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Communication

Enantioselective Carboetherification/Hydrogenation for the Synthesis of Amino Alcohols via a Catalytically Formed Chiral Auxiliary

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ABSTRACT: Chiral auxiliaries and asymmetric catalysis are the workhorses of enantioselective transformations, but they still remain limited in terms of either efficiency or generality. Herein, we present an alternative strategy for controlling the stereoselectivity of chemical reactions. Asymmetric catalysis is used to install a transient chiral auxiliary starting from achiral precursors, which then directs diastereoselective reactions. We apply this strategy to a palladium-catalyzed carboetherification/hydrogenation sequence on propargylic amines, providing fast access to enantioenriched chiral amino alcohols, important building blocks for medicinal chemistry and drug discovery. All stereoisomers of the product could be accessed by the choice of ligand and substituent on the propargylic amine, leading to a stereodivergent process.

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Currently, most enantioselective transformations rely on two strategies: (i) the use of chiral auxiliaries[1] and (ii) asymmetric catalysis.[2] The former allows the development of general and robust processes, but requires stoichiometric amounts of enantiopure precursors and multistep procedures. By contrast, asymmetric catalysis relies only on substoichiometric amounts of enantiopure molecules, but it generally requires an intensive optimization at the expense of robustness and generality. To overcome these limitations, we envisioned a catalytic enantioselective method, which would introduce a chiral auxiliary on the substrate from a cheap nonchiral tether in a synthetic useful step (Scheme 1A). This process would require only a catalytic amount of enantiopure species while providing a robust platform for further diastereoselective functionalizations, benefiting from the best aspects of the two traditional strategies. To the best of our knowledge, such an approach has not yet been realized, although different methods for improving asymmetric synthesis have been developed. A seminal work based on the formation of chiral aminals is the "self-reproduction of chirality" reported by Seebach for the stereoselective synthesis of amino acids. In this work, the existing stereocenter on the amino acid first controls the diastereoselective formation of the aminal by condensation with an aldehyde. The latter then shields one face of the enolate.[3,4] As another example based on an internal chirality transfer, Maulide and co-workers recently reported a redox-neutral coupling of alkenes and aldehydes via a "catch−release" tethering approach (Scheme 1B).[5] However, the resulting functional group (a ketone) remains in the product. Other researchers have worked on the concept of "transient chiral auxiliaries/tethers", which are easy to install and remove.[6−10] For example, Beauchemin and co-workers have used chiral aldehydes in substoichiometric amounts for the Cope-type hydroamination of allyl amines (Scheme 1C).[11] However, the scope of these transformations remains limited, and auxiliaries available from the chiral pool are generally required.

To implement our concept, we considered the palladium-catalyzed carboetherification of propargylic amines,[12] based on the use of trifluoroacetaldehyde-derived tethers (Scheme 1D).[13−15] The stereocenter formed in this step could direct a subsequent functionalization of the double bond, acting *de facto* as a chiral auxiliary. The rigid nature of the oxazolidine scaffold containing the stereocenter should secure a high level of diasteroselectivity to the following transformations.

Concerning the following diastereoselective functionalization, we found the hydrogenation of the formed double bond particularly attractive. By comparison, the enantioselective hydrogenation of alkyl- or heteroatom-tetrasubstituted olefins is highly challenging, with only few limited catalytic enantioselective systems reported.[16−18] After removal of the tether molecule, this process would provide amino alcohols, key building blocks in synthetic and medicinal chemistry, which have been the focus of intensive methodology development recently.[19−26] In particular, the diaryl-substituted amino alcohols obtained using this strategy can be found in antidepressants[27,28] and have served as intermediates for the synthesis of antimycotic, antibacterials[29] and antiviral molecules.[30,31] However, the selective synthesis of one of the four possible stereoisomers of the amino alcohols generally requires multistep processes.

To make this process successful, an enantioselective carboetherification step had to be developed. The reversible

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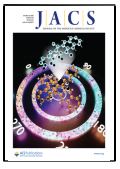

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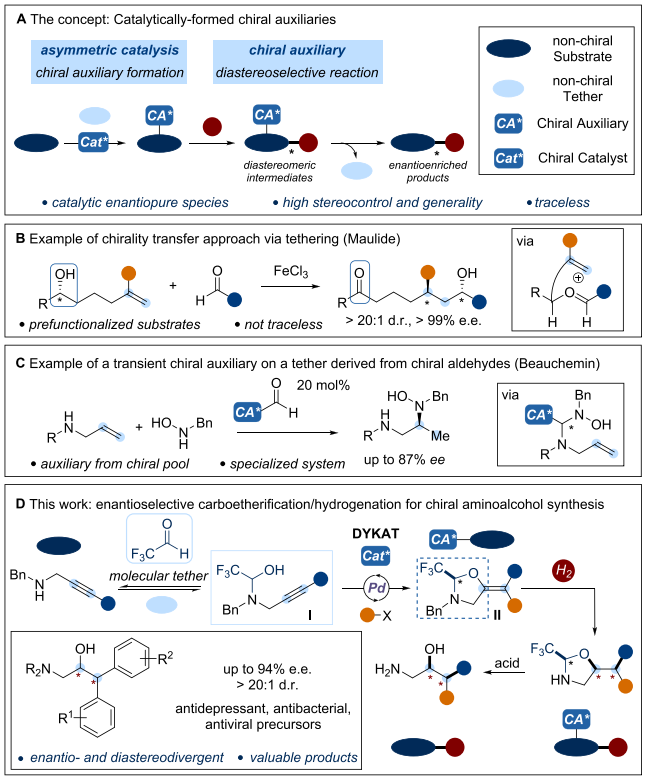
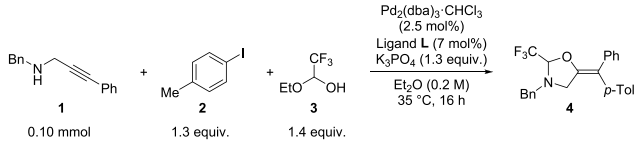
Scheme 1. (A) Our Concept: Catalytically Formed Chiral Auxiliaries; (B) Chirality Transfer via Tethering; (C) Transient Chiral Auxiliaries Introduced from Chiral Pool; (D) Implementation for the Stereodivergent Synthesis of Amino Alcohols

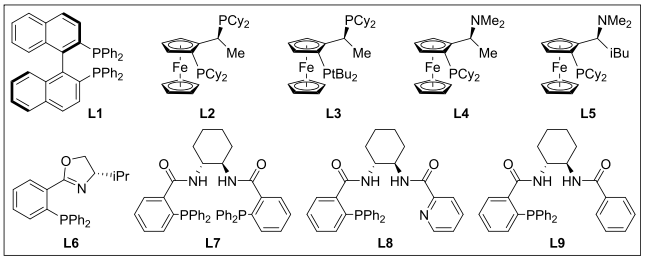


formation of the hemiaminal **I** from the propargylic amine prevents asymmetric induction at this stage (see Supporting Information (SI), section E for more details). Therefore, a dynamic kinetic asymmetric transformation (DYKAT) needs to take place: in the presence of a chiral catalyst, one enantiomer of **I** should react preferentially to give oxazolidine **II** enantioselectively. Although palladium-catalyzed DYKATs have been reported,[32] the envisaged process is highly challenging, due to the large distance between the chiral metal complex and the stereocenter. To the best of our knowledge, such a DYKAT process has never been realized in the palladium-catalyzed functionalization of alkynes. If successful, the selection of the substitution pattern on the alkyne and on the aryl electrophile, together with the choice of the suitable enantiomer of the chiral ligand on the palladium catalyst would provide a simple enantio- and diastereodivergent access to all four stereoisomers of the amino alcohol. This is especially attractive for medicinal chemistry, as each stereoisomer may have different bioactivity, and the development of stereodivergent methods has been the topic of intensive research in asymmetric catalysis recently.[33−35]

We tested the feasibility of our plan by examining the palladium-catalyzed tethered carboetherification of the readily available propargylic amine **1** with iodotoluene **2** to access tetrasubstituted olefin **4** bearing a chiral oxazolidine fragment (Table 1). 1-Ethoxy trifluoroethanol **3**, a commercially available ethyl hemiacetal of trifluoroacetaldehyde, was chosen as the electrophilic molecular tether, and $Pd_2(dba)_3{\cdot}CHCl_3$, as the palladium source.[12] We first focused on the identification of a suitable ligand that could secure a high level of

Table 1. Optimization Studies





entry	Conditions	4 yield (%)[a]	e.e. (%)
1	Ligand **L1**, **L2** or **L3**	<5	–
2	Ligand **L4**	44	20
3	Ligand **L5**	33	30
4	Ligand **L6**	72	40
5	Ligand **L7**	49	64
6	Ligand **L8**	45	74
7	Ligand **L9**	>95	90
8	**L9**, EtOAc instead of Et_2O	80	84
9	**L9**, MTBE instead of Et_2O	89	89
10	**L9**, Toluene instead of Et_2O	91	91
11[b]	**L9**, 0.40 mmol of **1**	>95	94

[a]NMR yields. [b]Reaction performed using 1.25 mol % of $Pd_2(dba)_3{\cdot}CHCl_3$ and 3.5 mol % of (S,S)-ligand.

stereoinduction in the process (for details, see SI, section C). Commonly used bidentate BINAP **L1** and Josiphos ligands **L2** and **L3** were not competent for this reaction (entry 1). The P,N ligands **L4** and **L5**, derived from the corresponding Ugi's amines,[36] delivered **4** in moderate yield and enantiomeric excess (entries 2 and 3), nevertheless demonstrating that a DYKAT was possible. However, higher asymmetric induction could not be achieved with this class of ligands. The P,N ligand S-*i*PrPhox **L6** yielded the desired product in 72% yield and 40% e.e. (entry 4). Promising results were obtained evaluating the Trost type ligands, commonly used for palladium catalyzed asymmetric allylation reactions.[37,38] In particular, the commercially available DACH-phenyl Trost ligand **L7** delivered product **4** in 49% yield and 64% e.e. (entry 5). Having in mind the previous positive results obtained with P,N ligands, we substituted the 2-(PPh_2)-aryl fragment with a 2-pyridine.[39] This change increased the e.e. to 74% (entry 6). Surprisingly, the best results were finally obtained employing the benzamide derived **L9** lacking a second strongly coordinating site, which delivered quantitatively **4** with 90% e.e. (entry 7). To the best of our knowledge, ligand **L9** has been reported only twice in the literature,[40,41] and it was not suitable for imparting high stereocontrol, as two strong coordinating sites were required for asymmetric induction. We developed a robust and operationally simple route for accessing both enantiomers of **L9** on multigram scale (SI, section B4). Demonstrating the process's robustness, the reaction could be performed in more "industrially preferred" solvents[42] (ethyl acetate, methyl *tert*-butyl ether and toluene, entries 8, 9 and 10), without loss of yield and enantioselectivity, except for ethyl acetate (entry 8). Finally, the reaction could be scaled up to a 0.40 mmol scale, reducing the catalyst and ligand loading to 1.25 and 3.5 mol %,

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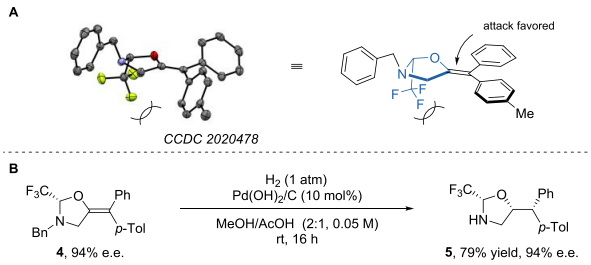
resulting in an improved stereoselectivity of 94% e.e. (entry 11).

The structure of **4**, obtained by X-ray single-crystal analysis (Scheme 2A), shows that the trifluoromethyl group is efficiently shielding one of the two enantiotopic faces of the olefin, setting the stage for the stereospecific hydrogenation. Indeed, when we submitted **4** to classical conditions for heterogeneous hydrogenation using Pearlman's catalyst,[43] the desired hydrogenated product **5** was obtained as a single diastereoisomer in 79% yield and 94% e.e. (Scheme 2B). The use of Pearlman's catalyst also allowed simultaneous removal of the benzyl protecting group.

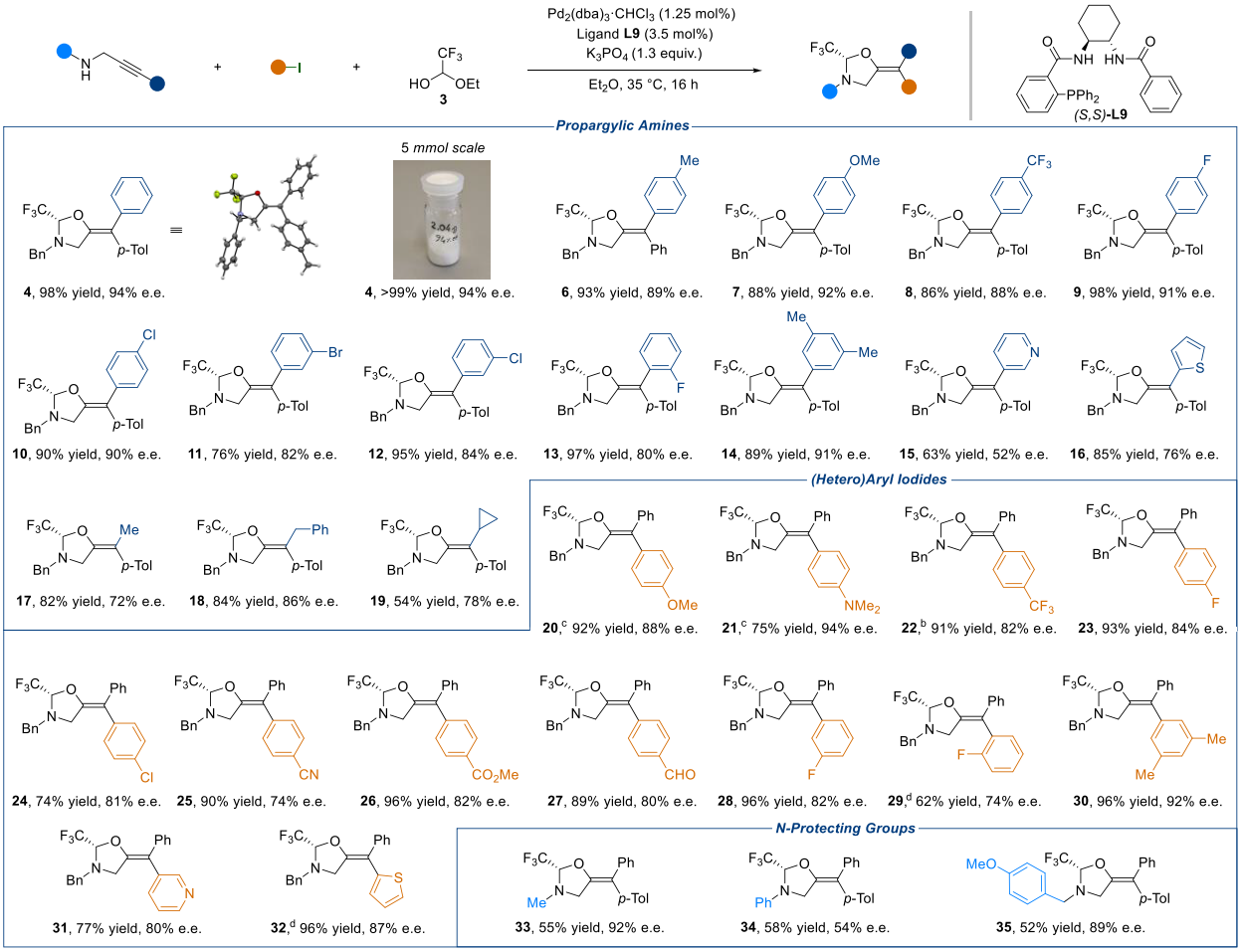
Scheme 2. (A) X-ray Crystal Structure of the Product 4; (B) Optimized Conditions for the Diastereoselective Hydrogenation



Various aryl propargylic amines were well tolerated in the reaction, regardless of the position of the substituents on the phenyl ring, as well as their electronic and steric properties (Scheme 3, **4**, **6**–**14**). The geometry of the olefin can be switched by just exchanging the aryl group on the alkyne and the aryl iodide (**4** vs **6**). The reaction tolerates heterocycles such as pyridine and thiophene on the alkyne, although an erosion of the enantioselectivity was observed (**15** and **16**). Alkyl propargylic amines delivered products **17**–**19** bearing a methyl, a benzyl, and a cyclopropyl group. The reaction could be performed on a 5 mmol scale providing 2.0 g of **4** (quantitative yield) without erosion of the optical purity. The absolute configuration of the products were assigned by X-ray analysis of **4**, confirming in addition that the aryl group coming from the iodide is incorporated in *trans* position to the oxygen.

The investigation of the scope of the iodoarene showed that numerous synthetically useful functional groups, including ethers, amines, halogens, esters, nitriles or aldehydes, are well tolerated independently from their electronic and steric properties or position on the benzene ring (**20**–**30**). 2-Iodothiophene and 3-iodopyridine delivered products **31** and

Scheme 3. Scope of the Enantioselective Carboetherification[a]



[a]Reactions performed on a 0.40 mmol scale using 1.3 equiv of aryl iodide and 1.4 equiv of 1-ethoxy trifluoroethanol (**3**). Isolated yields and HPLC enantiomeric excess are given. [b]Dichloroethane (DCE) instead of Et_2O. [c]Using 2.5 mol % of $Pd_2(dba)_3$·$CHCl_3$ and 7 mol % of ligand. [d]DCE at 60 °C.

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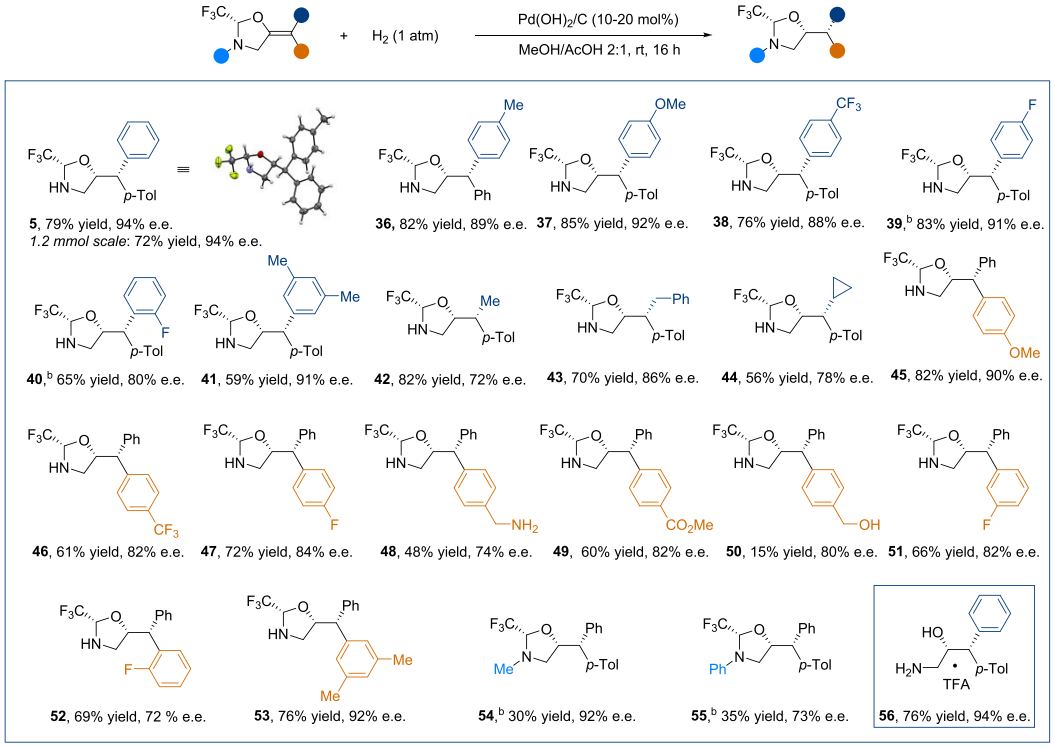
Scheme 4. Scope of the Stereoselective Hydrogenation[a]



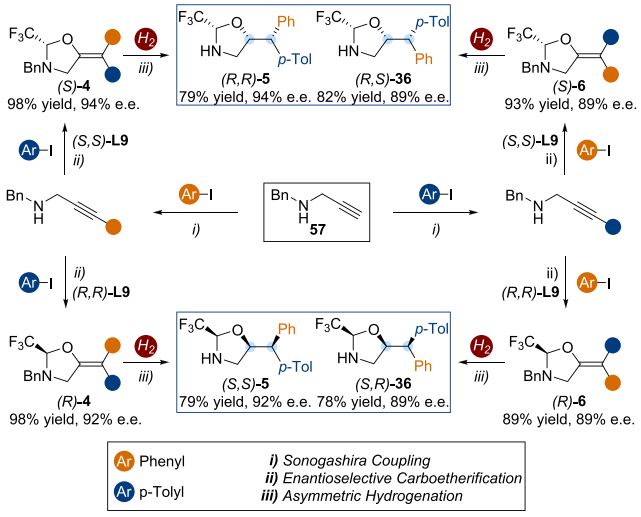
[a]Reactions performed on a 0.2 mmol scale using $Pd(OH)_2/C$ (~20 wt %). Isolated yields and HPLC enantiomeric excess are given. Product **56** was obtained after treating **5** with $TsOH·H_2O$ (7 equiv) in a 2:1 THF/H_2O mixture at room temperature for 16 h, the trifluoroacetate salt was obtained after purification by reversed phase preparative HPLC. [b]Pd/C (~5 wt %) was used instead of $Pd(OH)_2/C$.

32 in good yields. Finally, *N*-methyl, *N*-phenyl and *N*-*para*-methoxybenzyl (PMB) propargyl amines delivered products **33**−**35** in 52−58% yield and 54−92% e.e.

The obtained enantioenriched tetrasubstituted olefins were then submitted to the optimized conditions for the diastereoselective hydrogenation (Scheme 4). Products **36**−**55** were all obtained as single diastereoisomers, confirming the robustness of our approach. Scale-up was straightforward and compound **5** could be obtained in 72% yield on 1.2 mmol scale without erosion of stereoselectivity. Heterocycles and functional groups containing coordinating N or S atoms and chlorides were not tolerated in the hydrogenation step (for details, see SI, Section D5). The nitrile and the carbonyl group within **25** and **27** were reduced to the corresponding amine **48** and alcohol **50**.[44] Interestingly, **5**, **36**, **45**, **46**, **47** and **54** are precursors of bioactive compounds with antidepressive activity,[27,28] while the amino alcohols derived from **36** and **47** are intermediates for the synthesis of patented antiviral drugs candidates.[30] Remarkably, our method provides a high level of asymmetric induction even in the presence of sterically and electronically similar aryl substituents on the olefin, thus overcoming a common obstacle in the development of catalytic asymmetric reactions. Finally, to confirm the traceless nature of our strategy, we performed a mild acidic hydrolysis of the hemiaminal in **5**. The enantioenriched amino alcohol **56** was obtained in 76% yield without loss in optical purity.

We then demonstrated that this strategy provides a simple stereodivergent access to the four possible stereoisomers of chiral diaryl aminoalcohols by a judicious selection of the substrates and the ligands (Scheme 5). Starting from the benzyl propargyl amine **57**, a sequence of (i) Sonogashira coupling, (ii) enantioselective carboetherification and (iii) diastereoselective hydrogenation leads to all the stereoisomers of the desired products **5** and **36**. Permuting the iodoarenes in the cross-coupling and in the carboetherification steps allows the tuning of the *E*,*Z* geometry of the double bond. This selective process, combined with the choice of the enantiomer of the ligand, and the diasteroselectivity of the hydrogenation provide a selective access to the four stereoisomers of the diaryl amino alcohol precursors.

Scheme 5. Diastereo- and Enantiodivergent Access to Chiral Aminoalcohol Precursors[a]



[a]See SI for detailed reaction conditions.

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In summary, we have developed an innovative strategy to control the stereoselectivity of asymmetric transformations.[45] Our approach first capitalizes on the tools of asymmetric catalysis to forge a chiral oxazolidine from broadly available propargylic amines. This stereogenic element is then used to control the selectivity of the asymmetric hydrogenation of the tetrasubstituted double bond, giving access to valuable chiral amino alcohol precursors. The key for success was the first use of a "truncated" monophosphine Trost-type ligand to induce high enantioselectivity in an unprecedented DYKAT process. Combined with a Sonogashira cross-coupling, our approach gives a stereodivergent access to the four stereoisomers of protected diaryl amino alcohols in high yield and enantioselectivity. New opportunities for the design and development of asymmetric functionalizations of olefins can be expected based on the combination of the enantioselective introduction of a transient chiral auxiliary followed by a diastereoselective transformation. Such processes are currently under investigation in our laboratory.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/jacs.0c09177.

Experimental procedures and characterization data for starting materials, ligands and products; proposed reaction mechanism; copy of HPLC and NMR spectra (PDF)

Crystallographic data for the product **4** (CIF)

Crystallographic data for the product **5** (CIF)

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Author Contributions

‡L.B., M.P., and P.D.G.G. contributed equally.

Notes

The authors declare no competing financial interest.

Crystallographic data for the product **4** and **5** have been deposited at the Cambridge Crystallographic Data Centre, accession numbers CCDC 2020478 and 2020479, respectively. Raw HPLC, NMR, MS and IR data is available at https://doi.org/ 10.5281/zenodo.4046256.

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■ ABBREVIATIONS

Me, Methyl; Bu, Butyl; Pr, Propyl; Cy, Cyclohexyl; Ph, Phenyl; Bn, Benzyl; *p*-Tol, *p*-Tolyl; EtOAc, Ethyl acetate; MTBE, Methyl *tert*butyl ether; Et_2O, Diethyl ether; MeOH, Methanol; AcOH, Acetic acid; dba, Dibenzylideneacetone.

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(44) Product **55** was obtained with higher *e.e.* compared to its precursor **34**. The reasons for this surprising result are unclear at this stage. As **34** was not fully soluble under these conditions, a plausible explanation would be a lower solubility of the racemate salt, leading to a chiral resolution during hydrogenation.
(45) A previous version of this work appeared in a preprint: Buzzetti, L.; Purins, M.; Greenwood, P. D. G.; Waser, J. Enantioselective Carboetherification/Hydrogenation for the Synthesis of Amino Alcohols via a Catalytically-Formed Chiral Auxiliary ChemRxiv, August 25, **2020**, ver. 1, DOI: 10.26434/chemrxiv.12855218.v1.

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Supporting Information for

"Enantioselective Carboetherification/Hydrogenation for the Synthesis of Amino Alcohols via a Catalytically-Formed Chiral Auxiliary"

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Raw HPLC, NMR, MS and IR data is available at https://doi.org/ 10.5281/zenodo.4046256 .

Table of Contents

A. General Information

The NMR spectra were recorded on a Brucker DPX-400 spectrometer at 400 MHz for ^{1}H, 101 MHz for ^{13}C, 376 MHz for ^{19}F and 162 MHz for ^{31}P. The chemical shift (δ) for ^{1}H and ^{13}C are given in ppm relative to residual signals of the solvents (chloroform-d - 7.26 ppm ^{1}H NMR and 77.16 ppm ^{13}C NMR; methanol-d4 3.31 ppm ^{1}H NMR and 49.0 ppm ^{13}C NMR; dmso-d6 2.50 ppm ^{1}H NMR and 39.52 ppm ^{13}C NMR). Carbon spectra have been measured using broadband {^{1}H} decoupling. Coupling constants are given in Hertz. The following abbreviations are used to indicate the multiplicity: s, singlet; d, doublet; q, quartet; m, multiplet; bs, broad signal; app, apparent. Infrared spectra were recorded on a JASCO FT-IR B4100 spectrophotometer with an ATR PRO410-S and a ZnSe prisma and are reported as cm^{-1} (w = weak, m = medium, s = strong, br = broad). High resolution mass spectrometric measurements were performed by the mass spectrometry service of ISIC at the EPFL on a MICROMASS (ESI) Q-TOF Ultima API. The raw data obtained from the Q-TOF Waters instrument does not take into account the mass of the electron for the ion, the obtained raw data has been therefore corrected by removing the mass of the electron (5 mDa). The diffraction data for crystal structures were collected by mass spectrometry service of ISIC at the EPFL at low temperature using Cu (323) or Mo (520) K_a radiation on a Rigaku SuperNova dual system in combination with Atlas type CCD detector. The data reduction and correction were carried out by *CrysAlis^{Pro}* (Rigaku Oxford Diffraction, release 1.171.40.68a, **2019**). The solutions and refinements were performed by *SHELXT*[1] and *SHELXL*[2], respectively. The crystal structures were refined using full-matrix least-squares based on F^2 with all non-H atoms defined in anisotropic manner. Hydrogen atoms were placed in calculated positions by means of the "riding" model. Yields of isolated products refer to materials of >95% purity as determined by ^{1}H NMR.

The authors are indebted to the team of the research support service of ISIC at EPFL, particularly to the NMR, X-Ray, and the High Resolution Mass Spectrometry Units.

General Procedures. All reactions were set up under a nitrogen atmosphere in oven-dried glassware using standard Schlenk techniques, unless otherwise stated. Synthesis grade solvents were used as purchased; anhydrous solvents (THF, Et_2O, Toluene and DCM) were taken from a commercial SPS solvent dispenser (H_2O content < 10 ppm, *Karl-Fischer* titration). Chromatographic purification of products was accomplished using flash chromatography (FC) on SiliaFlash P60 silica gel (230 - 400 mesh). For thin layer chromatography (TLC) analysis throughout this work, Pre-coated TLC sheets ALUGRAM® Xtra SIL G/UV_{254} were employed, using UV light as the visualizing agent and basic aqueous potassium permanganate ($KMnO_4$) stain solutions, and heat as developing agents. Organic solutions were concentrated under reduced pressure on a Büchi rotatory evaporator.

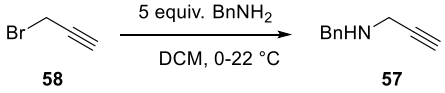
Determination of Enantiomeric Purity: HPLC analysis on chiral stationary phase was performed on a Agilent Acquity instrument using a Daicel CHIRALPAK IA, IB-N5 and IC chiral columns. The exact conditions for the analyses are specified within the characterization section. HPLC traces were compared to racemic samples prepared by running the reactions using racemic ligands. Absolute values of enantiomeric excesses are reported.

Materials. Most of the starting materials used in this study are commercial and were purchased in the highest purity available from Sigma-Aldrich, Fluka, Alfa Aesar, Fluorochem, Enamine and used as received, without further purifications. Tris(dibenzylideneacetone)dipalladium was purchased from Fluorochem and recrystalised in 200 mg portions following a reported procedure.[3] $Pd(OH)_2/C$ was purchased from Fluka (humid, Assay: ~20% (Pd), Analysis Number: 320400/1 1192). Pd/C was purchased from Sigma-Aldrich (~5 wt. % Pd (dry basis), matrix activated charcoal, wet support. Degussa type E105CA/W, Lot#MKBJ9424V). Deactivated silica gel was prepared by making a slurry of silica gel (230-400 mesh) with 5% Et_3N in pentane solution followed by complete removal of solvent by rotary evaporation until obtaining a free flowing powder. The synthesis of **1**, **63-65**, **68**, **71** and **73-78** has already been described by our group. The procedures are taken from the indicated publication[4] for clarity and to facilitate the reproduction of the results.

B. Synthesis of the Starting Materials and Ligands

B.1. Synthesis of the Propargylic Amines Precursors 57 and 62

N-Benzylprop-2-yn-1-amine (57)



Scheme 1. Synthesis of Benzyl Propargyl amine **57**.

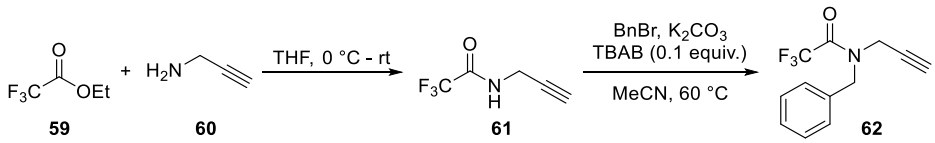
To a flame-dried 250 mL two-necked round-bottom flask, benzylamine (55 mL, 0.50 mol, 5.0 equiv.) and DCM (60 mL) were added. The mixture was cooled to 0 °C. Then, *via* an addition funnel, propargyl bromide (80 wt% solution in toluene, 10.8 mL, 100 mmol, 1.0 equiv.) in DCM (40 mL) was added dropwise over 1 hour. The reaction mixture was allowed to reach room temperature and stirred for 5 h. The reaction mixture was filtered through a plug of silica and concentrated *in vacuo* to approx. 100 mbar. The mixture was distilled under reduced pressure to give the *N*-benzylprop-2-yn-1-amine **57** as a colorless oil (7.3 g, 50 mmol, ~90% purity according to ^{1}H NMR (T = 50 – 55 °C, 0.35 mbar).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.31 (m, 4H, Ar*H*), 7.31 – 7.24 (m, 1H, ArH), 3.90 (s, 2H, PhCH_2), 3.44 (d, *J* = 2.4 Hz, 2H, CH_2C≡CH), 2.28 (t, *J* = 2.4 Hz, 1H, C≡C*H*), 1.49 (s, 1H, N*H*).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 139.5, 128.52, 128.49, 127.2, 82.2, 71.6, 52.4, 37.4.

Spectral data were consistent with the values reported in literature.[5]

N-Benzyl propynyl trifluoroacetamide (62)



Scheme 2. Synthesis of compound **62**.

Following a modified version of a reported procedure.[6] In a flame dried round-bottom flask, to a solution of ethyl trifluoroacetate (8.0 g, 56 mmol, 1.2 equiv.) in THF (12 mL) at 0 °C was slowly added propargyl amine (2.6 g, 47 mmol, 1 equiv.). The reaction mixture was stirred at 0 °C for 10 minutes; it was then allowed to reach 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 **61** as a colourless oil (5.5 g, 37 mmol, 78% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 6.94 (br. s., 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]

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 **61** (4.5 g, 30 mmol, 1 equiv.) and benzyl bromide (6.0 g, 33 mmol, 1.1 equiv.) and the reaction mixture was stirred at 60 °C. After 3 hours (progress determined by 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 pentane) afforded *N*-Benzyl propynyl trifluoroacetamide (**62**) as a colourless oil (5.0 g, 21 mmol, 71% yield)

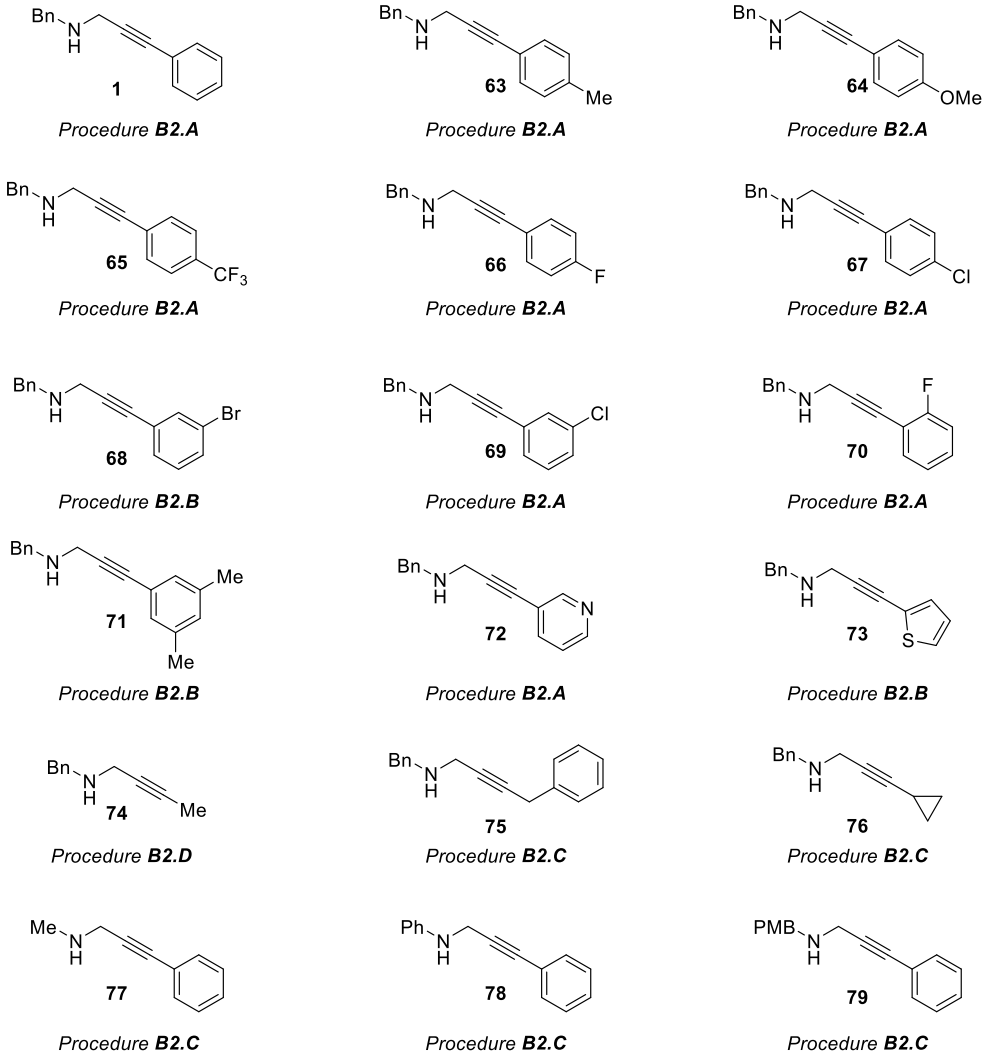
^{1}H NMR (400 MHz, Chloroform-*d*; 1:1.2 mixture of rotamers) δ 7.46 – 7.23 (m, 10H, Ar*H*), 4.79 (s, 2H, CH_2Ar), 4.77 (s, 2H, CH_2Ar), 4.12 (d, *J* = 2.5 Hz, 2H, CH_2C≡C), 4.06 (d, *J* = 2.4 Hz, 2H, CH_2C≡C), 2.37 (t, *J* = 2.4 Hz, 1H, C≡C*H*), 2.29 (t, *J* = 2.5 Hz, 1H, C≡C*H*).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*; 1:1.2 mixture of rotamers) δ 156.7 (q, *J* = 36.5 Hz, 2×C=O), 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.

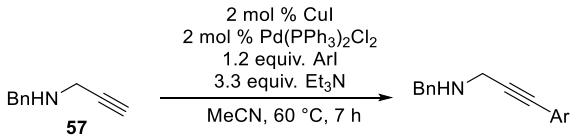
HRMS (LTQ-Orbitrap) m/z: $[M + H]^+$ Calculated for $C_{12}H_{11}F_3NO^+$ 242.0787; Found 242.0783.

B.2. Synthesis of the Propargylic Amines



Scheme 3. The propargylic amines synthesized according to the general procedures reported.

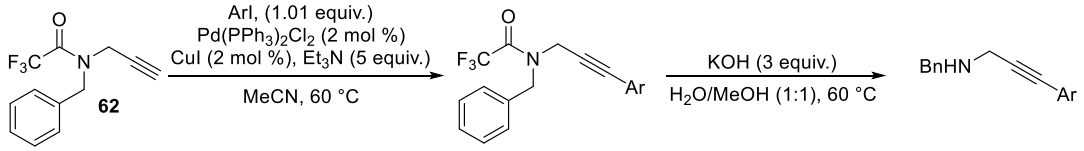
General Procedure B2.A



Scheme 4. General Procedure B2.A.

To a flame-dried 100 mL round bottom flask equipped with a Teflon-coated magnetic stirring bar, $Pd(PPh_3)_2Cl_2$ (42 mg, 60 µmol, 2 mol%), CuI (11 mg, 60 µmol, 2 mol%), Et_3N (0.90 g, 1.2 mL, 9.0 mmol, 3.3 equiv.) and degassed (by bubbling dry N_2 for 10 minutes) MeCN (30 mL) were added. Then, the iodoarene (1.1 equiv.) was added and the mixture was heated to 60 °C and stirred for 5 minutes. Benzyl propargyl amine **57** (0.39 g, 2.7 mmol, 1.0 equiv.) was added and the reaction mixture was stirred for 7 hours at 60 °C. Then, the reaction mixture was cooled down to ambient temperature and concentrated *in vacuo*. The resulting crude was dissolved in EtOAc (20 mL), then washed with water (20 mL) and brine (20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated *in vacuo*. The crude was purified with Biotage flash chromatography system using Buchi FlashPure cartridge with EcoFlex silica (10% – 40% EtOAc in pentane).

General Procedure B2.B

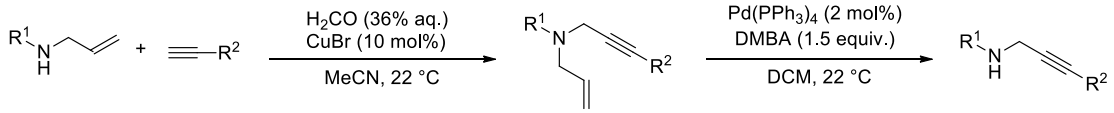


Scheme 5. General Procedure B2.B.

Following a modified version of a reported procedure.[7] To a solution of **62** (0.80 g, 3.3 mmol, 1 equiv.), ArI (1.01 equiv.) and Et_3N (2.3 mL, 17 mmol, 5 equiv.) in acetonitrile (30 mL) was added $PdCl_2(PPh_3)_2$ (47 mg, 0.066 mmol, 2 mol%) and CuI (13 mg, 0.066 mmol, 2 mol%) in a single portion. The resulting mixture was stirred for 7 hours at 60 °C. Water (20 mL) was then added and the reaction mixture extracted with EtOAc (3 x 30 mL); the combined organic layers 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).

Hydrolysis: following an adapted version of a reported procedure.[8] To the trifluoroacetamide obtained from the previous step (1 equiv.) was added a solution of KOH (3.0 equiv.) in water (15 mL) and methanol (15 mL) and the resulting mixture was stirred at 60 °C for 3 hours. The reaction was then cooled to room temperature and acidified with aq. HCl (1.0 M; 5 mL) followed by basification with sat. aq. $NaHCO_3$ (pH >7). The resulting mixture was extracted with DCM (3 x 10 mL), dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude material was purified by flash column chromatography (SiO_2, 10-30% EtOAc in pentane).

General Procedure B2.C

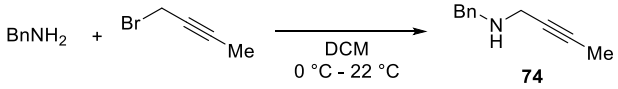


Scheme 6. General Procedure B2.C.

Following an adapted version of a reported procedure. [9] To a solution of CuBr (0.20 g, 1.4 mmol, 13 mol%) in MeCN (c = 0.15 M) was added allyl amine (1.3 equiv.), formaldehyde (3 equiv.) and alkyne (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 aq. NaOH solution (5.0 M; 3 x 10 mL), dried over $MgSO_4$, filtered and concentrated by rotary evaporation. The crude material was purified by flash column chromatography (SiO_2, 0-2% EtOAc in pentane).

Deallylation: The tertiary amine obtained from the previous step (1 equiv.) was added to a solution of $Pd(PPh_3)_4$ (2 mol%) and 1,3-dimethylbarbituric acid (1.5 equiv.) in DCM (c = 0.18 M) under an N_2 atmosphere. The reaction mixture was stirred at room temperature for 16 hours. The reaction mixture was concentrated to a quarter of its original volume and 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 and any precipitated solids 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. The crude material was purified by flash column chromatography (SiO_2, 20-50% EtOAc in pentane).

Procedure B2.D for the Synthesis of 74



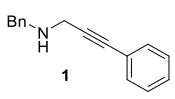
Scheme 7. General Procedure B2.D for the synthesis of **74**.

A solution of benzyl amine (4-6 equiv.) in DCM (15 mL) at 0 °C was stirred vigorously while a solution of bromo-2-butyne (2.5 mL, 27 mmol, 1 equiv.) in DCM (15 mL) was slowly added. The reaction mixture was then warmed to room temperature and stirred for 5 hours. It was then filtered through silica gel, eluting with 40% EtOAc in pentane and the resulting solution concentrated. Purification was performed by column chromatography (SiO_2, 10-40% EtOAc in pentane) to afford benzyl butynylamine **71** as a straw yellow oil (3.4 g, 21 mmol, 74% yield). 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.

Spectral data was consistent with the values reported in literature.[9]



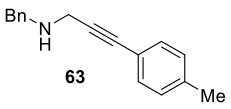
***N*-Benzyl-3-phenylprop-2-yn-1-amine (1)**

Prepared following an up-scaled general procedure B2.A using *N*-benzylprop-2-yn-1-amine **57** (2.20 g, 13.5 mmol, 1.0 equiv.), iodobenzene (3.1 g, 1.7 mL, 15 mmol, 1.1 equiv.), Et_3N (4.5 g, 6.3 mL, 45 mmol, 3.3 equiv.), $Pd(PPh_3)_2Cl_2$ (211 mg, 300 µmol, 2 mol%) and CuI (57 mg, 300 µmol, 2 mol%). Purification was performed by Biotage flash column chromatography system with a 120 g cartridge (SiO_2, 10 – 40% EtOAc in pentane) to afford *N*-benzyl-3-phenylprop-2-yn-1-amine (**1**) as an orange oil (2.5 g, 11 mmol, 75% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.52 – 7.20 (m, 9H, Ar*H*), 3.96 (s, 2H, PhC*H*$_2$), 3.66 (s, 2H, C*H*$_2$C≡C), 1.73 (br. s, 1H, N*H*).

^{13}C{^{1}H} 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.

Spectral data were consistent with the values reported in literature.[9]



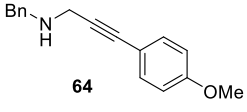
***N*-Benzyl-3-(*p*-tolyl)prop-2-yn-1-amine (63)**

Prepared following general procedure B2.A using *p*-tolyliodobenzene (667 mg, 3.06 mmol, 1.1 equiv.). Purification was performed by Biotage flash column chromatography system with a 25 g cartridge (SiO_2, 10 – 40% EtOAc in pentane) to afford *N*-benzyl-3-(p-tolyl)prop-2-yn-1amine (**63**) as an orange oil (512 mg, 2.13 mmol, 79% yield).

^{1}H NMR (400 MHz, Chloroform-d) δ 7.41 – 7.29 (m, 6H, Ar*H*), 7.29 – 7.22 (m, 1H, Ar*H*), 7.12 (d, *J* = 7.9 Hz, 2H, Ar*H*), 3.95 (s, 2H, PhC*H*$_2$), 3.65 (s, 2H, C*H*$_2$C-C≡C), 2.35 (s, 3H), 1.68 (br. s., 1H, N*H*)

^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ 139.7, 138.3, 131.7, 129.2, 128.62, 128.59, 127.3, 120.3, 86.7, 84.0, 52.6, 38.4, 21.6.

Spectral data were consistent with the values reported in literature.[9]



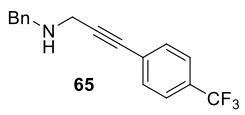
***N*-Benzyl-3-(4-methoxyphenyl)prop-2-yn-1-amine (64)**

Prepared following modified general procedure B2.A using $Pd(PPh_3)_2Cl_2$ (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-anisole (0.79 g, 6.4 mmol, 1.3 mmol) in DMSO (10 mL; degassed by bubbling N_2). The crude material was dry-loaded onto SiO_2 and purified by column chromatography (SiO_2, 15-30% EtOAc in pentane) affording *N*-benzyl-3-(4-methoxyphenyl)prop-2-yn-1-amine (**64**) 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, 7H, Ar*H*), 6.87 – 6.81 (m, 2H, 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.

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



***N*-Benzyl-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-amine (65)**

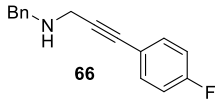
Prepared following modified general procedure B2.A using $Pd(PPh_3)_2Cl_2$ (90 mg, 0.13 mmol, 5 mol%), dppf (86 mg, 0.16 mmol, 6 mol%), CuI (25 mg, 0.13 mmol, 5 mol%), DABCO (0.76 g, 6.8 mmol, 2.6 equiv.) and 4-trifluro-Iodobenzene (0.92 g, 3.4 mmol, 1.3 equiv.) in DMSO (10 mL; degassed by bubbling N_2). The crude material was dry-loaded onto SiO_2 and purified by column chromatography (SiO_2, 10-20% EtOAc in pentane) affording *N*-benzyl-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-amine (**65**) as a dark orange oil (0.55 g, 1.9 mmol, 72% yield)

^{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), 1.76 (bs, 1H, N*H*).

^{13}C{^{1}H} 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), 123.91 (q, *J* = 272.2 Hz), 90.2, 82.5, 52.6, 38.2.

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

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



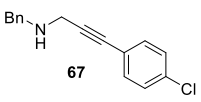
***N*-Benzyl-3-(4-fluorophenyl)prop-2-yn-1-amine (66)**

Prepared following general procedure B2.A using 4-fluoroiodobenzene (0.68 g, 0.35 mL, 3.1 mmol, 1.1 equiv.). Purification was performed by Biotage flash column chromatography system with a 25 g cartridge (SiO_2, 10 – 40 % EtOAc in pentane) to afford *N*-benzyl-3-(4-fluorophenyl)prop-2-yn-1-amine (**66**) as an orange oil (512 mg, 2.02 mmol, 79% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.48 – 7.30 (m, 6H, Ar*H*), 7.30 – 7.22 (m, 1H, Ar*H*), 7.07 – 6.91 (m, 2H, Ar*H*), 3.95 (s, 2H, PhCH_2), 3.64 (s, 2H, CH_2C≡C), 1.61 (br. s., 1H, N*H*).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 162.5 (d, *J* = 249.0 Hz), 139.7, 133.6 (d, *J* = 8.3 Hz), 128.61, 128.55, 127.3, 119.4 (d, *J* = 3.5 Hz), 115.7 (d, *J* = 22.0 Hz), 87.4, 82.8, 52.7, 38.3.
^{19}F NMR (376 MHz, Chloroform-*d*) δ -111.4 (tt, *J* = 8.7, 5.4 Hz).

Spectral data were consistent with the values reported in literature.[9]



***N*-Benzyl-3-(4-chlorophenyl)prop-2-yn-1-amine (67)**

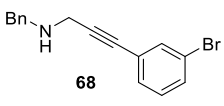
Prepared following general procedure B2.A using 4-chloroiodobenzene (730 mg, 3.06 mmol, 1.1 equiv.). Purification was performed by Biotage flash column chromatography system with a 25 g cartridge (SiO_2, 10 – 40% EtOAc in pentane) to afford *N*-benzyl-3-(4-chlorophenyl)prop-2yn-1-amine **67** as an orange oil (540 mg, 2.08 mmol, 77% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.28 (m, 6H, Ar*H*), 7.27 – 7.19 (m, 3H, Ar*H*), 3.91 (s, 2H, PhCH_2), 3.61 (s, 2H, CH_2C≡C), 2.35 (s, 3H, CH_3), 1.57 (br. s., 1H, N*H*).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 139.6, 134.2, 133.0, 129.1, 128.6, 128.6, 127.3, 121.9, 87.7, 82.8, 52.7, 38.3.

IR (cm^{-1}) 3327 (w), 3031 (m), 2921 (m), 2840 (m), 2104 (w), 1727 (m), 1487 (s), 1335 (m), 1254 (m), 1166 (m), 1094 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{16}H_{15}ClN^+$ 256.0888; Found 256.0890.



***N*-benzyl-3-(3-bromophenyl)prop-2-yn-1-amine (68)**

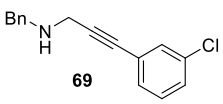
Prepared following general procedure B2.B using $PdCl_2(PPh_3)_2$ (47 mg, 66 µmol, 2 mol%), CuI (13 mg, 66 µmol, 2 mol%, **57** (0.80 g, 3.3 mmol, 1 equiv.), 1-bromo-3-iodobenzene (0.95 g, 3.4 mmol, 1.01 equiv.) and Et_3N (2.3 mL, 17 mmol, 5 equiv.) in acetonitrile (30 mL). The crude material was purified by flash column chromatography (SiO_2, 0-5% EtOAc in pentane) affording *N*-benzyl-*N*-(3-(3-bromophenyl)prop-2-yn-1-yl)-2,2,2-trifluoroacetamide as an yellow oil (1.2 g, 3.04 mmol, 92% yield).

Hydrolysis: the obtained trifluoroacetamide (1.2 g, 3.0 mmol, 1 equiv.) was treated with KOH (0.50 g, 9.0 mmol, 3.0 equiv.) in H_2O (15 mL) and MeOH (15 mL). Purification by column chromatography (SiO_2, 10-30% EtOAc in pentane) afforded *N*-benzyl-3-(3-bromophenyl)prop-2-yn-1-amine (**68**) as a light yellow oil (0.80 g, 2.7 mmol, 88% yield)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.59 (t, *J* = 1.7 Hz, 1H, Ar*H*), 7.45 (ddd, *J* = 8.0, 2.1, 1.1 Hz, 1H, Ar*H*), 7.43 – 7.24 (m, 6H, Ar*H*), 7.18 (t, *J* = 7.9 Hz, 1H, Ar*H*), 3.96 (s, 2H, ArC*H*$_2$), 3.66 (s, 2H, C*H*$_2$C≡C), 2.37 (s, 1H, N*H*).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 138.7, 134.4, 131.3, 130.2, 129.7, 128.5, 128.5, 127.4, 125.1, 122.1, 88.4, 82.6, 52.3, 37.9.

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{16}H_{15}{}^{79}BrN^+$300.0382; Found 300.0384.[4]



69

***N*-Benzyl-3-(3-chlorophenyl)prop-2-yn-1-amine (69)**

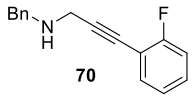
Prepared following general procedure B2.A using 3-chloroiodobenzene (730 mg, 3.06 mmol, 1.1 equiv.). Purification was performed by Biotage flash column chromatography system with a 25 g cartridge (SiO_2, 10 – 40% EtOAc in pentane) to afford *N*-benzyl-3-(3-chlorophenyl)prop-2yn-1-amine (**69**)as an orange oil (530 mg, 2.08 mmol, 77% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 – 7.40 (m, 1H, Ar*H*), 7.40 – 7.18 (m, 8H, Ar*H*), 3.94 (s, 2H, PhC*H*$_2$), 3.65 (s, 2H, C*H*$_2$C≡C), 1.60 (br. s., 1H. N*H*).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 139.6, 134.2, 131.7, 129.9, 129.6, 128.62, 128.56, 128.5, 127.4, 125.1, 89.1, 82.5, 52.7, 38.3.

IR (cm^{-1}) 3324 (m), 3030 (m), 2909 (m), 2833 (m), 2357 (w), 1589 (m), 1560 (m), 1465 (m).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{16}H_{15}ClN^+$ 256.0888; Found 256.0886.



70

***N*-Benzyl-3-(2-fluorophenyl)prop-2-yn-1-amine (70)**

Prepared following general procedure B2.A using 2-fluoroiodobenzene (0.80 g, 0.42 mL, 3.6 mmol, 1.2 equiv.). Purification was performed by Biotage flash column chromatography system with a 25 g cartridge (SiO_2, 10 – 40% EtOAc in pentane) to afford *N*-benzyl-3-(2-fluorophenyl)prop-2-yn-1-amine (**70**) as an orange oil (520 mg, 2.17 mmol, 72% yield).

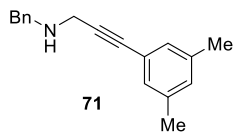
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.19 (m, 5H, Ar*H*), 7.19 – 7.10 (m, 2H, Ar*H*), 7.00 – 6.92 (m, 2H, Ar*H*), 3.86 (s, 2H, PhC*H*$_2$), 3.58 (s, 2H, C*H*$_2$C≡C), 1.48 (s, 1H, N*H*).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 163.0 (d, *J* = 250.9 Hz), 139.6, 133.7, 129.9 (d, *J* = 7.9 Hz), 128.7, 128.6, 127.3, 124.0 (d, *J* = 3.7 Hz), 115.6 (d, *J* = 21.0 Hz), 111.9 (d, *J* = 15.7 Hz), 93.2, 77.3, 52.5, 38.4.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -110.4 (d, 1F, *J* = 5.9 Hz, Ar*F*).

IR (cm^{-1}) 3324 (m), 3032 (m), 2912 (m), 2836 (m), 2104 (w), 1494 (s), 1451 (s), 1327 (m), 1214 (m), 1107 (m).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{16}H_{15}FN^+$ 240.1183; Found 240.1184.



71

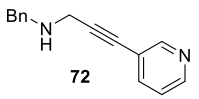
***N*-benzyl-3-(3,5-dimethylphenyl)prop-2-yn-1-amine (71)**

Prepared following modified general procedure B2.B using $PdCl_2(PPh_3)_2$ (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%). **57** (0.97 g, 4.0 mmol, 1 equiv.), 1-iodo-3,5-dimethylbenzene (1.1 g, 4.8 mmol, 1.2 equiv.) in DMF (3.3 mL) and Et_3N (10 mL). 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). Hydrolysis: the obtained trifluoroacetamide (0.84 g, 2.4 mmol, 1 equiv.) was treated with KOH (0.15 g, 2.7 mmol, 1.3 equiv.) in H_2O (5 mL) and MeOH (5 mL). Purification by column chromatography (SiO_2, 10-40% EtOAc in pentane) afforded *N*-benzyl-3-(3,5-dimethylphenyl)prop-2-ynylamine (**71**) 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, ArC*H*$_2$), 3.65 (s, 2H, C*H*$_2$C≡C), 2.29 (s, 6H, C*H*$_3$), 2.09 (bs, 1H, N*H*).

^{13}C{^{1}H} 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.

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



72

***N*-Benzyl-3-(pyridin-3-yl)prop-2-yn-1-amine (72)**

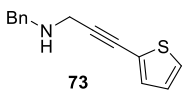
Prepared following general procedure B2.A using 3-bromopyridine (0.48 g, 0.30 mL, 3.06 mmol, 1.1 equiv.). Purification was performed by two sequential runs of Biotage flash column chromatography system with a 25 g cartridge (SiO_2, 0 – 10% MeOH in DCM) to afford *N*-benzyl-3-(pyridin-3-yl)prop-2-yn-1-amine (**72**) as a dark orange oil (401 mg, 1.80 mmol, 60% yield). The material was used without further purification.

^{1}H NMR (400 MHz, DMSO-*d6*) δ 8.62 (br. s, 1H, HetAr*H*), 8.55 (br. s, 1H, HetAr*H*), 7.84 (dt, *J* = 7.9, 1.9 Hz, 1H, HetAr*H*), 7.45 – 7.29 (m, 5H, HetAr*H* and Ar*H*), 7.26 – 7.19 (m, 1H, Ar*H*), 3.82 (s, 2H, PhCH_2), 3.56 (s, 2H, CH_2C≡C).

^{13}C{^{1}H} NMR (101 MHz, DMSO-*d6*) δ 151.6, 148.6, 140.1, 138.5, 128.1, 128.1, 126.7, 123.6, 119.8, 92.3, 79.8, 51.5, 37.4.

IR (cm^{-1}) 3649 (m), 3276 (m), 3032 (m), 2914 (m), 2831 (m), 2233 (w), 1663 (m), 1465 (m), 1112 (m).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{15}H_{15}N_2^+$ 223.1230; Found 223.1232.



73

***N*-benzyl-3-(thiophen-2-yl)prop-2-yn-1-amine (73)**

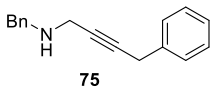
Prepared following general procedure B2.B using $PdCl_2(PPh_3)_2$ (36 mg, 51 µmol, 2 mol%), CuI (12 mg, 66 µmol, 3 mol%), **57** (0.50 g, 2.0 mmol, 1 equiv.), 2-iodothiophene (0.43 g, 2.0 mmol, 1.01 equiv.) and Et_3N (1.4 mL, 10 mmol, 5 equiv.) in acetonitrile (30 mL). The The crude material was purified by flash column chromatography (SiO_2, 0-5% EtOAc in pentane) afforded *N*-benzyl-2,2,2-trifluoro-*N*-(3-(thiophen-2-yl)prop-2-yn-1-yl)acetamide as an yellow oil (0.58 g, 1.8 mmol, 88% yield).

Hydrolysis: the obtained trifluoroacetamide (0.58 g, 1.8 mmol, 1 equiv.) was treated with KOH (0.30 g, 5.4 mmol, 3.0 equiv.) in H_2O (9 mL) and MeOH (9 mL). Purification by column chromatography (SiO_2, 10-30% EtOAc in pentane) afforded *N*-benzyl-3-(3-bromophenyl)prop-2-yn-1-amine (**73**) as an orange amorphous solid (0.38 g, 1.7 mmol, 93% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.27 (m, 5H, Ar*H*), 7.24 (dd, *J* = 5.2, 1.2 Hz, 1H, Ar*H*), 7.20 (dd, *J* = 3.6, 1.1 Hz, 1H, Ar*H*), 6.97 (dd, *J* = 5.2, 3.6 Hz, 1H, Ar*H*), 3.95 (s, 2H, ArCH_2), 3.68 (s, 2H, CH_2C≡C), 3.00 (s, 1H N*H*).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 138.8, 131.8, 128.5, 128.5, 127.3, 126.9, 126.8, 123.1, 91.0, 77.3, 52.3, 38.2.

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{14}H_{14}NS^+$ 228.0841; Found 228.0844.[4]



75

***N*-Benzyl 4-phenyl-but-2-ynylamine (75)**

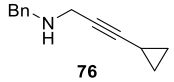
Prepared following general procedure B2.C using CuBr (0.18 g, 1.3 mmol, 12 mol%), allyl benzylamine (1.9 g, 13 mmol, 1.3 equiv), formaldehyde (2.5 mL, 33 mmol 36% aq. solution, 3.1 equiv) and phenylpropyne (1.2 g, 10 mmol, 1 equiv.) in MeCN (60 mL). Purification of the crude product by column chromatography (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).

Deallylation: the obtained tertiary amine (1.0 g, 3.6 mmol, 1 equiv.) was treated with $Pd(PPh_3)_4$ (84 mg, 73 µmol, 2 mol%) and 1,3-dimethylbarbituric acid (0.85 g, 5.5 mmol, 1.5 equiv.) in DCM (22 mL). Purification by flash column chromatography (SiO_2, 20-30% EtOAc in pentane) to afford *N*-benzyl-4-phenyl-but-2-ynylamine (**75**) 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 (br. s., 1H, N*H*).

^{13}C{^{1}H} 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.

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



76

***N*-Benzyl 4-phenyl-but-2-ynylamine (76)**

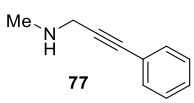
Prepared following general procedure B2.C using CuBr (0.36 g, 2.5 mmol, 12 mol%), allyl benzylamine (3.9 mL, 25 mmol, 1.3 equiv), formaldehyde (36% aq. solution; 5.0 mL, 65 mmol, 3.3 equiv.) and ethynylcyclopropane (1.7 mL, 20 mmol, 1 equiv.) in MeCN (130 mL). Purification of the crude material by column 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).

Deallylation: the obtained tertiary amine (1.0 g, 4.4 mmol, 1.0 equiv.) was treated with $Pd(PPh_3)_4$ (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 crude material was purified by column chromatography (SiO_3, 20-30% EtOAc in pentane) to afford *N*-benzyl 3-cyclopropyl-prop-2-ynylamine (**76**) 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, ArCH_2), 3.37 (d, *J* = 2.0 Hz, 2H, CH_2C≡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(CH_2)$_2$)).

^{13}C{^{1}H} 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.

Spectral data was consistent with the values reported in literature.[9]



77

***N*-methyl-3-phenylprop-2-yn-1-amine (77)**

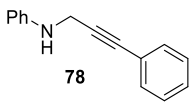
Prepared following general procedure B2.C using CuBr (0.20 g, 1.4 mmol, 13 mol%), allyl methylamine (0.98 g, 14 mmol, 1.3 equiv.), formaldehyde (2.5 mL, 33 mmol 36% aq. solution, 3 equiv.) and phenylpropyne (1.2 g, 11 mmol, 1 equiv.) in MeCN (70 mL). Purification of the crude product by column chromatography (SiO_2, 0-2% EtOAc in pentane) to afford *N*-allyl-N-benzyl-4-phenyl-but-2-ynylamine as a colourless oil (1.8 g, 9.7 mmol, 88% yield).

Deallylation: the obtained tertiary amine (1.0 g, 3.6 mmol, 1 equiv.), $Pd(PPh_3)_4$ (0.37 g, 0.32 mol, 6 mol%) and 1,3-dimethylbarbituric acid (1.7 g, 11 mmol, 2 equiv.) in DCM (50 mL). Purification by flash column chromatography (SiO_2, 20-50% EtOAc in pentane) to afford *N*-methyl-3-phenylprop-2-yn-1-amine (**77**) as an orange viscous oil (0.46 g, 3.1 mmol, 58% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 – 7.41 (m, 2H, Ar*H*), 7.33 (m, 3H, Ar*H*), 3.68 (s, 2H, NCH_2C≡C), 3.16 (s, 1H, N*H*), 2.59 (s, 3H, CH_3).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 131.7, 128.3, 128.1, 123.0, 86.5, 84.1, 40.5, 34.9.

Spectral data was consistent with the values reported in literature.[9]



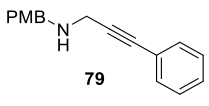
78

***N*-(3-phenylprop-2-yn-1-yl)aniline (78)**

Prepared following modified general procedure B2.A using phenyl propargylamine[12] (400 mg, 3.05 mmol, 1.0 equiv.), iodobenzene (684 mg, 3.35 mmol, 1.1 equiv.), $PdCl_2(PPh_3)_2$ (43 mg, 0.061 mmol, 2 mol%), CuI (6 mg, 0.03 mmol, 1 mol%) and Et_3N (0.31 g, 0.43 mL, 3.0 mmol, 1.0 equiv.). Purification by flash column chromatography (SiO_2, 2-6% EtOAc in pentane) afforded *N*-(3-phenylprop-2-yn-1-yl)aniline (**78**) as an orange solid (0.43 g, 1.9 mmol, 63% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.36 (m, 2H, Ar*H*), 7.35 – 7.27 (m, 3H, Ar*H*), 7.27 – 7.20 (m, 3H, Ar*H*), 6.86 – 6.73 (m, 3H, Ar*H* and N*H*), 4.17 (s, 2H, CH_2).
^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 146.9, 131.9, 129.4, 128.4 (2C), 123.0, 119.0, 114.1, 86.2, 83.7, 35.0.

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



79

***N*-(4-methoxybenzyl)-3-phenylprop-2-yn-1-amine (79)**

Prepared following general procedure B2.C using CuBr (0.22 g, 1.5 mmol, 13 mol%), N-(4-methoxybenzyl)prop-2-en-1-amine[13] (2.7 g, 15.0 mmol, 1.3 equiv.), formaldehyde (2.8 mL, 36.0 mmol 36% aq. solution, 3 equiv.) and phenylpropyne (1.2 g, 12.0 mmol, 1 equiv.) in MeCN (80 mL). Purification of the crude product by column chromatography (SiO_2, 0-2% EtOAc in pentane) afforded *N*-benzyl-*N*-(3-(4-methoxyphenyl)prop-2-yn-1-yl)prop-2-en-1-amine as a pale yellow oil (3.40 g, 11.7 mmol, 97% yield).

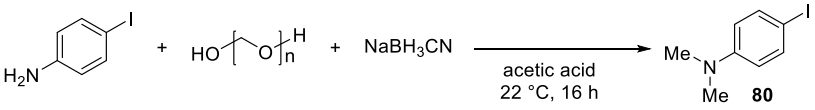
Deallylation: the obtained tertiary amine (3.40 g, 11.7 mmol, 1 equiv.) was treated with $Pd(PPh_3)_4$ (0.270 g, 0.233 mol, 2 mol%) and 1,3-dimethylbarbituric acid (2.70 g, 17.5 mmol, 1.5 equiv.) in DCM (58 mL). Purification by flash column chromatography (SiO_2, 20-50% EtOAc in pentane) to afford *N*-(4-methoxybenzyl)-3-phenylprop-2-yn-1-amine (**79**) as an orange viscous oil (2.3 g, 9.3 mmol, 80% yield).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.49 – 7.41 (m, 2H, Ar*H*), 7.34 – 7.28 (m, 5H, Ar*H*), 6.93 – 6.85 (m, 2H, Ar*H*), 3.89 (s, 2H, ArCH_2N), 3.81 (s, 3H, OCH_3), 3.64 (s, 2H, NCH_2C≡C) 1.54 (br. s., 1H, N*H*).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 158.9, 131.8 (2c), 129.8, 128.4, 128.1, 123.4, 114.0, 87.8, 83.8, 55.4, 52.0, 38.2.

Spectral data was consistent with the values reported in literature.[9]

B.3. Synthesis of the Substituted Aryl Iodide 80



Scheme 8. Synthesis of aryl iodide **80**.

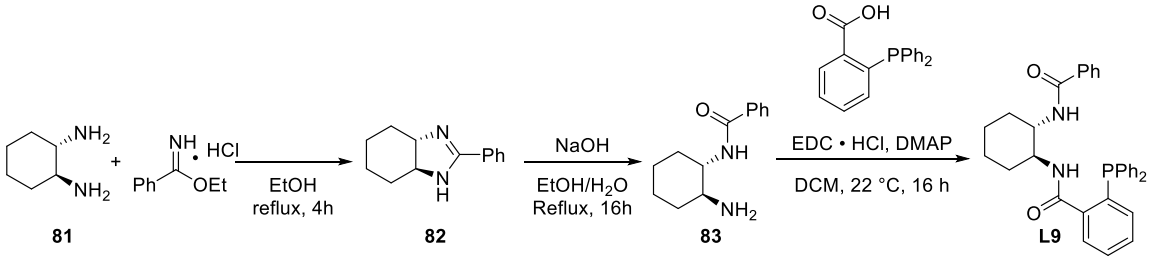
In accordance to a reported procedure,[14] 4-iodoaniline (4.00 g, 18.5 mmol, 1 equiv.) was dissolved in acetic acid (120 mL) and degassed. To the solution was added paraformaldehyde (6.00 g, 194 mmol, 10.5 equiv.) and slowly sodium cyanoborohydride (5.5 g, 87 mmol, 4.7 equiv.). The reaction mixture was stirred at room temperature for 12 h. Then, the mixture was cooled and neutralized by adding 1M NaOH solution and pure NaOH until basicity (pH >9). The suspension was extracted with DCM (3×150 mL). The combined organic layers were washed with brine and dried over sodium sulfate. After filtration, the solvent was removed in vacuum affording the product **80** as a grey solid (4.13 g, 16.7 mmol, 91%)

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (d, *J* = 9.1 Hz, 2H, Ar*H*), 6.49 (d, *J* = 9.1 Hz, 2H, Ar*H*), 2.92 (s, 6H, N(C*H*$_3$)$_2$).

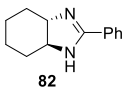
^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 150.1, 137.7, 114.9, 77.6, 40.5.

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

B.4. Synthesis of the Ligand L9



Scheme 9. Synthesis of ligand **L9**.



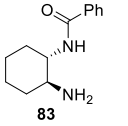
(3a*S*,7a*S*)-2-phenyl-3a,4,5,6,7,7a-hexahydro-1H-benzo[d]imidazole (82)

In accordance with a reported procedure,[15] ethyl benzimidate hydrochloride (3.3 g, 18 mmol, 1.2 equiv.) in ethanol (15 mL) was stirred at room temperature under nitrogen and (1*S*,2*S*)-cyclohexane-1,2-diamine (1.70 g, 15.0 mmol, 1.0 equiv.) was added to the solution in one portion. The solution was heated to reflux and stirred for 4 hours. 1 M NaOH (50 mL) was then added and the mixture was extracted with 5% MeOH in DCM. The organic layer was dried over sodium sulfate and concentrated to afford the crude product, which was purified by silica gel chromatography (gradient from DCM to DCM/MeOH/NH$_3$ 100:10:1) to obtain the product as a white solid (2.50 g, 12.5 mmol, 83%). [α]D^{20} = -132.8 (c = 0.51, CHCl$_3$).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.84 – 7.74 (m, 2H, Ar*H*), 7.40 (m, 3H, Ar*H*), 5.50-4.50 (bs, 1H, N*H*), 3.12 (m, 2H, NC*H*CH$_2$ and NHC*H*CH$_2$), 2.36 – 2.25 (m, 2H, NCHC*H*$_2$), 1.92 – 1.79 (m, 2H, NHCHC*H*$_2$), 1.62 – 1.49 (m, 2H, -CH$_2$C*H*$_2$CH$_2$-), 1.45 – 1.28 (m, 2H, -CH$_2$C*H*$_2$CH$_2$-).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 165.5, 131.0, 130.7, 128.6, 126.7, 69.8, 31.1, 25.2.

Spectral data was consistent with the values reported in literature.[15]



N-((1*S*,2*S*)-2-aminocyclohexyl)benzamide (83)

In accordance with a reported procedure,[15] to compound **83** (2.30 g, 11.5 mmol) was added 19 mL 5% NaOH and 42 mL EtOH/H$_2$O (2:1) and the solution was heated to reflux for 16 hours. After cooling to room temperature, the ethanol was removed in vacuum, and the crude product was extracted with DCM. The product was purified by silica column chromatography (gradient from DCM to DCM/MeOH/NH$_3$ 100:10:1) to provide the desired product as a white solid. (1.6 g, 7.3 mmol, 64%).

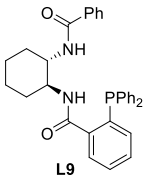
[α]D^{20} = -16.5 (c = 0.51, CHCl$_3$).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.82 – 7.76 (m, 2H, Ar*H*), 7.54 – 7.39 (m, 3H, Ar*H*), 6.12 (d, *J* = 8.4 Hz, 1H, N*H*), 3.71 (dddd, *J* = 11.9, 9.9, 8.3, 4.1 Hz, 1H, NHC*H*CH$_2$), 2.49 (td, *J* = 10.2, 3.9 Hz, 1H,

NH_2CHCH_2), 2.14 (ddd, *J* = 12.7, 4.0, 2.1 Hz, 1H, NHCHCH_aH_b), 2.08 – 1.98 (m, 1H, NHCHCH_aH_b), 1.76 (dq, *J* = 9.7, 2.7 Hz, 2H, NH_2CHCH_2), 1.54 – 1.12 (m, 6H, NH_2 and 2 x -$CH_2CH_2CH_2$-).

$^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 167.9, 134.9, 131.5, 128.7, 127.0, 56.8, 55.8, 35.9, 32.7, 25.3, 25.2.

Spectral data was consistent with the values reported in literature.[15]



L9

N-((1*S*,2*S*)-2-benzamidocyclohexyl)-2-(diphenylphosphino)benzamide (L9)

To a stirred solution of 2-(diphenylphosphino)benzoic acid (1.5 g, 5.0 mmol, 1.1 equiv.) and DMAP (280 mg, 2.30 mmol, 0.5 equiv.) in DCM (20 mL) was added EDC HCl (966 mg, 5.00 mmol, 1.1 equiv.) at 0 °C. The mixture was stirred for few minutes and allowed to reach room temperature. Then, compound **83** (1.0g, 4.6 mmol, 1 equiv.) was added followed by 8 mL of DCM. The resulting mixture was stirred at room temperature for 16 hours. The mixture was then quenched with 1 M HCl (50 mL) and extracted with DCM (2x50 mL). The combined organic layers were washed with brine and dried over sodium sulfate. The solvent was removed in vacuum and the crude mixture was purified by column chromatography (pentane/EtOAc up to 1:1) and recrystallized from boiling acetonitrile to obtain the desired compound **L9** as a white solid (1.4 g, 60%).

$[\alpha]D^{20}$ = +21.3 (c = 0.5, $CHCl_3$, >99% e.e.).

^1H NMR (400 MHz, Chloroform-*d*) δ 7.84 – 7.76 (m, 2H, Ar*H*), 7.51 – 7.12 (m, 16H, Ar*H*), 7.09 (d, *J* = 7.6 Hz, 1H, N*H*), 6.90 – 6.83 (m, 1H, Ar*H*), 6.19 (d, *J* = 8.4 Hz, 1H, N*H*), 3.96 (tdd, *J* = 11.8, 8.4, 3.9 Hz, 1H, NHC*H*CH_2), 3.83 (dtd, *J* = 10.8, 7.4, 3.9 Hz, 1H, NHC*H*CH_2), 2.21 (dd, *J* = 14.8, 7.6 Hz, 1H, NHCHCH_aH_b), 1.86 (dd, *J* = 12.9, 3.6 Hz, 1H, NHCHCH_aH_b), 1.80 – 1.67 (m, 2H, NHCHCH_aH_b and NHCHCH_aH_b), 1.29 (q, *J* = 12.7, 10.9 Hz, 3H, -$CH_2CH_2CH_2$-), 1.15 – 1.00 (m, 1H, -$CH_2CH_2CH_2$-).

$^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 170.2, 167.7, 141.2, 141.0, 137.4, 137.3, 137.2, 136.1, 135.9, 134.5, 134.3, 134.07, 134.05, 133.87, 133.85, 131.3, 130.4, 129.0, 128.9, 128.84, 128.76, 128.7, 128.6, 128.5, 127.7, 127.6, 127.3, 55.5, 53.3, 32.5, 32,0, 25.0, 24.7.[a]

^{31}P NMR (162 MHz, Chloroform-*d*) δ -10.97.

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{32}H_{32}N_2O_2P^+$ 507.2196; Found 507.2201.

IR (cm^{-1}) 3279 (m), 3064 (m), 2935 (m), 2860 (m), 1634 (s), 1545 (s), 1334 (m).

The (*R*,*R*)-**L9** ligand and the *rac*-**L9** were prepared using the same route starting from (*R*,*R*)-cyclohexane-1,2-diamine and racemic cyclohexane-1,2-diamine respectively.

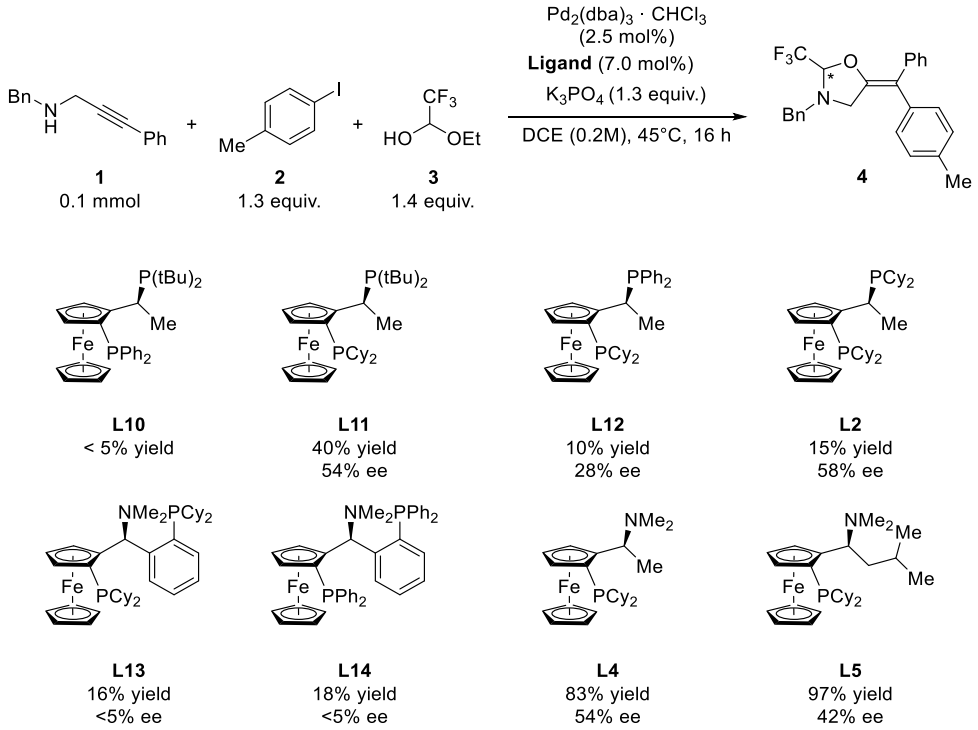
[a]The peaks are listed not accounting for C-P coupling

C. Optimization Studies

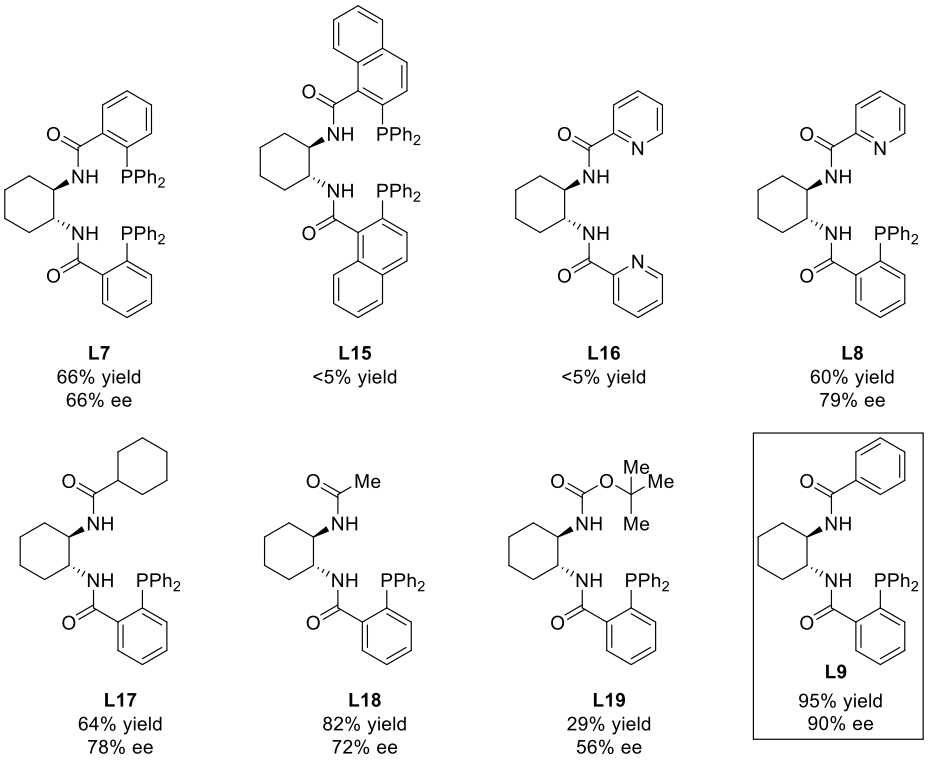
C.1. Carboetherification: Screening of Ligands

The optimization reactions were conducted on a 0.1 mmol scale (relative to the propargylic amine). Reactions were performed in 6 mL conical microwave vials equipped with Teflon-coated magnetic stirring bars. The vials were loaded with the palladium source, the base and the ligand. Part of the solvent (300 μL) was added and the mixture was stirred at the specified temperature for 10 minutes. Propargylic amine, tether, and the remaining solvent (200 μL) were then added and the reaction mixture was stirred for 16 hours. The crude mixture was filtered through a plug of deactivated silica eluting with 10 mL of pentane/EtOAc 9:1. The solvent was removed and yields were determined by ^{1}HNMR analysis of the crude mixture using 1 equiv. of trichloroethylene as the internal standard (IS). The enantiomeric excess was determined by HPLC analysis of a pure sample of product obtained by preparative TLC purification (pentane/EtOAc 100:3). HPLC method: Daicel Chiralpak IB N-5 column, 99:1 hexane/IPA, flow rate 1 mL/min. : τ_1 = 7.0 min τ_2 = 8.5 min.

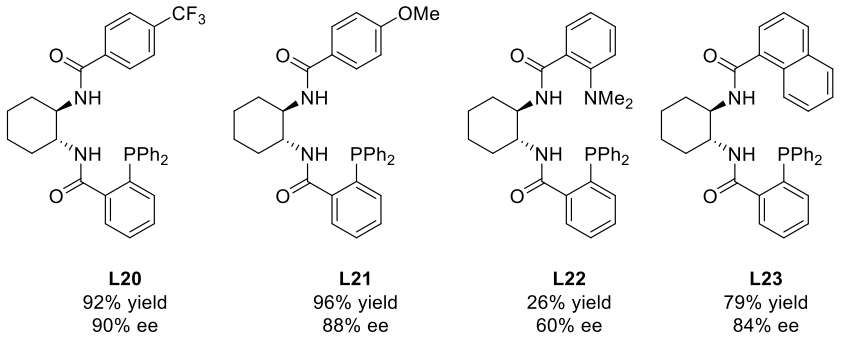
The ligands used in the optimization studies are commercially available or synthesized following reported procedures (**L4**-**L5**,[16] **L16**,[17] **L8**,[18] **L17**,[19] **L18**,[20] **L19**,[21] **L20**,[19] **L21**,[20] **L22**,[21] **L23**[20]).



Scheme 10. Screen 1 Evaluation of the JosiPhos and TaniaPhos type ligands and the corresponding P,N ligands.

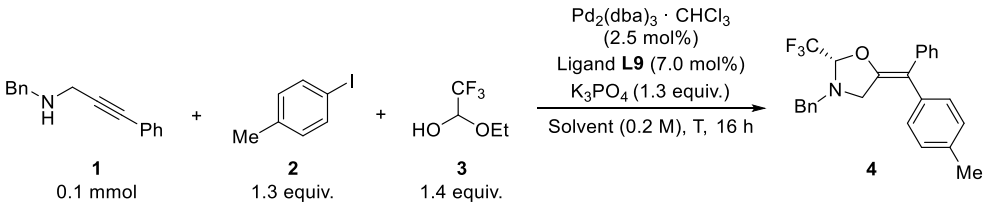


Scheme 11. Screen 2 Evaluation of the Trost type ligands and analogs.



Scheme 12. Screen 3 Variations on the benzoyl amide

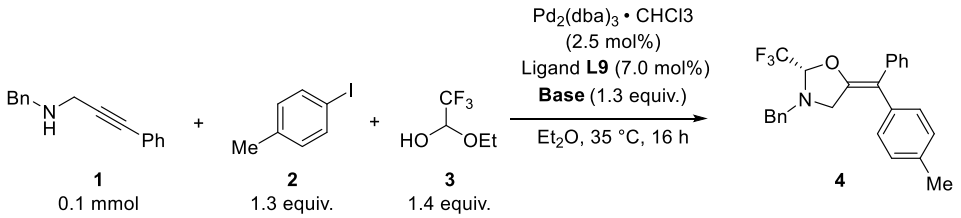
C.2. Carboetherification: Screening of Solvents and Temperatures



1 0.1 mmol + **2** 1.3 equiv. + **3** 1.4 equiv. → **4**

entry	Solvent (Temperature)	[%] yield **4**	ee **4**
1	DCE (45°C)	>95	90
2	MeOH (45°C)	25	48
3	DMSO (45°C)	78	50
4	DMF (45°C)	64	56
5	NMP (45°C)	40	44
6	MeCN (45°C)	94	72
7	Acetone (45°C)	35	74
8	EtOAc (45°C)	80	84
9	DCM (35°C)	>95	88
10	$CHCl_3$ (45°C)	80	89
11	PhCl (45°C)	93	90
12	DME (45°C)	87	82
13	THF (45°C)	84	89
14	Dioxane (45°C)	73	88
15	MTBE (45°C)	89	89
16	Et_2O (35°C)	>95	91
17	CPME (45°C)	90	90
18	MeTHF (45°C)	26	82
19	$PhCF_3$ (45°C)	88	90
20	Benzene (45°C)	93	90
21	Toluene (45°C)	91	91
22	*n*-hexane (45°C)	78	86

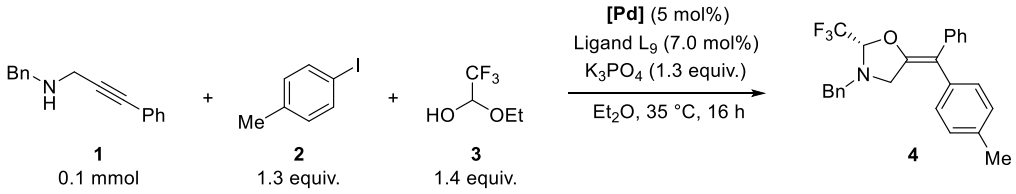
C.3. Carboetherification: Screening of Bases



1 0.1 mmol + **2** 1.3 equiv. + **3** 1.4 equiv. → **4**

entry	Base	[%] yield **4**	ee **4**
1	K_3PO_4	>95	91
2	CsOAc	<5	-
3	KH_2PO_4	<5	-
4	Li_2CO_3	<5	-
5	Na_2CO_3	<5	-
6	K_2CO_3	50	75
7	Cs_2CO_3	89	50
8	Li_3PO_4	<5	-
9	Na_3PO_4	<5	-
10	Cs_3PO_4	>95	86
11	LiOH	<5	-
12	NaOH	45	30
13	KOH	>95	82
14	NaOMe	30	89
15	NaO*t*Bu	80	82
16	KO*t*BU	56	40
17	NaHMDS	28	52
18	2,6-lutidine	<5	-
19	Et_3N	<5	-
20	DBU	<5	-

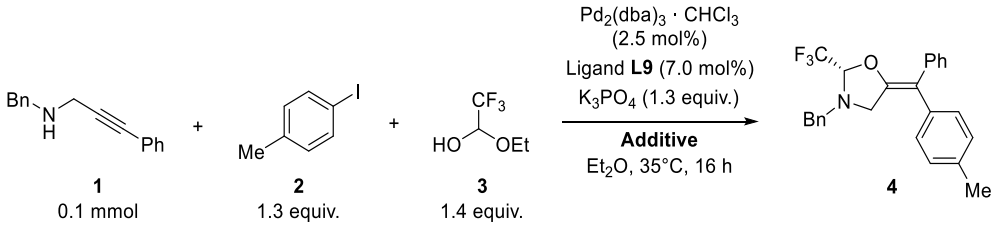
C.4. Carboetherification: Screening of Palladium Sources



1 0.1 mmol + **2** 1.3 equiv. + **3** 1.4 equiv. → **4**

entry	Pd source	[%] yield **4**[b]	ee **4**
1	Pd_2dba_3•$CHCl_3$	>95	91
2	$Pd_2(PhCN)_2Cl_2$	89	91
3	$(\eta^3\text{-}C_3H_4PdCl)_2$	94	91
4	CpPdCynnamil	90	91
5	$Pd(OAc)_2$	68	88
6	$Pd(acac)_2$	80	91
7	$Pd(PPh_3)_4$	20	82

C.5. Carboetherification: Screening of Additives

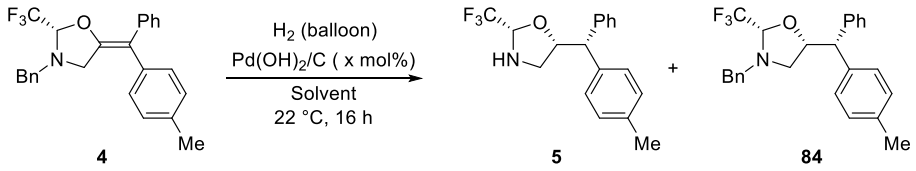


1 0.1 mmol + **2** 1.3 equiv. + **3** 1.4 equiv. → **4**

entry	Additive	[%] yield **4**	ee **4**
1	18-crown-6 (10 mol%)	>95	82
2	TBAB (10 mol%)	>95	88
3	LiCl (20 mol%)	>95	88
4	NaOTf (20 mol%)	>95	89
5	Perfluoroheptane (10% v/v)	91	91
6	HFiP (50 mol%)	>95	91
7	H_2O (10% v/v)	27	32

C.5. Asymmetric Hydrogenation: Optimization Studies

The optimization reactions were performed in 25 mL round-bottom flask equipped with Teflon-coated magnetic stir bars. The flasks were loaded with the palladium catalyst and the olefin substrate closed with a septum, and purged with nitrogen. The solvent mixture was added and the suspension was stirred under a nitrogen flow for 10 minutes. Then, a balloon of hydrogen was connected to the flask with a needle and the reaction was stirred for 16 h at room temperature. The crude mixture was degassed bubbling nitrogen for 10 minutes and filtered through a plug of celite eluting with 10 mL of MeOH. The crude extract was washed with saturated $NaHCO_3$ and extracted with DCM (3x20 mL). The combined organic layers were dried over sodium sulfate, filtered and concentrated in vacuum. Yields were determined by ^{1}HNMR analysis of the crude mixture using 1 equiv. of trichloroethylene as the internal standard (IS). The enantiomeric excess was determined by HPLC analysis of a pure sample obtained by preparative TLC purification (pentane/EtOAc 100:15). HPLC method: Daicel Chiralpak IA column, 95:5 hexane/IPA, flow rate 1 mL/min. τ_1 = 8.2 min, τ_2 = 12.5 min.



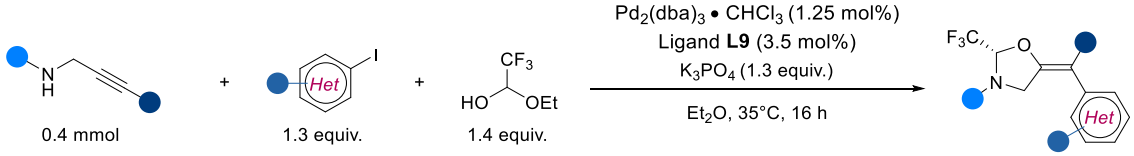
4 → **5** + **84**

entry	Scale (mmol)	Solvent	[Pd] loading	[%] yield **5**	[%] yield **84**
1	0.1	MeOH/EtOAc (2:1)	10	28	8
2	0.2	MeOH/EtOAc (2:1)	20	23	70
3	0.1	MeOH/AcOH (2:1)	20	77	-
4	0.1	MeOH/AcOH (2:1)	10	77	-
5	0.2	MeOH/AcOH (2:1)	10	80 (91% ee)[a]	-

a: ee starting material: 91%

D. Stereoselective Carboetherification of Propargylic Amines

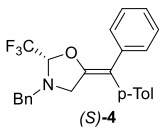
D.1. General Procedure for the Enantioselective Carboetherification of Propargylic Amines



Scheme 13. Enantioselevtive Carboetherification of Propargylic Amines

An oven-dried 8 mL microwave vial equipped with a Teflon coated stirring bar was charged with $Pd_2(dba)_3 \bullet CHCl_3$ (5.2 mg, 5.0 µmol, 1.25 mol%), the ligand (7.2 mg, 14 µmol, 3.5 mol%) and K_3PO_4 (0.11 g, 0.52 mmol, 1.3 equiv.). The vial was then sealed, purged with N_2 and placed in a heating metal block. 1.5 mL of Et_2O were added and the suspension was stirred at 35 °C for 10 minutes. Propargylic amine (0.40 mmol, 1.0 equiv) and 1-ethoxy-2,2,2-trifluoroethanol (85% in EtOH, 76 uL, 0.56 mmol 1.4 equiv.) were added followed by the aryl iodide (0.52 mmol, 1.3 equiv.) and the remaining 0.5 mL of Et_2O to rinse the wall of the vial. The resulting suspension was stirred at 35 °C for 16 hours. Next, the reaction mixture was filtered through a plug of deactivated silica gel eluting with 15 mL of pentane/EtOAc 9:1 and concentrated in vacuo. The crude material was purified by flash column chromatography on silica gel to afford the corresponding product.

D.2. Characterization of Products of the Enantioselevtive Carboetherification



(S)-**4**

(*S*,*E*)-3-Benzyl-5-(phenyl(p-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (*(S)*-4)

Prepared according to the general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 µL, 0.40 mmol, 1.0 equiv.) and 1-iodo-4-methylbenzene (113 mg, 0.520 mmol, 1.3 equiv). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:3) to give the corresponding olefin *(S)*-**4** (161 mg, 0.393 mmol, 98% yield) as a white solid (m.p. 118 °C). The enantiomeric excess was determined to be 94% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 6.9 min τ_{Major} = 8.4 min. Absolute configuration was determined by X-Ray diffraction analysis of a single crystal of *(S)*-**4** (details in section F).

$[\alpha]D^{20}$ = +67.5 (c = 0.37, $CHCl_3$, 94% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.26 (m, 9H, Ar*H*), 7.22 – 7.16 (m, 1H, Ar*H*), 7.14 (d, *J* = 7.8 Hz, 2H, Ar*H*), 7.05 (d, *J* = 8.1 Hz, 2H, Ar*H*), 5.13 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 3.99 (d, *J* = 13.3 Hz, 1H, PhCH_aH_b), 3.94 (d, *J* = 16.0 Hz, 1H, NCH_aH_bC=C), 3.89 (d, *J* = 13.2 Hz, 1H, PhCH_aH_b), 3.54 (d, *J* = 16.0 Hz, 1H, NCH_aH_bC=C),). 2.35 (s, 3H, CH_3).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 148.4, 138.8, 137.2, 137.1, 136.7, 130.0, 129.4, 129.1, 128.8 (2C), 128.04, 128.02, 126.3, 122.9 (q, J_{C-F} = 283.9 Hz), 112.9, 94.00 (q, J_{C-F} = 34.4 Hz), 60.5, 54.9, 21.3.

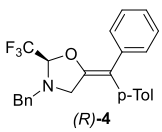
^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.3.

IR (cm^{-1}) 3031 (w), 1665 (w), 1503 (w), 1451 (w), 1293 (m), 1175 (s), 1153 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{25}H_{23}F_3NO^+$ 410.1726; Found 410.1728.

5 mmol scale reaction. The model reaction was repeated on 5 mmol scale. An oven dried 50 mL round-bottom flask equipped with a Teflon stir bar was charged with $Pd_2(dba)_3 \bullet CHCl_3$ (65 mg, 63 µmol, 1.25 mol%), the ligand (90 mg, 0.18 mmol, 3.5 mol%) and K_3PO_4 (1.38 g, 6.50 mmol, 1.3 equiv.). The flask was then purged with N_2 and placed in a heating metal block. 20 mL of Et_2O were added and the suspension was stirred at 35 °C for 10 minutes N-benzyl-3-phenylprop-2-yn-1-amine (1.11 g, 5.00 mmol, 1.0 equiv) and 1-ethoxy-2,2,2-trifluoroethanol (85% in EtOH, 0.96 mL, 7.0 mmol, 1.4 equiv.) were added followed by 1-iodo-4-methylbenzene (1.42 g, 6.50 mmol, 1.3 equiv.) and the remaining 5 mL of Et_2O to rinse the wall. The resulting suspension was stirred at 35 °C for 16 hours. Then, the reaction mixture was filtered through a plug of deactivated silica gel eluting with 50 mL of pentane/EtOAc 9:1 and concentrated in vacuo and analyzed by ^{1}H NMR with an internal standard (trichloroethylene, 0.1 equiv., NMR yield: >99%). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:3) to give the corresponding product *(S)*-**4** (2.04 g, 4.98 mmol, >99% yield) as a white solid. The enantiomeric

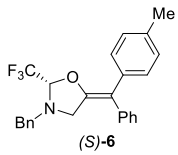
excess was determined to be 94% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 6.9 min τ_{Major} = 8.6 min.



(R)-**4**

(*R,E*)-3-Benzyl-5-(phenyl(p-tolyl)methylene)-2-(trifluoromethyl)oxazolidine ((*R)*-4)

Prepared according to the general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 µL, 0.40 mmol, 1.0 equiv.), 1-iodo-4-methylbenzene (113 mg, 0.520 mmol, 1.3 equiv) and the (*R,R*)-**L9** ligand**.** The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:3) to give the corresponding olefin **3** (160 mg, 0.390 mmol, 98% yield) as a white solid. The enantiomeric excess was determined to be 92% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Major} = 7.0 min τ_{Minor} = 8.6 min. $[\alpha]D^{20}$ = -52.3 (c = 0.50, $CHCl_3$, 92% ee). Absolute configuration determined in comparison to compound *(S)*-**4.**



(S)-**6**

(*S,Z*)-3-Benzyl-5-(phenyl(p-tolyl)methylene)-2-(trifluoromethyl)oxazolidine ((*S)*-6))

Prepared according to the general procedure D1 using N-benzyl-3-(p-tolyl)prop-2-yn-1-amine (94 mg, 0.40 mmol, 1.0 equiv.) and iodobenzene (108 mg, 58 µl, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin *(S)*-**6** (152 mg, 0.372 mmol, 93% yield) as colorless oil. The enantiomeric excess was determined to be 89% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 7.0 min, τ_{Major} = 8.1 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = 45.6 (c = 0.55, $CHCl_3$, 89% ee).

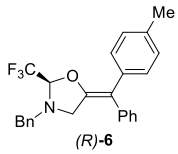
^{1}H NMR (400 MHz, Chloroform-d) δ 7.36 – 7.28 (m, 7H, Ar*H*), 7.27 – 7.21 (m, 3H, Ar*H*), 7.18 – 7.13 (m, 2H, Ar*H*), 7.10 (d, *J* = 8.0 Hz, 2H, Ar*H*), 5.11 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.03 – 3.83 (m, 3H, PhCH_2 and NC$H_a$$H_b$C=C), 3.52 (d, *J* = 15.7 Hz, 1H, NC$H_a$$H_b$C=C), 2.33 (s, 3H, ArC$H_3$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 148.1, 140.3, 137.1, 136.1, 135.8, 130.2, 129.0, 128.81, 128.77 (2C), 128.7, 128.0, 127.0, 122.9 (q, *J* = 284.0 Hz), 113.0, 93.9 (q, *J* = 34.3 Hz), 60.5, 54.8, 21.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.4 (d, 3F, *J* = 5.3 Hz).

IR (cm^{-1}) 3024 (w), 3023 (w), 1664 (w), 1505 (w), 1295 (m), 1214 (m), 1154 (m).

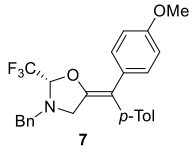
HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calculated for $C_{25}H_{22}F_3NNaO^+$ 432.1546; Found 432.1547.



(R)-**6**

(*R,Z*)-3-Benzyl-5-(phenyl(p-tolyl)methylene)-2-(trifluoromethyl)oxazolidine ((*R)*-6)

Prepared according to the general procedure D1 using N-benzyl-3-(p-tolyl)prop-2-yn-1-amine (94 mg, 0.40 mmol, 1.0 equiv.), iodobenzene (108 mg, 58 µl, 0.520 mmol, 1.3 equiv.) and the *(R,R)*-**L9** ligand. The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin *(R)*-**6.** (142 mg, 0.347 mmol, 87% yield) as colorless oil. The enantiomeric excess was determined to be 89% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Major} = 7.6 min, τ_{Minor} = 9.0 min. $[\alpha]D^{20}$ = -45.1 (c = 0.58, $CHCl_3$, 89% ee). Absolute configuration determined in comparison to compound *(S)*-**4.**



7

(*S,Z*)-3-Benzyl-5-((4-methoxyphenyl)(*p*-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (7)

Prepared according to the general procedure D1 using N-benzyl-3-(4-(methoxy)phenyl)prop-2-yn-1-amine (101 mg, 0.400 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin **7** (154 mg, 0.352 mmol, 88% yield) as amorphous white solid. The enantiomeric excess was determined to be 92% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 10.9 min, τ_{Major} = 22.6 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = 54.5 (c = 0.52, $CHCl_3$, 92% ee).

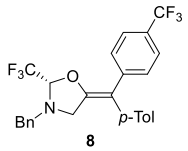
^{1}H NMR (400 MHz, Chloroform-d) δ 7.36 – 7.27 (m, 7H, Ar*H*), 7.16 – 7.09 (m, 2H, Ar*H*), 7.07 – 7.00 (m, 2H, Ar*H*), 6.87 – 6.78 (m, 2H, Ar*H*), 5.10 (q, *J* = 5.3 Hz, 1H, C*H*CF$_3$), 4.03 – 3.85 (m, 3H, PhC*H*$_2$ and NC*H*$_a$H$_b$C=C), 3.80 (s, 3H, OC*H*$_3$), 3.52 (dd, *J* = 15.7, 0.9 Hz, 1H, NCH$_a$*H*$_b$C=C), 2.34 (s, 3H, ArC*H*$_3$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 158.0, 147.3, 147.3, 137.4, 137.1, 136.7, 131.4, 130.2, 130.0, 129.4, 128.8, 128.0, 122.9 (q, *J* = 283.9 Hz), 113.5, 112.5, 93.8 (q, *J* = 34.2 Hz), 60.5, 55.4, 54.8, 21.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.3 (d, 3F, *J* = 5.3 Hz).

IR (cm^{-1}) 2941 (w), 2835 (w), 1664 (m), 1607 (m), 1512 (m), 1293 (m), 1247 (m), 1176 (s), 1155 (s), 1033 (m).

HRMS (ESI/QTOF) m/z: [M + Na]$^+$ Calculated for $C_{26}H_{24}F_3NNaO_2^+$ 462.1651; Found 462.1661.



8

(*S*,*Z*)-3-Benzyl-5-(*p*-tolyl(4-(trifluoromethyl)phenyl)methylene)-2-(trifluoromethyl)oxazolidine (8)

Prepared according to the general procedure D1 using N-benzyl-3-(4-(trifluoromethyl)phenyl)prop-2-yn-1-amine (116 mg, 0.400 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin **8** (165 mg, 0.346 mmol, 86% yield) as colorless oil. The enantiomeric excess was determined to be 88% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 6.8 min, τ_{Major} = 9.5 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

[α]D^{20} = 37.9 (c = 0.51, $CHCl_3$, 88% ee).

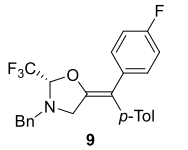
^{1}H NMR (400 MHz, Chloroform-d) δ 7.51 (d, *J* = 8.5 Hz, 2H, Ar*H*), 7.46 (d, *J* = 8.5 Hz, 2H, Ar*H*), 7.36 – 7.27 (m, 5H, Ar*H*), 7.15 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.02 (d, *J* = 8.0 Hz, 2H, Ar*H*), 5.17 (q, *J* = 5.2 Hz, 1H, C*H*CF$_3$), 3.99 (d, *J* = 13.3 Hz, 1H, PhC*H*$_a$H$_b$), 3.95 (d, *J* = 16.2 Hz, 1H, NC*H*$_a$H$_b$C=C), 3.90 (d, *J* = 13.3 Hz, 1H, PhCH$_a$*H*$_b$), 3.54 (d, *J* = 16.2 Hz, 1H, NCH$_a$*H*$_b$C=C), 2.36 (s, 3H, ArC*H*$_3$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 150.2, 142.4, 137.3, 138.8, 136.3, 130.0, 129.7, 129.1, 128.83, 128.78, 128.2, 127.9 (q, *J* = 32.0 Hz), 124.9 (q, *J* = 3.7 Hz), 124.5 (q, *J* = 272 Hz), 122.7 (q, *J* = 284.0 Hz) 111.7, 94.4 (q *J* = 34.4 Hz), 60.6, 55.1, 21.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.4 (s, 3F, ArC*F*$_3$), -80.4 (d, 3F, *J* = 5.2 Hz, CHC*F*$_3$).

IR (cm^{-1}) 2979 (m), 2901 (m), 1662 (m), 1616 (m), 1516 (m), 1329 (s), 1157 (s), 1122 (s), 1075 (m).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{26}H_{22}F_6NO^+$ 478.1600; Found 478.1607.



9

(*S*,*Z*)-3-Benzyl-5-((4-fluorophenyl)(*p*-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (9)

Prepared according to the general procedure D1 using N-benzyl-3-(4-(fluoro)phenyl)prop-2-yn-1-amine (96 mg, 0.40 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin **9** (168 mg, 0.392 mmol, 98% yield) as amorphous white solid. The enantiomeric excess was determined to be 91% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 6.5 min, τ_{Major} = 8.2 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

[α]D^{20} = 56.3 (c = 0.50, $CHCl_3$, 91% ee).

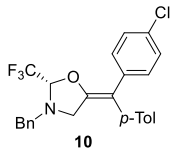
^{1}H NMR (400 MHz, Chloroform-d) δ 7.36 – 7.27 (m, 7H, Ar*H*), 7.13 (d, *J* = 7.8 Hz, 2H, Ar*H*), 7.06 – 6.99 (m, 2H, Ar*H*), 6.99 – 6.92 (m, 2H, Ar*H*), 5.12 (q, *J* = 5.3 Hz, 1H, C*H*CF$_3$), 4.02 – 3.83 (m, 3H, PhC*H*$_2$ and NC*H*$_a$H$_b$C=C), 3.52 (dd, *J* = 15.8, 1.0 Hz, 1H, NCH$_a$*H*$_b$C=C), 2.35 (s, 3H, ArC*H*$_3$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 161.3 (d, *J* = 245.8 Hz), 148.25, 148.24, 137.0 (2C), 136.9, 134.8 (d, *J* = 3.2 Hz), 130.7, 130.6, 129.9, 129.5, 128.79, 128.76, 122.82 (d, *J* = 284.0 Hz), 114.9 (d, *J* = 21.2 Hz), 94.0 (q, *J* = 34.2 Hz), 60.5, 54.8, 21.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.4 (d, 3F, *J* = 5.3 Hz, CHC*F*$_3$), -116.2 (tt, 1F, *J* = 8.8, 5.5 Hz, Ar*F*).

IR (cm^{-1}) 2979 (m), 2908 (m), 1665 (w), 1508 (m), 1402 (m), 1229 (s), 1154 (s), 1066 (s).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{25}H_{22}F_4NO^+$ 428.1632; Found 428.1627.



10

(*S*,*Z*)-3-Benzyl-5-((4-chlorophenyl)(*p*-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (10)

Prepared according to the general procedure D1 using N-benzyl-3-(4-(chloro)phenyl)prop-2-yn-1-amine (102 mg, 0.400 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin **10** (159 mg, 0.360 mmol, 90% yield) as colorless oil. The enantiomeric excess was determined to be 90% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 6.9 min, τ_{Major} = 9.1 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = 34.7 (c = 0.38, $CHCl_3$, 90% ee).

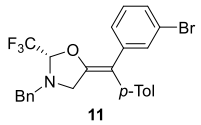
^{1}H NMR (400 MHz, Chloroform-d) δ 7.36 – 7.20 (m, 9H, Ar*H*), 7.14 (d, *J* = 7.9 Hz, 2H, Ar*H*), 7.01 (d, *J* = 7.9 Hz, 2H, Ar*H*), 5.14 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.03 – 3.81 (m, 3H, PhCH_2 and NC$H_a$$H_b$C=C), 3.52 (dd, *J* = 15.9, 0.9 Hz, 1H, NC$H_a$$H_b$C=C), 2.35 (s, 3H, ArC$H_3$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 148.9, 137.3, 137.0, 136.9, 136.7, 131.9, 130.3, 130.0, 129.6, 128.80, 128.76, 128.2, 128.1, 122.8 (q, *J* = 283.9 Hz), 111.8, 91.2 (q, *J* = 34.4 Hz), 60.5, 55.0, 21.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.4 (d, 3F, *J* = 5.3 Hz).

IR (cm^{-1}) 2928 (m), 2855 (m), 1664 (m), 1496 (m), 1292 (m), 1177 (s), 1154 (s), 1096 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{25}H_{22}ClF_3NO^+$ 444.1337; Found 444.1332.



11

(*S*,*Z*)-3-Benzyl-5-((3-bromophenyl)(*p*-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (11)

Prepared according to the general procedure D1 using N-benzyl-3-(3-bromophenyl)prop-2-yn-1-amine (120 mg, 0.400 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin **11** (149 mg, 0.304 mmol, 76% yield) as colorless oil. The enantiomeric excess was determined to be 82% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 8.4 min, τ_{Minor} = 10.4 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = 21.4 (c = 0.64, $CHCl_3$, 82% ee).

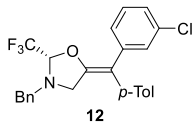
^{1}H NMR (400 MHz, Chloroform-d) δ 7.49 (t, *J* = 1.7 Hz, 1H, Ar*H*), 7.36 – 7.26 (m, 7H, Ar*H*), 7.17 - 7.09 (m, 3H, Ar*H*), 7.01 (d, *J* = 8.0 Hz, 2H, *o*-Me-Ar*H*), 5.15 (q, *J* = 5.3 Hz, 1H,C*H*CF_3), 4.01 – 3.81 (m, 3H, PhCH_2 and NC$H_a$$H_b$C=C), 3.50 (d, *J* = 16.1 Hz, 1H, NC$H_a$$H_b$C=C), 2.35 (s, 3H, ArC$H_3$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 149.5, 140.9, 137.1, 136.9, 136.4, 131.9, 130.0, 129.6, 129.5, 129.2, 128.81, 128.78, 128.1, 127.7, 122.7 (q, *J* = 284.1 Hz), 122.3, 111.6, 94.2 (q, *J* = 34.5 Hz), 60.6, 55.0, 21.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.3 (d, 3F, *J* = 5.3 Hz).

IR (cm^{-1}) 2927 (w), 2850 (w), 1664 (m), 1593 (m), 1480 (m), 1465 (m), 1292 (m), 1179 (s), 1154 (s), 1082 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{25}H_{22}{}^{79}BrF_3NO^+$ 488.0831; Found 488.0830.



12

(*S*,*Z*)-3-Benzyl-5-((3-chlorophenyl)(*p*-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (12)

Prepared according to the general procedure D1 using N-benzyl-3-(3-chlorophenyl)prop-2-yn-1-amine (102 mg, 0.400 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin **12** (168 mg, 0.380 mmol, 95% yield) as amorphous white solid. The enantiomeric excess was determined to be 84% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 8.2 min, τ_{Major} = 10.5 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = 33.0 (c = 0.48, $CHCl_3$, 84% ee).

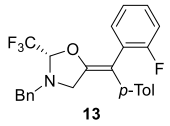
^{1}H NMR (400 MHz, Chloroform-d) δ 7.36 – 7.27 (m, 6H, Ar*H*), 7.25 – 7.16 (m, 2H, Ar*H*), 7.17 – 7.10 (m, 3H, Ar*H*), 7.04 – 6.97 (m, 2H, Ar*H*), 5.16 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.01 – 3.80 (m, 3H, PhCH_2 and NC$H_a$$H_b$C=C), 3.50 (dd, *J* = 16.0, 1.0 Hz, 1H, NC$H_a$$H_b$C=C), 2.35 (s, 3H, ArC$H_3$).

$^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-d) δ 149.4, 140.6, 137.1, 136.9, 136.4, 134.0, 130.0, 129.6, 129.2, 129.0, 128.80, 128.78, 128.1, 127.2, 126.3, 122.7 (q, *J* = 284.0 Hz), 111.7, 94.3 (q, *J* = 34.2 Hz), 60.6, 55.0, 21.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.3 (d, 3F, *J* = 5.3 Hz).

IR (cm^{-1}) 2842 (w), 1665 (m), 1589 (m), 1467 (w), 1293 (m), 1179 (s), 1154 (s), 1014 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{25}H_{22}ClF_3NO^+$ 444.1337; Found 444.1337.



13

(*S*,*Z*)-3-benzyl-5-((2-fluorophenyl)(p-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (13)

Prepared according to the general procedure D1 using N-benzyl-3-(2-fluorophenyl)prop-2-yn-1-amine (96 mg, 0.40 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin **13** (165 mg, 0.380 mmol, 97% yield) as amorphous white solid. The enantiomeric excess was determined to be 80% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 6.6 min, τ_{Minor} = 7.4 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = 6.2 (c = 0.54, $CHCl_3$, 80% ee).

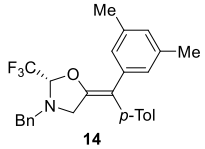
^{1}H NMR (400 MHz, Chloroform-d) δ 7.41 – 7.27 (m, 5H, Ar*H*), 7.26 – 7.16 (m, 2H, Ar*H*), 7.13 – 7.03 (m, 4H, Ar*H*), 7.04 – 6.94 (m, 2H, Ar*H*), 5.00 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.12 (dd, *J* = 15.6, 1.1 Hz, 1H, NC$H_a$$H_b$C=C), 3.99 (d, *J* = 13.3 Hz, 1H, PhC$H_a$$H_b$), 3.91 (d, *J* = 13.3 Hz, 1H, PhC$H_a$$H_b$), 3.72 (dd, *J* = 15.6, 1.3 Hz, 1H, NC$H_a$$H_b$C=C), 2.32 (s, 3H, ArC$H_3$).

$^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-d) δ 160.4 (d, *J* = 248.0 Hz), 149.5, 136.7 (d, *J* = 57.4 Hz), 136.6, 133.2 (d, *J* = 3.8 Hz), 129.2, 128.9, 128.82, 128.79, 128.6, 128.0, 126.6 (d, *J* = 15.8 Hz), 124.1, 123.91 (d, *J* = 3.5 Hz), 122.7 (q, *J* = 283.9 Hz), 115.8 (d, *J* = 22.5 Hz), 107.8, 93.2 (q, *J* = 34.3 Hz), 60.5, 54.0, 21.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.2 (d, 3F, *J* = 5.3 Hz, CHCF_3), -112.63 – -112.82 (m, 1F, Ar*F*).

IR (cm^{-1}) 2927 (w), 2858 (w), 1675 (m), 1492 (m), 1452 (m), 1294 (m), 1223 (m), 1176 (s), 1155 (s), 1021 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{25}H_{22}F_4NO^+$ 428.1632; Found 428.1640.



14

(*S*,*Z*)-3-Benzyl-5-((3,5-dimethylphenyl)(*p*-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (14)

Prepared according to the general procedure D1 using N-benzyl-3-(3,5-dimethylphenyl)prop-2-yn-1-amine (100 mg, 0.400 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin **14** (155 mg, 0.356 mmol, 89% yield) as colorless oil. The enantiomeric excess was determined to be 91% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 5.8 min, τ_{Major} = 7.2 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = 56.7 (c = 0.52, $CHCl_3$, 91% ee).

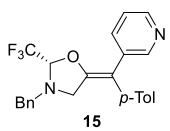
^{1}H NMR (400 MHz, Chloroform-d) δ 7.36 - 7.32 (m, 4H, Ar*H*), 7.32 – 7.27 (m, 1H, Ar*H*), 7.11 (d, *J* = 7.8 Hz, 2H, Ar*H*), 7.05 – 6.99 (m, 2H, Ar*H*), 6.96 (s, 2H, Ar*H*), 6.84 (s, 1H, Ar*H*), 5.09 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.04 – 3.81 (m, 3H, PhCH_2 and NC$H_a$$H_b$C=C), 3.53 (dd, *J* = 15.7, 0.9 Hz, 1H, NC$H_a$$H_b$C=C), 2.34 (s, 3H, ArC$H_3$), 2.26 (s, 6H, 2×ArC$H_3$).

$^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-d) δ 148.1, 138.7, 137.4 (2C), 137.2, 136.5, 129.9, 129.3, 128.8 (2C), 128.2, 128.0, 127.0, 122.9 (q, *J* = 284.1 Hz), 113.2, 93.8 (q, *J* = 34.2 Hz), 60.5, 54.8, 21.6, 21.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.3 (d, 3F, *J* = 5.3 Hz).

IR (cm^{-1}) 2925 (m), 2865 (w), 1664 (m), 1600 (m), 1506 (m), 1453 (m), 1295 (m), 1154 (s), 1077 (m).

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calculated for $C_{27}H_{26}F_3NNaO^+$ 460.1859; Found 460.1863.



15

(*S*,*Z*)-3-benzyl-5-(pyridin-3-yl(p-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (15)

Prepared according to the general procedure D1 using N-benzyl-3-(pyridin-3-yl)prop-2-yn-1-amine (89 mg, 0.40 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol,

1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 90:10 to 60:40) to give the corresponding olefin **15** (103 mg, 0.251 mmol, 63% yield) as orange oil. The enantiomeric excess was determined to be 52% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 90:10 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{minor} = 10.4 min, τ_{Major} = 11.2 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = 18.5 (c = 0.80, $CHCl_3$, 52% ee).

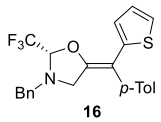
^{1}H NMR (400 MHz, Chloroform-d) δ 8.57 (br. s, 1H, HetAr*H*), 8.38 (br. s, 1H, HetAr*H*), 7.66 (dt, *J* = 8.1, 1.9 Hz, 1H, HetAr*H*), 7.37 – 7.25 (m, 5H, Ar*H*), 7.21 (dd, *J* = 8.1, 4.7 Hz, 1H, HetAr*H*), 7.15 (d, *J* = 7.8 Hz, 2H, Ar*H*), 7.06 – 6.99 (m, 2H, Ar*H*), 5.17 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.03 – 3.93 (m, 2H, NC$H_a$$H_b$C=C and PhC$H_a$$H_b$), 3.90 (d, *J* = 13.3 Hz, 1H, PhC$H_a$$H_b$), 3.54 (dd, *J* = 16.1, 1.4 Hz, 1H, NC$H_a$$H_b$C=C), 2.35 (s, 3H, ArC$H_3$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 150.6, 149.8, 146.6, 137.3, 136.8, 136.3, 135.7, 129.9, 129.7, 128.83, 128.78, 128.2, 126.4, 123.2, 122.7 (q, *J* = 283.9 Hz), 109.5, 94.3 (q, *J* = 34.5 Hz), 60.5, 54.9, 21.3.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.3 (d, 3F, *J* = 5.3 Hz).

IR (cm^{-1}) 3035 (m), 1664 (m), 1569 (m), 1515 (m), 1412 (m), 1292 (m), 1155 (s), 1076 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{24}H_{22}F_3N_2O^+$ 411.1679; Found 411.1679.



16

(*S*,*Z*)-3-Benzyl-5-(thiophen-2-yl(*p*-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (16)

Prepared according to the general procedure D1 using N-benzyl-3-(thiophen-2-yl)prop-2-yn-1-amine (91 mg, 0.40 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin **16** (142 mg, 0.340 mmol, 85% yield) as brown oil. The enantiomeric excess was determined to be 76% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 8.3 min, τ_{Major} = 13.9 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = 9.4 (c = 0.68, $CHCl_3$, 76% ee).

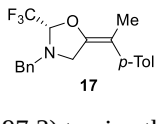
^{1}H NMR (400 MHz, Chloroform-d) δ 7.35 – 7.26 (m, 5H, Ar*H*), 7.24 – 7.13 (m, 5H, Ar*H*), 6.94 (dd, *J* = 5.1, 3.7 Hz, 1H, HetAr*H*), 6.79 (dd, *J* = 3.7, 1.0 Hz, 1H, HetAr*H*), 5.26 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.02 – 3.82 (m, 3H, PhCH_2 and NC$H_a$$H_b$C=C), 3.39 (dd, *J* = 16.1, 0.9 Hz, 1H, NC$H_a$$H_b$C=C), 2.38 (s, 3H, ArC$H_3$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 147.0, 142.2, 137.5, 137.0, 135.6, 130.2, 129.6, 128.8, 128.7, 128.0, 126.5, 125.3, 124.5, 122.7 (q, *J* = 283.7 Hz), 108.3, 94.7 (q, *J* = 34.5), 60.6, 54.6, 21.4.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.5 (d, 3F, *J* = 5.3 Hz).

IR (cm^{-1}) 2937 (m), 2834 (m), 1663 (m), 1512 (m), 1453 (m), 1294 (m), 1223 (s), 1170 (s), 1153 (s), 1077 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{23}H_{21}F_3NOS^+$ 416.1290; Found 416.1289.



17

(*S*,*E*)-3-Benzyl-5-(1-(*p*-tolyl)ethylidene)-2-(trifluoromethyl)oxazolidine (17)

Prepared according to the general procedure D1 using *N*-benzylbut-2-yn-1-amine (64 mg, 0.40 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin **17** (114 mg, 0.328 mmol, 82% yield) as amorphous white solid. The enantiomeric excess was determined to be 72% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 5.5 min, τ_{Major} = 6.4 min.. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = 27.5 (c = 0.54, $CHCl_3$, 72% ee)

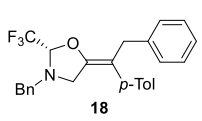
^{1}H NMR (400 MHz, Chloroform-d) δ 7.35 – 7.26 (m, 5H, Ar*H*), 7.10 (d, *J* = 8.0 Hz, 2H, *m*-Me-Ar*H*), 7.07 – 7.02 (m, 2H, *o*-Me-Ar*H*), 4.96 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 3.97 (d, *J* = 14.9 Hz, 1H, NC$H_a$$H_b$C=C), 3.92 (d, *J* = 13.3 Hz, 1H, PhC$H_a$$H_b$), 3.81 (d, *J* = 13.3 Hz, 1H, PhC$H_a$$H_b$), 3.45 (dt, *J* = 14.9, 1.3 Hz, 1H, NC$H_a$$H_b$C=C), 2.32 (s, 3H, ArC$H_3$), 2.07 (t, *J* = 1.7 Hz, 3H, C—CCH_3).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 146.9, 138.3, 137.3, 136.0, 129.1, 128.7 (2C), 127.9, 127.4, 123.0 (q, *J* = 283.9 Hz), 107.6, 94.6 (q, *J* = 34.0 Hz), 60.3, 53.3, 21.2, 16.6.

^{19}F NMR (376 MHz, Chloroform-*d*)) δ -80.6 (d, 3F, *J* = 5.3 Hz).

IR (cm^{-1}) 2979 (s), 2910 (m), 1689 (w), 1508 (w), 1451 (m), 1386 (m), 1292 (m), 1233 (m), 1157 (s), 1067 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{20}H_{21}F_3NO^+$ 348.1570; Found 348.1567.



18

(*S*,*E*)-3-Benzyl-5-(2-phenyl-1-(*p*-tolyl)ethylidene)-2-(trifluoromethyl)oxazolidine (18)

Prepared according to the general procedure D1 using *N*-benzyl-4-phenylbut-2-yn-1-amine (94 mg, 0.40 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin **18** (142 mg, 0.336 mmol, 84% yield) as amorphous white solid. The enantiomeric excess was determined to be 86% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 6.3 min, τ_{Major} = 6.9 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = 21.4 (c = 0.39, $CHCl_3$, 86% ee).

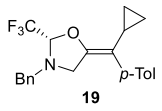
^{1}H NMR (400 MHz, Chloroform-d) δ 7.39 – 7.28 (m, 5H, Ar*H*), 7.25 – 7.18 (m, 2H, Ar*H*), 7.18 – 7.10 (m, 3H, Ar*H*), 7.03 (d, *J* = 8.0 Hz, 2H, *m*-Me-Ar*H*), 6.95 (d, *J* = 8.0 Hz, 2H, *o*-Me-Ar*H*), 5.02 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.03 – 3.94 (m, 2H, NC$H_a$$H_b$C=C and PhC*Ha*$H_b$N), 3.94 – 3.73 (m, 3H, PhCHaH_bN and C=CCH_2Ph), 3.47 (d, *J* = 15.2 Hz, 1H, NCHaH_bC=C), 2.28 (s, 3H, ArCH_3).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 148.0, 140.5, 137.2, 136.8, 136.2, 129.1, 128.74, 128.71, 128.6, 128.4, 128.3, 128.2, 127.9, 123.0 (q, *J* = 283.9 Hz), 111.4, 92.8 (q, *J* = 34.1 Hz), 60.4, 53.3, 37.2, 21.2.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.5 (d, 3F, *J* = 5.3 Hz).

IR (cm^{-1}) 2927 (m), 2851 (m), 1690 (m), 1504 (m), 1452 (m), 1293 (m), 1173 (s), 1154 (s), 1025 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{26}H_{25}F_3NO^+$ 424.1883; Found 424.1886.



19

(*S*,*E*)-3-Benzyl-5-(cyclopropyl(*p*-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (19)

Prepared according to the general procedure D1 using *N*-benzyl-3-cyclopropylprop-2-yn-1-amine (74 mg, 0.40 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin **19** (80 mg, 0.22 mmol, 54% yield) as amorphous white solid. The enantiomeric excess was determined to be 78% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 5.0 min, τ_{Major} = 5.8 min. $[\alpha]D^{20}$ = 22.6 (c = 0.53, $CHCl_3$, 78% ee). Absolute configuration determined in comparison to compound *(S)*-**4.**

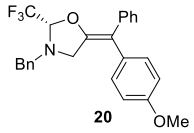
^{1}H NMR (400 MHz, Chloroform-d) δ 7.33 – 7.24 (m, 5H, Ar*H*), 7.07 (d, *J* = 7.9 Hz, 2H, Ar*H*), 6.95 (d, *J* = 7.9 Hz, 2H, Me-Ar*H*), 5.02 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 3.95 (d, *J* = 13.3 Hz, 1H, PhC$H_a$$H_b$), 3.81 (d, *J* = 13.3 Hz, 1H, PhC$H_a$$H_b$), 3.71 (d, *J* = 15.2 Hz, 1H, NC$H_a$$H_b$C=C), 3.21 (d, *J* = 15.2 Hz, 1H, NC$H_a$$H_b$C=C), 2.31 (s, 3H, ArC$H_3$), 2.01 – 1.88 (m, 1H, C*H*(CH_2)CH_2), 0.68 – 0.58 (m, 2H, CH(CH_2)CH_2), 0.37 – 0.18 (m, 2H, CH(CH_2)CH_2).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 147.6, 137.4, 136.5, 134.5, 129.7, 129.0, 128.69, 128.67, 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 -80.5 (d, 3F, *J* = 5.3 Hz).

IR (cm^{-1}) 3022 (w), 2946 (w), 2863 (w), 1665 (w), 1523 (w), 1425 (w), 1216 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{22}H_{23}F_3NO^+$ 374.1726; Found 374.1725.



20

(*S*,*E*)-3-Benzyl-5-((4-methoxyphenyl)(phenyl)methylene)-2-(trifluoromethyl)oxazolidine (20)

Prepared according to the general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 μL, 0.40 mmol, 1.0 equiv.) and 4-iodoanisole (122 mg, 0.520 mmol, 1.3 equiv). 2.5 mol% of $Pd_2(dba)_3$ • $CHCl_3$ (10.4 mg, 10.0 μmol) and 7 mol% of ligand (14.2 mg, 28.0 μmol) were used. The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:3) to give the corresponding olefin **20** (156 mg, 92% yield) as a white solid. The enantiomeric excess was determined to be 88% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 9.9 min, τ_{Major} = 14.7 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = +63.5 (c = 0.48, $CHCl_3$, 88% ee).

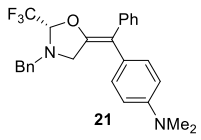
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.25 (m, 9H, Ar*H*), 7.22 – 7.15 (m, 1H, Ar*H*), 7.08 (d, *J* = 8.7 Hz, 2H, Ar*H*), 6.86 (d, *J* = 8.7 Hz, 2H, Ar*H*), 5.13 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.00 (d, *J* = 13.3 Hz, 1H, PhC$H_a$$H_b$), 3.96 – 3.85 (m, 2H, PhC$H_a$$H_b$ and NC$H_a$$H_b$C=C), 3.81 (s, 3H, OC$H_3$), 3.52 (dd, *J* = 15.6, 1.5 Hz, 1H, NC$H_a$$H_b$C=C).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 158.6, 148.4, 138.9, 137.1, 132.4, 131.3, 129.0, 128.77, 128.76, 128.0 (2C), 126.3, 122.9 (q, *J* = 284.0 Hz), 114.1, 112.5, 94.0 (q, *J* = 34.4 Hz), 60.5, 55.4, 54.9.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.3 (d, *J* = 4.9 Hz).

IR (cm^{-1}) 3032 (w), 2943 (w), 2841 (w), 1665 (m), 1606 (m), 1506 (m), 1453 (m), 1292 (m), 1246 (s), 1173 (s), 1153 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{25}H_{23}F_3NO_2^+$ 426.1675; Found 426.1678.



(*S*,*E*)-4-((3-Benzyl-2-(trifluoromethyl)oxazolidin-5-ylidene)(phenyl)methyl)-*N*,*N*-dimethylaniline (21)

Prepared according to the modified general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 μL, 0.40 mmol, 1.0 equiv.) and 4-iodo-N,N-dimethylaniline (128 mg, 0.520 mmol, 1.3 equiv). 2.5 mol% of $Pd_2(dba)_3$ • $CHCl_3$ (10.4 mg, 10.0 μmol) and 7 mol% of ligand (14.2 mg, 28.0 μmol) were used. The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:5) to give the corresponding olefin **21** (132 mg, 0.301 mmol, 75% yield) as a pale yellow solid. The enantiomeric excess was determined to be 94% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 9.9 min, τ_{Major} = 14.6 min.). Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = +79.1 (c = 0.64, $CHCl_3$, 94% ee

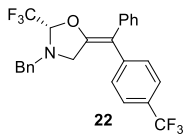
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.27 (m, 9H, Ar*H*), 7.20 – 7.14 (m, 1H, Ar*H*), 7.05 – 6.94 (m, 2H, Ar*H*), 6.73 – 6.64 (m, 2H, Ar*H*), 5.10 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.03 – 3.92 (m, 2H, PhC$H_a$$H_b$ and NC$H_a$$H_b$C=C), 3.89 (d, *J* = 13.4 Hz, 1H, PhC$H_a$$H_b$), 3.57 (dd, *J* = 15.7, 1.3 Hz, 1H, NC$H_a$$H_b$C=C), 2.96 (s, 6H, N($CH_3$)$_2$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) 149.4, 148.0, 139.3, 137.2, 130.9, 129.1, 128.8, 128.5, 128.00, 127.96, 126.2, 125.6, 122.9 (q, *J* = 284.2 Hz), 112.9, 112.5, 93.8 (q, *J* = 34.1 Hz), 60.5, 54.9, 40.6.

^{19}F{^{1}H}NMR (376 MHz, Chloroform-*d*) δ -80.3.

IR (cm^{-1}) 3030 (w), 2924 (w), 2855 (w), 2809 (w), 1662 (w), 1611 (m), 1522 (m), 1452 (w), 1351 (m), 1295 (m), 1223 (m), 1151 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{26}H_{26}F_3N_2O^+$ 439.1992; Found 439.1992.



(*S*,*E*)-3-Benzyl-5-(phenyl(4-(trifluoromethyl)phenyl)methylene)-2-(trifluoromethyl)oxazolidine (22)

Prepared according to the general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 μL, 0.40 mmol, 1.0 equiv.) and 4-iodobenzotrifluoride (76 μL, 0.52 mmol, 1.3 equiv). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:3) to give the corresponding olefin **22** (168 mg, 0.363 mmol, 91% yield) as a colorless oil. The enantiomeric excess was determined to be 82% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 10.7 min, τ_{Major} = 12.1 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = +47.8 (c = 0.77, $CHCl_3$, 82% ee).

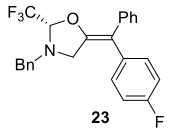
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.58 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.40 – 7.17 (m, 12H, Ar*H*), 5.16 (q, *J* = 5.2 Hz, 1H, C*H*CF_3), 4.01 (d, *J* = 13.3 Hz, 1H, PhC$H_a$$H_b$), 3.99 – 3.93 (m, 1H, NC$H_a$$H_b$C=C), 3.91 (d, *J* = 13.3 Hz, 1H, PhC$H_a$$H_b$), 3.54 (dd, *J* = 15.8, 1.4 Hz, 1H, NC$H_a$$H_b$C=C).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 149.4, 144.0, 138.0, 136.7, 130.4, 129.3 (q, *J* = 32.2 Hz), 129.2, 128.9, 128.8, 128.3, 128.2, 126.8, 125.7 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 275.6 Hz) 122.73 (q, *J* = 283.9 Hz), 112.2, 94.1 (q, *J* = 34.5 Hz), 60.5, 54.8.

^{19}F{^{1}H} NMR (377 MHz, Chloroform-*d*) δ -62.5, -80.3.

IR (cm^{-1}) 3042 (w), 2929 (w), 1664 (m), 1610 (w), 1404 (w), 1328 (s), 1293 (m), 1158 (s), 1130 (s), 1073 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{25}H_{20}F_6NO^+$ 464.1444; Found 464.1447.



(*S*,*E*)-3-Benzyl-5-((4-fluorophenyl)(phenyl)methylene)-2-(trifluoromethyl)oxazolidine (23)

Prepared according to the general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 μL, 0.40 mmol, 1.0 equiv.) and 4-fluoroiodobenzene (60 μL, 0.52 mmol, 1.3 equiv). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:3) to give the corresponding olefin **23** (154 mg, 0.373 mmol, 93% yield) as a colorless oil. The enantiomeric excess was determined to be 84% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 10.0 min, τ_{Major} = 11.9 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = +45.5 (c = 0.41, $CHCl_3$, 84% ee).

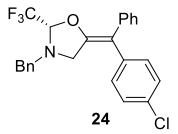
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.25 (m, 9H, Ar*H*), 7.24 – 7.17 (m, 1H, Ar*H*), 7.16 – 7.10 (m, 2H, Ar*H*), 7.02 (td, *J* = 8.3, 1.5 Hz, 2H, Ar*H*), 5.18 – 5.12 (m, 1H, C*H*CF_3), 4.00 (d, *J* = 13.4 Hz, 1H, PhCH_aH_b), 3.95 – 3.85 (m, 2H, PhCH_aH_b and NCH_aH_bC=C), 3.49 (d, *J* = 15.4 Hz, 1H, NCH_aH_bC=C).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 162.0 (d, *J* = 246.3 Hz), 148.8, 138.4, 136.9, 136.0 (d, *J* = 3.4 Hz), 131.8 (d, *J* = 8.0 Hz), 128.9, 128.82, 128.76, 128.14, 128.12, 126.5, 122.8 (q, *J* = 283.9 Hz), 115.7 (d, *J* = 21.3 Hz), 112.0, 94.1 (q, *J* = 34.4 Hz), 60.5, 54.9.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.3 (d, *J* = 4.2 Hz), -115.2.

IR (cm^{-1}) 3034 (w), 2929 (w), 2103 (w), 1665 (m), 1602 (m), 1503 (m), 1293 (m), 1226 (m), 1176 (s), 1153 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{24}H_{20}F_4NO^+$ 414.1476; Found 414.1476.



(*S*,*E*)-3-Benzyl-5-((4-chlorophenyl)(phenyl)methylene)-2-(trifluoromethyl)oxazolidine (24)

Prepared according to the general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 μL, 0.40 mmol, 1.0 equiv.) and 1-chloro-4-iodobenzene (124 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:3) to give the corresponding olefin **24** (128 mg, 0.298 mmol, 74% yield) as a pale yellow oil. The enantiomeric excess was determined to be 81% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 10.4 min, τ_{Major} = 11.9 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = +55.1 (c = 0.49, $CHCl_3$, 81% ee).

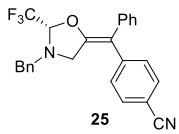
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.26 (m, 11H, Ar*H*), 7.23 – 7.17 (m, 1H, Ar*H*), 7.09 (d, *J* = 8.4 Hz, 2H, Ar*H*), 5.14 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 4.00 (d, *J* = 13.3 Hz, 1H, PhCH_aH_b), 3.96 – 3.85 (m, 2H, PhCH_aH_b and NCH_aH_bC=C), 3.51 (dd, *J* = 15.8, 1.5 Hz, 1H, NCH_aH_bC=C).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 148.9, 138.6, 138.2, 136.8, 133.0, 131.5, 129.03, 128.97, 128.84, 128.75, 128.18, 128.15, 126.6, 122.8 (q, *J* = 283.8 Hz), 112.0, 94.1 (q, *J* = 34.5 Hz), 60.5, 54.8.

^{19}F{^{1}H} NMR (376 MHz, Chloroform-*d*) δ -80.3.

IR (cm^{-1}) 3062 (w), 3032 (w), 2845 (w), 1664 (m), 1598 (w), 1494 (m), 1293 (m), 1176 (s), 1153 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{24}H_{20}ClF_3NO^+$ 430.1180; Found 430.1182.



(*S*,*E*)-4-((3-Benzyl-2-(trifluoromethyl)oxazolidin-5-ylidene)(phenyl)methyl)benzonitrile (25)

Prepared according to the general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 μL, 0.40 mmol, 1.0 equiv.) and 4-iodobenzonitrile (119 mg, 0.520 mmol, 1.3 equiv). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:10) to give the corresponding olefin **25** (152 mg, 0.362 mmol, 90% yield) as a white foam. The enantiomeric excess was determined to be 74% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Major} = 6.8 min, τ_{Minor} = 7.5 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = +50.3 (c = 0.52, $CHCl_3$, 74% ee).

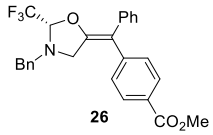
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.60 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.38 – 7.21 (m, 12H, Ar*H*), 5.16 (q, *J* = 5.1 Hz, 1H, C*H*CF$_3$), 4.02 (d, *J* = 13.3 Hz, 1H, PhC*H*$_a$H$_b$), 3.97 (d, *J* = 15.9 Hz, 1H, NC*H*$_a$H$_b$C=C), 3.90 (d, *J* = 13.3 Hz, 1H, PhCH$_a$*H*$_b$), 3.55 (d, *J* = 15.9, 1H, NCH$_a$*H*$_b$C=C).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 149.9, 145.3, 137.6, 136.6, 132.5, 130.6, 129.3, 128.9, 128.7, 128.4, 128.3, 127.1, 122.7 (q, *J* = 283.9 Hz), 118.9, 112.3, 110.7, 94.1 (q, *J* = 34.6 Hz) 60.4, 54.7.

^{19}F{^{1}H} NMR (376 MHz, Chloroform-*d*) δ -80.3.

IR (cm^{-1}) 3032 (w), 2928 (w), 2228 (m), 1663 (m), 1603 (m), 1501 (m), 1293 (m), 1178 (s), 1154 (s).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{25}H_{20}F_3N_2O^+$ 421.1522; Found 421.1529.



(*S*,*E*)-Methyl-4-((3-benzyl-2-(trifluoromethyl)oxazolidin-5-ylidene)(phenyl)methyl)benzoate (26)

Prepared according to the general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 μL, 0.40 mmol, 1.0 equiv.) and methyl 4-iodobenzoate (136 mg, 0.520 mmol, 1.3 equiv). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:10) to give the corresponding olefin **26** (175 mg, 0.386 mmol, 96% yield) as a white foam. The enantiomeric excess was determined to be 82% by HPLC analysis on a Daicel IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Major} = 6.2 min, τ_{Minor} = 7.1 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

[α]D^{20} = +49.8 (c = 0.76, $CHCl_3$, 82% ee).

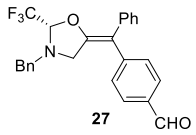
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.98 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.37 – 7.27 (m, 9H, Ar*H*), 7.21 (d, *J* = 8.4 Hz, 3H, Ar*H*), 5.15 (q, *J* = 5.2 Hz, 1H, C*H*CF$_3$), 4.00 (d, *J* = 13.3 Hz, 1H, PhC*H*$_a$H$_b$), 3.95 (d, *J* = 15.8, 1H, NC*H*$_a$H$_b$C=C), 3.91 (m, 4H, OC*H*$_3$ and PhCH$_a$*H*$_b$), 3.55 (dd, *J* = 15.8, 1.3 Hz, 1H, NCH$_a$*H*$_b$C=C).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 167.0, 149.3, 145.2, 138.0, 136.8, 130.1, 130.0, 129.2, 128.85, 128.79, 128.76, 128.22, 128.17, 126.8, 122.70 (q, *J* = 284.1 Hz), 112.7, 94.1 (q, *J* = 34.5 Hz), 60.5, 54.8, 52.3.

^{19}F{^{1}H} NMR (376 MHz, Chloroform-*d*) δ -80.3.

IR (cm^{-1}) 3029 (w), 2951 (w), 1721 (s), 1664 (m), 1604 (m), 1444 (m), 1284 (s), 1181 (s), 1153 (s), 1112 (m).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{26}H_{23}F_3NO_3^+$ 454.1625; Found 454.1624.



(*S*,*E*)-4-((3-Benzyl-2-(trifluoromethyl)oxazolidin-5-ylidene)(phenyl)methyl)benzaldehyde (27)

Prepared according to the general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 μL, 0.40 mmol, 1.0 equiv.) and 4-iodobenzaldehyde (121 mg, 0.520 mmol, 1.3 equiv). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:10) to give the corresponding olefin **27** (150 mg, 0.354 mmol, 89% yield) as a white foam. The enantiomeric excess was determined to be 80% by HPLC analysis on a Daicel IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Major} = 6.8 min, τ_{Minor} = 7.5 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

[α]D^{20} = +66.3 (c = 0.45, $CHCl_3$, 80% ee).

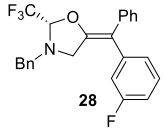
^{1}H NMR (400 MHz, Chloroform-*d*) δ 10.00 (s, 1H, C*H*O), 7.83 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.49 – 7.07 (m, 12H, Ar*H*), 5.16 (q, *J* = 5.2 Hz, 1H, C*H*CF$_3$), 4.09 – 3.94 (m, 2H, PhC*H*$_a$H$_b$ and NC*H*$_a$H$_b$C=C), 3.91 (d, *J* = 13.3 Hz, 1H, PhCH$_a$*H*$_b$), 3.59 (dd, *J* = 15.8, 1.4 Hz, 1H, NCH$_a$*H*$_b$C=C).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 191.8, 149.7, 146.9, 137.9, 136.7, 135.0, 130.6, 130.1, 129.3, 128.9, 128.8, 128.3, 128.2, 126.9, 122.7 (q, *J* = 285.6 Hz), 112.8, 94.0 (q, *J* = 34.5 Hz), 60.5, 54.7.

^{19}F{^{1}H} NMR (376 MHz, Chloroform-*d*) δ -80.3.

IR (cm^{-1}) 3031 (w), 2840 (w), 1700 (s), 1663 (m), 1602 (m), 1295 (m), 1174 (s), 1156 (s).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{25}H_{21}F_3NO_2^+$ 424.1519; Found 424.1522.



(*S*,*E*)-3-Benzyl-5-((3-fluorophenyl)(phenyl)methylene)-2-(trifluoromethyl)oxazolidine (28)

Prepared according to the general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 μL, 0.40 mmol, 1.0 equiv.) and 1-fluoro-3-iodobenzene (60 μL, 0.52 mmol,

1.3 equiv). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:3) to give the corresponding olefin **28** (158 mg, 0.382 mmol, 96% yield) as a colorless oil. The enantiomeric excess was determined to be 82% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 8.5 min, τ_{Major} = 10.5 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = +47.3 (c = 0.69, $CHCl_3$, 82% ee).

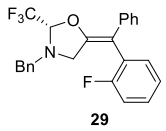
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.41 – 7.26 (m, 10H, Ar*H*), 7.24 – 7.17 (m, 1H, Ar*H*), 7.02 – 6.91 (m, 2H, Ar*H*), 6.86 (ddd, *J* = 9.8, 2.5, 1.6 Hz, 1H, Ar*H*), 5.15 (q, *J* = 5.2 Hz, 1H, C*H*CF_3), 4.00 (d, *J* = 13.3 Hz, 1H, PhCH_aH_b), 3.95 (d, *J* = 16.0 Hz, 1H, NCH_aH_bC=C), 3.90 (d, *J* = 13.3 Hz, 1H, PhCH_aH_b), 3.55 (dt, *J* = 16.0, 1.4 Hz, 1H, NCH_aH_bC=C).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 163.0 (d, *J* = 246.6 Hz), 149.1, 142.4 (d, *J* = 7.8 Hz), 138.1, 136.8, 130.2 (d, *J* = 8.5 Hz), 129.0, 128.83, 128.78, 128.19, 128.14, 126.7, 125.87 (d, *J* = 2.9 Hz), 122.8 (q, *J* = 283.8 Hz), 117.1 (d, *J* = 21.0 Hz), 114.1 (d, *J* = 21.0 Hz), 112.2 (d, *J* = 2.0 Hz), 94.1 (q, *J* = 34.4 Hz), 60.5, 54.8.

^{19}F{^{1}H} NMR (376 MHz, Chloroform-*d*) δ -80.3, -112.9.

IR (cm^{-1}) 3060 (w), 3033 (w), 2935 (w), 2102 (w), 1665 (m), 1604 (m), 1588 (m), 1489 (m), 1446 (m), 1293 (m), 1228 (m), 1175 (s), 1151 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{24}H_{20}F_4NO^+$ 414.1476; Found 414.1480.



29

(*S*,*E*)-3-Benzyl-5-((2-fluorophenyl)(phenyl)methylene)-2-(trifluoromethyl)oxazolidine (29)

Prepared according to the general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 μL, 0.40 mmol, 1.0 equiv.) and 2-iodofluorobenzene (61 μL, 0.52 mmol, 1.3 equiv). The reaction was conducted at 60 °C using 1,2-dichloroethane as the solvent. The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:3) to give the corresponding olefin **29** which was further purified using a chiral preparative HPLC (103 mg, 0.249 mmol, 62% yield) as a colorless oil (Chiral prep method: Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 15 mL/min). The enantiomeric excess was determined to be 74% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 7.3 min, τ_{Major} = 8.5 min. The e.e. was no affected by the preparative chiral HPLC purification. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = +60.9 (c = 0.32, $CHCl_3$, 74% ee).

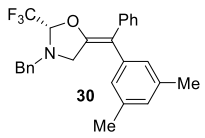
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.43 – 7.26 (m, 10H, Ar*H*), 7.21 – 7.06 (m, 4H, Ar*H*), 5.19 (q, *J* = 5.4 Hz, 1H, C*H*CF_3), 3.98 (d, *J* = 13.2 Hz, 1H, PhCH_aH_b), 3.90 (d, *J* = 13.3 Hz, 1H, PhCH_aH_b), 3.85 (d, *J* = 16.1 Hz, 1H, NCH_aH_bC=C), 3.43 (dd, *J* = 16.0, 1.4 Hz, 1H, NCH_aH_bC=C).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 160.5 (d, *J* = 246.1 Hz), 149.8, 137.7, 137.0, 132.9 (d, *J* = 3.2 Hz), 129.5 (d, *J* = 8.0 Hz), 128.9, 128.8, 128.4, 128.2, 128.1, 127.1 (d, *J* = 16.4 Hz), 126.5, 124.6 (d, *J* = 3.6 Hz), 122.74 (q, *J* = 283.8 Hz), 116.2 (d, *J* = 22.5 Hz), 106.0, 94.8 (q, *J* = 34.5 Hz), 60.7, 55.1.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.3 (d, *J* = 5.4 Hz), -113.7 – -115.9 (m).

IR (cm^{-1}) 3064 (w), 3031 (w), 1668 (m), 1491 (m), 1451 (m), 1294 (m), 1179 (s), 1155 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{24}H_{20}F_4NO^+$ 414.1476; Found 414.1482.



30

(*S*,*E*)-3-Benzyl-5-((3,5-dimethylphenyl)(phenyl)methylene)-2-(trifluoromethyl)oxazolidine (30)

Prepared according to the general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 μL, 0.40 mmol, 1.0 equiv.) and 1-iodo-3,5-dimethylbenzene (121 mg, 0.520 mmol, 1.3 equiv). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:3) to give the corresponding olefin **30** (162 mg, 0.383 mmol, 96% yield) as a colorless oil. The enantiomeric excess was determined to be 92% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 5.0 min, τ_{Major} = 6.2 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = +53.5 (c = 0.57, $CHCl_3$, 92% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.42 – 7.26 (m, 9H, Ar*H*), 7.22 – 7.14 (m, 1H, Ar*H*), 6.90 (s, 1H, Ar*H*), 6.78 (d, *J* = 1.6 Hz, 2H, Ar*H*), 5.13 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 3.99 (d, *J* = 13.3 Hz, 1H, PhCH_aH_b),

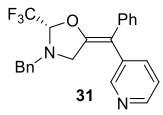
3.95 – 3.86 (m, 2H, PhCH$_a$H$_b$ and NCH$_a$H$_b$C=C), 3.53 (dd, *J* = 15.9, 1.5 Hz, 1H, NCH$_a$H$_b$C=C), 2.28 (s, 6H, 2 × ArCH$_3$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 148.4, 140.0, 138.8, 138.1, 137.1, 129.03, 128.83, 128.75 (2C), 128.03 (2C), 127.97, 126.3, 122.8 (q, *J* = 283.9 Hz), 113.1, 94.2 (q, *J* = 34.2 Hz), 60.6, 54.8, 21.4.

^{19}F{^{1}H} NMR (376 MHz, Chloroform-*d*) δ -80.3.

IR (cm^{-1}) 3028 (w), 2925 (w), 2862 (w), 1665 (m), 1600 (w), 1491 (w), 1453 (w), 1294 (m), 1174 (s), 1152 (s).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{26}H_{25}F_3NO^+$ 424.1883; Found 424.1885.



31

(*S*,*E*)-3-Benzyl-5-(phenyl(pyridin-3-yl)methylene)-2-(trifluoromethyl)oxazolidine (31)

Prepared according to the general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 µL, 0.40 mmol, 1.0 equiv.) and 3-iodopyridine (107 mg, 0.520 mmol, 1.3 equiv). The reaction was conducted at 60 °C using 1,2-dichloroethane as the solvent. The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 50:50) to give the corresponding olefin **31** (122 mg, 0.308 mmol, 77% yield) as an orange solid. The enantiomeric excess was determined to be 80% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 90:10 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 10.6 min, τ_{Major} = 19.8 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

[α]D^{20} = +47.3 (c = 0.55, $CHCl_3$, 80% ee).

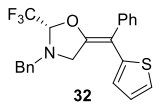
^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.49 (m, 2H, Ar*H*), 7.45 (dt, *J* = 7.9, 1.9 Hz, 1H, Ar*H*), 7.39 – 7.12 (m, 11H, Ar*H*), 5.17 (q, *J* = 5.2 Hz, 1H, C*H*CF$_3$), 4.01 (d, *J* = 13.3 Hz, 1H, PhCH$_a$H$_b$), 3.97 – 3.85 (m, 2H, PhCH$_a$H$_b$ and NCH$_a$H$_b$C=C), 3.55 (dd, *J* = 15.7, 1.4 Hz, 1H, NCH$_a$H$_b$C=C).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 150.8, 149.7, 148.4, 137.8, 137.7, 136.7, 136.0, 129.1, 128.9, 128.8, 128.3, 128.2, 126.8, 123.7, 122.7 (q, *J* = 283.8 Hz), 109.8, 94.2 (q, *J* = 34.5 Hz), 60.5, 54.8.

^{19}F{^{1}H} NMR (376 MHz, Chloroform-*d*) δ -80.3.

IR (cm^{-1}) 3345 (w), 3033 (w), 2970 (w), 1663 (m), 1488 (w), 1451 (w), 1409 (w), 1292 (m), 1173 (s), 1152 (s).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{23}H_{20}F_3N_2O^+$ 397.1522; Found 397.1524.



32

(*S*,*E*)-3-Benzyl-5-(phenyl(thiophen-2-yl)methylene)-2-(trifluoromethyl)oxazolidine (32)

Prepared according to the general procedure D1 using N-benzyl-3-phenylprop-2-yn-1-amine (76 µL, 0.40 mmol, 1.0 equiv.) and 2-iodothiophene (57 µL, 0.52 mmol, 1.3 equiv). The reaction was conducted at 60 C using DCE as the solvent. The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:3) to give the corresponding olefin **32** (154 mg, 0.384 mmol, 96% yield) as a brown solid. The enantiomeric excess was determined to be 87% by HPLC analysis on a Daicel IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 9.1 min, τ_{Major} = 10.2 min.). Absolute configuration determined in comparison to compound *(S)*-**4.**

[α]D^{20} = +46.9 (c = 0.65, $CHCl_3$, 87% ee

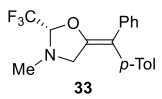
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.44 – 7.29 (m, 9H, Ar*H*), 7.28 – 7.23 (m, 2H, Ar*H*), 6.97 (dd, *J* = 5.2, 3.5 Hz, 1H, Ar*H*), 6.76 (dd, *J* = 3.6, 1.2 Hz, 1H, Ar*H*), 5.11 (q, *J* = 5.3 Hz, 1H, C*H*CF$_3$), 4.12 (dd, *J* = 16.1, 1.0 Hz, 1H, NCH$_a$H$_b$C=C), 4.01 (d, *J* = 13.3 Hz, 1H, PhCH$_a$H$_b$), 3.94 (d, *J* = 13.3 Hz, 1H, PhCH$_a$H$_b$), 3.80 (dd, *J* = 16.1, 1.4 Hz, 1H, NCH$_a$H$_b$C=C).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 149.8, 142.3, 138.3, 136.9, 129.1, 128.8, 128.2 (2C), 128.1, 127.1, 126.98, 126.91, 125.1, 122.7 (q, *J* = 283.6 Hz), 107.1, 94.1 (q, *J* = 34.5 Hz), 60.7, 55.2.

^{19}F{^{1}H} NMR (376 MHz, Chloroform-*d*) δ -80.4.

IR (cm^{-1}) 3064 (w), 3031 (w), 2935 (w), 2848 (w), 1658 (m), 1493 (w), 1449 (w), 1293 (m), 1226 (m), 1175 (s), 1150 (s).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{22}H_{19}F_3NOS^+$ 402.1134; Found 402.1134.



33

(*S*,*E*)-3-Methyl-5-(phenyl(p-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (33)

Prepared according to the general procedure D1 using *N*-methyl-3-phenylprop-2-yn-1-amine (58 mg, 0.40 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin **33** (74 mg, 0.22 mmol, 55% yield) as colorless oil. The enantiomeric excess was determined to be 92% by HPLC analysis on a Daicel Chiralpak IA column: 99.75:0.25 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 5.1 min, τ_{Major} = 5.4 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = 30.0 (c = 0.50, $CHCl_3$, 92% ee).

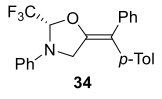
^{1}H NMR (400 MHz, Chloroform-d) δ 7.41 – 7.34 (m, 2H, Ar*H*), 7.32 – 7.26 (m, 2H, Ar*H*), 7.21 – 7.12 (m, 3H, Ar*H*), 7.09 – 7.01 (m, 2H, Ar*H*), 4.90 (q, *J* = 5.0 Hz, 1H, C*H*CF_3), 3.93 (d, *J* = 15.1 Hz, 1H, NC$H_a$$H_b$C=C), 3.43 (d, *J* = 15.1 Hz, 1H, NC$H_a$$H_b$C=C), 2.60 (s, 3H, NC$H_3$), 2.37 (s, 3H, ArC$H_3$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 148.2, 138.6, 137.2, 136.8, 130.0, 129.4, 129.1, 128.1, 126.4, 122.8 (q, *J* = 283.4 Hz), 113.0, 95.7 (q, *J* = 34.2 Hz), 56.8, 43.4, 21.3.

^{19}F NMR (376 MHz, Chloroform-d) δ -80.8 (d, *J* = 4.8 Hz).

IR (cm^{-1}) 2910 (w), 1660 (m), 1605 (m), 1451 (m), 1401 (m), 1284 (s), 1155 (s), 1064 (s).

HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{19}H_{19}F_3NO^+$ 334.1413; Found 334.1410.



34

(*S*,*E*)-3-Phenyl-5-(phenyl(p-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (34)

Prepared according to the general procedure D1 using *N*-(3-phenylprop-2-yn-1-yl)aniline (83 mg, 0.40 mmol, 1.0 equiv.) and *p*-iodotoluene (113 mg, 0.520 mmol, 1.3 equiv.). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding olefin **34** (91 mg, 0.23 mmol, 58% yield) as amorphous white solid. The enantiomeric excess was determined to be 54% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 6.2 min, τ_{Minor} = 11.6 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = 68.0 (c = 0.69, $CHCl_3$, 54% ee).

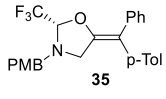
^{1}H NMR (400 MHz, Chloroform-d) δ 7.42 – 7.36 (m, 2H, Ar*H*), 7.34 – 7.27 (m, 4H, Ar*H*), 7.25 – 7.17 (m, 3H, Ar*H*), 7.17 – 7.10 (m, 2H, Ar*H*), 6.97 – 6.89 (m, 1H, Ar*H*), 6.79 – 6.67 (m, 2H, Ar*H*), 5.90 (q, *J* = 4.1 Hz, 1H, C*H*CF_3), 4.35 (d, *J* = 14.0 Hz, 1H, NC$H_a$$H_b$C=C), 4.21 (d, *J* = 14.0 Hz, 1H, NC$H_a$$H_b$C=C), 2.41 (s, 3H, ArC$H_3$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-d) δ 147.1, 144.6, 138.2, 137.2, 136.6, 123.0, 129.64, 129.62, 129.1, 128.2, 126.7, 123.3 (q, *J* = 287.4 Hz), 120.4, 114.0, 113.7, 88.2 (q, *J* = 35.4 Hz), 50.2, 21.4.

^{19}F NMR (376 MHz, Chloroform-d) δ -80.5 (d, *J* = 4.1 Hz).

IR (cm^{-1}) 3051 (m), 2926 (w), 1674 (m), 1602 (m), 1503 (s), 1358 (m), 1317 (m), 1183 (s), 1155 (s), 1077 (m).

HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{24}H_{21}F_3NO^+$ 396.1570; Found 396.1562.



35

(*S*,*E*)-3-(4-Methoxybenzyl)-5-(phenyl(p-tolyl)methylene)-2-(trifluoromethyl)oxazolidine (35)

Prepared according to the general procedure D1 using N-(4-methoxybenzyl)-3-phenylprop-2-yn-1-amine (101 mg, 0.400 mmol, 1.0 equiv.) and 1-iodo-4-methylbenzene (113 mg, 0.520 mmol, 1.3 equiv)**.** The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 100:3) to give the corresponding olefin **35** (92 mg, 0.21 mmol, 52% yield) as a colorless oil. The enantiomeric excess was determined to be 89% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Minor} = 9.4 min, τ_{Major} = 13.1 min. Absolute configuration determined in comparison to compound *(S)*-**4.**

$[\alpha]D^{20}$ = +55.0 (c = 0.60, $CHCl_3$, 89% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.40 – 7.34 (m, 2H, Ar*H*), 7.32 – 7.22 (m, 4H, Ar*H*), 7.21 – 7.09 (m, 3H), 7.07 – 7.00 (m, 2H, Ar*H*), 6.90 – 6.83 (m, 2H, Ar*H*), 5.11 (q, *J* = 5.4 Hz, 1H, C*H*CF_3), 3.94 – 3.81 (m, 3H, ArCH_2 and NC$H_a$$H_b$C=C), 3.80 (s, 3H, OC$H_3$), 3.53 (dd, *J* = 15.9, 1.4 Hz, 1H, NC$H_a$$H_b$C=C), 2.35 (s, 3H, ArC$H_3$).

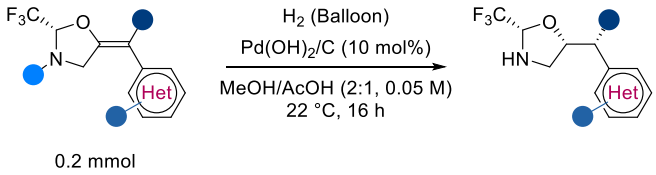
$^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 159.4, 148.5, 138.8, 137.2, 136.7, 130.09, 130.05, 129.4, 129.06, 129.04, 128.0, 126.3, 122.9 (q, *J* = 284.1 Hz), 114.12, 112.8, 93.8 (q, *J* = 34.2 Hz), 59.9, 55.4, 54.8, 21.3.

$^{19}F\{^{1}H\}$ NMR (376 MHz, Chloroform-*d*) δ -80.3.

IR (cm^{-1}) 3024 (w), 2931 (w), 2844 (w), 1665 (m), 1609 (m), 1514 (m), 1454 (m), 1295 (m), 1250 (s), 1175 (s), 1153 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{26}H_{25}F_3NO_2^+$ 440.1832; Found 440.1842.

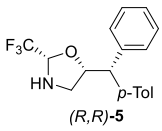
D.3. General Procedure for the Asymmetric Hydrogenation of the Tetrasubstituted Olefins.



Scheme 14. Palladium-catalyzed asymmetric hydrogenation of tetrasubstituted olefins.

An oven-dried 25 mL round-bottom flask equipped with a Teflon coated stirring bar was charged with $Pd(OH)_2/C$ (10 mol%, 14 mg) and the tetrasubstituted olefin (0.20 mmol). The flask was sealed and evacuated and back-filled with N_2 three times. MeOH (2.7 mL) and AcOH (1.3 mL) were added and the suspension was stirred at room temperature for 10 minutes under a nitrogen flow. Then, a hydrogen balloon was connected to the flask through a needle and the mixture was vigorously stirred at room temperature for 16 hours. Then, the reaction mixture was degassed by bubbling nitrogen for 10 minutes and filtered through a plug of celite eluting with 10 mL of MeOH. The crude extract was washed with saturated $NaHCO_3$ and extracted with DCM (3 x 25 mL). The combined organic layer was dried over sodium sulfate, filtered and concentrated in vacuum. The crude material was purified by flash column chromatography on silica gel to afford the corresponding product as a single diastereoisomer.

D.4. Characterization of Hydrogenated Products



(R,R)-**5**

(2*S*,5*R*)-5-((*R*)-Phenyl(p-tolyl)methyl)-2-(trifluoromethyl)oxazolidine ((*R*,*R*)-5)

Prepared according to the general procedure D5 using *(S)*-**4** (82 mg, 0.20 mmol, 1.0 equiv., 94% ee) and $Pd(OH)_2/C$ (10 mol%, 14 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product *(R,R)*-**5** (51 mg, 0.16 mmol, 79% yield) as a pale yellow solid (m.p. 72 °C).. The enantiomeric excess was determined to be 94% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 8.2 min, τ_{Minor} = 12.5 min. Absolute and relative configuration were determined by X-Ray diffraction analysis of a single crystal of *(R,R)*-**5** (Details in section F)

$[\alpha]D^{20}$ = +6.9 (c = 0.36, $CHCl_3$, 94% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.18 (m, 7H, Ar*H*), 7.12 (d, *J* = 7.9 Hz, 2H, Ar*H*), 4.97 (dq, *J* = 8.2, 5.6 Hz, 1H, C*H*CF_3), 4.62 (td, *J* = 9.4, 5.5 Hz, 1H, OC*H*), 3.97 (d, *J* = 9.5 Hz, 1H, Ar^{1}Ar^{2}C*H*), 3.15 (dt, *J* = 12.3, 6.2 Hz, 1H, NCH_aH$_b$), 2.80 (q, *J* = 11.0 Hz, 1H, NC$H_a$$H_b$), 2.72 – 2.58 (br. s., 1H, N*H*), 2.31 (s, 3H, CH_3).

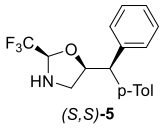
^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 141.5, 139.2, 136.3, 129.3, 128.9, 128.3, 128.2, 127.1, 123.4 (q, *J* = 282.9 Hz), 88.4 (q, *J* = 33.9 Hz), 82.2, 55.3, 50.7, 21.2.

^{19}F{^{1}H} NMR (376 MHz, Chloroform-*d*) δ -81.0.

IR (cm^{-1}) 3351 (w), 3024 (w), 2925 (m), 2861 (w), 1523 (w), 1454 (w), 1290 (m), 1166 (s), 1150 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{18}H_{19}F_3NO^+$ 322.1413; Found 322.1413.

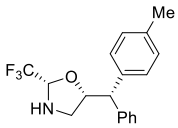
1.2 mmol scale reduction. The model reduction was repeated on 1.2 mmol scale. An oven dried 50 mL round-bottom flask equipped with a Teflon stir bar was charged with $Pd(OH)_2/C$ (10 mol%, 86 mg, 0.12 mmol) and olefin *(S)*-**4** (500 mg, 1.22 mmol, 1.0 equiv.). MeOH (16 mL) and AcOH (8 mL) were added and the suspension was stirred at 22 °C for 10 minutes under a nitrogen flow. Then, a hydrogen balloon was connected to the flask through a needle and the mixture was vigorously stirred at 22 °C for 16 hours. Then, the reaction mixture was degassed by bubbling nitrogen for 10 minutes and filtered through a plug of celite eluting with 20 mL of MeOH. The crude extract was washed with saturated $NaHCO_3$ and extracted with DCM (3×50 mL). The combined organic layer was dried over sodium sulfate, filtered and concentrated *in vacuo*. The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product *(R,R)*-**5** (284 mg, 0.884 mmol, 72% yield) as a colorless oil, which solidified upon vigorous scratching with a spatula. The enantiomeric excess was determined to be 94% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 8.2 min, τ_{Minor} = 12.6 min.



(S,S)-**5**

(2*R*,5*S*)-5-((*S*)-Phenyl(p-tolyl)methyl)-2-(trifluoromethyl)oxazolidine ((*S*,*S*)-5)

Prepared according to the general procedure D5 using *(R)*-**4** (82 mg, 0.20 mmol, 1.0 equiv., 92% ee) and $Pd(OH)_2/C$ (10 mol%, 14 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product *(S,S)*-**5** (51 mg, 0.16 mmol, 79% yield) as a pale yellow solid. The enantiomeric excess was determined to be 92% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Minor} = 7.8 min, τ_{Major} = 11.6 min. $[\alpha]D^{20}$ = -2.0 (c = 0.50, $CHCl_3$, 92% ee). Absolute configuration was determined in comparison to compound *(R,R)*-**5**.



(R,S)-**36**

(2*S*,5*R*)-5-((*S*)-Phenyl(*p*-tolyl)methyl)-2-(trifluoromethyl)oxazolidine ((*R*,*S*)-36)

Prepared according to the general procedure D5 using *(S)*-**6** (82 mg, 0.20 mmol, 1.0 equiv., 89% ee) and $Pd(OH)_2/C$ (20 mol%, 28 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product *(R,S)*-**36** (52 mg, 0.16 mmol, 82% yield) as colorless oil. The enantiomeric excess was determined to be 89% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 7.7 min, τ_{Minor} = 11.0 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

$[\alpha]D^{20}$ = -0.5 (c = 0.64, $CHCl_3$, 89% ee).

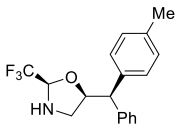
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.36 – 7.27 (m, 4H, Ar*H*), 7.23 – 7.16 (m, 1H, Ar*H*), 7.16 – 7.05 (m, 4H, Ar*H*), 4.98 (q, *J* = 5.5 Hz, 1H, C*H*CF_3), 4.61 (ddd, *J* = 11.5, 9.6, 5.6 Hz, 1H, OC*H*), 3.96 (d, *J* = 9.6 Hz, 1H, Ar^1Ar^2CH)), 3.16 (dd, *J* = 11.5, 5.6 Hz, 1H, NCH_aH_b), 2.81 (t, *J* = 11.5 Hz, 1H, NCH_aH_b), 2.66 (br. s, 1H, N*H*), 2.31 (s, 3H, CH_3).

$^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 142.4, 138.4, 136.8, 129.6, 128.5, 128.3, 128.2, 126.7, 123.4 (q, *J* = 283.0 Hz), 88.4 (q, *J* = 33.9 Hz), 81.1, 55.2, 50.8, 21.2.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.1 (d, 3F, *J* = 5.5 Hz).

IR (cm^{-1}) 3354 (w), 2927 (w), 1508 (m), 1453 (w), 1328 (m), 1290 (m), 1168 (s), 1150 (s).

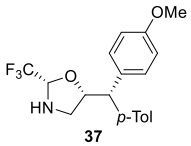
HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{18}H_{19}F_3NO^+$ 322.1413; Found 322.1417.



(S,R)-**36**

(2*R*,5*S*)-5-((*R*)-Phenyl(*p*-tolyl)methyl)-2-(trifluoromethyl)oxazolidine ((*S*,*R*)-36)

Prepared according to the general procedure D3 using *(R)*-**6** (82 mg, 0.20 mmol, 1.0 equiv., 89% ee) and $Pd(OH)_2/C$ (20 mol%, 28 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product *(S,R)*-**36** (50 mg, 0.16 mmol, 78% yield) as colorless oil. The enantiomeric excess was determined to be 89% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Minor} = 7.7 min, τ_{Major} = 10.9 min. $[\alpha]D^{20}$ = 2.7 (c = 0.50, $CHCl_3$, 89% ee). Absolute configuration was determined in comparison to compound *(R,R)*-**5**.



37

(2*S*,5*R*)-5-((*S*)-(4-Methoxyphenyl)(*p*-tolyl)methyl)-2-(trifluoromethyl)oxazolidine (37)

Prepared according to the general procedure D5 using **7** (88 mg, 0.20 mmol, 1.0 equiv., 92% ee) and $Pd(OH)_2/C$ (20 mol%, 28 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product **37** (60 mg, 0.17 mmol, 85% yield) as colorless oil The enantiomeric excess was determined to be 92% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 10.2 min, τ_{Minor} = 15.7 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

$[\alpha]D^{20}$ = -0.8 (c = 0.44, $CHCl_3$, 92% ee).

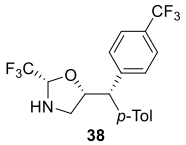
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.21 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.17 – 7.12 (m, 2H, Ar*H*), 7.11 (d, *J* = 8.0 Hz, 2H, Ar*H*), 6.87 – 6.78 (m, 2H, Ar*H*), 4.97 (q, *J* = 5.6 Hz, 1H, C*H*CF_3), 4.56 (dt, *J* = 9.6, 5.2 Hz, 1H, OC*H*), 3.91 (d, *J* = 9.6 Hz, 1H, Ar^1Ar^2CH)), 3.77 (s, 3H, OCH_3), 3.15 (dd, *J* = 11.6, 5.2 Hz, 1H, NCH_aH_b), 2.81 (dd, 1H, *J* = 11.6, 9.6, NCH_aH_b), 2.67 (br. s, 1H, N*H*), 2.30 (s, 3H, ArCH_3).

$^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 158.6, 139.5, 136.2, 133.7, 129.28, 129.25, 128.1, 123.5 (q, *J* = 282.9 Hz), 114.3, 88.4 (q, *J* = 33.9 Hz), 82.4, 55.4, 54.4, 50.8, 21.2.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.1 (d, 3F, *J* = 5.6 Hz).

IR (cm^{-1}) 3349 (m), 3010 (m), 2926 (m), 2839 (w), 1612 (m), 1513 (s), 1456 (m), 1293 (m), 1254 (s), 1171 (s), 1150 (s), 1038 (m).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{19}H_{21}F_3NO_2^+$ 352.1519; Found 352.1515.



38

((2*S*,5*R*)-5-((*S*)-*p*-Tolyl(4-(trifluoromethyl)phenyl)methyl)-2-(trifluoromethyl)oxazolidine (38)

Prepared according to the general procedure D5 using **8** (95 mg, 0.20 mmol, 1.0 equiv., 88% ee) and Pd(OH)$_2$/C (20 mol%, 28 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product **38** (59 mg, 0.15 mmol 76% yield) as colorless oil. The enantiomeric excess was determined to be 88% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 9.3 min, τ_{Minor} = 11.8 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

[α]D^{20} = 0.9 (c = 0.88, $CHCl_3$, 88% ee).

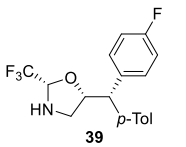
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.55 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.37 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.19 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.13 (d, *J* = 8.0 Hz, 2H, Ar*H*), 4.98 (q, *J* = 5.3 Hz, 1H, C*H*CF$_3$), 4.62 (ddd, *J* = 11.5, 9.1, 5.6 Hz, 1H, OC*H*), 4.04 (d, *J* = 9.1 Hz, 1H, Ar^{1}Ar^{2}C*H*), 3.17 (dd, *J* = 11.5, 5.6 Hz, 1H, NC*H*$_a$H$_b$), 2.78 (t, *J* = 11.5 Hz, 1H, NCH$_a$*H*$_b$), 2.68 (br. s, 1H, N*H*), 2.31 (s, 3H, C*H*$_3$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 145.6, 138.0, 136.8, 129.5, 129.4 (q, *J* = 32.5 Hz) 128.7, 128.3, 125.9 (q, *J* = 3.7 Hz), 124.2 (q, *J* = 271.9 Hz), 123.3 (q, *J* = 282.8 Hz), 88.4 (q, *J* = 34.0 Hz), 81.6, 55.0, 50.5, 21.2.

^{19}F NMR (376 MHz, Chloroform-*d*) δ -62.6 (s, 3F, ArC*F*$_3$), -81.0 (d, 3F, *J* = 5.3 Hz, CHC*F*$_3$).

IR (cm^{-1}) 3351 (w), 3017 (w), 2932 (w), 1620 (w), 1516 (w), 1421 (w), 1328 (s), 1165 (s), 1125 (s), 1074 (m).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{19}H_{18}F_6NO^+$ 390.1287; Found 390.1298.



39

(2*S*,5*R*)-5-((*S*)-(4-Fluorophenyl)(p-tolyl)methyl)-2-(trifluoromethyl)oxazolidine (39)

Prepared according to the general procedure D5 using **9** (85 mg, 0.20 mmol, 1.0 equiv., 91% ee) and Pd/C (20 mol%, 85 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product **39** (52 mg, 0.16 mmol, 83% yield) as colorless oil. The enantiomeric excess was determined to be 91% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 9.7 min, τ_{Minor} = 12.8 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

[α]D^{20} = 1.5 (c = 0.92, $CHCl_3$, 91% ee).

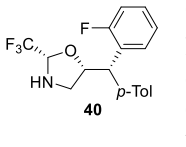
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.24 – 7.15 (m, 4H, Ar*H*), 7.15 – 7.08 (m, 2H, Ar*H*), 7.02 – 6.94 (m, 2H, Ar*H*), 4.97 (q, *J* = 5.5 Hz, 1H, C*H*CF$_3$), 4.57 (td, *J* = 9.3, 5.5 Hz, 1H, OC*H*), 3.96 (d, *J* = 9.3 Hz, 1H, Ar^{1}Ar^{2}C*H*), 3.15 (ddd, *J* = 12.3, 5.5, 1.5 Hz, 1H, NC*H*$_a$H$_b$),), 2.78 (ddd, *J* = 12.3, 9.3, 1.5 Hz, 1H, NCH$_a$*H*$_b$), 2.30 (s, 3H, ArC*H*$_3$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 161.9 (d, *J* = 245.8 Hz), 138.9, 137.4 (d, *J* = 3.5 Hz), 136.5, 129.8 (d, *J* = 7.8 Hz), 129.4, 128.2, 123.4 (q, *J* = 282.8 Hz), 115.8 (d, *J* = 21.2 Hz), 88.4 (q, *J* = 33.8 Hz), 82.1, 54.4, 50.6, 21.2.

^{19}F NMR (376 MHz, Chloroform-*d*) δ ^{19}F NMR (376 MHz, Chloroform-d) δ -81.0 (d, 3F, *J* = 5.5 Hz, CHC*F*$_3$), -115.7 (tt, 1F, *J* = 8.3, 5.4 Hz, Ar*F*).

IR (cm^{-1}) 3350 (w), 3016 (w), 2925 (w), 1611 (w), 1512 (m), 1329 (m), 1291 (m), 1226 (m), 1168 (s), 1137 (s).

HRMS (ESI/QTOF) m/z: [M + H]$^+$ Calculated for $C_{19}H_{21}F_3NO^+$ 336.1570; Found 336.1576.



40

(2S,5R)-5-((S)-(2-Fluorophenyl)(p-tolyl)methyl)-2-(trifluoromethyl)oxazolidine (40)

Prepared according to the general procedure D5 using **13** (85 mg, 0.20 mmol, 1.0 equiv., 80% ee) and Pd/C (20 mol%, 85 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product **40** (44 mg, 0.13 mmol, 65% yield) as colorless oil. The enantiomeric excess was determined to be 80% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1

mL/min, λ = 230 nm: τ_{Major} = 9.0 min, τ_{Minor} = 13.8 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

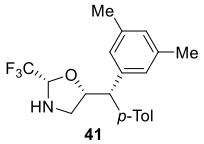
$[\alpha]D^{20}$ = 8.1 (c = 0.74, $CHCl_3$, 80% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.29 (td, *J* = 7.5, 1.8 Hz, 1H, Ar*H*), 7.27 – 7.16 (m, 3H, Ar*H*), 7.15 – 7.05 (m, 3H, Ar*H*), 7.02 (ddd, *J* = 10.5, 8.2, 1.3 Hz, 1H, Ar*H*), 4.98 (q, *J* = 5.6 Hz, 1H, C*H*CF_3), 4.68 (dtd, *J* = 9.2, 6.8, 5.9, 3.1 Hz, 1H, OC*H*), 4.28 (d, *J* = 9.4 Hz, 1H, Ar^1Ar^2CH), 3.22 (dd, *J* = 12.2, 5.1 Hz, 1H, NCH_aH_b), 2.80 (dd, *J* = 12.2, 9.3 Hz, 1H, NCH_aH_b), 2.30 (s, 3H, Ar^1CH_3).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 160.5 (d, *J* = 245.9 Hz), 138.1, 136.6, 129.8 (d, *J* = 4.5 Hz), 129.3, 128.7 (d, *J* = 8.4 Hz), 128.7 (d, *J* = 15.0 Hz), 128.3, 124.54 (d, *J* = 3.5 Hz), 123.4 (d, *J* = 283.0 Hz), 116.1 (d, *J* = 23.0 Hz), 88.5 (q, *J* = 34.1 Hz), 81.7 (d, *J* = 2.8 Hz), 50.4, 48.7, 21.2.
^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.0 (d, 3F, *J* = 5.6 Hz, CHC*F*$_3$), -115.9 (dt, 1F, *J* = 12.1, 6.5 Hz, Ar*F*).

IR (cm^{-1}) 3356 (w), 3039 (w), 2929 (w), 1496 (m), 1454 (m), 1290 (m), 1225 (m), 1169 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{18}H_{18}F_4NO^+$ 340.1319; Found 340.1318.



41

(2*S*,5*R*)-5-((*S*)-(3,5-Dimethylphenyl)(*p*-tolyl)methyl)-2-(trifluoromethyl)oxazolidine (41)

Prepared according to the general procedure D5 using **14** (87 mg, 0.20 mmol, 1.0 equiv., 91% ee) and $Pd(OH)_2$/C (20 mol%, 28 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product **41** (41 mg, 0.12 mmol, 59% yield) as colorless oil. The enantiomeric excess was determined to be 91% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 230 nm: τ_{Major} = 5.8 min, τ_{Minor} = 8.9 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

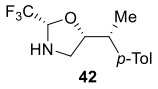
$[\alpha]D^{20}$ = 5.9 (c = 0.62, $CHCl_3$, 91% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.22 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.11 (d, *J* = 8.0 Hz, 2H, Ar*H*), 6.84 (s, 1H, Ar*H*), 6.84 (s, 2H, Ar*H*), 4.98 (q, *J* = 5.6 Hz, 1H, C*H*CF_3), 4.62 (td, *J* = 9.7, 5.6 Hz, 1H, OC*H*), 3.87 (d, *J* = 9.7 Hz, 1H, Ar^1Ar^2CH)), 3.19 (ddd, *J* = 12.2, 5.5, 1.0 Hz, 1H, NCH_aH_b), 2.80 (dd, *J* = 12.2, 9.7 Hz, 1H, NCH_aH_b, 2.79 (br. s, 1H, N*H*), 2.29 (s, 3H, Ar^2CH_3), 2.27 (s, 6H, Ar^1CH_3).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 141.3, 139.3, 138.3, 136.2, 129.3, 128.8, 128.1, 126.1, 123.3 (q, *J* = 283.0 Hz), 88.2 (q, *J* = 33.9 Hz), 82.3, 55.2, 50.6, 21.5, 21.2.
^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.8 (d, 3F, *J* = 5.6 Hz).

IR (cm^{-1}) 3353 (m), 3018 (m), 2923 (m), 1606 (m), 1515 (m), 1456 (m), 1290 (m), 1168 (s), 1043 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{20}H_{23}F_3NO^+$ 350.1726; Found 350.1733.



42

(2*S*,5*R*)-5-((*R*)-1-(*p*-Tolyl)ethyl)-2-(trifluoromethyl)oxazolidine (42)

Prepared according to the general procedure D5 using **17** (70 mg, 0.20 mmol, 1.0 equiv., 72% ee) and $Pd(OH)_2$/C (10 mol%, 14 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product **42** (43 mg, 0.16 mmol, 82% yield) as colorless oil. The enantiomeric excess was determined to be 72% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 7.7 min, τ_{Minor} = 9.3 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

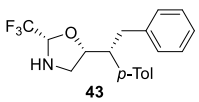
$[\alpha]D^{20}$ = 2.7 (c = 0.43, $CHCl_3$, 72% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.14 (s, 4H, Ar*H*), 4.87 (q, *J* = 5.6 Hz, 1H, C*H*CF_3), 3.93 (td, *J* = 8.8, 5.6 Hz, 1H, OC*H*), 3.32 (dd, *J* = 11.4, 5.6 Hz, 1H, NCH_aH_b), 2.94 – 2.79 (m, 2H, NCH_aH_b and $ArCHCH_3$), 2.67 (br. s, 1H, N*H*), 2.33 (s, 3H, $ArCH_3$), 1.24 (d, *J* = 7.1 Hz, 3H, $ArCHCH_3$).

^{13}C{^{1}H} 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, 3F, *J* = 5.6 Hz).

IR (cm^{-1}) 3348 (w), 2928 (w), 2887 (w), 1514 (m), 1456 (m), 1291 (m), 1166 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{13}H_{17}F_3NO^+$ 260.1257; Found 260.1259.



(2*S*,5*R*)-5-((*R*)-2-Phenyl-1-(p-tolyl)ethyl)-2-(trifluoromethyl)oxazolidine (43)

Prepared according to the general procedure D5 using **18** (85 mg, 0.20 mmol, 1.0 equiv., 86% ee) and $Pd(OH)_2/C$ (20 mol%, 28 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product **43** (47 mg, 0.14 mmol, 70% yield) as colorless oil. The enantiomeric excess was determined to be 86% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 7.1 min, τ_{Minor} = 11.4 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

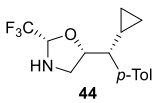
$[\alpha]D^{20}$ = -49.3 (c = 0.74, $CHCl_3$, 86% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.23 – 7.17 (m, 2H, Ar*H*), 7.17 – 7.11 (m, 1H, Ar*H*), 7.11 – 7.02 (m, 6H, Ar*H*), 4.84 (q, *J* = 5.5 Hz, 1H, C*H*CF_3), 4.04 (dt, *J* = 9.5, 5.6 Hz, 1H, OC*H*), 3.20 (dd, *J* = 12.0, 5.5 Hz, 1H, NC$H_a$$H_b$), 3.11 – 2.91 (m, 3H, PhCH_2CH and $PhCH_2$C*H*), 2.75 (t, *J* = 12.0, 9.5 Hz, 1H, NCH_aH_b), 2.46 (br. s, 1H, N*H*), 2.30 (s, 3H, $ArCH_3$).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 139.7, 137.6, 136.4, 129.2, 129.1, 128.6, 128.4, 126.2, 123.3 (q, *J* = 282.8 Hz), 87.5 (q, *J* = 33.9 Hz), 82.5, 50.4, 49.1, 38.5, 21.2.
^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.8 (d, 3F, *J* = 5.4 Hz, CHCF_3).

IR (cm^{-1}) 3349 (w), 3027 (w), 2927 (w), 1508 (m), 1451 (m), 1292 (m), 1165 (s), 1115 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{19}H_{21}F_3NO^+$ 336.1570; Found 336.1575.



(2*S*,5*R*)-5-((*R*)-Cyclopropyl(p-tolyl)methyl)-2-(trifluoromethyl)oxazolidine (44)

Prepared according to the general procedure D5 using **19** (75 mg, 0.20 mmol, 1.0 equiv., 78% ee) and $Pd(OH)_2/C$ (20 mol%, 28 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product **44** (32 mg, 0.11 mmol, 56% yield) as colorless oil. The enantiomeric excess was determined to be 78% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 7.1 min, τ_{Minor} = 9.2 min.). Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

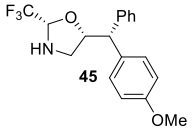
$[\alpha]D^{20}$ = -21.6 (c = 0.57, $CHCl_3$, 78% ee

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.14 (s, 4H, Ar*H*), 4.85 (q, *J* = 5.6 Hz, 1H, C*H*CF_3), 4.10 (td, *J* = 8.9, 5.5 Hz, 1H, OC*H*), 3.45 (ddd, *J* = 12.0, 5.5, 1.4 Hz, 1H, NC$H_a$$H_b$), 2.96 (dd, *J* = 12.0, 8.9 Hz, 1H, NCH_aH_b), 2.33 (s, 3H, ArCH_3), 1.93 (dd, *J* = 10.1, 8.3 Hz, 1H, Ar(CyPr)C*H*), 1.04 (dtt, *J* = 10.1, 8.1, 4.8 Hz, 1H, C*H*(CH_aH_b)CH_aH_b), 0.65 (dddd, *J* = 9.2, 8.1, 5.8, 4.5 Hz, 1H, CH(C$H_a$$H_b$)$CH_aH_b$), 0.44 (dddd, *J* = 9.2, 8.1, 5.6, 4.5 Hz, 1H, CH(CH_aH_b)C$H_a$$H_b$), 0.33 (ddt, *J* = 9.2, 5.6, 4.8 Hz, 1H, CH(CH_aH_b)CH_aH_b), 0.06 (ddt, *J* = 9.2, 5.8, 4.8 Hz, 1H, CH(CH_aH_b)CH_aH_b).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 139.4, 136.3, 129.2, 128.1, 123.4 (q, *J* = 282.8 Hz), 87.6 (q, *J* = 33.8 Hz), 84.3, 53.6, 49.6, 21.2, 13.4, 6.3, 3.3.
^{19}F NMR (376 MHz, Chloroform-*d*) δ -81.1 (d, 3F, *J* = 5.5 Hz, CHCF_3).

IR (cm^{-1}) 3343 (w), 3010 (w), 2927 (w), 2897 (w), 1515 (m), 1327 (m), 1291 (m), 1167 (s), 1116 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{15}H_{19}F_3NO^+$ 286.1413; Found 286.1416.



(2*S*,5*R*)-5-((*R*)-Phenyl(4-(trifluoromethyl)phenyl)methyl)-2-(trifluoromethyl)oxazolidine (45)

Prepared according to the general procedure D5 using **20** (85 mg, 0.20 mmol, 1.0 equiv., 88% ee) and $Pd(OH)_2/C$ (10 mol%, 14 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product **45** (55 mg, 0.16 mmol, 82% yield) as colorless oil. The enantiomeric excess was determined to be 90% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 12.6 min, τ_{Minor} = 20.2 min.). Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

$[\alpha]D^{20}$ = +13.0 (c = 0.32, $CHCl_3$, 90% ee

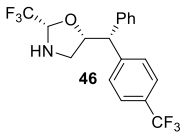
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.34 – 7.20 (m, 7H, Ar*H*), 6.88 – 6.82 (m, 2H, Ar*H*), 4.98 (br. s., 1H, C*H*CF_3), 4.58 (td, *J* = 9.3, 5.5 Hz, 1H, OC*H*), 3.95 (d, *J* = 9.4 Hz, 1H, Ar^1Ar^2C*H*), 3.77 (s, 3H, OCH_3), 3.14 (br.s.,1H, NC$H_a$$H_b$), 2.79 (br. s., 1H, NCH_aH_b), 2.65 (br. s., 1H, N*H*).

^{13}C{^{1}H} NMR (101 MHz, Chloroform-*d*) δ 158.4, 141.7, 134.3, 129.4, 128.9, 128.3, 127.1, 123.5 (q, *J* = 282.9 Hz), 113.9, 88.4 (q, *J* = 33.8 Hz), 82.3, 55.3, 54.8, 50.7.

$^{19}F\{^{1}H\}$ NMR (376 MHz, Chloroform-*d*) δ -81.0.

IR (cm^{-1}) 3353 (w), 3024 (w), 2933 (w), 2844 (w), 1610 (w), 1511 (m), 1455 (w), 1292 (m), 1251 (m), 1171 (s), 1152 (s).

HRMS (ESI/QTOF) m/z: $[M + Na]^+$ Calculated for $C_{18}H_{18}F_3NNaO_2^+$ 360.1182; Found 360.1184.



(2*S*,5*R*)-5-((*R*)-Phenyl(4-(trifluoromethyl)phenyl)methyl)-2-(trifluoromethyl)oxazolidine (46)

Prepared according to the general procedure D5 using **22** (93 mg, 0.20 mmol, 1.0 equiv., 82% ee) and $Pd(OH)_2/C$ (10 mol%, 14 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product **46** (46 mg, 0.12 mmol, 61% yield) as colorless oil. The enantiomeric excess was determined to be 82% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 12.0 min, τ_{Minor} = 14.2 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

$[\alpha]D^{20}$ = +5.0 (c = 0.30, $CHCl_3$, 82% ee).

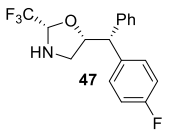
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.54 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.44 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.34 – 7.27 (m, 2H, Ar*H*), 7.27 – 7.19 (m, 3H, Ar*H*), 4.98 (dq, *J* = 8.5, 5.6 Hz, 1H, C*H*CF_3), 4.62 (td, *J* = 9.3, 5.5 Hz, 1H, OC*H*), 4.03 (d, *J* = 9.6 Hz, 1H, Ar^1Ar^2CH), 3.17 (dddd, *J* = 13.0, 7.2, 5.6, 1.5 Hz, 1H, NCH_aH_b), 2.89 – 2.75 (m, 1H, NCH_aH_b), 2.66 (br.s., 1H, N*H*).

$^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 146.1, 140.4, 129.2, 129.0 (q, *J* = 32.2 Hz) 128.8, 128.4, 127.6, 125.5 (q, *J* = 3.7 Hz), 124.3 (q, *J* = 271.6 Hz), 123.3 (q, *J* = 281.5 Hz), 88.6 (q, *J* = 34.0 Hz), 81.6, 55.5, 50.7.

$^{19}F\{^{1}H\}$ NMR (376 MHz, Chloroform-*d*) δ -62.5, -81.1.

IR (cm^{-1}) 2928 (w), 1613 (w), 1495 (w), 1455 (w), 1329 (s), 1292 (m), 1167 (s), 1136 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{18}H_{16}F_6NO^+$ 376.1131; Found 376.1141.



(2*S*,5*R*)-5-((*R*)-(4-Fluorophenyl)(phenyl)methyl)-2-(trifluoromethyl)oxazolidine (47)

Prepared according to the general procedure D5 using **23** (83 mg, 0.20 mmol, 1.0 equiv., 84% ee) and $Pd(OH)_2/C$ (10 mol%, 14 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 85:15) to give the corresponding product **47** (47 mg, 0.14 mmol, 72% yield) as colorless oil. The enantiomeric excess was determined to be 84% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 10.7 min, τ_{Minor} = 14.2 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

$[\alpha]D^{20}$ = +8.1 (c = 0.37, $CHCl_3$, 84% ee).

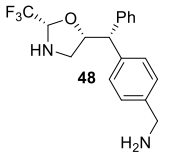
^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.19 (m, 7H, Ar*H*), 6.99 (t, *J* = 8.7 Hz, 2H, Ar*H*), 4.99 (dq, *J* = 8.5, 5.6 Hz, 1H, C*H*CF_3), 4.58 (td, *J* = 9.2, 5.5 Hz, 1H, OC*H*), 3.98 (d, *J* = 9.4 Hz, 1H, Ar^1Ar^2CH), 3.22 – 3.11 (m, 1H, NCH_aH_b), 2.87 – 2.72 (m, 1H, NCH_aH_b), 2.65 (br. s., 1H, N*H*).

$^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 161.7 (d, *J* = 244.9 Hz), 141.2, 137.8 (d, *J* = 3.3 Hz), 130.0 (d, *J* = 8.0 Hz), 129.0, 128.3, 127.3, 123.4 (q, *J* = 282.9 Hz), 115.3 (d, *J* = 21.2 Hz), 88.5 (q, *J* = 34.1 Hz), 82.1, 54.8, 50.7.

$^{19}F\{^{1}H\}$ NMR (376 MHz, Chloroform-*d*) δ -81.1, -116.6.

IR (cm^{-1}) 3357 (w), 2928 (w), 1605 (w), 1508 (m), 1454 (w), 1290 (m), 1226 (m), 1167 (s), 1154 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{17}H_{16}F_4NO^+$ 326.1163; Found 326.1164.



(4-((*R*)-Phenyl((2*S*,5*R*)-2-(trifluoromethyl)oxazolidin-5-yl)methyl)phenyl)methanamine (48)

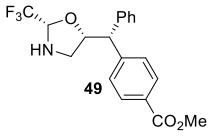
Prepared according to the general procedure D5 using **25** (84 mg, 0.20 mmol, 1.0 equiv., 73% ee) and $Pd(OH)_2/C$ (10 mol%, 14 mg). The crude material was purified by flash column chromatography (DCM/MeOH gradient 100:0 to 90:10) to give the corresponding product **48** (32 mg, 95 μmol, 48% yield) as colorless oil. The enantiomeric excess was determined to be 74% by HPLC analysis on a Daicel Chiralpak IC column: 85:15 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 17.4 min, τ_{Minor} = 24.7 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

$[\alpha]D^{20}$ = +10.1 (c = 0.33, $CHCl_3$, 74% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) ^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.38 – 7.09 (m, 9H, Ar*H*), 4.90 (q, *J* = 5.6 Hz, 1H, C*H*CF_3), 4.59 (td, *J* = 9.4, 5.5 Hz, 1H, OC*H*), 3.96 (dd, *J* = 9.6, 3.3 Hz, 1H, Ar^1Ar^2CH), 3.79 (d, *J* = 3.9 Hz, 2H, $ArCH_2NH_2$), 3.23 – 2.84 (m, 4H, NCH_aH_b, NCH_aH_b and NH_2), 2.84 – 2.70 (br. s., 1H, N*H*).

$^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 141.3, 141.2, 128.9, 128.6, 128.3, 127.8, 127.7, 127.2, 123.4 (q, *J* = 282.9 Hz), 88.4 (q, *J* = 34.0 Hz), 82.1, 55.4, 50.7, 45.6.
$^{19}F\{^1H\}$ NMR (376 MHz, Chloroform-*d*) δ -81.0.

IR (cm^{-1}) 3354 (w), 3027 (m), 2928 (m), 2865 (m), 1602 (w), 1505 (m), 1455 (w), 1291 (m), 1151 (s), 1092 (m).
HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{18}H_{20}F_3N_2O^+$ 337.1522; Found 337.1518.



Methyl-4-((*R*)-phenyl((2*S*,5*R*)-2-(trifluoromethyl)oxazolidin-5-yl)methyl)benzoate (49)

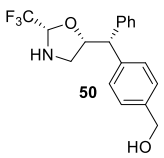
Prepared according to the general procedure D5 using **26** (91 mg, 0.20 mmol, 1.0 equiv., 82% ee) and $Pd(OH)_2/C$ (10 mol%, 14 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 80:20) to give the corresponding product **49** (44 mg, 0.12 mmol, 60% yield) as colorless oil. The enantiomeric excess was determined to be 82% by HPLC analysis on a Daicel Chiralpak IA column: 90:10 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 13.4 min, τ_{Minor} = 19.6 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

$[\alpha]D^{20}$ = +6.8 (c = 0.39, $CHCl_3$, 82% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.97 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.41 (d, *J* = 8.3 Hz, 2H, Ar*H*), 7.35 – 7.19 (m, 5H, Ar*H*), 4.99 (dq, *J* = 7.9, 5.6 Hz, 1H, C*H*CF_3), 4.64 (td, *J* = 9.3, 5.5 Hz, 1H, OC*H*), 4.05 (d, *J* = 9.5 Hz, 1H, Ar^1Ar^2CH), 3.88 (s, 3H, $COOCH_3$), 3.22 – 3.12 (m, 1H, NCH_aH_b), 2.82 (q, *J* = 10.9 Hz, 1H, NCH_aH_b), 2.68 (br. s., 1H, N*H*).

$^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 167.1, 147.3, 140.6, 129.9, 129.1, 128.6, 128.5, 128.4, 127.5, 123.4 (q, *J* = 282.8 Hz), 88.5 (q, *J* = 34.0 Hz), 81.6, 55.6, 52.2, 50.7.
$^{19}F\{^1H\}$ NMR (376 MHz, Chloroform-*d*) δ -81.1.

IR (cm^{-1}) 3349 (w), 2953 (w), 1718 (s), 1607 (w), 1444 (m), 1286 (s), 1169 (s), 1151 (s).
HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{19}H_{19}F_3NO_3^+$ 366.1312; Found 366.1320.



((4-((*R*)-Phenyl((2*S*,5*R*)-2-(trifluoromethyl)oxazolidin-5-yl)methyl)phenyl)methanol (50)

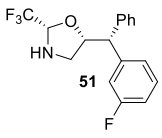
Prepared according to the general procedure D5 using **27** (85 mg, 0.20 mmol, 1.0 equiv., 80% ee) and $Pd(OH)_2/C$ (10 mol%, 14 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 60:40) to give the corresponding product **50** (10 mg, 30 μmol, 15% yield) as colorless oil. The enantiomeric excess was determined to be 80% by HPLC analysis on a Daicel Chiralpak IA column: 80:20 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 9.1 min, τ_{Minor} = 13.0 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

$[\alpha]D^{20}$ = +9.4 (c = 0.39, $CHCl_3$, 80% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.37 – 7.19 (m, 9H, Ar*H*), 4.97 (q, *J* = 5.7 Hz, 1H, C*H*CF_3), 4.64 (m, 3H, OC*H* and $ArCH_2OH$), 3.99 (d, *J* = 9.5 Hz, 1H, Ar^1Ar^2CH), 3.16 (dd, *J* = 12.2, 5.4 Hz, 1H, NCH_aH_b), 2.81 (br. s., 1H, NCH_aH_b), 2.66 (br. s., 1H, N*H*).

$^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 141.7, 141.2, 139.3, 129.0, 128.6, 128.3, 127.3, 127.2, 123.4 (q, *J* = 282.8 Hz), 88.4 (q, *J* = 34.2 Hz), 82.0, 65.3, 55.4, 50.7.
$^{19}F\{^1H\}$ NMR (376 MHz, Chloroform-*d*) δ -81.1.

IR (cm^{-1}) 3339 (m), 2925 (m), 1596 (w), 1454 (m), 1291 (m), 1151 (s).
HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{18}H_{19}F_3NO_2^+$ 338.1362; Found 338.1372.



(2*S*,5*R*)-5-((*R*)-(3-Fluorophenyl)(phenyl)methyl)-2-(trifluoromethyl)oxazolidine (51)

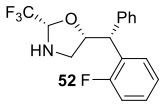
Prepared according to the general procedure D5 using **28** (83 mg, 0.20 mmol, 1.0 equiv., 82% ee) and $Pd(OH)_2/C$ (10 mol%, 14 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 80:15) to give the corresponding product **51** (43 mg, 0.14 mmol, 66% yield) as colorless oil. The enantiomeric excess was determined to be 82% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 9.2 min, τ_{Minor} = 13.4 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

$[\alpha]D^{20}$ = +3.3 (c = 0.25, $CHCl_3$, 82% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.39 – 7.19 (m, 6H, Ar*H*), 7.11 (dt, *J* = 7.8, 1.2 Hz, 1H, Ar*H*), 7.05 (dt, *J* = 10.3, 2.2 Hz, 1H, Ar*H*), 6.90 (tdd, *J* = 8.3, 2.6, 1.0 Hz, 1H, Ar*H*), 5.00 (dq, *J* = 8.4, 5.6 Hz, 1H, C*H*CF_3), 4.59 (td, *J* = 9.3, 5.5 Hz, 1H, OC*H*), 3.99 (d, *J* = 9.5 Hz, 1H, Ar^1Ar^2CH), 3.25 – 3.05 (br. s, 1H, NCH_aH_b), 2.89 – 2.74 (br. s, 1H, NCH_aH_b), 2.66 (br. s., 1H, N*H*).

$^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 162.9 (d, *J* = 245.4 Hz), 144.6 (d, *J* = 7.0 Hz), 140.7, 129.9 (d, *J* = 8.3 Hz), 129.1, 128.4, 127.5, 124.2 (d, *J* = 2.8 Hz), 123.4 (q, *J* = 282.9 Hz), 115.4 (d, *J* = 21.9 Hz), 113.7 (d, *J* = 21.1 Hz), 88.5 (q, *J* = 34.0 Hz), 81.8, 55.3 (d, *J* = 1.8 Hz), 50.7.
$^{19}F\{^1H\}$ NMR (376 MHz, Chloroform-*d*) δ -81.1, -113.2.

IR (cm^{-1}) 3354 (w), 2925 (w), 1597 (m), 1493 (m), 1451 (m), 1291 (m), 1168 (s), 1151 (s).
HRMS (APCI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{17}H_{16}F_4NO^+$ 326.1163; Found 326.1163.



(2S,5*R*)-5-((*R*)-(2-Fluorophenyl)(phenyl)methyl)-2-(trifluoromethyl)oxazolidine (52)

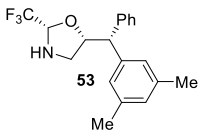
Prepared according to the general procedure D5 using **29** (83 mg, 0.20 mmol, 1.0 equiv., 74% ee) and $Pd(OH)_2/C$ (10 mol%, 14 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 80:15) to give the corresponding product **52** (45 mg, 0.14 mmol, 69% yield) as colorless oil. The enantiomeric excess was determined to be 72% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 254 nm: τ_{Major} = 8.1 min, τ_{Minor} = 14.0 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

$[\alpha]D^{20}$ = -12.8 (c = 0.26, $CHCl_3$, 72% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.45 (td, *J* = 7.6, 1.9 Hz, 1H, Ar*H*), 7.33 – 7.15 (m, 6H, Ar*H*), 7.12 (td, *J* = 7.5, 1.4 Hz, 1H, Ar*H*), 7.01 (ddd, *J* = 10.5, 8.0, 1.4 Hz, 1H, Ar*H*), 4.97 (br. s., 1H, C*H*CF_3), 4.71 (td, *J* = 9.1, 5.5 Hz, 1H, OC*H*), 4.34 (d, *J* = 9.2 Hz, 1H, Ar^1Ar^2CH), 3.18 (br. s, 1H, NCH_aH_b), 2.85 (br. s, 1H, NCH_aH_b), 2.66 (br. s., 1H, N*H*).

$^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 160.9 (d, *J* = 245.8 Hz), 140.5, 129.3 (d, *J* = 4.3 Hz), 129.0, 128.9, 128.4, 128.3, 127.3, 124.2 (d, *J* = 3.5 Hz), 123.3 (q, *J* = 282.8 Hz), 115.7 (d, *J* = 22.6 Hz), 88.4 (q, *J* = 34.0 Hz), 80.9, 50.6, 48.5 (d, *J* = 2.1 Hz).
$^{19}F\{^1H\}$ NMR (376 MHz, Chloroform-*d*) δ -81.1, -117.2.

IR (cm^{-1}) 3067 (w), 3025 (w), 2945 (w), 2891 (w), 2109 (w), 1715 (w), 1592 (w), 1494 (m), 1455 (m), 1291 (m), 1226 (m), 1167 (s), 1153 (s).
HRMS (ESI/QTOF) m/z: $[M + H]^+$ $C_{17}H_{16}F_4NO^+$ 326.1163; Found 326.1163.



(2*S*,5*R*)-5-((*R*)-(3,5-Dimethylphenyl)(phenyl)methyl)-2-(trifluoromethyl)oxazolidine (53)

Prepared according to the general procedure D5 using **30** (85 mg, 0.20 mmol, 1.0 equiv., 92% ee) and $Pd(OH)_2/C$ (10 mol%, 14 mg). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 80:15) to give the corresponding product **53** (51 mg, 0.15 mmol, 76% yield) as colorless oil. The enantiomeric excess was determined to be 92% by HPLC analysis on a Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 6.8 min, τ_{Minor} = 8.3 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

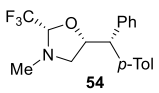
$[\alpha]D^{20}$ = -2.1 (c = 0.47, $CHCl_3$, 92% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.35 – 7.17 (m, 5H, Ar*H*), 6.95 (s, 2H, Ar*H*), 6.85 (s, 1H, Ar*H*), 4.97 (dq, *J* = 8.5, 5.6 Hz, 1H, C*H*CF_3), 4.63 (td, *J* = 9.3, 5.5 Hz, 1H, OC*H*), 3.91 (d, *J* = 9.4 Hz, 1H, Ar^1Ar^2CH), 3.21 – 3.09 (m, 1H, NCH_aH_b), 2.85 – 2.71 (m, 1H, NCH_aH_b), 2.63 (br. s., 1H, N*H*), 2.28 (s, 6H, $ArCH_3$).

$^{13}C\{^1H\}$ NMR (101 MHz, Chloroform-*d*) δ 141.9, 141.6, 137.9, 128.9, 128.6, 128.3, 127.0, 126.2, 123.4 (q, *J* = 283.1 Hz), 88.4 (q, *J* = 33.9 Hz), 82.1, 55.6, 50.7, 21.6.

$^{19}F\{^{1}H\}$ NMR (376 MHz, Chloroform-*d*) δ -81.0.

IR (cm^{-1}) 3355 (w), 3028 (w), 2923 (w), 1603 (w), 1492 (w), 1455 (w), 1292 (m), 1167 (s).
HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{19}H_{21}F_3NO^+$ 336.1570; Found 336.1564.



54

(2*S*,5*R*)-3-Methyl-5-((*R*)-phenyl(p-tolyl)methyl)-2-(trifluoromethyl)oxazolidine (54)

Prepared according to the general procedure D5 using **33** (33 mg, 0.10 mmol, 1.0 equiv., 92% ee) and Pd/C (20 mol%, 43 mg) in MeOH (1.3 mL) and AcOH (0.7 mL). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding product **54** (10 mg, 0.030 mmol, 30% yield) as colorless oil. The enantiomeric excess was determined to be 92% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 5.2 min, τ_{Minor} = 6.1 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**.

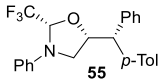
$[\alpha]D^{20}$ = 10.3 (c = 0.50, $CHCl_3$, 92% ee).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.33 – 7.27 (m, 2H, Ar*H*), 7.25 – 7.20 (m, 5H, Ar*H*), 7.11 (d, *J* = 8.0 Hz, 2H, Ar*H*), 4.86 (ddd, *J* = 9.9, 8.1, 5.8 Hz, 1H, OC*H*), 4.51 (q, *J* = 5.3 Hz, 1H, C*H*CF_3), 3.98 (d, *J* = 9.9 Hz, 1H, Ar^1Ar^2CH), 3.02 (ddd, *J* = 11.7, 8.1, 1.3 Hz, 1H, NCH_aH_b), 2.77 (ddd, *J* = 11.7, 5.8, 1.2 Hz, 1H, NCH_aH_b), 2.58 (s, 3H, NCH_3), 2.30 (s, 3H, $ArCH_3$).

$^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 141.6, 139.2, 136.3, 129.3, 128.9, 128.4, 128.2, 127.0, 123.4 (q, *J* = 283.2 Hz), 94.7 (q, *J* = 33.6 Hz), 79.6, 58.7, 55.3, 43.3, 21.2.
^{19}F NMR (376 MHz, Chloroform-*d*) δ -80.4 (d, 3F, *J* = 5.2 Hz, $CHCF_3$).

IR (cm^{-1}) 3023 (w), 2924 (m), 2867 (w), 1510 (w), 1459 (m), 1294 (m), 1161 (s), 1068 (m).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{19}H_{21}F_3NO^+$ 336.1570; Found 336.1576.



55

(2*S*,5*R*)-3-Phenyl-5-((*R*)-phenyl(p-tolyl)methyl)-2-(trifluoromethyl)oxazolidine (55)

Prepared according to the general procedure D5 using **34** (40 mg, 0.10 mmol, 1.0 equiv., 54% ee) and Pd/C (20 mol%, 43 mg) in MeOH (1.3 mL) and AcOH (0.7 mL). The crude material was purified by flash column chromatography (pentane/EtOAc gradient 100:0 to 97:3) to give the corresponding product **55** (14 mg, 0.035 mmol, 35% yield) as colorless oil. The enantiomeric excess was determined to be 73% by HPLC analysis on a Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 8.1 min, τ_{Minor} = 11.8 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5**. The olefin **34** was recovered (17 mg, 0.043 mmol, 43%, 24% e.e.).

$[\alpha]D^{20}$ = -23.7 (c = 0.50, $CHCl_3$, 73% ee).

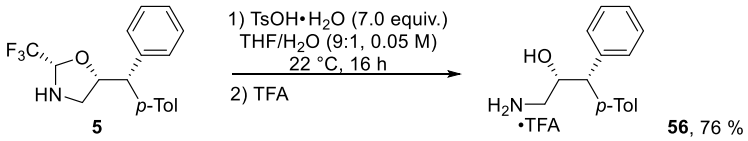
^{1}H NMR (400 MHz, Chloroform-*d*) 7.37 – 7.30 (m, 2H, Ar*H*), 7.30 – 7.26 (m, 3H, Ar*H*), 7.26 – 7.21 (m, 4H, Ar*H*), 7.13 (d, *J* = 8.0 Hz, 2H, Ar*H*), 6.88 (tt, *J* = 7.3, 1.1 Hz, 1H, Ar*H*), 6.77 – 6.70 (m, 2H, Ar*H*), 5.58 (q, *J* = 4.5 Hz, 1H, C*H*CF_3), 4.88 (td, *J* = 9.9, 6.1 Hz, 1H, OC*H*), 4.11 (d, *J* = 9.9 Hz, 1H, Ar^1Ar^2CH), 3.74 (ddd, *J* = 10.8, 6.1, 1.4 Hz, 1H, NCH_aH_b), 3.33 (dd, *J* = 10.8, 9.9 Hz, 1H, NCH_aH_b), 2.31 (s, 3H, $ArCH_3$).

$^{13}C\{^{1}H\}$ NMR (101 MHz, Chloroform-*d*) δ 145.3, 141.2, 138.6, 136.5, 129.5, 129.4, 129.1, 128.3, 128.2, 127.3, 123.7 (q, *J* = 286.8 Hz), 120.2, 114.5, 87.5 (q, *J* = 34.5 Hz), 80.5, 55.4, 52.3, 21.2.
^{19}F NMR (376 MHz, Chloroform-*d*) δ -79.6 (d, 3F. *J* = 4.6 Hz, $CHCF_3$).

IR (cm^{-1}) 3036 (w), 2924 (w), 1604 (m), 1506 (s), 1362 (m), 1323 (m), 1284 (m), 1168 (s), 1150 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{24}H_{23}F_3NO^+$ 398.1726; Found 398.1723.

(1*R*,2*R*)-3-Amino-1-phenyl-1-(p-tolyl)propan-2-ol trifluoroacetic acid salt (56)



Scheme 15. Acidic hydrolysis of the hemiaminal, synthesis of **56**

In 5 mL round bottom flask **5** (53 mg, 0.20 mmol, 94% ee) was dissolved in a mixture of THF (3.6 mL) and H_2O (0.4 mL). Tosylsulfonic acid (266 mg, 1.40 mmol, 7.0 equiv) was added and the mixture was stirred at room temperature for 16 hours. The reaction was diluted with DCM (5 mL) and quenched by

adding 1 M NaOH (4 mL). The layers were separated and the aqueous layer was extracted with DCM (2 x 5 mL). The combined organic layers were washed with brine, dried over Na_2SO_4, filtered and concentrated. The crude material was purified by preparative RP-HPLC on an Agilent 1260 HPLC system with a G2260A 1260 Prep ALS Autosampler, a G1361a 1260 Prep Pump, a G1365C 1260 MWD detector and a G1364B 1260 FC-PS collector, coupled with a Waters XBridge semi-preparative C18 column (19 x 150 mm, 5 µm). Water (solvent A) and water:acetonitrile 5:95 (solvent B), each containing 0.1% TFA, were used as the mobile phase at a flow rate of 20 mL.min-1. The following method was used: 100% A to 100% B in 20 minutes. The desired product (1*R*,2*R*)-3-amino-1-phenyl-1-(p-tolyl)propan-2-ol trifluoroacetic acid salt **56** was obtained as gummy solid (56 mg, 0.15 mmol, 76%). The enantiomeric excess was determined to be 94% by HPLC analysis on a Daicel Chiralpak IA column: 80:20 hexane/IPA, flow rate 1 mL/min, λ = 210 nm: τ_{Major} = 8.2 min, τ_{Minor} = 11.4 min. Absolute configuration was determined in comparison to compound *(R,R)*-**5.**

$[\alpha]D^{20}$ = -28.3 (c = 0.50, $CHCl_3$, 94% ee).

^{1}H NMR (400 MHz, Methanol-*d4*) δ 7.35 – 7.26 (m, 6H, Ar*H*), 7.24 – 7.17 (m, 1H, Ar*H*), 7.17 – 7.08 (m, 2H, Ar*H*), 4.53 (td, *J* = 9.8, 3.0 Hz, 1H, HOC*H*), 3.90 (d, *J* = 9.4 Hz, 1H, Ar^1Ar^2CH), 2.85 (dd, *J* = 12.8, 2.9 Hz, 1H, $H_2NCH_aH_b$), 2.75 (dd, *J* = 12.8, 9.9 Hz, 1H, $H_2NCH_aH_b$), 2.29 (s, 3H, $ArCH_3$).

^{13}C{^{1}H} NMR (101 MHz, Methanol-*d4*) δ 162.7 (q, *J* = 34.9 Hz), 143.1, 139.5, 137.4, 130.2, 129.9, 129.6, 129.2, 128.0, 118.1 (q, *J* = 292.3 Hz), 71.1, 57.8, 45.3, 21.0.

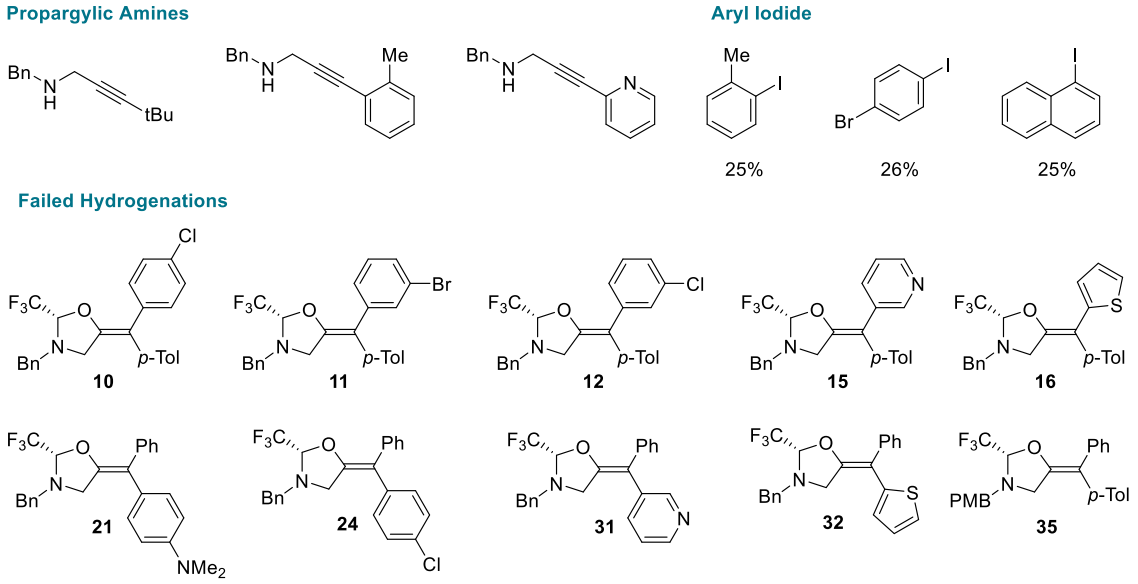
^{19}F NMR (376 MHz, Methanol-*d4*) δ -77.0 (s, 3F, $^-OOCCF_3$).

IR (cm^{-1}) 3031 (m), 2922 (m), 1679 (s), 1518 (m), 1200 (s), 1137 (s).

HRMS (ESI/QTOF) m/z: $[M + H]^+$ Calculated for $C_{16}H_{20}NO^+$ 242.1539; Found 242.1542.

D.5. Unsuccessful Substrates

Unreactive propargylic amines, aryl iodides and failed hydrogenations are reported in the following scheme. Yields are reported in the case of low conversions.



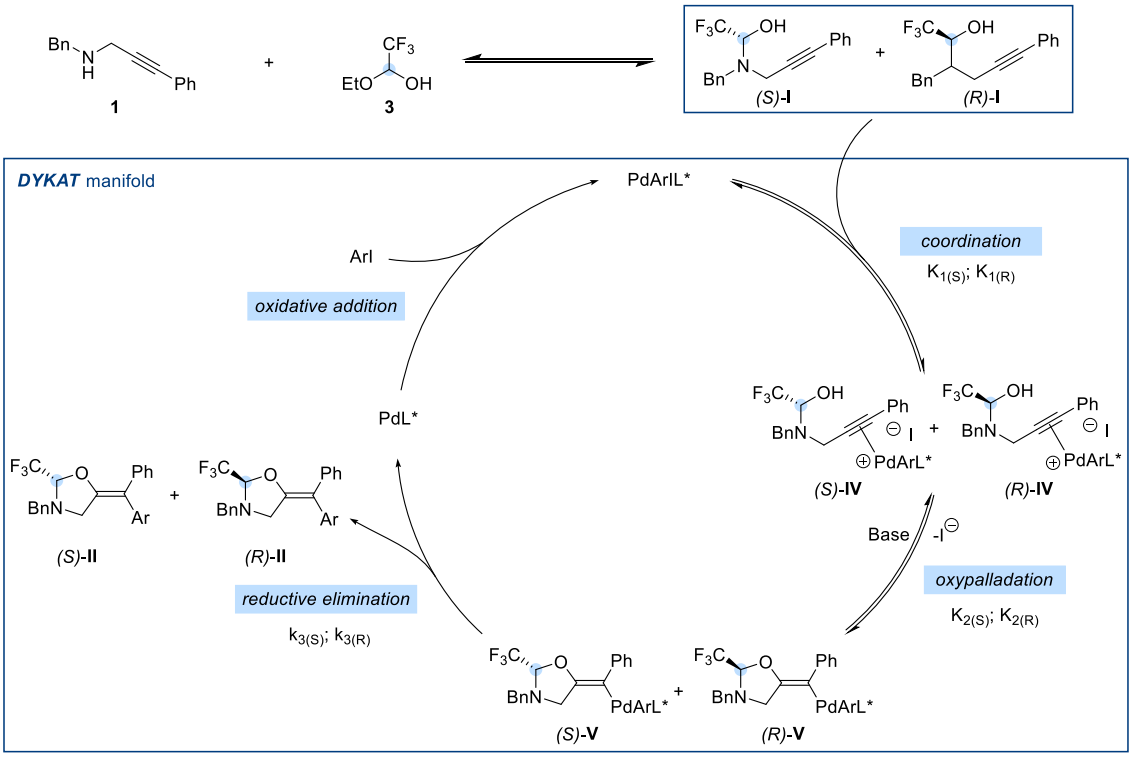
Scheme 16. Unsuccessful substrates and scope limitations.

E. Mechanistic Considerations

E.1. Proposed Reaction Mechanism

In the proposed reaction mechanism, the propargyl amine **1** condenses with the ethoxy trifluoroethanol **3** to give hemiaminal **I**. Then a ligand exchange onto the ArPdX species, obtained by oxidative addition of the Pd(0) catalyst with the aryl iodide, would provide the diastereomeric complexes **IV**. After a *trans*-oxypalladation step, (based on the observed geometry of the products[a]), the vinyl paladium species **V** could be obtained. Finally, a reductive elimination step would regenerate Pd(0) and provide the desired products **II**.

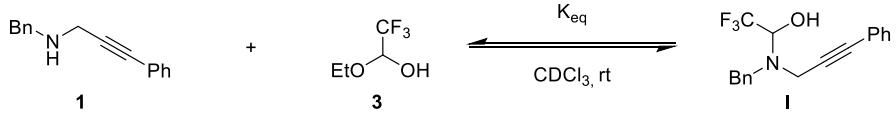
The origin of the asymmetric induction can be explained considering that the propargyl amine **1** and ethoxy trifluoroethanol **3** are in equilibrium with the hemiaminal **I**. This equilibrium provide the source of the racemization of the stereocenter in α to the CF_3-group. This racemization pathway is key for the development of a dynamic kinetic asymmetric transformation (DYKAT). In the presence of a chiral palladium complex, the two enantiomers of **IV** undergoes coordination, oxopalladation and reductive elimination with different kinetics ($K_{1(S)} \neq K_{1(R)}$, $K_{2(S)} \neq K_{2(R)}$, $k_{3(S)} \neq k_{3(R)}$) leading to the enantioenriched product **II**. Most likely, coordination proceed in a reversible fashion while the oxypalladation and/or the reductive elimination are irreversible thus constituting the enantiodeterming steps.



Scheme 17. Proposed reaction mechanism**.**

[a]An alternative *cis*-oxypalladation followed by isomerization cannot be excluded

E.2. NMR analysis of the equilibrium between Propargyl Amine 1, Tether 3 and hemiaminal I



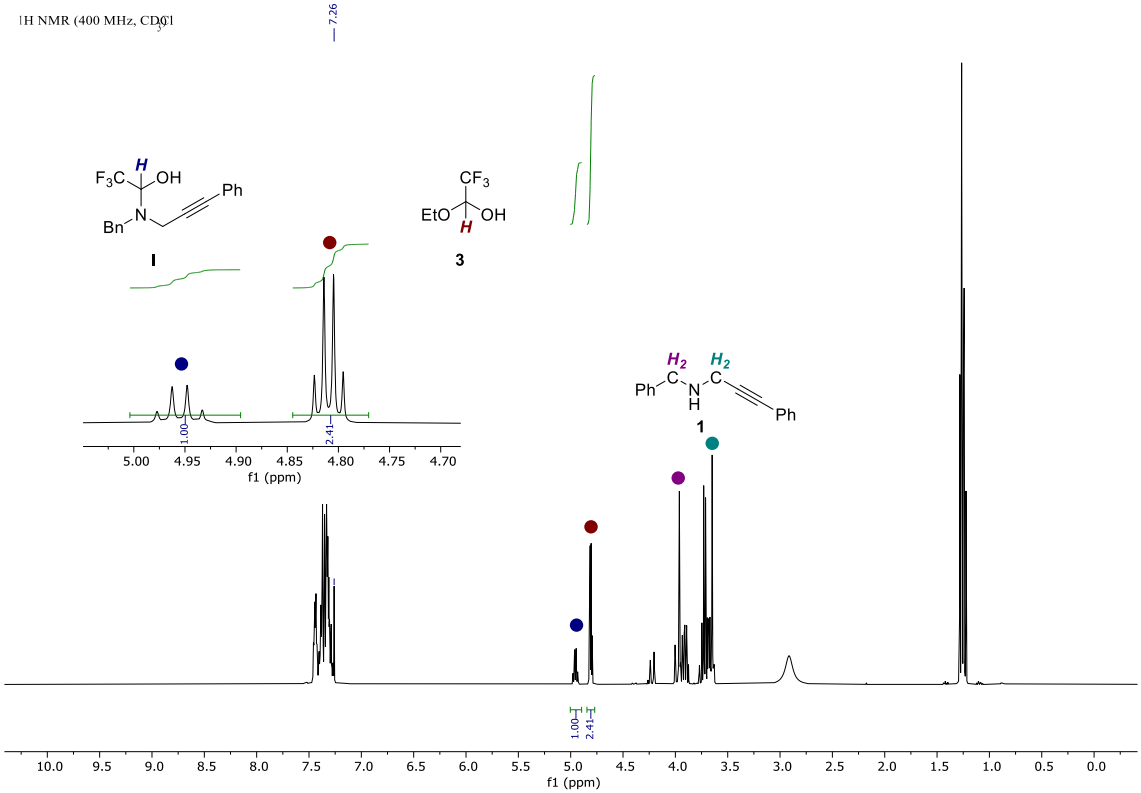
Scheme 18. Equilibrium between **1**, **3** and **I**.

An NMR tube (180×5 mm) was charged with propargylic amine **1** (21.5 µL, 22.0 mg, 0.10 mmol, 1.0 equiv) and 1-ethoxy-2,2,2-trifluoroethanol **3** (85% in EtOH, 19 uL, 0.14 mmol, 1.4 equiv.) and $CDCl_3$ (1.0 mL). ^{1}H NMR spectra was obtained using the following acquisition parameters: pulse program zg30, TD 65536, NS 16, D1 1.00000000 s, TE 298.0 K.

The integral ratio between the C*H*CF_3 protons of the heminal **I** and **3** was found to be 1.00:2.41. By simple calculation:

$$\begin{cases} [\mathbf{3}] + [\mathbf{I}] = 140\ \mu M \\ [\mathbf{3}] = 2.41 \cdot [\mathbf{I}] \end{cases}$$

This corresponds to approx. 41% conversion of the propargyl amine **1** to the hemiaminal **I**.



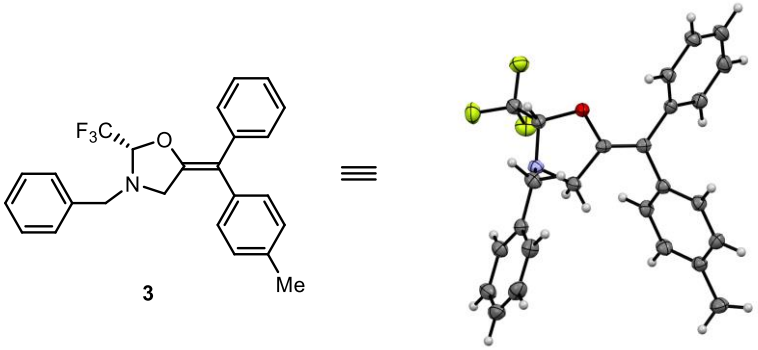
Scheme 19. ^{1}H-NMR spectrum of the equilibrium between **1**, **3** and **I**

F. X-Ray Crystallographic Data

F.1. Single Crystal X-Ray Diffraction for the chiral compound *(S)*-4

Crystals of the compound *(S)*-**4** were obtained by slow evaporation of a diethyl ether solution.

Data acquisition: Single clear pale colourless needle crystals of *(S)*-**4** were used as supplied. A suitable crystal with dimensions 0.78 × 0.13 × 0.07 mm^3 was selected and mounted on a SuperNova, Dual, Cu at home/near, Atlas diffractometer. The crystal was kept at a steady T = 140.01(10) K during data collection. The structure was solved with the **ShelXT** (Sheldrick, 2015) solution program using dual methods and by using **Olex 2** as the graphical interface. The model was refined with ShelXL 2018/3 (Sheldrick, 2015) using full matrix least squares minimisation on $\boldsymbol{F^2}$



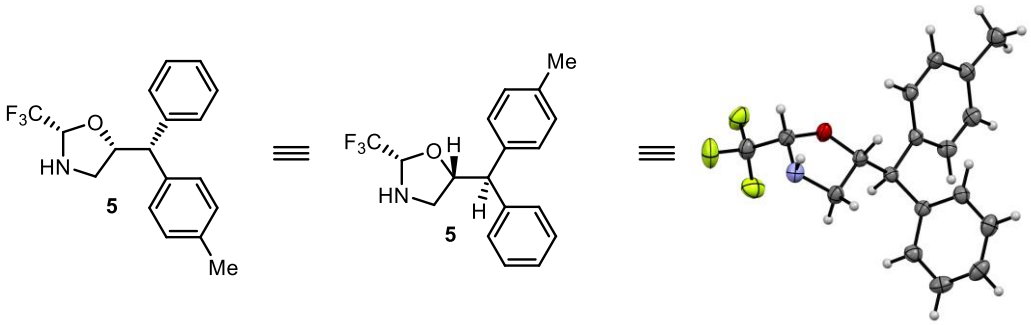
Scheme 20: Crystal data and structure refinement for ***(S)*-4. CCDC 2020478**

Compound	*(S)*-**4**
Formula	$C_{25}H_{22}F_3NO$
$D_{calc.}$/ g cm^{-3}	1.354
μ/mm^{-1}	0.843
Formula Weight	409.43
Colour	clear pale colourless
Shape	needle
Size/mm^3	0.78×0.13×0.07
T/K	140.01(10)
Crystal System	orthorhombic
Flack Parameter	0.02(5)
Hooft Parameter	0.04(4)
Space Group	$P2_12_12_1$
a/Å	5.80938(12)
b/Å	17.8312(3)
c/Å	19.3852(4)
α/°	90
β/°	90
γ/°	90
V/Å^3	2008.09(7)
Z	4
Z'	1
Wavelength/Å	1.54184
Radiation type	Cu K$_\alpha$
Θ_{min}/°	3.368
Θ_{max}/°	72.663
Measured Refl's.	14345
Ind't Refl's	3929
Refl's with I > 2σ(I)	3826
R_{int}	0.0255
Parameters	273
Restraints	0
Largest Peak	0.180
Deepest Hole	-0.155
GooF	1.048
wR_2 (all data)	0.0761
wR_2	0.0750
R_1 (all data)	0.0301
R_1	0.0291

F.2. Single Crystal X-Ray Diffraction for the chiral compound (*R,R*)-5

Crystals of the compound *(R,R)*-**5** were obtained by slow evaporation of an hexane/diethyl ether (10:1) solution.

Data Acquisition: Single clear pale colourless prism crystals of *(R,R)*-**5** were used as supplied. A suitable crystal with dimensions 0.23 × 0.17 × 0.09 mm^3 was selected and mounted on a SuperNova, Dual, Cu at home/near, AtlasS2 diffractometer. The crystal was kept at a steady T = 140.00(10) K during data collection. The structure was solved with the **ShelXT** (Sheldrick, 2015) solution program using dual methods and by using **Olex2** (Dolomanov et al., 2009) as the graphical interface. The model was refined with **ShelXL** 2018/3 (Sheldrick, 2015) using full matrix least squares minimisation on F^2.



Scheme 21: Crystal data and structure refinement for **5. CCDC2020479**

Compound	*(R,R)*-**5**
Formula	$C_{18}H_{18}F_3NO$
$D_{calc.}$/ g cm^{-3}	1.357
μ/mm^{-1}	0.916
Formula Weight	321.33
Colour	clear pale colourless
Shape	prism
Size/mm^3	0.23×0.17×0.09
T/K	140.00(10)
Crystal System	orthorhombic
Flack Parameter	0.01(7)
Hooft Parameter	0.05(5)
Space Group	$P2_12_12_1$
a/Å	5.83034(13)
b/Å	8.00767(18)
c/Å	33.6790(7)
α/°	90
β/°	90
γ/°	90
V/Å^3	1572.38(6)
Z	4
Z'	1
Wavelength/Å	1.54184
Radiation type	Cu K$_\alpha$
Θ_{min}/°	5.253
Θ_{max}/°	72.678
Measured Refl's.	3094
Ind't Refl's	3094
Refl's with I > 2σ(I)	2974
R_{int}	.
Parameters	218
Restraints	0
Largest Peak	0.336
Deepest Hole	-0.220
GooF	1.120
wR_2 (all data)	0.1374
wR_2	0.1360
R_1 (all data)	0.0468
R_1	0.0454

G. References

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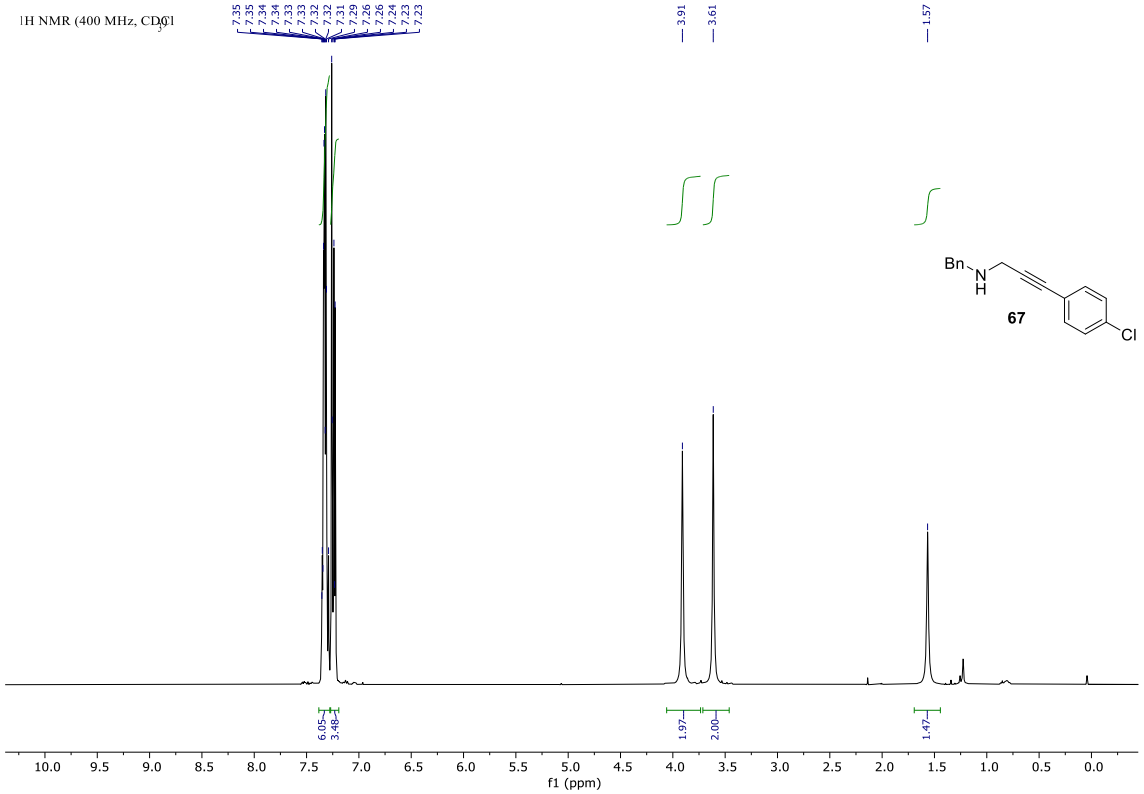
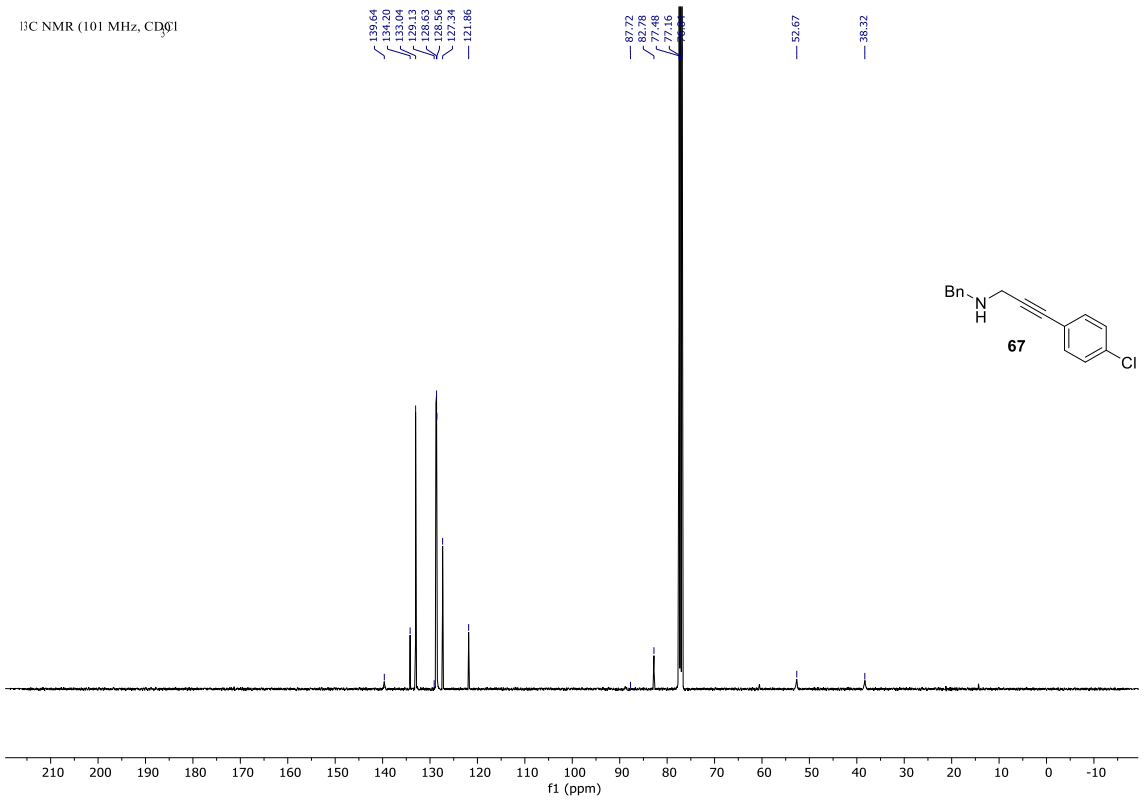
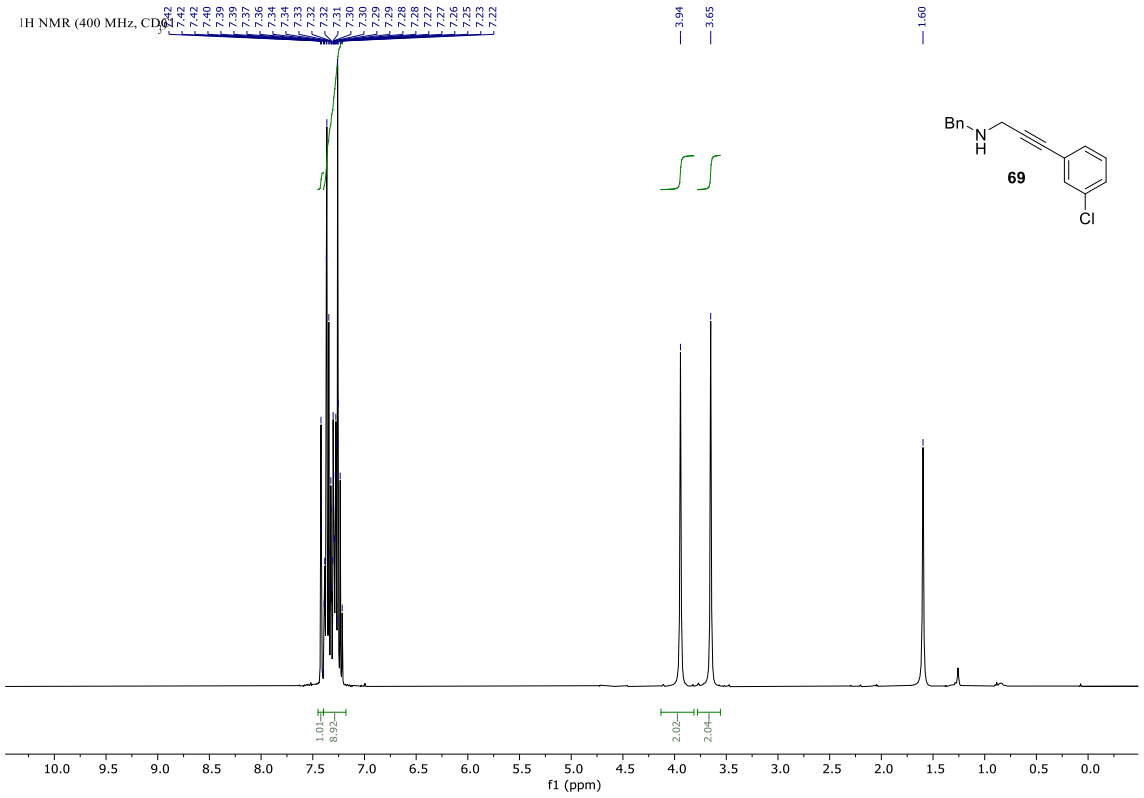
H. NMR Spectra

H.1.Starting Materials



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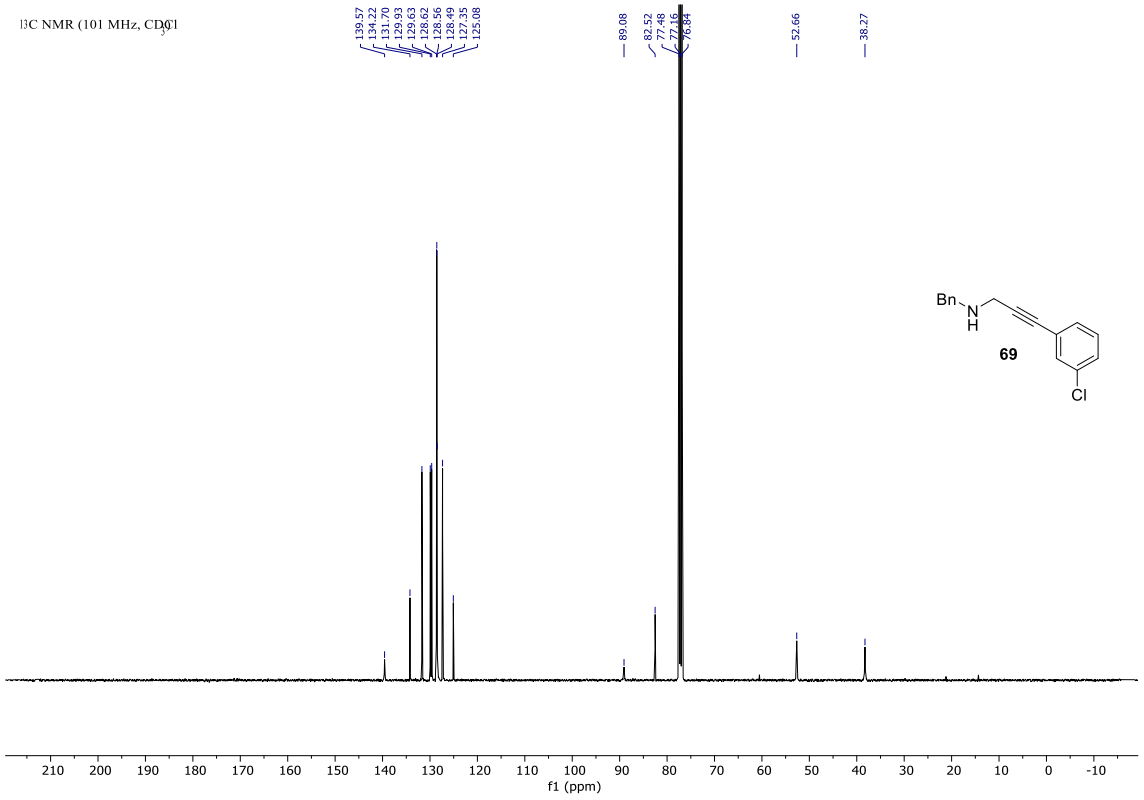
7.42
7.42
7.40
7.39
7.39
7.37
7.36
7.34
7.34
7.33
7.32
7.32
7.31
7.30
7.30
7.29
7.29
7.28
7.28
7.27
7.27
7.26
7.25
7.23
7.22
3.94
3.65
1.60
Bn
N
H
69
Cl
1.01
8.92
2.02
2.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)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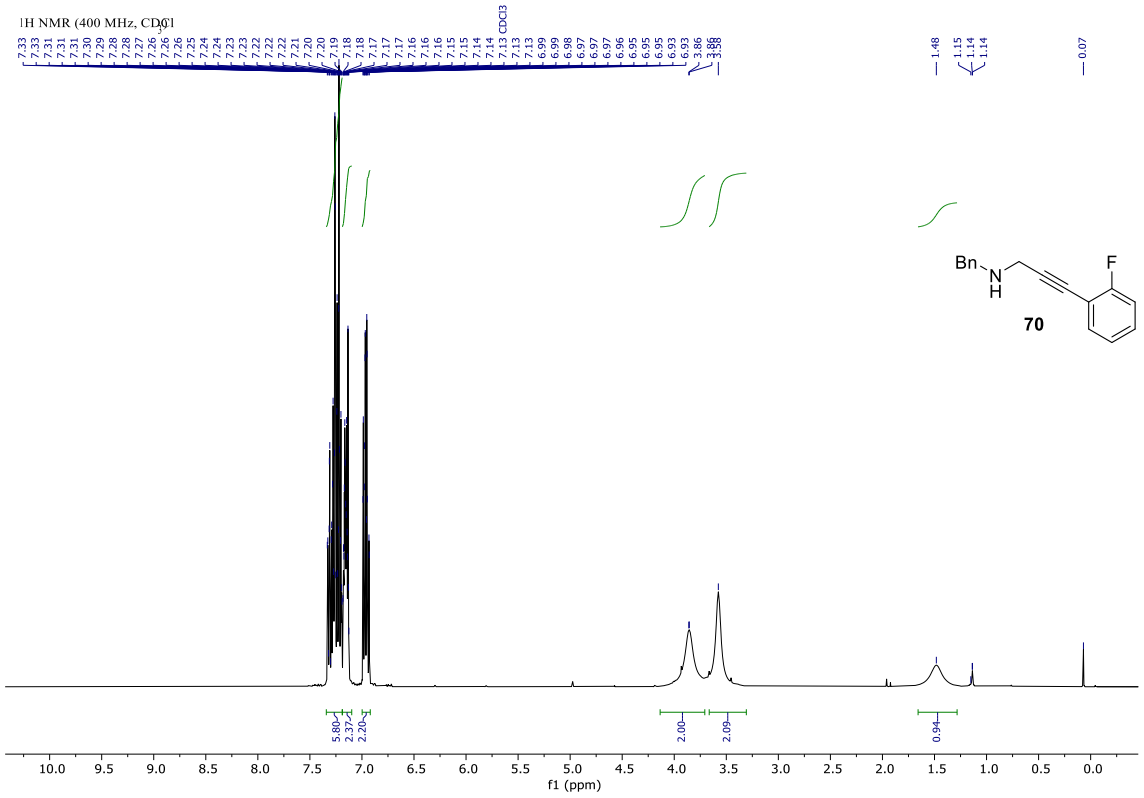
139.57
134.22
131.70
129.93
129.63
128.62
128.56
128.49
127.35
125.08
89.08
82.52
77.48
77.16
76.84
52.66
38.27
Bn
N
H
69
Cl
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)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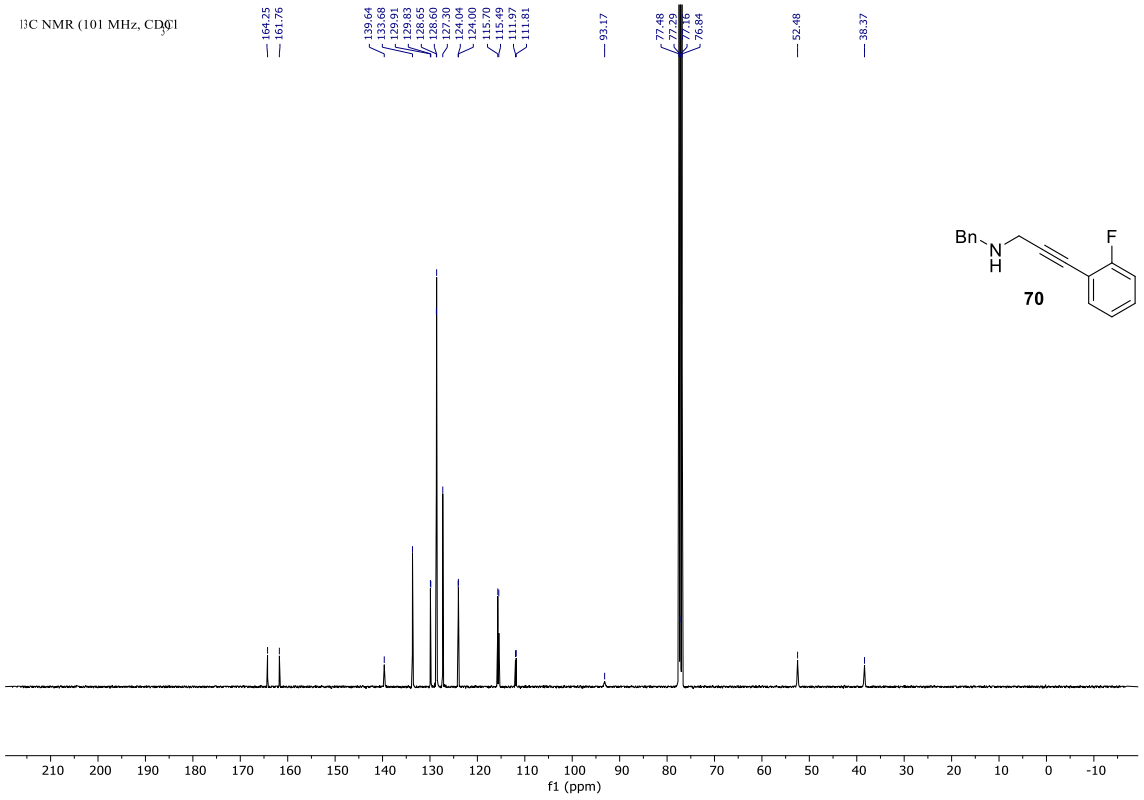
Bn
N
H
F
70
f1 (ppm)


13C NMR (101 MHz, CDCl3)
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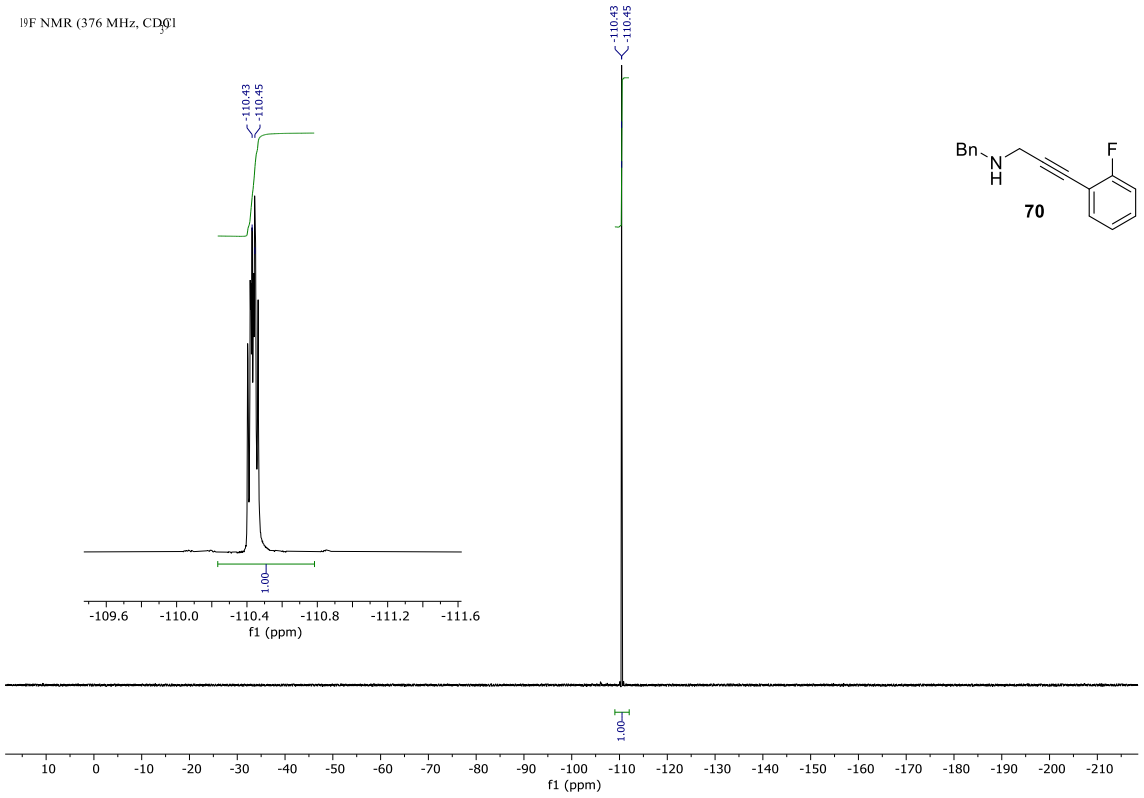
N
H
F
70
f1 (ppm)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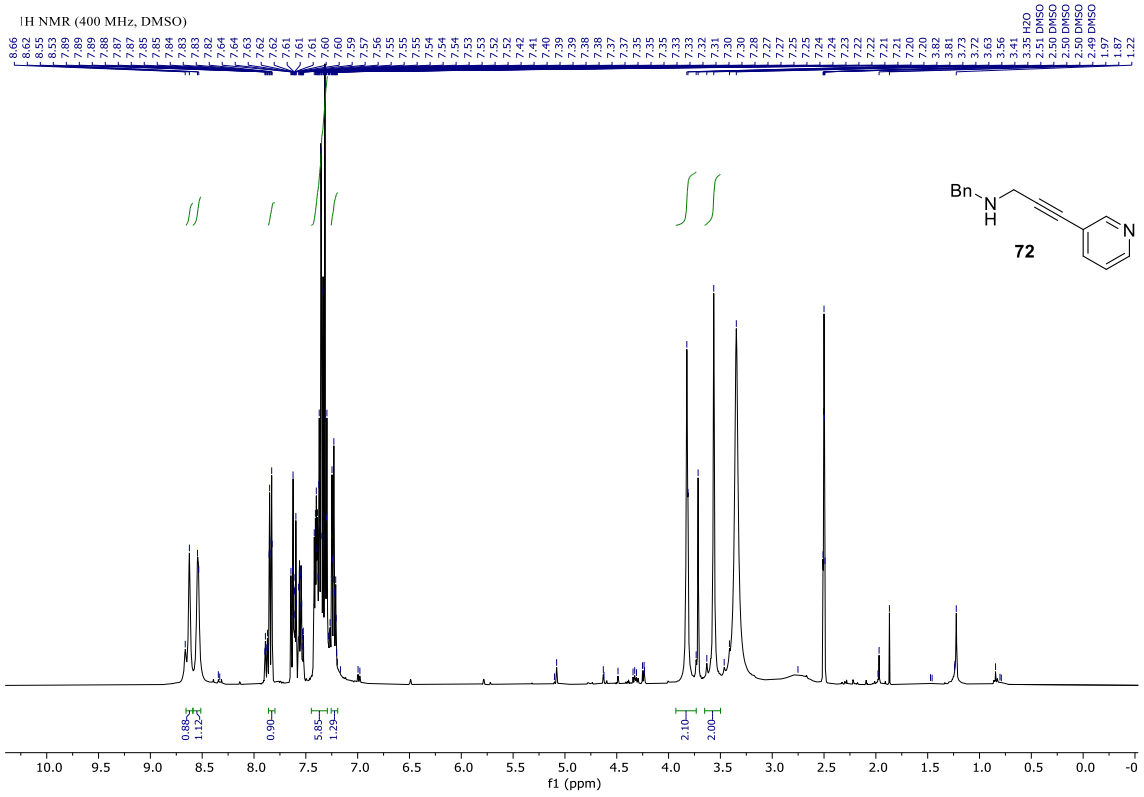
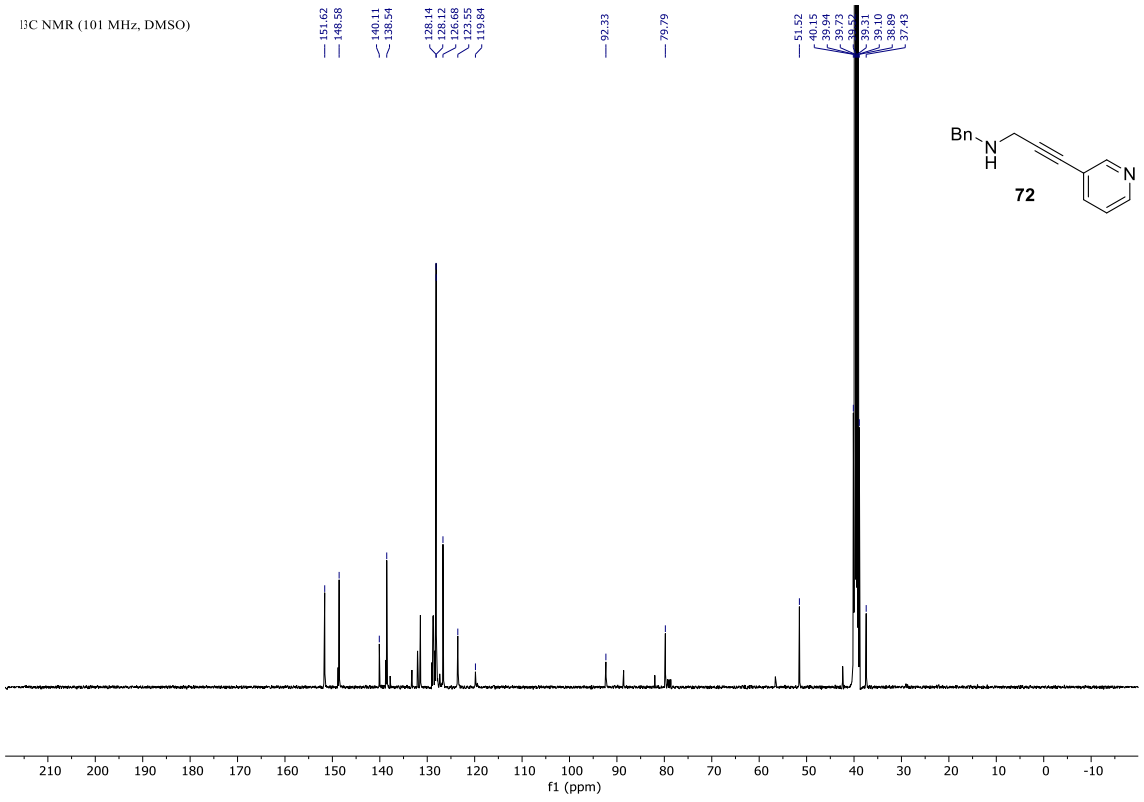
-110.43
-110.45
1.00
-109.6
-110.0
-110.4
-110.8
-111.2
-111.6
f1 (ppm)
Bn
N
H
F
70
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)


1H NMR (400 MHz, DMSO)
3.35 H2O
2.51 DMSO
2.50 DMSO
2.50 DMSO
2.50 DMSO
2.49 DMSO
0.88
1.12
0.90
5.85
1.29
2.10
2.00
Bn
N
H
N
72
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)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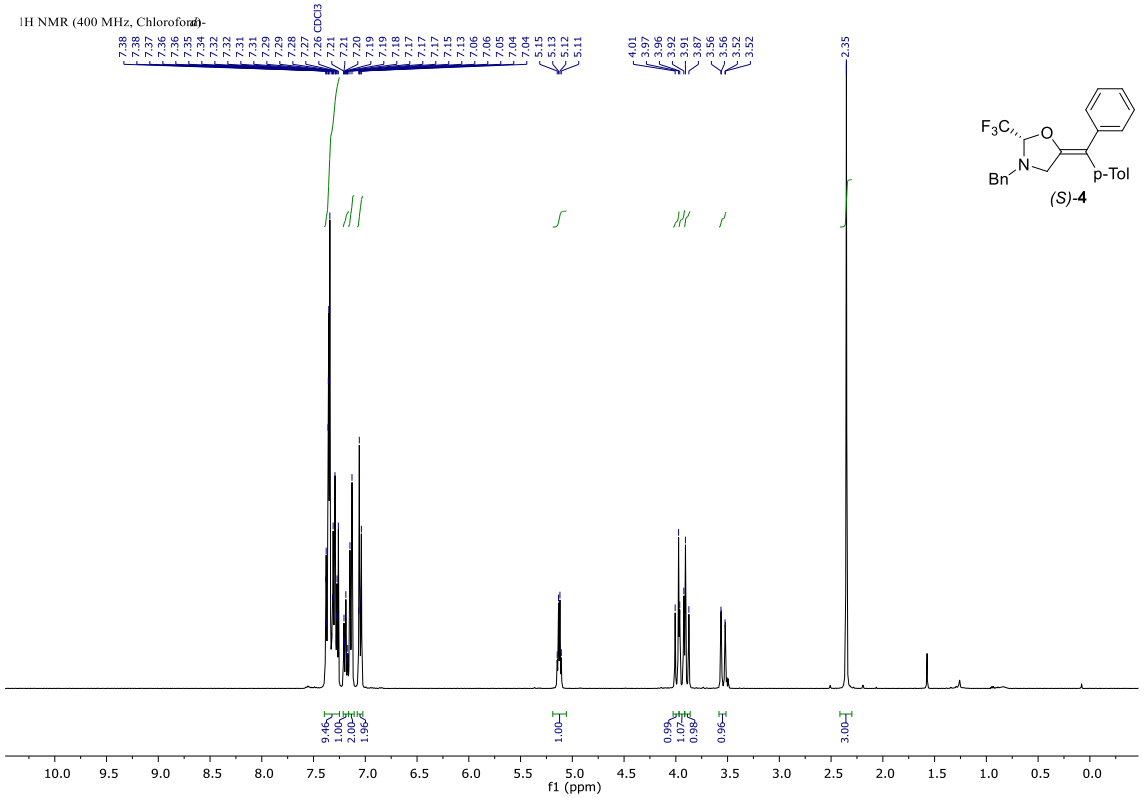
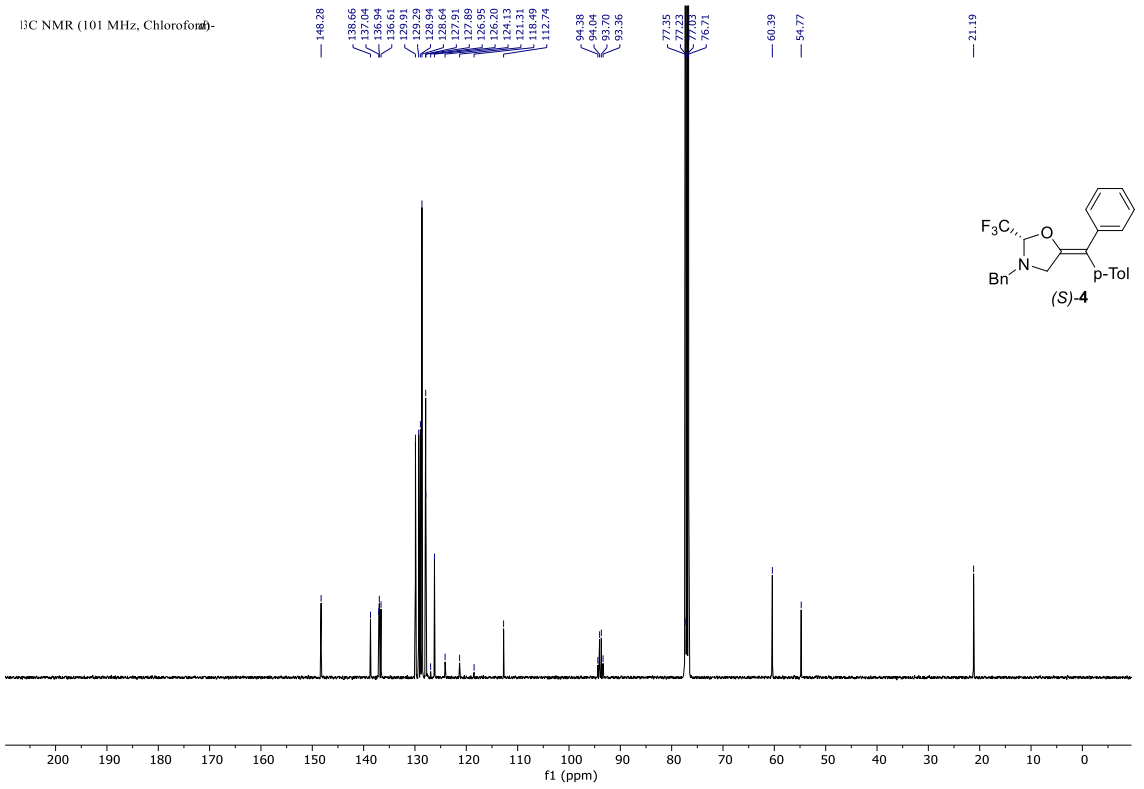
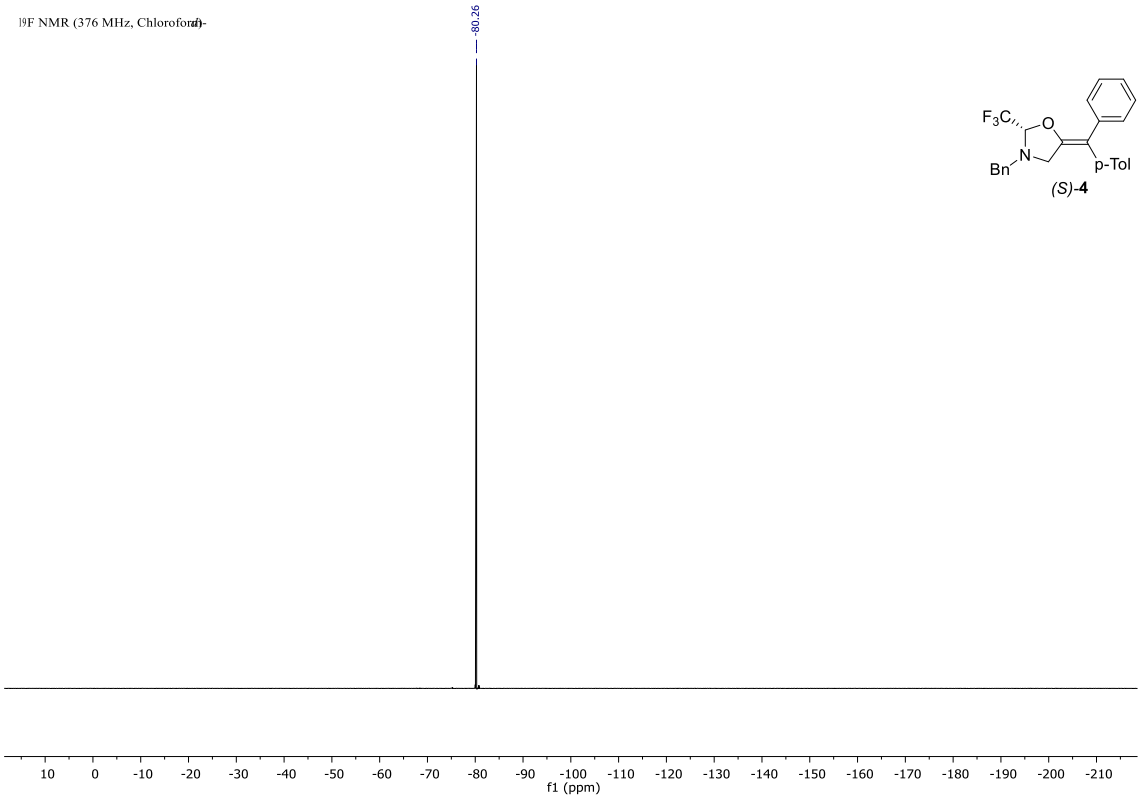
151.62
148.58
140.11
138.54
128.14
128.12
126.68
123.55
119.84
92.33
79.79
51.52
40.15
39.94
39.73
39.52
39.31
39.10
38.89
37.43
Bn
N
H
N
72
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)

H.2.Carboetherification Products



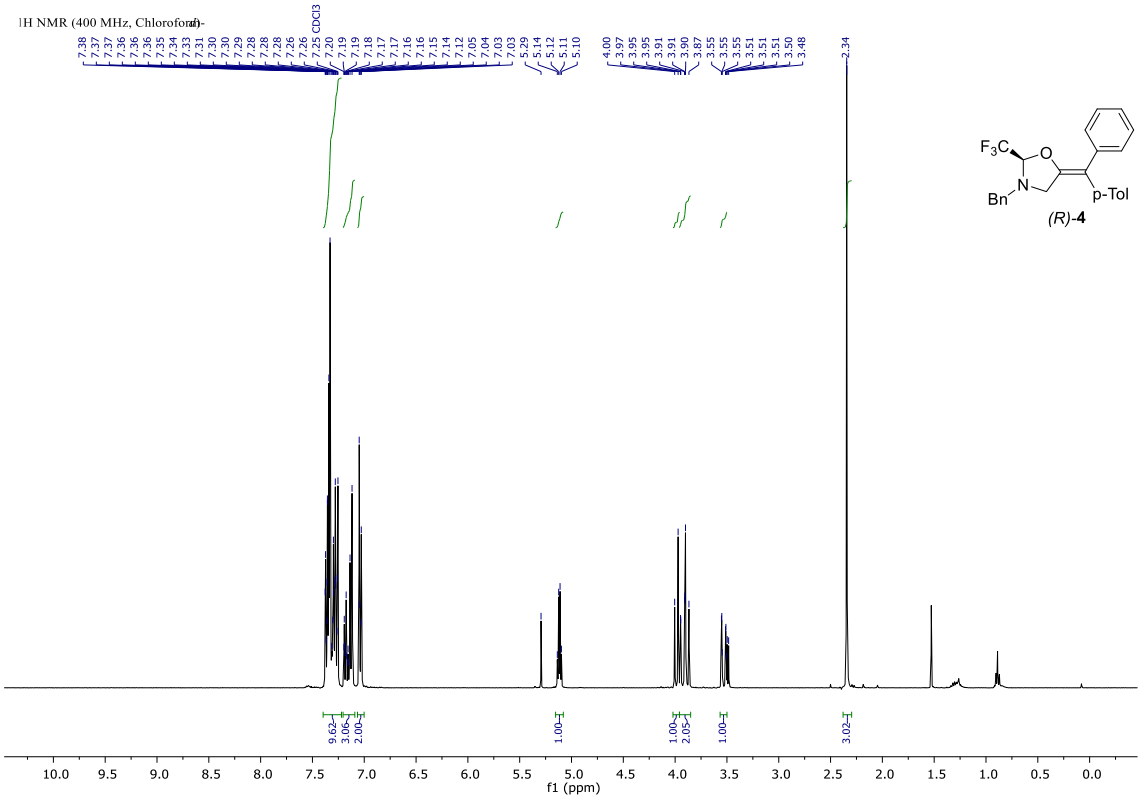


^{19}F NMR (376 MHz, Chloroform-*d*)



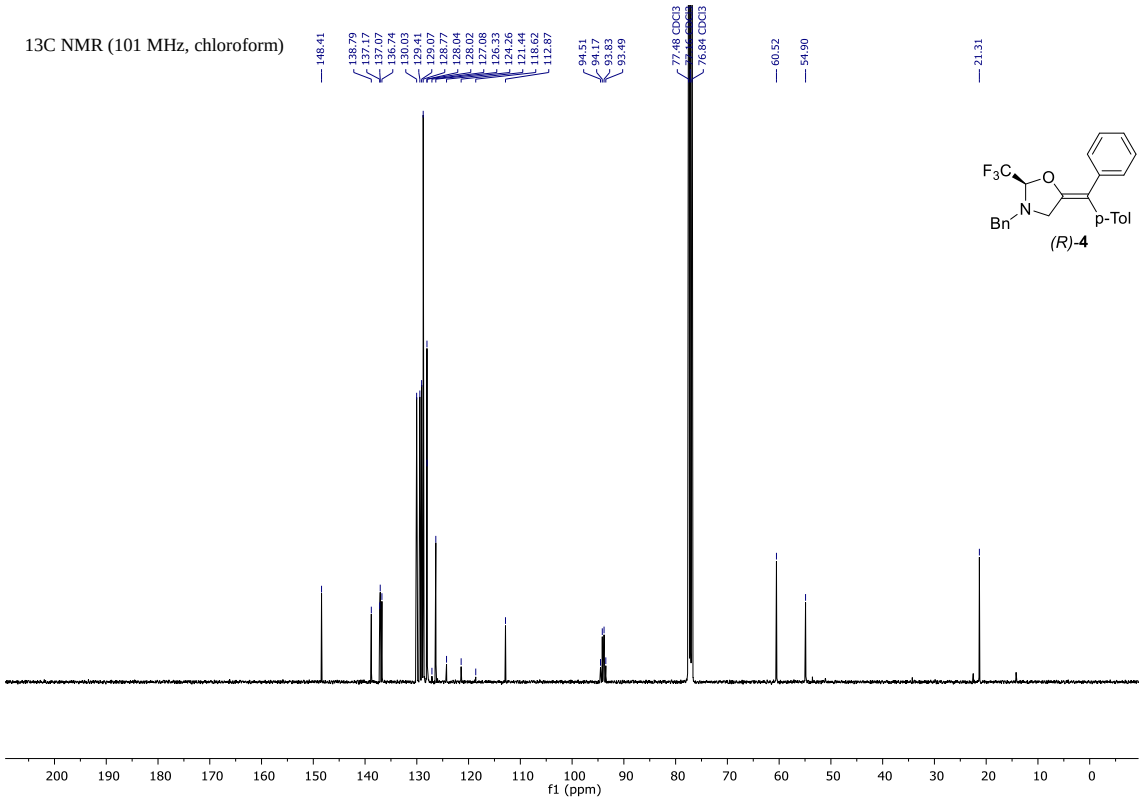
(S)-**4**

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

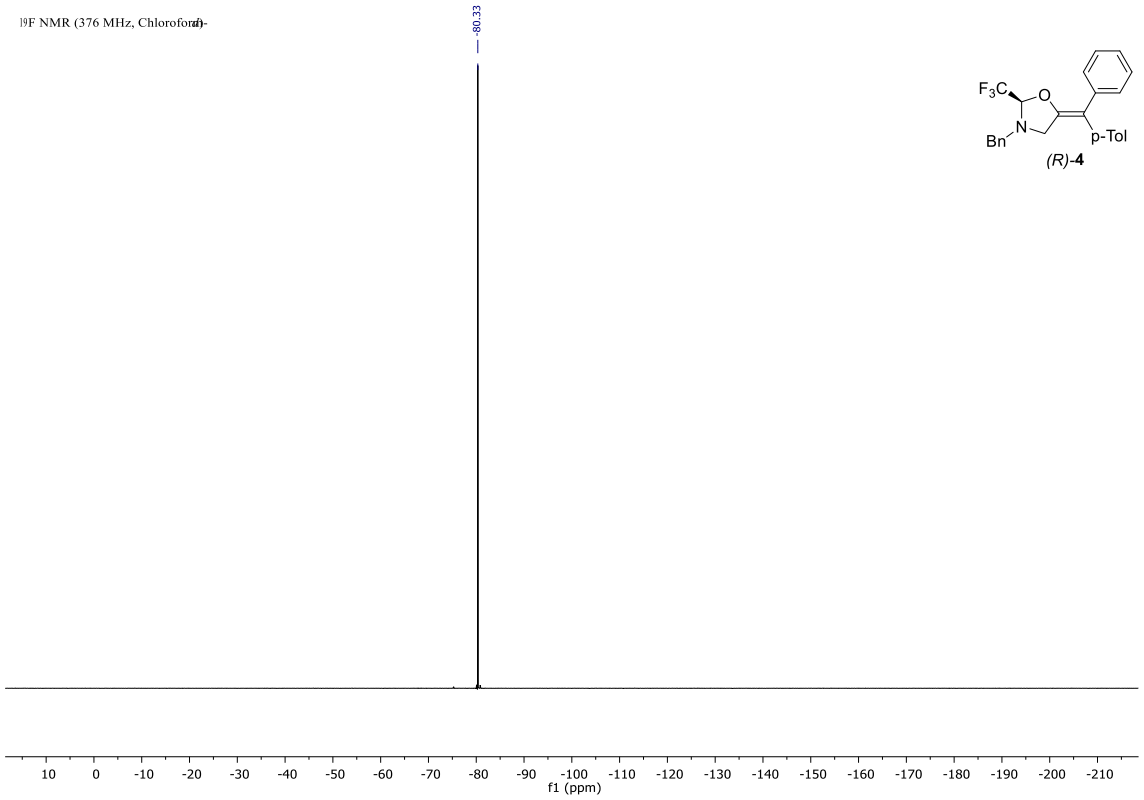


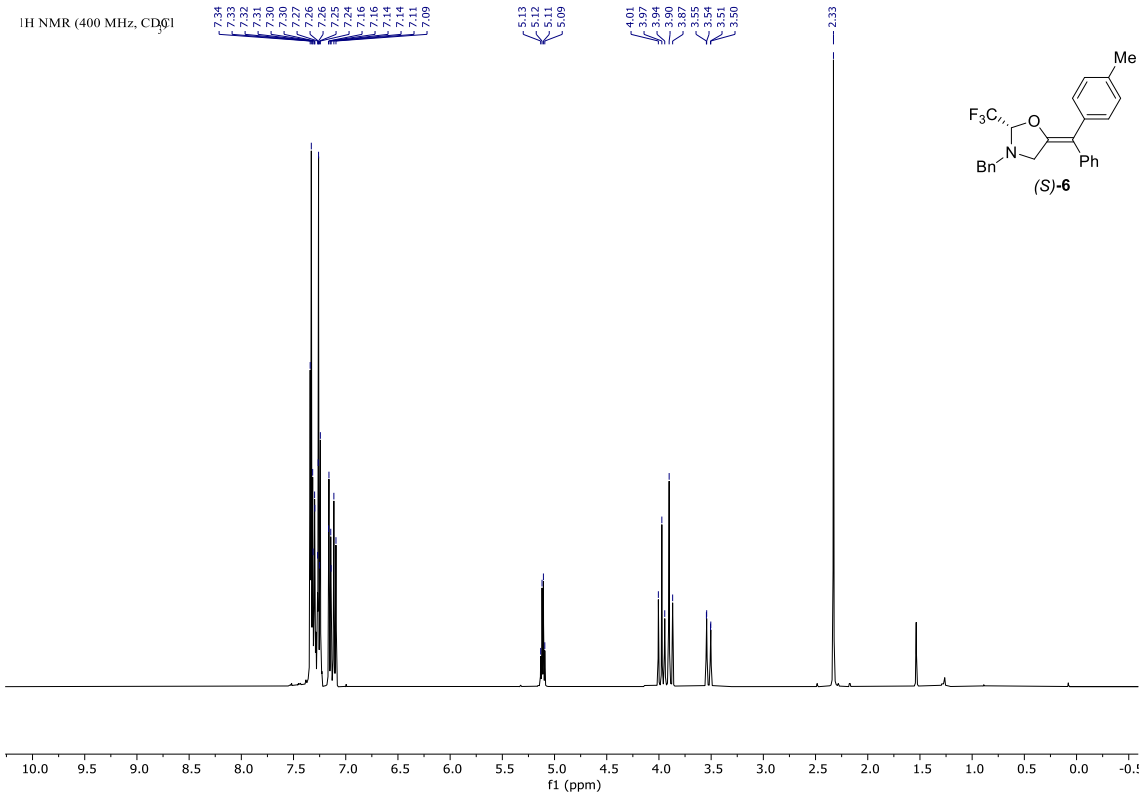
(R)-**4**

13C NMR (101 MHz, chloroform)



19F NMR (376 MHz, Chloroform-*d*)




1H NMR (400 MHz, CDCl3)
7.34
7.33
7.32
7.31
7.30
7.30
7.27
7.26
7.25
7.24
7.16
7.16
7.14
7.14
7.11
7.09
5.13
5.12
5.11
5.09
4.01
3.97
3.94
3.90
3.87
3.55
3.54
3.51
3.50
2.33
Me
F3C
O
N
Bn
Ph
(S)-6
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
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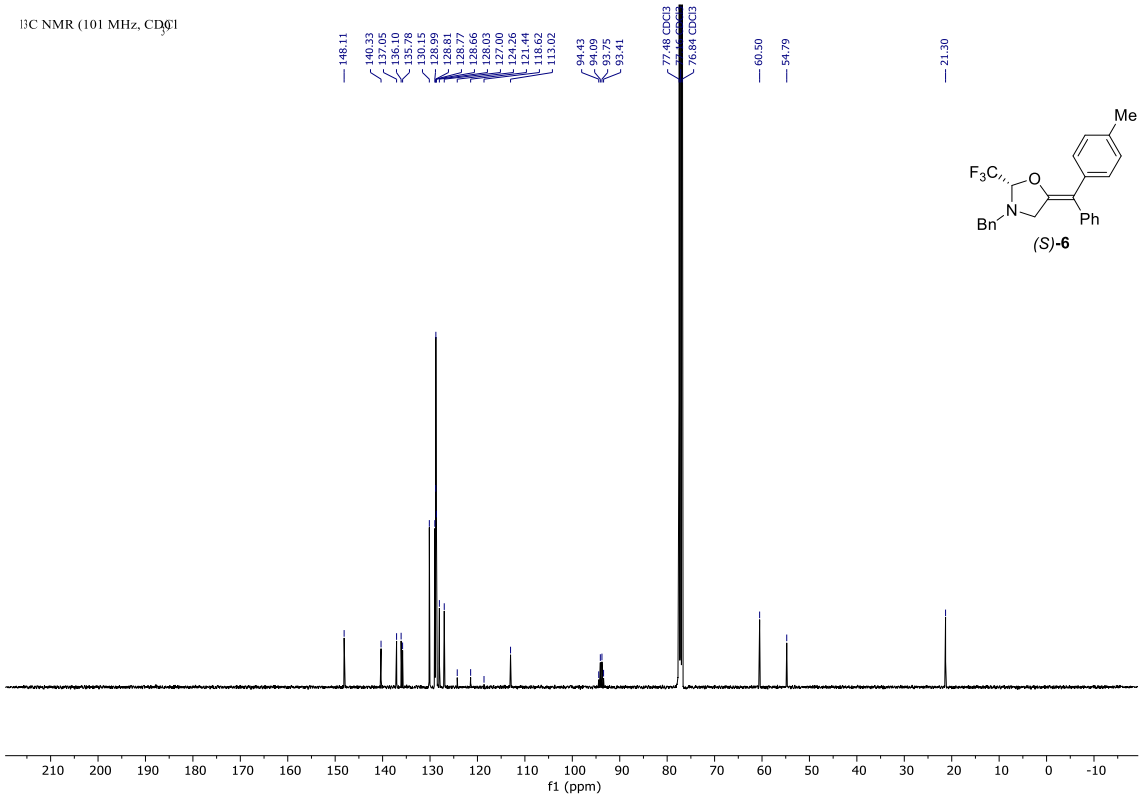
1.5
1.0
0.5
0.0
f1 (ppm)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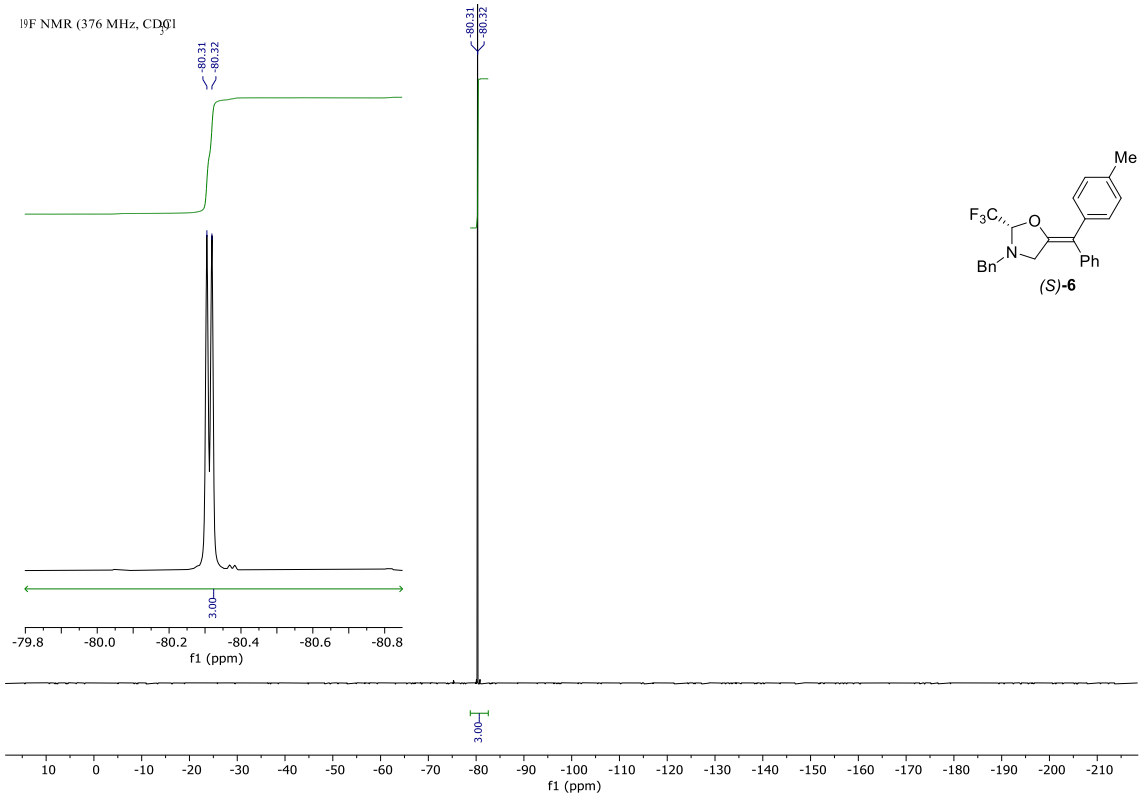
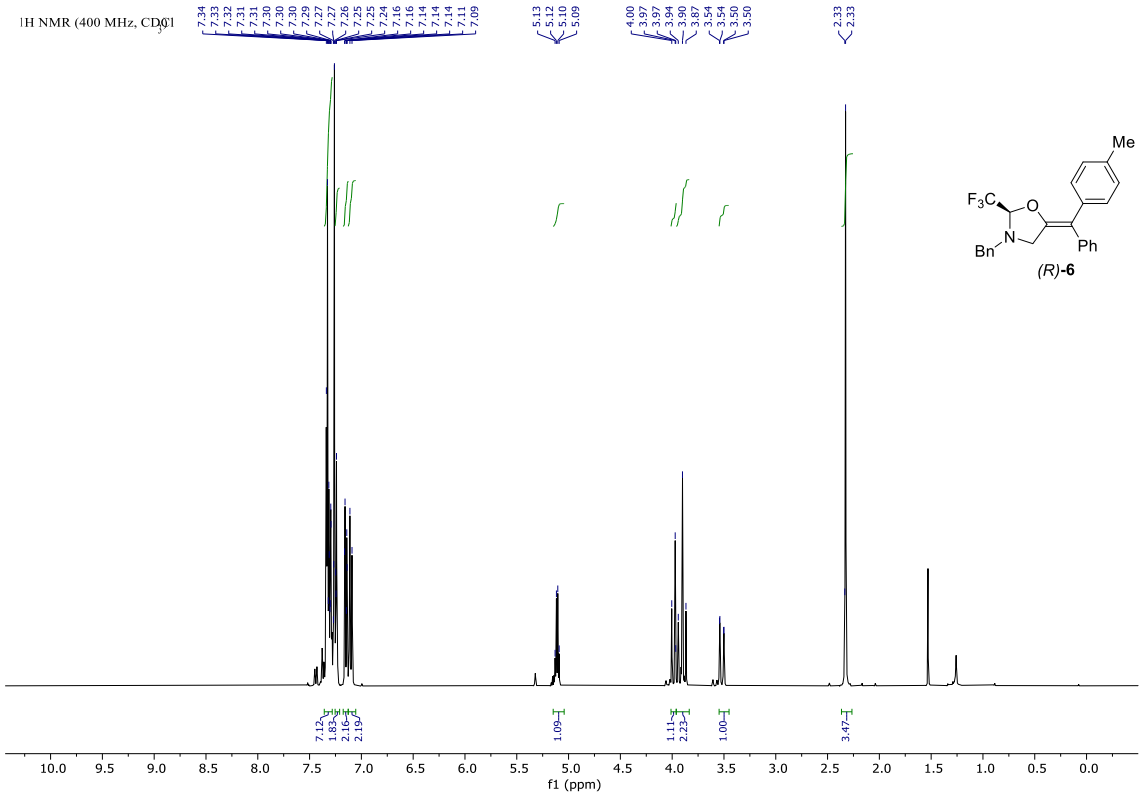
135.78
130.15
128.99
128.81
128.77
128.66
128.03
127.00
124.26
121.44
118.62
113.02
94.43
94.09
93.75
93.41
77.48 CDCl3
76.84 CDCl3
60.50
54.79
21.30
Me
F3C
O
N
Bn
Ph
(S)-6
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


19F NMR (376 MHz, CDCl3)
-80.31
-80.32
3.00
-79.8
-80.0
-80.2
-80.4
-80.6
-80.8
f1 (ppm)
3.00
10
0
-10
-20
-30
-40
-50
-60
-70
-80
-90
-100
-110
-120
-130
-140
-150
-160
-170
-180
-190
-200
-210
f1 (ppm)
Me
F3C
O
N
Bn
Ph
(S)-6


1H NMR (400 MHz, CDCl3)
7.34
7.33
7.32
7.31
7.31
7.30
7.30
7.30
7.29
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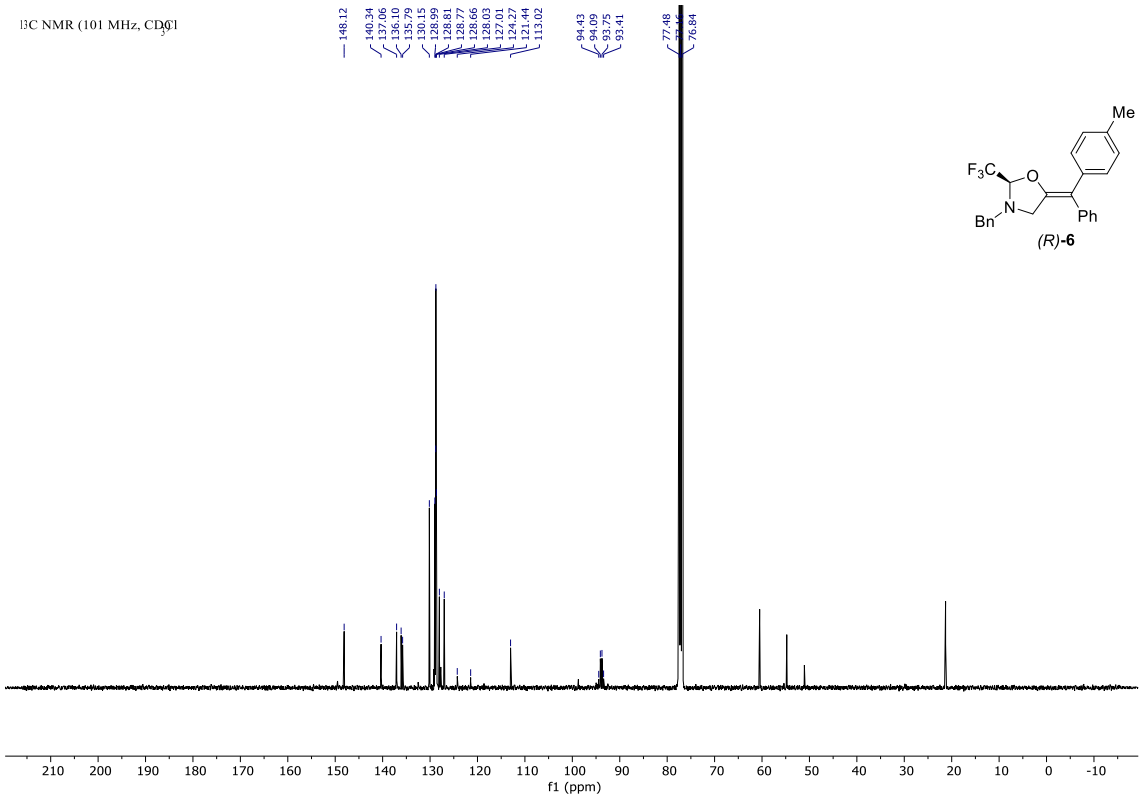
7.27
7.26
7.25
7.25
7.24
7.16
7.16
7.14
7.14
7.14
7.11
7.09
5.13
5.12
5.10
5.09
4.00
3.97
3.97
3.94
3.90
3.87
3.54
3.54
3.50
3.50
2.33
2.33
7.12
1.83
2.16
2.19
1.09
1.11
2.23
1.00
3.47
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
Me
F3C
O
N
Bn
Ph
(R)-6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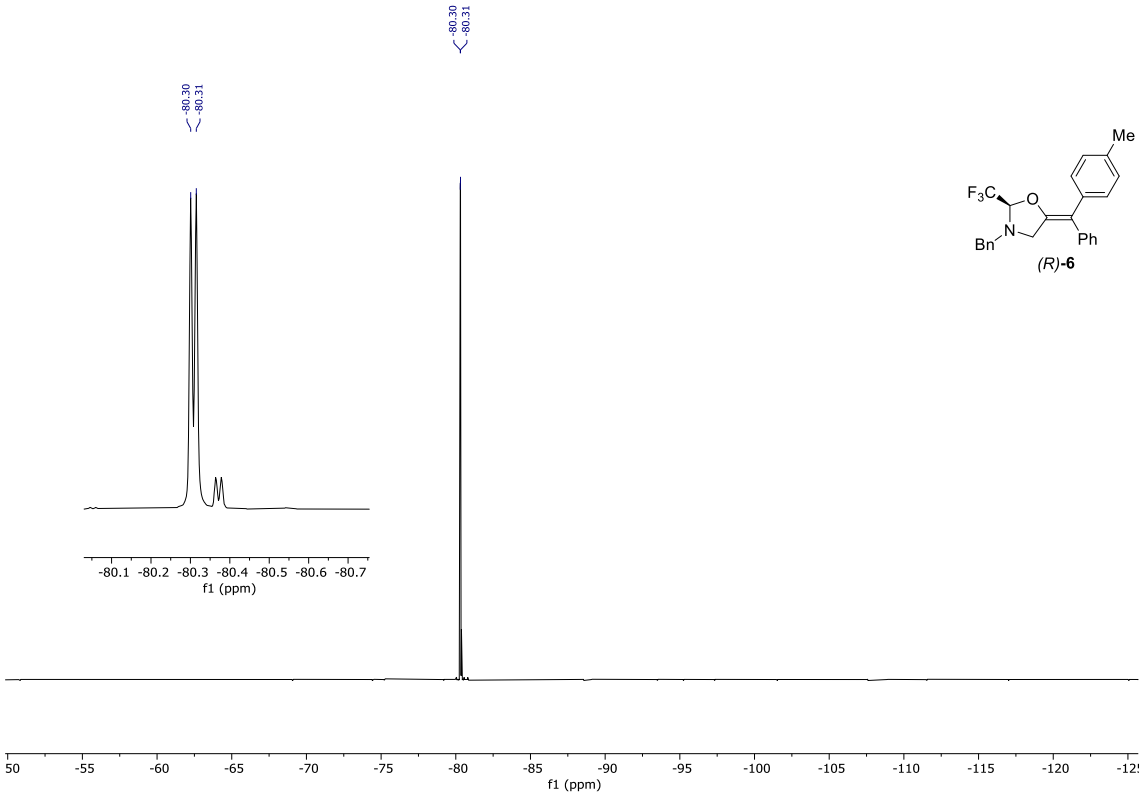
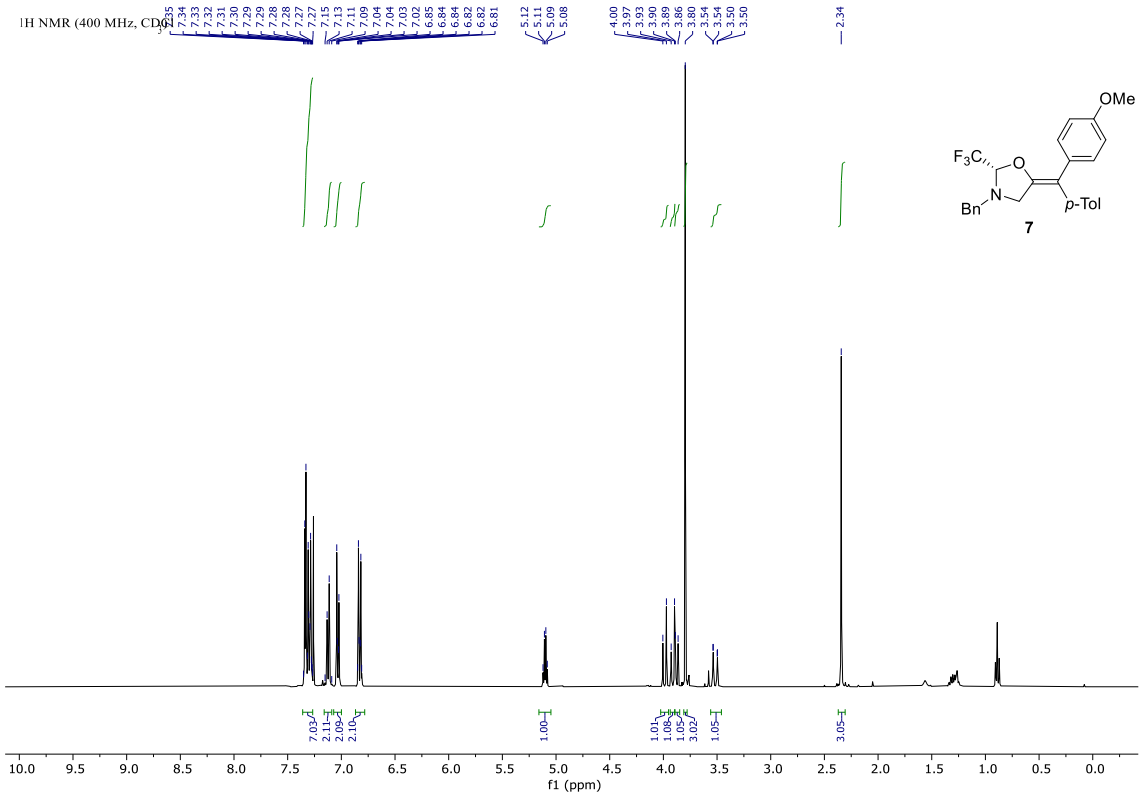
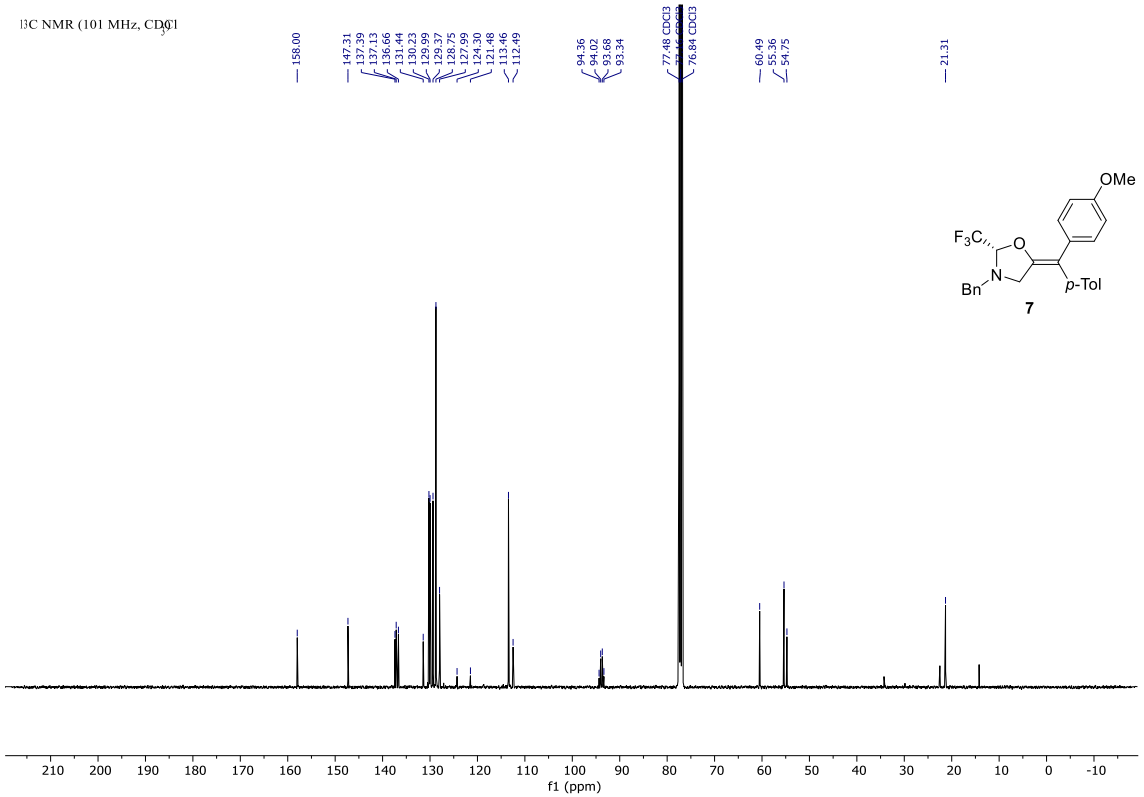
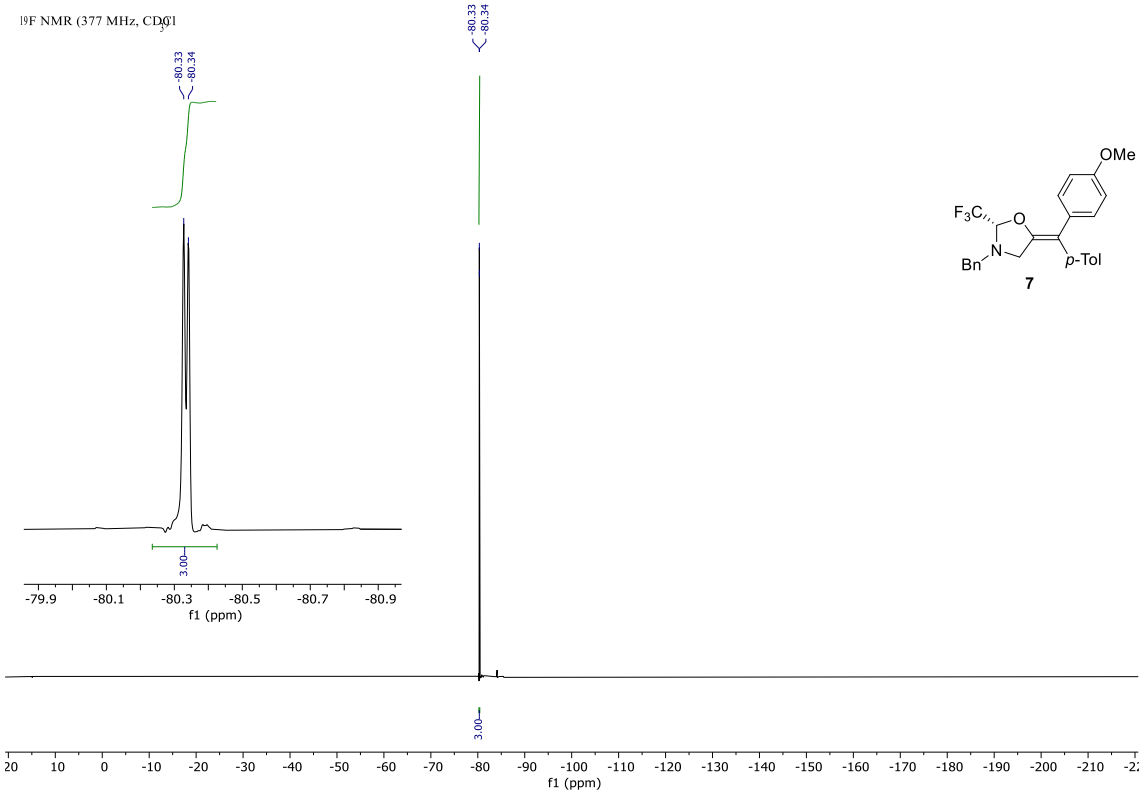
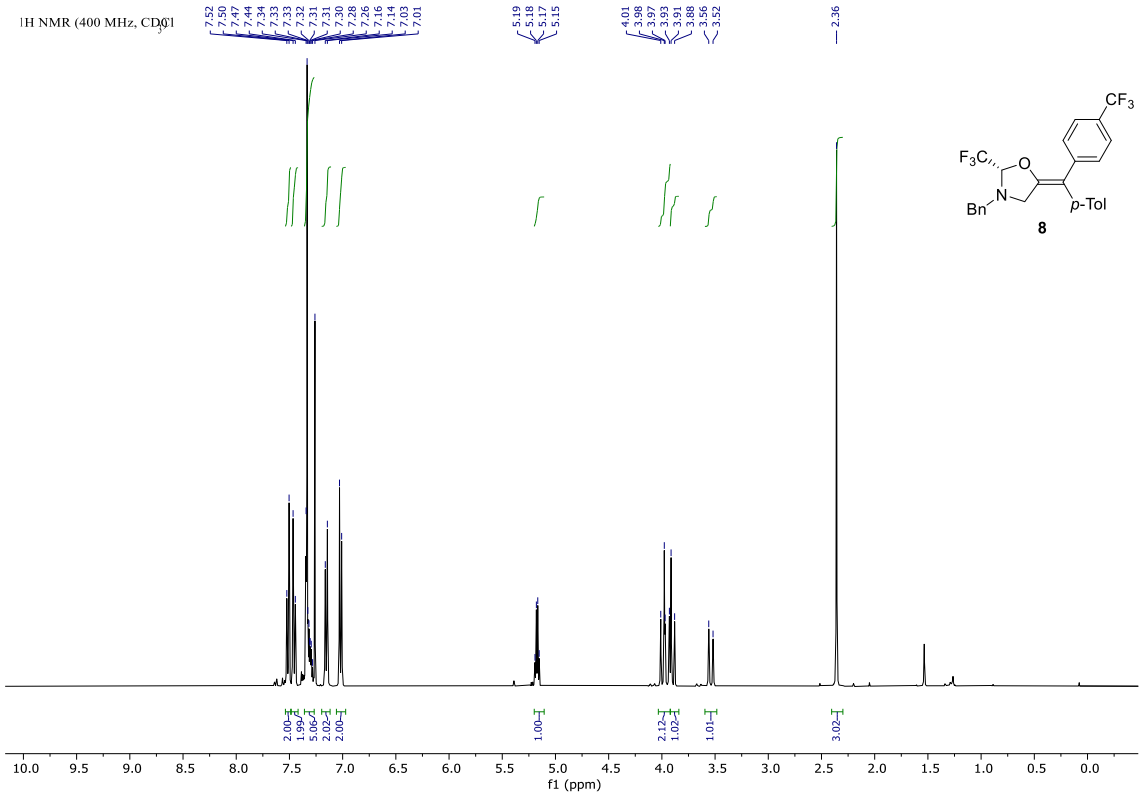
148.12
140.34
137.06
136.10
130.79
130.15
128.99
128.81
128.77
128.66
128.03
127.01
124.27
121.44
113.02
94.43
94.09
93.75
93.41
77.48
77.16
76.84
Me
F3C
O
N
Bn
Ph
(R)-6
f1 (ppm)

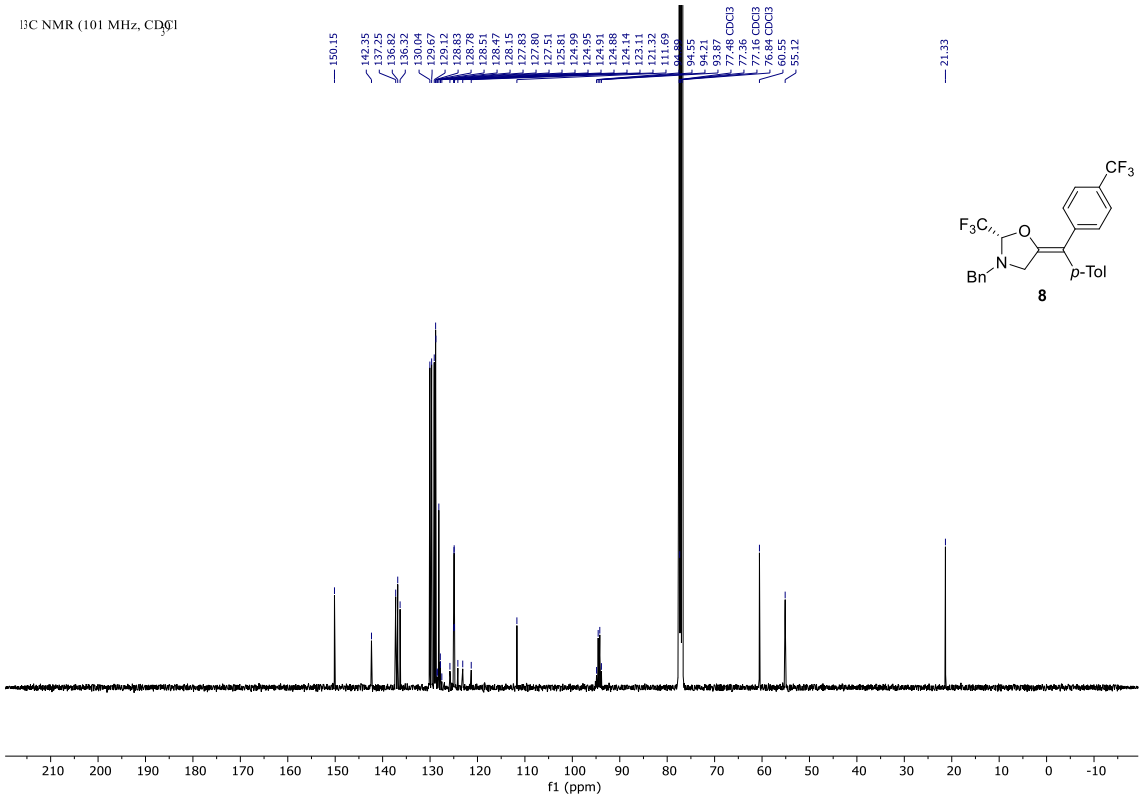

-80.30
-80.31
-80.1 -80.2 -80.3 -80.4 -80.5 -80.6 -80.7
f1 (ppm)
Me
F3C
O
N
Bn
Ph
(R)-6
f1 (ppm)

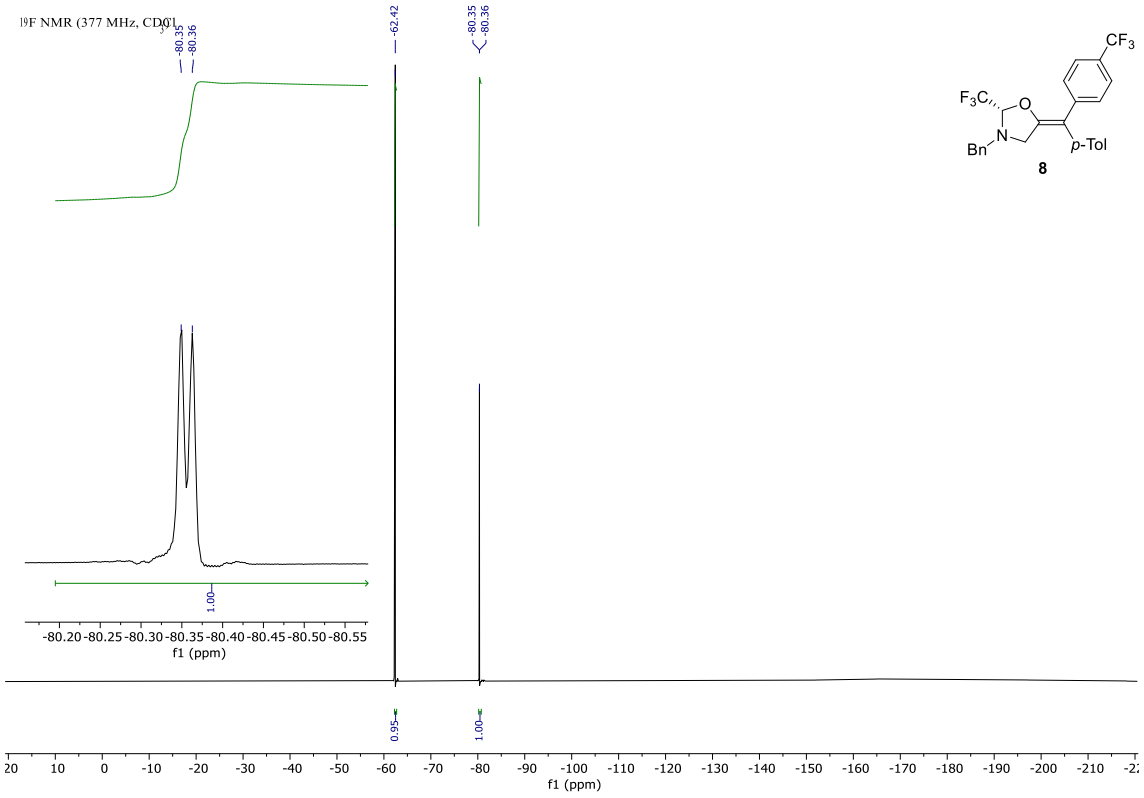

1H NMR (400 MHz, CDCl3)
OMe
F3C
O
N
Bn
p-Tol
7
f1 (ppm)

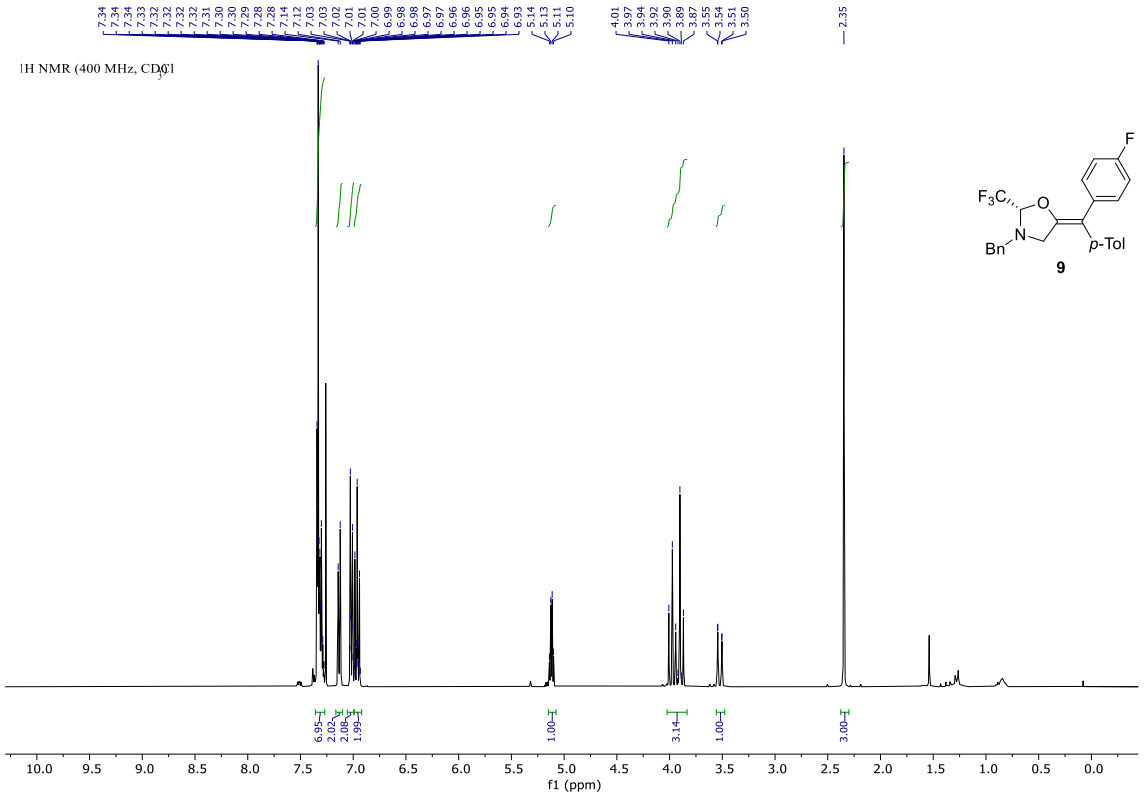

13C NMR (101 MHz, CDCl3)
OMe
F3C
O
N
Bn
p-Tol
7
f1 (ppm)

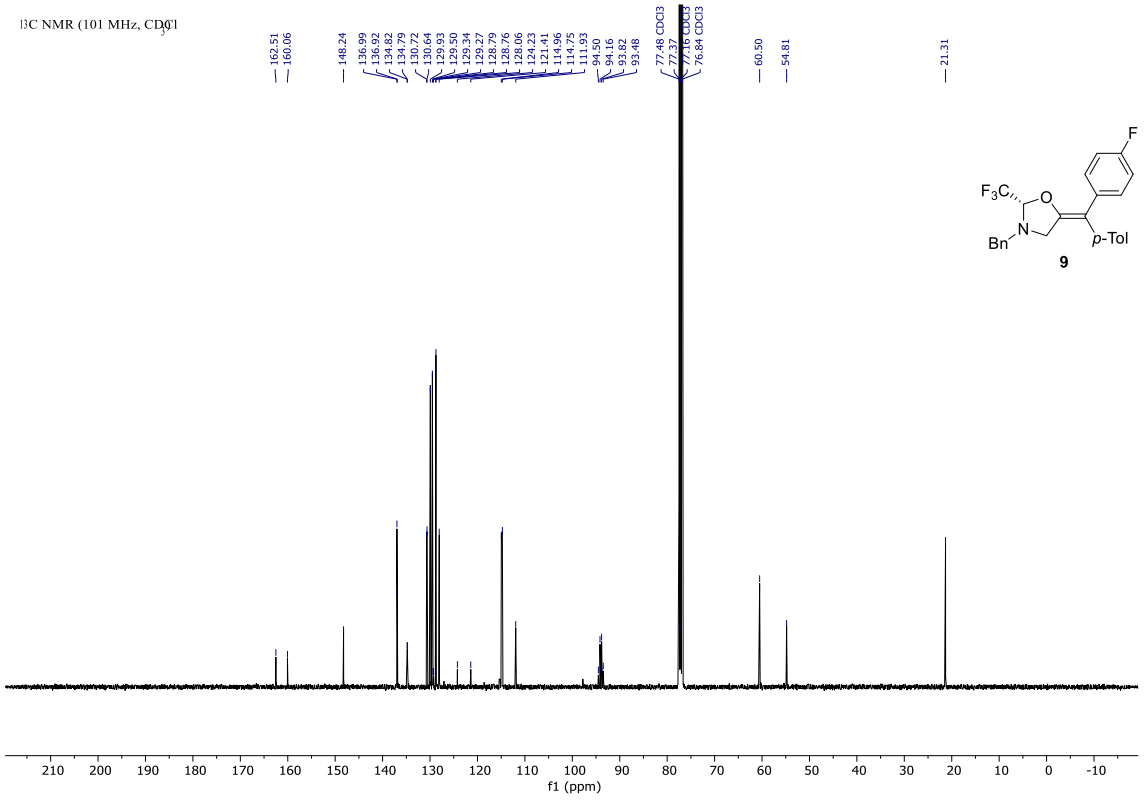

19F NMR (377 MHz, CDCl3)
-80.33
-80.34
3.00
-79.9
-80.1
-80.3
-80.5
-80.7
-80.9
f1 (ppm)
OMe
F3C
O
N
Bn
p-Tol
7

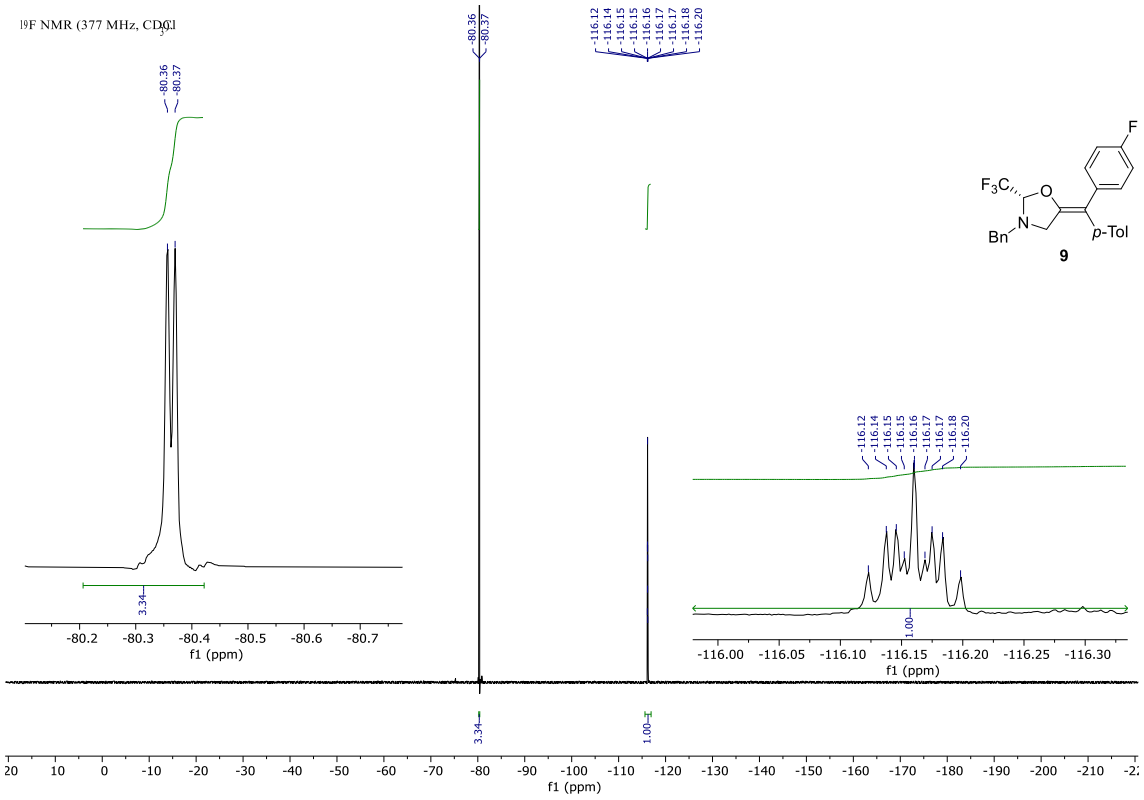

1H NMR (400 MHz, CDCl3)
7.52
7.50
7.47
7.44
7.34
7.33
7.32
7.31
7.31
7.30
7.28
7.26
7.16
7.14
7.03
7.01
5.19
5.18
5.17
5.15
4.01
3.98
3.97
3.93
3.91
3.88
3.56
3.52
2.36
2.00
1.99
5.06
2.02
2.00
1.00
2.12
1.02
1.01
3.02
f1 (ppm)
CF3
F3C
O
N
Bn
p-Tol
8

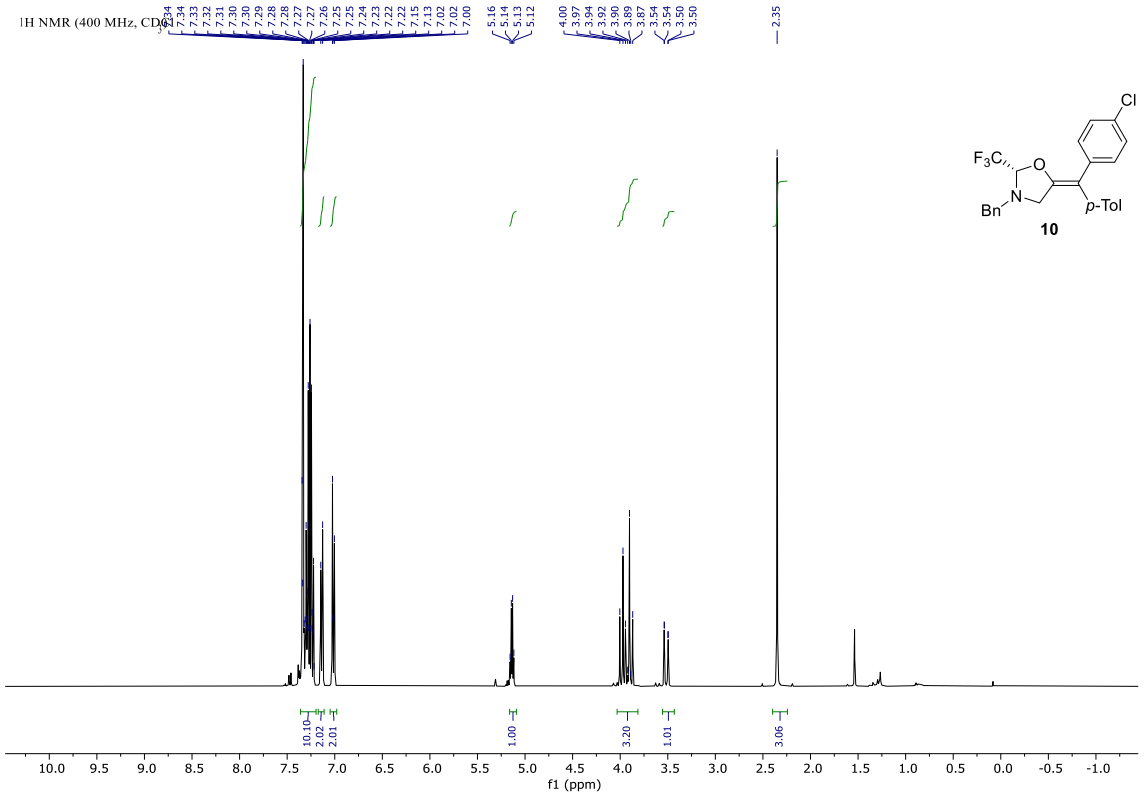

13C NMR (101 MHz, CDCl3)
150.15
142.35
137.25
136.82
136.32
130.04
129.67
129.12
128.83
128.78
128.51
128.47
128.15
127.83
127.80
127.51
125.81
124.99
124.95
124.91
124.88
124.14
123.11
121.32
111.69
94.55
94.21
93.87
77.36
77.16 CDCl3
76.84 CDCl3
60.55
55.12
21.33
CF3
F3C
O
N
Bn
p-Tol
8
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)


19F NMR (377 MHz, CDCl3)
-80.35
-80.36
-62.42
-80.35
-80.36
CF3
F3C
O
N
Bn
p-Tol
8
1.00
-80.20 -80.25 -80.30 -80.35 -80.40 -80.45 -80.50 -80.55
f1 (ppm)
0.95
1.00
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

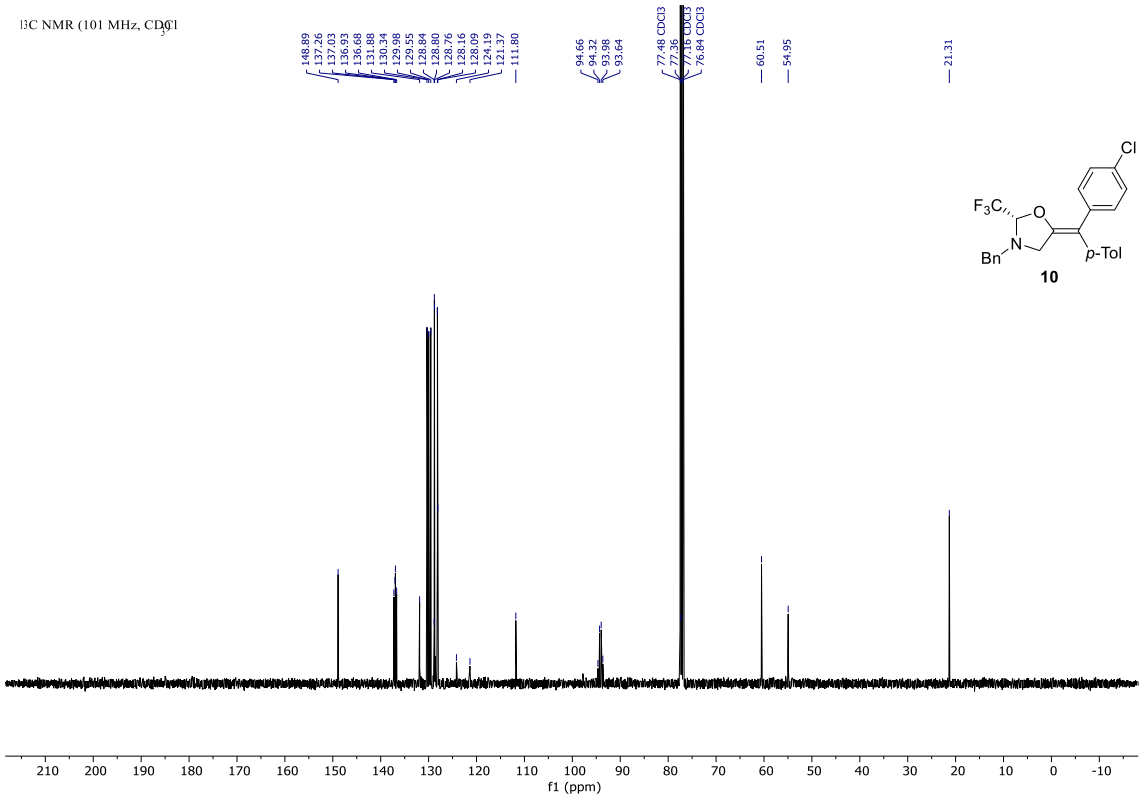

1H NMR (400 MHz, CDCl3)
F
F3C
O
N
Bn
p-Tol
9
f1 (ppm)


13C NMR (101 MHz, CDCl3)
F
F3C
O
N
Bn
p-Tol
9
f1 (ppm)

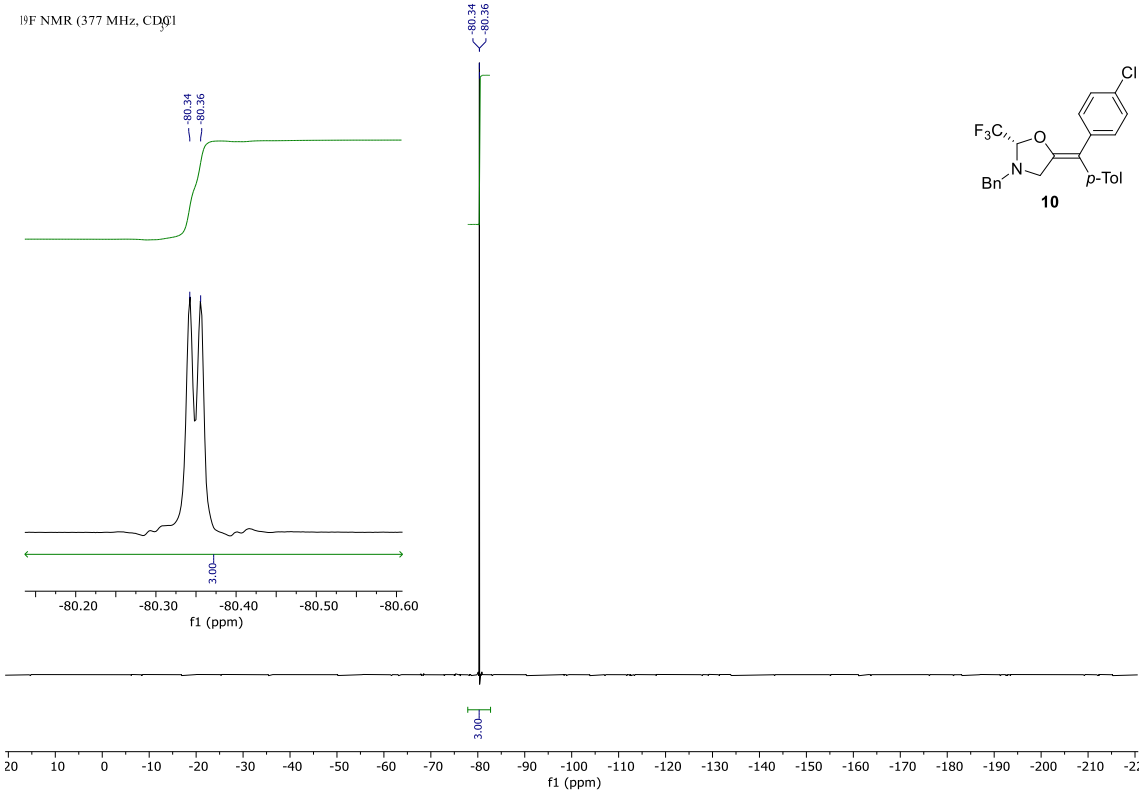

19F NMR (377 MHz, CDCl3)
-80.36
-80.37
-116.12
-116.14
-116.15
-116.15
-116.16
-116.16
-116.17
-116.17
-116.18
-116.20
F
F3C
O
N
Bn
p-Tol
9
3.34
1.00
f1 (ppm)

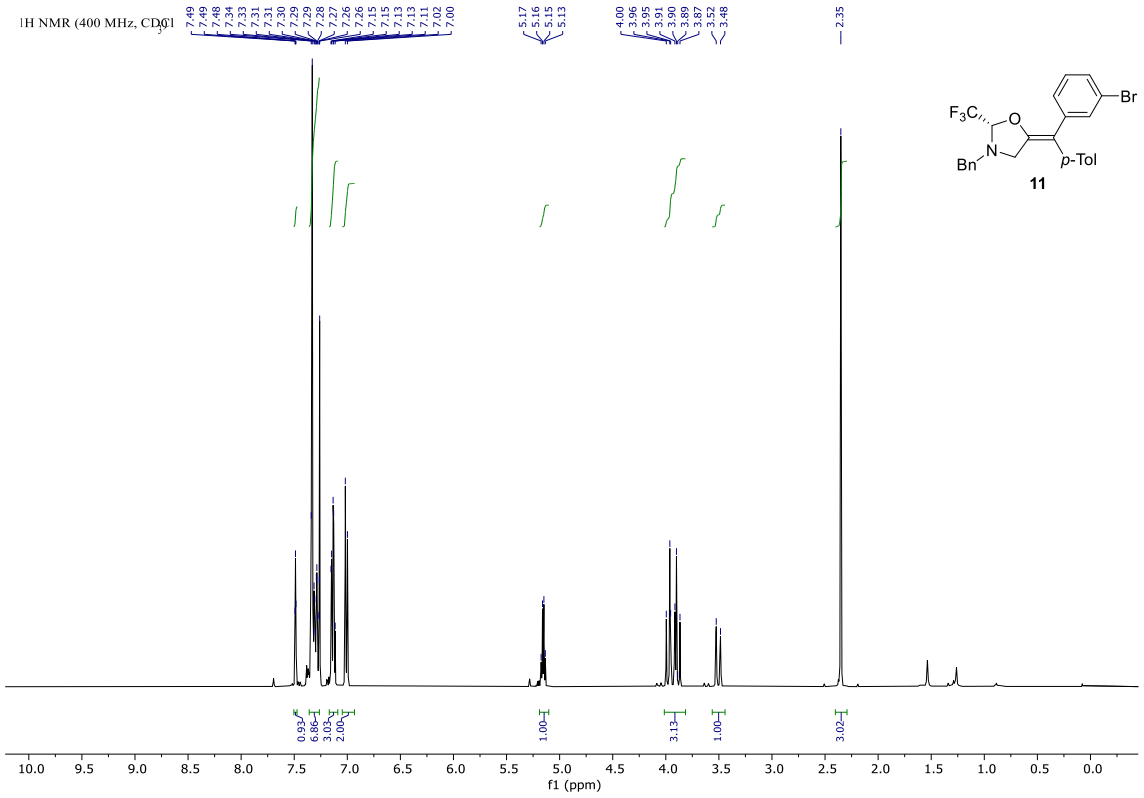

1H NMR (400 MHz, CDCl3)
7.34
7.33
7.32
7.31
7.30
7.30
7.29
7.28
7.28
7.27
7.27
7.26
7.25
7.25
7.24
7.23
7.22
7.22
7.15
7.13
7.02
7.02
7.00
5.16
5.14
5.13
5.12
4.00
3.97
3.94
3.92
3.90
3.89
3.87
3.54
3.54
3.50
3.50
2.35
Cl
F3C
O
N
Bn
p-Tol
10
10.10
2.02
2.01
1.00
3.20
1.01
3.06
f1 (ppm)

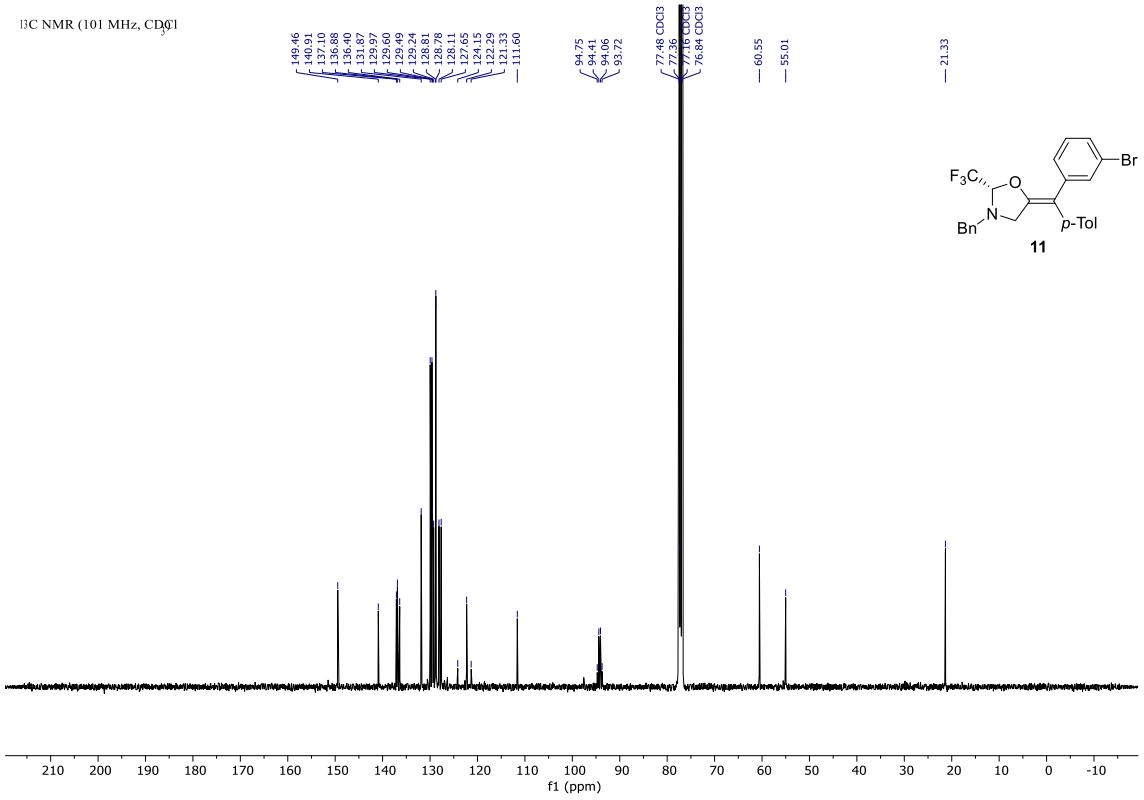
^{13}C NMR (101 MHz, $CDCl_3$)

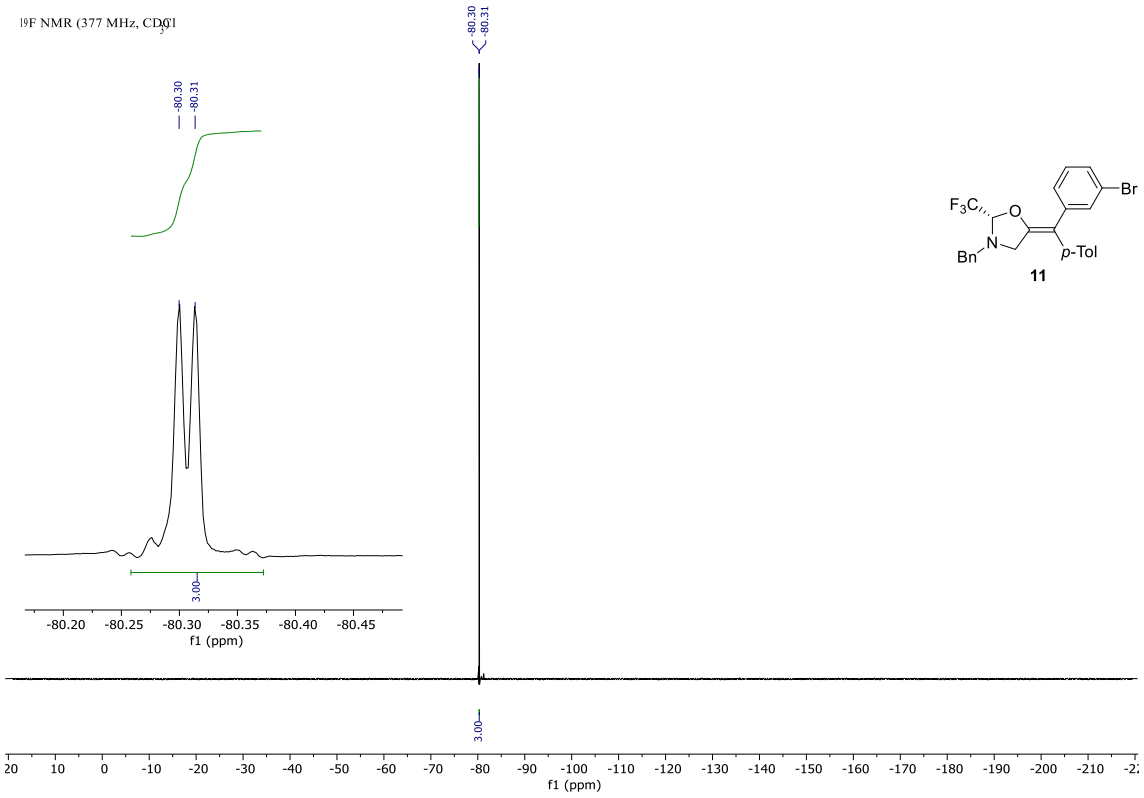


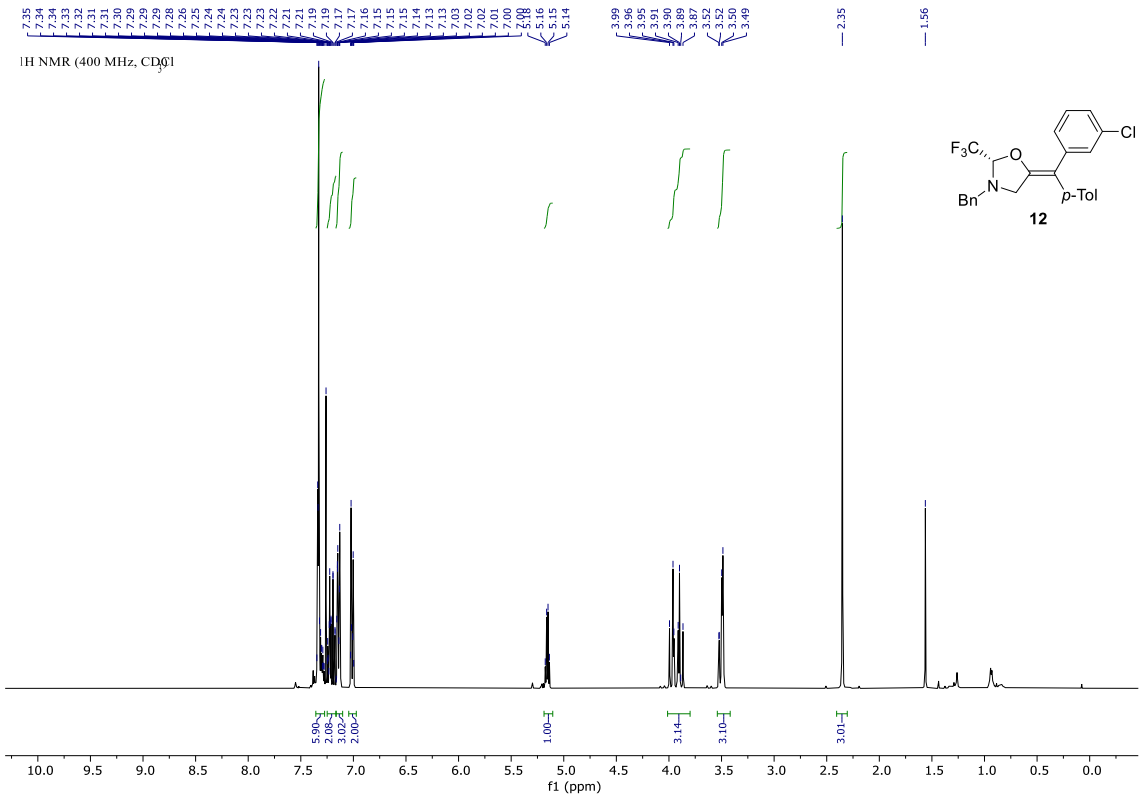
^{19}F NMR (377 MHz, $CDCl_3$)



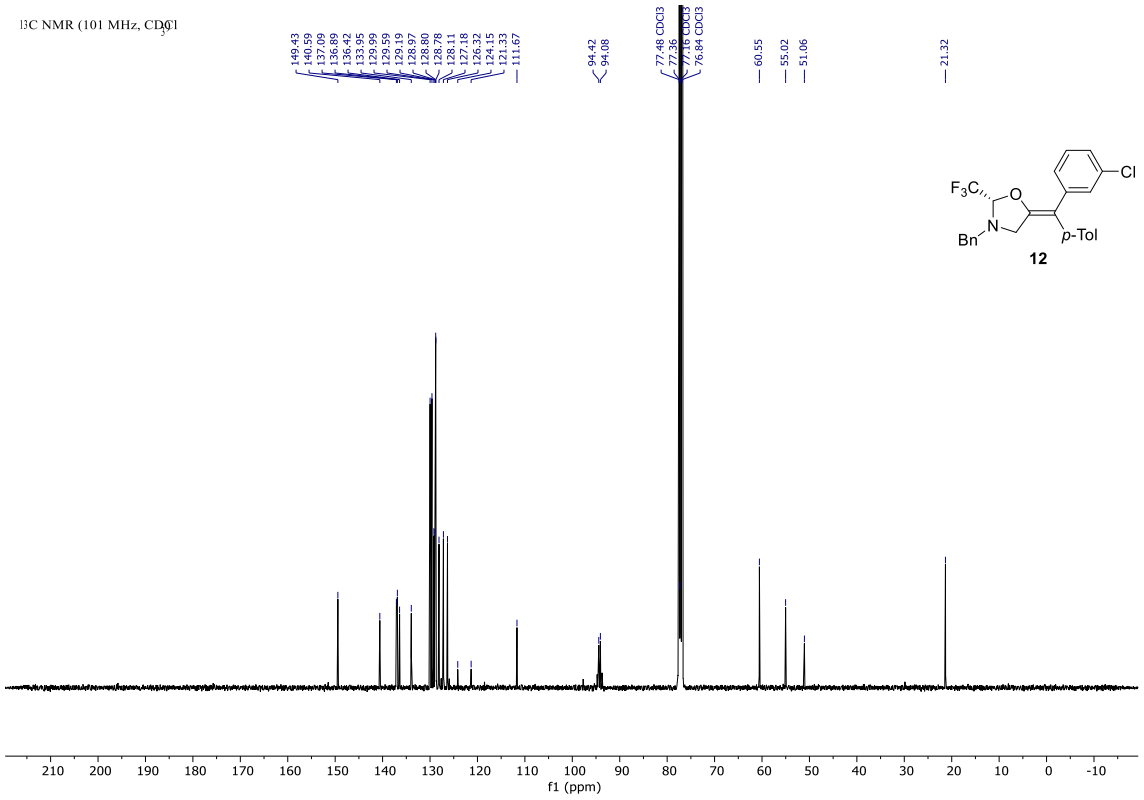

1H NMR (400 MHz, CDCl3)
7.49
7.49
7.48
7.34
7.33
7.31
7.31
7.30
7.29
7.29
7.28
7.27
7.26
7.26
7.15
7.15
7.13
7.13
7.11
7.02
7.00
5.17
5.16
5.15
5.13
4.00
3.96
3.95
3.91
3.90
3.89
3.87
3.52
3.48
2.35
Br
F3C
O
N
Bn
p-Tol
11
0.93
6.86
3.03
2.00
1.00
3.13
1.00
3.02
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


13C NMR (101 MHz, CDCl3)
149.46
140.91
137.10
136.88
136.40
131.87
129.97
129.60
129.49
129.24
128.81
128.78
128.11
127.65
124.15
122.29
121.33
111.60
94.75
94.41
94.06
93.72
77.48 CDCl3
77.36
77.16 CDCl3
76.84 CDCl3
60.55
55.01
21.33
Br
F3C
O
N
Bn
p-Tol
11
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


19F NMR (377 MHz, CDCl3)
-80.30
-80.31
3.00
-80.20 -80.25 -80.30 -80.35 -80.40 -80.45
f1 (ppm)
F3C
O
N
Bn
Br
p-Tol
11
20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

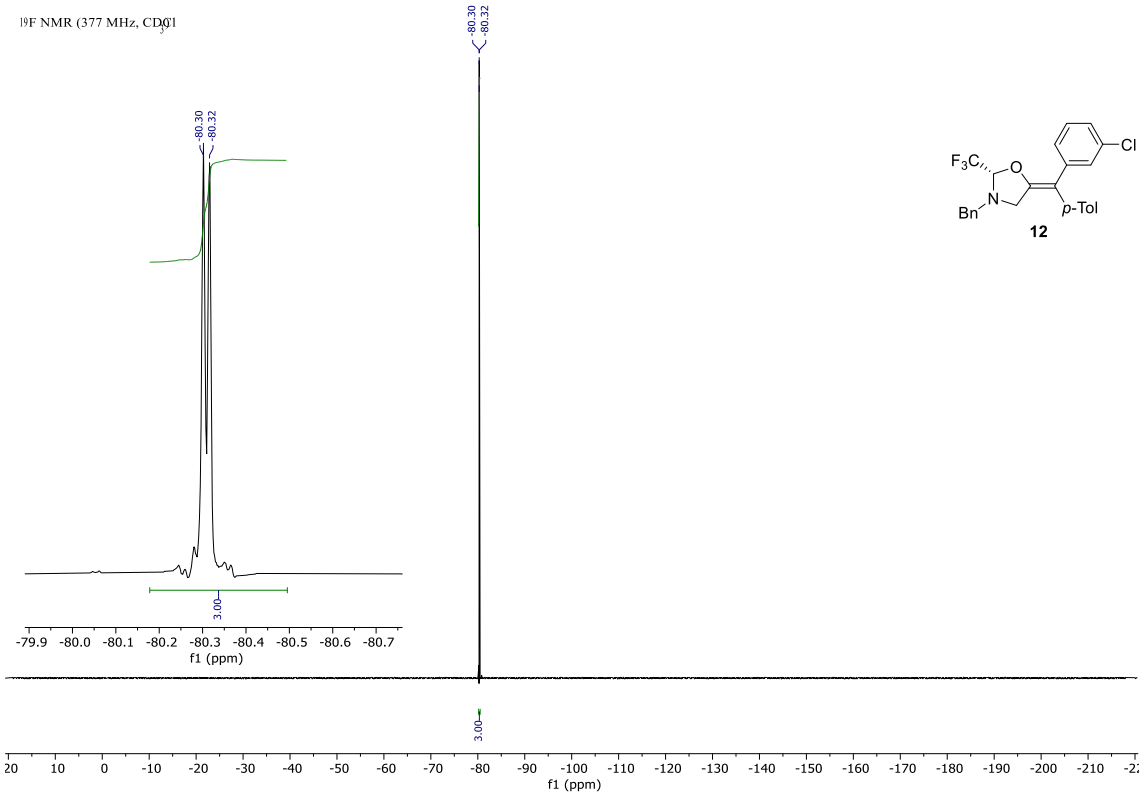

1H NMR (400 MHz, CDCl3)
7.35 7.34 7.34 7.33 7.32 7.31 7.31 7.30 7.29 7.29 7.28 7.26 7.25 7.24 7.24 7.23 7.23 7.22 7.21 7.21 7.19 7.19 7.17 7.17 7.16 7.15 7.15 7.15 7.14 7.13 7.13 7.03 7.02 7.02 7.01 7.00 7.00 5.18 5.16 5.15 5.14
3.99 3.96 3.95 3.91 3.90 3.89 3.87 3.52 3.52 3.50 3.49
2.35
1.56
5.90 2.08 3.02 2.00 1.00 3.14 3.10 3.01
F3C
O
N
Bn
Cl
p-Tol
12
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

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

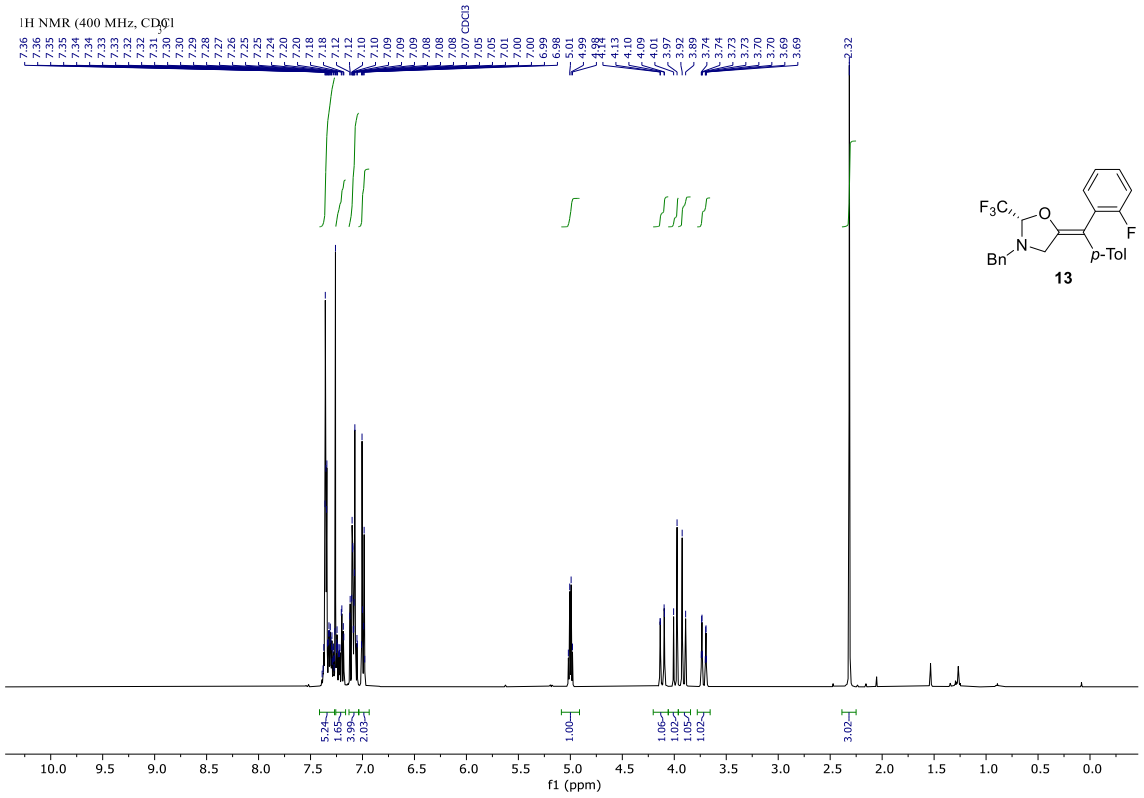


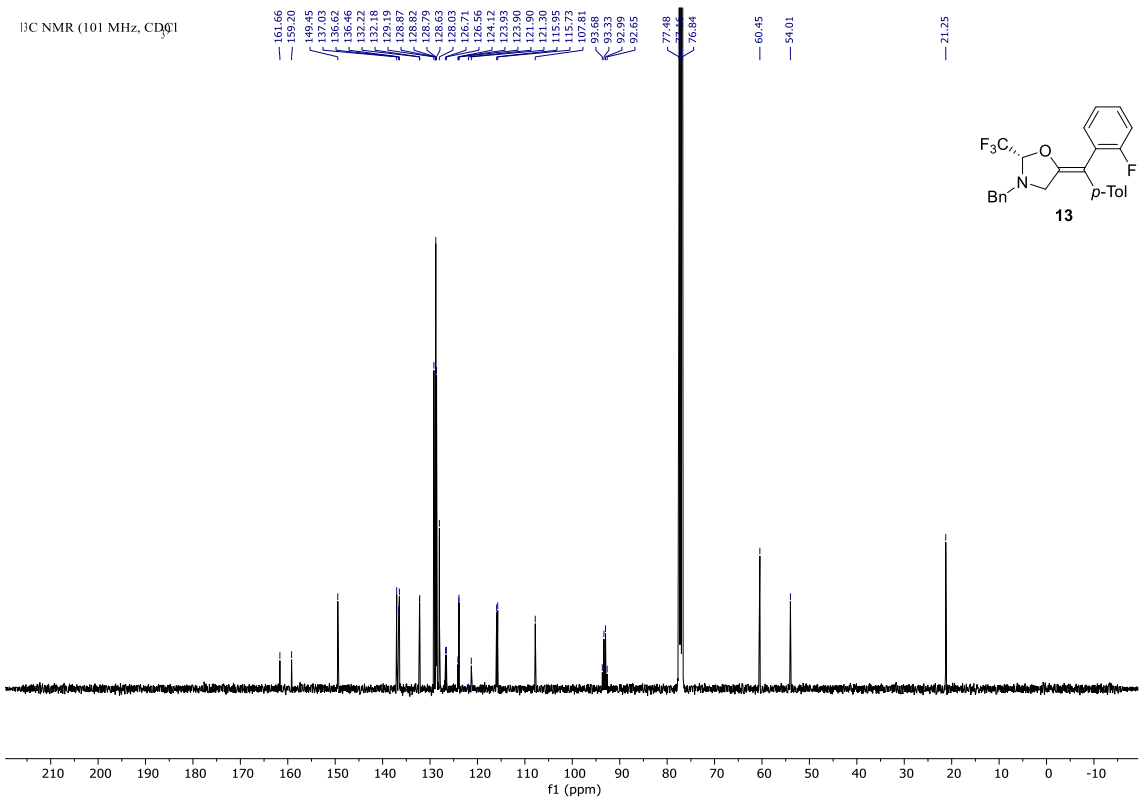
12

^{19}F NMR (377 MHz, $CDCl_3$)

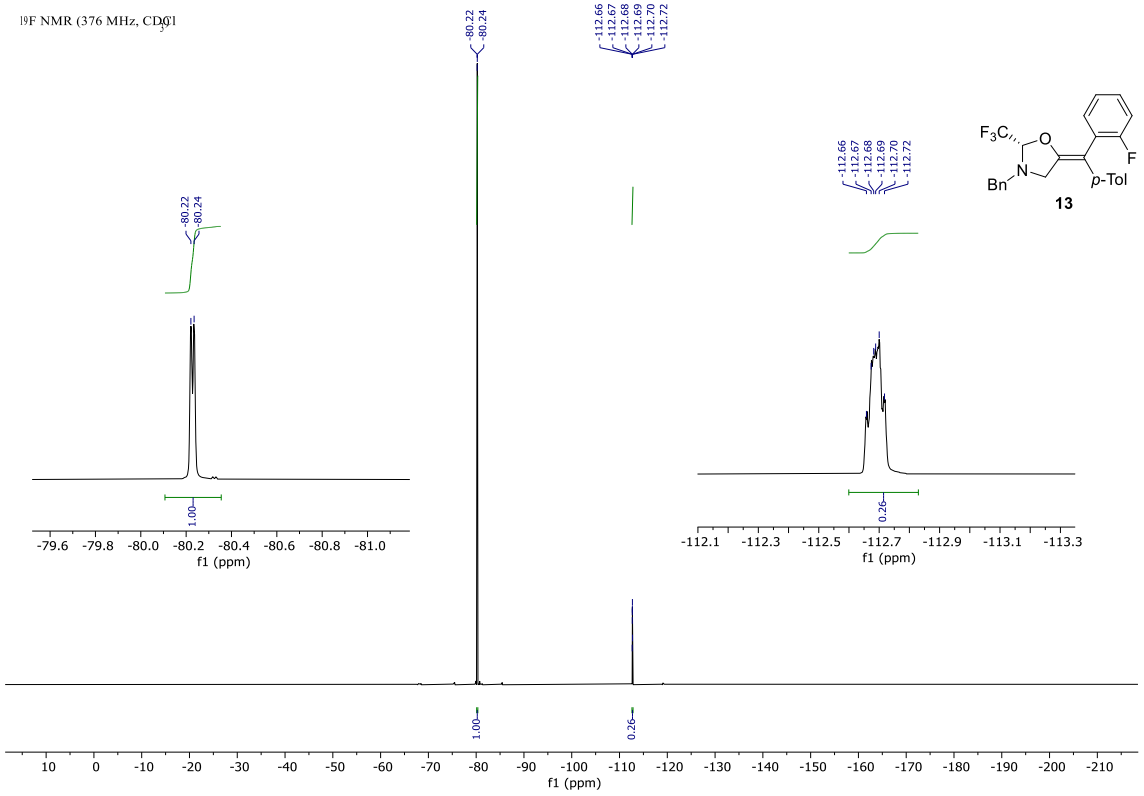


12

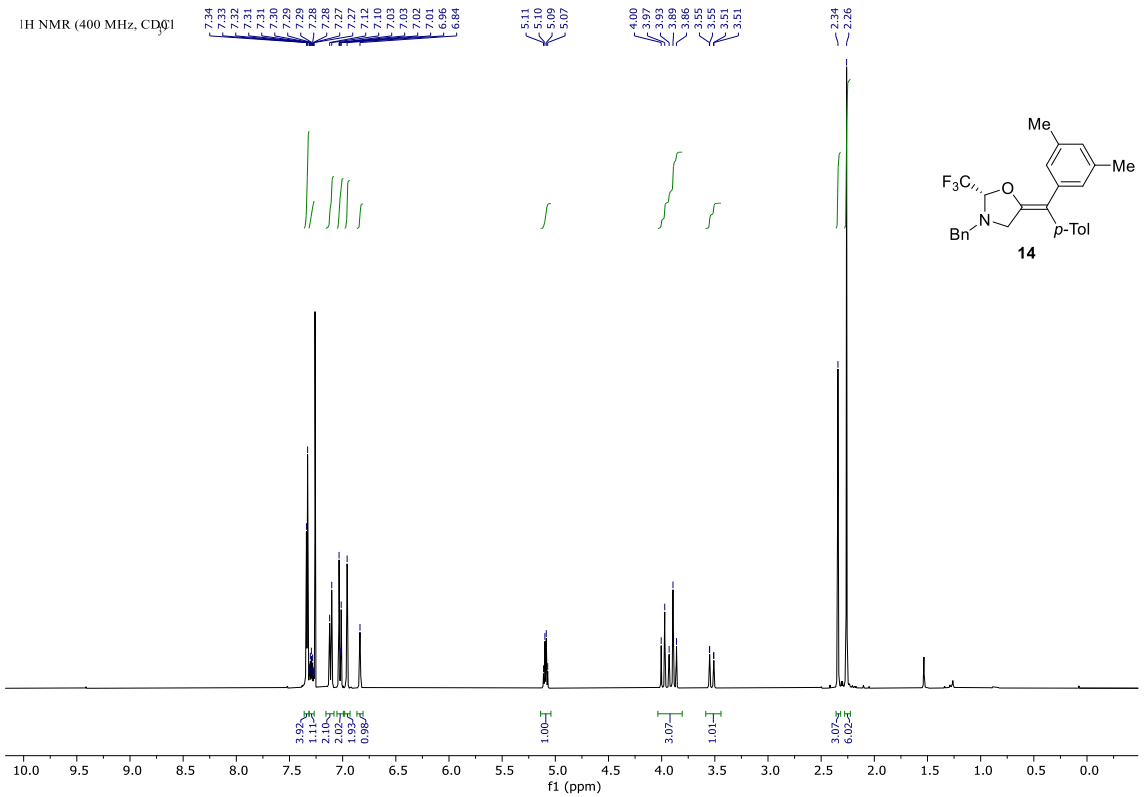

1H NMR (400 MHz, CDCl3)
CDCl3
2.32
5.24
1.65
3.99
2.03
1.00
1.06
1.02
1.05
1.02
3.02
f1 (ppm)
F3C
O
N
Bn
F
p-Tol
13


13C NMR (101 MHz, CDCl3)
161.66
159.20
149.45
137.03
136.62
136.46
132.22
132.18
129.19
128.87
128.82
128.79
128.63
128.03
126.71
126.56
124.12
123.93
123.90
121.90
121.30
115.95
115.73
107.81
93.68
93.33
92.99
92.65
77.48
77.16
76.84
60.45
54.01
21.25
f1 (ppm)
F3C
O
N
Bn
F
p-Tol
13

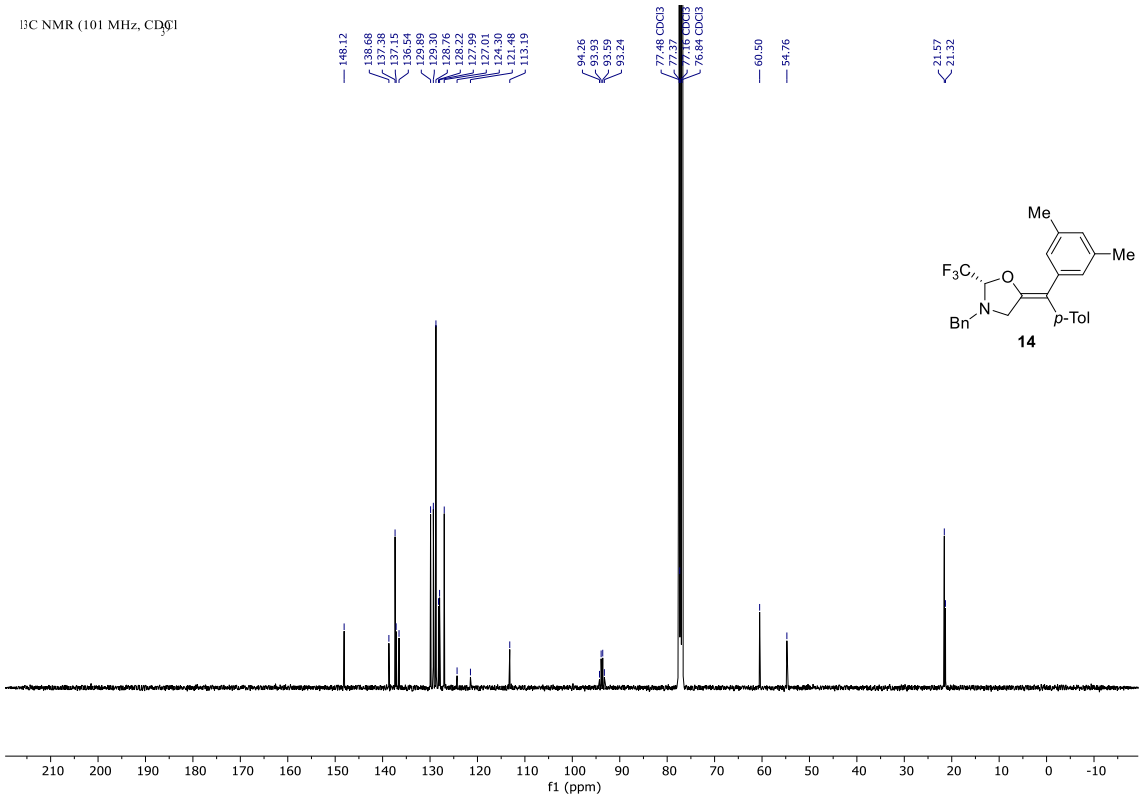
^{19}F NMR (376 MHz, $CDCl_3$)



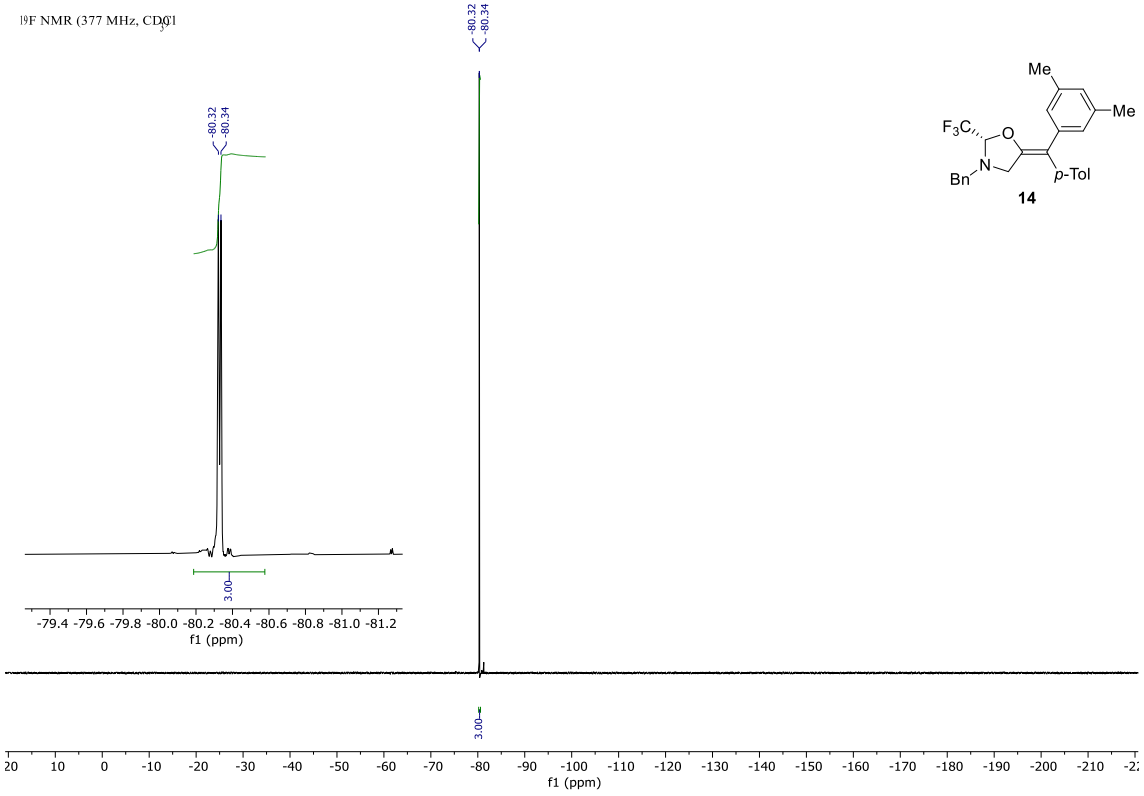
^{1}H NMR (400 MHz, $CDCl_3$)

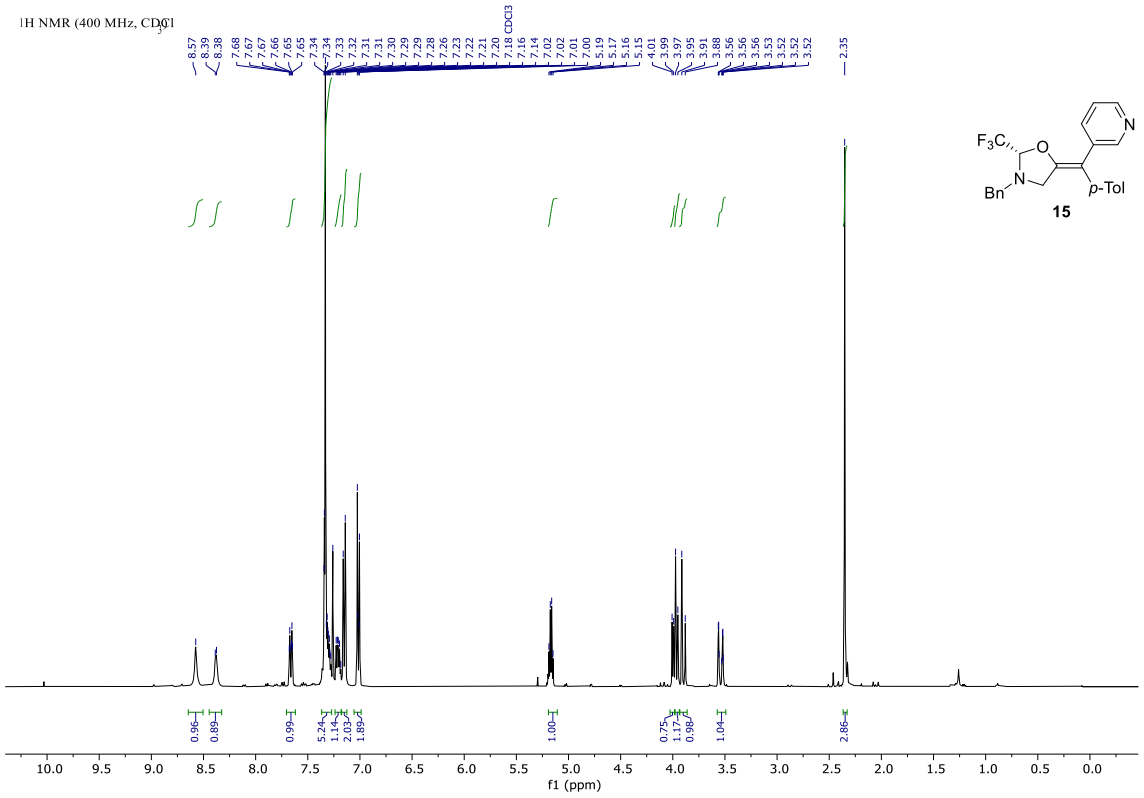


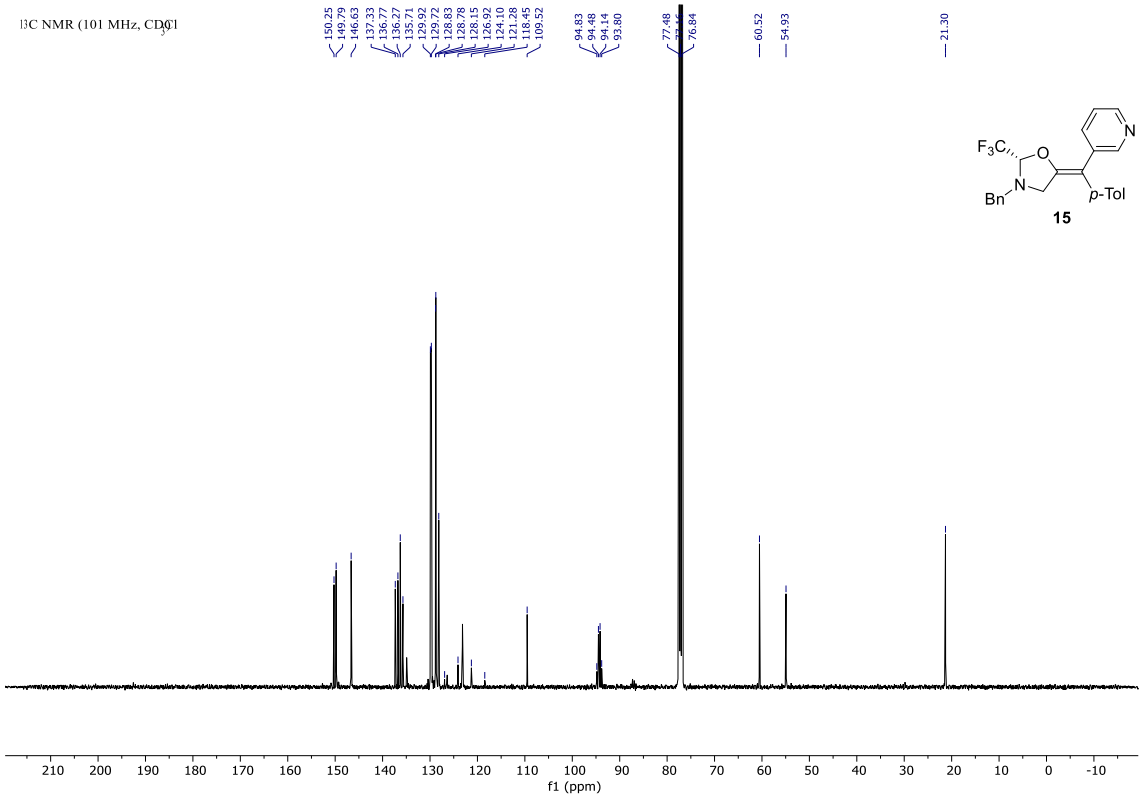
^{13}C NMR (101 MHz, $CDCl_3$)

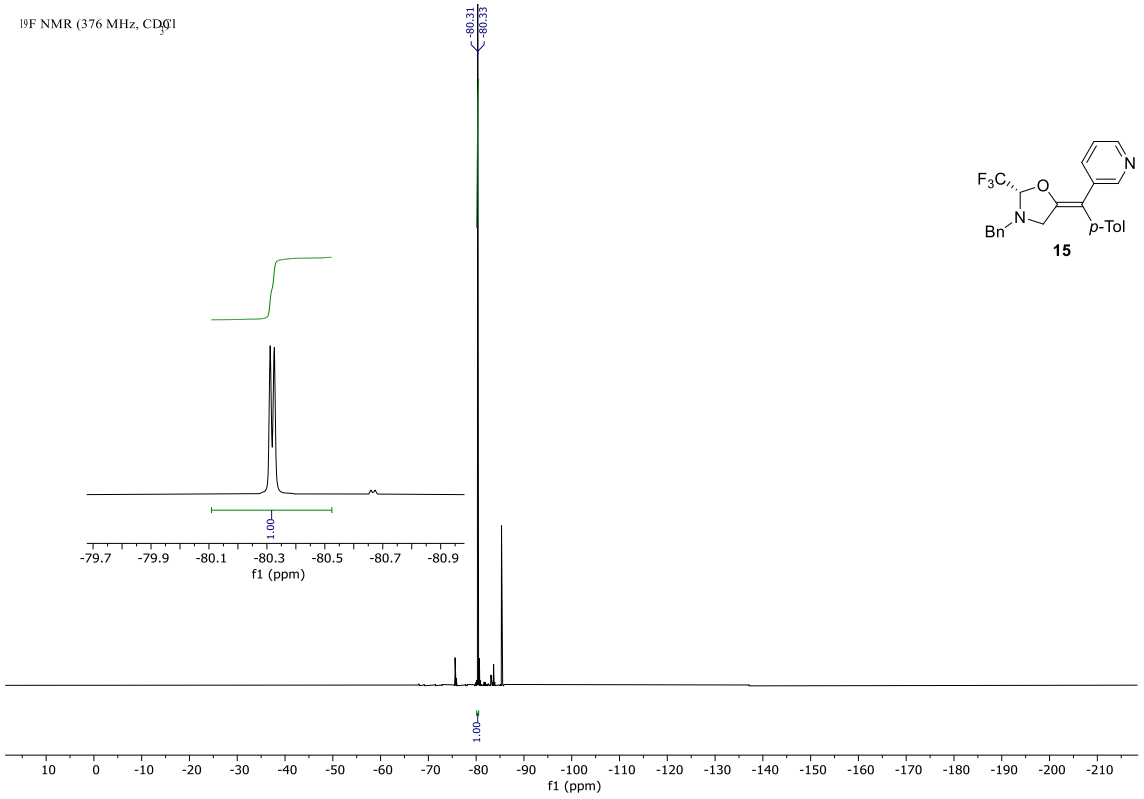


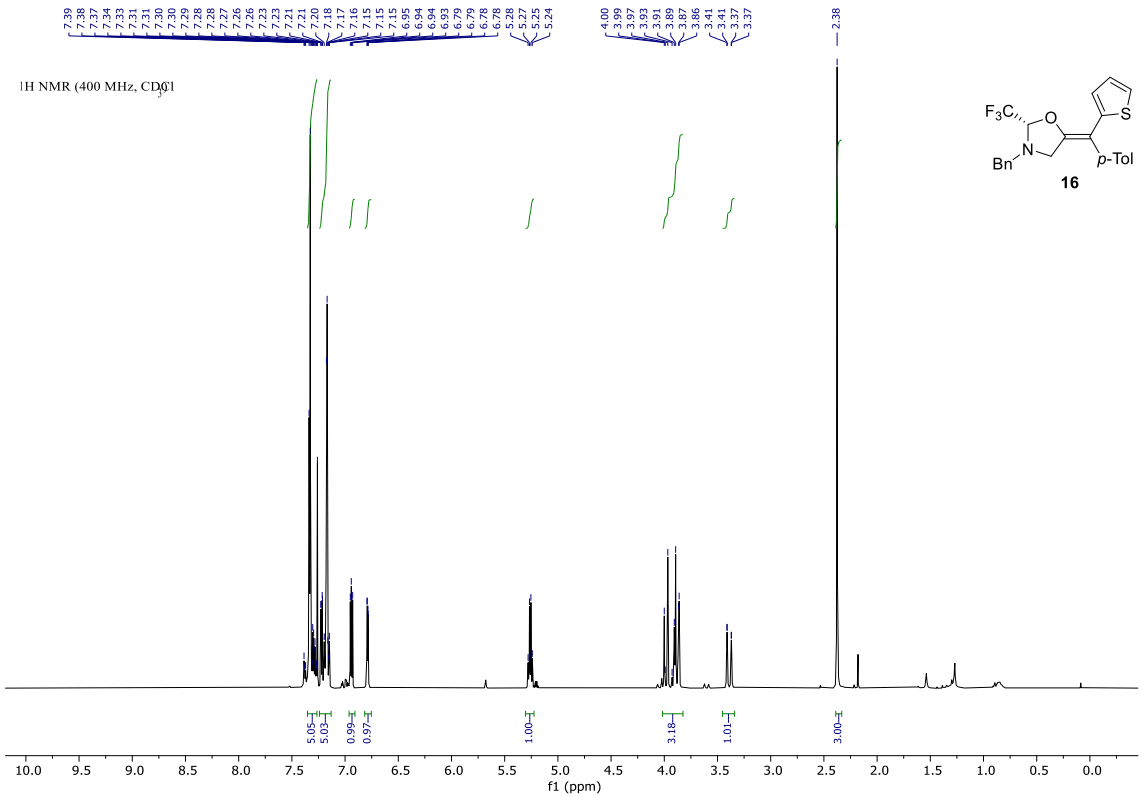
^{19}F NMR (377 MHz, $CDCl_3$)

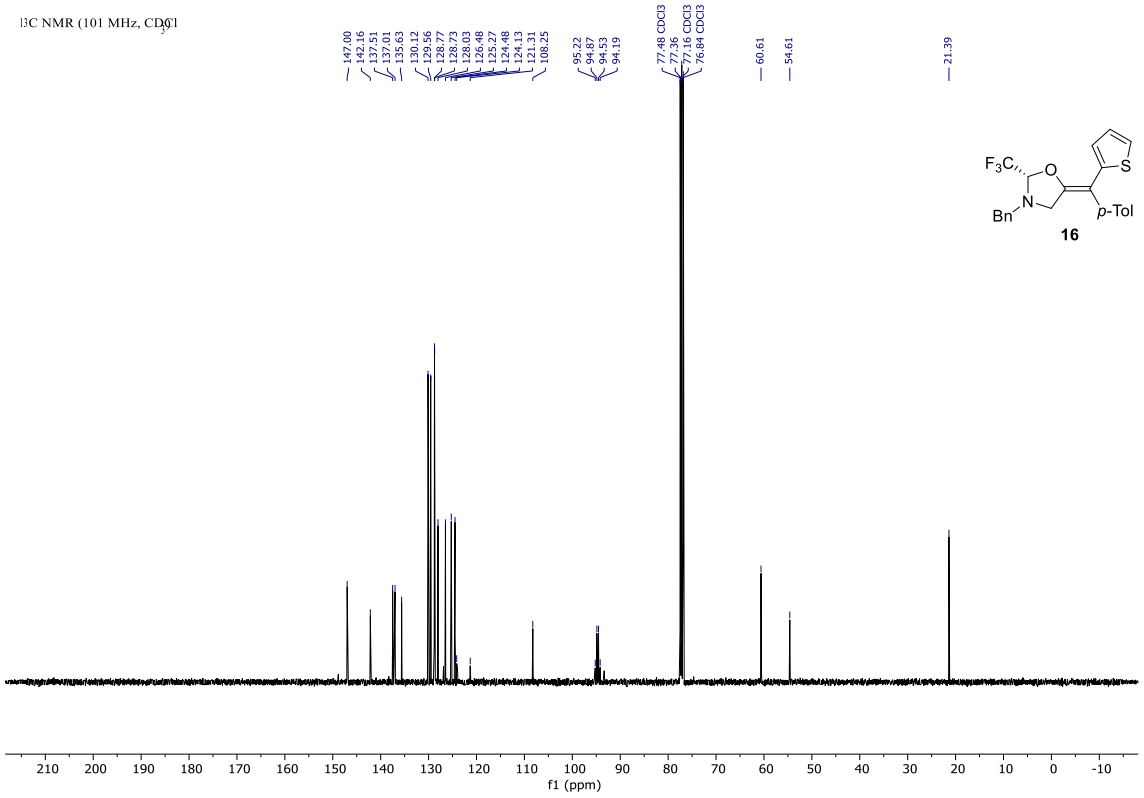


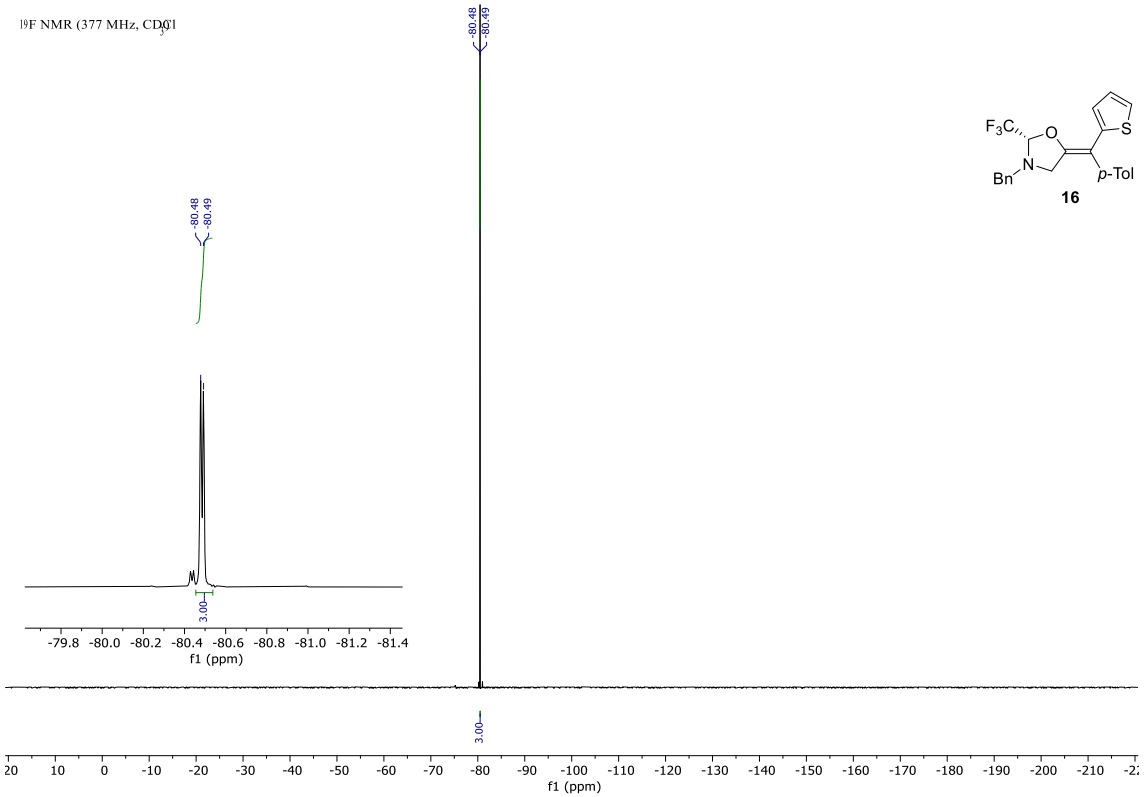

1H NMR (400 MHz, CDCl3)
F3C
O
N
Bn
p-Tol
15
f1 (ppm)

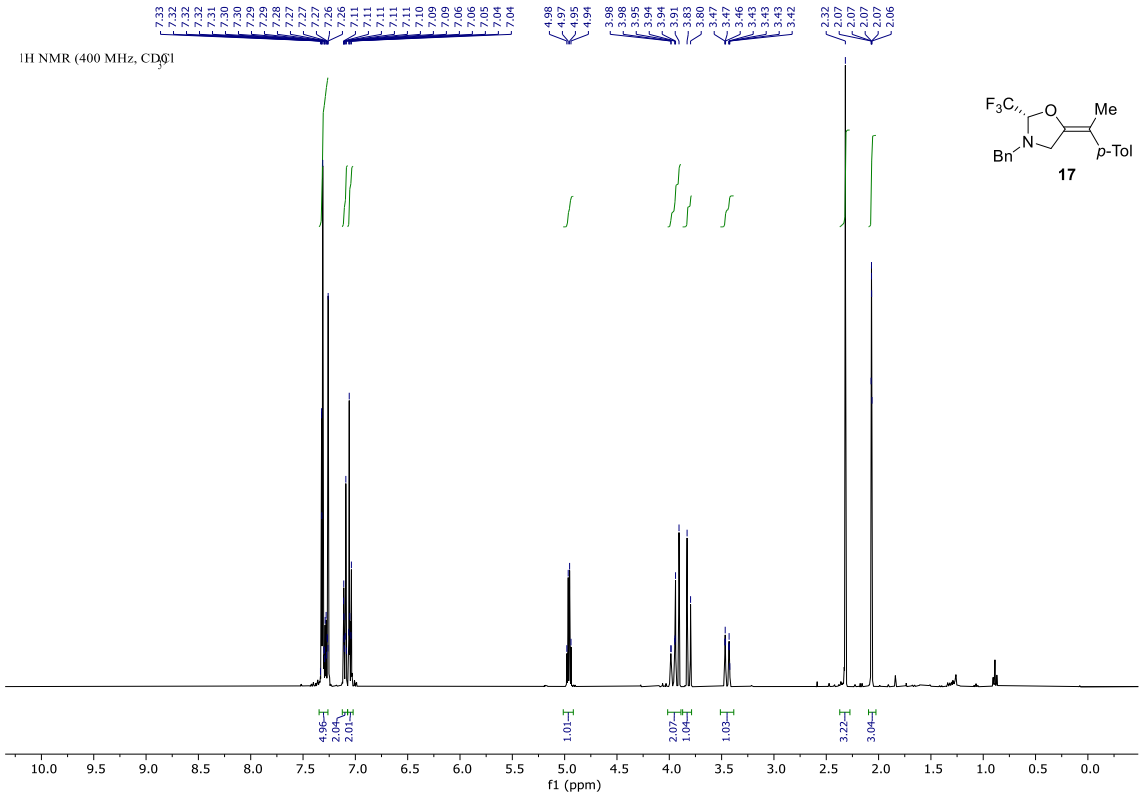

13C NMR (101 MHz, CDCl3)
F3C
O
N
Bn
p-Tol
15
f1 (ppm)

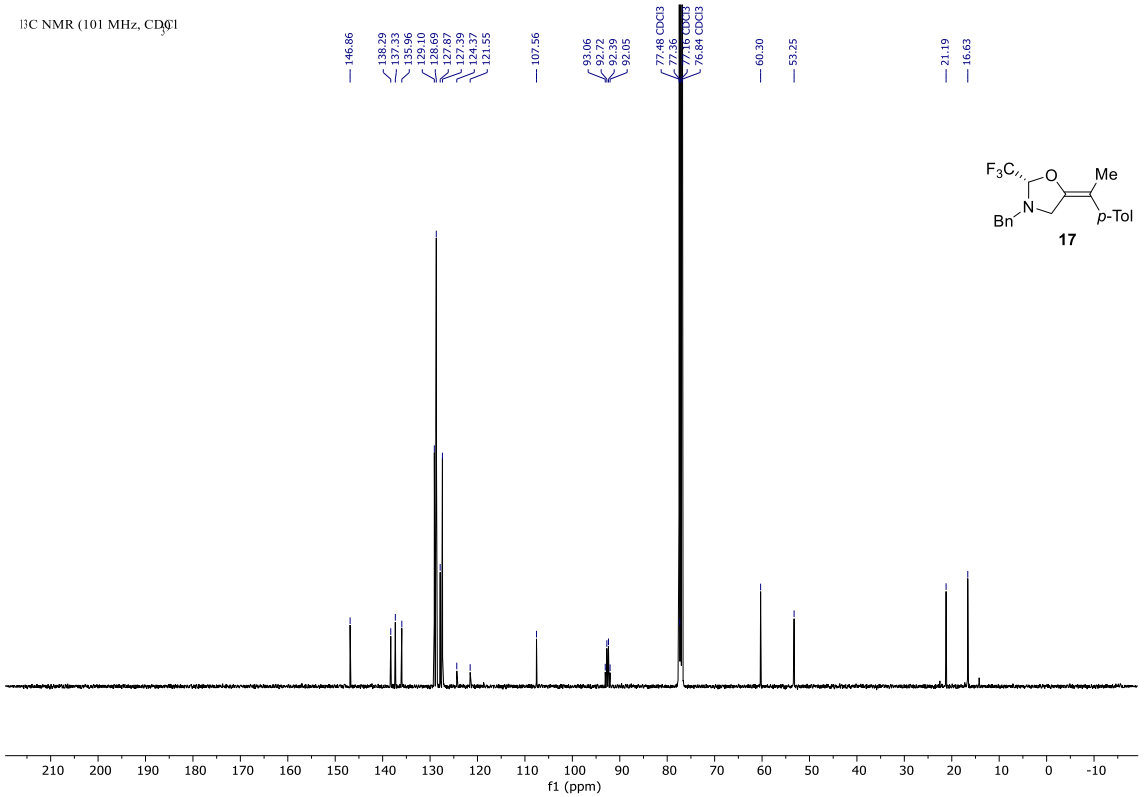

19F NMR (376 MHz, CDCl3)
-80.31
-80.33
1.00
-79.7 -79.9 -80.1 -80.3 -80.5 -80.7 -80.9
f1 (ppm)
1.00
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)
F3C
O
N
Bn
p-Tol
15


7.39 7.38 7.37 7.34 7.33 7.31 7.31 7.30 7.30 7.29 7.28 7.28 7.27 7.26 7.26 7.23 7.23 7.21 7.21 7.20 7.18 7.17 7.16 7.15 7.15 6.95 6.94 6.94 6.93 6.79 6.79 6.78 6.78 5.28 5.27 5.25 5.24
4.00 3.99 3.97 3.93 3.91 3.89 3.87 3.86 3.41 3.41 3.37 3.37
2.38
1H NMR (400 MHz, CDCl3)
5.05 5.03 0.99 0.97 1.00 3.18 1.01 3.00
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
F3C
O
S
N
Bn
p-Tol
16

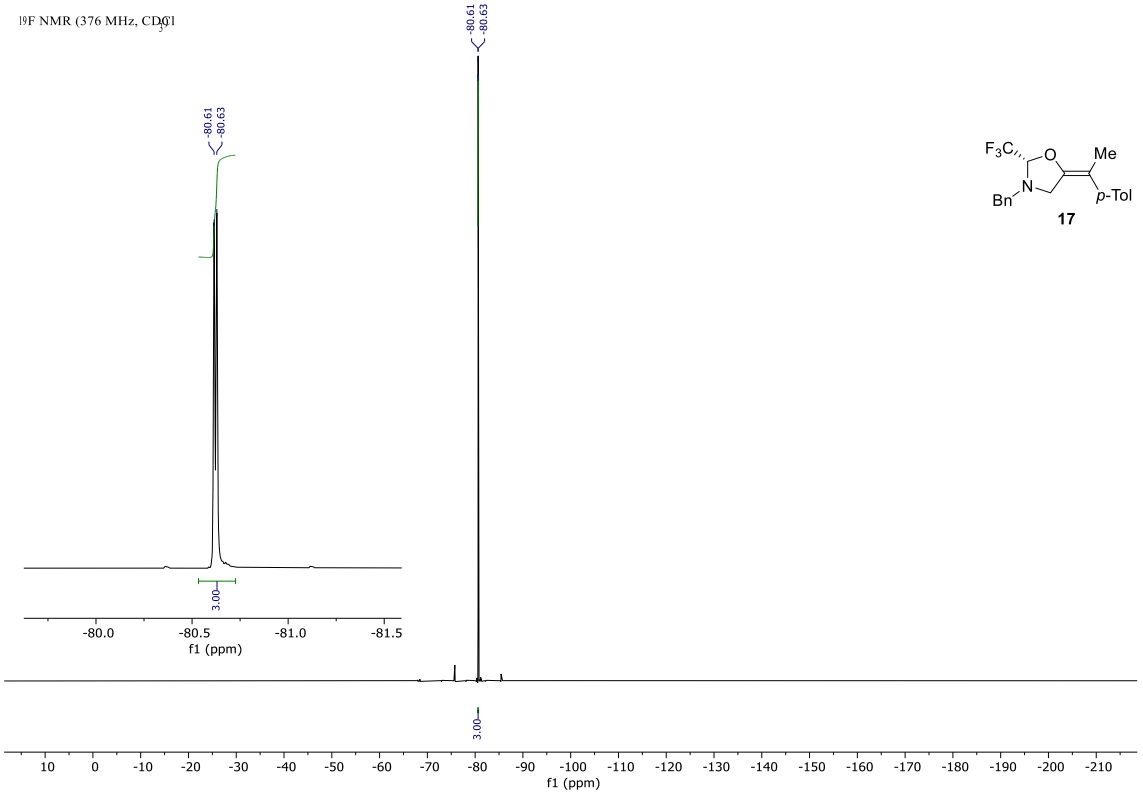

13C NMR (101 MHz, CDCl3)
147.00
142.16
137.51
137.01
135.63
130.12
129.56
128.77
128.73
128.03
126.48
123.27
124.48
124.13
121.31
108.25
95.22
94.87
94.53
94.19
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
60.61
54.61
21.39
F3C
O
S
N
Bn
p-Tol
16
f1 (ppm)


19F NMR (377 MHz, CDCl3)
-80.48
-80.49
3.00
F3C
O
S
N
Bn
p-Tol
16
f1 (ppm)


1H NMR (400 MHz, CDCl3)
7.33 7.32 7.32 7.32 7.31 7.30 7.29 7.29 7.28 7.27 7.27 7.27 7.26 7.26 7.11 7.11 7.11 7.11 7.10 7.09 7.09 7.06 7.06 7.05 7.04 7.04
4.98 4.97 4.95 4.94
3.98 3.98 3.95 3.94 3.94 3.91 3.83 3.80 3.47 3.46 3.43 3.43 3.43 3.42
2.32 2.07 2.07 2.07 2.07 2.06
4.96 2.04 2.01 1.01 2.07 1.04 1.03 3.22 3.04
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
F3C
O
N
Me
Bn
p-Tol
17

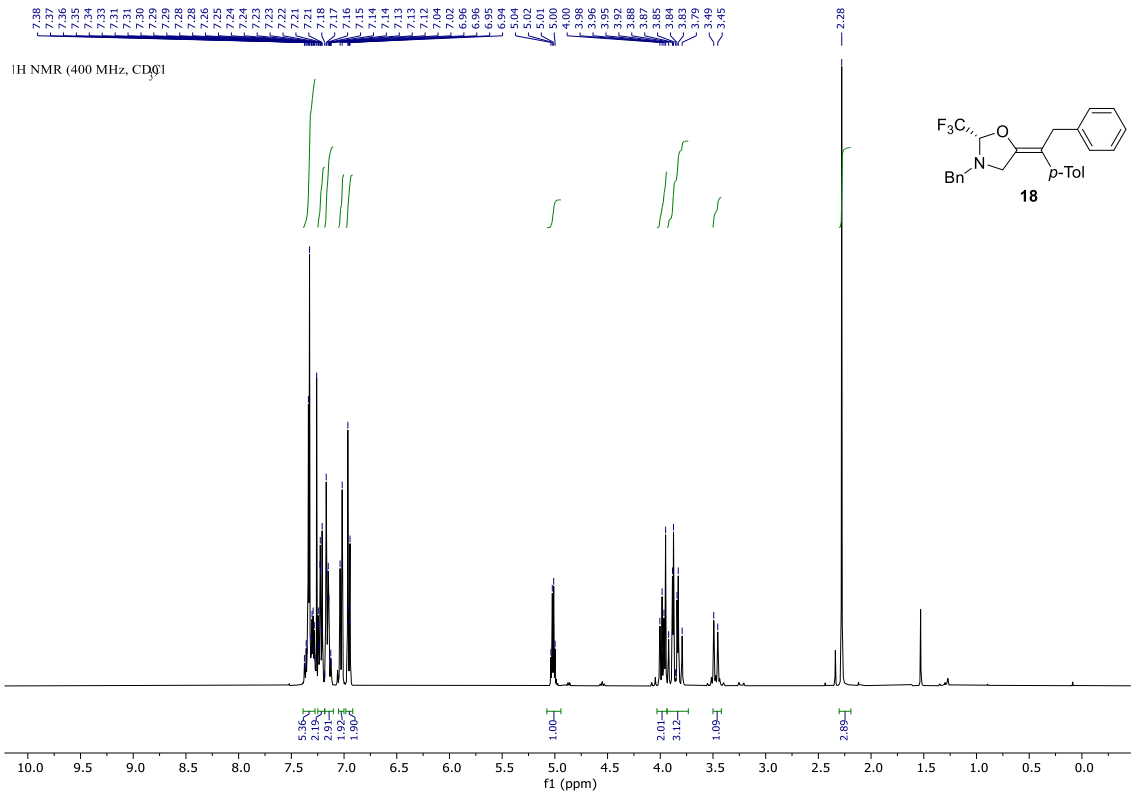

13C NMR (101 MHz, CDCl3)
146.86
138.29 137.33 135.96 129.10 128.69 127.87 127.39 124.37 121.55
107.56
93.06 92.72 92.39 92.05
77.48 CDCl3 77.36 77.16 CDCl3 76.84 CDCl3
60.30
53.25
21.19
16.63
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
F3C
O
N
Me
Bn
p-Tol
17

^{19}F NMR (376 MHz, $CDCl_3$)



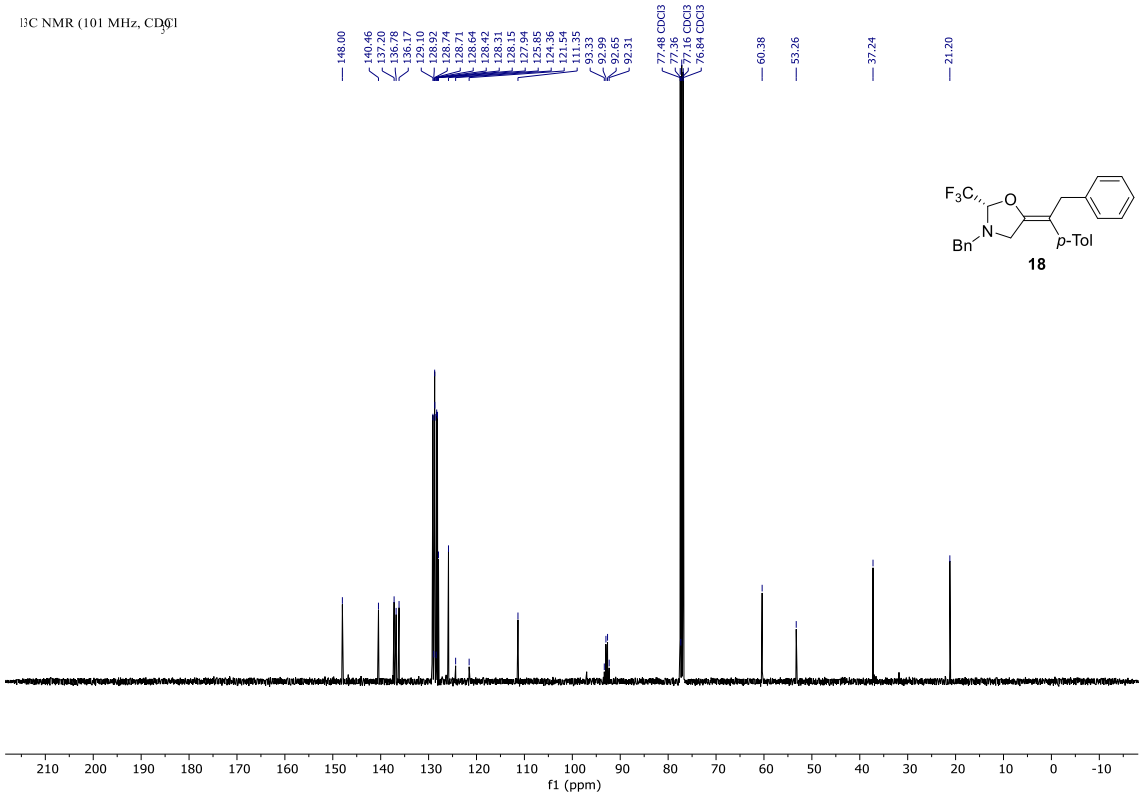
17

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

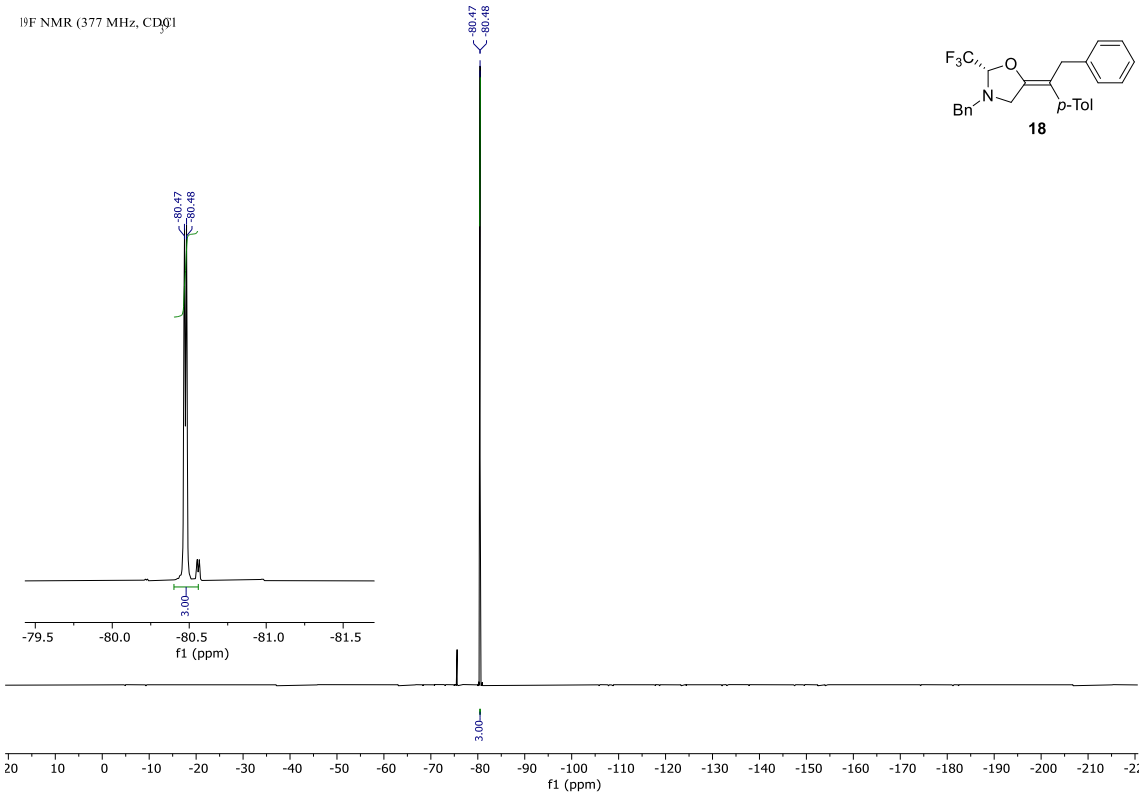


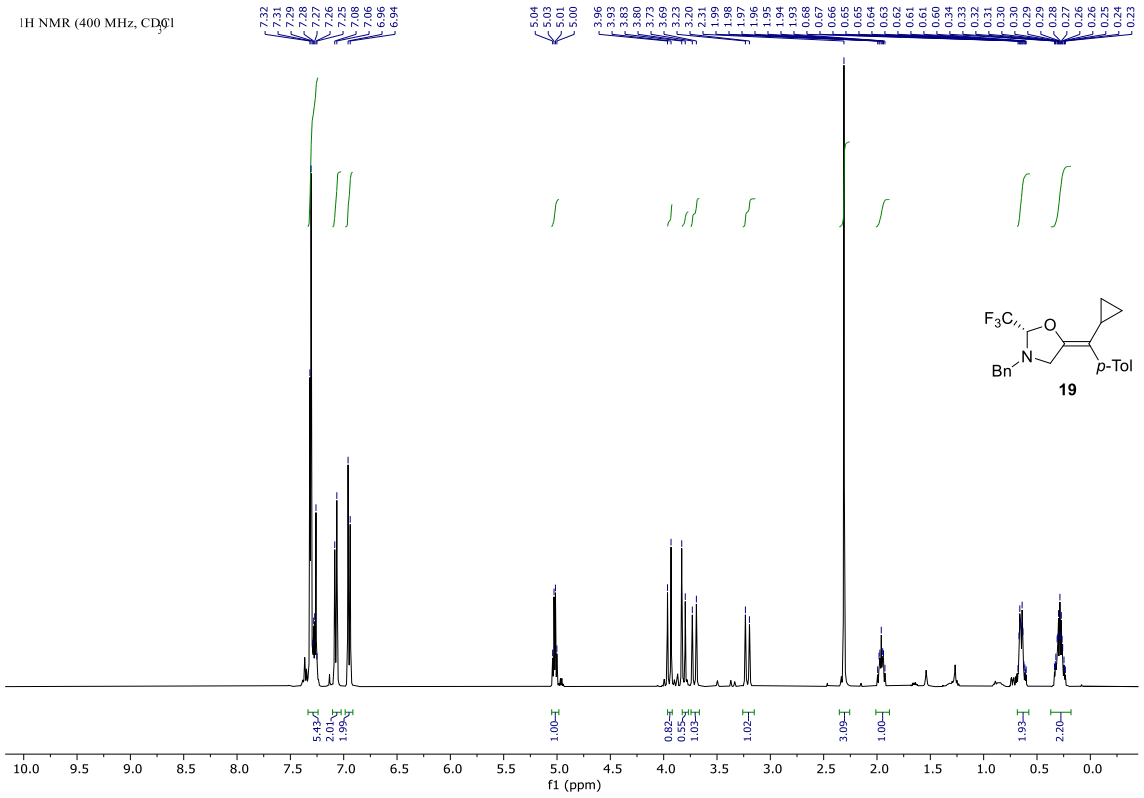
18

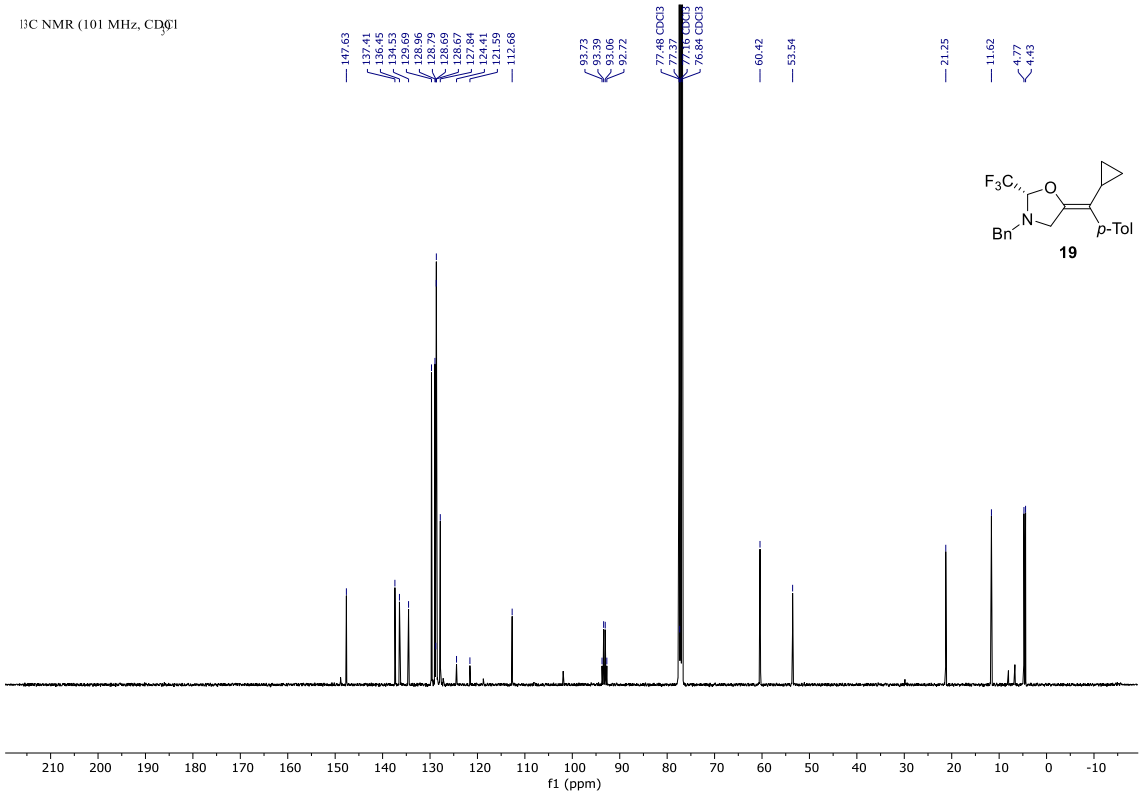
^{13}C NMR (101 MHz, $CDCl_3$)



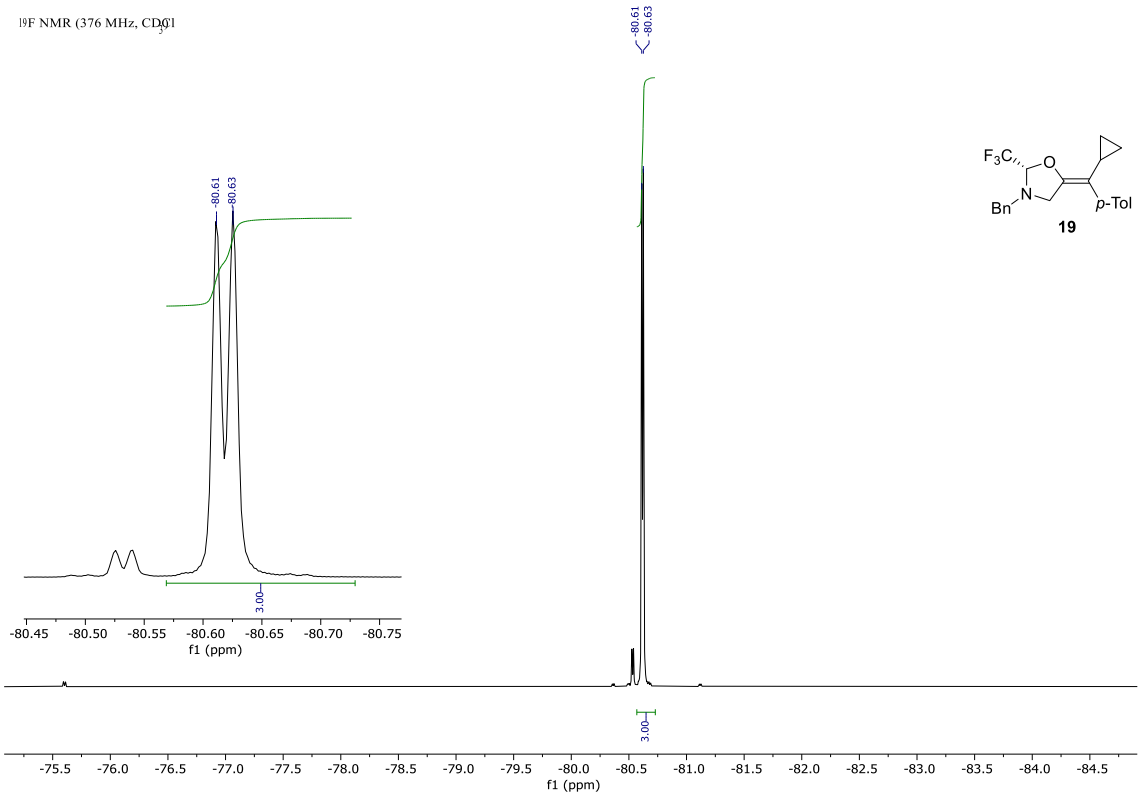
^{19}F NMR (377 MHz, $CDCl_3$)

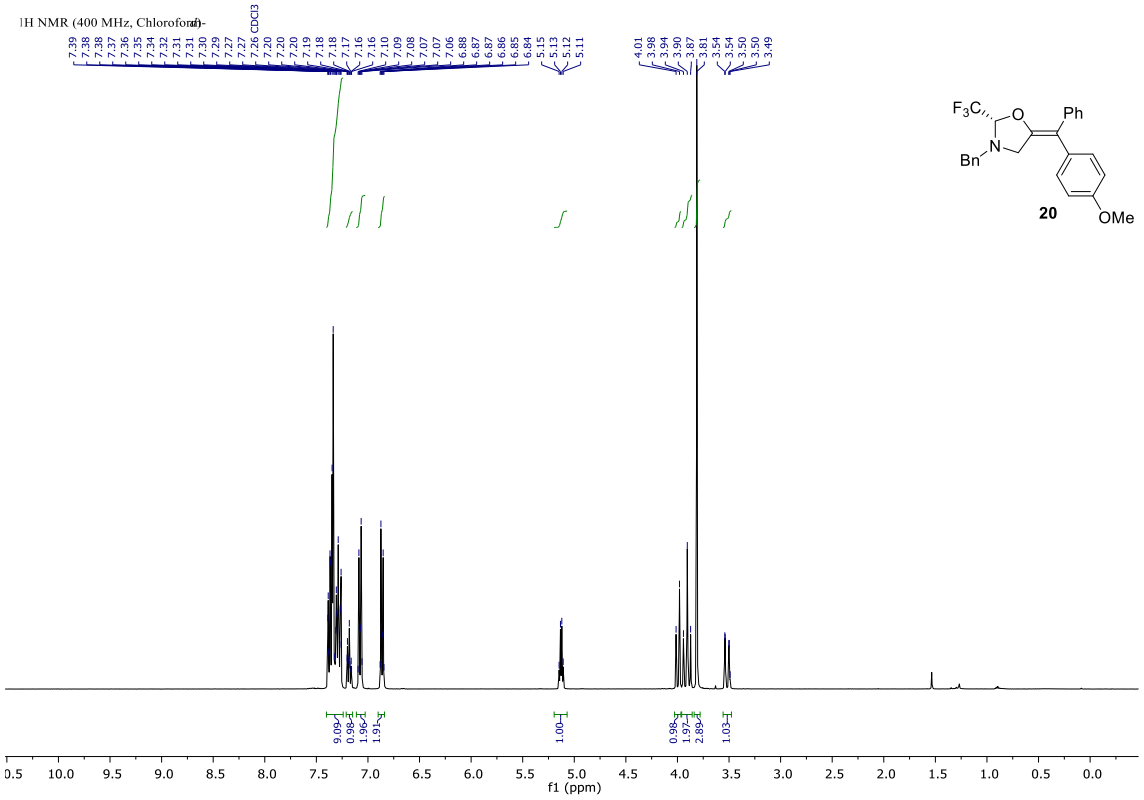


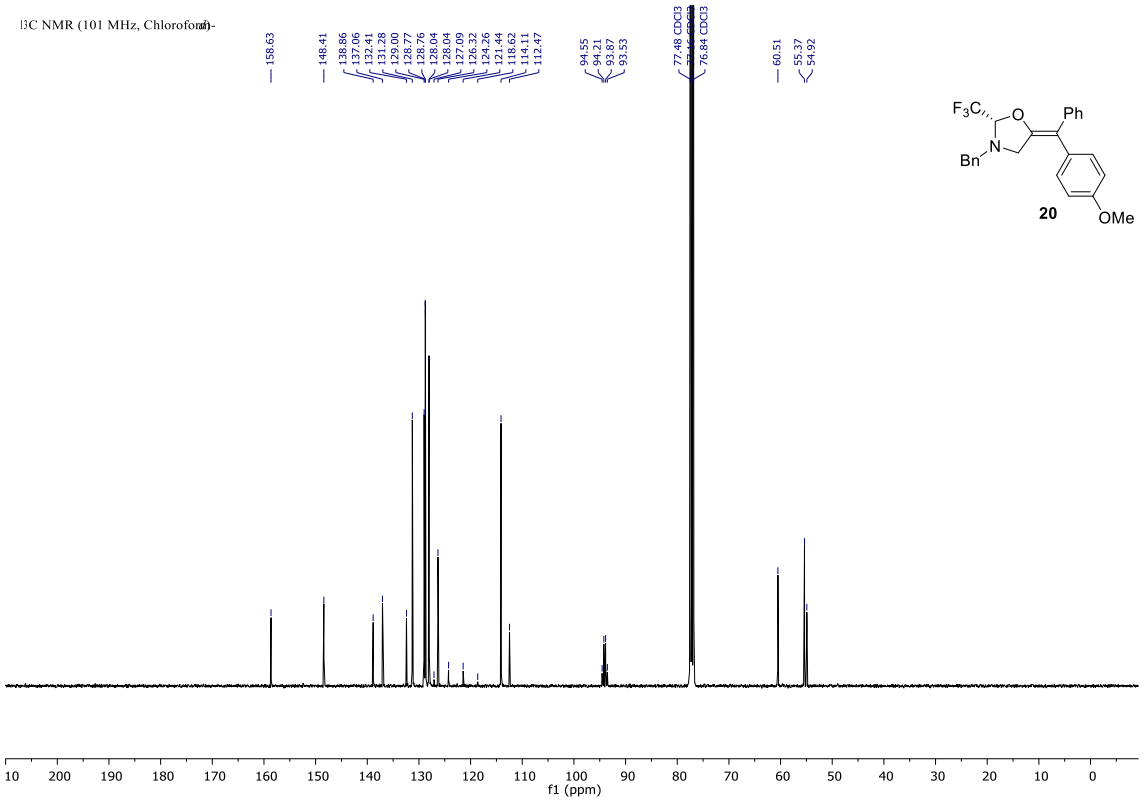

1H NMR (400 MHz, CDCl3)
F3C
O
N
Bn
p-Tol
19
f1 (ppm)


13C NMR (101 MHz, CDCl3)
F3C
O
N
Bn
p-Tol
19
f1 (ppm)

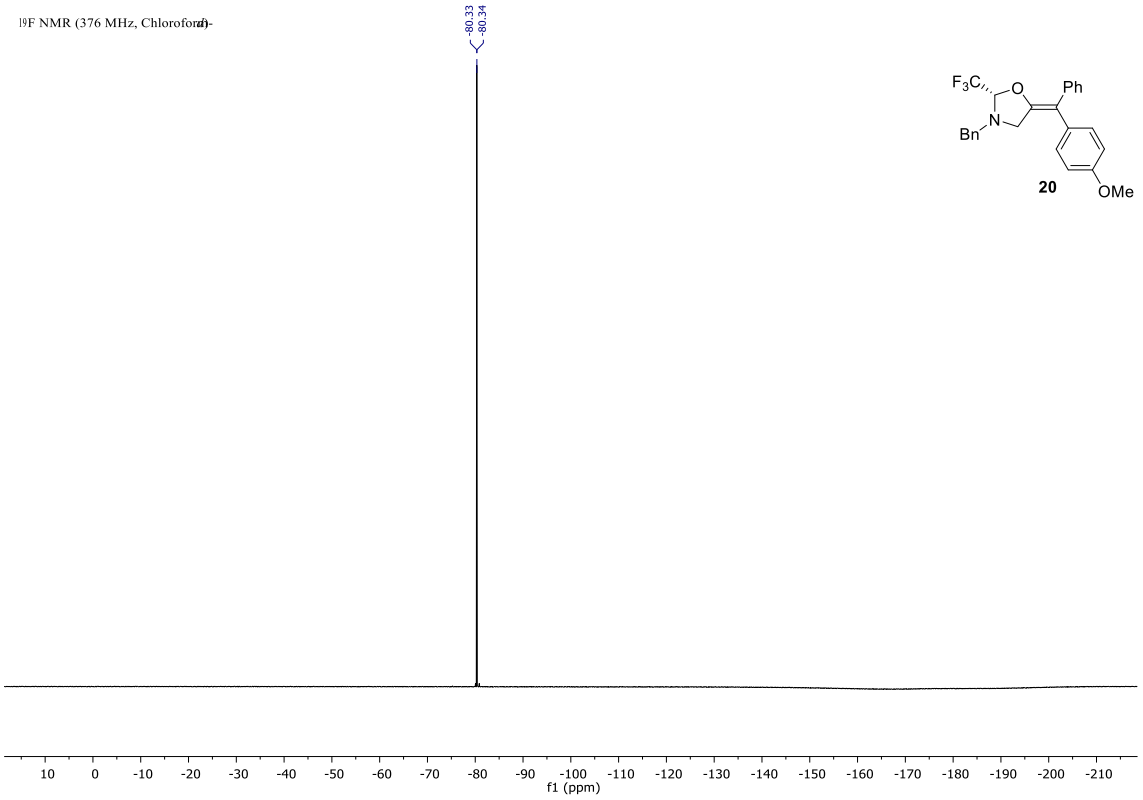
^{19}F NMR (376 MHz, CD_3Cl)



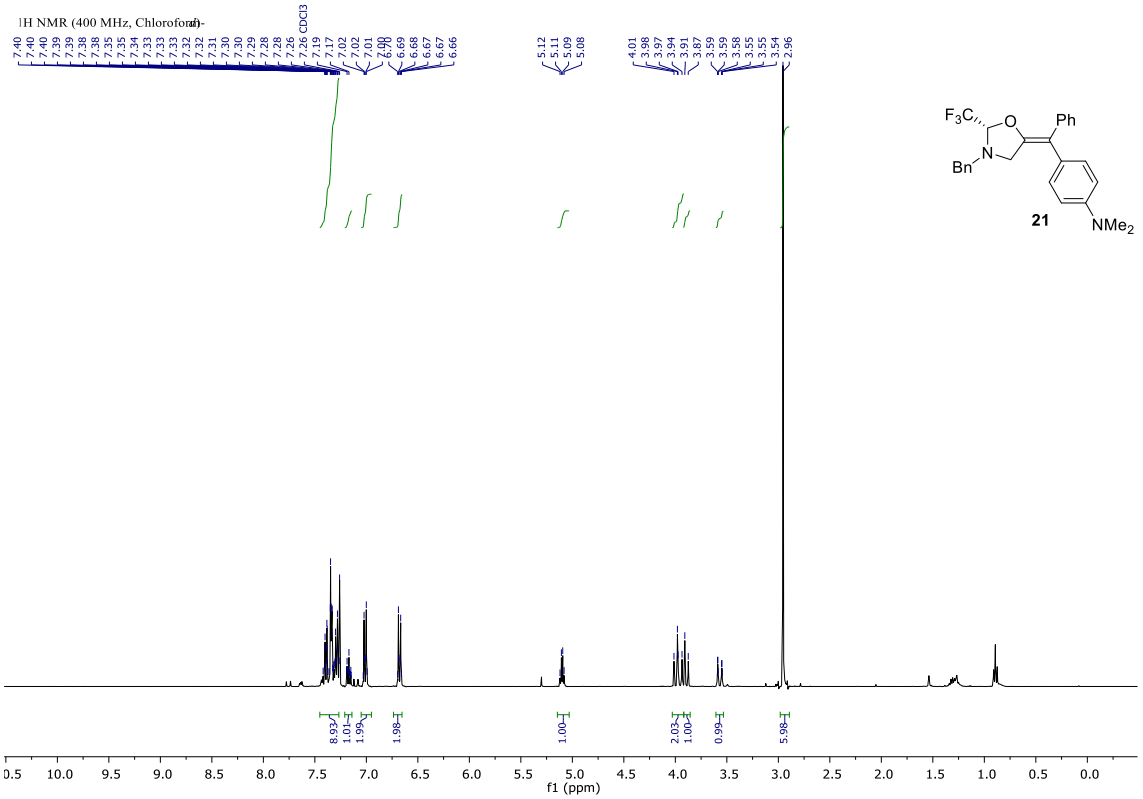

1H NMR (400 MHz, Chloroform-d)
CDCl3
F3C
O
Ph
N
Bn
20
OMe
f1 (ppm)


13C NMR (101 MHz, Chloroform-d)
CDCl3
F3C
O
Ph
N
Bn
20
OMe
f1 (ppm)

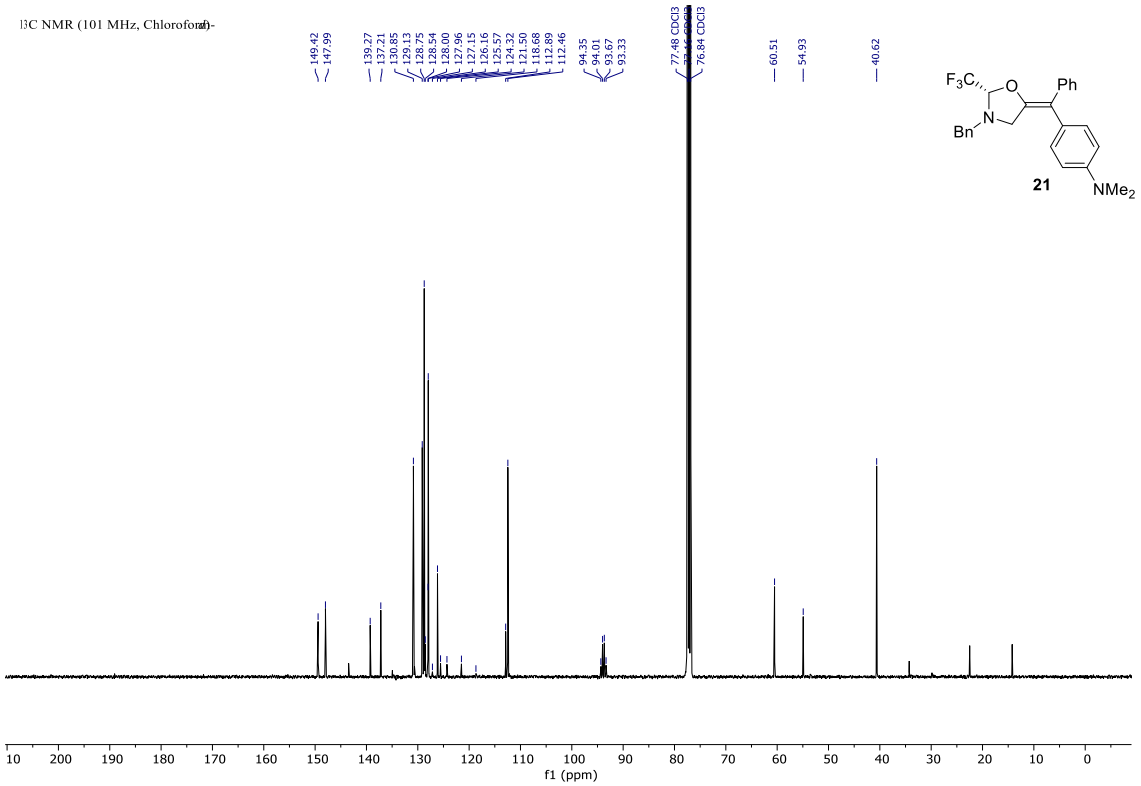
^{19}F NMR (376 MHz, Chloroform-*d*)



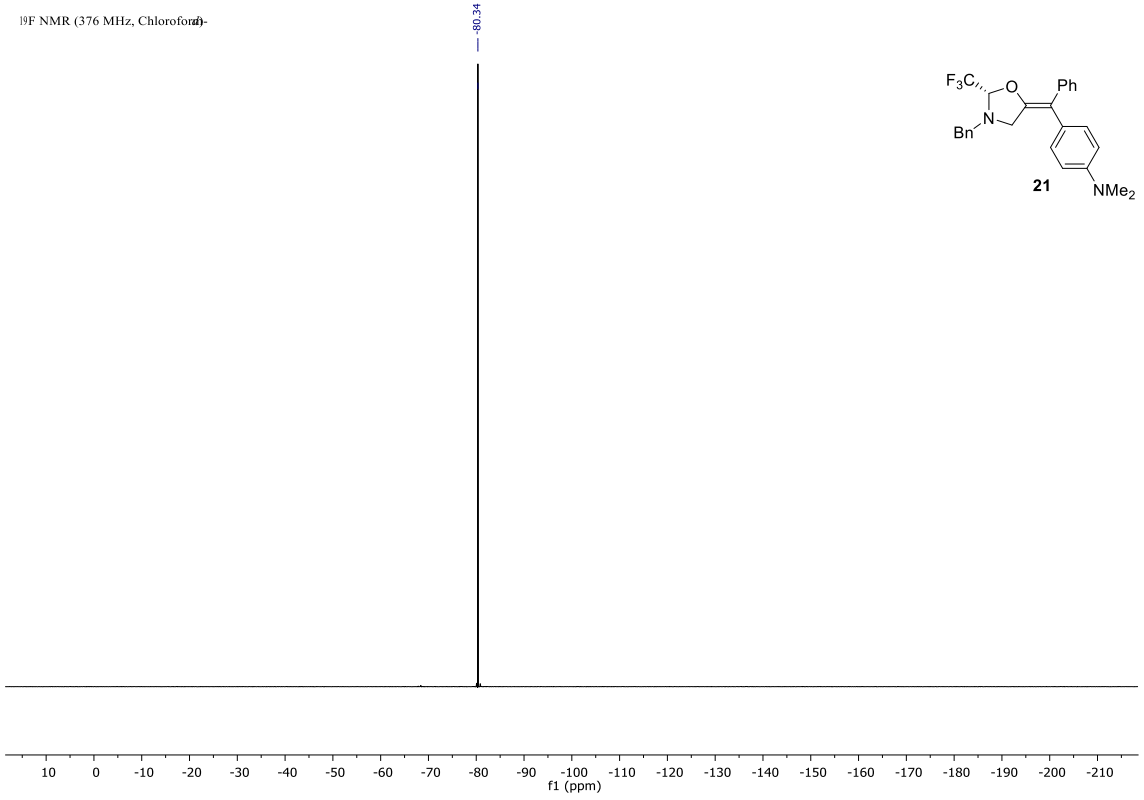
^{1}H NMR (400 MHz, Chloroform-*d*)

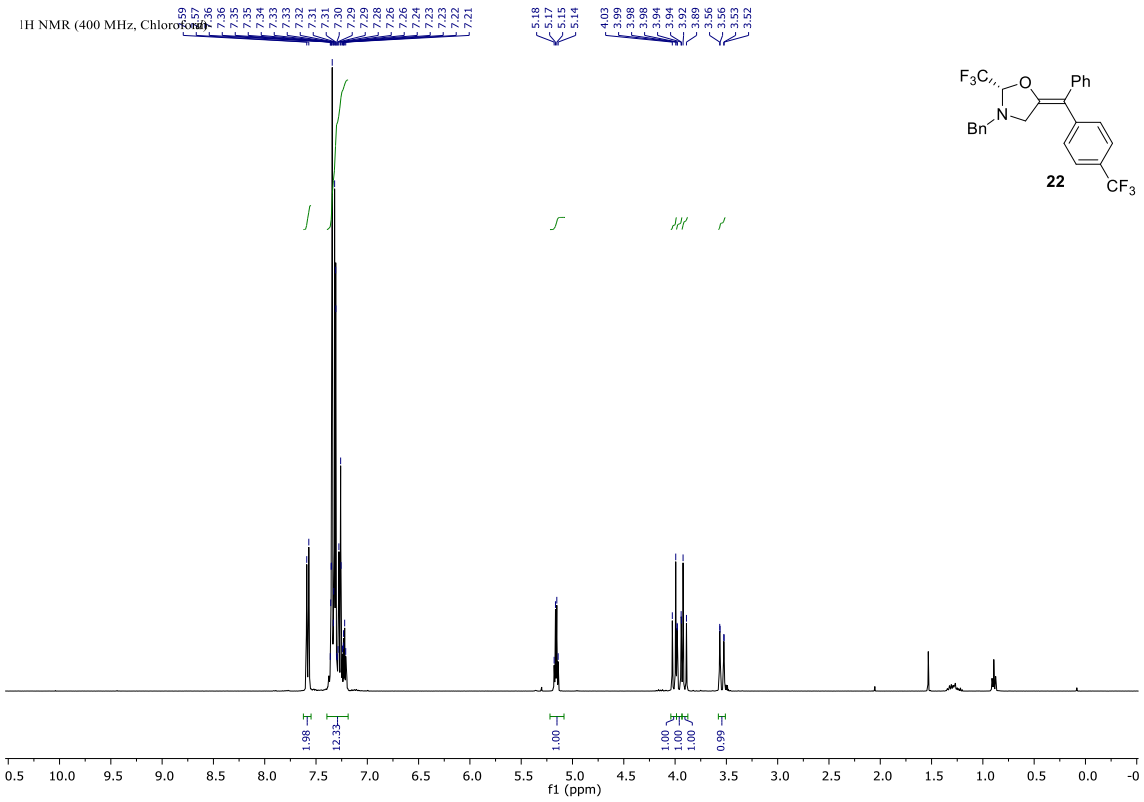


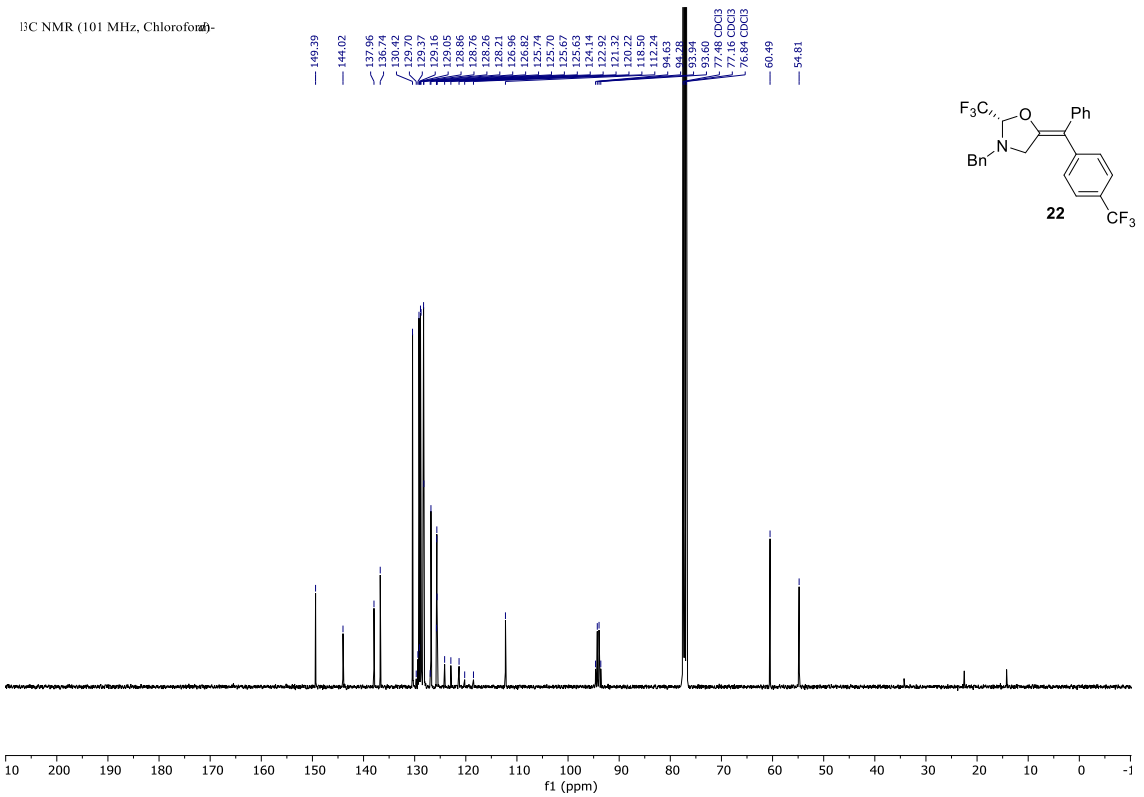
^{13}C NMR (101 MHz, Chloroform-*d*)

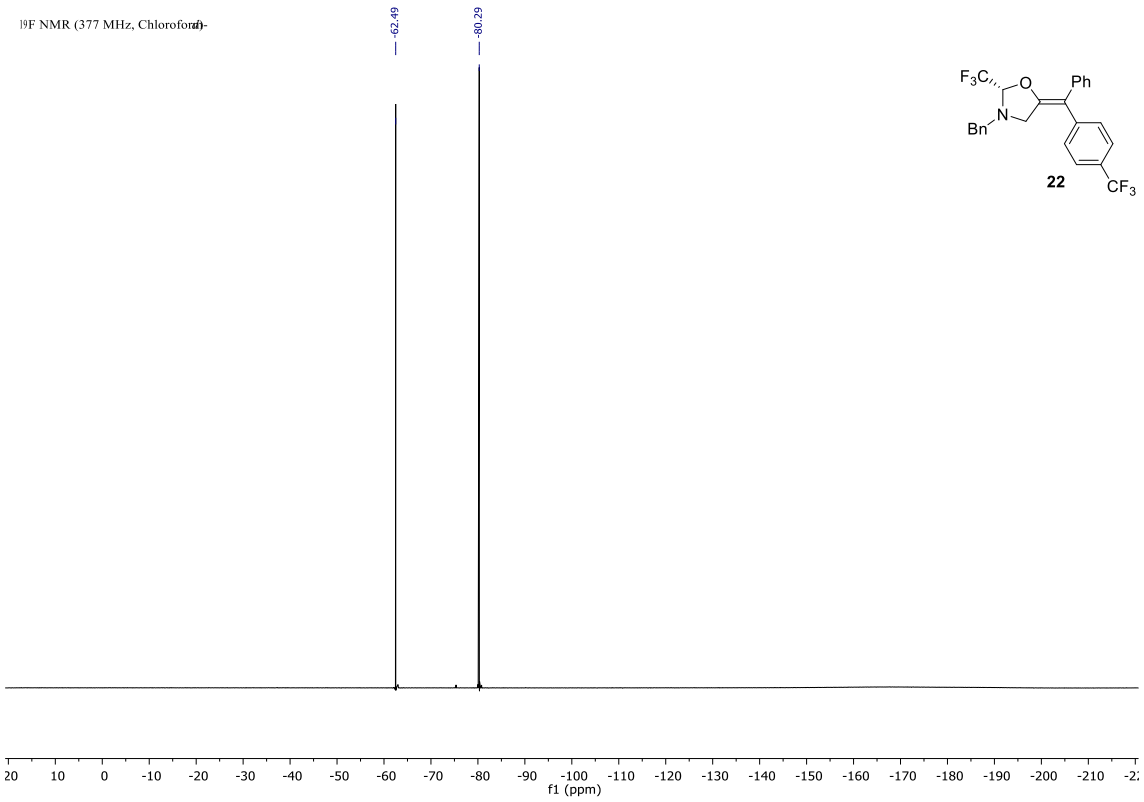


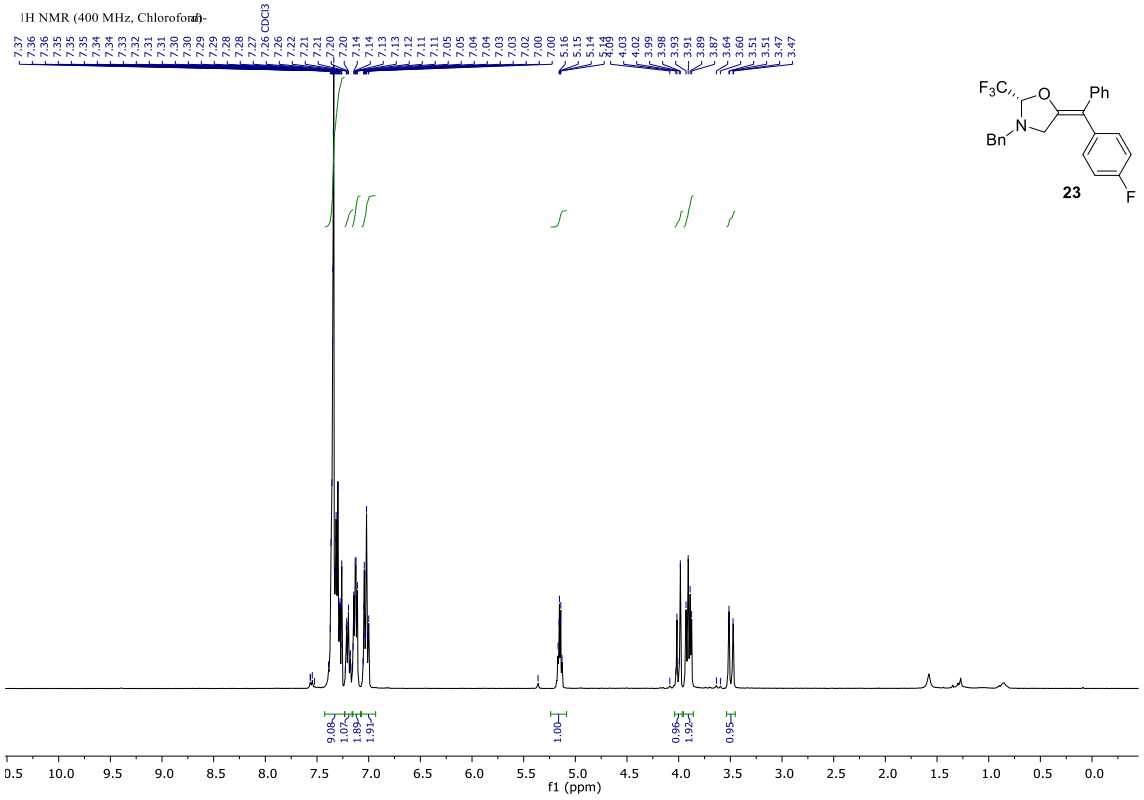
^{19}F NMR (376 MHz, Chloroform-*d*)



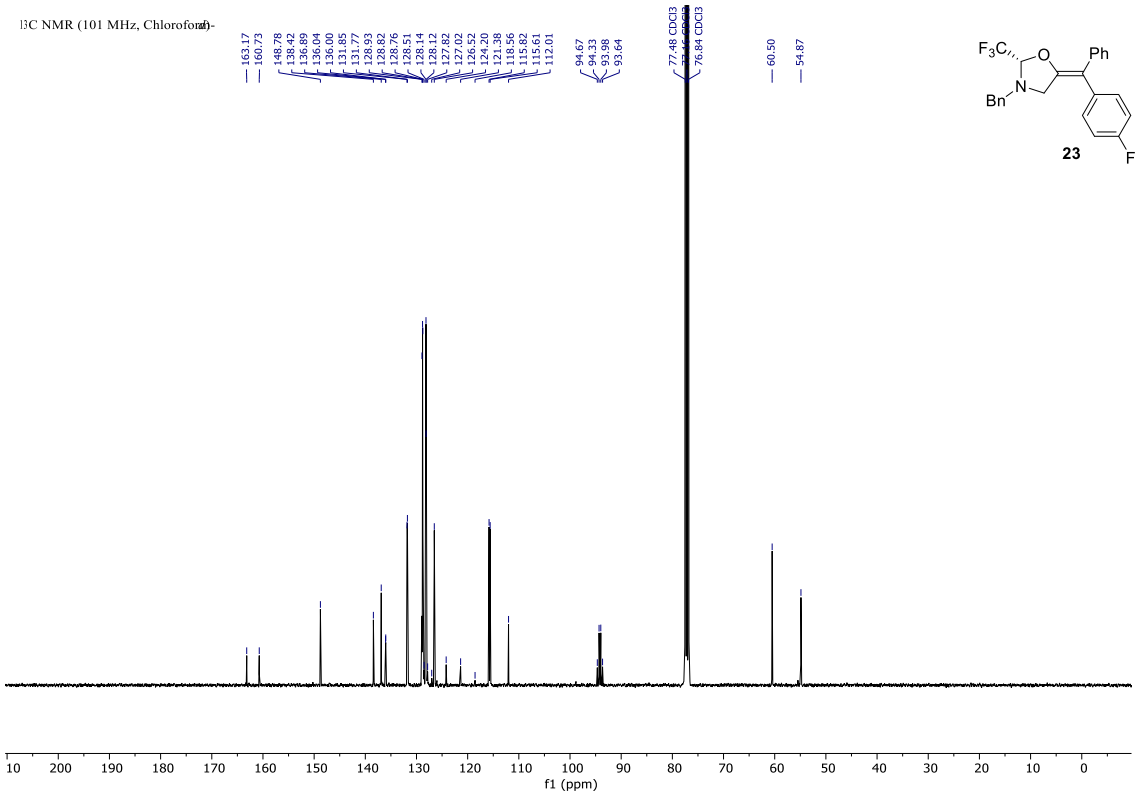

1H NMR (400 MHz, Chloroform-d)
7.59 7.57 7.36 7.36 7.35 7.35 7.34 7.33 7.33 7.32 7.31 7.31 7.30 7.29 7.28 7.26 7.26 7.24 7.23 7.23 7.22 7.21
5.18 5.17 5.15 5.14
4.03 3.99 3.98 3.98 3.94 3.94 3.92 3.89 3.56 3.56 3.53 3.52
F3C
O
Ph
N
Bn
22
CF3
1.98 12.33 1.00 1.00 1.00 1.00 0.99
f1 (ppm)


13C NMR (101 MHz, Chloroform-d)
149.39 144.02 137.96 136.74 130.42 129.70 129.37 129.16 129.05 128.86 128.76 128.26 128.21 126.96 126.82 125.74 125.70 125.67 125.63 124.14 122.92 121.32 120.22 118.50 112.24 94.63 93.28 93.94 93.60 77.48 CDCl3 77.16 CDCl3 76.84 CDCl3 60.49 54.81
F3C
O
Ph
N
Bn
22
CF3
f1 (ppm)


19F NMR (377 MHz, Chloroform-d)
-62.49
-80.29
F3C
O
Ph
N
Bn
22
CF3
f1 (ppm)

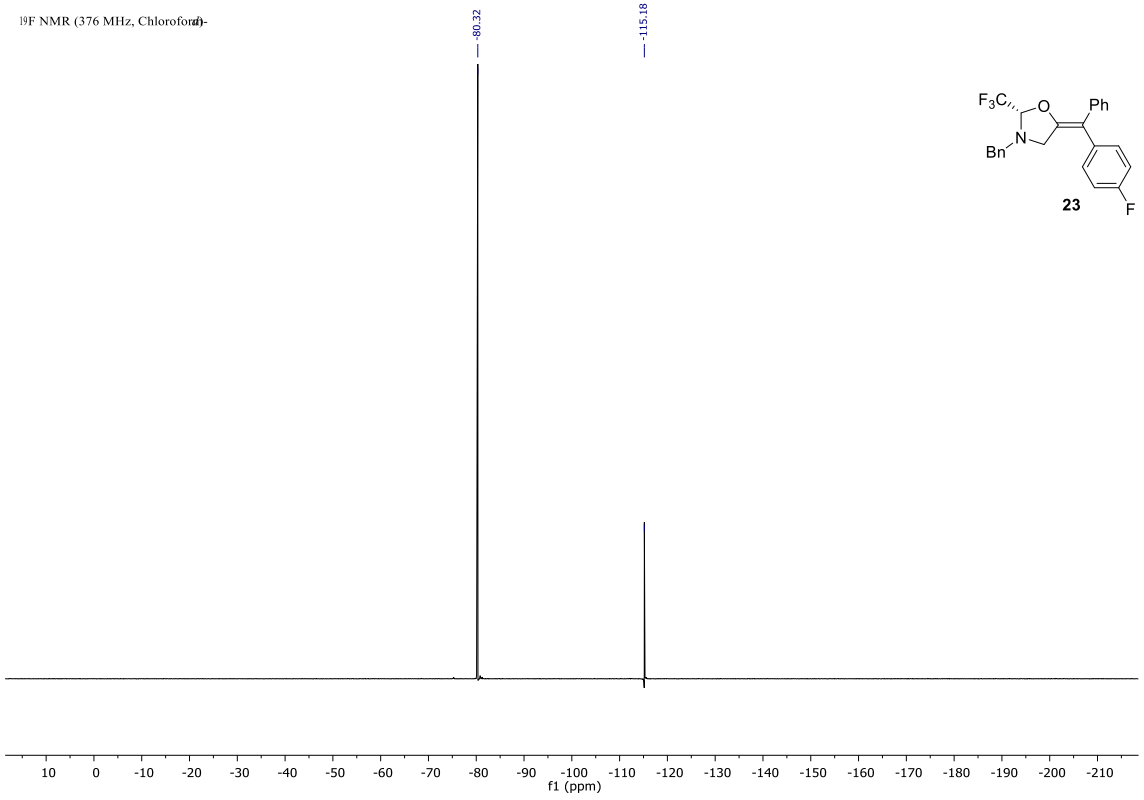

1H NMR (400 MHz, Chloroform-d)
CDCl3
F3C
O
Ph
N
Bn
23
F
9.08
1.07
1.89
1.91
1.00
0.96
1.92
0.95
f1 (ppm)

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

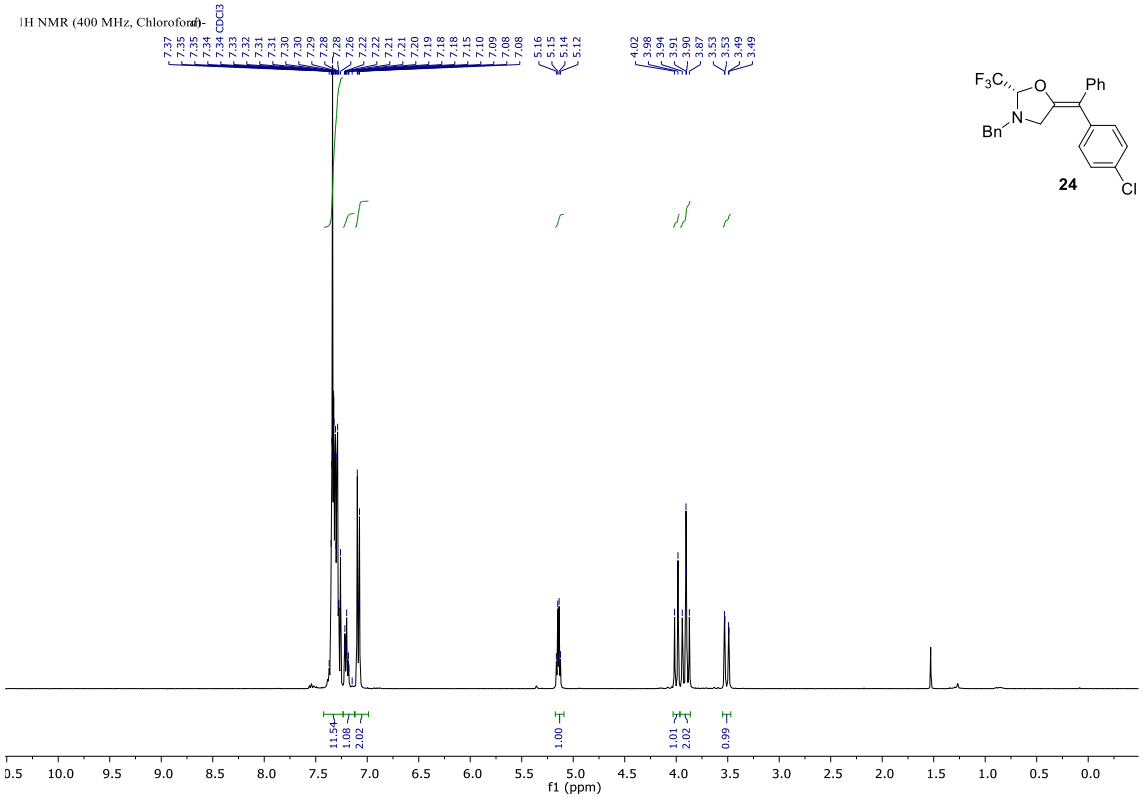


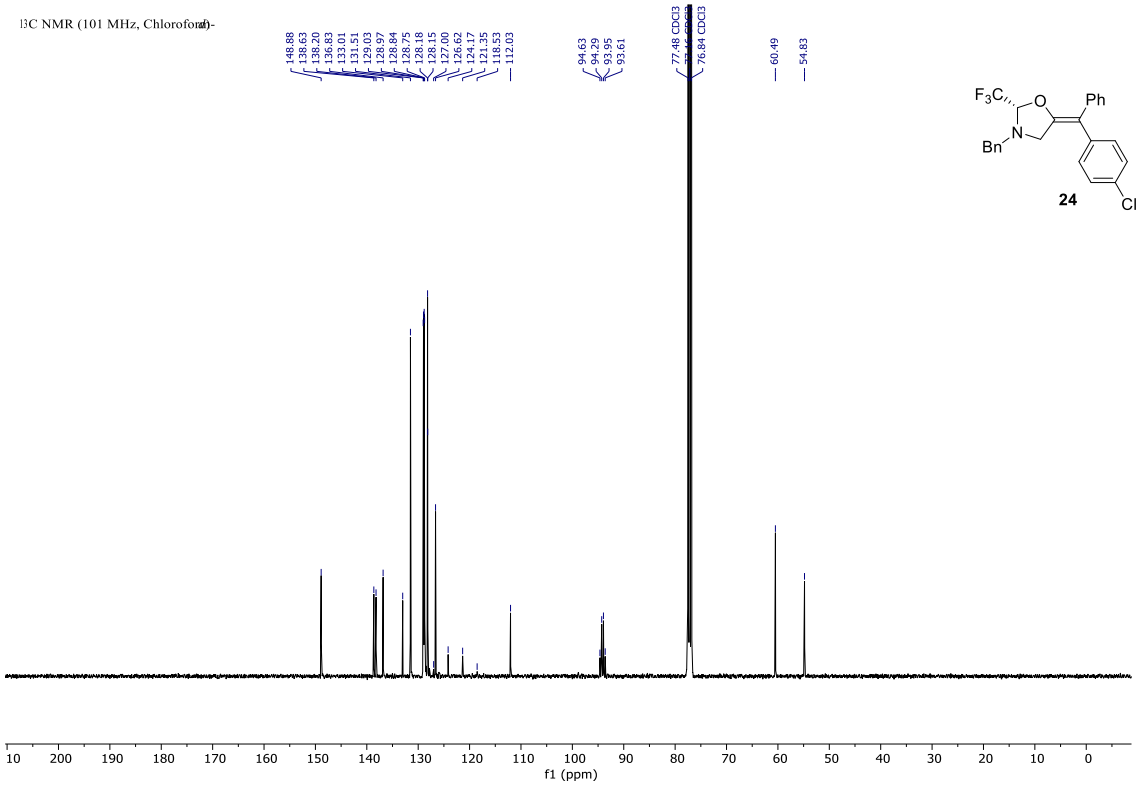
23

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

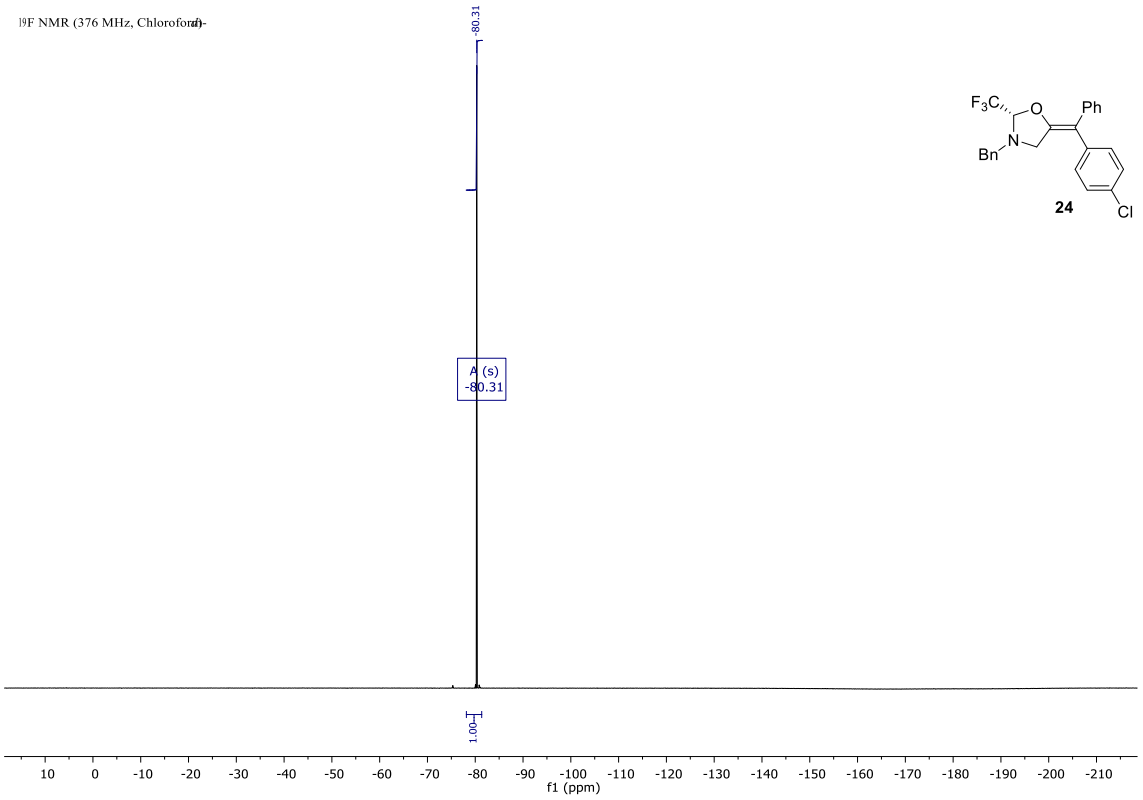


23


1H NMR (400 MHz, Chloroform-d)
7.37 7.35 7.35 7.34 7.34 CDCl3 7.33 7.32 7.31 7.31 7.30 7.30 7.29 7.28 7.28 7.26 7.22 7.21 7.21 7.20 7.19 7.18 7.18 7.15 7.10 7.09 7.08 7.08
5.16 5.15 5.14 5.12
4.02 3.98 3.94 3.91 3.90 3.87 3.53 3.53 3.49 3.49
F3C
O
Ph
N
Bn
Cl
24
11.54
1.08
2.02
1.00
1.01
2.02
0.99
f1 (ppm)

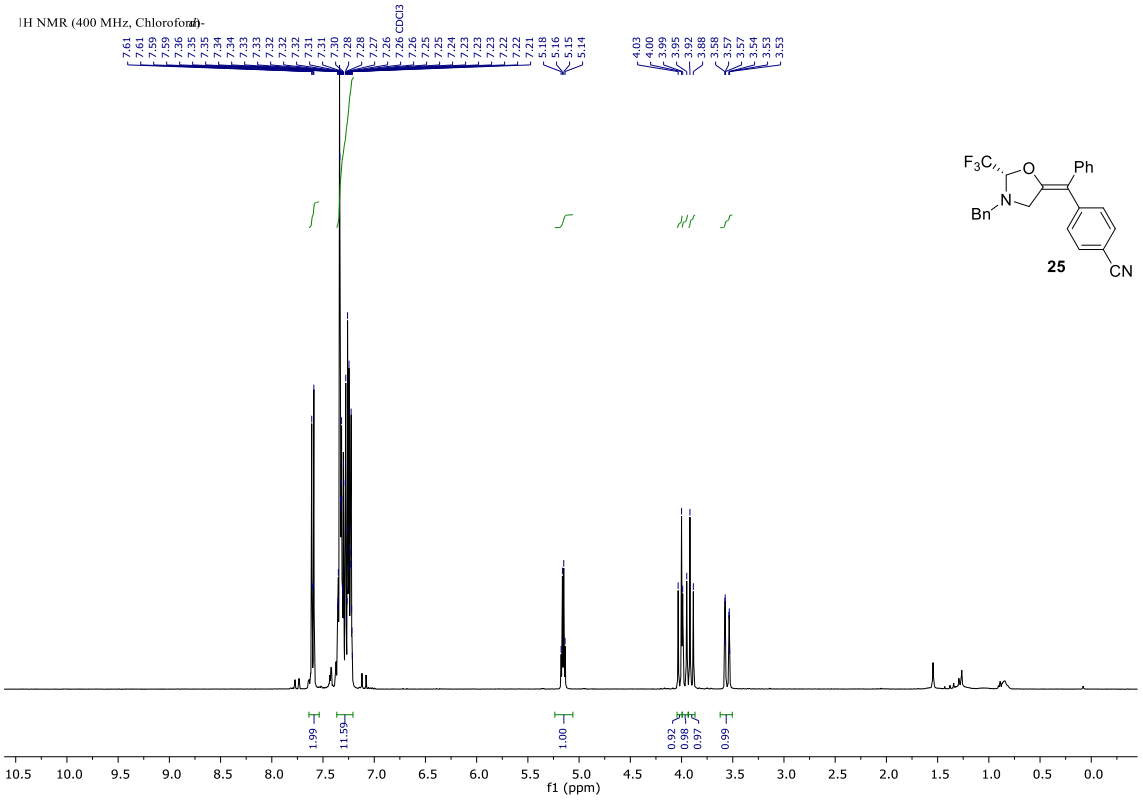

13C NMR (101 MHz, Chloroform-d)
148.88 138.63 138.20 136.83 133.01 131.51 129.03 128.97 128.84 128.75 128.18 128.15 127.00 126.62 124.17 121.35 118.53 112.03
94.63 94.29 93.95 93.61
77.48 CDCl3 77.16 76.84 CDCl3
60.49
54.83
F3C
O
Ph
N
Bn
Cl
24
f1 (ppm)

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



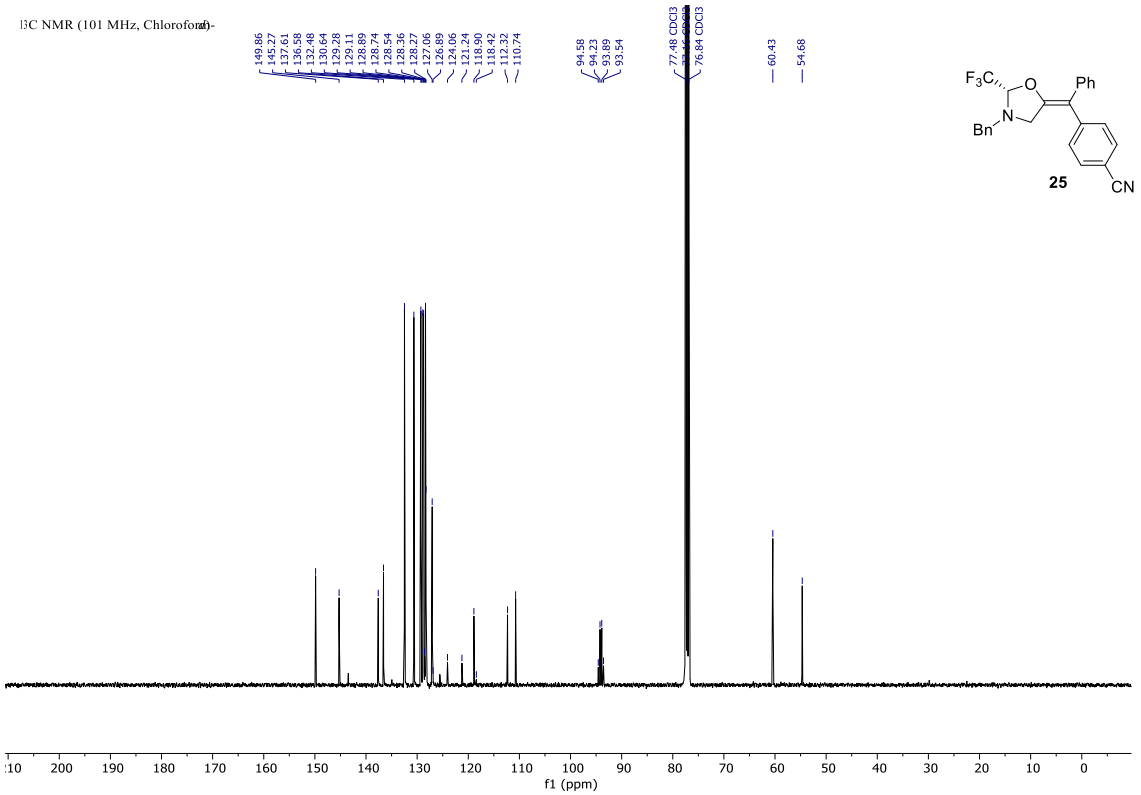
24

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



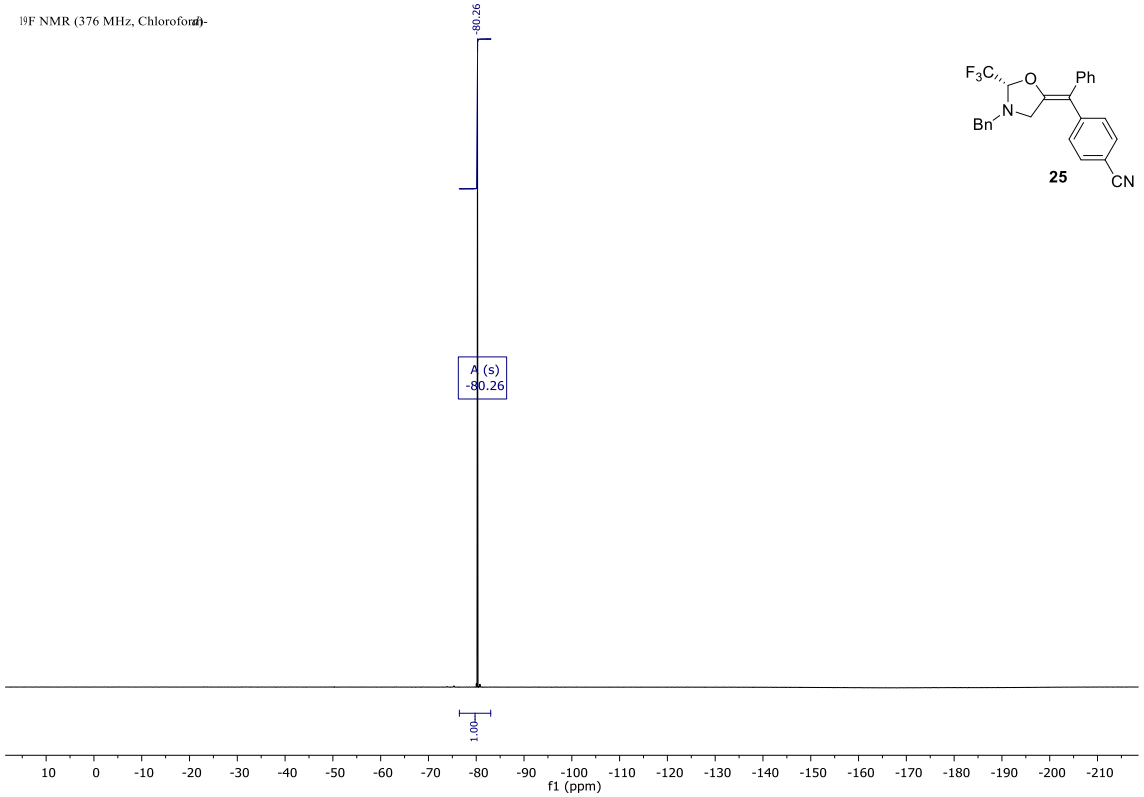
25

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

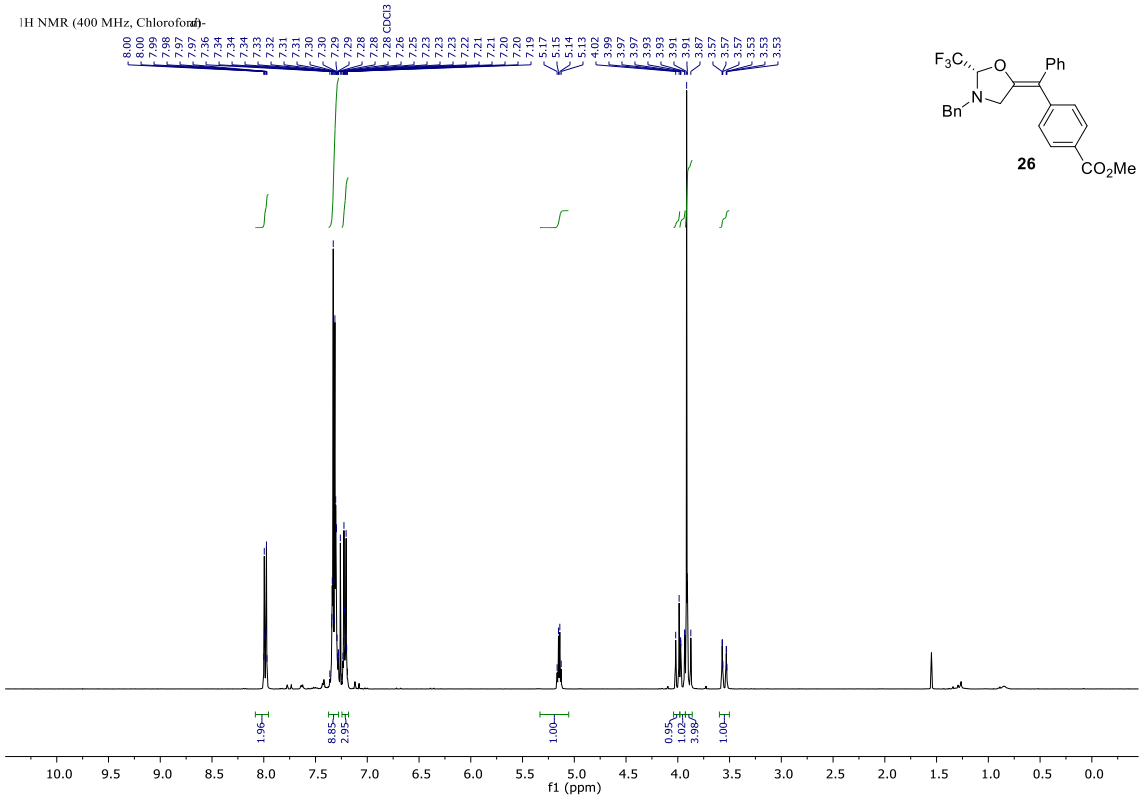


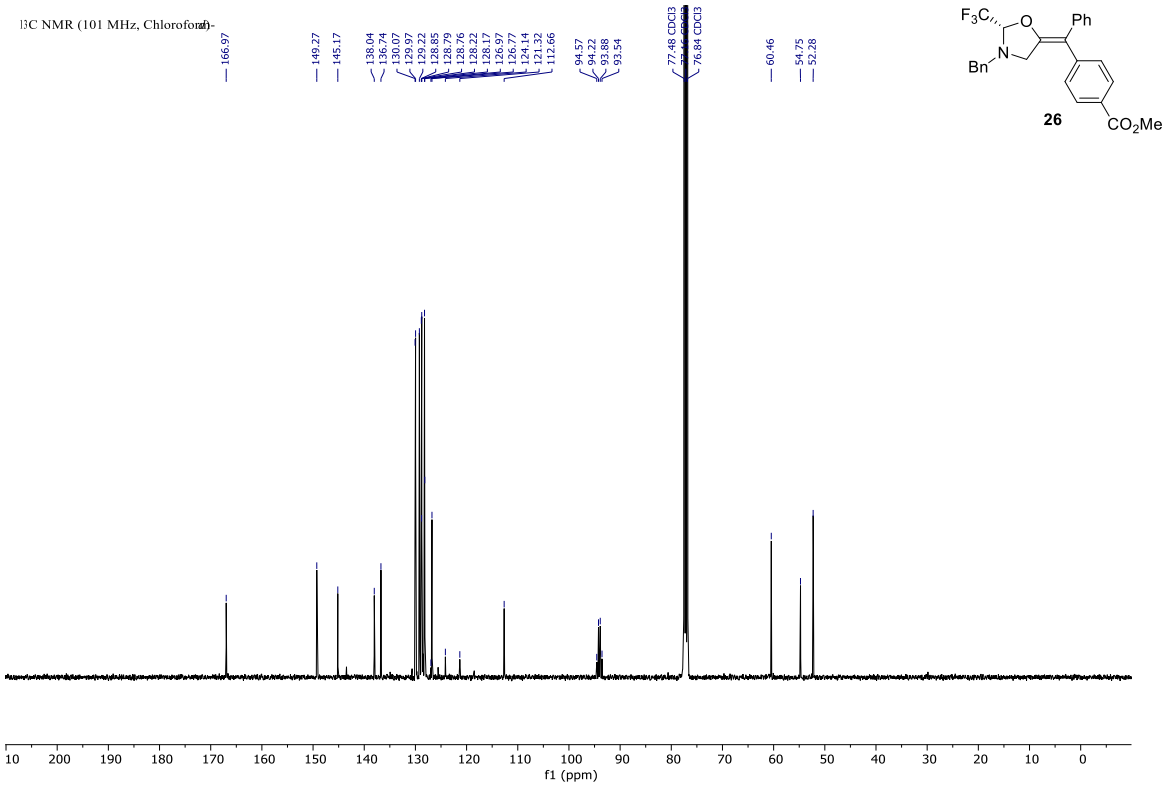
25

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

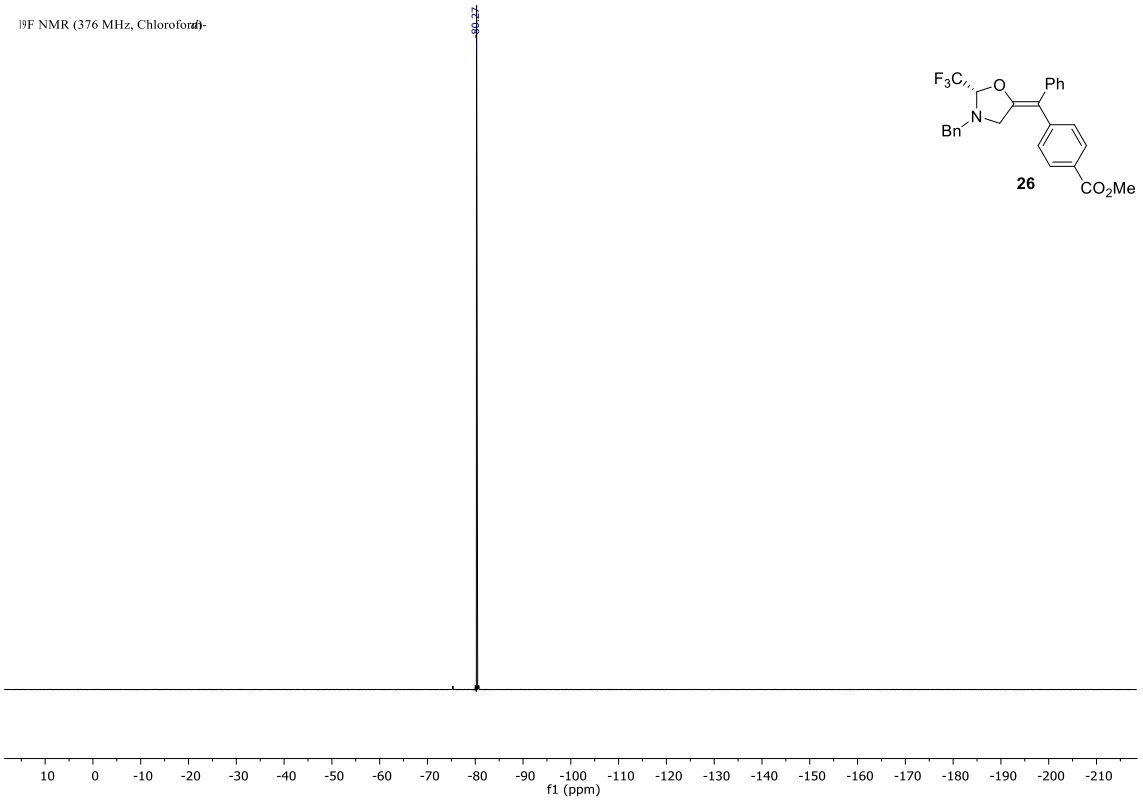


25


1H NMR (400 MHz, Chloroform-d)
7.28 CDCl3
1.96
8.85
2.95
1.00
0.95
1.02
3.98
1.00
f1 (ppm)
F3C
O
Ph
N
Bn
26
CO2Me

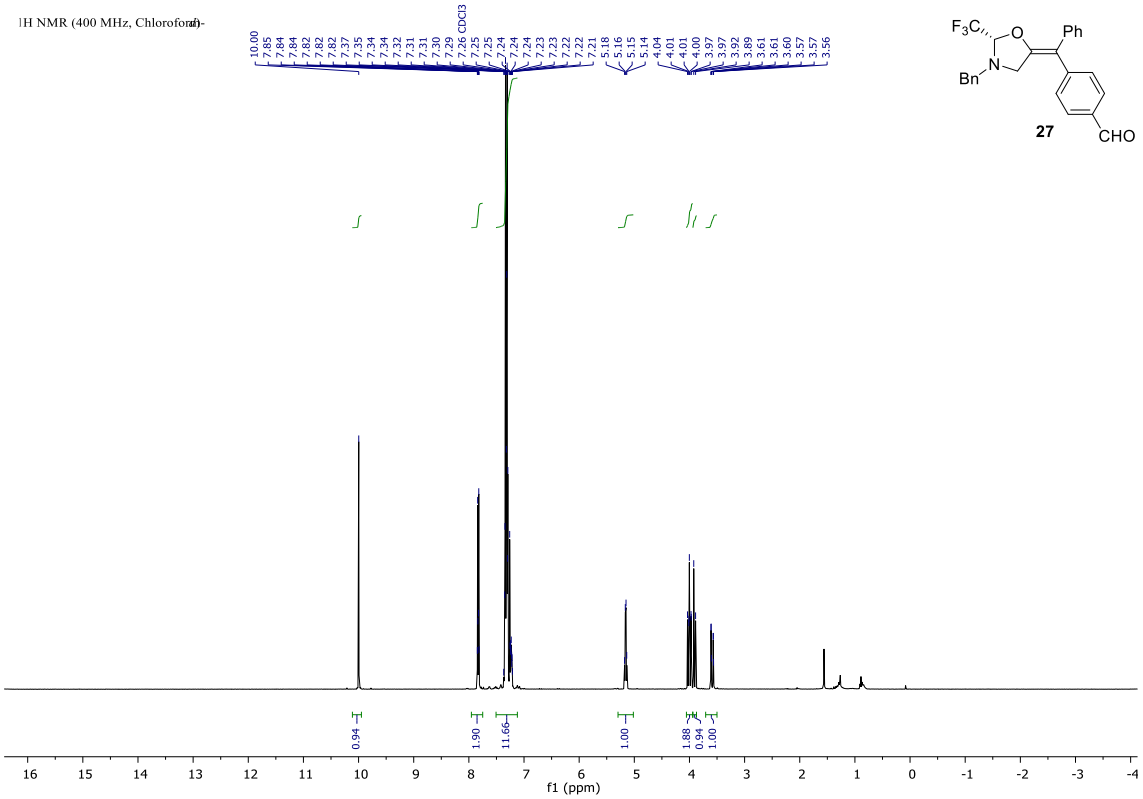

13C NMR (101 MHz, Chloroform-d)
166.97
149.27
145.17
138.04
136.74
130.07
129.97
129.22
128.85
128.79
128.76
128.22
128.17
126.97
126.77
124.14
121.32
112.66
94.57
94.22
93.88
93.54
77.48 CDCl3
76.84 CDCl3
60.46
54.75
52.28
f1 (ppm)
F3C
O
Ph
N
Bn
26
CO2Me

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

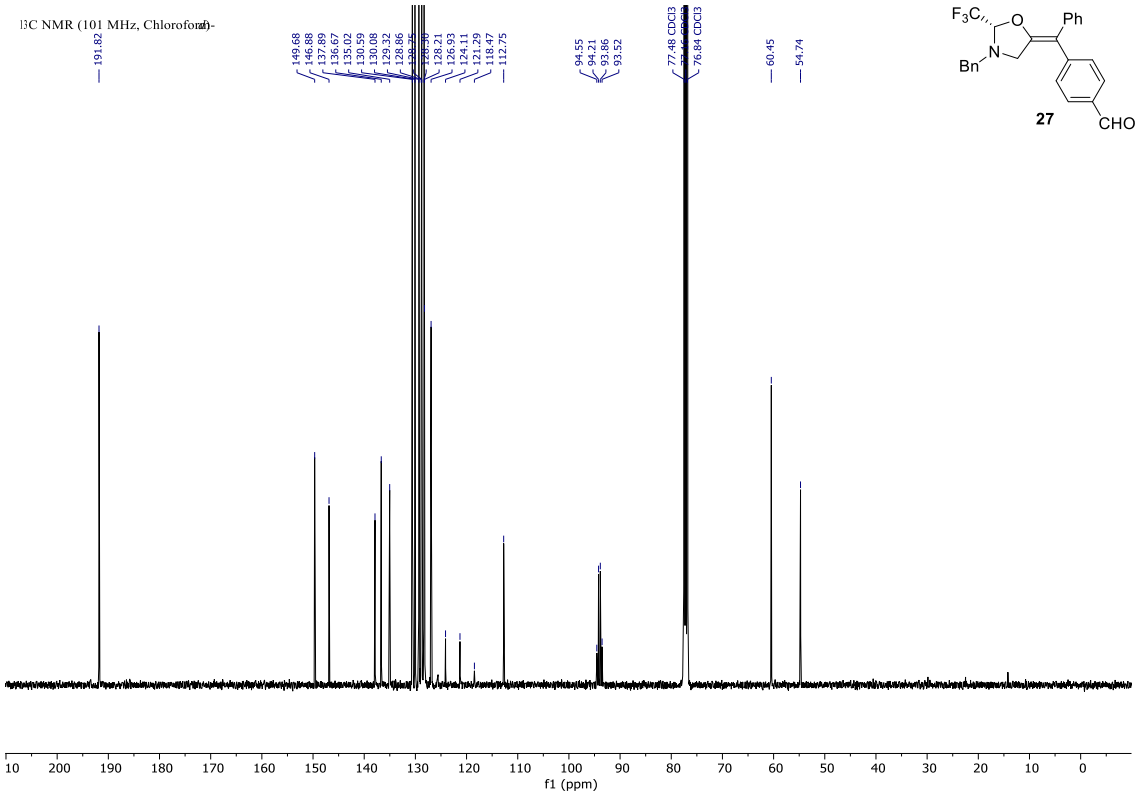


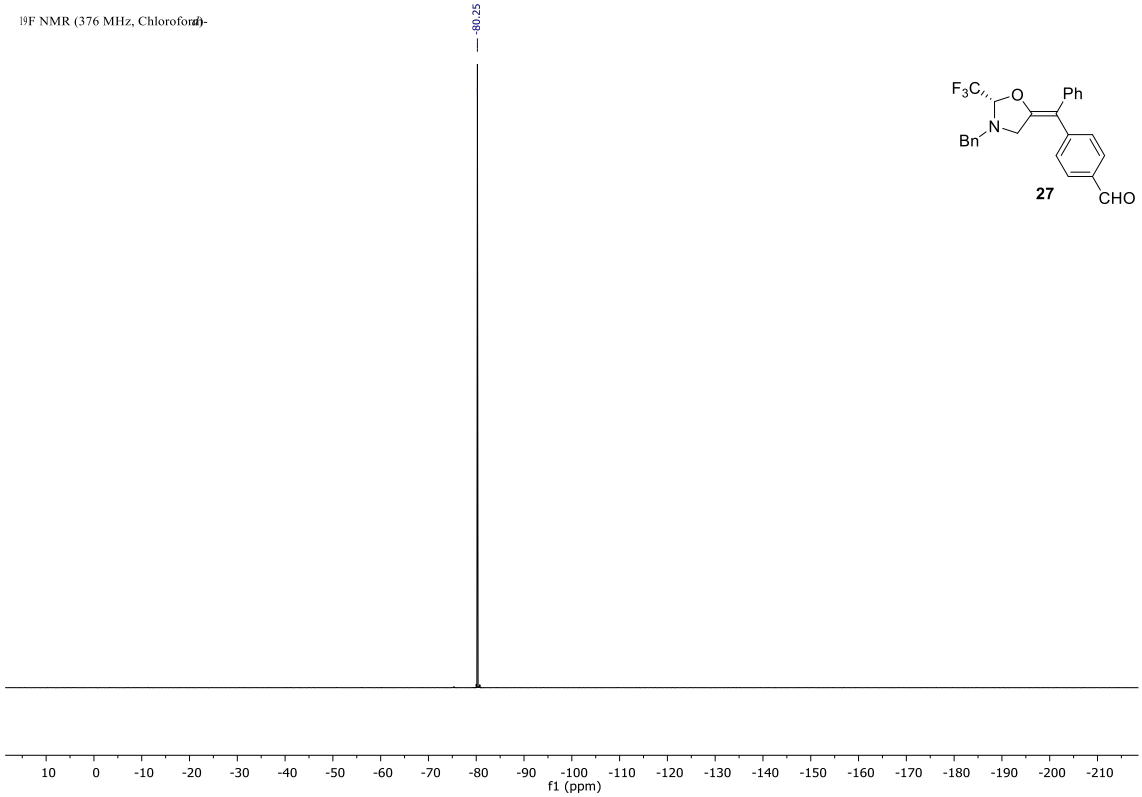
26

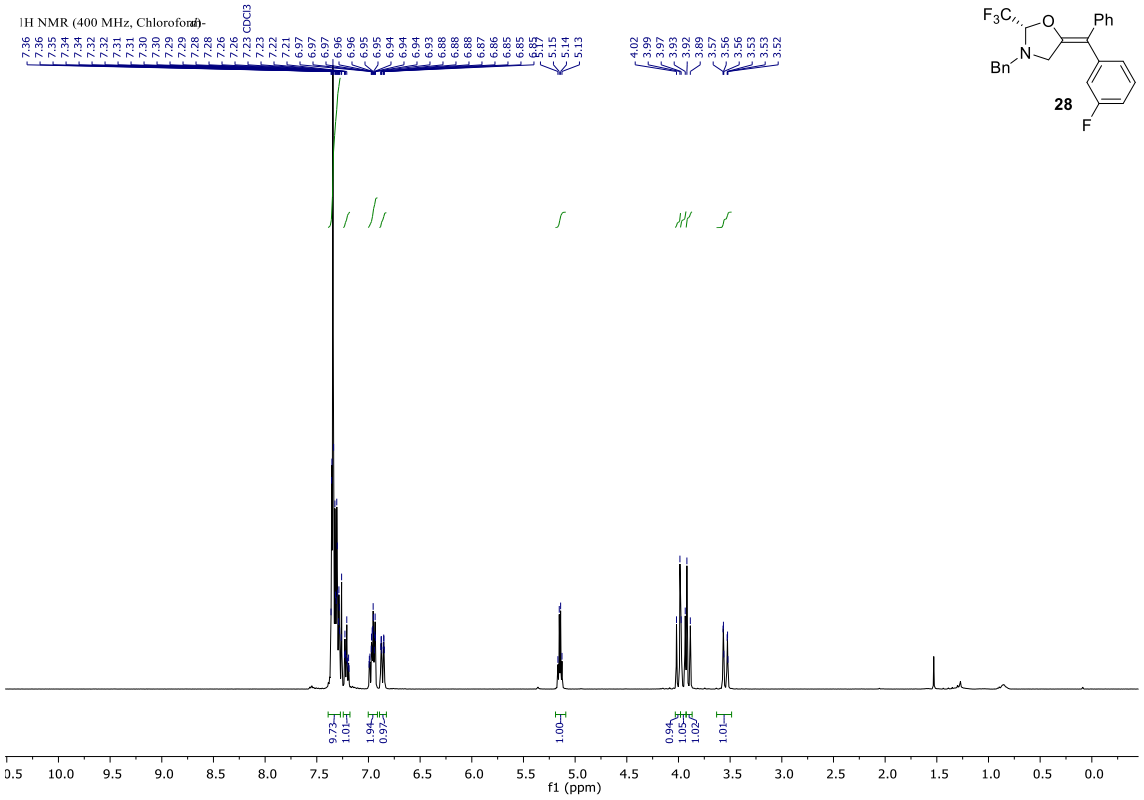
^{1}H NMR (400 MHz, Chloroform-*d*)

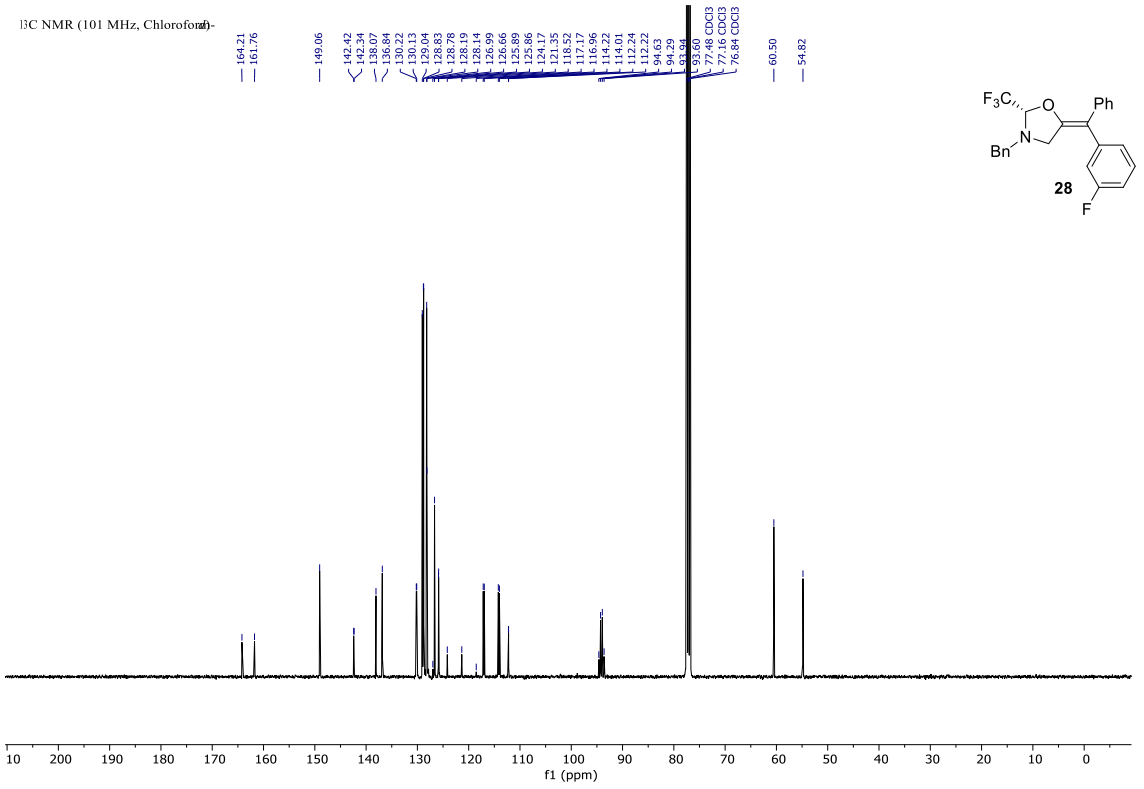


27

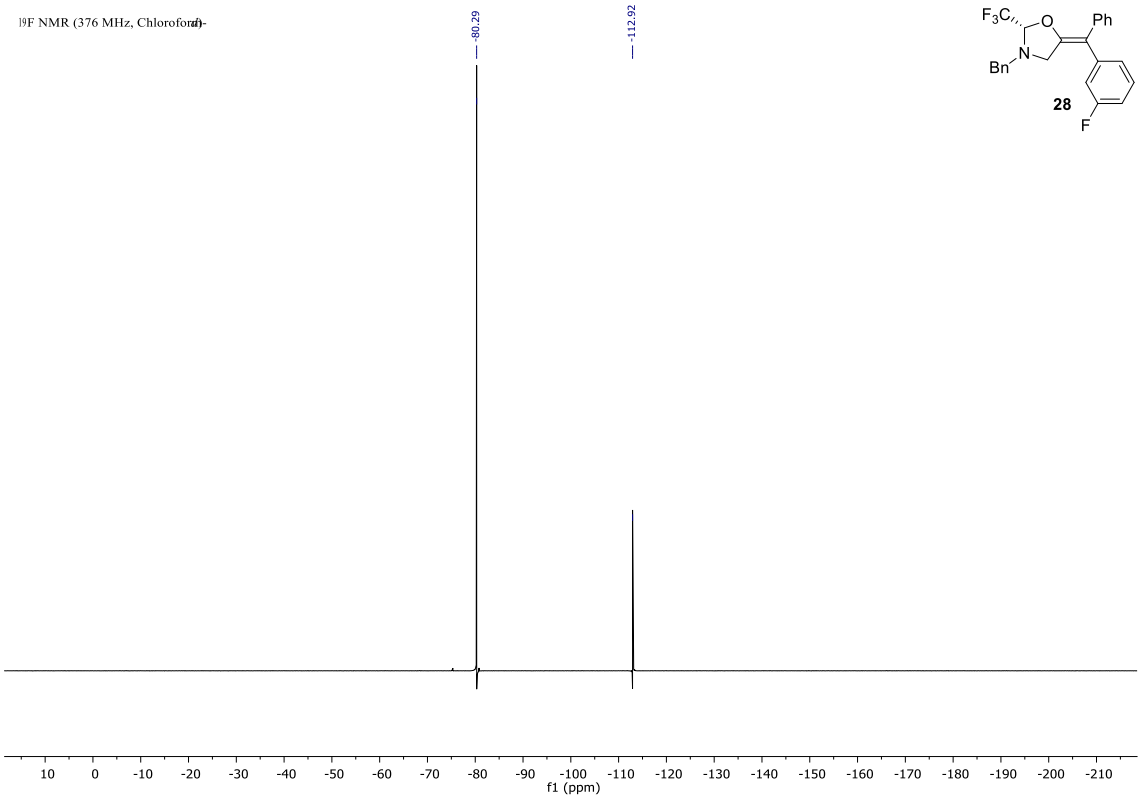

13C NMR (101 MHz, Chloroform-d)
191.82
149.68
146.88
137.89
136.67
135.02
130.59
130.08
129.32
128.86
128.21
126.93
124.11
121.29
118.47
112.75
94.55
94.21
93.86
93.52
77.48 CDCl3
76.84 CDCl3
60.45
54.74
F3C
O
Ph
N
Bn
27
CHO
10 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


19F NMR (376 MHz, Chloroform-d)
-80.25
F3C
O
Ph
N
Bn
27
CHO
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


1H NMR (400 MHz, Chloroform-d)
CDCl3
f1 (ppm)
28

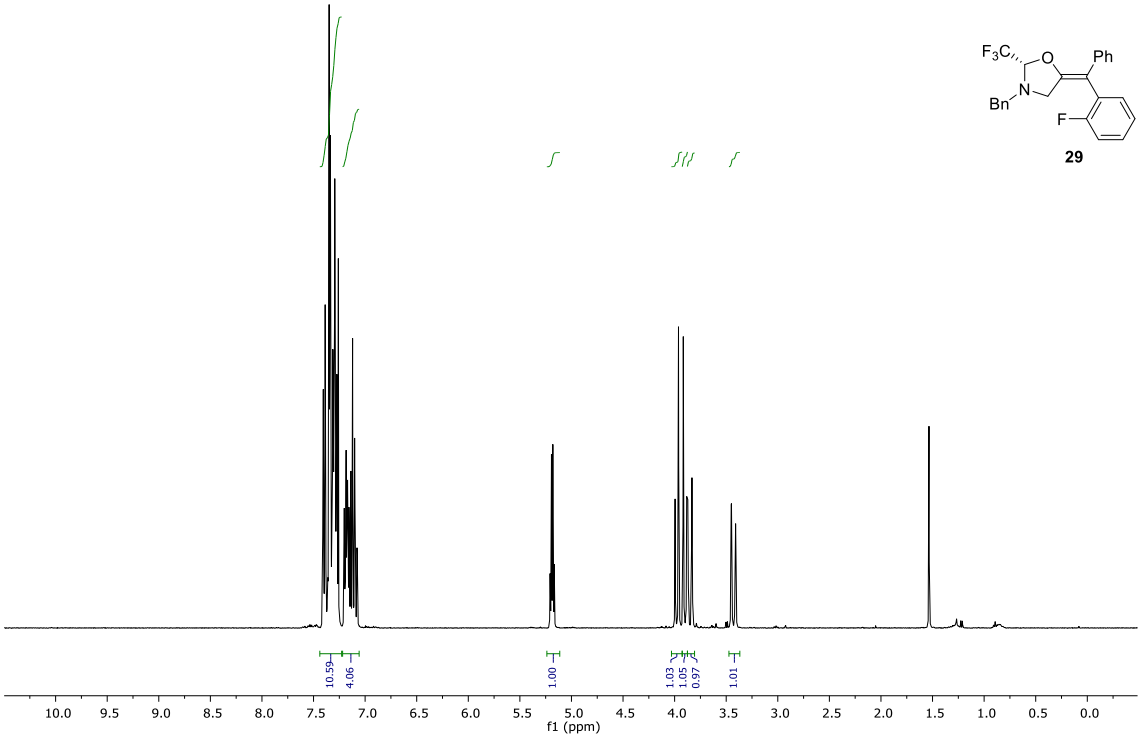

13C NMR (101 MHz, Chloroform-d)
CDCl3
f1 (ppm)
28

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



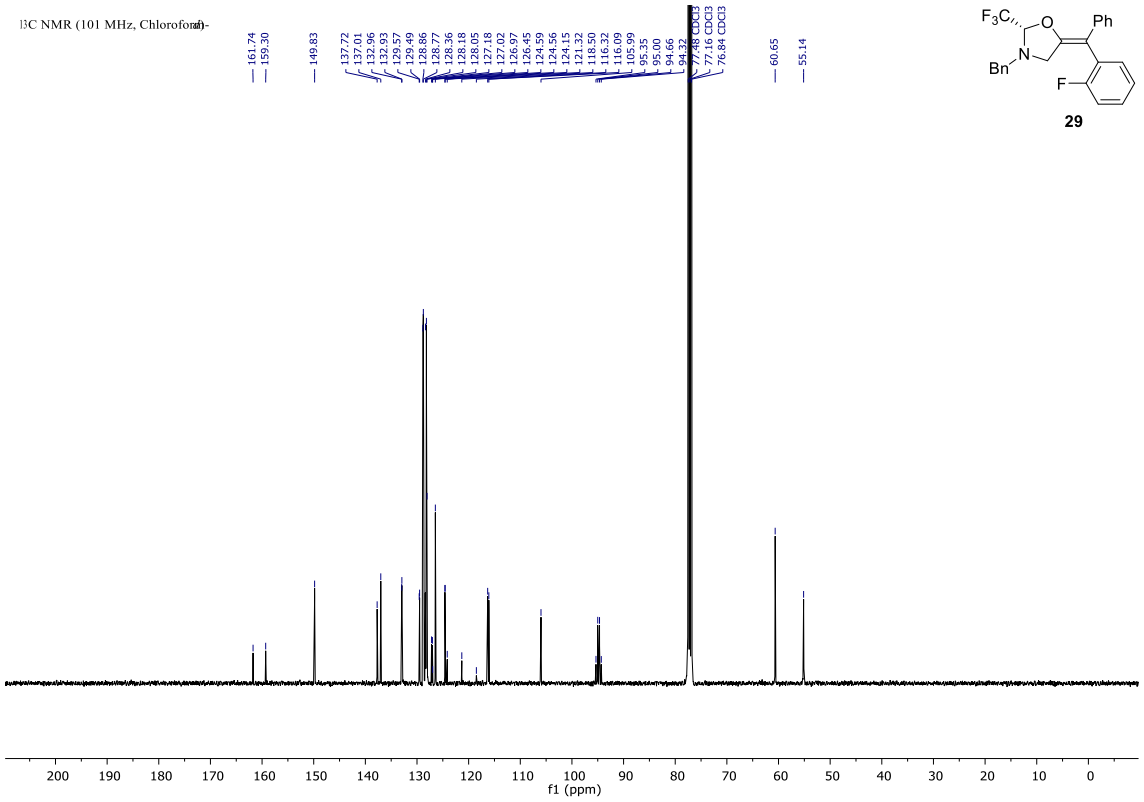
28

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



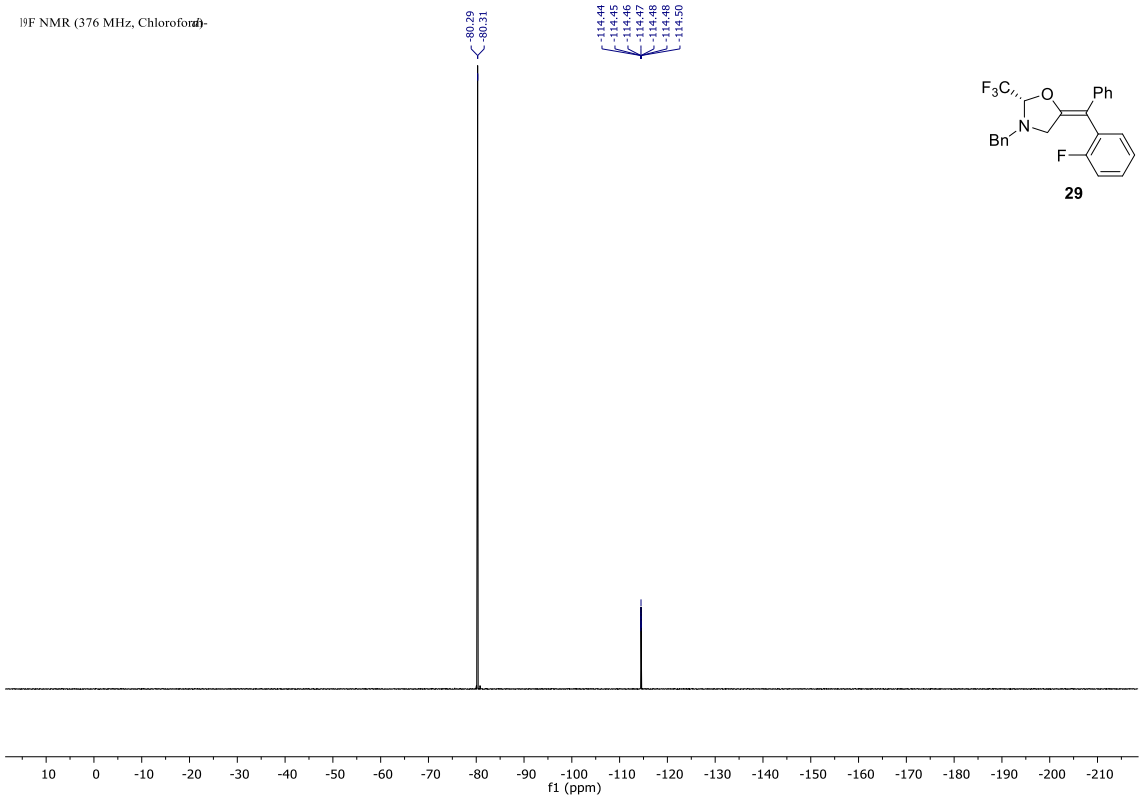
29

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

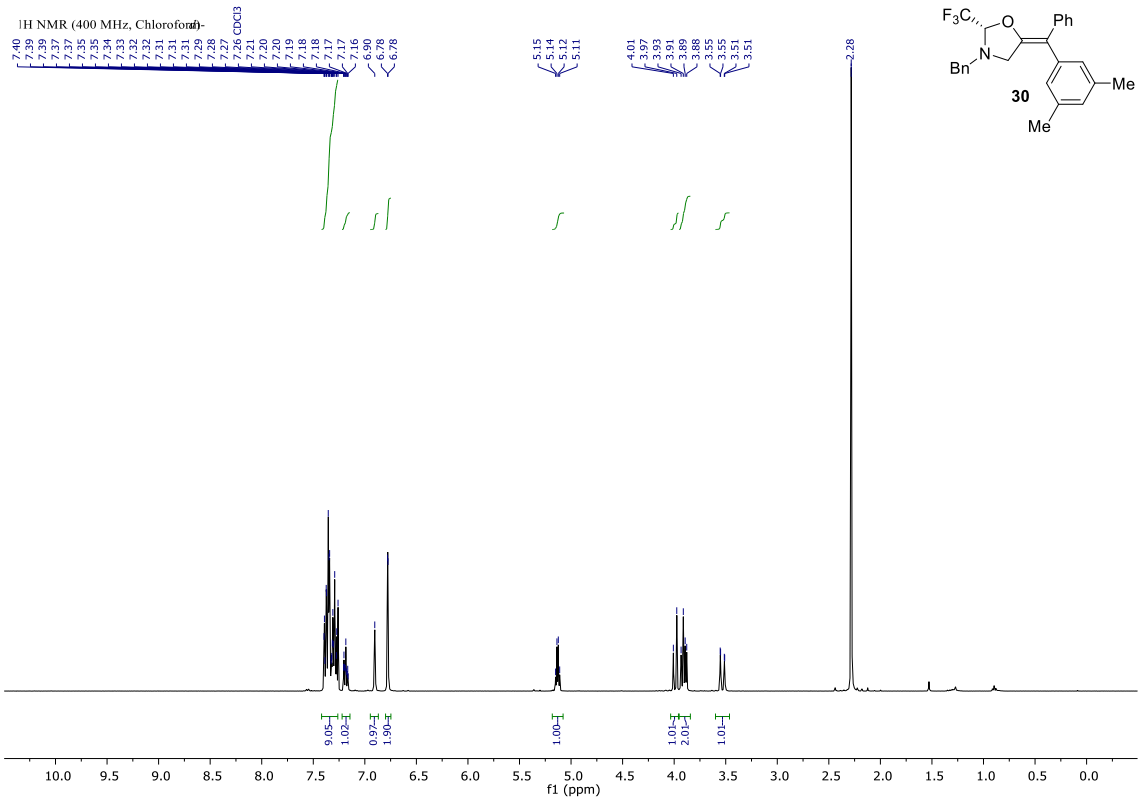


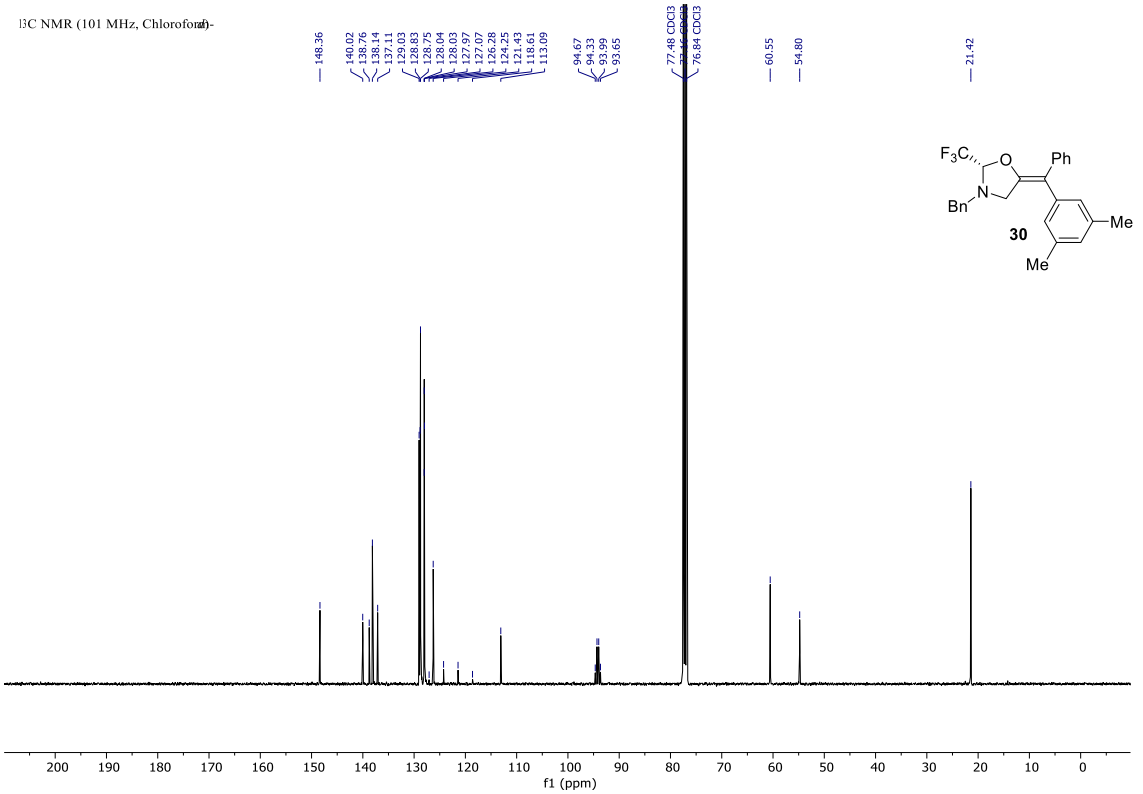
29

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

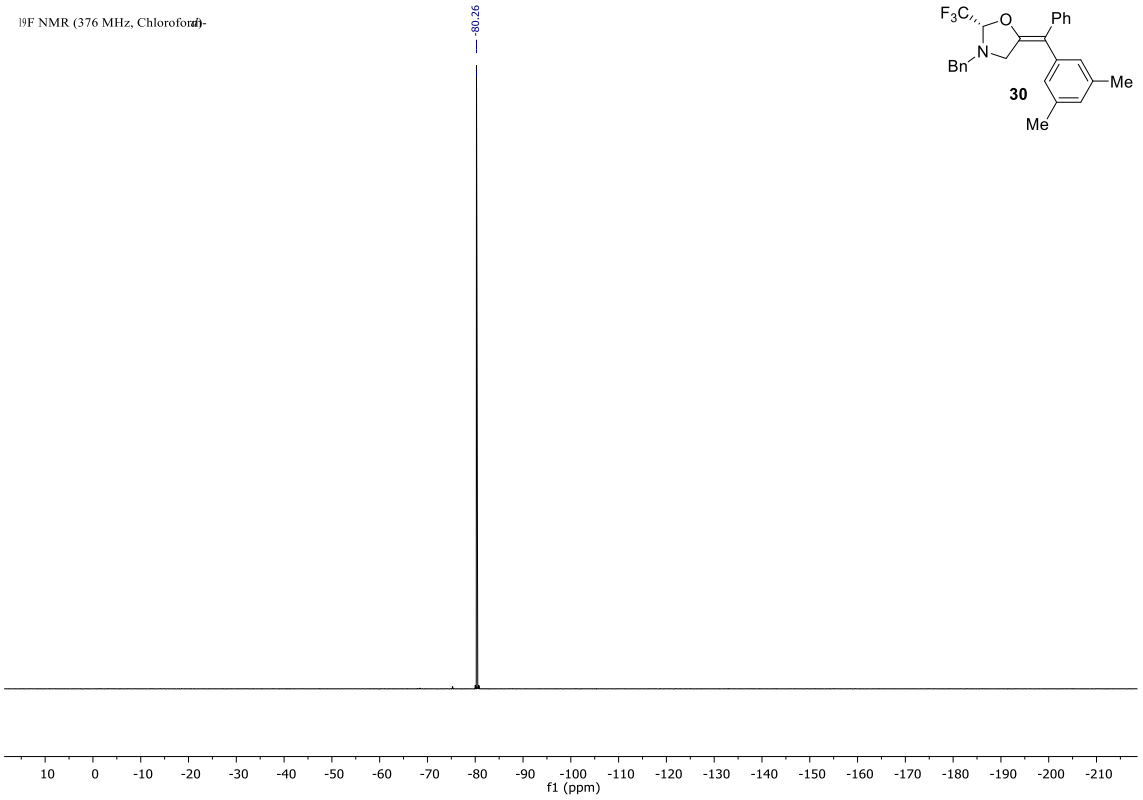


29


1H NMR (400 MHz, Chloroform-d)
7.40 7.39 7.39 7.37 7.37 7.35 7.35 7.34 7.33 7.32 7.32 7.31 7.31 7.31 7.29 7.28 7.27 7.26 CDCl3 7.21 7.20 7.20 7.19 7.18 7.18 7.17 7.17 7.16 6.90 6.78 6.78
5.15 5.14 5.12 5.11
4.01 3.97 3.93 3.91 3.89 3.88 3.55 3.55 3.51 3.51
2.28
9.05 1.02 0.97 1.90 1.00 1.01 2.01 1.01
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
F3C
O
Ph
N
Bn
Me
30
Me

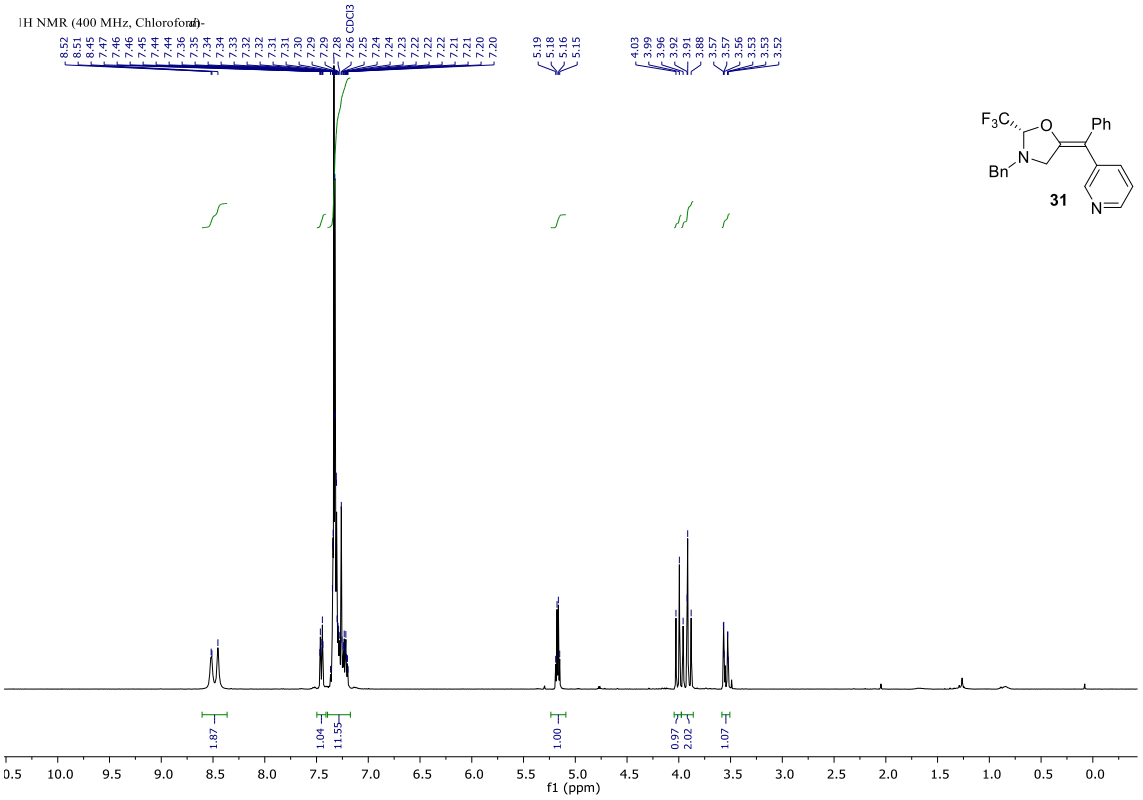

13C NMR (101 MHz, Chloroform-d)
148.36
140.02 138.76 138.14 137.11 129.03 128.83 128.75 128.04 128.03 127.97 127.07 126.28 124.25 121.43 118.61 113.09
94.67 94.33 93.99 93.65
77.48 CDCl3 76.84 CDCl3
60.55
54.80
21.42
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)
F3C
O
Ph
N
Bn
Me
30
Me

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



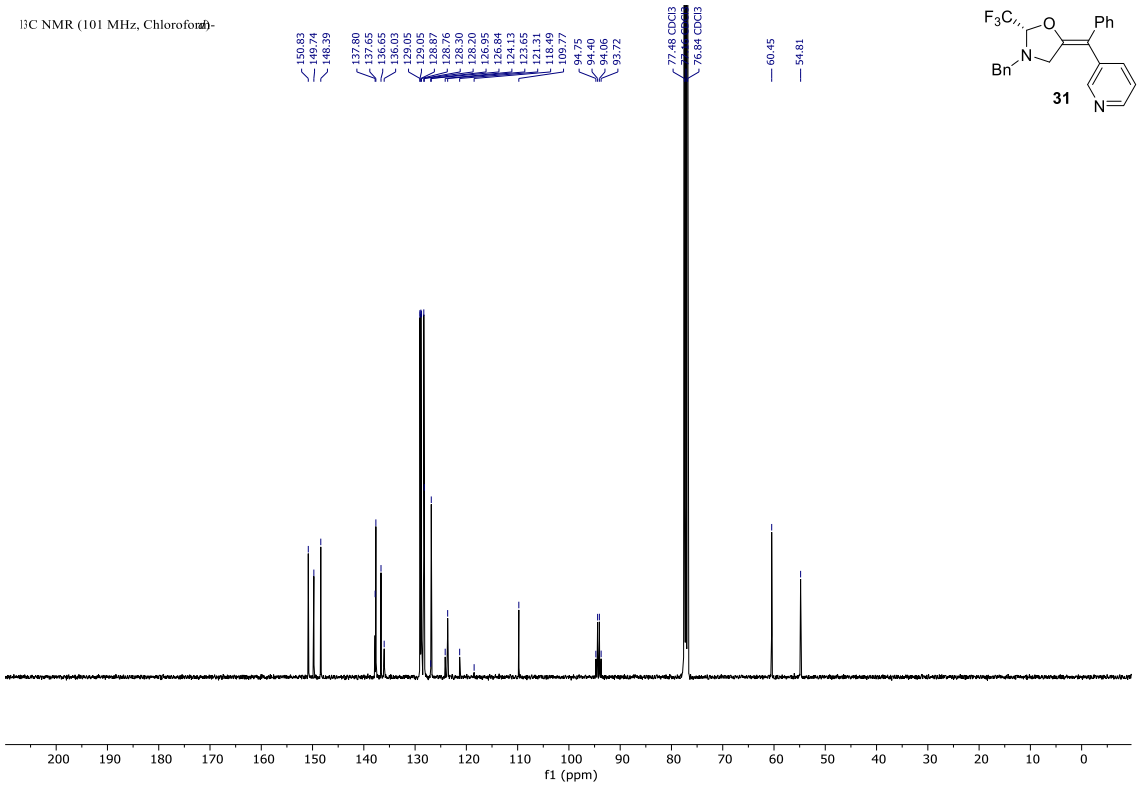
30

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



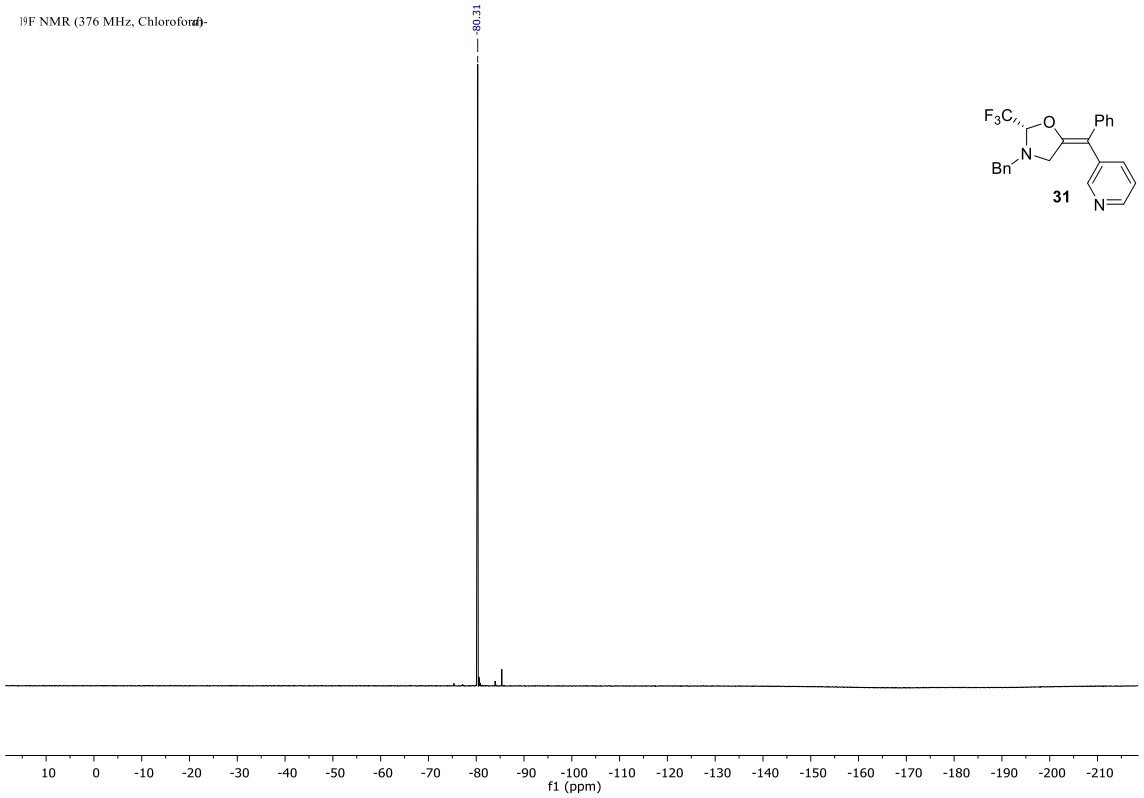
31

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

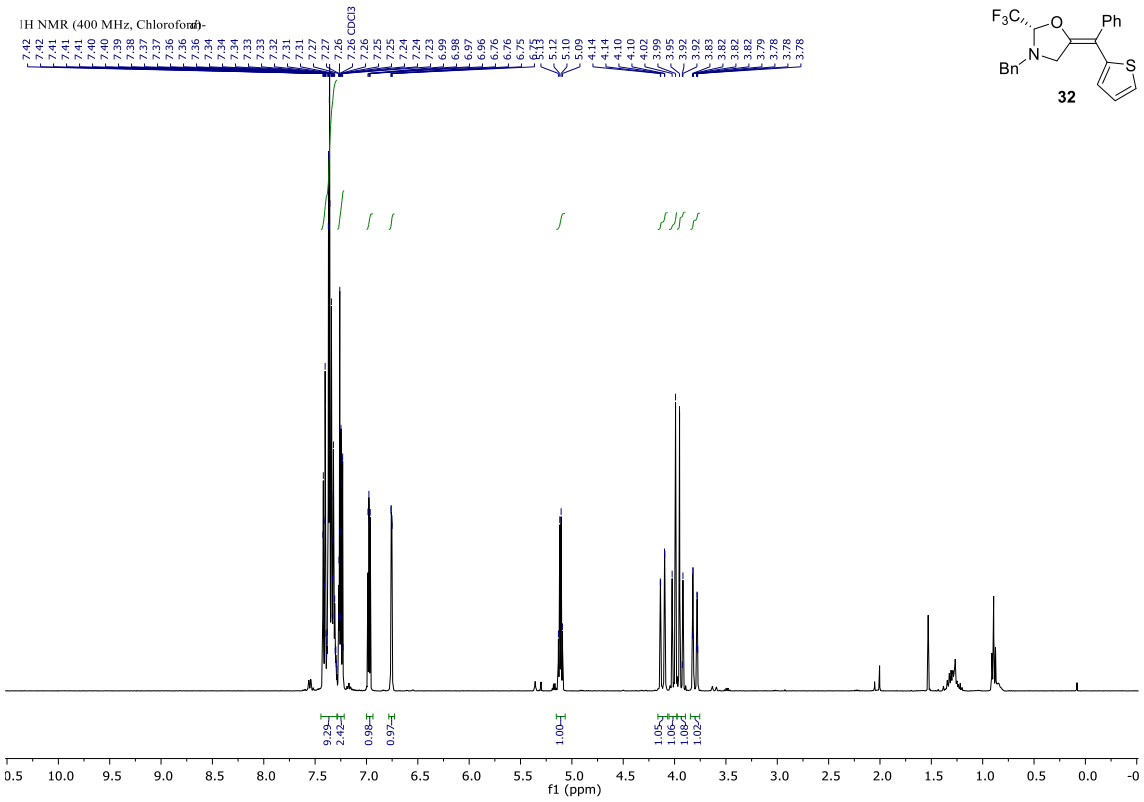


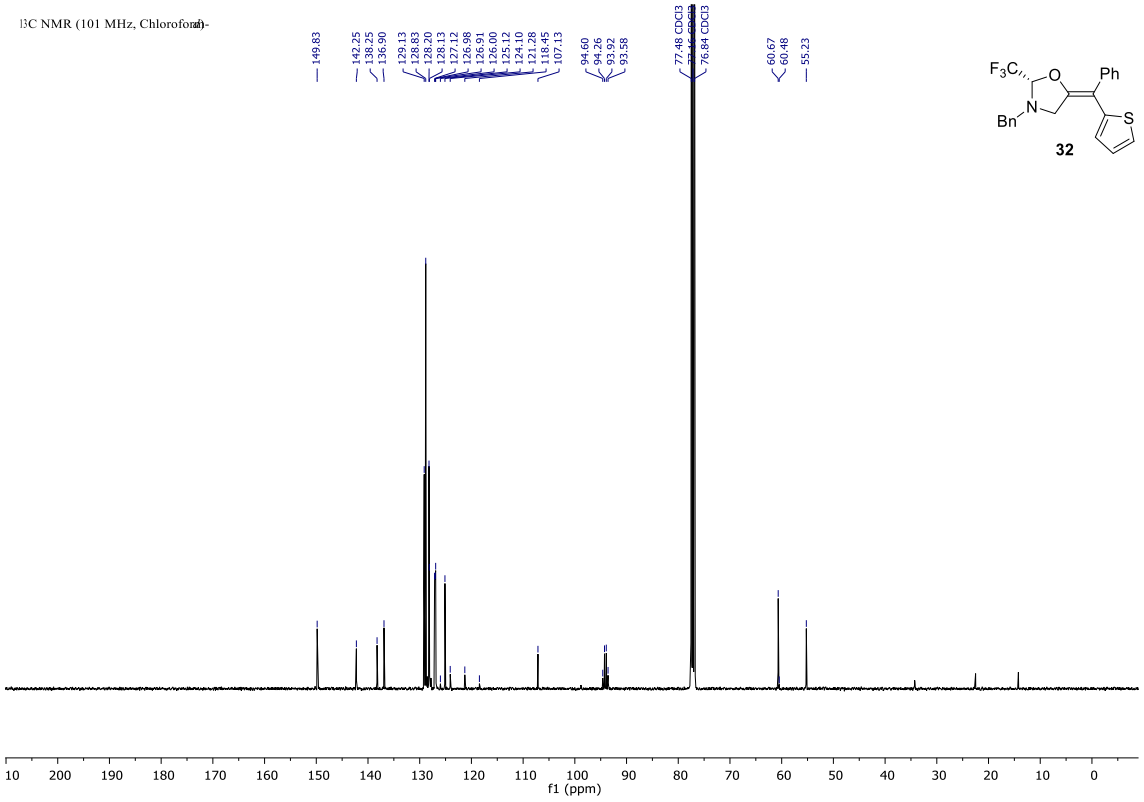
31

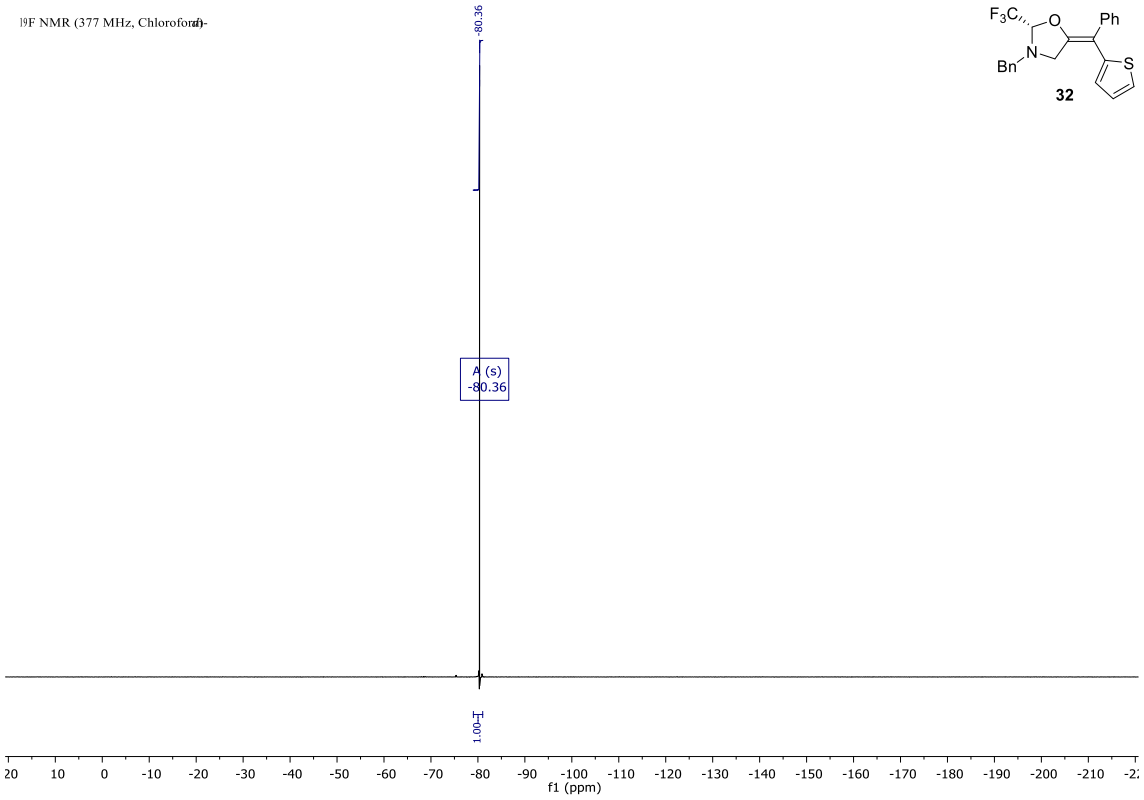
^{19}F NMR (376 MHz, Chloroform-*d*)

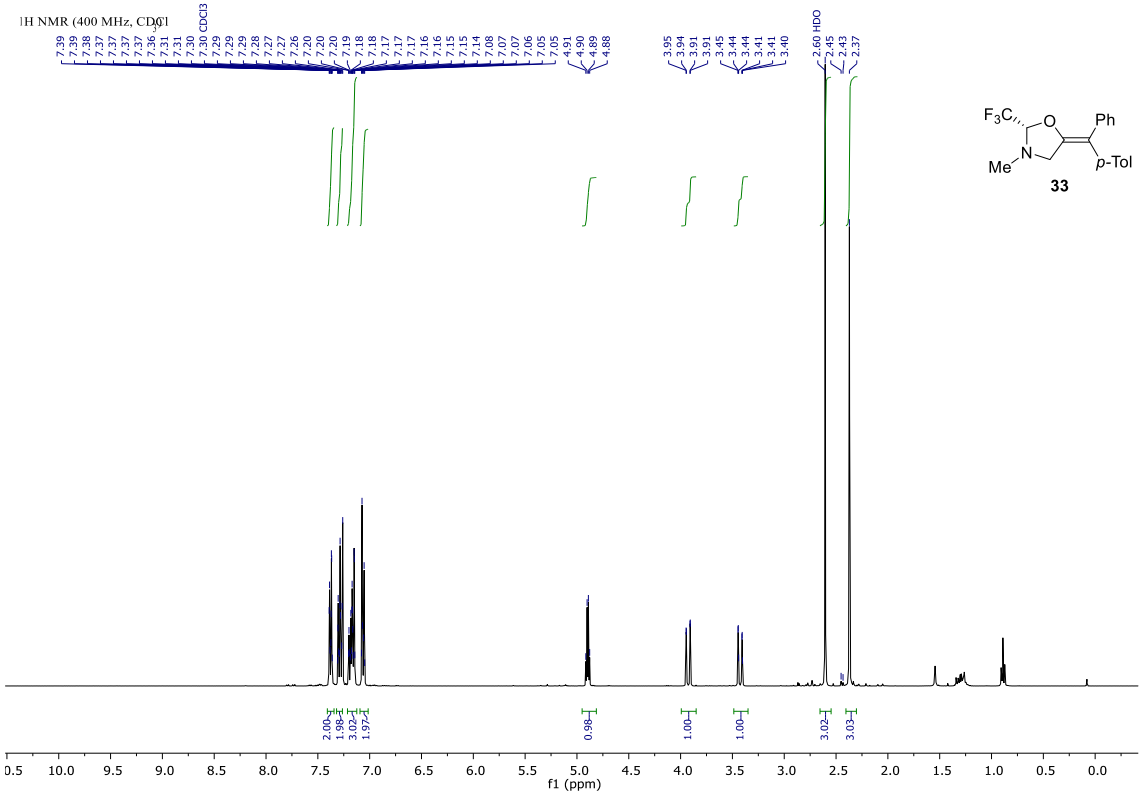


31

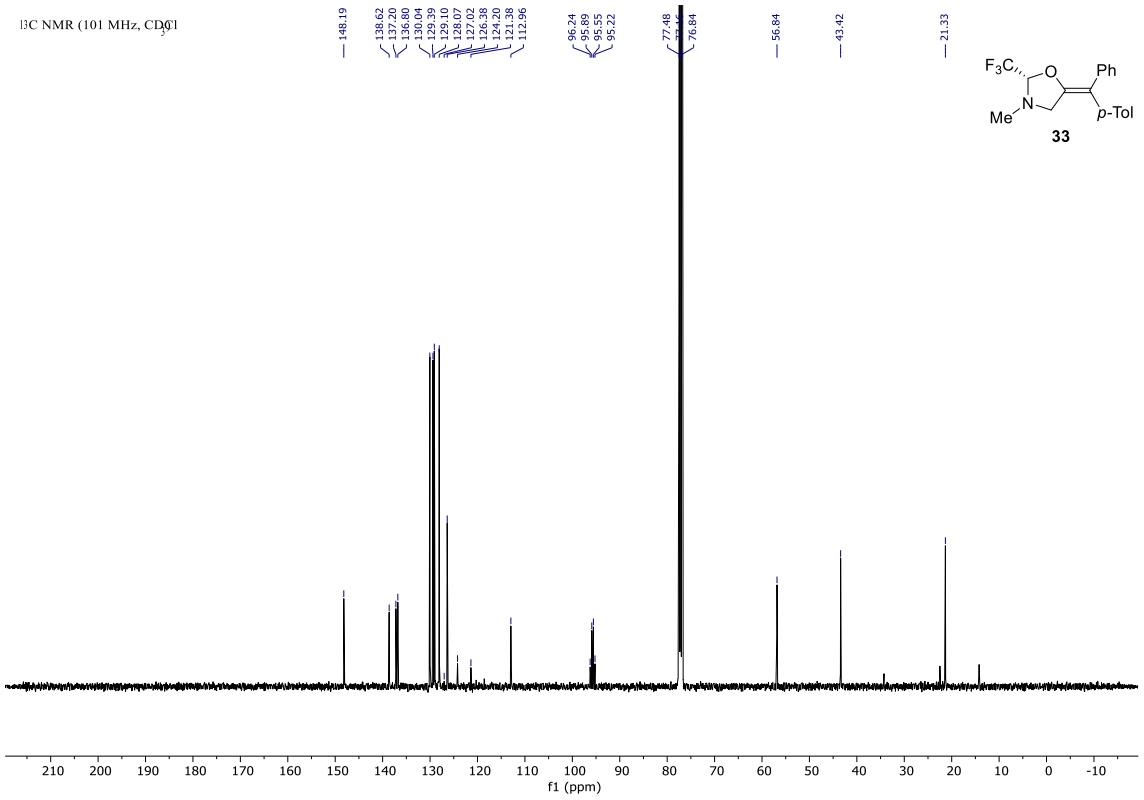

1H NMR (400 MHz, Chloroform-d)
CDCl3
9.29
2.42
0.98
0.97
1.00
1.05
1.06
1.08
1.02
f1 (ppm)
F3C
O
Ph
N
Bn
S
32


13C NMR (101 MHz, Chloroform-d)
149.83
142.25
138.25
136.90
129.13
128.83
128.20
128.13
127.12
126.98
126.91
126.00
125.12
124.10
121.28
118.45
107.13
94.60
94.26
93.92
93.58
77.48 CDCl3
76.84 CDCl3
60.67
60.48
55.23
f1 (ppm)
F3C
O
Ph
N
Bn
S
32


19F NMR (377 MHz, Chloroform-d)
-80.36
A (s)
-80.36
1.00
f1 (ppm)
F3C
O
Ph
N
Bn
S
32

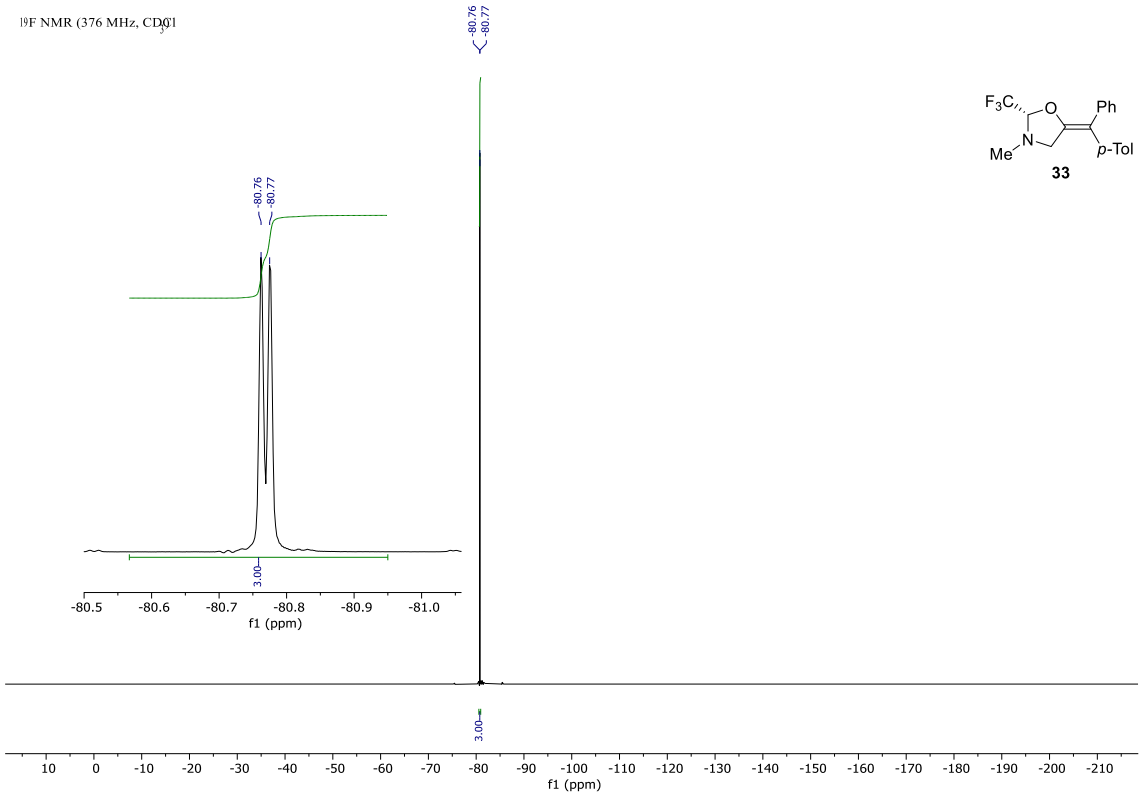

1H NMR (400 MHz, CDCl3)
7.30 CDCl3
2.60 HDO
2.00
1.98
3.02
1.97
0.98
1.00
1.00
3.02
3.03
f1 (ppm)
F3C
O
Ph
N
Me
p-Tol
33

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

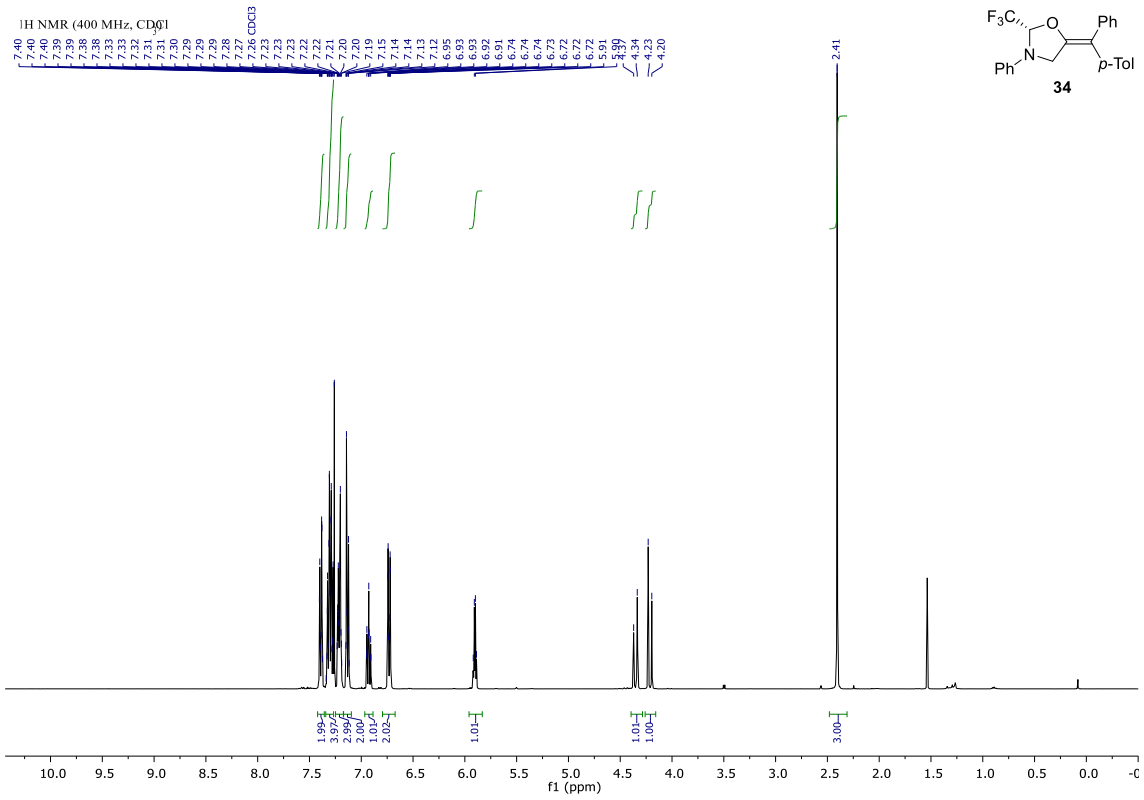


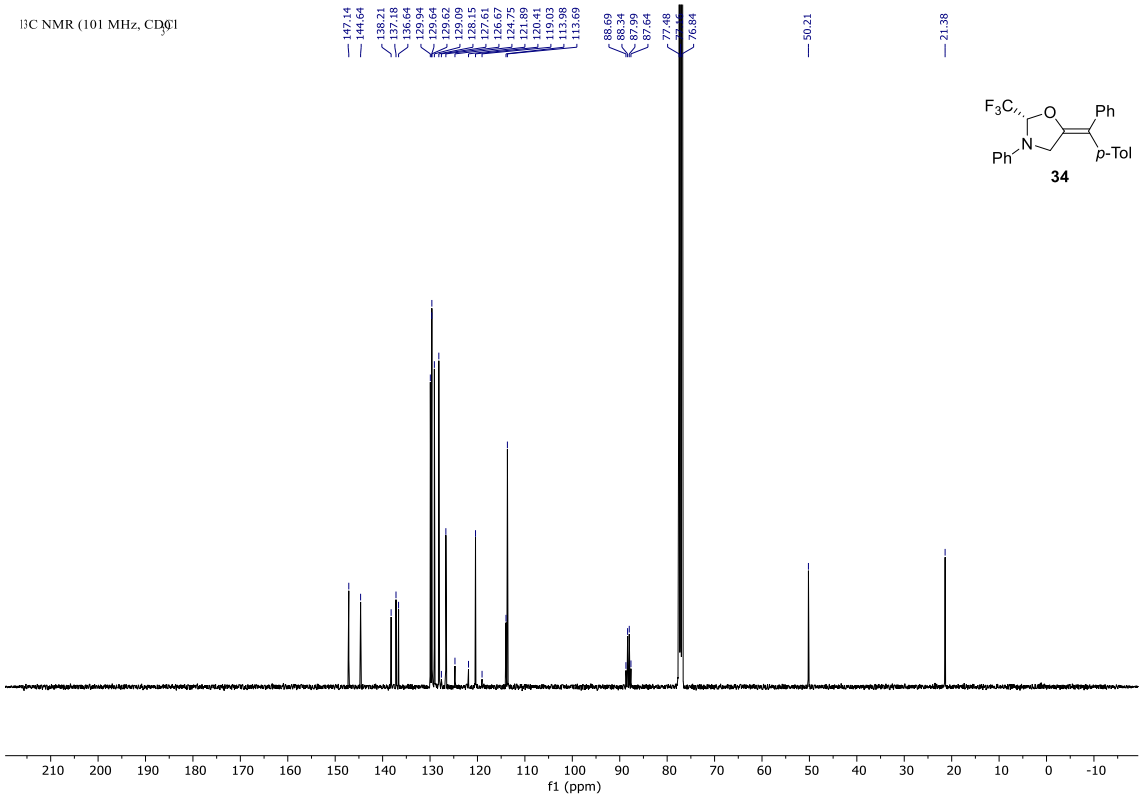
33

^{19}F NMR (376 MHz, $CDCl_3$)

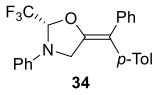


33

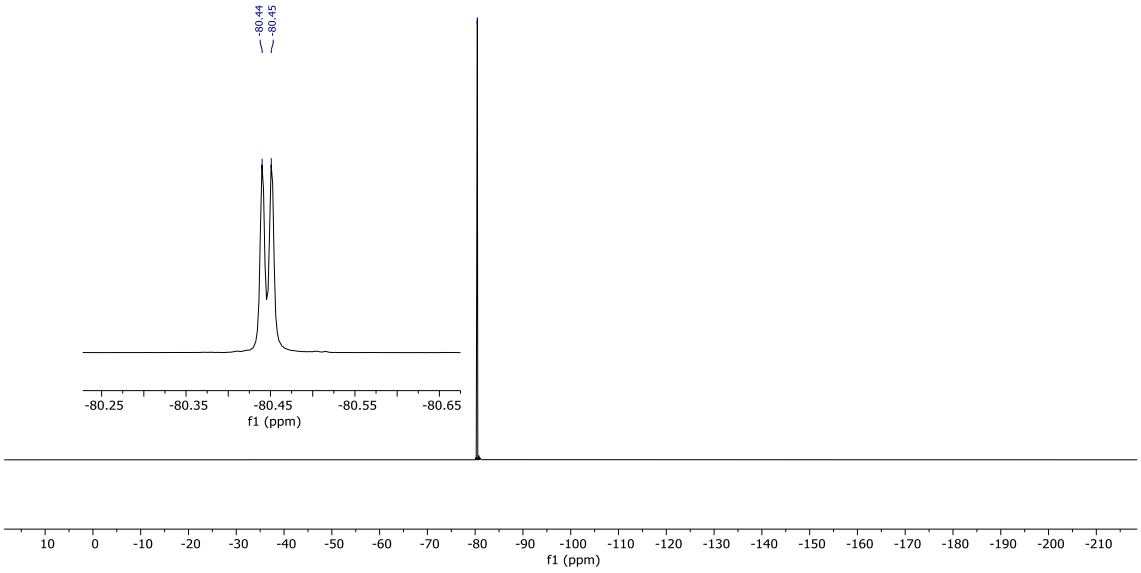

1H NMR (400 MHz, CDCl3)
F3C
O
Ph
N
Ph
p-Tol
34
f1 (ppm)


13C NMR (101 MHz, CDCl3)
F3C
O
Ph
N
Ph
p-Tol
34
f1 (ppm)

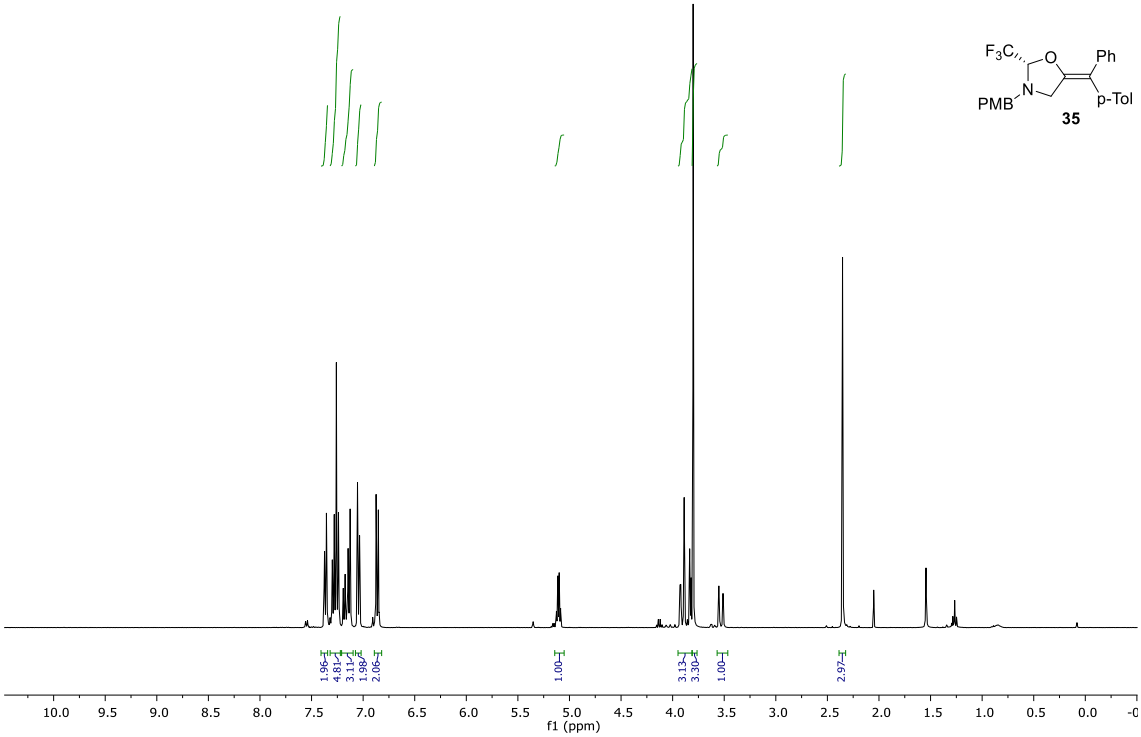
^{19}F NMR (376 MHz, $CDCl_3$)



34

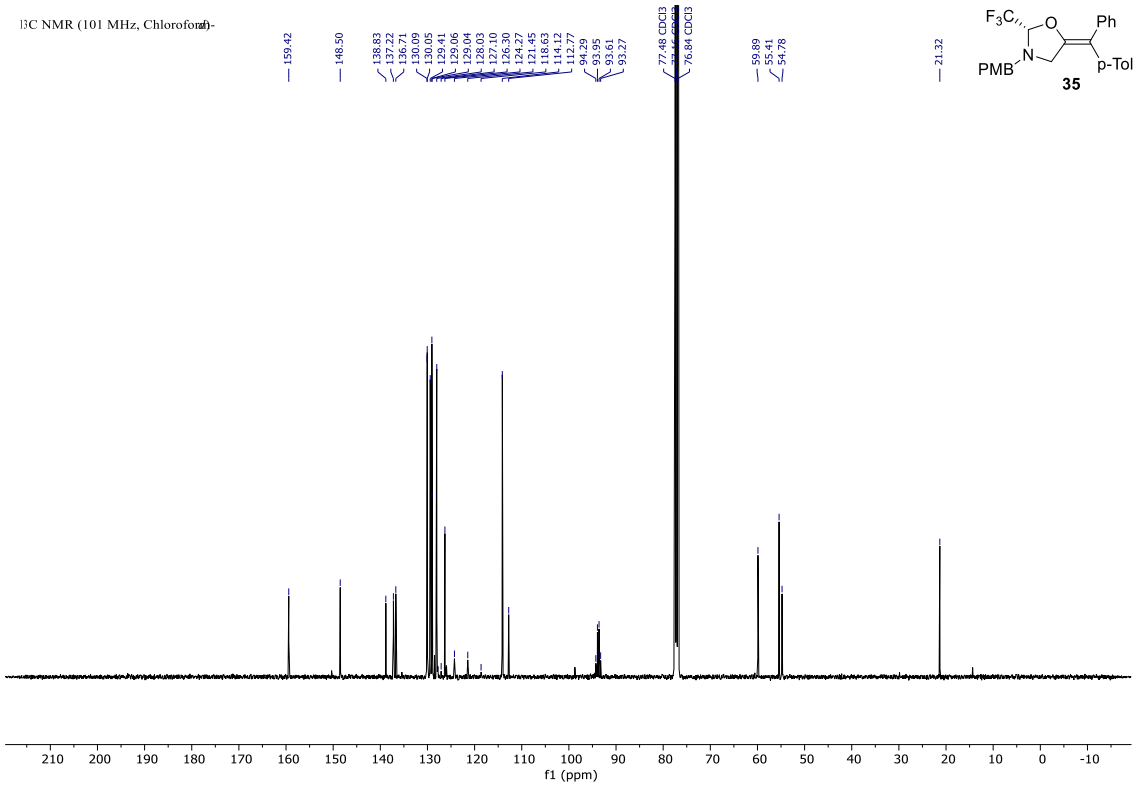


^{1}H NMR (400 MHz, Chloroform-*d*)

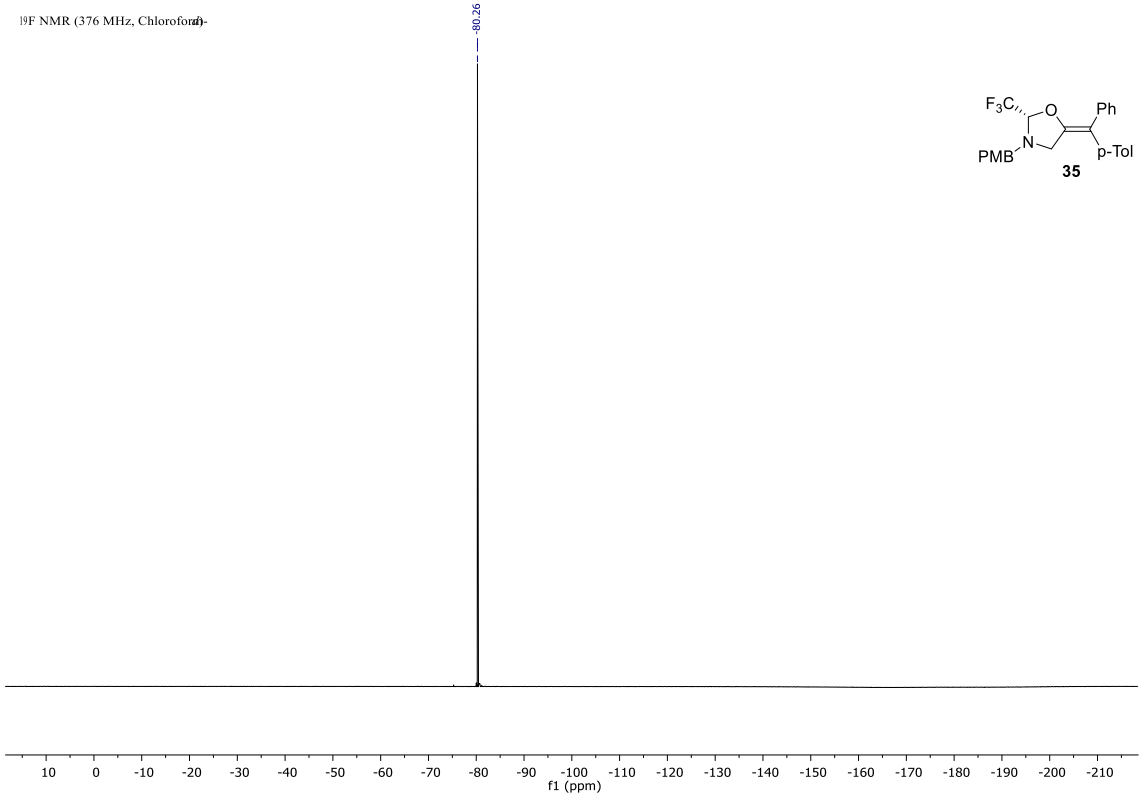


35

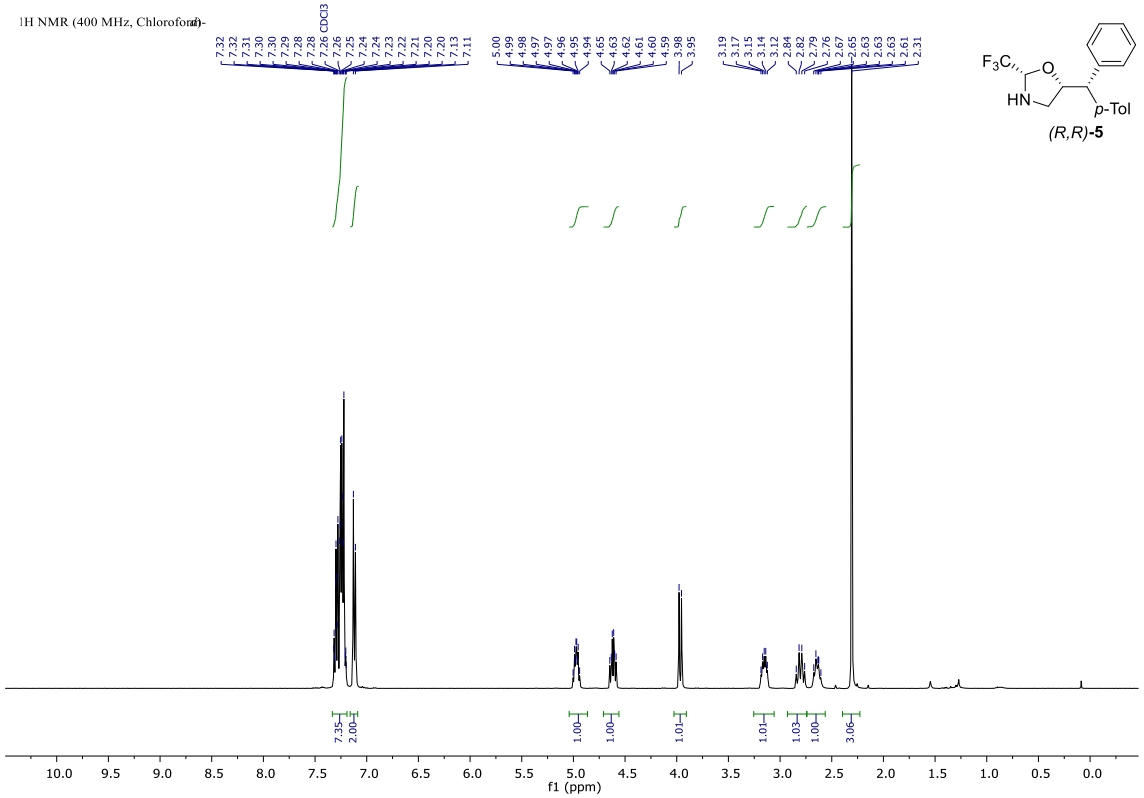
^{13}C NMR (101 MHz, Chloroform-*d*)

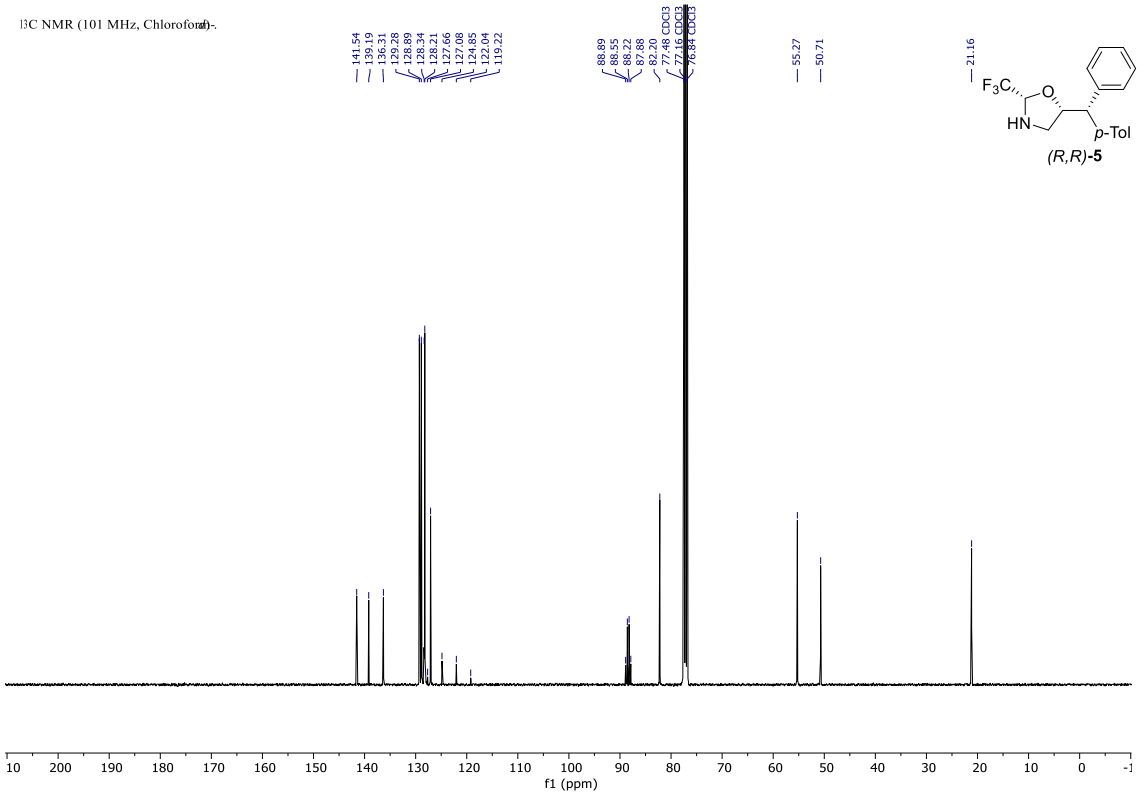


^{19}F NMR (376 MHz, Chloroform-*d*)

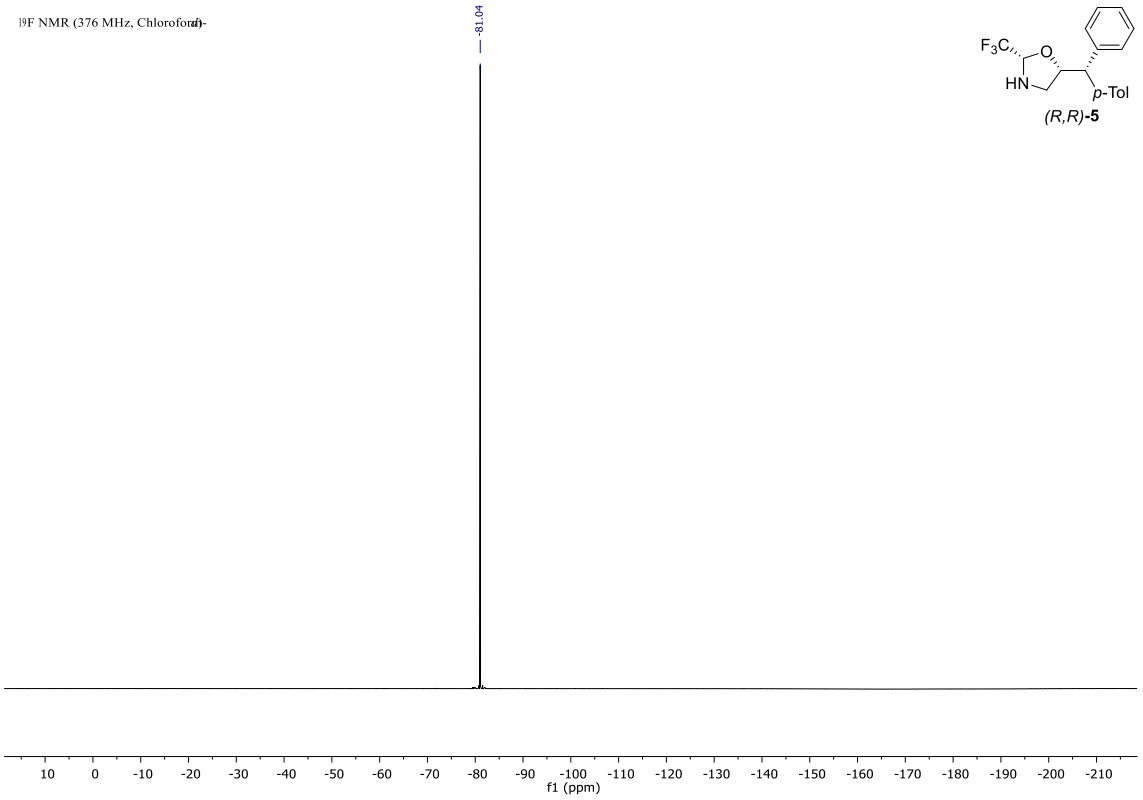


H.3. Asymmetric Hydrogenation Products



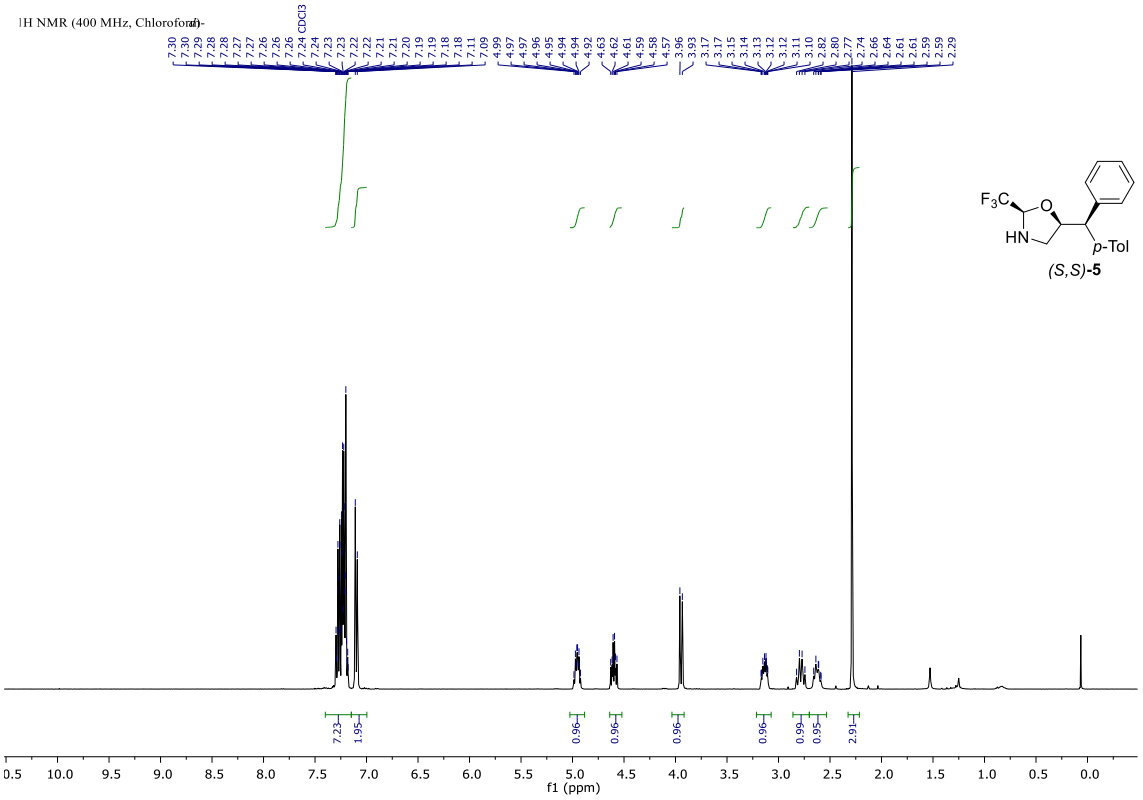


^{19}F NMR (376 MHz, Chloroform-*d*)



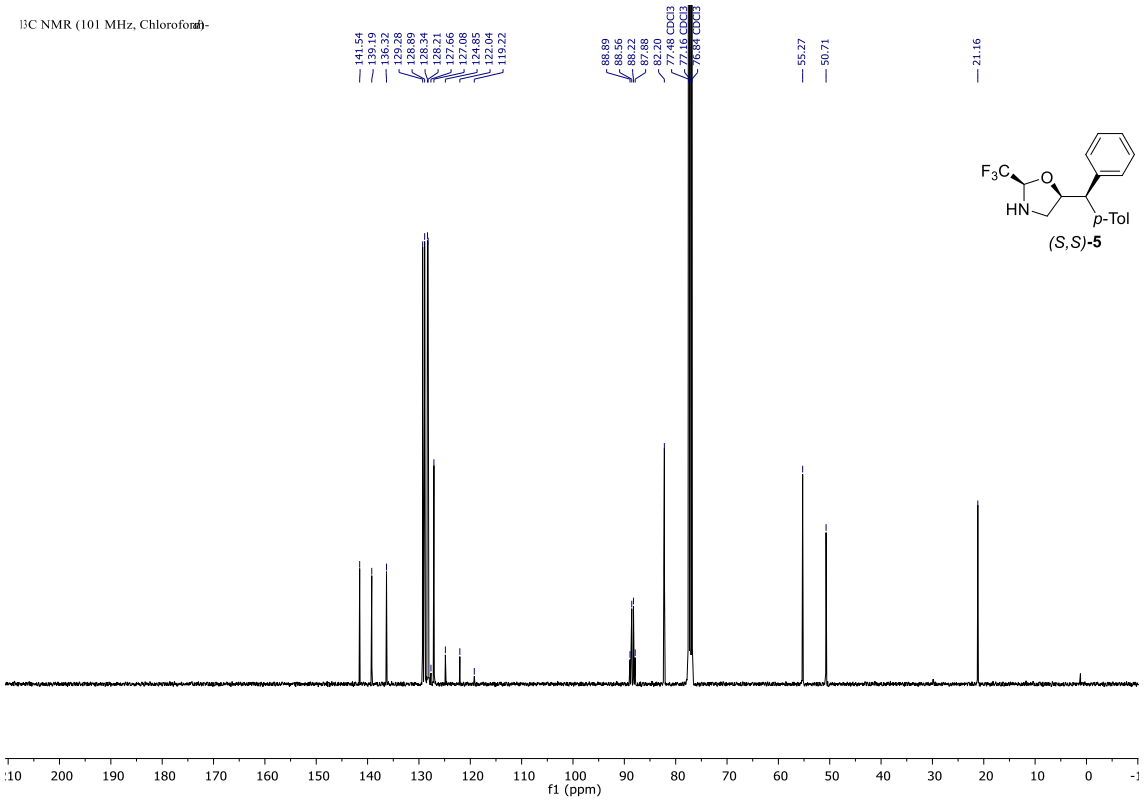
(R,R)-**5**

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



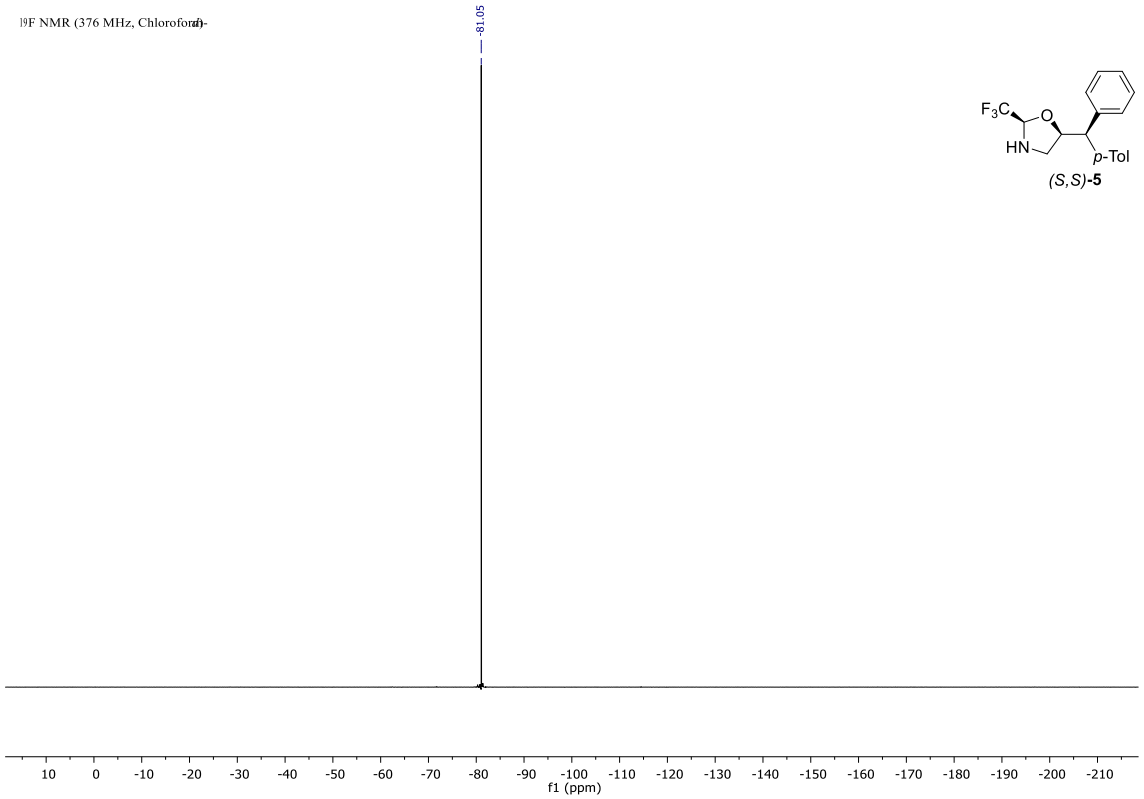
(S,S)-**5**

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

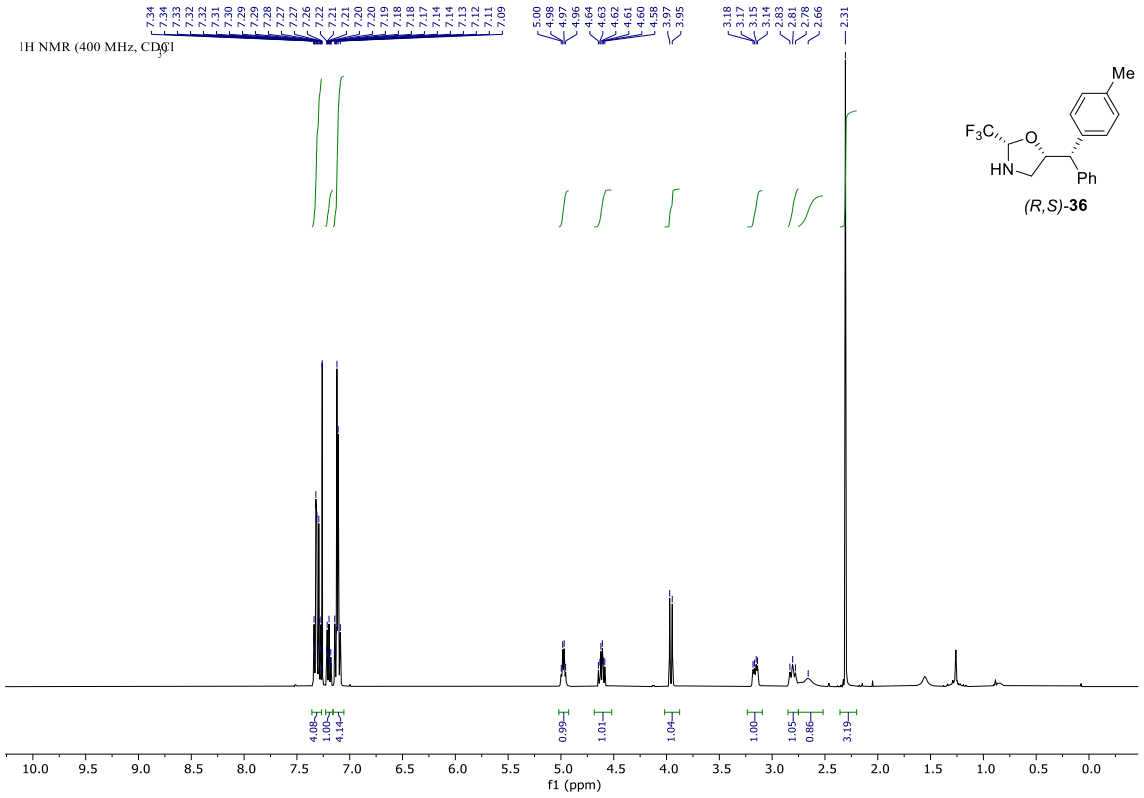


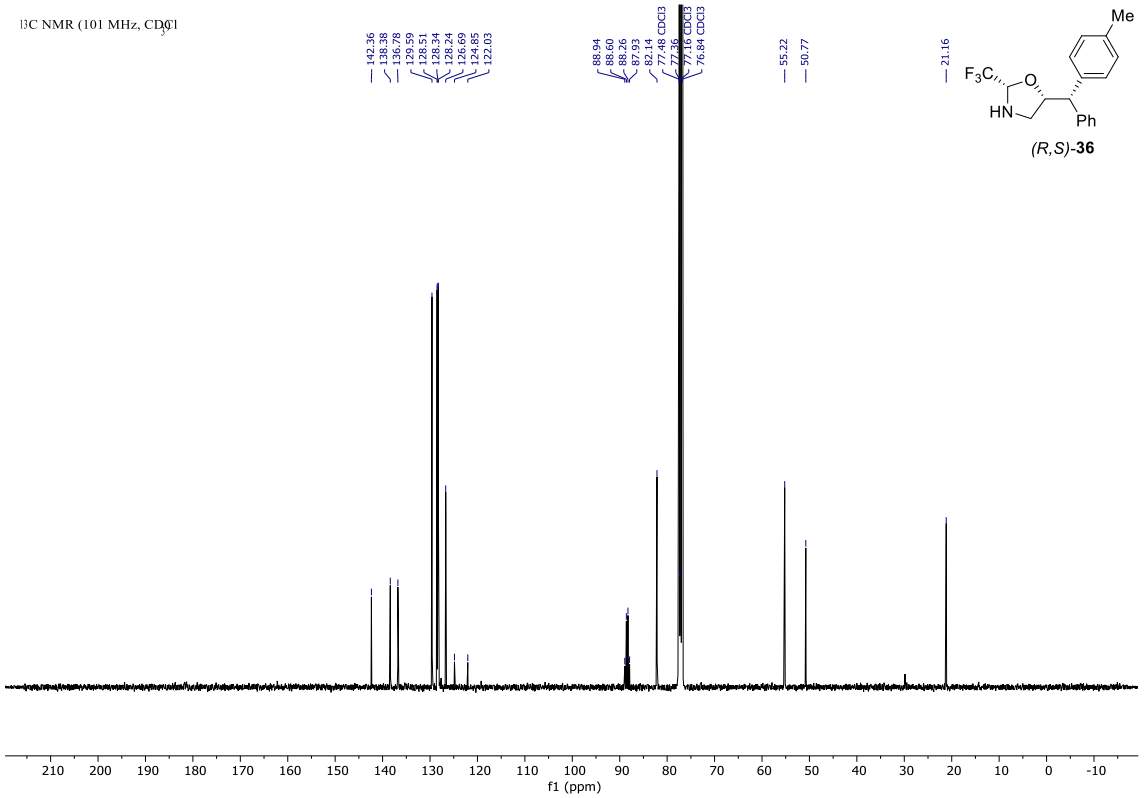
(S,S)-**5**

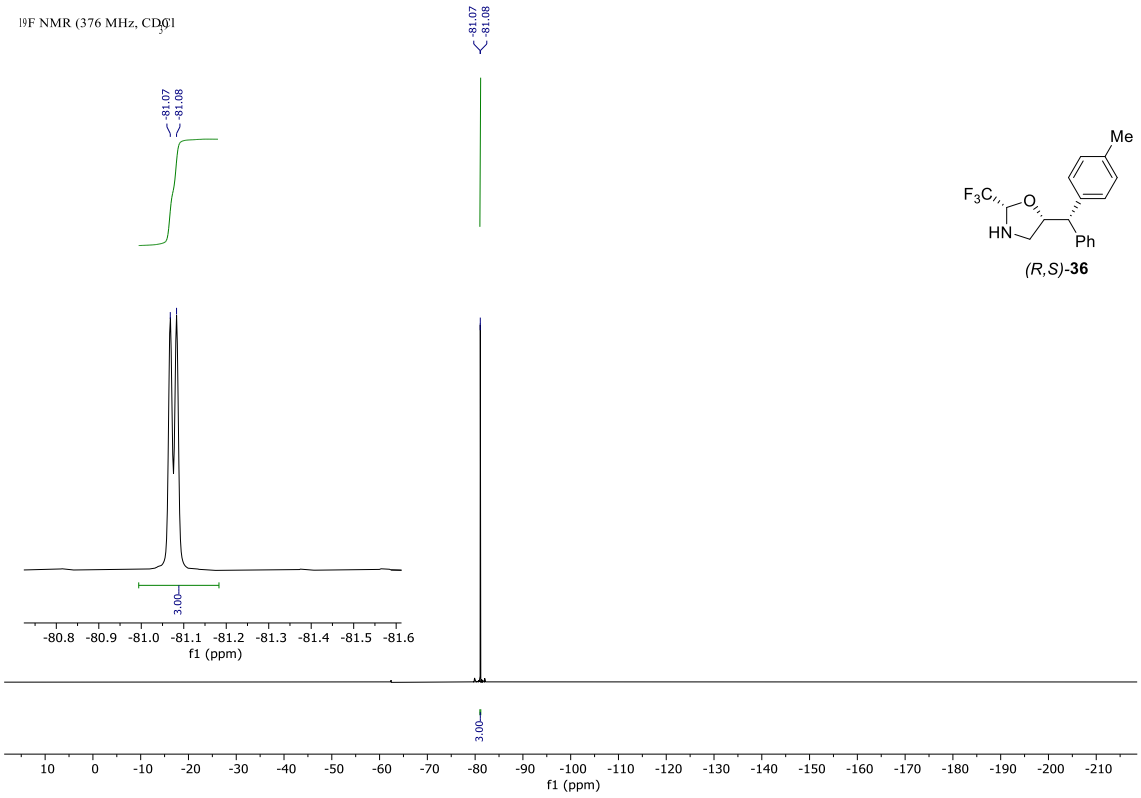
^{19}F NMR (376 MHz, Chloroform-*d*)



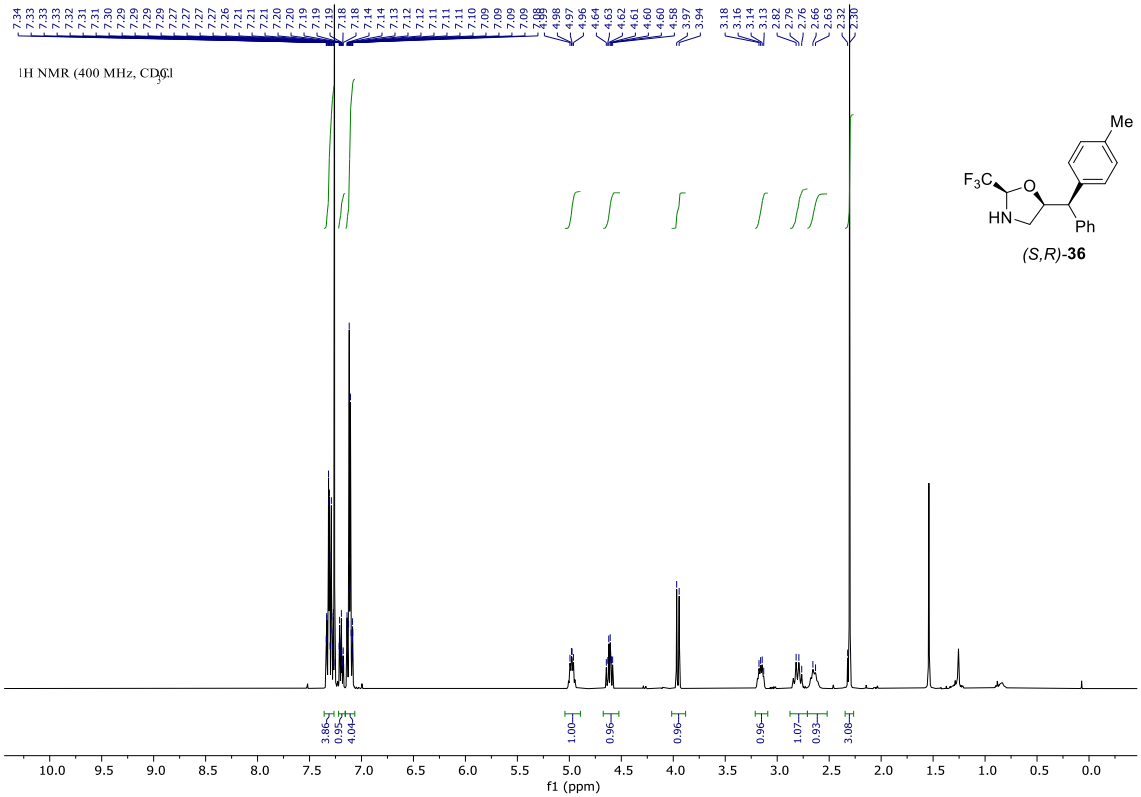
(S,S)-**5**


1H NMR (400 MHz, CDCl3)
7.34 7.34 7.33 7.32 7.32 7.31 7.30 7.29 7.29 7.28 7.27 7.27 7.26 7.22 7.21 7.21 7.20 7.20 7.19 7.18 7.18 7.17 7.14 7.14 7.13 7.12 7.11 7.09
5.00 4.98 4.97 4.96 4.64 4.63 4.62 4.61 4.60 4.58 3.97 3.95
3.18 3.17 3.15 3.14 2.83 2.81 2.78 2.66
2.31
4.08 1.00 4.14 0.99 1.01 1.04 1.00 1.05 0.86 3.19
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
Me
F3C
O
HN
Ph
(R,S)-36

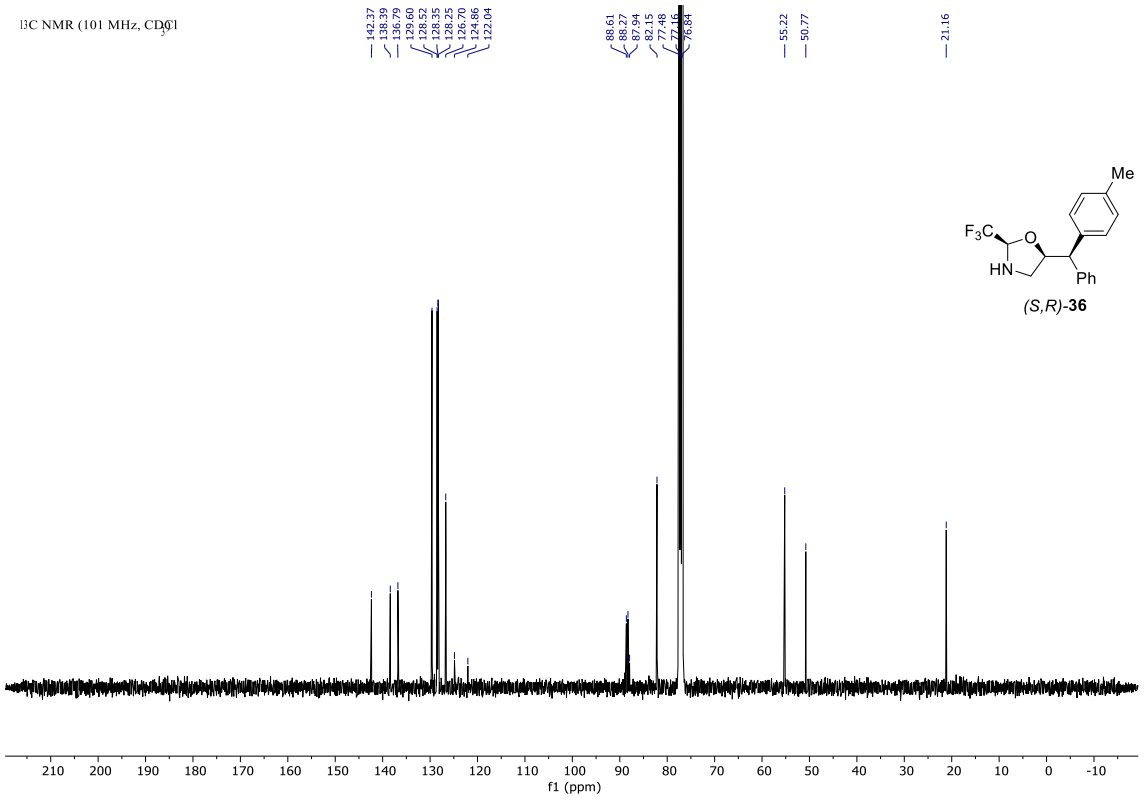

13C NMR (101 MHz, CDCl3)
142.36 138.38 136.78 129.59 128.51 128.34 128.24 126.69 124.85 122.03
88.94 88.60 88.26 87.93 82.14 77.48 CDCl3 77.16 CDCl3 76.84 CDCl3
55.22 50.77
21.16
210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10
f1 (ppm)
Me
F3C
O
HN
Ph
(R,S)-36

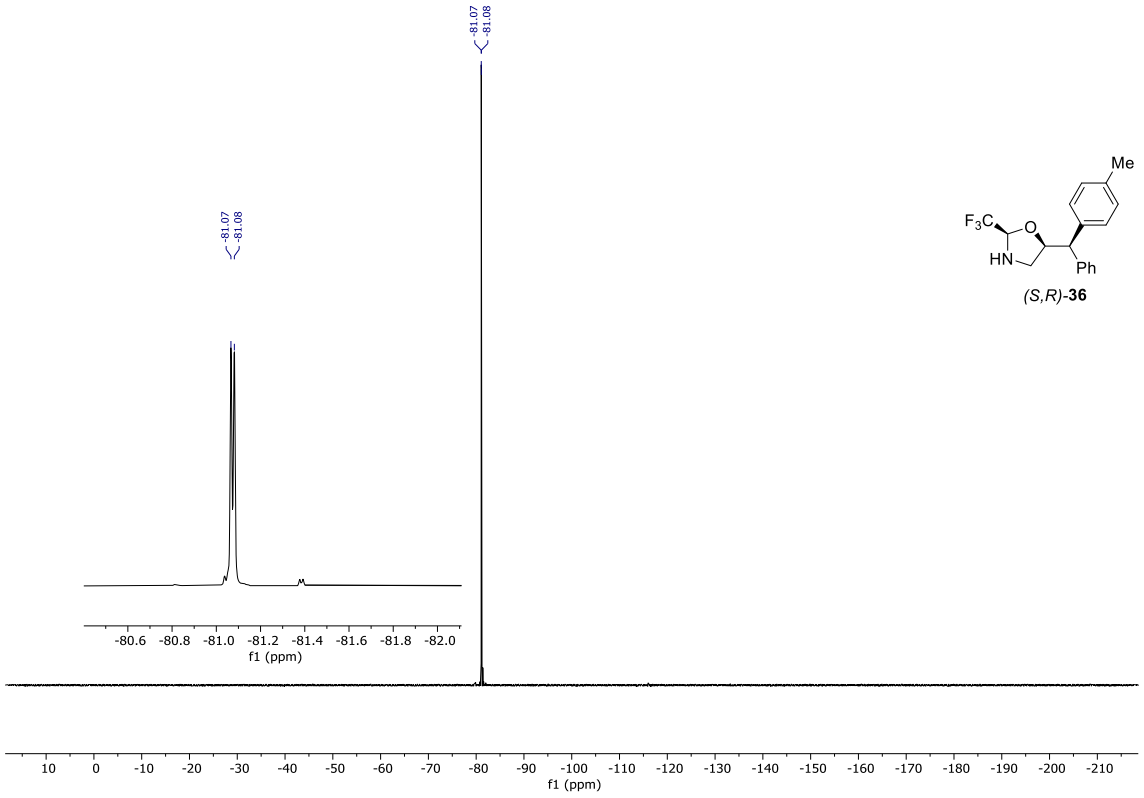

19F NMR (376 MHz, CDCl3)
-81.07
-81.08
3.00
-80.8 -80.9 -81.0 -81.1 -81.2 -81.3 -81.4 -81.5 -81.6
f1 (ppm)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)
Me
F3C
O
HN
Ph

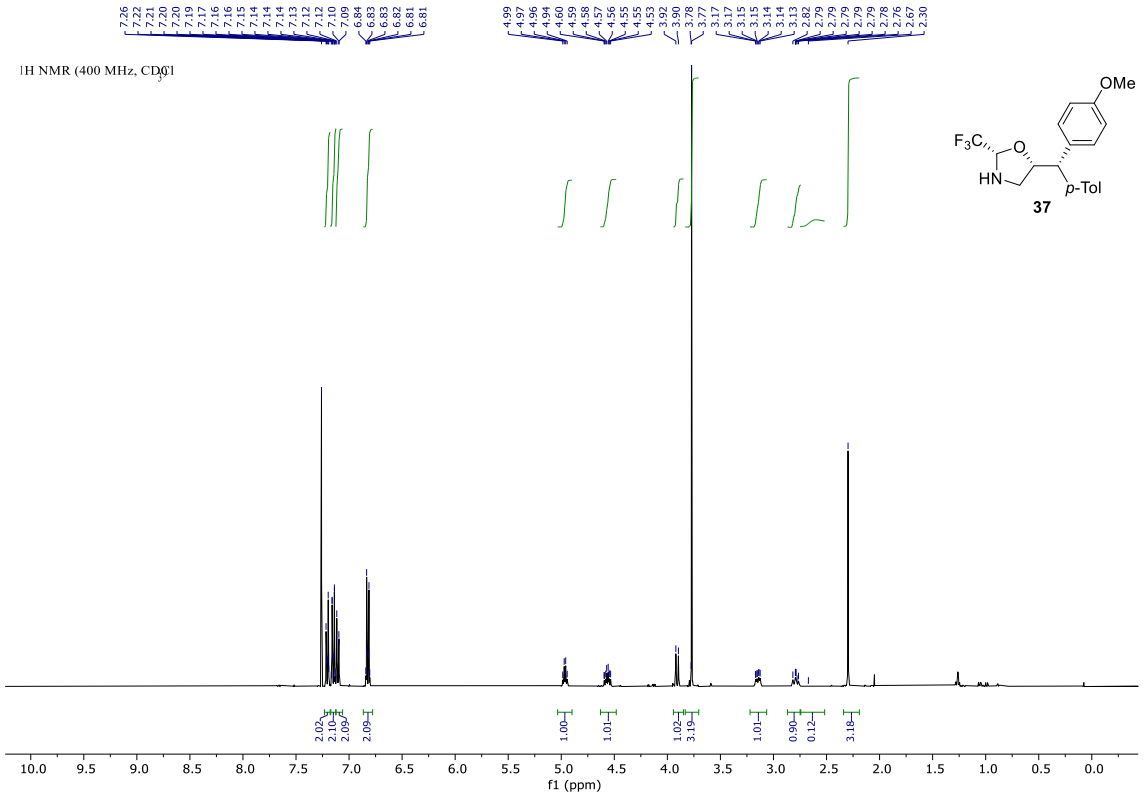
(R,S)-**36**

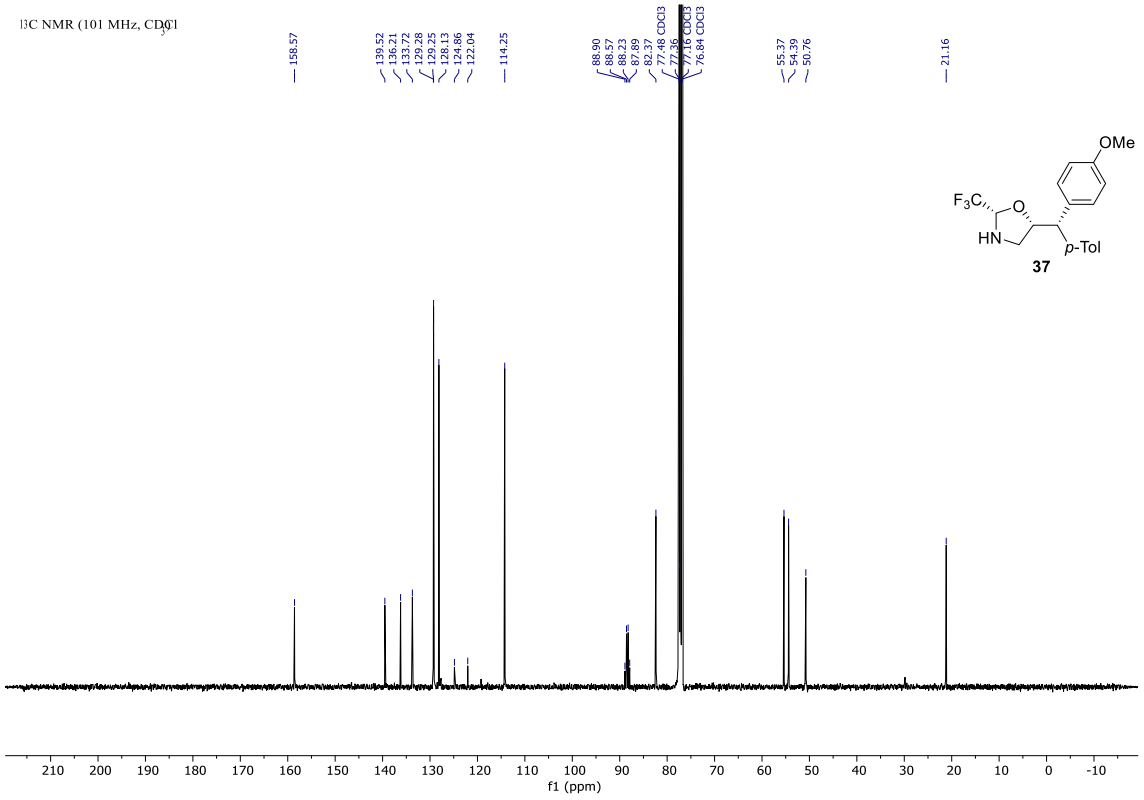

1H NMR (400 MHz, CDCl3)
3.86
0.95
4.04
1.00
0.96
0.96
0.96
1.07
0.93
3.08
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
Me
F3C
O
HN
Ph

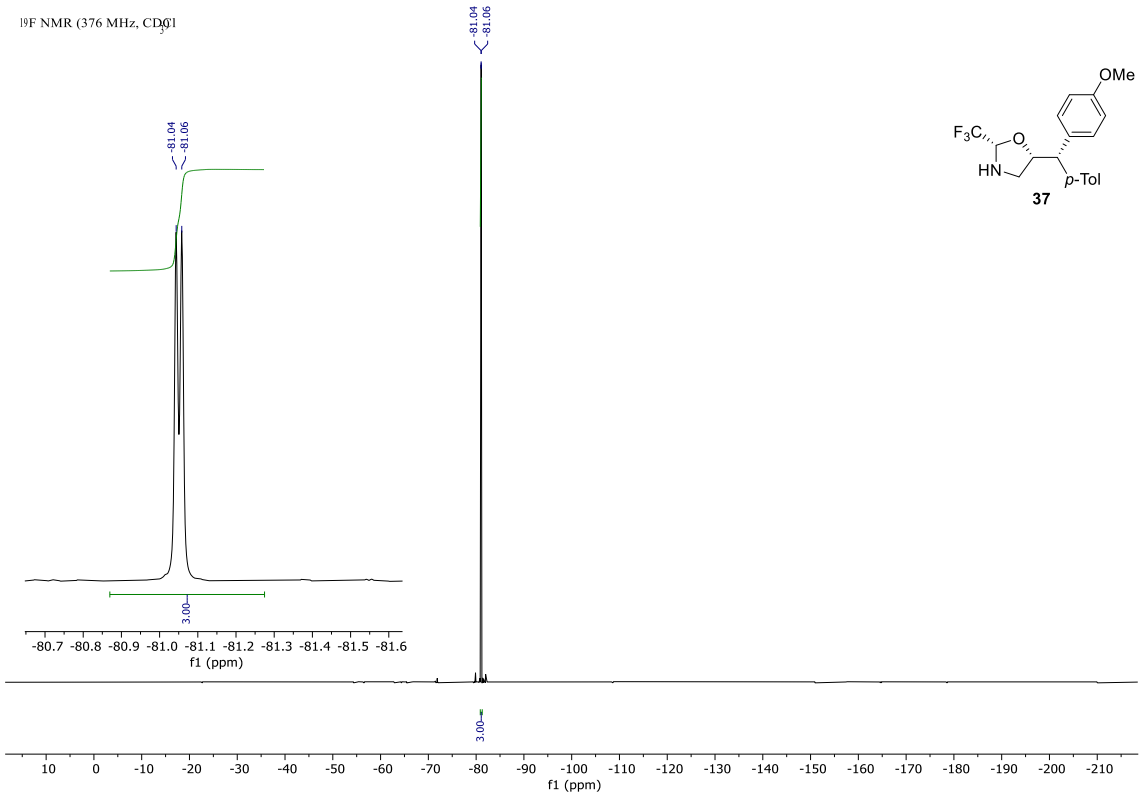
(S,R)-**36**

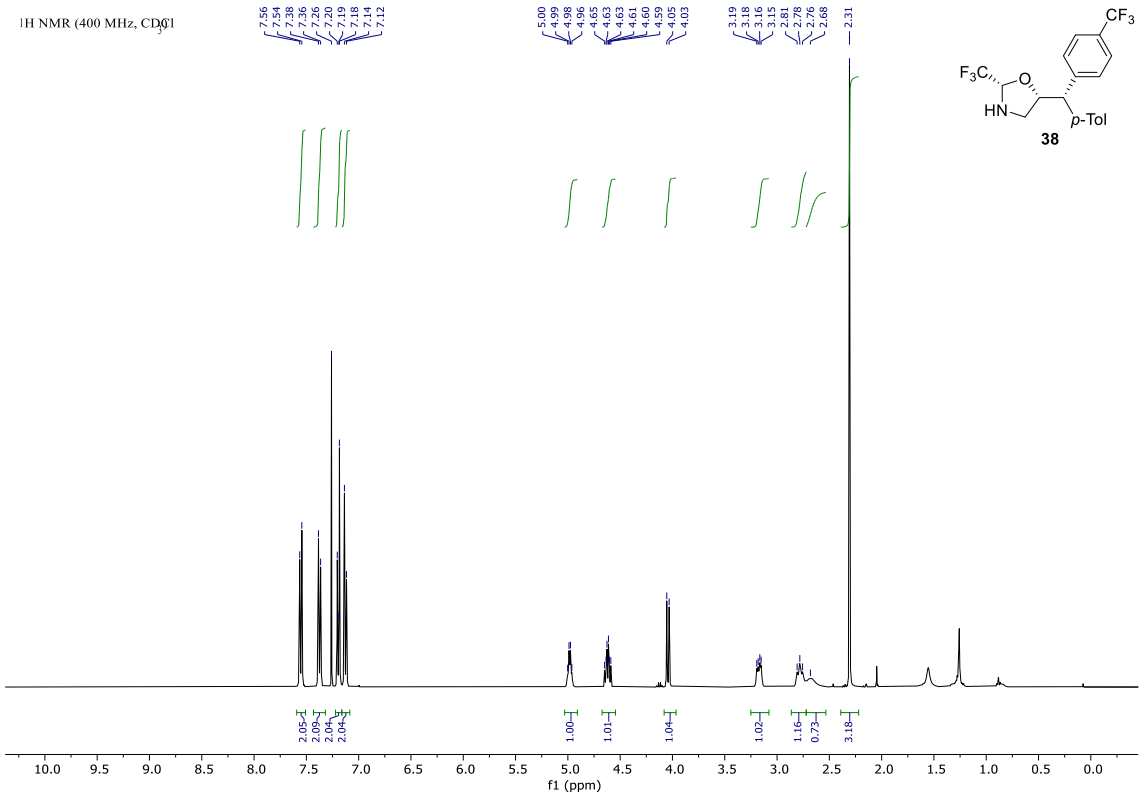

13C NMR (101 MHz, CDCl3)
142.37
138.39
136.79
129.60
128.52
128.35
128.25
126.70
124.86
122.04
88.61
88.27
87.94
82.15
77.48
77.16
76.84
55.22
50.77
21.16
Me
F3C
O
HN
Ph
(S,R)-36
f1 (ppm)


-81.07
-81.08
-80.6 -80.8 -81.0 -81.2 -81.4 -81.6 -81.8 -82.0
f1 (ppm)
Me
F3C
O
HN
Ph
(S,R)-36
f1 (ppm)

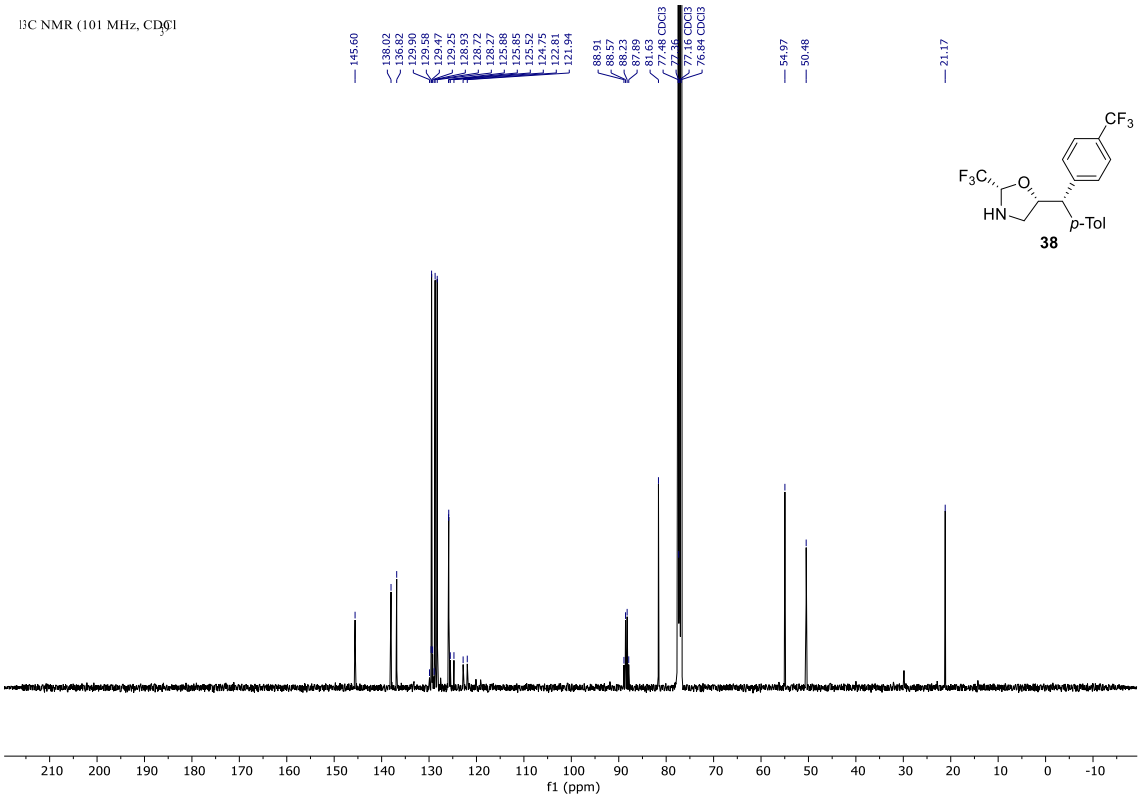

1H NMR (400 MHz, CDCl3)
OMe
F3C
O
HN
p-Tol
37
f1 (ppm)


13C NMR (101 MHz, CDCl3)
OMe
F3C
O
HN
p-Tol
37
f1 (ppm)


19F NMR (376 MHz, CDCl3)
-81.04
-81.06
3.00
-80.7 -80.8 -80.9 -81.0 -81.1 -81.2 -81.3 -81.4 -81.5 -81.6
f1 (ppm)
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)
OMe
F3C
O
HN
p-Tol
37

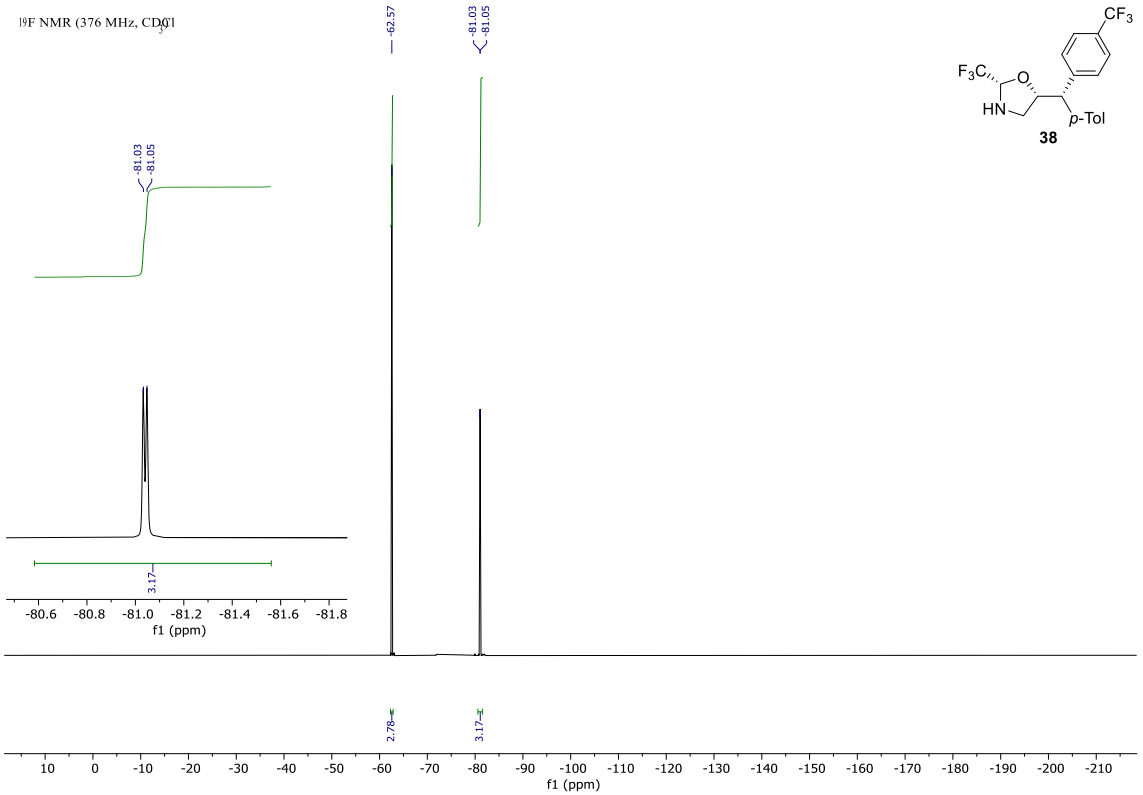

1H NMR (400 MHz, CDCl3)
7.56 7.54 7.38 7.36 7.26 7.20 7.19 7.18 7.14 7.12
5.00 4.99 4.98 4.96 4.65 4.63 4.63 4.61 4.60 4.59 4.05 4.03
3.19 3.18 3.16 3.15 2.81 2.78 2.76 2.68
2.31
2.05 2.09 2.04 2.04
1.00 1.01 1.04 1.02 1.16 0.73 3.18
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)
CF3
F3C
O
HN
p-Tol
38

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

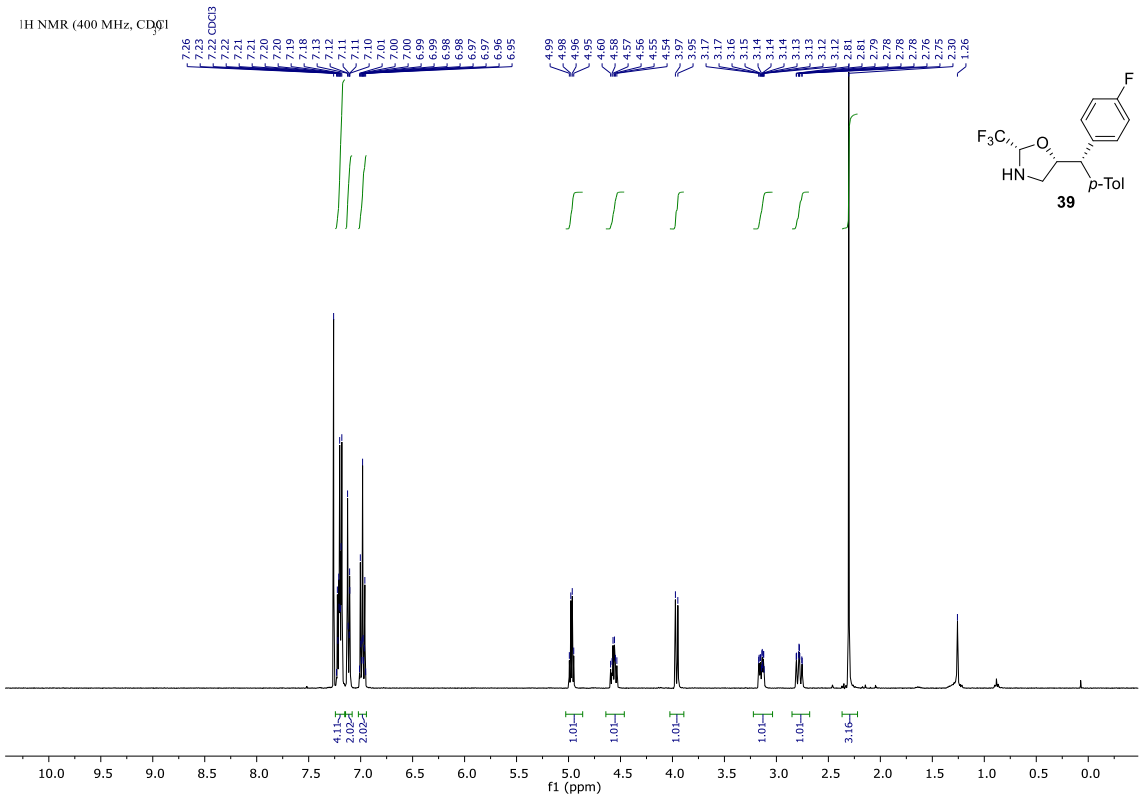


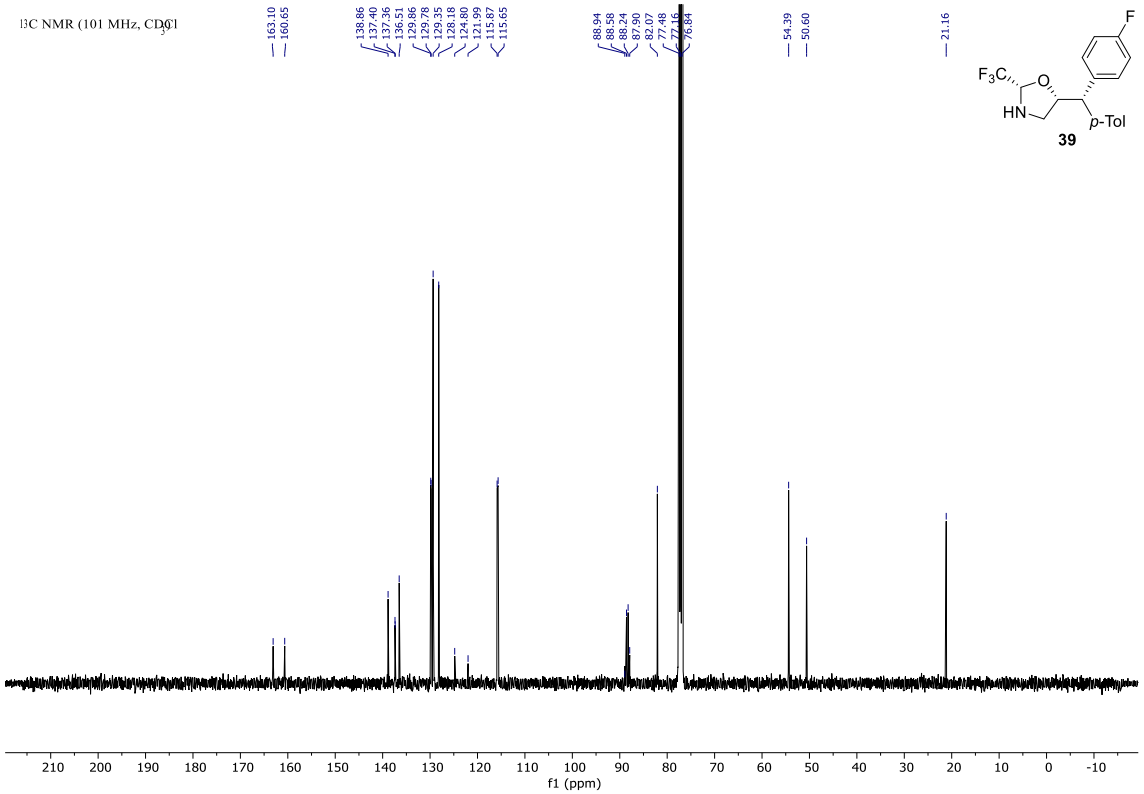
38

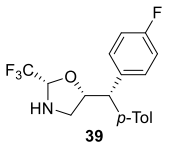
^{19}F NMR (376 MHz, $CDCl_3$)

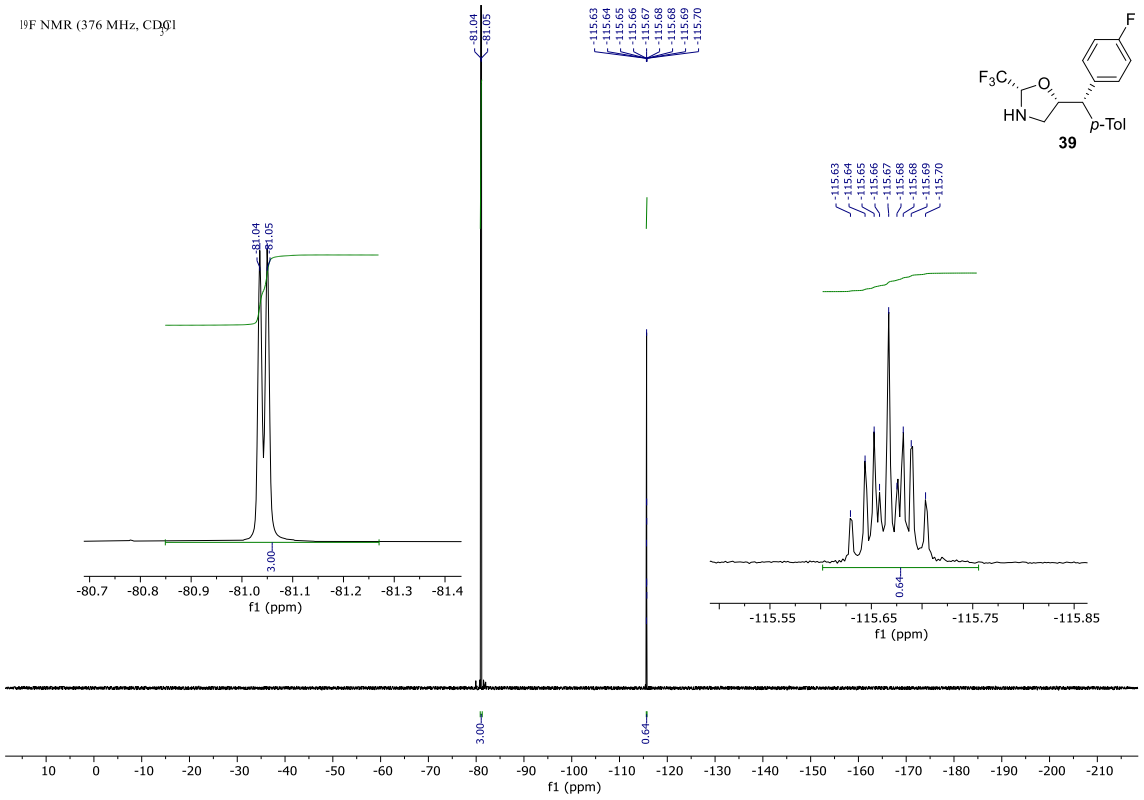


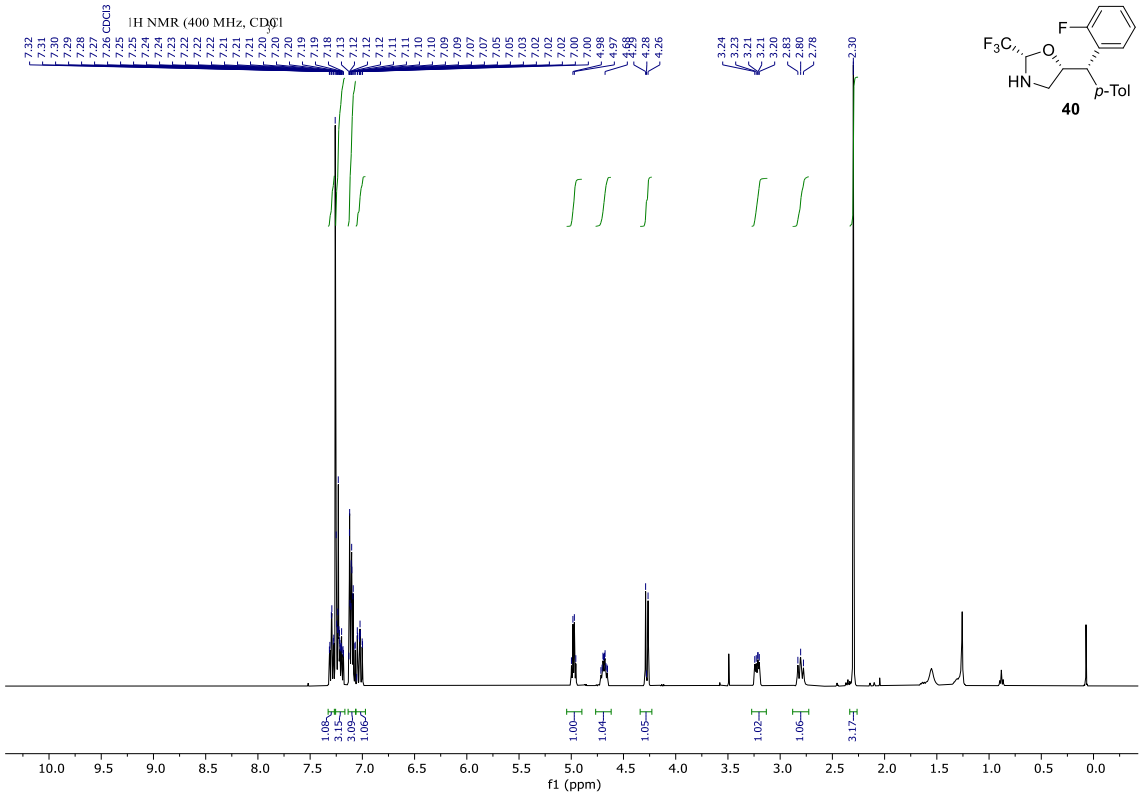
38

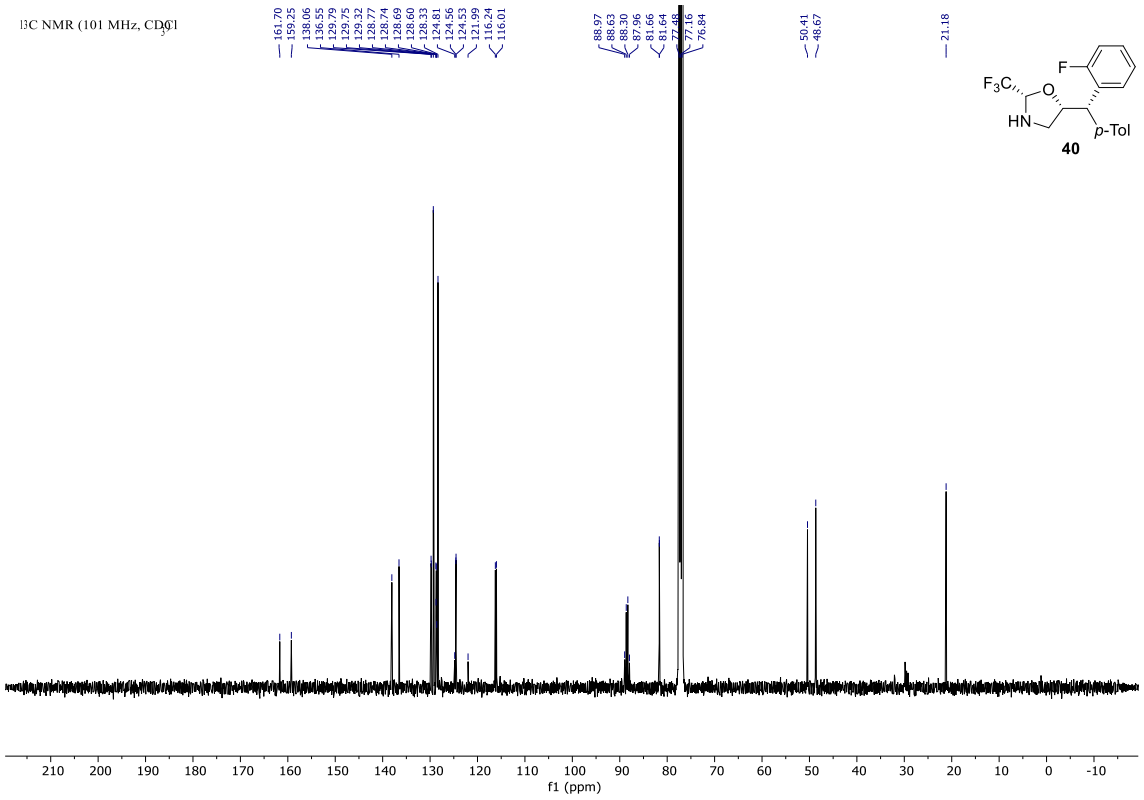

1H NMR (400 MHz, CDCl3)
CDCl3
F
F3C
O
HN
p-Tol
39
f1 (ppm)

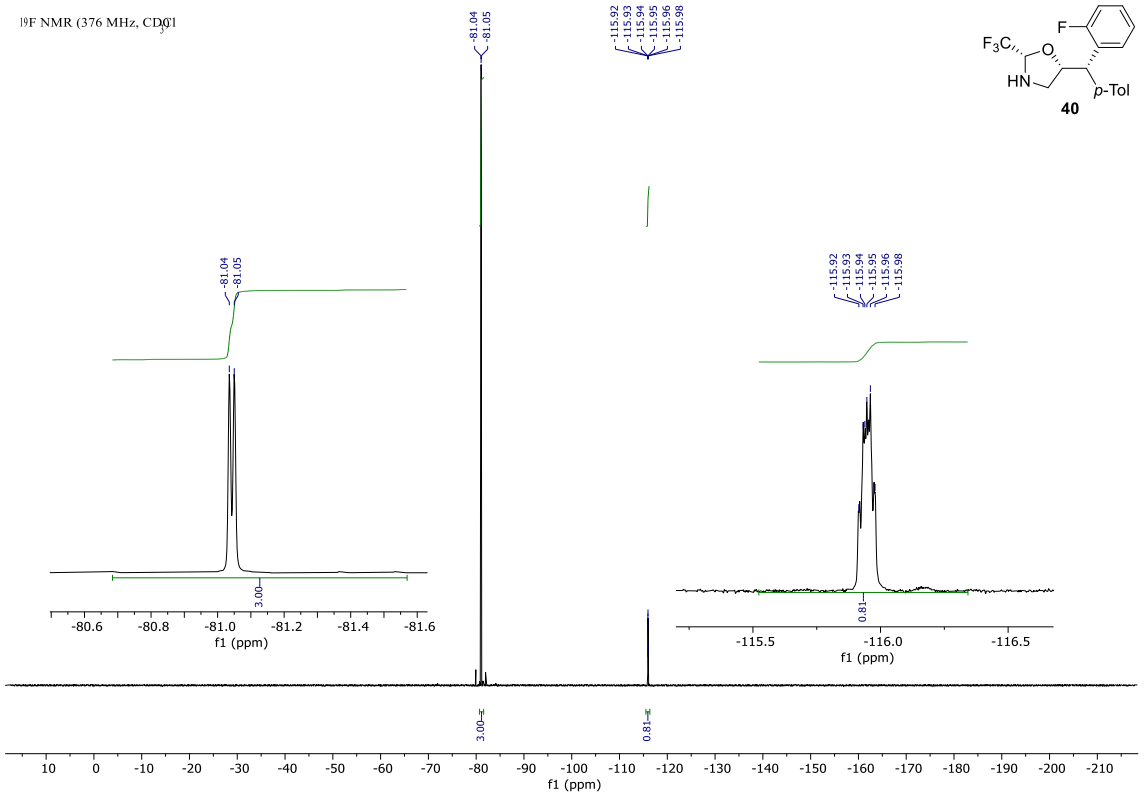

13C NMR (101 MHz, CDCl3)
F
F3C
O
HN
p-Tol
39
f1 (ppm)

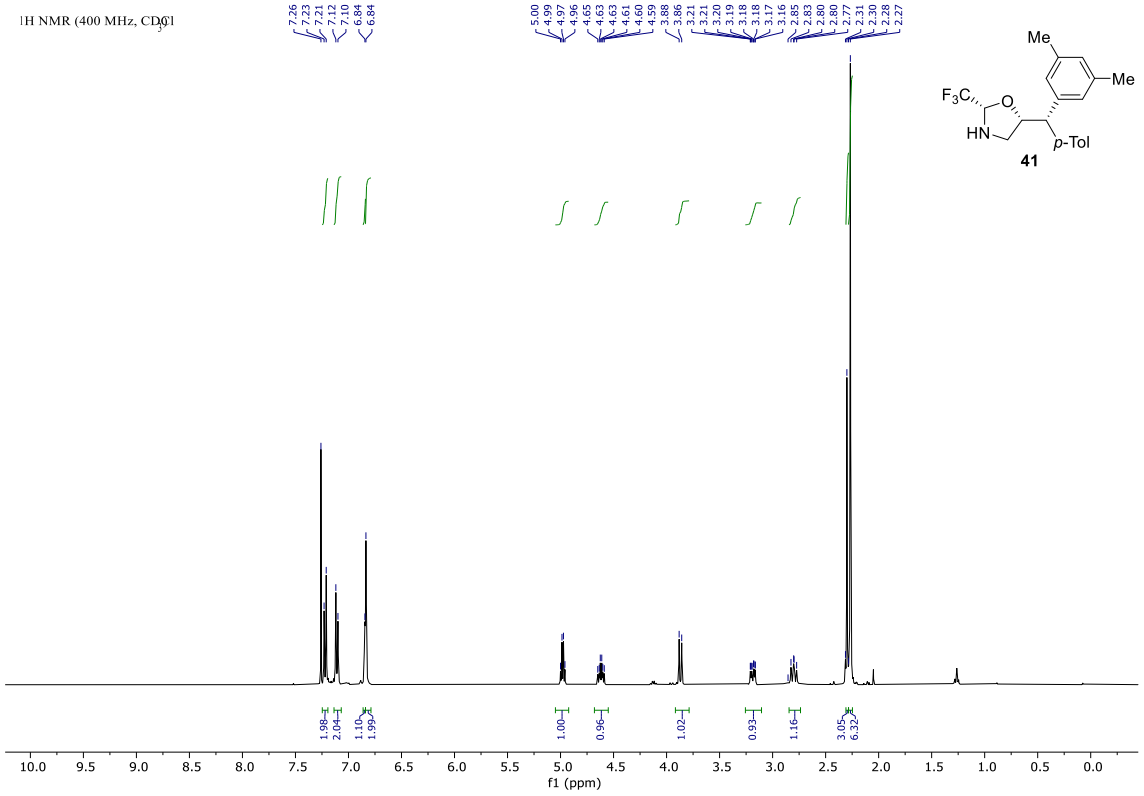

F
F3C
O
HN
p-Tol
39

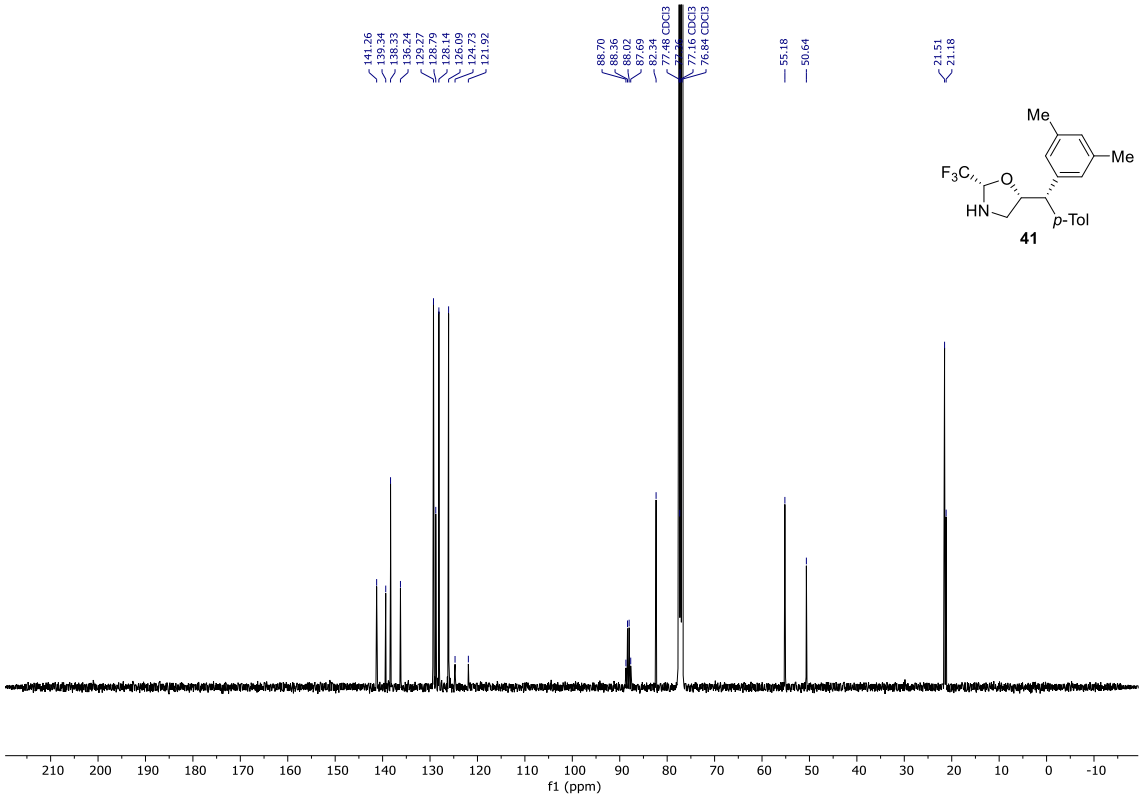

19F NMR (376 MHz, CDCl3)
F
F3C
O
HN
p-Tol
39
-81.04
-81.05
-115.63
-115.64
-115.65
-115.66
-115.67
-115.68
-115.68
-115.69
-115.70
3.00
0.64
f1 (ppm)


1H NMR (400 MHz, CDCl3)
F
F3C
O
HN
p-Tol
40
7.32
7.31
7.30
7.29
7.28
7.27
7.26 CDCl3
7.25
7.24
7.23
7.22
7.21
7.20
4.98
4.97
4.29
4.28
4.26
3.24
3.23
3.21
3.20
2.83
2.80
2.78
2.30
1.08
3.15
3.09
1.06
1.00
1.04
1.05
1.02
1.06
3.17
f1 (ppm)

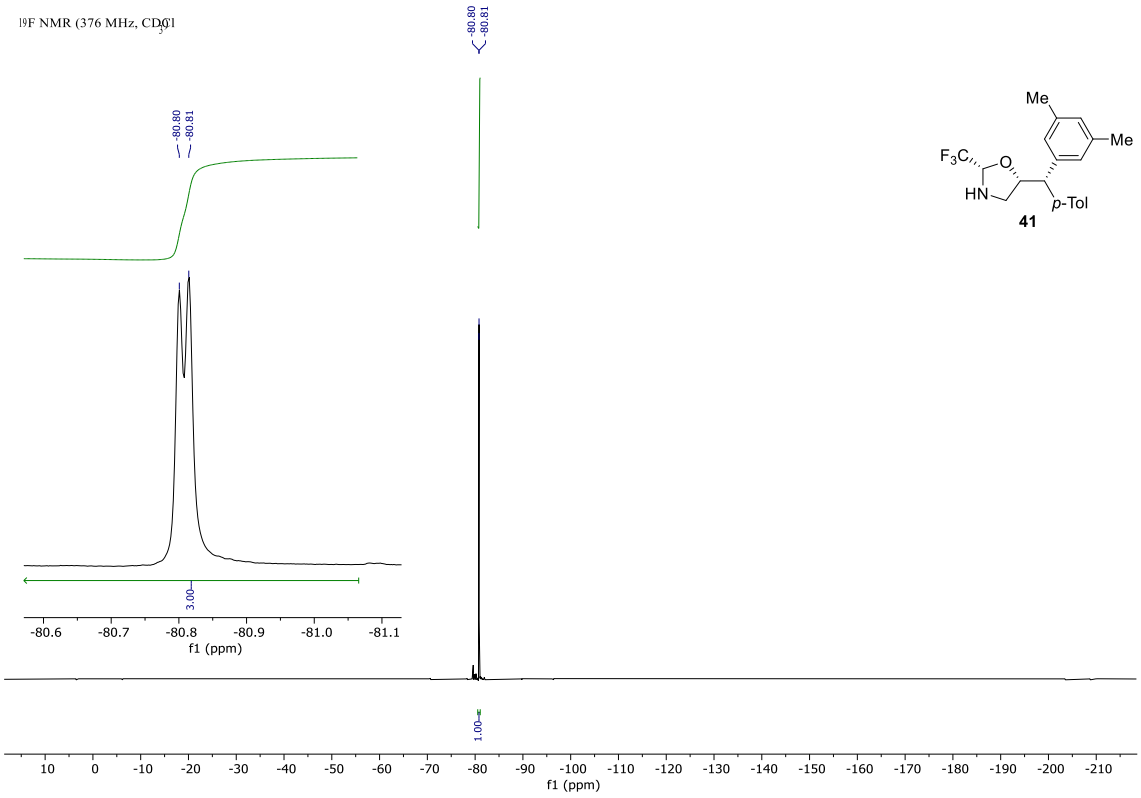

13C NMR (101 MHz, CDCl3)
161.70
159.25
138.06
136.55
129.79
129.75
129.32
128.77
128.74
128.69
128.60
128.33
124.81
124.55
124.53
121.99
116.24
116.01
88.97
88.63
88.30
87.96
81.66
81.64
77.48
77.16
76.84
50.41
48.67
21.18
F
F3C
O
HN
p-Tol
40
f1 (ppm)


19F NMR (376 MHz, CDCl3)
-81.04
-81.05
-115.92
-115.93
-115.94
-115.95
-115.96
-115.98
F
F3C
O
HN
p-Tol
40
3.00
0.81
f1 (ppm)


1H NMR (400 MHz, CDCl3)
Me
Me
F3C
O
HN
p-Tol
41
f1 (ppm)

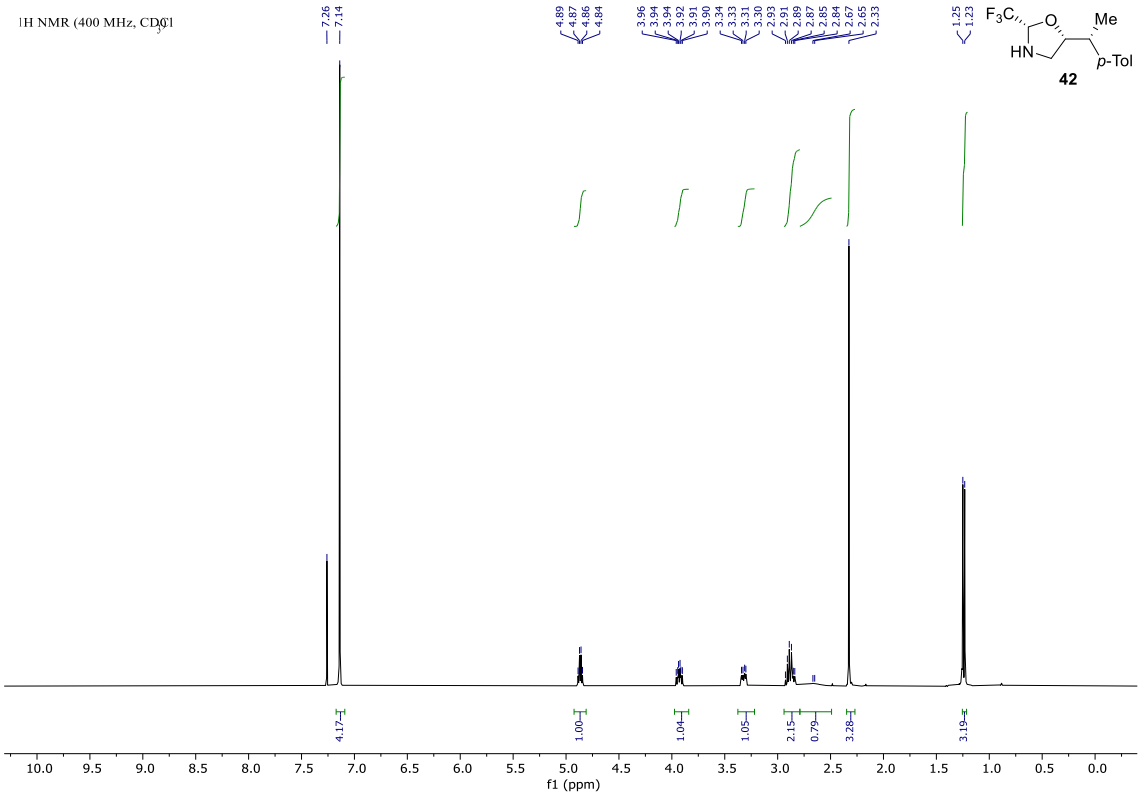

Me
Me
F3C
O
HN
p-Tol
41
f1 (ppm)

^{19}F NMR (376 MHz, CD_3Cl)

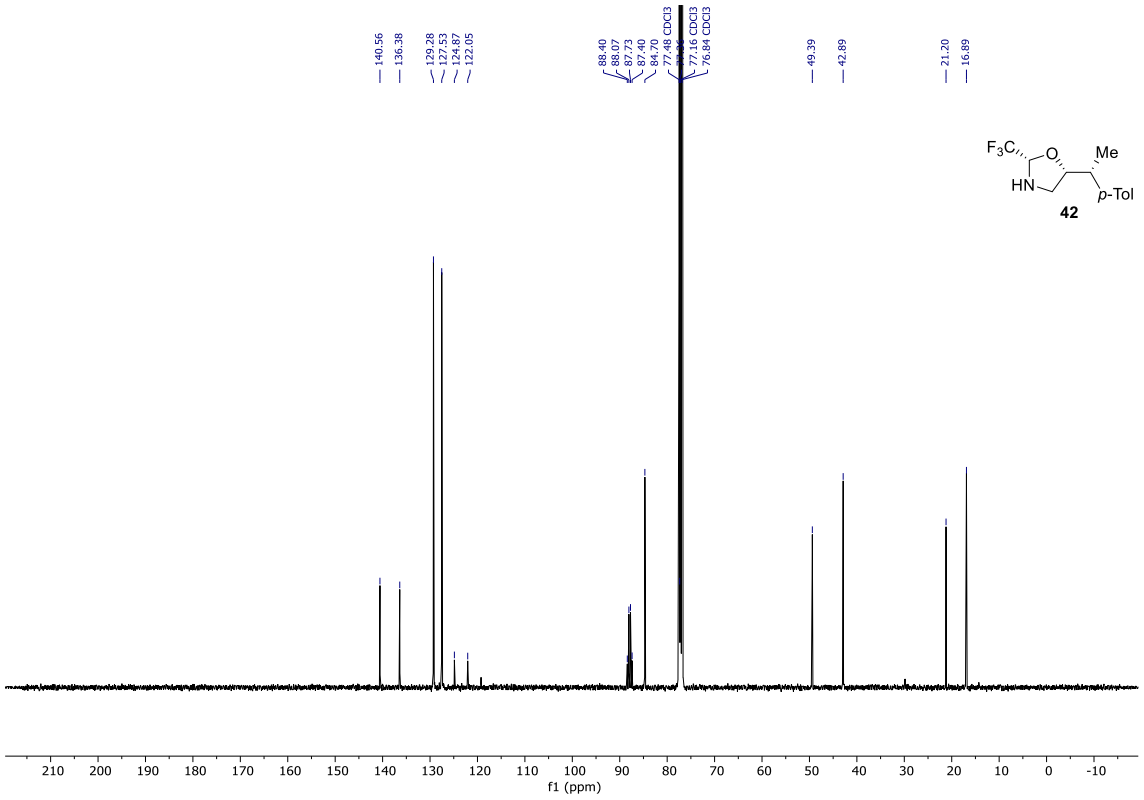


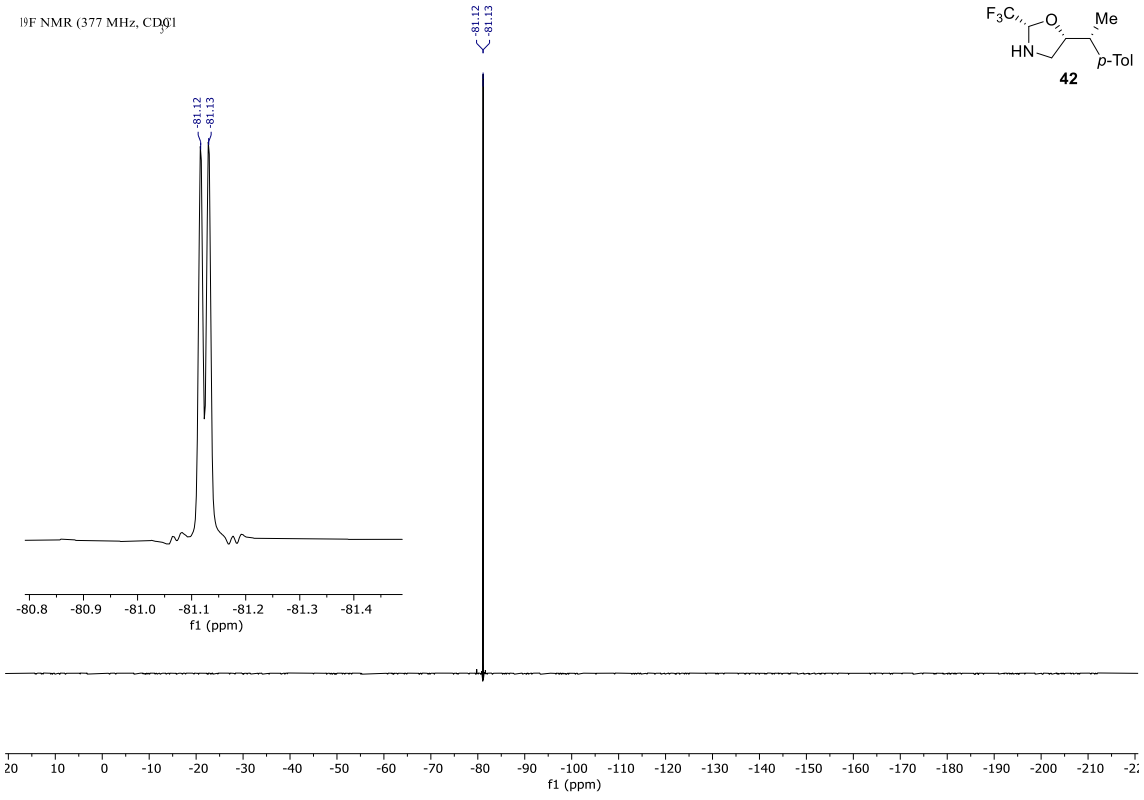
41

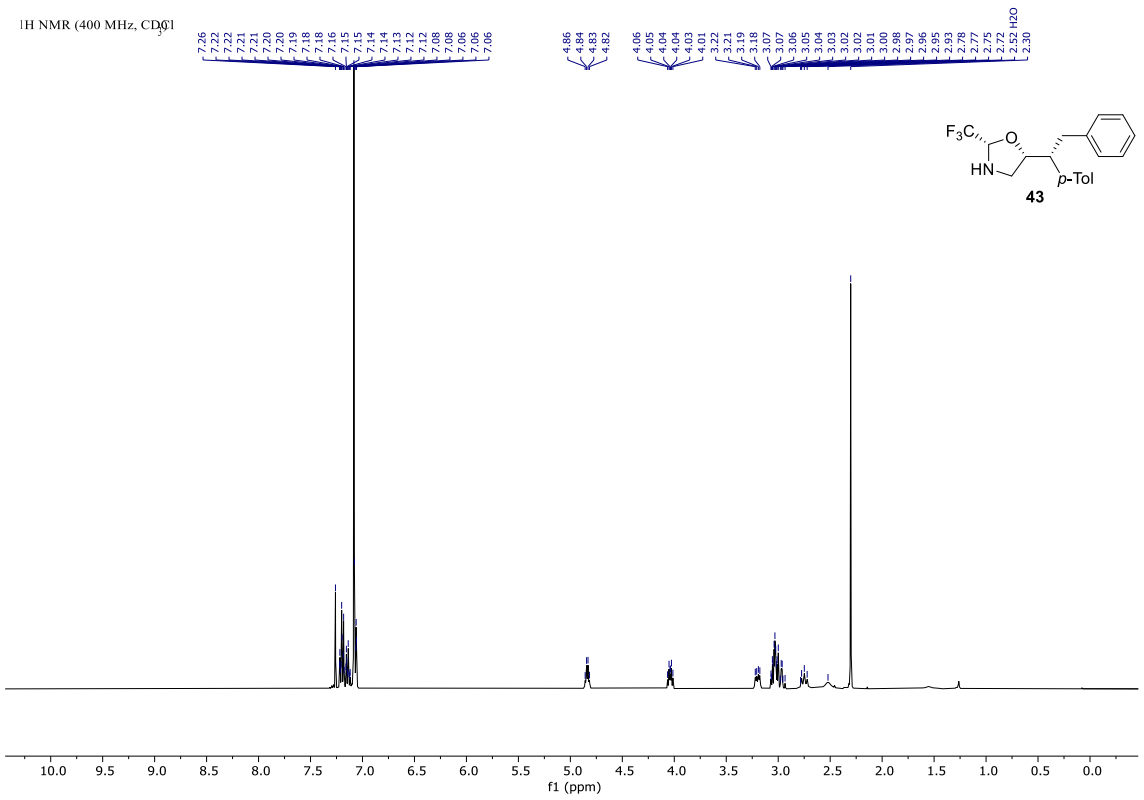
^{1}H NMR (400 MHz, CD_3Cl)

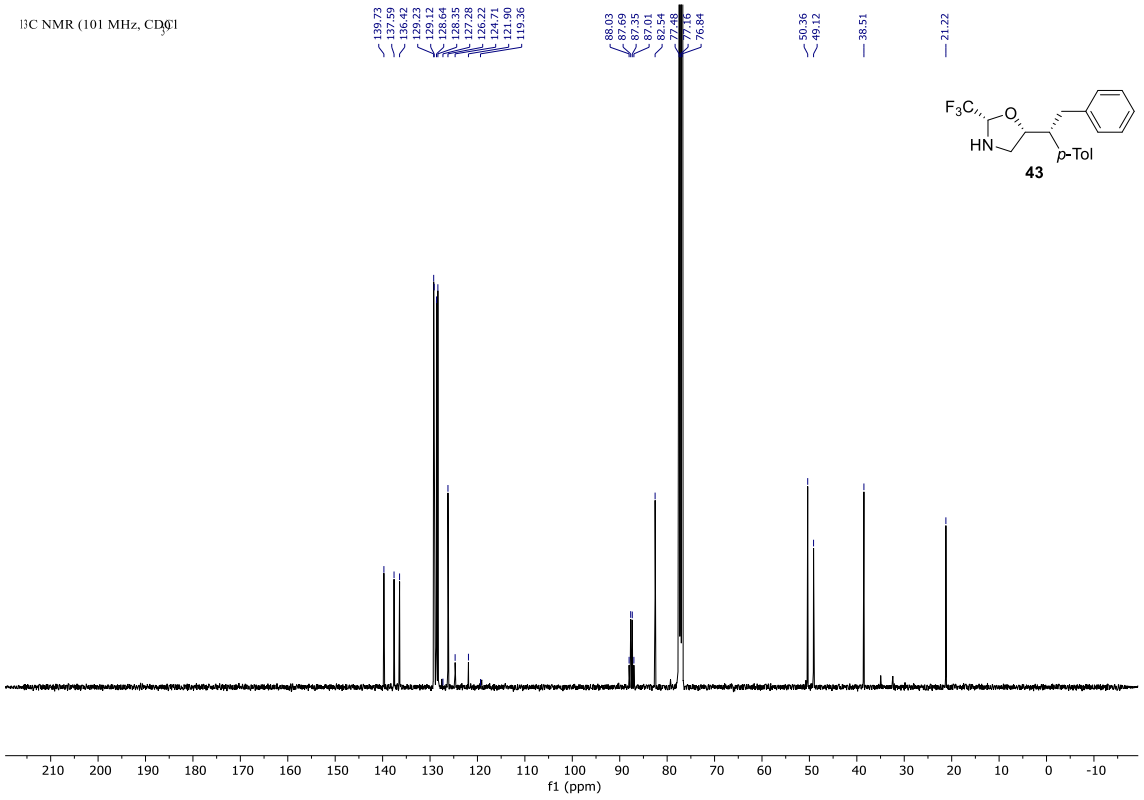


42

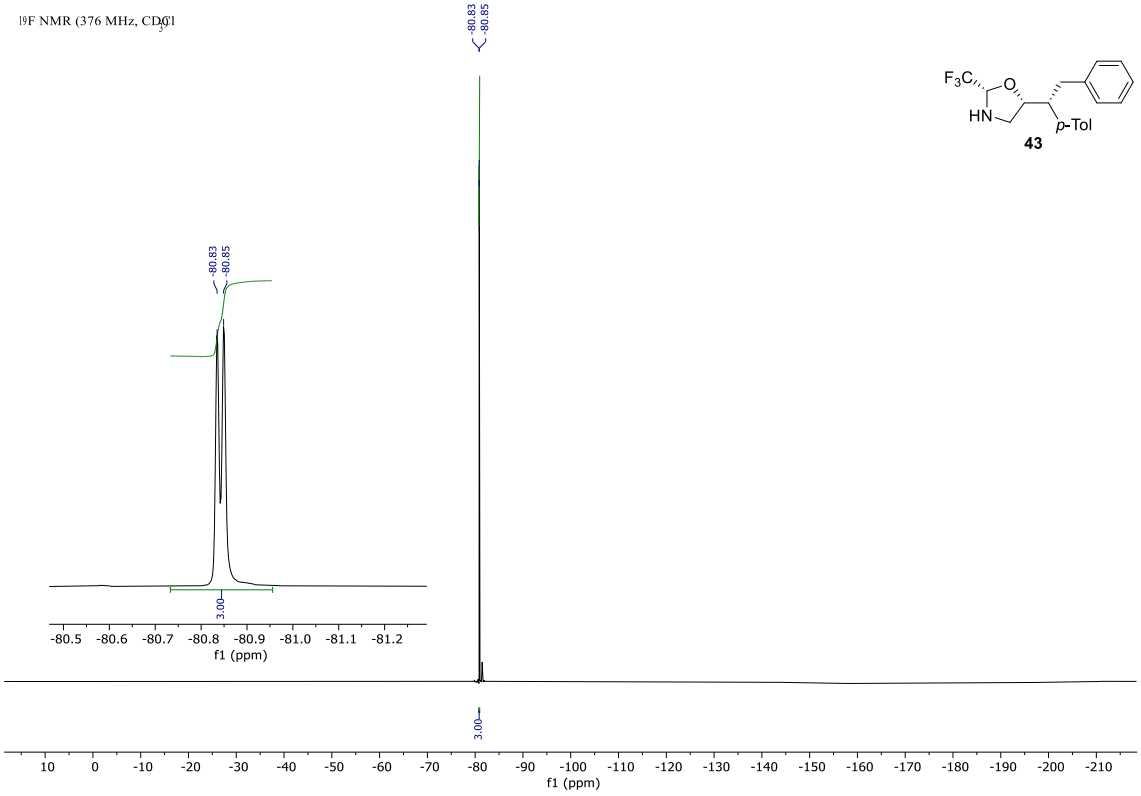

140.56
136.38
129.28
127.53
124.87
122.05
88.40
88.07
87.73
87.40
84.70
77.48 CDCl3
77.32
77.16 CDCl3
76.84 CDCl3
49.39
42.89
21.20
16.89
F3C
O
Me
HN
p-Tol
42
f1 (ppm)


19F NMR (377 MHz, CDCl3)
-81.12
-81.13
F3C
O
Me
HN
p-Tol
42
f1 (ppm)

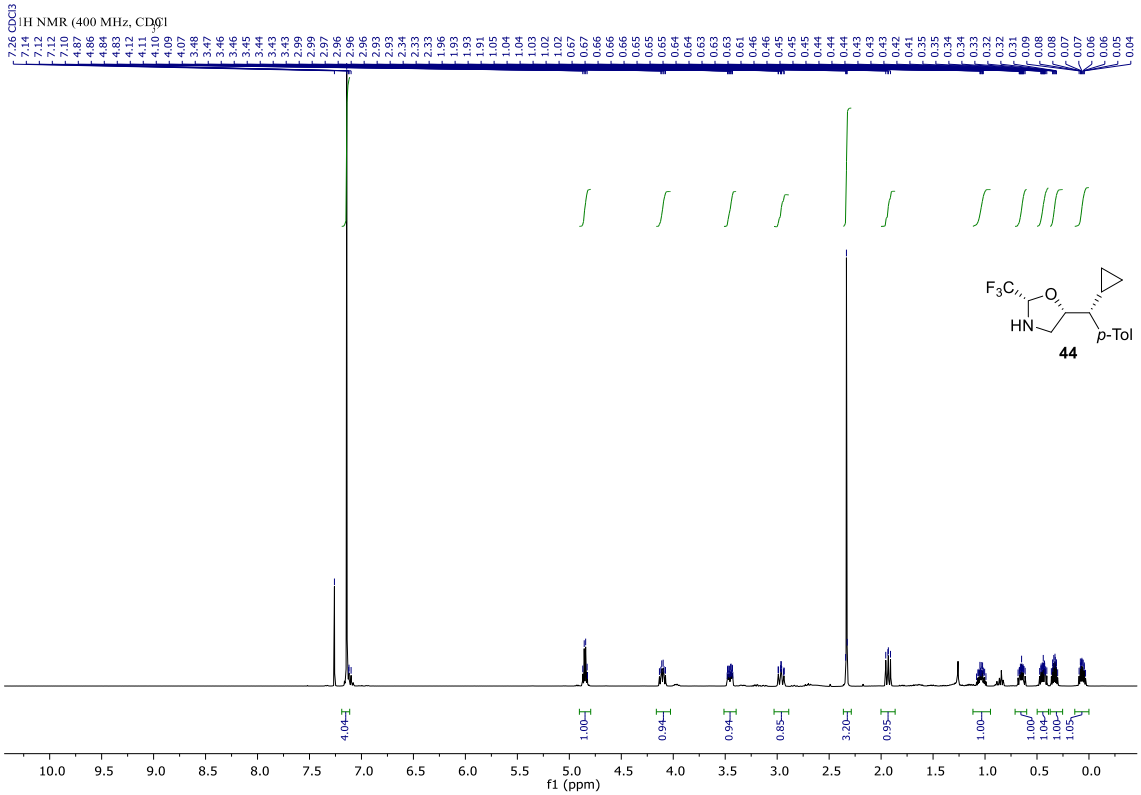

1H NMR (400 MHz, CDCl3)
F3C
O
HN
p-Tol
43
f1 (ppm)


13C NMR (101 MHz, CDCl3)
F3C
O
HN
p-Tol
43
f1 (ppm)

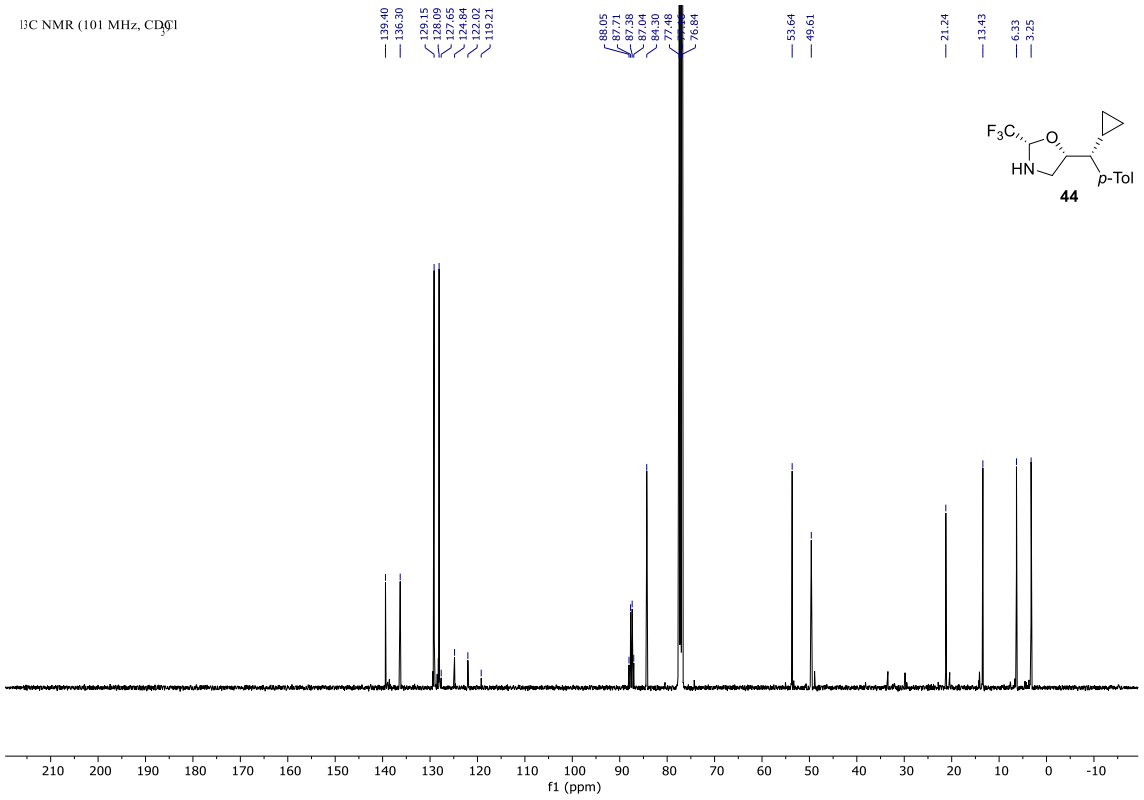
^{19}F NMR (376 MHz, $CDCl_3$)



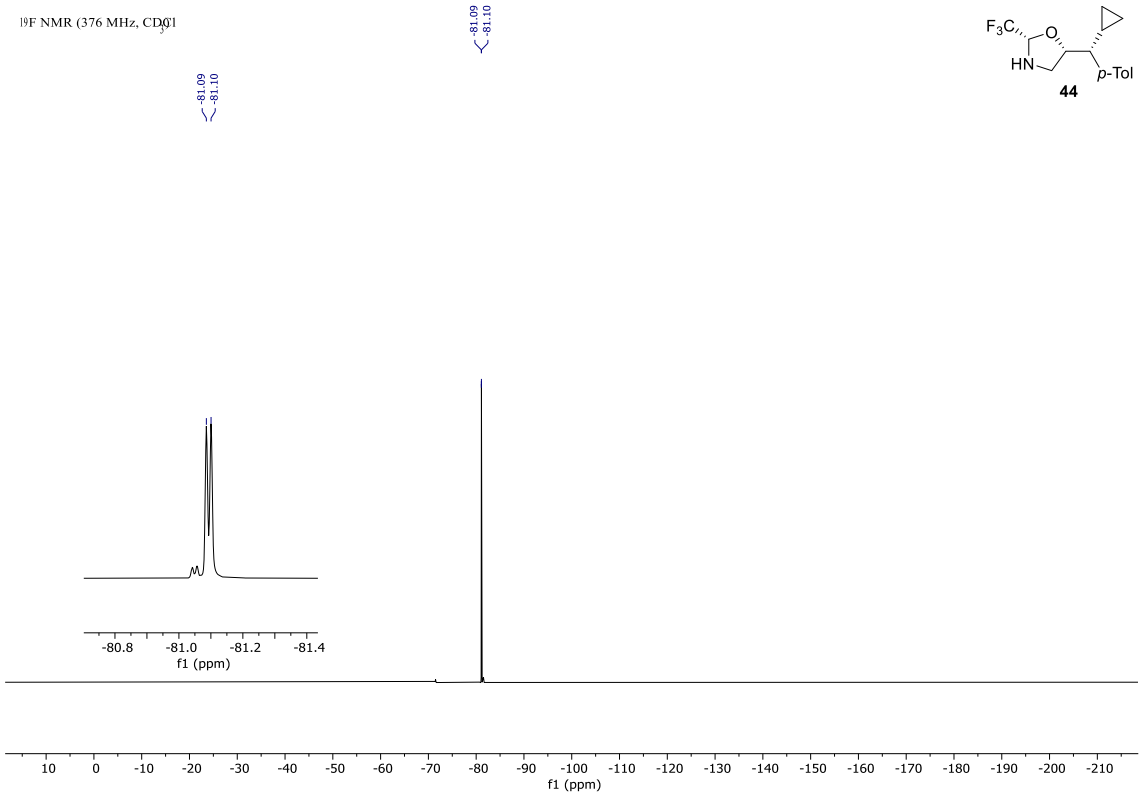
^{1}H NMR (400 MHz, $CDCl_3$)

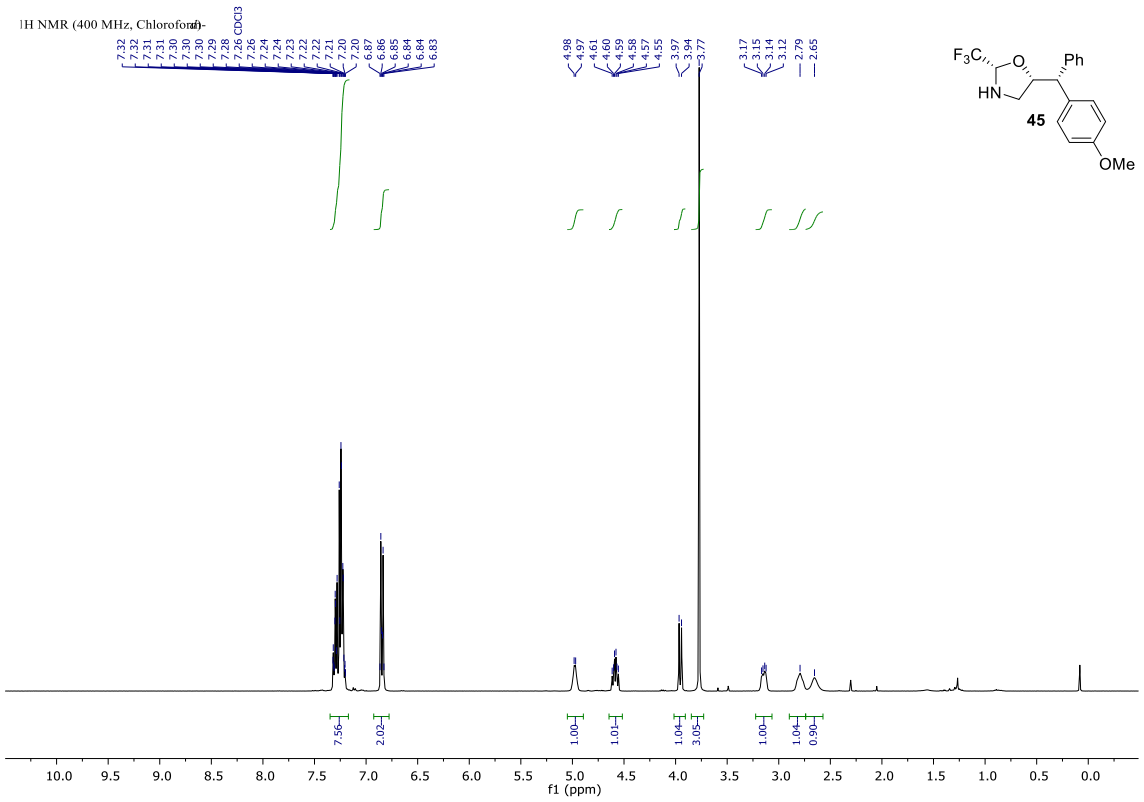


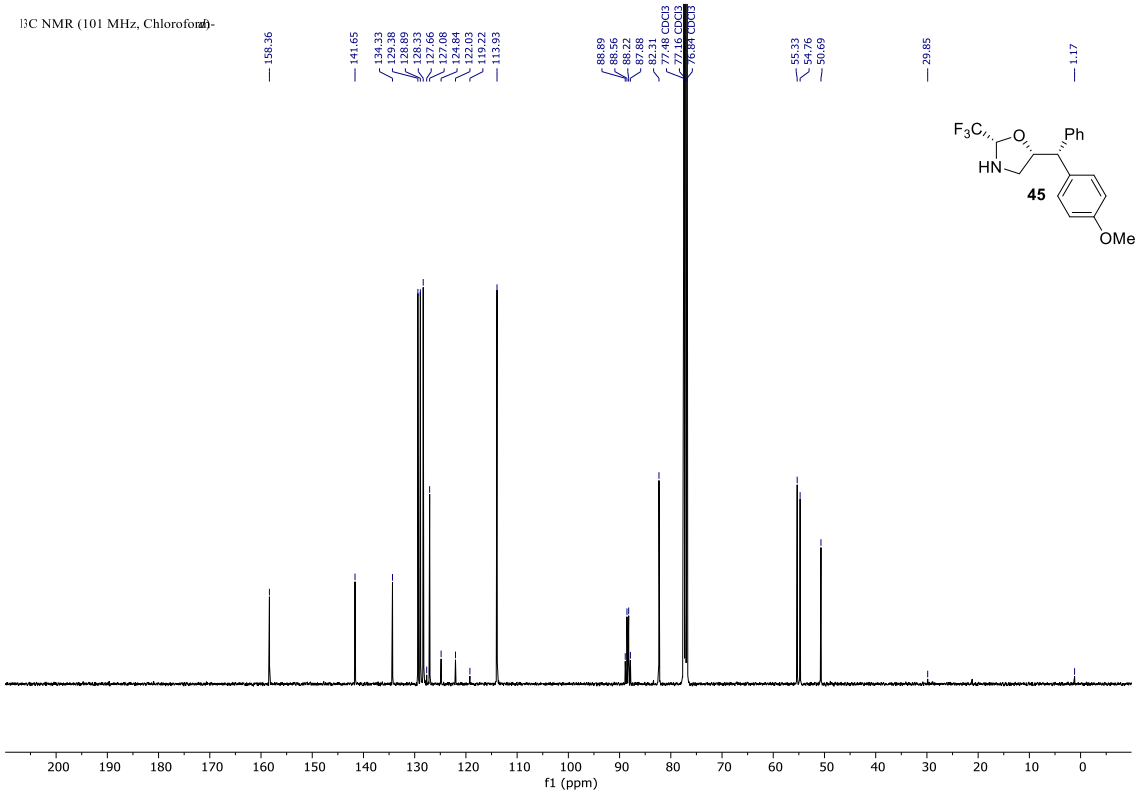
^{13}C NMR (101 MHz, $CDCl_3$)



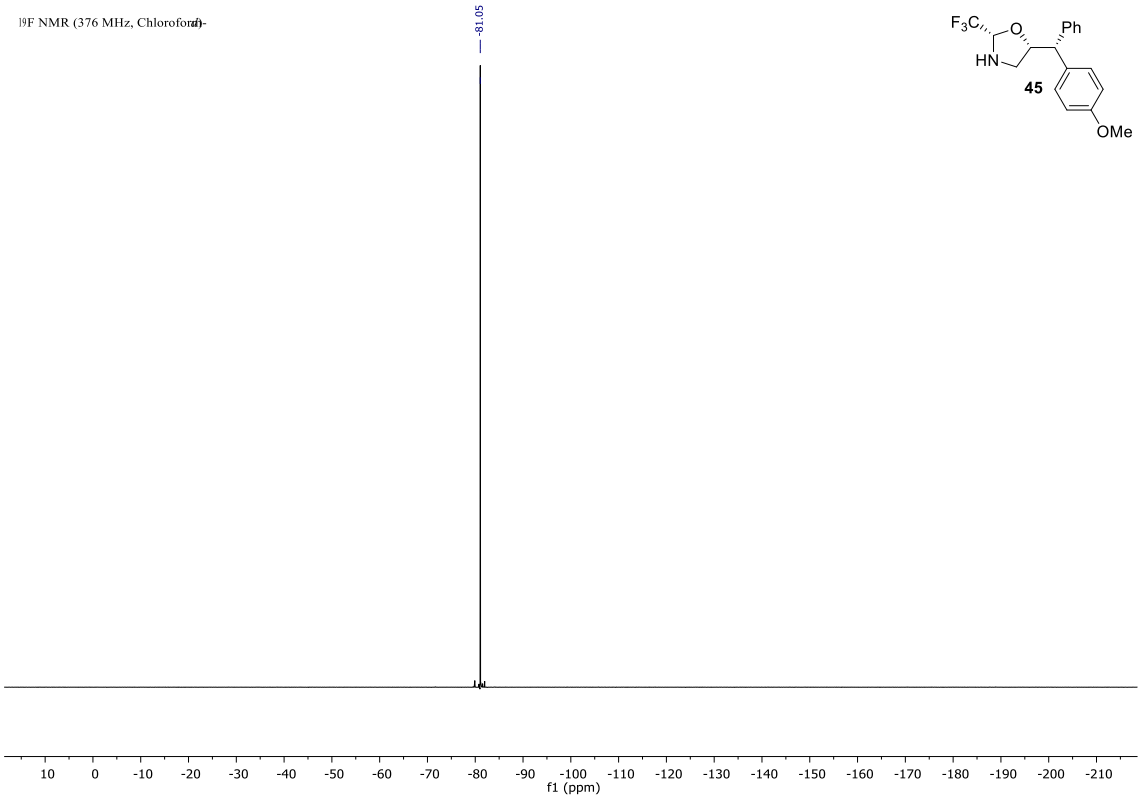
^{19}F NMR (376 MHz, $CDCl_3$)



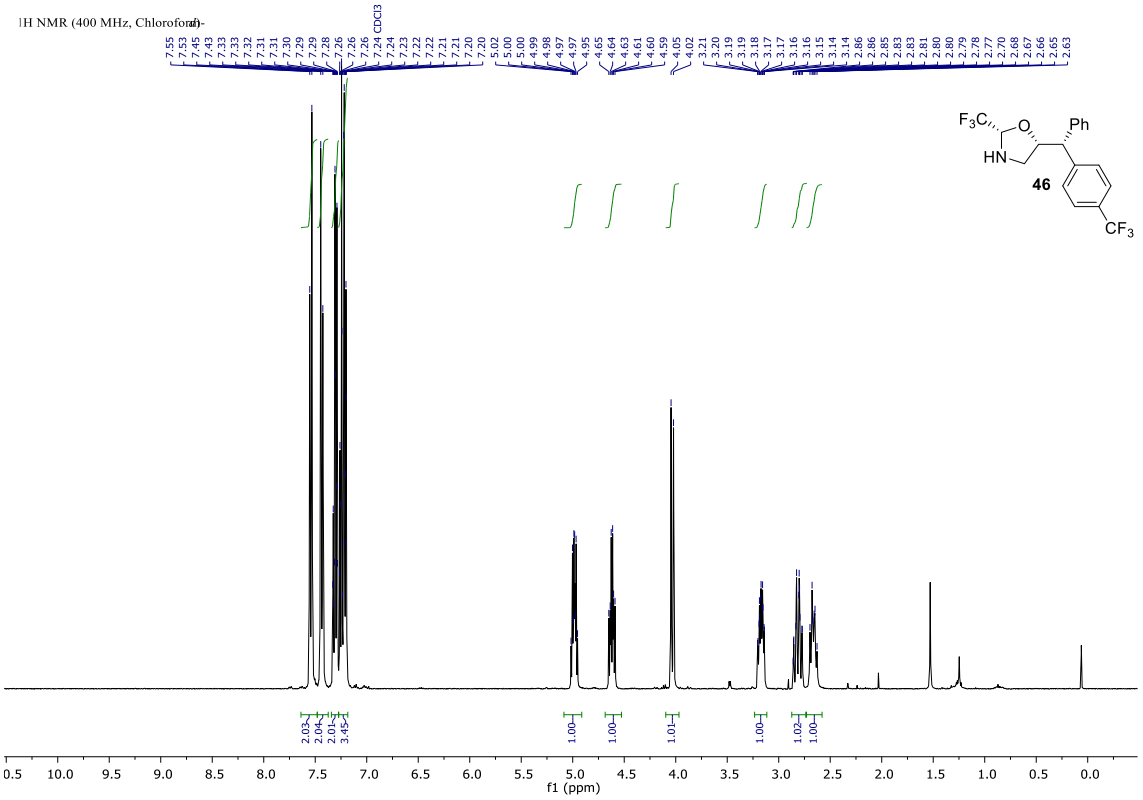

1H NMR (400 MHz, Chloroform-d)
7.32
7.32
7.31
7.31
7.30
7.30
7.30
7.29
7.28
7.26 CDCl3
7.26
7.24
7.24
7.23
7.22
7.22
7.21
7.20
7.20
6.87
6.86
6.85
6.84
6.84
6.83
4.98
4.97
4.61
4.60
4.59
4.58
4.57
4.55
3.97
3.94
3.77
3.17
3.15
3.14
3.12
2.79
2.65
F3C
O
Ph
HN
45
OMe
7.56
2.02
1.00
1.01
1.04
3.05
1.00
1.04
0.90
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)


13C NMR (101 MHz, Chloroform-d)
158.36
141.65
134.33
129.38
128.89
128.33
127.66
127.08
124.84
122.03
119.22
113.93
88.89
88.56
88.22
87.88
82.31
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.33
54.76
50.69
29.85
1.17
F3C
O
Ph
HN
45
OMe
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

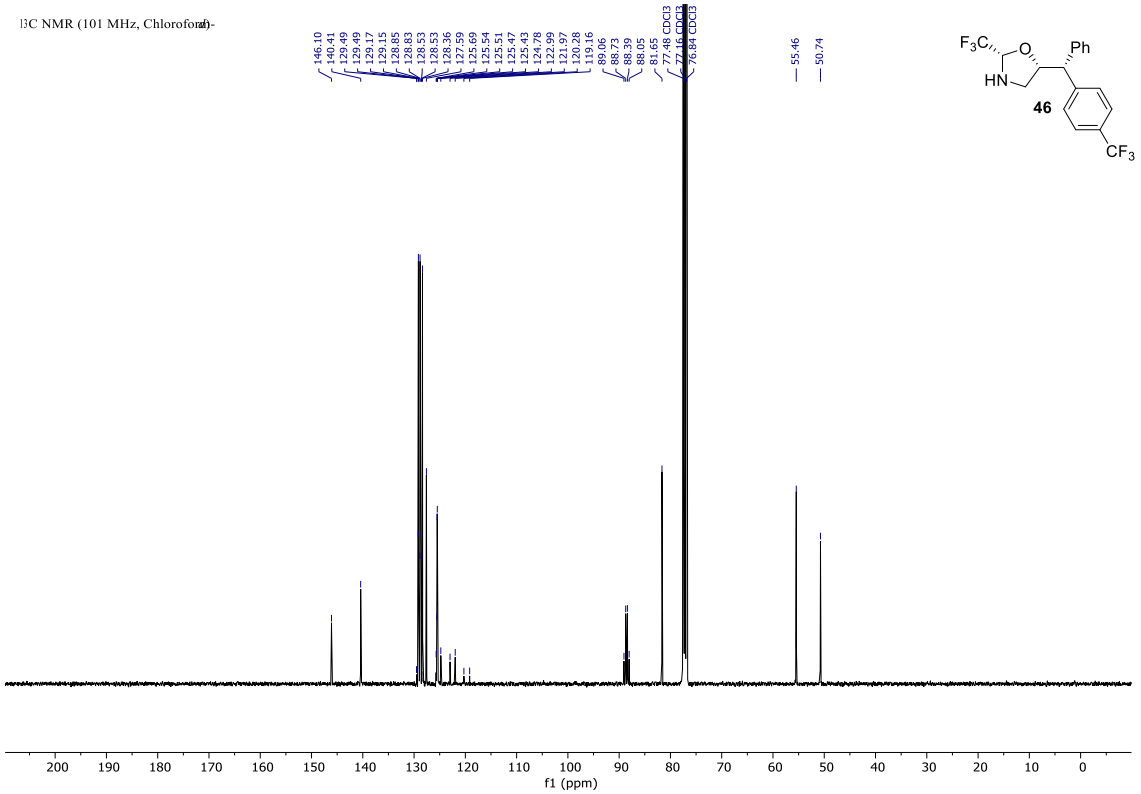
^{19}F NMR (376 MHz, Chloroform-*d*)



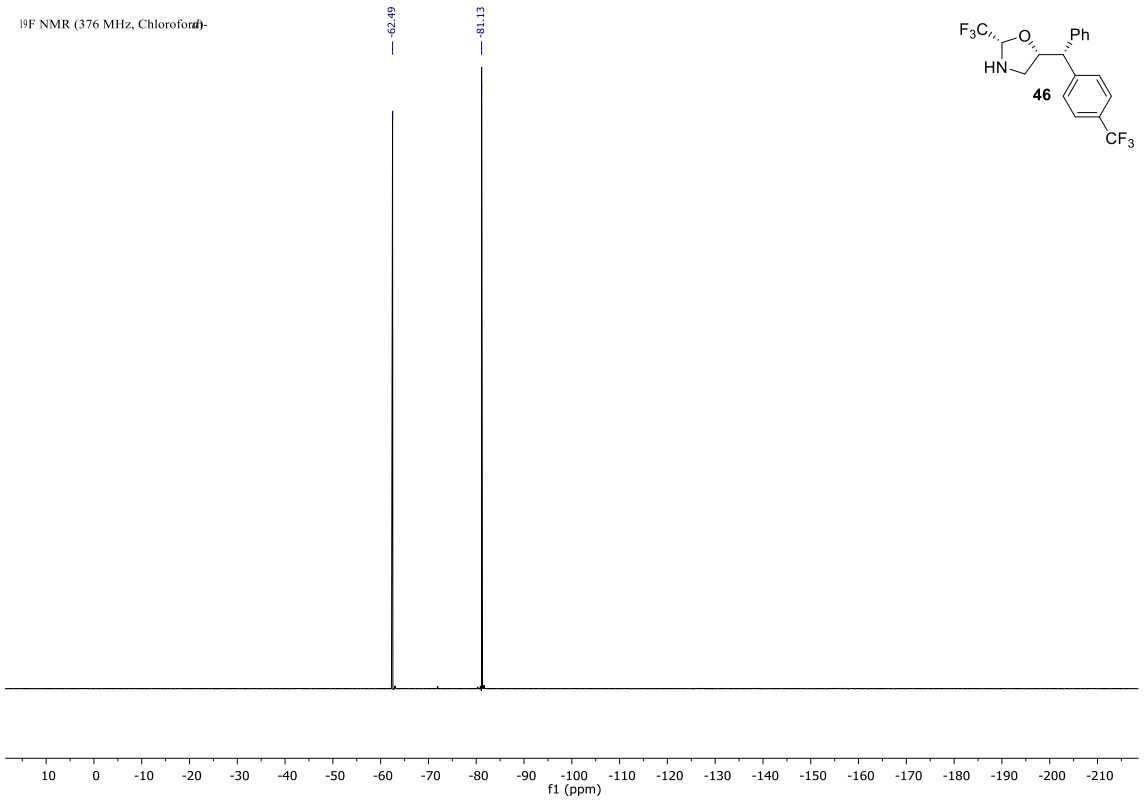
^{1}H NMR (400 MHz, Chloroform-*d*)

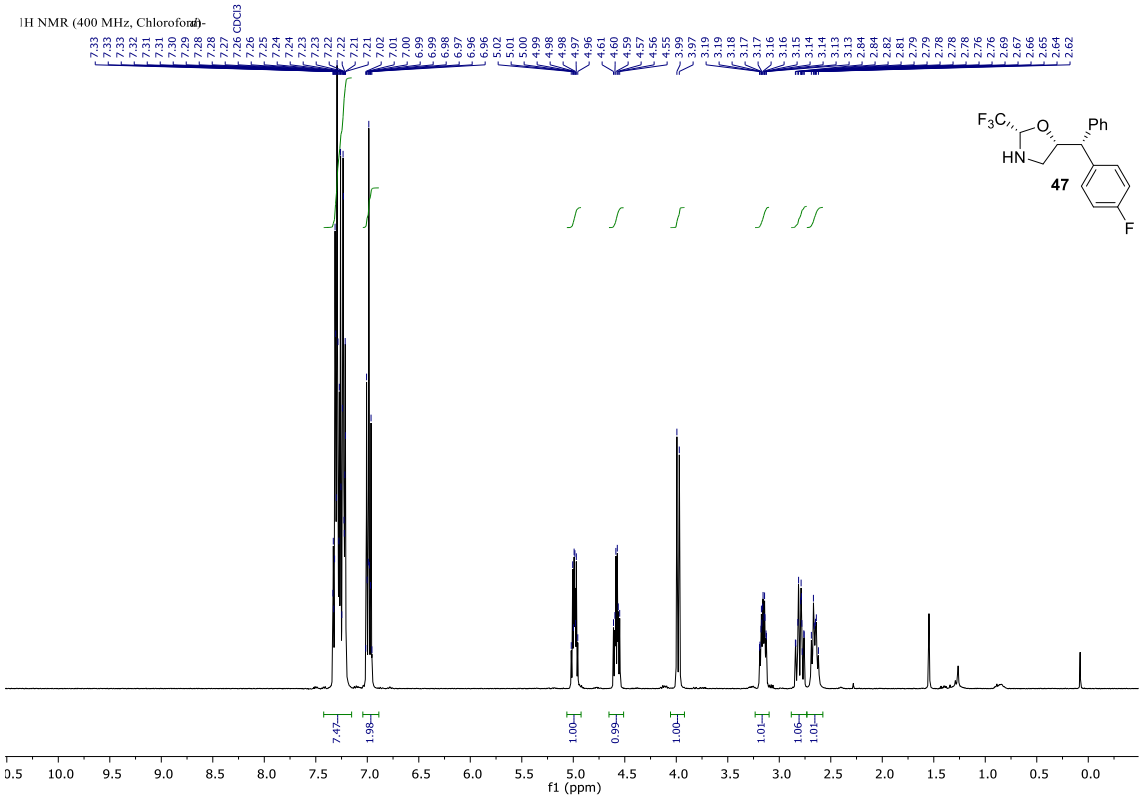


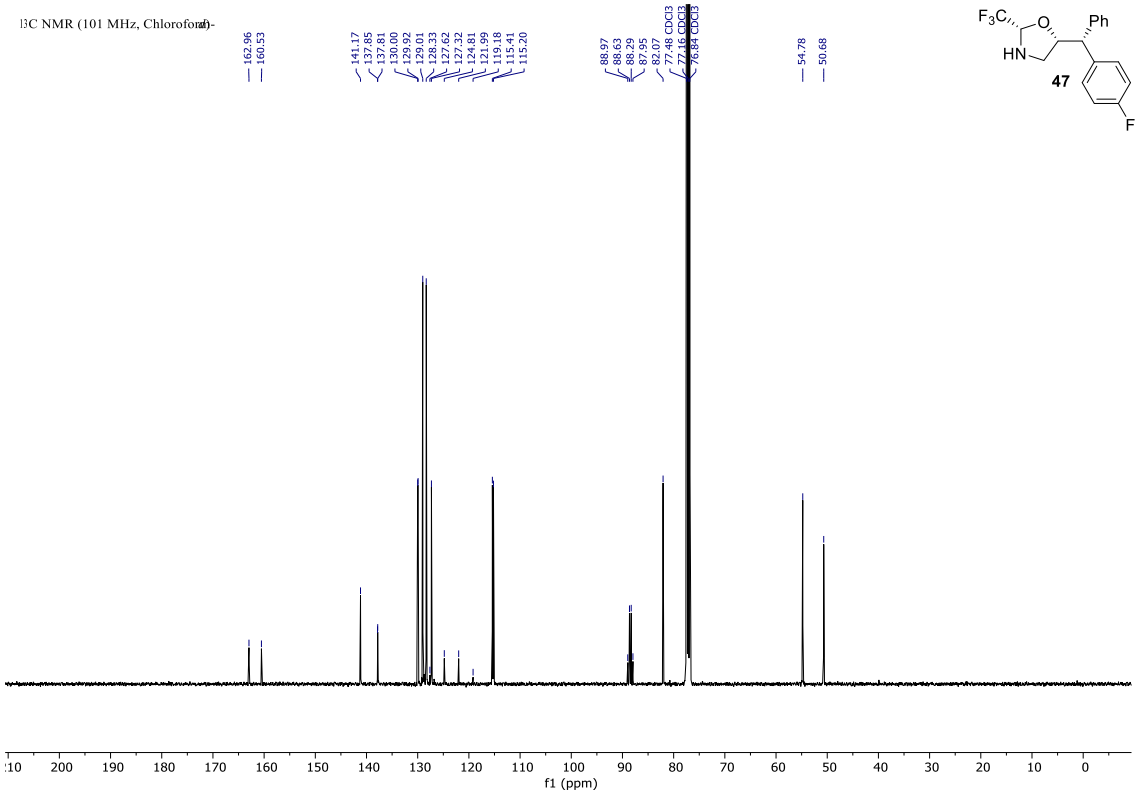
^{13}C NMR (101 MHz, Chloroform-*d*)



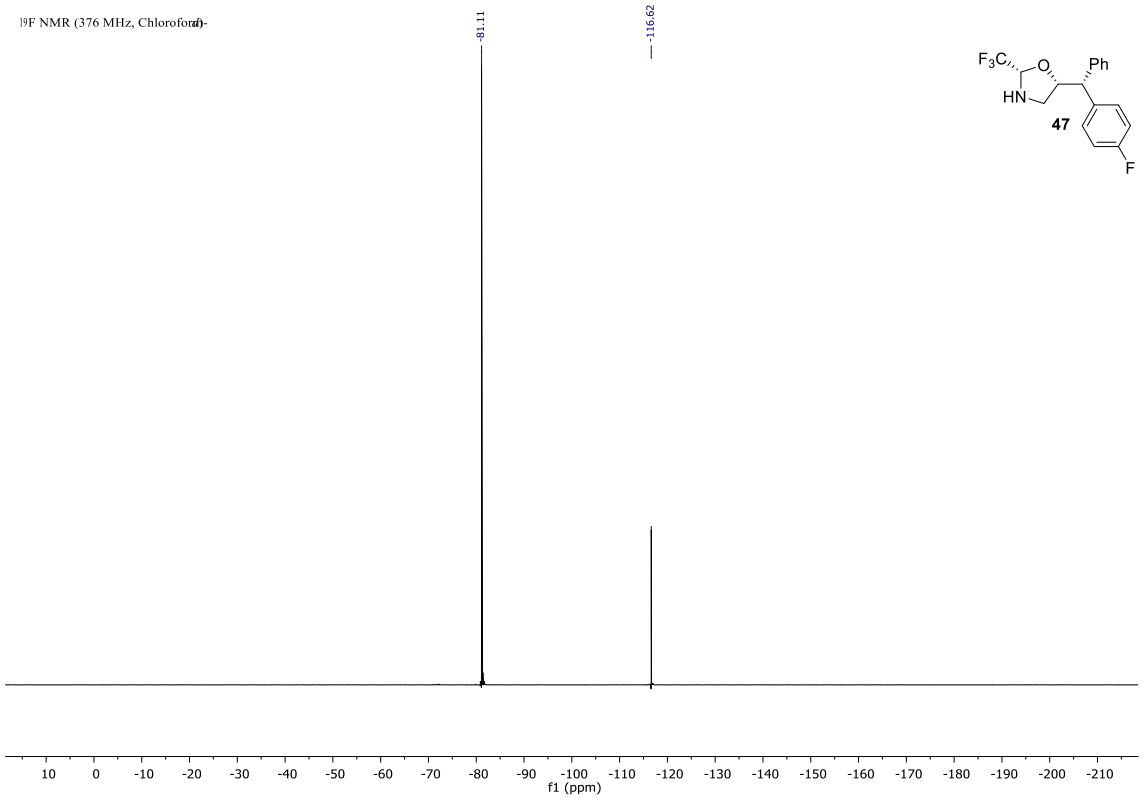
^{19}F NMR (376 MHz, Chloroform-*d*)



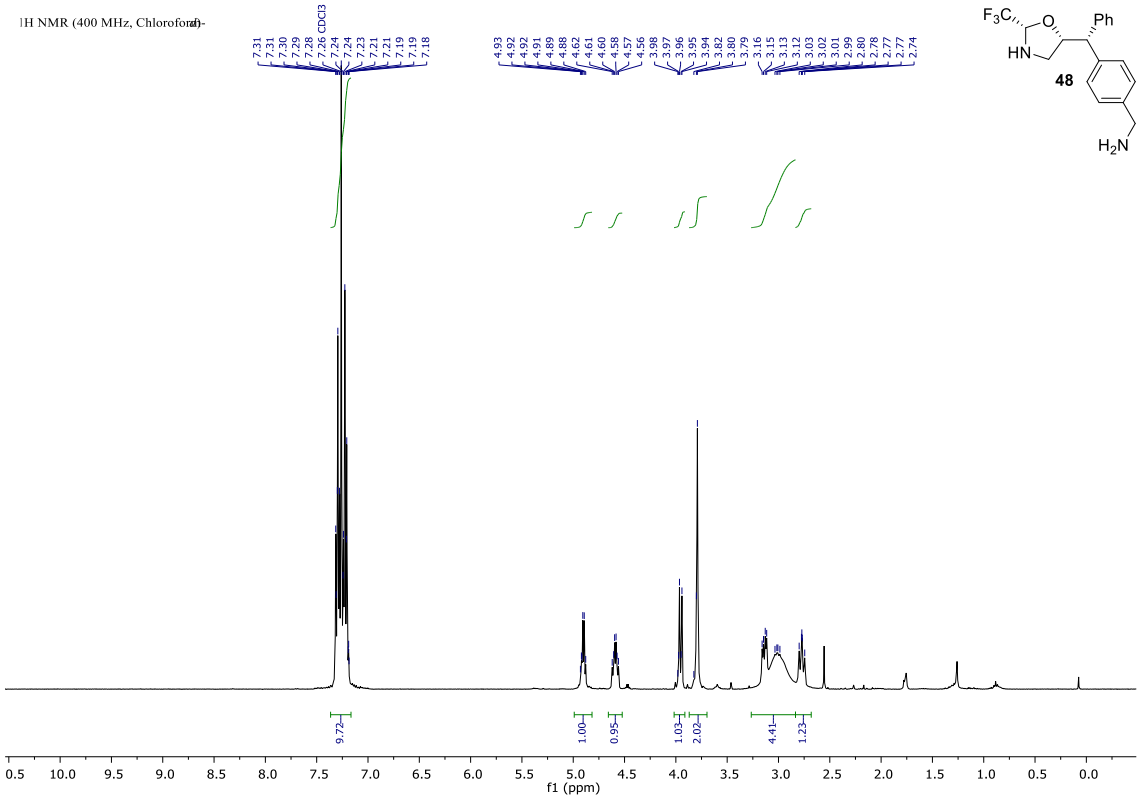

1H NMR (400 MHz, Chloroform-d)
CDCl3
7.42
1.98
1.00
0.99
1.00
1.01
1.06
1.01
f1 (ppm)
F3C
O
Ph
HN
47
F


13C NMR (101 MHz, Chloroform-d)
162.96
160.53
141.17
137.85
137.61
130.00
129.92
129.01
128.33
127.62
127.32
124.81
121.99
119.18
115.41
115.20
88.97
88.63
88.29
87.95
82.07
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
54.78
50.68
f1 (ppm)
F3C
O
Ph
HN
47
F

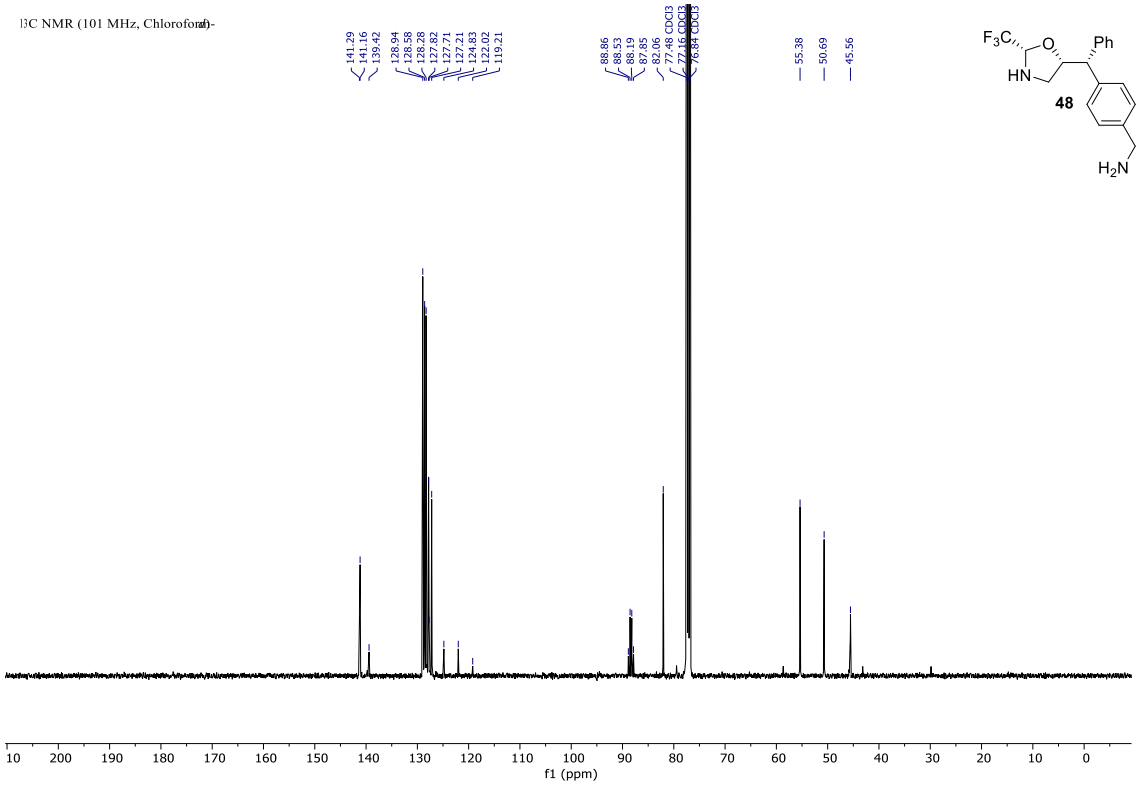
^{19}F NMR (376 MHz, Chloroform-*d*)



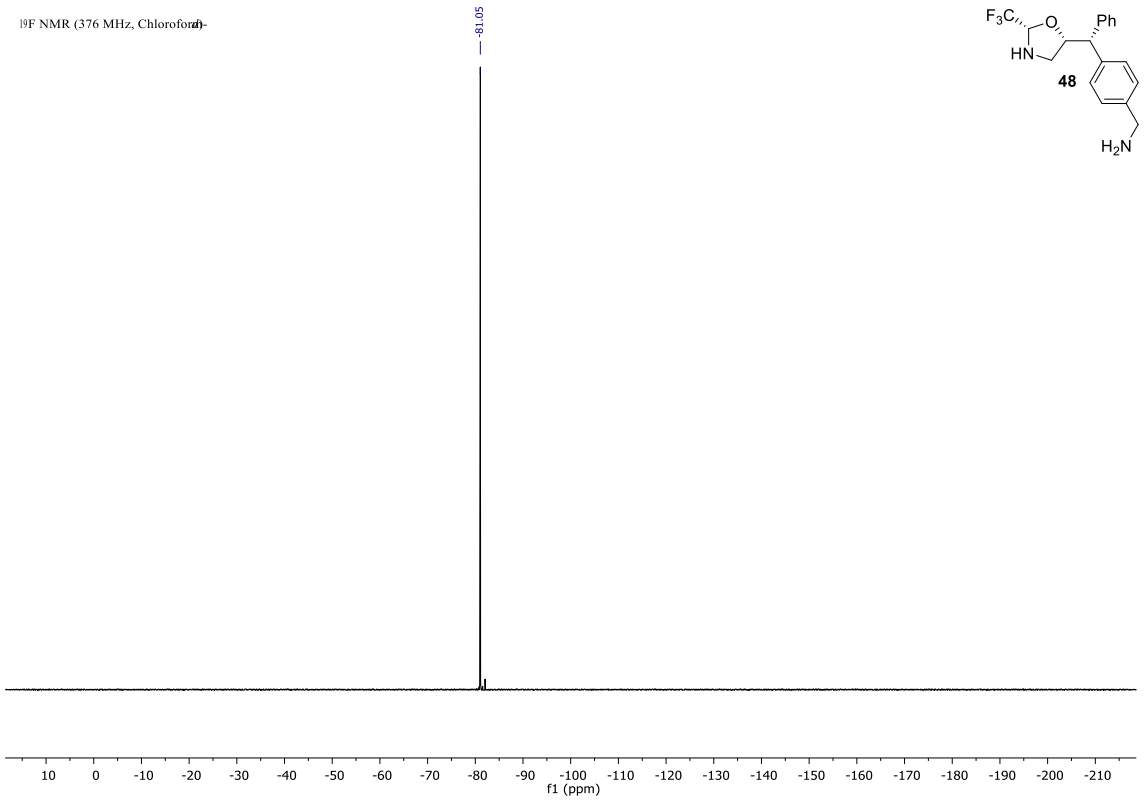
^{1}H NMR (400 MHz, Chloroform-*d*)

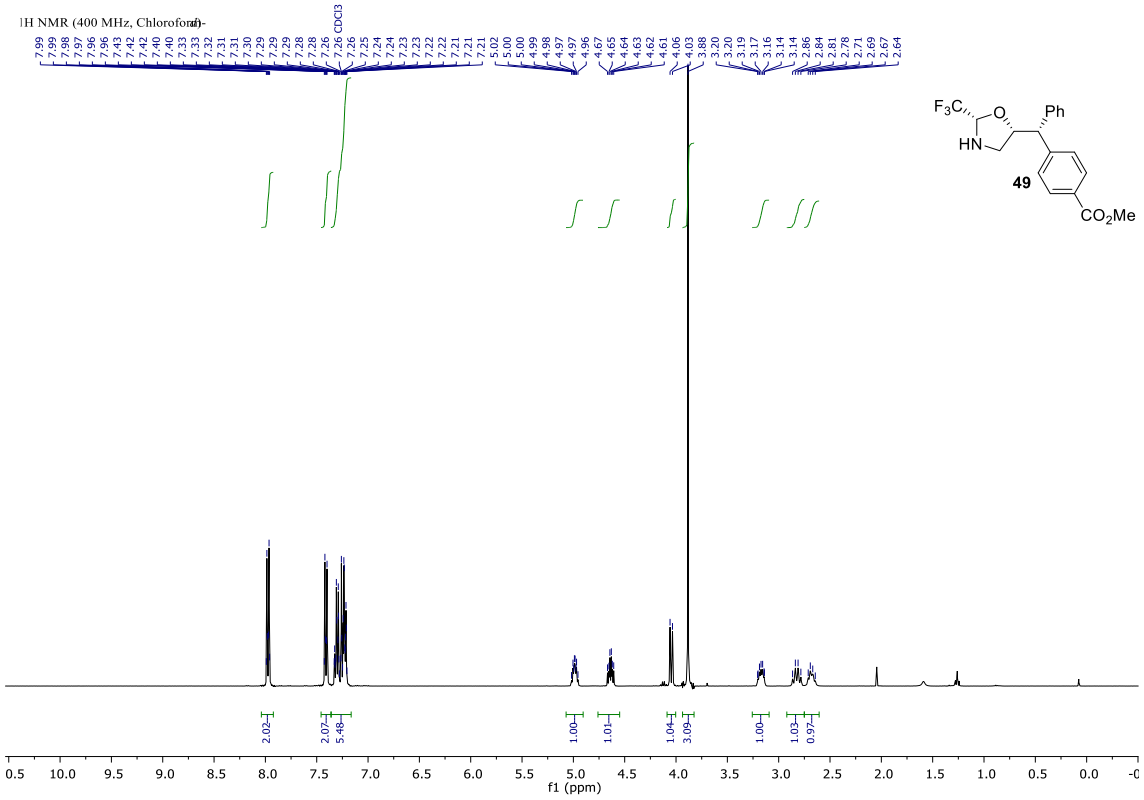


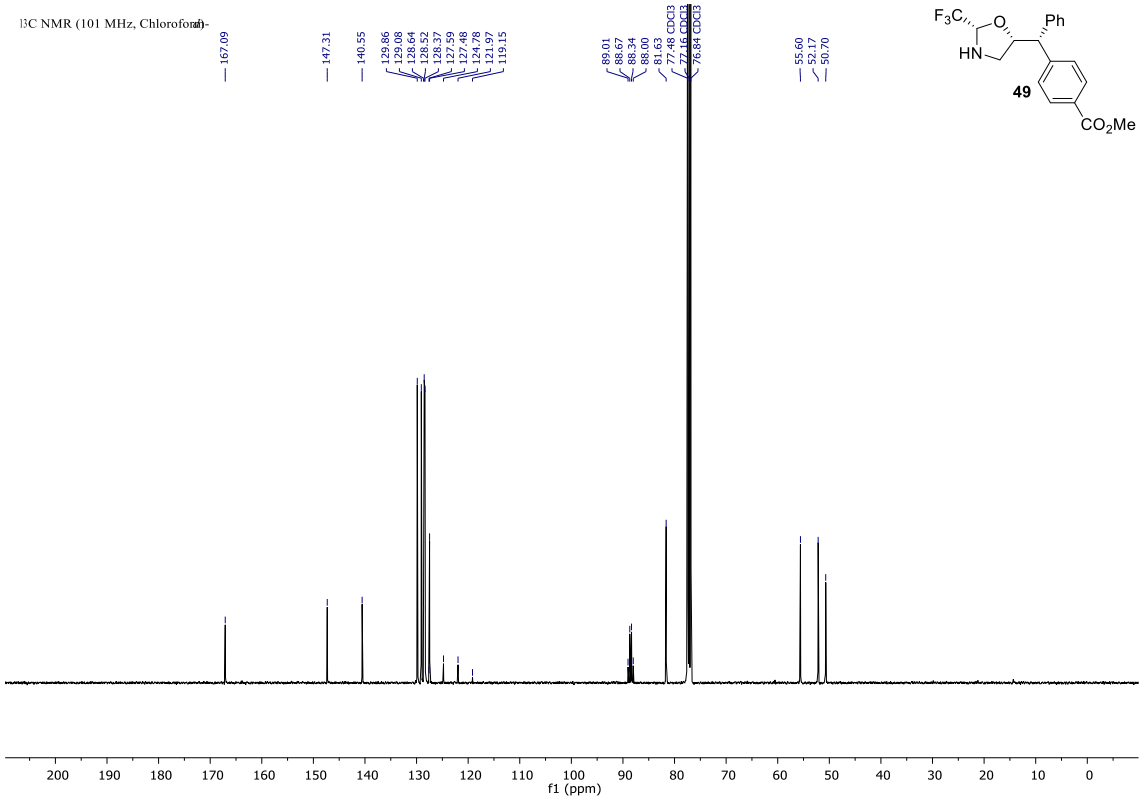
^{13}C NMR (101 MHz, Chloroform-*d*)



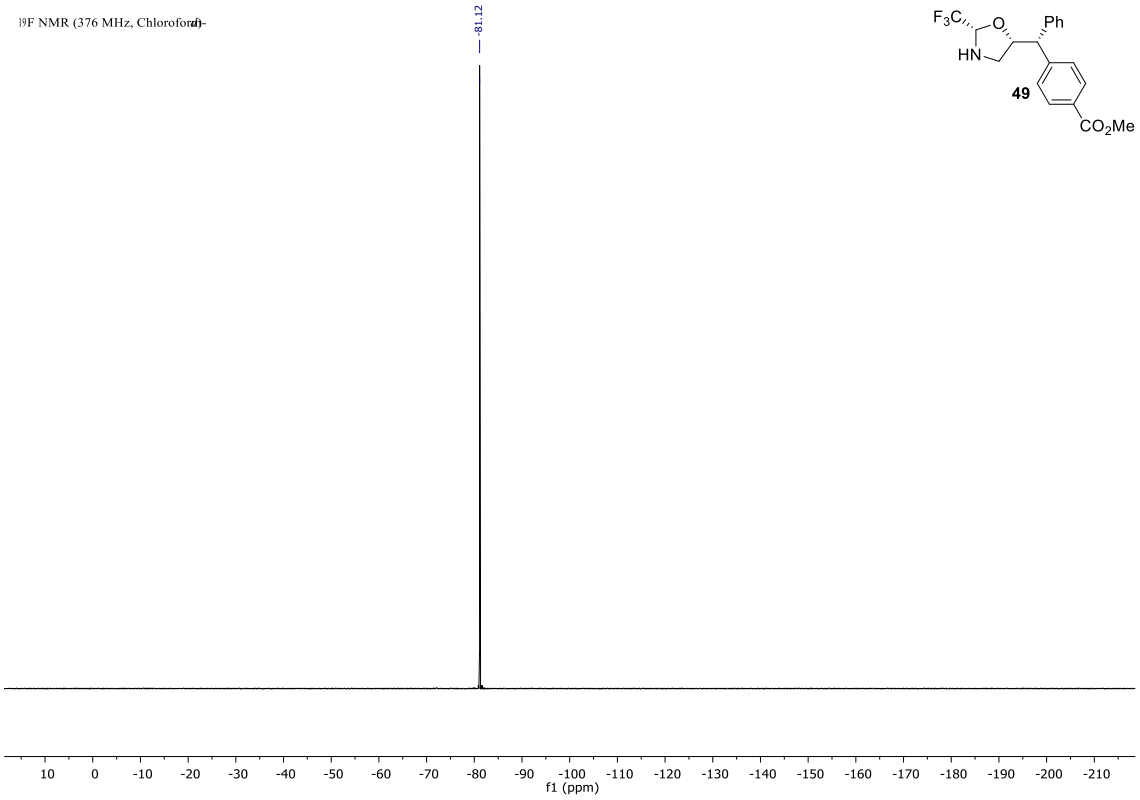
^{19}F NMR (376 MHz, Chloroform-*d*)



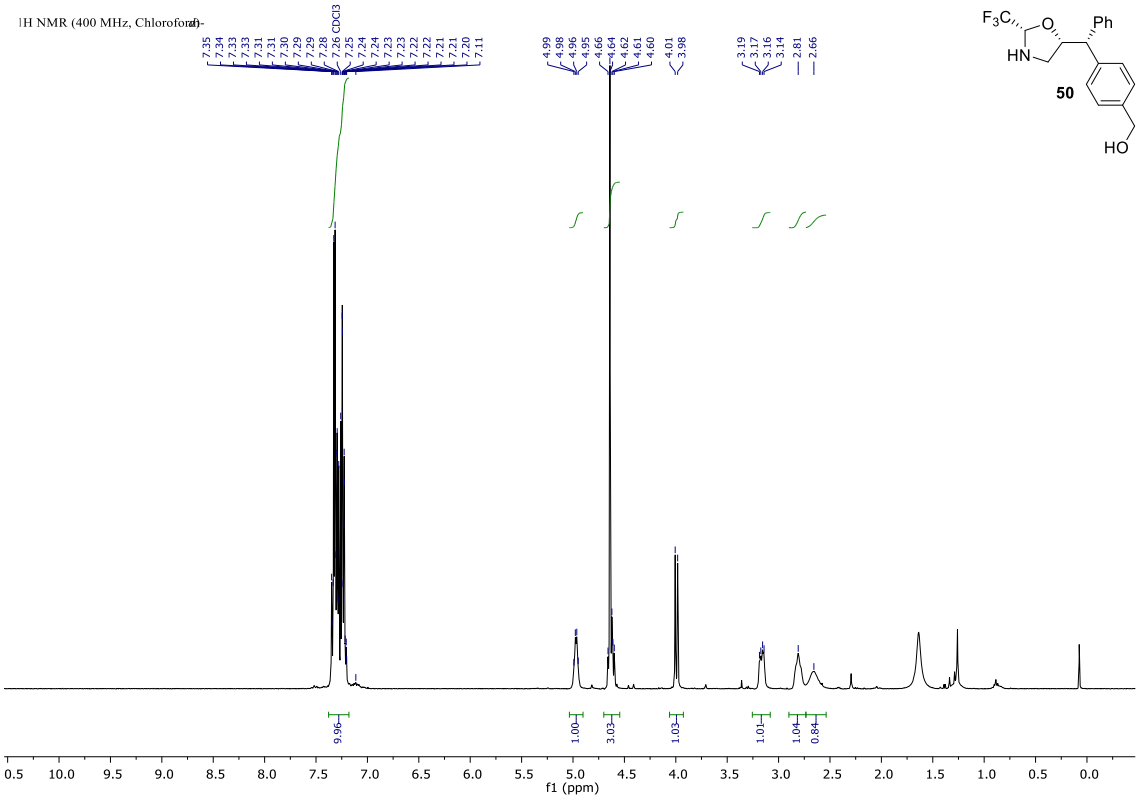

1H NMR (400 MHz, Chloroform-d)
CDCl3
F3C
O
Ph
HN
49
CO2Me
f1 (ppm)


13C NMR (101 MHz, Chloroform-d)
CDCl3
F3C
O
Ph
HN
49
CO2Me
f1 (ppm)

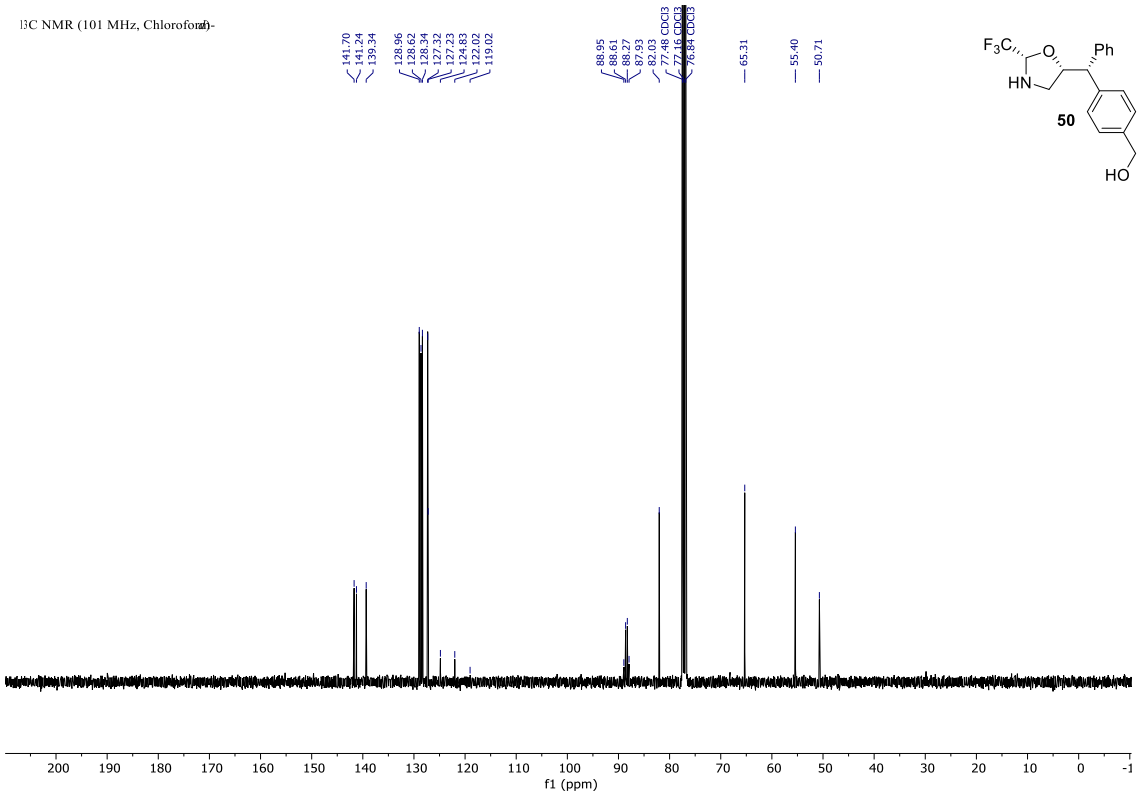
^{19}F NMR (376 MHz, Chloroform-*d*)



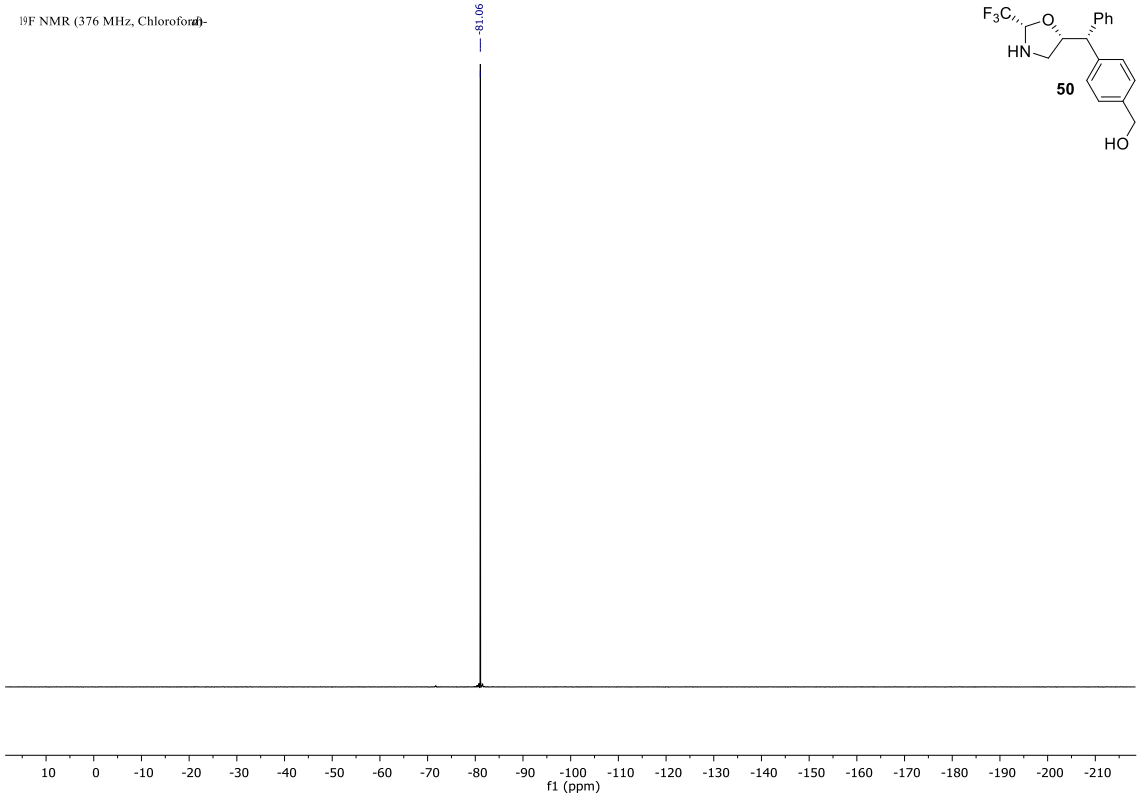
^{1}H NMR (400 MHz, Chloroform-*d*)

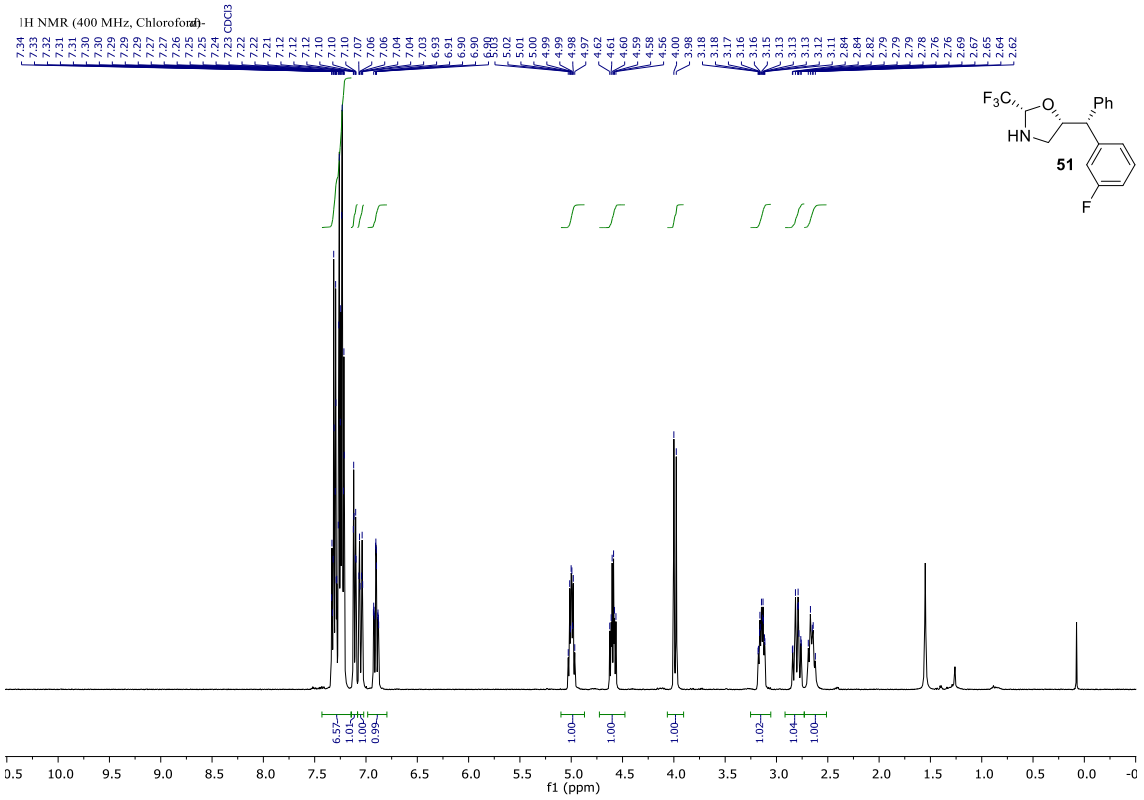


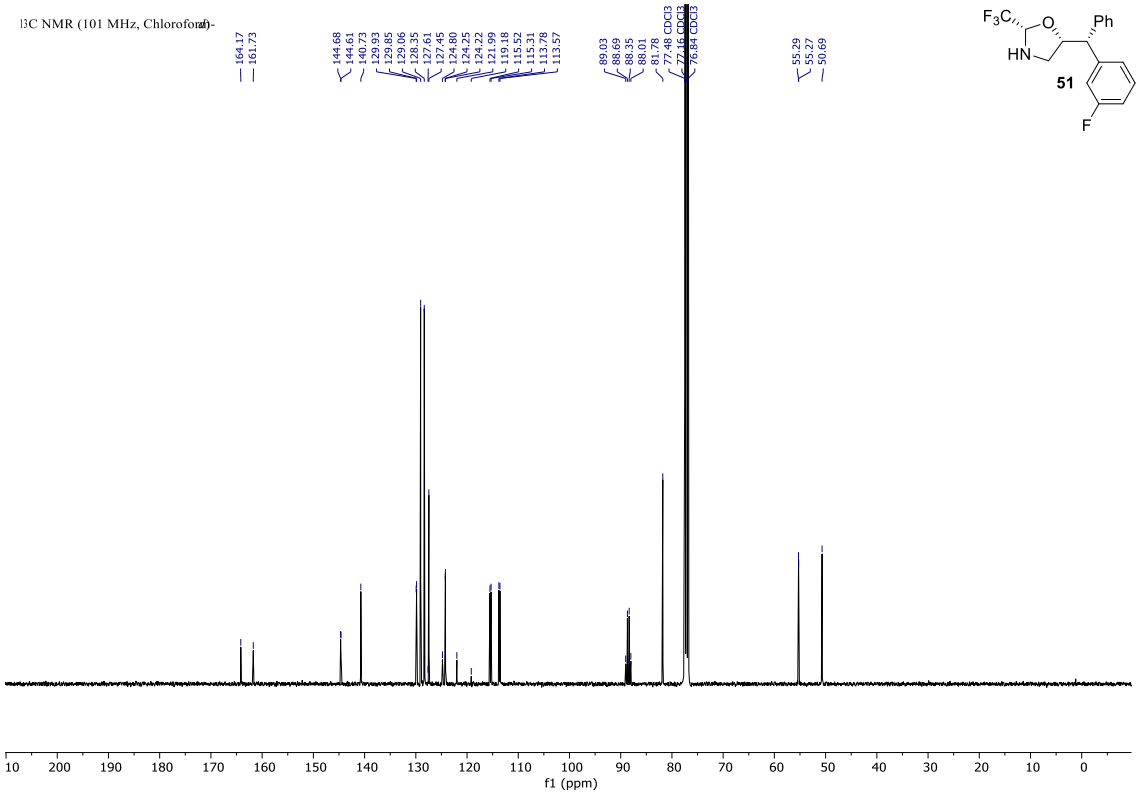
^{13}C NMR (101 MHz, Chloroform-*d*)

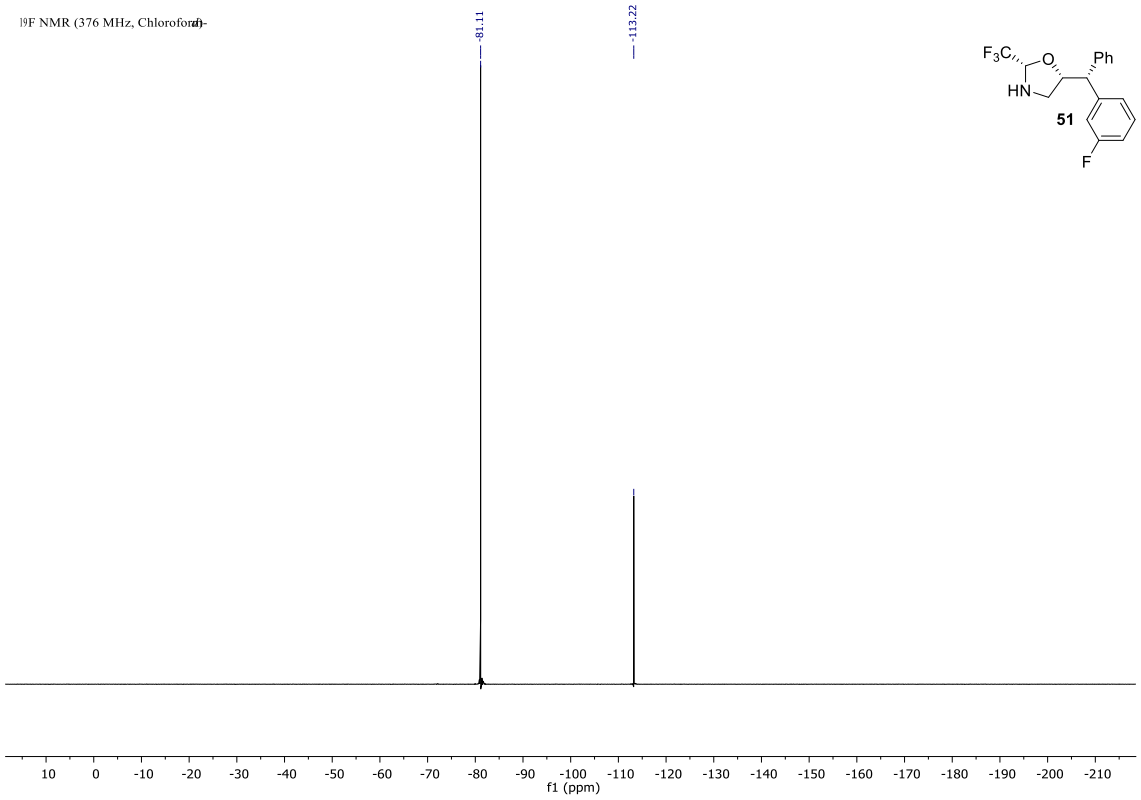


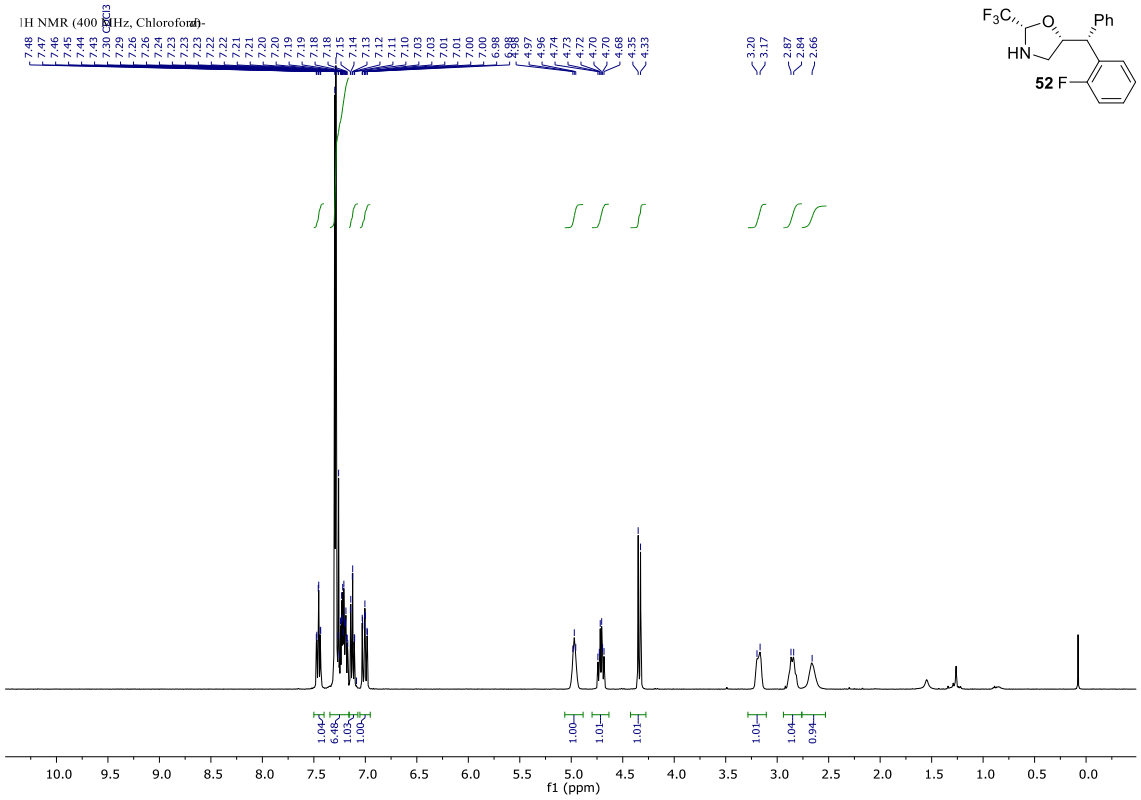
^{19}F NMR (376 MHz, Chloroform-*d*)



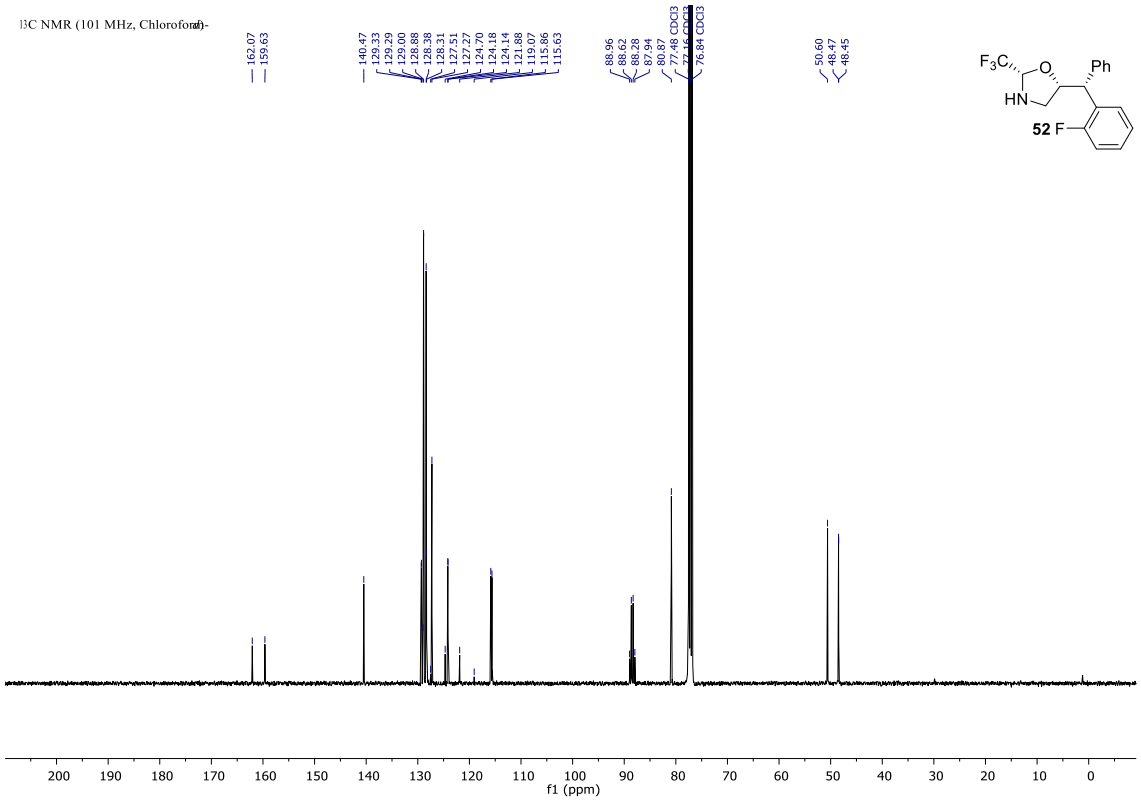

1H NMR (400 MHz, Chloroform-d)
CDCl3
F3C
O
Ph
HN
51
F
6.57
1.01
1.00
0.99
1.00
1.00
1.00
1.02
1.04
1.00
f1 (ppm)


13C NMR (101 MHz, Chloroform-d)
164.17
161.73
144.68
144.61
140.73
129.93
129.85
129.06
128.35
127.61
127.45
124.80
124.25
124.22
121.99
119.18
115.52
115.31
113.78
113.57
89.03
88.69
88.35
88.01
81.78
77.48 CDCl3
77.16 CDCl3
76.84 CDCl3
55.29
55.27
50.69
F3C
O
Ph
HN
51
F
f1 (ppm)

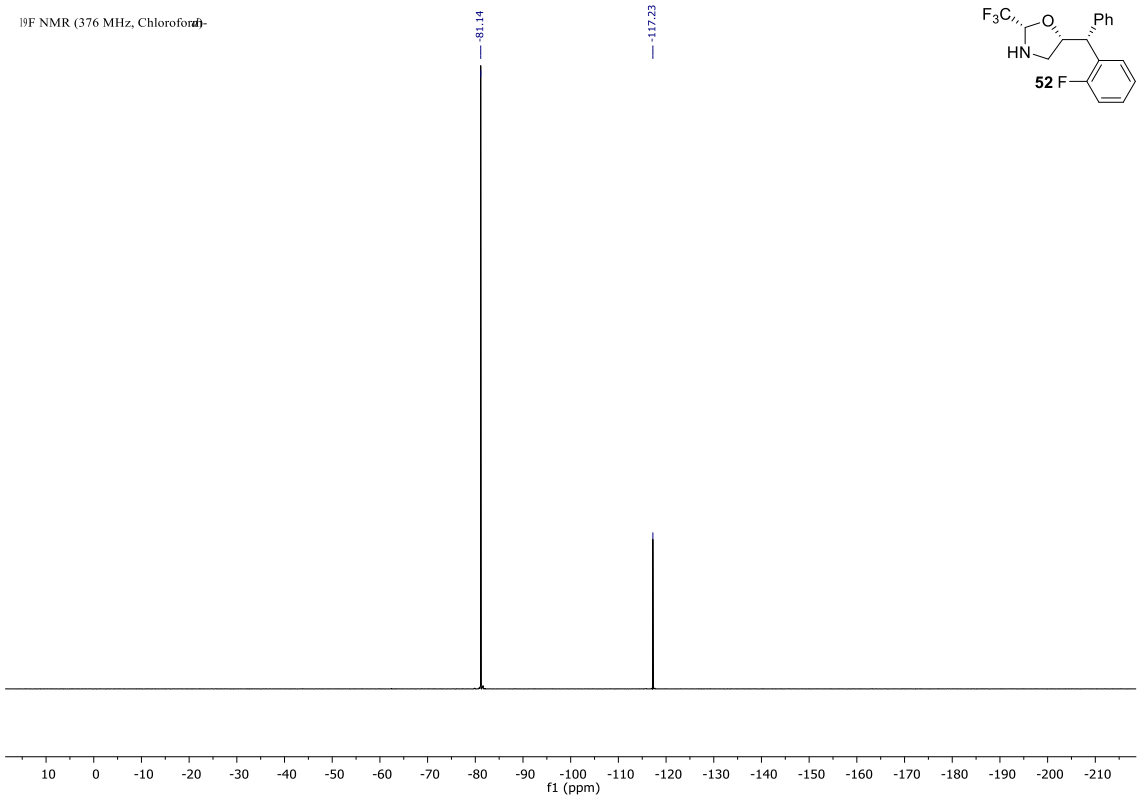

19F NMR (376 MHz, Chloroform-d)
-81.11
-113.22
F3C
O
Ph
HN
51
F
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

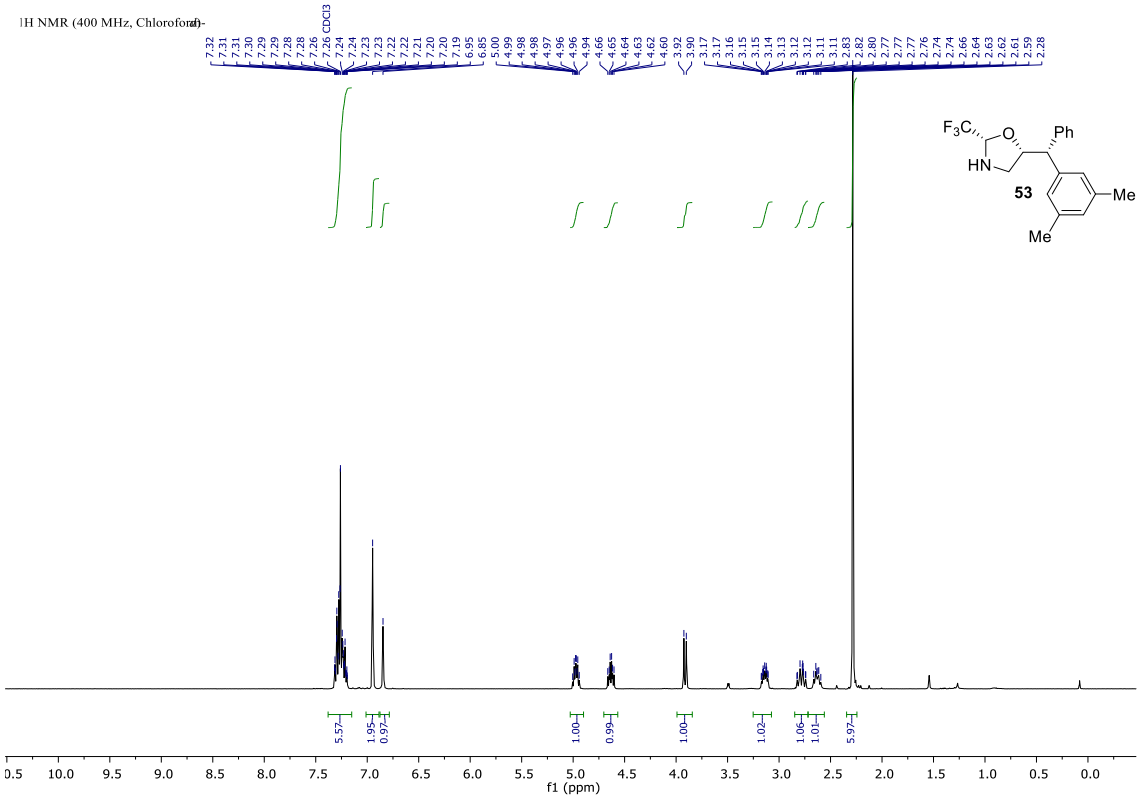

1H NMR (400 MHz, Chloroform-d)
7.48 7.47 7.46 7.45 7.44 7.43 7.30 CDCl3 7.29 7.26 7.26 7.24 7.23 7.23 7.23 7.22 7.22 7.21 7.21 7.20 7.20 7.19 7.19 7.18 7.18 7.15 7.14 7.13 7.12 7.11 7.10 7.03 7.03 7.01 7.01 7.00 7.00 6.98 4.97 4.96 4.74 4.73 4.72 4.70 4.70 4.68 4.35 4.33 3.20 3.17 2.87 2.84 2.66
F3C
O
Ph
HN
52 F
1.04 6.48 1.03 1.00 1.00 1.01 1.01 1.01 1.04 0.94
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

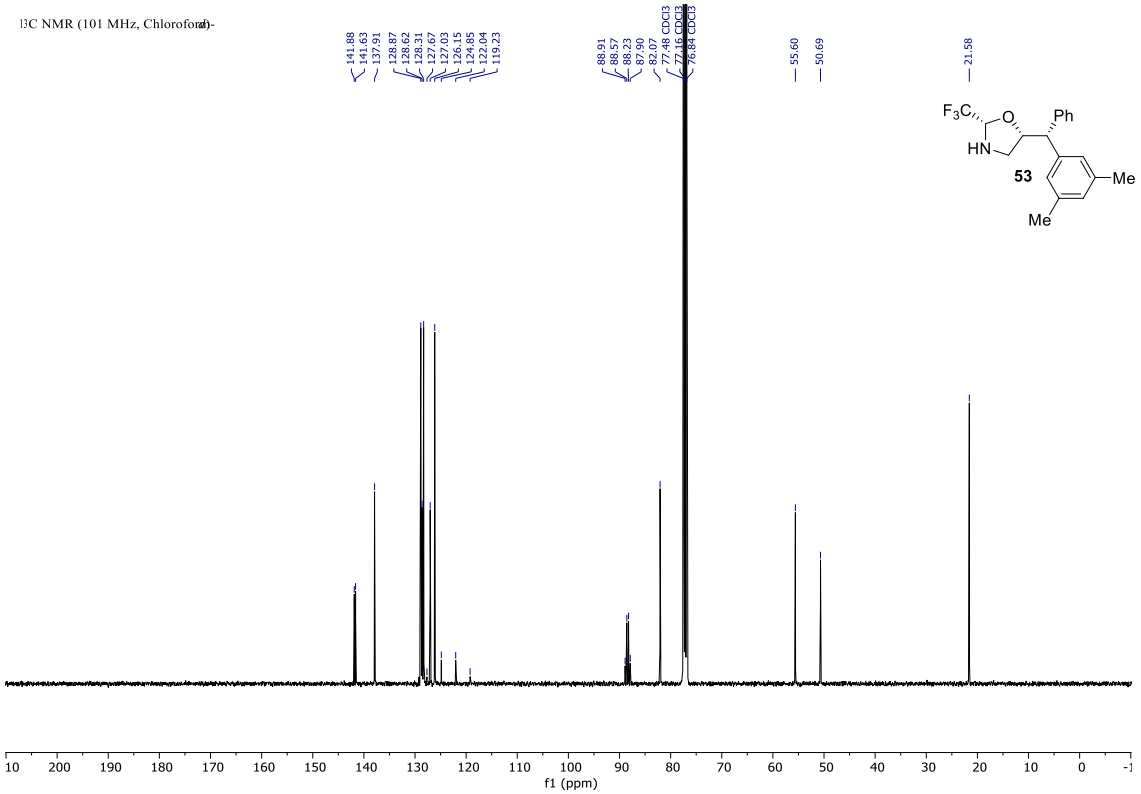
^{13}C NMR (101 MHz, Chloroform-*d*)

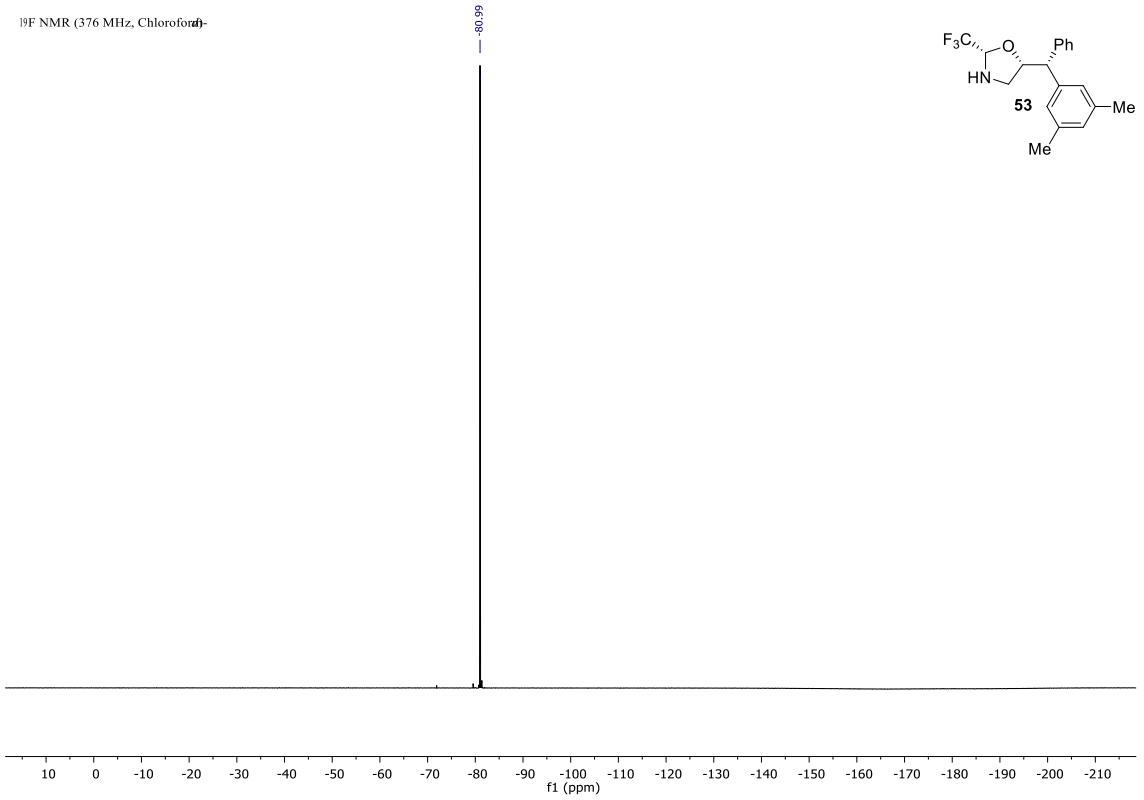


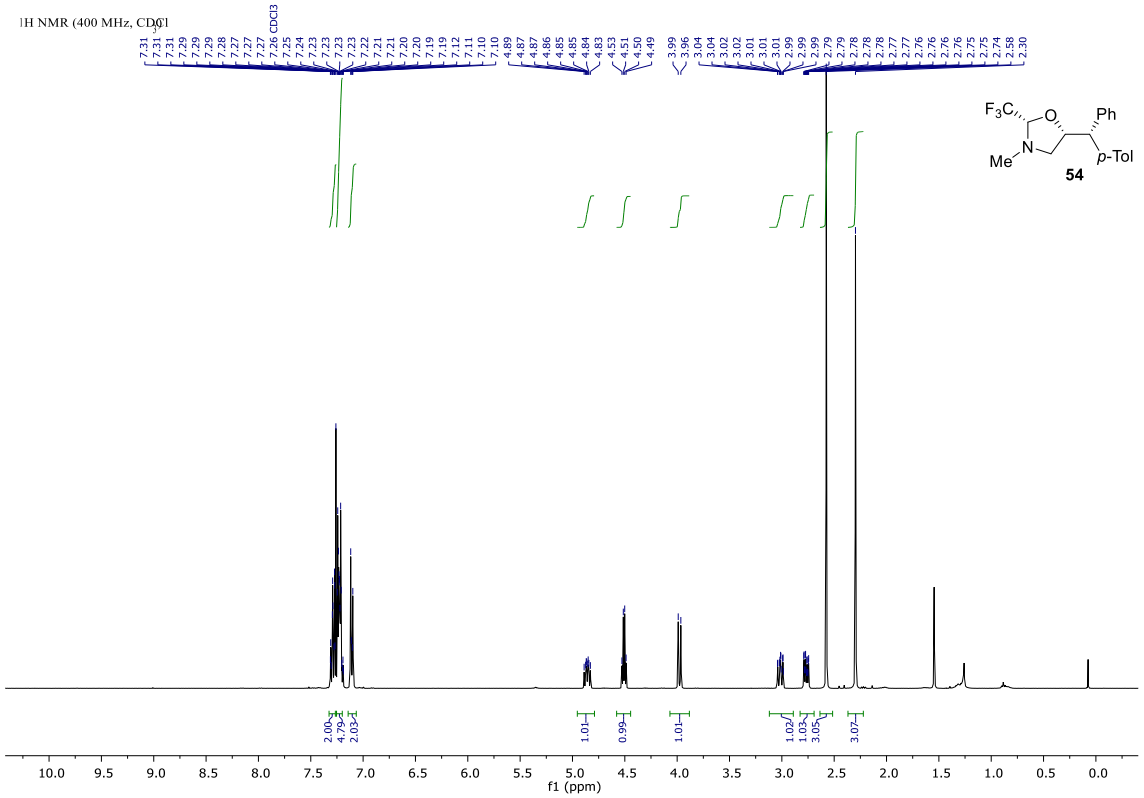
^{19}F NMR (376 MHz, Chloroform-*d*)



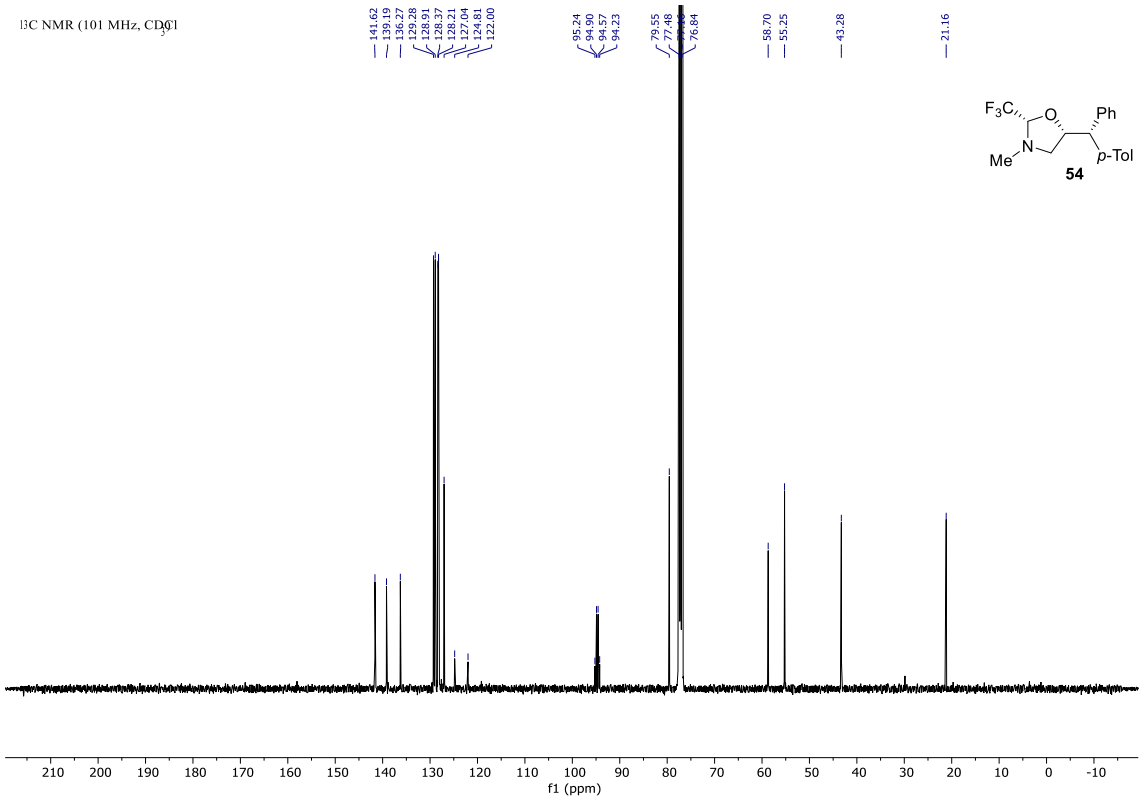

1H NMR (400 MHz, Chloroform-d)
7.32 7.31 7.31 7.30 7.29 7.29 7.28 7.28 7.26 7.26 CDCl3 7.24 7.24 7.23 7.23 7.22 7.22 7.21 7.20 7.20 7.19 6.95 6.85 5.00 4.99 4.98 4.98 4.97 4.96 4.96 4.94 4.66 4.65 4.64 4.63 4.62 4.60 3.92 3.90 3.17 3.17 3.16 3.15 3.15 3.14 3.13 3.12 3.12 3.11 3.11 2.83 2.82 2.80 2.77 2.77 2.77 2.76 2.74 2.74 2.66 2.64 2.63 2.62 2.61 2.59 2.28
5.57 1.95 0.97 1.00 0.99 1.00 1.02 1.06 1.01 5.97
f1 (ppm)
F3C
O
Ph
HN
53
Me
Me


13C NMR (101 MHz, Chloroform-d)
141.88 141.63 137.91 128.87 128.62 128.31 127.67 127.03 126.15 124.85 122.04 119.23 88.91 88.57 88.23 87.90 82.07 77.48 CDCl3 77.16 CDCl3 76.84 CDCl3 55.60 50.69 21.58
f1 (ppm)
F3C
O
Ph
HN
53
Me
Me

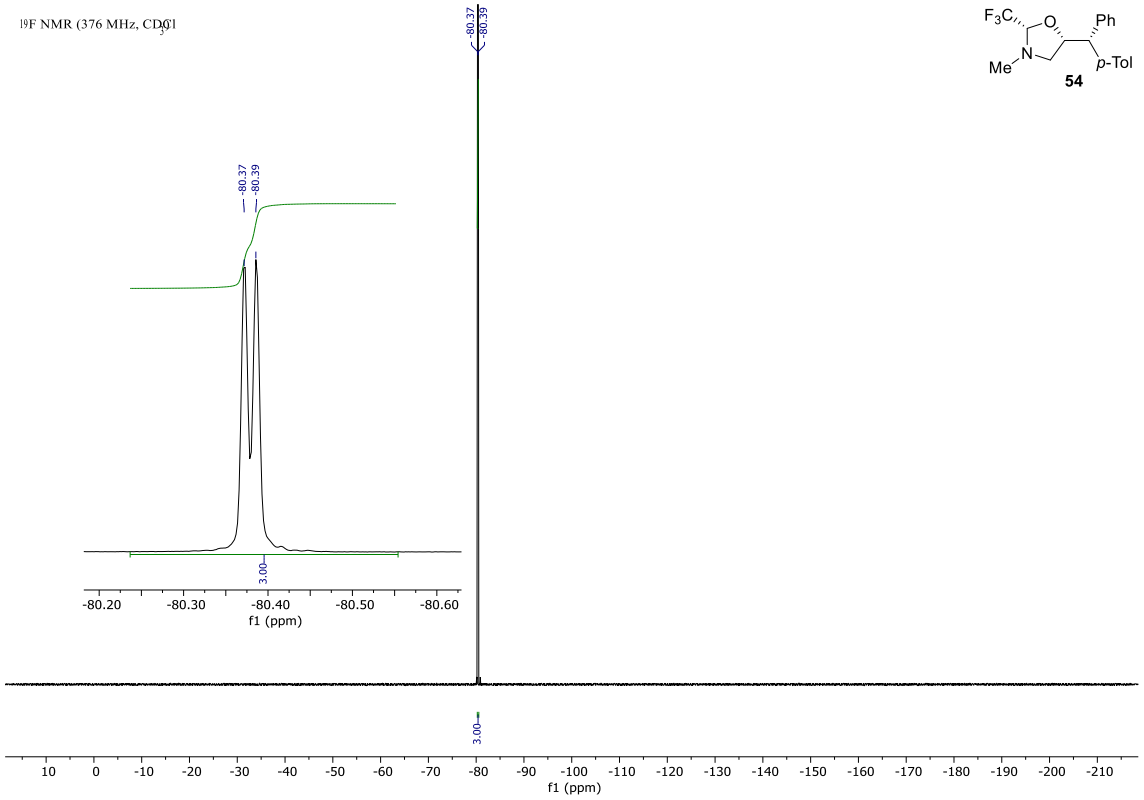

19F NMR (376 MHz, Chloroform-d)
-80.99
F3C
O
Ph
HN
53
Me
Me
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)

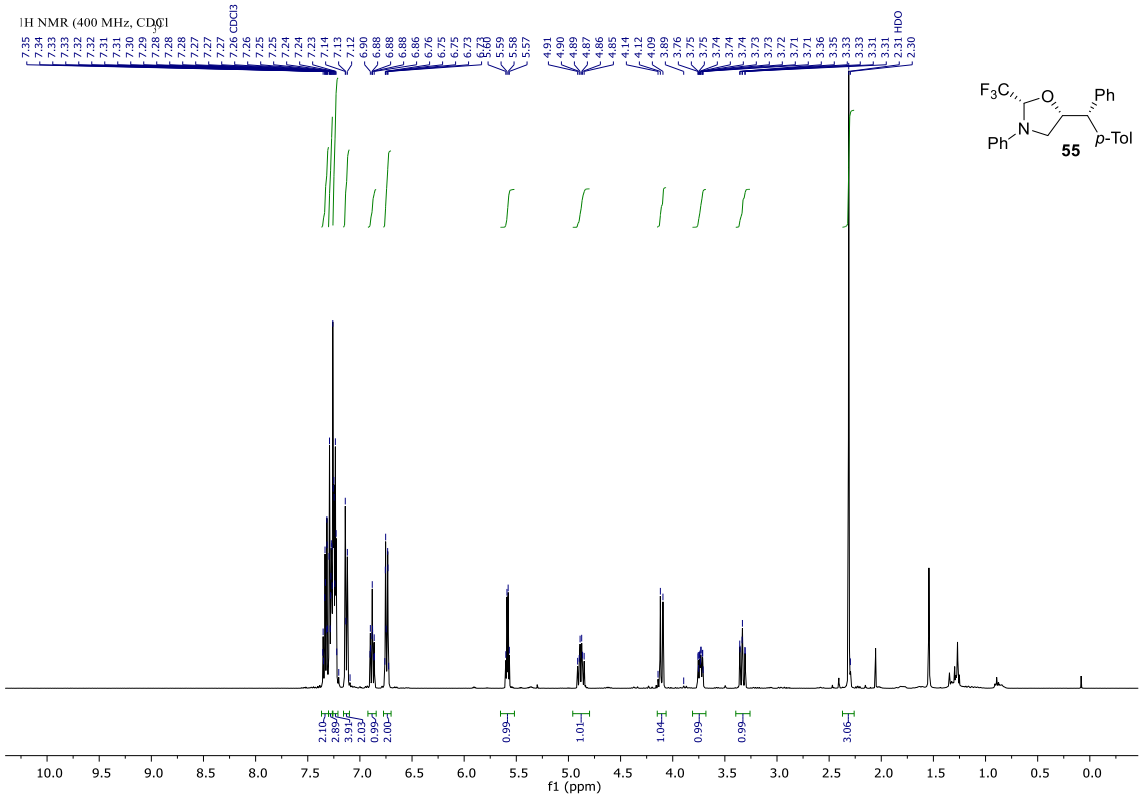

1H NMR (400 MHz, CDCl3)
CDCl3
F3C
O
Ph
N
Me
p-Tol
54
2.00
4.79
2.03
1.01
0.99
1.01
1.02
1.05
3.05
3.07
10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

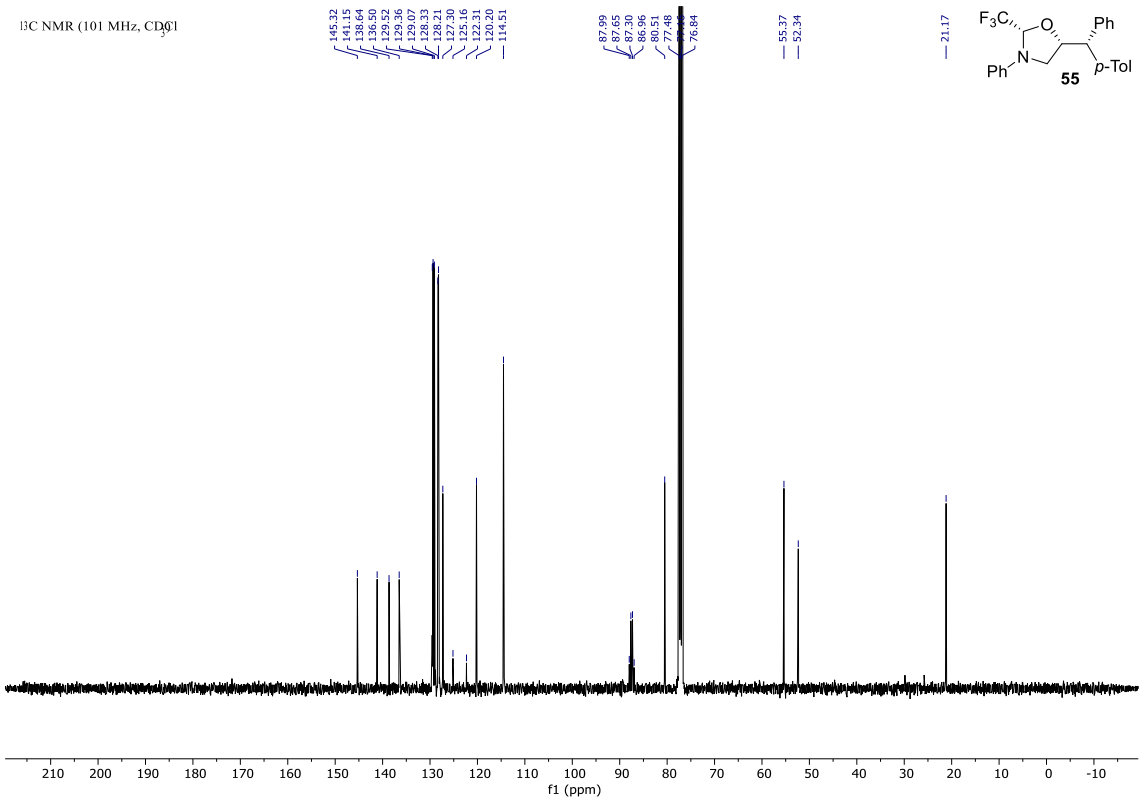
^{13}C NMR (101 MHz, $CDCl_3$)

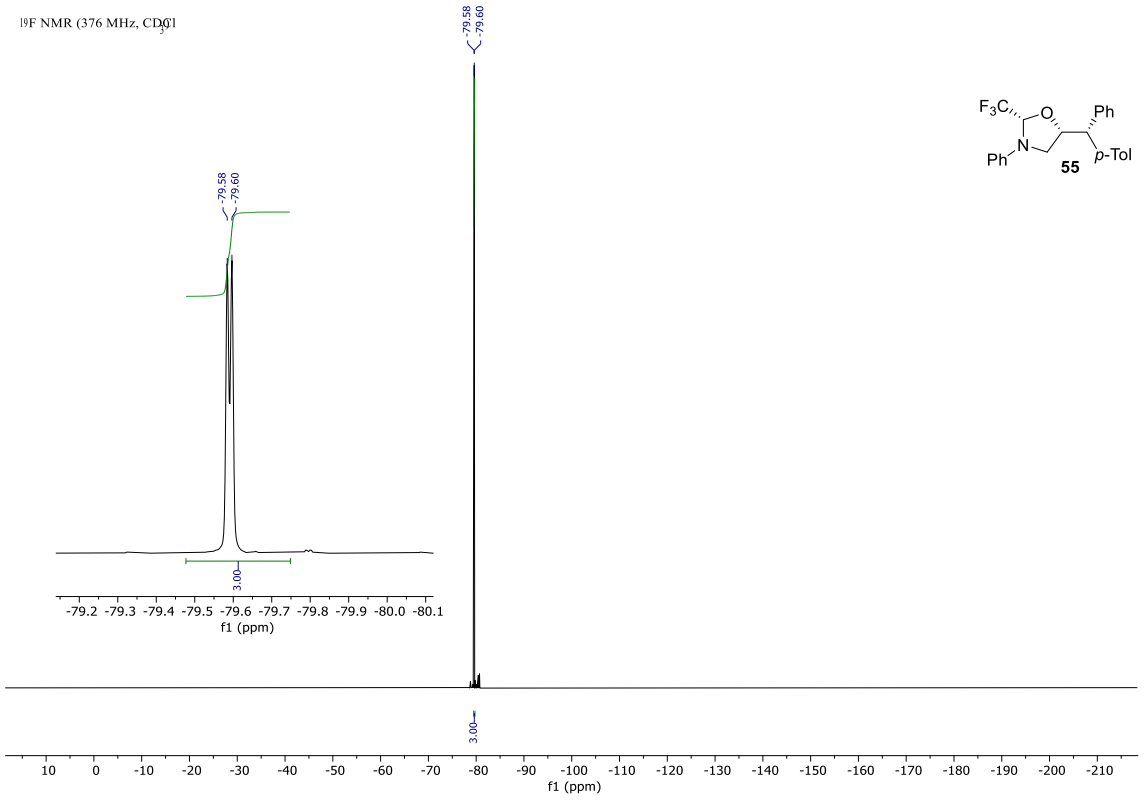


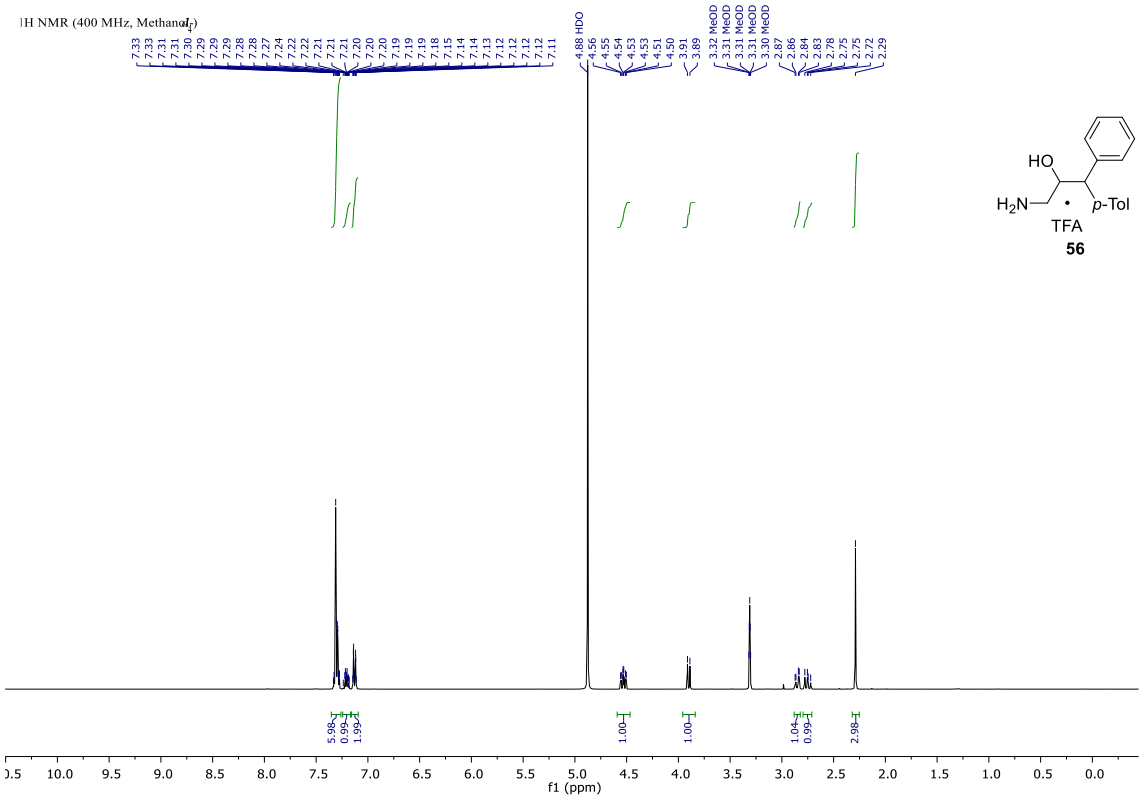
^{19}F NMR (376 MHz, $CDCl_3$)

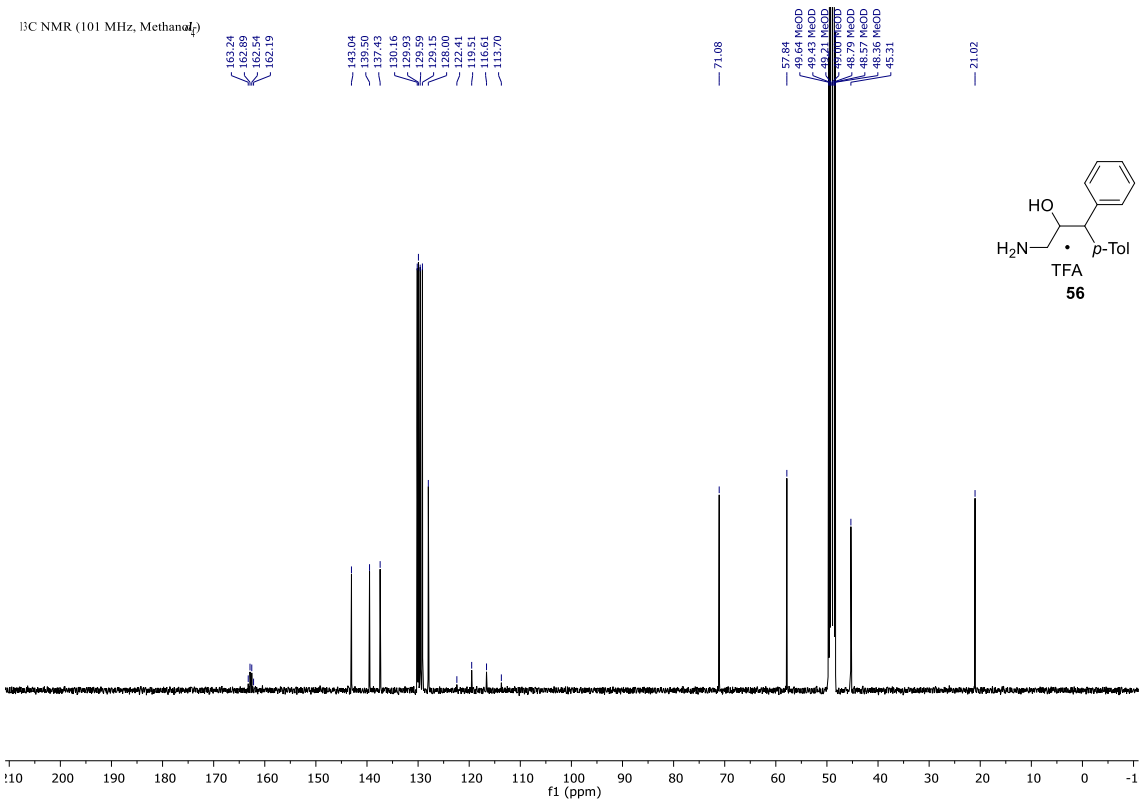



1H NMR (400 MHz, CDCl3)
F3C
O
Ph
N
Ph
p-Tol
55
f1 (ppm)

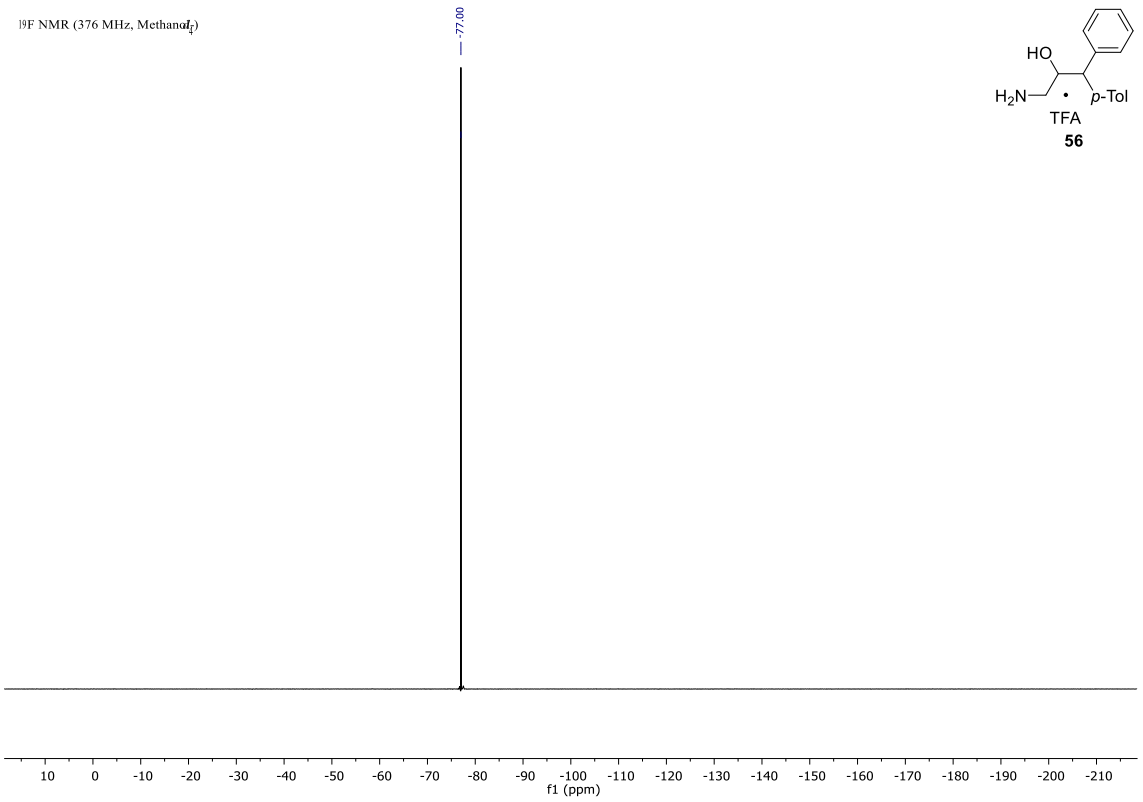

13C NMR (101 MHz, CDCl3)
F3C
O
Ph
N
Ph
p-Tol
55
f1 (ppm)


19F NMR (376 MHz, CDCl3)
-79.58
-79.60
F3C
O
Ph
N
Ph
p-Tol
55
3.00
-79.2 -79.3 -79.4 -79.5 -79.6 -79.7 -79.8 -79.9 -80.0 -80.1
f1 (ppm)
3.00
10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140 -150 -160 -170 -180 -190 -200 -210
f1 (ppm)


1H NMR (400 MHz, Methanol-d4)
HO
H2N
p-Tol
TFA
56
f1 (ppm)


13C NMR (101 MHz, Methanol-d4)
HO
H2N
p-Tol
TFA
56
f1 (ppm)

^{19}F NMR (376 MHz, Methanol-d_4)



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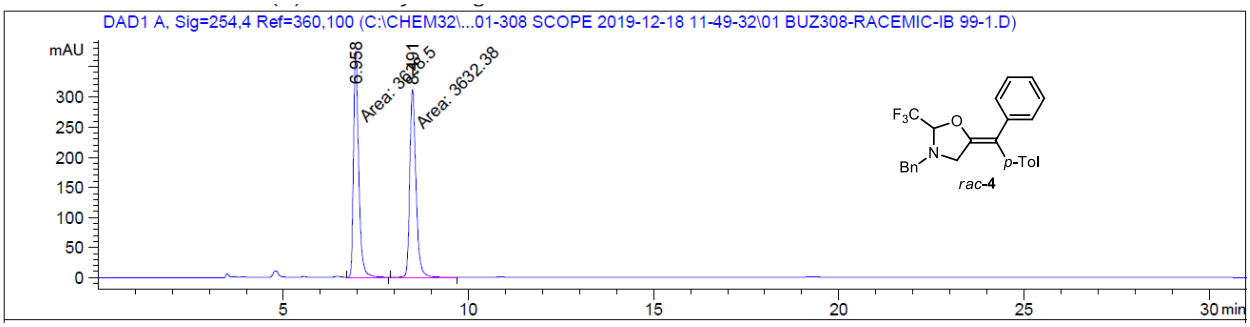
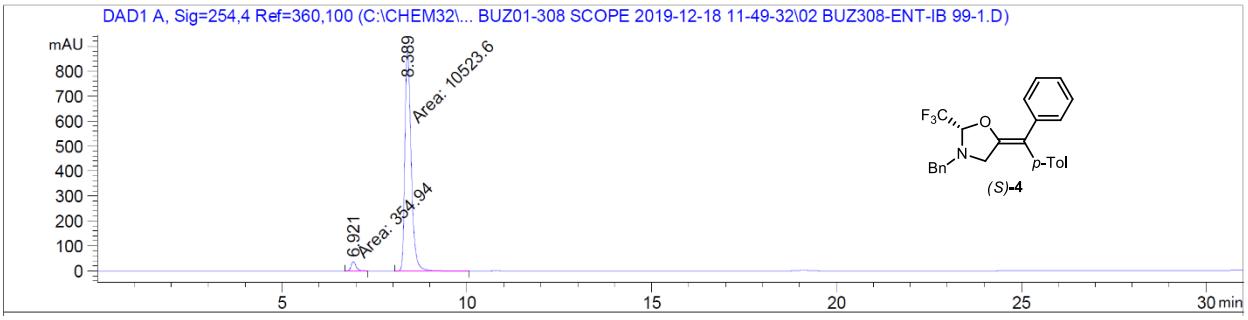
I. HPLC Traces

I.1. Carboetherification Products

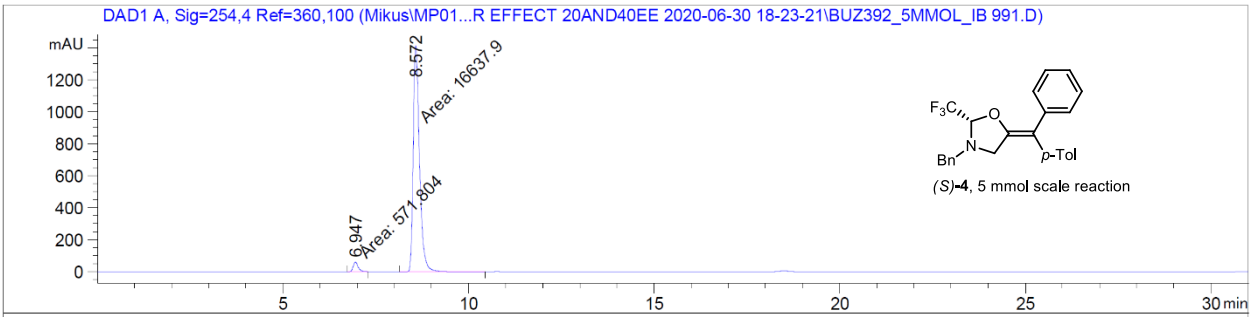
Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm



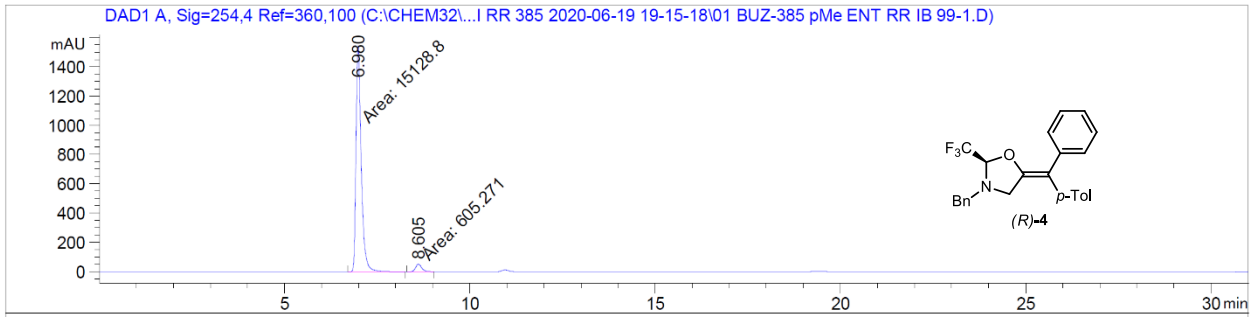
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.958	MM	0.1616	3628.49634	374.27448	49.9733
2	8.491	MM	0.1942	3632.37891	311.69940	50.0267



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.921	MM	0.1587	354.93954	37.28573	3.2628
2	8.389	MM	0.1949	1.05236e4	900.04584	96.7372

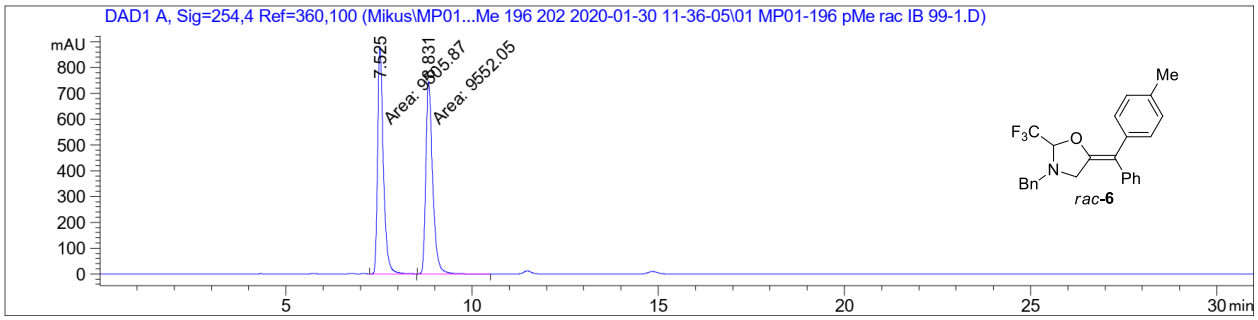


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.947	MM	0.1581	571.80402	60.28956	3.3226
2	8.572	MM	0.1961	1.66379e4	1414.37622	96.6774

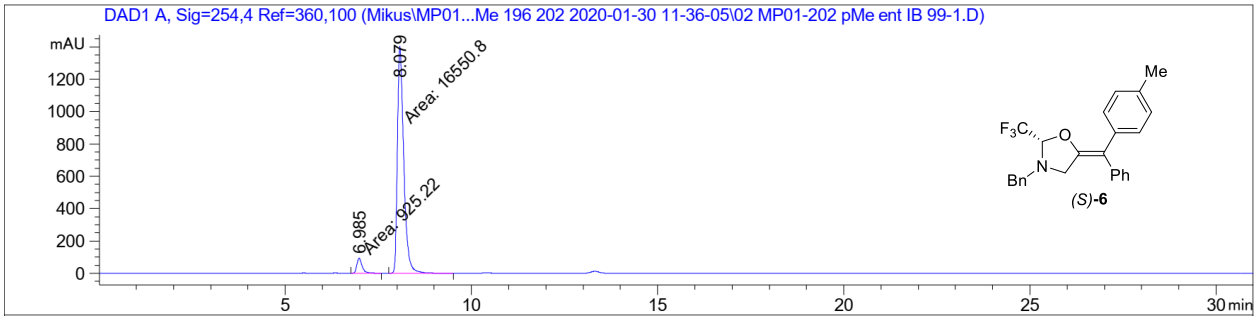


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.980	MM	0.1634	1.51288e4	1543.46191	96.1531
2	8.605	MM	0.1957	605.27081	51.55163	3.8469

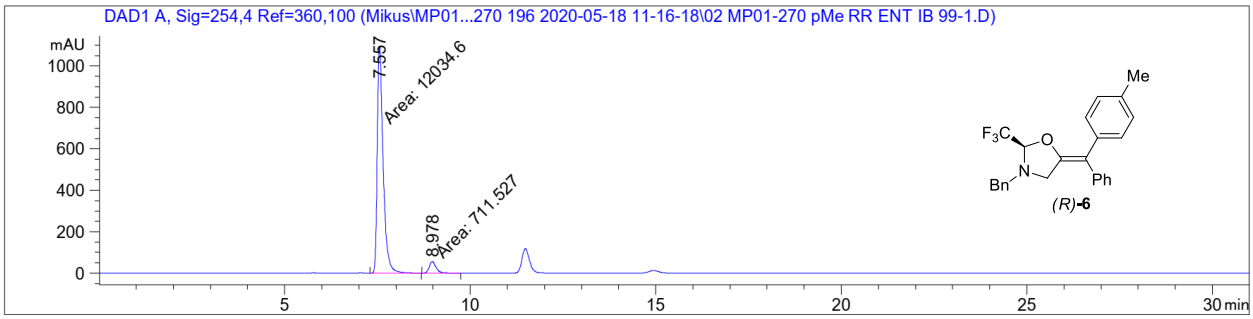
Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.525	MM	0.1801	9505.87305	879.81122	49.8789
2	8.831	MM	0.2139	9552.04980	744.29962	50.1211

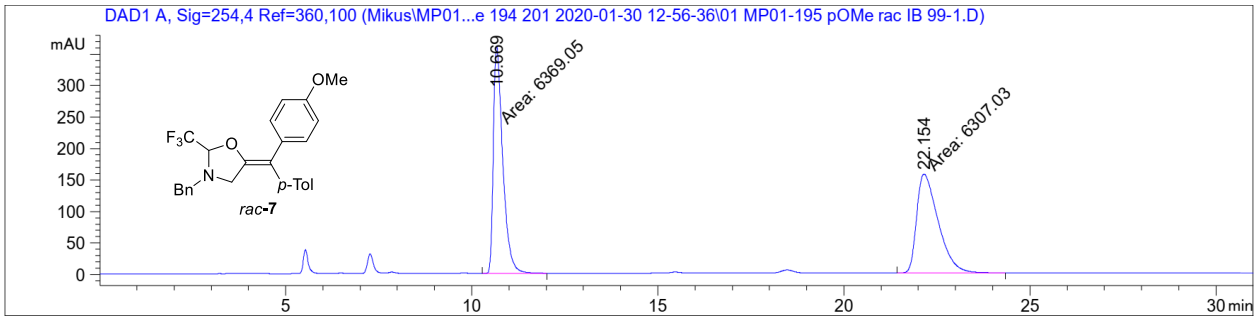


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.985	MM	0.1651	925.22040	93.38676	5.2942
2	8.079	MM	0.1962	1.65508e4	1406.06726	94.7058

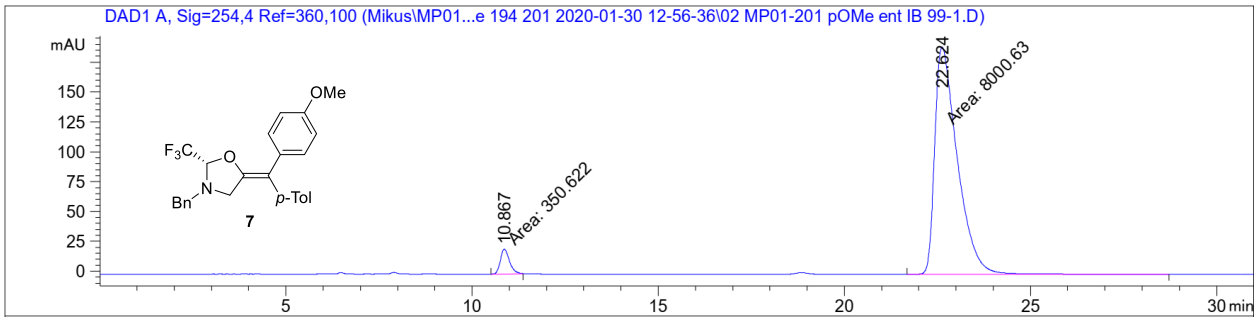


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.557	MM	0.1836	1.20346e4	1092.29956	94.4177
2	8.978	MM	0.2149	711.52716	55.18419	5.5823

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

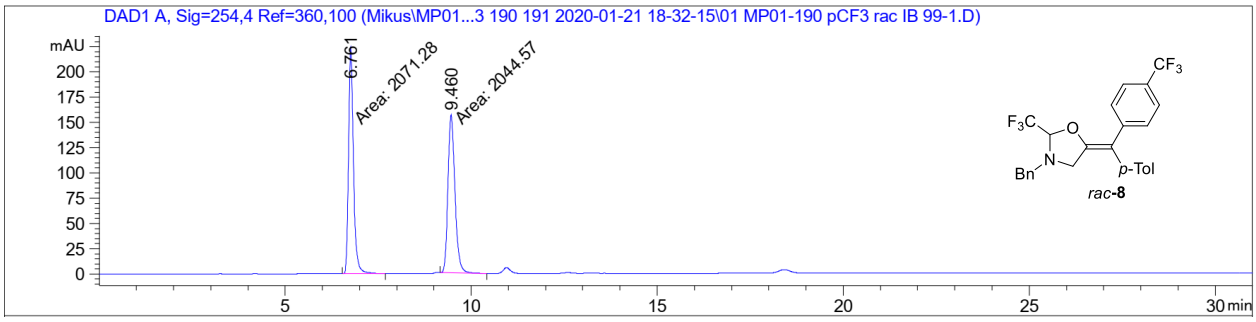


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.669	MM	0.2940	6369.04639	361.04782	50.2446
2	22.154	MM	0.6692	6307.02979	157.08136	49.7554

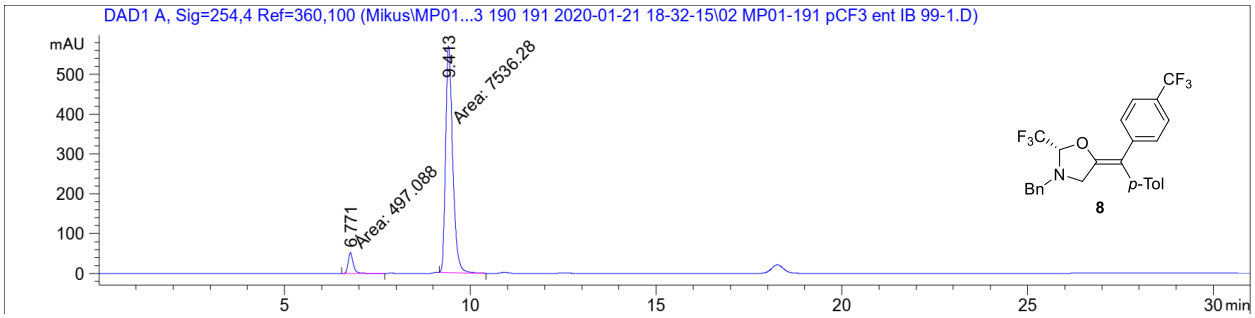


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.867	MM	0.2815	350.62244	20.76242	4.1984
2	22.624	MM	0.7010	8000.62646	190.21245	95.8016

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

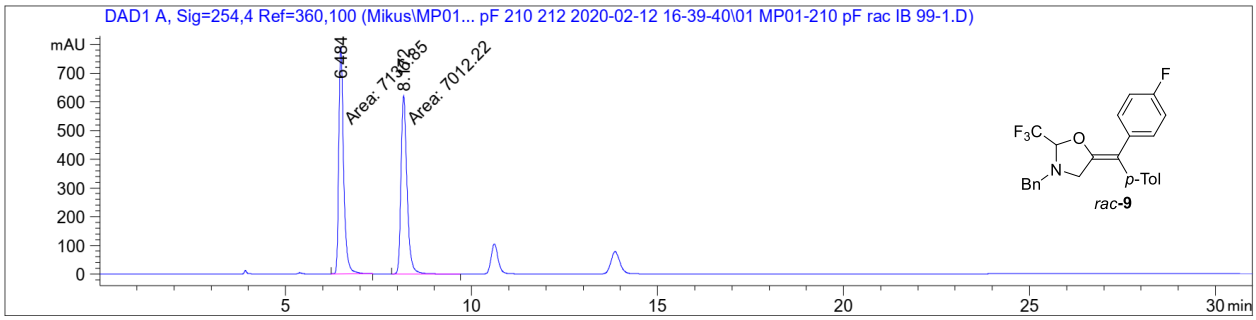


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.761	MM	0.1538	2071.27759	224.46736	50.3244
2	9.460	MM	0.2180	2044.57129	156.34639	49.6756

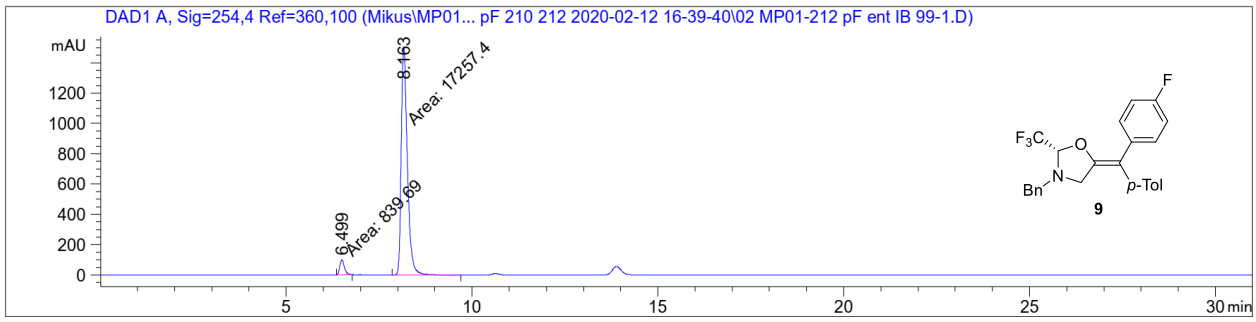


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.771	MM	0.1575	497.08813	52.59796	6.1878
2	9.413	MM	0.2209	7536.27637	568.60547	93.8122

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

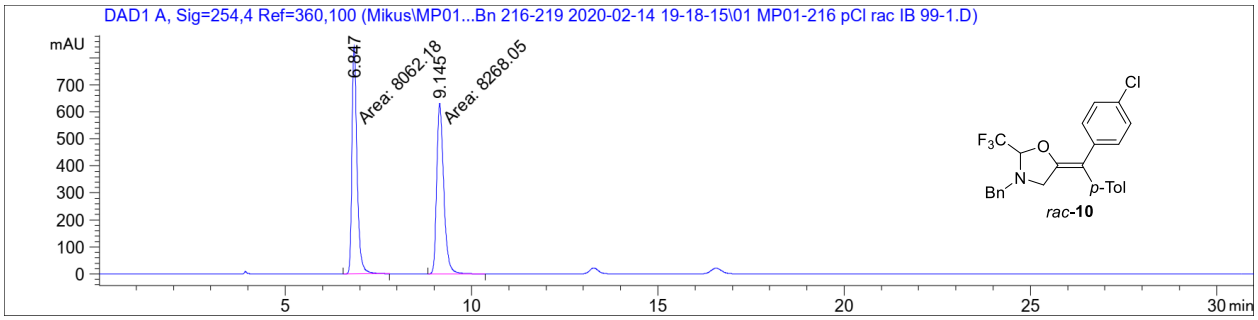


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.484	MM	0.1503	7136.85303	791.44922	50.4404
2	8.172	MM	0.1881	7012.22314	621.23798	49.5596

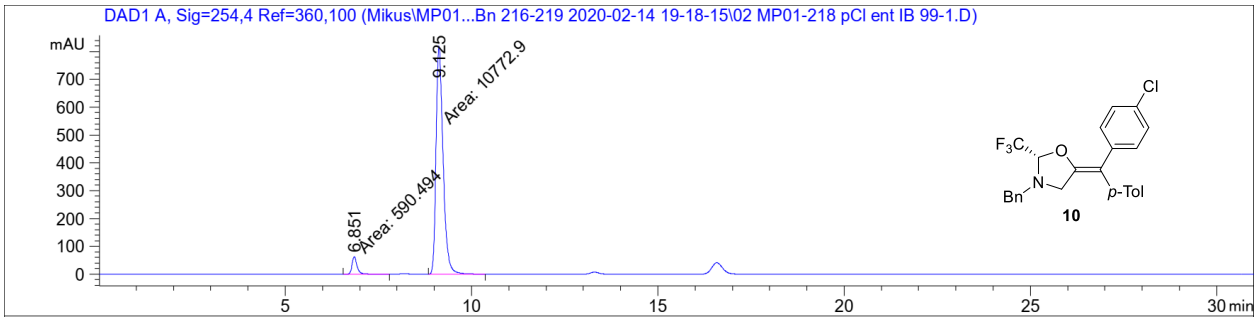


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.499	MM	0.1429	839.69019	97.94019	4.6399
2	8.163	MM	0.1918	1.72574e4	1499.87024	95.3601

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

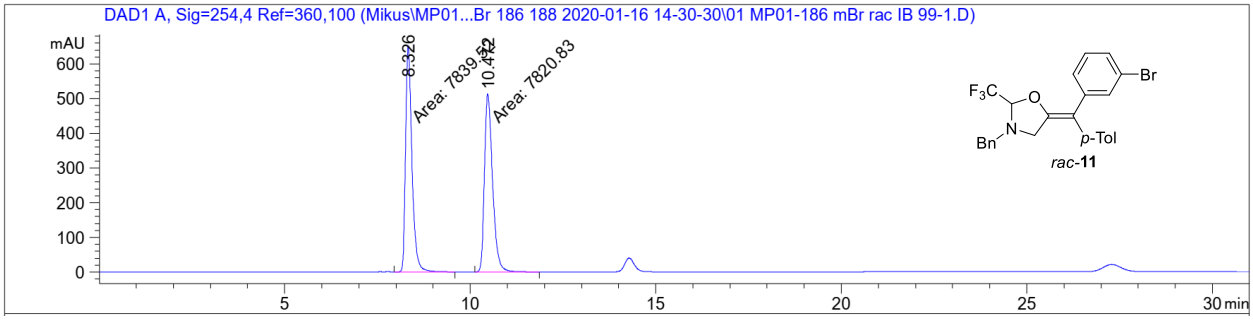


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.847	MM	0.1595	8062.17871	842.56726	49.3697
2	9.145	MM	0.2182	8268.05176	631.66949	50.6303

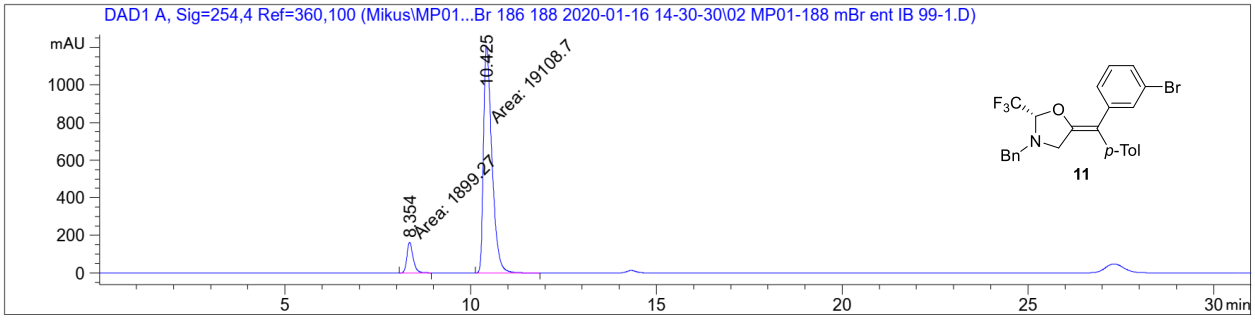


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.851	MM	0.1575	590.49353	62.46822	5.1965
2	9.125	MM	0.2194	1.07729e4	818.30353	94.8035

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

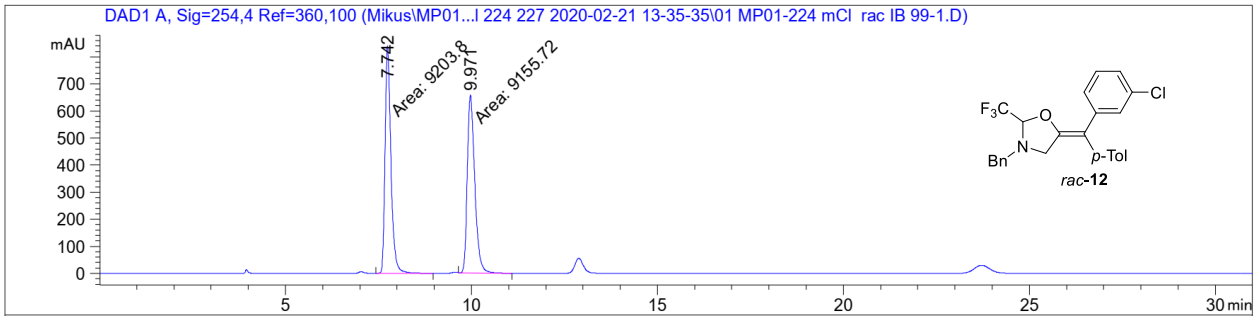


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.326	MM	0.2000	7839.51660	653.35144	50.0597
2	10.472	MM	0.2542	7820.83252	512.85229	49.9403

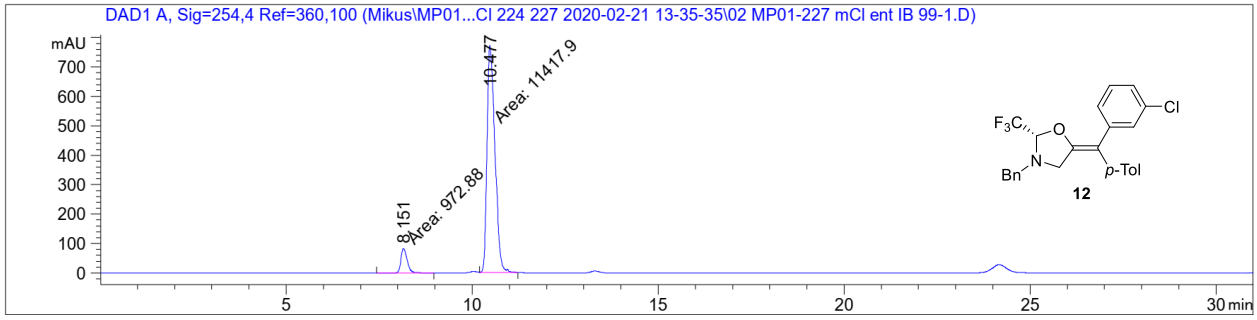


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.354	MM	0.1947	1899.26880	162.59052	9.0407
2	10.425	MM	0.2634	1.91087e4	1209.06799	90.9593

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

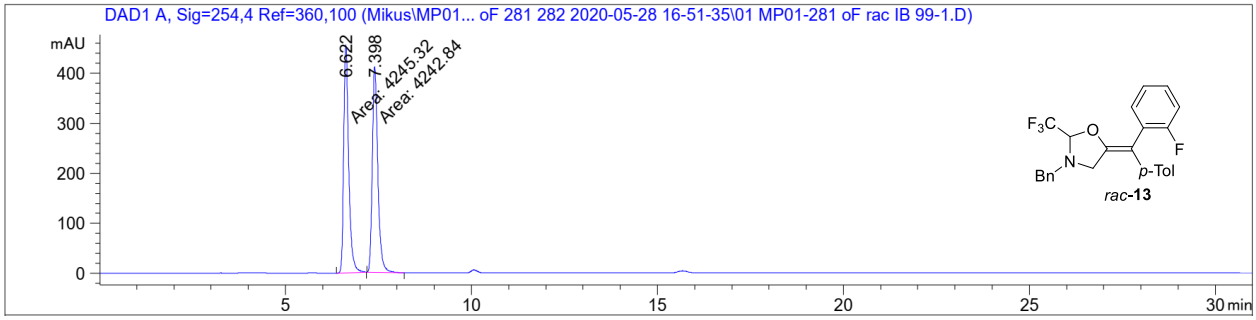


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.742	MM	0.1828	9203.80078	839.20245	50.1310
2	9.971	MM	0.2326	9155.71582	656.00647	49.8690

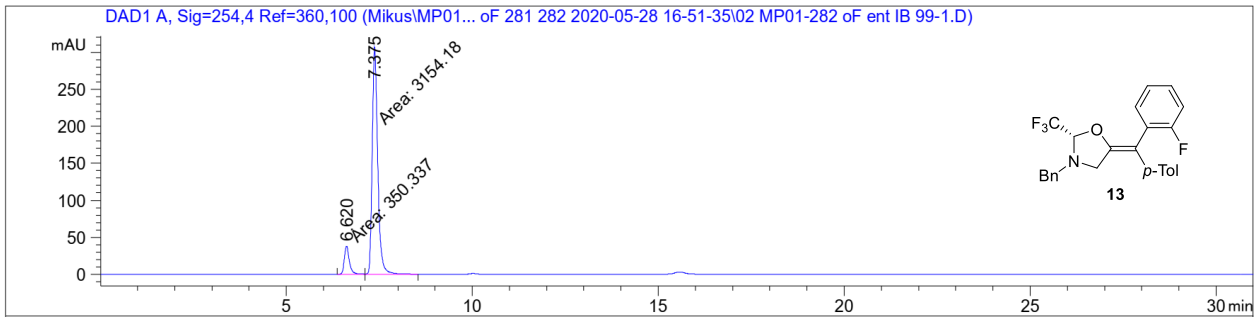


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.151	MM	0.1951	972.87964	83.09148	7.8516
2	10.477	MM	0.2469	1.14179e4	770.87140	92.1484

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

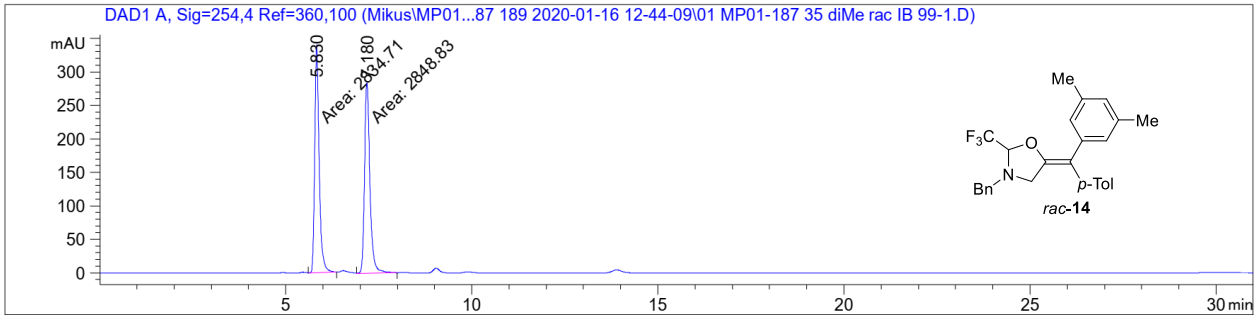


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.622	MM	0.1556	4245.32275	454.70941	50.0146
2	7.398	MM	0.1721	4242.84326	411.00439	49.9854

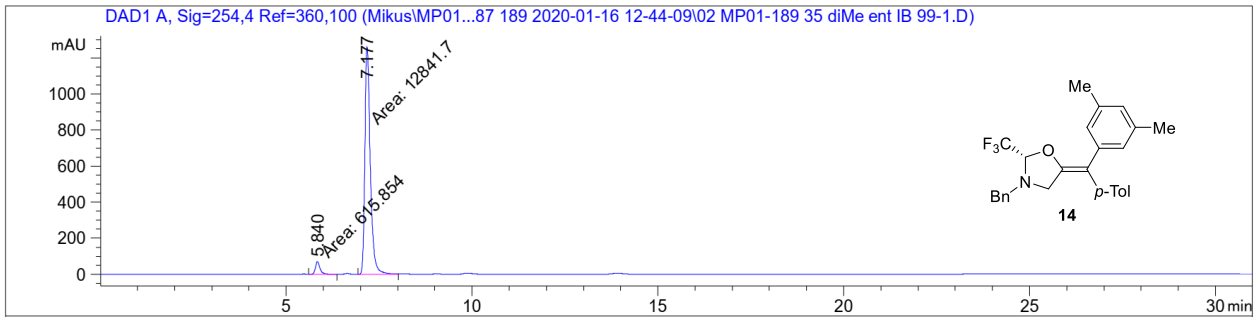


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.620	MM	0.1539	350.33701	37.93580	9.9967
2	7.375	MM	0.1714	3154.18433	306.79001	90.0033

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

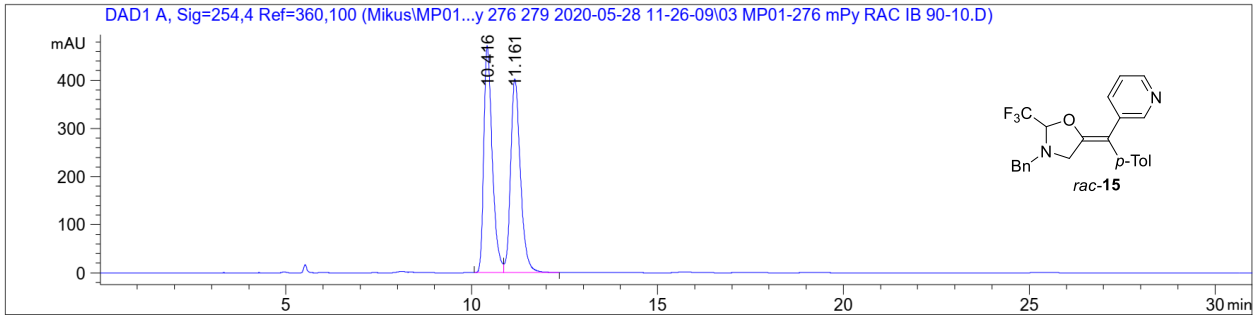


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.830	MM	0.1392	2834.70654	339.38593	49.8758
2	7.180	MM	0.1670	2848.82788	284.33942	50.1242

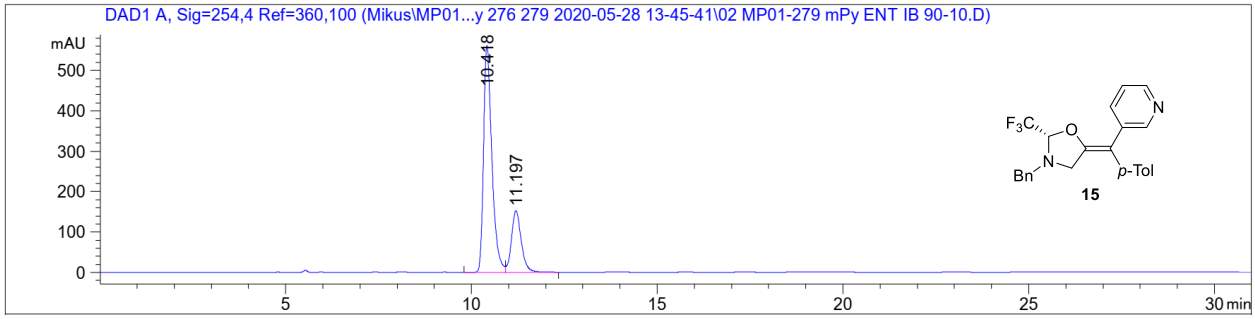


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.840	MM	0.1439	615.85376	71.33194	4.5763
2	7.177	MM	0.1698	1.28417e4	1260.57019	95.4237

Chiral HPLC Daicel Chiralpak IB N-5 column: 90:10 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

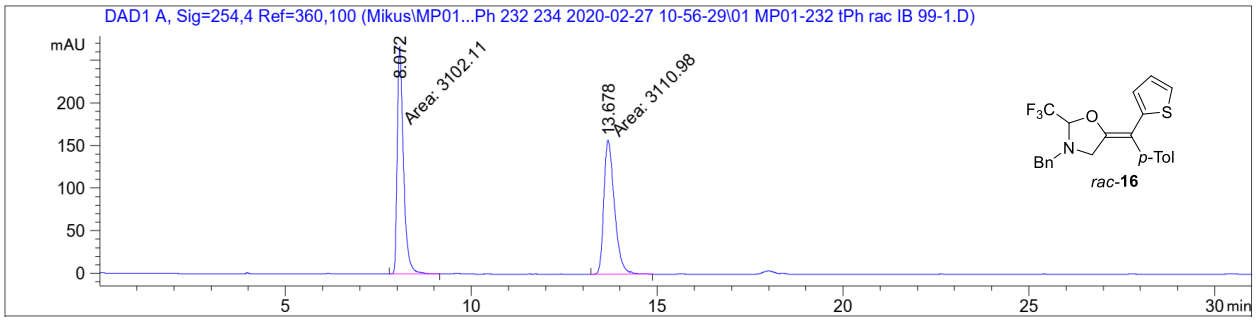


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.416	BV	0.2408	7469.38916	471.64029	50.2664
2	11.161	VB	0.2802	7390.22656	402.44556	49.7336

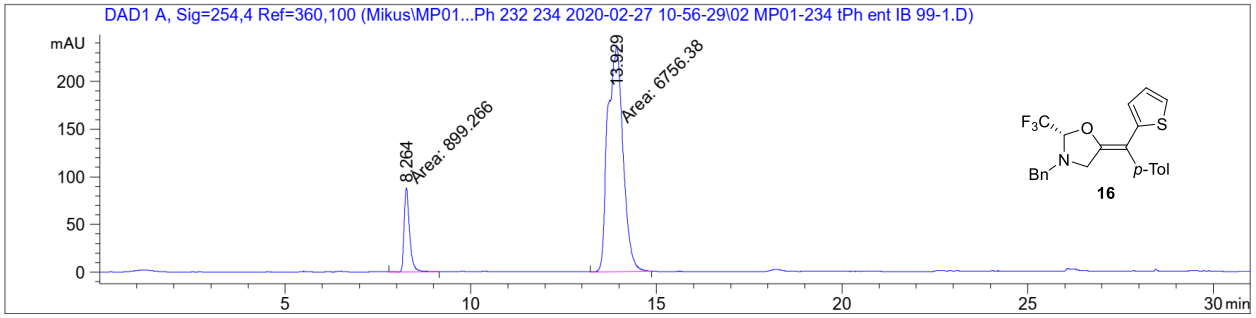


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.418	BV	0.2360	8751.86426	561.00800	75.8087
2	11.197	VB	0.2798	2792.81055	152.41017	24.1913

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

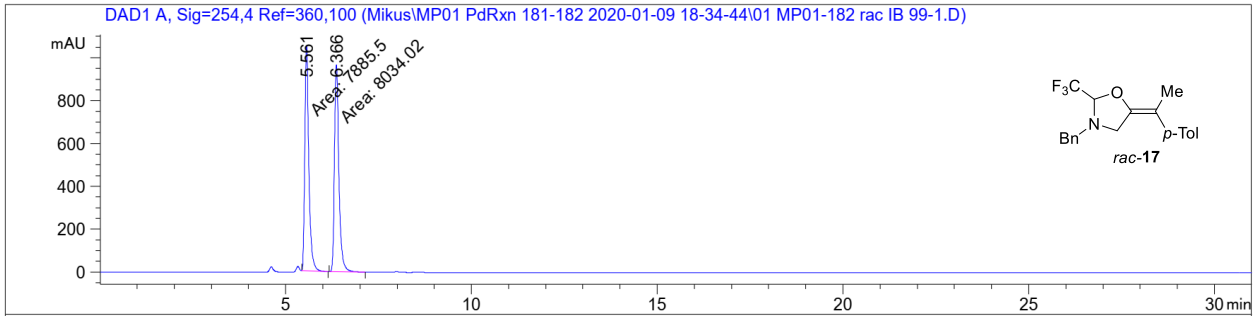


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.072	MM	0.1940	3102.10669	266.51071	49.9286
2	13.678	MM	0.3301	3110.97852	157.06339	50.0714

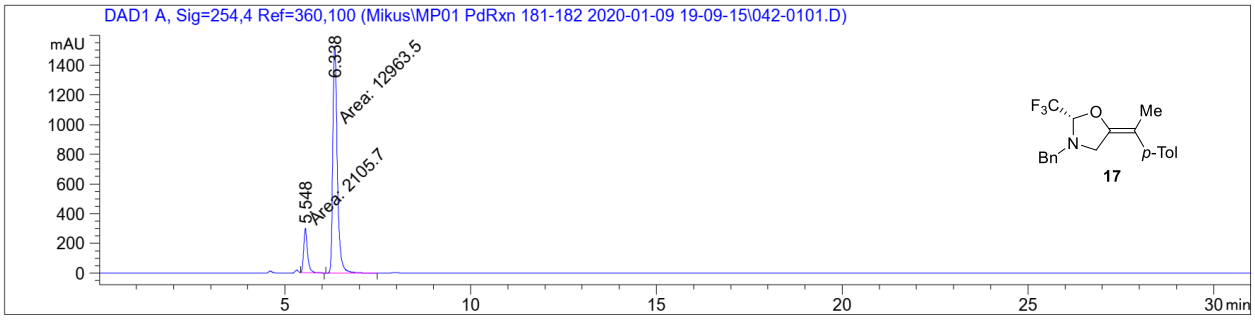


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.264	MM	0.1699	899.26599	88.19818	11.7464
2	13.929	MM	0.4756	6756.37939	236.79008	88.2536

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

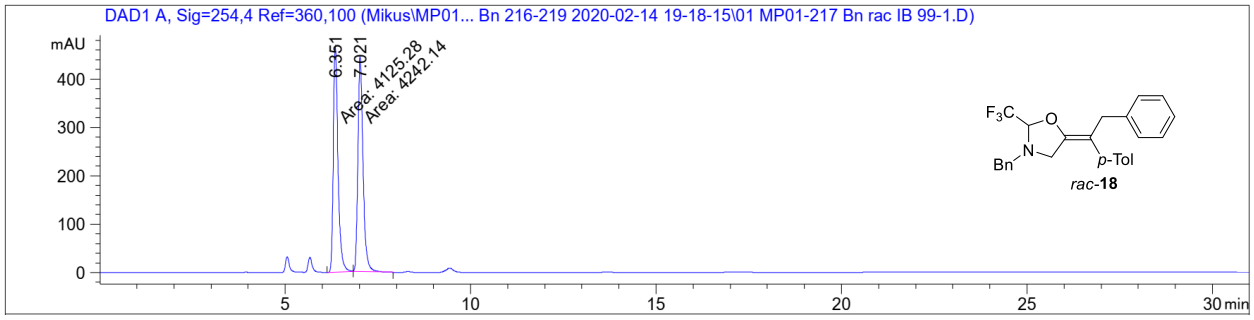


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.561	MM	0.1247	7885.49609	1054.21460	49.5335
2	6.366	MM	0.1383	8034.02002	968.16638	50.4665

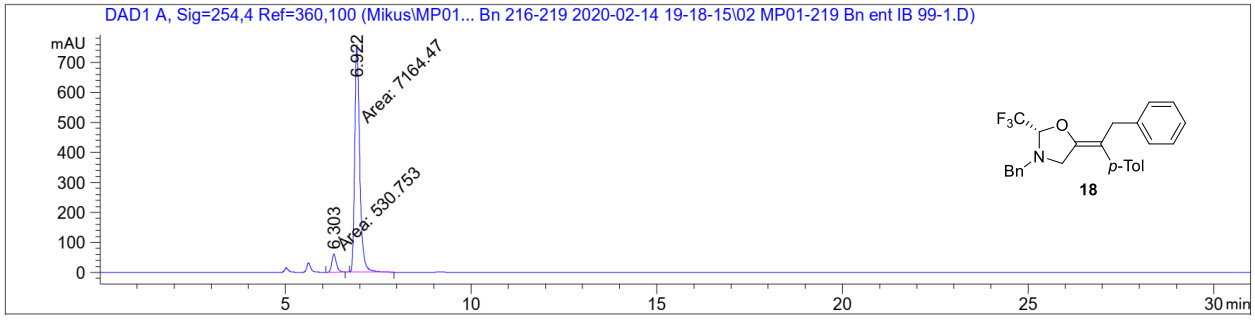


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.548	MM	0.1183	2105.70093	296.70862	13.9735
2	6.338	MM	0.1413	1.29635e4	1529.33142	86.0265

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

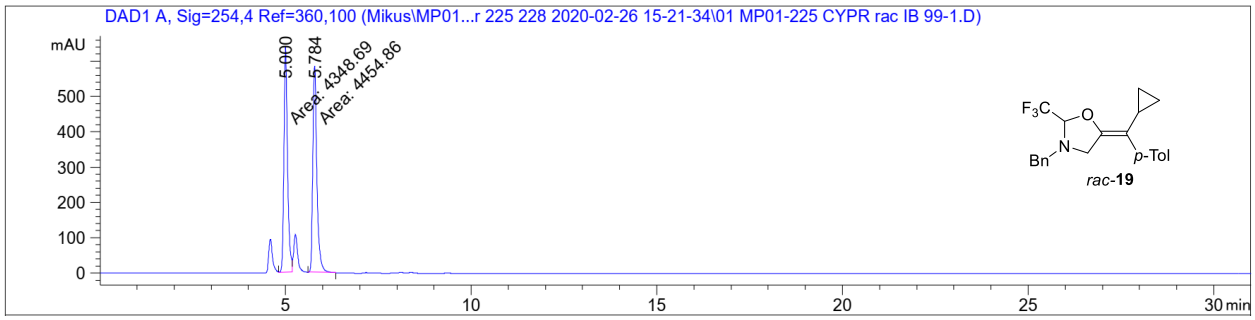


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.351	MM	0.1471	4125.28027	467.41537	49.3017
2	7.021	MM	0.1588	4242.14063	445.31125	50.6983

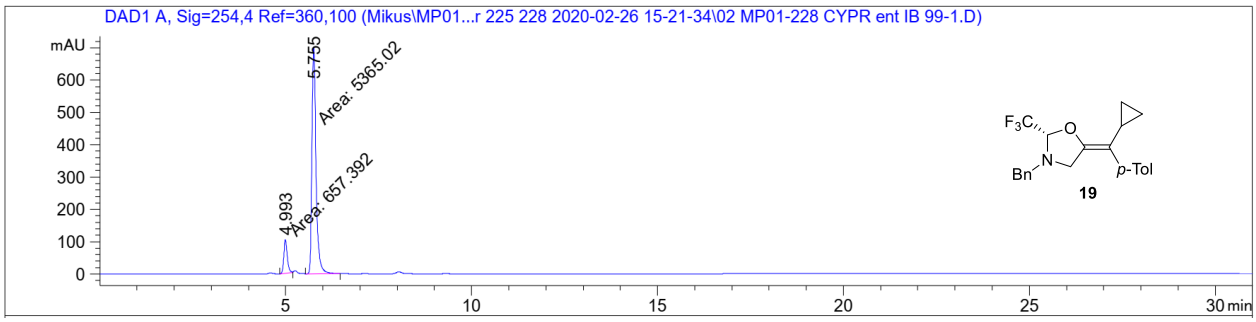


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.303	MM	0.1435	530.75311	61.65509	6.8972
2	6.922	MM	0.1580	7164.47070	755.93610	93.1028

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

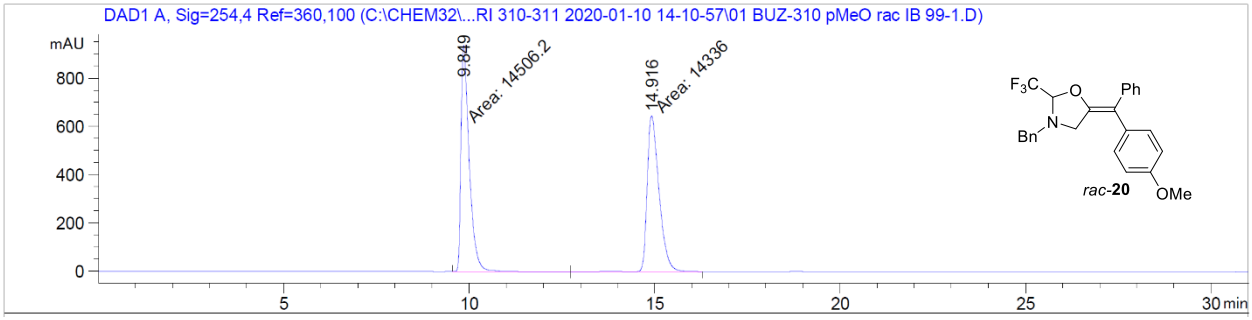


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.000	MM	0.1132	4348.69385	640.41498	49.3970
2	5.784	MM	0.1271	4454.86377	584.20685	50.6030

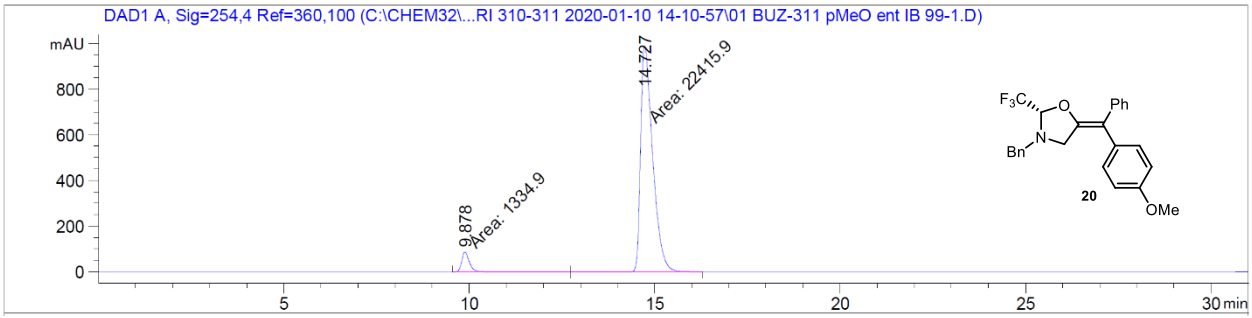


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	4.993	MM	0.1057	657.39233	103.61166	10.9158
2	5.755	MM	0.1275	5365.02002	701.19641	89.0842

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

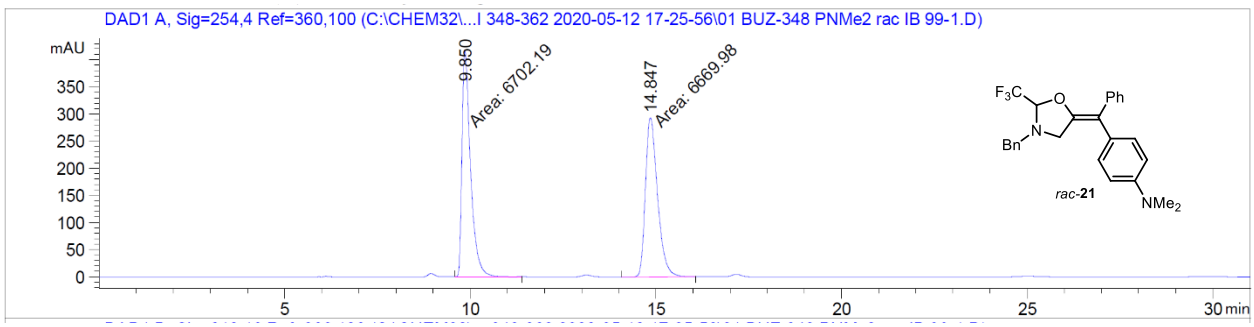


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.849	MF	0.2581	1.45062e4	936.69727	50.2952
2	14.916	FM	0.3703	1.43360e4	645.21008	49.7048

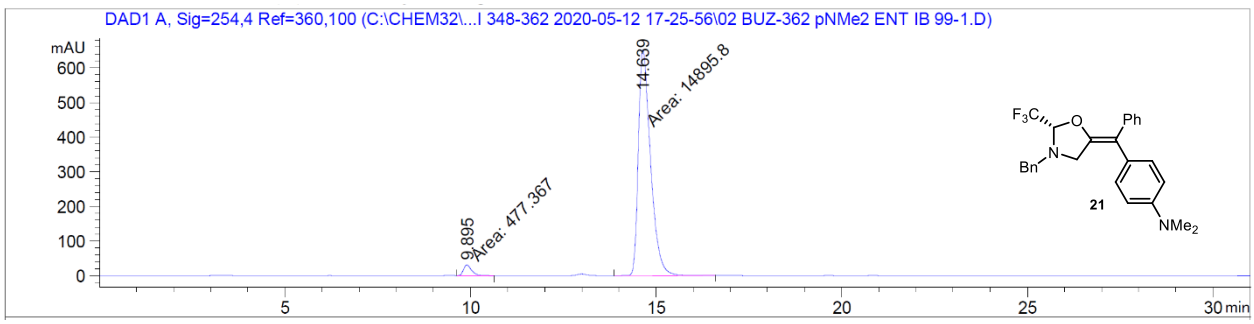


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.878	MF	0.2531	1334.90137	87.88715	5.6204
2	14.727	FM	0.3773	2.24159e4	990.31799	94.3796

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

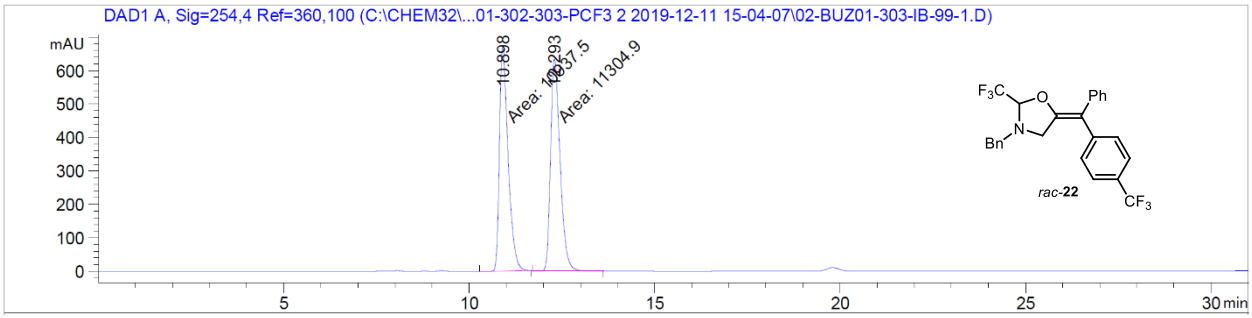


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.850	MM	0.2668	6702.18506	418.64359	50.1204
2	14.847	MM	0.3783	6669.97803	293.84787	49.8796

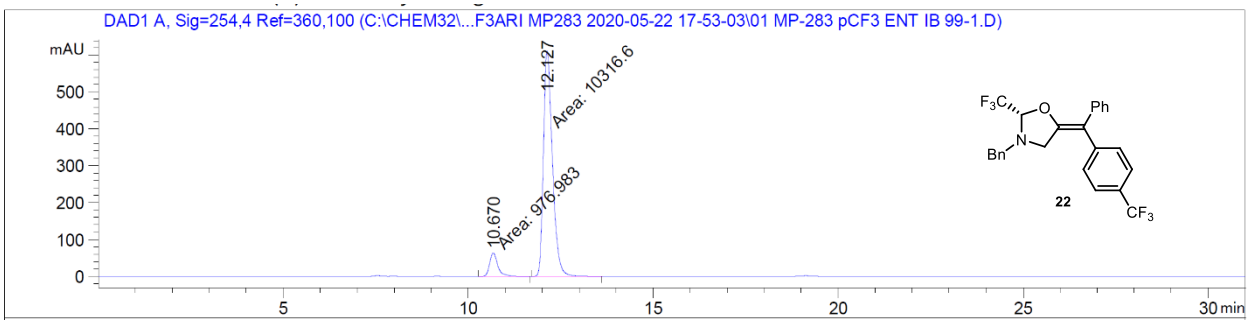


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.895	MM	0.2570	477.36749	30.95416	3.1052
2	14.639	MM	0.3806	1.48958e4	652.33496	96.8948

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

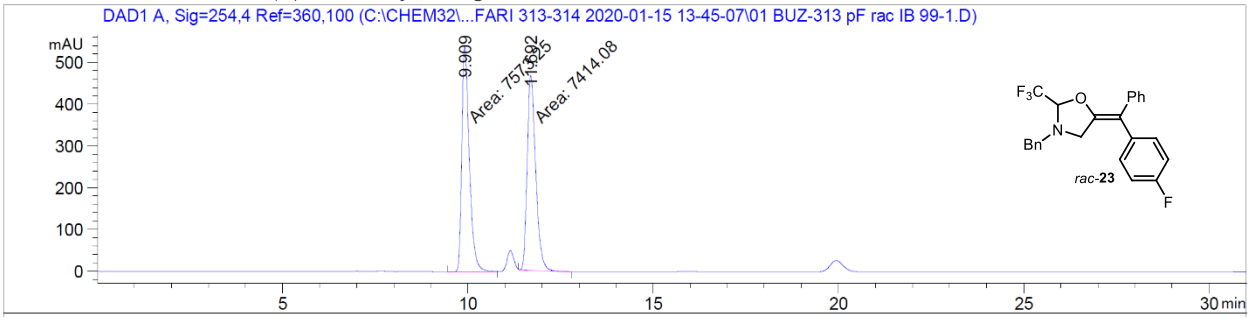


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.898	MM	0.2708	1.09375e4	673.26398	49.1741
2	12.293	MM	0.2970	1.13049e4	634.33032	50.8259

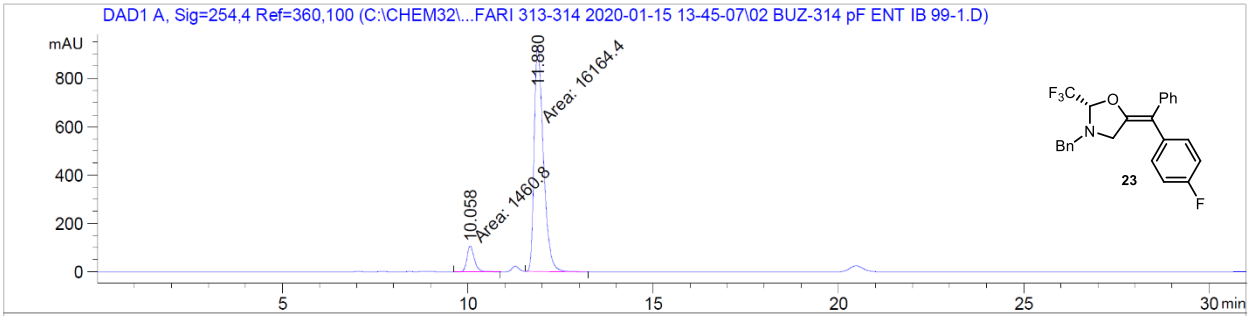


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.670	MM	0.2543	976.98279	64.04114	8.6508
2	12.127	MM	0.2817	1.03166e4	610.32190	91.3492

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

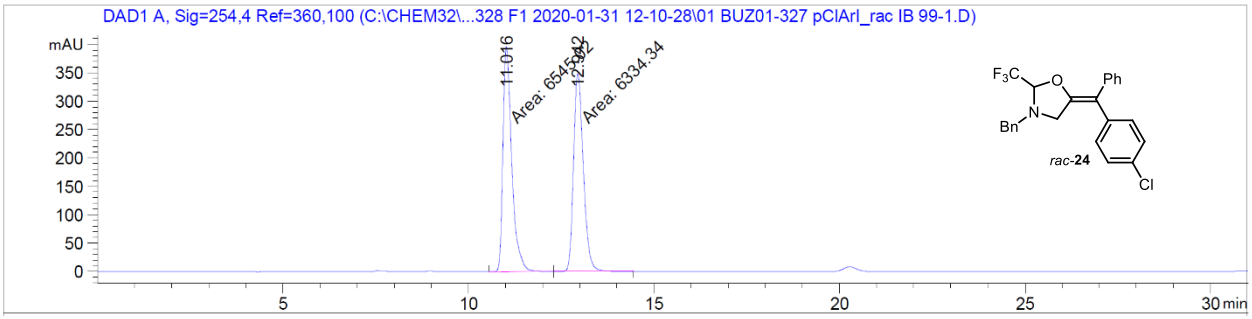


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.909	MM	0.2343	7573.24756	538.81549	50.5310
2	11.692	MM	0.2657	7414.08154	465.09402	49.4690

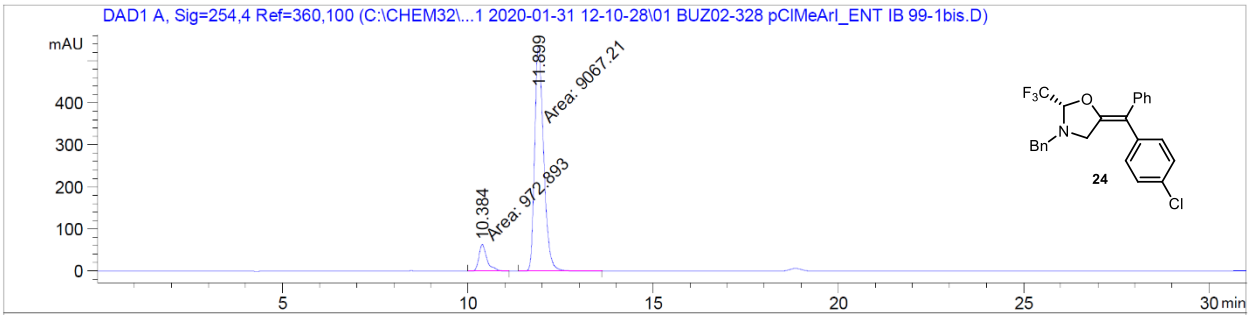


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.058	MM	0.2288	1460.80383	106.40328	8.2881
2	11.880	MM	0.2883	1.61644e4	934.54388	91.7119

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

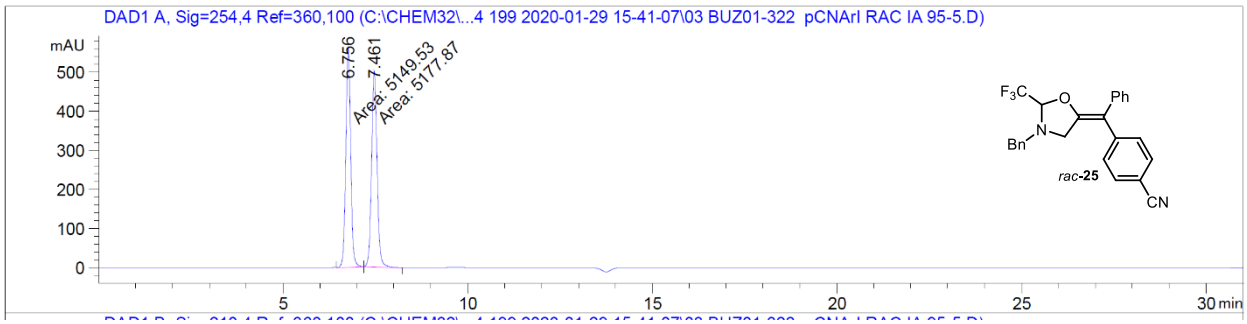


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	11.016	MM	0.2752	6545.02051	396.44269	50.8179
2	12.942	MM	0.3037	6334.33740	347.65237	49.1821

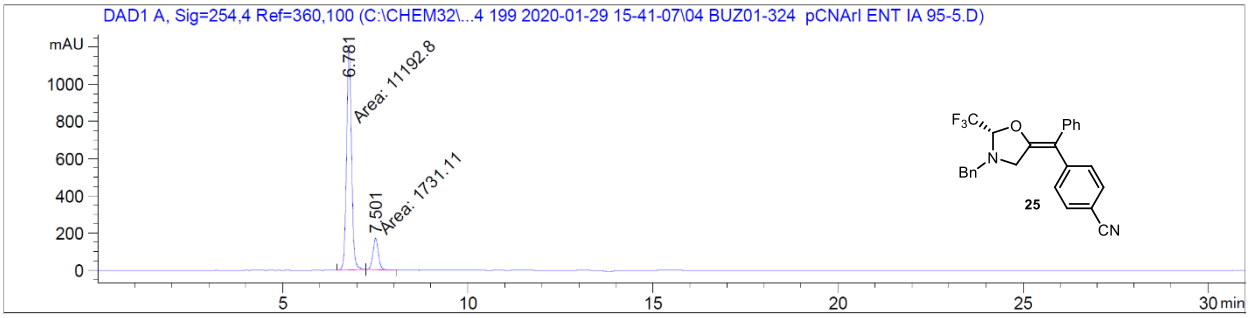


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.384	MM	0.2560	972.89252	63.33549	9.6901
2	11.899	MM	0.2822	9067.21387	535.55524	90.3099

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

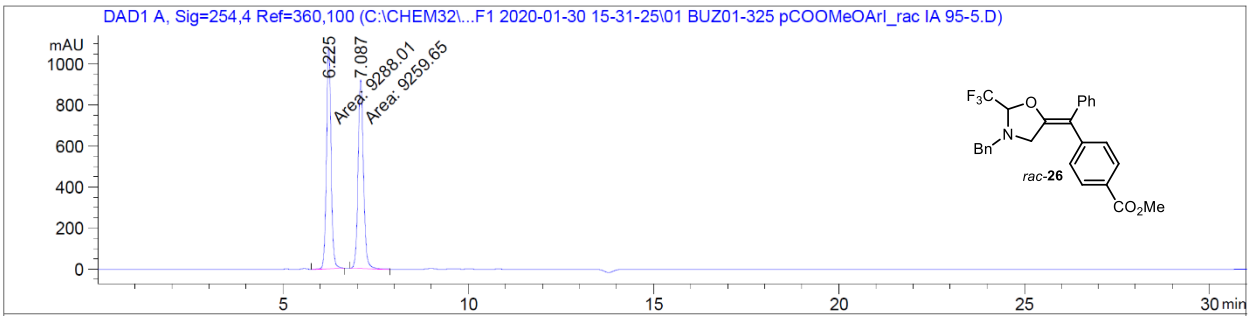


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.756	MM	0.1527	5149.52881	562.19830	49.8628
2	7.461	MM	0.1722	5177.86914	501.17307	50.1372

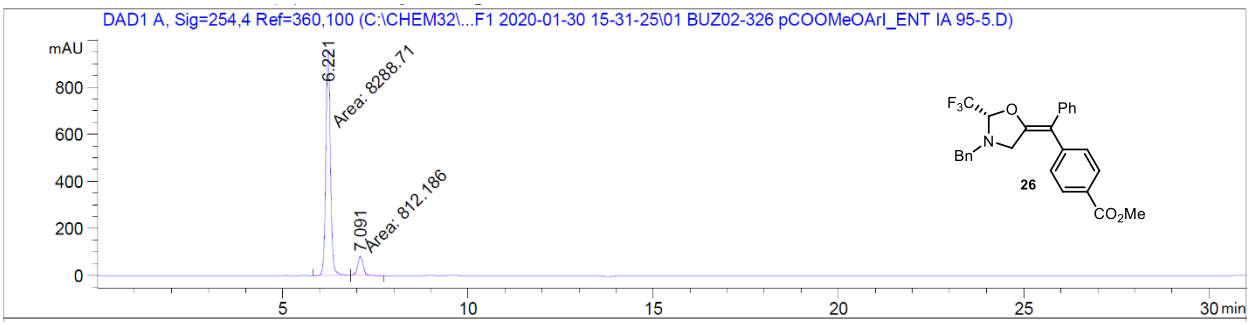


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.781	MM	0.1547	1.11928e4	1205.74072	86.6054
2	7.501	MM	0.1699	1731.10864	169.82246	13.3946

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

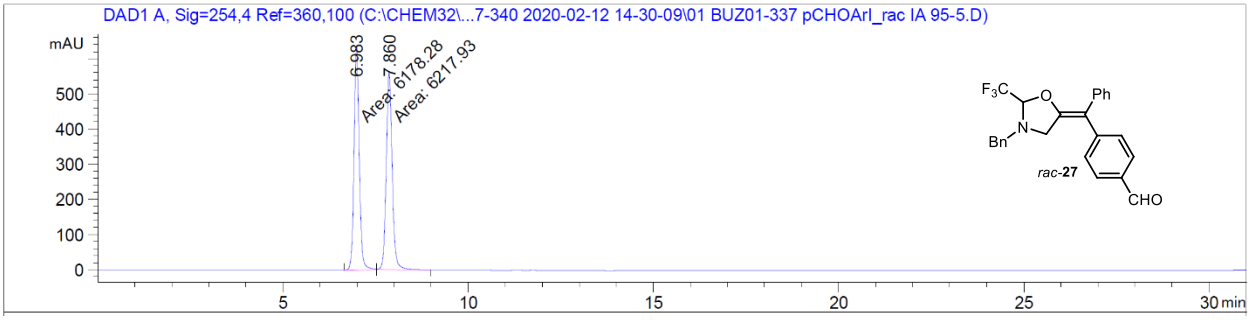


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.225	MM	0.1430	9288.00586	1082.22388	50.0764
2	7.087	MM	0.1676	9259.65234	920.65900	49.9236

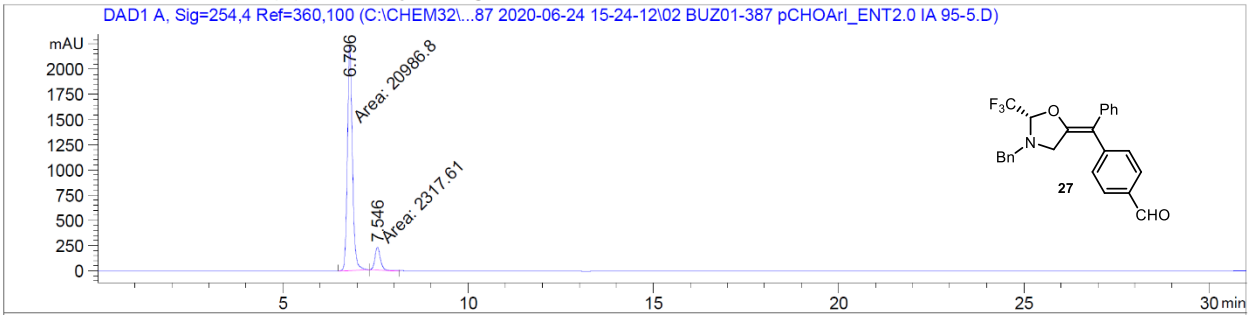


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.221	MM	0.1443	8288.71094	957.65491	91.0758
2	7.091	MM	0.1652	812.18579	81.92288	8.9242

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

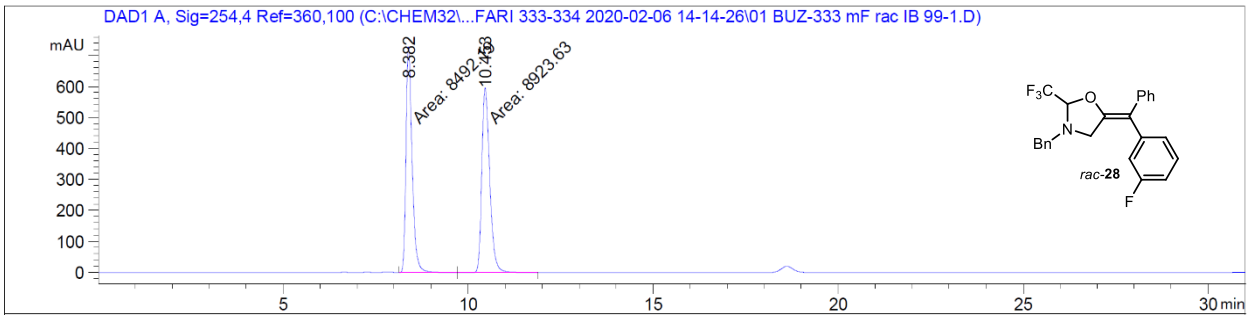


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.983	MM	0.1613	6178.28027	638.23871	49.8401
2	7.860	MM	0.1855	6217.93066	558.66156	50.1599

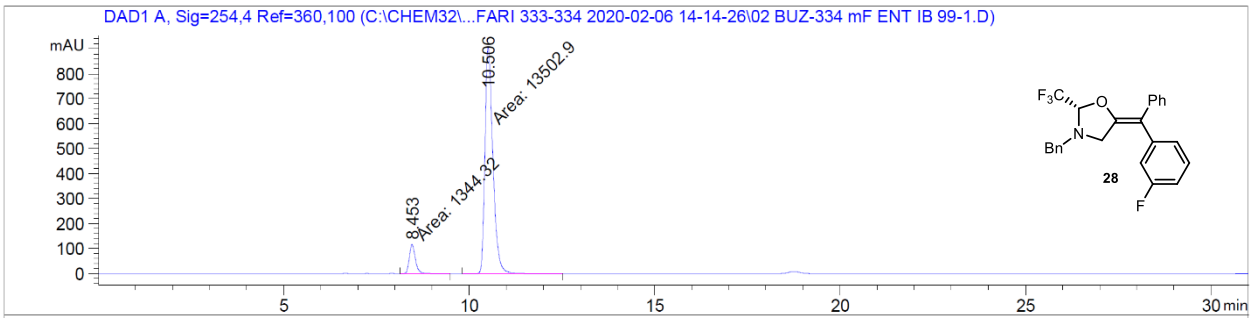


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.796	MM	0.1566	2.09868e4	2233.08179	90.0551
2	7.546	MM	0.1697	2317.60913	227.63397	9.9449

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

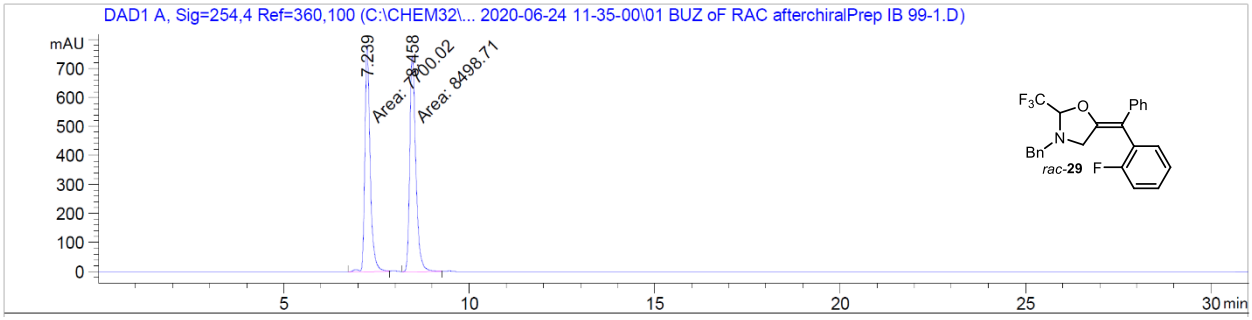


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.382	MF	0.1941	8492.19434	729.13214	48.7614
2	10.453	FM	0.2488	8923.62988	597.71075	51.2386

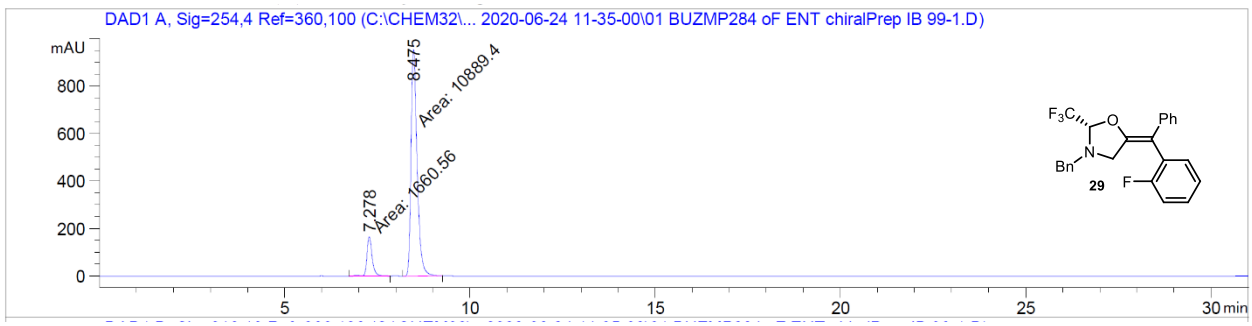


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.453	MM	0.1913	1344.32251	117.11890	9.0544
2	10.506	MM	0.2481	1.35029e4	907.05493	90.9456

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

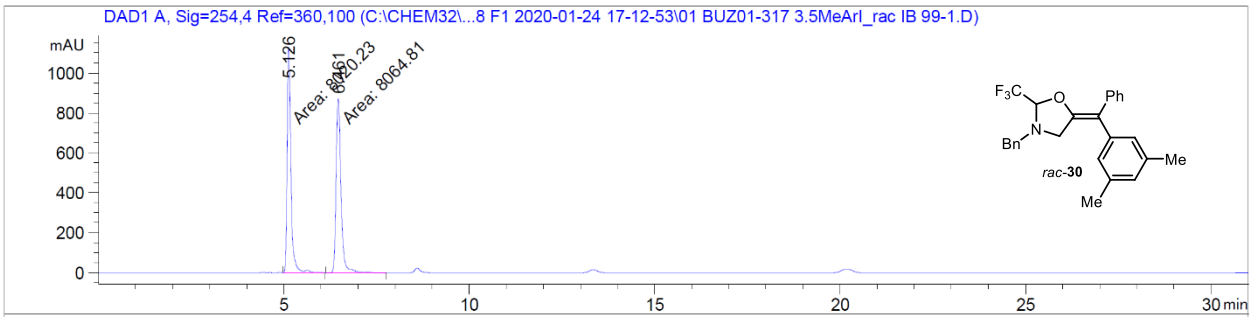


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.239	MM	0.1648	7700.02246	778.92145	47.5347
2	8.458	MM	0.1905	8498.70996	743.38043	52.4653

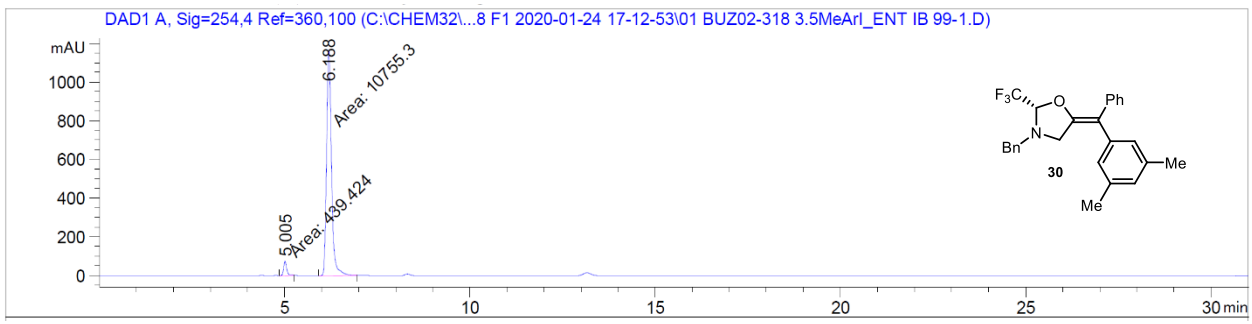


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.278	MM	0.1668	1660.55542	165.88861	13.2315
2	8.475	MM	0.1903	1.08894e4	953.67273	86.7685

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

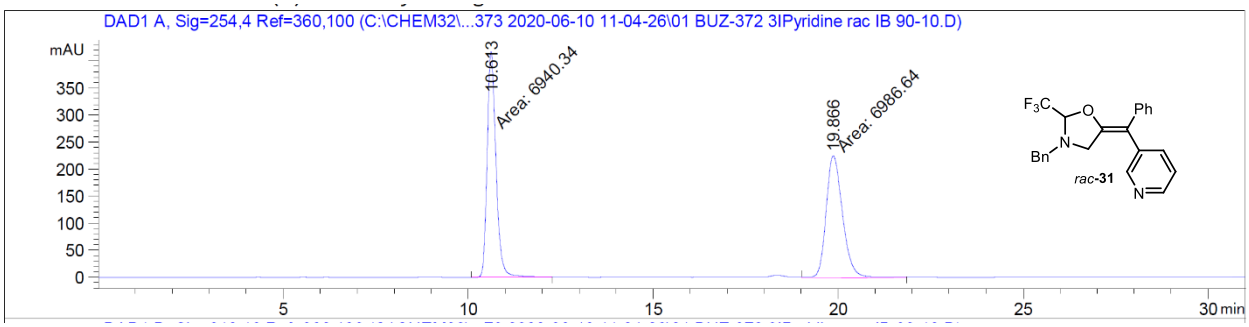


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.126	MM	0.1181	8020.22705	1132.02124	49.8614
2	6.461	MM	0.1543	8064.80762	871.38739	50.1386

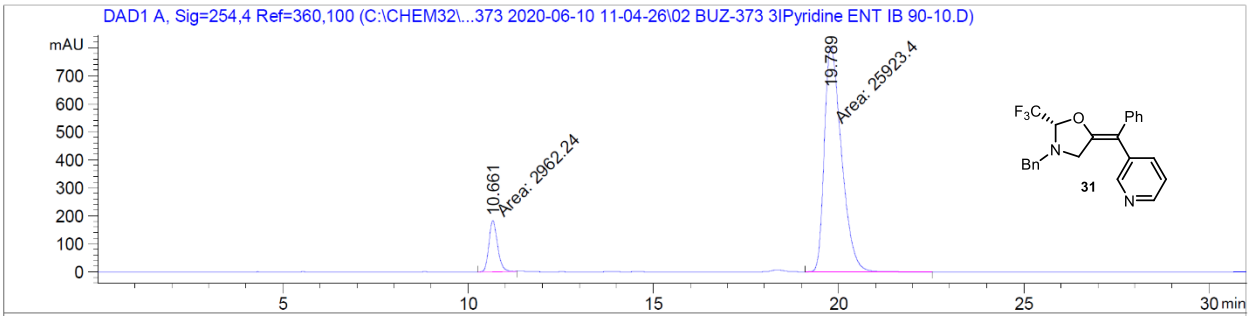


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.005	MM	0.0972	439.42377	75.32863	3.9253
2	6.188	MM	0.1534	1.07553e4	1168.46960	96.0747

Chiral HPLC Daicel Chiralpak IB N-5 column: 90:10 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

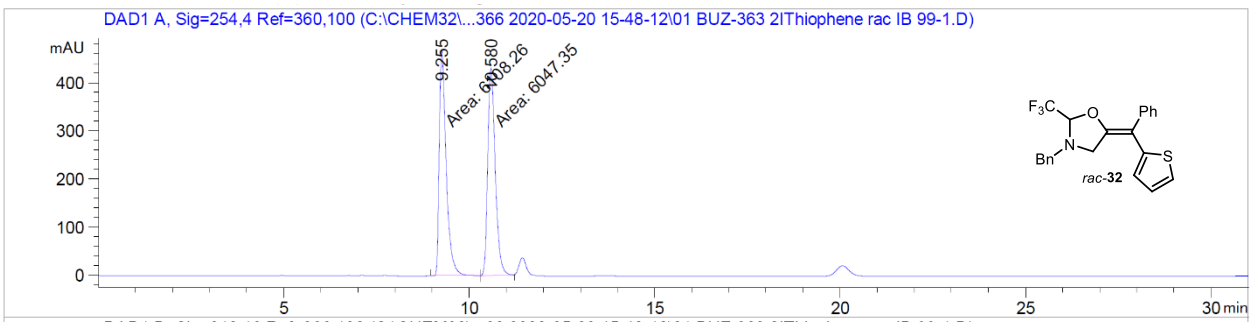


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.613	MM	0.2771	6940.34229	417.39124	49.8338
2	19.866	MM	0.5154	6986.64111	225.94112	50.1662

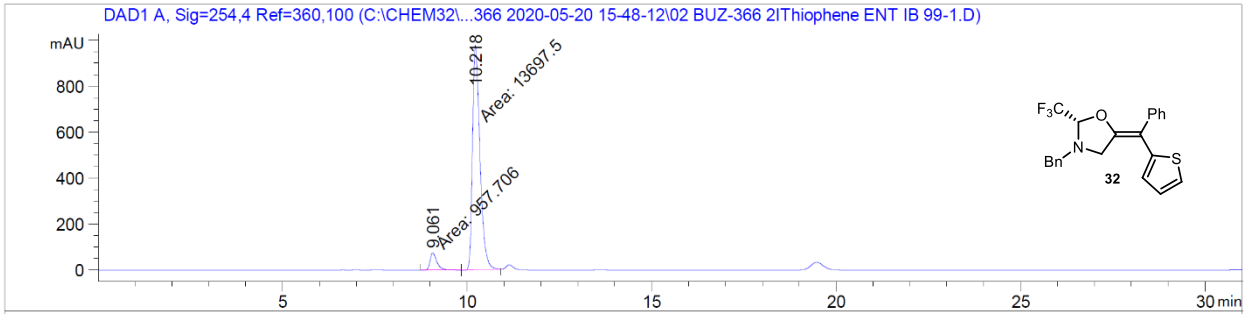


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.661	MM	0.2700	2962.23584	182.83882	10.2550
2	19.789	MM	0.5373	2.59234e4	804.11737	89.7450

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

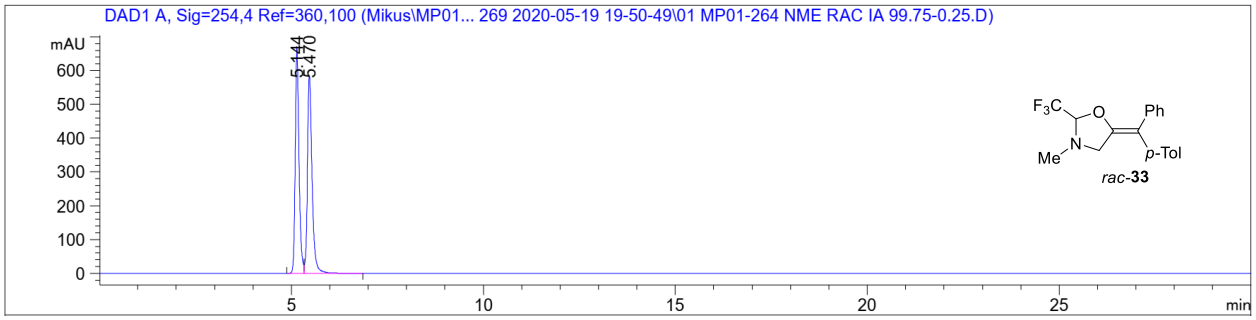


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.255	MM	0.2170	6108.25830	469.16779	50.2505
2	10.580	MM	0.2339	6047.34961	430.89670	49.7495

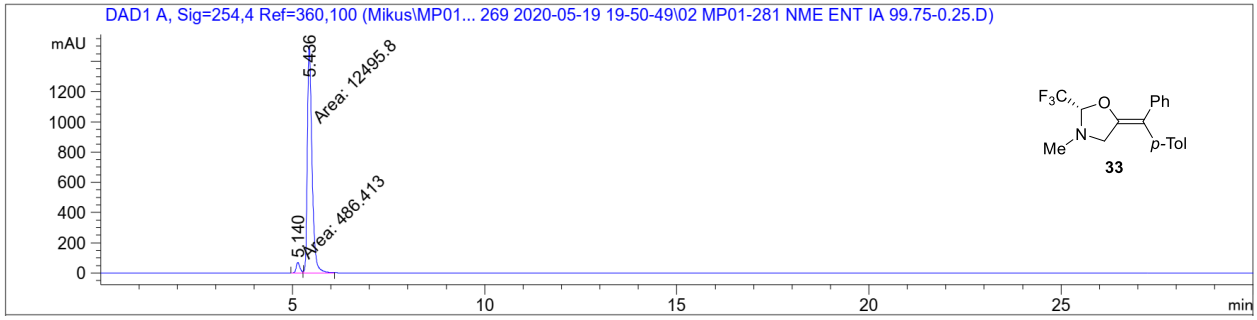


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.061	MM	0.2129	957.70569	74.95567	6.5349
2	10.218	MM	0.2336	1.36975e4	977.10193	93.4651

Chiral HPLC Daicel Chiralpak IA column: 99.75:0.25 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

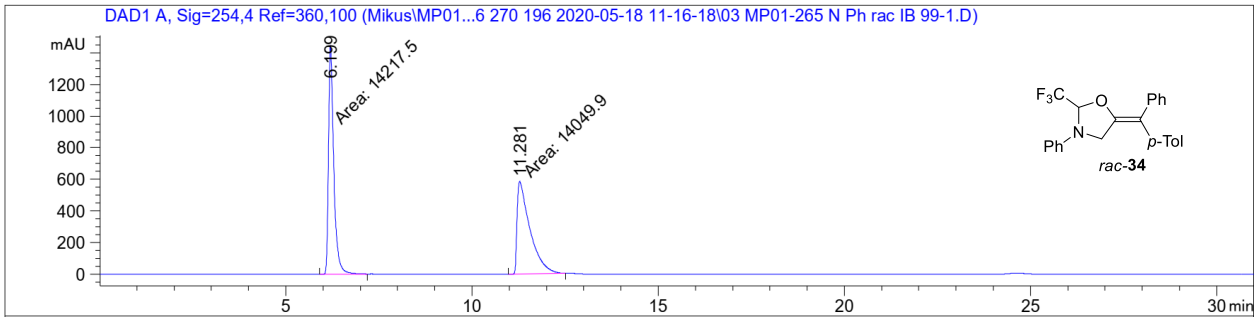


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.144	BV	0.1056	4701.87695	672.19818	48.8437
2	5.470	VB	0.1260	4924.50293	586.52747	51.1563

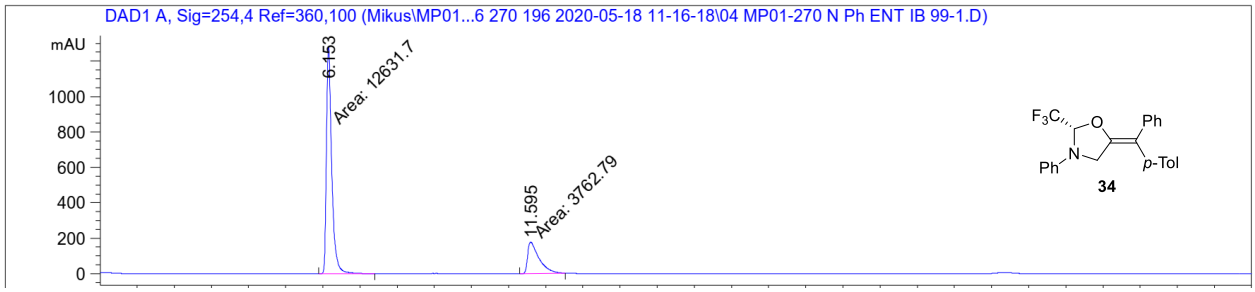


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.140	MM	0.1166	486.41333	69.51125	3.7468
2	5.436	MM	0.1384	1.24958e4	1505.25439	96.2532

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

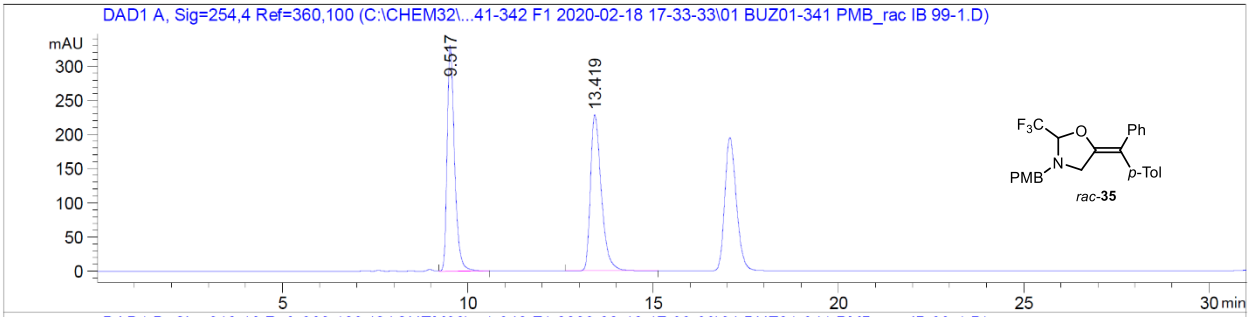


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.199	MM	0.1646	1.42175e4	1439.49976	50.2965
2	11.281	MM	0.3992	1.40499e4	586.51587	49.7035

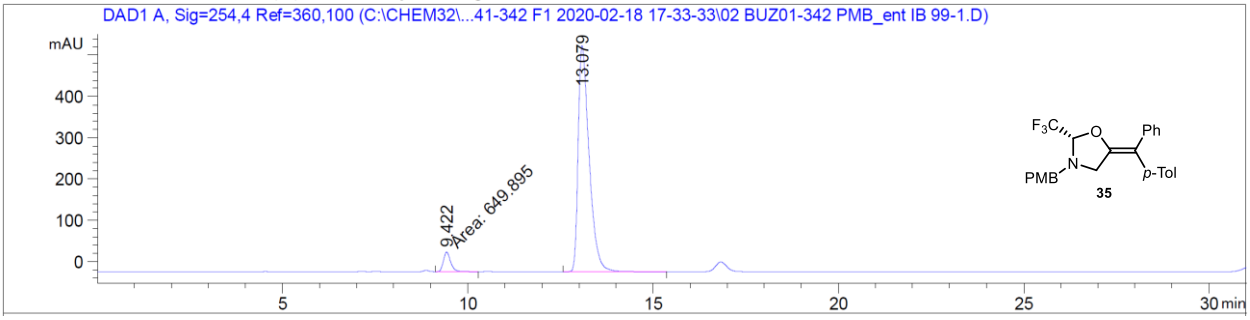


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.153	MM	0.1642	1.26317e4	1282.25012	77.0484
2	11.595	MM	0.3531	3762.79053	177.60005	22.9516

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

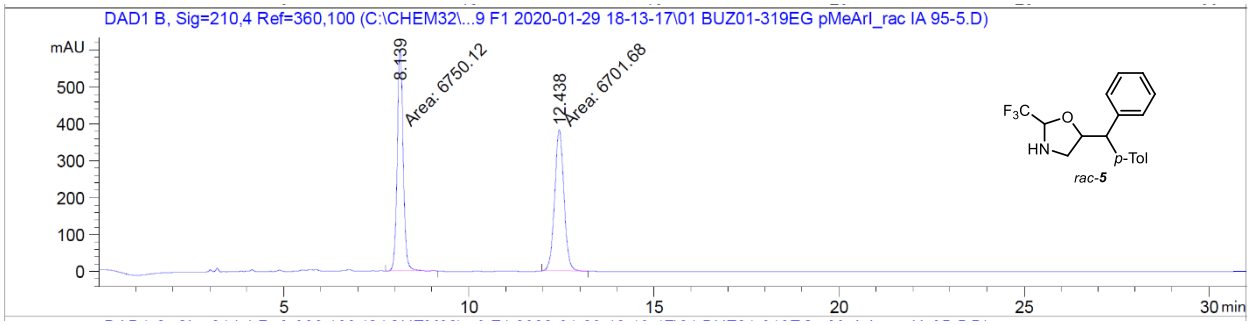


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.517	VB	0.2123	4588.63281	329.88892	49.5091
2	13.419	BB	0.3125	4679.63574	228.90796	50.4909

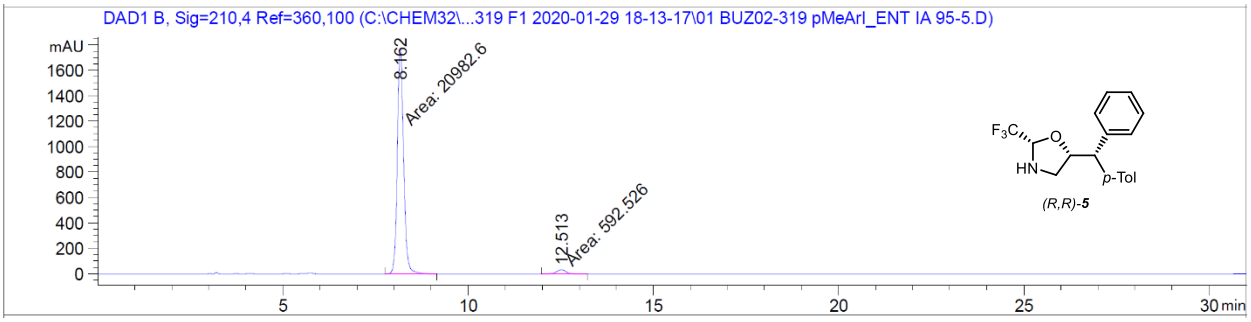


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.422	MM	0.2281	649.89478	47.48665	5.4671
2	13.079	BB	0.3096	1.12374e4	547.06708	94.5329

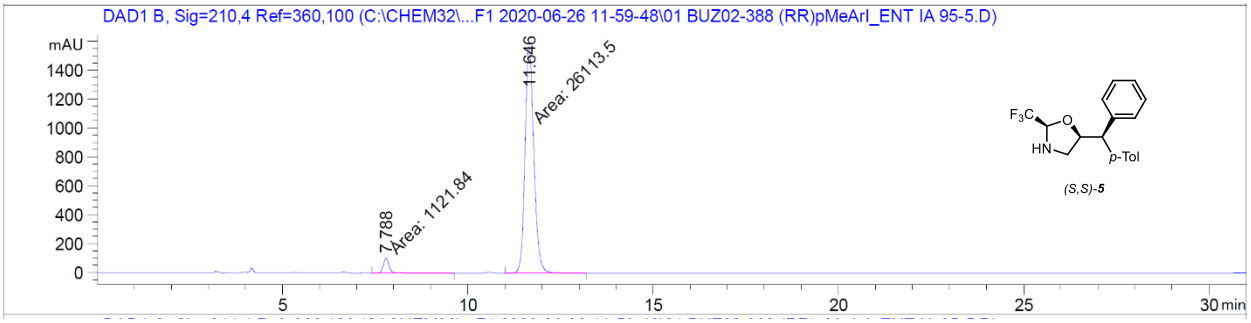
Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm



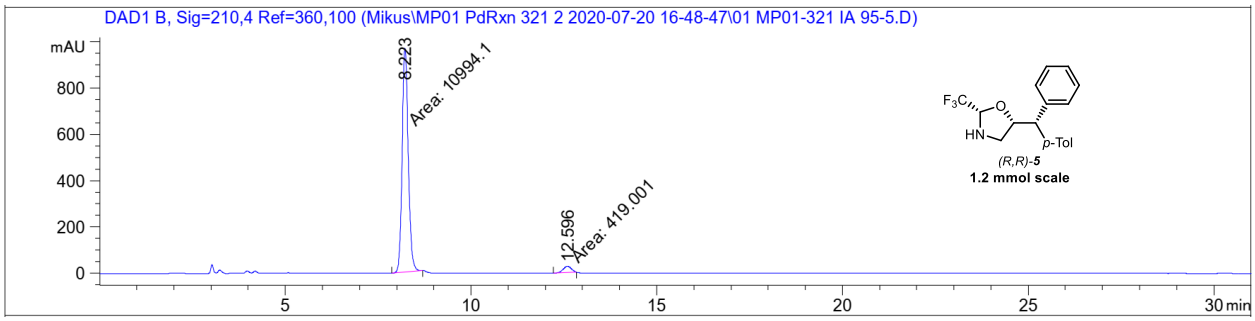
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.139	MM	0.1870	6750.12305	601.65063	50.1801
2	12.438	MM	0.2923	6701.67676	382.18515	49.8199



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.162	MM	0.1971	2.09826e4	1773.85559	97.2537
2	12.513	MM	0.2945	592.52631	33.52852	2.7463

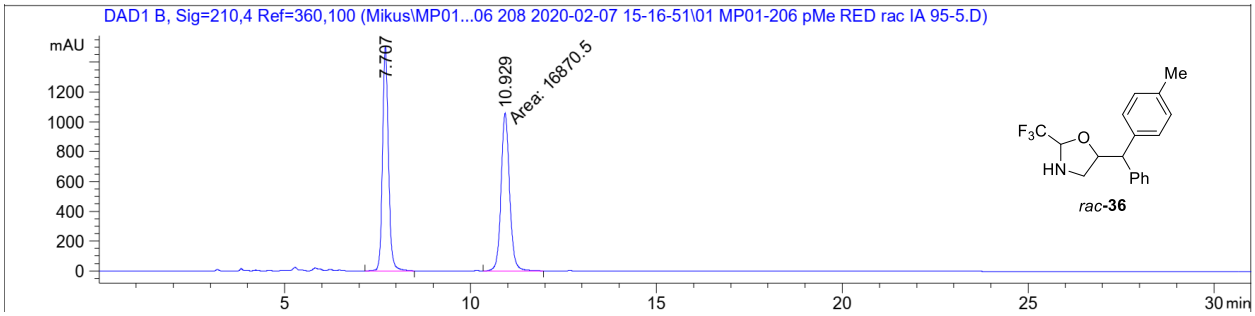


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.788	MM	0.1788	1121.83972	104.57675	4.1191
2	11.646	MM	0.2773	2.61135e4	1569.22839	95.8809

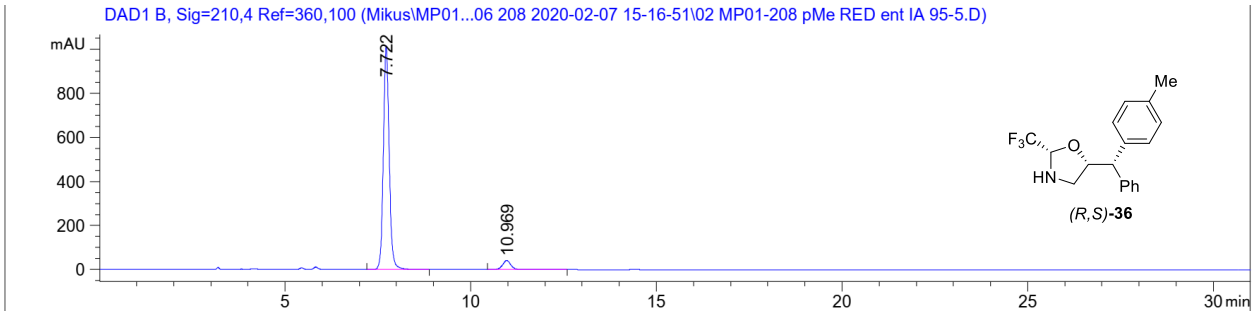


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.223	MM	0.1898	1.09941e4	965.64703	96.3288
2	12.596	MM	0.2552	419.00122	27.36468	3.6712

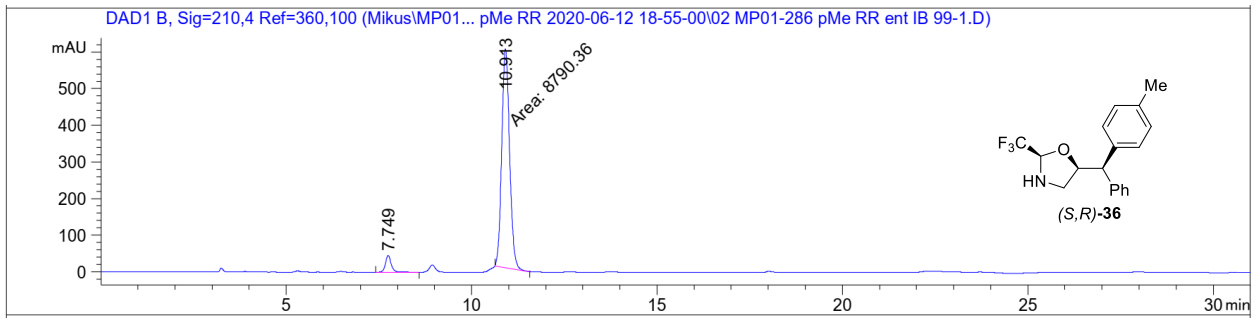
Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.707	BB	0.1689	1.66268e4	1505.27429	49.6362
2	10.929	MM	0.2652	1.68705e4	1060.31323	50.3638



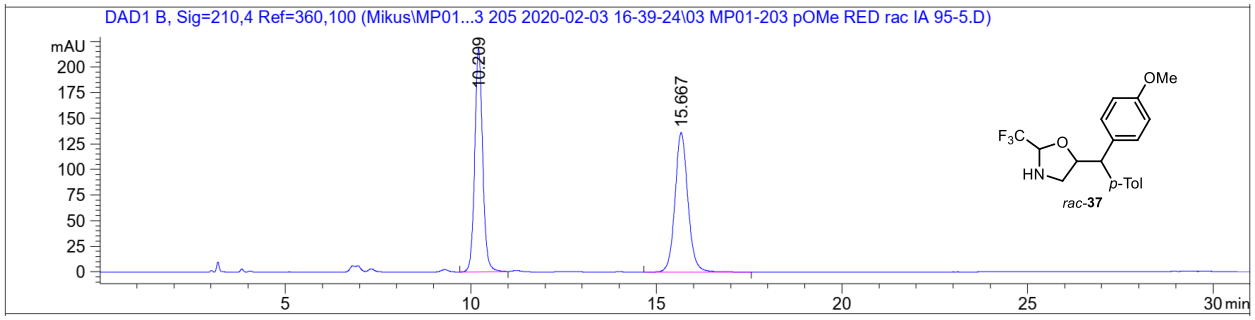
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.722	BB	0.1670	1.10836e4	1018.06122	94.4899
2	10.969	BB	0.2390	646.32837	41.20693	5.5101



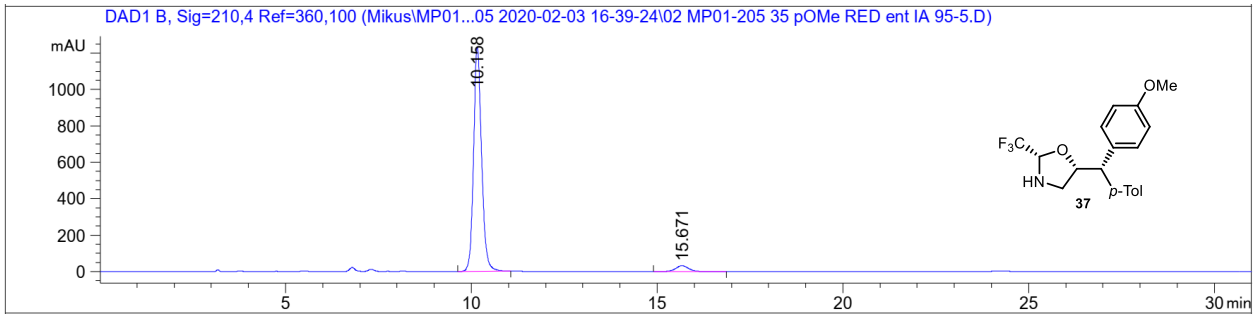
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.749	BB	0.1644	492.49951	45.44075	5.3055
2	10.913	MM	0.2449	8790.36035	598.13947	94.6945

I.2. Asymmetric Hydrogenation Products

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

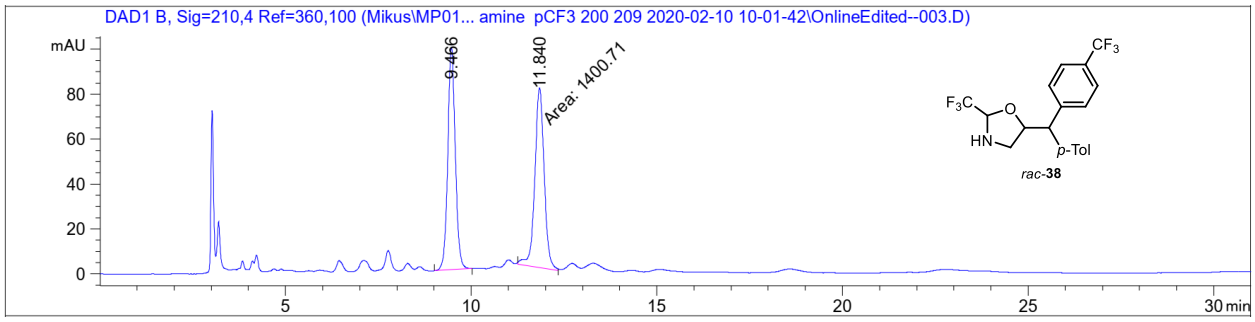


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.209	BB	0.2240	3224.11084	218.68341	49.4854
2	15.667	BB	0.3679	3291.16724	136.19072	50.5146

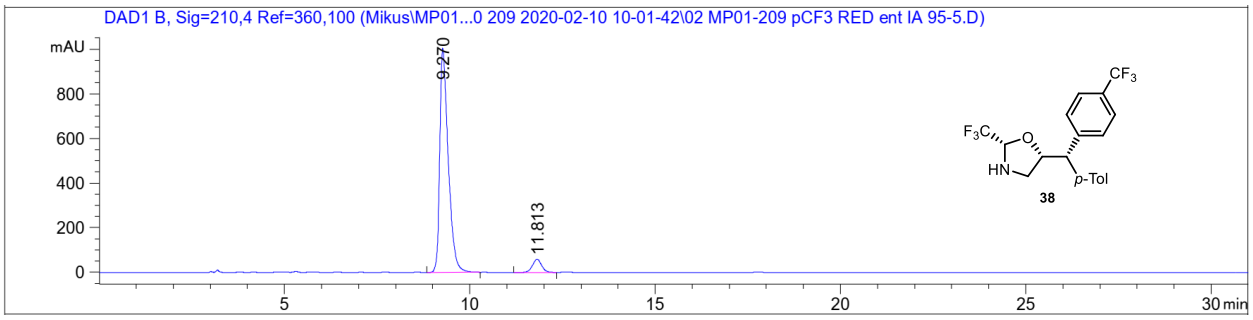


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.158	BB	0.2291	1.84721e4	1230.68018	95.9072
2	15.671	BB	0.3723	788.29559	32.34998	4.0928

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

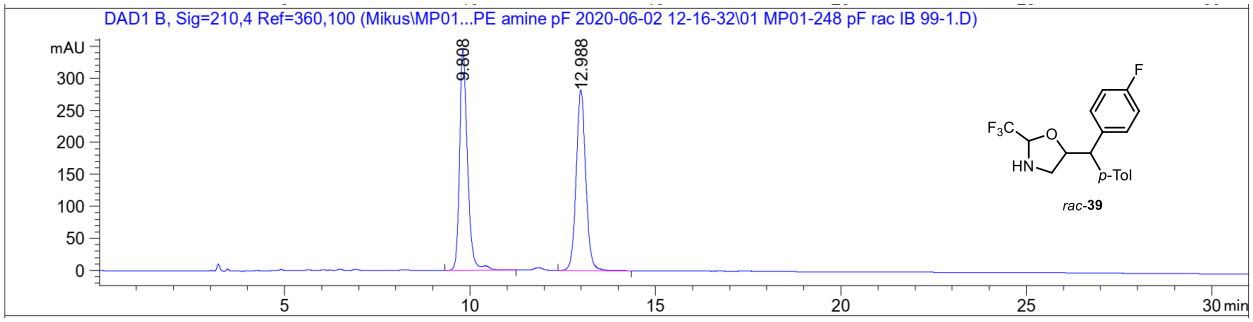


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.466	BB	0.2144	1396.00537	99.07581	49.9158
2	11.840	MM	0.2922	1400.71436	79.88445	50.0842

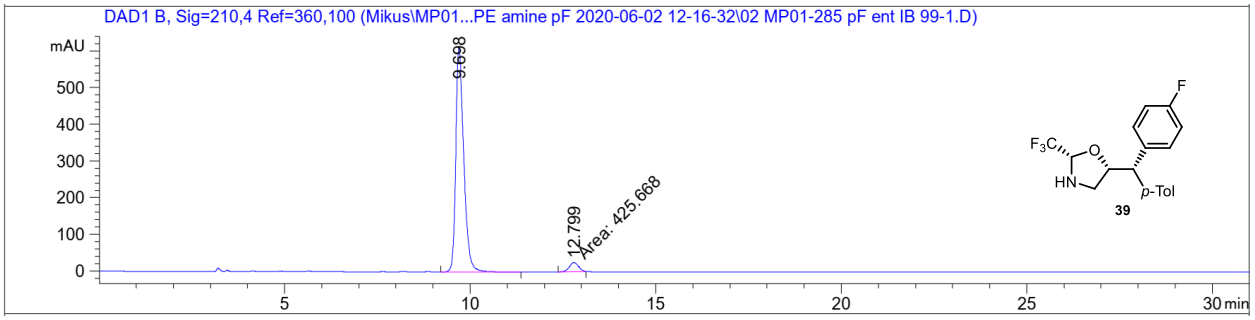


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.270	BB	0.2330	1.59401e4	1005.11450	94.0368
2	11.813	BB	0.2631	1010.81848	59.24051	5.9632

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

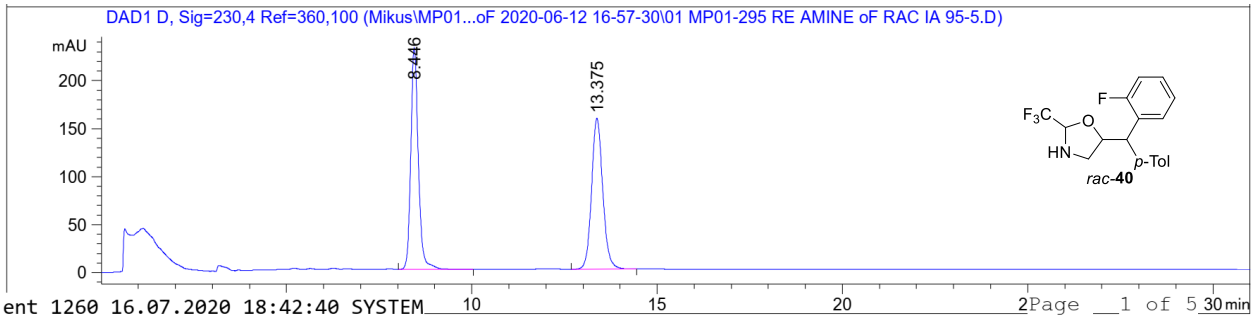


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.808	BV R	0.2199	5136.28760	345.08109	50.4463
2	12.988	BB	0.2750	5045.40527	281.61697	49.5537

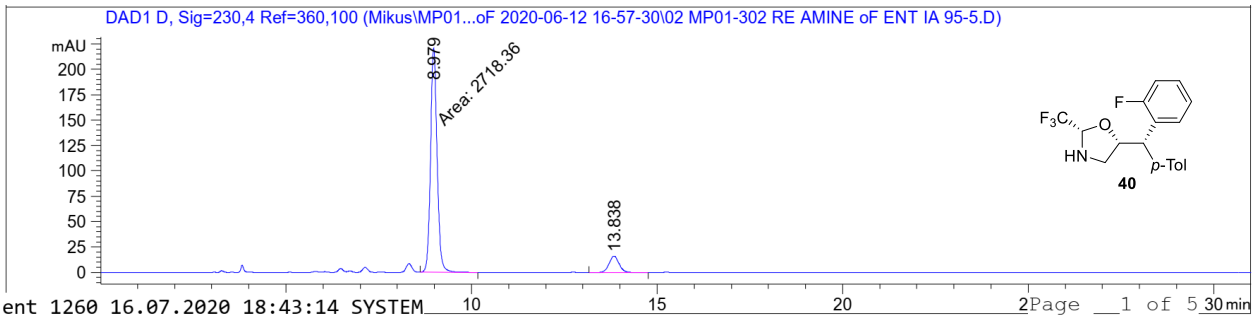


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.698	BB	0.2234	9107.40918	612.70685	95.5348
2	12.799	MM	0.2844	425.66833	24.94544	4.4652

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 230 nm

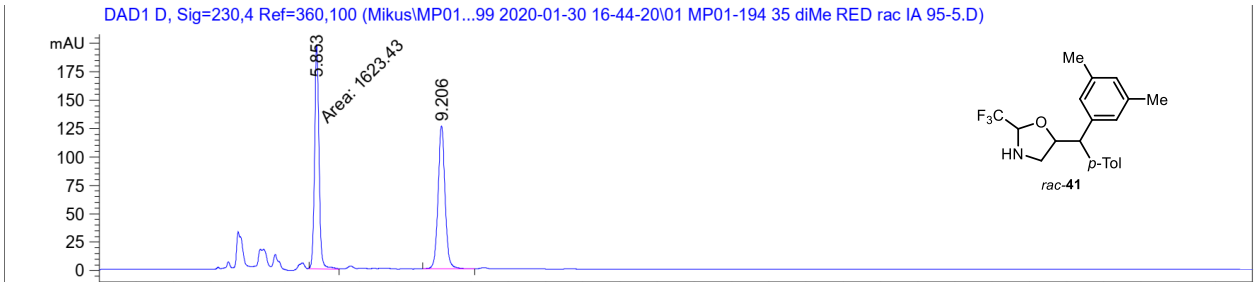


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.446	BB	0.2156	3278.09863	230.99530	49.7995
2	13.375	BB	0.3207	3304.48853	157.54460	50.2005

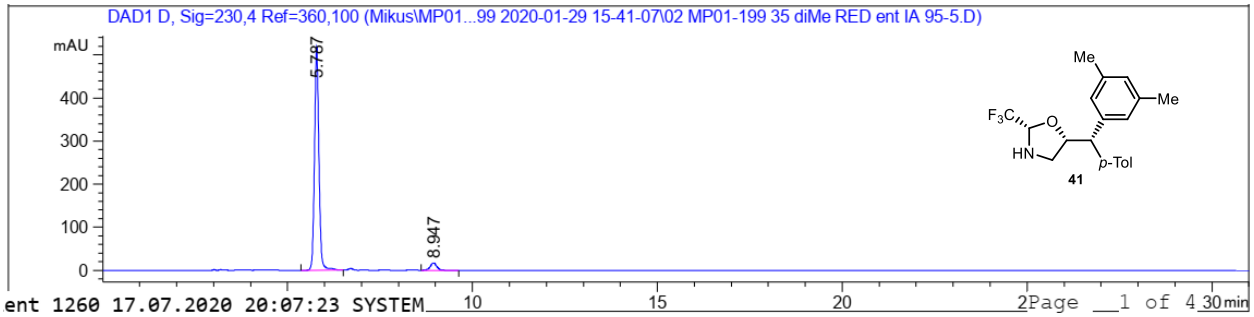


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.979	MM	0.2051	2718.36279	220.91415	89.7692
2	13.838	BB	0.2923	309.80426	16.26005	10.2308

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 230 nm

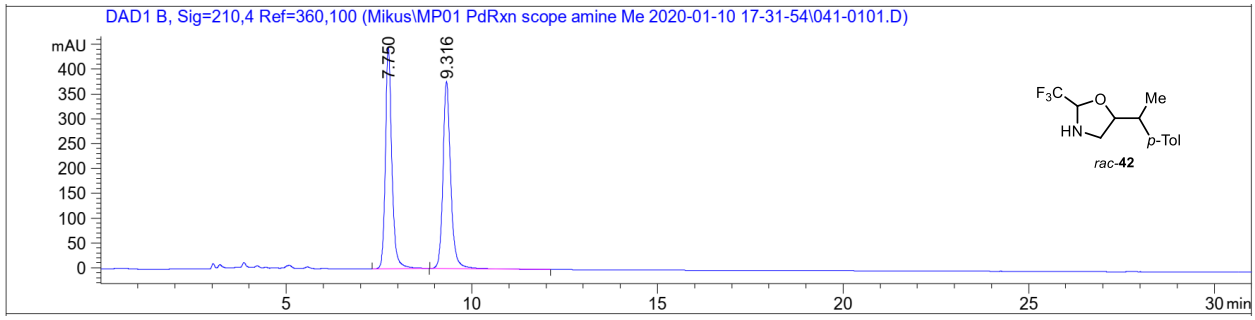


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.853	MM	0.1374	1623.43127	196.94261	49.7401
2	9.206	BB	0.2001	1640.39392	125.81128	50.2599

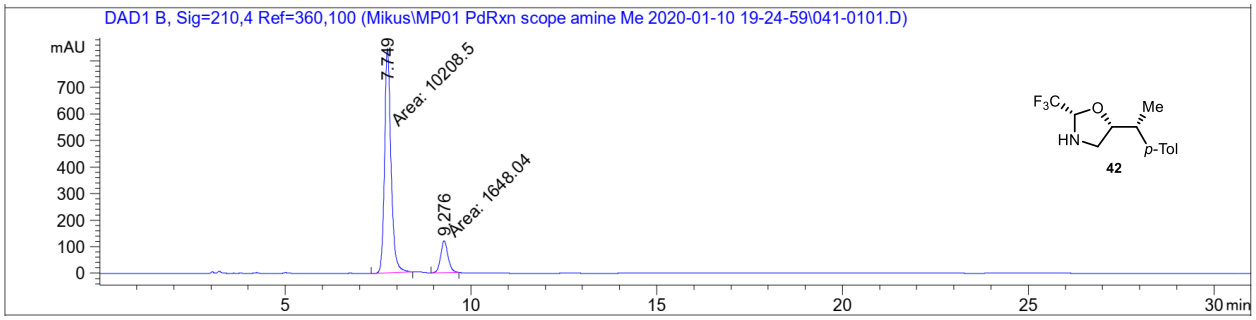


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.787	BB	0.1268	4301.36572	518.57843	95.3091
2	8.947	BB	0.1915	211.70566	16.97226	4.6909

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

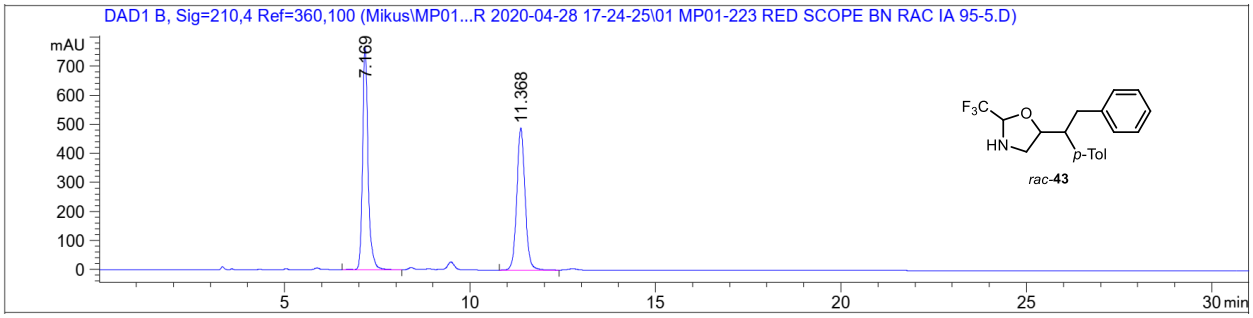


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.750	BB	0.1816	5410.29150	445.90652	49.7336
2	9.316	BB	0.2174	5468.25977	376.52570	50.2664

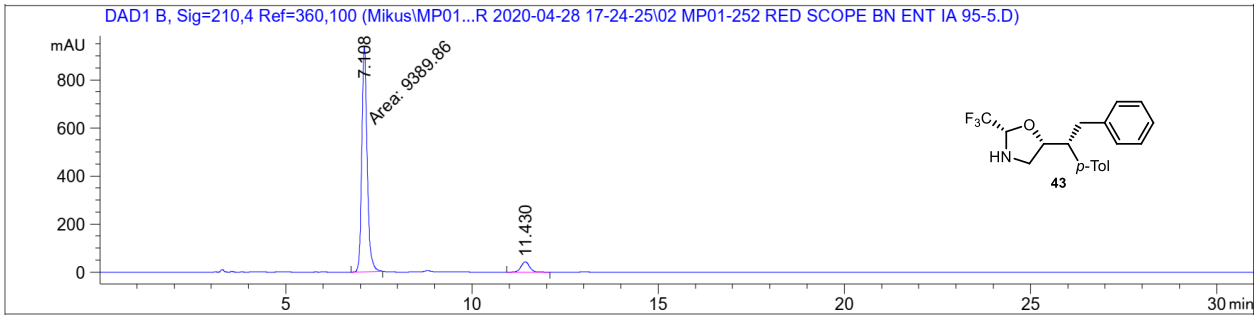


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.749	MM	0.2013	1.02085e4	845.34601	86.1001
2	9.276	MM	0.2287	1648.04089	120.09613	13.8999

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

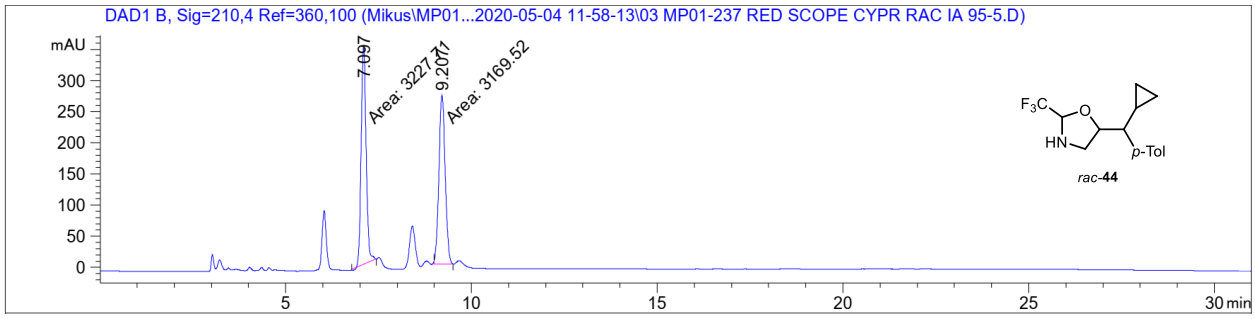


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.169	VB R	0.1568	7981.02490	768.78271	51.1646
2	11.368	BB	0.2398	7617.70557	488.75272	48.8354

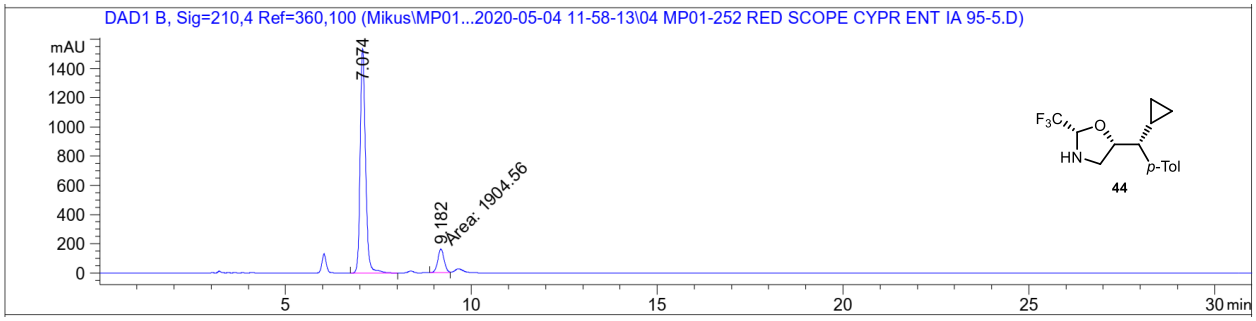


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.108	MM	0.1670	9389.86133	937.36621	93.2531
2	11.430	BB	0.2440	679.36102	43.07292	6.7469

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

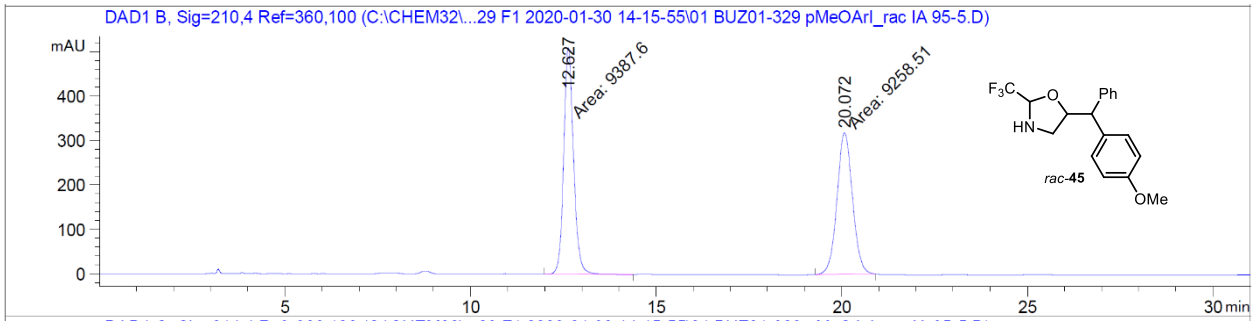


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.097	MM	0.1538	3227.70947	349.74594	50.4548
2	9.207	MM	0.1955	3169.52344	270.25354	49.5452

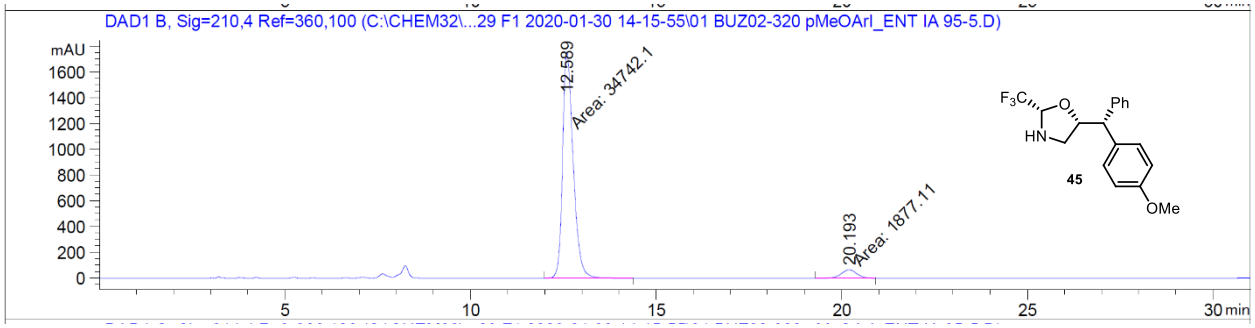


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	7.074	BB	0.1532	1.54350e4	1536.66870	89.0161
2	9.182	MM	0.1983	1904.55652	160.07146	10.9839

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

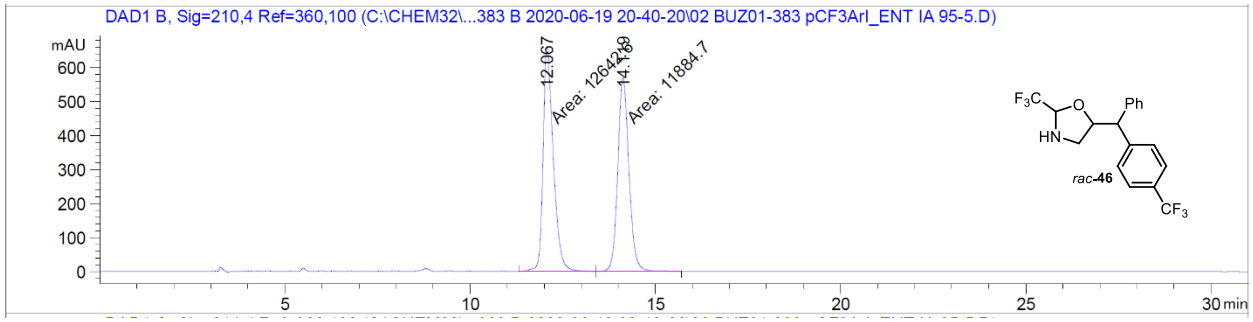


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.627	MM	0.3064	9387.59863	510.63348	50.3461
2	20.072	MM	0.4830	9258.51465	319.47153	49.6539

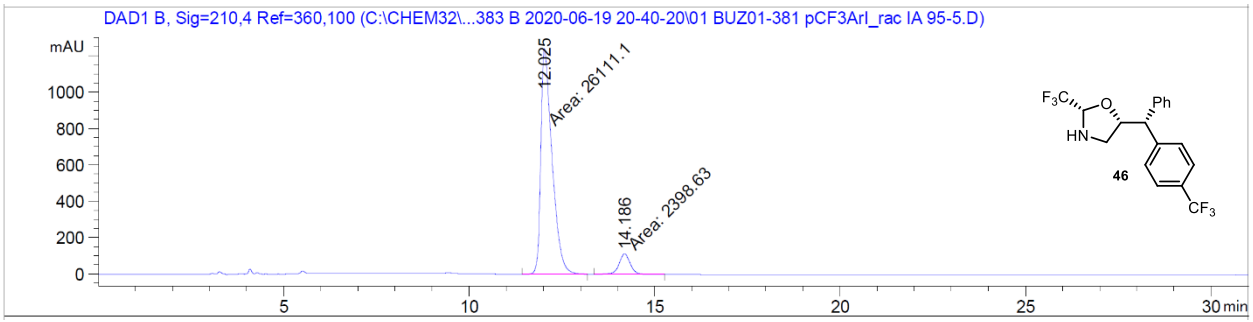


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.589	MM	0.3296	3.47421e4	1756.78882	94.8740
2	20.193	MM	0.4811	1877.10913	65.03127	5.1260

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

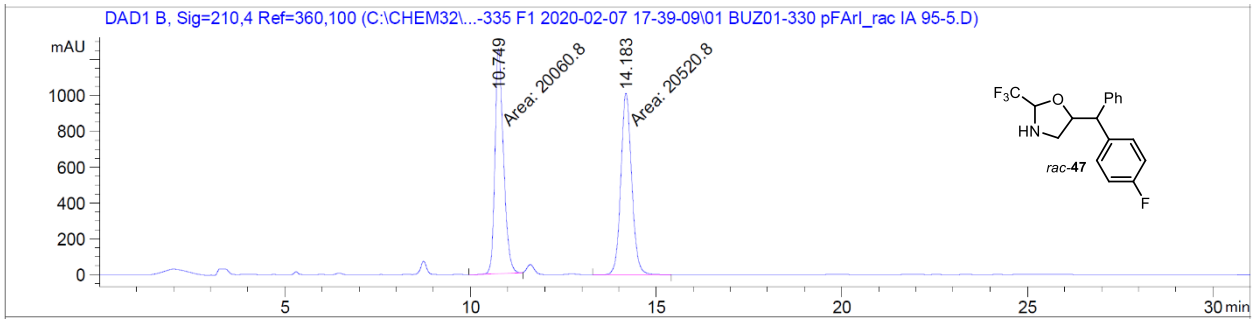


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.067	MM	0.3187	1.26426e4	661.17914	51.5451
2	14.119	MM	0.3477	1.18847e4	569.64447	48.4549

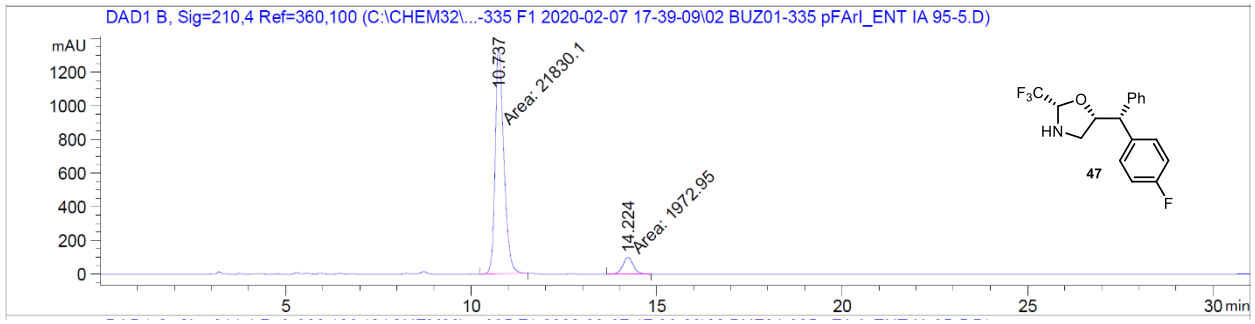


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	12.025	MM	0.3504	2.61111e4	1241.86218	91.5866
2	14.186	MM	0.3529	2398.63330	113.26971	8.4134

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

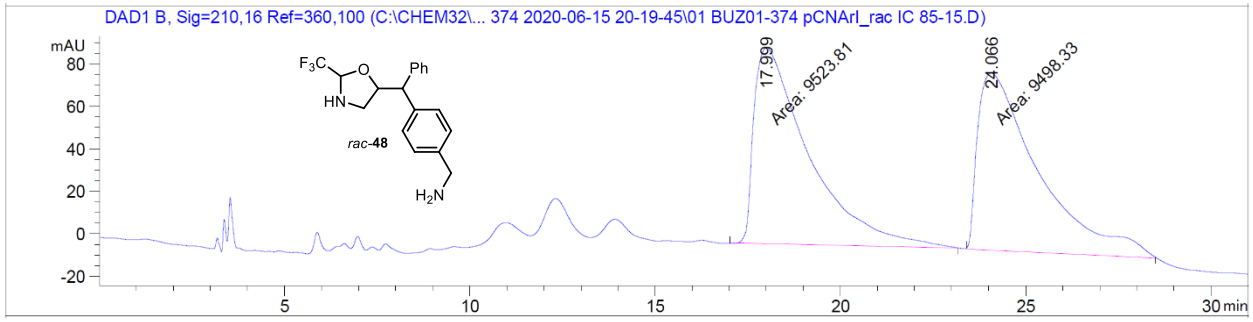


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.749	MM	0.2663	2.00608e4	1255.35925	49.4333
2	14.183	MM	0.3381	2.05208e4	1011.62799	50.5667

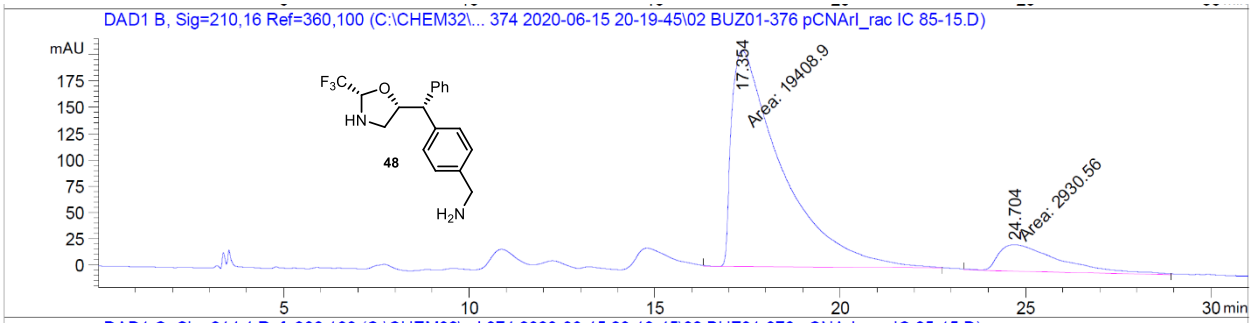


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	10.737	MM	0.2706	2.18301e4	1344.68372	91.7114
2	14.224	MM	0.3314	1972.94580	99.23210	8.2886

Chiral HPLC Daicel Chiralpak IC column: 85:15 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

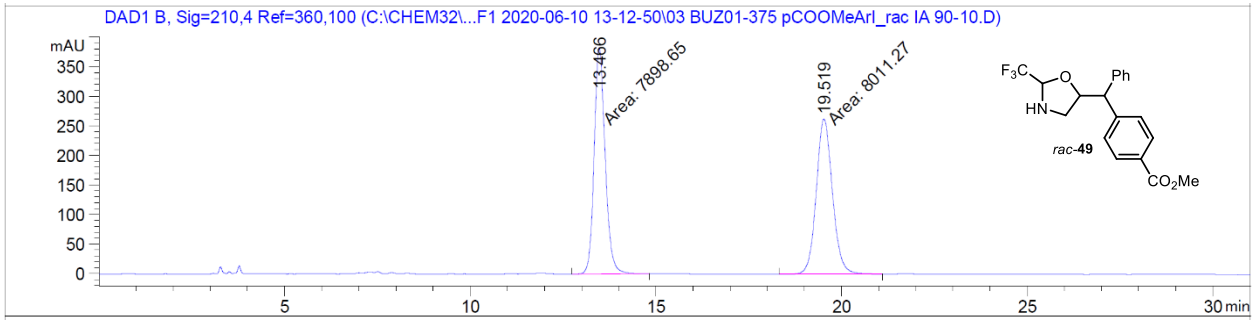


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.999	MM	1.7199	9523.80566	92.28851	50.0670
2	24.066	MM	1.8980	9498.33203	83.40444	49.9330

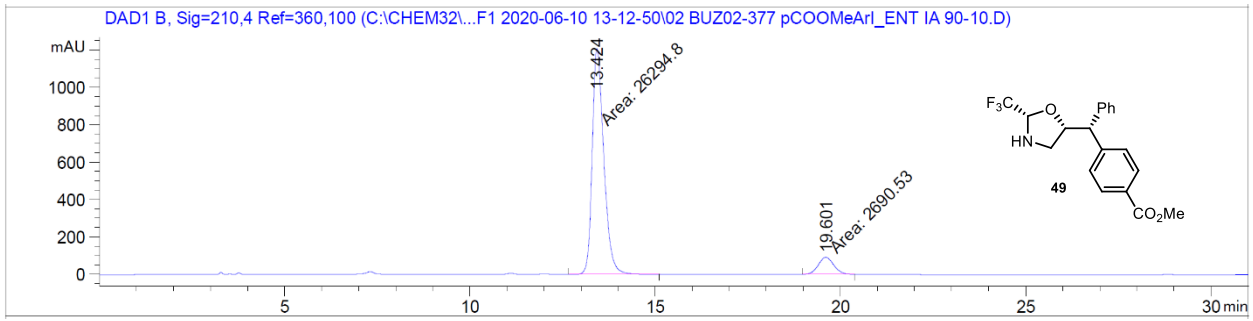


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	17.354	MM	1.5701	1.94089e4	206.02518	86.8817
2	24.704	MM	1.9329	2930.55688	25.26850	13.1183

Chiral HPLC Daicel Chiralpak IA column: 90:10 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

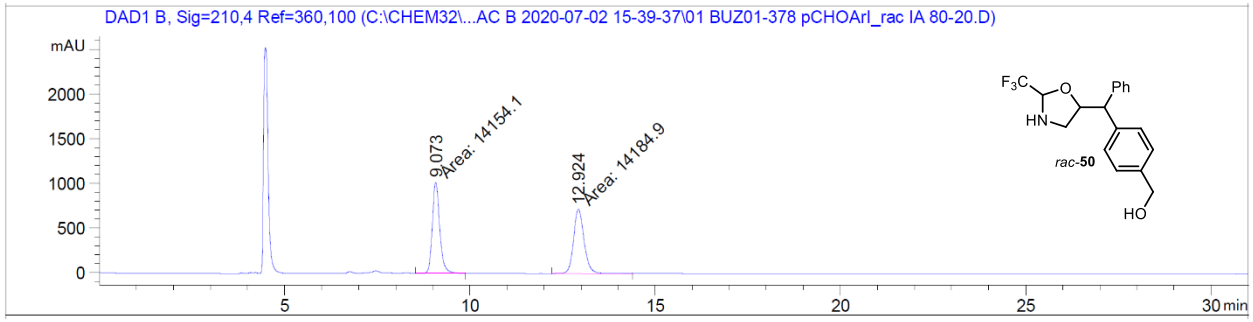


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.466	MM	0.3438	7898.64893	382.90601	49.6461
2	19.519	MM	0.5082	8011.26758	262.71729	50.3539

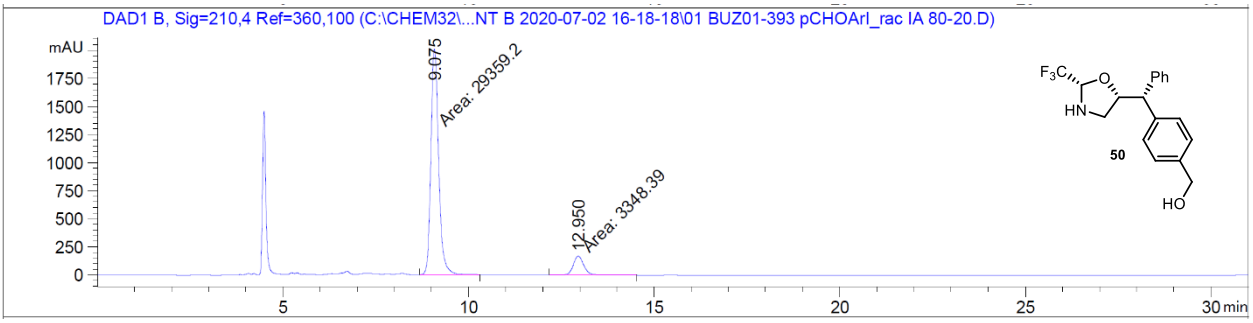


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	13.424	MM	0.3626	2.62948e4	1208.62793	90.7176
2	19.601	MM	0.4899	2690.53101	91.53439	9.2824

Chiral HPLC Daicel Chiralpak IA column: 80:20 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

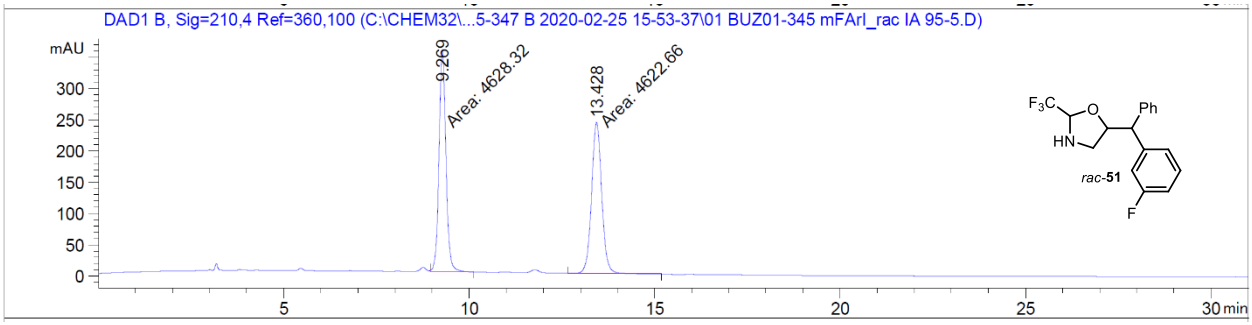


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.073	MM	0.2309	1.41541e4	1021.64856	49.9457
2	12.924	MM	0.3274	1.41849e4	721.98901	50.0543

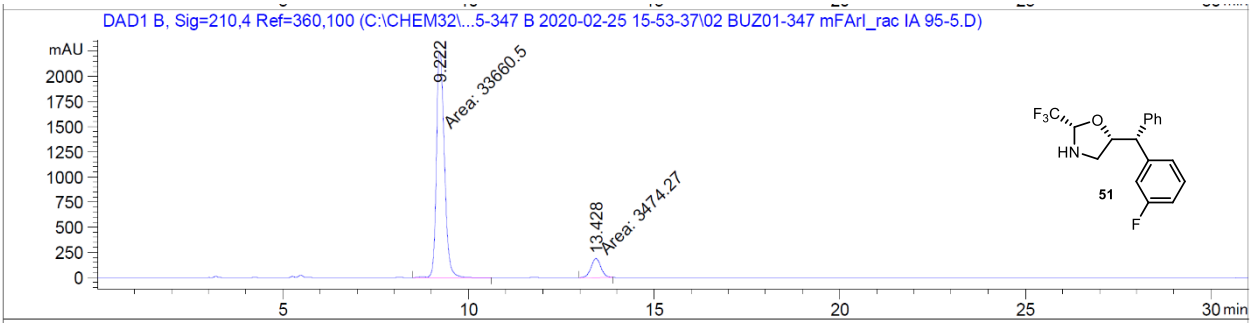


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.075	MM	0.2432	2.93592e4	2011.60852	89.7626
2	12.950	MM	0.3294	3348.38770	169.44325	10.2374

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

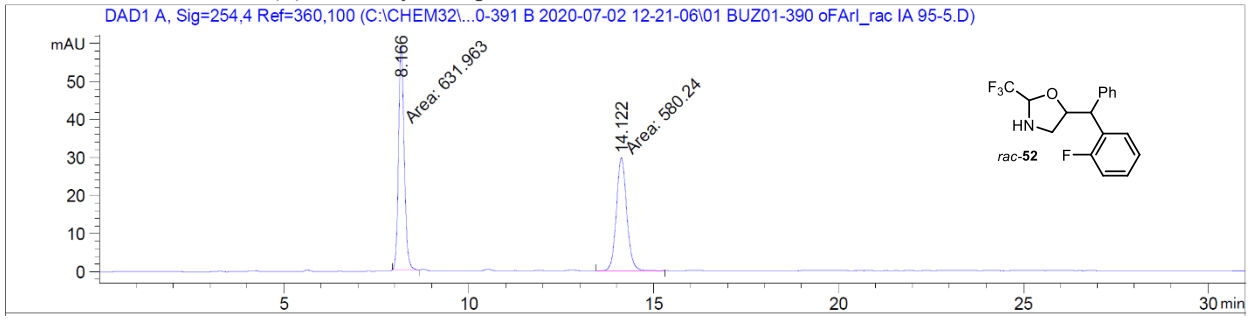


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.269	MM	0.2174	4628.32080	354.86615	50.0306
2	13.428	MM	0.3182	4622.65576	242.15567	49.9694

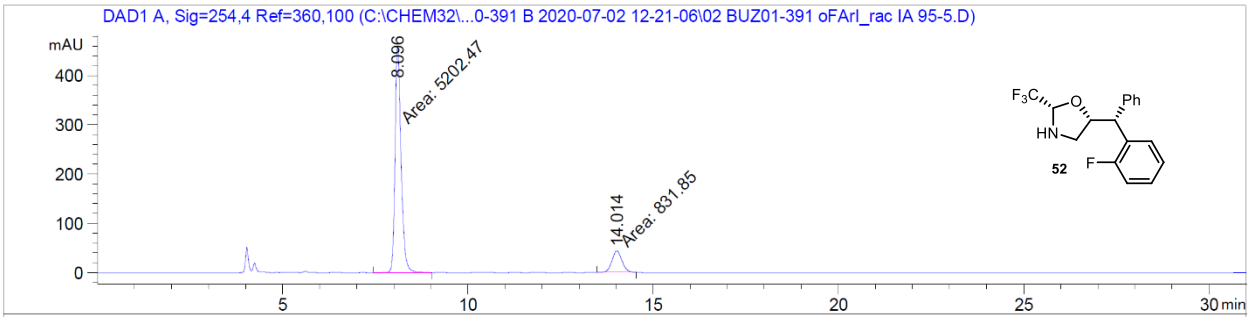


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	9.222	MM	0.2491	3.36605e4	2252.25830	90.6442
2	13.428	MM	0.3055	3474.27246	189.52641	9.3558

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 254 nm

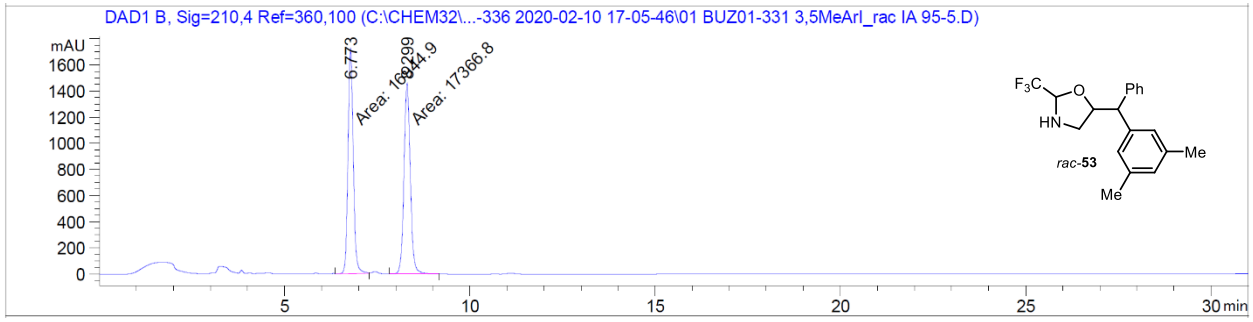


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.166	MM	0.1788	631.96338	58.90281	52.1335
2	14.122	MM	0.3250	580.23975	29.75735	47.8665

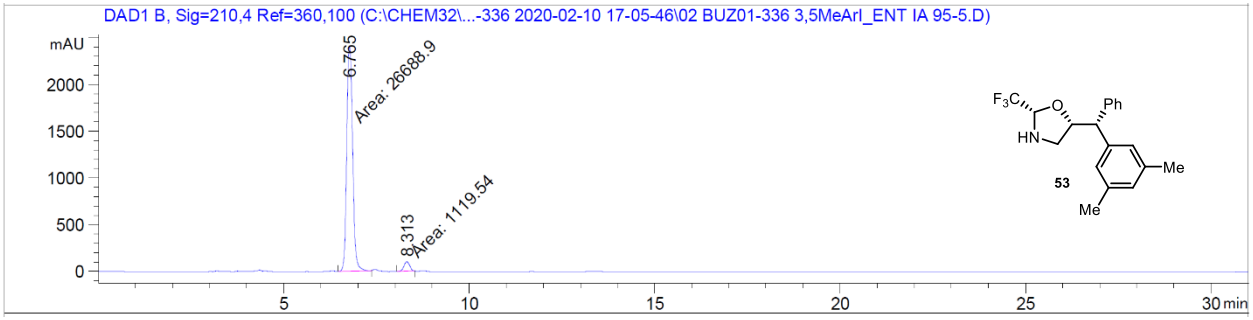


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.096	MM	0.1890	5202.46631	458.81155	86.2147
2	14.014	MM	0.3175	831.84991	43.66858	13.7853

Chiral HPLC Daicel Chiralpak IA column: 95:5 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

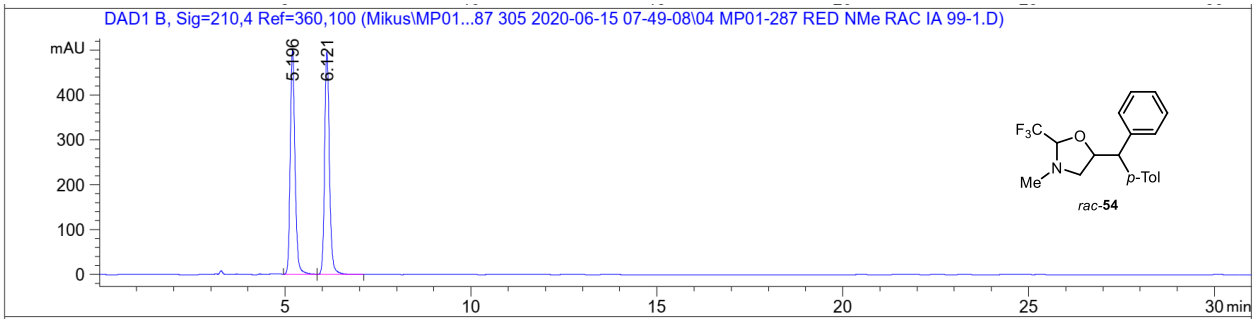


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.773	MM	0.1634	1.69449e4	1728.24072	49.3852
2	8.299	MM	0.1987	1.73668e4	1456.82104	50.6148

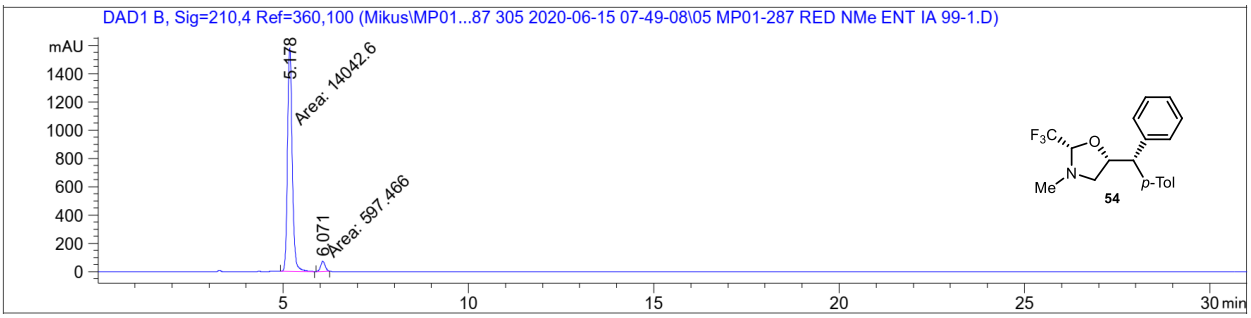


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.765	MM	0.1844	2.66889e4	2411.76831	95.9741
2	8.313	MM	0.1797	1119.54456	103.83485	4.0259

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

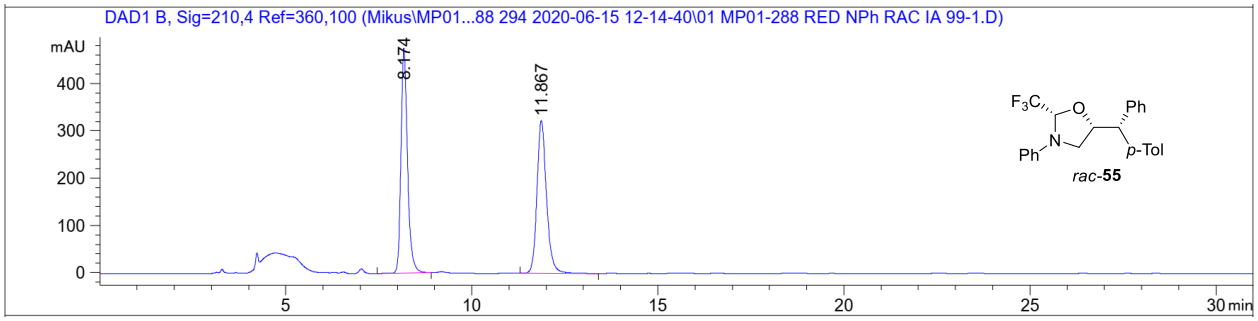


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.196	BB	0.1356	4445.54395	500.47305	50.0060
2	6.121	BB	0.1365	4444.47119	496.40112	49.9940

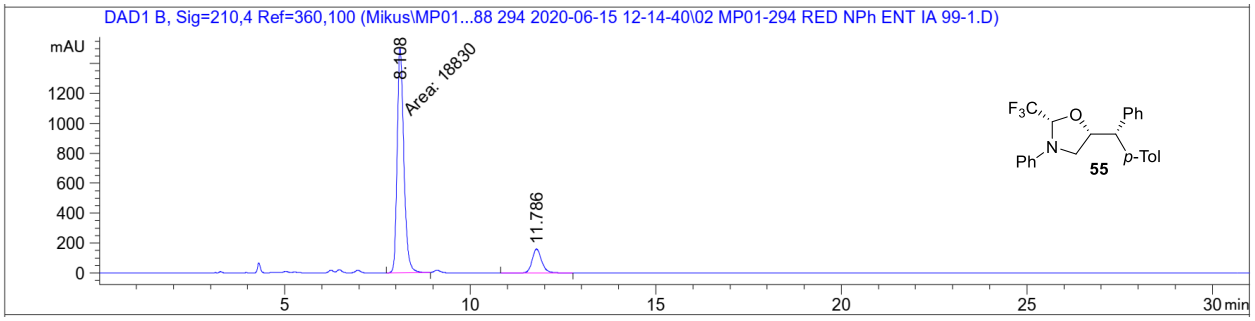


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	5.178	MM	0.1481	1.40426e4	1580.53882	95.9190
2	6.071	MM	0.1387	597.46625	71.80195	4.0810

Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 210 nm



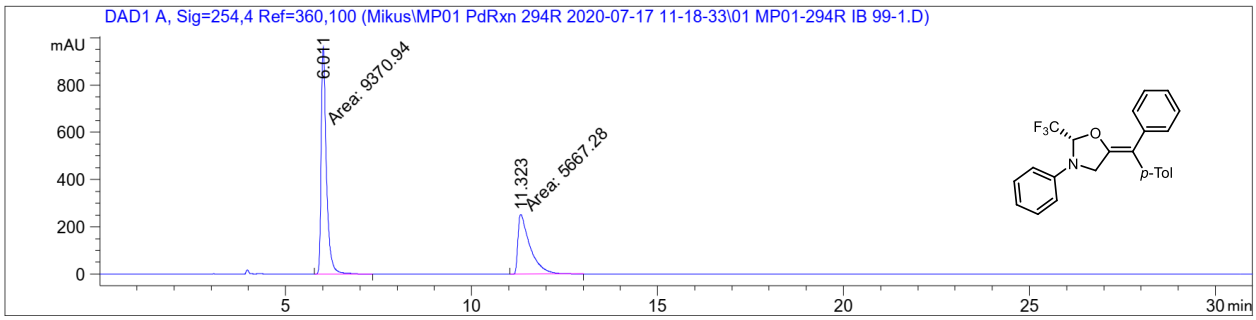
Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.174	BB	0.1844	5805.73877	475.57748	50.2076
2	11.867	BB	0.2702	5757.73145	322.67889	49.7924



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.108	MM	0.2087	1.88300e4	1504.10010	86.7448
2	11.786	BB	0.2707	2877.36133	160.87352	13.2552

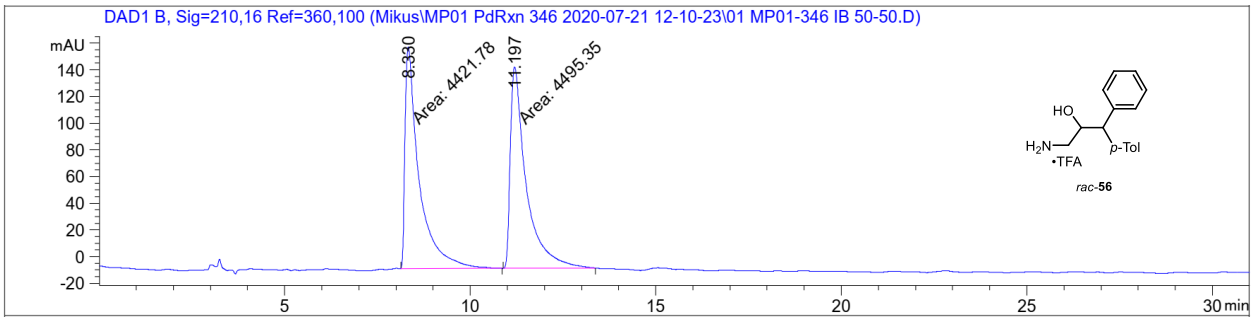
Chiral HPLC Daicel Chiralpak IB N-5 column: 99:1 hexane/IPA, flow rate 1 mL/min, λ = 210 nm

(Recovered from the reduction)

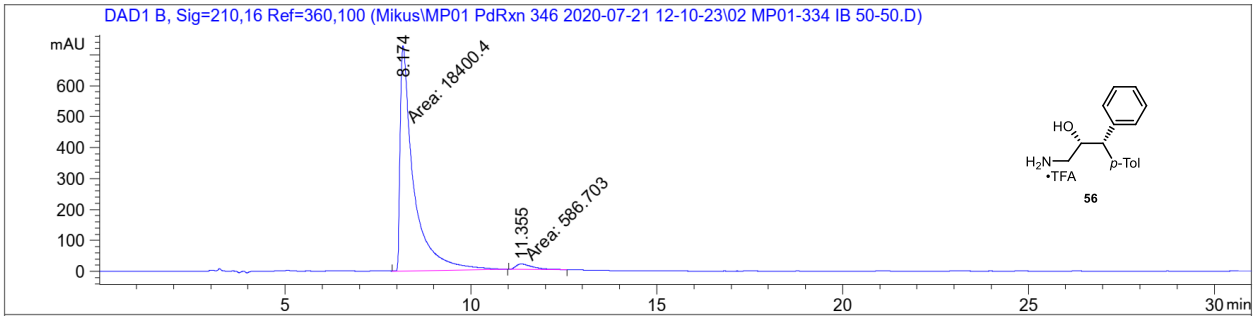


Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	6.011	MM	0.1628	9370.93945	959.58252	62.3142
2	11.323	MM	0.3742	5667.27588	252.38786	37.6858

Chiral HPLC Daicel Chiralpak IA column: 80:20 hexane/IPA, flow rate 1 mL/min, λ = 210 nms



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.330	MM	0.4435	4421.77979	166.16771	49.5875
2	11.197	MM	0.4967	4495.35107	150.85443	50.4125



Peak #	RetTime [min]	Type	Width [min]	Area [mAU*s]	Height [mAU]	Area %
1	8.174	MM	0.4213	1.84004e4	727.84509	96.9100
2	11.355	MM	0.5534	586.70251	17.67097	3.0900