Supporting Information for

Determination of orientational isomerism in rhodium(II) metallopeptides by pyrene fluorescence

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Contents

1. Experimental procedures and results:

1a. General Information:

All rhodium-catalyzed reactions were carried out in 4-mL vials. Reactions carried out below 0 °C were conducted in a Neslab CB-80 cold bath. Flash chromatography was performed with silica gel (40–63 μm). Optical rotations were measured using a JASCO DIP-370 digital polarimeter.

NMR Spectroscopy: NMR data was acquired with Bruker Avance 400 MHz or Bruker Avance 500 MHz instrument. ^{1}H and ^{13}C NMR spectra were referenced relative to residual solvent or TMS.

HPLC analysis: Reverse-phase HPLC analyses of the metallopeptides were performed on a Shimadzu CBM-20A instrument with Phenomenex Jupiter 4μ Proteo 90A (250 × 15 mm preparative) and Phenomenex Jupiter 4μ Proteo 90A (250 × 4.6 mm analytical) columns. Flow rates of 8 mL/min and 1.5 mL/min were used for the preparative and analytical columns, respectively. The analysis of the peptides and dirhodium complexes was done at two wavelengths (254 nm and 300 nm). Chiral HPLC analyses were performed on a Shimadzu SCL-10ADVP instrument with Phenomenex Lux 5u Cellulose-1 (250 x 4.6 mm analytical) or a Chiralpak IA (250 x 2 mm ID analytical) column with a flowrate of 1.6–1.9 mL/min.

Mass Spectrometry: MALDI-MS was performed on a Bruker Daltonics Autoflex MALDI-TOF/TOF mass spectrometer. Ethanolic solutions of analyte were cocrystallized on Bruker Daltonics PAC384 AnchorChip with Alpha-CHCA matrix (Agilent technologies). MALDI data analysis was performed using the mMass program.[1]

FluorescenceSpectroscopy: The fluorescence measurements were taken using a 1cm path length quartz cuvette in a HORIBA Jovin Yvon Fluorolog3 fluorometer. The sample concentration of Rh_2(**L***)$_2$ was 1μM in aqueous methanol. The excitation wavelength was 340 nm and the emission was measured from 350 to 600 nm with a slit width of 2 nm.

Circular Dichroism Spectroscopy: CD spectrum was obtained on a Jasco J-815 CD spectropolarimeter using a 0.1 cm cell. The spectrum was acquired with a 0.2-nm interval in the range of 180–250 nm at 20 °C. Concentration of the metallopeptide solution in 2,2,2-trifluoroethanol was 10 μM. The results were converted to mean residue ellipticity by the equation $[\theta] = \theta_{obs} / (10 \times l \times C \times N)$ where θ_{obs} is the ellipticity in millidegrees of rotation, l is the

optical path length of the cell in cm, *C* is the concentration of the metallopeptide in mol/L, and *N* is the number of residues in the metallopeptide.

Chemicals: The following chemicals were purchased and used as received: 1-pyrenebutyric acid (Aldrich), $Rh_2(OAc)_4$ (Pressure), 2,2,2-trifluoroethanol (Aldrich), phenylacetic acid (Matheson), diisopropylethylamine (Fisher), Styrene (Aldrich), 1,8-diazabicyclo[5.4.0]undec-7-ene (Acros), and phenyldimethylsilane (Gelest). All solvents were reagent grade.

Peptide Synthesis:

Peptide synthesis for solution-phase catalyst generation: Commercially available L-amino acids were used for peptide synthesis. All peptides were synthesized using standard solid-phase FMOC protocols.[2] Peptides were synthesized on Rink amide resin, manually or in an Advanced ChemTech APEX 396 Automated Multipeptide Synthesizer. In the synthesis of non-pyrene peptides, the peptides were subjected to acetylation after the last K^Z coupling step and then they were subjected to cleavage. For pyrene containing peptides, the N-terminal coupling was carried out with 1-pyrenebutyric acid and after this, the peptides were directly subjected to cleavage. After peptide synthesis, removal of side-chain protecting groups and peptide cleavage were accomplished using a cocktail of 25% trifluoroacetic acid, 70% dichloromethane and 5% triisopropylsilane. Crude peptides were taken up in trifluoroethanol, and diisopropylethylamine was added dropwise with simultaneous sonication until the peptide dissolved. The purification of peptides was accomplished by direct injection into reverse-phase HPLC with gradients of water-acetonitrile containing 0.1% trifluoroacetic acid, and the peptides were isolated by lyophilization. Analysis and purity assessment was attained by mass spectrometry and analytical HPLC.

Synthesis of known compounds: The dirhodium precursor $Rh_2(tfa)_4$ was prepared according to published procedure.[3] Diazo substrate methyl α-diazophenylacetate[4] has been previously reported and characterized and (*E*)-methyl 2-diazo-4-phenylbut-3-enoate was prepared according to the same reported protocol. For purpose of ee determination, racemic material was generated using $Rh_2(OAc)_4$. The absolute configuration of product **2** is assigned by comparison of the optical rotation to our previous paper[5] and that of products **3**[6,7] and **5**[8] is assigned by comparison to previous reports.

1b. Preparation of dirhodium metallopeptides:

General procedure for the synthesis of soluble Rh_2(peptide)$_2$ complexes: Synthesis of Rh_2(L16)$_2$-*para* (Rh_2(L16)$_2$-*iso*A) and Rh_2(L16)$_2$-*anti* (Rh_2(L16)$_2$-*iso*B)

Peptide **L16** (30 mg, 23.4 μmol) was weighed in a 4-mL vial and trifluoroethanol (3.9 mL) was added. Diisopropylethylamine (6.0 μL) was added, and the mixture was sonicated until the peptide was completely dissolved to give a clear solution. The peptide solution was then transferred to another 4-mL vial containing $Rh_2(tfa)_4$ (7.70 mg, 11.7 μmol), and the mixture was allowed to stir at 50 °C for 1 d. The reaction was monitored until complete disappearance of the $Rh_2(tfa)_4$ peak was observed by HPLC. Purification and isolation of the isomeric dirhodium–dipeptide complexes was achieved by direct injection of the reaction mixture on a preparative RP-HPLC column using isocratic conditions (54% acetonitrile/water). The isomers were isolated as blue solids (Rh_2(**L16**)$_2$-*para* = 8.71 mg, 27% and Rh_2(**L16**)$_2$-*anti* = 9.79 mg, 30%) upon lyophilization.

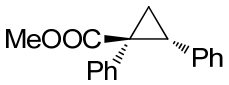
Rh_2(**L16**)$_2$-*para* calculated mass for $Rh_2C_{120}H_{176}N_{24}Na_1O_{38}$ $[M+Na]^+$: 2791.9262, found: 2792.6355

Rh_2(**L16**)$_2$-*anti* calculated mass for $Rh_2C_{120}H_{176}N_{24}Na_1O_{38}$ $[M+Na]^+$: 2791.9262, found: 2792.9023

1c. Catalytic asymmetric cyclopropanation:

General procedure for Rh-catalyzed cyclopropanations: Synthesis of

(*1S,2R*)-methyl 1,2-diphenylcyclopropanecarboxylate (3)



A solution of the catalyst Rh_2(**L16**)$_2$-*para* (Rh_2(**L16**)$_2$-*iso*A, 0.79 mg, 0.25 mol%) in trifluoroethanol (500 μL) was stirred at rt in a 4-mL vial. A mixture of methyl α-diazophenylacetate (20 mg, 0.11 mmol) and styrene (118 mg, 1.14 mmol) in 1,1,1-trifluoroethanol (1.5 mL) were stirred at the same temperature in another 4-mL vial. The catalyst solution was then quickly transferred to the vial containing the substrates and the reaction mixture was allowed to stir at rt until the diazo compound reacted fully. The mixture was concentrated under reduced pressure without further workup and purification of the product by flash chromatography on silicagel using a gradient from hexane to 2:8 diethyl ether/hexane gave the desired *(1S,2R)* product as a white crystalline solid in 95% yield. The enantiomeric excess

was determined to be 76%.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.12−7.11 (m, 3H), 7.07−7.01 (m, 5H), 6.77−6.75 (m, 2H), 3.66 (s, 3H), 3.11 (dd, *J* = 9.5, 7.0 Hz, 1H), 2.14 (dd, *J* = 9.5, 5.0 Hz, 1H), 1.88 (dd, *J* = 7.0, 5.0 Hz, 1H)

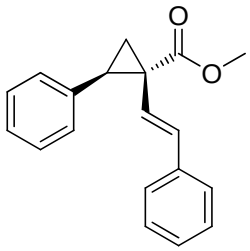
^{13}C NMR (500 MHz, $CDCl_3$) δ 174.6, 136.6, 134.9, 132.1, 128.2, 127.9, 127.9, 127.2, 126.5, 52.9, 37.6, 33.4, 20.7

GC-MS t_R 15.3 min, (> 95%) *m/z*: $[M]^+$ calcd for $C_{17}H_{16}O_2$: 252.3; found: 252.1

$[\alpha]_D^{23}$ +23.9 (*c* 1.1, $CHCl_3$); For (–)-(1*R*,2*S*) product, Lit[7] $[\alpha]_D^{23}$ –28.5 (*c* 1.3, $CHCl_3$) for 89% ee. Lit[6] $[\alpha]_D^{23}$ –20.0 (*c* 0.15, $CHCl_3$) for 90% ee.

Enantiomeric excess determined by HPLC; Chiralpak IA column, eluting with 97:3 hexanes/CH_2Cl_2, 1.5 mL/min, detection wavelength: 220 nm. (+)-(*1S,2R*)-methyl 1,2-diphenylcyclopropanecarboxylate t_R = 8.1 min and (–)-(*1R,2S*)-methyl 1,2-diphenylcyclopropanecarboxylate t_R = 7.2 min

(1*R*,2*R*)-methyl 2-phenyl-1-((*E*)-styryl)cyclopropanecarboxylate (5)



The general procedure was employed using Rh_2(**L16**)$_2$-*para* catalyst (*E*)-methyl 2-diazo-4-phenylbut-3-enoate on a 0.05 mmol scale. The reaction was carried out at –35 °C to afford the *(1R,2R)* product as a white solid in 80% yield and 92% ee. Chromatography eluent: gradient from hexane to 2:8 diethylether/hexane.

^{1}H NMR (500 MHz, $CDCl_3$) δ 7.24−7.20 (m, 4H), 7.18−7.12 (m, 6H), 6.34 (d, *J* = 16 Hz, 1H), 6.13 (d, *J* = 16 Hz, 1H), 3.76 (s, 3H), 3.00 (dd, *J* = 9.0, 7.0 Hz, 1H), 2.02 (dd, *J* = 9.0, 5.0, 1H), 1.83 (dd, *J* = 7.0, 5.0 Hz, 1H)

^{13}C NMR (500 MHz, $CDCl_3$) δ 174.4, 137.3, 135.7, 133.3, 129.3, 128.6, 128.2, 127.5, 127.0, 126.4, 124.3, 52.7, 35.2, 33.5, 18.8

GC-MS t_R 19.1 min, (> 95%) *m/z*: $[M]^+$ calcd for $C_{19}H_{18}O_2$: 278.3; found: 278.2

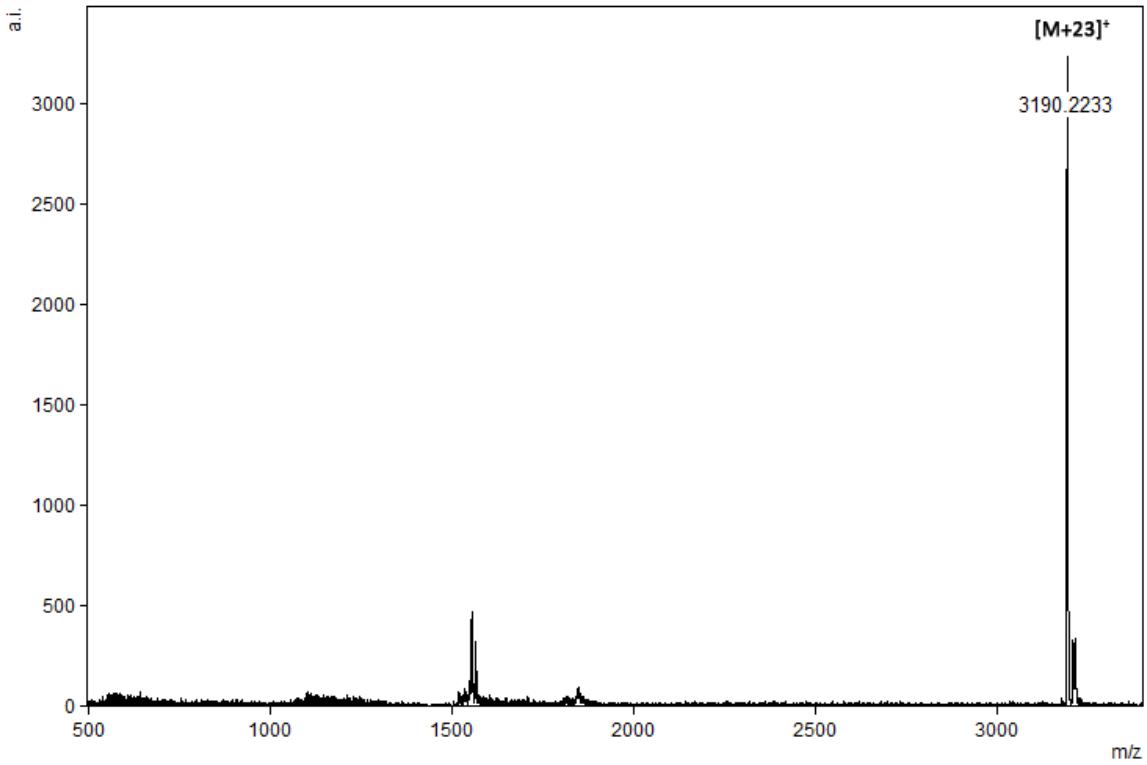
$[\alpha]_D^{23}$ +135.8 (*c* 1.1, $CHCl_3$); Lit[8] $[\alpha]_D^{25}$ +157.1 (*c* 1.1, $CHCl_3$).

Enantiomeric excess determined by HPLC; Phenomenex Lux 5u Cellulose-1 column, eluting with 99:1 hexanes/*i*-PrOH, 1.5 mL/min, detection wavelength: 220 nm. (+)-(*1R,2R*)-methyl 2-phenyl-1-((*E*)-styryl)cyclopropanecarboxylate t_R = 5.9 min and (–)-(*1S,2S*)-methyl 2-phenyl-1-((*E*)-styryl)cyclopropanecarboxylate t_R = 7.3 min

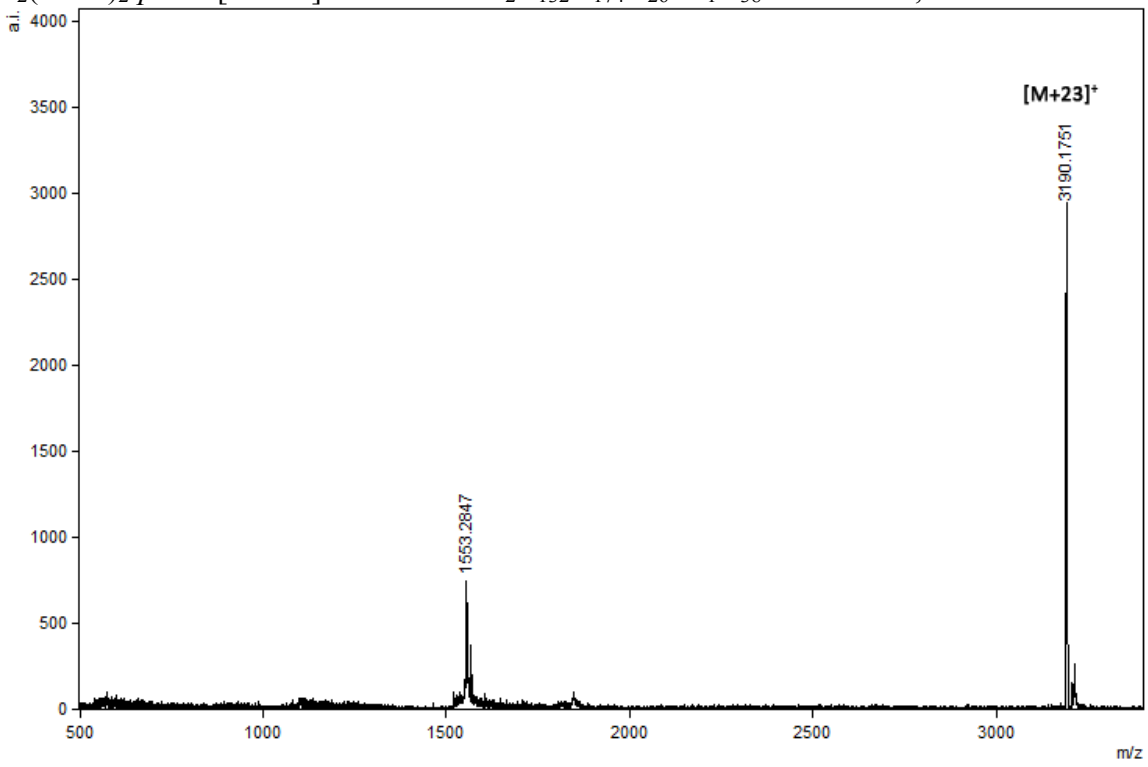
2. Characterization data:

2a.Mass spectra of pyrene-containing dirhodium metallopeptides:

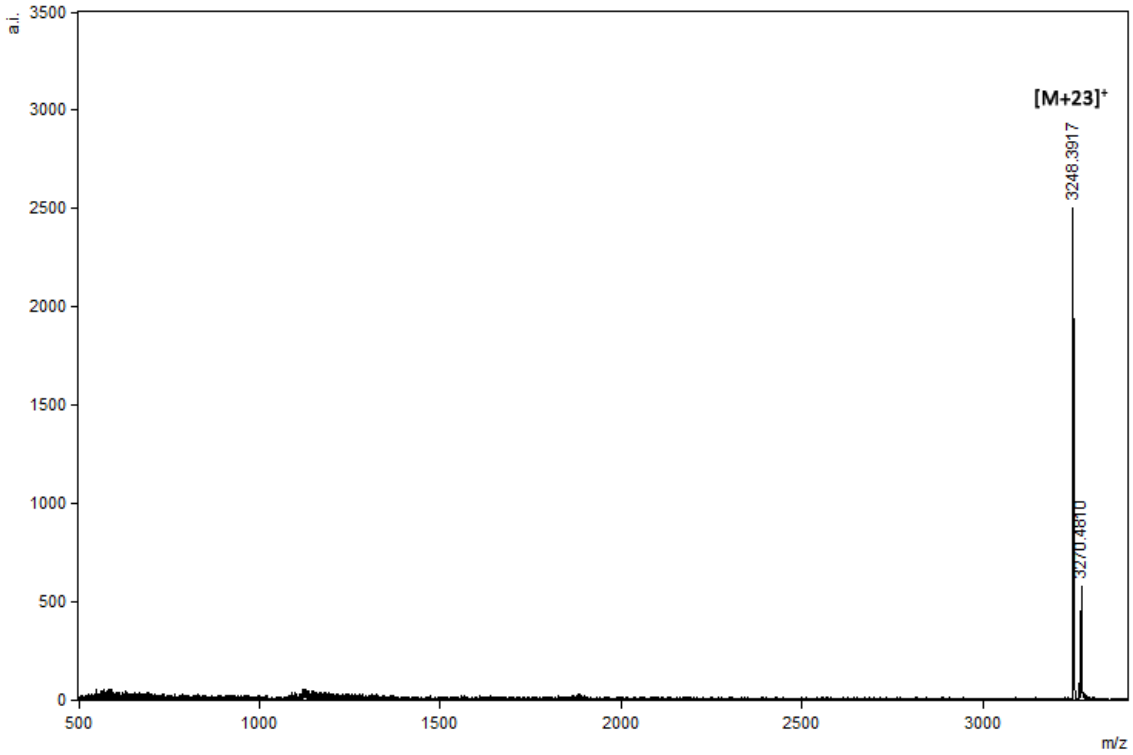
Rh_2(L21*)$_2$-*anti*: $[M+Na]^+$ calcd for $Rh_2C_{150}H_{186}N_{26}Na_1O_{38}$: 3190.1117, found: 3190.2233



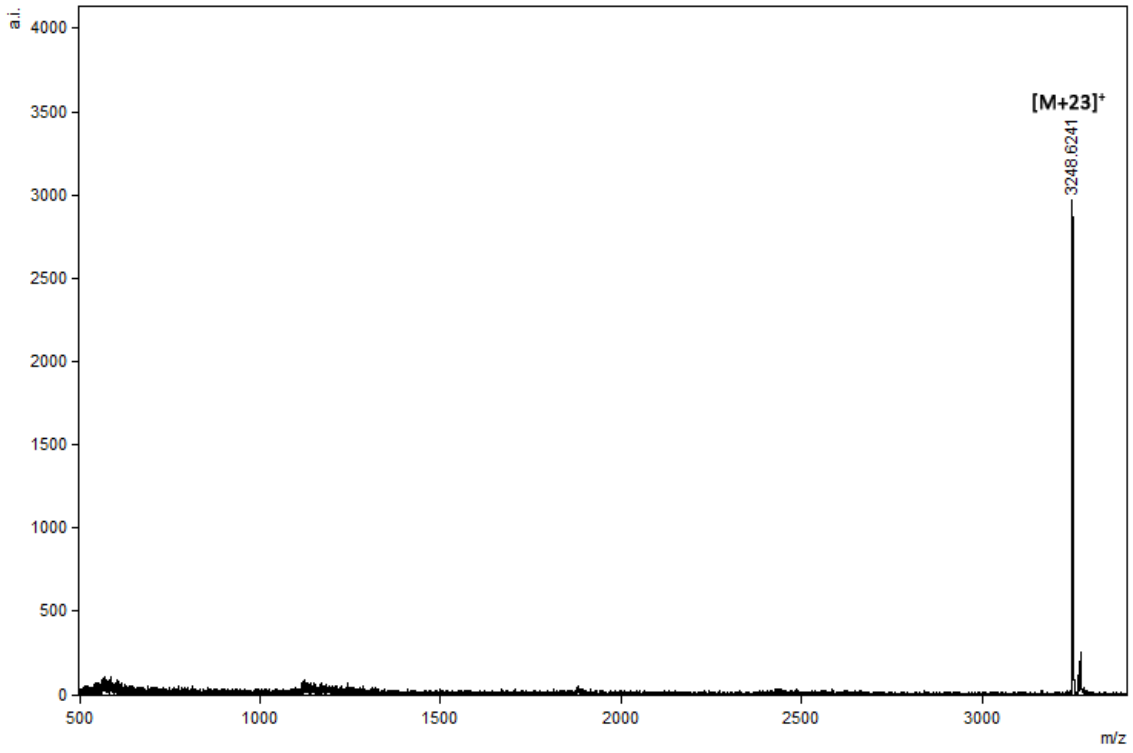
Rh_2(**L21***)$_2$-*para*: $[M+Na]^+$ calcd for $Rh_2C_{132}H_{174}N_{26}Na_1O_{38}$: 3190.1117, found: 3190.1751



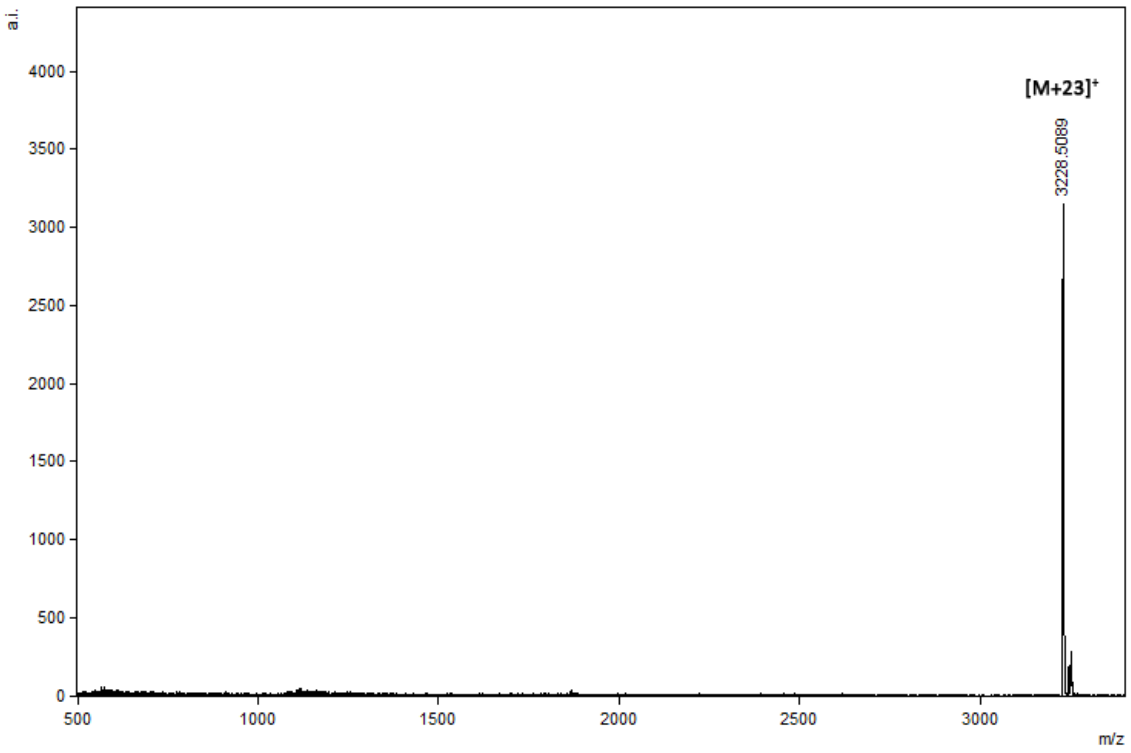
Rh_2(**L16***)$_2$-*para*: $[M+Na]^+$ calcd for $Rh_2C_{138}H_{188}N_{24}Na_1O_{38}$: 3248.2731, found: 3248.3917



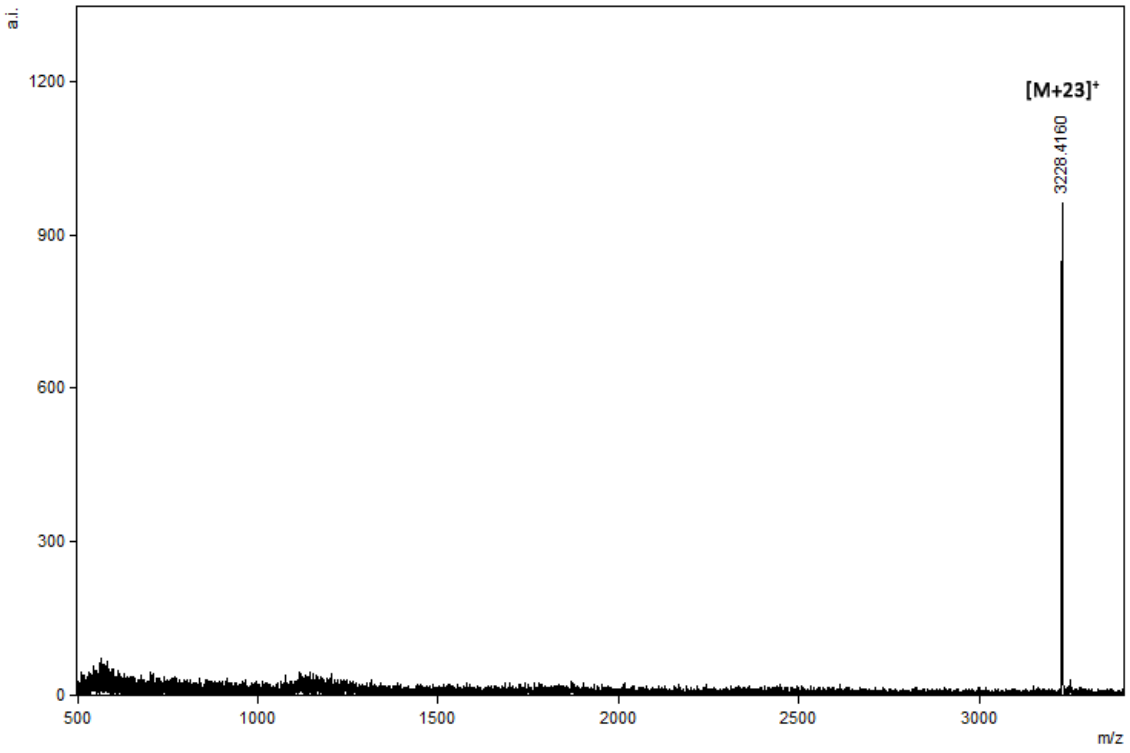
Rh_2(**L16***)$_2$-*anti*: $[M+Na]^+$ calcd for $Rh_2C_{138}H_{188}N_{24}Na_1O_{38}$: 3248.2731, found: 3248.6241



Rh_2(**L13***)$_2$-*anti*: $[M+Na]^+$ calcd for $Rh_2C_{140}H_{176}N_{24}Na_1O_{36}$: 3228.2009, found: 3228.5089

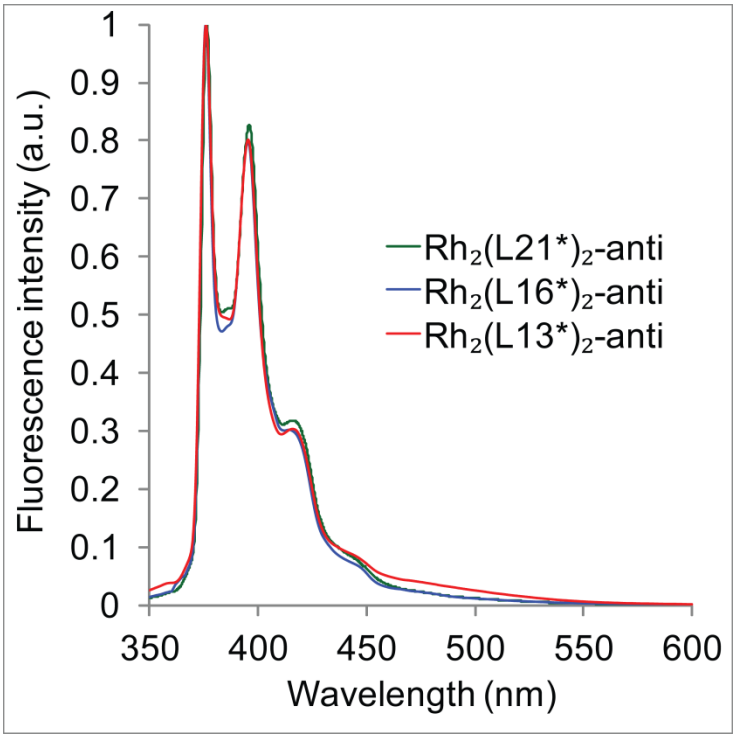


Rh_2(**L13***)$_2$-*para*: $[M+Na]^+$ calcd for $Rh_2C_{140}H_{176}N_{24}Na_1O_{36}$: 3228.2009, found: 3228.4160

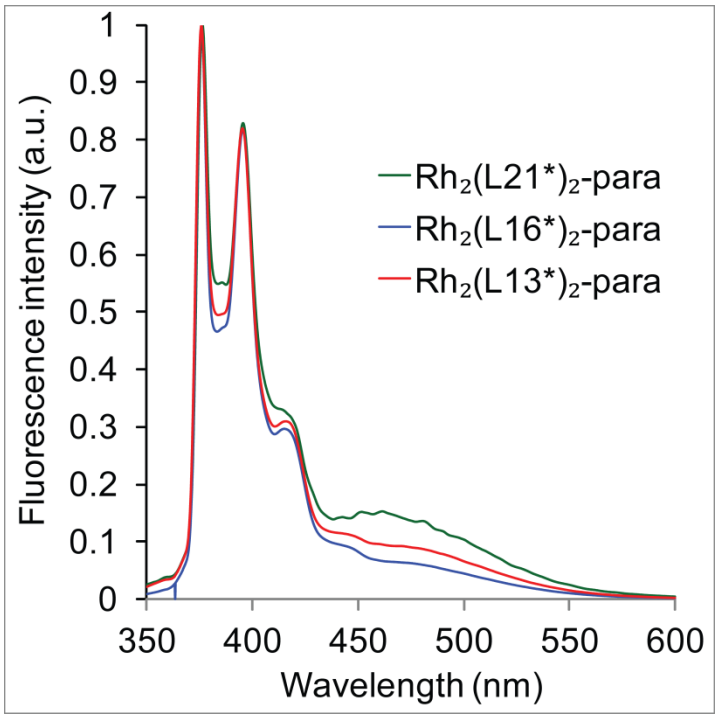


2b. Fluorescence emission spectra:

Antiparallel structures:

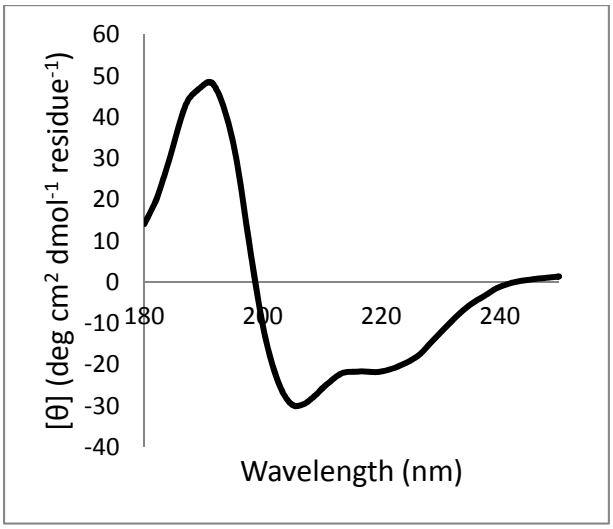


Parallel structures:

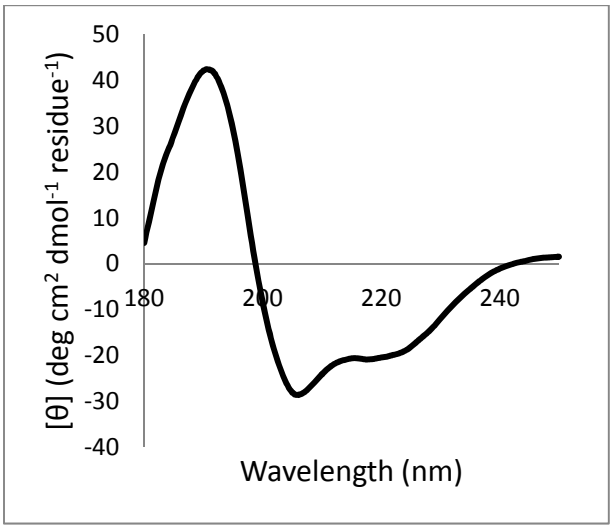


2c. CD spectra of dirhodium metallopeptides:

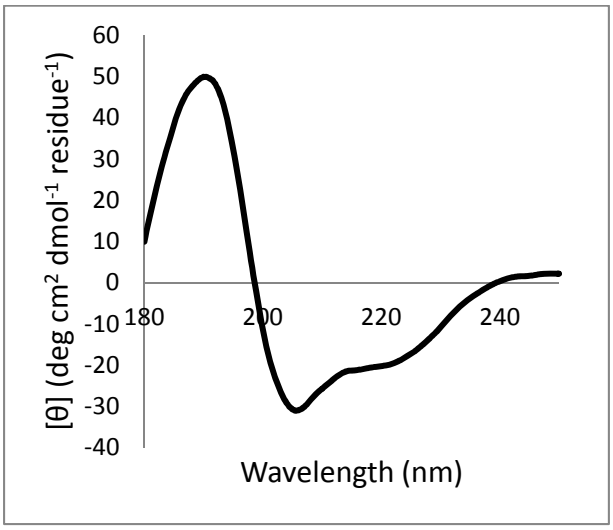
Rh_2(**L21**)$_2$-*para* (Rh_2(**L21**)$_2$-*iso*A)



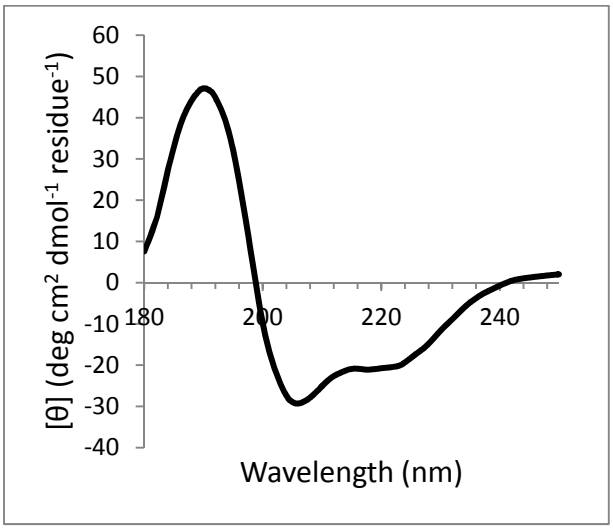
Rh_2(**L21**)$_2$-*anti* (Rh_2(**L21**)$_2$-*iso*B)



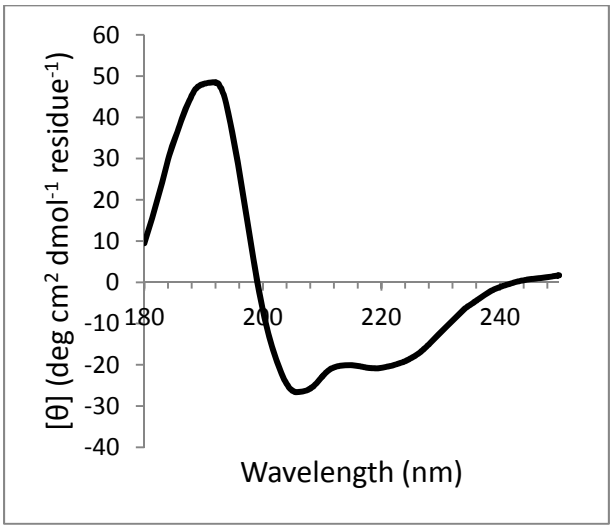
Rh_2(**L16**)$_2$-*para* (Rh_2(**L16**)$_2$-*iso*A)



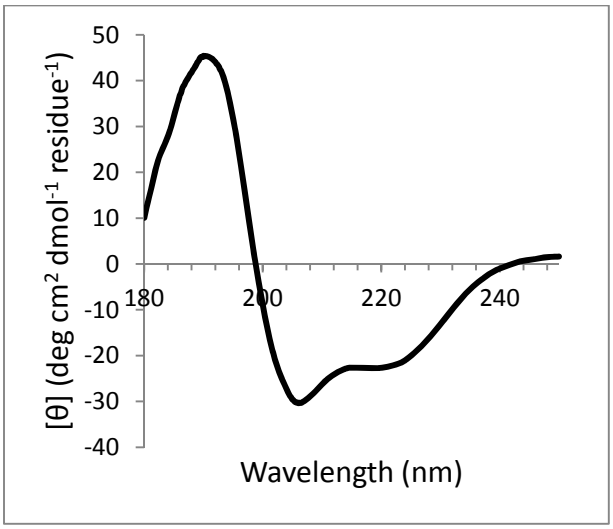
Rh_2(**L16**)$_2$-*anti* (Rh_2(**L16**)$_2$-*iso*B)



Rh_2(**L13**)$_2$-*para* (Rh_2(**L13**)$_2$-*iso*A)

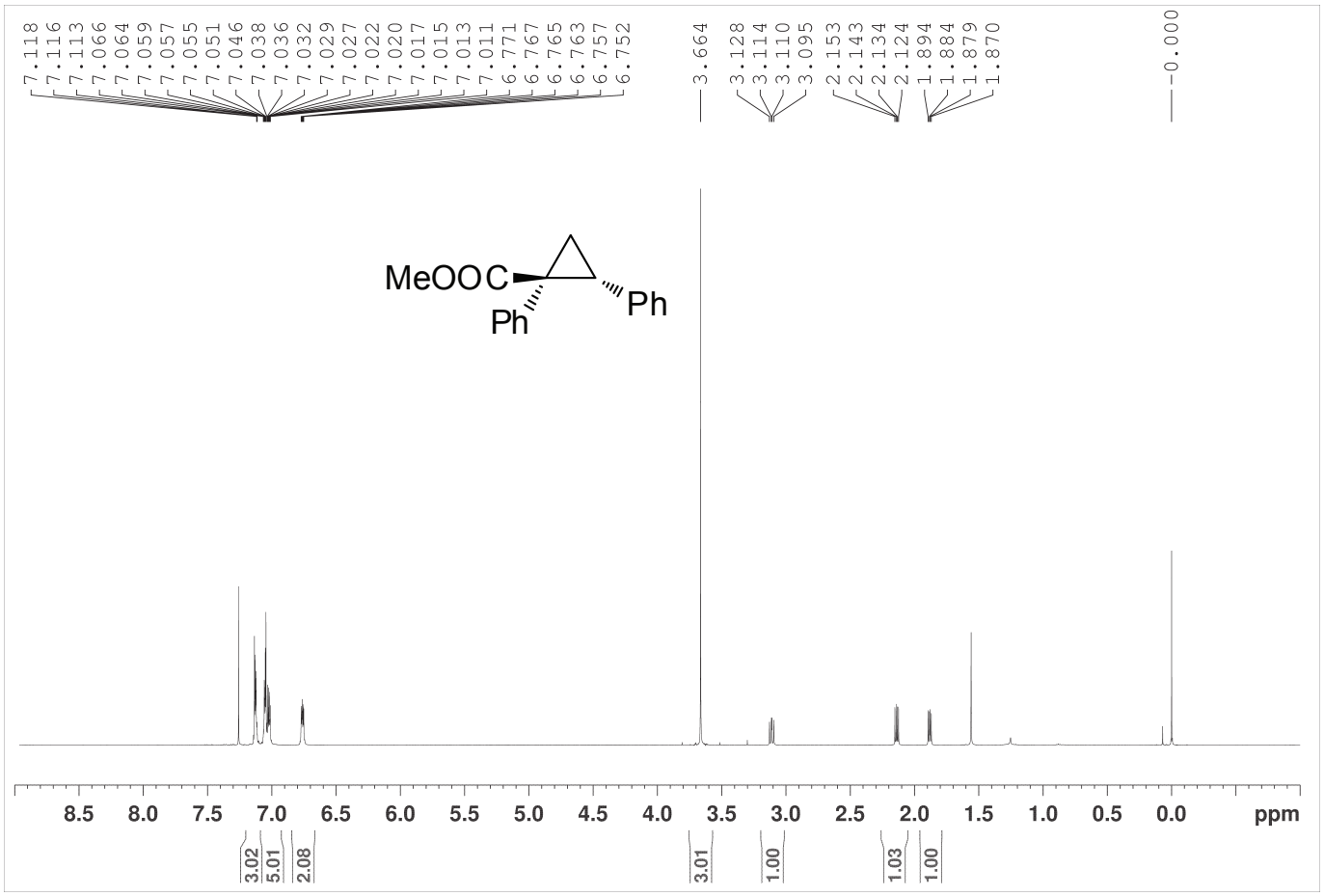


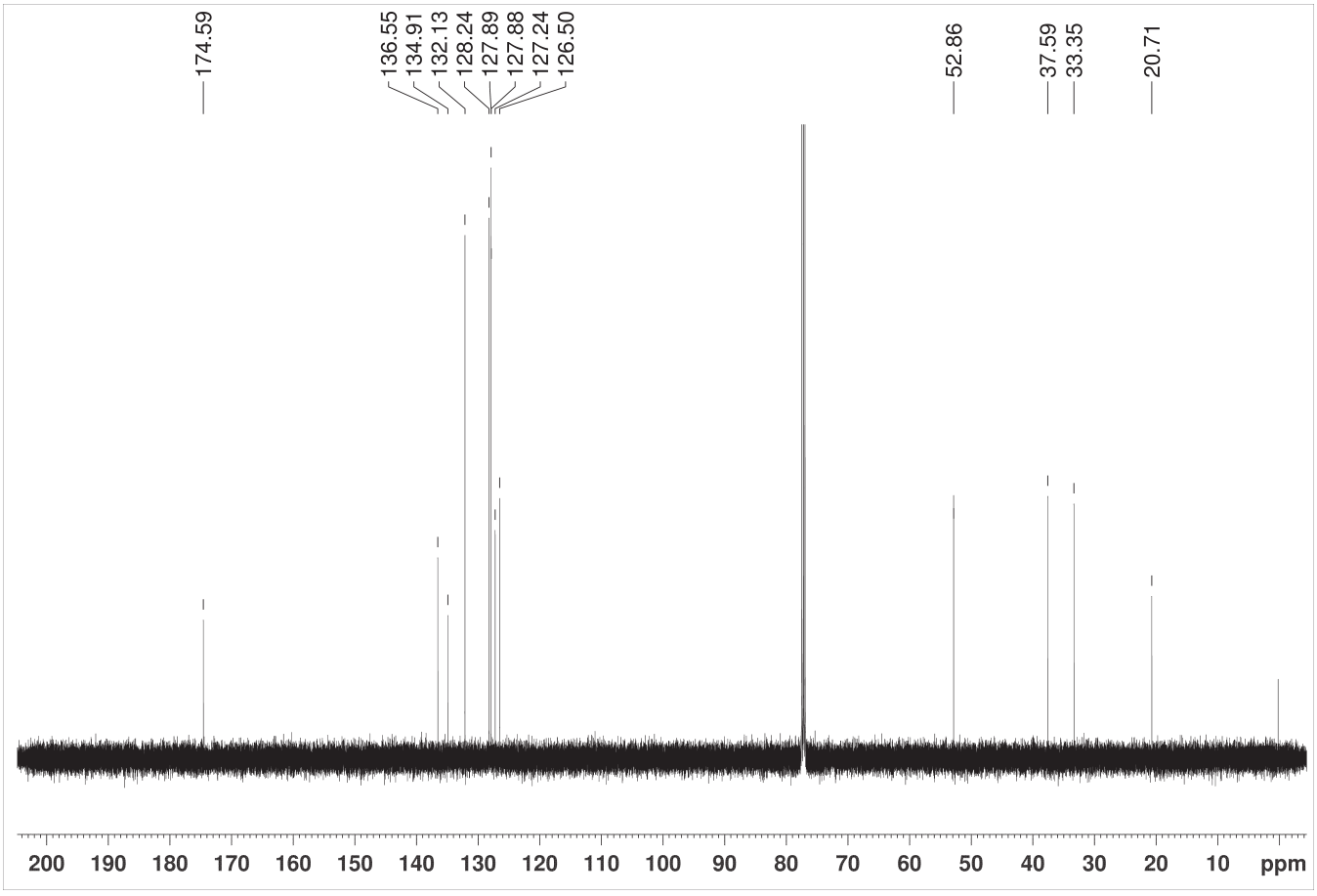
Rh_2(**L13**)$_2$-*anti* (Rh_2(**L13**)$_2$-*iso*B)



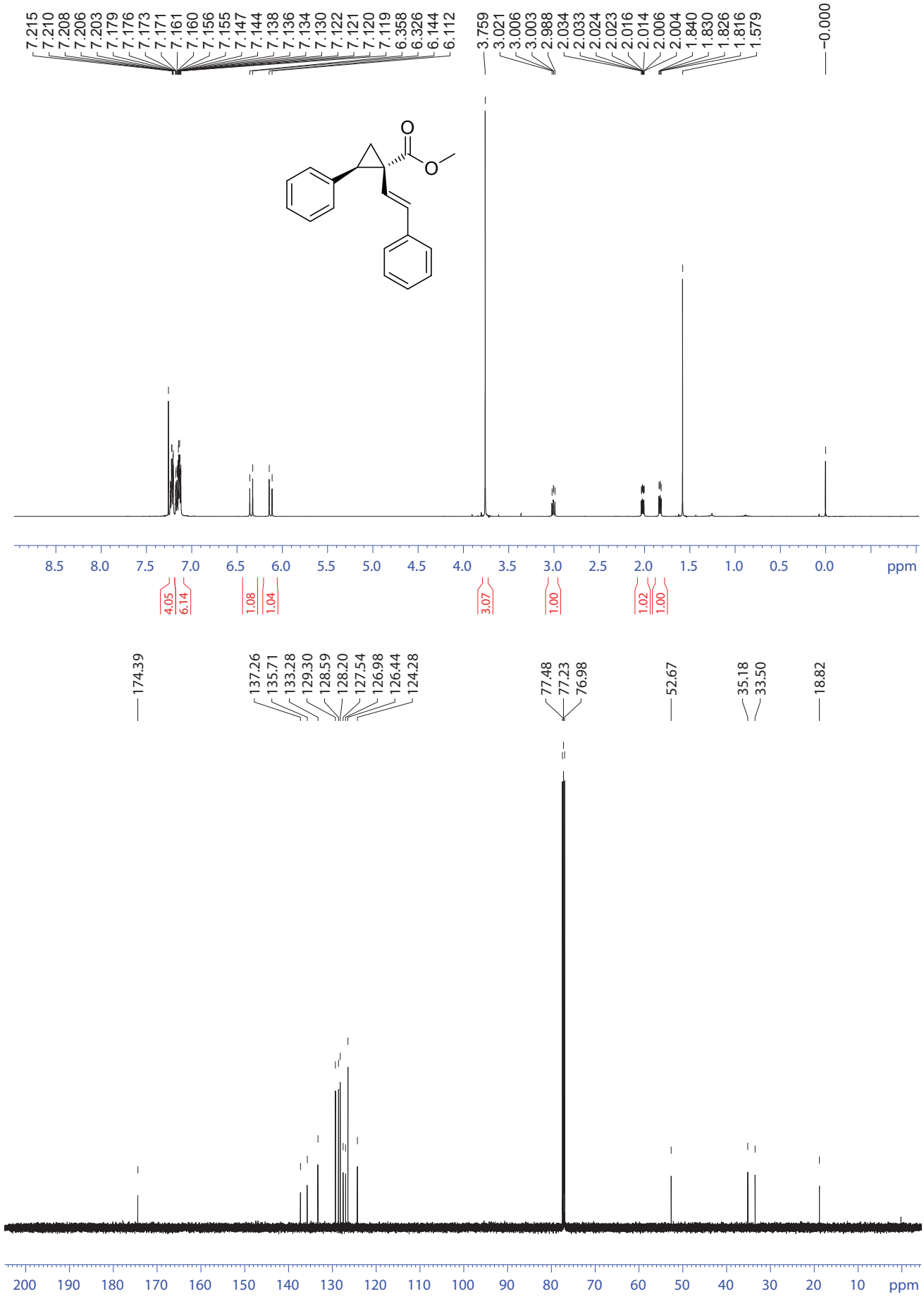
2d. NMR spectra of cyclopropane products:

(*1S,2R*)-methyl 1,2-diphenylcyclopropanecarboxylate (**3**)



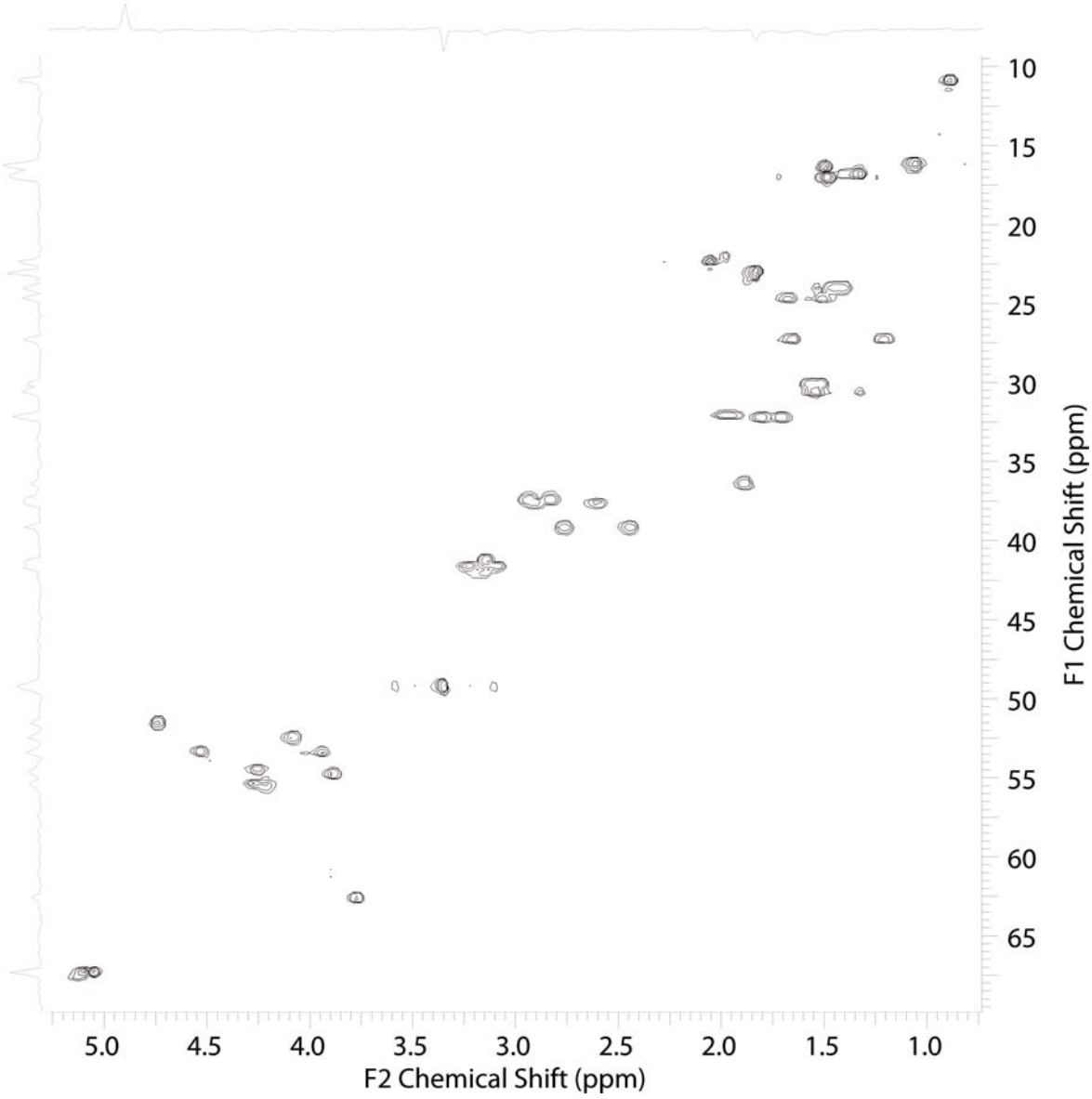


(1R,2R)-methyl 2-phenyl-1-((*E*)-styryl)cyclopropanecarboxylate (**5**)

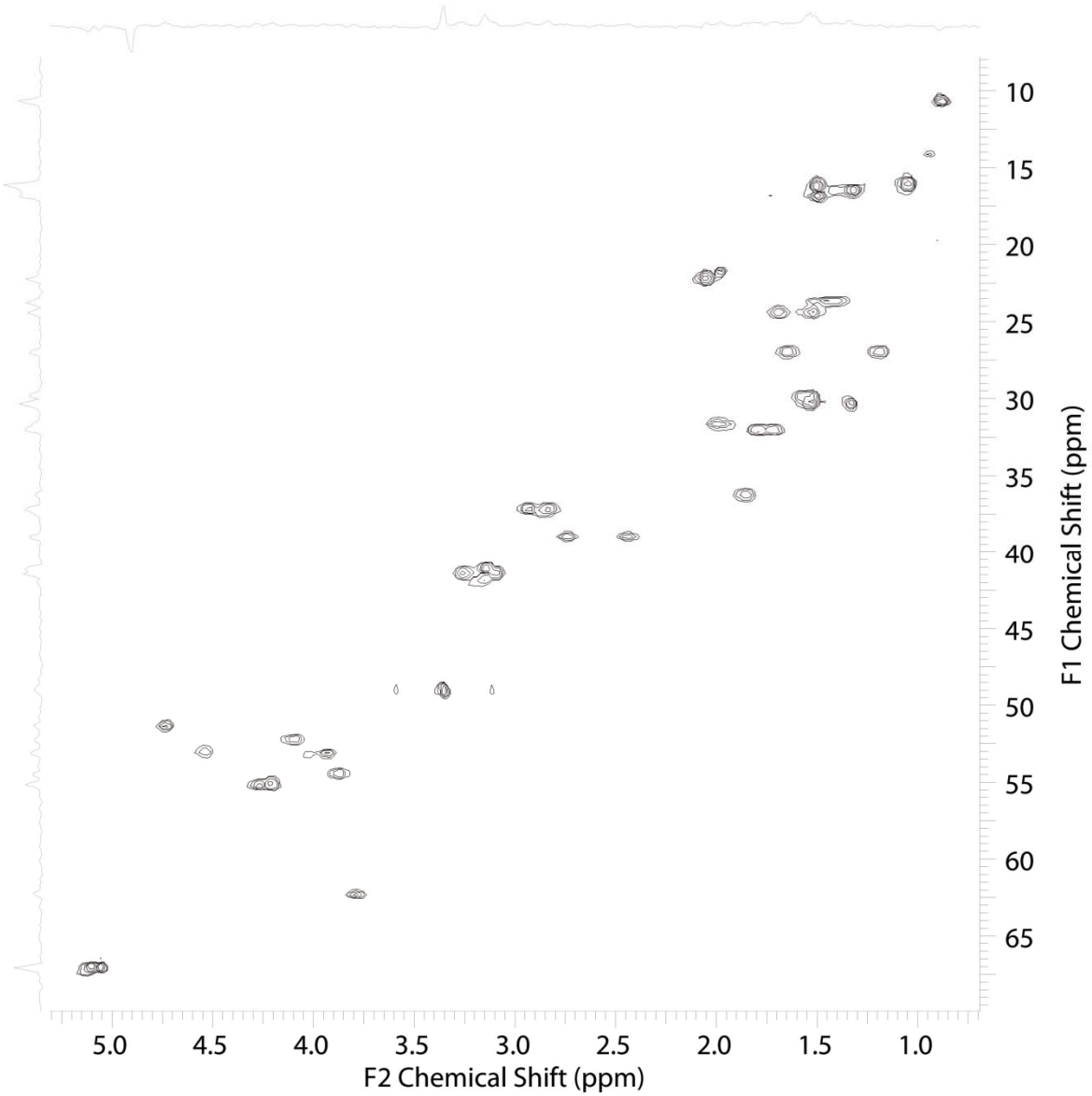


2e. HSQC of dirhodium metallopeptides of sequence L21:

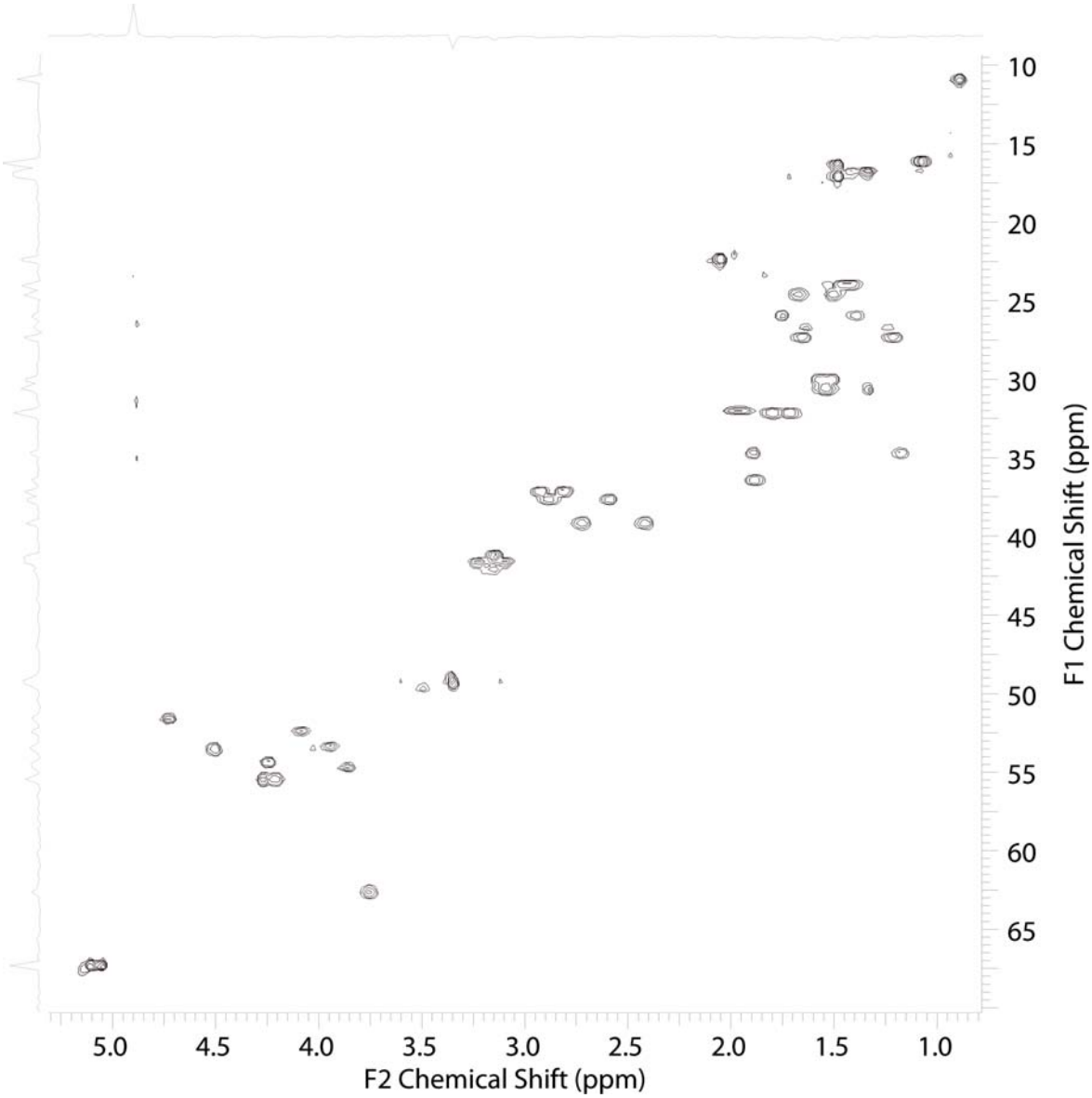
Rh_2(**L21**)$(OAc)_2$:



Rh_2(**L21**)$_2$-*para*:

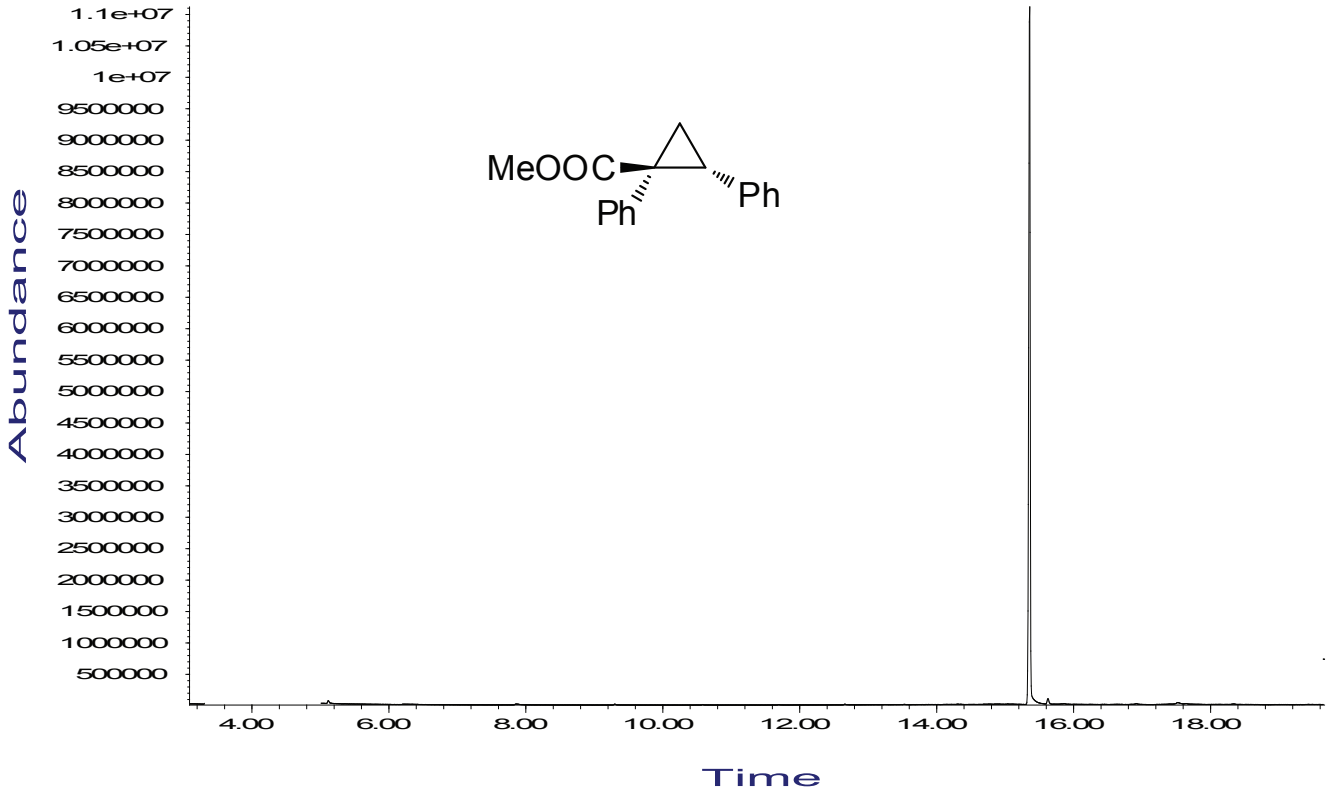


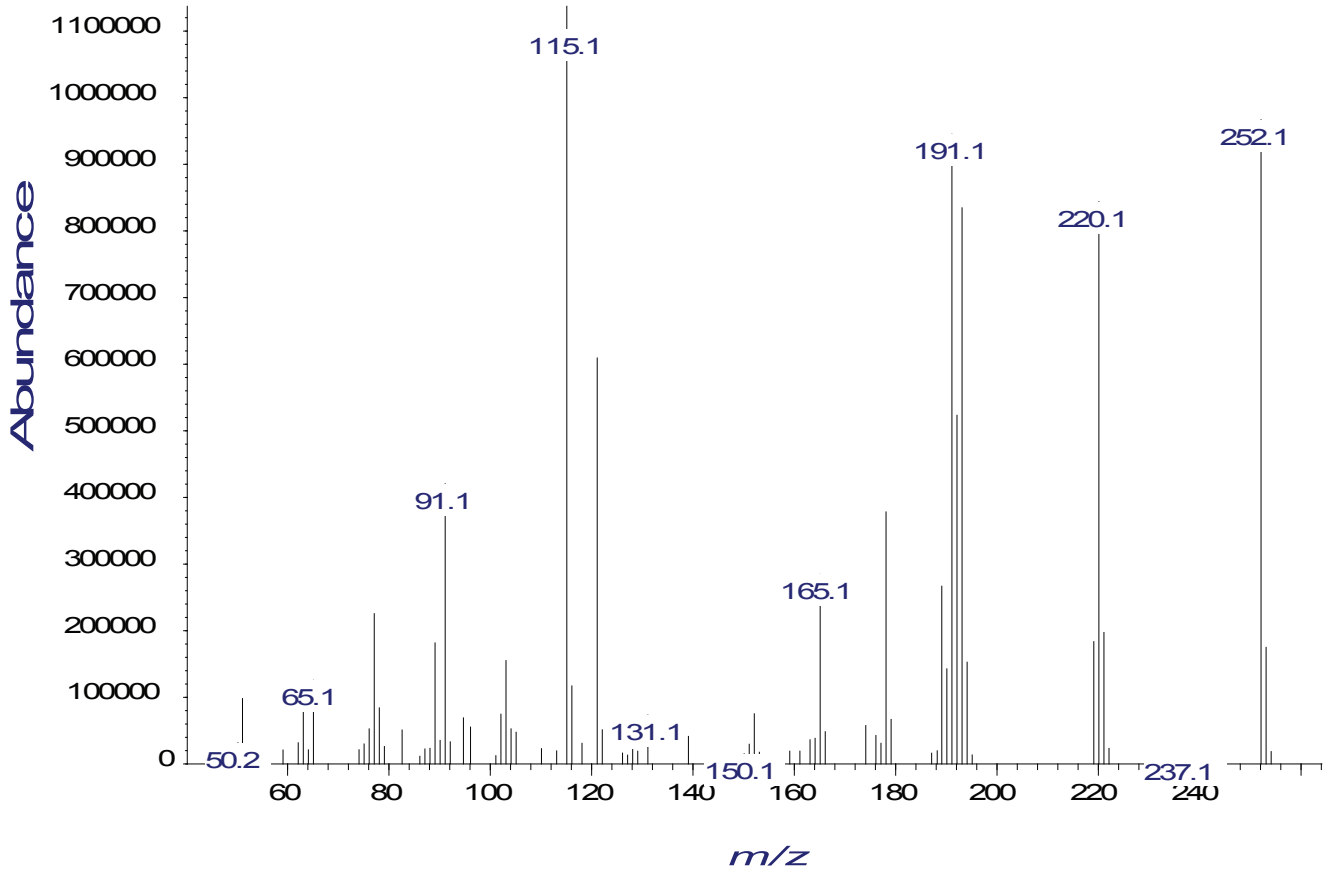
Rh_2(**L21**)$_2$-*anti*:



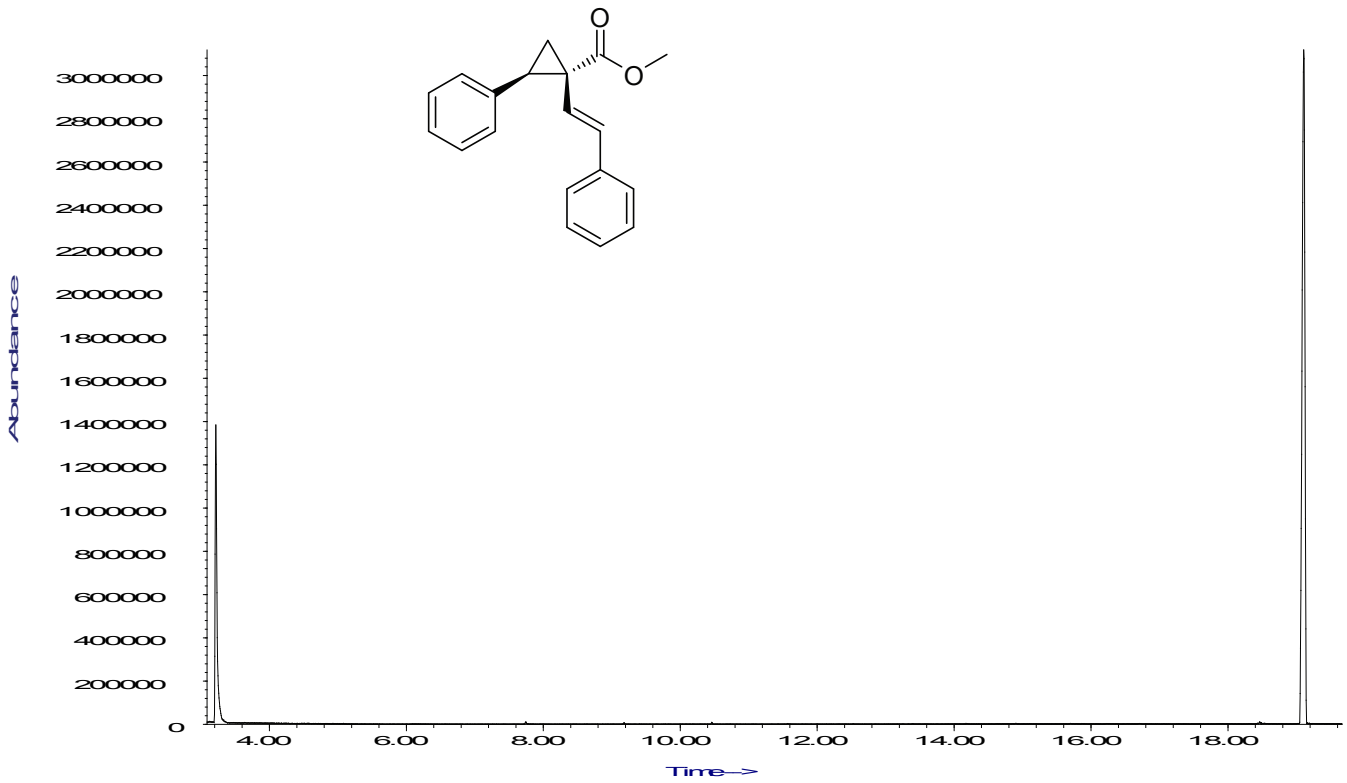
2f. GC-MS spectra of cyclopropane products:

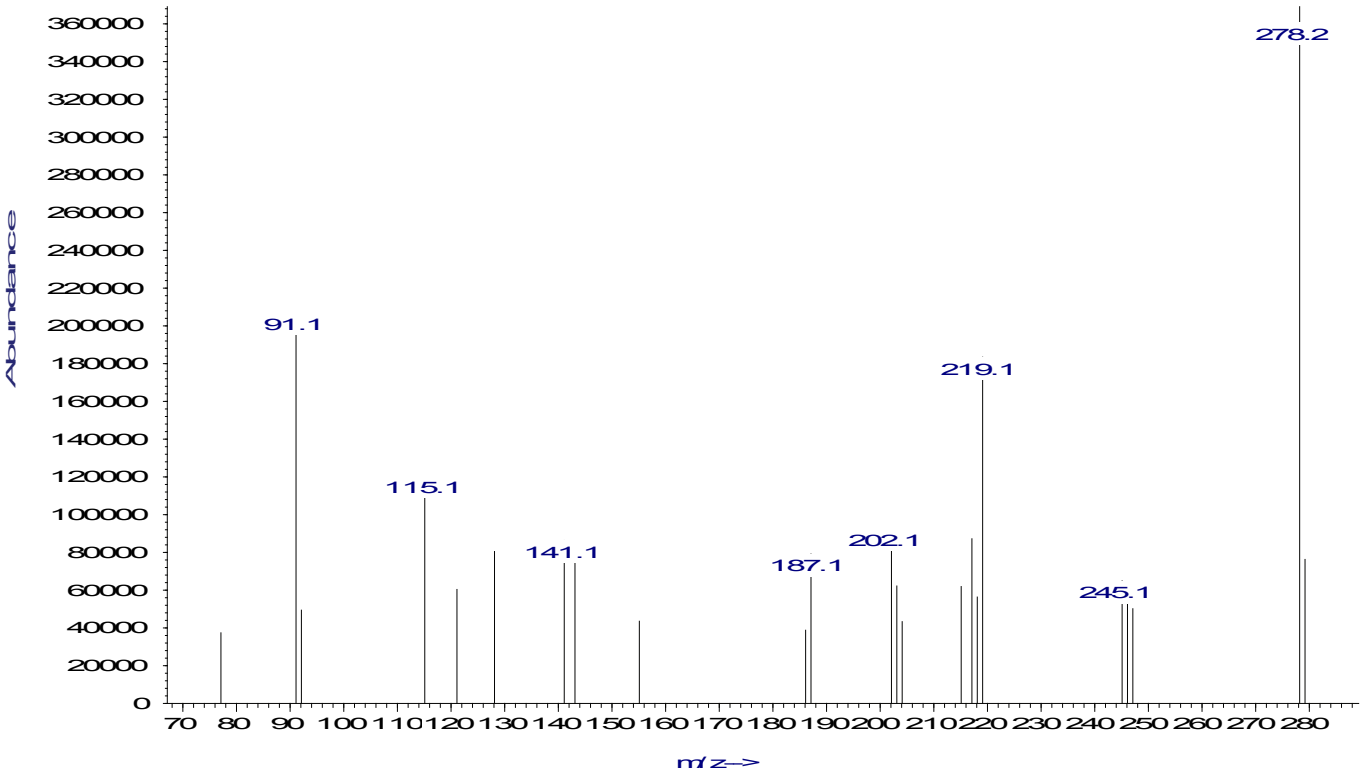
(*1S,2R*)-methyl 1,2-diphenylcyclopropanecarboxylate (**3**)





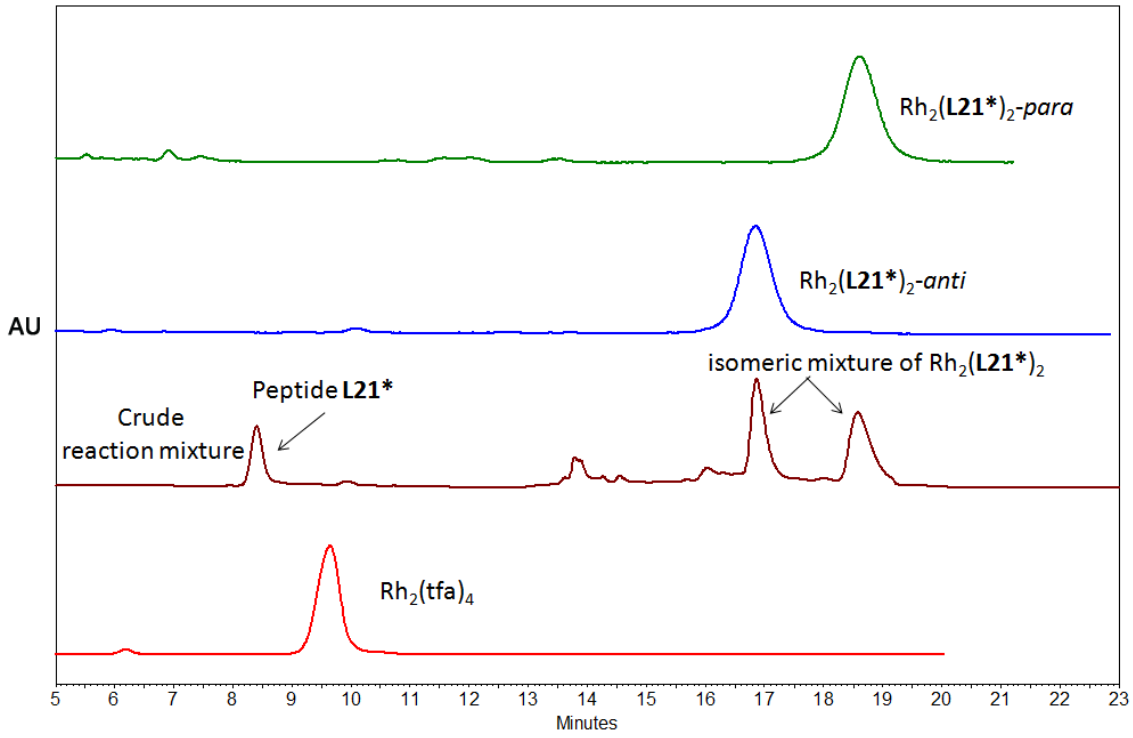
(1R,2R)-methyl 2-phenyl-1-((*E*)-styryl)cyclopropanecarboxylate (**5**)



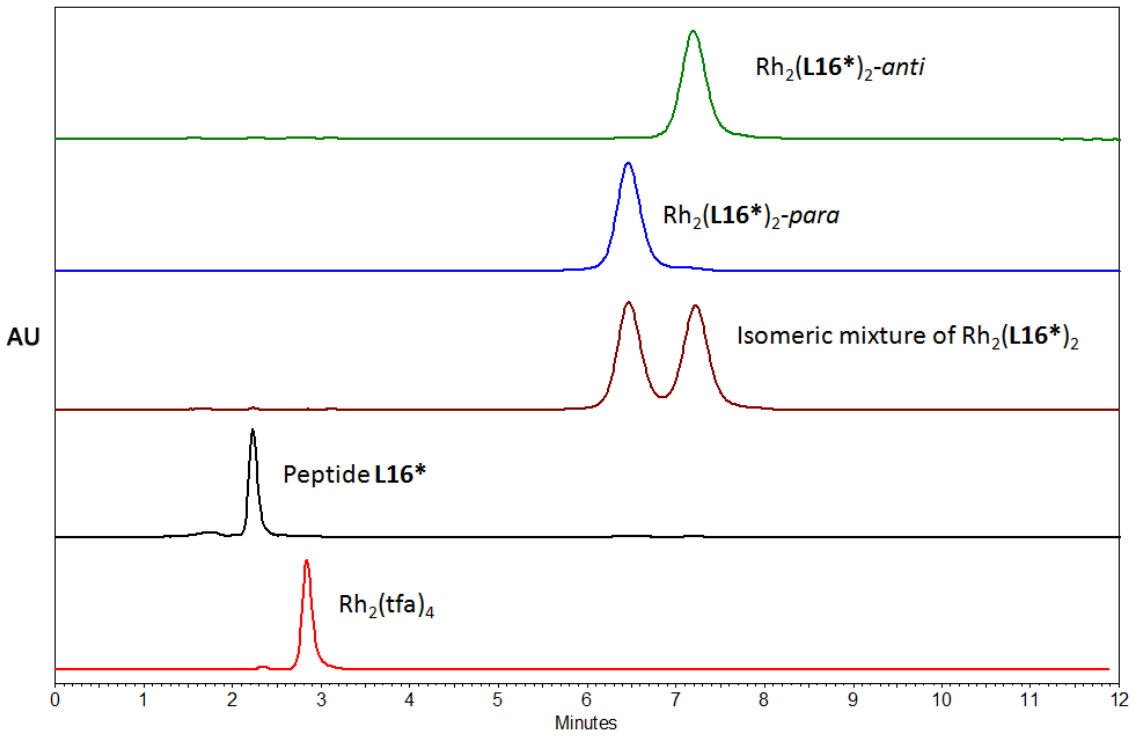


2g.HPLC analysis of pyrene-containing metallopeptides:

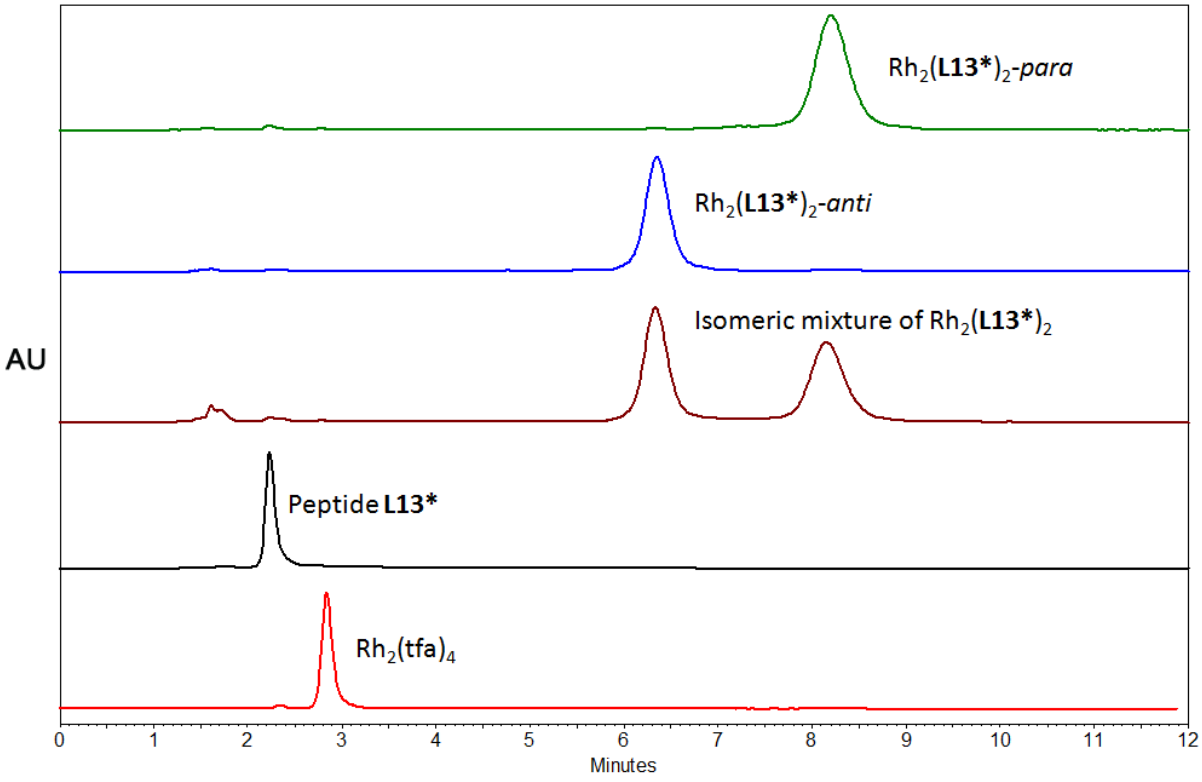
Rh_2(**L21***)$_2$



Rh_2(**L16***)$_2$

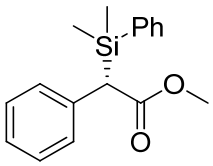


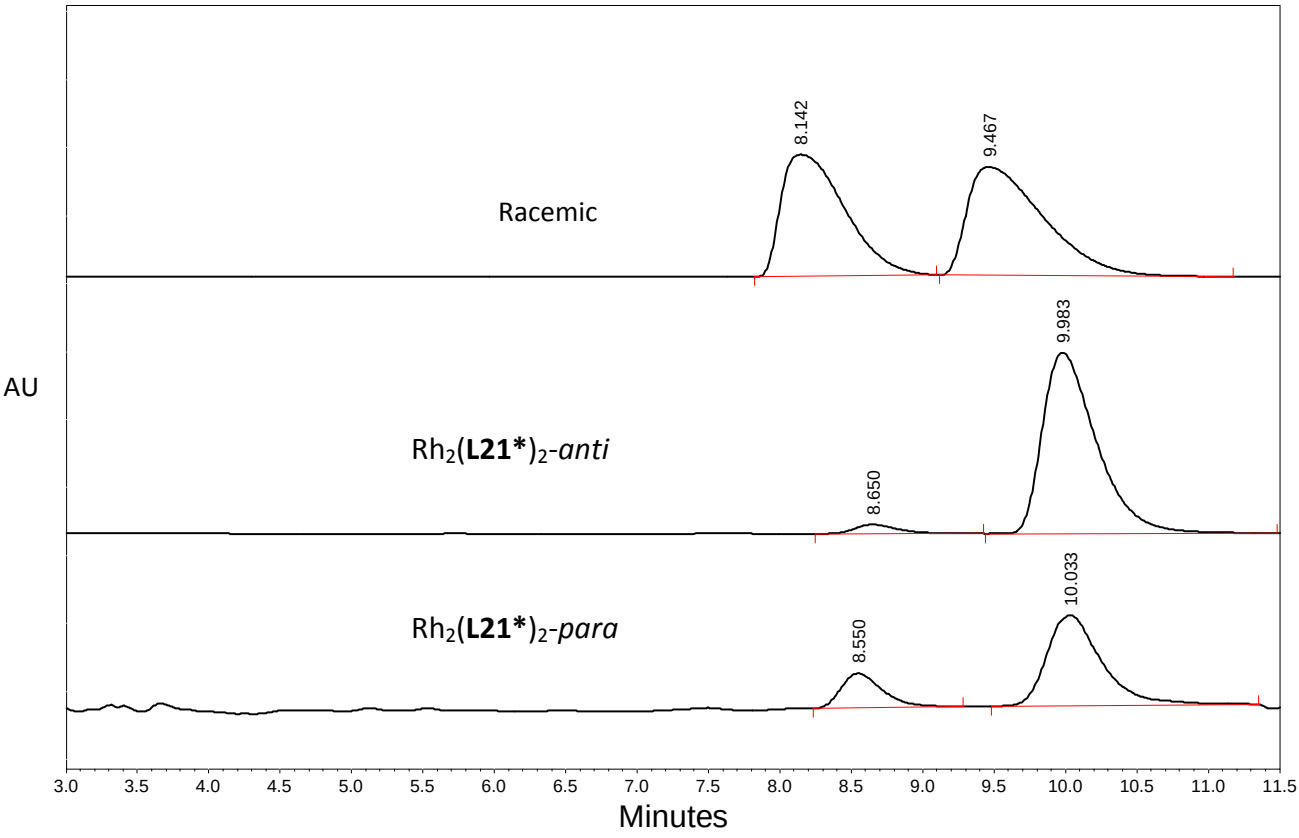
Rh_2(**L13***)$_2$



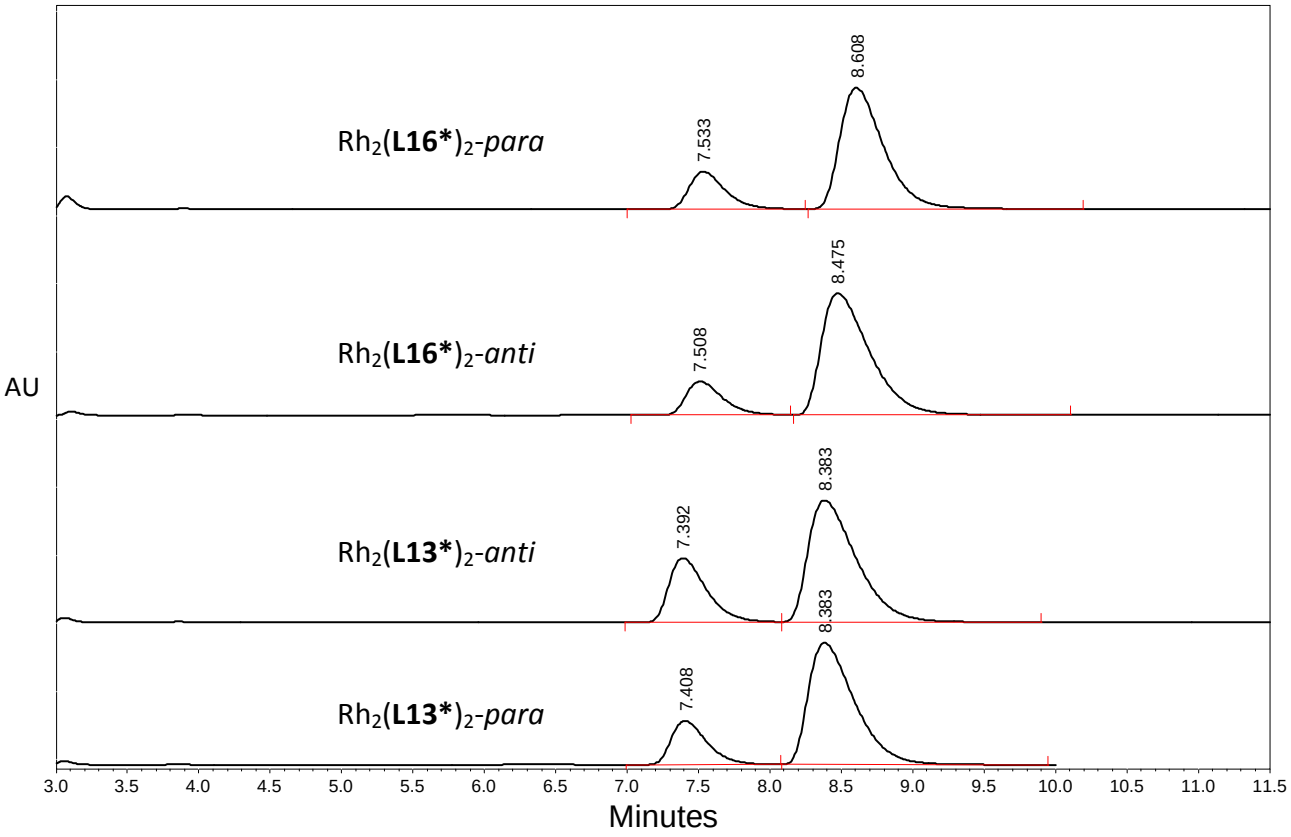
2h. Chiral HPLC analysis:

(*S*)-Methyl 2-dimethylphenylsilyl-2-phenylacetate (2):



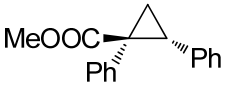


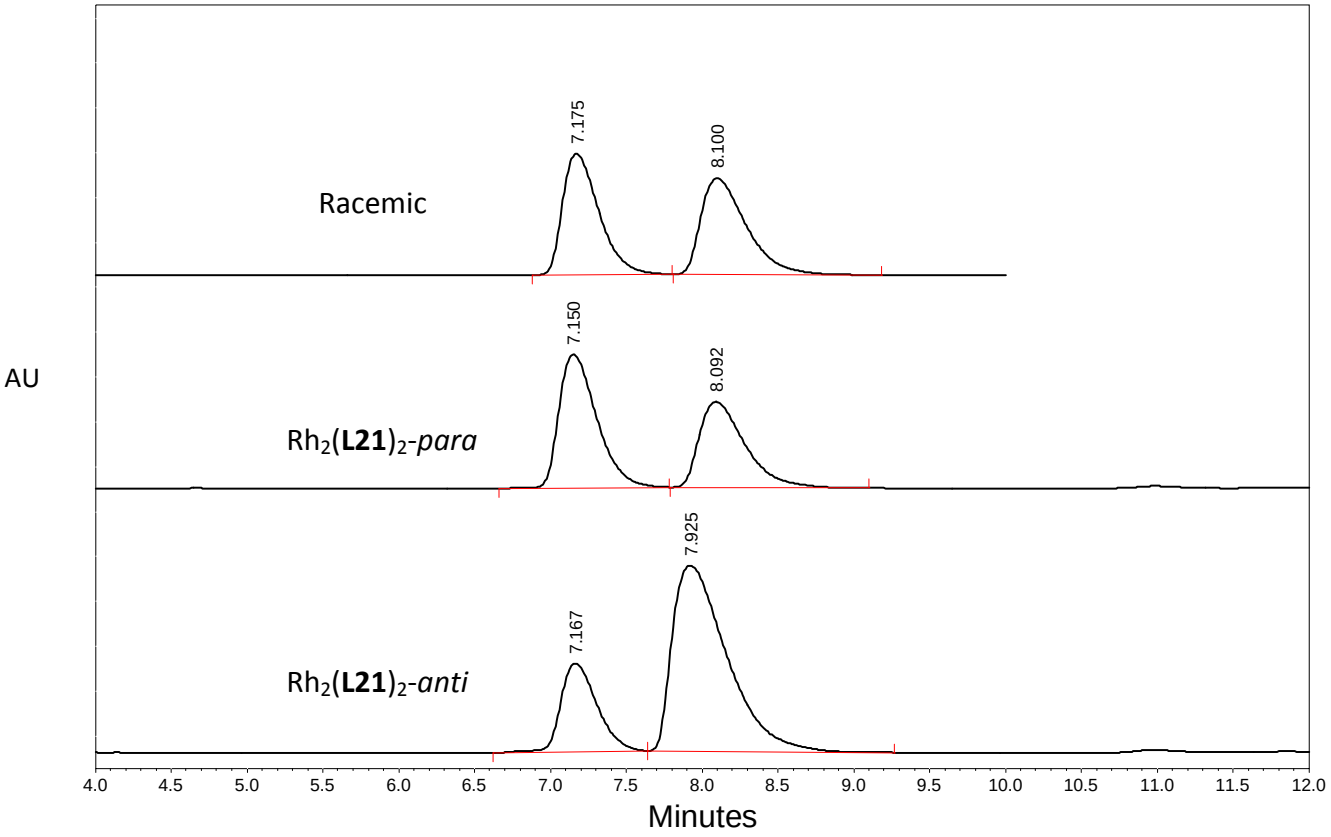
Catalyst	RT		Area		% Area		Height	
	Peak 1	Peak2	Peak1	Peak2	Peak1	Peak2	Peak1	Peak2
$Rh_2(OAc)_4$	8.142	9.467	55229209	59021753	48.34	51.660	1787891	1592384
Rh_2(**L21***)$_2$-*anti*	8.650	9.983	192988	4737040	3.915	96.085	9039	180002
Rh_2(**L21***)$_2$-*para*	8.550	10.033	30159	104357	22.420	77.580	1479	3860



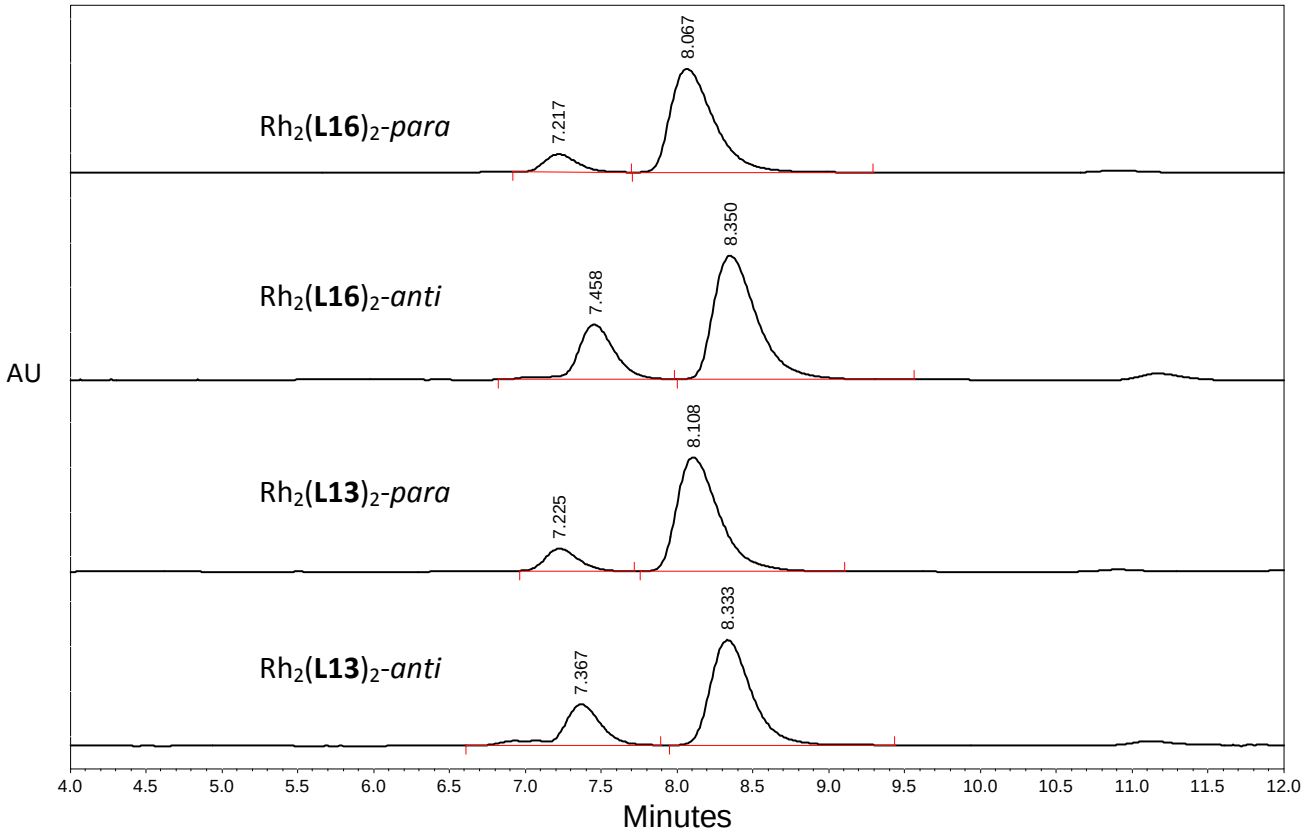
Catalyst	RT		Area		% Area		Height	
	Peak 1	Peak2	Peak1	Peak2	Peak1	Peak2	Peak1	Peak2
Rh_2(**L16***)$_2$-*para*	7.533	8.608	1498880	5927456	20.183	79.817	85325	274940
Rh_2(**L16***)$_2$-*anti*	7.508	8.475	3885505	18700682	17.203	82.797	219318	793270
Rh_2(**L13***)$_2$-*anti*	7.392	8.383	8170654	20197713	28.802	71.198	450282	855485
Rh_2(**L13***)$_2$-*para*	7.408	8.383	4452936	15929231	21.847	78.153	253934	702423

(*1S,2R*)-methyl 1,2-diphenylcyclopropanecarboxylate (**3**)

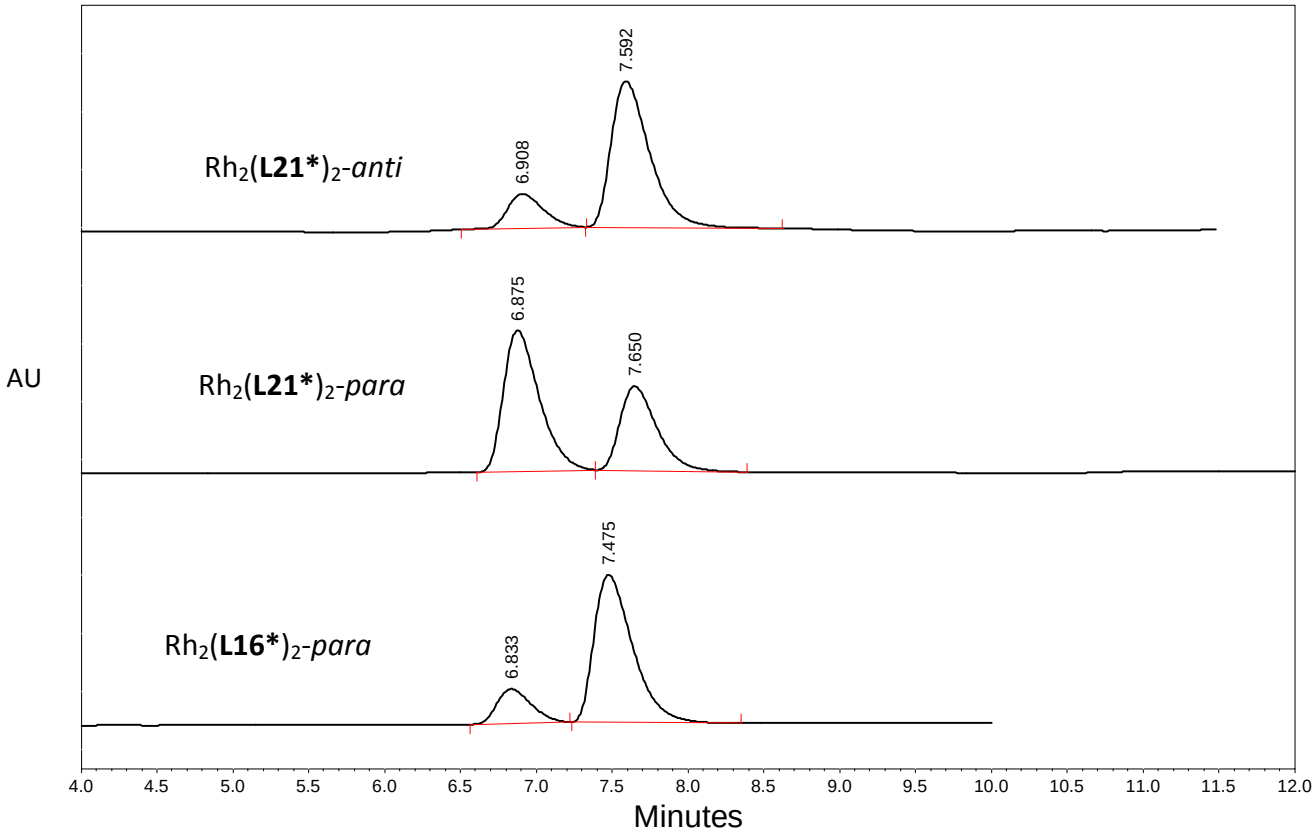




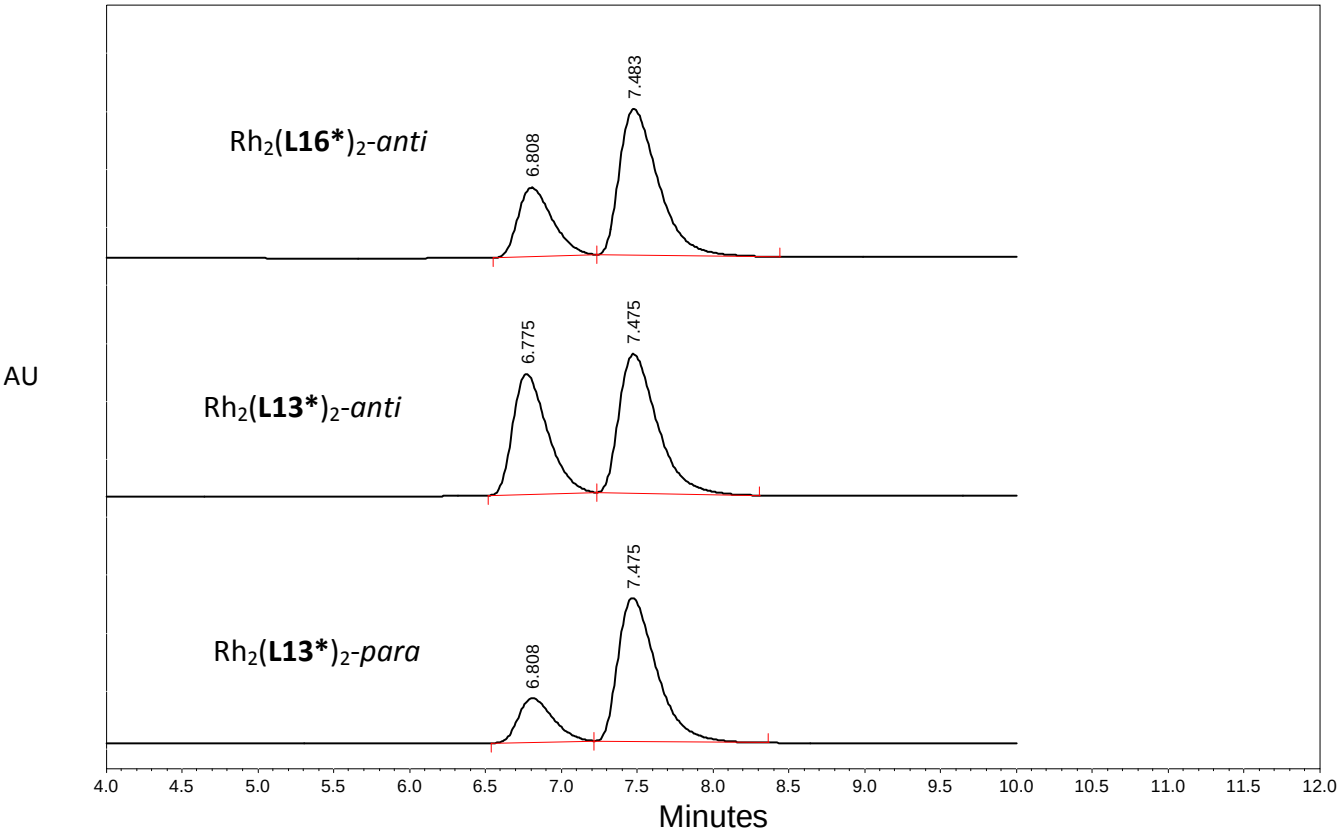
Catalyst	RT		Area		% Area		Height	
	Peak 1	Peak2	Peak1	Peak2	Peak1	Peak2	Peak1	Peak2
$Rh_2(OAc)_4$	7.175	8.100	11245778	11070563	50.393	49.607	674568	534165
Rh_2(**L21**)$_2$-*para*	7.150	8.092	12229089	9515859	56.239	43.761	706271	453932
Rh_2(**L21**)$_2$-*anti*	7.167	7.925	9033156	28585544	24.012	75.988	544388	1143021



Catalyst	RT		Area		% Area		Height	
	Peak 1	Peak2	Peak1	Peak2	Peak1	Peak2	Peak1	Peak2
Rh_2(**L16**)$_2$-*para*	7.217	8.067	793216	5913845	11.827	88.173	51584	296436
Rh_2(**L16**)$_2$-*anti*	7.458	8.350	1943000	5202667	27.191	72.809	116005	261511
Rh_2(**L13**)$_2$-*para*	7.225	8.108	571077	3754514	13.202	86.798	37774	193161
Rh_2(**L13**)$_2$-*anti*	7.367	8.333	406403	1083766	27.272	72.728	22419	57428

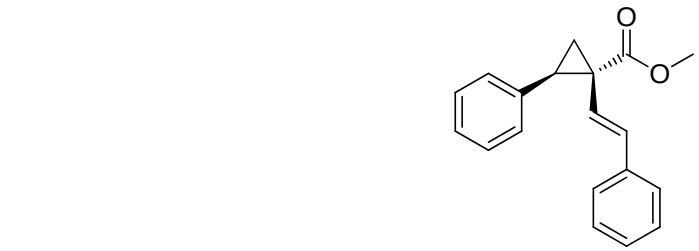


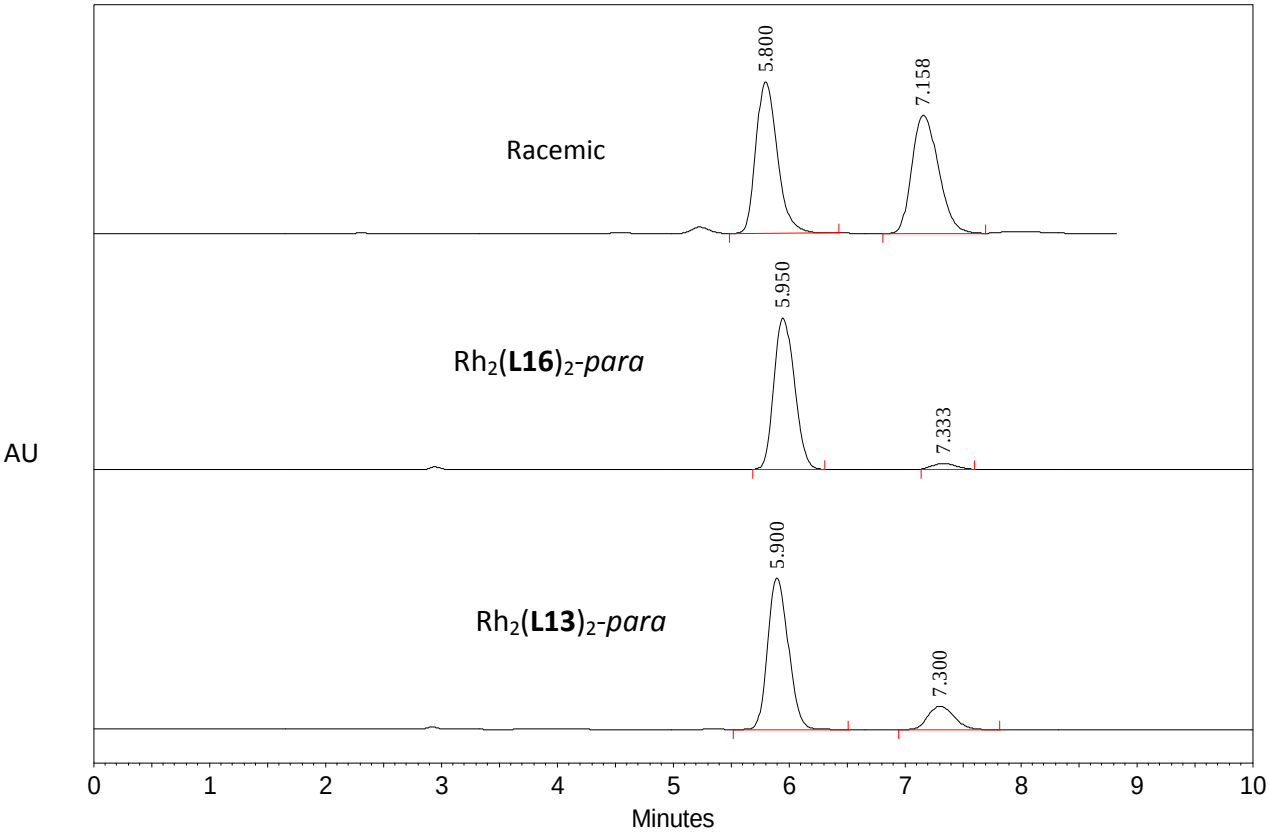
Catalyst	RT		Area		% Area		Height	
	Peak 1	Peak2	Peak1	Peak2	Peak1	Peak2	Peak1	Peak2
Rh_2(**L21***)$_2$-*anti*	6.908	7.592	630121	2913861	17.780	82.220	38515	163674
Rh_2(**L21***)$_2$-*para*	6.875	7.650	2044102	1274264	61.6	38.4	124643	74496
Rh_2(**L16***)$_2$-*para*	6.833	7.475	785842	3767253	17.260	82.740	49739	212701



Catalyst	RT		Area		% Area		Height	
	Peak 1	Peak2	Peak1	Peak2	Peak1	Peak2	Peak1	Peak2
Rh_2(**L16***)$_2$-*anti*	6.808	7.483	1521222	3626127	29.554	70.446	96370	203913
Rh_2(**L13***)$_2$-*anti*	6.775	7.475	2238556	2858734	43.917	56.083	141487	163945
Rh_2(**L13***)$_2$-*para*	6.808	7.475	878432	3181803	21.635	78.365	55546	180792

(1*R*,2*R*)-methyl 2-phenyl-1-((*E*)-styryl)cyclopropanecarboxylate (5)





Catalyst	RT		Area		% Area		Height	
	Peak 1	Peak2	Peak1	Peak2	Peak1	Peak2	Peak1	Peak2
$Rh_2(OAc)_4$	5.8	7.158	14838812	14443763	50.675	49.325	1151170	900577
Rh_2(**L16**)$_2$-*para*	5.95	7.333	9428815	412447	95.809	4.191	759451	29344
Rh_2(**L13**)$_2$-*para*	5.900	7.3	10674754	2067950	83.771	16.229	856017	132971

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