Pd(0)-Catalyzed Oxy- and Amino-Alkynylation of Olefins for the Synthesis of Tetrahydrofurans and Pyrrolidines.

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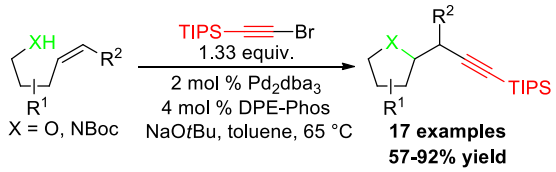
ABSTRACT



The first Pd(0)-catalyzed intramolecular oxy- and amino- alkynylation of non-activated olefins is reported. The reaction gives access to important tetrahydrofuran and pyrrolidine heterocycles with high diastereoselectivity. The unique synthetic potential of acetylenes is further exploited to access key building blocks for the synthesis of bioactive natural products.

Heterocycles are essential structural elements for the bioactivity of natural and synthetic molecules. Among them, tetrahydrofurans and pyrrolidines are particularly important in natural products, such as the antitumoral annonaceous acetogenins gigantecin (**1**) and squamostatin C (**2**),[1] or the antibiotic alkaloid preussin (**3**) (Figure 1).[2] Consequently, the stereoselective synthesis of tetrahydrofurans and pyrrolidines has been extensively investigated.[3] Particularly interesting are methods using cyclization of alcohols or amines onto non-activated olefins combined with a further bond forming event. Iodo-etherification or amination reactions have been often used in the synthesis of heterocycles.[4] Recently, the power of metal catalysis has been harnessed to achieve multiple functionalizations of olefins[5] for the synthesis of tetrahydrofurans and pyrrolidines together with further C-N,[6] C-O[7] or C-C bond formation.[8]

Impressive progress has been realized in Pd-catalyzed domino reactions involving cyclization on olefins to form a tetrahydrofuran or a pyrrolidine followed by carbonylation,[8a-c] vinylation[8d-e] or arylation.[8f-j] Despite these recent breakthroughs, there are currently no examples of an oxy- or amino- alkynylation reaction for the synthesis of tetrahydrofurans or pyrrolidines.[9] Such a process would be highly useful, as the functionalization of alkynes through cross-coupling, reduction, addition, cyclization, cycloisomerization or cycloaddition gives access to important building blocks used in synthetic chemistry, chemical biology and material sciences.[10]

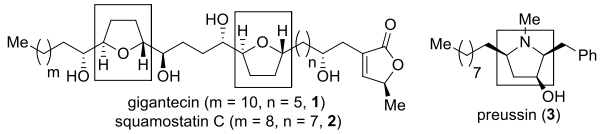
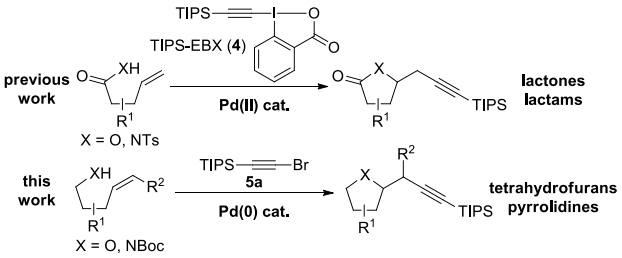


Figure 1. Tetrahydrofuran and pyrrolidines natural products.

Our group has developed the Pd(II)-catalyzed oxy- and amino-alkynylation of olefins with EBX (ethynyl benziodoxolone) reagent **4** for the synthesis of lactones and lactams (Scheme 1).[11] However, the developed

methods could not be used to access tetrahydrofurans or pyrrolidines and C-C bond formation was limited to primary positions. Herein, we report a different approach for the oxy- and amino- alkynylation of olefins using Pd(0) catalysis and tri*iso*propylsilyl ethynyl bromide (**5a**), which allowed us to override both limitations (Scheme 1). To the best of our knowledge, this is the first example of Pd(0) catalysis for the oxy- and amino- alkynylation of olefins or for any C-X/C(SP^3)-C(SP) domino sequence on alkenes. Tetrahydrofurans and pyrrolidines were obtained in good yields and diastereoselectivities, and examples of alkynylation at secondary positions are also reported. The synthetic potential of the obtained acetylenes is demonstrated in further transformations giving access to the core structures of acetogenin natural products.

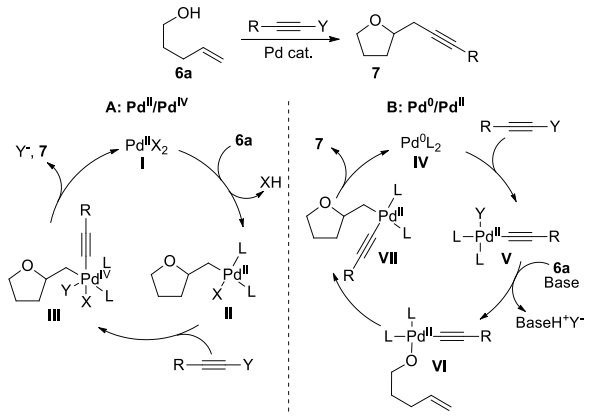
Scheme 1. Oxy- and Amino Alkynylation of Alkenes.



The oxyalkynylation of penten-5-ol (**6a**) with TIPS-EBX (**4**) as reagent and a Pd(II) catalyst gave only low yields (<25%), and no conversion was observed with halogeno acetylenes. At this point, we decided to reconsider our working model for the reaction (Scheme 2). For lactonization[11a] we had used an electron-poor Pd(II) catalyst **I**, which would react with the strong oxidant **4** to form a putative Pd(IV) intermediate **III** only after oxy-palladation to give **II** had occurred. However, the use of a Pd(0) catalyst **IV** with **4** led to fast formation of a diyne product and to silylation of alcohol **6a** (Table 1, entry 1).[12] We speculated that a weaker and less electrophilic oxidant, such as a halogeno acetylene should be less prone to the observed side reactions. Instead, oxypalladation and reductive elimination via **VI** and **VII** would give the product **7**, opening a new Pd(0)/Pd(II) manifold for the reaction.

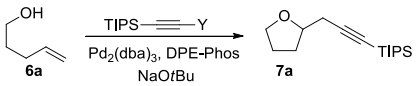
When Wolfe's conditions[8f-j] were used with phenyl- or phenylethyl- ethynyl bromides (**5b**) and (**5c**) (Table 1, entries 2-3), complex mixtures of products were obtained. At this point, we decided to turn towards tri*iso*propylsilyl acetylenes derivatives, which had demonstrated exceptional properties in metal catalysis.[11,13] Gratifyingly, whereas chloroacetylene **5d** displayed only low conversion (entry 4) and iodoacetylene **5e** lead to dimerization (entry 5),[14] a promising 69% of yield was obtained using 2 mol% $Pd_2(dba)_3$ and DPE-Phos as ligand with bromoacetylene **5a** (entry 6).

Scheme 2. Working Models for the Oxyalkynylation of Penten-5-ol (**6a**).



Further optimization studies allowed us to identify toluene as the optimal solvent and confirmed DPE-Phos as the ideal ligand (entry 7).[15] Under these conditions, **7a** could be isolated in 92% yield using only 1.33 equivalent of bromide **5a** (Table 2, entry 1).

Table 1. Optimization of the Oxyalkynylation Reaction.



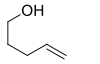
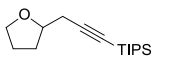
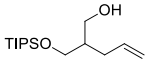
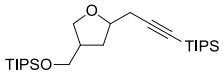
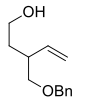
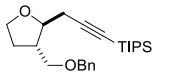
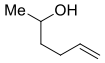
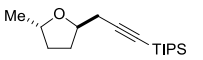
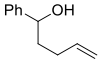
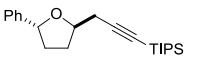
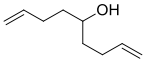
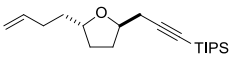
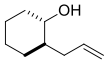
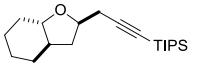
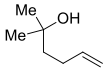
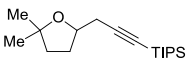
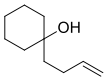
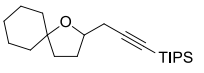
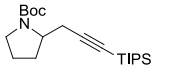
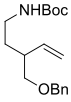
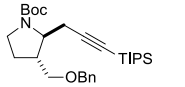
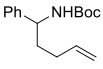
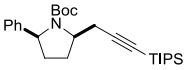
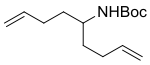
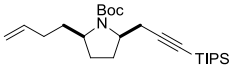
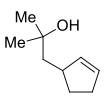
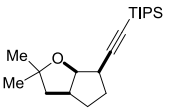
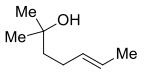
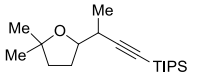
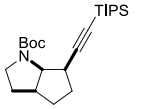
entry	reagent	ligand	solvent	yield[a]
1	TIPS-EBX	DPE-Phos	THF	<5%
2	Ph—≡—Br (**5b**)	DPE-Phos	THF	-[b]
3	$PhCH_2CH_2$—≡—Br (**5c**)	DPE-Phos	THF	-[b]
4	TIPS—≡—Cl (**5d**)	DPE-Phos	THF	22%
5	TIPS—≡—I (**5e**)	DPE-Phos	THF	31%
6	TIPS—≡—Br (**5a**)	DPE-Phos	THF	69%
7	TIPS—≡—Br (**5a**)	DPE-Phos	toluene	87%

[a]Reaction conditions: 0.15 mmol **6a**, 0.20 mmol **5**, 0.20 mmol NaO*t*Bu, 0.003 mmol $Pd_2(dba)_3$, 0.006 mmol ligand, 0.8 mL dry solvent under N_2 at 65-70 °C. Yield determined via GC-MS. [b]Complex mixture of non-separable products.

We then examined the scope of the reaction (Table 2). The cyclization of primary alcohols proceeded in 79-92% yield (entries 1-3). We then turned to the use of secondary alcohols in the cyclization reaction (entries 4-7). This class of substrates is particularly interesting, as *trans* 2,5-disubstituted tetrahydrofurans are often represented in natural products, such as acetogenins (Figure 1). The reaction worked in 60-80% yield and excellent *trans* diastereoselectivity (>95:5) (entries 5-7), with the exception of the small Me substituent (entry 4). The reaction tolerated a second double bond in the molecule (entry 6) and gave access to bicyclic heterocycles (entry 7). Useful yields could be obtained with tertiary alcohols

(entries 8-9), including for the formation of a spiro-bicyclic heterocycle **7i** (entry 9).

Table 2. Scope of the Alkynylation Reaction.

entry	substrate	product	yield[a]
1	 **6a**	 **7a**	92%
2	 **6b**	 **7b**	88% (67:33 dr)
3	 **6c**	 **7c**	80% (85:15 dr)
4	 **6d**	 **7d**	80% (87:13 dr)
5	 **6e**	 **7e**	60% (>95:5 dr)
6	 **6f**	 **7f**	65% (>95:5 dr)
7	 **6g**	 **7g**	79% (>95:5 dr)
8	 **6h**	 **7h**	69%
9	 **6i**	 **7i**	57%[b]
10	 **6j**	 **7j**	81%
11	 **6k**	 **7k**	76% (87:13 dr)
12	 **6l**	 **7l**	80% (94:6 dr)
13	 **6m**	 **7m**	57% (>95:5 dr)
14	 **6n**	 **7n**	86% (>95:5 dr)
15	 **6o**	 **7o**	71%[b] (>95:5 dr)
16	 **6p**	 **7p**	86% (>95:5 dr)

[a]Reaction conditions: 0.40 mmol **6**, 0.53 mmol alkyne **5a**, 0.53 mmol NaO*t*Bu, 0.008 mmol $Pd_2(dba)_3$, 0.016 mmol DPE-Phos, 2.1 mL toluene under N_2 at 65-70 °C for 3 h. Isolated yield after column chromatography. [b]At 110 °C.

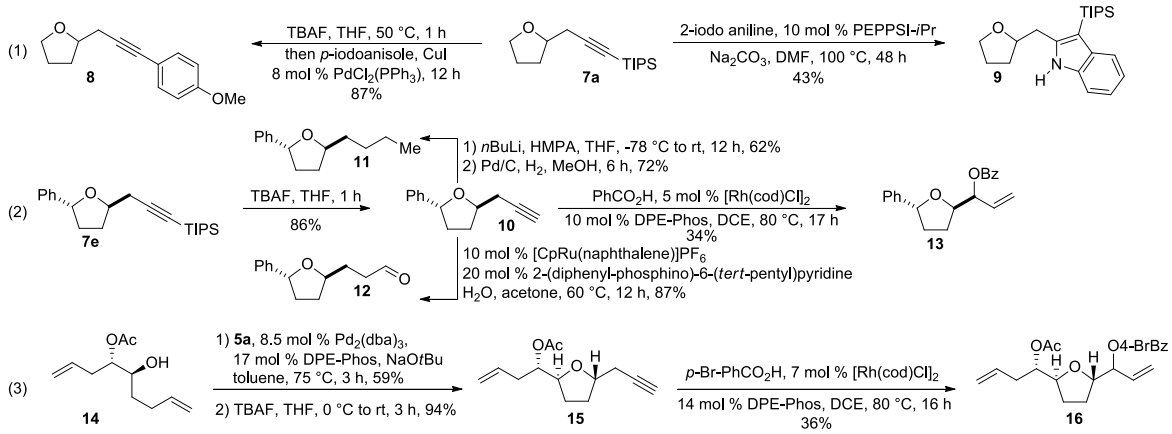
In our previous work, completely different conditions had to be used when going from lactonization to lactamization.[11] However, this was not the case when using Pd(0) catalysis, and no further optimization was required in the case of Boc-protected amines as substrates (entries 10-13). Excellent *cis* selectivity was observed in the formation of 2,5-disubstituted pyrrolidines (entries 12-13), which is the same relative stereochemistry as observed in preussin (**3**) (Figure 1). Up to now, we had examined only monosubstituted olefins involving most probably a primary Pd-alkyl intermediate. The use of 1,2 disubstituted olefins would require a challenging SP^3-SP reductive elimination at a secondary position. Such processes are difficult in Pd catalysis.[16] Gratifyingly, the reaction also worked well for disubstituted olefins, both in the case of alcohols and amines (entries 14-16). Pre-organization through rigidification was not required, and even simple acyclic substrate **6o** could be used (entry 15). In the case of bicyclic products **7n** and **7p**, an all-*cis* relationship of the substituents was observed. This is in accordance with the mechanism we proposed in our working model (Scheme 2) involving binding of the heteroatom to Pd, followed by *syn* oxy-palladation and reductive elimination.

We then shortly investigated the transformation of the obtained acetylenes into important building blocks (Scheme 3). TIPS deprotection and Sonogashira coupling on **7a** can be done in one-pot to give aryl acetylene **8** in 87% yield (Scheme 3, (1)).[17] A Larock annulation[18] gave indole **9** with perfect regioselectivity, albeit in moderate yield (43%). With **7e**, deprotection proceeded in good yield, and the terminal alkyne could be converted in two steps to known **11**,[19] which allowed us to confirm definitively the *trans* relationship of the substituents (Scheme 3, (2)). Hydration using the method developed by Hintermann[20] gave access to versatile aldehyde **12** in 87% yield, resulting in an overall addition of an oxygen atom and acetaldehyde to an olefin. We then introduced an oxygen group in propargylic position using Breit's method.[21] The desired allylic ester **13** was obtained in 34% yield and 73:27 dr. This preliminary result is highly interesting, especially when considering that the reaction had been reported for the acid as limiting agent, and no effort has yet been done to improve the reaction with only one equivalent of alkyne. Building blocks for the synthesis of acetogenins were accessed starting from enantioenriched alcohol **14** (Scheme 3, (3)).[22] High diastereoselectivity for the desired *trans* product **15** was observed, giving an asymmetric entry to the α-monohydroxylated tetrahydrofuran ring of gigantecin (**1**) or squamostatin C (**2**) (Figure 1). A second hydroxy group could be introduced using Breit's method to access the bis α-hydroxylated tetrahydrofuran ring.

In summary, we have reported the first oxy- and amino-alkynylation reactions of alkenes catalyzed by a Pd(0) catalyst. Tetrahydrofurans and pyrrolidines were obtained in good yield and diastereoselectivity with simultaneous installation of a triple bond. The utility of the alkyne was demonstrated through its transformation in other functional groups and into key building blocks for the synthesis of acetogenin natural products. Principles applied in arylation chemistry could be transferred to alkynylation reactions if a tri*iso*propylsilyl protecting group was present. This discovery will probably be of

broad use in the development of other reactions involving acetylenes. Further investigations along this line, as well as the development of asymmetric methods, are currently ongoing in our group.

Scheme 3. Functionalization of the Products.



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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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(1) (a) Crimmins, M. T.; She, J. *J. Am. Chem. Soc.* **2004**, *126*, 12790. (b) Spurr, I. B.; Brown, R. C. D. *Molecules* **2010**, *15*, 460.

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(12) On a 0.40 mmol scale, 1,4-bis(tri*iso*propylsilyl)buta-1,3-diyne and tri*iso*propyl(pent-4-enyloxy)silane were obtained in 8 and 84% yield respectively using the conditions of entry 1, Table 1. See supporting information.

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(14) On a 0.40 mmol scale, 1,4-bis(tri*iso*propylsilyl)buta-1,3-diyne and tetrahydrofuran **7a** were both obtained in 34% yield using the conditions of entry 5, Table 1. See supporting information.

(15) See supporting information for further tested conditions.

(16) (a) Altenhoff, G.; Wurtz, S.; Glorius, F. *Tetrahedron Lett.* **2006**, *47*, 2925. (b) de Carne-Carnavalet, B.; Archambeau, A.; Meyer, C.; Cossy, J.; Folleas, B.; Brayer, J. L.; Demoute, J. P. *Org. Lett.* **2011**, *13*,

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Supporting information

Pd(0)-Catalyzed Oxy- and Amino- Alkynylation of Olefins for the Synthesis of Tetrahydrofurans and Pyrrolidines.

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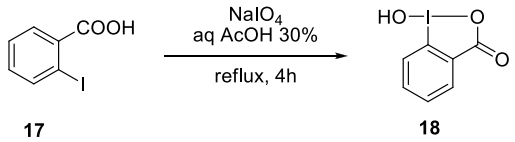
1. General Methods

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). 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 (unprotected pyrrolidines were eluted using DCM/ULTRA; ULTRA; ULTRA: DCM/MeOH/(NH_3 25% inwater) 75/25/5). 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, all signals are reported in ppm with the internal chloroform signal at 7.26 ppm. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, quint = quintet, m = multiplet or unresolved, br = 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. 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, br = broad). 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 the reagents

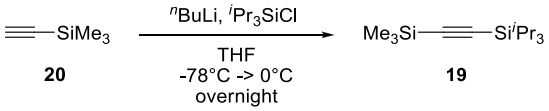
1-Hydroxy-1,2-benziodoxol-3-(1*H*)-one (18)



Following the reported procedure,[1] $NaIO_4$ (7.24 g, 33.8 mmol, 1.05 equiv) and 2-iodobenzoic acid (**17**) (8.00 g, 32.2 mmol, 1.00 equiv) were suspended in 30% (v:v) aq. AcOH (48 mL). The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (180 mL) and allowed to cool to rt, protecting it from light. After 1 h, the crude product was collected by filtration, washed on the filter with ice water (3 x 20 mL) and acetone (3 x 20 mL), and air-dried in the dark to give the pure product **18** (8.3 g, 31 mmol, 98%) as a colorless solid.

^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.02 (dd, 1 H, *J* = 7.7, 1.4 Hz, Ar*H*), 7.97 (m, 1 H, Ar*H*), 7.85 (dd, 1 H, *J* = 8.2, 0.7 Hz, Ar*H*), 7.71 (td, 1 H, *J* = 7.6, 1.2 Hz, Ar*H*); ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4; IR ν 3083 (w), 3060 (w), 2867 (w), 2402 (w), 1601 (m), 1585 (m), 1564 (m), 1440 (m), 1338 (s), 1302 (m), 1148 (m), 1018 (w), 834 (m), 798 (w), 740 (s), 694 (s), 674 (m), 649 (m); the reported values correspond to the ones in literature.[1]

Tri*iso*propylsilyl trimethylsilylacetylene (19)

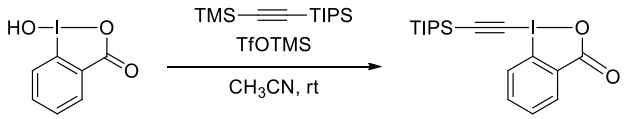


Following a reported procedure,[2] *n*-butyllithium (2.5 M in hexanes, 12.0 mL, 29.9 mmol, 0.98 equiv) was added dropwise to a stirred solution of ethynyltrimethylsilane (**20**) (3.0 g, 30 mmol, 1.0 equiv) in THF (48 mL) at -78 °C. The mixture was then warmed to 0 °C and stirred for 5 min. The mixture 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 **19** (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 **19** corresponded to the literature values.[2]

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

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

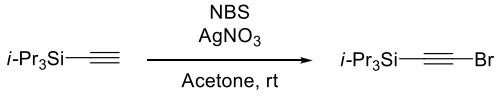


18 **4**

Following a reported procedure,[3] 2-iodosylbenzoic acid (**18**) (21.7 g, 82.0 mmol, 1.0 equiv) was charged in oven-dried three-neck 1L flask equipped with a magnetic stirrer. After 3 vacuum/nitrogen cycles, anhydrous acetonitrile (500 mL) was added via canula and cooled to 4 °C. Trimethylsilyltriflate (16.4 mL, 90.0 mmol, 1.1 equiv) was added dropwise via a dropping funnel over 30 min (no temperature increase was observed). After 15 min, (trimethylsilyl)(tri*iso*propylsilyl)acetylene (**19**) (23.0 g, 90.0 mmol, 1.1 equiv) was added via canula over 15 min (no temperature increase was observed). After 30 min, the suspension became an orange solution. After 10 min, pyridine (7.0 mL, 90 mmol, 1.1 equiv) was added via syringe. After 15 min, the reaction mixture was transferred in a one-neck 1L flask and reduced under vacuum until a solid was obtained. The solid was dissolved in DCM (200 mL) and transferred in a 1L separatory funnel. The organic layer was added and washed with 1 M HCl (200 mL) and the aqueous layer was extracted with CH_2Cl_2 (200 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (2 x 200 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. Recrystallization from acetonitrile (*ca* 120 mL) afforded **4** (30.1 g, 70.2 mmol, 86%) as colorless cristals.

^{1}H NMR (400 MHz, $CDCl_3$) δ 8.44 (m, 1 H, Ar*H*), 8.29 (m, 1 H, Ar*H*), 7.77 (m, 2 H, Ar*H*), 1.16 (m, 21 H, TIPS). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 134.6, 132.3, 131.4, 131.4, 126.1, 115.6, 114.1, 64.6, 18.4, 11.1. IR ν 2943 (m), 2865 (m), 1716 (m), 1618 (m), 1604 (s), 1584 (m), 1557 (m), 1465 (m), 1439 (w), 1349 (m), 1291 (m), 1270 (w), 1244 (m), 1140 (m), 1016 (m), 999 (m), 883 (m), 833 (m), 742 (m), 702 (s), 636 (m); Melting point (Dec.) 170-176°C; The values for the characterization of **TIPS-EBX** correspond to the ones reported in literature.[3]

2-Bromo-1-tri*iso*propylsilyl acetylene (5a)



21 **5a**

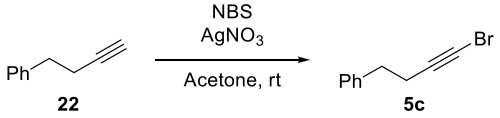
Following a reported procedure,[4] tri*iso*propylsilylacetylene (**21**) (813 mg, 4.45 mmol, 1.00 equiv) was dissolved in acetone (30 mL). *N*-bromosuccinimide (925 mg, 5.19 mmol, 1.16 equiv) was added, followed by $AgNO_3$ (76 mg, 0.44 mmol, 0.1 equiv). The resulting mixture was stirred at room temperature for 3 h and it was then poured onto ice. After ice being allowed to melt, the aqueous layer was extracted with pentane (3 x 30 mL). The combined organic layers

(3) J. P. Brand, J. Waser, *Angew. Chem., Int. Ed.* **2010**, *49*, 7304.
(4) Jiang, M. X.; Rawat, M.; Wulff, W. D. *J. Am. Chem. Soc.*, **2004**, *126*, 5970.

were dried over $MgSO_4$, filtered and concentrated *in vacuo* to afford pure 2-bromo-1-tri*iso*propylsilyl acetylene (**5a**) (1.16 g, 4.43 mmol, 99%) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.20-0.97 (m, 21 H, TIPS); ^{13}C NMR (101 MHz, $CDCl_3$) δ 83.5, 61.7, 18.5, 11.3; the reported values corresponded to the ones in literature.[4]

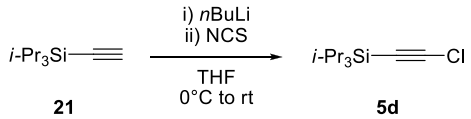
(4-Bromobut-3-ynyl)benzene (5c)



Following a reported procedure,[5] 4-phenyl-1-butyne (**22**) (0.432 mg, 3.07 mmol, 1.00 equiv) was dissolved in acetone (20 mL). *N*-bromosuccinimide (637 mg, 3.58 mmol, 1.16 equiv) was added, followed by $AgNO_3$ (50 mg, 0.30 mmol, 0.1 equiv). The resulting mixture was stirred at room temperature for 5 h. The solids were then filtered off and the solvent was removed by distillation under reduced pressure. The residual oil was treated with hexane (10 mL) to induce the further precipitation of solids, which were also removed by filtration. After removal of the organic solvent *in vacuo*, the resulting crude oil was purified by column chromatography (SiO_2, pentane) to afford pure alkyne **5c** (608 mg, 2.91 mmol, 95% yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (m, 2 H, Ar H), 7.22 (m, 3 H, Ar H), 2.83 (t, 2 H, J = 7.5 Hz, CH_2), 2.49 (t, 2 H, J = 7.7 Hz, CH_2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 140.2, 128.4, 128.4, 126.4, 79.6, 65.8, 34.7, 21.8. The ^{1}H NMR values for the characterization of **5c** correspond to the ones reported in literature.[5]

(Chloroethynyl)tri*iso*propylsilane (5d)

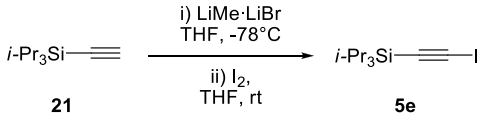


Following a reported procedure,[6] tri*iso*propyl silyl acetylene (**21**) (2.2 mL, 10 mmol, 1.0 equiv) was dissolved in THF (12.5 mL) and the solution was stirred at 0°C for 5 min. *n*BuLi (2.5 M in hexanes, 4.4 mL, 11 mmol, 1.1 equiv) was added dropwise and the resulting mixture was stirred at 0°C for 30 min. *N*-chloro succinimide (1.6 g, 12 mmol, 1.2 equiv) was added and the mixture was stirred at 0°C for 5 min and then at rt overnight. The reaction was then quenched by the addition of water (12.5 mL). The two layers were separated and the aqueous one was extracted with EtOAc (3 x 12 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, hexane) afforded 2-iodo-1-tri*iso*propylsilyl acetylene (**5d**) (1.67 mg, 7.70 mmol, 77% yield) as a yellow oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.14-1.06 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 80.0, 71.2, 18.5, 11.3. The values for the characterization of **5d** correspond to the ones reported in literature.[6]

(5) Mu, F.; Lee, D. J.; Pryor, D. E.; Hamel, E.; Cushman, M. *J. Med. Chem.*, **2002**, *45*, 4774.
(6) Wada, T. ; Masayuki, J.; Azusa, K.; Hideki, Y.; Oshima, K. *Chem. Eur. J.* **2010**, *16*, 10671.

2-Iodo-1-tri*iso*propylsilyl acetylene (5e)

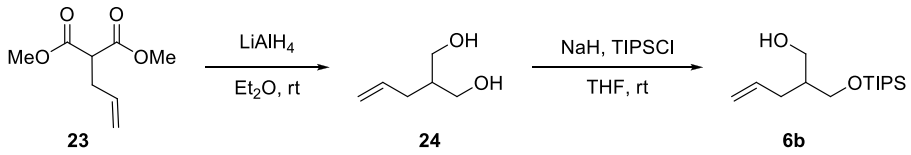


Following a reported procedure,[7] MeLi•LiBr (1.5 M in diethyl ether, 1.1.mL, 1.6 mmol, 1.0 equiv) was added to a stirred solution of tri*iso*propylsilylacetylene (**21**) (0.36 mL, 1.6 mmol, 1.0 equiv) in dry THF (1.8 mL), cooled at -78 °C, and the mixture was allowed to react for 1 h at that temperature. 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 (**5e**) (0.470 g, 1.52 mmol, 94% yield) as a colorless oil.

^{1}H NMR (400 MHz, $CDCl_3$) δ 1.10-1.04 (m, 21 H, TIPS); ^{13}C NMR (100 MHz, $CDCl_3$) δ 100.8, 18.5, 11.4 (one acetylene carbon was not resolved); the reported values correspond to the ones in literature.[7]

3. Preparation of the substrates

2-((Triisopropylsilyloxy)methyl)pent-4-en-1-ol (6b):



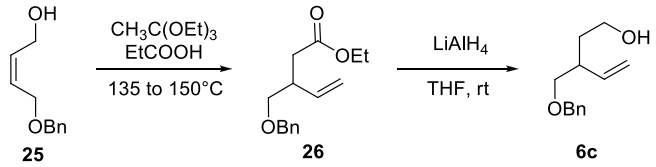
According to a reported procedure,[8] a solution of dimethyl 2-allylmalonate (**23**) (1.77 mL, 11.0 mmol, 1.0 equiv) in Et_2O (25 mL) was added dropwise to a suspension of $LiAlH_4$ (1.25 g, 33.0 mmol, 3.0 equiv) in Et_2O (31 mL) at 0°C. The resulting mixture was stirred at rt for 3 h; it was then cooled back to 0°C and the reaction was quenched by slow addition of water (1.05 mL). The mixture was allowed to warm to rt and treated with aqueous NaOH (15%, 1.05 mL) and water (3.2 mL). The resulting white slurry was filtered through Celite and then washed with EtOAc (4 x 50 mL). After removal of the solvent by distillation under reduced pressure, the crude product was purified by column chromatography (SiO_2, Et_2O) to afford diol **24** as a colorless oil (744 mg, 6.40 mmol, 58% yield).

(7) López S.; Fernández-Trillo F.; Midón P.; Castedo L.; Saá *J. Org. Chem.*, **2005**, *70*, 6346.
(8) Macsári, I.; Szabó, K. J. *Chem. Eur. J.* **2001**, *7*, 4097.

Following a reported procedure,[9] a solution of diol **24** (581 mg, 5.00 mmol, 1.0 equiv) in THF (4.0 mL) was added dropwise to a suspension of NaH (60% dispersion in mineral oil, 120 mg, 5.00 mmol, 1.0 equiv) in THF (10 mL). The mixture was stirred at rt for 50 min and then a solution of triisopropyl silyl chloride (0.96 mL, 4.5 mmol, 0.9 equiv) in THF (4.0 mL) was slowly added. After stirring for 2 h, the reaction was quenched by treatment with aqueous K_2CO_3 (1.0 M, 15 mL). The aqueous layer was separated from the organic one and extracted with Et_2O (3 x 15 mL). The combined organic layers were washed with brine (15 mL), dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 95/5) afforded the monoprotected diol **6b** as a colorless oil (1.15 g, 4.23 mmol, 85% yield).

R_f 0.57 (Pentane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.77 (ddt, 1 H, *J* = 17.2, 10.1, 7.2 Hz, *CH*=CH_2), 5.07-4.98 (m, 2 H, CH=*CH*$_2$), 3.88 (dd, 1 H, *J* = 9.8, 4.1 Hz, *CH*$_2$OTIPS), 3.79-3.58 (m, 3 H, *CH*$_2$OTIPS and *CH*$_2$OH), 2.96 (m, 1 H, *OH*), 2.03 (t, 2 H, *J* = 7.3 Hz, *CH*$_2$CH=CH_2), 1.86 (m, 1 H, *CH*CH_2OTIPS), 1.23-0.94 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.3, 116.3, 67.2, 66.3, 41.9, 32.4, 17.9, 11.7; IR 3419 (br, w), 3078 (w), 2943 (m), 2922 (m), 2892 (m), 2866 (m), 2726 (w), 1642 (w), 1464 (m), 1442 (w), 1416 (w), 1385 (w), 1368 (w), 1249 (w), 1099 (m), 1040 (m), 1014 (m), 995 (m), 913 (m), 882 (s), 787 (m), 736 (w), 681 (s), 660 (s), 652 (s), 637 (s), 627 (m), 613 (w); HRMS (ESI) calcd for $C_{15}H_{33}O_2Si^+$ $[M+H]^+$ 273.2244; found 273.2253.

3-(Benzyloxymethyl)pent-4-en-1-ol (6c)



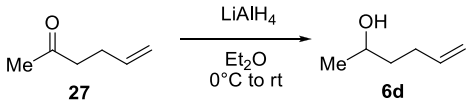
Following a reported procedure,[10] *cis*-4-(benzyloxy)but-2-en-1-ol (**25**) (5.11 g, 28.6 mmol, 1.0 equiv) was dissolved in triethyl orthoacetate (31.5 mL, 171 mmol, 6.0 equiv). Propionic acid (0.75 mL, 10 mmol, 0.35 equiv) was added and the mixture was stirred at 135°C until no more EtOH could be distilled off. The mixture was then stirred at 150°C for 2.5 h. It was then allowed to cool down to rt. Et_2O (ca. 70 mL) and aqueous $KHSO_4$ (1.0 M, ca. 100 mL) were added and the biphasic system was stirred overnight at rt. The two layers were then separated and the aqueous one was extracted with Et_2O (3 x 70 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 80/20) afforded ester **26** as a pale yellow oil (4.42 g, 17.8 mmol, 62% yield).

(9) Zhang, Q.; Rivkin, A.; Curran, D. P. *J. Amer. Chem. Soc.* **2002**, *124*, 5774.
(10) S. Couty, C. Meyer, J. Cossy, *Tetrahedron* **2009**, *65*, 1809.

Following a reported procedure,[11] ester **26** (3.72 g, 15.0 mmol, 1.0 equiv) was carefully added dropwise to a suspension of $LiAlH_4$ (512 mg, 13.5 mmol, 0.9 equiv) in THF (12.5 mL) at rt. The mixture was stirred at rt for 2 h and then the reaction was quenched by addition of wet THF, until no more gas was released. Aqueous NH_4Cl (saturated solution, 3 mL) was added and the resulting slurry was filtered through Celite and washed with Et_2O (3 x 20 mL). After removal of the organic solvents in vacuo, the resulting crude product was purified by column chromatography (SiO_2, DCM/MeOH 97/3 to 95/5) to afford alcohol **6c** as a pale yellow oil (2.37 g, 11.5 mmol, 77% yield).

R_f 0.14 (Hexane/EtOAc 20/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.27 (m, 5 H, *Ph*), 5.72 (ddd, 1 H, *J* = 17.3, 10.3, 8.3 Hz, *CH*=CH_2), 5.12 (ddd, 1 H, *J* = 17.4, 1.7, 1.0 Hz, CH=*CH*$_2$), 5.08 (ddd, 1 H, *J* = 10.5, 1.7, 0.9 Hz, CH=*CH*$_2$), 4.53 (s, 2 H, O*CH*$_2$Ph), 3.71 (m, 1 H, *CH*$_2$OH), 3.63 (m, 1 H, *CH*$_2$OH), 3.47 (dd, 1 H, *J* = 9.2, 5.5 Hz, *CH*$_2$OBn), 3.40 (dd, 1 H, *J* = 9.2, 7.1 Hz, *CH*$_2$OBn), 2.53 (m, 1 H, *CH*CH=CH_2), 2.02 (t, 1 H, *J* = 5.7 Hz, *OH*), 1.77 (m, 1 H, CH*CH*$_2$$CH_2$OH), 1.65 (dt, *J* = 7.9, 5.8 Hz, CH*CH*$_2$$CH_2$OH); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.4, 138.0, 128.3, 127.5, 127.5, 115.7, 73.7, 73.0, 60.6, 41.1, 34.7; IR 3390 (br, m), 2859 (m), 1767 (w), 1725 (w), 1698 (m), 1653 (w), 1641 (w), 1607 (w), 1587 (w), 1574 (w), 1569 (w), 1554 (w), 1537 (w), 1516 (w), 1496 (w), 1477 (w), 1455 (m), 1420 (w), 1360 (w), 1347 (w), 1313 (w), 1280 (w), 1279 (w), 1269 (w), 1205 (w), 1089 (m), 1061 (m), 1030 (w), 995 (w), 952 (w), 918 (m), 852 (w), 819 (w), 809 (w), 782 (w), 740 (s), 714 (w), 698 (s), 678 (s), 668 (w), 662 (w), 654 (w), 643 (w), 622 (w), 610 (w). The values for the characterization of **6c** correspond to the ones reported in literature.[11]

Hex-5-en-2-ol (6d)



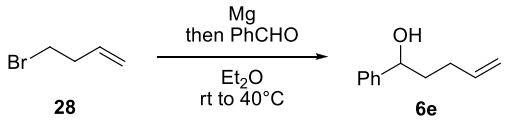
Following a reported procedure,[12] $LiAlH_4$ (708 mg, 18.6 mmol, 0.75 equiv) was suspended in Et_2O (52 mL) at 0°C. A solution of 5-hexen-2-one **27** (2.9 mL, 25 mmol, 1.0 equiv) in Et_2O (8.7 mL) was then added dropwise. The resulting mixture was stirred at 0°C for 5 min and then at rt for 3 h. The mixture was then cooled to 0°C and water (4.4 mL) was cautiously added. The resulting white slurry was filtered though Celite and washed with Et_2O (3 x 50 mL). The organic layers were combined and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, DCM/MeOH 97/3) afforded secondary alcohol **6d** as a pale yellow oil (1.27 g, 12.6 mmol, 51% yield).

R_f 0.30 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (ddt, 1 H, *J* = 16.9, 10.2, 6.6 Hz, *CH*=CH_2), 5.04 (dd, 1 H, *J* = 17.1, 1.4 Hz, CH=*CH*$_2$), 4.97 (d, 1 H, *J* = 10.1 Hz, CH=*CH*$_2$),

(11) Marotta, E.; Righi, P.; Rosini, G. *Org. Lett.* **2000**, *2*, 4145.
(12) Conti, P.; Dallanoce, C.; De Amici, M.; De Micheli, C.; Carrea, G.; Zambianchi, F. *Tetrahedron: Asymmetry* **1998**, *9*, 657.

3.82 (m, 1 H, *CH*OH), 2.15 (m, 2 H, *CH*$_2$CH=CH$_2$), 1.55 (m, 2 H, CH*CH*$_2$), 1.48 (m, 1 H, *OH*), 1.19 (d, 3 H, *J* = 6.2 Hz, *C*HC*H*$_3$); ^{13}C NMR (101 MHz, CDCl3) δ 138.4, 114.5, 67.3, 38.1, 30.0, 23.3; IR 3358 (m), 3079 (w), 2970 (m), 2931 (m), 2857 (w), 1692 (w), 1642 (m), 1454 (w), 1416 (w), 1375 (w), 1308 (w), 1122 (m), 1085 (w), 1033 (w), 995 (w), 952 (m), 935 (m), 910 (s), 847 (w), 735 (m), 714 (w), 700 (w), 678 (s), 667 (w), 645 (m), 632 (w), 617 (w); The values for the characterization of **6d** correspond to the ones reported in literature.[12]

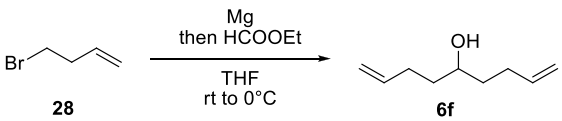
1-Phenylpent-4-en-1-ol (6e)



Following a reported procedure,[13] a solution of 4-bromobutene (**28**) (2.0 mL, 20 mmol, 1.15 equiv) in Et$_2$O (7.8 mL) was added dropwise to a suspension of Mg turnings (853 mg, 35.1 mmol, 2.05 equiv) in Et$_2$O (15.6 mL) at rt. The mixture was then stirred at rt for 1 h and further refluxed for 1 h. A solution of benzaldehyde (1.75 mL, 17.1 mmol, 1.0 equiv) in (7.8 mL) was then added dropwise and the mixture was refluxed for 2 h. It was then poured onto ice (ca. 10 g) and treated by dropwise addition of HCl (aqueous solution 2.0 M). The two layers were separated and the aqueous one was extracted with Et$_2$O (2 x 20 mL). The combined organic layers were washed with aqueous NaHCO$_3$ (saturated solution, 20 mL) and brine, dried over MgSO$_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO$_2$, pentane/EtOAc 95/5) afforded benzyl alcohol **6e** as a colorless oil (1.19 g, 7.35 mmol, 43% yield).

R$_f$ 0.30 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.38-7.33 (m, 3 H, *Ph*), 7.29 (m, 2 H, *Ph*), 5.85 (ddt, 1 H, *J* = 16.9, 10.2, 6.6 Hz, *CH*=CH$_2$), 5.05 (ddd, 1 H, *J* = 17.1, 3.4, 1.6 Hz, CH=*CH*$_2$), 4.99 (ddd, *J* = 10.1, 3.1, 1.2 Hz, CH=*CH*$_2$), 4.70 (ddd, 1 H, *J* = 7.9, 5.5, 3.4 Hz, *CH*OH), 2.15 (m, 2 H, *CH*$_2$CH=CH$_2$), 1.97-1.75 (m, 3 H, *CH*$_2$CH*OH*); ^{13}C NMR (101 MHz, CDCl$_3$) δ 144.6, 138.1, 128.5, 127.6, 125.9, 114.9, 74.0, 38.0, 30.0; IR 3359 (br, w), 2932 (w), 1721 (w), 1721 (w), 1642 (w), 1603 (w), 1591 (w), 1493 (w), 1453 (w), 1416 (w), 1416 (w), 1400 (w), 1305 (w), 1270 (w), 1239 (w), 1239 (w), 1200 (w), 1200 (w), 1175 (w), 1104 (w), 1061 (m), 1023 (m), 1013 (m), 913 (m), 760 (m), 701 (s), 675 (m), 668 (m), 667 (m), 650 (m), 638 (m), 629 (w), 616 (w), 606 (w). The values for the characterization of **6e** correspond to the ones reported in literature.[13]

Nona-1,8-dien-5-ol (6f)

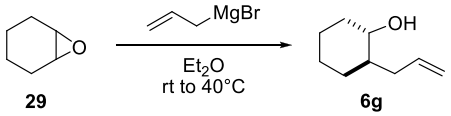


(13) Janza, B.; Studer, A. *J. Org. Chem.* **2005**, *70*, 6991.

Following a reported procedure,[14] a solution of 4-bromobutene (**28**) (2.0 mL, 20 mmol, 2.5 equiv) in THF (16 mL) was added dropwise to a suspension of Mg turnings (486 mg, 20 mmol, 2.5 equiv) in THF (2 mL) at rt. After stirring the resulting mixture for 1 h at rt, it was cooled to 0°C and a solution of ethyl formate (0.65 mL, 8.0 mmol, 1.0 equiv) in THF (10 mL) was added dropwise. The mixture was stirred at rt for 4 h and then the reaction was quenched with aqueous NH_4Cl (saturated solution, 30 mL). The two layers were separated and the aqueous one was extracted with Et_2O (3 x 30 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 90/10 to 70/30) afforded secondary alcohol **6f** as a colorless oil (1.03 g, 7.38 mmol, 92% yield).

R_f 0.29 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.83 (ddt, 2 H, *J* = 16.9, 10.2, 6.7 Hz, *CH*=CH_2), 5.04 (ddd, 2 H, *J* = 17.1, 3.4, 1.7 Hz, CH=*CH*$_2$), 4.96 (ddd, 2 H, *J* = 10.2, 3.2, 1.5 Hz, CH=*CH*$_2$), 3.64 (m, 1 H, *CH*OH), 2.16 (m, 4 H, *CH*$_2$CH=CH_2), 1.68-1.45 (m, 5 H, *CH*$_2$CH*CH*$_2$ and *OH*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.5, 114.7, 70.9, 36.4, 30.0; IR 3359 (w), 3078 (w), 2997 (w), 2979 (w), 2934 (m), 2869 (w), 2850 (w), 1642 (w), 1450 (w), 1416 (w), 1338 (w), 1317 (w), 1126 (w), 1126 (w), 1080 (w), 1061 (w), 1053 (w), 994 (m), 947 (w), 910 (s), 736 (w), 650 (w), 650 (w), 636 (w), 624 (w), 614 (w). The values for the characterization of **6f** correspond to the ones reported in literature.[14]

2-Allylcyclohexanol (6g)



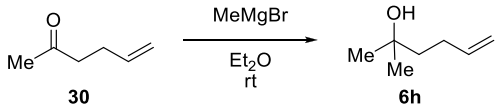
Following a reported procedure,[15] allyl magnesium bromide (1.0 M in Et_2O, 20 mL, 20 mmol, 3.0 equiv) was diluted with Et_2O (16 mL). Cyclohexene oxide **29** (0.67 mL, 6.6 mmol, 1.0 equiv) was added dropwise to the resulting solution at rt over 15 min. The mixture was refluxed for 3 h and then the reaction was quenched by addition of aqueous NH_4Cl (saturated solution, 30 mL). The two layers were separated and the aqueous one was extracted with Et_2O (3 x 30 mL). The combined organic layers were washed with water (3 x 20 mL) and brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, DCM/MeOH 99/1 to 96/4) afforded secondary alcohol **6g** as a colorless oil (0.838 g, 5.98 mmol, 90% yield).

R_f 0.44 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.89 (ddt, 1 H, *J* = 17.2, 10.1, 7.4 Hz, *CH*=CH_2), 5.09 (m, 1 H, CH=*CH*$_2$), 5.05 (m, 1 H, CH=*CH*$_2$), 3.30 (m, 1 H, *CH*OH), 2.48 (m, 1 H, *CH*$_2$CH=CH_2), 2.09-1.92 (m, 2 H, *CH*$_2$CH=CH_2 and *OH*), 1.79 (m, 2 H, *Cy*), 1.65 (m, 2 H,

(14) Lemière, G.; Gandon, V.; Cariou, K.; Hours, A.; Fukuyama, T.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. *J. Am. Chem. Soc.* **2009**, *131*, 2993.
(15) Schomaker, J. M.; Travis, B. R.; Borhan, B. *Org. Lett.*, **2003**, *5*, 3089.

Cy), 1.43-1.12 (m, 4 H, *Cy*), 0.98 (m, 1 H, *Cy*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.5, 115.9, 74.5, 44.8, 37.4, 35.5, 30.3, 25.5, 24.9; IR 3332 (w), 2927 (s), 2856 (s), 1639 (w), 1462 (w), 1462 (w), 1449 (m), 1415 (w), 1352 (w), 1308 (w), 1234 (w), 1214 (w), 1195 (w), 1151 (w), 1132 (w), 1081 (w), 1061 (s), 1037 (s), 997 (w), 965 (w), 965 (w), 940 (w), 908 (m), 844 (w), 824 (w), 790 (w), 736 (m), 709 (w), 697 (w), 687 (w), 666 (w), 647 (m), 638 (m), 629 (w), 629 (w), 620 (w), 611 (m). The values for the characterization for **6g** correspond to the ones reported in literature.[16]

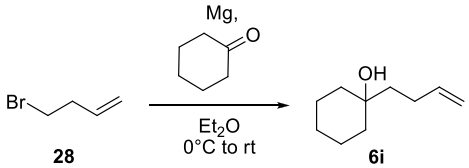
2-Methylhex-5-en-2-ol (6h)



Following a reported procedure,[17] methyl magnesium bromide (3.0 M in Et_2O, 6.3 mL, 19 mmol, 1.1 equiv) was diluted with Et_2O (10.3 mL). 5-hexen-2-one **30** (2.0 mL, 17 mmol, 1.0 equiv) was cautiously added dropwise at rt and the resulting mixture was stirred for 1 h at rt. The reaction was then quenched by addition of aqueous NH_4Cl (saturated solution, 5.1 mL) followed by aqueous $NaHSO_4$ (1.0 M, 3.4 mL). The two layers were separated and the aqueous one was extracted with Et_2O (3 x 15 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, DCM/MeOH 99/1 to 96/4) afforded tertiary alcohol **6h** as a colorless oil (1.38 g, 12.1 mmol, 71% yield).

R_f 0.40 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.85 (ddt, 1 H, *J* = 16.9, 10.2, 6.6 Hz, *CH*=CH_2), 5.04 (ddd, 1 H, *J* = 17.1, 3.5, 1.7 Hz, CH=*CH*$_2$), 4.95 (ddd, 1 H, *J* = 10.2, 3.1, 1.3 Hz, CH=*CH*$_2$), 2.14 (m, 2 H, *CH*$_2$CH=CH_2), 1.57 (m, 2 H, *CH*$_2$C(CH_3)$_2$), 1.34 (m, 1 H, *OH*), 1.23 (s, 6 H, C(*CH*$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.0, 114.4, 70.9, 42.8, 29.3, 28.8; IR 3381 (br, w), 3079 (w), 2974 (m), 2931 (w), 2879 (w), 2852 (w), 1642 (w), 1559 (w), 1542 (w), 1471 (w), 1456 (w), 1436 (w), 1416 (w), 1378 (w), 1290 (w), 1221 (w), 1149 (w), 1082 (w), 995 (w), 909 (s), 772 (w), 759 (w), 735 (s), 700 (w), 686 (w), 671 (w), 666 (w), 640 (w), 629 (w), 620 (w), 610 (w). The values for the characterization of **6h** correspond to the ones reported in literature.[17]

1-(But-3-enyl)cyclohexanol (6i)

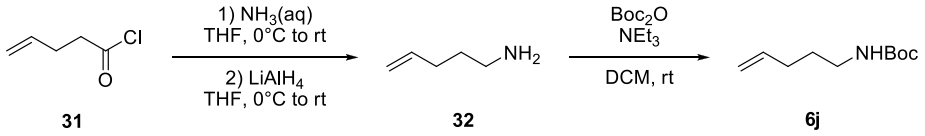


(16) Wang, L.; Thai, K.; Gravel, M. *Org. Lett.*, **2009**, *11*, 891.
(17) Dragoli, D. R.; Burdett, M. T.; Ellman, J. A. *J. Am. Chem. Soc.*, **2001**, *123*, 10127.

4-Bromobutene **28** (0.140 mL, 0.138 mmol, 0.115 equiv) was added dropwise to a suspension of Mg turnings (350 mg, 14.4 mmol, 1.2 equiv) in THF (2.9 mL), with only occasional stirring. A solution of 4-bromobutene (1.26 mL, 13.7 mmol, 1.03 equiv) in THF (2.9 mL) was then added dropwise. The resulting mixture was refluxed for 2 h and then diluted with THF (5.4 mL) and cooled to 0°C. Cyclohexanone (1.24 mL, 12.0 mmol, 1.0 equiv) dissolved in THF (11.0 mL) was added at the same temperature and the mixture was allowed to warm to rt under stirring over 3 h. The reaction was then quenched by addition of aqueous NH_4Cl (saturated solution, 20 mL). The two layers were separated and the aqueous one was extracted with EtOAc (3 x 20 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 98/2 to 90/10) afforded tertiary alcohol **6i** as a colorless oil (0.556 g, 3.60 mmol, 30% yield).

R_f 0.34 (Hexane/EtOAc 20/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (ddt, 1 H, *J* = 16.9, 10.2, 6.6 Hz, *CH*=CH_2), 5.04 (dd, 1 H, *J* = 17.1, 1.6 Hz, CH=*CH*$_2$), 4.95 (dd, 1 H, *J* = 10.2, 1.2 Hz, CH=*CH*$_2$), 2.20-2.10 (m, 2 H, *CH*$_2$CH=CH_2), 1.68-1.38 (m, 11 H, Cy, *CH*$_2$$CH_2$CH=$CH_2$), 1.28 (m, 1 H, Cy), 1.22 (s, 1 H, *OH*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 139.3, 114.2, 71.3, 41.3, 37.4, 27.4, 25.8, 22.2; IR 3385 (w), 3077 (w), 2976 (w), 2931 (s), 2853 (m), 1676 (w), 1641 (m), 1449 (m), 1415 (w), 1415 (w), 1346 (w), 1294 (w), 1259 (w), 1259 (w), 1164 (w), 1149 (w), 1149 (w), 1141 (w), 1120 (w), 1120 (w), 1084 (w), 1067 (w), 1040 (w), 1040 (w), 997 (w), 982 (w), 982 (w), 964 (m), 911 (s), 853 (w), 853 (w), 836 (w), 836 (w), 773 (w), 744 (w), 716 (w), 665 (w), 664 (w), 654 (w), 645 (w), 637 (m), 629 (w). The values for the characterization for **6i** correspond to the ones reported in literature.[18]

Tert-butyl pent-4-enylcarbamate (6j)



31 **32** **6j**

Following a reported procedure,[19] a solution of 4-pentenoyl chloride (**31**) (3.72 g, 31.4 mmol) in THF (63 mL) was added dropwise to an aqueous solution of NH_3 (25% w/w, 63 mL) at 0°C. The resulting mixture was allowed to warm to rt and stirred for 6 h. THF then was removed by distillation under reduced pressure and the residual aqueous layer was diluted with water (20 mL) and extracted with EtOAc (3 x 60 mL). The combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo* to afford 4-pentenamide (2.66 g, 26.5 mmol, 85% yield), which did not require further purification.

(18) Caggiano, L.; Fox, D. J.; House, D.; Jones, Z. A.; Kerr, F.; Warren, S. *J. Chem. Soc., Perkin Trans. 1*, 2002, 2634

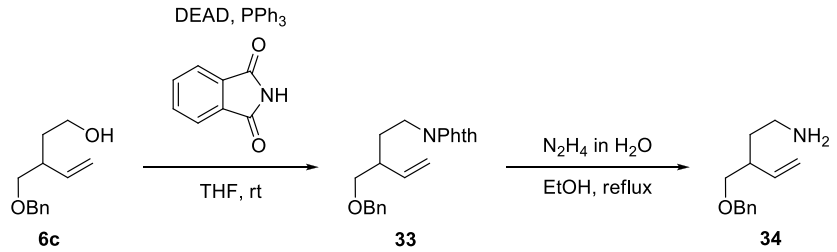
(19) Bertrand, M. B.; Wolfe, J. P. *Tetrahedron* **2005**, *61*, 6447.

Following a reported procedure,[20] a suspension of $LiAlH_4$ (1.72 g, 45.1 mmol, 1.7 equiv) in Et_2O (45 mL) was slowly added to a solution of 4-pentenamide (2.65 g, 26.5 mmol, 1.0 equiv) in Et_2O (26 mL) at 0°C. The resulting mixture was stirred at rt overnight and then diluted with Et_2O (300 mL). Aqueous NaOH (10.0 M) was cautiously added dropwise, until complete precipitation of the insoluble materials. After filtration, the solids were washed with Et_2O (3 x 100 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, DCM/ULTRA 95/5 to 50/50) afforded 4-pentenamine (**32**) as a colorless oil (0.907 g, 10.5 mmol, 40% yield).

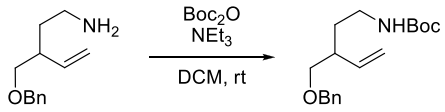
Following a slightly modified version of a reported procedure,[21] triethyl amine (3.25 mL, 23.4 mmol, 2.2 equiv) was added to a solution of ditert-butyl dicarbonate (1.27 g, 5.83 mmol, 1.1 equiv) in DCM (16 mL) and the mixture was stirred at 0°C for 5 min. 4-Pentenamine (**32**) (0.907 g, 10.6 mmol, 1.0 equiv) in DCM (16 mL) was then added at 0°C and the resulting mixture was stirred at rt overnight. The solution was then washed with aqueous citric acid (0.1 M, 20 mL). The aqueous layer was extracted with DCM (3 x 20 mL); the combined organic layers were washed with aqueous $NaHCO_3$ (saturated solution, 20 mL) and brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 95/5 to 80/20) afforded protected pentenamine **6j** as a pale yellow oil (0.678 g, 3.66 mmol, 63% yield).

R_f 0.32 (Hexane/EtOAc 20/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 (ddt, 1 H, *J* = 16.9, 10.2, 6.7 Hz, *CH*=CH_2), 5.03 (dq, 1 H, *J* = 17.1, 1.7 Hz, CH=*CH*$_2$), 4.97 (ddd, 1 H, *J* = 11.3, 2.0, 1.1 Hz, CH=*CH*$_2$), 4.52 (m, 1 H, *NH*), 3.13 (q, 2 H, *J* = 6.6 Hz, *CH*$_2$N), 2.08 (m, 2 H, *CH*$_2$CH=CH_2), 1.58 (quint, 1 H, *J* = 7.4 Hz, *CH*$_2$$CH_2$CH=$CH_2$), 1.44 (s, 9 H, *Boc*); ^{13}C NMR (101 MHz, CDCl3) δ 155.9, 137.7, 114.9, 78.9, 40.0, 30.9, 29.1, 28.3; IR 3349 (w), 2978 (m), 2933 (m), 2870 (w), 1692 (s), 1643 (w), 1525 (m), 1453 (w), 1392 (w), 1367 (m), 1271 (m), 1252 (m), 1173 (s), 1044 (w), 995 (w), 977 (w), 913 (m), 874 (w), 782 (w), 666 (w), 638 (w). The ^{1}H NMR values for the characterization for **6j** correspond to the ones reported in literature.[21]

***Tert*-butyl 3-(benzyloxymethyl)pent-4-enylcarbamate (6k)**



(20) Yang, Q.; Ney, J. E.; Wolfe, J. P. *Org. Lett.*, **2005**, *7*, 2575.
(21) Michael, F. E.; Cochran, B. M. *J. Am. Chem. Soc.*, **2006**, *128*, 4246.



34 **6k**

Following a reported procedure,[22] phthalimide (1.65 g, 11.2 mmol, 1.25 equiv) and triphenyl phosphine (2.95 g, 11.2 mmol, 1.25 equiv) were dissolved in THF (63 mL). Primary alcohol **6c** (1.86 g, 9.00 mmol, 1.0 equiv) was added; DEAD (40% solution in toluene, 5.8 mL, 13 mmol, 1.4 equiv) was then added dropwise at rt over 20 min. The reaction mixture was stirred at rt for 23 h. The solvent was removed under reduced pressure and the resulting crude oil was triturated with petroleum ether/Et_2O (2:1 mixture) until complete precipitation of the solids. The latter were filtered off and washed with the same mixture of solvents. The organic layers were combined and the solvents were removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 90/10 to 80/20) afforded phthalimide **33** as a colorless oil (1.99 g, 5.94 mmol, 66% yield).

Phthalimide **33** (1.99 g, 5.94 mmol, 1.0 equiv) was dissolved in EtOH (52 mL). Hydrazine hydrate (0.610 mL, 12.5 mmol, 2.10 equiv) was added and the mixture was refluxed for 2 h (during this time a white solid precipitated). The mixture was allowed to cool down to rt and concentrated HCl (37% w/w) was added dropwise to quench the reaction. The solid was filtered off and the organic solvent was removed *in vacuo*. The residual aqueous solution was washed with Et_2O (2 x 30 mL) and treated with solid NaOH until pH 12. It was then extracted with DCM (3 x 50 mL). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was removed *in vacuo*. Primary amine **34** was obtained as a pale yellow oil (1.09 g, 5.30 mmol, 89% yield), which did not require further purification.

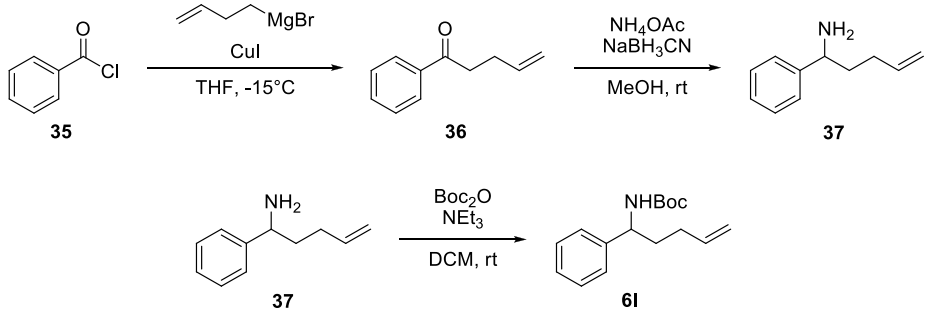
Following a reported procedure, primary amine **34** (0.616 g, 3.00 mmol, 1.0 equiv) was dissolved in DCM (9 mL). Triethyl amine (freshly distilled on CaH_2, 0.92 mL, 6.6 mmol, 2.2 equiv) was added and the solution was cooled to 0°C. Ditert-butyl dicarbonate (0.720 g, 3.30 mmol, 1.1 equiv) was added in two portions and the resulting mixture was stirred at rt for 6 h. The solution was then washed with aqueous citric acid (0.1 M, 10 mL). The aqueous layer was extracted with DCM (3 x 10 mL); the combined organic layers were washed with aqueous $NaHCO_3$ (saturated solution, 10 mL) and brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 95/5 to 90/10) afforded protected amine **6k** as a pale yellow oil (0.800 g, 2.61 mmol, 87% yield).

R_f 0.51 (Pentane/EtOAc 20/3); ^1H NMR (400 MHz, $CDCl_3$) δ 7.36-7.23 (m, 5 H, *Ph*), 5.67 (ddt, 1 H, *J* = 10.3, 8.5, 8.5 Hz, *CH*=CH_2), 5.11 (d, 1 H, *J* = 7.6 Hz, CH=*CH*$_2$), 5.08 (br s, 1 H, CH=*CH*$_2$), 4.62 (s, 1 H, *NH*), 4.50 (s, 2 H, O*CH*$_2$Ph), 3.43 (dd, 1 H, *J* = 9.2, 6.2 Hz, *CH*$_2$OCH_2Ph), 3.37 (dd, 1 H, *J* = 8.8, 6.6 Hz, *CH*$_2$OCH_2Ph), 3.18 (m, 1 H, CH_2*CH*$_2$N), 3.09 (m, 1 H, CH_2*CH*$_2$N), 2.40 (m, 1 H, *CH*CH=CH_2), 1.72 (m, 1 H, *CH*$_2$$CH_2$N), 1.53-1.36 (m, 10 H,

(22) Ma, S.; Ni, B. *Chem. Eur. J.* **2004**, *10*, 3286.

CH$_2$CH$_2$N and *Boc*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.8, 139.1, 138.3, 128.3, 127.5, 127.5, 116.3, 79.0, 73.5, 73.0, 42.0, 38.5, 31.5, 28.4; IR 3426 (sh, w), 3359 (br, w), 3067 (w), 3031 (w), 3003 (w), 2978 (w), 2933 (w), 2862 (w), 2248 (w), 1698 (s), 1642 (w), 1512 (m), 1480 (w), 1455 (w), 1392 (w), 1366 (m), 1271 (w), 1249 (m), 1170 (s), 1100 (m), 1077 (w), 1041 (w), 1029 (w), 1014 (w), 996 (w), 914 (m), 870 (w), 780 (w), 733 (s), 698 (m), 681 (w), 672 (w), 662 (w), 648 (w), 647 (w), 624 (w), 610 (w); HRMS (ESI) calcd for $C_{18}H_{28}NO_3^+$ $[M+H]^+$ 306.2064; found 306.2065.

***Tert*-butyl 1-phenylpent-4-enylcarbamate (6l)**



Following a reported procedure,[23] a solution of 4-bromobutene (1.6 mL, 16 mmol, 1.0 equiv) in THF (18 mL) was added dropwise to a suspension of Mg turnings (397 mg, 16.3 mmol, 1.02 equiv) in THF (2 mL) at rt; the resulting mixture was then stirred at rt for 1 h. CuI (152 mg, 0.798 mmol, 0.05 equiv) was added to a solution of benzoyl chloride (**35**) (1.9 mL, 16 mmol, 1.0 equiv) in THF (17 mL) at -15°C and the resulting mixture was stirred at the same temperature for 10 min. The Grignard reagent previously prepared was then added dropwise over 1 h at -15°C. The mixture was stirred at -15°C for additionally 2 h and then allowed to warm to rt. THF was removed by distillation under reduced pressure and the residue was treated with DCM (30 mL) and aqueous HCl (1.0 M, 20 mL). The two layers were separated and the aqueous one was extracted with DCM (3 x 30 mL). The combined organic layers were washed with aqueous $NaHCO_3$ (saturated solution), dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 95/5) afforded ketone **36** as a pale yellow oil (2.44 g, 15.2 mmol, 95% yield).

Ketone **36** (2.30 g, 14.3 mmol, 1.0 equiv) was dissolved in MeOH (43 mL). Ammonium acetate (18.0 g, 233 mmol, 16.3 equiv), $NaBH_3CN$ (1.53 g, 24.4 mmol, 1.7 equiv) and activated molecular sieves 4Å were added and the resulting mixture was stirred at rt for 24 h. The reaction was then quenched by dropwise addition of aqueous HCl (37% w/v, ca. 20 mL) until pH 2. The organic solvent was removed under reduced pressure and the residue diluted with water (15 mL). The aqueous layer was washed with Et_2O (2 x 35 mL) and treated by addition of solid KOH until pH 12. It was then extracted with Et_2O (4 x 25 mL), the combined organic layers were dried over

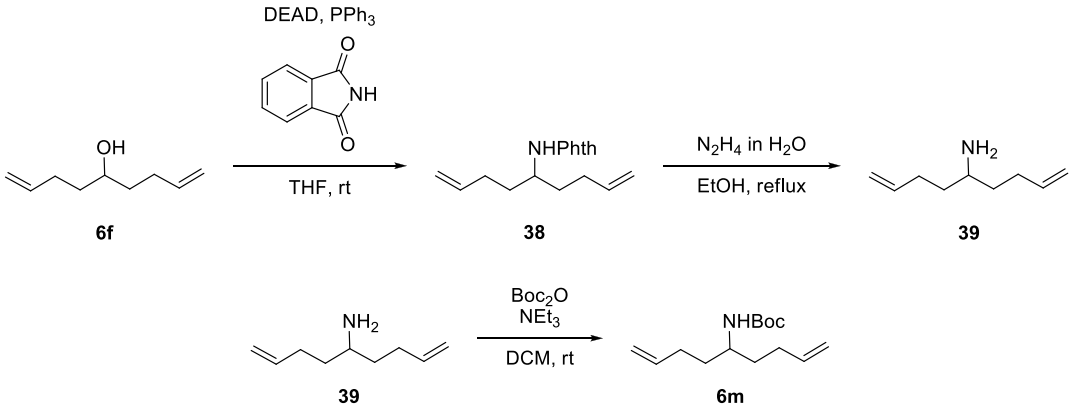
(23) Gribkov, D. V.; Hultzsch,K. C.; Hampel, F. *J. Am. Chem. Soc.*, **2006**, *128*, 3748.

KOH, filtered and the solvent was removed in vacuo to afford secondary amine **37** as a colorless oil (1.44 g, 8.95 mmol 62% yield), which was not further purified.

Secondary amine **37** (0.564 g, 3.50 mmol, 1.0 equiv) was dissolved in DCM (10.5 mL). Triethyl amine (freshly distilled on CaH_2, 1.1 mL, 7.7 mmol, 2.2 equiv) was added and the solution was cooled to 0°C. Ditert-butyl dicarbonate (0.840 g, 3.85 mmol, 1.1 equiv) was added in two portions and the resulting mixture was stirred at rt overnight. The solution was then washed with aqueous citric acid (0.1 M, 10 mL). The aqueous layer was extracted with DCM (3 x 12 mL); the combined organic layers were washed with aqueous $NaHCO_3$ (saturated solution, 12 mL) and brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 98/2 to 95/5) afforded protected amine **6l** as a colorless solid (0.815 g, 3.11 mmol, 89% yield).

R_f 0.51 (Pentane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 2 H, *Ph*), 7.25 (m, 3 H, *Ph*), 5.81 (ddt, 1 H, *J* = 16.8, 10.2, 6.5 Hz, *CH*=CH_2), 5.01 (ddd, *J* = 16.1, 3.5, 2.0 Hz, CH=*CH_2*), 4.99-4.96 (m, 1 H, CH=*CH_2*), 4.78 (m, 1 H, *CH*N), 4.64 (m, 1 H, *NH*), 2.09 (m, 2 H, *CH_2*CH=CH_2), 1.78 (m, 2 H, NCH*CH_2*), 1.42 (s, 9 H, *Boc*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.2, 142.7, 137.6, 128.5, 127.2, 126.3, 115.2, 79.3, 55.1, 36.0, 30.4, 28.4; IR 3382 (w), 3078 (w), 3064 (w), 3030 (w), 3004 (w), 2978 (w), 2933 (w), 2360 (w), 2342 (w), 1685 (s), 1643 (w), 1519 (s), 1452 (w), 1414 (w), 1391 (w), 1365 (m), 1321 (w), 1297 (m), 1254 (m), 1213 (w), 1175 (s), 1122 (w), 1047 (m), 1026 (w), 1018 (w), 1000 (w), 912 (m), 868 (w), 779 (w), 765 (m), 752 (m), 703 (s), 686 (w), 670 (w), 660 (w), 648 (w), 632 (w), 613 (w); Melting Point: 81.9-84.4°C. The values for the characterization for **6l** correspond to the ones reported in literature.[19]

***Tert*-butyl nona-1,8-dien-5-ylcarbamate (6m)**



Following a reported procedure,[22] phthalimide (1.93 g, 13.1 mmol, 1.40 equiv) and triphenyl phosphine (3.44 g, 13.1 mmol, 1.40 equiv) were dissolved in THF (74 mL). Secondary alcohol **6f** (1.59 g, 10.5 mmol, 1.0 equiv) was added; DEAD (40% solution in toluene, 6.6 mL, 15 mmol, 1.4 equiv) was then added dropwise at rt over 20 min. The reaction mixture was stirred at rt for 23 h. The solvent was removed under reduced pressure and the resulting crude oil was triturated

with petroleum ether/Et_2O (2:1 mixture) until complete precipitation of the solids. The latter were filtered off and washed with the same mixture of solvents. The organic layers were combined and the solvents were removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 98/2 to 95/5) afforded phthalimide **38** as a colorless oil (2.32 g, 8.61 mmol, 82% yield).

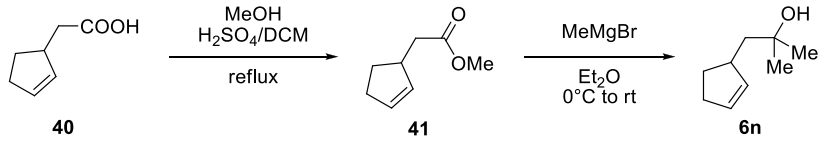
Phthalimide **38** (2.32 g, 8.61 mmol, 1.0 equiv) was dissolved in EtOH (76 mL). Hydrazine hydrate (0.870 mL, 17.8 mmol, 2.07 equiv) was added and the mixture was refluxed for 7 h (during this time a white solid precipitated). The mixture was allowed to cool down to rt and concentrated HCl (37% w/w, ca. 20 mL) was added dropwise to quench the reaction. The solvent was removed by distillation under reduced pressure and the residual aqueous solution was washed with Et_2O (2 x 30 mL) and treated with solid NaOH until pH 12. It was then extracted with Et_2O (4 x 100 mL). The combined organic layers were washed with brine and dried over Na_2SO_4, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, DCM/ULTRA 95/5 to 50/50) afforded secondary amine **39** as a colorless oil (0.631 g, 4.53 mmol, 53% yield).

Secondary amine **39** (0.631 g, 4.53 mmol, 1.0 equiv) was dissolved in DCM (10.5 mL). Triethyl amine (freshly distilled on CaH_2, 1.6 mL, 11 mmol, 2.5 equiv) was added and the solution was cooled to 0°C. Di*tert*-butyl dicarbonate (1.38 g, 6.34 mmol, 1.4 equiv) was added in two portions and the resulting mixture was stirred at rt overnight. The solution was then washed with aqueous citric acid (0.1 M, 10 mL). The aqueous layer was extracted with DCM (3 x 10 mL); the combined organic layers were washed with aqueous $NaHCO_3$ (saturated solution, 10 mL) and brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 95/5 to 90/10) afforded protected amine **6m** as a colorless solid (0.749 g, 3.13 mmol, 69% yield).

R_f 0.59 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.81 (ddt, 2 H, *J* = 16.9, 10.2, 6.6 Hz, *CH*=CH_2), 5.02 (ddd, 2 H, *J* = 17.1, 3.2, 1.5 Hz, CH=*CH*$_2$), 4.96 (d, 2 H, *J* = 10.2 Hz, CH=*CH*$_2$), 4.25 (m, 1 H, *NH*), 3.59 (m, 1 H, *CH*N), 2.10 (m, 4 H, *CH*$_2$CH=CH_2), 1.56 (m, 4 H, NCH(*CH*$_2$)$_2$), 1.44 (s, 9 H, *Boc*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.6, 138.2, 114.8, 78.9, 49.9, 34.8, 30.2, 28.4; IR 3439 (w), 3341 (w), 3077 (w), 3002 (w), 2978 (m), 2933 (m), 2853 (w), 1685 (s), 1642 (w), 1525 (m), 1452 (w), 1391 (w), 1366 (m), 1302 (w), 1269 (w), 1248 (m), 1172 (s), 1102 (w), 1046 (w), 1023 (w), 994 (w), 910 (s), 875 (w), 861 (w), 778 (w), 748 (w), 681 (w), 664 (w), 644 (w), 631 (w), 610 (w); Melting Point: 35.8 - 36.8 °C (expected), 38.5 - 40.5°C (found). The values for the characterization for **6m** correspond to the ones reported in literature.[24]

1-(Cyclopent-2-enyl)-2-methylpropan-2-ol (6n)

(24) Legeay, J. C.; Lewis, W.; Stockman R. A. *Chem. Comm.* **2009**, 2207.

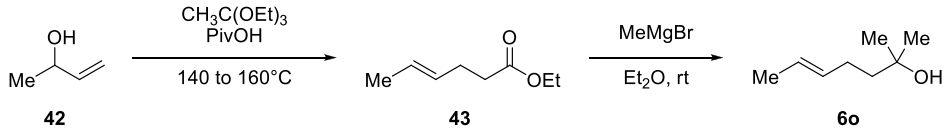


Following a reported procedure,[25] 2-cyclopentene-1-acetic acid (**40**) (1.92 mL, 15.8 mmol, 1.0 equiv) was dissolved in DCM (5 mL). MeOH (1.9 mL, 48 mmol, 3.0 equiv) and H_2SO_4 (96% w/w, 0.120 mL) were added and the mixture was stirred at reflux for 24 h. It was then allowed to cool down to rt and treated with water (7 mL). The two layers were separated and the aqueous one was extracted with DCM (3 x 10 mL). The combined organic layers were washed with aqueous Na_2CO_3 (saturated solution, 2 x 10 mL), water (1 x 10 mL) and brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, DCM) afforded methyl ester **41** as a pale yellow oil (2.16 g, 15.4 mmol, 97% yield).

Methyl magnesium bromide (3.0 M in Et_2O, 6.6 mL, 20 mmol, 3.3 equiv) was diluted with Et_2O (12 mL) and the resulting solution was cooled to 0°C. Methyl ester **41** (0.84 g, 6.0 mmol, 1.0 equiv) was then added dropwise and the mixture was stirred at rt for 1.5 h. The reaction was then quenched by dropwise addition of aqueous NH_4Cl (saturated solution, ca. 18 mL). The aqueous layer was extracted with EtOAc (3 x 18 mL), the combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, DCM/MeOH 99/1 to 97/3) afforded tertiary alcohol **6n** as a colorless oil (0.547 g, 3.90 mmol, 65% yield).

R_f 0.27 (Hexane/EtOAc 20/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76-5.67 (m, 2 H, *CH*=*CH*), 2.81 (m, 1 H, *CH*CH=CH), 2.34 (m, 1 H, *CH*$_2$CH=CH), 2.25 (m, 1 H, *CH*$_2$CH=CH), 2.15 (dddd, 1 H, *J* = 16.4, 8.1, 4.0, 4.0 Hz, *CH*$_2$CH), 1.67 (dd, 1 H, *J* = 14.1, 5.9 Hz, $CH_2C(CH_3)_2$), 1.49 (dd, 1 H, *J* = 14.3, 7.6 Hz, $CH_2C(CH_3)_2$), 1.45 (m, 1 H, *CH*$_2$CH), 1.26 (s, 6 H, $C(CH_3)_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.1, 129.9, 71.2, 50.0, 41.4, 32.1, 32.0, 30.1, 29.5; IR 3404 (br, m), 3052 (w), 2968 (m), 2915 (m), 2875 (w), 2849 (m), 1614 (w), 1469 (w), 1441 (w), 1428 (w), 1399 (w), 1378 (m), 1362 (m), 1341 (w), 1314 (w), 1288 (w), 1223 (m), 1147 (m), 1117 (s), 1075 (w), 1023 (w), 994 (w), 958 (w), 907 (s), 843 (w), 767 (w), 717 (s), 687 (w), 682 (w), 674 (w), 657 (w), 648 (w), 638 (w), 630 (w), 614 (w); Low resolution mass (obtained by GC-MS): calcd for $C_9H_{20}NO^+$ $[M+NH_4]^+$ 158; found 158. The compound is reported in the literature.[25]

2-Methylhept-5-en-2-ol (6o)



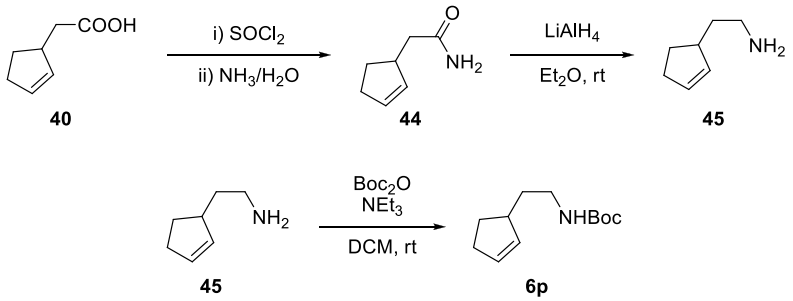
(25) Chapman, O. L.; Mattes, K. C.; Sheridan, R. S.; Klun, J. A. *J. Am. Chem. Soc.*, **1978**, *100*, 4878.

Following a modified version of a reported procedure,[26] *3*-buten-2-ol (**42**) (1.74 mL, 20.0 mmol, 1.0 equiv) was dissolved in triethyl orthoacetate (26 mL, 140 mmol, 7.0 equiv). Pivalic acid (0.24 g, 1.2 mmol, 0.12 equiv) was added and the mixture was stirred at 140°C until no more EtOH could be distilled off. The temperature was then increased to 160°C and the mixture was stirred overnight. It was then allowed to cool down to rt, diluted with THF (40 mL) and stirred with aqueous HCl (1.0 M, 40 mL) for 1 h. The two layers were separated, the aqueous one was extracted with Et_2O (40 mL) and the combined organic layers were washed with aqueous $NaHCO_3$ (saturated solution, 40 mL), dried over $MgSO_4$, filtered and the solvent was removed *in vacuo* to afford ethyl ester **43** as a pale yellow oil (1.70 g, 11.9 mmol, 60% yield), which was not subjected to further purification.

Methyl magnesium bromide (3.0 M in Et_2O, 6.0 mL, 18 mmol, 3.0 equiv) was diluted with Et_2O (11.5 mL) and the resulting solution was cooled to 0°C. Ethyl ester **43** (0.80 g, 5.6 mmol, 1.0 equiv) was then added dropwise and the mixture was stirred at rt for 4 h. The reaction was then quenched by dropwise addition of aqueous NH_4Cl (saturated solution, ca. 18 mL). The aqueous layer was extracted with EtOAc (3 x 18 mL), the combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, DCM/MeOH 99/1 to 97/3) afforded tertiary alcohol **6o** as a colorless oil (0.520 g, 4.06 mmol, 73% yield).

R_f 0.35 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.46-5.40 (m, 2 H, *CH*=*CH*), 2.05 (m, 2 H, *CH*$_2$CH=CH), 1.74 (br s, 1 H, *OH*), 1.62 (m, 3 H, *CH*$_3$CH=CH), 1.50 (m, 2 H, *CH*$_2$C(CH$_3$)$_2$), 1.19 (s, 6 H, C(*CH*$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 131.3, 124.7, 70.8, 43.4, 29.1, 27.5, 17.8; IR 3373 (m), 3017 (w), 2970 (s), 2934 (s), 2887 (w), 2856 (m), 2360 (w), 2337 (w), 2336 (w), 1470 (w), 1453 (w), 1379 (m), 1366 (m), 1260 (w), 1216 (m), 1151 (m), 1088 (w), 966 (s), 935 (s), 914 (m), 796 (w), 760 (w), 750 (w), 741 (w), 704 (w), 694 (w), 676 (w), 663 (w), 654 (w), 636 (w), 606 (w). The values for the characterization for **6o** correspond to the ones reported in literature.[26]

Tert-butyl 2-(cyclopent-2-enyl)ethylcarbamate (6p)



(26) Hay, M. B.; Wolfe, J. P. *J. Am. Chem. Soc.*, **2005**, *127*, 16468.

Following a reported procedure,[27] thionyl chloride (6.9 mL, 95 mmol, 4.0 equiv) was cautiously added dropwise to 2-cyclopentene-1-acetic acid (**40**) (2.85 mL, 23.8 mmol, 1.0 equiv) and the mixture was stirred at rt for 3 h. The excess of thionyl chloride was then removed by simple distillation and the resulting acyl chloride was added dropwise to aqueous NH_3 (25% w/w, 140 mL). The mixture was stirred at rt for 60 h and then the aqueous solution was extracted with EtOAc (3 x 80 mL). The combined organic layers were washed with aqueous $NaHCO_3$ (saturated solution, 80 mL), brine and dried over $MgSO_4$. Removal *in vacuo* of the solvent afforded the amide **44** as a colorless solid (1.51 g, 12.0 mmol, 51% yield), which was not further purified.

Amide **44** (1.51 g, 12.0 mmol, 1.0 equiv) was dissolved in Et_2O (14 mL). A suspension of $LiAlH_4$ (1.59 g, 41.9 mmol, 3.47 equiv) in Et_2O (42 mL) was added dropwise to the previous solution at rt and the resulting mixture was stirred at rt for 24 h. It was then diluted with Et_2O (150 mL), cooled to 0°C and the reaction was quenched by dropwise addition of aqueous NaOH (10.0 M) until no more solid precipitated. The resulting slurry was filtered through Celite and washed with Et_2O (3 x 50 mL). After removal of the aqueous layer, the organic one was further diluted with pentane (100 mL), dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, DCM/ULTRA 30/70 to 70/30) afforded primary amine **45** as a pale yellow oil (1.33 g, 12.0 mmol, 85% yield).

Primary amine **45** (0.400 g, 3.60 mmol, 1.0 equiv) was dissolved in DCM (10.5 mL). Triethyl amine (freshly distilled on CaH_2, 1.3 mL, 9.5 mmol, 2.6 equiv) was added and the solution was cooled to 0°C. Di*tert*-butyl dicarbonate (1.04 g, 4.76 mmol, 1.3 equiv) was added in two portions and the resulting mixture was stirred at rt overnight. The solution was then washed with aqueous citric acid (0.1 M, 10 mL). The aqueous layer was extracted with DCM (3 x 10 mL); the combined organic layers were washed with aqueous $NaHCO_3$ (saturated solution, 10 mL) and brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 98/2 to 95/5) afforded protected amine **6p** as a colorless oil (0.627 g, 2.97 mmol, 82% yield).

R_f 0.31 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.76 (m, 1 H, *CH=CH*), 5.68 (ddd, 1 H, *J* = 6.1, 4.2, 2.1 Hz, *CH=CH*), 4.53 (m, 1 H, *NH*), 3.18 (m, 2 H, CH_2NH), 2.70 (m, 1 H, *CH*CH=CH), 2.43-2.24 (m, 2 H, CH_2CH=CH), 2.08 (m, 1 H, CH_2CHCH$_2$CH$_2$NH), 1.62 (m, 1 H, CH_2CHCH$_2$CH$_2$NH), 1.55-1.34 (m, 11 H, CH_2CH$_2$NH and *Boc*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 155.9, 134.3, 130.7, 78.9, 43.0, 39.3, 36.2, 31.9, 29.6, 28.4; IR 3456 (sh, w), 3360 (br, w), 3051 (w), 2977 (m), 2933 (m), 2862 (w), 2853 (w), 1691 (s), 1517 (m), 1455 (w), 1392 (w), 1366 (m), 1271 (m), 1251 (m), 1170 (s), 1087 (w), 1041 (w), 1009 (w), 968 (w), 952 (w), 912 (w), 912 (w), 867 (w), 782 (w), 758 (w), 719 (m), 696 (w), 696 (w), 687 (w), 687 (w), 678 (w), 653 (w), 639 (w), 627 (w). The values for the characterization for **6p** correspond to the ones reported in literature.[19]

(27) Ney, J. E.; Wolfe, J. P. *J. Am. Chem. Soc.*, **2005**, *127*, 8644.

4. Optimization of the Reaction

General procedure for reaction optimization:

Under inert atmosphere $Pd_2(dba)_3$ (2.7 mg, 0.0030 mmol, 0.02 equiv), the ligand (0.06 mmol, 0.04 equiv) and the base (0.2 mmol, 1.33 equiv) were introduced into a 2 mL vial, which was then sealed. The solvent was added (0.8 mL), followed by the alkyne reagent (0.2 mmol, 1.33 equiv), 4-penten-1-ol (15.5 μL, 0.150 mmol, 1.00 equiv) and the internal standard (pentadecane, 21 μL, 0.076 mmol). The mixture was stirred at 65-70°C (or 110°C, where specified) for 3 h and then allowed to cool to room temperature. Circa 0.2 mL of the reaction mixture were filtered through a short plug of Celite, which was then washed with DCM (2 mL). The so obtained solution was injected into a GC-MS chromatographer (the following oven program was followed: Initial temperature: 50°C, Ramp: 10.0 °C/min to 250 °C, hold 25 min at 250 °C). Yield was determined by GC-MS, based on the following calibration.

Preparative Reaction for the conditions of Table 1, Entry 1

1,4-Bis(tri*iso*propylsilyl)buta-1,3-diyne (46)

Under inert atmosphere $Pd_2(dba)_3$ (7.3 mg, 0.0080 mmol, 0.02 equiv), DPE-Phos (8.6 mg, 0.016 mmol, 0.04 equiv) and NaO*t*Bu (51.2 mg, 0.533 mmol, 1.33 equiv) were introduced into a 5 mL vial, which was then sealed. Toluene was added (2.1 mL), followed by bromo triisopropylsilyl acetylene (139 mg, 0.533 mmol, 1.33 equiv) and the starting material (0.4 mmol, 1.00 equiv). The mixture was stirred at 65-70°C (or 110°C, where specified) for 3 h and then allowed to cool to room temperature. The solvent was evaporated under reduced pressure. The crude mixture was then directly purified by column chromatography (SiO_2, pentane/EtOAc 98/2 to 95/5). R_f (Pentane/EtOAc 20/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ ; ^{13}C NMR (101 MHz, $CDCl_3$) δ ; IR . The values for the characterization for **6p** correspond to the ones reported in literature.[28]

GC-MS Quantification:

A 0.0.25 M standard solution was prepared by dissolving pentadecane (0.200 mL, 0.728 mmol) in DCM (28.8 mL).

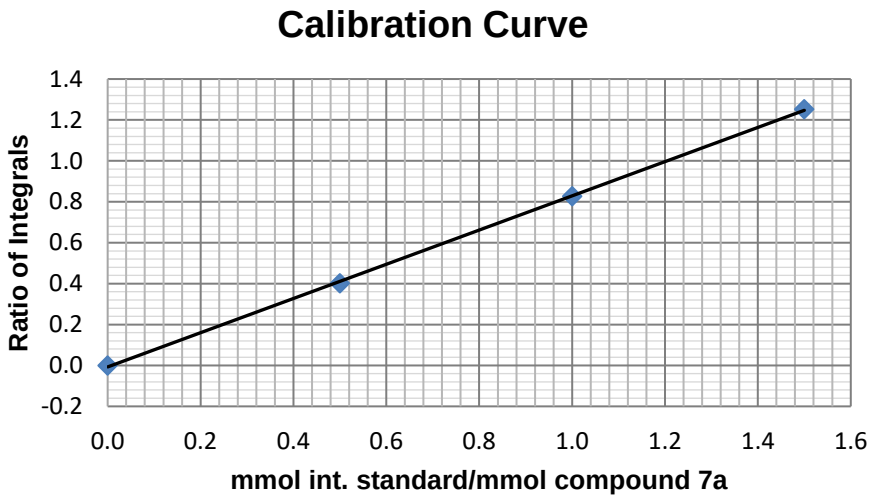
Triisopropyl(3-(tetrahydrofuran-2-yl)prop-1-ynyl)silane (**7a**) (24.8 mg, 0.0931 mmol) was dissolved in DCM (ca. 3.72 mL) (solution O).

- 0.1 mL of solution O were diluted by adding DCM (0.9 mL) to obtain solution A;
- 0.1 mL of solution O were mixed with 0.05 mL standard solution 0.025 M and diluted by adding DCM (0.85 mL) to obtain solution B;
- 0.1 mL of solution O were mixed with 0.10 mL standard solution 0.025 M and diluted by adding DCM (0.80 mL) to obtain solution C;

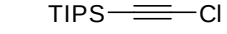
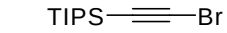
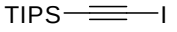
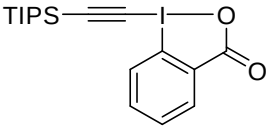
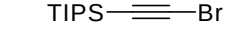
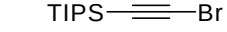
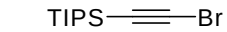
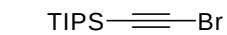
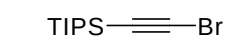
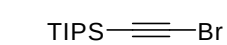
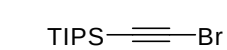
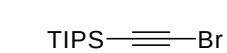
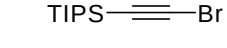
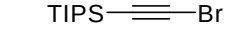
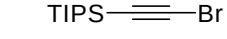
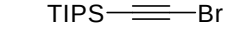
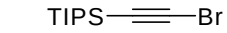
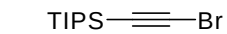
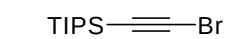
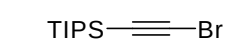
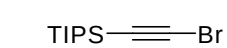
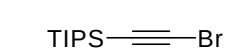
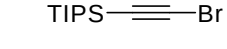
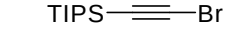
(28) Alonso, D. A.; Najera, C.; Pacheco, M. C. *Adv. Synth. Catal.* **2003,** *345*, 1146.

- 0.1 mL of solution O were mixed with 0.15 mL standard solution 0.025 M and diluted by adding DCM (0.75 mL) to obtain solution D.

GC-MS chromatograms were acquired for solutions A, B, C and D and in each of them the ratio between the integrals of the signals corresponding to the internal standard (retention time: 16.7 min) and to the compound **7a** (retention time: 19.8 min) was calculated. These observed ratios by integration of the chromatogram peaks and the ratios (mmol pentadecane/mmol **7a**) were used as the axis of the calibration graph.



Detailed results for the optimization studies

Entry	Reagent	Catalyst	Base	Solvent	Yield
1		DPE-Phos	NaO*t*Bu	THF	15%; 22% (14 hrs)
2		DPE-Phos	NaO*t*Bu	THF	69%
3		DPE-Phos	NaO*t*Bu	THF	31%
4		DPE-Phos	NaO*t*Bu	THF	< 5%
5		DPE-Phos	NaO*t*Bu	THF	48%[a]
6		DPE-Phos	NaO*t*Bu	THF	47%[b]
7		DPE-Phos	NaO*t*Bu	THF	71%[c]
8		DPE-Phos	NaO*t*Bu	THF	72%[d]
9		DPE-Phos	NaO*t*Bu	THF	78%[e]
10		DPE-Phos	NaO*t*Bu	THF	57%[f]
11		DPE-Phos	NaO*t*Bu	DME	80%
12		DPE-Phos	NaO*t*Bu	Toluene	87%
13		DPE-Phos	NaO*t*Bu	DCE	34%
14		DPE-Phos	NaO*t*Bu	DMF	nr
15		DPE-Phos	NaO*t*Bu	MeCN	nr
16		DPE-Phos	LiO*t*Bu	Toluene	75%
17		DPE-Phos	KO*t*Bu	Toluene	nr
18		DPE-Phos	CsO*t*Bu	Toluene	< 5%
19		DPE-Phos	DBU	Toluene	nr
20		DPE-Phos	Hünig's Base	Toluene	nr
21		dppp	NaO*t*Bu	Toluene	< 5%
22		dppe	NaO*t*Bu	Toluene	< 5%
23		Xant-Phos	NaO*t*Bu	Toluene	50%
24		Ru-Phos	NaO*t*Bu	Toluene	18%
25		Seg-Phos	NaO*t*Bu	Toluene	20%
26		BINAP	NaO*t*Bu	Toluene	32%

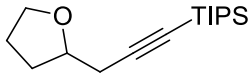
Standard conditions: 0.15 mmol 4-pentenol, 0.2 mmol reagent (1.33 equiv), 0.2 mmol base (1.33 equiv), 0.003 mmol $Pd_2(dba)_3$ (2 mol %), 0.006 mmol ligand (4 mol %) in 0.8 mL solvent at 65-70°C; (a) 0.003 mmol ligand (2 mol %); (b) Premixing of catalyst and ligand in 0.4 mL THF before the starting material and the reagent were added and heating was started; (c) in 0.3 mL THF; (d) in 3 mL THF; (e) 0.0075 mmol catalyst (5 mol %), 0.015 mmol ligand (10 mol %); (f) 0.0015 mmol catalyst (1 mol %), 0.03 mmol ligand (2 mol %);

5. Scope of the Reaction

General procedure for the intramolecular oxy- and aminoalkynylation of olefins (GP1): Under inert atmosphere $Pd_2(dba)_3$ (7.3 mg, 0.0080 mmol, 0.02 equiv), DPE-Phos (8.6 mg, 0.016 mmol, 0.04 equiv) and NaO*t*Bu (51.2 mg, 0.533 mmol, 1.33 equiv) were introduced into a 5 mL vial, which was then sealed. Toluene was added (2.1 mL), followed by bromo triisopropylsilyl acetylene (139 mg, 0.533 mmol, 1.33 equiv) and the starting material (0.4 mmol, 1.00 equiv). The mixture was stirred at 65-70°C (or 110°C, where specified) for 3 h and then allowed to cool to room temperature. The solvent was evaporated under reduced pressure. The crude mixture was then directly purified by column chromatography (SiO_2, pentane/EtOAc 98/2 to 95/5).

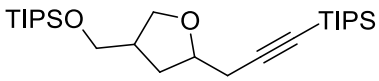
General procedure for the deprotection of 2-propargyl *N*-Boc pyrrolidines (GP2): The *N*-Boc pyrrolidine is dissolved in DCM (20 mL per mmole of protected pyrrolidine) and the resulting solution is cooled to 0°C. Trifluoroacetic acid (10 mL per mmole of protected pyrrolidine) was added dropwise and the mixture was stirred at 0°C for 40 min. The volatiles were then removed by distillation under reduced pressure. The residue was taken up in DCM and the solution as washed with aqueous NaOH (2 M, three times). The combined organic layers were dried over Na_2SO_4, filtered and concentrated under reduced pressure. The crude product was purified by column chromatography (SiO_2, short plug; DCM/ULTRA 85/15 to 70/30).

Tri*iso*propyl(3-(tetrahydrofuran-2-yl)prop-1-ynyl)silane (7a): was obtained as a pale yellow oil (100 mg, 0.370 mmol, 92% yield); R_f 0.53 (Pentane/EtOAc 20/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.07 (ddd, 1 H, *J* = 14.6, 6.9, 4.3 Hz, O*CH*CH_2C≡C), 3.92 (m, 1 H, O*CH*$_2$), 3.79 (m, 1 H, O*CH*$_2$), 2.60 (dd, 1 H, *J* = 16.6, 4.3 Hz, *CH*$_2$C≡C), 2.43 (dd, 1 H, *J* = 16.6, 7.9 Hz, *CH*$_2$C≡C), 2.10 (m, 1 H, CH_2CH_2), 2.04-1.76 (m, 3 H, CH_2CH_2), 1.14-0.98 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 105.2, 81.8, 77.4, 68.5, 30.6, 26.7, 25.8, 18.6, 11.2; IR 2957 (s), 2956 (s), 2942 (s), 2891 (m), 2175 (m), 1746 (w), 1463 (m), 1383 (w), 1367 (w), 1239 (w), 1033 (m), 1018 (w), 1017 (w), 997 (m), 921 (w), 884 (s), 842 (w), 810 (w), 744 (w), 674 (s), 641 (s), 633 (s), 618 (m), 607 (w); HRMS (ESI) calcd for $C_{16}H_{30}AgOSi^+$ $[M+Ag]^+$ 373.1111; found 373.1112.



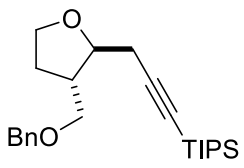
The same reaction was performed on a 5.00 mmol scales using: 4-penten-1-ol (431 mg, 5.00 mmol, 1.0 equiv), bromo triisopropyl silyl acetylene (1.74 g, 6.67 mmol, 1.33 equiv), $Pd_2(dba)_3$ (91.7 mg, 0.100 mmol, 0.02 equiv), DPE-Phos (108 mg, 0.200 mmol, 0.04 equiv) and NaO^{t}Bu (0.641 g, 6.67 mmol, 1.33 equiv). Compound **7a** (1.15 g, 4.30 mmol) was obtained in 86% yield.

Triisopropyl((5-(3-(tri*iso*propylsilyl)prop-2-ynyl)tetrahydrofuran-3-yl)methoxy)silane (7b): was obtained as a pale yellow oil (160 mg, 0.352 mmol, 88% yield; mixture of inseparable diastereoisomers, d.r. 67:33); R_f 0.76 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10 (ddd, 1 H, *J* = 14.6, 7.0, 4.5 Hz, O*CH*CH_2C≡C), 4.05-4.00 (m, 1 H, O*CH*CH_2C≡C, *minor diaster.*), 4.00 (dd, 1 H, *J* = 8.5, 7.0 Hz, O*CH*$_2$), 3.84 (dd, 1 H, *J* = 8.5, 8.0 Hz, O*CH*$_2$, *minor diaster.*), 3.73 (dd, 1 H, *J* = 8.5, 6.5 Hz,



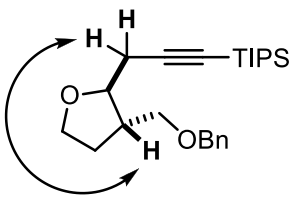
O*CH*$_2$, *minor diaster.*), 3.70-3.58 (m, 3 H, OCH$_2$, both diaster.), 2.62 (dd, 1 H, *J* = 16.6, 4.4 Hz, *CH*$_2$C≡C, *minor diaster.*), 2.56-2.48 (m, 1 H, OCH$_2$*CH*CH$_2$, both diaster.) 2.55 (dd, 1 H, *J* = 16.6, 4.5 Hz, , *CH*$_2$C≡C), 2.43 (dd, 1 H, *J* = 16.6, 8.0 Hz, *CH*$_2$C≡C, *minor diaster.*), 2.41 (dd, 1 H, *J* = 16.6, 7.9 Hz, *CH*$_2$C≡C), 2.18 (ddd, 1 H, *J* = 14.1, 8.0, 6.0 Hz, CH*CH*$_2$CH, *minor diaster.*), 1.94-1.89 (m, 2 H, CH*CH*$_2$CH), 1.47 (ddd, 1H, *J* = 12.5, 8.5, 8.5 Hz, CH*CH*$_2$CH, *minor diaster.*), 1.14-0.96 (m, 21 H, *TIPS*, both diaster.).; ^{13}C NMR (101 MHz, CDCl$_3$, the signals for the minor diastereoisomer are indicated in *italics*, some of them being not resolved) δ 105.1, *104.9*, *81.9*, 81.9, *77.8*, 77.1, *71.0*, 70.9, *65.4*, 64.8, *42.6*, 41.8, *34.3*, 33.4, 26.9, *26.6*, 18.6, *18.0*, 11.9, *11.2*; IR 2942 (s), 2891 (m), 2865 (s), 2724 (w), 2175 (w), 1463 (m), 1432 (w), 1384 (w), 1367 (w), 1246 (w), 1159 (w), 1103 (s), 1072 (m), 1030 (w), 1014 (m), 996 (m), 920 (w), 883 (s), 793 (m), 738 (w), 678 (s), 665 (s), 638 (m), 613 (w), 606 (w); HRMS (ESI) calcd for $C_{26}H_{53}O_2Si_2^+$ $[M+H]^+$ 453.3579; found 453.3589.

(3-(3-(Benzyloxymethyl)tetrahydrofuran-2-yl)prop-1-ynyl)tri*iso*propylsilane (7c): was



obtained as a pale yellow oil (142 mg, 0.314 mmol, 80% yield; mixture of inseparable diastereoisomers, d.r. 85:15); R$_f$ 0.33 (Hexane/EtOAc 20/2); ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.45-7.20 (m, 5 H, *Ph*, both diast.), 4.53 (s, 2 H, Ph*CH*$_2$O, both diast.), 4.08 (ddd, 1 H, *J* = 8.0, 6.5, 5.0 Hz, O*CH*$_2$CH, *minor diaster.*), 4.01 (dt, 1 H, *J* = 8.0, 5.5 Hz, O*CH*$_2$CH, *minor diaster.*), 3.94 (dt, 1 H, *J* = 8.5, 7.0 Hz, O*CH*$_2$CH), 3.85-3.74 (m, 2 H, *CH*$_2$OBn, *minor diaster.*), 3.82 (td, 1 H, *J* = 8.5, 3.0, O*CH*$_2$CH), 3.80-3.73 (m, 1 H, O*CH*$_2$CH), 3.58 (dd, 1 H, *J* = 9.0, 6.5 Hz, *CH*$_2$OBn), 3.49 (dd, 1 H, *J* = 9.0, 7.0 Hz, *CH*$_2$OBn), 2.64 (dd, 2 H, *J* = 13.0, 7.0 Hz, *CH*$_2$C≡C, *minor diaster.*), 2.59 (d, 2 H, *J* = 5.5 Hz, *CH*$_2$C≡C), 2.57-2.44 (m, 1 H, *CH*CH$_2$OBn; 2 H, *CH*CH$_2$OBn and OCH$_2$*CH*$_2$, *minor diaster.*), 2.12 (m, 1 H, OCH$_2$*CH*$_2$), 2.17-1.96 (m, 1 H, OCH$_2$*CH*$_2$, *minor diaster.*), 1.78 (ddd, 1 H, *J* = 13.6, 12.5, 6.5 Hz, OCH$_2$*CH*$_2$), 1.20-0.96 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, CDCl$_3$; the signals for the minor diastereoisomer are indicated in *italics*, some of them being not resolved) δ 138.3, *138.2*, 128.3, *128.3*, 127.5, *127.5*, 127.4, *105.4*, 105.1, 81.9, 79.8, *78.6*, *73.2*, 73.0, 72.2, *69.2*, 67.7, *67.1*, 43.5, *41.3*, 29.9, *29.1*, 26.3, *22.2*, 18.6, 11.2; IR 2942 (s), 2890 (m), 2174 (m), 1739 (w), 1496 (w), 1496 (w), 1462 (m), 1381 (w), 1381 (w), 1365 (w), 1244 (w), 1243 (w), 1205 (w), 1205 (w), 1205 (w), 1098 (m), 1077 (m), 1030 (w), 1018 (w), 996 (m), 969 (w), 969 (w), 919 (w), 918 (w), 884 (m), 843 (w), 842 (w), 836 (w), 822 (w), 821 (w), 736 (s), 698 (m), 674 (s), 667 (s), 660 (s), 650 (m), 636 (m), 626 (m), 614 (w); HRMS (ESI) calcd for $C_{24}H_{39}O_2Si^+$ $[M+H]^+$ 387.2714; found 387.2708.

The relative stereochemistry of the major diastereoisomer was assigned based on ROESY correlation between signals at δ 3.82 (O*CH*CH$_2$C≡C) and δ 2.59 (*CH*$_2$C≡C).



Tri*iso*propyl(3-(5-methyltetrahydrofuran-2-yl)prop-1-ynyl)silane (7d): was obtained as a pale yellow oil (89.7 mg, 0.320 mmol, 80% yield; mixture of inseparable diastereoisomers, d.r. 87:13); R_f 0.58 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.16 (m, 2 H, O*CH*CH_2C≡C and O*CH*CH_3), *3.98* (m, 2 H, O*CH*CH_2C≡C and O*CH*CH_3, *minor diast.*), *2.60* (dd, 1 H, *J* = 16.6, 4.0 Hz, *CH_2*C≡C, *minor diast.*), 2.55 (dd, 1 H, *J* = 16.6, 4.0 Hz, *CH_2*C≡C), 2.42 (dd, 1 H, *J* = 16.6, 8.0 Hz, *CH_2*C≡C), *2.41* (dd, 1 H, *J* = 16.6, 8.0 Hz, *minor diast.*), 2.20-2.03 (m, 2 H, CH_2CH_2, both diast.), 1.92-1.81 (m, 1 H, CH_2CH_2, both diast.), 1.47 (m, 1 H, CH_2CH_2, both diast.), *1.24* (d, 3 H, *J* = 6.0 Hz, *CH_3*CH, *minor diast.*), 1.21 (d, 3 H, *J* = 6.1 Hz, *CH_3*CH), 1.12-0.97 (m, 21 H, *TIPS*, both diast.); ^{13}C NMR (101 MHz, $CDCl_3$, only major diastereoisomer) δ 105.2, 81.9, 76.9, 75.5, 33.9, 31.4, 27.0, 21.1, 18.6, 11.2; IR 2960 (w), 2942 (w), 2924 (w), 2865 (w), 2173 (w), 1717 (w), 1684 (w), 1559 (w), 1542 (w), 1508 (w), 1471 (w), 1471 (w), 1459 (w), 1420 (w), 1383 (w), 1376 (w), 1367 (w), 1088 (w), 1088 (w), 1018 (w), 996 (w), 996 (w), 919 (w), 918 (w), 883 (m), 723 (w), 713 (w), 677 (s), 660 (s), 648 (m), 641 (s), 605 (w); HRMS (ESI) calcd for $C_{17}H_{32}AgOSi^+$ $[M+Ag]^+$ 387.1268; found 387.1276. The relative stereochemistry was assigned based on analogy with compound **7e**.

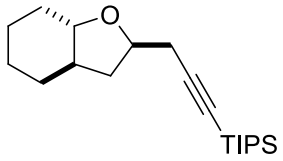
Tri*iso*propyl(3-(5-phenyltetrahydrofuran-2-yl)prop-1-ynyl)silane (7e): was obtained as a pale yellow oil (82.3 mg, 0.240 mmol, 60% yield); R_f 0.65 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (m, 4 H, *Ph*), 7.25 (m, 1 H, *Ph*), 5.09 (dd, 1 H, *J* = 8.1, 6.3 Hz, *CH*Ph), 4.40 (ddd, *J* = 14.0, 7.3, 4.4 Hz, O*CH*CH_2C≡C), 2.67 (dd, 1 H, *J* = 16.6, 4.2 Hz, *CH_2*C≡C), 2.56 (dd, 1 H, *J* = 16.6, 7.7 Hz, *CH_2*C≡C), 2.41 (m, 1 H, PhCH*CH_2*), 2.25 (m, 1 H, PhCHCH_2*CH_2*), 2.02 (m, 1 H, PhCHCH_2*CH_2*), 1.89 (m, 1 H, PhCH*CH_2*), 1.15-1.00 (m, 21 H, TIPS); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2, 128.2, 127.1, 125.5, 105.1, 82.1, 81.1, 77.9, 35.2, 31.4, 27.1, 18.6, 11.3; IR 3288 (w), 2966 (w), 2941 (m), 2925 (w), 2893 (w), 2864 (m), 2174 (m), 1690 (w), 1494 (w), 1464 (w), 1449 (w), 1448 (w), 1383 (w), 1366 (w), 1314 (w), 1288 (w), 1284 (w), 1216 (w), 1198 (w), 1186 (w), 1181 (w), 1168 (w), 1159 (w), 1142 (w), 1112 (w), 1081 (w), 1060 (s), 1030 (m), 994 (m), 967 (w), 939 (w), 919 (w), 883 (s), 837 (w), 789 (w), 758 (m), 699 (s), 673 (s), 660 (s), 648 (m), 633 (w), 626 (w), 613 (w); HRMS (ESI) calcd for $C_{22}H_{35}OSi^+$ $[M+H]^+$ 343.2452; found 343.2462. The relative stereochemistry was assigned based on transformation into known compound **11**.

The same reaction was performed on a 2.00 mmol scale using: 1-Phenylpent-4-en-1-ol (**6e**) (325 mg, 2.00 mmol, 1.0 equiv), bromo tri*iso*propyl silyl acetylene (0.695 g, 2.66 mmol, 1.33 equiv), $Pd_2(dba)_3$ (37 mg, 0.040 mmol, 0.02 equiv), DPE-Phos (43 mg, 0.080 mmol, 0.04 equiv) and NaO^tBu (0.236 g, 2.66 mmol, 1.33 equiv). Compound **7e** (0.431 g, 1.26 mmol) was obtained in 63% yield.

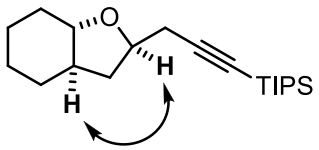
(3-(5-(But-3-enyl)tetrahydrofuran-2-yl)prop-1-ynyl)tri*iso*propylsilane (7f): was obtained as a pale yellow oil (79.8 mg, 0.249 mmol, 65% yield; 95% pure based

on ^{1}H NMR); R_f 0.65 (Pentane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.82 (m, 1 H, *CH*=CH_2), 5.03 (m, 1 H, CH=*CH*$_2$), 4.95 (m, 1 H, CH=*CH*$_2$), 4.13 (ddd, 1 H, *J* = 13.6, 7.5, 4.0 Hz, O*CH*CH_2C≡C), 4.03 (ddd, 1 H, *J* = 14.1, 8.0, 6.0 Hz, O*CH*CH_2), 2.55 (dd, 1 H, *J* = 16.6, 4.3 Hz, *CH*$_2$C≡C), 2.42 (dd, 1 H, *J* = 16.6, 7.8 Hz, *CH*$_2$C≡C), 2.21-2.00 (m, 4 H, *CH*$_2$*CH*$_2$CH=CH_2), 1.84 (m, 1 H, *CH*$_2$*CH*$_2$), 1.68 (m, 1 H, *CH*$_2$*CH*$_2$), 1.61-1.45 (m, 2 H, *CH*$_2$*CH*$_2$CH=CH_2 and *CH*$_2$*CH*$_2$), 1.12-1.01 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.5, 114.5, 105.4, 81.9, 79.2, 76.9, 35.0, 31.9, 31.2, 30.4, 27.0, 18.6, 11.3; IR 3079 (w), 2943 (w), 2923 (w), 2907 (w), 2895 (w), 2865 (w), 2845 (w), 2360 (w), 2342 (w), 2332 (w), 2174 (w), 1722 (w), 1721 (w), 1643 (w), 1464 (w), 1444 (w), 1418 (w), 1383 (w), 1366 (w), 1345 (w), 1192 (w), 1163 (w), 1124 (w), 1095 (w), 1075 (w), 1030 (w), 1017 (w), 996 (w), 958 (w), 941 (w), 912 (m), 883 (m), 737 (w), 678 (m), 670 (m), 664 (m), 635 (s), 627 (m), 613 (w); HRMS (ESI) calcd for $C_{20}H_{37}OSi^+$ $[M+H]^+$ 321.2608; found 321.2600. The relative stereochemistry was assigned based on analogy with compound **7e**.

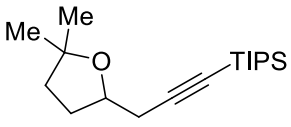
Tri*iso*propyl(3-(octahydrobenzofuran-2-yl)prop-1-ynyl)silane (7g): was obtained as a pale yellow oil (101 mg, 0.316 mmol, 79% yield); R_f 0.65 (Pentane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.18 (m, 1 H, O*CH*CH_2C≡C), 3.30 (m, 1 H, Cy*CH*O), 2.58 (br s, 1 H, *CH*$_2$C≡C), 2.56 (d, 1 H, *J* = 1.9 Hz, *CH*$_2$C≡C), 2.17 (ddd, 1 H, *J* = 12.1, 6.2, 6.2 Hz, CyCH*CH*$_2$), 2.06 (m, 1 H, *CH*$_2$CHO in Cy), 1.93 (m, 1 H, *Cy*), 1.81 (m, 1 H, *Cy*), 1.72 (m, 1 H, *Cy*), 1.59 (m, 1 H, dd, *J* = 20.6, 12.0 Hz, CyCH*CH*$_2$), 1.45 (m, 1 H, *CH*CH_2CHCH_2C≡C), 1.35-1.10 (m, 4 H, *Cy*), 1.12-0.95 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 105.2, 83.0, 82.0, 76.1, 46.3, 36.9, 31.3, 28.9, 27.4, 25.7, 24.3, 18.6, 11.3; IR 2935 (s), 2864 (s), 2173 (m), 1716 (w), 1462 (m), 1383 (w), 1366 (w), 1351 (w), 1243 (w), 1142 (w), 1071 (m), 1057 (m), 1025 (w), 1008 (w), 994 (m), 972 (w), 922 (w), 883 (m), 864 (w), 735 (w), 699 (w), 677 (s), 667 (s), 653 (m); HRMS (ESI) calcd for $C_{20}H_{37}OSi^+$ $[M+H]^+$ 321.2608; found 321.2610.



The relative stereochemistry was assigned based on ROESY correlation between signals at δ 4.18 (O*CH*CH_2C≡C) and 1.45 (m, 1 H, *CH*CH_2CHCH_2C≡C).

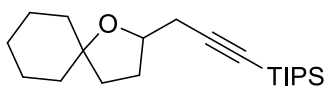


(3-(5,5-Dimethyltetrahydrofuran-2-yl)prop-1-ynyl)tri*iso*propylsilane (7h): was obtained as a pale yellow oil (81.0 mg, 0.275 mmol, 69% yield); R_f 0.66 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.10 (ddd, 1 H, *J* = 14.9, 7.0, 4.1 Hz, O*CH*CH_2C≡C), 2.59 (dd, 1 H, *J* = 16.6, 4.0 Hz, *CH*$_2$C≡C), 2.38 (dd, 1 H, *J* = 16.6, 8.2 Hz, *CH*$_2$C≡C), 2.10 (m, 1 H, CH_2CH_2), 1.96-1.67 (m, 3 H, CH_2CH_2), 1.25 (s, 3 H, *CH*$_3$), 1.20 (s, 3 H, *CH*$_3$), 1.11-0.92 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 105.2, 81.4, 81.3, 76.7, 38.2, 31.1, 29.0, 27.9, 27.2,

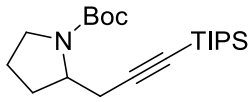


18.6, 11.3; IR 2962 (m), 2942 (m), 2930 (m), 2893 (m), 2865 (s), 2174 (m), 1463 (m), 1381 (w), 1367 (m), 1302 (w), 1241 (w), 1145 (w), 1059 (m), 1027 (m), 996 (w), 964 (w), 953 (w), 920 (w), 884 (m), 864 (w), 736 (w), 677 (s), 663 (s), 628 (m), 617 (w); HRMS (ESI) calcd for $C_{18}H_{35}OSi^+$ $[M+H]^+$ 295.2452; found 295.2459.

(3-(1-oxaspiro[4.5]decan-2-yl)prop-1-ynyl)tri*iso*propylsilane (7i): The reaction was performed at 110°C. The product was obtained as a pale yellow oil (75.9 mg, 0.227 mmol, 57% yield); R_f 0.48 (Hexane/EtOAc 20/1.5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.09 (ddd, 1 H, *J* = 14.1, 6.5, 4.0 Hz, O*CH*CH_2C≡C), 2.59 (dd, 1 H, *J* = 16.6, 4.2 Hz, *CH*$_2$C≡C), 2.37 (dd, 1 H, *J* = 16.6, 8.1 Hz, *CH*$_2$C≡C), 2.08 (m, 1 H, CH_2CH_2), 1.94-1.63 (m, 5 H, CH_2CH_2, cyclohexyl), 1.59-1.44 (m, 4 H, cyclohexyl), 1.44-1.28 (m, 4 H, cyclohexyl), 1.16-0.93 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 105.5, 83.4, 81.7, 76.3, 38.5, 37.4, 35.7, 30.7, 27.4, 25.7, 24.1, 23.8, 18.6, 11.3; IR 2931 (s), 2892 (m), 2864 (s), 2174 (m), 2074 (w), 1660 (w), 1615 (w), 1615 (w), 1615 (w), 1567 (w), 1463 (m), 1449 (m), 1383 (w), 1383 (w), 1365 (w), 1365 (w), 1345 (w), 1345 (w), 1345 (w), 1323 (w), 1310 (w), 1305 (w), 1255 (w), 1251 (w), 1240 (w), 1240 (w), 1213 (w), 1209 (w), 1199 (w), 1199 (w), 1199 (w), 1150 (w), 1150 (w), 1128 (w), 1075 (m), 1059 (m), 1025 (m), 996 (w), 969 (w), 969 (w), 951 (w), 951 (w), 950 (w), 950 (w), 920 (w), 920 (w), 884 (m), 847 (w), 742 (w), 742 (w), 717 (w), 696 (w), 677 (s), 661 (s), 640 (w), 632 (w), 621 (w), 614 (w); HRMS (ESI) calcd for $C_{21}H_{39}OSi^+$ $[M+H]^+$ 335.2765; found 335.2758.

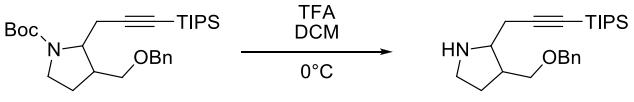


***Tert*-butyl 2-(3-(tri*iso*propylsilyl)prop-2-ynyl)pyrrolidine-1-carboxylate (7j):** was obtained as a pale yellow oil (118 mg, 0.323 mmol, 81% yield; mixture of rotamers); R_f 0.65 (Pentane/EtOAc 20/2); ^{1}H NMR (400 MHz, 55°C, $CDCl_3$) δ 3.81 (br s, 1 H, N*CH*CH_2C≡C), 3.34 (m, 2 H, *CH*$_2$N), 2.62 (m, 1 H, CH_2C≡C), 2.51 (br m, 1 H, CH_2C≡C), 2.09-1.71 (m, 4 H, *CH*$_2$*CH*$_2$), 1.45 (m, 9 H, *Boc*), 1.14-0.92 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, $CDCl_3$) (rotamers!) δ 154.3, 105.9, 105.6, 81.9, 81.5, 79.2, 79.0, 56.2, 47.1, 46.6, 30.7, 29.8, 28.4, 25.4, 24.5, 23.6, 22.9, 11.2; IR 2960 (m), 2943 (m), 2904 (w), 2891 (w), 2866 (m), 2365 (w), 2359 (w), 2341 (w), 2331 (w), 2173 (w), 1698 (s), 1654 (w), 1463 (w), 1394 (s), 1366 (m), 1341 (w), 1329 (w), 1254 (w), 1246 (w), 1213 (w), 1173 (m), 1120 (m), 1097 (w), 1030 (w), 1019 (w), 996 (w), 954 (w), 920 (w), 905 (w), 884 (m), 866 (w), 774 (w), 756 (w), 744 (w), 740 (w), 679 (m), 662 (m), 634 (m), 619 (w), 609 (w); HRMS (ESI) calcd for $C_{21}H_{40}NO_2Si^+$ $[M+H]^+$ 366.2823; found 366.2825.



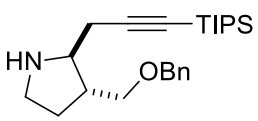
***Tert*-butyl 3-(benzyloxymethyl)-2-(3-(tri*iso*propylsilyl)prop-2-ynyl)pyrrolidine-1-carboxylate (7k):** was obtained as a mixture of separable diastereoisomers. Major diastereoisomer: pale yellow oil (128 mg, 0.263 mmol, 66% yield); R_f 0.66 (Pentane/EtOAc 20/3). Minor diastreoisomer: pale yellow oil (19.2 mg, 0.0395 mmol, 10% yield); R_f 0.57 (Pentane/EtOAc 20/3). 76% overall yield, d.r.: 87:13.

Both diastereoismers were obtained as mixtures of rotamers. In order to characterize them, they were subjected to deprotection of the amino group according to the general procedure GP2.

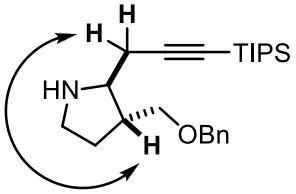


7k **7k'**

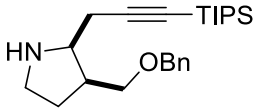
Major Diastereoisomer: pale yellow oil (99.1 mg, 0.256 mmol, quant. yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.26 (m, 5 H, *Ph*), 4.51 (s, 2 H, Ph*CH*$_2$O), 3.50 (m, 2 H, CH*CH*$_2$OBn), 3.04 (ddd, 1 H, *J* = 10.5, 7.6, 5.5 Hz, *CH*$_2$N), 2.97 (q, 1 H, *J* = 5.8 Hz, N*CH*CH$_2$ C≡C), 2.88 (ddd, 1 H, *J* = 10.4, 7.4, 7.4 Hz, *CH*$_2$N), 2.59 (dd, 1 H, *J* = 16.9, 5.2 Hz, *CH*$_2$C≡C), 2.50 (dd, 1 H, *J* = 16.9, 5.8 Hz, *CH*$_2$C≡C), 2.22 (m, 1 H, NCH$_2$*CH*$_2$), 1.96 (m, 1 H, NCH$_2$*CH*$_2$), 1.80 (br s, 1 H, NH), 1.59 (ddd, 1 H, *J* = 13.0, 13.0, 6.0 Hz, *CH*CH$_2$OBn), 1.17-0.95 (m, 21 H, TIPS); ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.2, 138.5, 128.3, 127.5, 105.9, 82.1, 73.1, 73.0, 60.8, 45.9, 43.4, 30.1, 25.9, 18.6, 11.2; IR 3032 (w), 2942 (m), 2942 (m), 2890 (m), 2890 (m), 2864 (s), 2864 (s), 2170 (m), 1697 (w), 1629 (w), 1558 (w), 1507 (w), 1497 (w), 1462 (m), 1457 (m), 1406 (w), 1383 (w), 1365 (w), 1242 (w), 1203 (w), 1098 (m), 1076 (m), 1029 (w), 1018 (w), 996 (w), 919 (w), 910 (w), 884 (m), 811 (w), 735 (s), 698 (m), 678 (s), 669 (s), 662 (s), 639 (s), 628 (s), 619 (m); HRMS (ESI) calcd for $C_{24}H_{40}NOSi^+$ $[M+H]^+$ 386.2874; found 386.2868.



The relative stereochemistry of the major diastereoisomer was assigned based on the ROESY correlation observed between signals at δ 3.50 (CH*CH*$_2$OBn) and δ 2.97 (N*CH*CH$_2$C≡C).

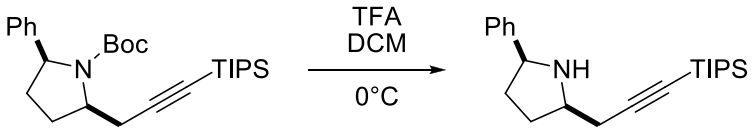


Minor Diastereoisomer: pale yellow oil (15.3 mg, 0.0394 mmol, quant. yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41-7.27 (m, 5 H, *Ph*), 4.50 (s, 2 H, Ph*CH*$_2$O), 3.57 (d, 2 H, *J* = 6.0 Hz, CH*CH*$_2$OBn), 3.40 (dd, 1 H, *J* = 14.0, 7.0 Hz, N*CH*CH$_2$C≡C), 3.45-3.26 (br s, 1 H, *NH*), 3.17 (ddd, 1 H, *J* = 10.4, 9.1, 4.7 Hz, *CH*$_2$N), 2.97 (ddd, 1 H, *J* = 10.3, 8.5, 7.6 Hz, *CH*$_2$N), 2.61-2.43 (m, 3 H, *CH*$_2$C≡C and *CH*CH$_2$OBn), 2.02 (m, 1 H, NCH$_2$*CH*$_2$), 1.73 (m, 1 H, NCH$_2$*CH*$_2$), 1.16-0.93 (m, 21, *TIPS*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 138.0, 128.4, 127.7, 127.7, 105.7, 82.5, 73.4, 70.2, 59.4, 44.8, 40.4, 28.5, 21.4, 18.6, 11.2; IR 2946 (w), 2923 (w), 2891 (w), 2881 (w), 2864 (m), 2170 (w), 1676 (w), 1463 (w), 1463 (w), 1421 (w), 1420 (w), 1378 (w), 1366 (w), 1202 (w), 1188 (w), 1182 (w), 1161 (w), 1132 (w), 1100 (w), 1081 (w), 1073 (w), 1029 (w), 1015 (w), 997 (w), 884 (w), 799 (w), 741 (m), 738 (m), 721 (w), 714 (w), 696 (m), 679 (s), 662 (m), 657 (m), 645 (w), 636 (m), 621 (w), 611 (w); HRMS (ESI) calcd for $C_{24}H_{40}NOSi^+$ $[M+H]^+$ 386.2874; found 386.2876.



***Tert*-butyl 2-phenyl-5-(3-(tri*iso*propylsilyl)prop-2-ynyl)pyrrolidine-1-carboxylate (7l):** was obtained as a pale yellow oil (141 mg, 0.319 mmol, 80% yield; mixture of inseparable

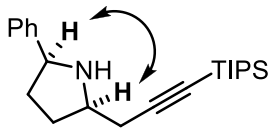
diastereosiomers, d.r. 94:6); R_f 0.64 (Pentane/EtOAc 20/3). The product was obtained as a mixture of rotamers. In order to characterize it, it was subjected to deprotection of the amino group according the general procedure GP2.



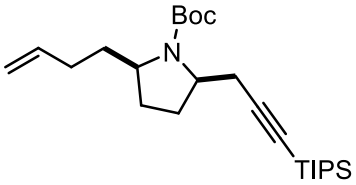
7l **7l'**

2-Phenyl-5-(3-(tri*iso*propylsilyl)prop-2-ynyl)pyrrolidine (7l') was obtained as a pale yellow oil (109 mg, 0.319 mmol, quantitative yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40 (m, 2 H, *Ph*), 7.31 (m, 2 H, *Ph*), 7.24 (m, 1 H, *Ph*), 4.20 (t, 1 H, *J* = 7.9 Hz, Ph*CH*N), 3.43 (dt, *J* = 13.6, 6.0 Hz, N*CH*CH_2C≡C), 2.54 (d, 2 H, *J* = 5.9 Hz, *CH_2*C≡C), 2.30 (br s, 1 H, NH), 2.17 (m, 1 H, *CH_2CH_2*), 2.02 (m, 1 H, *CH_2CH_2*), 1.74 (m, 2 H, *CH_2CH_2*), 1.13-1.00 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.4, 128.3, 126.8, 126.5, 106.3, 81.7, 62.8, 57.6, 34.2, 30.7, 27.1, 18.6, 11.3; IR 3064 (w), 3026 (w), 2955 (s), 2941 (s), 2891 (m), 2865 (s), 2171 (m), 1604 (w), 1491 (w), 1463 (m), 1435 (w), 1427 (w), 1413 (w), 1402 (w), 1383 (w), 1366 (w), 1279 (w), 1249 (w), 1106 (w), 1074 (w), 1030 (w), 1016 (m), 996 (w), 971 (w), 920 (w), 883 (s), 756 (m), 701 (s), 678 (s), 667 (s), 666 (s), 654 (s), 643 (m), 634 (m), 620 (w), 607 (w); HRMS (ESI) calcd for $C_{22}H_{36}NSi^+$ $[M+H]^+$ 342.2617; found 342.2602.

The relative stereochemistry of the major diastereoisomer was assigned based on the ROESY correlation observed between signals at δ 4.20 (Ph*CH*N) and δ 3.43 (N*CH*CH_2C≡C).

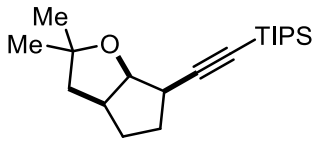


***Tert*-butyl 2-(but-3-enyl)-5-(3-(tri*iso*propylsilyl)prop-2-ynyl)pyrrolidine-1-carboxylate (7m):** was obtained as a dark yellow oil (103 mg, 0.245 mmol, 57% yield); R_f 0.66 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, 57°C, $CDCl_3$) δ 5.81 (ddt, 1 H, *J* = 16.8, 10.2, 6.5 Hz, *CH*=CH_2), 5.01 (ddd, *J* = 17.1, 3.5, 1.5 Hz, CH=*CH_2*), 4.94 (d, 1 H, *J* = 10.2 Hz, CH=*CH_2*), 3.87 (m, 1 H, N*CH*CH_2C≡C), 3.79 (m, 1 H, N*CH*CH_2CH_2C=CH_2), 2.81 (dd, 1 H, *J* = 16.5, 2.5 Hz, *CH_2*C≡C), 2.36 (dd, 1 H, *J* = 16.6, 9.0 Hz, *CH_2*C≡C), 2.16-1.83 (m, 7 H, *CH_2CH_2*C=CH_2 and CH*CH_2CH_2*CH), 1.69 (m, 1 H, CH*CH_2CH_2*CH), 1.47 (s, 9 H, *Boc*), 1.15-0.94 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, 57°C, $CDCl_3$) δ 154.8, 138.4, 114.5, 106.0, 82.1, 79.3, 58.7, 57.8, 35.0, 30.8, 29.1, 28.7, 28.6, 26.4, 18.6, 11.5; IR 3079 (w), 3078 (w), 2972 (w), 2962 (w), 2942 (w), 2933 (w), 2865 (w), 2364 (w), 2358 (w), 2171 (w), 1695 (s), 1642 (w), 1462 (w), 1426 (w), 1389 (s), 1366 (m), 1322 (w), 1254 (w), 1173 (m), 1109 (m), 1030 (w), 995 (w), 969 (w), 940 (w), 911



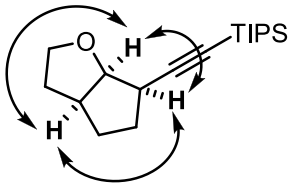
(m), 884 (m), 858 (w), 774 (w), 735 (w), 678 (m), 668 (m), 660 (m), 635 (w), 622 (w), 612 (w); HRMS (ESI) calcd for $C_{25}H_{46}NO_2Si^+$ $[M+H]^+$ 420.3292; found 420.3279. The relative stereochemistry was assigned based on analogy with compound (**7l**).

((2,2-Dimethylhexahydro-*2H*-cyclopenta[b]furan-6-yl)ethynyl)tri*iso*propylsilane (7n): was

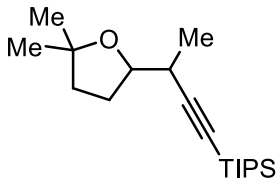


obtained as a pale yellow oil (111 mg, 0.345 mmol, 86% yield); R_f 0.64 (Hexane/EtOAc 20/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.38 (dd, 1 H, *J* = 6.8, 6.2 Hz, *CH*O), 2.82 (m, 1 H, *CH*C≡C), 2.51 (ddd, *J* = 10.6, 6.2, 5.7 Hz, CH_2CHCH_2), 1.98 (dd, 1 H, *J* = 12.1, 9.1 Hz, CH_2CHC≡C), 1.90-1.74 (m, 2 H, $CH_2C(CH_3)_2$), 1.62-1.45 (m, 2 H, CH_2CH_2CHC≡C), 1.27 (s, 3 H, CH_3), 1.26 (dd, 1 H, *J* = 12.2, 8.4 Hz, CH_2CHC≡C), 1.12 (s, 3 H, CH_3), 1.10-0.97 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 108.8, 82.9, 82.1, 81.9, 46.6, 43.4, 38.1, 31.5, 31.4, 27.8, 26.0, 18.7, 11.4; IR 2960 (s), 2942 (s), 2893 (m), 2865 (s), 2723 (w), 2717 (w), 2359 (w), 2240 (w), 2180 (m), 2153 (w), 2152 (w), 1463 (m), 1382 (w), 1367 (m), 1302 (w), 1273 (w), 1246 (w), 1159 (m), 1112 (w), 1091 (w), 1080 (m), 1065 (m), 1034 (w), 1010 (m), 994 (m), 925 (m), 911 (s), 884 (s), 821 (w), 788 (w), 736 (s), 687 (s), 674 (s), 657 (s), 643 (m), 629 (m), 618 (m), 606 (w); HRMS (ESI) calcd for $C_{20}H_{37}OSi^+$ $[M+H]^+$ 321.2608; found 321.2607.

The relative stereochemistry of the major diastereoisomer was assigned based on the ROESY correlations observed between signals at δ 4.38 (*CH*O), δ 2.82 (*CH*C≡C) and δ 2.51 (CH_2CHCH_2).



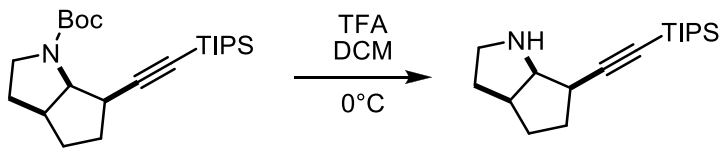
(3-(5,5-Dimethyltetrahydrofuran-2-yl)but-1-ynyl)tri*iso*propylsilane (7o): The reaction was



performed at 110°C. The product was obtained as a yellow oil (87.4 mg, 0.283 mmol, 71% yield); R_f 0.77 (Hexane/EtOAc 20/2); ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.08 (td, 1 H, *J* = 7.1, 4.1 Hz, *CH*O), 2.72 (ddd, 1 H, *J* = 14.1, 7.0, 4.1 Hz, *CH*(CH_3)C≡C), 2.05-1.87 (m, 2 H, $CH_2CH_2C(CH_3)_2$), 1.78-1.67 (m, 2 H, $CH_2CH_2C(CH_3)_2$), 1.27 (s, 3 H, C(CH_3)$_2$), 1.22 (s, 3 H, C(CH_3)$_2$), 1.18 (d, 3 H, *J* = 7.0 Hz, CH(CH_3)C≡C), 1.11-1.01 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 110.9, 81.2, 81.0, 80.1, 38.4, 31.4, 28.5, 28.1, 27.7, 18.6, 15.8, 11.3; IR 2965 (s), 2942 (s), 2906 (m), 2892 (m), 2866 (s), 2165 (m), 1463 (m), 1380 (w), 1366 (m), 1301 (w), 1246 (w), 1155 (w), 1061 (m), 1051 (m), 998 (m), 912 (m), 884 (s), 867 (w), 867 (w), 862 (w), 862 (w), 822 (w), 785 (w), 737 (w), 737 (w), 675 (s), 634 (w), 634 (w); HRMS (ESI) calcd for $C_{19}H_{37}OSi^+$ $[M+H]^+$ 309.2608; found 309.2605.

***Tert*-butyl 6-((tri*iso*propylsilyl)ethynyl)hexahydrocyclopenta[b]pyrrole-1(*2H*)-carboxylate (7p):** was obtained as a yellow oil (134 mg, 0.346 mmol, 86% yield); R_f 0.48 (Hexane/EtOAc

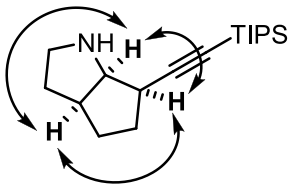
20/3). The product was obtained as a mixture of rotamers. In order to characterize it, it was subjected to deprotection of the amino group according the general procedure GP2.



7p **7p'**

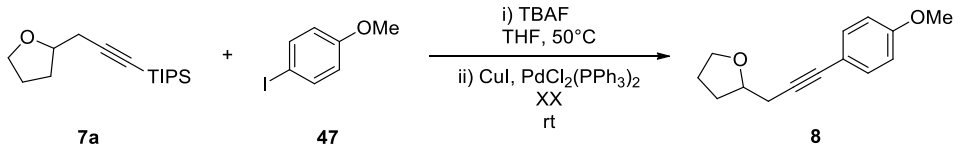
((Triisopropylsilyl)ethynyl)octahydrocyclopenta[b]pyrrole **(7p')** was obtained as a yellow oil (79.2 mg, 0.272 mmol, 85% yield); ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.63 (t, 1 H, *J* = 6.9 Hz, *CH*N), 2.98 (dt, 1 H, *J* = 9.1, 7.2 Hz, *CH*$_2$N), 2.82 (dt, 1 H, *J* = 9.1, 6.4 Hz, *CH*$_2$N), 2.73 (dt, 1 H, *J* = 10.1, 6.5 Hz, *CH*C≡C), 2.62 (m, 1 H, *CH*CHN), 2.09-1.82 (m, 3 H, *CH*$_2$CH$_2$N, CH$_2$*CH*$_2$CHC≡C and NH), 1.78-1.59 (m, 2 H, *CH*$_2$CH$_2$CHC≡C), 1.49 (m, 1 H, CH$_2$*CH*$_2$CHC≡C), 1.40 (m, 1 H, *CH*$_2$CH$_2$N), 1.16-0.95 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 108.7, 83.1, 64.4, 47.4, 42.2, 38.8, 34.2, 33.4, 32.7, 18.6, 11.2; IR 2942 (s), 2892 (w), 2864 (s), 2175 (w), 1710 (w), 1462 (m), 1383 (w), 1365 (w), 1312 (w), 1116 (w), 1077 (w), 1015 (w), 997 (w), 919 (w), 883 (m), 829 (w), 806 (w), 734 (w), 674 (s), 662 (m), 643 (s), 633 (m), 622 (m), 607 (w); HRMS (ESI) calcd for $C_{18}H_{34}NSi^+$ $[M+H]^+$ 292.2455; found 292.2453.

The relative stereochemistry was assigned based on ROESY correlations observed between signals at δ 3.63 (*CH*N), δ 2.73 (*CH*C≡C) and δ 2.62 (*CH*CHN).



6. Functionalizations of the products

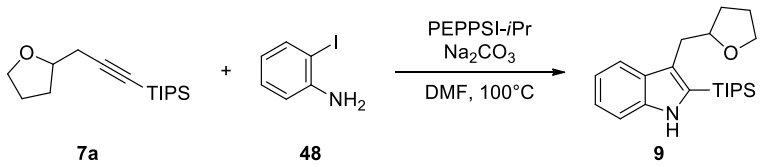
2-(3-(4-Methoxyphenyl)prop-2-ynyl)tetrahydrofuran (8)



Following a reported procedure,[29] TBAF (1.0 M in THF, 0.6 mL, 0.6 mmol, 2.0 equiv) was added dropwise to a solution of propargyl tetrahydrofuran **7a** (80 mg, 0.30 mmol, 1.0 equiv) in THF (1.5 mL) and the mixture was stirred at 50°C for 1 h. It was then allowed to cool down to rt and *p*-iodoanisole (**47**) (87 mg, 0.36 mmol, 1.2 equiv) was added, followed by $PdCl_2(PPh_3)_2$ (17 mg, 0.024 mmol, 0.08 equiv) and CuI (69 mg, 0.36 mmol, 1.2 equiv). After stirring at rt overnight, SiO_2 was added and the solvent was removed in vacuo. Column chromatography purification of the crude product preadsorbed on silica gel (SiO_2, Hexane/EtOAc 95/5) afforded alkyne **8** (56.8 mg, 0.262 mmol, 87%) as a pale yellow oil.

R_f 0.46 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.33 (m, 2 H, *Ar*), 6.80 (m, 2 H, *Ar*), 4.10 (dt, *J* = 12.0, 6.7 Hz, O*CH*CH_2C≡C), 3.93 (m, 1 H, O*CH*$_2$), 3.82-3.73 (m, 1 H, OCH_2), 3.78 (s, 3 H, OCH_3), 2.66 (dd, 1 H, *J* = 16.6, 5.2 Hz, *CH*$_2$C≡C), 2.57 (dd, 1 H, *J* = 16.6, 6.8 Hz, *CH*$_2$C≡C), 2.09 (m, 1 H, CH_2CH_2), 2.02-1.83 (m, 2 H, CH_2CH_2), 1.78 (m, 1 H, CH_2CH_2); ^{13}C NMR (101 MHz, $CDCl_3$) δ 159.1, 132.9, 115.8, 113.7, 85.0, 81.4, 77.4, 68.4, 55.2, 30.7, 26.2, 25.7; IR 2954 (w), 2930 (w), 2908 (w), 2868 (w), 2839 (w), 1607 (m), 1569 (w), 1509 (s), 1462 (w), 1442 (w), 1417 (w), 1365 (w), 1290 (m), 1246 (s), 1173 (m), 1107 (w), 1067 (s), 1034 (m), 920 (w), 832 (s), 811 (w), 801 (w), 735 (w), 647 (w), 636 (m); HRMS (ESI) calcd for $C_{14}H_{17}O_2^+$ $[M+H]^+$ 217.1223; found 217.1217.

3-((Tetrahydrofuran-2-yl)methyl)-2-(tri*iso*propylsilyl)-1H-indole (9)



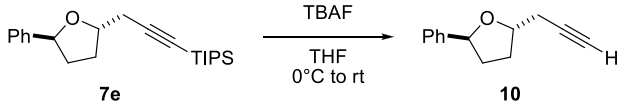
Following a reported procedure,[30] 2-iodo aniline (**48**) (92 mg, 0.42 mmol, 1.2 equiv), Na_2CO_3 (185 mg, 1.75 mmol, 5.0 equiv) and PEPPSI-*i*Pr (24 mg, 0.035 mmol, 0.1 equiv) were introduced into a vial, which was then sealed. Propargyl tetrahydrofuran **7a** (93 mg, 0.35 mmol, 1.0 equiv) was added by syringe, followed by DMF (previously degassed, 2.1 mL). The mixture was stirred at 100°C for 40 h and then allowed to cool down to rt, diluted with water (5 mL) and extracted with EtOAc (4 x 10 mL). The combined organic layers were washed with brine and

(29) Sun, J. ; Conley, M. P.; Zhang, C.; Kosmin, S. A. *J. Am. Chem. Soc.* **2006**, *128*, 9705.
(30) Grunenthal GMBH, Patent: US2009/247505 A1, **2009.**

dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, hexane/EtOAc 99/1 to 98/2) afforded indole **9** (54.5 mg, 0.152 mmol, 43% yield) as a colorless solid.

R_f 0.54 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (s, 1 H, NH *indole*), 7.76 (d, 1 H, *J* = 7.9 Hz, *indole*), 7.38 (m, 1 H, *indole*), 7.20 (m, 1 H, *indole*), 7.11 (m, 1 H, *indole*), 4.28 (dt, 1 H, *J* = 13.3, 6.7 Hz, O*CH*CH_2C≡C), 3.98 (dt, *J* = 7.6, 6.5 Hz, *CH*$_2$O), 3.78 (dt, 1 H, *J* = 7.1, 5.7 Hz, *CH*$_2$O), 3.23 (dd, 1 H, *J* = 14.2, 6.2 Hz, CH_2indole), 3.03 (dd, 1 H, *J* = 14.2, 7.1 Hz, CH_2indole), 1.92 (m, 3 H, CH_2CH_2), 1.68 (m, 1 H, CH_2CH_2), 1.51 (quint, 3 H, *J* = 7.5 Hz, Si*CH*$(CH_3)_2$), 1.26-1.10 (m, 18 H, SiCH(*CH*$_3$)$_2$); ^{13}C NMR (101 MHz, $CDCl_3$, TIPS carbon partially splitted) δ 138.6, 130.0, 129.1, 123.3, 122.0, 119.8, 118.8, 110.6, 80.4, 67.7, 33.0, 31.7, 25.8, 18.9, 18.8, 12.2; IR 3480 (w), 3361 (w), 3058 (w), 3057 (w), 2940 (m), 2890 (m), 1723 (w), 1504 (w), 1462 (m), 1419 (w), 1382 (w), 1368 (w), 1336 (w), 1285 (w), 1235 (w), 1151 (w), 1126 (w), 1092 (w), 1016 (w), 1016 (w), 996 (w), 909 (m), 884 (m), 801 (w), 740 (s), 679 (m), 672 (m), 660 (m), 648 (m); Melting point: 121.7 – 124.8°C; HRMS (ESI) calcd for $C_{22}H_{36}NOSi^+$ $[M+H]^+$ 358.2561; found 358.2557.

2-Phenyl-5-(prop-2-ynyl)tetrahydrofuran (10)

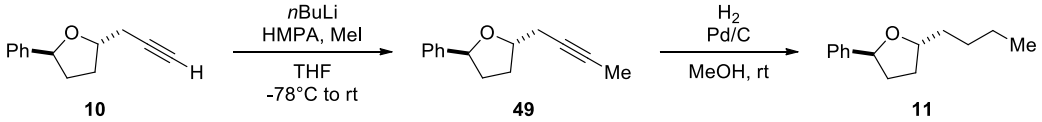


7e **10**

TBAF (1.0 M in THF, 2.6 mL, 2.6 mmol, 2.0 equiv) was added dropwise to a solution of tetrahydrofuran **7e** (431 mg, 1.26 mmol, 1.0 equiv) in THF (5.8 mL) at 0°C. The resulting mixture was stirred at 0°C for 2 h and at further rt for 1 h. The reaction was then quenched by addition of aqueous NH_4Cl (saturated solution, 7 mL). The two layers were separated and the aqueous one was extracted with Et_2O (4 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 98/2) afforded compound **10** (202 mg, 1.09 mmol, 86% yield) as a yellow oil.

R_f 0.59 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.39-7.32 (m, 4 H, *Ph*), 7.28 (m, 1 H, *Ph*), 5.11 (m, 1 H, O*CH*Ph), 4.43 (m, 1 H, O*CH*CH_2C≡C), 2.61 (ddd, 1 H, *J* = 16.6, 5.0, 2.7 Hz, *CH*$_2$C≡C), 2.52 (ddd, 1 H, *J* = 16.6, 6.9, 2.7 Hz, *CH*$_2$C≡C), 2.43 (m, 1 H, PhCH*CH*$_2$), 2.26 (m, 1 H, PhCH*CH*$_2$), 2.05 (t, 1 H, *J* = 2.7 Hz, C≡*CH*), 2.02-1.86 (m, 2 H, PhCHCH_2*CH*$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.2, 128.3, 127.2, 125.5, 81.1, 81.0, 77.6, 69.8, 35.1, 31.4, 25.6; IR 3298 (w), 3032 (w), 3028 (w), 2973 (w), 2938 (w), 2909 (w), 2873 (w), 2362 (w), 1493 (w), 1452 (w), 1435 (w), 1428 (w), 1420 (w), 1360 (w), 1343 (w), 1333 (w), 1332 (w), 1290 (w), 1217 (w), 1181 (w), 1083 (m), 1060 (s), 1029 (w), 1002 (w), 970 (w), 943 (w), 912 (w), 881 (w), 867 (w), 828 (w), 753 (m), 740 (m), 733 (m), 720 (m), 701 (s), 673 (s), 653 (s), 642 (s), 633 (s), 621 (s), 607 (m); HRMS (ESI) calcd for $C_{13}H_{15}O^+$ $[M+H]^+$ 187.1117; found 187.1113.

2-Butyl-5-phenyltetrahydrofuran (11)



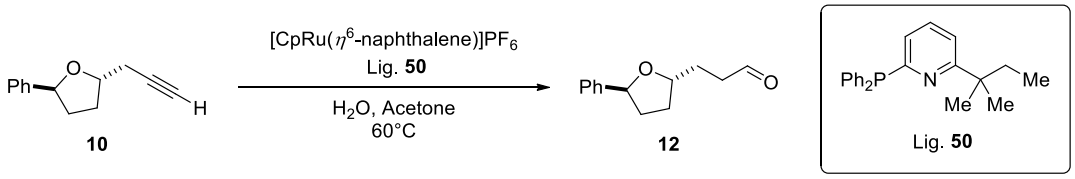
Following a reported procedure,[31] *n*BuLi (2.5 M in hexanes, 0.15 mL, 0.38 mmol, 1.09 equiv) was added dropwise to a solution of phenyl propargyl tetrahydrofuran **10** (65 mg, 0.35 mmol, 1.00 equiv) in THF (0.8 mL) at -78°C. The resulting mixture was stirred at -78°C for 45 min, then at 0°C for 5 min and cooled back to -78°C before adding methyl iodide (110 μL, 1.75 mmol, 5.00 equiv) and HMPA (70 μL, 0.40 mmol, 1.13 equiv). The mixture was stirred at -78°C for additional 40 min and then at rt overnight. The reaction was then diluted with Et_2O (5 mL) and quenched by addition of water (5 mL). The two layers were separated and the aqueous one was extracted with Et_2O (4 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 99/1 to 98/2) afforded alkyne **49** (43.1 mg, 0.215 mmol, 62% yield) as colorless oil.

Alkyne **49** (37 mg, 0.18 mmol) was dissolved in MeOH (2 mL) and palladium on charcoal (40 mg) was added. The mixture was stirred under an H_2 atmosphere at rt for 6 hours and it was then filtered through a Celite pad (which was washed several times with MeOH and DCM). The solvent was removed *in vacuo* and the crude product was purified by column chromatography (SiO_2, pentane/EtOAc 99/1 to 98/2) to afford butyl phenyl tetrahydrofuran **11** (27.2 mg, 0.133 mmol, 72% yield) as a colorless oil.

R_f 0.51 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.40-7.29 (m, 4 H, *Ph*), 7.25 (m, 1 H, *Ph*), 5.00 (dd, 1 H, *J* = 8.0, 6.5 Hz, Ph*CH*O), 4.19 (ddd, 1 H, *J* = 14.1, 8.0, 6.0 Hz, Bu*CH*O), 2.37 (m, 1 H, PhCH*CH*$_2$), 2.13 (m, 1 H, PhCH*CH*$_2$), 1.86 (m, 1 H, PhCHCH$_2$*CH*$_2$), 1.77-1.58 (m, 2 H, PhCHCH$_2$*CH*$_2$ and *Bu*), 1.58-1.27 (m, 5 H, *Bu*), 0.93 (t, 4 H, *J* = 6.8 Hz, *CH*$_3$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.0, 128.2, 127.0, 125.6, 80.1, 80.1, 35.9, 35.4, 32.4, 28.4, 22.8, 14.1; IR 3064 (w), 3029 (w), 3029 (w), 2960 (m), 2930 (m), 2888 (w), 2872 (m), 2859 (m), 2363 (w), 1716 (w), 1493 (w), 1493 (w), 1465 (w), 1453 (w), 1379 (w), 1379 (w), 1368 (w), 1368 (w), 1363 (w), 1363 (w), 1362 (w), 1362 (w), 1361 (w), 1361 (w), 1329 (w), 1329 (w), 1215 (w), 1092 (m), 1088 (m), 1051 (m), 1029 (m), 957 (w), 957 (w), 937 (w), 937 (w), 910 (w), 910 (w), 877 (w), 877 (w), 753 (m), 699 (s), 682 (w), 668 (w), 654 (w), 653 (w), 642 (w), 630 (w), 619 (w). The ^{1}H NMR and ^{13}C NMR values for the characterization for **11** correspond to the ones reported in literature.[32]

3-(5-Phenyltetrahydrofuran-2-yl)propanal (12)

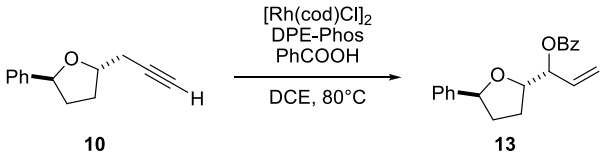
(31) Schweizer, S.; Tokan, W. M.; Parsons, P. J.; de Meijere, A. *Eur. J. Org. Chem.* ***2010***, 4687.
(32) Shi, H.; Liu, H.; Bloch, R.; Mandville, G. *Tetrahedron* **2001**, *57*, 9335.



Following a reported procedure,[33] [CpRu(η^6-naphthalene)]PF_6 (13 mg, 0.030 mmol, 0.1 equiv) and ligand **50** (20 mg, 0.06 mmol, 0.2 equiv) were stirred in previously degassed CH_3CN (1.8 mL) at 60°C for 6 hours. Passed this time, the solvent was removed by distillation under reduced pressure to afford a yellow resinous solid. A solution of tetrahydrofuran **10** (56 mg, 0.30 mmol, 1.0 equiv) in acetone (0.8 mL) was prepared. Water (162 μL, 9.00 mmol, 30 equiv) was added and the resulting solution was degassed and added to the previously prepared solid. The mixture was then stirred at 55°C for 12 h, before the solvent was removed *in vacuo*. The resulting crude oil was purified by column chromatography (SiO_2, pentane/EtOAc 95/5 to 90/10) to afford aldehyde **12** (59.5 mg, 0.291 mmol, 87% yield) as a colorless oil.

R_f 0.35 (Hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 9.81 (t, 1 H, *J* = 1.6 Hz, *HC*=O), 7.38-7.28 (m, 4 H, *Ph*), 7.25 (m, 1 H, *Ph*), 4.96 (dd, 1 H, *J* = 8.1, 6.4 Hz, Ph*CH*O), 4.24 (m, 1 H, O*CH*CH_2), 2.62 (m, 2 H, *CH*$_2$CHO), 2.37 (m, 1 H, PhCH*CH*$_2$), 2.15 (m, 1 H, PhCH*CH*$_2$), 2.00-1.80 (m, 3 H, *CH*$_2$$CH_2$CHO and PhCHCH$_2$*CH*$_2$), 1.68 (m, 1 H, PhCHCH$_2$*CH*$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 202.2, 143.4, 128.3, 127.1, 125.5, 80.2, 78.7, 40.7, 35.2, 32.0, 28.3; IR 3063 (w), 3029 (w), 2962 (w), 2937 (w), 2872 (w), 2725 (w), 1722 (s), 1604 (w), 1493 (w), 1452 (w), 1412 (w), 1390 (w), 1353 (w), 1342 (w), 1335 (w), 1307 (w), 1306 (w), 1215 (w), 1186 (w), 1107 (w), 1082 (m), 1069 (m), 1027 (m), 993 (w), 987 (w), 975 (w), 953 (w), 912 (m), 878 (w), 756 (m), 733 (s), 701 (s), 676 (w), 667 (w), 648 (w), 623 (w); HRMS (ESI) calcd for $C_{13}H_{17}O_2^+$ $[M+H]^+$ 205.1223; found 205.1222.

1-(5-Phenyltetrahydrofuran-2-yl)allyl benzoate (13)



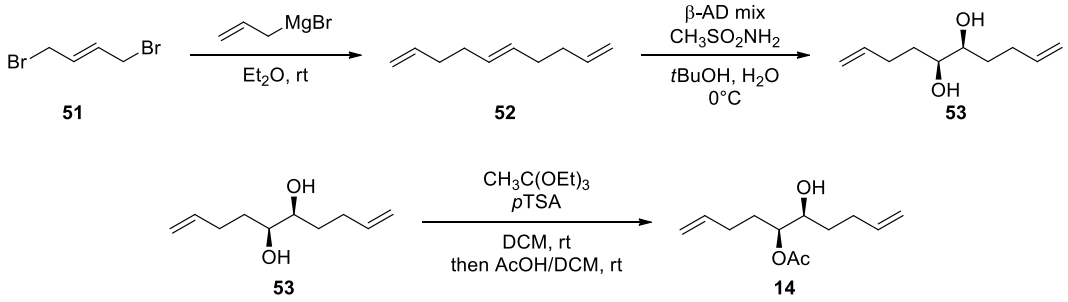
Following a reported procedure,[34] $[Rh(cod)Cl]_2$ (8.0 mg, 0.016 mmol, 0.05 equiv), DPE-Phos (17.3 mg, 0.0322 mmol, 0.10 equiv) and benzoic acid (59 mg, 0.48 mmol, 1.5 equiv) were introduced into a vial, which was then sealed. Alkyne **10** (60 mg, 0.32 mmol, 1.0 equiv) was added, followed by DCE (freshly distilled on CaH_2 and degassed, 3.2 mL). The resulting mixture was stirred at 80°C for 17 h. It was then allowed to cool down to rt and filtered through a short plug of silica gel, which was then washed several times with DCM. After removal of the solvent by distillation under reduced pressure, the crude product was purified by column

(33) Labonne, A. l.; Kribber, T.; Hintermann, L. *Org. Lett.*, **2006**, *8*, 5853.
(34) Lumbroso, A.; Koschker, P.; Vautravers, N. R.; Breit, B. *J. Am. Chem. Soc.*, **2011**, *133*, 2386.

chromatography (SiO_2, pentane/EtOAc 98/2 to 95/5) to afford the pure compound **13** (34 mg, 0.11 mmol, 34% yield, mixture of inseparable diastereoisomers, d.r.: 73:27) as a pale yellow oil.

R_f 0.48 (pentane/EtOAc 20/1.5); ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (m, 2 H, *Ph*CO, both diaster.), 7.58 (m, 1 H, *Ph*CO, both diaster.), 7.47 (m, 2 H, *Ph*CO, both diaster.), 7.41-7.15 (m, 5 H, CH*Ph*, both diaster.), 6.02 (ddd, *J* = 17.0, 10.5, 6.2 Hz, *CH*=CH_2), 6.01 (m, 1 H, *CH*=CH_2, *minor diaster.*), 5.68 (dd, 1 H, *J* = 5.8, 4.8 Hz, *CH*OBz), 5.65 (m, 1 H, *CH*OBz, *minor diaster.*), 5.48 (dt, *J* = 17.2, 1.5 Hz, CH=*CH_2*), 5.45 (dt, *J* = 17.4, 1.5 Hz, CH=*CH_2*, *minor diaster.*), 5.35 (d, 1 H, *J* = 10.6 Hz, CH=*CH_2*, both diaster.), 5.09 (dd, *J* = 8.1, 6.5 Hz, Ph*CH*O, *minor diaster.*), 5.05 (dd, 1 H, *J* = 8.1, 6.2 Hz, Ph*CH*O), 4.43-4.55 (m, 1 H, O*CH*CHOBz, *minor diaster.*), 4.49 (ddd, 1 H, *J* = 7.1, 7.1, 4.8 Hz, O*CH*CHOBz), 2.44 (m, 1 H, CH_2CH_2, both diaster.), 2.29-1.99 (m, 2 H, CH_2CH_2, both diaster.), 1.95 (m, 1 H, CH_2CH_2, both diaster.); ^{3}C NMR (101 MHz, $CDCl_3$; some peaks are not resolved) δ 165.8, 165.6, 142.8, 133.2, 133.1, 133.0, 133.0, 130.3, 129.9, 129.7, 129.6, 128.4, 128.3, 128.3, 127.2, 125.6, 125.5, 118.5, 81.6, 81.1, 80.6, 80.1, 77.1, 76.7, 35.0, 28.1, 27.8; IR 3087 (w), 3063 (w), 3030 (w), 3009 (w), 2972 (w), 2945 (w), 2906 (w), 2874 (w), 1720 (s), 1602 (w), 1585 (w), 1585 (w), 1493 (w), 1452 (m), 1337 (w), 1315 (w), 1268 (s), 1177 (w), 1111 (m), 1097 (m), 1061 (m), 1027 (m), 991 (w), 991 (w), 957 (w), 935 (m), 883 (w), 883 (w), 805 (w), 756 (m), 710 (s), 700 (s), 674 (w), 668 (w), 649 (w), 632 (w); HRMS (ESI) calcd for $C_{20}H_{21}O_3^+$ $[M+H]^+$ 309.1485; found 309.1490.

6-Hydroxydeca-1,9-dien-5-yl acetate (14)



Following a reported procedure,[35] a solution of *trans*-1,4-dibromobutene (**51**) (2.99 g, 14.0 mmol, 1.0 equiv) in Et_2O (5 mL) was added dropwise to an solution of allyl magnesium bromide (1.0 M in Et_2O, 45 mL, 45 mmol, 3.2 equiv) at 0°. The resulting mixture was stirred overnight, allowing the temperature to increase to 22°C. The reaction was then quenched by addition of aqueous acetic acid (10.5 M, 1.55 mL) at 0°C. The mixture was poured onto ice (ca. 70 g). The two layers were separated and the aqueous one was extracted with Et_2O (3 x 50 mL). The combined organic layers were washed with aqueous $NaHCO_3$ (10% w/w, 2 x 50 mL) and brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. The crude product was purified by filtration through a short silica plug (elution with pentane) to afford triene **52** (1.505 g, 11.07 mmol, 79% yield) as a colorless oil.

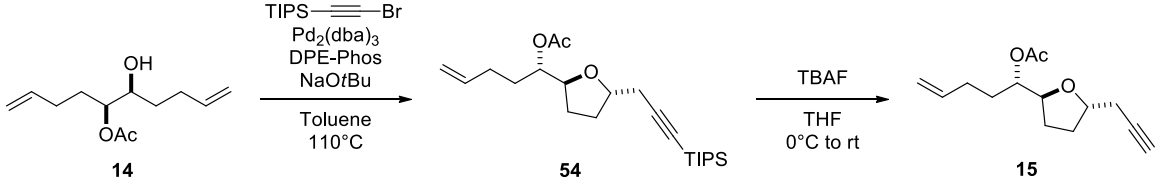
(35) Braddock, D. C.; Cansell, G.; Hermitage, S. A.; White, A. J. P. *Tetrahedron: Asymmetry* **2004**, *15*, 3123.

Following a reported procedure,[34] triene **52** (1.50 g, 11.0 mmol, 1.0 equiv) was added to a suspension of Admix β (15.4 g: $(DHQD)_2Phal$, 0.105 mmoles (0.0095 equiv); K_2CO_3, 32.7 mmoles (3.0 equiv); $K_3Fe(CN)_6$, 32.7 mmoles (3.0 equiv); K_2OsO_4 H_2O, 0.0459 mmoles (0.0042 equiv)) and methanesulfonamide (1.05 g, 11.1 mmol, 1.01 equiv) in a solution of *tert*-butanol and water (54 mL/54 mL).The resulting mixture was stirred at 0°C for 7 h and then the reaction was quenched by the addition of Na_2SO_3 (ca. 15 g) and allowed to warm to rt. The aqueous layer was extracted with EtOAc (4 x 50 mL) and the combined organic layers were washed with brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 75/25 to 40/60) afforded diol **53** (0.782 g, 4.60 mmol, 41% yield) as colorless oil.

Following a reported procedure,[36] triethyl orthoacetate (1.8 mL, 9.7 mmol, 3.0 equiv) and *p*-TSA (62 mg, 0.32 mmol, 0.1 equiv) were added to a solution of diol **53** (0.553 g, 3.25 mmol, 1.0 equiv) in DCM (6.5 mL). The mixture was stirred at rt overnight and then the solvent was removed by distillation under reduced pressure. The residue was taken up in DCM (4.4 mL) and treated with aqueous acetic acid (80% v/v, 2.4 mL) for 1.5 h. The two layers were then separated and the aqueous one was extracted with DCM (2 x 5 mL). The combined organic layers were washed with aqueous $NaHCO_3$ (saturated solution, 5 mL), water and brine, dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, pentane/EtOAc 90/10 to 80/20) afforded compound **14** (0.634 g, 2.99 mmol, 92% yield) as colorless oil.

R_f 0.56 (hexane/EtOAc 17/7); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.80 (m, 2 H, *CH*=CH_2), 5.08-4.94 (m, 4 H, CH=*CH*$_2$), 4.86 (ddd, 1 H, *J* = 7.6, 6.2, 4.0 Hz, *CH*OAc), 3.62 (ddd, 1 H, *J* = 12.2, 8.2, 4.2 Hz, *CH*OH), 2.29-2.01 (m, 4 H, *CH*$_2$CH=CH_2), 2.09 (s, 3 H, *Ac*), 1.73 (m, 2 H, *CH*$_2$$CH_2$CH=$CH_2$), 1.50 (m, 2 H, *CH*$_2$$CH_2$CH=$CH_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 138.0, 137.5, 115.2, 115.2, 75.9, 71.8, 32.8, 29.8, 29.8, 29.6, 21.0; IR 3384 (w), 3076 (w), 2937 (w), 2854 (w), 1737 (s), 1721 (s), 1642 (w), 1450 (w), 1417 (w), 1374 (m), 1239 (s), 1028 (m), 999 (w), 912 (s), 673 (w), 637 (w), 630 (w); $[\alpha]_D^{20}$= +18.8°. The values for the characterization for **14** correspond to the ones reported in the literature.[35]

1-(5-(Prop-2-ynyl)tetrahydrofuran-2-yl)pent-4-enyl acetate (15)



Under inert atmosphere $Pd_2(dba)_3$ (172 mg, 0.187 mmol, 0.085 equiv), DPE-Phos (202 mg, 0.187 mmol, 0.17 equiv) and NaO*t*Bu (303 mg, 3.15 mmol, 1.43 equiv) were introduced into a

(36) Zhao, H. ; Gorman, J. T. ; Pagenkopf, B. L. *Org. Lett.* **2006**, *8*, 4379.

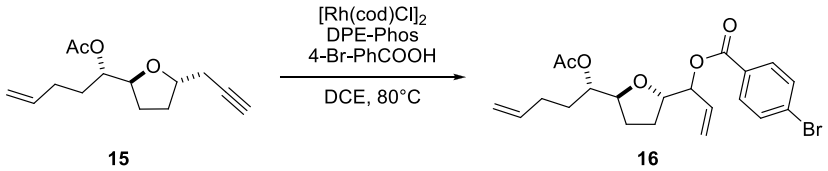
20 mL vial, which was then sealed. Toluene was added (21 mL), followed by bromo tri*iso*propylsilyl acetylene (**5a**) (3.15 g, 3.15 mmol, 1.43 equiv) and alcohol **14** (465 mg, 2.20 mmol, 1.00 equiv). The mixture was stirred at 75°C for 3 h and then allowed to cool to room temperature. The solvent was evaporated under reduced pressure. The crude mixture was then directly purified by column chromatography (SiO_2, pentane/EtOAc 98/2 to 95/5) to afford compound **54** (510 mg, 1.30 mmol, 59% yield) as a pale yellow oil.

R_f 0.79 (hexane/EtOAc 17/7); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (ddt, *J* = 16.8, 10.1, 6.5 Hz, *CH*=CH_2), 5.08-4.94 (m, 2 H, CH=*CH*$_2$), 4.89 (dt, 1 H, *J* = 8.6, 4.8 Hz, OCH*CH*O), 4.13 (ddd, 1 H, *J* = 13.7, 7.6, 4.5 Hz, O*CH*CH_2C≡C), 4.08 (td, 1 H, *J* = 7.2, 5.5 Hz, OCH*CH*O), 2.54 (dd, 1 H, *J* = 16.6, 4.3 Hz, *CH*$_2$C≡C), 2.40 (dd, 1 H, *J* = 16.6, 7.6 Hz, *CH*$_2$C≡C), 2.17-1.96 (m, 4 H, *CH*$_2$CH=CH_2 and *CH*$_2$*CH*$_2$), 2.08 (s, 3 H, *Ac*), 1.83 (m, 1 H, *CH*$_2$*CH*$_2$), 1.65 (m, 3 H, *CH*$_2$*CH*$_2$), 1.09-1.01 (m, 21 H, *TIPS*); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.8, 137.7, 115.0, 105.0, 82.0, 80.0, 77.5, 74.6, 31.0, 30.3, 29.6, 28.1, 26.7, 21.2, 18.6, 11.2; IR 2942 (m), 2895 (w), 2865 (m), 2364 (w), 2336 (w), 2174 (w), 1742 (s), 1643 (w), 1464 (w), 1373 (m), 1236 (s), 1072 (m), 1028 (m), 996 (m), 974 (w), 948 (w), 914 (m), 884 (m), 735 (m), 701 (w), 677 (s), 661 (m), 646 (w), 639 (w), 628 (w), 620 (w); HRMS (ESI) calcd for $C_{23}H_{41}O_3Si^+$ $[M+H]^+$ 393.2819; found 393.2811.

TBAF (1.0 M in THF, 2.3 mL, 2.3 mmol, 2.0 equiv) was added dropwise to a solution of tetrahydrofuran **54** (450 mg, 1.15 mmol, 1.0 equiv) in THF (5.2 mL) at 0°C. The resulting mixture was stirred at 0°C for 2 h and at further rt for 1 h. The reaction was then quenched by addition of aqueous NH_4Cl (saturated solution, 7 mL). The two layers were separated and the aqueous one was extracted with Et_2O (4 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and the solvent was removed *in vacuo*. Purification by column chromatography (SiO_2, hexane/EtOAc 96/4) afforded compound **15** (256 mg, 1.08 mmol, 94% yield) as a yellow oil.

R_f 0.39 (hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.79 (ddt, *J* = 16.9, 10.2, 6.6 Hz, *CH*=CH_2), 5.02 (m, 1 H, CH=*CH*$_2$), 4.97 (m, 1 H, CH=*CH*$_2$), 4.90 (dt, 1 H, *J* = 8.6, 4.8 Hz, OCH*CH*O), 4.18-4.04 (m, 2 H, O*CH*CH_2C≡C and OCH*CH*O), 2.47 (ddd, 1 H, *J* = 16.5, 4.6, 2.6 Hz, *CH*$_2$C≡C), 2.36 (ddd, 1 H, *J* = 16.5, 7.0, 2.6 Hz, *CH*$_2$C≡C), 2.18-1.98 (m, 4 H, *CH*$_2$CH=CH_2 and *CH*$_2$*CH*$_2$), 2.09 (s, 3 H, *Ac*), 1.96 (t, 1 H, *J* = 2.7 Hz, C≡*CH*), 1.84-1.58 (m, 4 H, *CH*$_2$$CH_2$CH=$CH_2$ and *CH*$_2$*CH*$_2$); ^{13}C NMR (101 MHz, $CDCl_3$) δ 170.7, 137.5, 115.0, 79.8, 77.0, 74.5, 69.7, 69.7, 30.9, 30.1, 29.6, 27.9, 25.0, 21.1; IR 3299 (w), 3290 (w), 3078 (w), 2976 (w), 2953 (w), 2918 (w), 2876 (w), 1736 (s), 1643 (w), 1464 (w), 1447 (w), 1437 (w), 1374 (w), 1239 (s), 1073 (m), 1030 (m), 1001 (w), 943 (w), 917 (w), 916 (w), 886 (w), 740 (w), 732 (w), 711 (w), 696 (w), 670 (s), 656 (m), 644 (m), 633 (w), 611 (w); $[\alpha]_D^{20}$= +25.1°; HRMS (ESI) calcd for $C_{14}H_{21}O_3^+$ $[M+H]^+$ 237.1485; found 237.1492.

1-(5-(1-Acetoxypent-4-enyl)tetrahydrofuran-2-yl)allyl 4-bromobenzoate (16)

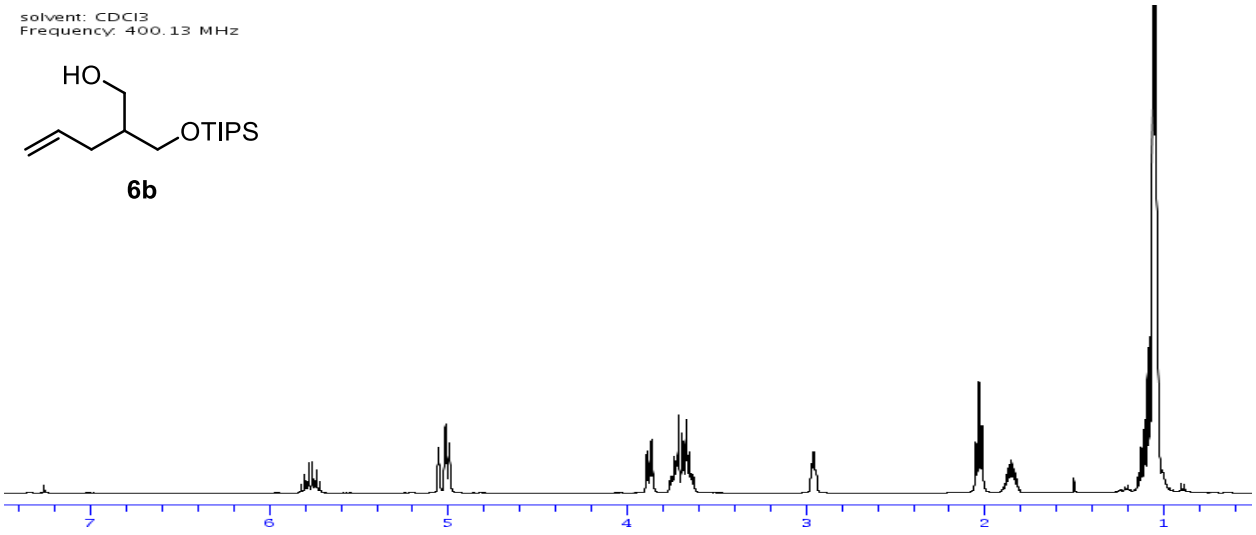


15 16

Following a reported procedure,[33] $[Rh(cod)Cl]_2$ (8.6 mg, 0.017 mmol, 0.07 equiv), DPE-Phos (18.8 mg, 0.0350 mmol, 0.14 equiv) and 4-bromobenzoic acid (75.4 mg, 0.375 mmol, 1.5 equiv) were introduced into a vial, which was then sealed. Alkyne **15** (59 mg, 0.25 mmol, 1.0 equiv) was added, followed by DCE (freshly distilled on CaH_2 and degassed, 2.5 mL). The resulting mixture was stirred at 80°C for 16 h. It was then allowed to cool down to rt and filtered through a short plug of silica gel, which was then washed several times with DCM. After removal of the solvent by distillation under reduced pressure, the crude product was purified by column chromatography (SiO_2, pentane/EtOAc 97/3 to 90/10) to afford the pure compound **16** (39.8 mg, 0.0.910 mmol, 36% yield, mixture of inseparable diastereoisomers, d.r.: 64:36) as a colorless oil.

R_f 0.33 (hexane/EtOAc 20/3); ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.91 (m, 2 H, *Ar*), 7.58 (m, 2 H, *Ar*), 5.99-5.85 (m, 1 H, OCH*CH*=CH_2, both diaster.), 5.86-5.73 (m, 1 H, CH_2*CH*=CH_2), 5.57 (ddt, 1 H, *J* = 7.5, 2.5, 1.5 Hz, O*CH*CH=CH_2), 5.49 (tt, 1 H, *J* = 6.0, 1.0 Hz, O*CH*CH=CH_2, *minor diaster.*), 5.46-5.28 (m, 2 H, OCHCH=*CH_2*, both diaster.), 5.06-4.95 (m, 2 H, CH_2CH=*CH_2*), 4.91 (ddd, 1 H, *J* = 13.8, 4.7, 4.7 Hz, O*CH*CHOAc, both diaster.), 4.29-4.18 (m, 1 H, O*CH*CHCH=CH_2, both diaster.), 4.05 (ddd, 1 H, *J* = 19.3, 6.8, 6.8 Hz, OCH*CH*OAc, both diaster.), 2.13-1.86 (m, 4 H, *CH_2*CH=CH_2 and CH_2CH_2, both diaster.), 2.07 (s, 3 H, *Ac*), 1.98 (s, 3 H, *Ac*, *minor diaster.*), 1.79-1.51 (m, 4 H, CH_2CH_2, both diaster.); ^{13}C NMR (101 MHz, CDCl3) δ 170.8, 164.8, 137.6, 132.9, 132.8, 131.8, 131.7, 131.7, 131.4, 131.2, 131.1, 129.2, 129.2, 128.1, 128.0, 118.9, 118.5, 115.1, 115.1, 80.4, 79.9, 79.8, 79.4, 76.9, 76.7, 74.3, 74.2, 30.1, 30.1, 29.6, 29.6, 28.0, 27.9, 27.8, 27.2, 21.1, 21.0; IR 3077 (w), 2973 (w), 2955 (w), 2927 (w), 2872 (w), 2858 (w), 2857 (w), 2358 (w), 1728 (s), 1727 (s), 1643 (w), 1591 (m), 1486 (w), 1464 (w), 1448 (w), 1398 (w), 1373 (w), 1269 (s), 1238 (s), 1174 (w), 1103 (m), 1069 (w), 1027 (w), 1012 (m), 994 (w), 921 (w), 848 (w), 757 (s), 726 (w), 708 (w), 684 (w), 673 (w), 660 (w), 652 (w), 643 (w), 633 (w), 619 (w), 604 (w); HRMS (ESI) calcd for $C_{21}{}^{79}BrH_{26}O_5^+$ $[M+H]^+$ 437.0958; found 437.0967.

8. Spectra of New Compounds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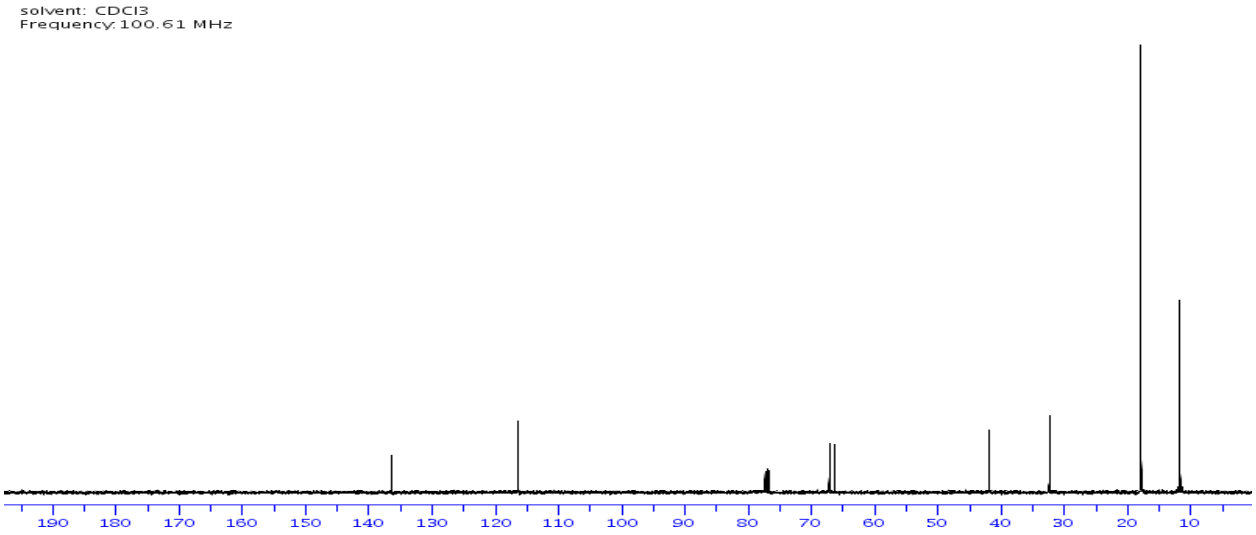
6b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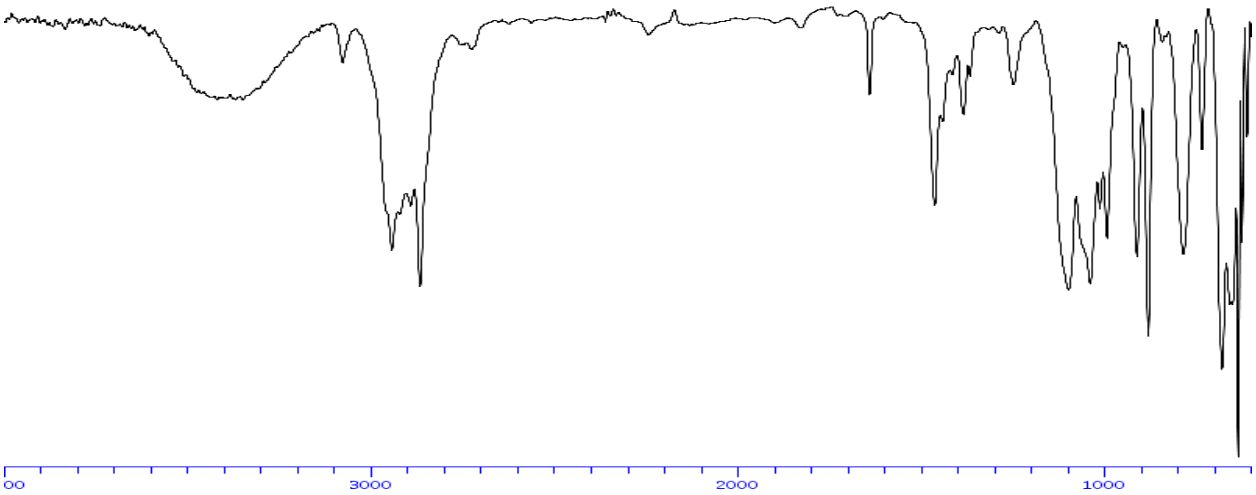
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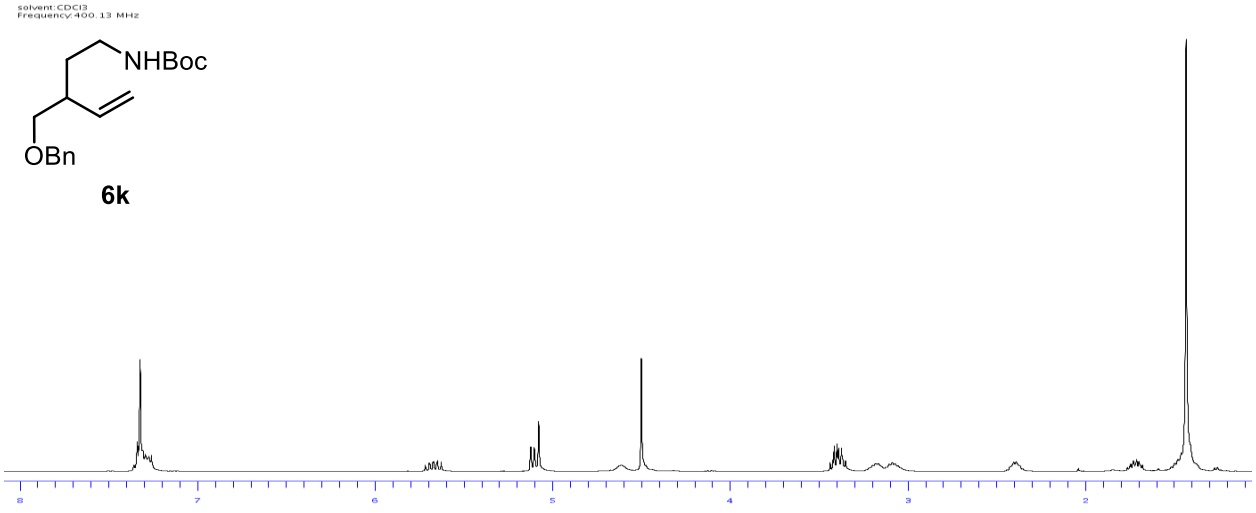
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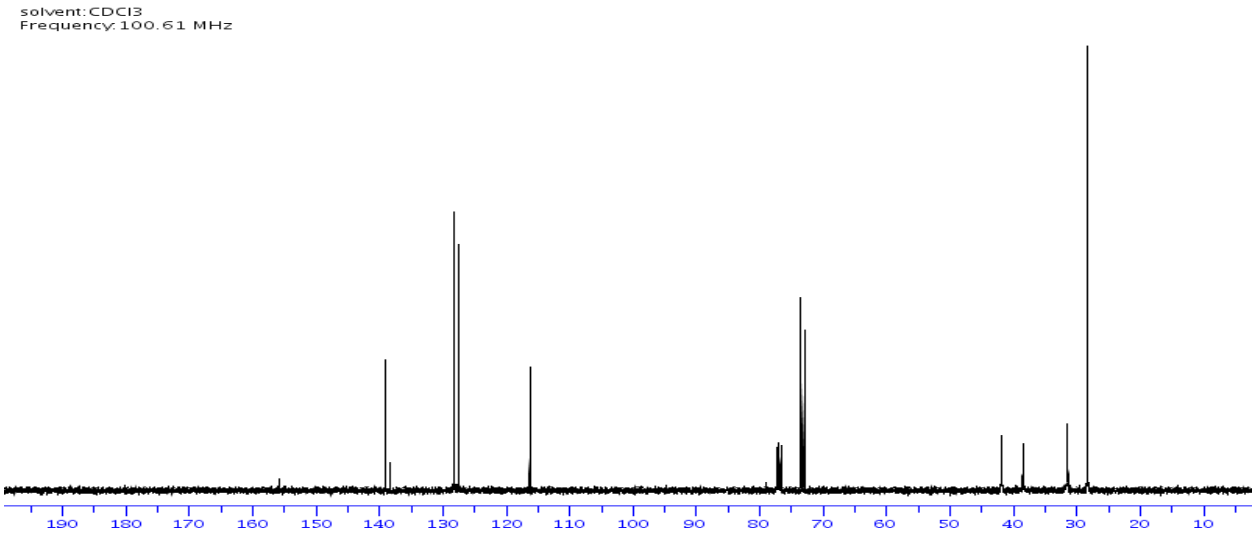
OBn
6k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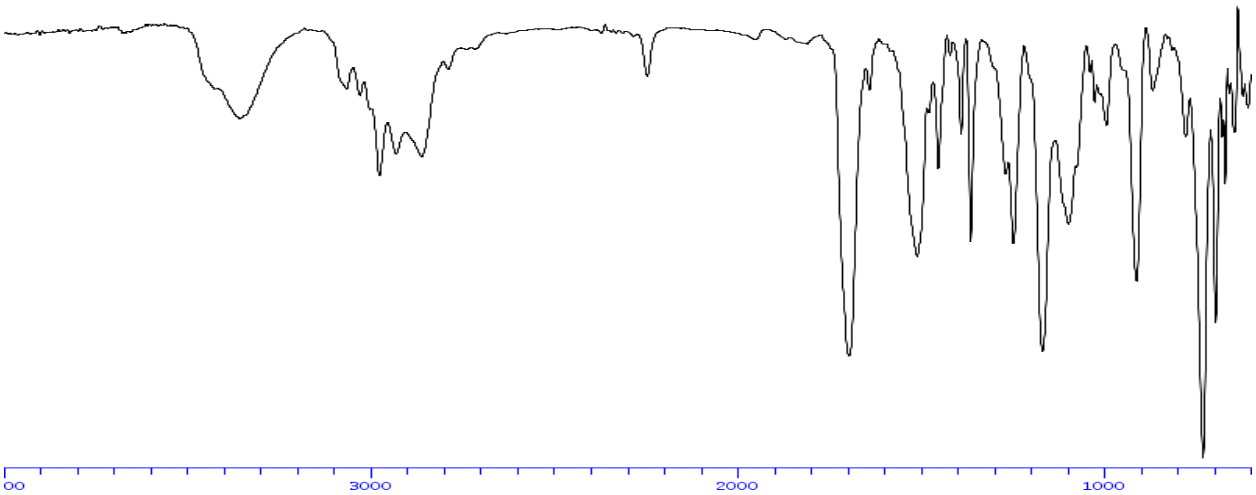

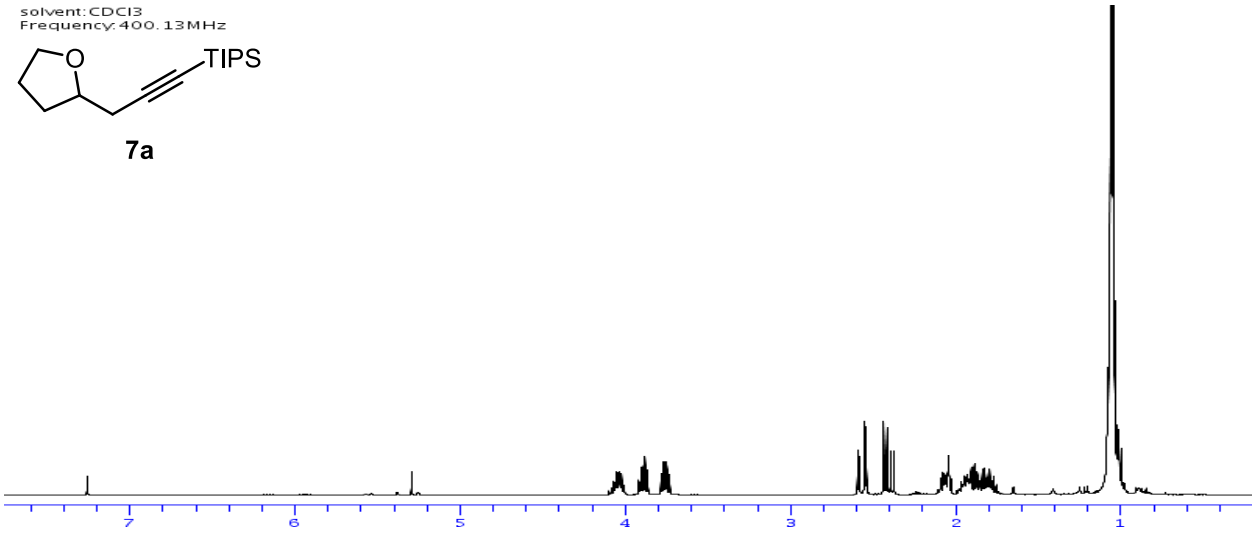
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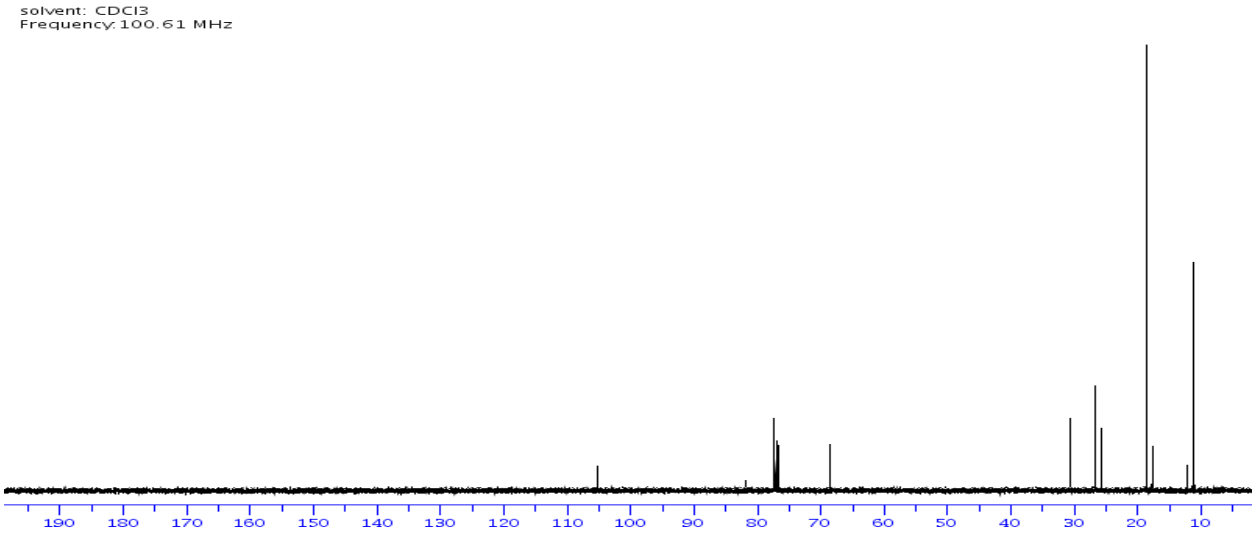
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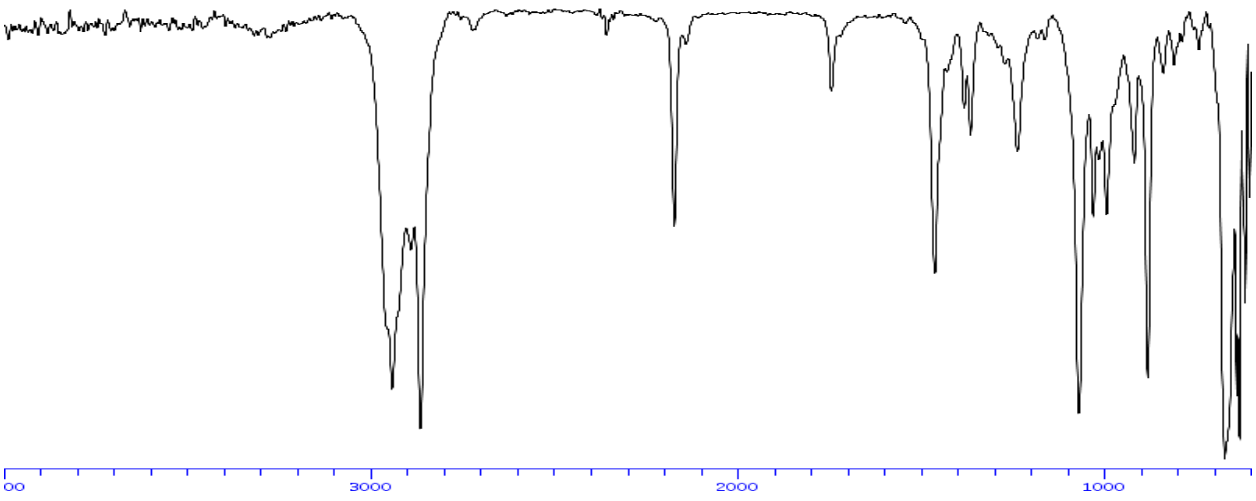
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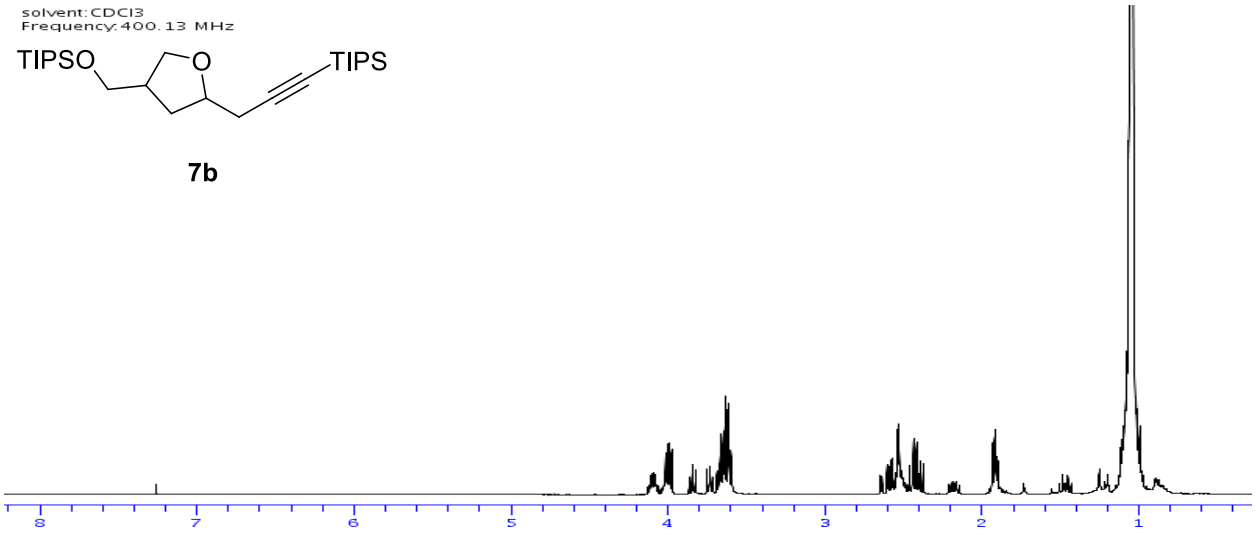
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TIPS
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3
2
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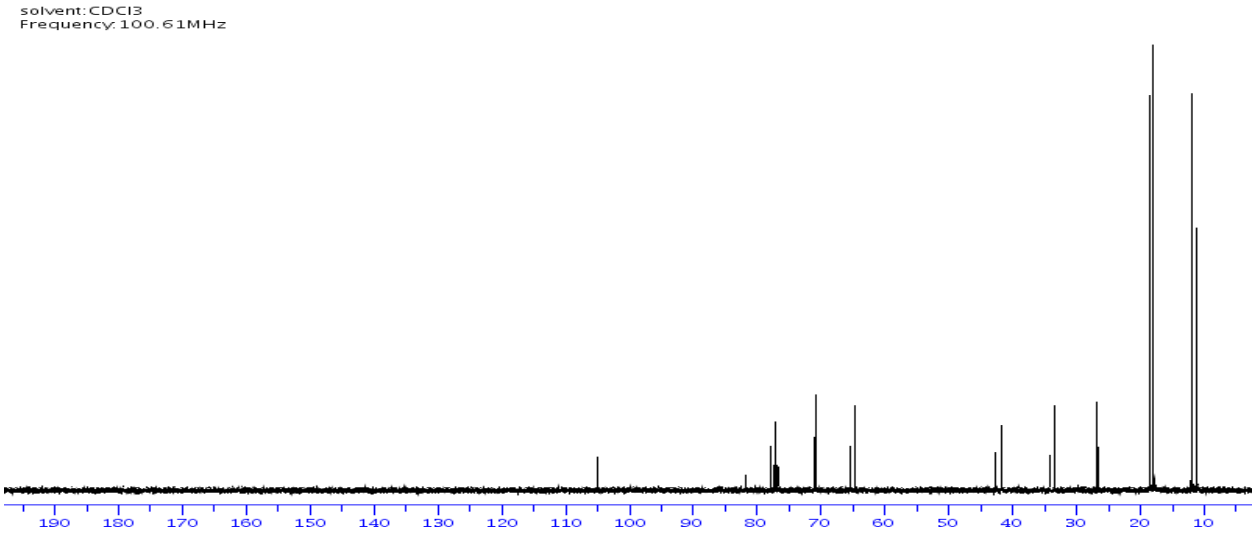
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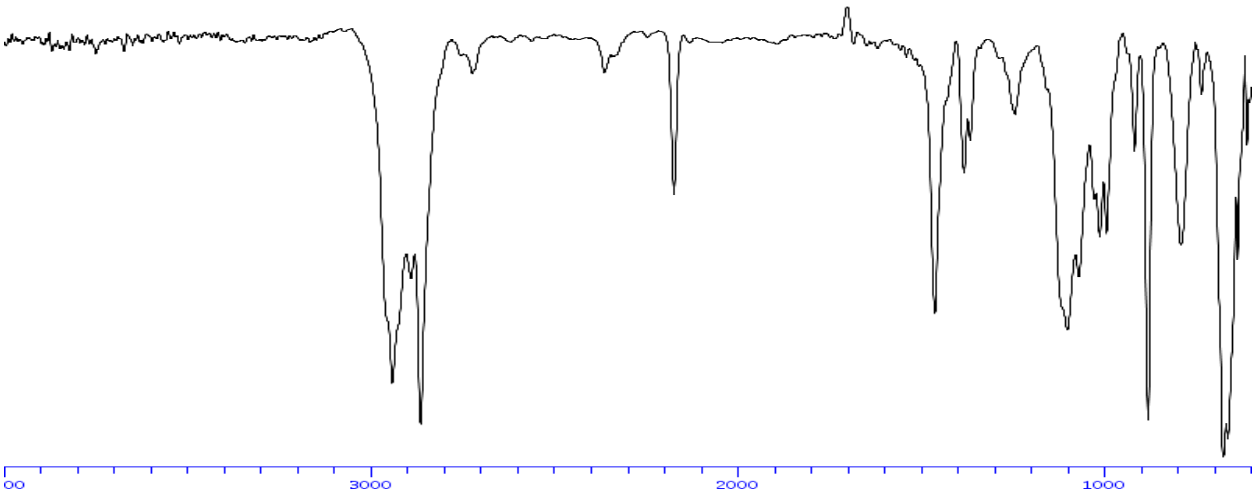
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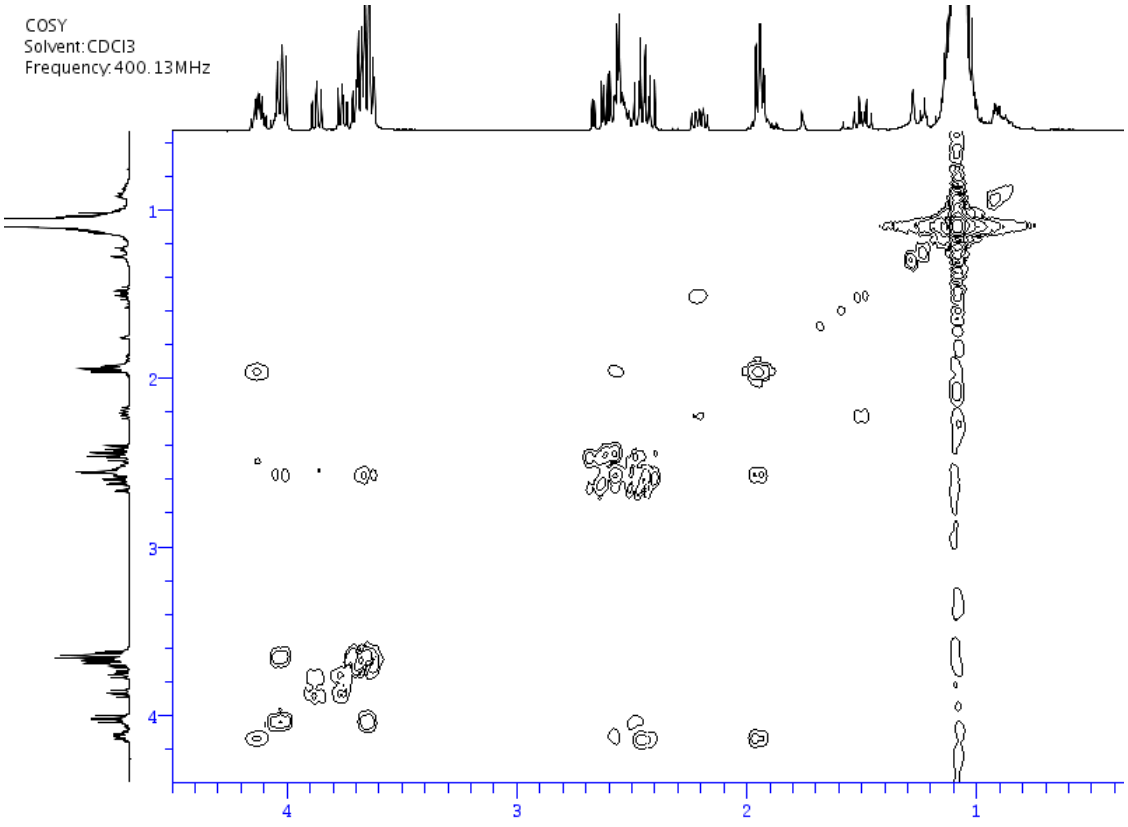
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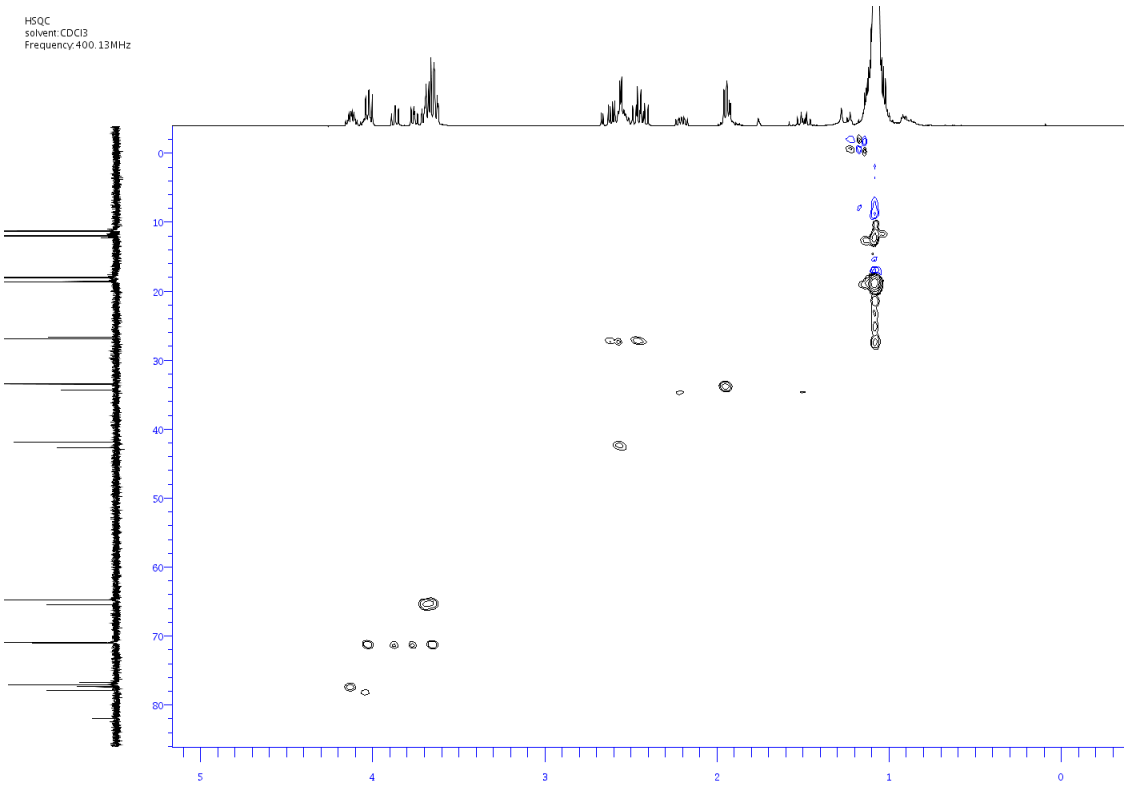
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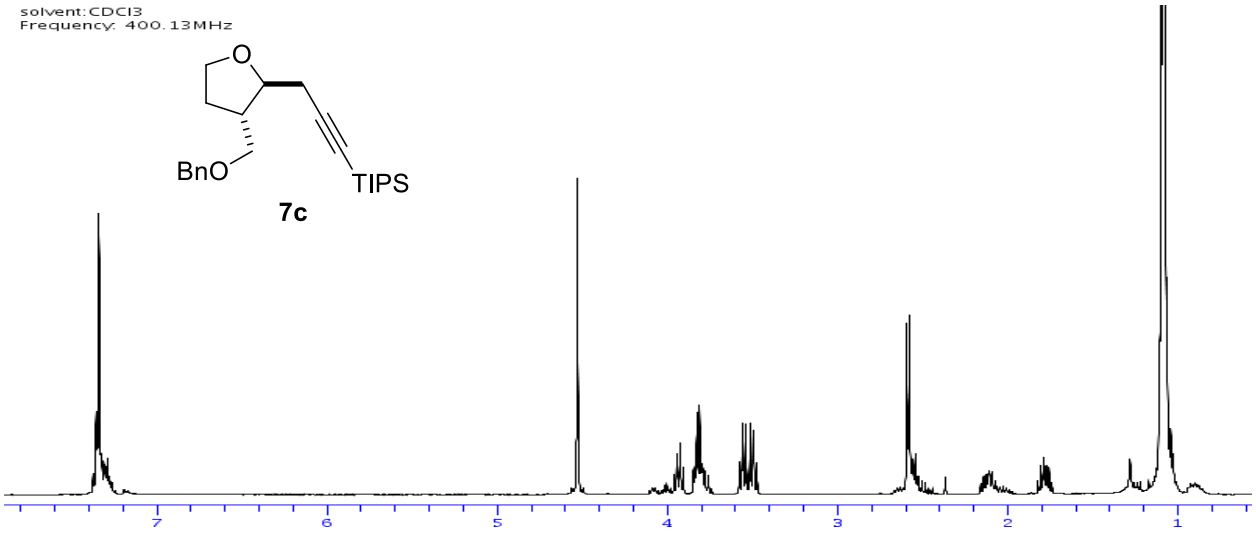
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BnO
TIPS
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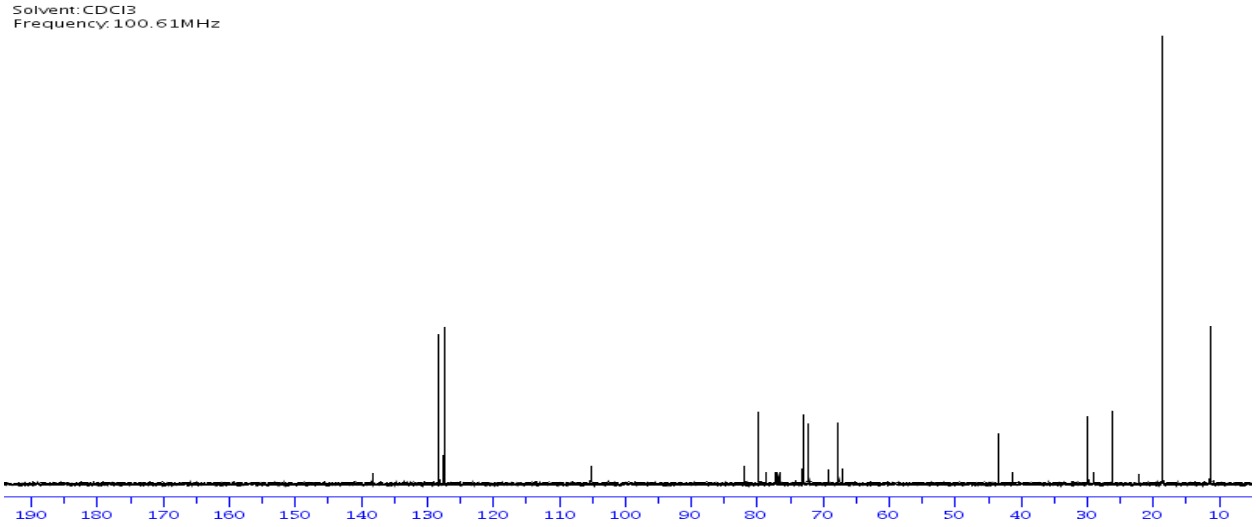
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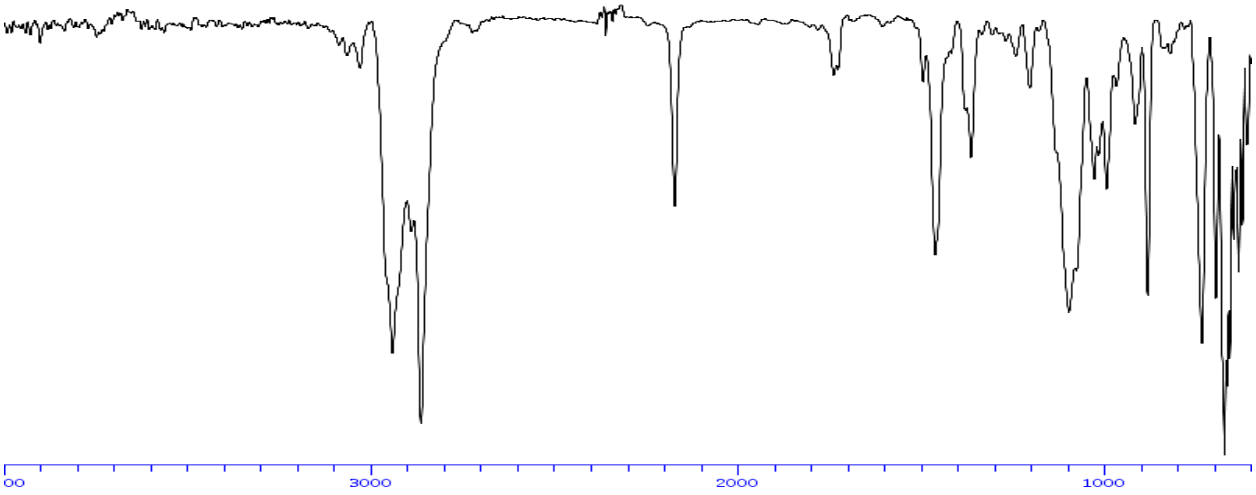
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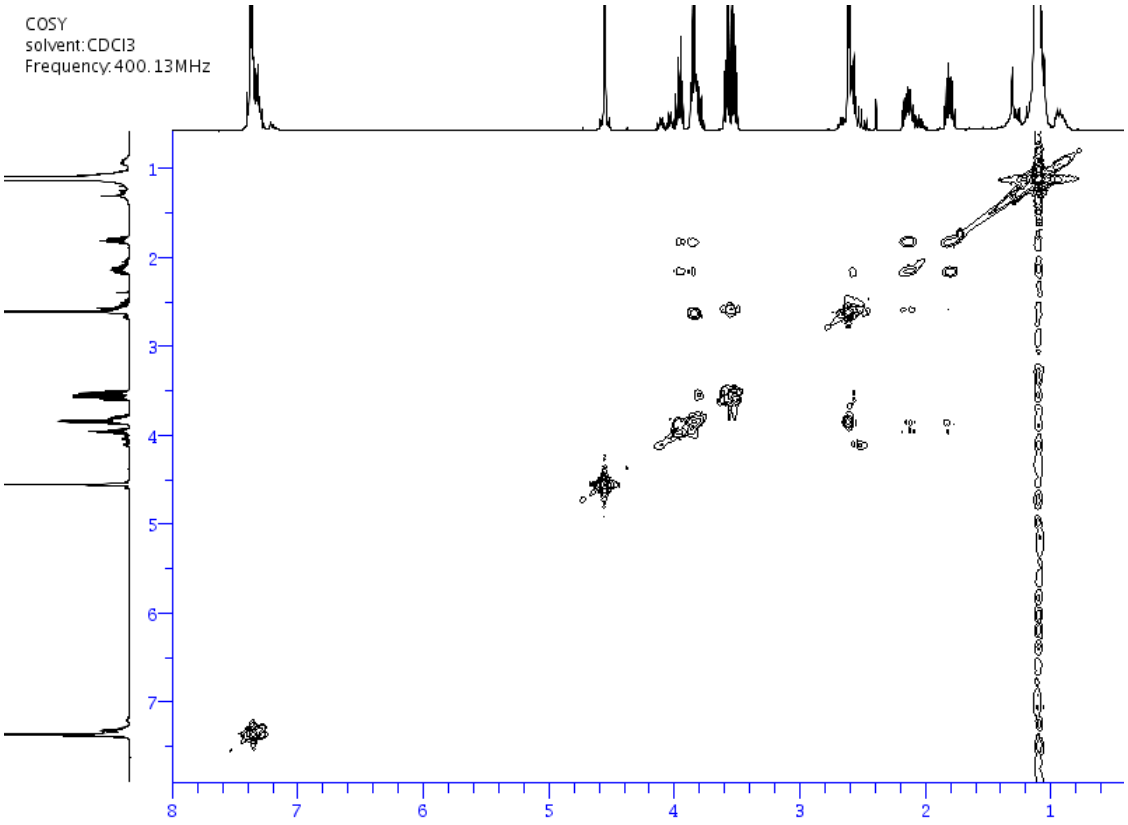
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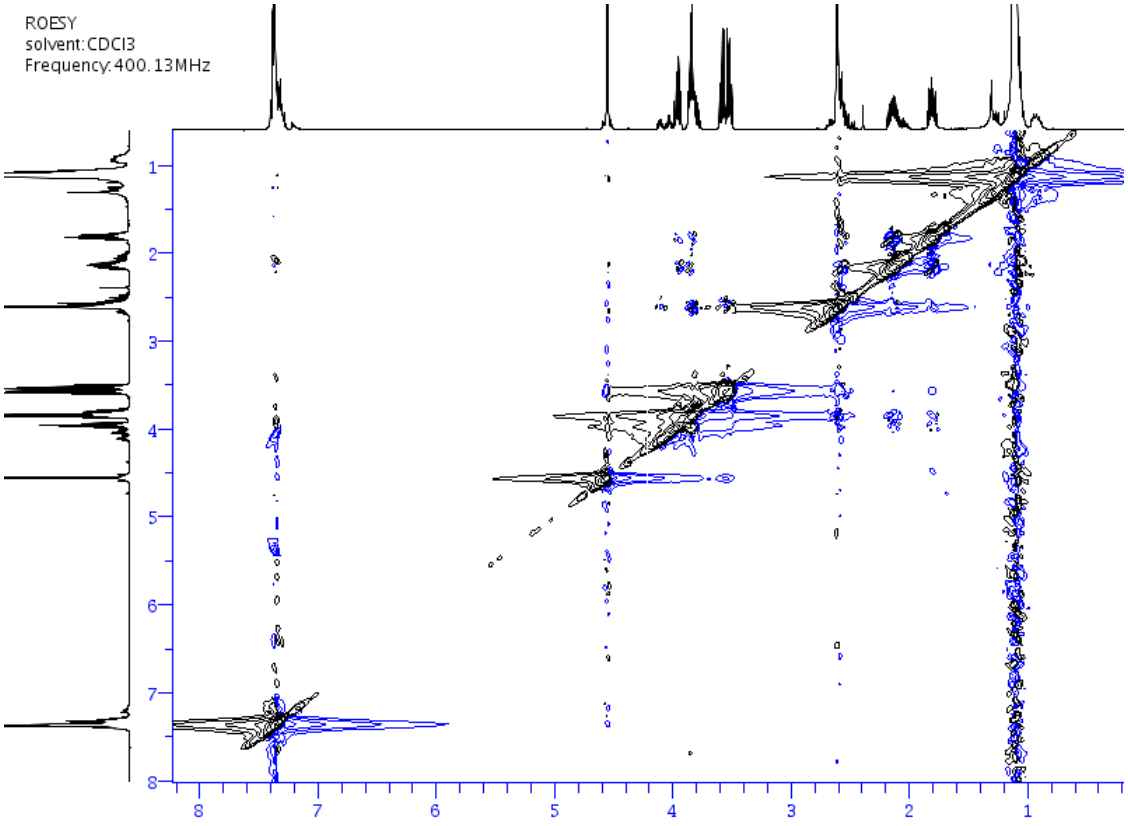
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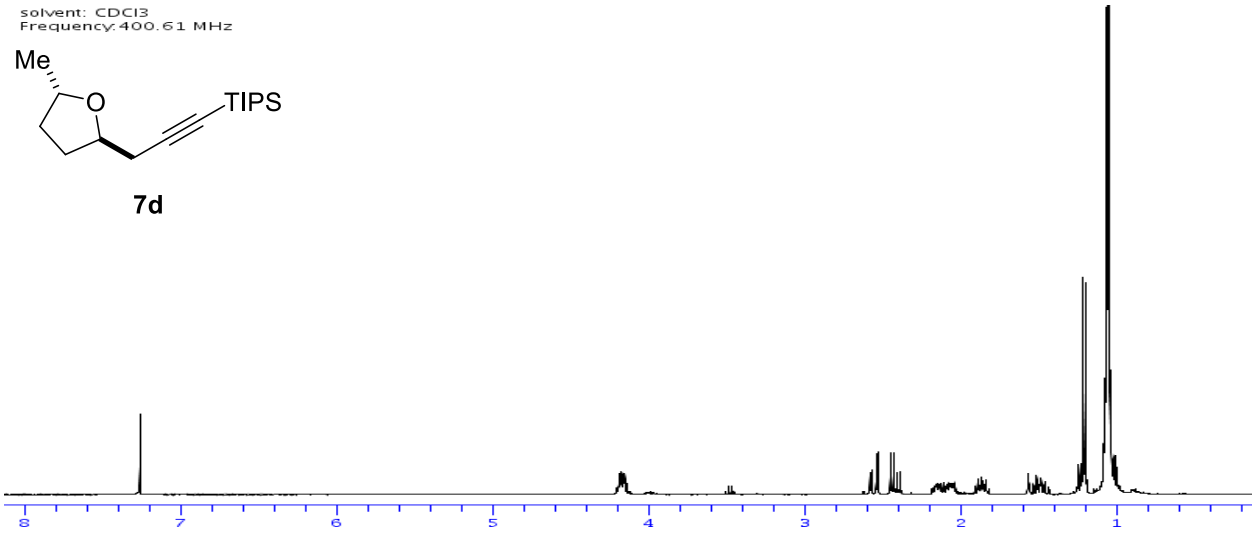
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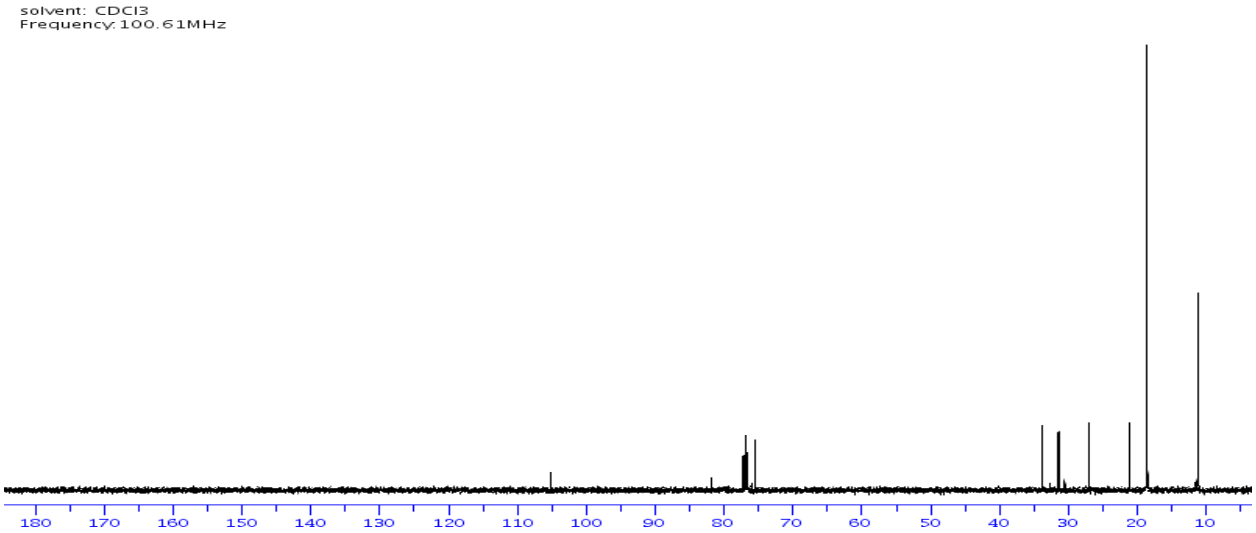
7d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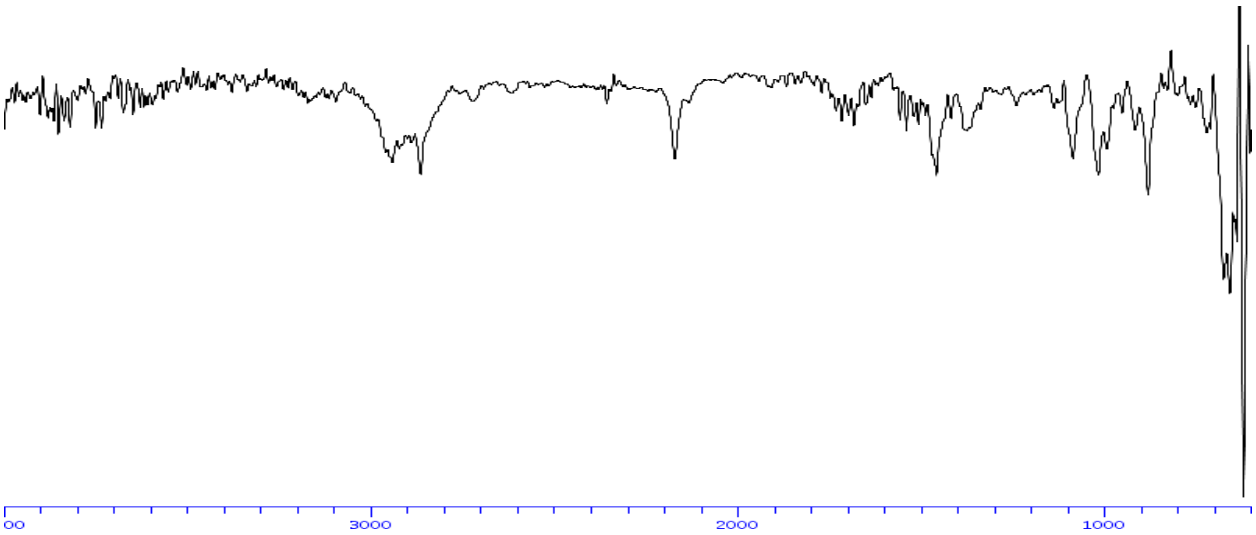
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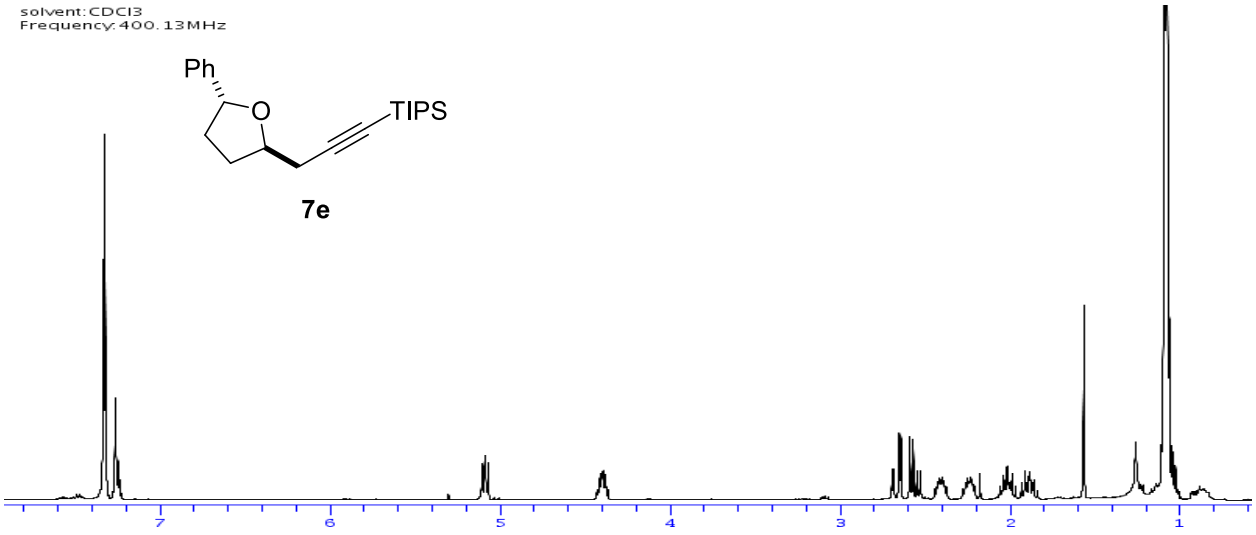
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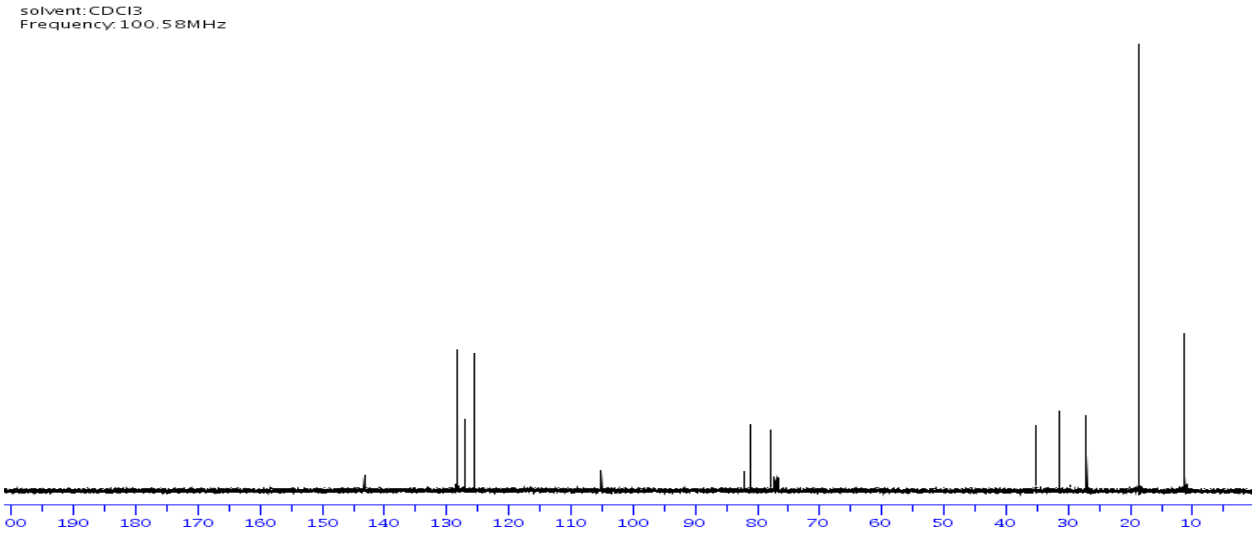
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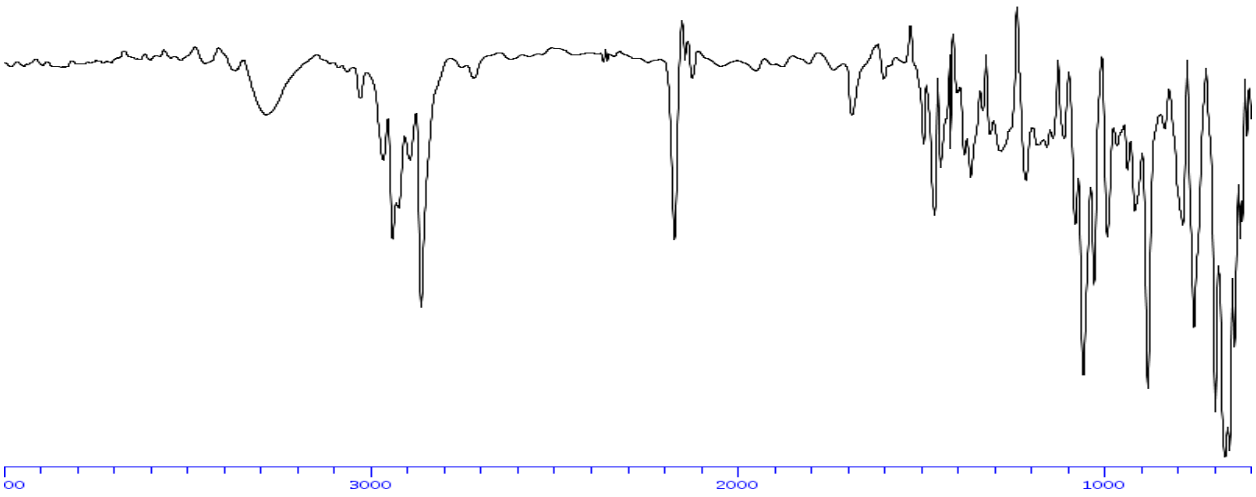
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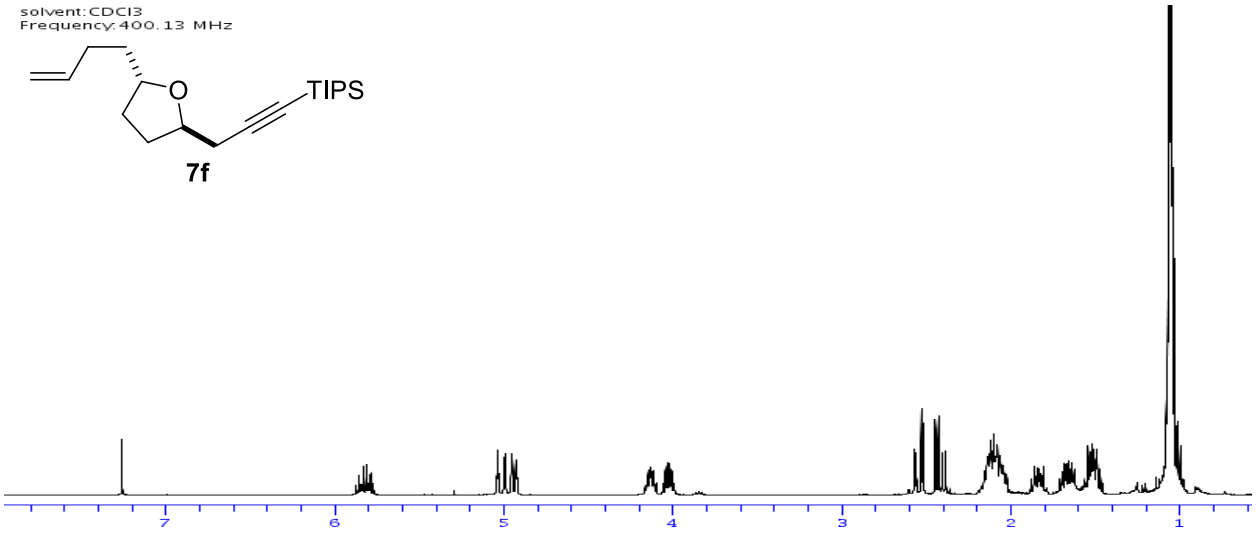
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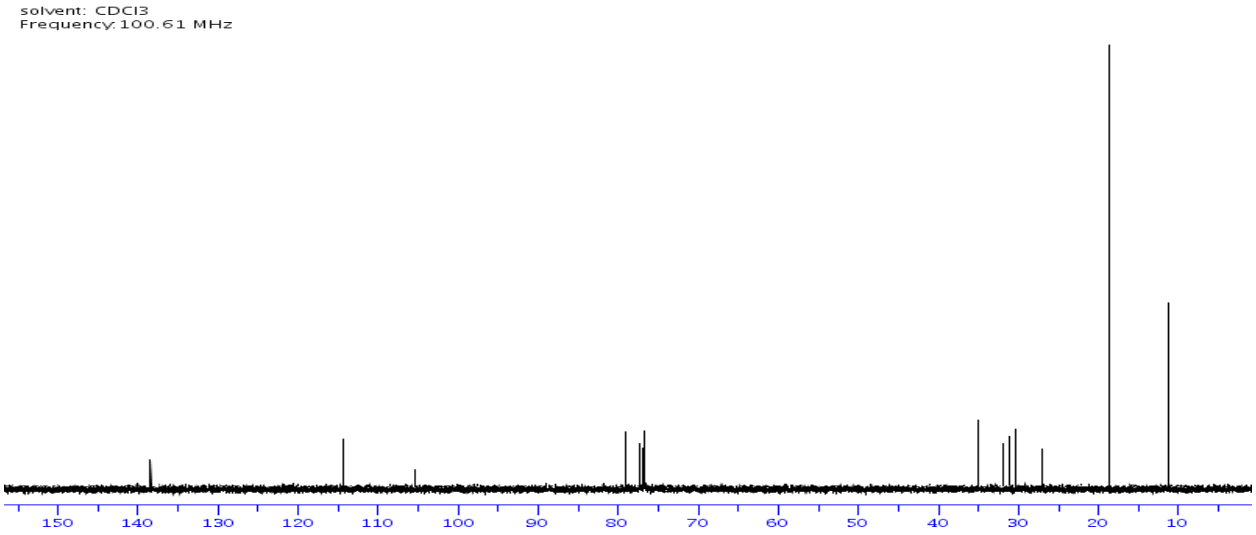
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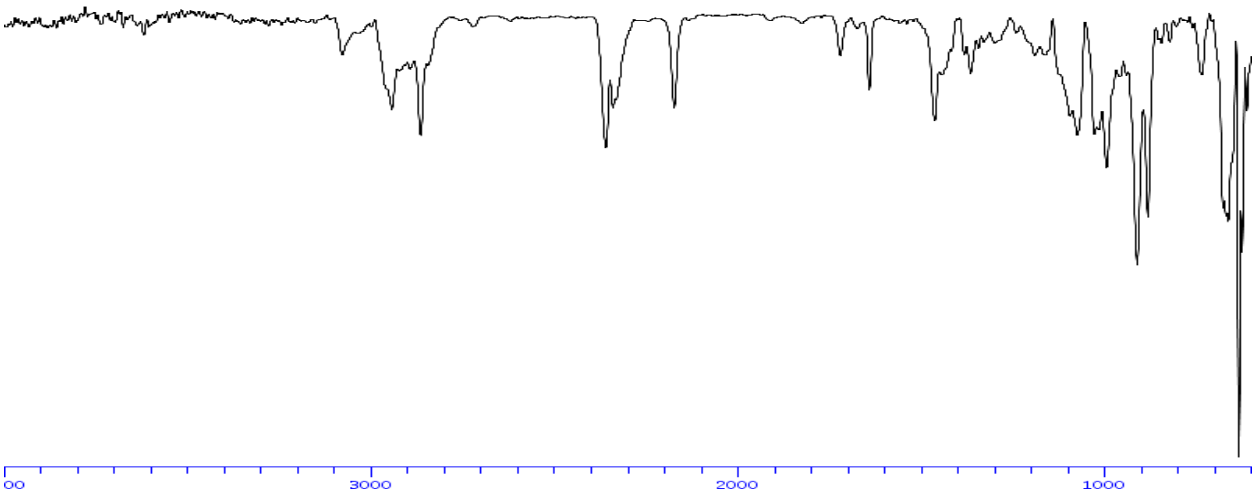
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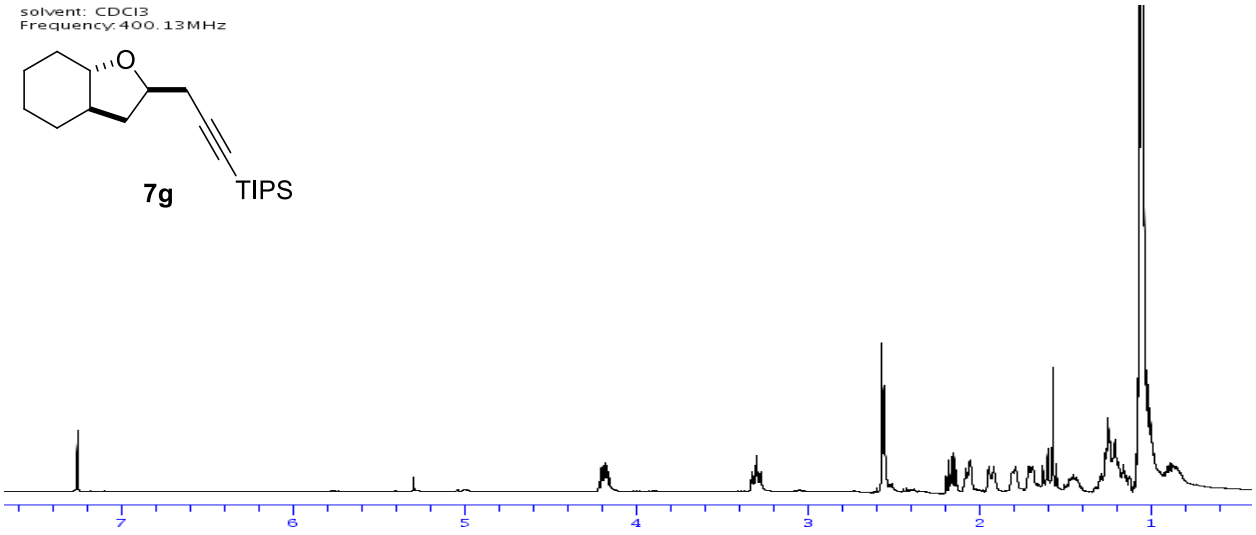
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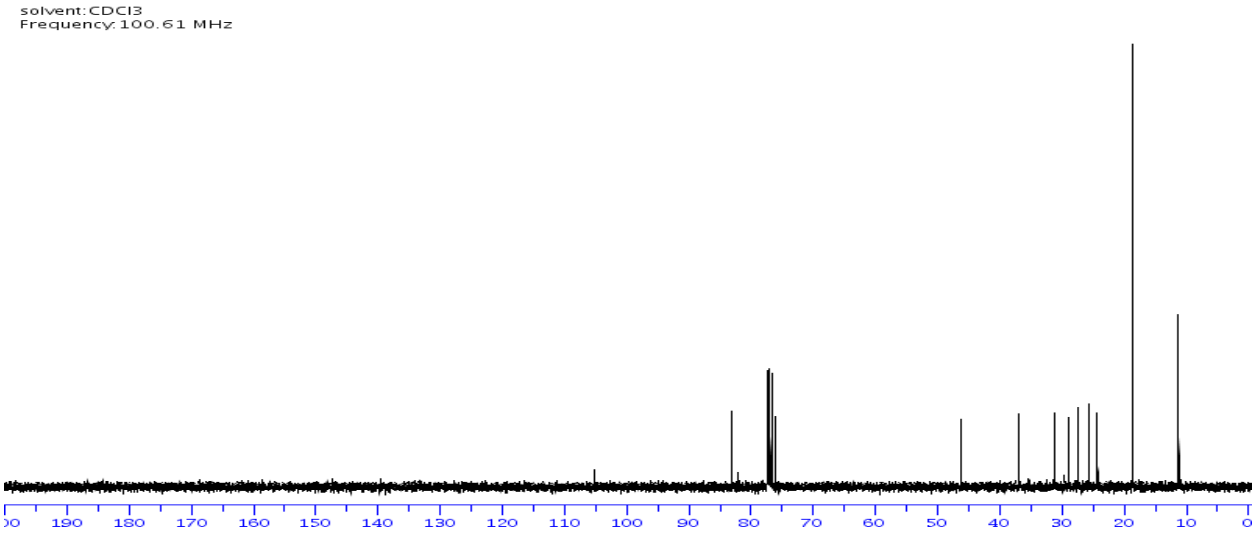
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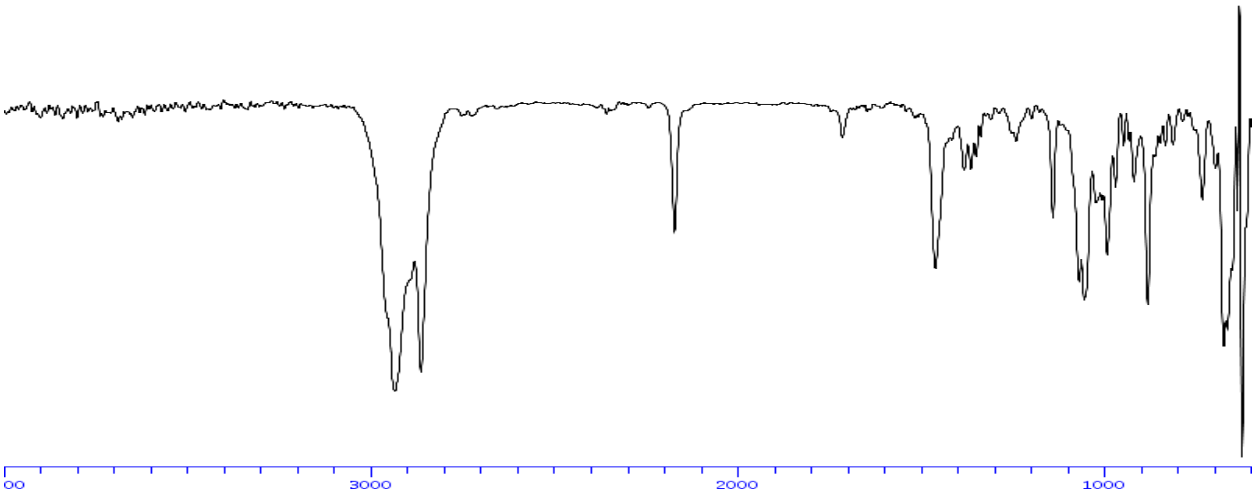
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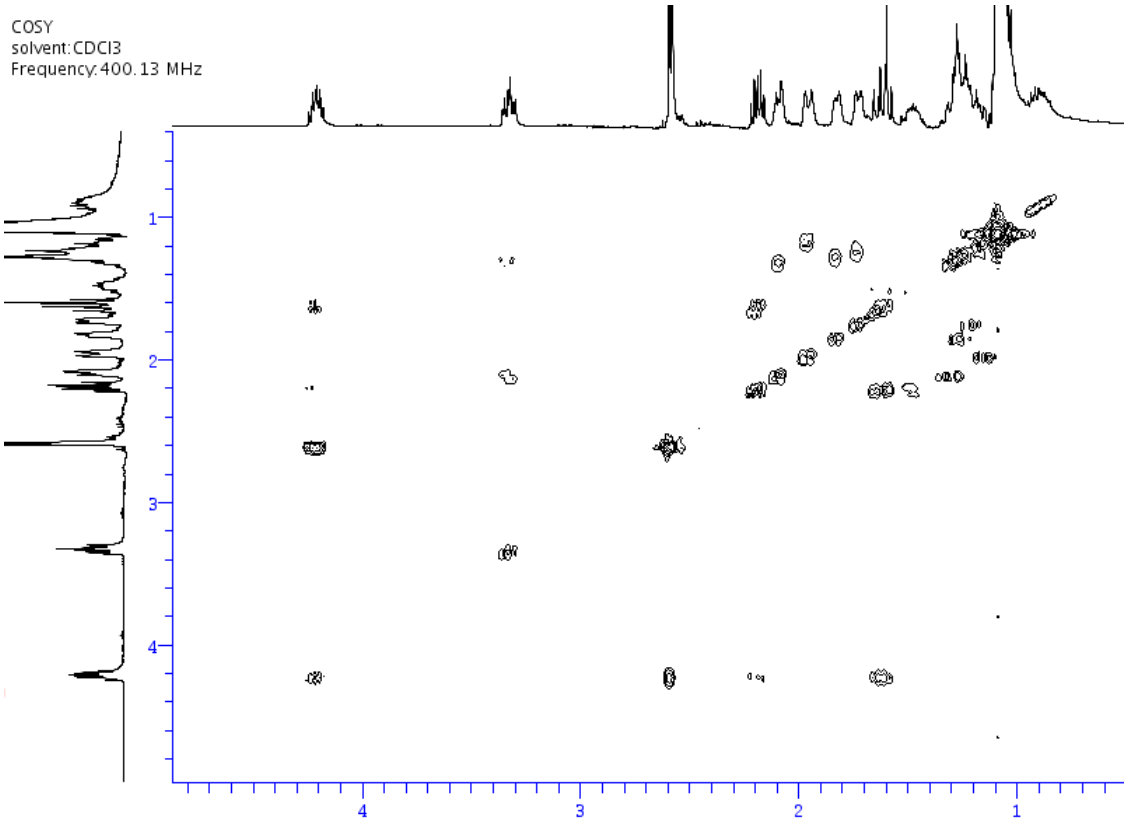
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Frequency: 400.13 MHz
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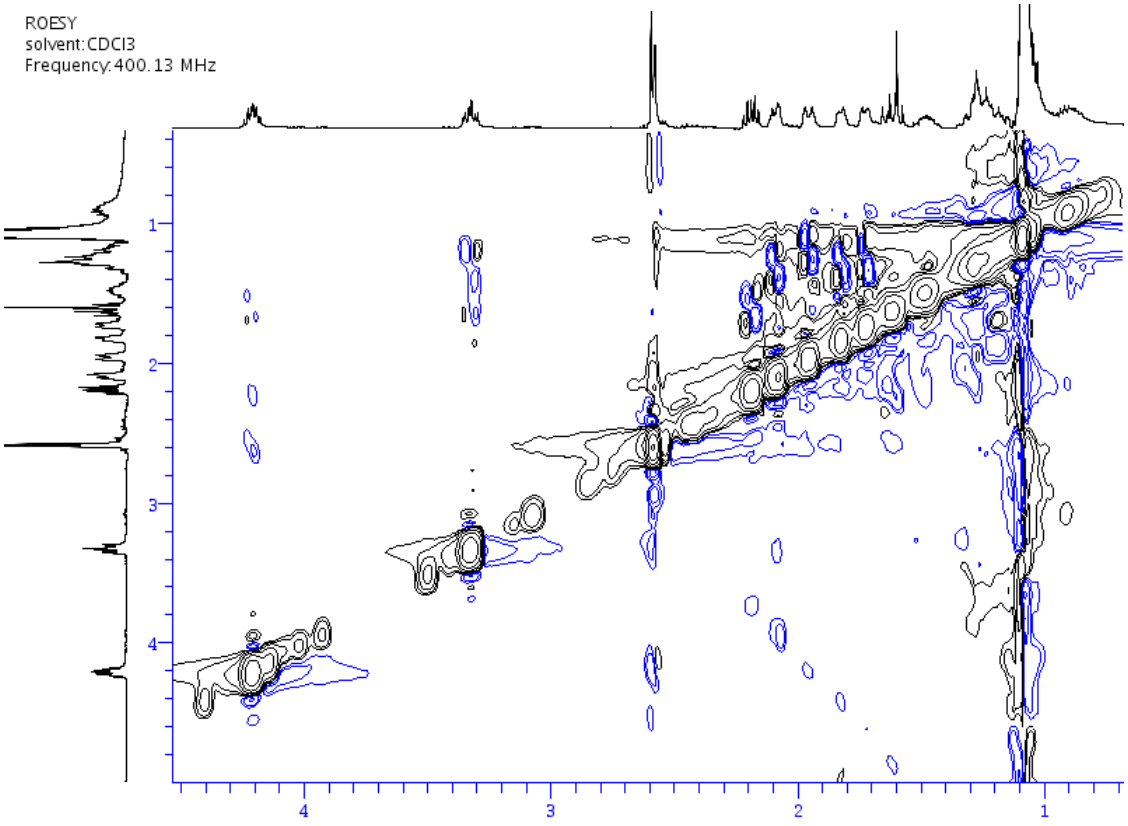
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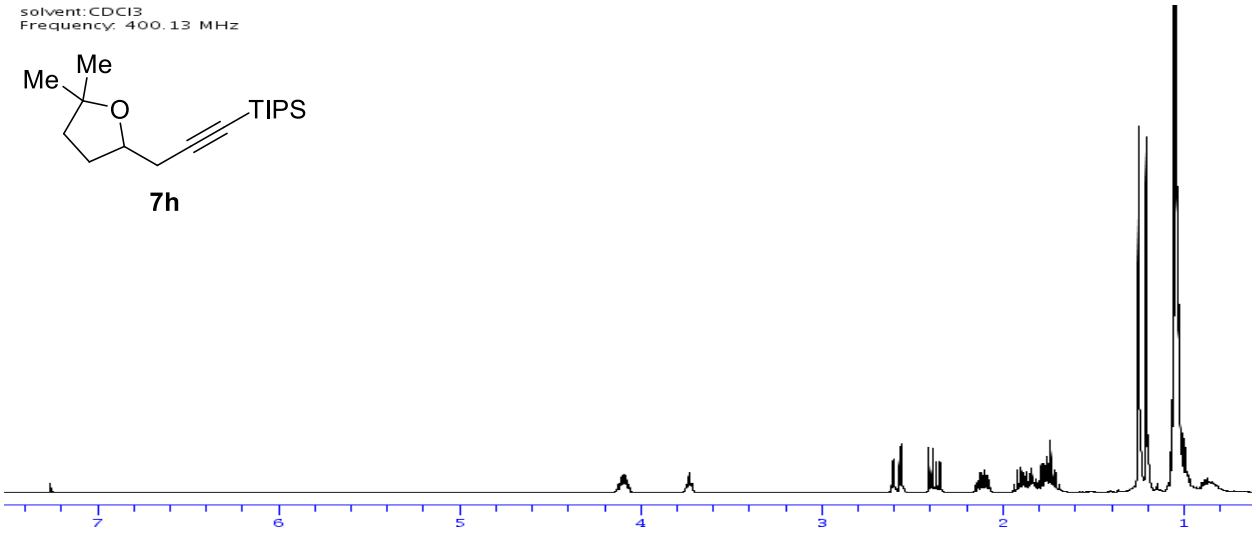
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TIPS
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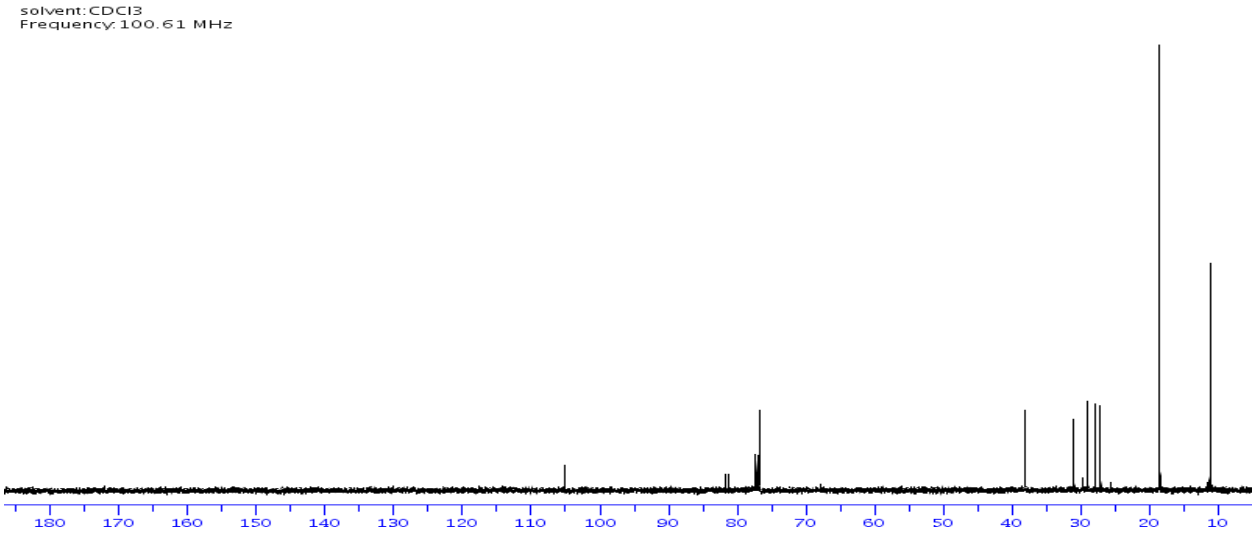
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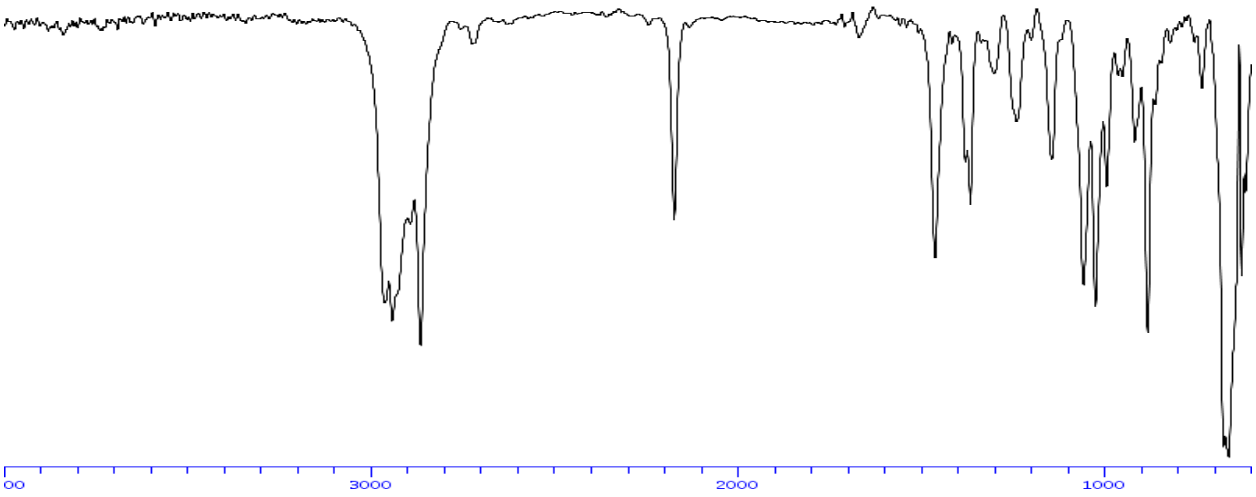
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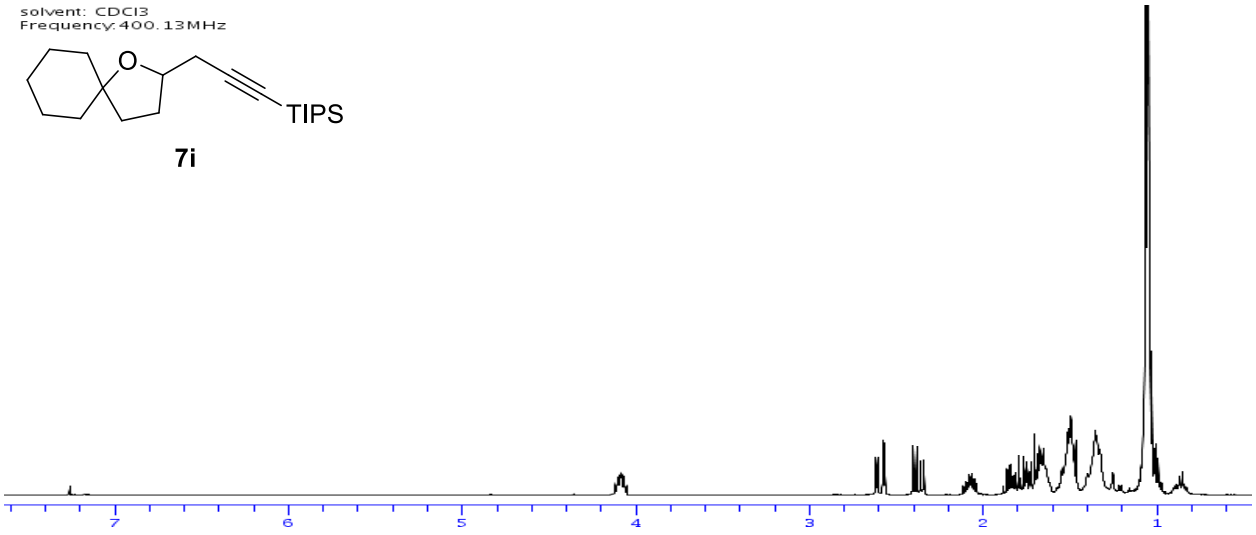
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TIPS
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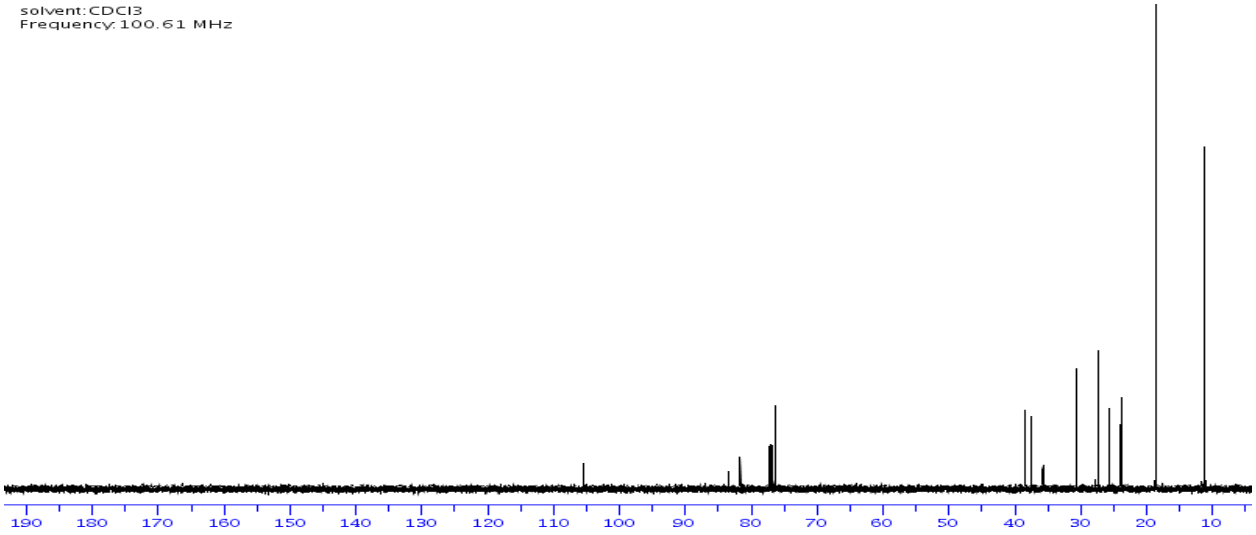
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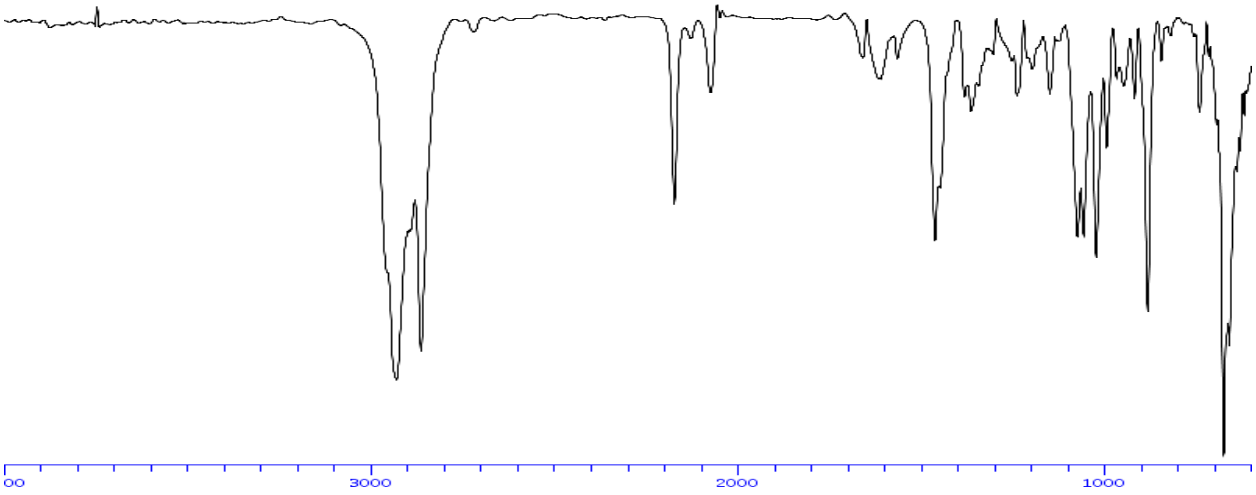
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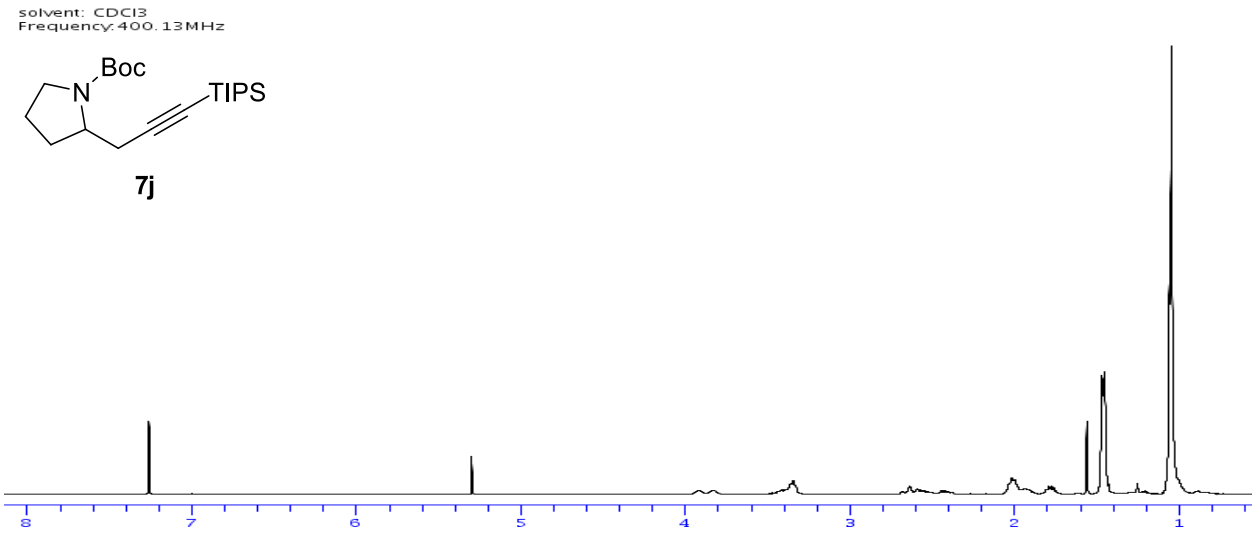
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TIPS
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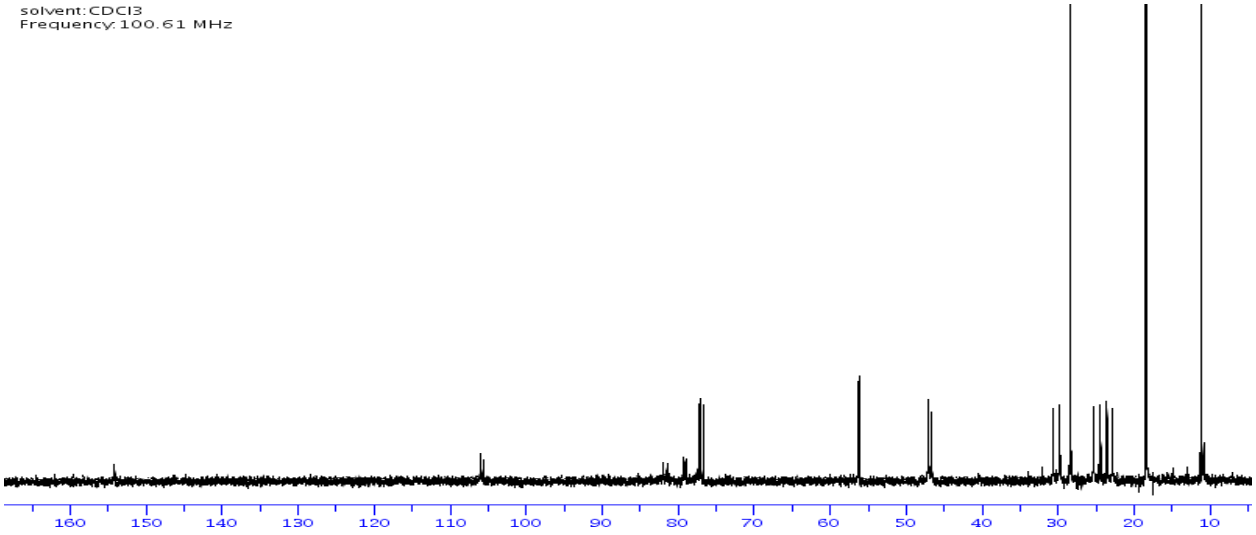
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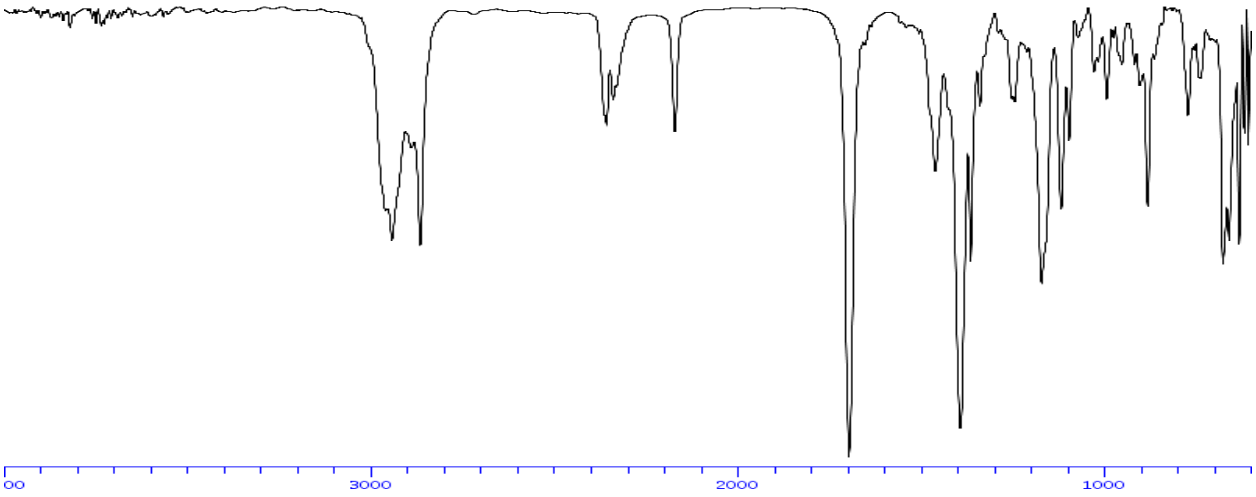
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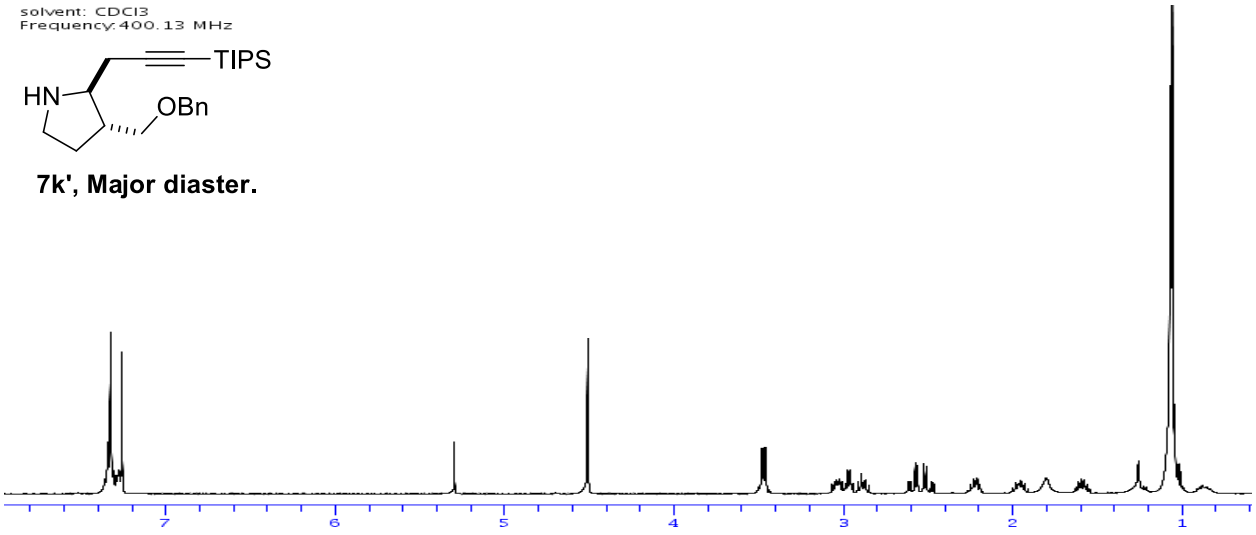
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TIPS
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7k', Major diaster.
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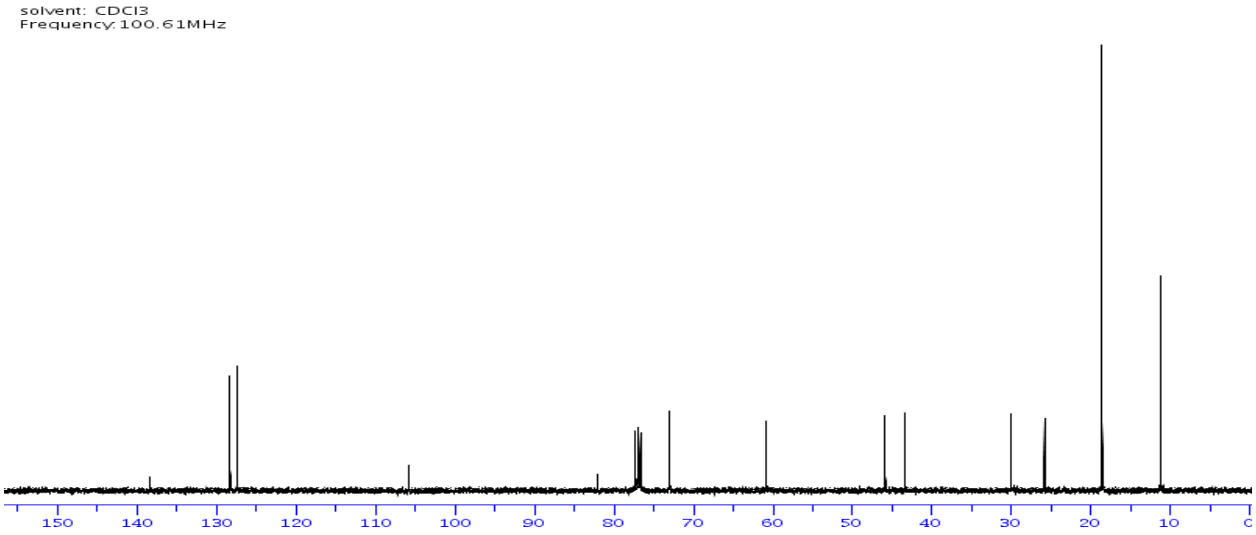
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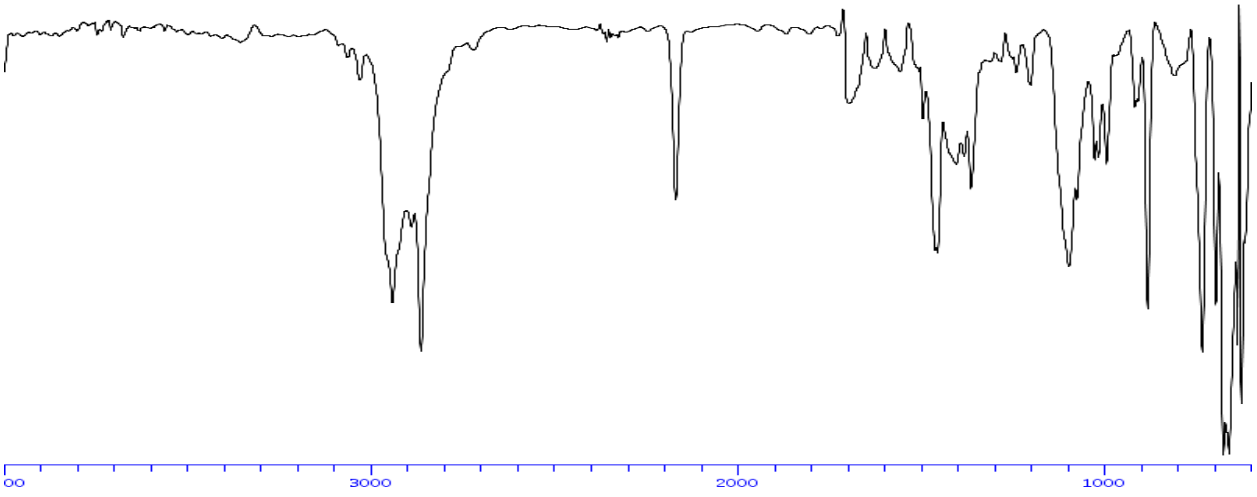
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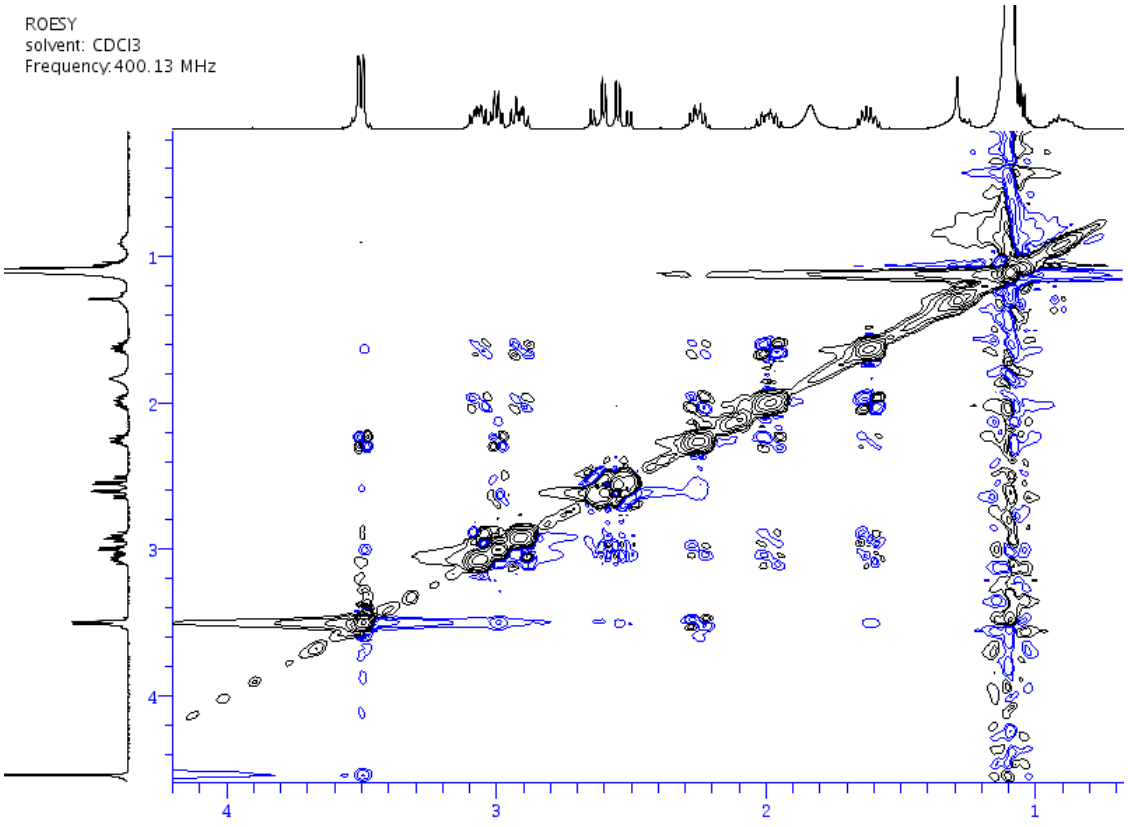
ROESY
solvent: CDCl3
Frequency: 400.13 MHz
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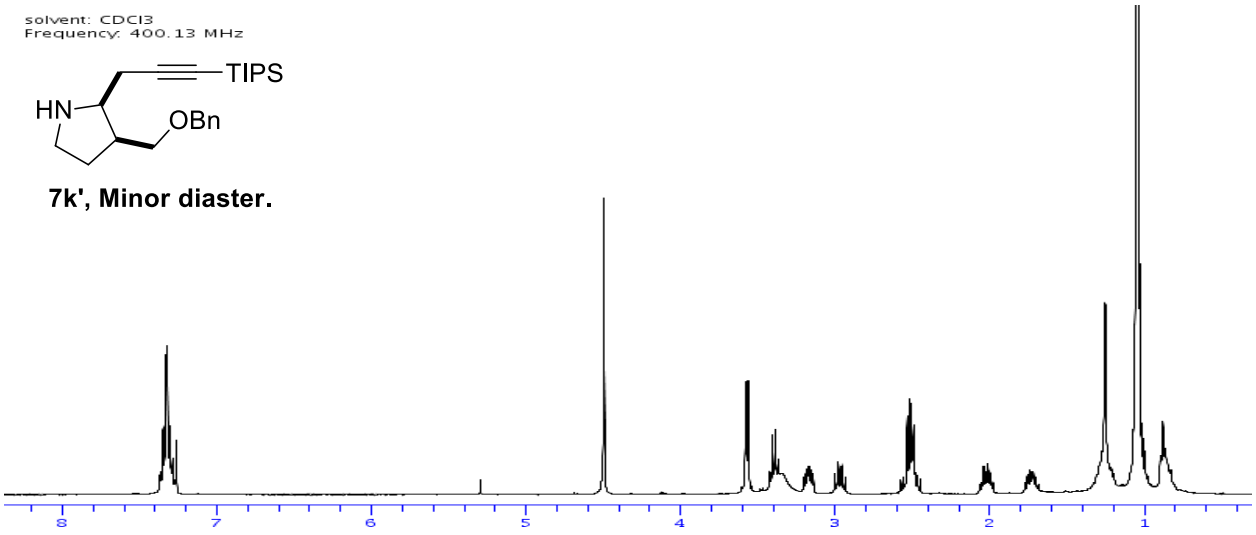
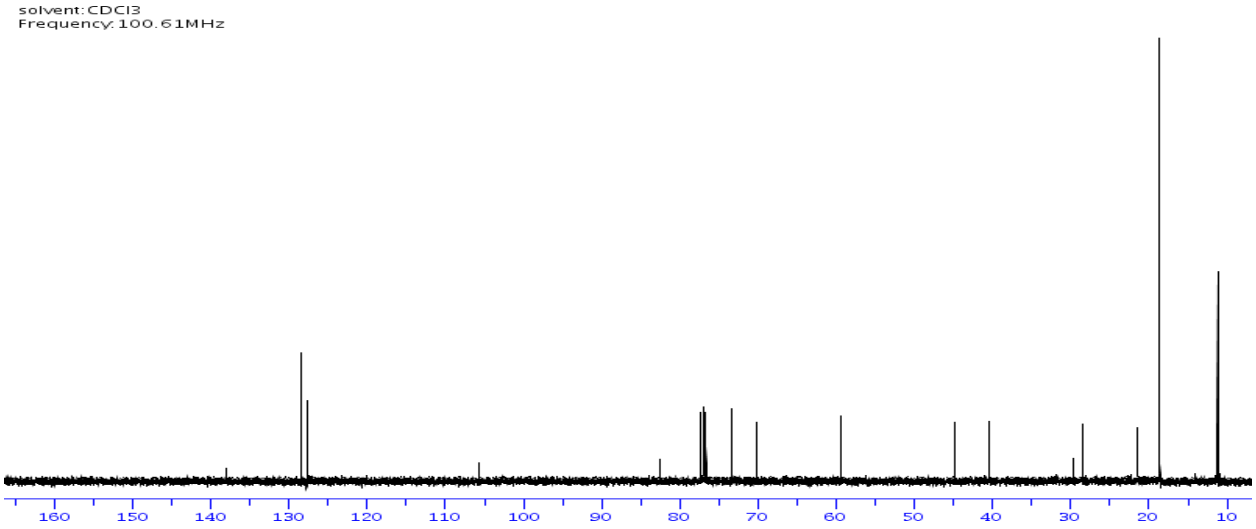
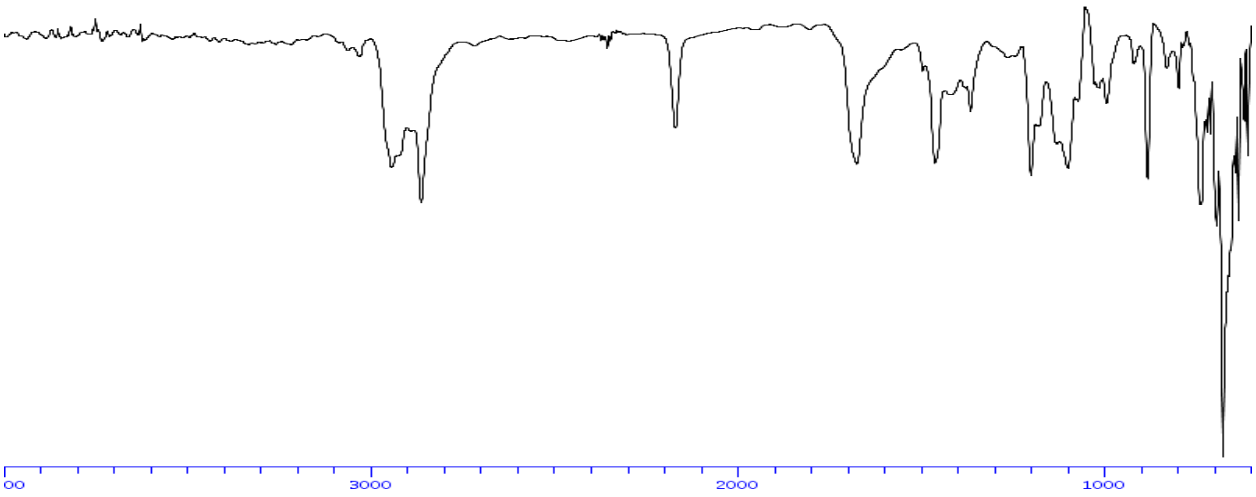
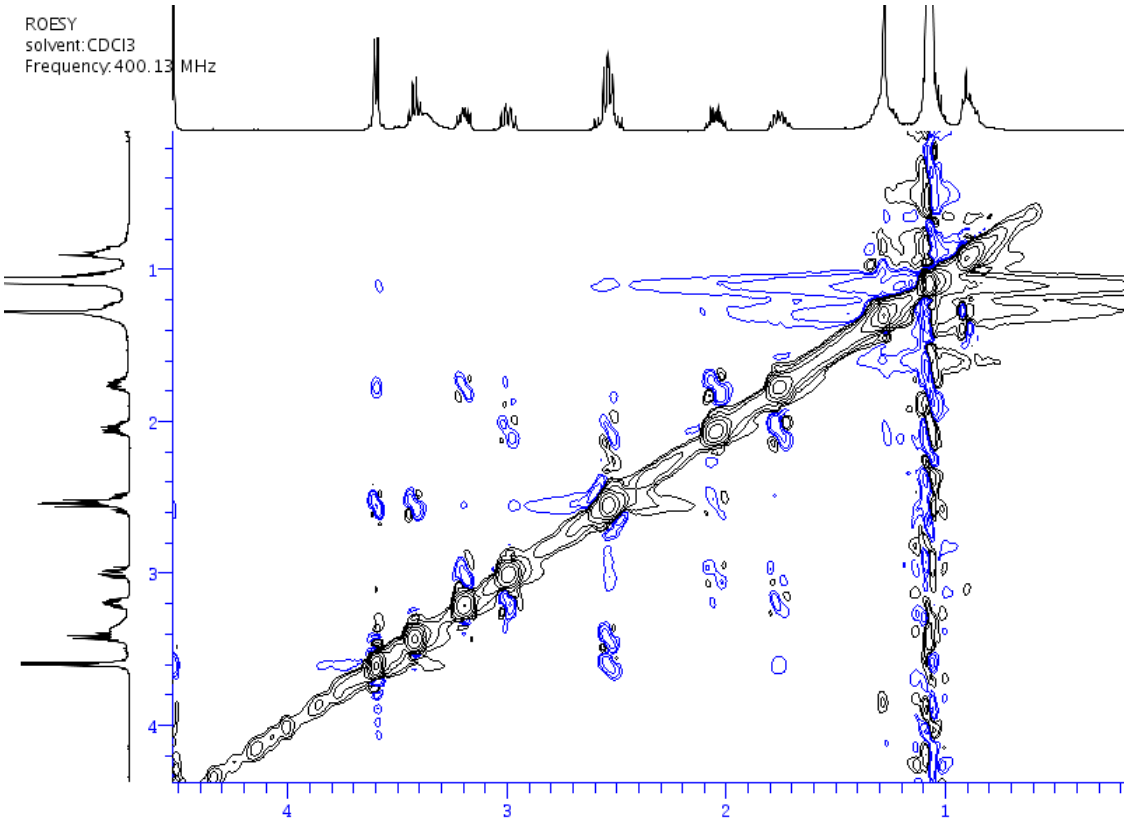


7k', Minor diaster.






ROESY
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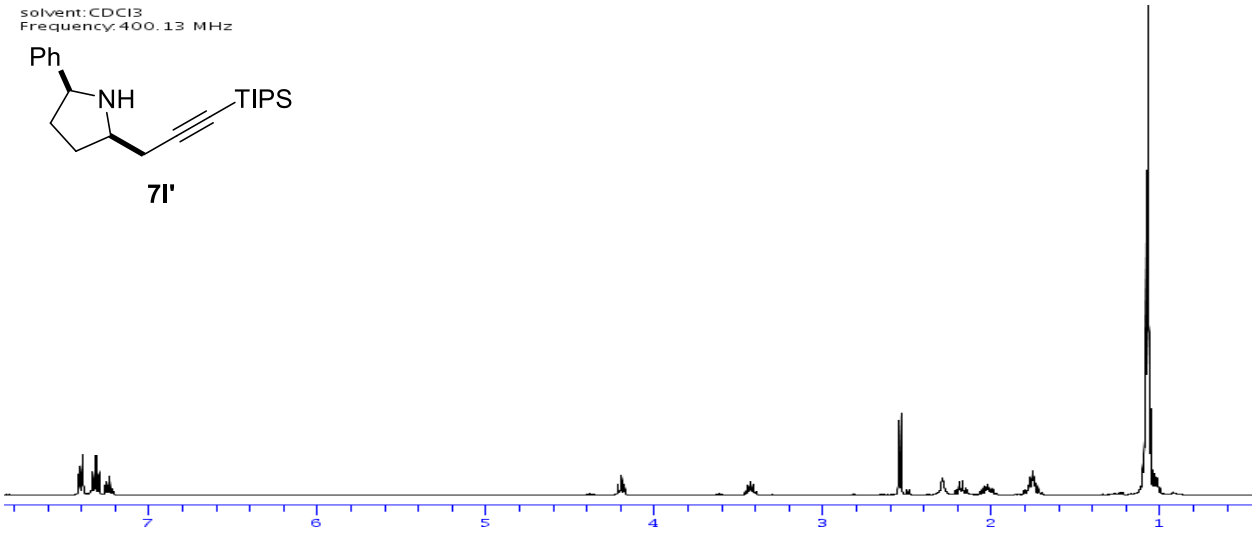
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Frequency:400.13 MHz
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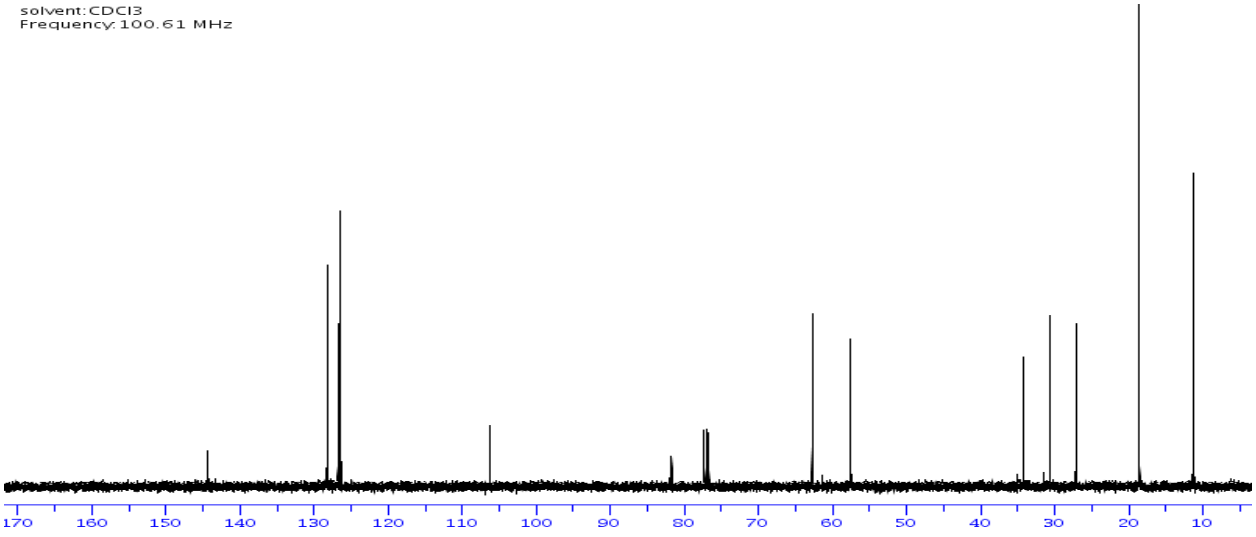
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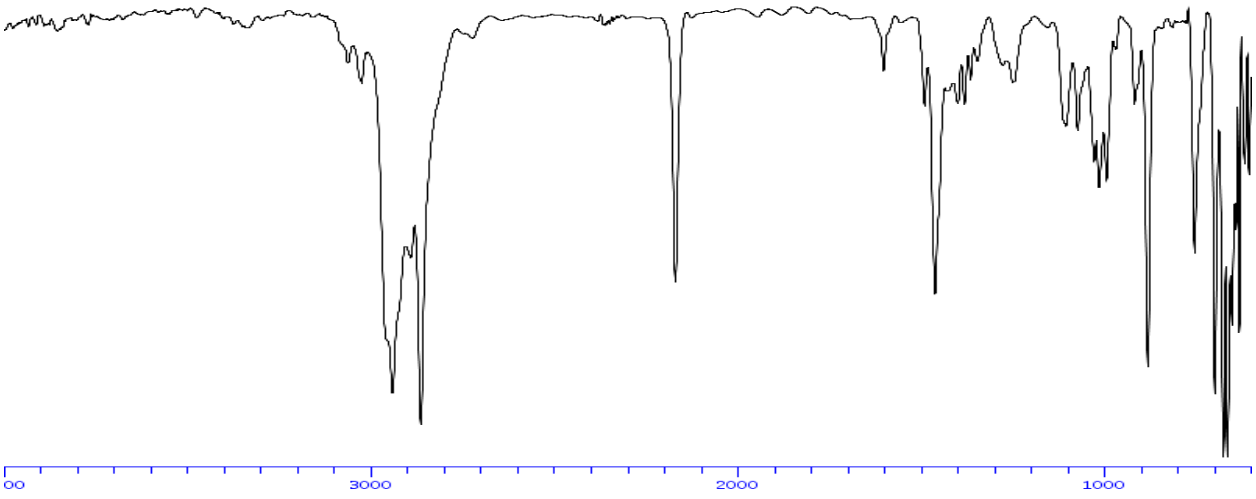
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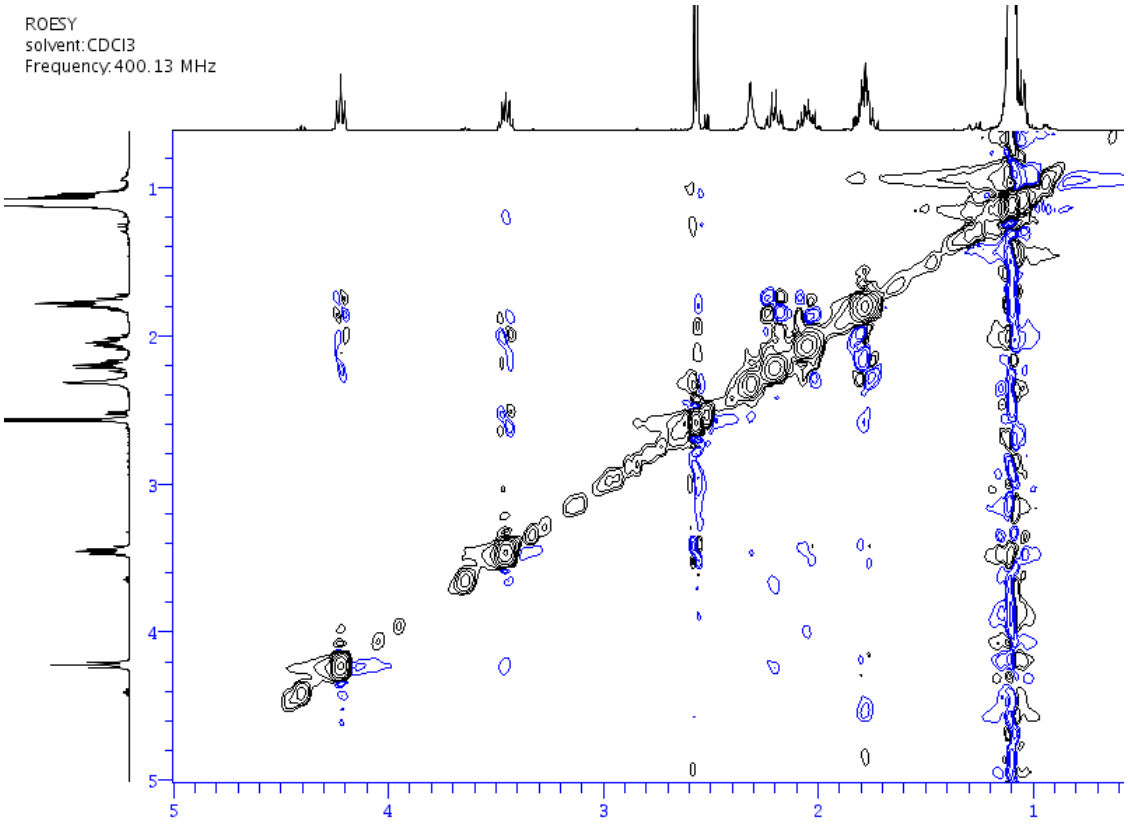
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solvent:CDCl3
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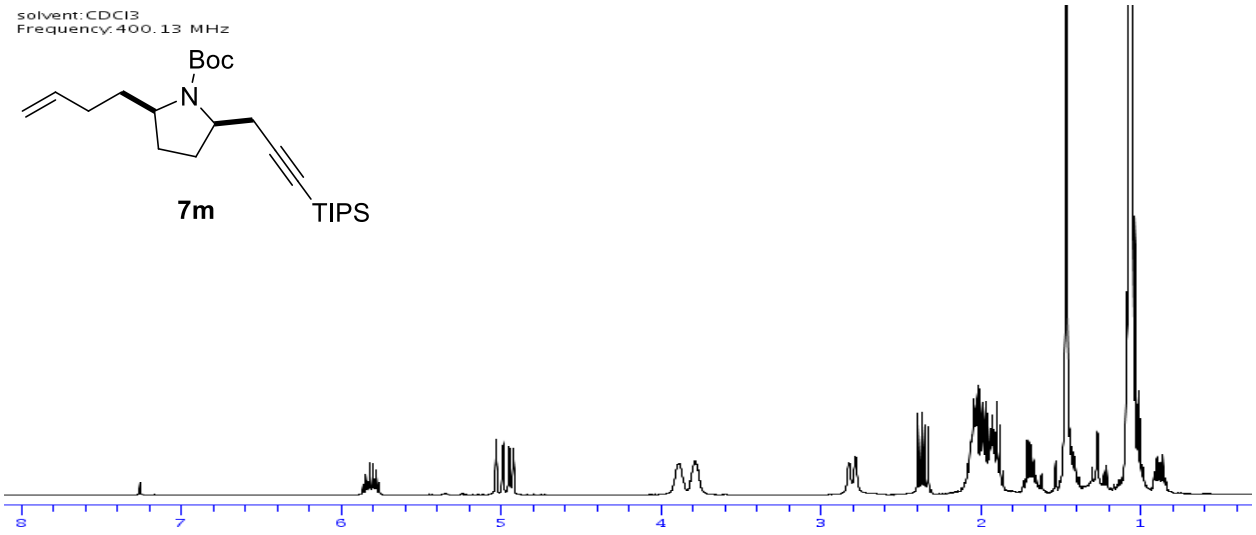
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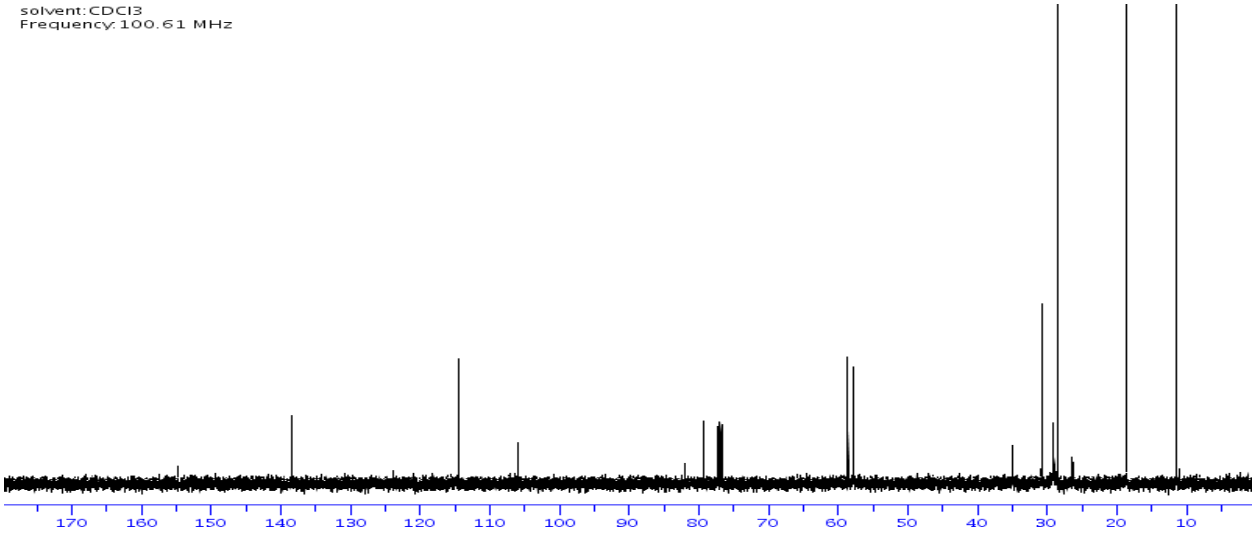
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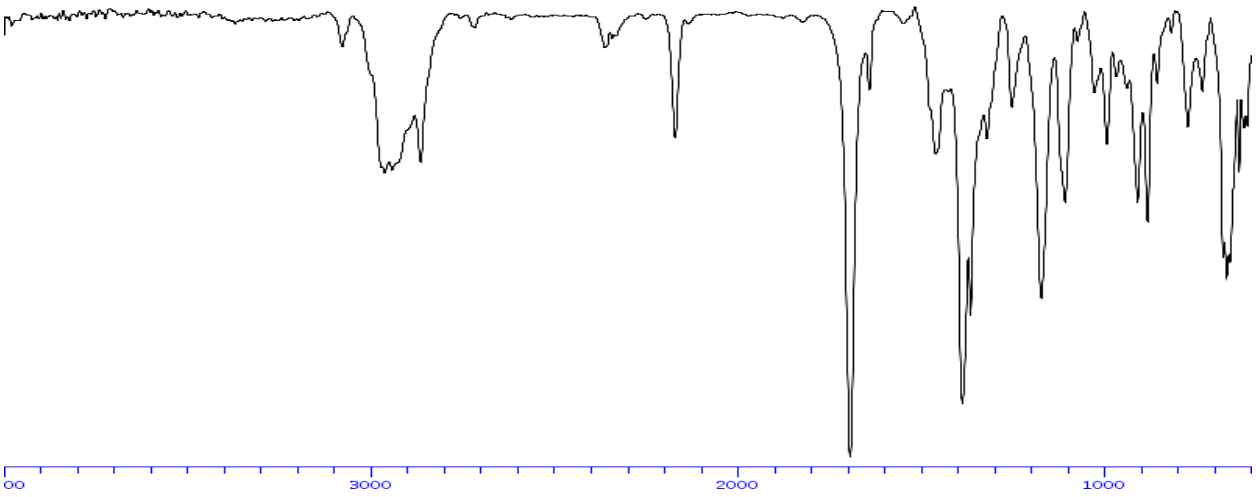
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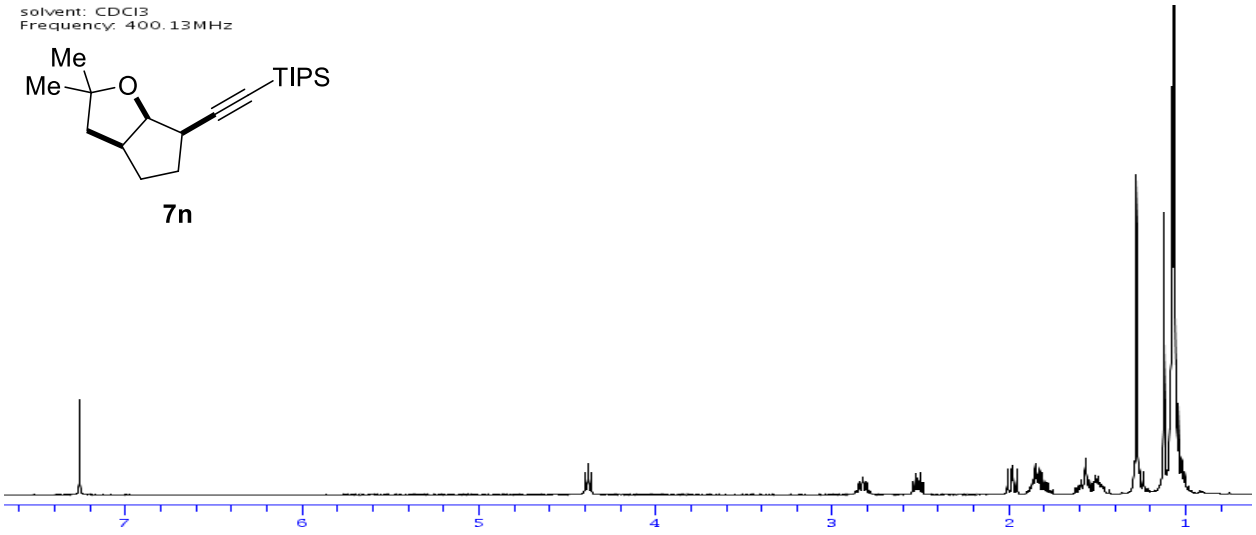
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Frequency: 400.13MHz
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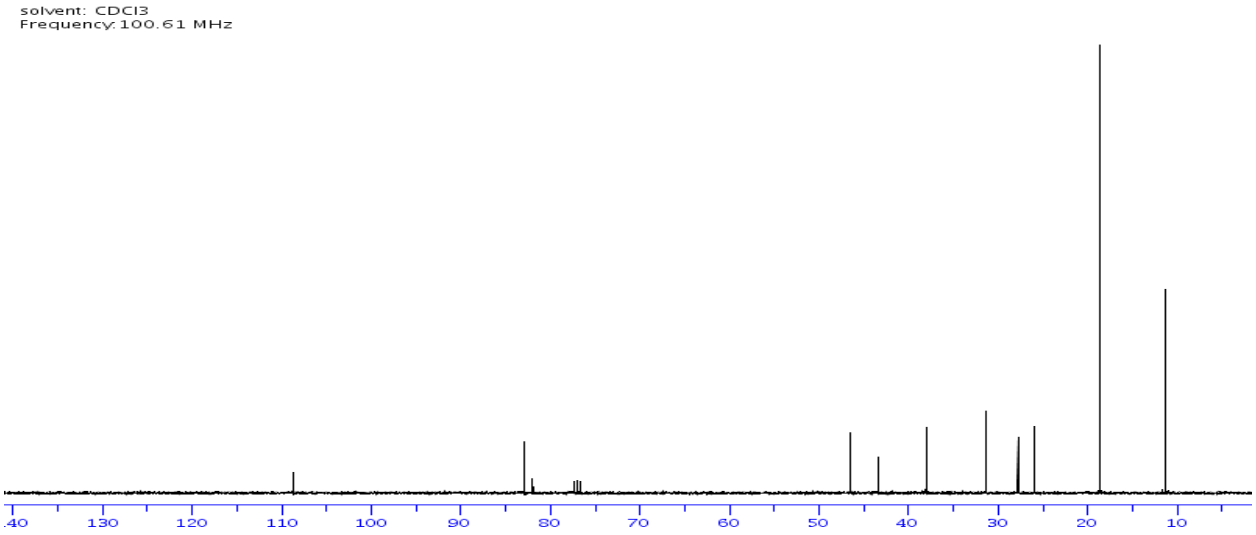
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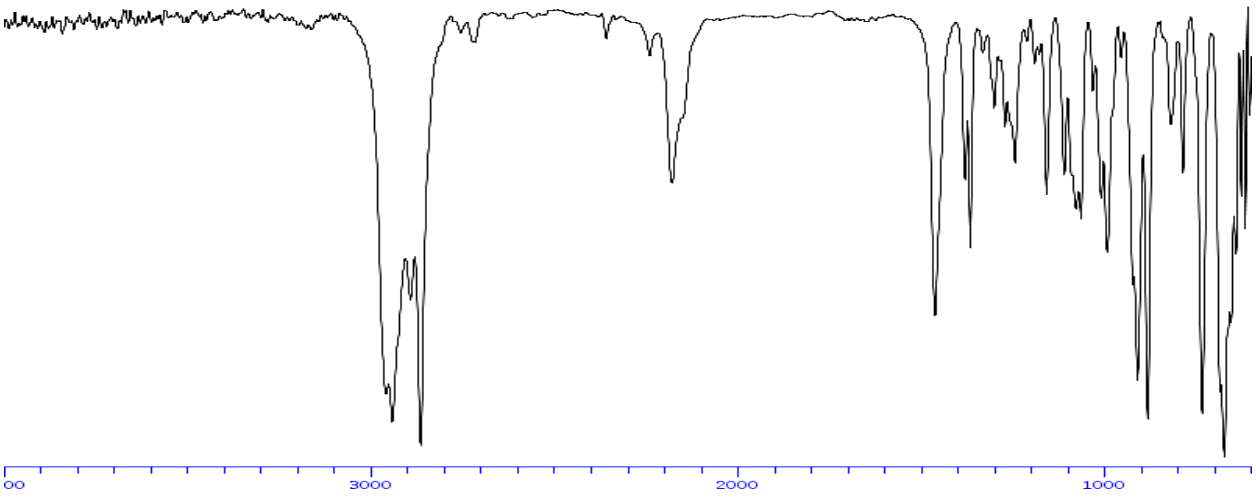
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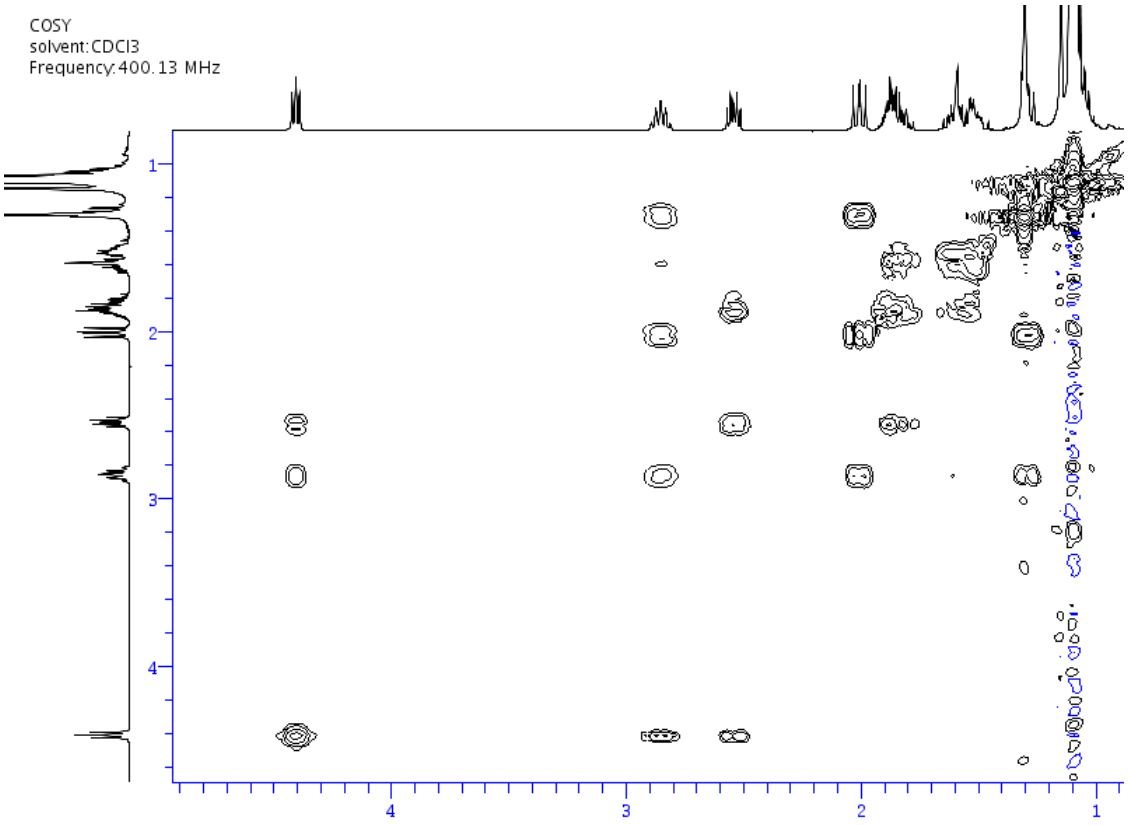
COSY
solvent:CDCl3
Frequency:400.13 MHz
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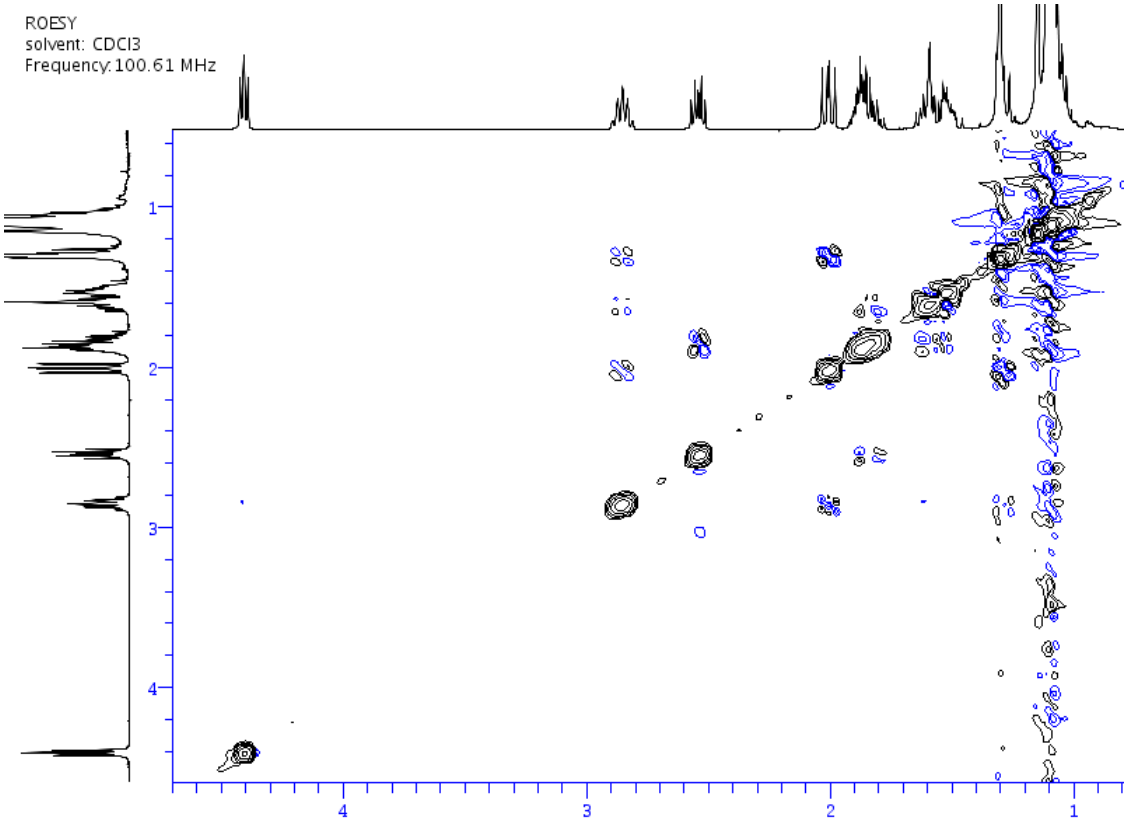
ROESY
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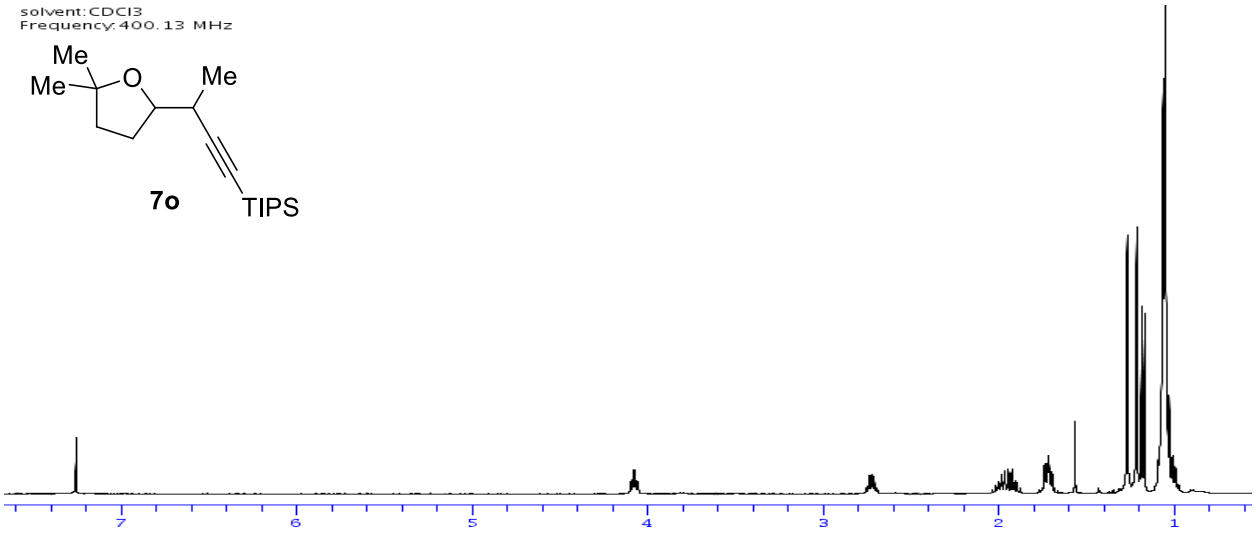
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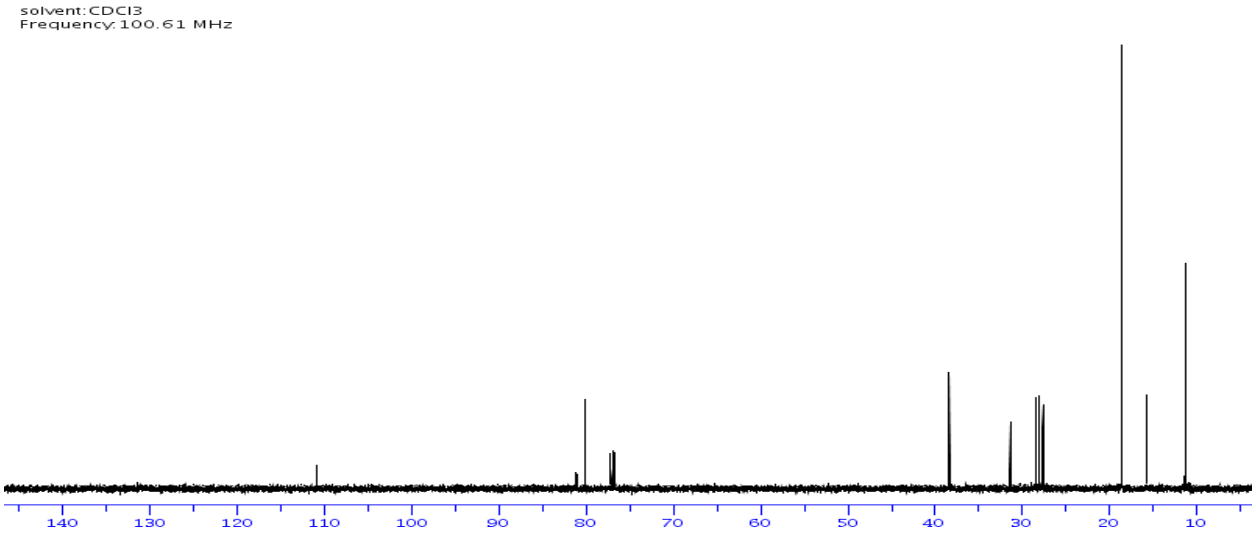
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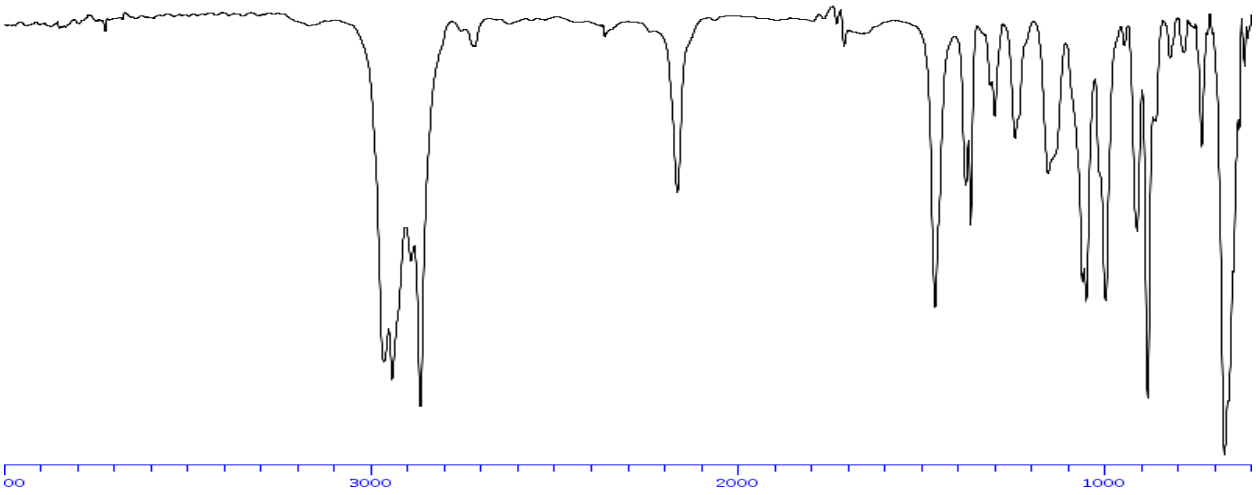
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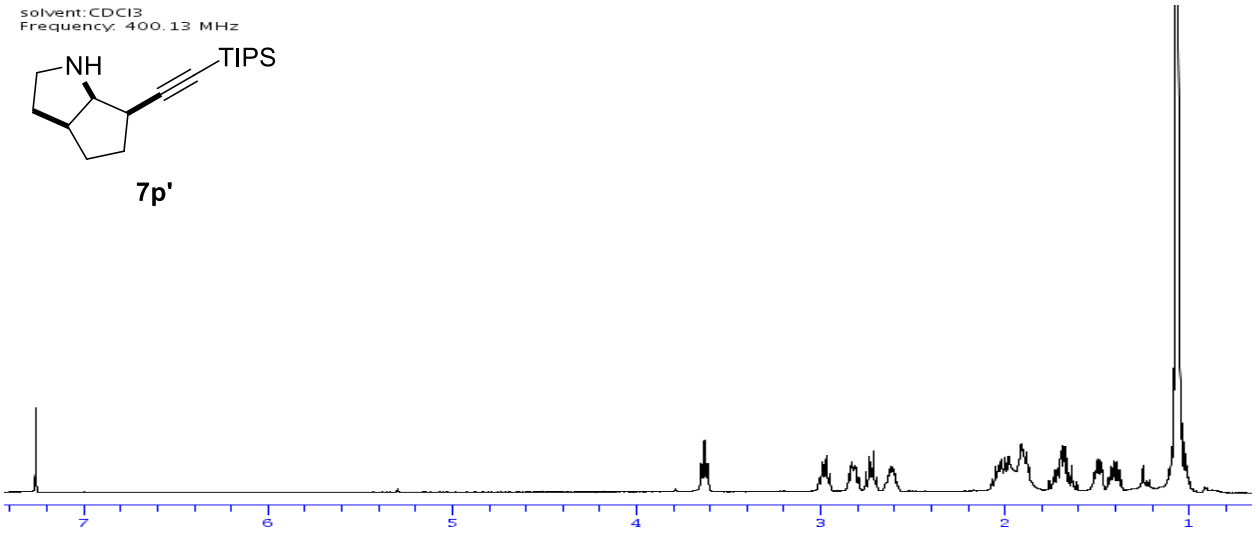
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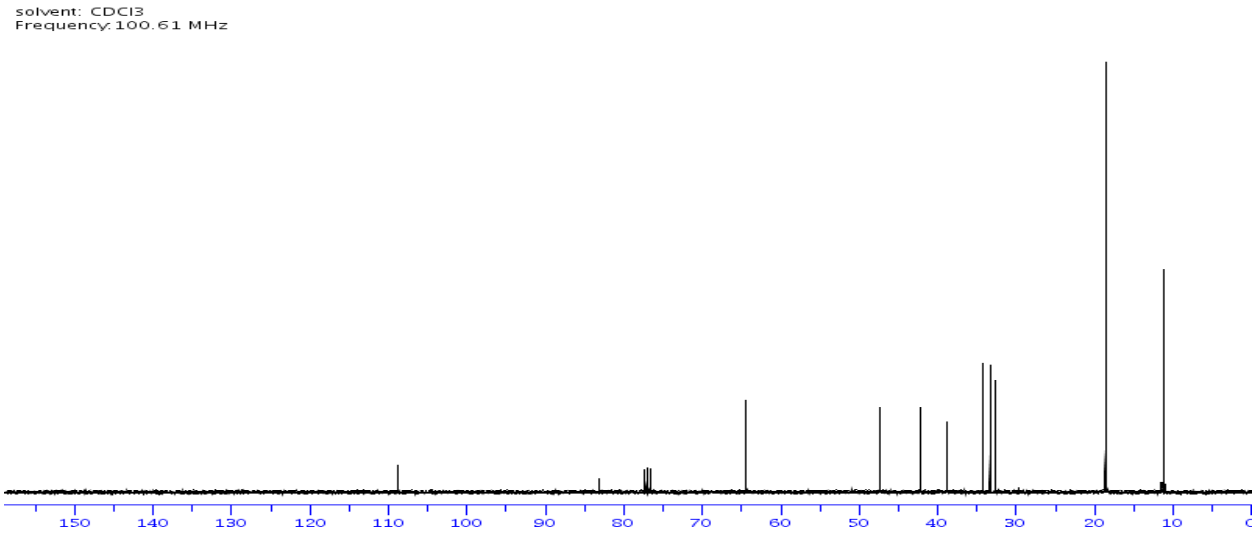
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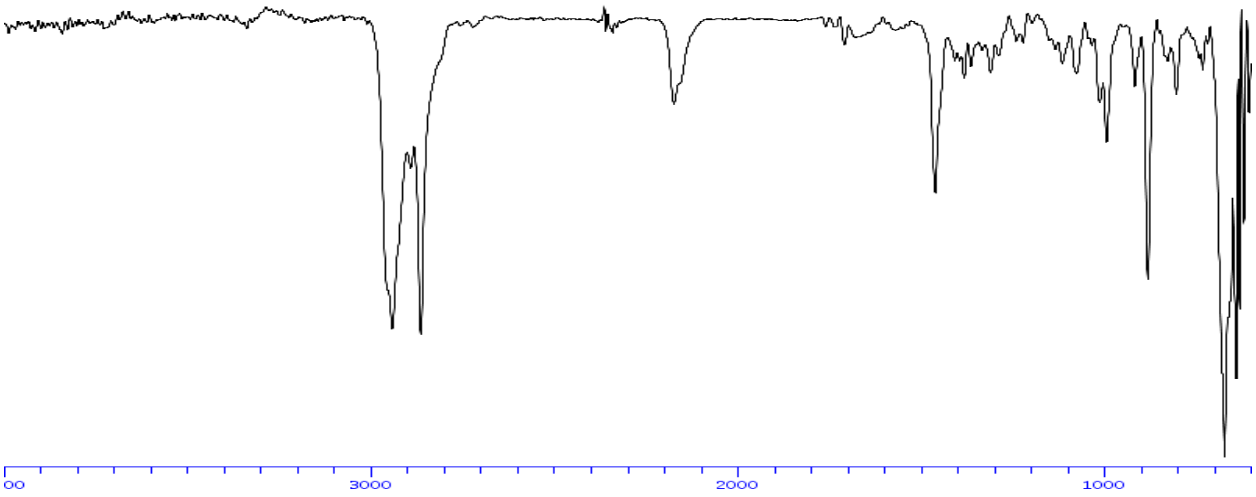
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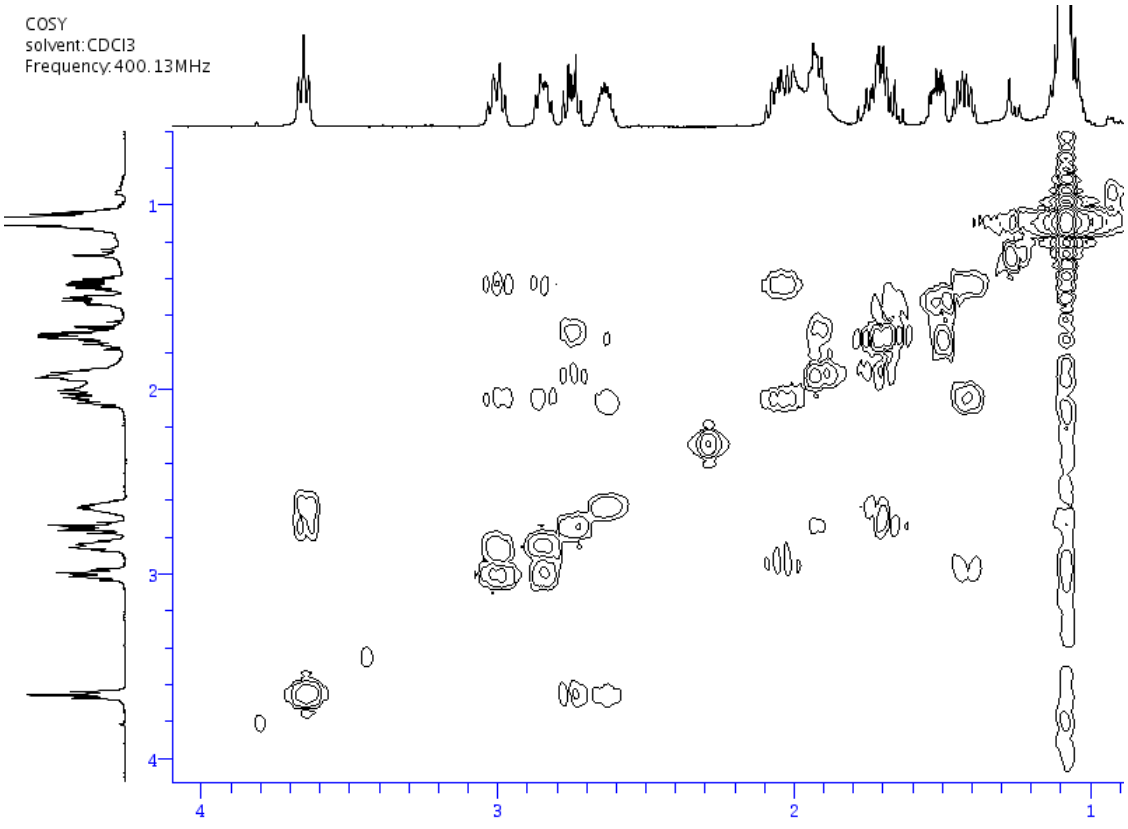
COSY
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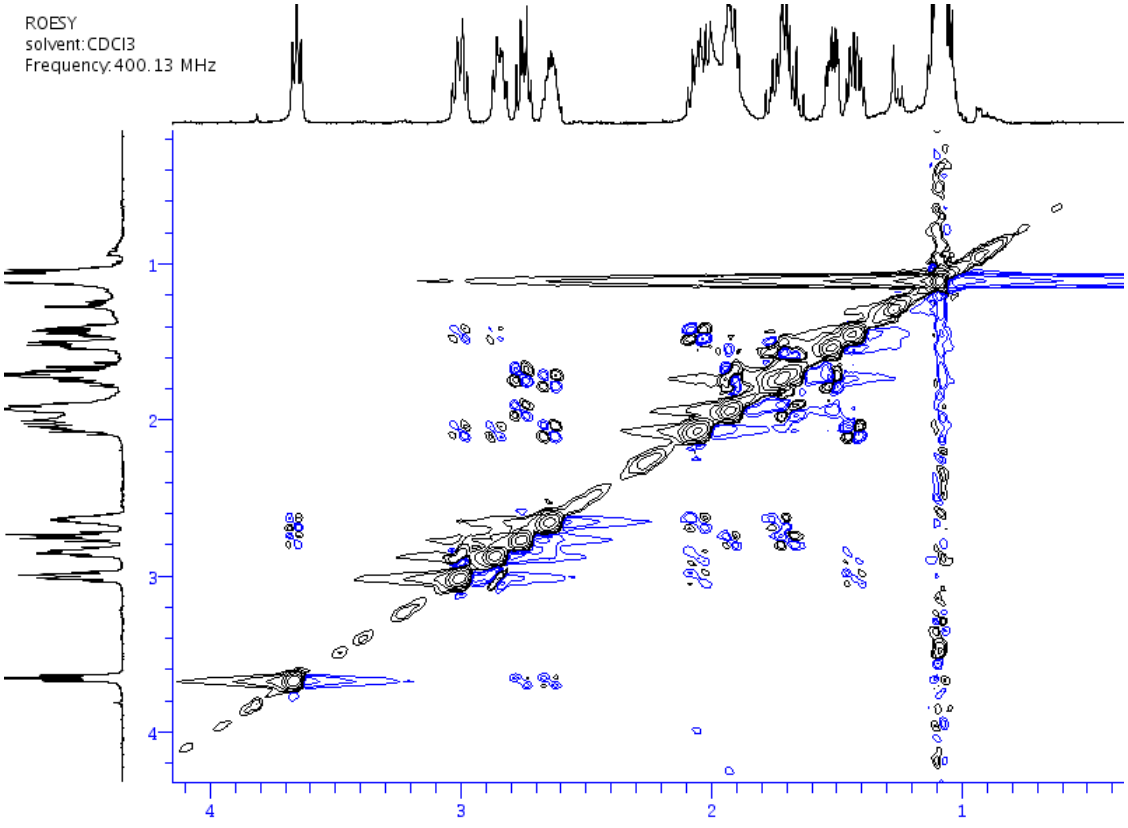
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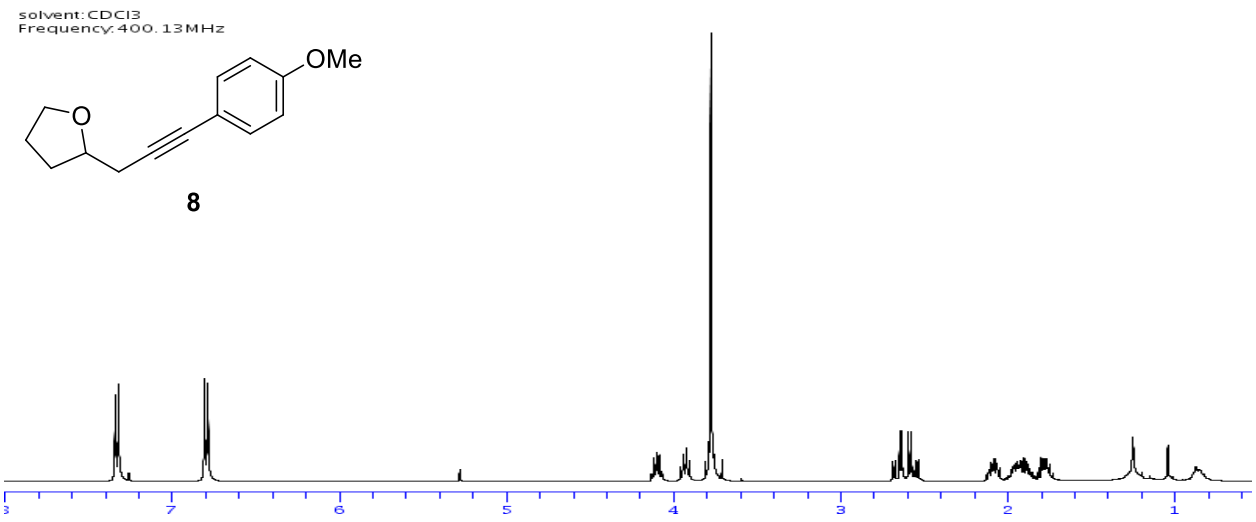
solvent:CDCl3
Frequency:400.13MHz
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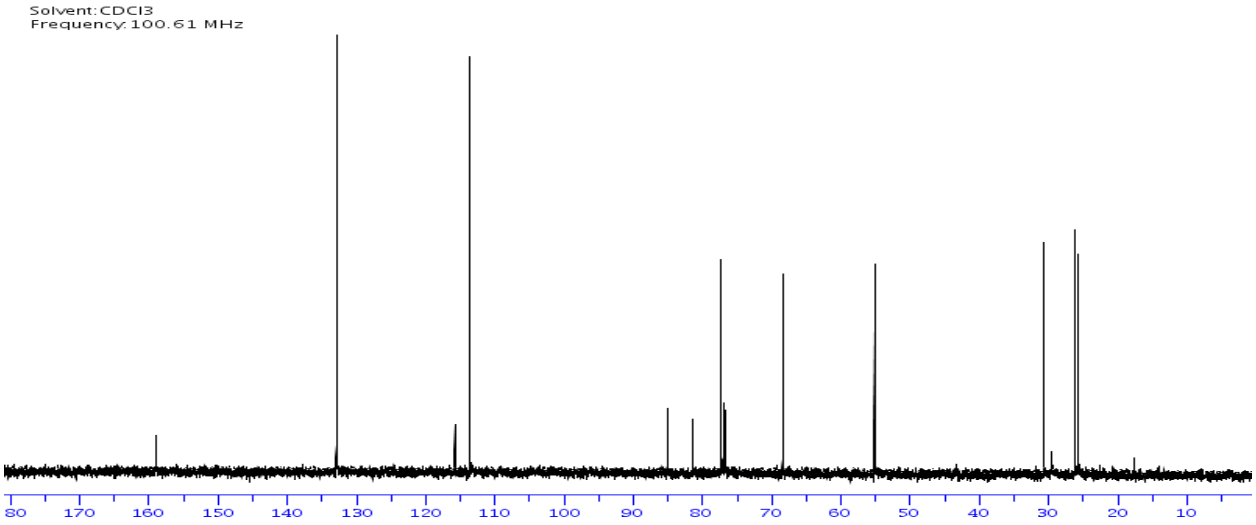
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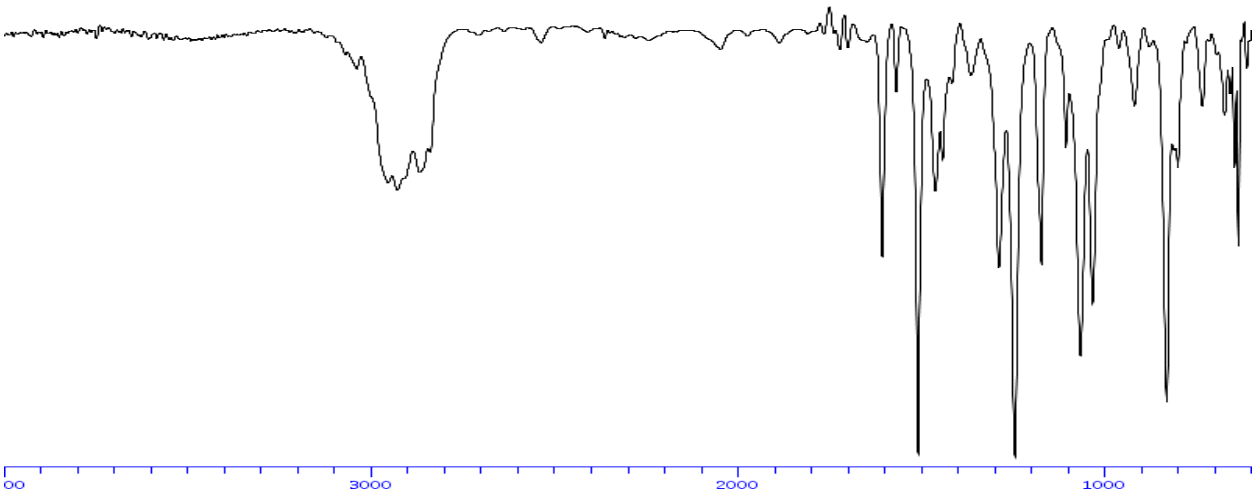
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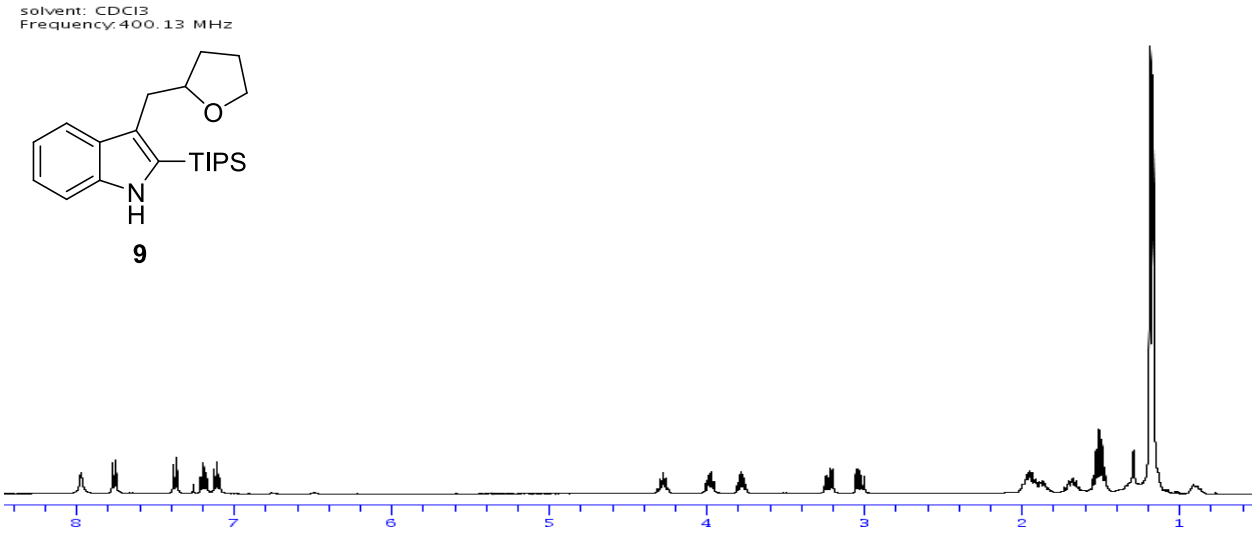
solvent: CDCl3
Frequency: 400.13 MHz
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TIPS
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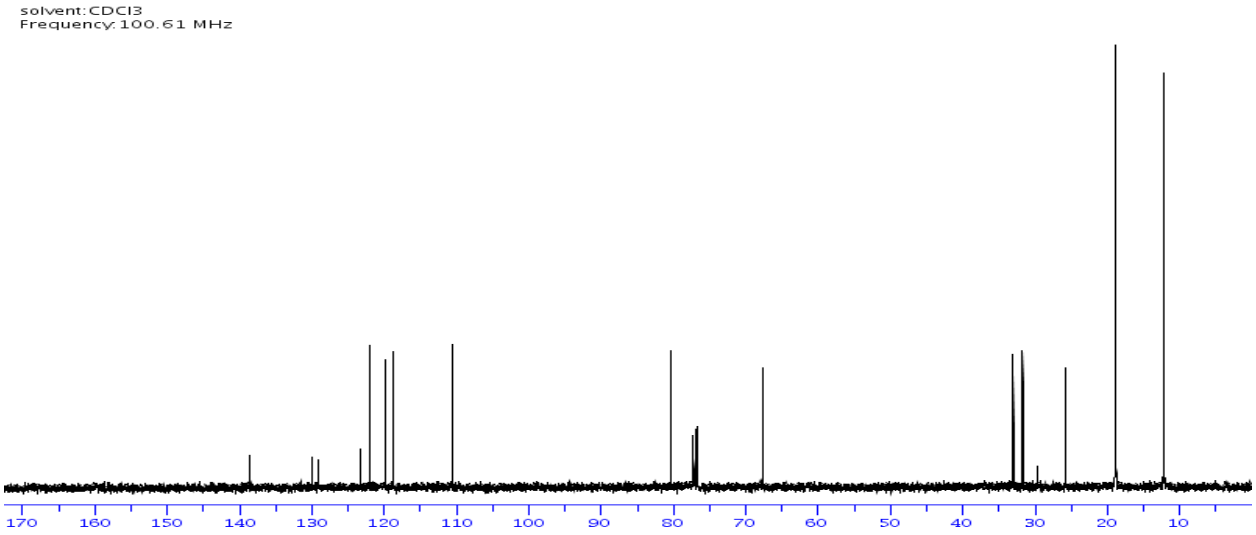
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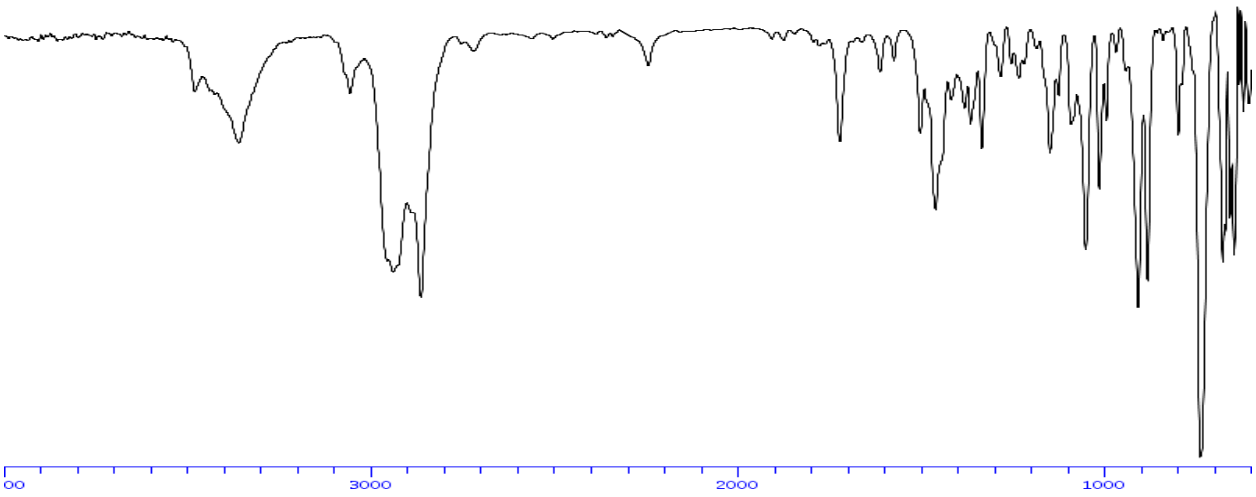
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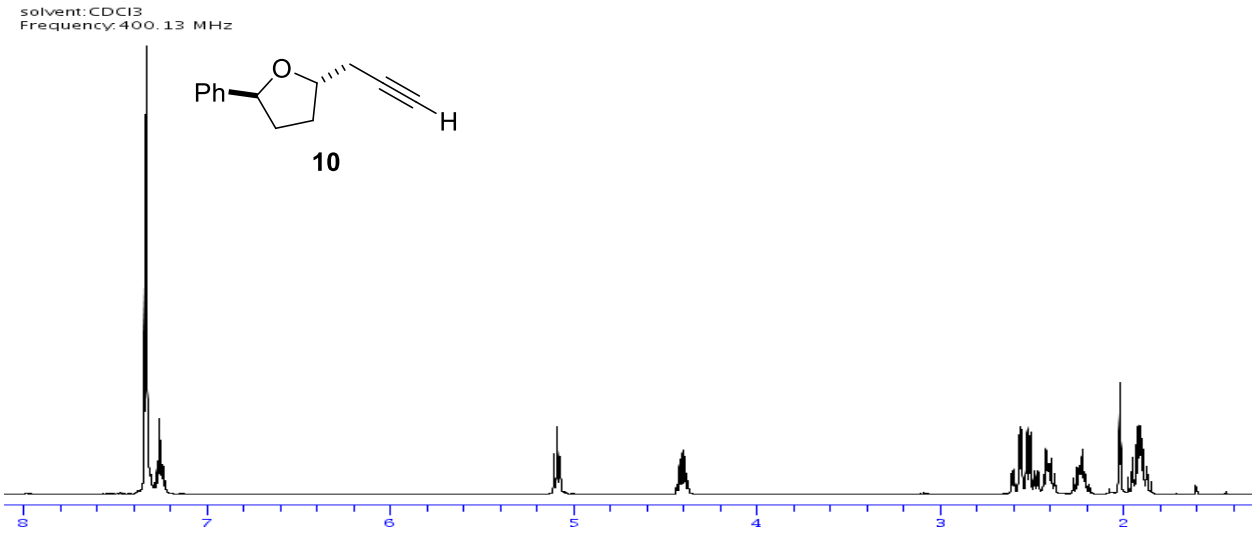
solvent:CDCl3
Frequency:400.13 MHz
Ph
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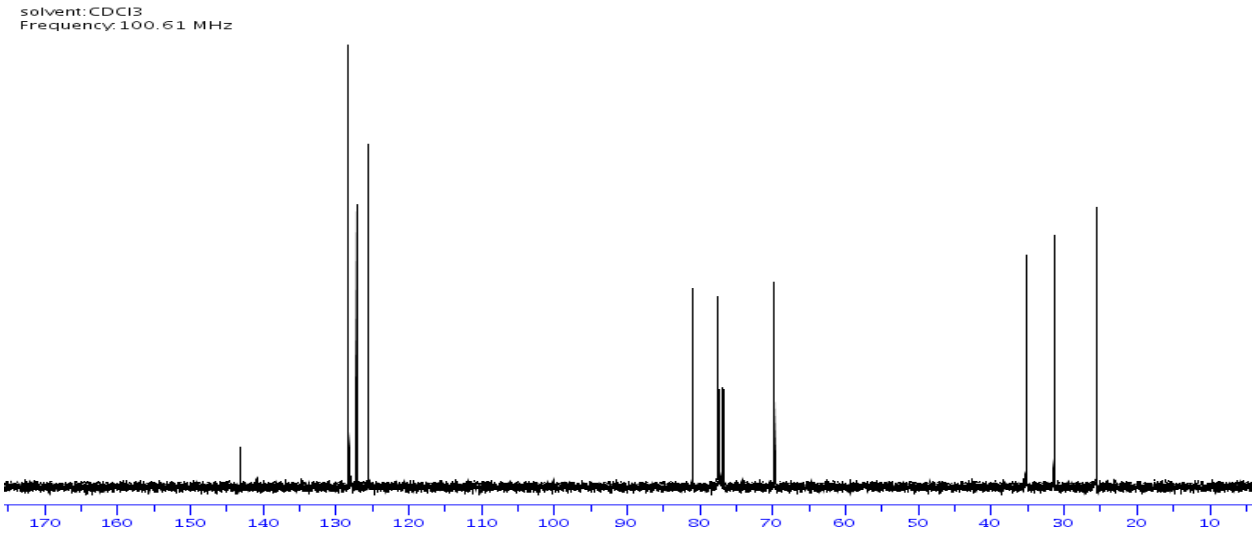
solvent:CDCl3
Frequency:100.61 MHz
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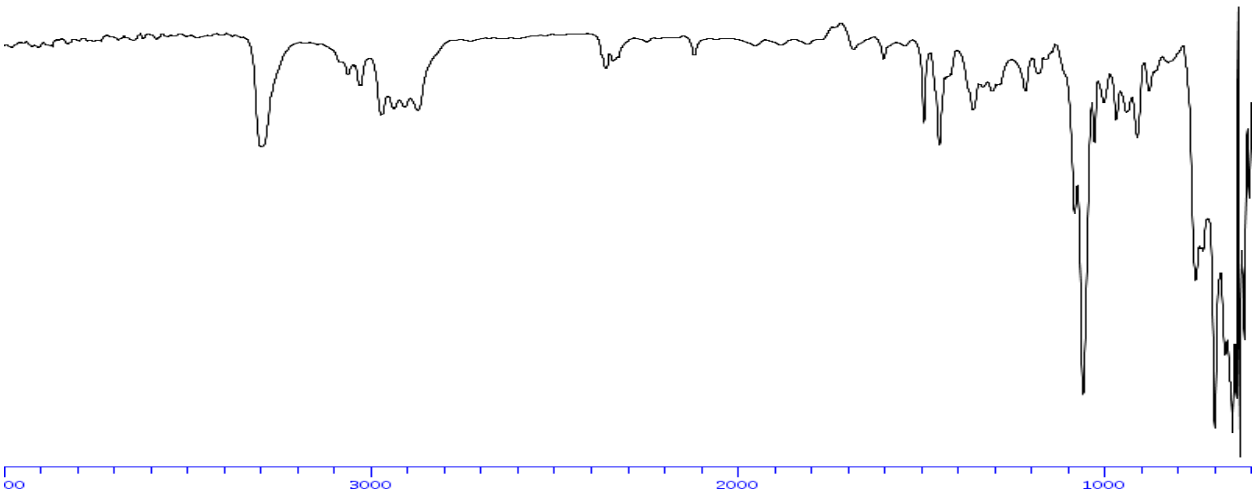
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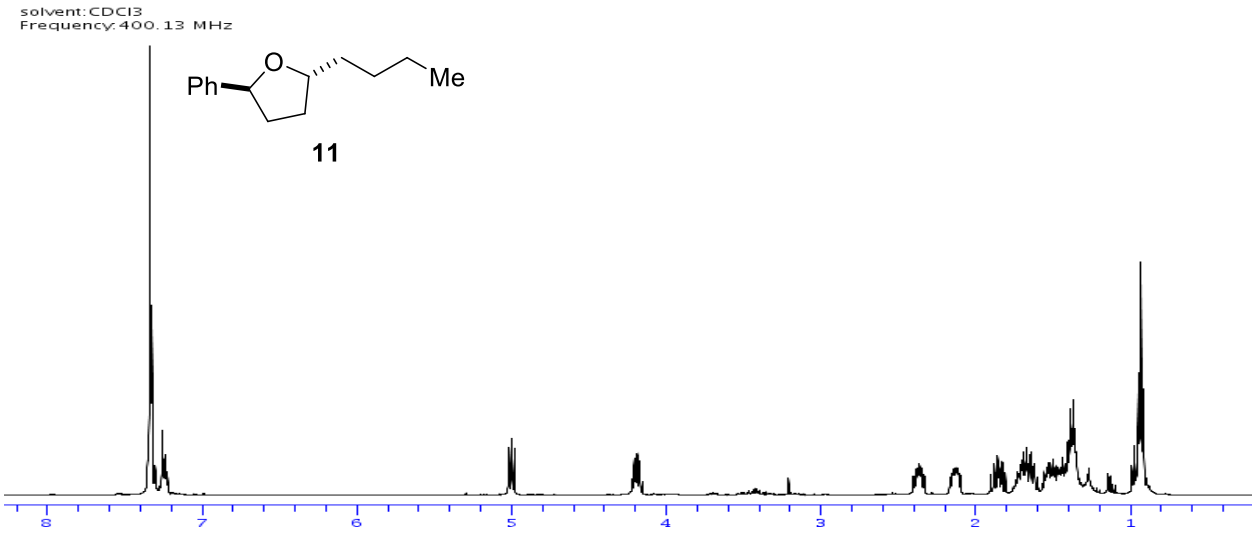
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Ph
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11
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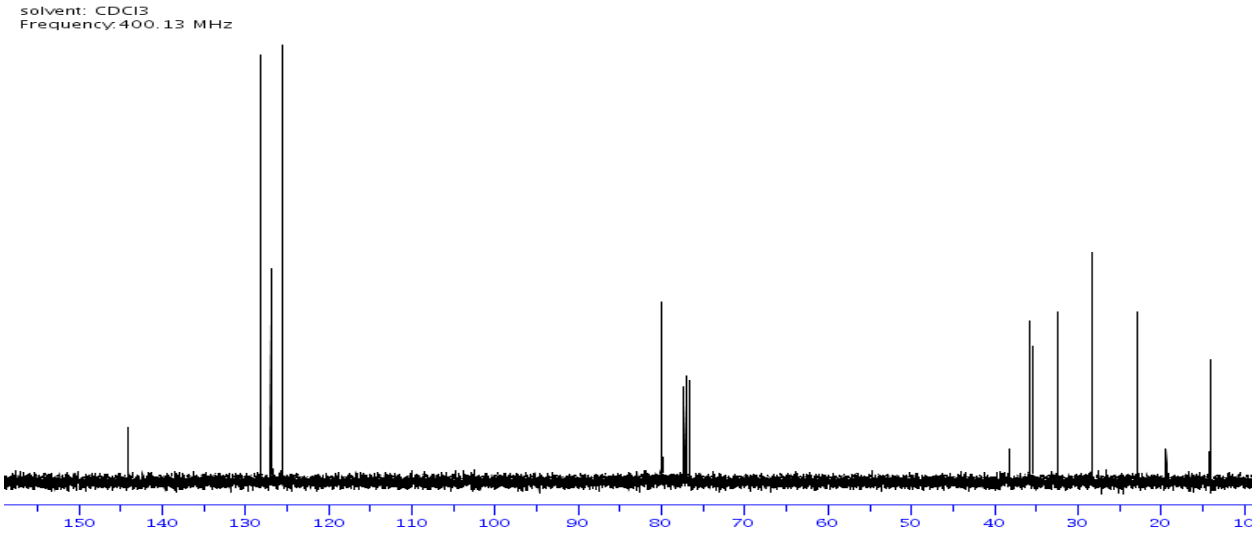
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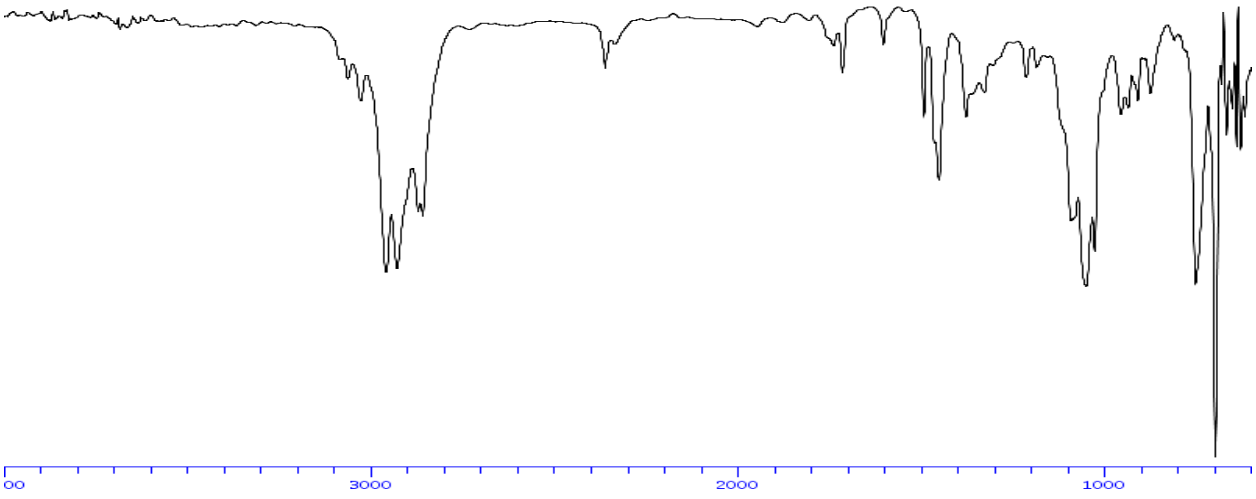
20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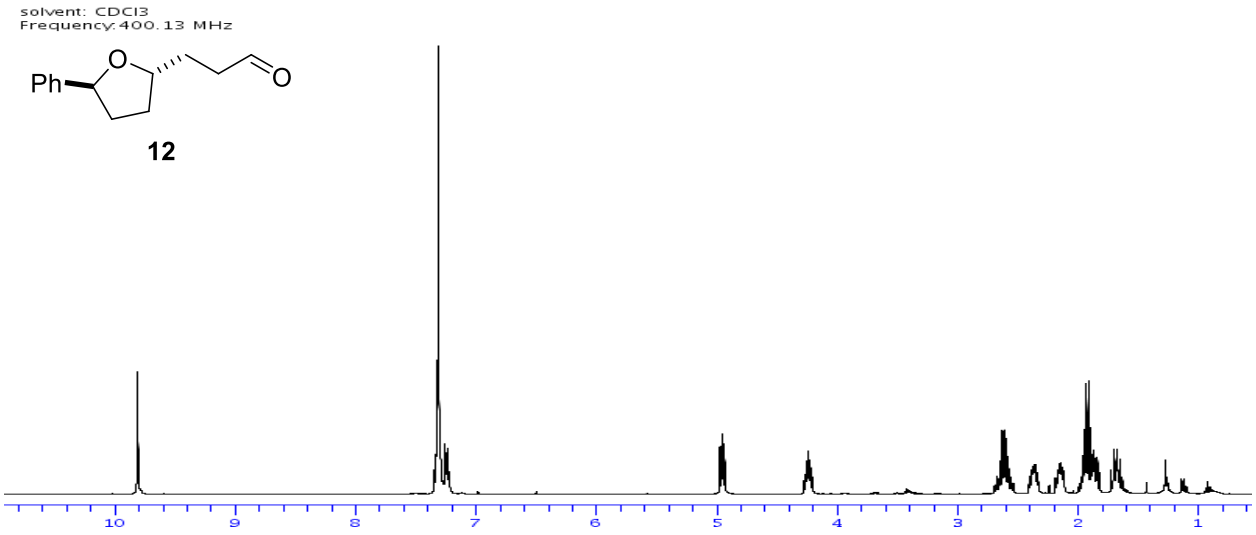
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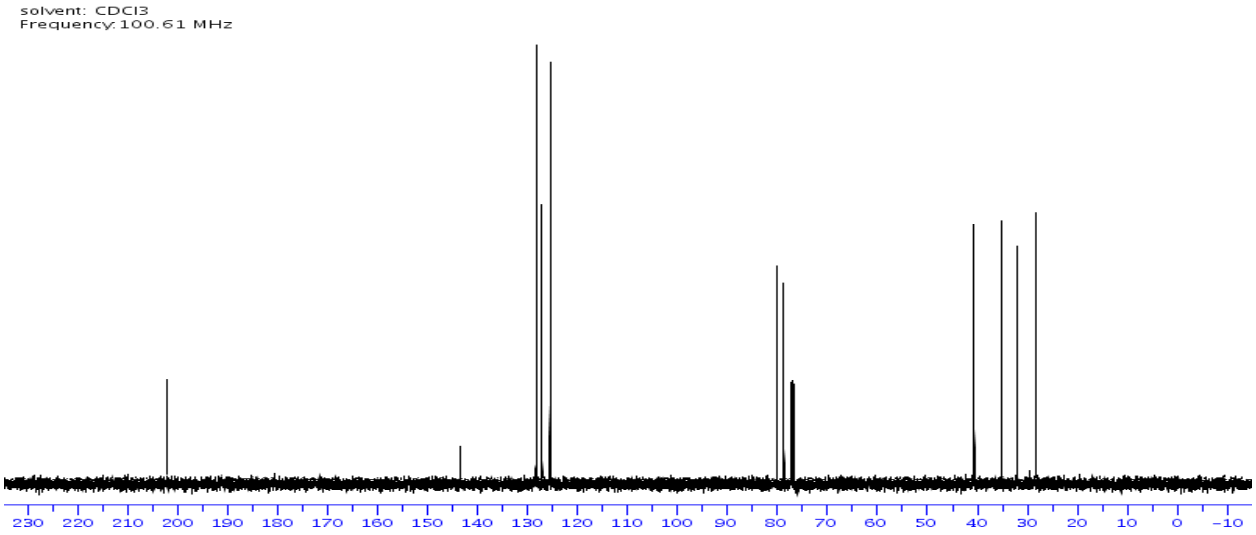
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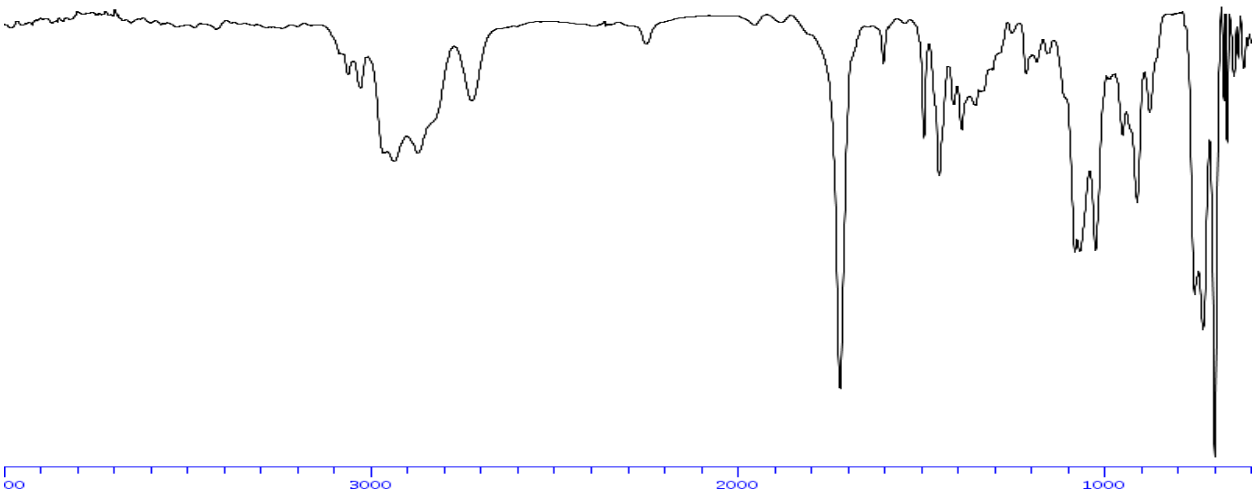
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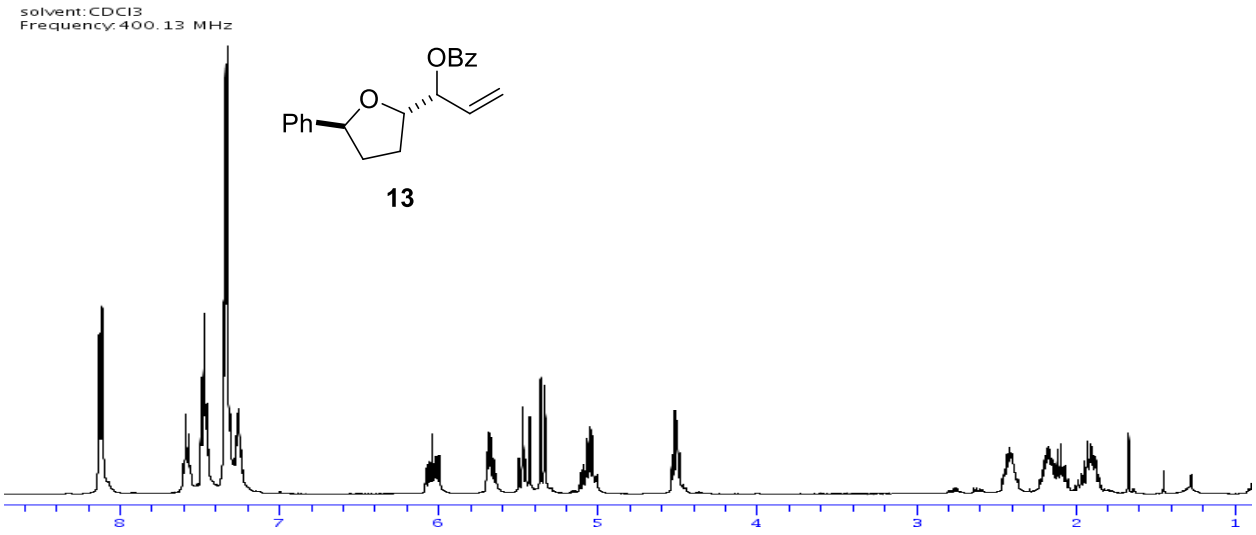
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Frequency:400.13 MHz
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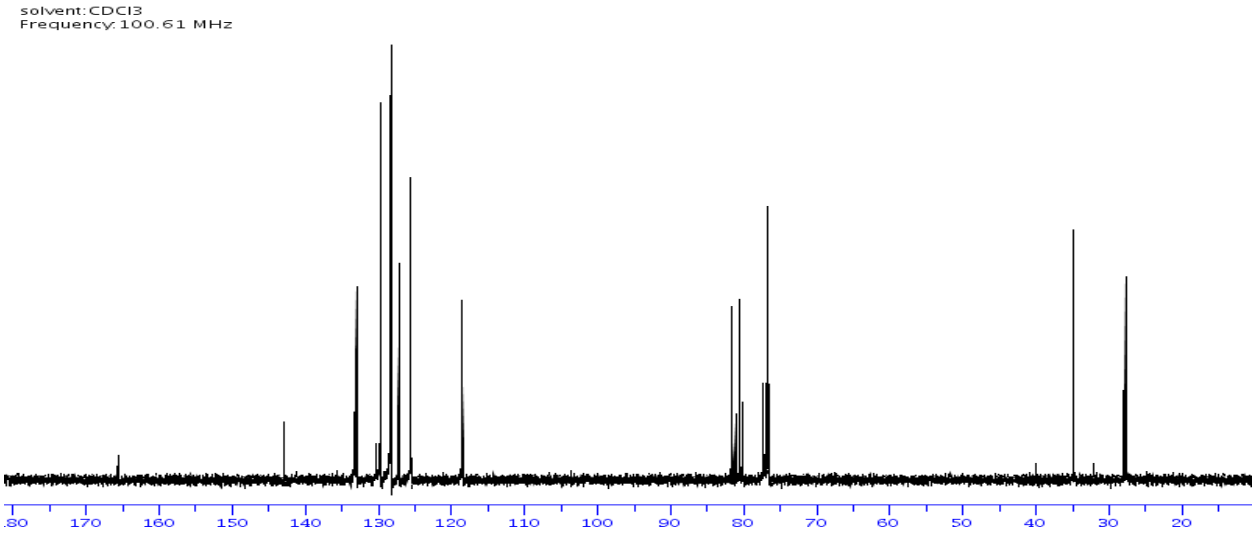
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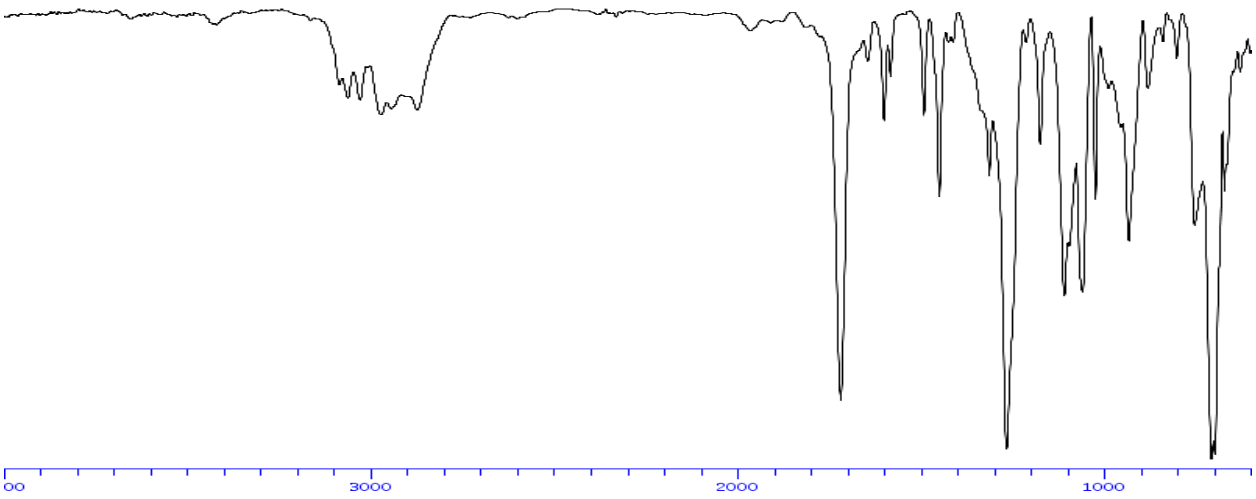
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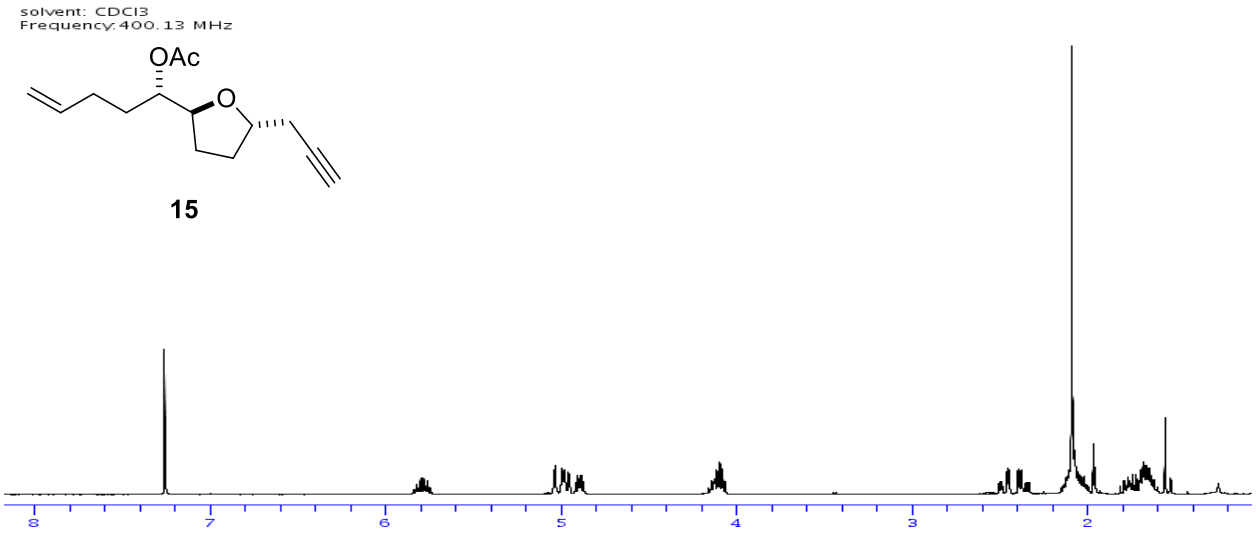
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Frequency: 400.13 MHz
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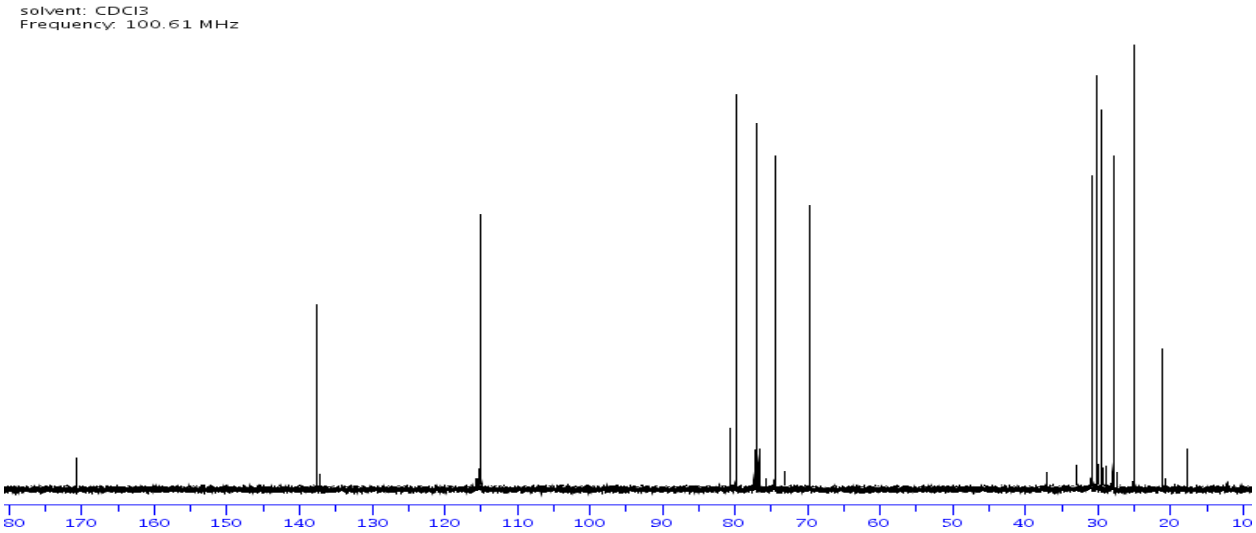
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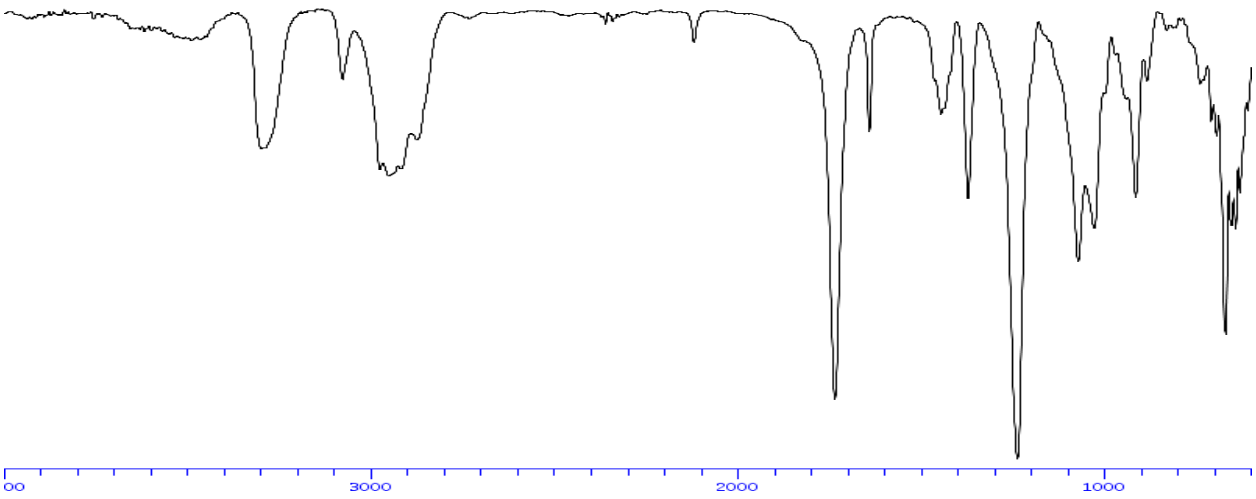
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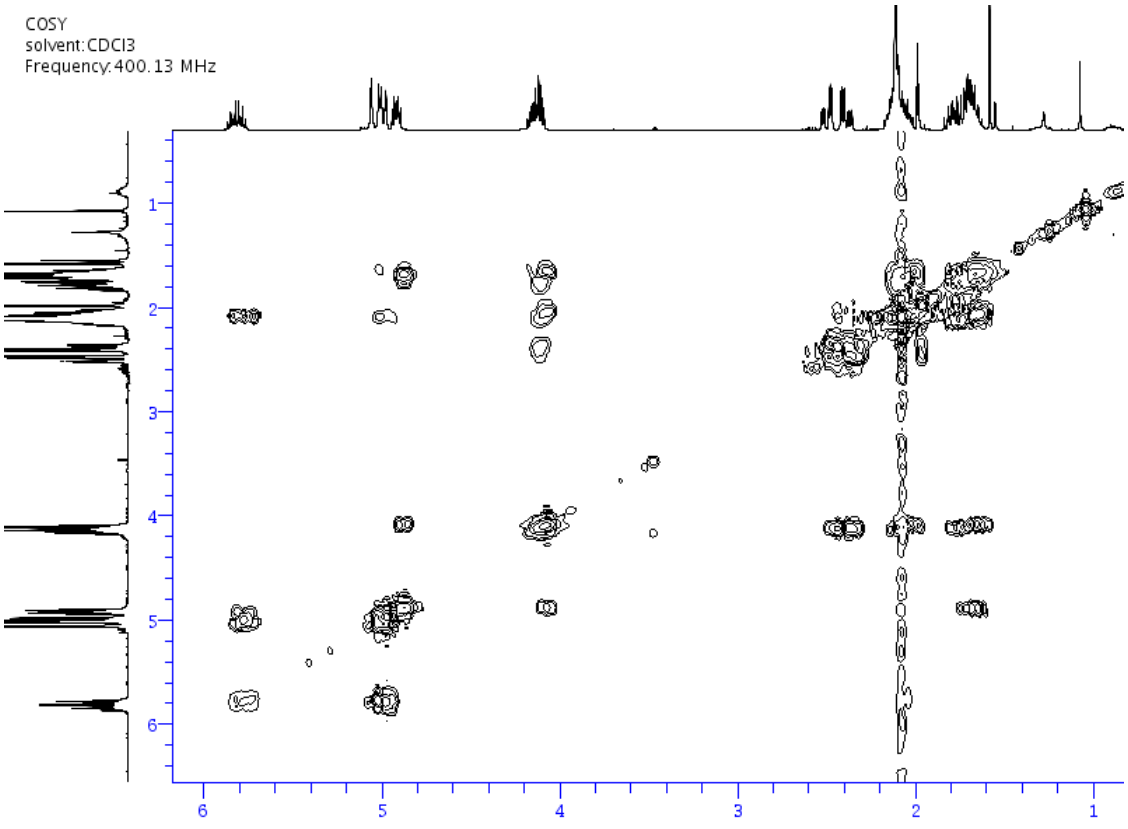
COSY
solvent:CDCl3
Frequency:400.13 MHz
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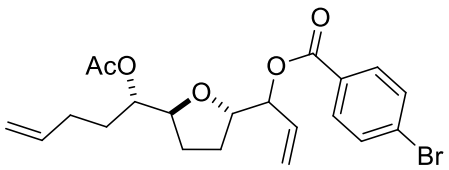
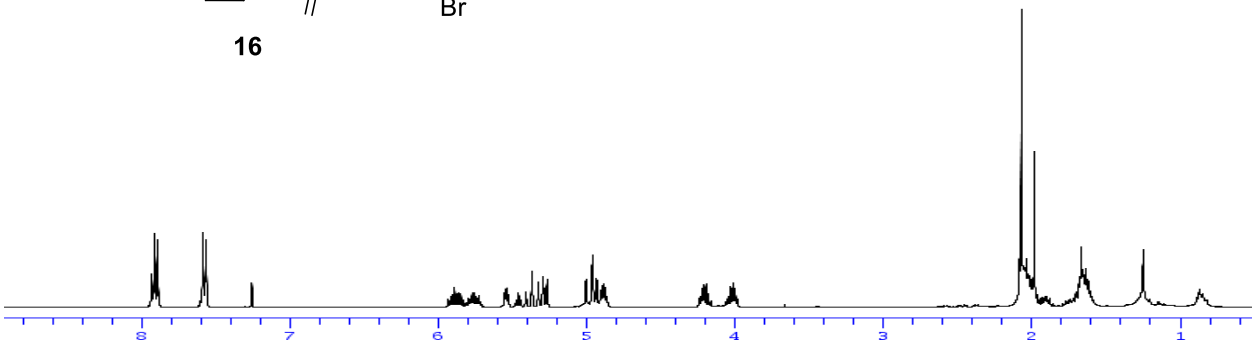
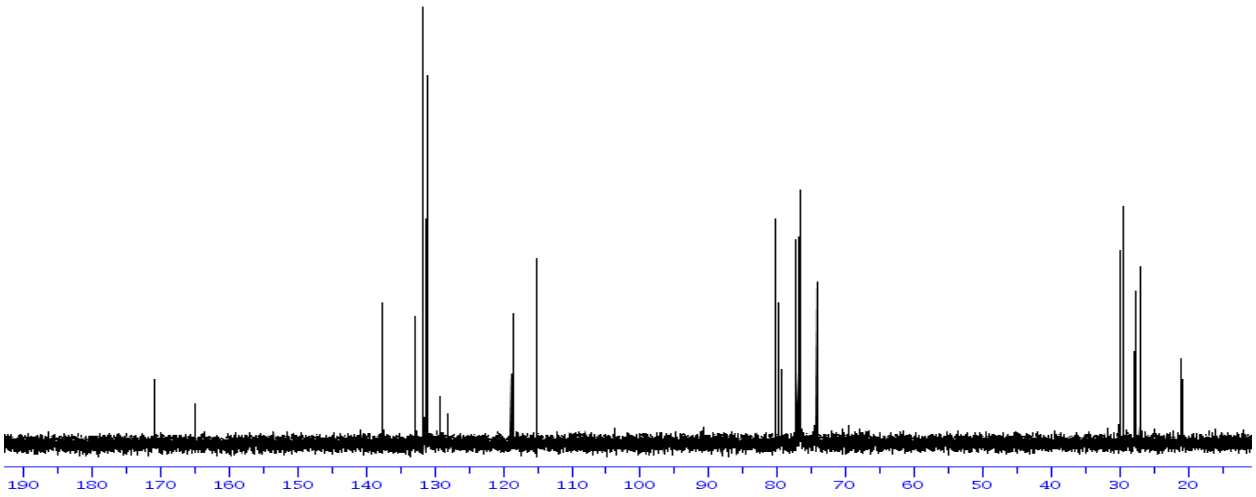
solvent:CDCl3
Frequency:400.13MHz

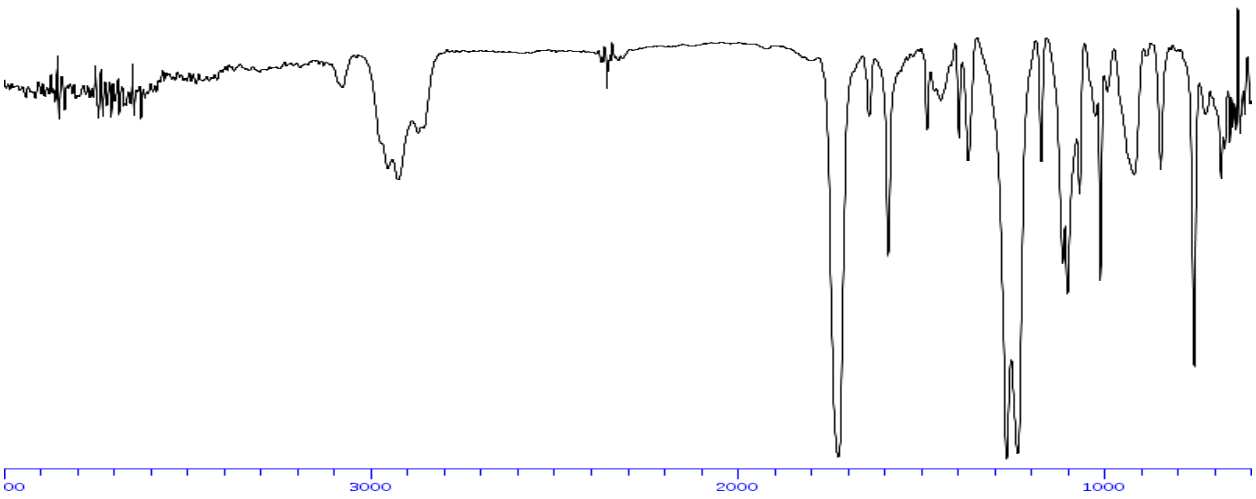


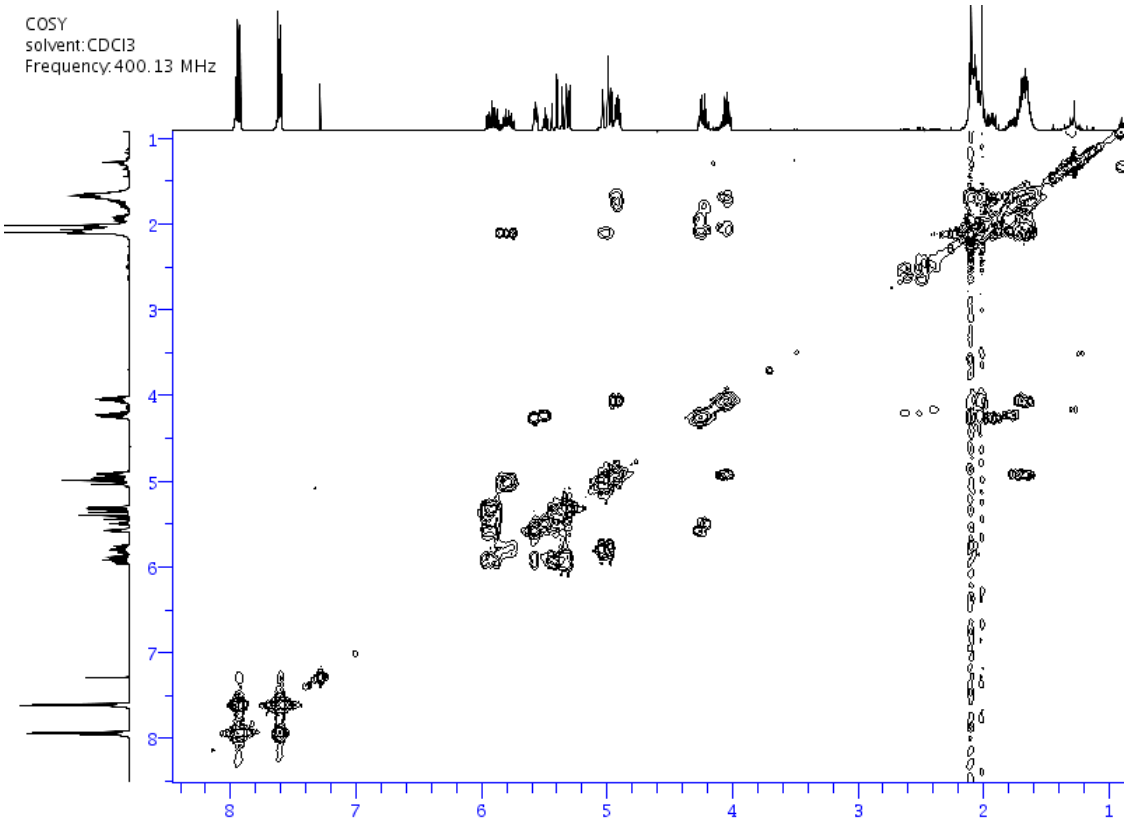
16



solvent:CDCl3
Frequency:100.61MHz






COSY
solvent:CDCl3
Frequency:400.13 MHz
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