Supporting Information

Supramolecularly regulated copper-bisoxazoline catalysts for the efficient insertion of carbenoid species into hydroxyl bonds

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Supporting Information

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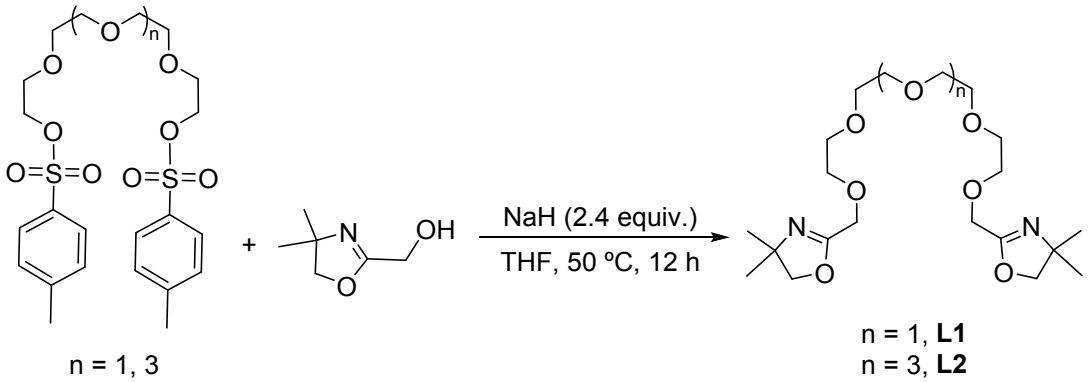
1. General remarks

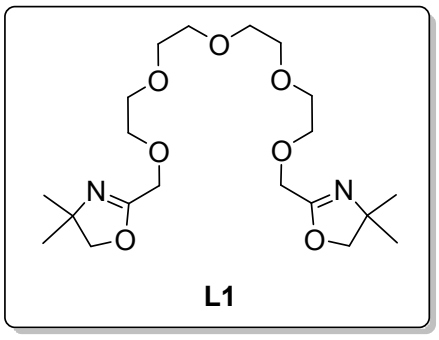
All syntheses were carried out using chemicals as purchased from commercial sources unless otherwise stated. Air- and moisture-sensitive manipulations or reactions were run under inert atmosphere, either in a N_2-filled glove box or with standard Schlenk techniques. Glassware was dried *in vacuo* before use with a hot air gun. All solvents were dried with a Solvent Purification System (SPS) and thoroughly deoxygenated by freeze-thaw cycles. Silica gel 60 Å (230 − 400 mesh particle size) was used for column chromatography, unless otherwise stated. NMR spectra were recorded at room temperature in 400 MHz or 500 MHz spectrometers in $CDCl_3$ or CD_2Cl_2, unless otherwise mentioned. ^{1}H and $^{13}C\{^{1}H\}$ NMR chemical shifts are quoted in ppm relative to residual solvent peaks. $^{11}B\{^{1}H\}$ NMR chemical shifts are quoted in ppm relative to $BF_3{\cdot}(CH_3)_2O$ in $CDCl_3$. $^{19}F\{^{1}H\}$ NMR chemical shifts are quoted in ppm relative to $CFCl_3$ in $CDCl_3$. High resolution mass spectra (HRMS) were recorded by using ESI ionization in positive mode. IR spectra were recorded using Attenuated Total Reflection (ATR) technique, unless otherwise cited.

2. Synthesis of bisoxazoline ligands L1 and L2



Scheme SI 1. General procedure for the synthesis of ligands **L1** and **L2**.

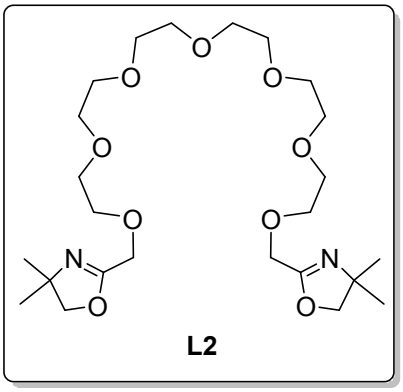
In a dried 100 mL flask, a slurry of NaH (4.78 mmol) in dry THF (4.0 mL) was prepared under inert atmosphere and cooled at 0 ºC. A solution of (2,2-dimethyl-2,5-dihydrooxazol-4-yl)methanol[1] (4.18 mmol) in dry THF (4.0 mL) was slowly syringed into the NaH suspension at 0 ºC. The resulting mixture was allowed to reach room temperature and stirred for further 30 minutes. Then, a solution of polyethylene glycol ditosylate (1.99 mmol) in dry THF (4.0 mL) was syringed into the reaction mixture at room temperature. The resulting reaction mixture was heated at 50 ºC and stirred for 12 hours. Solvent was removed under reduced pressure. The residue obtained was dissolved in CH_2Cl_2 (20 mL) and filtered on Celite®. The filtrate was evaporated *in vacuo* and the residue was finally purified by silica gel column chromatography using EtOAc/MeOH (95:5 v/v) as the eluent to provide the corresponding bisoxazoline ligands as yellowish oils.



Ligand **L1** was synthesised following the general procedure from tetraethylene glycol bis(tosylate) (1.99 mmol, 1.0 g), NaH (4.78 mmol, 121.0 mg), and (2,2-dimethyl-2,5-dihydrooxazol-4-yl)methanol (4.18 mmol, 540.0 mg). After purification by silica gel column chromatography, ligand **L1** was obtained as a yellowish oil (500.0 mg, 60% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.19 (s, 4H), 3.97 (s, 4H), 3.73 - 3.64 (m, 16H) and 1.29 (s, 12H) ppm; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 162.4 (C), 79.3

[1] (2,2-dimethyl-2,5-dihydrooxazol-4-yl)methanol was synthesised following the reported procedure: M. B. M. de Mello, G. C. Clososki, L. Piovan and A. R. M. de Oliveira, *J. Organomet. Chem.*, 2015, **794**, 11-16.

(CH_2), 70.68 (CH_2), 70.66 (CH_2), 70.65 (CH_2), 70.56 (CH_2), 67.3 (C), 65.9 (CH_2) and 28.4 (CH_3) ppm; IR (neat): 2965, 2868, 1666, 1461, 1349, 1294, 1253, 1101, 980, 924, 876 and 815 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{20}H_{36}N_2O_7Na$ $[M+Na]^+$ 439.2415, found 439.2417.

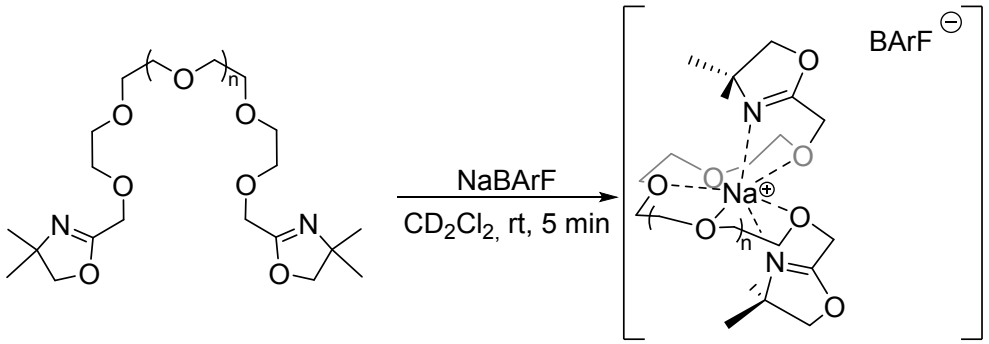


L2

Ligand **L2** was synthesised following the general procedure from hexaethylene glycol bis(tosylate) (1.64 mmol, 1.0 g), NaH (3.94 mmol, 99.6 mg), and (2,2-dimethyl-2,5-dihydrooxazol-4-yl)methanol (3.28 mmol, 424.0 mg). After purification by silica gel column chromatography, ligand **L2** was obtained as a yellowish oil (527.0 mg, 64% yield). ^1H NMR (400 MHz, $CDCl_3$) δ: 4.19 (s, 4H), 3.97 (s, 4H), 3.75 - 3.64 (m, 24H) and 1.29 (s, 12H) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 162.4 (C), 79.4 (CH_2), 70.74 (CH_2), 70.73 (CH_2), 70.71 (CH_2), 70.6 (CH_2), 67.3 (C), 65.9 (CH_2) and 28.5 (CH_3) ppm; IR (neat) : 3390, 2868, 1665, 1527, 1460, 1349, 1295, 1251, 1098 and 981 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{24}H_{45}N_2O_9$ $[M+H]^+$ 505.3120, found 505.3102.

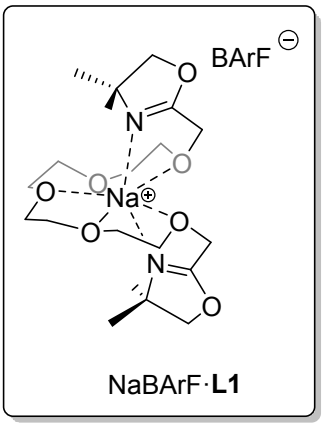
3. Preparation and characterization of copper(I)-complexes derived from NaBArF and ligands L1 or L2

3.1. Complexation of L1 and L2 with NaBArF

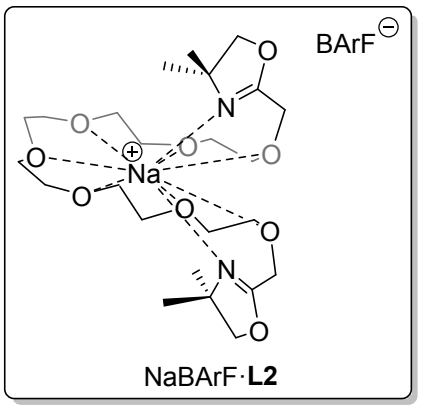


Scheme SI 2. Preparation of NaBArF·**L1** and NaBArF·**L2**.

In a N_2-filled glove box, a solution of NaBArF (0.06 mmol) in CD_2Cl_2 (0.5 mL) was prepared. Then, a solution of desired ligand (0.05 mmol) in CD_2Cl_2 (0.4 mL) was added dropwise to the previous solution. The resulting mixture was stirred for 5 minutes at room temperature. NMR characterization studies were made directly with this solution, which was subsequently concentrated under reduce pressure to isolate the complex as a solid in a quantitative manner.

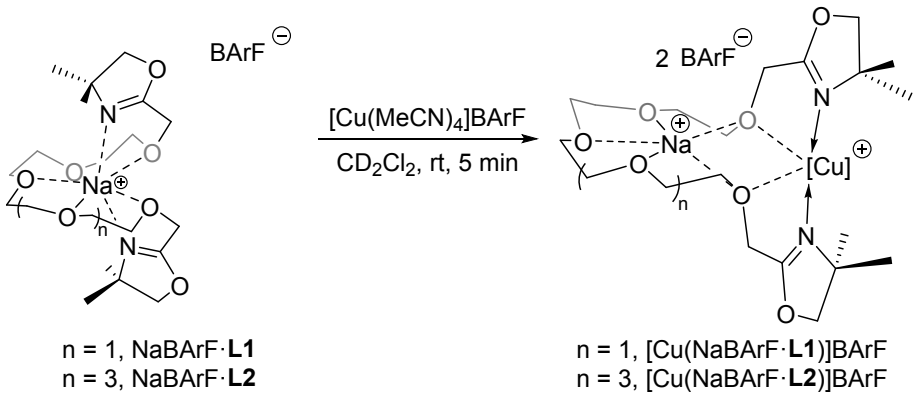


Complex NaBArF·**L1** was prepared following the general procedure from ligand **L1** (0.05 mmol, 20.8 mg) and NaBArF (0.06 mmol, 48.7 mg). The complex NaBArF·**L1** was obtained as whitish foamy solid. ^{1}H NMR (400 MHz, CD_2Cl_2) δ: 7.74 - 7.73 (m, 8H), 7.58 - 7.57 (m, 4H), 4.11 (s, 4H), 4.02 (s, 4H), 3.68 - 3.59 (m, 16H) and 1.27 (s, 12H) ppm; ^{13}C{^{1}H} NMR (101 MHz, CD_2Cl_2) δ: 164.7 (C), 162.2 (q, $J_{C–B}$ = 50.2 Hz, C), 135.2 (CH), 129.8 - 128.8 (C), 125.0 (q, $J_{C–F}$ = 272.4 Hz, C) 118.1 - 117.7 (CH), 80.3 (CH_2), 70.6 (CH_2), 69.4 (CH_2), 69.0 (CH_2), 68.5 (CH_2), 67.5 (C), 65.5 (CH_2) and 28.6 (CH_3) ppm; ^{19}F{^{1}H} NMR (376 MHz, CD_2Cl_2) δ: –63.0 ppm; ^{11}B{^{1}H} NMR (128 MHz, CD_2Cl_2) δ: –6.6 ppm; IR (neat): 2929, 1673, 1612, 1353, 1275, 1113, 944, 888, 839, 745, 715, 681 and 668 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{20}H_{36}N_2NaO_7$ $[M]^+$ 439.2415, found 439.2401.



Complex NaBArF·**L2** was prepared following the general procedure from ligand **L2** (0.05 mmol, 25.2 mg) and NaBArF (0.06 mmol, 48.7 mg). The complex NaBArF·**L2** was obtained as yellowish foamy solid. ^{1}H NMR (400 MHz, CD_2Cl_2) δ: 7.74 - 7.73 (m, 8H), 7.59 - 7.57 (m, 4H), 4.14 (s, 4H), 3.99 (s, 4H), 3.71 - 3.63 (m, 24H) and 1.25 (s, 12H) ppm; ^{13}C{^{1}H} NMR (101 MHz, CD_2Cl_2) δ: 163.7 (C), 162.2 (q, $J_{C–B}$ = 49.8 Hz, C), 135.2 (CH), 129.8 - 128.9 (C), 125.0 (q, $J_{C–F}$ = 272.6 Hz, C), 118.1 – 117.7 (CH), 80.0 (CH_2), 70.2 (CH_2), 69.4 (CH_2), 69.3 (CH_2), 69.0 (CH_2), 68.9 (CH_2), 68.7 (CH_2), 67.5 (C), 65.5 (CH_2) and 28.5 (CH_3) ppm; ^{19}F{^{1}H} NMR (376 MHz, CD_2Cl_2) δ: –63.0 ppm; ^{11}B{^{1}H} NMR (128 MHz, CD_2Cl_2) δ: –6.6 ppm; IR (neat): 2920, 1673, 1611, 1464, 1353, 1273, 1114, 947, 886, 839, 745, 713, 682 and 669 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{24}H_{44}N_2NaO_9$ $[M]^+$ 527.2939, found 527.2922.

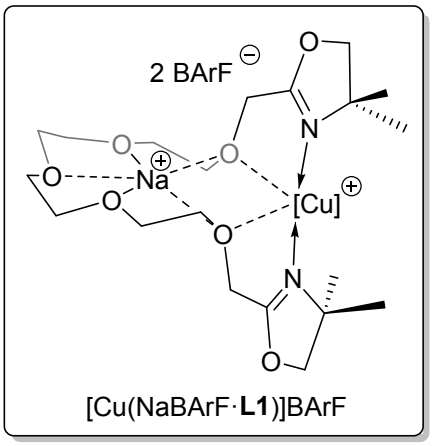
3.2. Complexation of NaBrF·L1 and NaBArF·L2 with [Cu(MeCN)$_4$]BArF



Scheme SI 3. Preparation of complexes [Cu(NaBArF·**L1**)]BArF and [Cu(NaBArF·**L2**)]BArF.

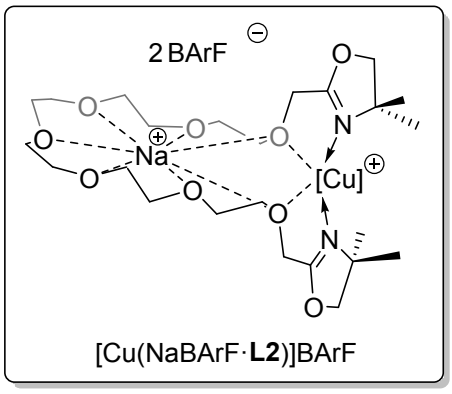
In a N_2-filled glove box, a solution of [Cu(MeCN)$_4$]BArF[2] (0.05 mmol) in CD_2Cl_2 (0.3 mL) was prepared at room temperature. A solution of NaBArF·**L1** (0.05 mmol) in CD_2Cl_2 (0.9 mL) was prepared as indicated in Section 3.1 and added dropwise to the solution containing the copper precursor. NMR characterization studies were made directly with this solution, which was subsequently concentrated under reduce pressure to isolate the complex as a solid in a quantitative manner.

[2] Y. Zhang, W. Sun, C. Freund, A. M. Santos, E. Herdtweck, J. Mink and F. E. Kuehn, *Inorg. Chim. Acta*, 2006, **359**, 4723-4729.



[Cu(NaBArF·**L1**)]BArF

Complex [Cu(NaBArF·**L1**)]BArF was synthesised following the general procedure from $[Cu(MeCN)_4]BArF$ (0.05 mmol, 51.6 mg), NaBArF (0.06 mmol, 51.2 mg), and ligand **L1** (0.05 mmol, 21.9 mg). The complex [Cu(NaBArF·**L1**)]BArF was obtained as a yellowish foamy solid. ^{1}H NMR (400 MHz, CD_2Cl_2) δ: 7.75 - 7.74 (m, 16H), 7.59 - 7.57 (m, 8H), 4.34 (s, 4H), 4.29 (s, 4H), 3.80 - 3.57 (m, 16H), 1.99 (s, 12H) and 1.37 (s, 12H) ppm; $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_2Cl_2) δ: 171.6 (C), 162.4 (q, $J_{C–B}$ = 49.8 Hz, C), 135.3 (CH), 130.0 - 129.1 (C), 125.1 (q, $J_{C–F}$ = 272.0 Hz, C), 118.1 - 117.8 (CH), 117.0 (C), 81.4 (CH_2), 72.0 (CH_2), 71.0 (CH_2), 70.8 (CH_2), 70.7 (CH_2), 67.1 (C), 64.9 (CH_2), 28.8 (CH_3) and 1.8 (CH_3) ppm; $^{19}F\{^{1}H\}$ NMR (376 MHz, CD_2Cl_2) δ: –63.1 ppm; $^{11}B\{^{1}H\}$ NMR (128 MHz, CD_2Cl_2) δ: –6.6 ppm; IR (neat): 2932, 1667, 1611, 1354, 1274, 1111, 945, 886, 838, 712, 681 and 669 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{20}H_{36}CuN_2O_7$ $[M–Na]^+$ 479.1813, found 479.1819.



[Cu(NaBArF·**L2**)]BArF

Complex [Cu(NaBArF·**L2**)]BArF was synthesised following the general procedure from $[Cu(MeCN)_4]BArF$ (0.05 mmol, 55.3 mg), NaBArF (0.06 mmol, 54.9 mg), and ligand **L2** (0.05 mmol, 28.4 mg). The complex [Cu(NaBArF·**L2**)]BArF was obtained as a yellowish foamy solid. ^{1}H NMR (400 MHz, CD_2Cl_2) δ: 7.76 - 7.73 (m, 16H), 7.60 - 7.58 (m, 8H), 4.36 (s, 4H), 4.31 (s, 4H), 3.77 - 3.56 (m, 24H), 2.01 (s, 12H) and 1.40 (s, 12H) ppm; $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_2Cl_2) δ: 171.2 (C), 162.2 (q, $J_{C–B}$ = 49.6 Hz, C), 135.3 (CH), 129.9 - 128.9 (C), 125.0 (q, $J_{C–F}$ = 272.0 Hz, C), 118.1 - 117.8 (CH), 117.2 (C), 81.4 (CH_2), 71.9 (CH_2), 69.7 (CH_2), 69.4 (CH_2), 68.8 (CH_2), 68.4 (CH_2), 68.3 (CH_2), 67.9 (C), 65.4 (CH_2), 29.0 (CH_3) and 1.8 (CH_3) ppm; $^{19}F\{^{1}H\}$ NMR (376 MHz, CD_2Cl_2) δ: –62.9 ppm; $^{11}B\{^{1}H\}$ NMR (128 MHz, CD_2Cl_2) δ: –6.7 ppm; IR (neat): 2932, 1657, 1354, 1274, 1115, 886, 839, 712 and 669 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{24}H_{44}CuN_2O_9$ $[M–Na]^+$ 567.2337, found 567.2354.

3.3. Stacked plots of the ^{1}H- and ^{13}C{^{1}H} spectra of L/NaBArF·L/ [Cu(NaBArF·L)]BArF for L1 and L2

The corresponding solutions were prepared as described previously (sections 3.1 and 3.2) and transferred to NMR J-Young tubes.

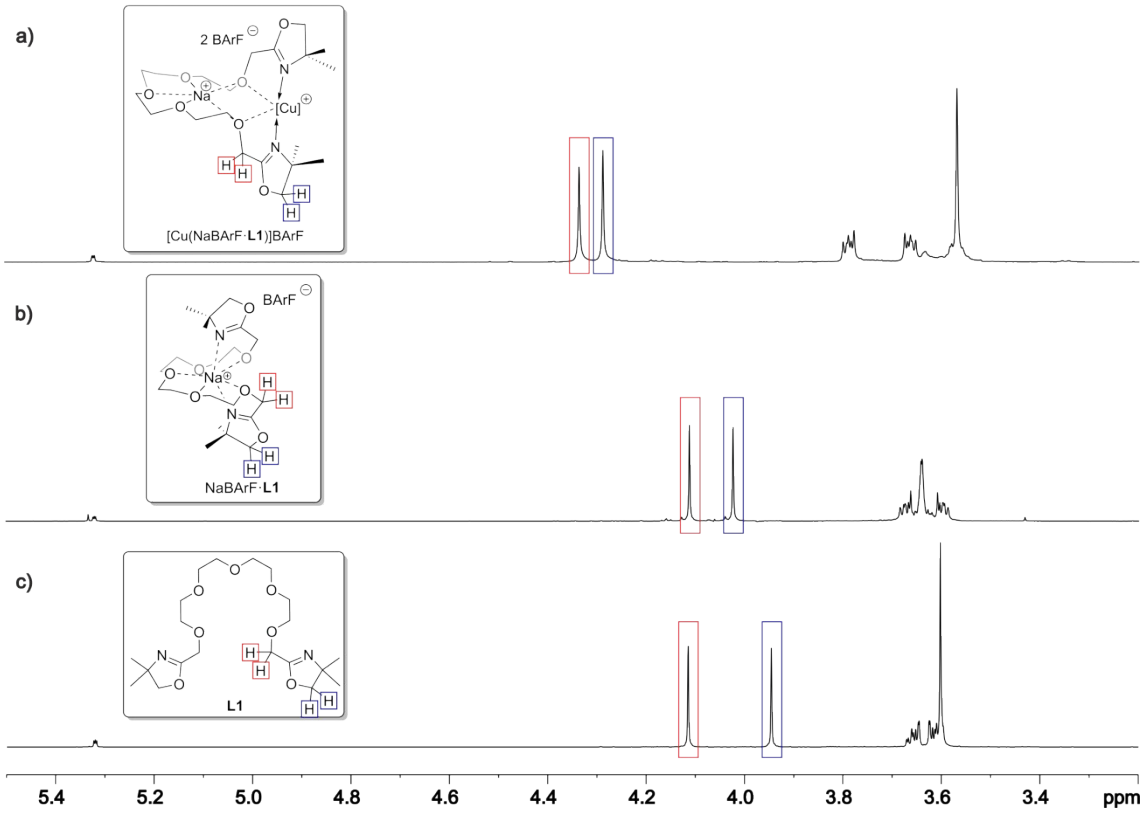


Figure SI 1. Aliphatic region of the ^{1}H NMR spectra (400 MHz, CD_2Cl_2) acquired at 298 K of **L1** (c) NaBArF·**L1** (b) and [Cu(NaBArF·**L1**)]BArF (a) (*ca.* 0.08 M).

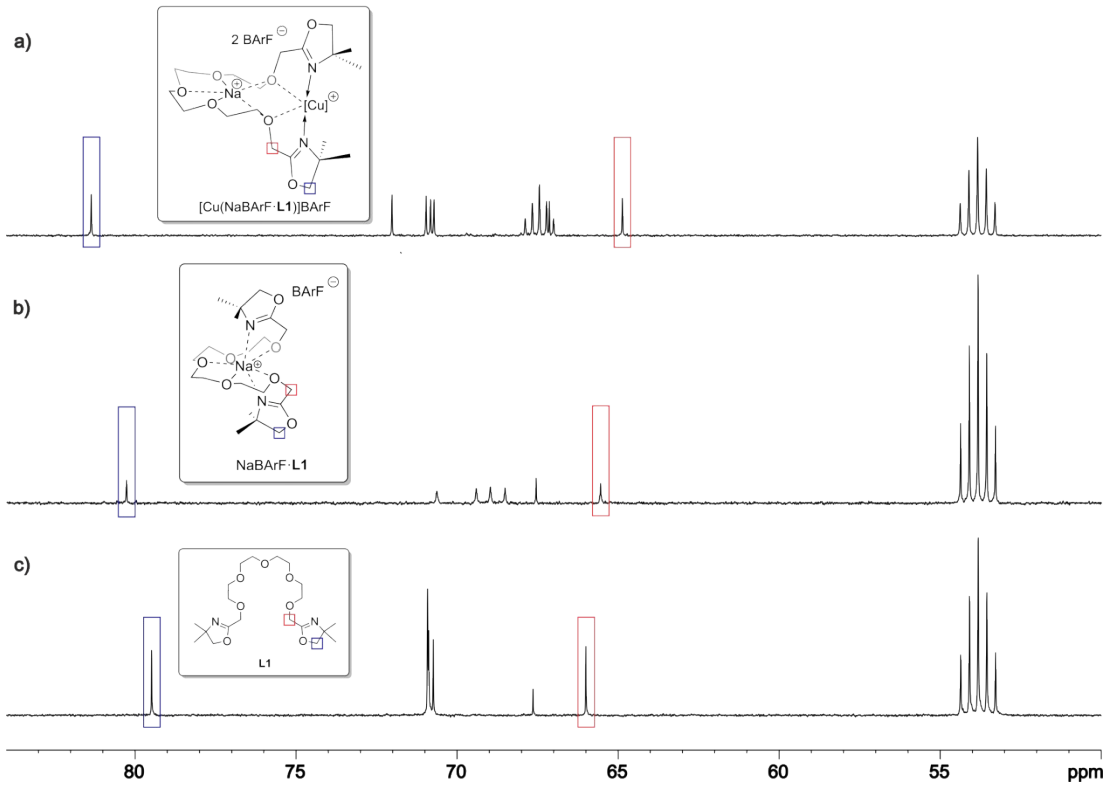


Figure SI 2. Aliphatic region of the $^{13}C\{^{1}H\}$ NMR spectra (101 MHz, CD_2Cl_2) acquired at 298 K of **L1** (c) NaBArF·**L1** (b) and [Cu(NaBArF·**L1**)]BArF (a) (*ca.* 0.08 M).

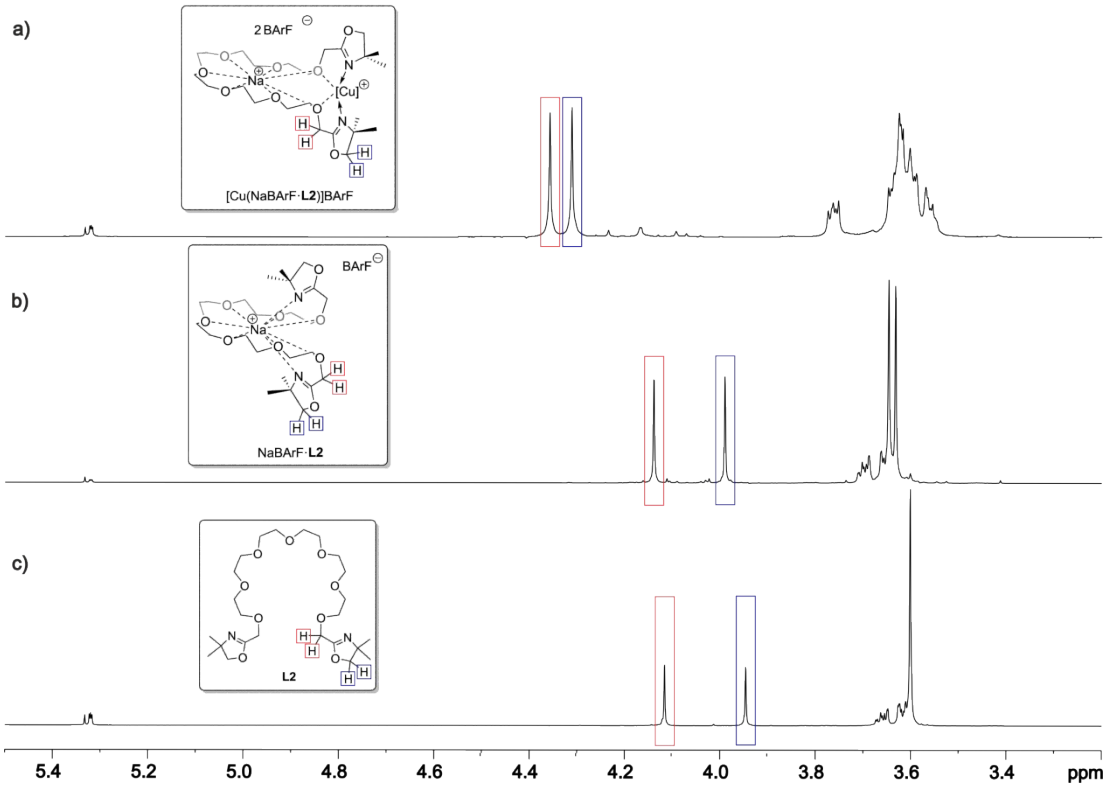


Figure SI 3. Aliphatic region of the ^{1}H NMR spectra (400 MHz, CD_2Cl_2) acquired at 298 K of **L2** (c) NaBArF·**L2** (b) and [Cu(NaBArF·**L2**)]BArF (a) (*ca.* 0.08 M).

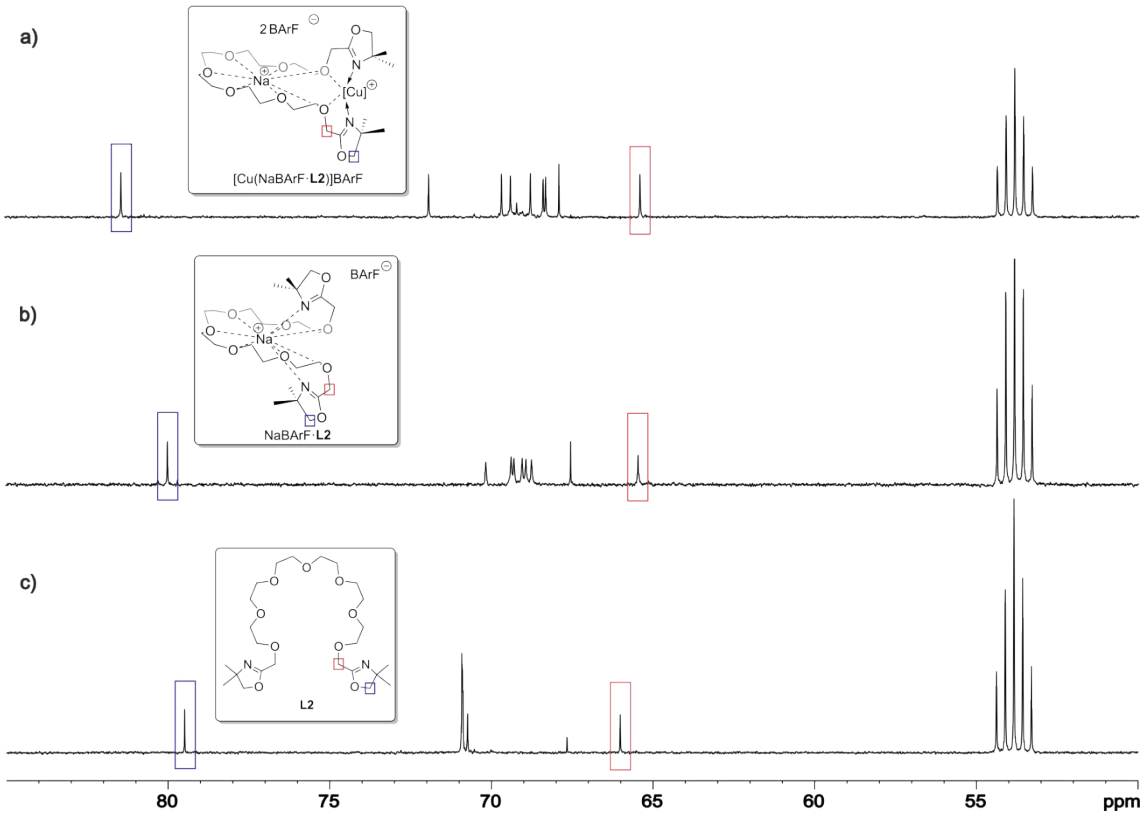


Figure SI 4. Aliphatic region of the $^{13}C\{^1H\}$ NMR spectra (101 MHz, CD_2Cl_2) acquired at 298 K of **L2** (c) NaBArF·**L2** (b) and [Cu(NaBArF·**L2**)]BArF (a) (*ca.* 0.08 M).

3.4. NMR titrations and measurement of binding constants by NMR

3.4.1. Qualitative titrations

Titrations were carried out on a 400 MHz spectrometer by using a solution of ligand **L1** (*ca.* 1 x 10^{-3} M) in $CDCl_3$ and adding aliquots of a solution of the corresponding regulation agent in the same solvent at 298 K.

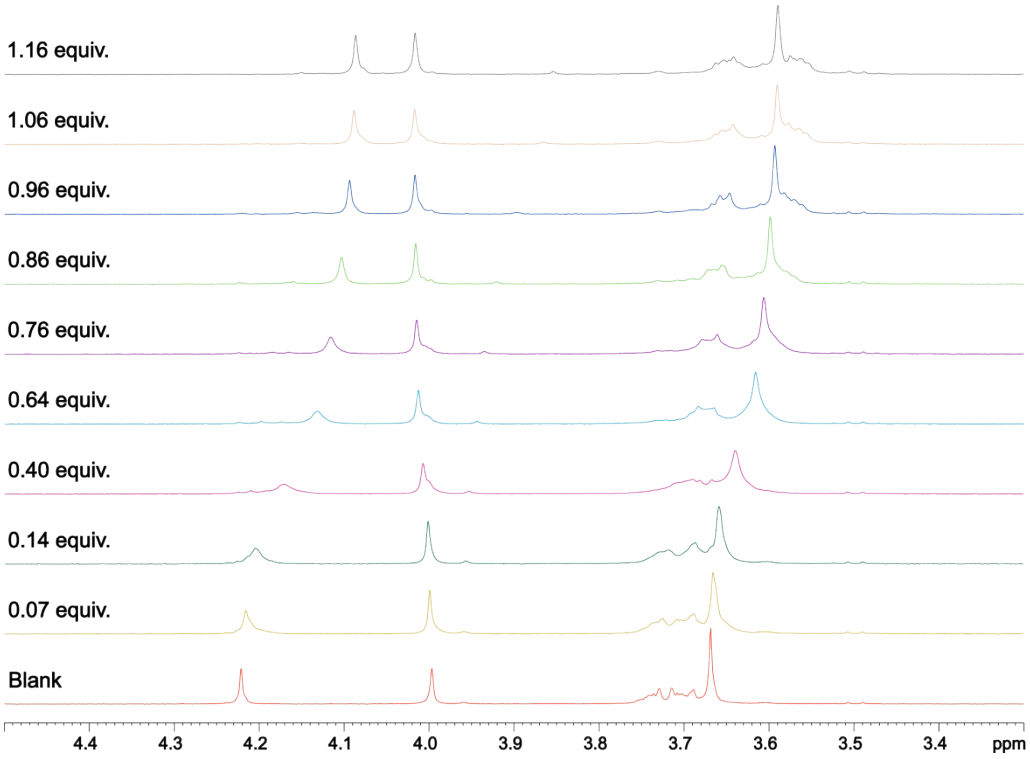


Figure SI 5. Changes in the ^{1}H NMR spectra (400 MHz, $CDCl_3$) acquired at 298 K during the titration of **L1** (2.54 x 10^{-3} M) with NaBArF.

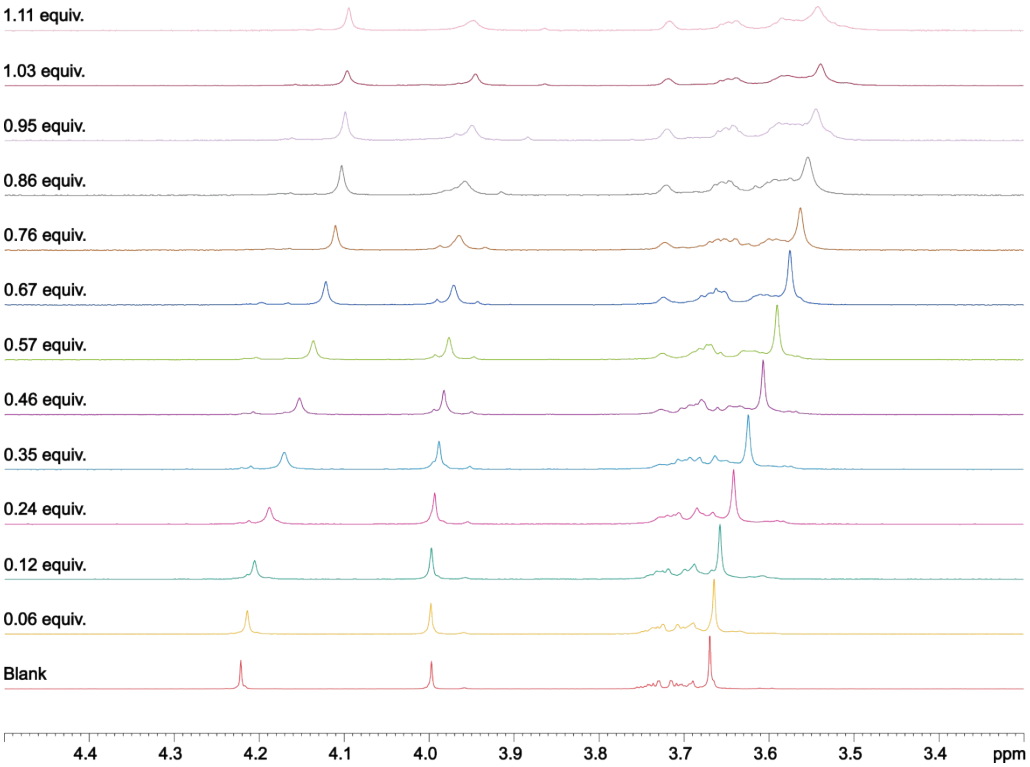


Figure SI 6. Changes in the ^{1}H NMR (400 MHz, $CDCl_3$) spectra acquired at 298 K during the titration of **L1** (2.51 x 10^{-3} M) with RbBArF.

3.4.2. Measurement of binding constants by NMR spectroscopy

A solution of ligand **L1** (*ca*. 10^{-3} M) was prepared in $CDCl_3$. Solutions of NaBArF and RbBArF were also prepared in the same solvent. The host solution (0.5 mL) was placed in a NMR tube. The titration was carried out adding at 298 K incremental amounts of guest (NaBArF or RbBArF) to the host (**L1**) solution. This process led to changes in the chemical shift in the NMR spectra. Binding constants were calculated by multivariate factor analysis of the ^{1}H NMR chemical shift values, considering a 1:1 binding model in the fast exchange-limit. SPECFIT software (Version 3.0; Spectra Software Associates)[3] was used.

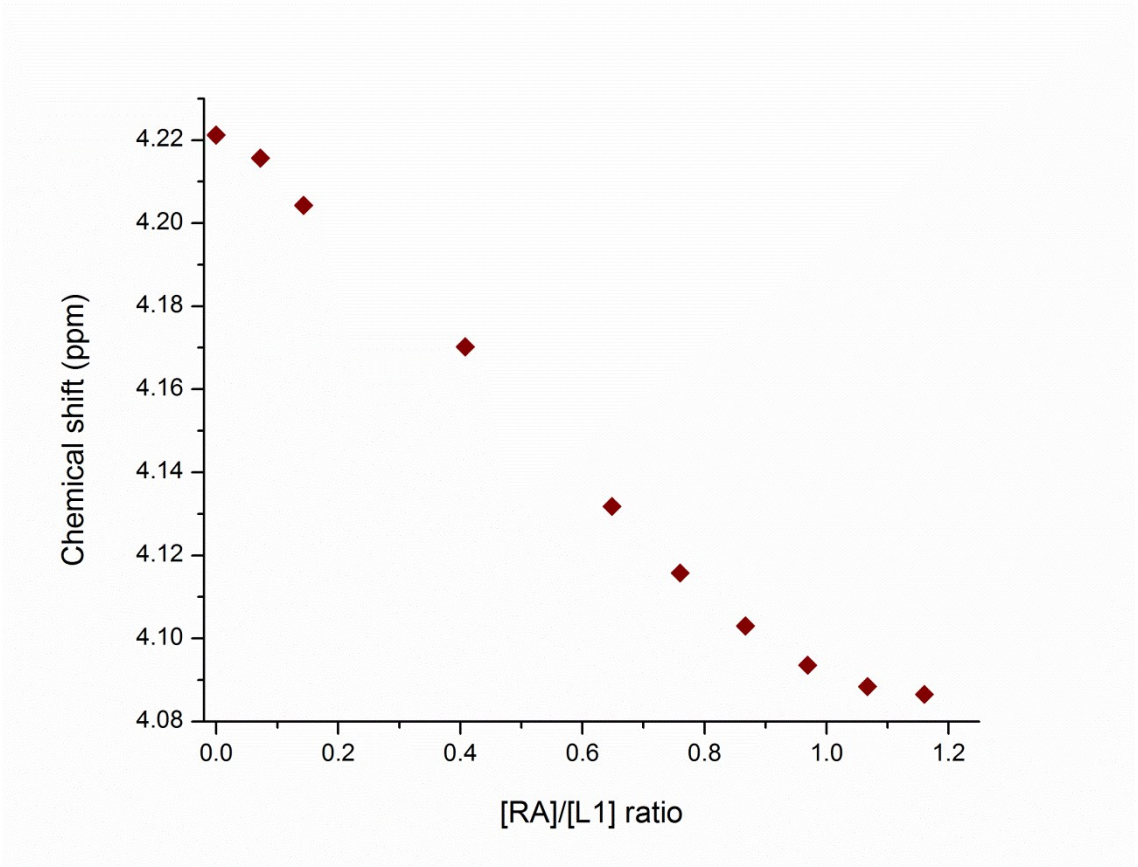


Figure SI 7. NMR titration to measure the binding constant between **L1** (2,54 x 10^{-3} M) and NaBArF as RA. Changes (ppm) in the ^{1} H NMR (400 MHz, $CDCl_3$) upon addition of a NaBArF solution in $CDCl_3$ (14.0 x 10^{-3} M).

[3] (a) H. Gampp, M. Maeder, C. J. Meyer and A. D. Zuberbühler, *Talanta*, 1986, **33**, 943-951. (b) H. Gampp, M. Maeder, C. J. Meyer and A. D. Zuberbühler, *Talanta*, 1985, **32**, 95-101.

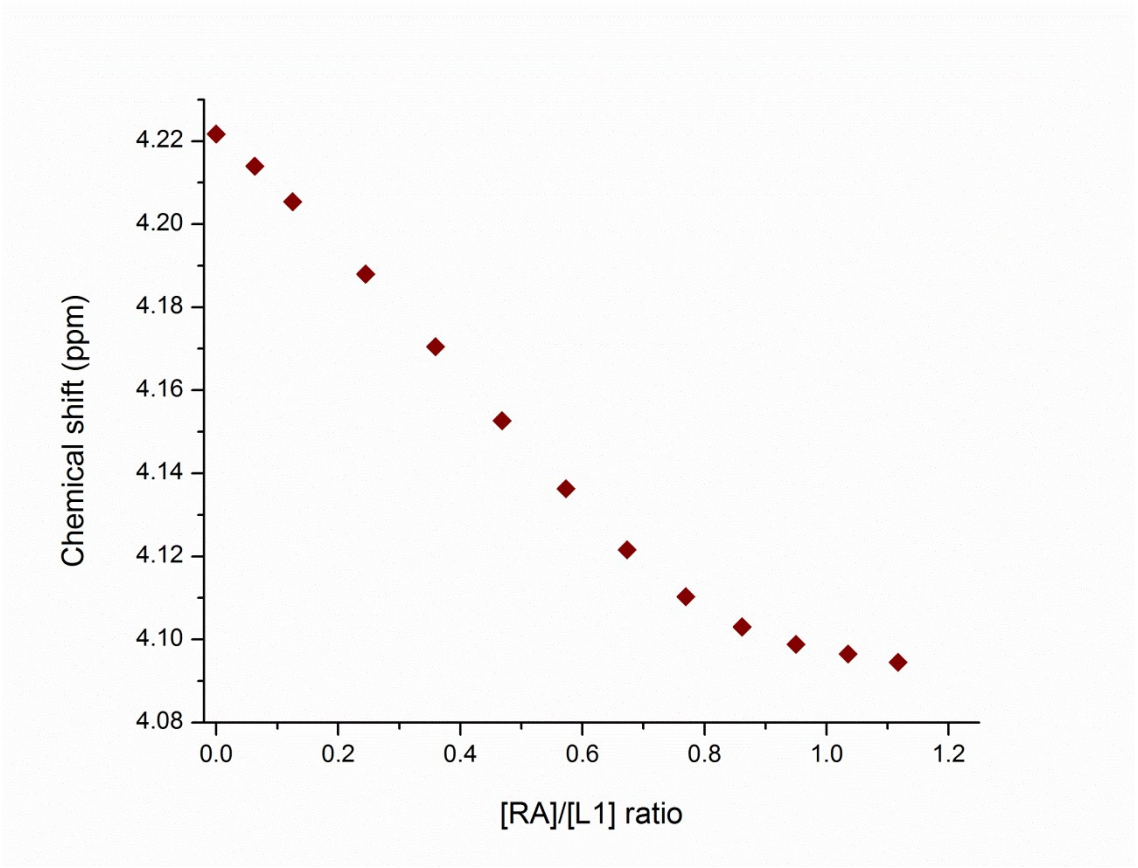


Figure SI 8. NMR titration to measure the binding constant between **L1** (2,51 x 10^{-3} M) and RbBArF as RA. Changes (ppm) in the ^{1}H NMR (400 MHz, $CDCl_3$) upon addition of RbBArF (13.4 x 10^{-3} M).

3.5. Preparation of [Cu($NaPF_6$·L1)]PF_6 and [Cu($NaPF_6$·L2)]PF_6

Complexes [Cu($NaPF_6$·**L1**)]PF_6 and [Cu($NaPF_6$·**L2**)]PF_6 were prepared by following analogous synthetic protocols to those indicated in sections 3.1 and 3.2 and employing the corresponding molar amounts of $NaPF_6$ instead of NaBArF. The resulting solids were dissolved in CH_2Cl_2 and diethyl ether was carefully layered on top of the previous solution. Single crystals were obtained by allowing diethyl ether to slowly diffuse into the CH_2Cl_2 solution.

4. Single crystal X-ray structure determinations

Crystal preparation: Crystals of NaBArF·**L1**, [Cu(NaPF$_6$·**L1**]PF$_6$ and [Cu(NaPF$_6$·**L2**)]PF$_6$ were grown by slow diffusion of Et_2O in CH_2Cl_2. The crystals used for X-ray measurements were selected using a Zeiss stereomicroscope using polarised light and prepared under inert conditions immersed in perfluoropolyether as protecting oil for manipulation.

Data collection: Crystal structure determination for samples NaBArF·**L1**, [Cu(NaPF$_6$·**L1**)]PF$_6$ and [Cu(NaPF$_6$·**L2**)]PF$_6$ were carried out using a Apex DUO Kappa 4-axis goniometer equipped with an APPEX 2 4K CCD area detector, a Microfocus Source E025 IμS using MoK$_\alpha$ radiation, Quazar MX multilayer Optics as monochromator and an Oxford Cryosystems low temperature device Cryostream 700 plus (T = –173 ˚C). Full-sphere data collection was used with ω and φ scans. *Programs used:* Bruker Device: Data collection APEX-2,[4] data reduction Bruker Saint[5] V/.60A and absorption correction SADABS.[6]

Structure Solution and Refinement: Crystal structure solution was achieved using the computer program SHELXT.[7] Visualization was performed with the program SHELXle.[8] Missing atoms were subsequently located from difference Fourier synthesis and added to the atom list. Least-squares refinement on F^2 using all measured intensities was carried out using the program SHELXL 2015.[9] All non-hydrogen atoms were refined including anisotropic displacement parameters.

Comments to the structure of NaBArF·L1: The asymmetric unit contains one molecule of the cationic sodium complex and one molecule of the BArF anion. The central part of the ligand in the sodium complex is disordered in two orientations. Also the CF_3 groups in the BArF anion are disordered in different orientations.

Comments to the structure of [Cu(NaPF$_6$·L1)]PF$_6$: The asymmetric unit contains one molecule of the metal complex (with a copper and a sodium atom), two PF_6 anions and a half diethyl ether molecule. The two PF_6 anions are located in three positions with

[4] Data collection with APEX II version 2013.4-1. Bruker (2007). Bruker AXS Inc., Madison, Wisconsin, USA.
[5] Data reduction with Bruker SAINT version 8.30c. Bruker (2007). Bruker AXS Inc., Madison, Wisconsin, USA.
[6] SADABS: V2012/1 Bruker (2001). Bruker AXS Inc., Madison, Wisconsin, USA.See the following reference: A. Pereira, Y. Champouret, C. Martin, E. Alvarez, M. Etienne, T. R. Belderrain and P. J. Perez, *Chem. - Eur. J.*, 2015, **21**, 9769-9775.
[7] SHELXT. V2014/4 (Sheldrick 2014). See the following reference: G. Tseberlidis, A. Caselli and R. Vicente, *J. Organomet. Chem.*, 2017, **835**, 1-5.
[8] SHELXle; See the following reference: S. Ferrer and A. M. Echavarren, *Organometallics*, 2018, **37**, 781-786.
[9] SHELXL; SHELXL-2014/7 (Sheldrick 2014). See the following reference: M. M. Hansmann, F. Rominger, M. P. Boone, D. W. Stephan and A. S. K. Hashmi, *Organometallics*, 2014, **33**, 4461-4470.

a ratio 1:0.5:0.5. The two half PF_6 anions are shared with neighbouring symmetry equivalent units. The sodium cation is coordinated to two of the PF_6 anions forming a two dimensional chain. One of the PF_6 anions is disordered in three rotated orientations with a ratio of 55:30:15. The half diethyl ether molecule is disordered in two orientations also shared with a neighbouring symmetry equivalent unit.

Comments to the structure of [Cu(NaPF$_6$·L2)]PF$_6$: The asymmetric unit contains one molecule of the metal complex (Cu and Na) and two PF_6 anions. The atoms belonging to the ether part with the free oxygen atom (not coordinated to the sodium atom) are disordered in two orientations with an occupancy of 67:33.

(a) (b)

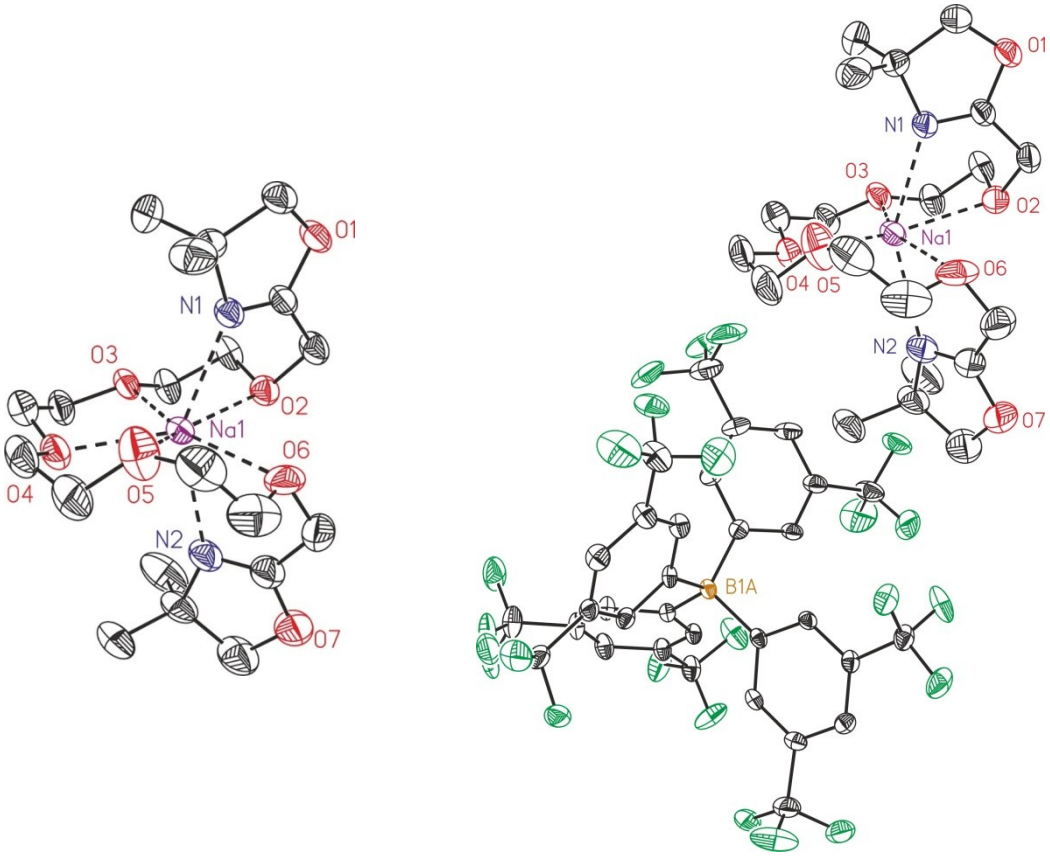


Figure SI 9. ORTEP drawing (thermal ellipsoids drawn at a 50% probability level) showing the structure of NaBArF·**L1**. (a) The BArF anion and hydrogen atoms have been omitted for clarity; (b) hydrogen atoms have been omitted for clarity. Colour scheme: C: black, O: red, N: dark blue, Na: purple, F: green, B: light brown.

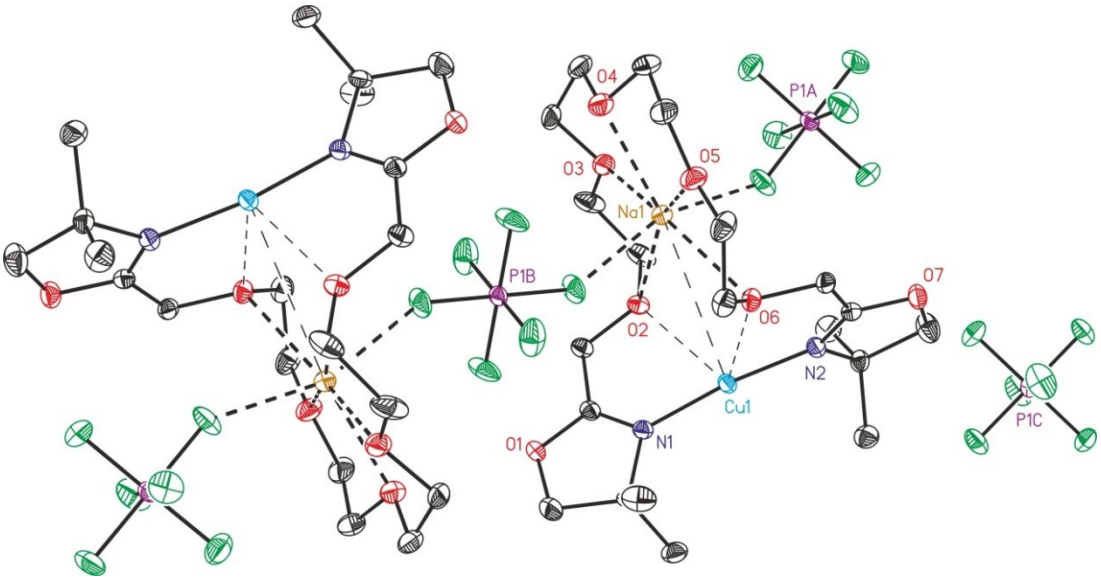


Figure SI 10. ORTEP drawing (thermal ellipsoids drawn at a 50% probability level) showing the structure of [Cu($NaPF_6$·**L1**)]PF_6. Hydrogen atoms have been omitted for clarity. Colour scheme: C: black, O: red, N: dark blue, Na: light brown, Cu: light blue, F: green, P: purple.

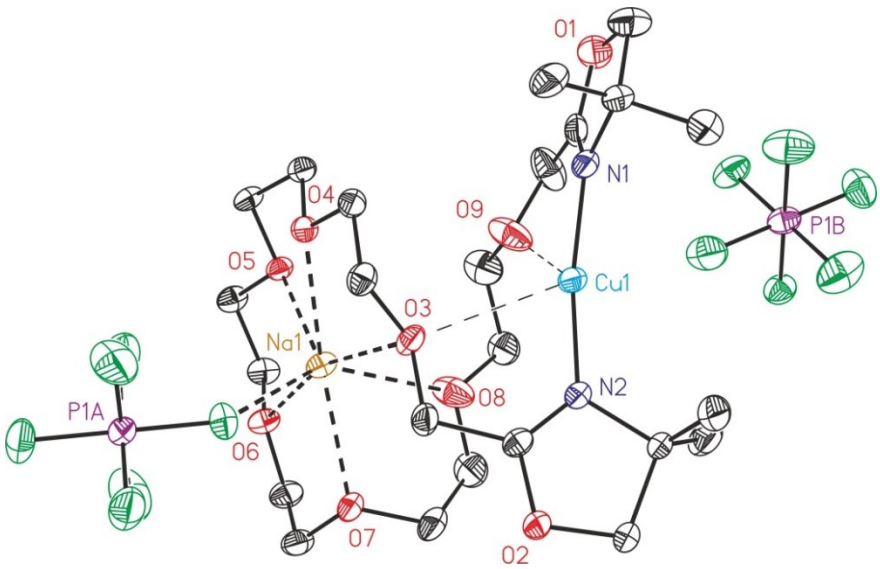
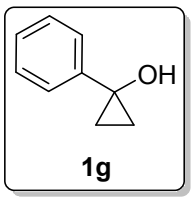


Figure SI 11. ORTEP drawing (thermal ellipsoids drawn at a 50% probability level) showing the structure of [Cu($NaPF_6$·**L2**)]PF_6. Hydrogen atoms have been omitted for clarity. Colour scheme: C: black, O: red, N: dark blue, Na: light brown, Cu: light blue, F: green, P: purple.

CCDC 1900983-1900985 contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from "The Cambridge Crystallographic Data Centre" via www.ccdc.cam.ac.uk/data_request/cif.

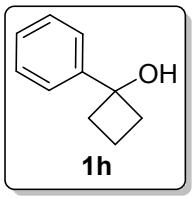
5. Synthesis of substrates 1g, 1h, 1i, 2a and 2b

5.1. Synthesis of 1-phenylcyclopropan-1-ol, 1g



The preparation of **1g** was performed adapting a reported procedure.[10] In a flame dried Schlenk flask under inert atmosphere, MeMgBr (3 M in Et_2O, 10 mL, 30 mmol) was added dropwise to a solution of titanium isopropoxide (6.1 mL, 20 mmol) in anhydrous Et_2O (20 mL). The resulting yellow solution was cooled to 0 ºC and a solution of methyl benzoate (2.63 mL, 20 mmol) in Et_2O (20 mL) was then added. A second fraction of EtMgBr (3 M in Et_2O, 10 mL, 30 mmol) was then added dropwise and the resulting reaction mixture was allowed to warm to room temperature and then stirred for an additional hour. The reaction was quenched at 0 ºC by careful addition of an ice-cooled 10% H_2SO_4 solution (80 mL), and extracted with Et_2O (3 x 20 mL). The combined organic layers were washed with saturated $NaHCO_3$ solution (60 mL), brine (60 mL) and dried ($MgSO_4$). After removal of the solvent under reduced pressure, **1g** was isolated by purification on silica gel column chromatography using Cy/EtOAc (10:1) as the eluent as a colourless oil (1.33 g, 50% yield). Spectroscopic data were in agreement with those previously reported.[10] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.36 - 7.30 (m, 4H), 7.25 - 7.22 (m, 1H), 2.44 (broad signal, 1H), 1.28 - 1.25 (m, 2H) and 1.06 - 1.04 (m, 2H) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 144.4 (C), 128.5 (CH), 126.5 (CH), 124.5 (CH), 56.8 (C) and 18.0 (CH_2) ppm.

5.2. Synthesis of 1-phenylcyclobutan-1-ol, 1h

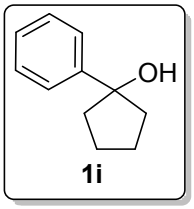


The preparation of **1h** was performed adapting a reported procedure.[11] In a flame dried Schlenk under inert atmosphere, a solution of cyclobutanone (0.90 mL, 12.2 mmol) in dry THF (25.0 mL) was cooled to 0 ºC. Phenylmagnesium bromide (2.8 M in Et_2O, 4.8 mL, 13.4 mmol) was added dropwise with stirring at the same temperature. The mixture was allowed to warm to room temperature, stirred for 12 h and quenched with a sat. NH_4Cl solution (25 mL). The aqueous layer was extracted with EtOAc (3 x 40 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated

[10] G. Z. Elek, V. Borovkov, M. Lopp and D. G. Kananovich, *Org. Lett.*, 2017, **19**, 3544-3547.
[11] Y. Sun, X. Huang, X. Li, F. Luo, L. Zhang, M. Chen, S. Zheng and B. Peng, *Adv. Synth. Catal.*, 2018, **360**, 1082-1087.

under reduced pressure. The crude mixture was purified by silica gel column chromatography using Cy/EtOAc (10:1) as the eluent to yield **1h** as yellow solid (852 mg, 46 % yield). Spectroscopic data were in agreement with those previously reported.[11] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.53 - 7.49 (m, 2H), 7.40 - 7.37 (m, 2H), 7.30 - 7.27 (m, 1H), 2.61 - 2.55 (m, 2H), 2.41 - 2.35 (m, 2H), 2.06 - 2.02 (m, 2H), 1.73 - 1.67 (m, 1H) ppm; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 146.4 (C), 128.6 (CH), 127.4 (CH), 125.1 (CH), 77.4 (C) 37.0 (CH_2), 13.1 (CH_2) ppm.

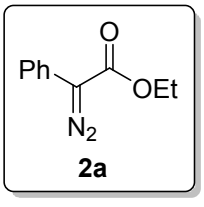
5.3. Synthesis of 1-phenylcyclopentan-1-ol, 1i



1i

The preparation of **1i** was performed adapting a reported procedure.[11] In a flame dried Schlenk under inert atmosphere, a solution of cyclopentanone (1.29 mL, 14.5 mmol) in dry THF (25.0 mL) was cooled to 0 ºC. Phenylmagnesium bromide (2.8 M in Et_2O, 10.4 mL, 29.1 mmol) was added dropwise with stirring at the same temperature. The mixture was allowed to warm to room temperature, stirred for 12 h and quenched with a sat. NH_4Cl solution (25 mL). The aqueous layer was extracted with EtOAc (3 x 40 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure. The crude mixture was purified by silica gel column chromatography using Cy/EtOAc (10:1) as the eluent to yield **1i** as yellow oil (1.3 g, 55 % yield). Spectroscopic data were in agreement with those previously reported.[11] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.52 - 7.50 (m, 2H), 7.37 - 7.34 (m, 2H), 7.30 - 7.26 (m, 1H), 2.02 - 1.98 (m, 6H), 1.91 - 1.84 (m, 2H), 1.58 (broad signal, 1H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ: 147.2 (C), 128.4 (CH), 126.9 (CH), 125.2 (CH), 83.6 (C), 42.0 (CH_2), 24.0 (CH_2) ppm.

5.4. Synthesis of phenyl diazoacetate (PhEDA), 2a



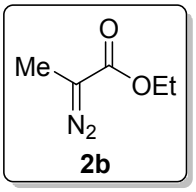
2a

The preparation of **2a** was performed adapting a reported procedure.[12] A solution of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU, 1.19 g, 7.78 mmol) in dry CH_3CN (20.0 mL) was added dropwise at 0 ºC to a solution of methyl 2-phenylacetoacetate (1.07 g, 5.19 mmol) and *p*-acetamidobenzenesulfonylazide (*p*-ABSA, 1.87 g, 7.78 mmol) in dry CH_3CN (50.0 mL). The mixture was then stirred at 0 ºC for 1 hour and allowed to reach room

[12] V. Tyagi, H. Alwaseem, K. M. O'Dwyer, J. Ponder, Q. Y. Li, C. T. Jordan and R. Fasan, *Bioorg. Med. Chem.*, 2016, **24**, 3876-3886.

temperature and then stirred for 8 hours. The reaction was quenched by addition of water (50 mL) and Et_2O (100 mL). The two layers were separated and the aqueous layer was extracted with Et_2O (2 x 50 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The product was purified by silica gel column chromatography using Cy/EtOAc (30:1) as the eluent to yield **2a** as a red oil (560.4 mg, 57% yield). Spectroscopic data were in agreement with those previously reported.[13] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.50 - 7.48 (m, 2H), 7.41 - 7.36 (m, 2H), 7.20 - 7.16 (m, 1H), 4.34 (q, J = 7.1 Hz, 2H) and 1.35 (t, J = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 165.4 (C), 129.1 (C), 125.9 (CH), 125.8 (CH), 124.1 (CH), 63.4 (C), 61.1 (CH_2) and 14.6 (CH_3) ppm.

5.5. Synthesis of methyl diazoacetate (MeEDA), 2b

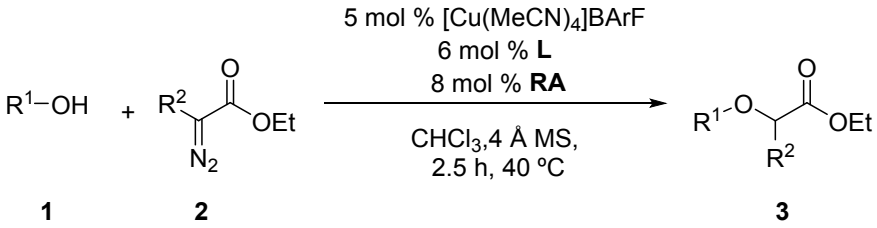


2b

The preparation of **2b** was performed adapting a reported procedure.[12] A solution of DBU (1.71 g, 11.30 mmol) in dry CH_3CN (20 mL) was added dropwise at 0 ºC to a solution of 2-methyl-3-oxo-butyric acid ethyl ester (1.08 g, 7.50 mmol) and *p*-ABSA (2.79 g, 11.30 mmol) in dry CH_3CN (20 mL). Then, the reaction mixture was stirred at 0 ºC for 1 hour and allowed to reach room temperature and then stirred for 8 hours. The reaction was quenched by addition of water (25 mL) and Et_2O (50 mL). The two layers were separated and the aqueous layer was extracted with Et_2O (2 x 25 mL). The combined organic layers were dried over $MgSO_4$, filtered and concentrated *in vacuo*. The product was purified by silica gel column chromatography using pentane/Et_2O (20:1) as the eluent to yield **2b** as yellowish liquid (379.0 mg, 40% yield). Spectroscopic data were in agreement with those previously reported.[13] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 4.20 (q, J = 7.1 Hz, 2H), 1.95 (s, 3H) and 1.26 (t, J = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 168.1 (C), 62.8 (C), 60.9 (CH_2), 14.6 (CH_3) and 8.5 (CH_3) ppm.

[13] H. Keipour and T. Ollevier, *Org. Lett.*, 2017, **19**, 5736-5739.

6. General procedure for the Cu-catalysed insertion of carbenoid species into hydroxyl bonds and characterization of the resulting insertion products 3

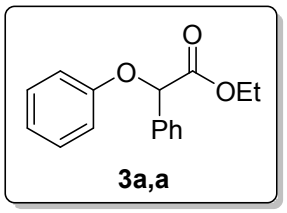


Scheme SI 4. General procedure for the catalysed insertion of copper-carbenoids into O–H bonds.

In a flame-dried Schlenk flask under inert atmosphere, a solution of the corresponding BArF salt[14] (0.016 mmol) was prepared in dry and deoxygenated $CHCl_3$ (0.5 mL). A solution of ligand (0.012 mmol) in $CHCl_3$ (0.5 mL) was added to the previous solution and the mixture was stirred for 5 min at room temperature. This mixture was then added dropwise to a solution of $[Cu(MeCN)_4]BArF$ (0.01 mmol) in $CHCl_3$ (0.5 mL) and, subsequently, 770 mg of 4 Å molecular sieves were added. After stirring for 5 min at room temperature, a solution of substrate **1** (1.0 mmol) in $CHCl_3$ (0.5 mL) was added dropwise and the mixture was stirred for another 5 minutes. Then, the corresponding diazoderivative **2** (0.20 mmol) was added dropwise (an intense bubbling was observed due to N_2 release) and the resulting mixture was stirred for 2.5 h at 40 ºC. After the stated time, the crude mixture was filtered, the residue washed with 1 mL of $CHCl_3$ and the combined organic solutions were evaporated *in vacuo*. The resulting mixture was analysed by ^1H NMR using 1,3,5-trimethoxybenzene as internal standard to quantify the amount of O–H insertion product.[15] For the best catalytic result for a given substrate **1** and diazoderivative **2**, the residue after evaporating the organic solvent was purified by silica gel column chromatography using Cy/EtOAc (98:2) as the eluent, unless otherwise stated. The target product was obtained as a yellowish oil.

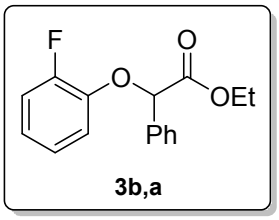
[14] L. Carreras, L. Rovira, M. Vaquero, I. Mon, E. Martin, J. Benet-Buchholz and A. Vidal-Ferran, *RSC Adv.*, 2017, **7**, 32833-32841.

[15] *para*-C–H insertion product **7** was formed in low amounts when **L2** was used as the ligand and was identified according to previous reports in the literature. See: (a) Z. Yu, B. Ma, M. Chen, H.-H. Wu, L. Liu and J. Zhang, *J. Am. Chem. Soc.*, 2014, **136**, 6904-6907. (b) Y. Xi, Y. Su, Z. Yu, B. Dong, E. J. McClain, Y. Lan and X. Shi, *Angew. Chem., Int. Ed.*, 2014, **53**, 9817-9821.



3a,a

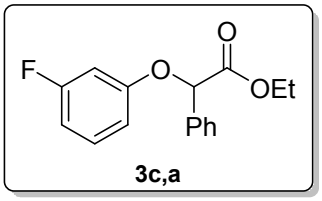
Compound 3a,a: This compound was synthesised following the general procedure indicated at the beginning of this section from phenol **1a** (94.0 mg, 1.0 mmol) and diazo compound **2a** (35 μL, 0.20 mmol) as substrates, using $[Cu(MeCN)_4]BArF$ (11.4 mg, 0.01 mmol), **L1** (5.0 mg, 0.012 mmol) and RbBArF (15.2 mg, 0.016 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography, product **3a,a** was obtained as a yellowish oil (46.1 mg, 81% yield). Spectroscopic data were in agreement with those previously reported.[16] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 - 7.58 (m, 2H), 7.43 - 7.34 (m, 3H), 7.29 - 7.25 (m, 2H), 7.00 - 6.95 (m, 3H), 5.63 (s, 1H), 4.27 - 4.13 (m, 2H) and 1.21 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 170.1 (C), 157.5 (C), 135.7 (C), 129.7 (CH), 129.0 (CH), 128.9 (CH), 127.2 (CH), 121.9 (CH), 115.6 (CH), 78.8 (CH), 61.7 (CH_2) and 14.2 (CH_3) ppm.



3b,a

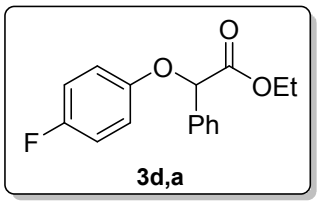
Compound 3b,a: This compound was synthesised following the general procedure indicated at the beginning of this section from 2-fluorophenol **1b** (112.0 mg, 1.0 mmol) and diazo compound **2a** (35 μL, 0.20 mmol) as substrates, using $[Cu(MeCN)_4]BArF$ (11.4 mg, 0.01 mmol), **L1** (4.99 mg, 0.012 mmol) and RbBArF (15.2 mg, 0.016 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography, product **3b,a** was obtained as a yellowish oil (30.3 mg, 55% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.60 - 7.58 (m, 2H), 7.42 - 7.36 (m, 3H), 7.12 - 7.07 (m, 1H), 7.00 - 6.94 (m, 3H), 5.65 (s, 1H), 4.25 - 4.16 (m, 2H) and 1.20 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 169.7 (C), 153.5 (d, J_{C-F} = 246.9 Hz, C), 145.4 (d, J_{C-F} = 10.3 Hz, C), 135.3 (C), 129.2 (CH), 128.9 (CH), 127.3 (CH), 124.4 (d, J_{C-F} = 4.1 Hz, CH), 123.0 (d, J_{C-F} = 7.1 Hz, CH), 117.9 (d, J_{C-F} = 1.3 Hz, CH), 116.8 (d, J_{C-F} = 18.6 Hz, CH), 80.3 (CH), 61.8 (CH_2) and 14.1 (CH_3) ppm; ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ: −132.2 ppm; IR (neat): 3069, 2989, 2925. 2853, 1734, 1613, 1592, 1506, 1258, 1212, 1178, 1110, 1055, 1019 and 752 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{16}H_{15}FO_3Na$ $[M+Na]^+$ 297.0897, found 297.0887.

[16] P. Berglund, I. Vallikivi, L. Fransson, H. Dannacher, M. Holmquist, M. Martinelle, F. Bjorkling, O. Parve and K. Hult, *Tetrahedron: Asymmetry*, 1999, **10**, 4191-4202.



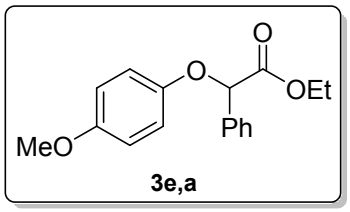
3c,a

Compound 3c,a: This compound was synthesised following the general procedure indicated at the beginning of this section from 3-fluorophenol **1c** (114.0 mg, 1.0 mmol) and diazo compound **2a** (35 μL, 0.20 mmol) as substrates, using [Cu(MeCN)$_4$]BArF (11.4 mg, 0.01 mmol), **L1** (4.99 mg, 0.012 mmol) and CsBArF (15.9 mg, 0.016 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography, product **3c,a** was obtained as a yellowish oil (35.0 mg, 64% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.58 - 7.57 (m, 2H), 7.43 - 7.36 (m, 3H), 7.24 - 7.19 (m, 1H), 6.75 - 6.68 (m, 3H), 5.60 (s, 1H), 4.27 - 4.15 (m, 2H) and 1.21 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ: 169.6 (C), 163.6 (d, $J_{C–F}$ = 245.9 Hz, C), 158.7 (d, $J_{C–F}$ = 10.6 Hz, C), 135.2 (C), 130.4 (d, $J_{C–F}$ = 10.2 Hz, CH), 129.2 (CH), 129.0 (CH), 127.2 (CH), 111.2 (d, $J_{C–F}$ = 2.7 Hz, CH), 108.8 (d, $J_{C–F}$ = 21.7 Hz, CH), 103.6 (d, $J_{C–F}$ = 24.9 Hz, CH), 79.0 (CH), 61.9 (CH_2) and 14.1 (CH_3) ppm; ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ: −111.3 ppm; IR (neat): 2982, 1751, 1610, 1594, 1488, 1261, 1182, 1165, 1134, 1024 and 695 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{16}H_{15}FO_3Na$ [M+Na]$^+$ 297.0897, found 297.0890.



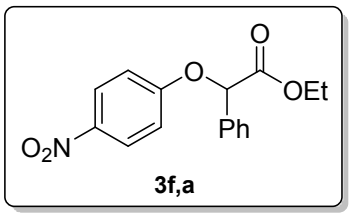
3d,a

Compound 3d,a: This compound was synthesised following the general procedure indicated at the beginning of this section from 4-fluorophenol **1d** (112.0 mg, 1.0 mmol) and diazo compound **2a** (35 μL, 0.20 mmol) as substrates, using [Cu(MeCN)$_4$]BArF (11.4 mg, 0.01 mmol), **L1** (4.99 mg, 0.012 mmol) and NaBArF (14.2 mg, 0.016 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography, product **3d,a** was obtained as a yellowish oil (43.7 mg, 80% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.58 - 7.56 (m, 2H), 7.42 - 7.35 (m, 3H), 6.97 - 6.89 (m, 4H), 5.55 (s, 1H), 4.24 - 4.16 (m, 2H) and 1.21 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ: 170.0 (C), 158.0 (d, $J_{C–F}$ = 239.6 Hz, C), 153.7 (d, $J_{C–F}$ = 1.8 Hz, C), 135.6 (C), 129.2 (CH), 129.0 (CH), 127.3 (CH), 117.1 (d, $J_{C–F}$ = 7.9 Hz, CH), 116.2 (d, $J_{C–F}$ = 23.1 Hz, CH), 79.7 (CH), 61.9 (CH_2) and 14.2 (CH_3) ppm; ^{19}F{^{1}H} NMR (376 MHz, $CDCl_3$) δ: −122.5 ppm; IR (neat): 3072, 2996, 2963, 1736, 1504, 1186, 1153, 1091, 1061, 830 and 728 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{16}H_{15}FO_3Na$ [M+Na]$^+$ 297.0897, found 297.0897.



3e,a

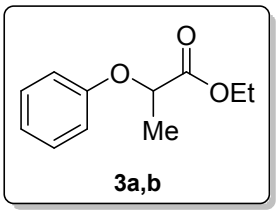
Compound 3e,a: This compound was synthesised following the general procedure indicated at the beginning of this section from 4-methoxyphenol **1e** (124.0 mg, 1.0 mmol) and diazo compound **2a** (35 μL, 0.20 mmol) as substrates, using $[Cu(MeCN)_4]BArF$ (11.4 mg, 0.01 mmol), **L1** (4.99 mg, 0.012 mmol) and NaBArF (14.2 mg, 0.016 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography, product **3e,a** was obtained as a yellowish oil (52.0 mg, 91% yield). Spectroscopic data were in agreement with those previously reported.[17] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.58 - 7.56 (m, 2H), 7.41 - 7.34 (m, 3H), 6.92 - 6.89 (m, 2H), 6.82 - 6.79 (m, 2H), 5.54 (s, 1H), 4.25 - 4.15 (m, 2H), 3.75 (s, 3H) and 1.21 (t, J = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ: 170.3 (C), 154.8 (C), 151.7 (C), 136.0 (C), 129.1 (CH), 128.9 (CH), 127.3 (CH), 117.1 (CH), 114.9 (CH), 80.0 (CH), 61.8 (CH_2), 55.9 (CH_3) and 14.3 (CH_3) ppm.



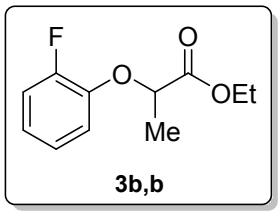
3f,a

Compound 3f,a: This compound was synthesised following the general procedure indicated at the beginning of this section from 4-nitrophenol **1f** (139.0 mg, 1.0 mmol) and diazo compound **2a** (35 μL, 0.20 mmol) as substrates, using $[Cu(MeCN)_4]BArF$ (11.4 mg, 0.01 mmol) and **L1** (4.99 mg, 0.012 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography using a mixture of Cy/EtOAc that ranged from 98:2 to 90:10 (v/v), product **3f,a** was obtained as a yellowish oil (23.1 mg, 38% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 8.20 - 8.18 (m, 2H), 7.58 - 7.56 (m, 2H), 7.43 - 7.41 (m, 3H), 7.04 - 7.00 (m, 2H), 5.70 (s, 1H), 4.29 - 4.15 (m, 2H) and 1.22 (t, J = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 168.8 (C), 162.2 (C), 142.4 (C), 134.3 (C), 129.6 (CH), 129.1 (CH), 127.2 (CH), 126.0 (CH), 115.5 (CH), 79.0 (CH), 62.2 (CH_2) and 14.1 (CH_3) ppm; IR (neat): 2983, 1748, 1591, 1513, 1493, 1455, 1370, 1341, 1299, 1247, 1183, 1111, 1051, 913, 843, 751, 729, 695 and 663 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{16}H_{15}NO_5Na$ $[M+Na]^+$ 324.0842, found 324.0840.

[17] E. J. Miller, W. Zhao, J. D. Herr and A. T. Radosevich, *Angew. Chem., Int. Ed.*, 2012, **51**, 10605-10609.

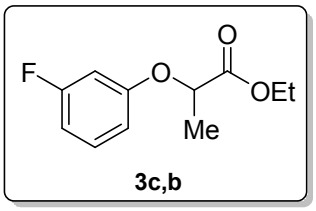


Compound 3a,b: This compound was synthesised following the general procedure indicated at the beginning of this section from phenol **1a** (94.0 mg, 1.0 mmol) and diazo compound **2b** (25.6 mg, 0.20 mmol) as substrates, using $[Cu(MeCN)_4]BArF$ (11.4 mg, 0.01 mmol), **L1** (4.99 mg, 0.012 mmol) and KBArF (14.4 mg, 0.016 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography, product **3a,b** was obtained as a yellowish oil (29.2 mg, 75% yield). Spectroscopic data were in agreement with those previously reported.[18] ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.26 - 7.22 (m, 2H), 6.96 - 6.92 (m, 1H), 6.86 - 6.84 (m, 2H), 4.72 (q, J = 6.8 Hz, 1H), 4.19 (q, J = 7.1 Hz, 2H), 1.59 (d, J = 6.8 Hz, 3H) and 1.22 (t, J = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ: 172.4 (C), 157.7 (C), 129.7 (CH), 121.7 (CH), 115.2 (CH), 72.8 (CH), 61.4 (CH_2), 18.7 (CH_3) and 14.3 (CH_3) ppm.



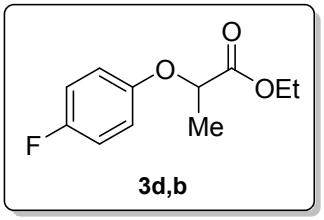
Compound 3b,b: This compound was synthesised following the general procedure indicated at the beginning of this section from 2-fluorophenol **1b** (112.0 mg, 1.0 mmol) and diazo compound **2b** (25.6 mg, 0.20 mmol) as substrates, using $[Cu(MeCN)_4]BArF$ (11.4 mg, 0.01 mmol), **L1** (4.99 mg, 0.012 mmol) and NaBArF (14.2 mg, 0.016 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography, product **3b,b** was obtained as a yellowish oil (26.7 mg, 63% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.11 - 6.90 (m, 4H), 4.76 (q, J = 6.8 Hz, 1H), 4.27 - 4.18 (m, 2H), 1.65 (d, J = 6.8 Hz, 3H) and 1.25 (t, J = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 171.8 (C), 153.3 (d, J_{C-F} = 245.8 Hz, C), 145.7 (d, J_{C-F} = 10.3 Hz, C), 124.3 (d, J_{C-F} = 4.0 Hz, CH), 122.7 (d, J_{C-F} = 6.5 Hz, CH), 117.5 (d, J_{C-F} = 1.8 Hz, CH), 116.7 (d, J_{C-F} = 18.9 Hz, CH), 74.7 (CH), 61.4 (CH_2), 18.7 (CH_3) and 14.2 (CH_3) ppm; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ: –132.9 ppm; IR (neat): 2987, 1750, 1504, 1257, 1191, 1132, 1095, 1049 and 744 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{11}H_{13}FO_3Na$ $[M+Na]^+$ 235.0741, found 235.0737.

[18] C. Chen, S.-F. Zhu, B. Liu, L.-X. Wang and Q.-L. Zhou, *J. Am. Chem. Soc.*, 2007, **129**, 12616-12617.



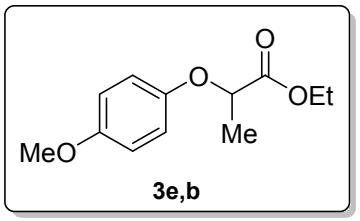
3c,b

Compound 3c,b: This compound was synthesised following the general procedure indicated at the beginning of this section from 3-fluorophenol **1c** (114.0 mg, 1.0 mmol) and diazo compound **2b** (25.6 mg, 0.20 mmol) as substrates, using $[Cu(MeCN)_4]BArF$ (11.4 mg, 0.01 mmol), **L1** (4.99 mg, 0.012 mmol) and NaBArF (14.2 mg, 0.016 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography, product **3c,b** was obtained as a yellowish oil (25.5 mg, 60% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.24 - 7.18 (m, 1H), 6.70 - 6.58 (m, 3H), 4.72 (q, J = 6.8 Hz, 1H), 4.22 (q, J = 7.1 Hz, 2H), 1.62 (d, J = 6.8 Hz, 3H) and 1.25 (t, J = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 171.9 (C), 163.6 (d, J_{C-F} = 245.8 Hz, C), 159.0 (d, J_{C-F} = 10.9 Hz, C), 130.4 (d, J_{C-F} = 9.9 Hz, CH), 110.8 (d, J_{C-F} = 3.9 Hz, CH), 108.5 (d, J_{C-F} = 21.9 Hz, CH), 103.2 (d, J_{C-F} = 24.8 Hz, CH), 73.0 (CH), 61.5 (CH_2), 18.6 (CH_3) and 14.2 (CH_3) ppm; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ: −111.5 ppm; IR (neat): 2988, 1752, 1593, 1489, 1278, 1197, 1168, 1134, 1094, 1049, 978, 766 and 680 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{11}H_{13}FO_3Na$ $[M+Na]^+$ 235.0741, found 235.0742.



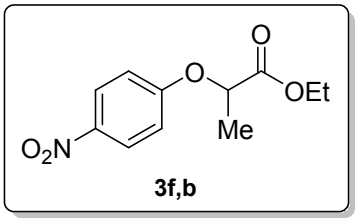
3d,b

Compound 3d,b: This compound was synthesised following the general procedure indicated at the beginning of this section from 4-fluorophenol **1d** (112.0 mg, 1.0 mmol) and diazo compound **2b** (25.6 mg, 0.20 mmol) as substrates, using $[Cu(MeCN)_4]BArF$ (11.4 mg, 0.01 mmol), **L1** (4.99 mg, 0.012 mmol) and NaBArF (14.2 mg, 0.016 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography, product **3d,b** was obtained as a yellowish oil (28.7 mg, 68% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 6.98 - 6.92 (m, 2H), 6.85 - 6.81 (m, 2H), 4.67 (q, J = 6.8 Hz, 1H), 4.21 (q, J = 7.1 Hz, 2H), 1.60 (d, J = 6.8 Hz, 3H) and 1.25 (t, J = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 172.2 (C), 157.8 (d, J_{C-F} = 239.6 Hz, C), 153.9 (d, J_{C-F} = 2.3 Hz, C), 116.6 (d, J_{C-F} = 8.0 Hz, CH), 116.1 (d, J_{C-F} = 23.5 Hz, CH), 73.6 (CH), 61.4 (CH_2), 18.7 (CH_3) and 14.3 (CH_3) ppm; $^{19}F\{^1H\}$ NMR (376 MHz, CDCl3) δ: −122.9 ppm; IR (neat): 2987, 1750, 1503, 1196, 1132, 1095, 1050, 827 and 746 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{11}H_{13}FO_3Na$ $[M+Na]^+$ 235.0741, found 235.0749.



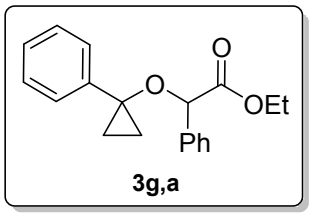
3e,b

Compound 3e,b: This compound was synthesised following the general procedure indicated at the beginning of this section from phenol **1e** (124.0 mg, 1.0 mmol) and diazo compound **2b** (25.6 mg, 0.20 mmol) as substrates, using $[Cu(MeCN)_4]BArF$ (11.4 mg, 0.01 mmol), **L1** (4.99 mg, 0.012 mmol) and RbBArF (15.2 mg, 0.016 mmol) as supramolecular catalyst. After purification by silica gel column chromatography, product **3e,b** was obtained as yellowish oil (31.8 mg, 71% yield). The spectroscopic data is consistent with those previously reported.[18] ^1H NMR (400 MHz, $CDCl_3$) δ: 6.87 - 6.65 (m, 4H), 4.65 (q, J = 6.8 Hz, 1H), 4.21 (q, J = 7.2 Hz, 2H), 3.76 (s, 3H), 1.59 (d, J = 6.8 Hz, 3H), 1.25 (t, J = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 172.6 (C), 154.6 (C), 151.9 (C), 116.7 (CH), 116.2 (CH), 115.0 (CH), 114.8 (CH), 73.8 (CH), 61.3 (CH_2), 55.8 (CH_3), 18.8 (CH_3) and 14.3 (CH_3) ppm.



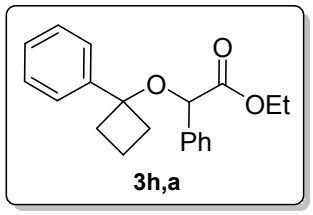
3f,b

Compound 3f,b: This compound was synthesised following the general procedure indicated at the beginning of this section from 4-nitrophenol **1f** (139.0 mg, 1.0 mmol) and diazo compound **2b** (25.6 mg, 0.20 mmol) as substrates, using $[Cu(MeCN)_4]BArF$ (11.4 mg, 0.01 mmol), **L1** (4.99 mg, 0.012 mmol) and KBArF (14.9 mg, 0.016 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography using a mixture of Cy/EtOAc that ranged from 98:2 to 90:10 (v/v), product **3f,b** was obtained as a yellowish oil (13.8 mg, 29% yield). ^1H NMR (500 MHz, $CDCl_3$) δ: 8.21 - 8.15 (m, 2H), 6.94 - 6.91 (m, 2H), 4.84 (q, J = 6.8 Hz, 1H), 4.24 (q, J = 7.1 Hz, 2H), 1.67 (d, J = 6.8 Hz, 3H) and 1.26 (d, J = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ: 171.1 (C), 162.7 (C), 142.2 (C), 126.1 (CH), 115.1 (CH), 73.1 (CH), 61.9 (CH_2), 18.5 (CH_3) and 14.3 (CH_3) ppm; IR (neat): 2919, 2850, 1745, 1592, 1513, 1494, 1342, 1257, 1198, 1094, 1048, 1016, 845, 751 and 654 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{11}H_{13}NO_5Na$ $[M+Na]^+$ 262.0686, found 262.0688.



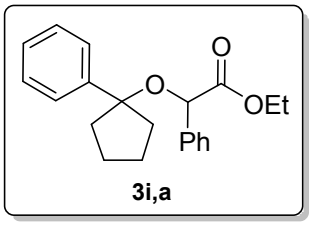
3g,a

Compound 3g,a: This compound was synthesised following the general procedure indicated at the beginning of this section from compound **1g** (134.0 mg, 1.0 mmol) and diazo compound **2a** (35.0 μL, 0.20 mmol) as substrates, using [Cu(MeCN)$_4$]BArF (11.4 mg, 0.01 mmol), **L1** (4.99 mg, 0.012 mmol) and NaBArF (14.2 mg, 0.016 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography, product **3g,a** was obtained as a yellowish oil (33.2 mg, 56% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.37 - 7.23 (m, 10H), 4.97 (s, 1H), 4.10 - 3.97 (m, 2H), 1.42 - 1.38 (m, 1H), 1.18 - 1.16 (m, 1H), 1.14 (t, J = 7.1 Hz, 3H) and 0.99 - 0.89 (m, 2H) ppm; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 171.6 (C), 140.5 (C), 137.5 (C), 128.6 (CH), 128.48 (CH), 128.45 (CH), 127.51 (CH), 127.49 (CH), 127.1 (CH), 79.2 (CH), 64.9 (C), 61.2 (CH_2), 14.43 (CH_2), 14.36 (CH_2) and 14.1 (CH_3) ppm; IR (neat): 2981, 1748, 1453, 1230, 1203, 1173, 1088, 1063, 1024 and 696 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{19}H_{20}O_3Na$ [M+Na]$^+$ 319.1305, found 319.1294.



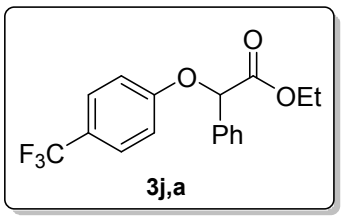
3h,a

Compound 3h,a: This compound was synthesised following the general procedure indicated at the beginning of this section from compound **1h** (156.0 mg, 1.0 mmol) and diazo compound **2a** (35.0 μL, 0.20 mmol) as substrates, using [Cu(MeCN)$_4$]BArF (11.4 mg, 0.01 mmol), **L1** (4.99 mg, 0.012 mmol) and LiBArF (16.3 mg, 0.016 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography, product **3h,a** was obtained as a yellowish oil (40.2 mg, 83% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.48 - 7.46 (m, 2H), 7.37 - 7.26 (m, 8H), 4.65 (s, 1H), 4.00 - 3.90 (m, 2H), 2.65 - 2.58 (m, 1H), 2.48 - 2.38 (m, 2H), 2.37 - 2.28 (m, 1H), 1.96 - 1.92 (m, 1H), 1.64 - 1.59 (m, 1H), 1.10 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 171.8 (C), 142.6 (C), 138.0 (C), 128.5 (CH), 128.3 (CH), 128.2 (CH), 127.8 (CH), 127.1 (CH), 127.0 (CH), 83.3 (C), 75.7 (CH), 61.0 (CH_2), 34.2 (CH_2), 33.3 (CH_2), 14.1 (CH_3), 13.5 (CH_2) ppm; IR (neat): 2982, 2946, 1749, 1172, 1095, 1057, 1026, 696 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{20}H_{22}O_3Na$ [M+Na]$^+$ 333.1461, found 333.1454.



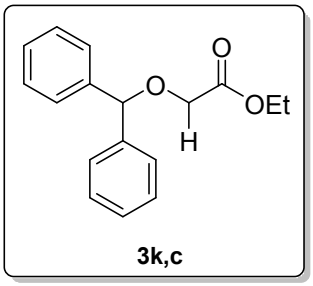
3i,a

Compound 3i,a: This compound was synthesised following the general procedure indicated at the beginning of this section from compound **1i** (171.0 mg, 1.0 mmol) and diazo compound **2a** (35.0 μL, 0.20 mmol) as substrates, using $[Cu(MeCN)_4]BArF$ (11.4 mg, 0.01 mmol), **L1** (4.99 mg, 0.012 mmol) and NaBArF (14.4 mg, 0.016 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography, product **3i,a** was obtained as a yellowish oil (31.7 mg, 32% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.50 - 7.37 (m, 2H), 7.35 - 7.21 (m, 8H), 4.67 (s, 1H), 4.05 - 3.87 (m, 2H), 2.40 - 2.29 (m, 1H), 2.22 - 2.10 (m, 1H), 2.10 - 1.97 (m, 1H), 1.95 - 1.88 (m, 2H), 1.82 - 1.62 (m, 3H), 1.09 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ: 172.1 (C), 142.9 (C), 138.6 (C), 128.4 (CH), 128.2 (CH), 128.0 (CH), 127.7 (CH), 127.5 (CH), 126.8 (CH), 91.2 (C), 75.6 (CH), 60.9 (CH_2), 38.2 (CH_2), 36.7 (CH_2), 23.2 (CH_2), 23.1 (CH_2), 14.1 (CH_3) ppm; IR (neat): 2961, 2873, 1750, 1171, 1091, 1066, 1029, 698 cm^{-1}. HRMS (ESI) *m/z*: calcd for $C_{21}H_{24}O_3Na$ $[M+Na]^+$ 347.1618, found 347.1616.



3j,a

Compound 3j,a: This compound was synthesised following the general procedure indicated at the beginning of this section from 4-(trifluoromethyl)phenol **1j** (166.0 mg, 1.0 mmol) and diazo compound **2a** (35 μL, 0.20 mmol) as substrates, using $[Cu(MeCN)_4]BArF$ (11.4 mg, 0.01 mmol) and **L1** (4.99 mg, 0.012 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography, product **3j,a** was obtained as a yellowish oil (32.3 mg, 50% yield). ^{1}H NMR (500 MHz, $CDCl_3$) δ: 7.59 - 7.53 (m, 4H), 7.44 - 7.39 (m, 3H), 7.05 - 7.01 (m, 2H), 5.66 (s, 1H), 4.28 - 4.15 (m, 2H) and 1.21 (t, J = 7.1 Hz, 3H) ppm; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 169.4 (C), 159.8 (C), 134.9 (C), 129.4 (CH), 129.0 (CH), 127.2 (CH), 127.1 (q, J_{C-F} = 3.5 Hz, CH), 124.4 (q, J_{C-F} = 270.0 Hz, C), 124.1 (q, J_{C-F} = 33.3 Hz, C), 115.5 (CH), 78.8 (CH), 62.0 (CH_2) and 14.1 (CH_3) ppm; ^{19}F{^{1}H} NMR (471 MHz, $CDCl_3$) δ: –61.8 ppm; IR (neat): 2992, 1733, 1614, 1520, 1326, 1253, 1213, 1192, 1152, 1106, 1069, 1054, 1021, 873, 727, 694 and 648 cm^{-1}; HRMS (ESI) *m/z*: calcd for $C_{17}H_{15}F_3O_3Na$ $[M+Na]^+$ 347.0865, found 347.0862.



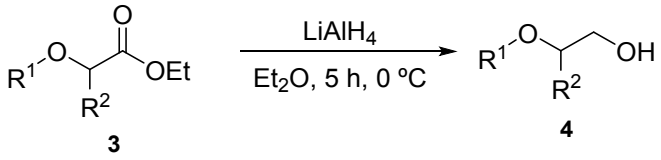
3k,c

Compound 3k,c: This compound was synthesised following the general procedure indicated at the beginning of this section from diphenylmethanol **1k** (185.0 mg, 1.0 mmol) and the commercial available ethyl 2-diazoacetate **2c** (24.3 μL, 0.20 mmol) as substrates, using $[Cu(MeCN)_4]BArF$ (11.4 mg, 0.01 mmol) and **L1** (4.99 mg, 0.012 mmol) and NaBArF (14.2 mg, 0.016 mmol) to generate *in situ* the supramolecular catalyst. After purification by silica gel column chromatography, product **3k,c** was obtained as a yellowish oil (40.7 mg, 75% yield). Spectroscopic data were in agreement with those previously reported.[19] ^1H NMR (500 MHz, $CDCl_3$) δ: 7.37 - 7.35 (m, 4H), 7.32 - 7.29 (m, 4H), 7.26 - 7.23 (m, 2H), 5.56 (s, 1H), 4.19 (q, J = 7.1 Hz, 2H), 4.07 (s, 2H), 1.25 (t, J = 7.1 Hz, 3H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ: 170.6 (C), 141.2 (C), 128.6 (CH), 127.9 (CH), 127.5 (CH), 83.7 (CH), 66.1 (CH_2), 60.9 (CH_2) and 14.3 (CH_3) ppm.

[19] P. R. Krishna, Y. L. Prapurna and M. Alivelu, *Tetrahedron Lett.*, 2011, **52**, 3460-3462.

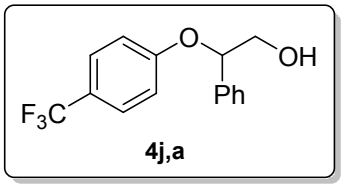
7. Transformation of O–H insertion products into advanced synthetic intermediates of APIs

7.1. General procedure for the reduction of an ester group into the corresponding primary alcohol 4



Scheme SI 5. General synthesis for products **4**.

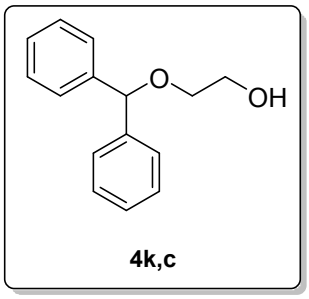
To a flame-dried Schlenk flask, $LiAlH_4$ (19.1 mg, 0.503 mmol) was added, suspended in anhydrous Et_2O (0.5 mL) and cooled at 0 °C. Then, a solution of **3** (100.0 mg, 0.370 mmol) in anhydrous Et_2O (0.5 mL) was slowly cannulated into the $LiAlH_4$ suspension. The reaction mixture was allowed to reach room temperature and stirred for 4.5 h. The reaction was then cooled down to 0 °C, diluted with Et_2O (0.5 mL), and carefully quenched with a saturated aqueous solution (1.0 mL) of Rochelle salt (*i.e.*, sodium potassium L(+)-tartrate tetrahydrate). The biphasic mixture was vigorously stirred overnight at room temperature. The two phases were then separated and the aqueous phase was extracted with Et_2O (2 x 5.0 mL). The combined organic phases were washed with brine (1 x 5.0 mL), dried over $MgSO_4$, filtered, and concentrated *in vacuo.* The desired product was obtained after purification by silica gel column chromatography using Cy/EtOAc (98:2) as eluent.



Compound **4j,a** was synthesised following the general procedure from $LiAlH_4$ (0.419 mmol, 15.9 mg) and **3j,a** (0.308 mmol, 100 mg). After purification by silica gel column chromatography, product **4j,a** (43.2 mg, 50% yield) was obtained as a colourless oil (43.2 mg, 50% yield). Spectroscopic data were in agreement with those previously reported.[20] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.47 - 7.44 (m, 2H), 7.39 - 7.30 (m, 5H), 6.95 - 6.93 (m, 2H), 5.32 (dd, J = 8.1, 3.6 Hz, 1H), 3.97 (dd, J = 12.1, 8.1 Hz, 1H), 3.85 (dd, J = 12.1, 3.6 Hz, 1H) and 2.32 (broad signal, 1H) ppm; ^{13}C{^{1}H} NMR (101 MHz, $CDCl_3$) δ: 160.3 (C), 137.1 (C), 129.1 (CH), 128.6 (CH), 127.0 (q, $J_{C–F}$ = 3.7 Hz, CH), 126.4 (CH), 124.5 (q, $J_{C–F}$ = 270.8 Hz, C), 123.5 (q,

[20] P. N. Devine, R. M. Heid, Jr. and D. M. Tschaen, *Tetrahedron*, 1997, **53**, 6739-6746.

J_{C-F} = 32.8 Hz, C), 116.0 (CH), 81.6 (CH) and 67.5 (CH_2) ppm; $^{19}F\{^1H\}$ NMR (376 MHz, $CDCl_3$) δ: −61.7 ppm.



4k,c

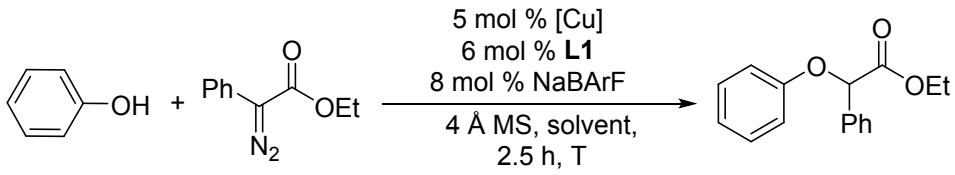
Compound **4k,c** was synthesised following the general procedure from $LiAlH_4$ (0.503 mmol, 19.1 mg) and **3k,c** (0.370 mmol, 100 mg). After purification by silica gel column chromatography, product **4k,c** was obtained as a colourless oil (41.0 mg, 49% yield). Spectroscopic data were in agreement with those previously reported.[21] ^1H NMR (500 MHz, $CDCl_3$) δ: 7.37 - 7.24 (m, 10H), 5.41 (s, 1H), 3.79 (broad multiplet, 2H), 3.61 - 3.59 (m, 2H) and 2.01 (broad signal, 1H) ppm; $^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$) δ: 142.0 (C), 128.6 (CH), 127.8 (CH), 127.1 (CH), 84.2 (CH) , 70.5 (CH_2) and 62.2 (CH_2) ppm.

[21] M. H. S. A. Hamid, C. L. Allen, G. W. Lamb, A. C. Maxwell, H. C. Maytum, A. J. A. Watson and J. M. J. Williams, *J. Am. Chem. Soc.*, 2009, **131**, 1766-1774.

8. Complete set of results for catalysed insertion of copper-carbenoids into O–H bonds

8.1. Background experiments

A full set of experiments on the optimization of the reaction conditions, as well as background experiments, is summarised below (Table SI 1). See section 6 for the general procedure and experimental details to carry out the O–H insertion reactions.



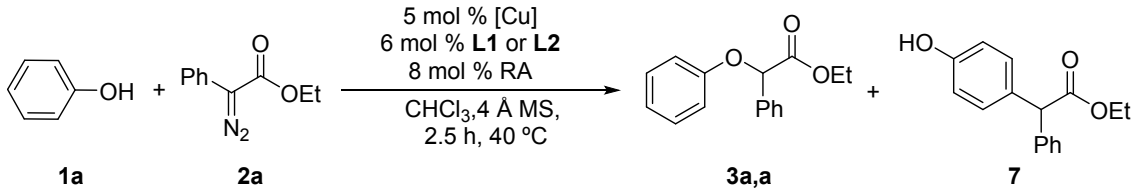
1a **2a** **3a,a**

Table SI 1. Optimization for the Cu-mediated carbene insertion into O–H bonds.

Entry	[Cu]	Ligand	NaBArF	Molecular sieves	Solvent	T (ºC)	Yield [%][a]
1	--	--	--	yes,[b]	$CHCl_3$	40	<1
2	$[Cu(MeCN)_4]BArF$	--	--	--	$CHCl_3$	40	48
3	--	**L1**	--	--	$CHCl_3$	40	<1
4	--	--	NaBArF	--	$CHCl_3$	40	<1
5	--	**L1**	NaBArF	--	$CHCl_3$	40	<1
6	$[Cu(MeCN)_4]BArF$	--	NaBArF	--	$CHCl_3$	40	51
7	$[Cu(MeCN)_4]BArF$	**L1**	NaBArF	--	$CHCl_3$	40	64
8	$[Cu(MeCN)_4]BArF$	--	NaBArF	yes,[b]	$CHCl_3$	40	53
9	$[Cu(MeCN)_4]BArF$	**L1**	NaBArF	yes,[b]	$CHCl_3$	40	66
10	$[Cu(MeCN)_4]BArF$	**L1**	--	yes,[b]	$CHCl_3$	40	67
11	$[Cu(MeCN)_4]BArF$	**Ox**[c]	--	yes,[b]	$CHCl_3$	40	47
12	$[Cu(MeCN)_4]BArF$	**L1**	NaBArF	yes,[b]	CH_2Cl_2	40	62
13[d]	$[Cu(MeCN)_4]BArF$	**L1**	NaBArF	yes,[b]	PhMe	40	47
14	$[Cu(MeCN)_4]BArF$	**L1**	NaBArF	yes,[b]	PhCl	40	59
15[e]	$[Cu(MeCN)_4]BArF$	**L1**	NaBArF	yes,[b]	$CHCl_3$	0	42
16	$[Cu(MeCN)_4]BArF$	**L1**	NaBArF	yes,[b]	$CHCl_3$	rt	64
17	$[Cu(MeCN)_4]BF_4$	**L1**	$NaBF_4$	yes,[b]	$CHCl_3$	40	15

[a] Yields were determined by ^1H NMR using 1,3,5-trimethoxybenzene as the internal standard. [b] 4 Å molecular sieves were used in a 95:5 ratio with respect to **2a**. [c] 2.0 equiv. of 4,4-dimethyl-4,5-dihydrooxazole was added. [d] The reaction was performed adding a 3% of THF. [e] Reaction time was 5 h.

8.2. Comparative study of the reactivity of L1 and L2



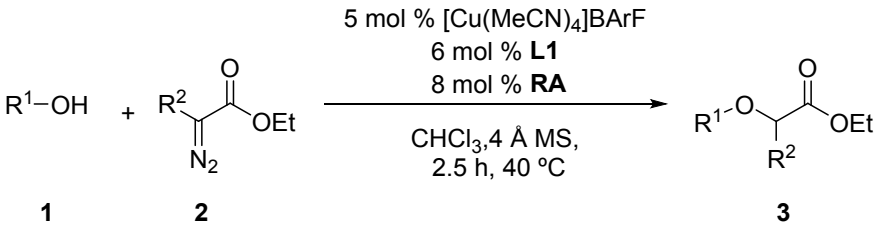
1a **2a** **3a,a** **7**

Table SI 2. Study between ligands **L1** and **L2.**

Entry	Substrate 1	Substrate 2	L	RA	3 yield [%][a]	7 yield [%][a]
1	**1a**	**2a**	**L1**	None	67	nd[b]
2				LiBArF	84	nd
3				NaBArF	66	nd
4				KBArF	77	nd
5				RbBArF	85 (81)[c]	nd
6				CsBArF	65	nd
7	**1a**	**2a**	**L2**	None	50	6
8				LiBArF	77	5
9				NaBArF	64	nd
10				KBArF	79	4
11				RbBArF	71	nd
12				CsBArF	60	14

[a] Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as the internal standard. [b] Not detected. [c] Isolated yield.

8.3. Full set of results for the catalysed insertion of copper-carbenoids into the O–H bonds of compounds 1a-i



1 **2** **3**

See section 6 for the general procedure and experimental details to carry out the O–H insertion reactions.

Table SI 3. Catalysed insertion of copper-carbenoids into the O–H bonds of compounds **1a-i**.

Entry	Substrate 1	Substrate 2	RA	3 yield [%][a]
1	**1b**	**2a**	None	49
2			LiBArF	52
3			NaBArF	56
4			KBArF	50
5			RbBArF	59 (55)[b]
6			CsBArF	51
7	**1c**	**2a**	None	54
8			LiBArF	53
9			NaBArF	55
10			KBArF	51
11			RbBArF	61
12			CsBArF	69 (64)[b]
13	**1d**	**2a**	None	32
14			LiBArF	82
15			NaBArF	87 (80)[b]
16			KBArF	82
17			RbBArF	83
18			CsBArF	80
19	**1e**	**2a**	None	70
20			LiBArF	98
21			NaBArF	99 (91)[b]
22			KBArF	97
23			RbBArF	88
24			CsBArF	80

Table SI 2 cont.

Entry	Substrate 1	Substrate 2	RA	3 yield [%][a]
25	**1f**	**2a**	None	41 (38)[b]
26			LiBArF	28
27			NaBArF	30
28			KBArF	20
29			RbBArF	24
30			CsBArF	17
31[c]			NaBArF	10
32	**1a**	**2b**	None	66
33			LiBArF	70
34			NaBArF	72
35			KBArF	77 (75)[b]
36			RbBArF	77
37			CsBArF	72
38	**1b**	**2b**	None	54
39			LiBArF	21
40			NaBArF	69 (63)[b]
41			KBArF	65
42			RbBArF	53
43			CsBArF	58
44	**1c**	**2b**	None	44
45			LiBArF	61
46			NaBArF	62 (60)[b]
47			KBArF	62
48			RbBArF	59
49			CsBArF	62
50	**1d**	**2b**	None	64
51			LiBArF	72
52			NaBArF	74 (68)[b]
53			KBArF	65
54			RbBArF	19
55			CsBArF	43
56	**1e**	**2b**	None	50
57			LiBArF	59
58			NaBArF	63
59			KBArF	58
60			RbBArF	74 (71)[b]
61			CsBArF	72

Table SI 2 cont.

Entry	Substrate 1	Substrate 2	RA	3 yield [%][a]
62	**1f**	**2b**	None	19
63			LiBArF	16
64			NaBArF	38
65			KBArF	42 (29)[b]
66			RbBArF	25
67			CsBArF	34
68	**1g**	**2a**	None	11
69			LiBArF	57
70			NaBArF	64 (56)[b]
71			KBArF	61
72			RbBArF	61
73			CsBArF	59
74	**1h**	**2a**	None	82
75			LiBArF	85 (83)[b]
76			NaBArF	80
77			KBArF	81
78			RbBArF	71
79			CsBArF	71
80[d]	**1i**	**2a**	None	12
81			LiBArF	36
82			NaBArF	39 (32)[b]
83			KBArF	38
84			RbBArF	37
85			CsBArF	38
86	**1j**	**2a**	None	54 (50)[b]
87			LiBArF	43
88			NaBArF	35
89			KBArF	35
90			RbBArF	54
91			CsBArF	52
92	**1k**	**2c**	None	72
93			LiBArF	69
94			NaBArF	76 (75)[b]
95			KBArF	75
96			RbBArF	68
97			CsBArF	73

[a] Yields were determined by ^{1}H NMR using 1,3,5-trimethoxybenzene as the internal standard. [b] Isolated yield. [c] Addition time of **2a** was 6 h and reaction time 24 h. [d] Reaction time was 24 h.

9. Reaction monitoring

Monitorization of the reaction between **2a** and phenol by ^{1}H NMR at different reaction times was performed following the general procedure (see section 6), in the absence and in the presence of RbBArF as RA. The yields for **2a**, **3a,a**, **5** and **6** were quantified by ^{1}H NMR using 1,3,5-trimethoxybenzene as internal standard. The resulting plots are shown in Figure SI 12 and Figure SI 13.

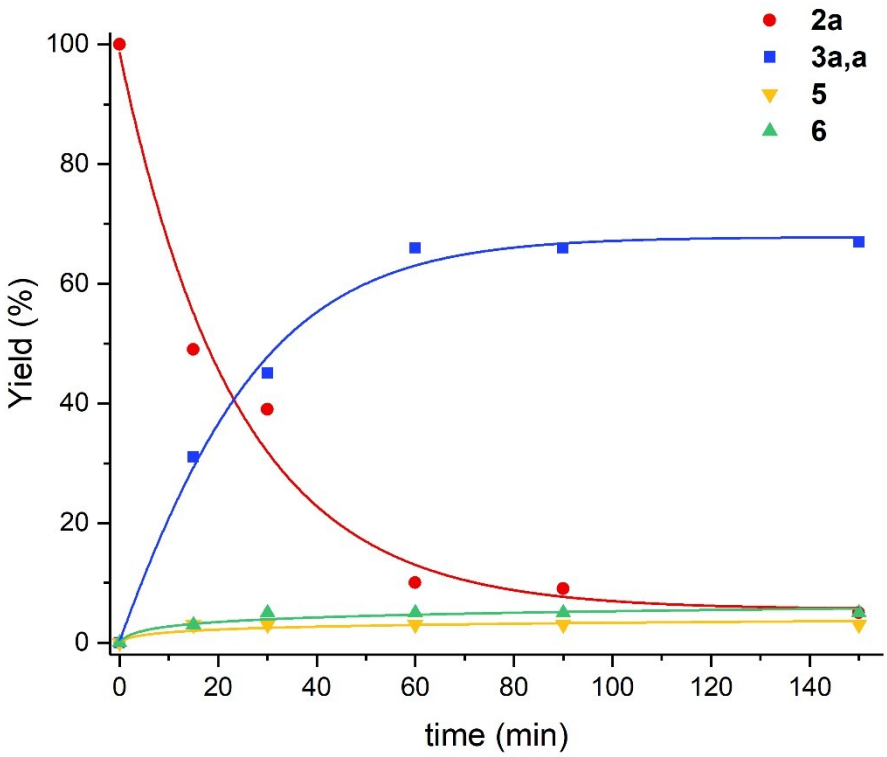


Figure SI 12. Reaction monitoring in the absence of RA (solid lines correspond to eye guidelines).

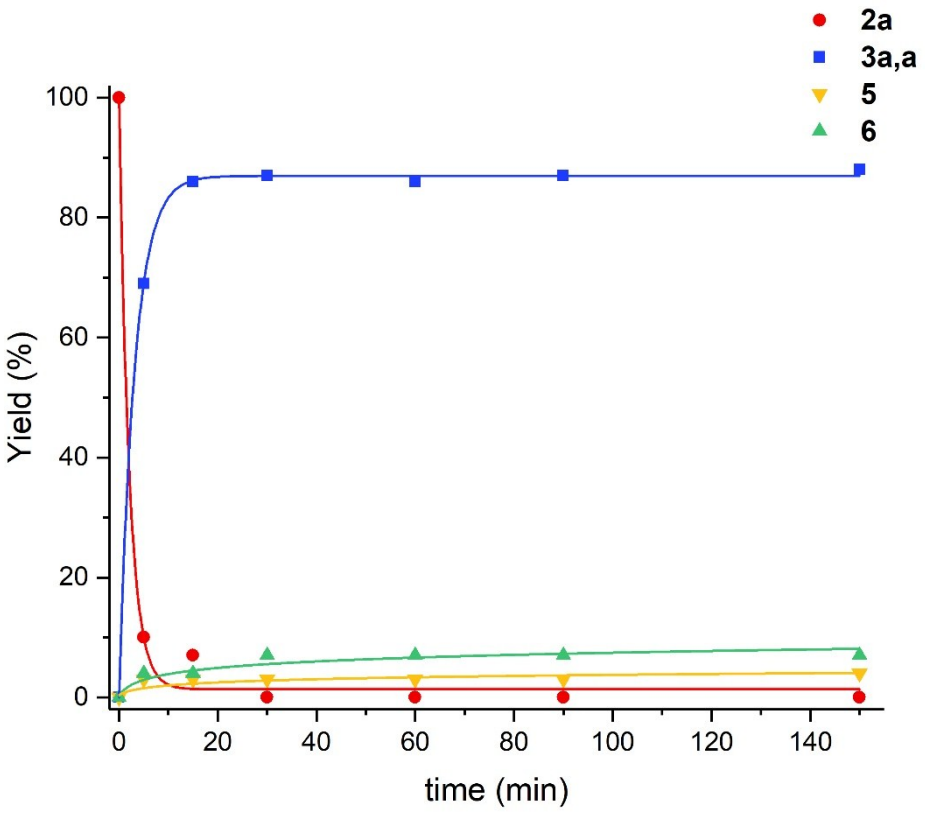


Figure SI 13. Reaction monitoring in the presence of RbBArF as RA (solid lines correspond to eye guidelines).

10. Studies on the stability of the copper-based supramolecular catalyst

Two independents reactions, one without RA and the other with RbBArF as regulation agent, were performed following the general procedure between **1a** and **2a** as substrates (see section 6). After two and a half hours, a second batch of **1a** and **2a** (the same amounts than before) were added to each reaction mixture. It should be mentioned that no amounts of ligand, copper precursor or regulation agent were added to the reaction mixtures at this point. The formation of **3a,a** as a function of time was monitored by ^{1}H NMR analysis of the corresponding reaction mixtures using 1,3,5-trimethoxybenzene as internal standard. The resulting plots are shown in Figure SI 14 and Figure SI 15.

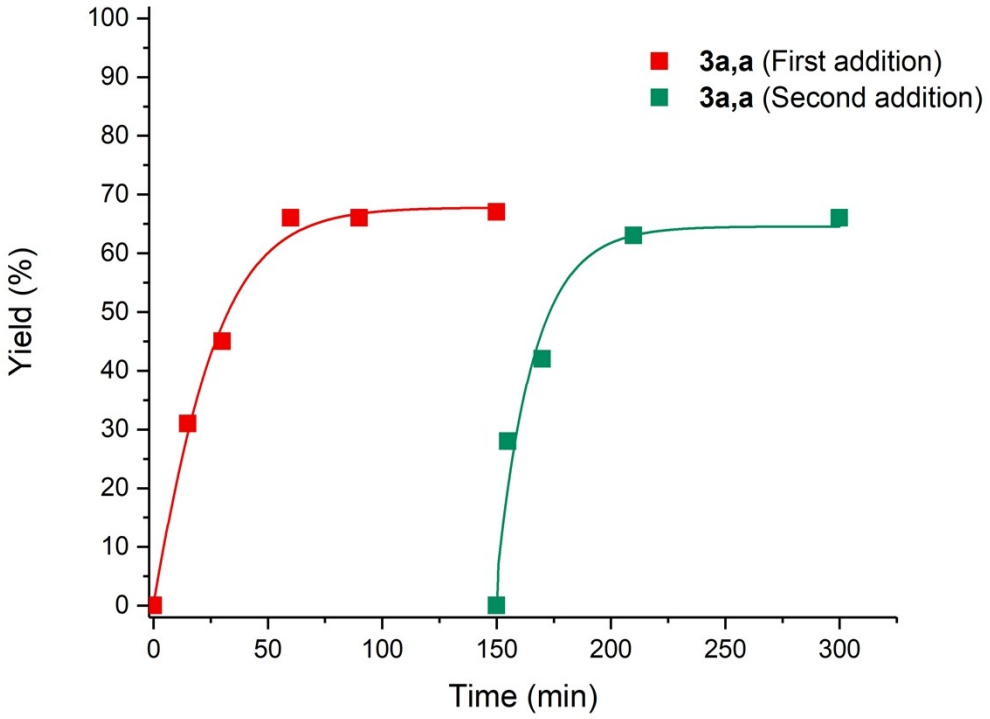


Figure SI 14. Reaction monitoring of two reaction cycles in the absence of RA. Red line corresponds to the yield towards **3a,a** for the first reaction cycle (from 0 to 150 min) and the green one for the second reaction cycle (from 150 to 300 min; solid lines correspond to eye guidelines).

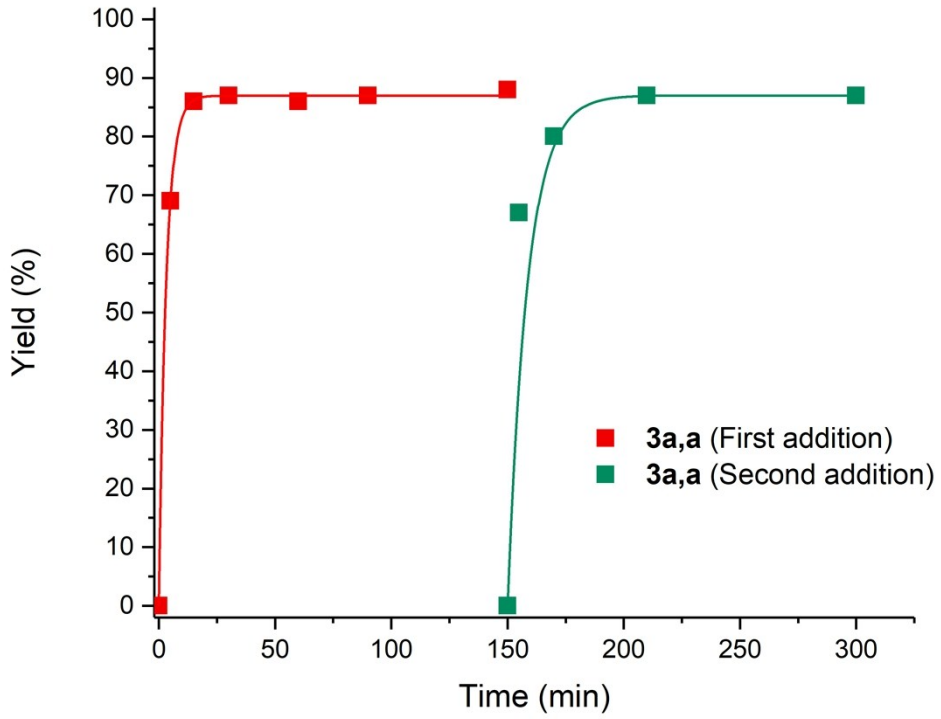
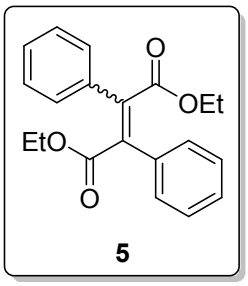


Figure SI 15. Reaction monitoring of two reaction cycles with RbBArF as the RA. Red line corresponds to the yield towards **3a,a** for the first reaction cycle (from 0 to 150 min) and the green one for the second reaction cycle (from 150 to 300 min; solid lines correspond to eye guidelines).

As it can be seen in the conversion curves in Figures SI-14 and SI-15, the rate of formation of product **3a,a** during the first (from 0 to 150 min) and second (from 150 to 300 min) reaction cycles are very similar. These experiments demonstrate that the catalytic species survive the first reaction cycle and remain active to transform a second batch of reagents into the corresponding product with very similar catalytic efficiency. Hence, these experiments rule out a deactivation process of the catalyst, as the supramolecular catalytic system remains active in solution.

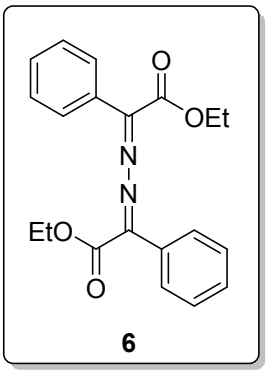
11. Characterization of products 5 and 6

Products **5** and **6** (see section 9) were identified in the crude mixture. Both compounds were independently synthesised.



5

Product **5** was prepared reacting PhEDA **2a** (0.26 mmol) with $AgBF_4$ (10 mol%) in 2 mL of CH_2Cl_2 for 1 hour. After evaporation, the reaction crude mixture was purified by column chromatography using SiO_2 and Cy and AcOEt as the eluents (30:1, Cy:AcOEt), to afford **5** as a pale yellow oil (18.3 mg, 22% yield). Spectroscopic data were in agreement with those previously reported.[22] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.45-7.34 (m, 10H), 4.00 (q, J = 7.1 Hz, 4H), 0.94 (t, J = 7.1 Hz, 6H) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 168.2 (C), 137.8 (C), 135.7 (C), 128.8 (CH), 128.5 (CH), 128.3 (CH), 61.5 (CH_2), 13.7 (CH_3) ppm.



6

Product **6** was prepared reacting PhEDA **2a** (0.26 mmol) with $AgBF_4$ (10 mol%) in 2 mL of CH_2Cl_2 for 1 hour. After evaporation, the reaction crude mixture was purified by column chromatography using SiO_2 and Cy and AcOEt as the eluents (30:1, Cy:AcOEt), to afford **6** as a yellow solid (9.1 mg, 10% yield). Spectroscopic data were in agreement with those previously reported.[23] ^{1}H NMR (400 MHz, $CDCl_3$) δ: 7.81-7.78 (m, 4H), 7.50-7.41 (m, 6H), 4.50 (q, J = 7.1 Hz, 4H), 1.42 (t, J = 7.1 Hz, 6H) ppm; $^{13}C\{^1H\}$ NMR (101 MHz, $CDCl_3$) δ: 165.3 (C), 162.3 (C), 132.1 (C), 131.4 (CH), 128.9 (CH), 128.0 (CH), 61.7 (CH_2), 14.5 (CH_3) ppm.

[22] The *E*- or *Z*-configuration could not be unequivocally assigned according to previous reports. See the following references: (a) C. Zhou and R. C. Larock, *J. Org. Chem.*, 2005, **70**, 3765-3777.(b) L. Zhou, W. Zhang and H. Jiang, *Sci. China, Ser. B: Chem.*, 2008, **51**, 241-247.

[23] R. Glaser, G. S. Chen and C. L. Barnes, *J. Org. Chem.*, 1993, **58**, 7446-7455.

12. Copies of NMR spectra

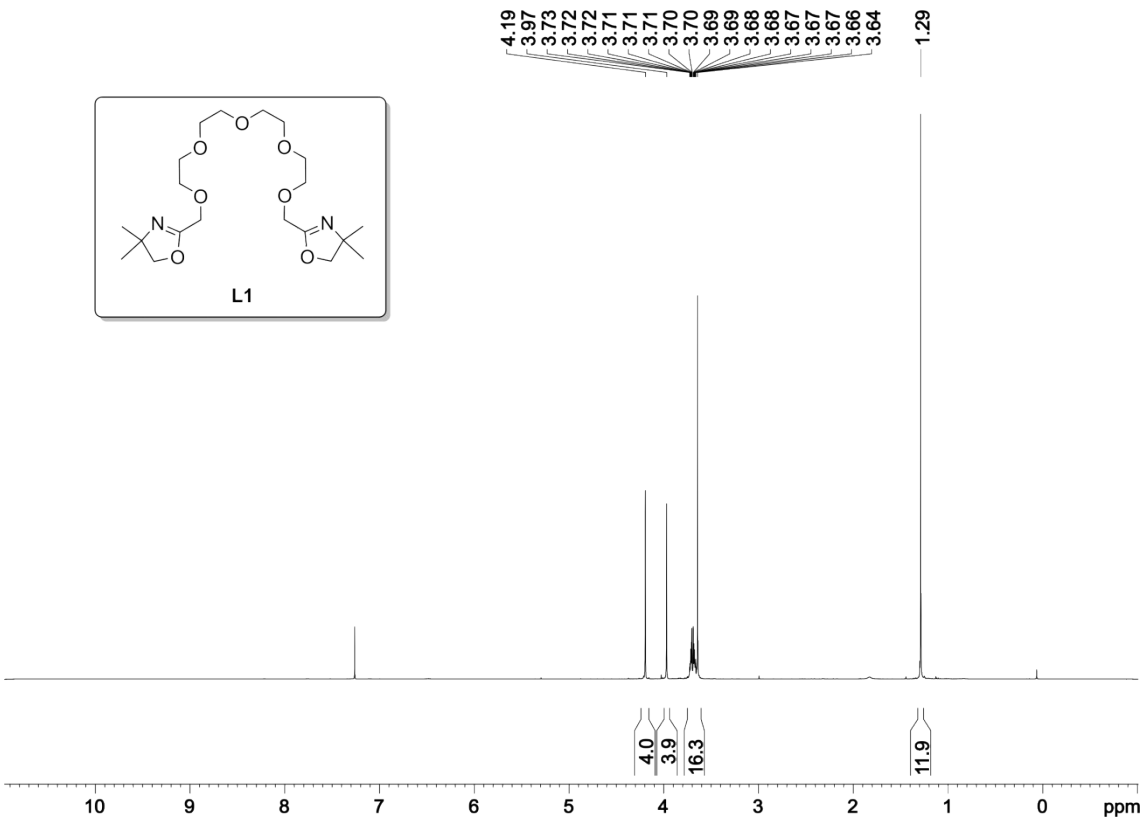


Figure SI 16. ^{1}H NMR (400 MHz, $CDCl_3$) of **L1.**

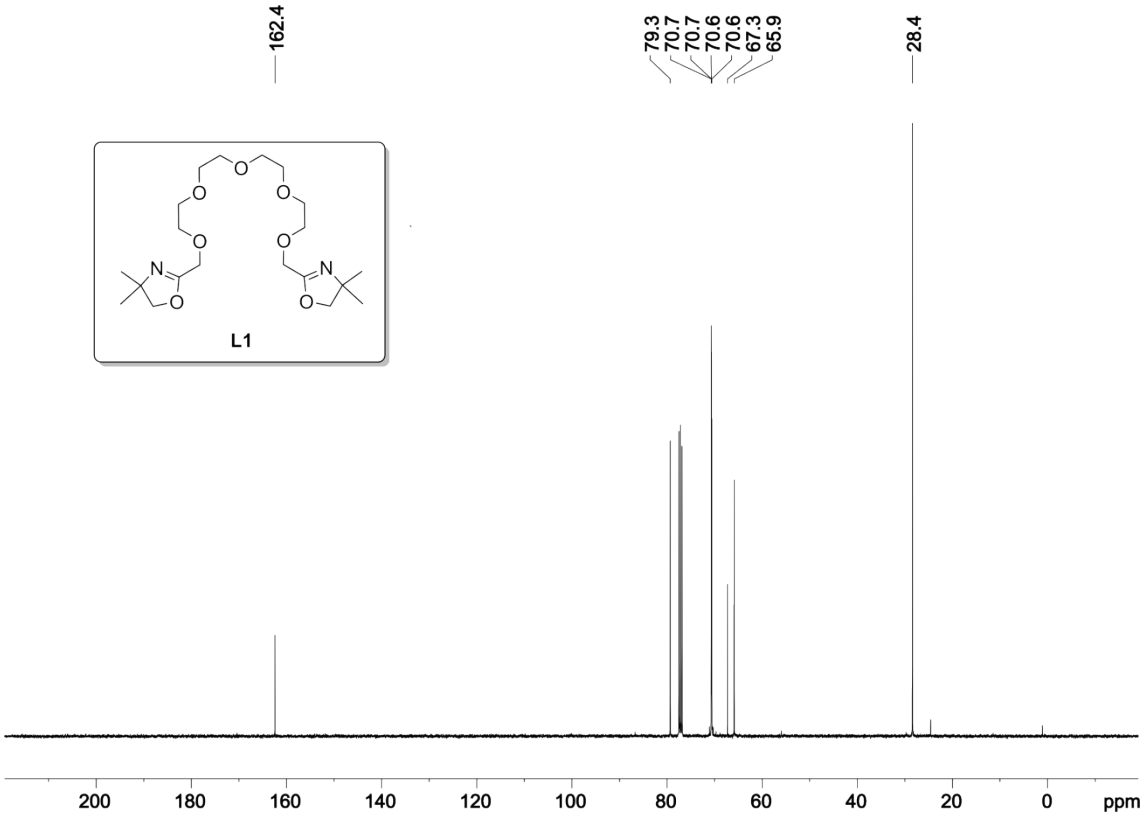


Figure SI 17. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **L1**.

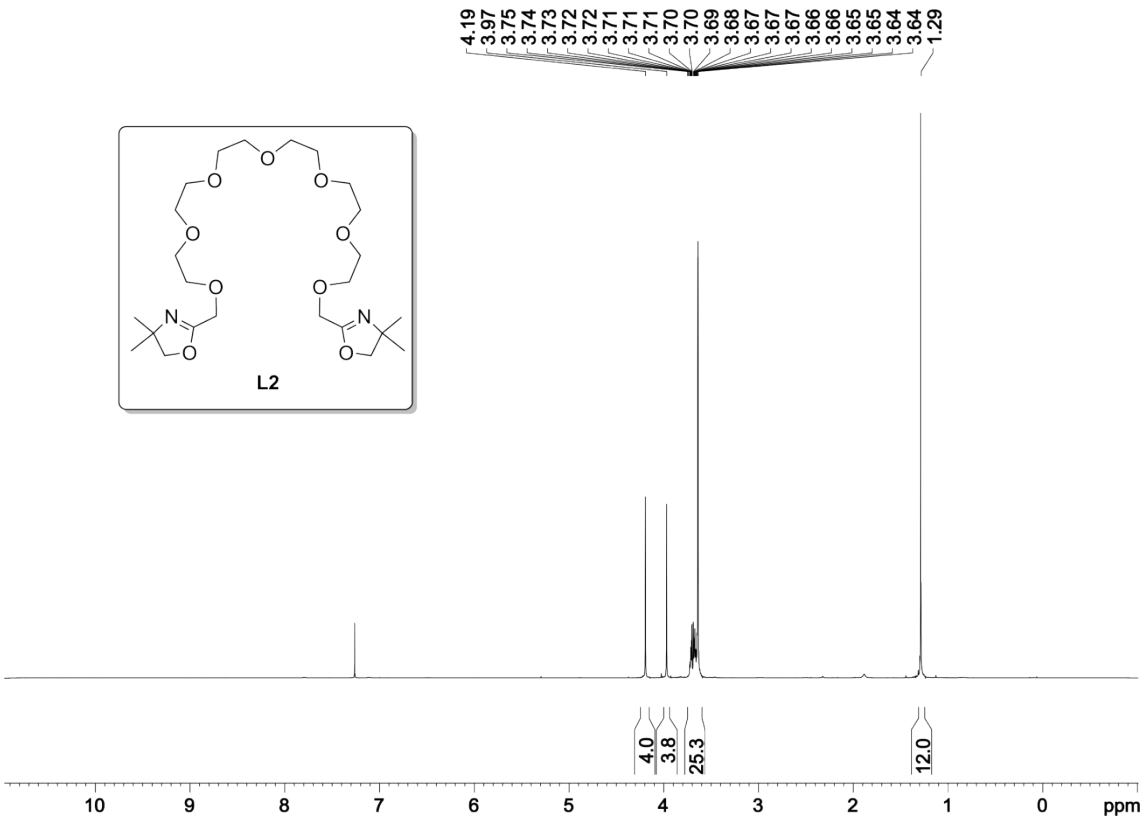


Figure SI 18. ^{1}H NMR (400 MHz, $CDCl_3$) of **L2**.

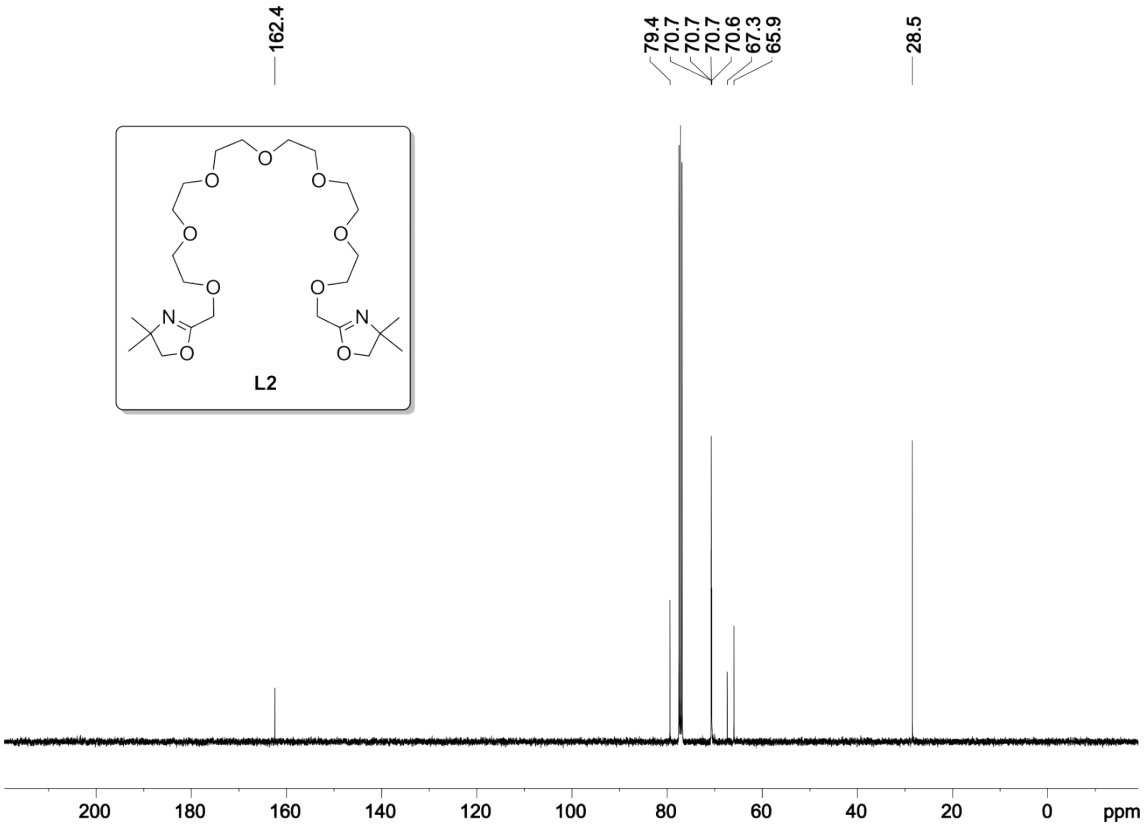


Figure SI 19. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **L2**.

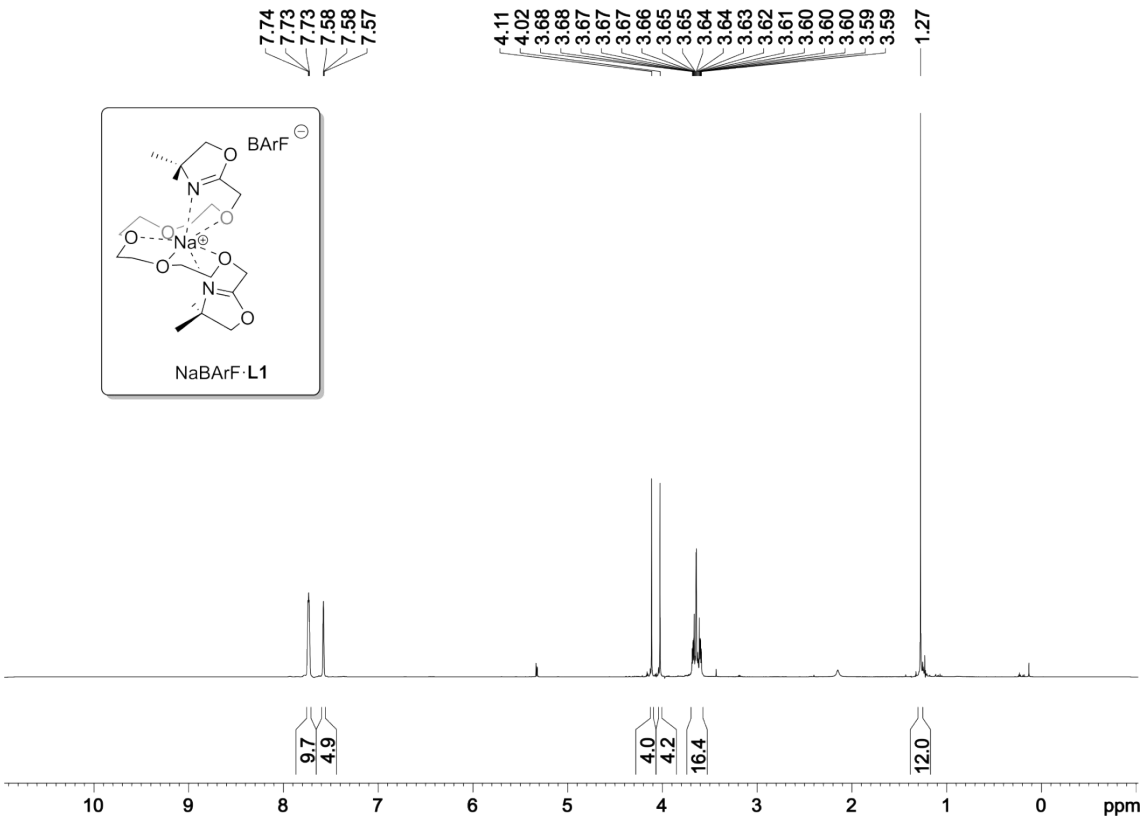


Figure SI 20. ^{1}H NMR (400 MHz, CD_2Cl_2) of NaBArF·**L1**.

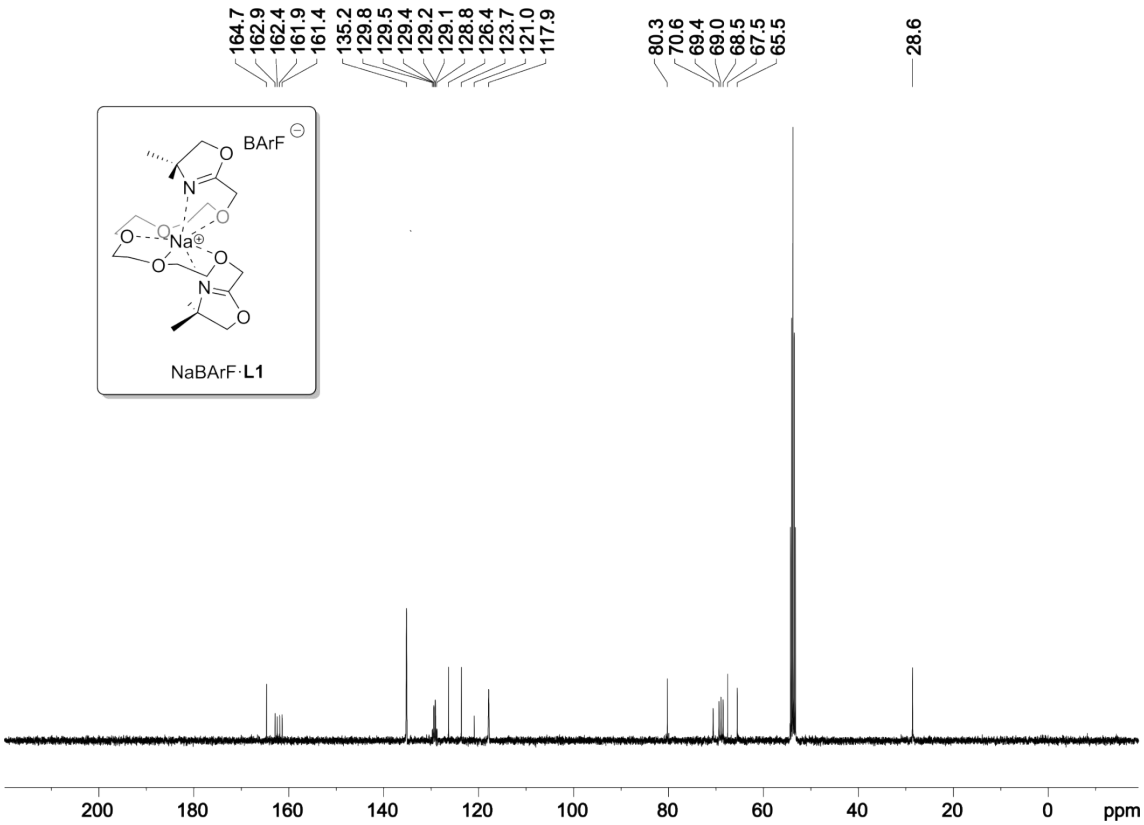


Figure SI 21. ^{13}C{^{1}H} NMR (101 MHz, CD_2Cl_2) of NaBArF·**L1**.

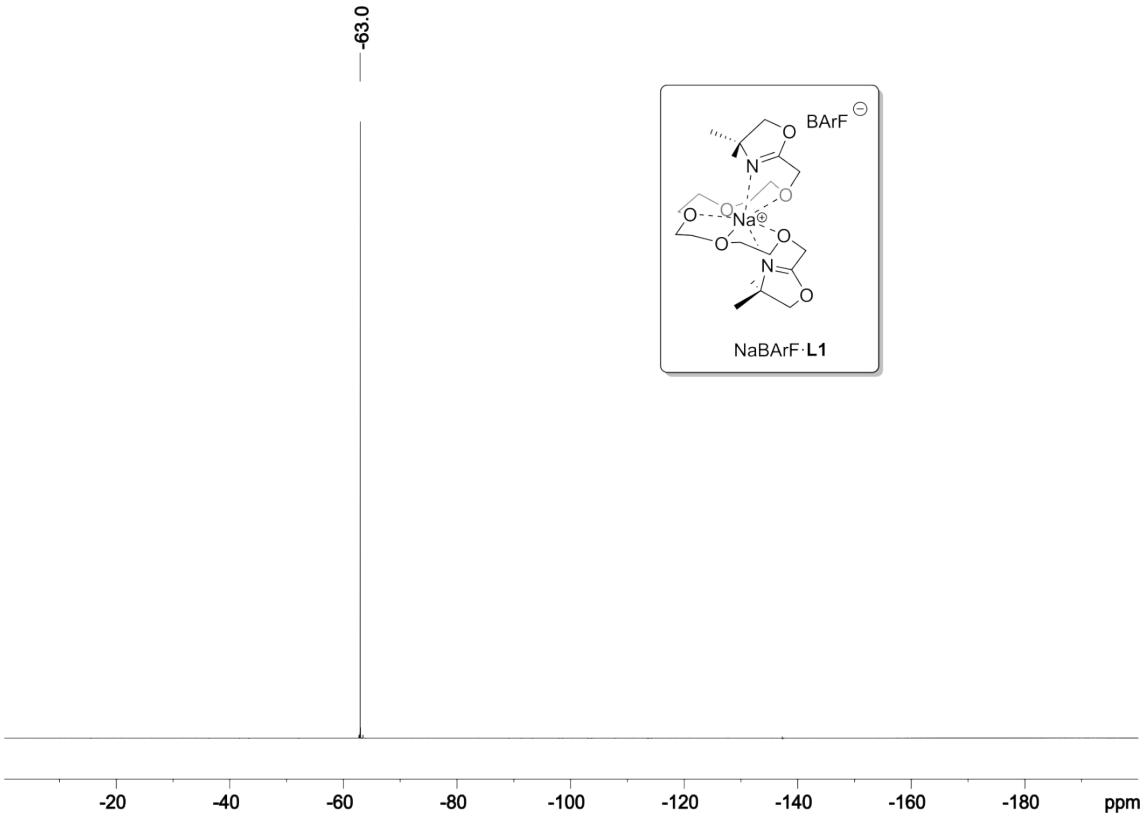


Figure SI 22. $^{19}F\{^{1}H\}$ NMR (376 MHz, CD_2Cl_2) of NaBArF·**L1**.

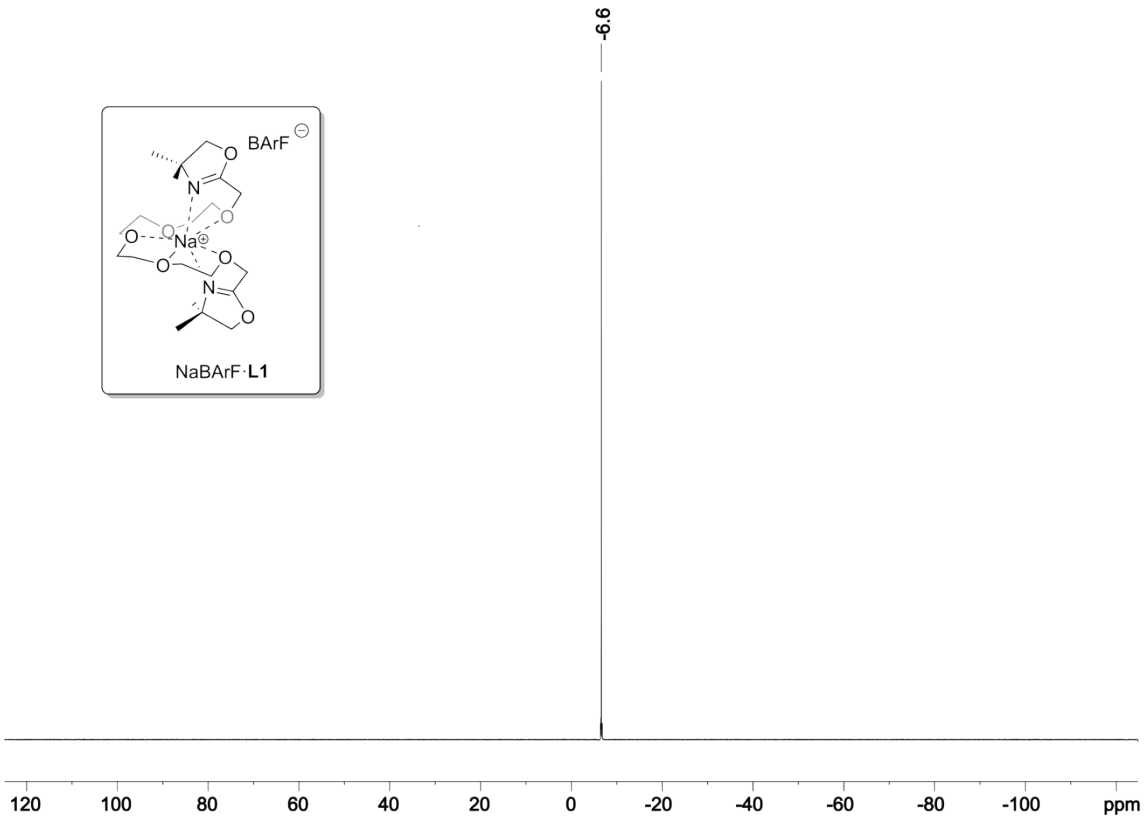


Figure SI 23. $^{11}B\{^{1}H\}$ NMR (128 MHz, CD_2Cl_2) of NaBArF·**L1**.

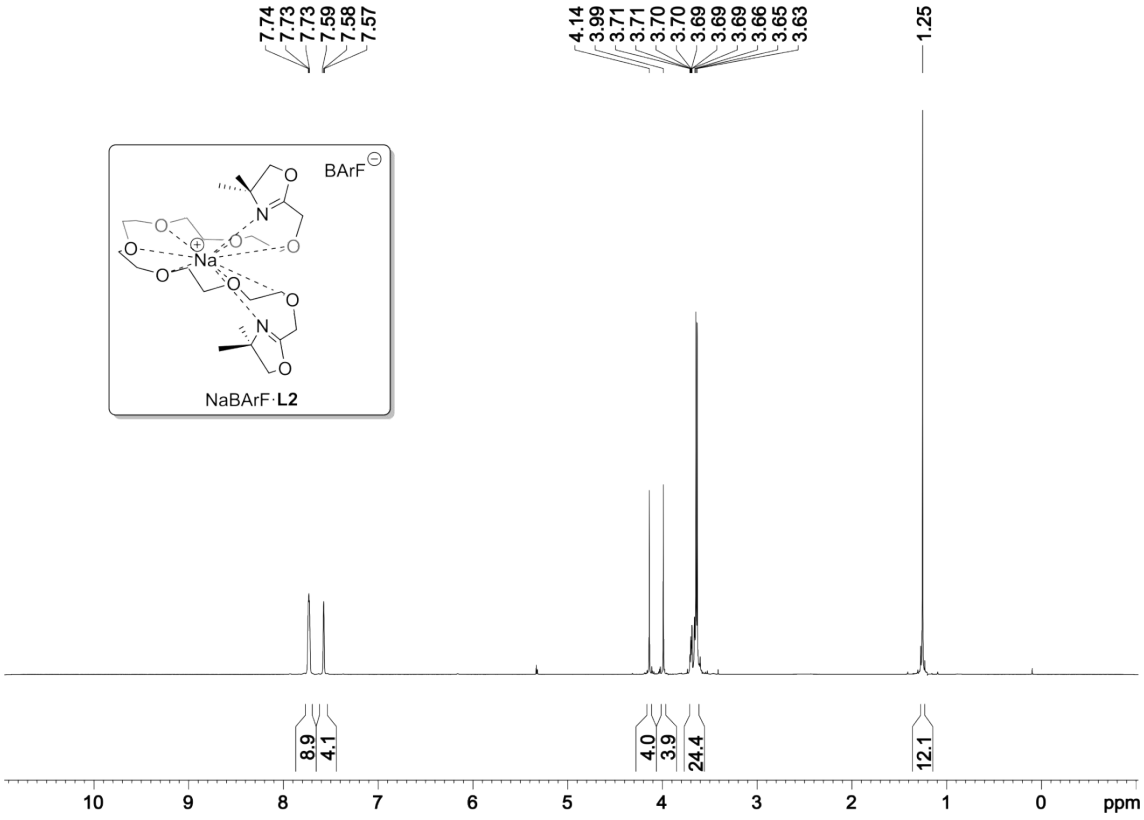


Figure SI 24. ^{1}H NMR (400 MHz, CD_2Cl_2) of NaBArF·**L2**.

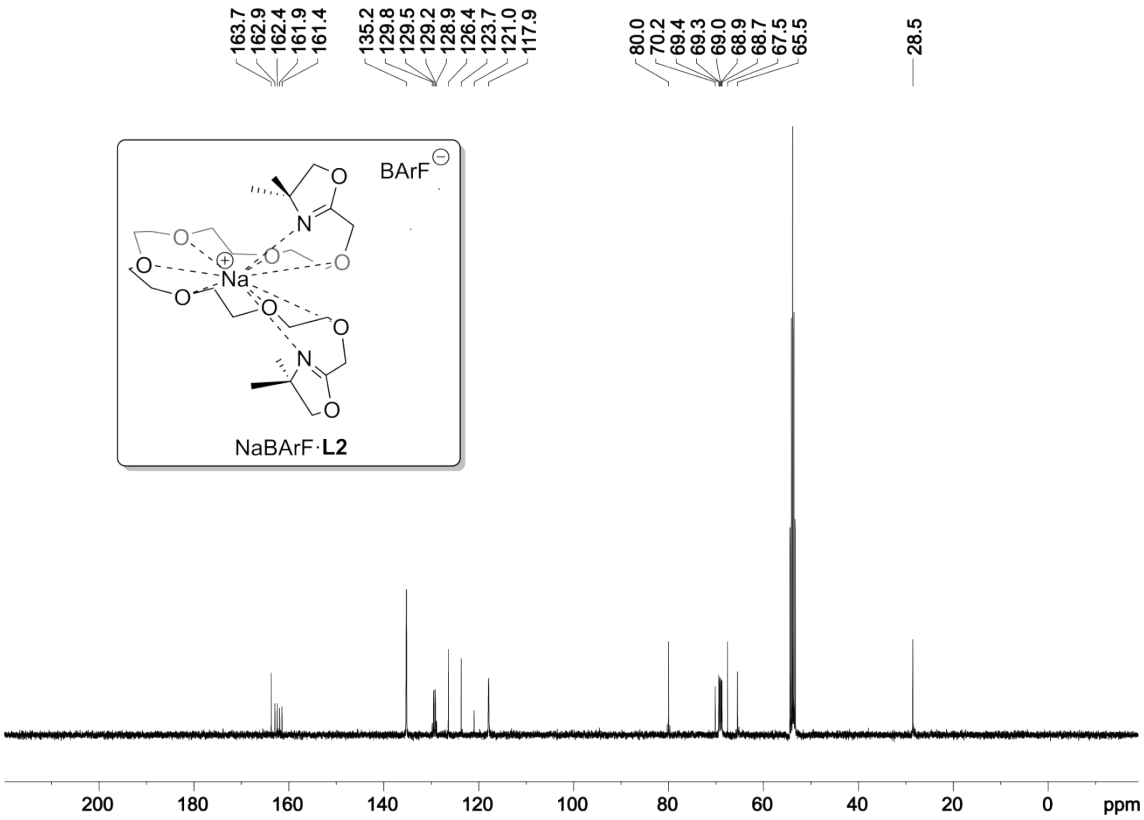


Figure SI 25. $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_2Cl_2) of NaBArF·**L2**.

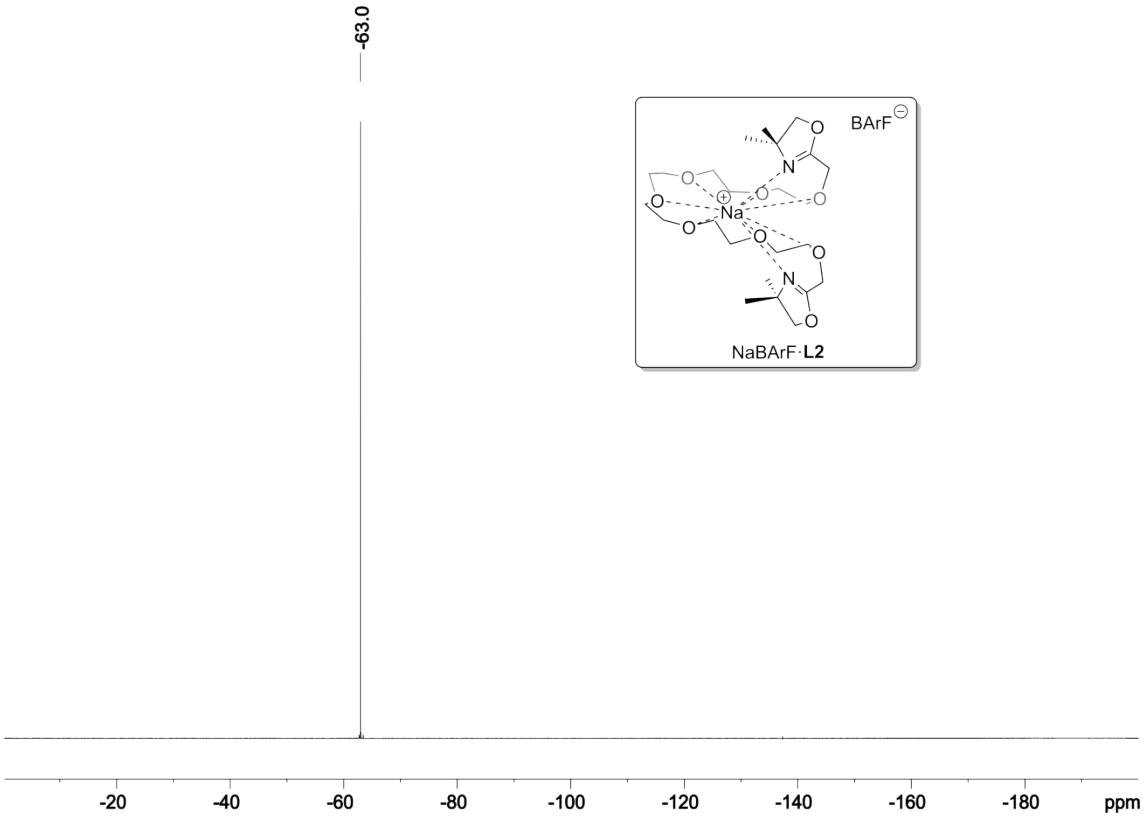


Figure SI 26. $^{19}F\{^{1}H\}$ NMR (376 MHz, CD_2Cl_2) of NaBArF·**L2**.

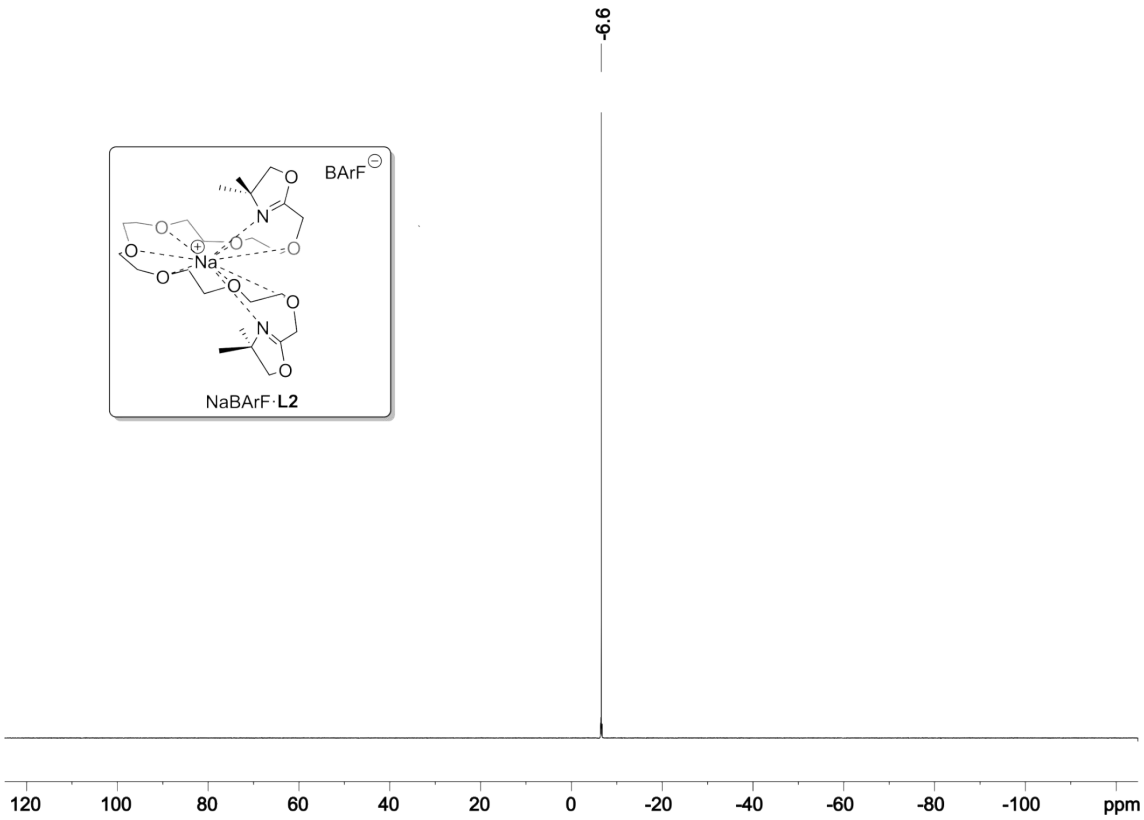


Figure SI 27. $^{11}B\{^{1}H\}$ NMR (128 MHz, CD_2Cl_2) of NaBArF·**L2**.

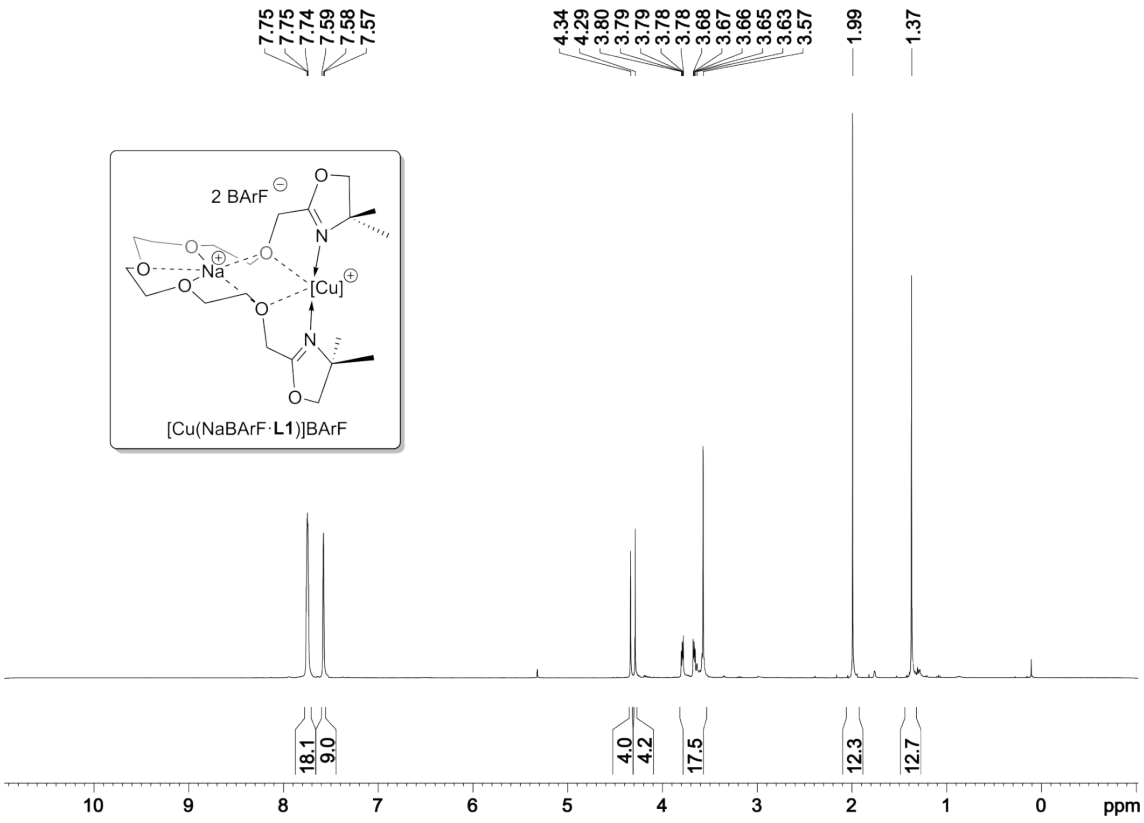


Figure SI 28. ^{1}H NMR (400 MHz, CD_2Cl_2) of [Cu(NaBArF·**L1**)]BArF.

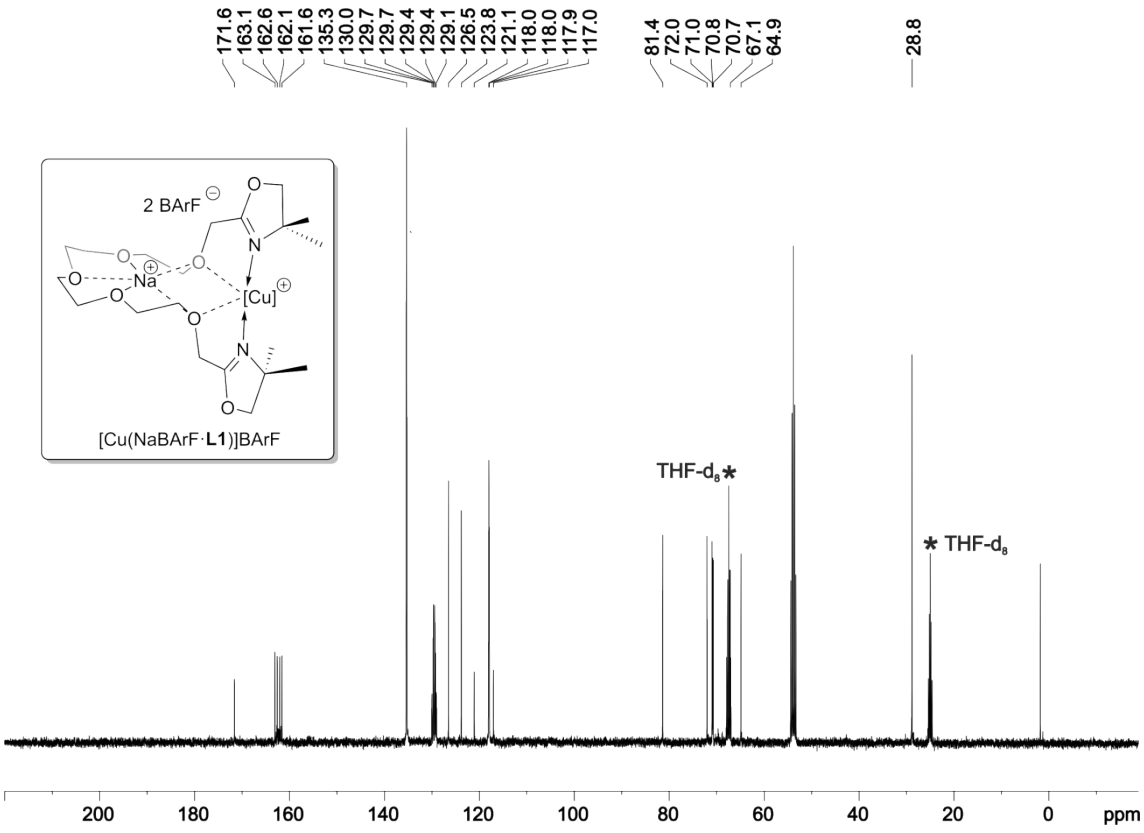


Figure SI 29. $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_2Cl_2) of [Cu(NaBArF·**L1**)]BArF.

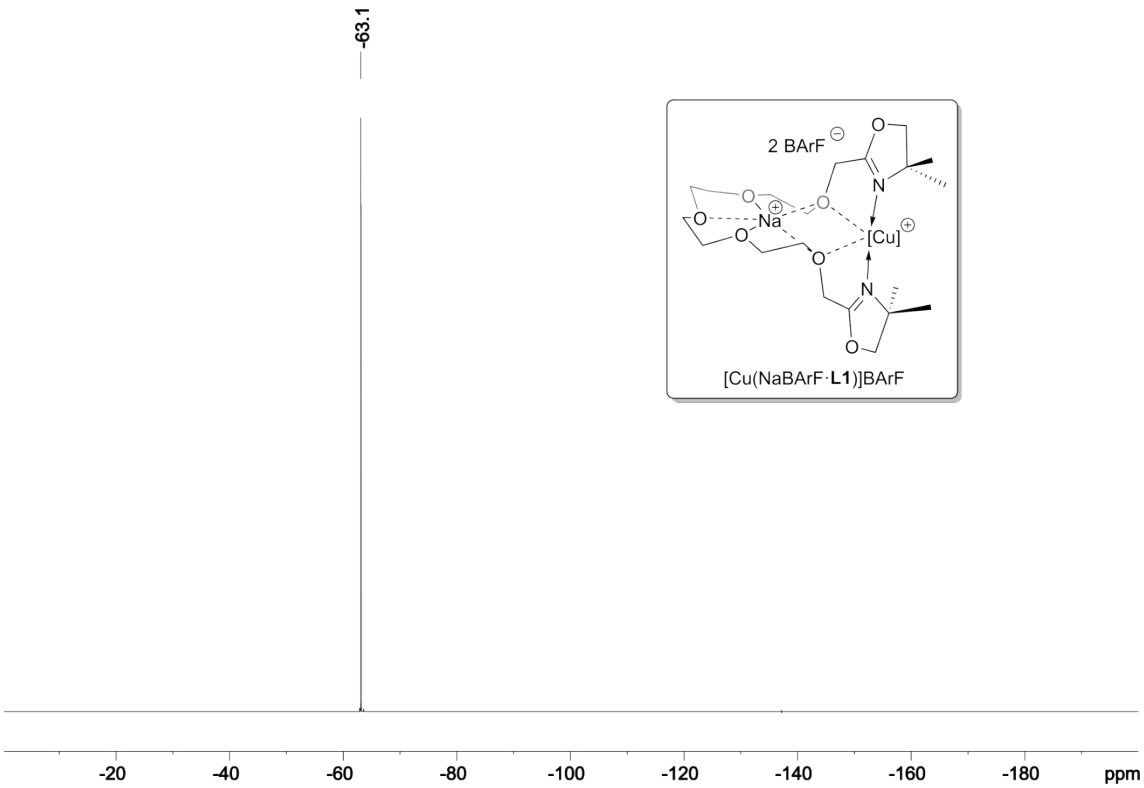


Figure SI 30. $^{19}F\{^{1}H\}$ NMR (376 MHz, CD_2Cl_2) of [Cu(NaBArF·**L1**)]BArF.

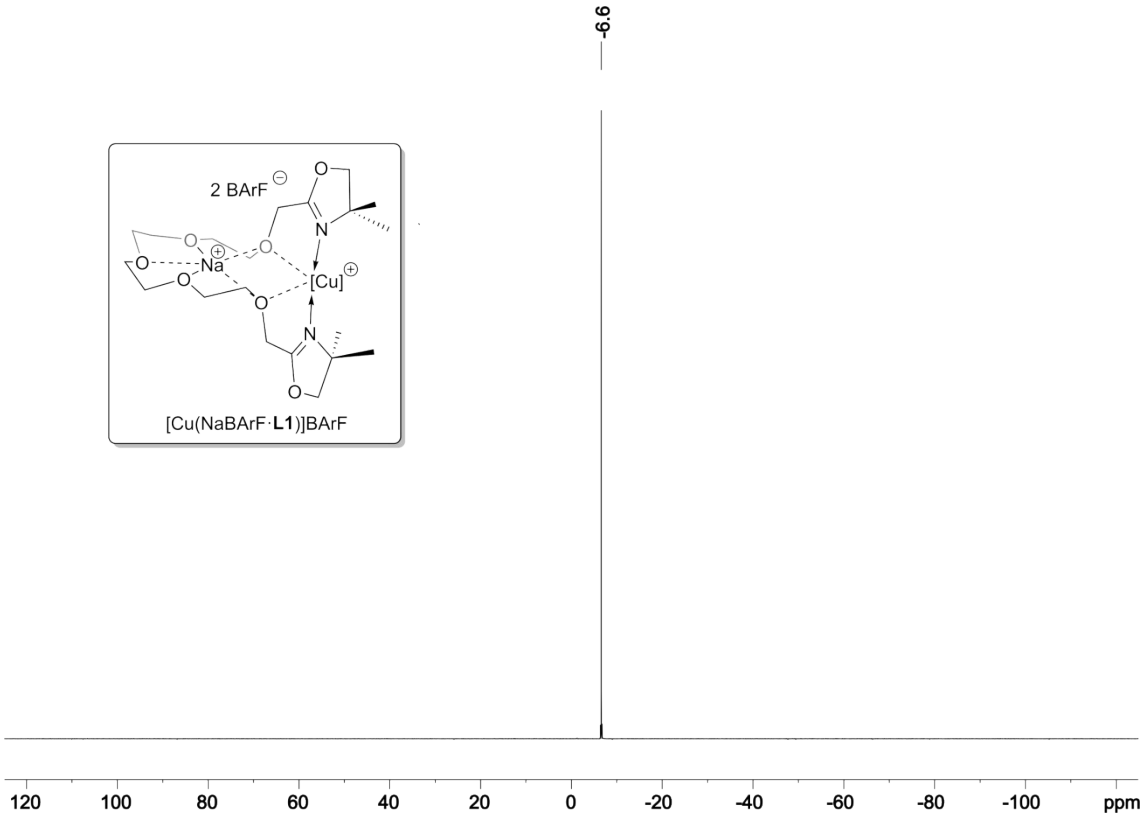


Figure SI 31. $^{11}B\{^{1}H\}$ NMR (128 MHz, CD_2Cl_2) of [Cu(NaBArF·**L1**)]BArF.

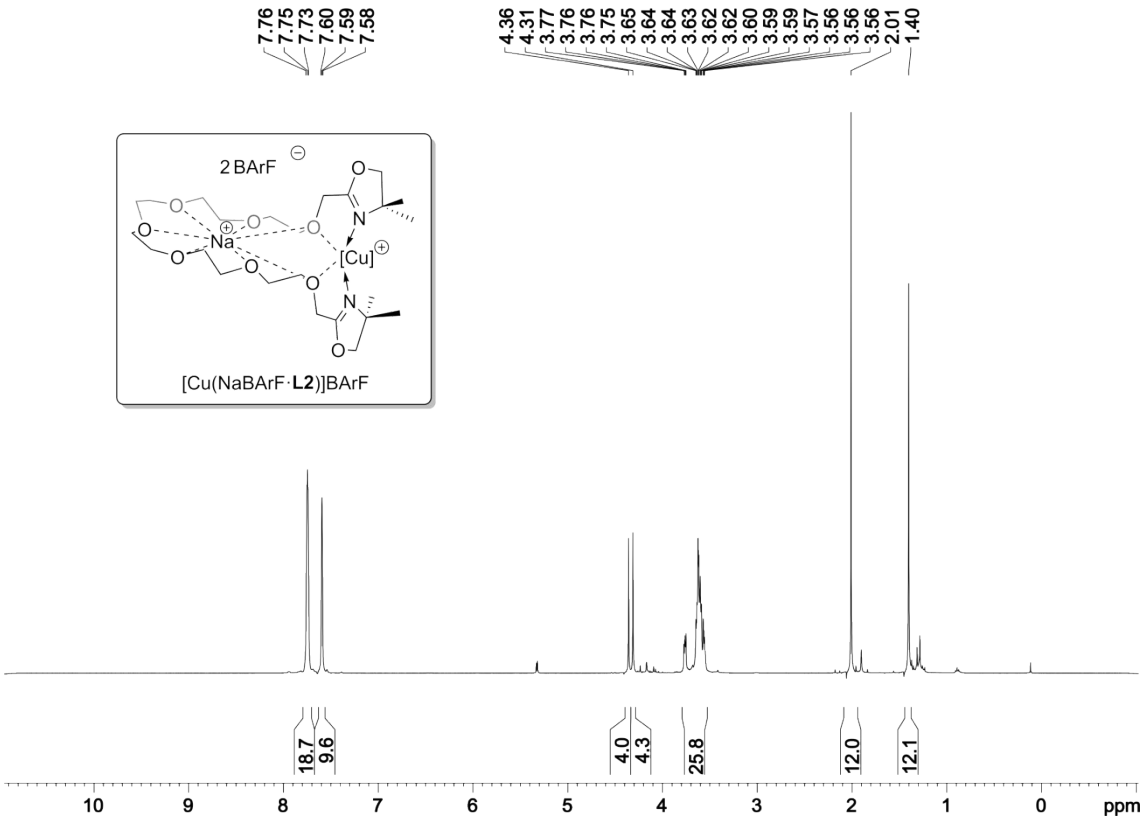


Figure SI 32. ^{1}H NMR (400 MHz, CD_2Cl_2) of [Cu(NaBArF·**L2**)]BArF.

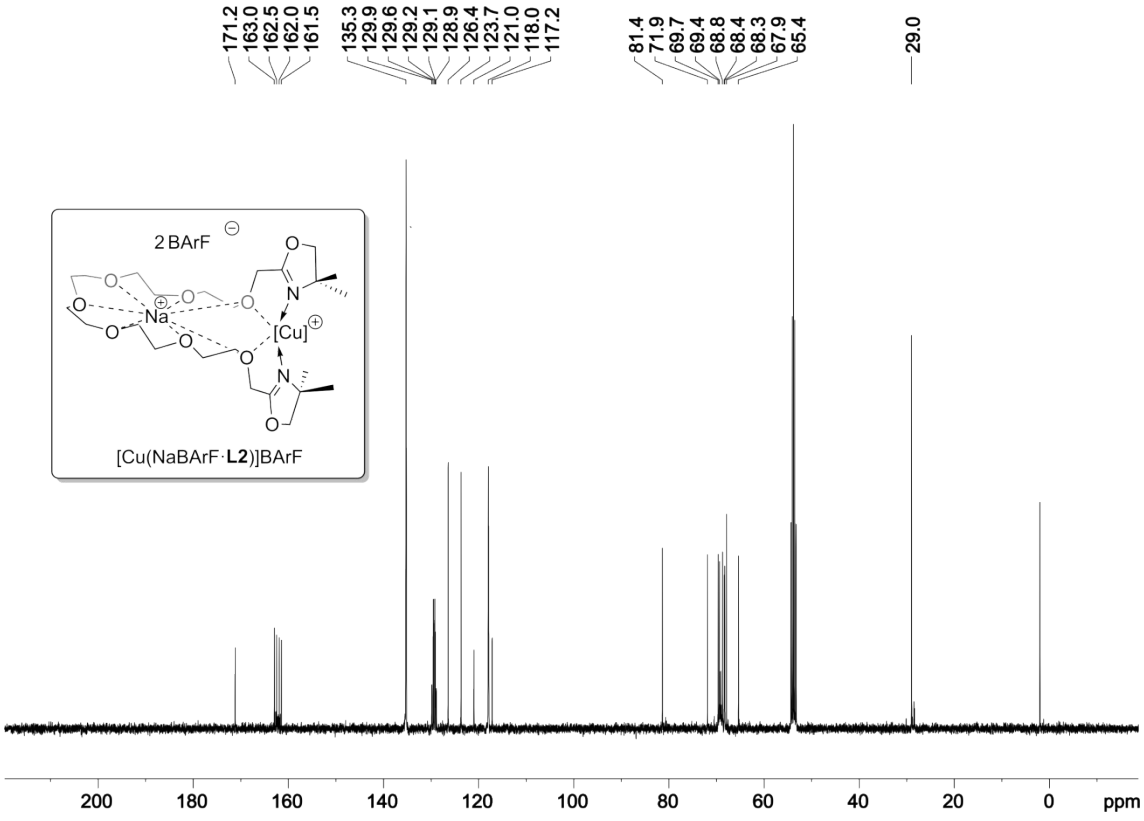


Figure SI 33. $^{13}C\{^{1}H\}$ NMR (101 MHz, CD_2Cl_2) of [Cu(NaBArF·**L2**)]BArF.

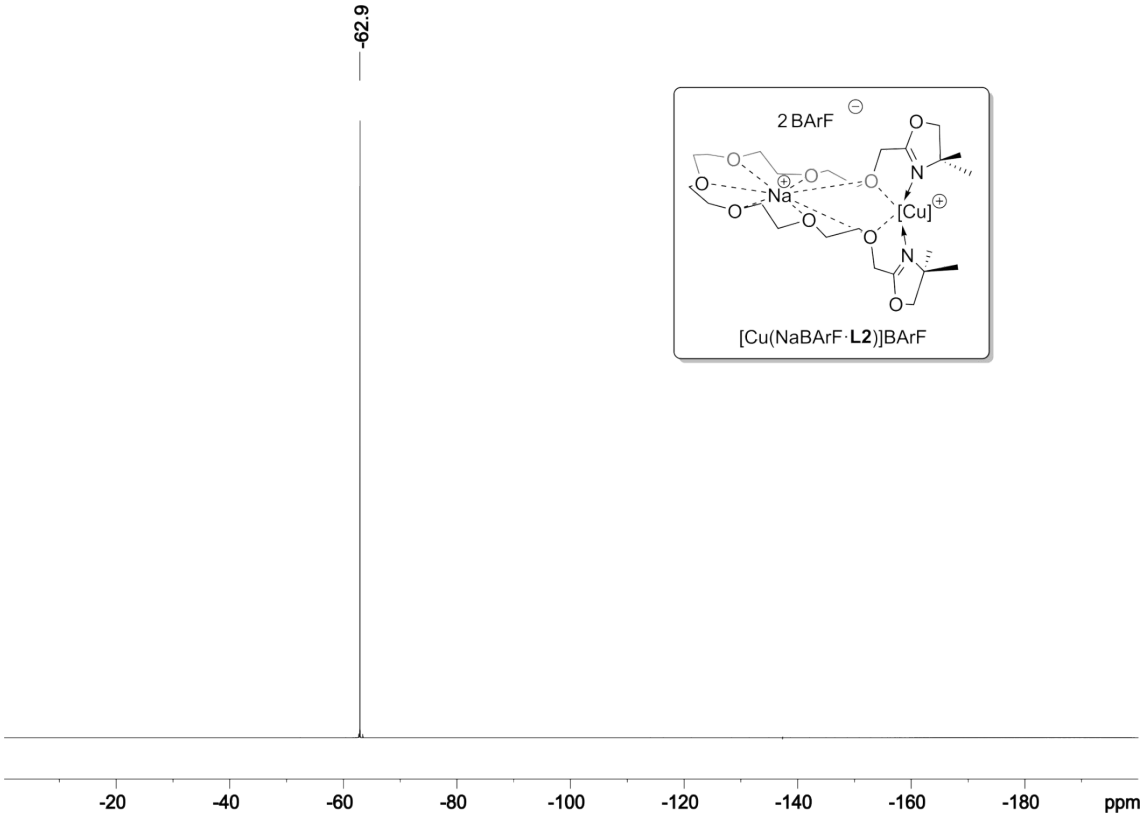


Figure SI 34. $^{19}F\{^{1}H\}$ NMR (376 MHz, CD_2Cl_2) of [Cu(NaBArF·**L2**)]BArF.

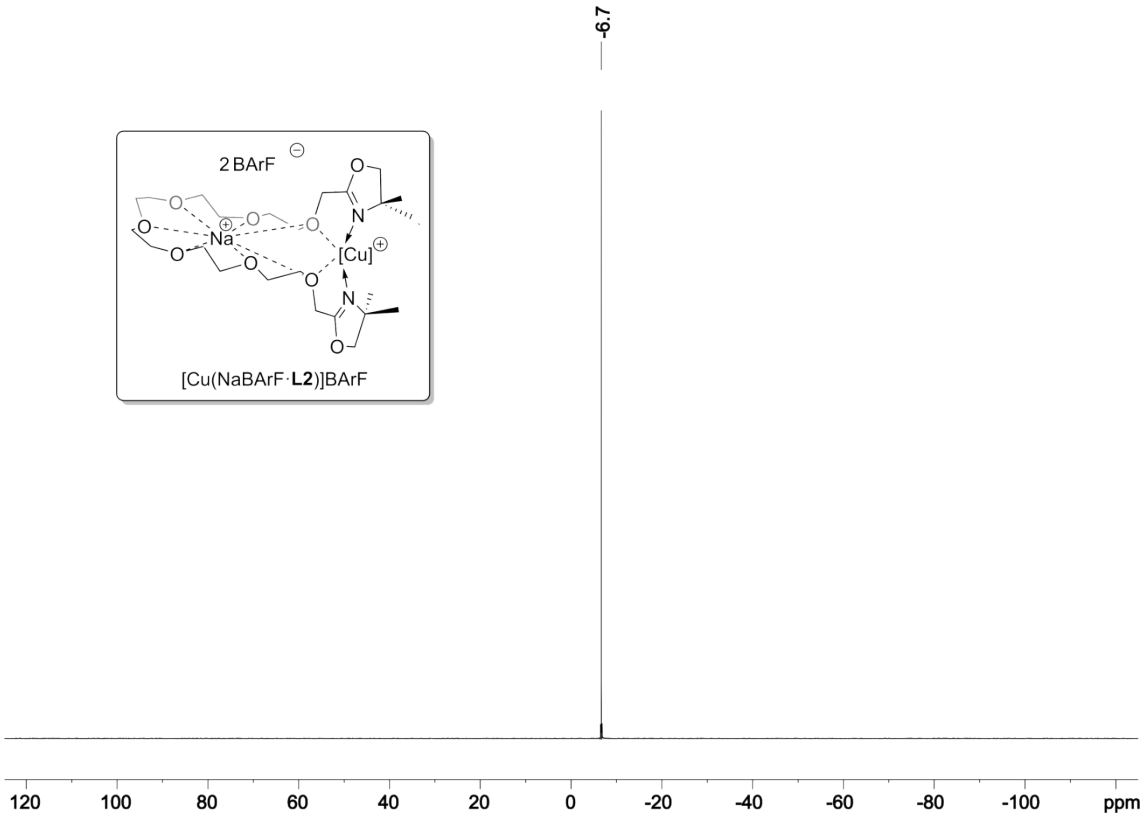


Figure SI 35. $^{11}B\{^{1}H\}$ NMR (128 MHz, CD_2Cl_2) of [Cu(NaBArF·**L2**)]BArF.

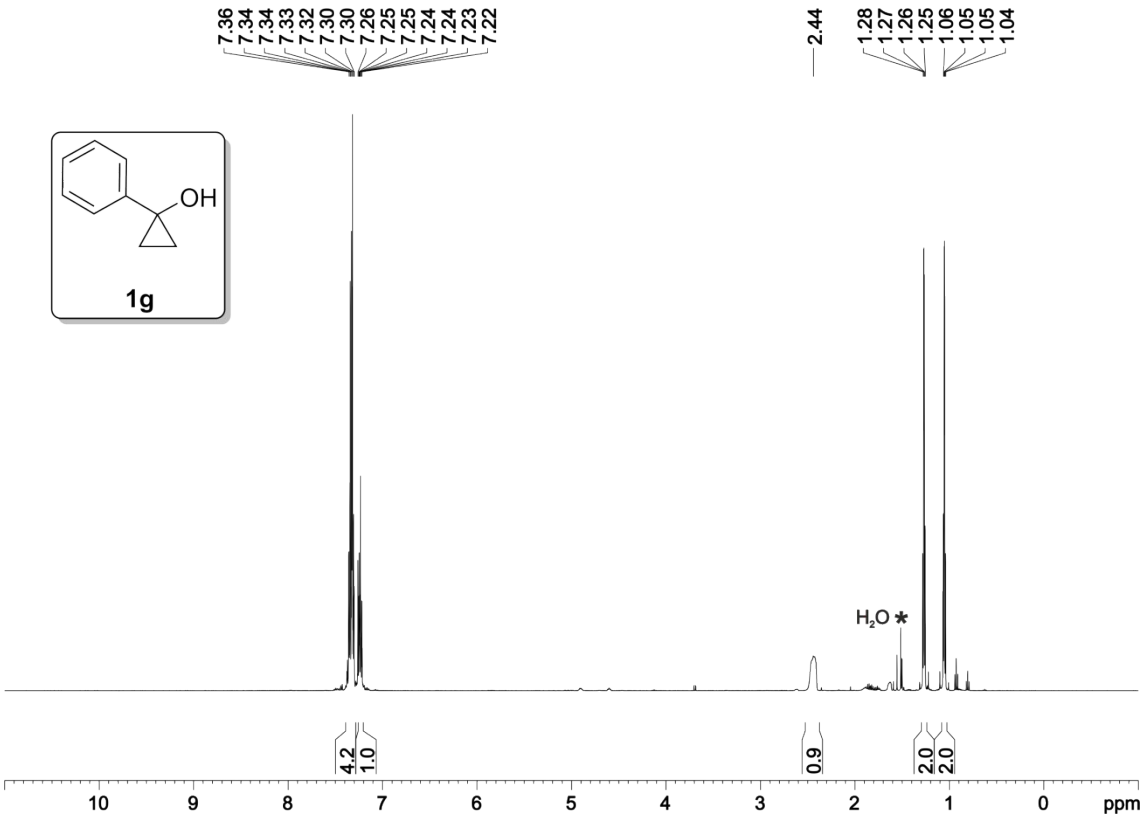


Figure SI 36. ^{1}H NMR (500 MHz, $CDCl_3$) of **1g**.

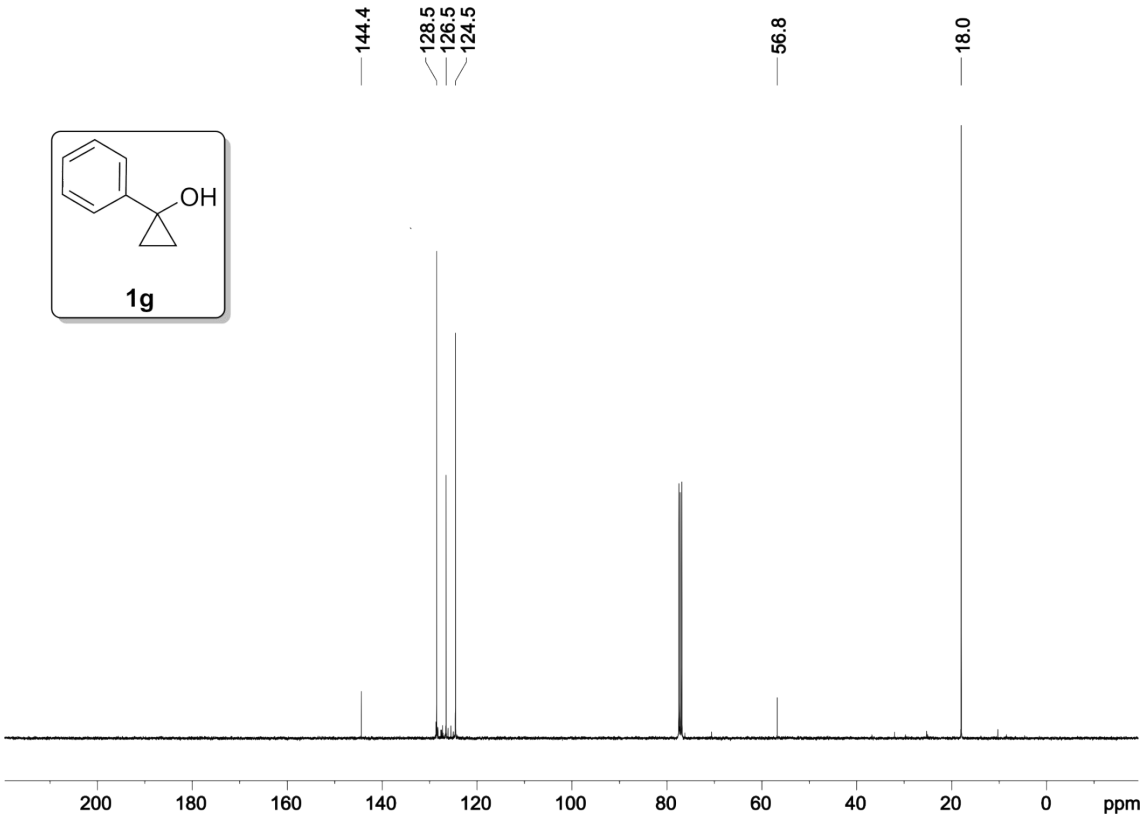


Figure SI 37. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **1g.**

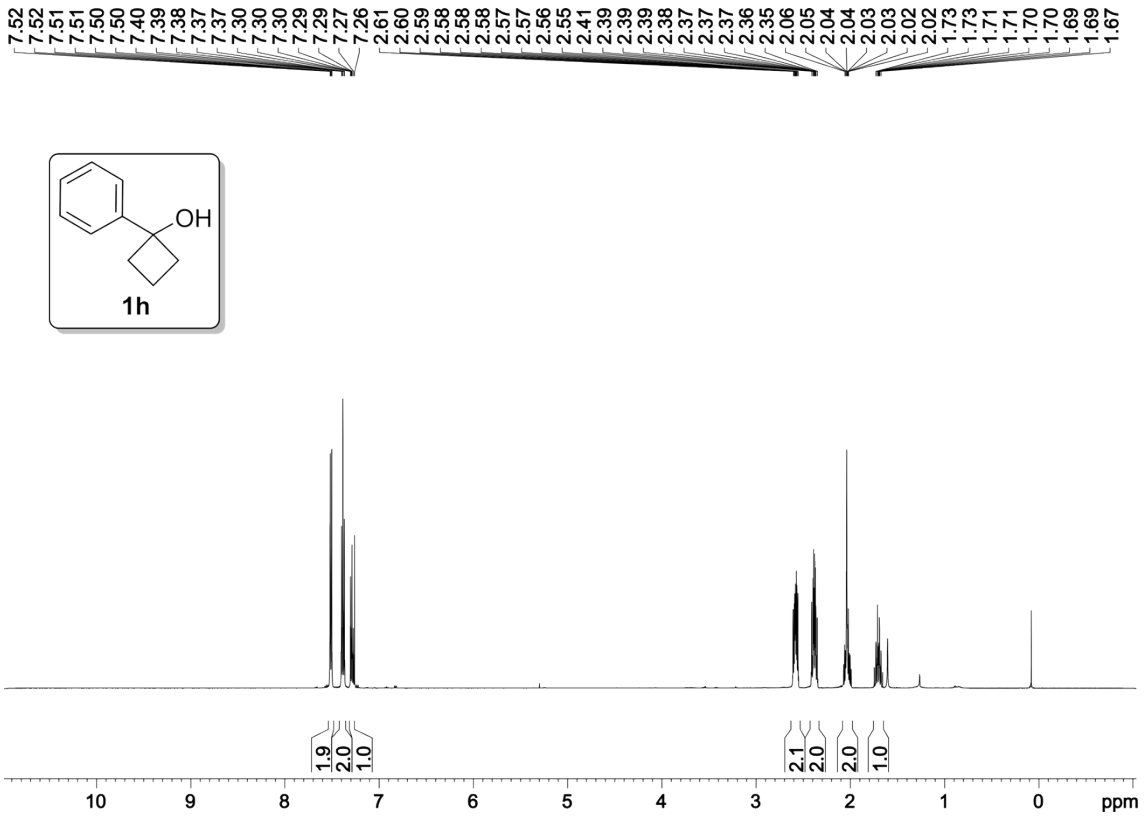


Figure SI 38. ^{1}H NMR (500 MHz, $CDCl_3$) of **1h.**

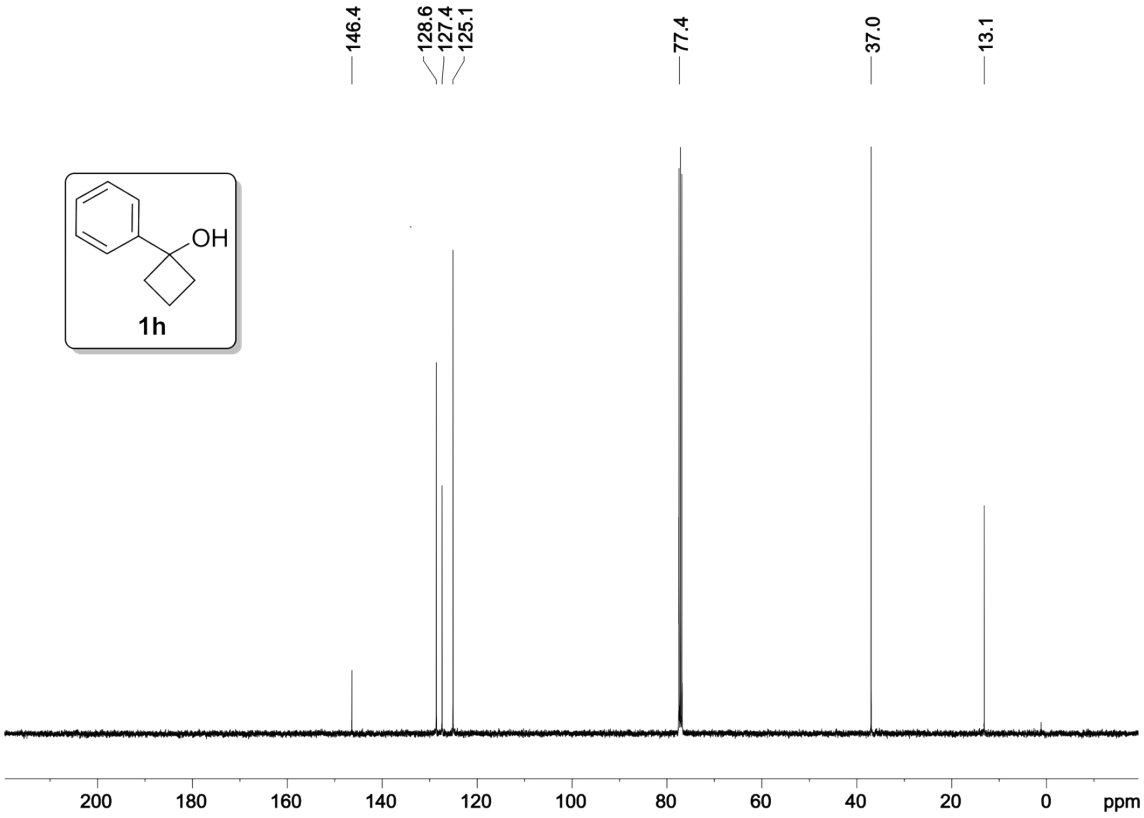


Figure SI 39. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **1h.**

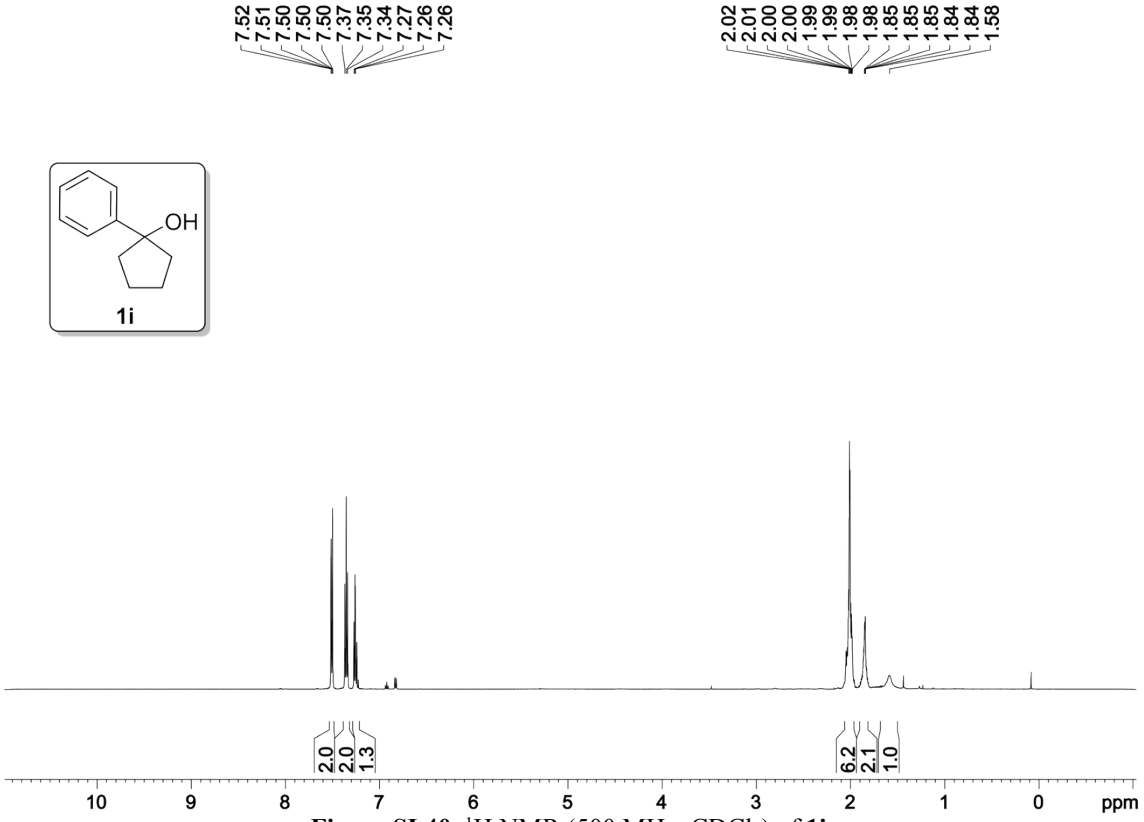


Figure SI 40. ^{1}H NMR (500 MHz, $CDCl_3$) of **1i.**

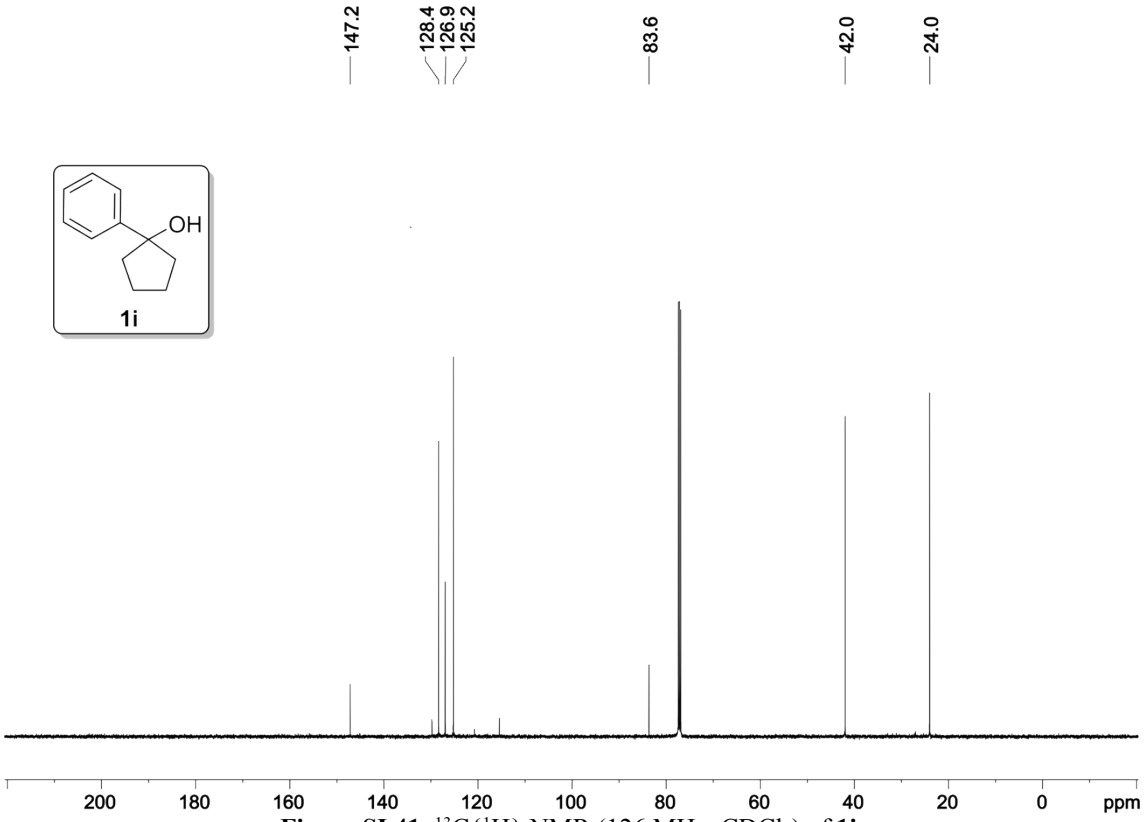


Figure SI 41. $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of **1i.**

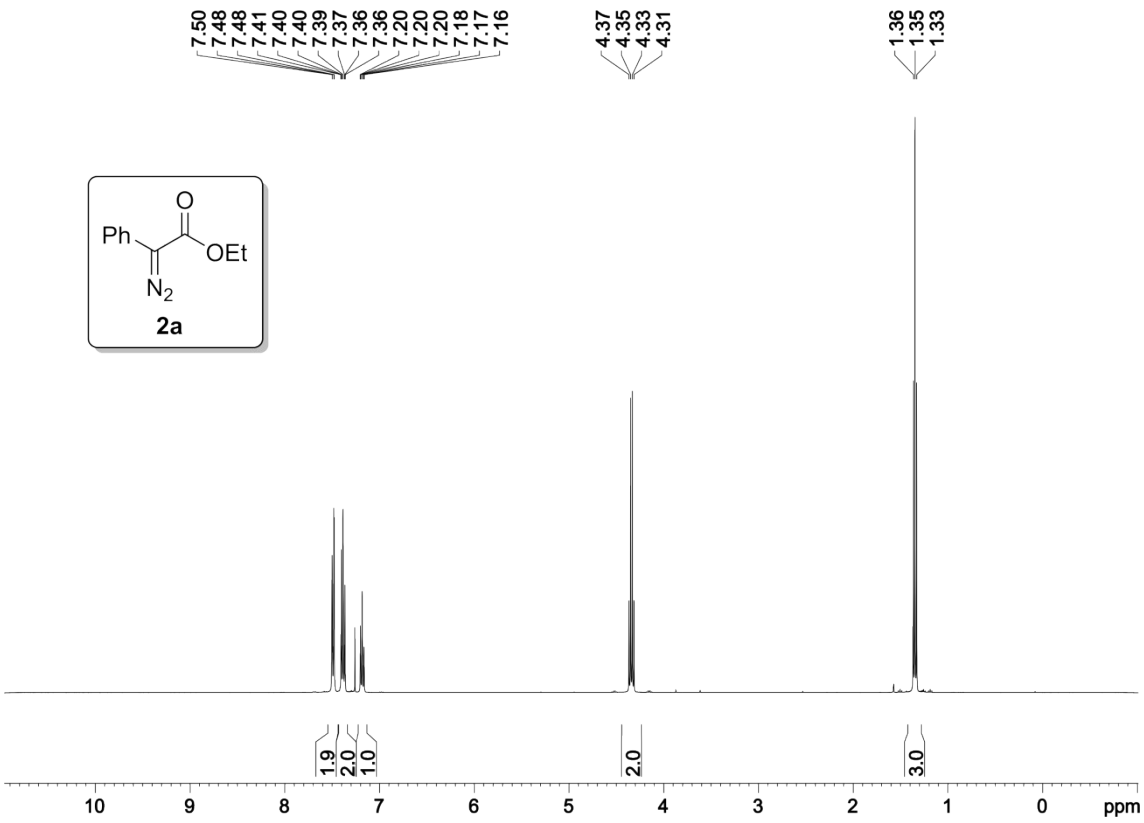


Figure SI 42. ^{1}H NMR (400 MHz, $CDCl_3$) of **2a**.

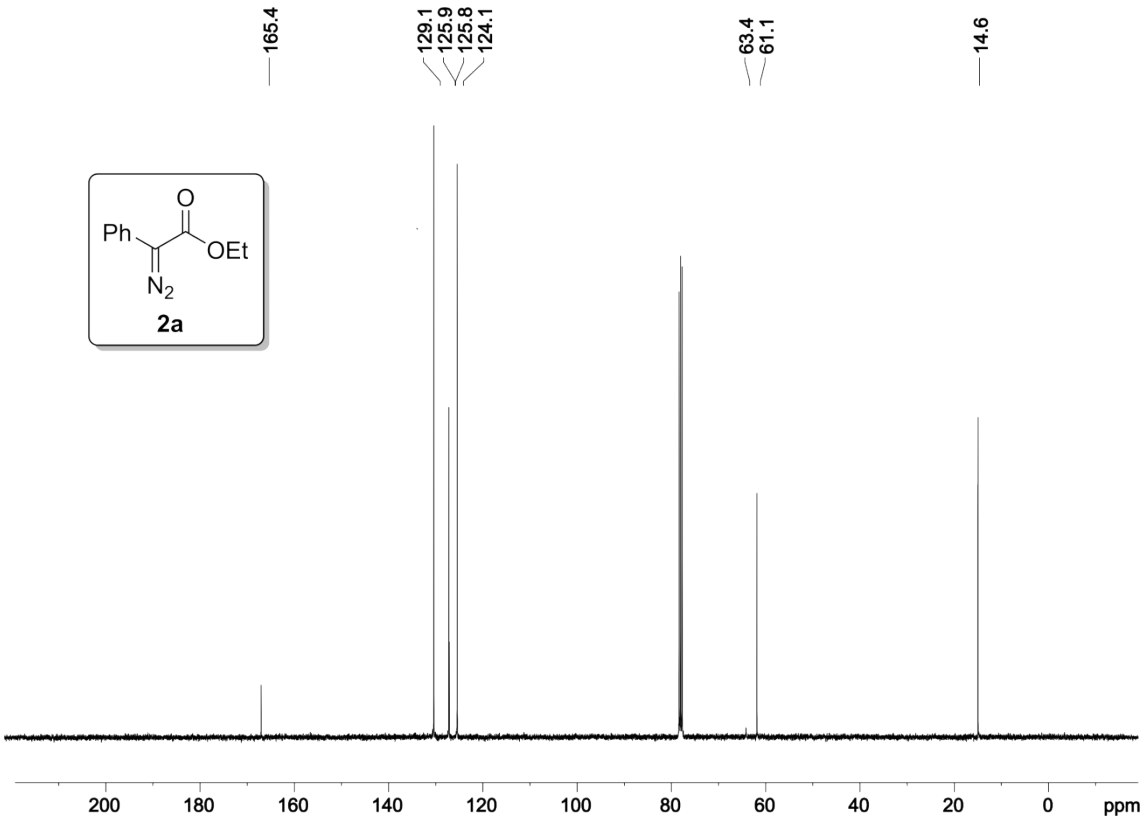


Figure SI 43. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **2a**.

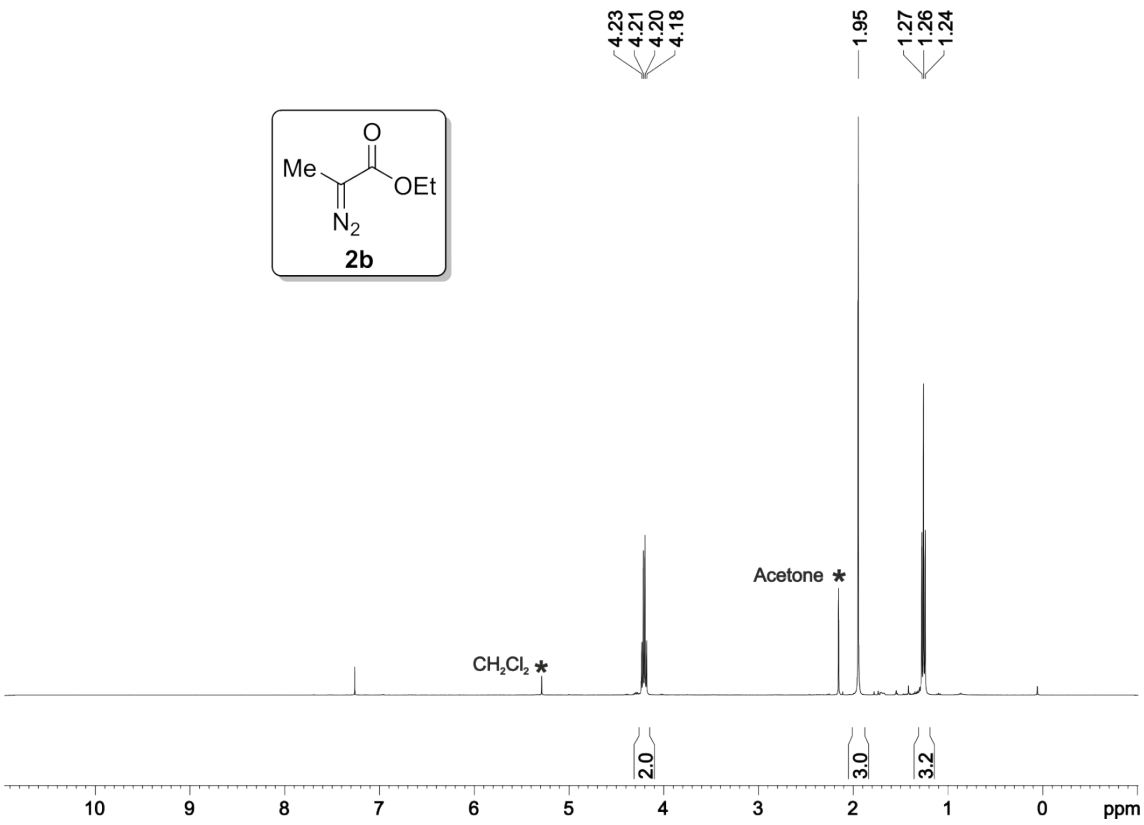


Figure SI 44. ^{1}H NMR (400 MHz, $CDCl_3$) of **2b**.

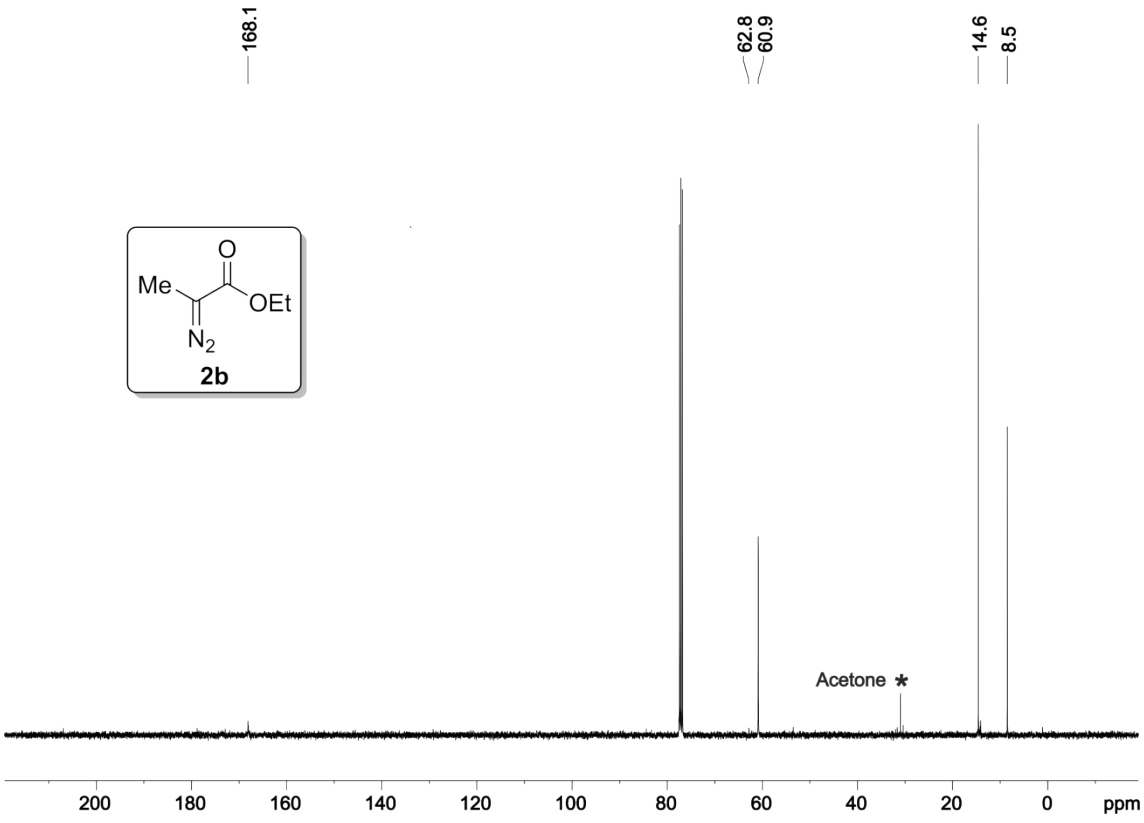


Figure SI 45. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **2b**.

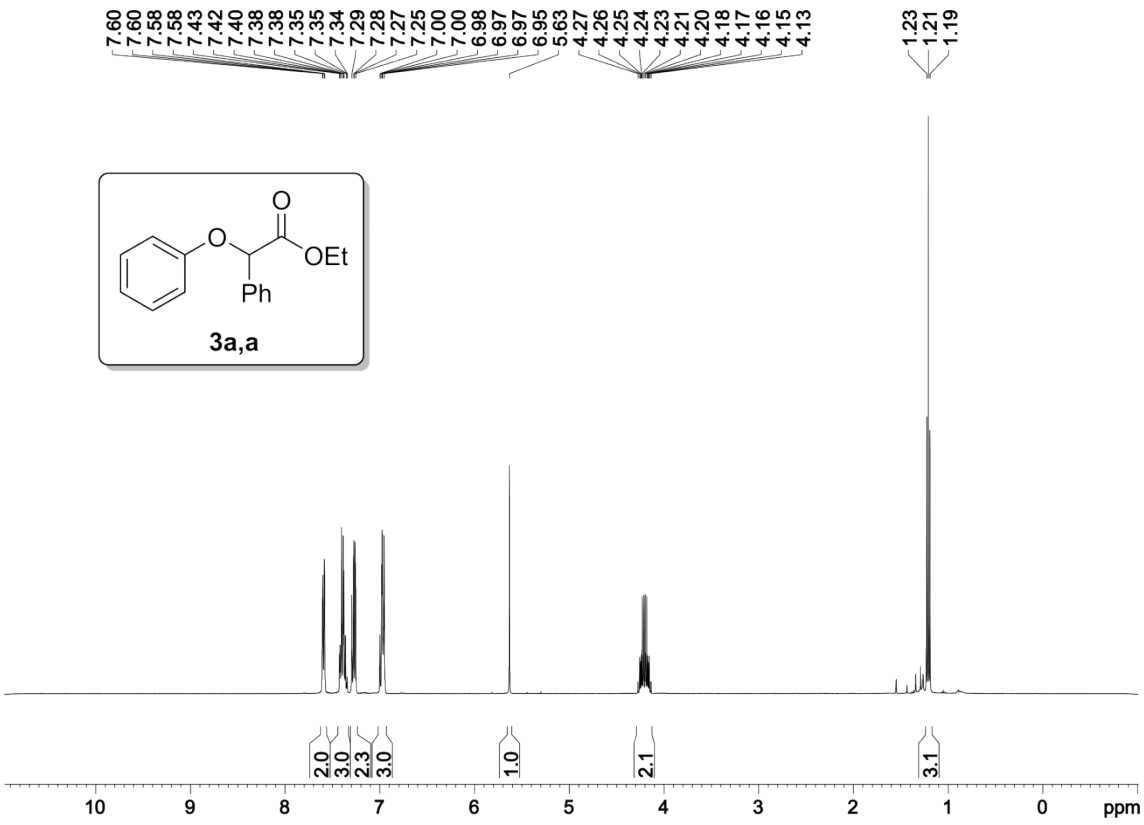


Figure SI 46. ^{1}H NMR (400 MHz, $CDCl_3$) of **3a,a**.

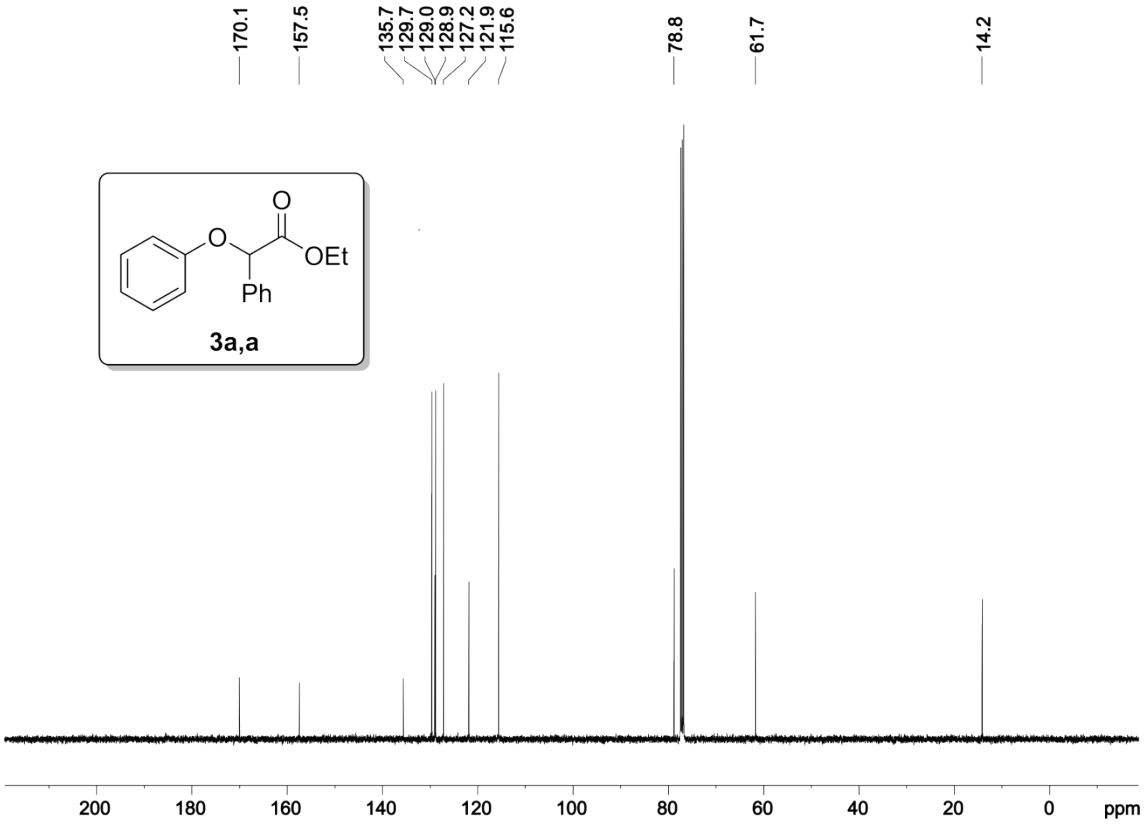


Figure SI 47. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **3a,a**.

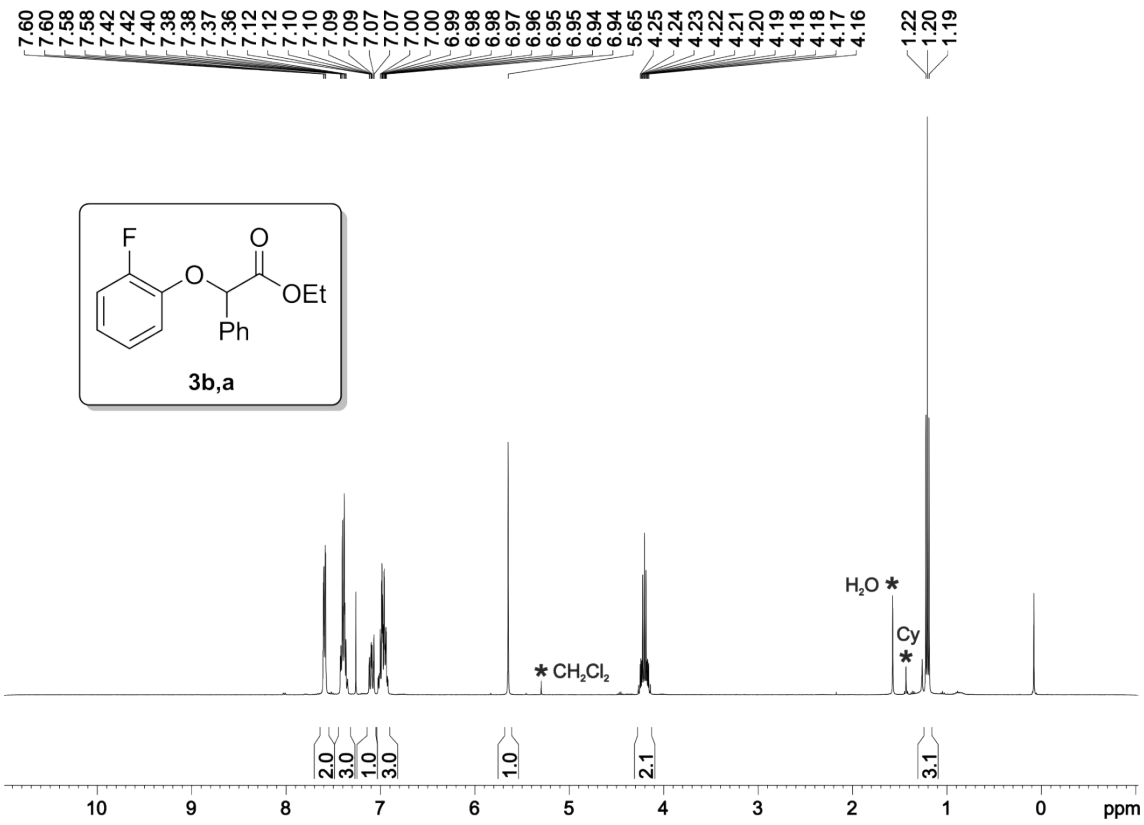


Figure SI 48. ^{1}H NMR (400 MHz, $CDCl_3$) of **3b,a**.

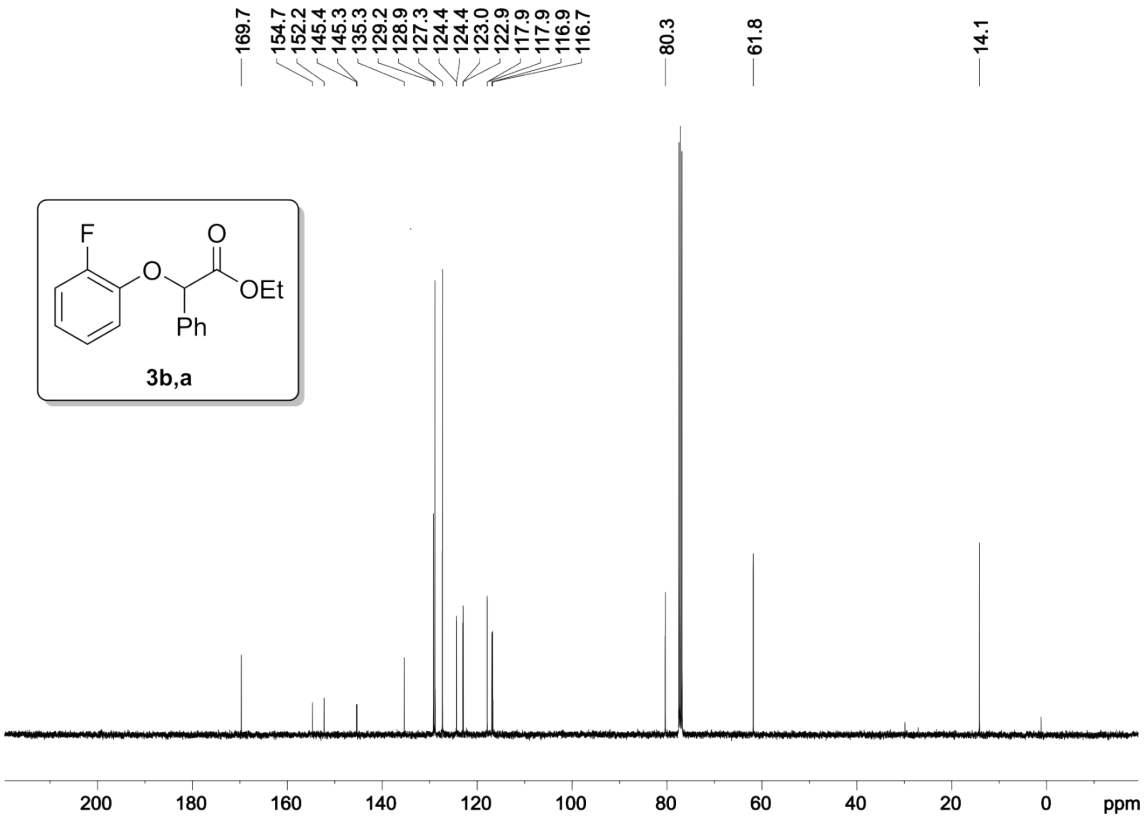


Figure SI 49. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **3b,a**.

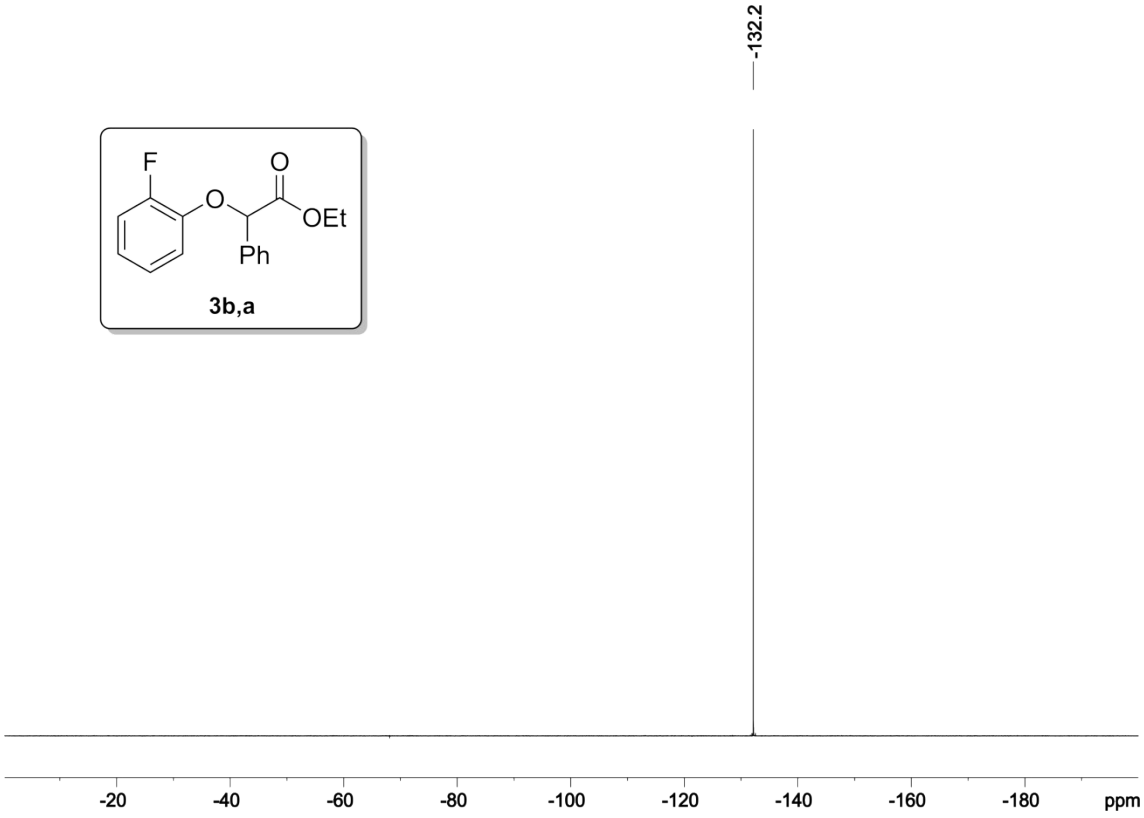


Figure SI 50. $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) of **3b,a**.

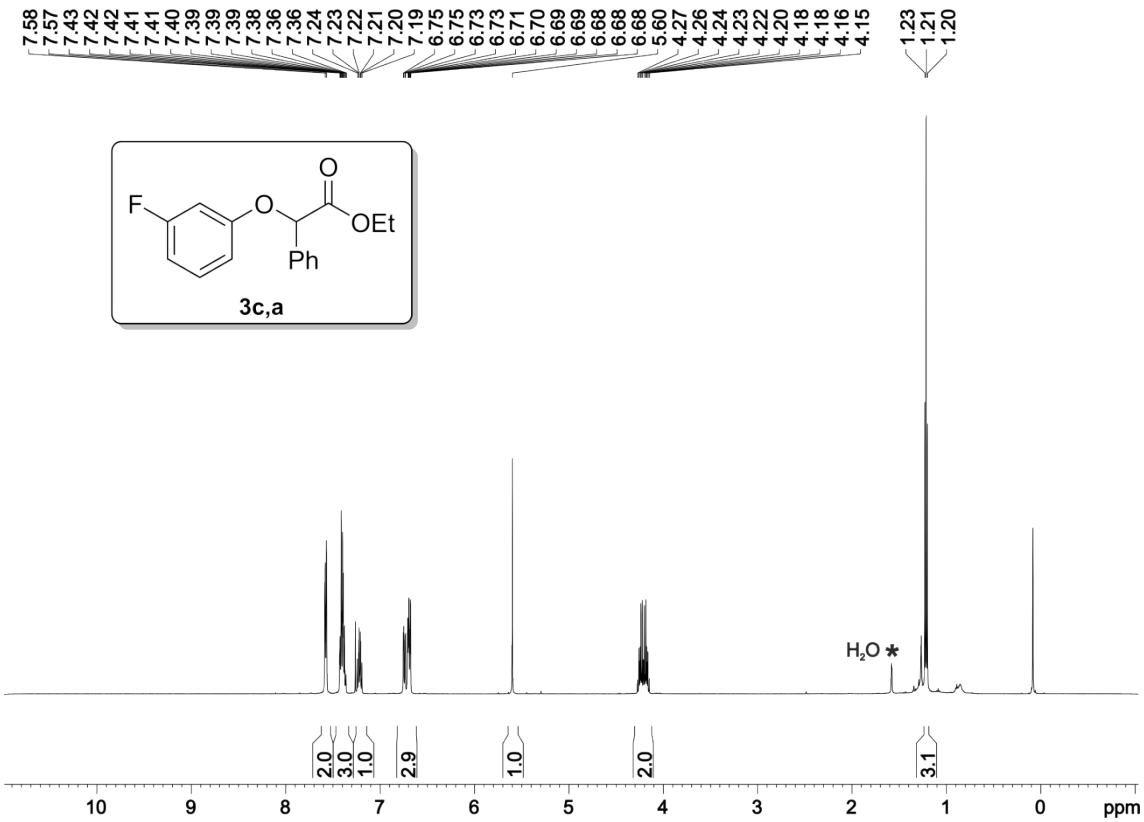


Figure SI 51. ^{1}H NMR (500 MHz, $CDCl_3$) of **3c,a**.

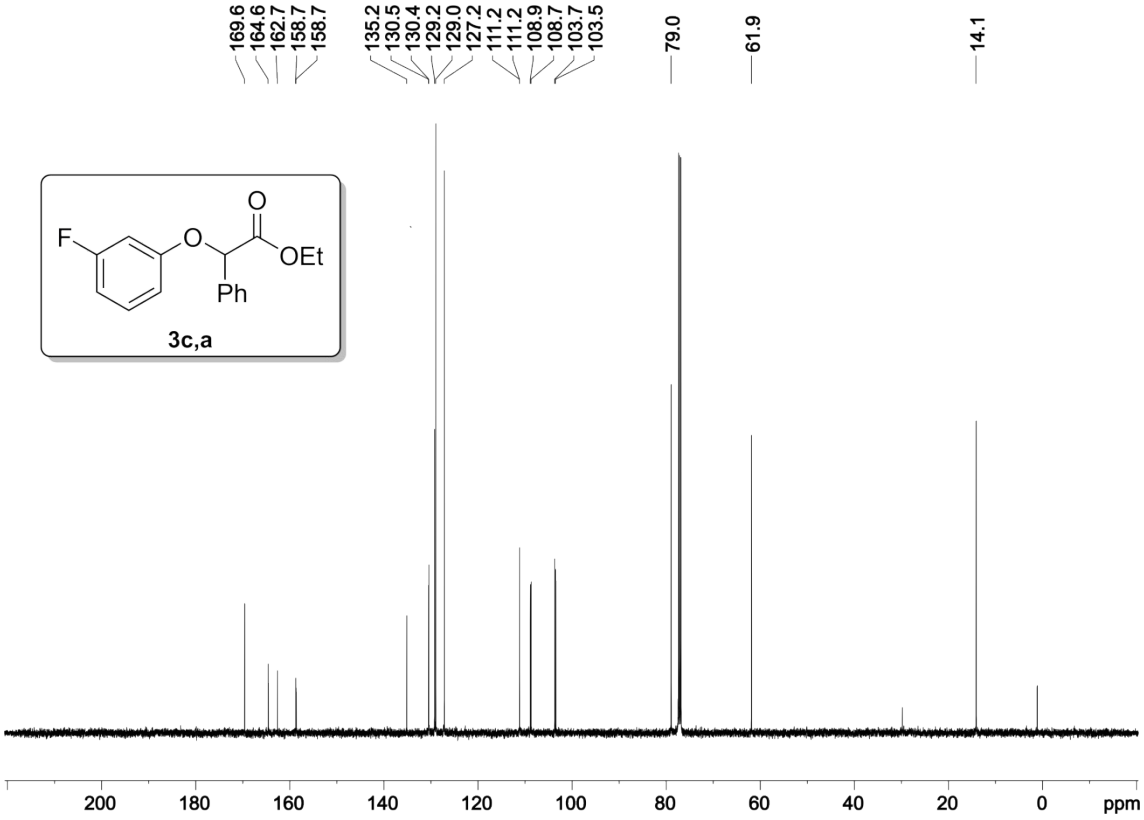


Figure SI 52. $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of **3c,a**.

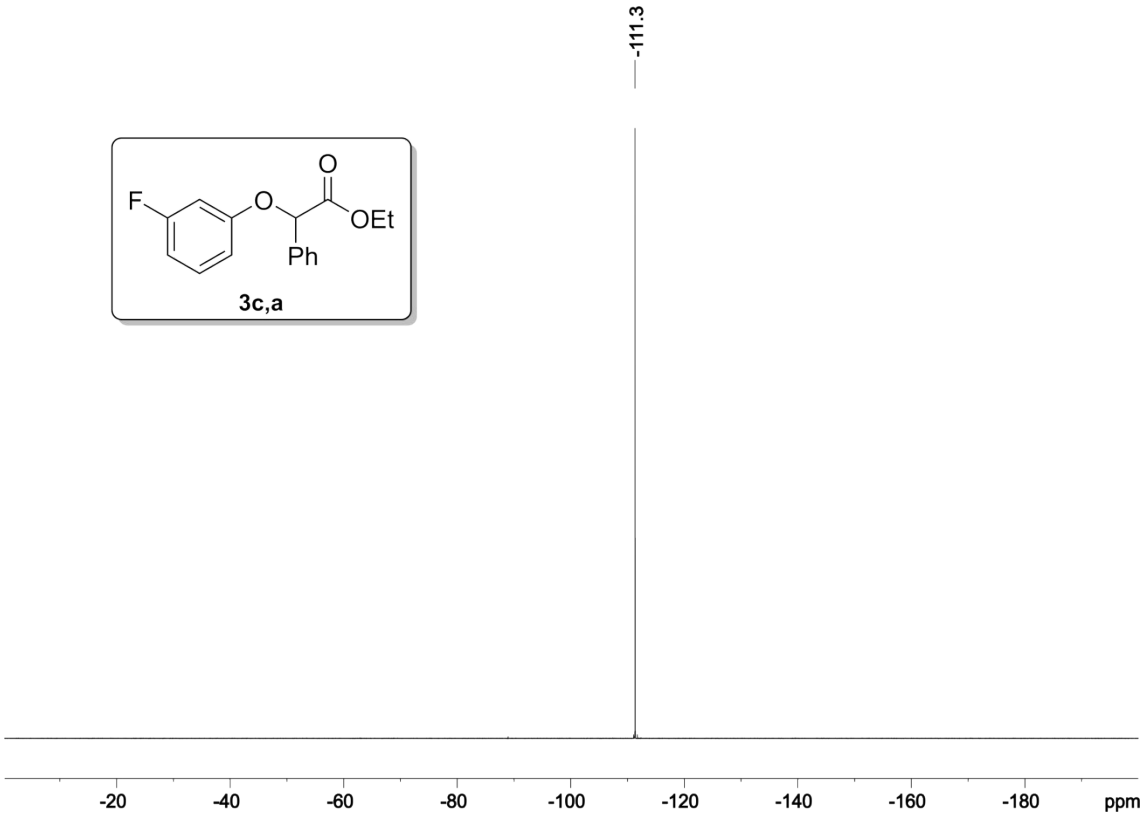


Figure SI 53. $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) of **3c,a**.

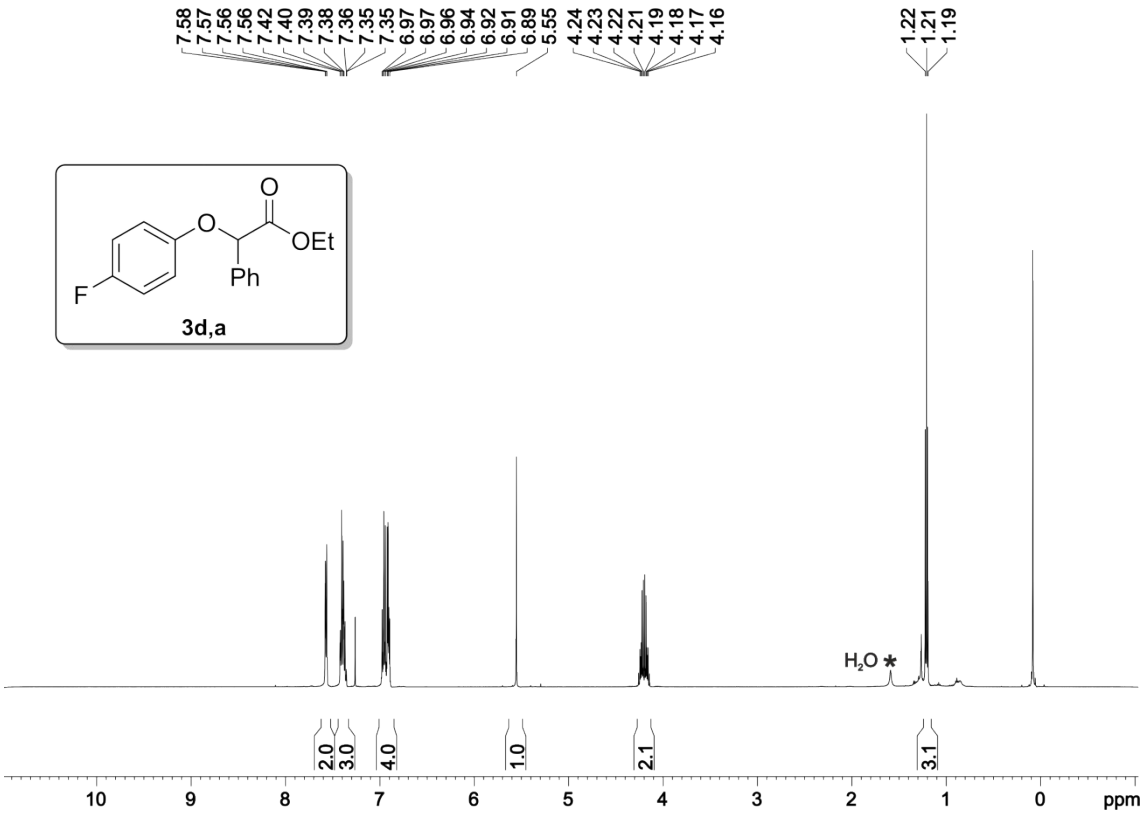


Figure SI 54. ^{1}H NMR (500 MHz, $CDCl_3$) of **3d,a**.

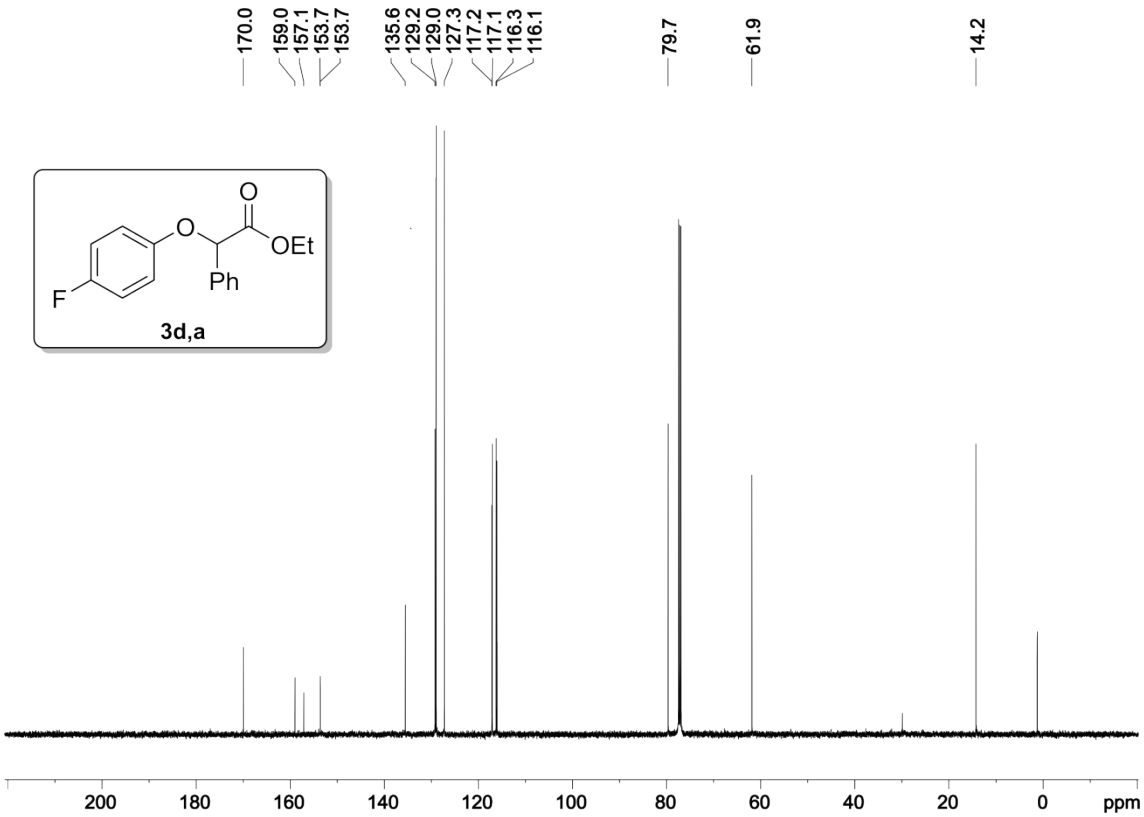


Figure SI 55. $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of **3d,a**.

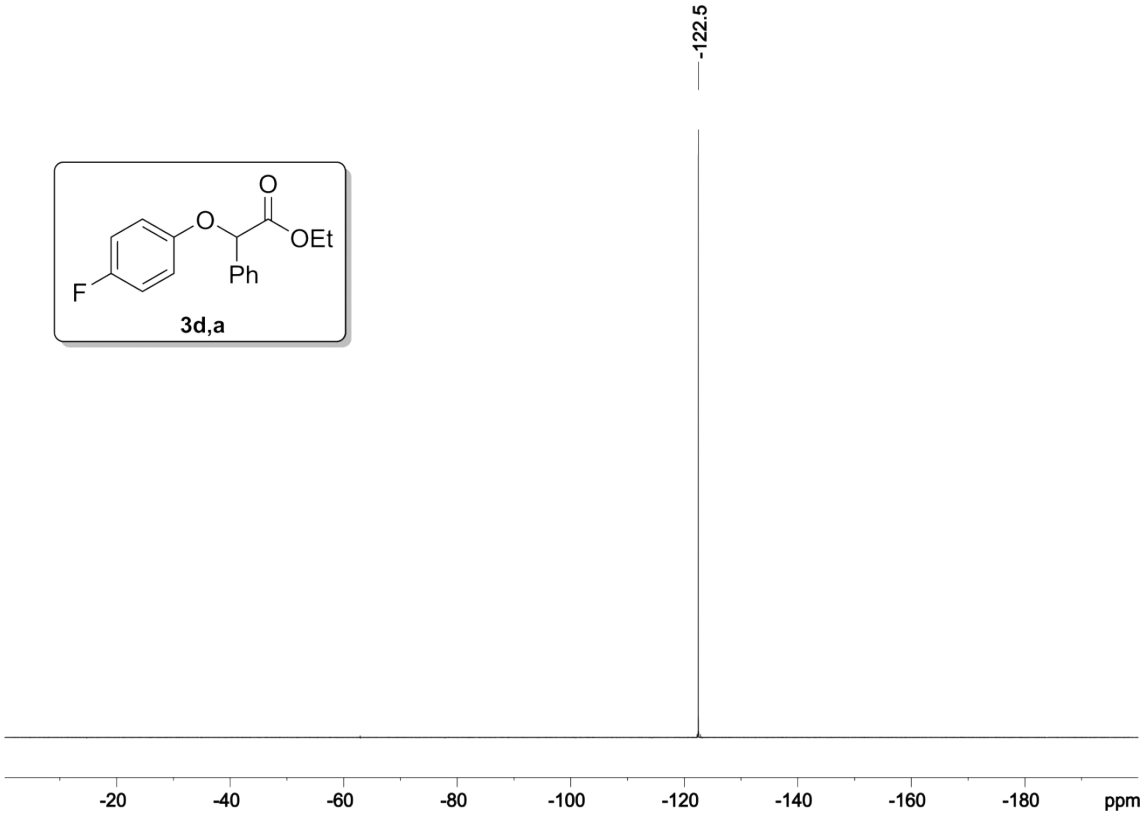


Figure SI 56. $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) of **3d,a**.

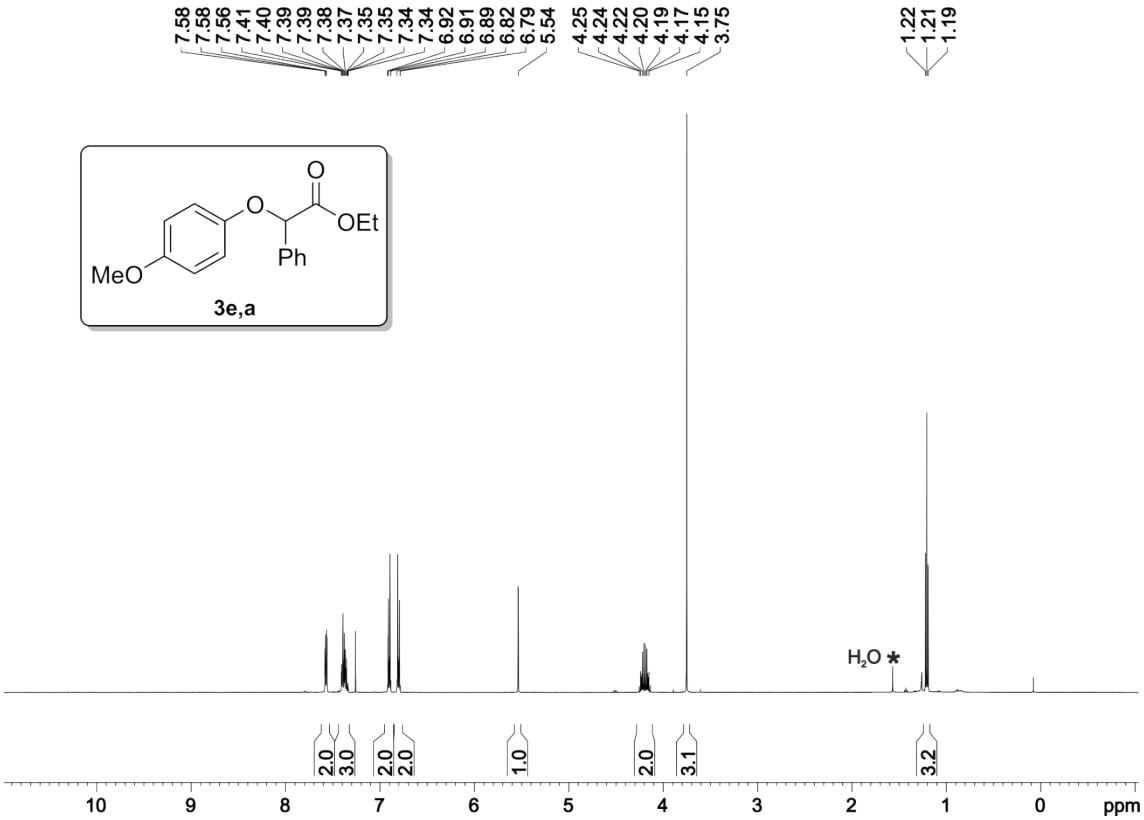


Figure SI 57. ^{1}H NMR (500 MHz, $CDCl_3$) of **3e,a**.

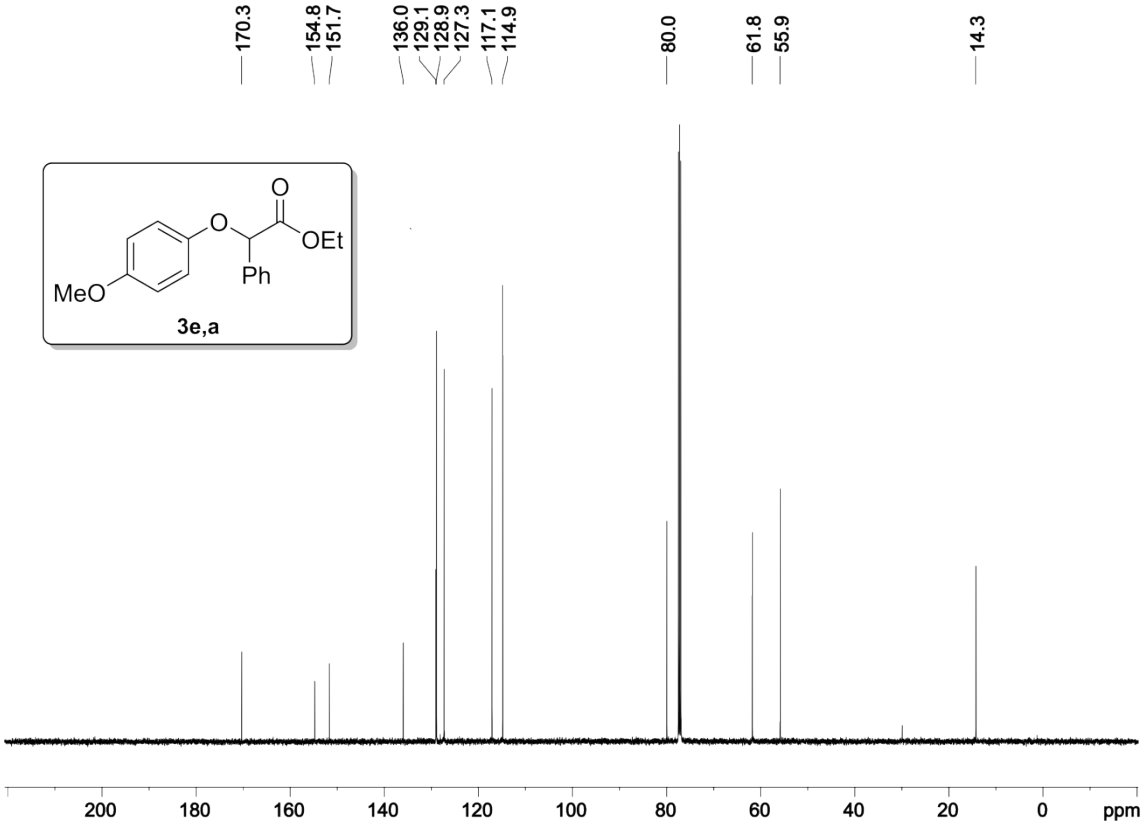


Figure SI 58. $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of **3e,a**.

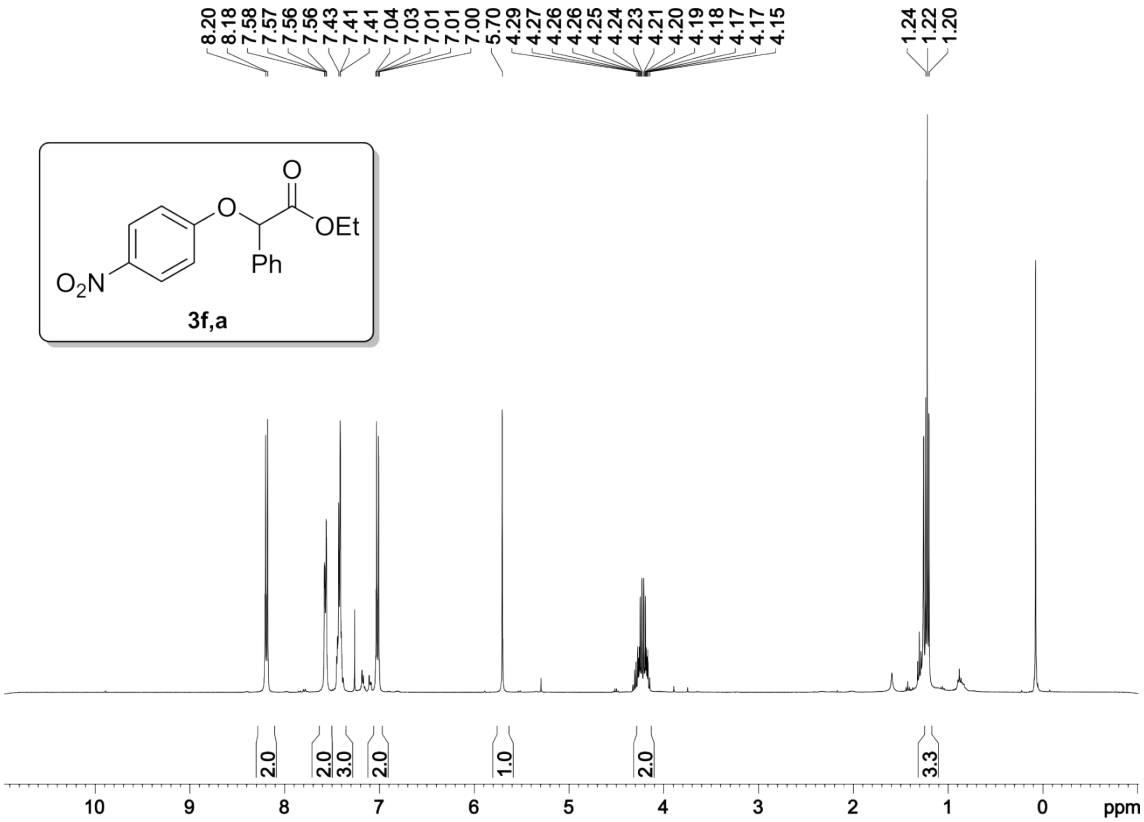


Figure SI 59. ^{1}H NMR (400 MHz, $CDCl_3$) of **3f,a**.

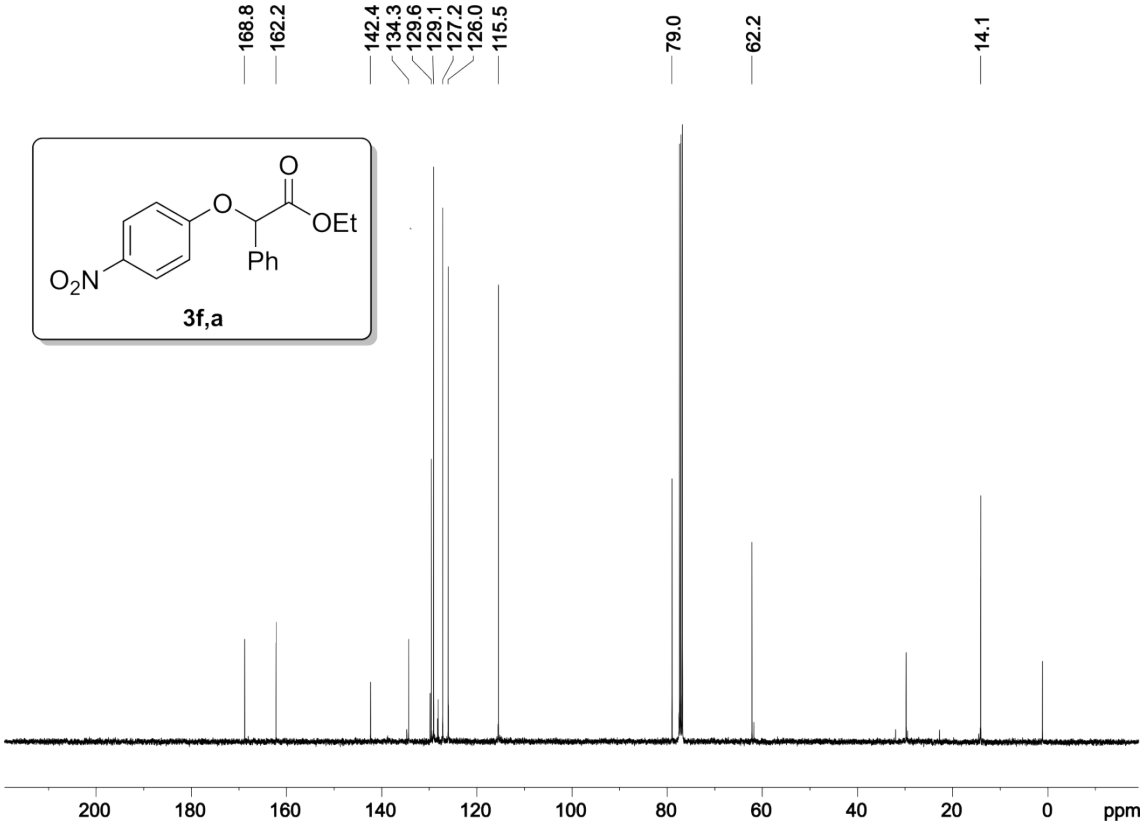


Figure SI 60. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **3f,a**.

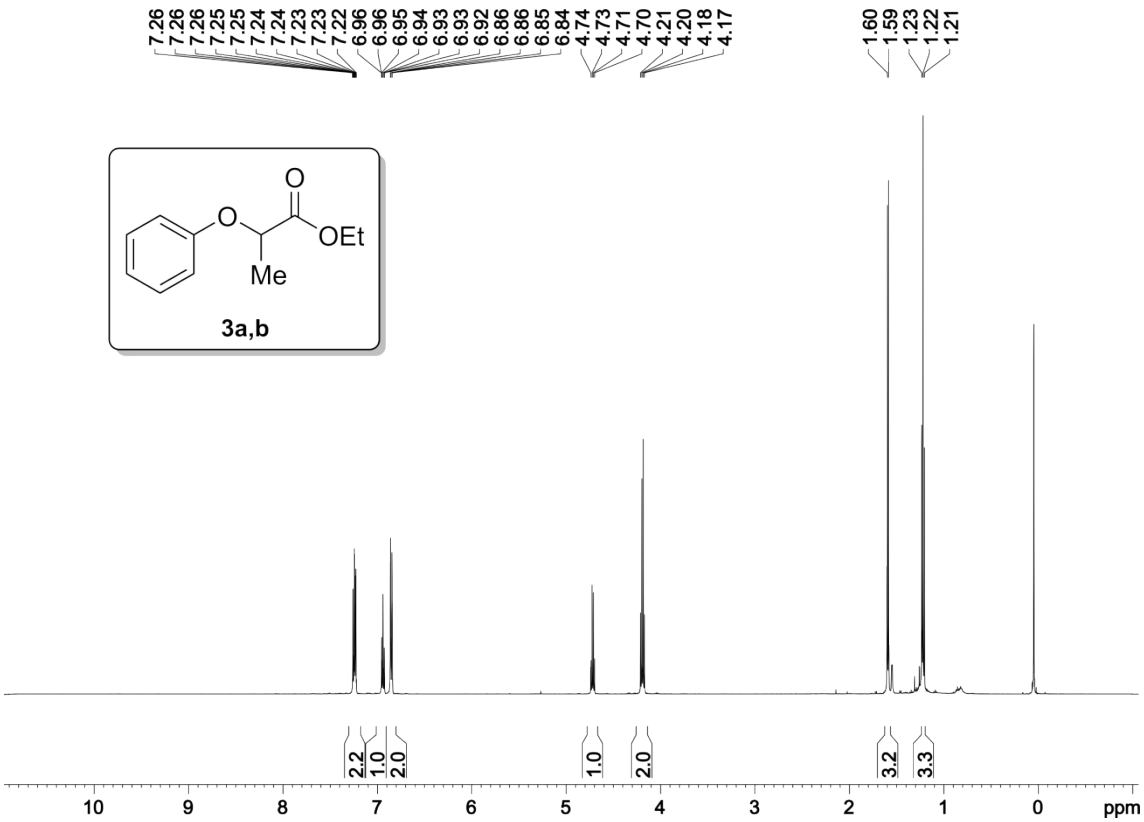


Figure SI 61. ^{1}H NMR (500 MHz, $CDCl_3$) of **3a,b**.

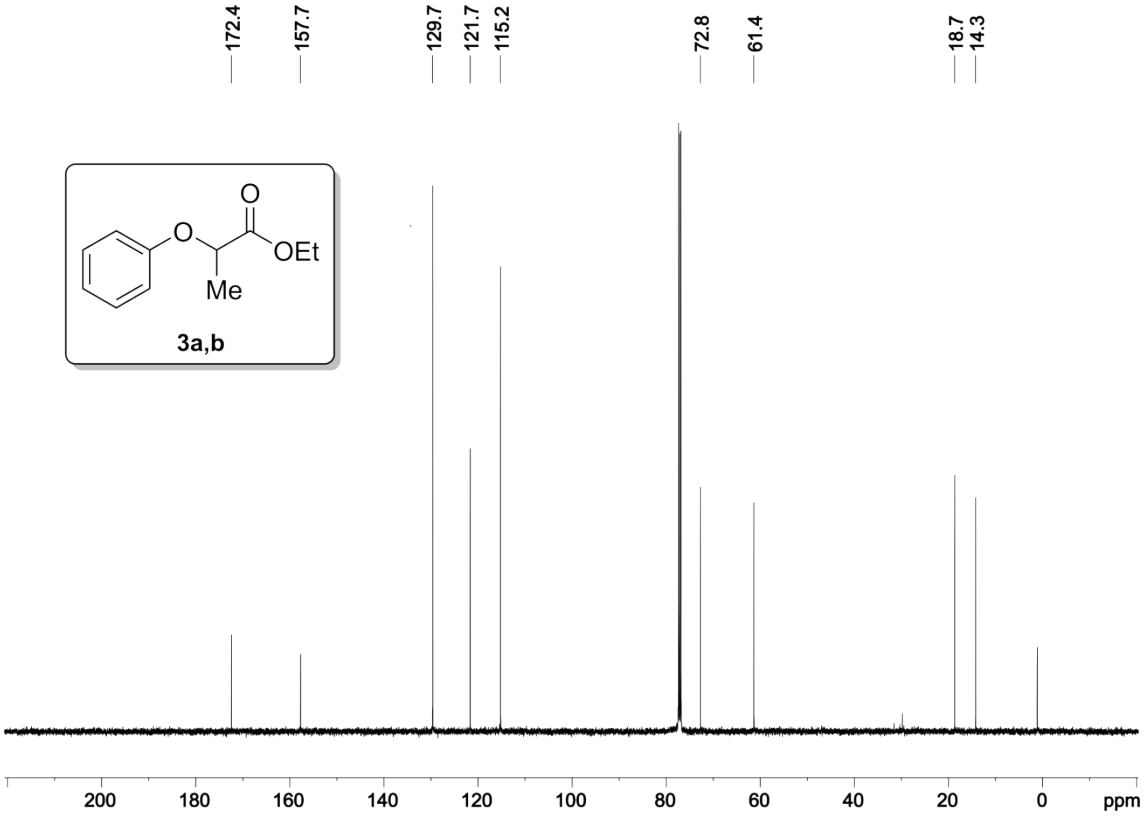


Figure SI 62. $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of **3a,b**.

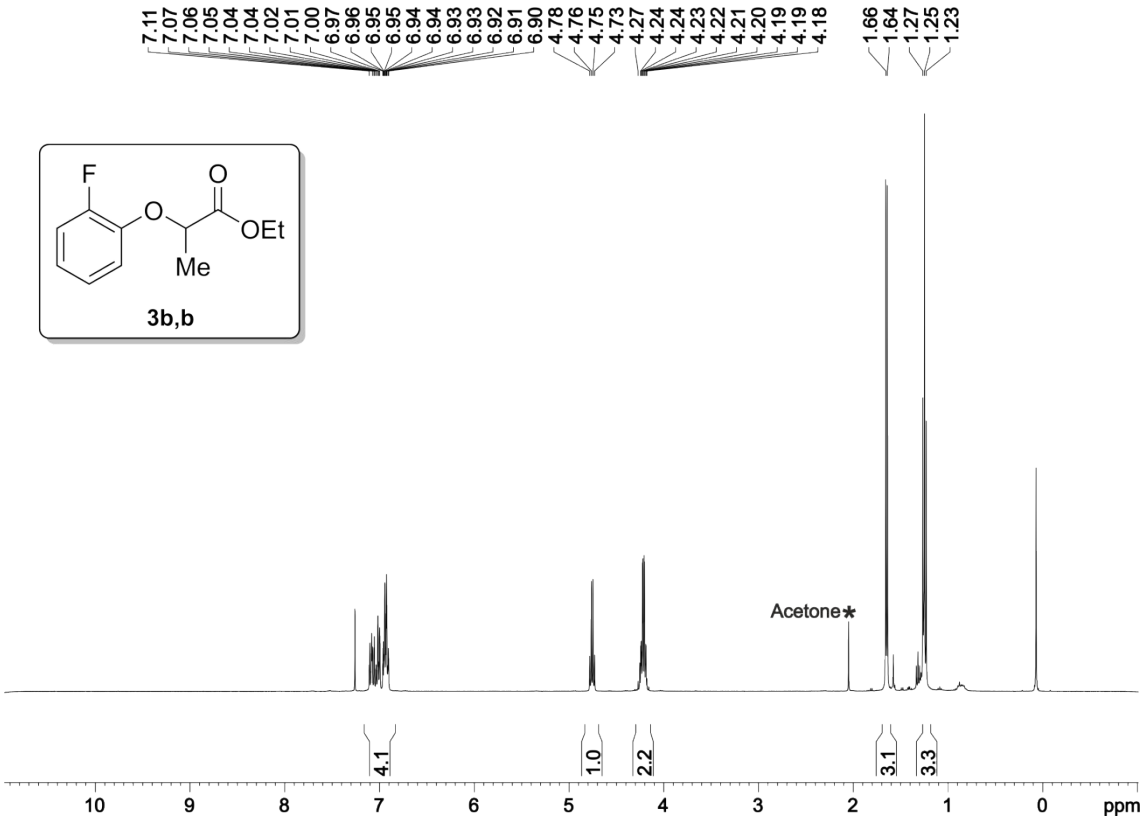


Figure SI 63. ^{1}H NMR (400 MHz, $CDCl_3$) of **3b,b**.

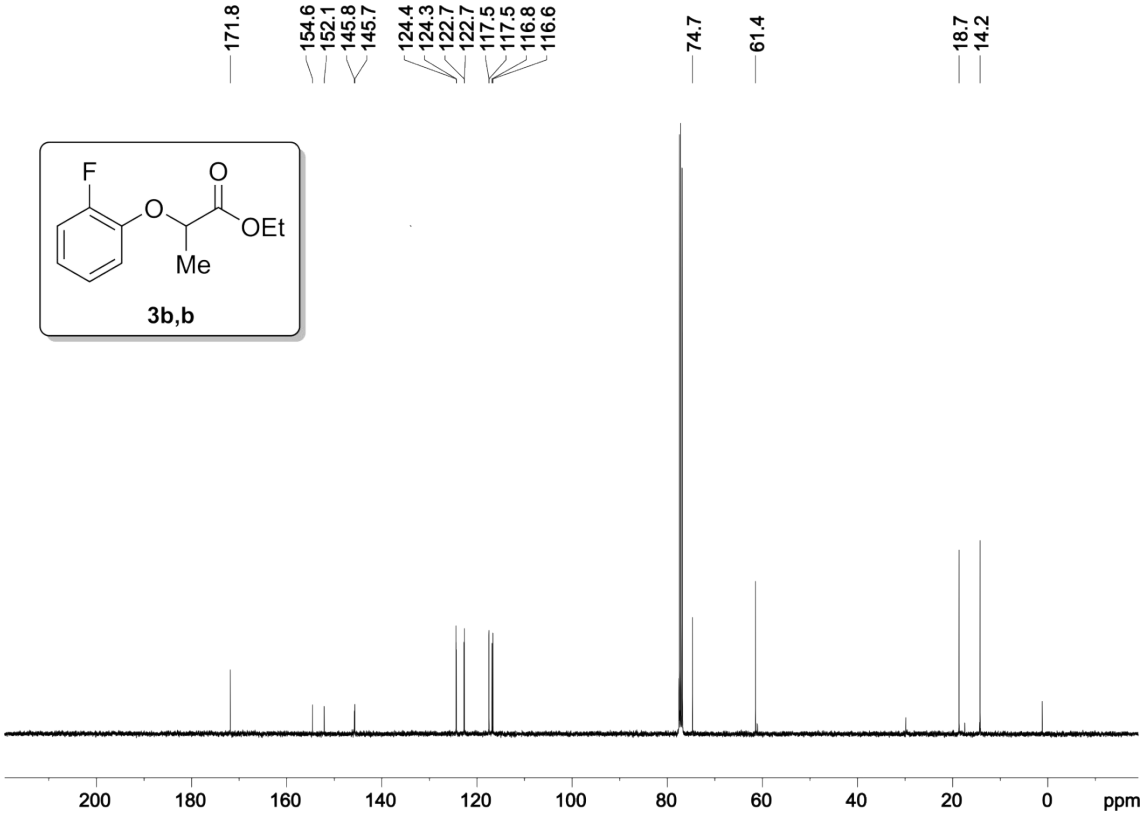


Figure SI 64. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **3b,b**.

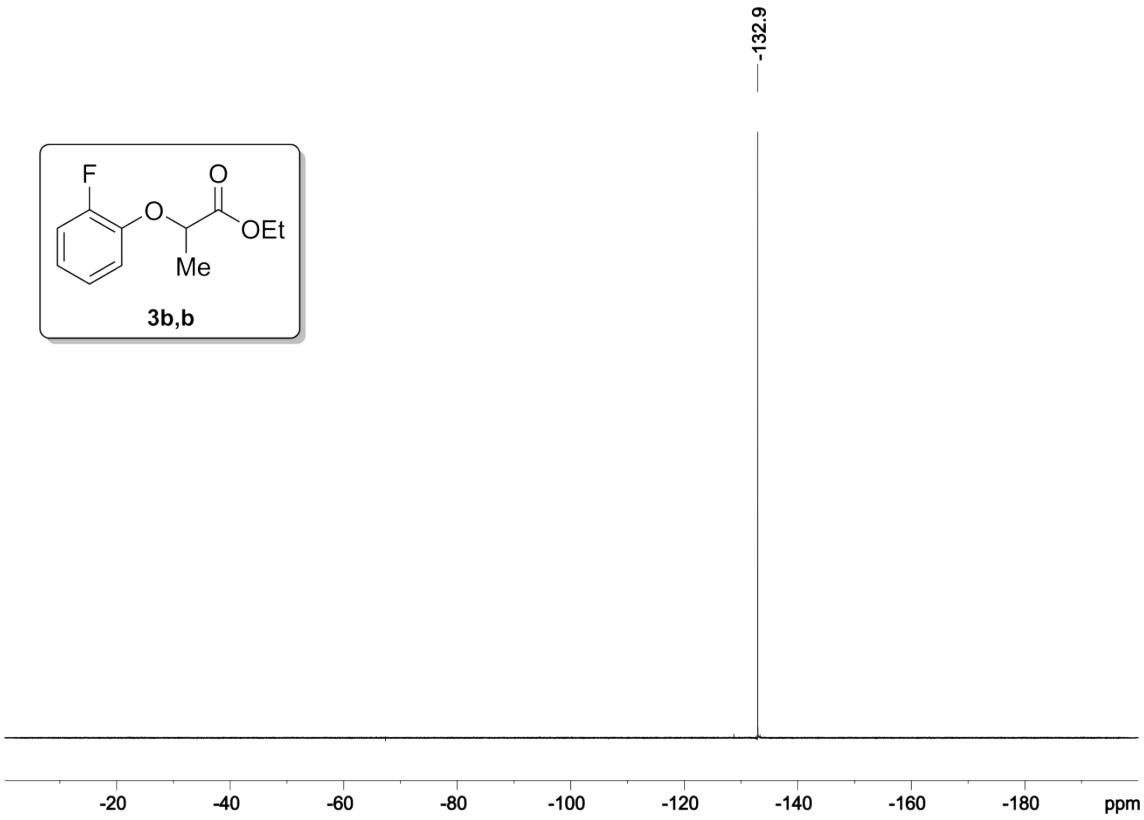


Figure SI 65. $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) of **3b,b**.

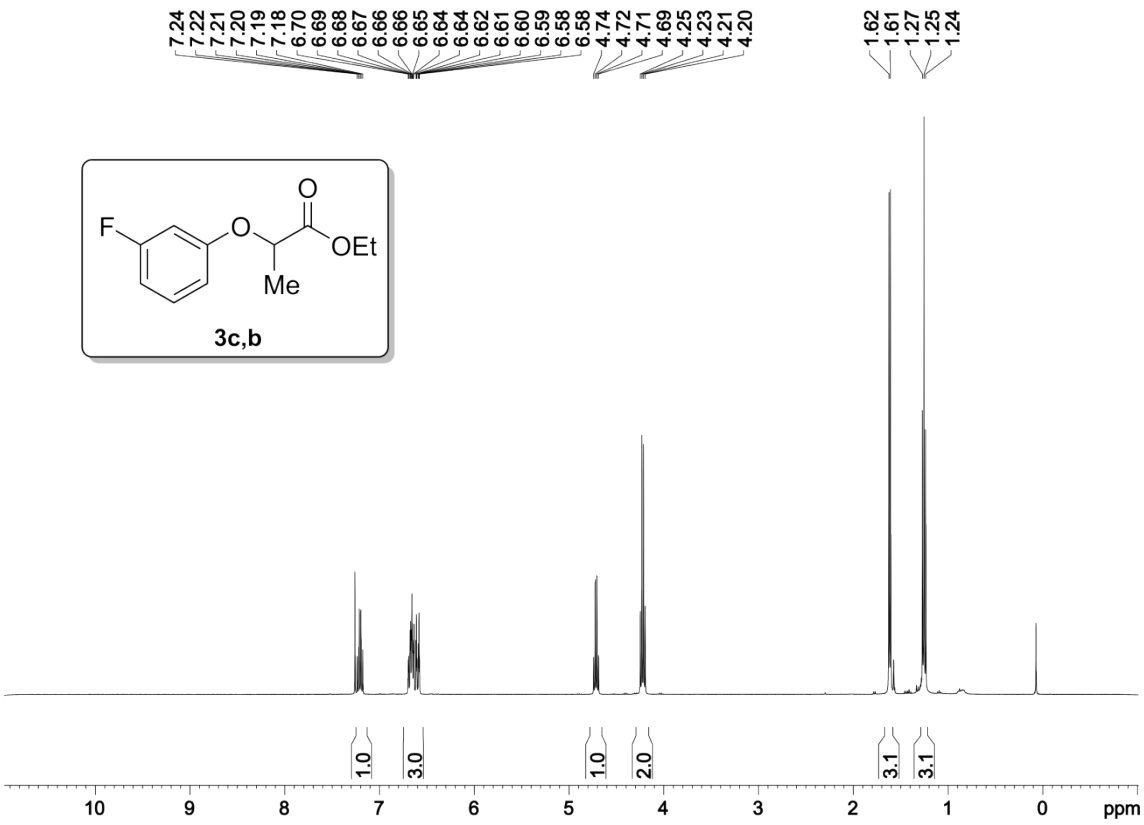


Figure SI 66. ^{1}H NMR (400 MHz, $CDCl_3$) of **3c,b**.

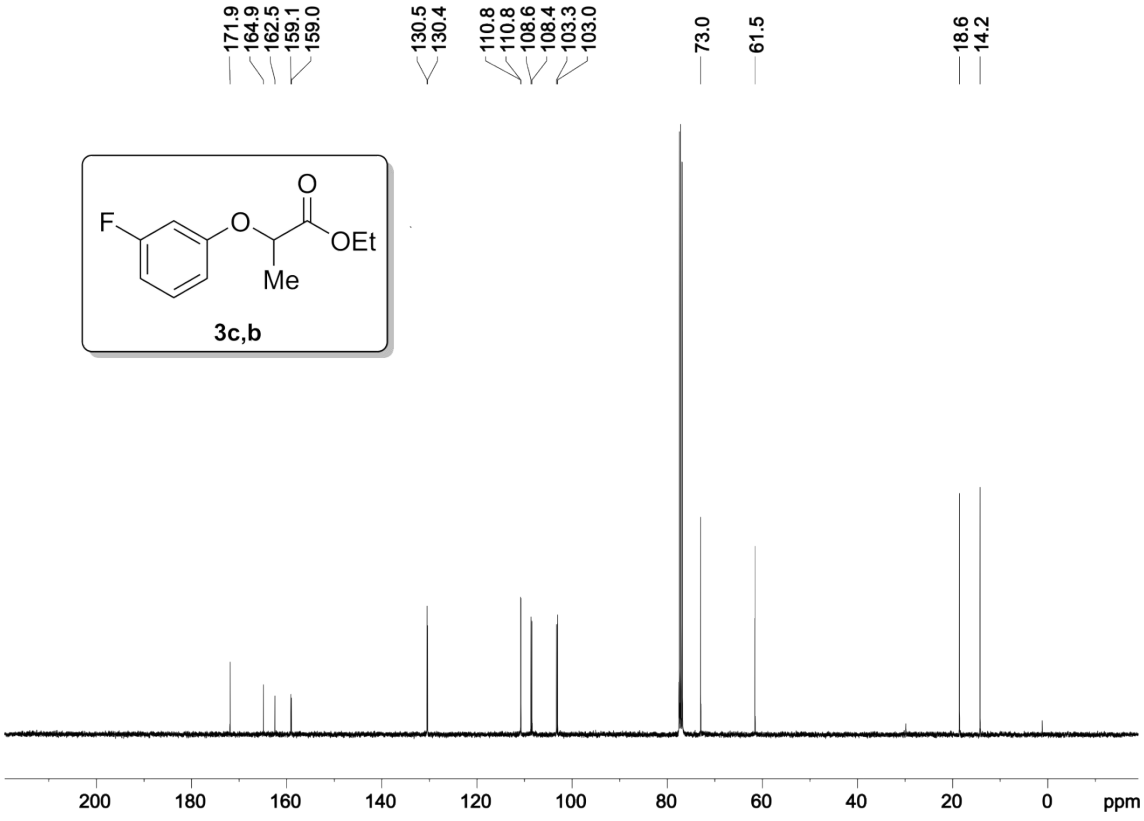


Figure SI 67. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **3c,b**.

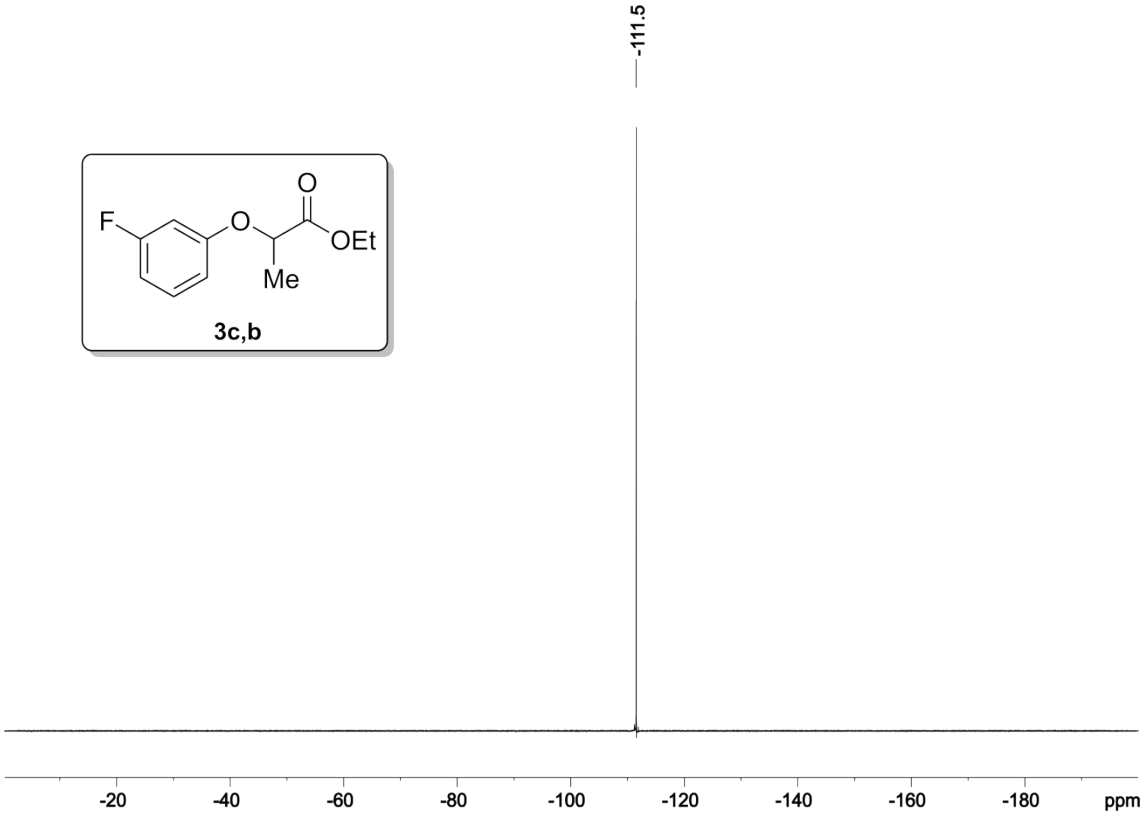


Figure SI 68. $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) of **3c,b**.

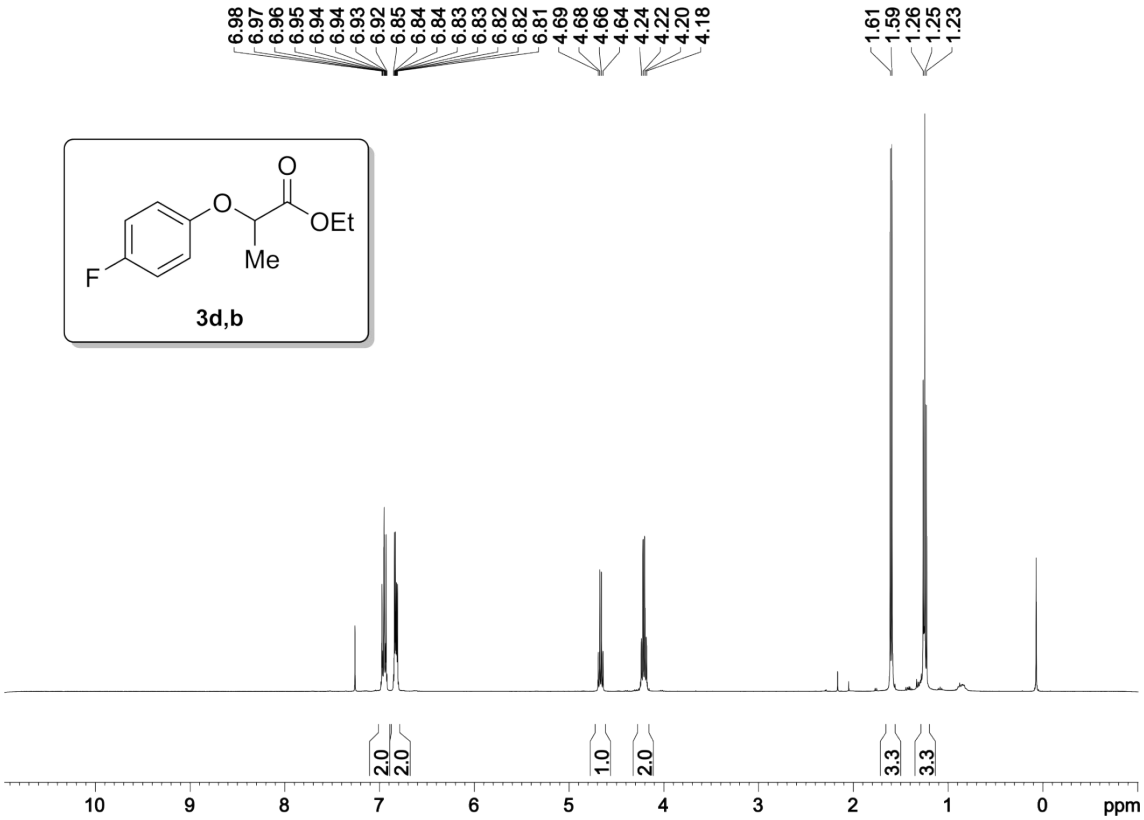


Figure SI 69. ^{1}H NMR (400 MHz, $CDCl_3$) of **3d,b**.

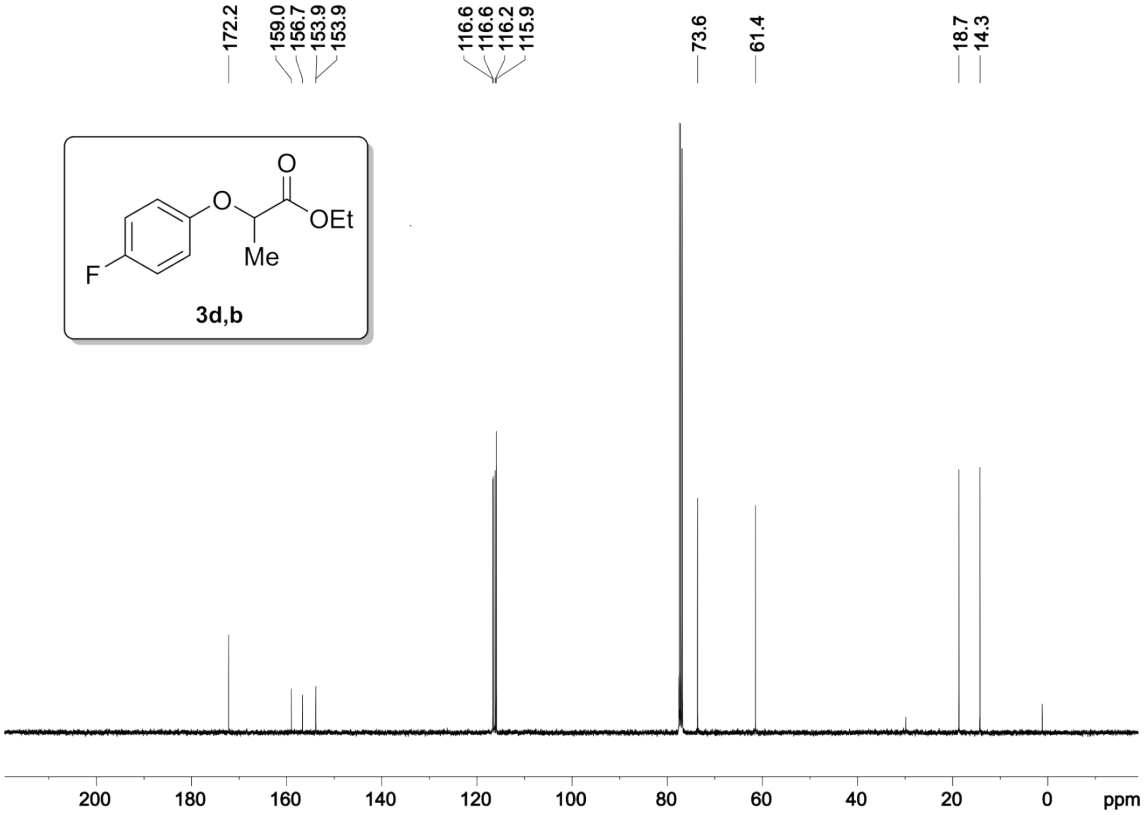


Figure SI 70. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **3d,b**.

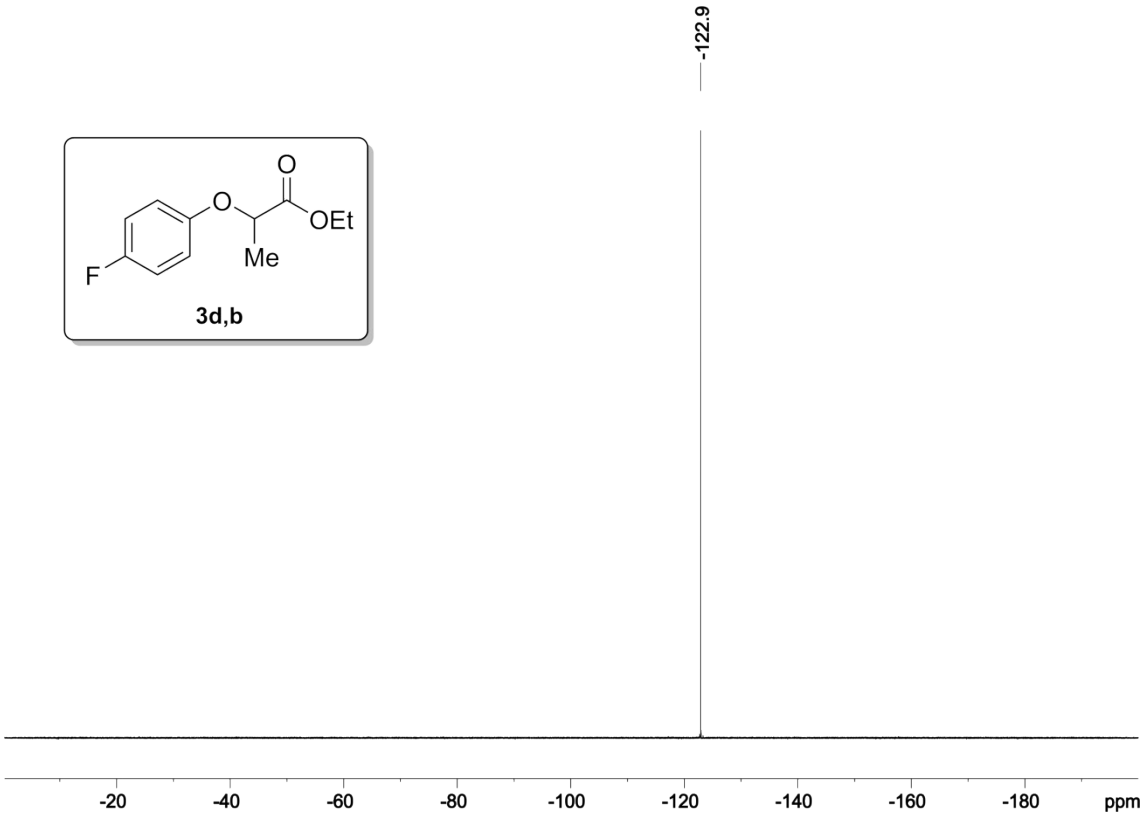


Figure SI 71. $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) of **3d,b**.

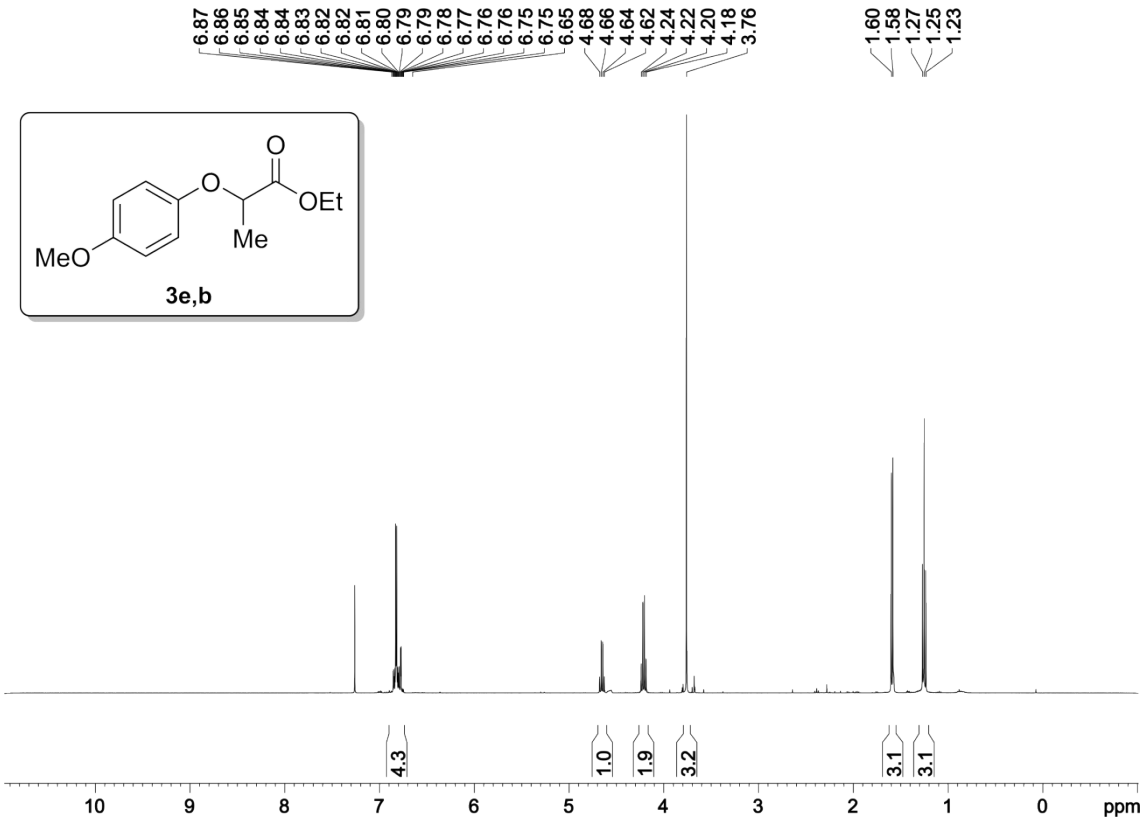


Figure SI 72. ^{1}H NMR (400 MHz, $CDCl_3$) of **3e,b**.

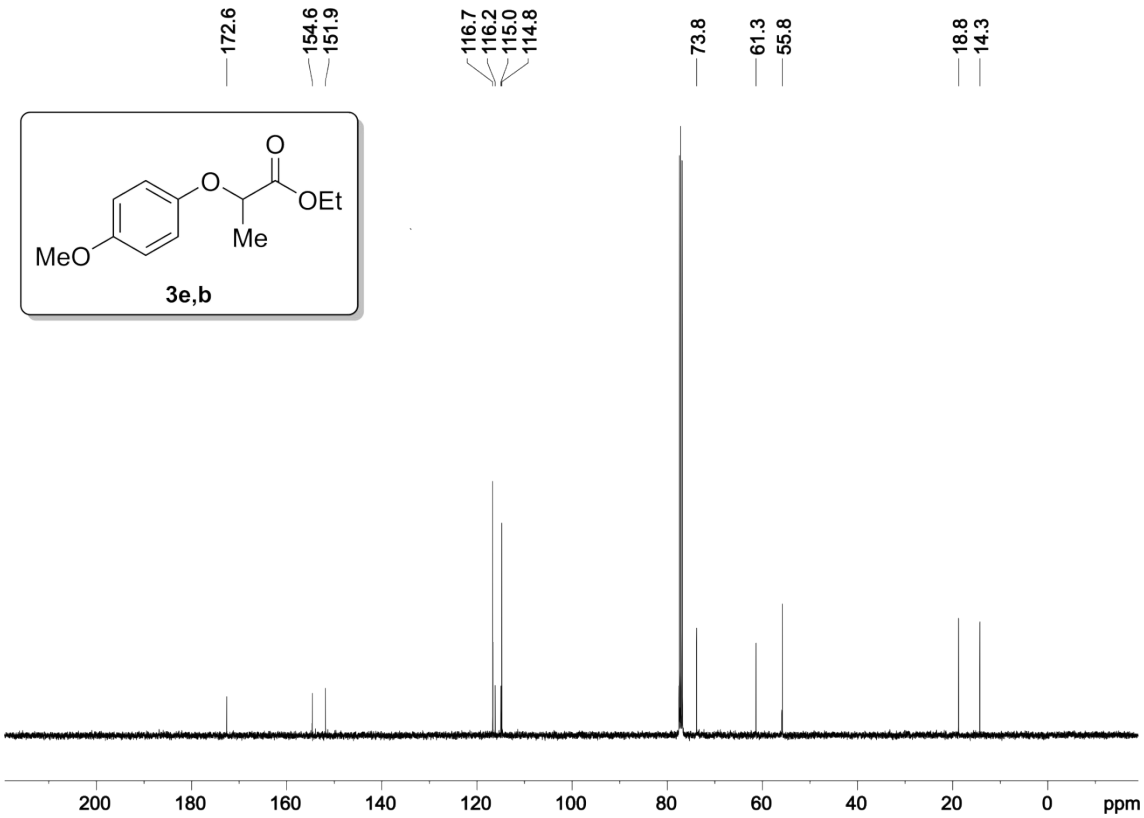


Figure SI 73. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **3e,b**.

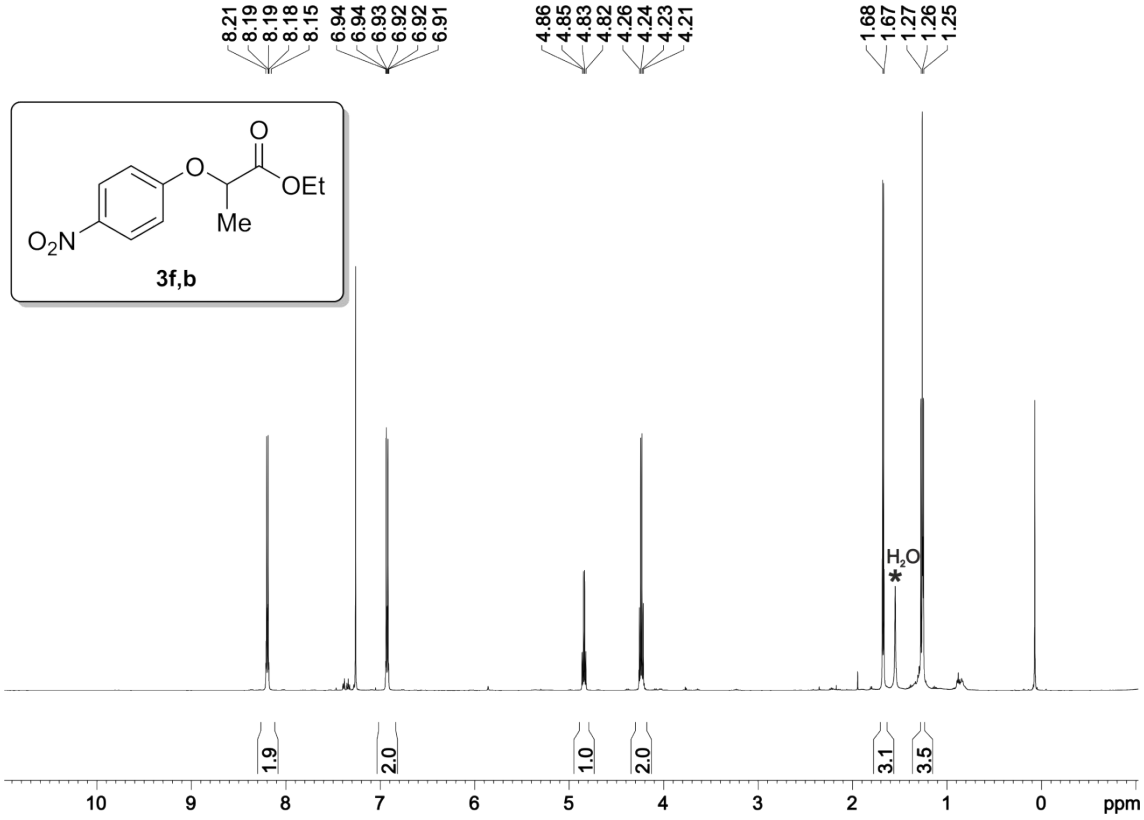


Figure SI 74. ^{1}H NMR (500 MHz, $CDCl_3$) of **3f,b**.

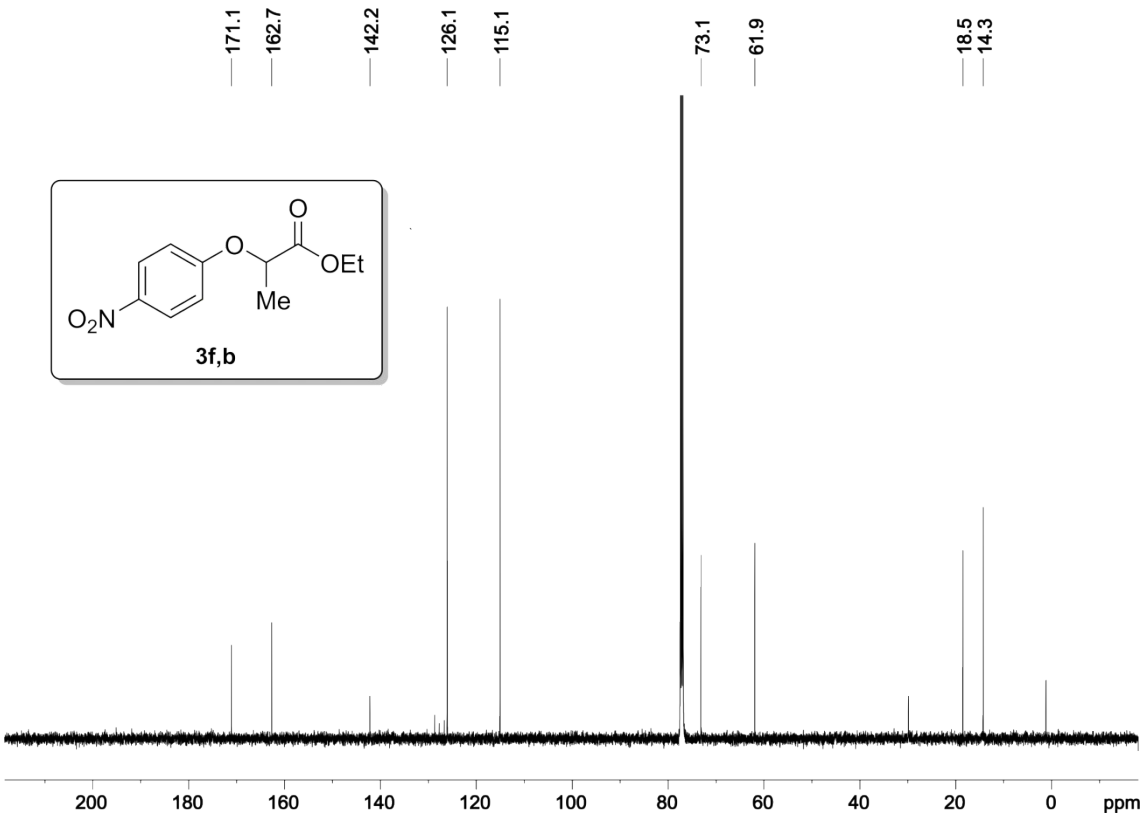


Figure SI 75. $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of **3f,b**.

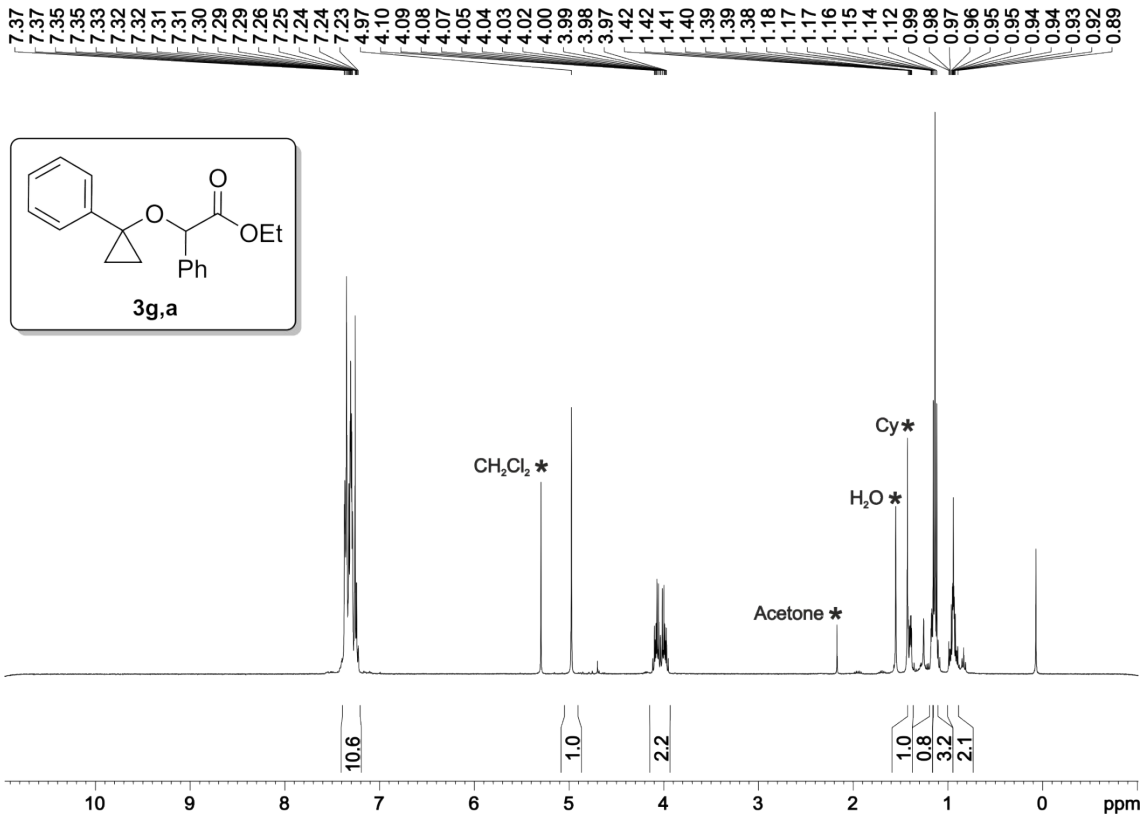


Figure SI 76. ^{1}H NMR (400 MHz, $CDCl_3$) of **3g,a**.

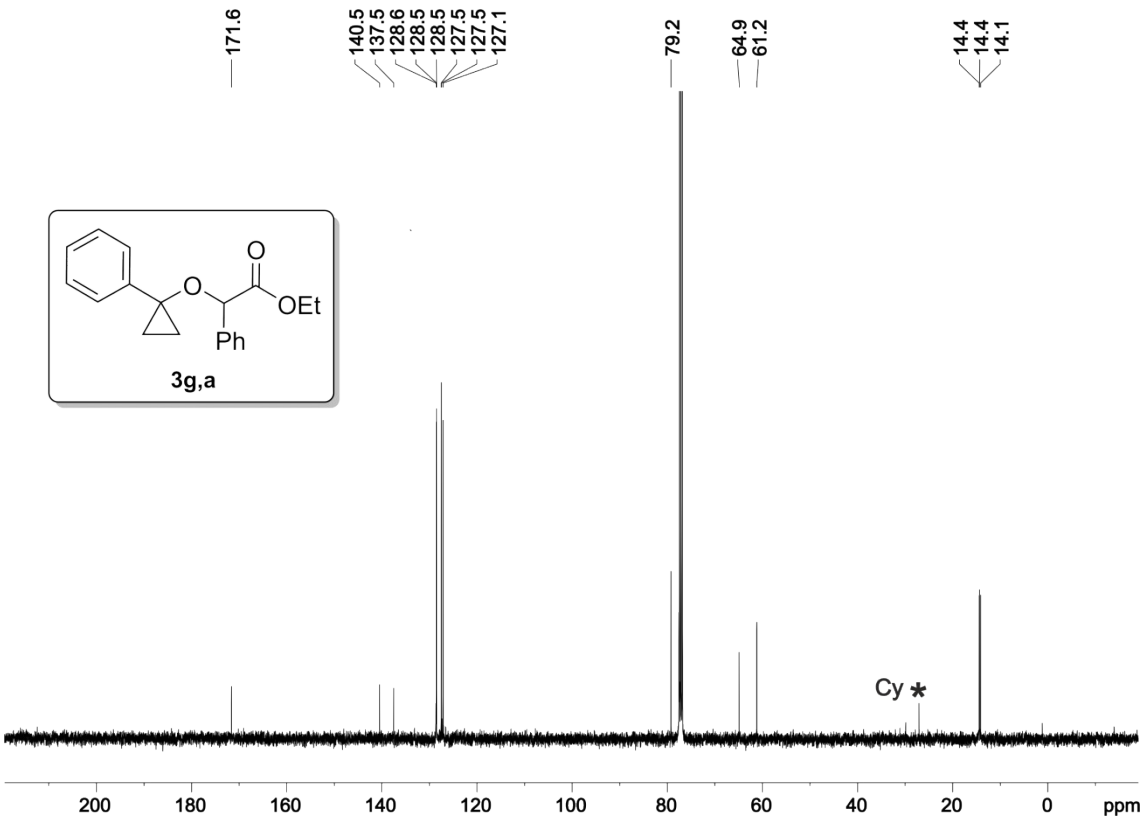


Figure SI 77. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **3g,a**.

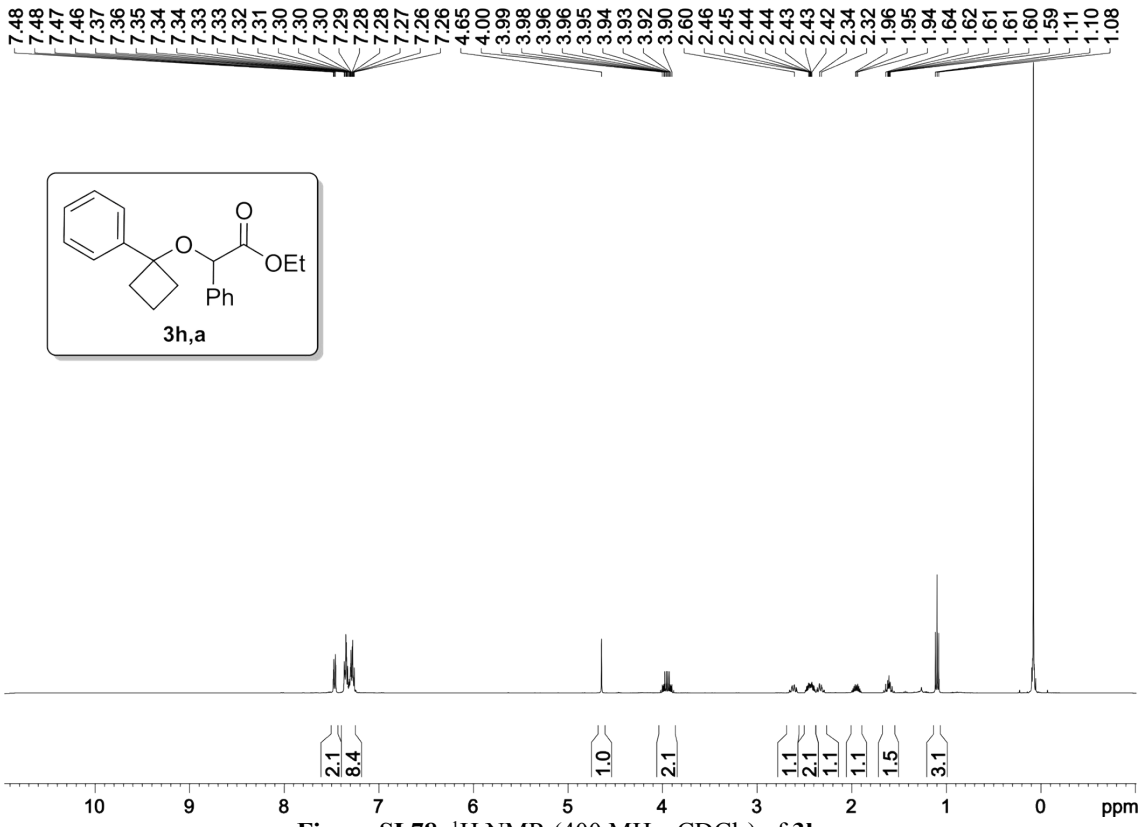


Figure SI 78. ^{1}H NMR (400 MHz, $CDCl_3$) of **3h,a**.

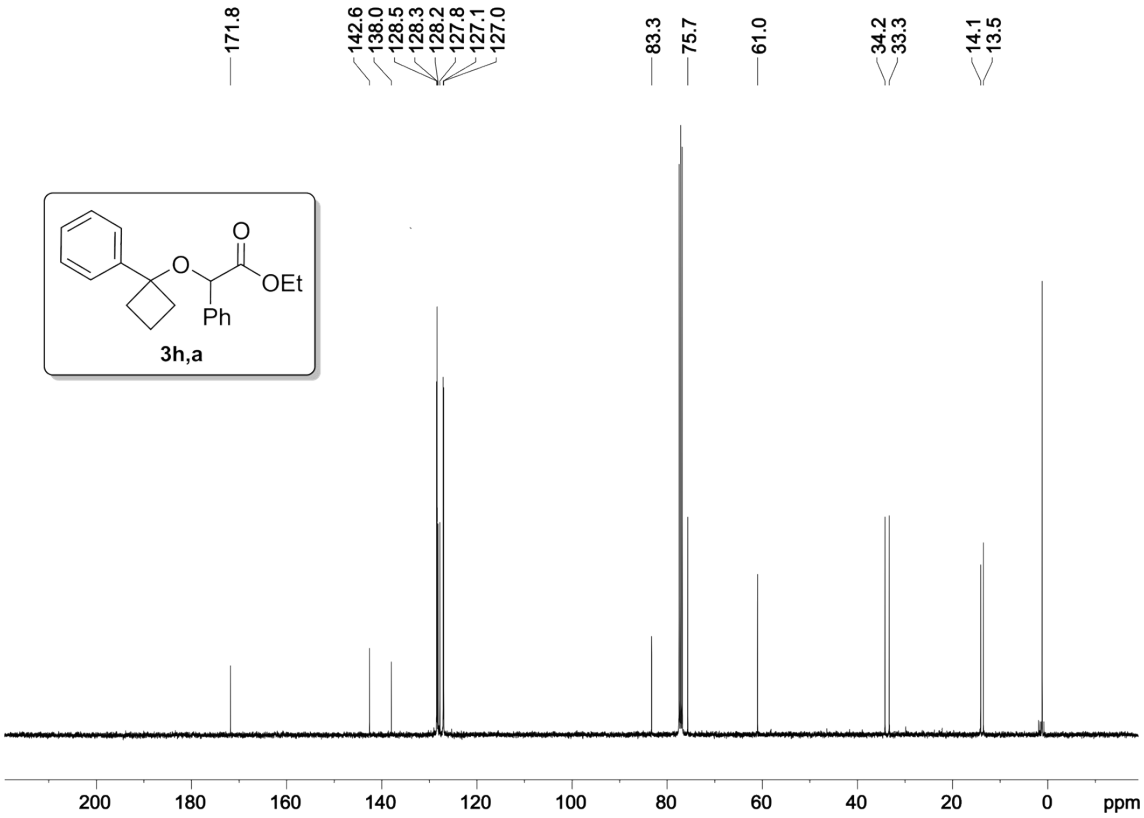


Figure SI 79. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **3h,a**.

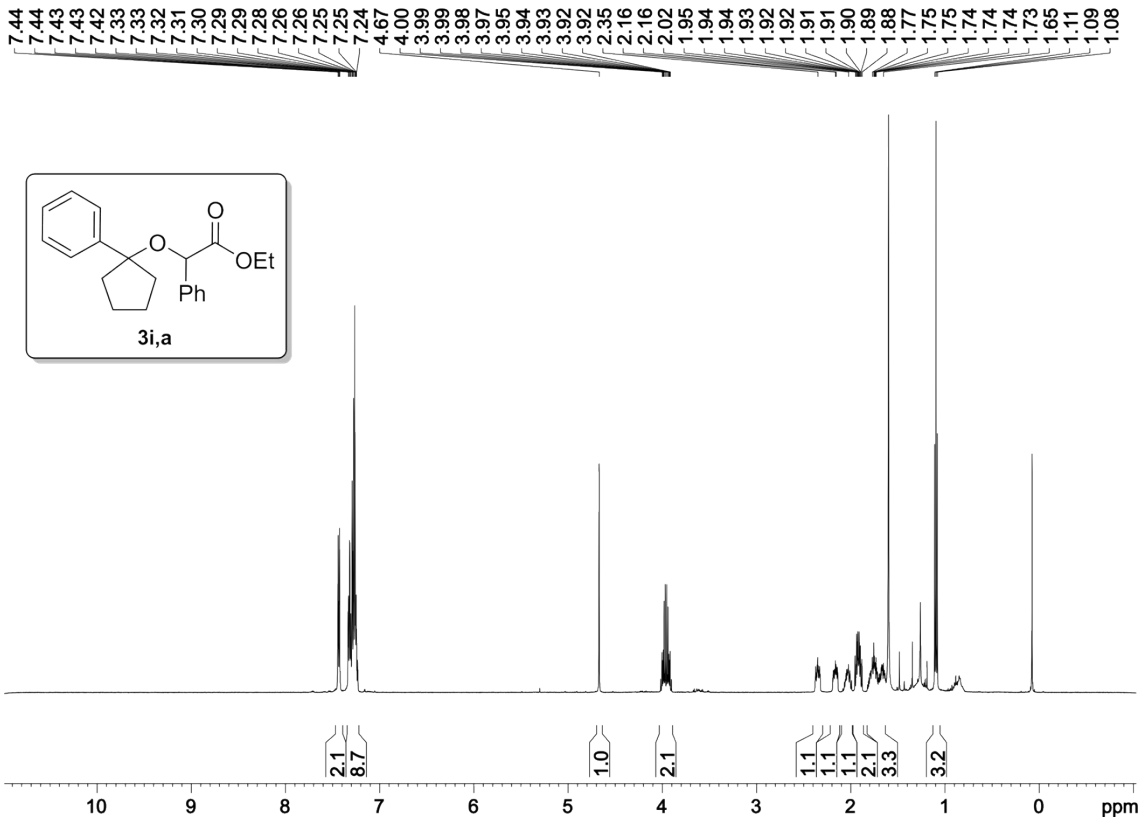


Figure SI 80. Figure SI 81. ^{1}H NMR (500 MHz, $CDCl_3$) of **3i,a**.

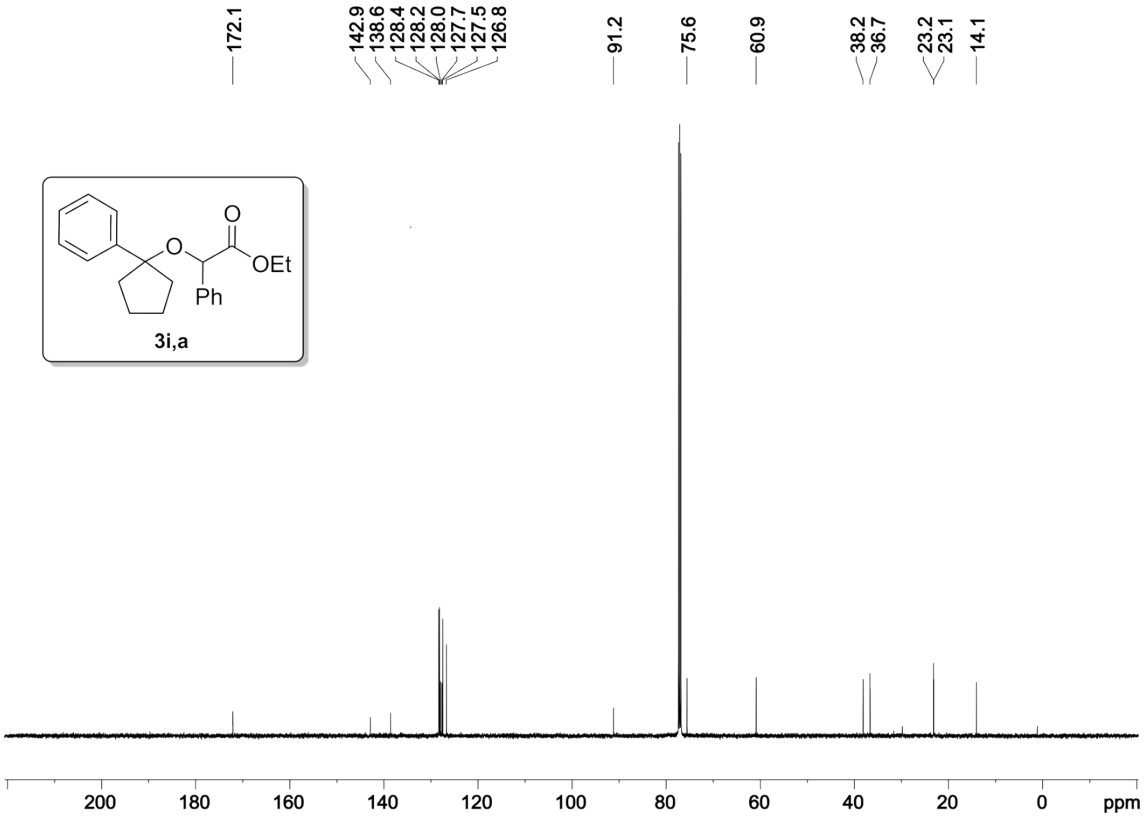


Figure SI 82. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **3i,a**.

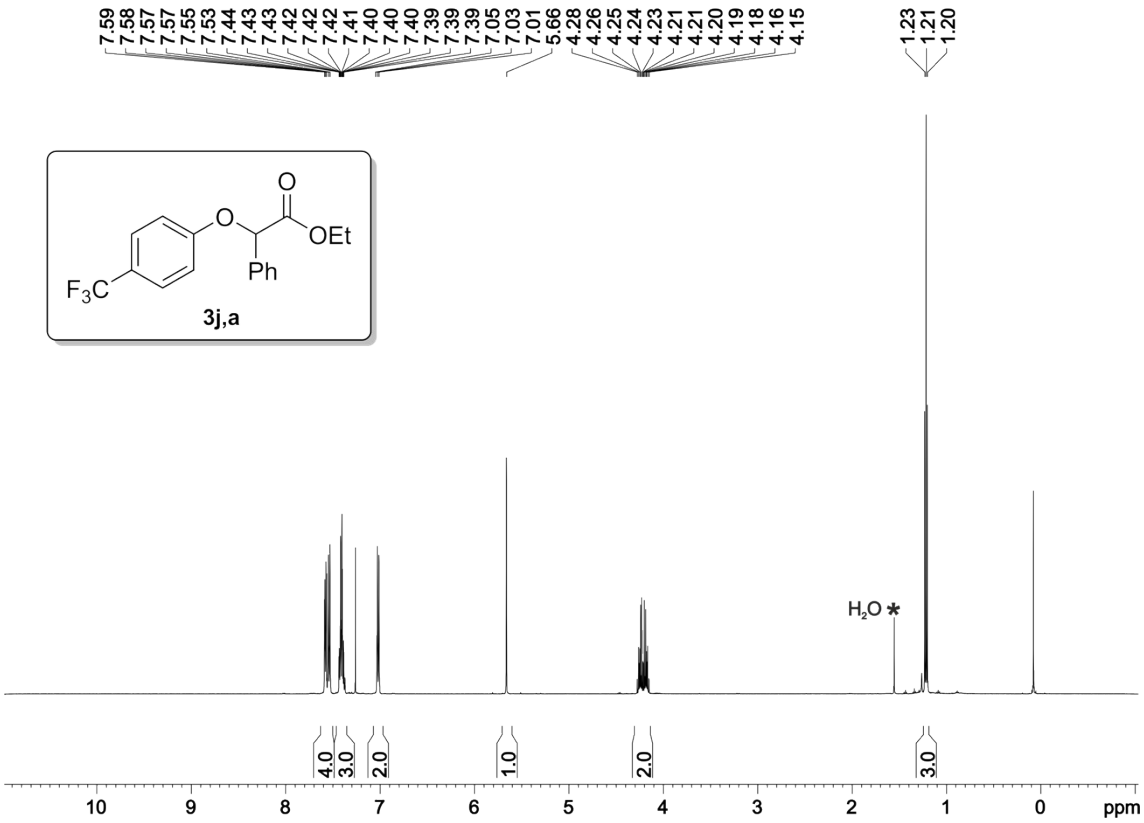


Figure SI 83. ^{1}H NMR (500 MHz, $CDCl_3$) of **3j,a**.

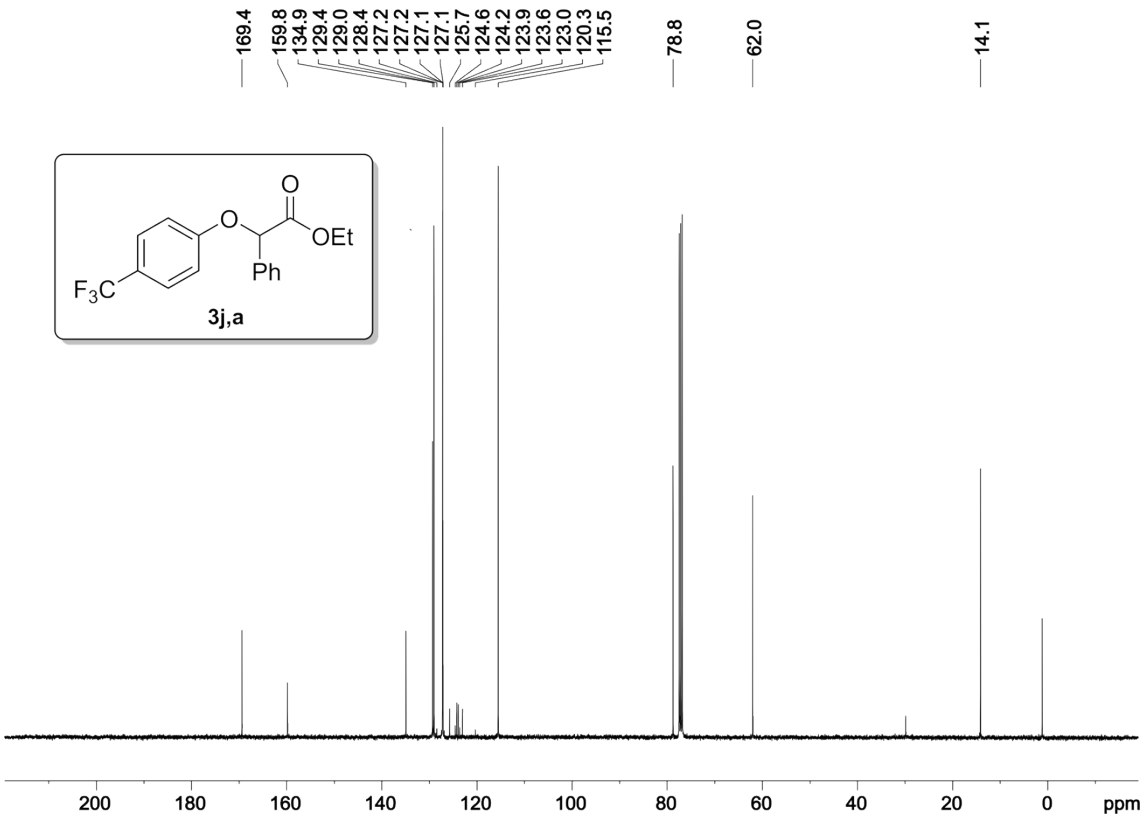


Figure SI 84. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **3j,a**

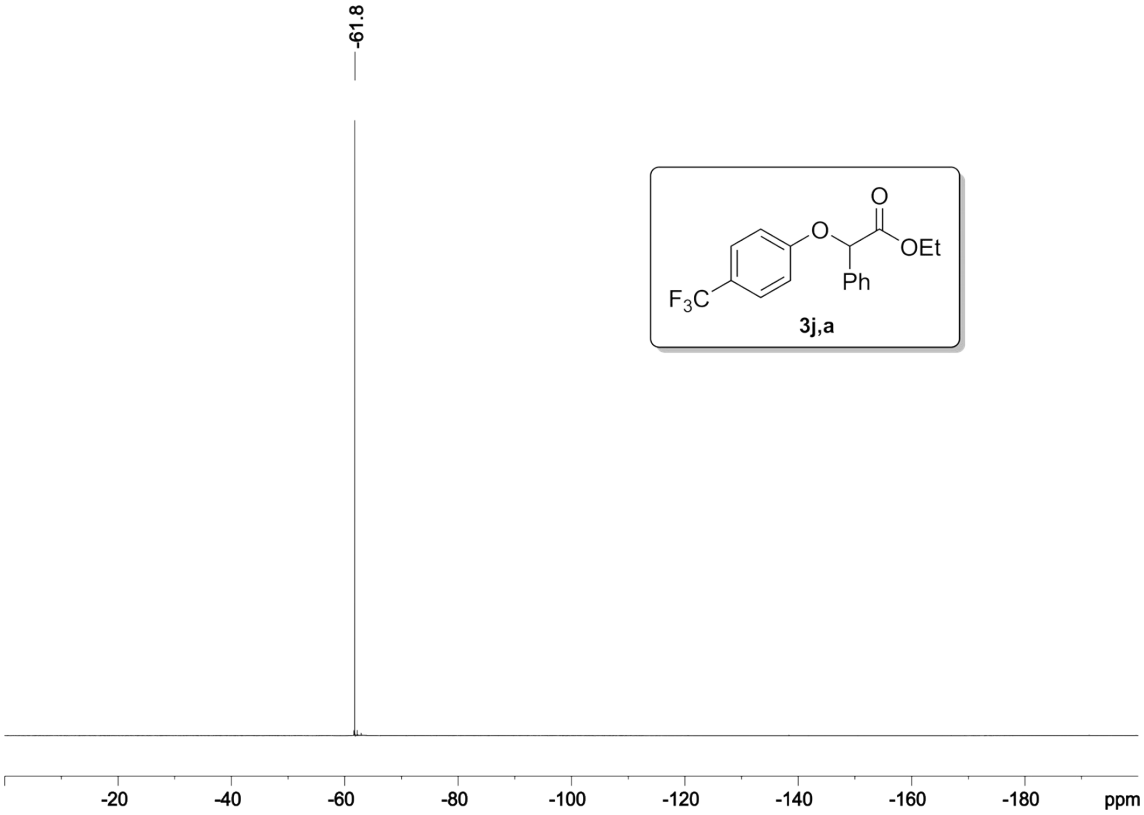


Figure SI 85. $^{19}F\{^{1}H\}$ NMR (471 MHz, $CDCl_3$) of **3j,a**.

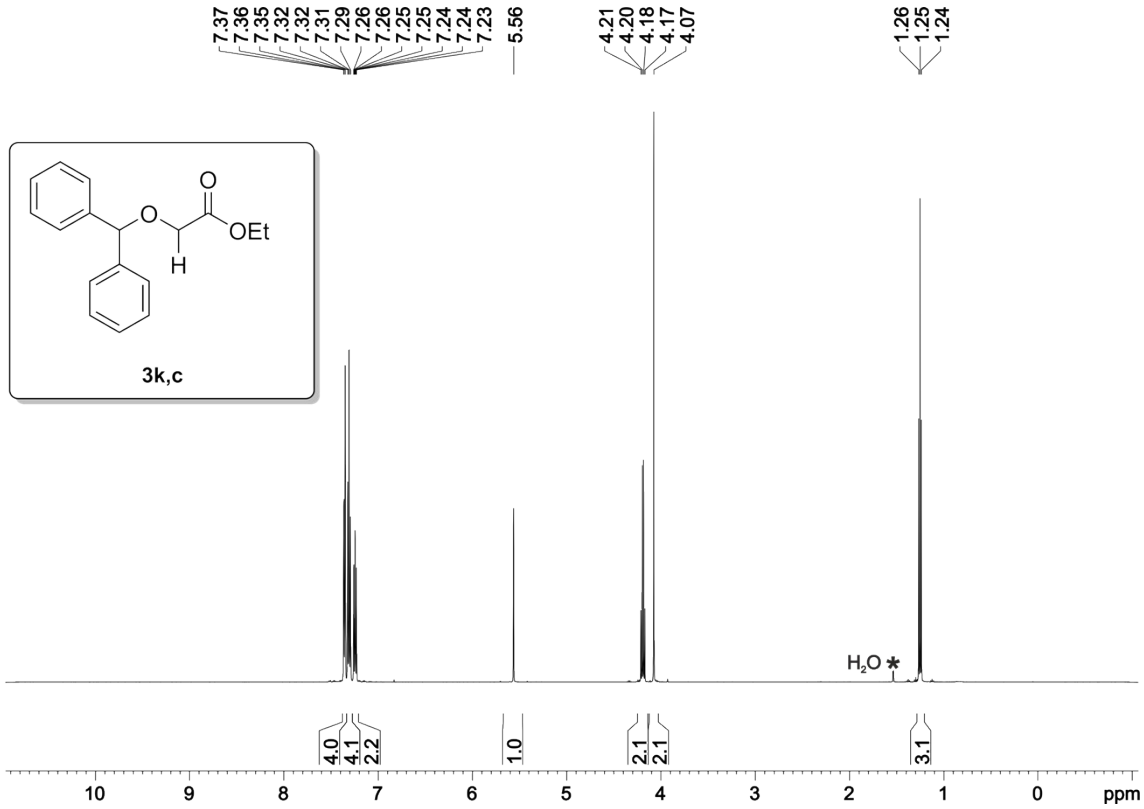


Figure SI 86. ^{1}H NMR (500 MHz, $CDCl_3$) of **3k,c**.

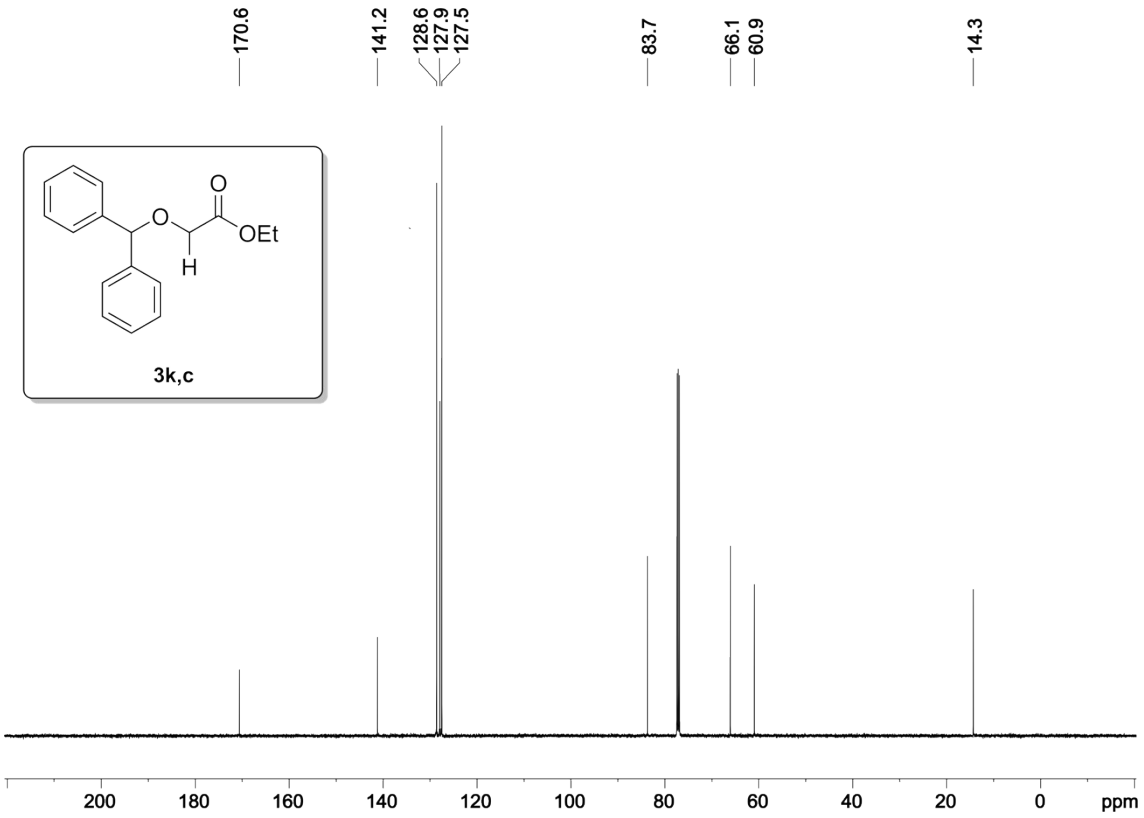


Figure SI 87. $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of **3k,c**.

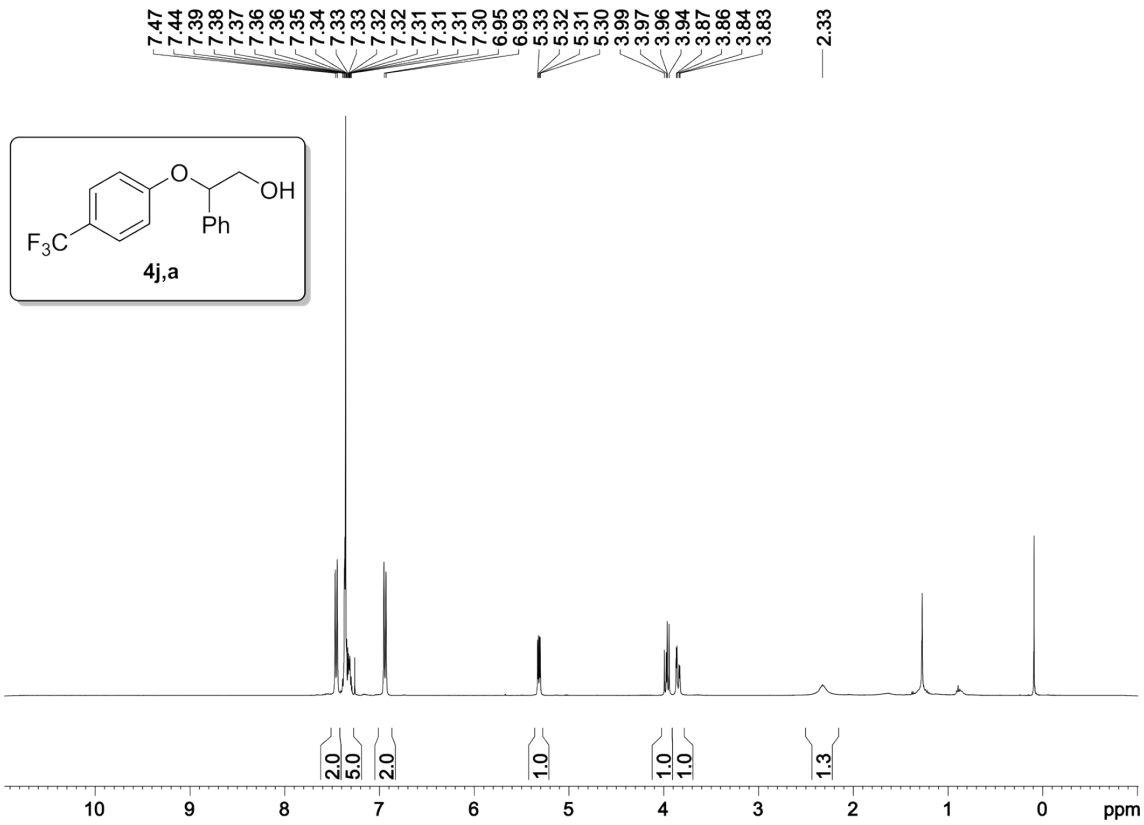


Figure SI 88. ^{1}H NMR (400 MHz, $CDCl_3$) of **4j,a**.

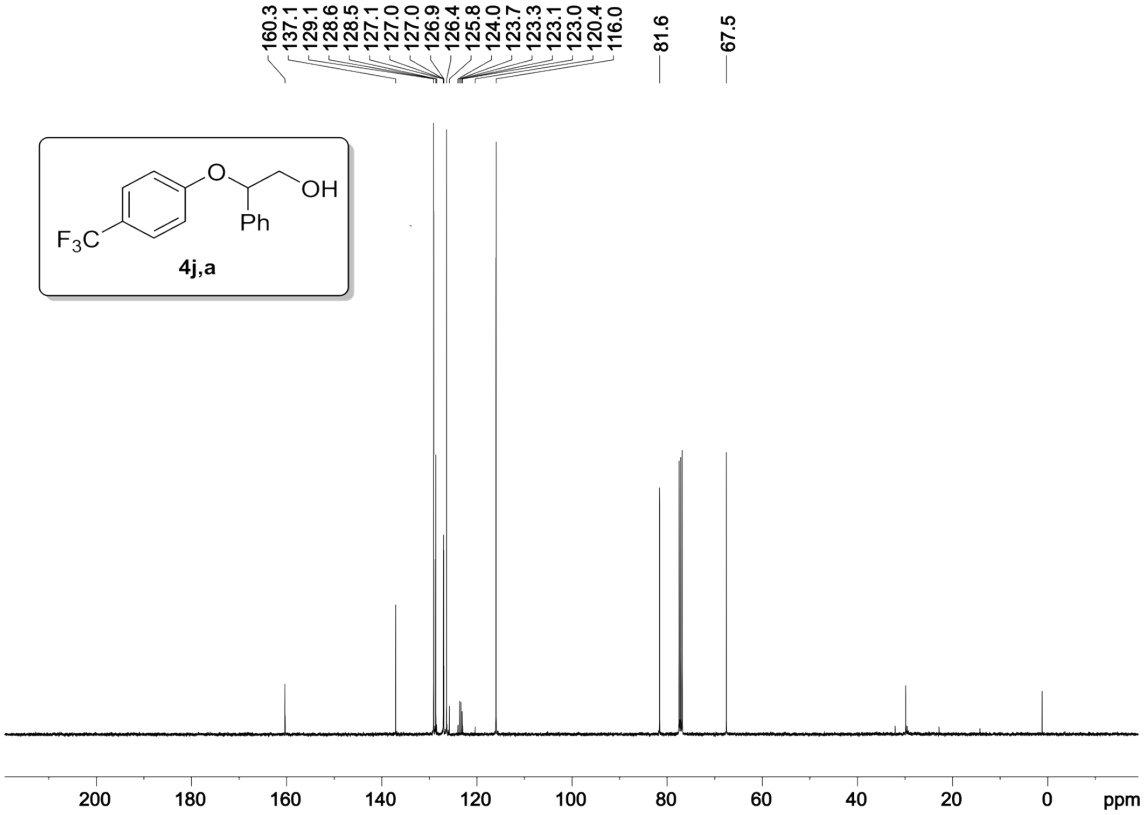


Figure SI 89. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **4j,a**.

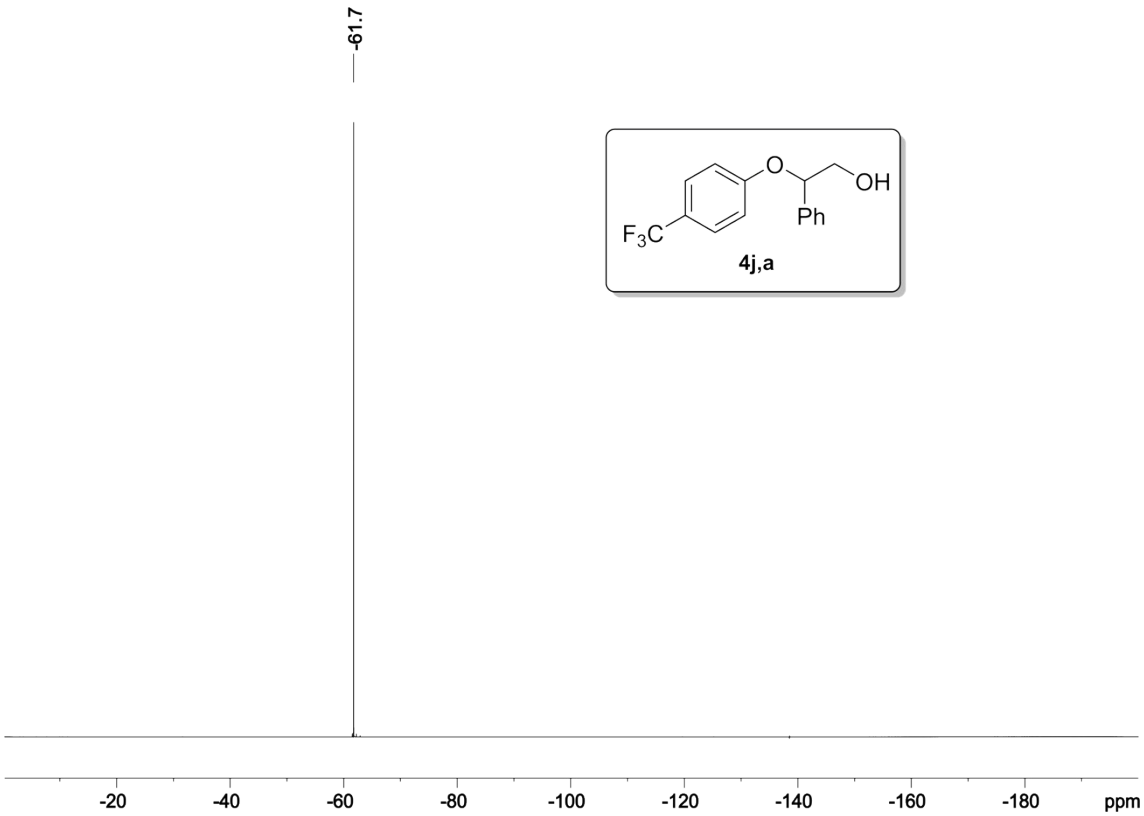


Figure SI 90. $^{19}F\{^{1}H\}$ NMR (376 MHz, $CDCl_3$) of **4j,a**.

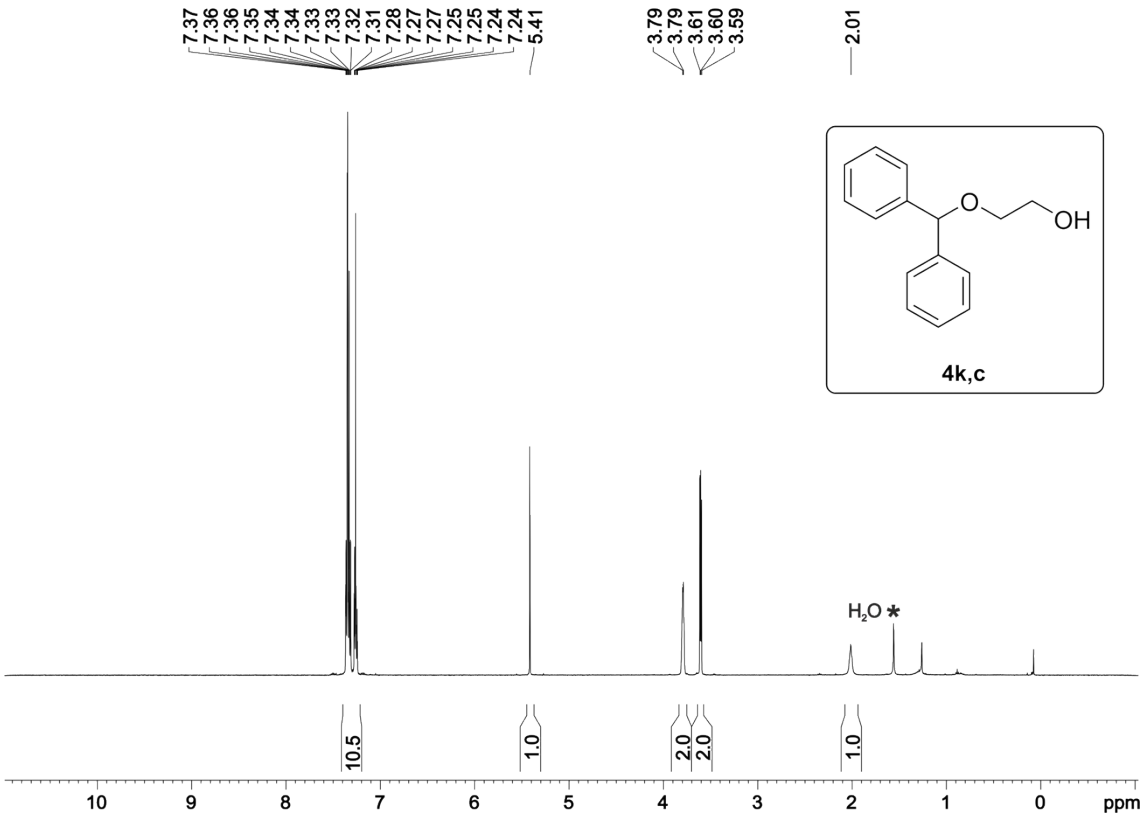


Figure SI 91. ^{1}H NMR (500 MHz, $CDCl_3$) of **4k,c**.

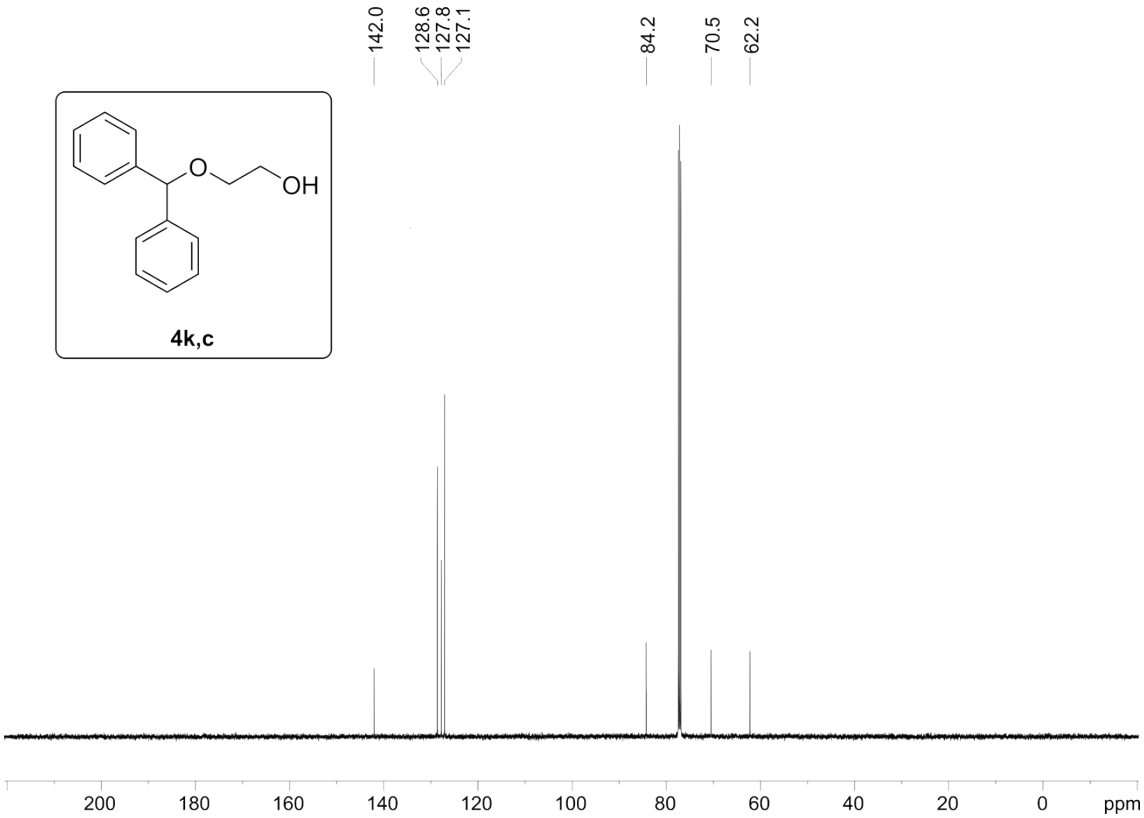


Figure SI 92. $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) of **4k,c**.

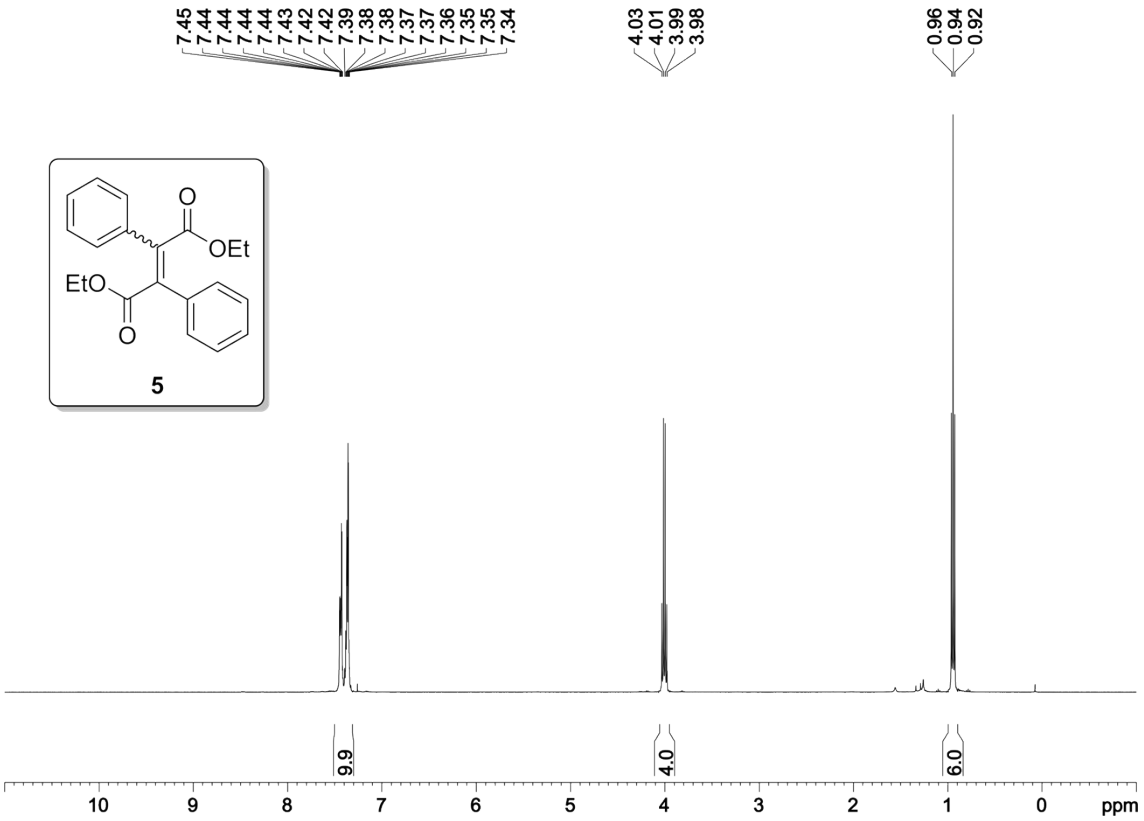


Figure SI 93. ^{1}H NMR (400 MHz, $CDCl_3$) of **5**.

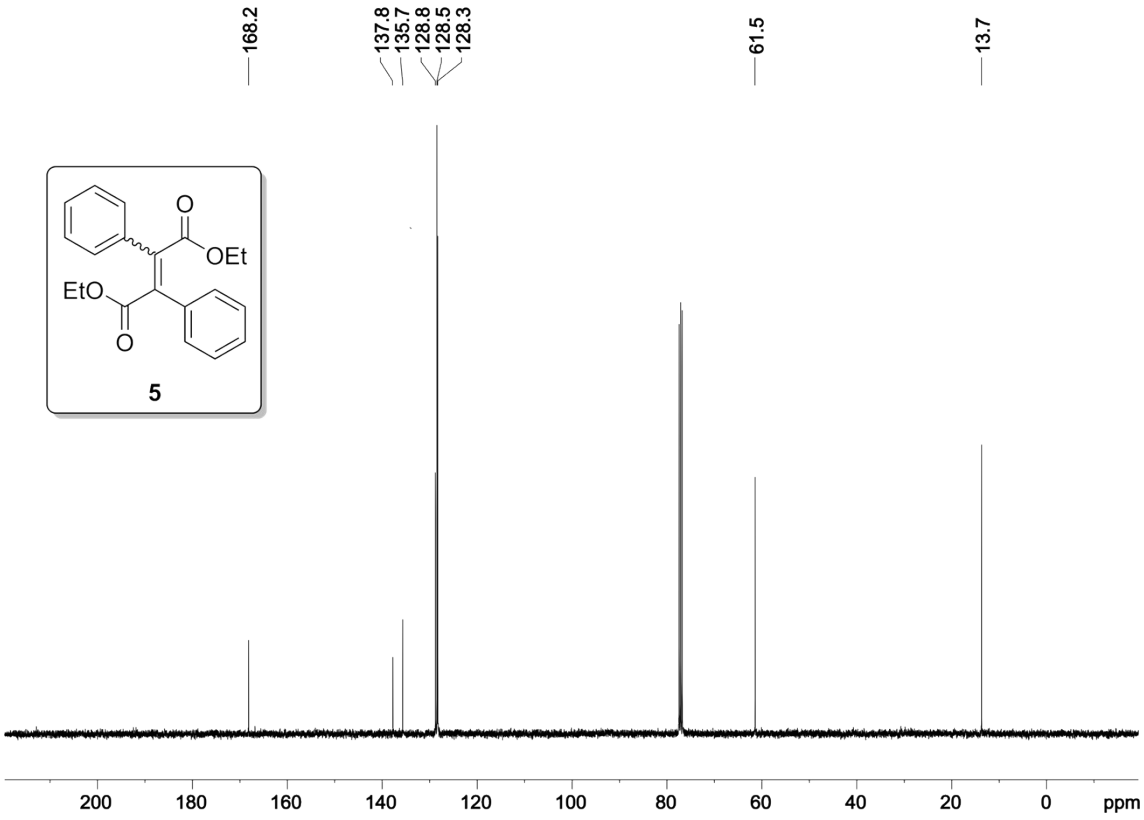


Figure SI 94. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **5**.

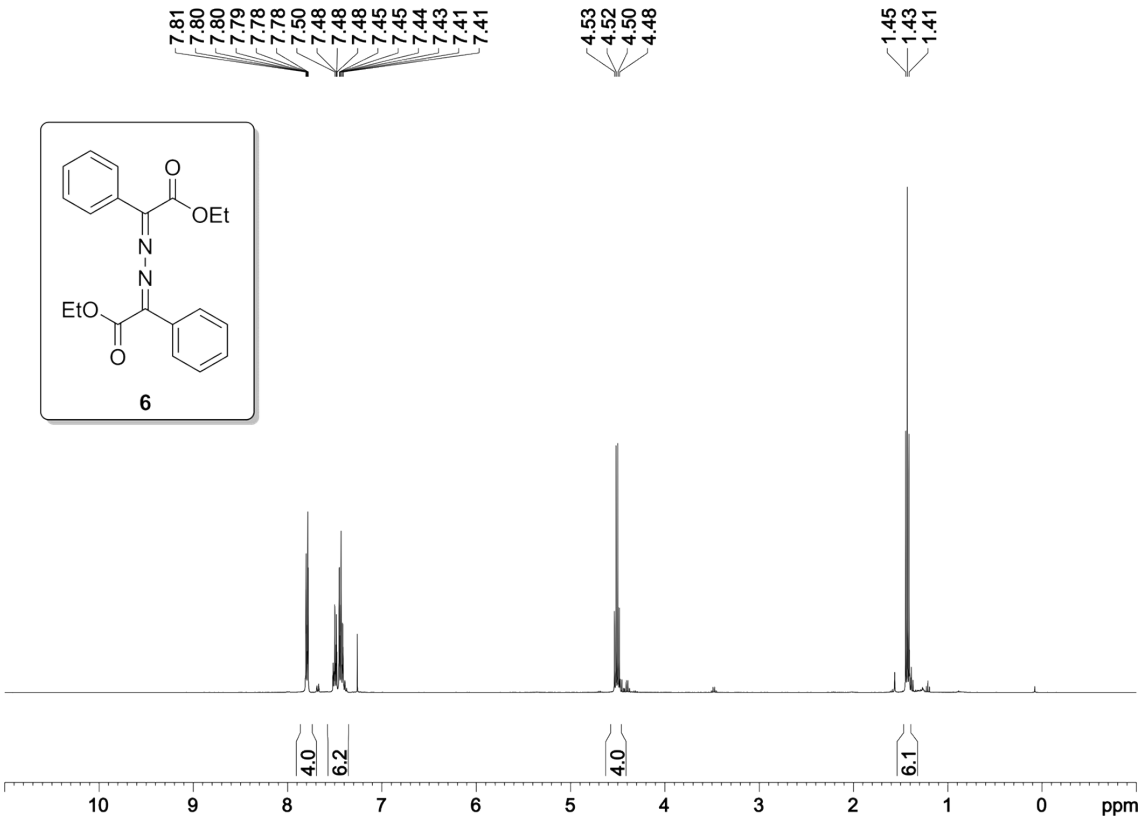


Figure SI 95. ^{1}H NMR (400 MHz, $CDCl_3$) of **6**.

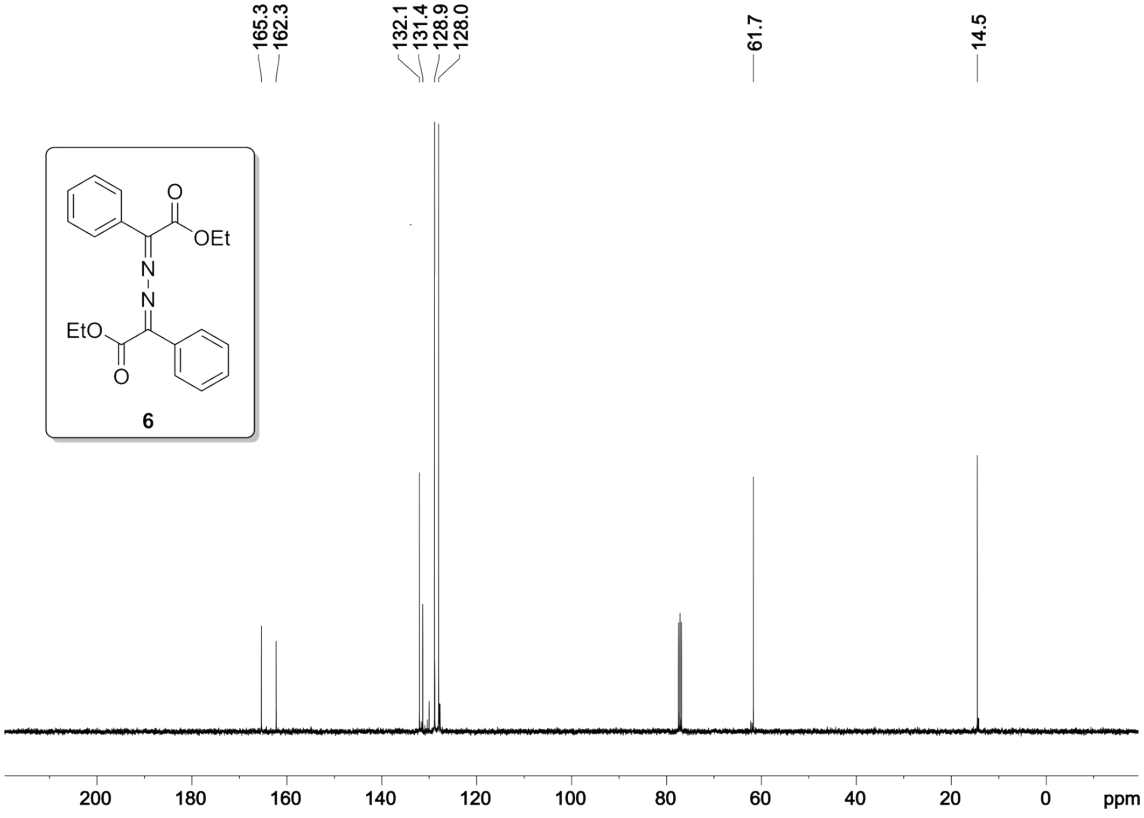


Figure SI 96. $^{13}C\{^{1}H\}$ NMR (101 MHz, $CDCl_3$) of **6**.