Palladacycle Promoted Base Controlled Regio- and Enantioselective Hydrophosphination of 2-Pyridylacrylate/amide and the Cytotoxicity of their Gold Complexes

Yuxiang Jia,[a] Renta Jonathan Chew,[a] BinBin Li,[a] Pengcheng Zhu,[b] Yongxin Li,[a] Sumod A. Pullarkat,[a] Nguan Soon Tan*[b,c] and Pak-Hing Leung**[a]

[a]*Division of Chemistry & Biological Chemistry, School of Physical and Mathematical Sciences, Nanyang Technological University, Singapore 637371, Singapore*

[b]*School of Biological Sciences, Nanyang Technological University, Singapore 637551, Singapore*

[c]*Institute of Molecular and Cell Biology, 61 Biopolis Drive, Proteos, 138673, Singapore*

* E-mail: nstan@ntu.edu.sg

**E-mail: pakhing@ntu.edu.sg

Supporting Information

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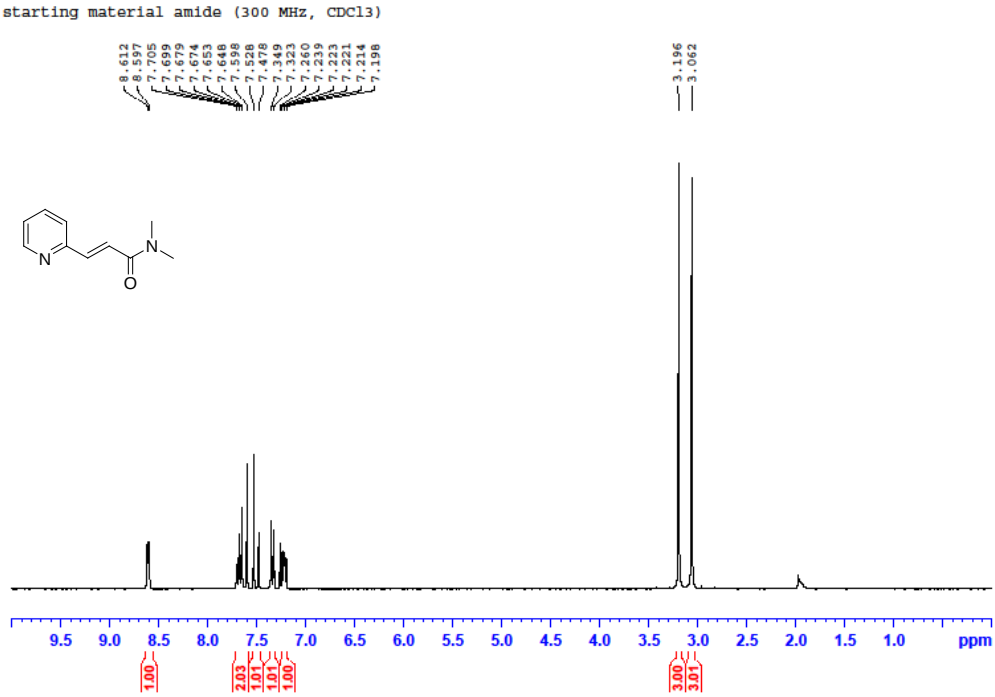
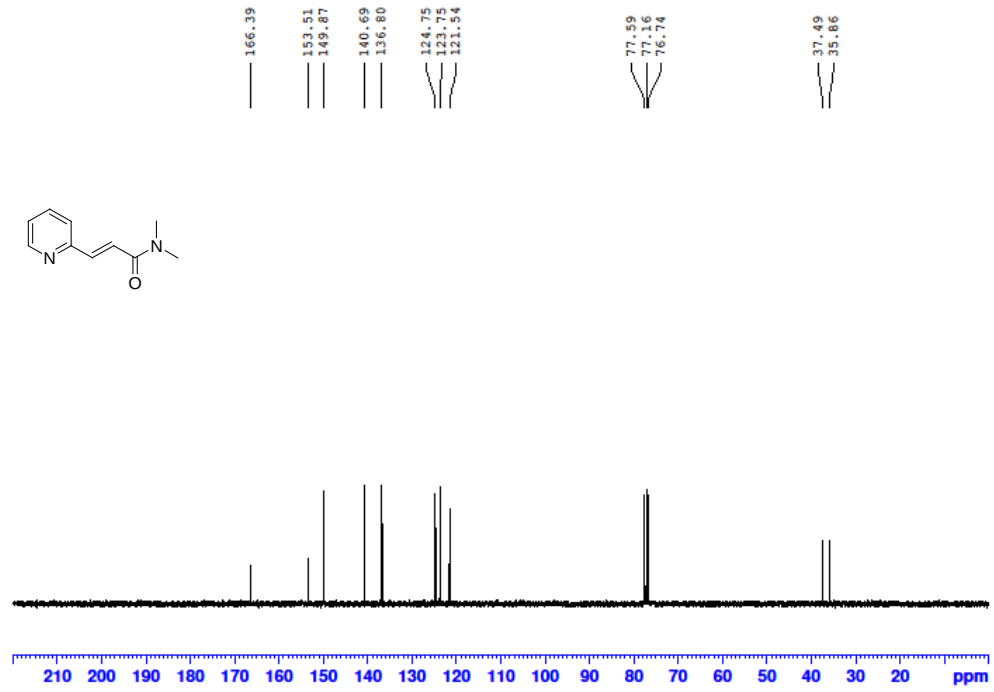
I. NMR spectra





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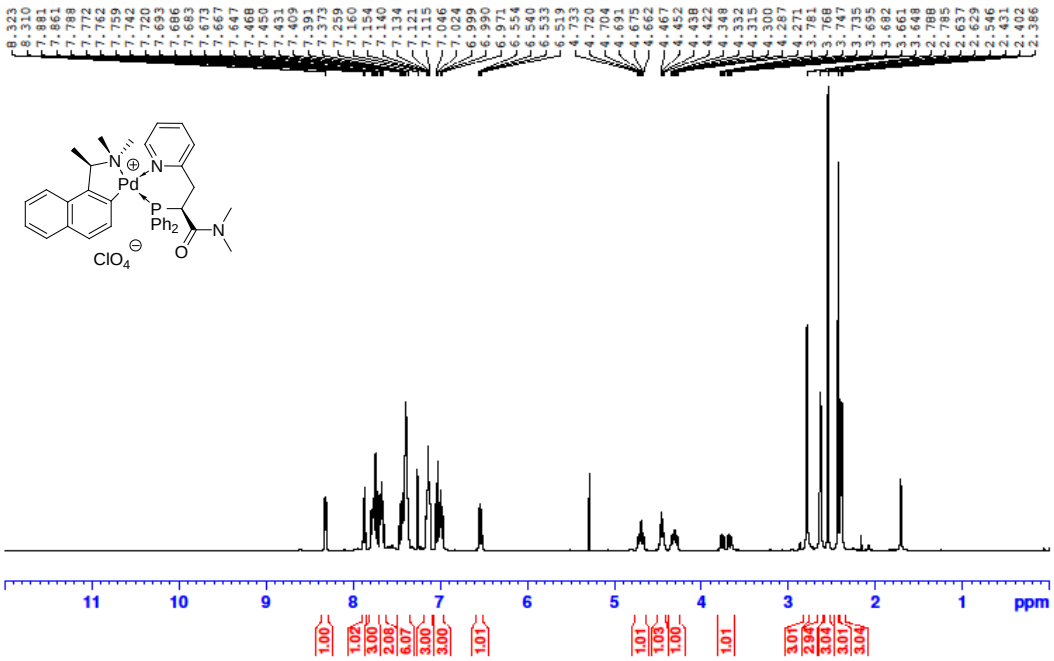

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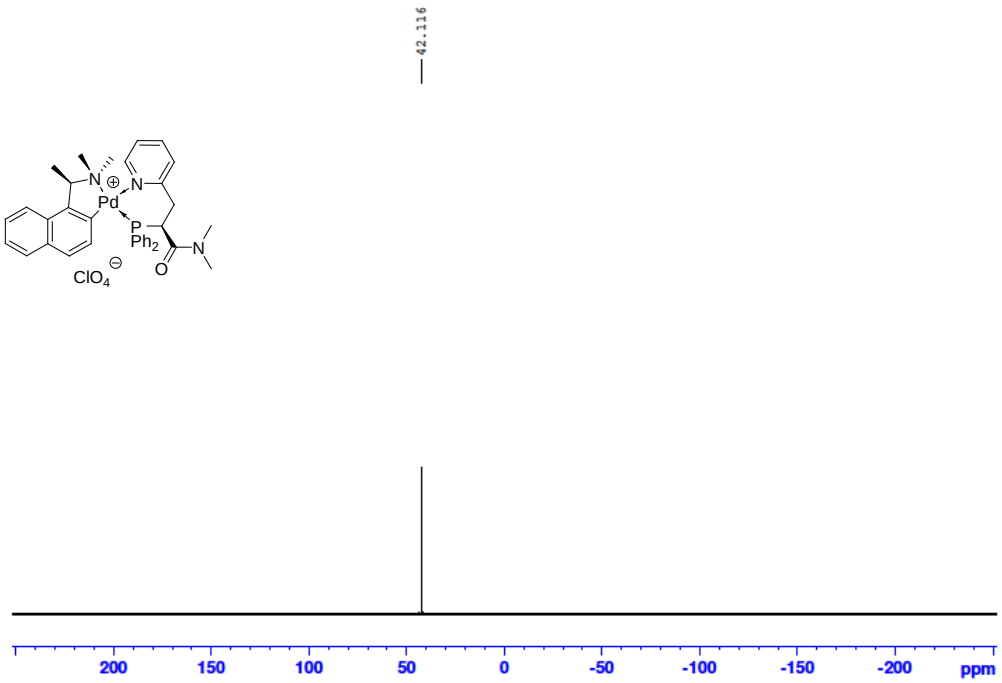

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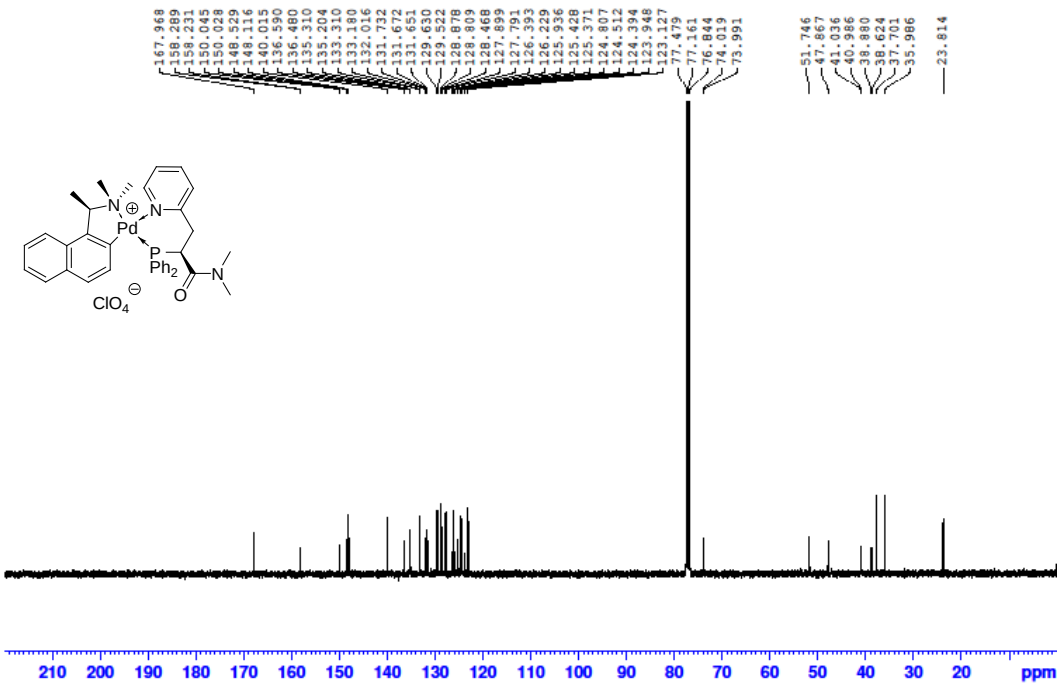

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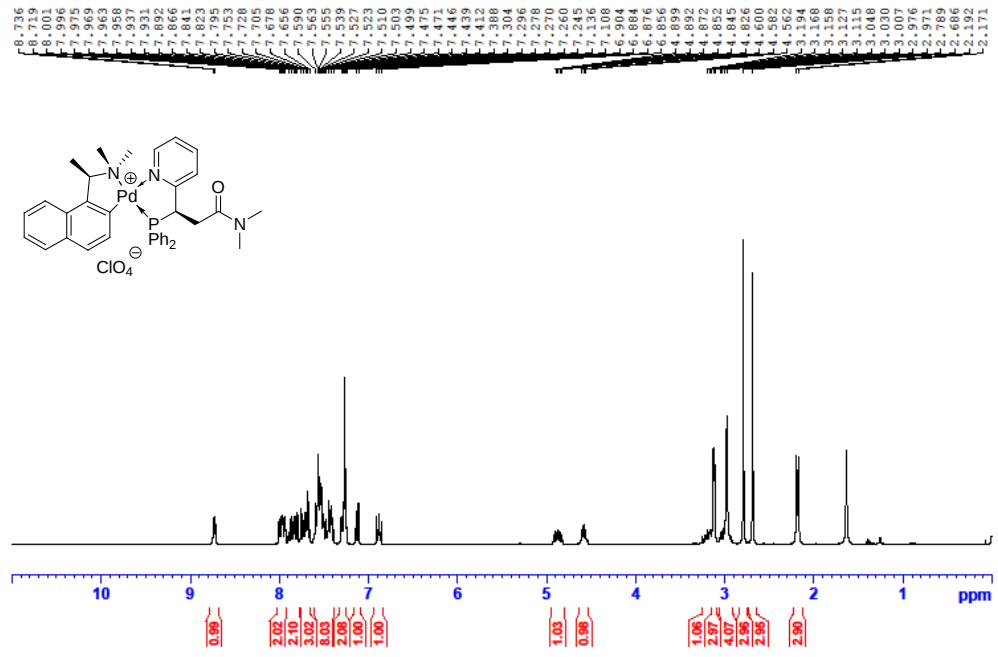

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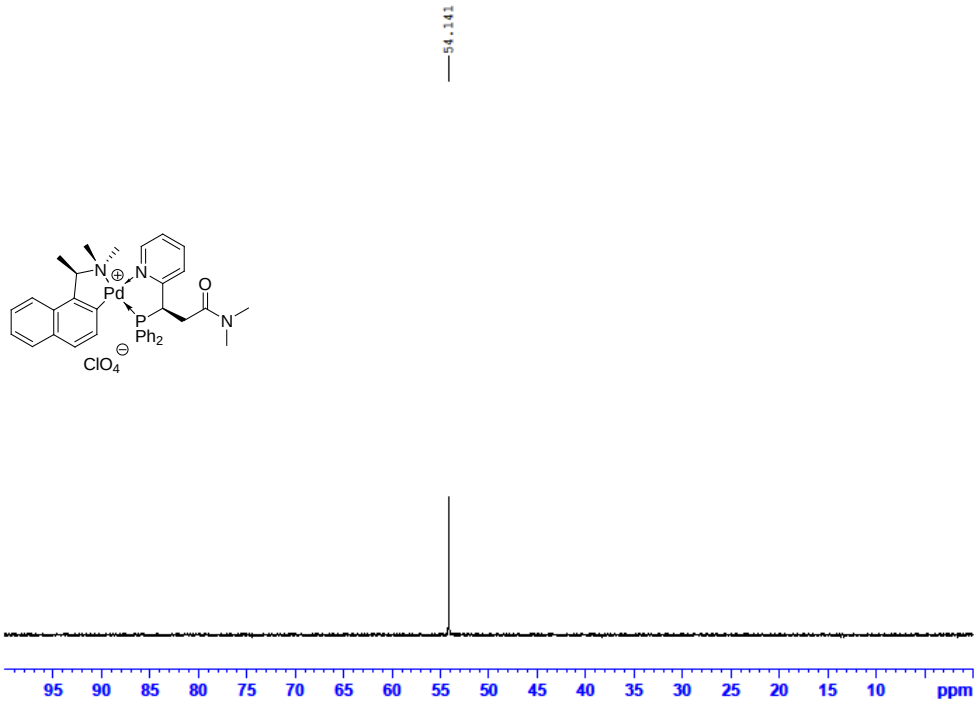

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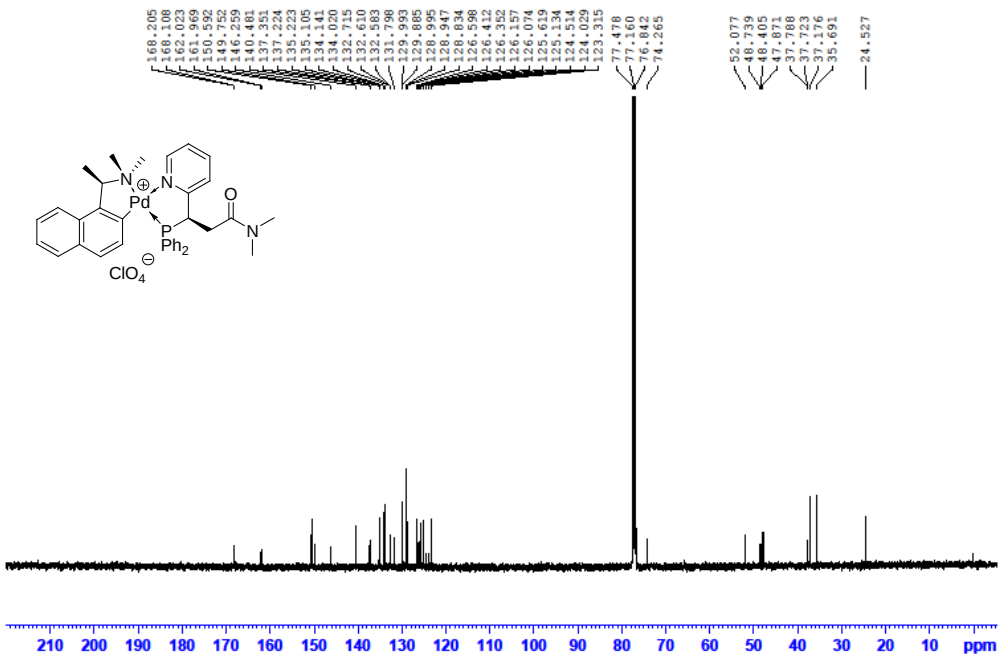

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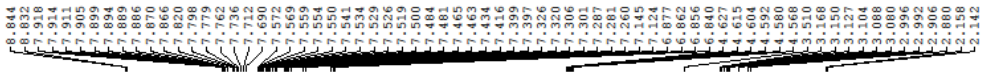

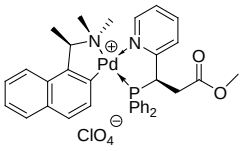

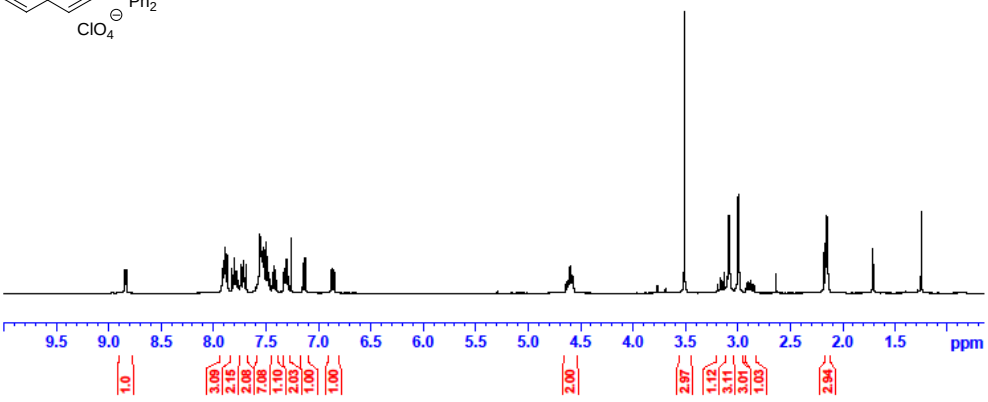

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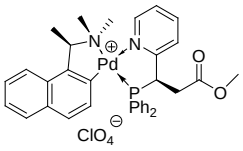

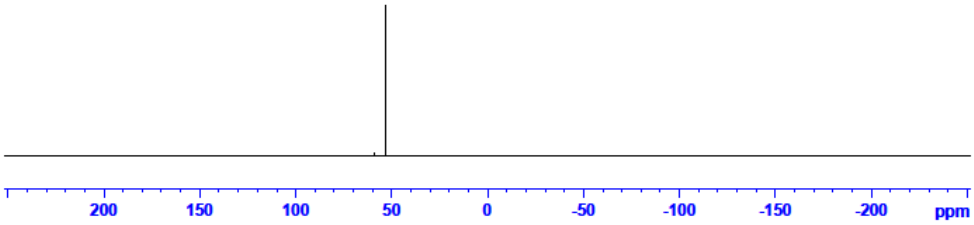

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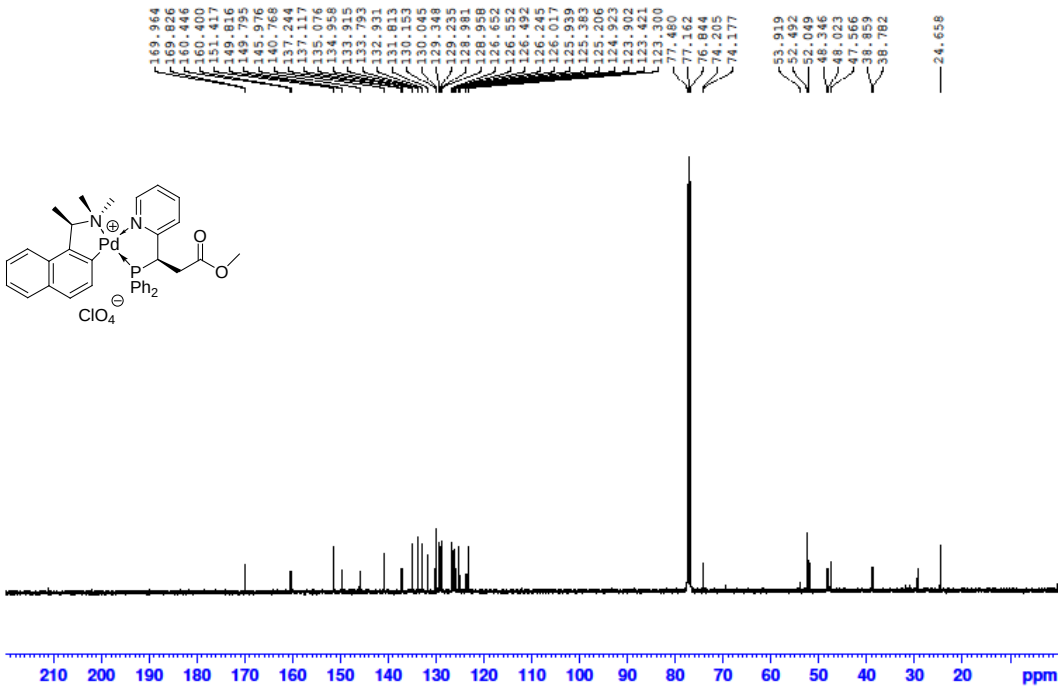

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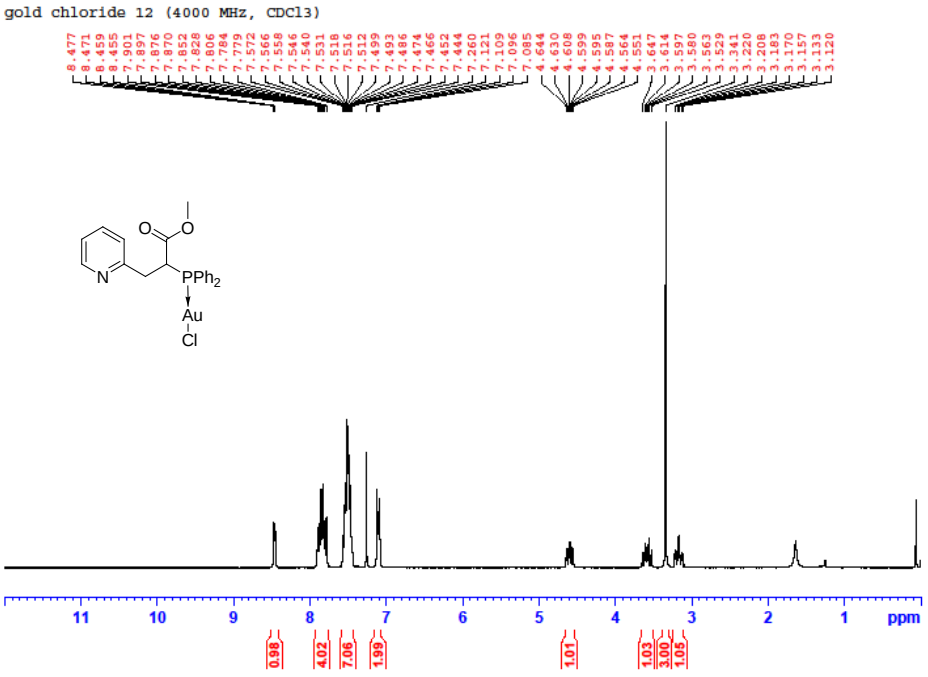

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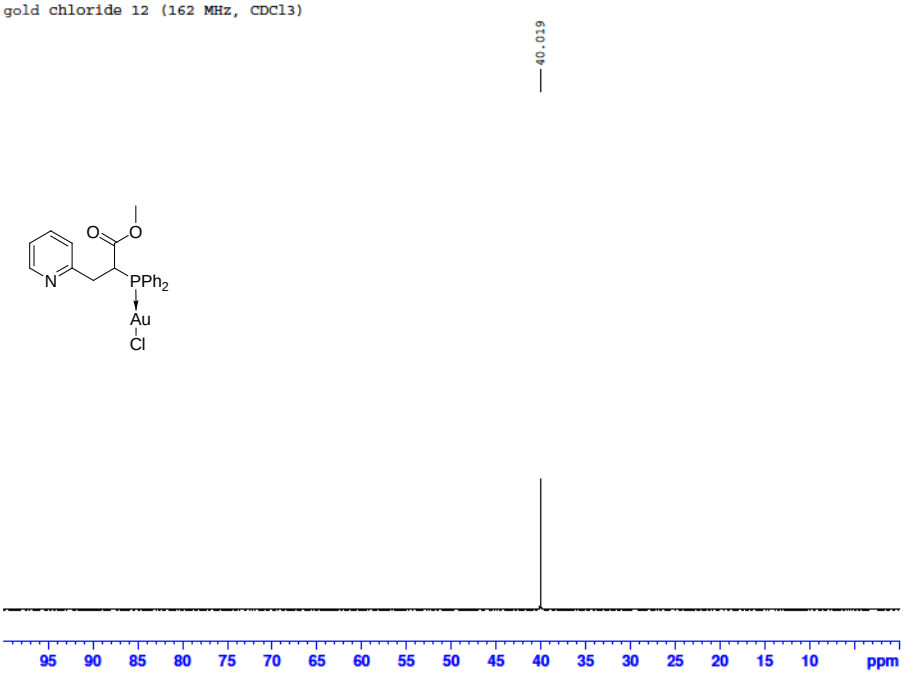

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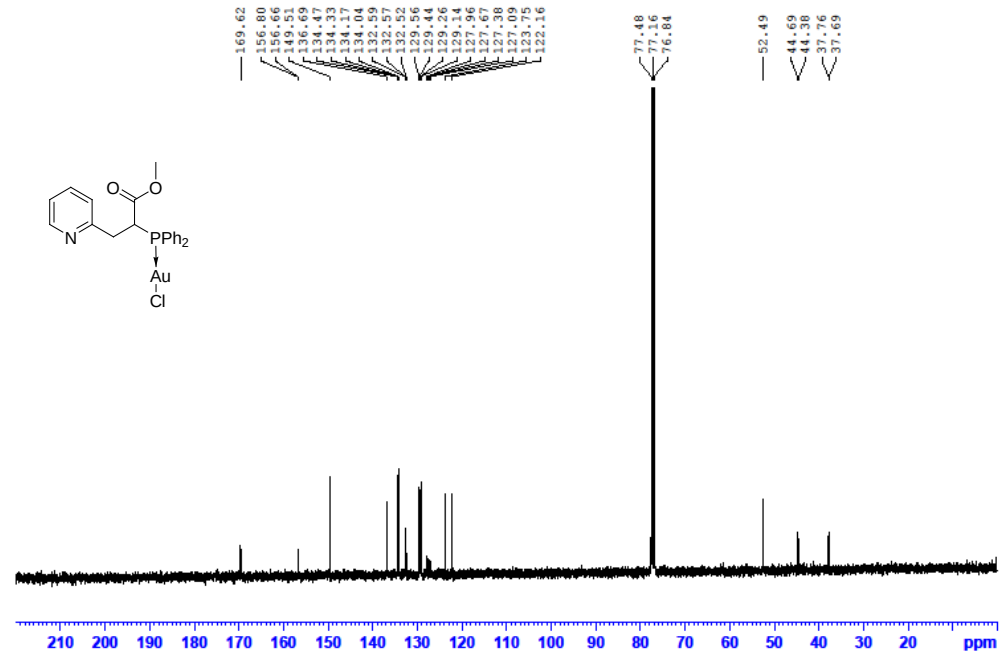

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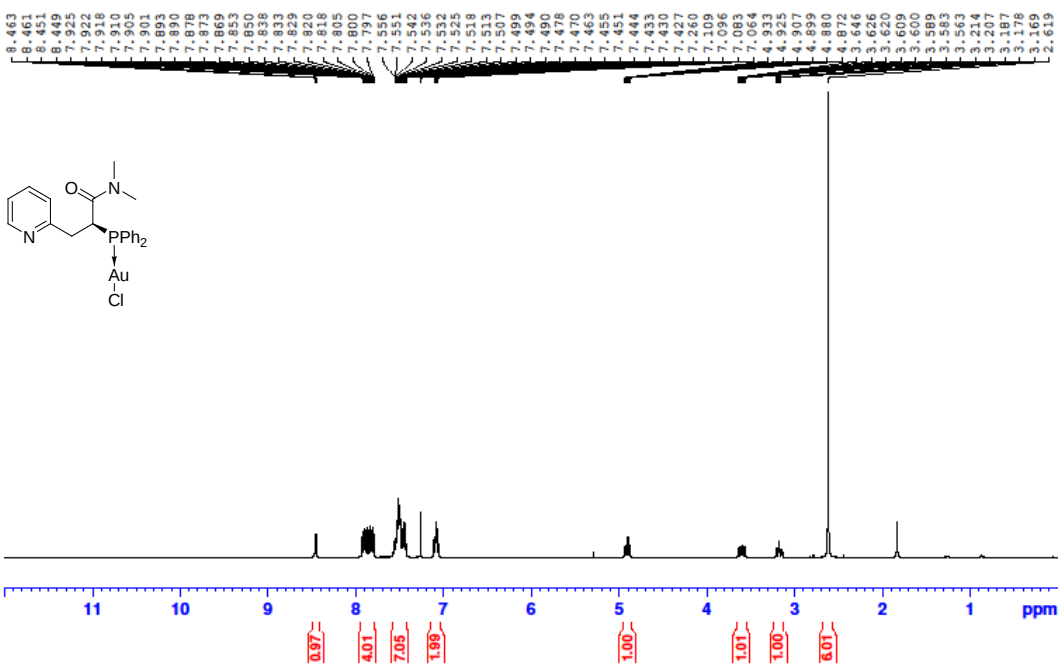

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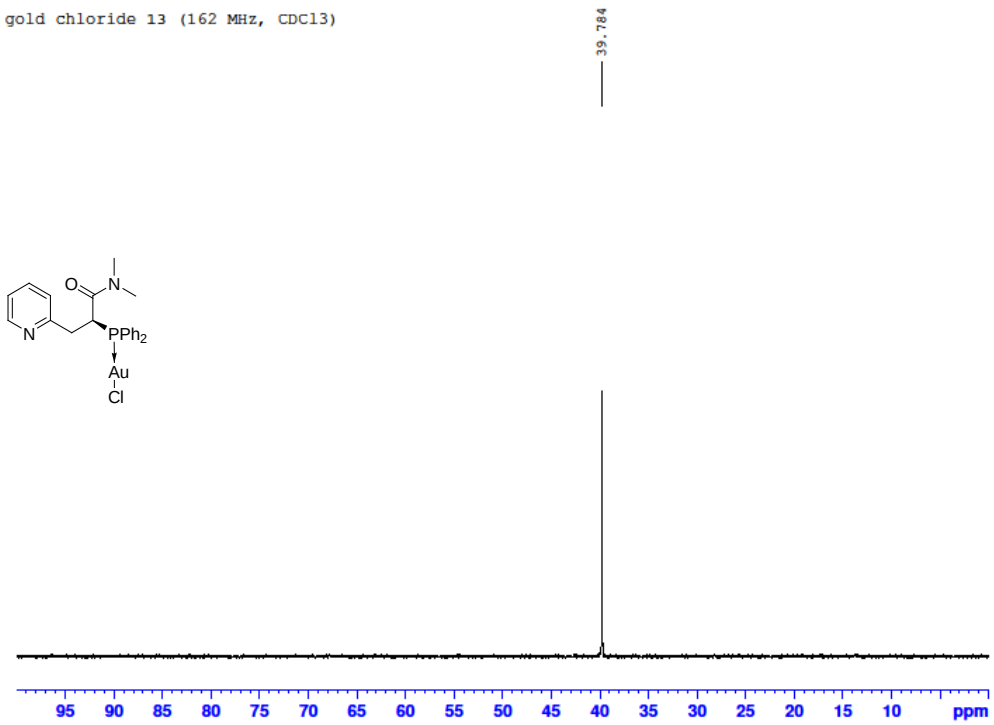

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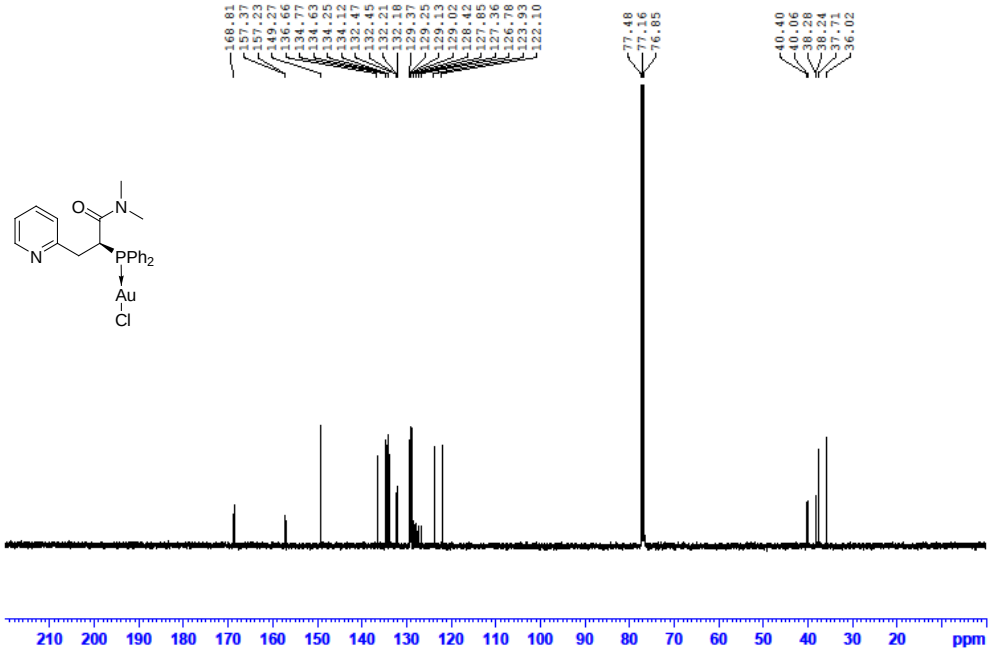

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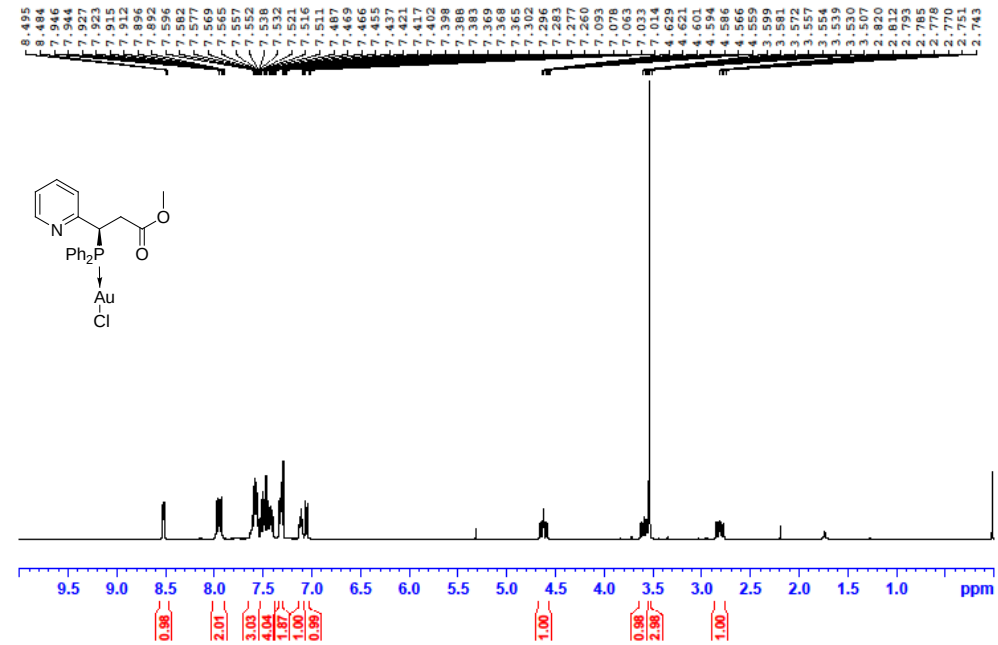

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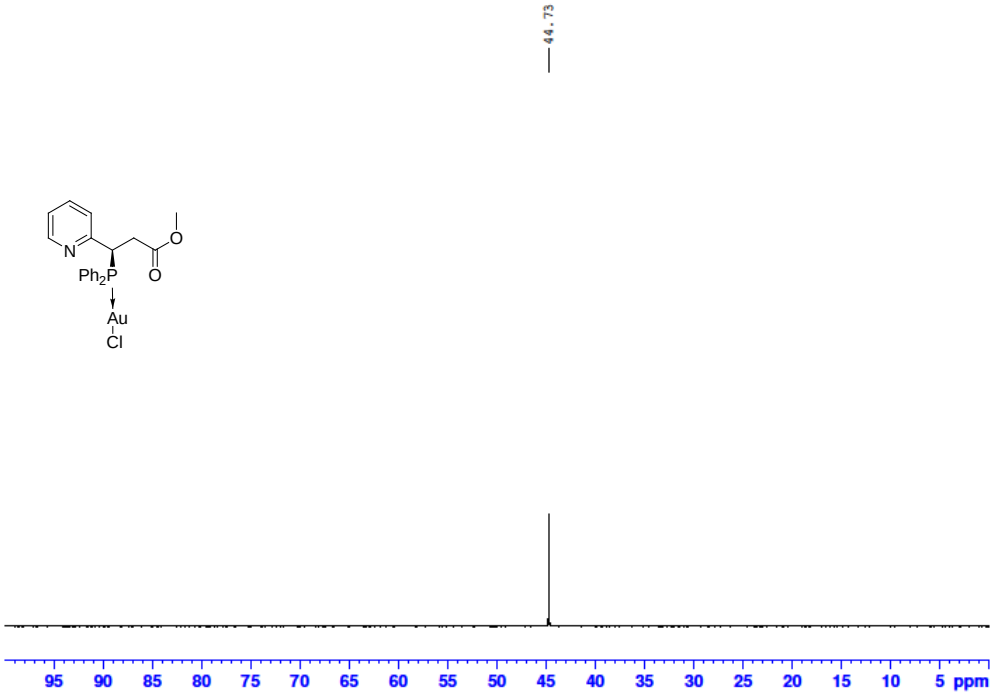

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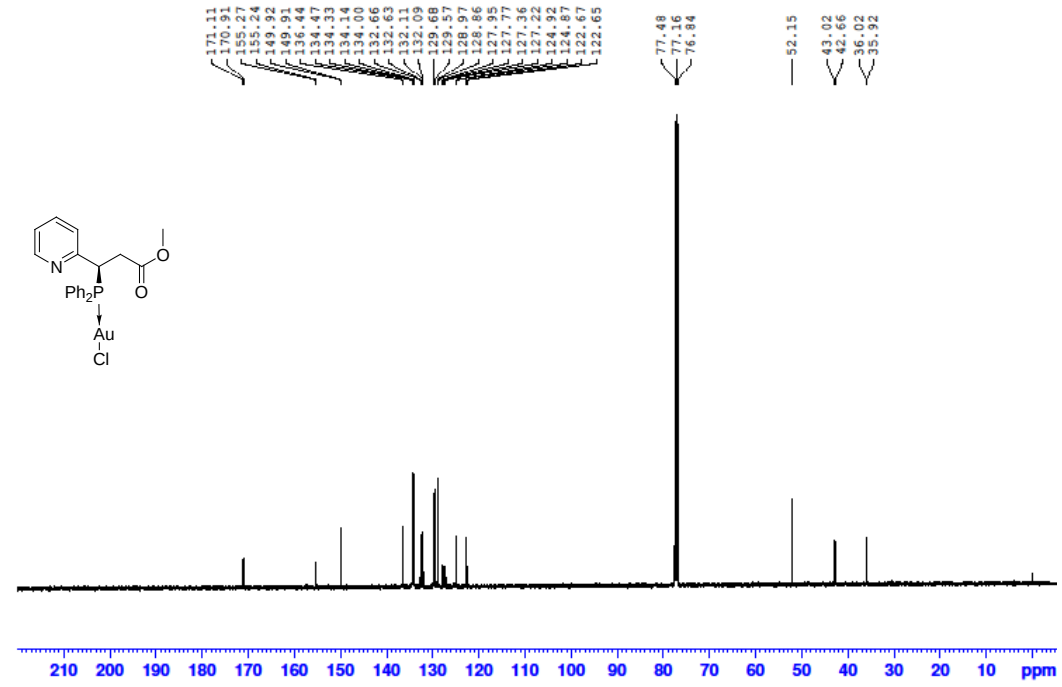

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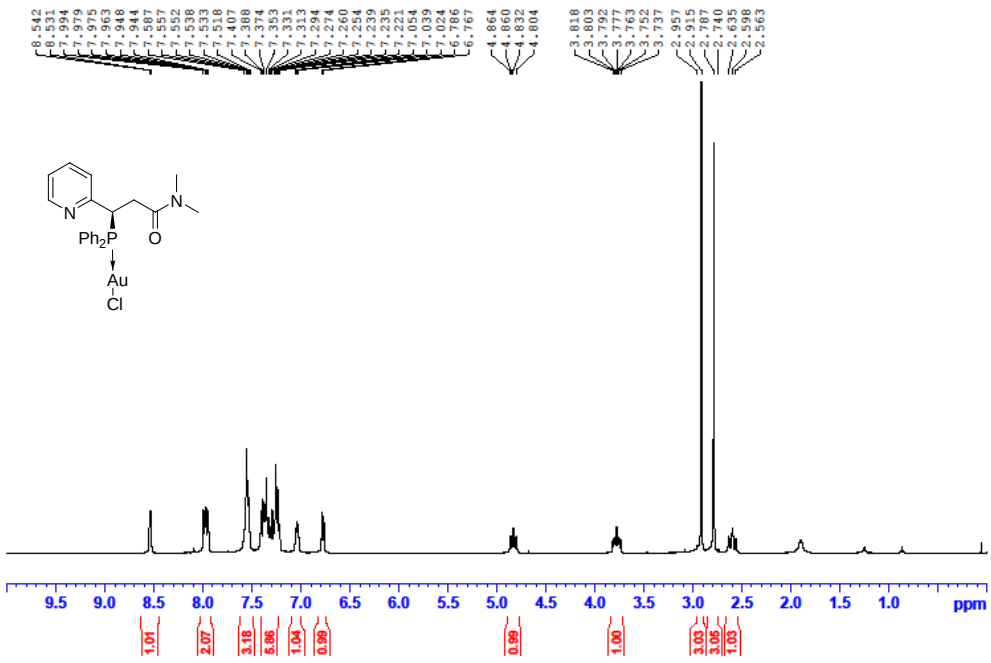

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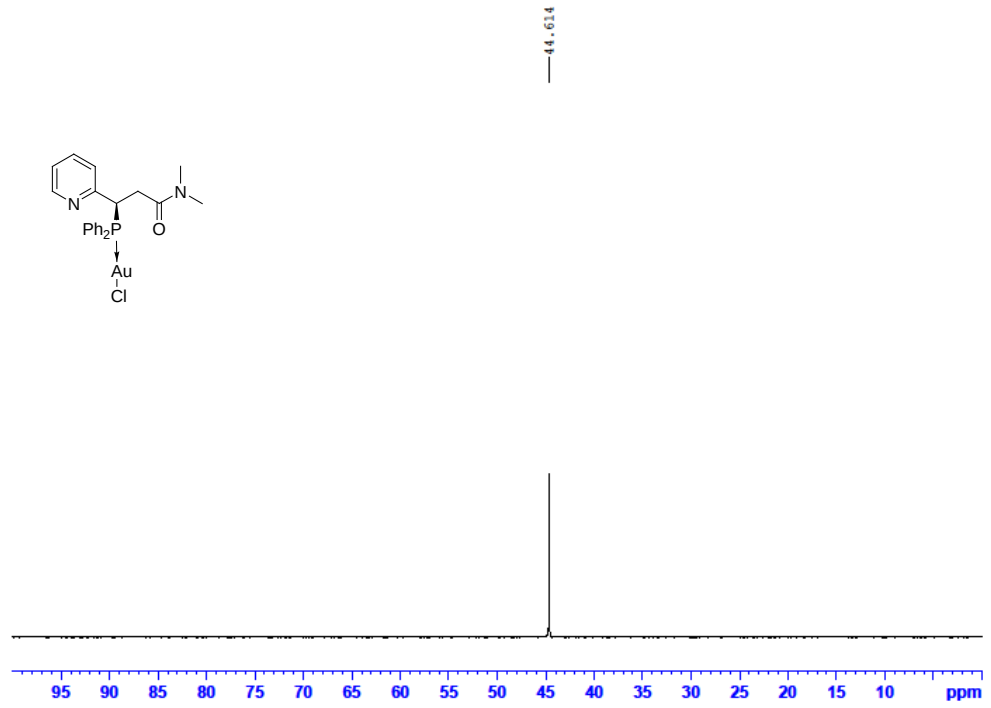

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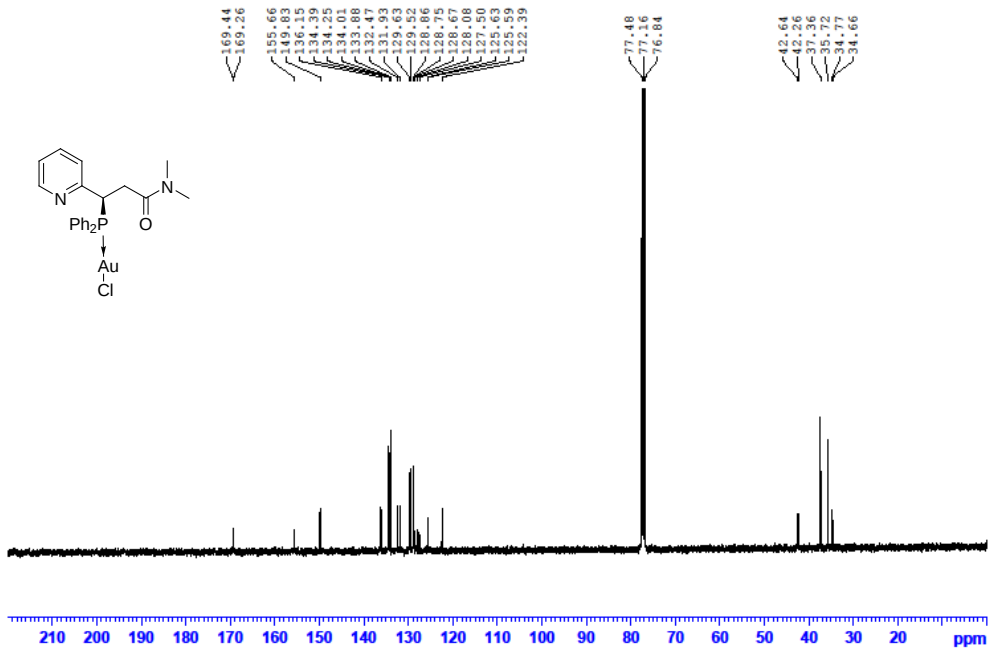
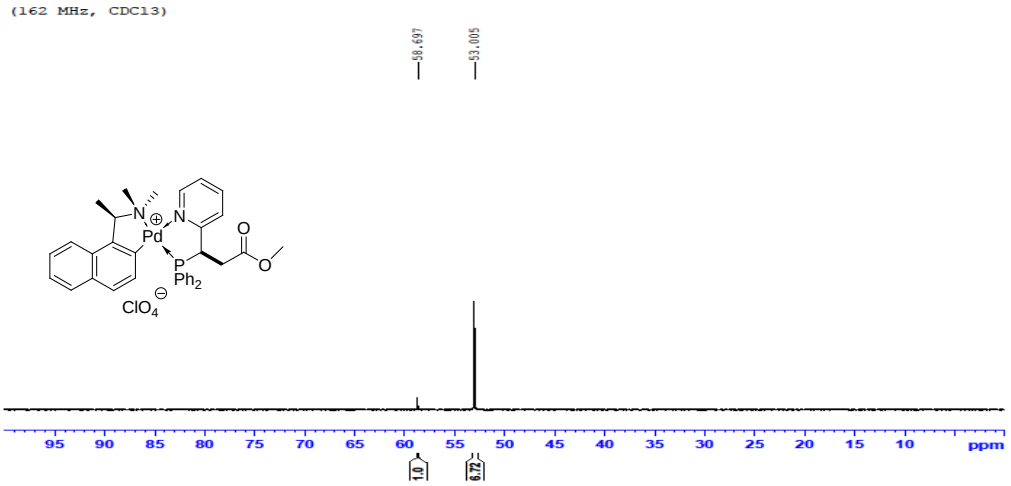


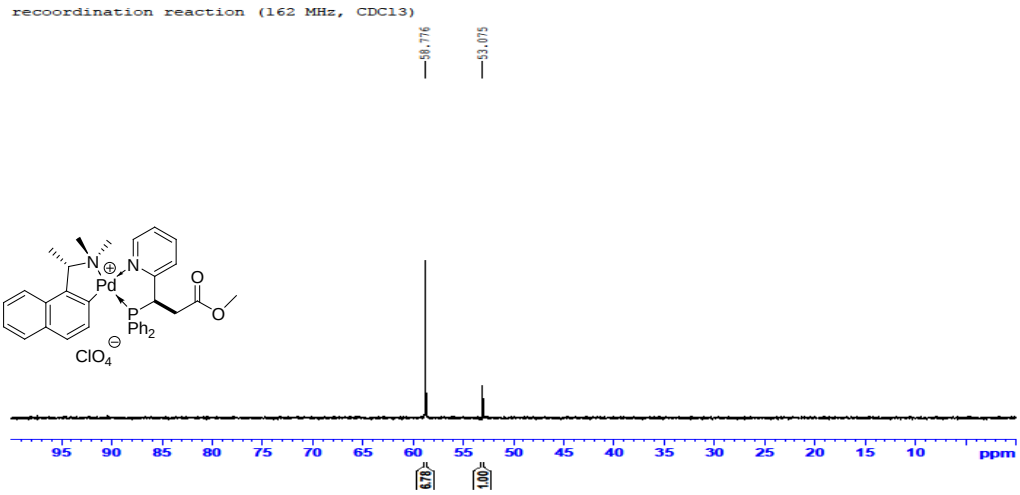
Recoordination reaction

To a solution of **6** (10 mg, 0.013 mmol)) in dichloromethane (2 mL) was added aqueous solution of potassium cyanide (excessive, 2 mL). The reaction mixture was stirred for 10 min. The aqueous phase was removed and (*S*)-1 (19.0 mg, 0.039 mmol) was added and stirred for 30 min. The reaction mixture was concentrated and detected with $^{31}P\{^{1}H\}$ NMR (162 MHz, $CDCl_3$): δ 58.78 (s, 6.78 H), 53.08 (s, 1.00 H).

NMR before liberation:



NMR after coordination:



II. Cytotoxicity test data

Apoptosis Index of MDA-MB-231(%)					
Drug Concentration(μM)	0.5	1.0	1.5	2.0	2.5
Gold Chloride 12	25.0	56.0	58.6	83.1	88.3
Gold Chloride 13	14.5	36.4	46.6	73.7	74.3
Gold Chloride 14	45.3	68.5	92.8	97.4	99.1
Gold Chloride 15	17.9	29.5	52.3	58.1	55.4
Cisplatin	4.9	4.1	6.6	14.7	23.0

Apoptosis Index of MCF-10A (%)					
Drug Concentration(μM)	0.5	1.0	1.5	2.0	2.5
Gold Chloride 12	10.7	22.9	19.0	31.5	39.4
Gold Chloride 13	10.1	12.9	16.0	26.7	22.7
Gold Chloride 14	8.0	30.5	41.0	56.4	65.6
Gold Chloride 14	8.0	6.6	15.7	18.0	20.7

III. Single crystal X-Ray diffraction data

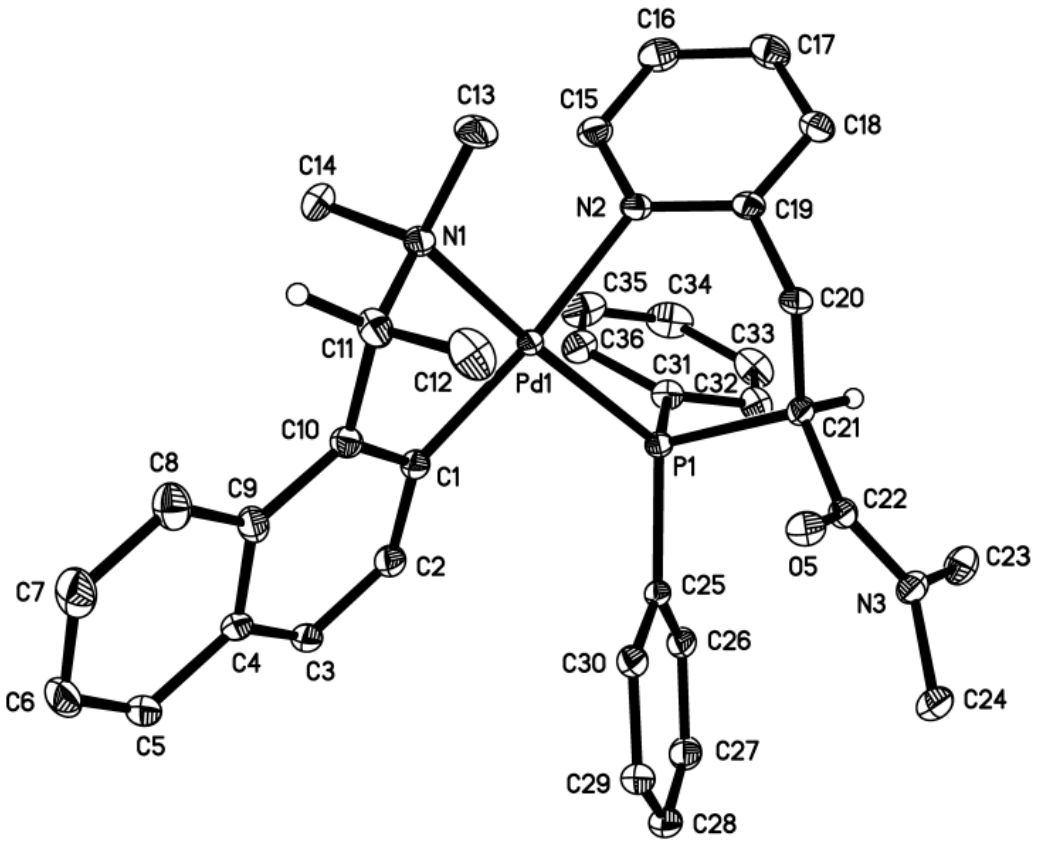


Figure 1. Molecular structure and absolute stereochemistry of (*R*,*S*)-**5** with 50% thermal ellipsoids shown. Hydrogen atoms except those on the chiral center are omitted for clarity (CCDC 1403563).

Table 1. Crystal data and structure refinement for (*R*,*S*)-**5**.

Identification code	leung646s
Empirical formula	C37 H41 Cl3 N3 O5 P Pd
Formula weight	851.45
Temperature	103(2) K
Wavelength	0.71073 Å
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)

Unit cell dimensions	a = 8.4252(2) Å	a= 90°.
	b = 17.7922(4) Å	b= 90°.
	c = 24.7267(6) Å	g = 90°.
Volume	3706.60(15) $Å^3$	
Z	4	
Density (calculated)	1.526 Mg/m^3	
Absorption coefficient	0.807 mm^{-1}	
F(000)	1744	
Crystal size	0.40 x 0.38 x 0.22 mm^3	
Theta range for data collection	1.41 to 32.85°.	
Index ranges	-12<=h<=5, -26<=k<=26, -37<=l<=37	
Reflections collected	27070	
Independent reflections	12372 [R(int) = 0.0251]	
Completeness to theta = 26.00°	99.6 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8425 and 0.7385	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	12372 / 0 / 456	
Goodness-of-fit on F^2	1.105	
Final R indices [I>2sigma(I)]	R1 = 0.0272, wR2 = 0.0730	
R indices (all data)	R1 = 0.0342, wR2 = 0.0908	
Absolute structure parameter	-0.019(19)	
Largest diff. peak and hole	0.853 and -1.016 $e.Å^{-3}$	

Tabel 2 Selected Bond Lengths (Å) and Angles (°) of complex (*R*,*S*)-**5**

Pd(1)-C(1)	2.002(2)	Pd(1)-N(1)	2.1267(18)
Pd(1)-N(2)	2.1270(18)	Pd(1)-P(1)	2.2651(5)
C(1)-C(10)	1.383(3)	C(10)-C(11)	1.508(3)
C(11)-N(1)	1.515(3)	C(19)-N(2)	1.350(3)
C(19)-C(20)	1.502(3)	C(20)-C(21)	1.539(3)
C(21)-P(1)	1.895(2)	C(1)-Pd(1)-N(1)	80.73(8)
C(1)-Pd(1)-N(2)	174.65(7)	N(1)-Pd(1)-N(2)	95.90(7)
C(1)-Pd(1)-P(1)	101.03(6)	N(1)-Pd(1)-P(1)	170.81(5)
N(2)-Pd(1)-P(1)	82.97(5)	C(10)-C(11)-N(1)	106.34(17)
C(11)-N(1)-Pd(1)	104.50(13)	C(19)-N(2)-Pd(1)	121.27(14)
N(2)-C(19)-C(20)	116.24(18)	C(10)-C(1)-Pd(1)	113.48(15)
C(21)-P(1)-Pd(1)	105.13(7)	C(20)-C(21)-P(1)	110.56(14)
C(19)-C(20)-C(21)	110.88(17)	C(1)-C(10)-C(11)	116.82(19)

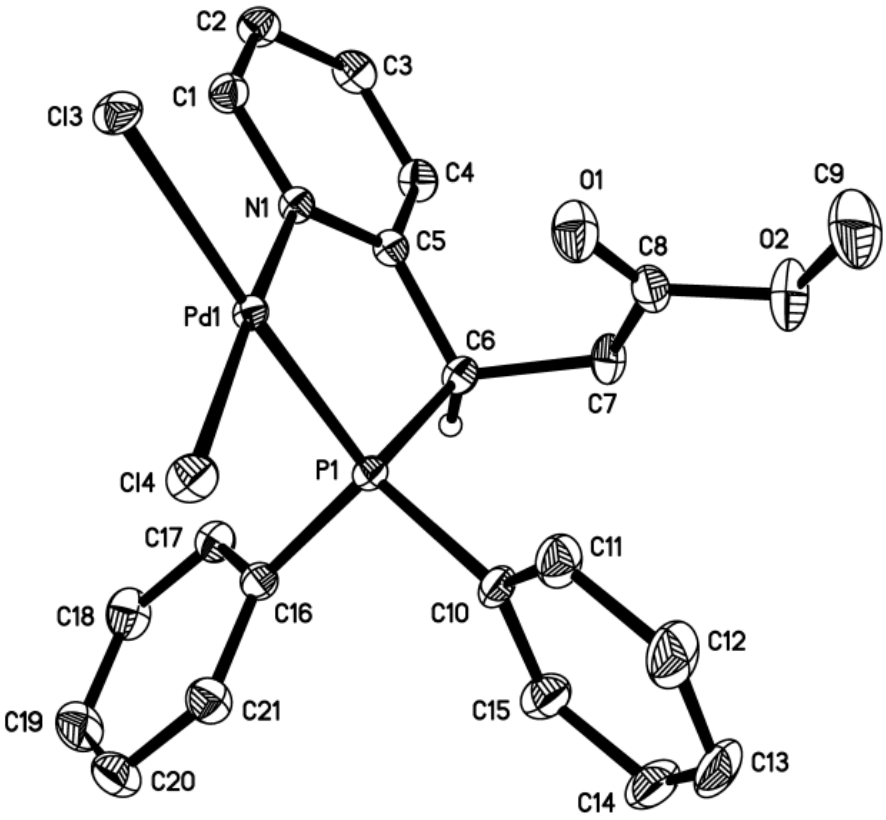


Figure 2. Molecular structure and absolute stereochemistry of (*R*)-**8** with 50% thermal ellipsoids shown (CCDC 1403564).

Table 3. Crystal data and structure refinement for (*R*)-**8**.

Identification code	leung721s
Chemical formula	C22H22Cl4NO2PPd
Formula weight	611.58
Temperature	153(2) K
Wavelength	0.71073 Å
Crystal size	0.080 x 0.260 x 0.400 mm
Crystal habit	yellow block
Crystal system	orthorhombic

Space group	P 21 21 21	
Unit cell dimensions	a = 8.7889(10) Å	α = 90°
	b = 10.1423(13) Å	β = 90°
	c = 26.660(4) Å	γ = 90°
Volume	2376.5(5) Å3	
Z	4	
Density (calculated)	1.709 g/cm3	
Absorption coefficient	1.318 mm-1	
F(000)	1224	
Theta range for data collection	1.53 to 31.25°	
Index ranges	-6<=h<=12, -14<=k<=14, -35<=l<=38	
Reflections collected	20515	
Independent reflections	7702 [R(int) = 0.0382]	
Coverage of independent reflections	99.5%	
Absorption correction	multi-scan	
Max. and min. transmission	0.9019 and 0.6206	
Structure solution technique	direct methods	
Structure solution program	SHELXS-97 (Sheldrick, 2008)	
Refinement method	Full-matrix least-squares on F2	
Refinement program	SHELXL-97 (Sheldrick, 2008)	
Function minimized	Σ w(Fo2 - Fc2)2	
Data / restraints / parameters	7702 / 33 / 300	
Goodness-of-fit on F2	1.134	

Δ/σmax	0.001	
Final R indices	7215 data; I>2σ(I)	R1 = 0.0266, wR2 = 0.0653
	all data	R1 = 0.0307, wR2 = 0.0814
Weighting scheme	w=1/[σ2(Fo2)+(0.0388P)2+0.0000P] where P=(Fo2+2Fc2)/3	
Absolute structure parameter	0.0(0)	
Largest diff. peak and hole	0.616 and -0.769 eÅ-3	
R.M.S. deviation from mean	0.206 eÅ-3	

Table 4 Selected Bond Lengths (Å) and Angles (°) of complex (*R*)-**8**

Pd1-N1	2.060(2)	Pd1-P1	2.1832(7)
Pd1-Cl4	2.2907(7)	Pd1-Cl3	2.3806(7)
C5-N1	1.352(3)	C5-C6	1.508(3)
C6-P1	1.845(3)	C8-O1	1.188(3)
C8-O2	1.335(3)	O1-C8-O2	124.1(3)
N1-Pd1-P1	83.04(6)	N1-Pd1-Cl4	172.01(6)
P1-Pd1-Cl4	90.23(2)	N1-Pd1-Cl3	94.76(6)
P1-Pd1-Cl3	177.08(2)	Cl4-Pd1-Cl3	92.10(2)
C5-N1-Pd1	121.28(16)	C6-P1-Pd1	103.58(8)
N1-C5-C6	118.5(2)	C5-C6-P1	108.54(16)

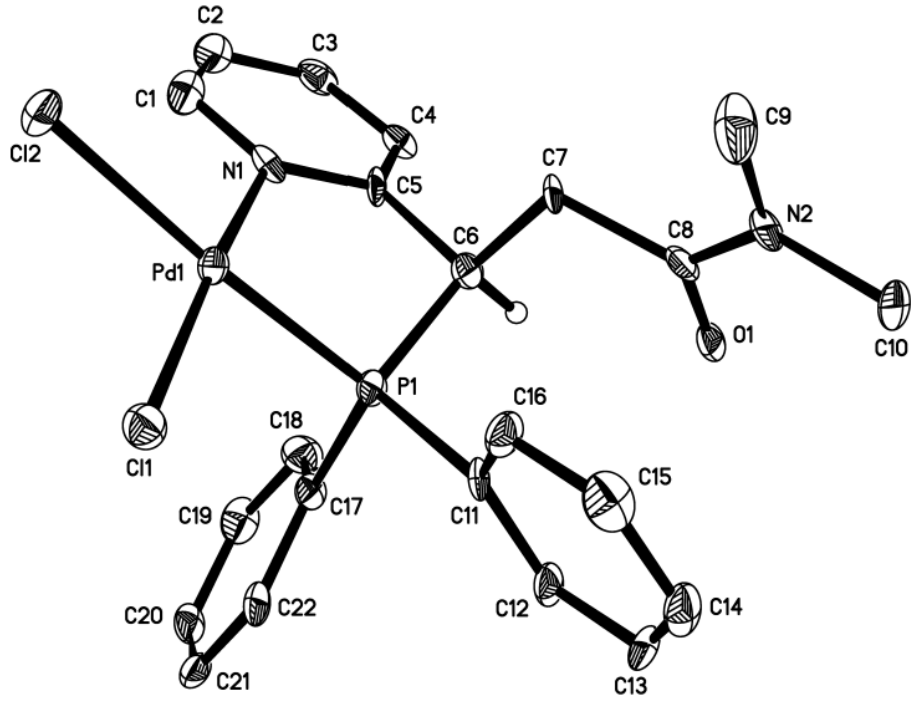


Figure 3. Molecular structure and absolute stereochemistry of (*R*)-**9** with 50% thermal ellipsoids shown (CCDC 1403565).

Table 5. Crystal data and structure refinement for (*R*)-**9**.

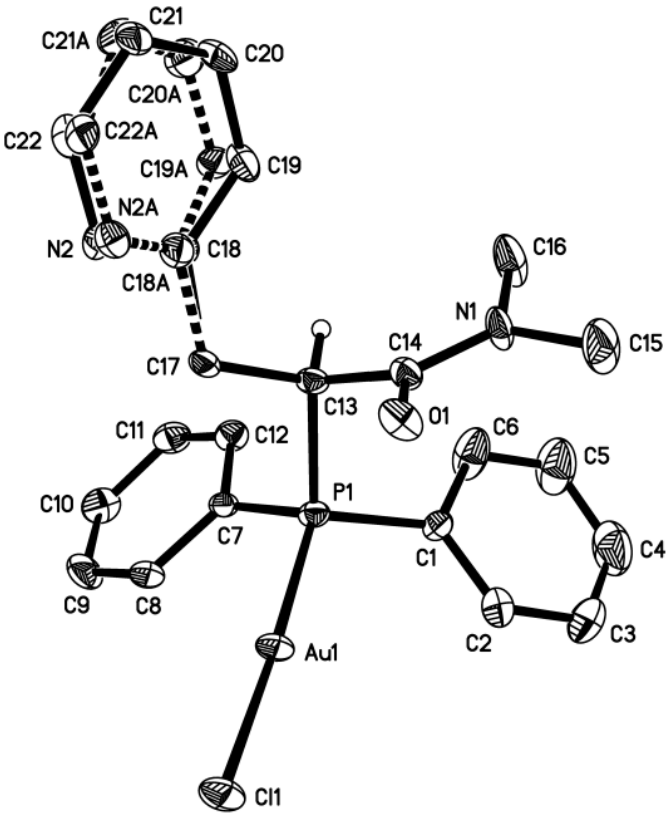
Identification code	leung641_0t	
Empirical formula	C22.50 H24 Cl3 N2 O P Pd	
Formula weight	582.16	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Tetragonal	
Space group	P4(3)2(1)2	
Unit cell dimensions	a = 9.5802(3) Å	a= 90°.
	b = 9.5802(3) Å	b= 90°.
	c = 52.123(2) Å	g = 90°.
Volume	4783.9(3) Å^3	

Z	8
Density (calculated)	1.617 Mg/m^3
Absorption coefficient	1.196 mm^{-1}
F(000)	2344
Crystal size	0.20 x 0.16 x 0.14 mm^3
Theta range for data collection	2.16 to 28.33°.
Index ranges	-9<=h<=9, -12<=k<=12, -67<=l<=69
Reflections collected	13584
Independent reflections	13584 [R(int) = 0.0000]
Completeness to theta = 28.33°	98.5 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.8505 and 0.7960
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	13584 / 30 / 279
Goodness-of-fit on F^2	1.082
Final R indices [I>2sigma(I)]	R1 = 0.0780, wR2 = 0.1858
R indices (all data)	R1 = 0.1083, wR2 = 0.2137
Absolute structure parameter	0.00(5)
Largest diff. peak and hole	1.137 and -2.527 $e.Å^{-3}$

Table 6 Selected Bond Lengths (Å) and Angles (°) of complex (*R*)-**9**

Pd(1)-N(1)	2.083(5)	Pd(1)-P(1)	2.1980(18)
Pd(1)-Cl(1)	2.3040(18)	Pd(1)-Cl(2)	2.3607(18)
C(5)-N(1)	1.368(8)	C(6)-P(1)	1.847(7)

C(5)-C(6)	1.538(9)	C(8)-O(1)	1.236(8)
C(8)-N(2)	1.350(8)	N(1)-Pd(1)-P(1)	82.20(16)
N(1)-Pd(1)-Cl(1)	169.69(15)	P(1)-Pd(1)-Cl(1)	91.17(7)
N(1)-Pd(1)-Cl(2)	95.64(16)	P(1)-Pd(1)-Cl(2)	176.20(7)
Cl(1)-Pd(1)-Cl(2)	91.39(6)	C(5)-N(1)-Pd(1)	120.4(4)
C(6)-P(1)-Pd(1)	100.7(2)	N(1)-C(5)-C(6)	115.5(6)
O(1)-C(8)-N(2)	121.4(6)	C(5)-C(6)-P(1)	105.7(4)



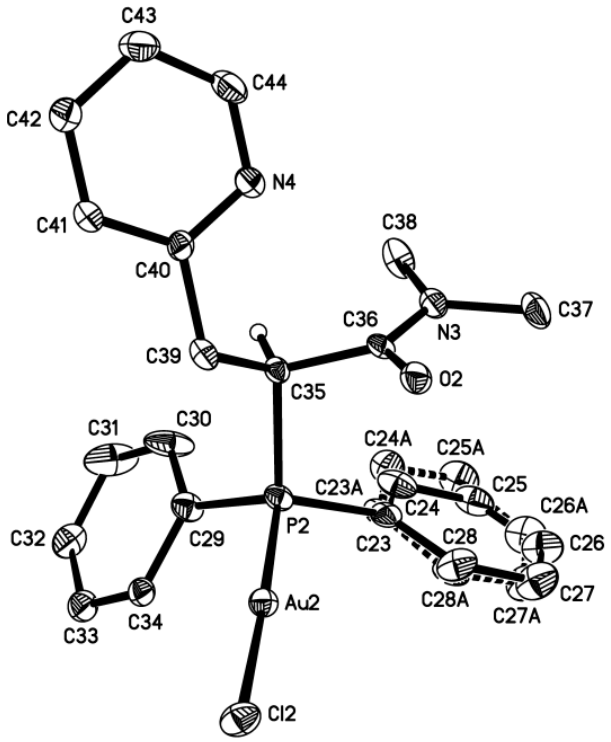


Figure 4. Molecular structures and absolute stereochemistry of phosphine gold complex **13** with 50% thermal ellipsoids shown (CCDC 1403566).

Table 7. Crystal data and structure refinement for phosphine gold complex **13**.

Identification code	leung655	
Empirical formula	C22 H23 Au Cl N2 O P	
Formula weight	594.81	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P1	
Unit cell dimensions	a = 9.8221(4) Å	a= 66.396(2)°.
	b = 10.6843(4) Å	b= 80.267(2)°.
	c = 12.2336(5) Å	g = 64.934(2)°.
Volume	1065.62(7) Å^3	

Z	2
Density (calculated)	1.854 Mg/m^3
Absorption coefficient	7.118 mm^{-1}
F(000)	576
Crystal size	0.40 x 0.20 x 0.18 mm^3
Theta range for data collection	1.82 to 31.07°.
Index ranges	-14<=h<=14, -15<=k<=15, -17<=l<=17
Reflections collected	16770
Independent reflections	11846 [R(int) = 0.0259]
Completeness to theta = 26.00°	98.9 %
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.3606 and 0.1630
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	11846 / 523 / 589
Goodness-of-fit on F^2	0.982
Final R indices [I>2sigma(I)]	R1 = 0.0323, wR2 = 0.0716
R indices (all data)	R1 = 0.0379, wR2 = 0.0902
Absolute structure parameter	0.013(6)
Largest diff. peak and hole	2.434 and -2.795 $e.Å^{-3}$

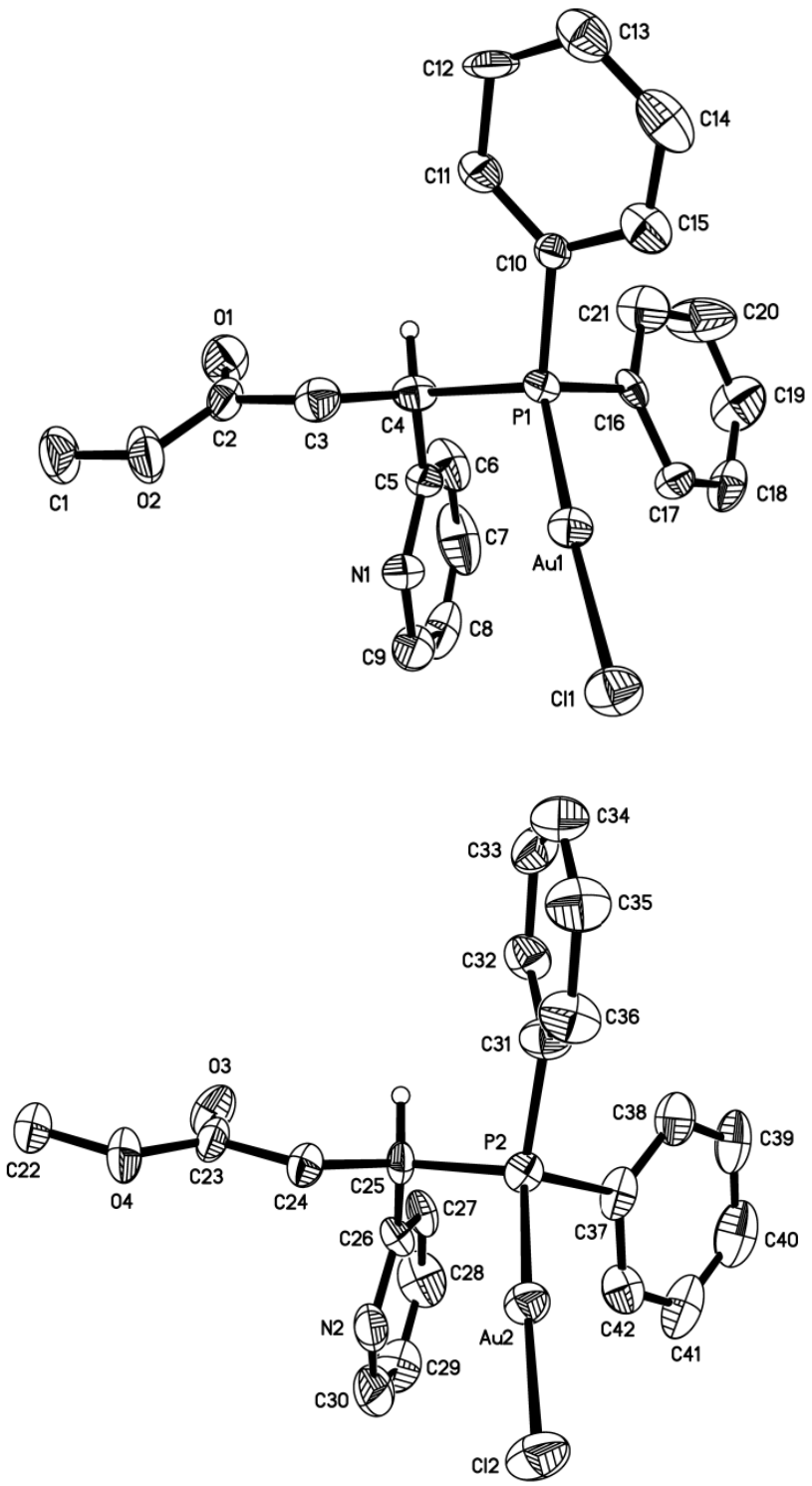


Figure 5. Molecular structure and absolute stereochemistry of phosphine gold complex **14** with 50% thermal ellipsoids shown (CCDC 1403567).

Table 8. Crystal data and structure refinement for phosphine gold complex **14**.

Identification code	leung720s	
Chemical formula	C21H20AuClNO2P	
Formula weight	581.77	
Temperature	173(2) K	
Wavelength	0.71073 Å	
Crystal size	0.060 x 0.100 x 0.140 mm	
Crystal habit	colorless block	
Crystal system	monoclinic	
Space group	P 1 21 1	
Unit cell dimensions	a = 8.5246(13) Å	α = 90°
	b = 17.622(3) Å	β = 91.475(2)°
	c = 13.569(2) Å	γ = 90°
Volume	2037.7(6) Å3	
Z	4	
Density (calculated)	1.896 g/cm3	
Absorption coefficient	7.445 mm-1	
F(000)	1120	
Theta range for data collection	1.50 to 31.00°	
Index ranges	-12<=h<=12, -25<=k<=25, -19<=l<=19	
Reflections collected	12458	
Coverage of independent reflections	98.1%	
Absorption correction	multi-scan	
Max. and min. transmission	0.6636 and 0.4221	

Structure solution technique	direct methods
Structure solution program	SHELXS-97 (Sheldrick, 2008)
Refinement method	Full-matrix least-squares on F2
Refinement program	SHELXL-97 (Sheldrick, 2008)
Function minimized	Σ w(Fo2 - Fc2)2
Data / restraints / parameters	12458 / 38 / 479
Goodness-of-fit on F2	1.040
Δ/σmax	0.001
Final R indices	10020 data; I>2σ(I) R1 = 0.0534, wR2 = 0.1161
	all data R1 = 0.0749, wR2 = 0.1410
Weighting scheme	w=1/[σ2(Fo2)+(0.0621P)2+0.5201P] where P=(Fo2+2Fc2)/3
Absolute structure parameter	0.0(0)
Largest diff. peak and hole	2.626 and -3.081 eÅ-3
R.M.S. deviation from mean	0.302 eÅ-3

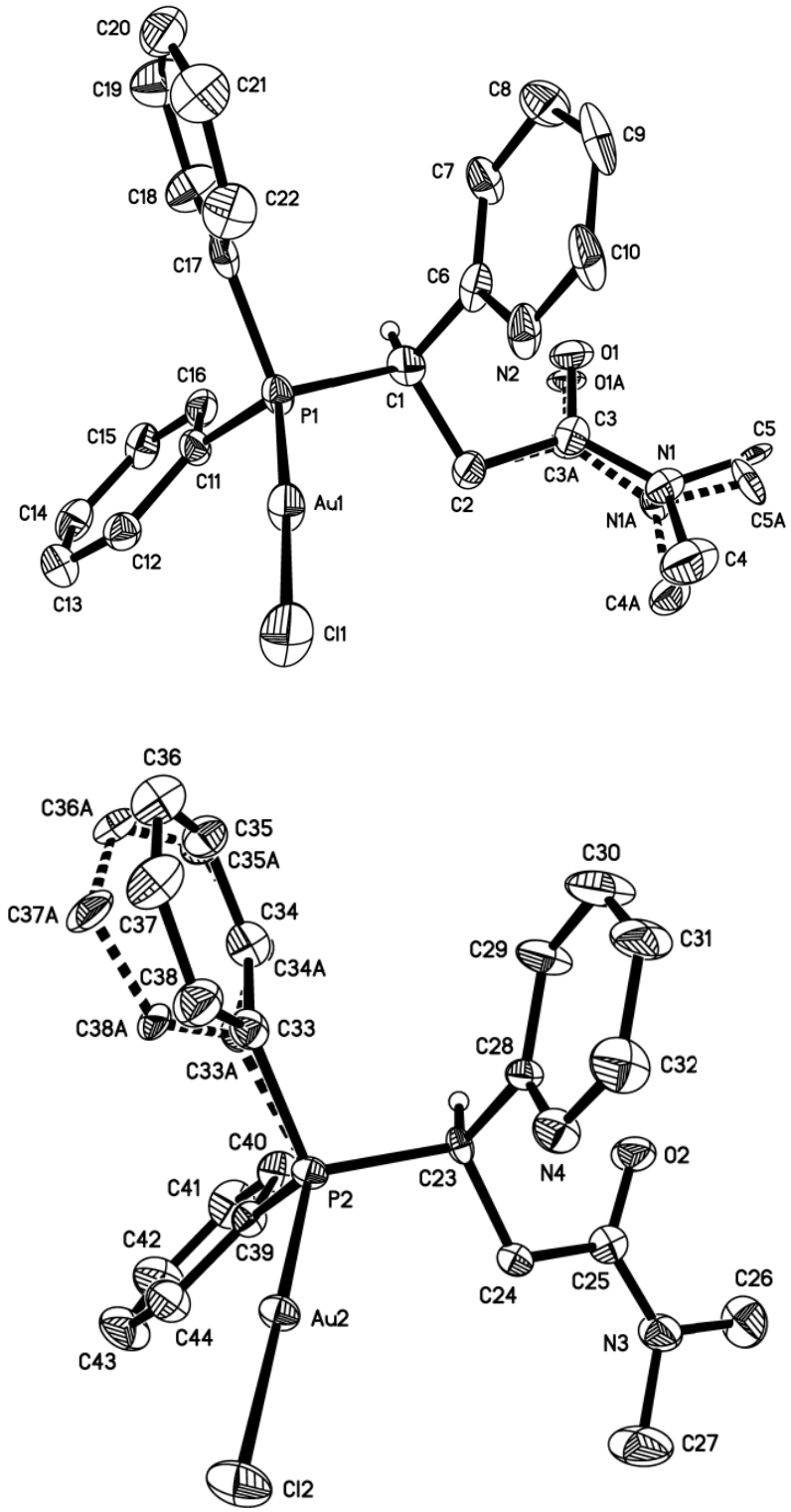


Figure 6. Molecular structure and absolute stereochemistry of phosphine gold complex **15** with 50% thermal ellipsoids shown (CCDC 1403568).

Table 9. Crystal data and structure refinement for phosphine gold complex **15**.

Identification code	leung648s	
Empirical formula	C23 H24 Au Cl4 N2 O P	
Formula weight	714.18	
Temperature	103(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	P2(1)	
Unit cell dimensions	a = 14.6585(4) Å	a= 90°.
	b = 9.3247(2) Å	b= 102.985(2)°.
	c = 19.8149(5) Å	g = 90°.
Volume	2639.16(11) $Å^3$	
Z	4	
Density (calculated)	1.797 Mg/m^3	
Absorption coefficient	6.058 mm^{-1}	
F(000)	1384	
Crystal size	0.40 x 0.10 x 0.06 mm^3	
Theta range for data collection	1.57 to 30.52°.	
Index ranges	-20<=h<=20, -12<=k<=12, -28<=l<=25	
Reflections collected	29774	
Independent reflections	14989 [R(int) = 0.0400]	
Completeness to theta = 27.00°	99.1 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7126 and 0.1955	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	14989 / 594 / 721	

Goodness-of-fit on F^2	1.045
Final R indices [I>2sigma(I)]	R1 = 0.0406, wR2 = 0.0863
R indices (all data)	R1 = 0.0737, wR2 = 0.1153
Absolute structure parameter	-0.023(6)
Largest diff. peak and hole	2.793 and -2.450 e.$Å^{-3}$

Table 10 Selected Bond Lengths (Å) and Angles (°) of gold complexes

	Au-P	Au-Cl	P-Au-Cl
12	2.2305(18)	2.2834(18)	175.97(6)
13	2.2340(16)	2.2878(15)	177.20(7)
	2.2375(18)	2.2877(17)	177.44(7)
14	2.231(3)	2.286(3)	176.16(13)
	2.221(3)	2.278(4)	177.82(15)
15	2.231(3)	2.301(3)	176.56(9)
	2.234(3)	2.295(3)	175.69(8)