Electronic Supplementary Material (ESI) for ChemComm.

Enantioselective Aryl-Aryl Coupling facilitated by Chiral Binuclear Gold Complexes

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Supporting Information

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1. General Information

^{1}H NMR, ^{13}C NMR, ^{31}P NMR spectra were recorded on a Bruker Ascend 400 spectrometer. The chemical shifts are reported in ppm relative to solvent residual peak.[1] The peak patterns are indicated as follows: br, broad; s, singlet; d, doublet; t, triplet; m, multiplet; dd, doublet of doublets; dt, doublet of triplets. The enantiomeric excess was determined by HPLC with a chiral stationary phase. Mass spectrometry was performed on either a Waters AQUITY UPLC system equipped with PDA and SQD2 electrospray (ESI) MS detector (direct injection). Dichloromethane and toluene were dried/purified using the solvent purification system Puresolv MD-7. DMS•AuCl, ligands, and CsF were used as received without further purification. 2-Methoxynaphthaleneboronic acid was repurified by washing the solid with CH_2Cl_2:hexane (1:2). DMS•AuCl, CsF (99.9% trace metal basis), and 2-methoxynaphthaleneboronic acid were purchased from Sigma-Aldrich. Ligands were purchased from Sigma-Aldrich: ((*R*)-BINAP, (*S*)-BINAP, (*R*)-Tol-BINAP, (*S*)-Xyl-BINAP, (*R*)-H_8-BINAP, (*R*)-SEGPHOS, (*R*)-DM-SEGPHOS, (*R*)-DTBM-SEGPHOS, (*R*)-MeO-BIPHEP); Strem Chemicals: ((*R*)-Tol-MeO-BIPHEP, (*R*)-Xyl-MeO-BIPHEP, (*R*)-SYNPHOS, (*R*)-DIFLUORPHOS, (*R*)-C_3-TUNEPHOS); and TCI Chemicals: ((*S*)-Xyl-BINAP). $PhICl_2$ was prepared according to literature procedure.[2]

2. General Procedure for Synthesis of Chiral Gold Complexes

In an argon-filled glovebox, DMS•AuCl (0.250 mmol; 2.00 equiv), bisphosphine ligand (0.125 mmol; 1.00 equiv), and CH_2Cl_2 (5 mL; 0.05M relative to DMS•AuCl) was added to a 20 mL vial. The vial was capped with a PTFE-lined septum cap, and then removed from the glovebox. After stirring 1 hour at room temperature, hexane (3 mL) was added, and the solvents were removed in vacuo. After drying in vacuo overnight, the complex was dissolved in CH_2Cl_2, filtered through 2-3 syringe filters (0.22 μm), and then concentrated again. The resulting colorless solid was recrystallized from CH_2Cl_2/hexane.

Most of the gold complexes have been characterized previously: BINAP$(AuCl)_2$[3], (*R*)-Tol-BINAP$(AuCl)_2$[3], (*S*)-Xyl-BINAP$(AuCl)_2$[4], (*R*)-H_8-BINAP$(AuCl)_2$[5], (*R*)-SYNPHOS$(AuCl)_2$[6], (*R*)-MeO-BIPHEP$(AuCl)_2$[7], (*R*)-Xyl-MeO-BIPHEP$(AuCl)_2$[8], (*R*)-SEGPHOS$(AuCl)_2$[4], (*R*)-DTBM-SEGPHOS$(AuCl)_2$[4], and (*R*)-DIFLUORPHOS$(AuCl)_2$[6]. For these complexes, the spectroscopic data were in accordance with the previously characterized complexes. See Table S-1 (Section 2) and Section 6 for ^{31}P NMRs and chemical shifts for all complexes.

Characterization of New Complexes

(*R*)-Tol-MeO-BIPHEP$(AuCl)_2$

The title complex was obtained in 65% yield (90 mg) as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (dt, *J* = 8.2, 2.6 Hz, 2H), 7.39 – 7.26 (m, 8H), 7.22 (dd, *J* = 8.2, 2.4 Hz, 4H), 7.17 (dd, *J* = 8.2, 2.4 Hz, 4H), 6.98 – 6.91 (m, 4H), 2.99 (s, 6H), 2.39 (s, 6H), 2.35 (s, 6H). ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.6. MS (ESI) *m/z* ($M–Cl^-$) calcd for $C_{42}H_{40}Au_2ClO_2P_2$: 1067, found 1067.

(*R*)-C_3-TUNEPHOS$(AuCl)_2$

The title complex was obtained in 81% yield (107 mg) as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.78 (dd, *J* = 13.2, 7.3 Hz, 4H), 7.43 (td, *J* = 8.0, 2.2 Hz, 4H), 7.39 – 7.32 (m, 6H), 7.23 (td, *J* = 7.8, 2.4, 4H), 7.18 – 7.09 (m, 4H), 7.00 (d, *J* = 8.1 Hz, 2H), 6.95 (dd, *J* = 10.7, 7.8 Hz, 2H), 4.04 (dt, *J* = 11.8, 5.7 Hz, 2H), 3.95 (dt, *J* = 11.8, 4.4 Hz, 2H), 1.67 – 1.58 (m, 2H). ^{31}P NMR (162 MHz, $CDCl_3$) δ 25.0. MS (ESI) *m/z* ($M–Cl^-$) calcd for $C_{39}H_{32}Au_2ClO_2P_2$: 1023, found 1023.

(*R*)-DM-SEGPHOS$(AuCl)_2$

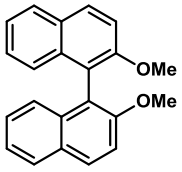
The title complex was obtained in 86% yield (128 mg) as a colorless solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.21 (s, 2H), 7.17 (s, 2H), 7.08 (s, 2H), 6.99 (s, 4H), 6.96 (s, 2H), 6.91 (d, *J* = 8.2 Hz, 2H), 6.77 (dd, *J* = 11.6, 8.2 Hz, 2H), 5.71 (s, 2H), 4.93 (s, 2H), 2.30 (s, 12H), 2.27 (s, 12H). ^{31}P NMR (162 MHz, $CDCl_3$) δ 23.6. MS (ESI) *m/z* ($M–Cl^-$) calcd for $C_{46}H_{44}Au_2ClO_4P_2$: 1151, found 1151.

3. General Procedure for Enantioselective Aryl-Aryl Coupling facilitated by Chiral Gold Complexes

In an argon-filled glovebox, a 4 mL vial was charged with the chiral binuclear gold complex (0.0580 mmol; 1.00 equiv), 2-methoxy-naphthalene-1-boronic acid (35.2 mg, 0.174 mmol; 3.00 equiv), and CsF (52.8 mg, 0.348 mmol; 6.00 equiv). Then, a Teflon stir bar was added followed by CH_2Cl_2 (1.7 mL). The vial was capped with a PTFE-lined septum cap and removed from the glovebox. The vial was placed in an aluminum heating block on a heated stir plate, and the reaction mixture stirred at 30 °C until ^{31}P NMR of an aliquot, diluted with $CDCl_3$, showed complete double transmetalation (48 h unless otherwise noted). The reaction mixture was cooled to –78 °C, using a dry-ice bath, followed by slow addition of a solution of $PhICl_2$ (31.9 mg, 0.116 mmol; 2.00 equiv) in CH_2Cl_2 (0.67 mL); addition over one minute. The reaction was stirred one hour at –78 °C, then the dry-ice bath was removed, and the reaction mixture allowed to heat to room temperature. Then toluene (12 µL) was added and an aliquot of the reaction mixture analyzed by ^1H NMR for determination of yield and ^{31}P NMR for determination of the fate of the gold complex. A portion of the reaction mixture was purified by preparative-TLC (75:25 CH_2Cl_2:hexane) for determination of the enantiomeric excess.

The enantiomeric excess was determined by HPLC with an OD-H column (2% *i*-PrOH/hexane, flow rate 1.0 mL/min); retention times (*R*)-**2**: 7.07 min, (*S*)-**2**: 7.93 min. The absolute configuration of the enantiomers was determined by comparison of optical rotation with literature[9] and by comparison of the retention time for an authentic sample of (*R*)-**2** purchased from Sigma-Aldrich.

2,2'-Dimethoxy-1,1'-binaphthalene (**2**)[10]



Colorless solid. ^1H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, *J* = 9.0 Hz, 2H), 7.87 (d, *J* = 8.1 Hz, 2H), 7.46 (d, *J* = 9.0 Hz, 2H), 7.35-7.28 (m, 2H), 7.24-7.16 (m, 2H), 7.12 (d, *J* = 8.5 Hz, 2H), 3.77 (s, 6H).

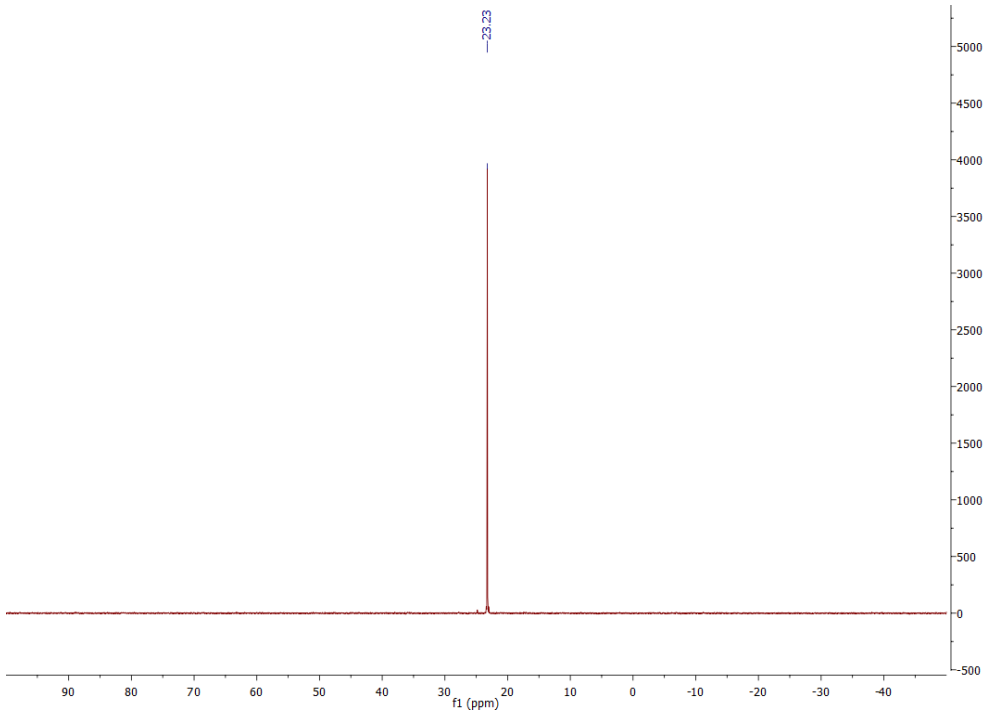
Table S-1 ^{31}P NMR Chemical Shifts for $L(AuCl)_2$ and $L(AuAr)_2$ Complexes (after transmetalation).

Entry	Starting Complex	$L(AuCl)_2$ (ppm)	$L(AuAr)_2$ (ppm)
1	(*S*)-BINAP$(AuCl)_2$	23.2	38.1
2	(*R*)-BINAP$(AuCl)_2$	23.2	38.2
3	(*R*)-Tol-BINAP$(AuCl)_2$	21.7	36.5
4	(*S*)-Xyl-BINAP$(AuCl)_2$	22.0	37.6
5	(*R*)-H_8-BINAP$(AuCl)_2$	20.3	35.2
6	(*R*)-SYNPHOS$(AuCl)_2$	22.1	37.2
7	(*R*)-MeO-BIPHEP$(AuCl)_2$	23.1	37.8
8	(*R*)-Tol-MeO-BIPHEP$(AuCl)_2$	23.6	36.1
9	(*R*)-Xyl-MeO-BIPHEP$(AuCl)_2$	22.1	37.0[a]
10	(*R*)-C_3-TUNEPHOS$(AuCl)_2$	25.0	38.8
11	(*R*)-SEGPHOS$(AuCl)_2$	24.8	37.9
12	(*R*)-DM-SEGPHOS$(AuCl)_2$	23.6	37.5
13	(*R*)-DTBM-SEGPHOS$(AuCl)_2$	27.3	40.8
14	(*R*)-DIFLUORPHOS$(AuCl)_2$	23.6	38.0

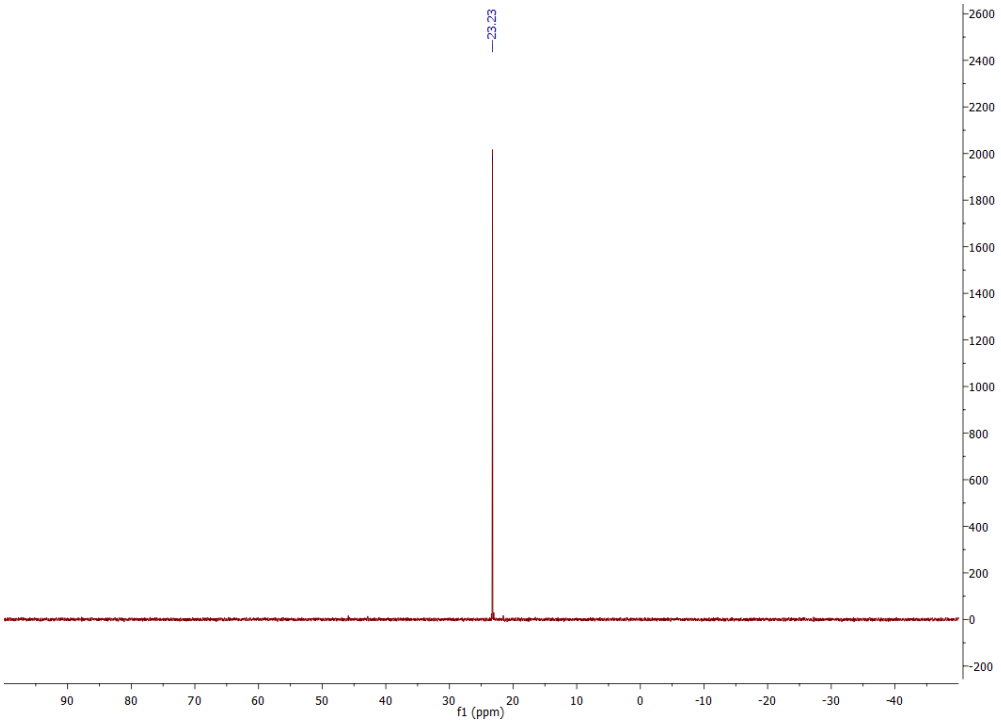
[a] Multiple large peaks observed after transmetalation.

4. ^{1}H and ^{31}P NMR of Previously Uncharacterized Gold Complexes and ^{31}P NMR for Previously Characterized Complexes

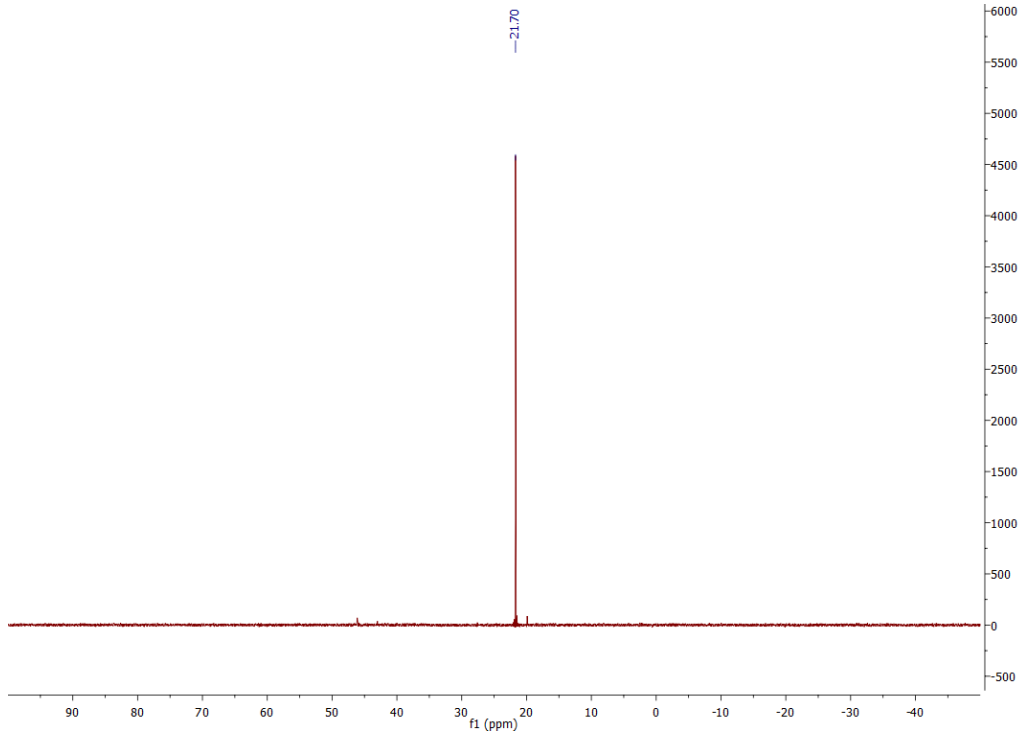
(*S*)-BINAP(AuCl)$_2$:



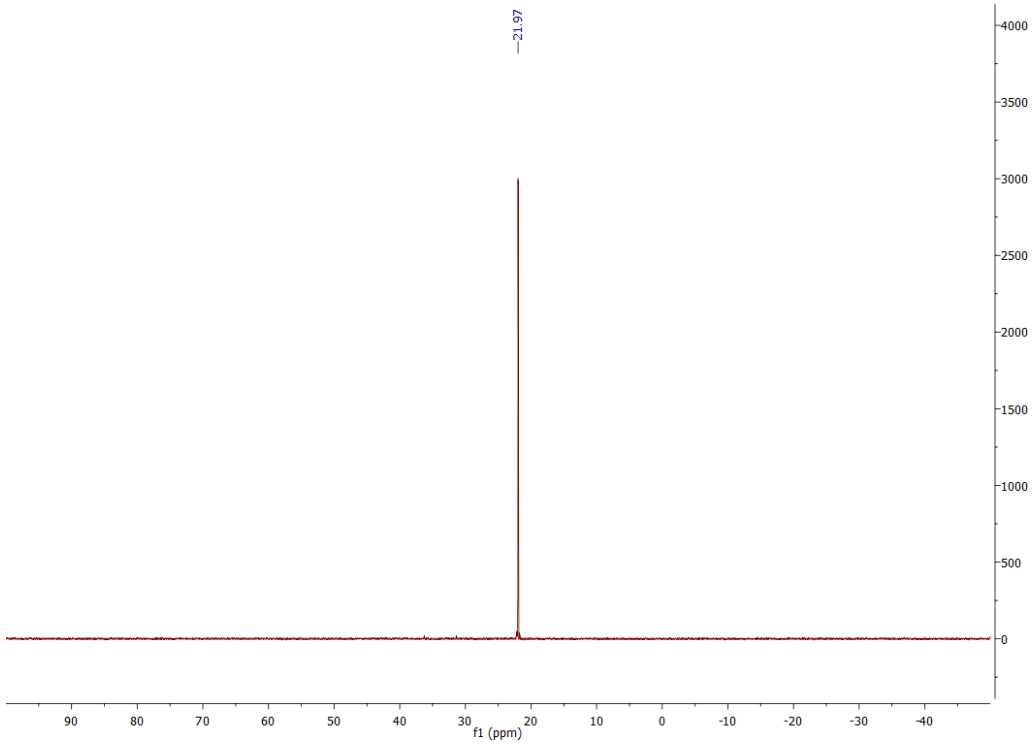
(*R*)-BINAP(AuCl)$_2$:



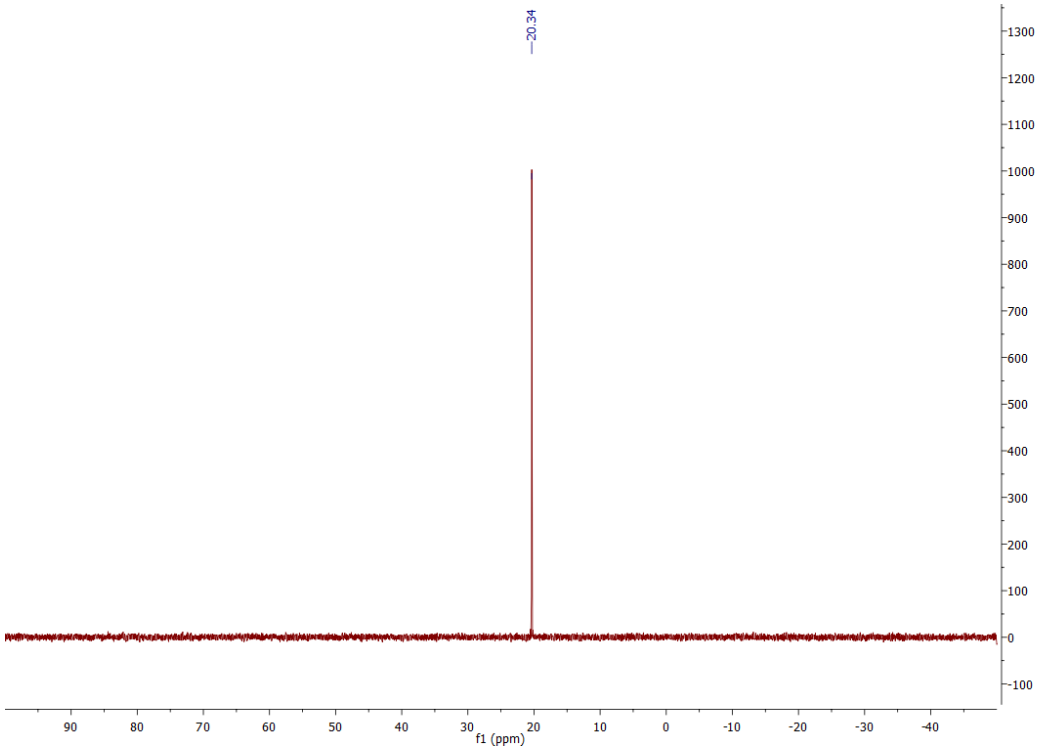
(*R*)-Tol-BINAP(AuCl)$_2$:



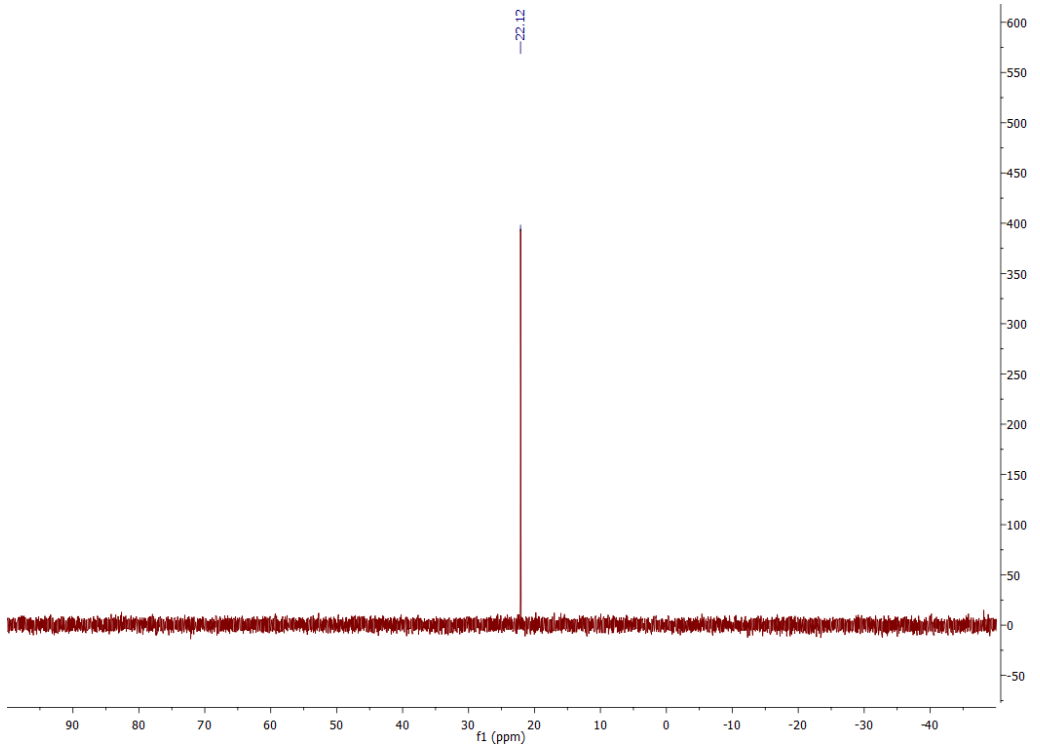
(*S*)-Xyl-BINAP(AuCl)$_2$:



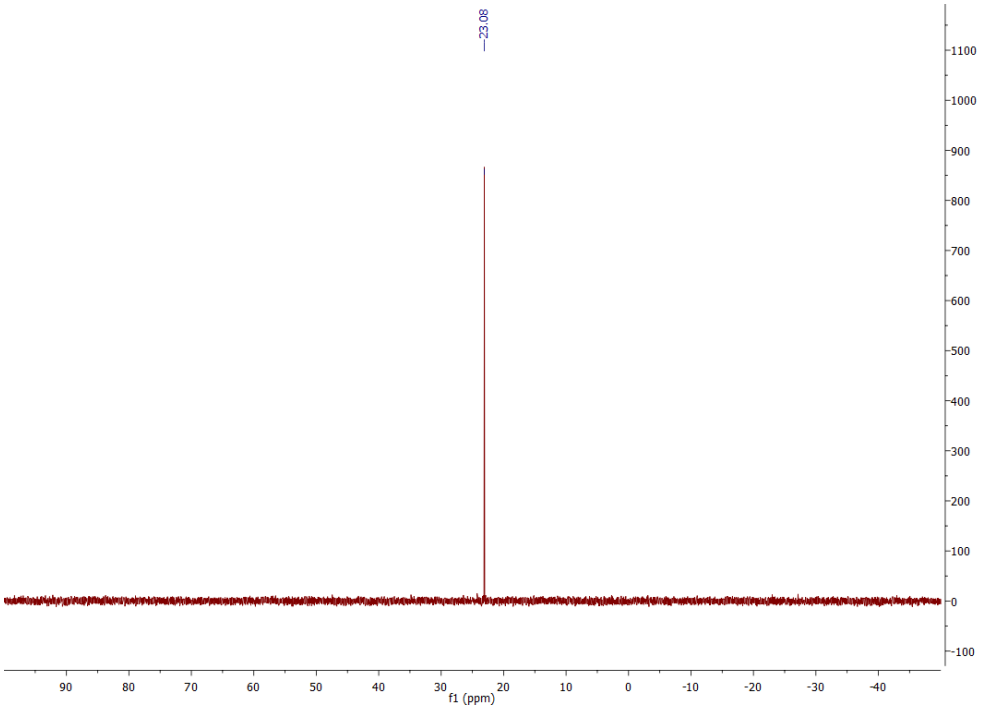
(*R*)-H_8-BINAP$(AuCl)_2$:



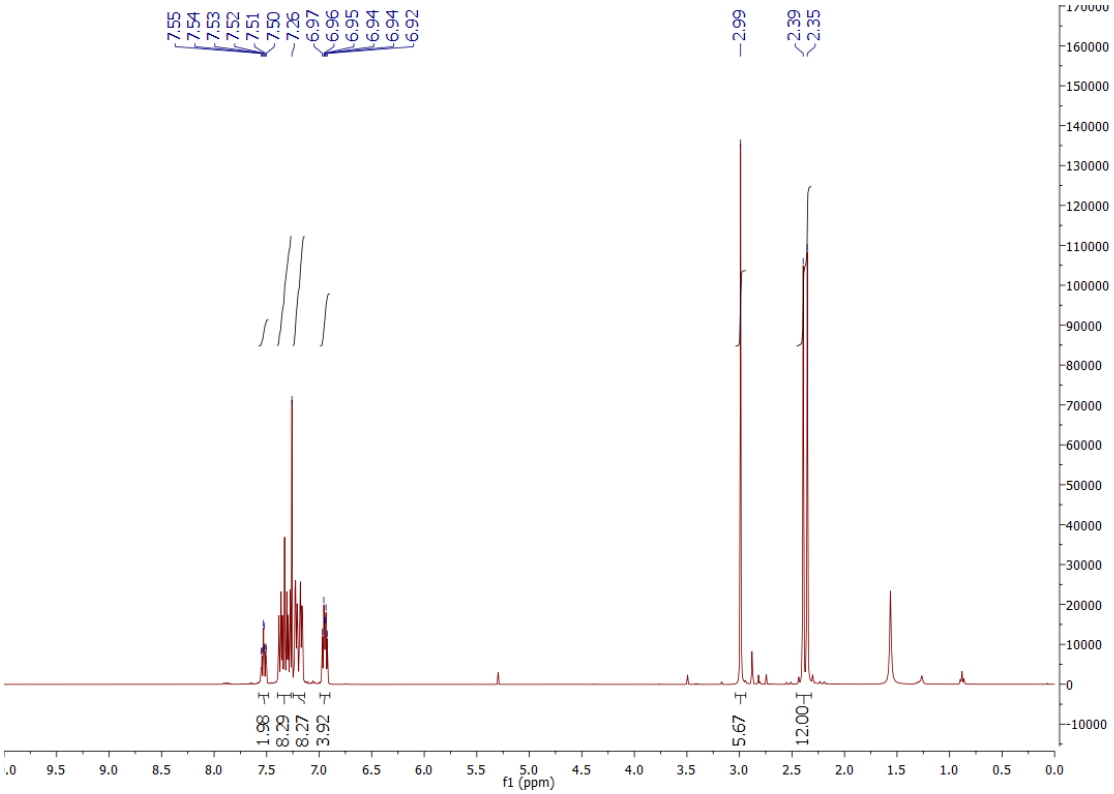
(*R*)-SYNPHOS$(AuCl)_2$:

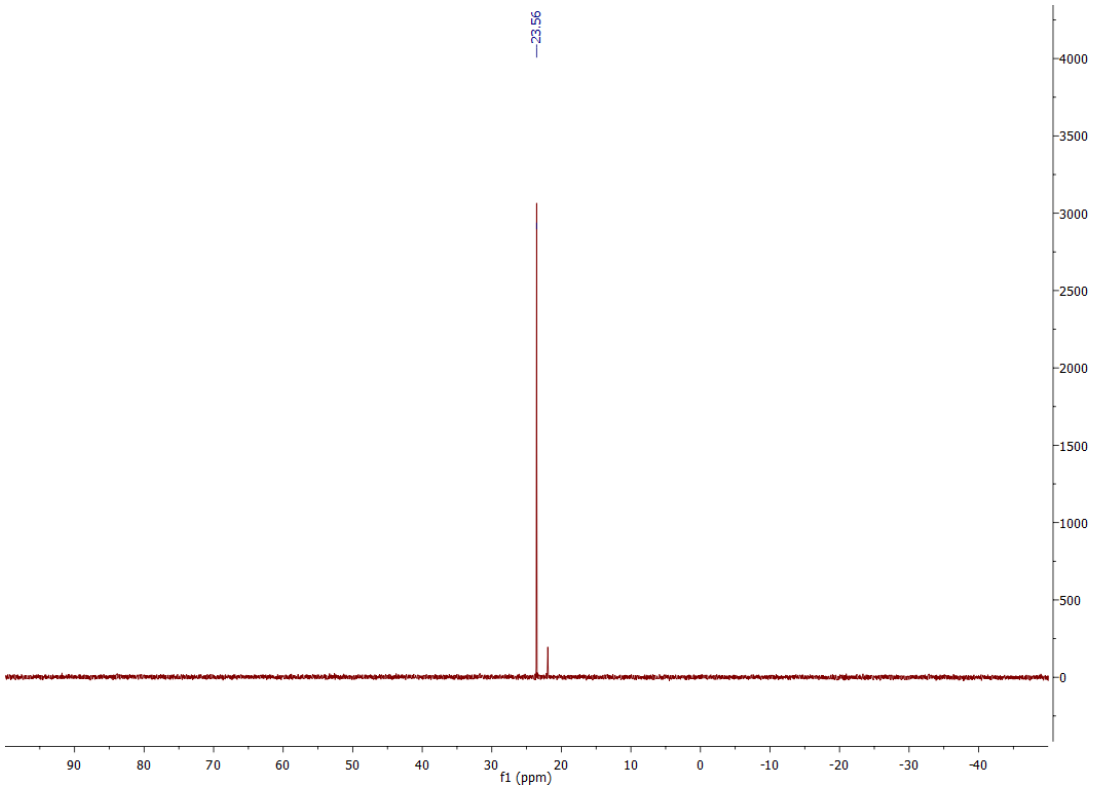


(*R*)-MeO-BIPHEP(AuCl)$_2$:

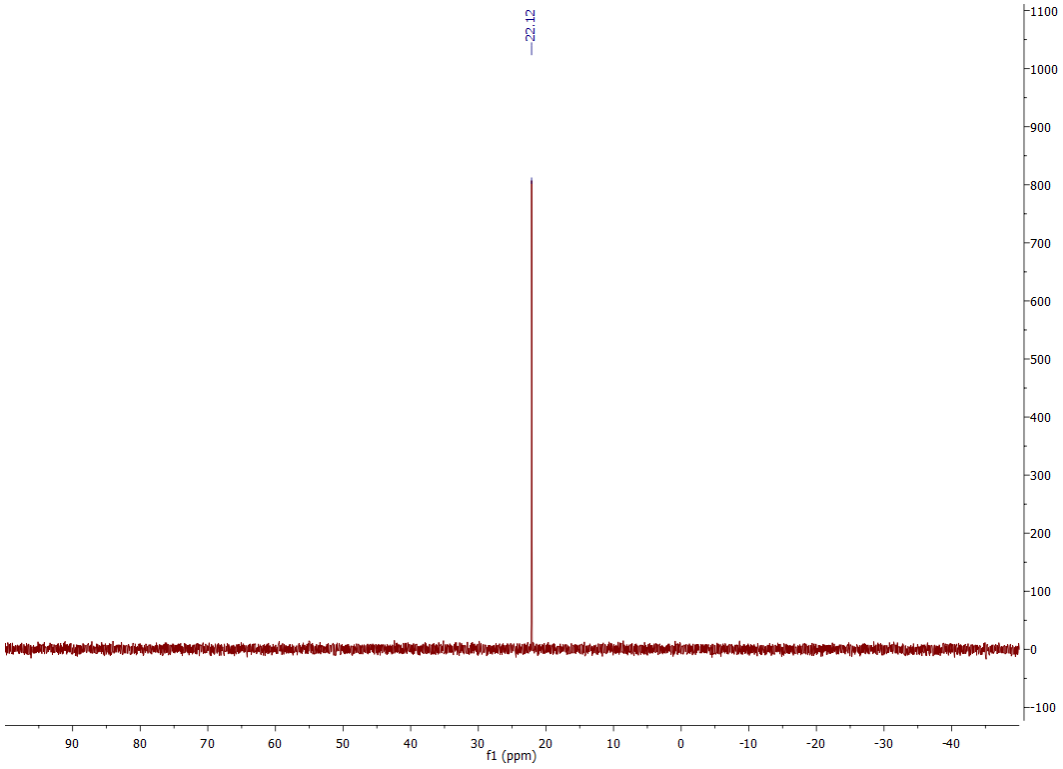


(*R*)-Tol-MeO-BIPHEP(AuCl)$_2$:

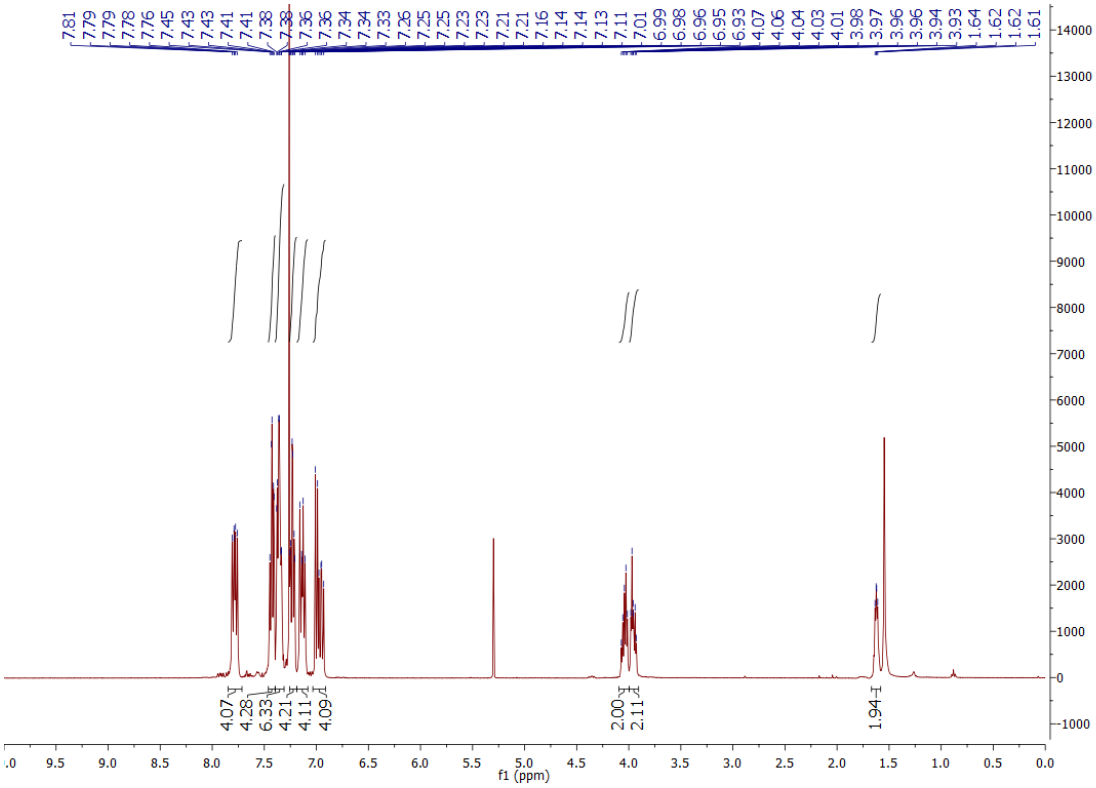


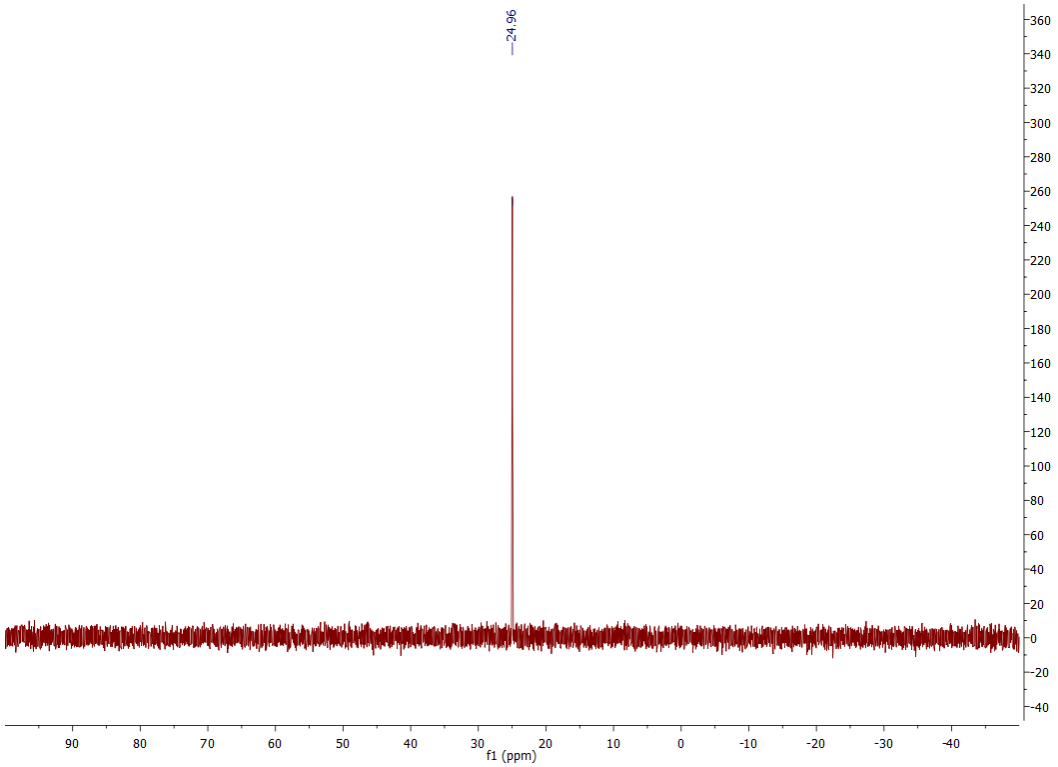


(*R*)-Xyl-MeO-BIPHEP(AuCl)$_2$:

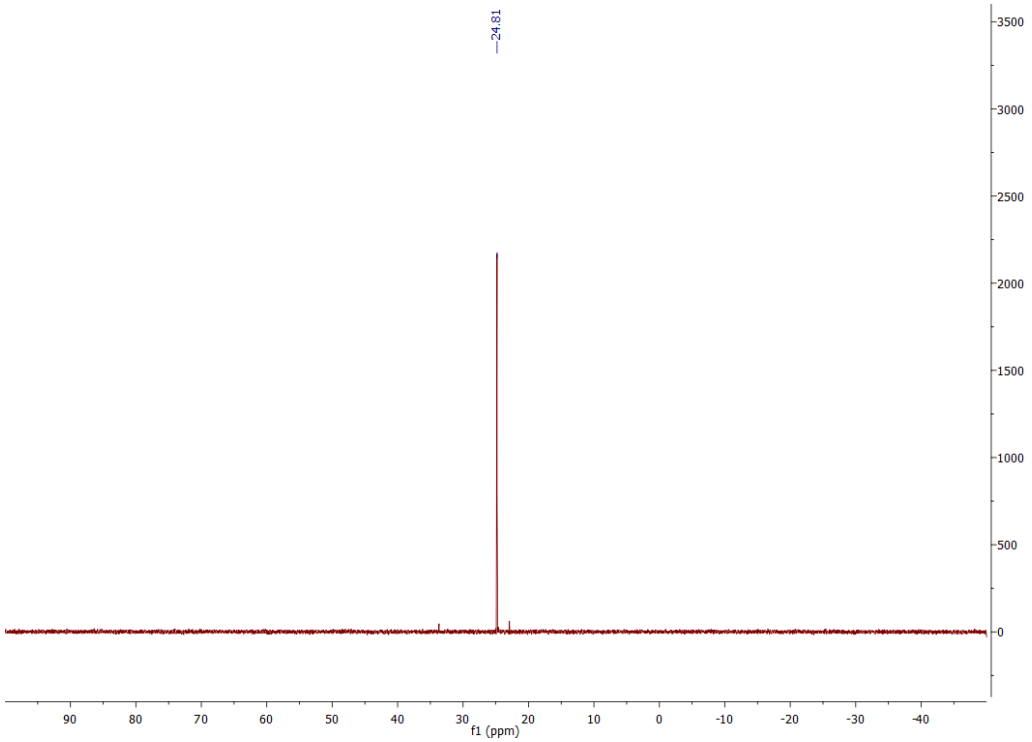


(*R*)-C_3-TUNEPHOS$(AuCl)_2$:

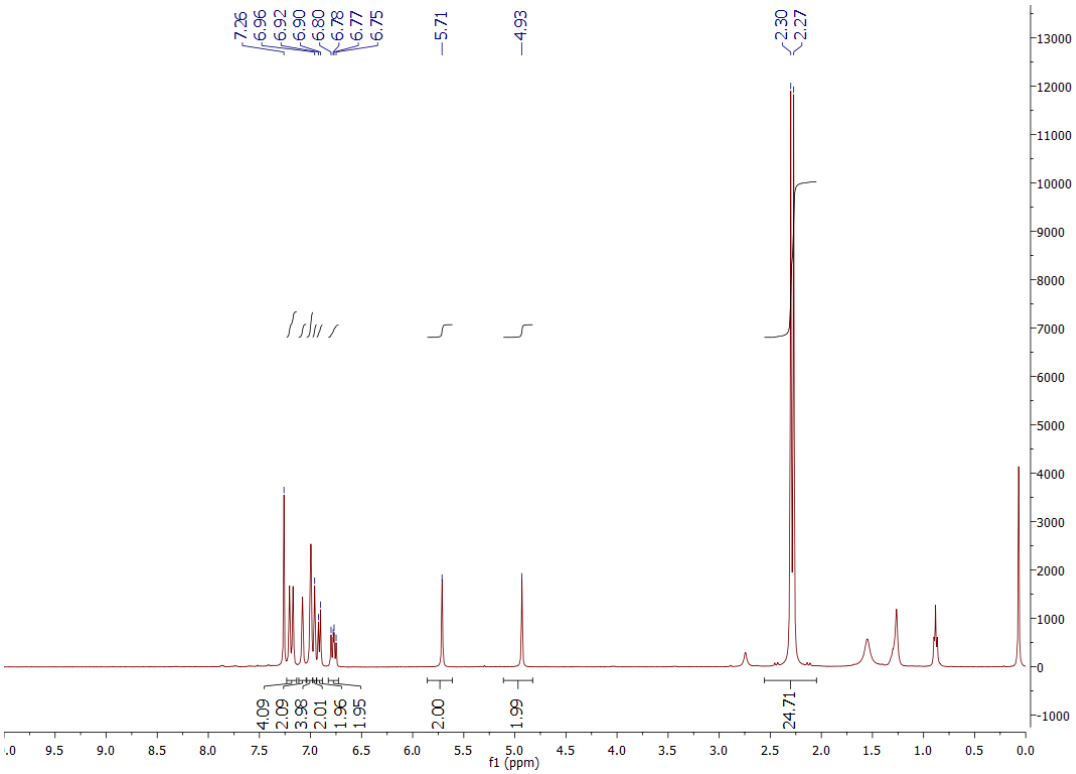


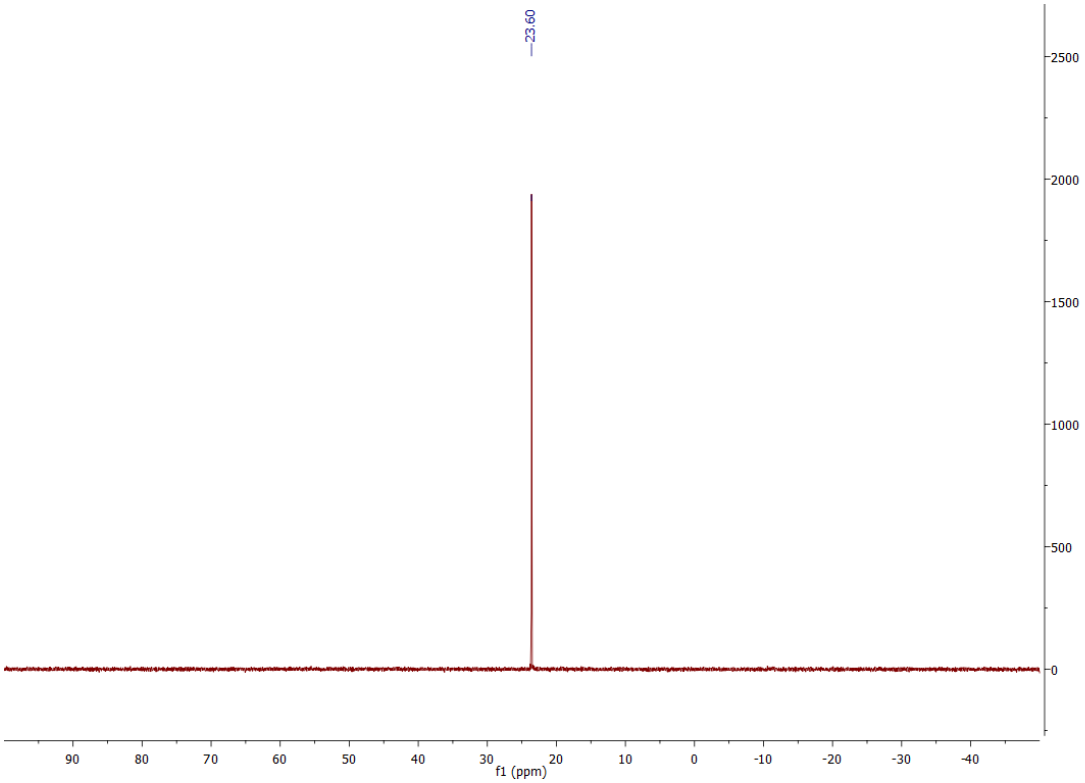


(*R*)-SEGPHOS(AuCl)$_2$:

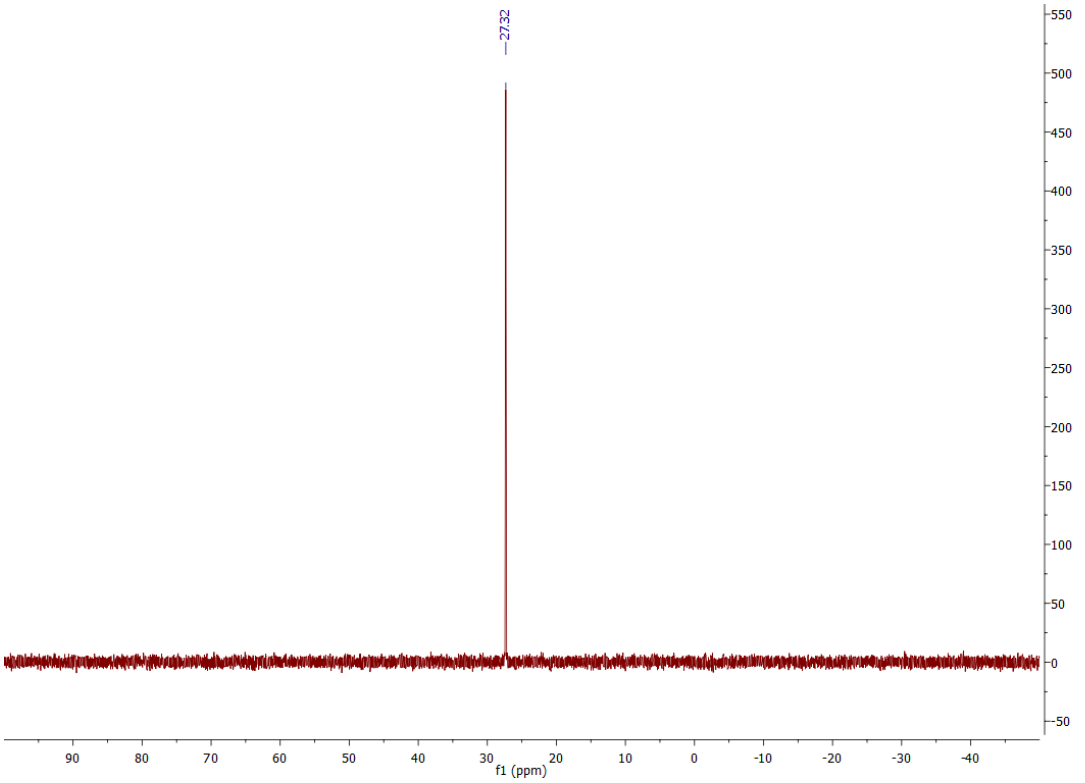


(*R*)-DM-SEGPHOS(AuCl)$_2$:

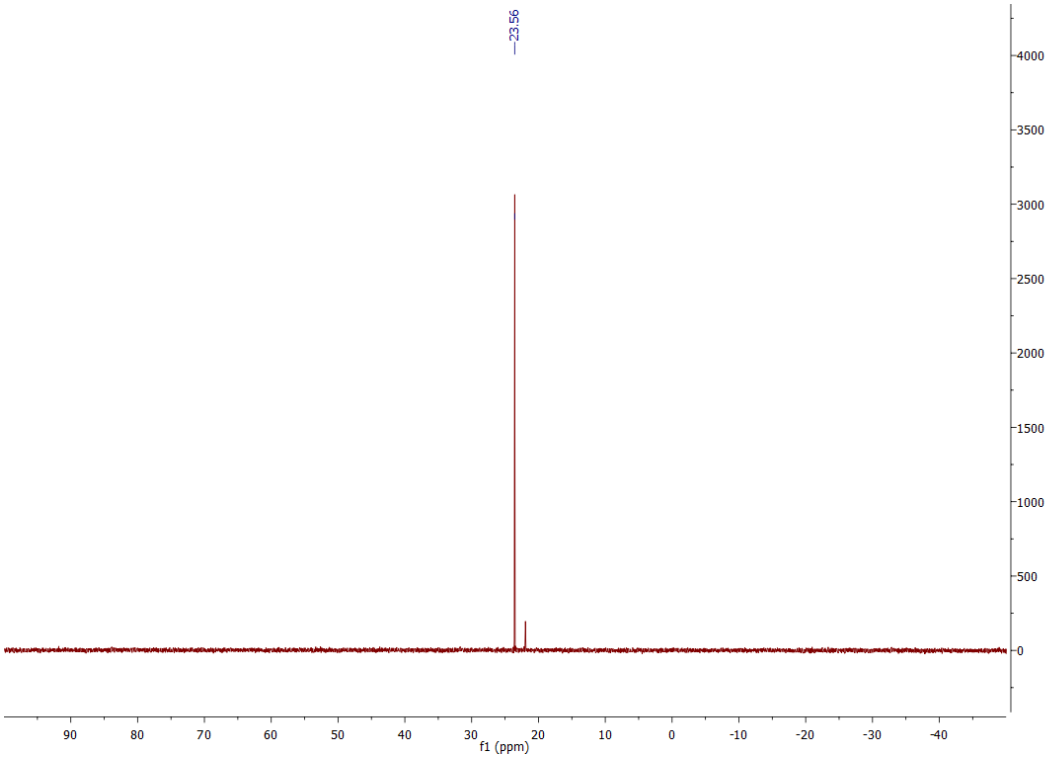




(*R*)-DTBM-SEGPHOS(AuCl)$_2$:

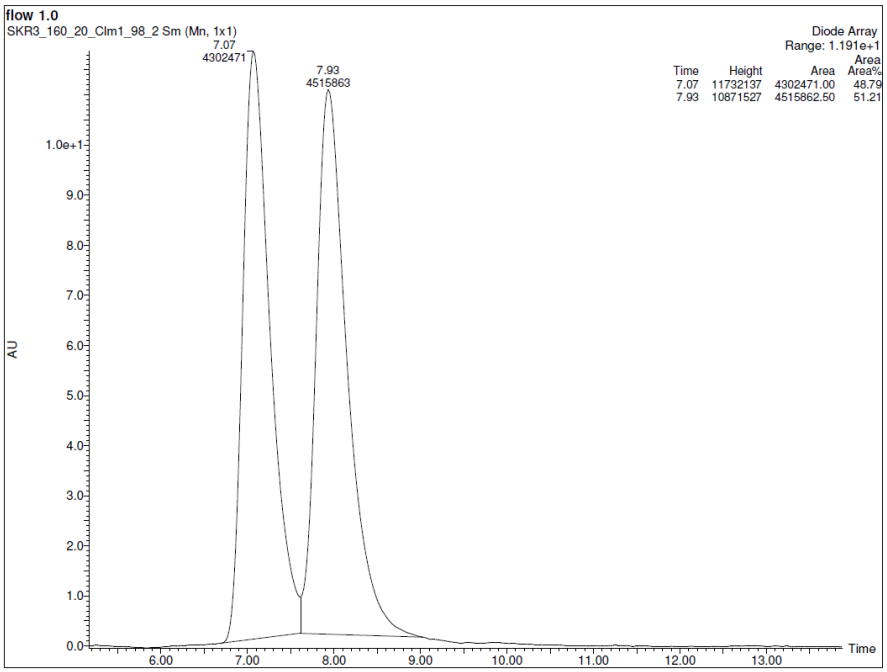


(*R*)-DIFLUORPHOS(AuCl)$_2$:

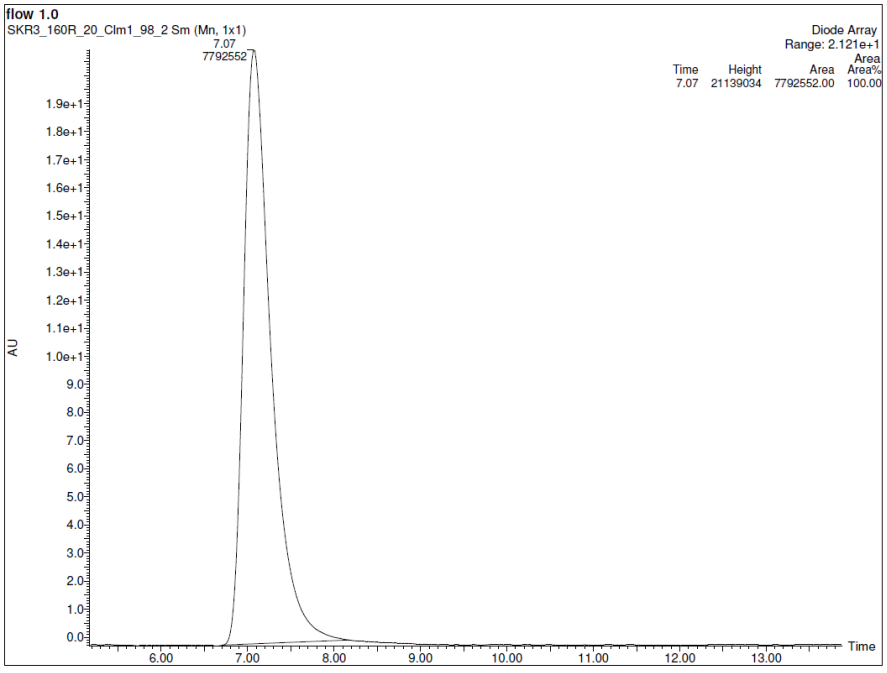


5. HPLC Traces of Biaryl Product (2) isolated from the Aryl-Aryl Coupling Reactions in Table 2

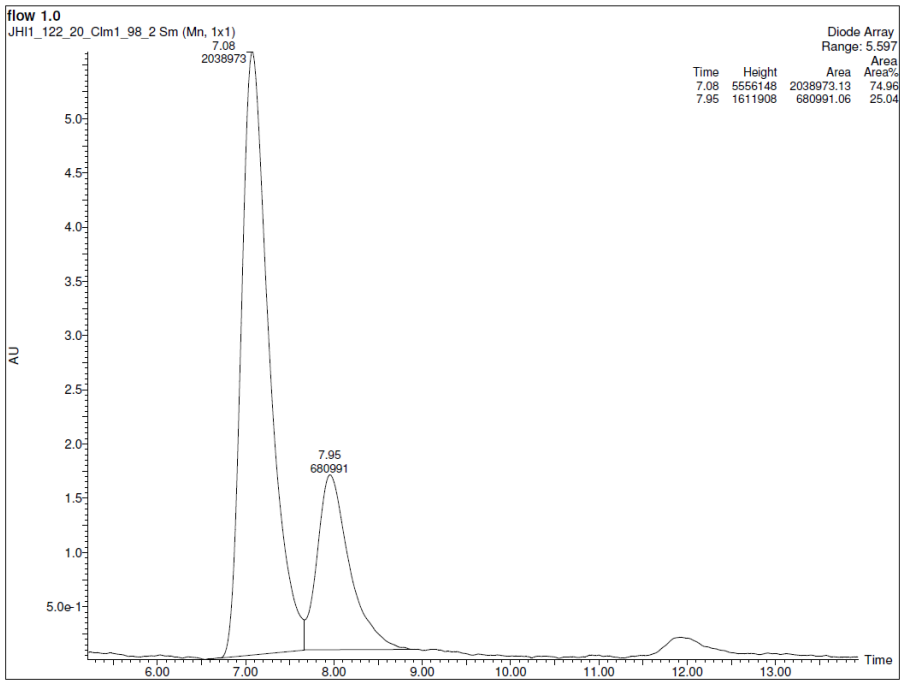
Racemic Sample:



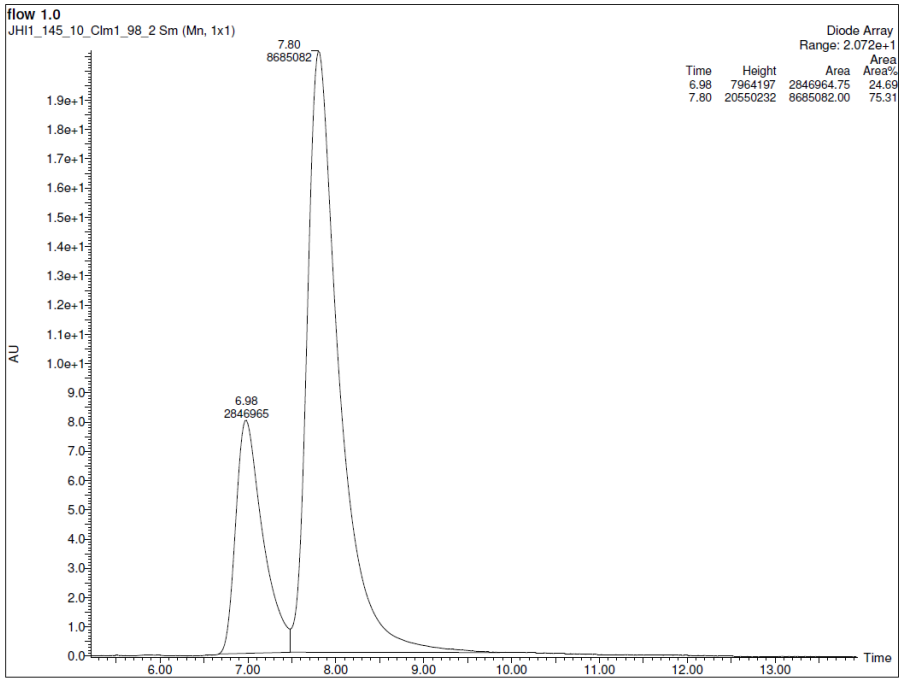
(*R*)-**2** purchased from Sigma-Aldrich:



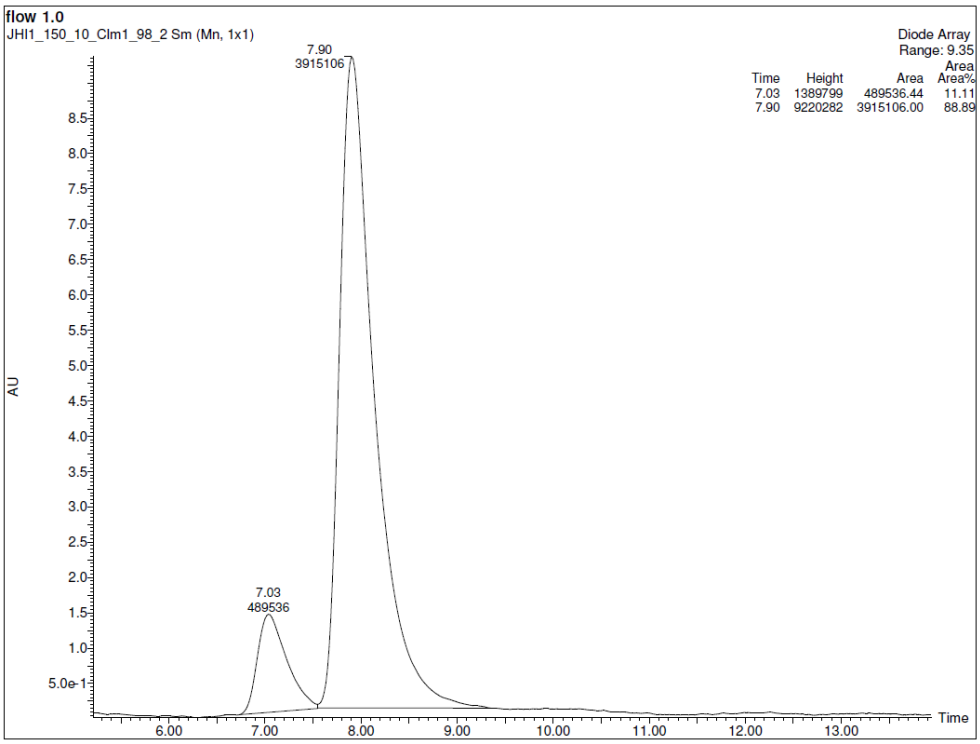
From (*S*)-BINAP(AuCl)$_2$:



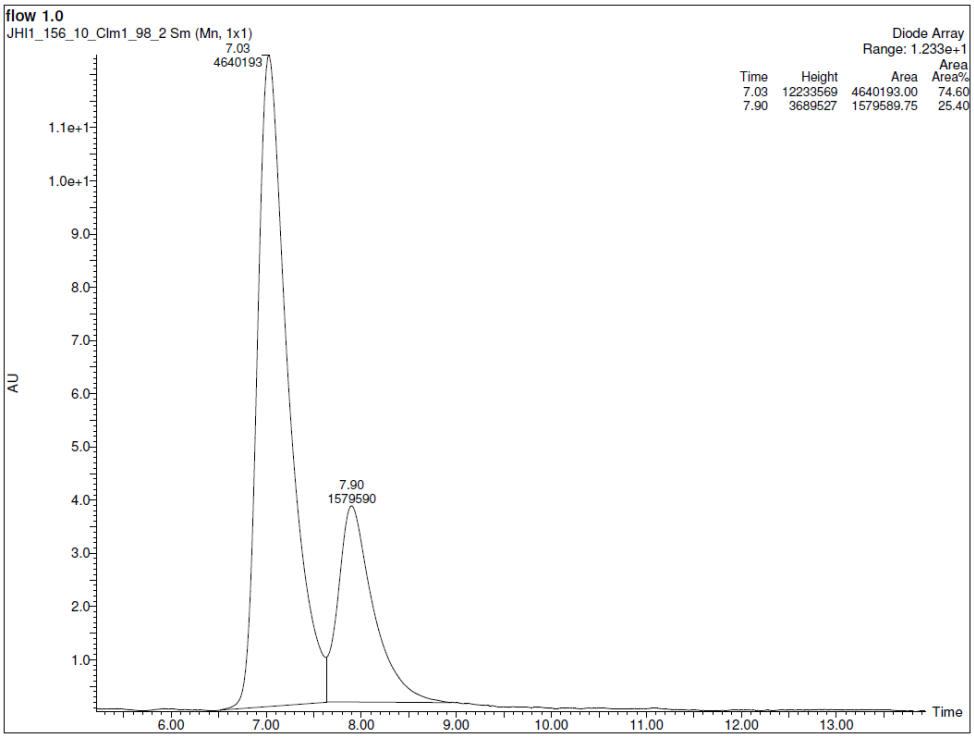
From (*R*)-BINAP(AuCl)$_2$:



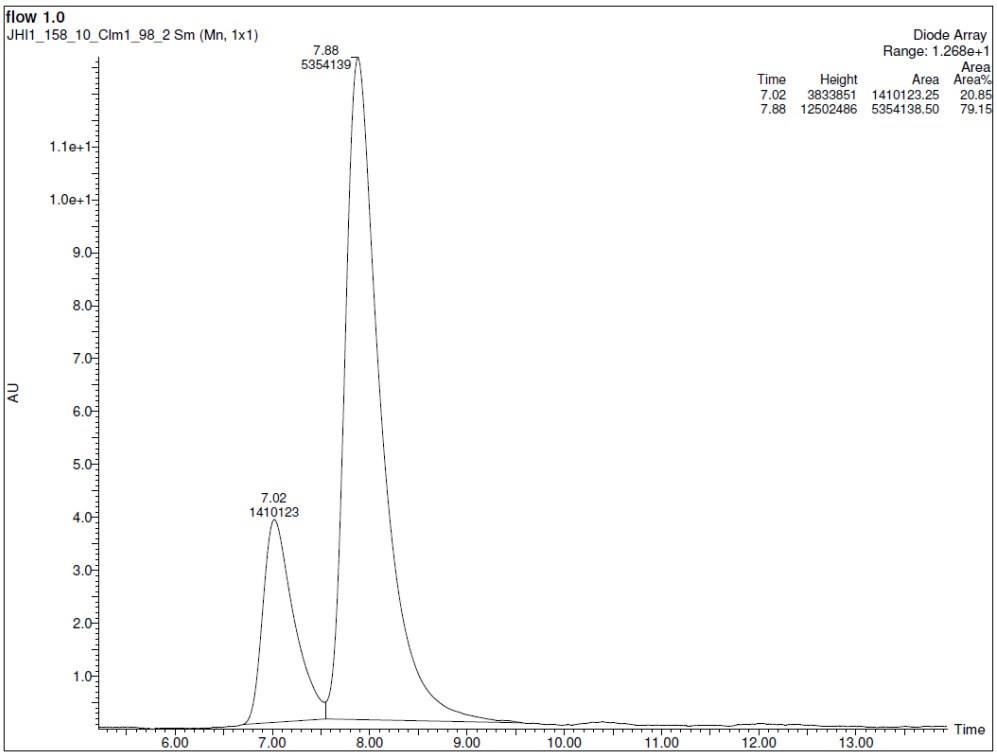
From (*R*)-Tol-BINAP(AuCl)$_2$:



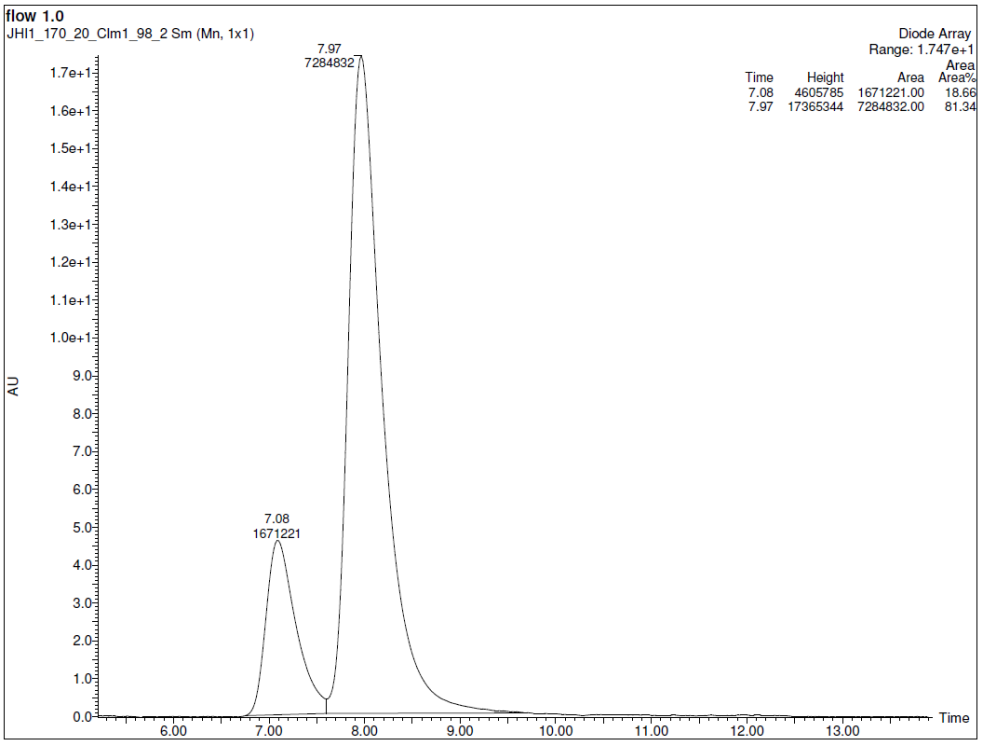
From (*S*)-Xyl-BINAP(AuCl)$_2$:



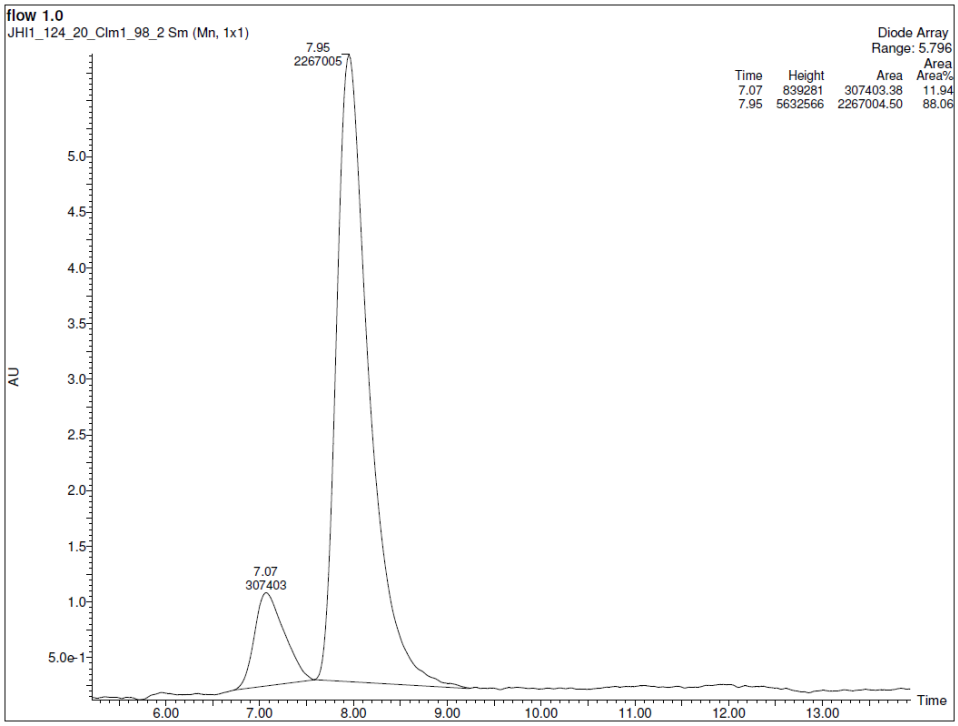
From (*R*)-H_8-BINAP$(AuCl)_2$:



From (*R*)-SYNPHOS$(AuCl)_2$:



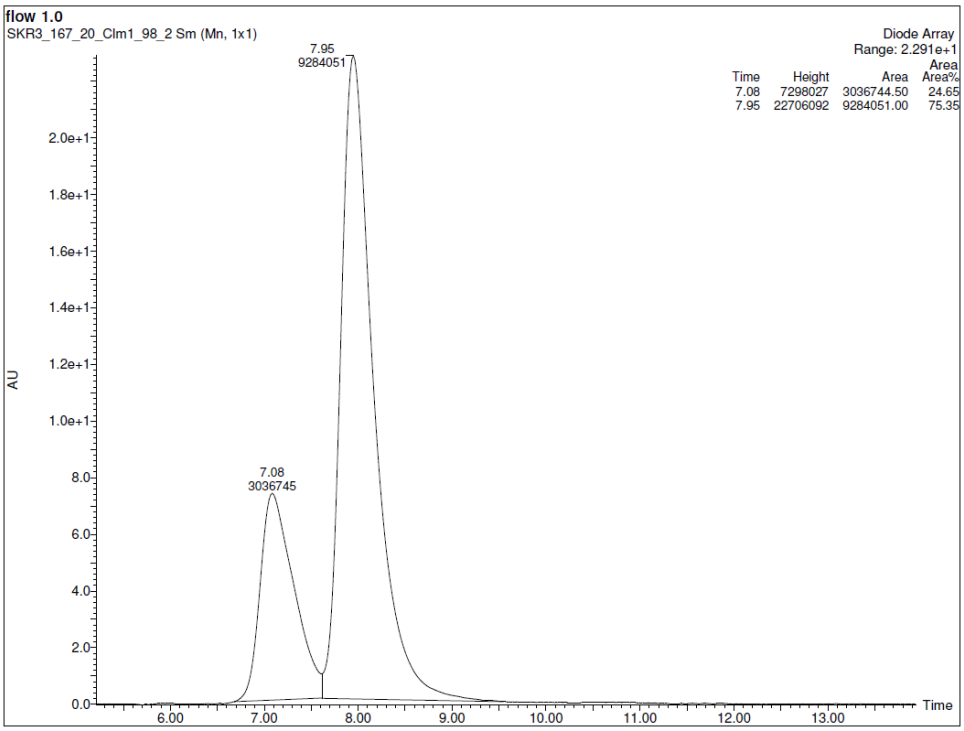
From (*R*)-MeO-BIPHEP(AuCl)$_2$:



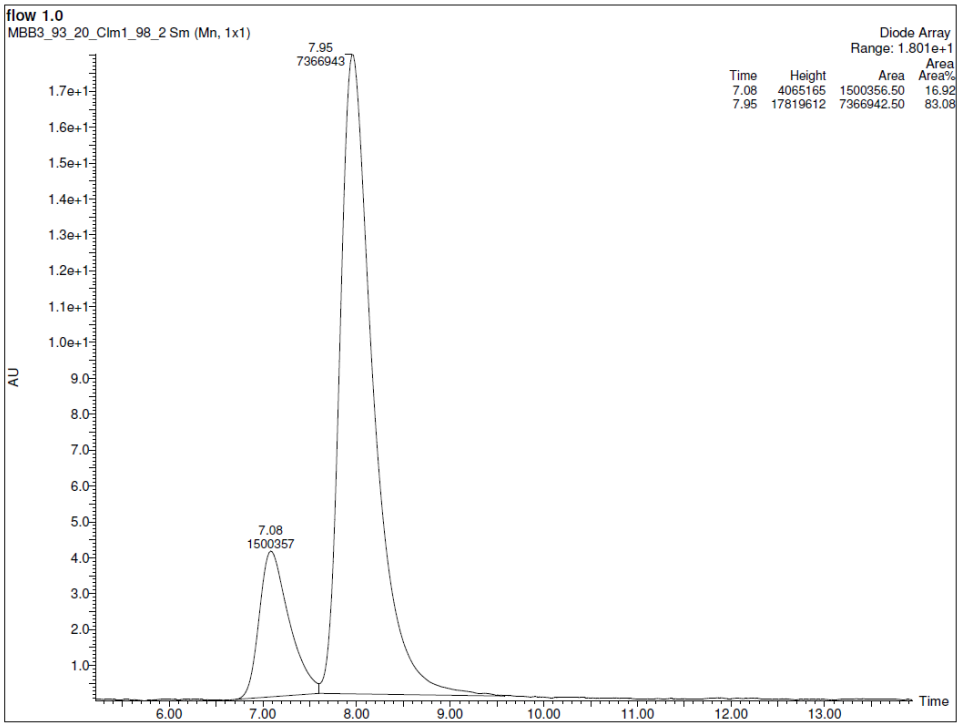
From (*R*)-Tol-MeO-BIPHEP(AuCl)$_2$:

Not Determined

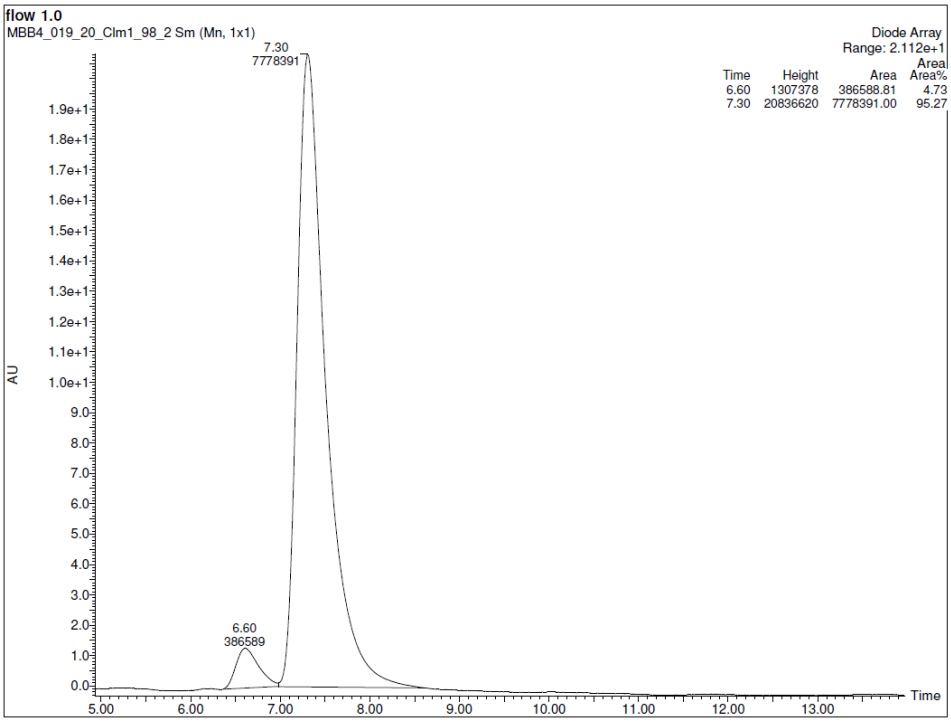
From (*R*)-Xyl-MeO-BIPHEP(AuCl)$_2$:



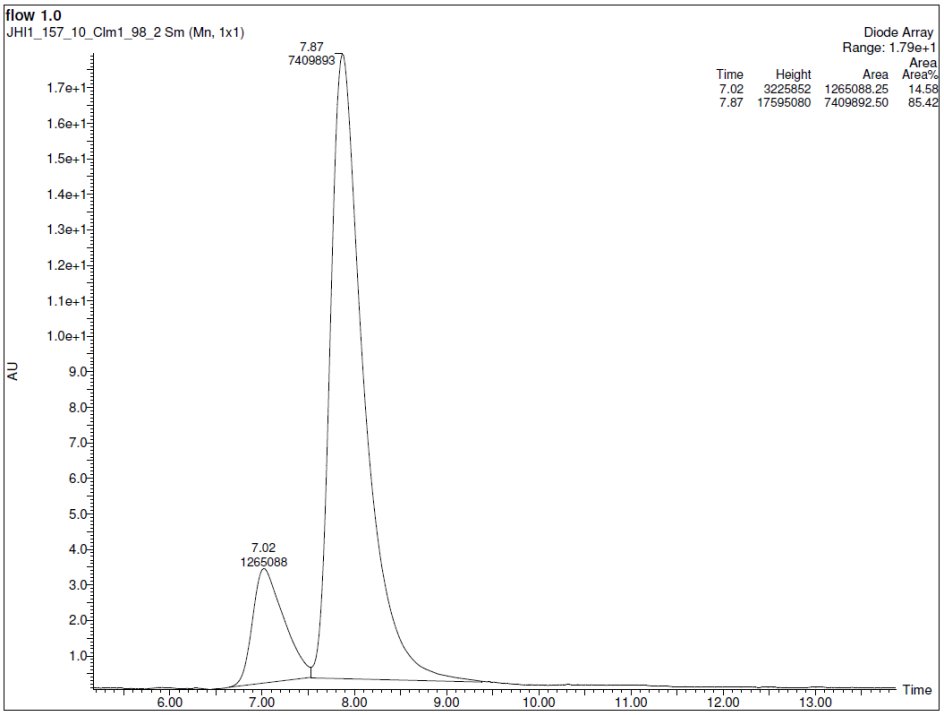
From (*R*)-C$_3$-TUNEPHOS(AuCl)$_2$:



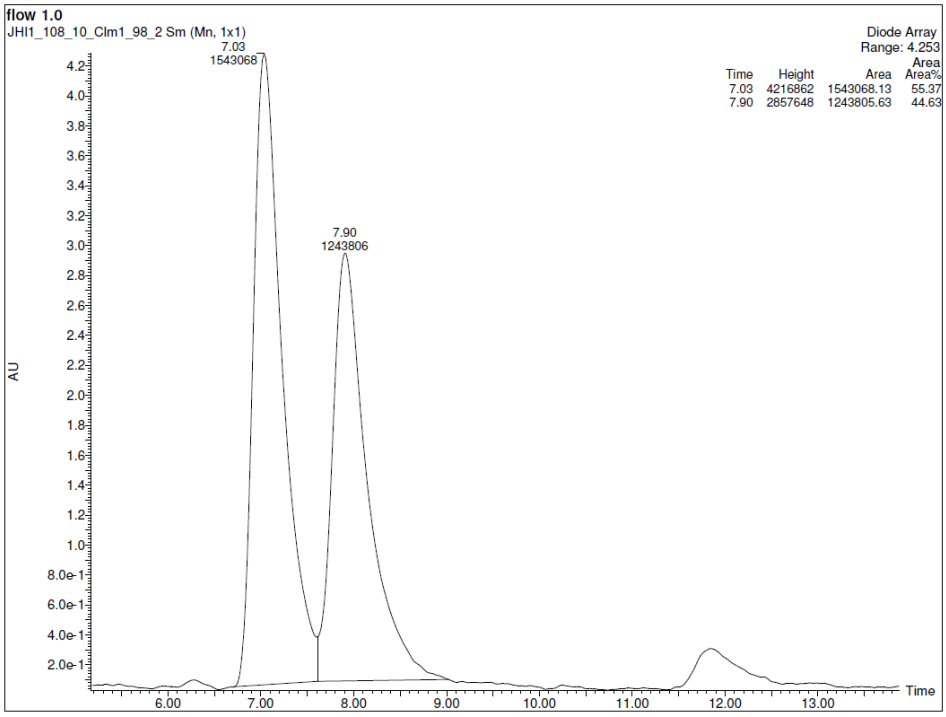
From (*R*)-SEGPHOS(AuCl)$_2$:



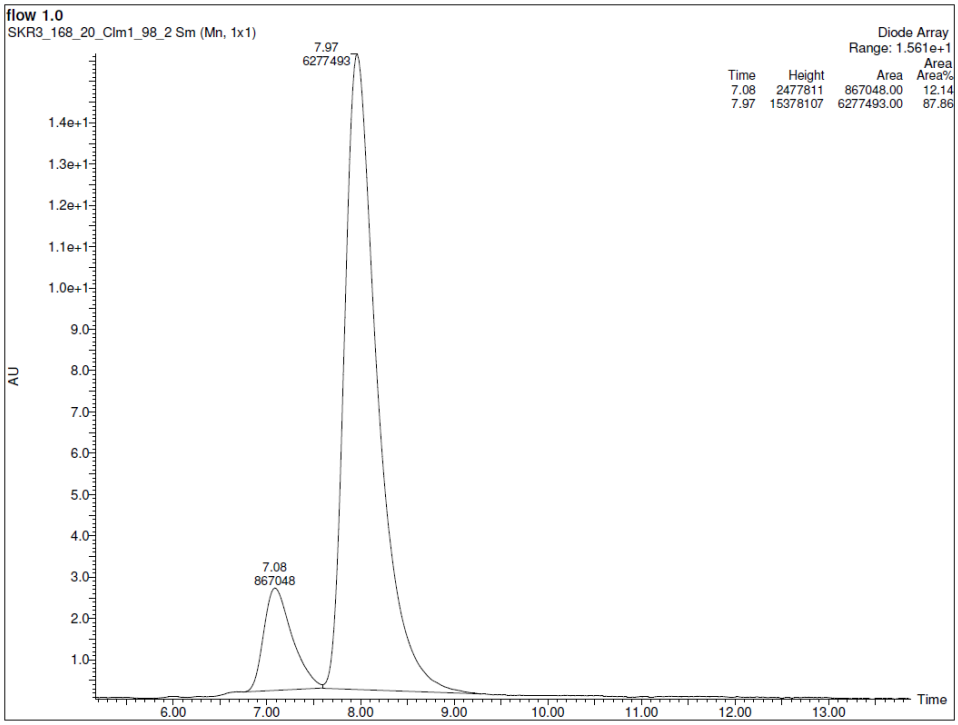
From (*R*)-DM-SEGPHOS(AuCl)$_2$:



From (*R*)-DTBM-SEGPHOS(AuCl)$_2$:

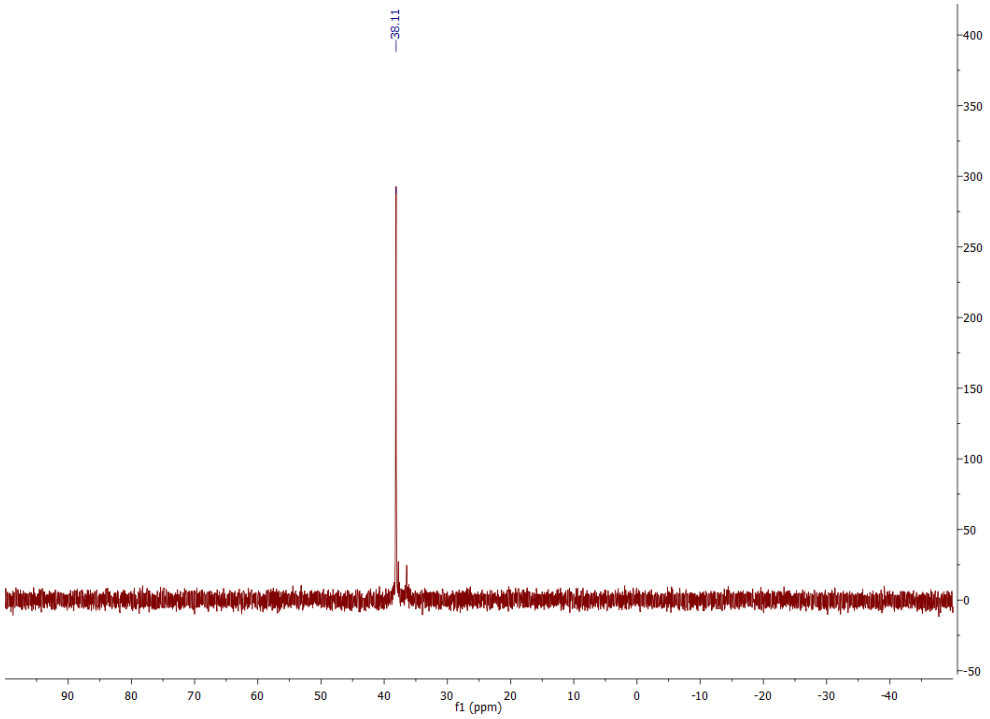


From (*R*)-DIFLUORPHOS(AuCl)$_2$:

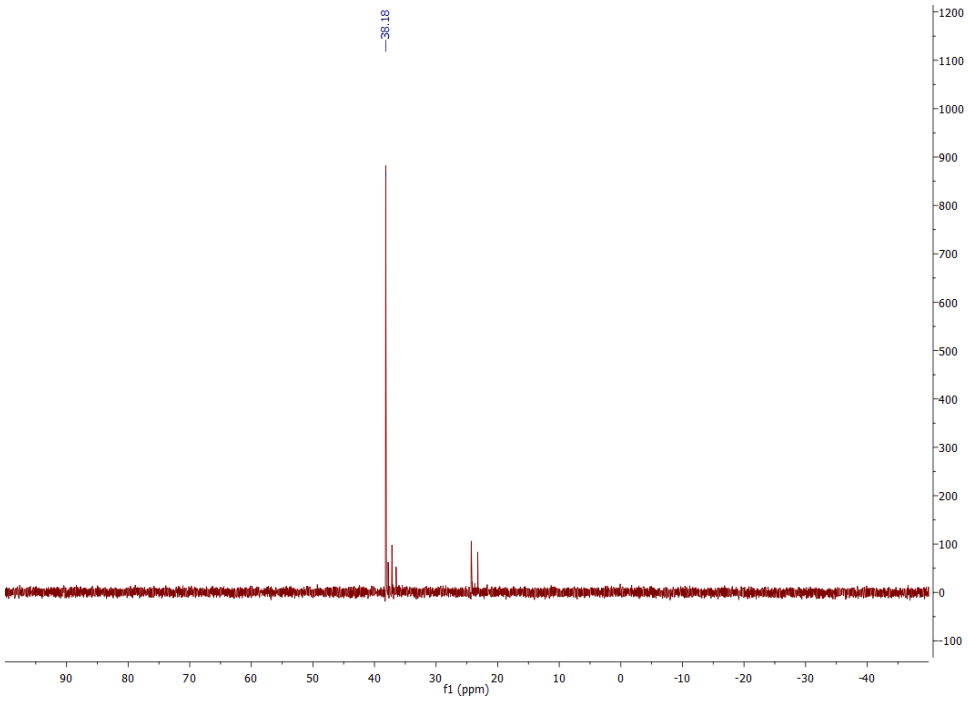


6. ^{31}P NMR Spectra of All Transmetalations

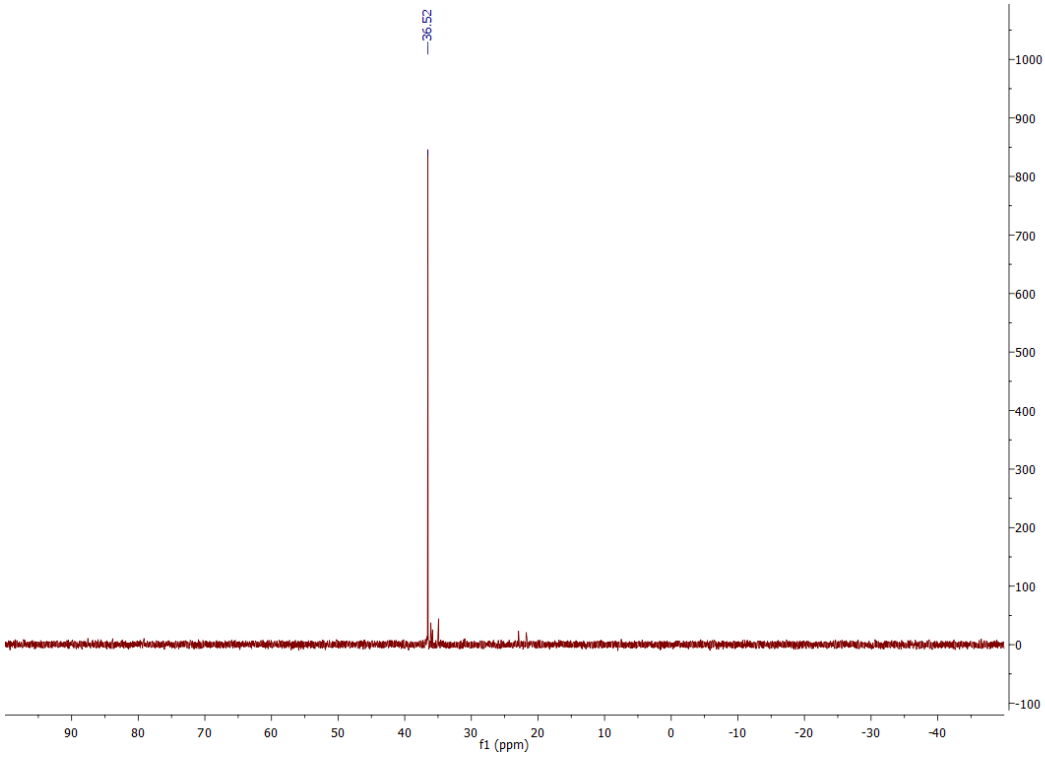
(*S*)-BINAP(AuAr)$_2$:



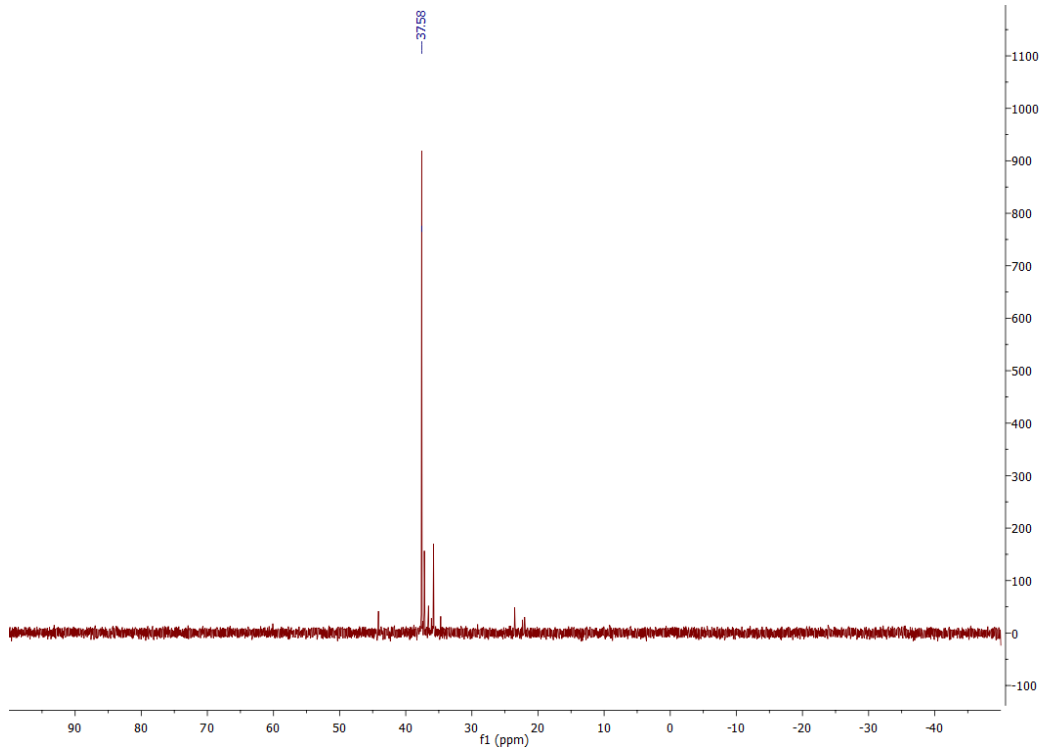
(*R*)-BINAP(AuAr)$_2$:



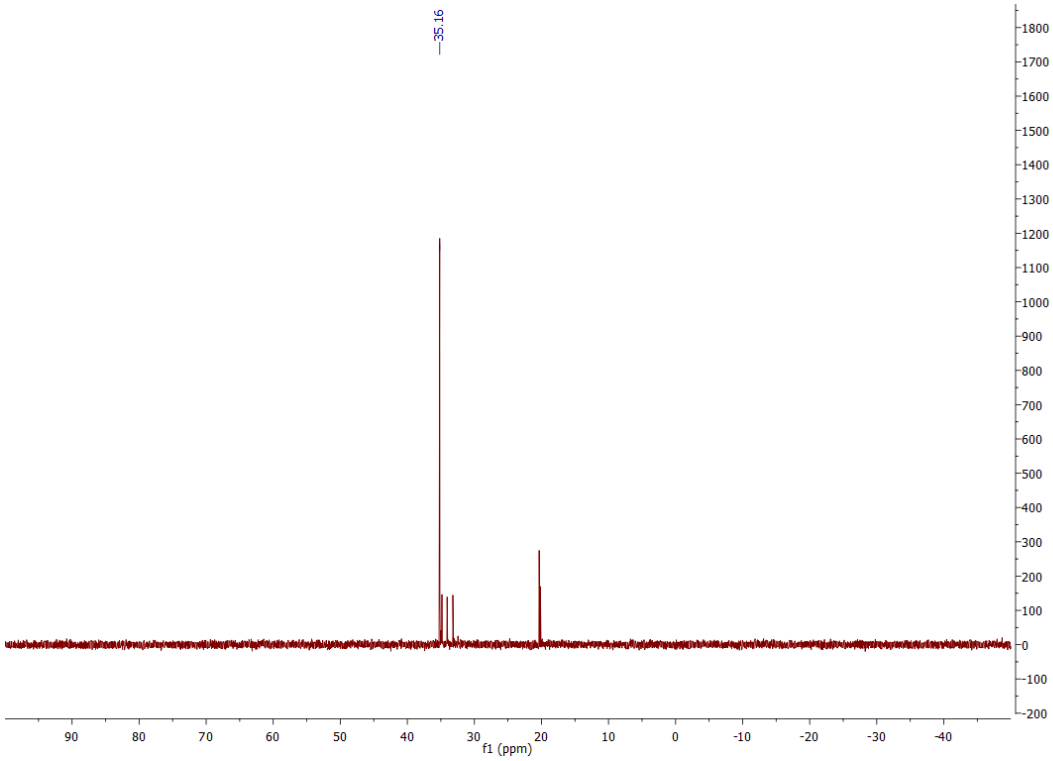
(*R*)-Tol-BINAP(AuAr)$_2$:



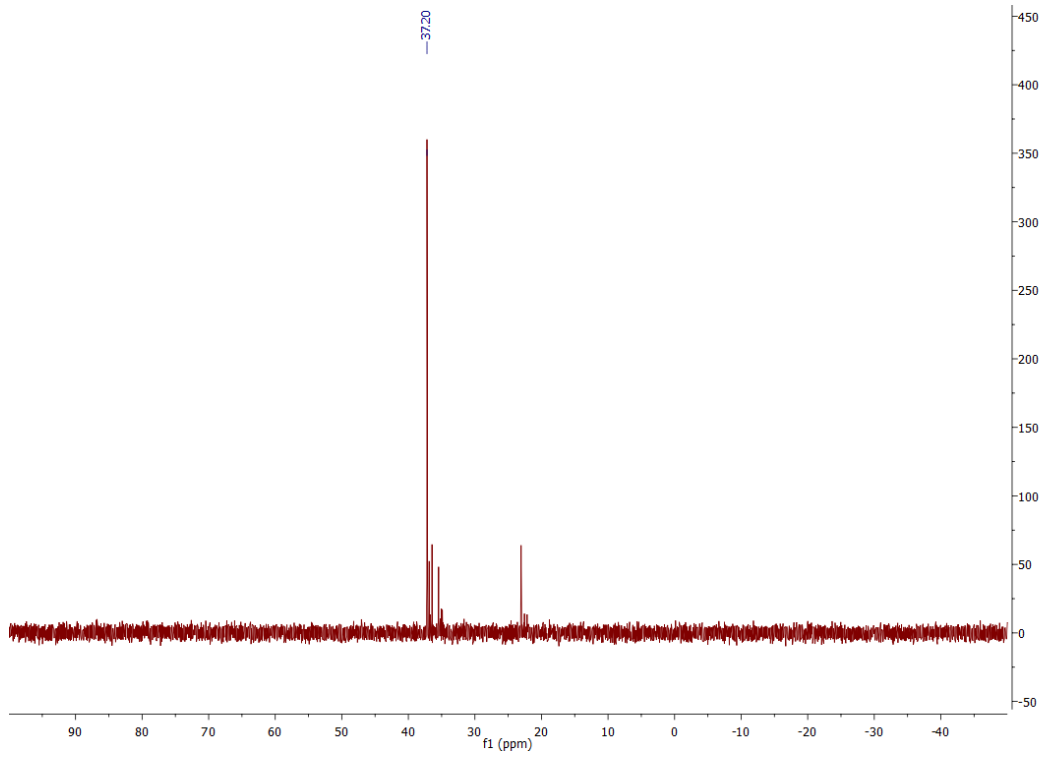
(*S*)-Xyl-BINAP(AuAr)$_2$:



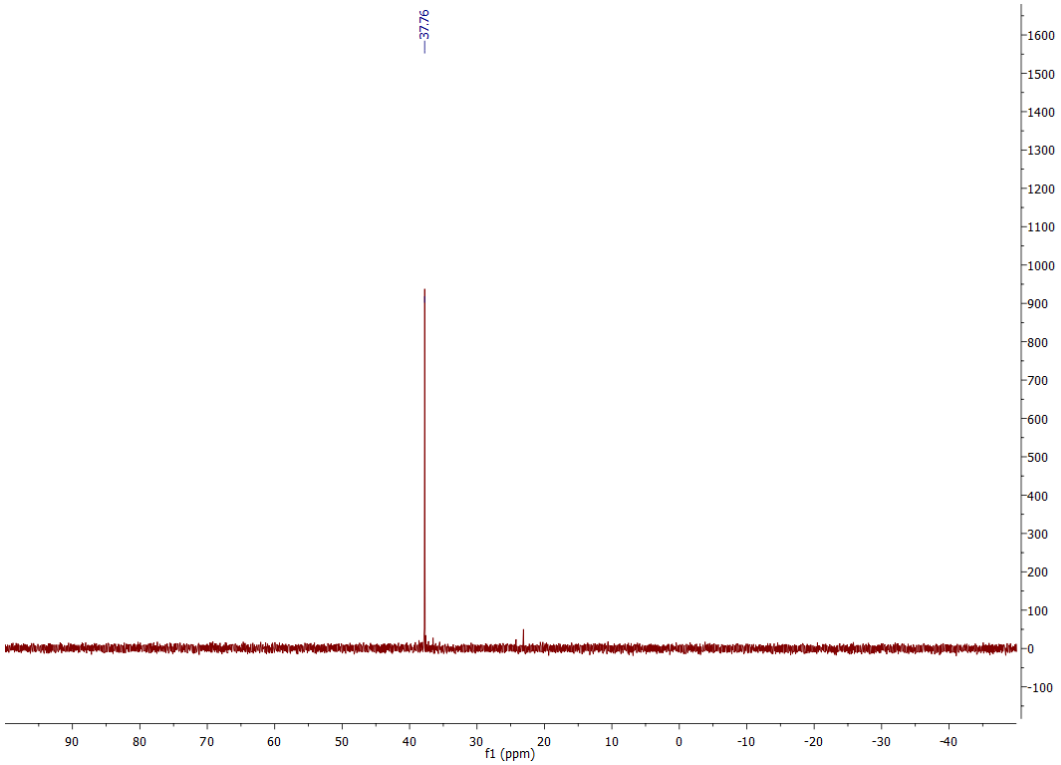
(*R*)-H_8-BINAP(AuAr)$_2$:



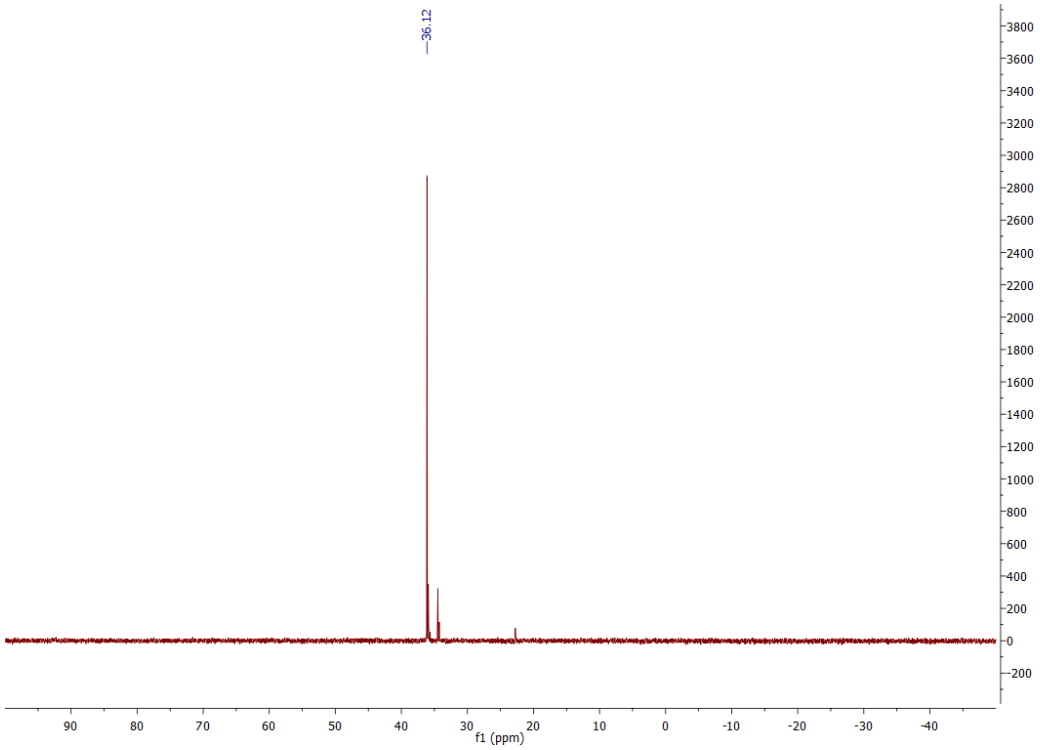
(*R*)-SYNPHOS(AuAr)$_2$:



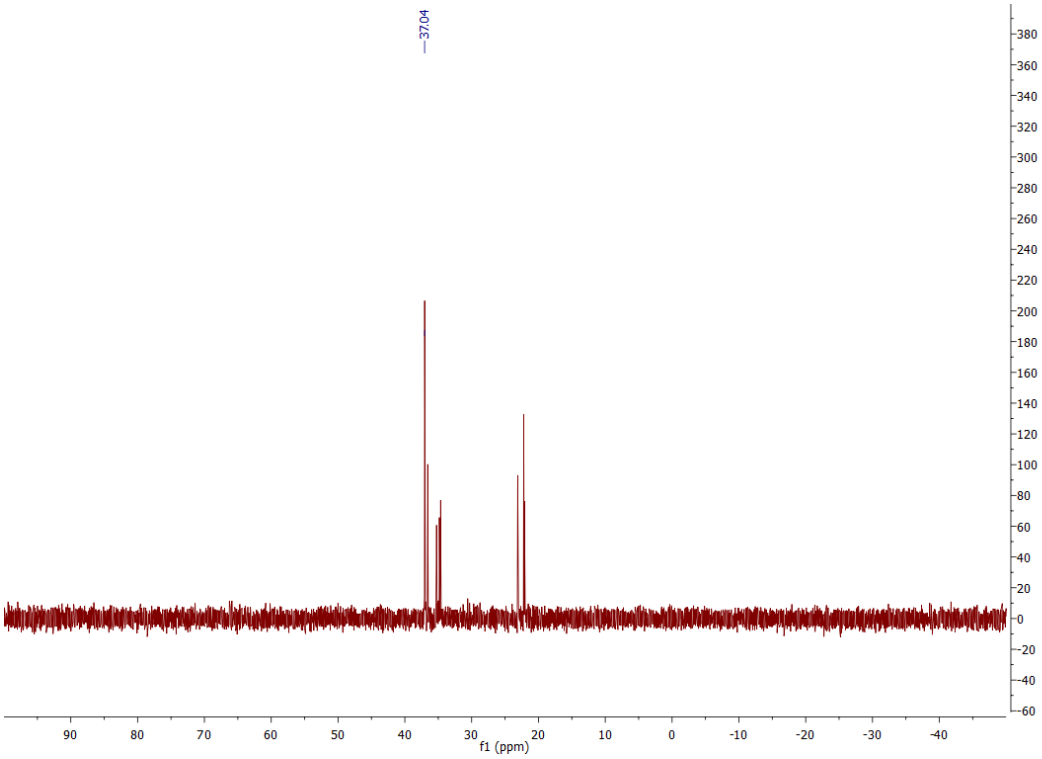
(*R*)-MeO-BIPHEP(AuAr)$_2$:



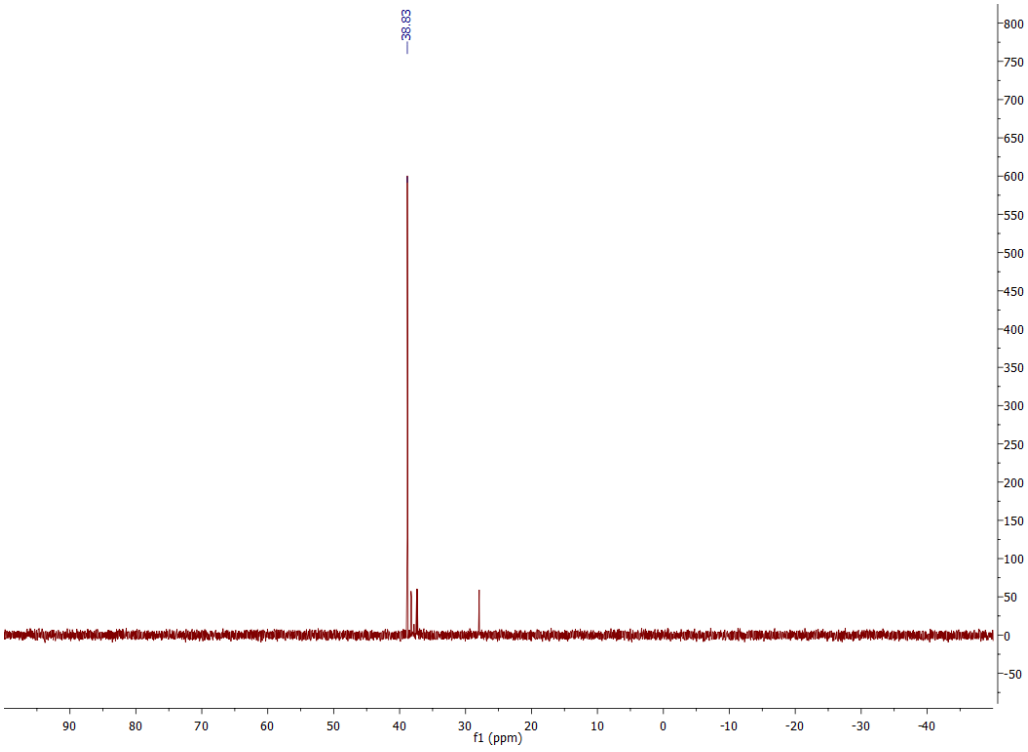
(*R*)-Tol-MeO-BIPHEP(AuAr)$_2$:



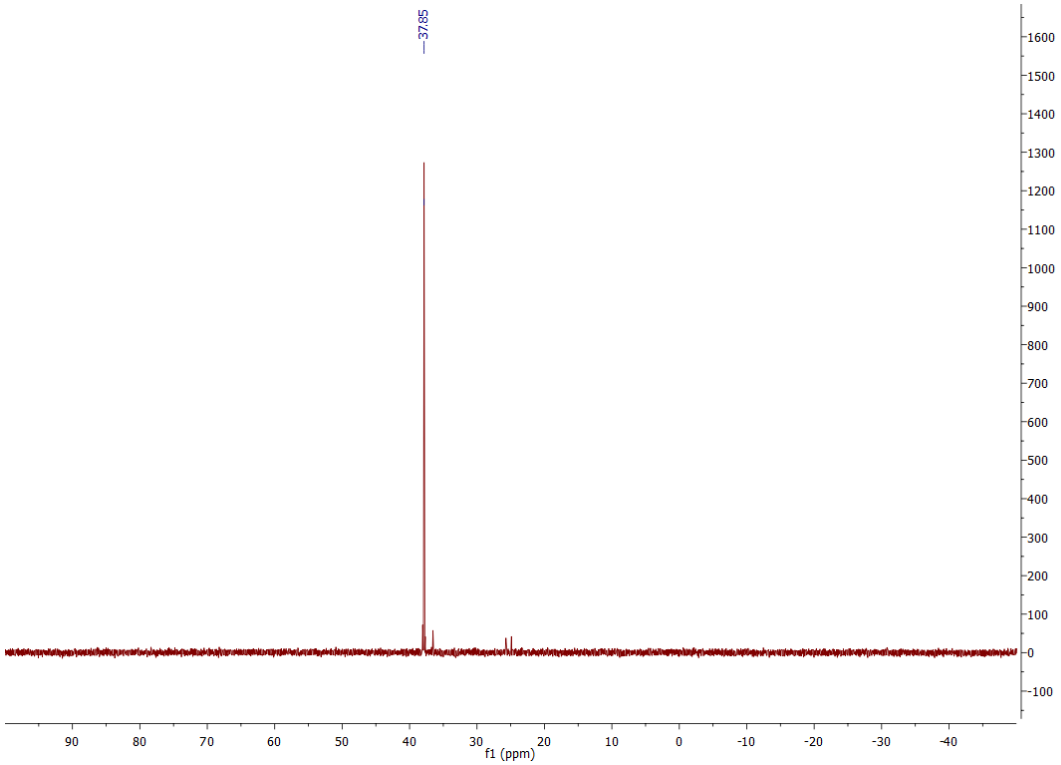
(*R*)-Xyl-MeO-BIPHEP(AuAr)$_2$:



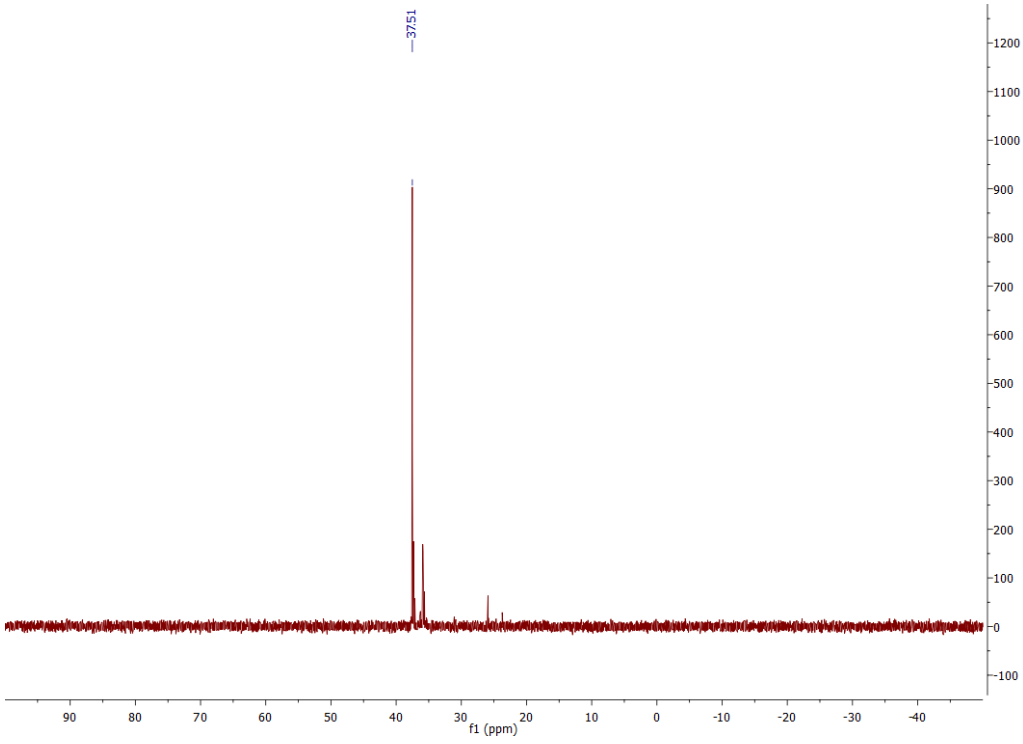
(*R*)-C$_3$-TUNEPHOS(AuAr)$_2$:



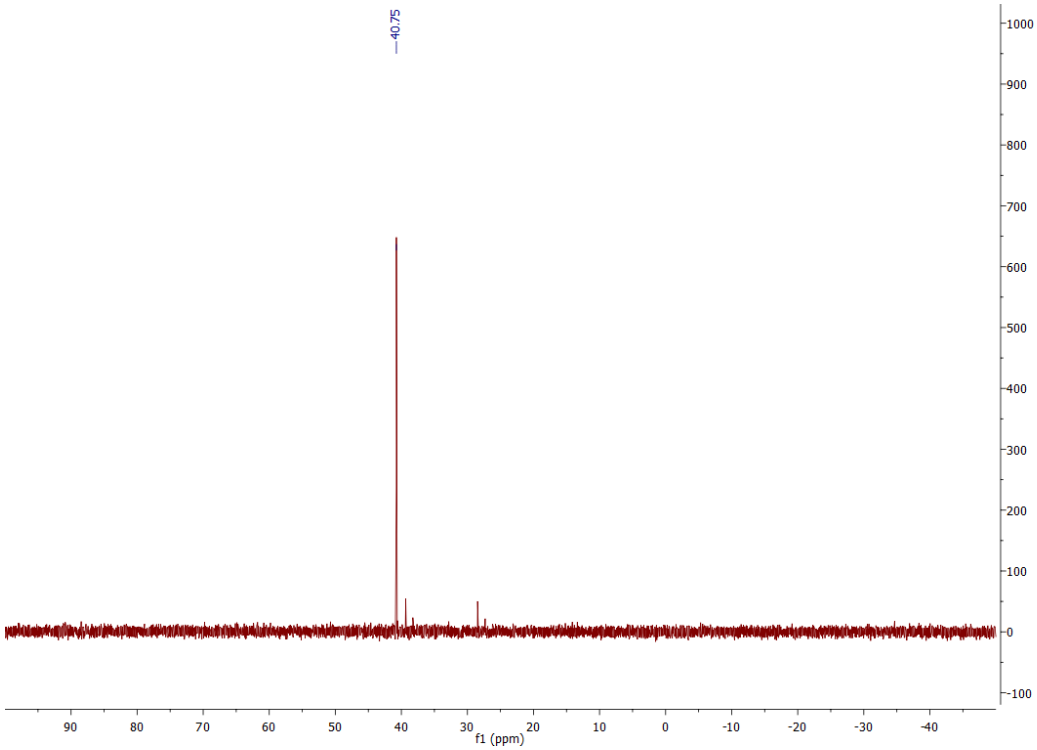
(*R*)-SEGPHOS(AuAr)$_2$:



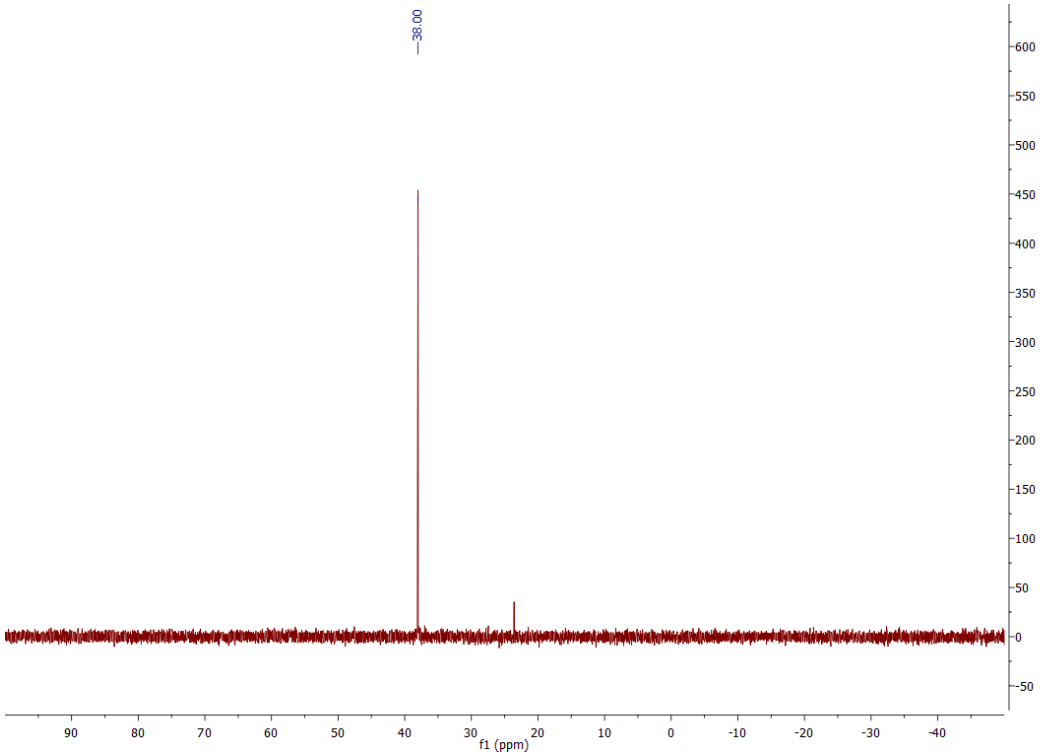
(*R*)-DM-SEGPHOS(AuAr)$_2$:



(*R*)-DTBM-SEGPHOS(AuAr)$_2$:



(*R*)-DIFLUORPHOS(AuAr)$_2$:



7. References

1) H. E. Gottlieb, V. Kotlyar, A. Nudelman, *J. Org. Chem.* 1997, **62**, 7512–7515.
2) M. Sawaguchi, S. Ayuba, S. Hara, *Synthesis* 2002, **13**, 1802–1803.
3) M. P. Munoz, J. Adrio, J. C. Carretero, A. M. Echavarren, *Organometallics* 2005, **24**, 1293–1300.
4) M. J. Johansson, D. J. Gorin, S. T. Staben, F. D. Toste, *J. Am. Chem. Soc.* 2005, **127**, 18002–18003.
5) S. Handa, D. J. Lippincott, D. H. Aue, B. H. Lipshutz, *Angew. Chem. Int. Ed.* 2014, **53**, 10658–10662.
6) A. D. Melhado, M. Luparia, F. D. Toste, *J. Am. Chem. Soc.* 2007, **129**, 12638–12639.
7) E. S. Andreiadis, M. R. Vitale, N. Mezailles, X. Le Goff, P. Le Floch, P. Y. Toullec, V. Michelet, *Dalton Trans.* 2010, **39**, 10608–10616.
8) F. Kleinbeck, F. D. Toste, *J. Am. Chem. Soc.* 2009, **131**, 9178–9179.
9) M. Genov, A. Almorin, P. Espinet, *Chem. Eur. J.* 2006, **12**, 9346–9352.
10) (a) J. Buter, D. Heijnen, C. Vila, V. Hornillos, E. Otten, M. Giannerini, A. J. Minnaard, B. L. Feringa, *Angew. Chem. Int. Ed.* 2016, **55**, 3620–3624; (b) T. Tu, Z. Sun, W. Fang, M. Xu, Y. Zhou, *Org. Lett.* 2012, **14**, 4250–4253.