C2-Selective Direct Alkynylation of Indoles

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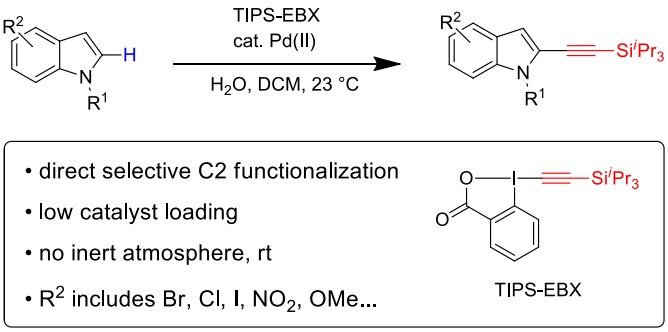
ABSTRACT



The first C2-selective alkynylation of indoles using the hypervalent iodine reagent triisopropylsilylethynyl-1,2-benziodoxol-3(*1H*)-one (TIPS-EBX) with Pd(II) as a catalyst is described. This convenient and robust method gives a single-step access to substituted alkynyl indoles with very high C2 selectivity. The reaction is orthogonal to classical Pd(0) cross-coupling reactions as it is tolerant to bromide and iodide substituents. The used silyl protecting group can be easily removed to give terminal acetylenes.

Since the first synthesis of indole by Baeyer almost 150 years ago,[1] interest in the preparation and functionalization of this privileged heterocycle has constantly grown.[2] Indoles can indeed be found in numerous important molecules such as pharmaceuticals, dyes and natural products. Consequently, methods to synthesize and modify this heterocycle are of utmost importance in organic chemistry.

Metal-catalyzed cross-coupling reactions constitute an efficient tool for the modification of aromatic rings,[3] but the need for pre-functionalization makes this method less efficient. In comparison, C-H functionalization constitutes a more direct alternative for the introduction of various valuable functional groups. Recently, the direct functionalization of indoles has been intensively examined using metal catalysts to complement traditional Friedel-Crafts reactions. Efficient methods have been developed to introduce vinyl[4], aryl,[5] alkyl[6] and cyano[7]

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(1) Baeyer, A. *Liebigs. Ann. Chem.* **1866**, 140, 295.

(2) (a) Sundberg, R.J. *Indoles*; Academic: New York, USA, 1996. (b) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2005**, *105*, 2873. (c) Humphrey, G. R.; Kuethe, J. T. *Chem. Rev.* **2006**, *106*, 2875. (d) Bandini, M.; Eichholzer, A. *Angew. Chem., Int. Ed.* **2009**, *48*, 9608. (e) Cacchi, S.; Fabrizi, G. *Chem. Rev.* **2011**, *111*, PR215-PR283.

(3) de Meijere, A.; Diedrich, F. *Metal-Catalyzed Cross-Coupling Reactions, 2nd, Completely Revised and Enlarged Edition*; Wiley-WCH: Weinheim, Germany, 2004.

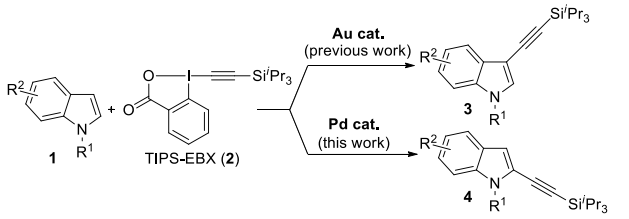
(4) Selected examples: (a) Grimster, N. P.; Gauntlett, C.; Godfrey, C. R. A.; Gaunt, M. J. *Angew. Chem., Int. Ed.* **2005**, *44*, 3125. (b) Garcia-Rubia, A.; Arrayas, R. G.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2009**, *48*, 6511. (c) Ding, Z. H.; Yoshikai, N. *Angew. Chem., Int. Ed.* **2012**, *51*,

groups among others.[8] In several cases, the C2/C3 regioselectivity of these functionalizations could be controlled by the reaction conditions or using directing groups.[4,9]

Despite the important applications of acetylenes in synthetic chemistry, biochemistry, and material sciences,[10] there are only a few methods for the direct alkynylation of the indole core.[11] In 2009, Gu and Wang first introduced the C3-selective alkynylation of indoles using bromoacetylenes and a Pd catalyst.[11a] C2-selective alkynylation is especially challenging and only two examples have been reported so far. Li and co-workers described an oxidative Heck-Cassar-Sonogashira type method for the alkynylation of 1,3-dimethylindole.[11f] This reaction could be applied to a broad scope of acetylenes, but only 3-methylindoles were reported. More recently, a method for the alkynylation of lithiated indoles using ethynylsulfonates as reagents was reported by Garcia Ruano and co-workers.[11g,h] Depending of the sterical hinderance of the substituent on the indole nitrogen, C2 or C3 alkynylation could be obtained. Nevertheless, the requirement for a strong base such as butyl lithium limited the scope of this transformation. Consequently, the most frequently used methods to access 2-alkynylated indoles are often based on the formation of the heterocycles via cyclisation reactions.[12]

In 2009, our group introduced the hypervalent iodine compound triisopropylsilylethynyl-1,2-benziodoxol-3(*1H*)-one (TIPS-EBX, **2**)[13] as an efficient reagent for the gold-catalyzed C3 alkynylation of indoles (Scheme 1). During our first investigation, palladium catalysts gave only traces of product, albeit with very high C2 selectivity.[11b] We later demonstrated that efficient acetylene transfer with Pd catalysts was possible for the amino- and oxy- alkynylation of olefins.[14] Building upon these results, we report herein the first Pd-catalyzed C2-selective alkynylation of 3H-indoles using TIPS-EBX (**2**), which proceeds at room temperature under air in presence of a broad range of functional groups (Scheme 1). In contrast to Gu and Wang's work, exclusive C2-alkynylation was observed. To the best of our knowledge, our work constitutes also the first example of Pd-catalyzed direct alkynylation of a heterocycle using a hypervalent iodine reagent.

Scheme 1. Regioselective alkynylation of indoles.



During preliminary investigations on indole itself, a broad screen of Pd catalysts, solvents and reaction conditions was not successful to improve the yield beyond 20%. More promising results were obtained in the case of N-methyl indole (**1a**) using a dichloromethane/water mixture as solvent and three equivalents of TIPS-EBX (**2**) (Table 1).[15] In this case, the reaction did not proceed without catalyst (entry 1) or with the Pd(0) source $Pd(PPh_3)_4$ (entry 2), but Pd(II) salts such as $Pd(OAc)_2$ and $PdCl_2$ gave promising yields (entries 3 and 4). A further increase in yield was observed with $Pd(MeCN)_4(BF_4)_2$, which has a less coordinating counteranion (entry 5). In this case, the importance of water was confirmed, as a lower yield was obtained under dry conditions (entry 6). The catalyst loading had a strong influence on the yield, with 2% being the optimal amount (entries 7-9). Further screening of catalysts did not lead to better yields and confirmed that the reaction did not proceed in the presence of phosphine ligands (entries 10-12). When the reaction was scaled up to 0.5 mmol, the

4698. (d) Kandukuri, S. R.; Schiffner, J. A.; Oestreich, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 1265.

(5) Selected examples: (a) Lane, B. S.; Sames, D. *Org Lett* **2004**, *6*, 2897. (b) Wang, X.; Lane, B. S.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 4996. (c) Lane, B. S.; Brown, M. A.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 8050. (d) Deprez, N. R.; Kalyani, D.; Krause, A.; Sanford, M. S. *J. Am. Chem. Soc.* **2006**, *128*, 4972. (e) Stuart, D. R.; Fagnou, K. *Science* **2007**, *316*, 1172. (f) Lebrasseur, N.; Larrosa, I. *J. Am. Chem. Soc.* **2008**, *130*, 2926. (g) Phipps, R. J.; Grimster, N. P.; Gaunt, M. J. *J. Am. Chem. Soc.* **2008**, *130*, 8172. (h) Cornella, J.; Lu, P. F.; Larrosa, I. *Org. Lett.* **2009**, *11*, 5506. (i) Potavathri, S.; Pereira, K. C.; Gorelsky, S. I.; Pike, A.; LeBris, A. P.; DeBoef, B. *J. Am. Chem. Soc.* **2010**, *132*, 14676.

(6) Jiao, L.; Bach, T. *J. Am. Chem. Soc.* **2011**, *133*, 12990.

(7) (a) Yan, G. B.; Kuang, C. X.; Zhang, Y.; Wang, J. B. *Org. Lett.* **2010**, *12*, 1052. (b) Xu, S.; Huang, X.; Hong, X.; Xu, B. *Org. Lett* **2012**, *14*, 4614.

(8) Reviews: (a) Beck, E. M.; Gaunt, M. J., Pd-Catalyzed C-H Bond Functionalization on the Indole and Pyrrole Nucleus. In *C-H Activation*, Yu, J. Q.; Shi, Z., Eds. Springer-Verlag Berlin: Berlin, 2010; Vol. 292, pp 85-121. (b) Lebrasseur, N.; Larrosa, I., Recent Advances in the C2 and C3 Regioselective Direct Arylation of Indoles. In *Advances in Heterocyclic Chemistry, Vol 105*, Katritzky, A. R., Ed. Elsevier Academic Press Inc: San Diego, 2012; Vol. 105, pp 309-351.

(9) Huestis, M. P.; Chan, L.; Stuart, D. R.; Fagnou, K. *Angew Chem, Int. Ed.* **2011**, *50*, 1338.

(10) Diedrich, F.; Stang, P. J.; Tykwinsky, R. R. *Acetylene Chemistry*; Wiley-WCH: Weinheim, Germany, **2004**.

(11) (a) Gu, Y. H.; Wang, X. M. *Tetrahedron Lett.* **2009**, *50*, 763. (b) Brand, J. P.; Charpentier, J.; Waser, J. *Angew. Chem., Int. Ed.* **2009**, *48*, 9346. (c) Brand, J. P.; Chevalley, C.; Waser, J. *Beilstein J. Org. Chem.* **2011**, *7*, 565. (d) Brand, J. P.; Chevalley, C.; Scopelliti, R.; Waser, J. *Chem. Eur. J.* **2012**, *18*, 5655. (e) de Haro, T.; Nevado, C. *J. Am. Chem. Soc.* **2010**, *132*, 1512. (f) Yang, L.; Zhao, L.; Li, C. J. *Chem. Commun.* **2010**, *46*, 4184. (g) García Ruano, J. L.; Alemán, J.; Marzo, L.; Alvarado, C.; Tortosa, M.; Díaz-Tendero, S.; Fraile, A. *Angew. Chem., Int. Ed.* **2012**, *51*, 2712. (h) García Ruano, J. L.; Alemán, J.; Marzo, L.; Alvarado, C.; Tortosa, M.; Díaz-Tendero, S.; Fraile, A. *Chem. Eur. J.* **2012**, *18*, 8414.

(12) Mothe, S. R.; Kothandaraman, P.; Lauw, S. J.; Chin, S. M.; Chan, P. W. *Chem. Eur J.* **2012**, *18*, 6133. And references herein.

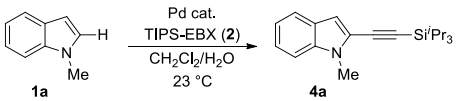
(13) TIPS-EBX is commercially avaible, and easily preparable in a two step protocol from iodobenzoic acid in high yield on a 30 g scale: Brand, J. P.; Waser, J. *Synthesis* **2012**, *44*, 1155.

(14) (a) Nicolai, S.; Erard, S.; Fernandez Gonzalez, D.; Waser, J. *Org. Lett.* **2010**, *12*, 384. (b) Nicolai, S.; Piemontesi, C.; Waser, J. *Angew. Chem., Int. Ed.* **2011**, *50*, 4680.

(15) A broad range of other solvents and additives were examined, but without positive effect on the reaction outcome. A steady improvement of the yield was observed with increasing amounts of TIPS-EBX (**2**) up to three equivalents. Other silyl substituted alkynes gave lower yields and no product was observed with aryl or alkyl substituted acetylenes. See Supporting Information for details.

alkynylation product was obtained in 66% isolated yield with $Pd(MeCN)_4(BF_4)_2$ (entry 13). In contrast to the work of Gu and Wang,[11a] only the C2-alkynylated product was isolated from the reaction mixture. This transformation consequently was the first C2-selective direct alkynylation of 3-unsubstituted indoles.

Table 1. Optimization of the C2 selective alkynylation.



1a 4a

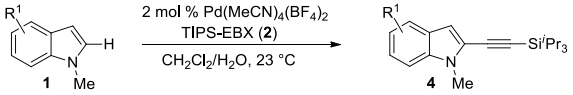
entry	catalyst loading	Pd source	yield(%)[a]
1		-	0
2	10%	$Pd(PPh_3)_4$	0
3	10%	$Pd(OAc)_2$	34
4	10%	$PdCl_2$	40
5	10%	$Pd(MeCN)_4(BF_4)_2$	50
6	10%	$Pd(MeCN)_4(BF_4)_2$	23[b]
7	25%	$Pd(MeCN)_4(BF_4)_2$	19
8	0.5%	$Pd(MeCN)_4(BF_4)_2$	37
9	2%	$Pd(MeCN)_4(BF_4)_2$	61
10	2%	$[Pd(allyl)Cl]_2$	60
11	2%	$Pd(PPh_3)_2Cl_2$	traces
12	2%	Pd_2dba_3	57
13	2%	$Pd(MeCN)_4(BF_4)_2$	66[c]

[a]0.2 mmol **1a**, 0.6 mmol **2**, 2 mL CH_2Cl_2, 0.04 mL water, overnight; GC-MS yields, using dodecanitrile as standard. [b]In dry CH_2Cl_2. [c]Isolated yield on a 0.5 mmol scale.

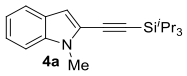
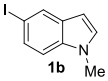
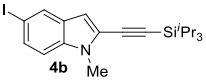
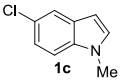
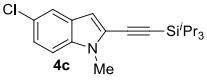
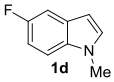
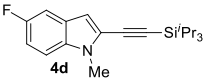
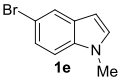
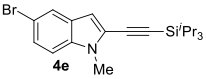
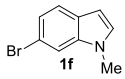
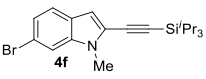
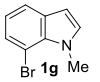
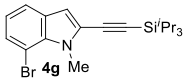
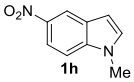
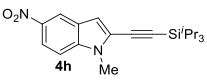
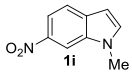
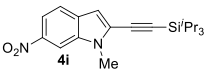
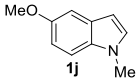
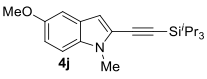
The reaction worked well with different halogens on various positions on the benzene ring (Table 2, entries 2-7), which has two main advantages. First, halogen substituents can be used to adjust the polarity, liphophilicity and metabolic stability of dyes or pharmaceuticals. Second, halogens allow further modification using cross-coupling reactions for the elaboration of molecule libraries. These results also indicated that the reaction most likely did not proceed via a Pd(0) intermediate, as oxidative addition on the carbon-halogen bond would have been expected in this case. This is an important advantage when compared with previously published methods involving Pd(0) catalysis.[11a] Furthermore, both electron-withdrawing (entries 8-9) and electron-donating (entry 10) groups were tolerated on the benzene ring.

In general, N-alkylated indoles are very important building blocks for the synthesis of bioactive compounds, in particular for natural indole alkaloids. We consequently decided to further examine the scope of alkyl groups on the nitrogen (Table 3).[16] Propylphenyl substituted indole **1k** gave 58% yield, demonstrating that the reaction was not limited to the small methyl group (entry 1). Allyl or benzyl groups on nitrogen could present a serious issue in the presence of a palladium catalyst. Nevertheless, the alkynylation products could still be obtained in moderate yields in this case (entries 2-4). Conversely, a TIPSO-ethyl and a sensitive bromo ethyl groups gave good yields, opening the door for a wide range of further synthetic modifications (entries 5-6). Finally, indole **1q**, bearing an acetal protected aldehyde, could also be alkynylated in 66% yield (entry 7).

Table 2. Scope of substituents on the benzene ring.



1 4

entry	indole	product	yield(%)[a]
1	 1a	 4a	66
2	 1b	 4b	68
3	 1c	 4c	54
4	 1d	 4d	45
5	 1e	 4e	54
6	 1f	 4f	72
7	 1g	 4g	72
8	 1h	 4h	48
9	 1i	 4i	45
10	 1j	 4j	55

[a]Isolated yields with 0.5 mmol indole **1**, 1.5 mmol (**2**), 5 mL CH_2Cl_2, 0.1 mL water, 10 µmol $Pd(MeCN)_4(BF_4)_2$.

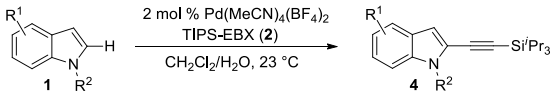
Based on precedence from other Pd-mediated transformations, in particular arylation,[5] a speculative mechanism may possibly involve a Pd(II)/(IV) cycle (Scheme 2). The reaction could be initiated by a C2-palladation to give intermediate **II**, either via direct concerted metallation-deprotonation (CMD, path **a**) [5i,17] or via electrophilic palladation at the C3 position to give **I**,

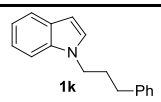
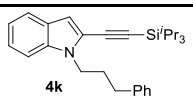
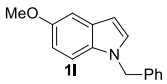
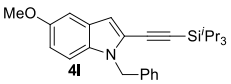
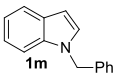
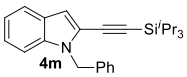
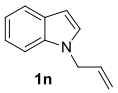
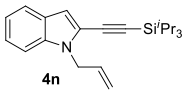
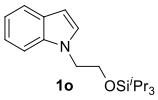
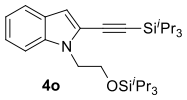
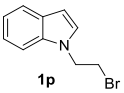
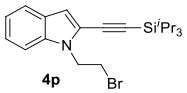
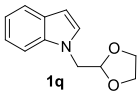
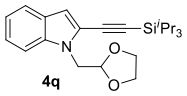
(16) The required substrates were synthesized using known procedures: (a) Guida, W. C.; Mathre, D. J. *J. Org. Chem.* **1980**, *45*, 3172. (b) Ottoni, O.; Cruz, R.; Alves, R. *Tetrahedron* **1998**, *54*, 13915. (c) Bode, J. W.; Carreira, E. M. *J. Org. Chem.* **2001**, *66*, 6410. (d) Bressy, C.; Alberico, D.; Lautens, M. *J. Am. Chem. Soc.* **2005**, *127*, 13148. (e) Jorapur, Y. R.; Jeong, J. M.; Chi, D. Y. *Tetrahedron Lett.* **2006**, *47*, 2435. See Supporting Information for further details.

(17) Lafrance, M.; Fagnou, K. *J. Am. Chem. Soc.* **2006**, *128,* 16496.

followed by Pd migration (path **b**).[5d,18] Water or water-clusters could play a key role in promoting this metallation-deprotonation step. The indole Pd complex **II** can then be oxidatively alkynylated by TIPS-EBX (**2**), to give Pd(IV) intermediate **III**,[19] which undergoes reductive elimination to give the product **4a** and regenerate the Pd(II) catalyst.

Table 3. Scope of substituents on the nitrogen.

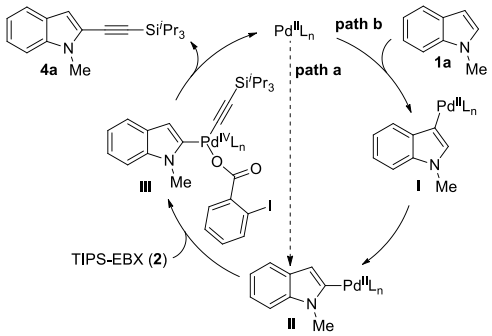


entry	indole	product	yield(%)[a]
1			58
2			41
3			41
4			44
5			68
6			61
7			66

[a]Isolated yields, 0.5 mmol indole **1**, 1.5 mmol **2**, 5 mL CH_2Cl_2, 0.1 mL water, 10 µmol $Pd(MeCN)_4(BF_4)_2$.

In conclusion, we have described the first Pd-catalyzed alkynylation of indoles proceeding with high C2 regioselectivity. The reaction is orthogonal to classical cross-coupling reactions, and has a wide range of functional group tolerance both on the indole core and the alkyl substituent on the nitrogen. The mild and neutral reaction conditions and the tolerance of the process towards air and moisture lead to a convenient method for the direct C2 alkynylation of indoles.

Scheme 2. Speculative mechanism for the alkynylation reaction.



Supporting Information. Experimental procedures and analytical data for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) Li, Y.; Wang, W.-H.; He, K.-H.; Shi, Z. J. *Organometallics* **2012**, *31*, 4397.

(19) (a) Canty, A. J.; Rodemann, T.; Skelton, B. W.; White, A. H. *Organometallics* **2006**, *25*, 3996. For a recent review on high valent metal catalysis, see: (b) Hickman, A. J.; Sanford, M. S. *Nature* **2012**, *484*, 177. The involvement of Pd(IV) or Pd(III) dimers in catalytic cycles is currently a topic of intensive discussion, see for example: (c) Powers, D. C.; Ritter, T. *Nat. Chem.* **2009**, *1*, 302. (d) Powers, D. C.; Lee, E.; Ariafard, A.; Sanford, M. S.; Yates, B. F.; Canty, A. J.; Ritter, T. *J. Am. Chem. Soc.* **2012**, *134*, 12002.

C2 Selective Direct Alkynylation of Indoles

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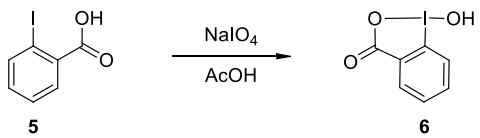
General Methods

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et_2O, CH_3CN, toluene, hexane and CH_2Cl_2 were dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 10 ppm, *Karl-Fischer* titration). All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Fluorochem, Aplichem or Merck and used without further purification, unless stated otherwise. Chromatographic purification was performed as flash chromatography using Macherey-Nagel silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F_{254} TLC aluminium plates and visualized with UV light and anisaldehyde stain. Melting points were measured on a calibrated Büchi B-540 melting point apparatus using open glass capillaries. ^{1}H-NMR spectra were recorded on a Bruker DPX-400 400 MHz spectrometer in chloroform-d and/or DMSO-d_6. All signals are reported in ppm with the internal chloroform signal at 7.26 ppm or the internal DMSO signal at 2.50 ppm as standard. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, br = broad signal, app = apparent, coupling constant(s) in Hz, integration, interpretation).^{13}C-NMR spectra were recorded with ^{1}H-decoupling on a Bruker DPX-400 100 MHz spectrometer in chloroform-d and/or DMSO-d_6. All signals are reported in ppm with the internal chloroform signal at 77.0 ppm or the internal DMSO signal at 39.5 ppm as standard. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm^{-1} (w = weak, m = medium, s = strong, br = broad). 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.

Synthesis of Reagent

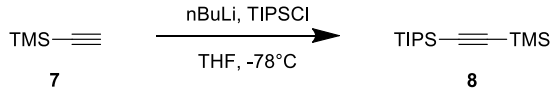
1-Hydroxy-1,2-benziodoxol-3(*1H*)-one (**6**)



5 **6**

Caution: This reaction should be carried out behind a safety shield! Following a reported procedure[1], $NaIO_4$ (77.2 g, 361 mmol, 1.0 equiv) and 2-iodobenzoic acid (**5**) (89.5 g, 361 mmol, 1.0 equiv) were suspended in 30% (v:v) aq. AcOH (700 mL) under air in a 4-neck sulfonation flask equipped with a mechanic stirrer, a thermometer and a condenser. The mixture was vigorously stirred and refluxed for 4 h. The reaction mixture was then diluted with cold water (500 mL) and allowed to cool to room temperature, protecting it from light. After 45 min, the suspension was added to water (1.5 L) and the crude product was collected by filtration, washed on the filter with ice cold water (3 x 300 mL) and cold acetone (3 x 300 mL), and air-dried in the dark overnight to give the pure product 1-hydroxy-1,2-benziodoxol-3(*1H*)-one (**6**) (77.3 g, 0.292 mol, 81% yield) as a colorless solid. ^{1}H NMR (400 MHz, $(CD_3)_2SO$) δ 8.02 (dd, *J* = 7.7, 1.4 Hz, 1 H, Ar*H*), 7.97 (m, 1 H, Ar*H*), 7.85 (dd, *J* = 8.2, 0.7 Hz, 1 H, Ar*H*), 7.71 (td, *J* = 7.6, 1.2 Hz, 1 H, Ar*H*). ^{13}C NMR (100 MHz, $(CD_3)_2SO$) δ 167.7, 134.5, 131.5, 131.1, 130.4, 126.3, 120.4. IR ν 3083 (w), 3060 (w), 2867 (w), 2402 (w), 1601 (m), 1585 (m), 1564 (m), 1440 (m), 1338 (s), 1302 (m), 1148 (m), 1018 (w), 834 (m), 798 (w), 740 (s), 694 (s), 674 (m), 649 (m).[1]

Trimethylsilyl(triisopropylsilyl)acetylene (**8**)



7 **8**

Following a modified reported procedure[2], a 4-neck 500 mL flask equipped with a thermometer, a dropping funnel, a magnetic stirrer and a nitrogen inlet was charged with trimethylsilylacetylene (**7**) (30.3 ml, 213 mmol, 1.0 equiv.) under nitrogen . THF (330 mL) was added via a dropping funnel and the solution was cooled to -78°C. ^{n}BuLi (2.5 M in hexanes, 86 mL, 0.21 mol, 0.98 equiv) was added and the reaction mixture was stirred for 5 minutes at -78°C, then warmed to 0°C and stirred for 5 minutes. ^{i}Pr$_3$SiCl (45.5 mL, 213 mmol, 1 equiv) was added dropwise via a dropping funnel at -78°C. The mixture was then allowed to warm to r.t. and stirred overnight. A saturated solution of NH_4Cl_{aq} (300 mL) was added and the reaction was extracted with Et_2O (2 x 300 mL). The organic layer was dried over $MgSO_4$, filtered and concentrated. Distillation of the crude product (1.4 mbar, 55°C) afforded trimethylsilyl (triisopropylsilyl) acetylene (**8**) (51.4 g, 203 mmol, 95%) 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).[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*propyllsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (TIPS-EBX, (2))

6 **8** **2**

Caution: This reaction should be carried out behind a safety shield![3] Following a modified reported procedure,[4] a 4-neck flat-bottom flask equipped with a thermometer, a dropping funnel, a mechanic stirrer and a nitrogen inlet was charged with 2-iodosylbenzoic acid (**6**) (26.4 g, 100 mmol, 1.0 equiv). The system was flushed with N_2 by three vacuum/N_2 cycles. Anhydrous acetonitrile (350 mL) was then canulated. The reaction mixture (white suspension) was cooled to 4°C and then trimethylsilyltriflate (20.0 mL, 110 mmol, 1.1 equiv) was added dropwise for 15 min via a dropping funnel. The dropping funnel was rinsed with anhydrous acetonitrile (10 mL). No increase of temperature was observed. The ice bath was removed and the reaction stirred for 15 min. Trimethylsilyl(tri*iso*propylsilyl)acetylene (**8**) (28.0 g, 110 mmol, 1.1 equiv) was added dropwise via dropping funnel over 15 min (the colorless suspension was converted to a yellow solution). The dropping funnel was rinsed with anhydrous acetonitrile (10 mL) and the reaction was stirred for 30 min. Then pyridine (9.9 mL, 25 mmol, 1.1 equiv) was added dropwise via a dropping funnel over 5 min. After 15 min, the reaction mixture was transferred in a one-neck 1L flask and concentrated under reduced pressure until a solid was obtained. The solid was dissolved in CH_2Cl_2 (250 mL) and transferred in a 2 L separatory funnel. The organic layer was added and washed with 1 M HCl (150 mL) and the aqueous layer was extracted with CH_2Cl_2 (250 mL). The organic layers were combined, washed with a saturated solution of $NaHCO_3$ (2x250 mL), dried over $MgSO_4$, filtered and the solvent was evaporated under reduced pressure. The resulting solid (44.8 g) was then recristallized in CH_3CN (110 mL). The colorless solid obtained over cooling down was then filtered over a Büchner funnel, washed with hexanes (2x40 mL) and dried for 1 h at 40°C at 5 mbar. TIPS-EBX (**2**) (36.2 g, 84.5 mmol, 85%) was obtained as white crystals. Mp 173-177°C (decomposition). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (m, 1 H, ArH), 8.28 (m, 1 H, ArH), 7.72 (m, 2 H, ArH), 1.13 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 166.4, 134.5, 132.3, 131.4, 131.4, 126.1, 115.6, 113.9, 64.7, 18.4, 11.1.[4]

[3] Differential scanning calorimetry showed that TIPS-EBX undergoes exothermic degradation at 187 °C.
[4] Zhdankin, V. V.; Kuehl, C. J.; Krasutsky, A. P.; Bolz, J. T.; Simonsen, A. J. J. *Org. Chem*. **1996**, *61*, 6547.

Synthesis of tetrakis(acetonitrile)palladium(II)tetrafluoroborate

Using a slight modification of a literature procedure,[5] a solution of palladium(II)chloride (0.80 g, 4.5 mmol, 1.0 equiv.) in anhydrous MeCN (40 mL, degassed by 3 "Freeze-Pump-Thaw" cycles) was prepared in a 250 mL 2-necked flask. Then $AgBF_4$ (1.7 g, 9.0 mmol, 2.0 equiv.) was added as a solid. The flask was rinsed with anhydrous MeCN (24 mL). After 1.5 h, the formed yellowish precipitate was filtered under nitrogen atmosphere. The filtrate was reduced to half of its original volume under vacuum. In order to precipitate the product, anhydrous Et_2O (120 mL) was canulated to the remaining solution. After filtration under nitrogen atmosphere and washing the solid with anhydrous Et_2O (2 x 20 mL), the remaining solid was dried under vacuum overnight to afford $Pd(MeCN)_4(BF_4)_2$ (2.1 g, 4.5 mmol, quant.) as grey solid, which was used without further purification (no difference of activity was observed compared to a recrystallized product from MeCN from another synthesis). IR 3007 (w), 2948 (w), 2352 (w), 2321 (w), 1418 (w), 1370 (w), 1287 (w), 1056 (s), 1024 (s), 964 (w), 769 (w), 623 (w). IR data corresponded to the literature values.[6]

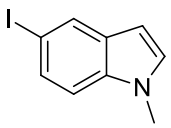
Synthesis of starting materials

1-methyl-1*H*-indole (**1a**) and 6-bromo-1-methyl-1*H*-indole (**1f**) are commercially available.

General procedure for methylation of indoles:

The indole (1 equiv., 0.6 - 6.4 mmol, 200 - 1000 mg) was dissolved in dry THF in a 10 or 25 mL round-bottomed flask to give a 0.3 M solution. Sodium hydride (60% in mineral oil, 1.5 equiv.) was slowly added under a N_2 flow at 0 °C to give a suspension. After stirring for 15 min at 0°C the reaction mixture was allowed to warm to r.t.. After 1.5 h it was cooled back to 0°C and methyl iodide (1.3 equiv.) was added. The mixture was then warmed up to r.t. and stirred overnight. After cooling back to 0°C, it was quenched with water (10 mL), extracted with Et_2O (3 x 10 mL), the organic layer was dried over $MgSO_4$, filtered and then the solvent was evaporated under reduced pressure. The residue was purified via flash column chromatography (Hex:EtOAc 1:99-20:80), and recrystallized from hexane to give the N-methylated indole.

5-Iodo-1-methyl-1*H*-indole (1b)

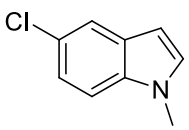


Starting from 5-iodo-1*H*-indole (1.00 g, 4.11 mmol), 5-iodo-1-methyl-1*H*-indole (**1b**) (0.768 g, 2.99 mmol, 73 % yield) was obtained as a white solid. R_f: 0.65 (hexanes:EtOAc 10:1). Mp: 76-78°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (s, 1 H, ArH), 7.49 (d, 1 H, *J* = 8.6 Hz, ArH), 7.13 (d, 1 H, *J* = 8.6 Hz, ArH), 7.04 (s, 1 H, ArH), 6.43 (s, 1 H, ArH), 3.80 (s, 3 H, Me). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.8, 131.0, 129.8, 129.7, 129.6, 111.3, 100.3, 82.9, 33.0. IR 3093 (w), 3053 (w), 2940 (w), 2919 (w), 2886 (w),

[5] Werner, H.; Bertleff, W.; Schubert, U., *Inorg. Chim. Acta*. **1980**, *43*, 199.
[6] Wayland, B. B.; Schramm, R. F. *Inorg. Chem.* **1969**, *8*, 971.

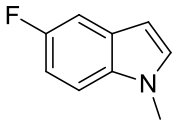
2876 (w), 2856 (w), 1557 (m), 1510 (s), 1473 (s), 1432 (m), 1420 (s), 1379 (w), 1329 (m), 1277 (s), 1242 (s), 1193 (w), 1151 (w), 1103 (m), 1079 (m), 1045 (w), 1007 (m), 888 (s), 868 (m). HRMS (ESI) calcd for $C_9H_9IN^+$ $[M+H]^+$ 257.9774; found 257.9776. NMR data is corresponding to the reported values.[7]

5-Chloro-1-methyl-1H-indole (1c)



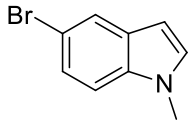
Starting from 5-chloro-1*H*-indole (364 mg, 2.40 mmol), 5-chloro-1-methyl-1*H*-indole (**1c**) (268 mg, 1.62 mmol, 81 % yield) was obtained as a white solid. R_f: 0.60 (hexanes:EtOAc 10:1). Mp: 33-34°C, Lit 35°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 (dd, 1 H, *J* = 1.9, 0.5 Hz, ArH), 7.19-7.30 (m, 2 H), 7.10 (d, 1 H, *J* = 3.1 Hz, ArH), 6.47 (dd, 1 H, *J* = 3.1, 0.7 Hz, ArH), 3.80 (s, 3 H, Me). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.1, 130.1, 130.1, 125.1, 121.8, 120.2, 110.2, 100.6, 33.1. IR 3102 (w), 2943 (w), 2913 (w), 2881 (w), 2817 (w), 1567 (w), 1513 (m), 1475 (s), 1441 (m), 1421 (s), 1379 (w), 1331 (m), 1278 (s), 1241 (s), 1199 (m), 1146 (m), 1106 (w), 1082 (m), 1063 (s), 1009 (m), 909 (m), 870 (m), 869 (m). HRMS (ESI) calcd for $C_9ClH_9N^+$ $[M+H]^+$ 166.0418; found 166.0423. The NMR spectroscopic data is in accordance to those ones reported.[8]

5-Fluoro-1-methyl-1*H*-indole (1d)



Starting from 5-fluoro-1*H*-indole (541 mg, 4.00 mmol), purification by column chromatography (SiO_2, hexane) gave pure 5-fluoro-1-methyl-1*H*-indole (**1d**) (536 mg, 3.59 mmol, 90 % yield) as a white solid. R_f: 0.70 (hexanes:EtOAc 10:1). Mp: 51-53°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.31 (dd, 1 H, *J* = 9.7, 2.4 Hz, ArH), 7.26 (m, 1 H ArH), 7.12 (d, 1 H, *J* = 3.1 Hz, ArH), 7.01 (1 H, dt, *J* =9.1, 2 Hz, ArH), 6.48 (dd, 1 H, *J* = 3.1, 0.7 Hz, ArH). 3.81 (s, 3 H, Me) ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.0 (d, *J* C-F = 232 Hz), 133.4, 130.4, 128.7 (d, *J* C-F = 10 Hz), 109.9 (d, *J* C-F = 15 Hz), 109.8, 105.5 (d, *J* C-F = 23 Hz), 100.8 (d, *J* C-F = 5 Hz), 33.1. IR 3104 (w), 2946 (w), 2922 (w), 2907 (w), 2887 (w), 2362 (w), 2343 (w), 1626 (w), 1576 (w), 1514 (m), 1492 (s), 1449 (m), 1423 (m), 1340 (m), 1283 (m), 1238 (s), 1228 (s), 1140 (m), 1129 (m), 1122 (m), 1100 (m), 1081 (m), 1013 (w), 949 (m), 859 (m), 811 (s). ^{1}H NMR is corresponding to the literature data. [9]

5-Bromo-1-methyl-1*H*-indole (1e)



Starting from 5-bromo-1*H*-indole (294 mg, 1.50 mmol), 5-bromo-1-methyl-1*H*-indole (**1e**) (229 mg, 1.10 mmol, 73%) was obtained as an off-white solid. R_f: 0.45 (hexanes:EtOAc 10:1). Mp. 40-41°C, Lit.:41°C.[8] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, 1 H, *J* = 1.7 Hz, ArH), 7.19 (m, 1 H, ArH), 7.07 (d, 1 H, *J* = 8.7 Hz, ArH), 6.93 (d, 1 H, *J* = 3.1 Hz, ArH), 6.32 (dd, 1 H, *J* = 3.1, 0.8 Hz, ArH), 3.64 (s, 3 H, C*H*$_3$). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.4, 130.1, 130.0, 124.3, 123.3, 112.7, 110.7, 100.6, 33.0. IR 3101 (w), 3065 (w), 2983 (w), 2947 (w), 2917 (w), 2869 (w), 2842 (w), 1606 (w), 1557 (m), 1517 (w), 1486 (m), 1468 (m), 1445 (m), 1422 (w), 1421 (w), 1408 (m), 1384 (w), 1353 (w), 1334 (m), 1320 (s), 1302 (s), 1266 (w), 1216 (m), 1200 (w), 1139 (w), 1100 (s), 1087 (m), 1071 (w), 1052 (w), 1011 (w), 951 (w), 917 (m), 882 (w), 853 (w), 832 (w), 814 (m). HRMS (ESI)

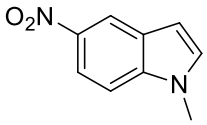
[7] René, O.; Fagnou, K. *Org. Lett.* **2010**, *12*, 2116.
[8] Klare, H. F.; Oestreich, M.; Ito, J.; Nishiyama, H.; Ohki, Y.; Tatsumi, K. *J. Am. Chem. Soc.* **2011**, *133*, 3312.5
[9] Xu, X.-H.; Liu, G.-K.; Azuma, A.; Tokunaga, E.; Shibata, N. *Org. Lett.* **2011**, *13*, 4854.

calcd for $C_9{}^{79}BrH_9N^+$ $[M+H]^+$ 209.9913; found 209.9901. The NMR corresponds to the reported data.[10]

7-Bromo-1-methyl-1*H*-indole (1g)

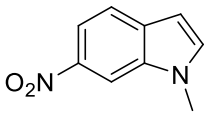
Starting from 7-bromo-1*H*-indole (392 mg, 2.00 mmol), 7-bromo-1-methyl-1*H*-indole (**1g**) (385mg, 1.833 mmol, 92 % yield) was obtained as white solid. R_f: 0.80 (hexanes:EtOAc 10:1). Mp 46-48°C, Lit 52°C.[10] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.57 (dd, *J* = 7.8, 1.0 Hz, 1 H, ArH), 7.37 (dd, 1 H, *J* = 7.4, 0.4 Hz, ArH), 7.03 (d, 1 H, *J* = 3.1 Hz, ArH), 6.95 (t, 1 H, *J* = 7.7 Hz, ArH), 6.49 (d, 1 H, *J* = 3.1 Hz, ArH), 4.19 (s, 3 H, Me).^{13}C NMR (101 MHz, $CDCl_3$) δ 133.1, 131.8, 131.7, 126.6, 120.5, 120.4, 103.9, 101.2, 36.9. IR 3100 (w), 3066 (w), 3065 (w), 2947 (w), 2920 (m), 2854 (w), 1557 (m), 1517 (w), 1487 (m), 1467 (m), 1445 (m), 1408 (m), 1335 (m), 1320 (s), 1303 (s), 1216 (m), 1200 (w), 1101 (s), 1087 (w), 1052 (w), 917 (m), 815 (m). HRMS (ESI) calcd for $C_9{}^{79}BrH_9N^+$ $[M+H]^+$ 209.9913; found 209.9912. The NMR corresponds to the reported data.[10]

1-Methyl-5-nitro-1*H*-indole (1h)



Starting from 5-nitro-1*H*-indole (1.00 g, 6.17 mmol), 1-methyl-5-nitro-1*H*-indole (**1h**) (0.789 g, 4.48 mmol, 73 % yield) was obtained as yellow crystals. R_f: 0.20 (hexanes:EtOAc 10:1). Mp.: 170-172°C, Lit.: 169°C.[11] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.60 (d, 1 H, *J* = 2.2 Hz, ArH), 8.14 (dd, 1 H, *J* = 9.1, 2.2 Hz, ArH), 7.36 (d, 1 H, *J* = 9.1 Hz, ArH), 7.23 (d, 1 H, *J* = 3.2 Hz, ArH), 6.69 (dd, 1 H, *J* = 3.2, 0.8 Hz, ArH), 3.88 (s, 3 H, Me) ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.9, 135.3, 134.6, 133.3, 120.7, 114.8, 106.4, 102.2, 33.3. IR 3104 (w), 2946 (w), 2936 (w), 2926 (w), 2919 (w), 2904 (w), 1614 (w), 1580 (w), 1519 (s), 1481 (m), 1466 (m), 1465 (m), 1398 (w), 1333 (s), 1285 (m), 1243 (m), 1067 (m), 895 (w), 813 (w). HRMS (ESI) calcd for $C_9H_9N_2O_2^+$ $[M+H]^+$ 177.0659; found 177.0662. The NMR corresponds to the literature data.[12]

1-Methyl-6-nitro-1*H*-indole (1i)



Starting from 6-nitro-1*H*-indole (649 mg, 4.00 mmol), 1-methyl-6-nitro-1*H*-indole (**1i**) (298 mg, 1.69 mmol, 42 % yield) was obtained as yellow needles. R_f: 0.30 (hexanes:EtOAc 10:1). Mp.: 78-80°C. Lit: 77°C.[13] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.32 (d, 1 H, *J* = 1.8 Hz), 8.02 (dd, 1 H, *J* = 8.8, 2.0 Hz, ArH), 7.66 (d, 1 H, *J* = 8.8 Hz, ArH), 7.36 (d, 1 H, *J* = 3.1 Hz, ArH), 6.61 (dd, 1 H, *J* = 3.0, 0.8 Hz, ArH), 3.91 (s, 3 H, Me). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.9, 135.3, 134.6, 133.3, 120.7, 114.8, 106.4, 102.2, 33.3. IR 3135 (w), 3122 (w), 3103 (w), 3079 (w), 2938 (w), 2909 (w), 2885 (w), 2813 (w), 1610 (w), 1584 (w), 1498 (s), 1463 (m), 1419 (m), 1408 (m), 1362 (m), 1335 (s), 1324 (s), 1300 (s), 1288 (s), 1235 (m), 1215 (w), 1134 (s), 1085 (w), 1063 (m), 933 (w), 880 (w), 843 (m), 817 (m). HRMS (ESI) calcd for $C_9H_9N_2O_2^+$ $[M+H]^+$ 177.0659; found 177.0659. The NMR corresponds to the literature data.[14]

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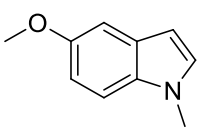
[10] Stadlwieser, J. F.; Dambaur, M. E. *Helv. Chim. Acta* **2006**, *89*, 936.
[11] Challis, B. C.; Lawson, A. J. *J. Chem Soc., Perkin Trans. 2* **1973**, 918.
[12] US patent, WO2009/42907, **2009**.
[13] Coullet, F.; Morel, S.; Boyer, G.; Galy, J. P. *Synth. Commun.* **1998**, *28*, 147.
[14] Lane, B. S.; Brown, M. A.; Sames, D. *J. Am. Chem. Soc.* **2005**, *127*, 8050.

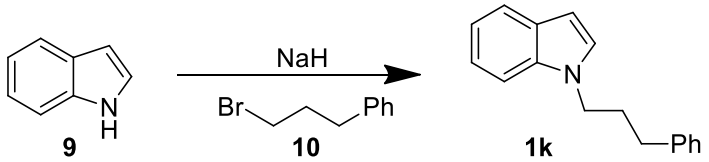
5-Methoxy-1-methyl-1*H*-indole (1j)



Starting from 5-methoxy-1*H*-indole (221 mg, 1.50 mmol) 5-methoxy-1-methyl-1*H*-indole (104 mg, 0.645 mmol, 43 % yield) was obtained as white crystals. R_f: 0.60 (hexanes:EtOAc 10:1). Mp.: 99-102°C, Lit.: 102-103°C.[15] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30 (d, 1H, *J* = 8.5 Hz, ArH) 7.13 (s, 1 H, ArH), 7.05 (s, 1 H, ArH), 6.92 (d, 1 H, *J* = 8.8 Hz, ArH), 6.43 (d, 1 H, *J* = 1.0 Hz, ArH), 3.90 (s, 3 H), 3.80 (s, 3 H, Me). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.0, 132.2, 129.3, 128.8, 111.9, 109.9, 102.5, 100.4, 55.9, 33.0. IR 2952 (w), 2918 (w), 2834 (w), 1622 (m), 1608 (w), 1577 (w), 1496 (s), 1459 (w), 1450 (m), 1449 (m), 1421 (s), 1347 (w), 1293 (w), 1243 (s), 1191 (m), 1152 (s), 1102 (w), 1026 (m), 942 (w), 855 (m), 845 (w), 805 (s). HRMS (ESI) calcd for $C_{10}H_{12}NO^+$ $[M+H]^+$ 162.0913; found 162.0914. The NMR corresponds to the spectral data from literature.[16]

Other N substituted indoles

1-(3-phenylpropyl)-1*H*-indole (1k)

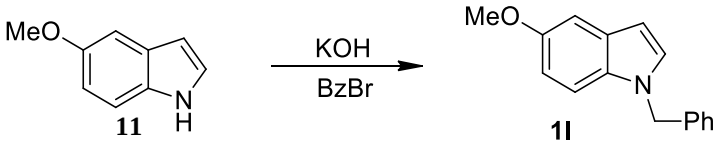


Following a reported procedure,[17] in an oven-dried 10 mL round-bottomed flask 1*H*-indole (**9**) (0.644 g, 5.50 mmol, 1.1 equiv.) was dissolved in THF (5 mL) to give a colorless solution. Sodium hydride (60% in mineral oil, 0.240 g, 6.00 mmol, 1.2 equiv.) was added at 0°C and the reaction mixture was stirred for 30 min. (3-bromopropyl) benzene (**10**) (0.644 mL, 5.00 mmol, 1 eq.) was added dropwise. After 15 min the ice bath was removed and the reaction mixture was stirred for additional 4 hours, until there was no alkylating reagent (**10**) left according to TLC (Rf: 1.0, Hexanes:EtOAc 10:1) The reaction was cooled back to 0°C, quenched with water, diluted with EtOAc (10 mL), extracted with water (2 x 10 mL), washed with brine (10 mL) and dried over $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure. The crude product was purified by column chromatography (SiO_2, hexane:EtOAc 1% to 10%) to give a colorless oil. This oil was then distillated (short path, Kugelrohr, 0.4 mbar, 167-173°C) to remove the 1,3-bis-alkylated indole. 1-(3-phenylpropyl)-1H-indole (**1k**) (0.794 g, 3.37 mmol, 68 % yield) was obtained as a colorless oil. R_f: 0.75 (hexanes:EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (d, 1 H, *J* = 8 Hz, ArH), 7.53-7.23 (m, 9 H, ArH), 6.72 (dd, 1 H, *J* = 3.1, 0.8 Hz, ArH), 4.26 (t, 2 H, *J* = 7.1 Hz, CH_2), 2.77 (t, 2 H, *J* = 8Hz, CH_2), 2.34 (qi, 2 H, *J* = 7.8 Hz, -CH_2-C*H*$_2$-CH_2-). ^{13}C NMR (101 MHz, $CDCl_3$) δ 141.2, 136.2, 128.7, 128.7, 128.6, 128.0, 126.3, 121.6, 121.2, 119.5, 109.6, 101.3, 45.8, 33.2, 31.7. IR 3085 (w), 3057 (w), 3026 (w), 3004 (w), 2946 (w), 2945 (w), 2870 (w), 1780 (w), 1738 (s), 1717 (s), 1612 (w), 1603 (w), 1511 (m), 1497 (m), 1483 (m), 1464 (s), 1455 (s), 1400 (m), 1377 (s), 1354 (s), 1336 (s), 1315 (s), 1254 (s), 1207 (s), 1179 (m), 1166 (m), 1143 (m), 1143 (m), 1122 (m), 1114 (m), 1080 (m), 1031 (m), 1020 (m), 1004 (w), 952

[15] Flaugh, M. E.; Crowell, T. A.; Clemens, J. A.; Sawyer, B. D. *J. Med. Chem.* **1979**, *22*, 63.
[16] US patent, US2004/59131 A1, **2004**.

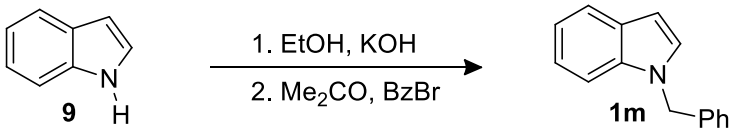
(w), 928 (w), 909 (w), 885 (m), 855 (w), 838 (w), 821 (w), 811 (w), 802 (w). HRMS (ESI) calcd for $C_{17}H_{18}N^+$ $[M+H]^+$ 236.1434; found 236.1440. The NMR spectra correspond to the literature.[17]

1-Benzyl-5-methoxy-1*H*-indole (1l)



Following a reported method,[18] 5-methoxy-1*H*-indole (**11**) (300 mg, 2.04 mmol, 1 equiv.) was dissolved in dry EtOH (17 mL), to give a pale yellow solution. KOH (143 mg, 2.60 mmol, 1.25 equiv.) was added, and the reaction mixture was stirred until the base was dissolved. The solvent was evaporated under reduced pressure. The residue was dissolved in 17 mL acetone to give an orange solution. Then benzyl-bromide (244 µl, 349 mg, 2.04 mmol, 1 equiv.) was added, while a white solid precipitated from the mixture. The reaction was stirred for 15 min, then the solid was filtered off, the liquid was concentrated, and purified by column chromatography (SiO_2, 5% Et_2O in pentane), to give 1-benzyl-5-methoxy-1*H*-indole (**1l**) (199 mg, 0.839 mmol, 41%) as a yellowish solid. R_f: 0.33 (5% Et_2O in pentane). Mp.: 69-72 °C Lit: 66-68 °C.[19] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.24 (m, 3 H, ArH), 7.20-7.09 (m, 5 H, ArH), 6.85 (ddd, 1 H, *J* = 8.8, 2.5, 0.3 Hz, ArH), 6.49 (dd, 1 H, *J* = 3.1, 0.8 Hz, ArH), 5.31 (s, 2 H, Bz CH_2), 3.86 (s, 3 H, OCH_3). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.1, 137.6, 129.1, 128.9, 128.8, 127.6, 126.7, 112.0, 110.5, 102.6, 101.2, 55.9, 50.3.[20] IR 3063 (w), 3030 (w), 2995 (w), 2935 (w), 2917 (w), 2853 (w), 2853 (w), 2852 (w), 2831 (w), 1622 (w), 1576 (w), 1486 (s), 1448 (m), 1398 (w), 1356 (w), 1347 (w), 1297 (w), 1255 (m), 1238 (s), 1192 (w), 1183 (w), 1149 (s), 1132 (m), 1030 (m), 836 (w), 797 (m), 752 (m), 718 (s), 717 (s), 705 (s), 704 (s), 627 (w). NMR is corresponding to the one in the literature.[19]

1-Benzyl-1*H*-indole (1m)

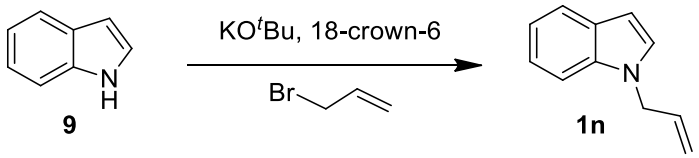


Following a reported method,[18] 1*H*-indole (**9**) (1.17 g, 10.0 mmol, 1.00 equiv.) was dissolved in ethanol (50 mL). KOH (566 mg, 10.0 mmol, 1.00 equiv.) was added and the reaction mixture was stirred until the base dissolved. The solvent was evaporated under reduced pressure. The residue was dissolved in acetone (30 mL), and benzyl bromide was added dropwise, an exothermic reaction and precipitation was observed. After stirring for 30 minutes, the solid was filtered off. The liquid was concentrated under vacuum, and purified via column chromatography to give 1-benzyl-1*H*-indole (**1m**) (586 mg, 28% yield) as a white solid. R_f: 0.75 (hexanes:EtOAc 10:1) Mp.: 42-43°C, Lit: 41-43°C,[21] ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, 1 H, *J* = 7.7 Hz, ArH),

[17] Jorapur, Y. R.; Jeong, J. M.; Chi, D. Y. *Tetrahedron Lett.* **2006**, *47*, 2435.
[18] Ottoni, O.; Cruz, R.; Alves, R. *Tetrahedron* **1998**, *54*, 13915.
[19] Evans, D. A.; Scheidt, K. A.; Fandrick, K. R.; Lam, H. W.; Wu, J. *J. Am. Chem. Soc.* **2003**, *125*, 10780.
[20] One Carbon signal was not resolved.
[21] Gribble, G. W.; Leiby, R. W.; Sheehan, M. N. *Synthesis* **1977**, 856.

7.41-7.09 (m, 9 H, ArH), 6.59 (d, 1 H, *J* = 5 Hz, ArH), 5.35 (s, 2 H, Bz CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.6, 136.3, 128.8, 128.3, 127.6, 126.8, 121.7, 121.0, 119.6, 109.7, 101.7, 50.1. IR 3099 (w), 3087 (w), 3086 (w), 3056 (w), 3030 (w), 3029 (w), 2919 (w), 2858 (w), 1613 (w), 1612 (w), 1512 (s), 1496 (m), 1485 (m), 1464 (s), 1455 (s), 1439 (m), 1398 (m), 1357 (s), 1335 (s), 1318 (s), 1302 (s), 1256 (m), 1235 (w), 1208 (w), 1197 (m), 1182 (s), 1079 (w), 1062 (w), 1046 (w), 1030 (m), 1012 (m), 884 (w), 842 (w), 822 (w). MS (ESI) calcd for $C_{15}H_{14}N^+$ $[M+H]^+$ 208.1121; found 208.1122, The NMR spectral data is the same as in the literature.[22]

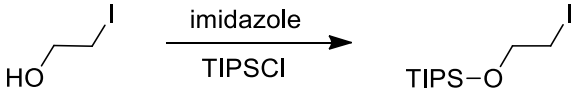
1-Allyl-1*H*-indole (1n)



9 **1n**

Following a reported procedure,[23] potassium *tert*butoxide (1234 mg, 11.00 mmol, 1.1 equiv.) was added to a solution of 18-crown-6 (26.4 mg, 0.100 mmol, 0.01 equiv.) in dry THF (25 mL). The mixture was stirred while 1*H*-indole (**9**) (1.17 g, 10.0 mmol, 1 equiv.) was added in a single portion. The reaction was cooled to 0 °C in an ice bath. A solution of allyl bromide (952 µl, 11.0 mmol, 1.1 equiv.) in THF (10 mL) was added dropwise to the reaction mixture. After stirring for 4 h, water (20 mL) was added to the reaction mixture, the layers were separated, and the aqueous layer was extracted with Et_2O (2 x 20 mL). The combined organic layers were extracted with bringe (50 mL) and then dried over anhydrous $MgSO_4$. The solvent was removed by evaporation under reduced pressure, and the residue was purified by column chromatography to give a mixture of 1-allylindole and 1,3-diallyl indole (1.24 g) as a colorless oil. The mixture was purified by short-path (Kugelrohr) distillation (104-105 °C, 0.4 mbar) to give 1-allyl-1*H*-indole (**1n**) (95% pure, 266 mg, 1.69 mmol, 17 % yield). R_f: 0.60 (hexanes:EtOAc 10:1), co-spotting with impurity. ^1H NMR (400 MHz, $CDCl_3$) δ 7.75 (d, 1 H, *J* = 6.7, ArH), 7.42 (d, 1 H, *J* = 8.2 Hz, ArH), 7.31 (t, 1 H, *J* = 7.0 Hz, ArH), 7.22 (t, 1 H, *J* = 6.5 Hz, ArH), 7.18 (d, 1 H, *J* = 3.3Hz, ArH), 6.63 (dd, 1 H, *J* = 3.2, 0.8 Hz) 6.13-6.02 (m, 1 H, Allyl H), 5.31-5.14 (m, 2 H, allyl CH_2), 4.80 (dt, 2 H, *J* = 5.4, *J* = 1.4, allyl CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.2, 133.6, 128.8, 127.9, 121.6, 121.1, 119.5, 117.3, 109.7, 101.5, 48.9. NMR is corresponding to the literature data.[24]

(2-Iodoethoxy)tri*iso*propylsilane (13)



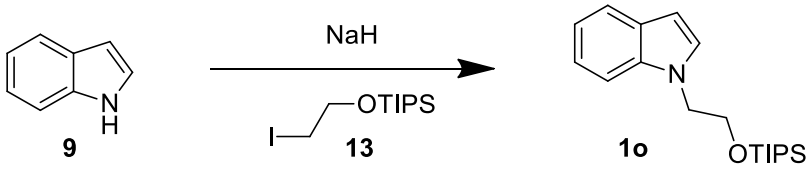
12 **13**

Following a reported procedure,[25] 2-iodoethanol (**12**) (1.10 mL, 10.0 mmol, 1 equiv.) was added to a solution of imidazole (0.885 g, 13.0 mmol, 1.3 equiv.) in DMF (5 mL) under an atmosphere of N_2. Chlorotriisopropylsilane (2.75 mL, 13.0 mmol, 1.3 equiv.) was added dropwise. After 1 h the reaction turned into a thick suspension, as a white solid precipitated. The ice bath was

[22] Kim, J.; Kim, H.; Chang, S. *Org. Lett.* **2012**, *14*, 3924.
[23] Guida, W. C.; Mathre, D. J. *J. Org. Chem.* **1980**, *45*, 3172.
[24] Choy, P. Y.; Lau, C. P.; Kwong, F. Y. *J. Org. Chem.* **2010**, *76*, 80.
[25] Bode, J. W.; Carreira, E. M. *J. Org. Chem.* **2001**, *66*, 6410.

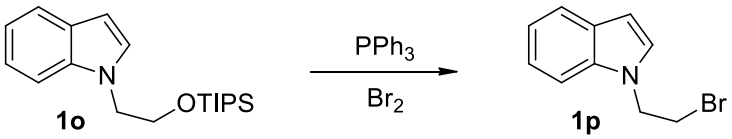
removed and the reaction mixture was stirred for an additional hour. Water (5 mL) was added to dissolve the solid. The organic layer was separated and washed through a SiO_2 pad with pentane (100 mL). The solvent was evaporated, and the crude product was dried under vacuum to give (2-iodoethoxy)triisopropylsilane (**13**) (3.21 g, 9.78 mmol, 98 % yield) as a colorless liquid. ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.85 (t, *J* = 6.9 Hz, 2 H, CH_2), 3.15 (t, *J* =7.0 Hz. 2 H, CH_2), 1.11-0.88 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 64.6, 18.0, 12.1, 6.9. IR 2958 (m), 2942 (m), 2891 (w), 2866 (m), 1464 (m), 1384 (w), 1275 (w), 1249 (w), 1190 (w), 1169 (w), 1123 (s), 1092 (s), 1069 (s), 1013 (w), 999 (m), 943 (w), 920 (w), 882 (s), 857 (w). The NMR spectra is corresponding to the literature data.[25]

1-(2-((Tri*iso*propylsilyl)oxy)ethyl)-1*H*-indole (1o)



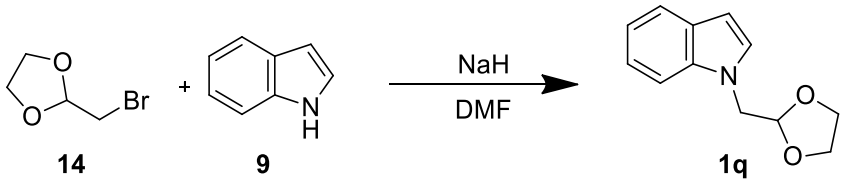
1*H*-indole (**9**) (0.843 g, 7.20 mmol, 1.2 equiv.) was dissolved in N,N-dimethylformamide (6 mL) and NaH (60% in mineral oil, 0.360 g, 9.00 mmol, 1.33 equiv., 1.25 equiv. compared to indole) was added at RT under strong stirring and the reaction mixture was stirred for one hour. N,N-Dimethylformamide (18 mL) was added to dissolve the white precipitae and to give a greenish solution. The reaction was cooled to 0 °C and (2-iodoethoxy)triisopropylsilane (**13**) (1.97 g, 6.00 mmol, 1equiv.) was added dropwise. The reaction was stirred overnight and let to slowly warm up to RT. The reaction was then quenched with water (20 mL) and the reaction mixture was extracted with EtOAc (3 x 25 mL). The combined organic layers were washed with water (10 mL), brine (3x10 mL) and dried over $MgSO_4$. The solvent was evaporated and the crude product was dried under vacuum with stirring. The crude NMR did not show the presence of the alkylating agent. TLC (10:1 hexanes: EtOAc, Rf prod.: 0.7). Purification by flash chromatography (SiO_2, 1% to 10% EtOAc in hexane) gave 1-(2-((triisopropylsilyl)oxy)ethyl)-1*H*-indole (**1o**) (1.56 g, 4.91 mmol, 82 % yield) as a colorless oil, R_f: 0.65 (hexanes:EtOAc 10:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 (m, 1 H, ArH), 7.38 (dd, 1 H, *J* = 8.2, 0.8 Hz, ArH), 7.25-7.19 (m, 2H, ArH) 7.13 (m, 1 H, ArH), 6.52 (dd, 1 H, *J* = 3.1, 0.8 Hz, ArH), 4.30 (t, 2 H, *J* = 6.0 Hz, CH_2), 4.04 (t, 2 H, *J* = 5.8 Hz, CH_2), 1.17-0.85 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.1, 128.7, 128.6, 121.3, 120.9, 119.2, 109.3, 101.0, 62.8, 48.8, 17.9, 11.9. IR 3056 (w), 2942 (m), 2891 (m), 2865 (s), 1514 (w), 1464 (s), 1439 (w), 1400 (w), 1387 (w), 1360 (w), 1334 (w), 1317 (m), 1250 (w), 1200 (w), 1115 (s), 1077 (m), 1013 (m), 997 (w), 923 (m), 883 (s), 819 (w). HRMS (ESI) calcd for $C_{19}H_{32}NOSi^+$ $[M+H]^+$ 318.2248; found 318.2236.

1-(2-Bromoethyl)-1*H*-indole (1p)



Following a modification of a reported procedure,[26] Br_2 (0.170 mL, 3.30 mmol, 1.1 equiv.) was added dropwise in 5 minutes to a solution of triphenylphosphine (866 mg, 3.30 mmol, 1.1 equiv.) in DCM (3 mL) to give a slightly brownish suspension. The reaction mixture was stirred for 15 min, then 1-(2-((triisopropylsilyl)oxy)ethyl)-1*H*-indole (953 mg, 3.00 mmol, 1 equiv.) was added dropwise as a solution in DCM (3 mL). After 48 h, the mixture became a pale yellow solution, and the TLC did not show any starting material. The reaction was quenched with water (10 mL), the layers were separated, and the organic layer was washed with water (2 x 10 mL) and dried over $MgSO_4$. After filtration, the solvent was removed under reduced pressure. Purification by column chromatography (SiO_2, hexane/EtOAc, 95/5 to 85/15) gave pure 1-(2-bromoethyl)-1*H*-indole (**1p**) (534 mg, 2.38 mmol, 79 % yield) as a colorless oil. R_f: 0.45 (hexanes : EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.73-7.63 (m, 1 H, ArH), 7.41-7.25 (m, 2 H, ArH), 7.23-7.15 (m, 2 H, ArH), 6.58 (dd, 1 H, *J* = 3.2, 0.8 Hz, ArH), 4.59-4.49 (m, 2 H, CH_2), 3.72-3.62 (m, 2 H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 128.8, 127.9, 122.0, 121.3, 119.9, 108.9, 102.0, 48.0, 29.8. IR 3101 (w), 3100 (w), 3086 (w), 3053 (w), 3027 (w), 2962 (w), 2961 (w), 2917 (w), 1612 (w), 1514 (m), 1485 (m), 1477 (m), 1464 (s), 1453 (m), 1452 (m), 1436 (m), 1399 (m), 1355 (m), 1334 (m), 1314 (s), 1279 (m), 1241 (s), 1232 (m), 1218 (m), 1196 (m), 1166 (m), 1158 (m), 1119 (w), 1089 (w), 1040 (w), 1013 (m), 927 (w), 884 (m), 847 (w). HRMS (ESI) calcd for $C_{10}{}^{79}BrH_{11}N^+$ $[M+H]^+$ 224.0069; found 224.0072. The obtained NMR data is in accordance with reported NMR values.[26]

1-((1,3-Dioxolan-2-yl)methyl)-1*H*-indole (1q)



1*H*-indole (**9**) (586 mg, 5.00 mmol, 1 equiv) was dissolved in dry DMF (5 mL). The solution was then cooled to 0 °C and NaH (60% in mineral oil, 300 mg, 7.50 mmol, 1.5 equiv) was added. The reaction mixture was stirred for 1 h at RT and a white solid precipitated. Additional DMF (15 mL) was added, and 2-(bromomethyl)-1,3-dioxolane (**14**) (0.622 mL, 6.00 mmol, 1.2 equiv.) was added. The reaction mixture was stirred overnight at 50°C, then cooled to RT, quenched with water and extracted with EtOAc (3 x 25 mL). The combined organic layers were washed with water (25 mL), then brine (2x25 mL), dried over $MgSO_4$ and the solvent was evaporated to give a brownish crude oil. Purification by column chromatography (SiO_2, hexane/EtOAc 95/5 to 80/20) gave 1-((1,3-dioxolan-2-yl)methyl)-1*H*-indole (**1q**) (680 mg, 3.35 mmol, 67 % yield) as colorless oil. R_f: 0.2 (hexanes:EtOAc 10:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.68 (d, 1 H, *J* = 7.9 Hz, ArH), 7.49 (d, 1 H, *J* = 8.3 Hz, ArH), 7.32-7.07 (m, 3 H, ArH), 6.58 (d, 1 H, *J* = 3.1 Hz, ArH), 5.27 (t, 1 H, *J* = 3.4 Hz, CH_2-C*H*), 4.37-4.24 (m, 2 H, N-CH_2), 3.81 (m, 4 H, CH_2-CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.8, 129.0, 128.5, 121.6, 120.8, 119.5, 109.8, 102.5, 101.7, 65.3, 49.2. IR 3053 (w), 2973 (w), 2939 (w), 2887 (w), 2886 (w), 1683 (w), 1613 (w), 1514 (m), 1485 (m), 1475 (m), 1464 (s), 1398 (m), 1385 (w), 1366 (w), 1335 (m), 1316 (s), 1259 (m), 1258 (m), 1229 (w), 1228

[26] Bressy, C.; Alberico, D.; Lautens, M. *J. Am. Chem. Soc.* **2005**, *127*, 13148.

(w), 1196 (m), 1142 (s), 1141 (s), 1093 (w), 1061 (m), 1036 (s), 1012 (s), 946 (m), 884 (w), 844 (m), 843 (m). HRMS (ESI) calcd for $C_{12}H_{14}NO_2^+$ $[M+H]^+$ 204.1019; found 204.1025.

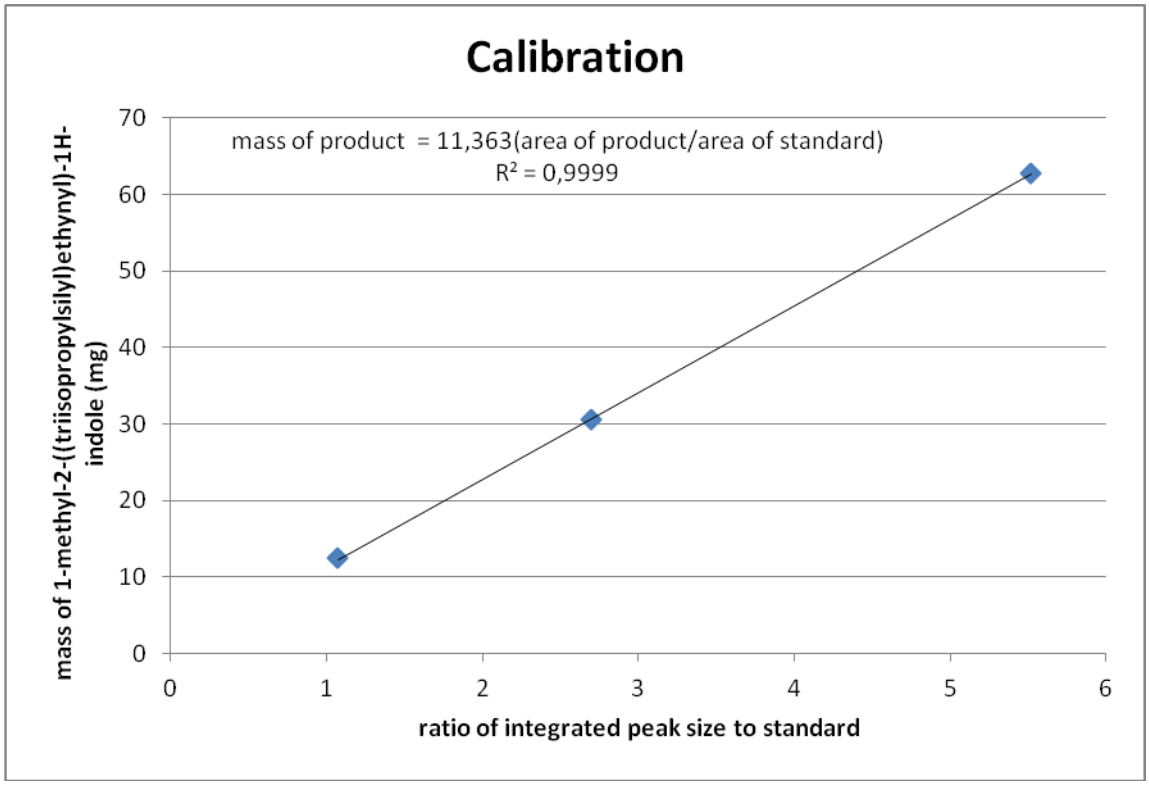
Optimization of the alkynylation reaction

With isolated yields

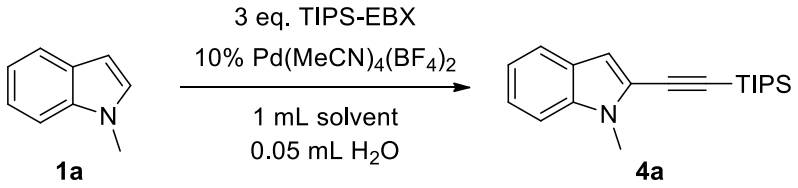
The optimization was carried out as following: TIPS EBX (**2**) was suspended/dissolved in the solvent, 1-methyl-1*H*-indole (**1a**) (25 µl, 26 mg, 0.20 mmol, 1 equiv.) was added via a Hamilton syringe, then the additive was added, followed by the catalyst. The reaction was stirred overnight, the solvent was evaporated, the residue was taken up in EtOAc (10 mL), washed with 0.1 M NaOH (10 mL), saturated $NaHCO_3$ (2 x10 mL) and brine (10 mL), and dried over $MgSO_4$. After filtration, the solvent was evaporated under reduced pressure, and purified via column chromatography.

With GC yield

The optimization was carried out as following: TIPS EBX (**2**) was suspended/dissolved in the solvent, 1-methyl-1H-indole (**1a**) (25 µl, 26 mg, 0.20 mmol, 1 equiv.) was added via a Hamilton syringe, then the additive was added, followed by the catalyst. The reaction was stirred overnight. Then 10 µl dodecanitrile was added via a Hamilton syringe. The mixture was homogenized then¸ ca. 100 µl were transferred to a vial of 1 mL DCM. The GC yield was determined by the following calibration curve, using the ratio of the area of the product peak and the standard peak of the FID detector.

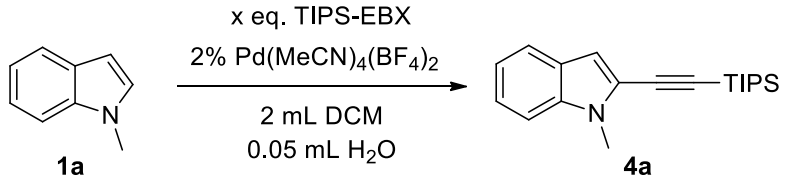


Solvent effect



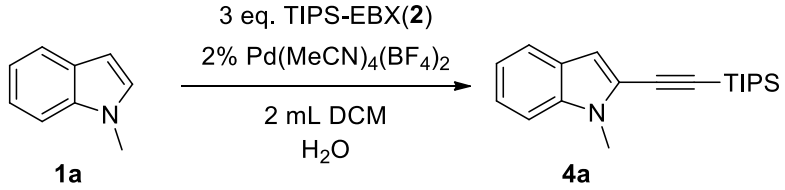
Entry	Solvent	Isolated yield (%)
1	Et_2O	47
2	Toluene	48
3	Acetonitrile	16
4	Isopropanol	32
5	Ethyl-acetate	44
6	THF	50
7	DMF	37
8	DMSO	0
9	EtOH	6
10	MeOH	10

TIPS-EBX dependence



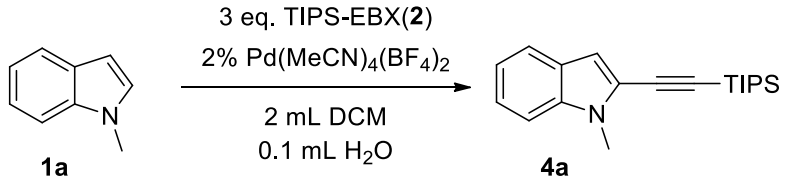
Entry	Equivalent of TIPS EBX (2)	GC yield (%)
1	0.5	16
2	1	29
3	2	51
4	3	59
5	5	57

Water dependence



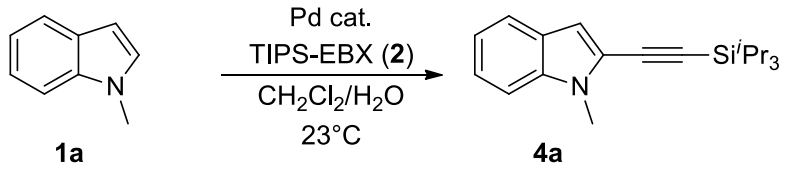
Entry	Water content (µl)	GC yield (%)
1	0 (dry DCM)	22
2	1.8	37
3	100	61
4	500	61
5	1000	53
6	2000	60

Selected additive screening



Entry	Equivalent	Additive	GC yield (%)
1	-	-	61
2	1	Na_2CO_3	16
3	1	$NaHCO_3$	17
4	1	PivOH	56
5	10	PivOH	14
6	5	TFA	Traces
7	1	Cs_2CO_3	Traces
8	1	CsOPiv	Traces
9	0.1	TMEDA	0
10	0.1	DMEDA	0
11	1	Ethylene glycol	8

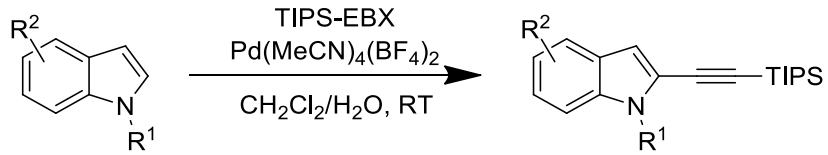
Catalyst screening



1a **4a**

Entry	loading	Pd source	ligand	GC yield (%)
1	2%	$Pd(MeCN)_4(BF_4)_2$	-	61
2	2%	$PdCl_2$	-	22
3	2%	Pd_2dba_3	-	57
4	2%	$Pd(allyl)codBF_4$	-	44
5	2%	Pd(allyl)Cl dimer	-	60
6	2%	$Pd(PPh_3)_4$	-	traces
7	2%	$Pd(dba)_2$	-	44
8	2%	$Pd_2(dba)_3CHCl_3$	-	54
9	2%	$Pd_2(dba)_3$	dppp	24
10	2%	$Pd_2(dba)_3$	Xphos	26
11	10%	$Pd(TFA)_2$	-	42
12	10%	$Pd(MeCN)_4(BF_4)_2$	-	50

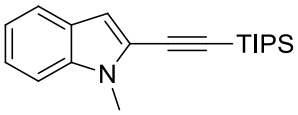
General procedure for C2 selective alkynylation of indoles.



In a 10 mL round bottom-flask, the corresponding indole (0.500 mmol, 1.0 equiv.) and 1-[(triisopropylsilyl)ethynyl]-1,2-benziodoxol-3(1*H*)-one (TIPS-EBX, **2**) (643 mg, 1.50 mmol, 3 equiv.) were dissolved in DCM (5 mL) under air, then water was added (0.10 mL). Lastly $Pd(MeCN)_4(BF_4)_2$ (4.4 mg, 10 µmol, 2%) was added with strong stirring. The flask was closed and the reaction mixture was stirred overnight (the reaction is generally completed after 4-6 h), when it became brownish. The solvent was evaporated under reduced pressure. EtOAc (25 mL) was added to the crude product, and the solution was washed with $NaOH_{aq}$ (0.1 M, 25 mL), conc. $NaHCO_3$ (2 x 25 mL) and brine (25 mL). The organic layer was dried over $MgSO_4$, filtered and

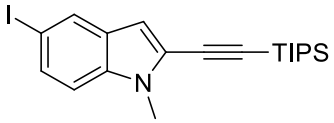
the solvent was evaporated under reduced pressure. Purification by column chromatography gave the pure alkynylated product. [27]

1-Methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4a)



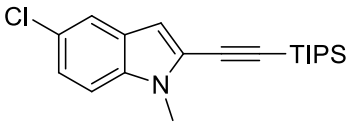
Starting from 1-methyl-1*H*-indole (**1a**) (64 µl, 66 mg, 0.50 mmol), 1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (**4a**) (102 mg, 0.33 mmol, 66%) was obtained as a pale yellow oil after purification by column chromatography (SiO_2, hexane to hexane/DCM 90/10), R_f: 0.75 (hexanes:EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 (dt, 1 H, *J* = 8.0, 0.9 Hz, ArH), 7.33-7.28 (m, 2 H, ArH), 7.16 (q, 1 H, *J* = 4 Hz, ArH), 6.86 (s, 1 H, ArH), 3.78 (s, 3 H, Me), 1.30-1.09 (m, 21 H, TIPS) ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.1, 127.1, 123.1, 122.3, 121.1, 120.1, 109.4, 107.7, 98.2, 97.8, 30.6, 18.8, 11.4. IR 3058 (w), 2942 (s), 2891 (m), 2864 (s), 2150 (s), 1463 (s), 1429 (w), 1383 (m), 1364 (m), 1339 (s), 1317 (m), 1238 (m), 1170 (w), 1152 (w), 1073 (w), 1012 (m), 997 (m), 920 (m), 883 (s), 854 (m). HRMS (ESI) calcd. for $C_{20}H_{30}NSi^+$ $[M+H]^+$ 312.2142; found 312.2147.

5-Iodo-1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4b)



Starting from 5-iodo-1-methyl-1*H*-indole (**1b**) (129 mg, 0.500 mmol), 5-iodo-1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (**4b**) (148 mg, 0.339 mmol, 68 % yield) was obtained as a white solid after purification by column chromatography (SiO_2, hexane to hexane/DCM 90/10). R_f: 0.85 (hexanes:EtOAc 10:1). Mp.: 76-78°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.71 (d, 1 H, *J* = 1.2 Hz, ArH), 7.29 (dd, 1 H, *J* = 8.6, 1.5 Hz, ArH), 6.84 (d, 1 H, *J* = 8.6 Hz, ArH), 6.51 (s, 1 H, ArH), 3.60 (s, 3 H, Me), 1.15-0.88 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.1, 131.3, 129.6, 129.5, 123.1, 111.4, 106.7, 98.7, 97.4, 83.6, 30.7, 18.7, 11.3. IR 2957 (s), 2942 (s), 2891 (m), 2890 (m), 2865 (s), 2154 (m), 1557 (w), 1516 (w), 1465 (s), 1426 (w), 1425 (w), 1383 (m), 1367 (w), 1326 (m), 1274 (w), 1236 (w), 1169 (w), 1147 (w), 1101 (w), 1075 (w), 1063 (w), 1044 (w), 1018 (w), 997 (m), 911 (m), 883 (s). HRMS (ESI) calcd for $C_{20}H_{29}INSi^+$ $[M+H]^+$ 438.1109; found 438.1113.

5-Chloro-1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4c)

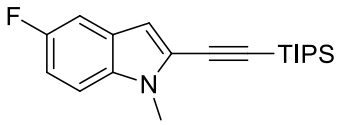


Starting from 5-chloro-1-methyl-1*H*-indole (83 mg, 0.50 mmol 5-chloro-1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (**4c**) (94.2 mg, 0.272 mmol, 54 % yield) was obtained as a white solid after purification by column chromatography (SiO_2, hexane to hexane/DCM 90/10). Mp.: 36-38°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34 (d, 1 H, *J* = 1.4 Hz, ArH), 7.03-6.95 (m, 2 H, ArH), 6.53 (s, 1 H, ArH), 3.61 (s, 3 H, Me), 1.11-0.87 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.5, 127.9, 125.8, 123.7, 123.4, 120.2, 110.4, 107.1, 98.7, 97.5, 30.8, 18.7, 11.3. IR 2943 (s), 2892 (w), 2865 (s), 2362 (w), 2341 (w), 2331 (w), 2153 (m), 1467 (s), 1427 (w), 1384 (m), 1330 (m), 1272 (w), 1235 (w), 1169 (w), 1160 (w), 1146 (w), 1101 (w),

[27] No dry glassware is needed. The starting materials are giving a brownish-red color on anisaldehyde stain, while the less polar products are purple. The reaction is never observed to go until full conversion. The order of addition is crucial in term of yield.

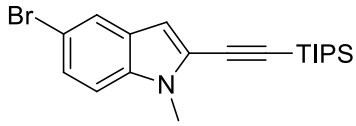
1064 (m), 1017 (w), 997 (w), 923 (m), 883 (s), 866 (w). HRMS (ESI) calcd for $C_{20}ClH_{29}NSi^+$ $[M+H]^+$ 346.1752; found 346.1753.

5-Fluoro-1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4d)



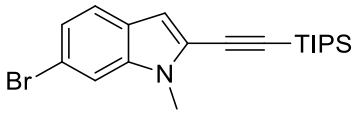
Starting from 5-fluoro-1-methyl-1*H*-indole (**1d**) (74.6 mg, 0.500 mmol), 5-fluoro-1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (**4d**) (74 mg, 0.23 mmol, 45 % yield) was obtained as a yellow oil after purification by column chromatography (SiO_2, hexane). R_f: 0.30 (Hexanes) 0.9 (hexanes/EtOAc 10:1), ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.03-6.95 (m, 2 H, ArH), 6.81 (td, 1 H, *J* = 9.1, 2.5 Hz, ArH), 6.55 (d, 1 H, *J* = 0.7 Hz, ArH), 3.61 (s, 3H, Me), 1.16-0.87 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 158.3 (d, *J* C-F = 233 Hz), 133.8, 127.1 (d, *J* C-F = 10 Hz), 123.8, 111.7 (d, *J* C-F = 26 Hz), 110.1 (d, *J* C-F = 9.4 Hz), 107.4 (d, *J* C-F = 5.8 Hz), 105.5(d, *J* C-F = 23 Hz), 98.4, 97.7, 30.8, 18.7, 11.3. IR 2943 (m), 2891 (w), 2865 (m), 2151 (m), 1624 (w), 1580 (w), 1477 (s), 1430 (w), 1389 (m), 1366 (w), 1342 (m), 1282 (m), 1232 (w), 1191 (s), 1130 (w), 1116 (m), 1101 (w), 1073 (w), 1017 (w), 997 (m), 955 (m), 921 (w), 883 (s), 853 (m). HRMS (ESI) calcd for $C_{20}FH_{29}NSi^+$ $[M+H]^+$ 330.2048; found 330.2039.

5-Bromo-1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4e)



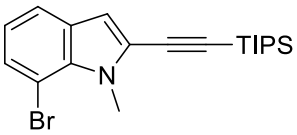
Starting from 5-bromo-1-methyl-1H-indole (**1e**) (105 mg, 0.500 mmol), 5-bromo-1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (**4e**) (105 mg, 0.269 mmol, 54 % yield) as a white solid after purification by column chromatography (SiO_2, hexane). R_f: 0.70 (hexanes:EtOAc 10:1) Mp.: 59-60°C, ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (s, 1 H, ArH), 7.13 (d, 1 H, *J* = 8.7 Hz, ArH), 6.93 (d, 1 H, *J* = 8.7 Hz, ArH), 6.52 (s, 1 H, ArH), 3.60 (s, 3 H, Me), 1.05-0.89 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 135.7, 128.6, 125.9, 123.5, 123.3, 113.4, 110.8, 106.9, 98.7, 97.4, 30.8, 18.7, 11.3. IR 2943 (s), 2890 (w), 2865 (s), 2362 (m), 2341 (w), 2335 (w), 2153 (m), 1517 (w), 1494 (m), 1466 (s), 1426 (w), 1386 (w), 1366 (w), 1330 (m), 1283 (w), 1272 (w), 1238 (m), 1191 (w), 1170 (w), 1141 (w), 1131 (w), 1124 (w), 1101 (w), 1074 (w), 1052 (w), 1014 (w), 998 (w), 951 (w), 916 (m), 884 (s), 866 (w), 857 (w), 837 (w), 826 (w), 812 (w). HRMS (ESI) calcd for $C_{20}{}^{79}BrH_{29}NSi^+$ $[M+H]^+$ 390.1247; found 390.1252.

6-Bromo-1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4f)



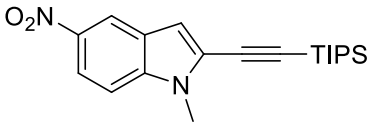
Starting from 6-bromo-1-methyl-1*H*-indole (**1f**) (105 mg, 0.500 mmol), 6-bromo-1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole **(4f)** (140 mg, 0.359 mmol, 72 % yield) was obtained as a brown oil after purification by column chromatography (SiO_2, hexane), R_f: 0.80 (hexanes:EtOAc 10:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.22 (m, 2 H, ArH), 7.01 (d, 1 H, *J* = 8.4 Hz, ArH), 6.55 (s, 1 H, ArH), 3.57 (s, 3 H, Me), 1.07-0.86 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.8, 125.9, 123.4, 123.0, 122.2, 116.9, 112.4, 107.8, 98.6, 97.6, 30.7, 18.7, 11.3; IR 2942 (m), 2891 (w), 2864 (m), 2151 (m), 1605 (w), 1464 (s), 1383 (w), 1339 (m), 1330 (m), 1229 (w), 997 (w), 922 (w), 883 (s), 855 (m), 808 (s). HRMS (ESI) calcd for $C_{20}{}^{79}BrH_{29}NSi^+$ $[M+H]^+$ 390.1247; found 390.1243.

7-Bromo-1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4g)



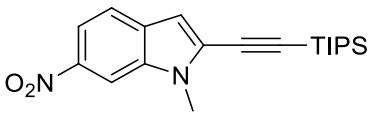
Starting from 7-bromo-1-methyl-1*H*-indole (**1g**) (105 mg, 0.500 mmol), 7-bromo-1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (**4g**) (141 mg, 0.361 mmol, 72 % yield) was obtained as as a white solid after purification by column chromatography (SiO_2, hexane). R_f: 0.95 (hexanes/EtOAc 10/1). Mp.: 39-42°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.47 (dd, 1 H, *J* = 7.9, 0.9 Hz, ArH), 7.37 (dd, 1 H, *J* = 7.6, 0.9 Hz, ArH), 6.90 (t, 1 H, *J* = 7.7 Hz, ArH), 6.76 (s, 1 H, ArH), 4.22 (s, 3 H, Me), 1.05-1.23 (m, 21 H, TIPS) ^{13}C NMR (101 MHz, $CDCl_3$) δ 133.5, 130.1, 128.2, 124.7, 121.1, 120.4, 108.2, 103.8, 99.2, 97.6, 34.0, 18.7, 11.3. IR 2942 (s), 2891 (w), 2865 (s), 2153 (m), 1557 (w), 1483 (w), 1463 (m), 1449 (m), 1406 (w), 1381 (w), 1368 (w), 1347 (m), 1317 (s), 1308 (m), 1208 (w), 1162 (w), 1099 (s), 1073 (w), 1055 (w), 1017 (w), 997 (m), 922 (m), 883 (s). HRMS (ESI) calcd for $C_{20}{}^{79}BrH_{29}NSi^+$ $[M+H]^+$ 390.1247; found 390.1232.

1-Methyl-5-nitro-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4h)



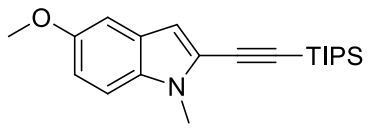
Starting from 1-methyl-5-nitro-1*H*-indole (**1h**) (88 mg, 0.50 mmol), 1-methyl-5-nitro-2-((triisopropylsilyl)ethynyl)-1*H*-indole (**4h**) (86 mg, 0.24 mmol, 48 % yield) was obtained as a yellow solid, after purification by column chromatography (SiO_2, hexane to hexane/DCM 8/2, then hexane/EtOAc 98/2 to 95/5) R_f: 0.65 (hexanes:EtOAc 10:1). Mp.: 57-59°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.53 (d, 1 H, *J* = 2.2 Hz, ArH), 8.15 (dd, 1 H, *J* = 9.1, 2.2 Hz, ArH), 7.30 (d, 1 H, *J* = 9.1 Hz, ArH), 6.94 (s, 1 H, ArH), 3.88 (s, 3 H, Me), 1.18 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 142.1, 139.6, 126.2, 125.8, 118.5, 118.1, 109.7, 109.3, 100.4, 96.4, 31.1, 18.7, 11.2, IR 2942 (w), 2890 (w), 2865 (w), 2360 (w), 2343 (w), 2154 (w), 1520 (m), 1463 (m), 1390 (w), 1348 (m), 1329 (s), 1068 (m), 997 (w), 883 (m), 784 (w), 752 (m), 721 (s), 677 (m), 662 (m), 647 (m), 617 (m), 574 (w), 512 (m), 498 (m), 491 (s), 461 (s), 445 (m), 430 (s), 403 (s). HRMS (ESI) calcd for $C_{20}H_{29}N_2O_2Si^+$ $[M+H]^+$ 357.1993; found 357.1997.

1-Methyl-6-nitro-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4i)



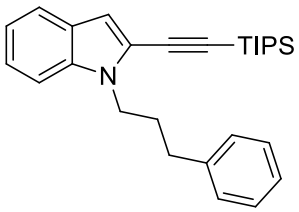
Starting from 1-methyl-6-nitro-1*H*-indole (**1i**) (88 mg, 0.50 mmol), 1-methyl-6-nitro-2-((triisopropylsilyl)ethynyl)-1*H*-indole (**4i**) (81 mg, 0.23 mmol, 45 % yield) obtained as a brown solid after purification by column chromatography (SiO_2, hexane to hexane/DCM 70/30) R_f: 0.70 (hexanes/EtOAc 10/1). Mp.: 89-96°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.18 (d, 1 H**,** *J* = 1.8 Hz, ArH), 7.93 (dd, 1 H, *J* = 8.8, 2.0 Hz, ArH), 7.53 (d, 1 H, *J* = 8.8 Hz, ArH), 6.77 (d, 1 H, *J* = 0.7 Hz, ArH), 3.84 (s, 3 H, Me), 1.20-0.94 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.9, 135.6, 131.8, 128.0, 120.8, 115.5, 108.0, 106.4, 101.5, 96.5, 31.1, 18.7, 11.3. IR 2956 (m), 2941 (m), 2889 (w), 2864 (m), 2154 (w), 1751 (w), 1519 (m), 1503 (s), 1463 (s), 1385 (w), 1362 (m), 1344 (s), 1330 (s), 1300 (m), 1256 (w), 1235 (m), 1234 (m), 1143 (w), 1129 (m), 1072 (m), 1063 (m), 1039 (w), 1020 (m), 1012 (m), 996 (m), 922 (w), 883 (s), 862 (w), 844 (w), 822 (m). HRMS (ESI) calcd for $C_{20}H_{29}N_2O_2Si^+$ $[M+H]^+$ 357.1993; found 357.1990.

5-Methoxy-1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4j)



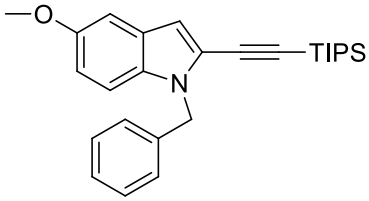
Starting from 5-methoxy-1-methyl-1*H*-indole (**1j**) (81 mg, 0.50 mmol), 5-methoxy-1-methyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (**4j**) (94.5 mg, 0.277 mmol, 55 % yield) was obtained as a brownish solid, after purification by column chromatography (SiO_2, hexane to hexane/DCM 90/10) giving a highly fluorescent spot on TLC. R_f: 0.75 (hexanes/EtOAc 10/1). Mp.: 113-118°C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.17 (d, 1 H, *J* = 6.4 Hz, ArH), 7.02 (d, 1 H, *J* = 2.3 Hz, ArH), 6.95 (d, 1 H, *J* = 2.4 Hz, ArH), 6.72 (d, 1 H, *J* = 0.8 Hz, ArH), 3.86 (s, 3 H, Me), 3.81 (s, 3 H, Me), 1.19 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.5, 132.6, 127.3, 122.7, 113.9, 110.2, 107.1, 102.0, 98.3, 97.6, 55.8, 30.7, 18.7, 11.4. IR 2944 (m), 2891 (w), 2865 (m), 2834 (w), 2146 (m), 1621 (w), 1518 (w), 1474 (m), 1464 (m), 1429 (m), 1385 (w), 1366 (w), 1349 (m), 1293 (m), 1265 (m), 1242 (m), 1215 (s), 1179 (m), 1163 (w), 1142 (m), 1101 (w), 1072 (w), 1030 (m), 1018 (w), 996 (m), 946 (w), 921 (w), 883 (s), 846 (m), 804 (m). HRMS (ESI) calcd for $C_{21}H_{32}NOSi^+$ $[M+H]^+$ 342.2248; found 342.2253.

1-(3-Phenylpropyl)-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4k)



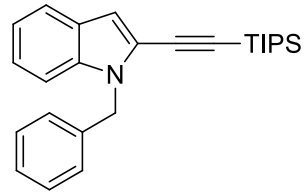
Starting from 1-(3-phenylpropyl)-1*H*-indole (**1k**) (0.118 g, 0.500 mmol), 1-(3-phenylpropyl)-2-((triisopropylsilyl)ethynyl)-1*H*-indole (**4k**) (0.120 g, 0.289 mmol, 58 % yield) was obtained as a yellow oil after purification by column chromatography (SiO_2, hexane to hexane/DCM 80/20). R_f: 0.75 (hexanes:EtOAc 10:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (dd, 1 H, *J* = 7.9, 0.8 Hz, ArH), 7.12-6.88 (m, 8 H, ArH), 6.62 (d, 1 H, *J* = 0.6 Hz, ArH), 4.12 (t, 2 H, *J* = 7.3 Hz, CH_2), 2.52-2.46 (m, 2 H, CH_2), 1.97 (m, 2 H, CH_2), 1.10-0.85 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.6, 137.7, 132.0, 128.6, 127.7, 127.3, 126.7, 122.5, 114.0, 110.8, 107.8, 102.1, 98.2, 98.0, 44.3, 33.4, 31.8, 18.8, 11.4. IR 3057 (w), 2942 (s), 2865 (s), 2361 (w), 2341 (w), 2152 (m), 1520 (w), 1458 (s), 1388 (m), 1346 (m), 1216 (w), 1166 (w), 1073 (w), 996 (m), 922 (m), 883 (s), 851 (m). HRMS (ESI) calcd for $C_{28}H_{38}NSi^+$ $[M+H]^+$ 416.2768; found 416.2762.

1-Benzyl-5-methoxy-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4l)



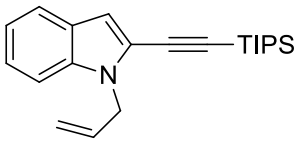
Starting from 1-benzyl-5-methoxy-1*H*-indole (**1l**) (119 mg, 0.500 mmol), 1-benzyl-5-methoxy-2-((triisopropylsilyl)ethynyl)-1*H*-indole (**4l**) (86 mg, 0.21 mmol, 41 % yield) was obtained as a redish-brown oil after purification by column chromatography (SiO_2, hexane to hexane/DCM 90/10). R_f: 0.70 (hexanes:EtOAc 10:1), 0.35 (hexanes:EtOAc 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.16-6.95 (m, 6 H, ArH), 6.90 (d, 1 H, *J* = 2.3 Hz, ArH), 6.73 (dd, 1 H, *J* = 8.9, 2.5 Hz, ArH), 6.66 (d, 1 H, *J* = 0.8 Hz, ArH), 5.30 (s, 2 H, Bz CH_2), 3.72 (s, 3 H, OMe), 1.10-0.89 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 154.6, 137.7, 132.0, 128.6, 127.7, 127.3, 126.7, 122.5, 114.1, 110.8, 107.9, 102.1, 98.3, 98.1, 55.8, 48.1, 18.7, 11.3; IR 2942 (m), 2891 (w), 2864 (m), 2148 (m), 1789 (w), 1624 (w), 1475 (s), 1453 (s), 1392 (m), 1346 (m), 1294 (m), 1222 (s), 1175 (m), 1134 (w), 1113 (m), 1037 (m), 997 (m), 883 (s), 836 (m). HRMS (ESI) calcd for $C_{27}H_{36}NOSi^+$ $[M+H]^+$ 418.2561; found 418.2563.

1-Benzyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4m)



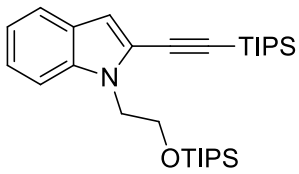
Starting from 1-benzyl-1*H*-indole (**1m**) (104 mg, 0.500 mmol), 1-Benzyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole **(4m)** (79.8 mg, 0.205 mmol, 41 % yield) was obtained as a brownish oil after purification by column chromatography (SiO_2, hexane to hexane/DCM 90/10). R_f: 0.65 (hexanes:EtOAc 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.50 (d, 1 H, *J* = 7.9 Hz, ArH), 7.19-6.98 (m, 8 H, ArH), 6.78 (s, 1 H, ArH), 5.37 (s, 2 H, Bz CH_2), 1.07-0.92 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.6, 136.7, 128.6, 127.3, 126.8, 123.3, 122.2, 121.2, 120.3, 110.0, 108.4, 98.2, 98.2, 47.9, 18.7, 11.3. IR 3062 (w), 3032 (w), 2942 (s), 2891 (m), 2864 (s), 2150 (m), 1606 (w), 1455 (s), 1388 (m), 1342 (s), 1316 (m), 1213 (w), 1163 (w), 1075 (w), 999 (m), 919 (w), 883 (s), 851 (w).[28] HRMS (ESI) calcd for $C_{26}H_{34}NSi^+$ $[M+H]^+$ 388.2455; found 388.2436.

1-Allyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4n)



Starting from 1-allyl-1*H*-indole (**1n**) (79 mg, 0.50 mmol), 1-allyl-2-((triisopropylsilyl)ethynyl)-1*H*-indole (**4n**) (74 mg, 0.22 mmol, 44 % yield) was obtained as a yellow oil after purification by column chromatography (SiO_2, hexane). R_f: 0.70 (hexanes:EtOAc 20:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.41 (dt, 1 H, *J* = 8.0, 0.9 Hz, ArH), 7.10-7.03 (m, 2 H, ArH), 6.93 (m, 1 H, ArH), 6.64 (m, 1 H, ArH), 5.82-5.73 (m, 1 H, allyl H), 4.97 (dq, 1 H, *J* = 10.3, 1.5 Hz, allyl CH_2), 4.82 (m, 1 H, allyl CH), 4.70 (dt, 2 H, *J* = 5.1, 1.7 Hz, allyl CH_2), 1.06-0.81 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.5, 133.1, 127.2, 123.1, 121.8, 121.1, 120.2, 116.7, 109.9, 108.1, 97.9, 97.8, 46.7, 18.7, 11.4; IR 2942 (s), 2891 (m), 2865 (s), 2361 (w), 2341 (w), 2150 (s), 1458 (s), 1388 (m), 1343 (m), 1316 (m), 1216 (w), 1165 (w), 1073 (w), 996 (m), 922 (m), 883 (s), 851 (m). HRMS (ESI) calcd for $C_{22}H_{32}NSi^+$ $[M+H]^+$ 338.2299; found 338.2300.

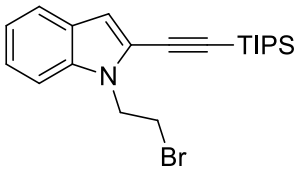
2-((Triisopropylsilyl)ethynyl)-1-(2-((triisopropylsilyl)oxy)ethyl)-1*H*-indole (4o)



Starting from 1-(2-((triisopropylsilyl)oxy)ethyl)-1*H*-indole (**1o**) (159 mg, 0.500 mmol), 2-((triisopropylsilyl)ethynyl)-1-(2-((triisopropylsilyl) oxy)ethyl)-1*H*-indole (**4o**) (170 mg, 0.341 mmol, 68 % yield) was obtained as a colorless oil after purification by column chromatography (SiO_2, hexane to hexane/DCM 90/10). R_f: 0.70 (hexanes:EtOAc 20:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36 (d, 1 H, *J* = 7.9 Hz, ArH), 7.17 (dd, 1 H, *J* = 8.3, 0.7 Hz, ArH), 7.06-7.01 (m, 1 H, ArH), 6.92-6.87 (m, 1 H, ArH), 6.61 (d, 1 H, *J* = 0.7 Hz, ArH), 4.22 (t, 2 H, *J* = 6.3 Hz, CH_2), 3.85 (t, 2 H, *J* = 6.2 Hz, CH_2), 1.03-0.94 (m, 21H, TIPS), 0.87-0.67 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.3, 127.0, 123.0, 121.5, 120.9, 120.0, 110.1, 108.3, 98.3, 97.6, 62.7, 46.7, 18.7, 17.9, 11.9, 11.4; IR 2942 (s), 2891 (w), 2865 (s), 2150 (m), 1459 (m), 1388 (w), 1366 (w), 1344 (w), 1318 (w), 1250 (w), 1166 (w), 1123 (m), 1072 (w), 1015 (w), 997 (m), 936 (w), 921 (w), 882 (s). HRMS (ESI) calcd for $C_{30}H_{52}NOSi_2^+$ $[M+H]^+$ 498.3582; found 498.3589.

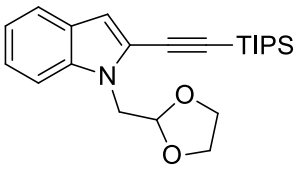
[28] One carbon signal could not be resolved.

1-(2-Bromoethyl)-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4p)



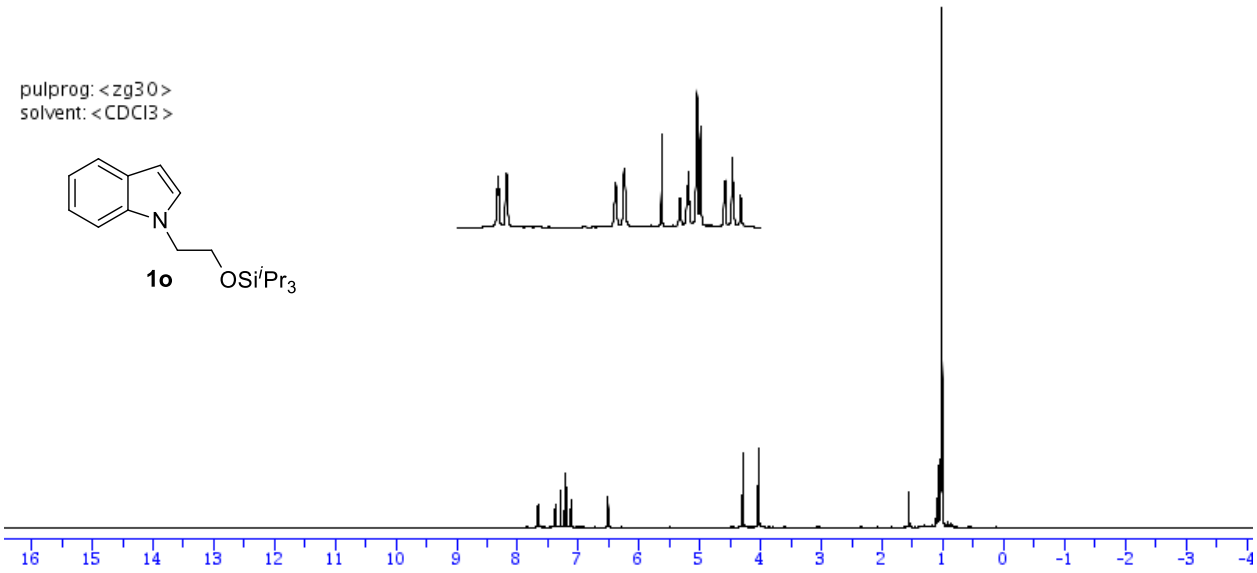
Starting from 1-(2-bromoethyl)-1*H*-indole (**1p**) (112 mg, 0.500 mmol), 1-(2-bromoethyl)-2-((triisopropylsilyl)ethynyl)-1*H*-indole (**4p**) (124 mg, 0.307 mmol, 61 % yield) was obtained as a colorless oil after purification by column chromatography (SiO_2, hexane to hexane/DCM 90/10). R_f: 0.65 (hexanes:EtOAc 20:1), Rf: 0.30 (hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.38 (d, 1 H, *J* = 7.9 Hz, ArH), 7.13-7.03 (m, 2 H, ArH), 6.93 (m, 1 H, ArH), 6.63 (s, 1 H, ArH), 4.41 (t, 2 H, *J* = 7.7 Hz, CH_2), 3.41 (t, 2 H, *J* = 7.8 Hz, CH_2), 1.10-0.77 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 136.3, 127.2, 123.6, 121.4, 121.3, 120.6, 109.3, 108.9, 98.7, 97.4, 45.7, 28.6, 18.8, 11.4. IR 3059 (w), 2942 (s), 2890 (m), 2864 (s), 2150 (m), 1480 (w), 1457 (s), 1437 (w), 1386 (m), 1367 (m), 1340 (s), 1316 (m), 1281 (w), 1233 (w), 1219 (m), 1177 (w), 1160 (m), 1073 (w), 1016 (m), 997 (m), 919 (w), 882 (s), 857 (m), 843 (w). HRMS (ESI) calcd for $C_{21}{}^{79}BrH_{31}NSi^+$ $[M+H]^+$ 404.1404; found 404.1389.

1-((1,3-Dioxolan-2-yl)methyl)-2-((triisopropylsilyl)ethynyl)-1*H*-indole (4q)



Starting from 1-((1,3-dioxolan-2-yl)methyl)-1*H*-indole (**1q**) (102 mg, 0.500 mmol), 1-((1,3-dioxolan-2-yl)methyl)-2-((triisopropylsilyl)ethynyl)-1*H*-indole (**4q**) (126 mg, 0.328 mmol, 66 % yield) was obtained as a brown oil after purification by column chromatography (SiO_2, hexane to hexane/DCM 80/20). R_f: 0.40 (hexanes:EtOAc 20:1) ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.45 (d, 1 H, *J* = 7.9 Hz, ArH), 7.31 (m, 1 H, ArH), 7.19-7.12 (m, 1 H, ArH), 7.04-6.98 (m, 1 H, ArH), 6.72 (s, 1 H, ArH), 5.16 (t, 1 H, *J* = 4.2 Hz, CH_2-C*H*-O), 4.36-4.28 (m, 2 H, N-C*H*$_2$-CH), 3.75 (m, 4 H, -CH_2-CH_2-), 1.25-0.76 (m, 21 H, TIPS). ^{13}C NMR (101 MHz, $CDCl_3$) δ 137.2, 127.2, 123.3, 122.2, 121.0, 120.3, 110.3, 108.7, 102.6, 98.1, 97.9, 65.2, 47.5, 18.7, 11.4. IR 3058 (w), 2942 (m), 2890 (m), 2864 (s), 2150 (m), 1480 (w), 1457 (s), 1437 (w), 1386 (m), 1367 (m), 1340 (s), 1315 (m), 1281 (w), 1233 (w), 1219 (m), 1177 (w), 1161 (m), 1160 (m), 1073 (w), 1016 (w), 997 (m), 916 (w), 882 (s), 857 (m), 843 (w). HRMS (ESI) calcd for $C_{23}H_{34}NO_2Si^+$ $[M+H]^+$ 384.2353; found 384.2357.

Spectra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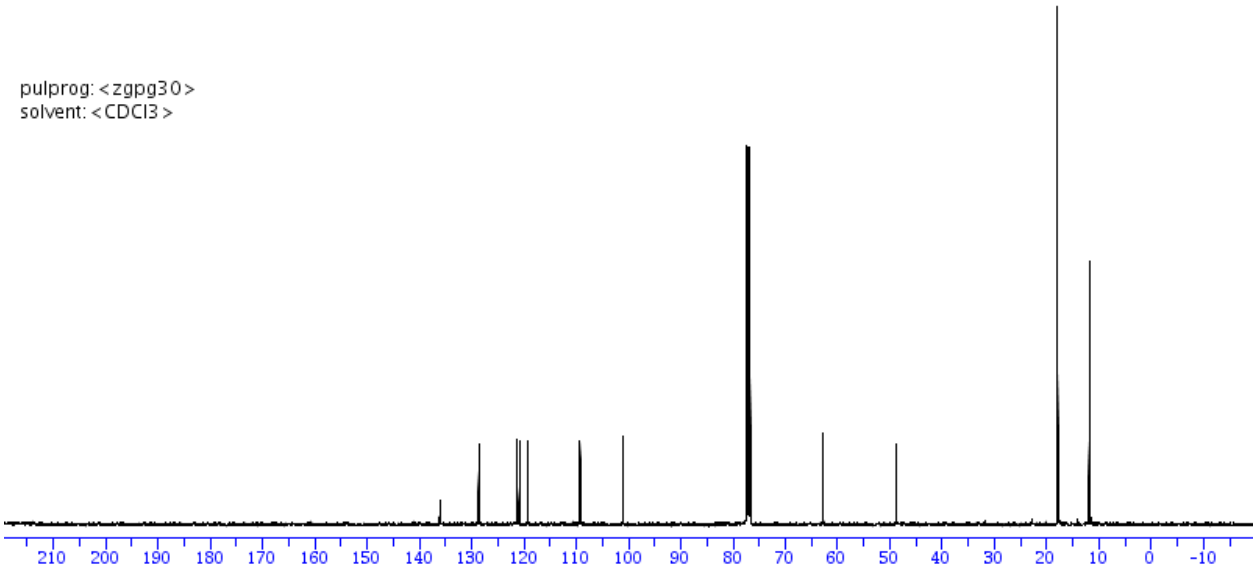
OSi^{i}Pr$_3$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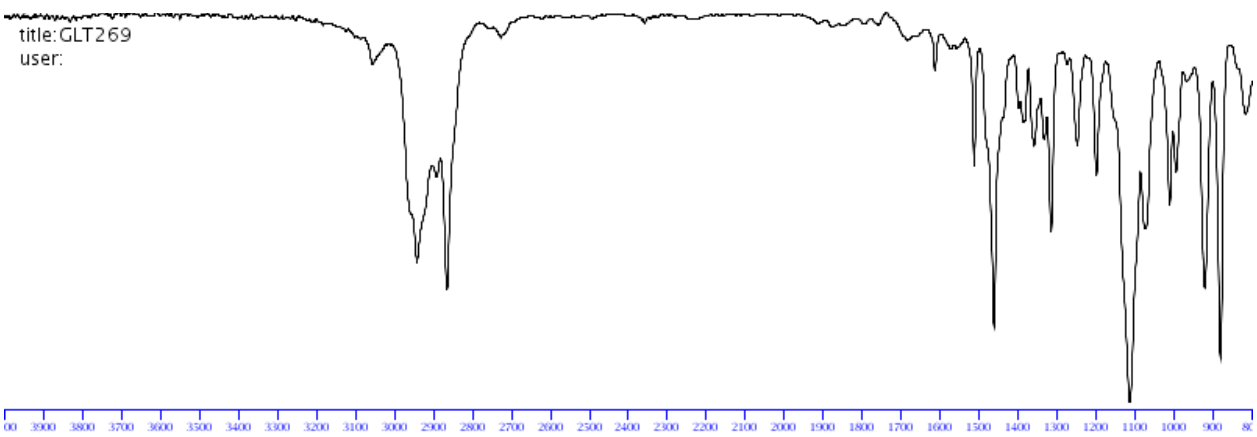
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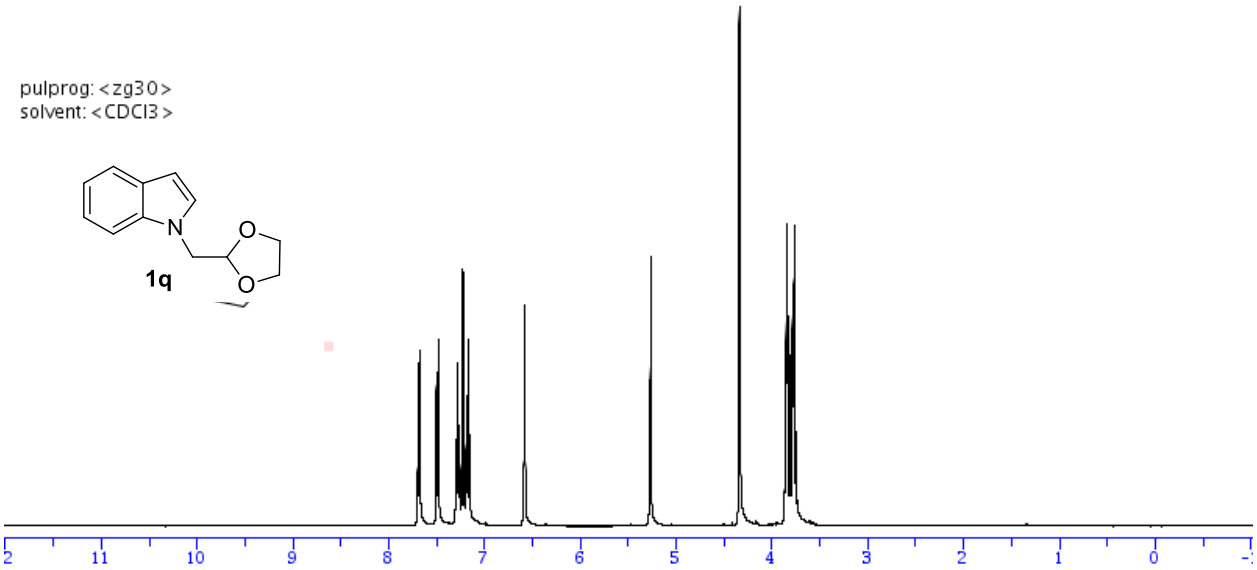
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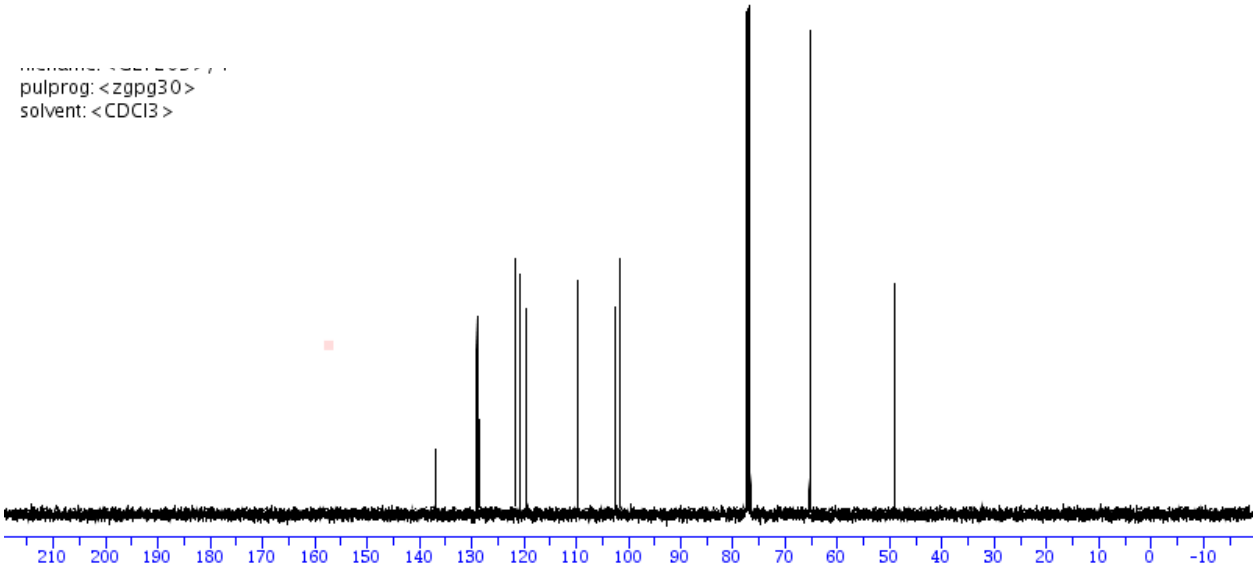
1
0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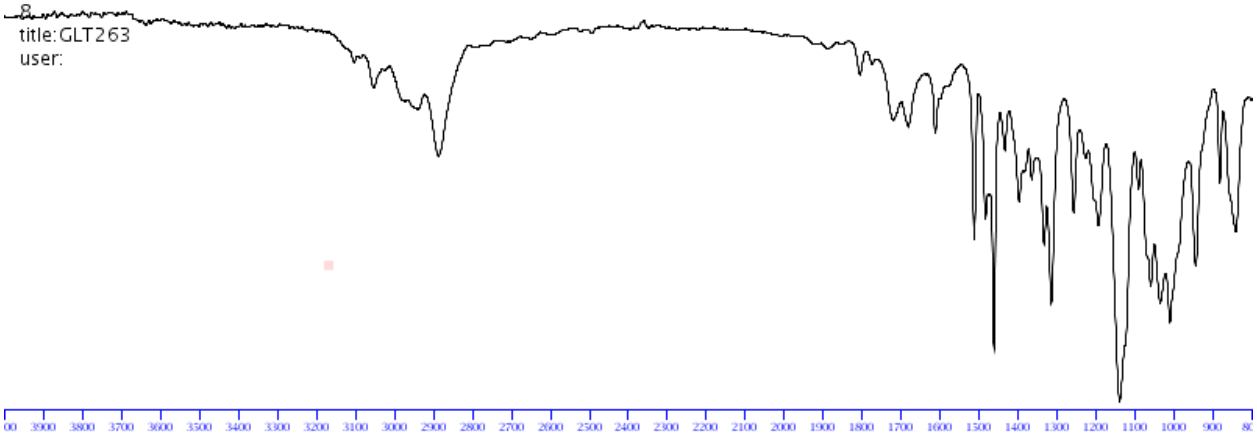
0
-10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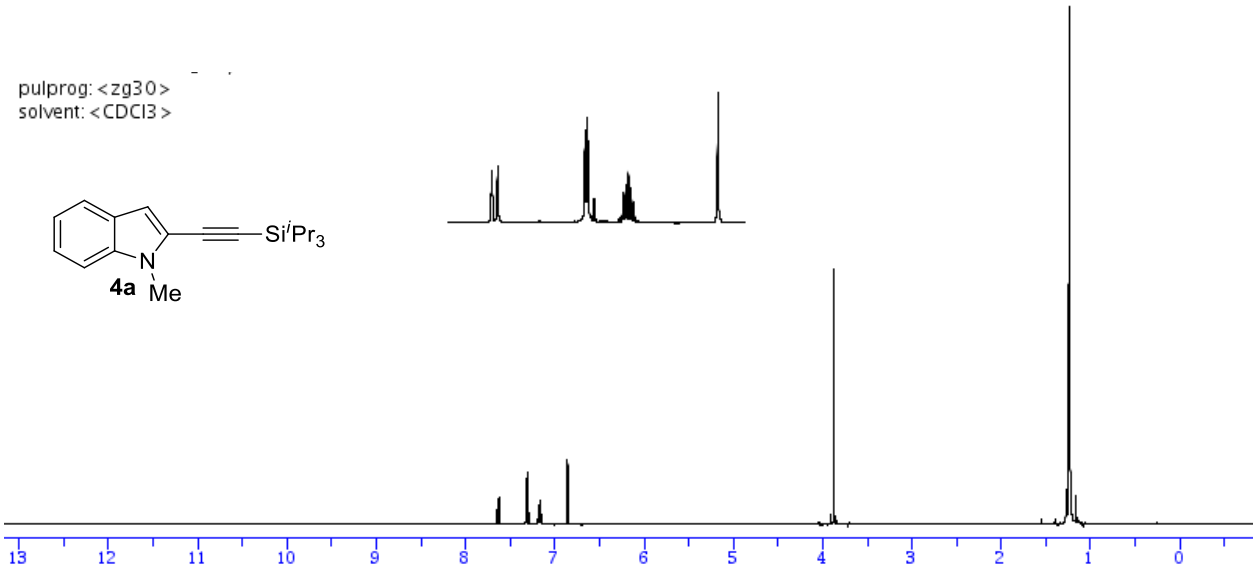
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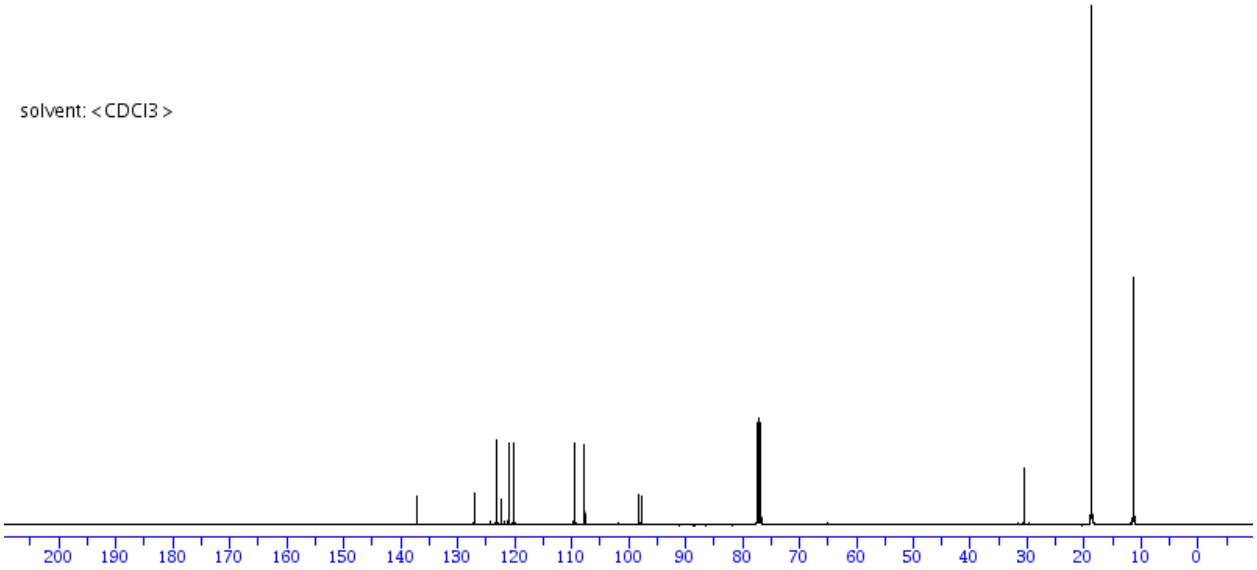
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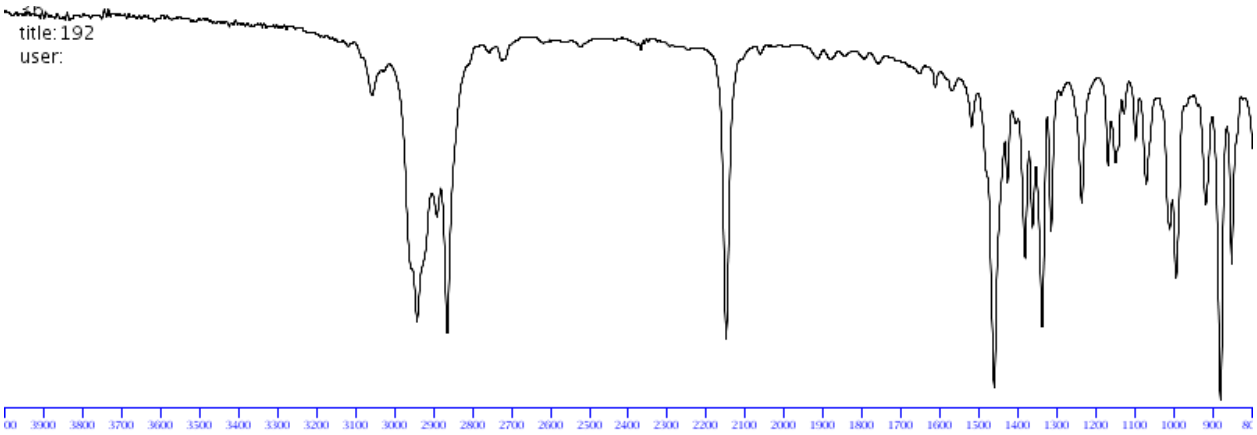
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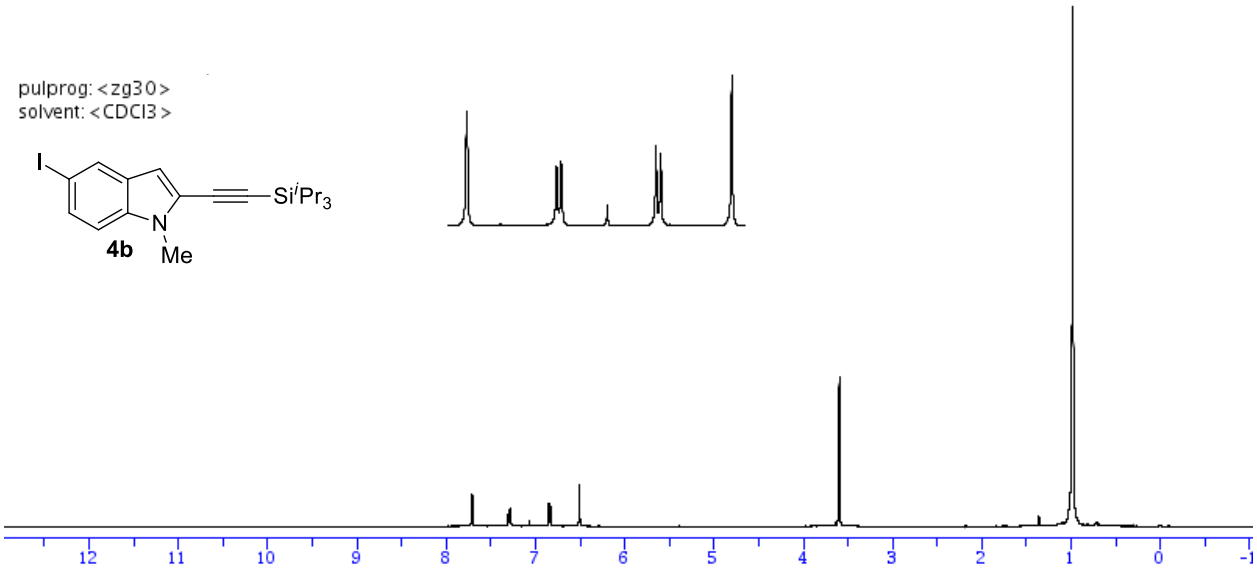
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Me
4b
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7
6
5
4
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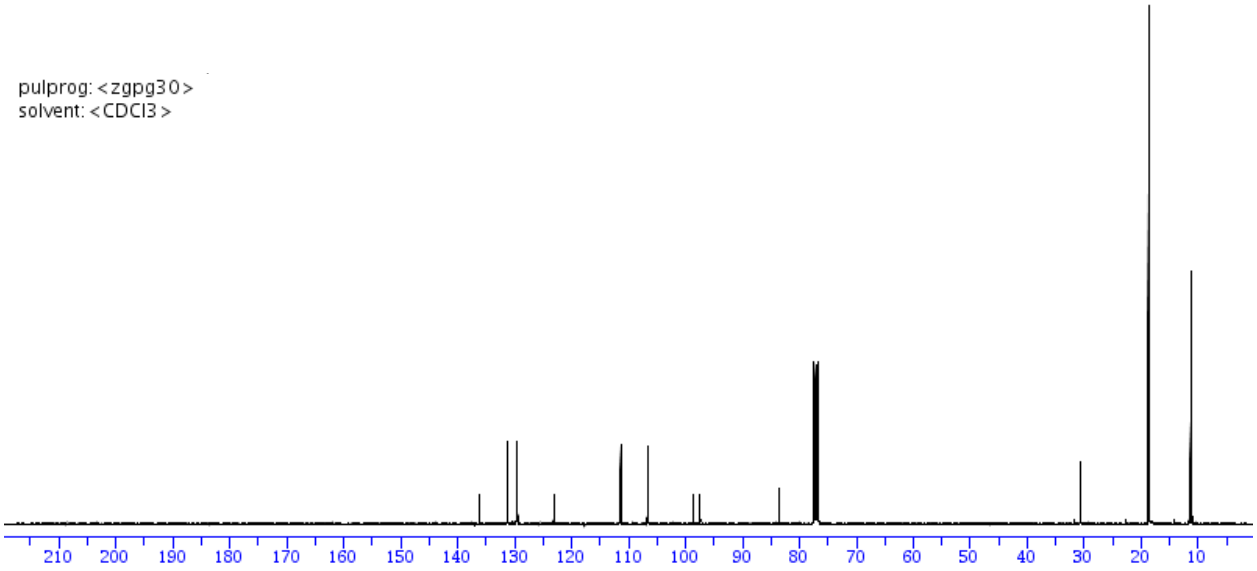
2
1
0
-1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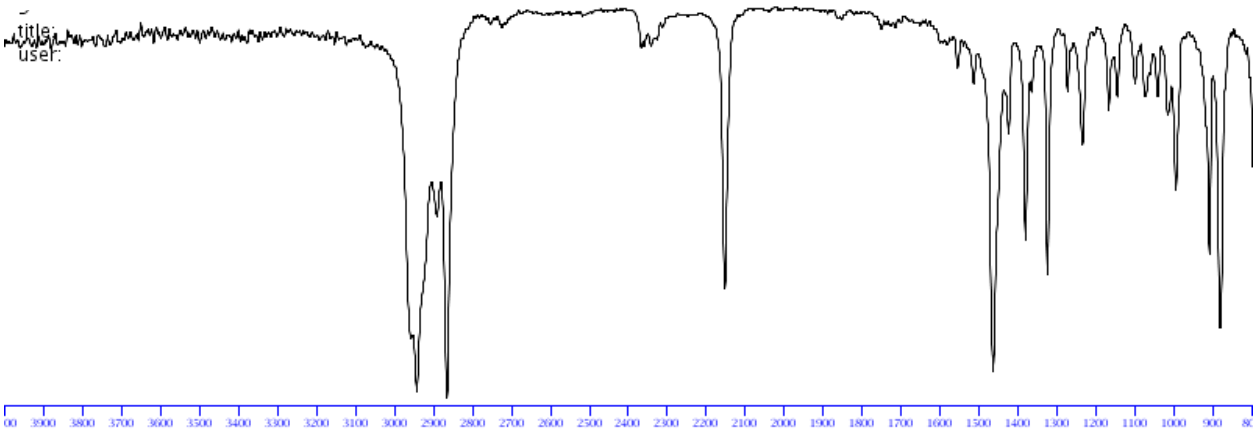
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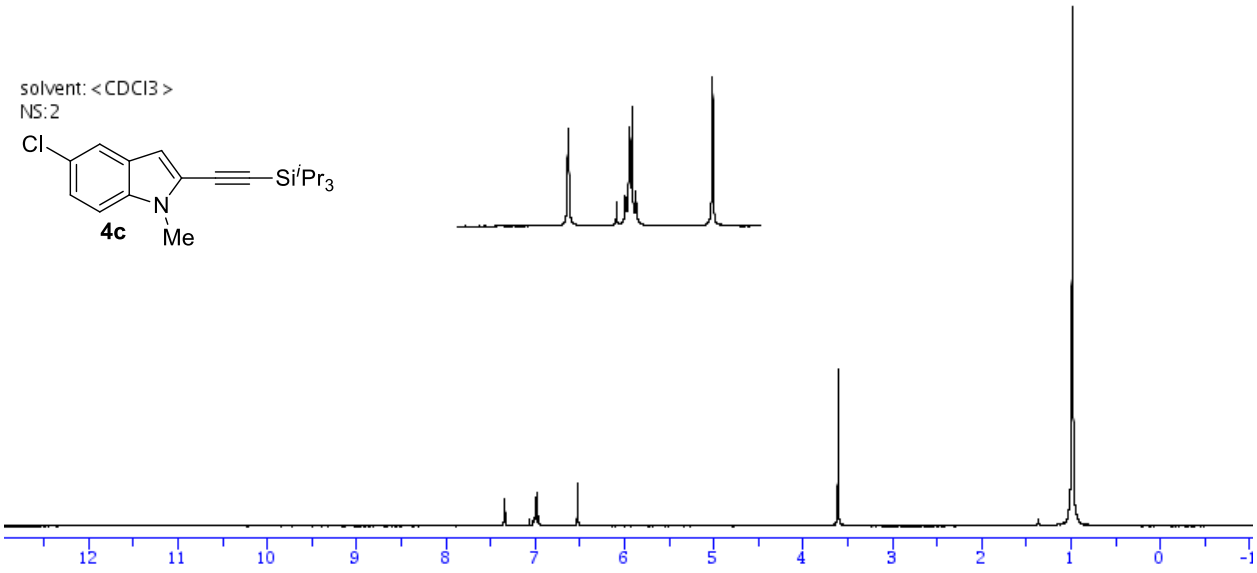
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Si^{i}Pr$_3$
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4c
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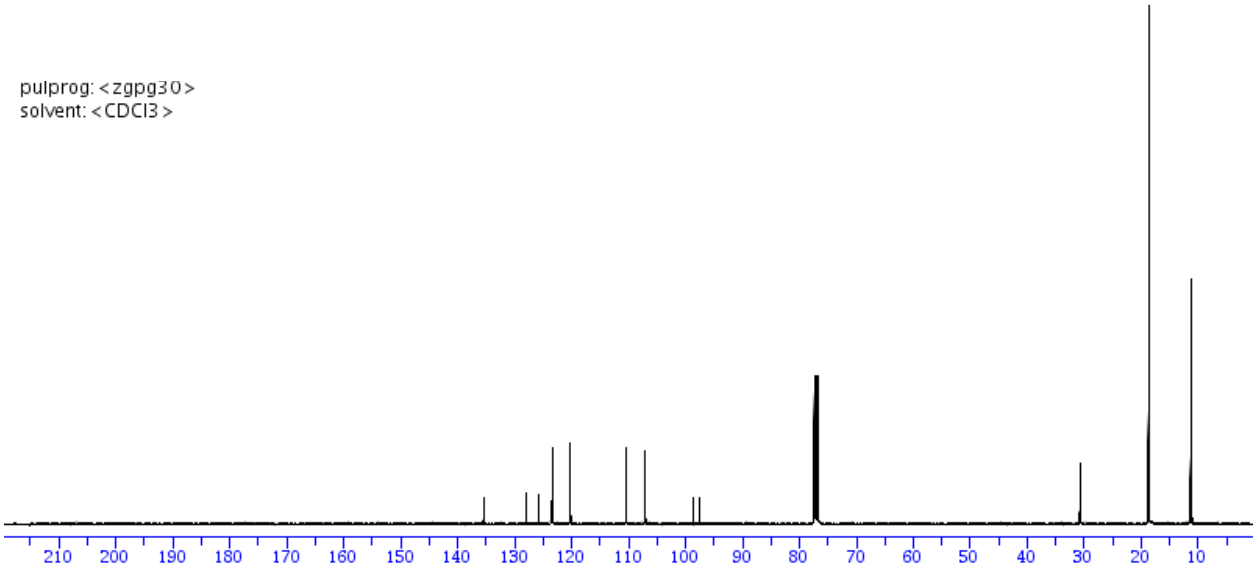
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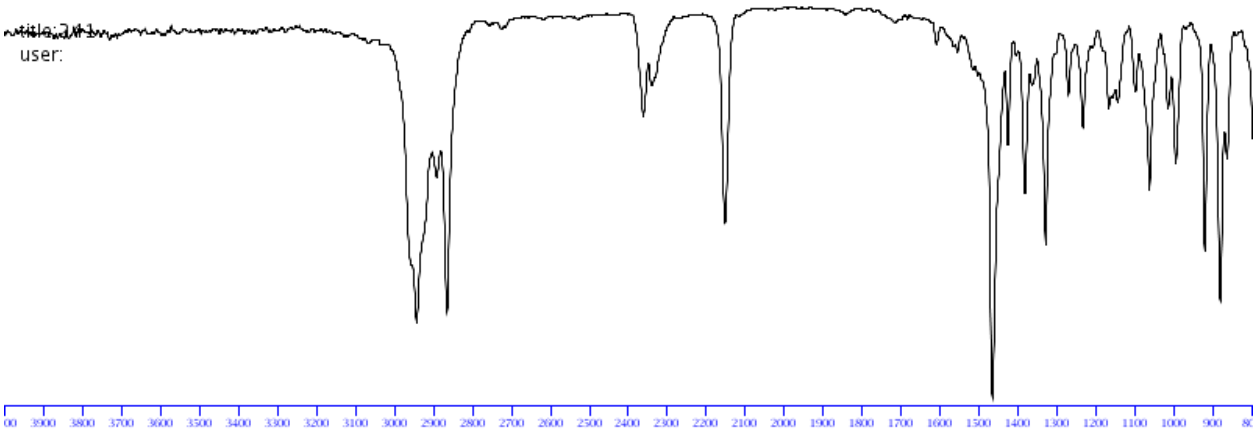
10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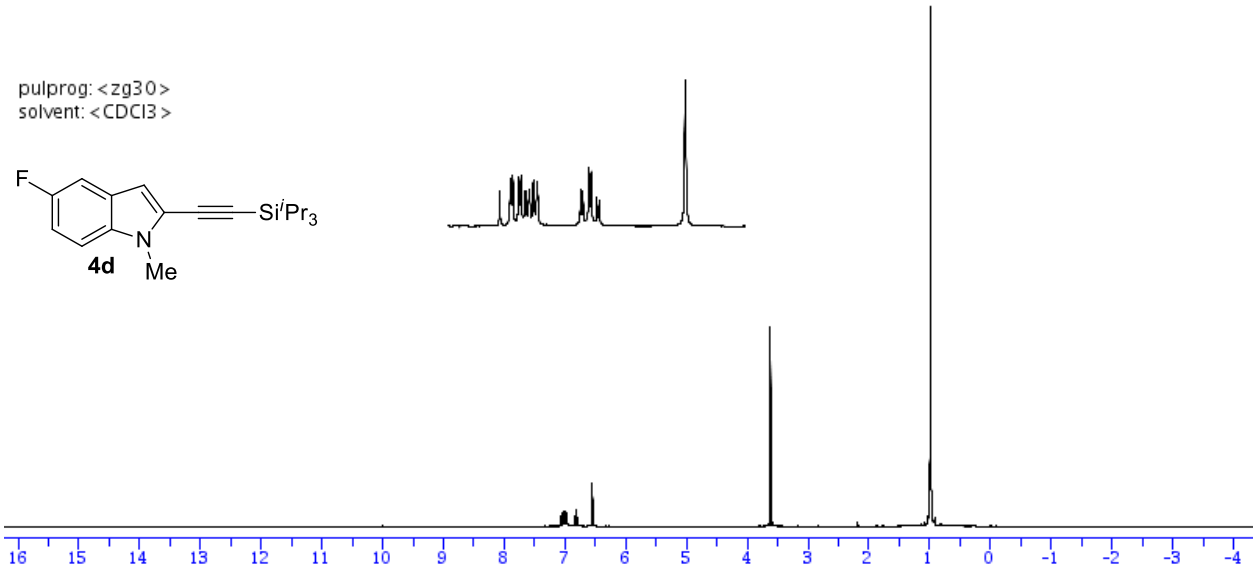
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4d
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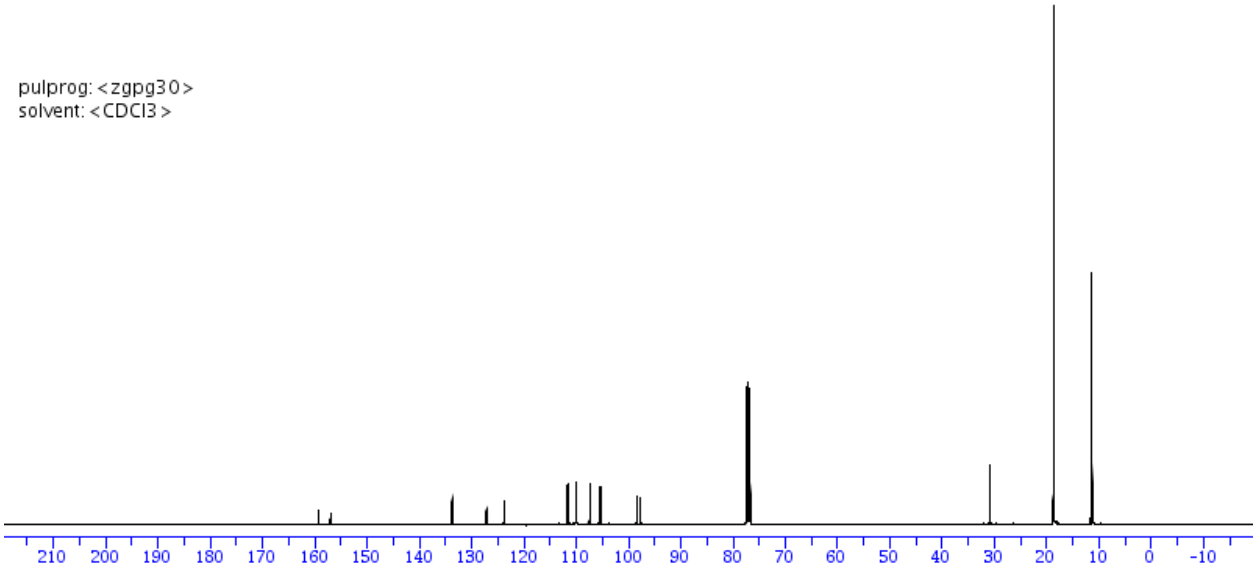
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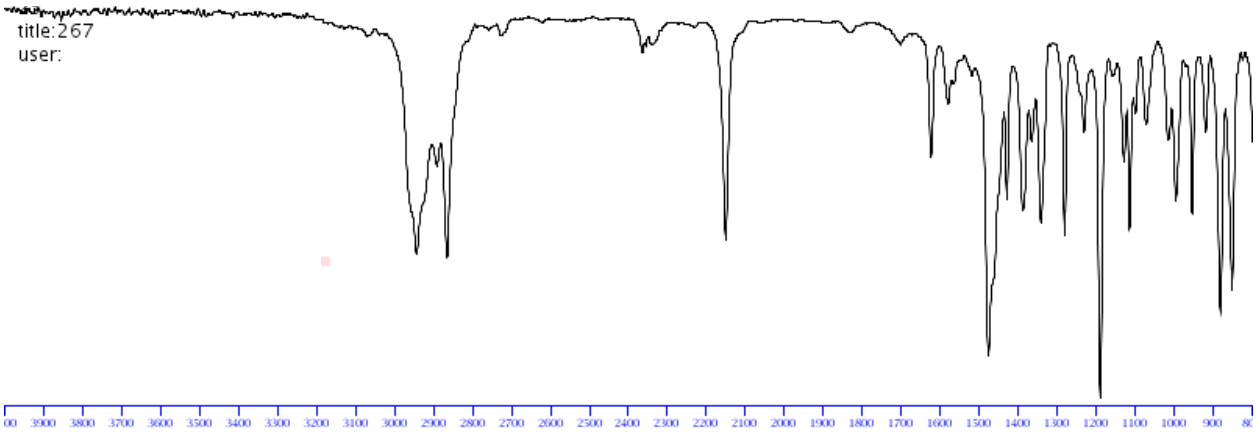
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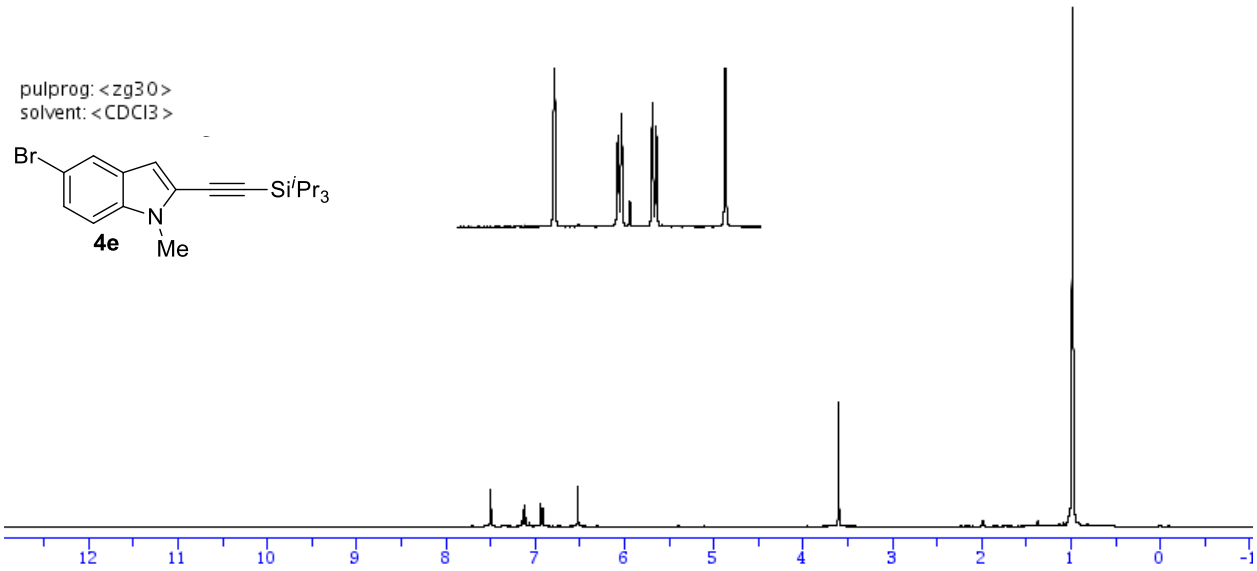
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Me
4e
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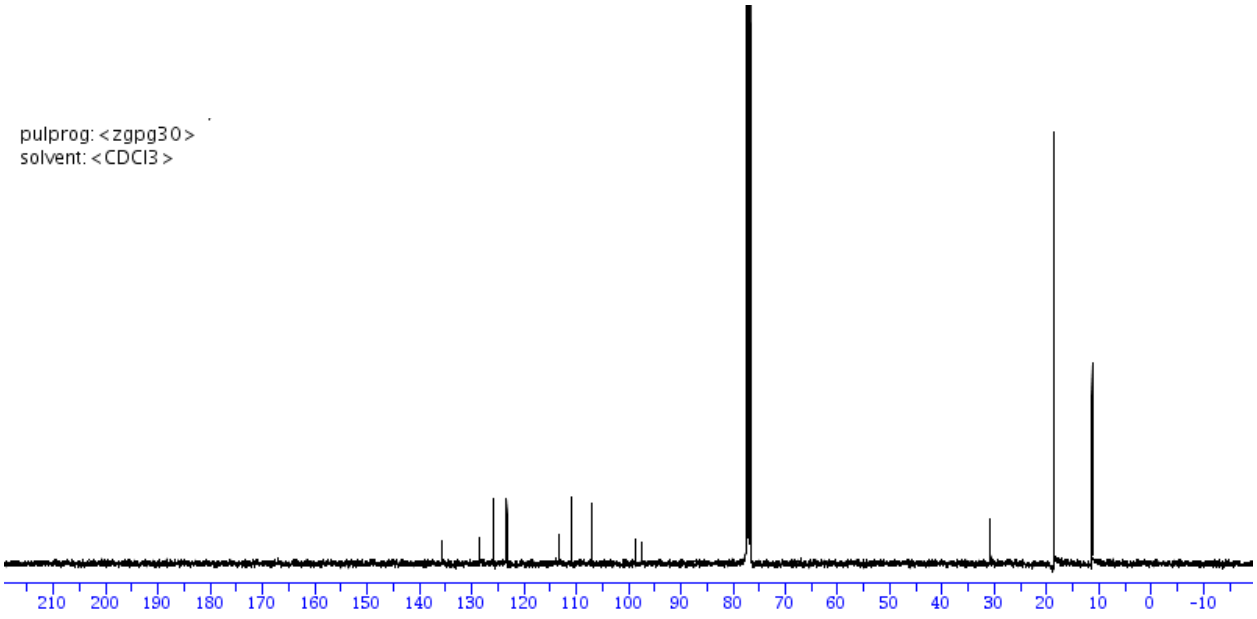
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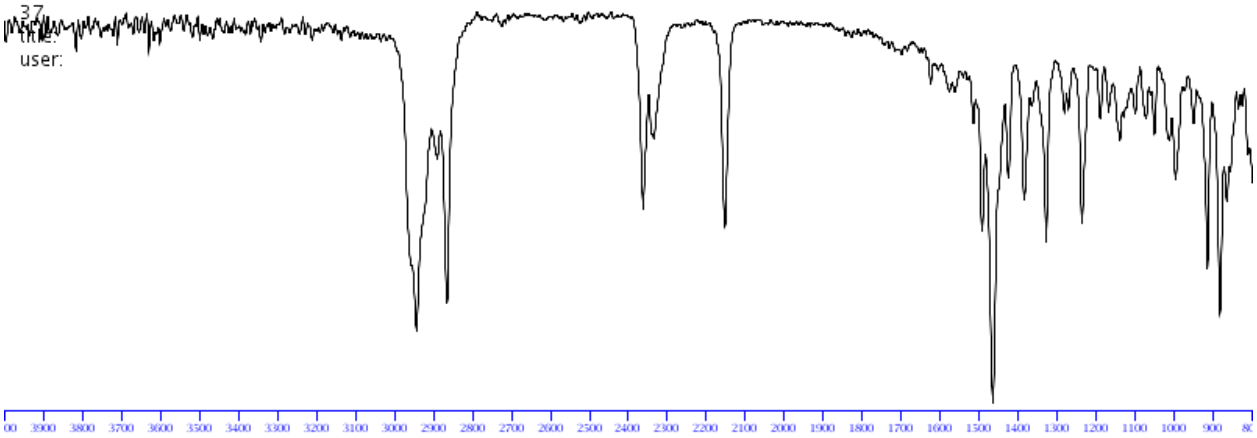
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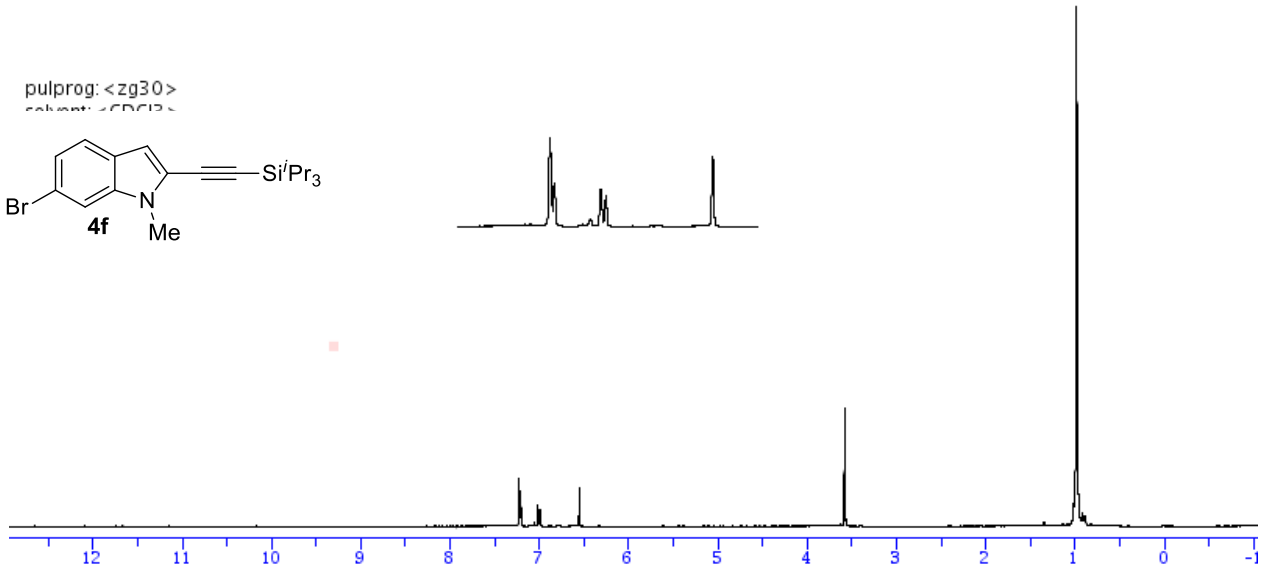
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Me
Si^{i}Pr$_3$
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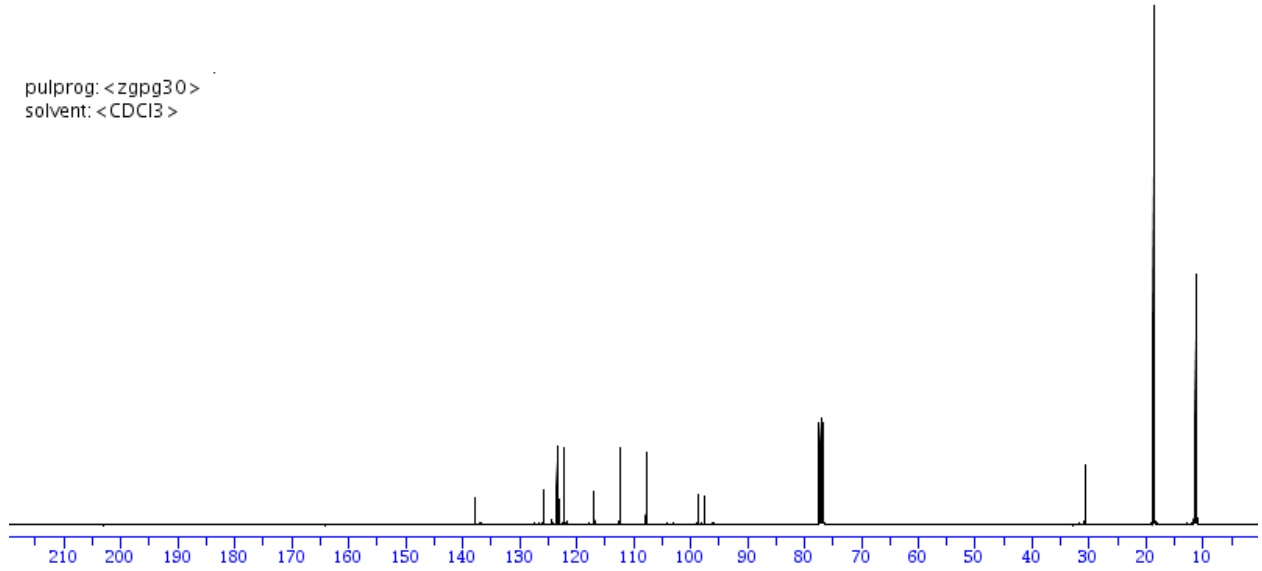
-1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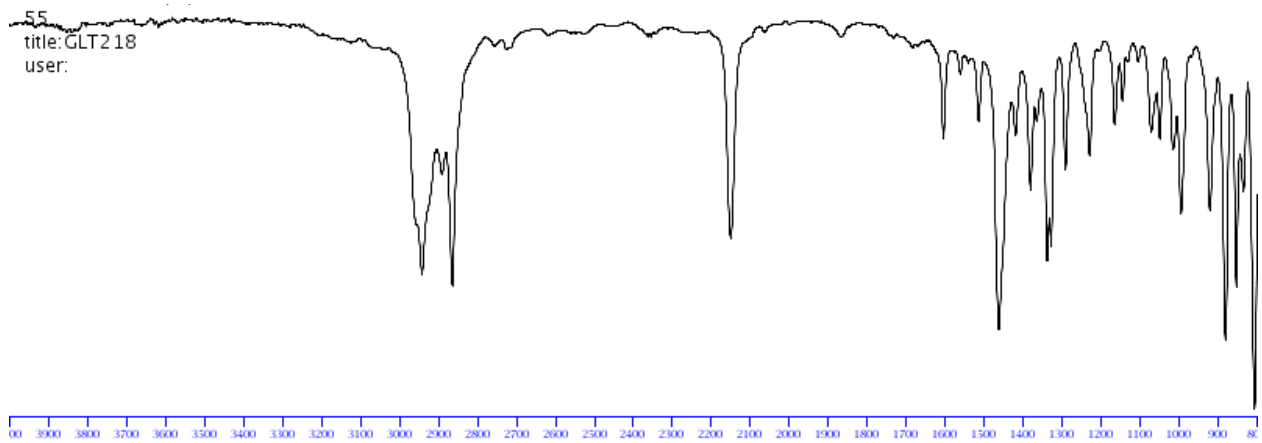
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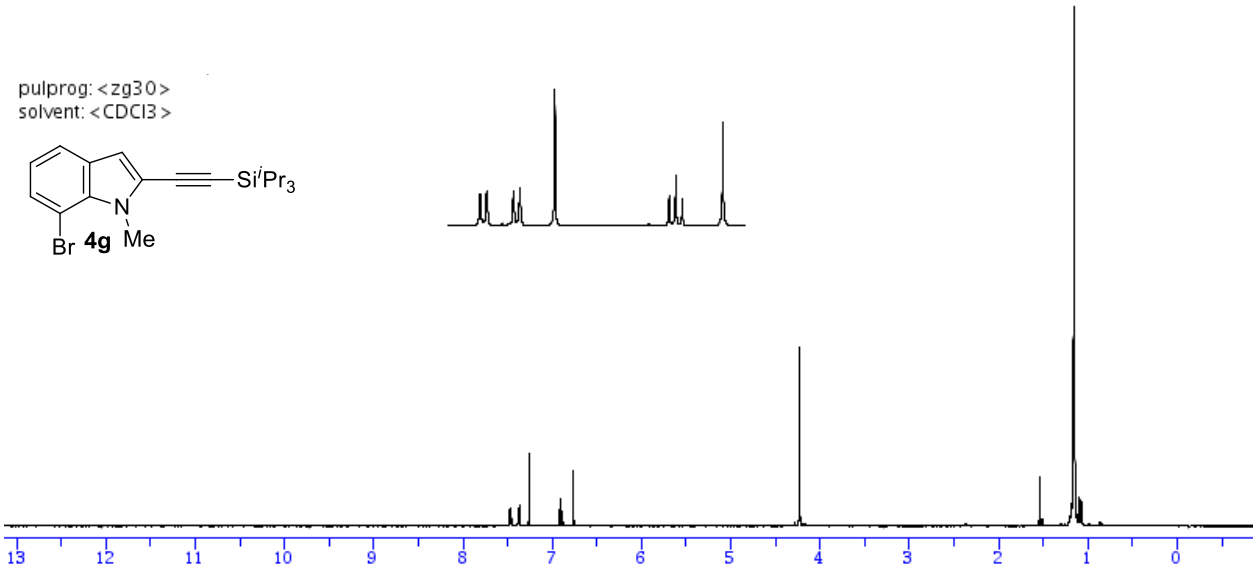
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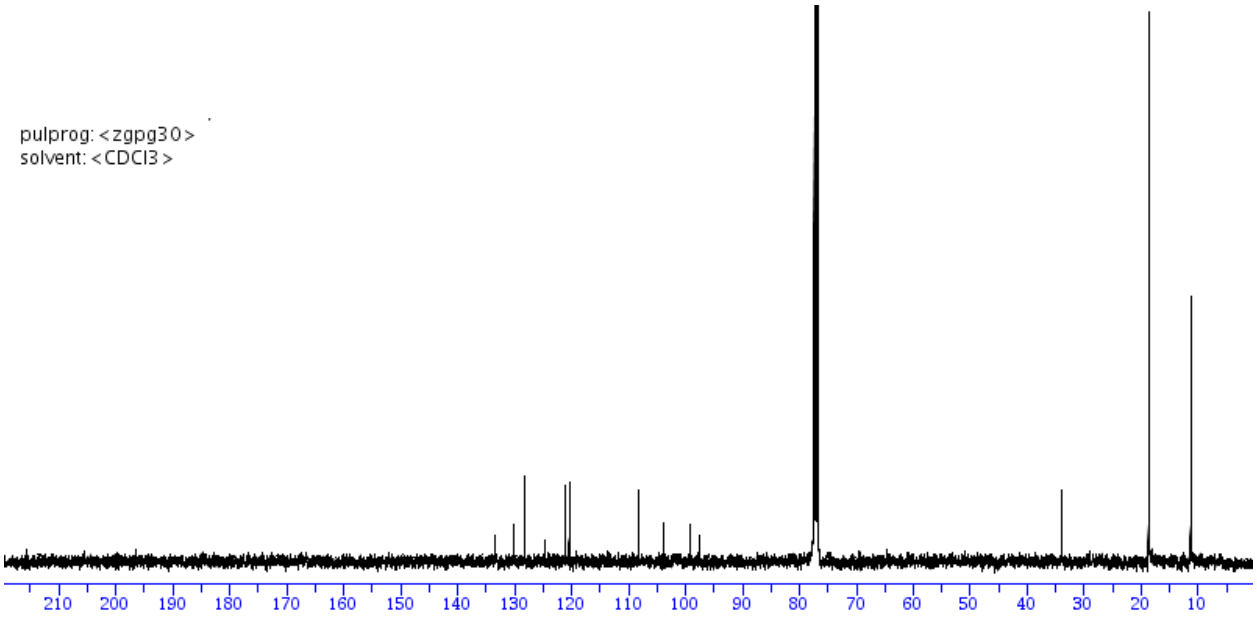
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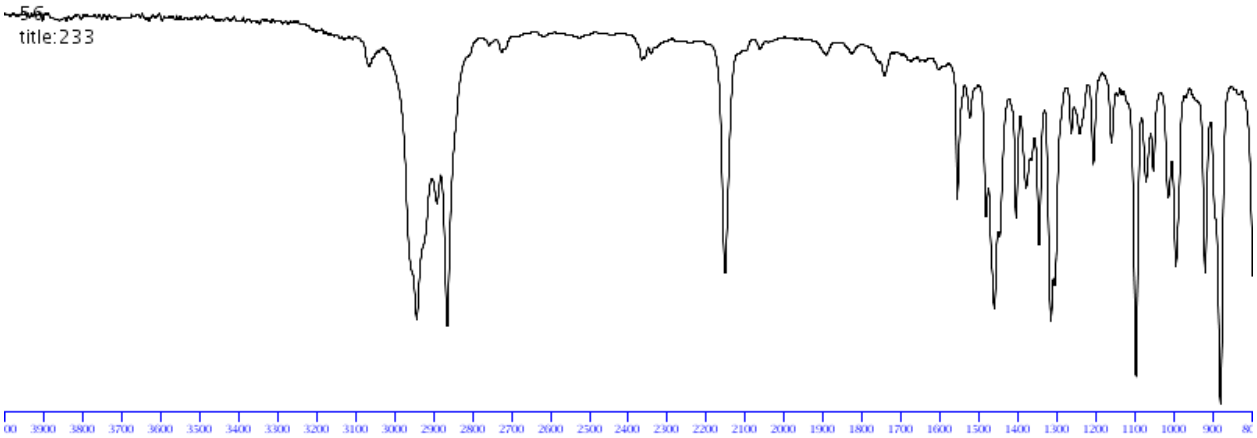
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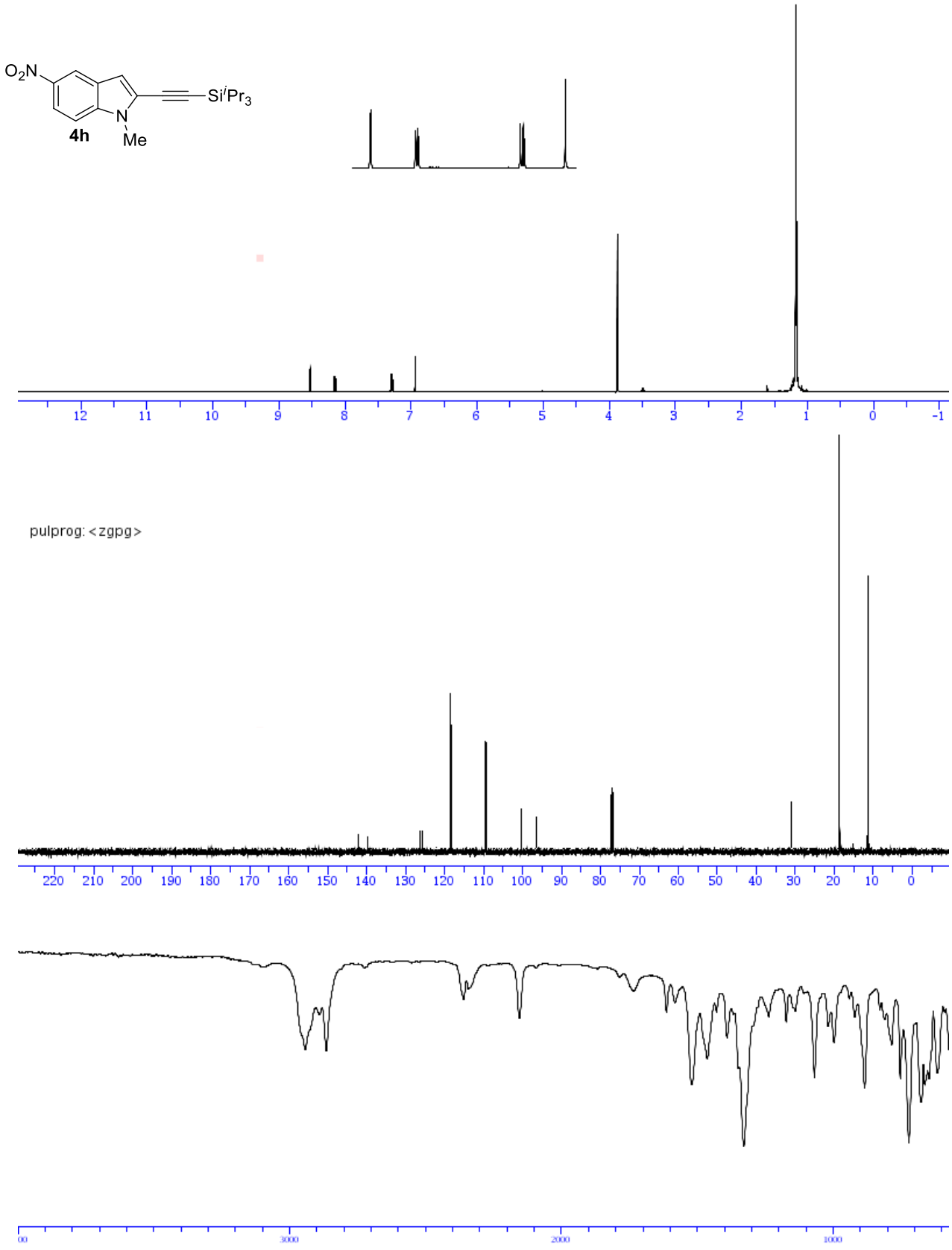
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4h
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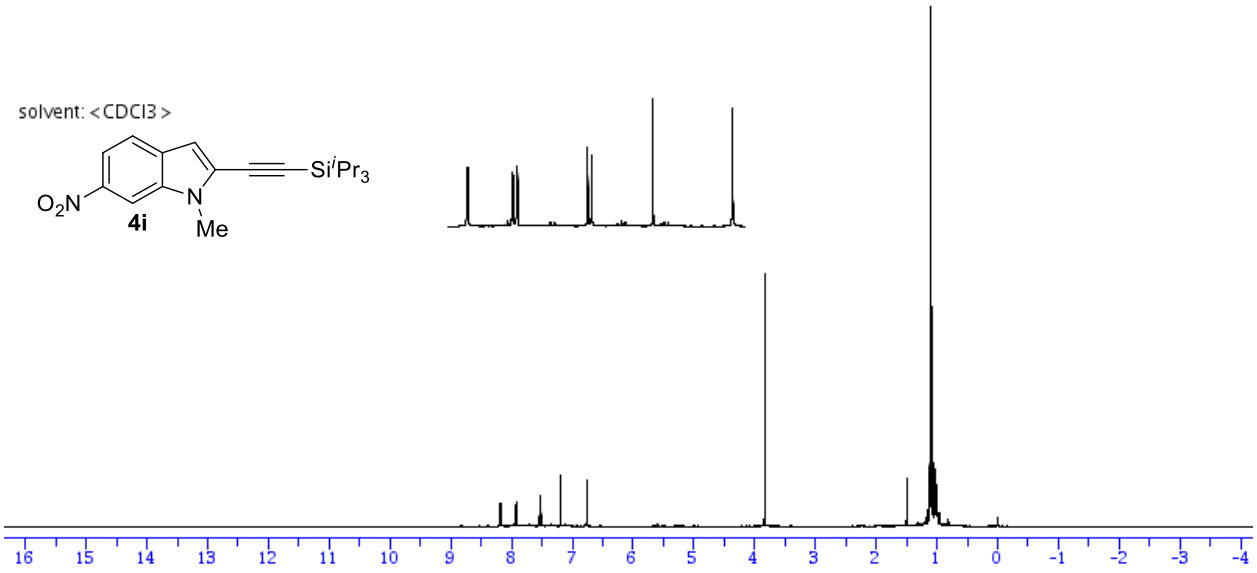
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4i
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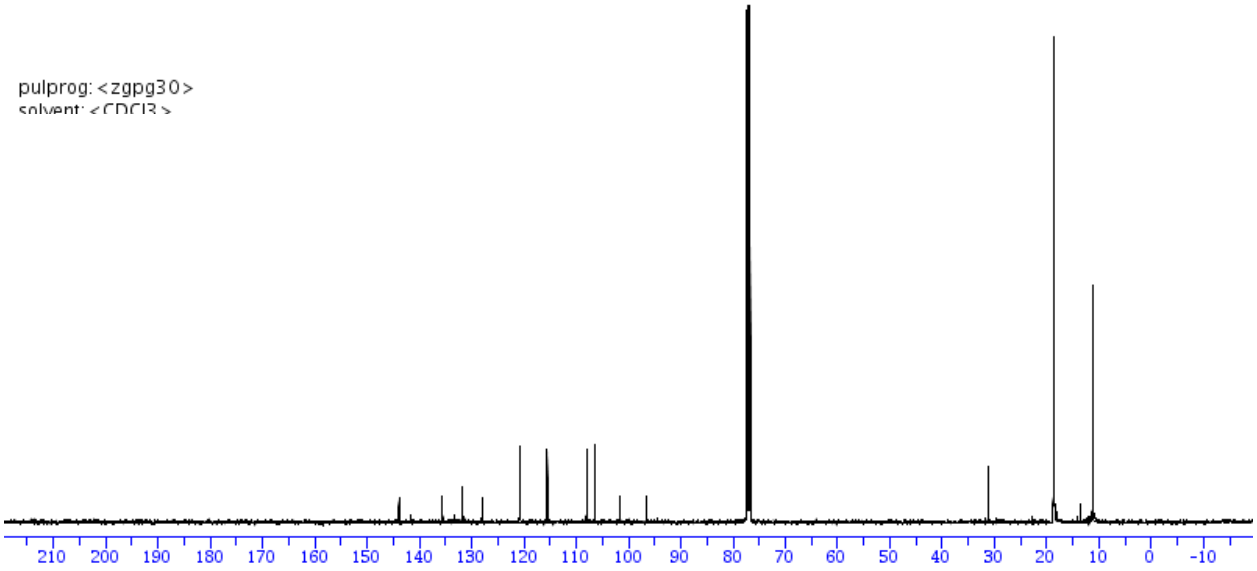
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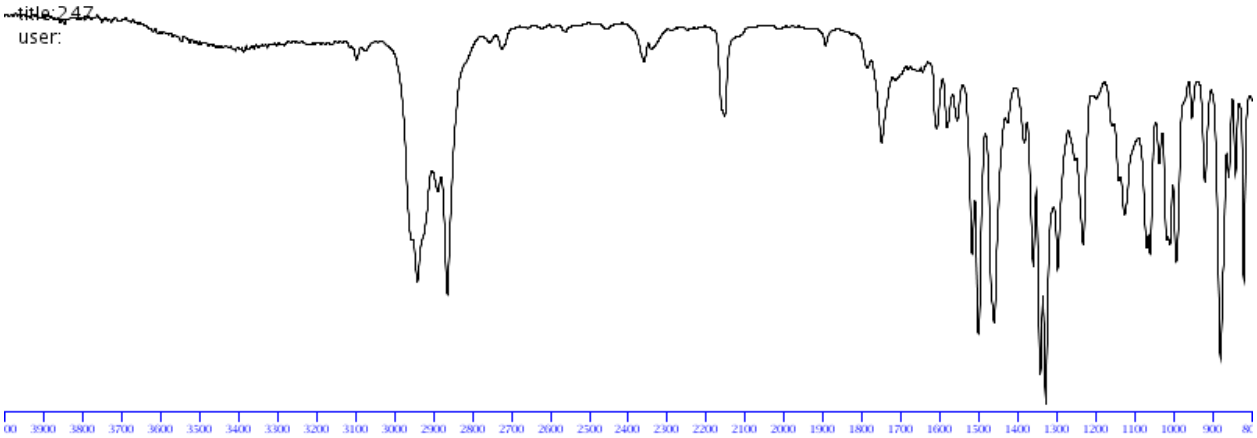
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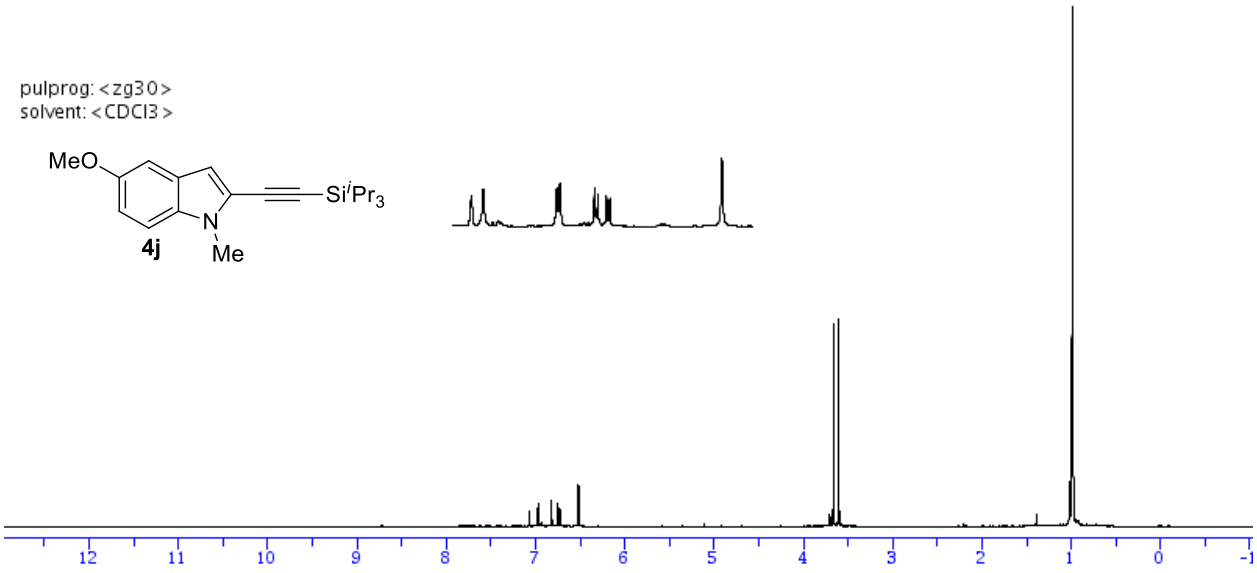
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Me
4j
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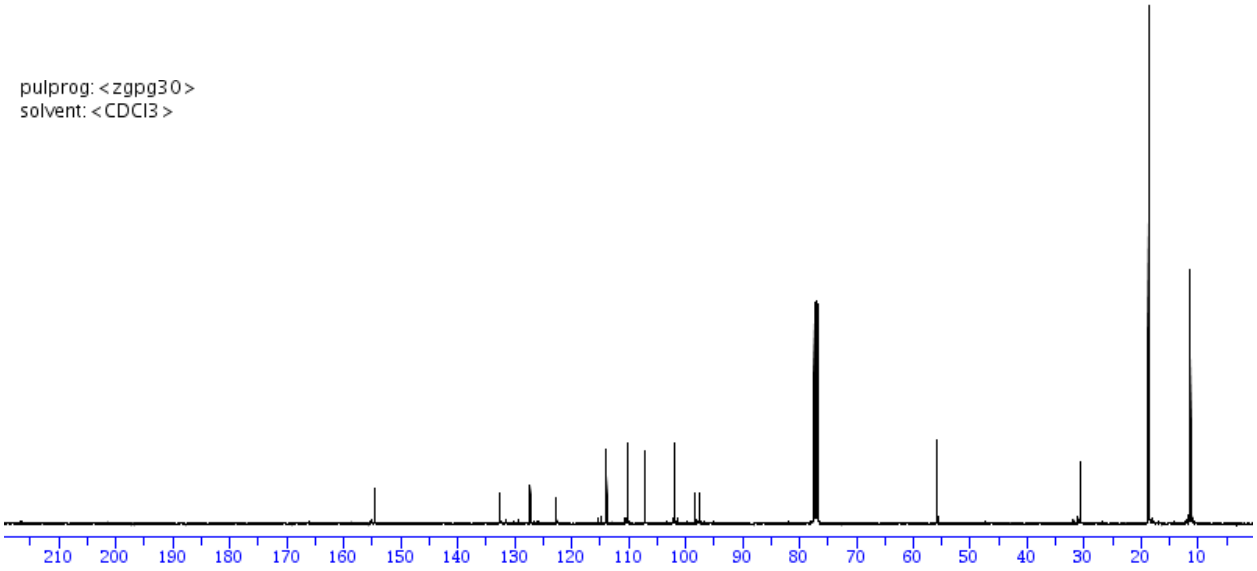
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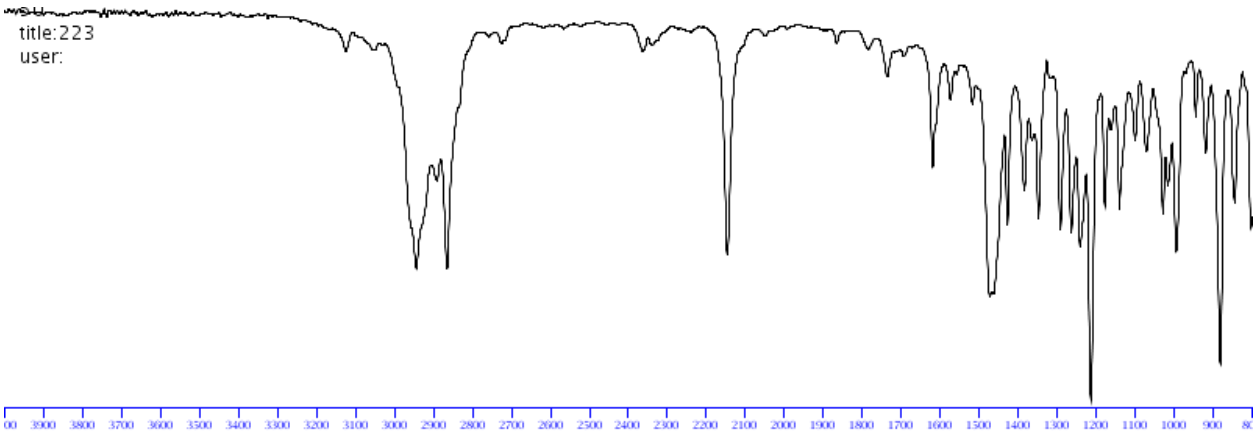
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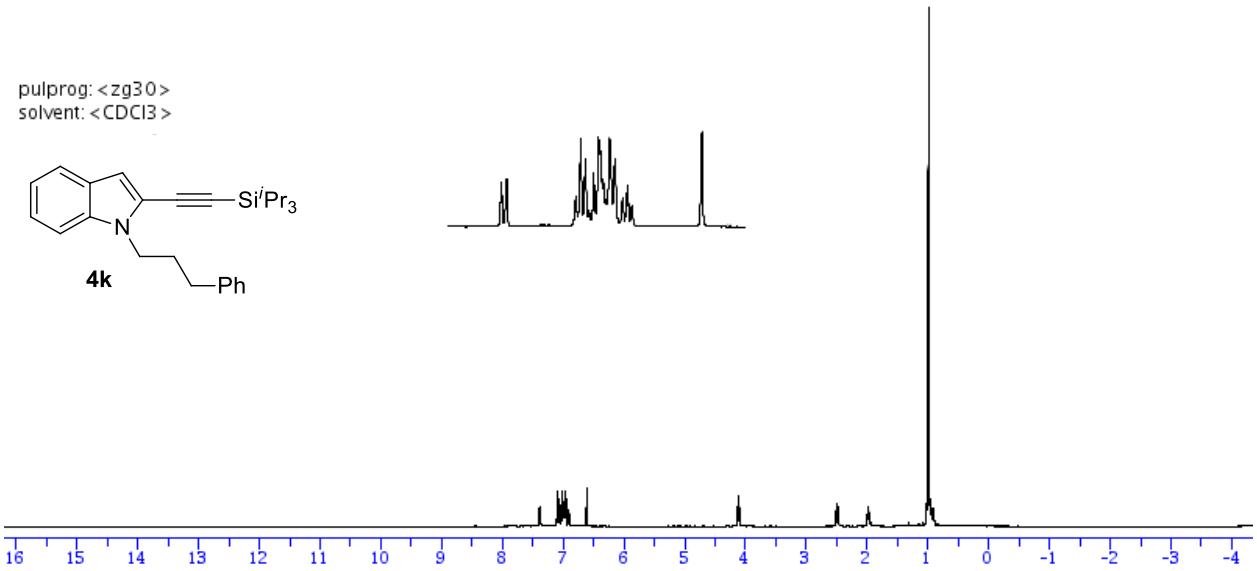
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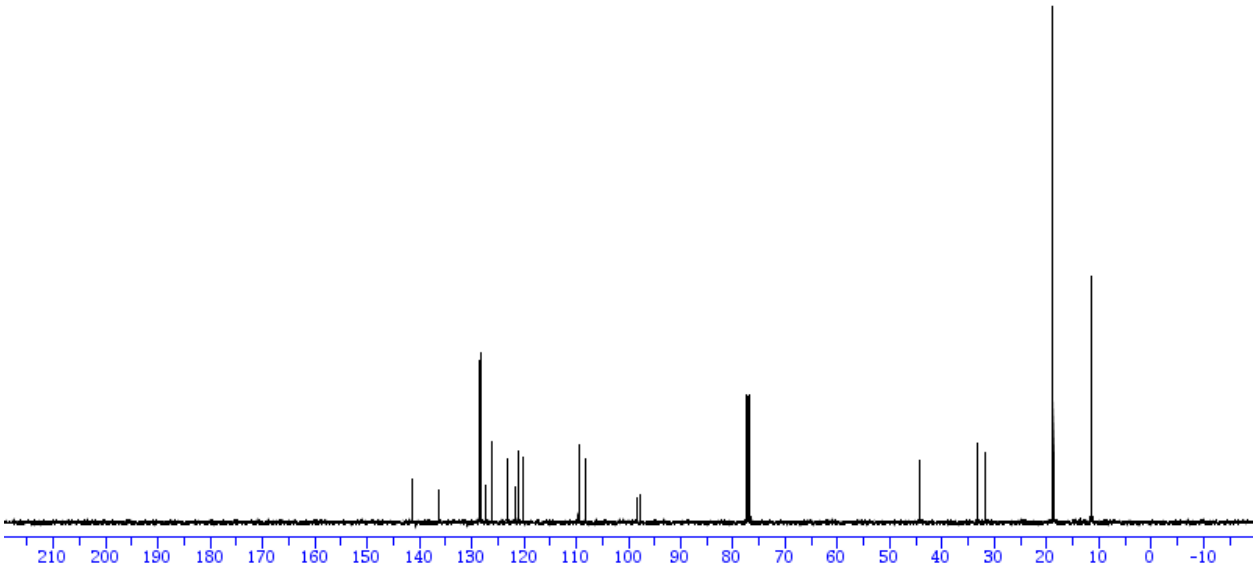
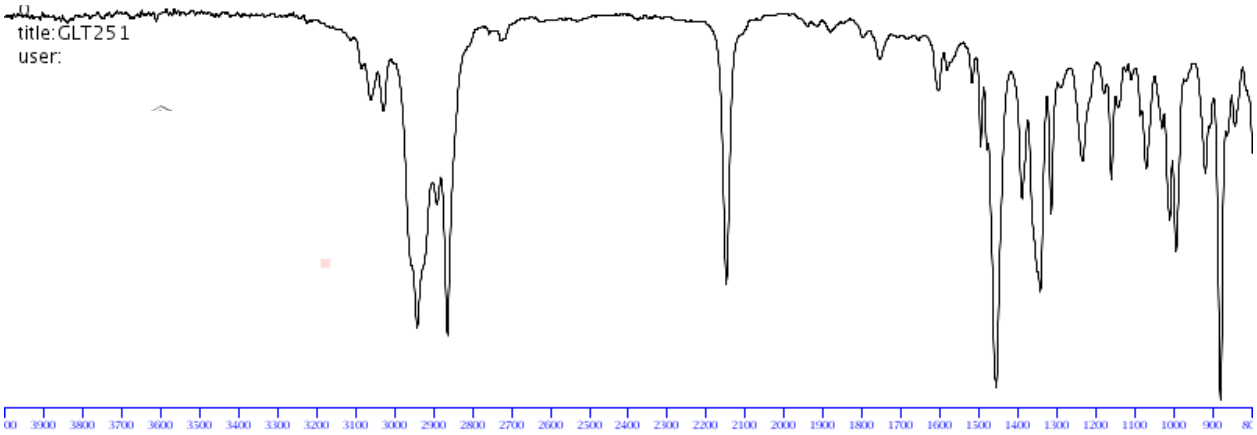
Ph
4k

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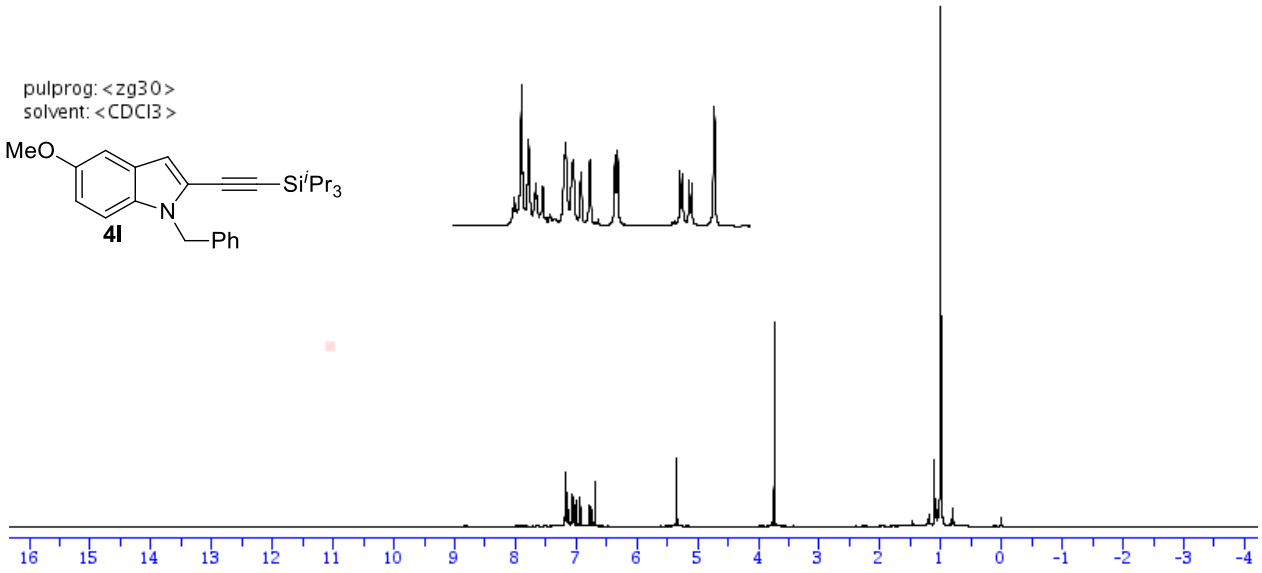
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Si^{i}Pr$_3$
N
Ph
4l
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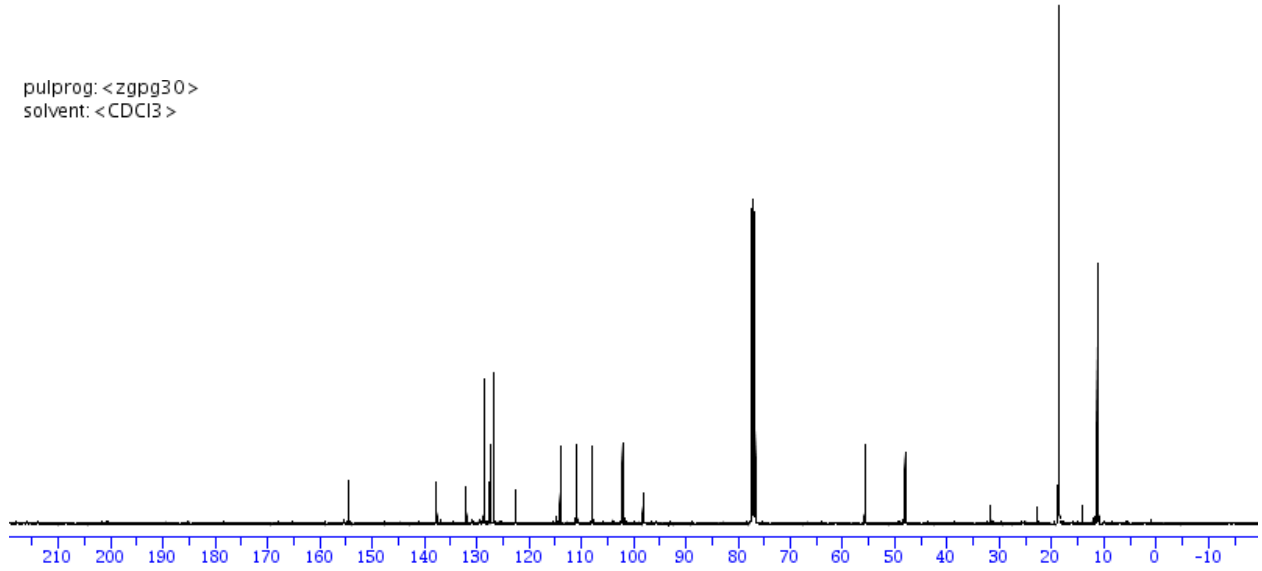
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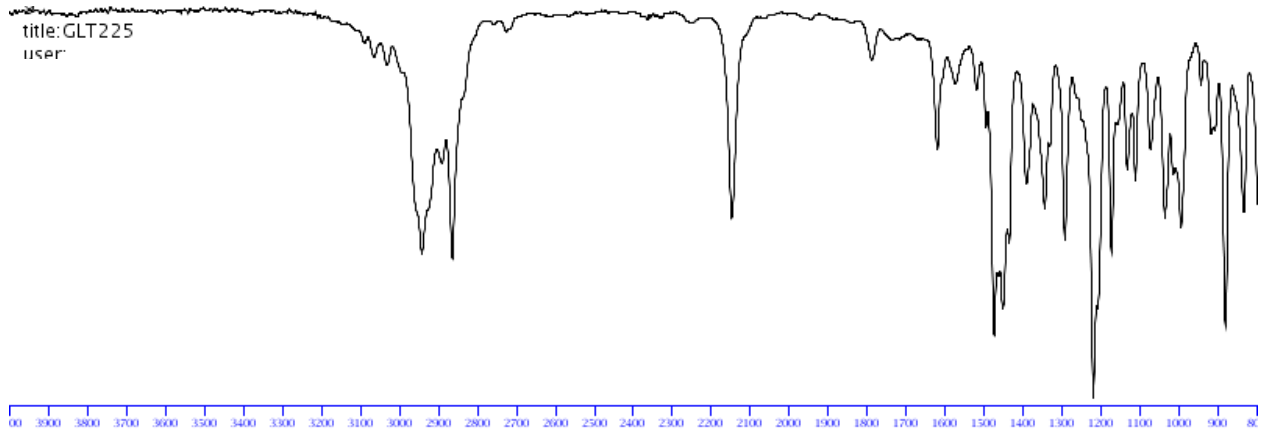
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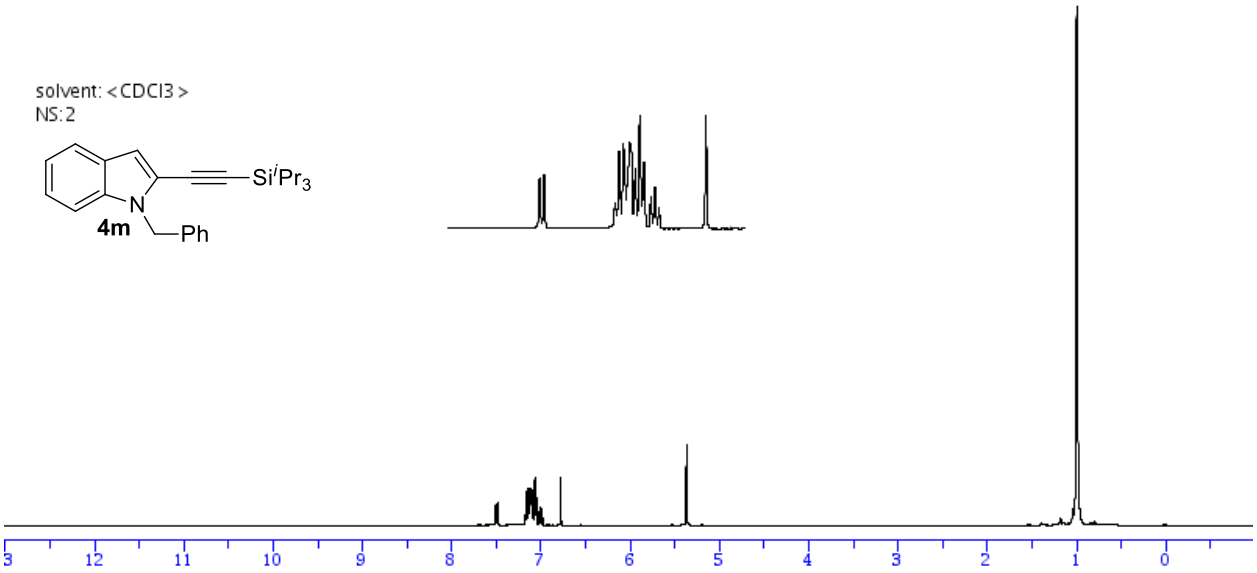
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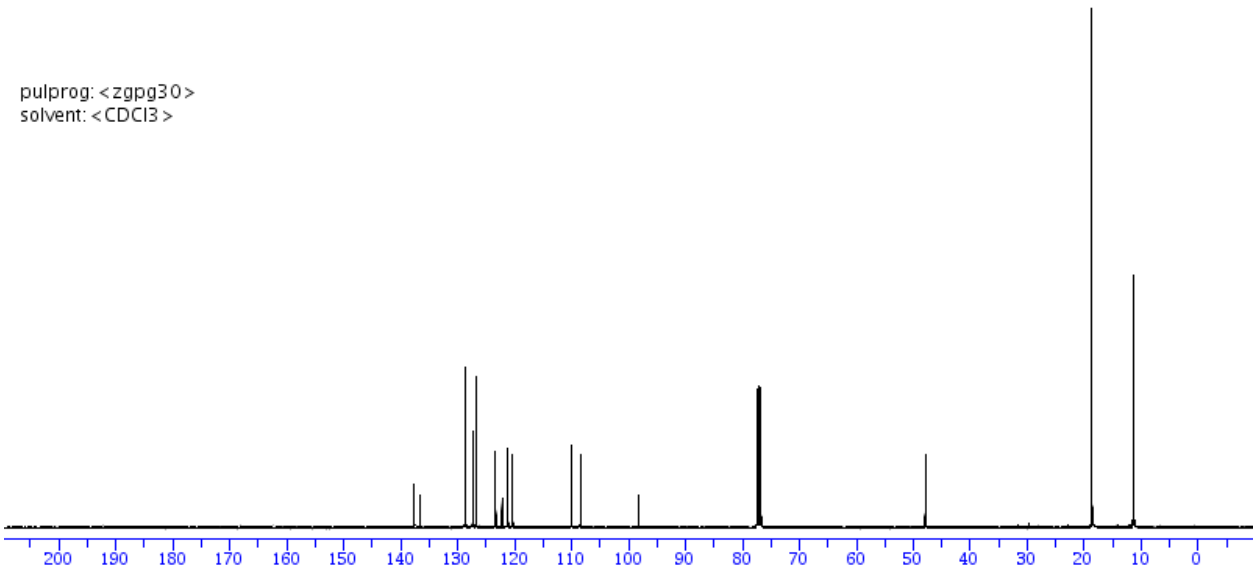
Si^{i}Pr$_3$
N
Ph
4m
3
12
11
10
9
8
7
6
5
4
3
2
1
0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200
190
180
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60
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30
20
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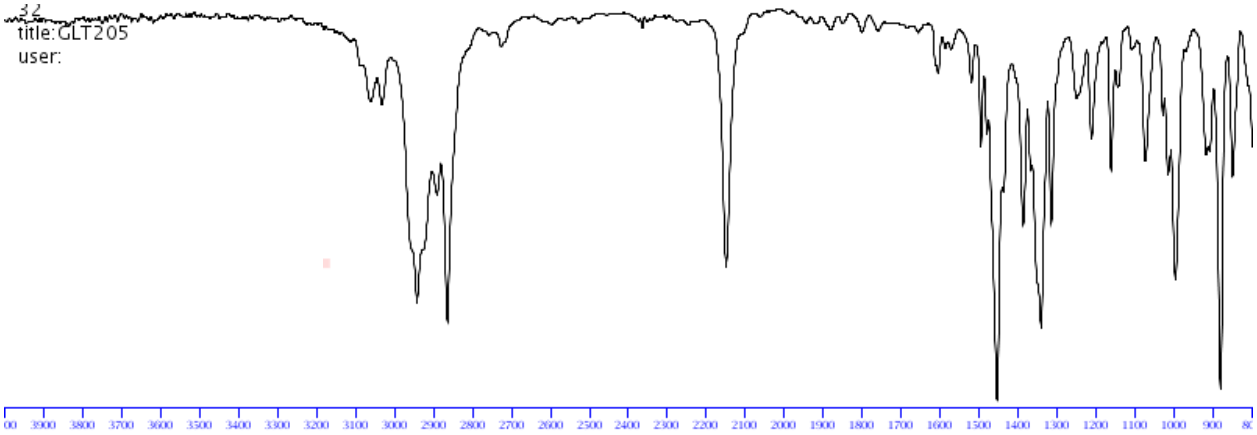
0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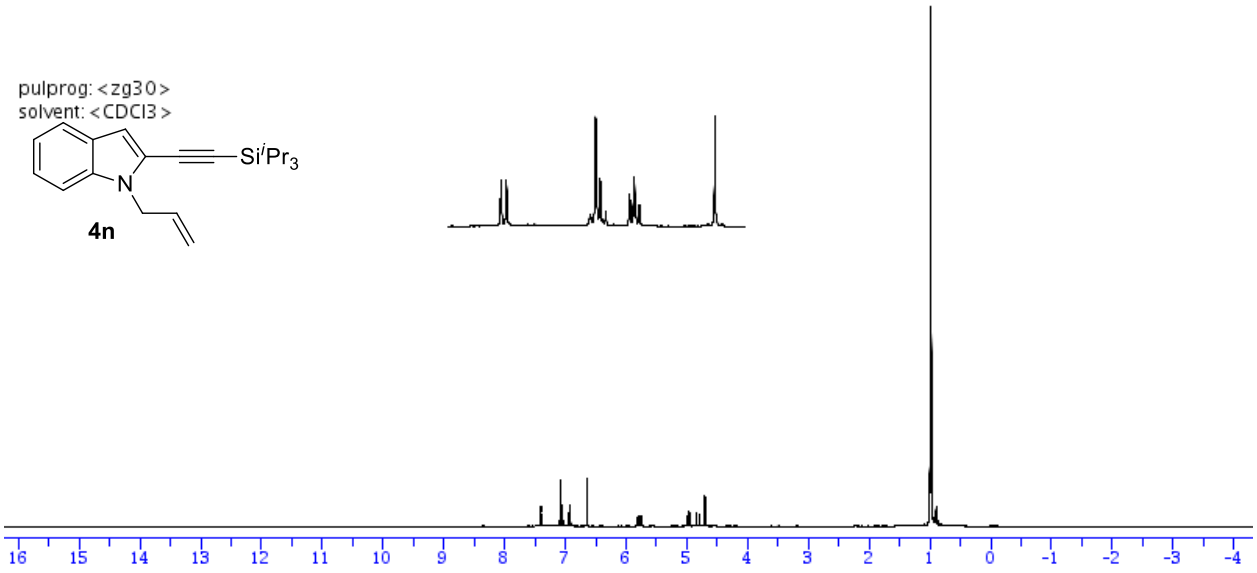
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Si^{i}Pr$_3$
N
4n
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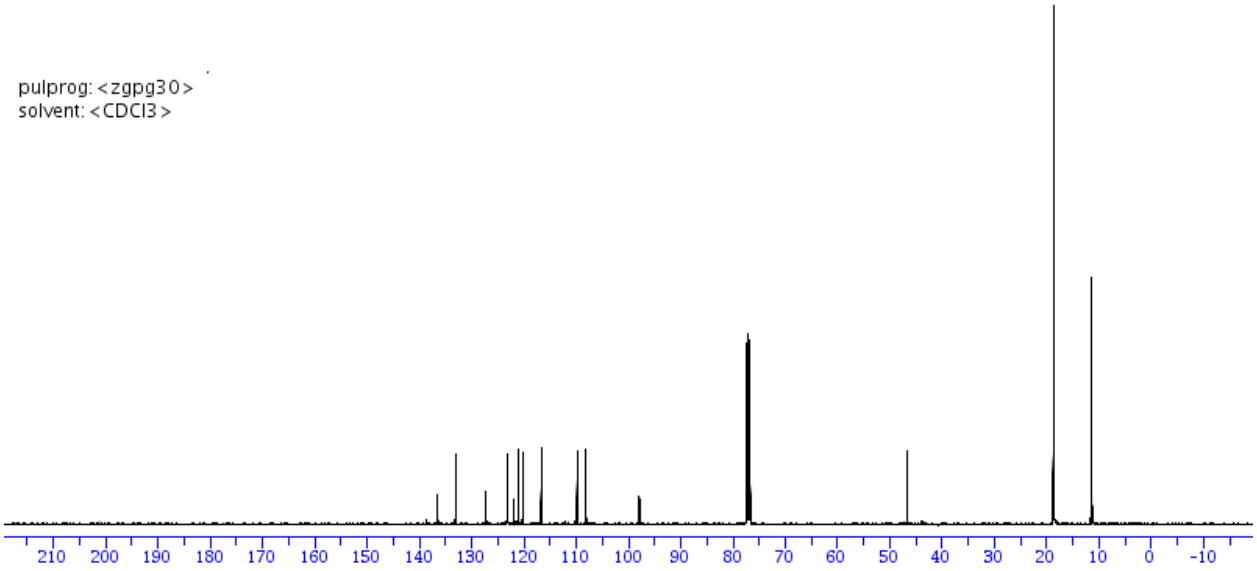
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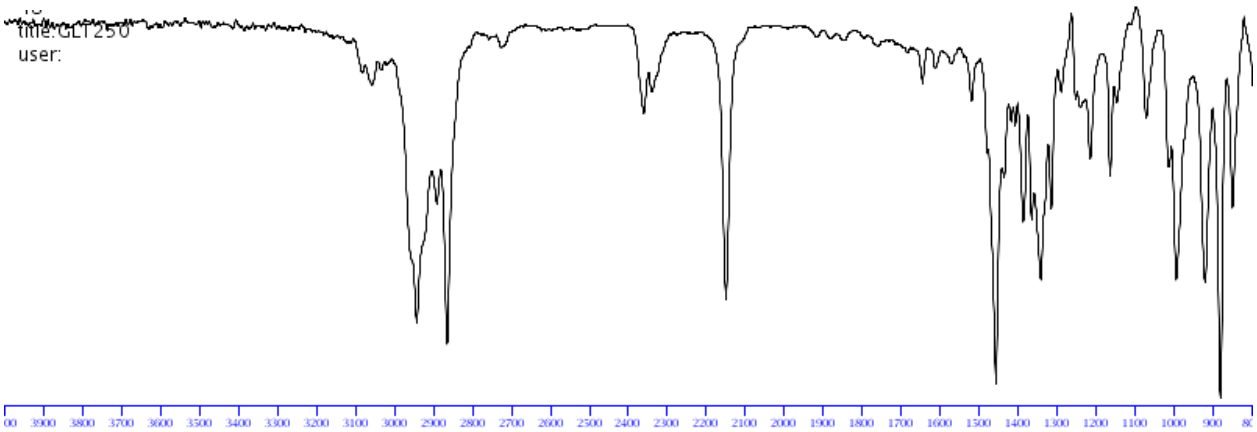
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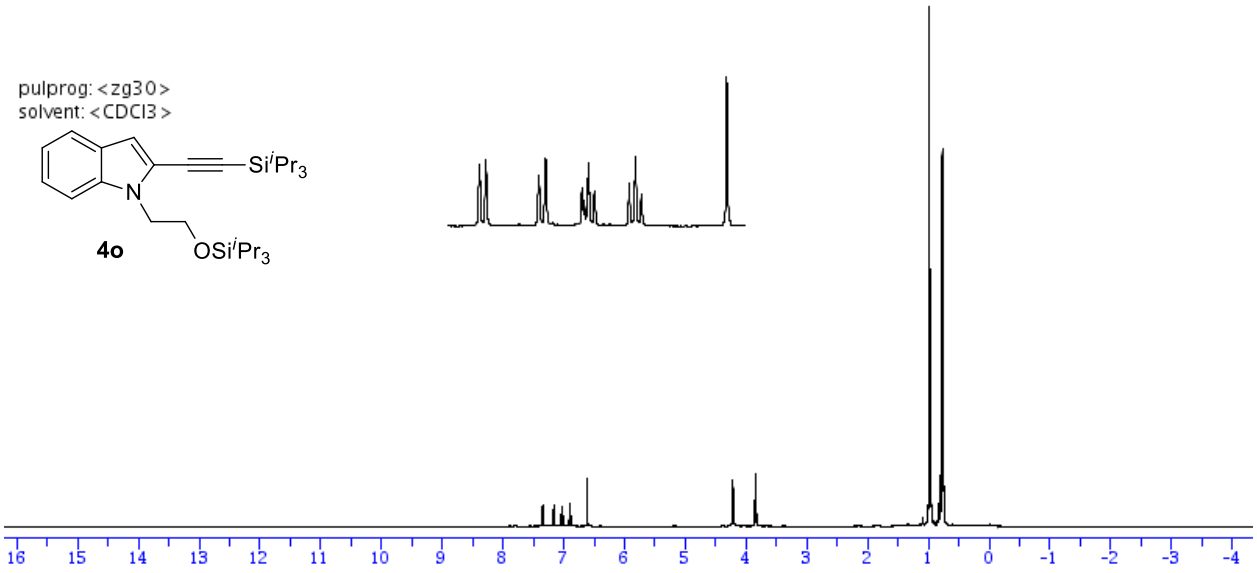
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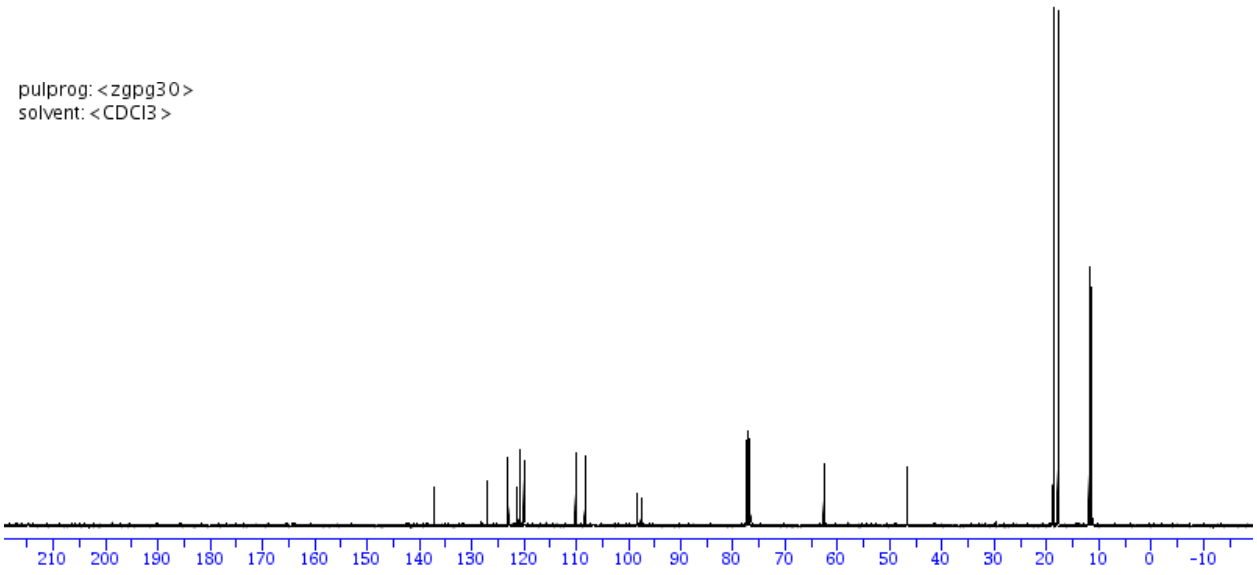
Si^{i}Pr$_3$
N
OSi^{i}Pr$_3$
4o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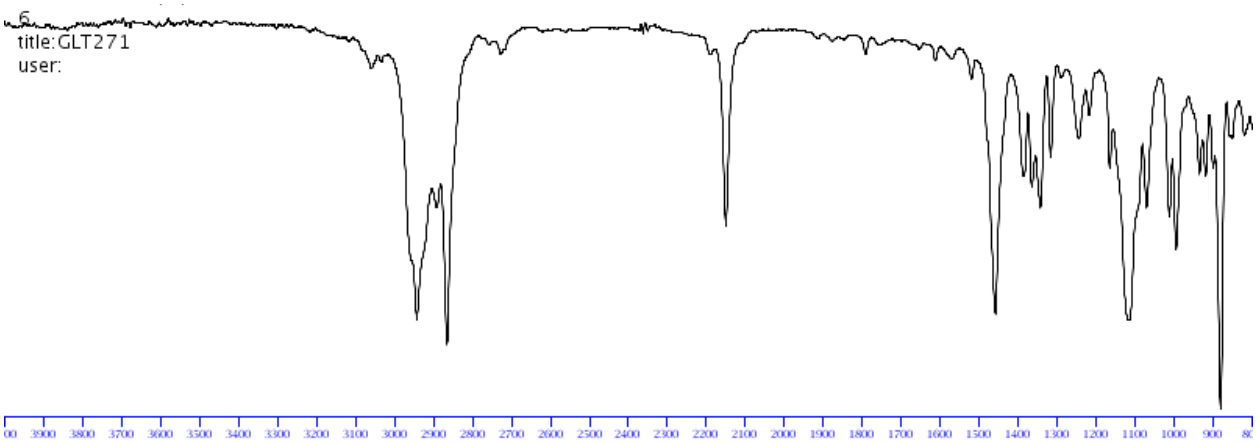
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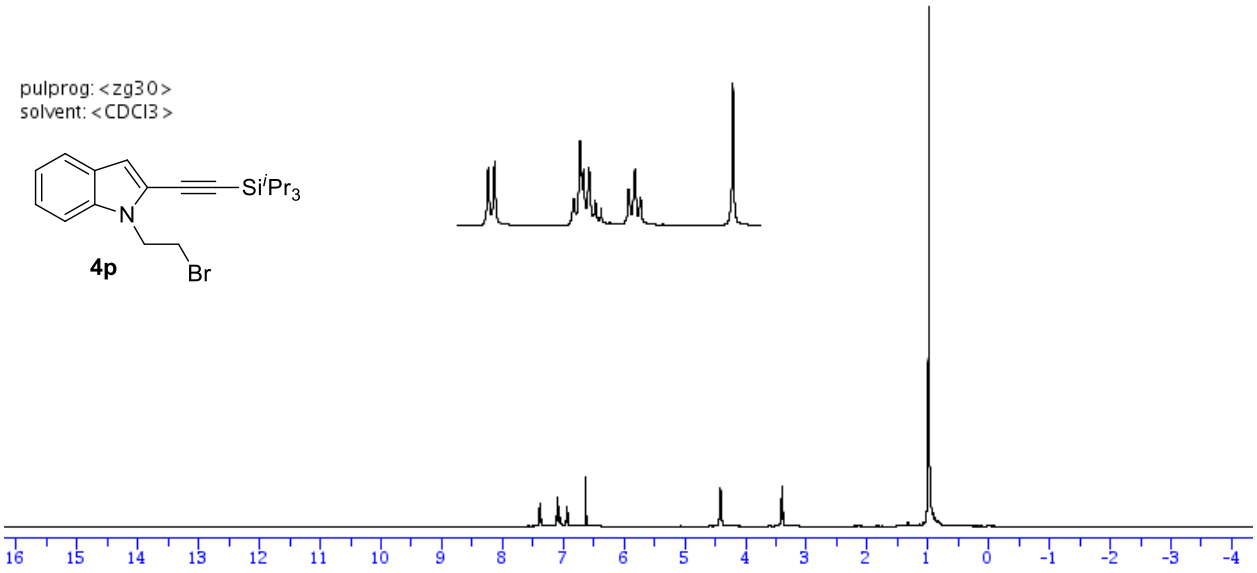
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Si^{i}Pr$_3$
N
Br
4p
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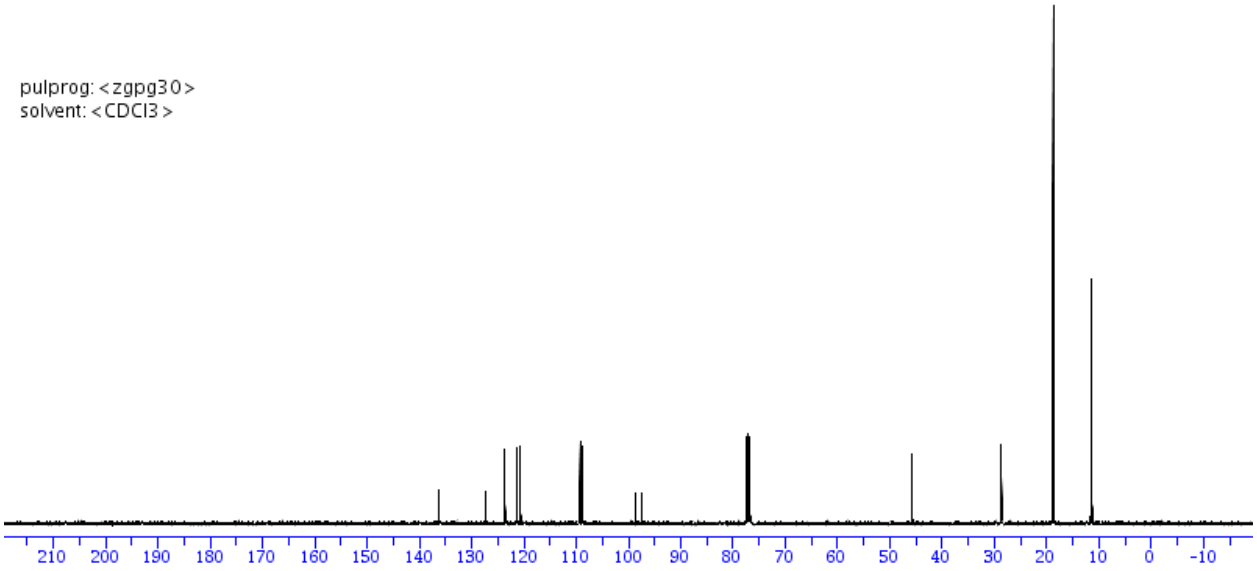
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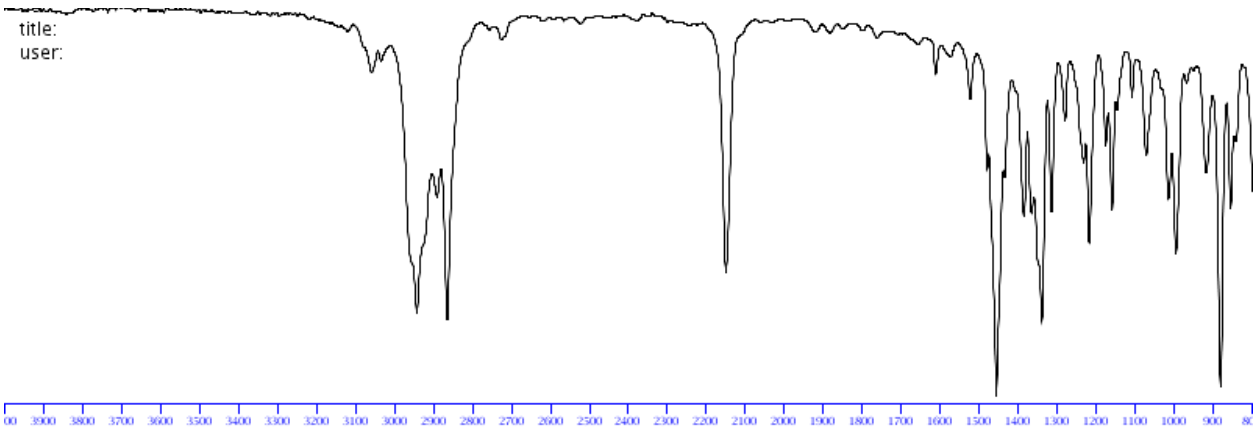
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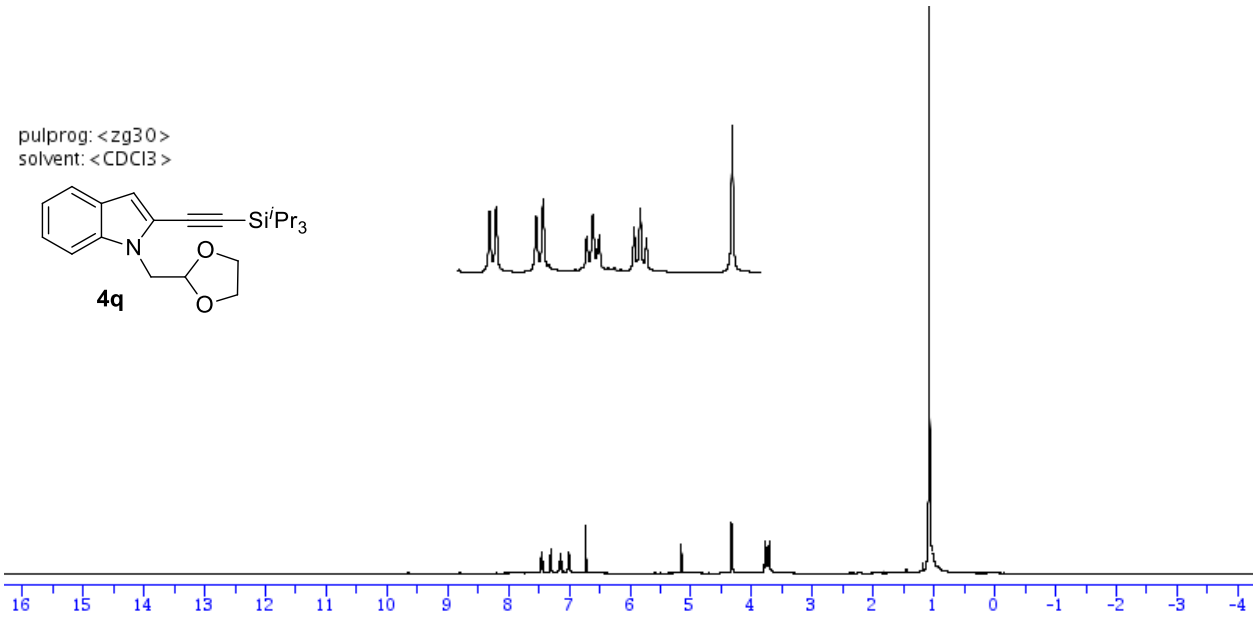
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Si^{i}Pr$_3$
N
O
O
4q
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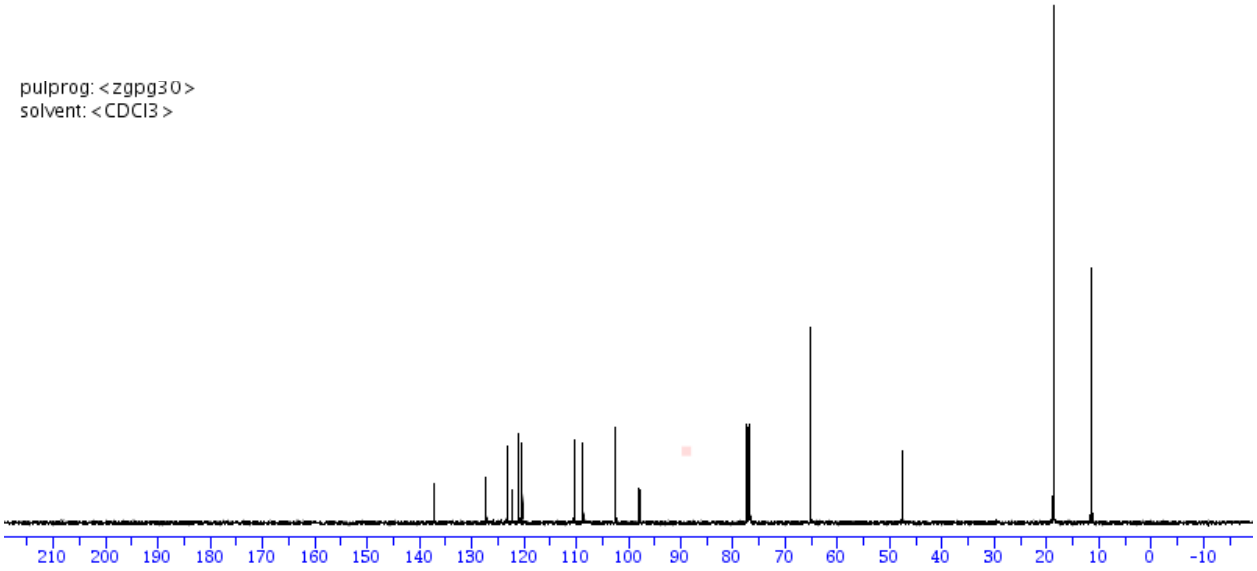
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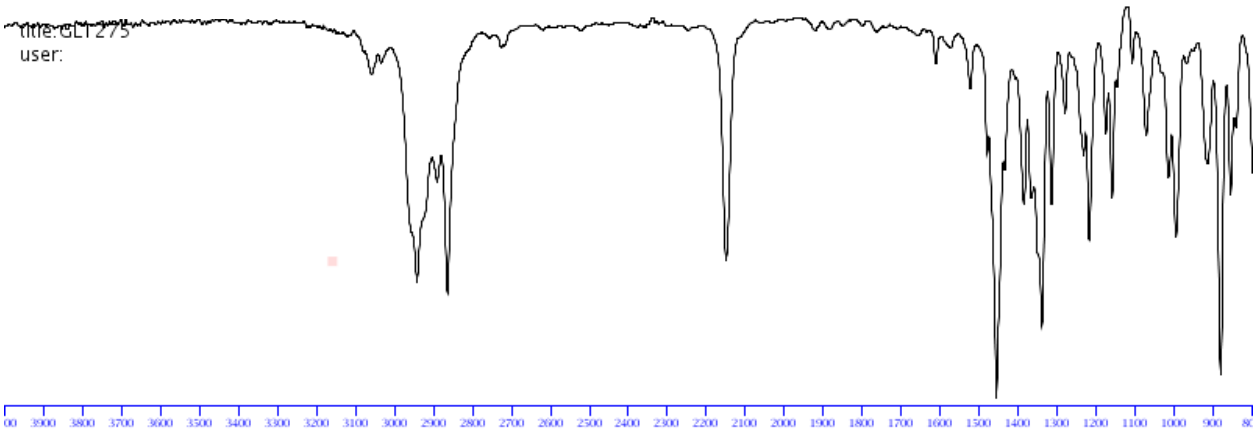
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