



Supporting Information

for

Asymmetric synthesis of fluorinated derivatives of aromatic and γ -branched amino acids via a chiral Ni(II) complex

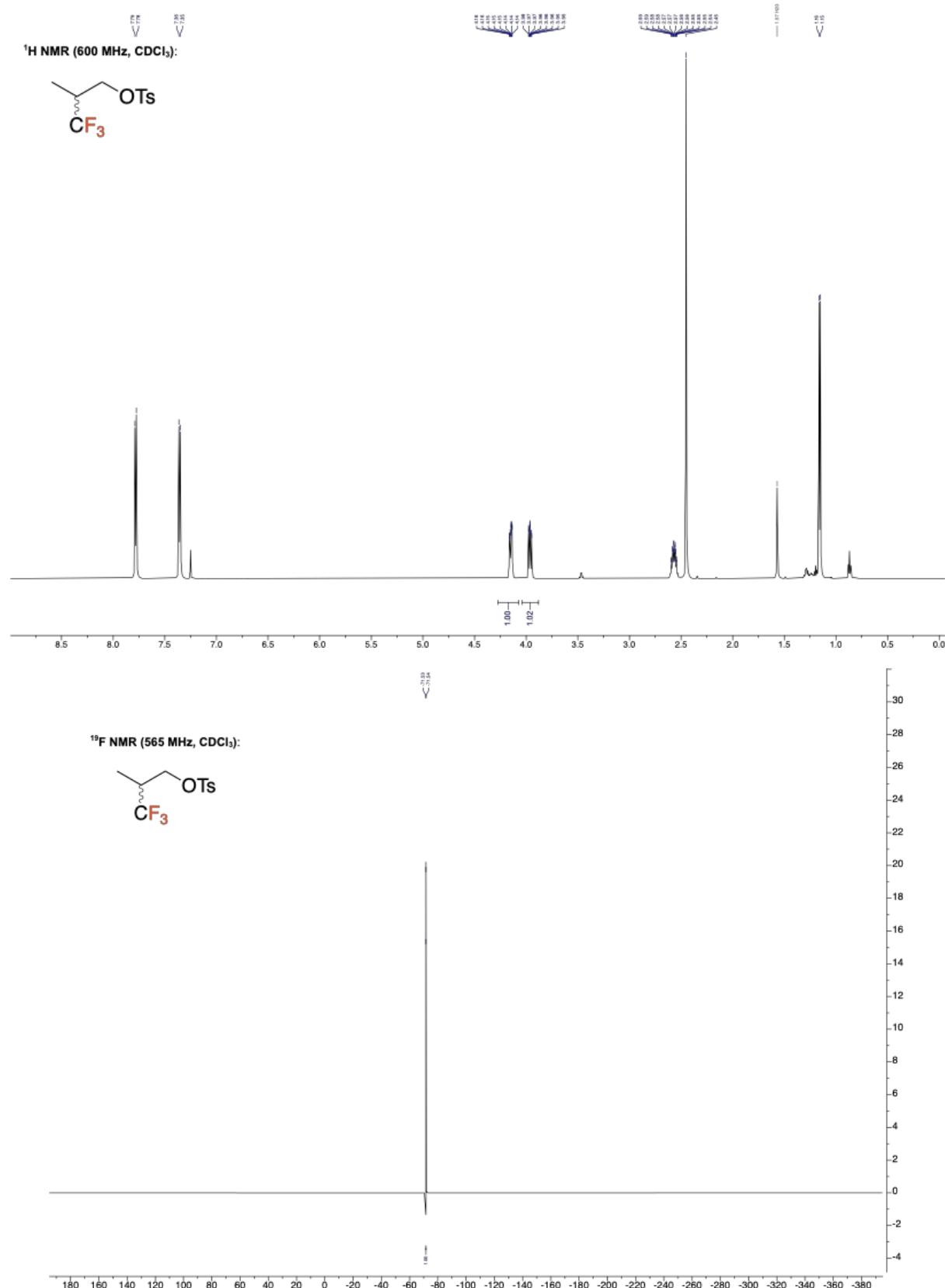
Maurizio Iannuzzi, Thomas Hohmann, Michael Dyrks, Kilian Haoues,
Katarzyna Salamon-Krokosz and Beate Koksch

Beilstein J. Org. Chem. **2025**, 21, 659–669. doi:10.3762/bjoc.21.52

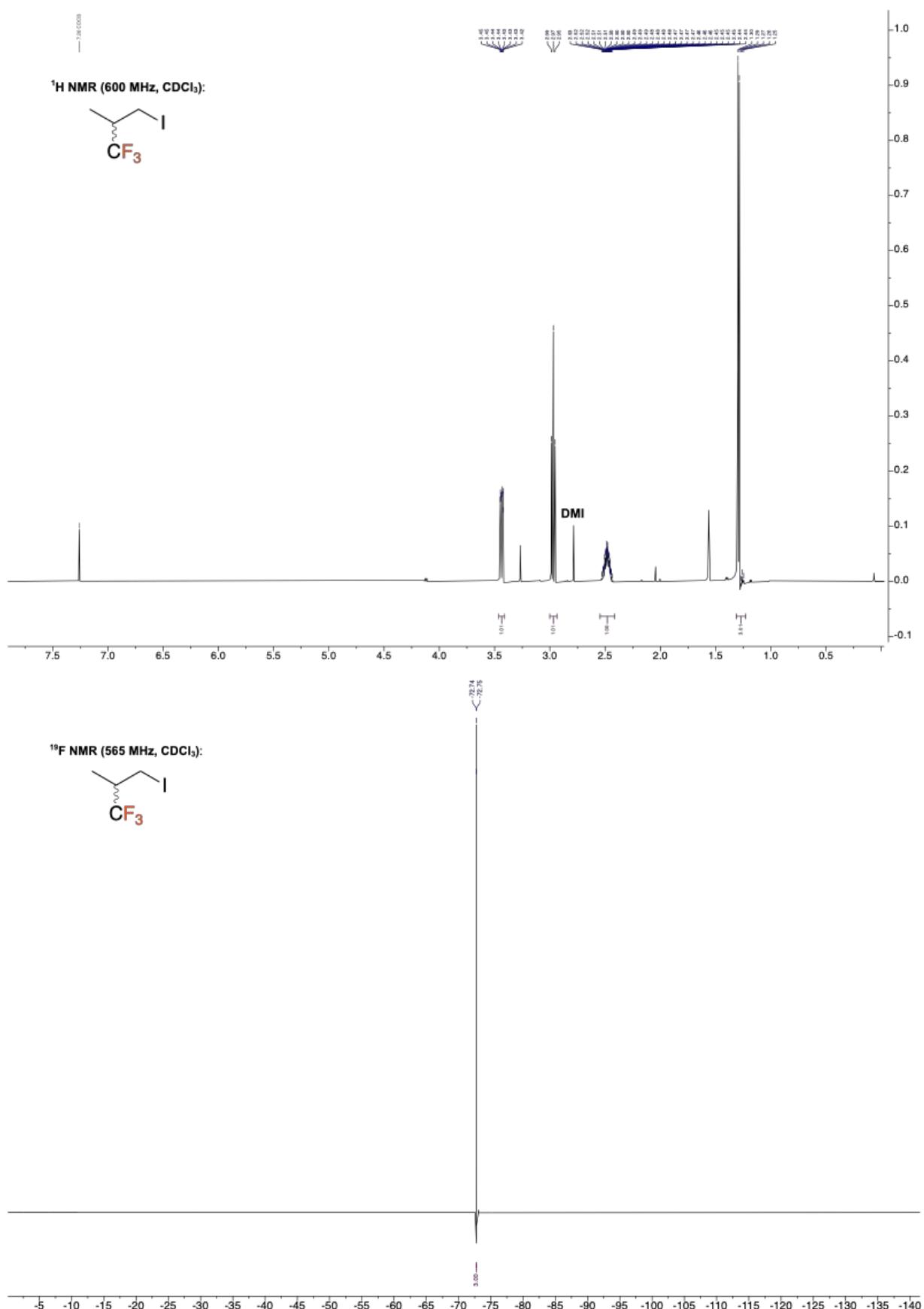
NMR spectra and HPLC chromatograms

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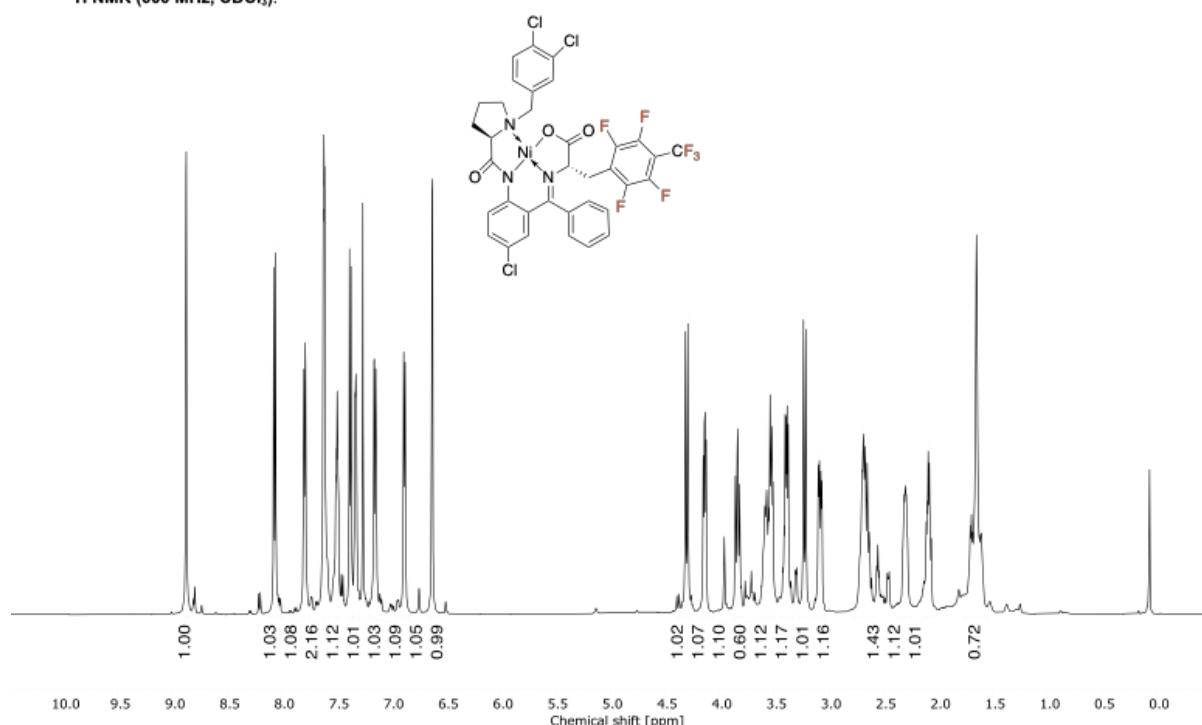
3,3,3-Trifluoro-2-methylpropyl 4-methylbenzene-1-sulfonate (**9**)



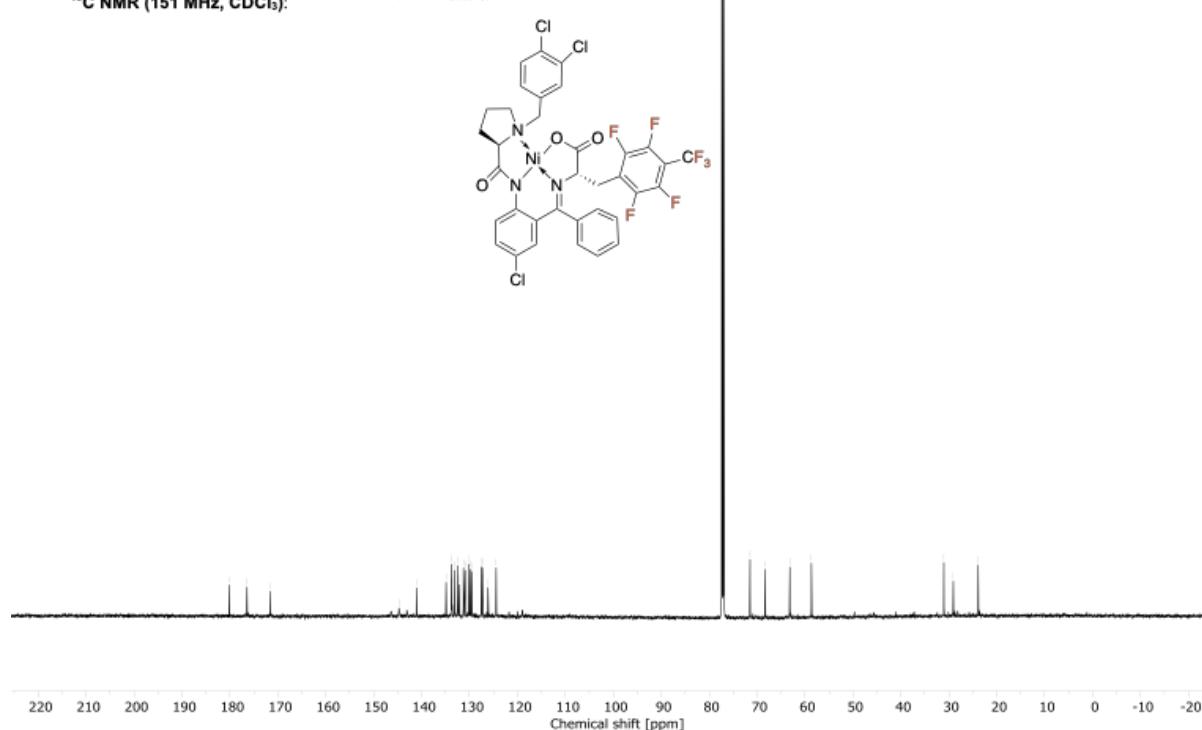
1,1,1-Trifluoro-3-iodo-2-methylpropane (10)



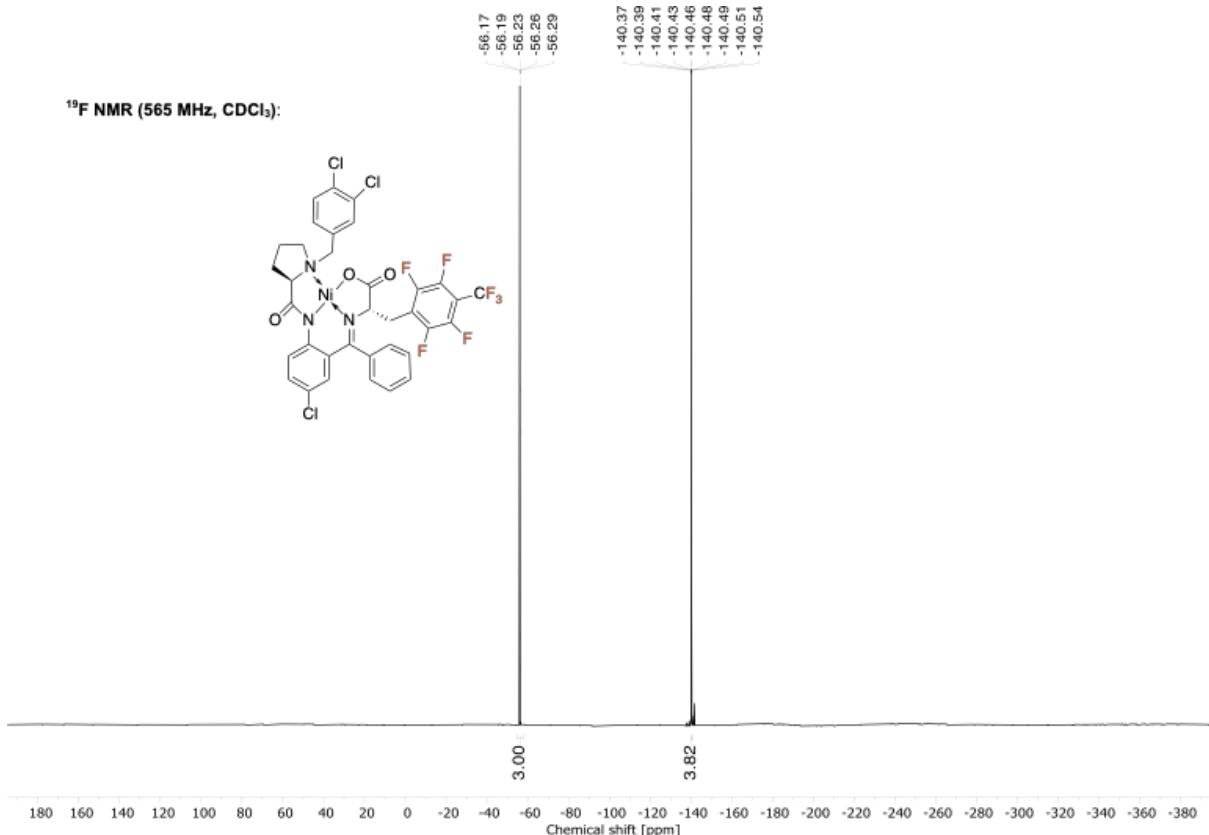
Ni(II)-Schiff base complex of [2.3.5.6F]TfMePhe 6



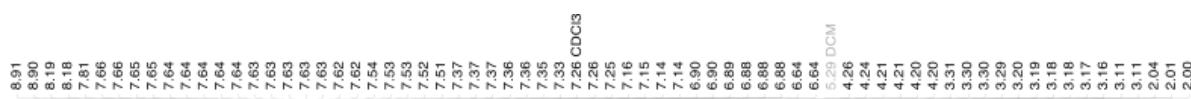
¹³C NMR (151 MHz, CDCl₃): δ 18.0, 17.7, 17.5, 14.4, 13.9, 13.8, 13.7, 13.6, 13.5, 13.4, 13.3, 13.2, 13.1, 13.0, 12.9, 12.8, 12.7, 12.6, 12.5, 12.4, 12.3, 12.2, 12.1, 12.0, 11.9, 11.8, 11.7, 11.6, 11.5, 11.4, 11.3, 11.2, 11.1, 11.0, 10.9, 10.8, 10.7, 10.6, 10.5, 10.4, 10.3, 10.2, 10.1, 10.0, 9.9, 9.8, 9.7, 9.6, 9.5, 9.4, 9.3, 9.2, 9.1, 9.0, 8.9, 8.8, 8.7, 8.6, 8.5, 8.4, 8.3, 8.2, 8.1, 8.0, 7.9, 7.8, 7.7, 7.6, 7.5, 7.4, 7.3, 7.2, 7.1, 7.0, 6.9, 6.8, 6.7, 6.6, 6.5, 6.4, 6.3, 6.2, 6.1, 6.0, 5.9, 5.8, 5.7, 5.6, 5.5, 5.4, 5.3, 5.2, 5.1, 5.0, 4.9, 4.8, 4.7, 4.6, 4.5, 4.4, 4.3, 4.2, 4.1, 4.0, 3.9, 3.8, 3.7, 3.6, 3.5, 3.4, 3.3, 3.2, 3.1, 3.0, 2.9, 2.8, 2.7, 2.6, 2.5, 2.4, 2.3, 2.2, 2.1, 2.0, 1.9, 1.8, 1.7, 1.6, 1.5, 1.4, 1.3, 1.2, 1.1, 1.0, 0.9, 0.8, 0.7, 0.6, 0.5, 0.4, 0.3, 0.2, 0.1, 0.0.



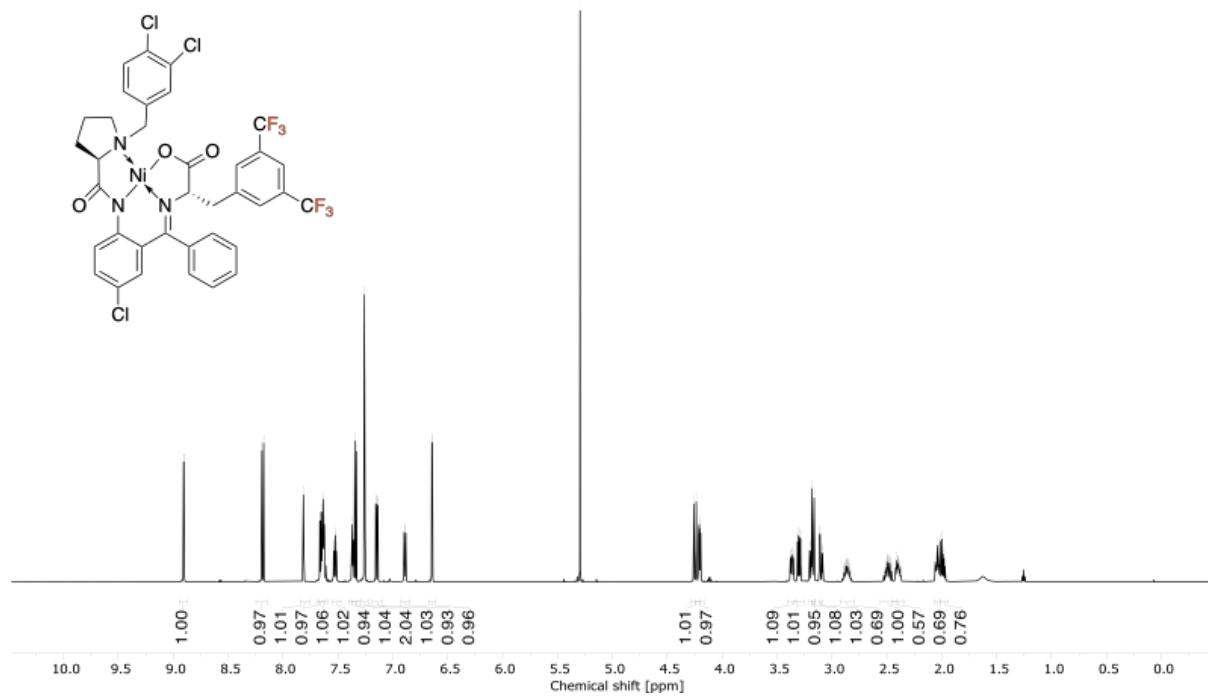
¹⁹F NMR (565 MHz, CDCl₃):



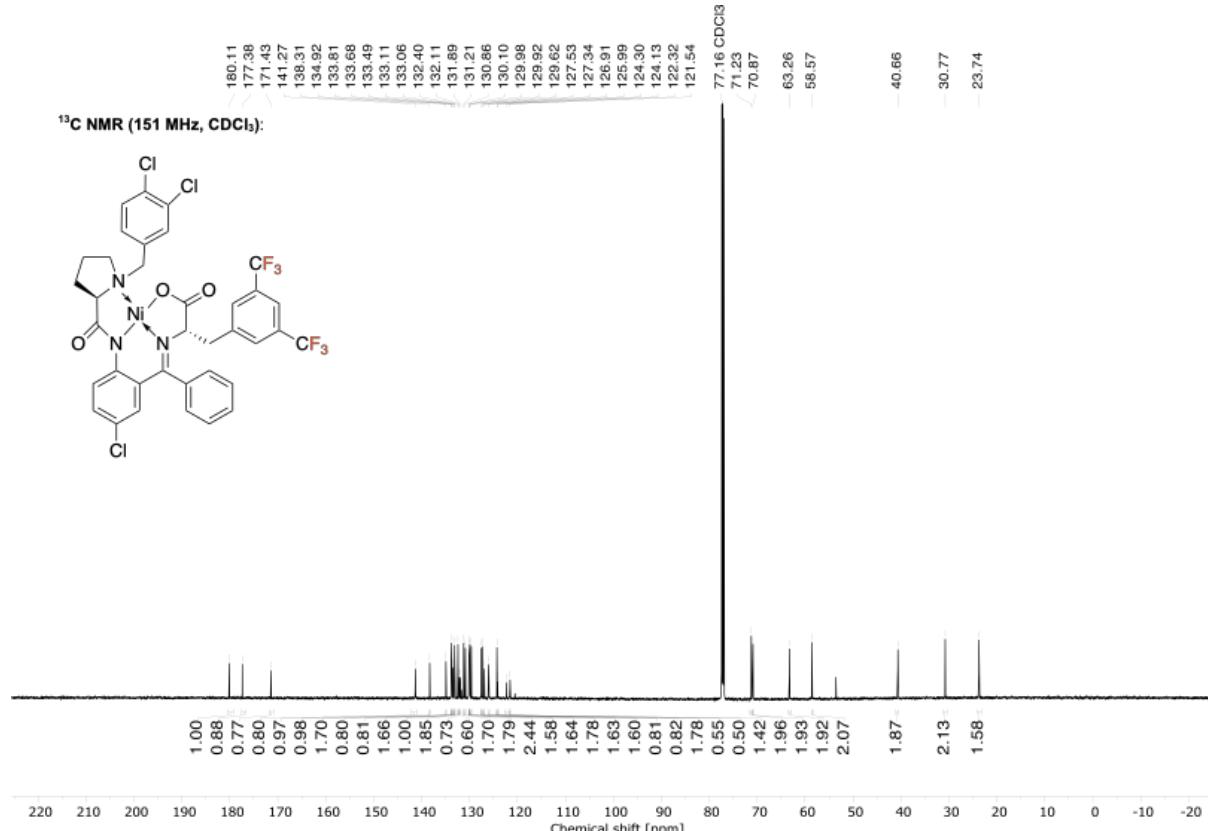
Ni(II)-Schiff base complex of bisTfMePhe 7



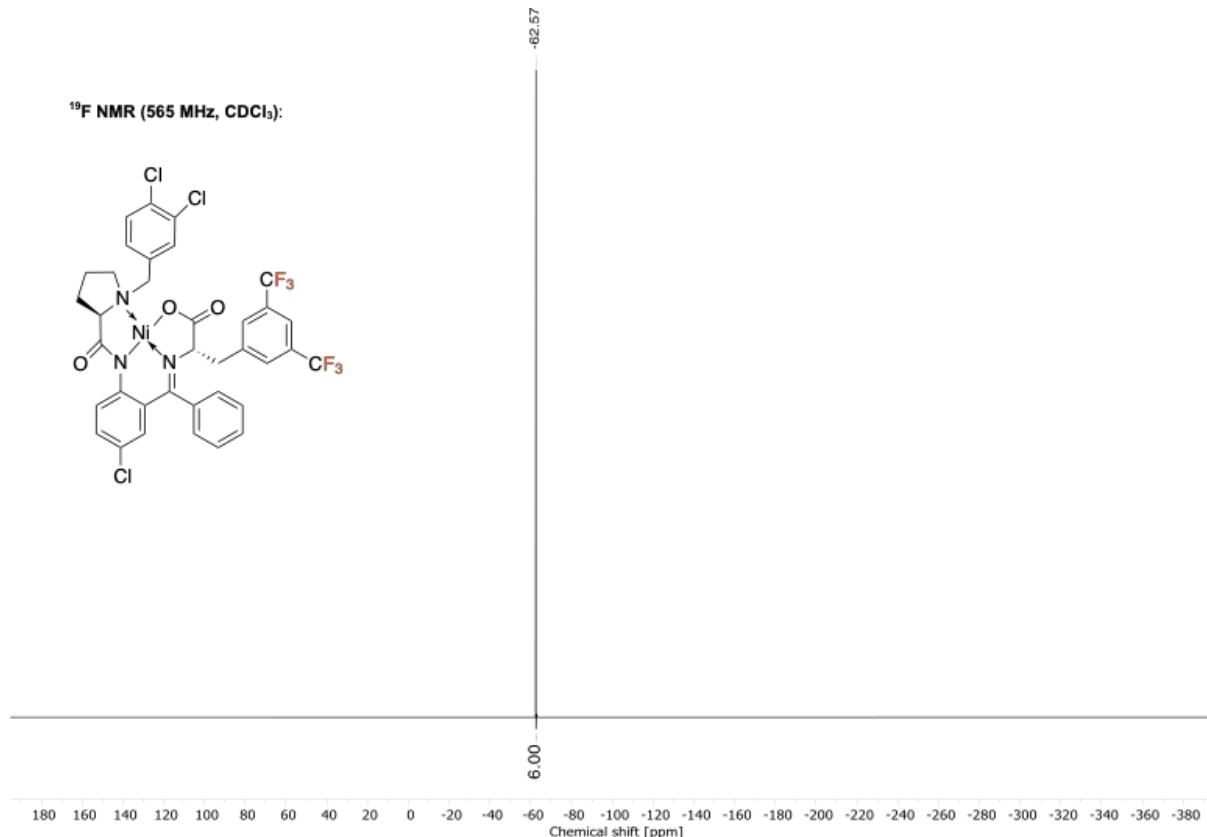
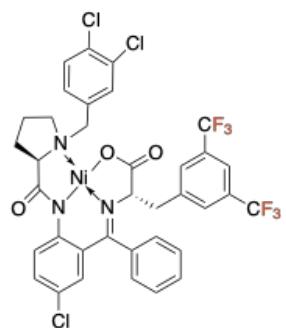
¹H NMR (600 MHz, CDCl₃):



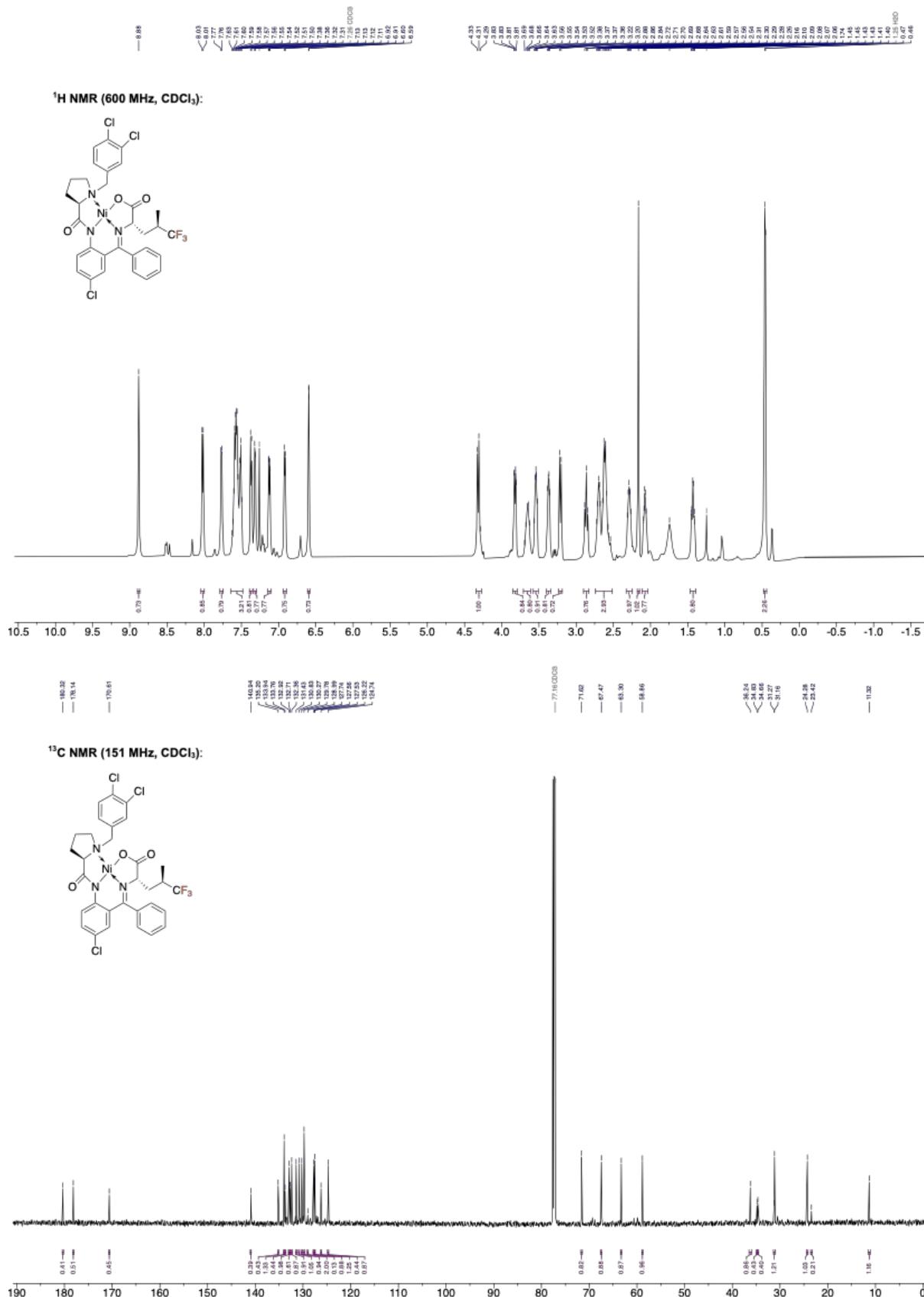
¹³C NMR (151 MHz, CDCl₃):



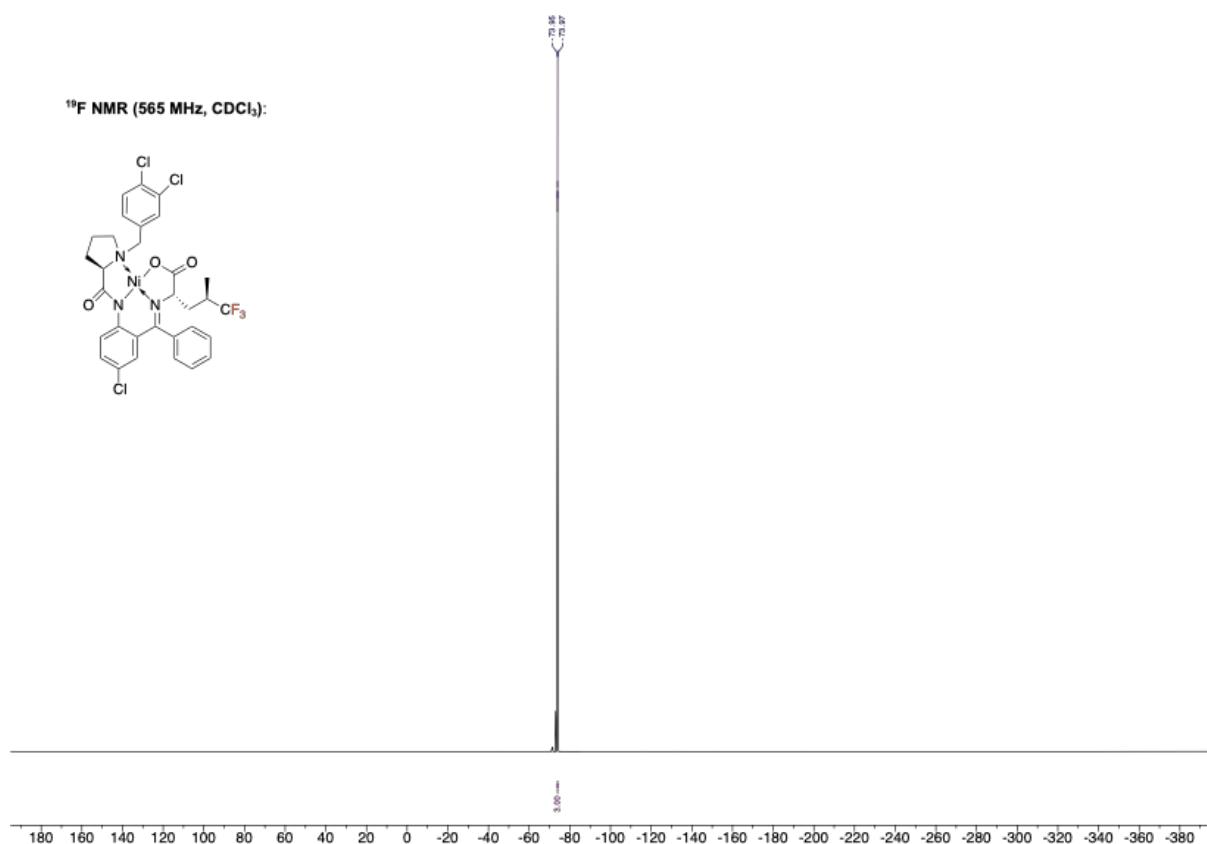
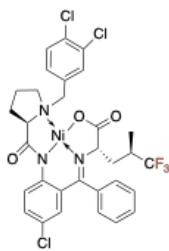
¹⁹F NMR (565 MHz, CDCl₃):



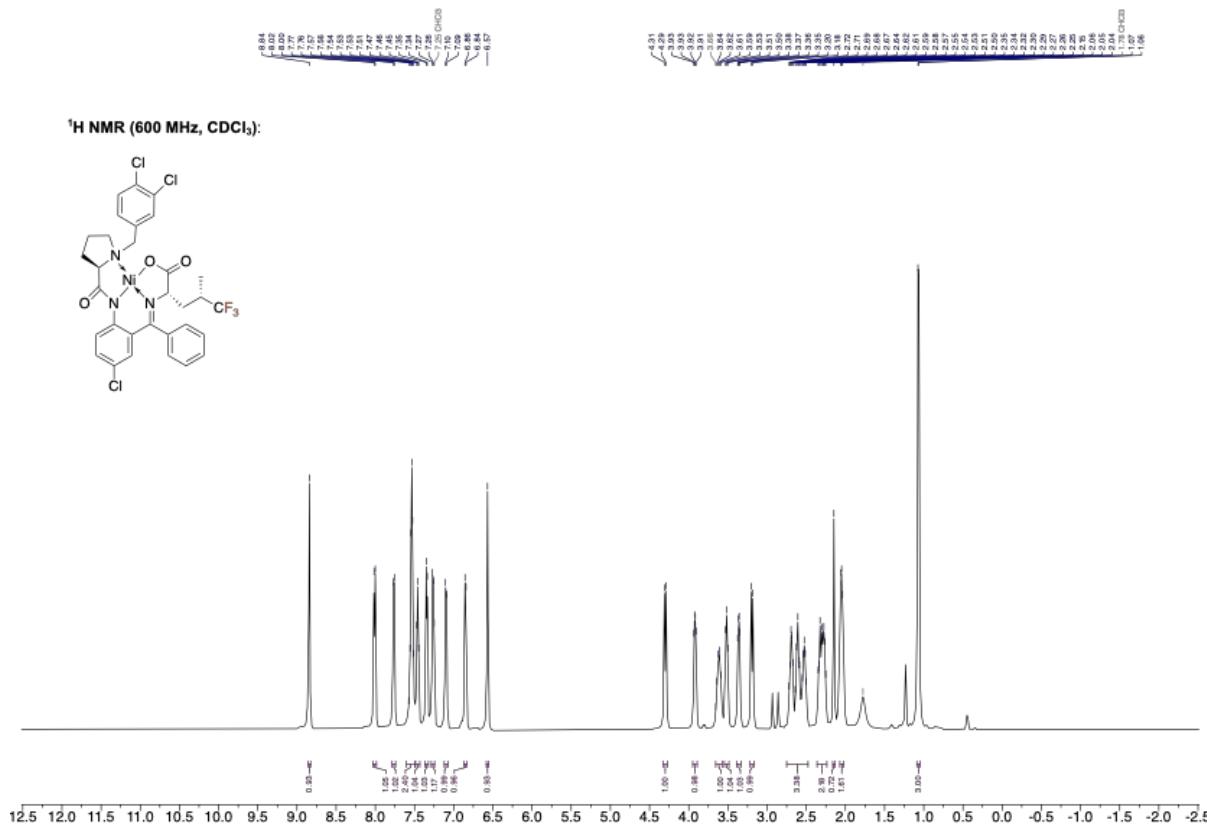
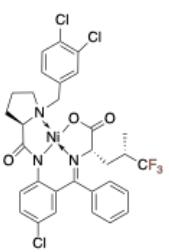
Ni(II)-Schiff base complexes of (2S,4R)-TfLeu 11a, (2S,4S)-TfLeu 11b

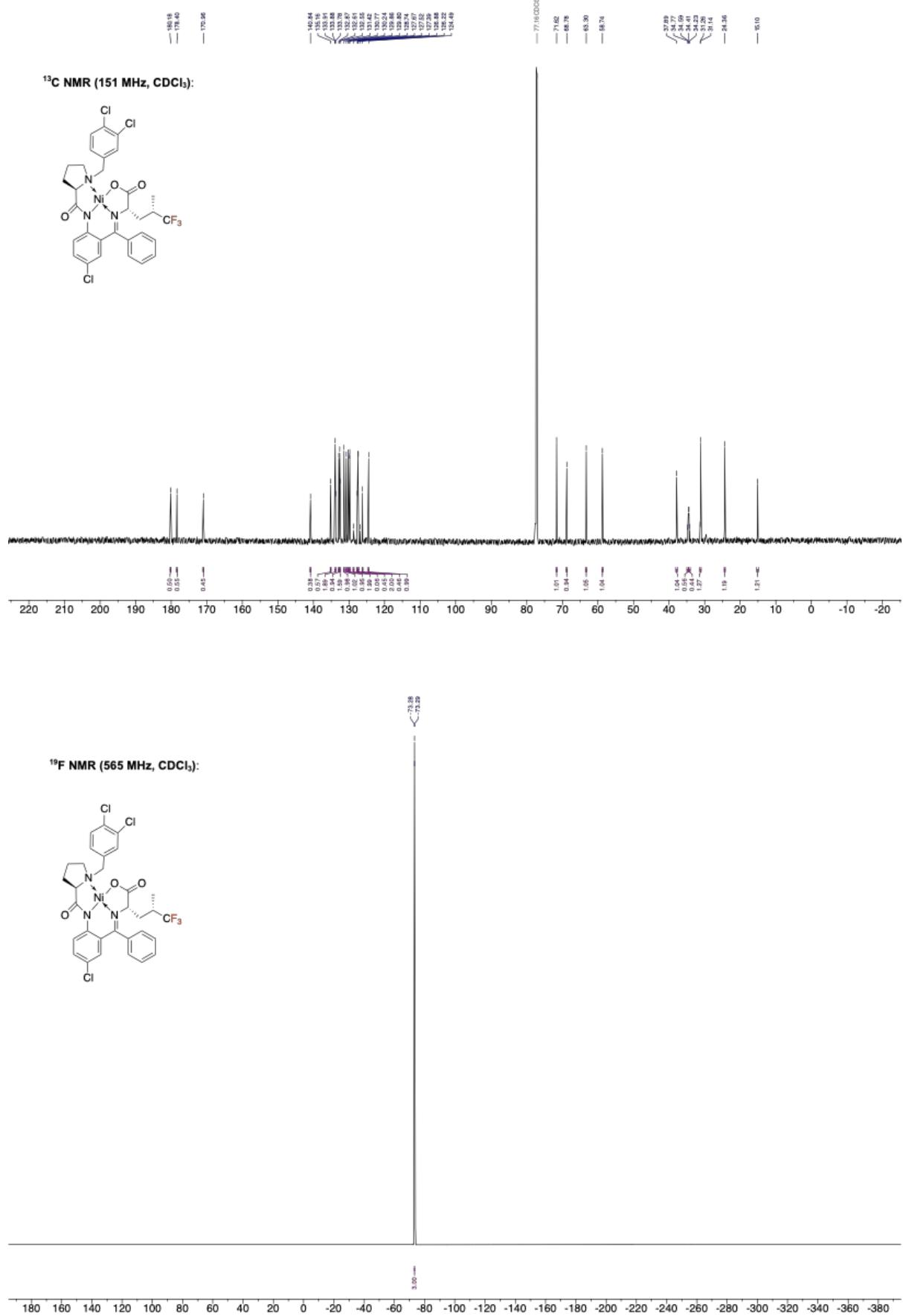


¹⁹F NMR (565 MHz, CDCl₃):

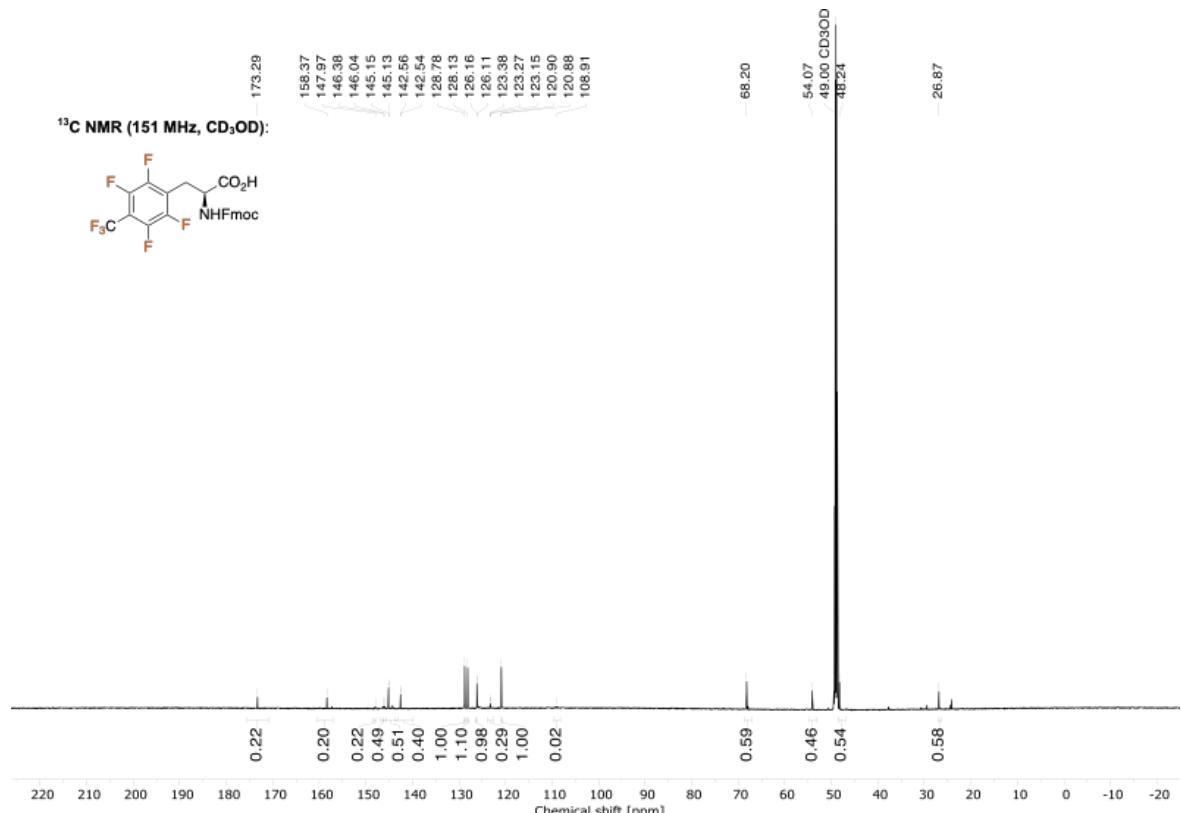
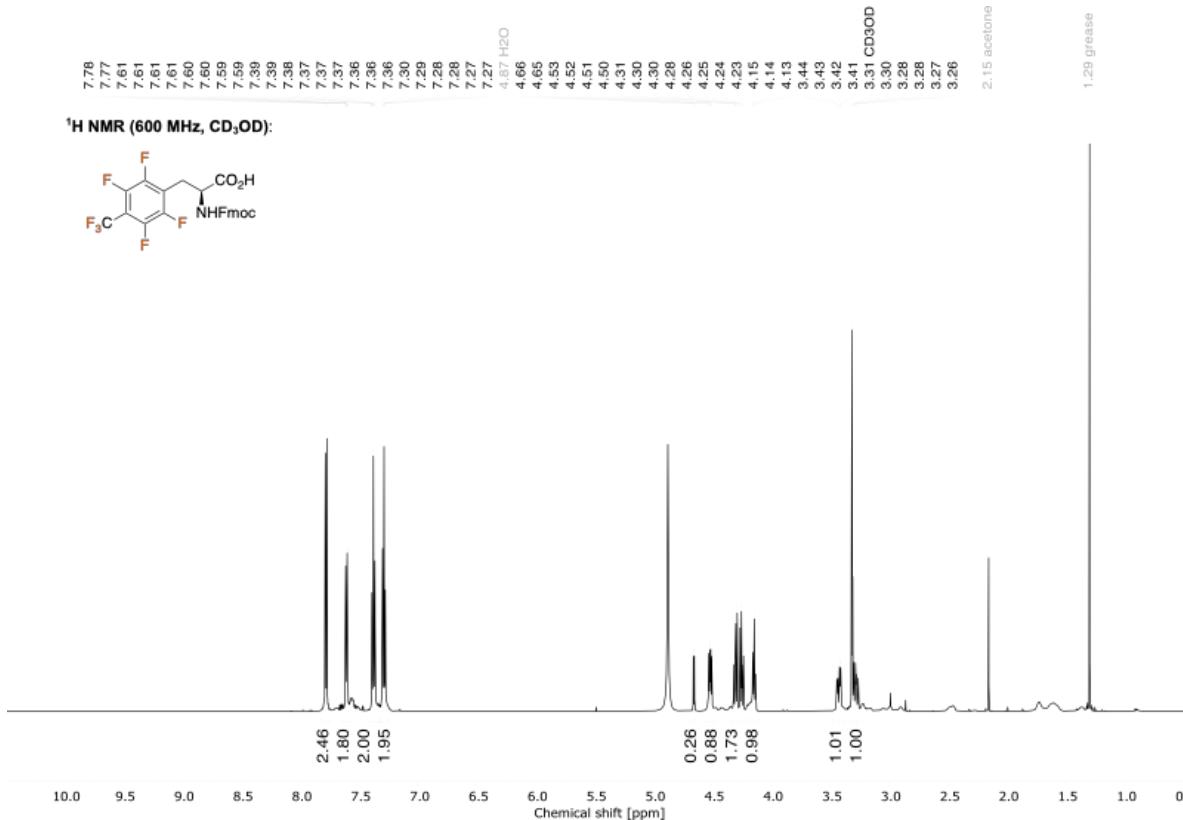


¹H NMR (600 MHz, CDCl₃):

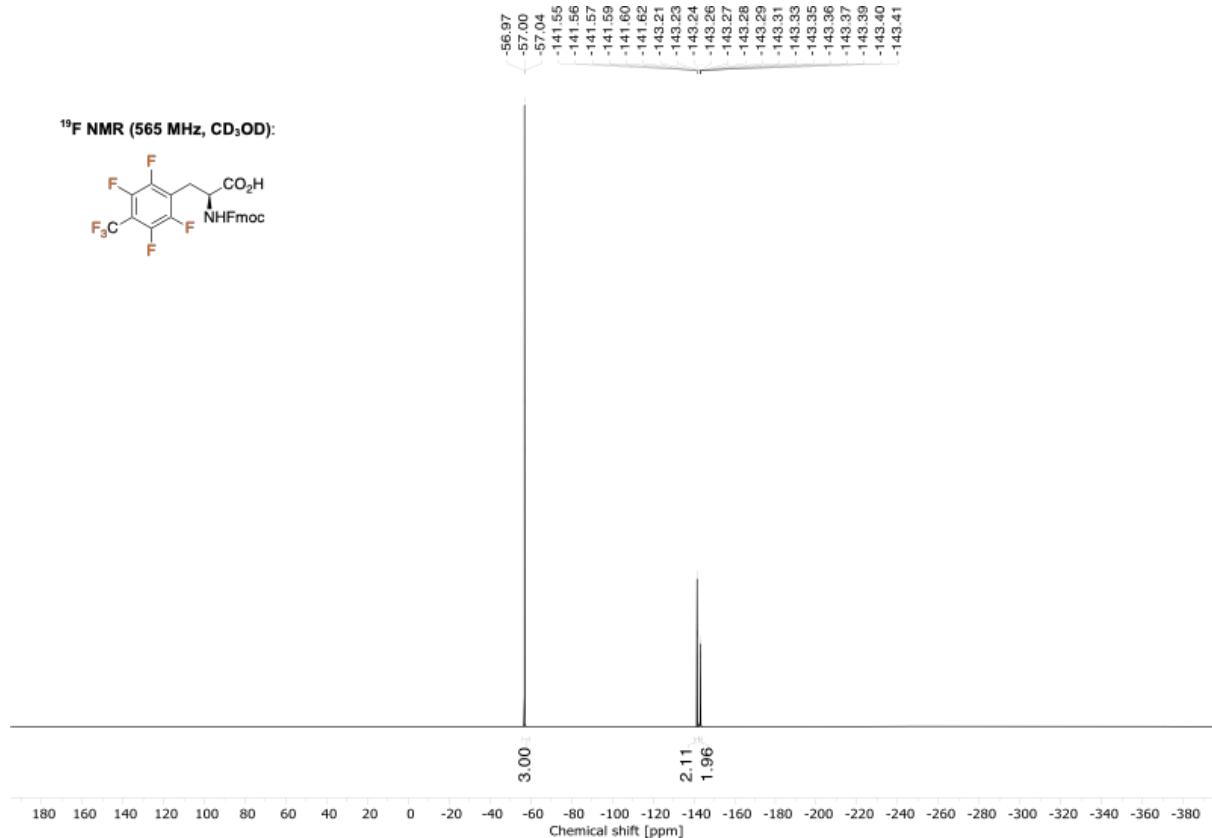




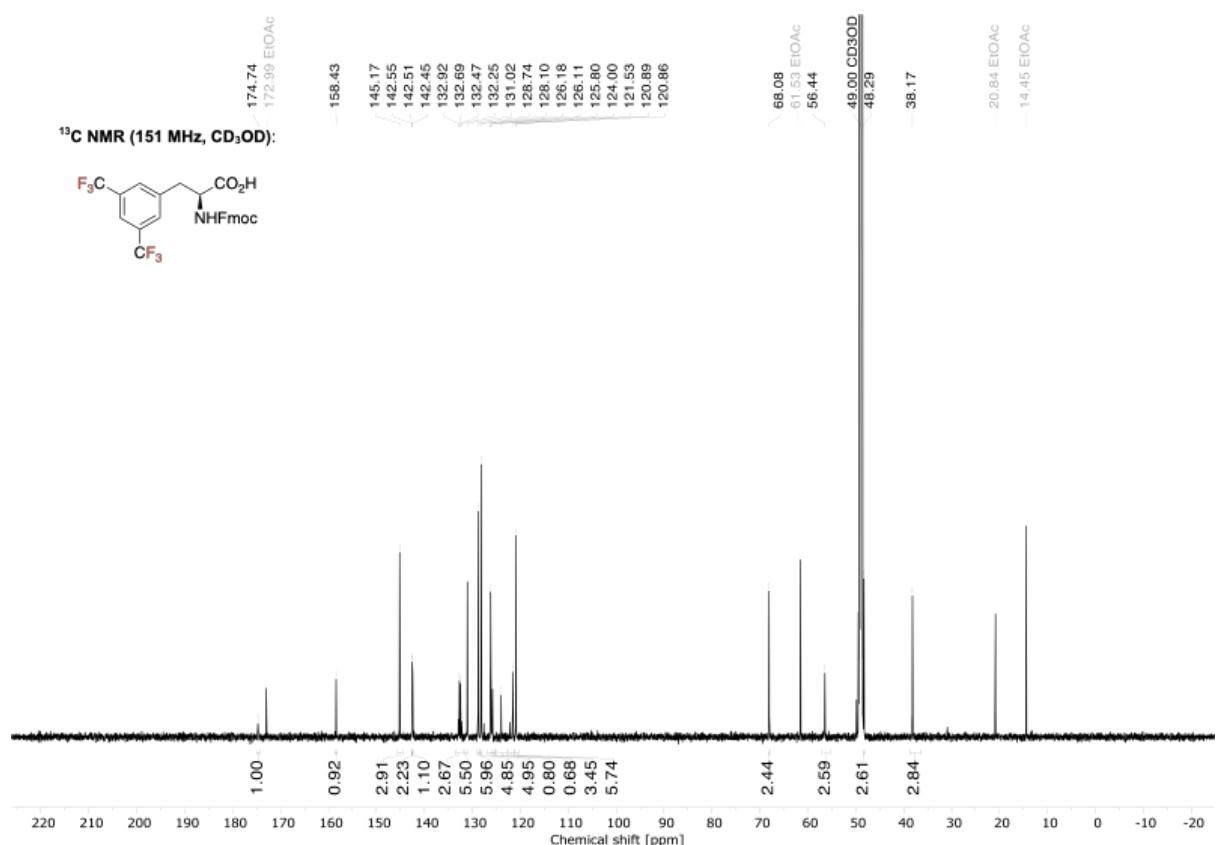
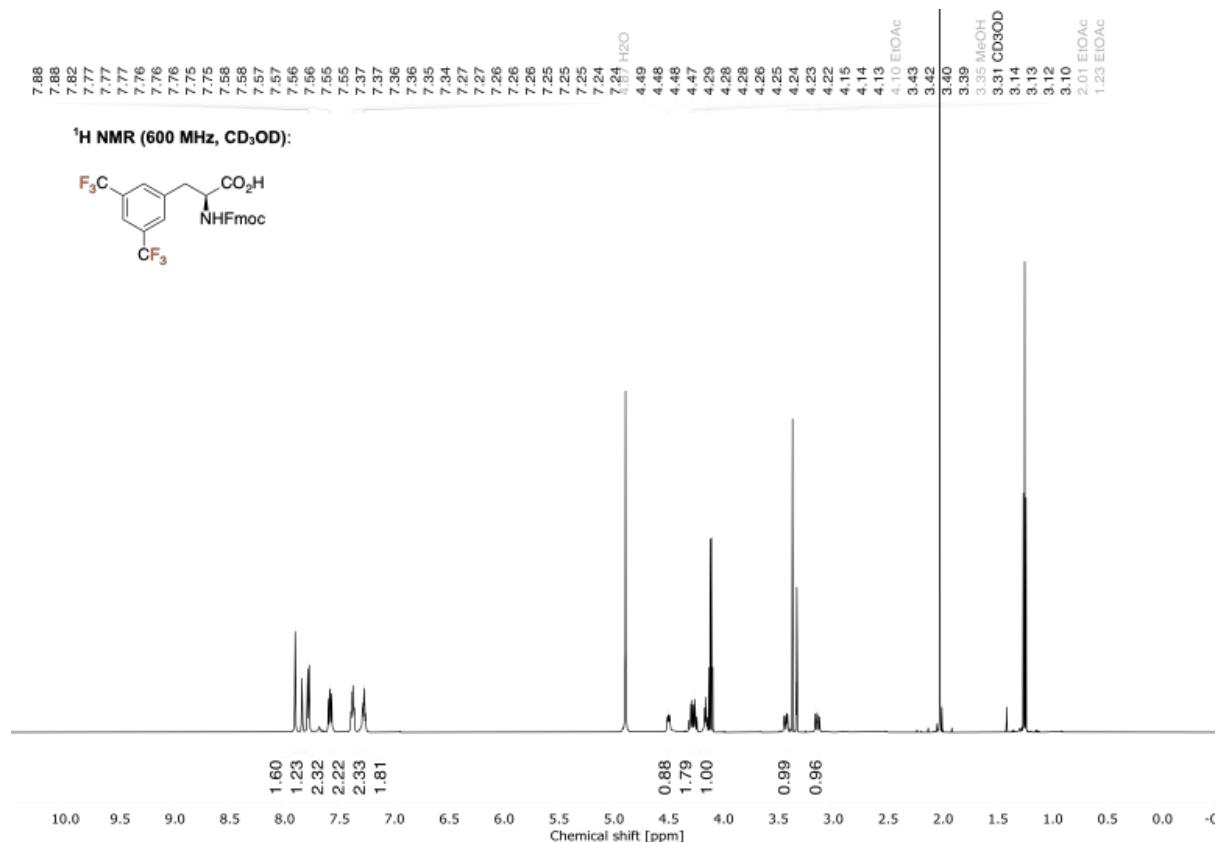
(S)-2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(2,3,5,6-tetrafluoro-4-(trifluoromethyl)phenyl)propanoic acid [tetrafluoro(trifluoromethyl)phenylalanine, [2.3.5.6F]TfMePhe] 2



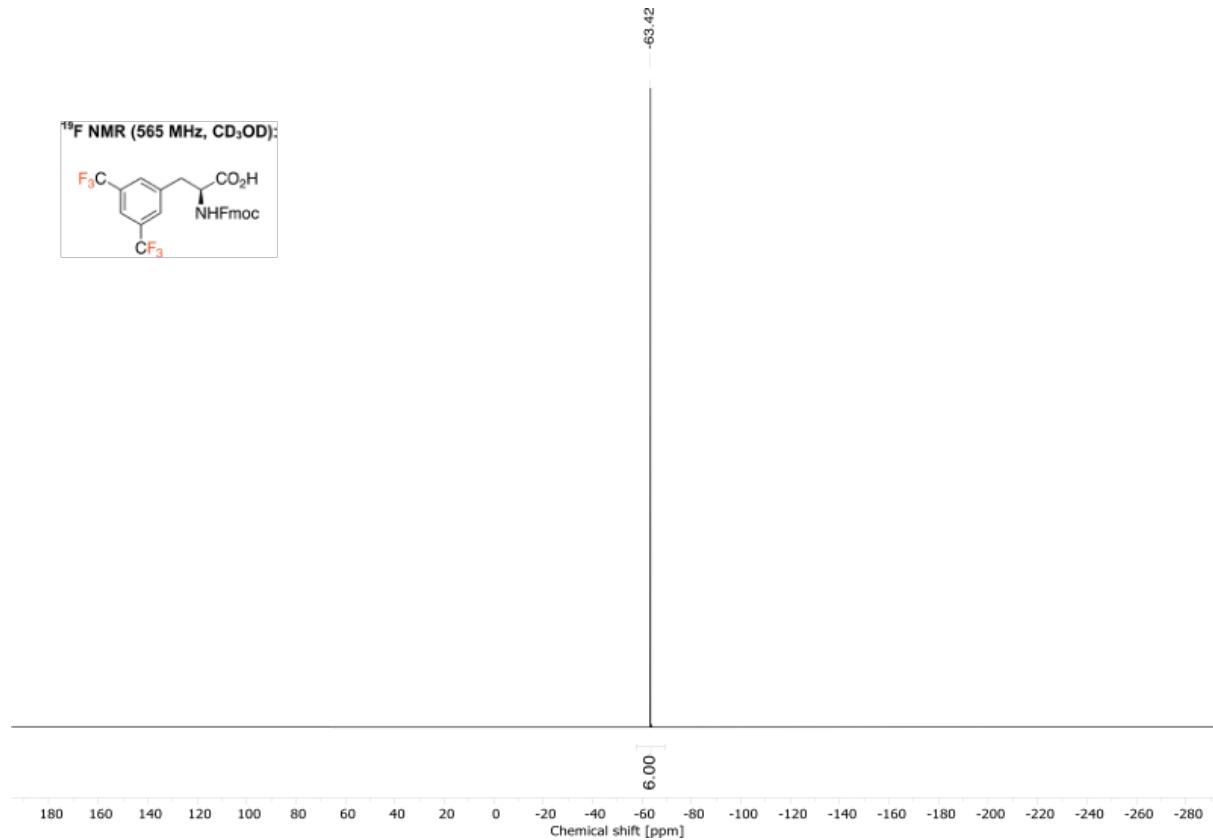
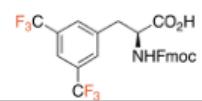
¹⁹F NMR (565 MHz, CD₃OD):



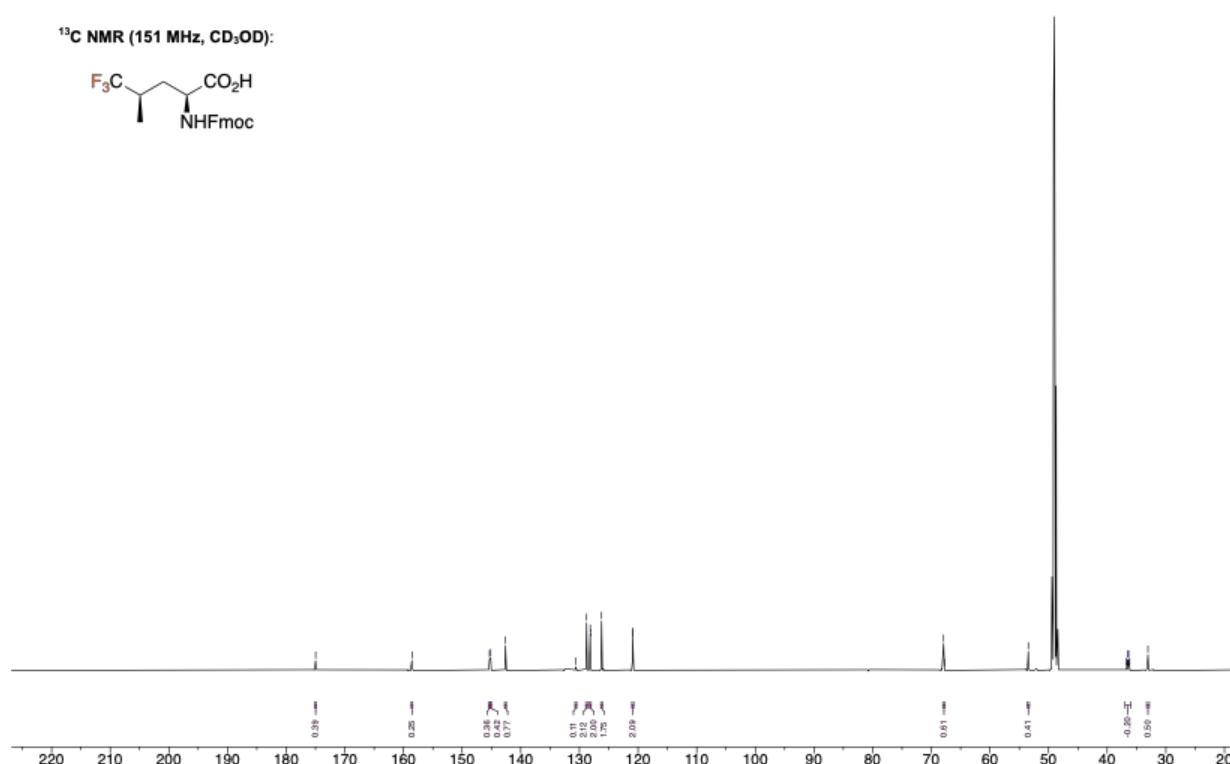
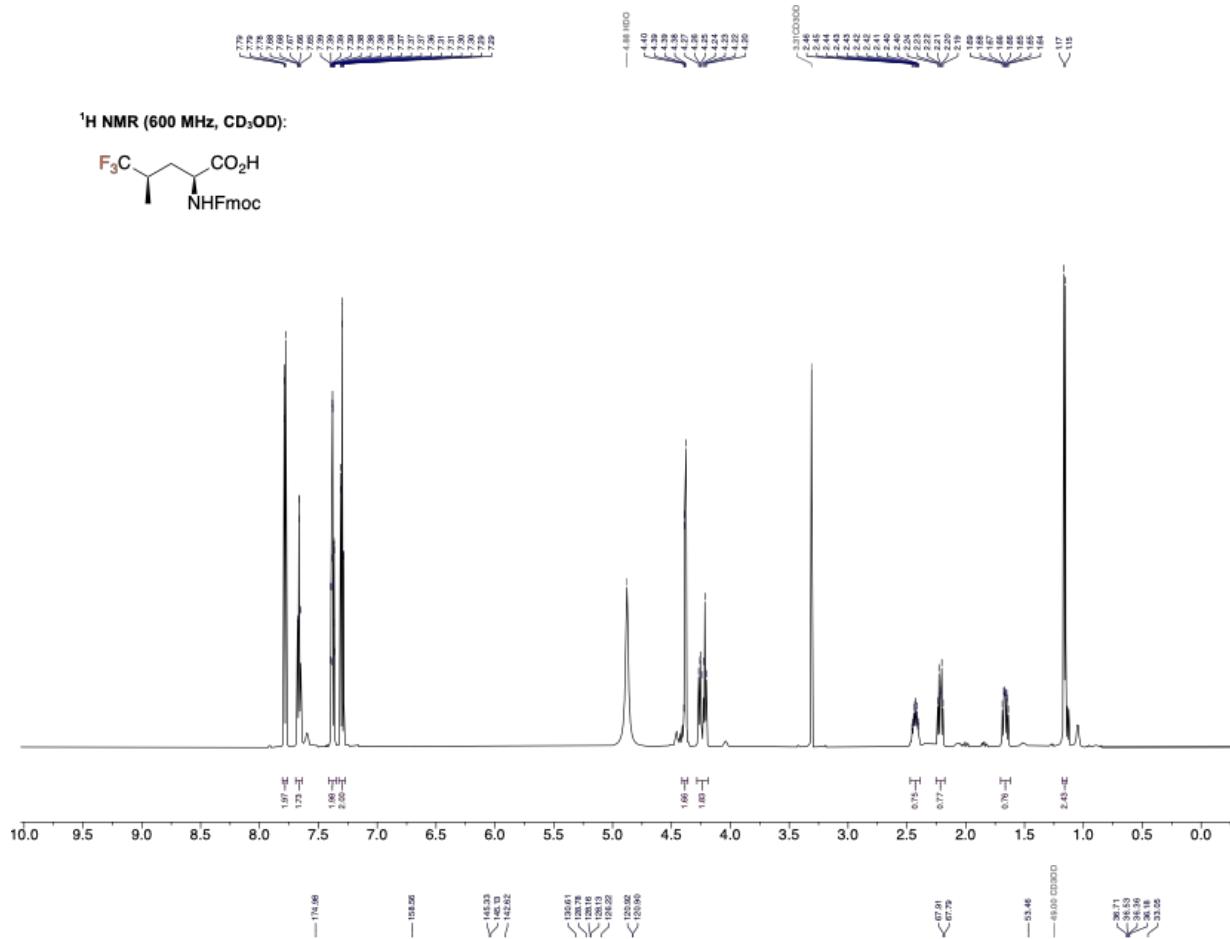
(S)-2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-3-(3,5-bis(trifluoromethyl)phenyl)propanoic acid [bis(trifluoromethyl)phenylalanine, bisTfMePhe] 3



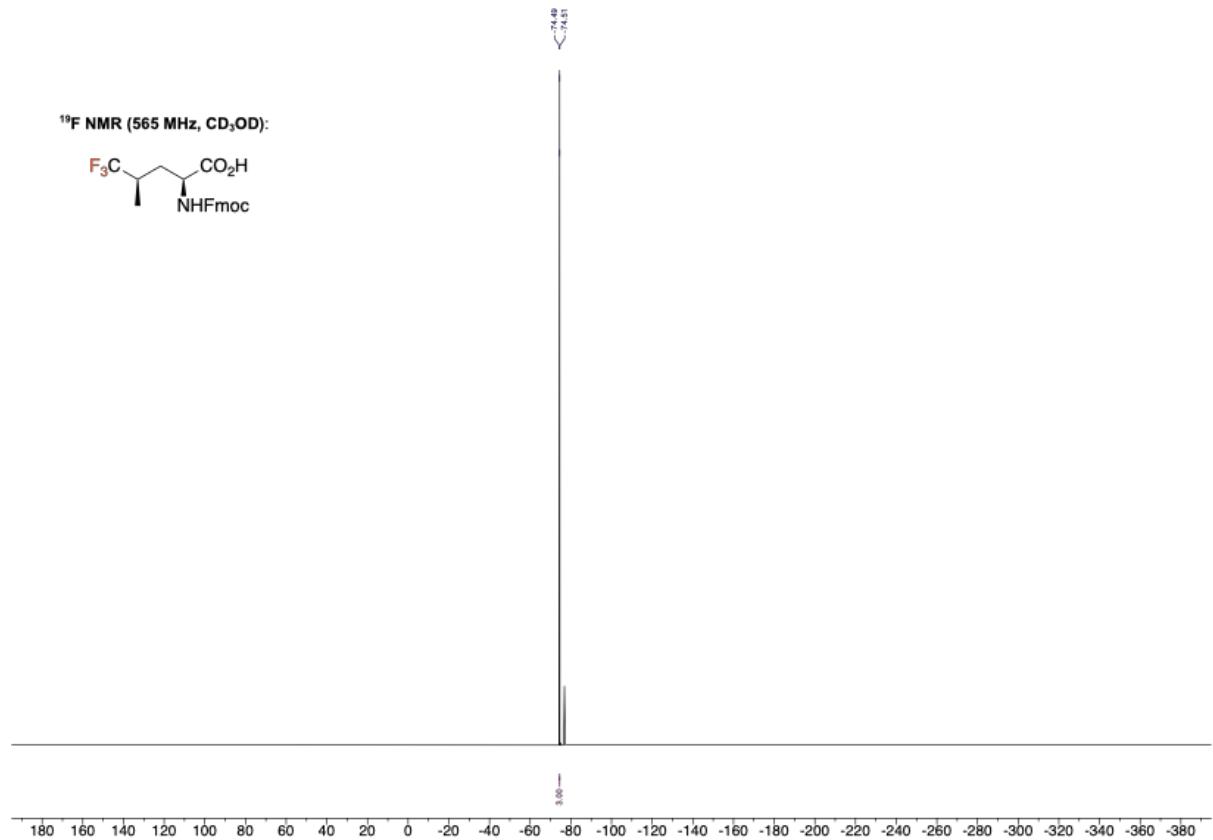
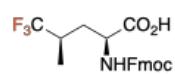
¹⁹F NMR (565 MHz, CD₃OD):

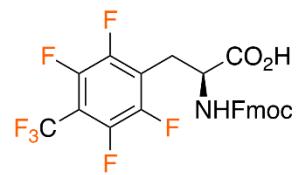
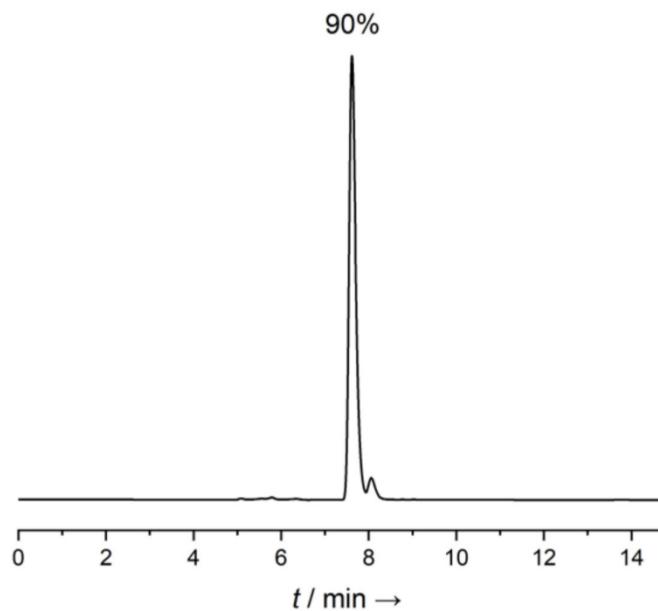


(2S,4R)-2-(((9H-fluoren-9-yl)methoxy)carbonyl)amino)-5,5,5-trifluoro-4-methylpentanoic acid
[Trifluoroleucine, TfLeu] 12a

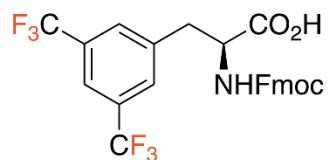
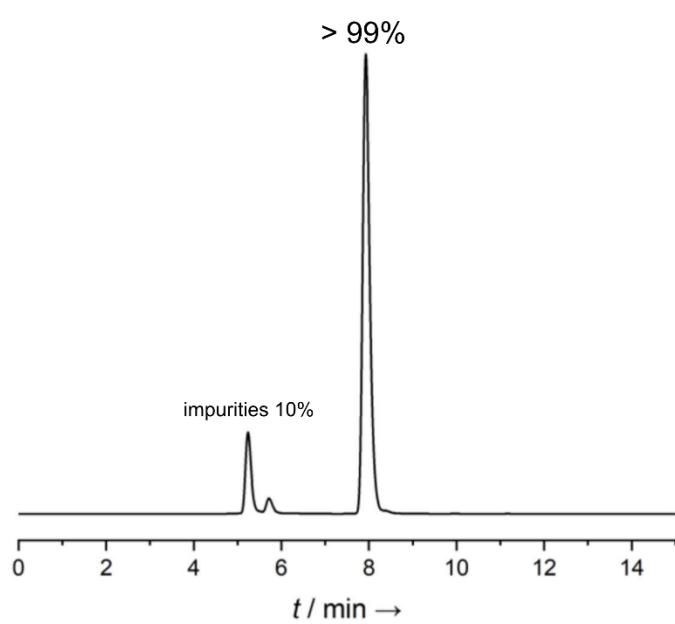


¹⁹F NMR (565 MHz, CD₃OD):

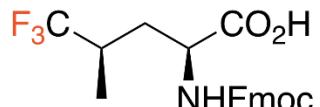
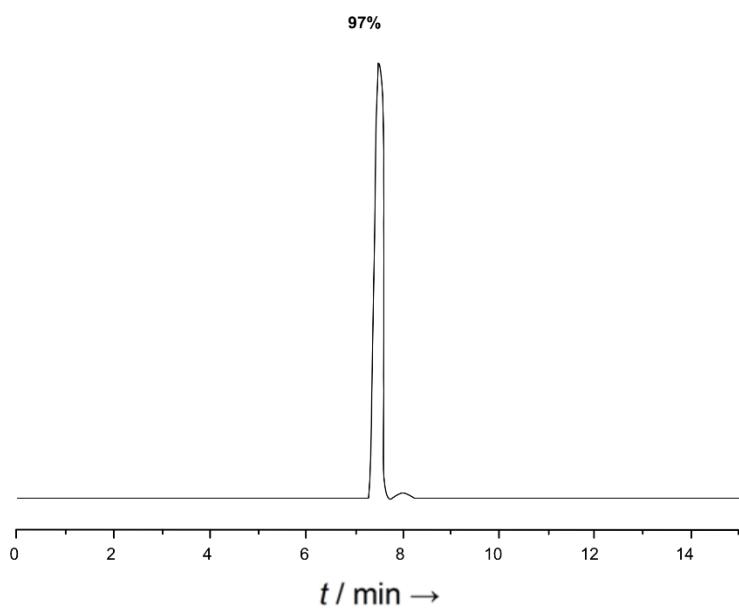




Chiral HPLC, Method:
MeCN:MeOH:H₂O = 148:850:2, 15 min



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MeCN:MeOH:H₂O = 148:850:2, 15 min



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MeCN:MeOH:H₂O = 148:850:2, 15 min

In order to validate the separation efficiency of the HPLC method to determine the enantiomeric purity of the fluorinated amino acids in our previous publication racemic mixtures of the corresponding fluorinated amino acids were prepared by a procedure described by Yamada et al. and subsequently analyzed [1].

References

1. Yamada, S.H., C.; Yoshioka, R.; Chibata, I. , *Method for the racemization of optically active amino acids*. Journal of Organic Chemistry, 1983. **48**(6): p. 843-846.