Electronic Supplementary Information (ESI)

Hydrogen bonding-enabled gold catalysis: Ligand effects in gold-catalyzed cycloisomerizations in hexafluoroisopropanol (HFIP)

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Gold catalysis has witnessed immense evolution in recent years, yet it still requires the use of activators to render the common [AuCl(L)] complexes catalytically active. Herein, the H-bonding donor properties of hexafluoroisopropanol (HFIP) are utilized for Au-Cl bond activation and the ancillary ligand and counteranion effects on cycloisomerization reactions are showcased in HFIP as solvent.

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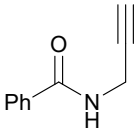
General considerations

All reactions were carried out in air unless otherwise noted. When chemicals were used for experiments under inert atmosphere (Innovative technologies glovebox or Schlenk line), they were either dried under vacuum (solids) or dried and degassed using argon (solvents). Solvents and all other reagents were purchased and used as received unless otherwise stated. [AuCl(DMS)] was prepared from $HAuCl_4 \cdot nH_2O$, which was supplied by Umicore, according to a modified known procedure. [Au(PPh_3)Cl] and the ligands JohnPhos, CyJohnPhos and PCy_3 were purchased from Strem Chemicals Inc.. 5-hexynoic acid was purchased from TCI and 6-heptynoic acid was purchased from Fluorochem. All [M(NHC)Cl] and [Au(PR_3)Cl] complexes were synthesized according to known procedures.[1-2] [Au(IPr)(MeCN)][BF_4] (**24**) and [Au(IPr)OTf] (**25**) were synthesized according to the reported procedures.[3] [Au(IPr)Cbz] (**26**) and [Au(IPr)OH] (**27**) were synthesized according to the reported procedures.[1,4] Purification of compounds by filtration was performed using celite purchased from Sigma Aldrich, or syringe membrane filters purchased from Carl Roth. Absolute ethanol, reagent grade acetone and freshly crushed anhydrous bases were used. ^{1}H, ^{13}C-{^{1}H} and ^{19}F Nuclear Magnetic Resonance (NMR) spectra were recorded on a Bruker Avance 400 Ultrashield, or Bruker Avance 300 Ultrashield spectrometer at 298 K using the residual solvent peak as reference ($CDCl_3$: δ_H = 7.26 ppm, δ_C = 77.16 ppm; CD_2Cl_2: δ_H = 5.32 ppm, δ_C = 53.84 ppm, C_6D_6: δ_H = 7.16 ppm, δ_C = 128.0 ppm). Chemical shifts δ are given in ppm. Peaks are assigned as: s (singlet), d (doublet), t (triplet), h (heptuplet) and m (multiplet). Elemental analyses were performed at Université de Namur, rue de Bruxelles, 55 B-5000 Namur, Belgium.

Procedures

Synthesis of N-Propargyl benzamide 1

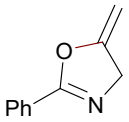


Synthesized according to a published procedure.[5] 4.0 mL (34.46 mmol, 1.0 equiv) of benzoyl chloride were dissolved in 70 mL dry DCM in a three-necked round bottom flask under argon. The solution was cooled at 0 °C using an ice bath and 2.16 ml (33.78 mmol, 0.98 equiv) of propargylamine and 2.87 mL (41.36 mmol, 1.2 equiv, 5.74 mL) of triethylamine were added. After the addition was complete, the ice bath was removed. The reaction progress was monitored by NMR. After 1.5 hours, the reaction was quenched with a saturated ammonium chloride solution, the organic phase was washed with brine, dried over anhydrous Na_2SO_4, filtered and the solvent was removed under vacuum. Purification by column chromatography on silica gel with DCM led to N-(prop-2-yn-1-yl)benzamide as a white solid which was further recrystallized from refluxing diethyl ether/petroleum ether 2/1 and was obtained as a white crystalline solid (3.8 g, 69% yield).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.88 – 7.71 (m, 2H, CH_{Ar}), 7.59 – 7.49 (m, 1H, CH_{Ar}), 7.44 (m, 2H, CH_{Ar}), 6.29 (s, 1H, NH), 4.26 (dd, *J* = 5.2, 2.6 Hz, 2H, CH_2), 2.29 (t, *J* = 2.6 Hz, 1H, CCH).

^{13}C NMR (75 MHz, $CDCl_3$) δ 167.3 (C=O), 133.9 (C_{Ar}), 131.9 (CH_{Ar}), 128.8 (CH_{Ar}), 127.2 (CH_{Ar}), 79.6 (CCH), 72.0 (CCH), 29.9 (CH_2).

Procedure for catalytic propargylamide cyclization



In a 4 mL vial equipped with a stirring bar and septum-equipped cap were added [Au], substrate (79.6 mg, 0.5 mmol) and 0.250 mL HFIP. The clear solution was stirred at room temperature for the required time and was then diluted with 1.0 mL of a 0.5 M solution of 1,3,5-trimethoxybenzene (ACS reagent grade >99%). When cationic gold catalysts were used, a drop of triethylamine was added at this stage to quench the catalyst as it would continue to be active in chlorinated solvents. An aliquot was taken after stirring for 1 minute and the solvents were evaporated to dryness. This sample was used to quantify the yield by ^{1}H NMR in Chloroform-d by integration of the characteristic TMB peaks and the olefinic CH peaks of the product and the Me peak of the byproduct and the CCH, CH_2 peaks of the starting material.

In a 4 mL vial equipped with a stirring bar and septum-equipped cap were added **12** (2.2 mg, 0.005 mmol, 1 mol%), substrate (79.6 mg, 0.5 mmol) and 0.250 mL HFIP. The clear solution was stirred at room temperature for 4 hours and then HFIP was removed under vacuum and ethyl acetate was used to filter the mixture through a silica gel plug. The solvent was removed and the residue was loaded on top of a chromatography column with silica gel and was purified by eluting with hexane/ethyl acetate 9/1. The reaction conversion as judged by ^{1}H NMR of the crude product was 87%. The pure product was isolated as a white solid in 70% yield (55.7 mg, 0.35 mmol).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 8.03 – 7.95 (m, 2H), 7.60 – 7.48 (m, 1H), 7.49 – 7.37 (m, 2H), 4.83 (q, *J* = 3.0 Hz, 1H), 4.66 (t, *J* = 2.9 Hz, 2H), 4.38 (q, *J* = 2.7 Hz, 1H).

Analytical data obtained are in agreement with the literature.[6]

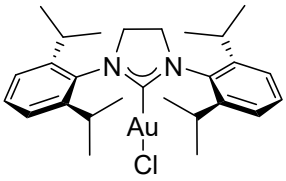
Additional screening results for propargylamide cyclization

The reactions were carried out as explained above and in the legend of table 1 in the main text or the article. In all cases, the amounts of **3** were negligible.

Table S1

Entry	[M]	Time	Solvent	2 (%)
1	[AuCl(IPr)] **4**	1h	DCM/HFIP 1:1	50
2	[AuCl(IPr)] **4**	1h	DCM/HFIP 9:1	21
3	[AuCl(JohnPhos)] **21**	1h	HFIP	95
4	[AuCl(PPh_3)] **9**	1h	HFIP	95
5	-	1h	HFIP	0

Synthesis of [AuCl(SIPr)] 5



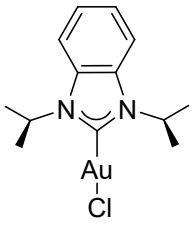
A 250 mL round bottom flask equipped with a magnetic stirring bar was charged with [Au(DMS)Cl] (6.9 g, 23.4 mmol) and SIPr•HCl (1 equiv., 10 g, 23.4 mmol) which were dissolved in acetone (80 mL) and the yellow solution was left to stir at 60 °C (metal heating mantle) with a Dean-Stark apparatus and condenser equipped in order to collect the DMS (ca. 20 minutes, DMS was disposed of in a bleach bath). Afterwards, the Dean-Stark was removed and the condenser was fitted on the reaction after freshly crushed K_2CO_3 (4 equiv., 12.9 g, 93.6 mmol) was added and the yellow mixture was stirred at 60 °C for 24 h. A violet color appeared after this time. The solvent was evaporated to dryness and the residue was then filtered over a pad of silica on a frit using dichloromethane (500 mL). The colorless (to golden yellow) filtrate was subsequently concentrated on the rotary evaporator until the product started to precipitate (ca. 100 mL) and pentane (400 mL) was added to completely precipitate the product, which was collected by filtration, washed with pentane (2x50 mL) and dried under high vacuum. The final product was obtained as a white solid in 76% yield (11.0 g, 17.8 mmol).

^{1}H NMR (300 MHz, CD_2Cl_2) δ 7.48 (t, *J* = 7.7, 2H, CH_{Ar}), 7.29 (d, *J* = 7.7, 4H, CH_{Ar}), 4.06 (s, 4H, NCH_2-imid), 3.07 (hept, *J* = 6.9 Hz, 4H, C*H*$(CH_3)_2$), 1.40 (d, *J* = 6.9, 12H, CH(C*H*$_3)_2$), 1.34 (d, *J* = 6.9, 12H, CH(C*H*$_3)_2$).

^{13}C NMR(75 MHz, CD_2Cl_2) δ 196.2 (s, C-Au), 147.2 (s, C_{Ar}), 134.5 (s, C_{Ar}), 130.3 (s, CH_{Ar}), 125.0 (s, CH_{Ar}), 53.9 (s, NCH_2-imid), 29.3 (s, *C*H$(CH_3)_2$), 25.2 (s, CH(*C*H$_3)_2$), 24.3 (s, CH(*C*H$_3)_2$).

Analytical data obtained are in agreement with the literature.[1]

Synthesis of [AuCl(BzIiPr)] (BzIiPr = N,N'-diisopropyl(benzimidazolylidene)) 12



The imidazolium bromide salt BzIiPr•HBr was synthesized according to known procedures.[7] Amberlite (IRA402 chloride form) resin was dried on a rotary evaporator at 80 °C for 30 minutes and then dried overnight in a vacuum oven. 50 g of this material were added to an oven dried round bottom flask along with 5.0 g of BzIiPr •HBr and 400 mL of MeOH. The mixture was stirred at room temperature for 16 hours. The resin was removed by filtration through a frit and washed with dichloromethane (300 mL). The filtrate was concentrated and transferred to a 100 mL flask. The solvents were evaporated until a sticky solid remained and then 50 mL ethyl acetate was added and removed under vacuum to give a white solid, then 50 mL of pentane were added and the mixture was sonicated. The solvents were decanted and the BzIiPr•HCl salt was dried under vacuum in a vacuum oven and used directly in the next step as it was found to be moderately hydroscopic (4.2 g, 99% yield).

A 100 mL round bottom flask equipped with a magnetic stirring bar was charged with [Au(DMS)Cl] (4.95 g, 16.8 mmol) and BzIiPr•HCl (1 equiv., 4.0 g, 16.8 mmol) which were dissolved in acetone (48 mL) and the yellow solution was left to stir at 60 °C (metal heating mantle) with a Dean-Stark apparatus and condenser equipped in order to collect the DMS (ca. 20 minutes, DMS was disposed of in a bleach bath). Afterwards, the Dean-Stark was removed and the condenser was fitted on the reaction after freshly crushed K_2CO_3 (3 equiv., 6.96 g, 50.4 mmol) was added and the yellow mixture was stirred at 60 °C for 1 h. A purple color appeared after this time. The reaction was completed as judged by NMR of an aliquot. The solvent was evaporated to dryness and the residue was then filtered over a pad of silica on a frit using dichloromethane (500 mL). The filtrate was subsequently concentrated on the rotary evaporator until the product started to precipitate and hexane (300 mL) was added to completely precipitate the product, which was collected by filtration, washed with hexane (2x100 mL)

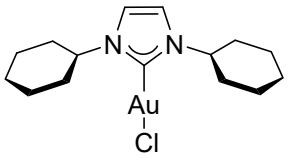
and dried under high vacuum. The final product was obtained as a white solid in 86% yield (6.3 g, 14.5 mmol).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.65 (dd, *J* = 6.2, 3.2 Hz, 2H, CH_A), 7.37 (dd, *J* = 6.3, 3.2 Hz, 2H), 5.52 (hept, *J* = 6.9 Hz, 2H, NCH), 1.73 (d, *J* = 7.0 Hz, 12H, Me).

^{13}C NMR (75 MHz, $CDCl_3$) δ 176.2 (Au-C), 132.5 (C_A), 124.0 (CH_A), 113.3 (CH_A), 54.5 (NCH), 21.8 (Me).

Analytical data obtained are in agreement with the literature.[7]

Synthesis of [AuCl(ICy)] 14

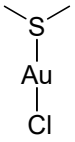


A 250 mL round bottom flask equipped with a magnetic stirring bar and reflux condenser was charged with [Au(DMS)Cl] (6.6 g, 22.3 mmol) and ICy•HCl (1 equiv., 6 g, 22.3 mmol) which were suspended in acetone (80 mL) and the mixture was left to stir at 60 °C (metal heating mantle) freshly crushed K_2CO_3 (3 equiv., 12.9 g, 66.9 mmol) was added and the red mixture was stirred at 60 °C for 5 h. The solvent was evaporated to dryness and the residue was then filtered over a pad of silica on a frit using dichloromethane (500 mL). The golden yellow filtrate was subsequently concentrated to dryness and was recrystallized by dissolving it in the minimum amount of DCM and adding diethyl ether (150 mL), then it was collected by filtration, washed with ether and pentane (2x50 mL) and dried under high vacuum. The final product was obtained as a white solid in 60% yield (6.2 g, 13.3 mmol).

^{1}H NMR (300 MHz, CD_2Cl_2) δ 6.99 (s, 2H, NCH_{imid}), 4.56 (tt, *J* = 11.9, 3.9 Hz, 2H, NCH), 2.08 (dd, *J* = 12.7, 2.0 Hz, 4H, CH_2), 1.89-1.86 (m, 4H, CH_2), 1.76-1.73 (m, 2H, CH_2), 1.61 (qd, *J* = 12.4, 3.4 Hz, 4H, CH_2), 1.47 (qt, *J* = 13.1, 3.2 Hz, 4H, CH_2), 1.22 (qt, *J* = 12.9, 3.7 Hz, 2H, CH_2).

Analytical data obtained are in agreement with the literature.[1]

Synthesis of [AuCl(DMS)] (dms = dimethyl sulfide) 16

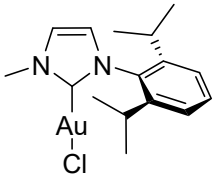


Tetrachloroauric(III) acid (“auric acid”), $HAuCl_4$ (anhydrous), was weighed and transferred using only glassware to a 1L round bottom flask equipped with a stirring bar, septum cap and ice bath (20 g, 58.8 mmol). This process is performed in a fumehood, avoiding light and taking into account the hydroscopic and corrosive nature of auric acid. Ethanol (250 mL) was added to submerge all of the solid and the orange mixture was stirred, leading to a solution. DMS was added (slowly while stirring rapidly in the ice bath) with a disposable syringe (8.6 mL, 2 equiv.) and a yellow precipitate formed at once. The syringe is washed and disposed of in a bleach bath. Simultaneously with this process, a sulfuric acid solution needs to be prepared, by simply adding the concentrated acid (75 mL) to ice (75 g) slowly and stirring in an ice bath. The cold acid solution was then added to an addition funnel which was adapted on top of the reaction vessel. The acid solution was added dropwise to the reaction over the course of 10 minutes, until the mixture is completely white. It is not necessary to add the entire amount of acid, and at this point corrections can be made (i.e. addition of excess DMS if the mixture is not turning white). At this point the reaction was complete and the white product was filtered on a frit and the filtrate was disposed of in appropriate gold waste containers. The product was washed with

ethanol (2x75 mL), diethyl ether (2x75 mL) and finally pentane (2x75 mL). The solid was left to dry for a few minutes on the frit and then was collected in a round bottom flask and placed under high vacuum for 10 minutes. The desired product was kept in a plastic vessel covered with aluminium foil in the freezer (14.025 g, 47.6 mmol, 81% yield). The yield can vary depending on the quality and water content of the starting material, even on larger scale.

^{1}H NMR (300 MHz, Chloroform-*d*) δ 2.75 (s, 6H, S(CH_3)$_2$).

Synthesis of [AuCl(MeIDipp)] (MeIDipp = 1-(2,6-Diisopropylphenyl)-3-methyl-imidazol-2-ylidene) 17



The imidazolium iodide salt MeIDipp•HI was synthesized according to known procedures.[8] Amberlite (IRA402 chloride form) resin was dried on a rotary evaporator at 80 °C for 30 minutes and then dried overnight in a vacuum oven. 5.0 g of this material were added to an oven dried round bottom flask along with 500 mg of MeIDipp•HI and 50 mL of MeOH. The mixture was stirred at room temperature for 16 hours. The resin was removed by filtration through a frit and washed with dichloromethane (50 mL). The filtrate was concentrated and transferred to a 20 mL scintillation vial. The solvents were evaporated until a viscous oil remained and then a few drops of acetone were added, followed by 10 mL of diethyl ether to precipitate the product. The solvents were decanted and the MeIDipp•HCl salt was dried under vacuum and used directly in the next step (369 mg, 98% yield).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.75 (s, 1H, NC*H*N), 7.71 (t, *J* = 1.6 Hz, 1H, NC*H*), 7.59 – 7.48 (t, *J* = 7.8 Hz, 1H, CH_{Ar}), 7.30 (d, *J* = 7.8 Hz, 2H), 7.13 (t, *J* = 1.7 Hz, 1H, NC*H*), 4.45 (s, 3H, Me), 2.30 (h, *J* = 6.8 Hz, 2H, C*H*(CH$_3$)$_2$)), 1.25 (d, *J* = 6.8 Hz, 6H, CH(CH_3)$_2$)), 1.14 (d, *J* = 6.8 Hz, 6H, CH(CH_3)$_2$)).

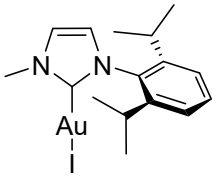
A 4 mL scintillation vial equipped with a magnetic stirring bar and a septum-equipped cap was charged with [Au(DMS)Cl] (211 mg, 0.717 mmol) and MeIDipp•HCl (1 equiv., 200 mg, 0.717 mmol) which were dissolved in acetone (3.1 mL) and the reaction was left to stir at 40°C for 20 minutes. Afterwards, K_2CO_3 (1.2 equiv., 109 mg, 0.861 mmol) was added and the mixture was stirred at 60 °C for 16 h. The solvent was evaporated and the residue was then filtered over silica using dichloromethane (8 mL). The solution was subsequently concentrated on the rotary evaporator until a viscous oil remained and pentane (5 mL) was added to precipitate the product, which was collected by filtration, washed with pentane (2x3 mL) and dried under high vacuum. The final product was obtained as a white solid in 51% yield (172 mg, 0.366 mmol).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.52 – 7.38 (t, 1H, *J* = 7.8 Hz, CH_{Ar}), 7.24 (d, *J* = 7.8 Hz, 2H, CH_{Ar}), 7.15 (d, *J* = 1.9 Hz, 1H, NCH), 6.92 (d, *J* = 1.9 Hz, 1H, NCH), 3.97 (s, 3H, NCH_3), 2.38 (hept, *J* = 6.9 Hz, 2H, C*H*(CH$_3$)$_2$)), 1.28 (d, *J* = 6.9 Hz, 6H, CH(CH_3)$_2$)), 1.11 (d, *J* = 6.9 Hz, 6H, CH(CH_3)$_2$)).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 173.6 (Au-C), 145.9 (iP-C_{Ar}), 134.1 (N-C_{Ar}), 130.7 (*ortho*-CH_{Ar}), 124.4 (*meta*-CH_{Ar}), 123.5 (DippNCH$_{Imid}$), 121.6 (MeNCH$_{Imid}$), 38.6 (N-Me), 28.5 (*C*H(CH$_3$)$_2$), 24.5 (CH(*C*H$_3$)$_2$), 24.5 (CH(*C*H$_3$)$_2$).

Anal. Calcd for $C_{16}H_{22}AuClN_2$: C, 40.48; H, 4.67; N, 5.90. Found: C, 40.44; H, 4.47; N, 5.34.

Synthesis of [AuI(MeIDipp)] (MeIDipp = 1-(2,6-Diisopropylphenyl)-3-methyl-imidazol-2-ylidene) 18

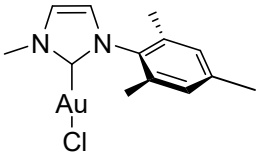


The imidazolium iodide salt MeIDipp•HI was synthesized according to known procedures.[8] A 4 mL scintillation vial equipped with a magnetic stirring bar and a septum-equipped cap was charged with [Au(DMS)Cl] (159 mg, 0.540 mmol) and MeImDipp•Hl (1 equiv., 200 mg, 0.540 mmol) which were dissolved in acetone (2.1 mL) and the reaction was left to stir at 40°C for 20 minutes. Afterwards, K_2CO_3 (1.0 equiv., 74.6 mg, 0.540 mmol) was added and the mixture was stirred at 60 °C for 16 h. The solvent was evaporated and the residue was then filtered over silica using dichloromethane (8 mL). The solution was subsequently concentrated on the rotary evaporator until a viscous oil remained and pentane (5 mL) was added to precipitate the product, which was collected by filtration, washed with pentane (2x3 mL) and dried under high vacuum. The final product was obtained as a brown solid in 80% yield (246 mg, 0.434 mmol).

^{1}H NMR (400 MHz, Chloroform-*d*) δ 7.47 (t, *J* = 7.8 Hz, 1H, CH_{Ar}), 7.25 (d, *J* = 7.8 Hz, 2H, CH_{Ar}), 7.14 (d, *J* = 1.9 Hz, 1H, NCH), 6.92 (d, *J* = 1.8 Hz, 1H, NCH), 3.99 (s, 3H, Me), 2.40 (hept, *J* = 6.8 Hz, 2H, C*H*$(CH_3)_2$)), 1.28 (d, *J* = 6.8 Hz, 6H, CH(C*H*$_3$)$_2$)), 1.11 (d, *J* = 6.9 Hz, 6H, CH(C*H*$_3$)$_2$)).

Analytical data obtained are in agreement with the literature.[8]

Synthesis of [AuCl(MeIMes)] (MeIMes = 1-(2,6-Dimesityl)-3-methyl-imidazol-2-ylidene) 19



The imidazolium iodide salt MeIMes•HI was synthesized according to known procedures.[9] Amberlite (IRA402 chloride form) resin was dried on a rotary evaporator at 80 °C for 30 minutes and then dried overnight in a vacuum oven. 5.0 g of this material were added to an oven dried round bottom flask along with 500 mg of MeIMes•HI and 50 mL of MeOH. The mixture was stirred at room temperature for 16 hours. The resin was removed by filtration through a frit and washed with dichloromethane (50 mL). The filtrate was concentrated and transferred to a 20 mL scintillation vial. The solvents were evaporated until a viscous oil remained and then a few drops of acetone were added, followed by 10 mL of diethyl ether to precipitate the product. The solvents were decanted and the MeIMes•HCl salt was dried under vacuum and used directly in the next step (351 mg, 97% yield).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 10.51 (s, 1H, NC*H*N), 8.01 (t, *J* = 1.7 Hz, 1H, NCH), 7.14 (t, *J* = 1.8 Hz, 1H, NCH), 6.95 (s, 2H, CH_{Ar}), 4.32 (s, 3H, NMe), 2.30 (s, 3H, Me), 2.02 (s, 6H, Me).

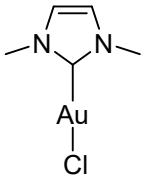
A 4 mL scintillation vial equipped with a magnetic stirring bar and a septum-equipped cap was charged with [Au(DMS)Cl] (249 mg, 0.717 mmol) and MeIMes•HCl (1 equiv., 200 mg, 0.845 mmol) which were dissolved in acetone (3.7 mL) and the reaction was left to stir at 40°C for 20 minutes. Afterwards, K_2CO_3 (1.2 equiv., 140 mg, 1.014 mmol) was added and the mixture was stirred at 60 °C for 16 h. The solvent was evaporated and the residue was then filtered over silica using dichloromethane (8 mL). The

solution was subsequently concentrated on the rotary evaporator until a viscous oil remained and pentane (5 mL) was added to precipitate the product, which was collected by filtration, washed with pentane (2x3 mL) and dried under high vacuum. The final product was obtained as a white solid in 70% yield (255 mg, 0.592 mmol).

1H NMR (300 MHz, Chloroform-d) δ 7.14 (d, J = 1.9 Hz, 1H, NCH), 6.95 (s, 2H, CH_{Ar}), 6.88 (d, J = 1.9 Hz, 1H, NCH), 3.95 (s, 3H, NMe), 2.32 (s, 3H, Me), 2.00 (s, 6H, Me).

Analytical data obtained are in agreement with the literature.[9]

Synthesis of [AuCl(IMe)] (IMe = 1,3-dimethyl-imidazol-2-ylidene) 20



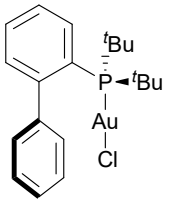
A 4 mL scintillation vial equipped with a magnetic stirring bar and a septum-equipped cap was charged with [Au(DMS)Cl] (222 mg, 0.754 mmol) and IMe•HCl (1 equiv., 100 mg, 0.754 mmol) which were dissolved in acetone (3.2 mL) and the reaction was left to stir at 60°C for 10 minutes. Afterwards, K_2CO_3 (2 equiv., 208 mg, 1.51 mmol) was added and the mixture was stirred at 60 °C for 3h. The solvent was evaporated and the residue was then filtered over silica using dichloromethane (8 mL). The solution was subsequently concentrated on the rotary evaporator until a viscous oil remained and pentane (5 mL) was added to precipitate the product, which was collected by filtration, washed with pentane (2x3 mL) and dried under high vacuum. The final product was obtained as a white solid in 83% yield (205 mg, 0.624 mmol).

^{1}H NMR (300 MHz, Chloroform-*d*) δ 6.94 (s, 2H, CH_{Imid}), 3.82 (s, 6H, CH_3).

^{13}C NMR (101 MHz, Chloroform-*d*) δ 171.7 (Au-C), 121.9 (CH_{Imid}), 38.3 (CH_3).

Analytical data obtained are in agreement with the literature.[9]

Synthesis of [AuCl(JohnPhos)] 21



Inside a glovebox, a 20 mL vial equipped with magnetic stirring bar and septum-equipped cap was charged with [Au(DMS)Cl] (1 equiv.,294.5 mg, 1.00 mmol) and JohnPhos (1 equiv., 298.4 mg, 1.00 mmol). DCM (3.0 mL) was added to solubilize the solids and the golden yellow solution was stirred at room temperature for 16 hours. Afterwards, outside the glovebox the resulting mixture was passed through a syringe filter using DCM. After removing the solvent in vacuo and washing with pentane (3x3 mL), a white solid was obtained in 97% yield (515 mg, 0.97 mmol).

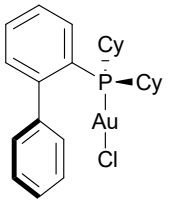
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.89 – 7.82 (m, 1H), 7.59 – 7.54 (m, 1H), 7.54 – 7.46 (m, 2H), 7.45 – 7.39 (m, 2H), 7.33 – 7.28 (m, 1H), 7.16 – 7.10 (m, 2H), 1.41 (d, $J_{H\text{-}P}$ = 15.6 Hz, 18H).

^{31}P NMR (121 MHz, $CDCl_3$) δ 59.94.

^{13}C NMR (75 MHz, Chloroform-*d*) δ (J = J_{C-P}) 150.3 (d, *J* = 13.5 Hz), 142.3 (d, *J* = 6.5 Hz), 133.6 (d, *J* = 2.8 Hz), 133.4 (d, *J* = 7.4 Hz), 130.7 (d, *J* = 2.3 Hz), 129.1 (d, *J* = 39.2 Hz), 128.4, 126.8 (d, *J* = 6.8 Hz), 126.2 (d, *J* = 45.4 Hz), 37.9 (d, *J* = 25.7 Hz), 31.0 (d, *J* = 6.7 Hz).

Analytical data obtained are in agreement with the literature.[2]

Synthesis of [AuCl(CyJohnPhos)] 22



Inside a glovebox, a 20 mL vial equipped with magnetic stirring bar and septum-equipped cap was charged with [Au(DMS)Cl] (1 equiv.,294.5 mg, 1.00 mmol) and CyJohnPhos (1 equiv., 350.5 mg, 1.00 mmol). DCM (3.0 mL) was added to solubilize the solids and the golden yellow solution was stirred at room temperature for 16 hours. Afterwards, outside the glovebox the resulting mixture was passed through a syringe filter using DCM. After removing the solvent in vacuo and washing with pentane (3x3 mL), a white solid was obtained in 99% yield (582 mg, 0.99 mmol).

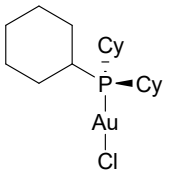
^{1}H NMR (300 MHz, Chloroform-*d*) δ 7.81 – 7.65 (m, 1H), 7.64 – 7.37 (m, 5H), 7.35 – 7.27 (m, 1H), 7.23 – 7.07 (m, 2H), 2.17 – 1.90 (m, 4H), 1.87 – 1.71 (m, 4H), 1.68 – 1.55 (m, 4H), 1.51 – 1.39 (m, 2H), 1.35 – 1.11 (m, 8H).

^{31}P NMR (162 MHz, $CDCl_3$) δ 43.96.

^{13}C NMR (75 MHz, Chloroform-*d*) δ (J = J_{C-P}) 149.0 (d, *J* = 10.5 Hz), 141.5 (d, *J* = 5.2 Hz), 134.3 (d, *J* = 7.3 Hz), 132.6 (d, *J* = 7.4 Hz), 130.8 (s), 129.0 (d, *J* = 94.3 Hz), 128.4 (s), 127.6 (d, *J* = 8.9 Hz), 124.9 (d, *J* = 51.6 Hz), 36.7 (d, *J* = 33.6 Hz), 31.7 (d, *J* = 3.7 Hz), 29.5 (s), 26.6 (s), 26.6 (d, *J* = 26.0 Hz), 25.7 (d, *J* = 1.5 Hz).

Analytical data obtained are in agreement with the literature.[2]

Synthesis of [AuCl(PCy_3)] 23



Inside a glovebox, a 20 mL vial equipped with magnetic stirring bar and septum-equipped cap was charged with [Au(DMS)Cl] (1 equiv.,294.5 mg, 1.00 mmol) and PCy_3 (1 equiv., 280.4 mg, 1.00 mmol). DCM (3.0 mL) was added to solubilize the solids and the golden yellow solution was stirred at room temperature for 16 hours. Afterwards, outside the glovebox the resulting mixture was passed through a syringe filter using DCM. After removing the solvent in vacuo and washing with pentane (3x3 mL), a white solid was obtained in 98% yield (505 mg, 0.98 mmol).

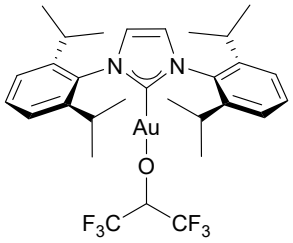
^{1}H NMR (300 MHz, Chloroform-*d*) δ 2.04 – 1.90 (m, 9H), 1.90 – 1.78 (m, 6H), 1.75 – 1.67 (m, 3H), 1.52 – 1.38 (m, 6H), 1.36 – 1.18 (m, 9H)

^{31}P NMR (162 MHz, $CDCl_3$) δ 54.03.

^{13}C NMR (75 MHz, Chloroform-*d*) δ (J = J_{C-P}) 33.44 (d, *J* = 31.0 Hz), 30.89 (s), 27.10 (d, *J* = 12.2 Hz), 25.94 (d, *J* = 1.2 Hz).

Analytical data obtained are in agreement with the literature.[2]

Synthesis of [AuOCH(CF_3)$_2$(IPr)] 28



Procedure A: A 4 mL scintillation vial equipped with a magnetic stirring bar and a septum-equipped cap was charged with [Au(OH)(IPr)] (100 mg, 0.166 mmol) which was suspended in benzene (1 mL and HFIP (1.1 equiv., 0.019 mL, 0.166 mmol) was added via a micropipette. The mixture became a clear solution at once, and was left to stir for 1 hour at room temperature. The solution was subsequently concentrated on the rotary evaporator until a viscous oil remained and pentane (5 mL) was added to precipitate the product, which was collected by filtration, washed with pentane (2x3 mL) and dried under high vacuum. The final product was obtained as a white solid in 86% yield (108 mg, 0.144 mmol). Crystals that were suitable for single crystal Xray diffraction were grown via vapor diffusion of hexane into a saturated solution of the product in benzene.

Procedure B: A 4 mL scintillation vial equipped with a magnetic stirring bar and a septum-equipped cap was charged with [AuCl(IPr)] (200 mg, 0.322 mmol) and K_2CO_3 (3 equiv., 134 mg, 0.966 mmol) which were suspended in ethanol (1 mL). HFIP (2 equiv., 68 µL) was added and the reaction was left to stir at room temperature for 16 hours. The solvent was evaporated and the residue was then microfiltered and filtered over basic alumina using benzene (8 mL). The solution was subsequently concentrated on the rotary evaporator until a viscous oil remained and pentane (5 mL) was added to precipitate the product, which was collected by filtration, washed with pentane (2x3 mL) and dried under high vacuum. The final product was obtained as a white solid in 95% yield (230 mg, 0.306 mmol).

^{1}H NMR (400 MHz, Benzene-d_6) δ 7.21 (t, *J* = 7.8 Hz, 2H, CH_{Ar}), 7.03 (d, *J* = 7.8 Hz, 4H, CH_{Ar}), 6.24 (s, 2H, NCH_{Imid}), 4.69 (hept, J_{H-F} = 6.4 Hz, 1H, C*H*(CF_3)), 2.48 (hept, J = 6.9 Hz, 4H, C*H*(CH_3)$_2$)), 1.36 (d, *J* = 6.9 Hz, 12H, CH(C*H*$_3$)$_2$)), 1.03 (d, *J* = 6.9 Hz, 12H, CH(C*H*$_3$)$_2$)).

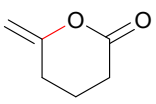
^{13}C NMR (101 MHz, Benzene-d_6) δ 169.2 (Au-C), 145.7 (C_{Ar}), 134.4(C_{Ar}), 131.0 (CH_{Ar}), 124.4 (CH_{Ar}), 126.2 – 123.3 (m, CF_3, seen in HMBC), 122.7 (NCH_{Imid}), 77.9 (p, J_{C-F} = 30.0 Hz, *C*H(CF_3)), 29.02 (*C*H(CH_3)$_2$)), 24.3 (CH(*C*H$_3$)$_2$)), 24.0, (CH(*C*H$_3$)$_2$)).

^{19}F-{H) NMR (376 MHz, C_6D_6) δ -75.99 (s, CF_3).

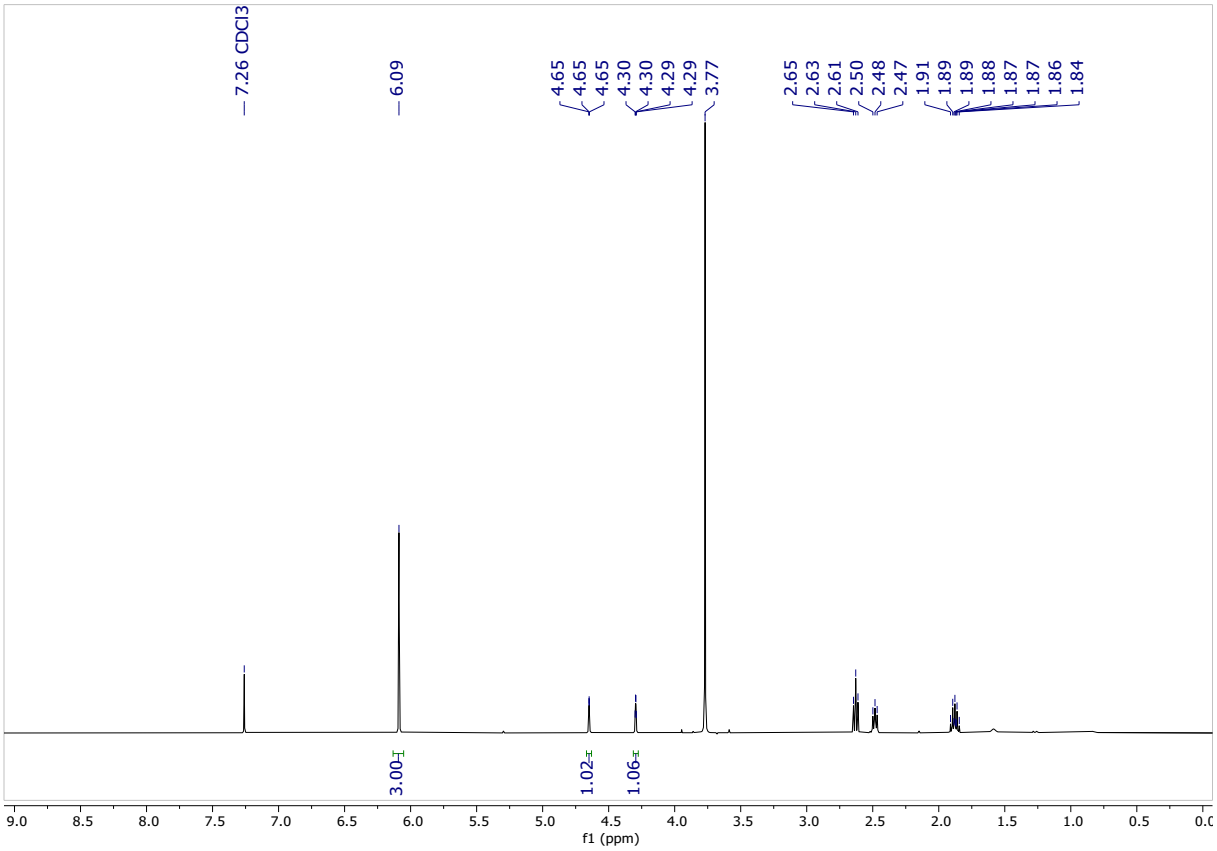
Anal. Calcd for $C_{30}H_{37}AuF_6N_2O$: C, 47.88; H, 4.96; N, 3.72. Found: C, 47.92; H, 4.89; N, 3.60.

Procedures for catalytic 5-hexynoic acid and 6-heptynoic acid cyclization

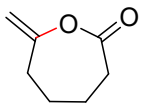
5-Hexynoic acid cyclization:



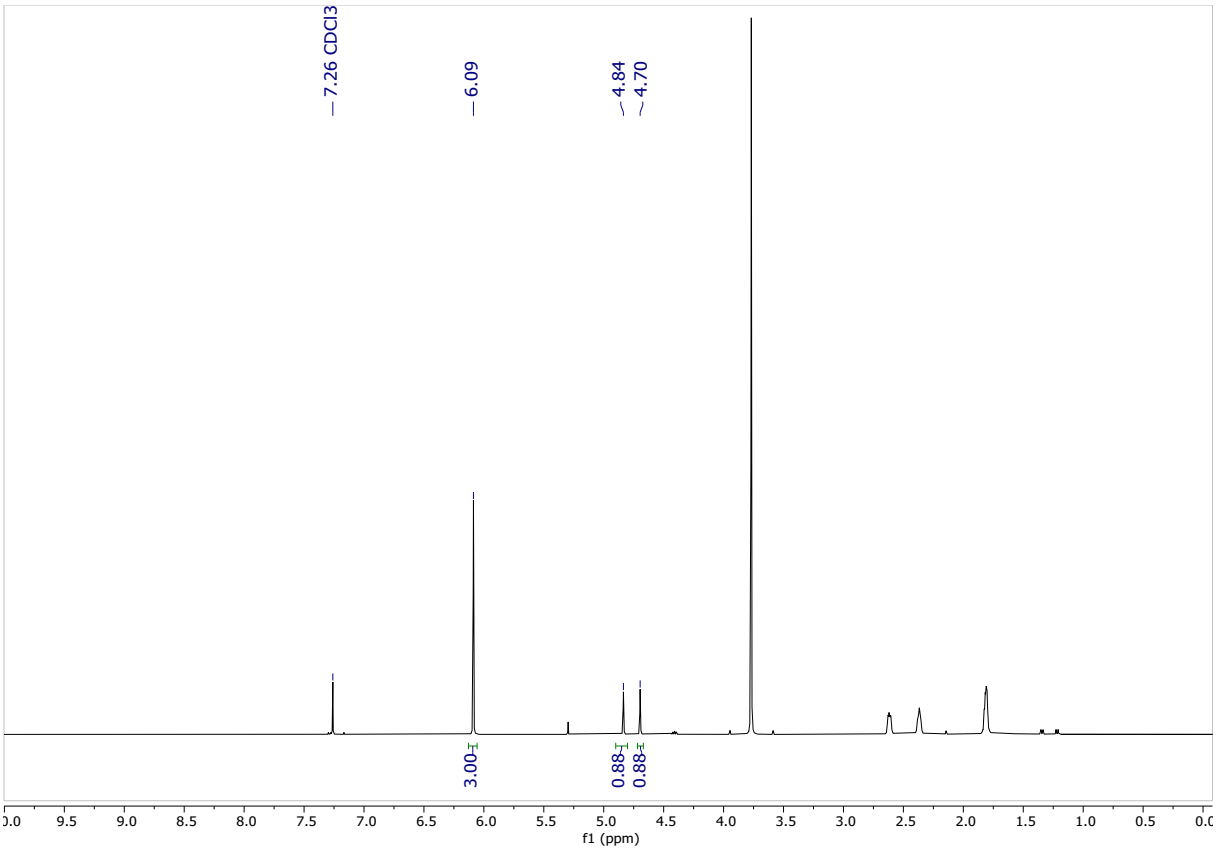
In a 4 mL vial equipped with a stirring bar and septum-equipped cap were added substrate (0.055 mL, 0.5 mmol) and 0.230 mL HFIP. Then, 0.020 mL of a freshly prepared HFIP stock solution of [Au] corresponding to 0.01 mol% catalyst loading (0.00005 mmol [Au]) were added. The clear solution was stirred at room temperature for 10 minutes and was then diluted with 1.0 mL of a 0.5 M solution of 1,3,5-trimethoxybenzene (ACS reagent grade >99%). An aliquot was taken after stirring for 1 minute and the solvents were evaporated to dryness at room temperature. This sample was used to quantify the yield by ^{1}H NMR in Chloroform-d by integration of the characteristic TMB peaks (6.09 ppm) and the olefinic CH peaks of the product (4.65 and 4.30 ppm) as shown below in an example.



6-Heptynoic acid cyclization:

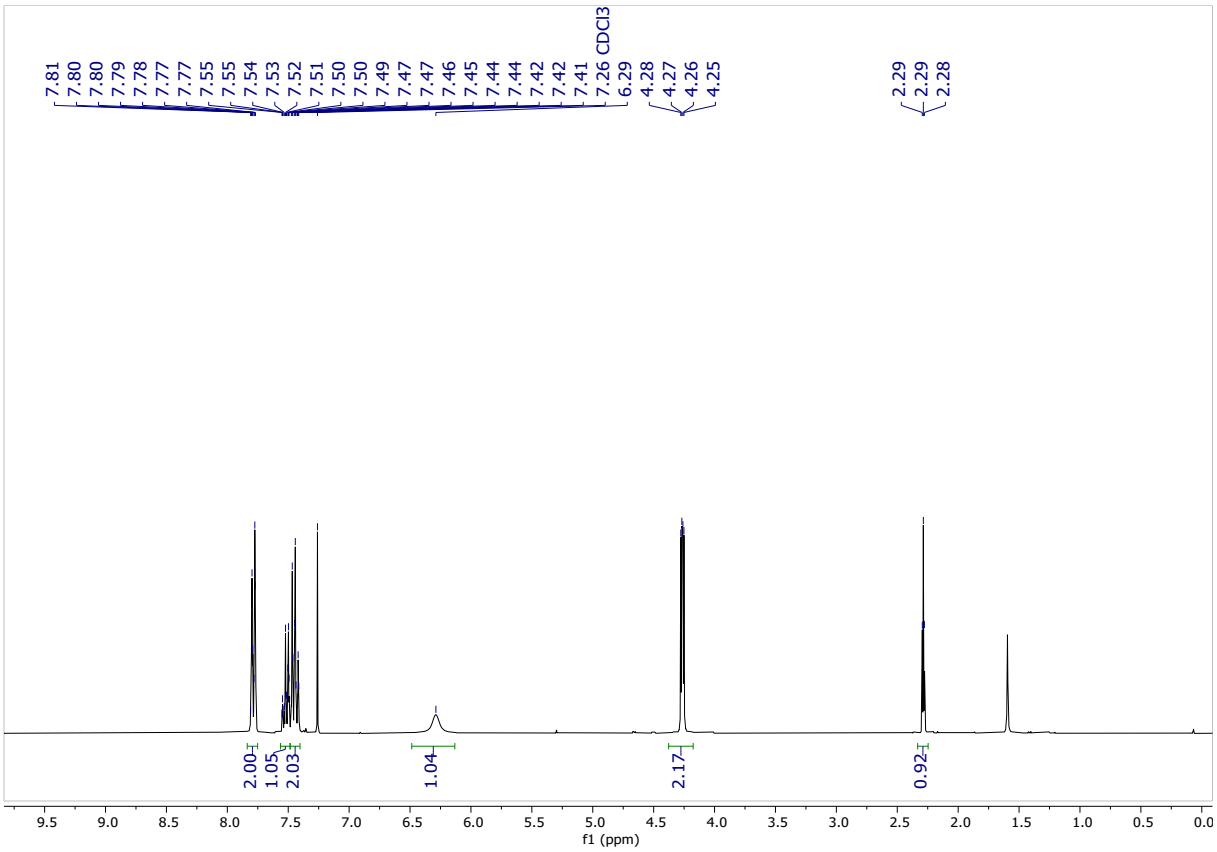


In a 4 mL vial equipped with a stirring bar and septum-equipped cap were added [Au], substrate (0.063 mL, 0.5 mmol) and 0.250 mL HFIP. The clear solution was stirred at room temperature 16 hours and was then diluted with 1.0 mL of a 0.5 M solution of 1,3,5-trimethoxybenzene (ACS reagent grade >99%). An aliquot was taken after stirring for 1 minute and the solvents were evaporated to dryness. This sample was used to quantify the yield by ^{1}H NMR in Chloroform-d by integration of the characteristic TMB peaks (6.09 ppm) and the olefinic CH peaks of the product (4.84 and 4.70 ppm) as shown below in an example. The conversion corresponds to the NMR yield and the starting material was also detected as conversion was not complete after 16 h.

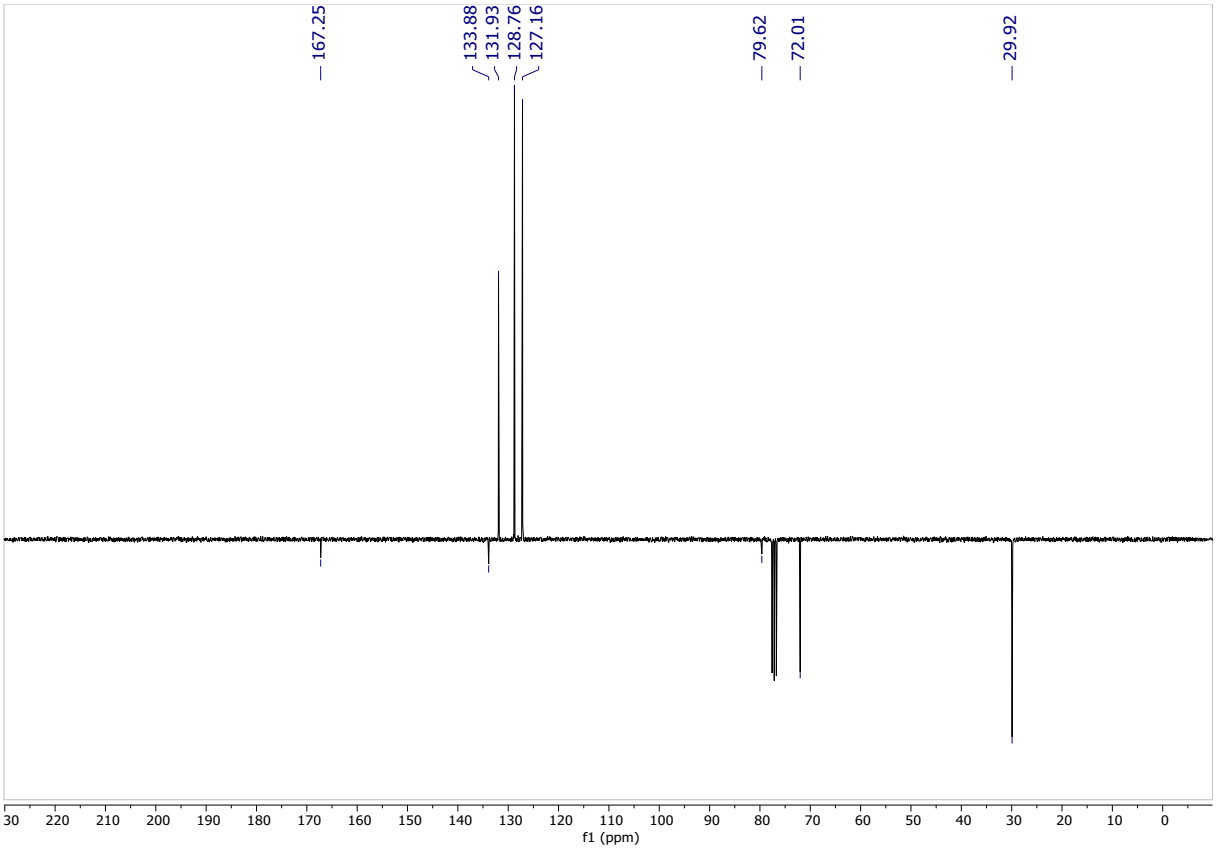

7.26 CDCl3
6.09
4.84
4.70
3.00
0.88
0.88
f1 (ppm)

NMR spectra

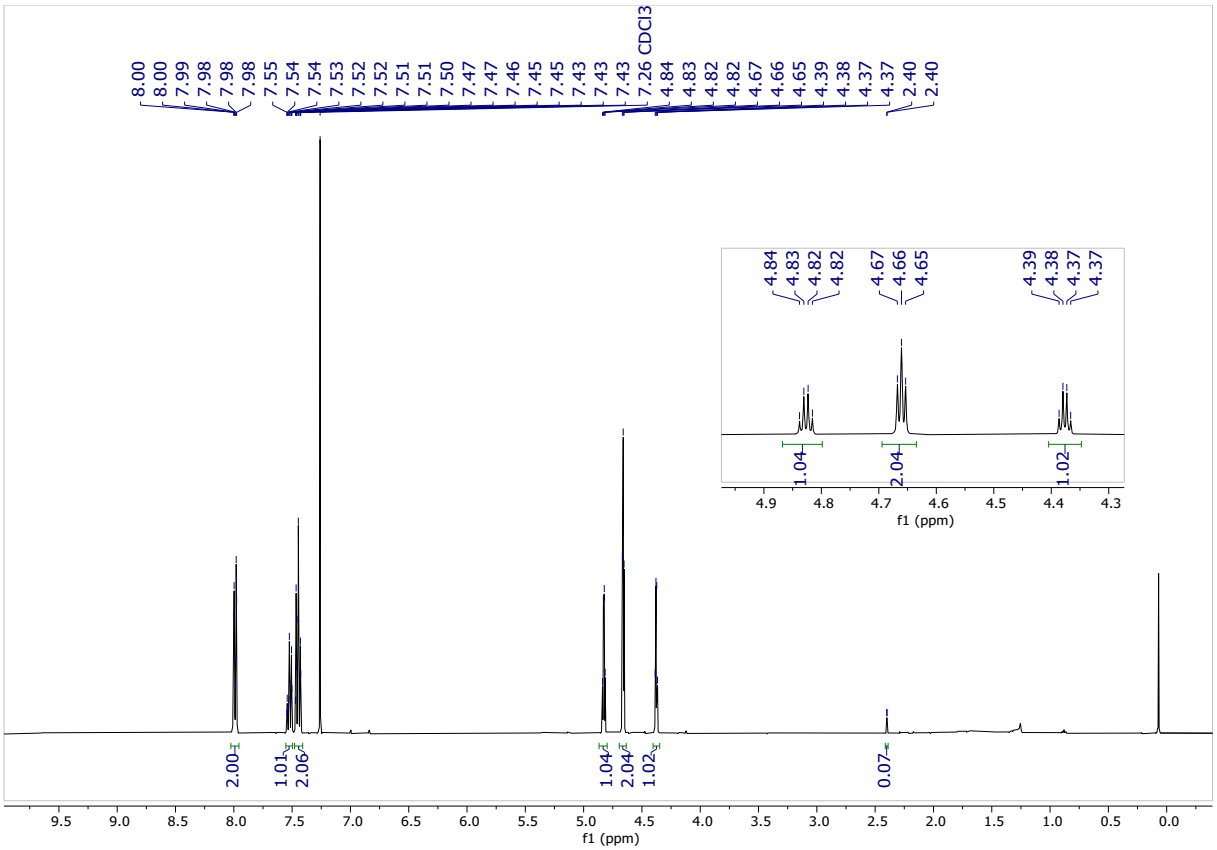
^{1}H NMR of N-Propargyl benzamide 1



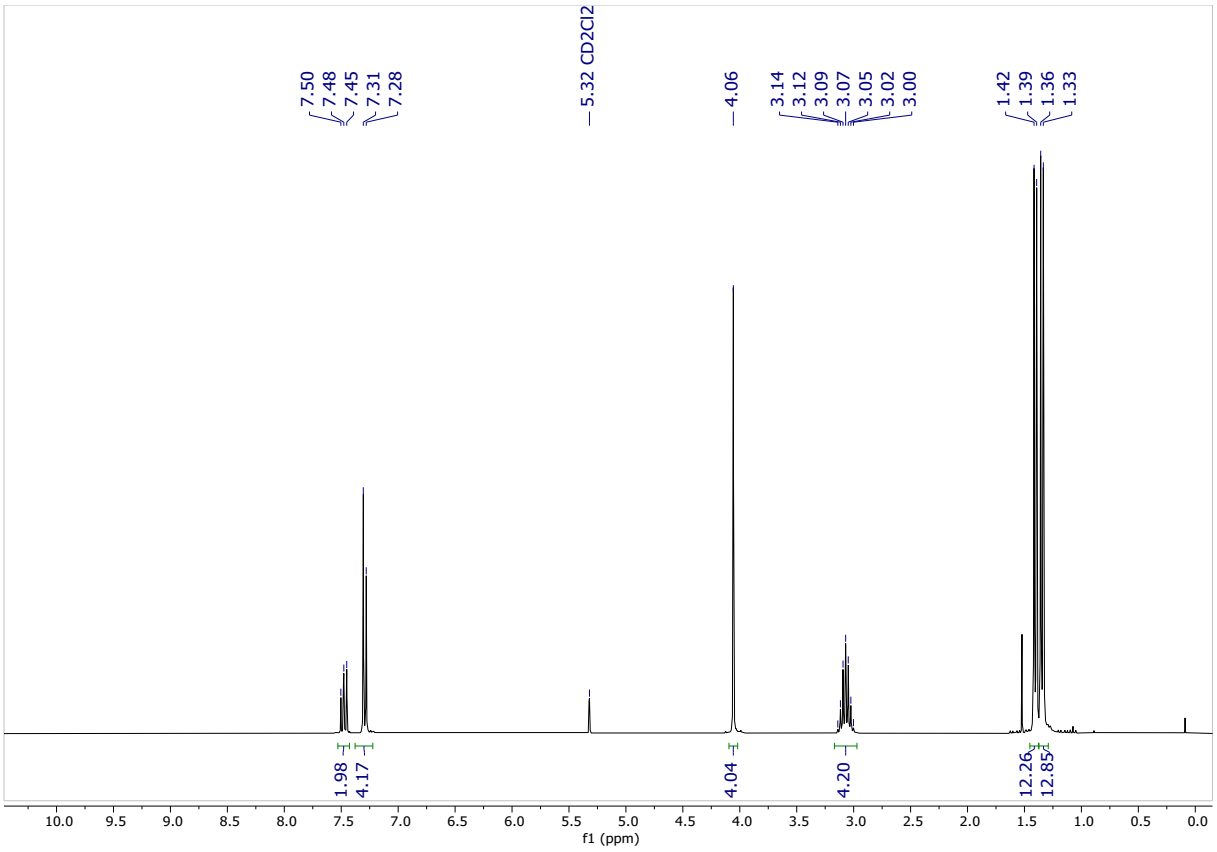
^{13}C NMR of N-Propargyl benzamide 1



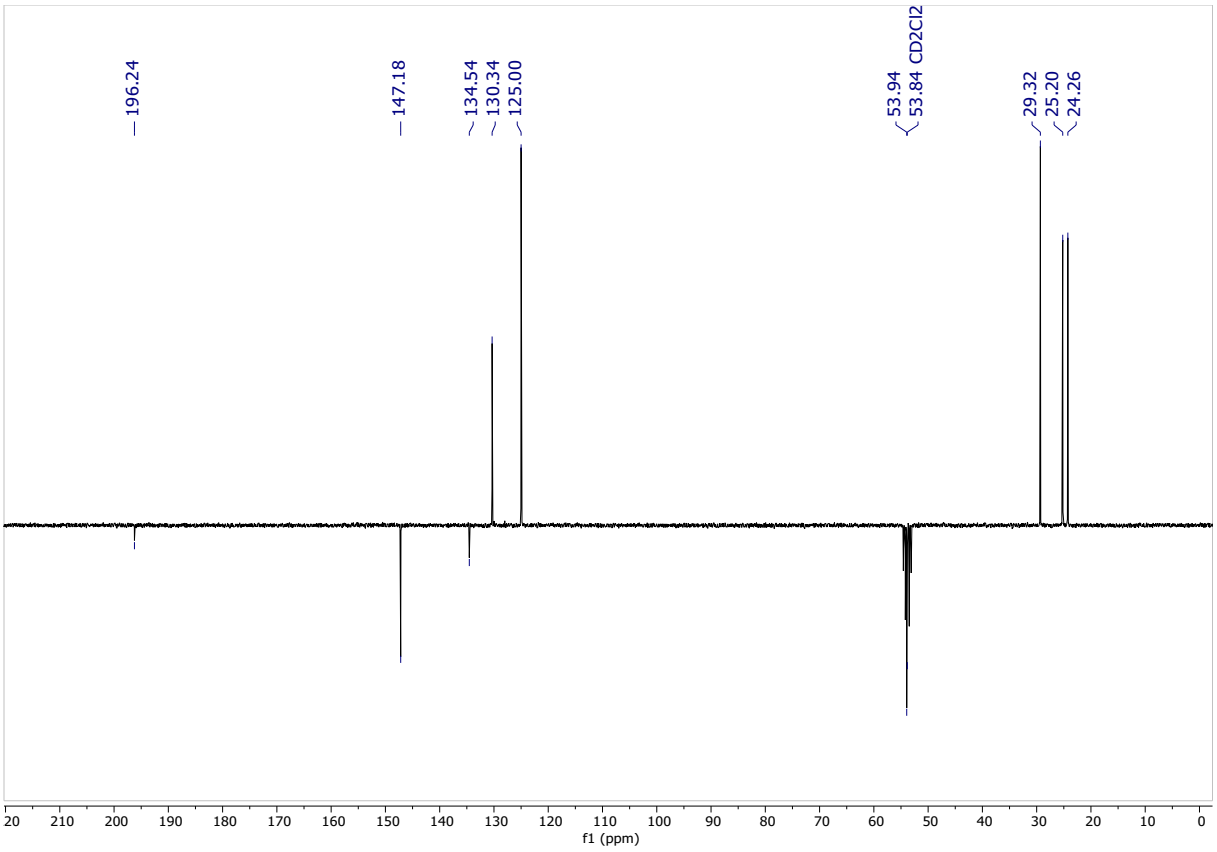
^{1}H NMR of 2


8.00
8.00
7.99
7.98
7.98
7.98
7.55
7.54
7.54
7.53
7.52
7.52
7.51
7.51
7.50
7.47
7.47
7.46
7.45
7.45
7.43
7.43
7.26 CDCl3
4.84
4.83
4.82
4.82
4.67
4.66
4.65
4.39
4.38
4.37
4.37
2.40
2.40
2.00
1.01
2.06
1.04
2.04
1.02
0.07
f1 (ppm)
1.04
2.04
1.02
f1 (ppm)

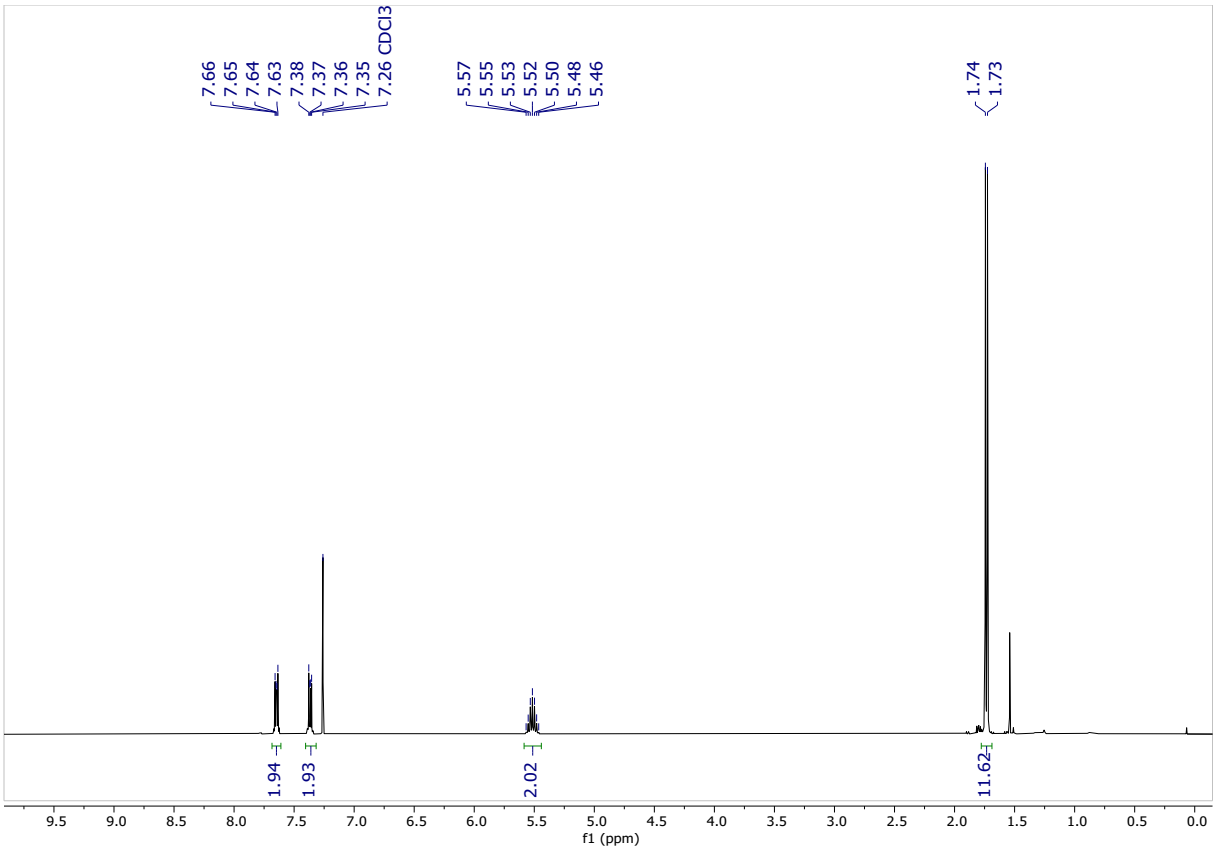
^{1}H NMR of [AuCl(SIPr)] 5



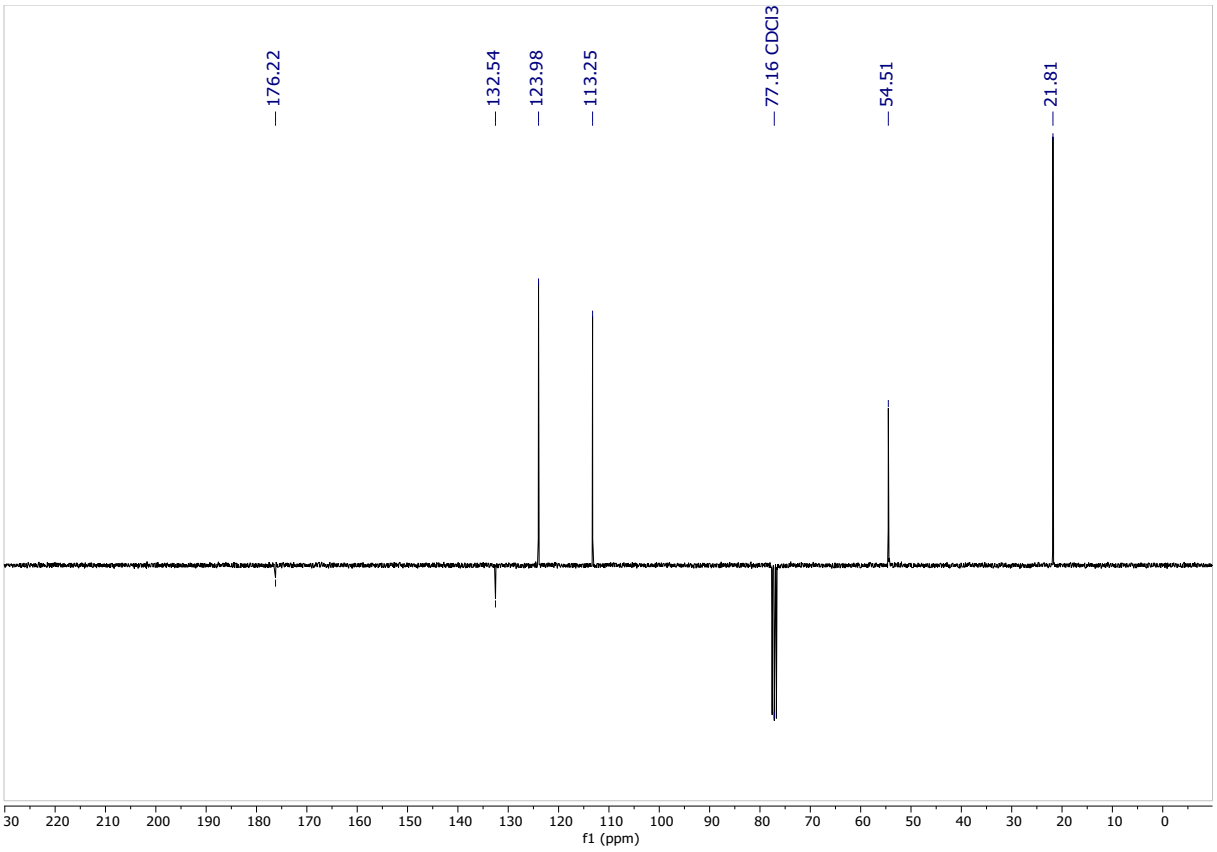
^{13}C NMR of [AuCl(SIPr)] 5



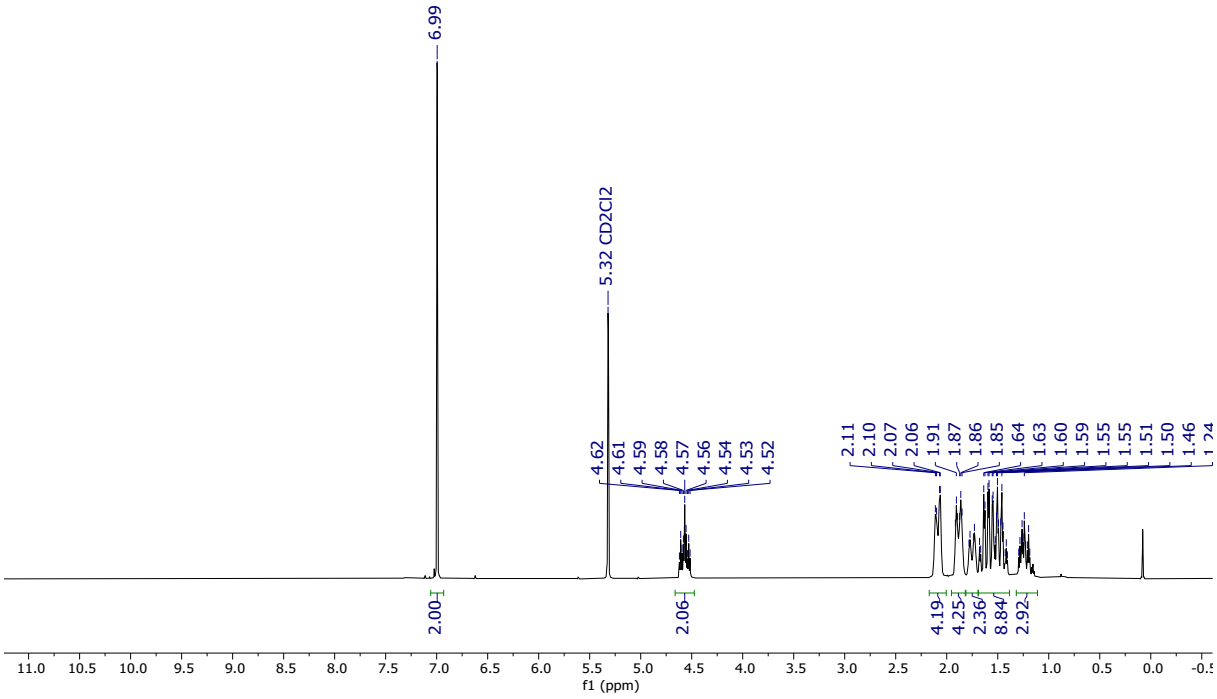
^{1}H NMR of [AuCl(BzIiPr)] 12



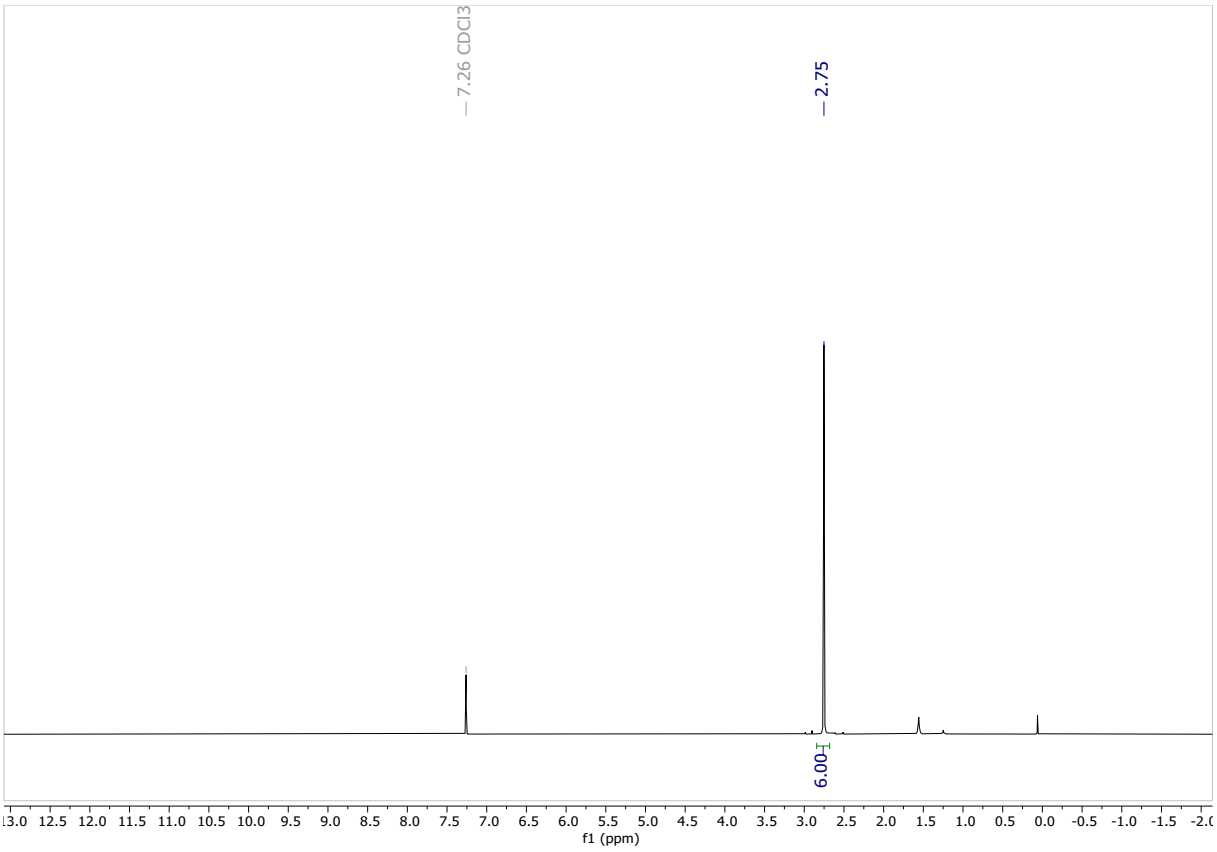
^{13}C NMR of [AuCl(BzIiPr)] 12



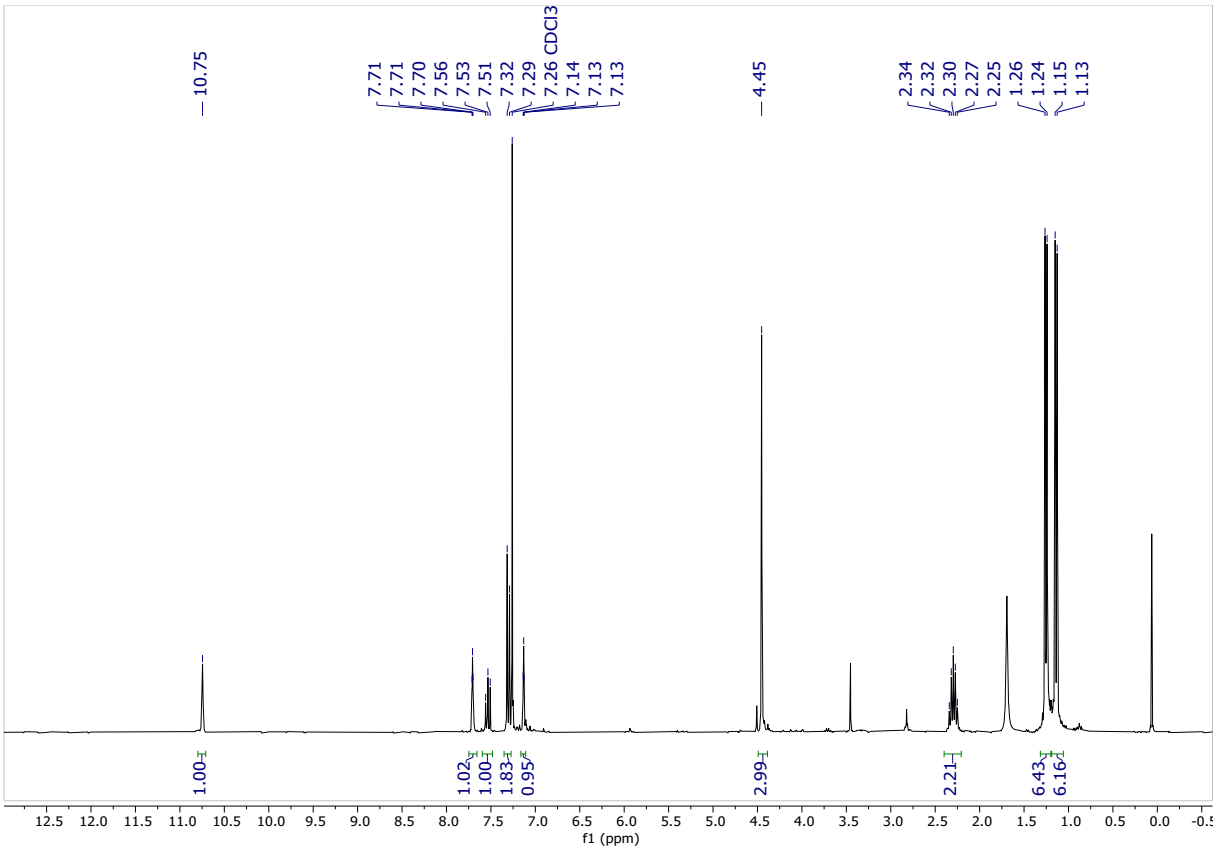
^{1}H NMR of [AuCl(ICy)] 14



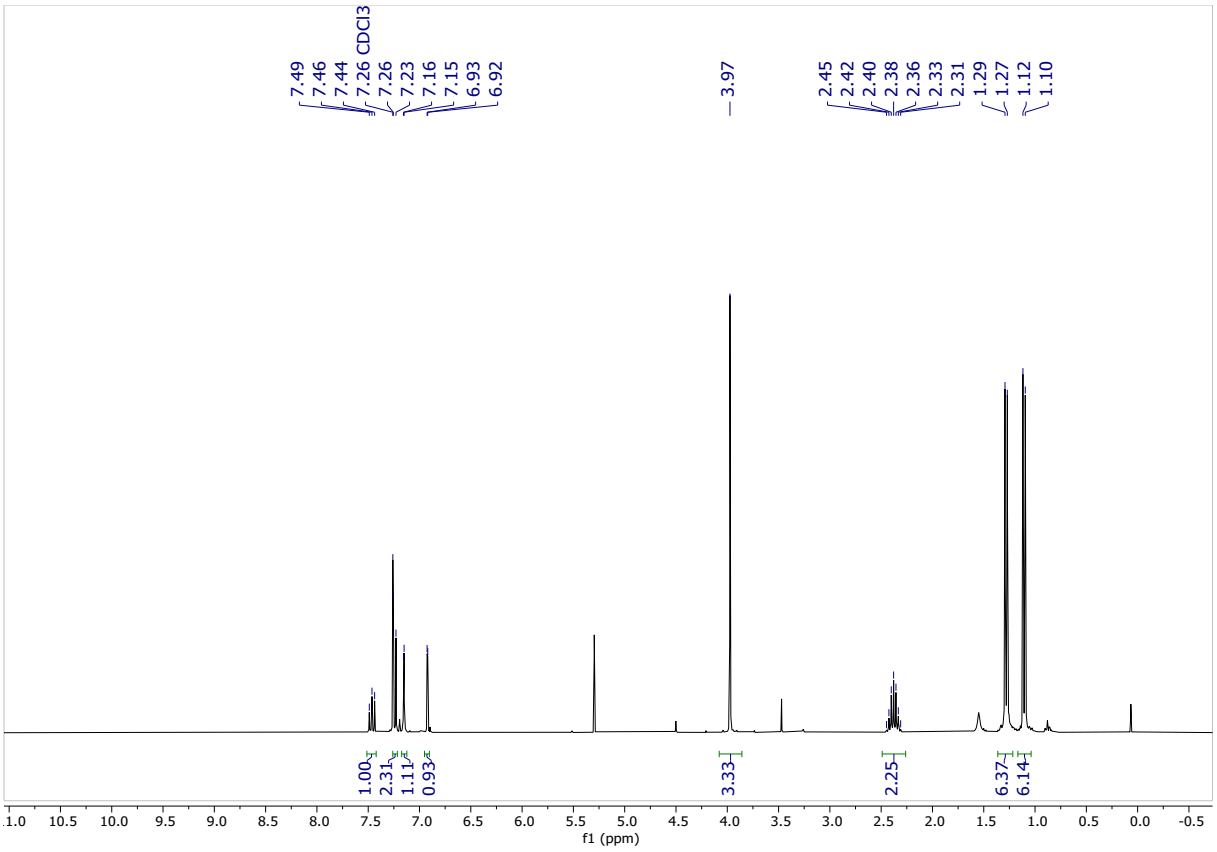
^{1}H NMR of [AuCl(DMS)] 14



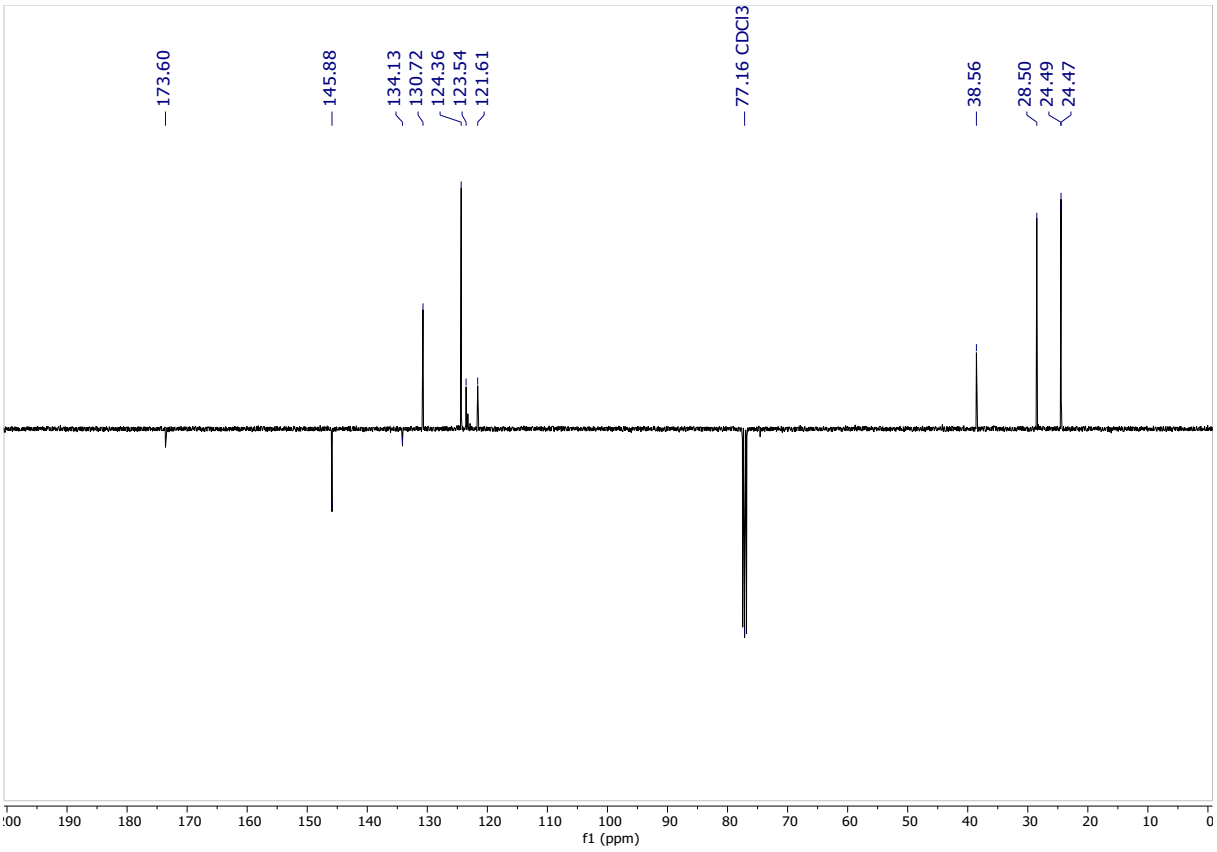
^{1}H NMR of MeImDipp HCl



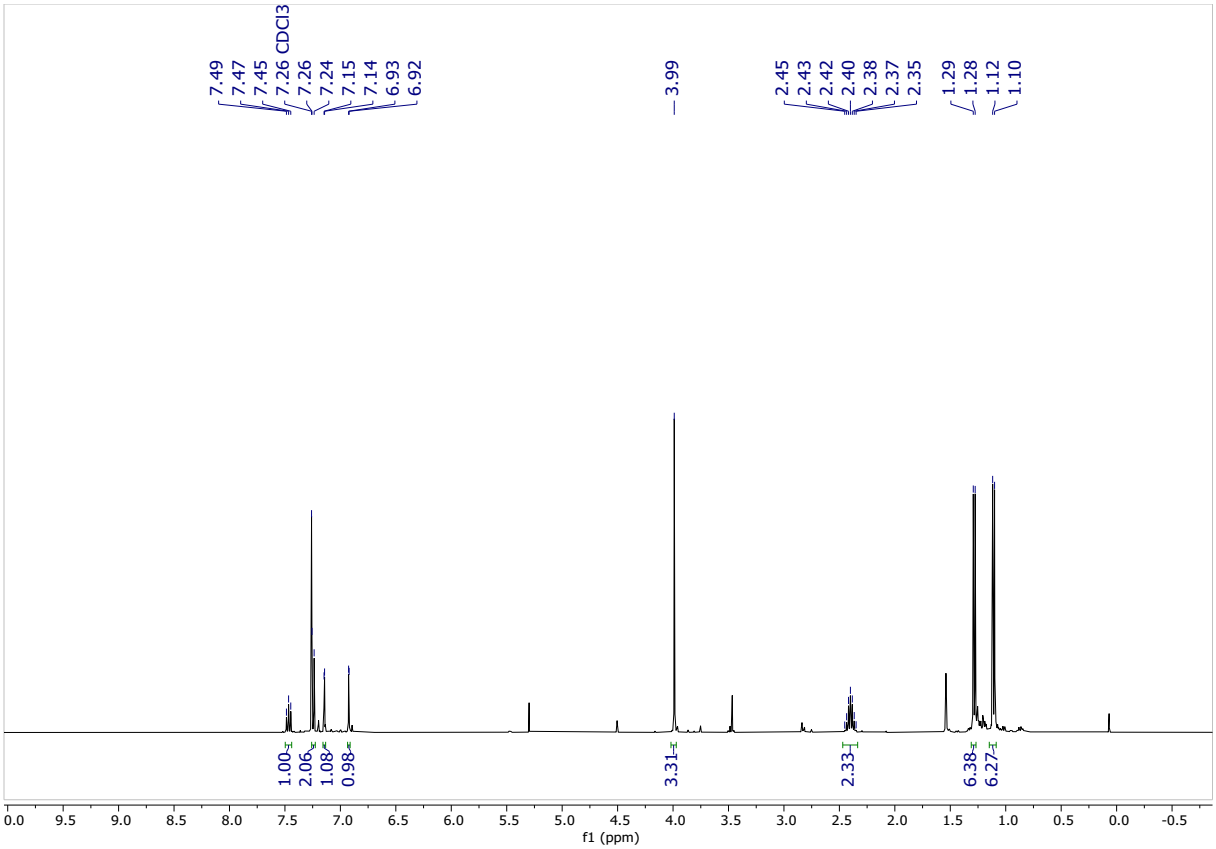
^{1}H NMR of [AuCl(MeImDipp)] 17



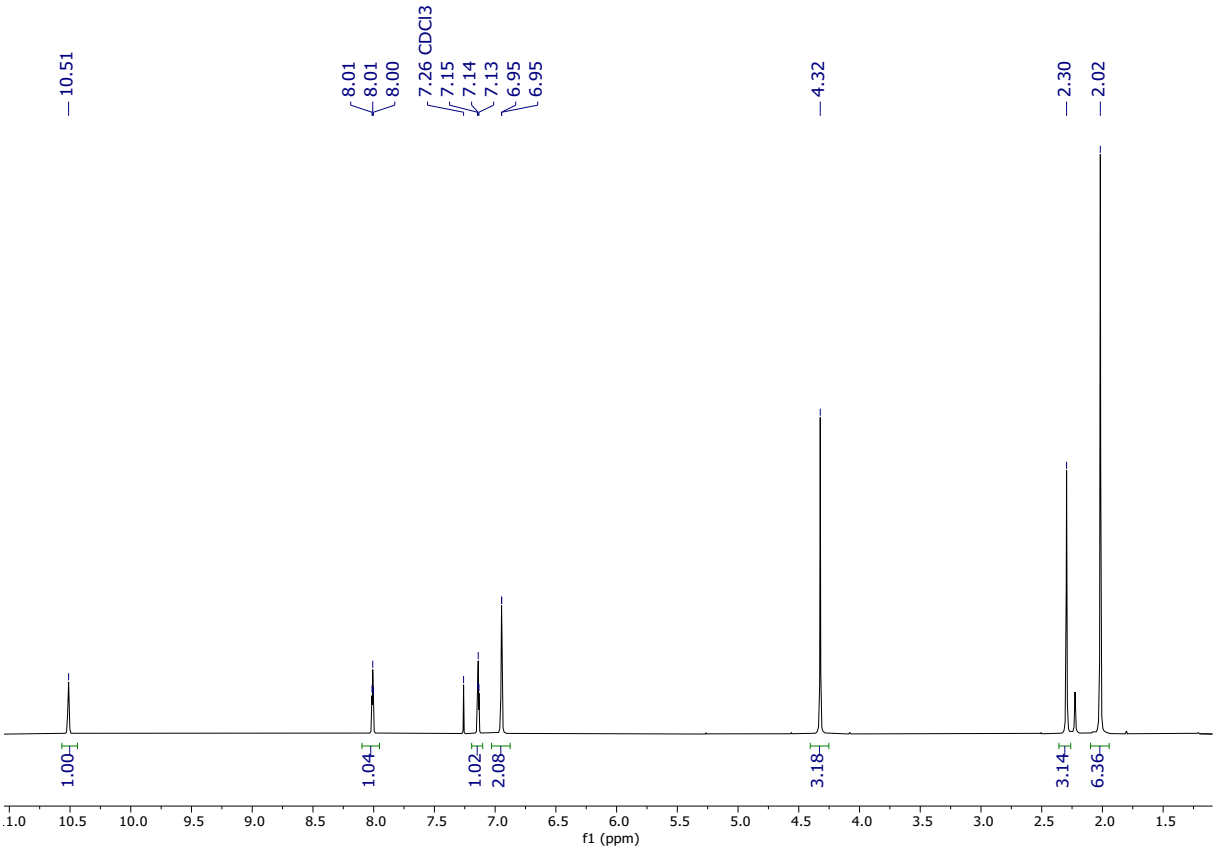
^{13}C NMR of [AuCl(MeImDipp)] 17



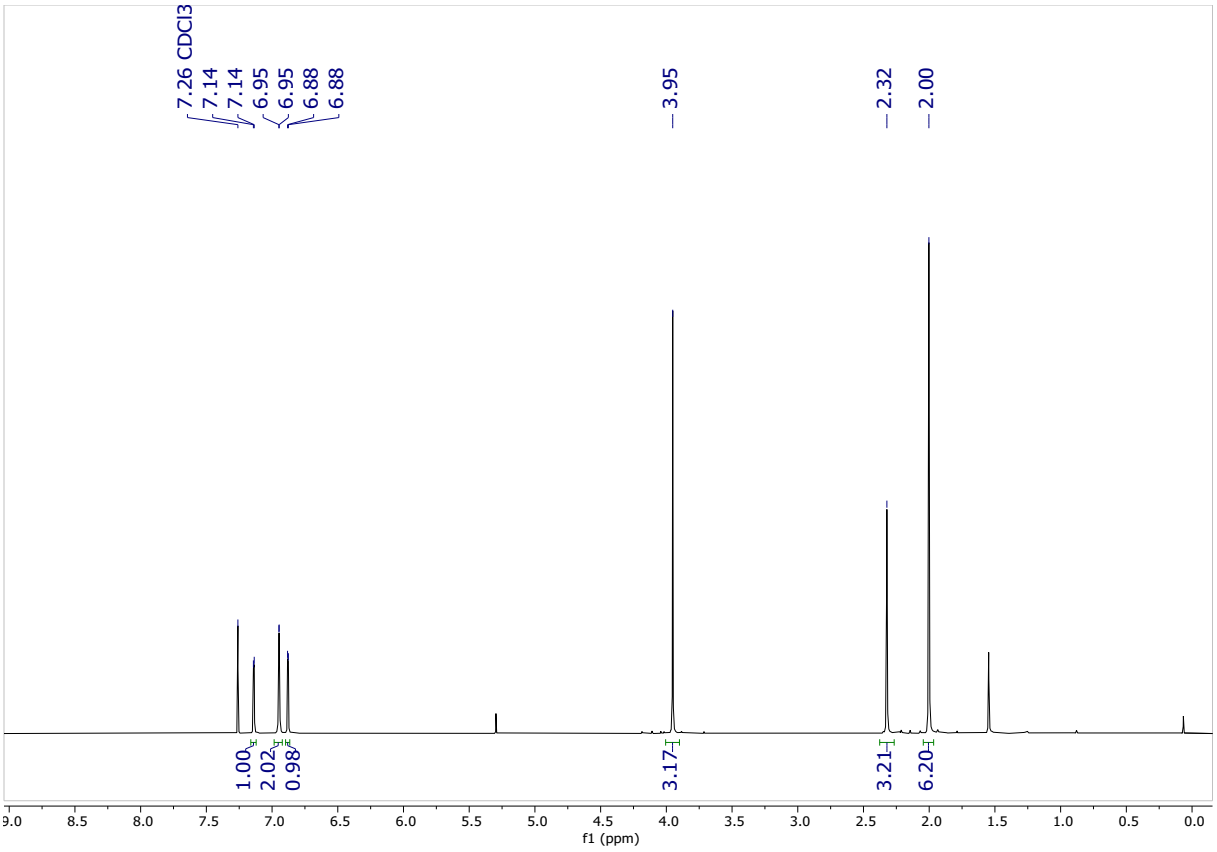
^{1}H NMR of [AuI(MeImDipp)] 18



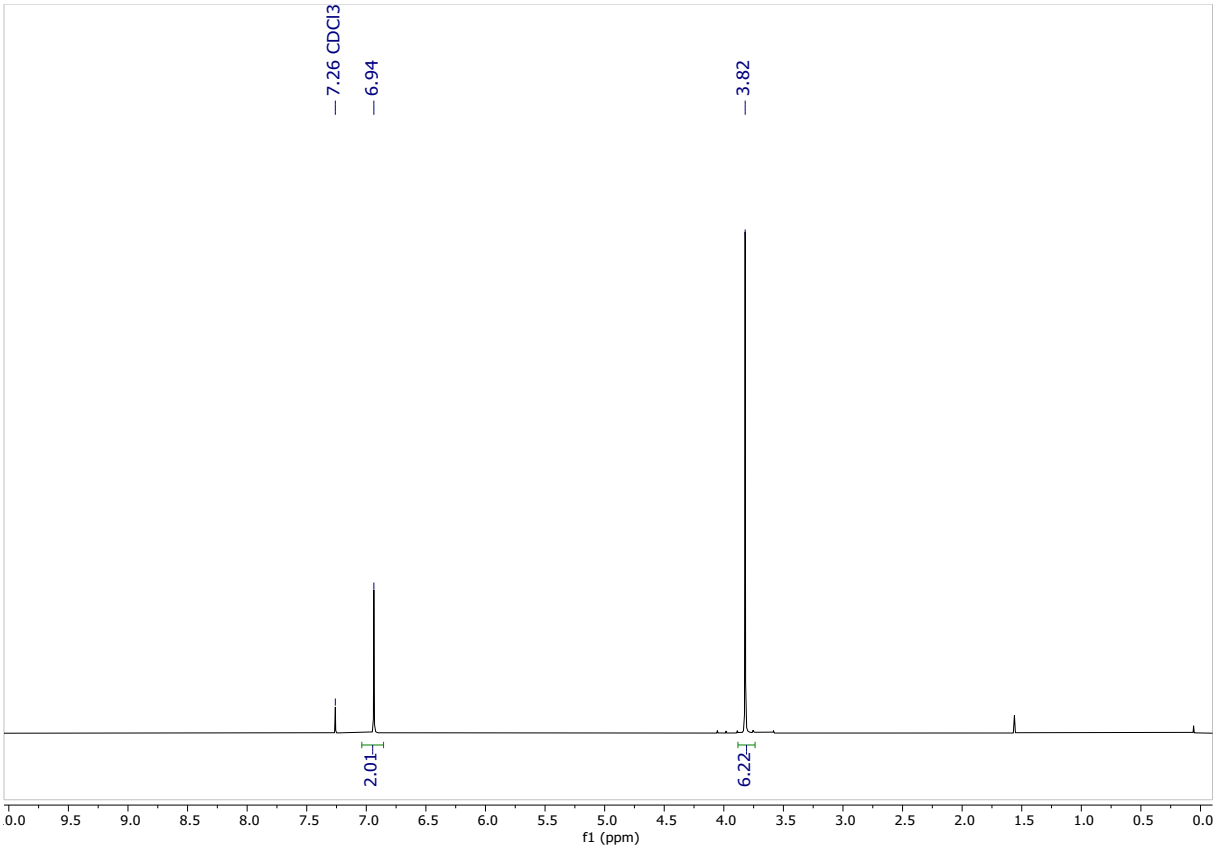
^{1}H NMR of MeImMes HCl



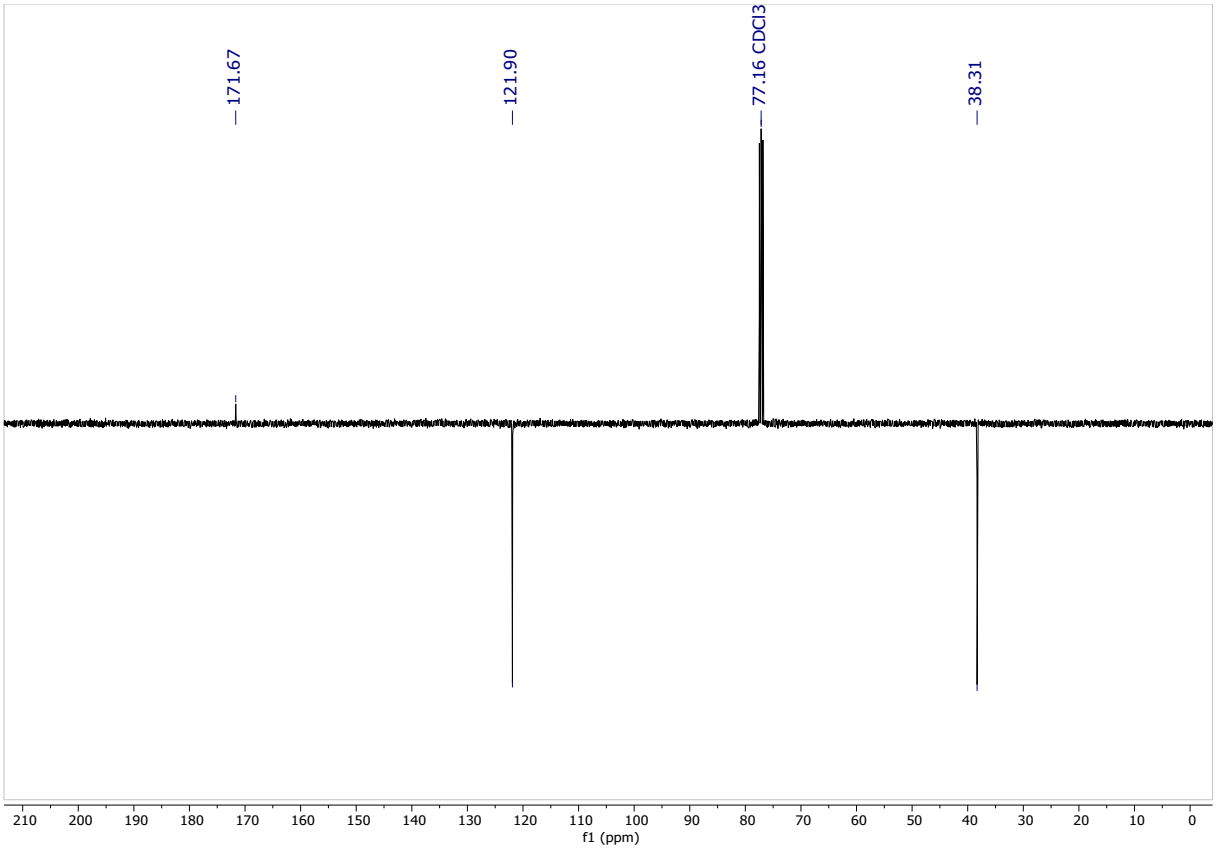
^{1}H NMR of [AuCl(MeImMes)] 19



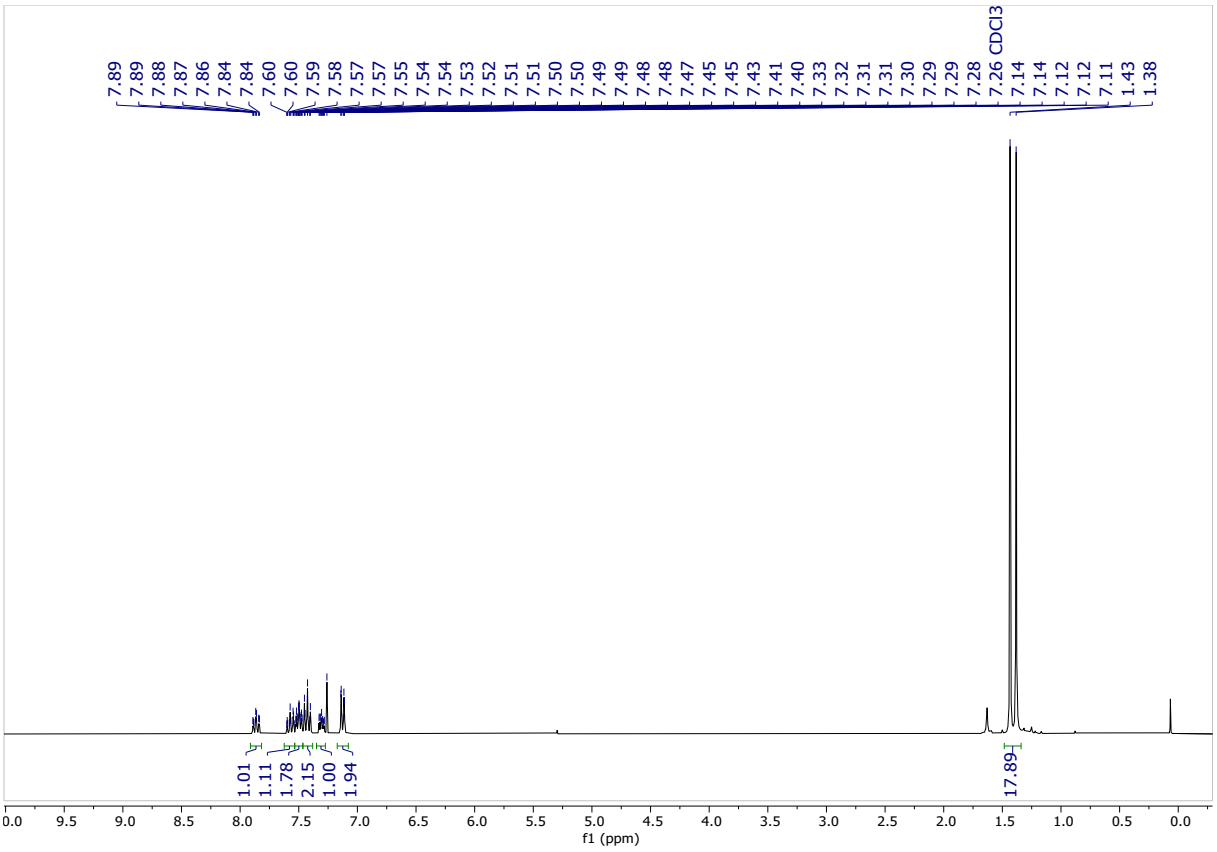
^{1}H NMR of [AuCl(IMe)] 20



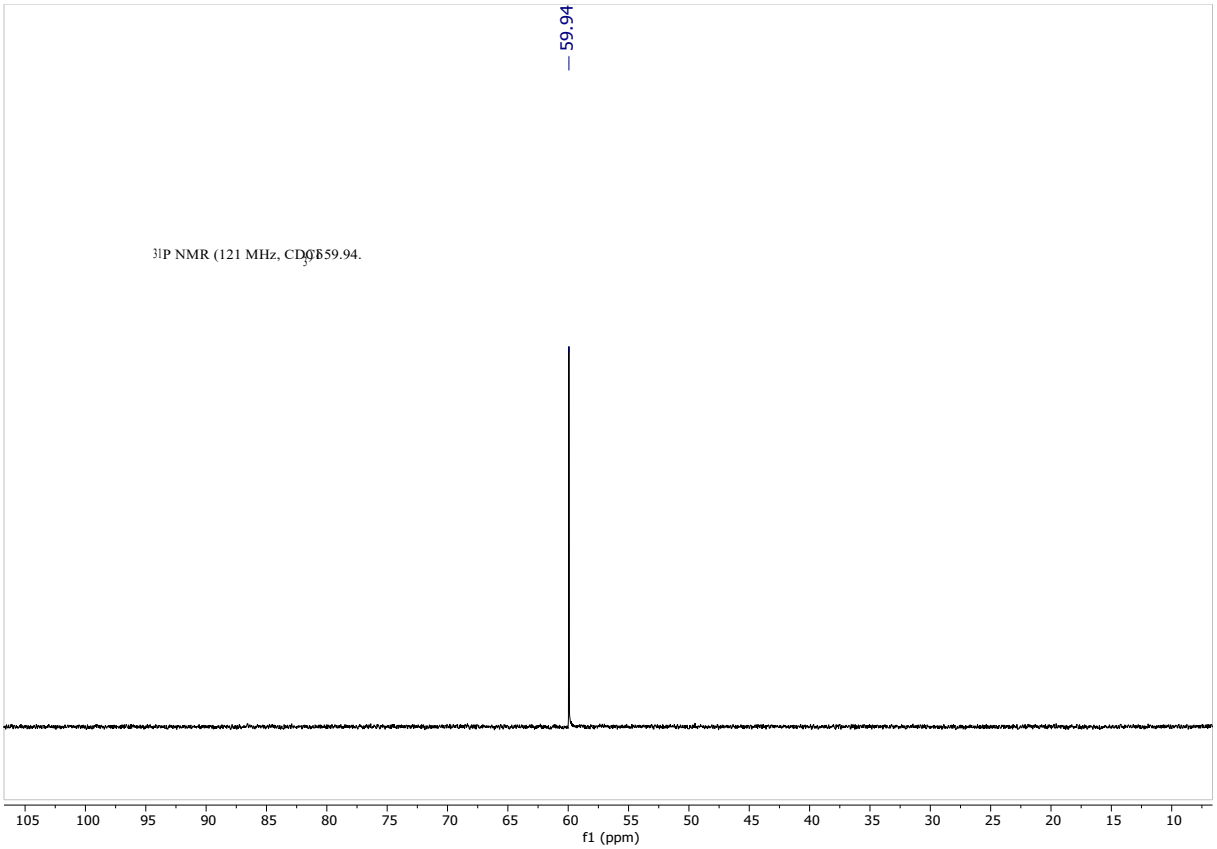
^{13}C NMR of [AuCl(IMe)] 20



^{1}H NMR of [AuCl(JohnPhos)] 21

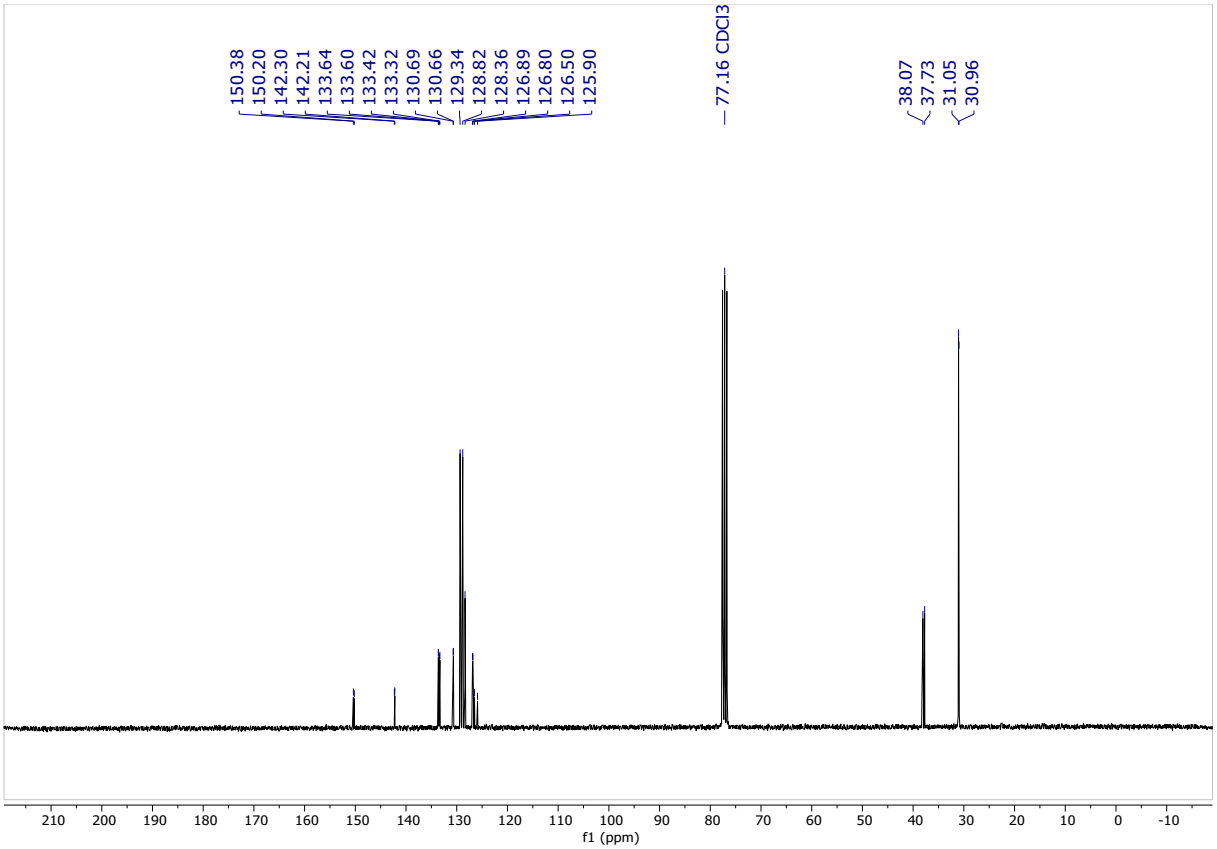


^{31}P NMR of [AuCl(JohnPhos)] 21

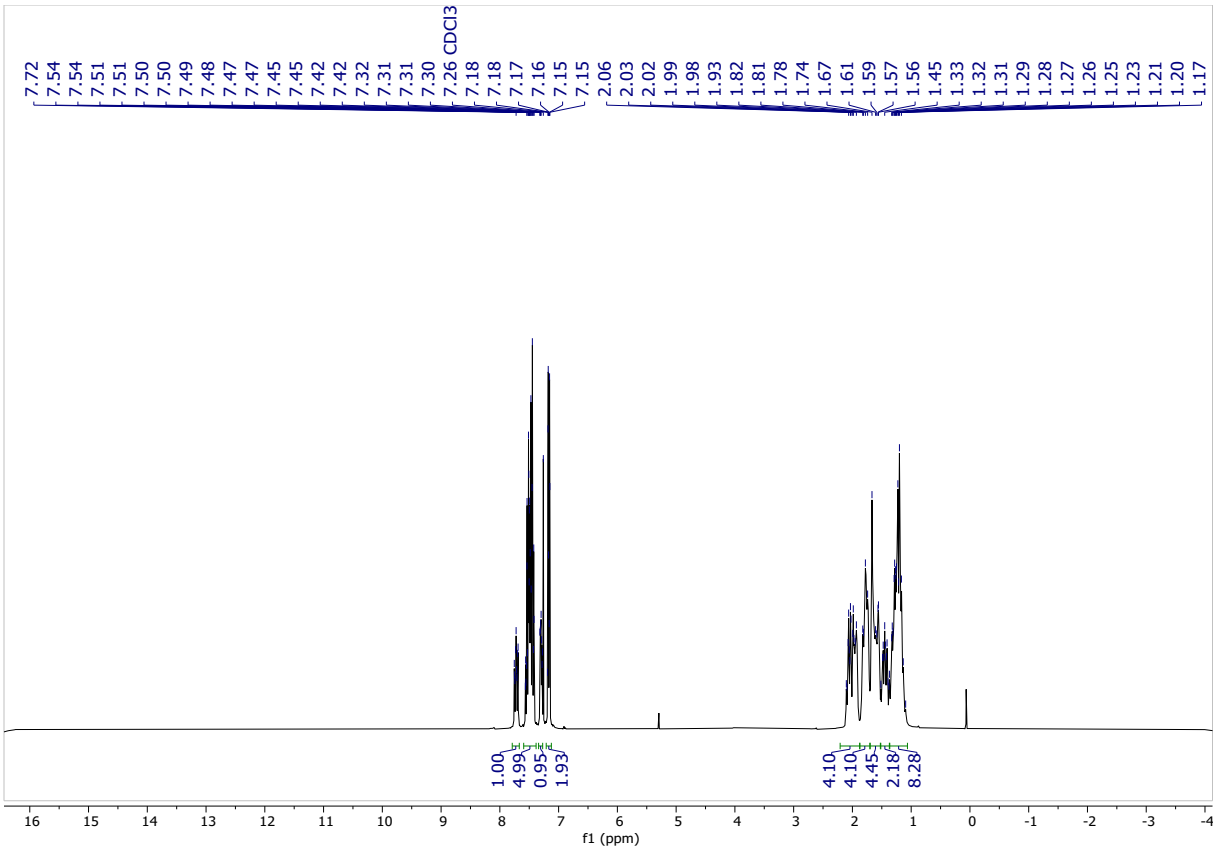


^{31}P NMR (121 MHz, CD_3CN) δ 59.94.

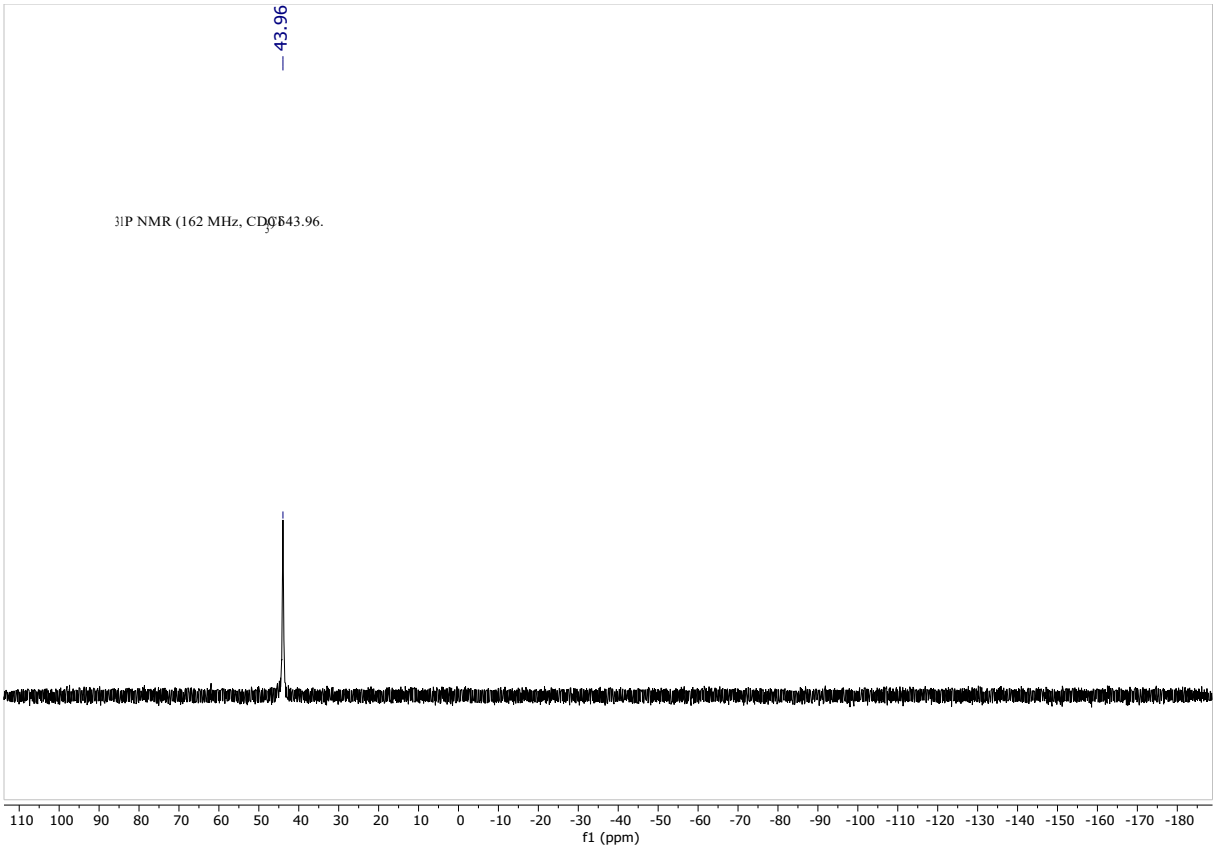
^{13}C NMR of [AuCl(JohnPhos)] 21



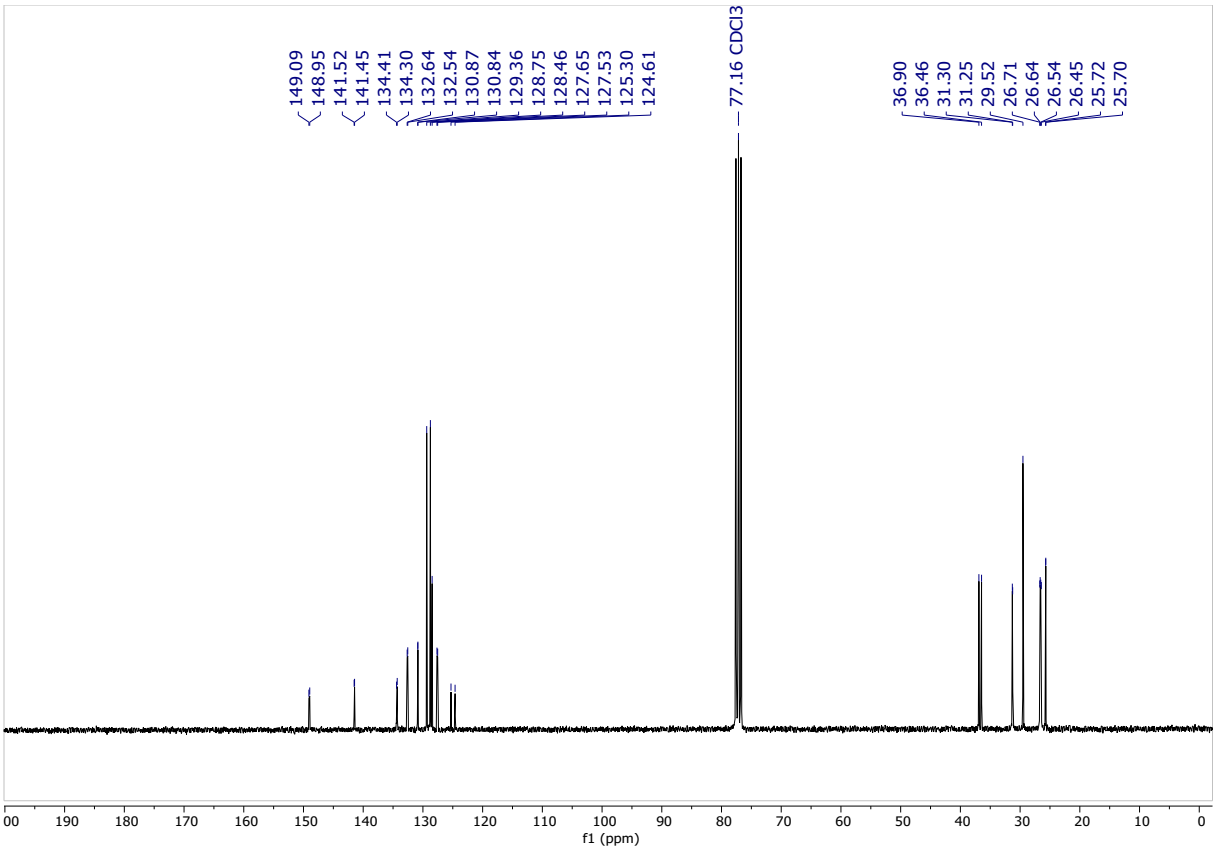
^{1}H NMR of [AuCl(CyJohnPhos)] 22



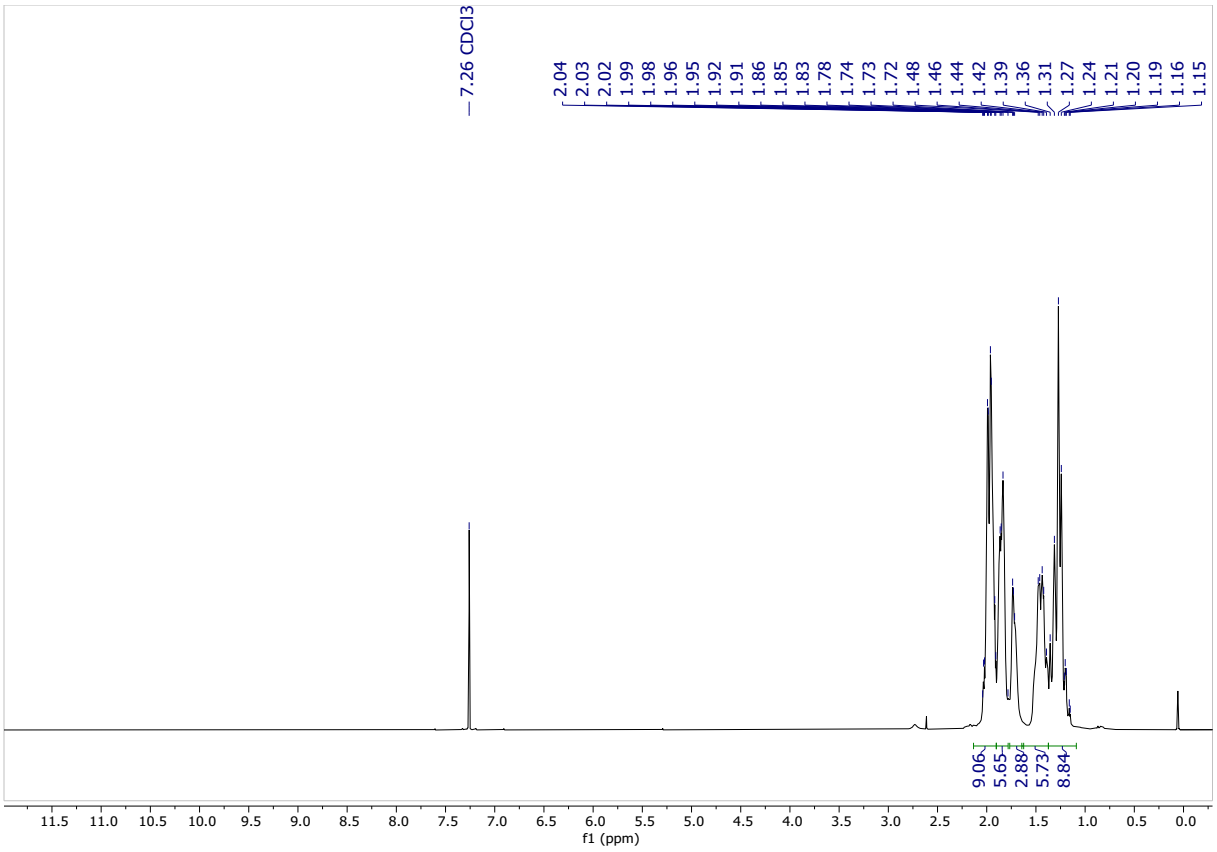
^{31}P NMR of [AuCl(CyJohnPhos)] 22



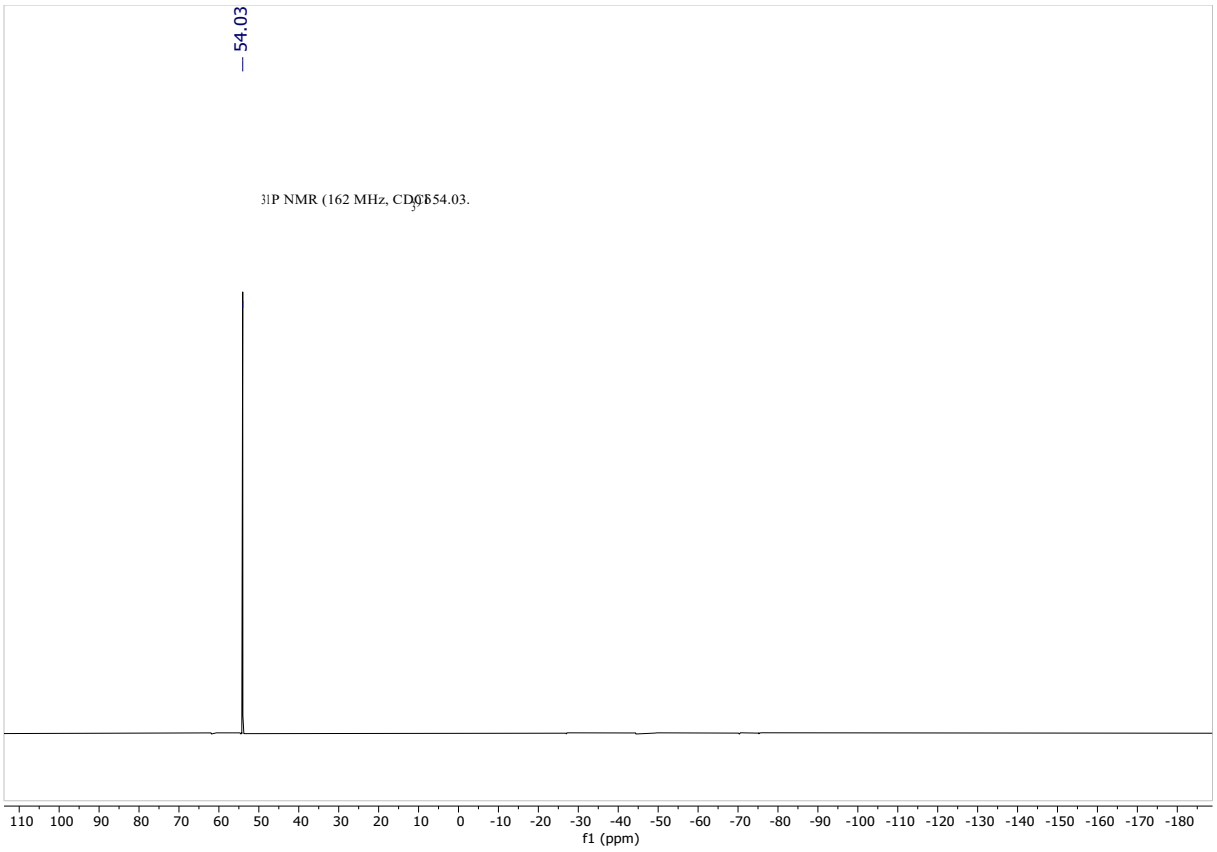
^{13}C NMR of [AuCl(CyJohnPhos)] 22



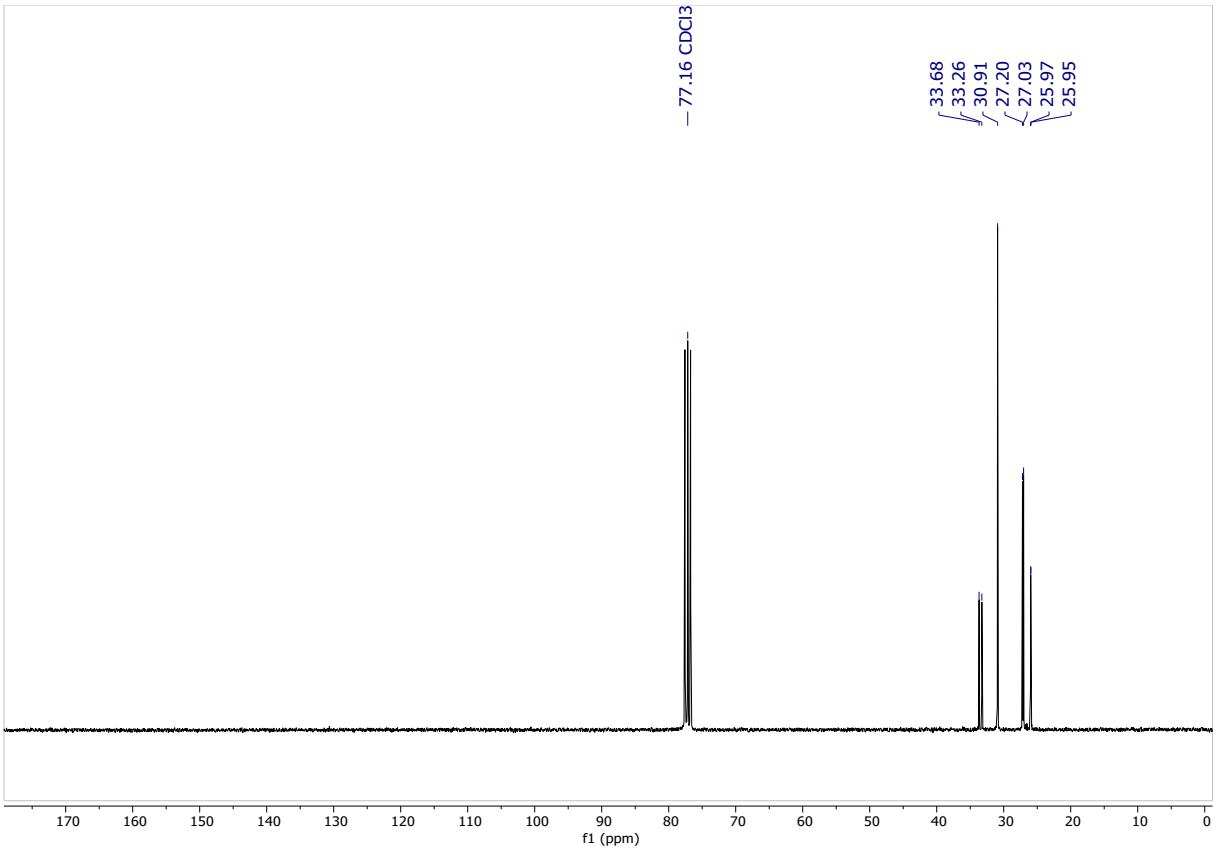
^{1}H NMR of [AuCl(PCy$_3$)] 23



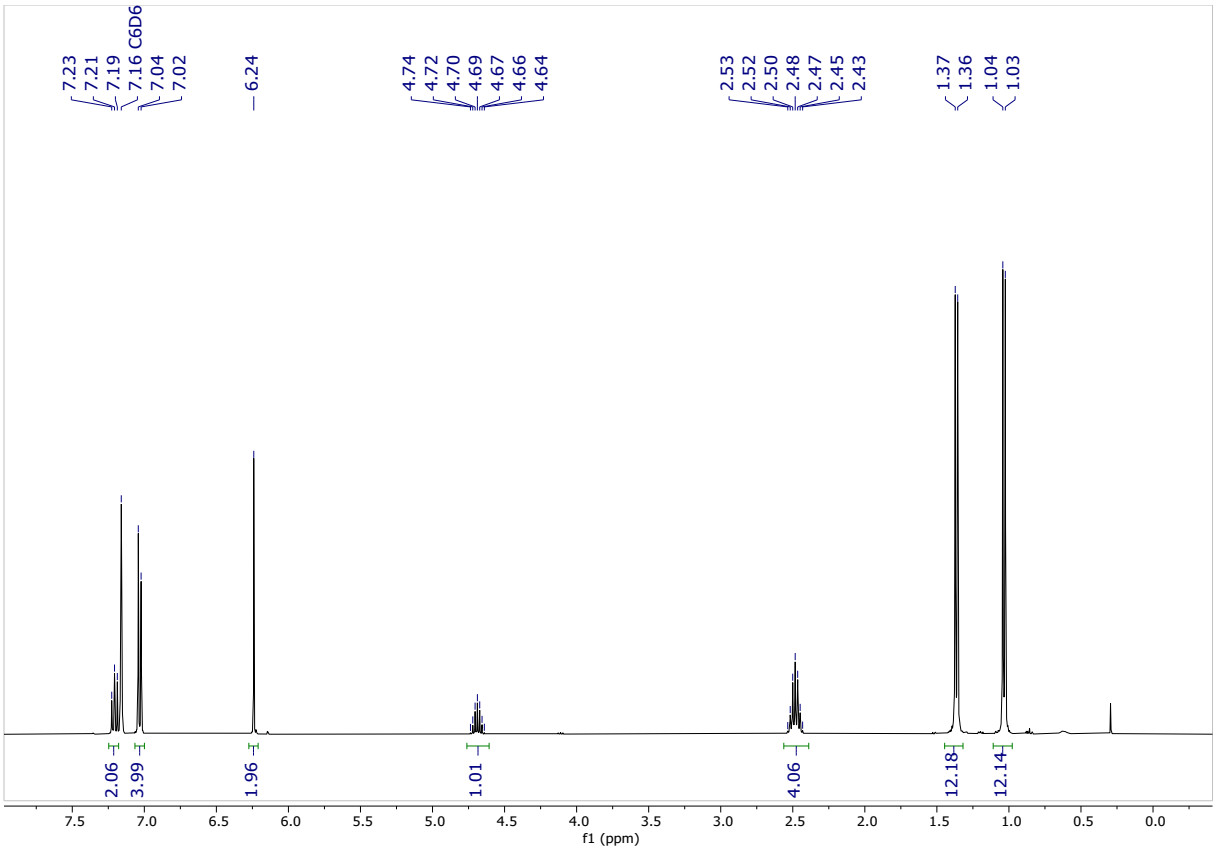
^{31}P NMR of [AuCl(PCy_3)] 23



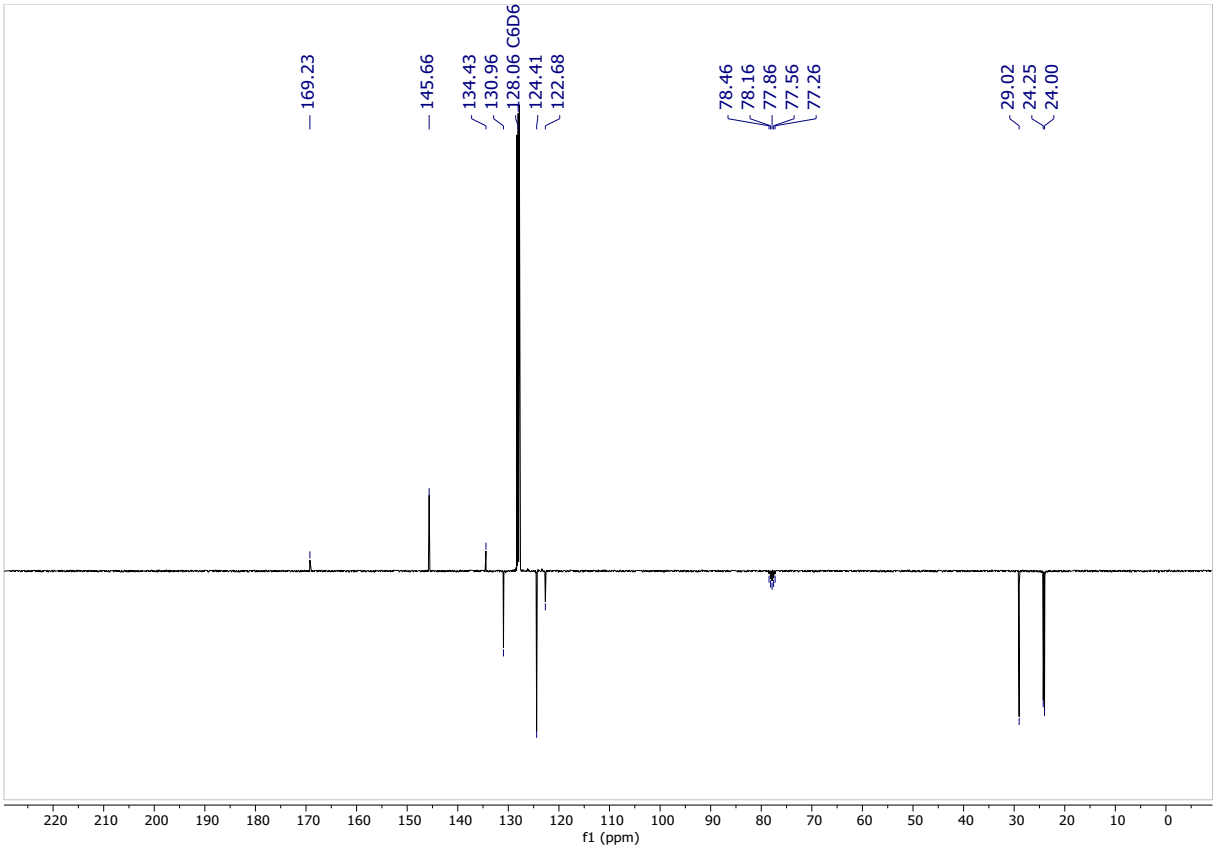
^{13}C NMR of [AuCl(PCy$_3$)] 23



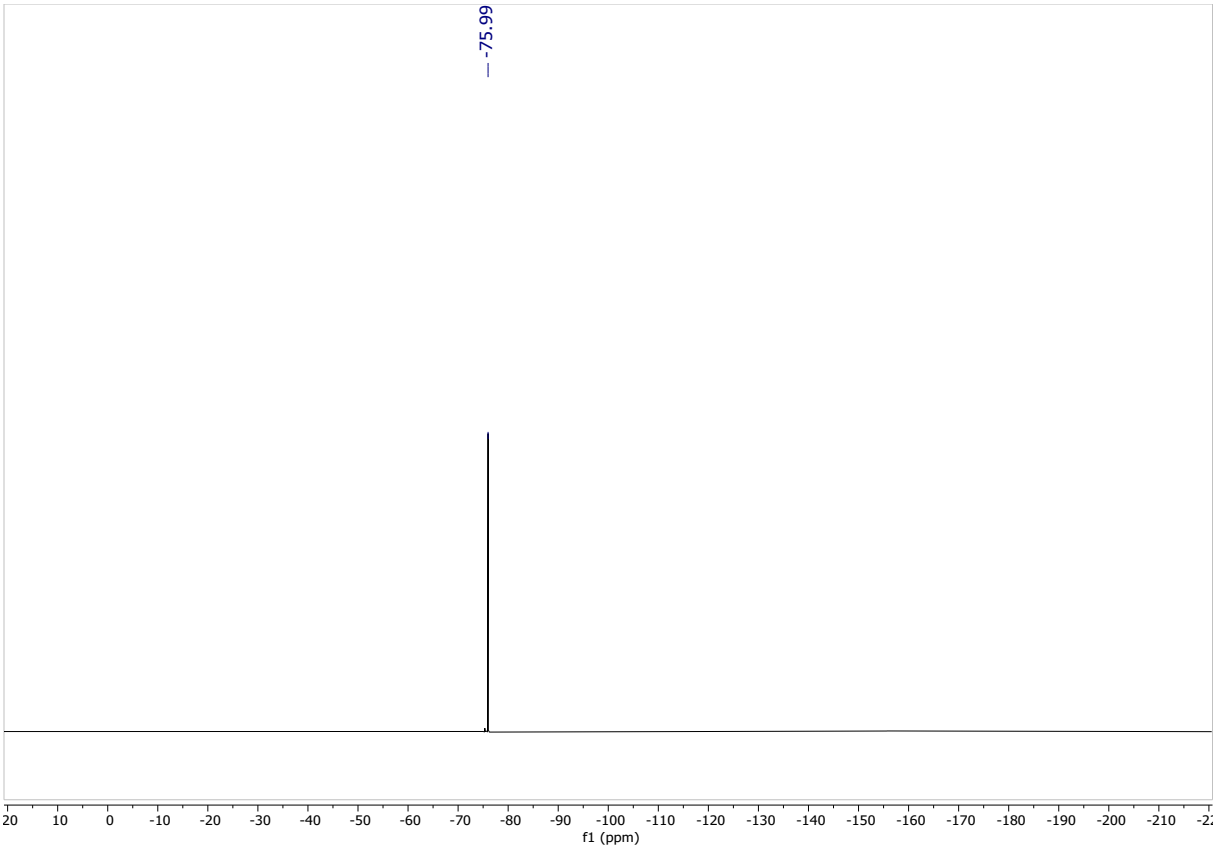
^{1}H NMR of [AuOCH(CF$_3$)$_2$(IPr)] 28



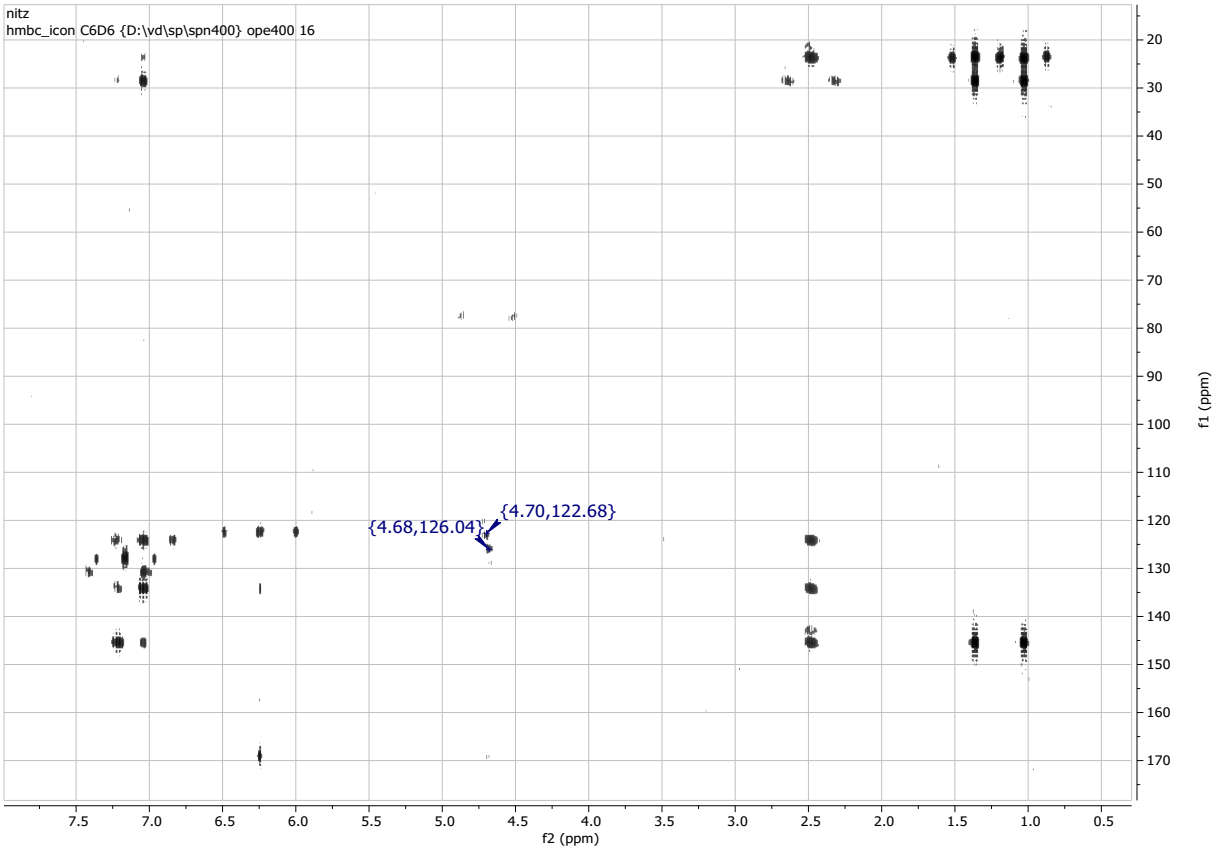
^{13}C NMR of [AuOCH(CF$_3$)$_2$(IPr)] 28



^{19}F NMR of [$AuOCH(CF_3)_2(IPr)$] 28



2D HMBC of [AuOCH(CF_3)$_2$(IPr)] 28 showing the chemical shift of the CF_3 groups by correlation to the O-C*H* signal



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