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Palladium-Catalyzed Carbo-oxygenation of Propargylic Amines using In Situ Tether Formation

Phillip D. G. Greenwood, Erwann Grenet and Jerome Waser*[a]

Dedication ((optional))

Abstract: 1,2-Amino alcohols and α-aminocarbonyls are frequently found in natural products, drugs, chiral auxiliaries and catalysts. Herein, we report a new method for the palladium-catalyzed oxyalkynylation and oxyarylation of propargylic amines. The reaction is perfectly regioselective based on the *in situ* introduction of a hemiacetal tether derived from trifluoroacetaldehyde. *Cis*-selective carbo-oxygenation was achieved for terminal alkynes, whereas internal alkynes gave *trans*-carbo-oxygenation products. The obtained enol ethers could be easily transformed into 1,2-amino alcohols or α-amino ketones using hydrogenation or hydrolysis respectively.

Compounds containing vicinal oxygen- and nitrogen-functionalities are highly represented among bioactive molecules. Examples of α-amino ketones include the protease inhibitor Rupintrivir (**1**)[1] and the antidepressant Bupropion (**2**).[2] Bioactive amino alcohols are even more widespread, with a broad range of bioactivities, as shown by the well-known stimulant pseudoephedrine (**3**), the gastroprotective AI-77-B (**4**)[3] or the antidepressant **5**.[4] Chiral amino alcohols have also found applications as ligands or organocatalysts in asymmetric synthesis, as exemplified by the Jorgensen-Hayashi catalyst **6**.[5]

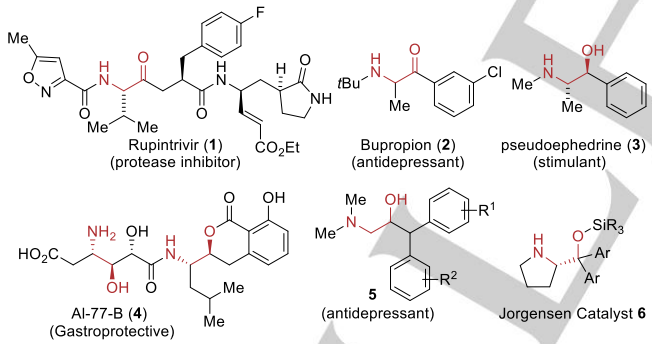
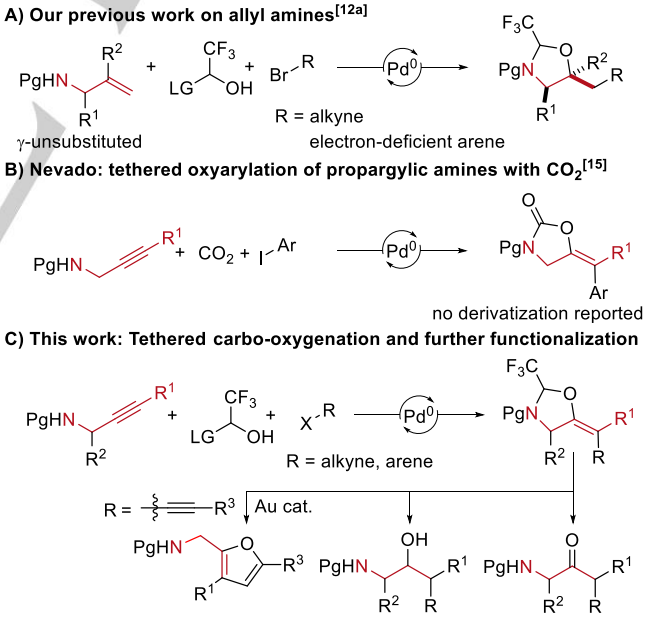


Figure 1. Important organic compounds containing amino ketones and amino alcohols.

The synthesis of amino alcohols from broadly available unsaturated hydrocarbons such as alkenes and alkynes is particularly attractive, but leads to formidable challenges in reactivity, regio- and stereo-selectivity.[6] The use of tethering groups installed onto existing functional groups such as alcohols or amines allows the functionalization of π bonds under mild conditions with high regioselectivity, but several steps are usually required to install and remove the tether.[7] Inspired by pioneering works of Beauchemin,[8] Hiemstra,[9] Stahl[10] and Menche,[11] our group has developed new tethers based on acetaldehydes for the palladium-catalyzed functionalization of allylic alcohols and amines.[12] In particular, a one-pot tether introduction/olefin carbo-oxygenation of allyl amines was developed for the synthesis of aminoalcohols (Scheme 1A).[12a] Nevertheless, important limitations remain for this transformation due to the challenging carbon-carbon formation on a sp^3 center: only alkyne and electron-deficient arene halogenides could be used as electrophiles and only primary positions could be functionalized. Therefore, products bearing a stereocenter in γ position to the amine could not be accessed.



Scheme 1. Allyl and propargyl amines as precursors for the tethered carbooxygenation of olefins.

To overcome these limitations, we considered propargylic amines as widely available starting materials.[13] After oxypalladation, the formed palladium-Csp^2 intermediate should undergo reductive elimination more efficiently, leading to a broader scope. Furthermore, both amino ketones and amino alcohols could be accessed from the products via hydrolysis and hydrogenation respectively. Such a transformation will also give access to highly

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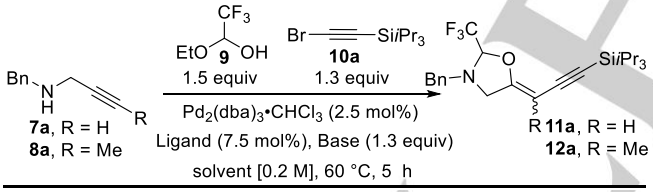
substituted enol ethers, which are challenging to synthesize stereoselectivity, in particularly starting from non-heteroatom substituted alkynes.[14] When considering the synthetic versatility of enol derivatives, new synthetic methods are urgently needed. In comparison to olefins, the tethered multi-functionalization of alkynes has been less investigated. Most success has been met using CO_2 as tether precursor from propargylic amines for the synthesis of oxazolidinones.[15] However, only one new C-O bond is formed in these processes. Using palladium catalysis, an important breakthrough was reported by Nevado and co-workers in 2016, with the oxyarylation of propargylic amines using CO_2 as tether precursor (Scheme 1B).[16] Multi-functionalized oxazolidinones were obtained as products, but no transformation into other valuable building blocks was reported.

Herein, we report the first successful use of acetaldehyde-derived tethers for both the oxy-alkynylation and -arylation of propargylic amines (Scheme 1C). In contrast to our previous work with allyl amines, substituted alkynes could also be used, resulting in the highly stereoselective synthesis of tetrasubstituted alkenes. The tether could be easily removed, enabling the synthesis of amino ketones, amino alcohols and furan heterocycles.

We started our investigations with the oxyalkynylation of simple benzylated propargylic amine **7a** (Table 1). Using silylated bromoalkyne **10a** and the conditions developed previously for allylic amines (Pd(0) catalyst,[17] hemiacetal **9**, DPEPhos as ligand, cesium carbonate as a base, in toluene), the desired product could be obtained in 82% yield and 4:1 *Z:E* ratio (entry 1).[18] In contrast, P(2-furyl)$_3$, which was one of the best ligands in the case of allylic amines, led to inferior results (entry 2). An improvement in *Z*:*E* selectivity could be achieved using dichloroethane (DCE) as solvent (entry 3).

Table 1. Optimization of the oxyalkynylation of amine **7a** and **8a**



Entry	R	Ligand	Base/solvent	Yield[a]/ Z:E ratio
1	H	DPEPhos	Cs_2CO_3/toluene	82%/4:1
2	H	P(2-furyl)$_3$	Cs_2CO_3/toluene	23%/3:1
3	H	DPEPhos	Cs_2CO_3/DCE	83%/9:1
4	Me	DPEPhos	Cs_2CO_3/DCE	40%/1:7
5	Me	DPEPhos	Cs_2CO_3/toluene	20%/1:5
6	Me	P(2-furyl)$_3$	Cs_2CO_3/DCE	-
7	Me	DPEPhos	CsOAc/DCE	19%/ND
8	Me	DPEPhos	K_3PO_4/DCE	67%/1:6
9	Me	XantPhos	K_3PO_4/DCE	73%/1:10

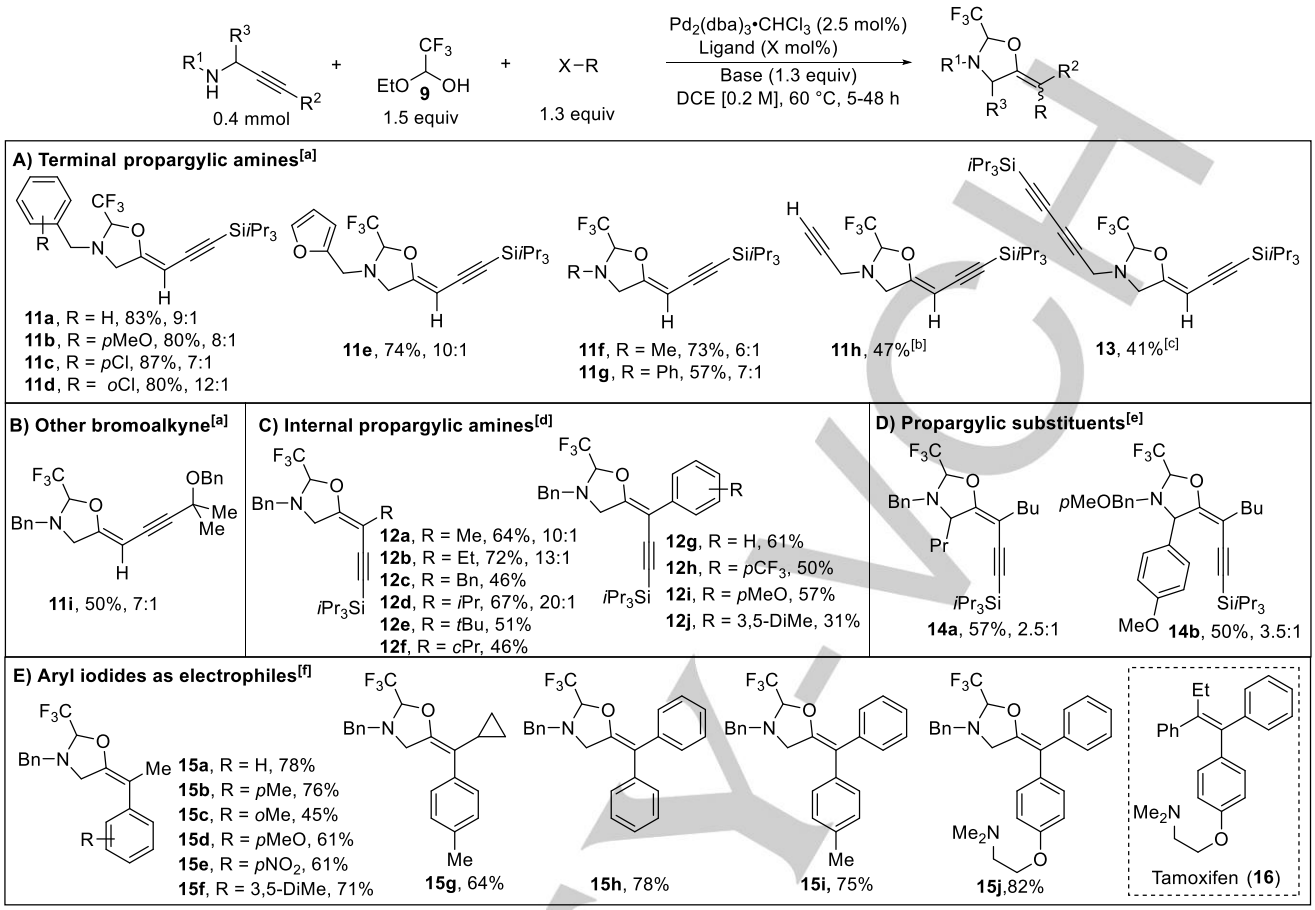
[a]NMR yields using *p*-difluorobenzene as internal standard.[19]

These reactions conditions were then applied to the more challenging internal alkyne **8a**. We were pleased to see that the desired product **12a** could be obtained in 40% yield (entry 4), whereas β-substituted allyl amines could not be used in our previous work.[12a] Interestingly, formation of the *E* product was now favored. Attempts to increase the yield by changing the solvent or ligand were not successful (entries 5 and 6). In contrast, a strong effect of the base was observed: the use of cesium acetate led to low yield (entry 7), but 67% of **12a** could be obtained using potassium phosphate (entry 8). Finally, using XantPhos as ligand allowed increasing both yield and selectivity (entry 9).

With optimized conditions in hand, we investigated first the functional group tolerance on the amine substituent with terminal propargylic alkynes and bromide **10a** as electrophile (Scheme 2A). Methoxy- and chloro- substituted benzyl amines **11b-d** were obtained in more than 80% yield with good *Z* selectivity. In addition, a furyl, a methyl and a phenyl group were also tolerated (products **11e-g**). When a bis-propargylic amine was used as starting material, enyne **11h** was obtained as the *Z* isomer only. The moderate yield was due to the formation of diyne **13** as side product through sp-sp coupling. The formation of **13** could be increased to 41% by doubling the number of equivalents of bromide **10a**. The carbo-oxygenation was also successful in case of an aliphatic alkynyl bromide as partner to give product **11i** (Scheme 2B).

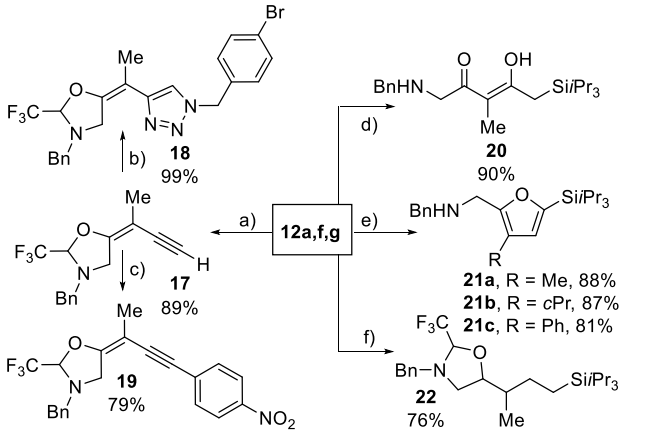
We then turned to the more challenging internal alkynes (Scheme 2C), which are a particular interesting class of substrates, as the corresponding olefins did not react in our previous work. Gratifyingly, primary, secondary, tertiary and cyclic alkyl groups were all well tolerated on the alkyne (products **12a-f**). With bulky alkyl groups, only the *E* isomer was obtained. Aryl-substituted enynes **12g-j** were also obtained with perfect *E* selectivity. When substituents were introduced at the propargylic position of the amine, the reaction was too slow with bidentate phosphine ligands. Fortunately, useful yields could be still obtained using tris(2-furyl)phosphine as ligand (Scheme 2D). Enynes **14a-b** were obtained as mixtures of two diastereoisomers.

Next, aryl iodides were examined as electrophiles (Scheme 2E). Only low yields were obtained with DPEPhos or XantPhos as ligands, but better results were obtained with RuPhos.[19] The reaction of propargylamine **8a** with phenyl iodide gave enol ether **15a** in 78% yield and complete *E* selectivity.[20] This result is noteworthy, as only electron-poor aryl electrophiles could be used in our previous work on allyl amines. Aryl electrophiles bearing electron-rich or –poor substituents could be used to give the desired products **15b-f** in good yields. Only in the case of an *ortho*-methyl substituent the yield decreased to 45% (product **15c**). A cyclopropyl substituent on the alkyne was also well tolerated to give alkene **15g**. Finally, difficult to access tetrasubstituted olefins **15h-j** bearing two aryl groups were also obtained with perfect *E* selectivity. Such compounds are important pharmacophores: for example, the drug tamoxifen (**16**), which is used to treat breast cancer, bears an olefin with the same two aryl substituents as compound **15j**.

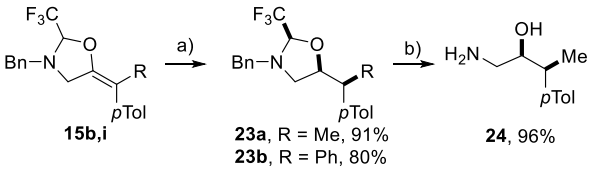


Scheme 2. Scope of the carbooxygenation reaction with alkynyl bromides and aryl iodides. The olefins are obtained with >20:1 stereoselectivity, unless noted otherwise. The major isomer obtained is drawn. [a]DPEPhos as (7.5 mol%) ligand, Cs_2CO_3 as base. [b]**13** also isolated in 13% yield. [c]2.6 equiv. bromoalkyne used. [d]XantPhos (7.5 mol%) as ligand, K_3PO_4 as base. [e]P(2-furyl)$_3$ (15 mol%) as ligand, K_3PO_4 as base. [f]RuPhos (7.5 mol%) as ligand, K_3PO_4 as base.

With a broad range of enynes and styrene derivatives in hand, we turned to the functionalization of the obtained products. Deprotection of product **12a** with TBAF gave surprisingly stable electron-rich terminal enyne **17** in 89% yield (Scheme 3). Enyne **17** could be easily further modified to give products **18** and **19** via [3+2] addition and Sonogashira coupling respectively. The main objective of this work was to access both amino ketone and amino alcohol building blocks. Therefore, the removal of the acetal functionality was investigated next. Hydrolysis in presence of trifluoroacetic acid (TFA) was successful, but hydration of the alkyne occurred upon isolation to give diketone **20** in 90% yield. When a gold catalyst was added directly after acetal removal, furan **21a** was obtained in 88% yield. This transformation was also successful with a cyclopropyl or phenyl substituent on the alkyne (products **21b-c**). Finally, hydrogenation of enyne **12a** gave protected amino alcohol **22** in 76% yield. In the case of styrene derivatives **15**, hydrogenation was completely stereoselective with both alkyl and aryl substituents to give **23a** and **23b** in 91% and 80% yield respectively (Scheme 4). The latter is especially interesting, due to the importance of diarylmethane derivatives as bioactive compounds, such as antidepressant **5**. Compound **23a** was easily deprotected to give amino alcohol **24** in 96% yield.



Scheme 3. Transformations of enyne products **12**. Reaction conditions: a) TBAF, THF, 0 °C; b) *p*Br-BnN$_3$, $CuSO_4$; Na-ascorbate, THF:H_2O, rt; c) *p*NO_2-Ph-I, $Pd(OAc)_2$, DABCO, MeCN; d) TFA, H_2O, $CHCl_3$, rt; e) TFA, H_2O, $CHCl_3$, rt *then* $Au(PPh_3)_2Cl_2$, $Ag(SbF_6)$, rt; f) H_2, Pd/$BaSO_4$, EtOH, 55 °C.



Scheme 4. Hydrogenation and deprotection of styrene derivatives **15**. Reaction conditions: a) H_2, $Pd(OH)_2$/C, MeOH, rt; b) TsOH, THF/H_2O, rt.

In summary, we have described a new tethered carbo-oxygenation of propargylic amines using palladium catalysis. The reaction was successful with trifluoroacetaldehyde derived tethers with both alkynyl bromides and aryl iodides as nucleophiles and could be used for the stereoselective synthesis of tri- and tetra-substituted olefins with high stereoselectivity. The switch of Z- to *E*- selectivity observed when going from terminal to internal alkynes as starting material may indicate a switch from *syn*- to *anti*- palladation in the C-O bond forming step, but further mechanism studies will be required to fully understand the observed selectivity and the subtle ligand effects observed.[21] The obtained products could be easily transformed into useful building blocks, such as amino ketones, amino alcohols or furans. Further studies are currently ongoing for applying the tether strategy to other classes of substrates and chemical transformations.

Acknowledgements

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Keywords: alkynes • tethers • amino alcohols • stereoselective synthesis • palladium catalysis

[1] S. L. Binford, F. Maldonado, M. A. Brothers, P. T. Weady, L. S. Zalman, J. W. Meador, D. A. Matthews, A. K. Patick, *Antimicrob. Agents Chemother.* **2005**, *49*, 619; b) X. N. Zhang, Z. G. Song, B. Y. Qin, X. L. Zhang, L. X. Chen, Y. W. Hu, Z. H. Yuan, *Antiviral Res.* **2013**, *97*, 264.

[2] a) J. A. Ascher, J. O. Cole, J. N. Colin, J. P. Feighner, R. M. Ferris, H. C. Fibiger, R. N. Golden, P. Martin, W. Z. Potter, E. Richelson, F. Sulser, *J. Clin. Psychiatry* **1995**, *56*, 395; b) A. J. Rush, M. H. Trivedi, S. R. Wisniewski, J. W. Stewart, A. A. Nierenberg, M. E. Thase, L. Ritz, M. M. Biggs, D. Warden, J. F. Luther, K. Shores-Wilson, G. Niederehe, M. Fava, S. D. S. Team, *N. Engl. J. Med.* **2006**, *354*, 1231.

[3] A. Kawai, O. Hara, Y. Hamada, T. Shioiri, *Tetrahedron Lett.* **1988**, *29*, 6331.

[4] J. A. Clark, M. S. G. Clark, D. V. Gardner, L. M. Gaster, M. S. Hadley, D. Miller, A. Shah, *J. Med. Chem.* **1979**, *22*, 1373.

[5] K. L. Jensen, G. Dickmeiss, H. Jiang, L. Albrecht, K. A. Jorgensen, *Acc. Chem. Res.* **2012**, *45*, 248.

[6] a) S. C. Bergmeier, *Tetrahedron* **2000**, *56*, 2561; b) T. J. Donohoe, C. K. A. Callens, A. Flores, A. R. Lacy, A. H. Rathi, *Chem. Eur. J.* **2011**, *17*, 58; c) Z. J. Garlets, D. R. White, J. P. Wolfe, *Asian J. Org. Chem.* **2017**, *6*, 636.

[7] Review: a) F. Diederich, P. J. Stang, *Templated Organic Synthesis*, Wiley-VCH, Chichester, UK, **2000**; Selected examples: a) Y. Tamaru, H. Tanigawa, S. Itoh, M. Kimura, S. Tanaka, K. Fugami, T. Sekiyama, Z. I. Yoshida, *Tetrahedron Lett.* **1992**, *33*, 631; b) H. Harayama, A. Abe, T. Sakado, M. Kimura, K. Fugami, S. Tanaka, Y. Tamaru, *J. Org. Chem.* **1997**, *62*, 2113; c) T. J. Donohoe, P. D. Johnson, A. Cowley, M. Keenan, *J. Am. Chem. Soc.* **2002**, *124*, 12934; d) T. J. Donohoe, M. J. Chughtai, D. J. Klauber, D. Griffin, A. D. Campbell, *J. Am. Chem. Soc.* **2006**, *128*, 2514; e) E. J. Alexanian, C. Lee, E. J. Sorensen, *J. Am. Chem. Soc.* **2005**, *127*, 7690. f) S. Li, J. Ye, W. Yuan, S. Ma, *Tetrahedron* **2013**, *69*, 10450.

[8] a) M. J. MacDonald, D. J. Schipper, P. J. Ng, J. Moran, A. M. Beauchemin, *J. Am. Chem. Soc.* **2011**, *133*, 20100; b) N. Guimond, M. J. MacDonald, V. Lemieux, A. M. Beauchemin, *J. Am. Chem. Soc.* **2012**, *134*, 16571; c) M. J. MacDonald, C. R. Hesp, D. J. Schipper, M. Pesant, A. M. Beauchemin, *Chem. Eur. J.* **2013**, *19*, 2597; d) B. J. Li, C. Ei-Nachef, A. M. Beauchemin, *Chem. Commun.* **2017**, *53*, 13192.

[9] a) R. A. T. M. Van Benthem, H. Hiemstra, W. N. Speckamp, *J. Org. Chem.* **1992**, *57*, 6082; b) R. A. T. M. van Benthem, H. Hiemstra, G. R. Longarela, W. N. Speckamp, *Tetrahedron Lett.* **1994**, *35*, 9281.

[10] A. B. Weinstein, D. P. Schuman, Z. X. Tan, S. S. Stahl, *Angew. Chem., Int. Ed.* **2013**, *52*, 11867.

[11] a) L. Wang, D. Menche, *Angew. Chem., Int. Ed.* **2012**, *51*, 9425; b) B. Tang, L. Wang, D. Menche, *Synlett* **2013**, *24*, 625.

[12] a) U. Orcel, J. Waser, *Angew. Chem., Int. Ed.* **2015**, *54*, 5250; b) U. Orcel, J. Waser, *Angew. Chem., Int. Ed.* **2016**, *55*, 12881; c) B. Muriel, U. Orcel, J. Waser, *Org. Lett.* **2017**, *19*, 3548; d) U. Orcel, J. Waser, *Chem. Sci.* **2017**, *8*, 32.

[13] K. Lauder, A. Toscani, N. Scalacci, D. Castagnolo, *Chem. Rev.* **2017**, *117*, 14091.

[14] Selected recent examples: a) M. G. Suero, E. D. Bayle, B. S. L. Collins, M. J. Gaunt, *J. Am. Chem. Soc.* **2013**, *135*, 5332; b) M. V. Pham, N. Cramer, *Angew. Chem., Int. Ed.* **2014**, *53*, 14575; For an elegant approach based on the use of ynamides, see: c) Y. Minko, M. Pasco, L. Lercher, M. Botoshansky, I. Marek, *Nature* **2012**, *490*, 522.

[15] a) T. Mitsudo, Y. Hori, Y. Yamakawa, Y. Watanabe, *Tetrahedron Lett.* **1987**, *28*, 4417; b) M. Costa, G. P. Chiusoli, M. Rizzardi, *Chem. Commun.* **1996**, 1699; c) Y. Kayaki, M. Yamamoto, T. Suzuki, T. Ikariya, *Green Chem.* **2006**, *8*, 1019; d) M. Yoshida, T. Mizuguchi, K. Shishido, *Chem. Eur. J.* **2012**, *18*, 15578; e) S. Hase, Y. Kayaki, T. Ikariya, *Organometallics* **2013**, *32*, 5285; f) T. Ishida, S. Kikuchi, T. Tsubo, T. Yamada, *Org. Lett.* **2013**, *15*, 848; g) J. Hu, J. Ma, Q. Zhu, Z. Zhang, C. Wu, B. Han, *Angew. Chem., Int. Ed.* **2015**, *54*, 5399; h) P. Brunel, J. Monot, C. E. Kefalidis, L. Maron, B. Martin-Vaca, D. Bourissou, *ACS Catal.* **2017**, *7*, 2652; i) B. B. Wang, S. Sun, J. Cheng, *Synlett* **2018**, *29*, 1814; j) Z. Zhang, J. H. Ye, D. S. Wu, Y. Q. Zhou, D. G. Yu, *Chem. Asian J.* **2018**, *13*, 2292.

[16] P. García-Domínguez, L. Fehr, G. Rusconi, C. Nevado, *Chem. Sci.* **2016**, *7*, 3914.

[17] In our previous work (ref. 12a), Pd(Cp)cinnamyl had been used as palladium source, but as no difference was observed with the more convenient $Pd_2(dba)_3$•$CHCl_3$ with propargylic amines, the latter was used.

[18] The structure of **11e**, **12j**, **15b**, **15i** and **19** was confirmed by X-ray analysis. The data is available at the Cambridge Crystallographic Data Center (ccdc numbers: 1873997 (**11e**), 1874007 (**12j**), 1874005 (**15b**), 1874008 (**15i**), 1874014 (**19**)).

[19] See Supporting Information for a more detailed list of tested ligands and reaction conditions.

[20] A complex mixture of products was obtained using terminal alkynes as starting materials. As access to tetrasubstituted enol derivatives is generally more difficult and therefore synthetically more useful, no attempt was made to optimize the reaction for terminal alkynes.

[21] See Scheme S1 in Supporting Information for a speculative reaction mechanism. For a discussion of *syn*- vs- *anti* oxy-palladation on alkene substrates, see: J. S. Nakhla, J. W. Kampf, J. P. Wolfe, *J. Am. Chem. Soc.* **2006**, *128*, 2893.

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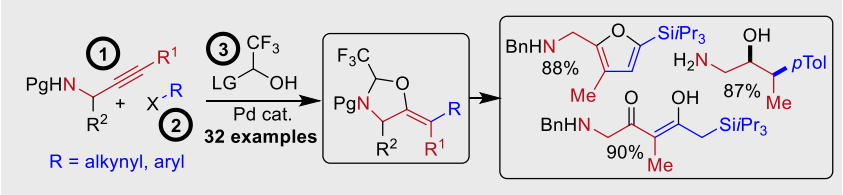

Tether control: *In-situ* tether formation allows the selective palladium-catalyzed oxyalkynylation and oxyarylation of propargyl amines in high yield and selectivity. The obtained products are easily transformed into useful building blocks, such as amino ketones, amino alcohols and furans.

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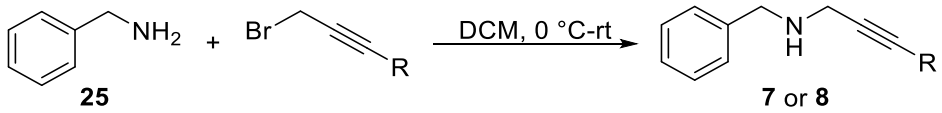
1. General methods.

All reactions were carried out in oven dried glassware under an atmosphere of nitrogen, unless stated otherwise. For quantitative flash chromatography technical grade solvents were used. For flash chromatography for analysis, HPLC grade solvents from Sigma-Aldrich were used. THF, Et_2O, CH_3CN, toluene, hexane and CH_2Cl_2 were dried by passage over activated alumina under nitrogen atmosphere (H_2O content < 10 ppm, *Karl-Fischer* titration). Unless otherwise stated, degassed solvents were degassed using freeze-thaw cycle. All chemicals were purchased from Acros, Aldrich, Fluka, VWR, Fluorochem or Merck and used without further purification. Chromatographic purification was performed as flash chromatography using Silicycle silica 40-63, 60 Å, using the solvents indicated as eluent with 0.1-0.5 bar pressure. TLC was performed on Merck silica gel 60 F254 TLC glass plates and visualized with UV light and potassium permanganate 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*.All signals are reported in ppm with the internal chloroform signal at 7.26 ppm. The data is being reported as (s = singlet, d = doublet, t = triplet, q = quadruplet, qi = quintet, m = multiplet or unresolved, bs = broad signal, coupling constant(s) in Hz, integration, assignment). ^{13}C-NMR spectra were recorded with {^{1}H} decoupling on a Bruker DPX-400 100 MHz spectrometer in chloroform-d unless otherwise stated. All signals are reported in ppm with the internal chloroform signal at 77.0 ppm as standard unless otherwise stated. ^{19}F-NMR spectra were recorded on a Bruker DPX-400 376 MHz spectrometer in chloroform-*d*. All signals are reported in ppm with 1,4-difluorobenzene as internal standard set at –120.1 ppm. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm-1 (w = weak, m = medium, s = strong, br = broad). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) QTOF. Technical grade trifluoroacetaldehyde ethyl hemiacetal was purchased from flurochem. Ultima API. Cesium carbonate was purchased from Aldrich and anhydrous potassium phosphate was purchased from acros, both were used without further purification. DPEPhos was purchased from Acros, Xantphos from flurochem and Ruphos and tri(2-furyl)phosphine were purchased from Aldrich. N-methylprop-2-yn-1-amine (**7f**) and Dipropargylamine (**7h**) are commercially available from Aldrich. Aryl iodides were bought from Aldrich, Acros, ABCR, TCI and Fluorochem, and used as received. Tris(Dibenzylideneacetone)dipalladium was purchased from flurochem and recrystalised in 200 mg portions following reported procedure.[2] Deactivated silica gel was prepared by making a slurry of silica gel (230-400mesh) with 5% Et_3N in pentane solution followed by complete removal of solvent by rotary evaporation until it is a free flowing powder. The solvent system ULTRA comprises 71% DCM, 24% methanol and 5% aq. ammonia (25% solution).

2. Synthesis of amine starting materials

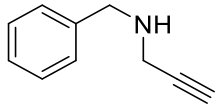
General procedure A:



25 **7** or **8**

Based on a literature procedure.[3] A solution of benzyl amine (**25**) (4-6 equiv.) in DCM (15 mL) at 0 °C was stirred vigorously while a solution of propargyl bromide (1 equiv.) in DCM (10 mL) was slowly added over 10 min. After complete addition, the reaction was allowed to warm to room temperature and stirring continued for 5 hours. The reaction was then filtered through silica gel eluting with 40% EtOAc in pentane and the resulting solution concentrated. The resulting crude material was purified by column chromatography (SiO_2, 10-40% EtOAc in Pent).

N-Benzyl propargylamine (7a)



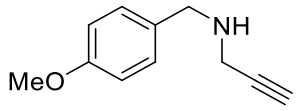
Synthesised following **general procedure A** using benzyl amine (9.8 g, 92 mmol, 4 equiv.) bromopropyne (2.5 mL, 23 mmol, 80%wt in toluene, 1 equiv.). Purification was performed by column chromatography (SiO_2, 10-40% EtOAc in Pent) followed by distillation (70 °C at $5x10^{-1}$ mbar) to obtain pure benzyl propargylamine (**7a**) as a clear straw yellow oil (2.2 g, 15 mmol, 68% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.22 (m, 5H, Ar*H*), 3.90 (s, 2H, CH_2Ar), 3.44 (d, *J* = 2.4 Hz, 2H, CH_2C≡C), 2.27 (t, *J* = 2.4 Hz, 1H, C≡C*H*), 1.85 (bs, 1H, N*H*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 139.1, 128.4, 128.4, 127.2, 81.8, 71.7, 52.2, 37.3.

Spectra data was consistent with the values reported in literature.[4]

4-Methoxybenzyl propargylamine (7b)



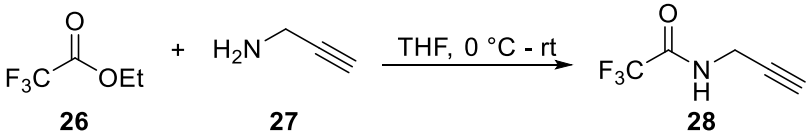
Synthesised following **general procedure A** using 4-methoxybenzyl amine (2.5 g, 18 mmol, 6 equiv.) and bromopropyne (0.32 mL, 3.0 mmol, 80%wtin in toluene, 1 equiv.). Purification was performed by column chromatography (SiO_2, 20-30% EtOAc in pentane) to afford 4-Methoxybenzyl propargylamine (**7b**) as a colourless oil. (0.37 g, 2.1 mml, 70 % yield)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.27 (d, *J* = 8.6 Hz, 2H, Ar*H*), 6.86 (d, *J* = 8.6 Hz, 2H, Ar*H*), 3.82 (s, 2H, ArCH_2), 3.80 (s, 3H, OCH_3), 3.41 (d, *J* = 2.4 Hz, 2H, CH_2C≡C), 2.27 (t, *J* = 2.4 Hz, 1H, C≡C*H*), 1.84 – 1.72 (bs, 1H, N*H*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.8, 131.4, 129.6, 113.8, 82.0, 71.5, 55.2, 51.6, 37.1.

Spectra data was consistent with the values reported in literature.[5]

Propynyl trifluoroacetamide (28)



26 **27** **28**

Following a modified version of a reported procedure.[6] In a flame dried round bottom flask, to a solution ethyl trifluoroacetate (**26**) (7.99 g, 56.2 mmol, 1.2 equiv.) in THF (12 mL) at 0 °C was slowly added propargylamine (**27**) (2.58 g, 46.8 mmol, 1 equiv.). The reaction mixture was stirred at this temperature for 10 minutes; it was then allowed to warm to room temperature and stirred for a further 7 hours. The solvent was removed by rotary evaporation and the product was isolated by distillation (90 °C at 17 mbar) to afford propynyl trifluoroacetamide (**25**) a colourless oil (5.53 g, 36.6 mmol, 78% yield).

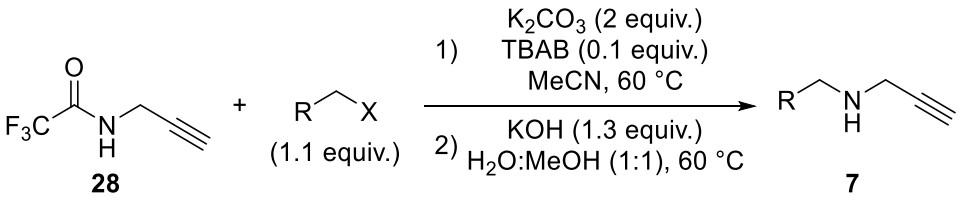
^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.94 (bs, 1H, N*H*), 4.14 (dd, *J* = 6.0, 2.5 Hz, 2H, CH_2C≡C, 2.32 (q, *J* = 2.2 Hz, 1H, C≡C*H*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.0 (q, *J* = 38.1 Hz), 115.5 (q, *J* = 287.5 Hz), 77.0, 73.1, 29.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -76.3.

Spectra data was consistent with the values reported in literature.[6]

General procedure B:

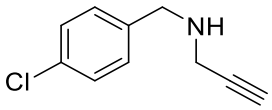


28 **7**

Following an adapted version of a reported procedure.[7]To a mixture of K_2CO_3 (0.69 g, 4.0 mmol, 2 equiv.) and TBAB (65 mg, 0.20 mmol, 0.1 equiv.) in MeCN (10 mL) was added propynyl trifluoroacetamide (**28**) (0.30 g, 2.0 mmol, 1 equiv.) and alkyl halide (1.1 equiv.) after which the reaction was stirred at 60 °C. The progress of the reaction was monitored by TLC. After completion has been determined (2-3 hours) based on TLC (SiO_2, 20% EtOAc in pentane), the mixture was filtered through a plug of Celite, which was washed with Et_2O. The resulting filtrate was concentrated by rotary evaporation to afford a crude material that could be used directly in the following step, without further purification.

Following an adapted version of a reported procedure.[8] To the crude material obtained in the previous step was added a solution of KOH (0.15 g, 2.7 mmol, 1.3 equiv.) in water (5 mL) and methanol (5 mL) and the resulting mixture was heated to 60 °C for 1 hour. The reaction mixture was then allowed to cool to room temperature, it was first quenched by the addition aq. HCl (1.0 M, 5.0 mL) followed by basification with sat. $NaHCO_3$ (until pH >7). The resulting aqueous solution was then extracted with DCM (3 x 10 mL), dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude propargylamine was purified by column chromatography.

4-Chlorobenzyl propargylamine (7c)



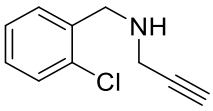
Synthesised following **general procedure B** using 4-chlorobenzyl bromide (0.45 g 2.2 mmol, 1.1 equiv) Purification was performed by column chromatography (SiO_2, 10-20% EtOAc in pentane) to afford 4-chlorobenzyl propargylamine (**7c**) as a straw yellow oil. (0.32 g, 1.8 mmol, 90 % yield)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (s, 4H, Ar*H*), 3.85 (s, 2H, ArCH_2), 3.41 (d, *J* = 2.4 Hz, 2H, CH_2C≡C), 2.26 (t, *J* = 2.4 Hz, 1H, C≡C*H*), 1.50 (bs, 1H, N*H*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 137.9, 132.9, 129.8, 128.6, 81.9, 71.7, 51.5, 37.3.

Spectra data was consistent with the values reported in literature.[4]

2-Chlorobenzyl propargylamine (7d)



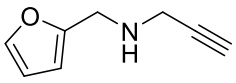
Synthesised following **general procedure B** using 2-chlorobenzyl chloride (0.35 g 2.2 mmol, 1.1 equiv) Purification was performed by column chromatography (SiO_2, 10-20% EtOAc in pentane) to afford 2-chlorobenzyl propargylamine (**7d**) as a straw yellow oil. (0.15 g, 0.77 mmol, 40 % yield)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.34 (m, 2H, Ar*H*), 7.25 – 7.18 (m, 2H, Ar*H)*, 3.98 (s, 2H, ArCH_2), 3.45 (d, *J* = 2.5 Hz, 2H, CH_2C≡C), 2.26 (t, *J* = 2.4 Hz, 1H, C≡C*H*), 1.67 (bs, 1H, N*H*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 136.8, 133.9, 130.3, 129.6, 128.5, 126.8, 81.8, 71.7, 49.9, 37.5.

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{10}H_{11}ClN^+$ 180.0575; Found 180.0577.

2-Frufuryl propargylamine (7e)



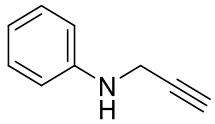
Synthesised following **general procedure B** using furfuryl bromide[9] (0.09M in THF, 40 mL, 5.2 mmol, 1.1 equiv.) Purification was performed by column chromatography (SiO_2, 10-20% EtOAc in pentane) to afford 2-frufuryl propargylamine (**7e**) as an orange oil. (0.29 g, 2.1 mmol, 53 % yield)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.71 (dd, *J* = 1.9, 0.9 Hz, 1H, Ar*H*), 6.65 (dd, *J* = 3.2, 1.9 Hz, 1H, Ar*H*), 6.56 (dq, *J* = 3.2, 0.8 Hz, 1H, Ar*H*), 4.22 (d, *J* = 0.7 Hz, 2H, ArCH_2), 3.77 (d, *J* = 2.5 Hz, 2H CH_2C≡C), 2.58 (t, *J* = 2.4 Hz, 1H, C≡C*H*), 1.92 (bs, 1H, N*H*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 152.9, 142.1, 110.1, 107.5, 81.6, 71.7, 44.6, 37.1.

Spectra data was consistent with the values reported in literature.[10]

Phenyl propargylamine (7g)



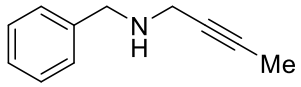
To K_2CO_3 (1.4 g, 10 mmol, 2 equiv.) in MeCN (10 mL) was added aniline (1.8 mL, 20 mmol, 4 equiv) and bromopropyne (0.56 mL, 5.0 mmol, 80%wt in toluene, 1 equiv.) and the resulting mixture was stirred at 55 °C for 7 hours. The reaction was then allowed to cool to room temperature, concentrated by rotary evaporation and loaded directly onto chromatography column for purification (SiO_2, 5-10% EtOAc in pentane) to afford phenyl propargylamine (**7g**) as a straw yellow oil. (0.27 g, 2.0 mmol, 41 % yield)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.27 – 7.18 (m, 2H, Ar*H*), 6.80 (tt, *J* = 7.4, 1.1 Hz, 1H, Ar*H)*, 6.74 – 6.66 (m, 2H, Ar*H*), 3.95 (dd, *J* = 6.0, 2.4 Hz, 2H, C*H*$_2$C≡C), 3.87 (bs, 1H, N*H*), 2.22 (t, *J* = 2.4 Hz, 1H, C≡C*H*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 146.8, 129.2, 118.6, 113.5, 81.0, 71.3, 33.6.

Spectra data was consistent with the values reported in literature.[11]

N-Benzyl but-2-ynylamine (8a)



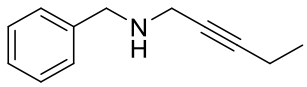
Synthesised following **general procedure A** using bromo-2-butyne (2.5 mL, 27 mmol, 1 equiv.). Purification was performed by column chromatography (SiO_2, 10-40% EtOAc in Pent) to afford benzyl butynylamine (**8a**) as a straw yellow oil (3.4g, 21 mmol, 74%). Further purification could be achieved by Kugelrohr distillation (86 °C at 5x10^{-1} mbar).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.21 (m, 5H, Ar*H*), 3.86 (s, 2H, ArC*H*$_2$), 3.38 (q, *J* = 2.4 Hz, 2H, C*H*$_2$C≡C), 1.85 (t, *J* = 2.4 Hz, 3H, C*H*$_3$), 1.57 (bs, 1H N*H*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 139.7, 128.4, 128.3, 127.0, 79.1, 77.1, 52.5, 37.8, 3.5.

Spectra data was consistent with the values reported in literature.[12]

N-Benzyl pent-2-ynylamine (8b)



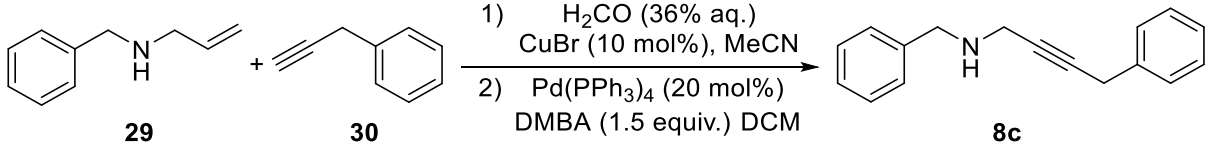
Synthesised following **general procedure A** using benzyl amine (2.4 g, 22 mmol, 6 equiv.) and bromo-2-pentyne (0.54 g, 3.7 mmol, 1 equiv.). Purification was performed by column chromatography (SiO_2, 10-20% EtOAc in Pent) to afford benzyl pent-2-ynylamine (**8b**) as straw yellow oil (0.54 g, 1.5 mmol, 40% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.21 (m, 5H, Ar*H*), 3.86 (s, 2H, ArCH_2), 3.40 (t, *J* = 2.2 Hz, 2H, CH_2C≡C), 2.22 (qt, *J* = 7.5, 2.2 Hz, 2H, CH_2CH$_3$), 1.68 (bs, 1H, N*H*), 1.15 (t, *J* = 7.5 Hz, 1H, CH$_2$CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 139.7, 128.4 (4C), 127.0, 85.3, 77.2, 52.5, 37.8, 14.1, 12.4.

Spectra data was consistent with the values reported in literature.[12]

N-Benzyl 4-phenyl-but-2-ynylamine (8c)



Following an adapted version of a reported procedure. [12] To a solution of CuBr (0.18 g, 1.3 mmol, 12 mol%) in MeCN (60 mL) was added allyl benzylamine (**29**) (1.9 g, 13 mmol, 1.3 equiv), formaldehyde (2.5 mL, 33 mmol 36% aq. solution, 3.1 equiv) and phenylpropyne (**30**) (1.2 g, 10 mmol, 1 equiv.). The reaction mixture was stirred at room temperature for 16 hours after which it was concentrated by rotary evaporation. The residue was diluted with Et_2O (20 mL) and washed with 5M NaOH solution (3 x 10 mL), dried over $MgSO_4$, filtered and concentrated by rotary evaporation. Purification of the crude product by column chromatography (SiO_2, 0-2% EtOAc in pentane) to afford N-allyl-N-benzyl-4-phenyl-but-2-ynylamine as a colourless oil (2.6 g, 9.3 mmol, 89% yield)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 – 7.28 (m, 10H, Ar*H*), 5.97 (dddd, *J* = 17.3, 12.4, 6.5, 2.3 Hz, 1H, C*H*=CH$_2$), 5.34 (dq, *J* = 17.2, 1.7 Hz, 1H, CH=CH_2), 5.24 (dq, *J* = 10.4, 1.6 Hz, 1H, CH=CH_2), 3.79 – 3.73 (m, 2.2 Hz, 4H, ArCH_2N, CH_2CH=CH$_2$), 3.44 (q, *J* = 2.5 Hz, 2H, C≡CCH_2Ph), 3.27 (dt, *J* = 6.6, 1.6 Hz, 2H, NjCH_2C≡C).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.7, 137.1, 135.7, 129.1, 128.4, 128.2, 127.8, 127.0, 126.5, 117.8, 82.9, 77.0, 57.3, 56.7, 41.8, 25.1.

The tertiary amine obtained from the previous step (1.0 g, 3.6 mmol, 1 equiv.) was added to a solution of $Pd(PPh_3)_4$ (84 mg, 73 µmol, 2 mol%) and 1,3-dimethylbarbituric acid (0.85 g, 5.5 mmol, 1.5 equiv.) in DCM (22 mL) under an N_2 atmosphere. The reaction mixture was stirred at room temperature for 6 hours. Reaction completion was checked by TLC (2 % EtOAc in pentane). The reaction mixture was diluted with ether (40 mL) and washed with sat. $NaHCO_3$ (3 x 15 mL). The Organic layer was extracted with aq. HCl (1.0 M; 3 x 15 mL) after which the combined aqueous layers were basified with K_2CO_3 (pH >7) and extracted with DCM (3 x 25 mL). The combined extracts were dried over $MgSO_4$, filtered and concentrated by rotary evaporation. Purification by flash column chromatography (SiO_2, 20-30 % EtOAc in pentane) to afford N-benzyl-4-phenyl-but-2-ynylamine (**8c**) as a straw coloured oil (0.76 g, 3.0 mmol, 83% yield)

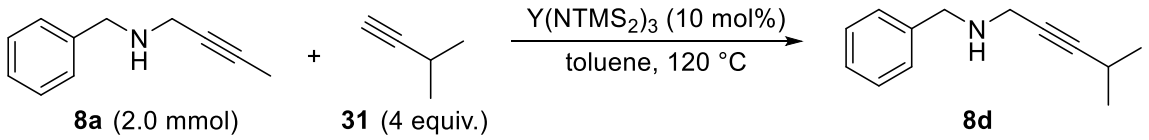
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.20 (m, 10H, Ar*H*), 3.90 (s, 2H, ArCH_2N), 3.65 (t, *J* = 2.3 Hz, 2H, C≡CCH_2Ph), 3.48 (t, *J* = 2.3 Hz, 2H, NCH_2C≡C), 1.65 (bs, 1H, N*H*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 139.5, 137.0, 128.5, 128.4 (2C), 127.9, 127.1, 126.6, 81.4, 80.2, 52.5, 37.9, 25.2.

IR (cm^{-1}) 3025 (s), 3063 (s), 2919 (s), 2838 (s), 1606 (s), 1496 (s), 1454 (s), 728 (s), 695 (s)

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{18}N^+$ 236.1434; Found 236.1436.

N-Benzyl 4-methyl-pent-2-ynylamine (8d)



8a (2.0 mmol) **31** (4 equiv.) **8d**

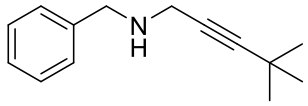
Following an adapted version of a reported procedure.[12] Into an oven dried microwave vial containing a stirrer bar was weighed $Y(N(TMS)_2)_3$) (0.11 g, 0.20 mmol, 10 mol%). Dry toluene (degassed; 13 mL), N-Benzyl but-2-ynylylamine (**8a**) (0.32 g, 2.0 mmol, 1 equiv.) and 3-methylbutyne (**31**) (0.55 g, 8.0 mmol, 4 equiv.) were added and reaction the reaction was stirred at 130 °C for 24 hours. After the reaction mixture had cooled to room temperature, the mixture was loaded directly onto a chromatography column for purification (SiO_2, 5:5:90-5:10:85 Ultra and EtOAc in pentane) to afford N-Benzyl 4-methyl-pent-2-ynylamine (**8d**) as a straw yellow oil (0.29 g, 1.6 mmol, 75% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.21 (m, 5H, Ar*H*), 3.86 (s, 2H, ArCH_2), 3.40 (d, *J* = 2.0 Hz, 2H, CH_2C≡C), 2.59 (tdd, *J* = 8.9, 6.9, 3.5 Hz, 1H, C*H*$(CH_3)_2$), 1.65 (bs, 1H, N*H*), 1.18 (d, *J* = 6.8 Hz, 6H, CH(CH_3)$_2$).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 139.6, 128.4, 128.4, 127.1, 89.7, 76.9, 52.4, 37.8, 23.2, 20.5.

Spectra data was consistent with the values reported in literature.[12]

N-Benzyl 4,4-dimethyl-pent-2-ynylamine (8e)



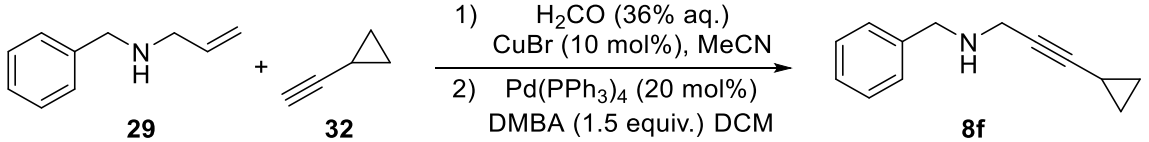
Following the same procedure as the synthesis of **8d**; using 3,3-dimethylbytyne (0.66 g, 8.0 mmol, 4 equiv.). After the reaction was finished, the reaction mixture was loaded directly onto a chromatography column for purification (SiO_2, 5:5:90-5:10:85 Ultra and EtOAc in pentane) afforded N-benzyl 4,4-dimethyl-pent-2-ynylamine (**8e**) as a straw yellow oil (0.27 g, 1.3 mmol, 66% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.21 (m, 5H, Ar*H*), 3.87 (s, 2H, ArCH_2), 3.40 (s, 2H, CH_2C≡C), 1.88 (bs, 1H, N*H*), 1.24 (s, 9H, C(CH_3)$_3$).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 139.4, 128.5, 128.4, 127.1, 92.8, 77.2, 52.2, 37.7, 31.2, 27.4.

Spectra data was consistent with the values reported in literature.[12]

N-Benzyl 3-cyclopropyl-prop-2-ynylamine (8f)



29 **32** **8f**

Following an adapted version of a reported procedure. [12] To a solution of CuBr (0.36 g, 2.5 mmol, 12 mol%) in MeCN (130 mL) was added allyl benzylamine (**29**) (3.9 mL, 25 mmol, 1.3 equiv), formaldehyde (36% aq. solution; 5.0 mL, 65 mmol, 3.3 equiv.) and ethenylcyclopropane (**32**) (1.7 mL, 20 mmol, 1 equiv.). The reaction was stirred at room temperature for 16 hours before being concentrated by

rotary evaporation. The resulting residue was diluted with Et_2O (20 mL) and washed with aq. NaOH (5.0 M; 3 x 10 mL), dried over $MgSO_4$, filtered and concentrated by rotary evaporation. Purification of the crude material by column chromatography (SiO_2, 0-2% EtOAc in pentane) afforded N-allyl-N-benzyl 3-cyclopropyl-prop-2-ynylamine as a colourless oil (4.0 g, 18 mmol, 89% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.19 (m, 5H, Ar*H*), 5.88 (ddt, *J* = 16.8, 10.1, 6.5 Hz, 1H, C*H*=CH$_2$), 5.25 (dq, *J* = 17.2, 1.6 Hz, 1H, CH=C*H*$_2$), 5.16 (ddt, *J* = 10.1, 2.2, 1.2 Hz, 1H, CH=C*H*$_2$), 3.61 (s, 2H, ArC*H*$_2$), 3.24 (d, *J* = 1.9 Hz, 2H, C*H*$_2$C≡C), 3.14 (dt, *J* = 6.5, 1.3 Hz, 2H, C*H*$_2$C=C), 1.28 (dddd, *J* = 10.1, 8.6, 5.0, 2.5 Hz, 1H, C*H*(CH$_2$)$_2$), 0.81 – 0.75 (m, 2H, CH(C*H*$_2$)$_2$), 0.70 – 0.66 (m, 2H, CH(C*H*$_2$)$_2$).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.7, 135.8, 129.2, 128.2, 127.0, 117.8, 88.9, 69.8, 57.2, 56.6, 41.8, 8.3, -0.5.

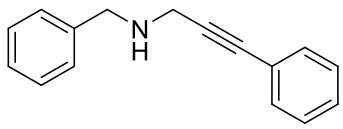
Under a nitrogen atmosphere, the tertiary amine obtained from the previous step (1.0 g, 4.4 mmol, 1.0 equiv.) was added to a solution of $Pd(PPh_3)_4$ (0.10 g, 89 µmol, 2 mol%) and 1,3-dimethylbarbituric acid (1.0 g, 6.7 mmol, 1.5 equiv.) in DCM (22 mL). The reaction mixture was stirred at room temperature for 6 hours. The mixture was then diluted with Et_2O (50 mL), washed with sat. aq. $NaHCO_3$ (3 x 20 mL) and then extracted with 1M HCl (3 x 20 mL). The combined aqueous layers were basified with K_2CO_3 (until pH >7) and then extracted with DCM (3 x 20 mL) after which the combined organic layers were dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude material was purified by column chromatography (SiO_3, 20-30% EtOAc in pentane) to afford N-benzyl 3-cyclopropyl-prop-2-ynylamine (**8f**) as a lightly straw coloured oil (0.82 g, 4.4 mmol, 99% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.19 (m, 5H, Ar*H*), 3.84 (s, 2H, ArC*H*$_2$), 3.37 (d, *J* = 2.0 Hz, 2H, C*H*$_2$C≡C), 1.50 (bs, 1H, N*H*), 1.25 (dddd, *J* = 10.1, 8.6, 5.0, 2.5 Hz, 1H, C*H*(CH$_2$)$_2$), 0.80 – 0.63 (m, 4H, CH(C*H*$_2$)$_2$).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 139.7, 128.4 (2C), 127.0, 87.0, 73.3, 52.5, 37.9, 8.1, -0.5.

Spectra data was consistent with the values reported in literature.[12]

N-benzyl-3-phenylprop-2-yn-1-amine (8g)



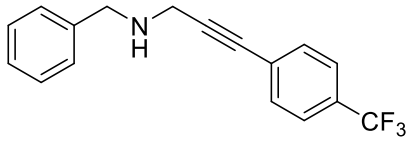
Synthesised following **general procedure A** using benzyl amine (2.9g, 27 mmol, 6 equiv.) and 3-phenyl-prop-2-ynyl p-toluenesulfonate[13] (1.3g, 4.4 mmol, 1 equiv.). Purification of the crude product by column chromatography (SiO_2, 10-40% EtOAc in Pent) afforded N-benzyl-3-phenylprop-2-yn-1-amine (**8f**) as a straw-coloured oil (0.78 g, 3.5 mmol, 79%).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 – 7.20 (m, 10H, Ar*H*), 3.96 (s, 2H, ArC*H*$_2$), 3.66 (s, 2H, C*H*$_2$C≡C), 1.73 (bs, 1H, N*H*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 139.5, 131.7, 128.5 (2C), 128.3, 128.1, 127.2, 123.2, 87.5, 83.8, 52.5, 38.3.

Spectra data was consistent with the values reported in literature.[12]

N-Benzyl-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-amine (8h)



Following a modified version of a reported procedure.[14] To a stirred solution of $Pd(PPh_3)_2Cl_2$ (90 mg, 0.13 mmol, 5 mol%), dppf (86 mg, 0.16 mmol, 6 mol%), CuI (25 mg, 0.13 mmol, 5 mol%), DABCO (0.76 g, 6.8 mmol, 2.6 equiv.) and 4-trifluro-Iodobenzene (0.92 g, 3.4 mmol, 1.3 equiv.) in DMSO (10 mL; degassed by bubbling N_2) under a N_2 atmosphere was added **7a** (0.38 g, 2.6 mmol, 1.0 equiv.). The reaction mixture was heated to 60 °C and stirred for 6 hours. The progress of the reaction was determined by TLC (30 % EtOAc in pentane). The reaction was then quenched by the addition of H_2O (10 mL) and the mixture diluted with EtOAc (12 mL). The layers were separated and the aqueous layer extracted with EtOAc (2 x 12 mL). The combined organic layers were washed with brine (2 x 24 mL), dried over $MgSO_4$ filtered through a pad of SiO_2 (washed with EtOAc) and concentrated under rotary evaporation. The crude material was dry-loaded onto SiO_2 and purified by column chromatography (SiO_2, 10-20% EtOAc in pentane) afforded N-benzyl-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-amine (**8h**) as a dark orange oil (0.55 g, 1.9 mmol, 72 %)

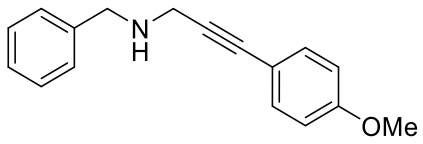
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.61 – 7.24 (m, 9H, Ar*H*), 3.95 (s, 2H, ArCH_2), 3.67 (s, 2H, CH_2C≡C), 1.64 (d, *J* = 2.5 Hz, 1H).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 139.3, 131.9, 129.8 (q, *J* = 32.7 Hz), 128.5, 128.4, 127.2, 127.0, 125.2 (q, *J* = 3.9 Hz), 90.2, 82.49, 52.6, 38.2.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -63.2.

Spectra data was consistent with the values reported in literature.[14]

N-Benzyl-3-(4-methoxyphenyl)prop-2-yn-1-amine (8i)



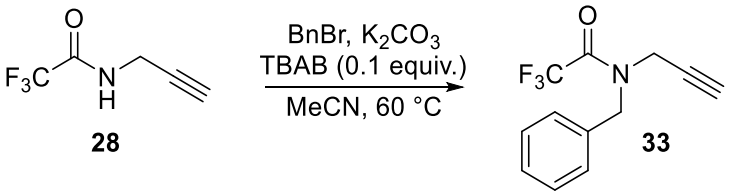
Following a modified version of a reported procedure.[14] To a stirred solution of $Pd(PPh_3)_2Cl_2$ (90 mg, 0.13 mmol, 5 mol%), dppf (86 mg, 0.16 mmol, 6 mol%), CuI (25 mg, 0.13 mmol, 5 mol%), DABCO (0.76 g, 6.8 mmol, 2.6 equiv.) and 4-iodo-anisol (0.79 g, 6.4 mmol, 1.3 mmol) in DMSO (10 mL; degassed by bubbling N_2) under a N_2 atmosphere was added **7a** (0.38 g, 2.6 mmol, 1.0 equiv.). The reaction mixture was heated to 60 °C and stirred for 6 hours. The progress of the reaction was determined by TLC (30 % EtOAc in pentane). The reaction was then quenched by the addition of H_2O (10 mL) and the mixture diluted with EtOAc (12 mL). The layers were separated and the aqueous layer extracted with EtOAc (2 x 12 mL). The combined organic layers were washed with brine (2 x 24 mL), dried over $MgSO_4$ filtered through a pad of SiO_2 (washed with EtOAc) and concentrated under rotary evaporation. The crude material was dry-loaded onto SiO_2 and purified by column chromatography (SiO_2, 15-30% EtOAc in pentane) afforded N-benzyl-3-(4-methoxyphenyl)prop-2-yn-1-amine (**8i**) as a light orange solid (0.28 g, 1.1 mmol, 43 % yield)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.23 (m, 9H, Ar*H*), 6.87 – 6.81 (m, 2H, C*H*$_3$O- Ar*H*), 3.95 (s, 2H, ArC*H*$_2$), 3.81 (s, 3H, C*H*$_3$), 3.64 (s, 2H, C*H*$_2$C≡C), 1.64 (bs, 1H, N*H*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.4, 139.6, 133.0, 128.4 (2C), 127.1, 115.3, 113.9, 86.0, 83.5, 55.3, 52.5, 38.3.

Spectra data was consistent with the values reported in literature.[14]

N-Benzyl Propynyl trifluoroacetamide (33)



Following an adapted version of a reported procedure.[7] To a mixture of K_2CO_3 (8.2 g, 59 mmol, 2 equiv.) and TBAB (0.95 g, 3.0 mmol, 0.1 equiv.) in MeCN (150 mL) was added propynyl trifluoroacetamide **28** (4.5 g, 30 mmol, 1 equiv.) and benzyl bromide (6.0 g, 33 mmol, 1.1 equiv.) after which the reaction mixture was stirred at 60 °C. The progress of the reaction was monitored. After completion has been determined (2-3 hours) based on TLC (SiO_2, 20% EtOAc in pentane), the mixture was filtered through a plug of Celite, which was washed with Et_2O. The resulting filtrate was concentrated by rotary evaporation. Purification of the crude product by column chromatography (SiO_2, 0-8% EtOAc in Pent) to afforded N-Benzyl propynyl trifluoroacetamide (**33**) as a colourless oil (5.0 g, 21 mmol, 71% yield)

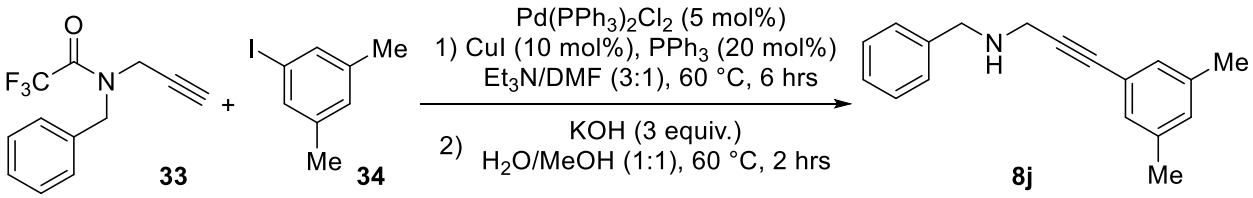
^{1}H NMR (400 MHz, Chloroform-*d*; 1:1.2 mixture of rotamers) δ 7.46 – 7.23 (m, 10H, Ar*H*), 4.79 (s, 2H, C*H*$_2$Ar), 4.77 (s, 2H, C*H*$_2$Ar), 4.12 (d, *J* = 2.5 Hz, 2H, C*H*$_2$C≡C), 4.06 (d, *J* = 2.4 Hz, 2H, C*H*$_2$C≡C), 2.37 (t, *J* = 2.4 Hz, 1H, C≡C*H*), 2.29 (t, *J* = 2.5 Hz, 1H, C≡C*H*).

^{13}C NMR (101 MHz, Chloroform-*d*; 1:1.2 mixture of rotamers) δ 156.7 (q, *J* = 36.5 Hz), 134.5, 133.8, 129.1, 129.0, 128.6, 128.6, 128.3, 127.7, 116.4 (q, *J* = 287.9 Hz), 116.3 (q, *J* = 288.1 Hz), 76.6 (overlapping with solvent), 76.5, 73.7, 73.3, 49.7 (q, *J* = 3.6 Hz), 48.7, 35.8 (q, *J* = 4.2 Hz), 34.4.

^{19}F NMR (376 MHz, Chloroform-*d*; 1:1.2 mixture of rotamers) δ -68.5, -69.3.

HRMS (LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{12}H_{11}F_3NO^+$ 242.0787; Found 242.0783.

N-Benzyl-3-(3,5-dimethylphenyl)prop-2-ynylamine (8j)



Following a modified version of a reported procedure.[14] To a solution of $PdCl_2(PPh_3)_2$ (0.14 g, 0.20 mmol, 5 mol%), PPh_3 (0.21 g, 0.80 mmol, 20 mol%) and CuI (76 mg, 0.40 mmol, 10 mol%) in DMF (3.3 mL) and Et_3N (10 mL) was added **33** (0.97 g, 4.0 mmol, 1 equiv.) and 1-Iodo-3,5-dimethylbenzene (**34**)

(1.1 g, 4.8 mmol, 1.2 equiv.). The resulting mixture was heated to 60 °C for 6 hours. After cooling to room temperature, water (25 mL) was added and the reaction mixture extracted with EtOAc (3 x 40 mL); the combined organics portions were dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude material was purified by flash column chromatography (SiO_2, 0-5% EtOAc in pentane) afforded N-benzyl-N-(3-(3,5-dimethylphenyl)prop-2-ynyl)-trifluoroacetamide as an orange oil (1.2 g, 3.6 mmol, 90% yield)

^{1}H NMR (400 MHz, Chloroform-*d*; mixture of rotamers) δ 7.44 – 7.29 (m, 10, CH_2Ar*H*, both rotamers), 7.06 (m, 4H, Ph*H*, both rotamers), 7.00 (s, 1H, Ph*H*), 6.99 (s, 1H, Ph*H*), 4.85 (s, 2H, ArCH_2), 4.83 (s, 2H, PhCH_2), 4.36 (s, 2H, CH_2C≡C), 4.29 (s, 1H, CH_2C≡C), 2.31 (s, 6H, CH_3), 2.30 (s, 6H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*; mixture of rotamers, some unresolved aromatic peaks) δ 156.75 (qd, *J* = 36.1, 10.0 Hz), 138.0, 138.0, 134.8, 134.1, 133.8, 133.7, 130.8, 130.7, 129.5, 129.5, 129.1, 129.0, 128.7, 128.6, 128.5, 128.5, 128.3, 127.8, 121.7, 121.4, 116.5 (qd, *J* = 288.1, 7.9 Hz), 85.8, 85.5, 81.1, 80.9, 49.74 (q, *J* = 3.6 Hz), 49.0, 36.9 (q, *J* = 4.3 Hz), 35.4, 21.1.

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{20}H_{18}F_3NNaO^+$ 368.1233; Found 368.1235.

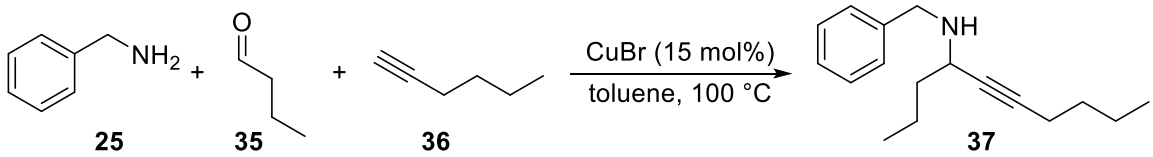
Following an adapted version of a reported procedure.[8] To the trifluoroacetamide obtained from the previous step (0.84 g, 2.4 mmol, 1 equiv.) was added a solution of KOH (0.15 g, 2.7 mmol, 1.3 equiv.) in water (5 mL) and methanol (5 mL) and the resulting mixture was heated to 60 °C for 2 hours. The reaction was then cooled to room temperature and acidified with aq. HCl (1.0 M; 5 mL) followed by basification with sat. $NaHCO_3$ (pH >7). The resulting mixture is extracted with DCM (3 x 10 mL), dried over $MgSO_4$, filtered and concentrated by rotary evaporation. Purification by column chromatography (SiO_2, 10-40% EtOAc in pentane) afforded N-benzyl-3-(3,5-dimethylphenyl)prop-2-ynylamine (**8j**) as an orange oil (0.49 g, 2.0 mmol, 76% yield)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.24 (m, 5H, Ar*H*), 7.08 (m, 2H, Ar*H*), 6.95 (m, 1H, Ar*H*), 3.96 (s, 2H, ArCH_2), 3.65 (s, 2H, CH_2C≡C), 2.29 (s, 6H, CH_3), 2.09 (bs, 1H, N*H*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 139.3, 137.8, 130.0, 129.3, 128.5, 128.4, 127.2, 122.8, 86.5, 84.2, 52.3, 38.1, 21.1.

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{20}N^+$ 250.1590; Found 250.1593.

N-benzyldec-5-yn-4-amine (37)



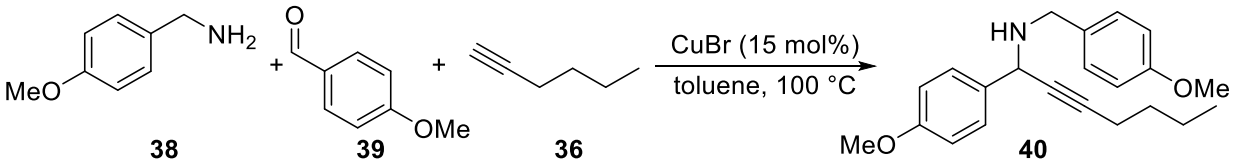
Following a modified reported procedure,[15] into a 20 mL μwave vial containing CuBr (0.26 g, 1.8 mmol, 15 mol%) in toluene (12 mL) was added benzylamine (**25**) (1.7 mL, 16 mmol, 1.3 equiv.), butyraldehyde (**35**) (1.1 mL, 12 mmol, 1 equiv.) and 1-hexyne (**36**) (2.3 mL, 19 mmol, 1.6 equiv.). The reaction mixture was heated to 100 °C for 12 hours, after which it was allowed to cool to room temperature and directly loaded onto a chromatography column for purification (SiO_2, 2-8% EtOAc in pentane) to obtain N-benzyldec-5-yn-4-amine (**37**) as an orange oil (1.9 g, 7.9 mmol, 64% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.20 (m, 5H, Ar*H*), 4.01 (d, *J* = 12.9 Hz, 1H, ArC*H*$_2$), 3.80 (d, *J* = 12.9 Hz, 1H, ArC*H*$_2$), 3.35 (ddt, *J* = 7.8, 5.8, 2.1 Hz, 1H, NC*H*), 2.24 (td, *J* = 6.9, 2.0 Hz, 2H, C≡CC*H*$_2$), 1.68 – 1.37 (m, 8H, CH_2), 1.30 (bs, 1H, N*H*), 0.98 – 0.87 (m, 6H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 140.4, 128.3, 128.3, 126.8, 83.9, 81.4, 51.4, 49.4, 38.6, 31.2, 21.9, 19.4, 18.4, 13.9, 13.6.

HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{17}H_{26}N^+$ 244.2060; Found 244.2052.

N-(4-methoxybenzyl)-1-(4-methoxyphenyl)hept-2-yn-1-amine (40)



38 39 36 40

Following a modified reported procedure,[15] Into a 20 mL µwave vial containing CuBr (0.29 mg, 2.0 mmol, 20 mol%) in toluene (10 mL) was added 4-methoxybenzylamine (**38**) (1.7 mL, 13 mmol, 1.3 equiv.), 4-methoxybenzaldehyde (**39**) (1.2 mL, 10 mmol, 1.0 equiv.) and 1-hexyne (**36**) (1.9 mL, 16 mmol, 1.6 equiv.). The reaction mixture was heated to 100 °C for 12 hours, after which it was allowed to cool to room temperature and directly loaded onto a chromatography column for purification (SiO_2, 5-20% EtOAc in pentane) to obtain N-(4-methoxybenzyl)-1-(4-methoxyphenyl)hept-2-yn-1-amine (**40**) as a dark orange oil (2.4 g, 7.7 mmol, 77% yield).

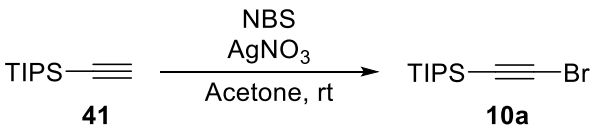
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 (m, 2H, Ar*H*), 7.28 (m, 2H, Ar*H*), 6.89 – 6.83 (m, 4H, Ar*H*), 4.48 (t, *J* = 2.1 Hz, 1H, NC*H*), 3.81 (d, *J* = 3.7 Hz, 2H, NC*H*$_2$Ar), 3.80 (s, 3H, OC*H*$_3$), 3.80 (s, 3H, OC*H*$_3$), 2.29 (td, *J* = 7.0, 2.1 Hz, 2H C≡CC*H*$_2$C), 1.60 – 1.40 (m, 4H, C*H*$_2$C*H*$_2$), 1.55 (bs, 1H, N*H*), 0.93 (t, *J* = 7.2 Hz, 3H, C*H*$_3$).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.9, 158.6, 133.3, 132.1, 129.6, 128.7, 113.7, 113.7, 85.7, 80.0, 55.3, 55.3, 52.5, 50.3, 31.0, 22.0, 18.5, 13.6.

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{28}NO_2^+$ 338.2115; Found 338.2114.

3. Synthesis of Bromoalkynes

Tri*iso*propylsilyl bromoacetylene 10a



41 10a

Following a reported procedure.[16] Tri*iso*propylsilylacetylene (**41**) (0.81 g, 4.5 mmol, 1.00 equiv.) was dissolved in acetone (30 mL). *N*-bromosuccinimide (0.93 g, 5.2 mmol, 1.16 equiv.) was added, followed by $AgNO_3$ (76 mg, 0.44 mmol, 0.1 equiv.). The resulting mixture was stirred at room temperature for 3 h and it was then poured onto ice. After ice being allowed to melt, the aqueous layer was extracted with pentane (3 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered through a plug

of silica and concentrated by rotary evaporation to afford pure tri*iso*propylsilyl bromoacetylene (**10a**) as a colourless oil. (1.16 g, 4.43 mmol, 99%)

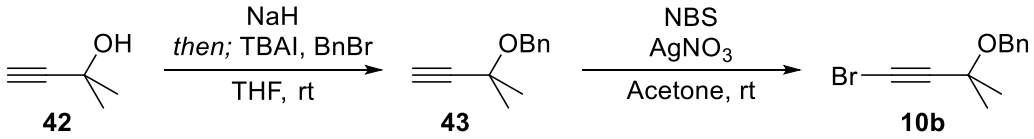
^{1}H NMR (400 MHz, Chloroform-*d*) δ 1.20-0.97 (m, 21H, TIPS).

^{13}C NMR (100 MHz, Chloroform-*d*) δ 83.5, 61.7, 18.5, 11.3.

Spectra data was consistent with the values reported in literature.[16]

Procedure copied from previous publication from the group.[1]

(((4-Bromo-2-methylbut-3-yn-2-yl)oxy)methyl)benzene (10b)



Following a reported procedure,[17] NaH (60% suspension in mineral oil, 240 mg, 6.00 mmol, 1.2 equiv.) was added portionwise to a solution of 2-methyl-3-butyn-2-ol (**42**) (0.49 mL, 5.0 mmol, 1.0 equiv.) in THF (24 mL). The mixture was stirred at rt for 1 hour and then TBAI (92.0 mg, 0.250 mmol, 0.050 equiv.) and benzyl bromide (0.72 mL, 6.0 mmol, 1.2 equiv.) were added in this order. The reaction mixture was stirred at rt overnight and then diluted with Et_2O (18 mL). The organic solution was washed with water (3 x 15 mL), brine and dried over $MgSO_4$. Upon filtration, it was concentrated by evaporation under reduced pressure and the resulting crude oil was purified by column chromatography (SiO_2, 5% Et2O in Pentane) to afford the pure O-benzylated alcohol **43** as a colourless oil (715 mg, 4.10 mmol, 82% yield) which was directly used in the next step.

O-Benzylated alcohol **43** (0.53 g, 3.0 mmol) was dissolved in acetone (25 mL). *N*-bromosuccinimide (0.64 g, 3.6mmol, 1.2 equiv.) was added, followed by $AgNO_3$ (51 mg, 0.30 mmol, 0.1 equiv.). The resulting mixture was stirred at room temperature for 3 h and it was then poured onto ice. After ice being allowed to melt, the aqueous layer was extracted with pentane (3 x 30 mL). The combined organic layers were dried over $MgSO_4$, filtered through a plug of silica and concentrated by rotary evaporation. Purification by column chromatography (SiO_2, 2% EtOAc in Pentane) afforded bromoalkyne **10b** was obtained as a pale yellow oil (0.63 mg, 2.5 mmol, 83% yield).

^{1}H NMR (400 MHz, CDCl3) δ 7.41-7.31 (m, 4H, Ar*H*), 7.27 (m, 1H, Ar*H*), 4.62 (s, 2H, CH_2Ar), 1.55 (s, 6H, CH_3).

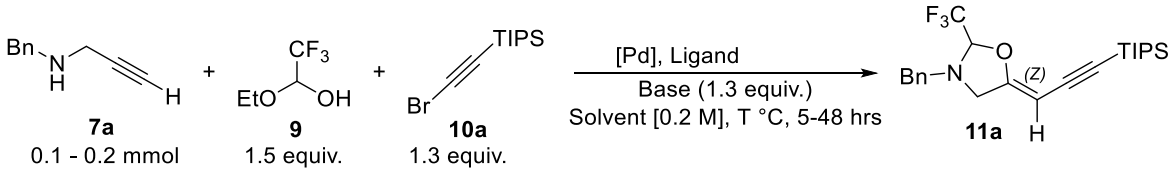
^{13}C NMR (101 MHz, CDCl3) δ 138.7, 128.3, 127.7, 127.4, 82.4, 71.7, 66.7, 44.1, 28.7.

Spectra data was consistent with the values reported in literature.[17]

Procedure copied from previous publication from the group.[1]

4. Optimisation of the Carbo-Oxygenation reaction.

Optimisation for reaction with terminal propargylic amines.

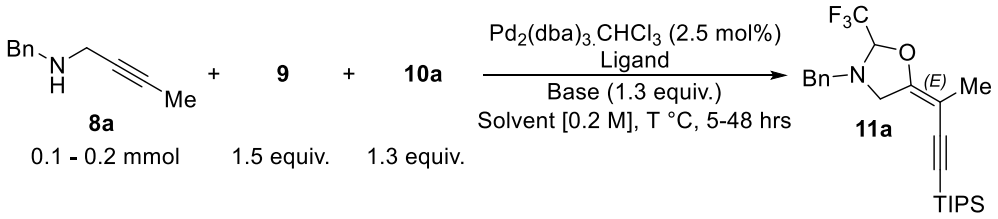


Entry	Pd source	Ligand	Base	Solvent	T (°C)	Yield[a] (E:Z)
1	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	P(2-furyl)$_3$	Cs_2CO_3	toluene	60	23% (1:3)
2	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	PPh_3	Cs_2CO_3	toluene	60	22% (1:4)
3	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	P(*o*Tol)	Cs_2CO_3	toluene	60	13% (1:2)
4	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	PPh_2Cy	Cs_2CO_3	toluene	60	3% (1:2)
5	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	P(*o*FPh)	Cs_2CO_3	toluene	60	37% (1:4)
6	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	P(*p*CF)Ph_3	Cs_2CO_3	toluene	60	35% (1:5)
7	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DavePhos	Cs_2CO_3	toluene	60	12% (1:3)
8	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	Xphos	Cs_2CO_3	toluene	60	12% (1:1)
9	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	toluene	60	82% (1:4)
10	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	dppf	Cs_2CO_3	toluene	60	83% (1:4)
11	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	N-XantPhos	Cs_2CO_3	toluene	60	12% (1:2)
12	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	dppe	Cs_2CO_3	toluene	60	72% (1:4)
13	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	dppp	Cs_2CO_3	toluene	60	79% (1:4)
14	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	BINAP	Cs_2CO_3	toluene	60	48% (1:4)
15	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPMPhos	Cs_2CO_3	toluene	60	79% (1:4)
16	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	Anthphos	Cs_2CO_3	toluene	60	36% (1:4)
17	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	CsHCO3	toluene	60	12% (1:1)
18	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Na2CO3	toluene	60	4% (--)
19	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	K2CO3	toluene	60	22% (1:5)
20	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	NaOtBu	toluene	60	20% (1:4)
21	$PdCl_2(PPh_3)_2$ (5 mol%)	DPEPhos	Cs_2CO_3	toluene	60	50% (1:4)
22	$Pd(OAc)_2$ (5 mol%)	DPEPhos	Cs_2CO_3	toluene	60	79% (1:4)
23	$Pd(Opiv)_2$ (5 mol%)	DPEPhos	Cs_2CO_3	toluene	60	36% (1:5)
24	$Pd(dba)_2$ (5 mol%)	DPEPhos	Cs_2CO_3	toluene	60	85% (1:4)[b]
25	Pd(allyl)(COD)BF_4 (5 mol%)	DPEPhos	Cs_2CO_3	toluene	60	60% (1:5)
26	Pd(Cp)Cinammyl	DPEPhos	Cs_2CO_3	toluene	60	87% (1:5)[b]
27	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	toluene	40	57% (1:5)
28	$Pd(dba)_2$ (5 mol%)	DPEPhos	Cs_2CO_3	toluene	40	51% (1:5)
29	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	toluene	50	62% (1:4)
30	$Pd(dba)_2$ (5 mol%)	DPEPhos	Cs_2CO_3	toluene	50	58% (1:4)
31	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	toluene	70	82% (1:3)
32	$Pd(dba)_2$ (5 mol%)	DPEPhos	Cs_2CO_3	toluene	70	81% (1:3)
33	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	THF	60	46% (1:3)
34	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	tol/THF (4:1)	60	65% (1:3)
35	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	F_3-toluene	60	45% (1:7)
36	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	Cl-benzene	60	39% (1:3)
37	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	DCE	60	83% (1:9)[b]
38	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	DCE	50	74% (1:11)
39[c]	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	DCE	60	77% (1:9)
40[d]	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	DCE	60	78% (1:8)
41[e]	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	DCE	60	81% (1:8)
42[f]	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	DCE	60	73% (1:7)
43[g]	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	DCE	60	78% (1:8)

44[h]	$Pd_2(dba)_3.CHCl_3$ (2.5 mol%)	DPEPhos	Cs_2CO_3	DCE	60	78% (1:8)

a) Yields were calculated from ^1H NMR spectra by using 1,2-diflurobenzene as internal standard. b) Isolated yield c) 10 min mixing for tether solution. d) 0 min mixing for tether solution. e) No premixing of tether solution. f) Addition of CsOTf (1.2 equiv.). g) Acetal (1.1 equiv). h) Acetal (3.0 equiv).

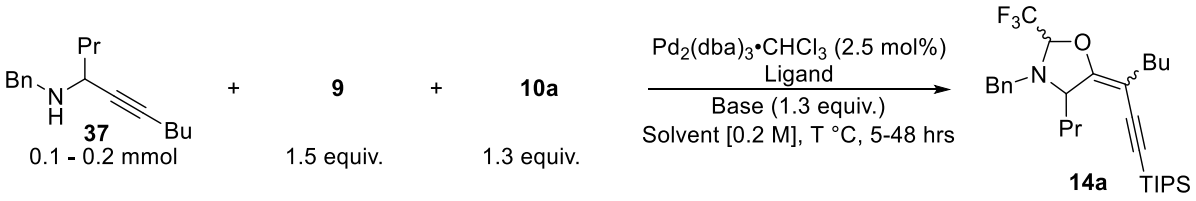
Optimisation for reaction with internal propargylic amines.



Entry	Ligand	Base	Solvent	Yield 11a (E:Z)[a]
1	DPEPhos	Cs_2CO_3	toluene	26% (4:1)
2	DPEPhos	Cs_2CO_3	DCE	45% (7:1)
3[b]	DPEPhos	Cs_2CO_3	DCE	43% (13:1)
4	P(2-furyl)$_3$	Cs_2CO_3	DCE	13% (--)
5[c]	DPEPhos	Cs_2CO_3	DCE	0%
6[c,d]	DPEPhos	Cs_2CO_3	DCE	0%
7	DPEPhos	CsOAc[e]	DCE	14%[e] (--)
8	DPEPhos	CsOBz	DCE	12%[e] (--)
9	DPEPhos	KO^{t}Bu	DCE	0%[e]
10	DPEPhos	KO^{t}Bu[f]	DCE	0%[e]
11	DPEPhos	K_3PO_4	DCE	60% (7:1)
12	DPEPhos	K_3PO_4[f]	DCE	48% (8:1)
13	DPEPhos	DIPEA	DCE	0%[e]
14	DPEPhos	DBU	DCE	0%[e]
15	DPEPhos	Cs_3PO_4[g]	DCE	58% (6:1)
16	DPEPhos	K_3PO_4[h]	DCE	67% (6:1)
17	DCEPhos	K_3PO_4[h]	DCE	20% (6:1)[e]
18	XantPhos	K_3PO_4[h]	DCE	73% (11:1)
19	N-XantPhos	K_3PO_4[h]	DCE	7% (--)
20	dppf	K_3PO_4[h]	DCE	80% (1:1)
21	dtpf	K_3PO_4[h]	DCE	22% (3:1)[e]
22	(+/-) BINAP	K_3PO_4[h]	DCE	0%
23	dppe	K_3PO_4[h]	DCE	33% (6:1)
24	dppp	K_3PO_4[h]	DCE	53% (3:1)

a) Yields were calculated from ^1H NMR spectra by using 1,2-diflurobenzene as internal standard. b) acetal (3.0 equiv.) bromo alkyne (2.6 equiv.) c) acetal (0 equiv) d) with CO_2 balloon e) incomplete conversion f) added CsOTf g) synthesised in oven h) new material, kept in in glovebox

Optimisation for reaction with internal and substituted propargylic amines with aryl iodides.

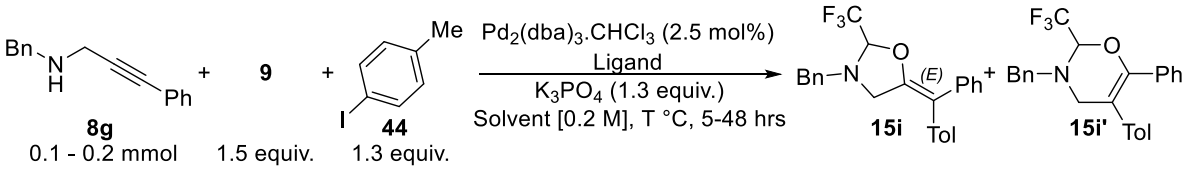


Entry	Ligand	T (°C)	Base	Remaining amine[a]	14a Yield (ratio)[a]
1	DPEPhos	60	K_3PO_4	100%	--
2	XantPhos	60	K_3PO_4	90%	--

3	P(2-furyl)$_3$	60	K_3PO_4	--	43% (3:1)
4	XPhos	60	K_3PO_4	42%	5% (4:1)
5	P(*t*Bu)$_3$	60	K_3PO_4	50	--
6	P(*n*Bu)$_3$	60	K_3PO_4	52	--
7	P(Cy)$_3$	60	K_3PO_4	80	--
8	PPh_2Cy	60	K_3PO_4	40	--
9	PPh_3	60	K_3PO_4	42	--
10	P(F_5-Ph)$_3$	60	K_3PO_4	50	--
11	P(2-thienyl)$_3$	60	K_3PO_4	--	44 (3:1)
12	P(2-furyl)$_3$	60	Cs_2CO_3	30	17
13	P(2-furyl)$_3$	60	CsOBz	71	--
14	P(2-furyl)$_3$	60	CsOPiv	81	--
15	P(2-furyl)$_3$	60	KO*t*Bu	81	--
16	P(2-furyl)$_3$	70	K_3PO_4	--	59% [b]
17[c]	P(2-furyl)$_3$	70	K_3PO_4	--	50% [b]
18[c]	P(2-furyl)$_3$	80	K_3PO_4	--	59% (2:1)
19[c]	P(2-furyl)$_3$	90	K_3PO_4	--	57% (2:1)

a) Yields were calculated from 1H NMR spectra by using 1,2-diflurobenzene as internal standard. b) Isolated yield c) Starting with amine **37'** bearing 4-methoxybenzyl protecting group

Optimisation for reaction with internal propargylic amines.



Entry	Ligand	Solvent	T (°C)	15i yield (E:Z) [a]	15i' yield [a,b]
1	SPhos	DCE	60	46% (--)	10%
2	RuPhos	DCE	60	62%	12%
3	DavePhos	DCE	60	60%	10%
4	PhDavePhos	DCE	60	14% (1:4)	0%
5	XPhos	DCE	60	21%	3%
6	BrettPhos	DCE	60	67% (16:1)	8%
7	BrettPhos[c]	DCE	60	55% (6:1)	6%
8	P(2-furyl)$_3$	DCE	60	16% (*z* isomer)	0%
9	XantPhos	DCE	60	33% (1:1)	1%
10	DPEPhos	DCE	60	11% (1:3)	1%
11	dppf	DCE	60	4% (--)	1%
12	RuPhos	Toluene	60	43%	9%
13	BrettPhos	Toluene	60	53%	5%
14	RuPhos	DCE	45	72%	14%
15	BrettPhos	DCE	45	37% (11:1)	4%
16	RuPhos	DCE	35	68%	14%
17	RuPhos	DMSO	35	0%	0%
18	BrettPhos	Toluene	35	64%	16%

a) Yields were calculated from 1H NMR spectra by using 1,2-diflurobenzene as internal standard. b) structure assigned by analogy to isolated and characterised **15a'** c) Repeat reaction.

5. Scope of the Carbo-Oxygenation Reaction.

Procedure C – Terminal propargyl amines

Tether solution: The solution terminal alkyne **7** (0.400 mmol), trifluoroacetaldehyde ethyl hemiacetal **9** (0.54 mmol, 1.35 equiv.) and tri*iso*propylsilyl bromoacetylene **10a** (136 mg, 0.520 mmol, 1.3 equiv.) were dissolved in DCE (0.50 mL). The resulting solution was then degassed by freeze-pump-thaw and placed under argon.

Catalyst mixture: A vial was charged with $Pd_2(dba)_3 \cdot CHCl_3$ (10.4 mg, 10.0 µmol, 2.5 mol%), DPEPhos (16.0 mg, 30.0 µmol, 7.5 mol%) and Cs_2CO_3 (169 mg, 0.520 mmol, 1.3 equiv.). The vial was sealed and the atmosphere purged and replaced with argon.

To the catalyst mixture vial was added DCE (0.5 mL) and the mixture was heated at 60 °C for 2-3 minutes, after which it took on an orange colour. The contents of the tether solution vial were transferred to the catalyst vial, using additional DCE (1.0 mL) to wash the flask. The resulting reaction mixture was stirred at 60 °C for 18-24 hours. After this time, the reaction mixture was removed from heating, cooled to room temperature, unsealed and diluted with pentane (4 mL) and passed through a small plug of silica gel (deactivated by Et_3N) rinsing with 5 % DCM in pentane (8 mL) and concentrated by rotary evaporation. The crude material was dry-loaded onto silica gel (deactivated by Et_3N) prior to column chromatography.

Procedure D – Internal propargyl amines

As “Procedure C” but the ligand DPEPhos was replaced with XantPhos (17.4, 30.0 µmol, 7.5 mol%) and the base Cs_2CO_3 was replaced with K_3PO_4 (110 mg, 0.520 mmol, 1.3 equiv.).

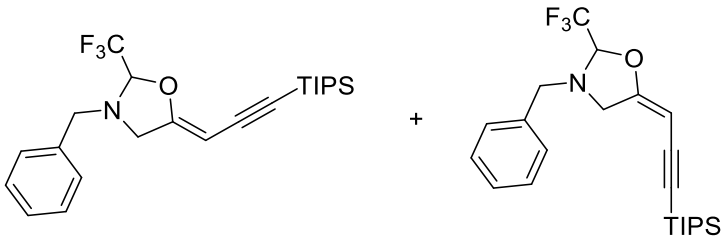
Procedure E – Internal propargyl amines with propargylic substitution

As “Procedure C” but the ligand DPEPhos was replaced with trifurylphosphine (14.0 mg, 60.0 µmol 0.15 mol%) and the base Cs_2CO_3 was replaced with K_3PO_4 (110 mg, 0.520 mmol, 1.3 equiv.).

Procedure F – Internal propargyl amines in combination with aryl electrophiles

As “Procedure C” but the ligand DPEPhos was replaced with RuPhos (14.0 mg, 30.0 µmol, 7.5 mol %) and the base Cs_2CO_3 was replaced with K_3PO_4 (110 mg, 0.520 mmol, 1.3 equiv.).

(Z)- and (E)-3-Benzyl-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11a)



Following **general procedure C**, using **7a** (58.1 mg, 0.400 mmol)**.** The crude product was purified through column chromatography (Et_3N-deactivated SiO_2; 0-2% DCM in pentane) affording the named compound **11a** as a straw yellow oil (141 mg, 0.334 mmol, 83% yield; separable Z:E isomers in 9:1 ratio)

Z-isomer (major)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.27 (m, 5H, Ar*H*), 5.11 (q, *J* = 5.2 Hz, 1H, C*H*CF$_3$), 4.63 (t, *J* = 1.6 Hz, 1H, C=C*H*), 3.99 (d, *J* = 13.1 Hz, 1H, ArC*H*$_2$), 3.92 (ddd, *J* = 16.1, 2.1, 1.0 Hz, 1H, NC*H*$_2$C=C), 3.86 (d, *J* = 13.1 Hz, 1H, ArC*H*$_2$), 3.50 (dq, *J* = 16.1, 1.4 Hz, 1H, NC*H*$_2$C=C), 1.10 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.5, 136.7, 128.7, 128.6, 128.0, 122.3 (q, *J* = 283.4 Hz), 100.7, 94.5 (q, *J* = 34.8 Hz), 93.9, 79.0, 60.2, 54.4, 18.6, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.1 (d, *J* = 5.2 Hz).

IR (cm^{-1}) 2946 (m), 2865 (m), 2128 (w), 1669 (m), 1463 (m), 1300 (m), 1180 (s), 1150 (s), 970 (m), 884 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{33}F_3NOSi^+$ 424.2278; Found 424.2273.

E-isomer (minor)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.17 (m, 5H, Ar*H*), 5.12 – 5.05 (t, *J* = 2.3 Hz, 1H, C=C*H*), 4.98 (q, *J* = 5.3 Hz, 1H, C*H*CF$_3$), 3.99 (d, *J* = 13.1 Hz, 1H, ArC*H*$_2$), 3.92 (d, *J* = 16.9 Hz, 1H, NC*H*$_2$C=C), 3.86 (d, *J* = 13.1 Hz, 1H, ArC*H*$_2$), 3.71 (dq, *J* = 16.8, 1.5 Hz, 1H, NC*H*$_2$C=C), 0.96 (m, 21H, *TIPS*).

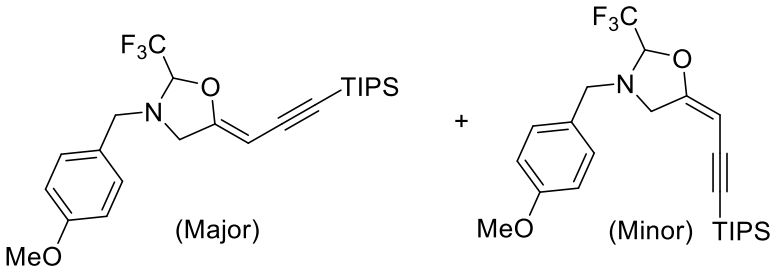
^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.2, 136.5, 128.8, 128.7, 128.0, 122.2 (q, *J* = 283.6 Hz), 102.5, 94.8 (q, *J* = 34.7 Hz), 93.1, 80.7, 60.5, 54.4, 18.6, 11.2.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.0 (d, *J* = 5.2 Hz).

IR (cm^{-1}) 2940 (m), 2866 (m), 2136 (m), 1661 (m), 1460 (w), 1292 (m), 1148 (s), 960 (m), 882 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{23}H_{33}F_3NOSi^+$ 424.2278; Found 424.2274.

(Z)- and (E)-3-(4-Methoxybenzyl)-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11b)



Following **general procedure C**, using **7b** (70.1 mg, 0.400 mmol)**.** The crude product was purified through column chromatography (Et_3N-deactivated SiO_2; 0-2% DCM in pentane) affording the named compound **11b** as a colourless oil (145 mg, 0.320 mmol, 80% yield; separable Z:E isomers in 8:1 ratio)

Z-isomer (major)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 (m, 2H, Ar*H*), 6.88 (m, 2H, Ar*H*), 5.09 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.62 (t, *J* = 1.6 Hz, 1H, C=C*H*), 3.93 – 3.76 (m, 3H, NCH_2C=C, ArCH_2), 3.81 (s, 3H, OCH_3), 3.50 (dq, *J* = 16.1, 1.4 Hz, 1H, ArCH_2), 1.09 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.6, 159.4, 130.0, 128.7, 122.3 (q, *J* = 283.2 Hz), 114.0, 100.8, 94.3 (q, *J* = 34.8 Hz), 93.8, 78.9, 59.6, 55.3, 54.3, 18.6, 11.4.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.0 (d, *J* = 5.4 Hz).

IR (cm^{-1}): 2945 (m), 2864 (m), 2358 (S), 2339 (m), 1514 (m), 1304 (m), 1252 (m), 1185 (S), 1151 (S).

E-isomer (minor)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.26 (d, *J* = 8.6 Hz, 2H, Ar*H*), 6.88 (m, 2H, Ar*H*), 5.15 (t, 1H, C=C*H*), 5.05 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.02 – 3.74 (m, 4H, NCH_2C=C, ArCH_2), 3.81 (s, 3H, OCH_3), 1.04 (m, 21H, *TIPS*).

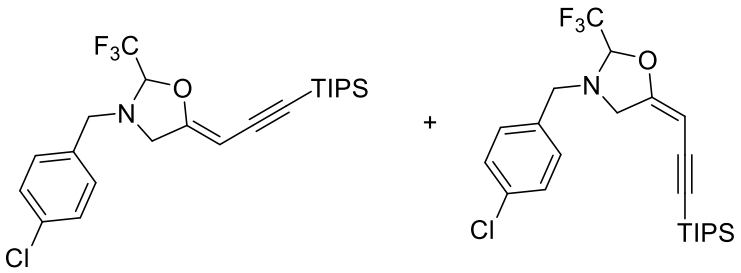
^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.3, 159.4, 130.2, 128.5, 122.2 (d, *J* = 283.5 Hz), 114.0 102.5, 94.6 (q, *J* = 34.6 Hz), 93.0, 80.6, 59.9, 55.3, 54.3, 18.6, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.9 (d, *J* = 5.3 Hz).

IR (cm^{-1}): 2940 (m), 2864 (m), 2137 (w), 1516 (m), 1659 (w), 1182 (S), 1148 (S).

HRMS (ESI) calcd for $C_{24}H_{35}F_3NO_2Si^+$ $[M+H]^+$ 454.2384; found 454.2399.

(Z)- and (E)-3-(4-Chlorobenzyl)-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11c)



Following **general procedure C**, using **7c** (72.0 mg, 0.400 mmol)**.** The crude product was purified through column chromatography (Et_3N-deactivated SiO_2; 0-3% DCM in pentane) affording the named compound **11c** as a colourless oil (160 mg, 0.349 mmol, 87% yield; separable Z:E isomers in 7:1 ratio)

Z-isomer (major)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.27 (m, 4H, Ar*H*), 5.07 (q, *J* = 5.2 Hz, 1H, C*H*CF_3), 4.63 (dd, *J* = 1.9, 1.3 Hz, 1H, C=C*H*), 4.01 – 3.79 (m, 3H, NCH_2C=C, ArCH_2), 3.47 (dp, *J* = 16.0, 1.4 Hz, 1H, NCH_2C=C), 1.09 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.2, 135.2, 133.9, 129.9, 128.9, 122.2 (q, *J* = 283.6 Hz), 100.6, 94.5 (q, *J* = 34.8 Hz), 94.1, 79.3, 59.6, 54.4, 18.6, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.7 (d, *J* = 5.1 Hz).

IR (cm^{-1}): 2945 (m), 2864 (m), 1669 (m), 1301 (m), 1182 (S), 1148 (S), 1086 (m).

HRMS (ESI) calcd for $C_{23}H_{32}ClF_3NOSi^+$ $[M+H]^+$ 458.1888; found 458.1888.

E-isomer (minor)

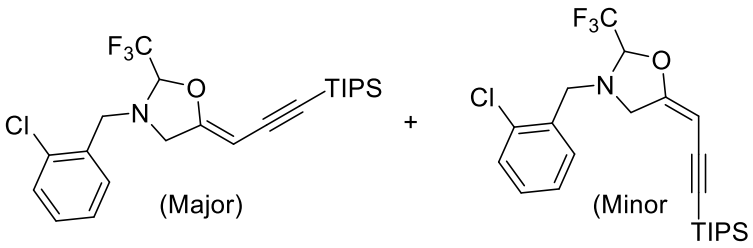
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.27 (m, 4H, Ar*H*), 5.17 (t, *J* = 2.1 Hz, 1H, C=C*H*), 5.02 (q, *J* = 5.2 Hz, 1H, C*H*CF_3), 4.02 – 3.83 (m, 3H, NCH_2C=C, ArCH_2), 3.74 (dt, *J* = 16.7, 1.6 Hz, 1H, NCH_2C=C), 1.03 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.9, 135.1, 133.9, 130.1, 128.9, 122.2 (q, *J* = 283.6 Hz), 102.3, 94.8 (q, *J* = 34.9 Hz), 93.3, 80.9, 59.8, 54.4, 18.6, 11.2.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.0 (d, *J* = 5.2 Hz).

IR (cm^{-1}) 2945 (m), 2864 (m), 1669 (m), 1301 (m), 1182 (s), 1148 (s), 1086 (m).

(Z)- and (E)-3-(2-Chlorobenzyl)-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11d)



Following **general procedure C**, using **7d** (72.0 mg, 0.400 mmol)**.** The crude product was purified through column chromatography (Et_3N-deactivated SiO_2; 0-3% DCM in pentane) affording the named compound **11d** as a colourless oil (146 mg, 0.320 mmol, 80% yield; separable Z:E isomers in 12:1 ratio)

Z-isomer (major)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 (m, 1H, Ar*H*), 7.38 (dd, *J* = 7.6, 1.6 Hz, 1H, Ar*H*), 7.33 – 7.20 (m, 2H, Ar*H*), 5.17 (q, *J* = 5.1 Hz, 1H, C*H*CF_3), 4.64 (t, *J* = 1.6 Hz, 1H, C=C*H*), 4.07 (s, 2H, ArCH_2), 3.95 (ddt, *J* = 16.0, 2.0, 1.0 Hz, 1H, NCH_2C=C), 3.52 (dp, *J* = 15.9, 1.4 Hz, 1H, NCH_2C=C), 1.10 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.3, 134.5, 133.8, 130.1, 129.7, 129.1, 127.1, 122.3 (q, *J* = 283.5 Hz), 100.6, 95.0 (q, *J* = 34.9 Hz), 94.1, 79.3, 57.5, 54.7, 18.6, 11.4.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.2 (d, *J* = 5.2 Hz).

IR (cm^{-1}) 2943 (s), 2864 (s), 2166 (s), 2128 (s), 1672 (s), 1464 (s), 1446 (s), 1303 (s), 1280 (s), 1183 (s), 1148 (s), 882 (s), 753 (s), 659 (s), 636 (s).

E-isomer (minor)

^{1}H NMR (400 MHz, Chloroform-*d*) 7.53 – 7.21 (m, 4H, Ar*H*), 5.18 (t, *J* = 2.1 Hz, 1H, C=C*H*), 5.12 (q, *J* = 5.2 Hz, 1H, C*H*CF_3), 4.14 – 3.99 (m, 3H, ArCH_2, NCH_2C=C), 3.79 (dt, *J* = 16.6, 1.5 Hz, 1H, NCH_2C=C), 1.04 (m, 21H, *TIPS*).

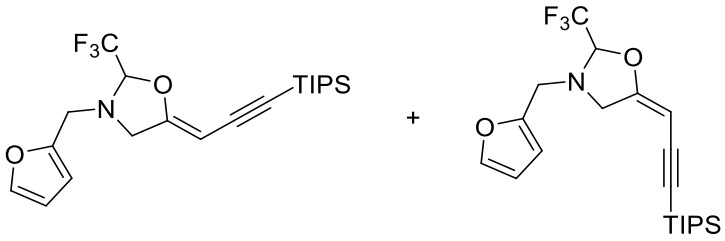
^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.9, 134.3, 134.1, 130.5, 129.8, 129.2, 127.0, 122.2 (q, *J* = 283.7 Hz), 102.3, 95.3 (q, *J* = 34.7 Hz), 93.3, 80.8, 57.5, 54.5, 18.6, 11.2.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.1 (d, *J* = 5.1 Hz).

IR (cm^{-1}) 2946 (m), 2867 (m), 2137 (w), 1663 (m), 1464 (w), 1293 (m), 1181 (m), 1149 (s), 882 (m).

HRMS (ESI) calcd for $C_{23}H_{32}ClF_3NOSi^+$ $[M+H]^+$ 458.1888; found 458.1887

(Z)- and (E)-3-(Furan-2-ylmethyl)-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11e)



Following **general procedure C**, using **7e** (54.1 mg, 0.400 mmol)**.** The crude product was purified through column chromatography (Et_3N-deactivated SiO_2; 0-2% DCM in pentane) affording the named compound **11e** as a colourless oil (107 mg, 0.261 mmol, 74% yield; separable Z:E isomers in 10:1 ratio)

Z-isomer (major)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (dd, *J* = 1.9, 0.9 Hz, 1H, Ar*H*), 6.34 (dd, *J* = 3.3, 1.9 Hz, 1H, Ar*H*), 6.29 (dd, *J* = 3.2, 0.8 Hz, 1H, Ar*H*), 5.19 (q, *J* = 5.1 Hz, 1H, C*H*CF_3), 4.59 (t, *J* = 1.6 Hz, 1H, C=C*H*), 3.96 (ddd, *J* = 15.9, 1.9, 0.9 Hz, 1H, NCH_2C=C), 3.98 – 3.84 (m, 2H, ArCH_2), 3.66 (dt, *J* = 15.9, 1.3 Hz, 1H, NCH_2C=C), 1.08 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.4, 149.9, 143.2, 122.3 (d, *J* = 283.5 Hz), 110.3, 109.7, 100.6, 93.8, 93.8 (q, *J* = 35.0 Hz), 78.9, 53.9, 51.7, 18.6, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.5 (d, *J* = 5.3 Hz).

IR (cm^{-1}) 2944 (m), 2866 (m), 2128 (w), 1671 (m), 1466 (w), 1304 (m), 1178 (s), 1147 (s), 1076 (m), 1013 (m).

HRMS (ESI) calcd for $C_{21}H_{31}F_3NO_2Si^+$ $[M+H]^+$ 414.2071; found 414.2082.

Cambridge Crystallographic Data Centre entry – 1873997

E-isomer (minor)

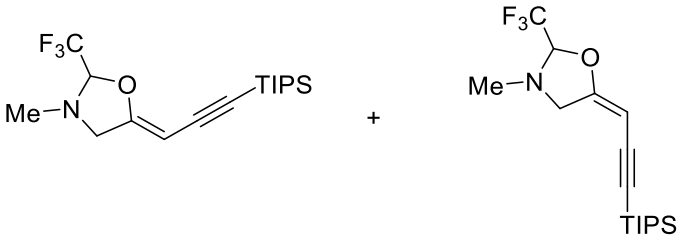
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 (dd, *J* = 1.9, 0.8 Hz, 1H, Ar*H*), 6.34 (dd, *J* = 3.3, 1.9 Hz, 1H, Ar*H*), 6.29 (dd, *J* = 3.2, 0.8 Hz, 1H, Ar*H*), 5.18 (q, *J* = 5.2 Hz, 1H, C*H*CF_3), 5.06 (t, *J* = 2.0 Hz, 1H, C=C*H*), 4.04 (ddd, *J* = 16.6, 2.3, 1.1 Hz, 1H, NCH_2C=C), 3.94 – 3.88 (m, 3H, NCH_2C=C, ArCH_2), 1.07 (s, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.1, 149.9, 143.2, 122.2 (d, *J* = 283.1 Hz), 110.4, 109.7, 102.4, 94.4 (q, *J* = 35.0 Hz), 93.0, 80.3, 53.8, 51.9, 18.6, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.5 (d, *J* = 5.3 Hz).

IR (cm^{-1}) 2944 (m), 2869 (m), 2138 (w), 1662 (m), 1466 (w), 1291 (m), 1151 (s), 1015 (m), 883 (m).

(Z)- and (E)-3-Methyl-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11f)



Following **general procedure C**, using N-methylpropargylamine (27.6 mg, 0.400 mmol)**.** The crude product was purified through column chromatography (Et_3N-deactivated SiO_2; 0-5% DCM in pentane) affording the named compound **11f** as a colourless oil (101 mg, 0.292 mmol, 73% yield; separable Z:E isomers in 6:1 ratio).

Z-isomer (major)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 4.90 (q, *J* = 5.0 Hz, 1H, C*H*CF_3), 4.63 (t, *J* = 1.6 Hz, 1H, C=C*H*), 3.98 (ddt, *J* = 15.5, 1.9, 1.0 Hz, 1H, NCH_2), 3.40 (dp, *J* = 15.5, 1.3 Hz, 1H, NCH_2), 2.61 (s, 3H, CH_3), 1.1 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.4, 122.2(q, *J* = 282.8 Hz), 100.6, 96.2(q, *J* = 34.7 Hz), 93.9, 79.1, 56.5, 43.5, 18.6, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.6 (d, *J* = 5.1 Hz).

IR (cm^{-1}) 2946 (m), 2865 (m), 1672 (w), 1302 (m), 1182 (s), 1150 (s), 1019 (m).

E-isomer (minor)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.16 (t, *J* = 2.1 Hz, 1H, C=C*H*), 4.87 (q, *J* = 5.0 Hz, 1H, C*H*CF_3), 4.13 – 4.04 (m, 1H, NCH_2), 3.63 – 3.55 (m, 1H, NCH_2), 2.64 (s, 3H, CH_3), 1.07 (m, 21H, *TIPS*).

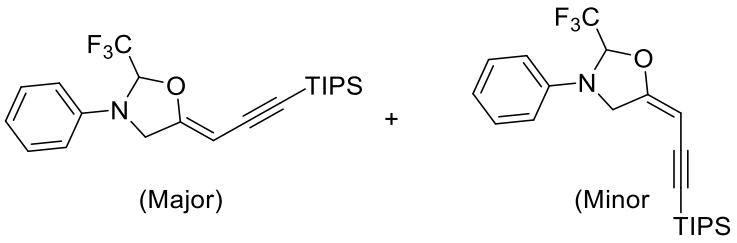
^{13}C NMR (101 MHz, Chloroform-*d*) δ 164.0, 122.2 (d, *J* = 283.2 Hz), 102.3, 96.6 (q, *J* = 34.6 Hz), 93.2, 80.7, 56.4, 43.7, 18.7, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.6 (d, *J* = 5.1 Hz).

IR (ν_{max}, cm^{-1}) 2947 (m), 2869 (m), 2128 (w), 1670 (w), 1304 (m), 1184 (s), 1152 (s), 1018 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{17}H_{29}F_3NOSi^+$ 348.1965; Found 348.1962.

(Z)- and (E)-3-Phenyl-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11g)



Following **general procedure C**, using **7g** (52.0 mg, 0.400 mmol). The crude product was purified through column chromatography (Et_3N-deactivated SiO_2; 0-5% DCM in pentane) affording the named compound **11g** as a colourless oil (92.5 mg, 0.226 mmol, 57% yield; separable Z:E isomers in 7:1 ratio)

Z-isomer (major)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.28 (m, 2H, Ar*H*), 6.96 (m, 1H, Ar*H*), 6.75 (dd, *J* = 7.6, 1.5 Hz, 2H, Ar*H*), 5.88 (q, *J* = 4.1 Hz, 1H, C*H*CF_3), 4.80 (t, *J* = 1.7 Hz, 1H, C=C*H*), 4.41 – 4.28 (m, 2H, NCH_2C=C), 1.10 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.4, 144.3, 129.6, 122.8 (q, *J* = 286.7 Hz), 120.7, 113.7, 99.9, 95.1, 88.7 (q, *J* = 35.8 Hz), 80.5, 50.0, 18.6, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.3 (d, *J* = 4.0 Hz).

IR (cm^{-1}) 2945(w), 2869(m), 2128(s), 1679(s), 1603(m), 1505(s), 1338(m), 1180(m), 1151(s), 882(s), 849(s).

E-isomer (minor)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.28 (m, 2H), 6.96 (tt, *J* = 7.4, 1.0 Hz, 1H), 6.79 – 6.71 (m, 2H), 5.85 (q, *J* = 4.1 Hz, 1H, C*H*CF_3), 5.23 (t, *J* = 2.2 Hz, 1H, C=C*H*), 4.52 (ddd, *J* = 15.1, 2.2, 1.1 Hz, 1H, NCH_2C=C), 4.42 (dd, *J* = 15.0, 2.3 Hz, 1H, NCH_2C=C), 1.11 (m, 21H, *TIPS*).

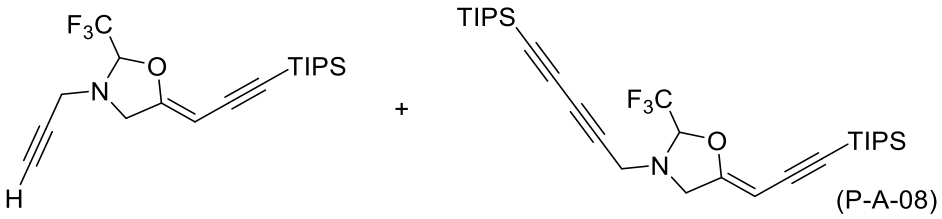
^{13}C NMR (101 MHz, Chloroform-*d*) δ 163.0, 144.2, 129.6, 122.7 (q, *J* = 286.9 Hz), 120.7, 113.6, 101.6, 94.4, 89.0 (q, *J* = 35.8 Hz), 81.8, 50.0, 18.7, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.2 (d, *J* = 4.2 Hz).

IR (cm^{-1}) 2944(m), 2855(m), 2133(s), 1668(s),1602(m), 1505(s), 1364(w), 1284(s), 1201(s), 996(m), 883(s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{31}F_3NOSi^+$ 410.2122; Found 410.2121.

(Z)- and (E)-3-(Prop-2-yn-1-yl)-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11h)



Following **general procedure C**, using dipropargylamine (37.3 mg, 0.400 mmol)**.** The crude product was purified through column chromatography (Et_3N-deactivated SiO_2; 0-2% DCM in pentane) affording the named compound **11h** as a colourless oil (69.6 mg, 0.187 mmol, 47% yield; single isomer) along with alkyne coupled product **13** (28.0 mg, 50.0 µmol, 13% yield; single isomer)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.19 (q, *J* = 4.7 Hz, 1H, C*H*CF_3), 4.64 (t, *J* = 1.7 Hz, 1H, C=C*H*), 3.94 (ddd, *J* = 15.2, 1.7, 0.7 Hz, 1H, NCH_2C=C), 3.75 (ddq, *J* = 15.3, 2.0, 1.0 Hz, 1H, NCH_2C=C), 3.58 (dd, *J* = 2.5, 1.3 Hz, 2H, CH_2C≡C), 2.32 (t, *J* = 2.4 Hz, 1H, C≡C*H*), 1.08 (m, 21H, *TIPS*).

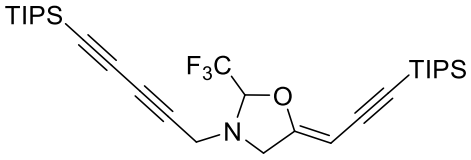
^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.4, 122.3 (q, *J* = 282.4 Hz), 100.4, 94.2, 93.0 (q, *J* = 35.1 Hz), 79.2, 77.1, 74.5, 53.4, 43.4, 18.6, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.8 (d, *J* = 4.7 Hz).

IR (cm^{-1}) 3311 (w), 2943 (m), 2868 (m), 2364 (m), 2339 (m), 2127 (w), 1672 (w), 1466 (w), 1310 (m), 1154 (s), 986 (w), 886 (m).

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{28}F_3NNaOSi^+$ 394.1784; Found 394.1791.

(Z)- and (E)-2-(Trifluoromethyl)-3-(5-(tri*iso*propylsilyl)penta-2,4-diyn-1-yl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (13)



Following **general procedure C**, using dipropargylamine (37.3 mg, 0.400 mmol) and **tri*iso*propylsilyl** bromoacetylene (272 mg, 1.04 mmol, 1.3 equiv)**.** The crude product was purified through column chromatography (Et_3N-deactivated SiO_2; 0-5% DCM in pentane) affording the named compound **13** as a colourless oil (90.7 mg, 0.164 mmol, 41% yield; single isomer).

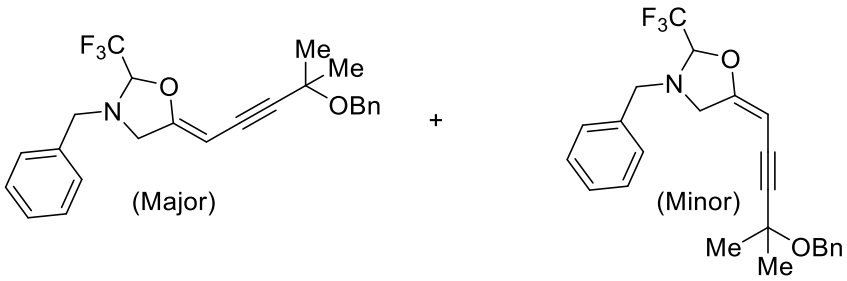
^{1}H NMR (400 MHz, Chloroform-*d*) δ 5.15 (q, *J* = 4.5 Hz, 1H, C*H*CF_3), 4.66 (t, *J* = 1.7 Hz, 1H, C=C*H*), 3.97 – 3.74 (m, 2H, NCH_2C=C), 3.68 (d, *J* = 0.9 Hz, 2H, CH_2C≡C), 1.08 (m, 42H, TIPS).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 161.1, 122.2 (q, *J* = 282.6 Hz), 100.3, 94.4, 92.6 (q, *J* = 35.3 Hz), 88.5, 84.5, 79.6, 71.6, 70.3, 53.3, 43.6, 18.6, 18.5, 11.3, 11.2.

IR (cm^{-1}) 2945 (s), 2865 (s), 2106 (w), 1674 (m), 1464 (m), 1307 (m), 1185 (s), 1153 (s), 1076 (m), 883 (s).

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{19}H_{29}F_3NOSi^+$ 552.3205; Found 552.3309.

(Z)- and (E)-3-Benzyl-5-(4-(benzyloxy)-4-methylpent-2-yn-1-ylidene)-2-(trifluoromethyl)oxazolidine (11i)



Following **general procedure C**, using **7a** (58.1 mg, 0.400 mmol) and bromoacetylene **10b** (132 g, 0.52 mmol, 1.3 equiv.). The crude product was purified through column chromatography (Et_3N-deactivated SiO_2; 5-10% EtOAc in pentane) affording the named compound **11i** as a colourless oil (83.0 mg, 0.200 mmol, 50% yield; separable Z:E isomers in 7:1 ratio).

Z-isomer (major)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.20 (m, 10H, Ar*H*), 5.10 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.67 (s, 2H, ArCH_2O), 4.61 (dd, *J* = 2.0, 1.2 Hz, 1H, C=C*H*), 4.00 – 3.83 (m, 3H, ArCH_2N, NCH_2C=C), 3.52 (dp, *J* = 16.1, 1.4 Hz, 1H, NCH_2C=C), 1.58 (d, *J* = 1.8 Hz, 6H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.2, 139.3, 136.6, 128.7, 128.2, 128.0, 127.9, 127.2, 122.3 (q, *J* = 283.5 Hz), 94.6, 94.6 (q, *J* = 34.5 Hz), 78.1, 72.1, 71.3, 66.6, 60.3, 54.4, 29.1.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (d, *J* = 5.3 Hz).

IR (cm^{-1}) 2987 (w), 1675 (m), 1454 (m), 1379 (m), 1303 (m), 1181 (s), 1147 (s), 1054 (m), 972 (m), 879 (m), 746 (m), 700 (s).

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{24}F_3NNaO_2^+$ 438.1651; Found 438.1657.

E-isomer (minor)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.20 (m, 10H, Ar*H*), 5.16 (t, *J* = 2.1 Hz, 1H, C=C*H*), 5.05 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.58 (s, 2H, ArCH_2O), 4.03 – 3.96 (m, 1H, NCH_2C=C), 3.96 – 3.87 (m, 2H ArCH_2N), 3.71 (dq, *J* = 16.6, 1.5 Hz, 1H, NCH_2C=C), 1.53 (s, 6H, CH_3).

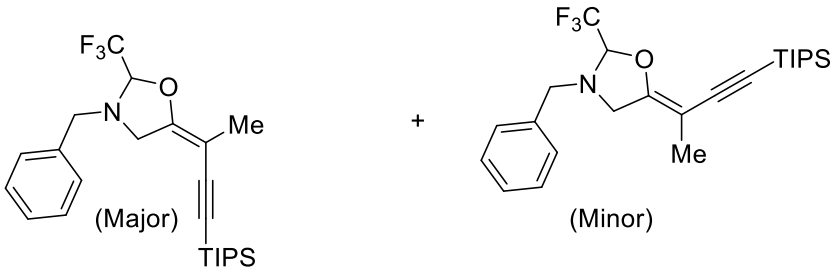
^{13}C NMR (101 MHz, Chloroform-*d*) δ 162.9, 139.1, 136.6, 128.7, 128.7, 128.3, 128.0, 127.6, 127.3, 122.2 (q, *J* = 284.3 Hz), 94.6 (q, *J* = 34.8 Hz), 94.3, 79.6, 71.2, 66.4, 60.5, 54.2, 29.1.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.0 (d, *J* = 5.3 Hz).

IR (cm^{-1}) 2987 (w), 1667 (m), 1452 (m), 1377 (m), 1290 (m), 1173 (s), 1146 (s), 1059 (m), 972 (m), 738 (s), 699 (s).

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{24}H_{24}F_3NNaO_2^+$ 438.1651; Found 438.1657.

(E)- and (Z)-3-Benzyl-2-(trifluoromethyl)-5-(4-(tri*iso*propylsilyl)but-3-yn-2-ylidene)oxazolidine (12a)



Following **general procedure D**, using **8a** (63.7 mg, 0.400 mmol). The crude product was purified through column chromatography (SiO_2; 0-5% DCM in pentane) affording the named compound **12a** as a colourless oil (112 mg, 0.256 mmol, 64%, 10:1 mixture of E:Z isomers). A sample of the mixture was further purified for characterisation by PrepTLC (SiO_2; 2% DCM in pentane) to obtain the major E-isomer as a single compound and a 1:5 mixture of E:Z isomers for assignment of the minor isomer.

E-isomer (major)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.27 (m, 5H, ArH), 5.07 (q, *J* = 5.3 Hz, 1H, C*H*CF$_3$), 4.87 (q, *J* = 6.2 Hz, C*H*CF$_3$), 3.98 (d, *J* = 15.6 Hz, 1H, NC*H*$_2$C=C), 3.96 (d, *J* = 12.7 Hz, 1H, ArC*H*$_2$), 3.88 (d, *J* = 12.9 Hz, 1H, ArC*H*$_2$), 3.75 (d, *J* = 16.2 Hz, 1H, NC*H*$_2$C=C), 1.83 (t, *J* = 1.7 Hz, 3H, C*H*$_3$), 1.10 – 1.03 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.6, 136.8, 128.9, 128.6, 127.9, 122.40 (q, *J* = 283.5 Hz), 106.8, 94.72 (q, *J* = 34.5 Hz), 91.1, 89.4, 60.5, 54.7, 18.6, 15.1, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.0 (d, *J* = 5.2 Hz)

IR (cm^{-1}) 2945 (m), 2865 (m), 2138 (m), 1675 (m), 1466 (m), 1299 (m), 1170 (s), 1149 (s), 969 (m), 882 (m).

Z-isomer (minor)

^{1}H NMR (400 MHz, Chloroform-*d*; characterised in a 5:1 mixture of E:Z isomers) δ 7.39 – 7.27 (m, 5H, Ar*H*), 4.87 (q, *J* = 6.2 Hz, 1H, C*H*CF$_3$), 4.02 – 3.92 (m, 2H, ArC*H*$_2$), 3.64 (d, *J* = 17.0 Hz, 1H, NC*H*$_2$C=C), 3.11 (d, *J* = 16.9 Hz, 1H, NC*H*$_2$C=C), 2.12 (t, *J* = 1.7 Hz, 3H, C*H*$_3$), , 1.10 – 1.03 (m, 21H, *TIPS*).

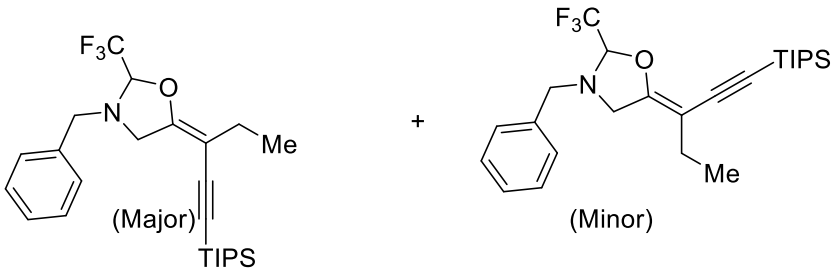
^{13}C NMR (101 MHz, Chloroform-*d*; characterised in a 1:1.6 mixture of E:Z isomers, some signals could not be attributed with certainty) δ 156.6, 137.1, 128.8, 127.8, 104.0, 93.4, 91.2, 85.24 (q, *J* = 34.1 Hz), 58.1, 46.2, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -76.4 (d, *J* = 6.3 Hz).

IR (cm^{-1}) 2945 (m), 2865 (m), 2138 (m), 1675 (m), 1466 (m), 1299 (m), 1170 (s), 1149 (s), 969 (m), 882 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{35}F_3NOSi^+$ 438.2435; Found 438.2432.

(E)- and (Z)-3-Benzyl-2-(trifluoromethyl)-5-(1-(tri*iso*propylsilyl)pent-1-yn-3-ylidene)oxazolidine (12b)



Following **general procedure D**, using **8b** (69.3 mg, 0.400 mmol. The crude product was purified through column chromatography (SiO_2; 0-5% DCM in pentane) affording the named compound **12b** as a colourless oil (130 mg, 0.288 mmol, 72%, 13:1 mixture of E:Z isomers). A sample of the mixture was further purified for characterisation by PrepTLC (SiO_2; 2% DCM in pentane) to obtain the major E-isomer as a single compound and a 1:1.4 mixture of E:Z isomers for assignment of the minor isomer.

E-isomer (major)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.25 (m, 5H, Ar*H*), 5.05 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 3.97 (m, 1H, NCH_2C=C), 3.95 (d, *J* = 12.9 Hz, 1H, ArCH_2), 3.88 (d, *J* = 12.9 Hz, 1H, ArCH_2), 3.73 (dq, *J* = 16.2, 1.2 Hz, 1H, NCH_2C=C), 2.29 – 2.12 (m, 2H, C$H_2$$CH_3$), 1.08 (t, *J* = 7.5 Hz, 3H, CH_2CH_3), 1.05 – 1.02 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.7, 136.8, 128.8, 128.6, 127.9, 122.4 (q, *J* = 283.8 Hz), 105.5, 96.1, 94.6 (q, *J* = 34.5 Hz), 92.3, 60.5, 54.7, 22.1, 18.6, 12.7, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.0 (d, *J* = 5.2 Hz)

IR (cm^{-1}) 2945 (m), 2865 (m), 2138 (m), 1669 (m), 1460 (m), 1293 (m), 1182 (s), 1148 (s), 1018 (m).

Z-isomer (minor)

^{1}H NMR (400 MHz, Chloroform-*d*; characterised in a 1:1.4 mixture of E:Z isomers) δ 7.39 – 7.23 (m, 5H, Ar*H*), 4.84 (qd, *J* = 6.3, 1.4 Hz, 1H, C*H*CF_3), 3.97 (d, *J* = 13.5 Hz, 1H, ArCH_2), 3.90 (d, *J* = 13.5 Hz, 1H, ArCH_2), 3.63 (dq, *J* = 16.9, 1.2 Hz, 1H, NCH_2C=C), 3.08 (dd, *J* = 16.8, 1.4 Hz, 1H, NCH_2C=C), 2.53 (dtd, *J* = 15.0, 7.4, 1.1 Hz, 1H, C$H_2$$CH_3$), 2.46 – 2.32 (m, 1H, C$H_2$$CH_3$), 1.13 (t, *J* = 7.5 Hz, 3H, CH_2CH_3), 1.06 (d, *J* = 2.0 Hz, 21H, *TIPS*).

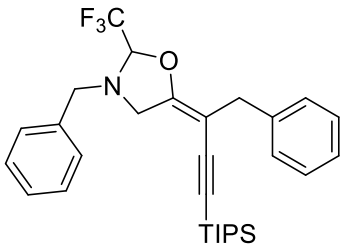
^{13}C NMR (101 MHz, Chloroform-*d*; characterised in a 1:1.6 mixture of E:Z isomers, some signals could not be attributed with certainty) δ 161.3, 137.0, 128.8, 128.6, 127.8, 123.8, 121.0, 103.7, 93.3, 90.0, 85.0 (q, *J* = 34.1 Hz), 58.2, 46.2, 26.1, 18.6, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -76.4 (d, *J* = 6.3 Hz),

IR (cm^{-1}) 2945 (m), 2865 (m), 2138 (m), 1669 (w), 1645 (m), 1460 (m), 1293 (m), 1182 (s), 1152 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{37}F_3NOSi^+$ 452.2591; Found 452.2590.

(E)-3-Benzyl-5-(1-phenyl-4-(tri*iso*propylsilyl)but-3-yn-2-ylidene)-2-(trifluoromethyl)oxazolidine (12c)



Following **general procedure D** using **8c** (94 mg, 0.400 mmol) with the reaction taking place over 48 hrs. The crude product was purified through column chromatography (SiO_2; 0-3% DCM in pentane) affording the named compound **12c** as a light yellow oil (95.3 mg, 0.186 mmol, 46% yield; single isomer). Additional purification of a sample of the obtained oil by PrepTLC (SiO_2, 1% Et_2O in pentane) was made for characterisation.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.13 (m, 10H, Ar*H*), 5.10 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.03 – 3.94 (m, 2H, NCH_2C=C, ArCH_2N), 3.89 (d, *J* = 13.0 Hz, 1H, ArCH_2N), 3.75 (dd, *J* = 16.5, 1.7 Hz, 1H, NCH_2C=C), 3.49 (m, 2H, CCH_2Ar), 0.99 – 0.95 (m, 21H, TIPS).

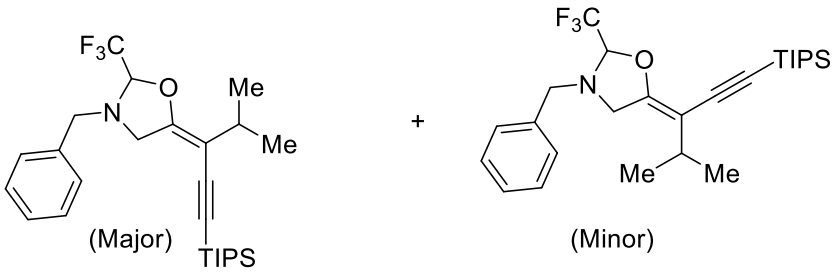
^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.6, 139.5, 136.6, 128.8, 128.8, 128.6, 128.1, 128.0, 126.0, 122.4 (q, *J* = 283.8 Hz), 105.3, 94.7 (q, *J* = 34.7 Hz), 94.3, 93.0, 60.5, 54.8, 35.4, 18.6, 11.2.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.0 (d, *J* = 5.4 Hz).

IR (cm^{-1}) 3029 (w), 2945 (m), 2865 (m), 2138 (w), 1677 (m), 1455 (m), 1291 (m), 1180 (s), 1144 (s), 883 (m).

HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{30}H_{39}F_3NOSi^+$ 514.2748; Found 514.2753.

(E)- and (Z)-3-Benzyl-5-(4-methyl-1-(tri*iso*propylsilyl)pent-1-yn-3-ylidene)-2-(trifluoromethyl)oxazolidine (12d)



Following **general procedure D**, using **8d** (74.9 mg, 0.400 mmol. The crude product was purified through column chromatography (SiO_2; 0-4% DCM in pentane) affording the named compound **12d** as a colourless oil (125.8 mg, 0.270 mmol, 67%, 20:1 mixture of E:Z isomers). A sample of the mixture was further purified for characterisation by PrepTLC (SiO_2; 2% DCM in pentane) to obtain the major E-isomer as a single compound and a 1.6:1 mixture of E:Z isomers for assignment of the minor isomer.

E-isomer (major)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.25 (m, 5H, Ar*H*), 5.05 (q, *J* = 5.3 Hz, 1H, C*H*CF$_3$), 4.01 – 3.91 (m, 2H, NC*H*$_2$C=C, ArC*H*$_2$), 3.88 (d, *J* = 13.0 Hz, 1H, ArC*H*$_2$), 3.72 (dd, *J* = 16.2, 1.4 Hz, 1H, NC*H*$_2$C=C), 2.81 (hept, *J* = 6.8 Hz, 1H, C*H*(CH$_3$)$_3$), 1.10 – 1.04 (m, 6H, CH(C*H*$_3$)$_3$), 1.07 – 1.01 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.7, 136.8, 128.8, 128.6, 127.9, 122.4 (q, *J* = 283.7 Hz), 103.6, 101.3, 94.46 (q, *J* = 34.4 Hz), 93.6, 60.5, 54.8, 27.0, 21.5, 21.3, 18.7, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.1 (d, *J* = 5.4 Hz).

IR (cm^{-1}) 2954 (m), 2865 (m), 2140 (m), 1671 (m), 1464 (m), 1299 (m), 1173 (s), 1145 (s), 1015 (m), 882 (m).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calcd for $C_{26}H_{39}F_3NOSi^+$ 466.2748; Found 466.2753.

Z-isomer (minor)

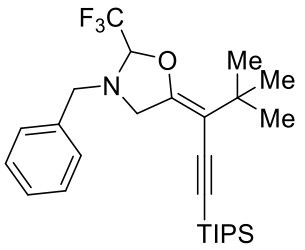
^{1}H NMR (400 MHz, Chloroform-*d*; characterised in a 1:1.6 mixture of E:Z isomers) δ 7.42 – 7.22 (m, 5H, Ar*H*), 4.84 (qd, *J* = 6.3, 1.5 Hz, 1H, C*H*CF$_3$), 4.00 – 3.84 (m, 2H, ArC*H*$_2$), 3.64 (dd, *J* = 17.0, 1.3 Hz, 1H, NC*H*$_2$C=C), 3.21 (hept, *J* = 7.0 Hz, 1H, C*H*(CH$_3$)$_3$), 3.07 (dt, *J* = 16.9, 1.2 Hz, 1H, NC*H*$_2$C=C), 1.13 (d, *J* = 6.9 Hz, 3H, CH(C*H*$_3$)$_3$), 1.10 (d, *J* = 6.9 Hz, 3H, CH(C*H*$_3$)$_3$), 1.08 – 1.02 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*; characterised in a 1:1.6 mixture of E:Z isomers) δ 163.8, 137.0, 128.8, 128.6, 127.8, 103.6, 93.6, 88.8, 84.8 (q, *J* = 33.8 Hz), 58.3, 46.2, 31.6, 19.1, 19.0, 18.7, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -76.4 (d, *J* = 5.8 Hz).

IR (cm^{-1}) 2946 (m), 2868 (m), 2139 (m), 1670 (w), 1462 (m), 1297 (m), 1180 (s), 1145 (s), 1063 (m).

(E)-3-Benzyl-5-(4,4-dimethyl-1-(tri*iso*propylsilyl)pent-1-yn-3-ylidene)-2-(trifluoromethyl)oxazolidine (12e)



Following **general procedure D** leaving the reaction for 48 hrs before work up, using **8e** (81.0 mg, 0.400 mmol. The crude product was purified through column chromatography (SiO_2; 0-3% DCM in pentane) affording the named compound **12e** as a colourless oil (98.9 mg, 0.206 mmol, 51% yield; single isomer)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.25 (m, 5H, Ar*H*), 5.11 (q, *J* = 5.3 Hz, 1H, C*H*CF$_3$), 3.98 (dd, *J* = 16.4, 1.1 Hz, 1H, NC*H*$_2$C=C), 3.96 (d, *J* = 12.9 Hz, 1H, ArC*H*$_2$), 3.87 (d, *J* = 13.0 Hz, 1H, ArC*H*$_2$), 3.76 (dq, *J* = 16.4, 1.5, 1.4 Hz, 1H, NC*H*$_2$C=C), 1.20 (s, 9H, ^{t}*Bu*), 1.04 – 1.00 (d, *J* = 2.0 Hz, 21H, *TIPS*).

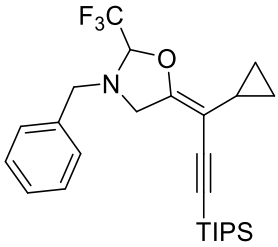
^{13}C NMR (101 MHz, Chloroform-*d*) δ 156.4, 136.8, 128.8, 128.6, 127.9, 122.4 (q, *J* = 283.9 Hz), 105.8, 103.4, 95.3 (q, *J* = 34.4 Hz), 93.1, 60.5, 56.7, 33.4, 29.6, 18.7, 11.4.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.2 (d, *J* = 5.4 Hz).

IR (cm^{-1}) 2945 (m), 2865 (m), 2131 (m), 1646 (m), 1462 (m), 1300 (m), 1174 (s), 1141 (s), 968 (m), 880 (m).

HRMS (APCI/QTOF) m/z: [M + H]$^+$ Calcd for $C_{27}H_{41}F_3NOSi^+$ 480.2904; Found 480.2914.

(E)-3-Benzyl-5-(1-cyclopropyl-3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)-2-(trifluoromethyl)oxazolidine (12f)



Following **general procedure D**, using **8f** (74.1 mg, 0.400 mmol. The crude product was purified through column chromatography (SiO_2; 0-3% DCM in pentane) affording the named compound **12f** as a colourless oil (85.0 mg, 0.183 mmol, 46%, >20:1 E:Z ratio)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.26 (m, 5H, Ar*H*), 5.09 (q, *J* = 5.3 Hz, 1H, C*H*CF$_3$), 3.99 (d, *J* = 16.4 Hz, 1H, NC*H*$_2$C=C), 3.97 (d, *J* = 12.9 Hz, 1H, ArC*H*$_2$), 3.89 (d, *J* = 12.9 Hz, 1H, ArC*H*$_2$), 3.74 (dt, *J* = 16.3, 1.5 Hz, 1H, NC*H*$_2$C=C), 1.76 (p, *J* = 6.6 Hz, 1H, C*H*), 1.06 – 1.00 (m, 21H, *TIPS*), 0.67 (d, *J* = 8.2 Hz, 4H, *c*Pr(C*H*$_2$)).

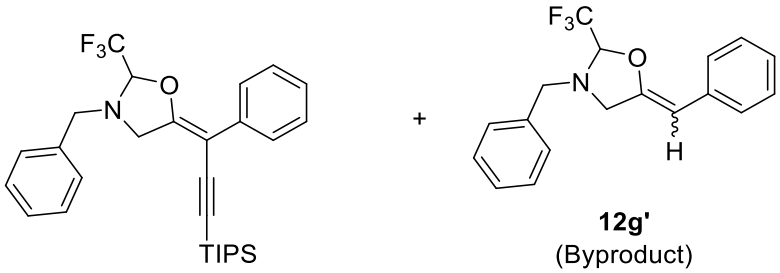
^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.1, 136.8, 128.9, 128.6, 127.9, 122.4 (q, *J* = 283.5 Hz), 101.9, 97.0, 94.8 (q, *J* = 34.5 Hz), 93.2, 60.5, 55.1, 18.6, 11.2, 8.7, 4.8, 4.6.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.9 (d, *J* = 5.5 Hz).

IR (cm^{-1}) 2945 (m), 2865 (m), 2144 (m), 1671 (m), 1463 (m), 1288 (m), 1176 (s), 1148 (s), 1011 (m), 881 (m).

HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{26}H_{37}F_3NOSi^+$ 464.2591; Found 464.2590.

(E)-3-Benzyl-5-(1-phenyl-3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)-2-(trifluoromethyl)oxazolidine (12g)



Following **general procedure D** using **8g** (89 mg, 0.400 mmol). The crude product was purified through column chromatography (SiO_2; 0-3% DCM in pentane) affording the named compound **12g** as an orange oil (122 mg, 0.245 mmol, 61% yield) along with 3-benzyl-5-benzylidene-2-(trifluoromethyl)oxazolidine by-product (**12g'**) (8.1 mg, 0.025 mmol, 6% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.86 – 7.79 (m, 2H, *Ph*), 7.42 – 7.27 (m, 7H, *Ar*, *Ph*), 7.25 – 7.21 (m, 1H, *Ph*), 5.29 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.26 – 4.20 (m, 1H, NCH_2C=C), 4.08 – 3.91 (m, 3H, NCH_2C=C, ArCH_2), 1.09 – 1.05 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.3, 136.4, 134.3, 128.9, 128.7, 128.1, 128.0, 127.4, 126.6, 122.2 (d, *J* = 283.4 Hz), 104.4, 96.4 (q, *J* = 34.9 Hz), 95.8, 93.6, 60.7, 57.2, 18.7, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (d, *J* = 5.5 Hz).

IR (cm^{-1}) 3028 (w), 2867 (m), 2945 (m), 2143 (m), 1637 (m), 1458 (m), 1293 (m), 1175 (s), 1153 (s), 1127 (s), 880 (m).

HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{29}H_{37}F_3NOSi^+$ 500.2591; Found 500.2590.

Byproduct - **3-Benzyl-5-benzylidene-2-(trifluoromethyl)oxazolidine (12g')**

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (m, 2H, Ar*H*), 7.43 – 7.28 (m, 7H, Ar*H*), 7.16 (m, 1H, Ar*H*), 5.35 (t, *J* = 1.5 Hz, 1H, C=C*H*), 5.17 (q, *J* = 5.4 Hz, 1H, C*H*CF_3), 4.06 (d, *J* = 15.5 Hz, 1H, NCH_2C=C), 4.03 – 3.86 (m, 2H, ArCH_2), 3.61 (dt, *J* = 15.4, 1.5 Hz, 1H, NCH_2C=C).

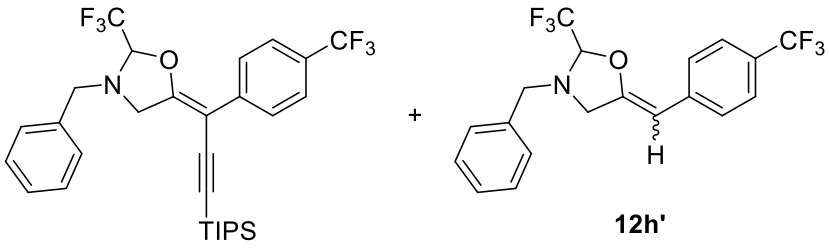
^{13}C NMR (101 MHz, Chloroform-*d*) δ 150.1, 136.9, 135.2, 128.7, 128.7, 128.4, 127.9, 127.7, 125.8, 122.52 (q, *J* = 283.2 Hz), 98.7, 94.80 (q, *J* = 34.5 Hz), 60.3, 55.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (d, *J* = 5.6 Hz).

IR (ν_{max}, cm^{-1}) 3027 (w), 2941 (w), 1689 (m), 1495 (w), 1454 (w), 1297 (m), 1181 (s), 1140 (s), 970 (m), 1016 (w).

HRMS (APPI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{18}H_{17}F_3NO^+$ 320.1257; Found 320.1261.

(E)-3-Benzyl-2-(trifluoromethyl)-5-(1-(4-(trifluoromethyl)phenyl)-3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (12h)



12h'
(Byproduct)

Following **general procedure D** using **8h** (116 mg, 0.400 mmol). The crude product was purified through column chromatography (SiO_2; 0-3% DCM in pentane) affording the named compound **12h** as a colourless oil (113.4 mg, 0.200 mmol, 50% yield) along with 3-benzyl-2-(trifluoromethyl)-5-(4-(trifluoromethyl)benzylidene)oxazolidine byproduct (**12h'**) (34.0 mg, 0.088 mmol, 22% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ7.94 (m, 2H, CF_3Ar*H*), 7.60 (m, 2H, CF_3Ar*H*), 7.44 – 7.28 (m, 5H, Ar*H*), 5.34 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.29 – 4.02 (m, 2H, NCH_2C=C), 4.06 – 3.91 (m, 2H, ArCH_2), 1.09 – 1.05 (m, 21H, TIPS).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.0, 138.0, 136.2, 128.9, 128.8, 128.2, 127.5, 125.1 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 272.1 Hz), 122.1 (q, *J* = 283.4 Hz), 103.5, 96.8 (q, *J* = 35.0 Hz), 94.9, 94.6, 60.7, 57.5, 18.7, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.9, -80.8 (d, *J* = 5.3 Hz).

IR (cm^{-1}) 2942 (m), 2866 (m), 2145 (w), 1641 (m), 1615 (m), 1324 (s), 1290 (m), 1156 (s), 1127 (s), 1108 (s), 1069 (s).

HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{30}H_{36}F_6NOSi^+$ 568.2465; Found 568.2471.

ByProduct - **3-Benzyl-2-(trifluoromethyl)-5-(4-(trifluoromethyl)benzylidene)oxazolidine (12h')**

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (m, 2H, CF_3Ar*H*), 7.48 (m, 2H, CF_3Ar*H*), 7.36 – 7.20 (m, 5H, Ar*H*), 5.32 (t, *J* = 1.4 Hz, 1H, , C=C*H*), 5.15 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.01 (d, *J* = 15.8 Hz, 1H, NCH_2C=C), 3.95 – 3.82 (m, 2H, ArCH_2), 3.58 (dt, *J* = 15.8, 1.4 Hz, 1H, NCH_2C=C).

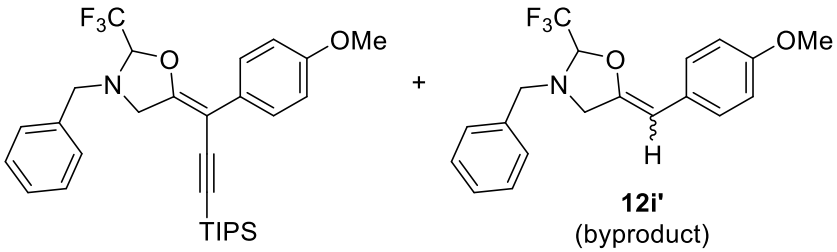
^{13}C NMR (101 MHz, Chloroform-*d*) δ 152.3, 138.8, 136.6, 128.8, 128.7, 128.7, 128.1, 127.6, 127.3, 125.2 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 271.6 Hz), 122.4 (q, *J* = 283.5 Hz), 97.6, 95.14 (q, *J* = 34.6 Hz), 60.3, 55.5.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.8, -80.8 (d, *J* = 5.5 Hz).

IR (cm^{-1}) 2945 (w), 2871 (w), 2359 (w), 1688 (m), 1616 (m), 1325 (s), 1144 (s), 1068 (s), 1017 (m), 969 (m), 1123 (s), 1166 (s).

HRMS (APPI/LTQ-Orbitrap) m/z: $[M]^+$ Calcd for $C_{19}H_{15}F_6NO^+$ 387.1052; Found 387.1045.

(E)-3-Benzyl-5-(1-(4-methoxyphenyl)-3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)-2-(trifluoromethyl)oxazolidine (12i)



Following **general procedure D** using **8i** (101 mg, 0.400 mmol). The crude product was purified through column chromatography (SiO_2; 0-10% DCM in pentane) affording the named compound **12i** as an orange oil (120 mg, 0.227 mmol, 57% yield) along with 3-benzyl-5-(4-methoxybenzylidene)-2-(trifluoromethyl)oxazolidine by-product (**12i'**) (13 mg, 0.037 mmol, 9% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.76 (m, 2H, Ph*H*), 7.42 – 7.27 (m, 5H, Ar*H*), 6.91 (m, 2H, Ph*H*), 5.26 (q, *J* = 5.3 Hz, 1H), 4.21 (dd, *J* = 17.0, 1.1 Hz, 1H, NC*H*$_2$C=C), 4.02 (dd, *J* = 17.0, 1.4 Hz, 1H, NC*H*$_2$C=C), 4.04 – 3.89 (m, 2H, ArC*H*$_2$), 3.83 (s, 3H, OC*H*$_3$), 1.10 – 1.06 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.2, 156.8, 136.5, 128.9, 128.7, 128.6, 128.0, 126.9, 122.3 (q, *J* = 283.6 Hz), 113.5, 104.7, 96.2 (q, *J* = 34.8 Hz), 95.4, 93.4, 60.6, 57.0, 55.2, 18.7, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (d, *J* = 5.3 Hz).

IR (cm^{-1}) 2944 (m), 2864 (m), 2139 (m), 1641 (m), 1609 (m), 1511 (s), 1459 (m), 1292 (m), 1249 (s), 1177 (s), 1157 (s), 1129 (s), 1109 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{30}H_{39}F_3NO_2Si^+$ 530.2697; Found 530.2704.

Byproduct - **3-Benzyl-5-(4-methoxybenzylidene)-2-(trifluoromethyl)oxazolidine (12i')**

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.50 (m, 2H, Ph*H*), 7.41 – 7.29 (m, 5H, Ar*H*), 6.88 (m, 2H, Ph*H*), 5.30 (m, 1H, C=C*H*), 5.14 (q, *J* = 5.4 Hz, 1H, C*H*CF$_3$), 4.03 (d, *J* = 15.4 Hz, 1H, NC*H*$_2$C=C), 4.00 – 3.88 (m, 2H, ArC*H*$_2$), 3.81 (s, 3H, OC*H*$_3$), 3.58 (dt, *J* = 15.3, 1.6 Hz, 1H, NC*H*$_2$C=C).

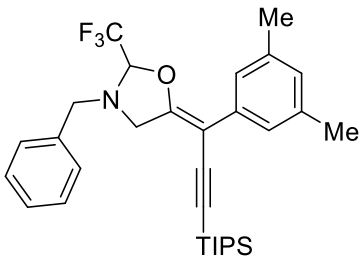
^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.7, 148.4, 137.0, 128.8, 128.7, 128.6, 128.1, 127.9, 122.57 (q, *J* = 283.7 Hz), 113.8, 98.1, 94.57 (q, *J* = 34.4 Hz), 60.3, 55.2, 55.1.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (d, *J* = 5.9 Hz).

IR (ν_{max}, cm^{-1}) 2922 (m), 2850 (m), 1694 (m), 1610 (m), 1509 (s), 1455 (w), 1299 (m), 1249 (s), 1177 (s), 1139 (s), 1034 (m), 1018 (m), 971 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{19}F_3NO_2^+$ 350.1362; Found 350.1363.

(E)-3-benzyl-5-(1-(3,5-dimethylphenyl)-3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)-2-(trifluoromethyl)oxazolidine (12j)



Following **general procedure D** using **8j** (100 mg, 0.400 mmol). The crude product was purified through column chromatography (SiO_2; 0-2% DCM in pentane) affording the named compound **12j** as a light yellow oil (67.0 mg, 0.127 mmol, 31% yield

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 (d, *J* = 1.4 Hz, 2H, Me_2ArH), 7.44 – 7.27 (m, 5H, Ar*H*), 6.88 (s, 1H, Me_2ArH), 5.28 (q, *J* = 5.4 Hz, 1H, $CHCF_3$), 4.21 (d, *J* = 17.0 Hz, 1H, $NCH_2C{\equiv}C$), 4.03 (m, 1H, $NCH_2C{\equiv}C$), 4.03 – 3.89 (m, 2H, $ArCH_2$), 2.32 (s, 6H, $ArCH_3$), 1.08 (s, 21H, *TIPS*).

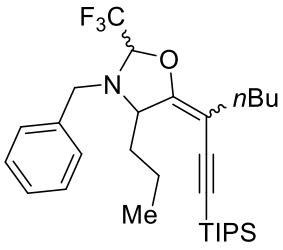
^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.9, 137.4, 136.5, 134.1, 128.9, 128.7, 128.3, 128.0, 125.3, 122.26 (q, *J* = 283.5 Hz), 104.8, 96.26 (q, *J* = 34.7 Hz), 95.8, 93.4, 60.7, 57.2, 21.5, 18.7, 11.3.

IR (cm^{-1}) 2944 (m), 2867 (m), 2143 (m), 1637 (m), 1599 (m), 1465 (m), 1298 (m), 1182 (s), 1154 (s), 1131 (s), 880 (m), 692 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{31}H_{41}F_3NOSi^+$ 528.2904; Found 528.2906.

Cambridge Crystallographic Data Centre entry – 1874007

(E)- and (Z)-3-benzyl-4-pentyl-2-(trifluoromethyl)-5-(1-(tri*iso*propylsilyl)hept-1-yn-3-ylidene)oxazolidine (14a)



Following **general procedure E** using **37** (97 mg, 0.400 mmol). The crude product was purified through column chromatography (SiO_2; 0-2% DCM in pentane) affording the named compound **14a** as a light yellow oil (118 mg, 0.226 mmol, 57% yield; 2.5:1 mixture of undetermined isomers).

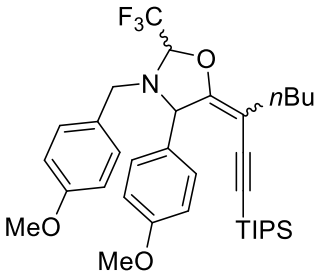
^{1}H NMR (400 MHz, Chloroform-*d*; characterised as a 2.5:1 mixture of major and minor isomers) δ 7.41 – 7.24 (m, 5H, Ar*H;* 5H, Ar*H*), 5.07 (q, *J* = 3.9 Hz, 1H, $CHCF_3$), 4.99 (q, *J* = 5.3 Hz, 1H, $CHCF_3$), 4.08 (d, *J* = 14.3 Hz, 1H, $ArCH_2$), 4.01 – 3.90 (m, 1H, $ArCH_2$, 1H, $NCH_2C{\equiv}C$; 2H, $ArCH_2$), 3.80 (dd, *J* = 10.1, 3.1 Hz, 1H, $NCH_2C{\equiv}C$), 2.02 – 1.85 (m, 2H, $C{\equiv}CCH_2CH_2$; 2H, $C{\equiv}CCH_2CH_2$), 1.66 – 1.39 (m, 2H, $NCHCH_2$; *2H,* $NCHCH$; CH_2 (unspecified)), 1.38 – 1.21 (m, CH_2 (unspecified)), 1.12 – 1.04 (m, 21H, *TIPS;* 21H, *TIPS*), 0.96 – 0.90 (m, 3H, CH_3),0.88 (t, *J* = 7.4 Hz, 3H, CH_3), 0.87 (t, *J* = 7.3 Hz, 3H, CH_3), 0.81 (t, *J* = 7.1 Hz, 3H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*; characterised as a 2.5:1 mixture of major and minor isomers) δ 160.6, 159.2, 137.5, 137.1, 129.3, 128.6 (both isomers), 128.5, 128.0, 127.9, 127.5, 122.9 (q, *J* = 285.6 Hz), 122.2 (q, *J* = 283.2 Hz), 103.9, 103.3, 95.4, 94.1 (q, *J* = 35.1 Hz), 93.9, 93.8, 93.3, 90.1 (q, *J* = 33.5 Hz), 65.1, 61.8, 58.5, 49.6, 36.7, 31.5, 30.6, 30.5, 30.3, 30.0, 22.2, 22.0, 19.2, 18.7, 18.6, 18.0, 14.1, 14.0 (both isomers), 13.8, 11.4, 11.4.

^{19}F NMR (376 MHz, Chloroform-*d*; characterised as a 2.5:1 mixture of major and minor isomers) δ -80.7 (d, *J* = 4.0 Hz), -81.1 (d, *J* = 5.3 Hz).

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{30}H_{46}F_3NNaOSi^+$ 544.3193; Found 544.3195.

(E)- and (Z)-3-(4-methoxybenzyl)-4-(4-methoxyphenyl)-2-(trifluoromethyl)-5-(1-(tri*iso*propylsilyl)hept-1-yn-3-ylidene)oxazolidine (14b)



Following **general procedure E** using **40** (97 mg, 0.400 mmol). The crude product was purified through column chromatography (SiO_2; 0-5% DCM in pentane) affording the named compound **14b** as a light yellow oil (122 mg, 0.199 mmol, 50% yield; 3.5:1 mixture of undetermined isomers).

Major isomer

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.07 – 6.98 (m, 4H, Ar*H*),6.89 – 6.76 (m, 4H, Ar*H*), 5.14 (q, *J* = 4.1 Hz, 1H, C*H*CF_3), 4.81 (s, 1H, NC*H*), 3.82 (s, 3H, CH_3), 3.85 – 3.76 (m, 1H, ArCH_2), 3.80 (s, 3H, CH_3), 3.45 (d, *J* = 13.9 Hz, 1H, ArCH_2), 1.77 – 1.55 (m, 2H, CH_2, *Bu*), 1.40 – 1.20 (m, 1H, *Bu*), 1.10 – 1.06 (m, 21H, *TIPS*), 1.14 – 0.94 (m, 1H, *Bu*), 0.68 (t, *J* = 7.1 Hz, 3H, *Bu*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 160.2, 159.5, 158.8, 130.2, 129.2, 129.1, 129.1, 123.2 (q, *J* = 287.7 Hz), 113.9, 113.6, 103.6, 95.4, 94.1, 89.47 (q, *J* = 33.4 Hz), 63.9, 55.3, 55.2, 49.0, 29.9, 29.3, 21.8, 18.6, 13.8, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.3 (d, *J* = 4.1 Hz).

Minor isomer

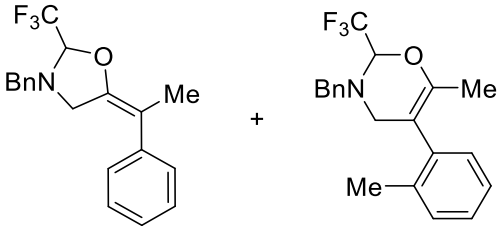
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.15 – 7.04 (m, 4H, Ar*H*), 6.85 – 6.74 (m, 4H, Ar*H*), 5.10 (q, *J* = 3.9 Hz, 1H, C*H*CF_3), 4.70 (s, 1H, NC*H*), 3.91 (d, *J* = 2.8 Hz, 2H, ArCH_2), 3.79 (s, 3H, *Me*O), 3.79 (s, 3H, *Me*O), 1.56 – 1.47 (m, 2H, *Bu*), 1.35 – 1.20 (m, 1H, *Bu*), 1.10 – 1.06 (m, 21H, *TIPS*), 1.13 – 0.92 (m, 3H, *Bu*), 0.67 (t, *J* = 7.1 Hz, 3H, *Bu*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 159.2 (2C), 159.2, 131.7, 130.7, 129.9, 127.3, 122.7 (q, *J* = 282.8 Hz), 113.8, 113.7, 103.8, 95.6, 94.4, 90.8 (q, *J* = 34.7 Hz), 66.5, 55.3, 55.3, 55.0, 30.0, 29.0, 22.0, 18.6, 13.8, 11.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.4 (d, *J* = 4.0 Hz).

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calcd for $C_{35}H_{48}F_3NNaO_3Si^+$ 638.3248; Found 638.3248.

(*E*)-3-benzyl-5-(1-phenylethylidene)-2-(trifluoromethyl)oxazolidine (15a)



15c'
(by-product)

Following **general procedure F**, using **8a** (63.7 mg, 0.400 mmol) and iodobenzene (106 mg, 0.52 mmol). The crude product was purified through column chromatography (SiO_2; 3% DCM in pentane) affording the named compound **15a** as a colourless oil (104 mg, 0.312 mmol, 78% yield; single isomer) and by-product **15a'** was also obtained as a colourless oil (17.4 mg, 52.0 µmol, 13% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.27 (m, 7H, Ar*H*), 7.21 – 7.14 (m, 3H, Ar*H*), 4.97 (q, *J* = 5.3 Hz, 1H, C*H*CF$_3$), 3.98 (d, *J* = 15.0 Hz, 1H, NC*H*$_2$C=C), 3.93 (d, *J* = 13.3 Hz, 1H, ArC*H*$_2$), 3.82 (d, *J* = 13.3 Hz, 1H, ArC*H*$_2$), 3.46 (d, *J* = 15.0 Hz, 1H, NC*H*$_2$C=C), 2.09 (s, 3H, C*H*$_3$).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 147.1, 141.1, 137.1, 128.5, 128.3, 127.7, 127.4, 126.2, 122.8 (d, *J* = 283.9 Hz), 107.6, 92.4 (q, *J* = 34.1 Hz), 60.1, 53.1, 16.4.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.6 (d, *J* = 5.3 Hz).

IR (cm^{-1}) 2925 (br), 1690 (w), 1496 (w), 1450 (w), 1292 (m), 1172 (s), 1147 (s), 1096 (m), 1025 (m), 970 (m), 856 (m), 761 (s), 733 (m), 698 (s).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calcd for $C_{19}H_{19}F_3NO^+$ 334.1413; Found 334.1414.

3-benzyl-6-methyl-5-phenyl-2-(trifluoromethyl)-3,4-dihydro-2*H*-1,3-oxazine (15a')

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 (d, *J* = 7.1 Hz, 2H, Ar*H*), 7.37 (t, *J* = 7.3 Hz, 2H, Ar*H*), 7.31 (t, *J* = 7.3 Hz, 3H, Ar*H*), 7.22 (m, 1H, Ar*H*), 7.11 (m, 2H, Ar*H*), 4.92 (q, *J* = 6.4 Hz, 1H, C*H*CF$_3$), 4.09 (d, J = 13.6 Hz, 1H, ArC*H*$_2$), 4.03 (d, J = 13.6 Hz, 1H, ArC*H*$_2$), 3.73 (d, *J* = 17.4 Hz, 1H, , NC*H*$_2$C=C), 3.22 (d, J = 17.4 Hz, 1H, , NC*H*$_2$C=C), 1.85 (s, 3H, C*H*$_3$).

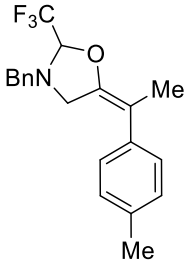
^{13}C NMR (101 MHz, Chloroform-*d*) δ 145.5, 138.9, 137.7, 129.0, 128.8, 128.7, 128.4, 127.8, 126.7, 123.0 (q, *J* = 285.7 Hz), 107.9, 85.0 (q, *J* = 33.6 Hz), 58.3, 48.1, 17.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -75.8 (d, *J* = 6.4 Hz).

IR (cm^{-1}) 3029 (w), 1676 (w), 1283 (m), 1264 (m), 1176 (m), 1138 (m), 1030 (m), 758 (s), 739 (s), 701 (s).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calcd for $C_{19}H_{19}F_3NO^+$ 334.1413; Found 334.1416.

(*E*)-3-benzyl-5-(1-(*p*-tolyl)ethylidene)-2-(trifluoromethyl)oxazolidine (15b)



Following **general procedure F**, using **8a** (63.7 mg, 0.400 mmol) and 4-iodotoluene (113 mg, 0.52 mmol). The crude product was purified through column chromatography (SiO_2; 3% DCM in pentane) affording the named compound **15b** as a colourless paste (106 mg, 0.304 mmol, 76% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ δ 7.33 (d, *J* = 4.4 Hz, 4H, Ar*H*), 7.29 (m, 1H, Ar*H*), 7.11 (m, 2H, Ar*H*), 7.06 (m, 2H, Ar*H*), 4.97 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 3.98 (d, *J* = 15.3 Hz, 1H, NCH_2C=C), 3.93 (d, *J* = 13.4 Hz, 1H, ArCH_2), 3.82 (d, *J* = 13.3 Hz, 1H, ArCH_2), 3.46 (d, *J* = 15.0 Hz, 1H, NCH_2C=C), 2.33 (s, 3H, ArCH_3), 2.08 (s, 3H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 146.9, 138.3, 137.3, 136.0, 129.1 (2C), 128.7 (3C), 127.9, 127.4 (2C), 123.0 (q, *J* = 283.9 Hz), 107.6, 92.6 (q, *J* = 34.0 Hz), 60.3, 53.2, 21.2, 16.6.

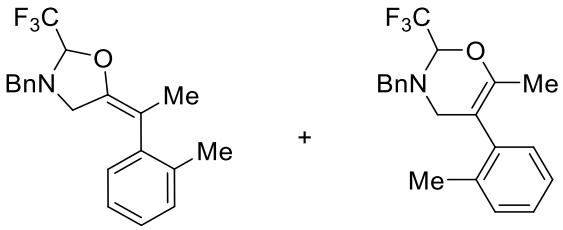
^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.6 (d, *J* = 5.3 Hz).

IR (cm^{-1}) 2944 (br), 1689 (w), 1516 (m), 1452 (w), 1294 (m), 1172 (s), 1145 (s), 1080 (s), 975 (m), 860 (m), 819 (s), 729 (m), 702 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{20}H_{21}F_3NO^+$ 348.1570; Found 348.1569.

Cambridge Crystallographic Data Centre entry – 1874005

(*E*)-3-benzyl-5-(1-(*o*-tolyl)ethylidene)-2-(trifluoromethyl)oxazolidine (15c)



Following **general procedure F** at 70 °C, using **8a** (63.7 mg, 0.400 mmol) and 2-iodotoluene (113 mg, 0.52 mmol). The crude product was purified through column chromatography (SiO_2; 3% DCM in pentane) affording a mixture of **15c** and **15c'** in 72:28 ratio (15c' was not isolated/characterised; the structure was assigned based on ^{1}H NMR signals in analogy to **15a'**) and the title compound **15c** (62.5 mg, 0.180 mmol, 45% yield). A sample of the mixture was further purified for characterisation by PrepTLC to furnish the pure title compound (**15c**) as a colourless oil.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.32 (d, *J* = 4.4 Hz, 4H, Ar*H*), 7.28 (m, 1H, Ar*H*), 7.19 – 7.09 (m, 3H, Ar*H*), 7.07 – 7.03 (m, 1H, Ar*H*), 5.02 (m, 1H, C*H*CF_3), 3.96 (d, *J* = 13.2 Hz, 1H, ArCH_2), 3.83 (d, *J* =

13.3 Hz, 1H, ArCH_2), 3.56 (d, *J* = 14.6 Hz, 1H, NCH_2C=C), 3.08 (d, *J* = 15.1 Hz, 1H, NCH_2C=C), 2.25 (s, 3H, ArCH_3), 1.97 (t, *J* = 1.7 Hz, 3H, CH_3).

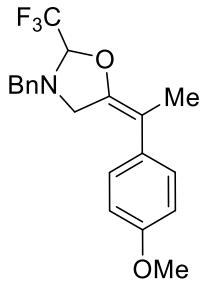
^{13}C NMR (101 MHz, Chloroform-*d*) δ 146.5, 140.6, 137.4, 136.2, 130.3, 129.3, 128.7 (2C), 128.7 (2C), 127.9, 127.2, 126.1, 123.0 (q, *J* = 284.0 Hz), 106.7, 93.3 (q, *J* = 33.9 Hz), 60.6, 52.9, 19.2, 17.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8.

IR (cm^{-1}) 2931 (br), 1712 (m), 1455 (m), 1294 (m), 1173 (s), 1149 (s), 1130 (s), 1080 (s), 1034 (m), 974 (m), 859 (m), 763 (m), 728 (s), 701 (s).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calcd for $C_{20}H_{21}F_3NO^+$ 348.1570; Found 348.1566.

(*E*)-3-benzyl-5-(1-(4-methoxyphenyl)ethylidene)-2-(trifluoromethyl)oxazolidine (15d)



Following **general procedure F**, using **8a** (63.7 mg, 0.400 mmol) and 4- iodoanisole (122 mg, 0.52 mmol). The crude product was purified through column chromatography (SiO_2; 10% DCM in pentane) affording the named compound **15d** as a colourless oil (88.5 mg, 0.244 mmol, 61% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.30 (m, 4H, *Ar*), 7.28 (m, 1H, Ar*H*), 7.07 (m, 2H, Ar*H*), 6.84 (m, 2H, Ar*H*), 4.96 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 3.97 – 3.91 (m, 2H, NCH_2C=C + ArCH_2), 3.82 (m, 1H, ArCH_2), 3.79 (s, 3H, OCH_3), 3.42 (ddt, *J* = 14.8, 2.5, 1.3 Hz, 1H, NCH_2C=C), 2.05 (t, *J* = 1.7 Hz, 3H, CH_3).

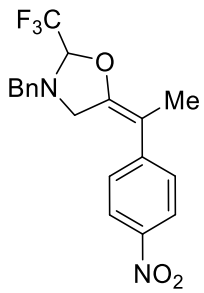
^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.1, 146.5, 137.3, 133.6, 128.7 (3C), 128.6 (2C), 127.9, 123.0 (q, *J* = 283.9 Hz), 113.8 (2C), 107.2, 92.6 (q, *J* = 34.0 Hz), 60.3, 55.4, 53.2, 16.7.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.6 (d, *J* = 5.3 Hz).

IR (cm^{-1}) 2921 (w), 2853 (w), 1673 (m), 1515 (m), 1288 (m), 1251 (s), 1168 (s), 1146 (s), 1135 (s), 1120 (s), 1090 (s), 1077 (s), 1061 (m), 1028 (s), 1014 (s), 972 (s), 858 (m), 830 (s), 758 (s), 728 (m), 702 (s).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calcd for $C_{20}H_{21}F_3NO_2^+$ 364.1519; Found 364.1521.

(*E*)-3-benzyl-5-(1-(4-nitrophenyl)ethylidene)-2-(trifluoromethyl)oxazolidine (15e)



Following **general procedure F**, using **8a** (63.7 mg, 0.400 mmol) and 1-iodo-4-nitrobenzene (130 mg, 0.52 mmol). The crude product was purified through column chromatography (SiO_2; 14% DCM in pentane) affording the named compound **15e** as a yellow oil (92.5 mg, 0.244 mmol, 61% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.14 (d, *J* = 9.0 Hz, 2H, Ar*H*), 7.35 – 7.27 (m, 7H, Ar*H*), 5.05 (q, *J* = 5.2 Hz, 1H, C*H*CF_3), 4.03 (d, *J* = 15.2 Hz, 1H, NCH_2C=C), 3.94 (d, *J* = 13.3 Hz, 1H, ArCH_2), 3.82 (d, *J* = 13.3 Hz, 1H, ArCH_2), 3.50 (dt, *J* = 15.2, 1.2 Hz, 1H, NCH_2C=C), 2.12 (dd, *J* = 1.8, 1.4 Hz, 3H, CH_3).

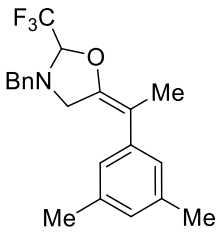
^{13}C NMR (101 MHz, Chloroform-*d*) δ 150.1, 148.2, 145.9, 136.7, 128.8 (2C), 128.7 (2C), 128.2, 127.8 (2C), 123.8 (2C), 122.7 (q, *J* = 283.6 Hz), 106.6, 93.0 (q, *J* = 34.4 Hz), 60.3, 53.5, 16.1.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.5 (d, *J* = 5.2 Hz).

IR (cm^{-1}) 2925 (w), 2856 (w), 1675 (m), 1594 (m), 1512 (s), 1342 (s), 1289 (m), 1172 (s), 1149 (s), 1076 (s), 973 (m), 846 (s), 755 (m), 734 (m), 697 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{19}H_{18}F_3N_2O_3^+$ 379.1264; Found 379.1258.

(*E*)-3-benzyl-5-(1-(3,5-dimethylphenyl)ethylidene)-2-(trifluoromethyl)oxazolidine (15f)



Following **general procedure F**, using **8a** (63.7 mg, 0.400 mmol) and 1-iodo-3,5-dimethylbenzene (121 mg, 0.52 mmol). The crude product was purified through column chromatography (SiO_2; 3% DCM in pentane) affording the named compound **15f** as a colourless oil (103 mg, 0.286 mmol, 71% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.26 (m, 5H, Ar*H*), 6.84 (s, 1H, Ar*H*), 6.78 (s, 2H, Ar*H*), 4.96 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 3.98 (d, *J* = 15.1 Hz, 1H, NCH_2C=C), 3.91 (d, *J* = 13.3 Hz, 1H, ArCH_2), 3.83 (d, *J* = 13.3 Hz, 1H, ArCH_2), 3.46 (d, *J* = 15.0 Hz, 1H, NCH_2C=C), 2.29 (s, 6H, ArCH_3), 2.06 (s, 3H, CH_3).

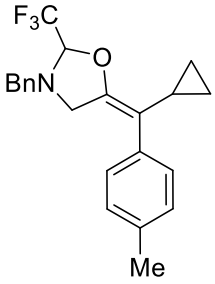
^{13}C NMR (101 MHz, Chloroform-*d*) δ 146.9, 141.3, 137.9 (2C), 137.4, 128.7 (2C), 128.7 (2C), 128.1, 127.9, 125.4 (2C), 123.0 (q, *J* = 283.8 Hz), 107.8, 92.6 (q, *J* = 34.0 Hz), 60.4, 53.3, 21.5 (2C), 16.7.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.5 (d, *J* = 5.3 Hz).

IR (cm^{-1}) 2925 (br), 1688 (w), 1601 (m), 1448 (w), 1289 (m), 1165 (s), 1147 (s), 1094 (s), 975 (m), 849 (m), 735 (m), 698 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{21}H_{23}F_3NO^+$ 362.1726; Found 362.1725.

(*E*)-3-benzyl-5-(cyclopropyl(*p*-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (15g)



Following **general procedure F**, using **8f** (74.1 mg, 0.400 mmol) and 4-iodotoluene (113 mg, 0.52 mmol). The crude product was purified through column chromatography (SiO_2; 10% DCM in pentane) affording the named compound **15g** as a colourless oil (95.6 mg, 0.256 mmol, 64% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.31 (d, *J* = 4.4 Hz, 4H, Ar*H*), 7.25 (m, 1H, Ar*H*), 7.07 (d, *J* = 7.8 Hz, 2H, Ar*H*), 6.95 (d, *J* = 8.0 Hz, 2H, Ar*H*), 5.02 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 3.95 (d, *J* = 13.3 Hz, 1H, ArCH_2), 3.81 (d, *J* = 13.3 Hz, 1H, ArCH_2), 3.71 (d, *J* = 15.2 Hz, 1H, NCH_2C=C), 3.21 (d, *J* = 15.2 Hz, 1H, NCH_2C=C), 2.31 (s, 3H, ArCH_3), 1.96 (tt, *J* = 8.4, 5.3 Hz, 1H, C*H*$(CH_2)_2$), 0.70 – 0.60 (m, 2H, CH(CH_2)$_2$), 0.33 – 0.23 (m, 2H, CH(CH_2)$_2$).

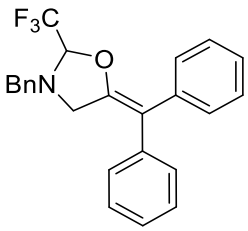
^{13}C NMR (101 MHz, Chloroform-*d*) δ 147.6, 137.4, 136.5, 134.5, 129.7, 129.0, 128.7, 128.7, 127.8, 123.0 (q, *J* = 284.0 Hz), 112.7, 93.2 (q, *J* = 34.0 Hz), 60.4, 53.5, 21.3, 11.6, 4.8, 4.4.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.6 (d, *J* = 5.0 Hz).

IR (cm^{-1}) 3019 (br), 1691 (w), 1290 (m), 1166 (s), 1148 (s), 1021 (m), 975 (m), 861 (m), 817 (s), 729 (m), 701 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{23}F_3NO^+$ 374.1726; Found 374.1721.

3-benzyl-5-(diphenylmethylene)-2-(trifluoromethyl)oxazolidine (15h)



Following **general procedure F**, using **8g** (86.0 mg, 0.400 mmol) and iodobenzene (104 mg, 0.52 mmol). The crude product was purified through column chromatography (SiO_2; 10% DCM in pentane) affording the named compound **15h** as a colourless solid (120 mg, 0.304 mmol, 78% yield), mp: 73-75 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.24 (m, 12H, Ar*H*), 7.22 – 7.14 (m, 3H, Ar*H*), 5.14 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 3.99 (d, *J* = 13.3 Hz, 1H, ArCH_2), 3.94 (d, *J* = 15.9 Hz, 1H, NCH_2C=C), 3.89 (d, *J* = 13.3 Hz, 1H, ArCH_2), 3.54 (d, *J* = 15.8 Hz, 1H, NCH_2C=C).

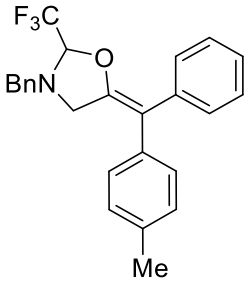
^{13}C NMR (101 MHz, Chloroform-*d*) δ 148.6, 140.2, 138.6, 137.0, 130.2, 129.1, 128.8, 128.7, 128.1, 128.1, 127.1, 126.4, 122.8 (q, *J* = 283.9 Hz), 113.1, 94.0 (q, *J* = 34.3 Hz), 60.5, 54.9.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.3 (d, *J* = 5.2 Hz).

IR (cm^{-1}) 3038 (w), 2837 (w), 1655 (w), 1300 (m), 1165 (m), 1145 (s), 1120 (m), 1057 (m), 1012 (m), 972 (s), 867 (m), 768 (s), 736 (m), 696 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{21}F_3NO^+$ 396.1570; Found 396.1561.

(*E*)-3-benzyl-5-(phenyl(*p*-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (15i)



Following **general procedure F**, using **8g** (86.0 mg, 0.400 mmol) and 4-iodotoluene (113 mg, 0.52 mmol). The crude product was purified through column chromatography (SiO_2; 10% DCM in pentane) affording the named compound **15i** as a colourless solid (120.8 mg, 0.300 mmol, 75% yield), mp: 122-124 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.26 (m, 9H, Ar*H*), 7.17 (m, 1H, Ar*H*), 7.13 (m, 2H, Ar*H*), 7.04 (d, *J* = 8.1 Hz, 2H, Ar*H*), 5.12 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 3.99 (d, *J* = 13.3 Hz, 1H, ArCH_2), 3.95 – 3.87 (m, 2H, ArCH_2 + NCH_2C=C), 3.53 (d, *J* = 15.8 Hz, 1H, NCH_2C=C), 2.35 (s, 3H, ArCH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 148.4, 138.8, 137.2, 137.1, 136.7, 130.0 (2C), 129.4 (2C), 129.1 (2C), 128.8 (4C), 128.0 (3C), 126.3, 122.9 (q, *J* = 284.4 Hz), 112.9, 94.0 (q, *J* = 34.5 Hz), 60.5, 54.9, 21.3.

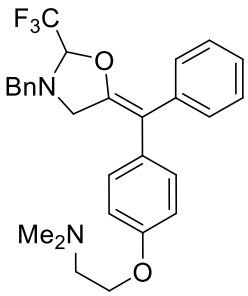
^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.3 (d, *J* = 5.3 Hz).

IR (cm^{-1}) 2975 (m), 2925 (m), 1674 (m), 1444 (m), 1293 (m), 1172 (s), 1147 (s), 1081 (s), 857 (m), 819 (s), 756 (m), 733 (m), 710 (m), 695 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{25}H_{23}F_3NO^+$ 410.1726; Found 410.1715.

Cambridge Crystallographic Data Centre entry – 1874008

(*E*)-2-(4-((3-benzyl-2-(trifluoromethyl)oxazolidin-5-ylidene)(phenyl)methyl)phenoxy)-*N*,*N*-dimethylethan-1-amine (15j)



Following **general procedure F**, using **8g** (86.0 mg, 0.400 mmol) and 2-(4-iodophenoxy)-N,N-dimethylethanamine (151 mg, 0.52 mmol). The crude product was purified through column chromatography (SiO_2; 1% MeOH in DCM) affording the named compound **15j** as a colourless oil (158 mg, 0.328 mmol, 82% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.24 (m, 9H, Ar*H*), 7.17 (m, 1H, Ar*H*), 7.05 (m, 2H, OAr*H*), 6.87 (m, 2H OAr*H*), 5.12 (q, *J* = 5.2 Hz, 1H, C*H*CF_3), 4.08 (t, *J* = 5.7 Hz, 2H, OC$H_2$$CH_2$N), 3.99 (d, *J* = 13.3 Hz, 1H, ArCH_2), 3.95 – 3.84 (m, 2H, NCH_2C=C, ArCH_2), 3.51 (d, *J* = 15.8 Hz, 1H, NCH_2C=C), 2.78 (t, *J* = 5.7 Hz, 2H, OCH_2CH_2N), 2.37 (s, 6H, NCH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 157.8, 148.4, 138.8, 137.0, 132.6, 131.3 (2C), 129.0 (2C), 128.8 (4C), 128.0 (3C), 126.3, 122.8 (q, J = 284.0 Hz), 114.7 (2C), 112.5, 94.0 (q, J = 34.2 Hz), 65.9, 60.5, 58.3, 54.9, 45.9.

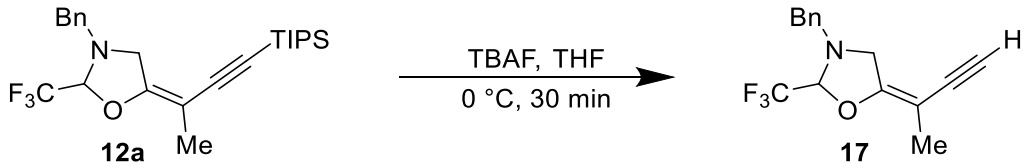
^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.3 (d, *J* = 5.2 Hz).

IR (cm^{-1}) 2932 (m), 2773 (w), 1608 (m), 1511 (m), 1291 (m), 1242 (m), 1176 (s), 1145 (s), 1031 (m), 971 (m), 832 (m), 698 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{28}H_{30}F_3N_2O_2^+$ 483.2254; Found 483.2260.

6. Transformations of the products

(E)- and (Z)-3-Benzyl-5-(but-3-yn-2-ylidene)-2-(trifluoromethyl)oxazolidine (17)



A solution of **12a** (0.52 g, 1.2 mmol, 1 equiv.; 12:1 E:Z ratio) in THF is added TBAF (1M, 1.4 mL, 1.4 mmol, 1.2 equiv.) was stirred at 0 °C for 30 minutes. After completion (consumption of starting material monitored by TLC (SiO_2, 5% DCM in pentane)) the reaction was quenched by the addition of sat. aq. $NaHCO_3$ (10 mL), the aqueous layer was extracted with DCM (3 x 10 mL) and the combined organic layers were dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude material was dry-loaded onto NEt_3-deactivated SiO_2 and then purified by column chromatography (NEt_3-deactivated SiO_2, 0-10% DCM in pentane) to afford the named compound **17** as a pale orange oil (0.30 g, 1.06 mmol, 89% yield; separable E:Z isomers in 12:1 ratio).

E-isomer (major)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 (dd, *J* = 19.7, 4.4 Hz, 5H, Ar*H*), 5.06 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.05 – 3.86 (m, 3H, ArC*H*$_2$, NC*H*$_2$C=C), 3.71 (dq, *J* = 16.3, 1.5 Hz, 1H, NC*H*$_2$C=C), 2.94 (s, 1H, C≡C*H*), 1.83 (t, *J* = 1.8 Hz, 3H, *CH*$_3$).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.0, 136.8, 128.7, 128.6, 127.9, 122.3 (q, *J* = 283.7 Hz), 94.6 (q, *J* = 34.5 Hz), 87.8, 83.4, 78.5, 60.5, 54.6, 14.9.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.2 (d, *J* = 4.6 Hz).

IR (cm^{-1}) 3308 (w), 2933 (w), 2094 (w), 1682 (m), 1657 (w), 1293 (m), 1299 (m), 1176 (s), 1145 (s), 967 (m).

HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{15}H_{15}F_3NO^+$ 282.1100; Found 282.1099.

Z-isomer (minor)

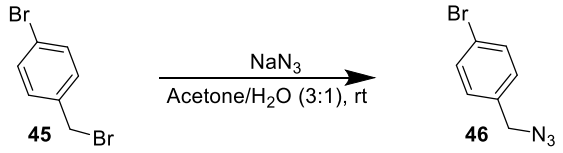
^{1}H NMR (400 MHz, Chloroform-*d*; characterised in a 4:1 mixture of E:Z isomers) δ 7.40 – 7.29 (m, 5H, Ar*H*), 4.86 (qd, *J* = 6.2, 1.5 Hz, 1H, C*H*CF_3), 4.00 – 3.87 (m, 2H, ArC*H*$_2$), 3.63 (d, *J* = 17.1 Hz, 1H, NC*H*$_2$C=C), 3.09 (m, 2H, NC*H*$_2$C=C, C≡C*H*), 2.09 (t, *J* = 1.7 Hz, 3H, *CH*$_3$).

^{13}C NMR (101 MHz, Chloroform-*d*; characterised in a 4:1 mixture of E:Z isomers) δ 157.2, 136.9, 128.7, 128.6, 127.8, 122.3 (d, *J* = 285.7 Hz), 89.5, 85.2 (q, *J* = 34.1 Hz), 80.8, 80.5, 58.2, 45.8, 18.4.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -76.4 (d, *J* = 6.6 Hz).

IR (cm^{-1}) 3302 (w), 2926 (w), 2094 (w), 1682 (m), 1299 (m), 1176 (s), 1145 (s), 1084 (m), 967 (m), 868 (w).

4-bromobenzyl azide (43)



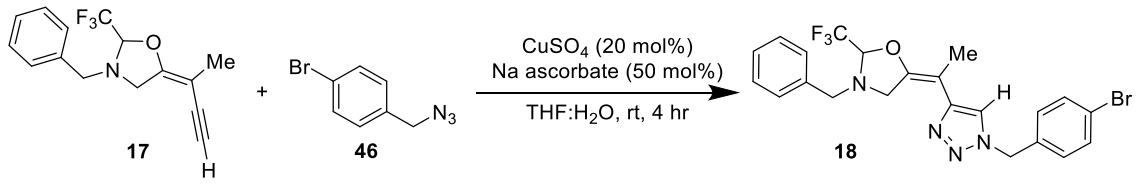
4-bromobenzyl bromide (**45**) (0.75 g, 3 mmol, 1 equiv.) and sodium azide (0.78 g, 12 mmol, 4 equiv.) were dissolved into a 3:1 acetone/water solution (5 mL) and stirred at room temperature for 6 hours. The reaction mixture was then diluted by the addition of H_2O (10 mL) and extracted with DCM (4 x 10 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated by rotary evaporation to provide 4-bromobenzyl azide (**46**) as a colourless oil (595 mg, 2.81 mmol, 94% yield). The azide was used without any further purification.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 (m, 2H, Ar*H*), 7.19 (m, 2H, Ar*H*), 4.30 (s, 2H, ArCH_2).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 134.3, 131.9, 129.8, 122.3, 54.0.

Spectra data was consistent with the values reported in literature.[18]

(E)-3-Benzyl-5-(1-(1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)ethylidene)-2-(trifluoromethyl)oxazolidine (18)



Following a modified version of a reported procedure.[19] To a solution of terminal alkyne (E)-**17** (56.0 mg, 0.200 mmol, 1 equiv.) and 4-bromobenzyl azide **43** (85.4 mg, 0.400 mmol, 2 equiv.) in a 1:1 mixture of THF and H_2O (1.2 mL; degassed by bubbling N_2) was quickly added $CuSO_4$ (9.0 mg, 0.060 mmol, 30 mol%) and sodium ascorbate (19.8 mg, 0.100 mmol, 50 mol%). The consumption of the starting material was monitored by TLC (SiO_2, 10% DCM in pentane). After 4 hours, the reaction was diluted with sat. $NaHCO_3$ (6 mL) and extracted with DCM (4 x 8 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude material was dry-loaded onto NEt_3-deactivated silica and purified by column chromatography (SiO_2 deac, 0-30% DCM in pentane) to afford the named compound **18** as a colourless viscous oil (97.2 mg, 0.197 mmol, 99% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 (d, *J* = 8.1 Hz, 2H, Br*Ar*), 7.41 – 7.25 (m, 5H, Ar*H*), 7.22 (s, 1H, C=C*H*), 7.13 (d, *J* = 8.1 Hz, 2H, Br*Ar*), 5.44 (s, 2H, BrArCH_2), 5.01 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.21 (q, *J* = 16.8 Hz, 2H, NCH_2C=C), 3.94 (s, 2H, ArCH_2), 2.00 (t, *J* = 1.7 Hz, 3H, CH_3).

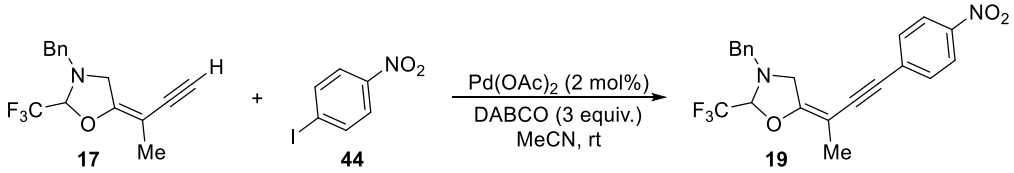
^{13}C NMR (101 MHz, Chloroform-*d*) δ 150.1, 148.8, 137.2, 133.9, 132.3, 129.6, 128.7, 128.6, 127.8, 122.9, 122.7 (q, *J* = 284.1 Hz), 118.9, 95.8, 92.6 (q, *J* = 34.1 Hz), 60.6, 55.3, 53.4, 13.9.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.1 (d, *J* = 5.4 Hz).

IR (cm^{-1}) 2859 (w), 3136 (w), 1694 (m), 1490 (m), 1454 (m), 1293 (m), 1176 (s), 1139 (s), 1013 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{22}H_{21}BrF_3N_4O^+$ 493.0845; Found 493.0852.

(Z)-3-benzyl-5-(4-(4-nitrophenyl)but-3-yn-2-ylidene)-2-(trifluoromethyl)oxazolidine (19)



Following a modified version of a reported procedure.[20] (E)-**17** (62 mg, 0.22 mmol, 1 equiv.) and 1-iodo-4-nitrobenzene (55 mg, 0.22 mmol) were dissolved into acetonitrile (1.5 mL) to which was added $Pd(OAc)_2$ (1.0 mg, 4.4 µmol, 2 mol%) and DABCO (74 mg, 0.66 mmol, 3 equiv.). The reaction mixture was stirred for 16 hours, after which it was diluted with EtOAc (5 mL) and filtered through a plug of Celite, and concentrated by rotary evaporation. The crude material was dry-loaded onto NEt_3-deactivated silica and purified by column chromatography (SiO_2, 5-20% DCM in pentane) which afforded the named compound **19** as an orange oil which later solidified after standing at 4 °C (71 mg, 0.18 mmol, 79% yield) The solid material was recrystallized from Et_2O:pent and was submitted for XDR for structure determination.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.15 (m, 2H, NO_2*Ph*), 7.46 (m, 2H, NO_2*Ph*), 7.42 – 7.27 (m, 5H, Ar*H*), 5.13 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.15 – 4.05 (m, 1H, NCH_2C≡C), 4.03 – 3.90 (m, 2H, ArCH_2), 3.80 (dp, *J* = 16.3, 1.4 Hz, 1H, NCH_2C≡C), 1.92 (t, *J* = 1.6 Hz, 3H, CH_3).

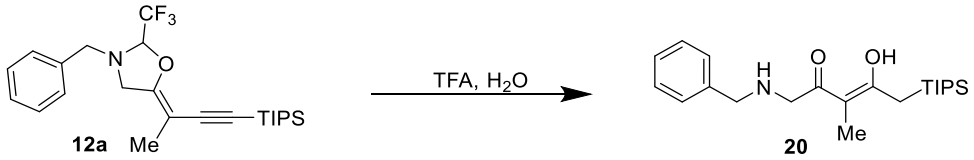
^{13}C NMR (101 MHz, Chloroform-*d*) δ 158.5, 146.4, 136.6, 131.4, 130.8, 128.7, 128.6, 128.1, 123.6, 122.27, (q, *J* = 283.9 Hz), 95.0, 94.89 (q, *J* = 34.7 Hz), 89.7, 88.6, 60.6 54.8, 15.1.

IR (cm^{-1}) 2926 (s), 2856 (s), 2193 (s), 1820 (s), 1671 (s), 1592 (s), 1516 (s), 1342 (s), 1294 (s), 1174 (s), 1139 (s), 963 (s), 853 (s), 751 (s), 702 (s).

HRMS (APPI/LTQ-Orbitrap) m/z: $[M + H]^+$ Calcd for $C_{21}H_{18}F_3N_2O_3^+$ 403.1264; Found 403.1257.

Cambridge Crystallographic Data Centre entry – 1874014

1-(benzylamino)-4-hydroxy-3-methyl-5-(tri*iso*propylsilyl)pent-3-en-2-one PM-B-03 (20)



To a solution of **12a** (0.13 mg, 0.30 mmol, 1 equiv.) in chloroform (3 mL) was added TFA (45 µL, 0.60 mmol, 2 equiv.) and H_2O (11 µL, 0.60 mmol, 2 equiv.). The resulting mixture was stirred at room temperature. The consumption of the starting material was monitored by TLC (SiO_2, 10% DCM in pentane). After 30 minutes, the reaction was quenched by the addition of sat. aq. $NaHCO_3$ (5 mL), the layers separated and the aqueous layer extracted with DCM (4 x 5 mL). The combined organic layers were washed with brine (10 mL), dried over $MgSO_4$, filtered and concentrated by rotary evaporation to afford the named compound **20** as an orange oil (0.10 mg, 0.27 mmol, 90% yield). Attempts at purification were unsuccessful.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.26 (m, 4H, Ar*H*), 7.08 (m, 1H, Ar*H*) 4.54 (s, 2H, ArCH_2), 3.62 (s, 2H, NCH_2C≡C), 2.10 (s, 2H, CH_2TIPS), 1.75 (s, 3H, CH_3), 1.11 – 1.07 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 196.2, 178.5, 136.7, 129.0, 127.8, 126.5, 107.1, 57.5, 50.1, 18.4, 12.0, 11.8, 7.7.

IR (cm^{-1}) 3333 (m), 2945 (s), 2865 (s), 1712 (m), 1632 (s), 1534 (s), 1454 (s), 1386 (s), 1139 (m).

HRMS (nanochip-ESI/LTQ-Orbitrap) m/z: [M – HO]$^+$ Calcd for $C_{22}H_{36}NOSi^+$ 358.2561; Found 358.2558.

N-benzyl-1-(3-methyl-5-(tri*iso*propylsilyl)furan-2-yl)methanamine (21a)

To a solution of **12a** (0.13 g, 0.30 mmol, 1 equiv.), $Au(PPh_3)Cl$ (29.7 mg, 60.6 µmol 20 mol%) and $AgSbF_6$ 20.6 mg, 60.6 µmol 20 mol%) in chloroform (3 mL) was added TFA (56.0 µL, 0.750 mmol, 2.5 equiv.) and H_2O (14 µL, 0.75 mmol, 2.5 equiv.), and the reaction mixture was stirred at 45 °C for 3 hours. To monitor consumption of starting material a small aliquot was removed, diluted with DCM and quenched with $NaHCO_3$. TLC (SiO_2, 30% DCM in pentane). After completion, the reaction was quenched by the addition of sat. aq. $NaHCO_3$ (5 mL) and diluted with DCM (5 mL). The reaction was transferred to a separatory funnel and the layers separated. The aqueous layer was extracted with DCM (2 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude material was dry-loaded onto silica and purified by column chromatography (SiO_2, 5-15% EtOAc in Pent) to afford the named compound **21a** as an orange oil. (94.1 mg, 0.209 mmol, 88% yield).

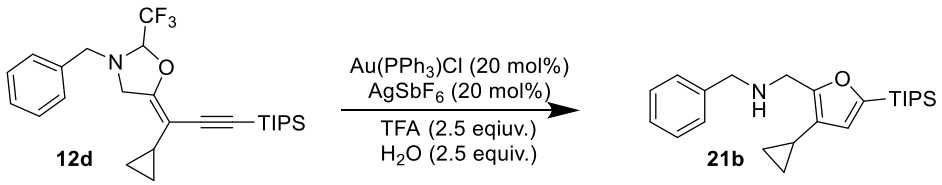
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.20 (m, 5H, Ar*H*), 6.48 (s, 1H, furan*H*), 3.77 (s, 2H, furanC*H*$_2$), 3.73 (s, 2H, ArC*H*$_2$), 1.98 (s, 3H, C*H*$_3$), 1.81 (s, 1H, N*H*), 1.35 – 1.05 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 154.8, 153.1, 140.1, 128.3, 128.3, 126.9, 125.1, 116.1, 52.5, 43.3, 18.6, 11.1, 9.7.

IR (cm^{-1}) 2944 (s), 2866 (s), 1496 (w), 1462 (m), 1139 (m), 884 (m).

HRMS (ESI/QTOF) m/z: [M – NHBn]$^+$ Calcd for $C_{15}H_{27}OSi^+$ found 251.1826; found 251.1841.

N-benzyl-1-(3-cyclopropyl-5-(tri*iso*propylsilyl)furan-2-yl)methanamine (21a)



Following the same procedure as for the synthesis of **21a**. To the starting enyne **12f** (93.0 mg, 0.200 mmol) dissolved in chloroform (1.3 mL) was added TFA (37 µL, 0.50 mmol, 2.5 equiv.) and H_2O (9.0 µL, 0.50 mmol, 2.5 equiv.). The reaction mixture was stirred for 10 min at 25 °C after which $Au(PPh_3)$ (19 mg, 40 µmol, 20 mol%) and $AgSbF_6$ (14 mg, 40 µmol, 20 mol%). The reaction mixture was stirred for another 3 hours. Consumption of starting material determined by TLC (SiO_2 30% DCM in pentane). After completion, the reaction was quenched by the addition of sat. aq. $NaHCO_3$ (5 mL) and diluted with DCM (5 mL). The reaction was transferred to a separatory funnel and the layers separated. The

aqueous layer was extracted with DCM (2 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude material was dry-loaded onto silica and purified by column chromatography (SiO_2, 5-15% EtOAc in Pent) to afford the named compound **21b** as a pale yellow oil. (67.1 mg, 0.175 mmol, 87% yield).

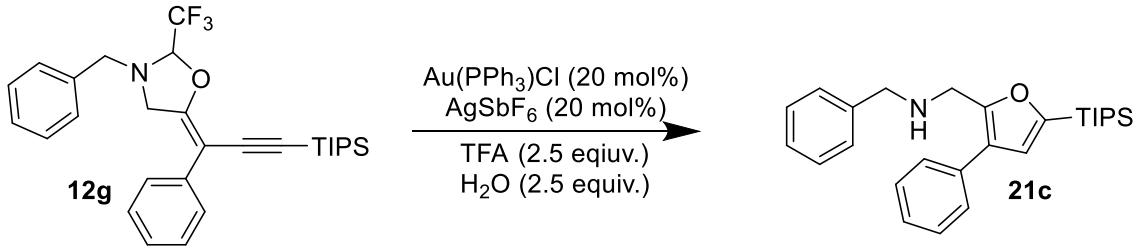
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.46 – 7.26 (m, 5H, Ar*H*), 6.30 (s, 1H, furan*H*), 3.95 (s, 2H, furanCH_2), 3.84 (s, 2H, ArCH_2), 2.23 (s, 1H, N*H*), 1.69 (tt, *J* = 8.4, 5.0 Hz, 1H, C*H*CH$_2$), 1.18 – 1.14 (m, 21H, *TIPS*), 0.92 – 0.86 (m, 2H, CHCH_2), 0.62 – 0.57 (m, 2H, CHCH_2).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.4, 153.1, 139.6, 128.5, 128.4, 127.0, 123.7, 120.4, 52.3, 43.4, 18.6, 11.0, 7.2, 5.9.

IR (cm^{-1}) 2943 (s), 2864 (s), 1496 (s), 1463 (s), 1105 (s), 1018 (s), 883 (s), 735 (s), 698 (s), 676 (s).

HRMS (ESI/QTOF) m/z: [M – NHBn]$^+$ Calcd for $C_{17}H_{29}OSi^+$ 277.1982; Found 277.1982.

N-benzyl-1-(3-phenyl-5-(tri*iso*propylsilyl)furan-2-yl)methanamine (21c)



Following the same procedure as for the synthesis of **21a**. To the starting enyne **12g** (100 mg, 0.200 mmol, 1equiv.) dissolved in chloroform (1.3 mL) was added TFA (37 µL, 0.50 mmol, 2.5 equiv.) and H_2O (9.0 µL, 0.50 mmol, 2.5 equiv.). The reaction mixture was stirred for 10 min at 25 °C after which $Au(PPh_3)$ (19 mg, 40 µmol, 20 mol%) and $AgSbF_6$ (14 mg, 40 µmol, 20 mol%). The reaction was allowed to stir for another 3 hours with reaction monitoring by TLC (SiO_2 35% DCM in pentane). After completion, the reaction was quenched by the addition of sat. aq. $NaHCO_3$ (5 mL) and diluted with DCM (5 mL). The reaction was transferred to a separatory funnel and the layers separated. The aqueous layer was extracted with DCM (2 x 5 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude material was dry-loaded onto silica and purified by column chromatography (SiO_2, 5-15% EtOAc in Pent) to afford the named compound **21c** as an orange oil. (67.6 mg, 0.61 mmol, 81%).

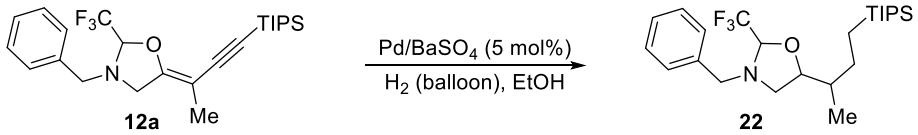
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.19 (m, 10H, Ar*H*), 6.82 (s, 1H, furan*H*), 3.96 (s, 2H, furanCH_2), 3.77 (s, 2H, ArCH_2), 1.93 (s, 1H, N*H*), 1.42 – 1.09 (m, 21H, *TIPS*).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 155.8, 153.4, 139.7, 133.8, 128.6, 128.4, 128.3, 127.8, 127.0, 126.5, 123.2, 123.1, 52.7, 44.2, 18.7, 11.0.

IR (cm^{-1}) 2946 (s), 2865 (s), 1461 (s), 882 (s), 765 (s), 734 (s), 698 (s), 680 (s).

HRMS (ESI/QTOF) m/z: [M – NHBn]$^+$ Calcd for $C_{20}H_{29}OSi^+$ 313.1982; Found 313.1989.

3-benzyl-2-(trifluoromethyl)-5-(4-(tri*iso*propylsilyl)butan-2-yl)oxazolidine (22)



Ethanol (1.5 mL) was added to **12a** (131 mg, 0.3 mmol, 1 equiv) and 5% Palladium on Barium sulfate (31.9 mg, 15 µmol, 5 mol%). The mixture was degassed by freeze pump thaw and the reaction vessel backfilled with H_2 from a balloon. The reaction mixture was stirred at 55 °C for 5 days under a balloon of H_2 (balloon). After cooling to room temperature, the mixture was filtered through a plug of Celite (washing with Et_2O (5 mL)) and concentrated by rotary evaporation. The crude material was dry loaded onto deactivated silica and purified by column chromatography (SiO_2, 4-10% DCM in pentane) to obtain the named compound **22** as colourless oil (98.6 mg, 0.229 mmol, 76% yield; as separable diastereomers 2:1 d.r.).

Major Diastereoisomer

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.23 (m, 5H, Ar*H*), 4.66 (q, *J* = 5.4 Hz, 1H, C*H*CF_3), 3.95 (d, *J* = 13.4 Hz, 1H, ArC*H*$_2$), 3.86 (m, 8.1 Hz, 2H, ArC*H*$_2$+C*H*O), 3.02 – 2.85 (m, 2H, C*H*$_2$CHO), 1.74 (tt, *J* = 13.7, 3.7 Hz, 1H, CHC*H*$_2$$CH_2$), 1.54 (m, 1H, C*H*$CH_3$), 1.27 – 1.14 (m, 1H, CHC*H*$_2$$CH_2$), 1.06 – 1.02 (m, 21H, *TIPS*), 0.80 (d, *J* = 6.7 Hz, 3H, C*H*$_3$), 0.70 (td, *J* = 14.1, 4.5 Hz, 1H, C*H*$_2$TIPS), 0.44 (ddd, *J* = 14.4, 13.3, 3.8 Hz, 1H, C*H*$_2$TIPS).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.1, 128.5, 128.5, 127.5, 123.4 (q, *J* = 283.7 Hz), 92.5 (q, *J* = 33.6 Hz), 81.1, 60.0, 55.2, 40.3, 27.7, 18.8, 14.5, 10.9, 5.5.

IR (cm^{-1}, major+minor 2:1) 2941 (m), 2865 (m), 1460 (m), 1291 (m), 1169 (s), 1131 (s), 883 (m), 738 (m), 698 (s).

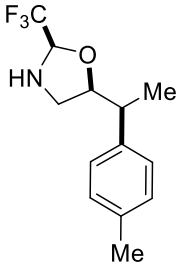
Minor Diastereoisomer

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.24 (m, 5H, Ar*H*), 4.66 (qd, *J* = 5.4, 2.2 Hz, 1H, C*H*CF_3), 3.95 (d, *J* = 13.5 Hz, 1H, ArC*H*$_2$), 3.91 – 3.84 (m, 2H, ArC*H*$_2$+C*H*O), 3.00 – 2.86 (m, 2H, C*H*$_2$CHO), 1.52 (m, 1H, C*H*CH_3), 1.44 – 1.32 (m, 1H, CHC*H*$_2$$CH_2$), 1.02 (d, *J* = 9.0 Hz, 25H, *TIPS*+C*H*$_3$+CHC*H*$_2$$CH_2$), 0.72 – 0.63 (m, 1H, C*H*$_2$TIPS), 0.48 – 0.37 (m, 1H, C*H*$_2$TIPS).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 138.0, 128.6, 128.5, 127.6, 123.4 (q, *J* = 283.8 Hz), 92.33 (q, *J* = 33.5 Hz), 81.5, 60.0, 54.9, 40.1, 27.0, 18.8, 10.9, 6.1.

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{24}H_{41}F_3NOSi^+$ 444.2904; Found 444.2912.

5-(1-(*p*-tolyl)ethyl)-2-(trifluoromethyl)oxazolidine (23a)



Palladium hydroxide on carbon (20%w, 53.4 mg, 76.0 µmol, 0.200 equiv.) was placed in a 10 mL flask under Ar. **20b** (132 mg, 0.380 mmol, 1.00 equiv.) was dissolved in MeOH (6.0 mL). After bubbling with N_2, the solution was added to the flask. The suspension was put under H_2 atmosphere and stirred overnight at rt. The solution was filtered on Celite (washing with MeOH) and concentrated under reduced pressure. A purification by preparative TLC (eluent Pentane/EtOAc 4:1) afford the named compound **23a** (89.4 mg, 0.345 mmol, 91% yield) as a colourless oil.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.14 (s, 4H, Ar*H*), 4.86 (q, *J* = 5.6 Hz, 1H, C*H*CF_3), 3.93 (ddd, *J* = 14.3, 8.8, 5.6 Hz, 1H, CH_2C*H*O), 3.32 (dd, *J* = 11.4, 5.1 Hz, 1H, NHCH_2), 2.93 – 2.84 (m, 2H, NHCH_2 + C*H*CH_3), 2.63 (br, 1H, N*H*), 2.33 (s, 3H, ArCH_3), 1.24 (d, *J* = 7.1 Hz, 3H, CH_3).

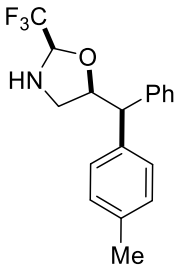
^{13}C NMR (101 MHz, Chloroform-*d*) δ 140.6, 136.4, 129.3, 127.5, 123.5 (q, *J* = 282.9 Hz), 87.9 (q, *J* = 33.8 Hz), 84.7, 49.4, 42.9, 21.2, 16.9.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.1 (d, *J* = 5.5 Hz).

IR (cm^{-1}) 3346 (br), 2972 (br), 2896 (br), 1517 (m), 1455 (m), 1289 (m), 1169 (s), 1141 (s), 1113 (s), 1088 (s), 1049 (s), 947 (m), 885 (m), 672 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{13}H_{17}F_3NO^+$ 260.1257; Found 260.1260.

5-(phenyl(*p*-tolyl)methyl)-2-(trifluoromethyl)oxazolidine (23b)



Palladium hydroxide on carbon (20%w, 14.3 mg, 20.0 µmol, 0.200 equiv.) was placed in a 10 mL flask under Ar. **20i** (40.9 mg, 0.100 mmol, 1.00 equiv.) was dissolved in MeOH (1.5 mL)/EtOAc (0.7 mL). After bubbling with N_2, the solution was added to the flask. The suspension was put under H_2 atmosphere and stirred overnight at rt. The solution was filtered on Celite (washing with MeOH) and concentrated under reduced pressure. A purification by preparative TLC (eluent Pentane/EtOAc 9:1) afford the named compound **23b** (25.6 mg, 80.0 µmol, 80% yield) as an off-white solid. **mp** 66-68 °C.

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.27 (m, 2H, Ar*H*), 7.26 – 7.19 (m, 5H, Ar*H*), 7.12 (d, *J* = 7.8 Hz, 2H, Ar*H*), 4.97 (q, *J* = 5.6 Hz, 1H, C*H*CF_3), 4.62 (ddd, *J* = 14.8, 9.3, 5.6 Hz, 1H, CH_2C*H*O), 3.96 (d, *J* = 9.6 Hz, 1H, C*H*Ph), 3.15 (dd, *J* = 11.8, 5.2 Hz, 1H, NHCH_2), 2.85 – 2.75 (m, 1H, NHCH_2), 2.67 (br, 1H, N*H*), 2.31 (s, 3H, ArCH_3).

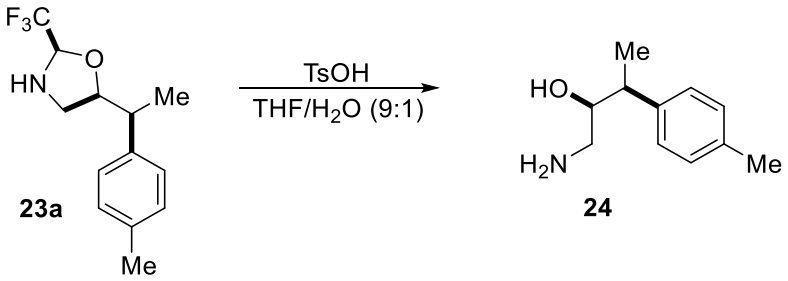
^{13}C NMR (101 MHz, Chloroform-*d*) δ 141.5, 139.2, 136.3, 129.3, 128.9, 128.3, 128.2, 127.1, 123.4 (q, *J* = 283.0 Hz), 88.4 (q, *J* = 33.9 Hz), 82.2, 55.3, 50.7, 21.2.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.0 (d, *J* = 5.1 Hz).

IR (cm^{-1}) 3276 (w), 2922 (w), 1283 (m), 1180 (s), 1146 (s), 1098 (s), 1014 (m), 937 (m), 797 (s), 739 (s), 697 (s), 686 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{18}H_{19}F_3NO^+$ 322.1412; Found 322.1409.

1-amino-3-(p-tolyl)butan-2-ol (24)



23a (60.0 mg, 0.231 mmol) was dissolved into a mixture of THF (4 mL) and H_2O (0.5 mL) to which was added tosylsulfonic acid (282 mg, 1.62 mmol, 7 equiv) and the reaction allowed to stir for 24 hr. The reaction was dissolved in DCM (5 mL) and quenched by the addition of 1M NaOH (4 mL) the layers were separated and the aqueous layer additionally extracted by DCM (2 x 5 mL). the organic layer was rinsed with brine, dried over $MgSO_4$ filtered and concentrated. No further purification was performed. The desired product 1-amino-3-(p-tolyl)butan-2-ol **24** was obtained as a viscous colourless oil (40 mg, 0.223 mmol, 96%) which was confirmed as a single diastereoisomer by ^{1}H NMR with an approximate purity of 95%

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.13 (s, 4H, Ar*H*), 3.60 (ddd, *J* = 8.3, 7.1, 3.1 Hz, 1H, C*H*OH), 2.92 (dd, *J* = 12.5, 1.4 Hz, 1H, H_2NC*H*H), 2.76 (p, *J* = 7.1 Hz, 1H, C*H*CH_3), 2.57 (dd, *J* = 12.7, 8.2 Hz, 1H, H_2NCH*H*), 2.33 (s, 3H, ArCH_3), 1.85 (s, 2H, NH_2), 1.26 (d, *J* = 7.1 Hz, 3H CHCH_3).

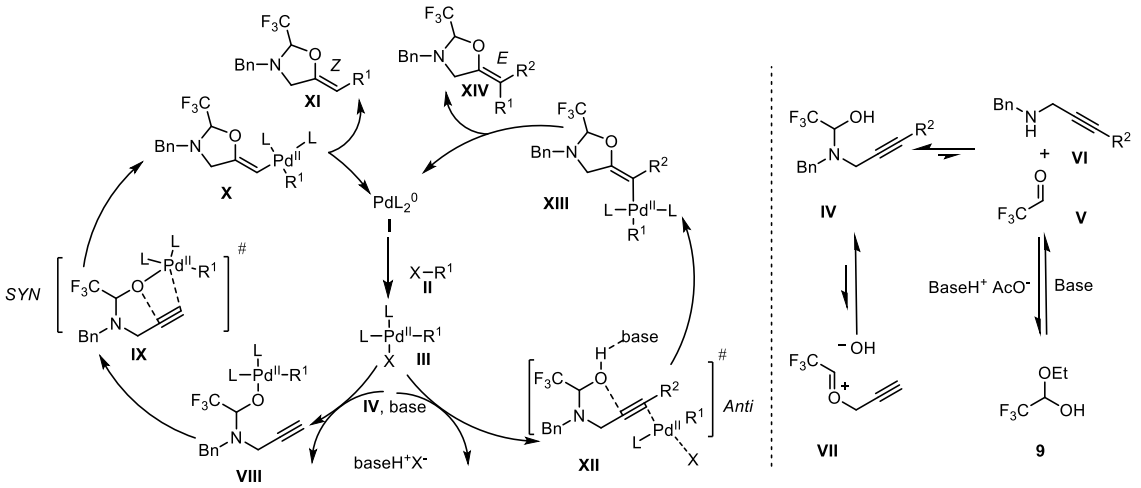
^{13}C NMR (101 MHz, Chloroform-*d*) δ 140.4, 136.1, 129.2, 127.9, 76.3, 45.0, 43.6, 21.0, 17.8.

IR (cm^{-1}) 3319 (b), 2926 (m), 1568 (s), 1515 (s), 1454 (s), 1313 (m), 1015 (m), 816 (s), 735 (m).

HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calcd for $C_{11}H_{18}NO^+$ 180.1383; Found 180.1384.

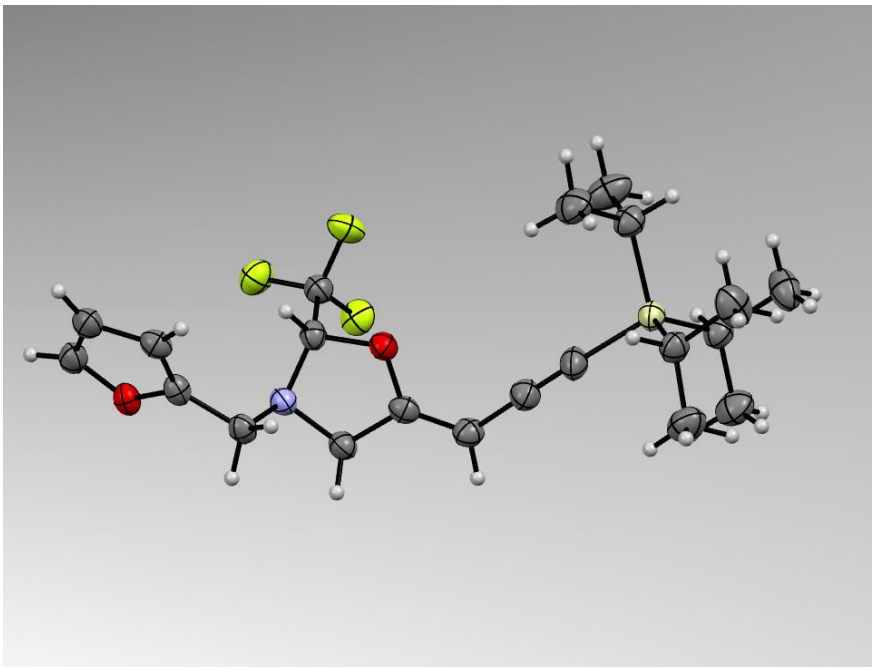
7. Speculative Reaction Mechanism

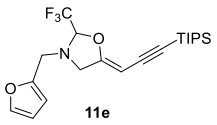
At this stage, no mechanism study has been performed. Nevertheless, a speculative mechanism can be proposed based on well-established fundamental steps of palladium catalysis (Scheme S1). The catalytic cycle is probably initiated by oxidative addition of Pd(0) complex **I** onto the halide **II**. Pd(II) complex **III** can then react with aminal **IV**, generated by the reaction of propargyl amine **VI** and trifluoroacetaldehyde (**V**), generated from precursor **9**. Aminal **IV** may be in equilibrium with oxonium **VII**. For terminal alkynes, the next step is probably a base-mediated ligand exchange to give palladium complex **VIII**. *Syn* oxy-palladation via transition state **IX** then give alkenyl-palladium complex **X**. Finally reductive elimination gives product **XI** and closes the catalytic cycle. Alternatively, *anti* oxy-palladation via transition state **XII** gives alkenyl palladium complex **XIII**. Reductive elimination then leads to *trans* product **XIV**. At this stage, the switch of selectivity observed when introducing a substituent on the alkyne is not clearly understood. One possibility would be that *syn* oxy palladation via **IX** becomes too high in energy due to steric hindrance. Interestingly, in the case of alkenes, no product could be obtained in this case.



Scheme S1. Speculative reaction mechanism.

8. Structures determined by X-ray measurement.





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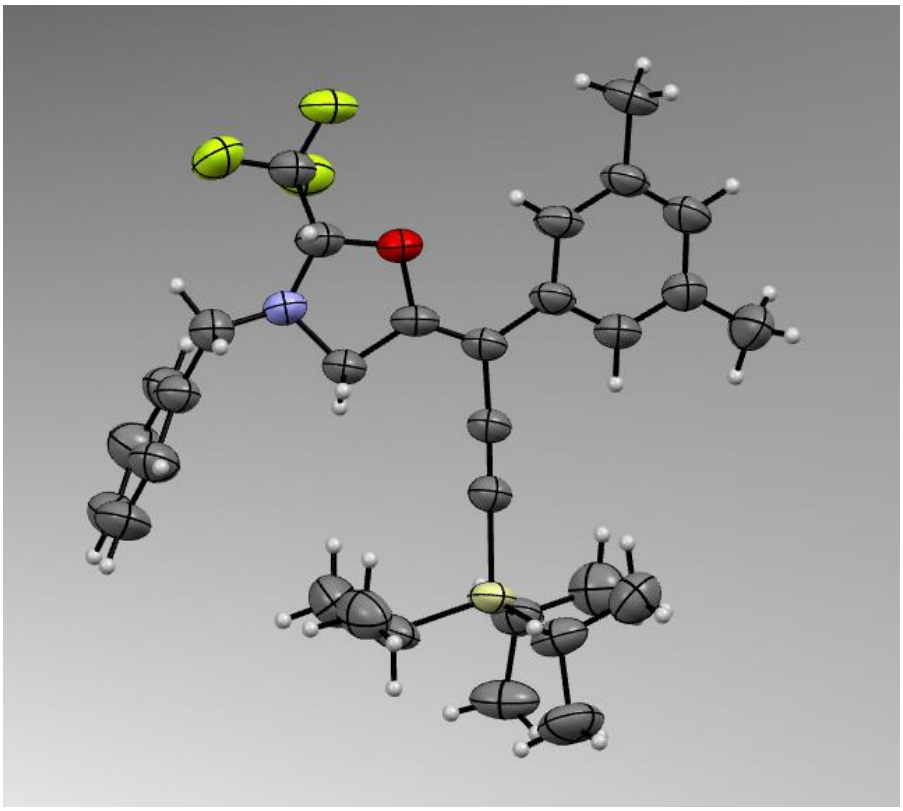

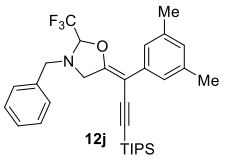

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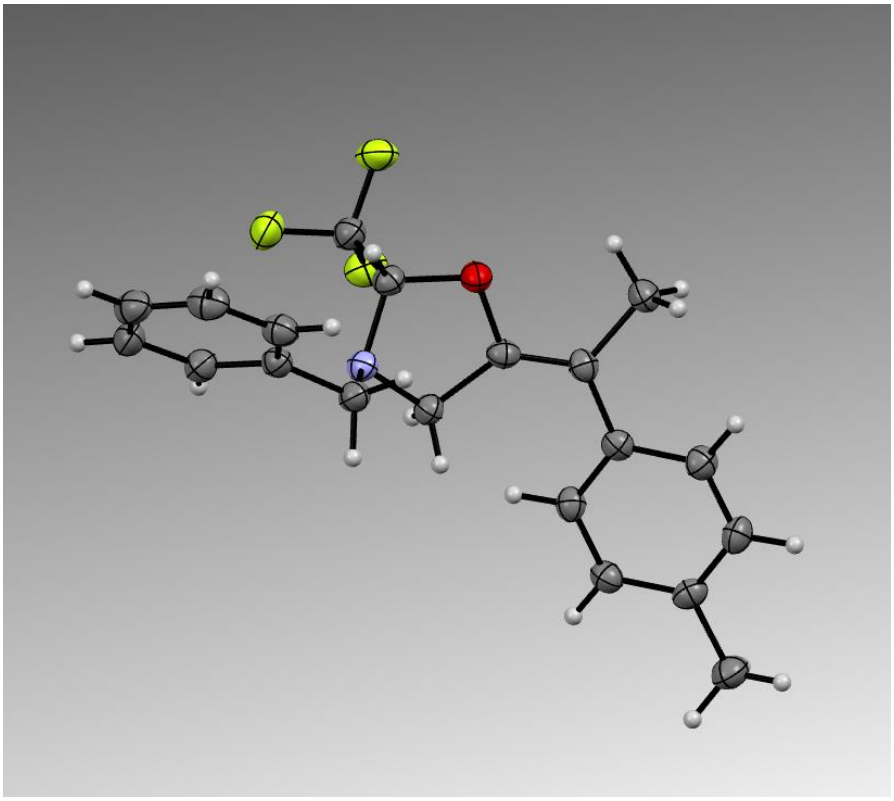

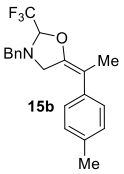

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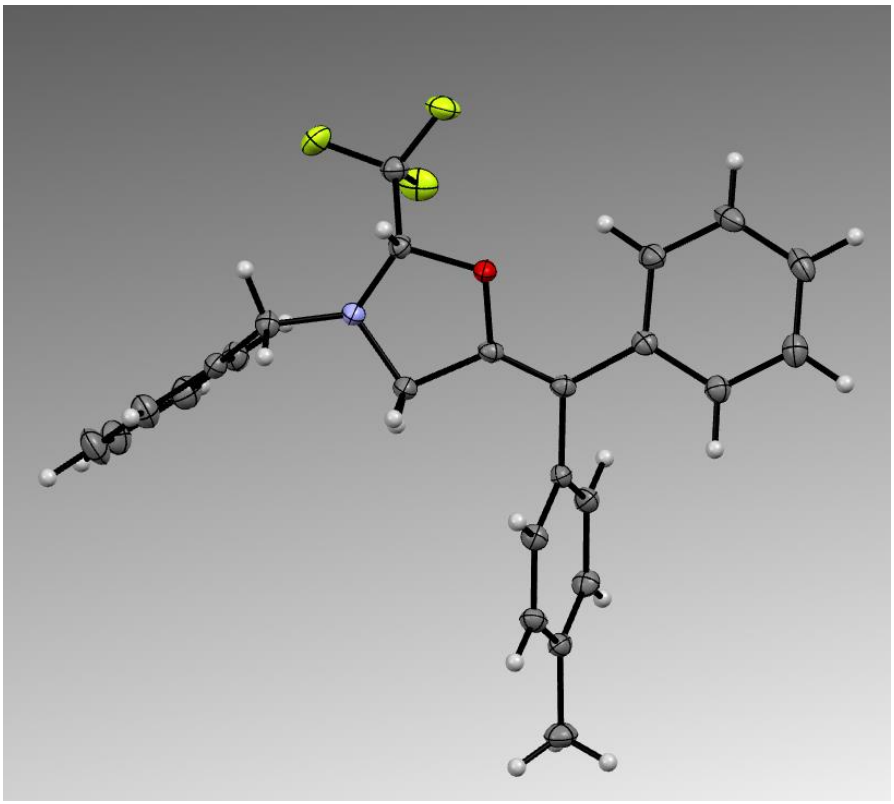

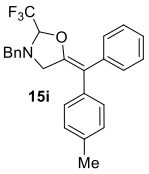

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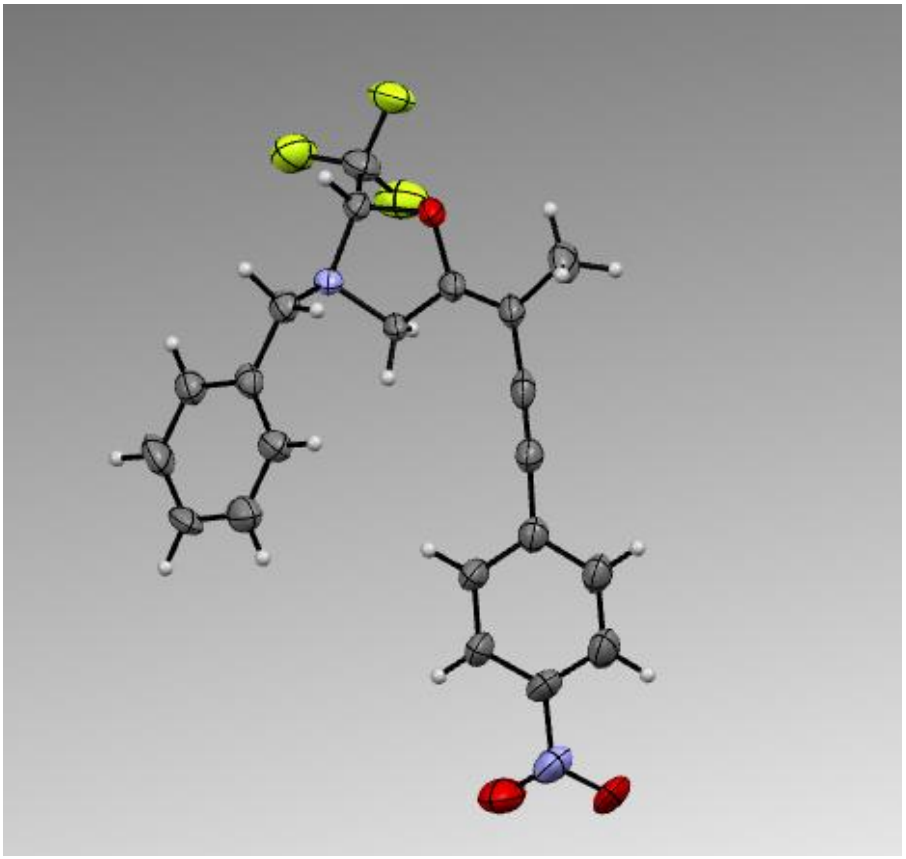
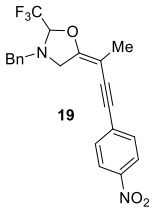




Cambridge Crystallographic Data Centre entry – 1874014

9. Bibliography

[1] U. Orcel, J. Waser, *Angew. Chemie Int. Ed.* **2016**, *55*, 12881–12885.

[2] S. S. Zalesskiy, V. P. Ananikov, *Organometallics* **2012**, *31*, 2302–2309.

[3] H. Mizoguchi, R. Watanabe, S. Minami, H. Oikawa, H. Oguri, *Org. Biomol. Chem.* **2015**, *13*, 5955–5963.

[4] D. Althuon, F. Rönicke, D. Fürniss, J. Quan, I. Wellhöfer, N. Jung, U. Schepers, S. Bräse, *Org. Biomol. Chem.* **2015**, *13*, 4226–4230.

[5] M. Yoshida, T. Mizuguchi, K. Shishido, *Chem. - A Eur. J.* **2012**, *18*, 15578–15581.

[6] A. S. K. Hashmi, T. Häffner, W. Yang, S. Pankajakshan, S. Schäfer, L. Schultes, F. Rominger, W. Frey, *Chem. - A Eur. J.* **2012**, *18*, 10480–10486.

[7] D. Landini, M. Penso, *Synth. Commun.* **1988**, *18*, 791–800.

[8] O. Reis, H. Koyuncu, I. Esiringu, Y. Sahin, O. H. Gulcan, *A New Method for the Synthesis of Rasagiline*, **2012**, WO2012096635.

[9] J. Oh, T. Kim, Y. Park, *Korean J. Women Heal. Nurs.* **2011**, *17*, 439.

[10] Z. Ma, F. Ni, G. H. C. Woo, S. M. Lo, P. M. Roveto, S. E. Schaus, J. K. Snyder, *Beilstein J. Org. Chem.* **2012**, *8*, 829–840.

[11] Y. Jeong, J. Lee, J. S. Ryu, *Bioorganic Med. Chem.* **2016**, *24*, 2114–2124.

[12] Y. Shao, F. Zhang, J. Zhang, X. Zhou, *Angew. Chemie Int. Ed.* **2016**, *55*, 11485–11489.

[13] H. M. Sheldrake, T. W. Wallace, *Tetrahedron Lett.* **2007**, *48*, 4407–4411.

[14] P. García-Domínguez, L. Fehr, G. Rusconi, C. Nevado, *Chem. Sci.* **2016**, *7*, 3914–3918.

[15] J. B. Bariwal, D. S. Ermolat'ev, E. V. Van der Eycken, *Chem. Eur. J.* **2010**, *16*, 3281-3284.

[16] M. X. W. Jiang, M. Rawat, W. D. Wulff, *J. Am. Chem. Soc.* **2004**, *126*, 5970–5971.

[17] B. M. Trost, D. R. Fandrick, D. C. Dinh, *J. Am. Chem. Soc.* **2005**, *127*, 14186–14187.

[18] C. Shu, Y. H. Wang, B. Zhou, X. L. Li, Y. F. Ping, X. Lu, L. W. Ye, *J. Am. Chem. Soc.* **2015**, *137*, 9567–9570.

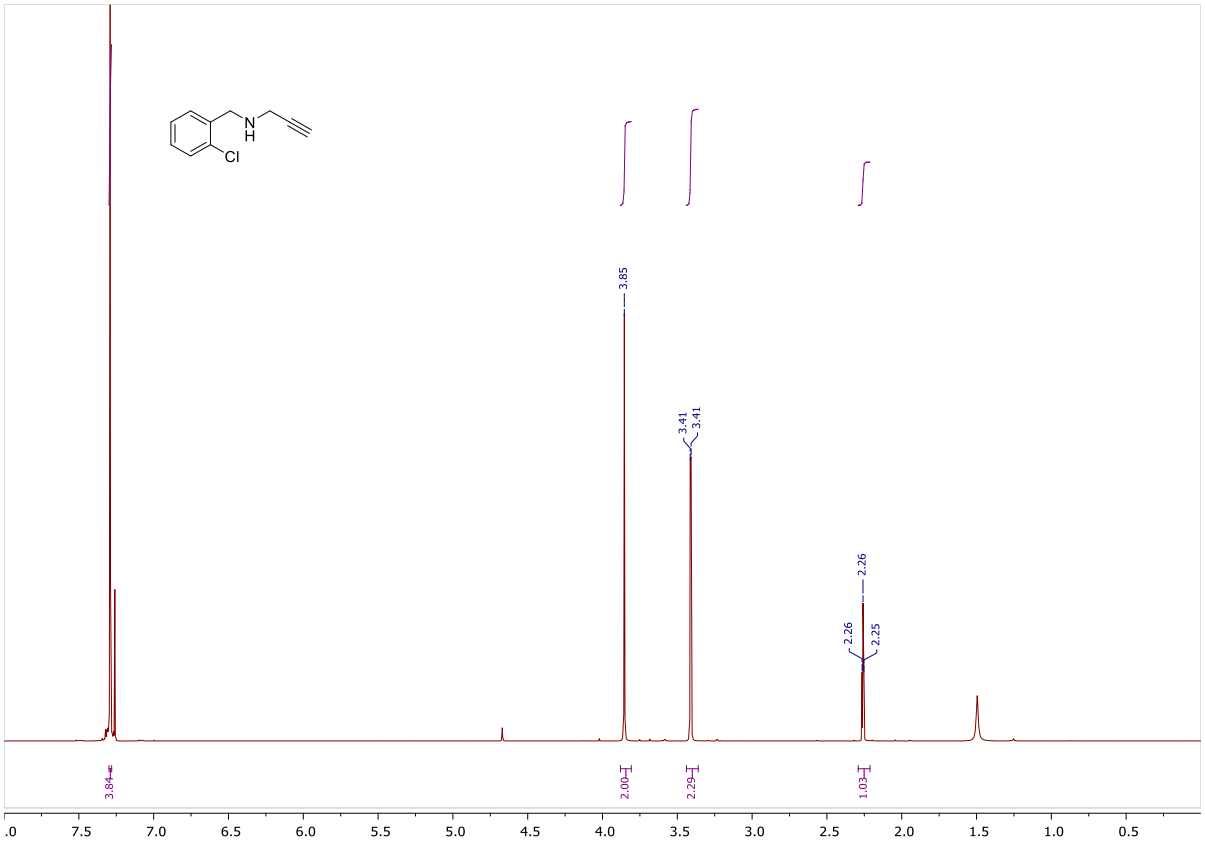
[19] M. Spain, J. K.-H. Wong, G. Nagalingam, J. M. Batten, E. Hortle, S. H. Oehlers, X. F. Jiang, H. E. Murage, J. T. Orford, P. Crisologo, et al., *J. Med. Chem.* **2018**, *61*, 3595–3608.

[20] J. Li, Y. Liang, Y. Xie, *J. Org. Chem.* **2005**, *70*, 4393–4396.

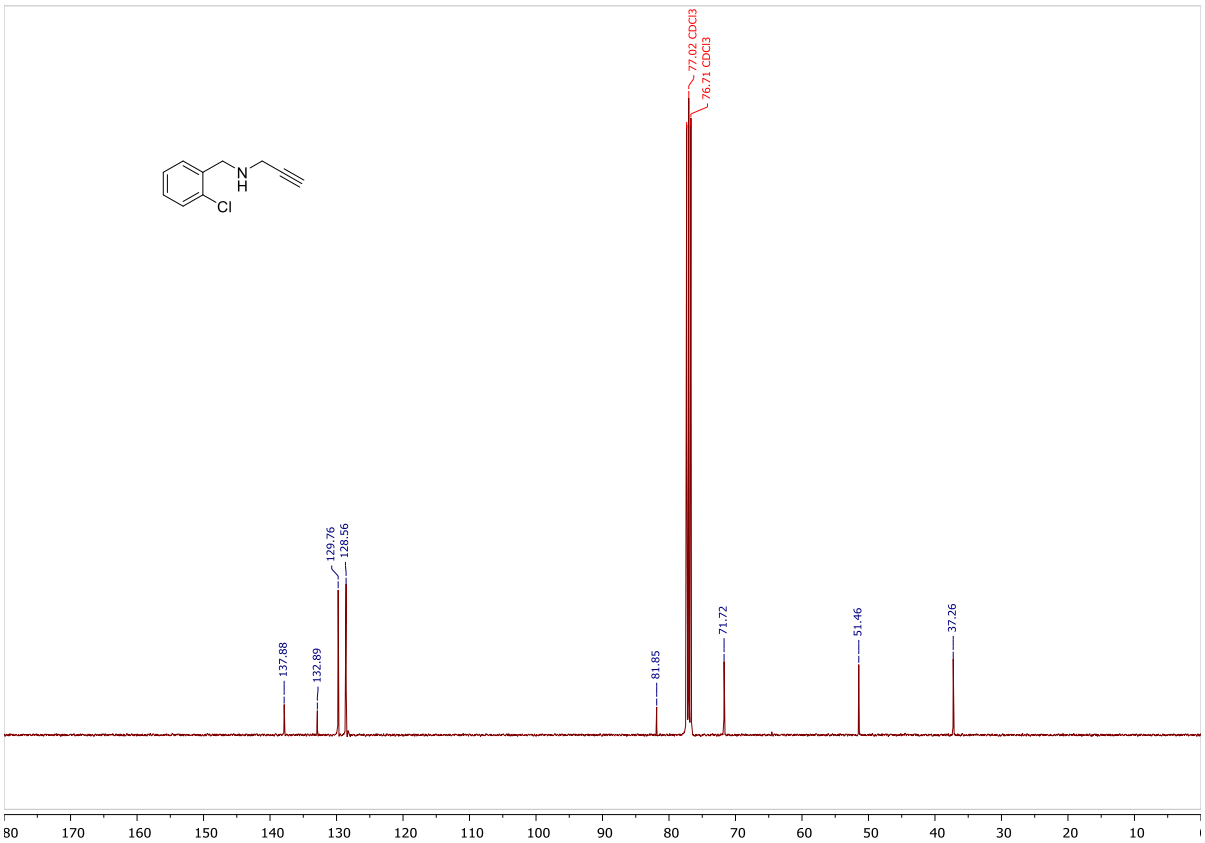
10. ^{1}H & ^{13}C NMR spectra of new compounds.

2-Chlorobenzyl propargylamine (7d)

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

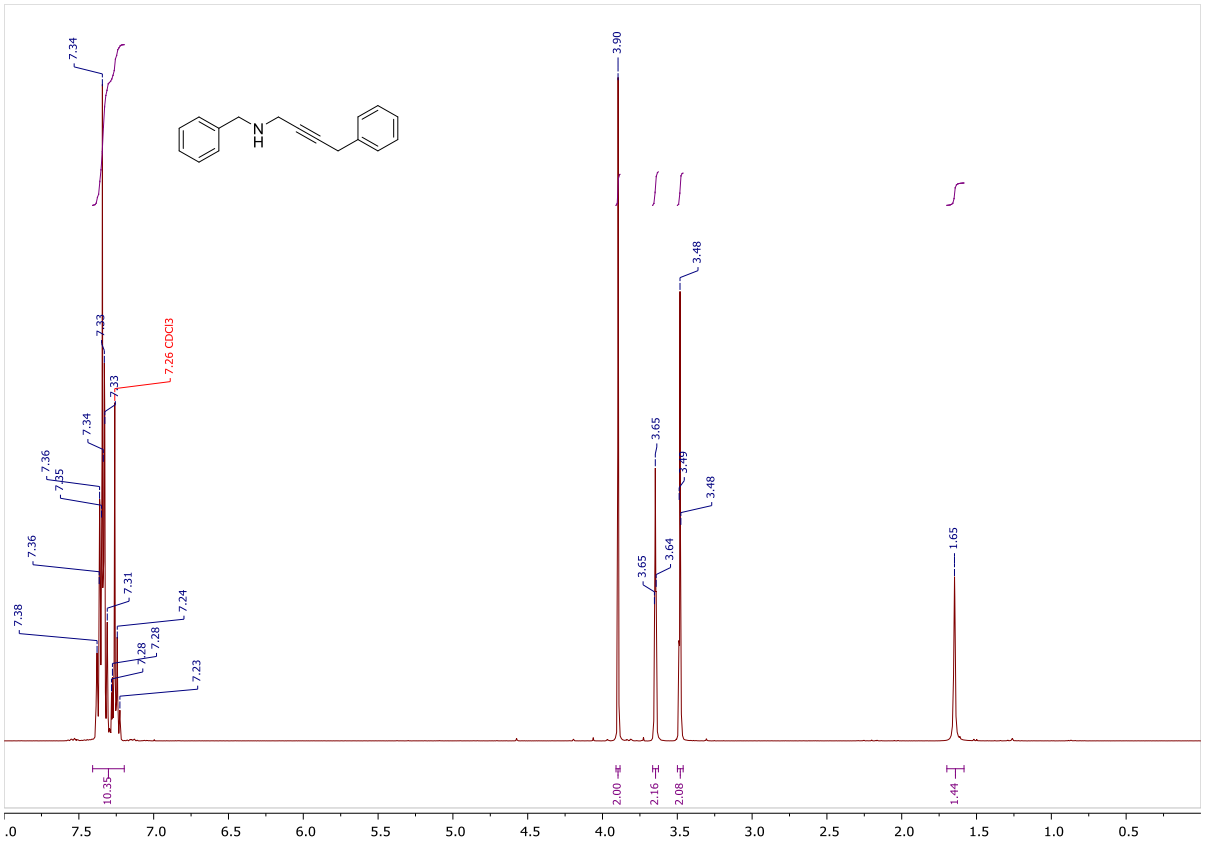


^{13}C-NMR (101 MHz, chloroform-*d*)



N-Benzyl 4-phenyl-but-2-ynylamine (8c)

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



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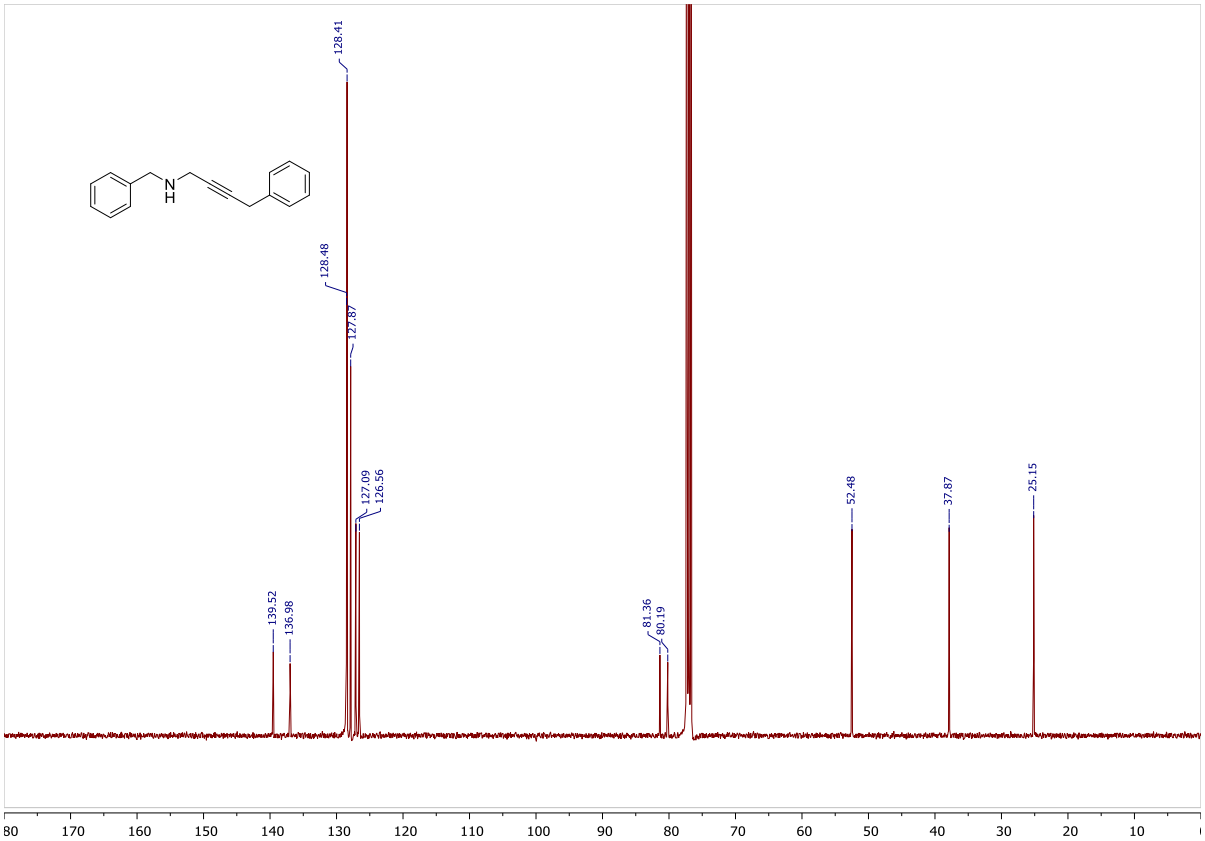

N-Benzyl Propynyl trifluoroacetamide (33)

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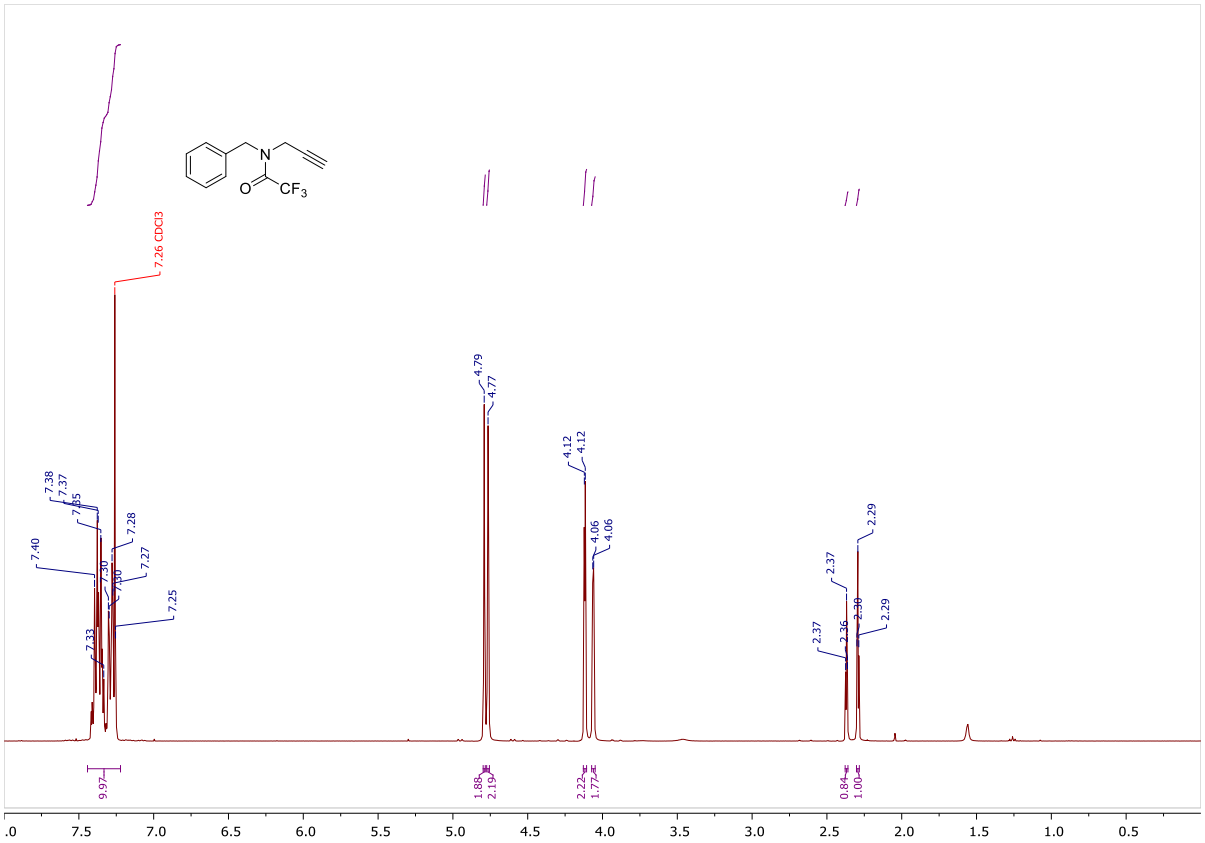

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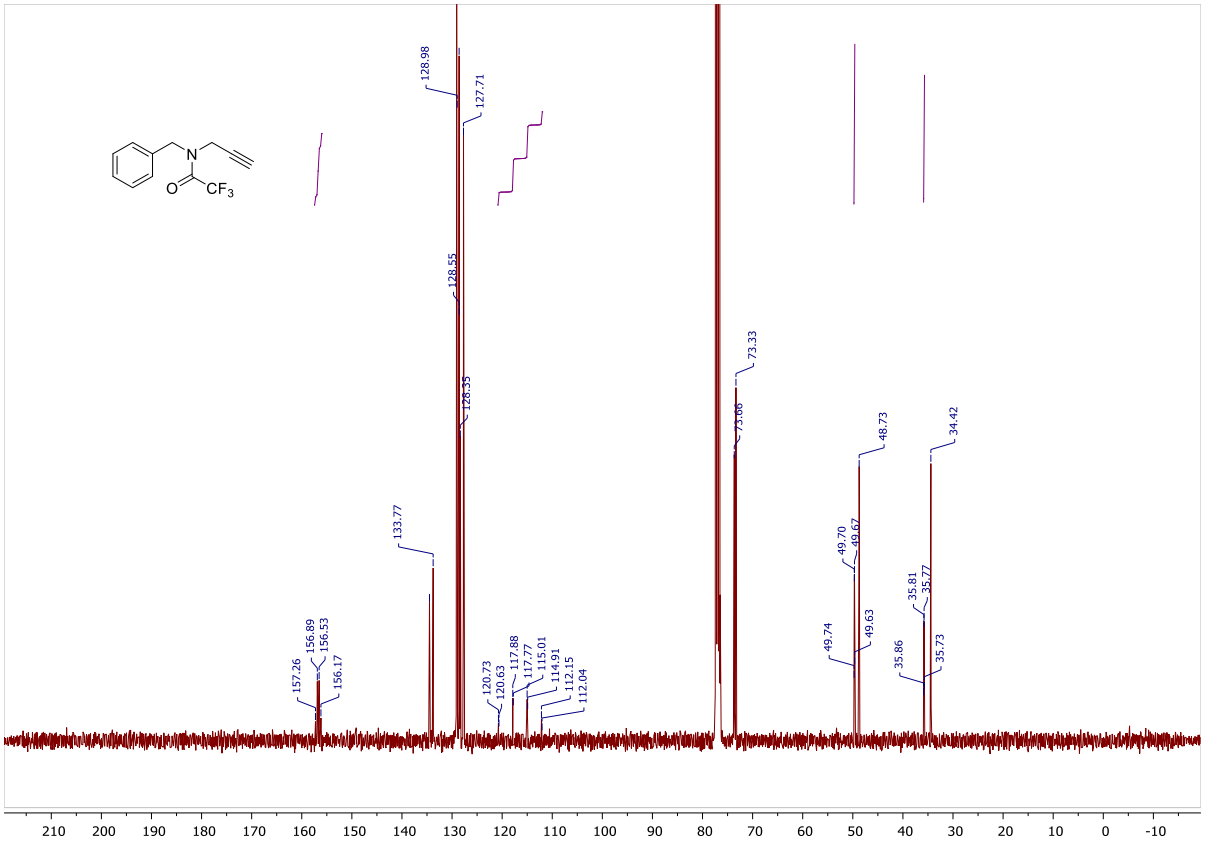

N-Benzyl-3-(3,5-dimethylphenyl)prop-2-ynylamine (8j)

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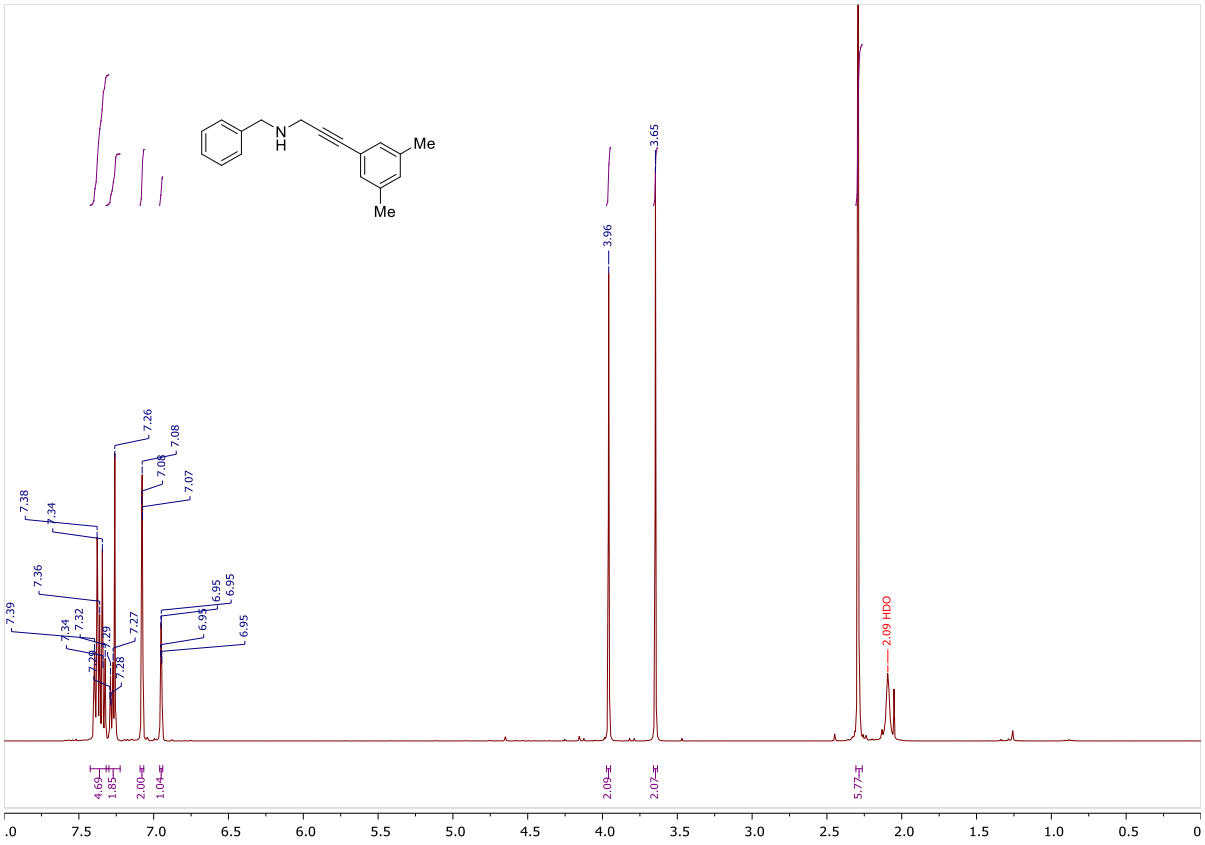

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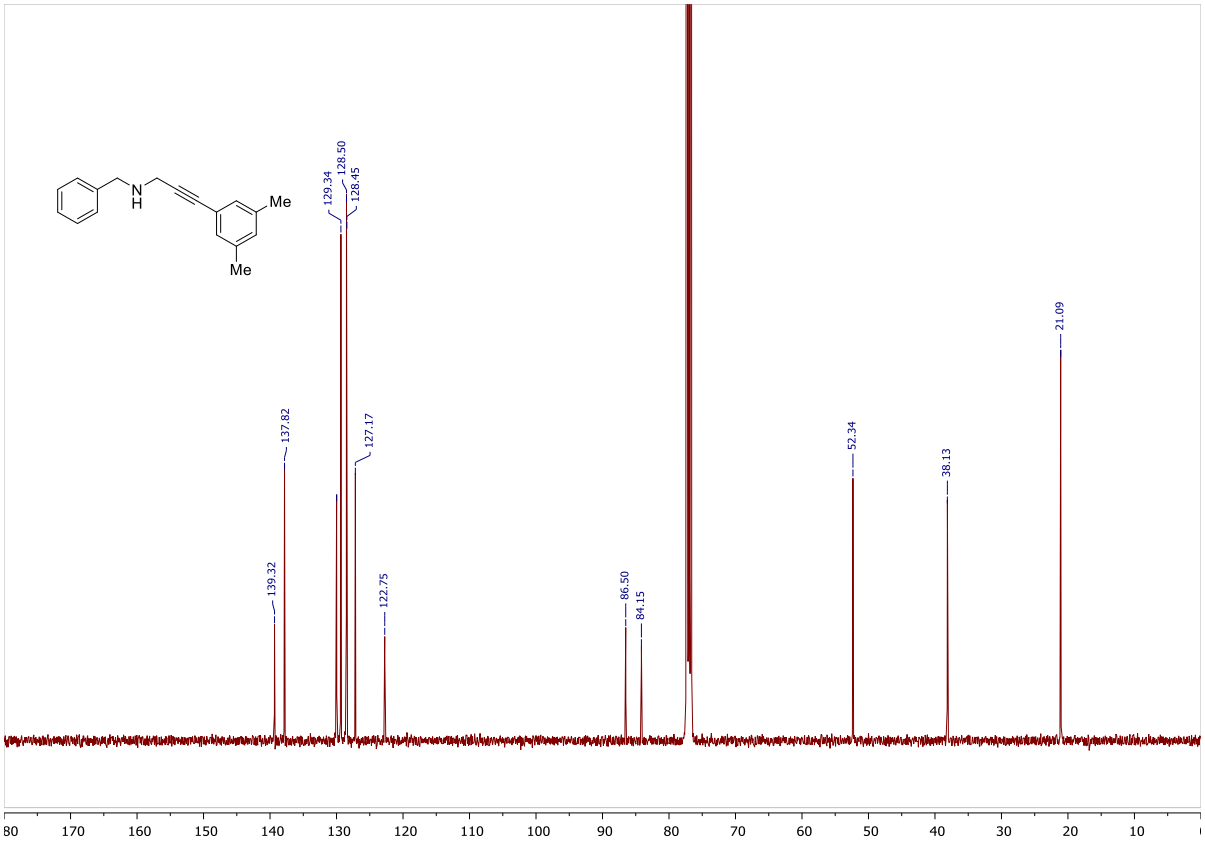

N-benzyldec-5-yn-4-amine (27)

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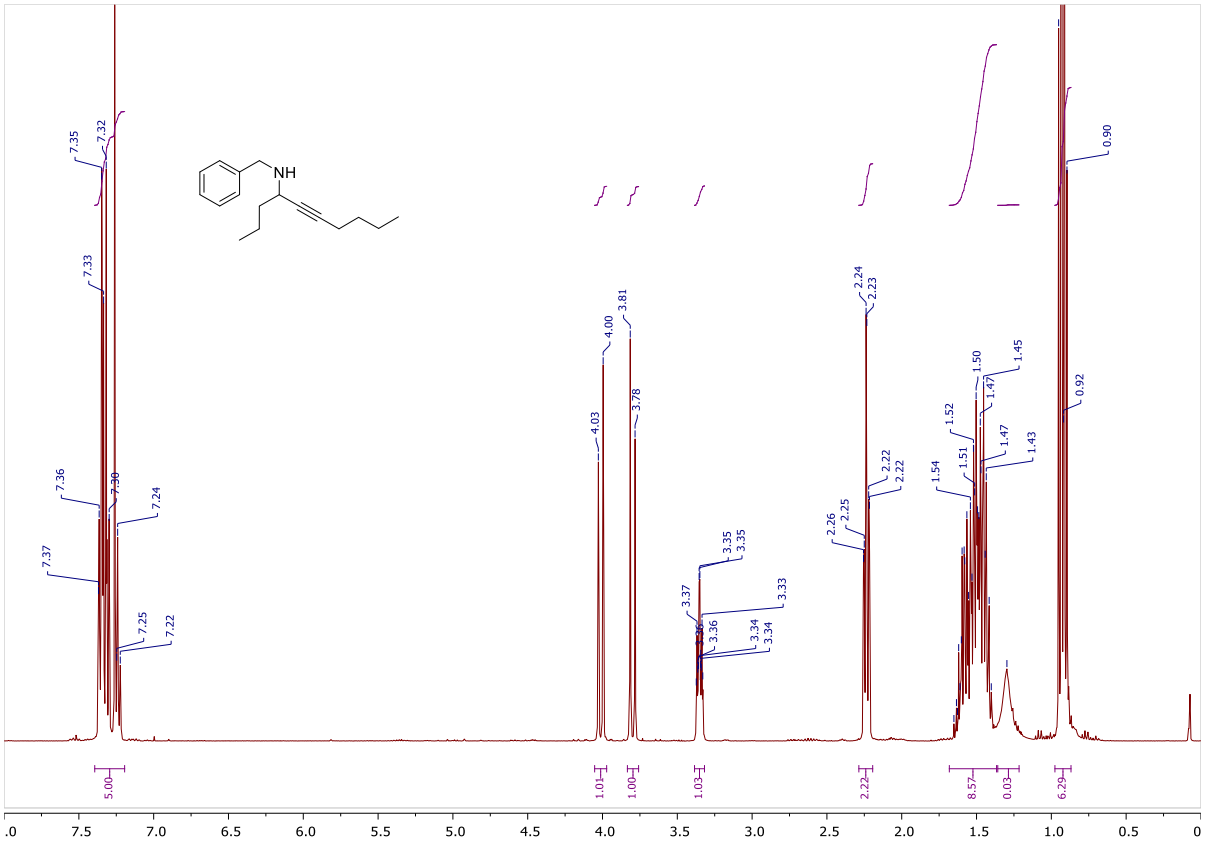

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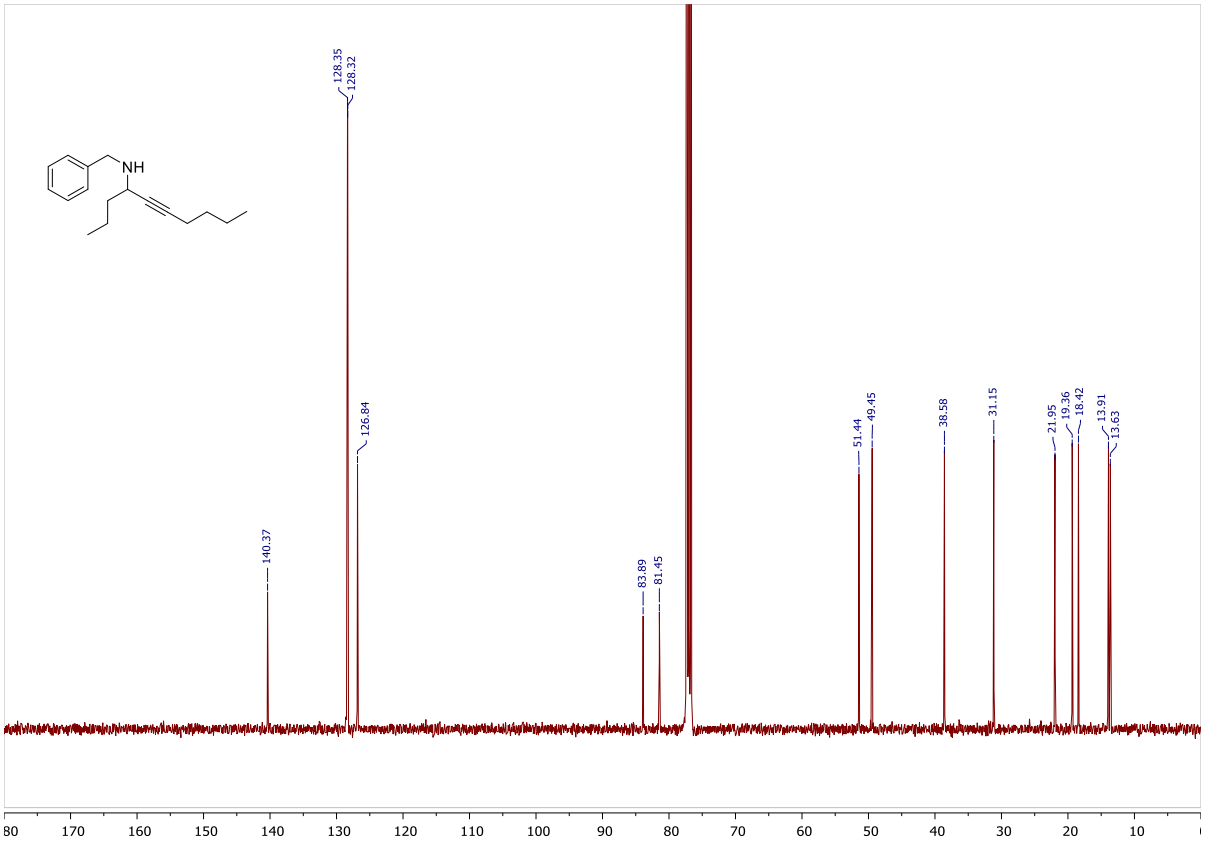
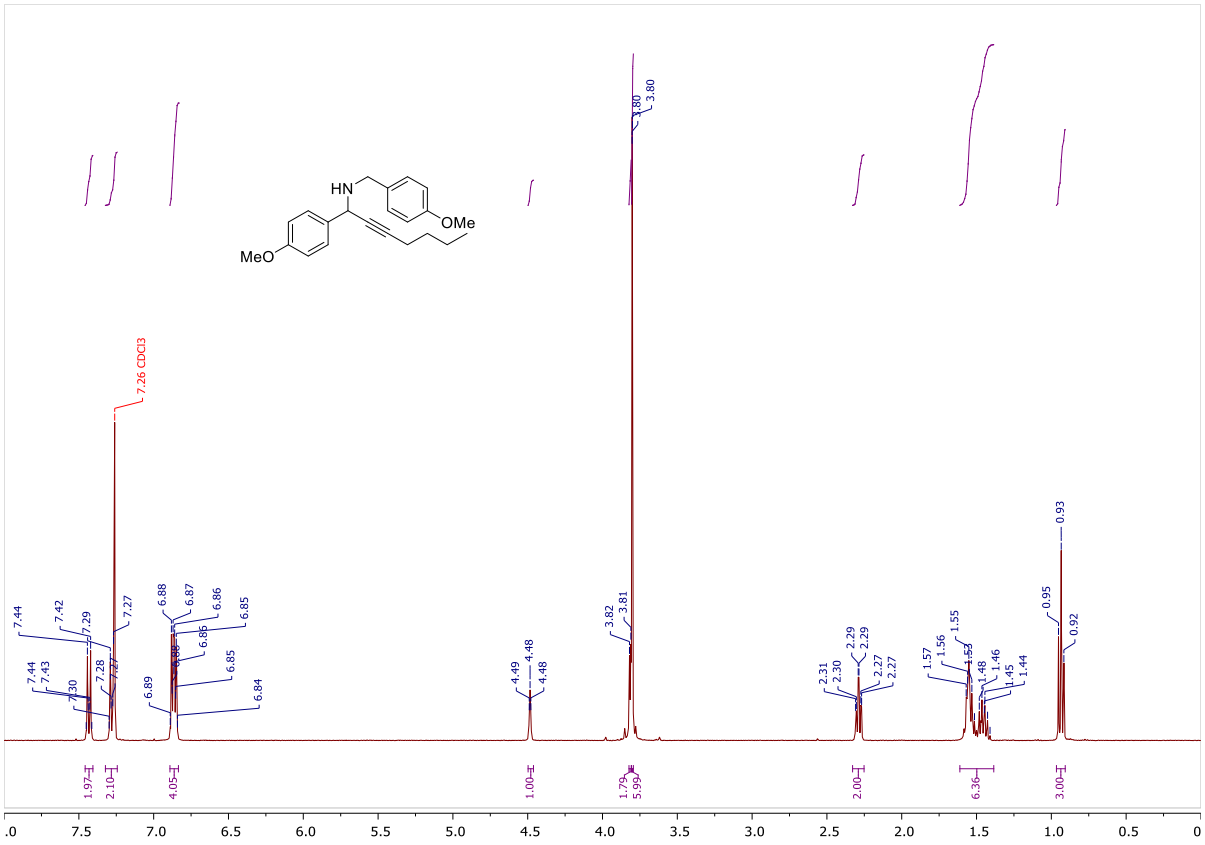


N-(4-methoxybenzyl)-1-(4-methoxyphenyl)hept-2-yn-1-amine (28)

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



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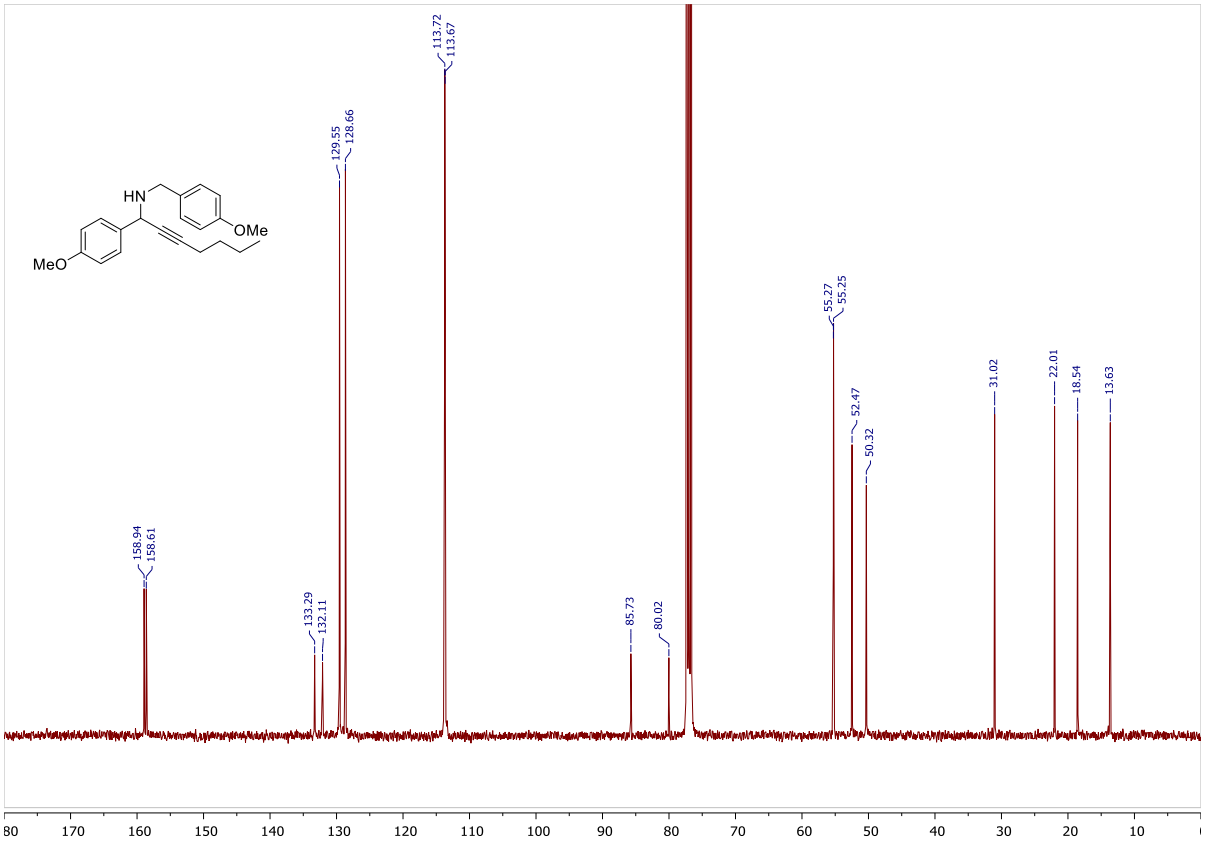
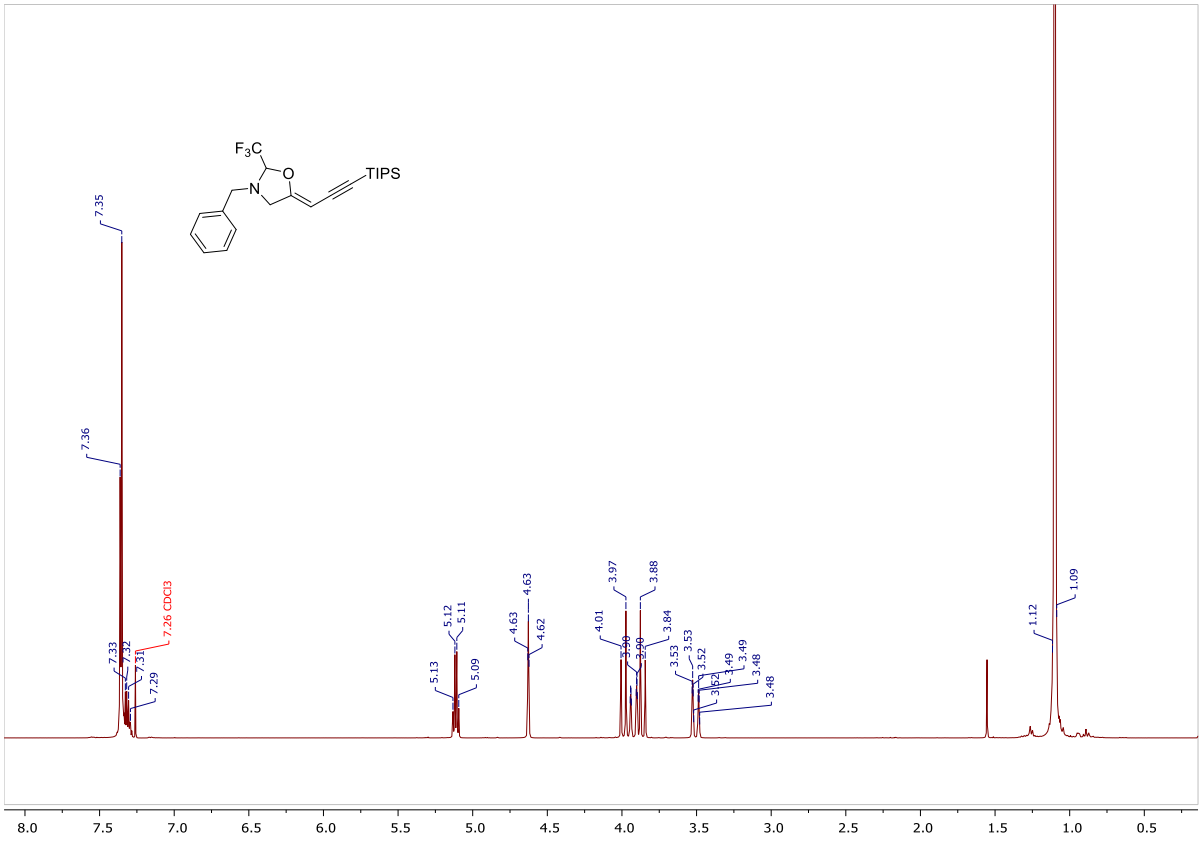
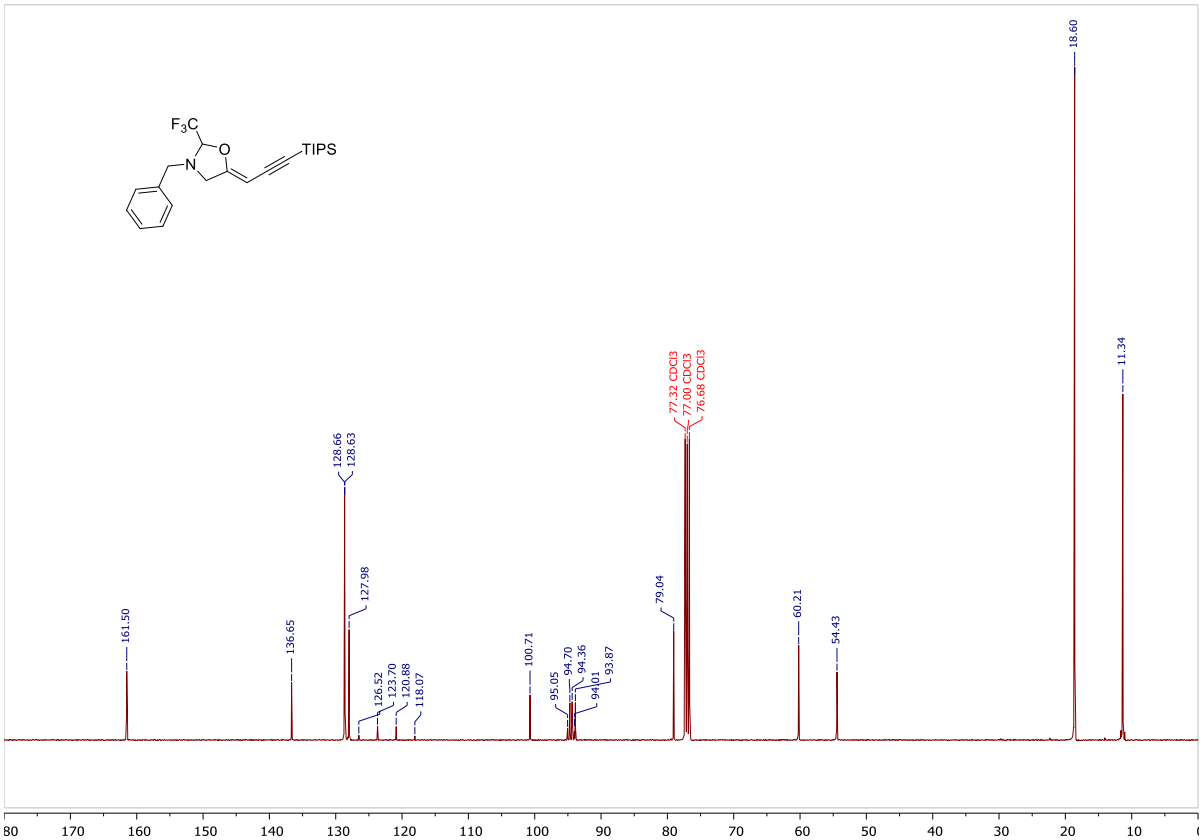


(Z)-3-Benzyl-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11a)

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

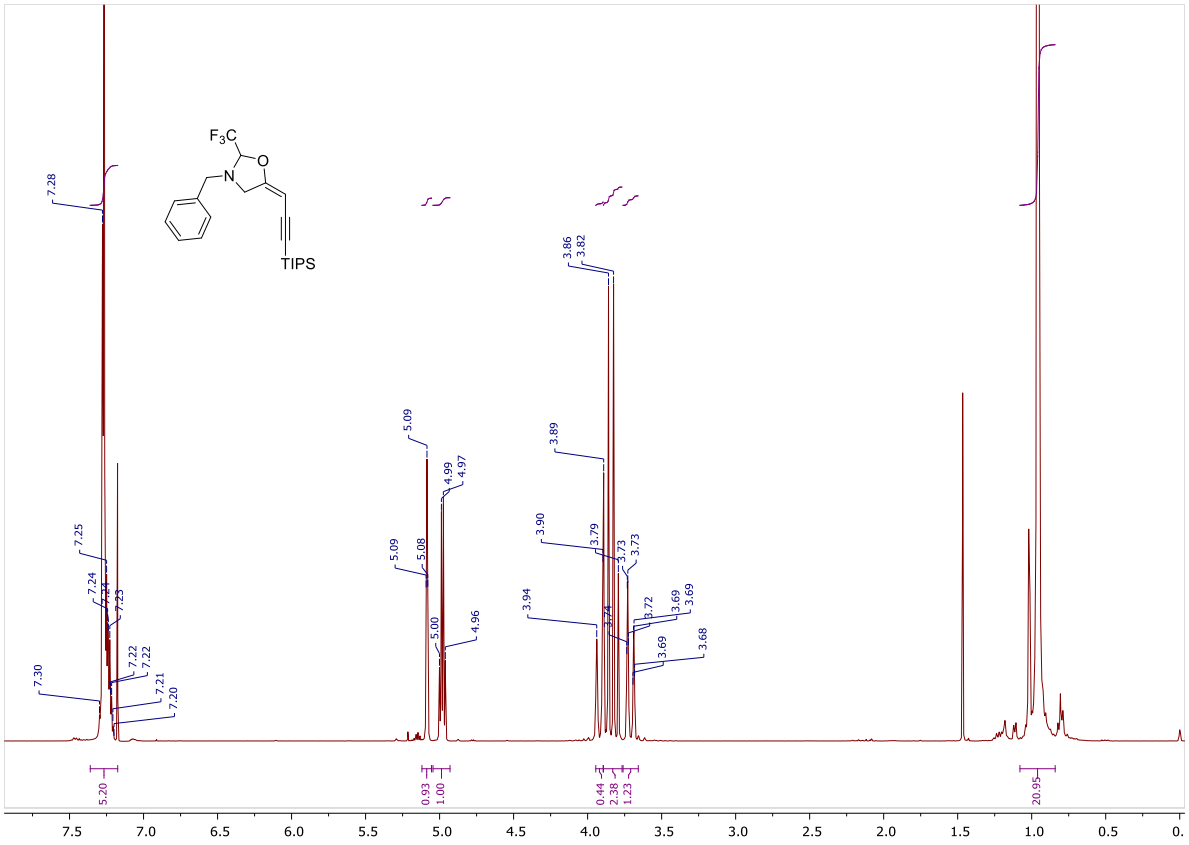


^{13}C-NMR (101 MHz, chloroform-*d*)



(E)-3-Benzyl-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11a)

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



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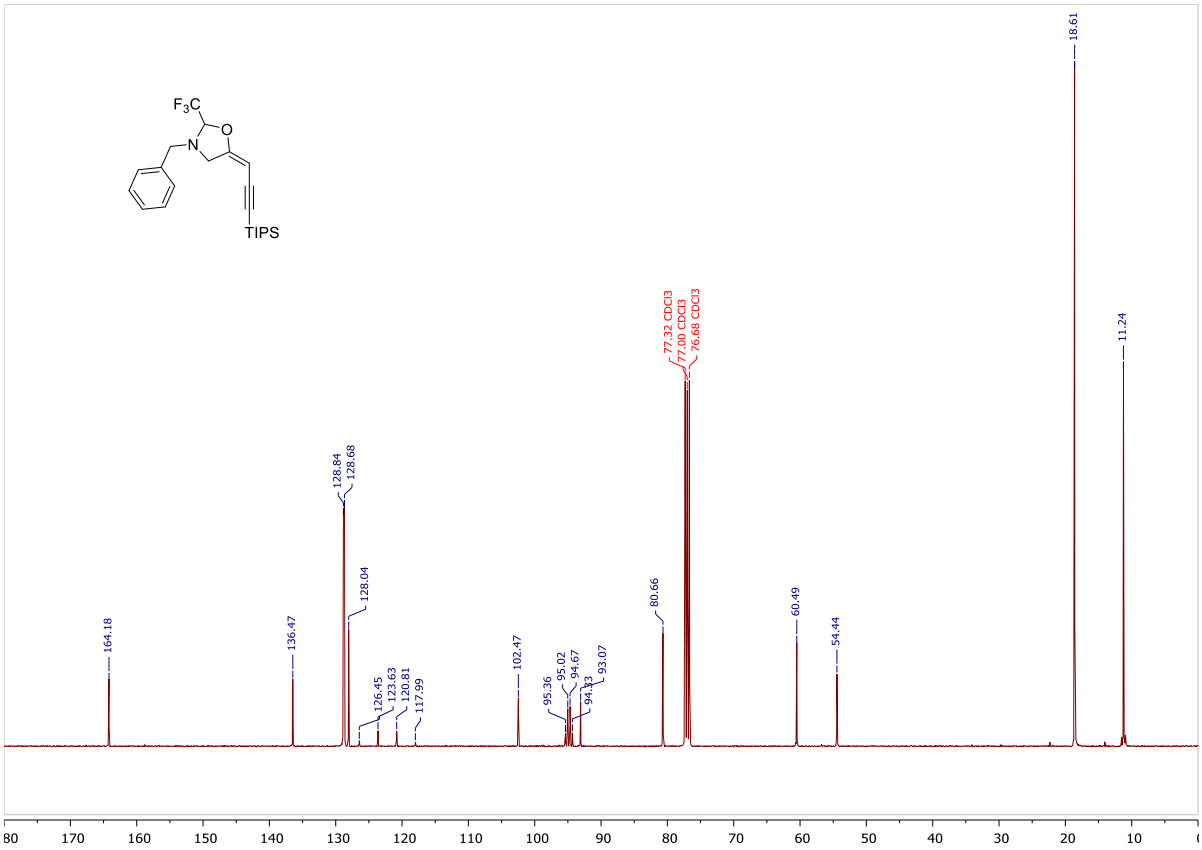
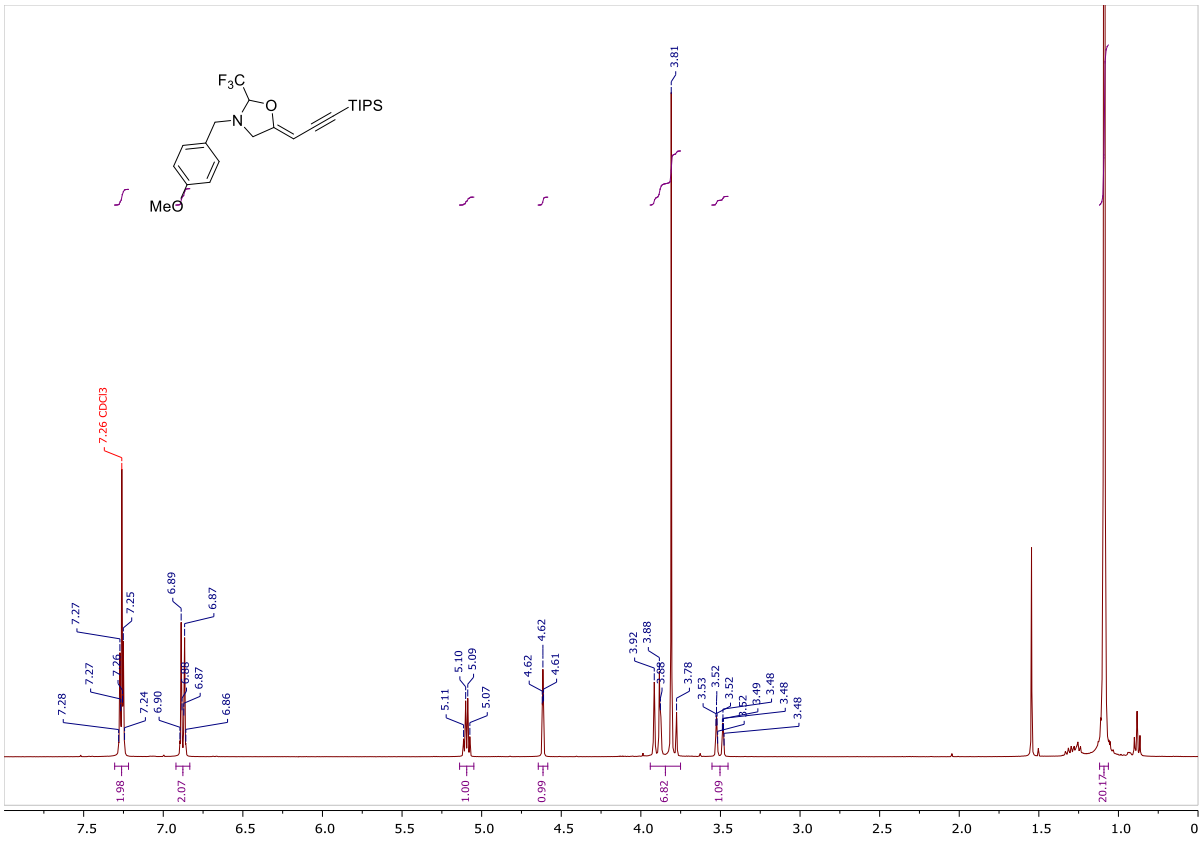


(Z)-3-(4-Methoxybenzyl)-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11b)

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



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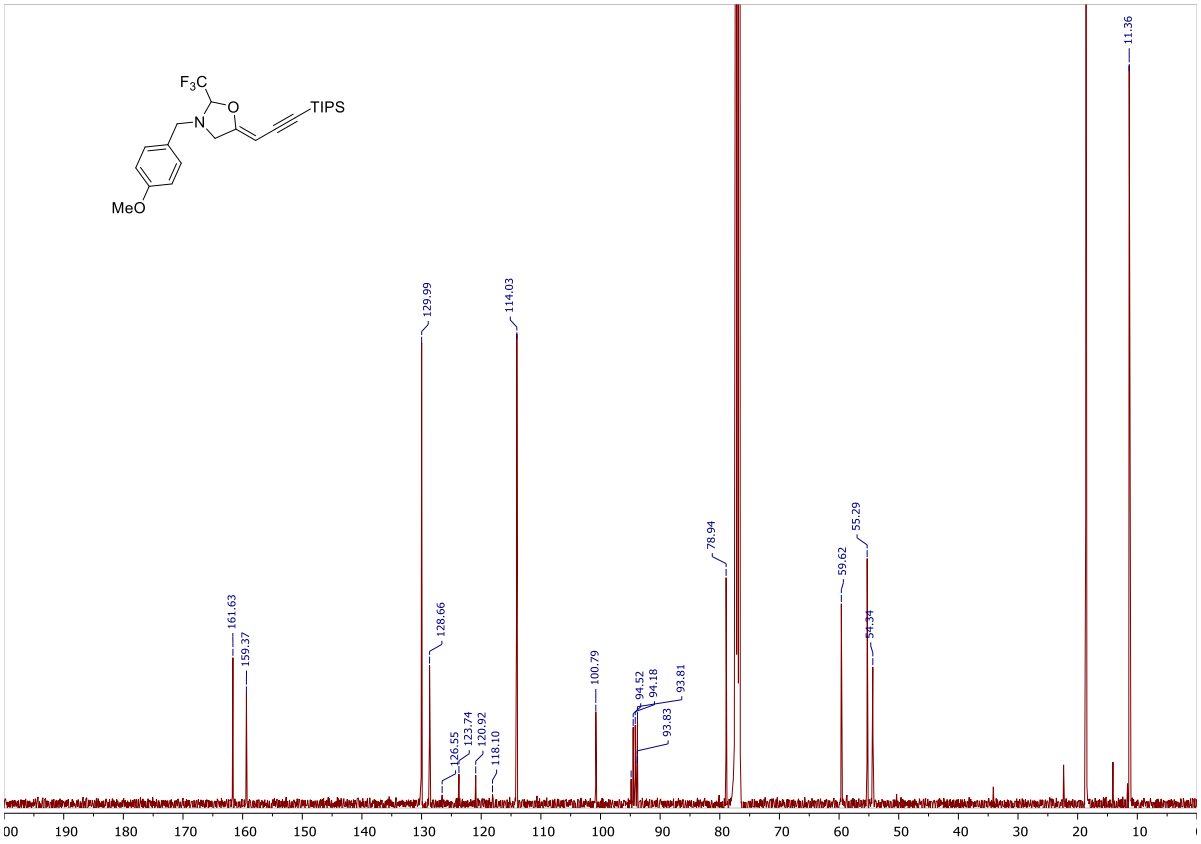
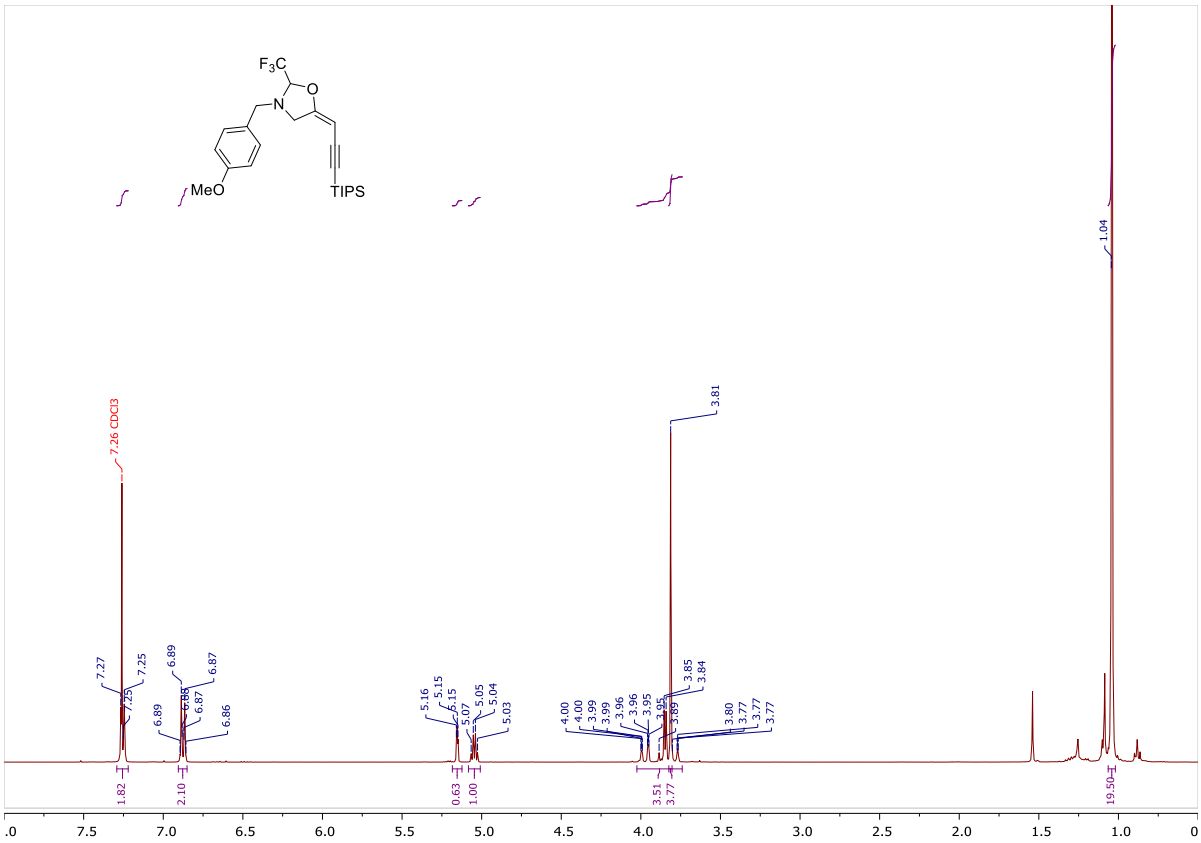


(E)-3-(4-Methoxybenzyl)-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11b)

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



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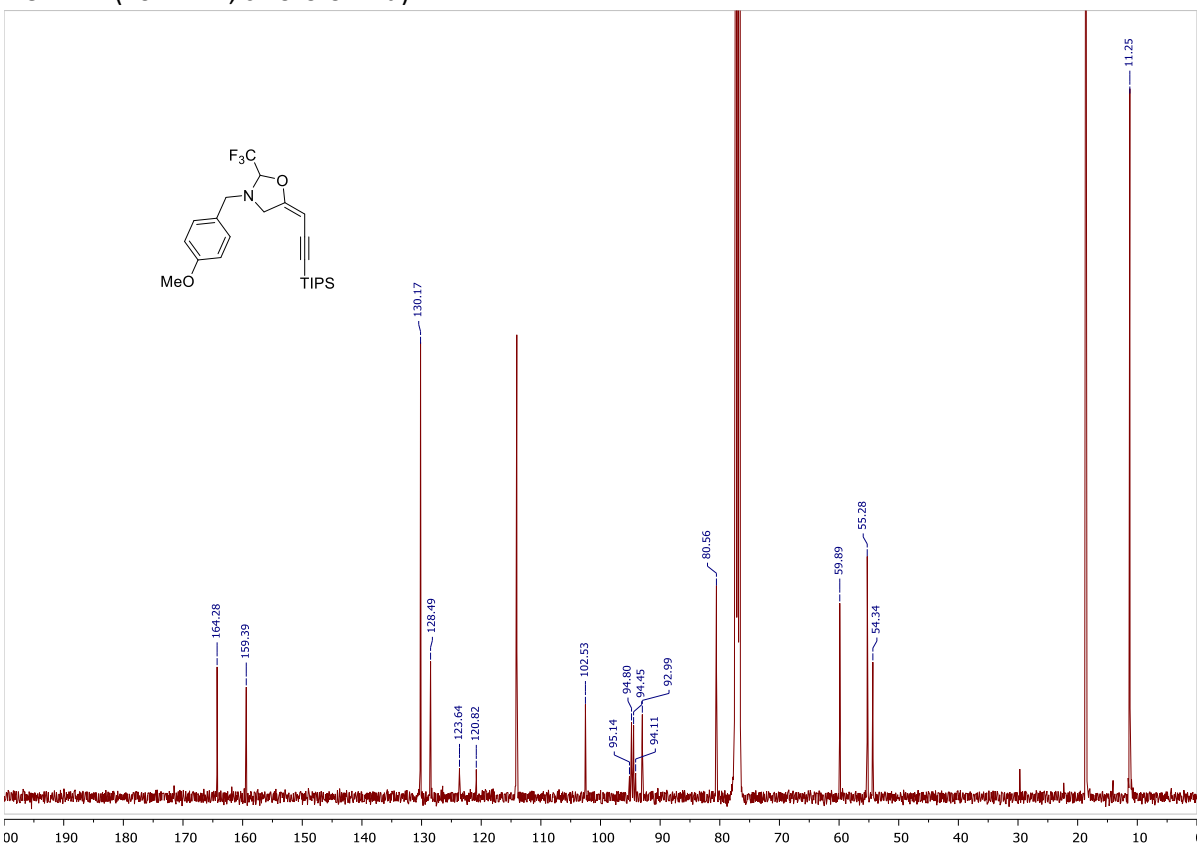
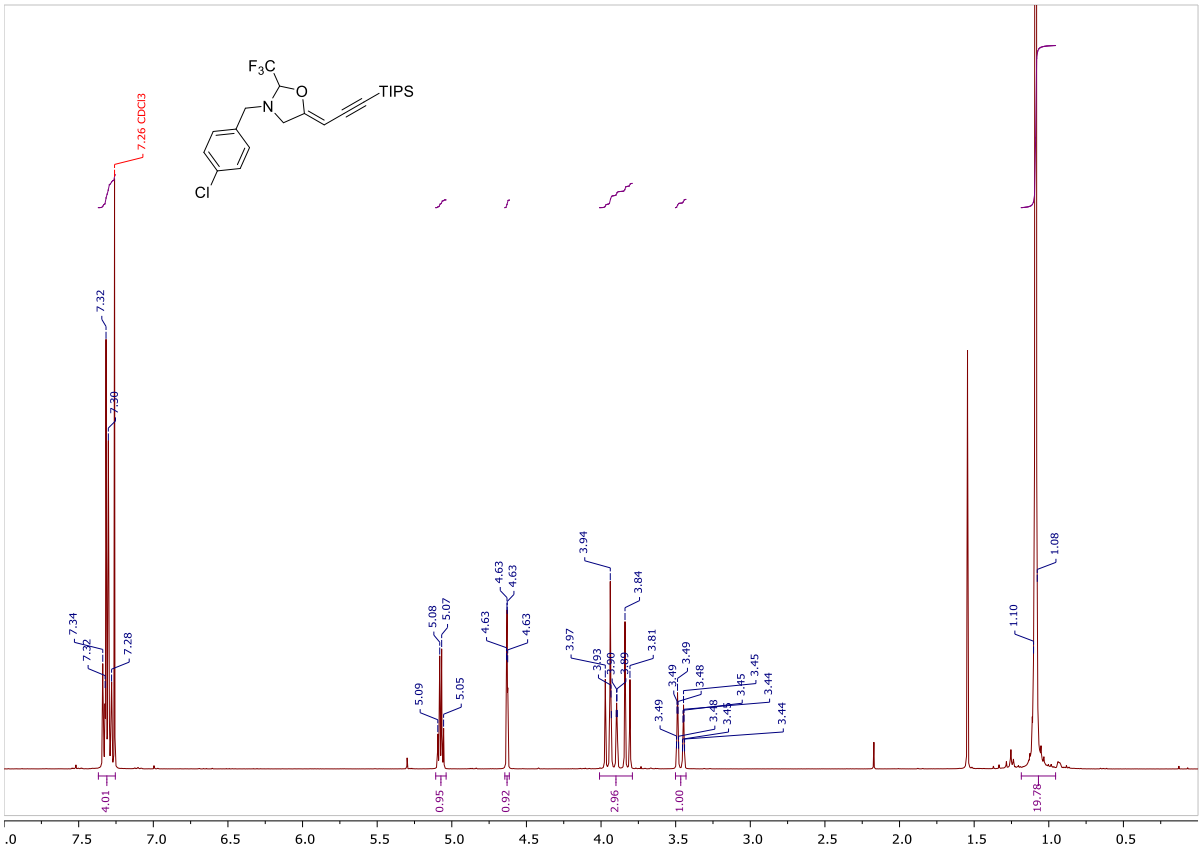


(Z)-3-(4-Chlorobenzyl)-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11c)

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



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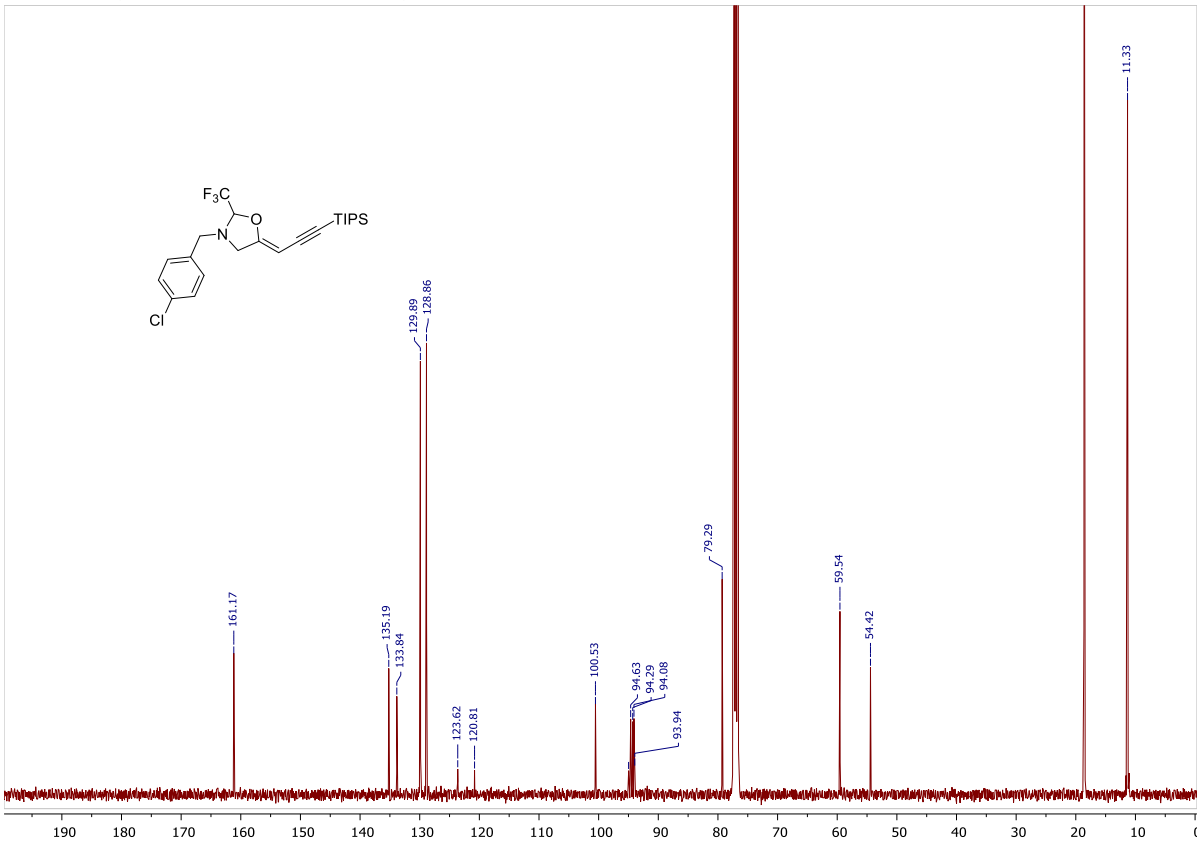
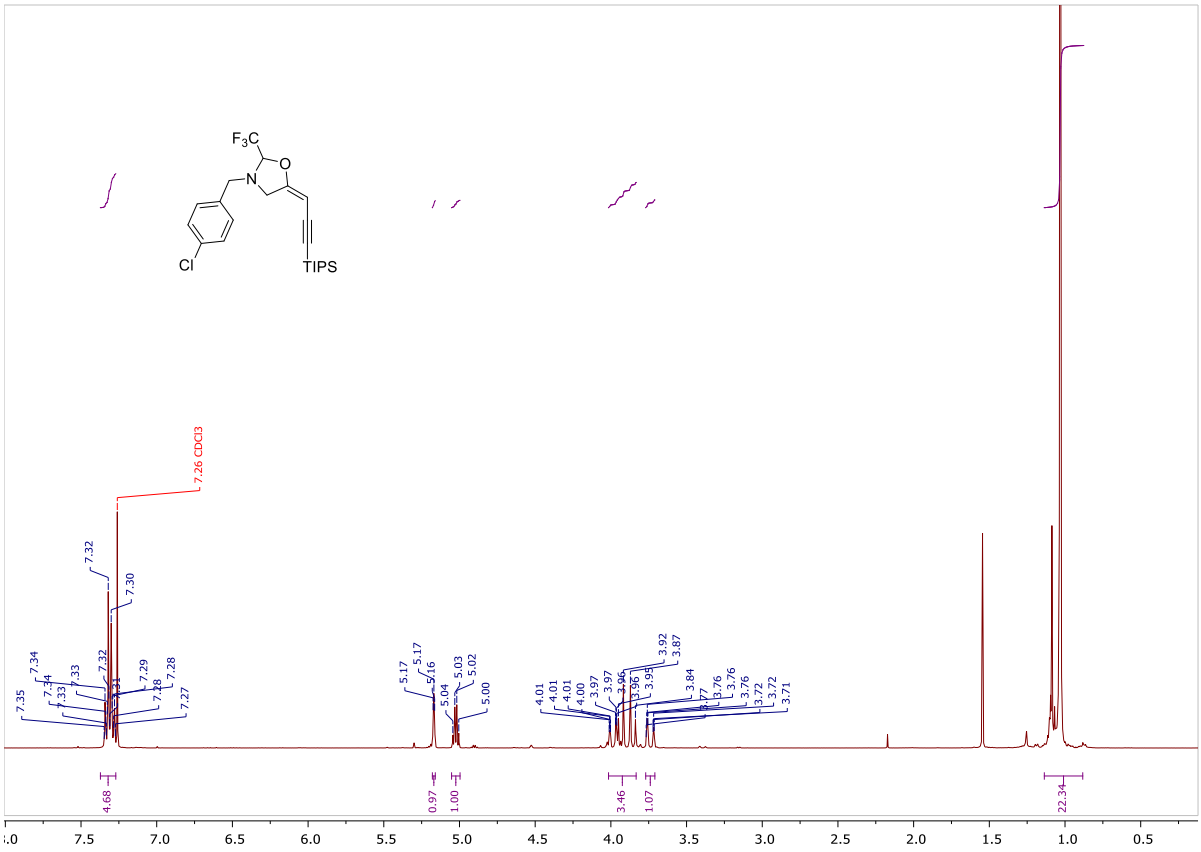


(E)-3-(4-Chlorobenzyl)-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11c)

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



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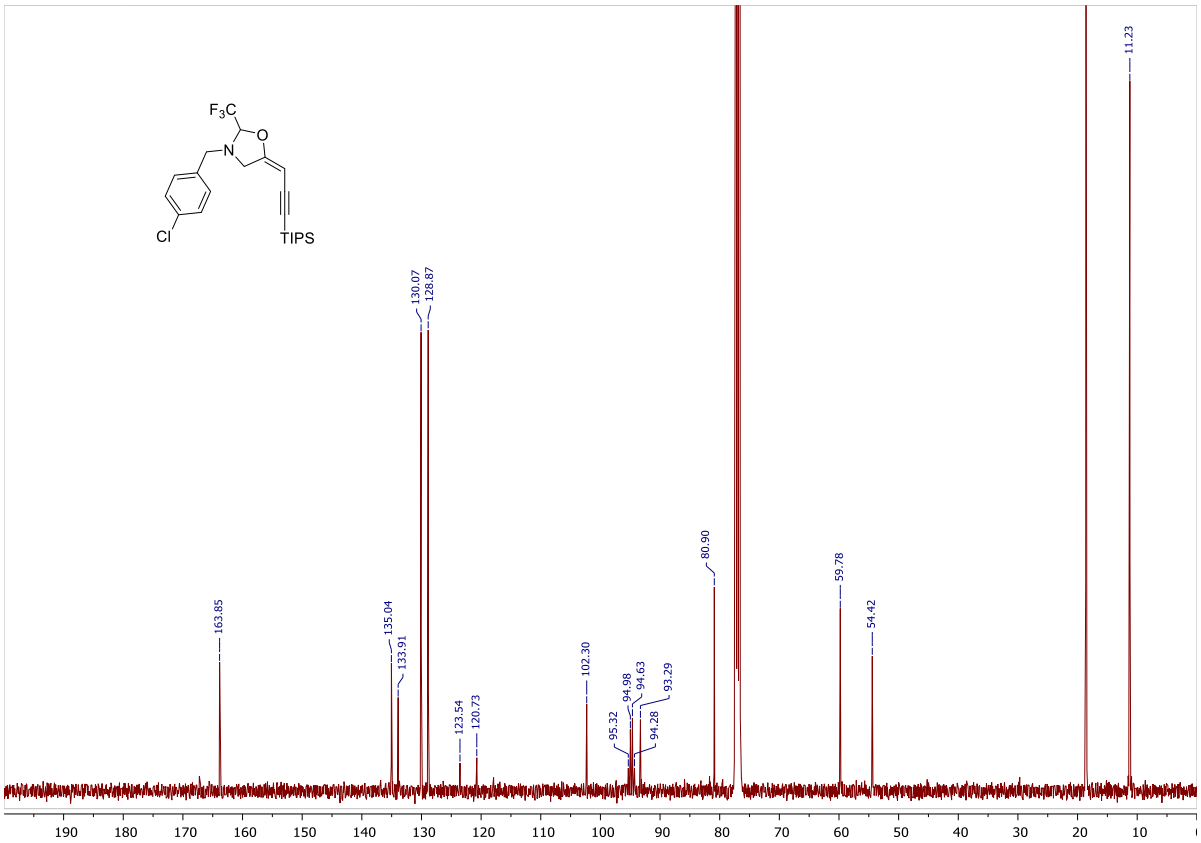
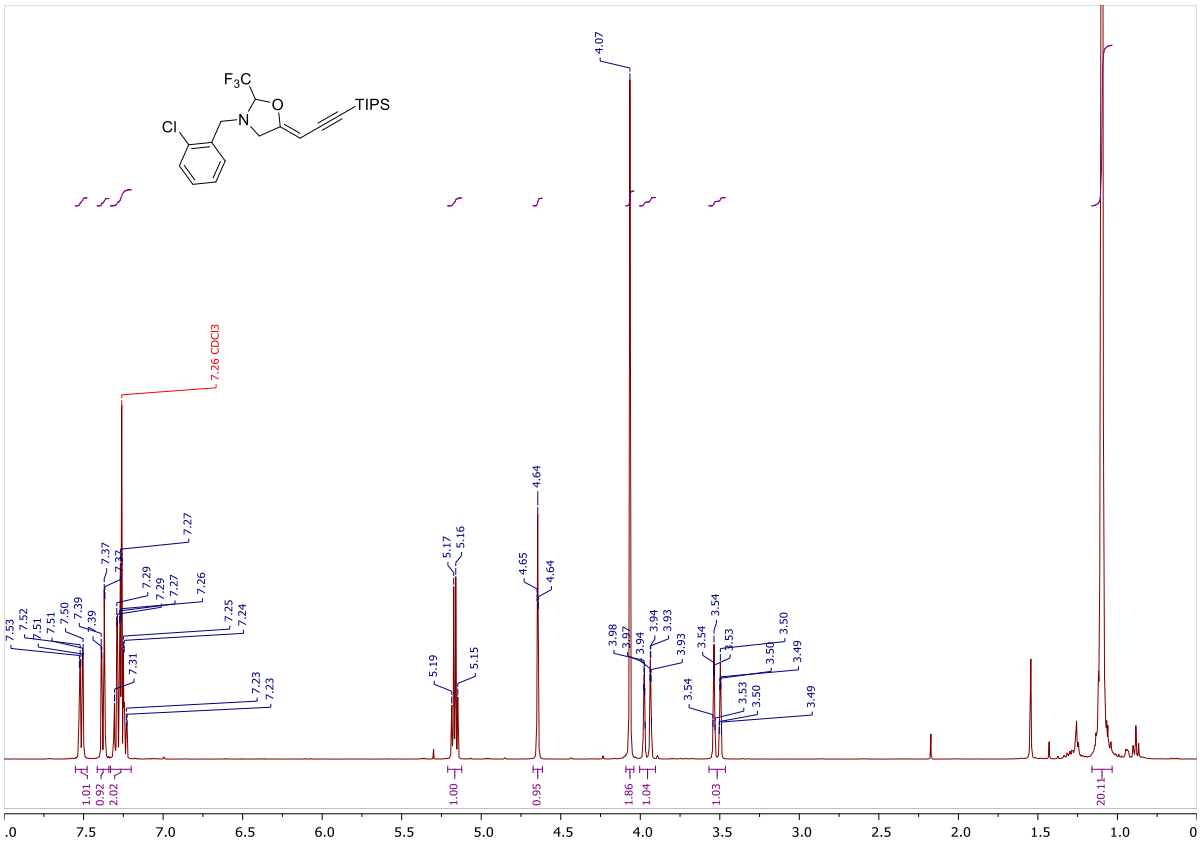


(Z)-3-(2-Chlorobenzyl)-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11d)

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



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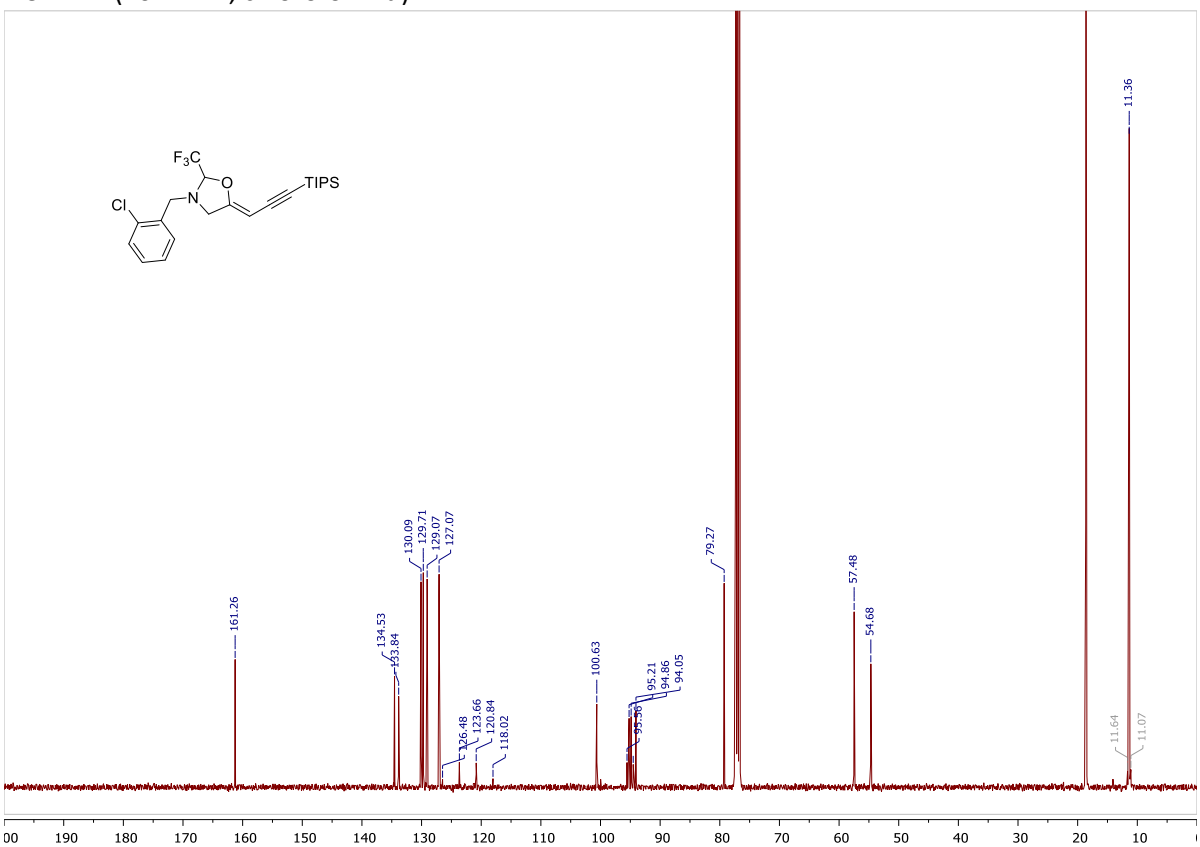
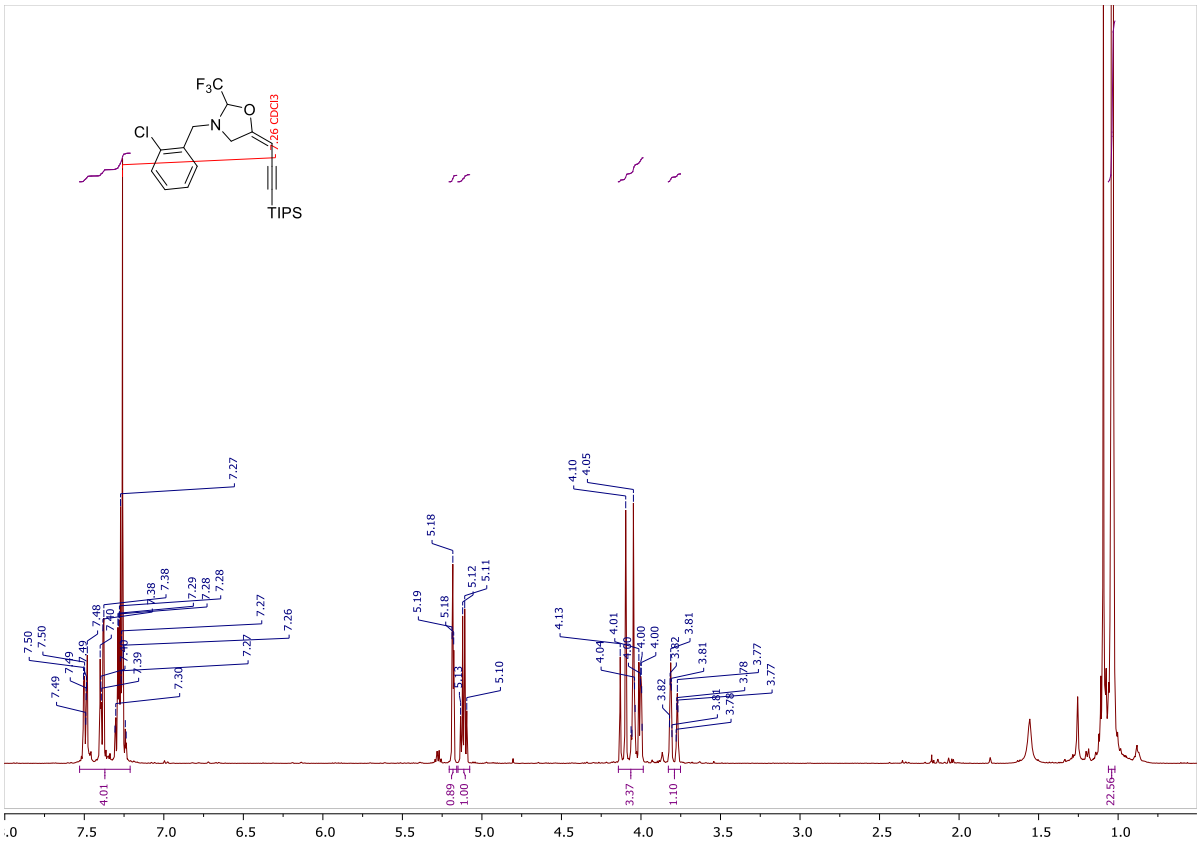


(E)-3-(2-Chlorobenzyl)-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11d)

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



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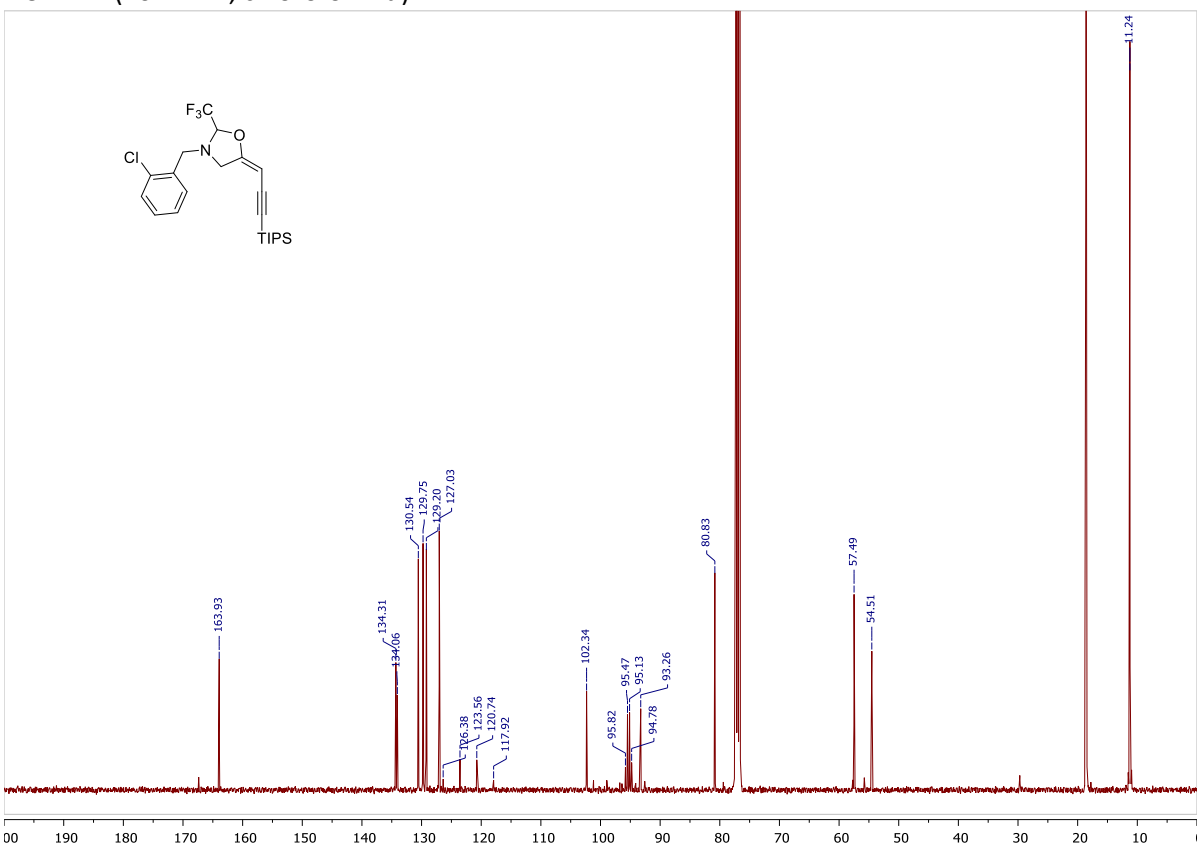
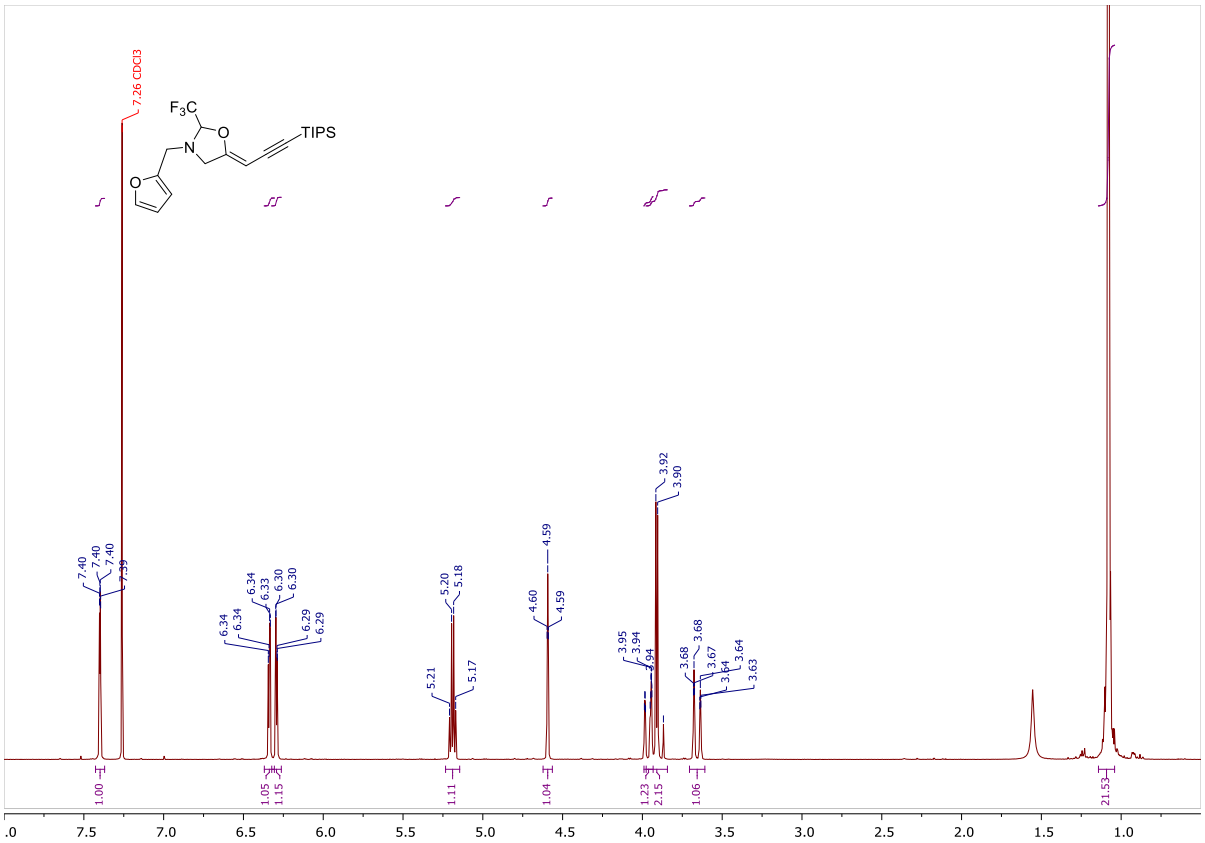
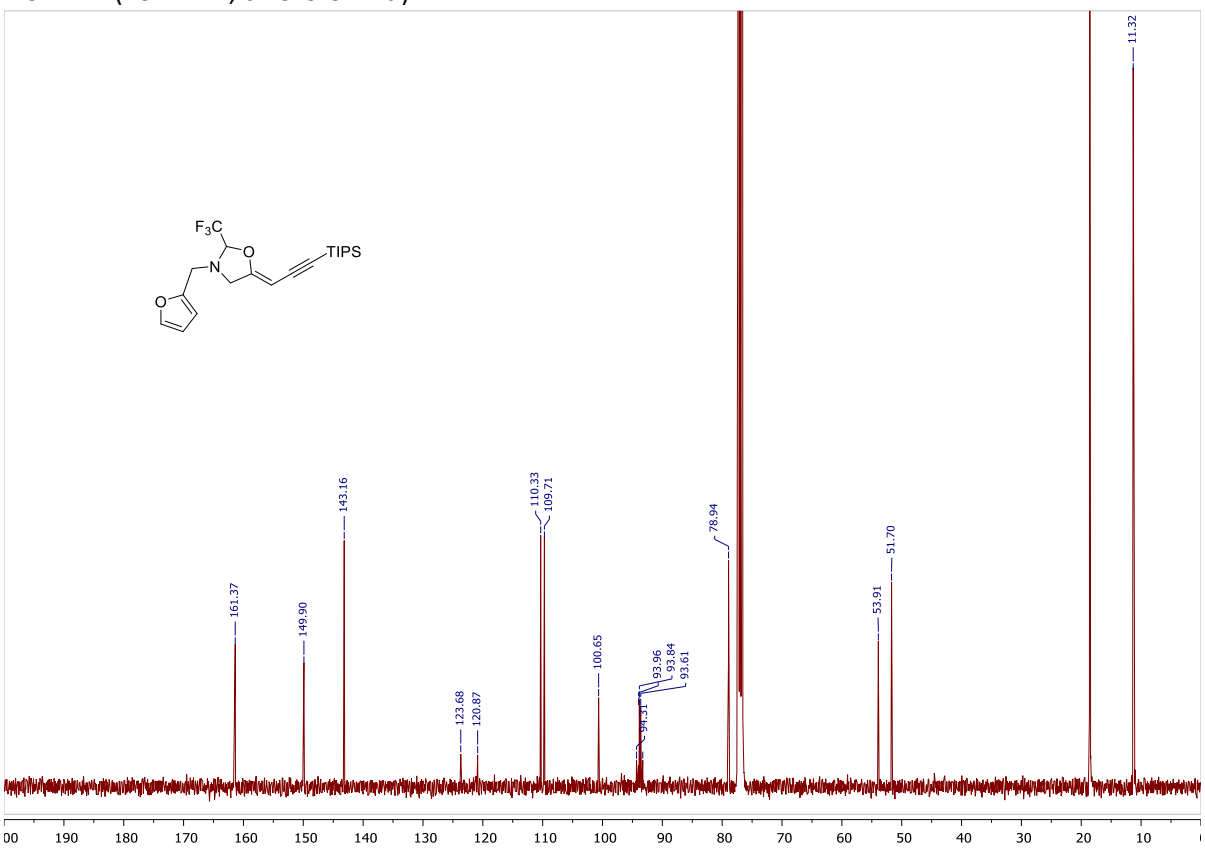


(Z)-3-(Furan-2-ylmethyl)-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11e)

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

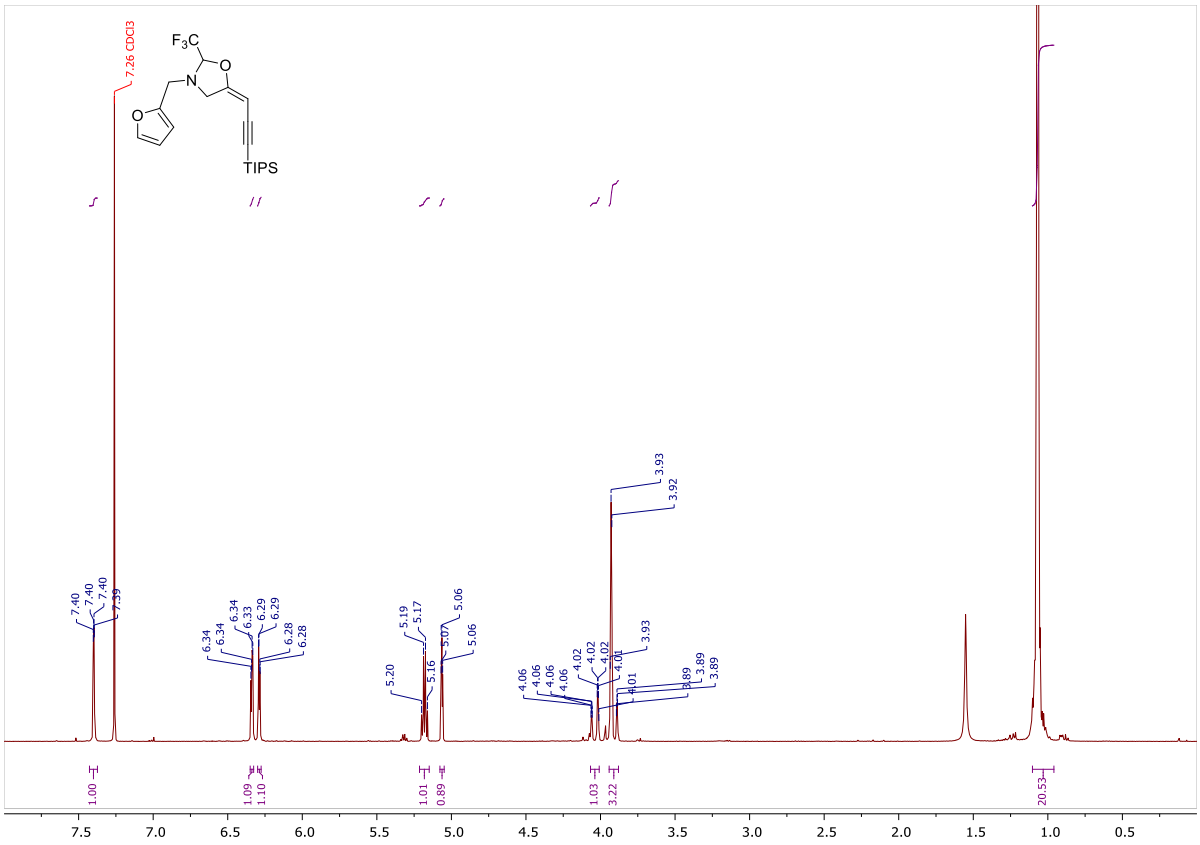


^{13}C-NMR (101 MHz, chloroform-*d*)

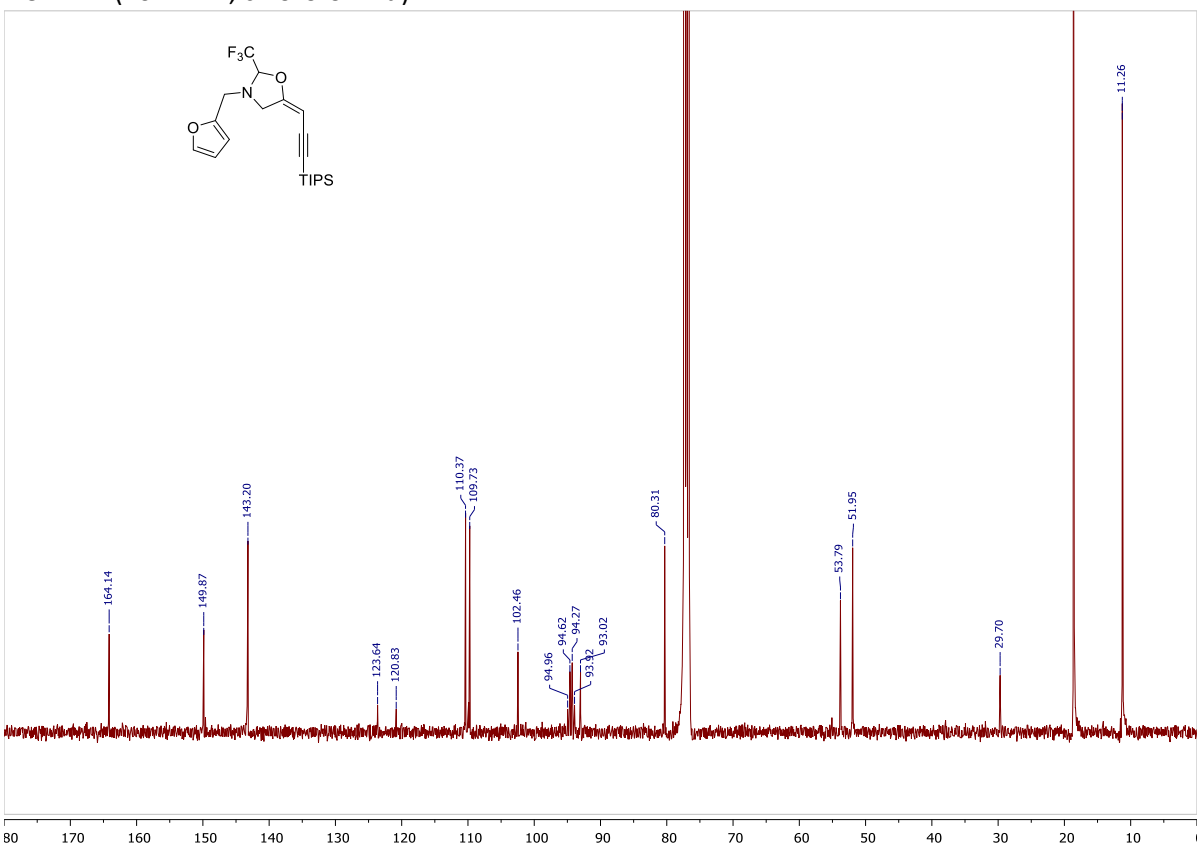


(E)-3-(Furan-2-ylmethyl)-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11e)

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

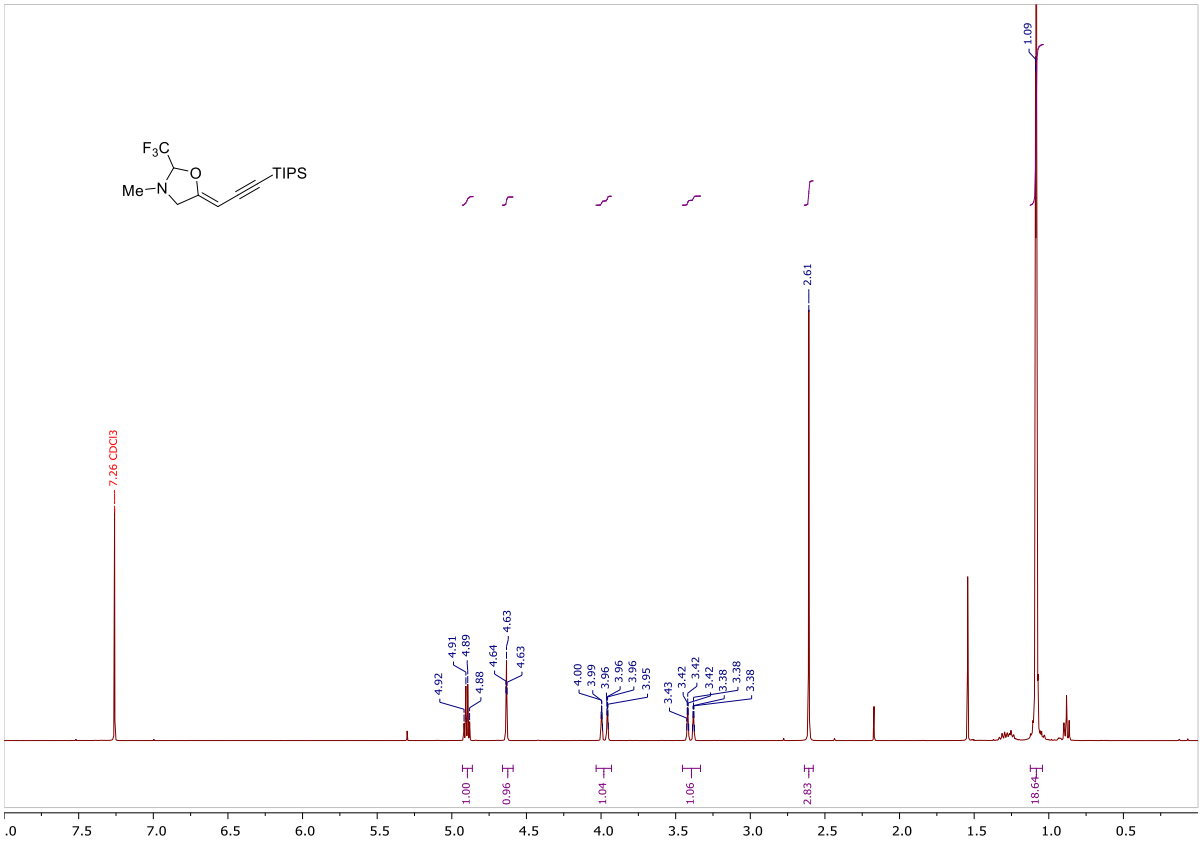


^{13}C-NMR (101 MHz, chloroform-*d*)

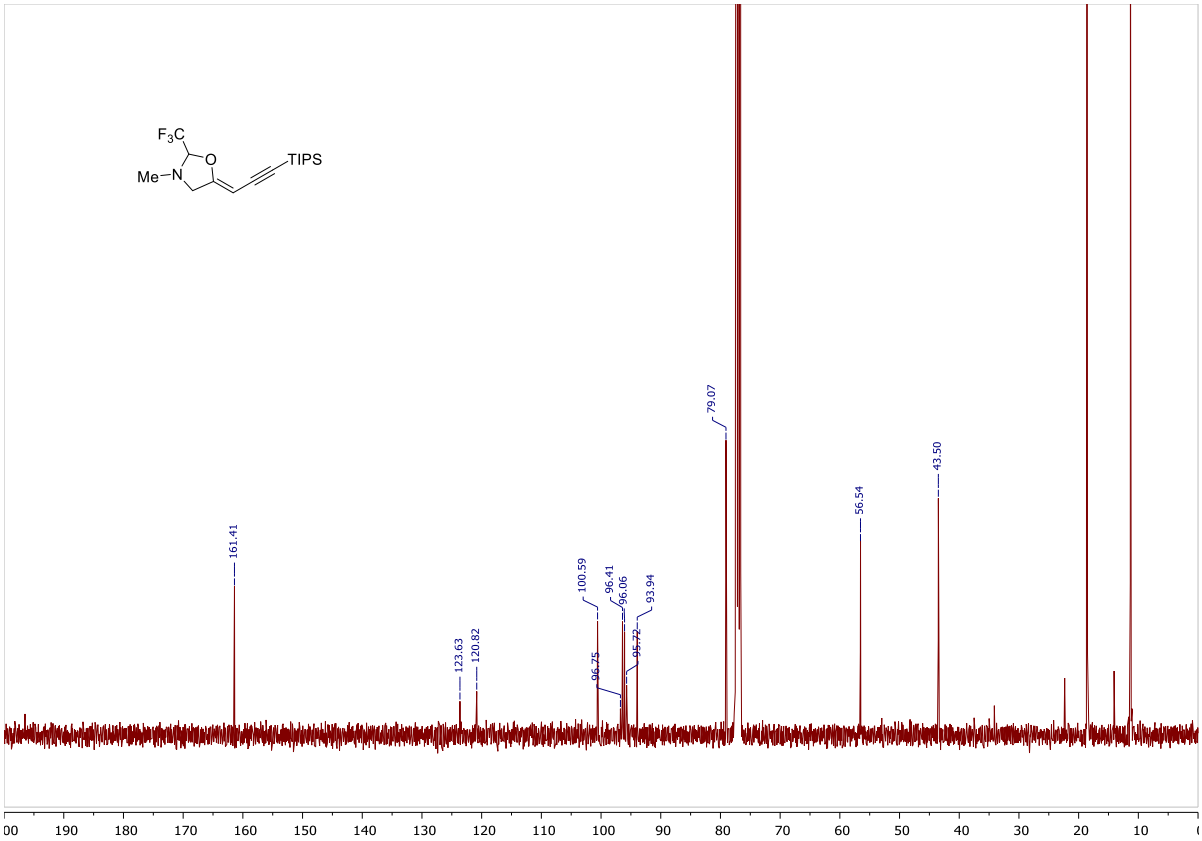


(Z)-3-Methyl-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11f)

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

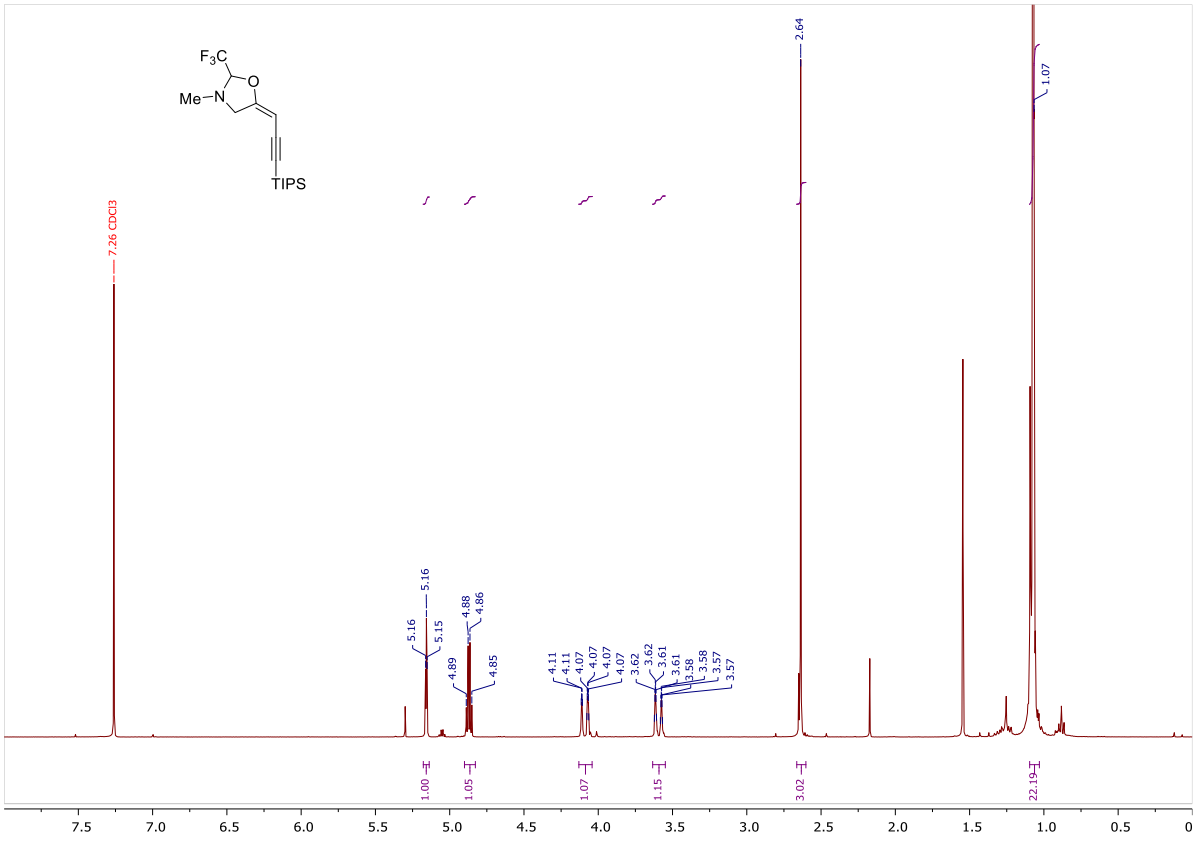


^{13}C-NMR (101 MHz, chloroform-*d*)

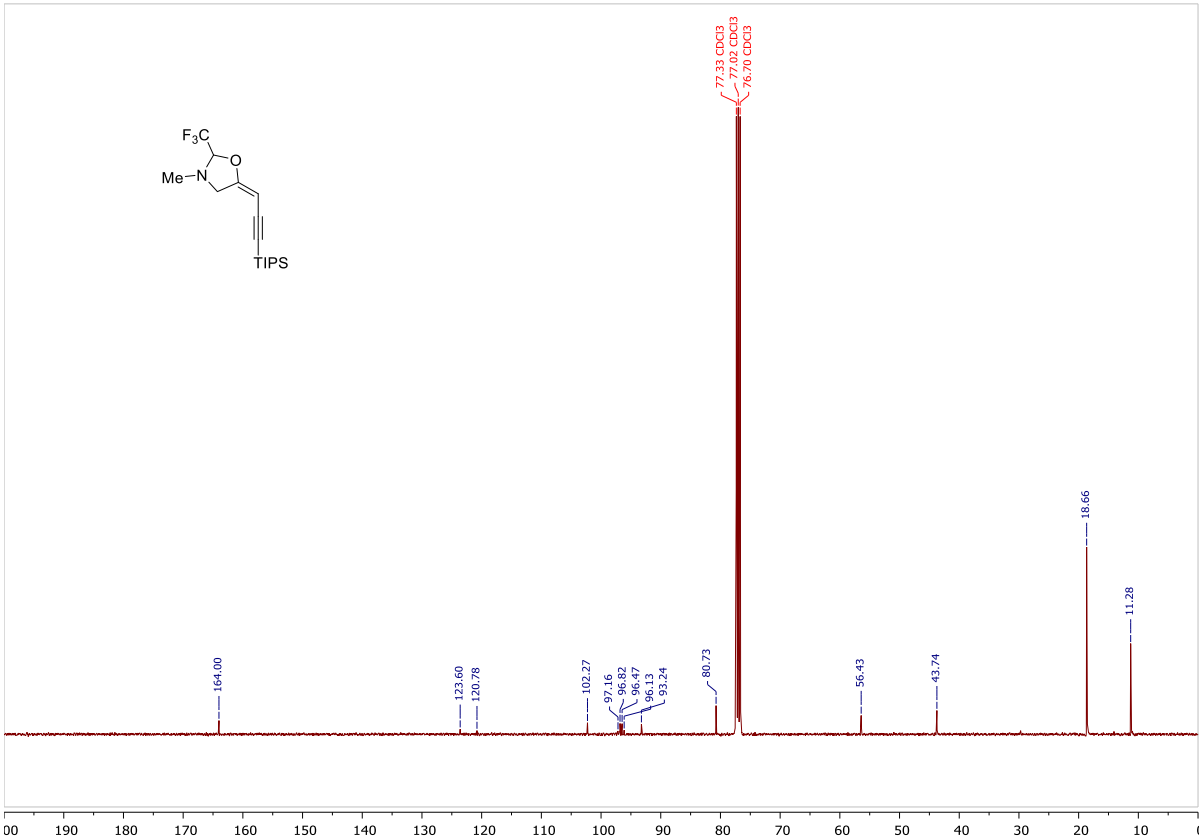


(E)-3-Methyl-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11f)

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

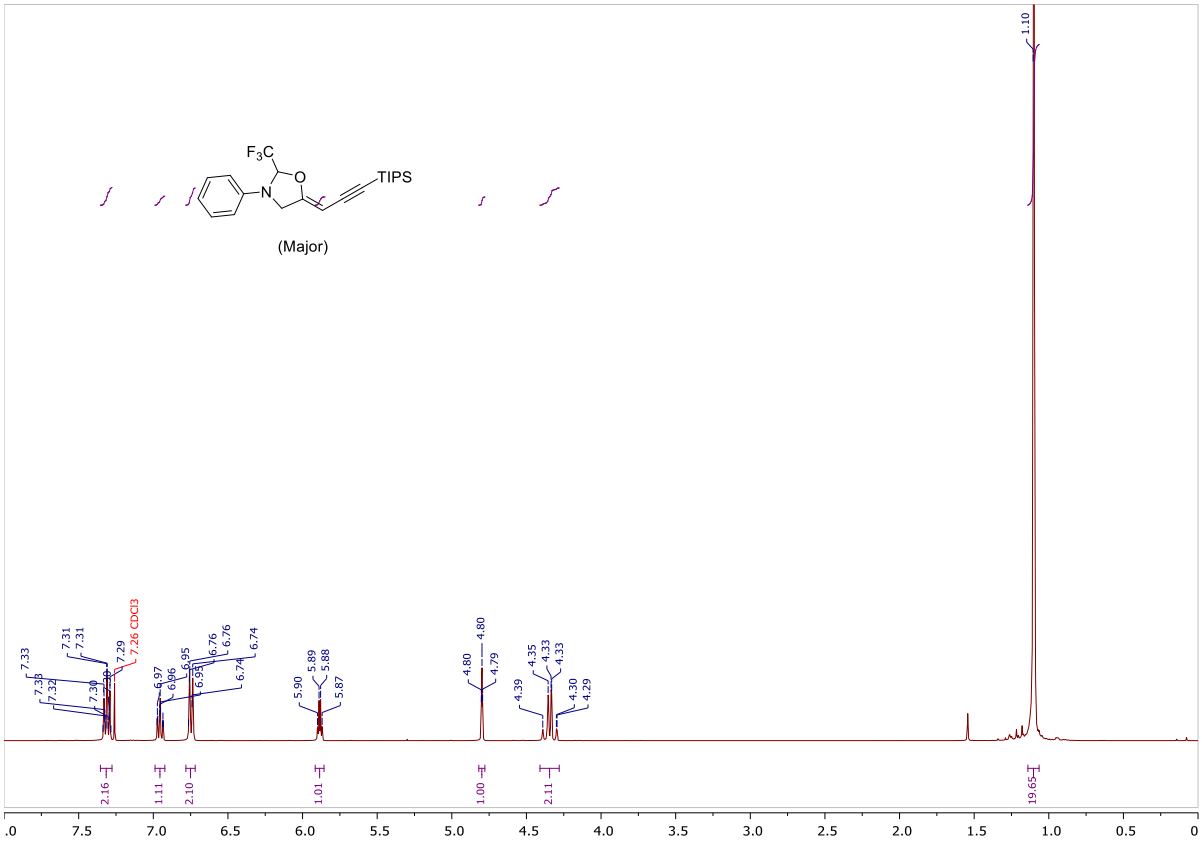


^{13}C-NMR (101 MHz, chloroform-*d*)

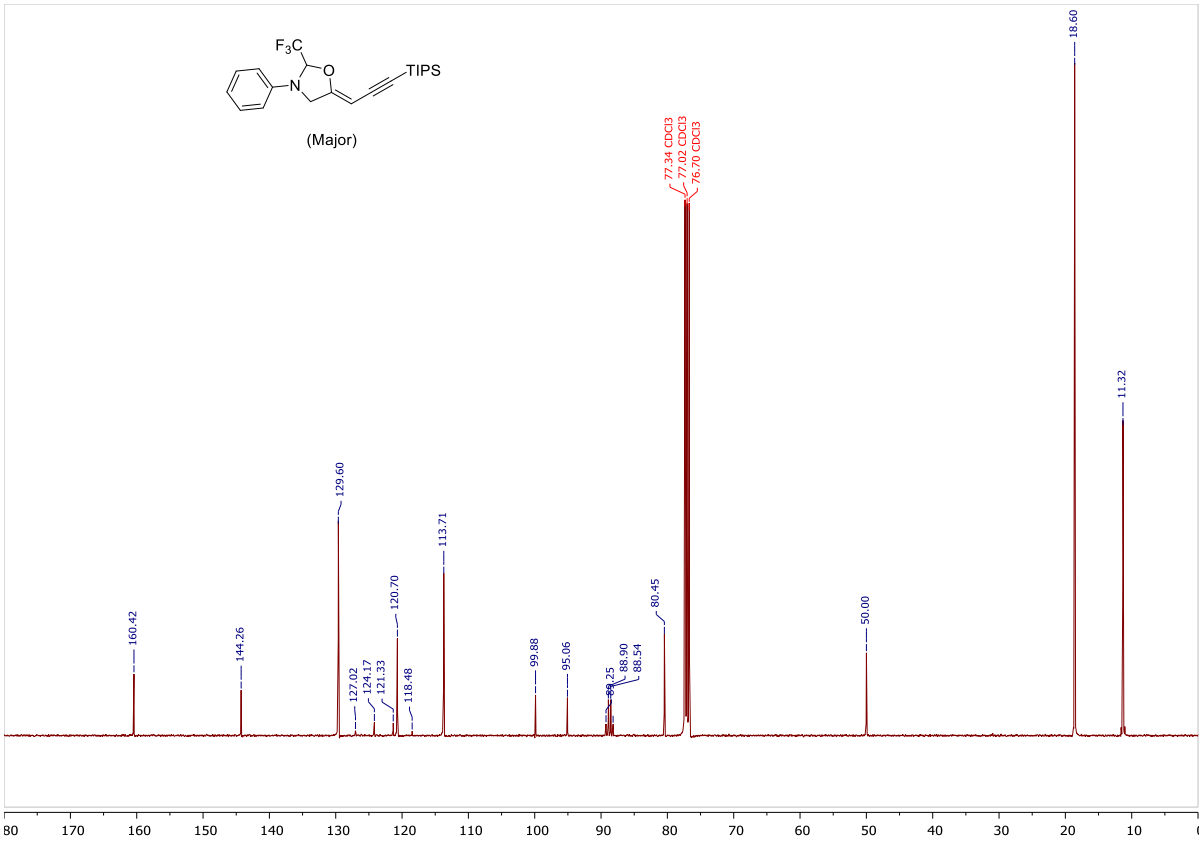


(Z)- -3-Phenyl-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11g)

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

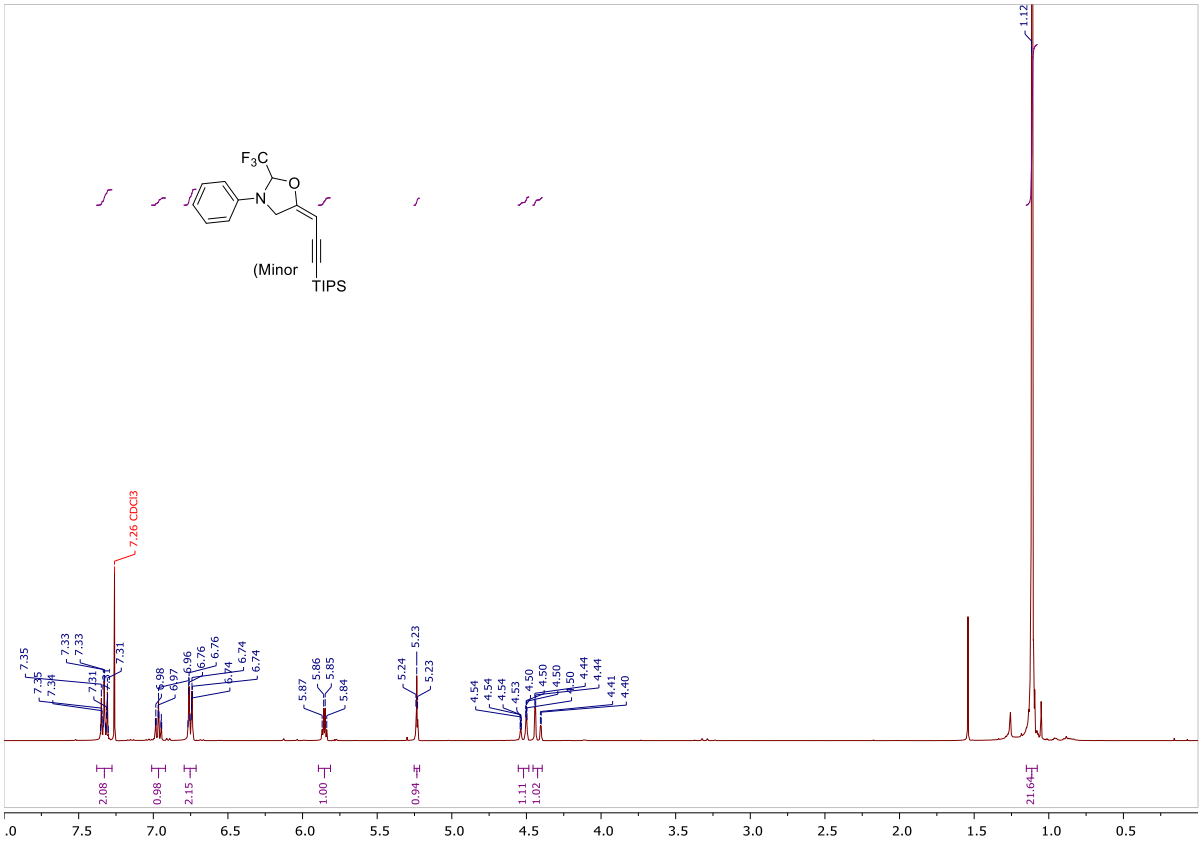


^{13}C-NMR (101 MHz, chloroform-*d*)

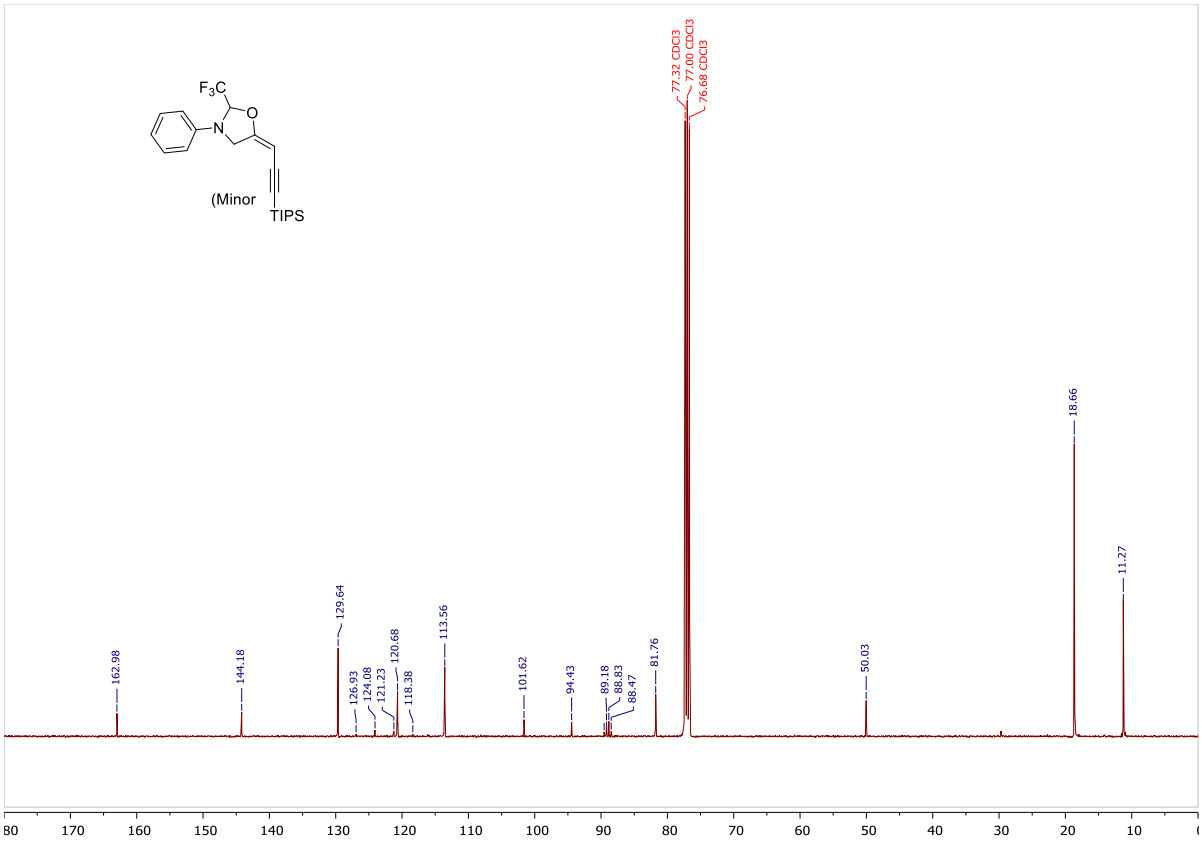


(E)-3-Phenyl-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11g)

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

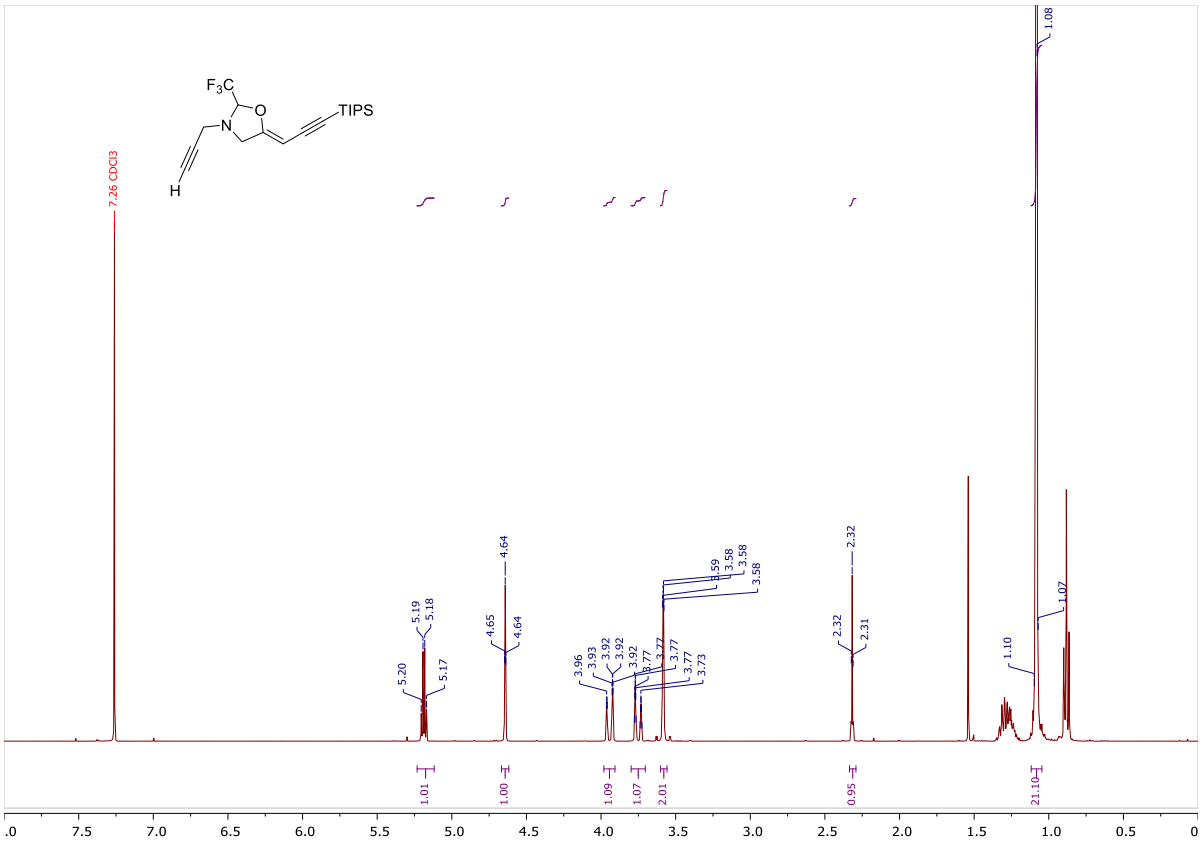


^{13}C-NMR (101 MHz, chloroform-*d*)

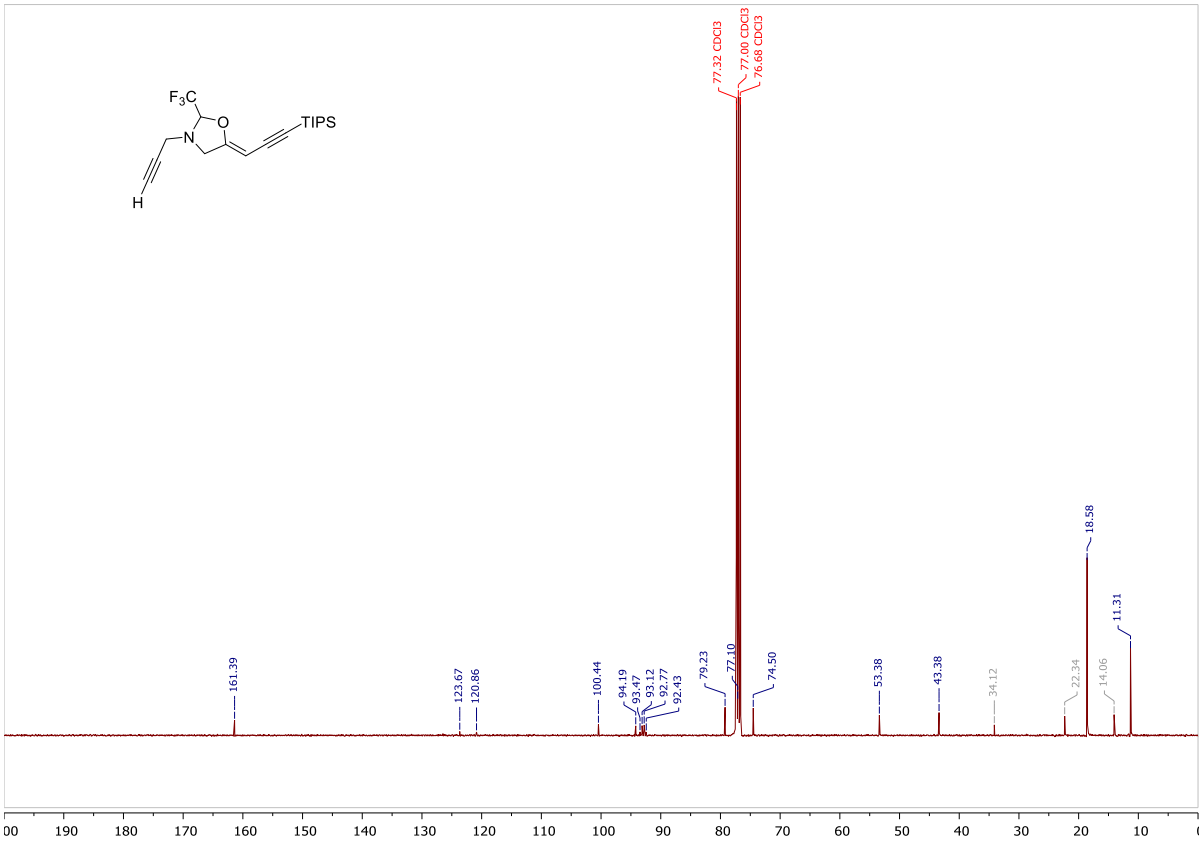


(Z)-3-(Prop-2-yn-1-yl)-2-(trifluoromethyl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (11h)

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

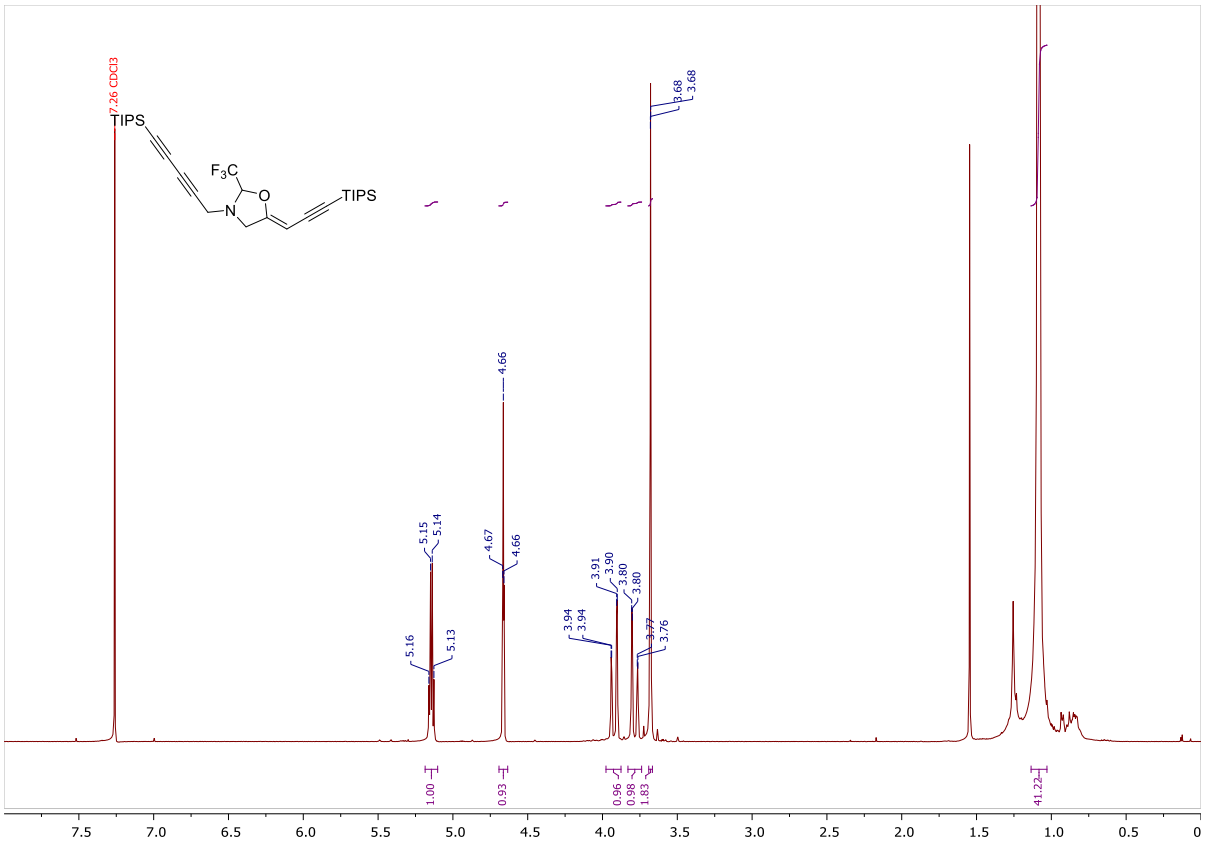


^{13}C-NMR (101 MHz, chloroform-*d*)

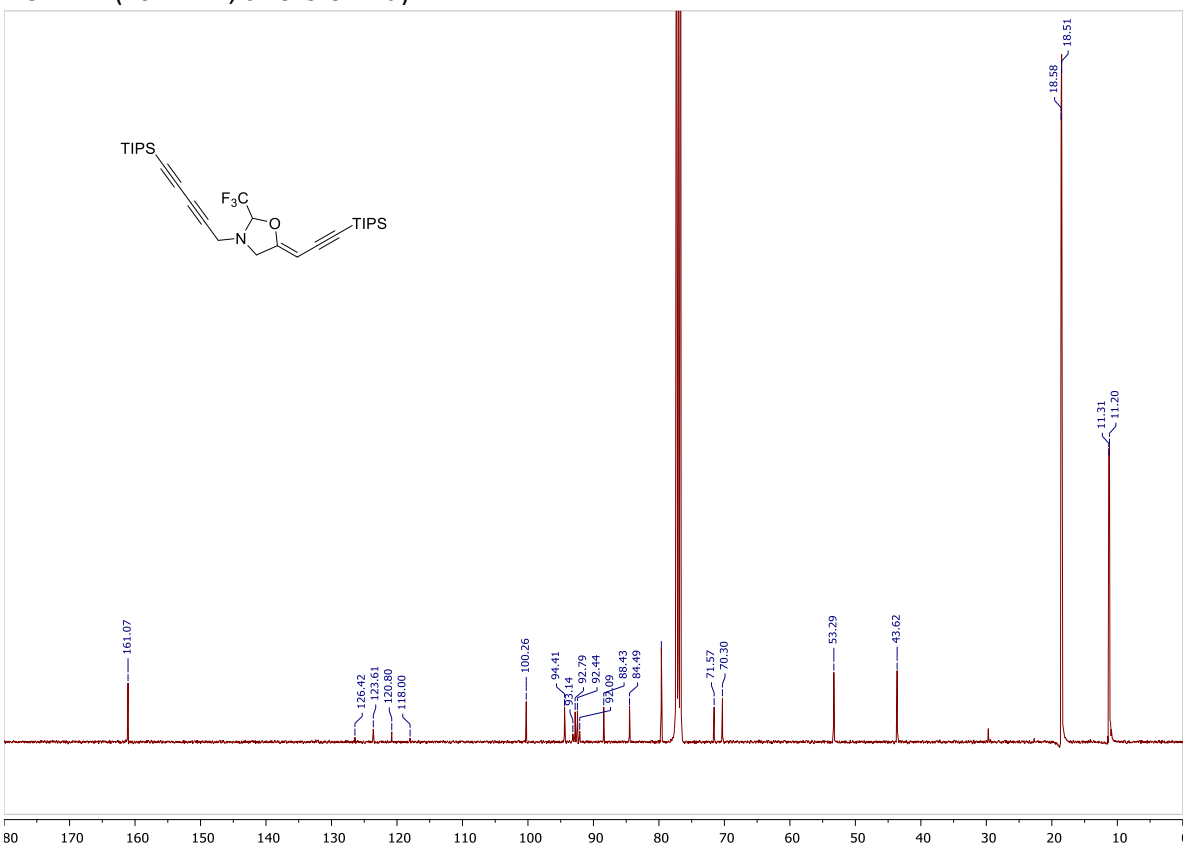


(Z)-2-(Trifluoromethyl)-3-(5-(tri*iso*propylsilyl)penta-2,4-diyn-1-yl)-5-(3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (13)

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

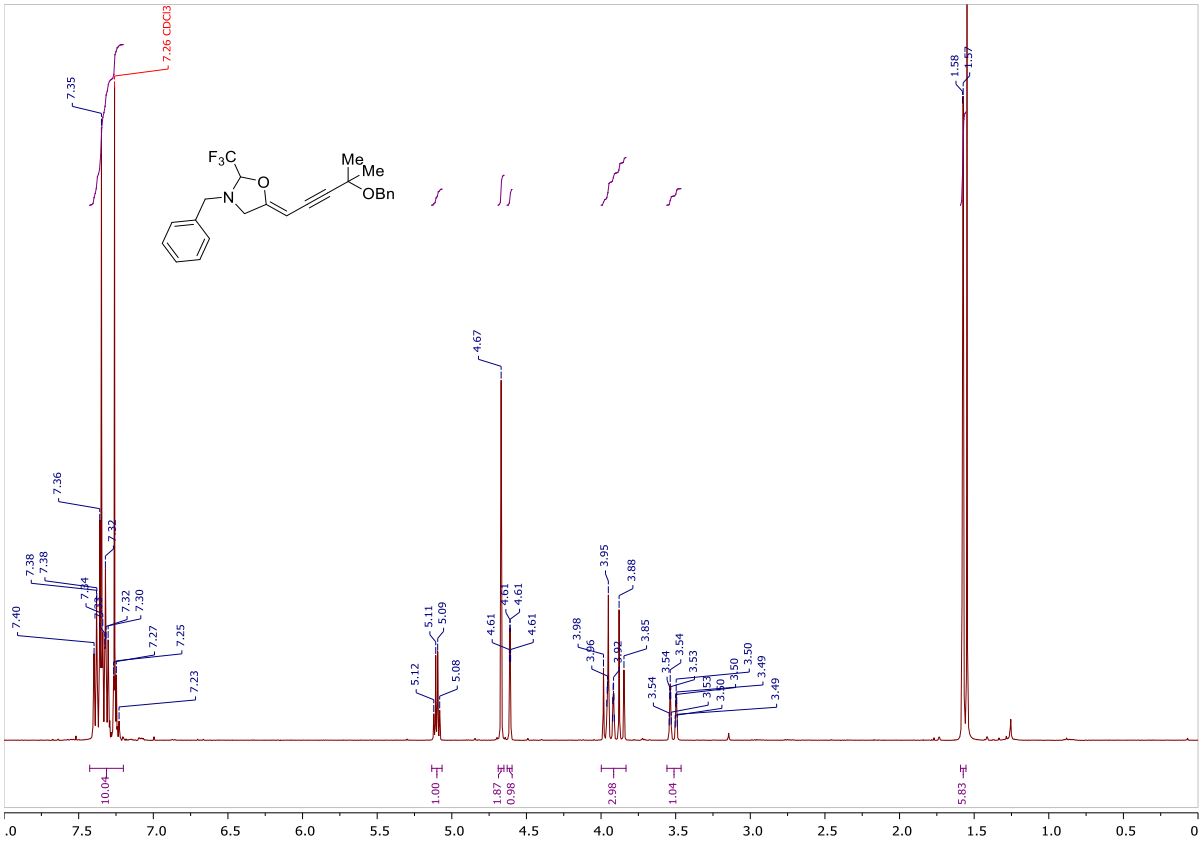


^{13}C-NMR (101 MHz, chloroform-*d*)

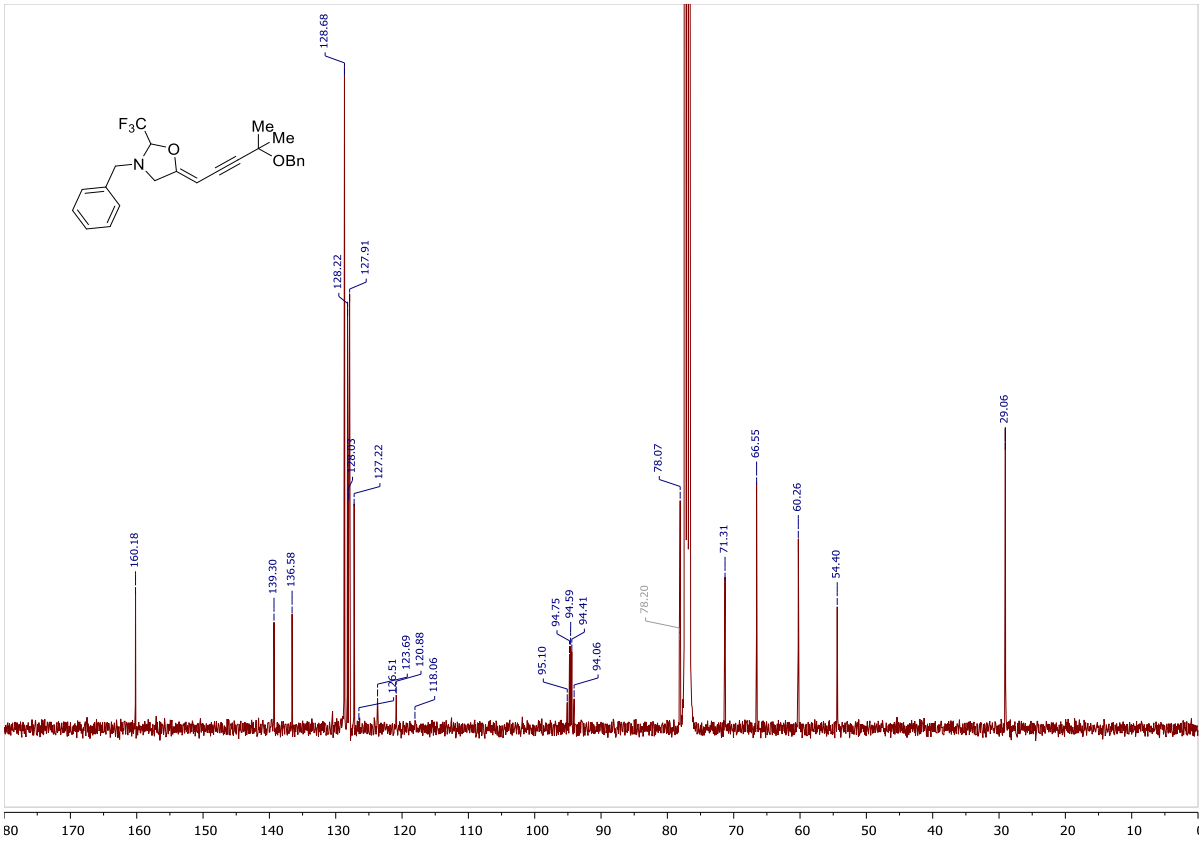


(Z)-3-Benzyl-5-(4-(benzyloxy)-4-methylpent-2-yn-1-ylidene)-2-(trifluoromethyl)oxazolidine (11i)

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

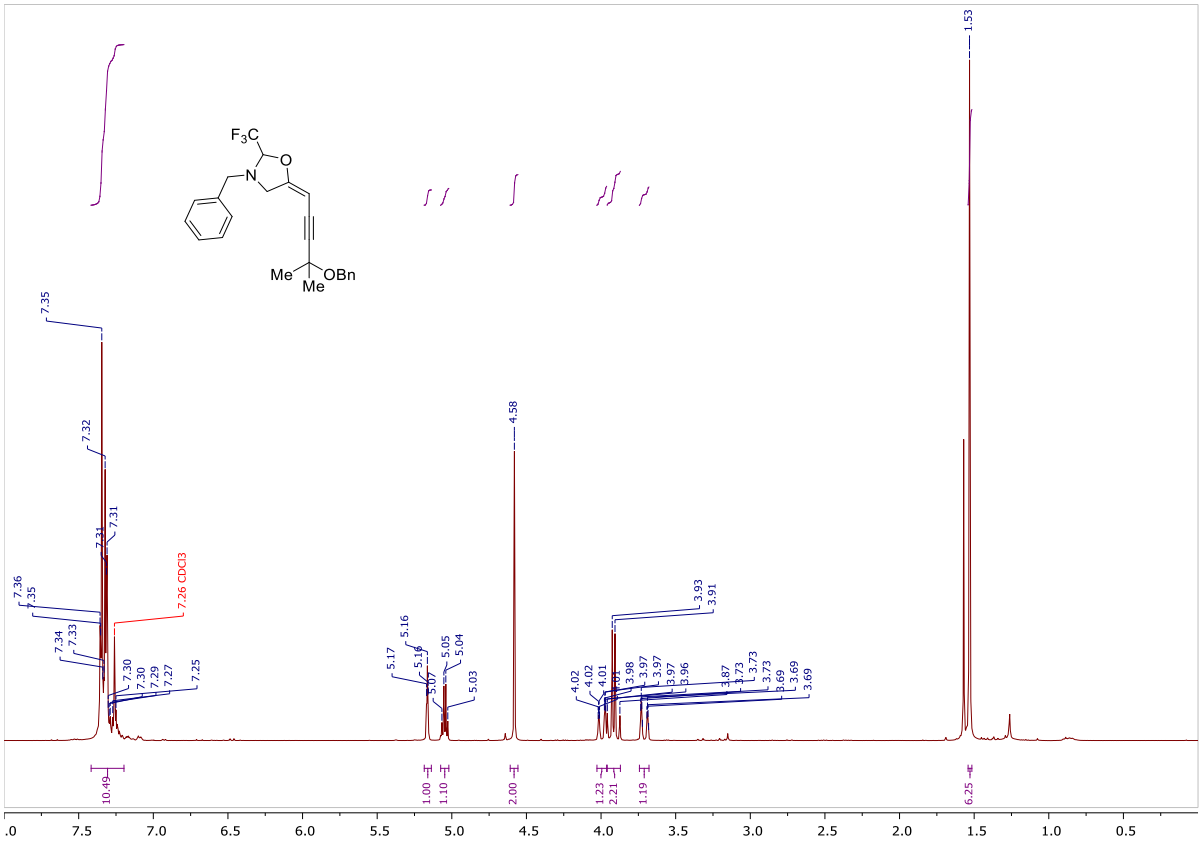


^{13}C-NMR (101 MHz, chloroform-*d*)

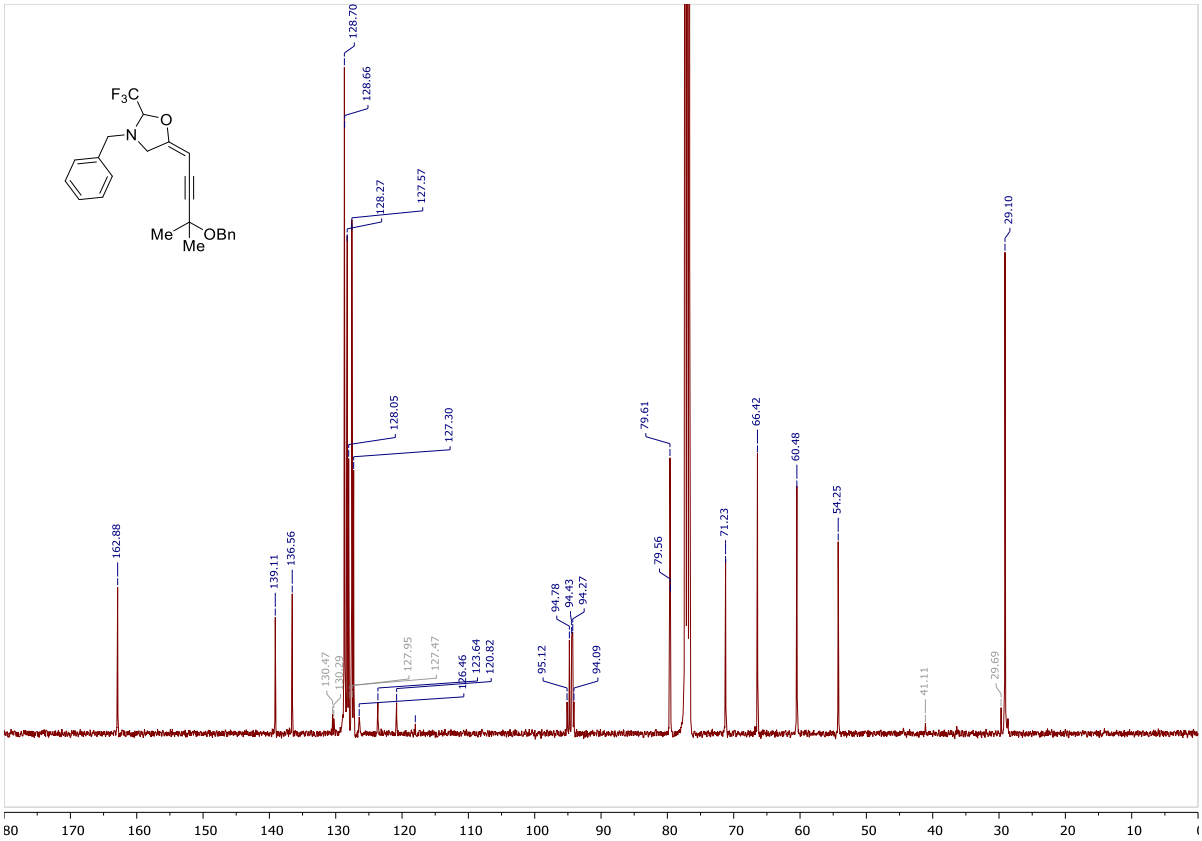


(E)-3-Benzyl-5-(4-(benzyloxy)-4-methylpent-2-yn-1-ylidene)-2-(trifluoromethyl)oxazolidine (11i)

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

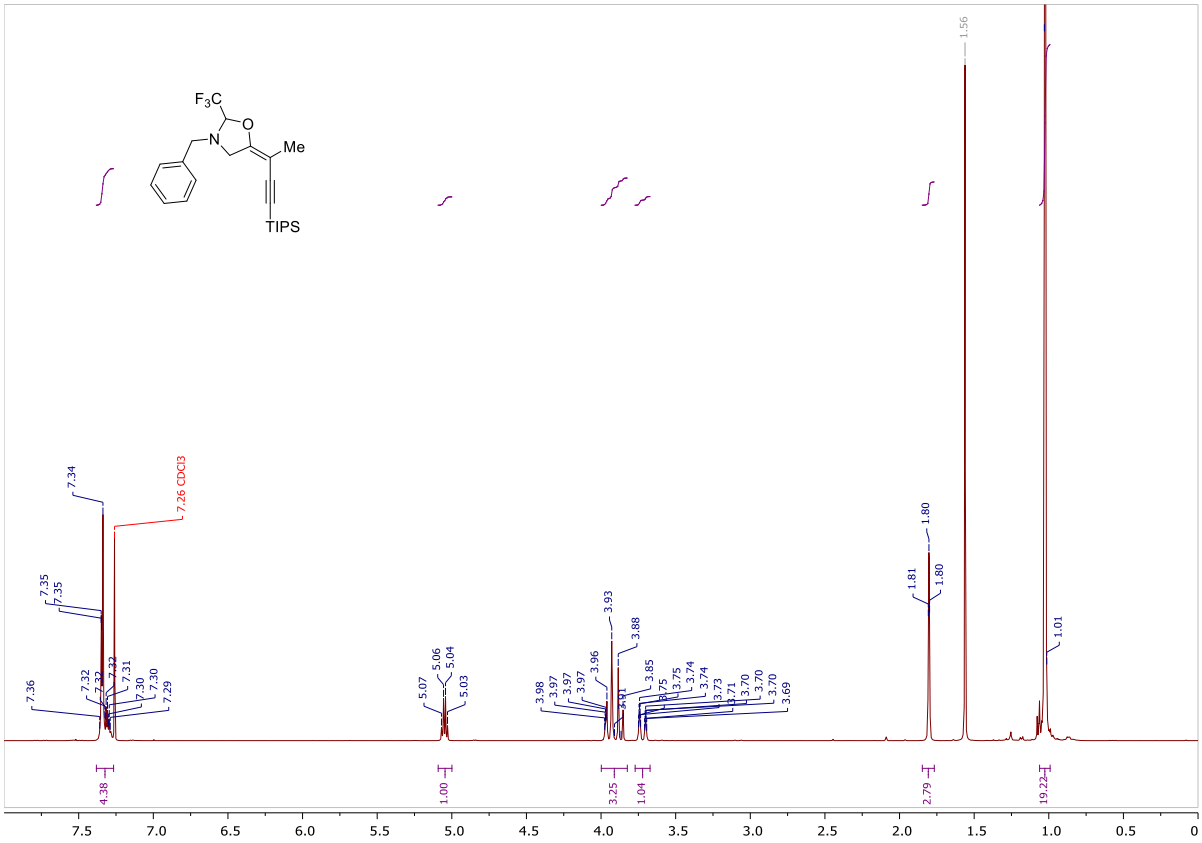


^{13}C-NMR (101 MHz, chloroform-*d*)

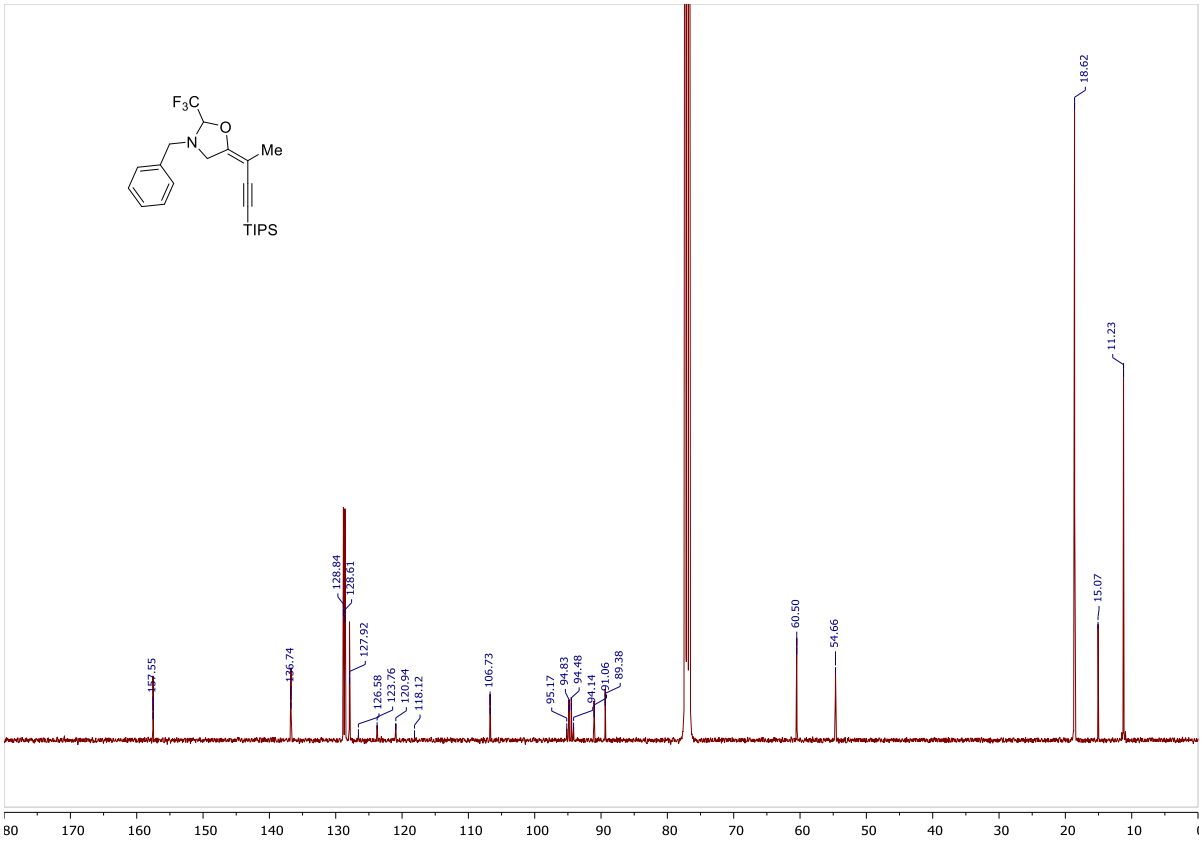


(E)-3-Benzyl-2-(trifluoromethyl)-5-(4-(tri*iso*propylsilyl)but-3-yn-2-ylidene)oxazolidine (12a)

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

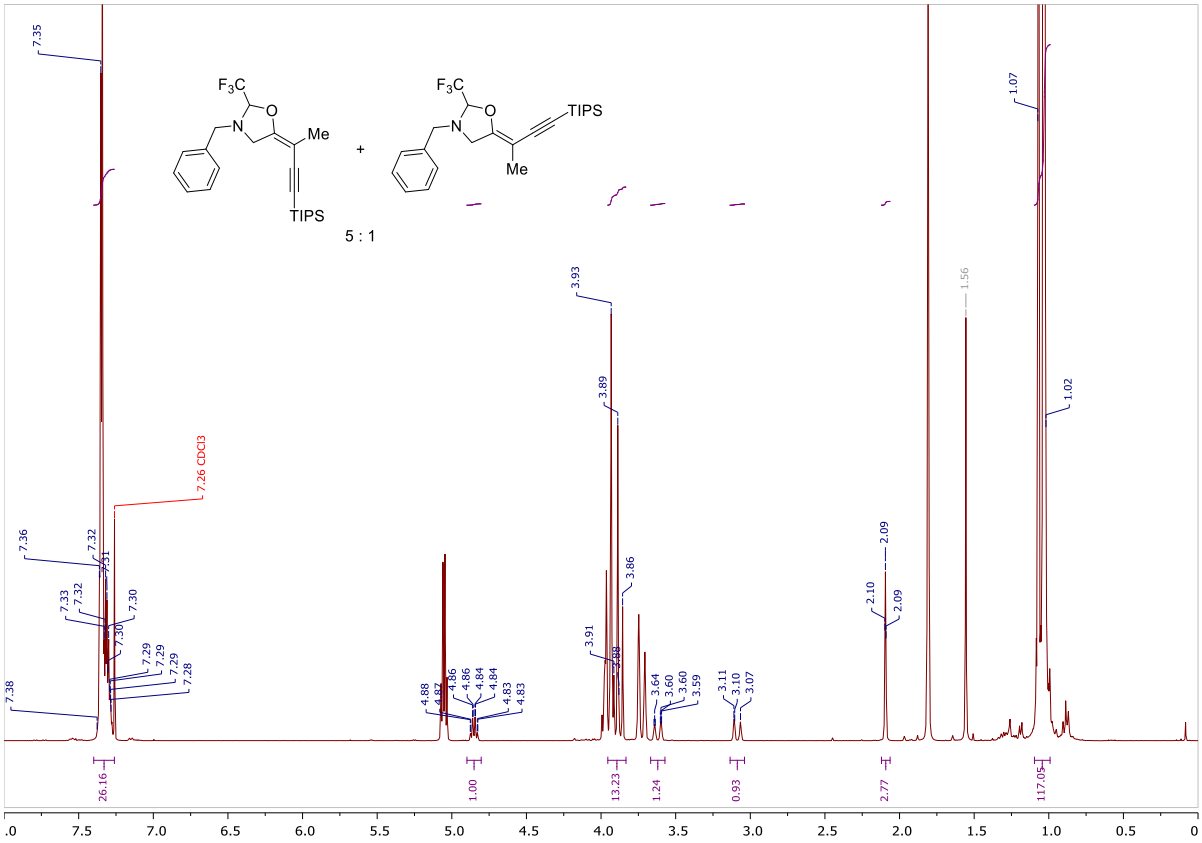


^{13}C-NMR (101 MHz, chloroform-*d*)

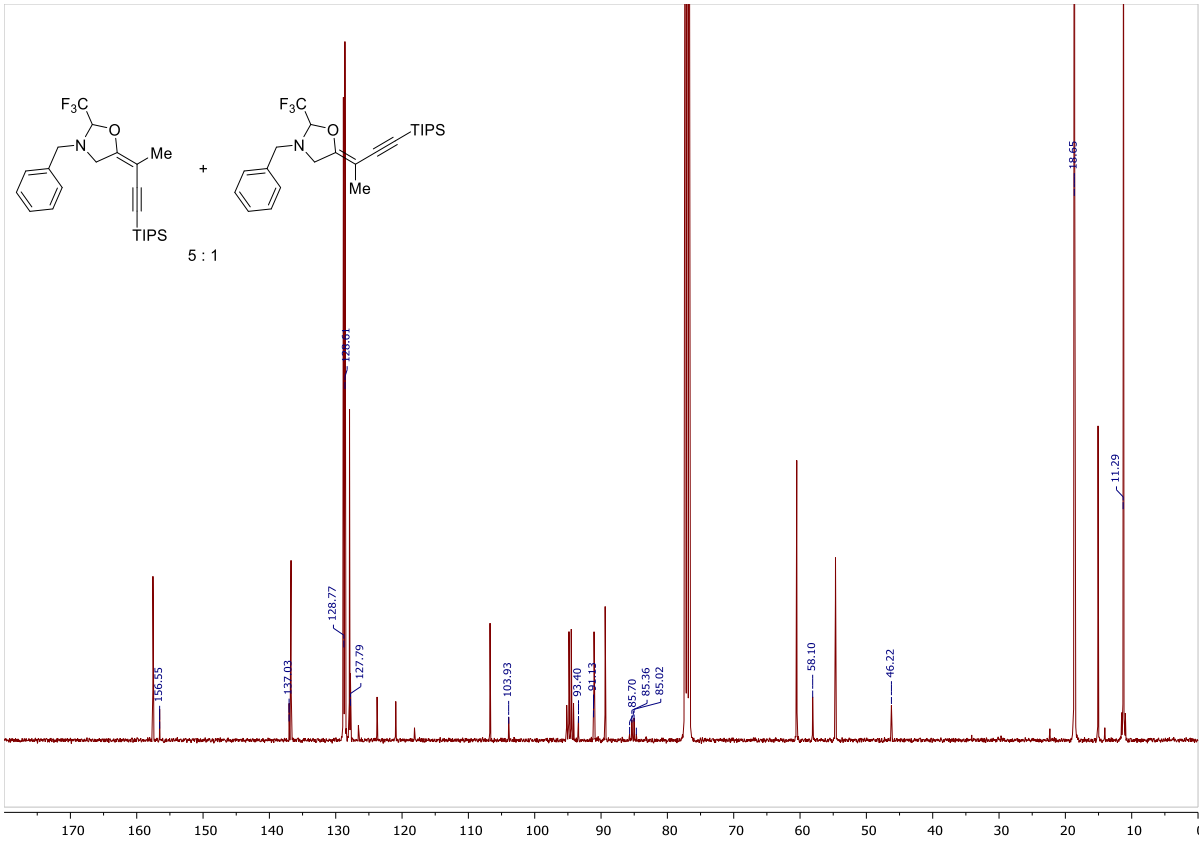


(E)- and (Z)-3-Benzyl-2-(trifluoromethyl)-5-(4-(tri*iso*propylsilyl)but-3-yn-2-ylidene)oxazolidine (12a)

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

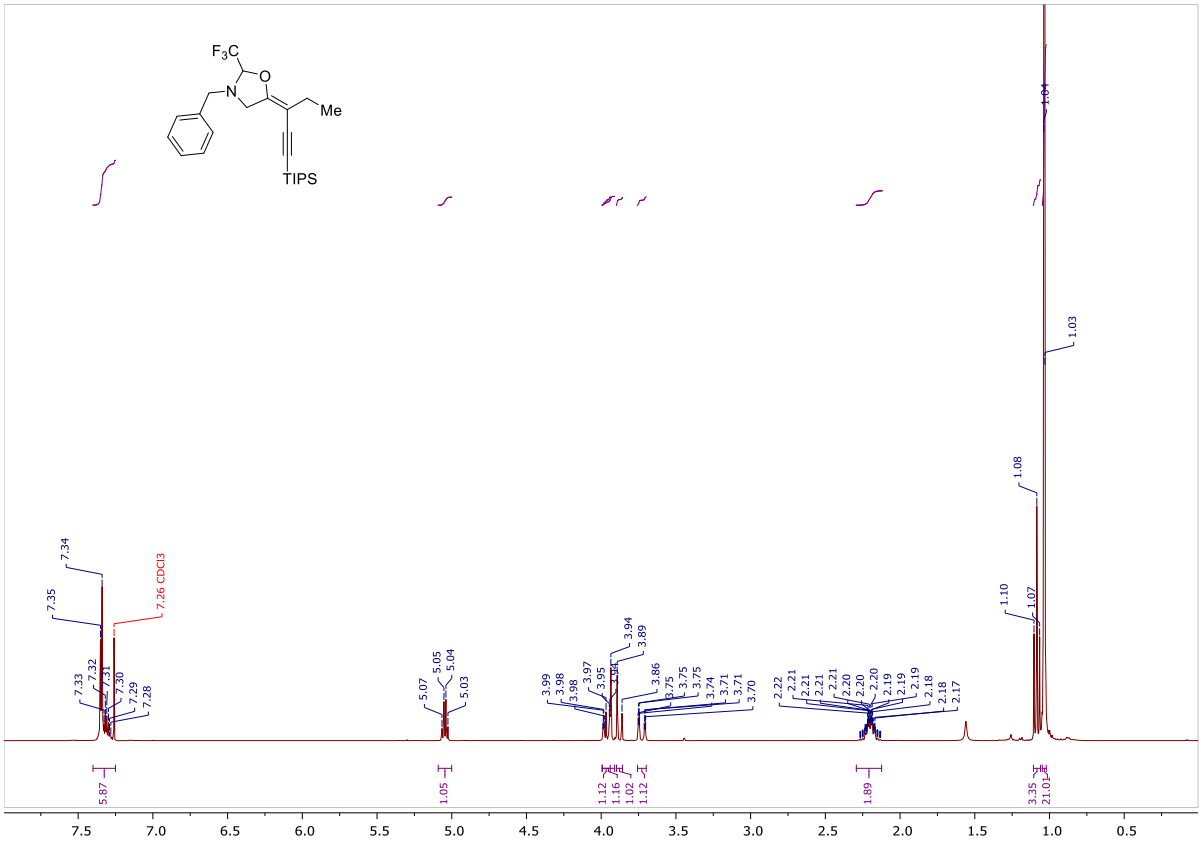


^{13}C-NMR (101 MHz, chloroform-*d*)

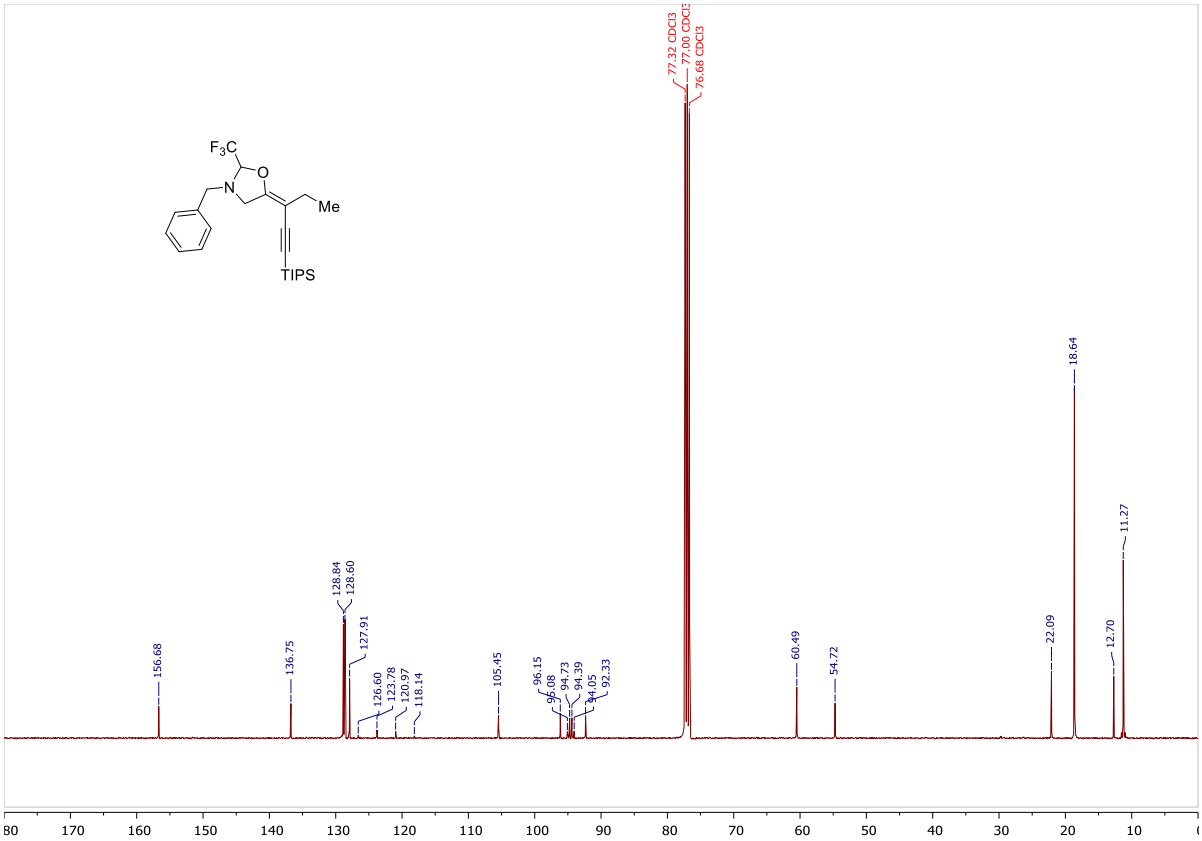


(E)-3-Benzyl-2-(trifluoromethyl)-5-(1-(tri*iso*propylsilyl)pent-1-yn-3-ylidene)oxazolidine (12b)

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

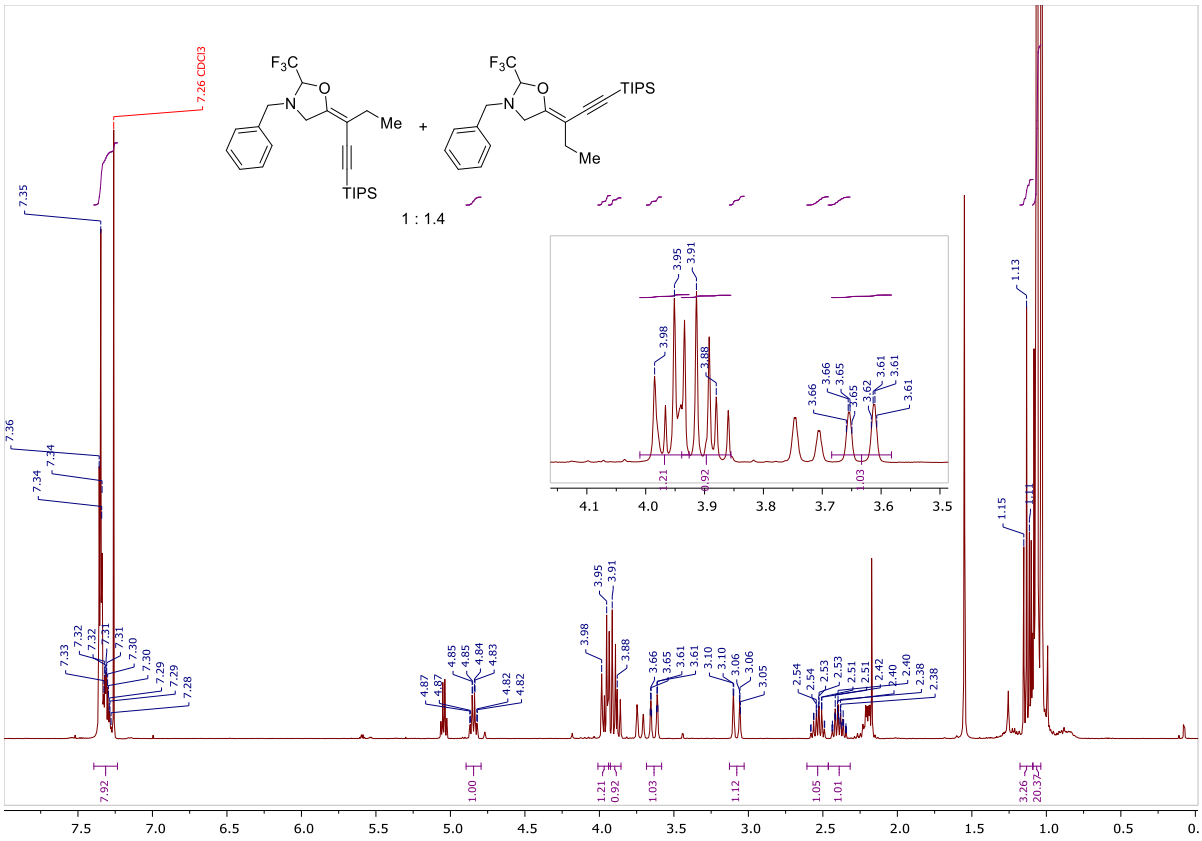


^{13}C-NMR (101 MHz, chloroform-*d*)

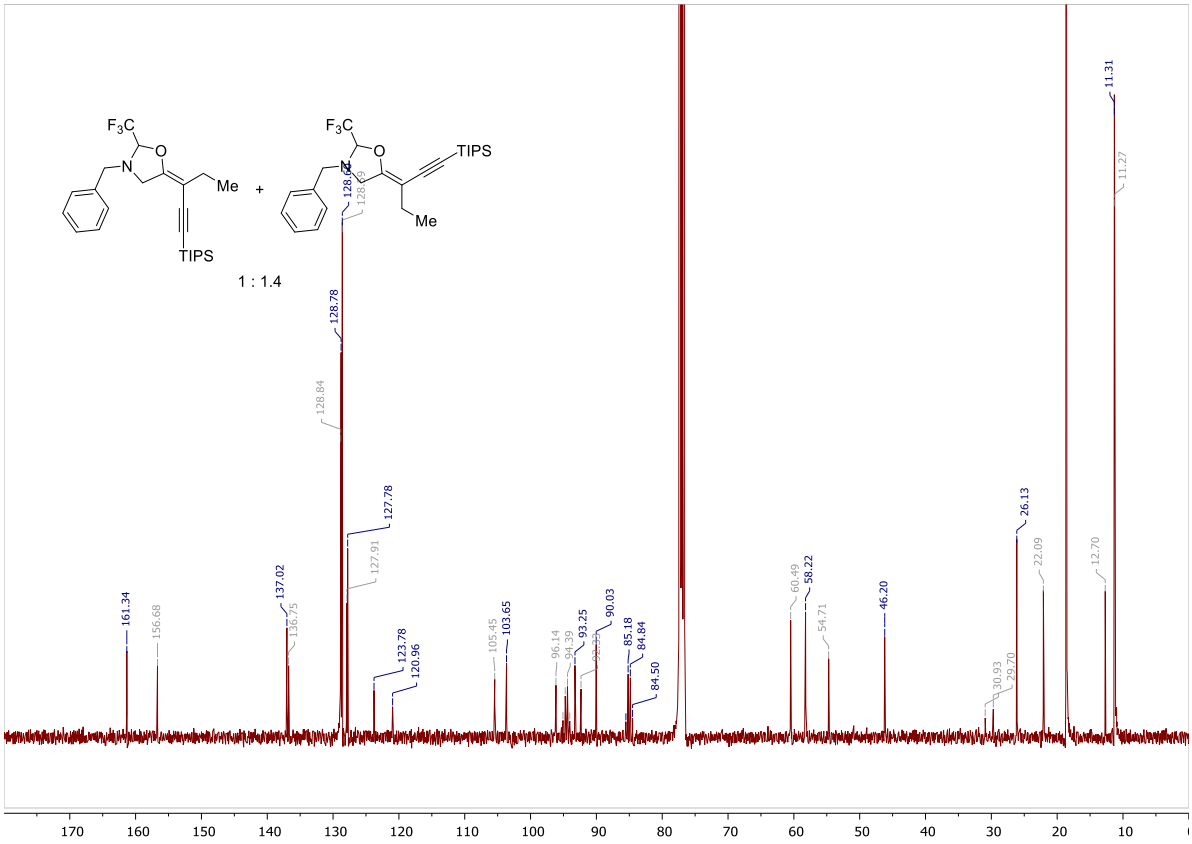


(E)- and (Z)-3-Benzyl-2-(trifluoromethyl)-5-(1-(tri*iso*propylsilyl)pent-1-yn-3-ylidene)oxazolidine (12b)

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

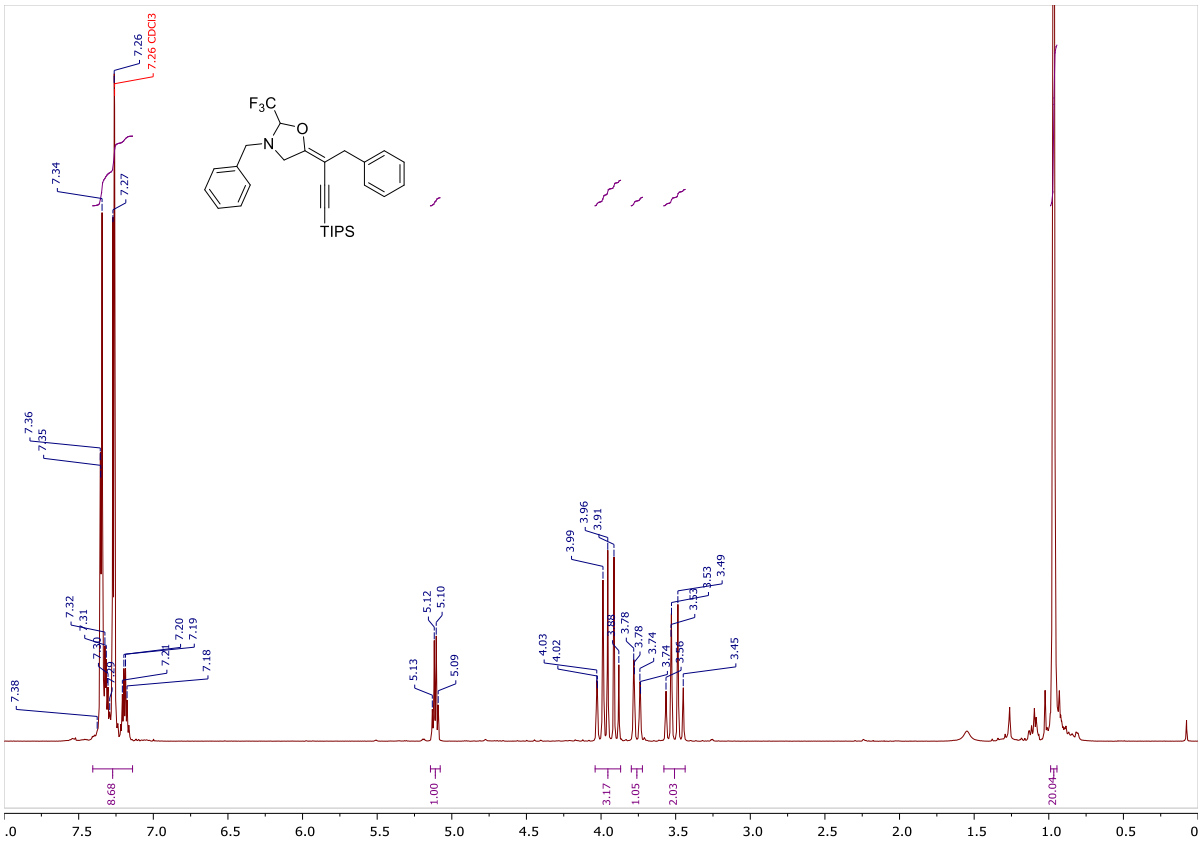


^{13}C-NMR (101 MHz, chloroform-*d*)

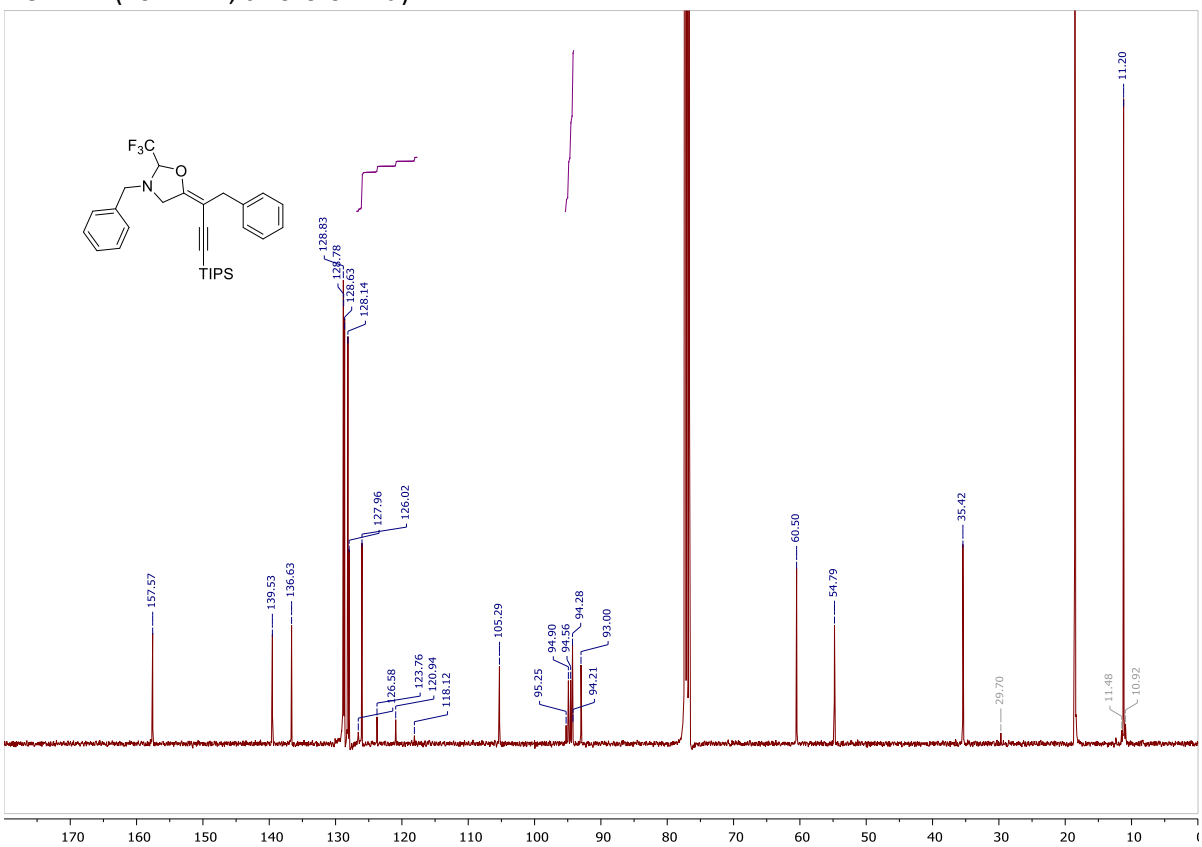


(E)-3-Benzyl-5-(1-phenyl-4-(tri*iso*propylsilyl)but-3-yn-2-ylidene)-2-(trifluoromethyl)oxazolidine (12c)

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

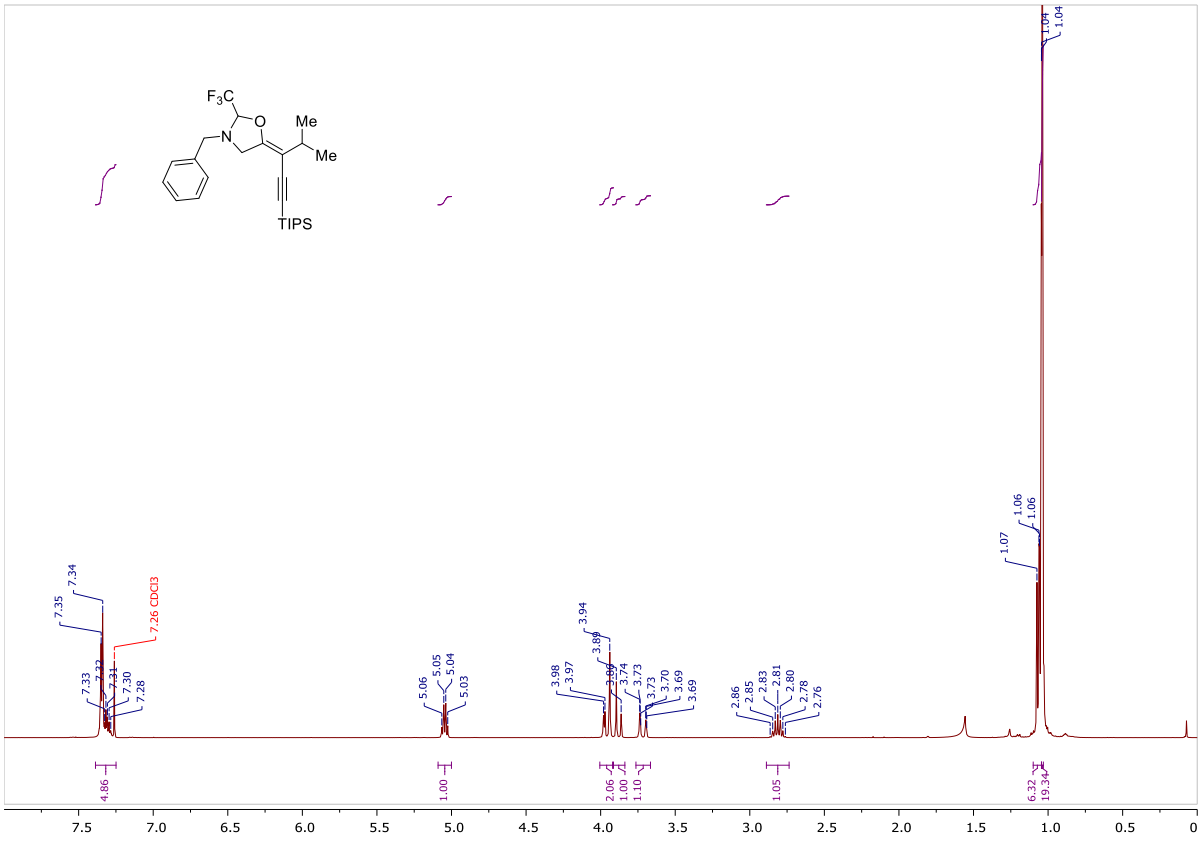


^{13}C-NMR (101 MHz, chloroform-*d*)

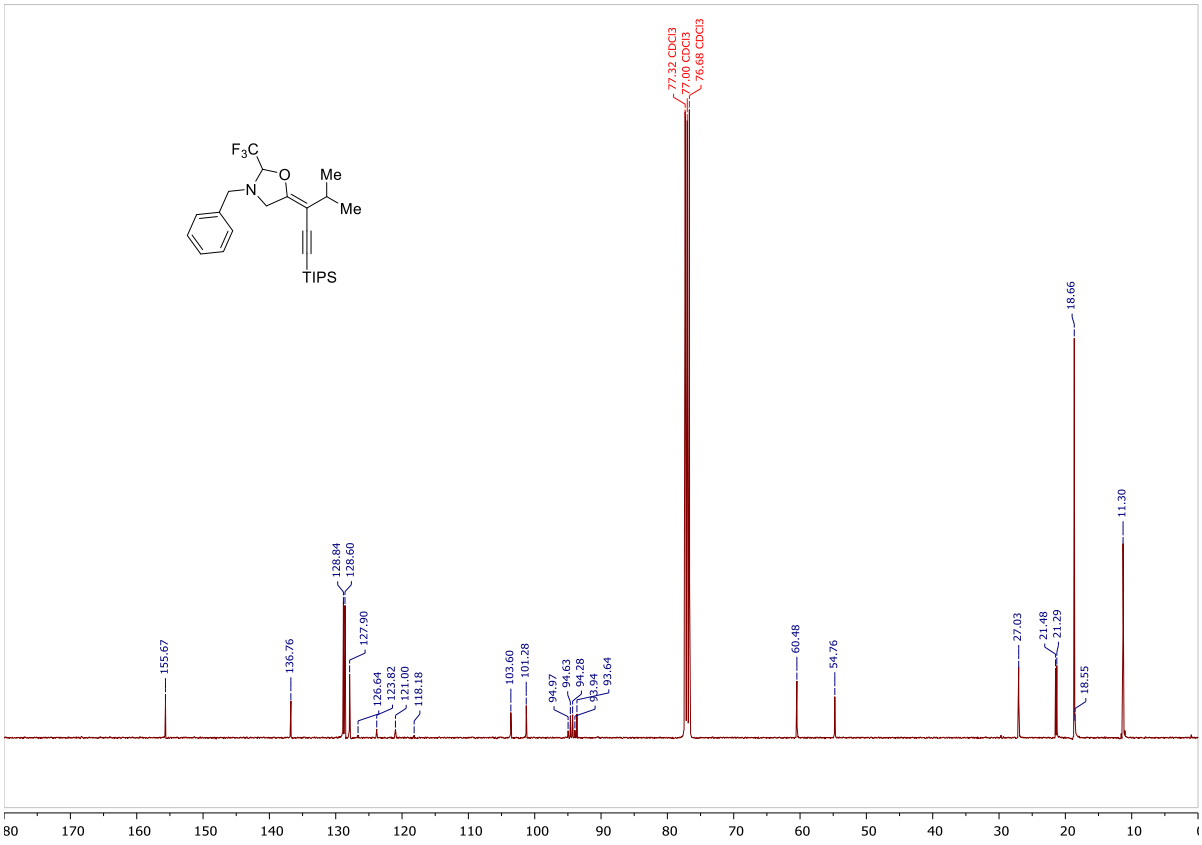


(E)-3-Benzyl-5-(4-methyl-1-(tri*iso*propylsilyl)pent-1-yn-3-ylidene)-2-(trifluoromethyl)oxazolidine (12d)

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

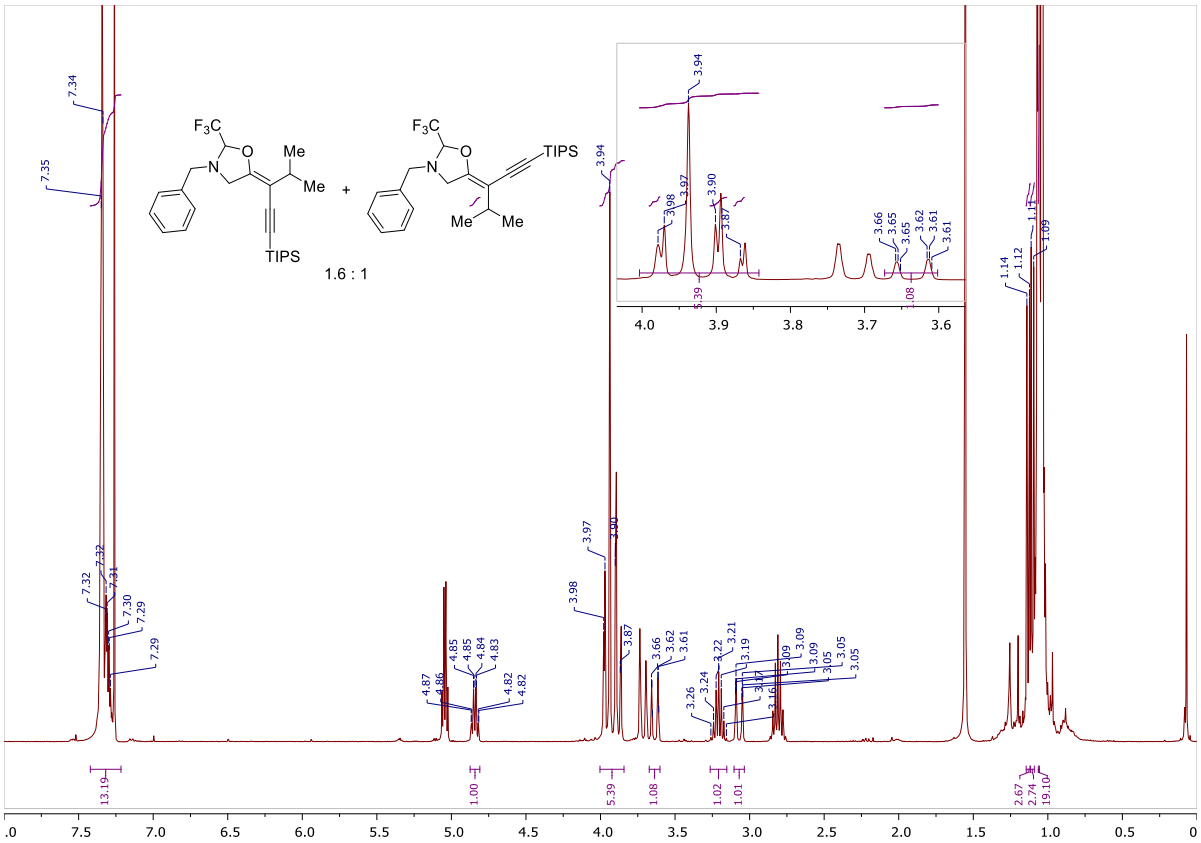


^{13}C-NMR (101 MHz, chloroform-*d*)

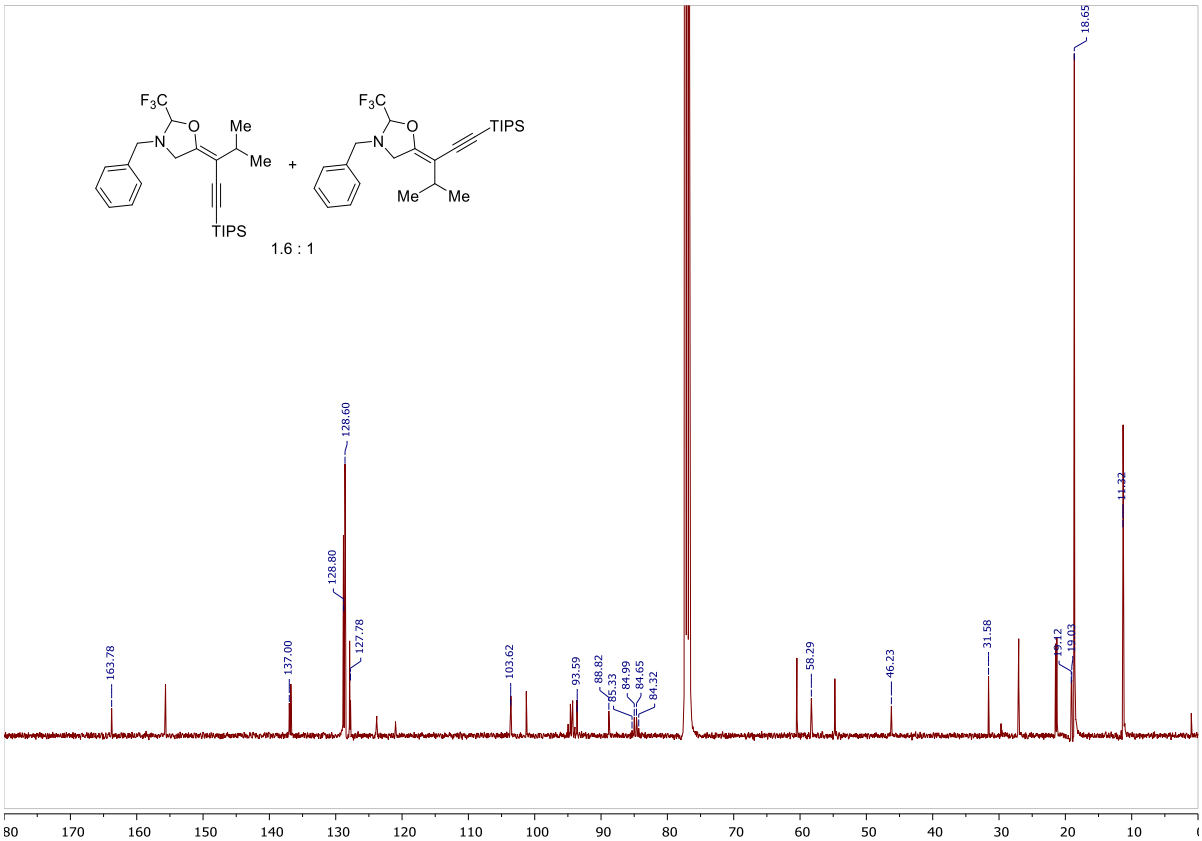


(E)- and (Z)-3-Benzyl-5-(4-methyl-1-(tri*iso*propylsilyl)pent-1-yn-3-ylidene)-2-(trifluoromethyl)oxazolidine (12d)

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

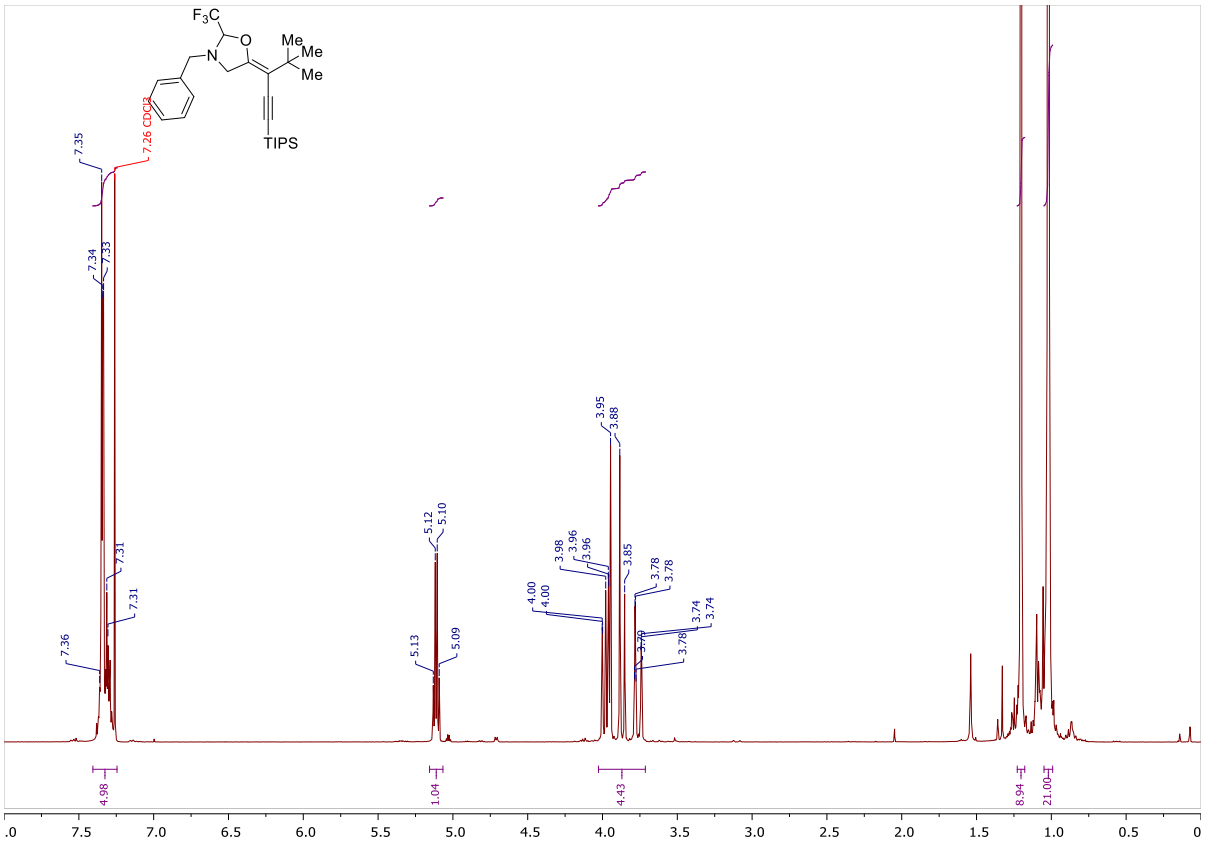


^{13}C-NMR (101 MHz, chloroform-*d*)

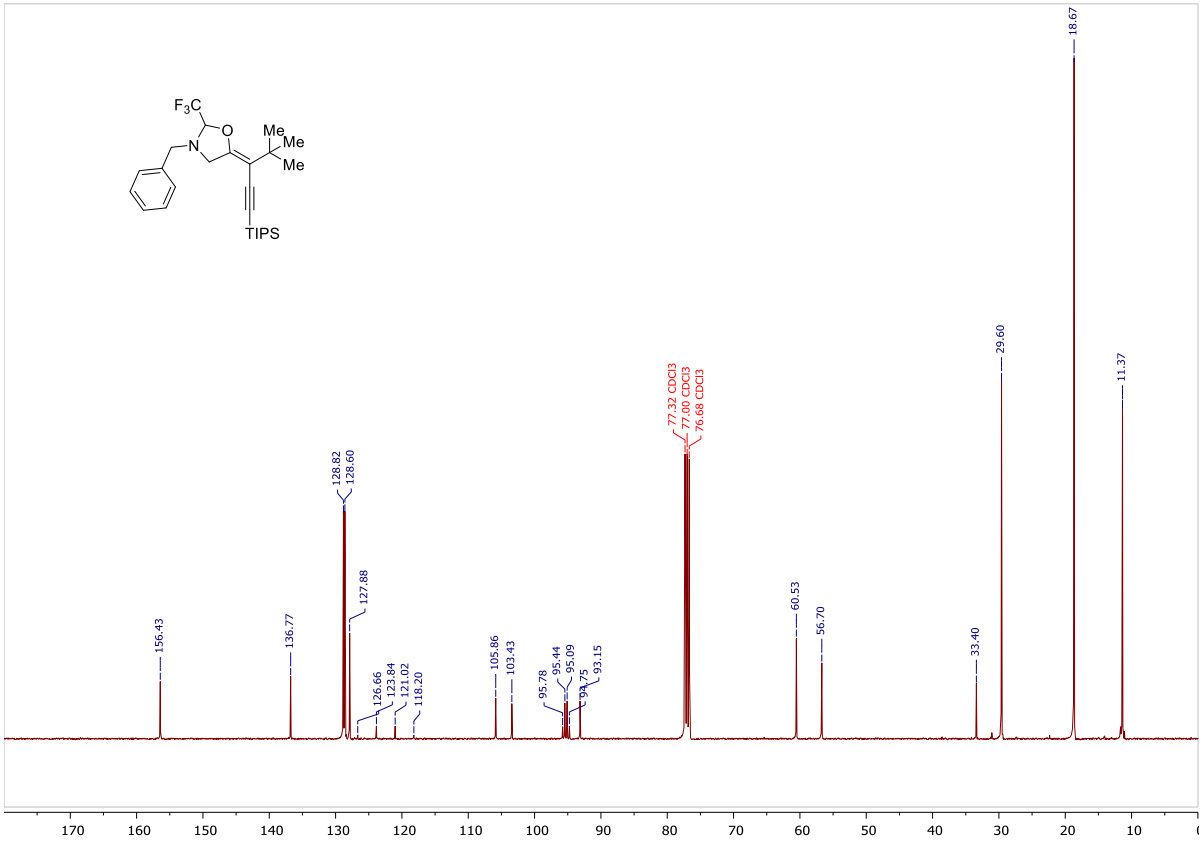


(E)-3-Benzyl-5-(4,4-dimethyl-1-(tri*iso*propylsilyl)pent-1-yn-3-ylidene)-2-(trifluoromethyl)oxazolidine (12e)

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

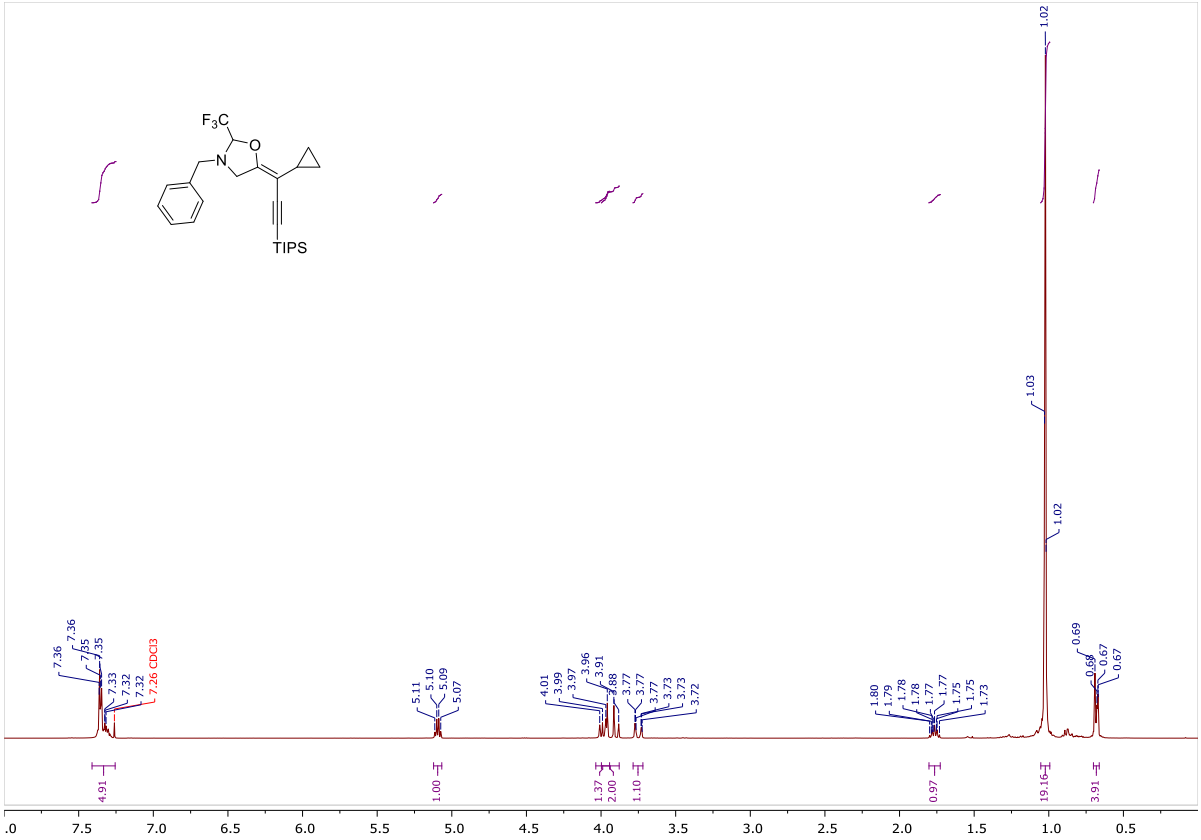


^{13}C-NMR (101 MHz, chloroform-*d*)

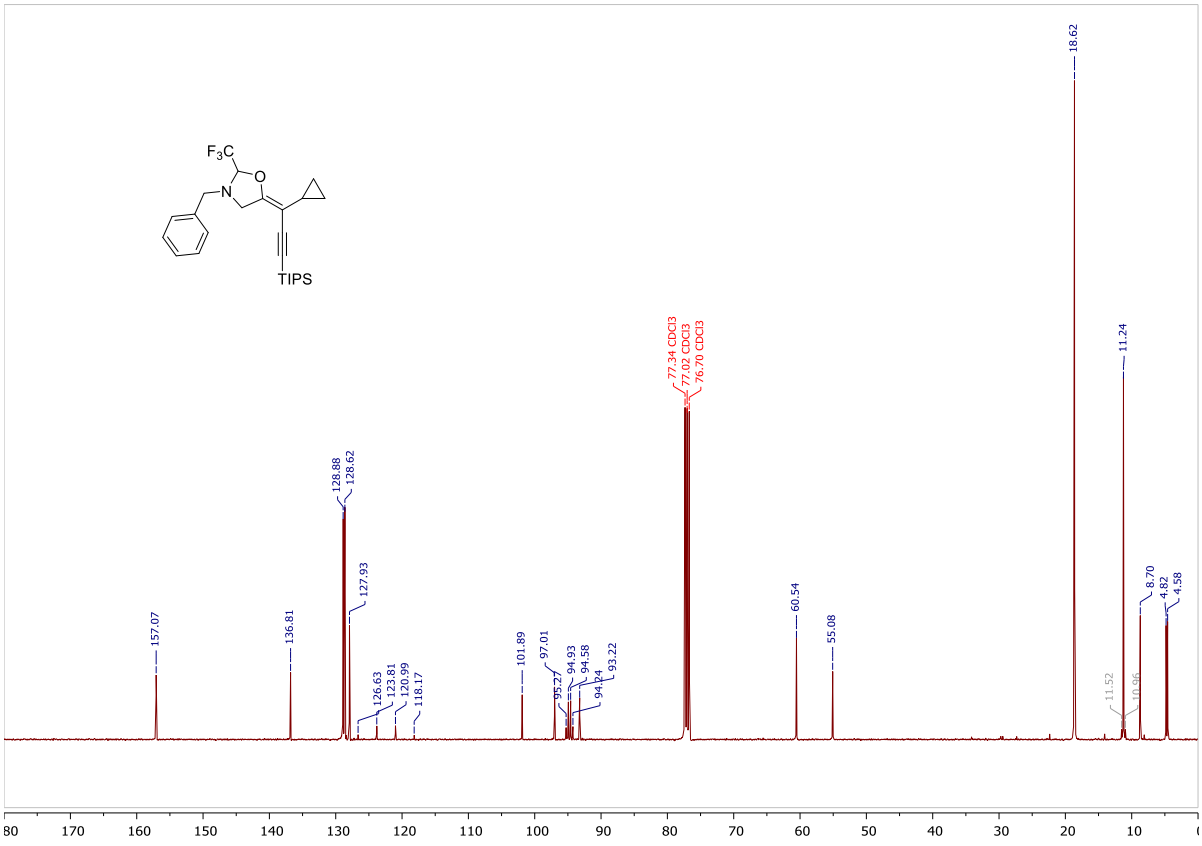


(E)-3-Benzyl-5-(1-cyclopropyl-3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)-2-(trifluoromethyl)oxazolidine (12f)

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

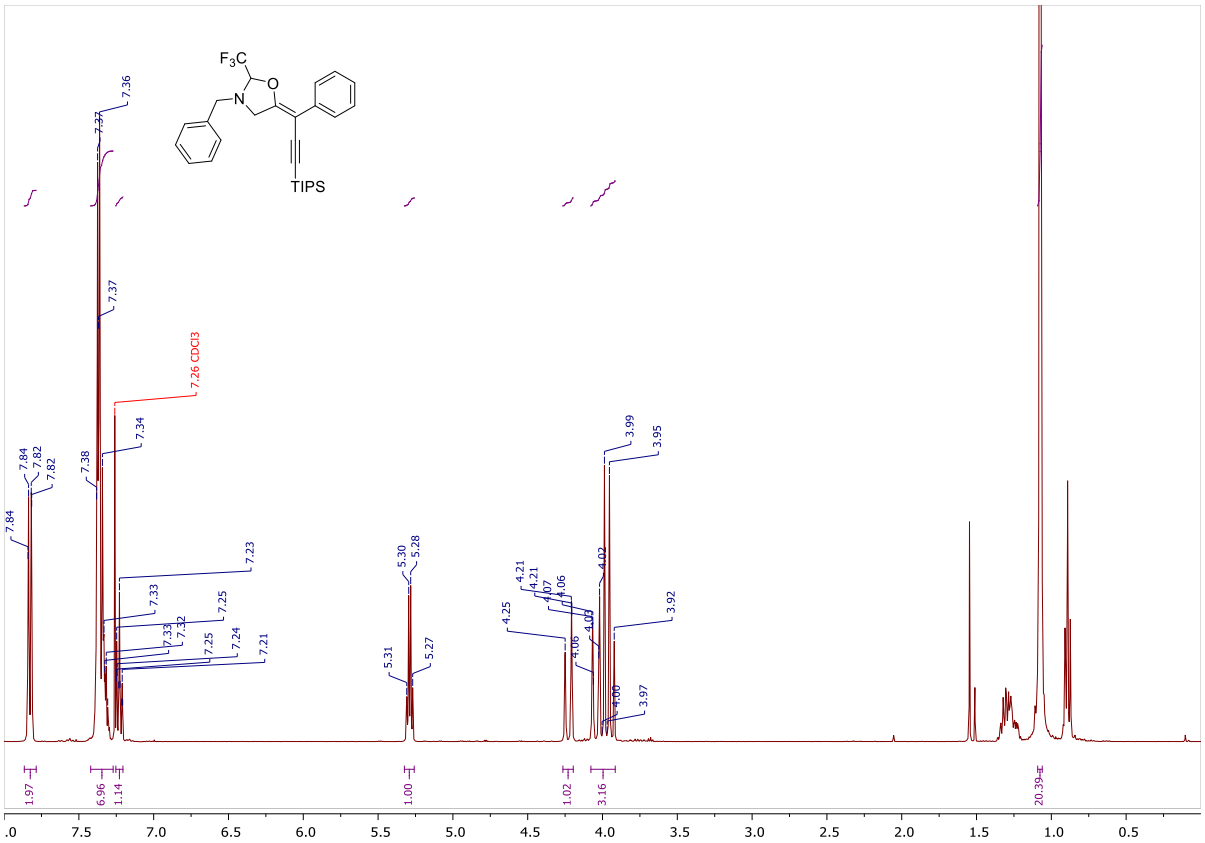


^{13}C-NMR (101 MHz, chloroform-*d*)

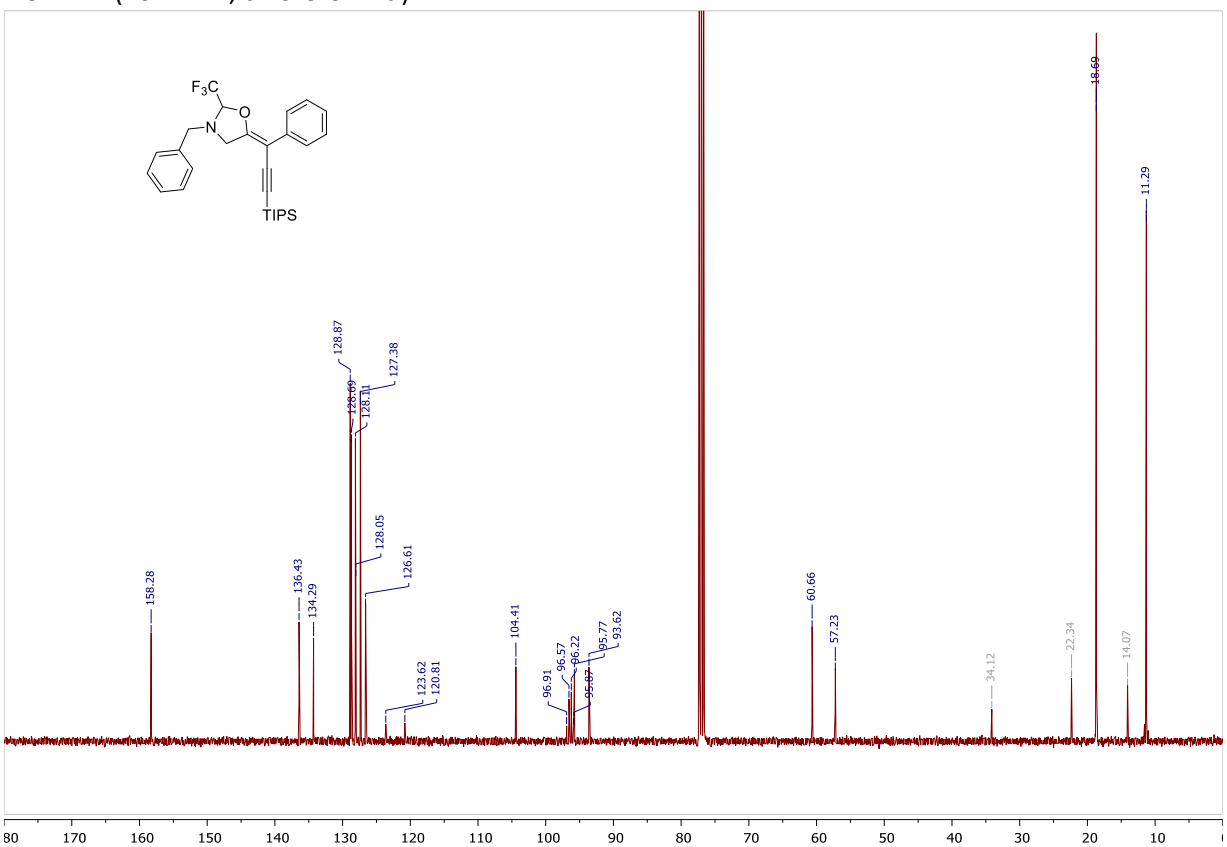


(E)-3-Benzyl-5-(1-phenyl-3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)-2-(trifluoromethyl)oxazolidine (12g)

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

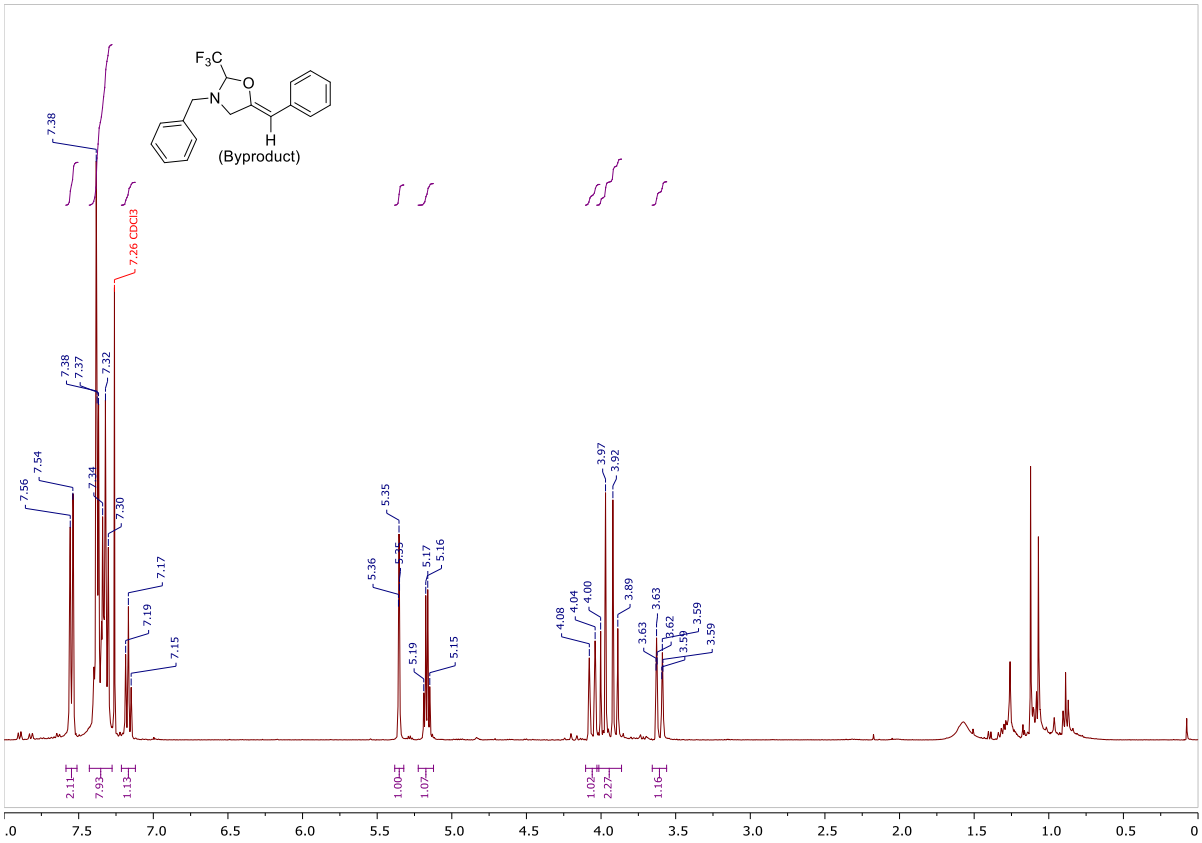


^{13}C-NMR (101 MHz, chloroform-*d*)

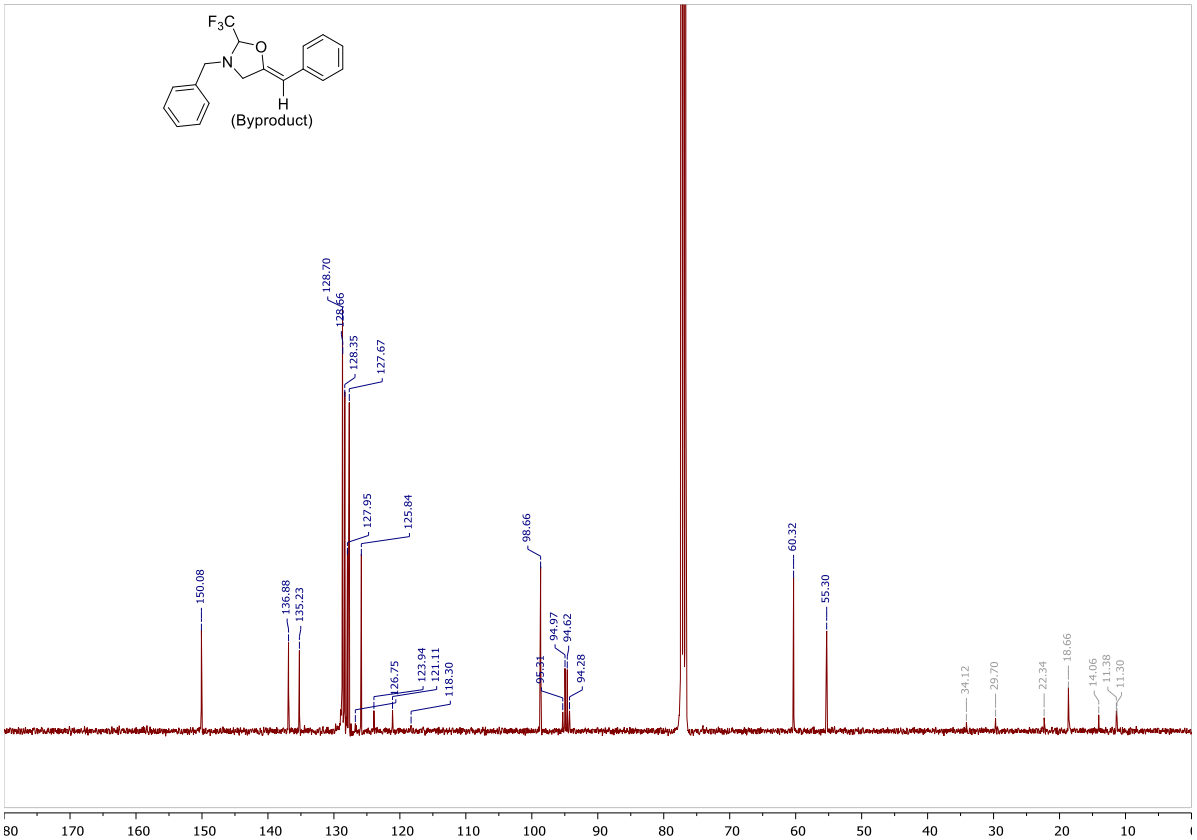


3-Benzyl-5-benzylidene-2-(trifluoromethyl)oxazolidine

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

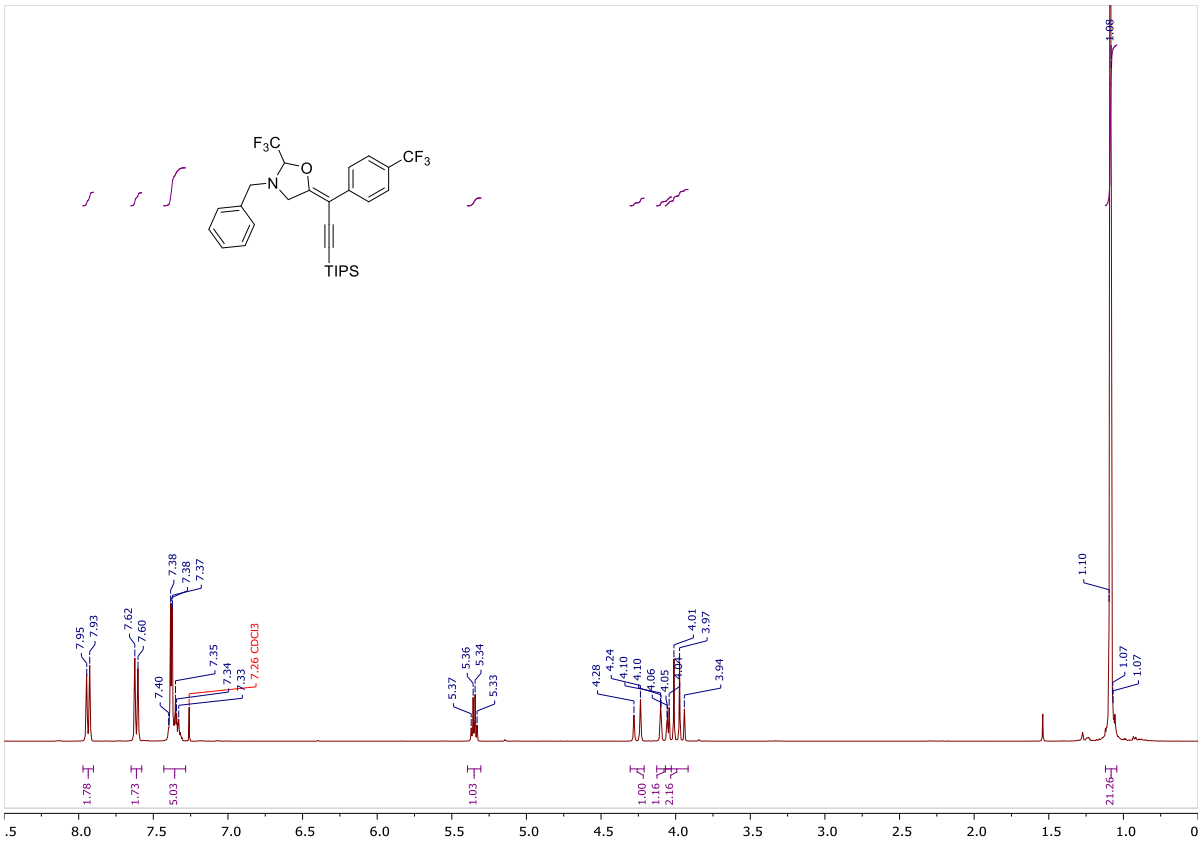


^{13}C-NMR (101 MHz, chloroform-*d*)

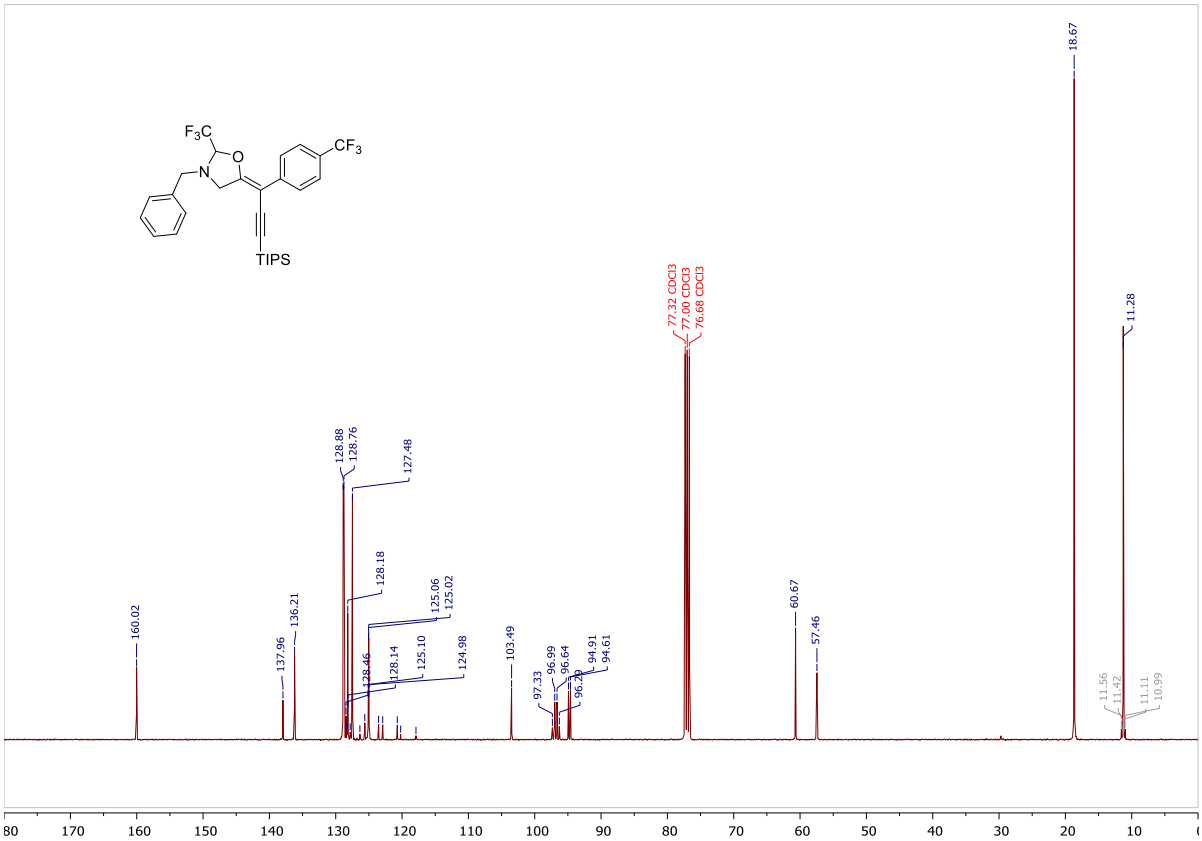


(E)-3-Benzyl-2-(trifluoromethyl)-5-(1-(4-(trifluoromethyl)phenyl)-3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)oxazolidine (12h)

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

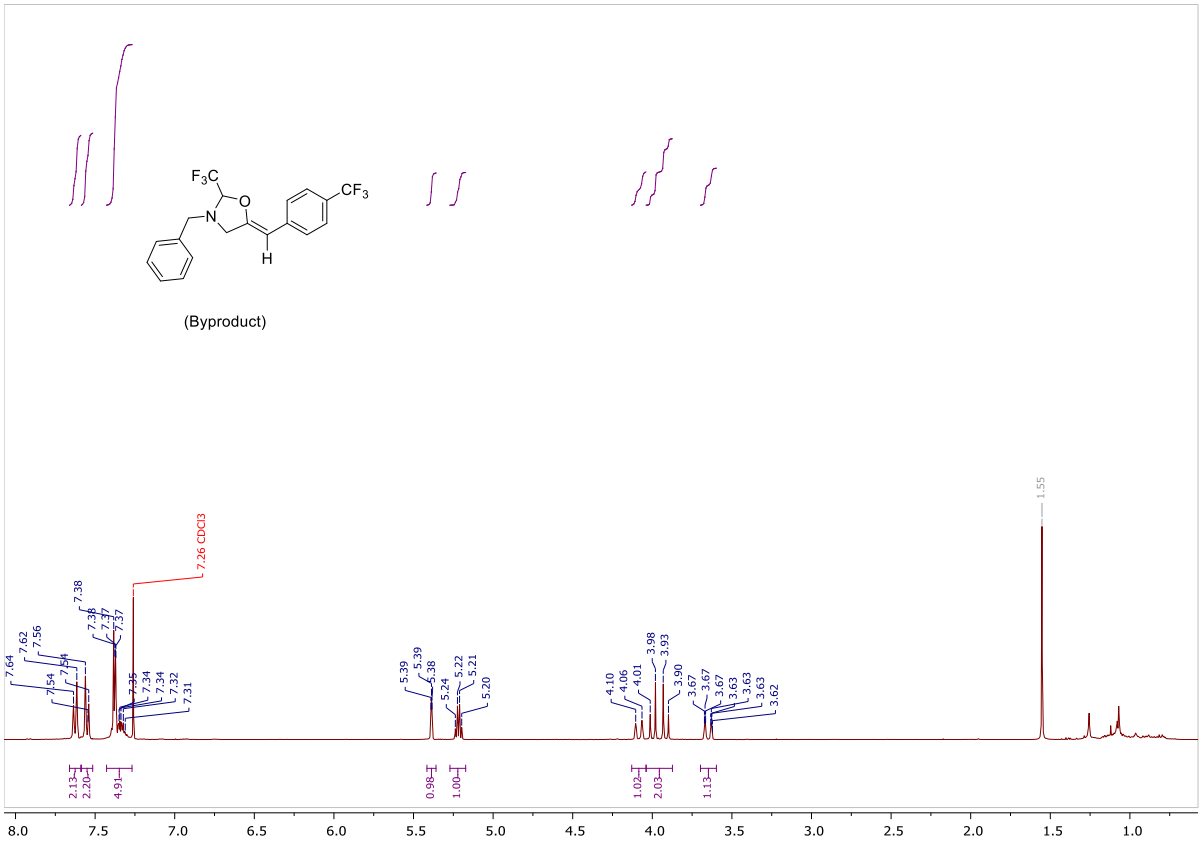


^{13}C-NMR (101 MHz, chloroform-*d*)

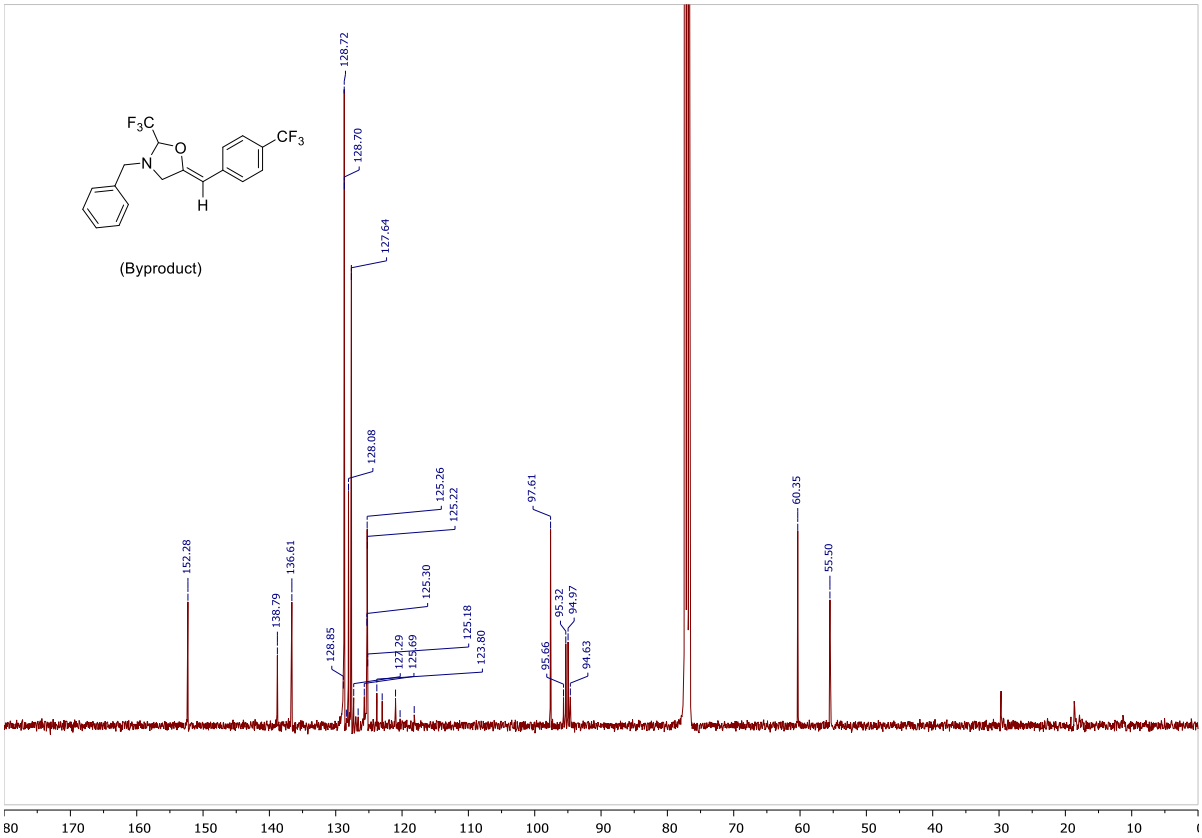


3-Benzyl-2-(trifluoromethyl)-5-(4-(trifluoromethyl)benzylidene)oxazolidine

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

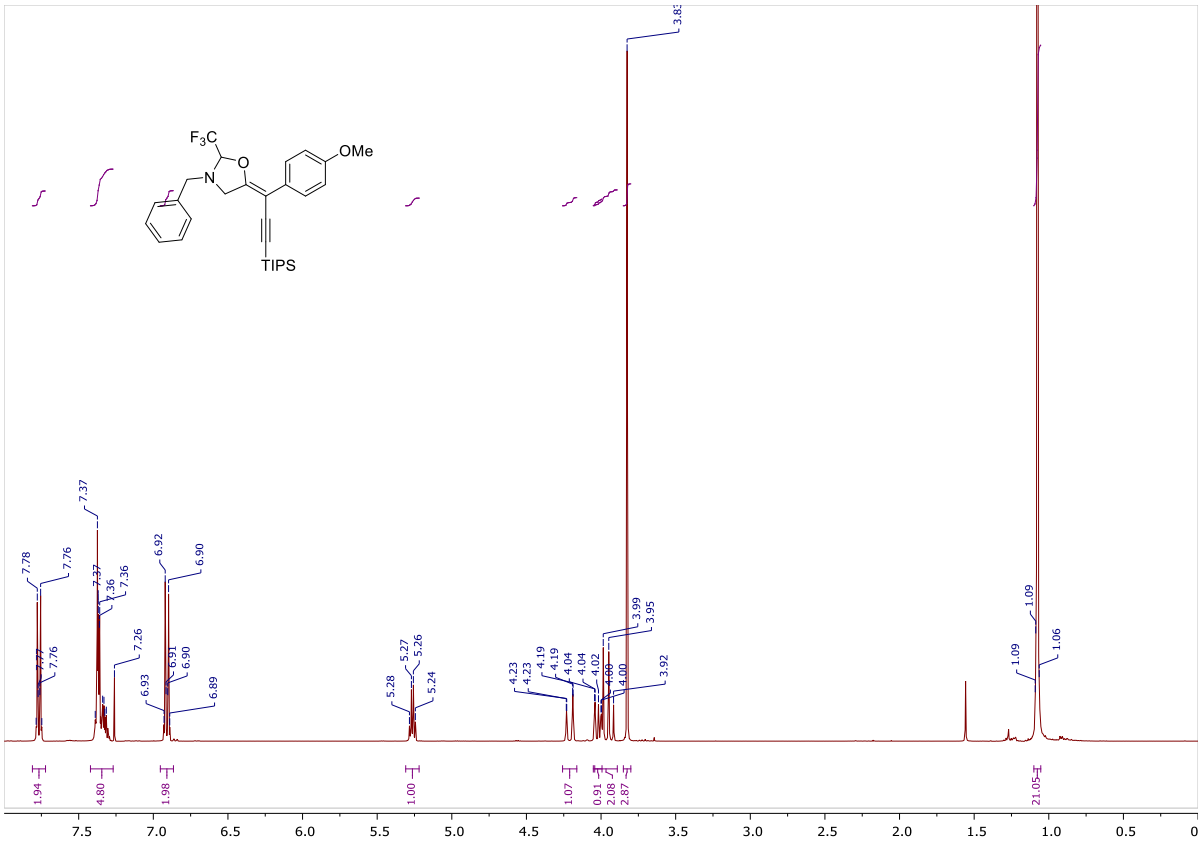


^{13}C-NMR (101 MHz, chloroform-*d*)

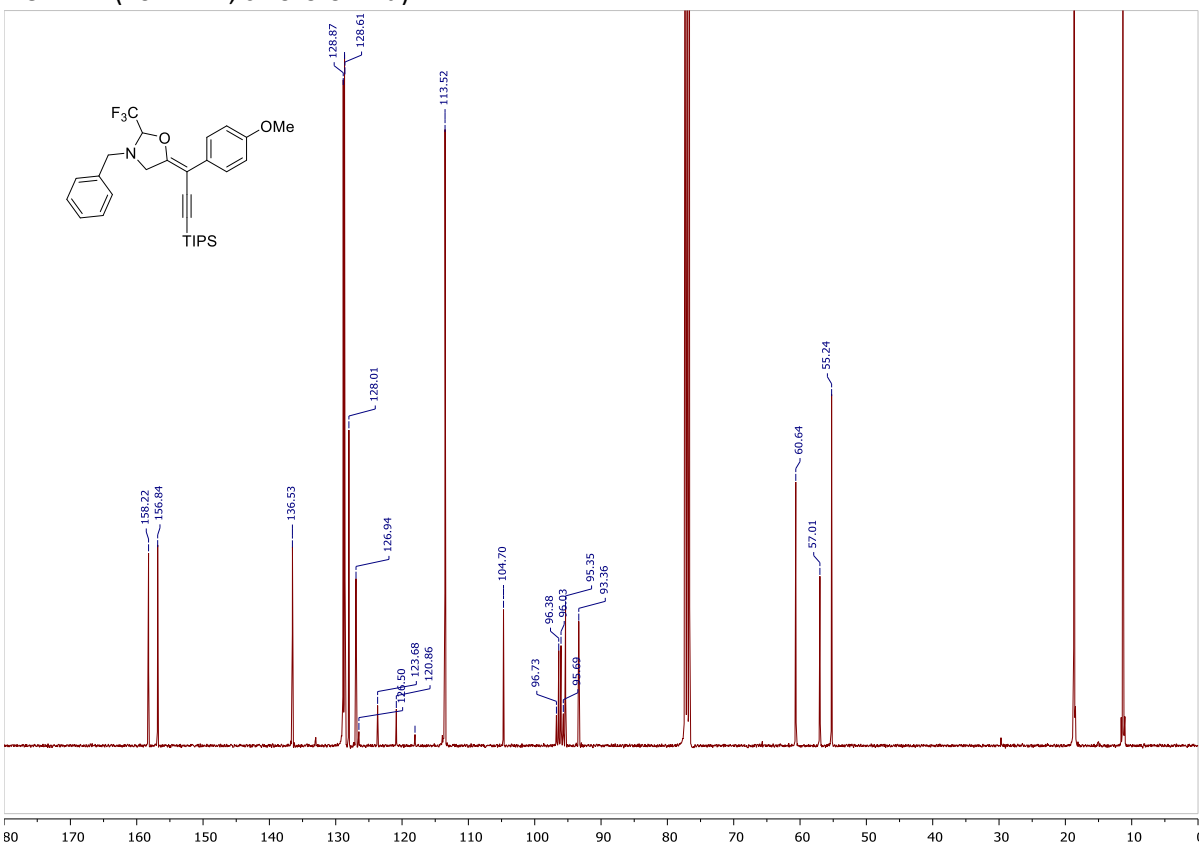


(E)-3-Benzyl-5-(1-(4-methoxyphenyl)-3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)-2-(trifluoromethyl)oxazolidine (12i)

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

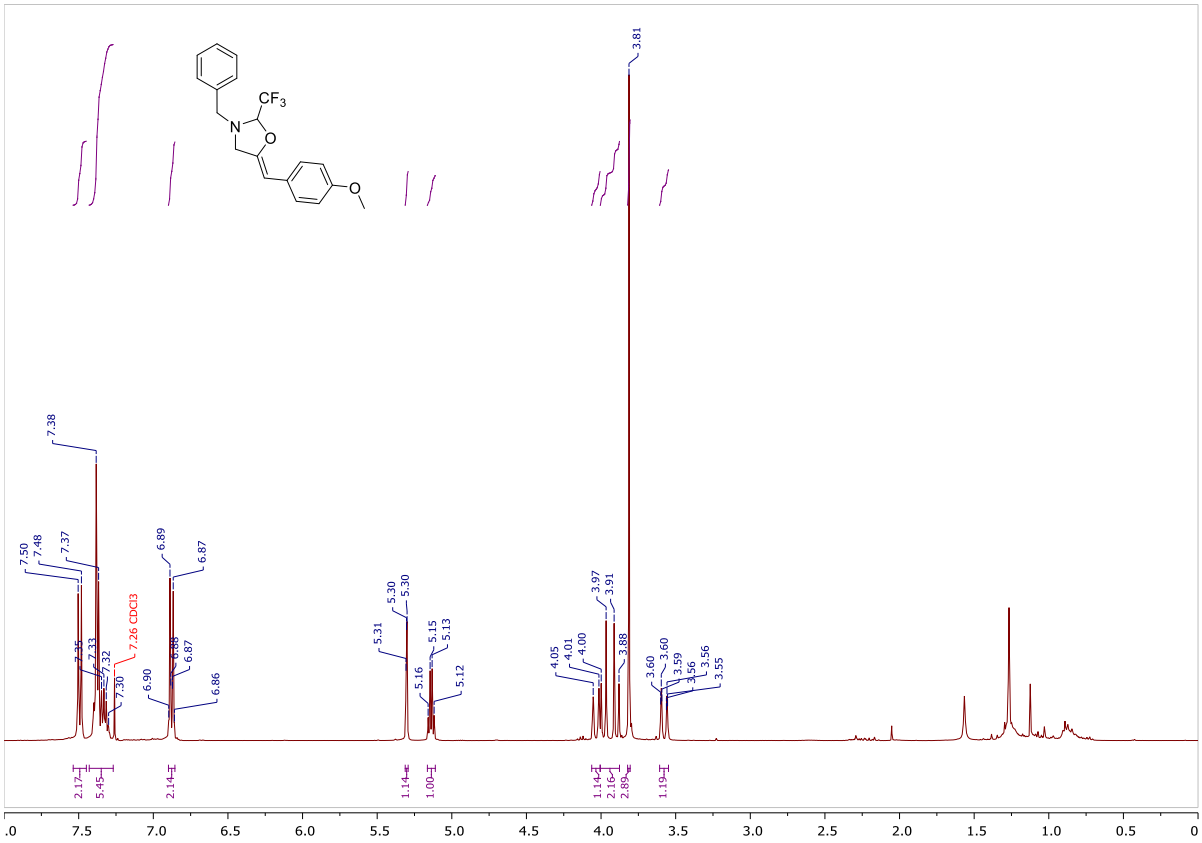


^{13}C-NMR (101 MHz, chloroform-*d*)

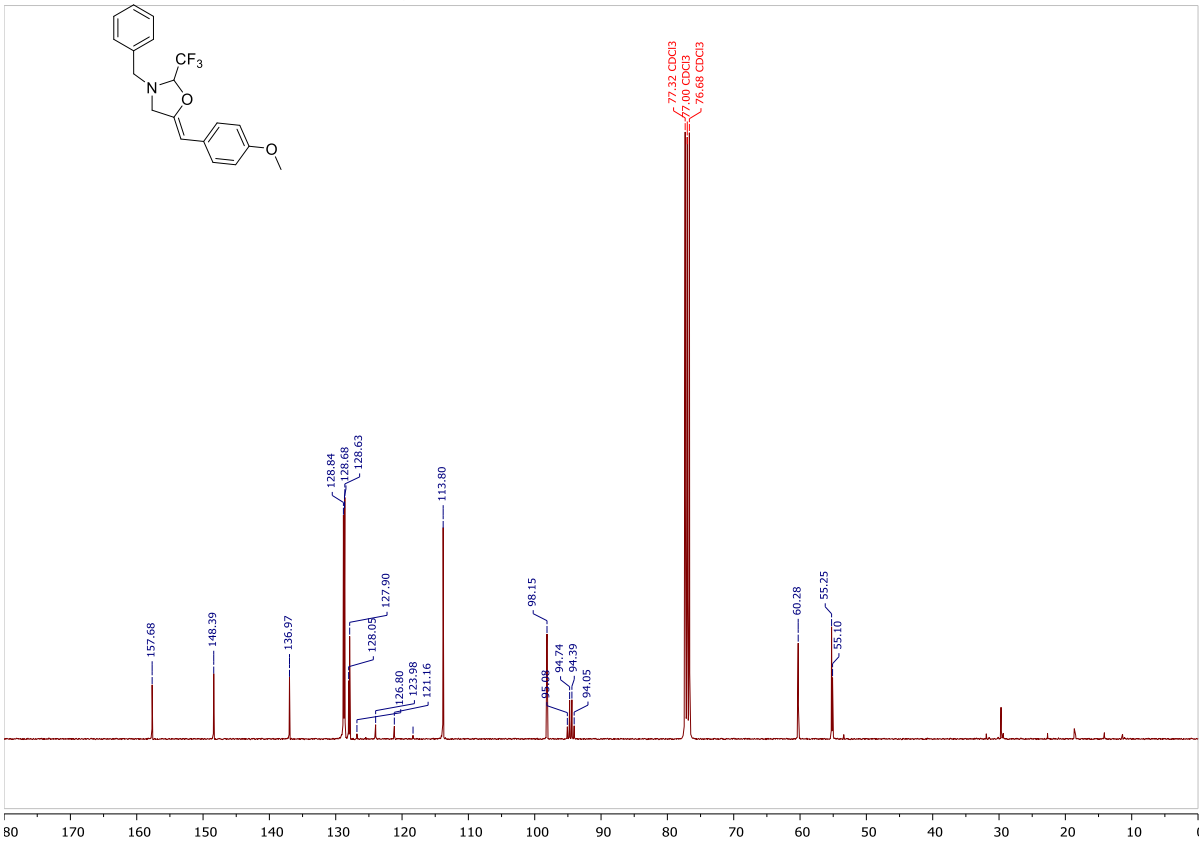


3-Benzyl-5-(4-methoxybenzylidene)-2-(trifluoromethyl)oxazolidine

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

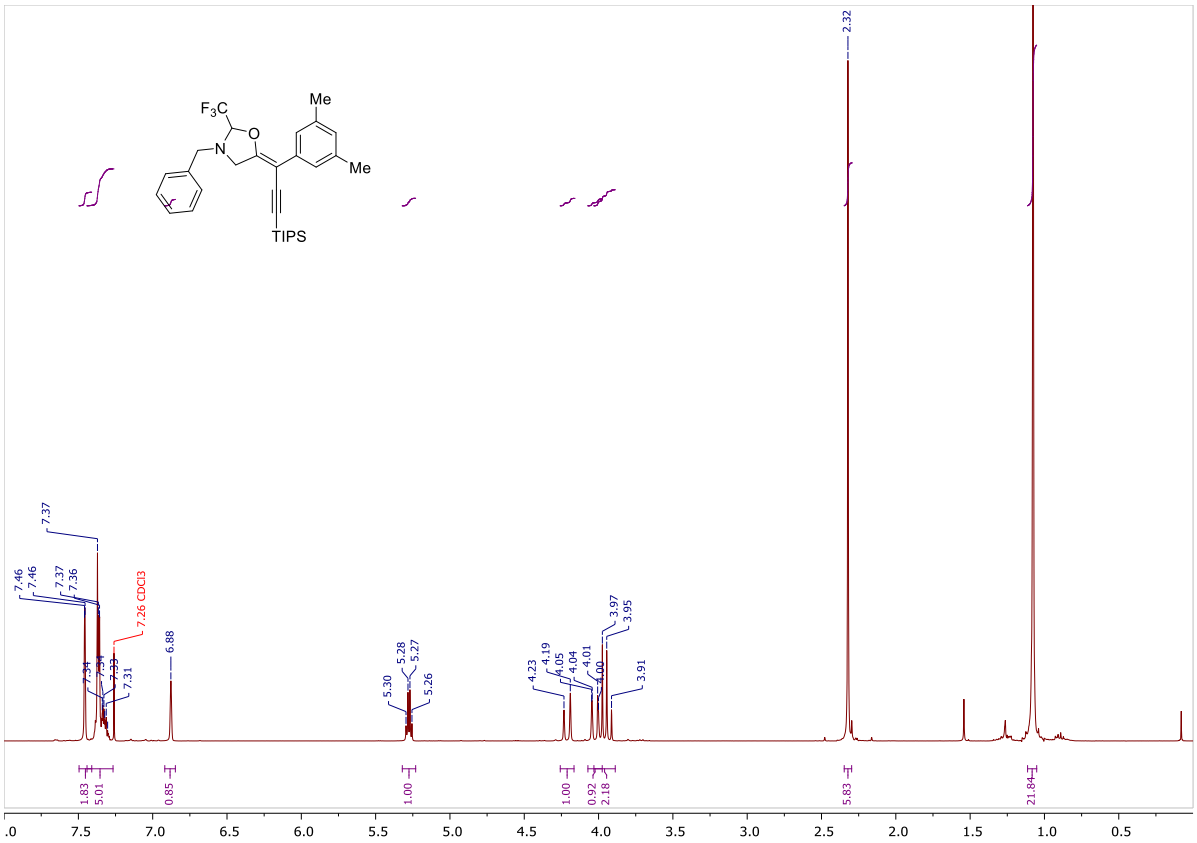


^{13}C-NMR (101 MHz, chloroform-*d*)

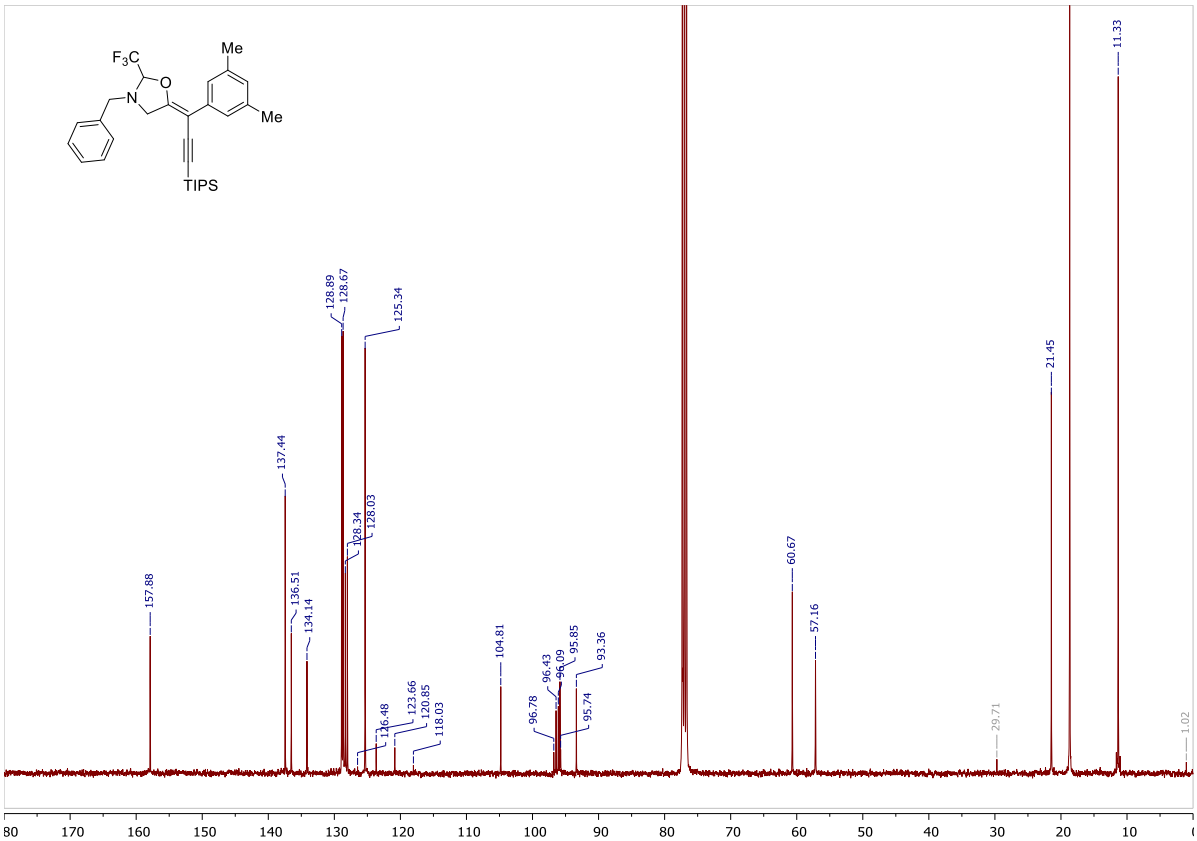


(E)-3-benzyl-5-(1-(3,5-dimethylphenyl)-3-(tri*iso*propylsilyl)prop-2-yn-1-ylidene)-2-(trifluoromethyl)oxazolidine (12j)

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

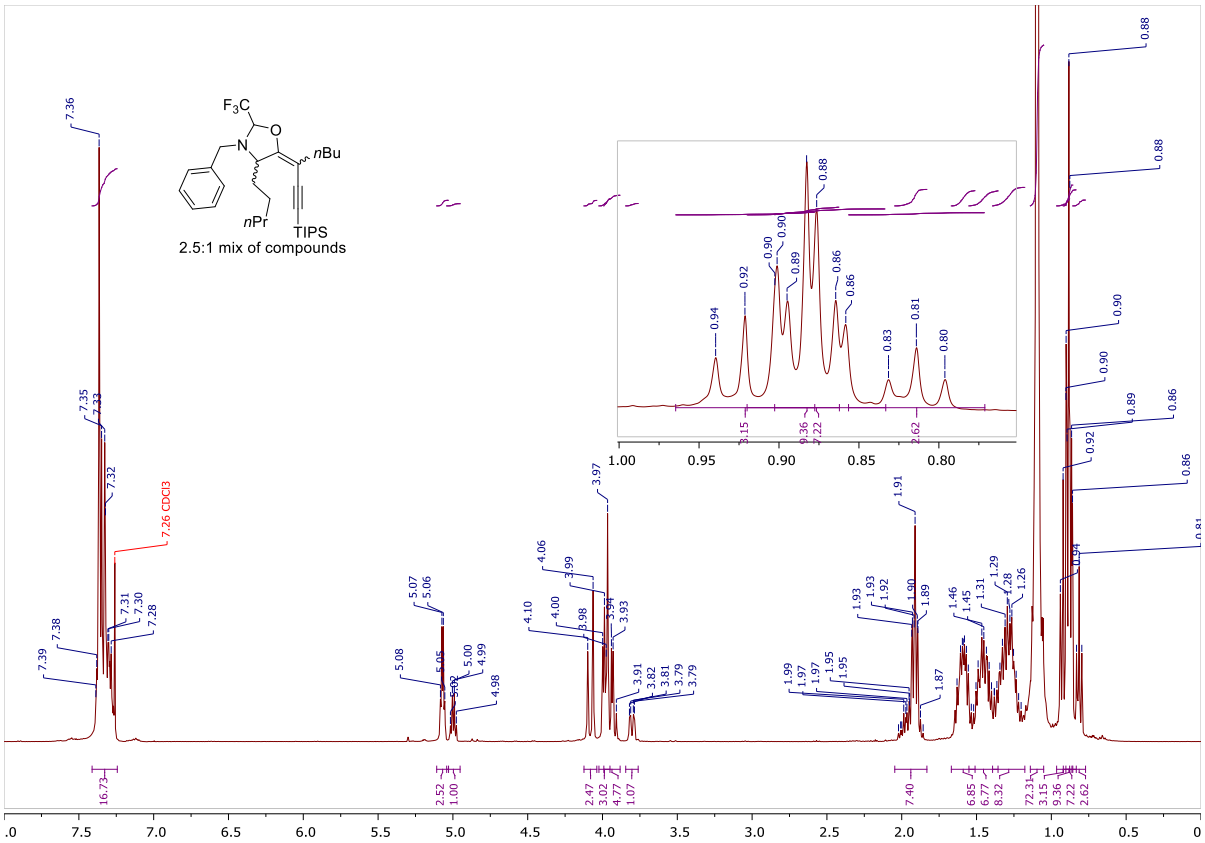


^{13}C-NMR (101 MHz, chloroform-*d*)

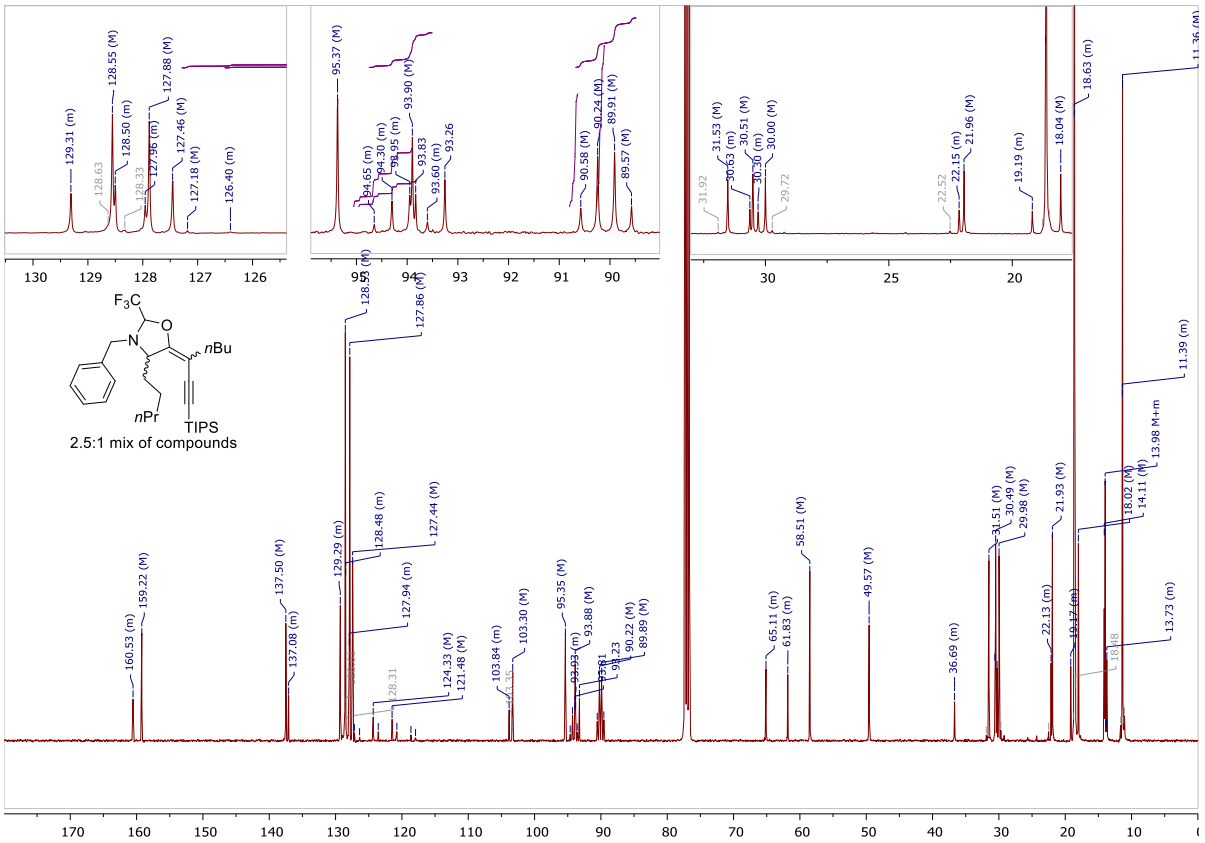


(E)- and (Z)-3-benzyl-4-pentyl-2-(trifluoromethyl)-5-(1-(tri*iso*propylsilyl)hept-1-yn-3-ylidene)oxazolidine (14a)

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

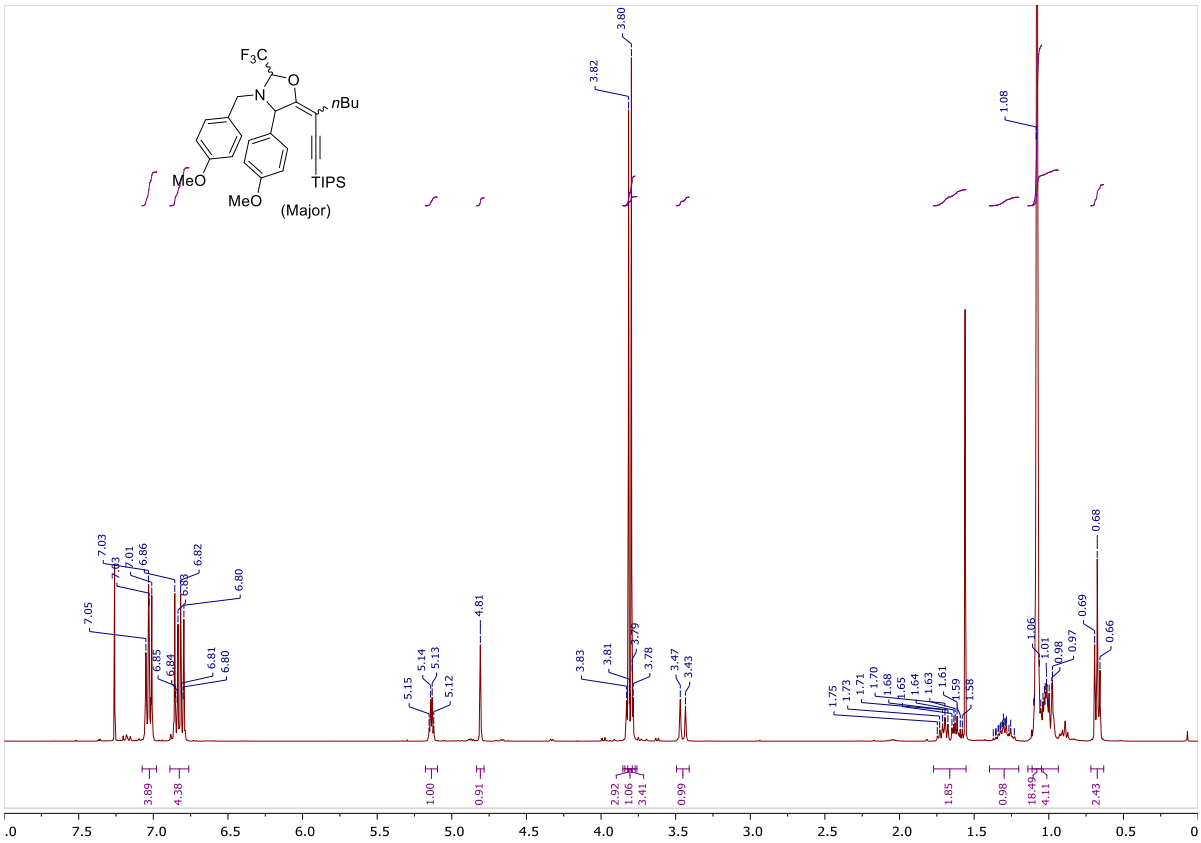


^{13}C-NMR (101 MHz, chloroform-*d*)

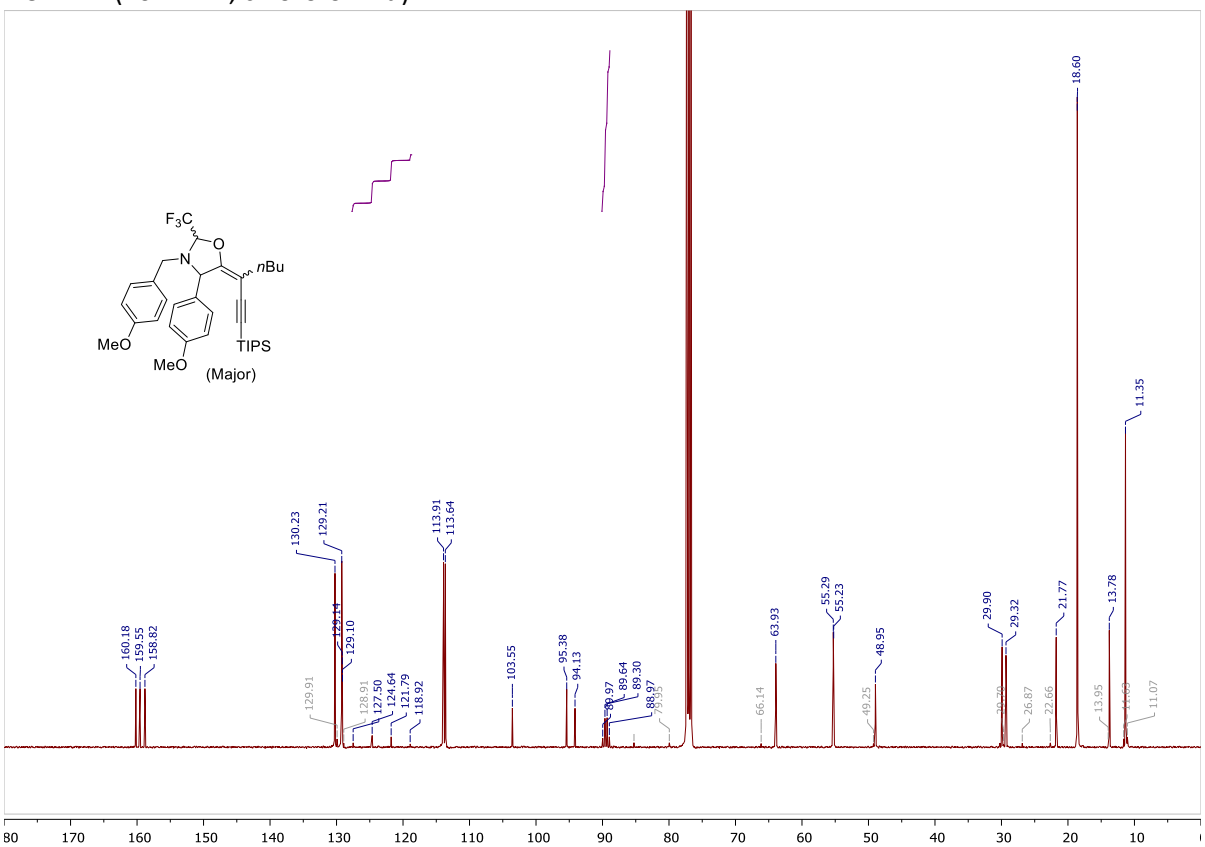


3-(4-methoxybenzyl)-4-(4-methoxyphenyl)-2-(trifluoromethyl)-5-(1-(tri*iso*propylsilyl)hept-1-yn-3-ylidene)oxazolidine (14b)

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

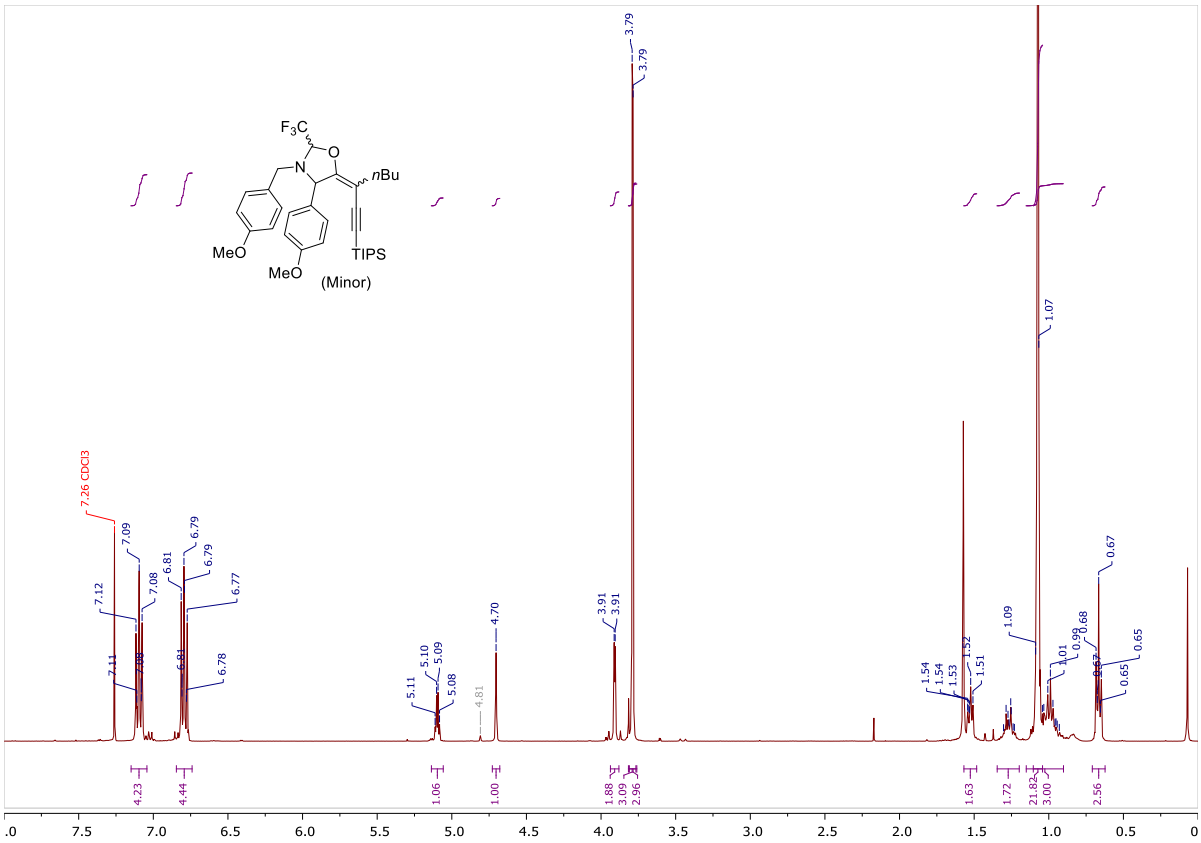


^{13}C-NMR (101 MHz, chloroform-*d*)

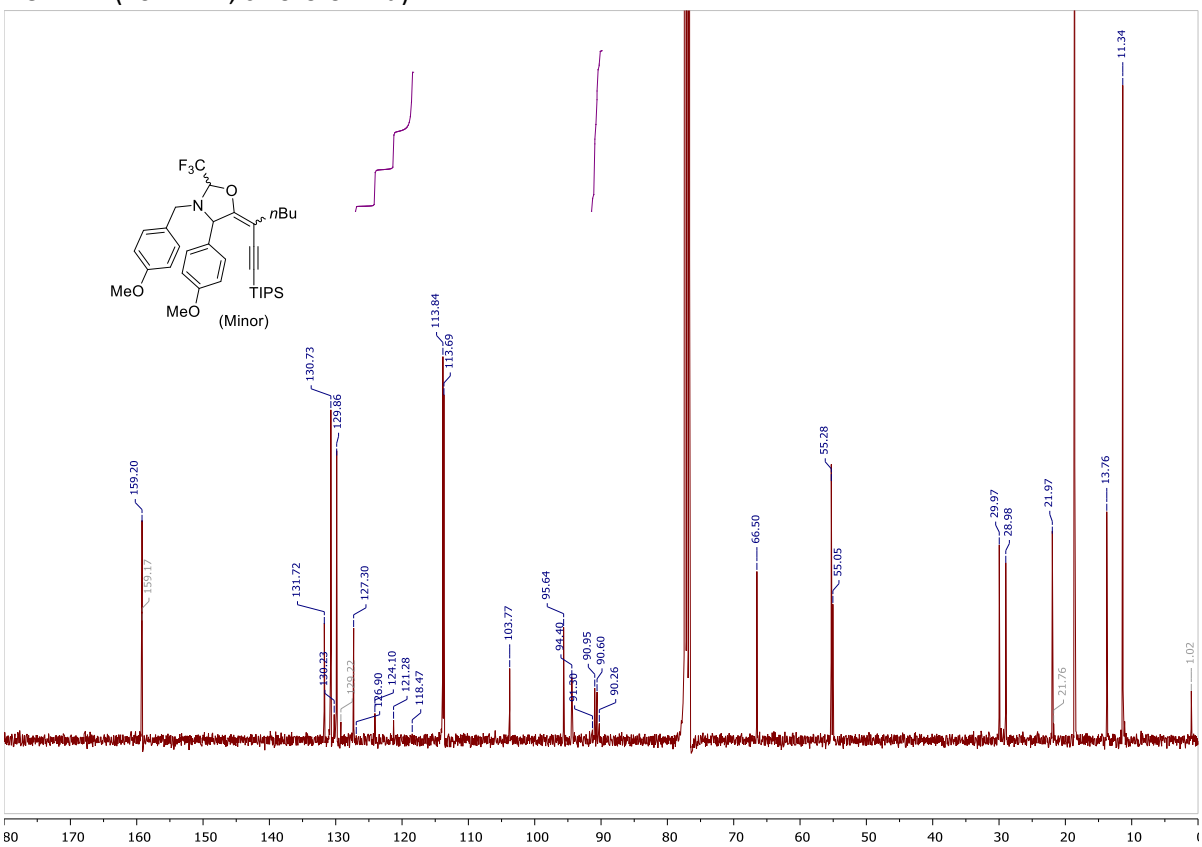


3-(4-methoxybenzyl)-4-(4-methoxyphenyl)-2-(trifluoromethyl)-5-(1-(tri*iso*propylsilyl)hept-1-yn-3-ylidene)oxazolidine (14b)

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

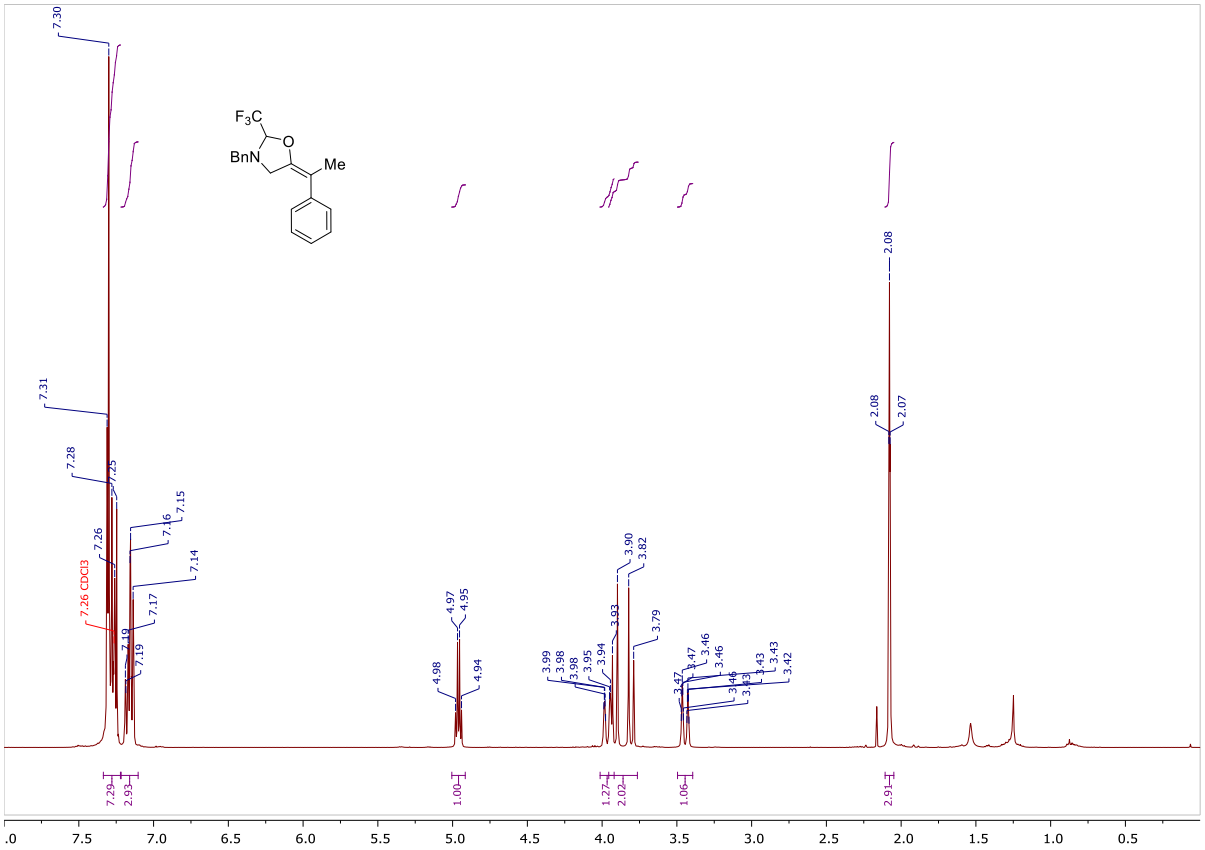


^{13}C-NMR (101 MHz, chloroform-*d*)

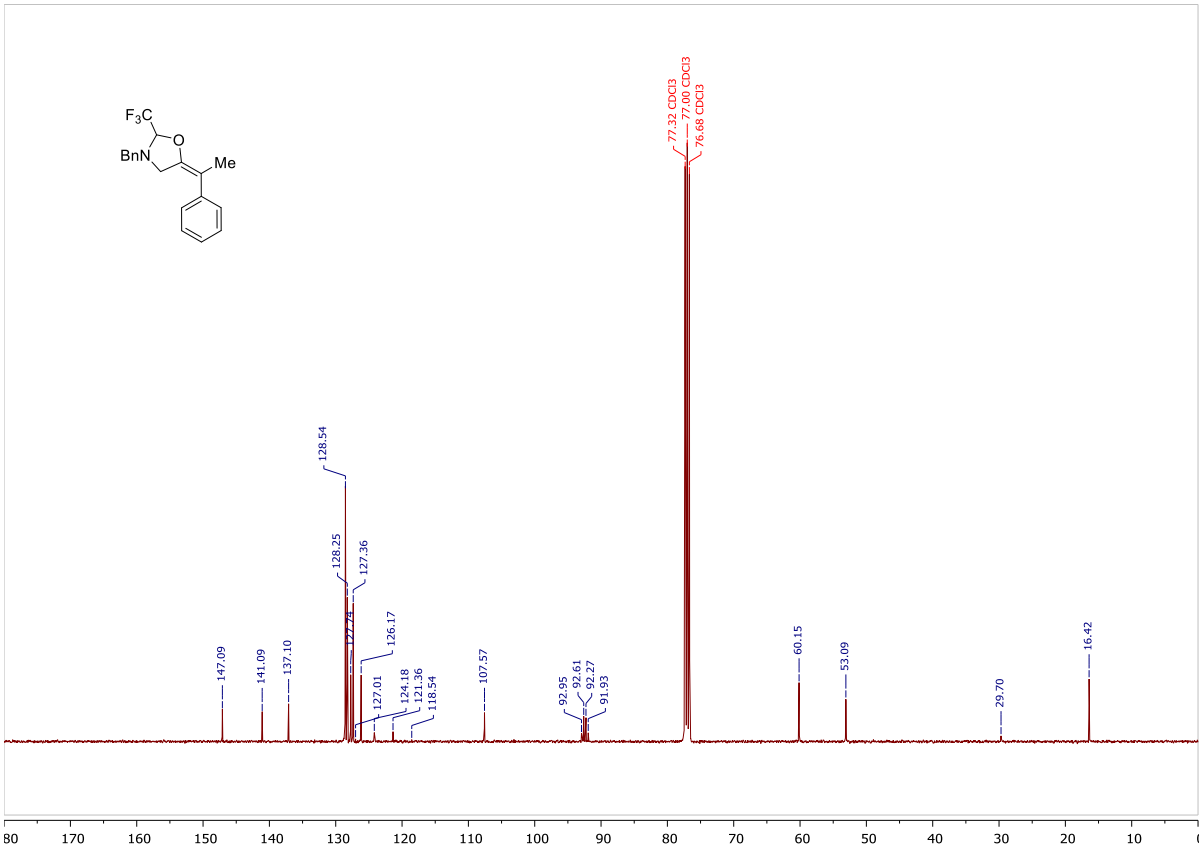


(*E*)-3-benzyl-5-(1-phenylethylidene)-2-(trifluoromethyl)oxazolidine (15a)

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

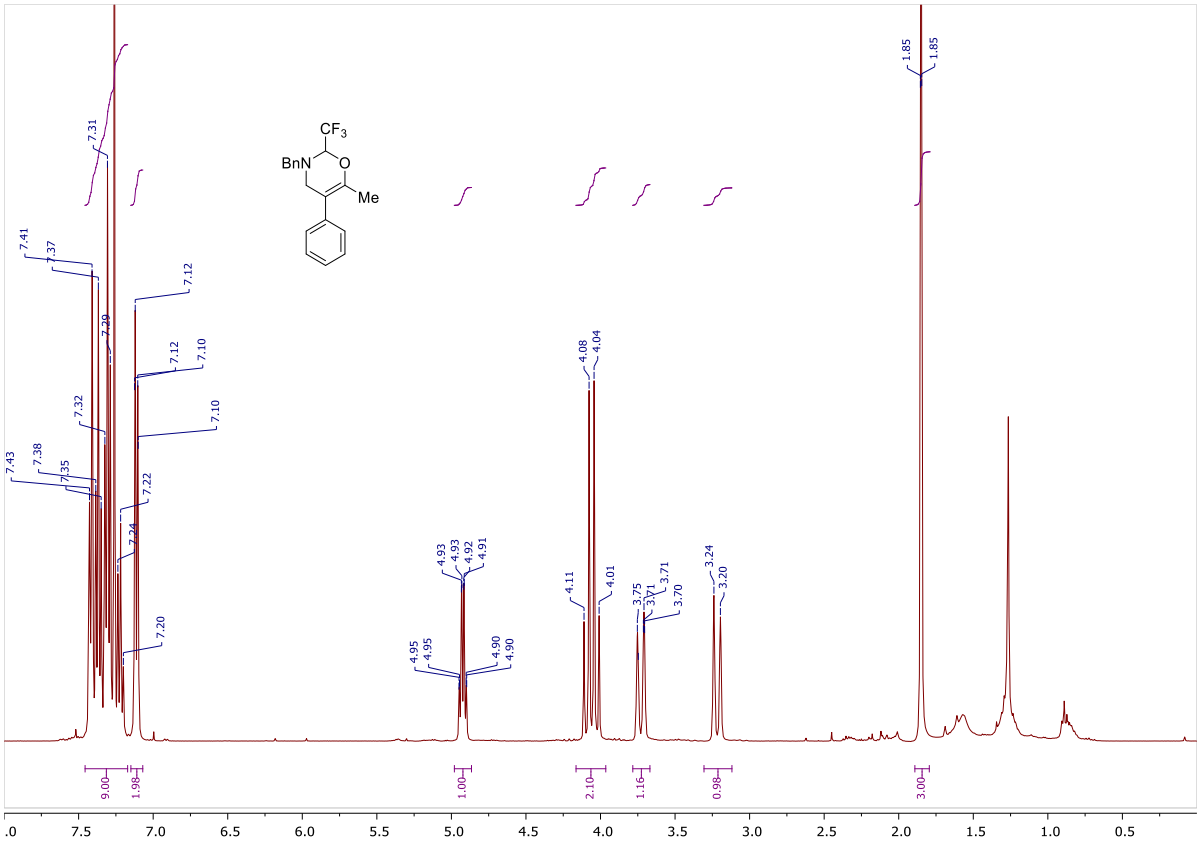


^{13}C-NMR (101 MHz, chloroform-*d*)

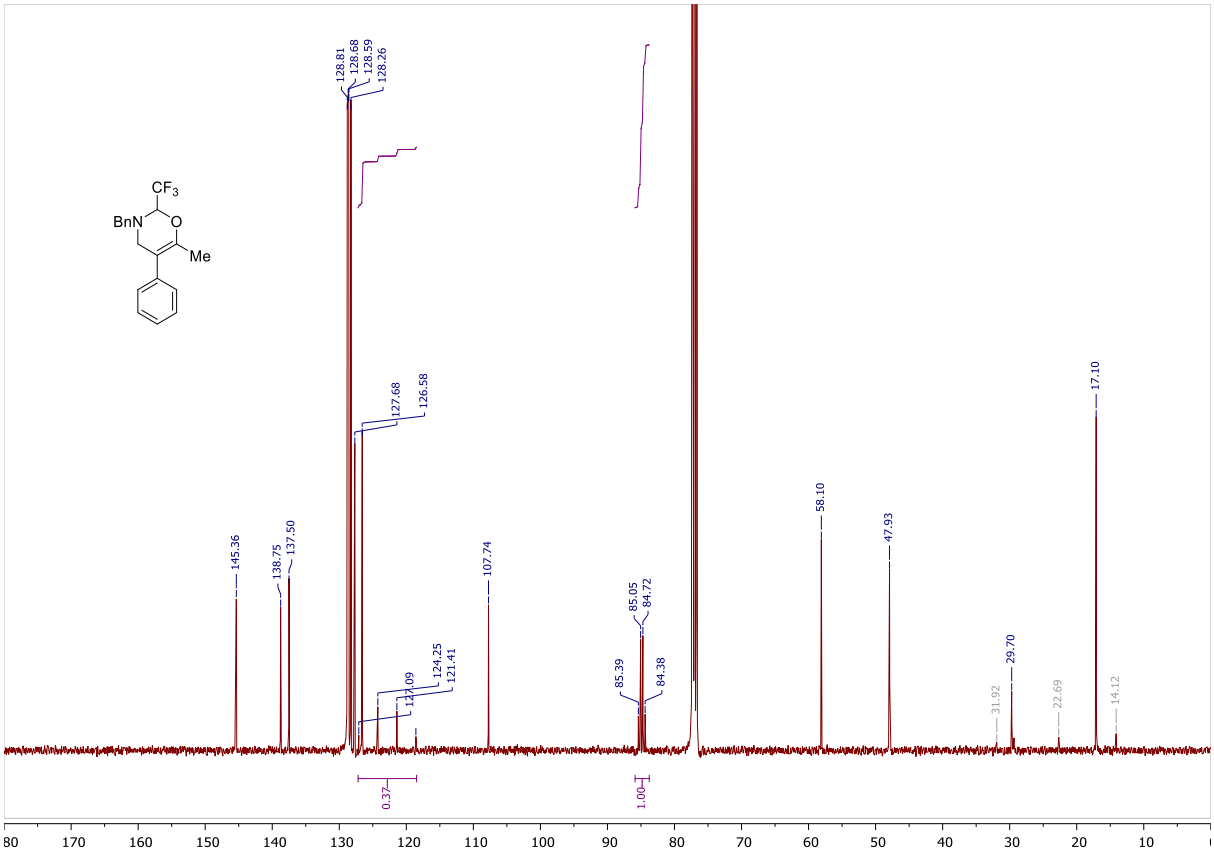


3-benzyl-6-methyl-5-phenyl-2-(trifluoromethyl)-3,4-dihydro-2*H*-1,3-oxazine (15a')

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

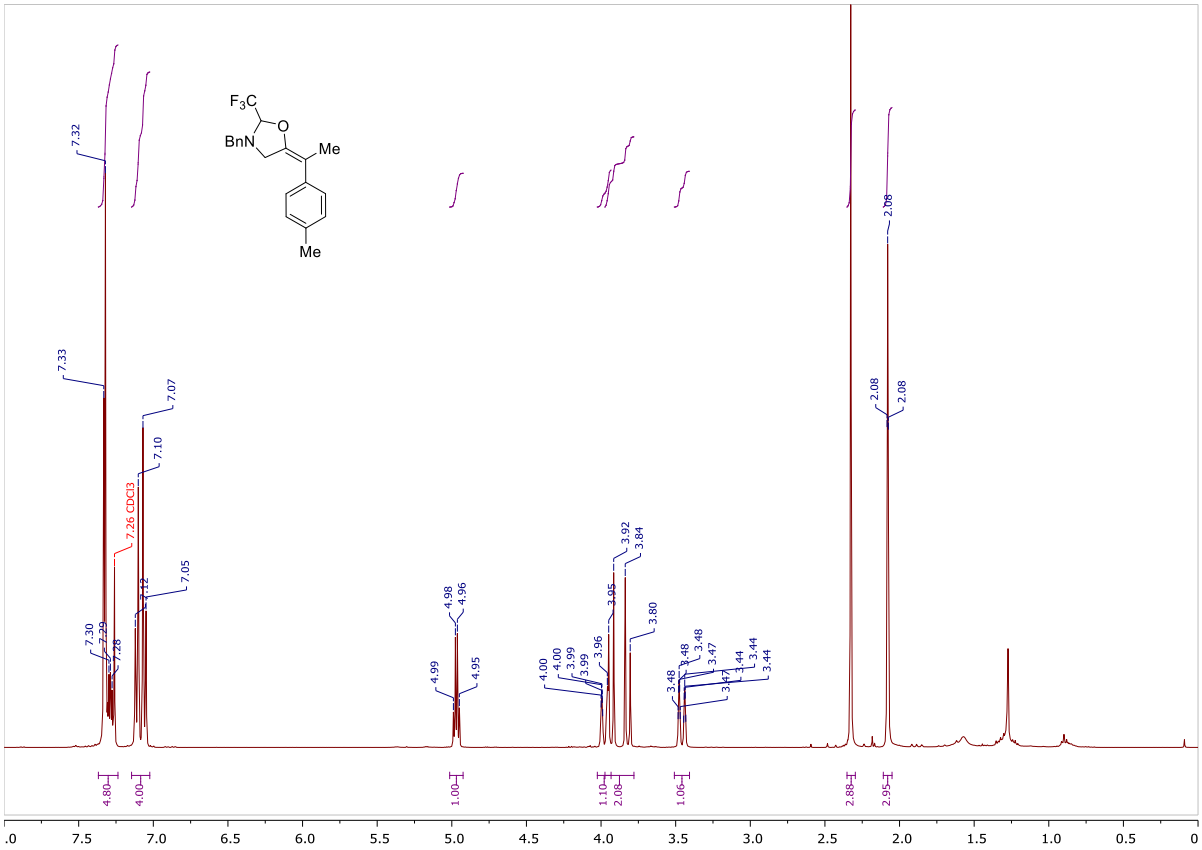


^{13}C-NMR (101 MHz, chloroform-*d*)

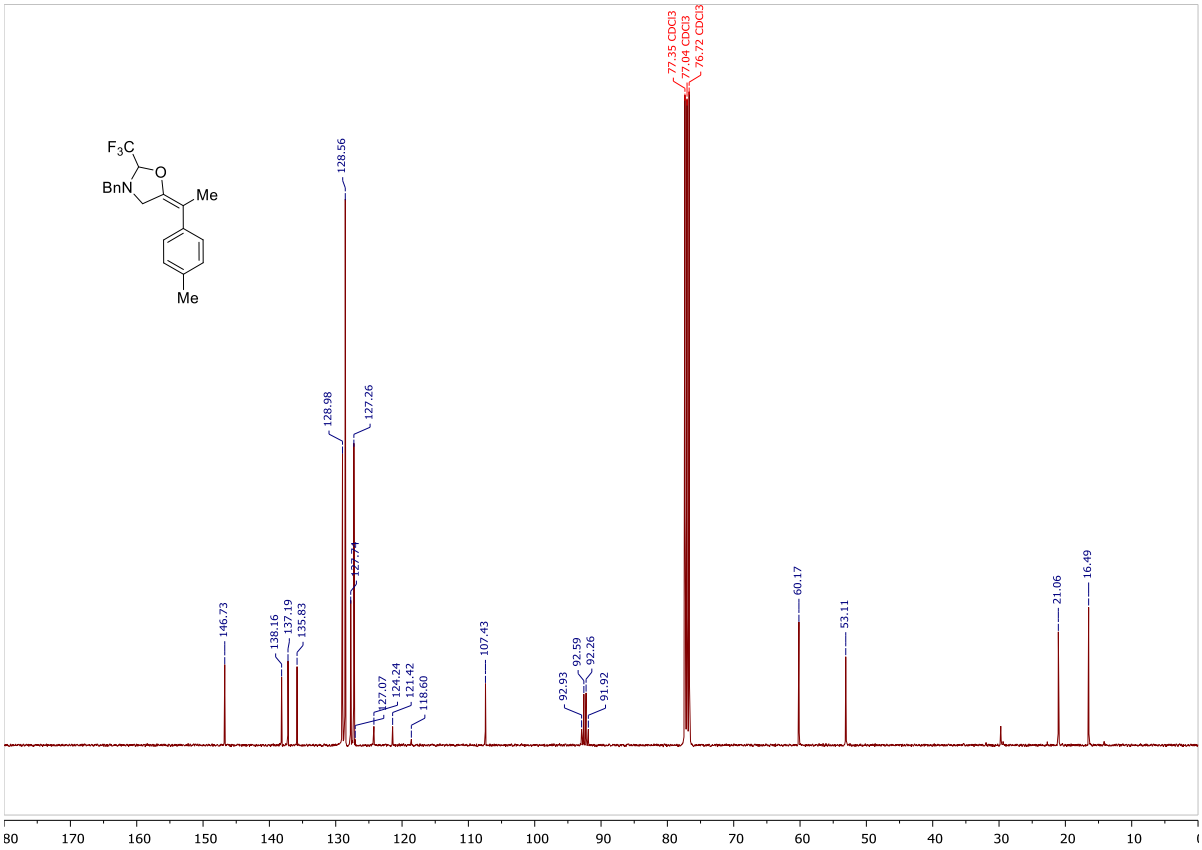


(*E*)-3-benzyl-5-(1-(*p*-tolyl)ethylidene)-2-(trifluoromethyl)oxazolidine (15b)

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

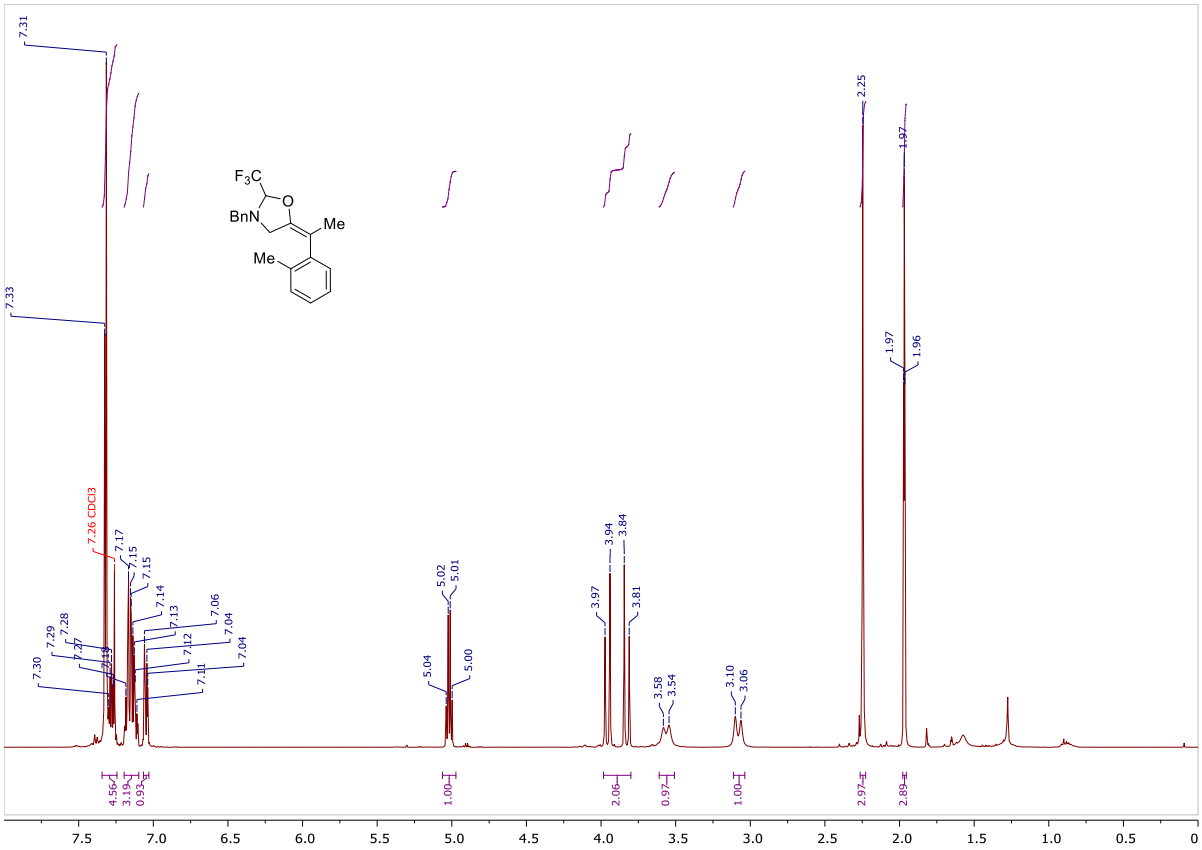


^{13}C-NMR (101 MHz, chloroform-*d*)

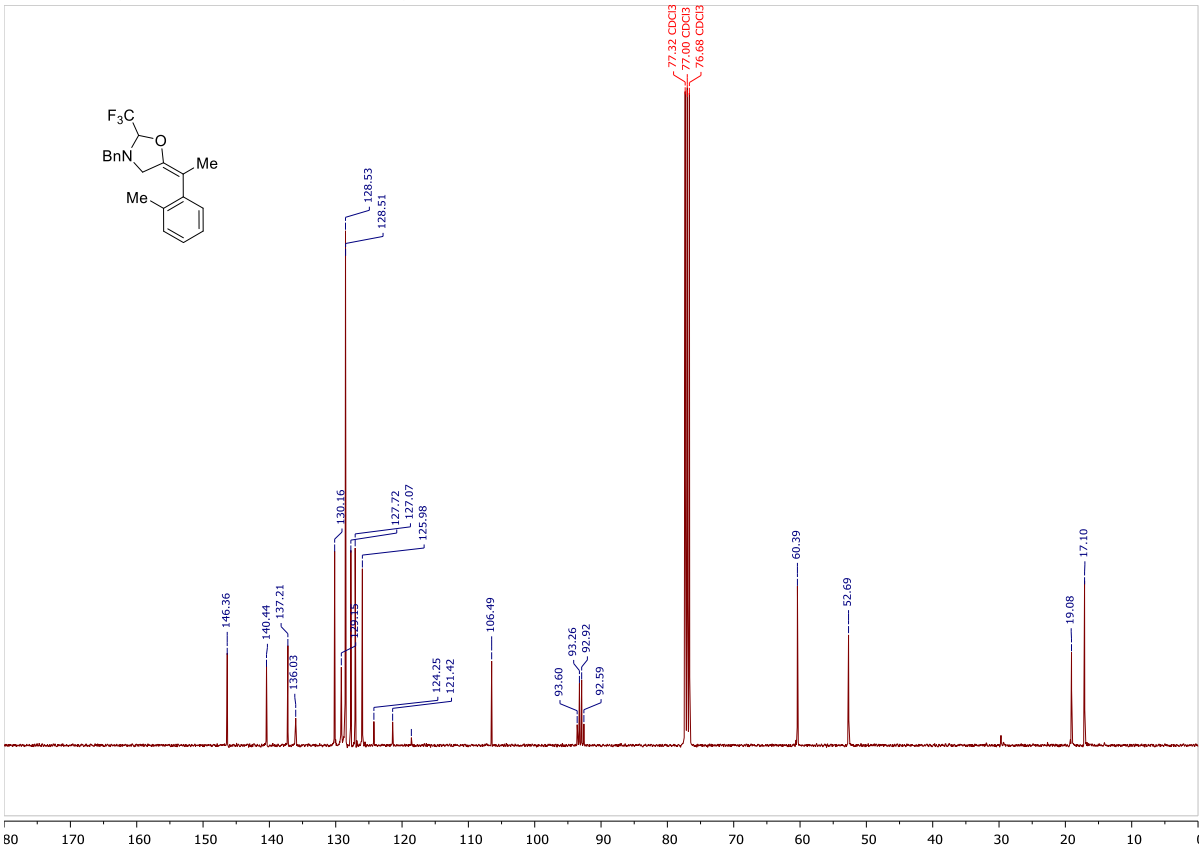


(*E*)-3-benzyl-5-(1-(*o*-tolyl)ethylidene)-2-(trifluoromethyl)oxazolidine (15c)

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

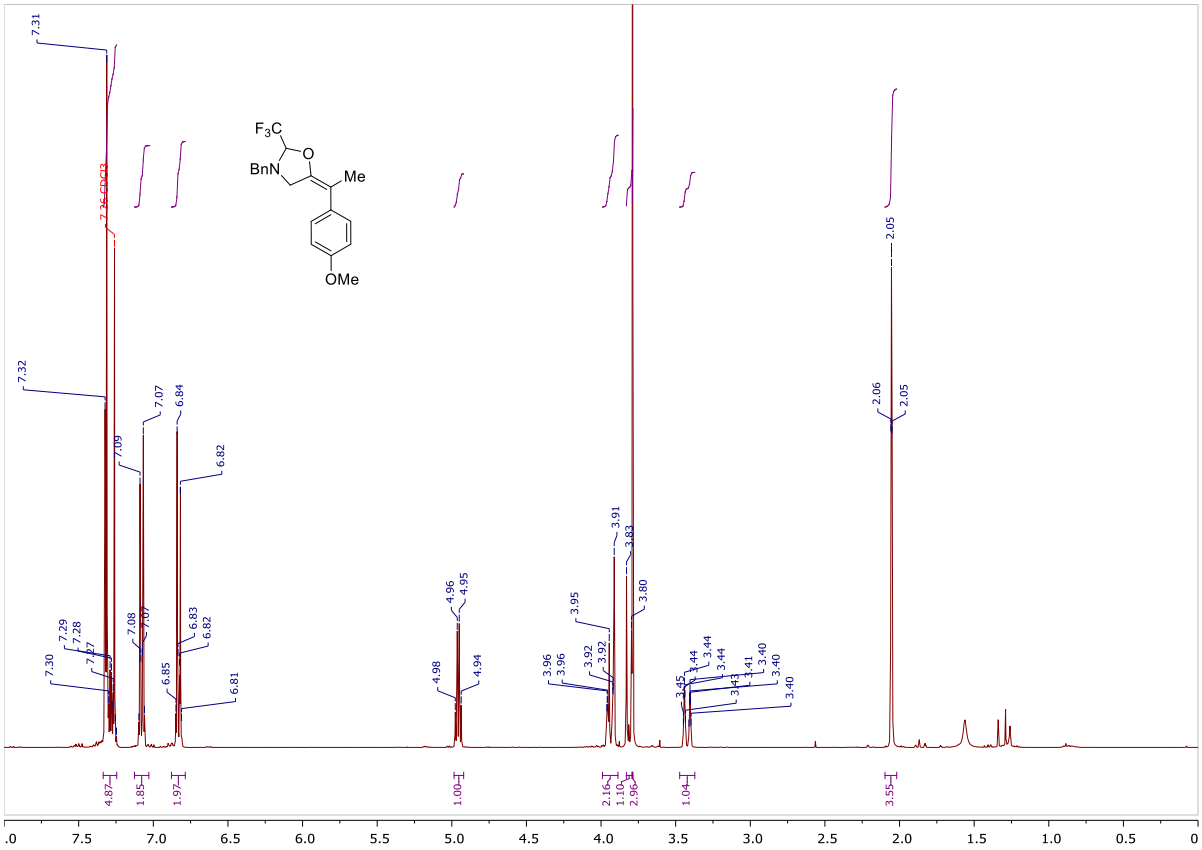


^{13}C-NMR (101 MHz, chloroform-*d*)

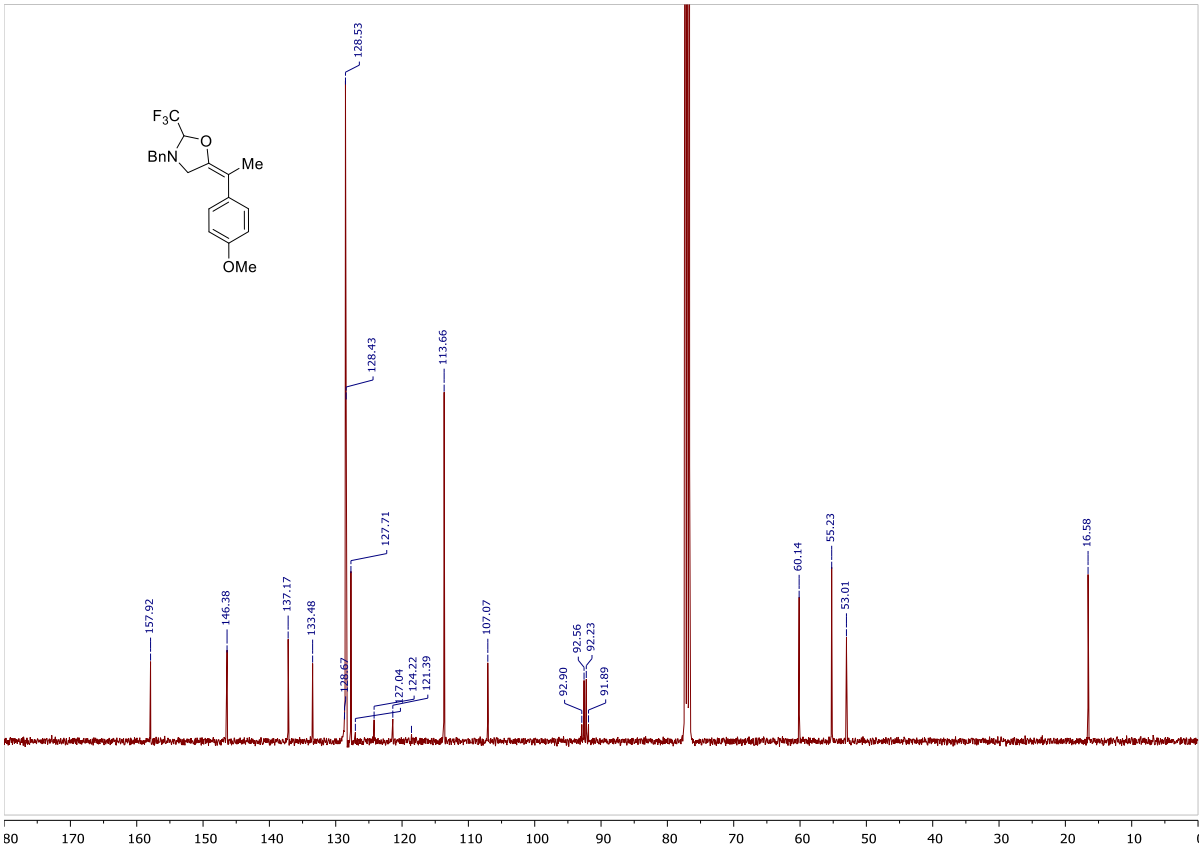


(*E*)-3-benzyl-5-(1-(4-methoxyphenyl)ethylidene)-2-(trifluoromethyl)oxazolidine (15d)

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

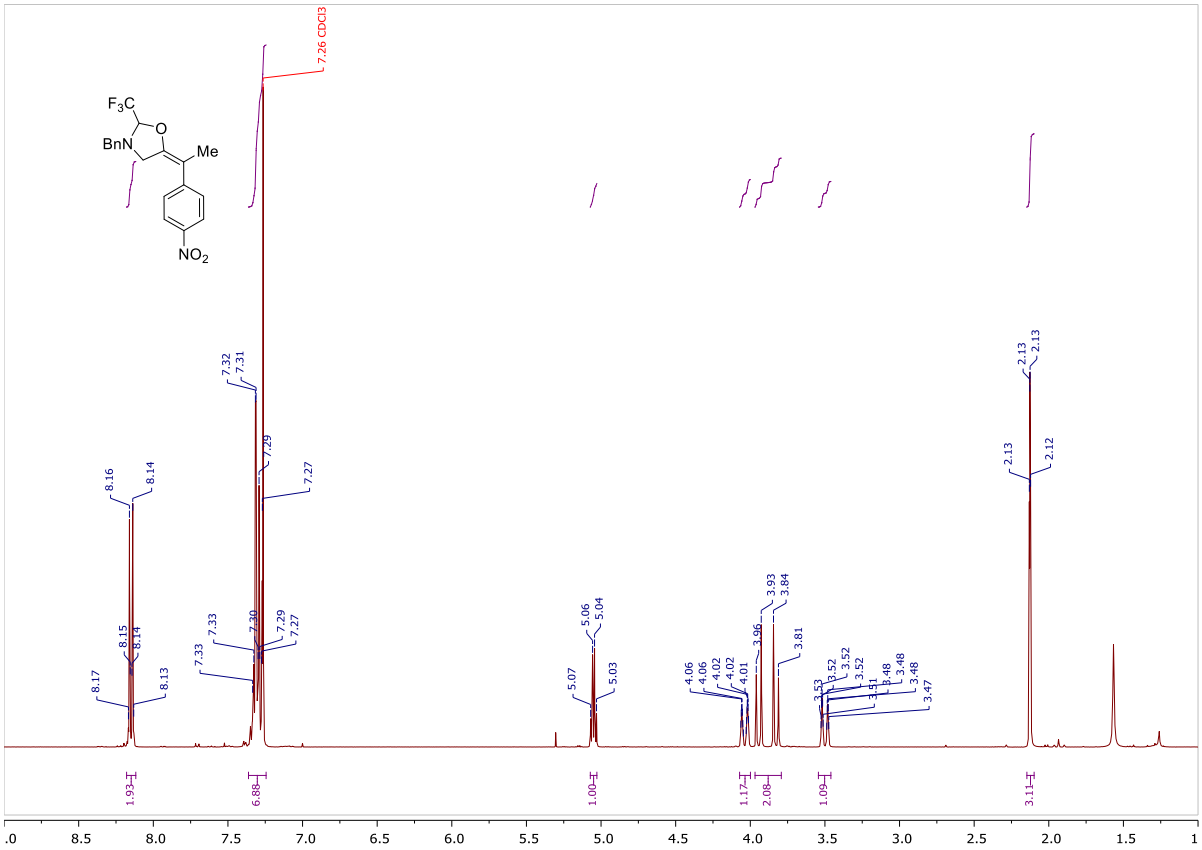


^{13}C-NMR (101 MHz, chloroform-*d*)

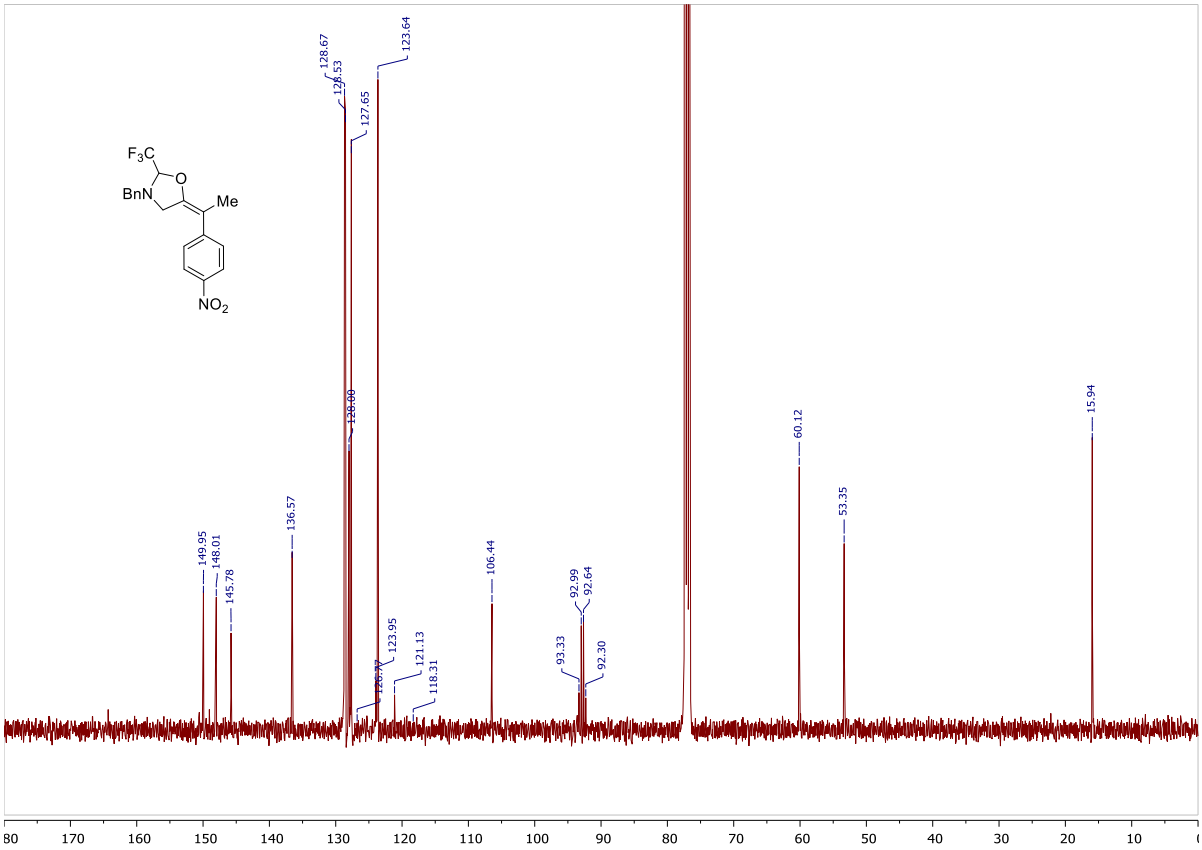


(*E*)-3-benzyl-5-(1-(4-nitrophenyl)ethylidene)-2-(trifluoromethyl)oxazolidine (15e)

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

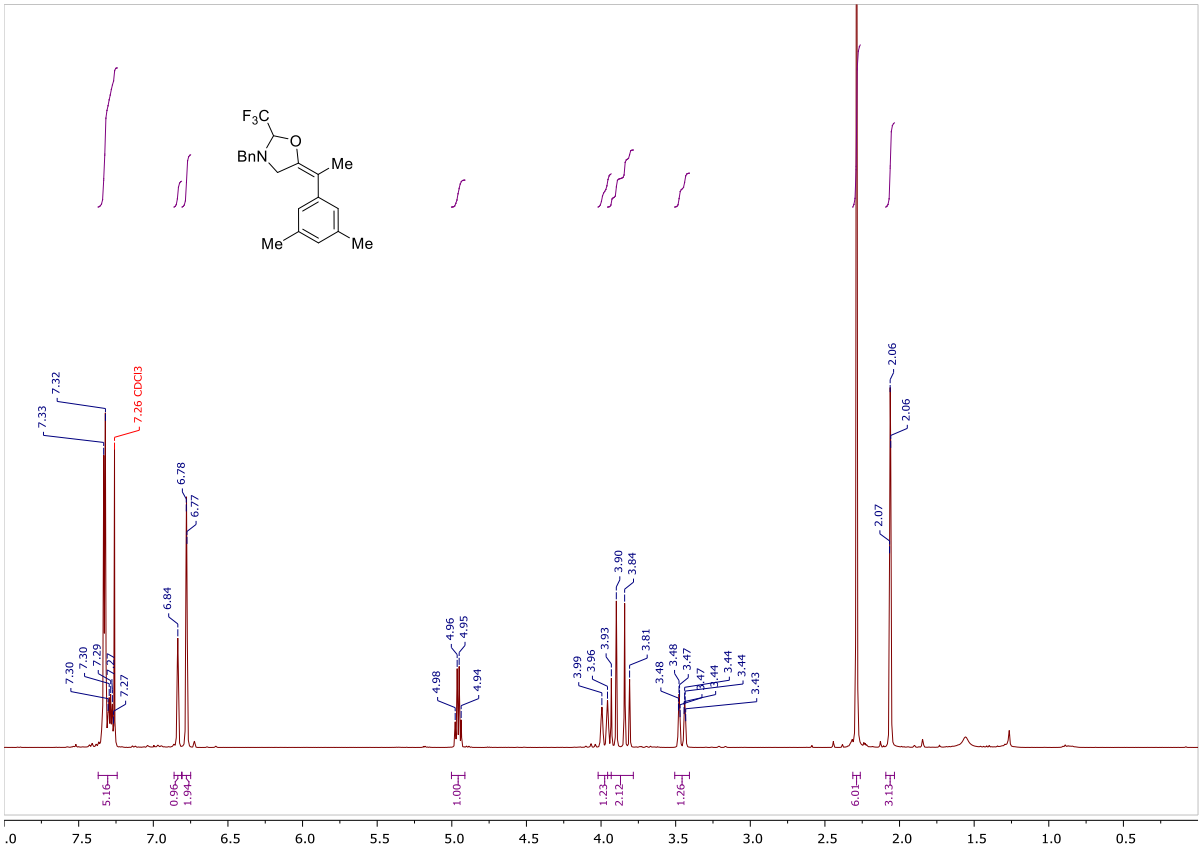


^{13}C-NMR (101 MHz, chloroform-*d*)

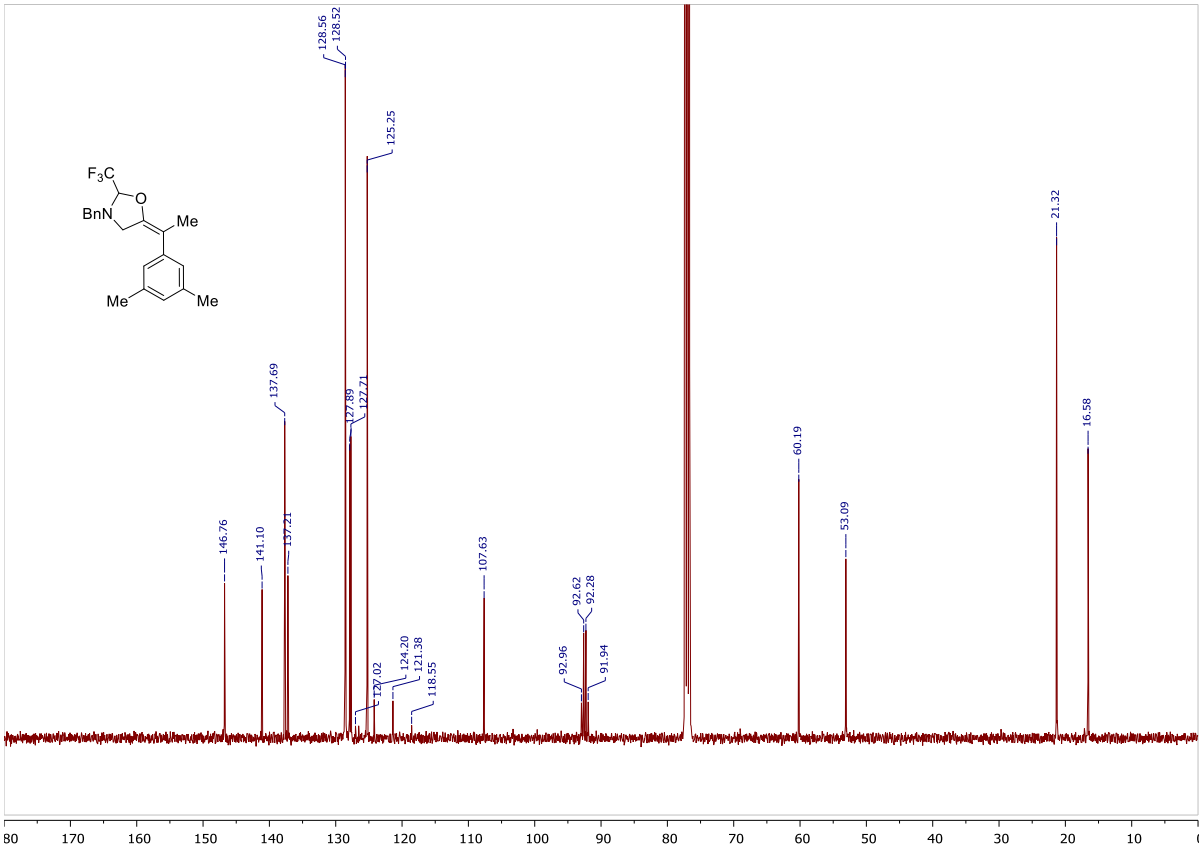


(*E*)-3-benzyl-5-(1-(3,5-dimethylphenyl)ethylidene)-2-(trifluoromethyl)oxazolidine (15f)

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

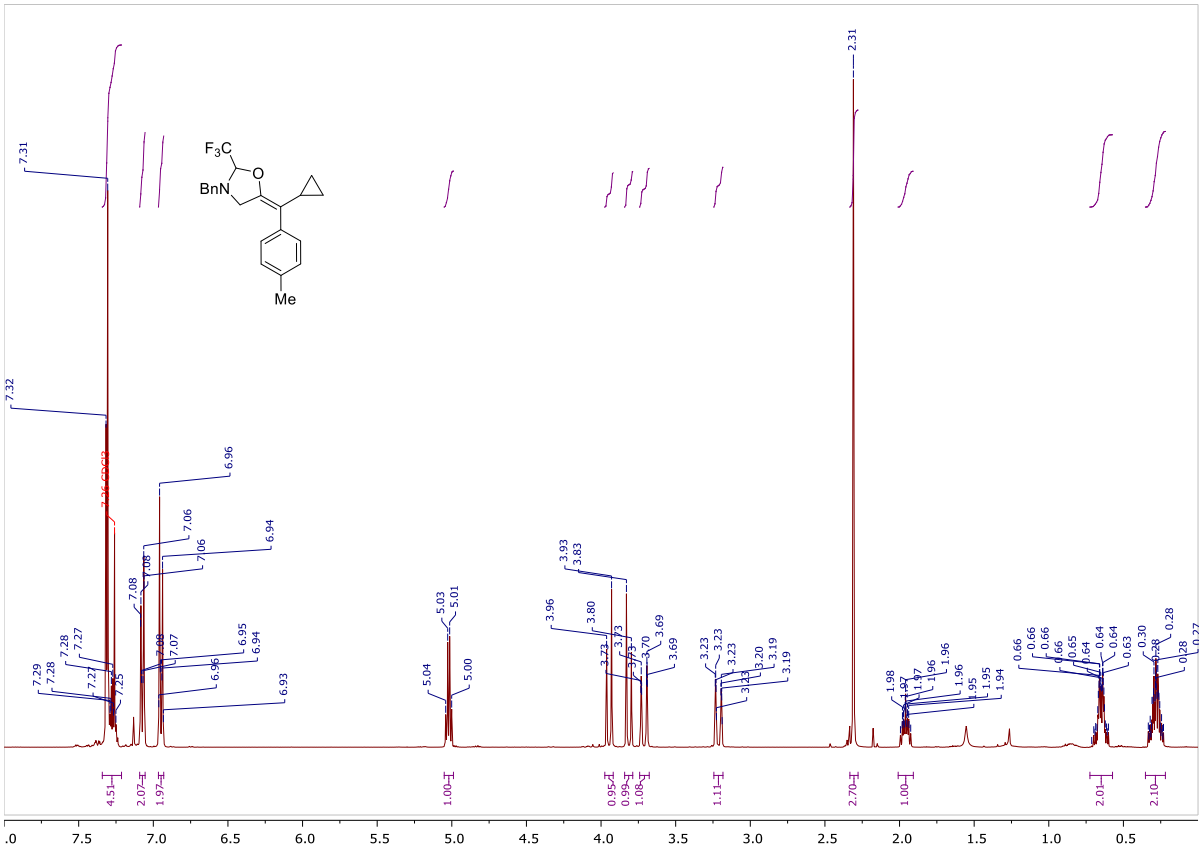


^{13}C-NMR (101 MHz, chloroform-*d*)

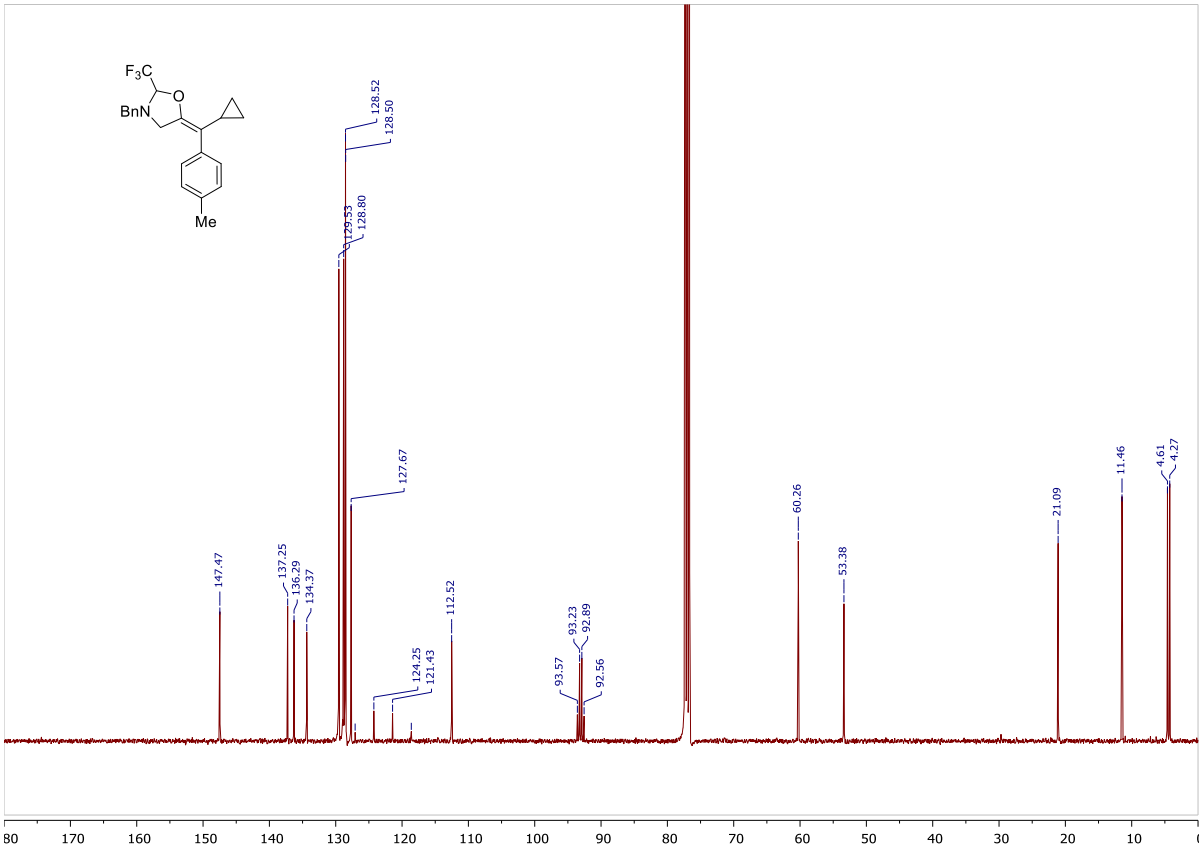


(*E*)-3-benzyl-5-(cyclopropyl(*p*-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (15g)

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

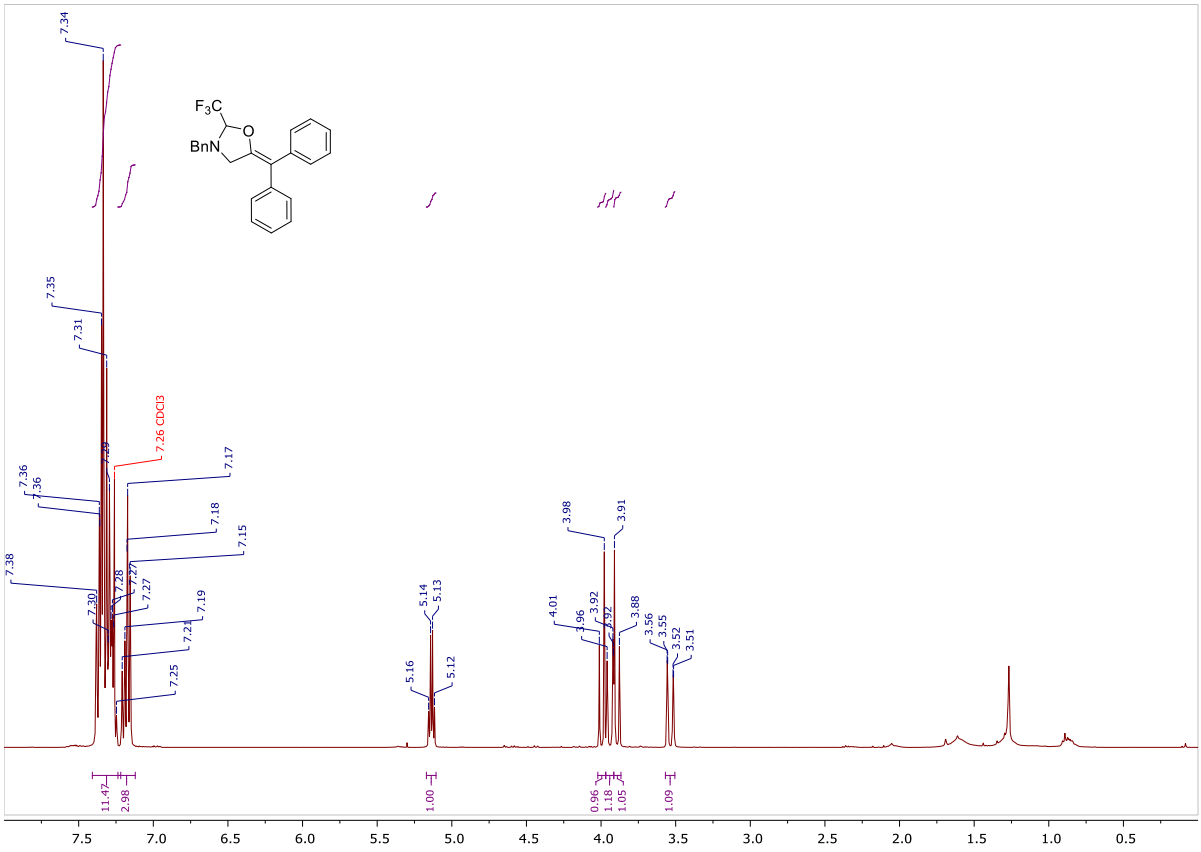


^{13}C-NMR (101 MHz, chloroform-*d*)

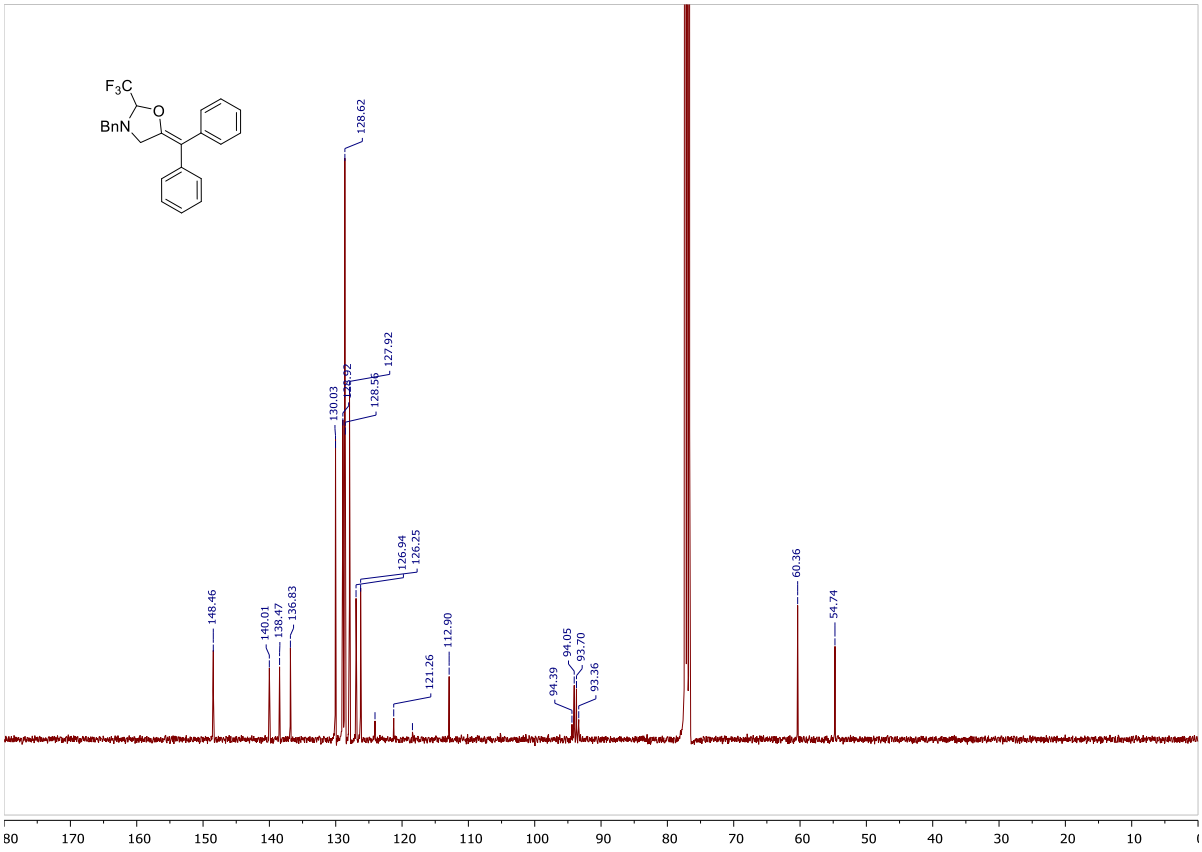


3-benzyl-5-(diphenylmethylene)-2-(trifluoromethyl)oxazolidine (15h)

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

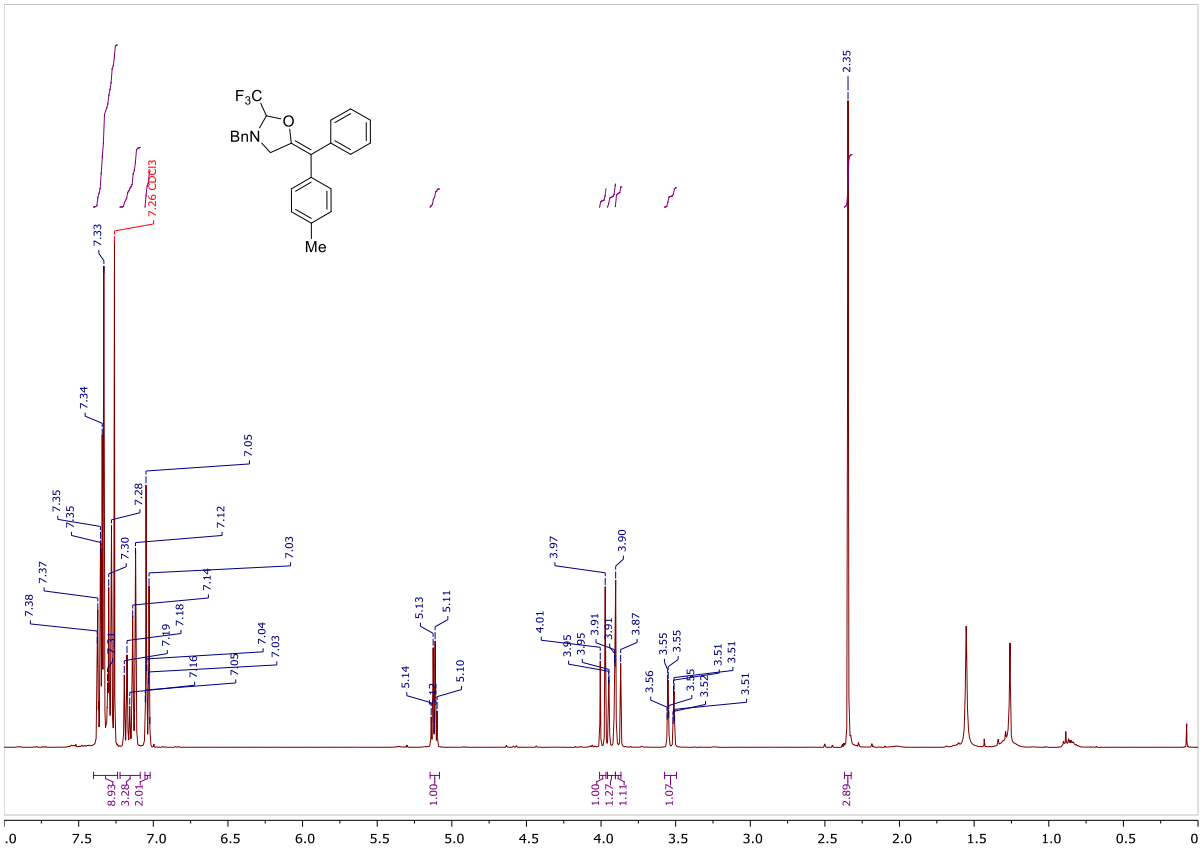


^{13}C-NMR (101 MHz, chloroform-*d*)

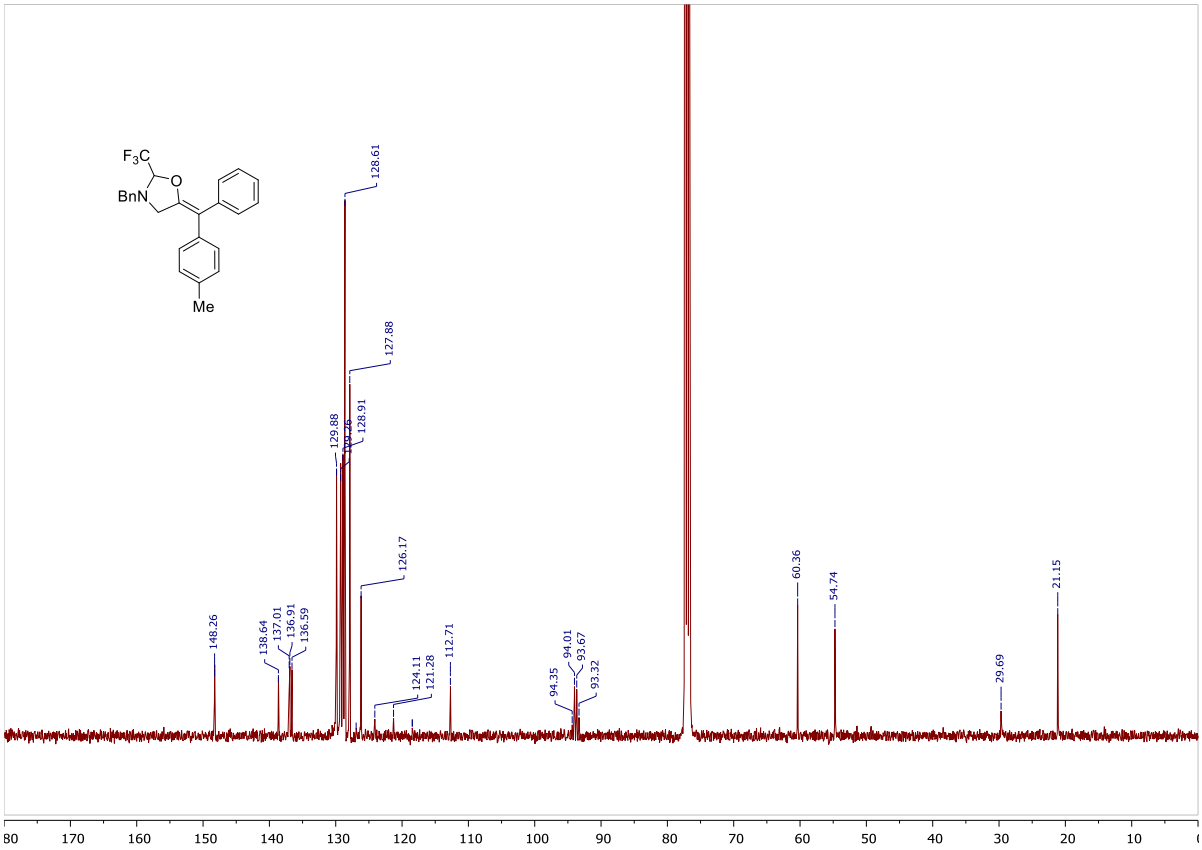


(*E*)-3-benzyl-5-(phenyl(*p*-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (15i)

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

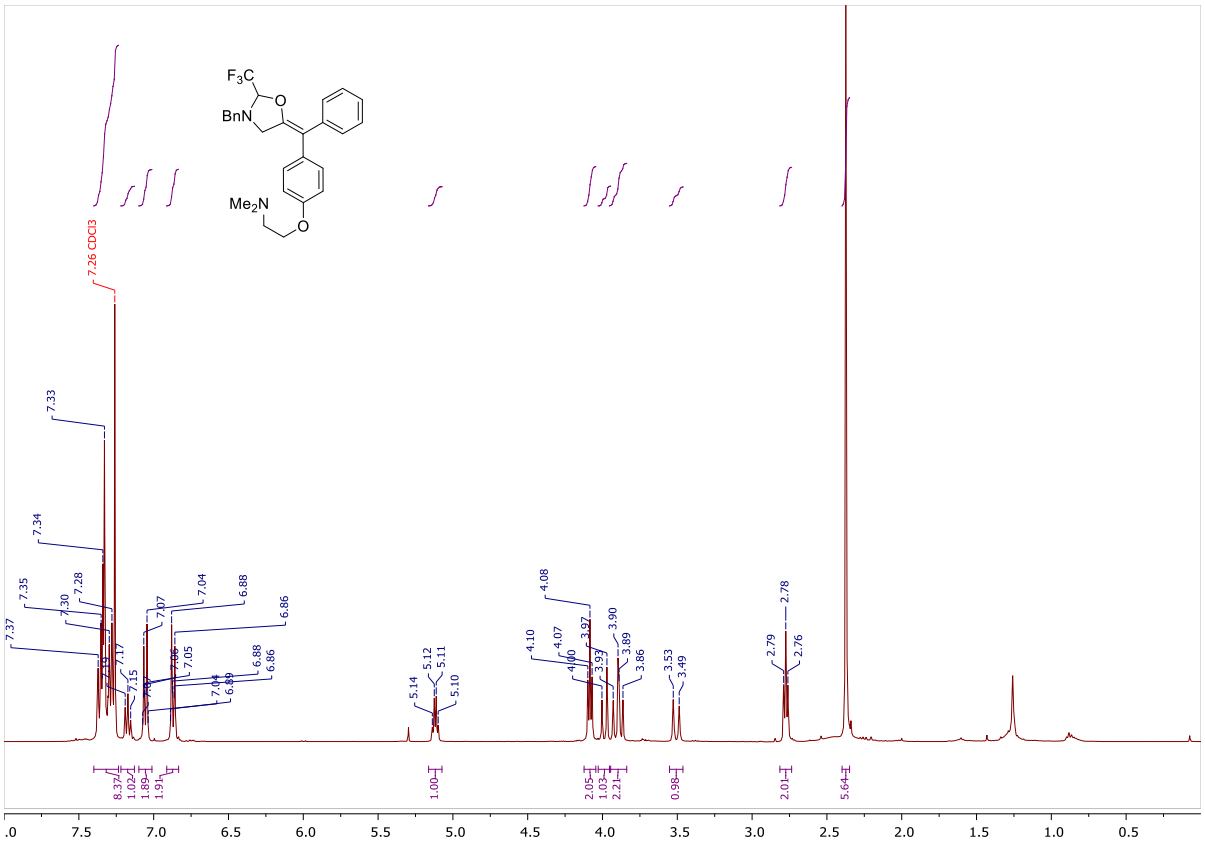


^{13}C-NMR (101 MHz, chloroform-*d*)

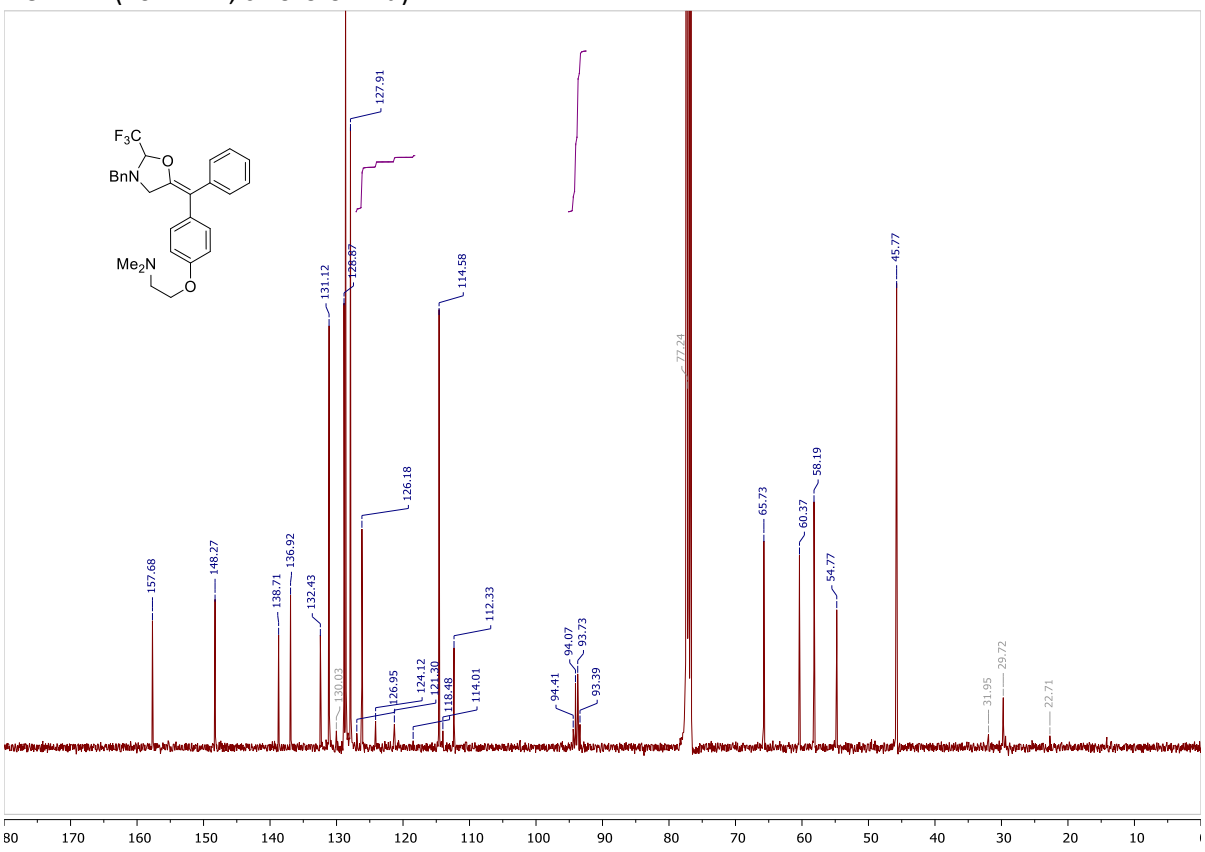


(*E*)-2-(4-((3-benzyl-2-(trifluoromethyl)oxazolidin-5-ylidene)(phenyl)methyl)phenoxy)-*N*,*N*-dimethylethan-1-amine (15j)

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



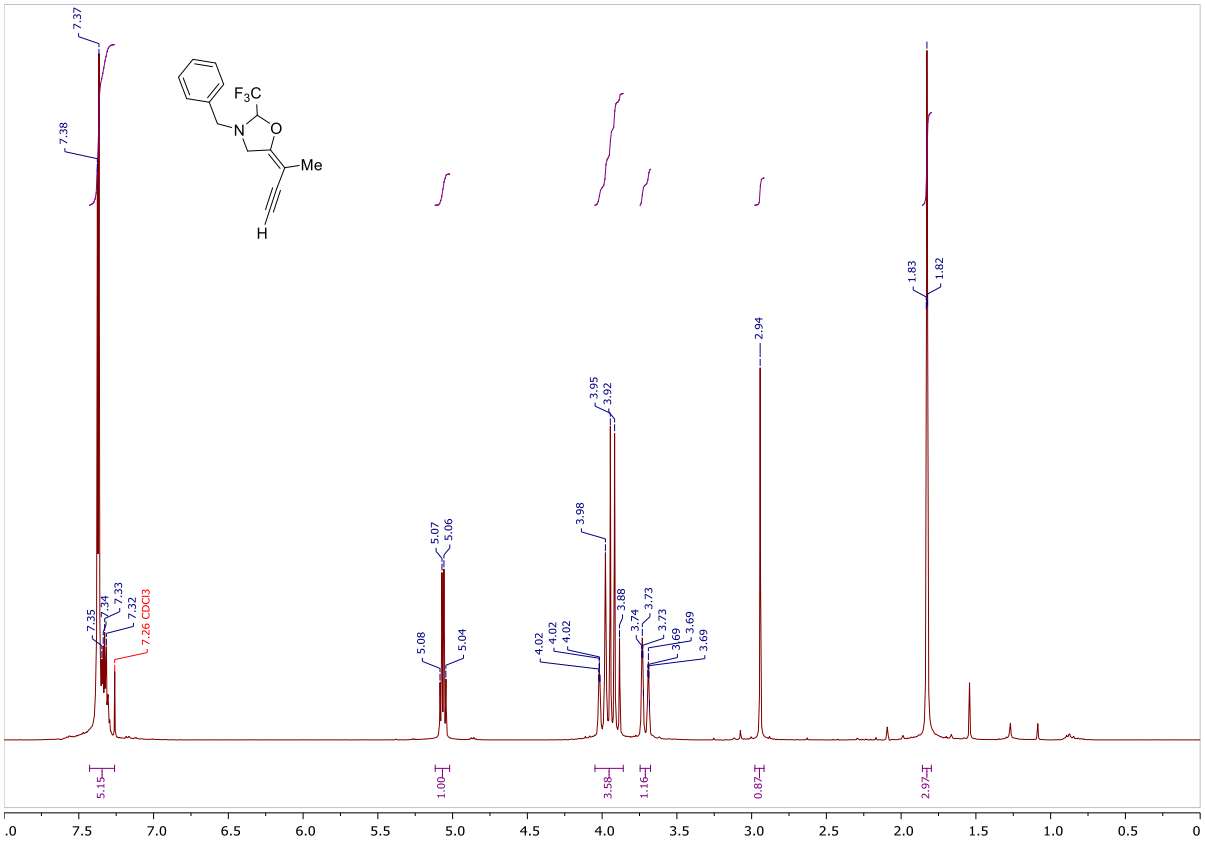
^{13}C-NMR (101 MHz, chloroform-*d*)



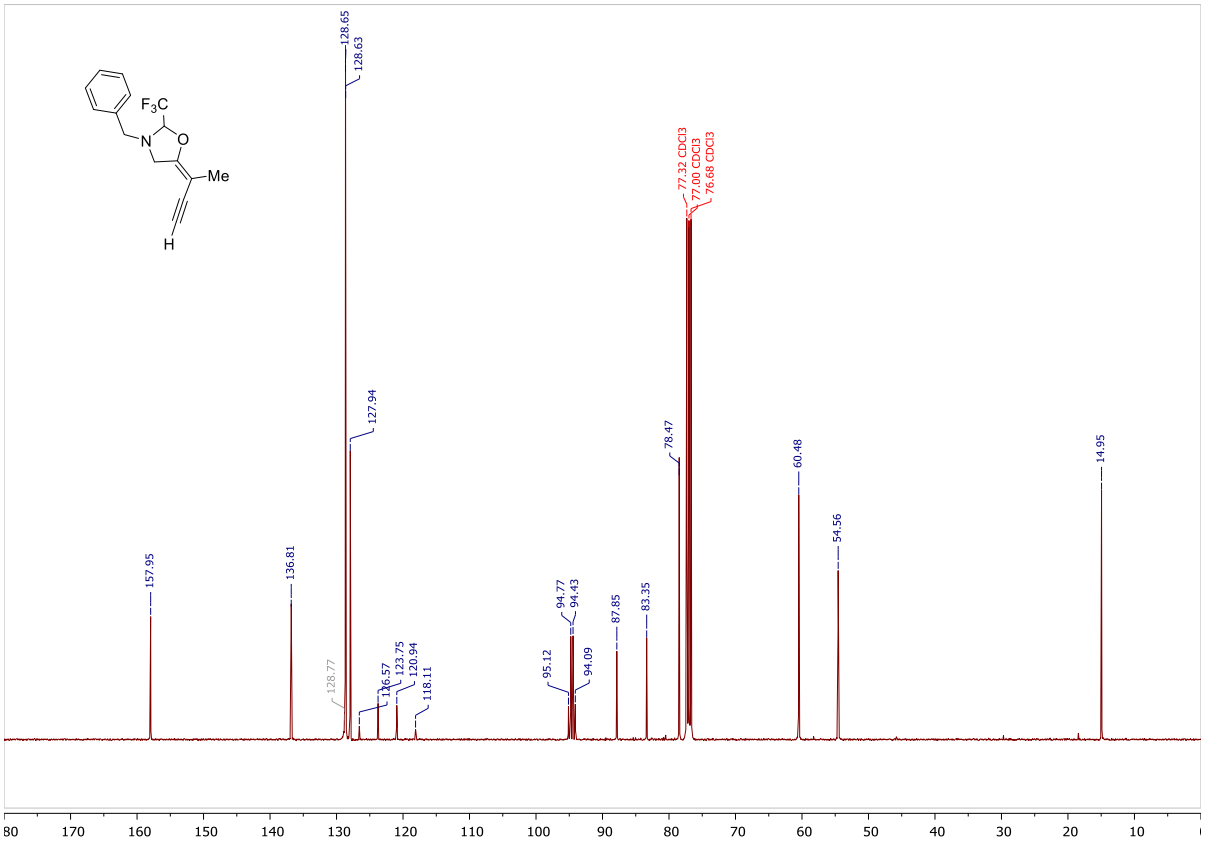
Product Modification

(E)-3-Benzyl-5-(but-3-yn-2-ylidene)-2-(trifluoromethyl)oxazolidine (17)

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

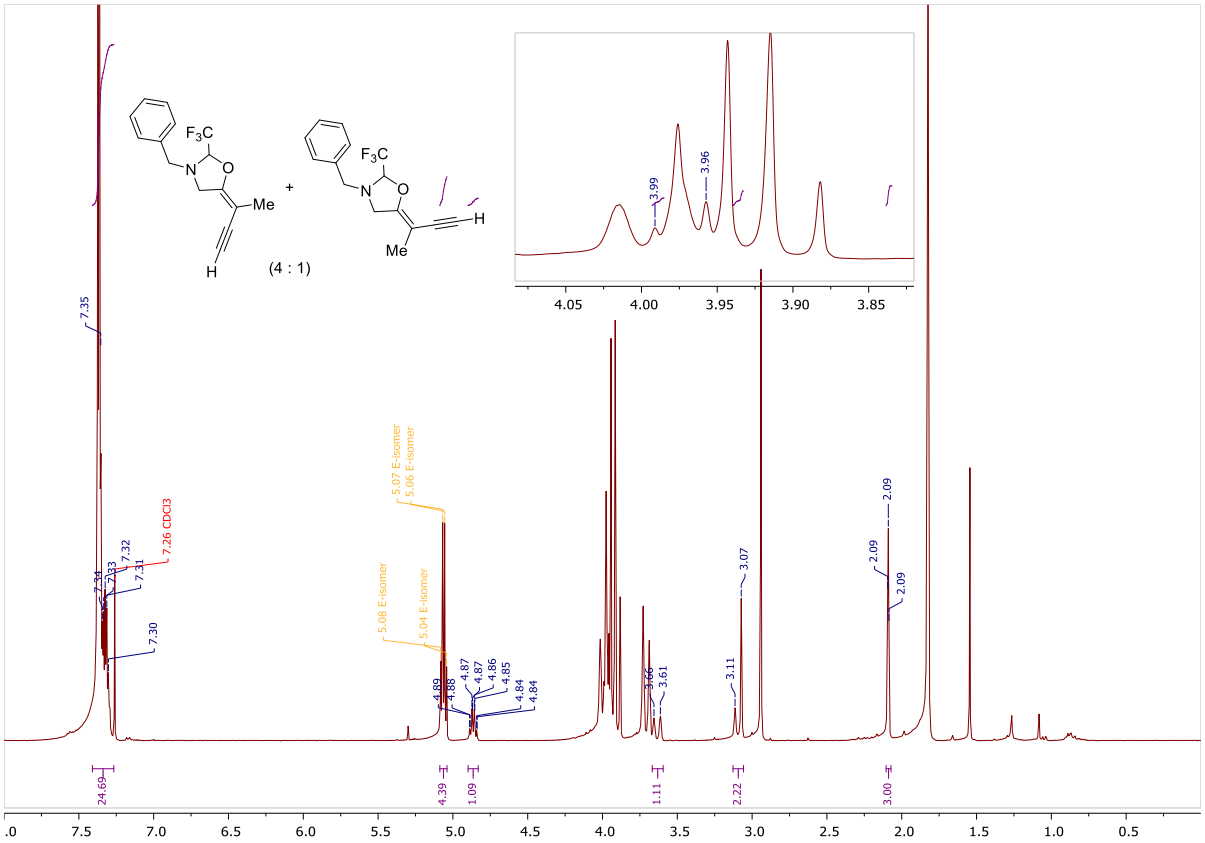


^{13}C-NMR (101 MHz, chloroform-*d*)

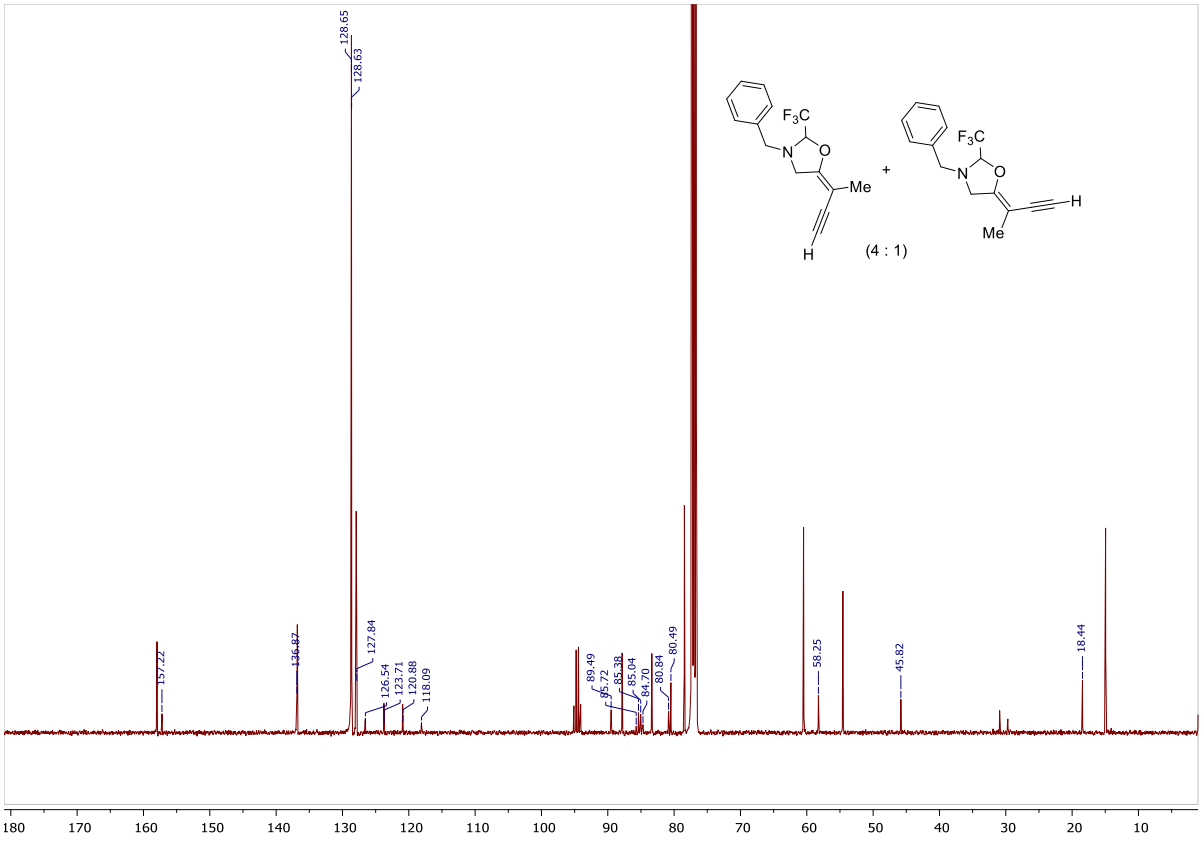


(E)- and (Z)-3-Benzyl-5-(but-3-yn-2-ylidene)-2-(trifluoromethyl)oxazolidine (17)

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

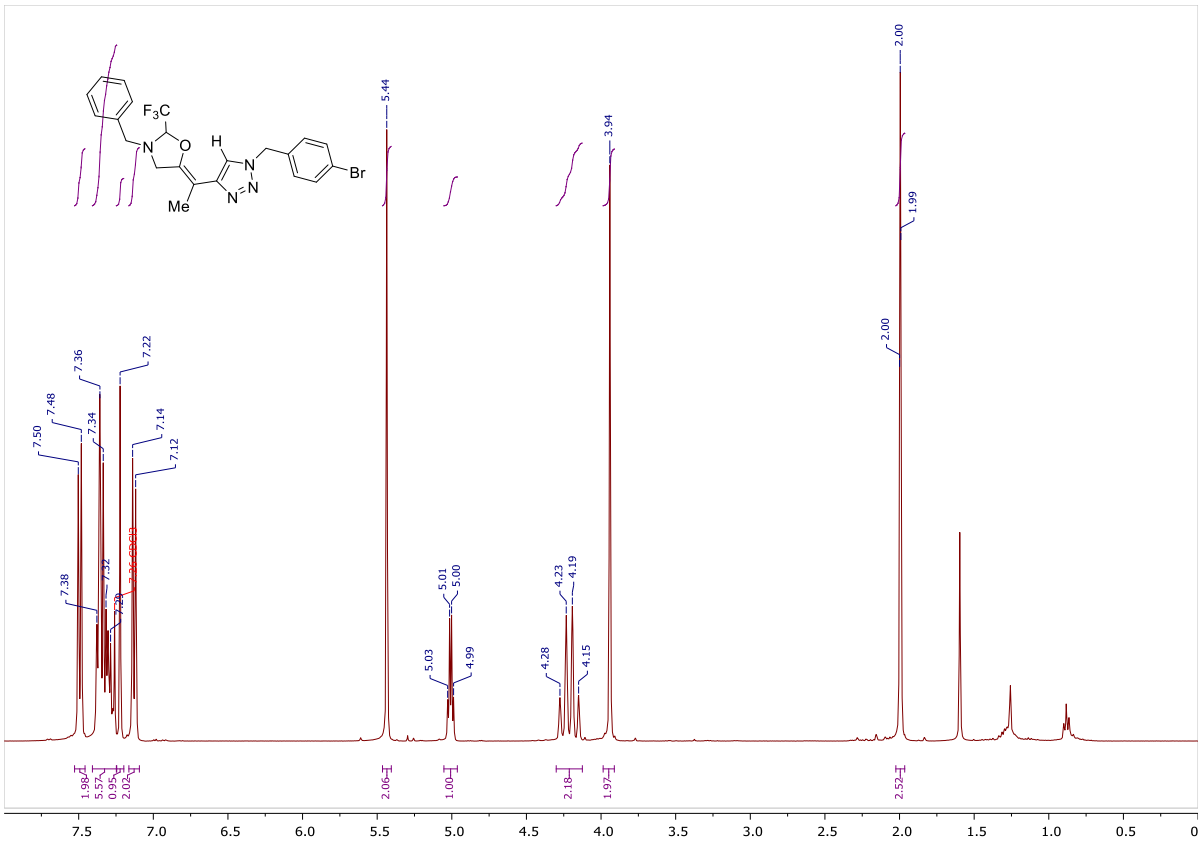


^{13}C-NMR (101 MHz, chloroform-*d*)

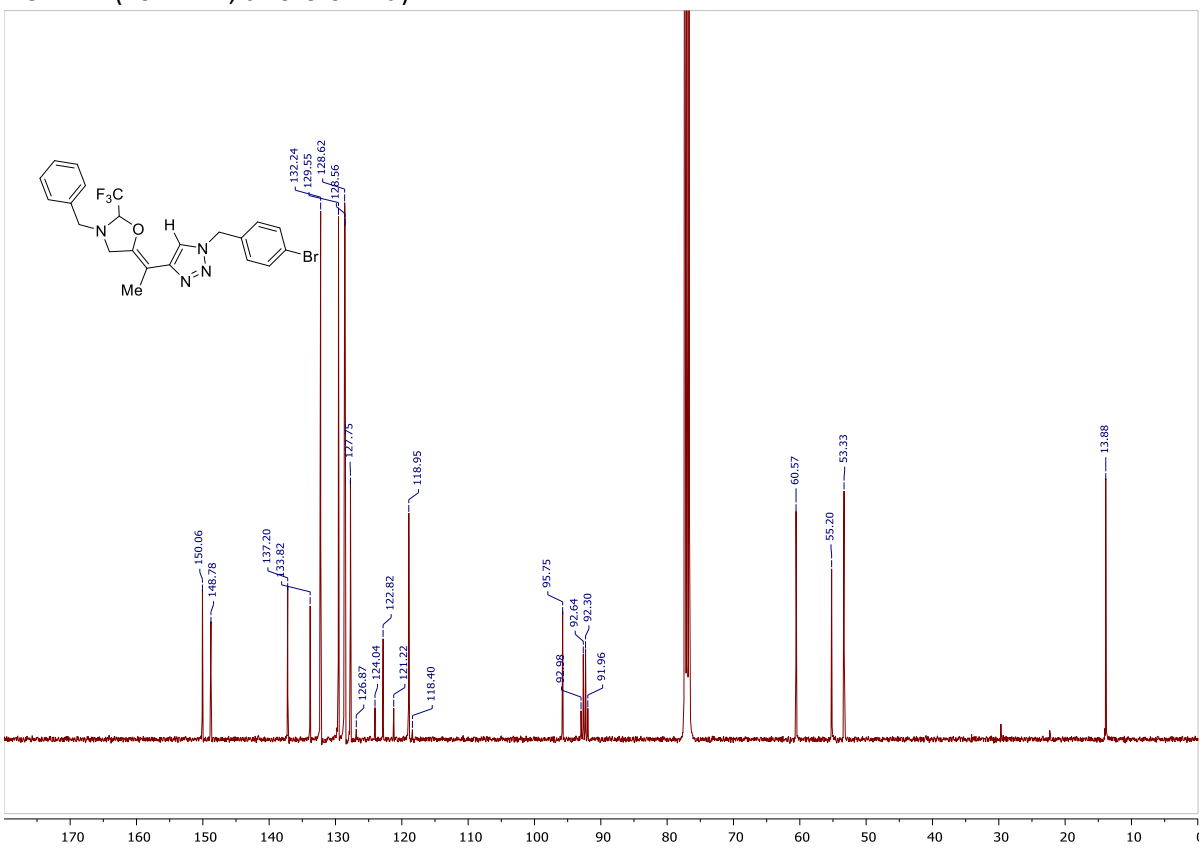


(E)-3-Benzyl-5-(1-(1-(4-bromobenzyl)-1H-1,2,3-triazol-4-yl)ethylidene)-2-(trifluoromethyl)oxazolidine (18)

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

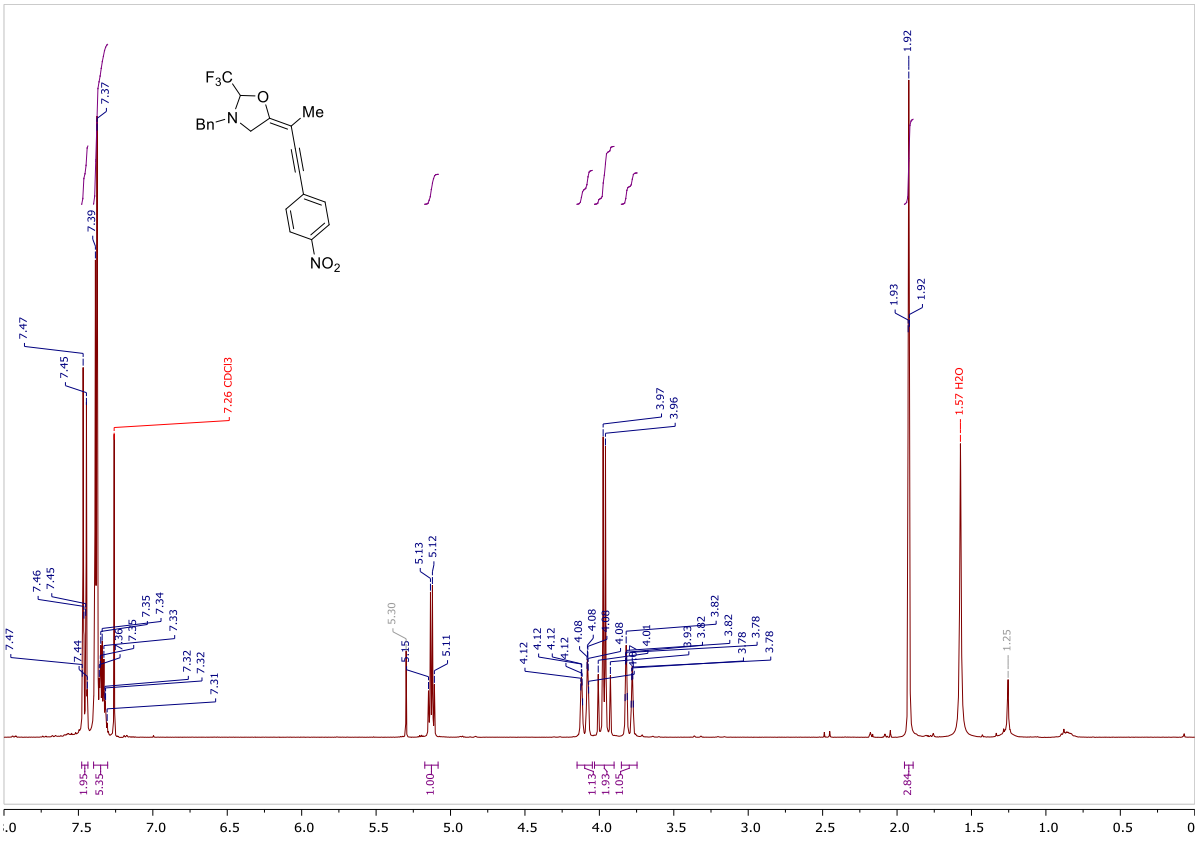


^{13}C-NMR (101 MHz, chloroform-*d*)

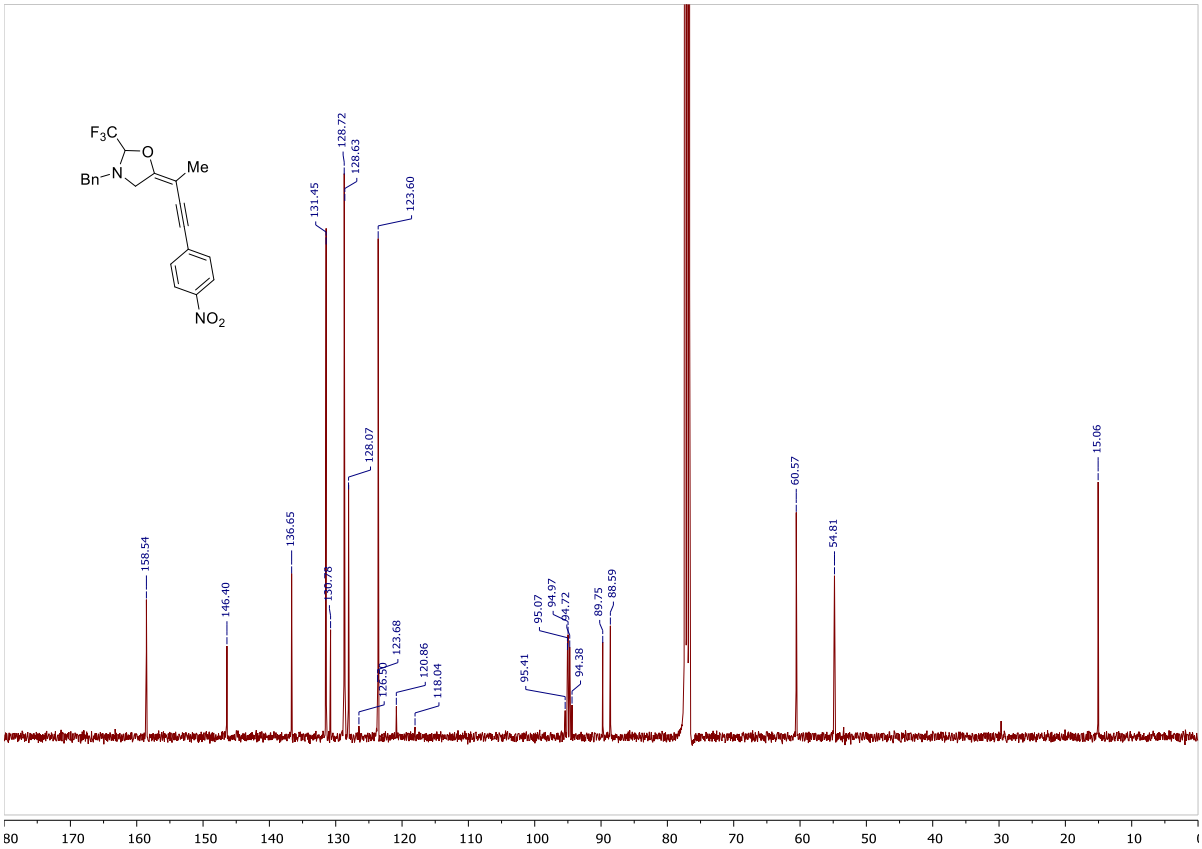


(Z)-3-benzyl-5-(4-(4-nitrophenyl)but-3-yn-2-ylidene)-2-(trifluoromethyl)oxazolidine (19)

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

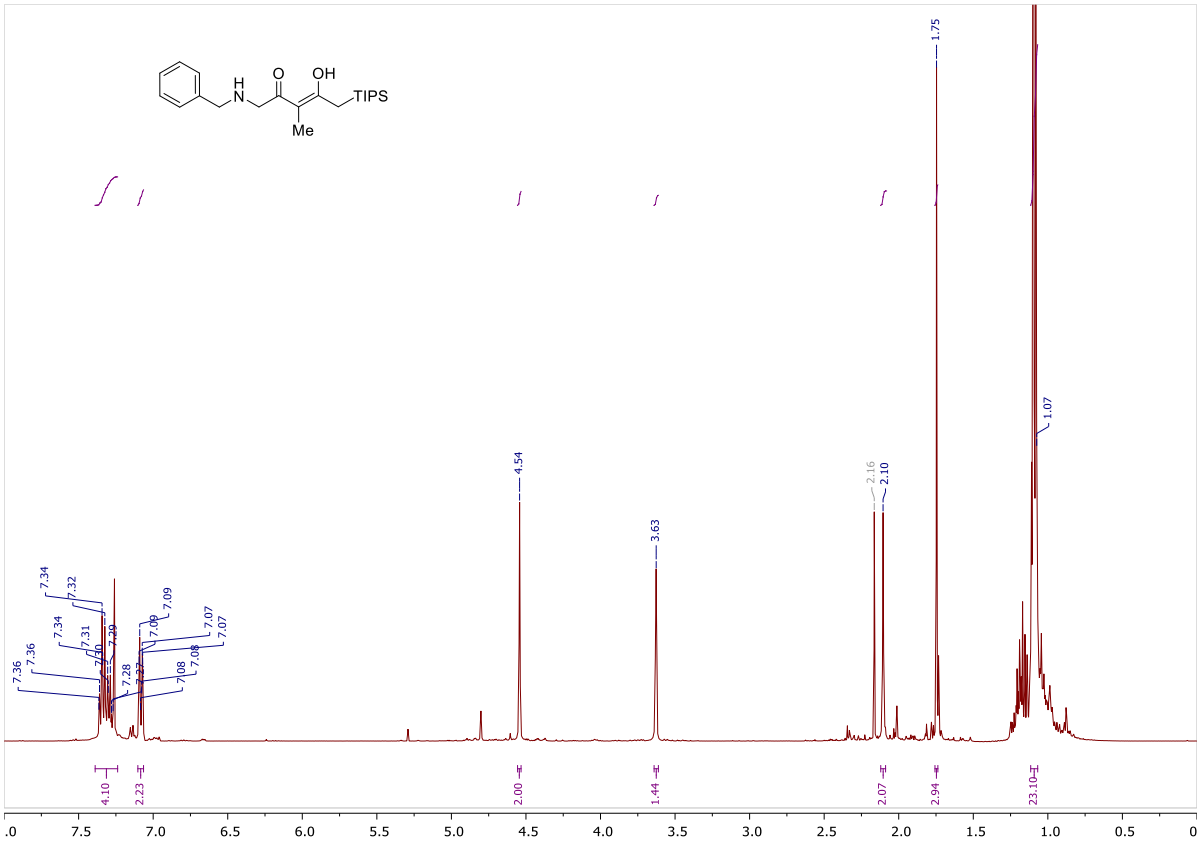


^{13}C-NMR (101 MHz, chloroform-*d*)

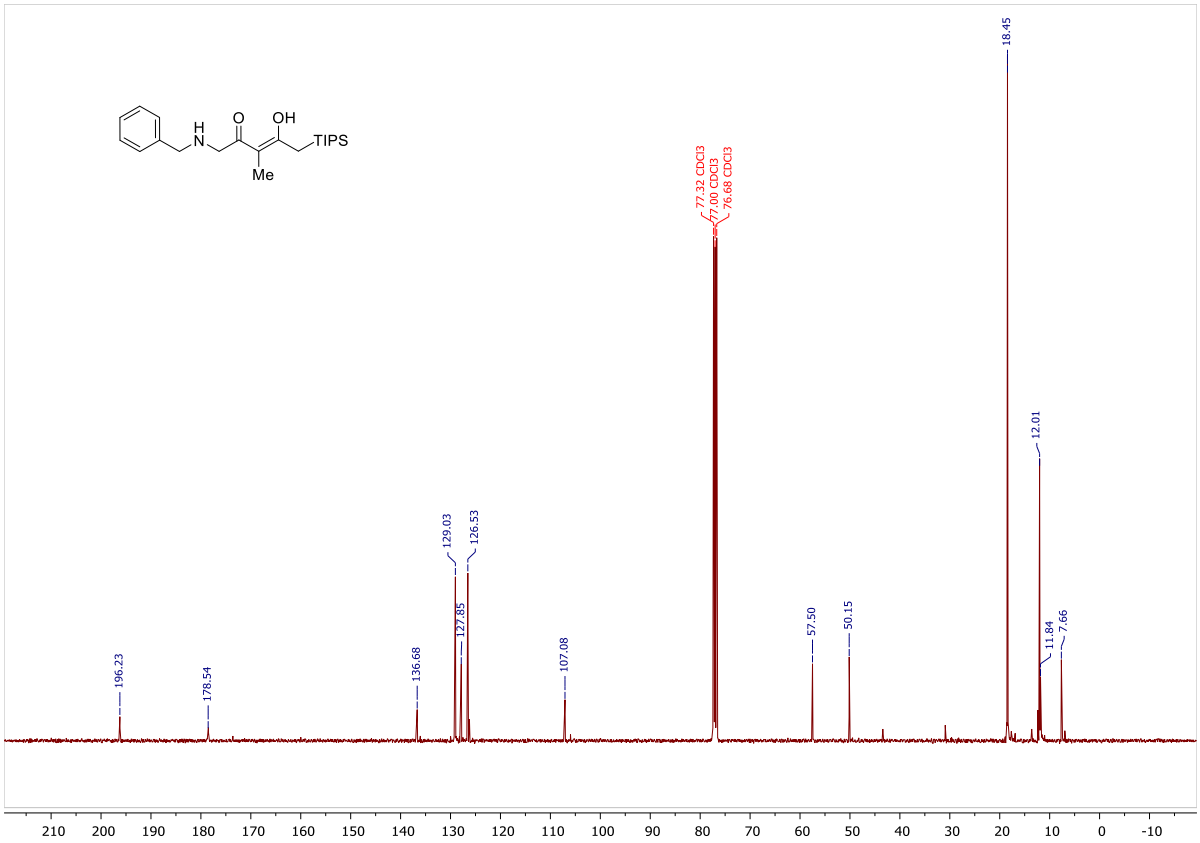


1-(benzylamino)-4-hydroxy-3-methyl-5-(tri*iso*propylsilyl)pent-3-en-2-one (20)

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

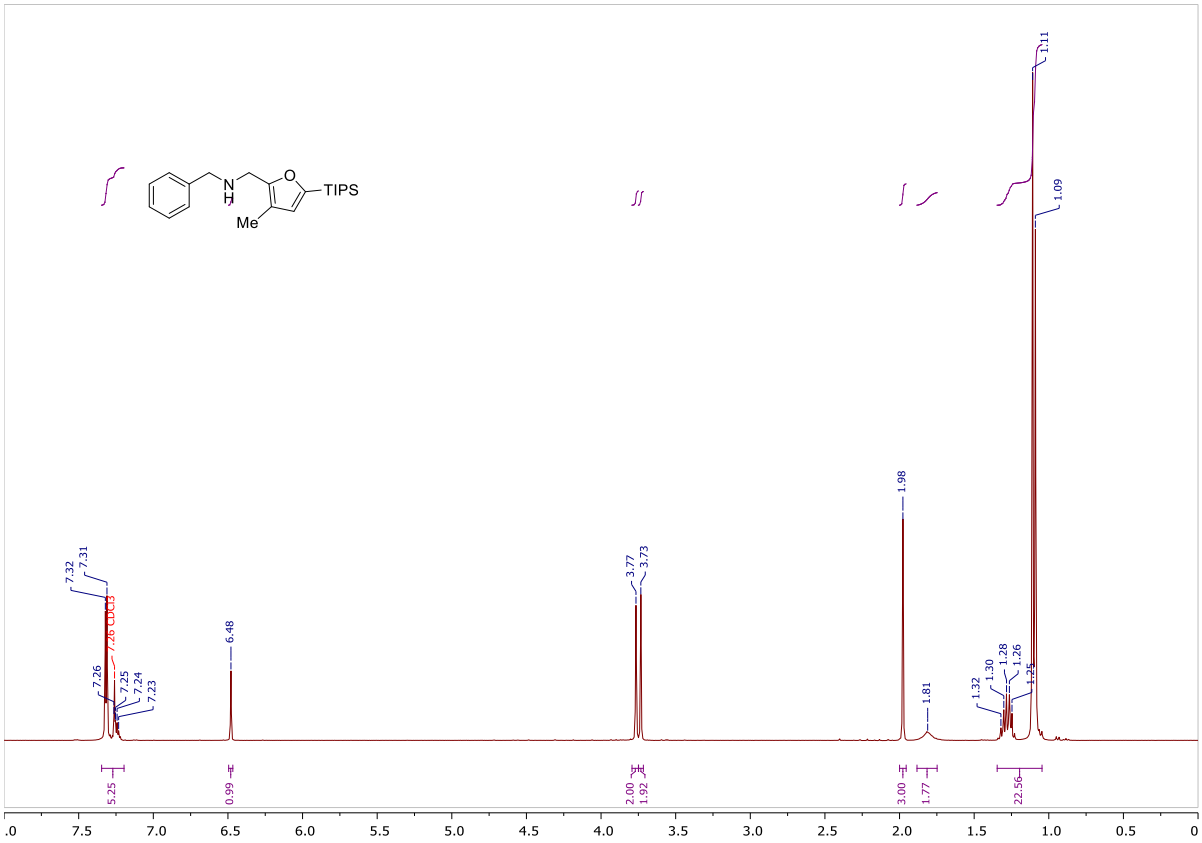


^{13}C-NMR (101 MHz, chloroform-*d*)

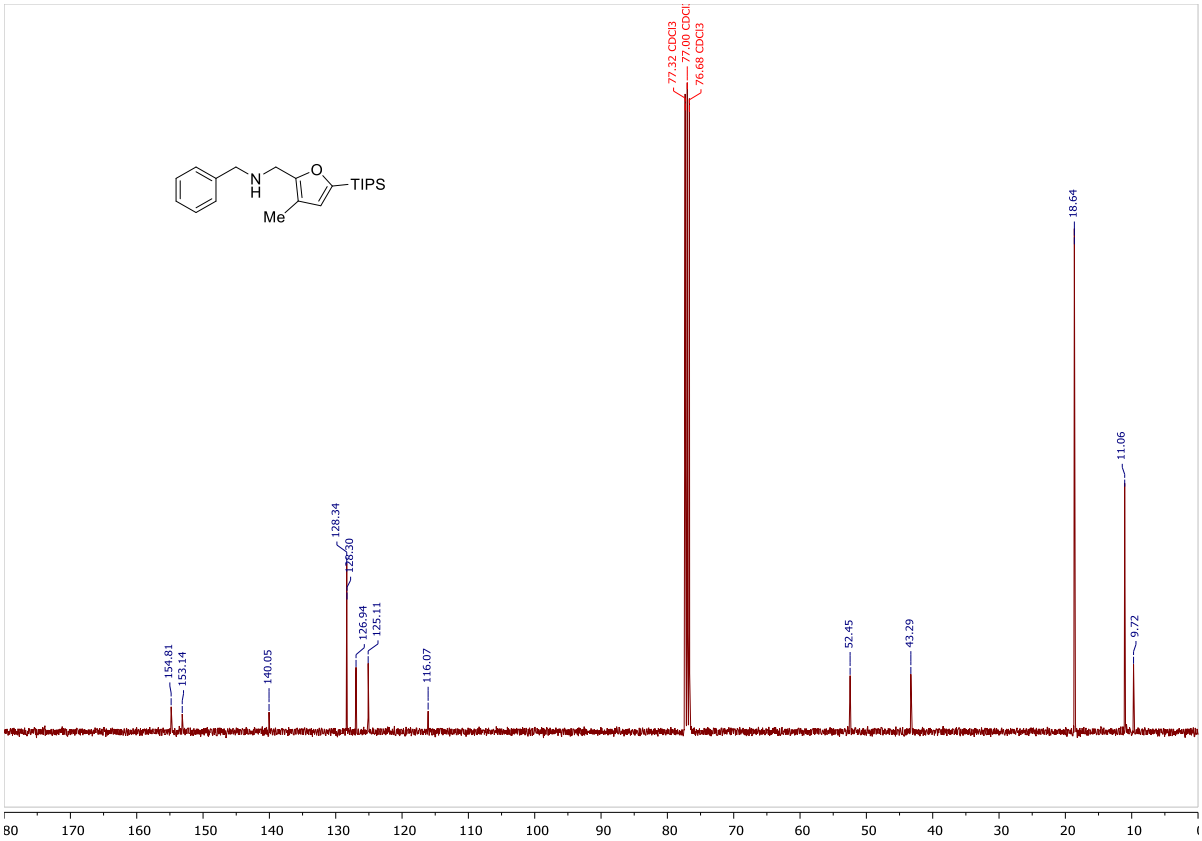


N-benzyl-1-(3-methyl-5-(tri*iso*propylsilyl)furan-2-yl)methanamine (21a)

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

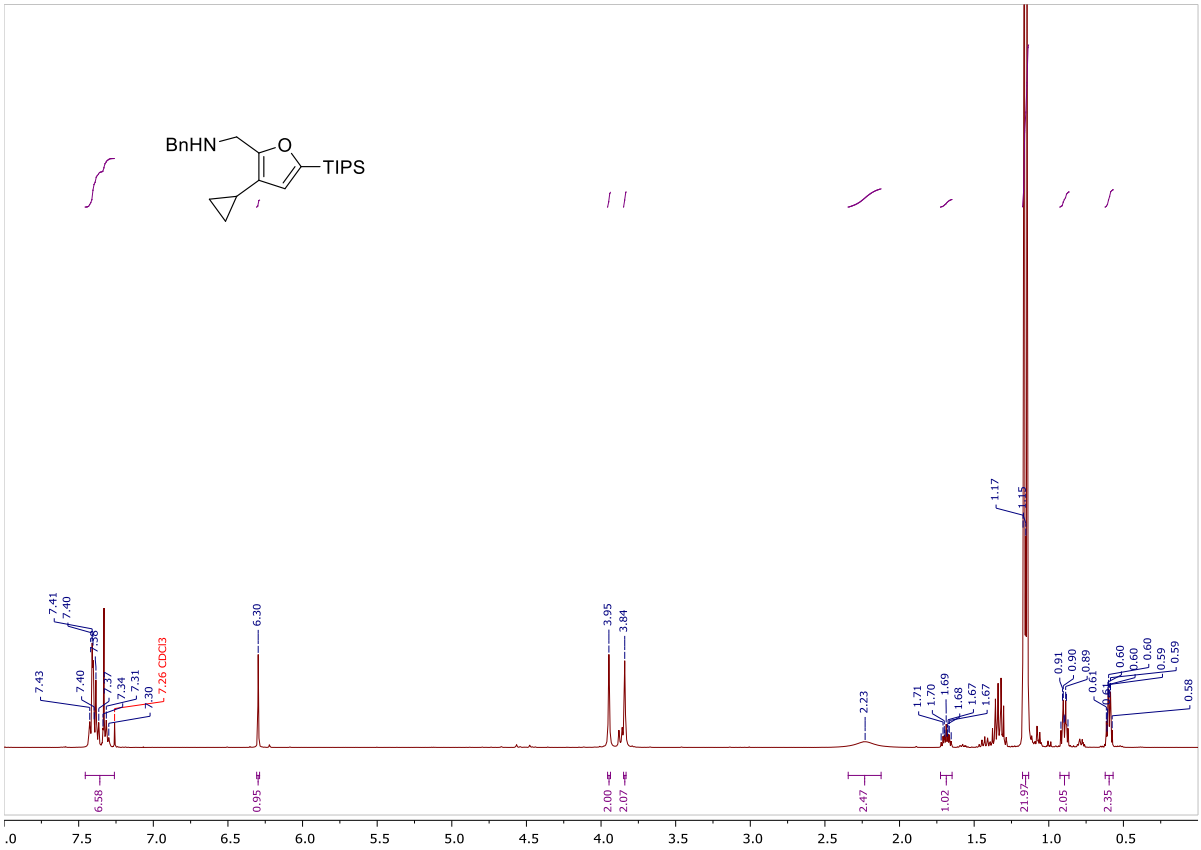


^{13}C-NMR (101 MHz, chloroform-*d*)

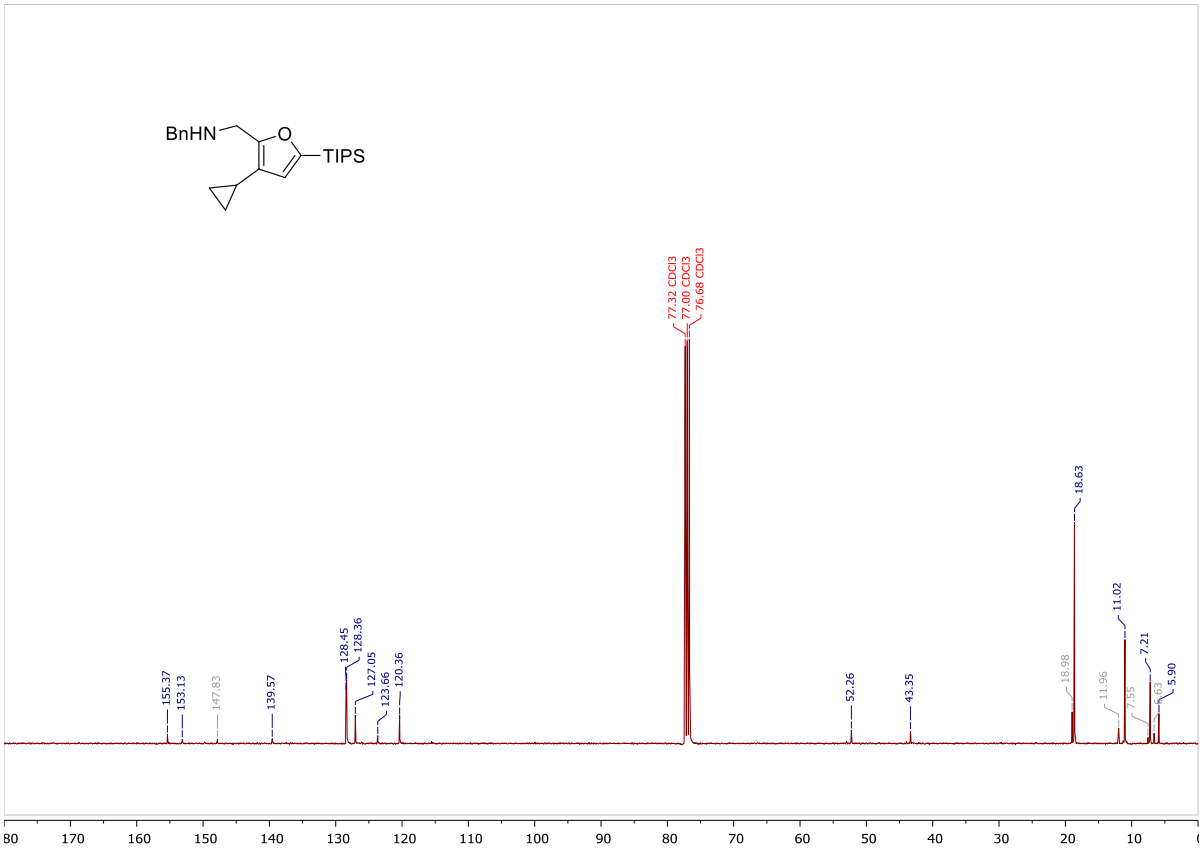


N-benzyl-1-(3-cyclopropyl-5-(tri*iso*propylsilyl)furan-2-yl)methanamine (21b)

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

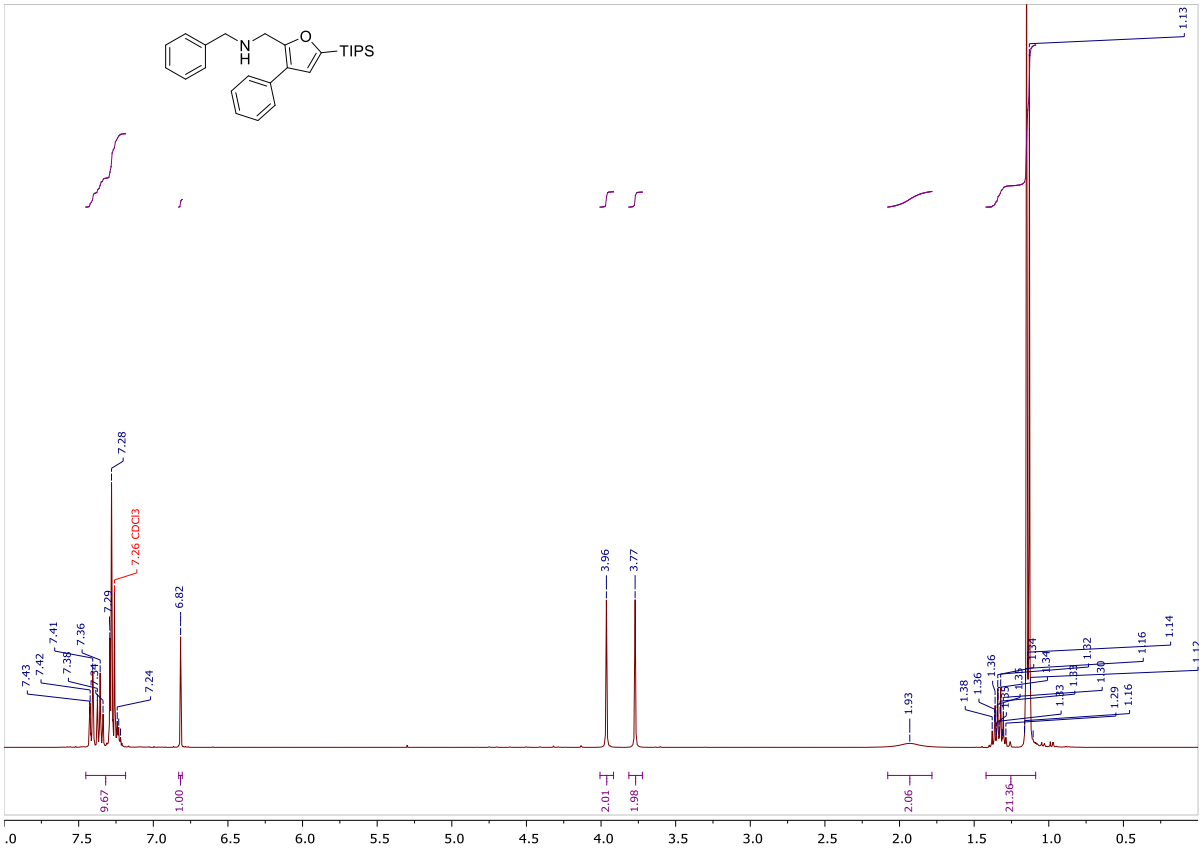


^{13}C-NMR (101 MHz, chloroform-*d*)

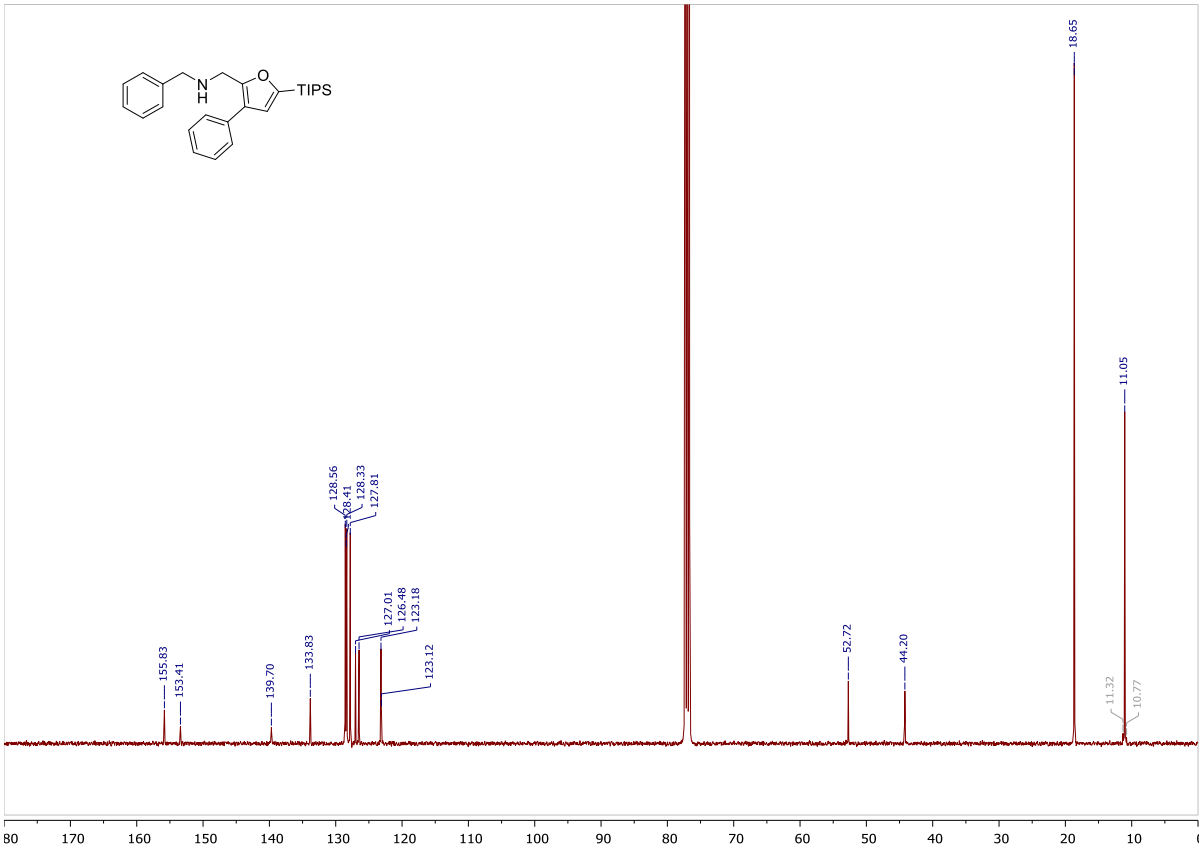


N-benzyl-1-(3-phenyl-5-(tri*iso*propylsilyl)furan-2-yl)methanamine (21c)

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

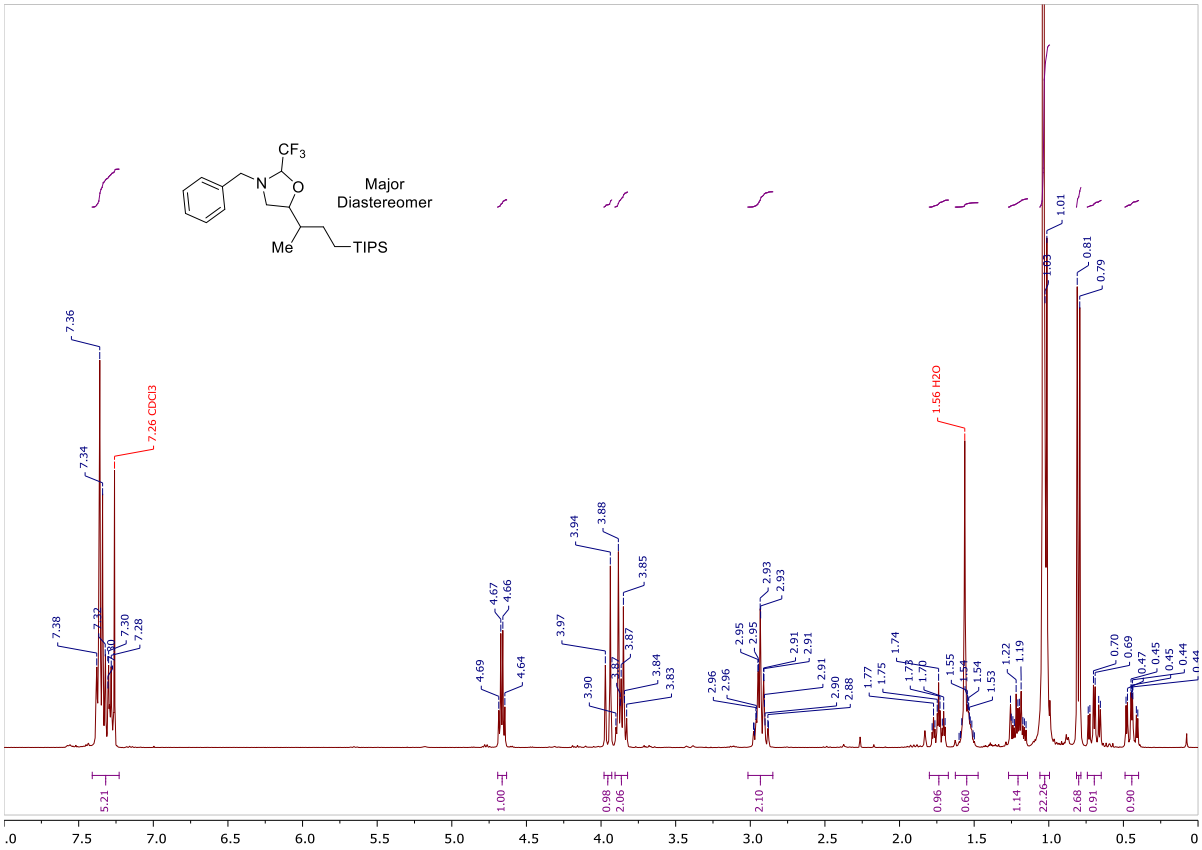


^{13}C-NMR (101 MHz, chloroform-*d*)

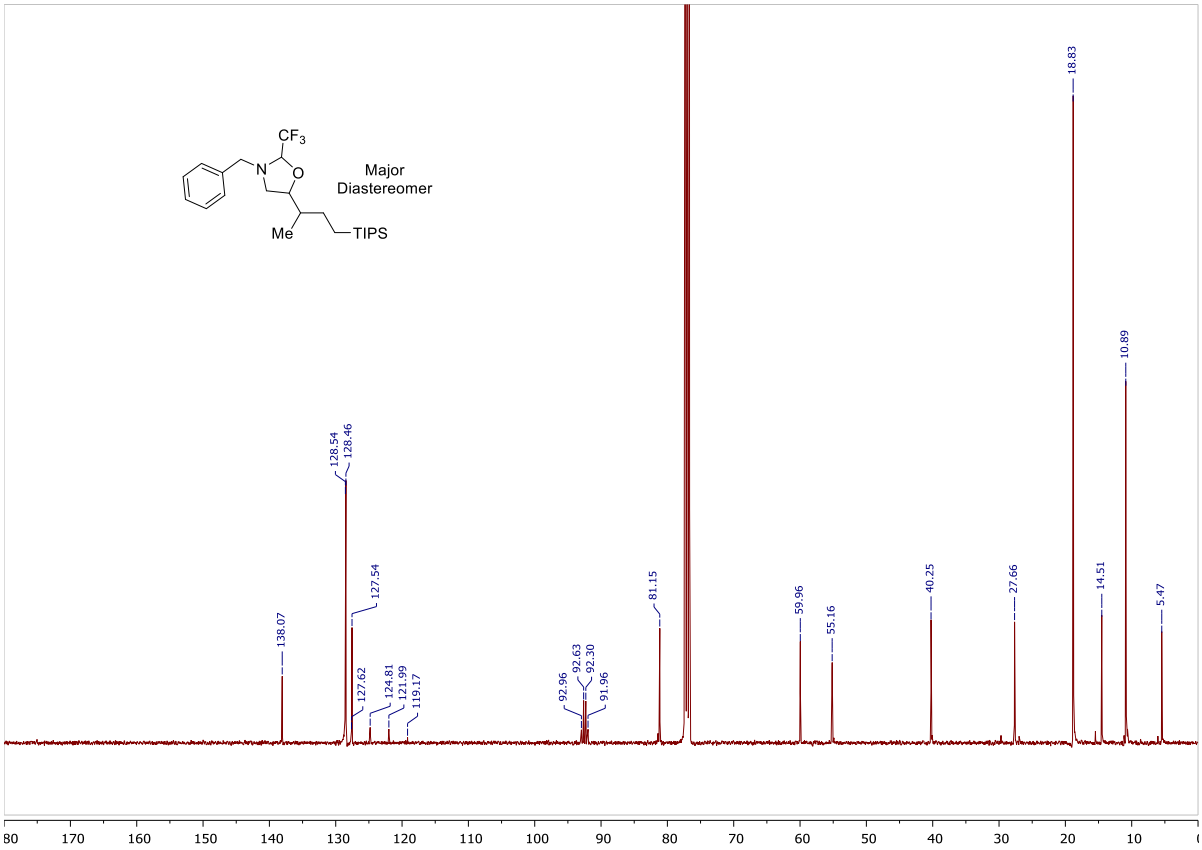


3-benzyl-2-(trifluoromethyl)-5-(4-(tri*iso*propylsilyl)butan-2-yl)oxazolidine (22)

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

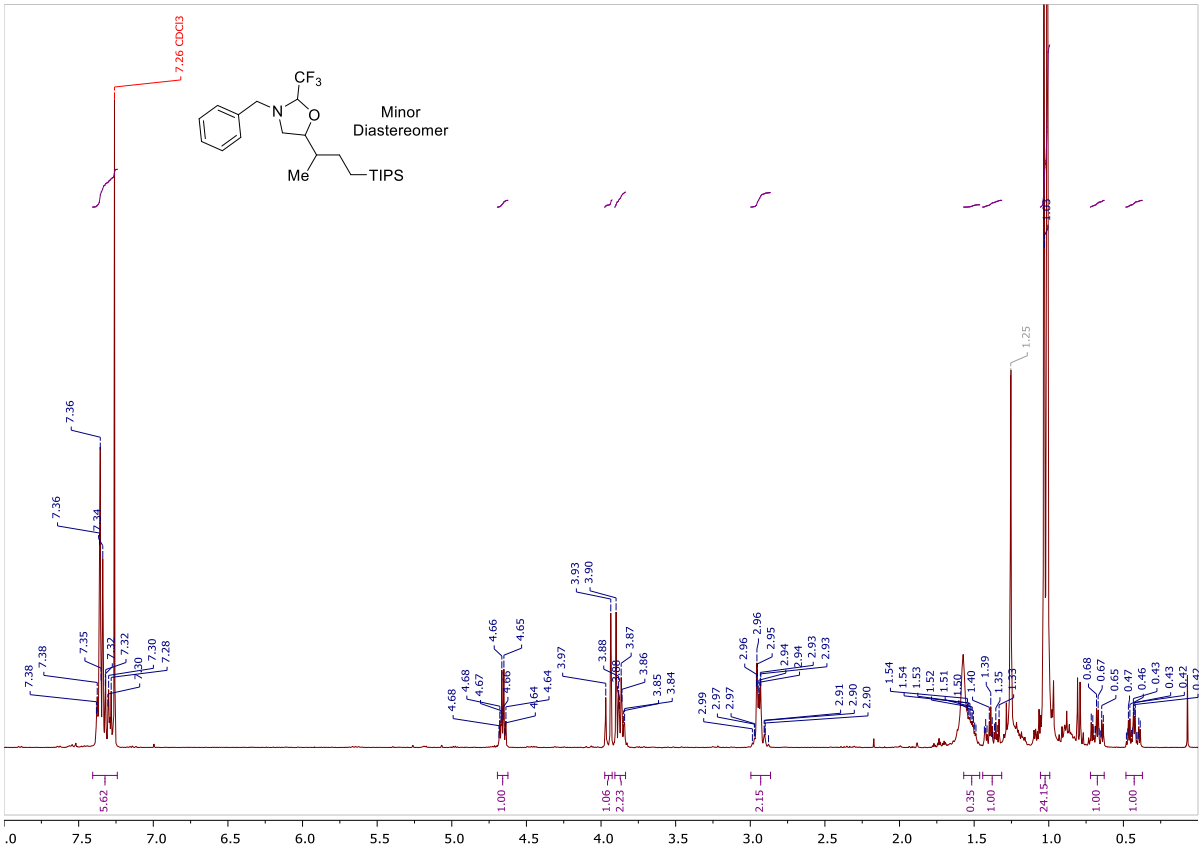


^{13}C-NMR (101 MHz, chloroform-*d*)

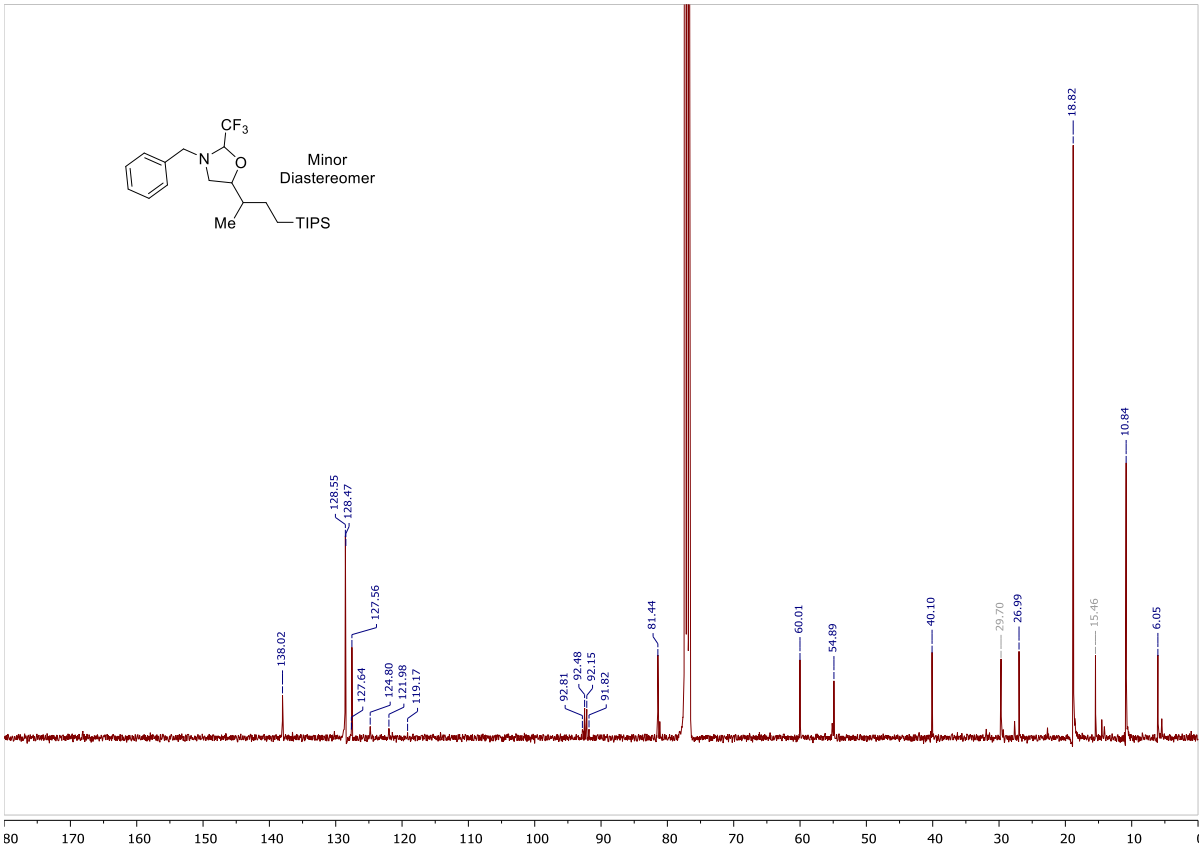


3-benzyl-2-(trifluoromethyl)-5-(4-(tri*iso*propylsilyl)butan-2-yl)oxazolidine (22)

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

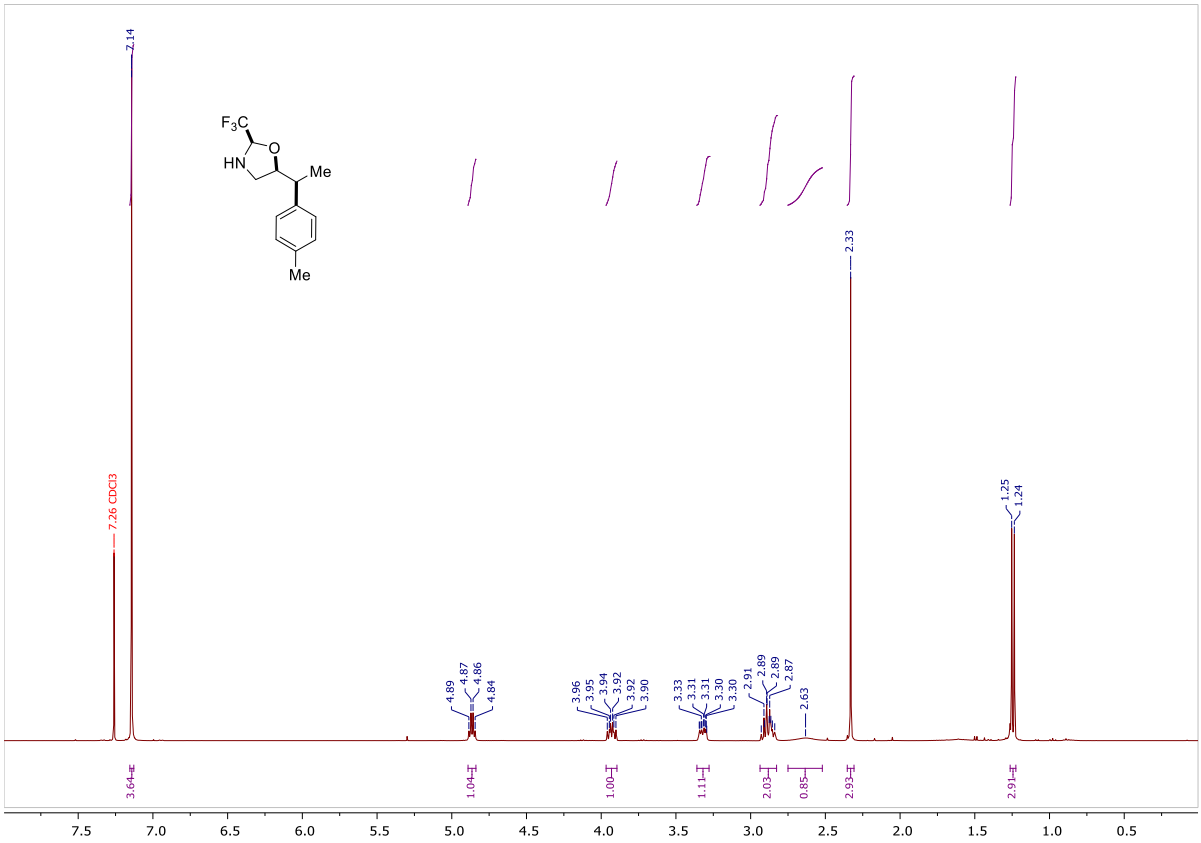


^{13}C-NMR (101 MHz, chloroform-*d*)

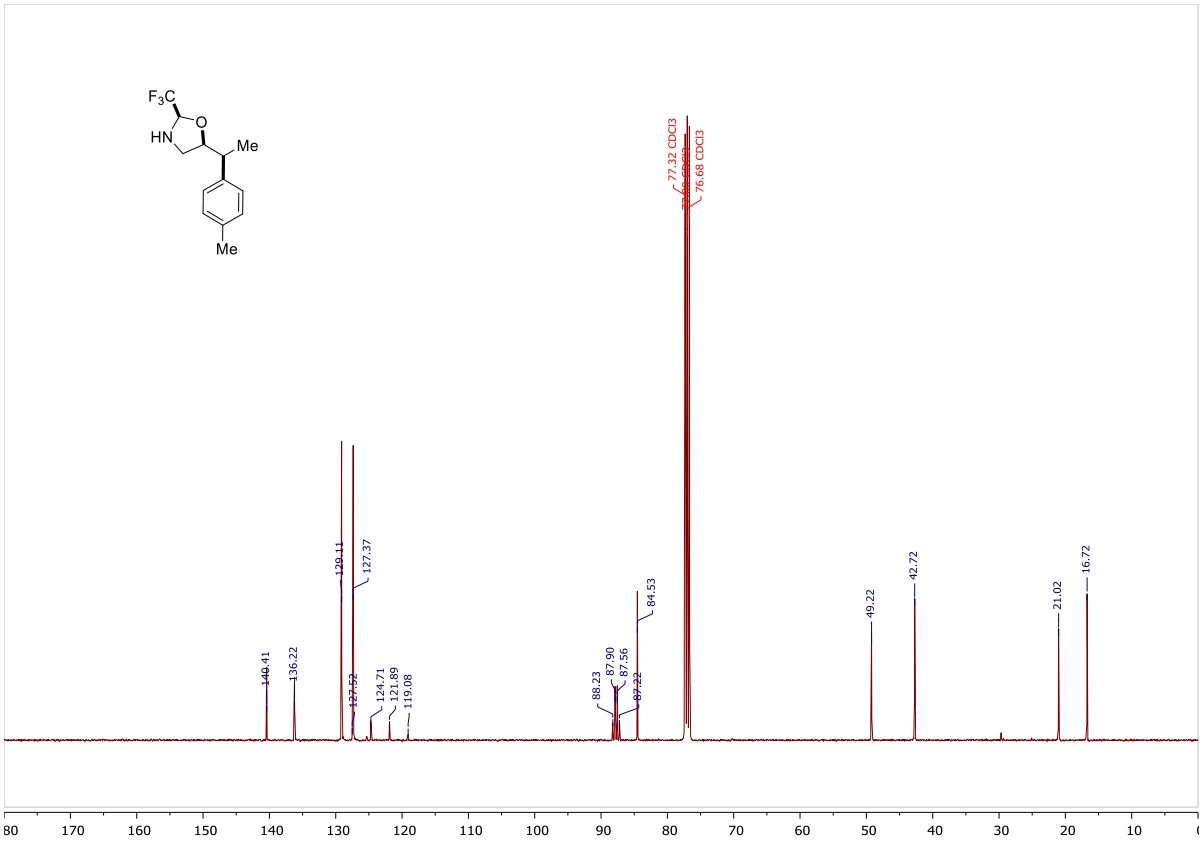


5-(1-(*p*-tolyl)ethyl)-2-(trifluoromethyl)oxazolidine (23a)

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

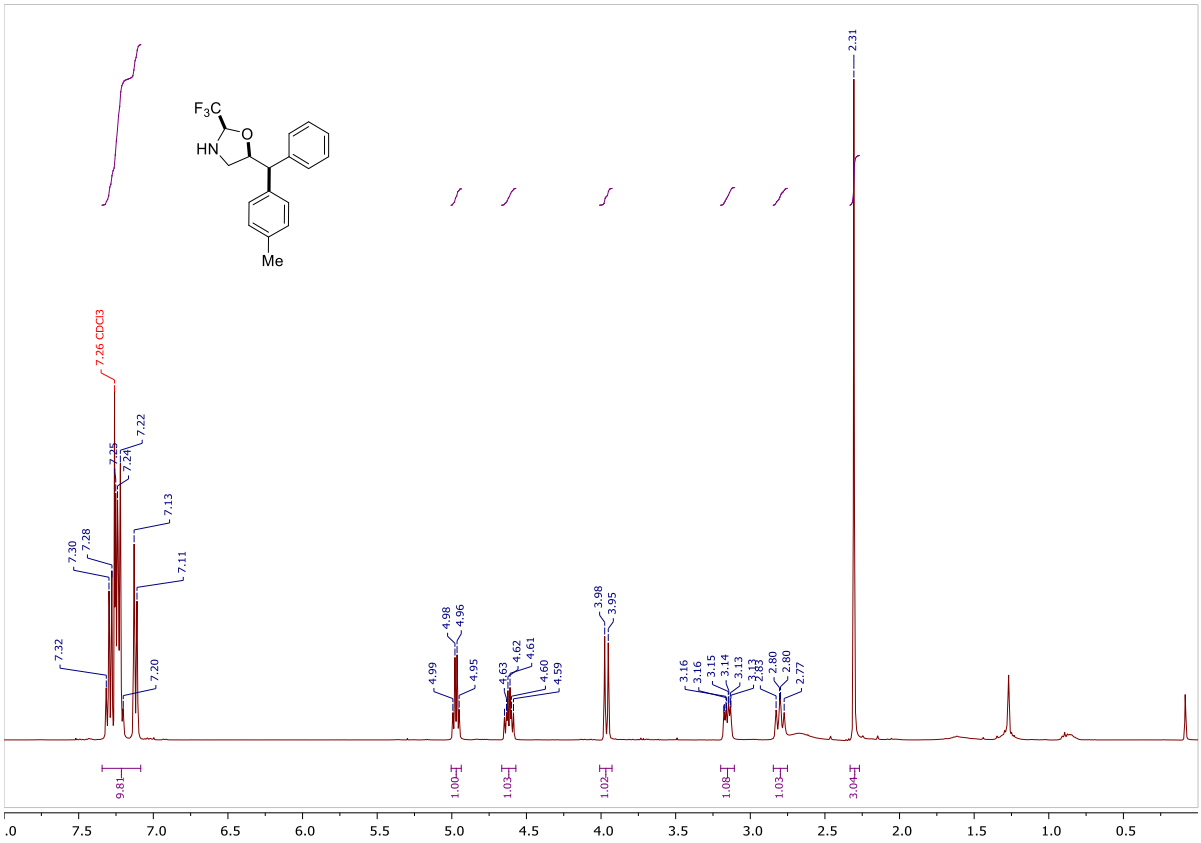


^{13}C-NMR (101 MHz, chloroform-*d*)

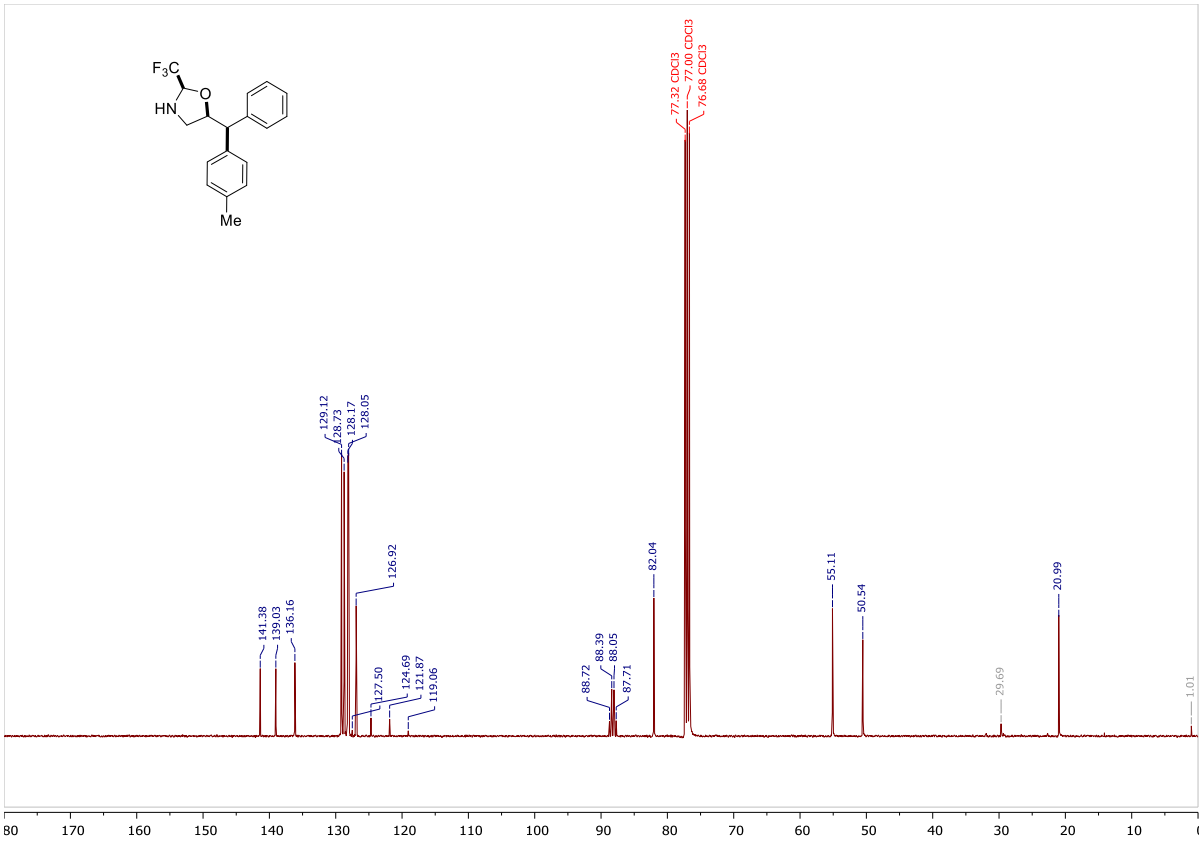


5-(phenyl(*p*-tolyl)methyl)-2-(trifluoromethyl)oxazolidine (23b)

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

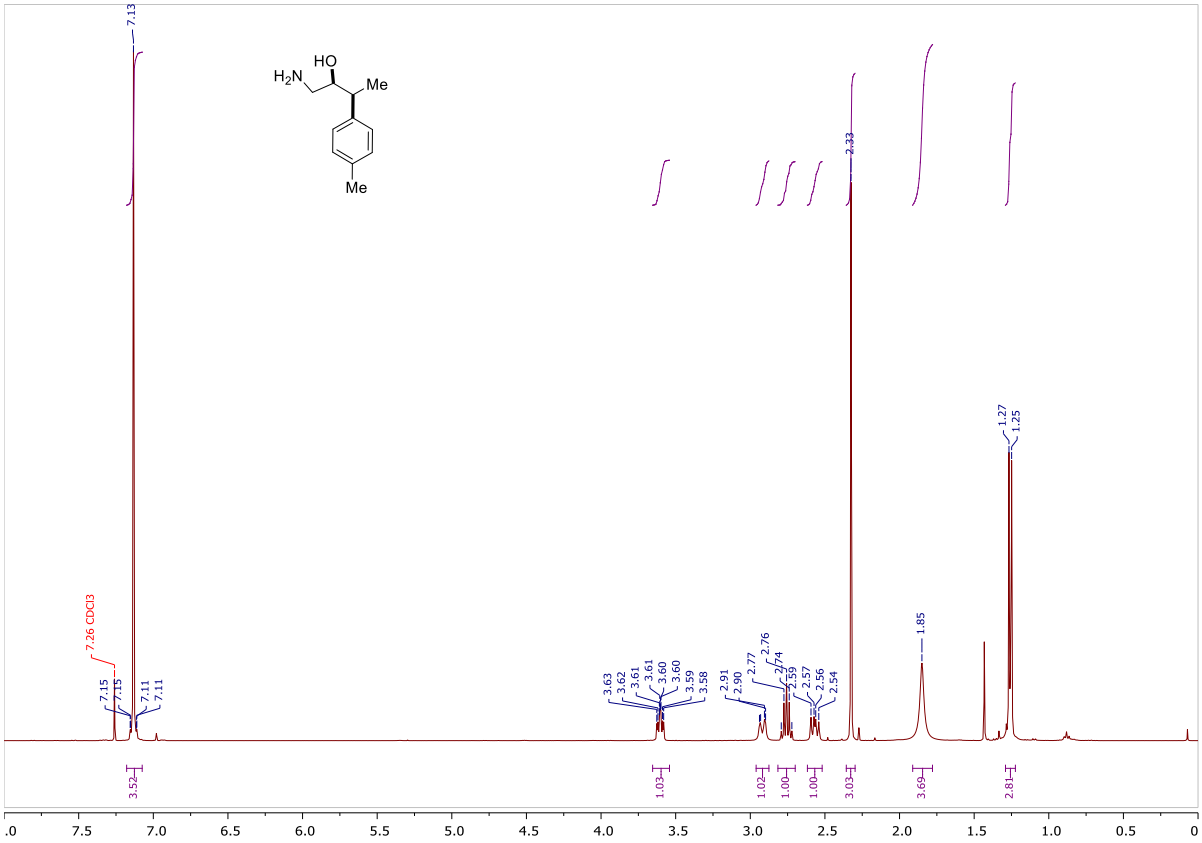


^{13}C-NMR (101 MHz, chloroform-*d*)



1-amino-3-(p-tolyl)butan-2-ol (24)

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



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