitrile (140 mL). (Trimethylsilyl)(tri*iso*propylsilyl)acetylene (**15**) (5.0 g, 20 mmol, 1.1 equiv) was then added dropwise, followed, after 15 min, by the addition of pyridine (1.5 mL, 20 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 (50 mL). The organic layer was washed with HCl 1 M (50 mL) and the aqueous layer was extracted with CH_2Cl_2 (50 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (2 * 50 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 35 mL) afforded **3d** (6.3 g, 15 mmol, 83%) as a colorless solid. 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

(4) Helal, C J.; Magriotis, P. A.; Corey, E. J. *J. Am. Chem. Soc.* **1996**, *118*, 10938.

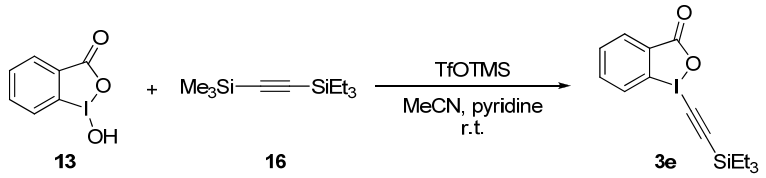
(w), 1349 (m), 1291 (m), 1270 (w), 1244 (m), 1140 (m), 1016 (m), 999 (m), 883 (m), 833 (m), 742 (m), 702 (s), 636 (m). Characterization data of **3d** corresponded to the literature values.[3]

Triethyl trimethylsilylacetylene (16)



Following a reported procedure,[4] *n*-butyllithium (2.5 M in hexanes, 5.4 mL, 14 mmol, 1.0 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (**14**) (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 concentrated under reduced pressure to obtain a colorless liquid which was further purified by Kugelrohr distillation to yield **16** (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).

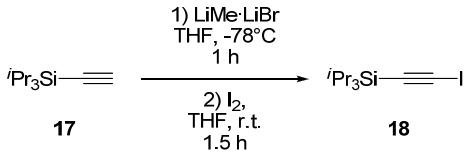
1-[(Triethylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (3e)



Following a reported procedure,[3] trimethylsilyltriflate (1.2 mL, 6.3 mmol, 1.4 equiv, freshly distilled) was added dropwise to a stirred solution of 2-iodosylbenzoic acid (**13**) (1.2 g, 4.5 mmol, 1.0 equiv) in acetonitrile (33 mL) until the mixture turned colorless. The mixture was cooled to 0°C and (Trimethylsilyl)(triethylsilyl)acetylene (**16**) (1.0 g, 4.9 mmol, 1.1 equiv) was then added dropwise. The reaction mixture was stirred at 0°C for 1 h and then allowed to warm to room temperature. After 20 min pyridine (0.50 mL, 6.4 mmol, 1.4 equiv) was added and the mixture was stirred for an additional 30 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 a large amount of water (80 mL), and the aqueous layer was extracted with CH_2Cl_2 (3 x 40 mL). The organic layer was washed with brine (80 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (1.5 mL) afforded **3e** (0.30 g, 0.80 mmol, 17% yield) as a colorless solid. Mp (Dec.) 111 – 130°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, $SiCH_2CH_3$), 0.73 (q, *J* = 8.0 Hz; 6H, $SiCH_2CH_3$). ^{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). HRMS (ESI) calcd for $C_{15}H_{20}IO_2Si^+$ (M+H) 387.0277; found 387.0290.

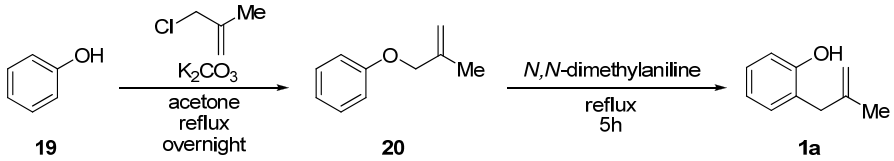
2-Iodo-1-tri*iso*propylsilyl acetylene (18)



Following a reported procedure,[5] 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 (**17**) (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 (**18**) (470 mg, 1.52 mmol, 94% yield) as a colorless oil. ^1H 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). Characterization data of **18** correspond to the literature values.[5]

3. Preparation of Substrates

2-(Methylallyl)phenol (1a)



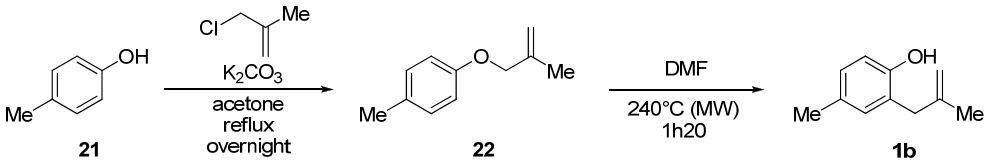
Following a reported procedure,[6] potassium carbonate (3.0 g, 22 mmol, 1.1 equiv) and methyl allyl chloride (2.15 mL, 22.0 mmol, 1.10 equiv) were added to a stirred solution of phenol (**19**) (1.9 g, 20 mmol, 1.0 equiv) in dry acetone (5.0 mL). The mixture was refluxed overnight. Then it was allowed to cool to room temperature and water (25 mL) was added, followed by extraction with ether (3 x 10 mL). The combined organic layers

(5) López, S.; Fernández-Trillo, F.; Midón, P.; Castedo, L.; Saá, L. *J. Org. Chem.*, **2005**, *70*, 6346.
(6) Goering, H. L.; Jacobson, R. R. *J. Am. Chem. Soc.* **1958**, *80*, 3277.

were then washed with 2 M NaOH (3 x 20 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo* to afford 1-(2-methylallyloxy)benzene (**20**) (1.2g, ≤ 8.1 mmol, ≤ 41% yield) which was used without further purification.

1-(2-Methylallyloxy)benzene (**20**) (1.2 g, 8.1 mmol, 1.0 equiv) was dissolved in *N,N*-dimethylaniline (1.0 mL, 8.1 mmol, 1.0 equiv) and the mixture was refluxed 5 h at 205 °C under N_2. It was then cooled to RT and diethyl ether (100 mL) was added and the reaction mixture washed with 1 M HCl (3x50 mL). The aqueous layer was further extracted with diethyl ether (3x50 mL). The organic layer was washed with water and brine. Then it was dried over $MgSO_4$ and concentrated under reduced pressure. The crude product was purified by flash chromatography (SiO_2, PET/EtOAc 30:1-5:1) to yield **1a** (0.357 g, 24.1 mmol, 30% yield) as a yellow oil. R_f 0.36, (PET/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (td, *J* = 7.7, 1.3 Hz, 1 H, Ar*H*), 7.13 (d, *J* = 7.4 Hz, 1 H, Ar*H*), 6.91 (t, *J* = 7.7 Hz, 1 H, Ar*H*), 6.86 (d, *J* = 8.0 Hz, 1 H, ArH), 5.34 (d, *J* = 1.6 Hz, 1 H, OH), 4.95 (s, 1 H, C=*CH*$_2$), 4.87 (s, 1 H, C=*CH*$_2$), 3.41 (s, 2 H, *CH*$_2$), 1.77 (s, 3 H, *CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 144.6, 130.9, 127.9, 124.8, 120.7, 116.0, 112.3, 39.7, 22.1. IR ν 3461 (m), 3072 (w), 3034 (w), 2971 (w), 2915 (w), 1650 (w), 1591 (w), 1489 (m), 1456 (s), 1375 (w), 1337 (w), 1331 (w), 1256 (m), 1227 (m), 1214 (m), 1171 (m), 1094 (m), 1042 (w), 893 (m), 856 (w), 753 (s), 721 (w). Characterization data corresponded to the literature values.[6]

4-Methyl-2(2-methylallyl)phenol (1b)

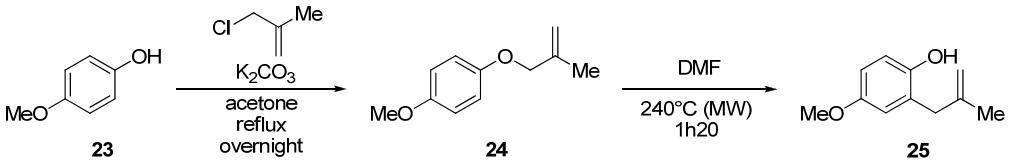


Following a slight modification of the reported procedure,[6] potassium carbonate (3.3 g, 24 mmol, 1.2 equiv) and methyl allyl chloride (2.4 mL, 24 mmol, 1.2 equiv) were added to a stirred solution of *p*-cresol (**21**) (2.2 g, 20 mmol, 1.0 equiv) in dry acetone (5.0 mL). The mixture was stirred under reflux overnight. Then it was allowed to cool to room temperature and water (25 mL) was added, followed by extraction with ether (3 x 10 mL). The combined organic layers were then washed with 2 M NaOH (3 x 20 mL) and dried with $MgSO_4$, filtered and concentrated *in vacuo* to afford 1-methyl-4-(2-methylallyloxy)benzene (**22**) (2.02 g, ≤ 12.5 mmol, ≤ 61% yield) which was used without further purification.

1-Methyl-4-(2-methylallyloxy)benzene (**22**) (0.80 g, 4.9 mmol) was dissolved in DMF (4.0 mL) and the mixture was stirred under N_2 at 240°C under microwave irradiation for 1h20. DMF was evaporated *in vacuo*. The resulting crude product was purified by chromatography (SiO_2, PET/EtOAc 30:1-15:1) to yield **1b** (404 mg, 2.49 mmol, 51% yield) as a yellow oil. R_f 0.63 (PET/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.94 (dd, *J* = 8.1, 1.7 Hz, 1 H, Ar*H*), 6.90 (m, 1 H, Ar*H*), 6.73 (d, *J* = 8.1 Hz, 1 H, Ar*H*), 4.98 (s, 1 H, OH), 4.92 (s, 1 H, C=*CH*$_2$), 4.85 (s, 1 H, C=*CH*$_2$), 3.34 (s, 2 H, *CH*$_2$), 2.27 (s, 3 H, Ph*CH*$_3$), 1.75 (s, 3 H, *CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.2, 144.7, 131.4, 129.8, 128.3, 124.6, 115.8, 112.1, 39.7, 22.1, 20.4. IR ν 3427 (broad, m),

3173 (w), 3075 (w), 3015 (m), 2971 (m), 2918 (m), 2863 (m), 1650 (w), 1614 (w), 1504 (s), 1442 (m), 1375 (m), 1337 (m), 1260 (s), 1229 (s), 1196 (s), 1150 (m), 1105 (s), 1040 (w), 1021 (w), 933 (sh), 890 (s), 812 (s), 782 (w), 748 (w), 716 (w), 696 (w), 695 (w), 683 (w), 664 (w), 652 (w), 634 (w), 620 (w). Characterization data corresponded to the literature values.[7]

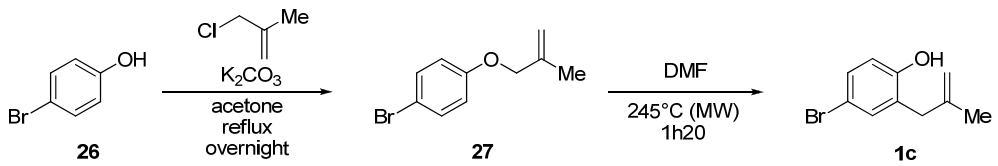
4-Methoxy-2(2-methylallyl)phenol (25)



Following a slight modification of the reported procedure,[6] potassium carbonate (2.9 g, 21 mmol, 1.3 equiv) and methyl allyl chloride (2.0 mL, 21 mmol, 1.3 equiv) were added to a stirred solution of *p*-methoxy phenol (**23**) (2.0 g, 16 mmol, 1.0 equiv) in dry acetone (4.0 mL). The mixture was stirred under reflux overnight. Then it was allowed to cool to room temperature and water (25 mL) was added, followed by extraction with ether (3 x 10 mL). The combined organic layers were then washed with 2 M NaOH (3 x 20 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo* to afford 1-methyl-4-(2-methylallyloxy)benzene (**24**) (2.01 g, ≤ 11.3 mmol, ≤ 70% yield), which was used without further purification.

1-Methyl-4-(2-methylallyloxy)benzene (**24**) (0.85 g, 4.8 mmol) was dissolved in DMF (3.8 mL) and the mixture was stirred under N_2 at 240°C under microwave irradiation for 1h20. DMF was evaporated *in vacuo*. The resulting crude product was purified by chromatography (SiO_2, PET/EtOAc 30:1-15:1) to yield **25** (684 mg, 3.84 mmol, 80% yield) as a yellow oil. R_f 0.23 (PET/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.77 (m, 1 H, Ar*H*), 6.72 – 6.65 (m, 2 H, Ar*H*), 4.92 (bs, 1 H, OH), 4.87 – 4.82 (m, 2 H, C=*CH*$_2$), 3.75 (s, 3 H, O*CH*$_3$), 3.34 (s, 2 H, *CH*$_2$), 1.75 (s, 3 H, *CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 148.6, 144.5, 126.5, 116.6, 116.5, 112.7, 112.2, 55.8, 39.5, 22.2. IR ν 3436 (sh), 3436 (m), 3384 (sh), 3076 (w), 3033 (w), 2971 (w), 2938 (w), 2911 (w), 2911 (w), 2835 (w), 1650 (w), 1611 (w), 1502 (s), 1432 (s), 1374 (m), 1344 (m), 1343 (w), 1274 (w), 1254 (s), 1205 (sh), 1182 (s), 1152 (w), 1106 (m), 1042 (s), 892 (m), 806 (m), 739 (s), 714 (sh), 666 (w), 633 (w), 609 (w). Characterization data corresponded to the literature values.[8]

4-Bromo-2-(2-methylallyl)phenol (1c)

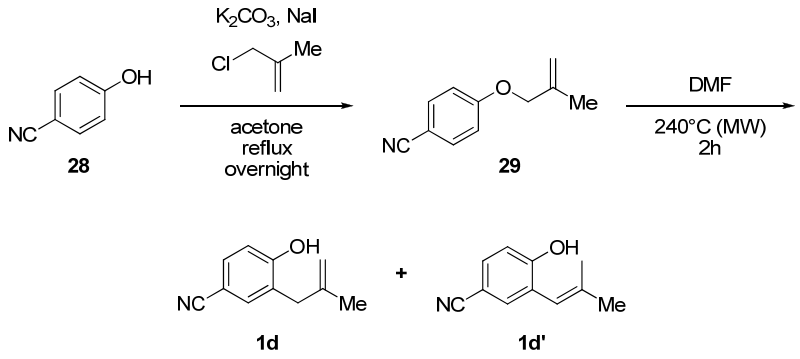


(7) Summermatter, W.; Heimgartner, H. *Helvetica Chimica Acta* **1984**, *67*, 1298.
(8) Mali, R. S.; Garkhedkar, M. P.; Sindkhedkar, M. D.; Dhavale, D. D. *J. Chem. Res., Synopses* **1996**, *7*, 342.

Following a slight modification of the reported procedure,[6] potassium carbonate (2.4 g, 17 mmol, 1.2 equiv) and methyl allyl chloride (1.7 mL, 17 mmol, 1.2 equiv) were added to a stirred solution of 4-bromo phenol (**26**) (2.5 g, 14 mmol, 1.0 equiv) in dry acetone (5.0 mL). The mixture was stirred under reflux overnight. Then it was allowed to cool to room temperature and water (25 mL) was added, followed by extraction with ether (3 x 10 mL). The combined organic layers were then washed with 2 M NaOH (3 x 20 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo* to afford 1-bromo-4-(2-methylallyloxy)benzene (**27**) (2.84 g, ≤ 12.5 mmol, ≤ 87% yield) which was used without further purification.

1-Methyl-4-(2-methylallyloxy)benzene (**27**) (1.1 g, 4.8 mmol) was dissolved in DMF (4.0 mL) and the mixture was stirred under N_2 at 245 °C under microwave irradiation for 1h20. DMF was evaporated *in vacuo*. The resulting crude product was purified by chromatography (SiO_2, PET/EtOAc 20:1-15:1) to yield **1c** (0.86 g, 3.8 mmol, 80% yield) as a yellow oil. R_f = 0.43, (PET/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 – 7.21 (m, 2 H, Ar*H*), 6.74 (d, *J* = 8.2 Hz, 1 H, Ar*H*), 5.22 (m, 1 H, OH), 4.97 (s, 1 H, C=*CH*$_2$), 4.89 (m, 1 H, C=*CH*$_2$), 3.36 (s, 2 H, *CH*$_2$), 1.76 (s, 3 H, *CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.7, 143.9, 133.4, 130.7, 127.4, 117.8, 113.0, 112.6, 39.4, 22.1; IR ν 3450 (broad), 3071 (w), 2972 (w), 2914 (w), 2851 (w), 1650 (m), 1603 (w),1584 (w), 1480 (s), 1420 (m),1411(s), 1376 (m), 1323 (m), 1266 (s), 1211 (s), 1168 (s), 1107 (s), 1020 (w), 891 (s), 809 (s), 779 (w), 672 (m). HRMS (ESI)[9] expected for $C_{10}H_{11}{}^{79}BrO^{107}Ag^+$ (M+^{107}Ag) 332.9035; found 332.8976.

4-Hydoxy-3-(2-methylallyl)benzonitrile (1d)



Following a slight modification of the reported procedure,[10] potassium carbonate (1.5 g, 11 mmol, 1.3 equiv), methyl allyl chloride (1.3 mL, 13 mmol, 1.5 equiv) and NaI (tip of a spatula) were added to a stirred solution of 4-hydroxy benzonitrile (**28**) (1.0 g, 8.5 mmol, 1.0 equiv) in dry acetone (5.2 mL). The mixture was stirred under reflux overnight. Then it was allowed to cool to room temperature and water (25 mL) was added, followed by extraction with ether (3 x 10 mL). The combined organic layers were then washed with 2 M NaOH

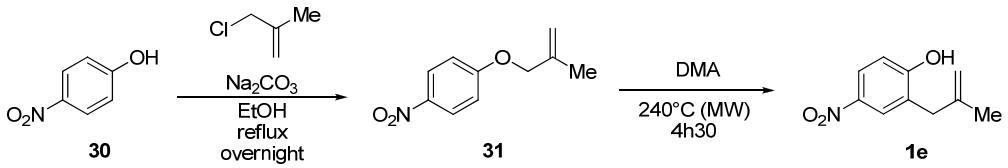
(9) ESI mass spectrum of compound **1c** was acquired after treatment of **1c** with $AgNO_3$, as a consequence of troublesome ionization of the pure compound.

(10) Stanetty, P.; Koller, H.; Pürstinger, G. *Monatsh. Chem.* **1990**, *121*, 883.

(3 x 20 mL). It was dried with $MgSO_4$, filtered and concentrated *in vacuo* to afford 4-(2-methylallyloxy)benzonitrile (**29**) (1.4 g, ≤ 8.1 mmol, ≤ 95% yield) which was used without further purification.

4-(2-Methylallyloxy)benzonitrile (**29**) (0.52 g, 3.0 mmol) was dissolved in DMF (2.4 mL) and the mixture was stirred under N_2 at 240 °C under microwave irradiation for 2 h. DMF was evaporated *in vacuo*. The resulting crude product was purified by chromatography (SiO_2, PET/EtOAc 20:1-5:1) to yield a yellowish solid (237 mg; mixture of inseparable isomers **1d**, **1d'**. Based on ^{1}H NMR, **1d** was the most abundant isomer, the ratio being 4.5:1; **1d**: 194 mg, 1.12 mmol, 37% yield. The mixture was used in the following reaction without separation, assuming **1d'** as a non reactive isomer). R_f = 0.33, (PET/EtOAc 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (dd, *J* = 2.0, 8.0 Hz, 1 H, Ar*H*), 7.42 (d, *J* = 2.0 Hz, 1 H, Ar*H*), *7.36 (d, J = 2.0 Hz)*, *6.96 (d, J = 8.5 Hz)*, 6.89 (d, *J* = 8.5 Hz, 1 H, Ar*H*), *6.05 (bs,1 H, OH or CH=C(CH$_3$)$_2$)*, 5.99 (s, 1 H, OH), *5.66 (s, 1 H, OH or CH=C(CH$_3$)$_2$)*, 4.98 (s, 1 H, C=*CH$_2$*), 4.86 (s, 1 H, C=*CH$_2$*), 3.38 (s, 2 H, *CH$_2$*), *1.97 (d, J = 1.5 Hz, 3 H, CH$_3$)*, 1.73 (s, 3 H, *CH$_3$*), *1.70-1.66 (m, 3 H, CH$_3$)*.[11]

2-(2-Methylallyl)-4-nitrophenol (1e)



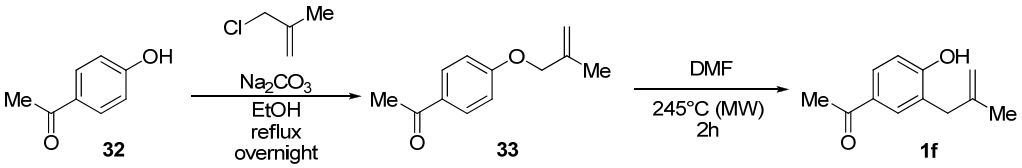
Following a slight modification of the reported procedure,[12] sodium carbonate (1.10 g, 10.3 mmol, 1.30 equiv) and methyl allyl chloride (1.0 mL, 10 mmol, 1.3 equiv) were added to a stirred solution of 4-nitro phenol (**30**) (1.1 g, 7.9 mmol, 1.0 equiv) in dry ethanol (3.0 mL). The mixture was stirred under reflux overnight. Then it was allowed to cool to room temperature and water (25 mL) was added, followed by extraction with ether (3 x 10 mL). The combined organic layers were then washed with 2 M NaOH (3 x 20 mL). It was dried with $MgSO_4$, filtered and concentrated *in vacuo* to afford 1-(2-methylallyloxy)-4-nitrobenzene (**31**) (1.29 g, ≤ 6.67 mmol, ≤ 84% yield) which was used without further purification.

1-(2-Methylallyloxy)-4-nitrobenzene (**31**) (500 mg, 2.58 mmol) was dissolved in DMA (2.3 mL) and the mixture was stirred under N_2 at 240 °C under microwave irradiation for 4h30. DMA was evaporated *in vacuo*. The resulting crude product was purified by chromatography (SiO_2, PET/EtOAc 9:1-7:3) to yield **1e** (179 mg, 0.926 mmol, 35% yield) as a brown solid. R_f = 0.23, (PET/EtOAc 10:1). Mp 56-58 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 – 8.03 (m, 2 H, Ar*H*), 6.91 (d, *J* = 9.0 Hz, 1 H, Ar*H*), 6.23 (s, 1 H, OH), 5.00 (s, 1 H, C=*CH$_2$*), 4.90 (s, 1 H, C=*CH$_2$*), 3.44 (s, 2 H, *CH$_2$*), 1.75 (s, 3 H, *CH$_3$*). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6, 143.2, 141.5, 126.9, 125.8, 124.5, 116.2, 113.8, 39.5, 22.1. IR ν 3389 (broad), 2941 (m), 2865 (m), 2175 (w), 1738 (m), 1650 (w), 1589 (m), 1523 (m), 1497 (m), 1451 (m), 1380 (w), 1338 (s), 1284 (s), 1237 (m), 1163 (w), 1129

(11) ^{1}H-NMR values for **1d'** are reported in italics. For signals at □ 6.05 and 5.99 the assigned proton is underlined.
(12) Buu-Hoi, N. P. ; Jacquignon, P. ; Dufour, M. *Bull. Soc. Chim. Fr.* **1964**, 23.

(w), 1081 (m), 1040 (w), 996 (w), 906 (m), 886 (m), 832 (m), 758 (m), 685 (m); 676 (m). HRMS (ESI)[13] calcd for $C_{10}H_{11}NO_3Ag^+$ (M+^{107}Ag, M+^{109}Ag) 299.9796, 301.9779; found 299.9731, 301.9746.

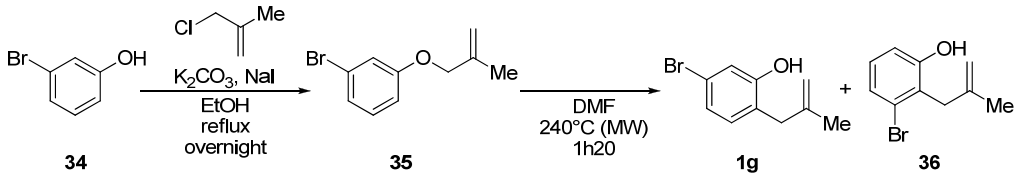
1-(4-Hydroxy-3-(2-methylallyl)phenyl)ethanone (1f)



Following a slight modification of the reported procedure,[12] sodium carbonate (1.0 g, 9.7 mmol, 1.2 equiv) and methyl allyl chloride (1.0 mL, 9.7 mmol, 1.2 equiv) were added to a stirred solution of 4-hydroxybenzophenone (**32**) (1.1 g, 8.0 mmol, 1.0 equiv) in ethanol (2.0 mL). The mixture was refluxed overnight. Then it was allowed to cool to room temperature and water (25 mL) was added, followed by extraction with ether (3 x 10 mL). The combined organic layers were then washed with 2 M NaOH (3 x 20 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo* to afford 1-(4-(2-methylallyloxy)phenyl)ethanone (**33**) (1.03 g, ≤ 5.40 mmol, ≤ 66% yield) which was used without further purification.

1-(4-(2-Methylallyloxy)phenyl)ethanone (**33**) (500 mg, 2.63 mmol) was dissolved in DMF (2.3 mL) and the mixture was stirred under N_2 at 245 °C under microwave irradiation for 2 h. DMF was evaporated *in vacuo*. The resulting crude product was purified by chromatography (SiO_2, PET/EtOAc 9:1-7:3) to yield **1f** (324 mg, 1.70 mmol, 64% yield) as a pale yellow oil. R_f = 0.28, (PET/EtOAc 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 – 7.76 (m, 2 H, Ar*H*), 6.87 (d, *J* = 8.2 Hz, 1 H, Ar*H*), 5.75 (s, 1 H, OH), 4.97 (s, 1 H, C=*CH*$_2$), 4.89 (s, 1 H, C=*CH*$_2$), 3.43 (s, 2 H, *CH*$_2$), 2.55 (s, 3 H, CO*CH*$_3$), 1.75 (s, 3 H, C=C*CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5, 160.0, 144.1, 132.0, 129.7, 129.4, 125.7, 115.7, 112.5, 38.9, 26.3, 22.3. IR ν 3225 (broad, w), 2942 (m), 2864 (m), 2361 (w), 2176 (m), 1676 (s), 1590 (s), 1523 (m), 1489 (m), 1463 (m), 1437 (m), 1380 (w), 1357 (s), 1326 (w), 1266 (s), 1245 (s), 1171 (w), 1112 (w), 1075 (m), 1057 (m), 1034 (m), 996 (w), 958 (w), 911 (m), 883 (s), 817 (m), 787 (w), 729 (w), 676 (s). HRMS (ESI) calcd for $C_{12}H_{15}O_2$ (M+H) 191.1072; found 191.1075.

5-Bromo-2-(2-methylallyl)phenol (1g)



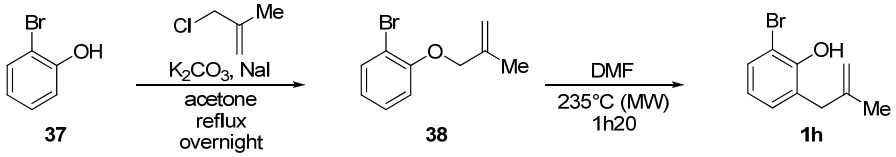
Following a slight modification of the reported procedure,[10] potassium carbonate (1.45 g, 10.5 mmol, 1.3 equiv), methyl allyl chloride (1.2 mL, 12 mmol, 1.5 equiv) and NaI (tip of a spatula) were added to a stirred solution of 3-bromo phenol (**34**) (1.4 g, 8.1 mmol, 1.0 equiv) in dry ethanol (4.5 mL). The mixture was stirred

(13) ESI mass spectrum of compound **1e** was acquired after treatment of **1e** with $AgNO_3$, as a consequence of troublesome ionization of the pure compound.

under reflux overnight. Then it was allowed to cool to room temperature and water (25 mL) was added, followed by extraction with ether (3 x 10 mL). The combined organic layers were then washed with 2 M NaOH (3 x 20 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo* to afford 1-bromo-3-(2-methylallyloxy)benzene (**35**) (1.3 g, ≤ 7.3 mmol, ≤ 90% yield) which was used without further purification.

1-Bromo-3-(2-methylallyloxy)benzene (**35**) (0.68 g, 3.0 mmol) was dissolved in DMF (2.4 mL) and the mixture was stirred under N_2 at 240 °C under microwave irradiation for 1h20. DMF was evaporated *in vacuo*. The resulting crude product was purified by chromatography (SiO_2, PET/EtOAc 97:3) to yield two products: **36** (R_f = 0.62, PET/EtOAc 10:1; not separable from a non identified by-product), and 5-bromo-2-(2-methylallyl)phenol **1g** (R_f = 0.51, PET/EtOAc 10:1; pure, 0.12 g, 0.53 mmol, 18% yield). Characterization data for **1g**: R_f = 0.62, (PET/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (dd, *J* = 8.2, 1.2 Hz, 1 H, Ar*H*), 7.00 (t, *J* = 8.2 Hz, 1 H, Ar*H*), 6.79 (d, *J* = 8.1 Hz, 1 H, Ar*H*), 5.30 (s, 1 H, OH), 4.91 (m, 1 H, C=*CH*$_2$), 4.74 (m, 1 H, C=*CH*$_2$), 3.62 (s, 2 H, *CH*$_2$), 1.80 (s, 3 H, *CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.6, 143.4, 128.6, 125.9, 125.3, 115.3, 115.3, 112.0, 38.8, 22.3. IR ν 3430 (broad), 3080 (w), 2973 (w), 2914 (w), 2847 (w), 1743 (m), 1650 (m), 1580 (s), 1448 (s), 1374 (w), 1320 (m), 1276 (s), 1226 (m), 1186 (m), 1120 (w), 1019 (w), 928 (s), 893 (m), 856 (s), 818 (w), 772 (s), 721 (m), 676 (w), 648 (w). HRMS (ESI)[14] expected for $C_{10}H_{11}{}^{79}BrO{}^{107}Ag^+$ (M+^{107}Ag) 332.9035; found 332.8206.

2-Bromo-6-(2-methylallyl)phenol (1h)



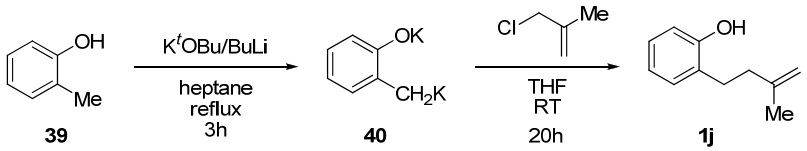
Following a slight modification of the reported procedure,[10] potassium carbonate (1.45 g, 10.5 mmol, 1.3 equiv), methyl allyl chloride (1.2 mL, 12 mmol, 1.5 equiv) and NaI (tip of a spatula) were added to a stirred solution of 2-bromophenol (**37**) (1.4 g, 8.1 mmol, 1.0 equiv) in dry acetone (4.5 mL). The mixture was stirred under reflux overnight. Then it was allowed to cool to room temperature and water (25 mL) was added, followed by extraction with ether (3 x 10 mL). The combined organic layers were then washed with 2 M NaOH (3 x 20 mL), dried with $MgSO_4$, filtered and concentrated *in vacuo* to afford 1-bromo-2-(2-methylallyloxy)benzene (**38**) (1.73 g, ≤ 7.69 mmol, ≤ 95% yield) which was used without further purification.

1-Bromo-2-(2-methylallyloxy)benzene (**38**) (650 mg, 2.87 mmol) was dissolved in DMF (2.3 mL) and the mixture was stirred under N_2 at 235°C under microwave irradiation for 1h20. DMF was evaporated *in vacuo*. The resulting crude product was purified by chromatography (SiO_2, PET/EtOAc 30:1-20:1) to yield **1h** (412 mg, 1.82 mmol, 61% yield) as a yellow oil. R_f 0.84 (PET/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (dd,

(14) ESI mass spectrum of compound **1g** was acquired after treatment of **1g** with $AgNO_3$, as a consequence of troublesome ionization of the pure compound.

J = 7.9, 1.4 Hz, 1 H, Ar*H*), 7.07 (d, *J* = 7.4 Hz, 1 H, Ar*H*), 6.76 (t, *J* = 7.7 Hz, 1 H, Ar*H*), 5.61 (s, 1 H, OH), 4.85 (s, 1 H, C=*CH*$_2$), 4.71 (s, 1 H, C=*CH*$_2$), 3.39 (s, 2 H, *CH*$_2$), 1.75 (s, 3 H, *CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.6, 144.1, 131.1, 130.3, 130.2, 121.4, 112.1, 110.6, 38.9, 22.4; IR ν 3511 (m), 3075 (w), 3028 (w), 2973 (w), 1915 (w), 1885 (w), 1797 (w), 1650 (m), 1599 (m), 1449 (s), 1375 (m), 1328 (s), 1238 (s), 1210 (m), 1166 (m), 1115 (m), 1014 (w), 893 (s), 863 (s), 820 (w), 764 (s), 732 (s), 636 (m). HRMS (ESI)[15] calcd for $C_{10}H_{11}{}^{79}BrO^{109}Ag^+$ (M+^{109}Ag), $C_{10}H_{11}{}^{81}BrO^{109}Ag^+$ (M+^{109}Ag) 334.9032, 336.9022; found 334.9037, 336.9014.

2-(3-Methylbut-3-enyl)phenol (1j)

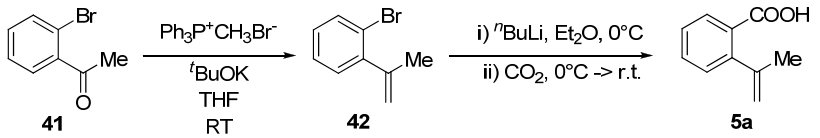


Following a reported procedure,[16] Ar was bubbled through heptane (130 mL) for 15 min, and ^{t}BuOK (5.0 g, 45 mmol, 4.0 equiv) and ^{n}BuLi (2.5 M in hexanes, 18 mL, 45 mmol, 4.0 equiv) were added. The resulting orange mixture was stirred under Ar at room temperature for 15 min and then *o*-cresol (**39**) (1.2 g, 11 mmol, 1.0 equiv) was added, whereas the reaction mixture turned to bright yellow; refluxing 3 h turned it brown. The mixture was then cooled to 0 °C and the dianion salt **40** was filtered via cannula and washed with dry hexane (100 mL).The salt was dissolved in THF (100 mL, previously cooled to 0°C) and the resulting suspension was transferred via cannula into a solution of methallyl chloride (3.3 mL, 33 mmol, 3.0 equiv) in THF (100 mL). The mixture was then stirred at room temperature for 20 h. Water was then added dropwise (10 mL) and the solution was acidified with 5 M HCl. The aqueous layer was separated and extracted with chloroform (3 x 50 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and evaporated under reduced pressure. The crude product was purified by column chromatography (SiO_2, PET/EtOAc 99:1–15:1) to afford **1j** (0.70 g, 3.9 mmol, 35% yield) as a yellow oil. Rf 0.64, (PET/EtOAc 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (dd, *J* = 7.4, 1.5 Hz, 1 H, Ar*H*), 7.09 (td, *J* = 7.6, 1.5 Hz, 1 H, Ar*H*), 6.88 (td, *J* = 7.2, 1.2 Hz, 1 H, Ar*H*), 6.76 (td, *J* = 7.9, 1.0 Hz, 1 H, Ar*H*), 4.76 (m, 2 H, C=*CH*$_2$), 4.69 (bs, 1 H, *OH*), 2.76 (m, 2 H, *CH*$_2$), 2.32 (m, 2 H, *CH*$_2$), 1.79 (s, 3 H, *CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.6, 145.8, 130.0, 128.3, 127.0, 120.5, 115.2, 110.1, 37.7, 28.5, 22.6. IR ν 3406 (broad, m), 3073 (m), 3035 (m), 2968 (m), 2932 (m), 2857 (m), 1785 (w), 1648 (m), 1609 (m), 1592 (m), 1500 (m), 1455 (s), 1374 (m), 1332 (m), 1296 (sh), 1236 (s), 1173 , (m) 1099 (m), 1045 (w), 932 (w), 889 (m), 838 (w), 752 (s), 708, 674 (w), 673 (w), 657(w), 647 (w), 633 (w), 632 (w), 609 (w). Characterization data corresponded to the literature values.[16]

2-(Prop-2-en-1-yl)benzoic acid (5a)

(15) ESI mass spectrum of compound **1h** was acquired after treatment of **1h** with $AgNO_3$, as a consequence of troublesome ionization of the pure compound.

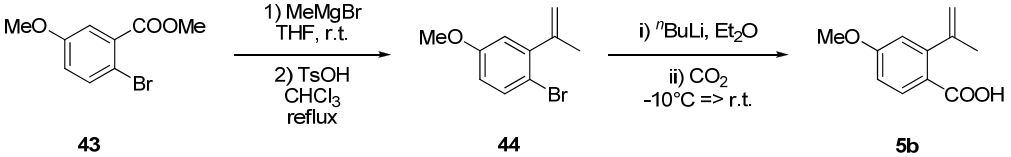
(16) Bates, R. B.; Siahaan, T. J. *J. Org. Chem.* **1986**, *51*, 1432.



Following a reported procedure,[17] a solution of potassium *tert*-butoxide (2.0 g, 18 mmol, 1.2 equiv) in THF (18 mL) was added to a stirred suspension of metylphenylphosphonium bromide (6.4 g, 18 mmol, 1.2 equiv) in THF (45 mL) under N_2 at room temperature. The mixture was stirred for 15 minutes and then a solution of 2'-bromoacetophenone (**41**) (2.0 mL, 15 mmol, 1.0 equiv) in THF (30 mL) was added via cannula. The resulting reaction mixture was stirred for 3 h at room temperature and quenched by the addition of a saturated solution of ammonium chloride (60 mL). The aqueous layer was extracted with ether (3 x 50 mL) and the combined organic layers were washed with water and brine, filtered and concentrated *in vacuo*. The resulting colorless solid was triturated with hexane (100 mL) to separate $Ph_3P=O$ which was removed by filtration. The filtrate was concentrated under reduced pressure. Purification by column chromatography (SiO_2, hexane) afforded bromostyrene **42** (2.45 g, 12.5 mmol, 83% yield) as a colorless oil.

A solution of bromostyrene **42** (600 mg, 3.06 mmol, 1.00 equiv) in Et_2O (6.1 mL, anhydrous, previously flushed with Ar) was treated dropwise with ^{n}BuLi (2.5 M in hexane, 1.5 mL, 3.7 mmol, 1.2 equiv) at 0 °C. The reaction mixture was stirred at 0 °C for 10 minutes and then anhydrous CO_2 was bubbled through it for 10 minutes. The mixture was allowed to warm to room temperature and stirred for an additional 30 minutes. The reaction was quenched with $NaHCO_3$ (saturated solution, 30 mL). The aqueous layer was washed with diethyl ether (2 x 30 mL) and then acidified with 2 N HCl to pH 1 and extracted with ether (3 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure to afford benzoic acid **5a** (414 mg, 2.55 mmol, 83% yield) as a colorless solid. R_f 0.33 (PET/EtOAc 5:1). Mp 67-69°C; 63-66°C.[17] ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.1 (bs, 1H, COO*H*), 7.98 (dd, *J* = 7.9, 1.4 Hz, 1 H, Ar*H*), 7.53 (td, *J* = 7.6, 1.4 Hz, 1 H, Ar*H*), 7.38 (td, *J* = 7.7, 1.4 Hz, 1 H, Ar*H*), 7.34-7.18 (m, 1 H, Ar*H*), 5.17 (q, *J* = 1.5 Hz, 1 H, C=*CH*$_2$), 4.96 (m, 1 H, C=*CH*$_2$), 2.15 (s, 3 H, *CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.5, 146.6, 146.3, 132.6, 130.8, 129.8, 128.0, 127.1, 114.0, 24.3. IR ν 3078 (m), 3077 (m), 3010 (m), 2978 (m), 2916 (m), 2863 (m), 2823 (m), 2652 (w), 1693 (s), 1641 (w), 1598 (w), 1570 (w), 1487(w), 1452 (w), 1408 (m), 1372 (w), 1299 (s), 1266 (s), 1141 (w), 1076 (w), 897 (s), 804 (w), 768 (s), 737 (m), 718 (m), 651 (m). ^{1}H NMR spectra corresponded to the literature values.[18]

4-methoxy-2-(prop-1-en-2-yl)benzoic acid (5b)



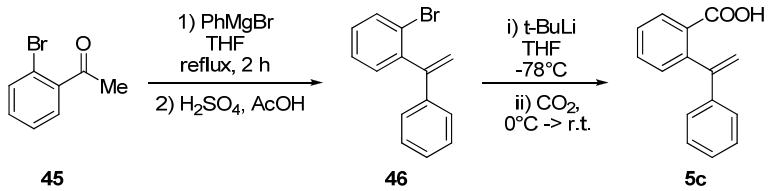
(17) Trend, R. M.; Ramtohul, Y. K.; Stoltz, B. M. *J. Am. Chem. Soc.* **2005**, *127*, 17778.
(18) Hellwinkel, D.; Aulmich, G.; Melan, M. *Chem. Ber.* **1981**, *114*, 86.

Following a slight modification of a reported procedure,[19]. methyl 2-bromo-5-methoxybenzoate (**43**) (0.73 g, 3.0 mmol, 1.0 equiv) was added dropwise to a solution of MeMgBr (3 M in Et_2O) (2.1 mL, 6.2 mmol, 2.1 equiv) in THF (6 mL). The resulting colorless suspension was stirred under nitrogen for 20 h and then the reaction was quenched by adding a saturated solution of NH_4Cl (7 mL). The aqueous layer was exctracted with Et_2O (3 x 10 mL) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford the expected tertiary alcohol (680 mg) as a colorless solid which was used without further purification. The alcohol was dissolved in chloroform (7.3 mL) and toluenesulfonic acid (7 mg, 0.04 mmol, 0.01 equiv) and the mixture was refluxed for 1 h. The reaction was then quenched by addition of a saturated solution of $NaHCO_3$ (10 mL) followed by extraction of the aqueous layer with Et_2O (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The crude procduct was purified by column chromatography (SiO_2, PET/EtOAc 98: 2) to afford the bromide **44** (513 mg, 2.26 mmol, 76% yield) as a colorless solid.

Following a reported procedure,[17] bromide **44** (0.25 g, 1.1 mmol, 1.0 equiv) was dissolved in Ar-flushed Et_2O (2.2 mL) and the solution was cooled to -10°C. After 5 minutes ^{n}BuLi (2.5 M in hexanes) (0.53 mL, 1.3 mmol, 1.2 equiv) was added dropwise and the resulting orange mixture was stirred at -10°C for 20 min. Then CO_2 was bubbled through the mixture for 15 min at -10°C and the solution was then allowed to warm to room temperature and stirred for 40 min. The reaction was quenched by adding a saturated solution of $NaHCO_3$ (5 mL). The organic layer was separated and washed with a 1 M solution of NaOH (3 x 10 mL). The combined basic layers were acidified with a 1 M solution of HCl until pH 1 and then extracted with Et_2O (3 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The crude yellow solid was purified by recrystallization from Hexane/EtOAc to furnish 4-methoxy-2-(prop-1-en-2-yl)benzoic acid (**5b**) (97 mg, 0.50 mmol, 46%) as a colorless solid. R_f 0.23 (PET/EtOAc 5: 1). Mp 109 – 111°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 12.00 (br s, 1 H, COO*H*), 8.01 (d, *J* = 8.7 Hz, 1 H, Ar*H*), 6.85 (dd, J_1 = 8.7, 2.6 Hz, 1 H, Ar*H*), 6.74 (d, *J* = 2.7 Hz, 1 H, Ar*H*), 5.11 (m, 1 H, C=*CH*$_2$), 4.88 (m, 1 H, C=*CH*$_2$), 3.87 (s, 3 H, O*CH*$_3$), 2.11 (s, 3 H, *CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 162.9, 149.2, 147.2, 133.5, 119.8, 115.3, 113.2, 112.2, 55.4, 24.2. IR ν 3380 (br, m), 2946 (s), 2893 (m), 2866 (s), 2177 (w), 2176 (s), 1780 (m), 1705 (w), 1541 (w), 1514 (w), 1462 (m), 1425 (w), 1389 (w), 1298 (w), 1274 (w), 1233 (w), 1179 (m), 1024 (m), 921 (w), 884 (m), 839 (w), 791 (w), 742 (w), 680 (m), 659 (m), 633 (m). HRMS (ESI) calcd for $C_{11}H_{13}O_3^+$ (M+H) 191.0708; found 191.0704.

2-(1-Phenylvinyl)benzoic acid (5c)

(19) Morrow, G. W.; Marks, T. M.; Sear, D. L. *Tetrahedron* **1995**, *51*, 10115.



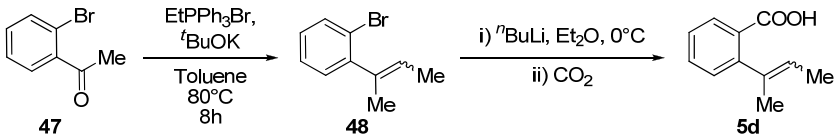
45 **46** **5c**

Following a reported procedure,[20] a solution of 2'-bromacetophenone (**45**) (2.0 mL, 15 mmol, 1.0 equiv) in THF (2 mL) was added dropwise to a stirred solution of phenyl magnesium bromide in THF (1 M, 16.6 mL, 16.6 mmol, 1.10 equiv). The resulting mixture was heated at reflux for 2 h. It was then allowed to cool to room temperature and the reaction was quenched by addition of saturated NH_4Cl (15 mL). The aqueous layer was extracted with diethyl ether (3 x 20 mL) and the combined organic layers were washed with water, dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford the crude carbinol (2.3 g, 8.5 mmol). The crude carbinol was treated with a solution of H_2SO_4 in acetic acid (4 mL, 20% v/v) at 50 °C for 5 minutes. The mixture was then poured into a Et_2O/water two-phase system (1:1, 100 mL). The aqueous layer was extracted with diethyl ether (2 x 100 mL) and the combined organic layers were washed with an aqueous solution of $NaHCO_3$ (1 M, 25 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (SiO_2, PET) to furnish 1-bromo-2-(1-phenylvinyl)benzene (**46**) (2.2 g, 8.5 mmol, 56% yield) as a colorless oil.

2-(1-Phenylvinyl)benzene (**46**) (0.60 g, 2.3 mmol, 1.0 equiv) was dissolved in Et_2O (4.5 mL, anhydrous, previously flushed with argon) and the resulting colorless mixture was cooled to -78 °C and stirred for 5 minutes. ^{t}BuLi (1.6 M in pentane, 3.4 mL, 5.5 mmol, 2.3 equiv) was added dropwise, whereas the reaction mixture turned to yellow. After 50 minutes, CO_2 was bubbled through the mixture for 10 minutes. The mixture turned to black, then to red and finally to yellow. It was then warmed to room temperature and stirred for an additional 30 minutes. The reaction was quenched by adding $NaHCO_3$ (saturated aqueous solution, 20 mL). The aqueous layer was washed with diethyl ether (3 x 20 mL), acidified to pH 1 with 2 N HCl and extracted with diethyl ether (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*, to afford the crude product as a yellow foam. Purification by crystallization from hexane furnished 2-(1-phenylvinyl)benzoic acid (**5c**) (90 mg, 0.40 mmol, 17% yield) as a colorless solid. R_f 0.10, (PET/EtOAc 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.8 (bs, 1H, COO*H*), 7.92 (dd, *J* = 7.7, 1.0 Hz, 1 H, Ar*H*), 7.56 (td, *J* = 7.6, 1.4 Hz, 1 H, Ar*H*), 7.43 (td, *J* = 7.7, 1.2 Hz, 1 H, Ar*H*), 7.36 (dd, *J* = 7.6, 0.7 Hz, 1 H, Ar*H*), 7.29 - 7.18 (m, 5 H, Ph*H*), 5.67 (d, *J* = 0.7 Hz, 1 H, C=*CH*$_2$), 5.22 (d, *J* = 0.7 Hz, 1 H, C=*CH*$_2$). Due to the low stability of the product, no further characterization was possible for **5c**.

2-(But-2-en-2-yl)benzoic acid (5d)

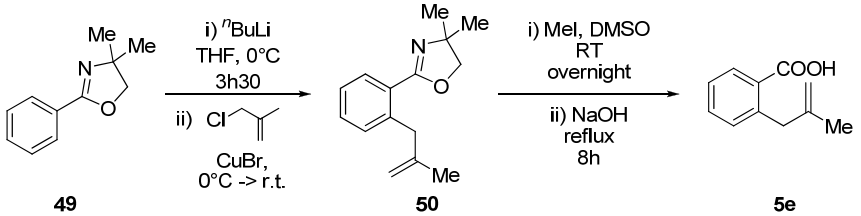
(20) Morrow, G. W.; Chen, Y.; Swenton, J. S. *Tetrahedron* **1991**, *47*, 655.



Following a reported procedure,[17] ethyltriphenylphosphonium bromide (4.4 g, 12 mmol, 2.7 equiv) was added to a suspension of potassium *t*-butoxide (1.35 g, 12.0 mmol, 2.70 equiv) in toluene (44 mL). The resulting orange suspension was stirred at 0 °C for 10 minutes, allowed to warm to room temperature and stirred for an additional 1 h. The mixture was cooled to 0 °C and 2'-bromoacetophenone (**47**) (0.88 g, 4.4 mmol, 1.0 equiv) was added dropwise. The mixture was heated at reflux for 8 h, then cooled to room temperature and quenched with NH_4Cl (saturated aqueous solution, 50 mL). The aqueous layer was extracted with diethyl ether (3 x 50 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The resulting colorless solid was triturated with hexane (50 mL) and $Ph_3P{=}O$ was removed by filtration. The filtrate was concentrated in vacuo and purified by column chromatography (SiO_2, hexane) to afford bromostyrene **48** (679 mg, 3.23 mmol, 73 % yield, mixture of E and Z isomers) as a colorless oil.

^{n}BuLi (2.5 M in hexanes, 0.80 mL, 2.1 mmol, 1.2 equiv) was added dropwise to a stirred solution of **48** (0.38 g, 1.8 mmol, 1.0 equiv) in diethyl ether (3.8 mL, anhydrous, previously flushed with Ar) at 0 °C. After 15 minutes CO_2 was bubbled through the reaction mixture for 10 minutes. The mixture was then allowed to warm to room temperature and stirred for an additional 30 minutes. The reaction was quenched with $NaHCO_3$ (saturated aqueous solution, 15 mL). The aqueous layer was washed with diethyl ether (3 x 15 mL), then acidified to pH 1 with 2 N HCl and extracted with Et_2O (3 x 15 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford benzoic acid **5d** (143 mg, 0.811 mmol, 45% yield; 2.6 :1, mixture of olefin isomers) as a colorless solid. Rf 0.23 (hexane/EtOAc 4:1). ^{1}H NMR (400 MHz, $CDCl_3$, data for a mixture 2.6 : 1 of olefin isomers based on the relative integration of peaks at δ 1.79 and 1.40**)** δ 11.2 (bs, 1H, COO*H*), 8.03 (dd, *J* = 7.9, 1.4 Hz, 1 H, Ar*H*), 7.92 (dd, *J* = 7.7, 1.4 Hz, 0.5 H, Ar*H*), 7.54 (td, *J* = 7.6, 1.4 Hz, 1 H, Ar*H*), 7.47 (td, *J* = 7.6, 1.5 Hz, 0.5 H, Ar*H*), 7.41 – 7.28 (m, 1.5 H, Ar*H*), 7.22 (dd, *J* = 7.7, 1.2 Hz, 0.5 H, Ar*H*), 7.15 (dd, *J* = 7.7, 1.2 Hz, 1 H, Ar*H*), 5.50 (m, 1 H, C=*CH*CH_3), 5.50 (m, 0.5 H, C=*CH*CH_3), 2.04 (m, 3 H, *CH_3*), 1.98 (m, 1.5 H, *CH_3*), 1.77 (dd, *J* = 6.7, 1.0 Hz, 1.5 H, *CH_3*), 1.38 (dd, *J* = 6.7, 1.5 Hz, 3 H, *CH_3*). ^{1}H NMR spectra corresponded to the literature values.[17]

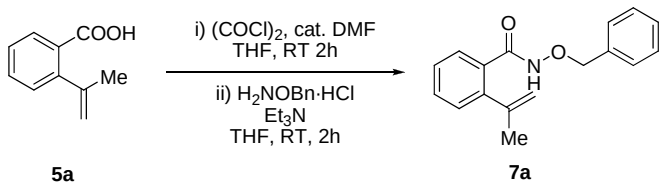
2-(2-Methylallyl)benzoic acid (5e)



Following a reported procedure,[21] *n*-BuLi (2.5 M in hexanes, 6.1 mL, 15 mmol, 1.3 equiv) was added dropwise to a solution of 4,4-dimethyl-2-phenyl-2-oxazoline (**49**) (2.0 g, 11 mmol, 1.0 equiv) in THF (34 mL, previously flushed with argon) at 0 °C. The mixture was stirred at 0°C for 3h30 and then it was transferred to a suspension of CuBr (1.61 g, 11.2 mmol, 0.99 equiv) in THF (10 mL) via cannula. The resulting green mixture was stirred at 0 °C for 1h30, methallyl chloride (1.0 mL, 10 mmol, 0.9 equiv) was added and the reaction mixture was stirred at room temperature overnight. The reaction was then quenched by addition of water (10 mL) and NH_3 (25% aq. solution, 10 mL). The aqueous layer was extracted with diethyl ether (3 x 20 mL) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification of the crude product by column chromatography (SiO_2, Hexane/EtOAc 10:1) afforded 4,4-dimethyl-2-(2-(2-methylallyl)phenyl)-4,5-oxazoline (**50**) (1.26 g, 5.49 mmol, 47 % yield) as a dark oil.

The oxazoline was converted to the methiodide salt by stirring in excess MeI (2.1 mL, 33 mmol, 6 equiv) and DMSO (1.2 mL) overnight at room temperature. The solvents were then evaporated *in vacuo* and the crude oxazoline methiodide was treated with 2 M NaOH (17.3 mL) at reflux for 9 h. The solution was then allowed to cool to room temperature and washed with DCM (3 x 20 mL). The aqueous layer was acidified to pH 1 with 12 N HCl and extracted with DCM (3 x 25 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was filtered on SiO_2 to afford 2-(2-methylallyl)benzoic acid (**5e**) (0.53 g, 3.1 mmol, 55% yield) as a colorless solid. R_f 0.42 (28:12:1 hexane-ether-formic acid). ^{1}H NMR (400 MHz, $CDCl_3$) δ 11.2 (bs, 1H, COO*H*), 8.03 (dd, *J* =0.9, 7.4, Hz, 1 H, Ar*H*), 7.49 (td, *J* =1.5, 7.6 Hz, 1 H, Ar*H*), 7.36 – 7.26 (m, 2 H, Ar*H*), 4.8 (d, *J* =0.7 Hz, 1 H, C=*CH*$_2$), 4.47 (d, *J* =0.7 Hz, 1 H, C=*CH*$_2$), 3.78 (s, 2 H, *CH*$_2$), 1.76 (s, 3 H, *CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.1, 145.4, 142.2, 132.7, 131.6, 131.5, 128.8, 126.3, 111.6, 41.8, 23.0. IR ν 3075 (m), 2972 (m), 2900 (m), 2817 (sh), 2653 (m), 2556 (m), 1688 (s), 1656 (sh), 1602 (w), 1576 (w), 1489 (w), 1449 (m), 1406 (m), 1378 (sh), 1301 (s), 1271 (s), 1196 (w), 1168 (w), 1142 (w), 1083 (w), 1051 (w), 1018 (w), 891 (s), 847 (w), 802 (m), 783 (s), 740 (s), 709 (w), 658 (m). Characterization data for **5e** corresponded to the literature values.[22]

***N*-(Benzyloxy)-2-(prop-2-en-1-yl)benzamide (7a)**



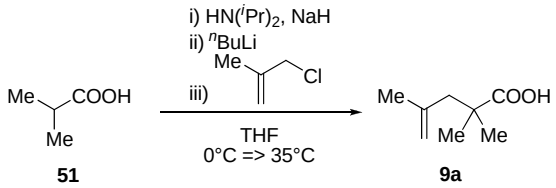
5a **7a**

Following a reported procedure,[17] oxalyl chloride (1.3 mL, 15 mmol, 5.0 equiv) was added to a stirred solution of acid **5a** (487 mg, 3.00 mmol, 1.00 equiv) in THF (16 mL), followed by a catalytic amount of DMF

(21) Ozaki, S.; Adachi, M.; Sekiya, S.; Kamikawa, R. *J. Org. Chem.* **2003**, *68*, 4586.
(22) Korte, D. E.; Hegedus, L. S.; Wirth, R. K. *J. Org. Chem.* **1977**, *42,* 1329.

(3 drops). After 2 h the solvent were evaporated under reduced pressure. The residue was diluted with THF (16 mL) and reacted with *O*-benzylhydroxylamine·hydrochloride (957 mg, 5.99 mmol, 2.00 equiv) and triethylamine (2.1 mL, 15 mmol, 5.0 equiv). The mixture was stirred for 2 h and then quenched by adding 2 M NaOH (24 mL). The aqueous layer was extracted with EtOAc (3 x 25 mL). The combined organic layers were washed with 2 M HCl (25 mL), dried over $MgSO_4$, filtered and the solvent was evaporated *in vacuo*. Purification by column chromatography (SiO_2, PET/EtOAc 4:1) afforded *N*-(benzyloxy)-2-(prop-2-en-1-yl)benzamide (**7a**) (635 mg, 2.37 mmol, 79% yield) as a pale yellow solid. R_f 0.15 (Hexane/EtOAc 1:1). Mp 84 – 88 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.92 (bs, 1 H, N*H*), 7.50 (d, *J* = 7.4 Hz, 1 H, Ar*H*), 7.47-7.31 (m, 6 H, 5 H Ph*H* and 1 H, Ar*H*), 7.27 (td, *J* = 7.6, 1.2 Hz, 1 H, Ar*H*), 7.20 (d, *J* = 7.6 Hz, 1 H, Ar*H*), 5.12 (t, *J* = 1.5 Hz, 1 H, C=C*CH*$_2$), 5.05-4.95 (m, 3 H, 1 H, C=C*CH*$_2$ and 2 H, Ph*CH*$_2$), 2.01 (m, 3 H, *CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.1, 145.1, 142.0, 135.3, 130.9, 130.5, 128.8, 128.7, 128.5, 128.4, 127.2, 116.1, 77.2, 24.0 (two carbons cannot be resolved). IR ν 3188 (m), 3087 (m), 3064 (m), 3031 (m), 2966 (m), 2948 (m), 2876 (m), 2349 (w), 1650 (s), 1598 (m), 1570 (w), 1497 (m), 1455 (m), 1371 (m), 1303 (m), 1212 (w), 1161 (w), 1088 (w), 1021 (s), 955 (w), 901 (s), 837 (w), 819 (w), 770 (s), 745 (s), 699 (s), 660 (m). HRMS (ESI) calcd for $C_{17}H_{18}NO_2$ (M + H) 268.1338; found 268.1328.

2,2,4-Trimethylpent-4-enoic acid (9a)



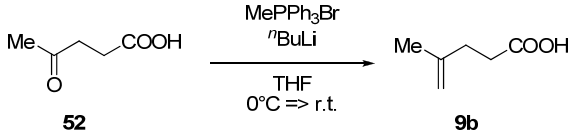
51 **9a**

Following a reported procedure,[23] isobutyric acid (**51**) (475 mg, 5.39 mmol, 1.0 equiv) was added dropwise to a stirred suspension of NaH (60% dispersion in mineral oil) (236 mg, 5.89 mmol, 1.1 equiv) and diisopropylamine (0.78 mL, 5.5 mmol, 1.0 equiv) in THF (7.5 mL). The resulting suspension was heated at reflux for 20 min and then cooled to 0°C for 15 min prior to the dropwise addition of ^{n}BuLi (2.5 M in hexanes) (2.2 mL, 5.4 mmol, 1.0 equiv). The resulting greenish suspension was stirred at 0°C for an additional 15 min and then heated to 35°C for 30 min. Then it was cooled to 0°C and methallyl chloride (0.54 mL, 5.5 mmol, 1.0 equiv) was added dropwise to give an off-white suspension which was stirred for 2 h at 35°C. The suspension was then cooled with an ice-bath and the excess of NaH was neutralized with water (10 mL). The organic layer was washed with a 1 M NaOH solution (3 x 20 mL) and the combined aqueous layers were then extracted with Et_2O (20 mL). The aqueous layer was acidified by addition of a 1 M HCl solution until pH 3 and was then extracted with ether (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated *in vacuo* to afford 2,2,4-trimethylpent-4-enoic acid (**9a**) (611 mg, 4.29 mmol, 79% yield) as a colorless oil. R_f 0.61 (Petroleum Ether/EtOAc 5/1). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* 9.91 (br s, 1 H, COO*H*), 4.83

(23) Davis, C. E., Duffy, B. C.; Coates, R. M. *J. Org. Chem.*, **2003**, *68*, 6935.

(m, 1 H, C=CH_2), 4.70 (m, 1 H, C=CH_2), 2.34 (d, J = 0.5 Hz, 2 H, CH_2), 1.71 (s, 3 H, CH_3C=C), 1.24 (s, 6 H, C(CH_3)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 185.2, 142.2, 114.4, 48.2, 42.0, 25.3, 23.6. IR ν 3126 (m), 3077 (m), 2976 (m), 2933 (m), 2883 (m), 2685 (w), 2619 (w), 1700 (s), 1647 (w), 1475 (m), 1453 (m), 1411 (m), 1371 (w), 1314 (m), 1281 (m), 1225 (m), 1165 (w), 1139 (w), 1021 (w), 943 (m), 897 (s), 870 (m), 829 (w), 811 (w), 790 (w), 767 (w). Characterization data for **9a** corresponded to the literature values.[22]

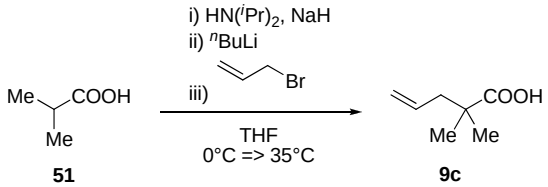
4-Methylpent-4-enoic acid (9b)



52 **9b**

Following a reported procedure,[24] methyltriphenylphosphonium bromide (3.75 g, 10.5 mmol, 3.0 equiv) was suspended in THF (46 mL). The colorless suspension was cooled to 0°C and ^{n}BuLi (2.5 M in hexanes) (4.2 mL, 10.5 mmol, 3.0 equiv) was added dropwise. The resulting bright orange solution was stirred at 0°C for 1 h before the dropwise addition of levulinic acid (**52**) (0.41 g, 3.5 mmol, 1.0 equiv). The suspension was allowed to warm to room temperature and stirred overnight. The reaction was then quench by adding a 1 M HCl solution (10 mL) and the aqueous layer was extracted with Et_2O (3 x 40 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (SiO_2, Petroleum ether/EtOAc/AcOH 85: 15: 0.1) to afford 4-methylpent-4-enoic acid (**9b**) (247 mg, 2.16 mmol, 62% yield) as a clear yellowish oil. R_f 0.47 (Petroleum Ether/EtOAc 4/1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.74 (br s, 1 H, COO*H*), 4.77 (m, 1 H, C=CH_2), 4.71 (d, J = 0.7 Hz, 1 H, C=CH_2), 2.54 (m, 2 H, CH_2COOH), 2.37 (t, J = 8.2 Hz, CH_2C=CH_2), 1.75 (d, J = 0.4 Hz, 3 H, CH_3C=CH_2). ^{13}C NMR (100 MHz, $CDCl_3$) δ 180.0, 143.7, 110.5, 32.4, 32.2, 22.5. IR ν 3080 (m), 3034 (m), 2974 (m), 2917 (m), 2857 (m), 2682 (w), 1710 (s), 1652 (w), 1444 (m), 1416 (m), 1379 (w), 1293 (m), 1245 (m), 1212 (m), 1164 (w), 1051 (w), 935 (w, sh), 891 (s), 841 (w), 787 (w). Characterization data for **9b** corresponded to the literature values.[25]

2,2-Dimethylpent-4-enoic acid (9c)



51 **9c**

Following a reported procedure,[22] isobutyric acid (**51**) (475 mg, 5.39 mmol, 1.0 equiv) was added dropwise to a stirred suspension of NaH (60% dispersion in mineral oil) (236 mg, 5.89 mmol, 1.1 equiv) and diisopropylamine (0.78 mL, 5.5 mmol, 1.0 equiv) in THF (7.5 mL). The resulting suspension was heated at

(24) Lee, E. E.; Rovis, T. *Org. Lett.*, **2008**, *10*, 1231.
(25) Braddock, D. C.; Cansell, G.; Hermitage, S. A. *Chem. Commun.*, **2006**, 2483.

reflux for 20 min and then cooled to 0°C for 15 min prior to the dropwise addition of ^{n}BuLi (2.5 M in hexanes) (2.2 mL, 5.4 mmol, 1.0 equiv). The resulting greenish suspension was stirred at 0°C for an additional 15 min and then heated to 35°C for 30 min. Passed this time it was cooled to 0°C and allyl bromide (0.48 mL, 5.5 mmol, 1.0 equiv) was added dropwise to give an off-white suspension which was stirred for 2 h at 35°C. The suspension was then cooled with an ice-bath and the excess of NaH was neutralized with water (10 mL). The organic layer was washed with a 1 M NaOH solution (3 x 20 mL) and the combined aqueous layers were then extracted with Et_2O (20 mL). The aqueous layer was acidified by addition of a 1 M HCl solution until pH 3 and it was then extracted with ether (3 x 20 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was evaporated *in vacuo*. The crude product was purified by column chromatography (SiO_2, Petroleum ether/EtOAc/AcOH 95: 5: 0.1) to afford 2,2-dimethylpent-4-enoic acid (**9c**) (150 mg, 1.17 mmol, 22%). R_f 0.56 (Petroleum ether/EtOAc/AcOH 80: 20: 0.1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.80 (br s, 1 H, COO*H*), 5.77 (m, 1 H, *CH*=CH_2), 5.10 (m, 1 H, CH=*CH*$_2$), 5.06 (m, 1 H, CH=*CH*$_2$), 2.31 (dt, J = 7.4,1.0 Hz, 2 H, *CH*$_2$CH=CH_2), 1.20 (s, 6 H, C(*CH*$_3$)$_2$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 184.6, 133.9, 118.2, 44.4, 41.5, 24.5. IR ν 3078 (m), 2979 (m), 2930 (m), 2879 (m), 2714 (w), 1702 (s), 1643 (w), 1475 (w), 1411 (w), 1388 (w), 1367 (w), 1315 (w), 1238 (w), 1207 (w), 1181 (w), 997 (w), 919 (m), 863 (w), 739 (w), 677 (w), 655 (w), 645 (w), 624 (w), 616 (w). Characterization data for **9c** corresponded to the literature values. [26]

4. Optimization of the Reaction

General procedure for reaction optimization:

The catalyst (0.014 mmol, 0.20 equiv) was dissolved in the dry solvent (5 mL) and the mixture was stirred under nitrogen. Methylallyl phenol (**1a**) (10 mg, 0.069 mmol, 1.0 equiv) was then added, followed by the hypervalent iodine reagent (35 mg, 0.084 mmol, 1.2 equiv). The mixture was stirred at room temperature overnight. It was then filtered over silica gel and the filtrate was concentrated *in vacuo*. The residue was diluted with dichloromethane (1 mL, solution **A**). 0.1 mL of a solution of decane 0.02 M in dichloromethane and 0.8 mL of dichloromethane were added to 0.1 mL of solution **A**. The resulting solution was injected into GC-MS and the following oven program was followed: Initial temperature: 50 min, Ramp: 10.0 °C/min to 250 °C, hold 15 min at 250 °C.

GC-MS Quantification

A solution of decane C = 0.02 M in dichloromethane and a solution of product **4** C = 0.02 M in dichloromethane were prepared. For the calibration, 3 points were measured corresponding to 3 different ratio (decane : **4**). The ratios used are 1:1, 1:2 and 2:1.

The observed ratio by integration of the GC peaks and the real ratios were used as the axis of the calibration graph (Figure S1 for the example of **4b**).

(26) de Almeida, M. I.; do Amaral, A. T.; do Amaral, L. *J. Org. Chem.* **1982,** *47***,** 1567.

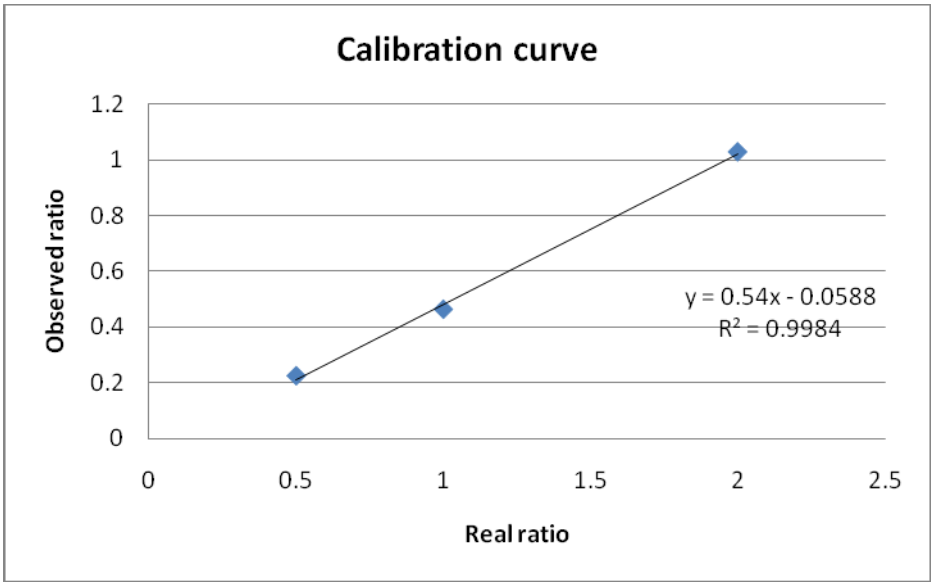
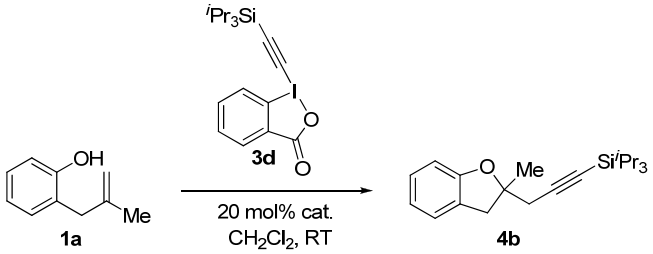
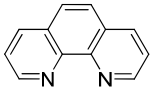
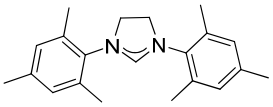
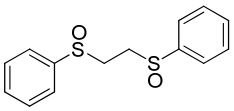


Figure S1: Calibration curve for GC yields calculation in the case of **4b**.

Detailed results for the optimization studies

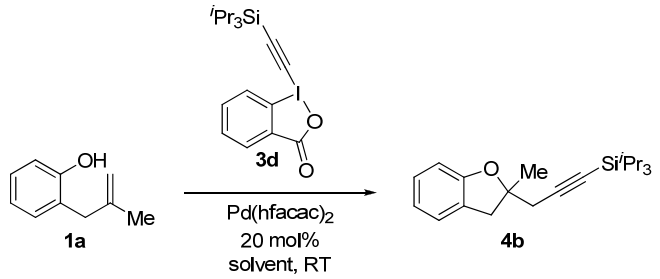
Table S1: Catalyst screening for the reaction of **1a** with **3d**.



Entry	Catalyst	Yield[a]
1	$Pd(TFA)_2$	17%
2	$Pd(OAc)_2$	18%
3	$PdCl_2(CH_3CN)_2$	40%
4	$[Pd(MeCN)_4](BF_4)_2$	21%
5	$Pd(acac)_2$	2%
6	$Pd(hfacac)_2$	73%
7	$PdCl_2(PPh_3)_2$	traces
8	$Pd(hfacac)_2/PPh_3$	traces
9	$Pd(II)(TFA)_2$, 	0%
10	$Pd(II)Cl_2$, 	0%
11	$Pd(OAc)_2$, 	31%
12	$Pd(dba)_2$	7%
13	$Pd_2(dba)_3 \cdot CHCl_3$	6%
14	10 mol% $Pd(hfacac)_2$	71%
15	5 mol% $Pd(hfacac)_2$	68%
16	40 mol% $Pd(hfacac)_2$	79%

[a]Reaction conditions: 0.069 mmol **1a**, 20% mol catalyst, 1.2 equiv reagent, 5 mL dry solvent under N_2. Yield was determined via GC-MS.

Table S2: Solvents screening for the reaction of **1a** with **3d**.

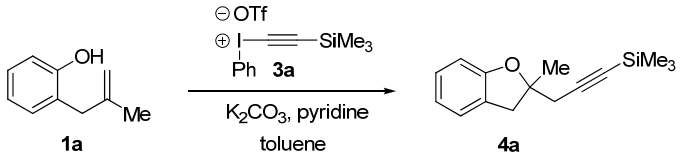


Entry	Solvent	Yield[a]
1	CH_2Cl_2	73%
2	$CHCl_3$	70%
3	$C_2H_4Cl_2$	67%
4	toluene	32%
5	hexane/toluene 1 : 1	42%
6	α,α,α-trifluorotoluene	67%
7	THF	12%
8	Et_2O	9%
9	acetone	9%
10	CH_3CN	21%
11	methanol	25%
12	DMF	traces

[a]Reaction conditions: 0.069 mmol **1a**, 20% mol catalyst, 1.2 equiv reagent, 5 mL dry solvent under N_2. Yield was determined via GC-MS.

5. Scope of the Reaction

Trimethyl-[3-(2-methyl-2,3-dihydro-benzofuran-2-yl)-prop-1-ynyl]-silane (4a)



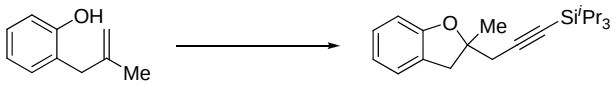
A small amount of **4a** was obtained using the conditions in entry 1, Table 1 on a preparative scale: 2-(methylallyl)phenol (**1a**) (85 mg, 0.57 mmol, 1.0 equiv) was added to a solution of Pd(II) bis(acetonitrile) (18 mg, 0.057 mmol, 0.10 equiv), pyridine (9 μL, 0.1 mmol, 0.2 equiv) and potassium carbonate (158 mg, 1.14 mmol, 2.00 equiv) in toluene (4.6 mL). Phenyl(trimethylsilylethynyl)iodonium triflate (**4a**) (308 mg, 0.685 mmol, 1.2 equiv) was then added and the mixture was stirred at 0 °C. After 1 h, the mixture was warmed to room temperature and stirred additionally 90 min. Then a solution of $NaHCO_3$ sat. was added, followed by water and a solution of NaCl sat., followed by an extraction with diethyl ether (3x20 ml). It was then dried with

$MgSO_4$ and evaporated under reduced pressure.The black crude oil was purified by chromatography (hexane/CH_2Cl_2 4:1) to yield **4a** (8.5 mg, 0.035 mmol, 6%) as a yellow oil, which was used for GC/MS calibration. R_f 0.56 (hexane/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.12 (m, 2 H, Ar H), 6.83 (t, J = 7.4 Hz, 1 H, Ar H), 6.74 (d, J = 8.0 Hz, 1 H, Ar H), 3.31 (m, 1 H, CH_2), 3.00 (d, J = 15.7 Hz, 1 H, CH_2), 2.62 (m, 2 H, CH_2), 1.58 (s, 3 H, Me), 0.11 (s, 9 H, TMS). MS (EI) found for $C_{15}H_{20}OSi^+$ (M) 244. GC Elution Time: 18.7 min.Due to the low amount of product **4a** and the low yield generally obtained, no further characterization was made.

General optimized procedure for the Wacker cyclization – alkynylation domino reaction:

Palladium (II) hexafluoroacetylacetonate (21 mg, 0.10 equiv.) was dissolved in dichloromethane (10 mL). The substrate (0.40 mmol) was then added, followed by 1-((tri*iso*propylsilyl)ethynyl)-1,2-benziodoxol-3(1 H)-one (**3d**). The resulting solution was stirred under N_2 at room temperature for 5 h. DCM was then removed under reduced pressure and the residue was treated with $NaHCO_3$ (saturated solution, 6 mL) and brine (6 mL). The mixture was extracted with diethyl ether (3 x 15 mL) and the combined organic layers were dried on $MgSO_4$, filtered and concentrated *in vacuo*. The brown crude oil was purified by column chromatography on silica gel.

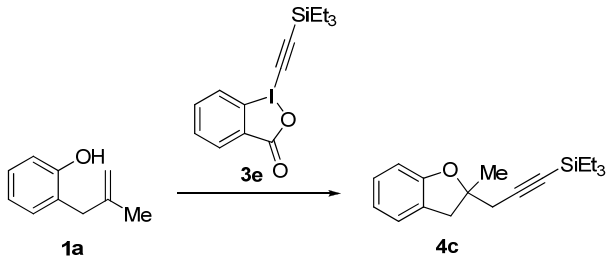
Tri*iso*propyl-[3-(2-methyl-2,3-dihydro-benzofuran-2-yl)-prop-1-ynyl]-silane (4b)



1a **4b**

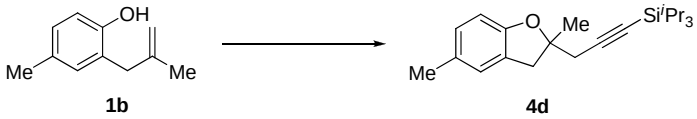
Column chromatography (SiO_2, PET/DCM 98:2) afforded product **4b** (92 mg, 0.28 mmol, 71% yield) as a yellow oil. R_f 0.41 (PET/DCM 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.15 (dd, J = 7.4, 0.7 Hz, 1 H, Ar*H*), 7.11 (m, 1 H, Ar*H*), 6.83 (td, J = 7.4, 0.9 Hz, 1 H, Ar*H*), 6.74 (d, J = 7.9 Hz, 1 H, Ar*H*), 3.39 (d, J = 15.8 Hz, 1 H, ArCH_2), 3.01 (d, J = 15.8 Hz, 1 H, ArCH_2), 2.67 (m, 2 H, CH_2C≡C), 1.60 (s, 3 H, CH_3), 1.05 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 128.0, 126.5, 125.1, 120.2, 109.5, 104.3, 87.3, 82.9, 40.6, 32.5, 26.1, 18.6, 11.2. IR ν 2956 (m), 2942 (m), 2892 (m), 2864 (m), 2176 (m), 1600 (w), 1481 (s), 1462 (m), 1380 (w), 1328 (w), 1239 (m), 1116 (w), 1069 (m), 1033 (m), 1017 (m), 996 (m), 921 (m), 883 (s), 796 (w), 785 (w), 747 (s), 710 (w), 677 (s), 660 (s), 636 (s). HRMS (ESI) calcd for $C_{21}H_{32}OSiNa^+$ (M+Na) 351.2120; found: 351.2139. GC Elution Time: 27.5 min.

Triethyl-[3-(2-methyl-2,3-dihydro-benzofuran-2-yl)-prop-1-ynyl]-silane (4c)



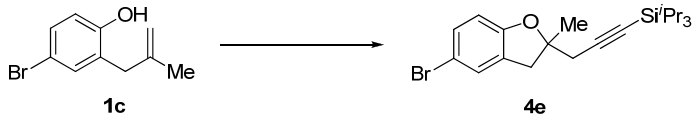
Following the general procedure, but using reagent **3e** (0.19 g, 0.48 mmol, 1.2 equiv) product **4c** (50 mg, 0.17 mmoles, 43% yield) was obtained as a yellow oil after purification by column chromatography (SiO_2, PET/DCM 98:2). R_f 0.82 (PET/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 (t, *J* = 7.2 Hz, 1 H, Ar*H*), 7.09 (d, *J* = 7.4 Hz, 1 H, Ar*H*), 6.83 (t, *J* = 7.4, 1 H, Ar*H*), 6.73 (d, *J* = 7.9 Hz, 1 H, Ar*H*), 3.35 (d, *J* = 15.8 Hz, 1 H, Ar*CH*$_2$), 3.00 (d, *J* = 15.8 Hz, 1 H, Ar*CH*$_2$), 2.68 (d, *J* = 16.7 Hz, 1 H, *CH*$_2$C≡C), 2.60 (d, *J* = 16.7 Hz, 1 H, *CH*$_2$C≡C), 1.58 (s, 3 H, *CH*$_3$), 0.95 (t, *J* = 7.9 Hz, 9 H, SiCH$_2$*CH*$_3$), 0.54 (q, *J* = Hz, 6 H, Si*CH*$_2$CH$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 128.0, 126.6, 125.1, 120.3, 109.5, 103.8, 87.3, 84.3, 40.6, 32.5, 26.1, 7.5, 4.5. IR ν 3093 (s), 2956 (m), 2933 (m), 2910 (w), 2878 (m), 2349 (w), 2177 (s), 1598 (m), 1481 (w), 1461 (w), 1416 (w), 1379 (s), 1325 (w), 1240 (s), 1116 (m), 1116 (w), 1070(w), 1034(m), 1017(m), 969 (w), 954 (w), 925 (w), 887 (w), 861 (w), 792 (w), 743 (s), 632 (w). HRMS (ESI) calcd for $C_{18}H_{26}OSi^+$ (M+H) 287.1831; found: 287.1833.

Tri*iso*propyl-[3-(2,5-dimethyl-2,3-dihydro-benzofuran-2-yl)-prop-1-ynyl]-silane (4d)



Column chromatography (SiO_2, PET/DCM 98:2) afforded product **4d** (48 mg, 0.13 mmol, 34% yield) as a yellow oil. R_f 0.80 (PET/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.97 (s, 1 H, Ar*H*), 6.90 (dd, *J* = 8.1, 1.0 Hz, 1 H, Ar*H*), 6.63 (d, *J* = 8.1 Hz, 1 H, Ar*H*), 3.35 (d, *J* = 15.6 Hz, 1 H, Ar*CH*$_2$), 2.97 (d, *J* = 15.6 Hz, 1 H, Ar*CH*$_2$), 2.65 (m, 2 H, *CH*$_2$C≡C), 2.28 (s, 3 H, *CH*$_3$), 1.59 (s, 3 H, *CH*$_3$), 1.09 - 0.99 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.6, 129.5, 128.3, 126.6, 125.7, 109.0, 104.5, 87.4, 82.8, 40.7, 32.5, 29.8, 26.1, 18.7, 11.2. IR ν 2941 (s), 2864 (s), 2175 (s), 1618 (w), 1491 (s), 1464 (s), 1380 (m), 1306 (m), 1249 (s), 1217 (m), 1125 (w), 1070 (s), 1034 (s), 995 (m), 923 (m), 882 (s), 811 (s), 676 (s), 634 (m). HRMS (ESI) calcd for $C_{22}H_{35}OSi^+$ (M+H) 343.2457; found: 343.2443.

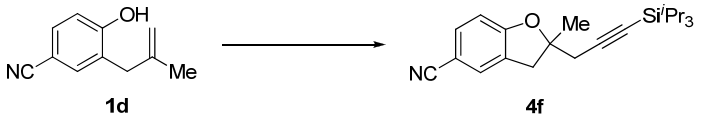
Tri*iso*propyl-[3-(5-bromo-2-methyl-2,3-dihydro-benzofuran-2-yl)-prop-1-ynyl]-silane (4e)



Column chromatography (SiO_2, PET/EtOAc 98:2) afforded product **4e** (0.11 g, 0.27 mmol, 68% yield) as a yellow oil. R_f 0.80 (PET/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.25 – 7.23 (m, 1 H, Ar*H*), 7.18 (dd, *J* =

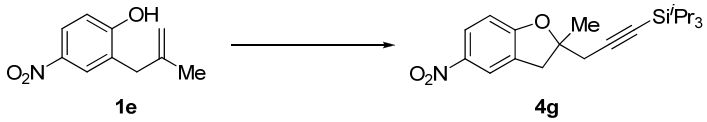
2.1, 8.4 Hz, 1H, Ar*H*), 6.56 (d, *J* = 8.4 Hz, 1 H, Ar*H*), 3.37 (d, *J* = 16.2 Hz, 1 H, ArCH_2), 2.98 (d, *J* = 16.2 Hz, 1 H, ArCH_2), 2.60 (m, 2 H, CH_2C≡C), 1.57 (s, 3 H, CH_3), 1.06 – 0.97 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.0, 130.8, 129.1, 128.0, 112.0, 111.0, 103.7, 88.2, 83.3, 40.4, 32.5, 26.3, 18.6, 11.2. IR ν 3730 (w), 2942 (m), 2864 (m), 2360 (w), 2340 (w), 2176 (m), 1659 (w), 1605 (w), 1490 (m), 1575 (s), 1381 (m), 1294 (m), 1239 (s), 1178 (m), 1107 (m), 1072 (s), 1034 (s), 995 (m), 960 (m), 920 (m), 884 (s), 810 (s), 785 (m), 678 (s), 629 (s). HRMS (ESI) calcd for $C_{21}H_{32}{}^{79}BrOSi^+$, $C_{21}H_{32}{}^{81}BrOSi^+$ (M+H) 407.1406, 409.1388; found: 407.1395, 409.1383.

2-Methyl-2-(3-(tri*iso*propylsilyl)prop-2-ynyl)-2,3-dihydro-1-benzofuran-5-carbonitrile (4f)



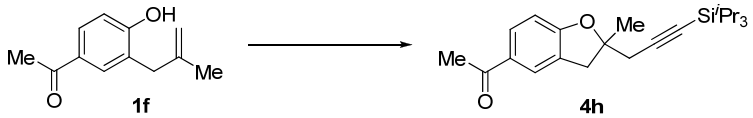
Column chromatography (SiO_2, PET/EtOAc 98:2) afforded product **4f** (107 mg, 0.303 mmol, 76% yield) as a yellow oil. R_f 0.74 (PET/EtOAc 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.48 – 7.40 (m, 2 H, Ar*H*), 6.78 (dd, *J* = 9.0, 3.0 Hz, 1H, Ar*H*), 3.45 (d, *J* = 16.1 Hz, 1 H, ArCH_2), 3.04 (d, *J* = 16.1 Hz, 1 H, ArCH_2), 2.72 (dm, *J* = 17.1 Hz, 1 H, CH_2C≡C), 2.62 (dm, *J* = 17.1 Hz, 1 H, CH_2C≡C), 1.60 (m, 3 H, CH_3), 1.15 – 0.88 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5, 133.6, 129.1, 128.4, 124.0, 119.7, 110.3, 103.0, 89.3, 83.7, 39.8, 32.7, 26.5, 18.5, 11.2. IR ν 2943 (s), 2865 (s), 2349 (w), 2224 (m), 2177 (m), 1770 (w), 1614 (m), 1487 (s), 1464 (m), 1382 (w), 1300 (m), 1266 (m), 1247 (m), 1112 (w), 1108 (w), 1069 (m), 1035 (m), 996 (w), 923 (w), 882 (m), 821 (m), 788 (w), 739 (w), 677 (s). HRMS (ESI) calcd for $C_{22}H_{32}NOSi^+$ (M+H) 354.2253; found: 354.2250.

Tri*iso*propyl-[3-(5-nitro-2-methyl-2,3-dihydro-benzofuran-2-yl)-prop-1-ynyl]-silane (4g)



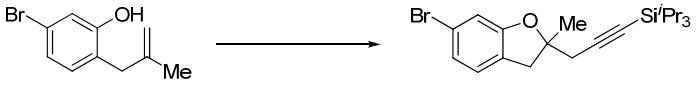
Column chromatography (SiO_2, PET/EtOAc 98:2) afforded product **4g** (108 mg, 0.289 mmol, 72% yield) as a yellow oil. R_f 0.85 (PET/EtOAc 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 – 8.03 (m, 2 H, Ar*H*), 6.75 (m, 1H, Ar*H*), 3.47 (d, *J* = 16.6 Hz, 1 H, ArCH_2), 3.06 (d, *J* = 16.6 Hz, 1 H, ArCH_2), 2.75 (d, *J* = 17.1 Hz, 1 H, CH_2C≡C), 2.65 (d, *J* = 17.1 Hz, 1 H, CH_2C≡C), 1.60 (s, 3 H, CH_3), 1.02 – 0.94 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.3, 141.8, 128.2, 125.8, 121.5, 109.2, 102.8, 90.4, 83.9, 39.7, 32.7, 26.5, 18.5, 11.2. IR ν 2942 (m), 2865 (m), 2349 (w), 2176 (w), 1621 (w), 1598 (m), 1523 (m), 1477 (m), 1339 (s), 1289 (m), 1272 (m), 1242 (m), 1120 (w), 1061 (m), 1035 (m), 997 (w), 925 (m), 883 (m), 810 (w), 783 (w), 739 (w), 665 (m), 636 (m). HRMS (ESI) calcd for $C_{21}H_{32}NO_3Si^+$ (M+H) 374.2151; found: 374.2133.

1-(2-Methyl-2-(3-(tri*iso*propylsilyl)prop-2-ynyl)-2,3-dihydro-1-benzofuran-5-yl)ethanone (4h)



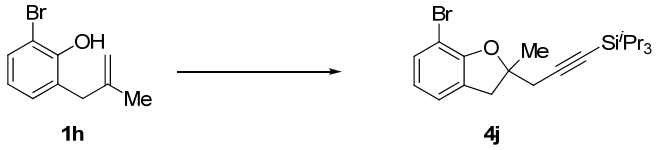
Column chromatography (SiO_2, PET/EtOAc 98:2) afforded product **4h** (128 mg, 0.345 mmol, 87% yield) as a yellow oil. Rf 0.54 (PET/EtOAc 8:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.78 (m, 1 H, Ar*H*), 7.75 (d, *J* = 1.9 Hz, 1 H, Ar*H*), 6.72 (d, *J* = 8.2 Hz, 1 H, Ar*H*), 3.40 (d, *J* = 16.0 Hz, 1 H, Ar*CH*$_2$), 3.01 (d, *J* = 16.0 Hz, 1 H, Ar*CH*$_2$), 2.70 (d, *J* = 16.8 Hz, 1 H, *CH*$_2$C≡C), 2.62 (d, *J* = 16.8 Hz, 1 H, *CH*$_2$C≡C), 2.51 (s, 3 H, CO*CH*$_3$), 1.58 (s, 3 H, *CH*$_3$), 1.09 – 0.85 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.6, 163.1, 130.6, 130.4, 127.4, 125.8, 109.1, 103.5, 89.2, 83.4, 39.9, 32.6, 26.4, 18.5, 11.2 (one carbon cannot be resolved). IR ν 2942 (s), 2864 (s), 2176 (m), 1676 (s), 1609 (s), 1589 (m), 1489 (m), 1464 (m), 1438 (m), 1381 (w), 1358 (m), 1305 (w), 1265 (s), 1170 (w), 1110 (w), 1075 (m), 1056 (m), 1034 (m), 996 (w), 956 (w), 911 (m), 883 (s), 816 (m), 787 (w), 729 (w), 675 (s), 634 (s), 612 (m). HRMS (ESI) expected for $C_{23}H_{34}O_2Si^+$ (M+H) 371.2406; found: 371.2419.

Tri*iso*propyl-[3-(6-bromo-2-methyl-2,3-dihydro-benzofuran-2-yl)-prop-1-ynyl]-silane (4i)



Column chromatography (SiO_2, PET/EtOAc 98:2) afforded product **4i** (107 mg, 0.263 mmol, 66% yield) as a yellow oil. R_f 0.86 (PET/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.98 – 6.94 (m, 2 H, Ar*H*), 6.65 (m, 1H, Ar*H*), 3.41 (d, *J* = 16.3 Hz, 1 H, Ar*CH*$_2$), 2.99 (d, *J* = Hz, 1 H, Ar*CH*$_2$), 2.72 (d, *J* = 16.7 Hz, 1 H, *CH*$_2$C≡C), 2.62 (d, *J* = 16.7 Hz, 1 H, *CH*$_2$C≡C), 1.58 (s, 3 H, *CH*$_3$), 1.07 – 0.95 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.2, 129.5, 128.0, 123.2, 119.3, 108.3, 103.6, 87.3, 83.4, 42.0, 32.8, 26.6, 18.6, 11.2. IR ν 3743 (w), 2941 (m), 2865 (m), 2176 (m), 1605 (m), 1584 (m), 1449 (s), 1382 (w), 1319 (w), 1266 (s), 1241 (s), 1171 (w), 1111 (w), 1074 (m), 995 (m), 936 (w), 906 (s), 882 (s), 825 (w), 765 (s), 707 (m), 664 (s). HRMS (ESI) calcd for $C_{21}H_{32}{}^{79}BrOSi^+$, $C_{21}H_{32}{}^{81}BrOSi^+$ (M+H) 407.1406, 409.1388; found: 407.1391, 409.1367.

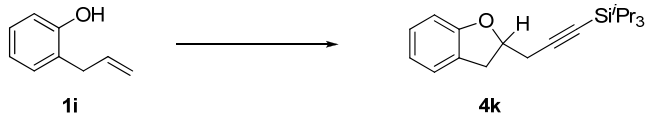
Tri*iso*propyl-[3-(7-bromo-2-methyl-2,3-dihydro-benzofuran-2-yl)-prop-1-ynyl]-silane (4j)



Column chromatography (SiO_2, PET/EtOAc 98:2) afforded product **4j** (84 mg, 0.21 mmol, 52% yield) as a yellow oil. R_f 0.78 (PET/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23-7.27 (m, 1 H, Ar*H*), 7.06 (dd, *J* = 7.4, 1.2 Hz, 1H, Ar*H*), 6.70 (t, *J* = 7.6 Hz, 1 H, Ar*H*), 3.48 (d, *J* = 16.0 Hz, 1 H, Ar*CH*$_2$), 3.08 (d, *J* = 16.0 Hz, 1 H, Ar*CH*$_2$), 2.71 (m, 2 H, *CH*$_2$C≡C), 1.62 (s, 3 H, *CH*$_3$), 0,99-1.05 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.2, 128.0, 131.1, 124.0, 121.5, 103.7, 102.7, 88.2, 83.2, 41.4, 32.6, 26.3, 18.6, 11.2. IR ν 2941 (m),

2864 (m), 2176 (w), 1648 (w), 1604 (w), 1584 (w), 1455 (s), 1382 (w), 1329 (w), 1291 (w), 1246 (w), 1216 (m), 1112 (w), 1072 (m), 1034 (m), 1028 (m), 994 (w), 920 (w), 882 (s), 783 (w), 759 (s), 714 (m), 664 (s), 644 (s). HRMS (ESI) calcd for $C_{21}H_{32}{}^{79}BrOSi^+$, $C_{21}H_{32}{}^{81}BrOSi^+$ (M+H) 407.1406, 409.1388; found: 407.1409, 409.1393.

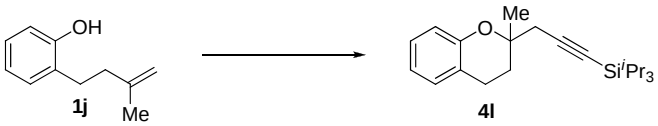
(3-(2,3-Dihydro-benzofuran-2-yl)-prop-1-ynyl)tri*iso*propyl silane (4k)



1i **4k**

Column chromatography (SiO_2, PET/DCM 95:5) afforded product **4k** (47 mg, 0.15 mmol, 37% yield) as a yellow oil. R_f 0.88 (PET/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, *J* = 7.2 Hz, 1 H, Ar*H*), 7.10 (t, *J* = 8.1 Hz, 1 H, Ar*H*), 6.83 (t, *J* = 7.4 Hz, 1 H, Ar*H*), 6.75 (d, *J* = 8.1 Hz, 1 H, Ar*H*), 4.92 (m, 1 H, *CH*), 3.36 (dd, *J* = 15.8, 9.1 Hz, 1 H, Ar*CH*$_2$), 3.19 (dd, *J* = 15.6, 6.5 Hz, 1 H, Ar*CH*$_2$), 2.76 (dd, *J* = 16.7, 4.5 Hz, 1 H, *CH*$_2$C≡C), 2.67 (dd, *J* = 16.7, 7.7 Hz, 1 H, *CH*$_2$C≡C), 1.09 – 0.97 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.4, 128.0, 126.3, 125.0, 120.5, 109.3, 103.3, 83.2, 80.5, 34.6, 27.0, 18.6, 11.2. IR ν 2942 (s), 2864 (s), 2176 (m), 1599 (m), 1481 (s), 1463 (s), 1383 (w), 1365 (w), 1336 (w), 1323 (w), 1294 (w), 1230 (s), 1172 (w), 1142 (w), 1098 (w), 1074 (w), 1026 (m), 1017 (m), 984 (m), 920 (w), 884 (s), 858 (m), 817 (w), 794 (w), 748 (s), 710 (m), 677 (s), 660 (s), 638 (s), 615(m). HRMS (ESI) calcd for $C_{20}H_{31}OSi^+$ (M+H) 315.2144; found: 315.2139.

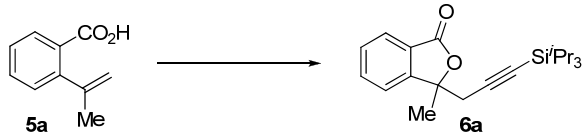
Tri*iso*propyl-(3-(2-methylchroman-2-yl)-prop-1-ynyl)-silane (4l)



1j **4l**

Column chromatography (SiO_2, PET/DCM 95:5) afforded product **4l** (63 mg, 0.18 mmol, 46% yield) as a colorless oil. R_f 0.94 (PET/EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.13 – 7.05 (m, 2 H, Ar*H*), 6.84 (td, *J* = 1.0, 7.4 Hz, 1 H, Ar*H*), 6.79 (d, *J* = 8.1 Hz, 1 H, Ar*H*), 2.80 (m, 2 H, Ar*CH*$_2$), 2.62 (d, *J* = 16.7 Hz, 1 H, *CH*$_2$C≡C), 2.53 (d, *J* = 16.7 Hz, 1 H, *CH*$_2$C≡C), 2.14 (m, 1 H, *CH*$_2$), 1.88 (m, 1 H, *CH*$_2$), 1.48 (s, 3 H, *CH*$_3$), 1.16 – 1.03 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 153.5, 129.5, 127.4, 121.1, 120.0, 117.3, 104.5, 83.1, 75.8, 30.6, 29.9, 25.1, 22.1, 18.7, 11.3. IR ν 2941 (s), 2864 (s), 2174 (m), 1612 (w), 1583 (m), 1489 (s), 1456 (s), 1379 (m), 1355 (w), 1306 (m), 1272 (w), 1270 (w), 1242 (s), 1216 (m), 1190 (w), 1148 (m), 1133 (m), 1111 (s), 1088 (s), 1037 (s), 995 (m), 948 (m), 928 (m), 883 (s), 830 (w), 753 (s), 728 (w), 710 (w), 677 (s), 667 (s), 637 (s). HRMS (ESI) calcd for $C_{22}H_{35}OSi^+$ (M+H) 343.2457; found: 343.2456.

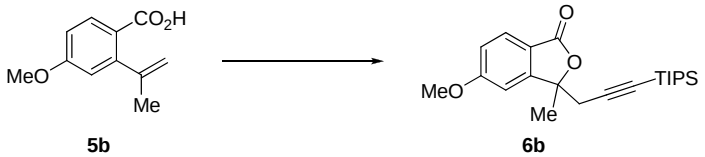
3-Methyl-3-(3-(tri*iso*propylsilyl)prop-2-ynyl)isobenzofuran-1(*3H*)-one (6a)



5a **6a**

Column chromatography (SiO_2, PET/EtOAc 98:2) afforded product **6a** (70 mg, 0.33 mmol, 83% yield) as a colorless solid. R_f 0.73 (PET/EtOAc 5:1). Mp 104 – 105 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.85 (d, *J* = 7.6 Hz, 1 H, Ar*H*), 7.64 (td, *J* = 7.7, 1.0 Hz, 1 H, Ar*H*), 7.59 (d, *J* = 7.6 Hz, 1 H, Ar*H*), 7.51 (td, *J* = 7.6, 1.2 Hz, 1 H, Ar*H*), 2.97 (d, *J* = 16.8 Hz, 1 H, *CH*$_2$C≡C), 2.83 (d, *J* = 16.8 Hz, 1 H, *CH*$_2$C≡C), 1.74 (s, 3 H, *CH*$_3$), 1.05 – 0.88 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 152.7, 133.9, 129.3, 126.0, 125.7, 121.5, 101.6, 85.2, 84.8, 32.3, 25.1, 19.0, 10.6. IR ν 2942 (s), 2864 (s), 2174 (m), 1767 (s), 1615 (w), 1465 (m), 1382 (w), 1363 (w), 1337 (w), 1312 (w), 1286 (m), 1248 (w), 1222 (w), 1164 (w), 1121 (m), 1077 (w), 1035 (s), 1001 (m), 916 (m), 884 (m), 805 (m), 765 (w), 726 (w), 696 (s), 674 (s), 618 (s). HRMS (ESI) calcd for $C_{21}H_{31}O_2Si^+$ (M+H) 343.2093; found: 343.2080.

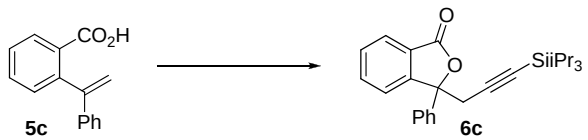
5-Methoxy-3-methyl-3-(3-(triisopropylsilyl)prop-2-ynyl)isobenzofuran-1(3H)-one (6b)



5b **6b**

Column chromatography (SiO_2, Hexane/EtOAc 95:5) afforded product **6b** (120 mg, 0.323 mmol, 80% yield) as a yellow solid. R_f 0.4 (PET/EtOAc 5:1). Mp 73 – 76°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (m, 1 H, Ar*H*), 7.07-7.00 (m, 2 H, Ar*H*), 3.91 (m, 3 H, O*CH*$_3$), 2.99 (d, *J* = 16.9 Hz, 1 H, *CH*$_2$C≡C), 2.83 (d, *J* = 16.9 Hz, 1 H, *CH*$_2$C≡C), 1.76 (s, 3 H, *CH*$_3$), 1.10-0.95 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.7, 155.5, 127.2, 118.2, 116.3, 105.8, 101.8, 84.6, 84.3, 55.8, 32.1, 25.1, 18.5, 11.1 (one aromatic carbon cannot be resolved). IR ν 2968 (m), 2943 (w), 2893 (m), 2865 (w), 2178 (s), 1760 (s), 1608 (m), 1492 (m), 1464 (m), 1382 (m), 1341 (m), 1330 (m), 1295 (m), 1247 (s), 1203 (w), 1180 (w), 1119 (m), 1069 (m), 1037 (s), 996 (w), 948 (w), 918 (w), 884 (m), 842 (w), 787 (w), 738 (w), 699 (m), 677 (m), 626 (m). HRMS (ESI) calcd for $C_{22}H_{33}O_3Si^+$ (M+H) 373.2199; found: 373.2204.

3-Phenyl-3-(3-(tri*iso*propylsilyl)prop-2-ynyl)isobenzofuran-1(*3H*)-one (6c)

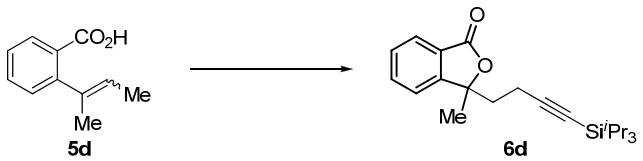


5c **6c**

Column chromatography (SiO_2, PET/EtOAc 98:2) afforded product **6c** (113 mg, 0.279 mmol, 70% yield) as a colorless solid. R_f 0.67 (PET/EtOAc 5:1). Mp 58 – 60 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J* = 7.6 Hz, 1 H, Ar*H*), 7.70 – 7.60 (m, 2 H, Ar*H*), 7.57 – 7.49 (m, 3 H, Ar*H,* Ph*H*), 7.42 – 7.27 (m, 3 H, Ph*H*), 3.41 (d, *J* =

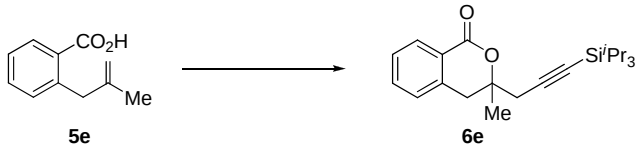
16.8 Hz, 1 H, CH_2C≡C), 3.28 (d, J = 16.8 Hz, 1 H, CH_2C≡C), 0.97 – 0.80 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.4, 151.3, 139.0, 134.1, 129.5, 128.7, 128.7, 126.4, 125.8, 125.5, 122.9, 101.1, 87.6, 85.2, 32.6, 18.4 11.1. IR ν 3062 (w), 2942 (m), 2864 (m), 2174 (w), 1772 (s), 1603 (w), 1496 (w), 1465 (m), 1419 (w),1386 (w), 1366 (w), 1339 (w), 1286 (m), 1228 (m), 1218 (m), 1189 (w), 1159 (w), 1094 (s), 1019 (m), 991 (s), 942 (m), 918 (w), 884 (s), 766 (s), 723 (w), 696 (s), 678 (s), 618 (m). HRMS (ESI) calcd for $C_{26}H_{33}O_2Si^+$ (M+H) 405.2250; found: 405.2259.

3-Methyl-3-(4-(tri*iso*propylsilyl)but-3-ynyl)benzofuran-1(3*H*)-one (6d)



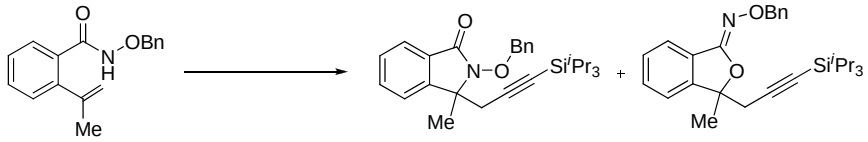
Column chromatography (SiO_2, PET/EtOAc 98:2) afforded product **6d** (80 mg, 0.22 mmol, 56% yield) as a yellow oil. R_f 0.75 (PET/EtOAc 5:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (dd, J = 8.0, 1.0 Hz, 1 H, ArH), 7.67 (td, J = 7.5, 1.0 Hz, 1 H, ArH), 7.51 (t, J = 7.5, 1 H, ArH), 7.40 (dd, J = 0.5, 7.5 Hz, 1 H, ArH), 2.31 (m, 2 H, CH_2CH$_2$C≡C), 2.12 (m, 1 H, CH$_2$$CH_2$C≡C), 1.96 (m, 1 H, CH$_2$$CH_2$C≡C), 1.66 (s, 3 H, CH_3), 1.11 – 0.91 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.6, 153.0, 134.3, 129.2, 125.9, 125.8, 121.0, 107.0, 86.7, 81.0, 39.2, 25.8, 18.6, 14.9, 11.2. IR ν 2942 (m), 2865 (m), 2174 (w), 1767 (s), 1615 (w), 1465 (m), 1382 (w), 1363 (w), 1312 (w), 1286 (m), 1248 (w), 1222 (w), 1164 (m), 1121 (w), 1035 (s), 1001 (m), 916 (m), 884 (m), 805 (w), 726 (w), 696 (m), 674 (s), 618 (m). HRMS (ESI) expected for $C_{22}H_{33}O_2Si^+$ (M+H) 357.2250; found: 357.2262.

3-Methyl-3-(3-(tri*iso*propylsilyl)prop-2-ynyl)isochroman-1-one (6e)



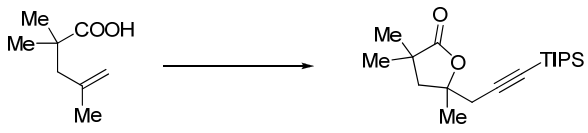
Column chromatography (SiO_2, PET/EtOAc 98:2) afforded product **6e** (115 mg, 0.322 mmol, 80% yield) as a colorless solid. R_f 0.72 (PET/EtOAc 5:1). Mp 71 – 73 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (dd, J = 7.7, 1.0 Hz, 1 H, ArH), 7.54 (td, J = 7.4, 1.4 Hz, 1 H, ArH), 7.38 (dt, J = 7.4, 0.5, Hz, 1 H, ArH), 7.22 (d, J = 7.4 Hz, 1 H, ArH), 3.33 (d, J = 16.3 Hz, 1 H, ArCH_2), 3.07 (d, J = 16.3 Hz, 1 H, ArCH_2), 2.68 (m, 2 H, CH_2C≡C), 1.56 (s, 3 H, CH_3), 1.08 – 1.03 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.4, 137.5, 134.0, 130.1, 128.1, 127.7, 124.6, 102.9, 84.5, 81.7, 36.5, 31.8, 25.3, 18.6, 11.2. IR ν 3330 (m), 3162 (m), 3067 (m), 3034 (m), 2943 (s), 2859 (s), 2177 (m), 2114 (m), 1727 (s), 1669 (m), 1649 (m), 1599 (m), 1550 (s), 1498 (m), 1463 (s), 1441 (m), 1385 (m), 1350 (m), 1314 (s), 1280 (s), 1226 (s), 1175 (m), 1114 (s), 1070 (s), 1034 (s), 885 (m), 845 (w), 798 (w), 746 (s), 677 (s); HRMS (ESI) calcd for $C_{22}H_{33}O_2Si^+$ (M+H) 357.2250; found: 356.2265.

2-(Benzyloxy)-3-methyl-3-(3-(tri*iso*propylsilyl)prop-2-ynyl)isoindolin-1-one (8a) and 3-methyl-3-(3-(tri*iso*propylsilyl)prop-2-ynyl)isobenzofuran-1(3*H*)-one *O*-benzyl oxime (8b)



Column chromatography (SiO_2, PET/EtOAc 19:1) afforded product **8a** (73 mg, 0.16 mmol, 41% yield) as a yellow solid and **8b** (49 mg, 0.11 mmol, 28% yield) as a yellow solid. Product **8a**: R_f 0.57 (PET/EtOAc 5:1). Mp 66-70 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J* = 7.6 Hz; Ar*H*), 7.61 – 7.52 (m, 4 H, Ph*H*), 7.71 – 7.35 (m, 4 H, Ar*H*, Ph*H*), 5.38 (d, *J* = 10.1 Hz, 1 H, *CH*$_2$OPh), 5.28 (d, *J* = 10.1 Hz, 1 H, *CH*$_2$OPh), 2.97 (d, *J* = 17.0 Hz, 1 H, *CH*$_2$C≡C), 2.71 (d, *J* = 17.0 Hz, 1 H, *CH*$_2$C≡C), 1.54 (s, 3 H, *CH*$_3$), 1.05 – 0.84 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.6, 146.4, 135.3, 132.0, 129.4, 129.1, 128.7, 128.5, 128.3, 123.6, 121.4, 102.5, 84.4, 79.0, 65.0, 29.5, 22.8, 18.4, 11.0. IR ν 3317 (broad, w), 3066 (w), 3034 (w), 2942 (s), 2892 (m), 2865 (s), 2249 (w), 2177 (m), 1713 (s), 1619 (w), 1464 (s), 1422 (w), 1375 (m), 1353 (w), 1319 (w), 1242 (w), 1219 (w), 1195 (w), 1161 (w), 1141 (w), 1141 (w), 1098 (w), 1065 (m), 1032 (m), 992 (m), 969 (m), 942 (m), 913 (s), 884 (s), 839 (w), 791 (w), 763 (m), 735 (s), 693 (s), 670 (s). HRMS (ESI) expected for $C_{28}H_{38}NO_2Si^+$ (M+H) 448.2672; found: 448.2678. Product **8b**: R_f 0.73 (PET/EtOAc 5:1). Mp 63 – 66 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 (d, *J* = 7.6 Hz; Ar*H*), 7.52 – 7.25 (m, 8 H, Ar*H*, Ph*H*), 5.13 (s, 2 H, *CH*$_2$OPh), 2.97 (d, *J* = 16.7 Hz, 1 H, *CH*$_2$C≡C), 2.82 (d, *J* = 16.7 Hz, 1 H, *CH*$_2$C≡C), 1.74 (s, 3 H, *CH*$_3$), 1.05 – 0.93 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.1, 147.0, 138.1, 130.5, 128.8, 128.5, 128.4, 128.2, 127.6, 121.7, 121.3, 102.3, 90.0, 84.1, 76.6, 32.9, 25.7, 18.5, 11.2. IR ν 3166 (w), 3065 (w), 3032 (s), 2941 (m), 2893 (s), 2865 (m), 2178 (sh), 1721 (sh), 1688 (s), 1662 (sh), 1493 (sh), 1466 (s), 1415 (sh), 1355 (m), 1304 (m), 1249 (w), 1209 (w), 1160 (w), 1122 (w), 1076 (sh), 1040 (s), 994 (sh), 964 (m), 914 (s), 884 (s), 838 (w), 807 (w), 756 (sh), 755 (s), 736 (s), 700 (s), 673 (s), 604 (m). HRMS (ESI) expected for $C_{28}H_{38}NO_2Si^+$ (M+H) 448.2672; found: 448.2660.

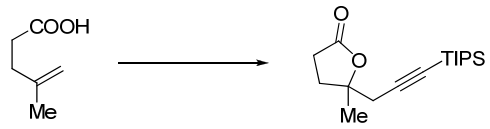
3,3,5-Trimethyl-5-(3-(tri*iso*propylsilyl)prop-2-ynyl)dihydrofuran-2(3H)-one (10a)



Column chromatography (SiO_2, PET/EtOAc 99:1) afforded product **10a** (91 mg, 0.28 mmol, 70% yield) as a yellow oil. R_f 0.69 (PET/EtOAc 5: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.66 (br m, 2 H, *CH*$_2$C≡C), 2.40 (d, *J* = 13.5 Hz, 1 H, *CH*$_2$C(CH$_3$)$_2$), 2.01 (d, *J* = 13.4 Hz, 1 H, *CH*$_2$C(CH$_3$)$_2$), 1.57 (s, 3 H, OC*CH*$_3$), 1.37 (s, 3 H, O=CC(*CH*$_3$)$_2$), 1.34 (s, 3 H, O=CC(*CH*$_3$)$_2$), 1.13-1.05 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.5, 102.8, 83.9, 81.2, 46.4, 40.8, 34.2, 27.8, 27.7, 27.0 18.6, 11.2. IR ν 2943 (s), 2894 (m), 2866 (s), 2176 (w), 1774

(s), 1463 (m), 1384 (w), 1290 (w), 1231 (m), 1203 (w), 1163 (w), 1089 (m), 1035 (w), 995 (w), 954 (w), 954 (w), 920 (w), 883 (m), 753 (w), 728 (w), 677 (s), 620 (m). HRMS (ESI) expected for $C_{19}H_{35}O_2Si^+$ (M+H) 323.2406; found: 323.2410.

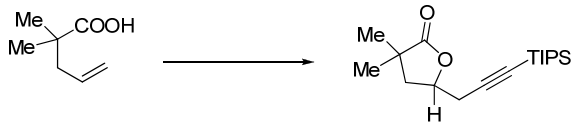
5-Methyl-5-(3-(triisopropylsilyl)prop-2-ynyl)dihydrofuran-2(3H)-one (10b)



9b **10b**

Column chromatography (SiO_2, PET/EtOAc 97:3) afforded product **10b** (86.5 mg, 0.287 mmol, 72% yield) as a yellow solid. R_f 0.57 (PET/EtOAc 4: 1). Mp 47 – 49°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 2.77-2.54 (m, 4 H, CH_2C≡C, CH_2C=O), 2.41 (ddd, J = 13.0, 10.1, 6.8 Hz, 1 H, CH_2C(CH_3)), 2.05 (ddd, J = 13.0, 9.7, 7.2 Hz, 1 H, CH_2C(CH_3)), 1.51 (s, 3 H, CH_3), 1.10-1.01 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.2, 102.6, 84.9, 84.1, 32.5, 32.0, 29.1, 26.1, 18.6, 11.2. IR ν 2943 (s), 2892 (m), 2866 (s), 2175 (m), 1778 (s), 1463 (m), 1419 (w), 1385 (w), 1295 (w), 1277 (w), 1248 (w), 1196 (s), 1172 (w), 1117 (m), 1087 (m), 1037 (m), 1013 (w), 994 (w), 946 (m), 918 (w), 884 (m), 735 (w), 677 (s). HRMS (ESI) expected for $C_{17}H_{31}O_2Si^+$ (M+H) 295.2093; found: 295.2079.

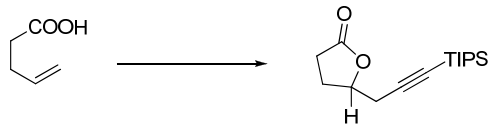
3,3-Dimethyl-5-(3-(triisopropylsilyl)prop-2-ynyl)dihydrofuran-2(3H)-one (10c)



9c **10c**

Column chromatography (SiO_2, PET/DCM/EtOAc 96: 3: 1) afforded product **10c** (94 mg, 0.30 mmol, 76% yield) as a yellow oil. R_f 0.39 (PET/EtOAc 10: 1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.54 (m, 1 H, CH), 2.75 (dd, J = 16.9, 4.4 Hz, 1 H, CH_2C≡C), 2.66 (dd, J = 16.9, 7.0 Hz, 1 H, CH_2C≡C), 2.19 (dd, J = 12.8, 6.1 Hz, 1 H, CH_2C(CH_3)$_2$), 2.05 (dd, J = 12.8, 9.7 Hz, 1 H, CH_2C(CH_3)$_2$), 1.29 (s, 3 H, CH_3), 1.26 (s, 3 H, CH_3), 1.08-1.01 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 181.3, 101.6, 84.2, 74.1, 42.0, 40.4, 26.2, 24.8, 24.7, 18.6, 11.1. IR ν 2943 (m), 2893 (w), 2866 (m), 2178 (w), 1777 (s), 1464 (m), 1384 (w), 1349 (w), 1231 (w), 1206 (m), 1147 (m), 1121 (m), 1074 (w), 1037, 1016 (m), 918 (m), 884 (m), 739 (w), 676 (s), 629 (m). HRMS (ESI) expected for $C_{18}H_{33}O_2Si^+$ (M+H) 309.2250; found: 309.2251.

5-(3-(triisopropylsilyl)prop-2-ynyl)dihydrofuran-2(3H)-one (10d)



9d **10d**

Column chromatography (SiO_2, PET/EtOAc 95: 5) afforded product **10d** (92 mg, 0.33 mmol, 82% yield – 95% purity according to ^{1}H-NMR) as a yellow oil. R_f 0.35 (PET/EtOAc 4:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.66 (qd, *J* = 7.0, 4.4 Hz, 1 H, *CH*), 2.85-2.51 (m, 4 H, CH_2C=O, CH_2C≡C), 2.43 (m, 1 H, CH_2), 2.20 (m, 1 H, CH_2), 1.20-0.95 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.7, 101.6, 84.3, 77.7, 28.4, 26.52, 26.5, 18.5, 11.0. IR ν 2943 (s), 2894 (m), 2866 (s), 2176 (w), 1781 (s), 1463 (m), 1382 (w), 1352 (w), 1291 (w), 1239 (w), 1177 (s), 1150 (sh), 1049 (sh), 1019 (s), 998 (m), 919 (m), 884 (s), 839 (w), 797 (w), 732 (m), 678 (s), 660 (s), 632 (m). HRMS (ESI) expected for $C_{16}H_{29}O_2Si^+$ (M+H) 281.1937; found: 281.1939.

6. Mechanistic Investigations

Stoichiometric NMR investigations

Experiment 1: Reagent **3d** (17 mg, 0.040 mmol, 1.0 equiv) was added to a solution of Pd (hfacac)$_2$ (21 mg, 0.040 mmol, 1.0 equiv) in CD_2Cl_2 (1 mL). ^{1}H-NMR spectra were acquired 10 min, 40 min and 3 h after mixing, whereas full decomposition of **3d** was observed.

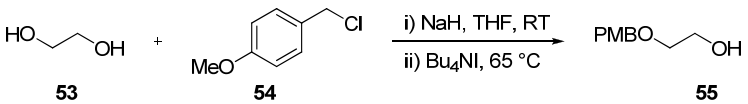
Experiment 2: Methylallyl-phenol (**1a**) (6 mg, 0.04 mmol, 1 equiv) was added to a solution of Pd (hfacac)$_2$ (21 mg, 0.040 mmol, 1.0 equiv) in CD_2Cl_2 (1 mL). ^{1}H-NMR spectra were acquired 10 min, 40 min and 8 h after mixing. Partially isomerization of the double bond into conjugation was observed.

Experiment 3: Reagent **3d** (17 mg, 0.040 mmol, 1.0 equiv) was added to a solution of Pd (hfacac)$_2$ (21 mg, 0.040 mmol, 1.0 equiv) in CD_2Cl_2 (1 mL). After 6 min Methylallyl phenol (**1a**) (6 mg, 0.04 mmol, 1 equiv) was added. ^{1}H-NMR spectra were acquired 5 minutes and 2 hours after the addition of **3d**. After 2 hours complete conversion to product **4b** was observed.

Experiment 4: Methylallyl phenol **1a** (6 mg, 0.04 mmol, 1 equiv) was added to a solution of Pd (hfacac)$_2$ (21 mg, 0.040 mmol, 1.0 equiv) in CD_2Cl_2 (1 mL). After 50 min, ^{1}H-NMR showed partial isomerization of the double bond. After 55 min reagent **3d** (17 mg, 0.040 mmol, 1.0 equiv) was added. ^{1}H-NMR spectra were acquired 5 minutes and 2 hours after the addition of **3d**. After 2 hours complete conversion to product **4b** was observed.

Preparation and reaction of ^{13}C-labeled reagent 3d'

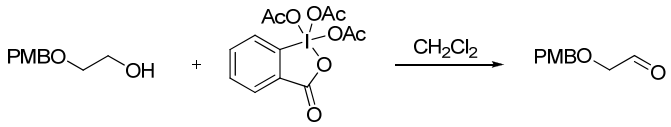
2-(4-Methoxybenzyloxy)ethanol (55)



53 **54** **55**

Following a reported procedure,[27] sodium hydride (60% in mineral oil, 0.70 g, 17 mmol, 1.0 equiv) was added to a solution of ethylene glycol (**53**) (freshly distilled from drierite (p = 0.3 mbar, T = 46 °C), 2.8 mL, 50 mmol, 3.0 equiv) in THF (30 mL). After stirring 30 min at RT, 4-methoxybenzyl chloride (**54**) (2.60 g, 16.6 mmol, 1.00 equiv) and Bu_4NI (0.61 g, 1.7 mmol, 0.10 equiv) were added, and the reaction mixture was heated to reflux. After 4.5 h, the reaction mixture was cooled to RT, the reaction was quenched with sat. NH_4Cl (30 mL) and extracted with Et_2O (3 x 30 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (PET/AcOEt 5/1-1/1) to yield protected alcohol **55** (2.54 g, 13.9 mmol, 84%) as a yellow oil. R_f (PET/AcOEt 1/1, $KMnO_4$) 0.25. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 7.27 (dm, J = 8.2 Hz, 2 H, ArH), 6.89 (dm, J = 8.6 Hz, 2 H, ArH), 4.49 (s, 2 H, benzyl CH_2), 3.81 (s, 3 H, OCH_3), 3.74 (t, J = 4.3 Hz, 2 H, CH_2OPMB), 3.57 (m, 2 H, CH_2OH), 2.08 (br s, 1 H, OH). ^{1}H NMR corresponded to the literature values.[22]

2-(4-Methoxybenzyloxy)acetaldehyde (57)

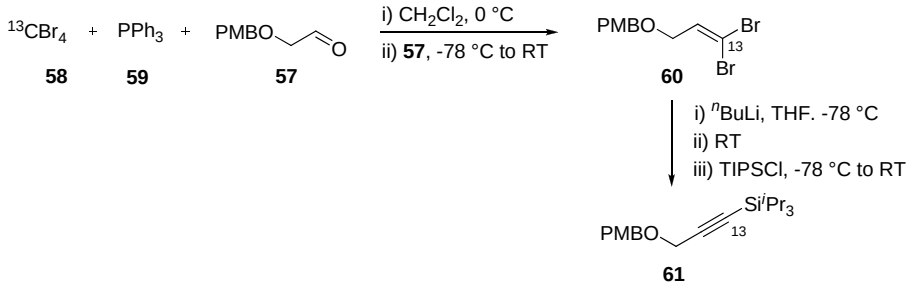


55 **56** **57**

Following a reported procedure,[28] Dess-Martin Periodinane (**56**) (0.53 g, 1.3 mmol, 1.1 equiv) was added to a solution of alcohol **55** (0.21 g, 1.2 mmol, 1.0 equiv) in wet CH_2Cl_2 (9 mL). After stirring 2.5 h at RT, the reaction was quenched with sat. $NaHCO_3$ (10 mL) and sat. sodium thiosulfate solution (10 mL) and the mixture was stirred vigorously for 10 min until two clear layers were obtained. The layers were separated and the water layer was extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give aldehyde **57** (0.21 g, 1.2 mmol, quant.) as a yellow oil, which was used immediately in the next step without further purification. R_f (PET/AcOEt 1/1 , $KMnO_4$) 0.35. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 9.71 (t, J = 0.9 Hz, CHO), 7.29 (dm, J = 8.8 Hz, 2 H, ArH), 6.90 (dm, J = 8.8 Hz, 2 H, ArH), 4.57 (s, 2 H, benzyl CH_2), 4.07 (d, J = 0.9 Hz, 2 H, CH_2CHO), 3.81 (s, 3 H, OCH_3). ^{1}H NMR corresponded to the literature values.[27]

Labeled 1-((3,3-dibromoallyloxy)methyl)-4-methoxybenzene (60) and tri*iso*propyl(3-(4-methoxybenzyloxy)prop-1-ynyl)silane (61)

(27) Masutani, K.; Minowa, T.; Hagiwara, Y.; Mukaiyama, T. *Bull. Chem. Soc. Jpn.* **2006**, *79*, 1106.
(28) Collins, I.; Caldwell, J.; Fonseca, T.; Donald, A.; Bavetsias, V.; Hunter, L. J. K.; Garrett, M. D.; Rowlands, M. G.; Aherne, G. W.; Davies, T. G.; Berdini, V.; Woodhead, S. J.; Davis, D.; Seavers, L. C. A.; Wyatt, P. G.; Workman, P.; McDonald, E. *Bioorg. Med. Chem.* **2006**, *14*, 1255.



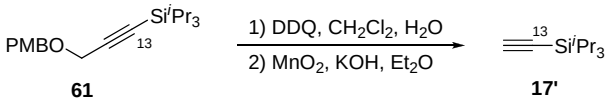
Following a slightly modified literature procedure,[29] a solution of PPh_3 (**57**) (1.6 g, 6.0 mmol, 2.0 equiv) in CH_2Cl_2 (9 mL) was added to a solution of CBr_4 (**58**) (1.0 g, 3.0 mmol, 1.0 equiv, 20% ^{13}C, prepared from 0.80 g natural CBr_4 and 0.20 g 99% ^{13}C-enriched CBr_4) in CH_2Cl_2 (12 mL) at 0 °C over 15 min. After stirring for 15 min at 0 °C, the yellow-orange solution was cooled to -78 °C and a solution of aldehyde **57** (freshly synthesized, 0.66 g, 3.6 mmol, 1.2 equiv) in CH_2Cl_2 (9 mL) was added over 10 min, whereas the reaction mixture turned dark red-brown. The reaction mixture was left to warm to RT over 17 h, quenched with sat. $NaHCO_3$ (30 mL) and extracted with CH_2Cl_2 (3 x 30 mL). The combined organic layers were washed with brine (30 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (PET/CH_2Cl_2 3/1-1.5/1) to yield dibromide **60** (501 g, 1.55 mmol, 52%) as a slightly yellow oil, which was used directly in the next step. R_f (PET/ CH_2Cl_2 2/1, $KMnO_4$) 0.30. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.28 (dm, J =8 .6 Hz, 2 H, ArH), 6.90 (dm, J = 8.6 Hz, 2 H, ArH), 6.64 (tm, J = 6.1 Hz, 1 H, alkene H), 4.46 (s, 2 H, benzyl CH_2), 4.04 (m, 2 H, alkene CH_2), 3.81 (s, 3 H, OCH_3). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.3, 135.6, 129.5, 129.4, 113.8, 91.3 (labeled 20x more intensive), 72.2, 69.4, 55.2.

Following a literature procedure,[30] ^{n}BuLi (2.5 M in hexane, 1.4 mL, 3.4 mmol, 2.2 equiv) was added dropwise to a solution of dibromide **60** (0.50 g, 1.5 mmol, 1.0 equiv) in THF (9 mL) at -78 °C. The yellow solution was stirred 1 h at -78 °C and 1 h at RT. After cooling to -78 °C, TIPSCl (0.43 mL, 2.0 mmol, 1.3 equiv) was added and the reaction was left to warm to RT over 12 h. The reaction was quenched with sat. $NaHCO_3$ (10 mL) and extracted with Et_2O (3 x 20 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. The crude product was purified by flash column chromatography (PET/CH_2Cl_2 4/1-2/1) to yield alkyne **61** (372 g, 1.12 mmol, 72%) as a colorless oil. Comparison of the ^{13}CNMR with an unlabeled sample (synthesized following the same procedure) showed 20% ^{13}C incorporation at the indicated position only. R_f (PET/CH_2Cl_2 2/1, $KMnO_4$) 0.35. ^1H NMR ($CDCl_3$, 400 MHz) δ 7.30 (dm, J = 8.4 Hz, 2 H, ArH), 6.89 (dm, J = 8.6 Hz, 2 H, ArH), 4.59 (s, 2 H, benzyl CH_2), 4.19 (s, 2 H, alkyne CH_2), 3.81 (s, 3 H, OCH_3), 1.12 (m, 21 H, TIPS). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 159.3, 129.8, 129.5, 113.8, 103.4, 87.7 (labeled 20x more intensive), 70.6, 57.4, 55.2, 18.6, 11.1. IR ν 2961 (w), 2944 (w), 2931 (w), 2866 (w), 2171 (w), 1663 (w), 1614 (w), 1515 (w), 1463 (w), 1444 (w), 1378

(29) Paquette, L. A.; Chang, J. Y.; Liu, Z. S. *J. Org. Chem.* **2004**, *69*, 6441.
(30) Corey, E. J.; Fuchs, P. L. *Tetrahedron Lett.* **1972**, 3769.

(w), 1250 (w), 1078 (m), 1036 (w), 907 (s), 730 (s), 651 (m). HRMS(ESI) calcd for $C_{15}H_{16}O_3^+$ (M+H) 333.2250, found 333.2254. Isotope repartition: expected for about 20% incorporation was obtained.

Labeled tri*iso*propyl acetylene (17')

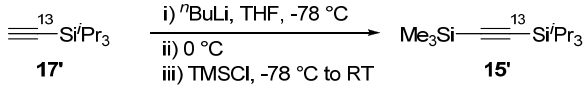


61 **17'**

Following a literature procedure,[31] DDQ (0.38 g, 1.7 mmol, 1.5 equiv) was added to a solution of protected alcohol **61** (372 mg, 1.12 mmol, 1.00 equiv) in CH_2Cl_2 (11 mL) and water (1.1 mL) at 0 °C. The reaction mixture was stirred 15 min at 0 °C and 3 h at RT. The resulting dark red thick suspension was quenched with sat. $NaHCO_3$ (20 mL) and extracted with CH_2Cl_2 (3 x 20 mL). The combined organic layers were washed with sat. $NaHCO_3$ (20 mL) and brine (20 mL), dried over $MgSO_4$ and the solvent was removed under reduced pressure. TLC (PET/AcOEt 6/1, $KMnO_4$) showed a mixture of two products, which were shown to be the corresponding propargylic alcohol (R_f = 0.50) and anisaldehyde (R_f = 0.45) by ^{1}H NMR. This mixture was directly used as such in the next step.

Following a literature procedure,[32] the obtained mixture was diluted in Et_2O (14 mL) and MnO_2 (Aldrich activated, 1.2 g, 13 mmol, 12 equiv) and KOH (freshly grounded, 0.38 g, 6.8 mmol, 6.0 equiv) were added in 4 portions every hour. After stirring for further 3 h, TLC (PET/AcOEt 6/1, $KMnO_4$) showed complete conversion and the reaction mixture was filtered over SiO_2 and the filter cake was washed with Et_2O (50 mL). The solvent was removed under reduced pressure and the crude mixture was purified by flash column chromatography (PET) to yield alkyne **17'** (167 mg, 0.915 mmol, 82%) as a colorless oil. Comparison of the ^{13}CNMR with an unlabeled sample (synthesized following the same procedure) showed 20% ^{13}C incorporation at the indicated position only. R_f (PET, $KMnO_4$) 0.80. ^{1}H NMR (CD_2Cl_2, 400 MHz) δ 2.38 (s, 1 H, alkyne H), 1.07 (m, 21 H, TIPS). ^{13}C NMR (CD_2Cl_2, 100 MHz) δ 94.9, 86.2 (labeled 20x more intensive), 18.3, 11.1.

Labeled tri*iso*propyl((trimethylsilyl)ethynyl)silane (15')



17' **15'**

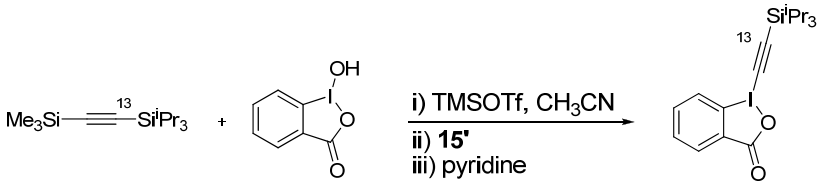
^{n}BuLi (2.5 M in hexane, 0.44 mL, 1.1 mmol, 1.2 equiv) was added to a solution of acetylene **17'** (167 mg, 0.915 mmol, 1.00 equiv) in THF (2 mL) at -78 °C. The reaction mixture was stirred 15 min at 0 °C and the yellow solution was cooled back to -78 °C. TMSCl (freshly distilled, 0.15 mL, 1.2 mmol, 1.3 equiv) was added and the colorless solution was left to warm to RT over 6 h. The reaction was quenched with sat. NH_4Cl (3 mL) and extracted with Et_2O (3 x 10 mL). The combined organic layers were washed with brine (5 mL), dried over

(31) Dimopoulos, P.; Athlan, A.; Manaviazar, S.; George, J.; Walters, M.; Lazarides, L.; Aliev, A. E.; Hale, K. J. *Org. Lett.* **2005**, *7*, 5369.

(32) Kukula, H.; Veit, S.; Godt, A. *Eur. J. Org. Chem.* **1999**, 277.

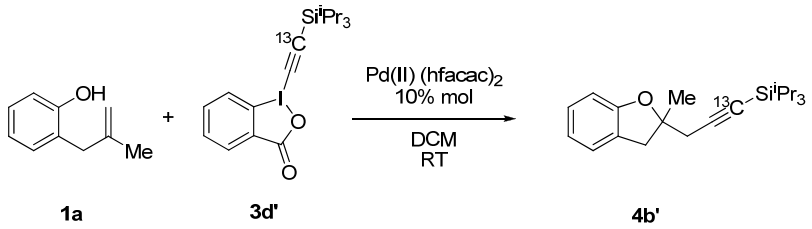
$MgSO_4$ and the solvent was removed under reduced pressure. The crude mixture was purified by flash column chromatography (PET) to yield protected alkyne **15'** (184 g, 0.722 mmol, 79%) as a colorless oil. Comparison of the ^{13}C NMR with an unlabeled sample showed 20% ^{13}C incorporation at the indicated position only. R_f (PET, $KMnO_4$) 0.80. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.07 (m, 21 H, TIPS), 0.17 (s, 9 H, TMS). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 116.2, 110.1 (labeled 20x more intensive), 18.6, 11.1, 0.0. 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). ^1H NMR corresponded to the literature values.[4]

Labeled 1-[(tri*iso*propyllsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (3d')



Following a slightly modified literature procedure,[3] TMSOTf (freshly distilled, 0.15 mL, 0.82 mmol, 1.1 equiv) was added to a suspension of iodinane **13** (freshly synthesized, 0.19 g, 0.72 mmol, 1.0 equiv) in CH_3CN (6.5 mL). After 10 min, a solution of acetylene **15'** (0.18 g, 0.72 mmol, 1.0 equiv) in CH_2Cl_2 (1.0 mL) was added to the slightly yellow solution. After stirring 15 min at RT, pyridine (70 µL, 0.87 mmol, 1.2 equiv) was added and the solvent was removed under reduced pressure below 30 °C. The reaction mixture was diluted with CH_2Cl_2 (15 mL) and washed with 1 M HCl (5 mL). The water layer was extracted with CH_2Cl_2 (2 x 5 mL) and the combined organic layers were washed with sat. Na_2CO_3 (2 x 10 mL). The combined basic aqueous layers were extracted with CH_2Cl_2 (10 mL) and the combined organic layers were dried over $MgSO_4$ and the solvent was removed under reduced pressure to give iodinane **3d'** (>95% pure by ^1HNMR, containing traces of acetylene **15'**, 259 mg, 0.604 mmol, 84%) as a slightly yellow solid. Comparison of the ^{13}C NMR with an unlabeled sample showed 20% ^{13}C incorporation at the indicated position only. ^1H NMR ($CDCl_3$, 400 MHz) δ 8.40 (m, 1 H, Ar H), 8.28 (m, 1 H, Ar H), 7.74 (m, 2 H, Ar H), 1.13 (m, 21 H, TIPS). ^{13}C NMR ($CDCl_3$, 100 MHz) δ 166.3, 134.6, 132.4, 131.5, 131.4, 126.0, 115.6, 114.1 (labeled 20x more intensive), 64.7, 18.4, 11.1.

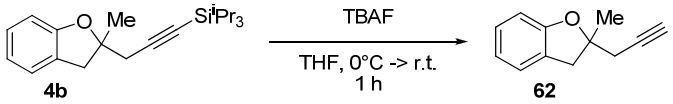
Labeled tri*iso*propyl-[3-(2-methyl-2,3-dihydro-benzofuran-2-yl)-prop-1-ynyl]-silane (4b')



Palladium (II) hexafluoroacetylacetonate (11 mg, 0.020 mmol, 0.10 equiv.) was dissolved in dichloromethane (5 mL). 2-(Methylallyl)phenol **(1a)** (30 mg, 0.20 mmol, 1.0 equiv) was then added, followed

by ^{13}C labeled 1-((tri*iso*propylsilyl)ethynyl)-1,2-benziodoxol-3(1*H*)-one (**3d'**) (1:1 mixture with non-labeled **3d**: 0.10 g, 0.24 mmol, 1.2 equiv overall). The resulting solution was stirred under N_2 at room temperature overnight. DCM was then removed under reduced pressure and the residue was treated with $NaHCO_3$ (saturated solution, 6 mL) and brine (6 mL). The mixture was extracted with diethyl ether (3 x 15 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. Column chromatography (SiO_2, PET/DCM 98:2) afforded product **4b'** (51 mg, 0.15 mmol, 75% yield) as a yellow oil. ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.7, 128.0, 126.6, 125.1, 120.2, 109.5, 104.3, 87.4, 82.9, 40.6, 32.5, 26.2, 18.6, 11.3. Intensity of peak at δ 82.9 was increased approximately 10 times when compared with the corresponding peak for the non-labeled compound **4b**.

2-Methyl-2-(prop-2-ynyl)-2,3-dihydrobenzofuran (62)



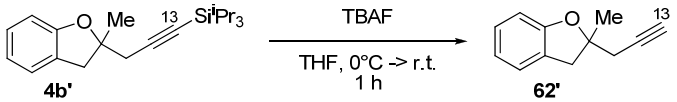
4b **62**

Following a reported procedure,[33] tri*iso*propyl-[3-(2-methyl-2,3-dihydro-benzofuran-2-yl)-prop-1-ynyl]-silane (**4b**) (197 mg, 0.600 mmol, 1.0 equiv) was dissolved in THF (2.5 mL) and the resulting solution was stirred at 0 °C for 5 min. TBAF (1 M solution in THF, 1.2 mL, 1.2 mmol, 2.0 equiv) was then added and the mixture was stirred a 0 °C for 50 min. The reaction mixture was allowed to warm to room temperature and stirred for 10 min. NH_4Cl (saturated solution, 25 mL) was added followed by water (17 mL). The aqueous layer was extracted with Et_2O (3 x 20 mL) and the combined organic layers were washed with NH_4Cl (saturated solution, 25 mL) and brine (25 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography (SiO_2, PET/EtOAc 99:1) afforded 2-methyl-2-(prop-2-ynyl)-2,3-dihydrobenzofuran (**62**) (80 mg, 0.46 mmol, 77% yield) as a colorless oil. R_f 0.82 (PET/EtOAc 10:1). ^1H NMR (400 MHz, $CDCl_3$) δ 7.18-7.09 (m, 2 H, Ar*H*), 6.85 (t, *J* = 7.4 Hz, 1 H, Ar*H*), 6.77 (d, *J* = 8.1 Hz, 1 H, ArH), 3.29 (d, *J* = 15.6 Hz, 1 H, Ar*CH*$_2$), 3.02 (d, *J* = 15.8 Hz, 1 H, Ar*CH*$_2$), 2.61 (d, *J* = 2.6 Hz, 2 H, C≡C*CH*$_2$), 2.03 (t, *J* = 2.7 Hz, 1 H, C≡C*H*), 1.59 (s, 3 H, *CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3 (aromatic C), 128.0 (aromatic CH), 126.3 (aromatic C), 125.0 (aromatic CH), 120.3 (aromatic CH), 109.6 (aromatic CH), 86.8 (quaternary CO), 80.2 (alkynyl C), 70.5 (alkynyl CH), 40.6 (CH_2), 30.9 (CH_2), 25.8 (CH_3). IR ν 3297 (m), 3053 (m), 2974 (m), 2931 (m), 2861 (m), 2651 (w), 2650 (w), 2562 (w), 2121 (w), 1691 (s), 1599 (m), 1576 (sh), 1482 (s), 1460 (s), 1409 (m), 1380 (m), 1325 (m), 1302 (sh), 1271 (sh), 1240 (s), 1186 (w), 1144 (w), 1116 (w), 1070 (m), 1017 (w), 957 (w), 920 (sh), 886 (s), 859 (sh), 786 (m), 749 (s), 711 (m), 649 (s). MS (EI) found for $C_{12}H_{12}O^+$ (M) 172. DEPT experiments (see spectra) was not conclusive to differentiate definitively the two acetylene carbons at 80.2 and 70.5 ppm, as even the quaternary carbon displayed a significant signal in all DEPT experiments. To confirm further the assignment, **62** was deprotonated with ^{n}BuLi in THF and the

(33) J. Bian, M. Van Wingerden, J. M. Ready *J. Am. Chem. Soc.* **2006**, *128*, 7428.

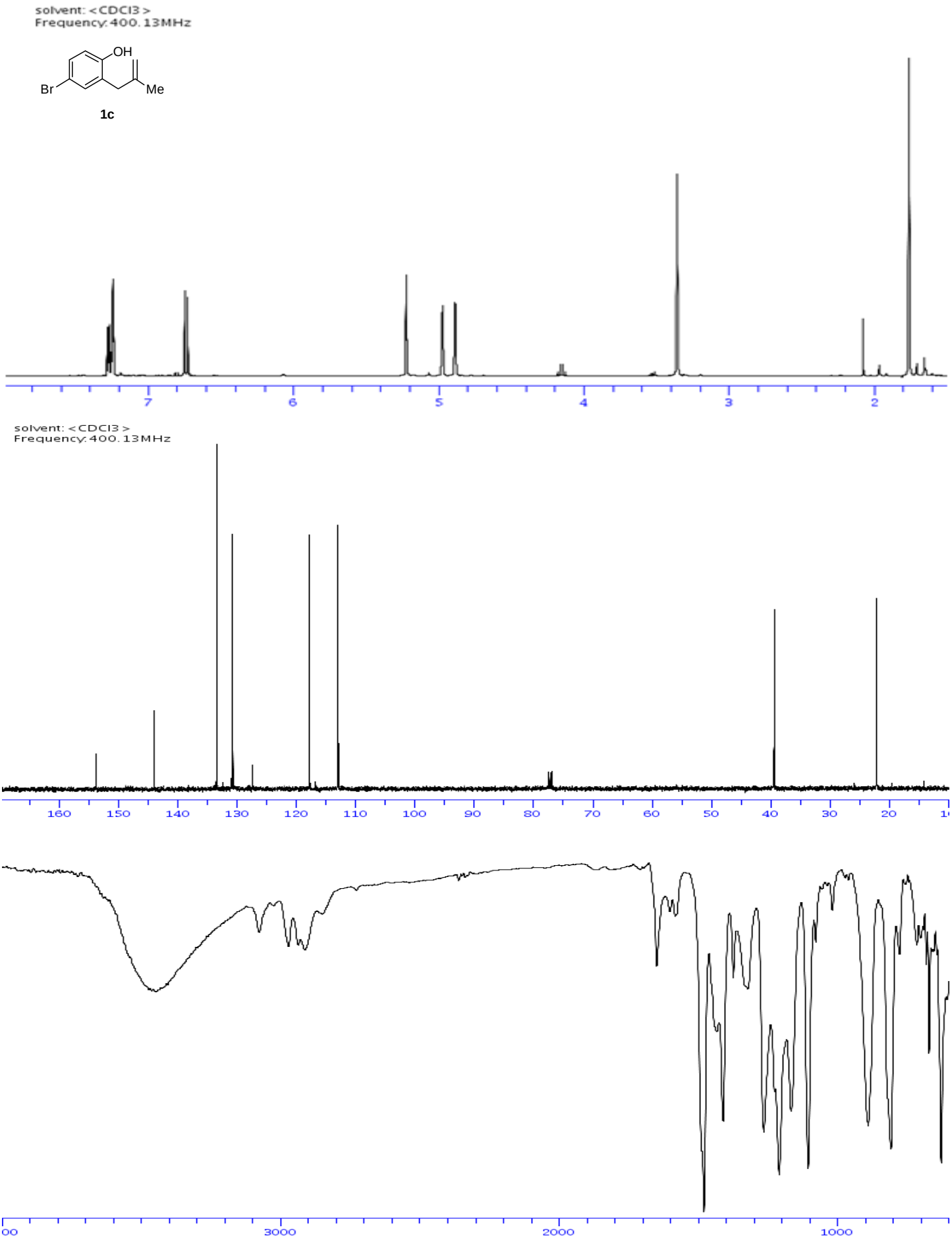
resulting organolithium was quenched with D_2O. The obtained C-D coupling was much larger at 70.2 ppm (39 Hz vs 7.7 Hz), confirming definitively this carbon to be the terminal one: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16 (d, *J* = 8.2 Hz, 1 H, Ar*H*), 7.12 (d, *J* = 7.7 Hz, 1 H, Ar*H*), 6.86 (t, *J* = 7.4 Hz, 1 H, Ar*H*), 6.78 (d, *J* = 8.1 Hz, 1 H, Ar*H*), 3.30 (d, *J* = 15.8 Hz, 1 H, Ar*CH*$_2$), 3.03 (d, *J* = 15.8 Hz, 1 H, Ar*CH*$_2$), 2.62 (s, 2 H, C≡C*CH*$_2$), 1.61 (s, 3 H, *CH*$_3$). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.5, 128.0, 126.4, 125.1, 120.3, 109.6, 86.9, 79.7 (t, ^2J(C,D)= 7.7 Hz, *C*≡CD), 70.2 (t, ^1J(C,D)=39 Hz, C≡*C*D), 40.7, 30.9, 25.7.

Labeled 2-methyl-2-(prop-2-ynyl)-2,3-dihydrobenzofuran (62')



The same procedure as for compounds **62** was used to prepare the ^{13}C labeled compound **62'**. ^{13}C labeled tri*iso*propyl-[3-(2-methyl-2,3-dihydro-benzofuran-2-yl)-prop-1-ynyl]-silane (**4b'**) (51 mg, 0.15 mmol, 1.0 equiv) was dissolved in THF (0.7 mL) and the resulting solution was stirred at 0 °C for 5 min. TBAF (1 M solution in THF, 0.3 mL, 0.3 mmol, 2.0 equiv) was then added and the mixture was stirred a 0 °C for 50 min. The reaction mixture was allowed to warm to room temperature and stirred for 10 min. NH_4Cl (saturated solution, 12 mL) was added followed by water (4 mL). The aqueous phase was extracted with Et_2O (3 x 5 mL) and the combined organic layers were washed with NH_4Cl (saturated solution, 12 mL) and brine (12 mL), dried over $MgSO_4$, filtered and concentrated under reduced pressure. Purification by column chromatography (SiO_2, PET/EtOAc 99:1) afforded ^{13}C labeled 2-methyl-2-(prop-2-ynyl)-2,3-dihydrobenzofuran (**62'**) (19 mg, 0.11 mmol, 71% yield) as a colorless oil. ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.3 (aromatic C), 128.0 (aromatic CH), 126.3 (aromatic C), 125.0 (aromatic CH), 120.3 (aromatic CH), 109.6 (aromatic CH), 86.8 (alkynyl C), 80.2 (quaternary C), 70.5 (10x more intensive, alkynyl CH), 40.6 (CH_2), 30.9 (CH_2), 25.8 (CH_3).

7. Spectra of New Compounds.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Me
1c
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6
5
4
3
2
solvent: <CDCl3 >
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150
140
130
120
110
100
90
80
70
60
50
40
30
20
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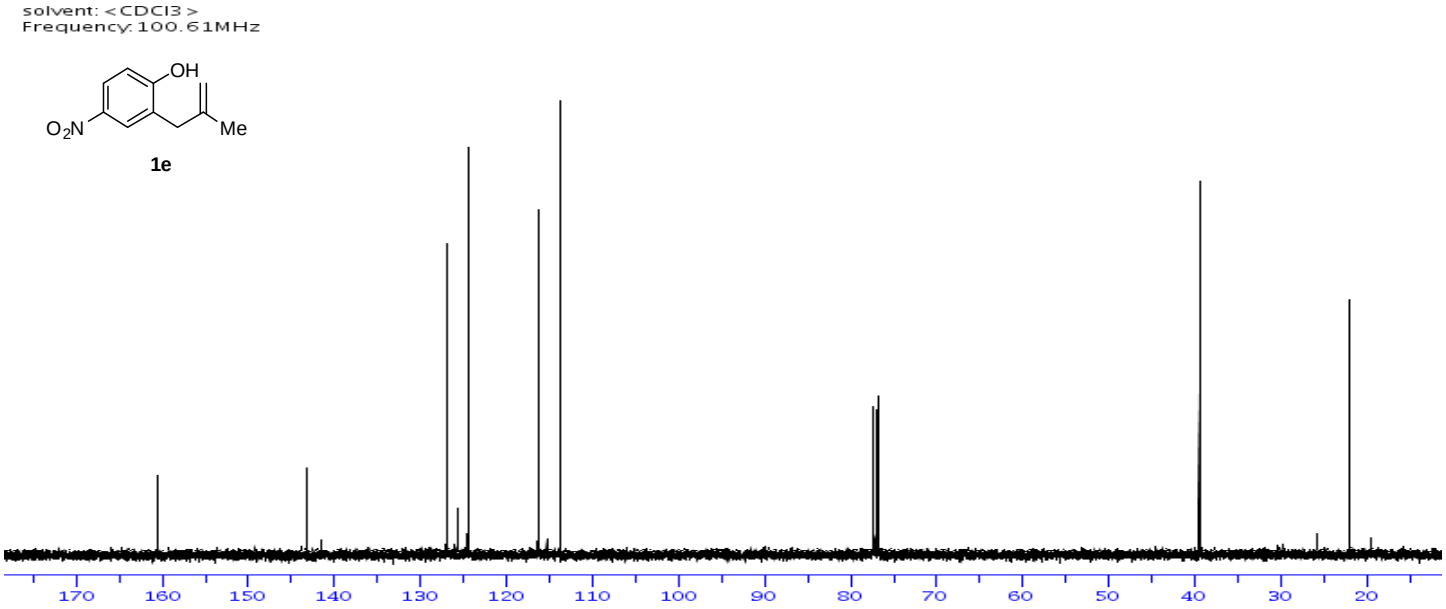
3000
2000
1000


solvent: <CDCl3 >
Frequency: 100.61MHz
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O2N
Me
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140
130
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100
90
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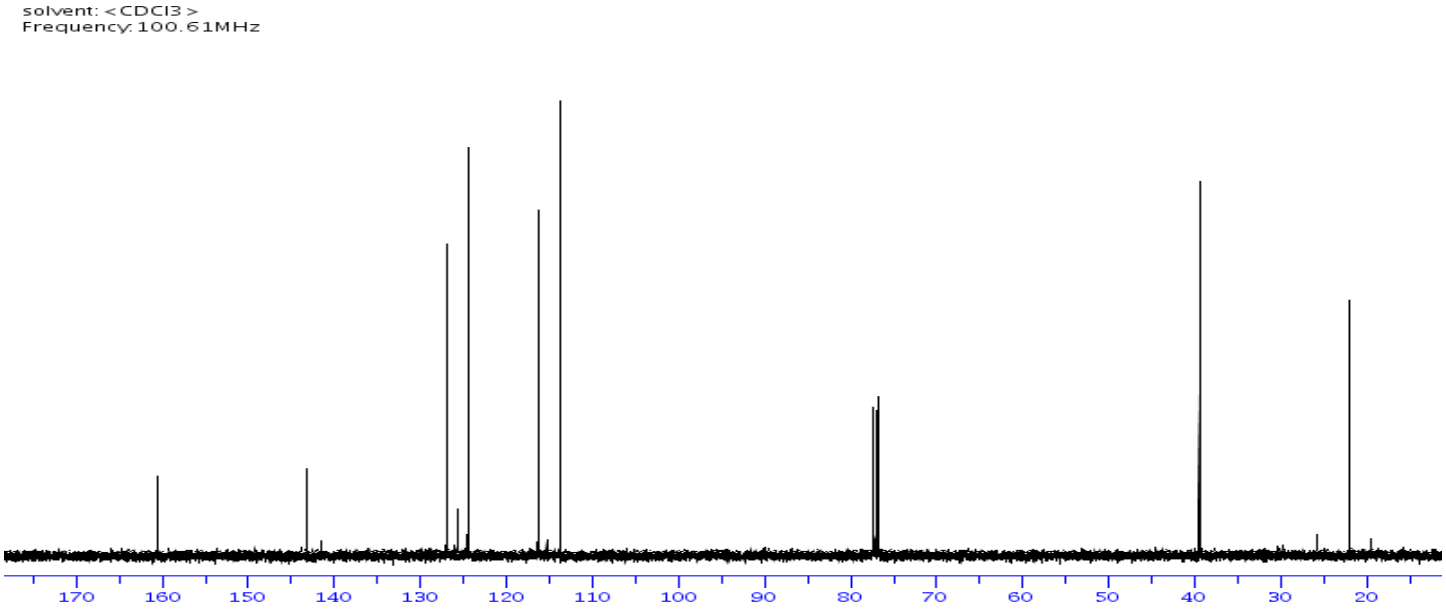
70
60
50
40
30
20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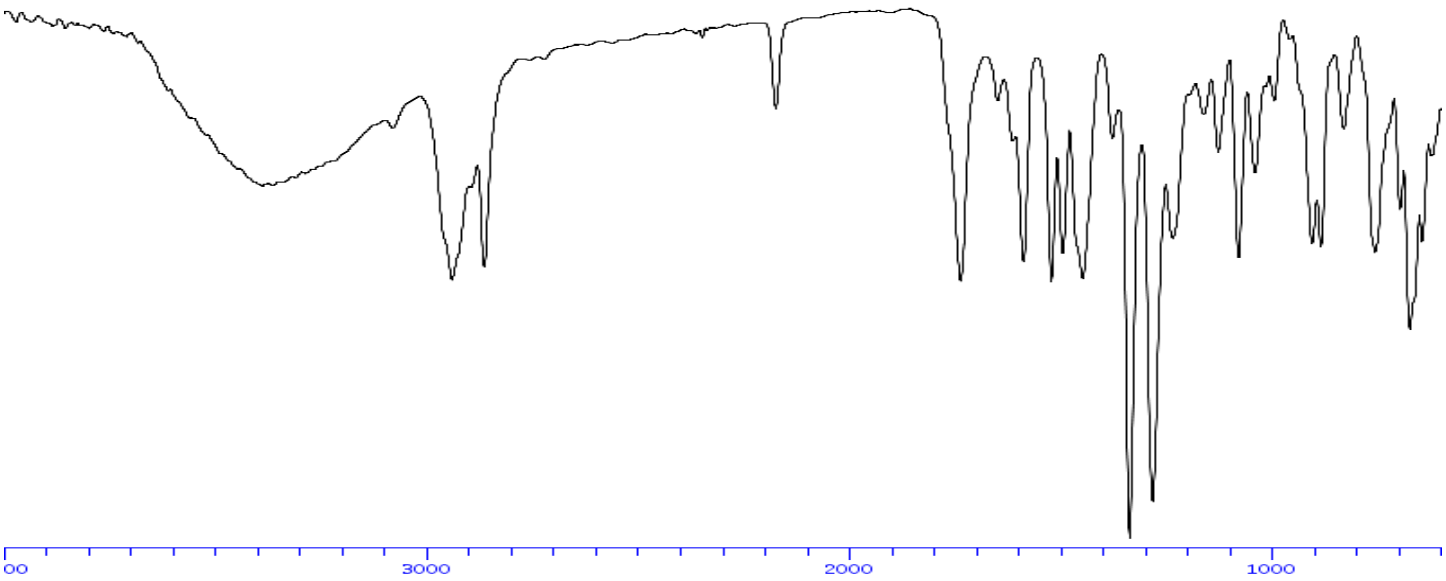
30
20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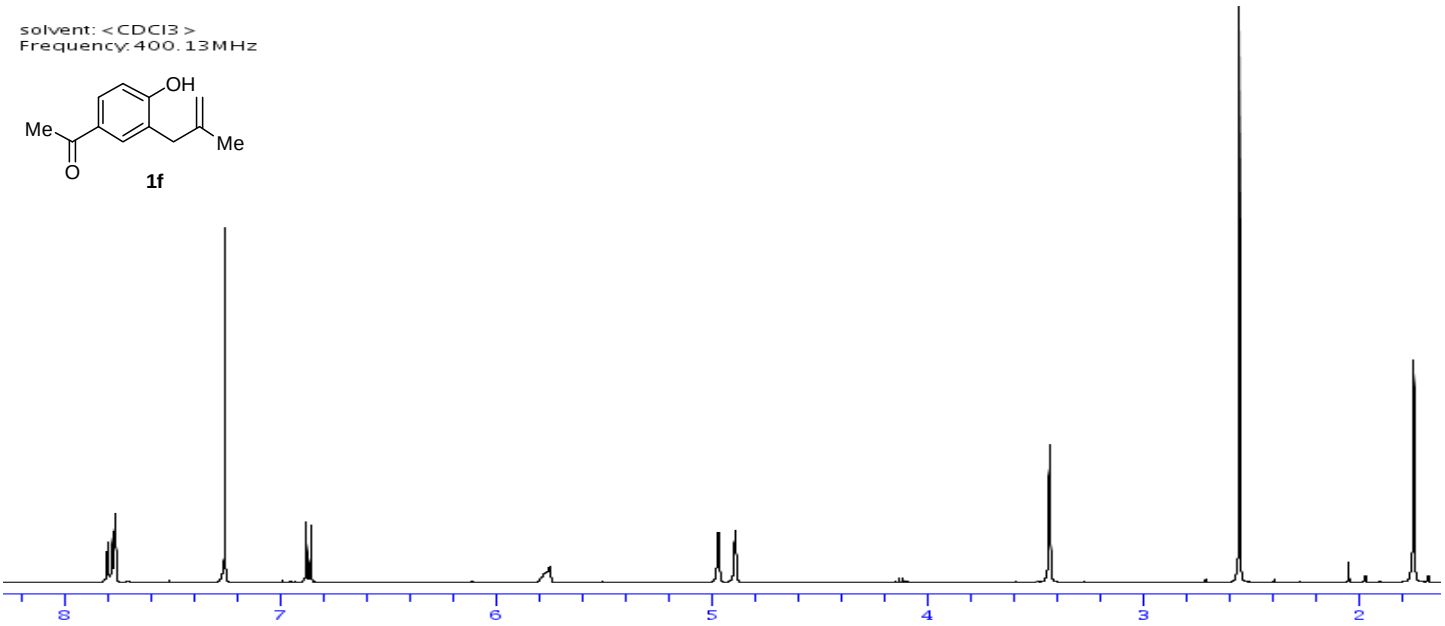
3000
2000
1000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OH
Me
Me
O
1f
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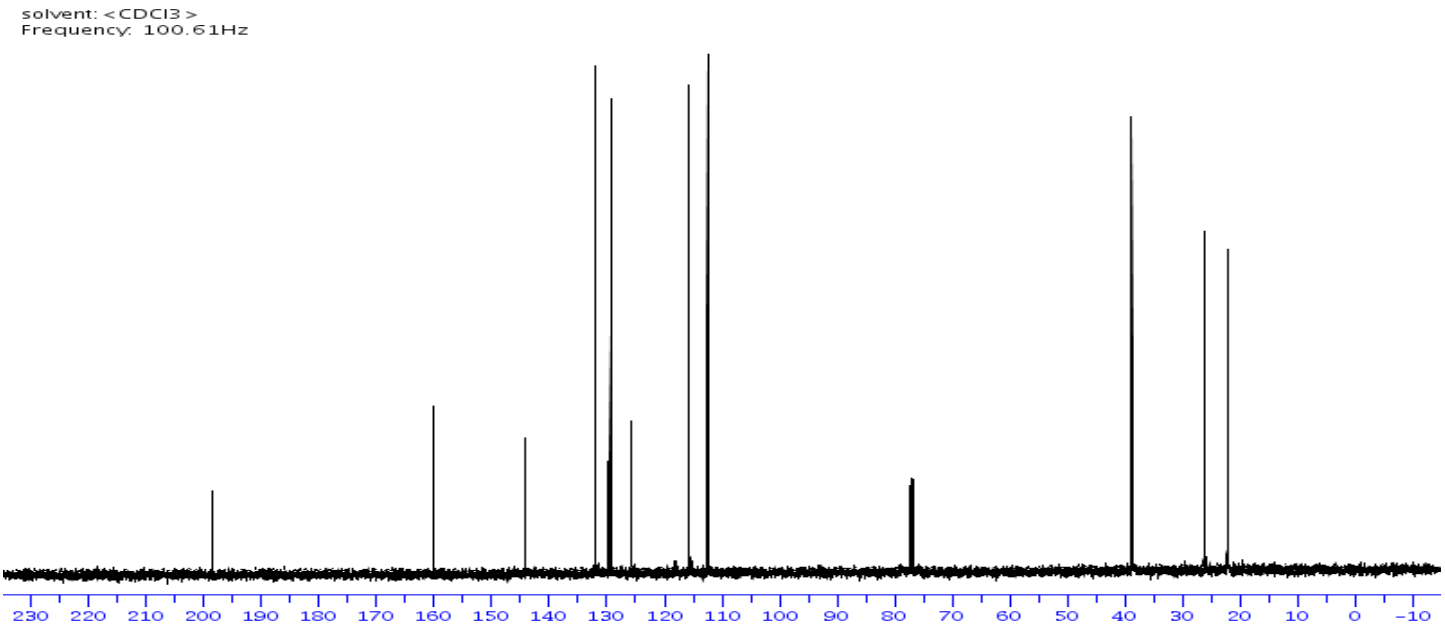
3
2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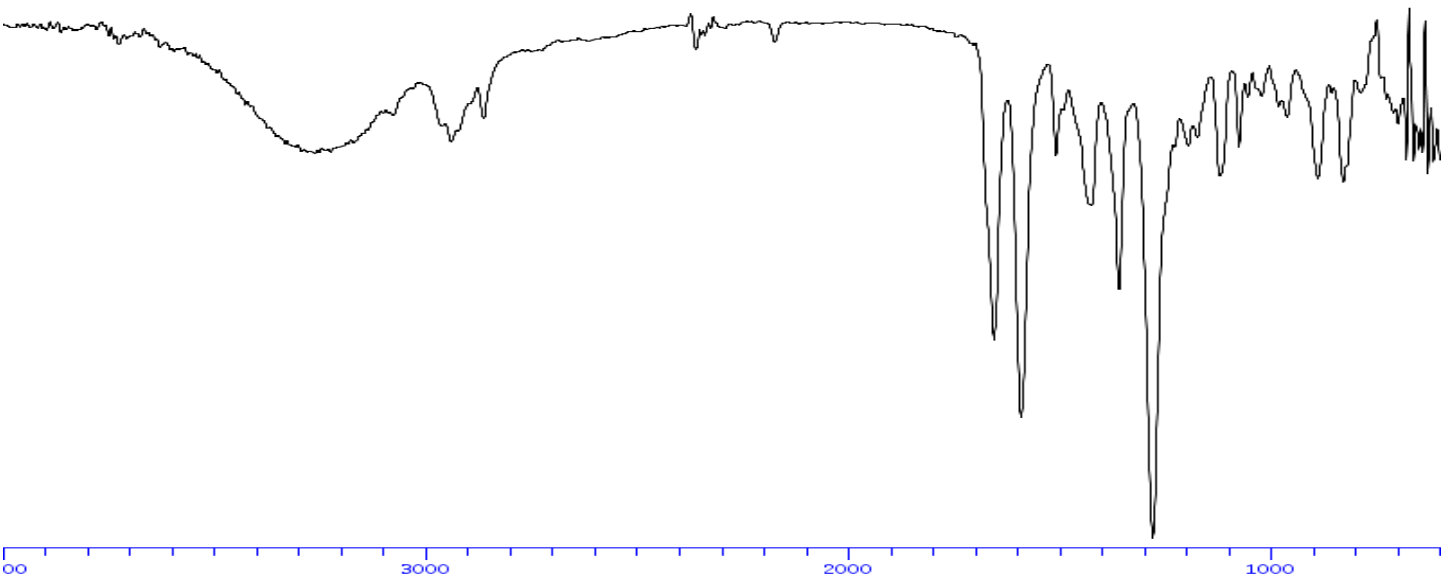
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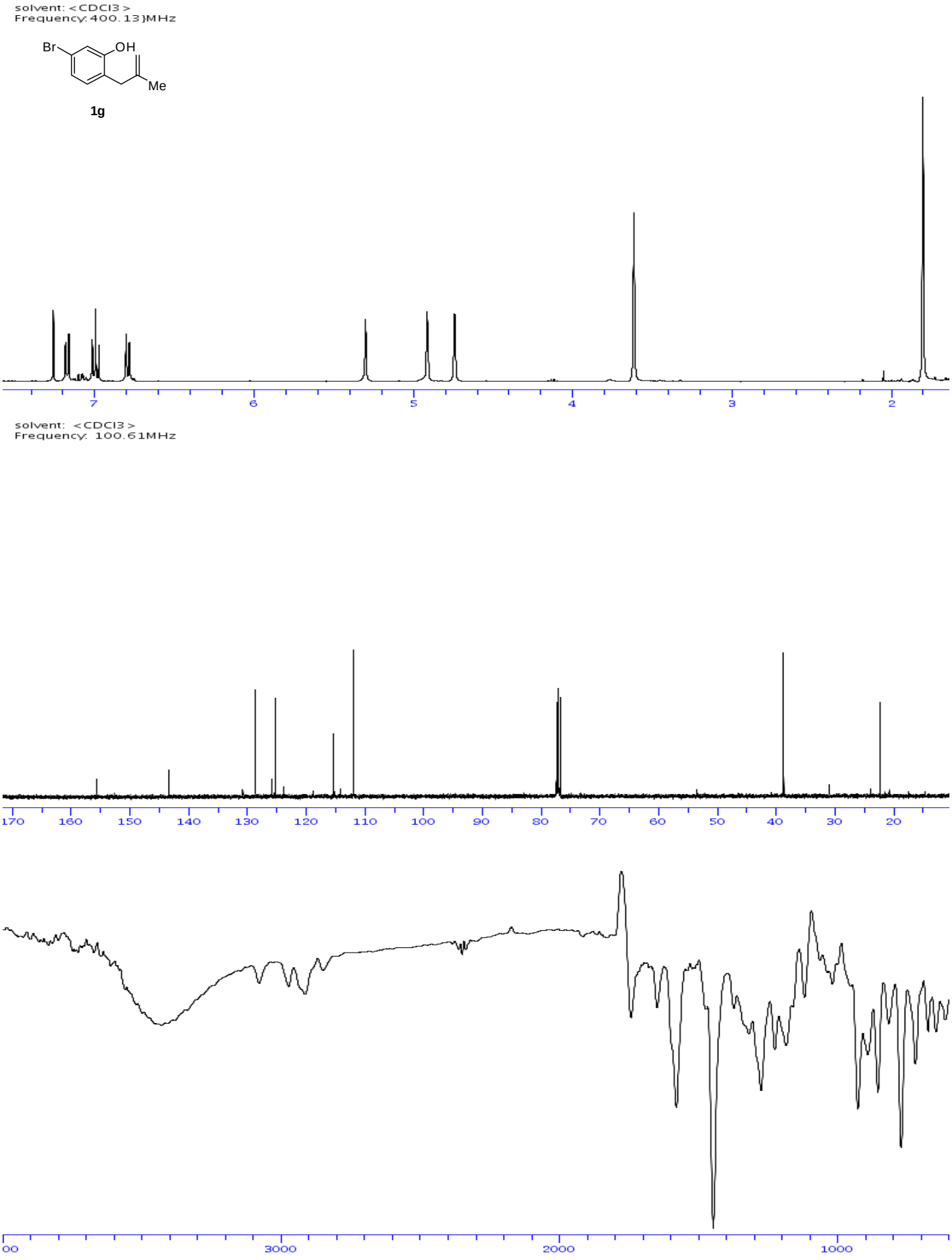
1000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Frequency: 400.13}MHz
Br
OH
Me
1g
7
6
5
4
3
2
solvent: <CDCl3 >
Frequency: 100.61MHz
170
160
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140
130
120
110
100
90
80
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50
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30
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00
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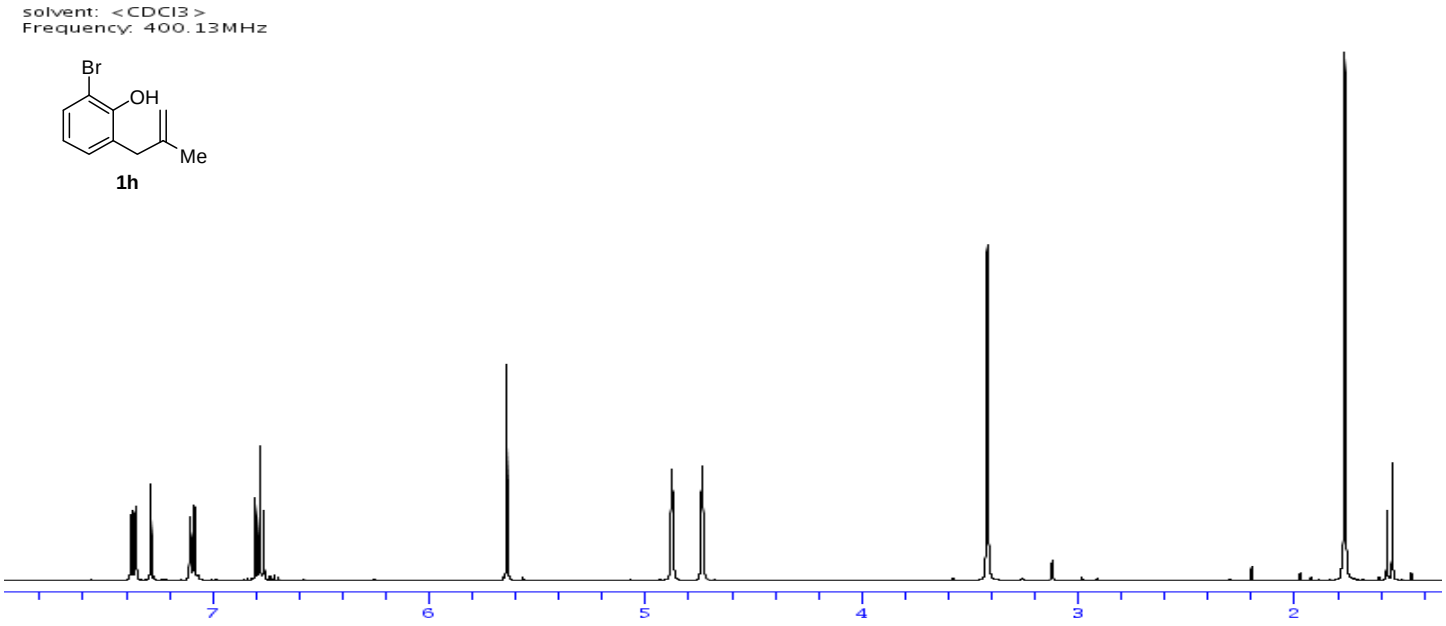
2000
1000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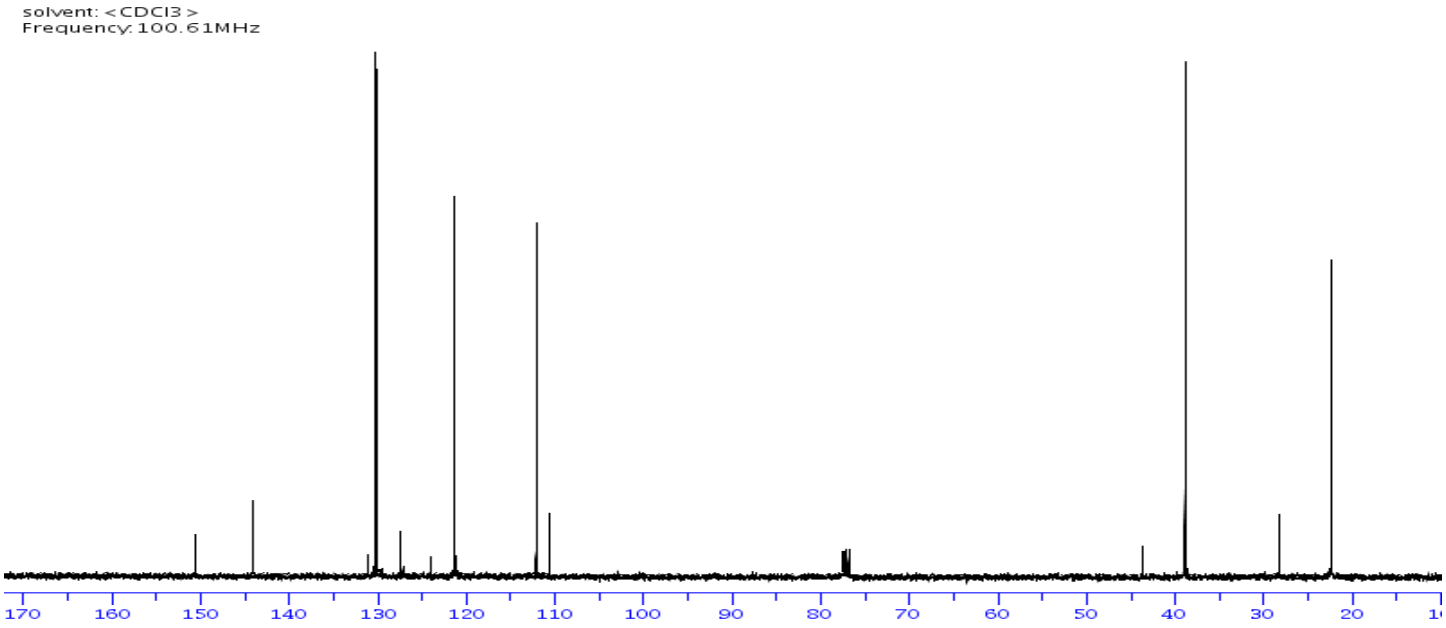
Br
OH
Me
1h
7
6
5
4
3
2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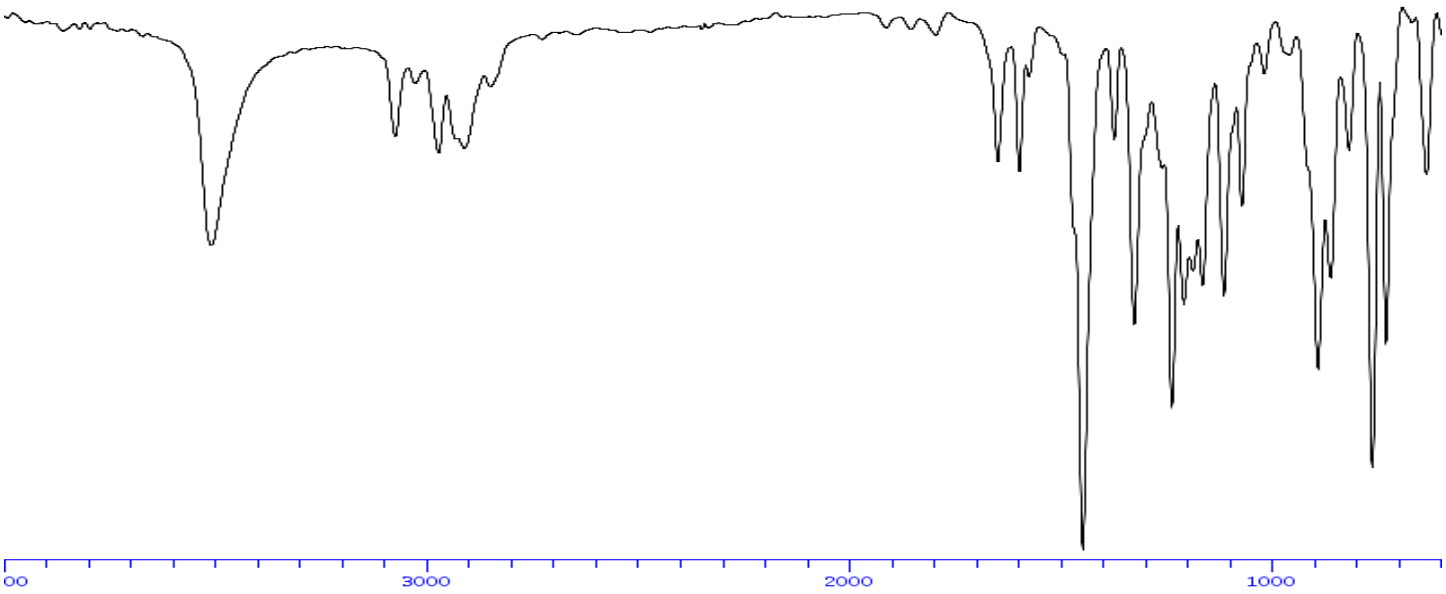
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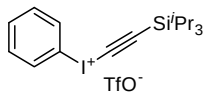
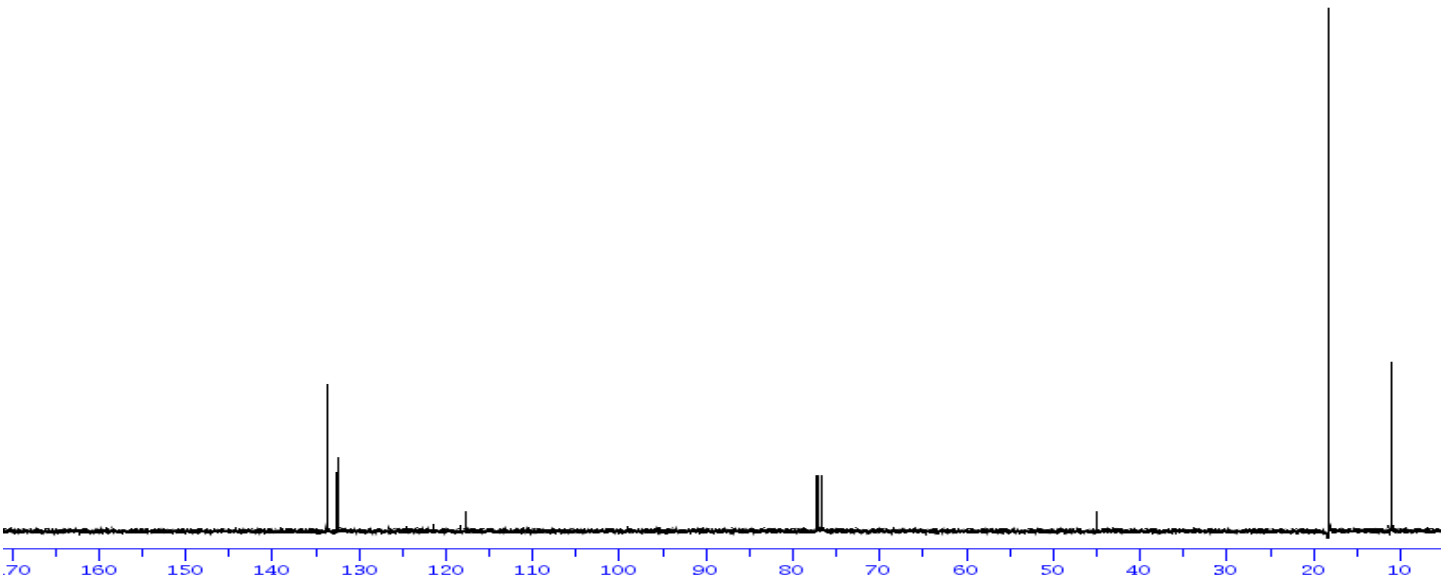
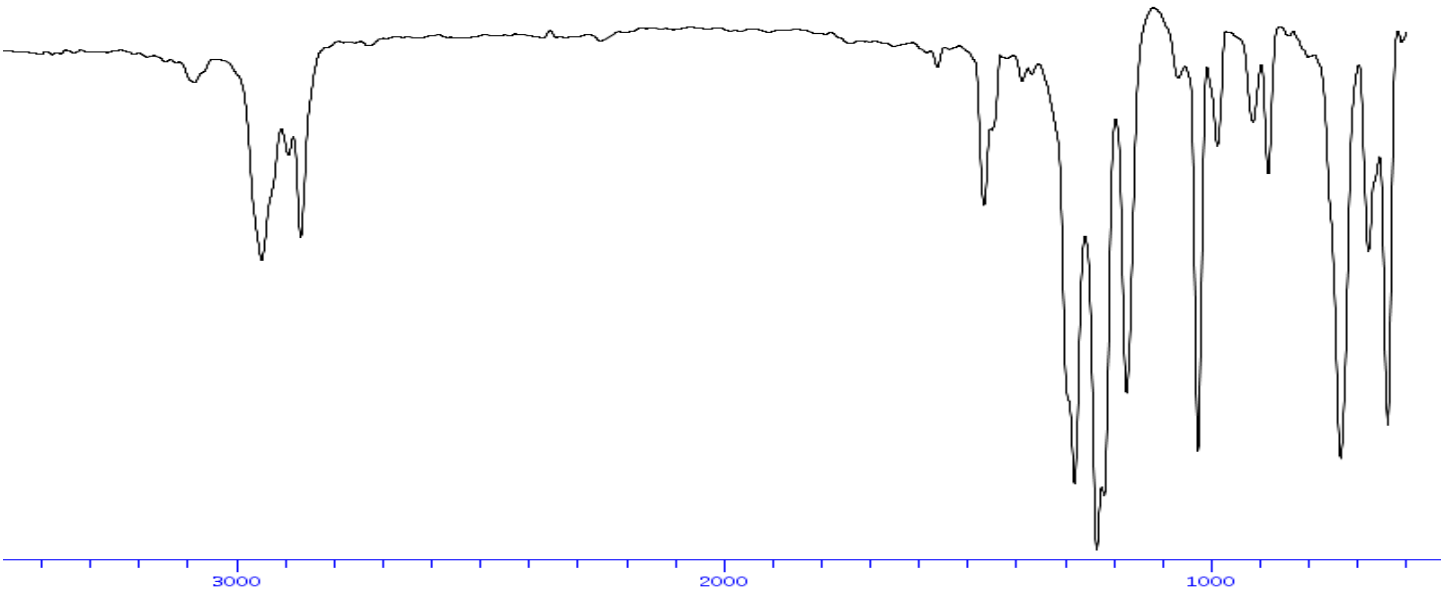
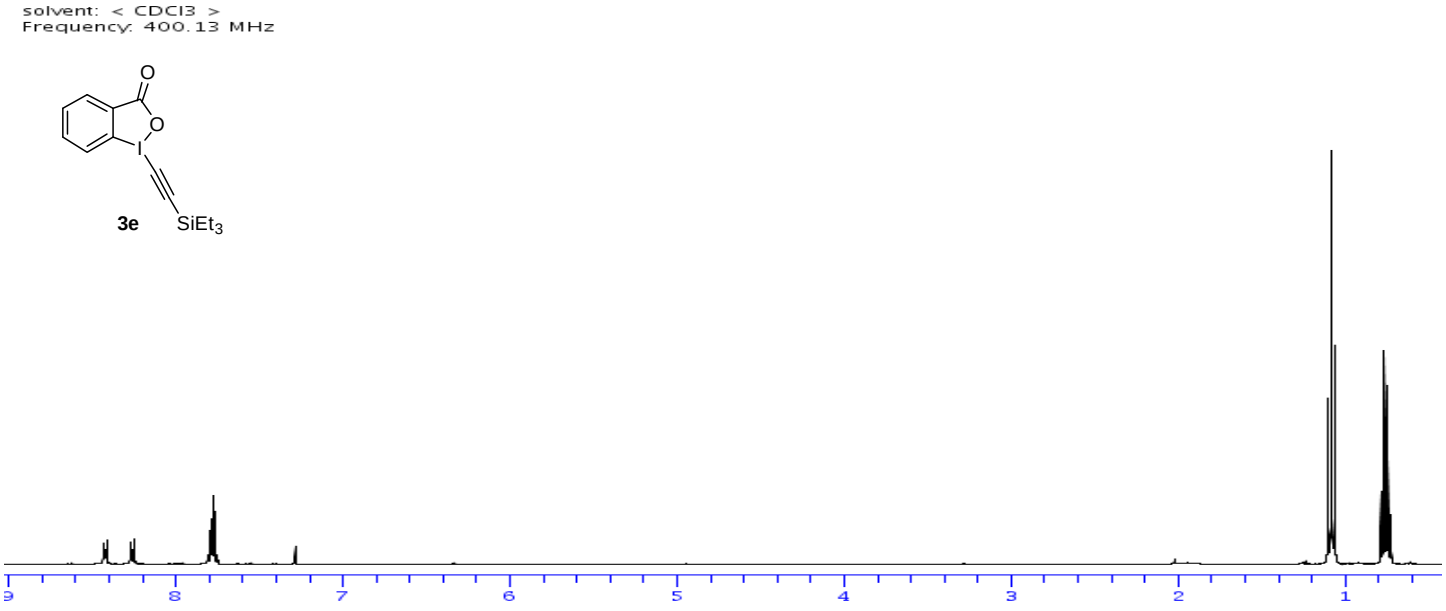


3b

solvent: <CDCl3>
Frequency: 100.61MHz



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O
O
I
3e
SiEt3
9
8
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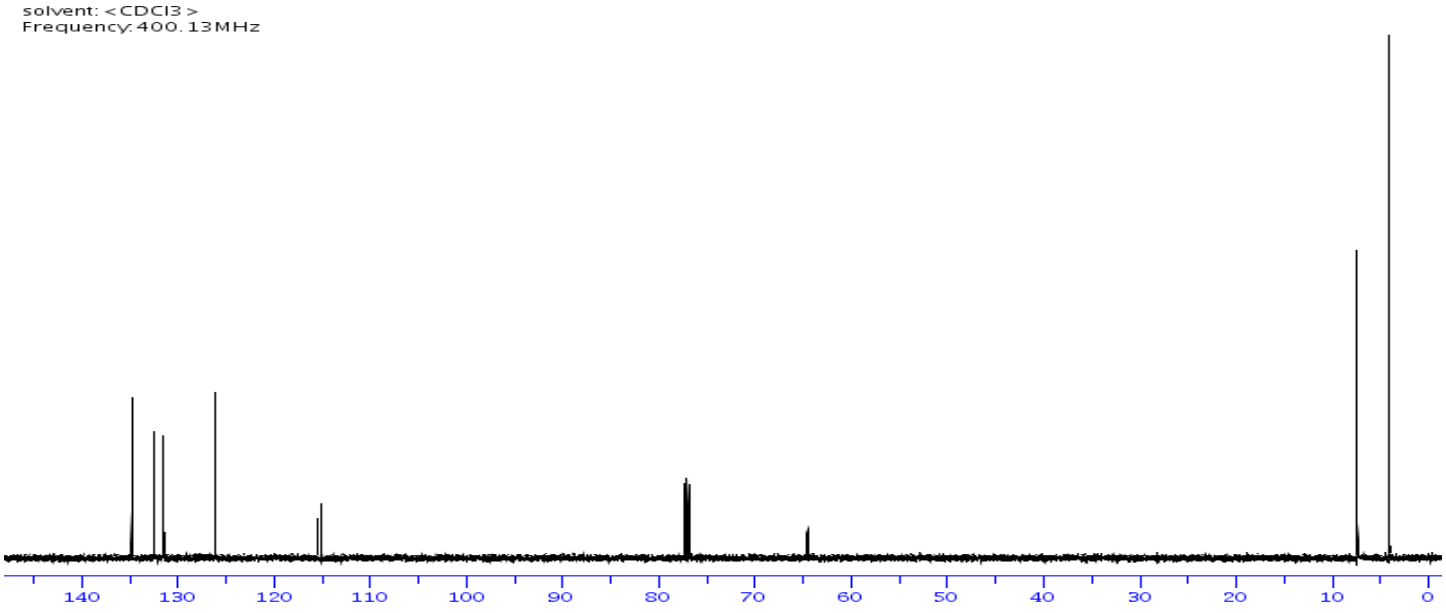
4
3
2
1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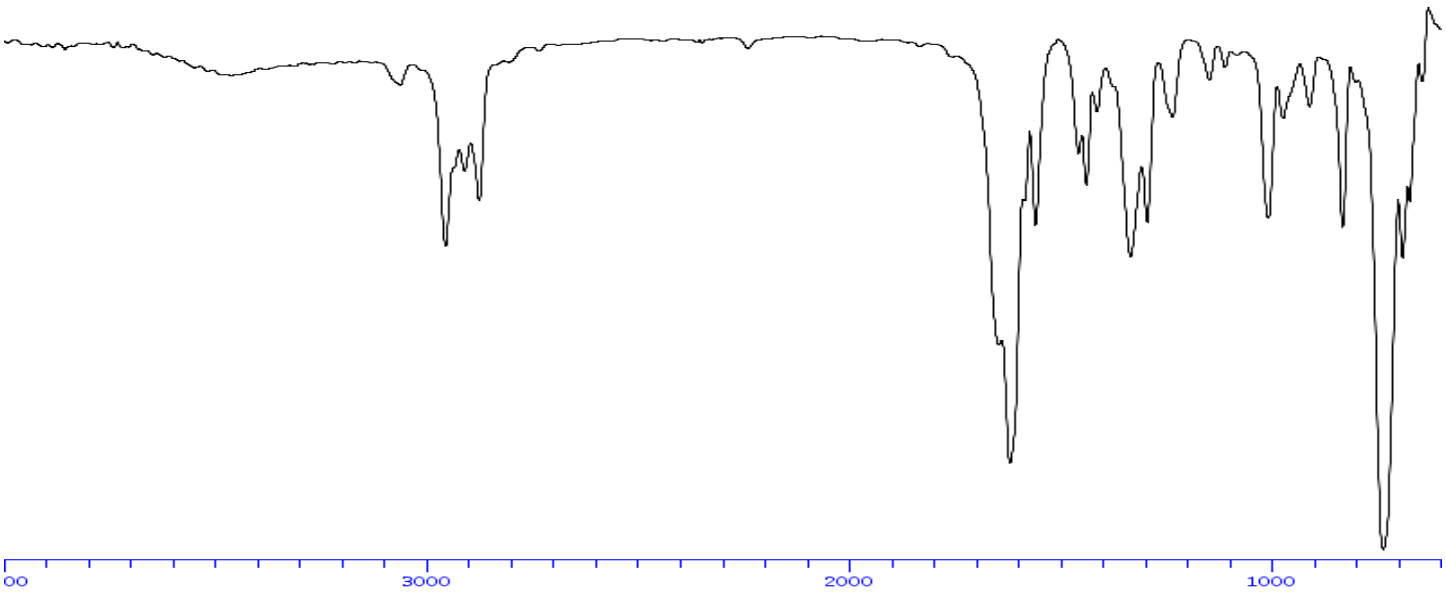
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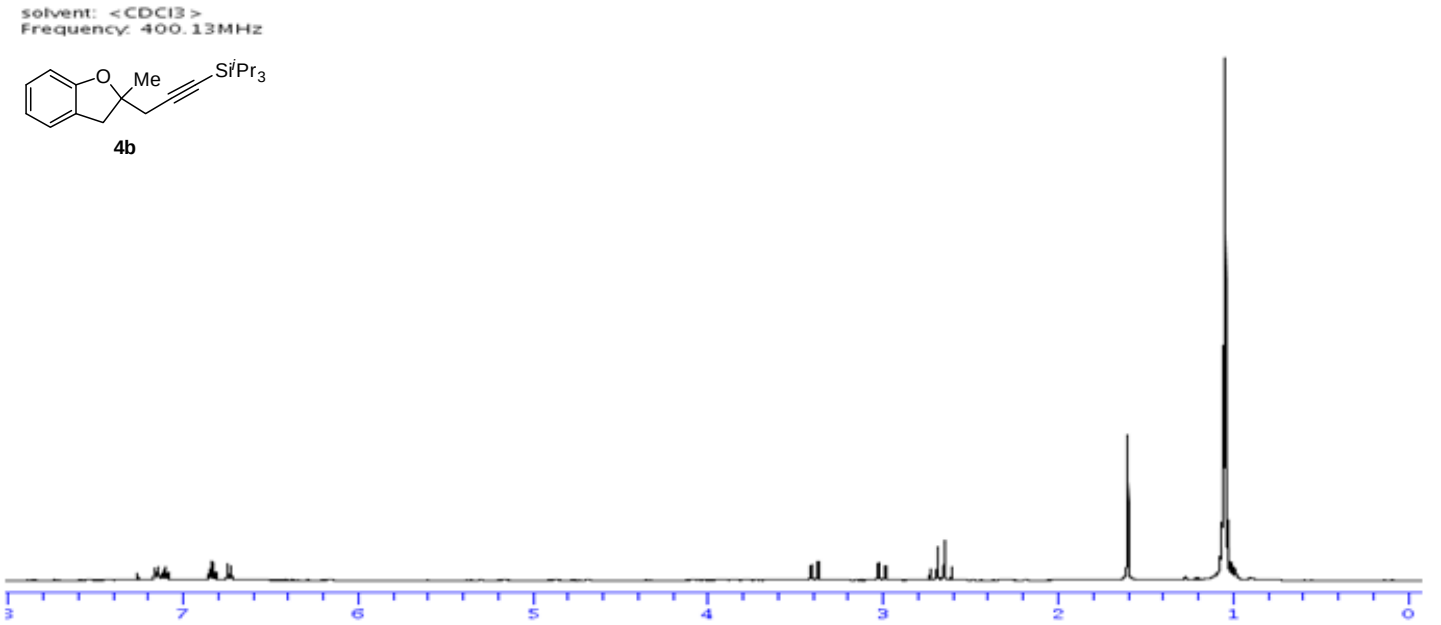
2000
1000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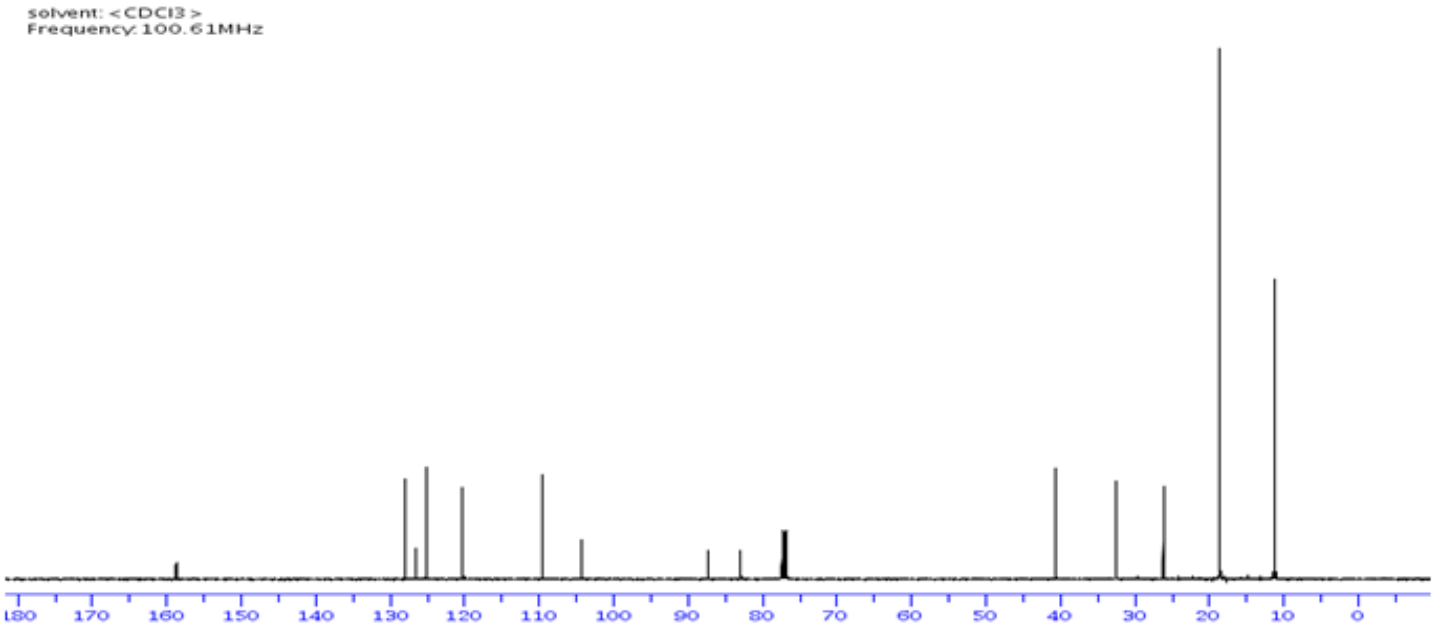
O
Me
SiiPr3
4b
3
7
6
5
4
3
2
1
0


solvent: <CDCl3>
Frequency: 100.61MHz
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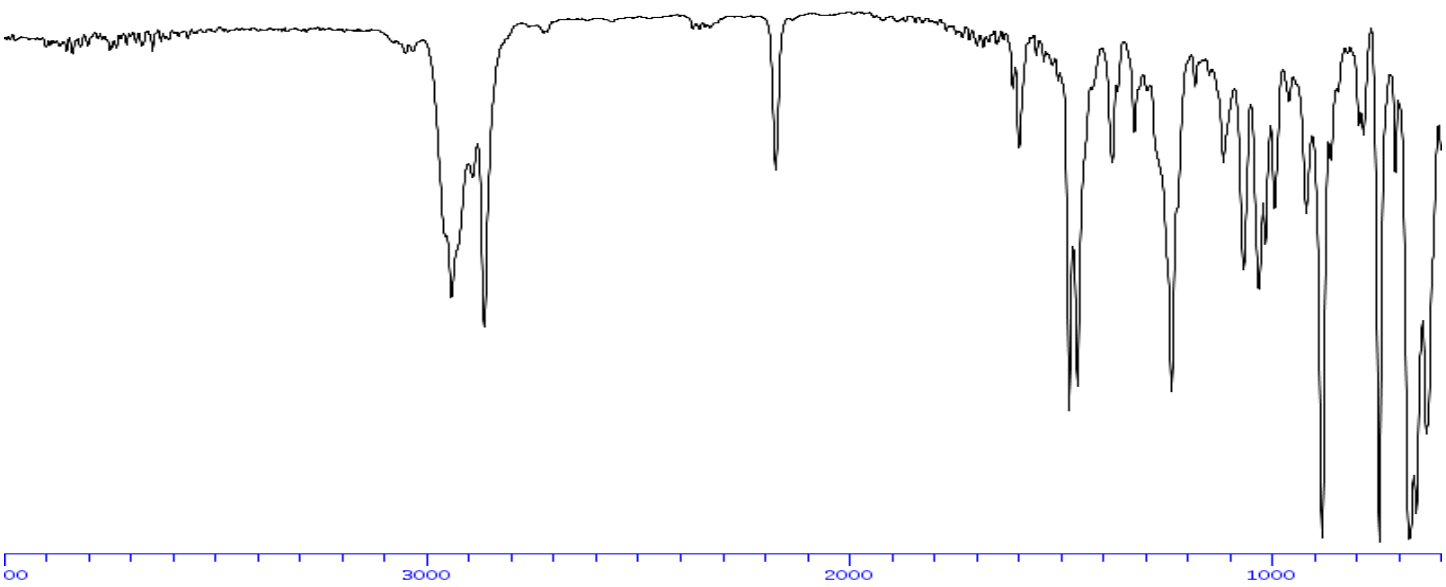
30
20
10
0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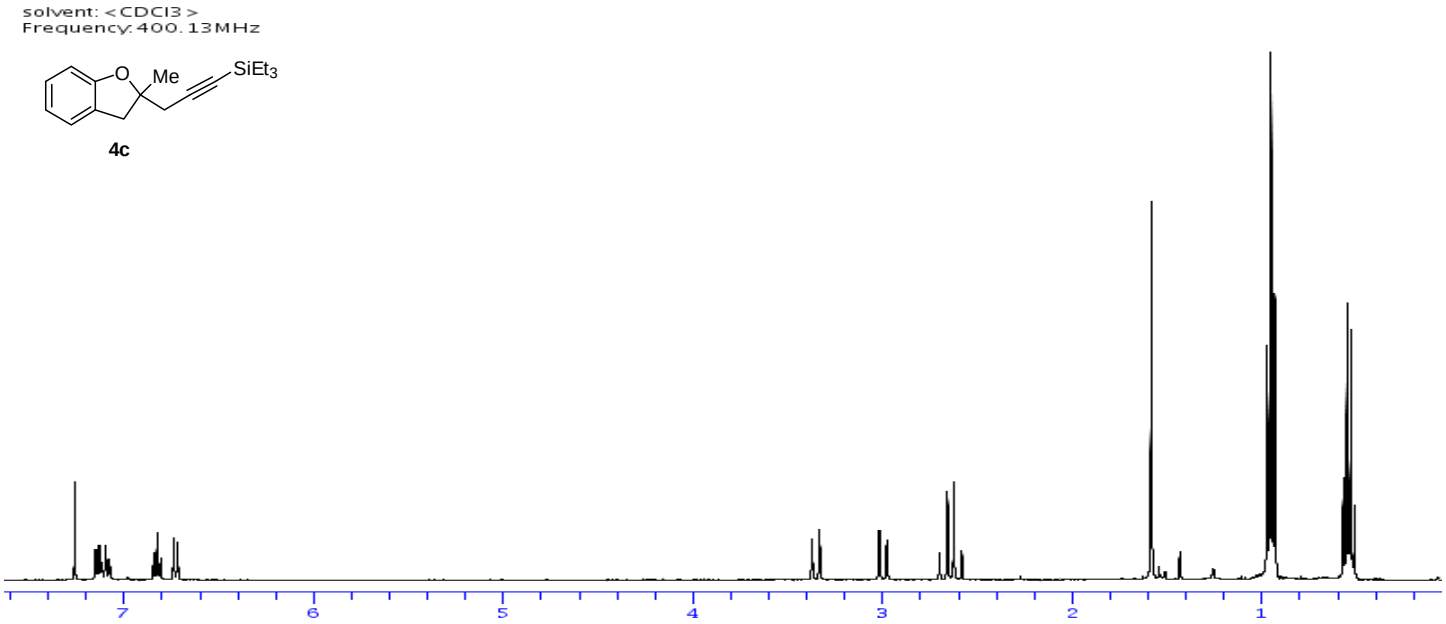
3000
2000
1000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Me
SiEt3
4c
7
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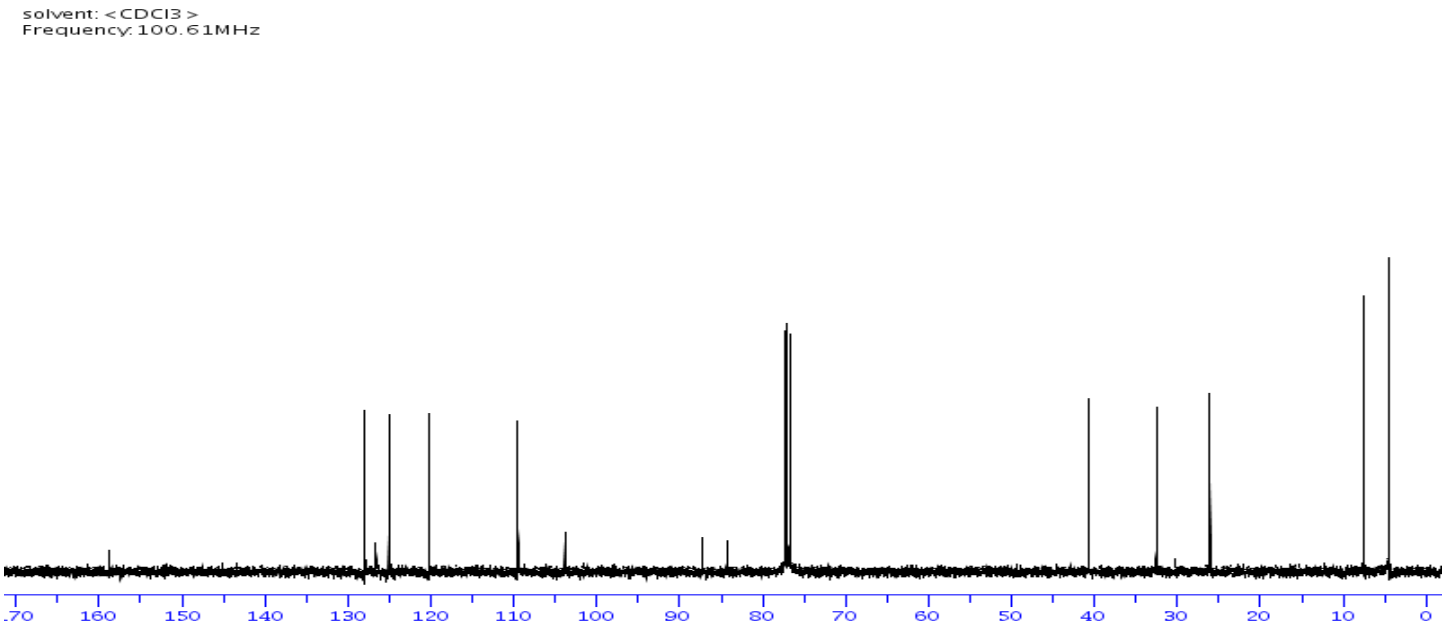
4
3
2
1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Frequency: 100.61MHz
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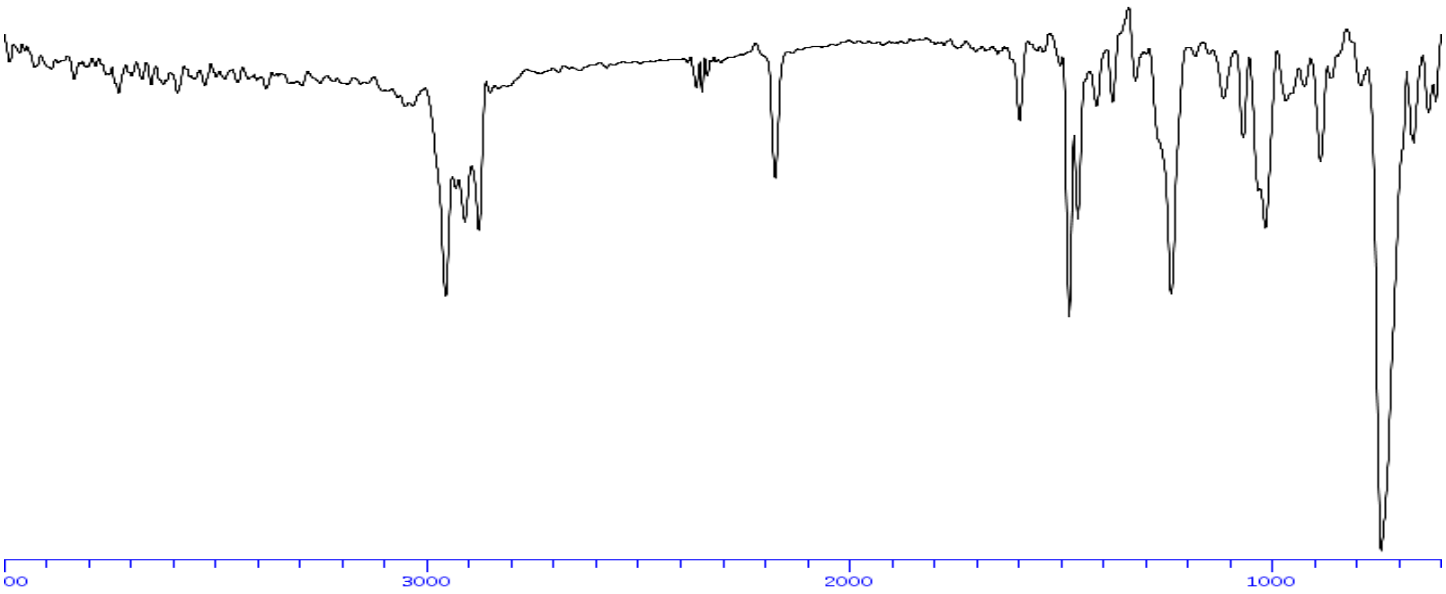
20
10
0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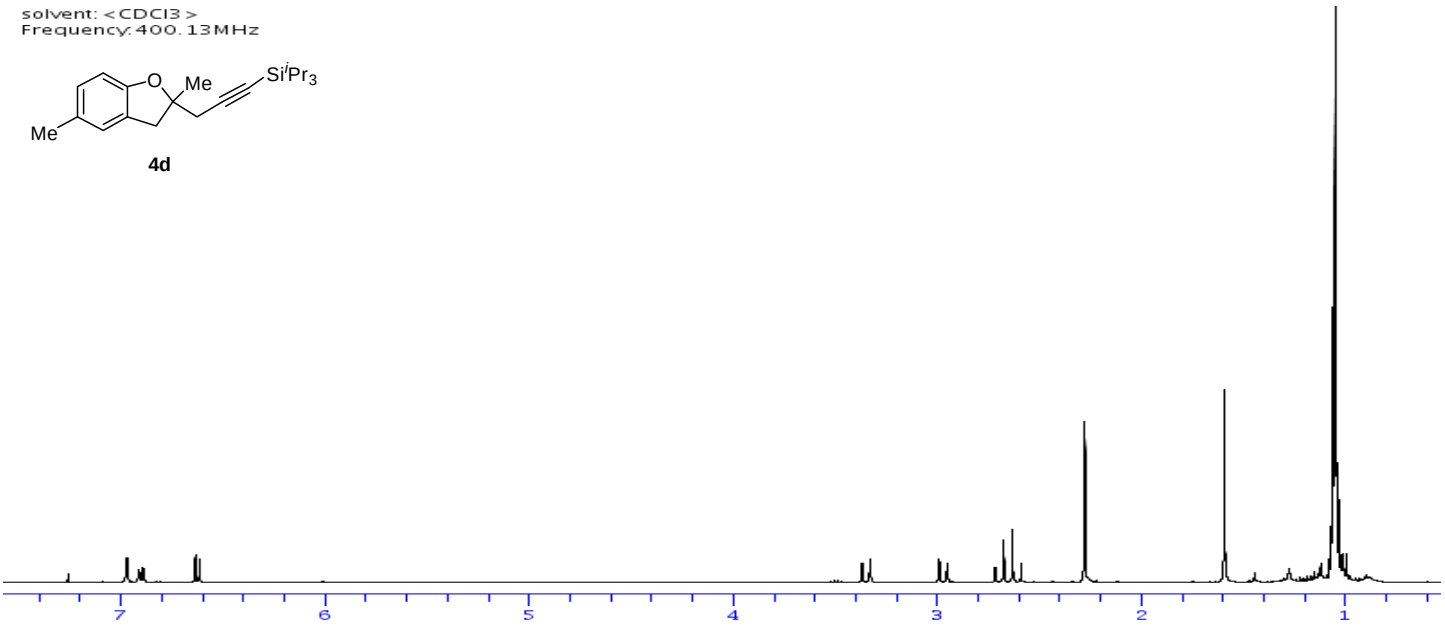
2000
1000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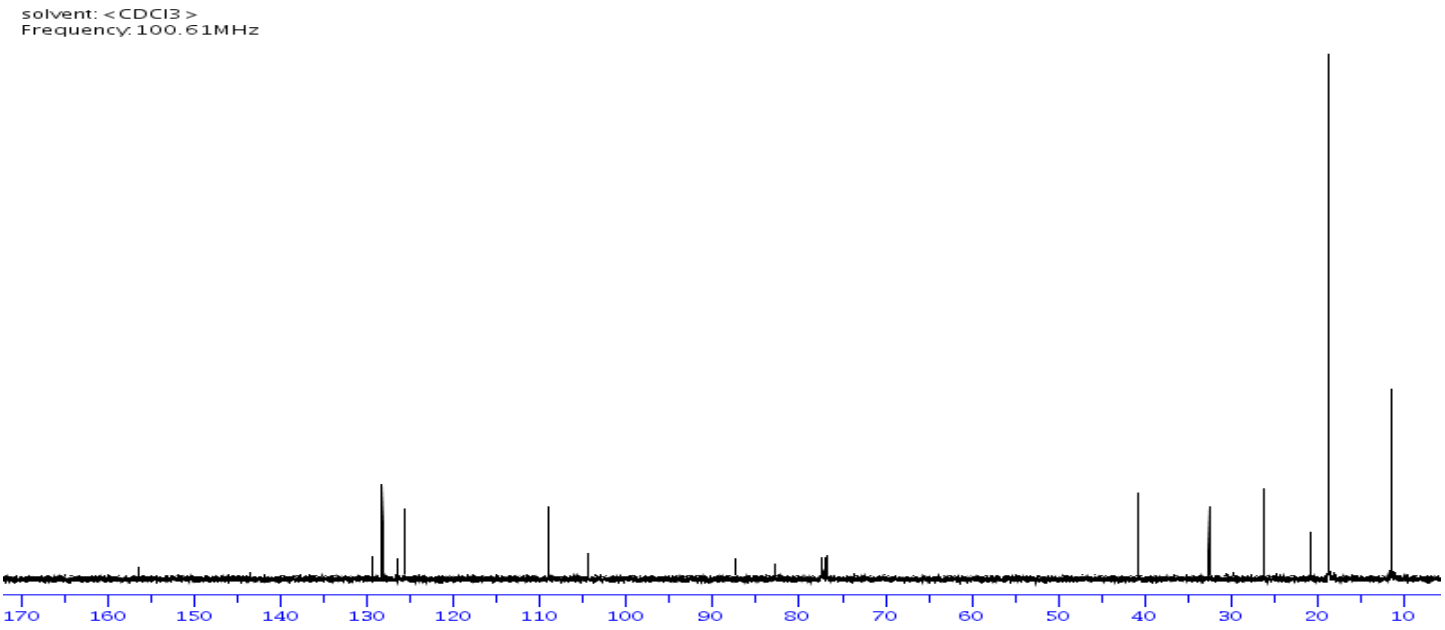
Me
Si^{i}Pr$_3$
Me
7
6
5
4
3
2
1

4d


solvent: <CDCl3 >
Frequency: 100.61MHz
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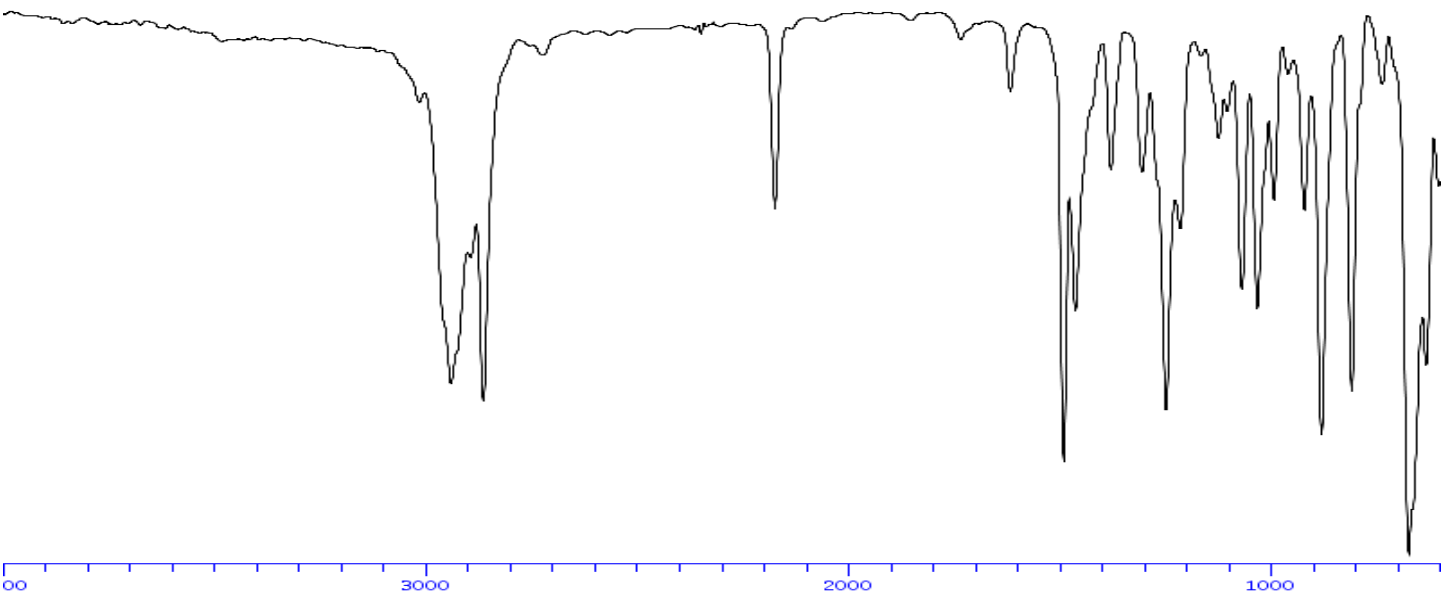
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2000
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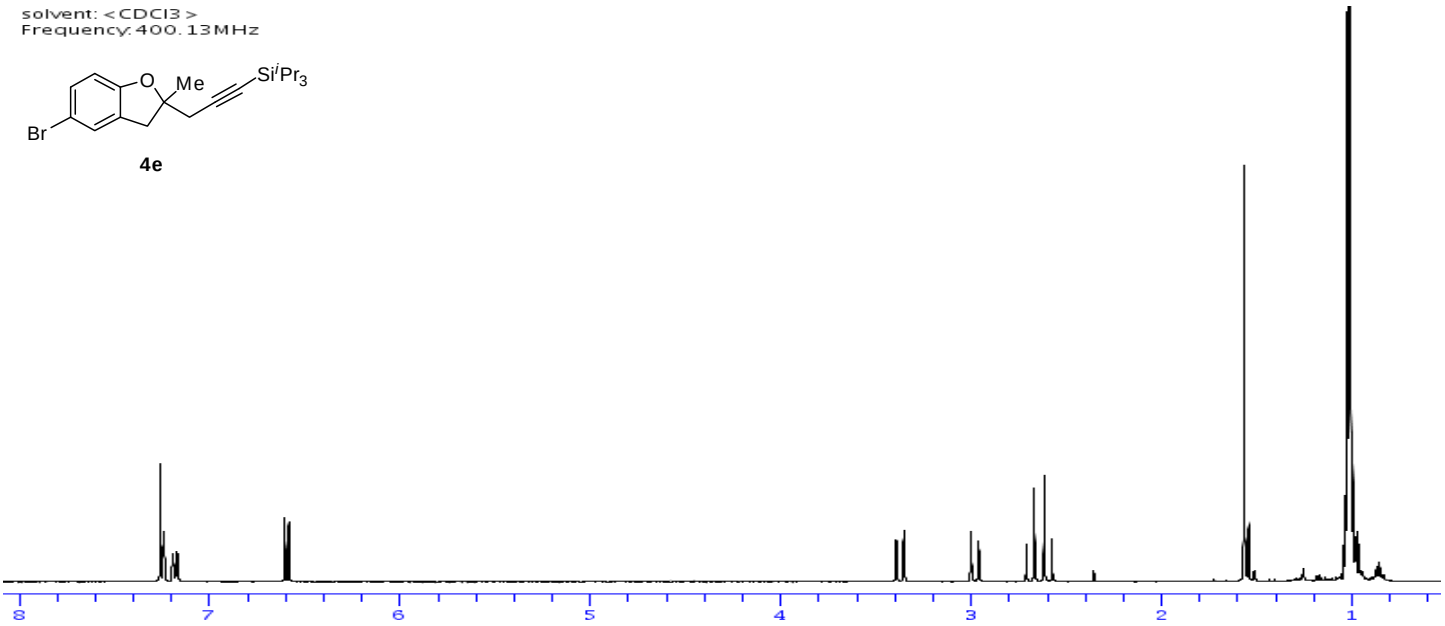
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Frequency: 400.13MHz
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Me
Si^{i}Pr$_3$
Br
8
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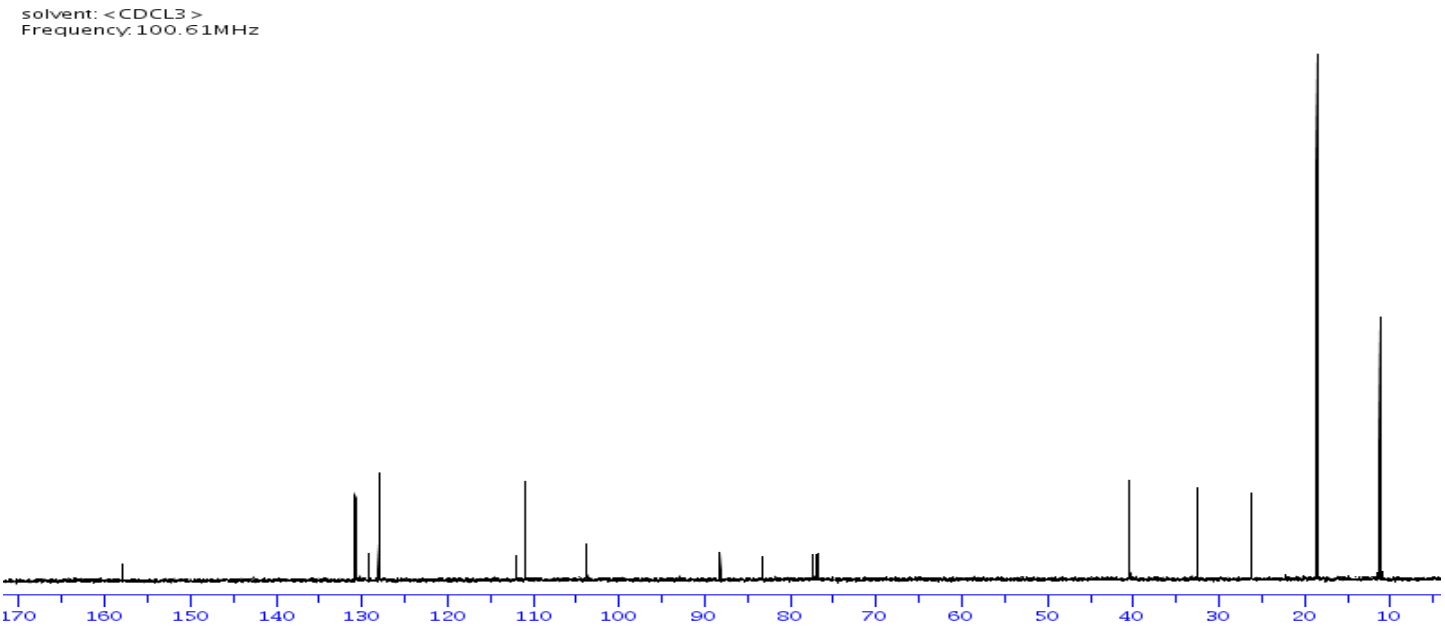
5
4
3
2
1

4e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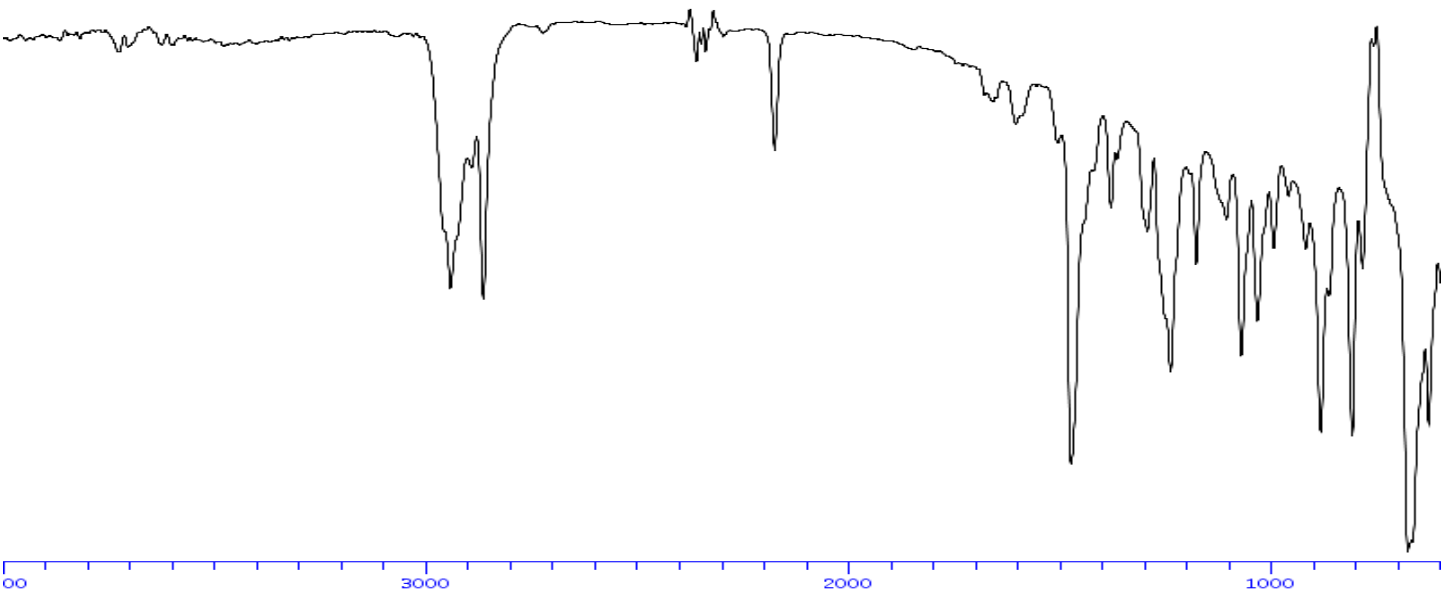
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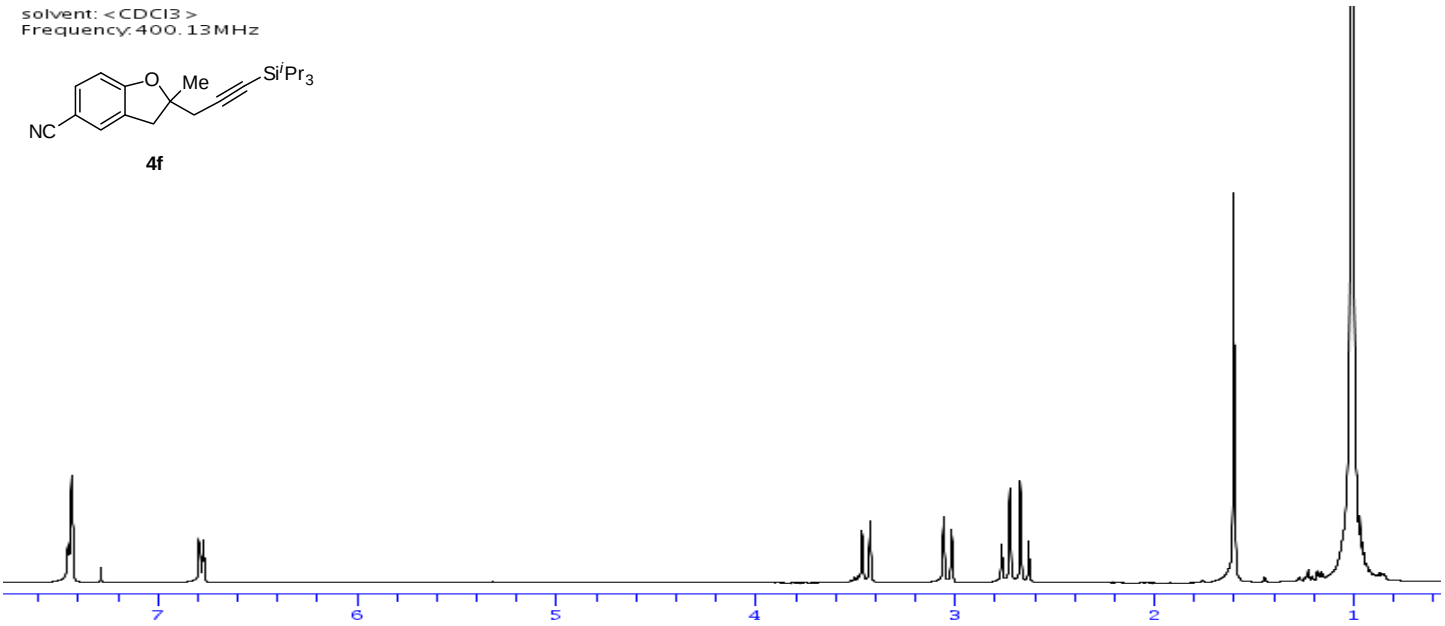
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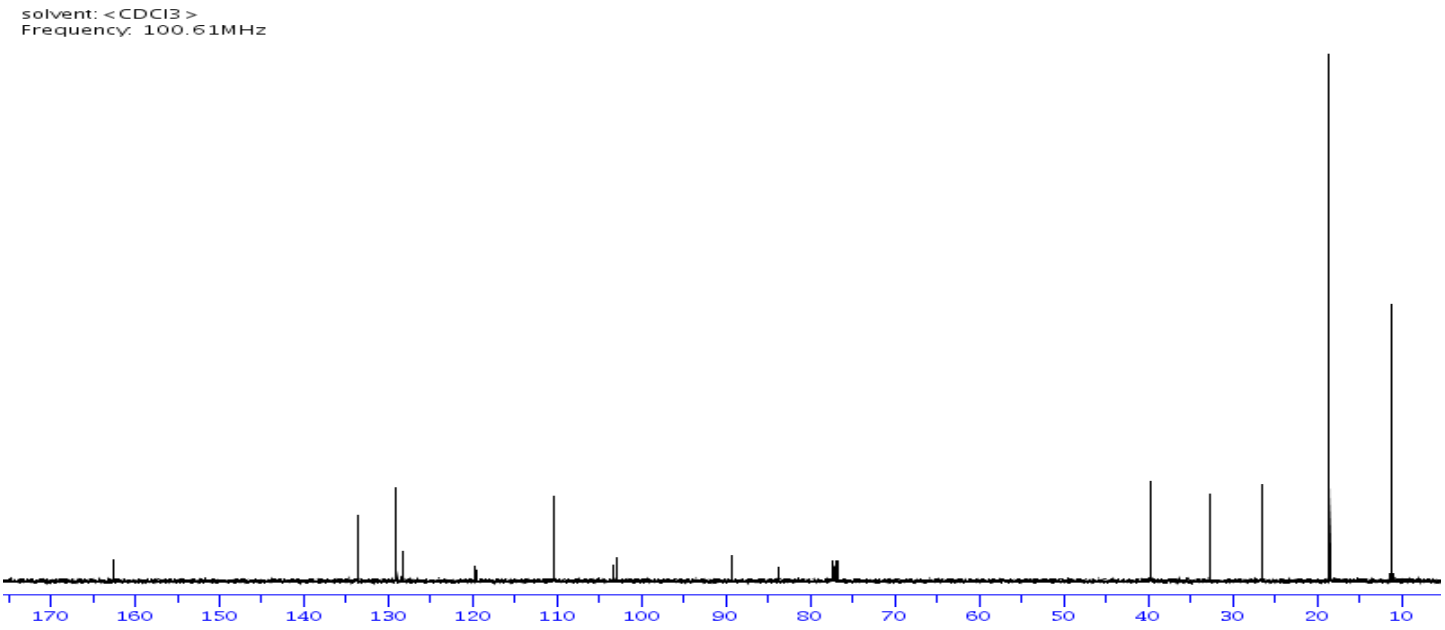
Si^{i}Pr$_3$
NC
7
6
5
4
3
2
1

4f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Frequency: 100.61MHz
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20
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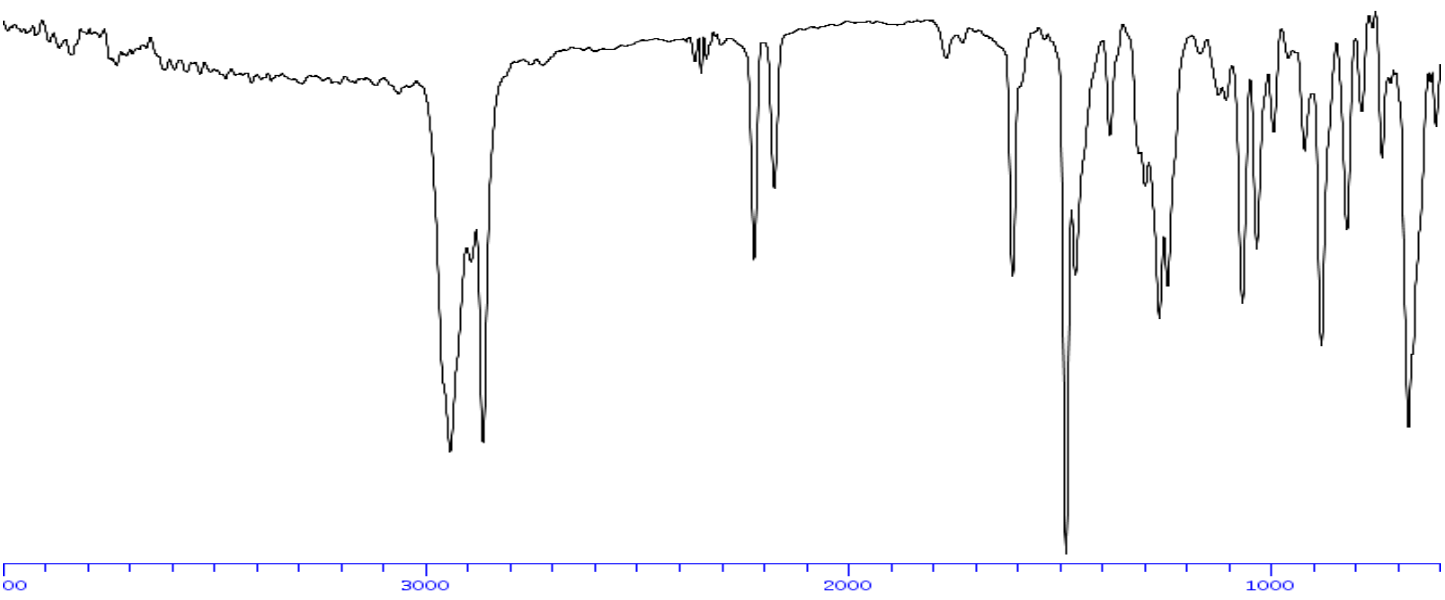
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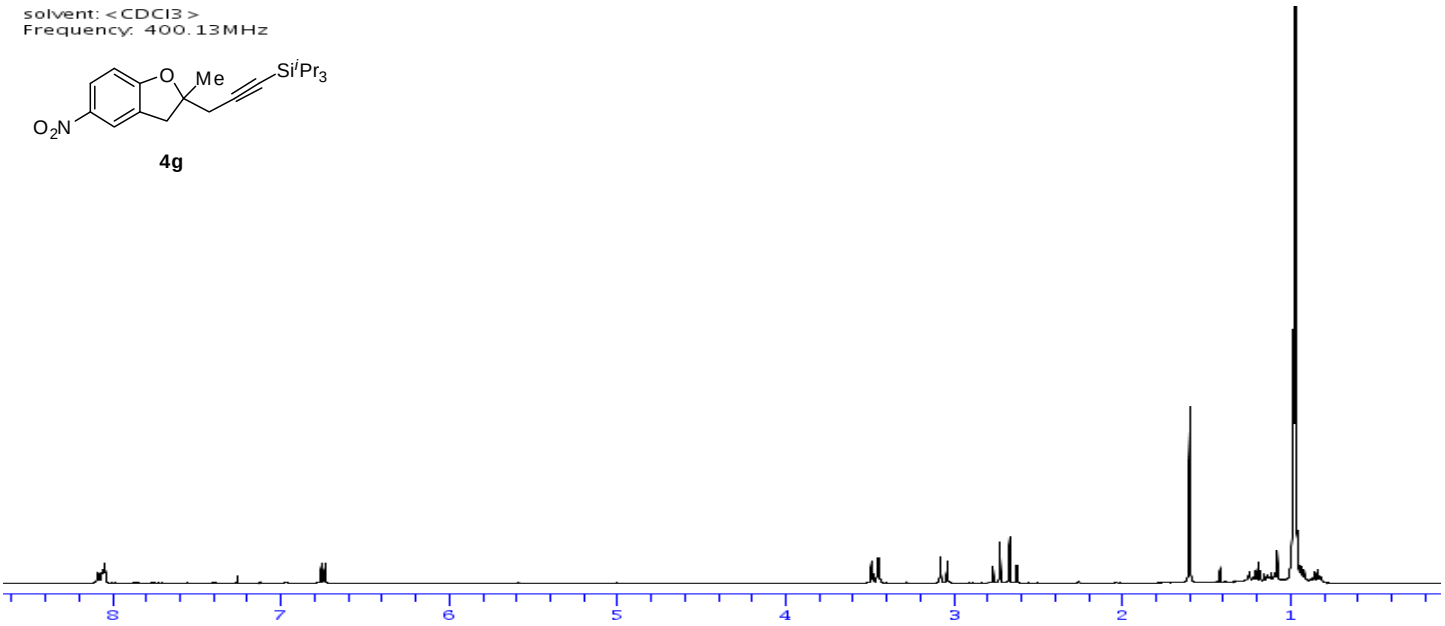
2000
1000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Frequency: 400.13MHz
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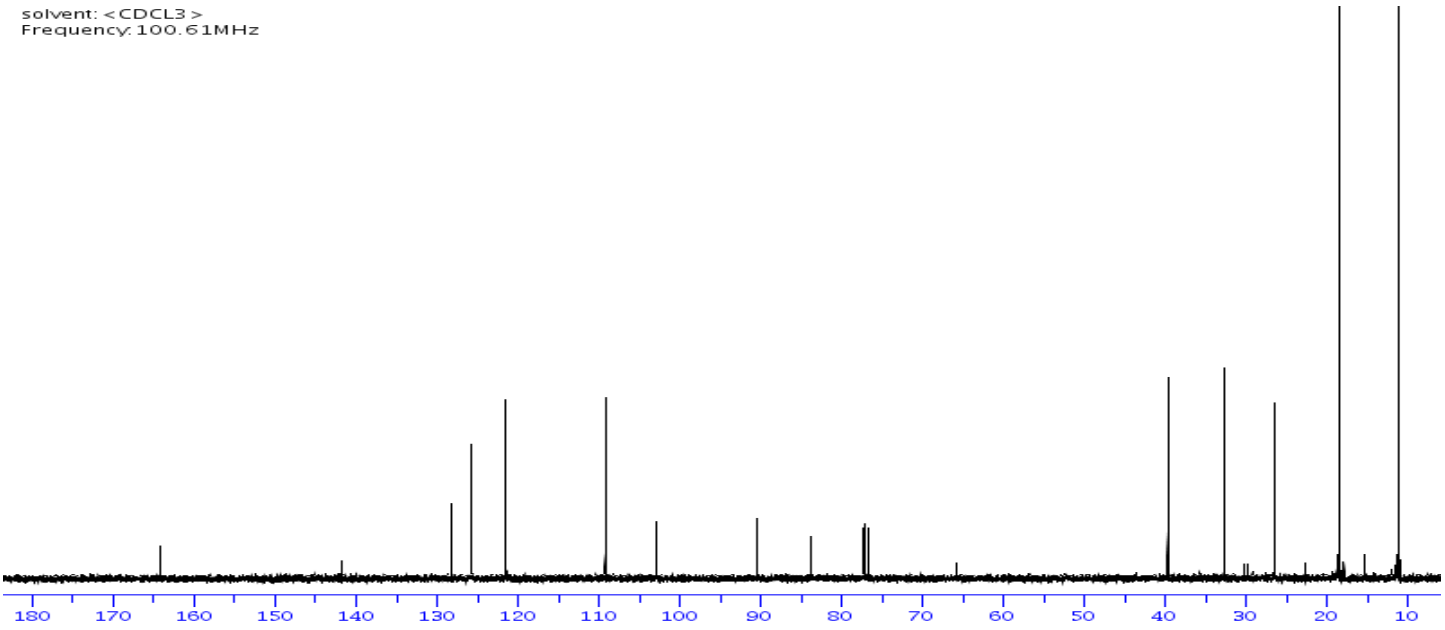
Me
Si^{i}Pr$_3$
O_2N
8
7
6
5
4
3
2
1

4g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20
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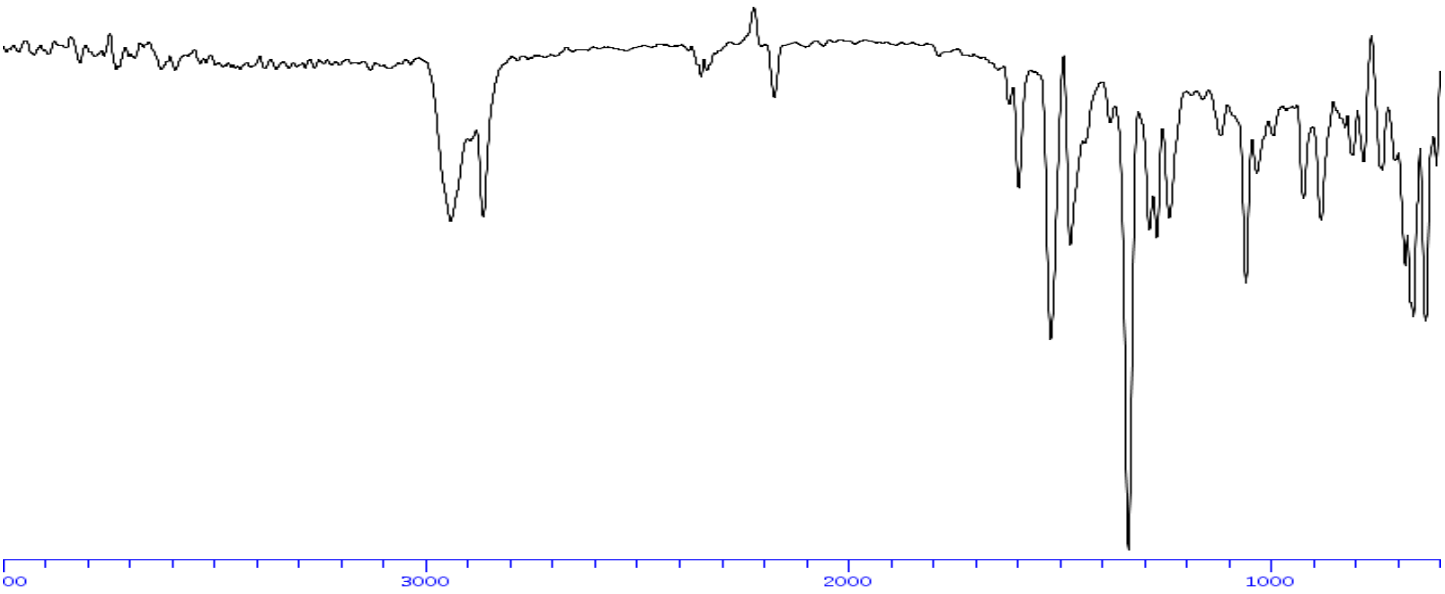
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2000
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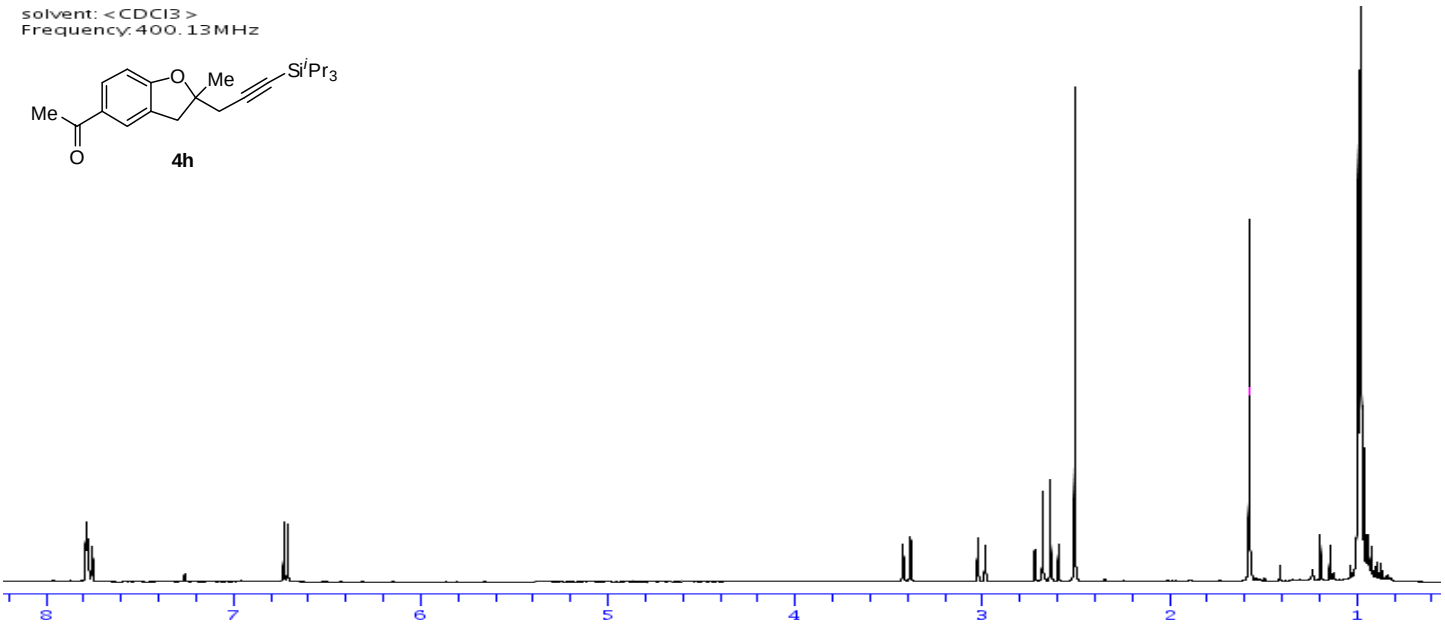
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Me
Si^{i}Pr$_3$
O
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8
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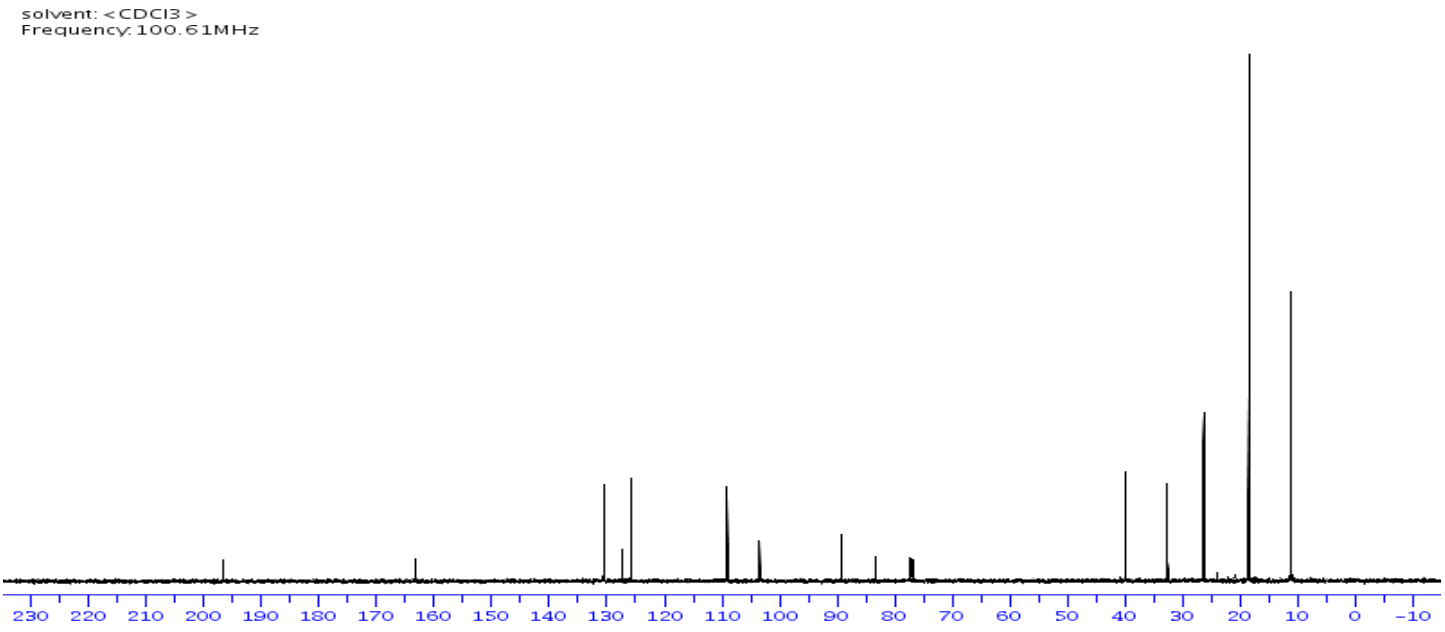
6
5
4
3
2
1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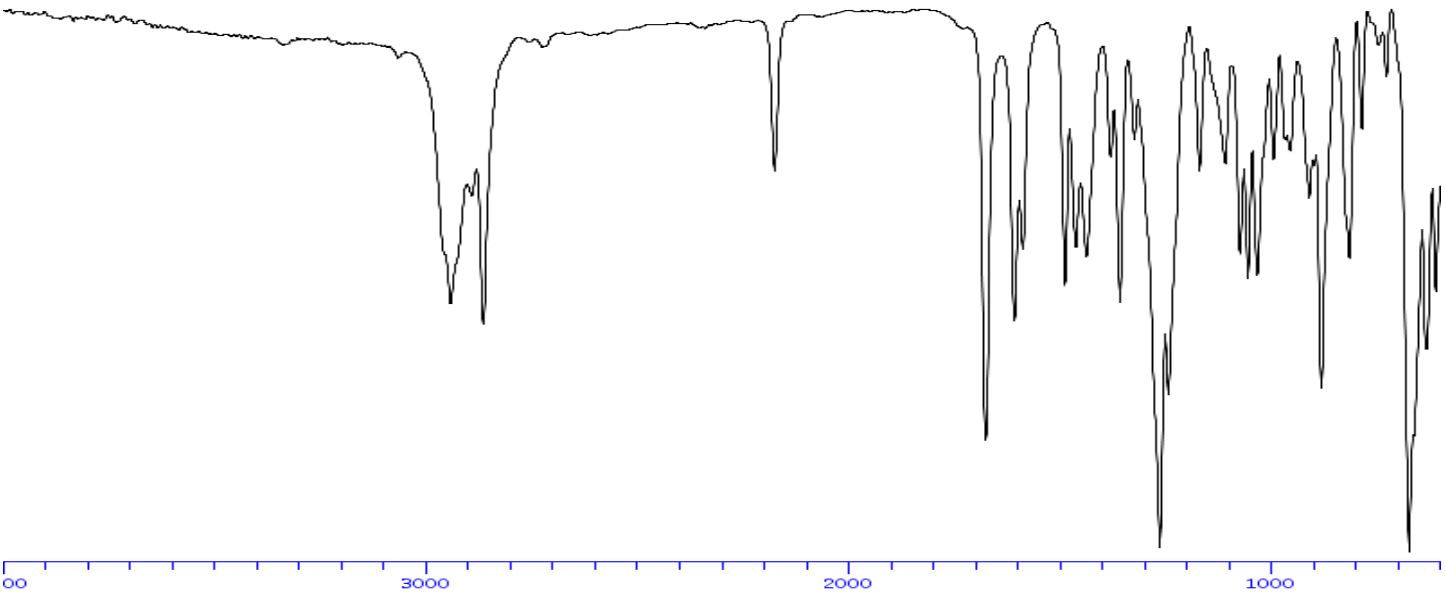
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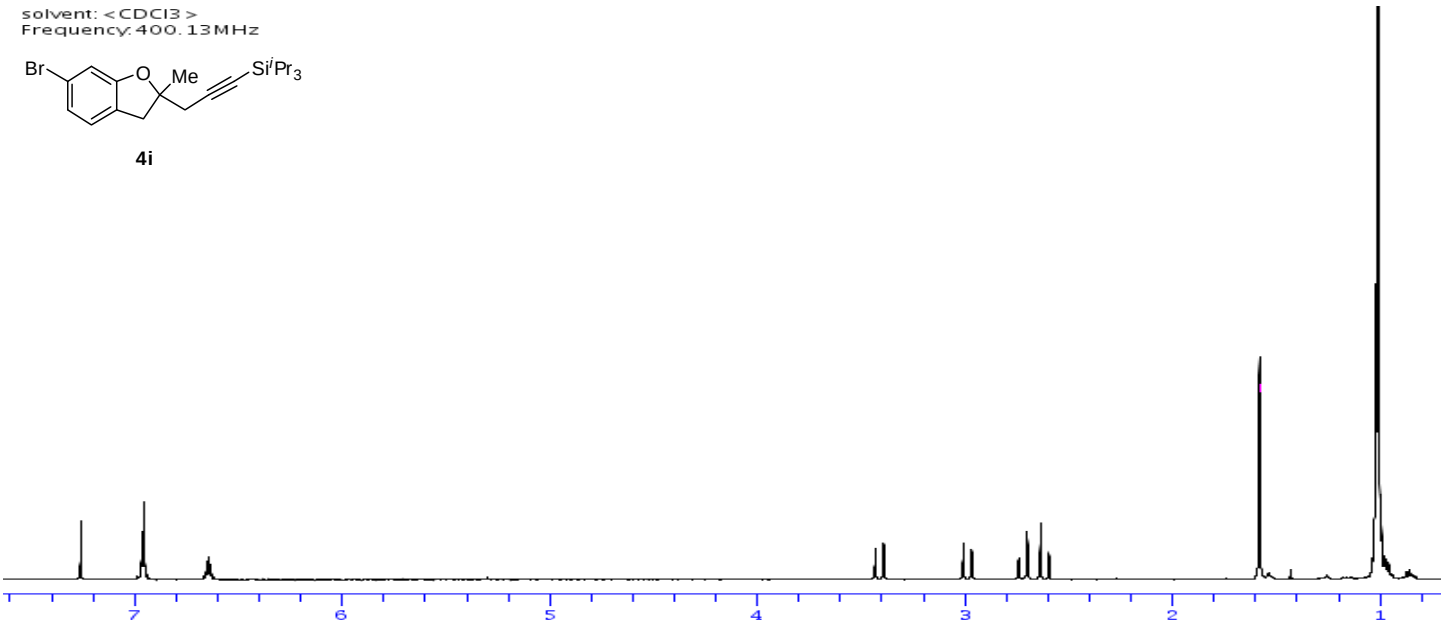
2000
1000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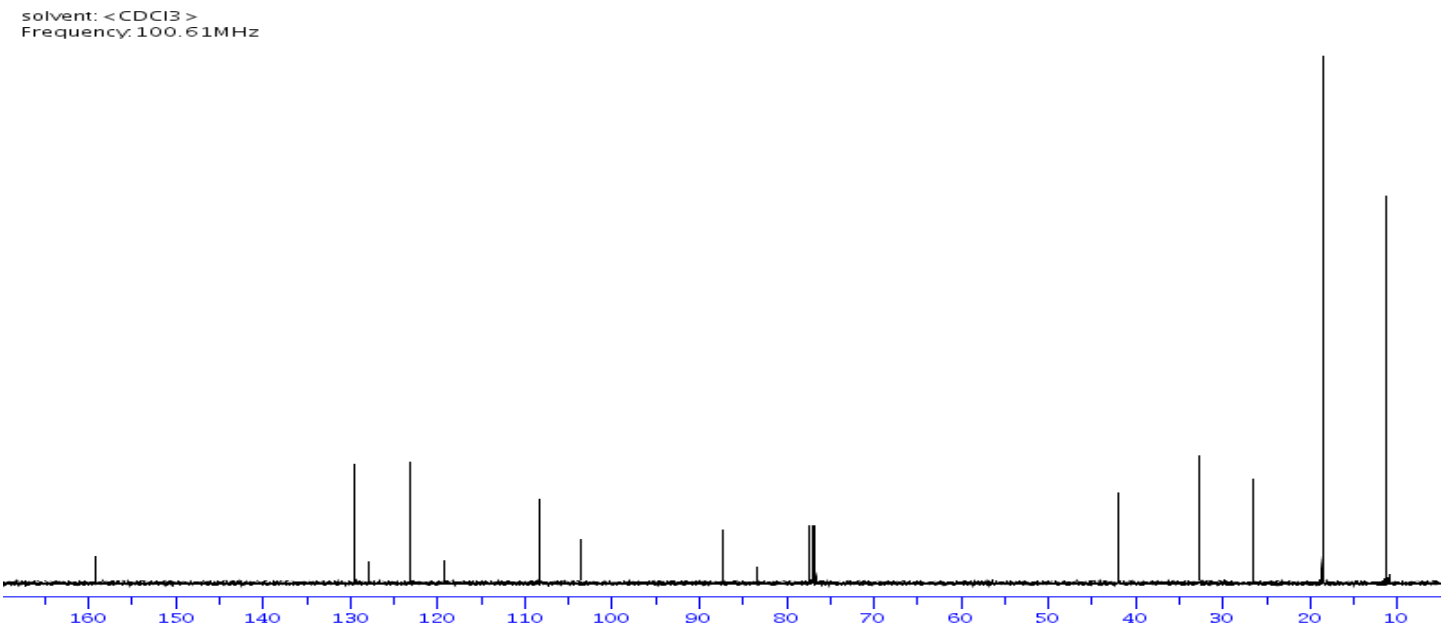
Frequency: 400.13MHz
Br
O
Me
Si^{i}Pr$_3$
7
6
5
4
3
2
1

4i


solvent: <CDCl3 >
Frequency: 100.61MHz
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80
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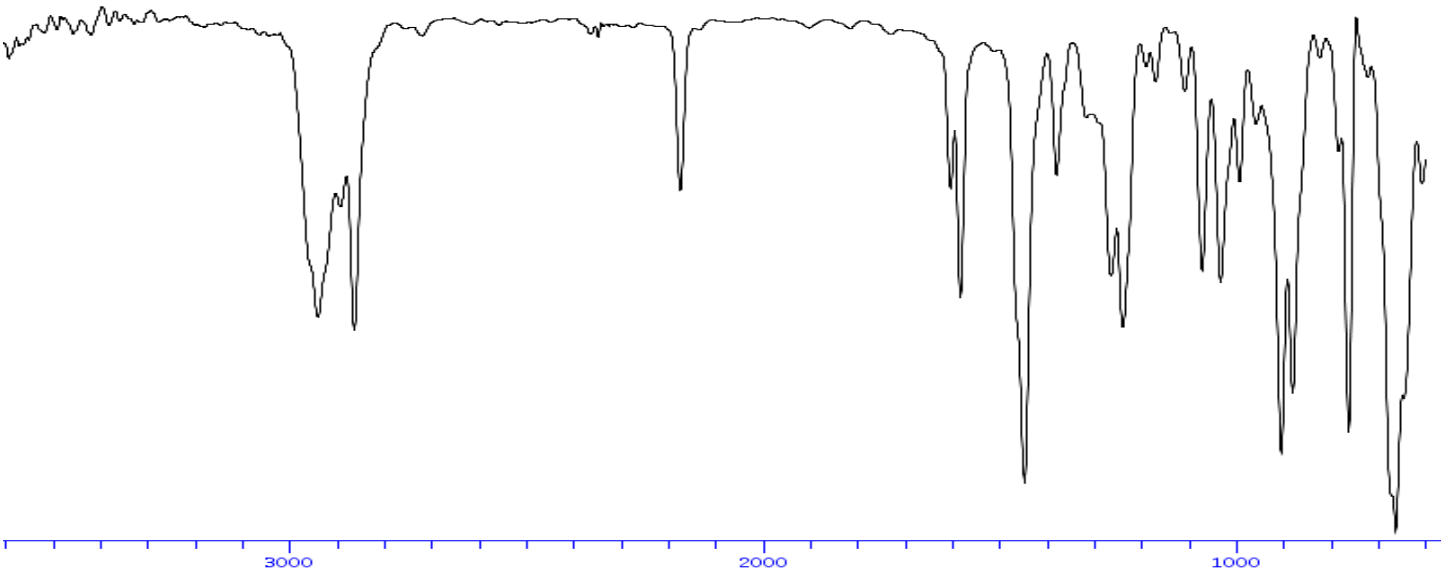
20
10


3000
2000
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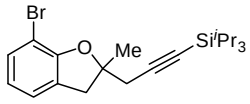
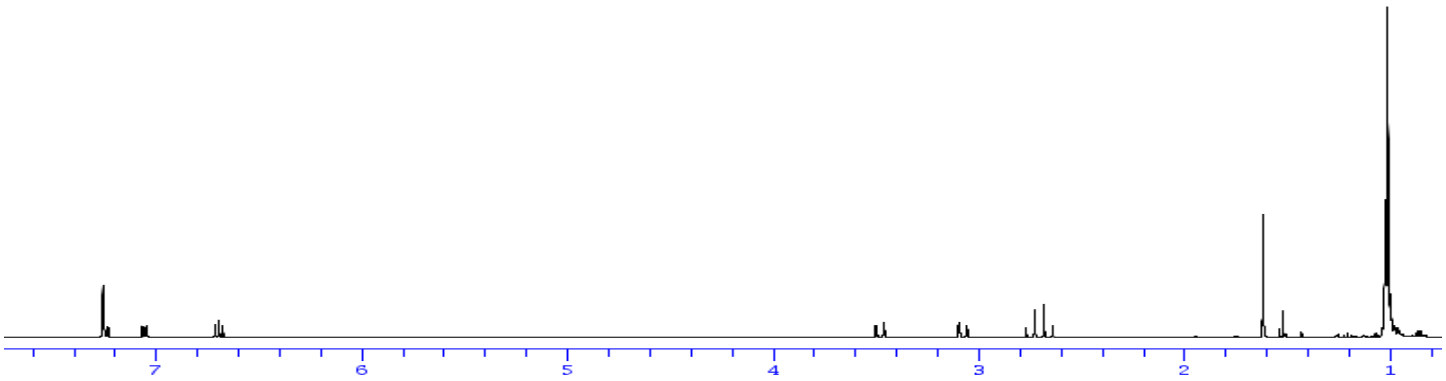
solvent: <CDCl3>
Frequency: 400.13MHz



4j



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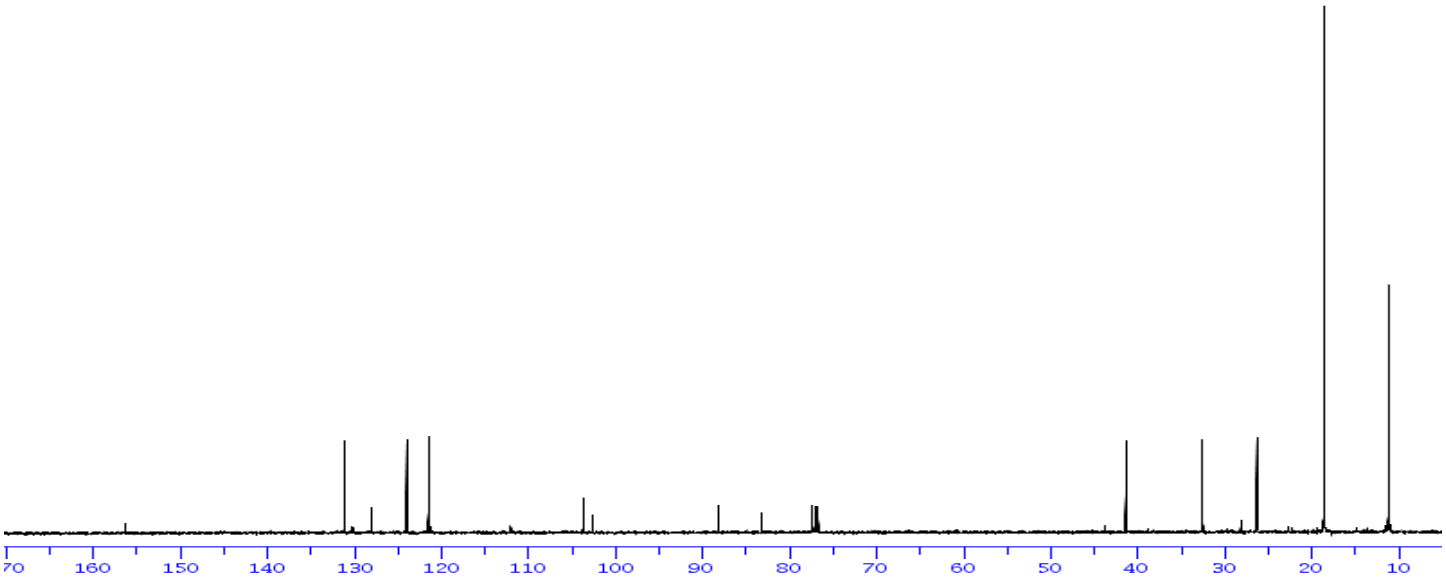

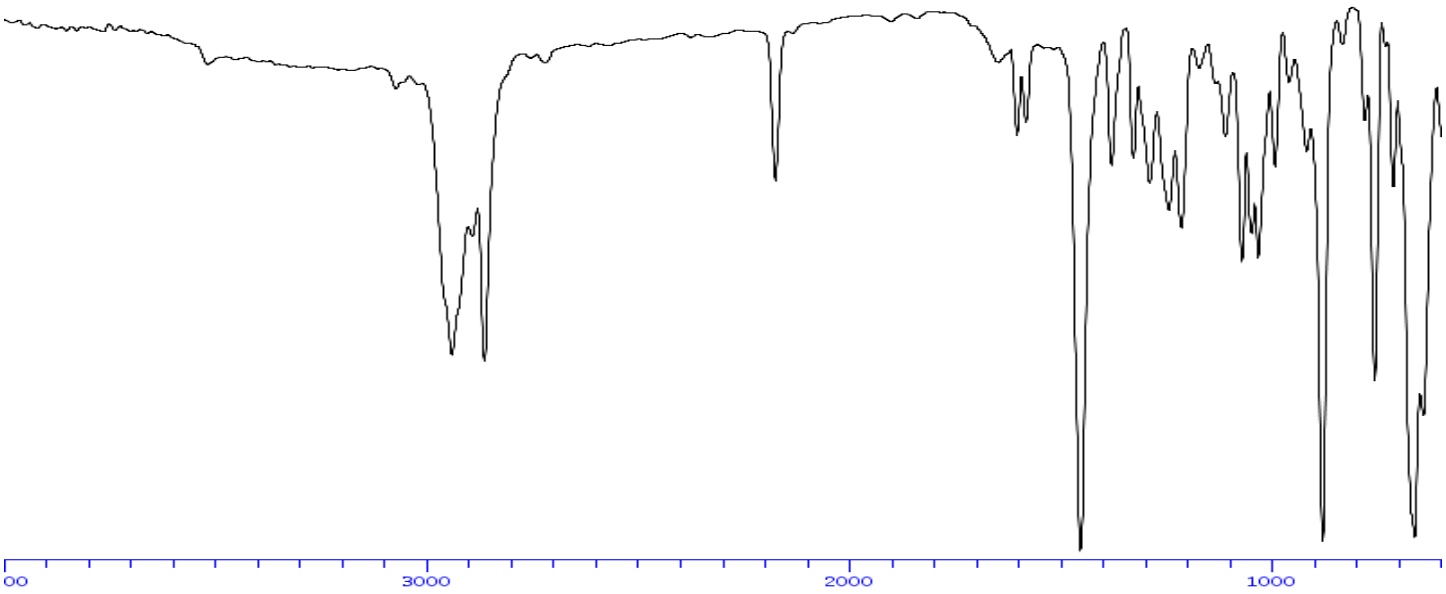

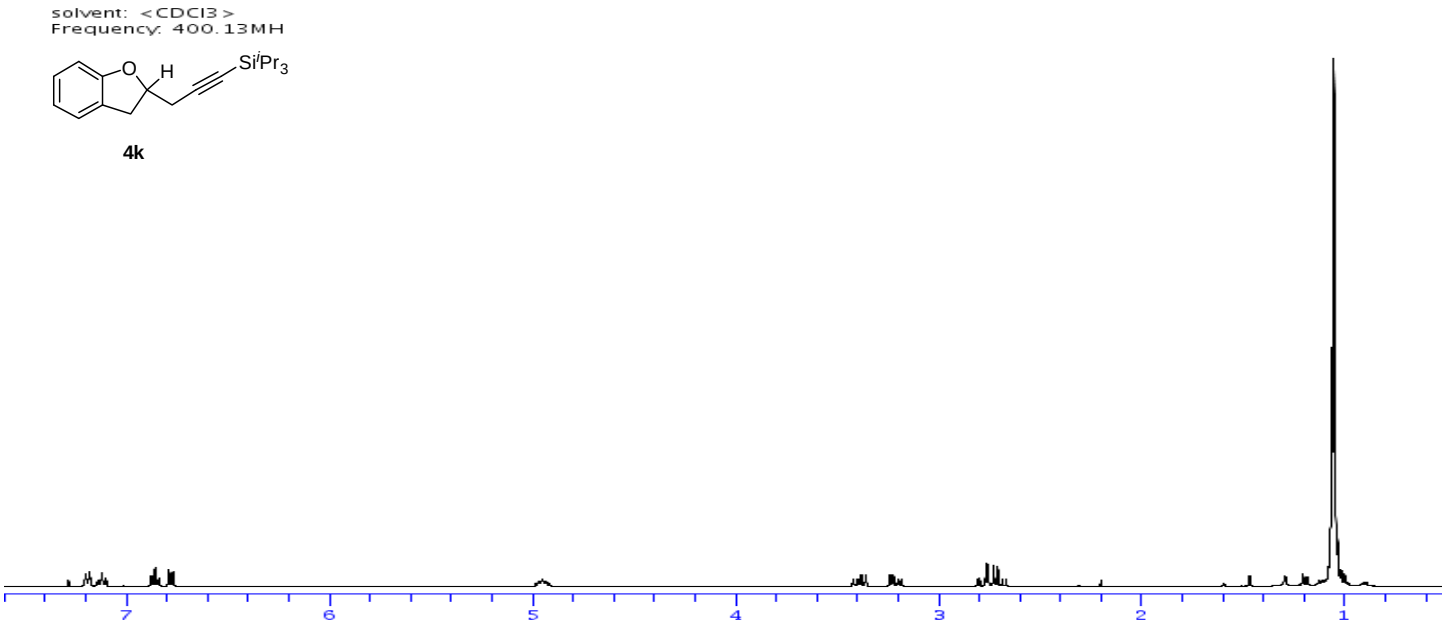
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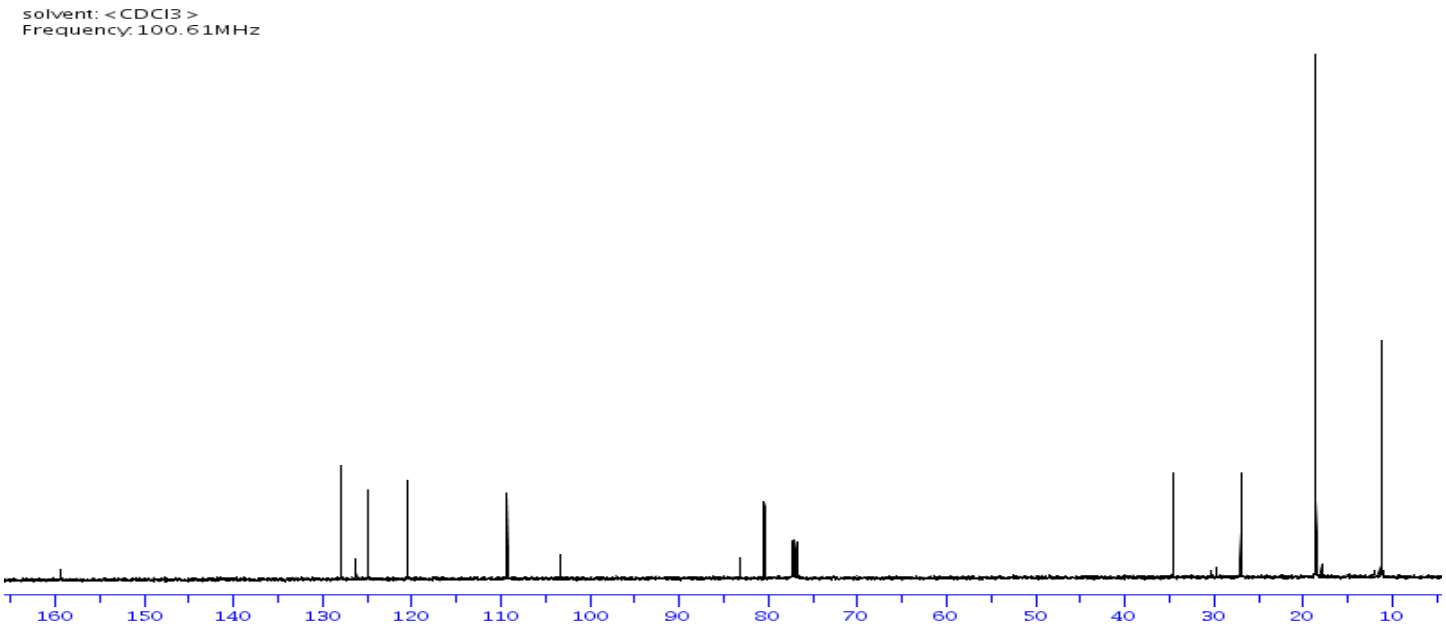
Frequency: 400.13MH
O
H
Si^{i}Pr$_3$
7
6
5
4
3
2
1

4k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120
110
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90
80
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20
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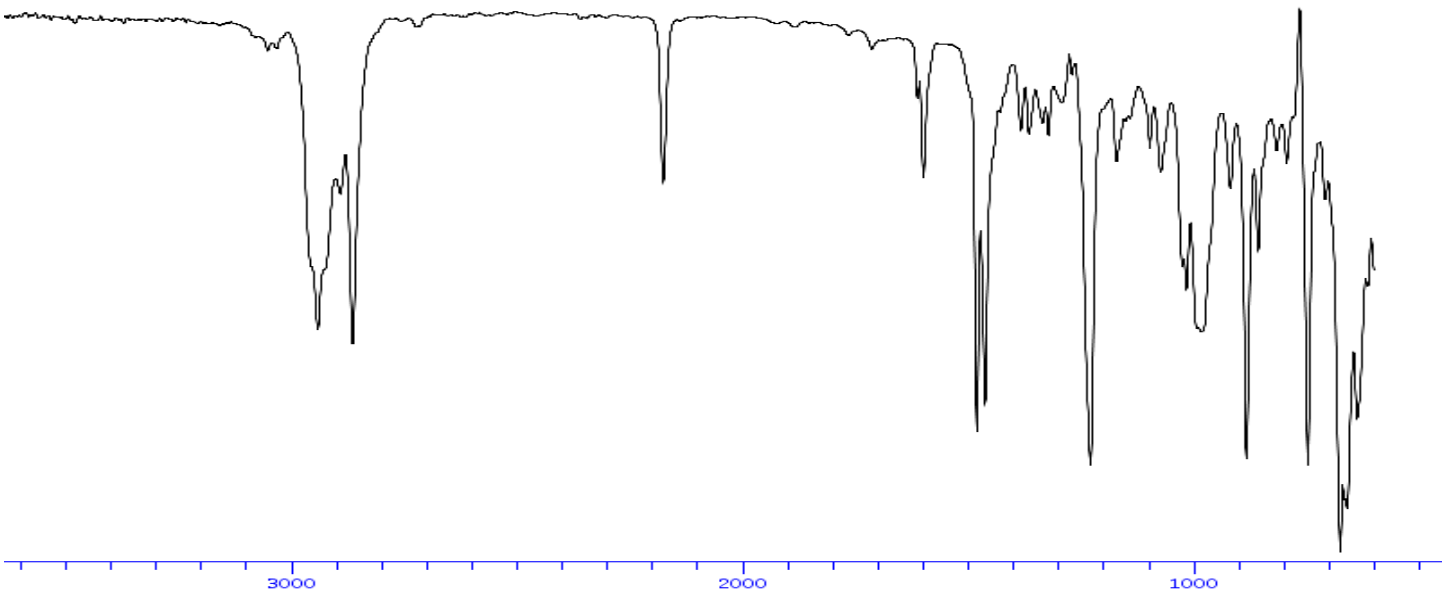
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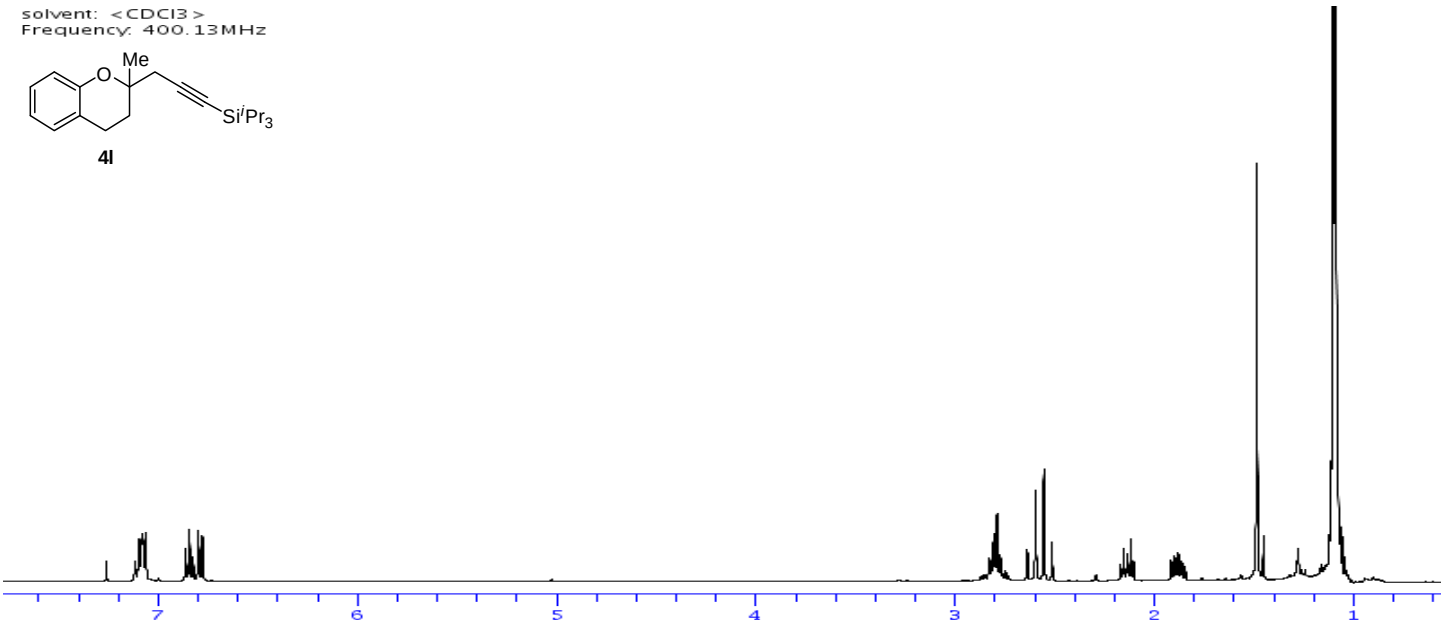
2000
1000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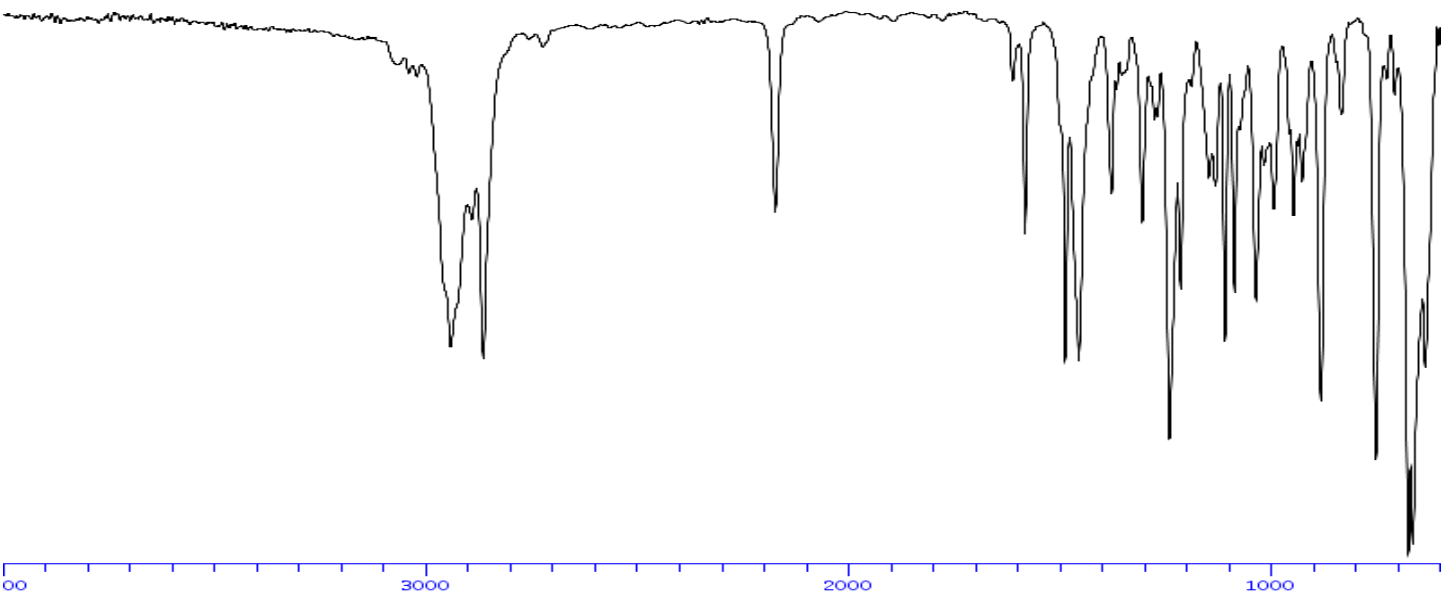
Frequency: 400.13MHz
Me
O
Si^{i}Pr$_3$
4l
7
6
5
4
3
2
1


solvent: <CDCl3>
Frequency: 100.61MHz
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10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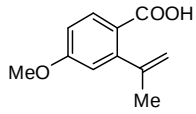
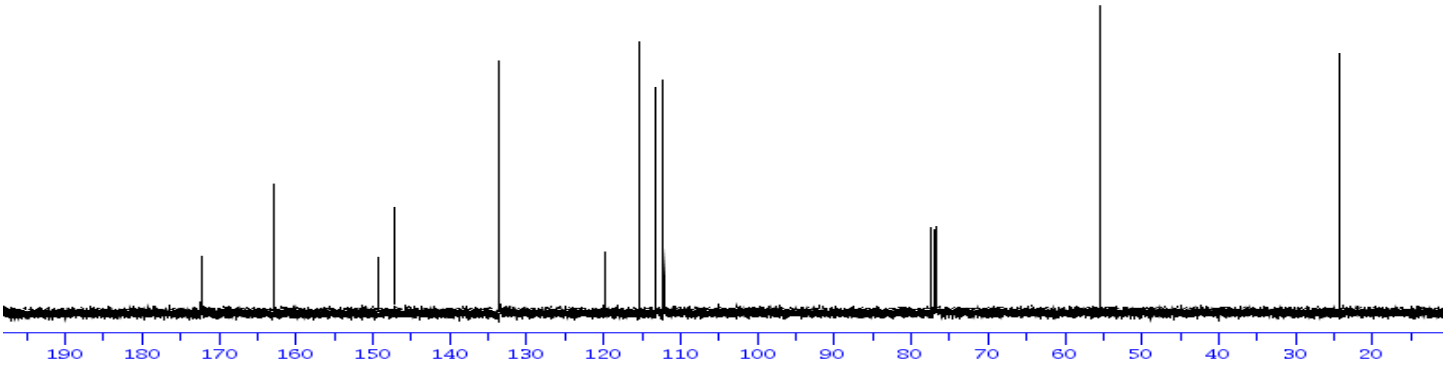
2000
1000

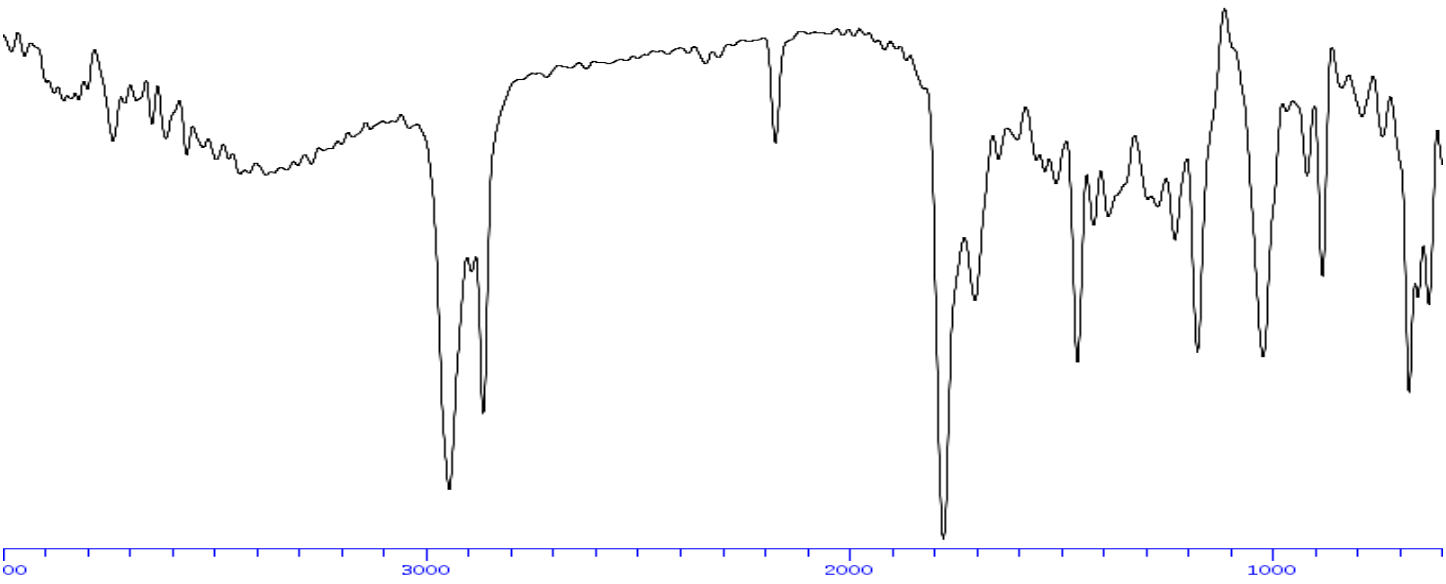
solvent: <CDCl3>
Frequency: 400.13 MHz

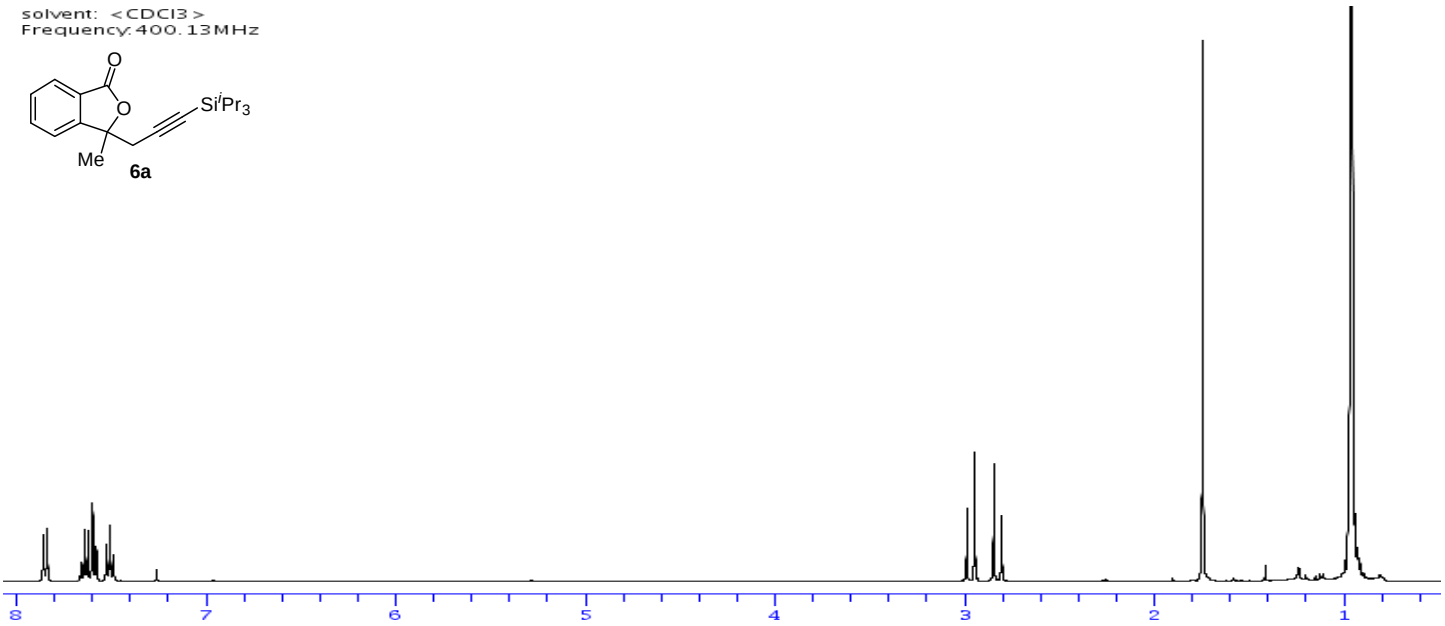


5b

solvent: <CDCl3>
Frequency: 100.61 MHz



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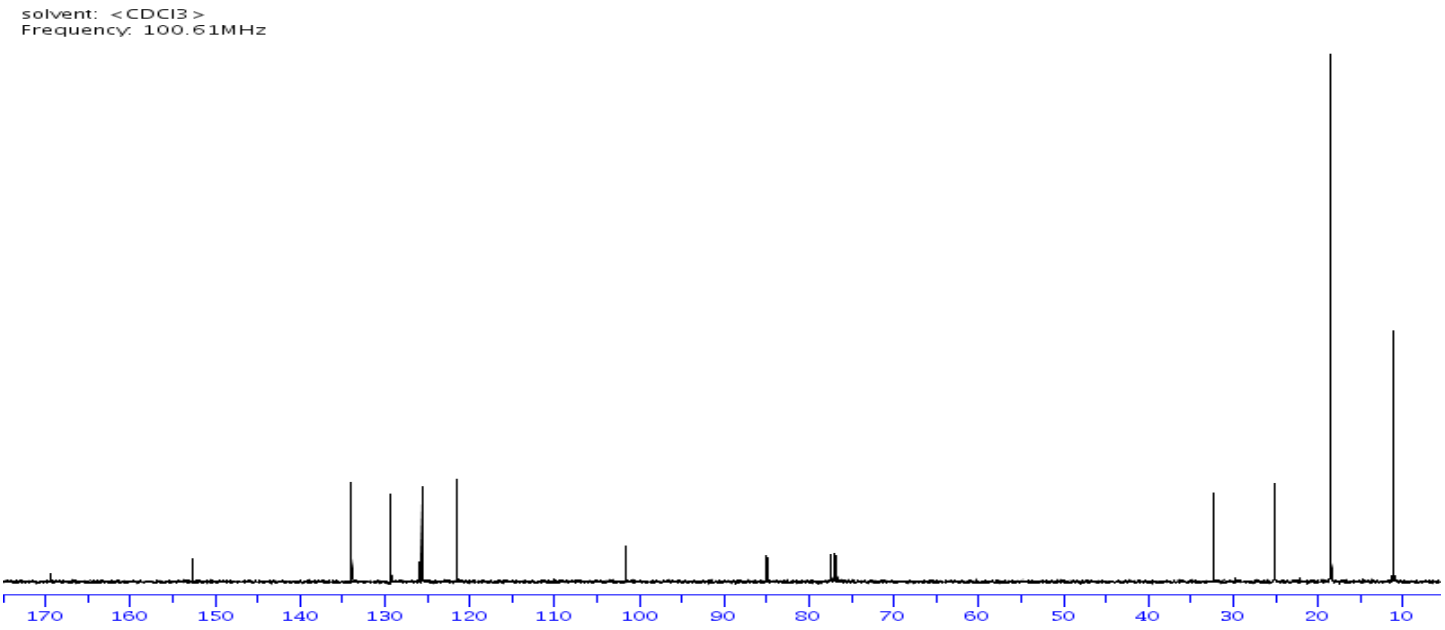
O
Si^{i}Pr$_3$
Me
8
7
6
5
4
3
2
1

6a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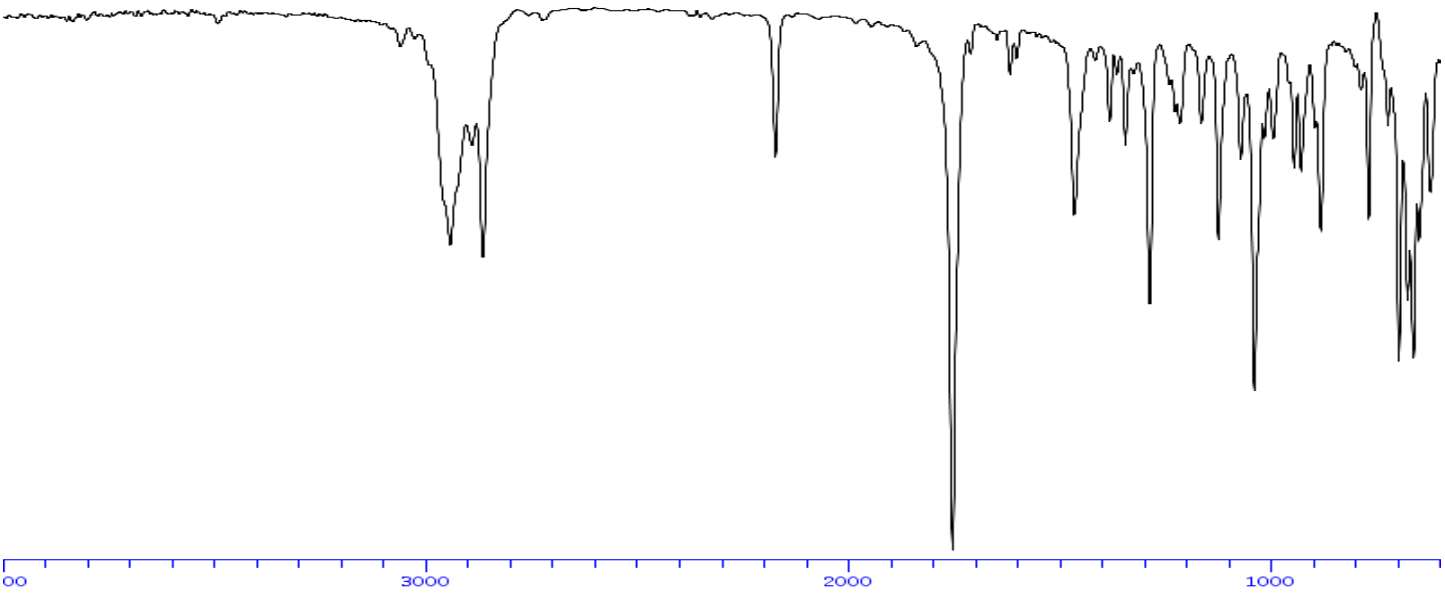
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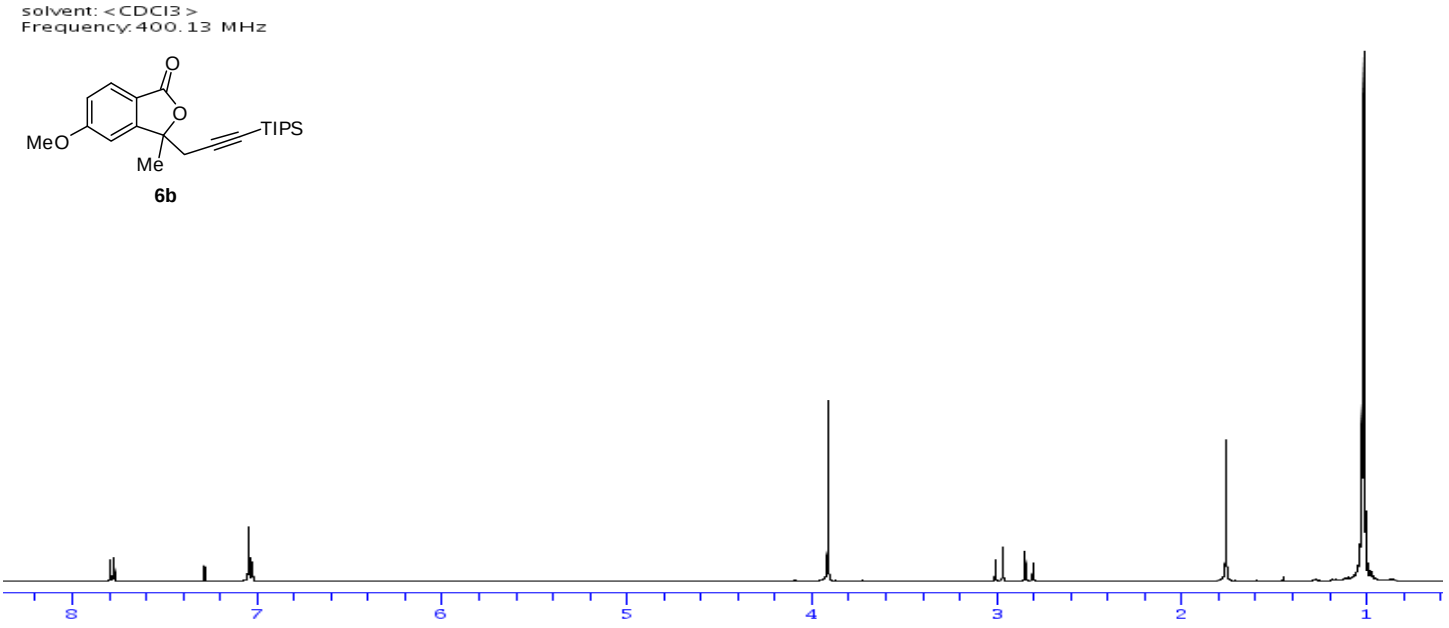
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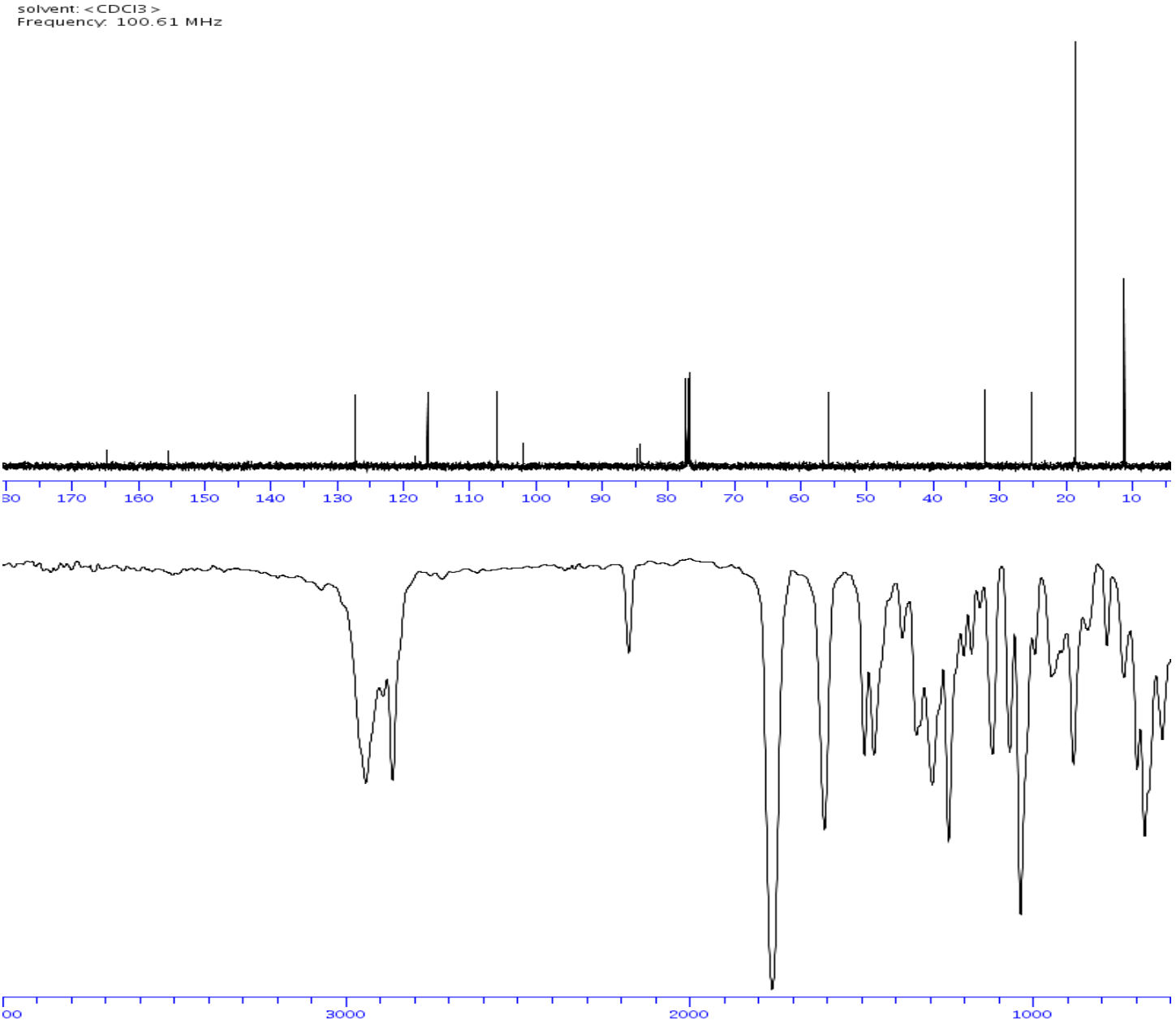
Frequency: 400.13 MHz
O
O
MeO
TIPS
Me
8
7
6
5
4
3
2
1

6b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Frequency: 100.61 MHz
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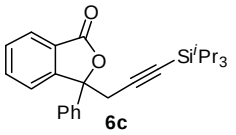
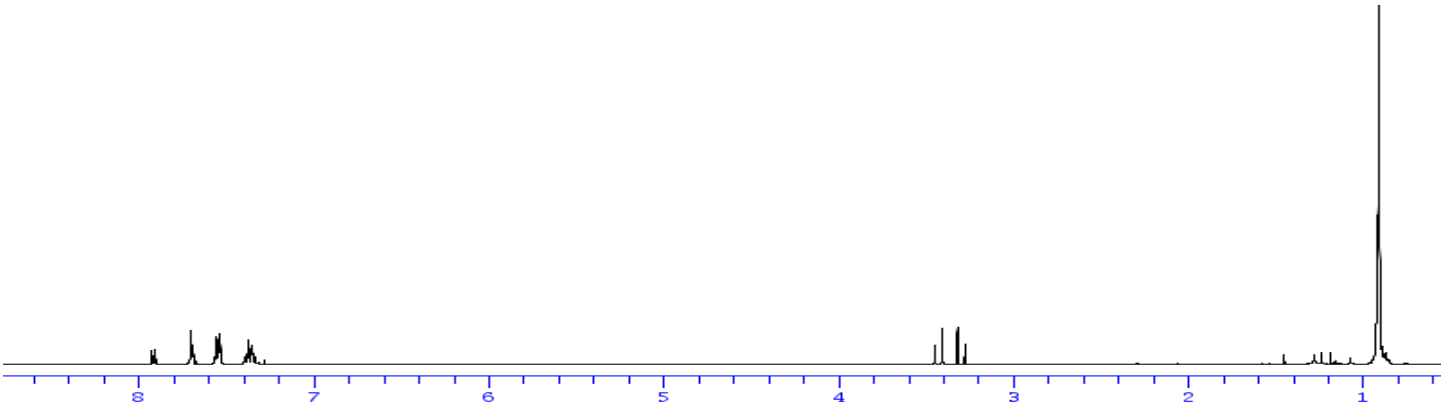
30
20
10
3000
2000
1000

solvent: <CDCl3>
Frequency: 400.13MHz



6c



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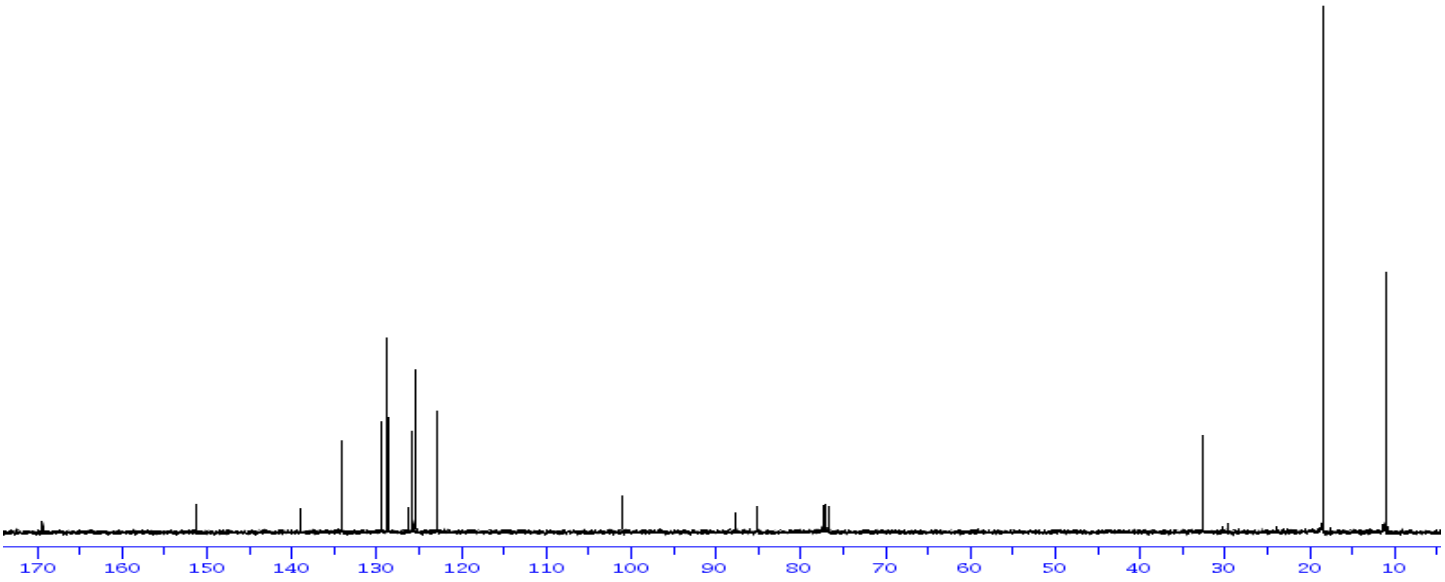

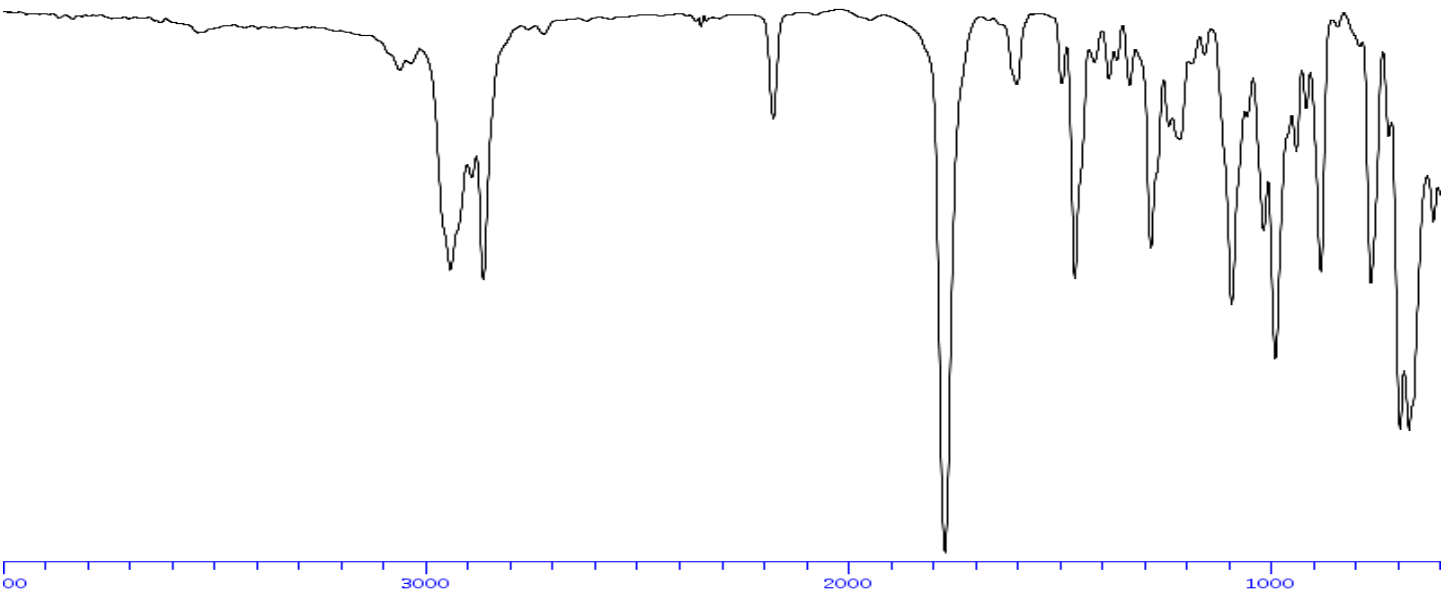

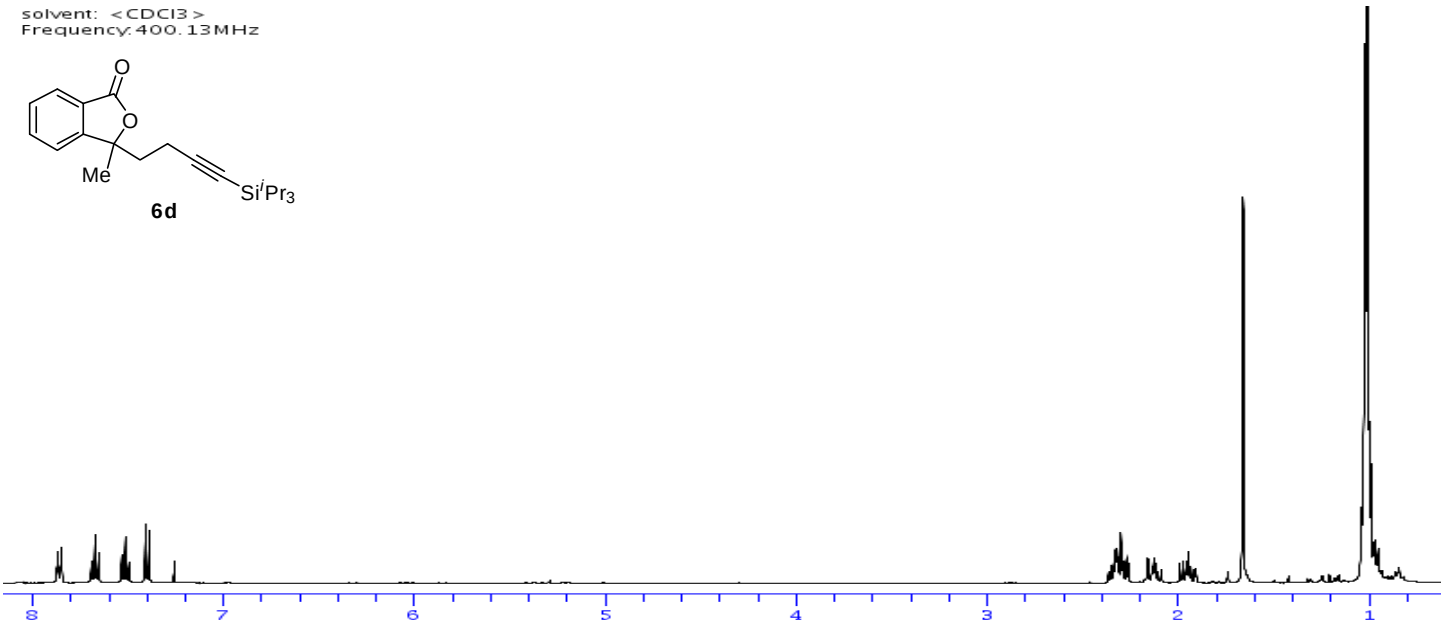
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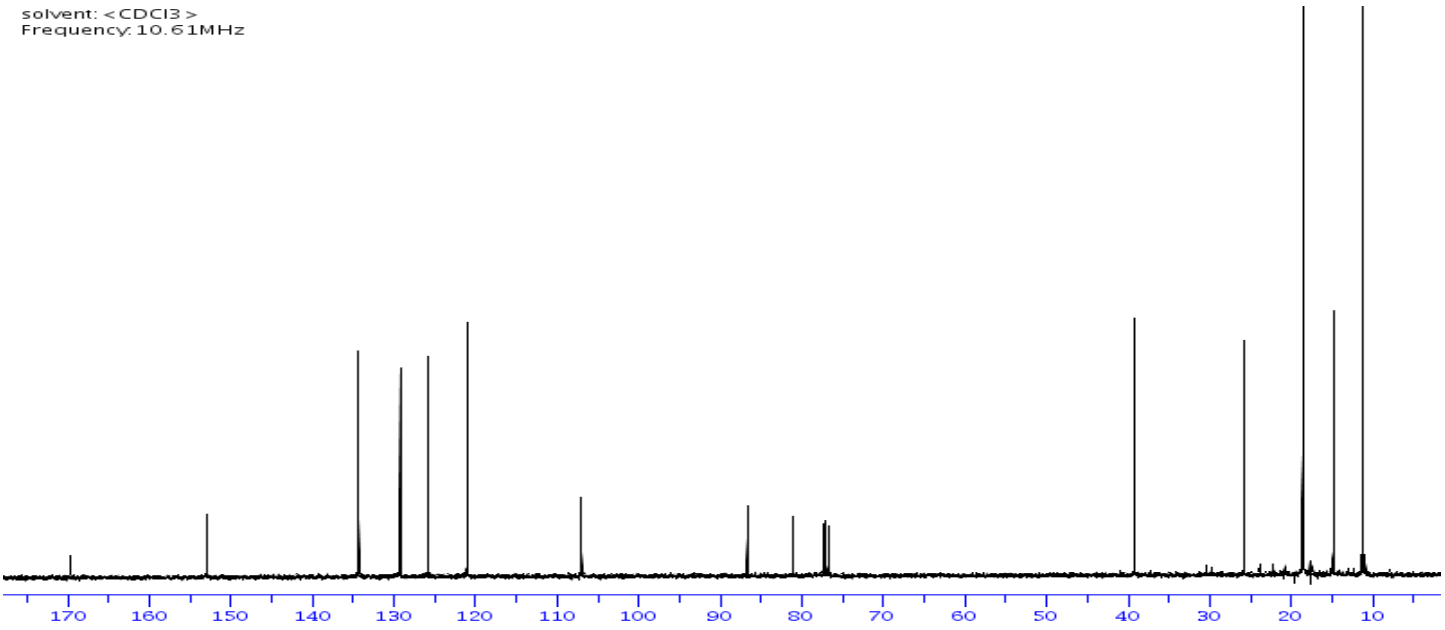
Frequency: 400.13MHz
O
O
Me
Si^{i}Pr$_3$
8
7
6
5
4
3
2
1

6d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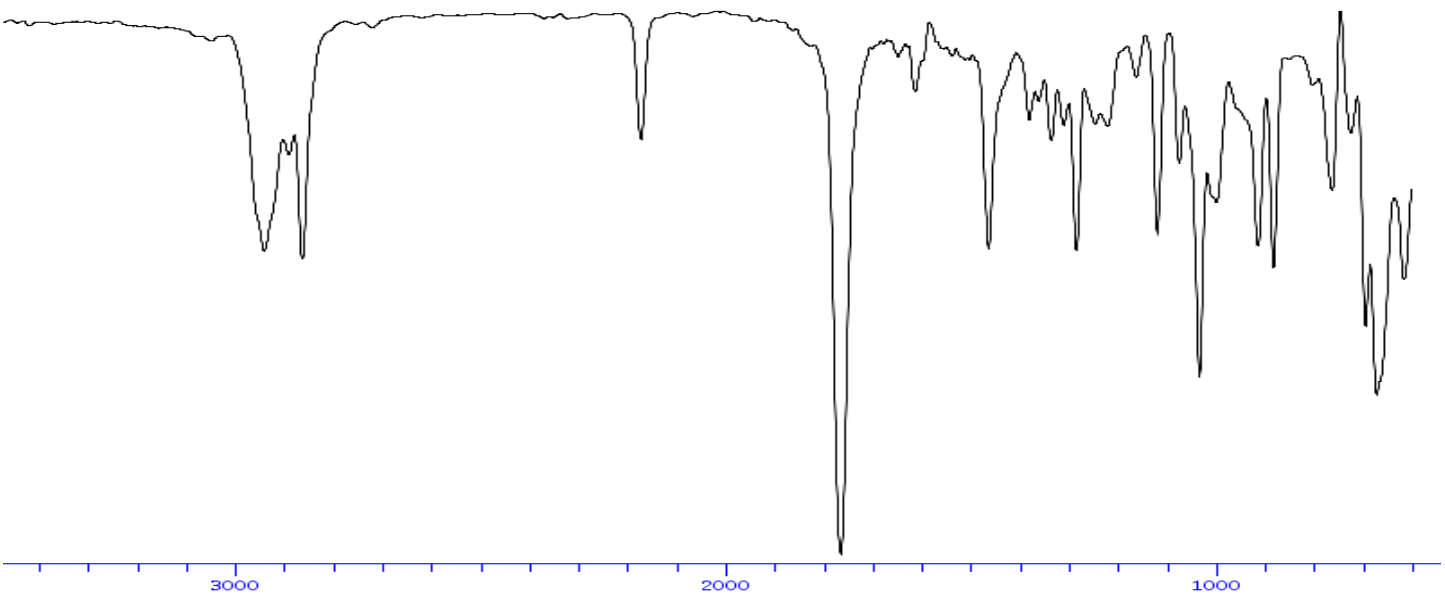
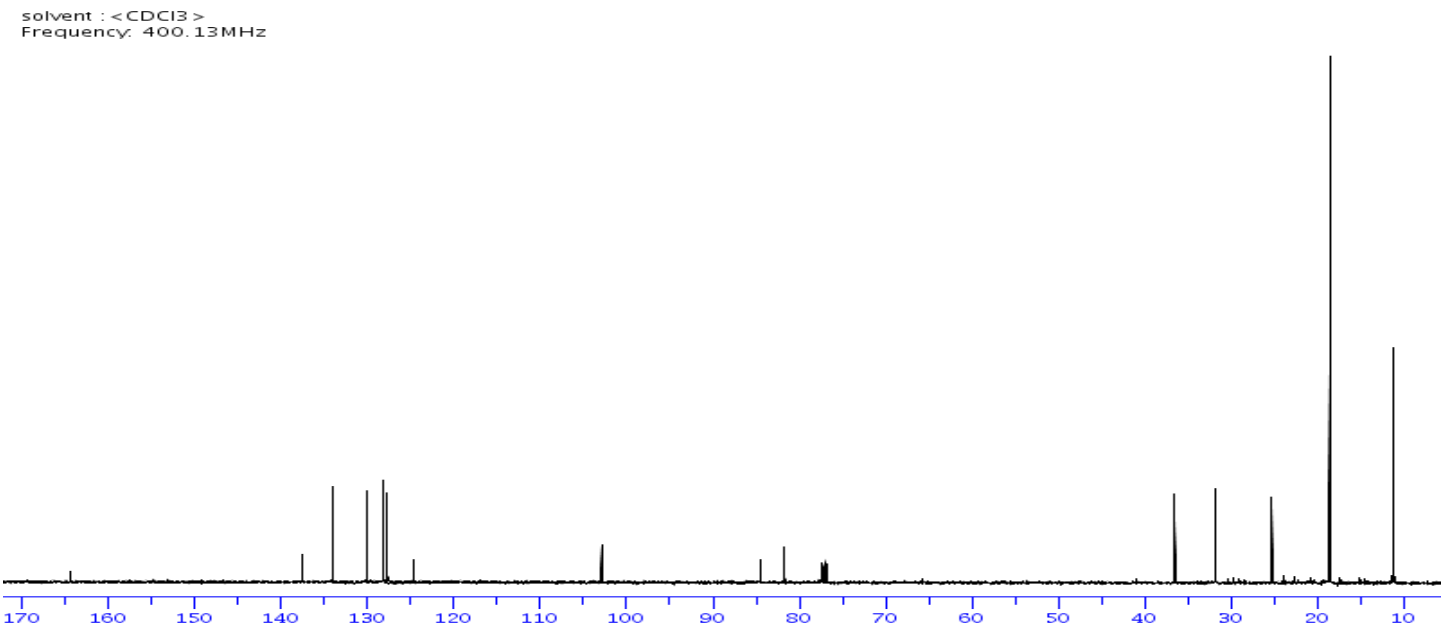
20
10


3000
2000
1000


solvent: <CDCl3 >
Frequency: 400.13MHz
O
O
Si^{i}Pr$_3$
Me
6e
8
7
6
5
4
3
2
1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Frequency: 400.13MHz
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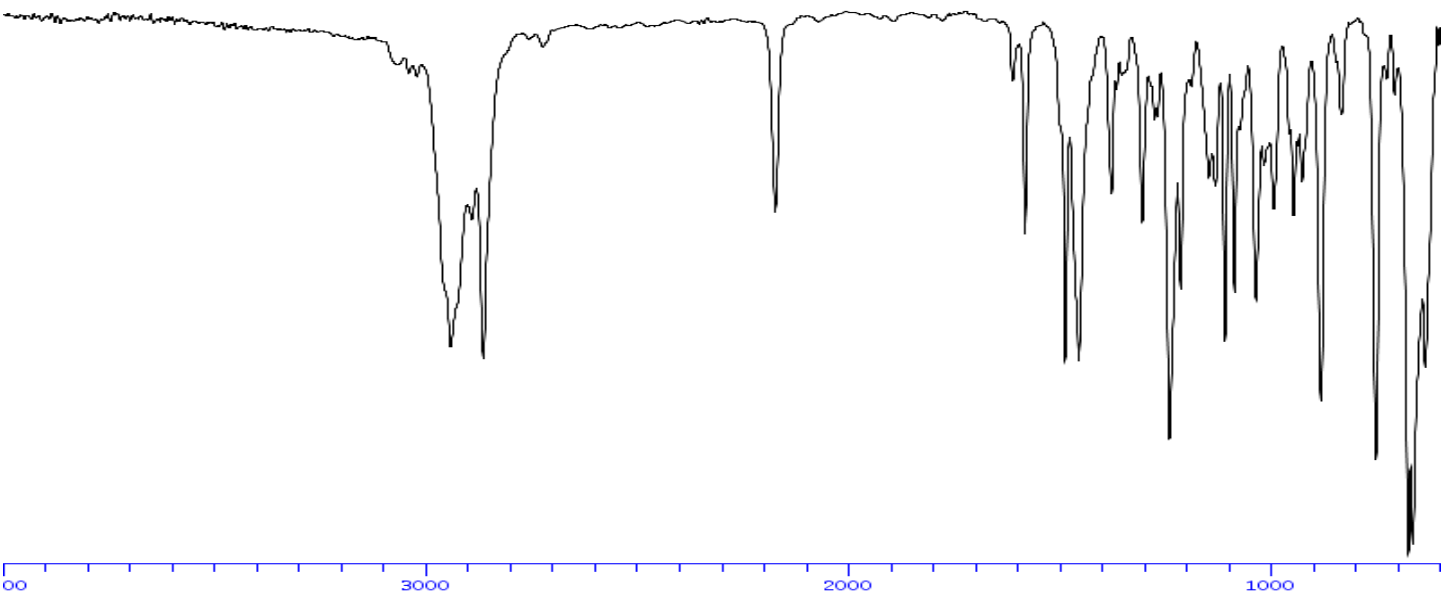
10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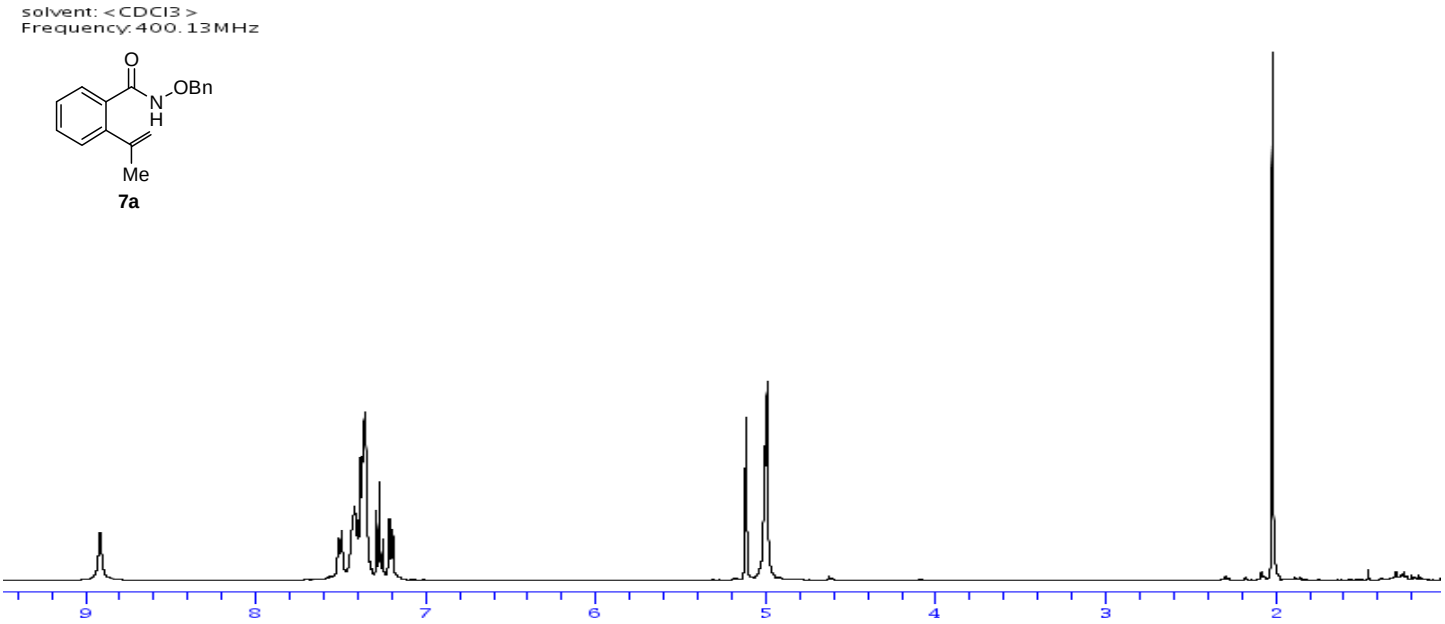
2000
1000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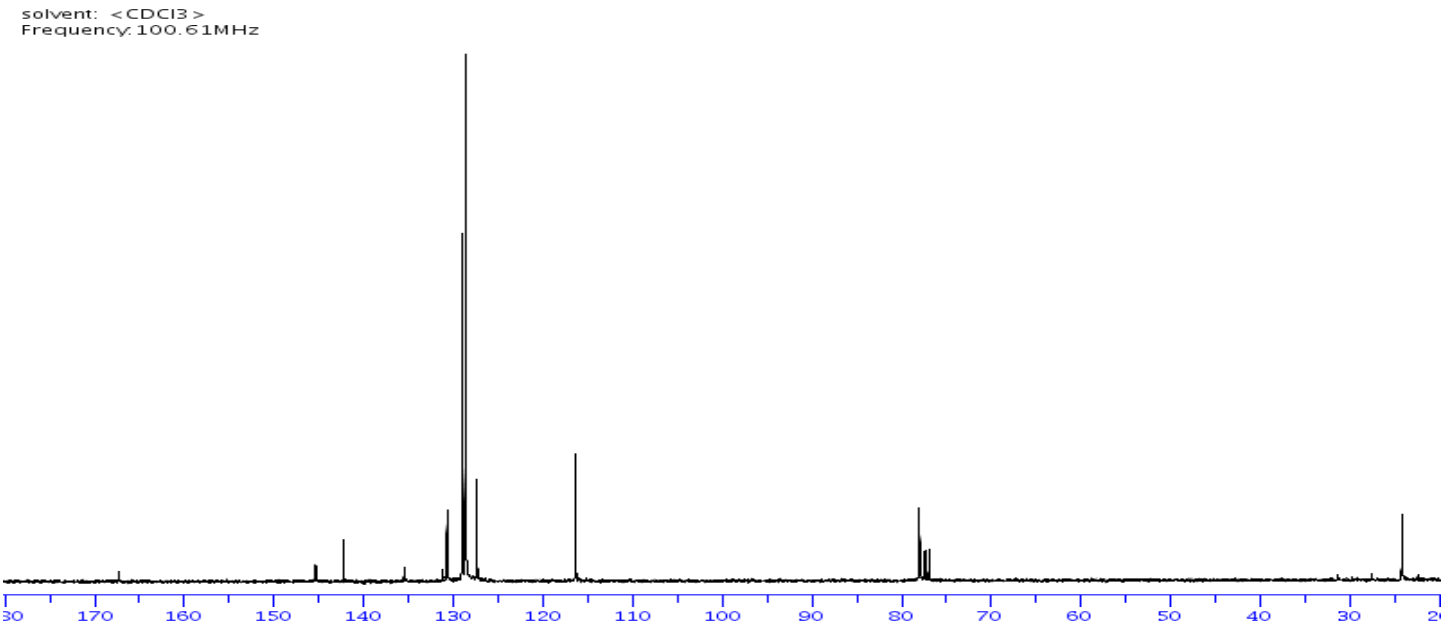
Frequency: 400.13MHz
O
N
H
OBn
Me
7a
9
8
7
6
5
4
3
2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Frequency: 100.61MHz
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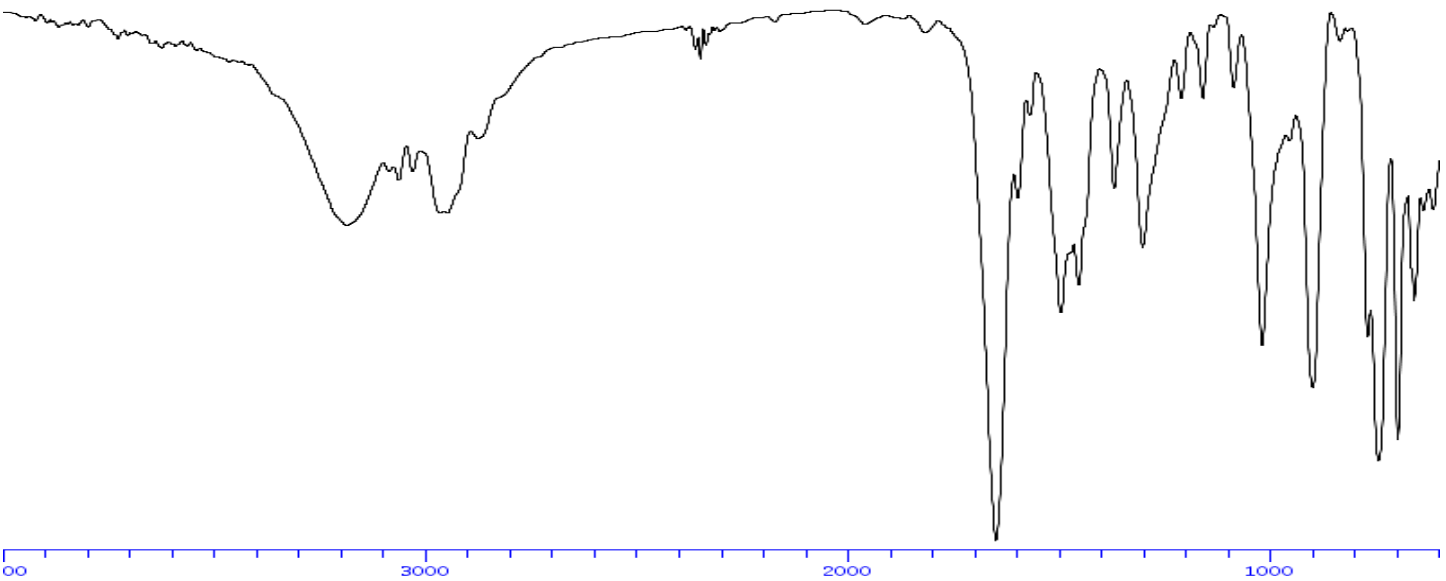
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solvent: <CDCl3>
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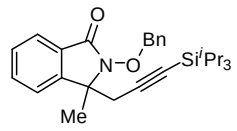
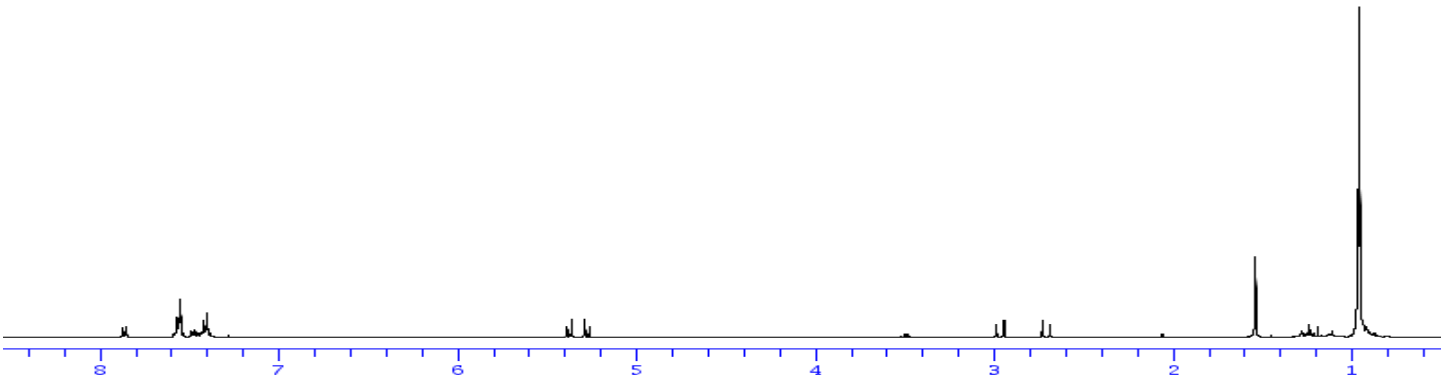


8a



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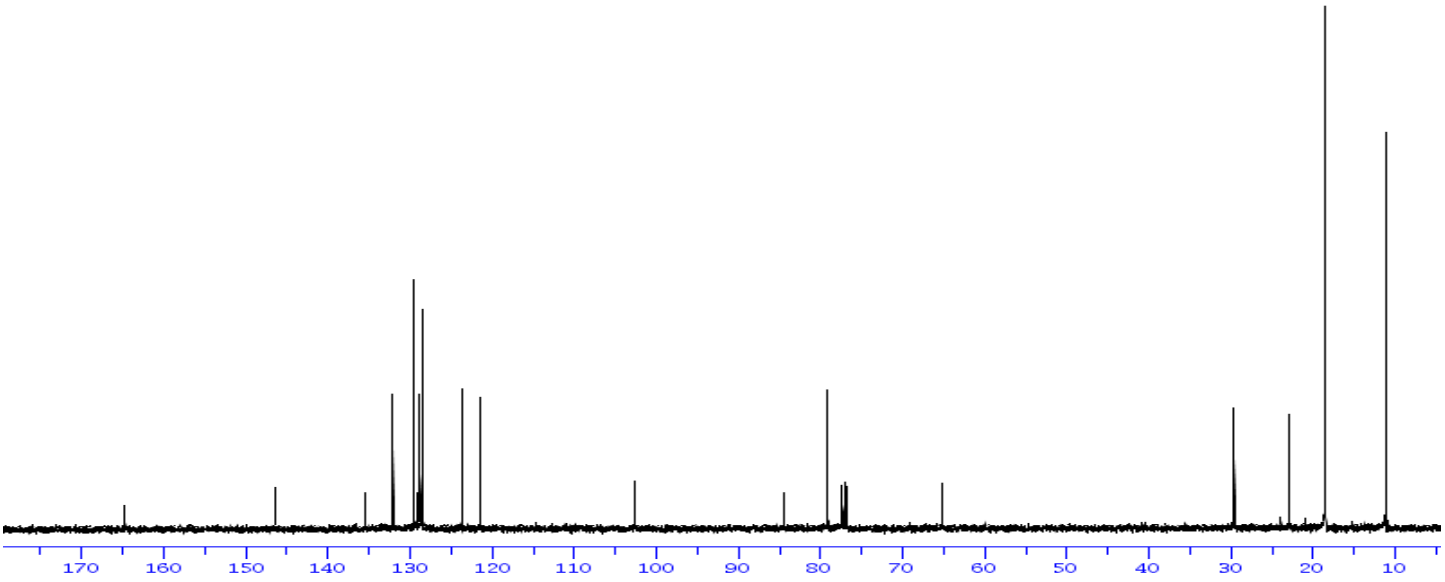

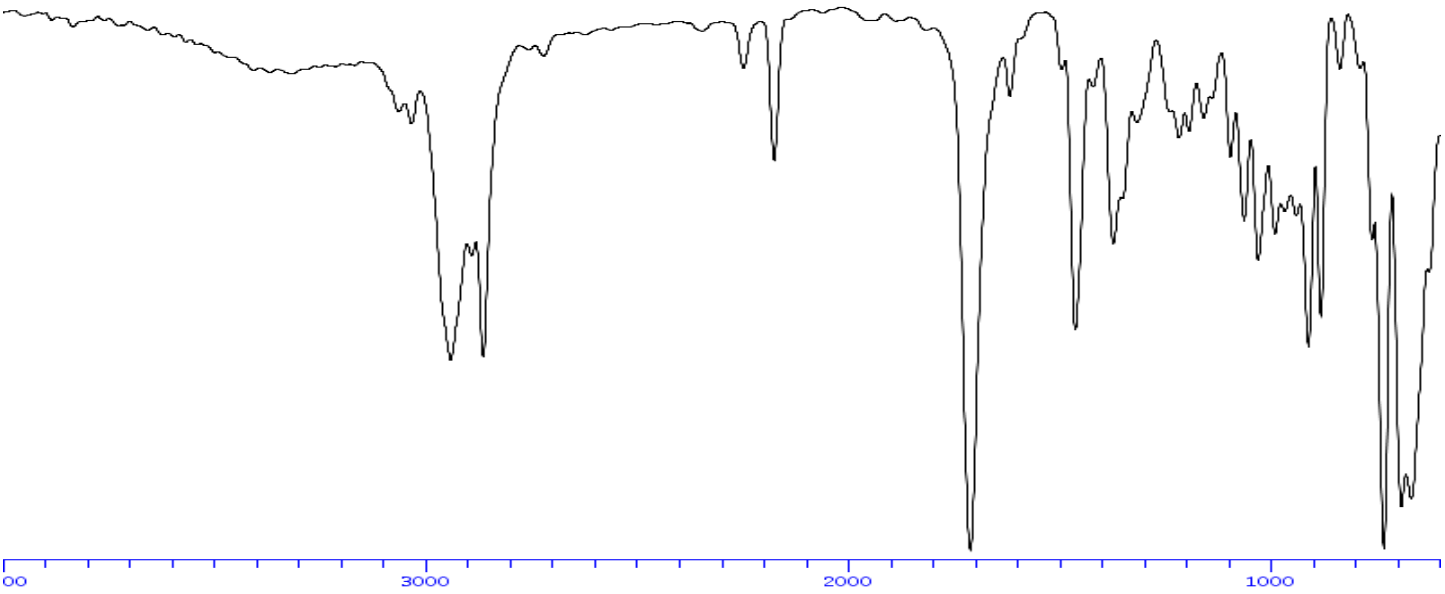

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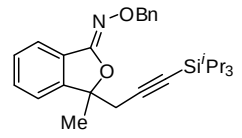

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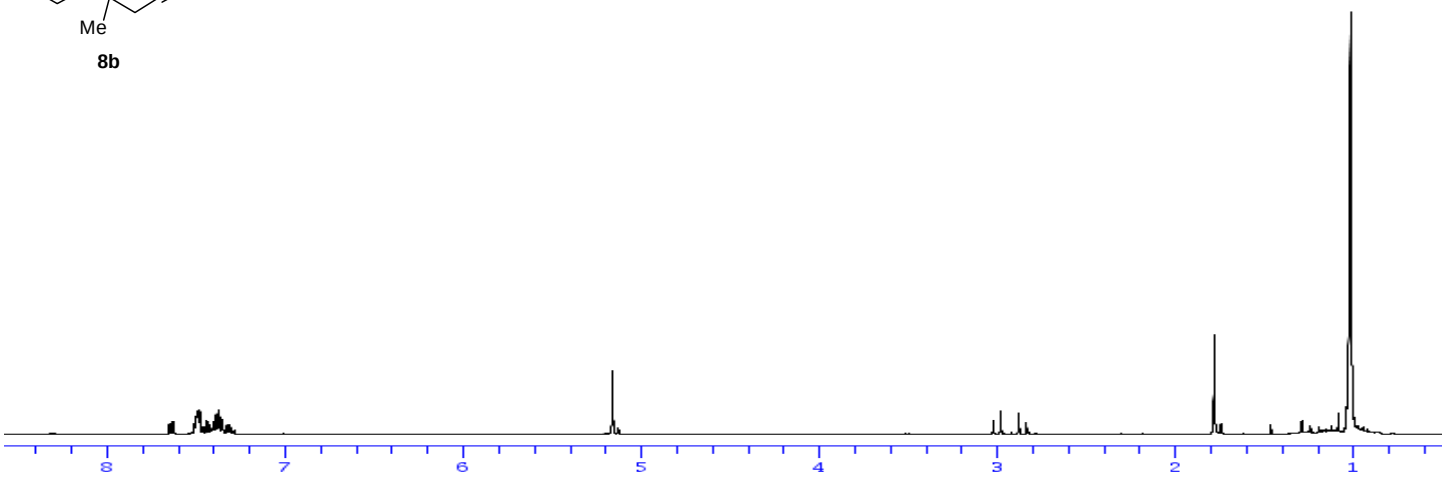

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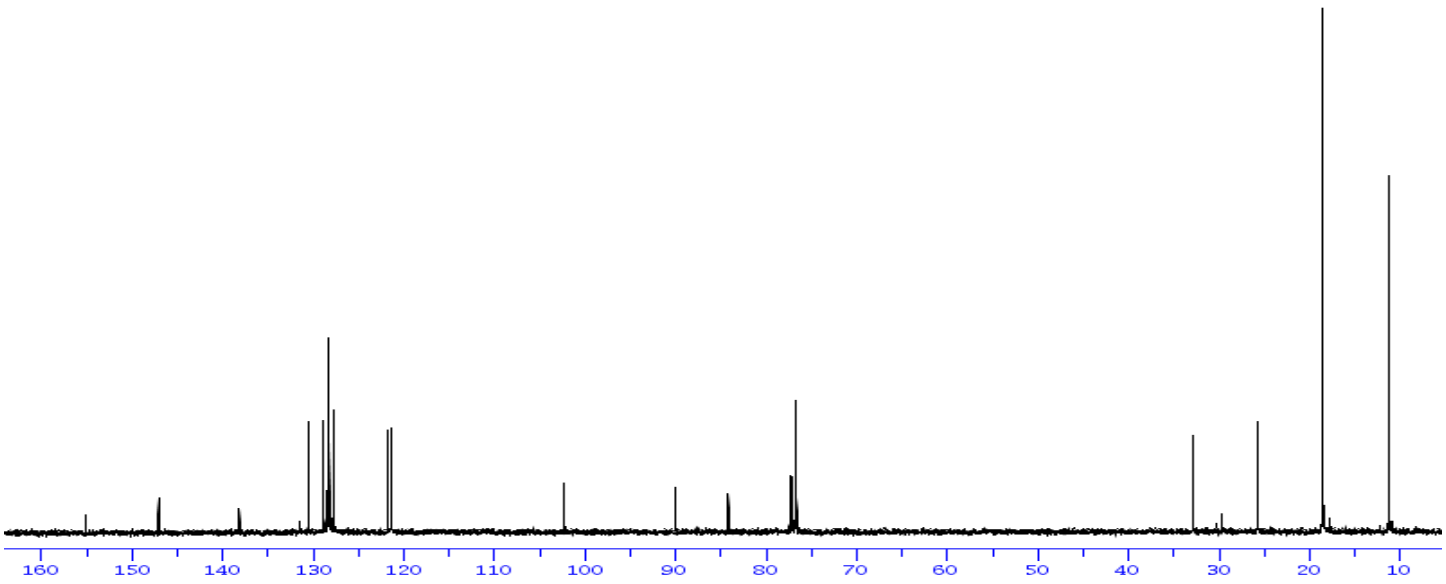
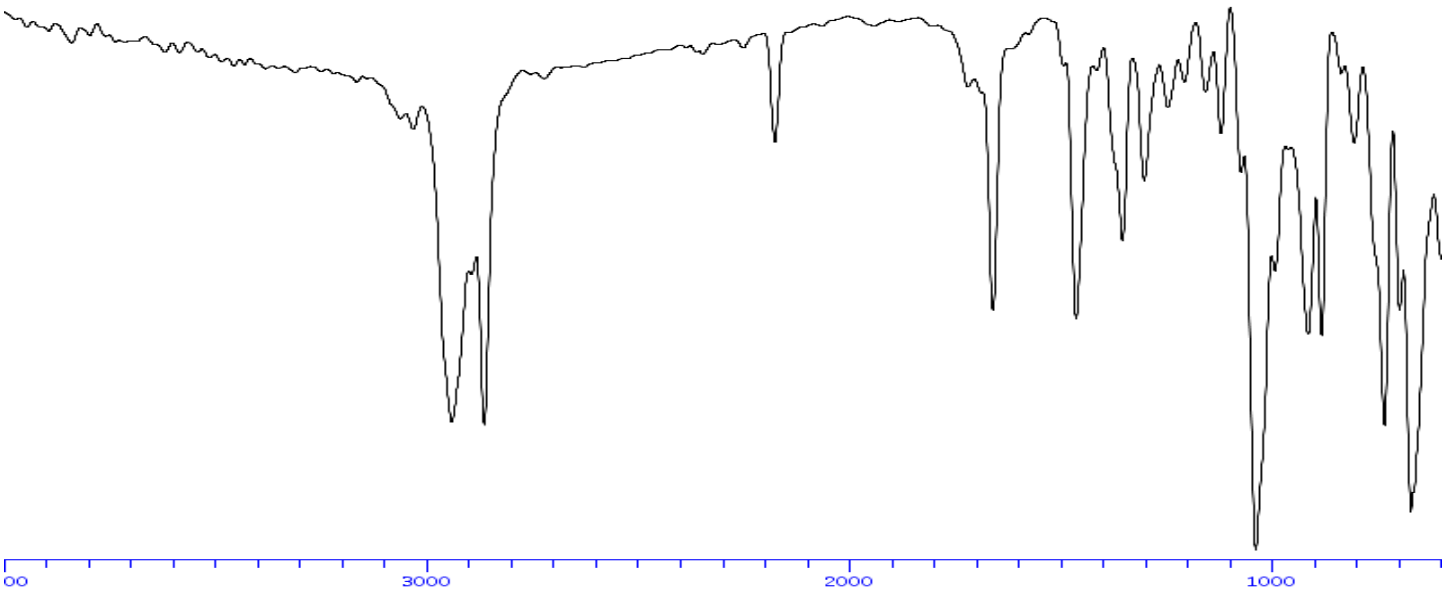
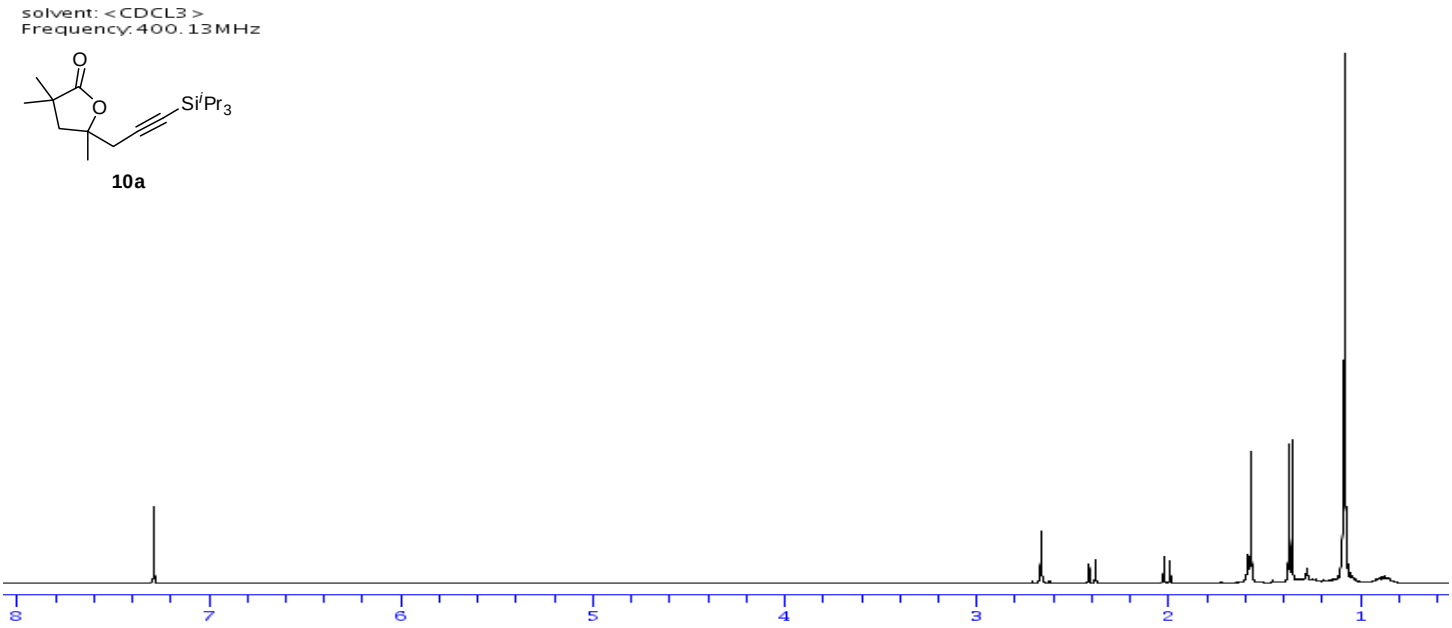
Frequency: 100.61MHz



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Frequency: 400.13MHz
O
O
SiiPr3
10a
8
7
6
5
4
3
2
1


solvent: <CDCl3 >
Frequency: 100.61MHz
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140
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120
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100
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40
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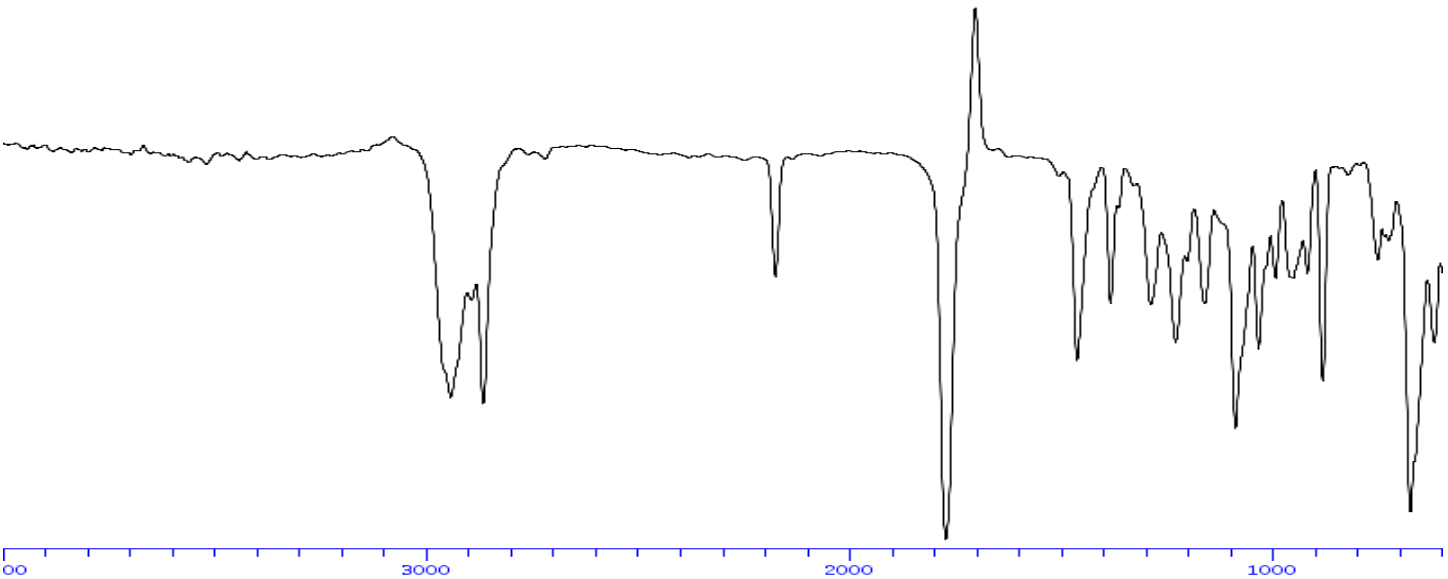
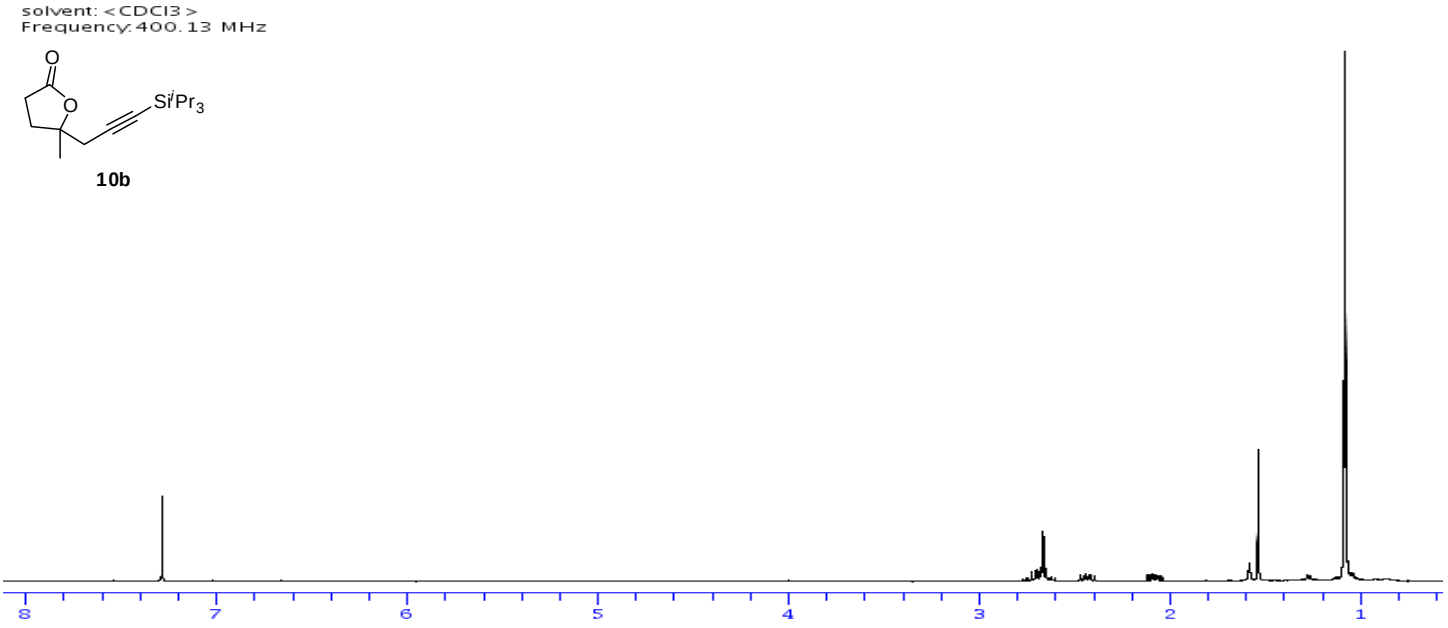
20
10


00
3000
2000
1000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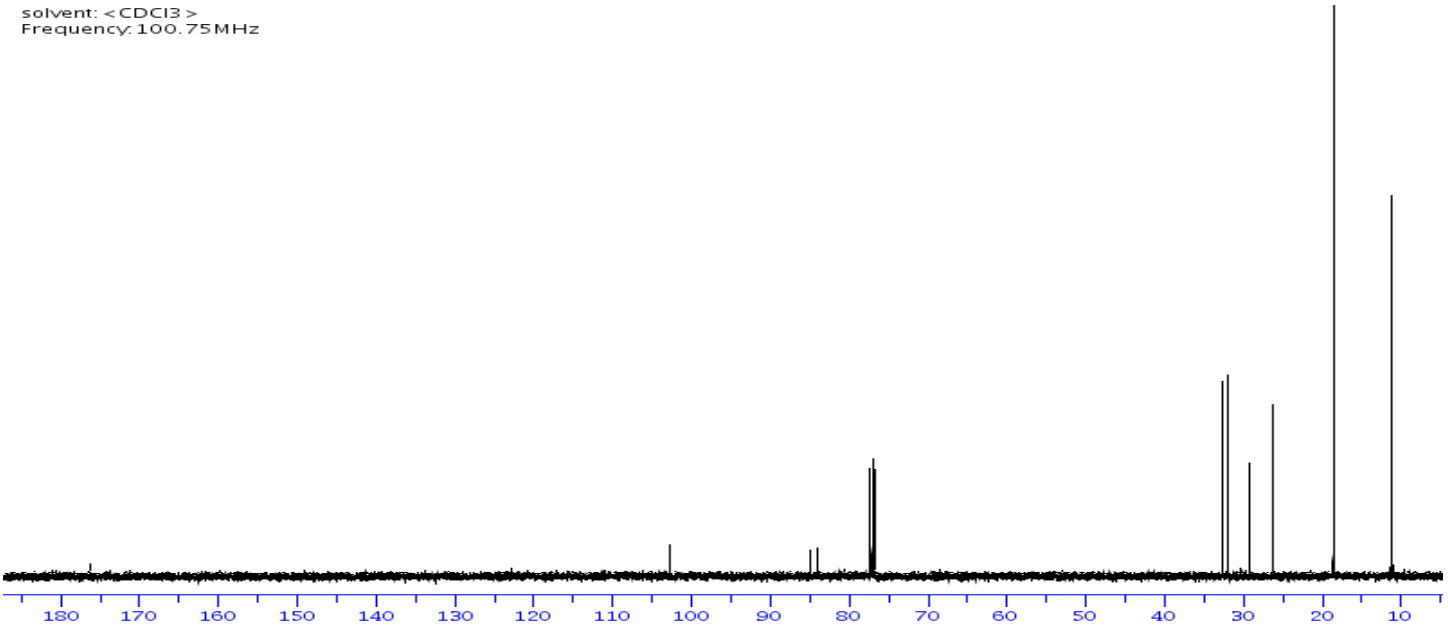
Frequency: 400.13 MHz
O
O
SiiPr3
8
7
6
5
4
3
2
1

10b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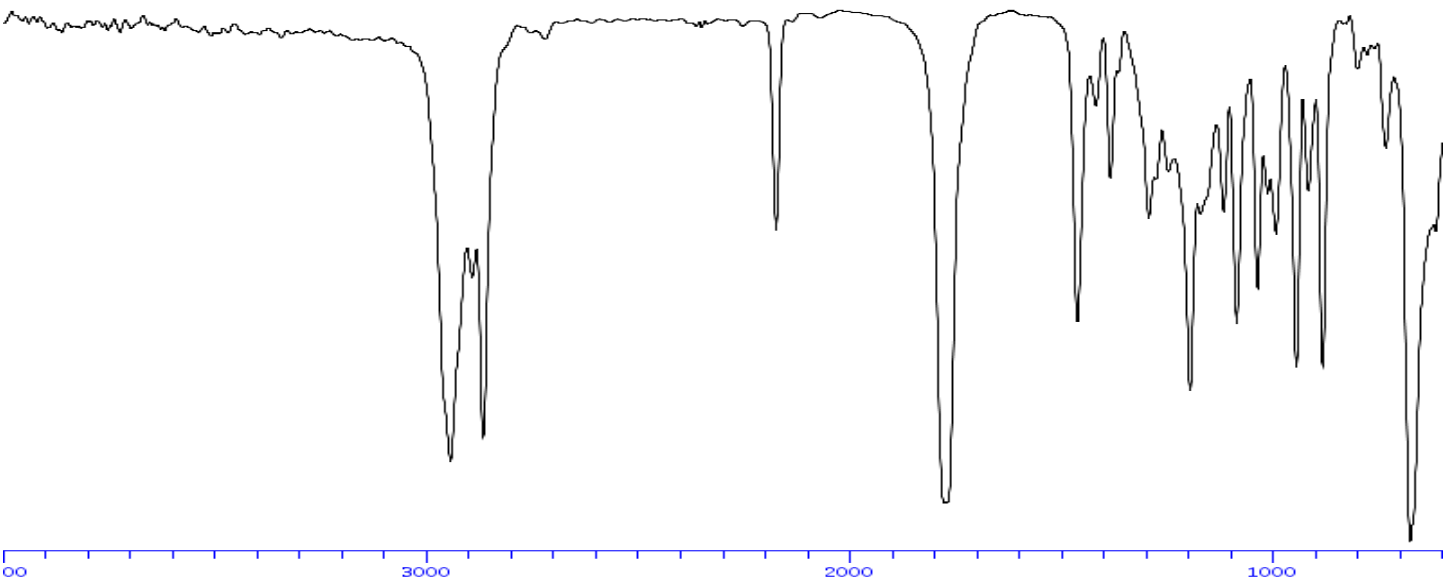
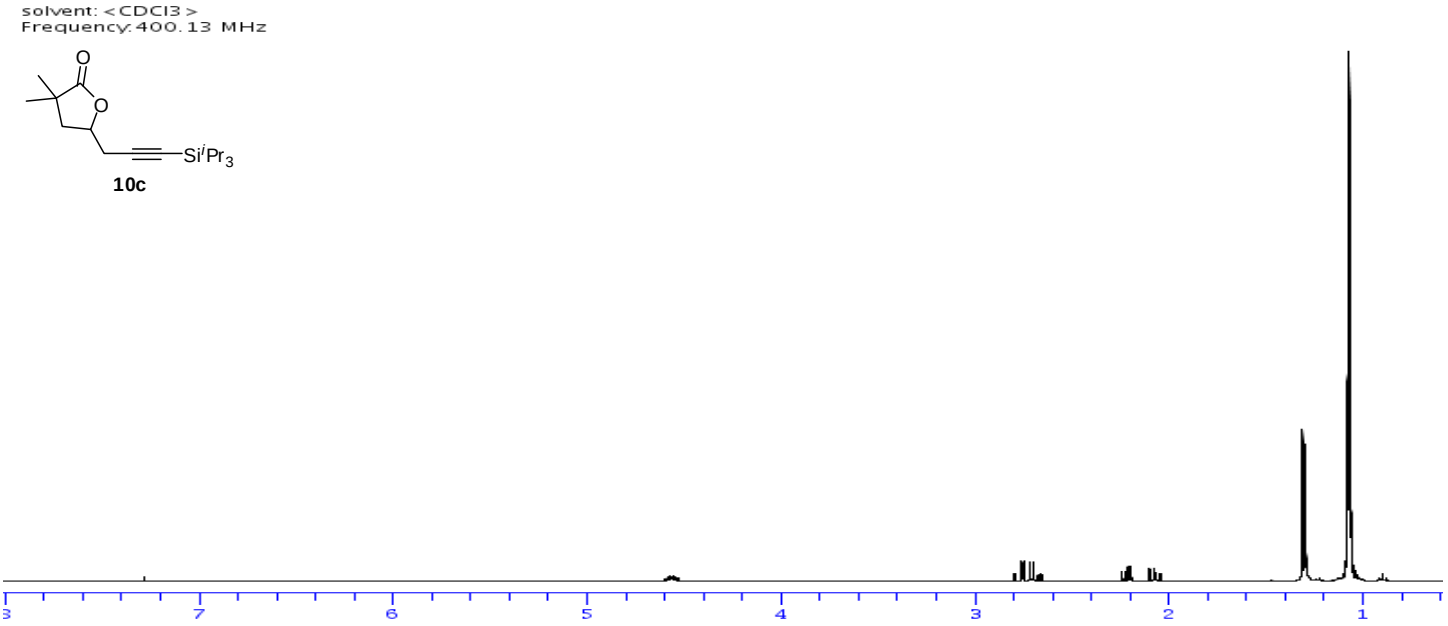
40
30
20
10


00
3000
2000
1000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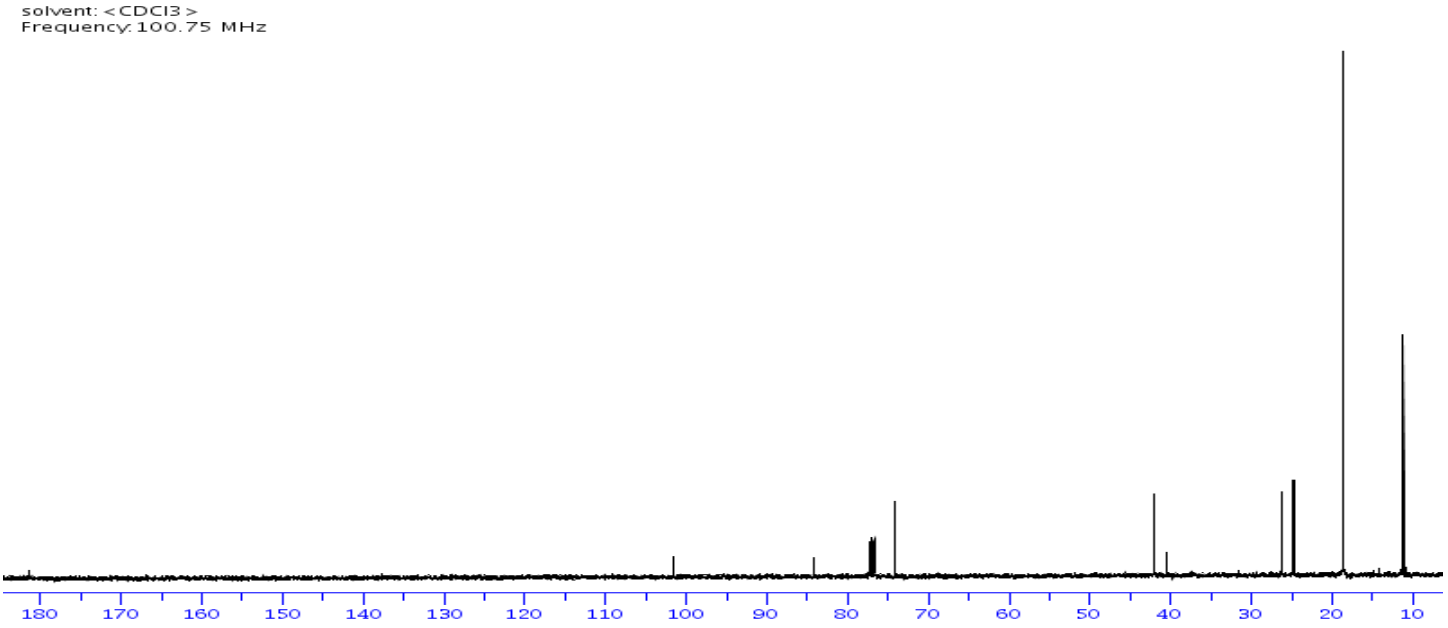
Frequency: 400.13 MHz
O
O
Si^{i}Pr$_3$
10c
7
6
5
4
3
2
1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Frequency: 100.75 MHz
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120
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100
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80
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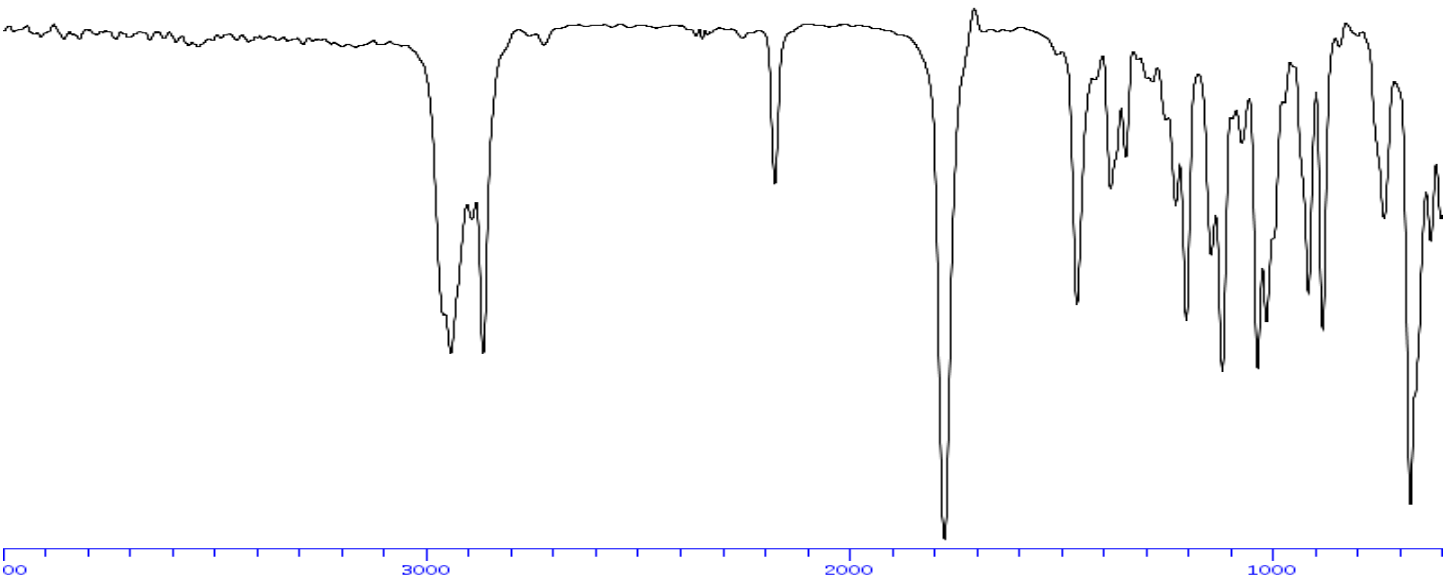
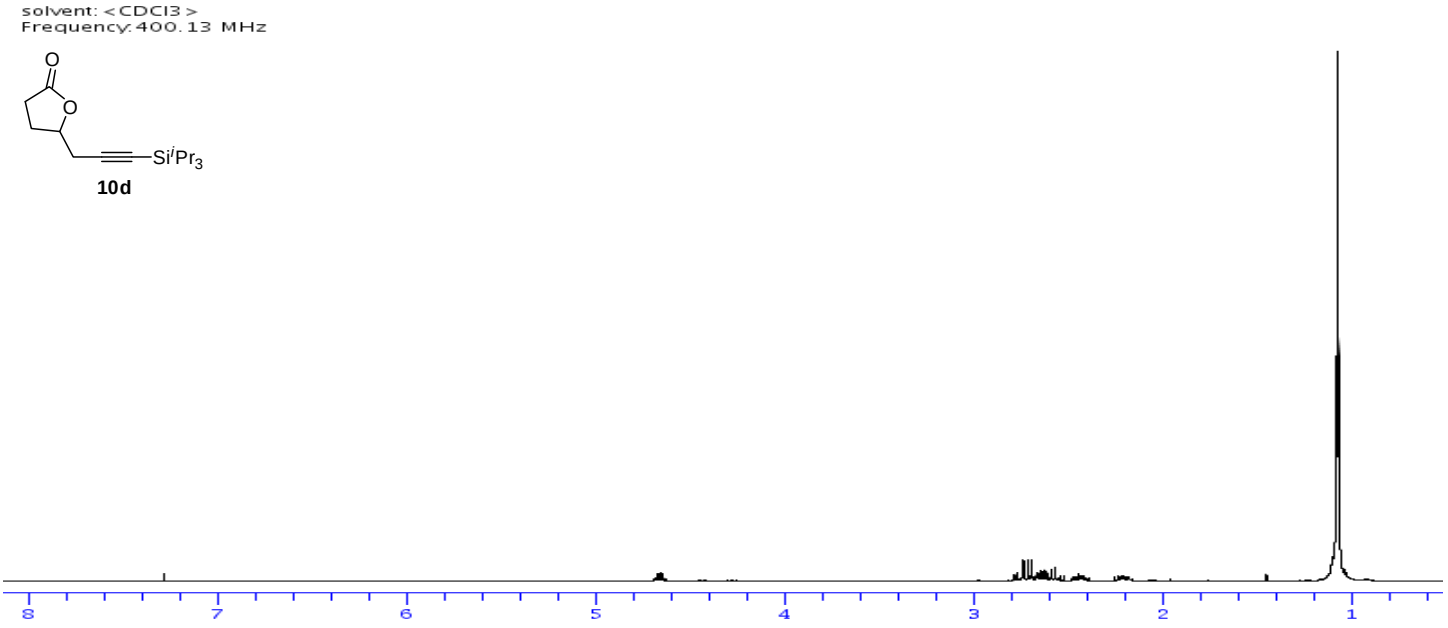
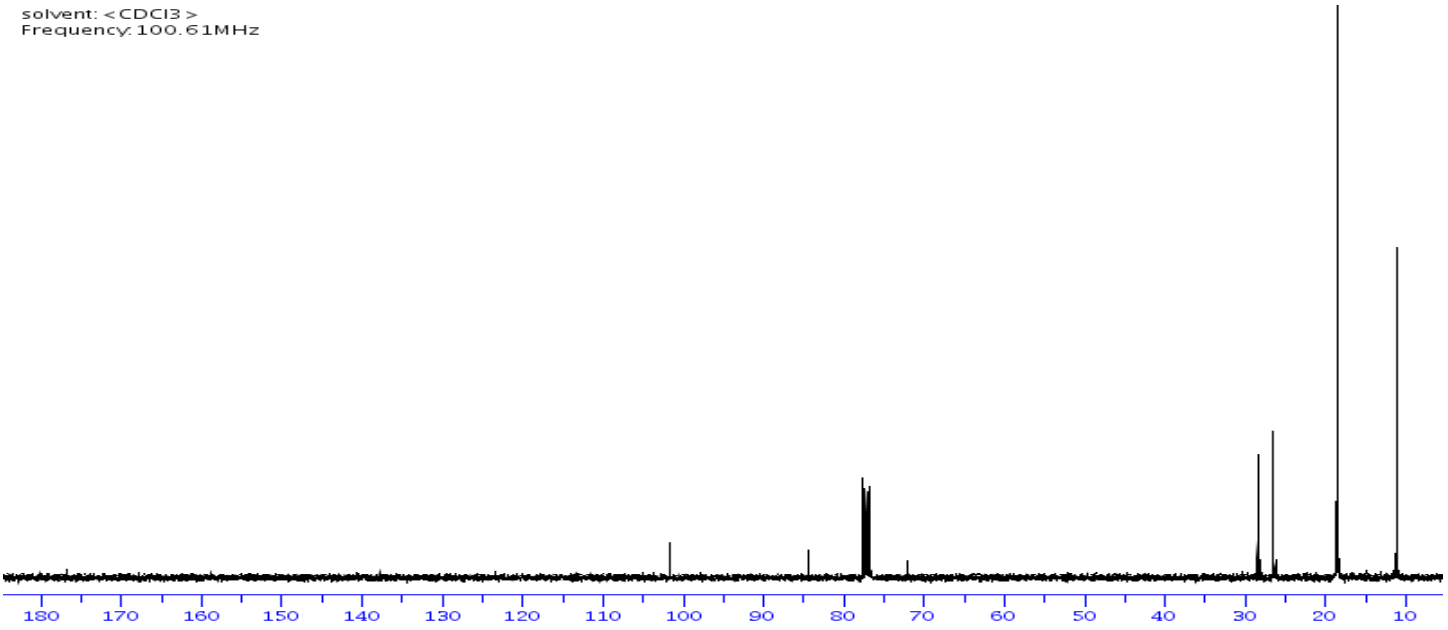
40
30
20
10


3000
2000
1000


solvent: <CDCl3 >
Frequency: 400.13 MHz
O
O
SiiPr3
10d
8
7
6
5
4
3
2
1


solvent: <CDCl3 >
Frequency: 100.61MHz
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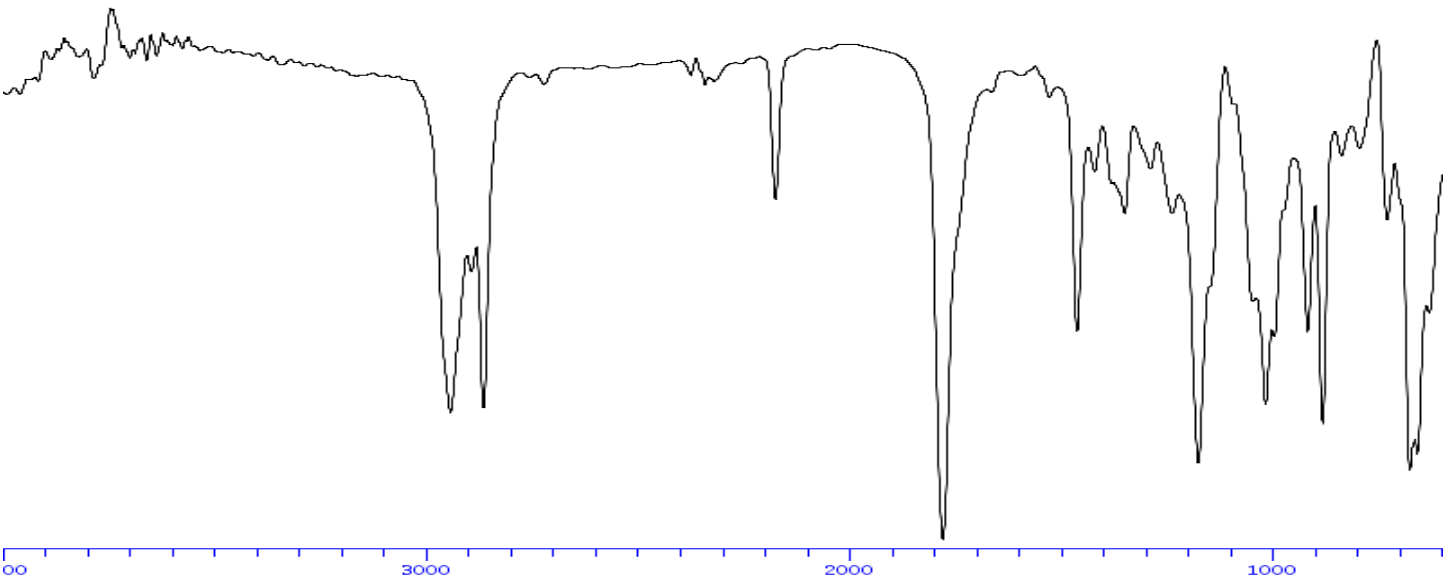
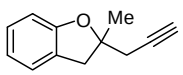
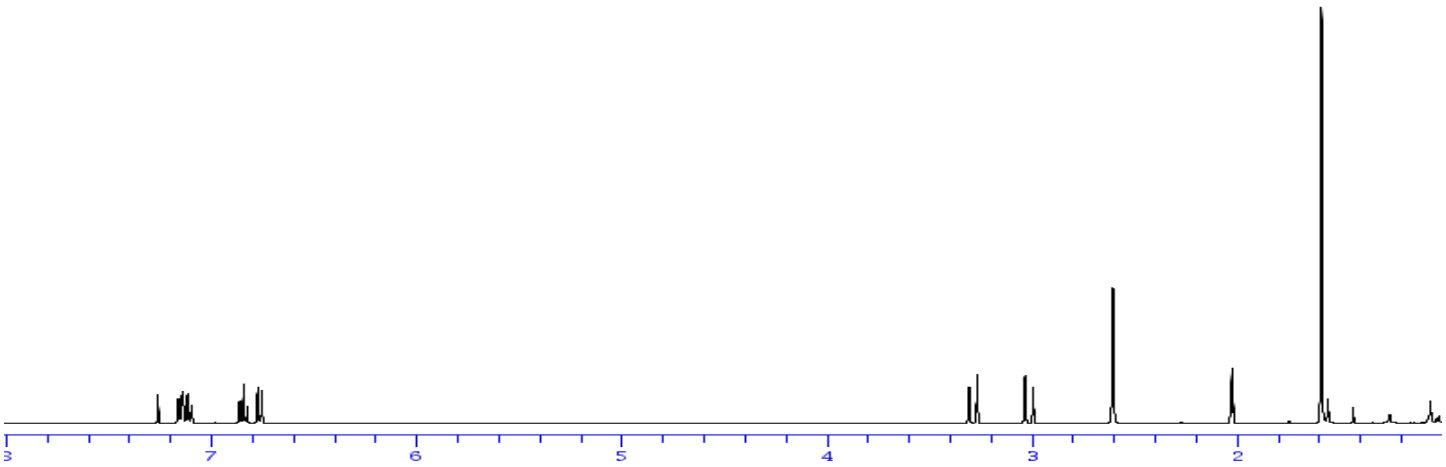
140
130
120
110
100
90
80
70
60
50
40
30
20
10


00
3000
2000
1000

solvent: <CDCl3>
Frequency: 400.13MHz



62



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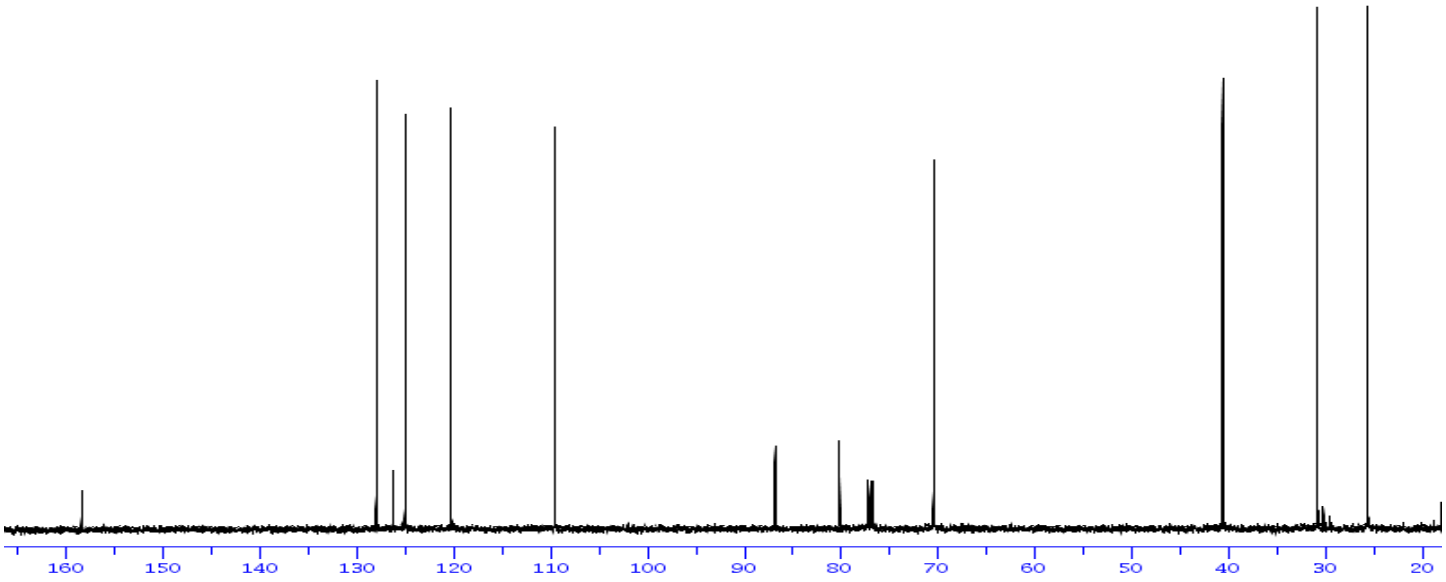

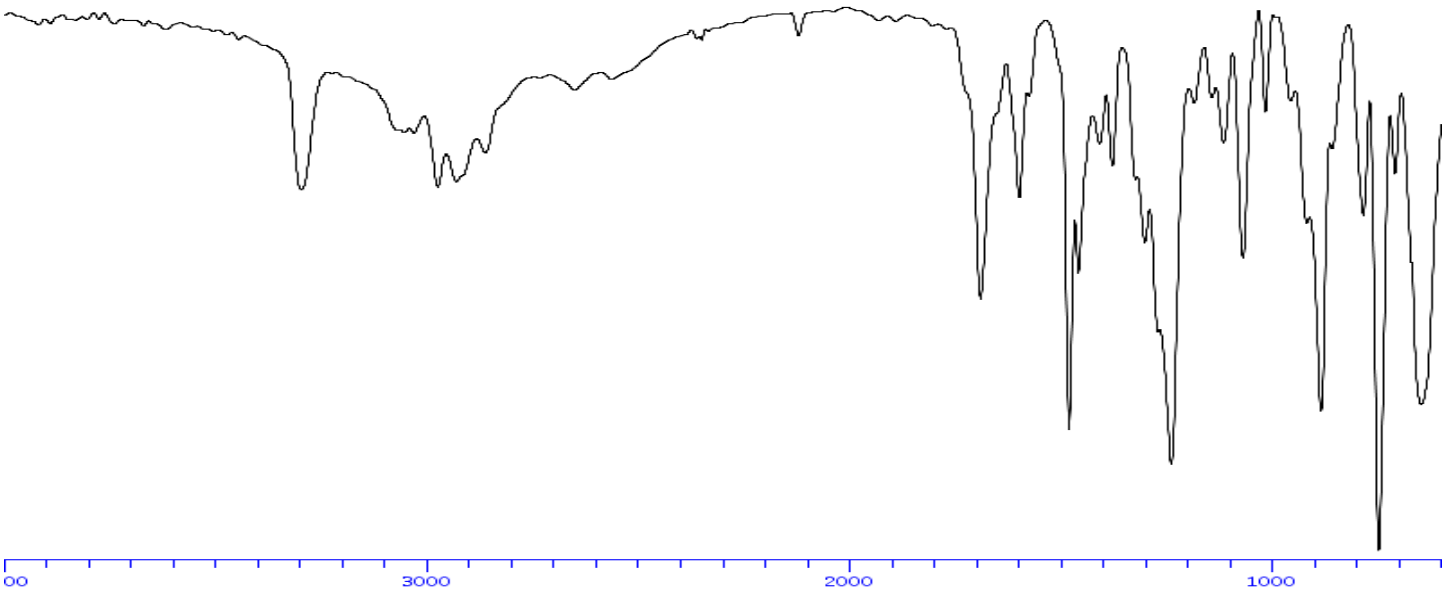

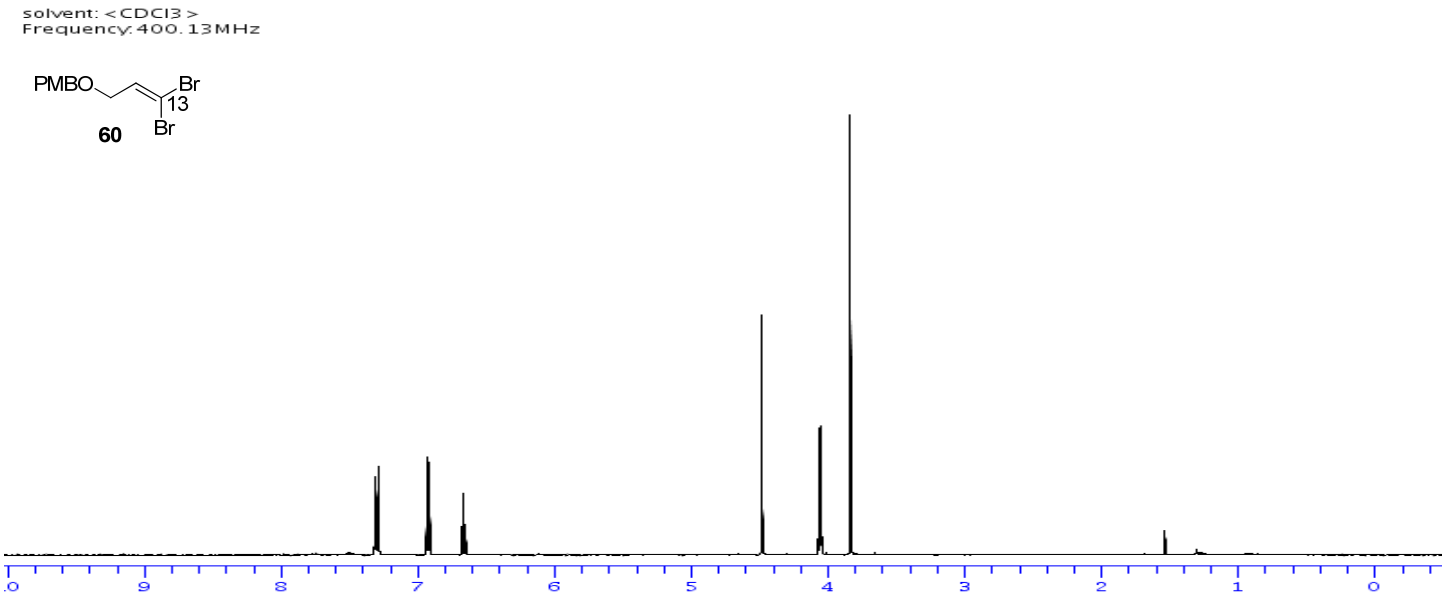
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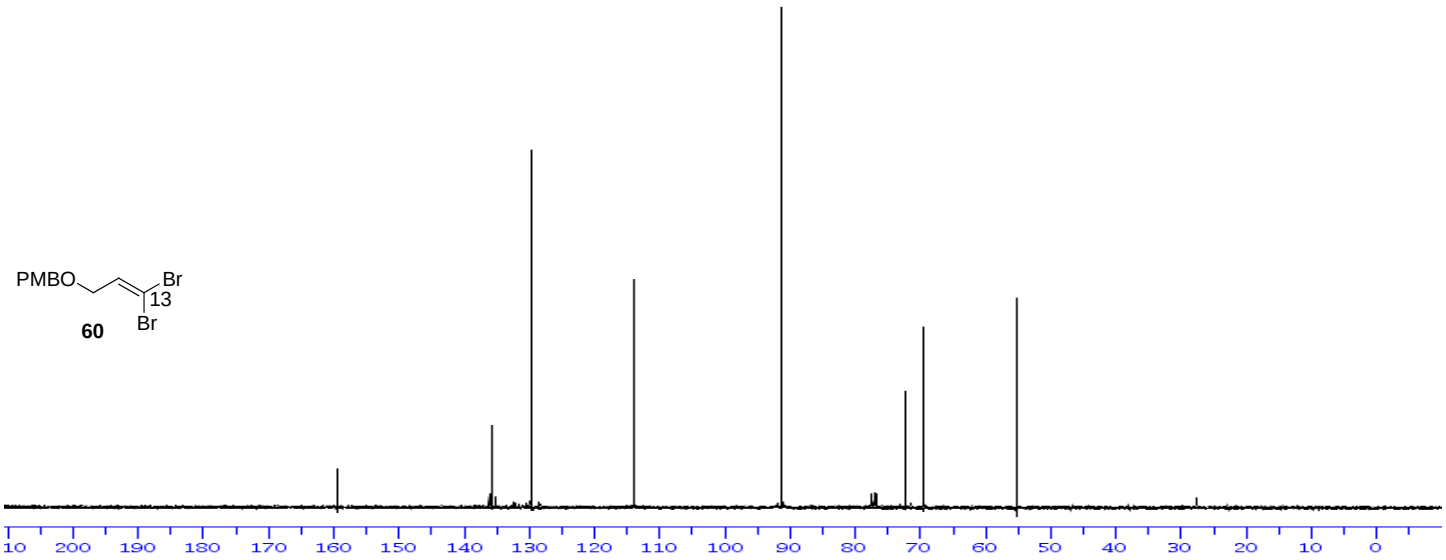
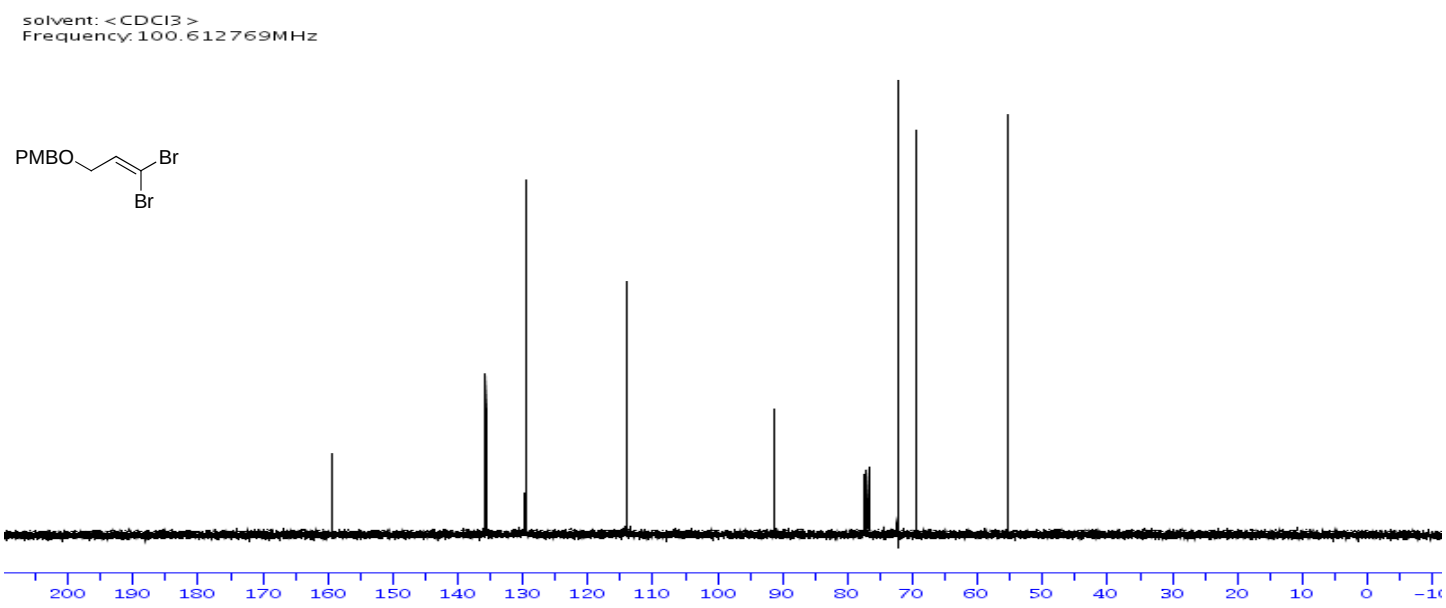
Br
13
Br
60


PMBO
Br
13
Br
60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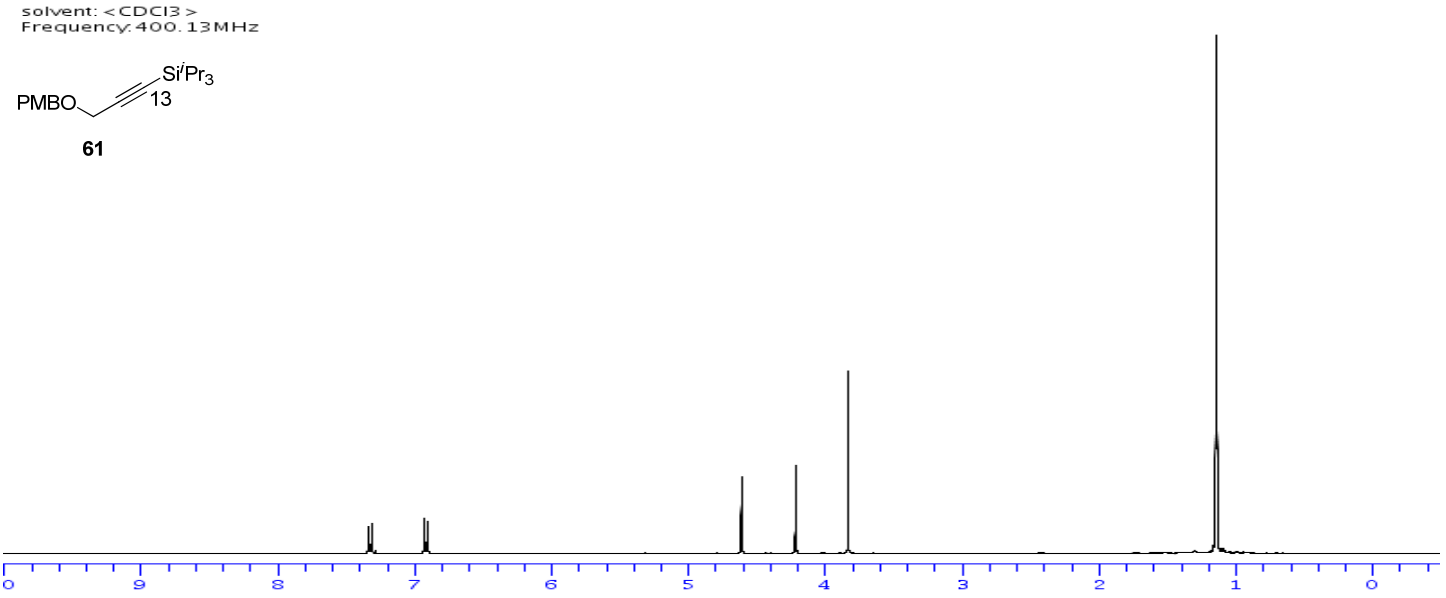
Frequency: 100.612769MHz
PMBO
Br
Br


solvent: <CDCl3 >
Frequency: 400.13MHz
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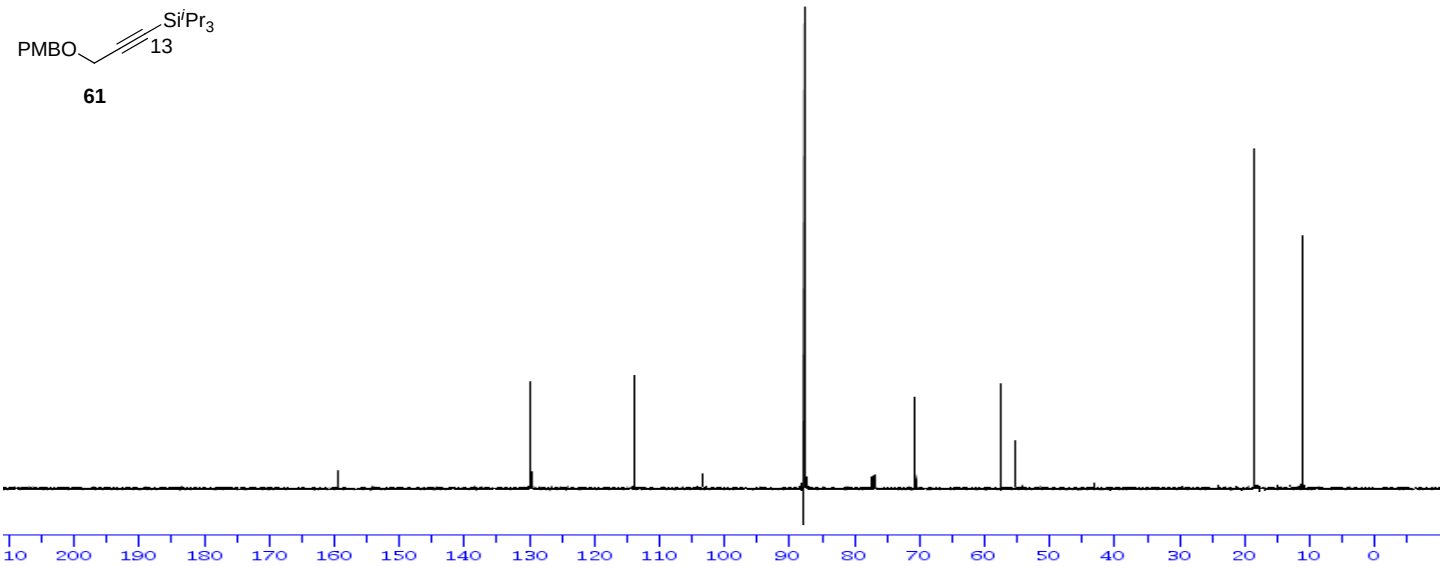
Si^{i}Pr$_3$
13
61
0
9
8
7
6
5
4
3
2
1
0


PMBO
Si^{i}Pr$_3$
13
61
10
200
190
180
170
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150
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130
120
110
100
90
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70
60
50
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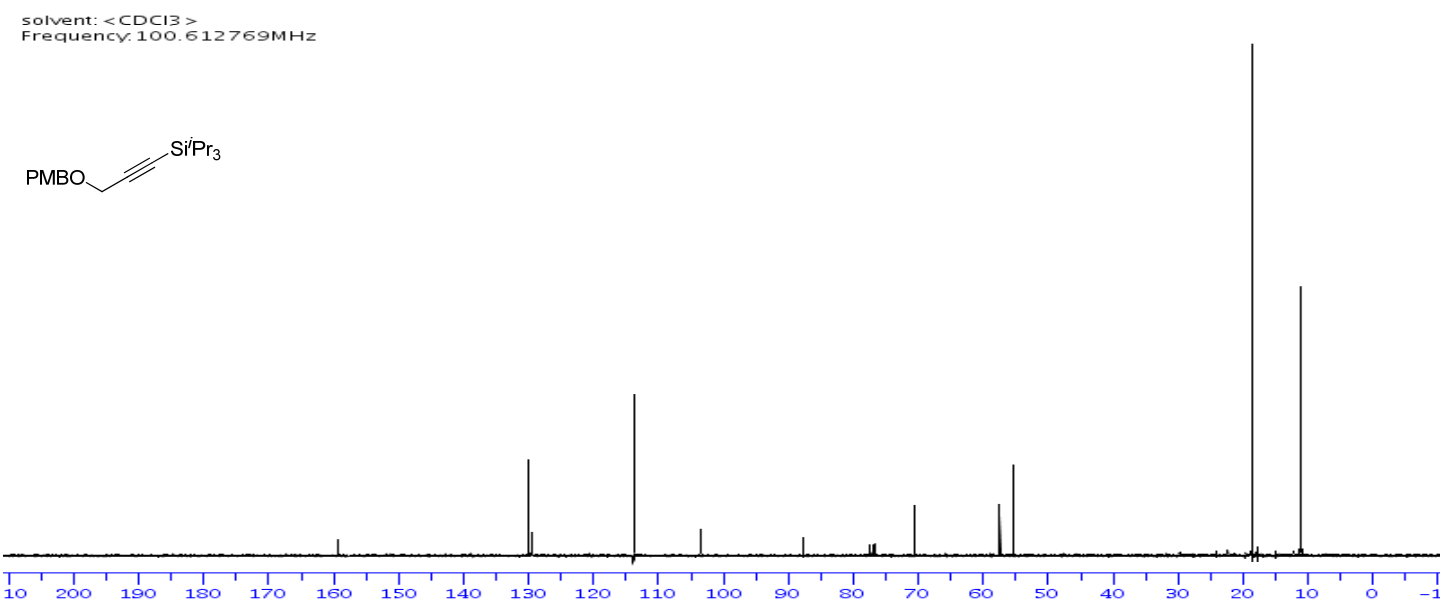
30
20
10
0


solvent: <CDCl3 >
Frequency: 100.612769MHz
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Si^{i}Pr$_3$
10
200
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180
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140
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120
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80
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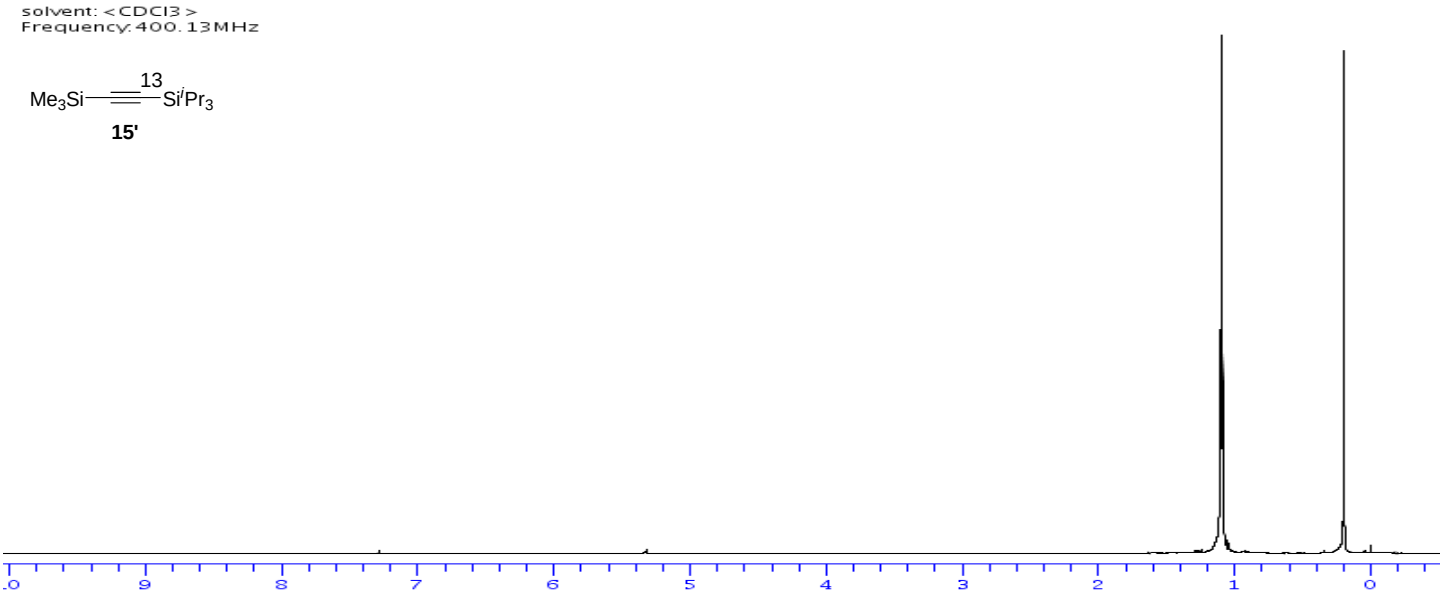
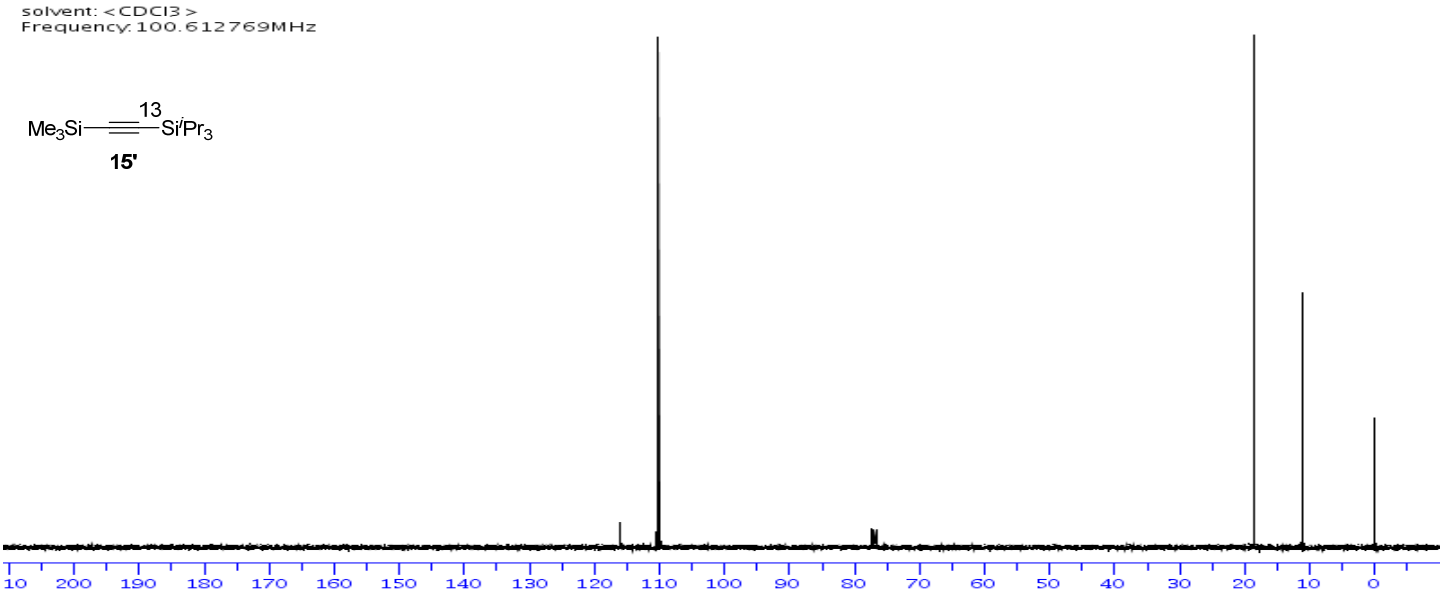
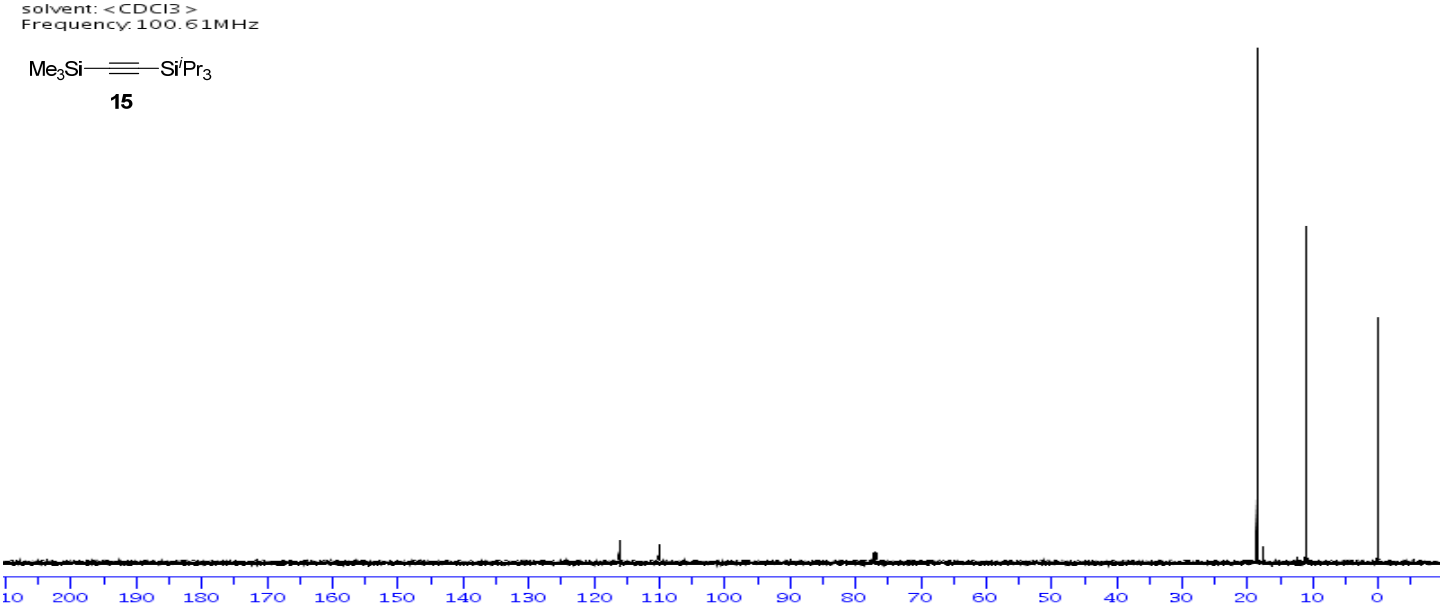
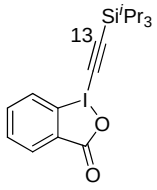
30
20
10
0
-1


solvent: <CDCl3 >
Frequency: 400.13MHz
13
Me3Si
SiiPr3
15'
.0
9
8
7
6
5
4
3
2
1
0


solvent: <CDCl3 >
Frequency: 100.612769MHz
13
Me3Si
SiiPr3
15'
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

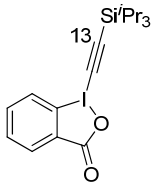

solvent: <CDCl3 >
Frequency: 100.61MHz
Me3Si
SiiPr3
15
10
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0

solvent: <CDCl3 >
Frequency: 400.13MHz



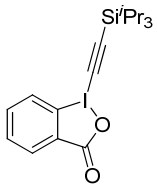
3d'

solvent: <CDCl3 >
Frequency: 100.612769MHz



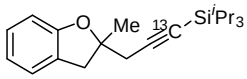
3d'

solvent: <CDCl3 >
Frequency: 100.61MHz



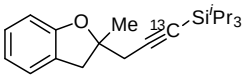
3d

solvent: <CDCl3 >
Frequency: 400.13MHz



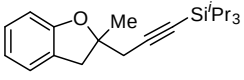
4b'

solvent: <CDCl3 >
Frequency: 100.61MHz



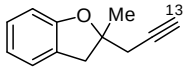
4b'

solvent: <CDCl3 >
Frequency: 100.61MHz



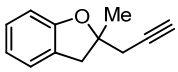
4b

solvent: <CDCl3>
Frequency: 100.61MHz



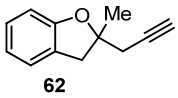
62'

solvent: <CDCl3>
Frequency: 100.61MHz



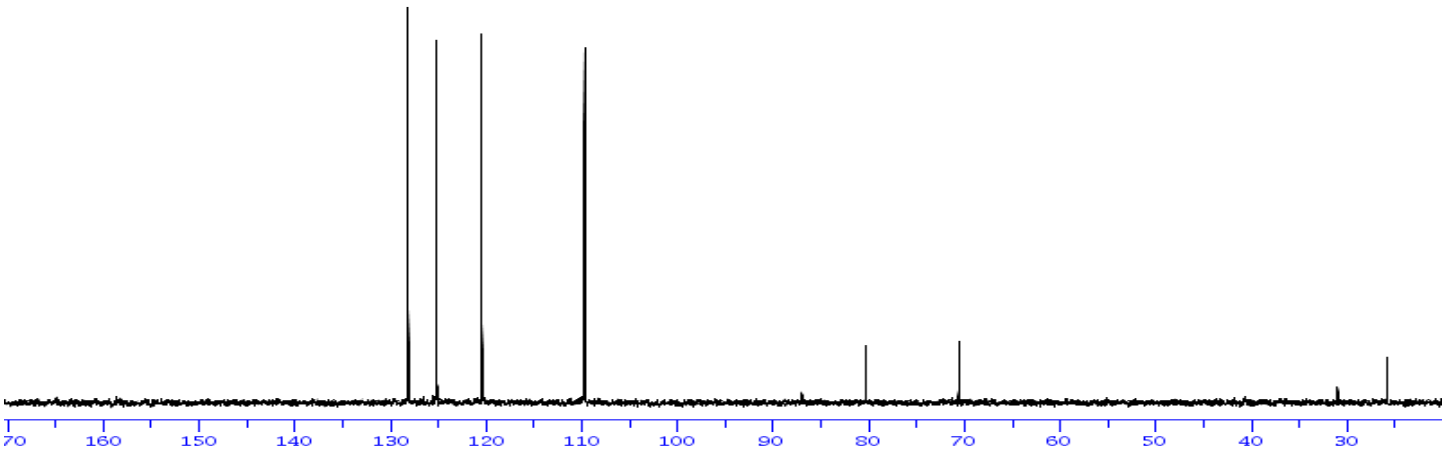
62

13C-NMR
solvent: <CDCl3>
Frequency: 100.61MHz

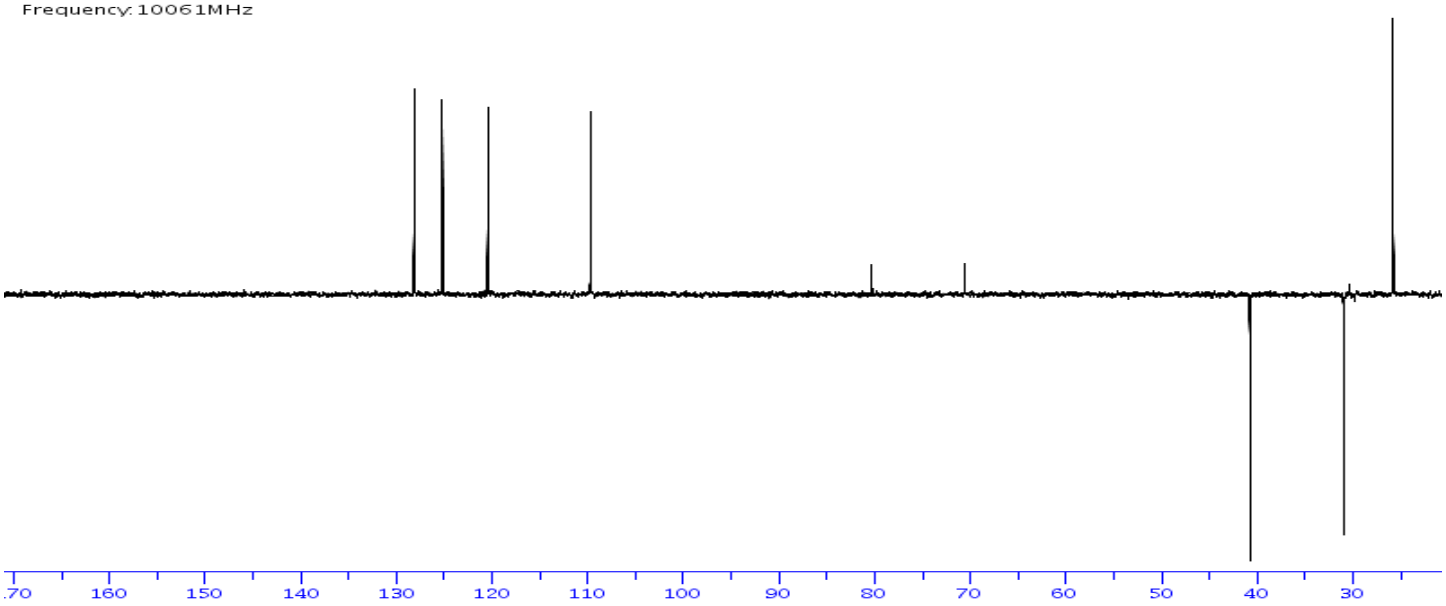


62

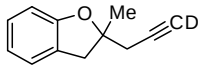
DEPT-90
solvent: <CDCl3>
Frequency: 100.61MHz

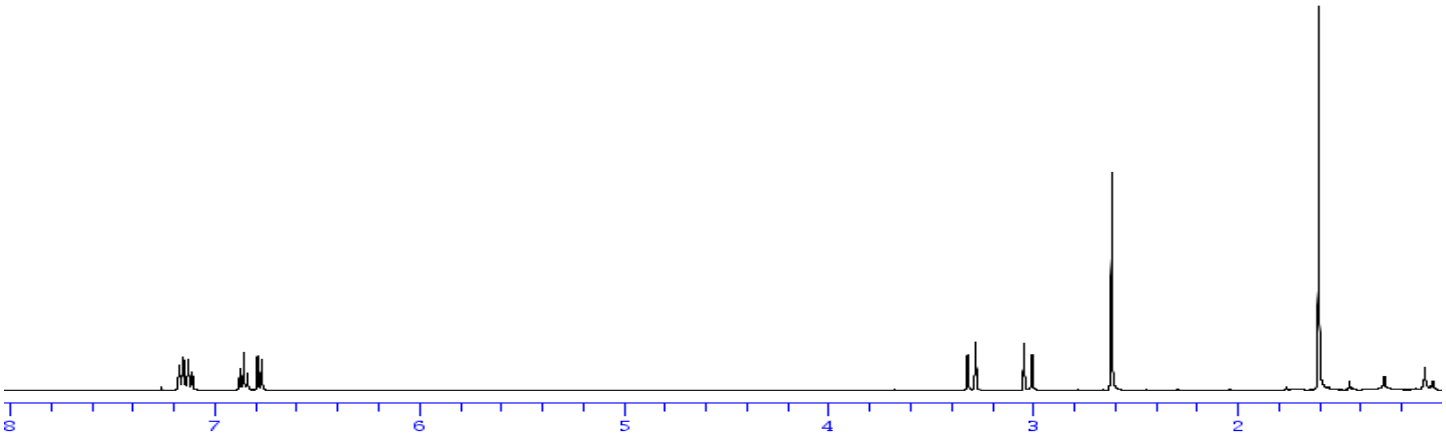


DEPT-135
solvent: <CDCl3>
Frequency: 10061MHz



solvent: <CDCl3 >
Frequency: 400.13MHz





solvent: <CDCl3 >
Frequency: 100.61MHz