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New Tetraphosphite Ligands for Regioselective Linear Hydroformylation of Terminal Olefins and Internal Olefin

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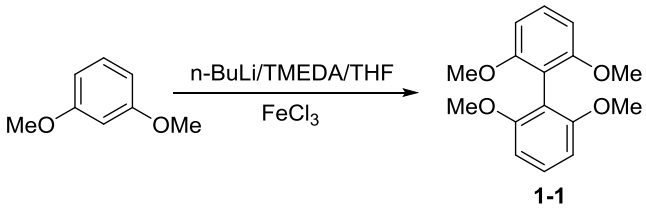
Contents

1. General Remarks

All reactions were performed in the argon-filled glovebox or under nitrogen using standard Schlenk techniques, unless otherwise noted. Solvents were dried with standard procedures and degassed with N_2. Column chromatography was performed using 200~400 mesh silica gel. Thin layer chromatography (TLC) was performed on EM reagents 0.25 mm silica 60-F plates. ^{1}H, ^{13}C, ^{31}P NMR spectrum were recorded on Bruker-400, with $CDCl_3$ as the solvents and tetramethylsilane (TMS) as the internal standard. Chemical shifts were reported in ppm, up field to TMS (0.00 ppm) for and relative to $(CD_3)_2SO$ (2.5ppm, 39.5ppm), $CDCl_3$ (7.26 ppm, 77.3 ppm) for ^{1}H NMR and ^{13}C NMR. GC analysis was carried out on SHIMADZU Lab Solution GC instrument using achiral capillary columns. Unless otherwise noted, all reagents and solvents were purchased from commercial suppliers and used without further purification.

2. Procedure for synthesis of tetraphosphite ligands

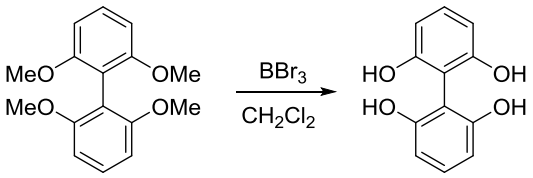
(1) Synthesis of 2,2',6,6'-Tetramethoxybiphenyl **1-1**[1]



1-1

To a mixture of 1,3-dimethoxybenzene (27.6 g, 200 mmol) and TMEDA (36.3 mL, 240 mmol) in THF at -78 ℃ was slowly added a solution of *n*-BuLi (1.5 M in hexane, 140 mL, 210 mmol). After being stirred for 2 hours at -78 ℃, the reaction mixture was warmed to 0 ℃. After being stirred for 1 h at 0 ℃, $FeCl_3$ (38.9 g, 240 mmol) was added, and the reaction mixture was warmed to room temperature. After 36 hours, 1.0 M HCl (aq.) was added and the resulting solid (target molecule) was collected by filtration. The filtrate was extracted with diethyl ether (x 3), washed with brine, and dried over Na_2SO_4. After removing solvent under reduced pressure, the residue was washed with ethyl acetate to give the product. 2,2',6,6'-tetramethoxybiphenyl **1-1** was obtained in 70% total yield (19.3 g). The NMR is in consistence with the literature data.[1]

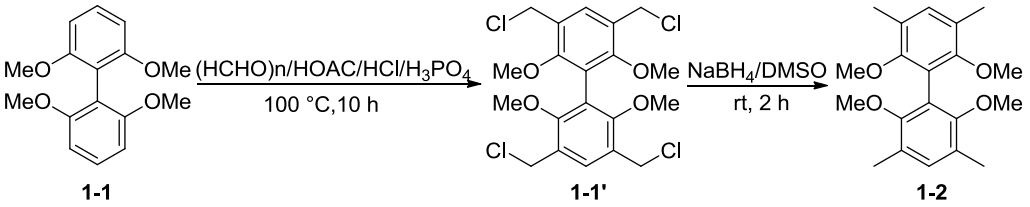
(2) Synthesis of 2,2',6,6'-Tetrahydroxybiphenyl **2-1**[1]



1-1 **2-1**

To a solution of 2,2',6,6'-tetramethoxybiphenyl **1-1** (11.1 g, 42.7 mmol) in CH_2Cl_2 (215 mL) at -78 ℃ was slowly added boron tribromide (50 g, 200 mmol). The reaction mixture was gradually warmed to room temperature over 2 hours, and stirred for 24 hours at room temperature. After complete consumption of the starting material, the reaction mixture was quenched by H_2O. The water layer was extracted with ether (x 2). The combined organic layers were washed with brine, dried over Na_2SO_4, and concentrated under reduced pressure to give 2,2',6,6'-tetrahydroxybiphenyl **2-1** as a yellow solid (7.23 g, 82%). The NMR is in consistence with the literature data.[1]

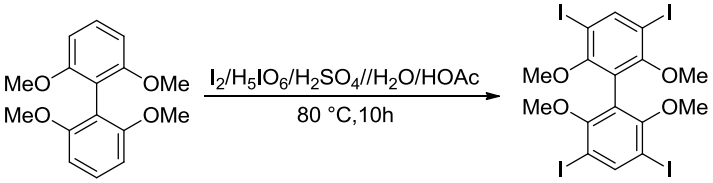
(3) Synthesis of 2,2’,6,6’-tetramethoxy-3,3’,5,5’-tetramethyl-1,1’-biphenyl **1-2**[2]



1-1 **1-1'** **1-2**

2,2,6,6-tetramethoxy biphenyl **1-1** (1.37 g, 5 mmol) with paraformaldehyde (30 equiv.) in the mixture acid of phosphoric acid, concentrated hydrochloric acid, and acetic acid (V = 1:1:1, 0.01 M) were heated to 100 ℃ for 10 h affording product **1-1’** (2.1 g) with 90% isolated yield. Then, reduction of **1-1’** by $NaBH_4$ gave desired product **1-2** (1.41 g) in 95% yield. The NMR is in consistence with the literature data.[2]

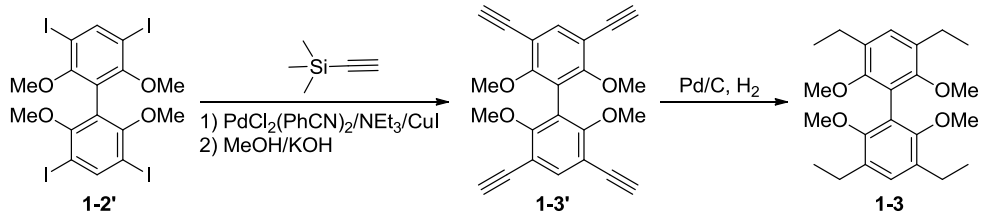
(4) Synthesis of 3,3’,5,5’-Tetraiodo-2,2’6,6’-Tetramethoxybiphenyl **1-2’**[3]



1-1 **1-2'**

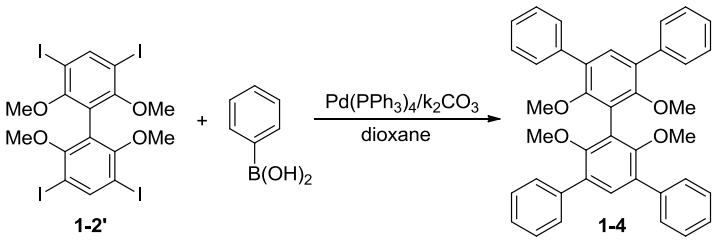
A 200 mL three-necked flask is charged with 2,2’6,6’-Tetramethoxybiphenyl **1-1** (13.8 g, 50.0 mmol), periodic acid dehydrate (9.1 g, 40.0 mmol), and iodine (20.4 g, 80.0 mmol). A solution of 3 mL of concentrated sulfuric acid and 20 mL of water in 100 mL of glacial acetic acid is added to this mixture. The resulting purple solution is heated at 80 ℃ with stirring for approximately 10 hours until the color of iodine disappears. The reaction mixture is diluted with approximately 250 mL of water, and the white-yellow solid that separates is collected on a Büchner funnel and washed three times with 100-mL portions of water. The product is recrystallized from boiling acetone as colorless, fine needles (34.9 g, 90%). The NMR is in consistence with the literature data.[3]

(5) Synthesis of 3, 3’, 5, 5’-Tetraethyl-2, 2’ 6, 6’-Tetramethoxybiphenyl **1-3**[3]



3,3',5,5'-Tetraiodo-2,2'6,6'-Tetramethoxybiphenyl **1-2'** (7.8 g, 10 mmol) and ethynyltrimethylsilane (8.2 mL, 58.0 mmol) in a mixture of triethylamine (100 mL) and piperidine (30 mL) was treated with $PdCl_2(PhCN)_2$, (0.4 mg, 1.0 mmol), triphenylphosphine (275 mg, 1.0 mmol), and CuI (80 mg). The originally yellow solution turned to green and then brown. After 3 h at room temperature it was heated at 80 ºC for 24 h. The precipitate was filted and the filtration was passed through a short silica gel plug. The obtained solution was evaporated and treated with a solution of KOH (6.0 g, 108.0 mmol) in methanol (40 mL). The reaction solution was stirred at room temperature for 2 h until TLC analysis indicated that the reaction was complete. Ether-water workup and the obtained yellow liquid was dissolved in 200 mL of mixture of ethyl acetate and methanol and combined with 5 wt% Pd/C (0.5 g) in an autoclave under a 200 psi of hydrogen atmosphere. The reaction was stirred at room temperature for 2 h until no hydrogen absorption was observed. Filtration and flash chromatography afford white solid 2.3 g in 58% yield. The NMR is in consistence with the literature data.[3]

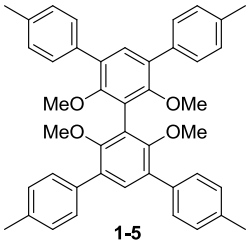
(6) Synthesis of 3,3',5,5'-Tetraphenyl-2,2',6,6'-Tetramethoxybiphenyl **1-4**[3]



A mixture of phenylboronic acid (14.6 g, 120.0mmol), 3,3',5,5'-Tetraiodo-2,2'6, 6'-Tetramethoxy biphenyl **1-2'** (7.8 g, 10 mmol), palladium tetrakistriphenylphosphine (1.0 g), and potassium carbonate (24 g, 160 mmol) in dry dioxane (150 mL) was stirred under nitrogen for 24 h at 85 ºC. The resulting mixture was cooled and poured into a solution of ice with concentrated hydrochloric acid (3:1) and the organic phase was extracted with dichloromethane (x 2), dried over magnesium sulfate. After evaporation of the solvent, the mixture was subjected to flash chromatography to give 3,3'5,5'-Tetraphenyl-2,2'6,6'-Tetramethoxybiphenyl **1-4** (4.0 g) as a

white solid in 70% yield. The NMR is in consistence with the literature data.[3]

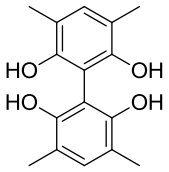
(7) Synthesis of 3,3’,5,5’-Tetratolyl-2,2’,6,6’-Tetramethoxybiphenyl **1-5**[3]



1-5

3,3’,5,5’-Tetratolyl-2,2’,6,6’-Tetramethoxybiphenyl **1-5** was prepared according to the general procedure for synthesis of 3,3’,5,5’-tetraphenyl-2,2’6,6’-tetramethoxybiphenyl **1-4** by using tolylboronic acid (24.5 g, 180.0 mmol), 3,3’,5,5’-tetraiodo-2,2’,6,6’-tetramethoxybiphenyl **1-2’** (11.9 g, 15.2 mmol). Purification by flash chromatography gave **1-5** (6.5 g) as a white solid in 69% yield. The NMR is in consistence with the literature data.[3]

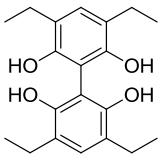
(8) Synthesis of 3,3’,5,5’-tetramethyl-[1,1'-biphenyl]-2,2',6,6'-tetraol **2-2**[2]



2-2

3,3',5,5'-tetramethyl-[1,1'-biphenyl]-2,2',6,6'-tetraol **2-2** was prepared according to the general procedure for synthesis of 2,2',6,6'-Tetrahydroxybiphenyl **2-1** in 81% yield. The NMR is in consistence with the literature data.[2]

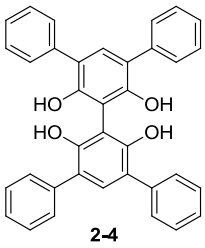
(9) Synthesis of 3,3’,5,5’-tetraethyl-[1,1'-biphenyl]-2,2',6,6'-tetraol **2-3**[3]



2-3

3,3',5,5'-tetraethyl-[1,1'-biphenyl]-2,2',6,6'-tetraol **2-3** was prepared according to the general procedure for synthesis of 2,2',6,6'-Tetrahydroxybiphenyl **2-1** in 85% yield. The NMR is in consistence with the literature data.[3]

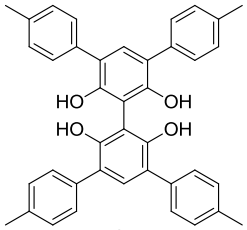
(10) Synthesis of 3, 3', 5, 5'-Tetraphenylbiphenyl-2, 2' 6, 6'-tetranol **2-4**[3]



2-4

3, 3', 5, 5'-Tetraphenylbiphenyl-2, 2' 6, 6'-tetranol **2-4** was prepared according to the general procedure for synthesis of 2,2',6,6'-Tetrahydroxybiphenyl **2-1** in 89% yield. The NMR is in consistence with the literature data.[3]

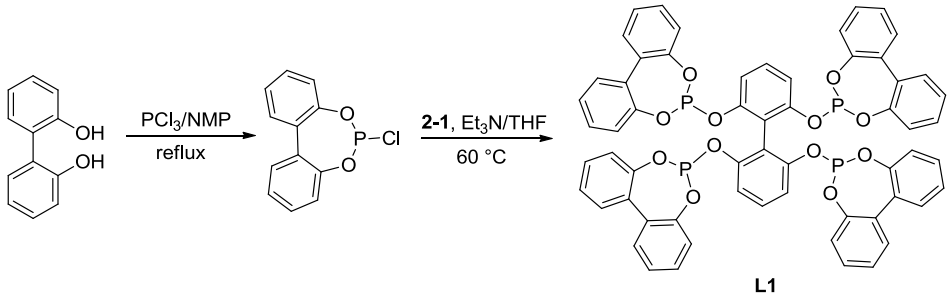
(11) Synthesis of 3, 3', 5, 5'-Tetratolyl-2, 2' 6, 6'-Tetramethoxybiphenyl **2-5**[3]



2-5

3, 3', 5, 5'-Tetratolyl-2, 2' 6, 6'-Tetramethoxybiphenyl **2-5** was prepared according to the general procedure for synthesis of 2,2',6,6'-Tetrahydroxybiphenyl **2-1** in 85% yield. The NMR is in consistence with the literature data.[3]

(12) Synthesis of ligand **L1**[4]

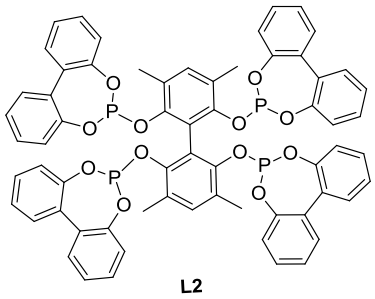


L1

To a 50 mL Schlenk flask was added 2,2'-biphenol (5.59 g, 30.0 mmol), a drop of NMP and 10 mL PCl_3. The resulting solution was refluxed for 6 hours and the excess PCl_3 was removed under reduced press. Trace amount of PCl_3 were azeotropically evaporated with toluene (2 × 10 mL) and the resulting oil was dissolved in 20 ml THF. The resulting mixture was added dropwise to the solution of 2,2',6,6'-Tetrahydroxybiphenyl **2-1** (1.09 g, 5 mmol), Et_3N (8.3 mL, 60 mmol),

THF (20 mL) at 60 ºC, and then stirred at 60 ºC for 12h. The mixture was concentrated under vacuum after the salts were filtered off. The crude product was purified by silica gel flash chromatography to get the pure product as a white solid (2.8 g, yield 52%). ^{1}H NMR (400 MHz, $(CD_3)_2SO$): δ = 6.89-6.92 (m, 6 H), 7.29-7.39 (m, 20 H), 7.49-7.56 (m, 10 H), 7.70-7.72 (m, 2 H); ^{13}C NMR (101 MHz, $CDCl_3$): 103.34, 108.63, 116.74, 121.49, 121.70, 121.74, 124.09, 127.00, 128.63, 129.78, 130.26, 130.37, 131.39, 131.87, 146.47, 153.01, 155.18; ^{31}P NMR: δ = 144.01 ppm.

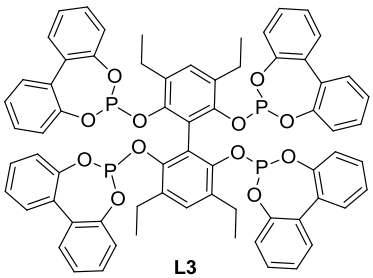
(13) Synthesis of ligand **L2**[4]



L2

Ligand **L2** was prepared according to the general procedure for synthesis of ligand **L1** in 61% yield (504 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.44 (s, 12 H), 6.83-6.85 (m, 8H), 7.15-7.29 (m, 16H), 7.42-7.43 (m, 10H); ^{13}C NMR (101 MHz, $CDCl_3$): 17.53, 122.41, 124.87, 126.52, 128.85, 129.47, 131.18, 133.16, 149.30; ^{31}P NMR: δ = 144.92 ppm.

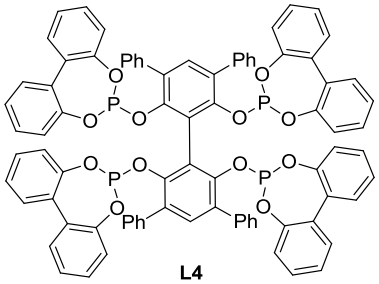
(14) Synthesis of ligand **L3**[4]



L3

Ligand **L3** was prepared according to the general procedure for synthesis of ligand **L1** in 59% yield (424 mg).^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.24 (t, *J* = 8.0 Hz, 12 H), 2.83-2.85 (m, 8H), 6.79-6.81 (m, 8H), 7.18-7.22 (m, 16H), 7.30-7.32 (m, 2H), 7.41-7.43 (m, 8H); ^{13}C NMR (101 MHz, $CDCl_3$) : 15.27, 23.76, 122.47, 124.84, 128.78, 129.05, 129.46, 130.40, 131.21, 132.78, 148.08, 149.39; ^{31}P NMR: δ = 144.55 ppm.

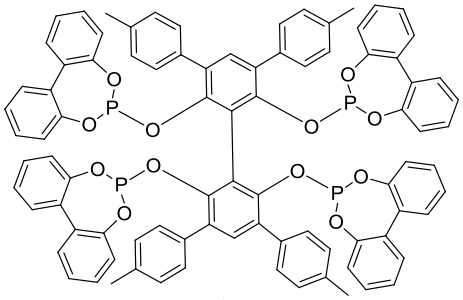
(15) Synthesis of ligand **L4**[4]



L4

Ligand **L4** was prepared according to the general procedure for synthesis of ligand **L1** in 57% yield (300 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 6.33 (d, *J* = 8.0 Hz, 8H), 7.12-7.17 (m, 16H), 7.35-7.36 (m, 8H), 7.42-7.50 (m, 20H), 7.74 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): 122.10, 124.87, 127.45, 128.44, 128.94, 129.04, 129.37, 130.93, 131.04, 132.07, 133.39, 137.42, 148.94; ^{31}P NMR: δ = 143.09 ppm.

(16) Synthesis of ligand **L5**[4]



L5

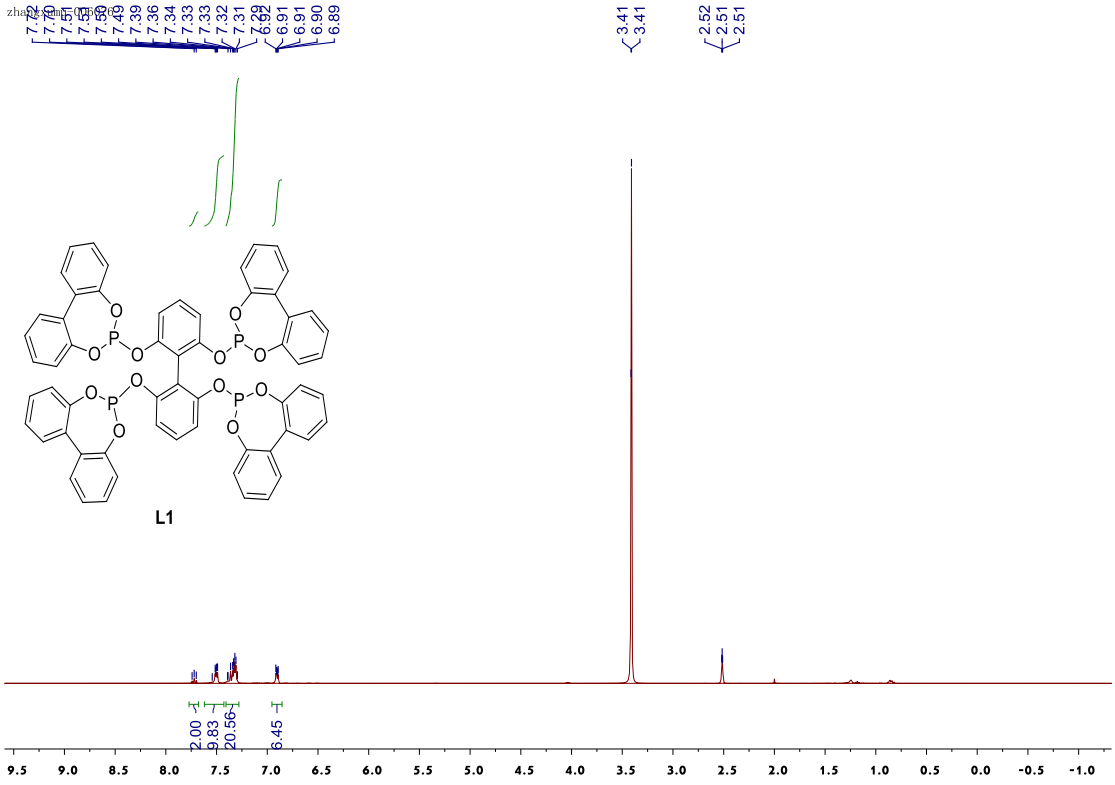
Ligand **L5** was prepared according to the general procedure for synthesis of ligand **L1** in 68% yield (337 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.50 (s, 12H), 6.33 (d, *J* = 8.0 Hz, 8H), 7.17-7.22 (m, 16H), 7.22-7.29 (m, 8H), 7.36-7.38 (m, 16H), 7.70 (s, 2H); ^{13}C NMR (101 MHz, $CDCl_3$): 21.39, 122.14, 124.77, 127.07, 128.81, 129.06, 129.32, 130.81, 130.95, 131.87, 133.35, 134.63, 136.98, 148.68, 149.03; ^{31}P NMR: δ = 142.92 ppm.

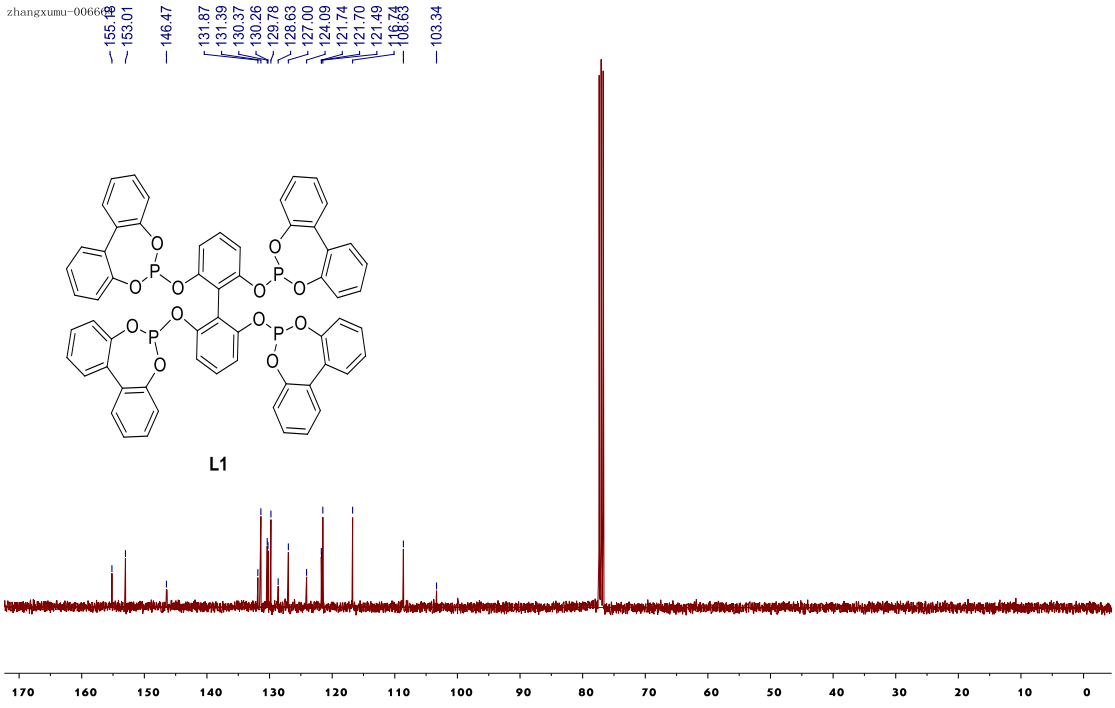
3. General procedure for regioselective linear hydroformylation of olefins

A 5 mL vial with a magnetic stirring bar was charged with ligands (0.6 umol in 0.3 mL CH_2Cl_2) and $Rh(acac)(CO)_2$ (0.2 umol in 0.1 mL CH_2Cl_2) in an argon filled glove box. The resulting mixture was stirred for 5 min. olefin (0.4 mmol) was then added, followed by decane (0.1 mL) as internal standard. Additional CH_2Cl_2 was added to bring the total reaction volume to

1.0 mL. The vial containing the reaction mixture was transferred to an autoclave which was subsequently purged with H_2 three times and then inletting H_2 (5 bar) and CO (5 bar). The autoclave was then heated to 80 ℃ (oil bath). After 2 h, the autoclave was cooled in icy water, and the pressure was carefully released in a well-ventilated hood. The resulting mixture was immediately analyzed by GC instrument.

4. NMR Spectra

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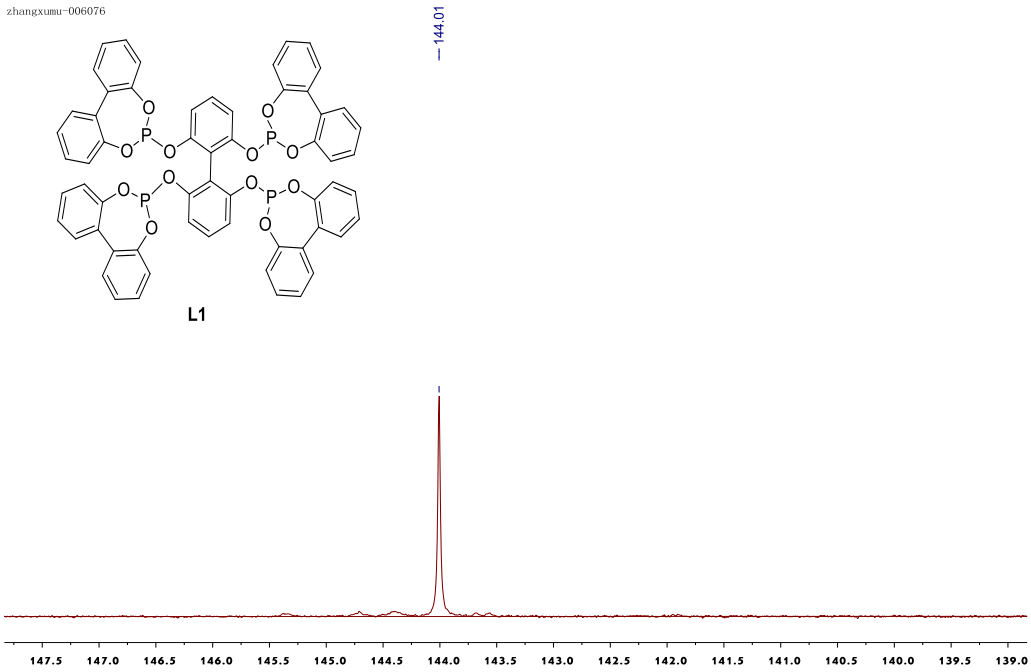
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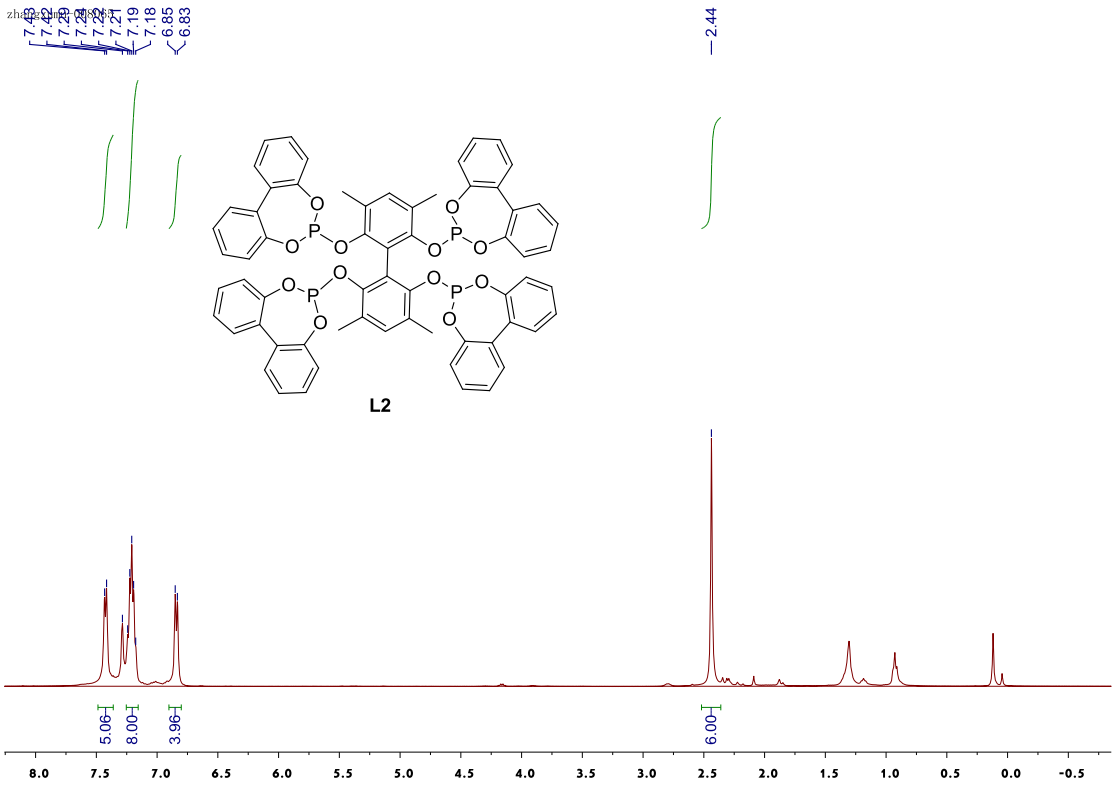
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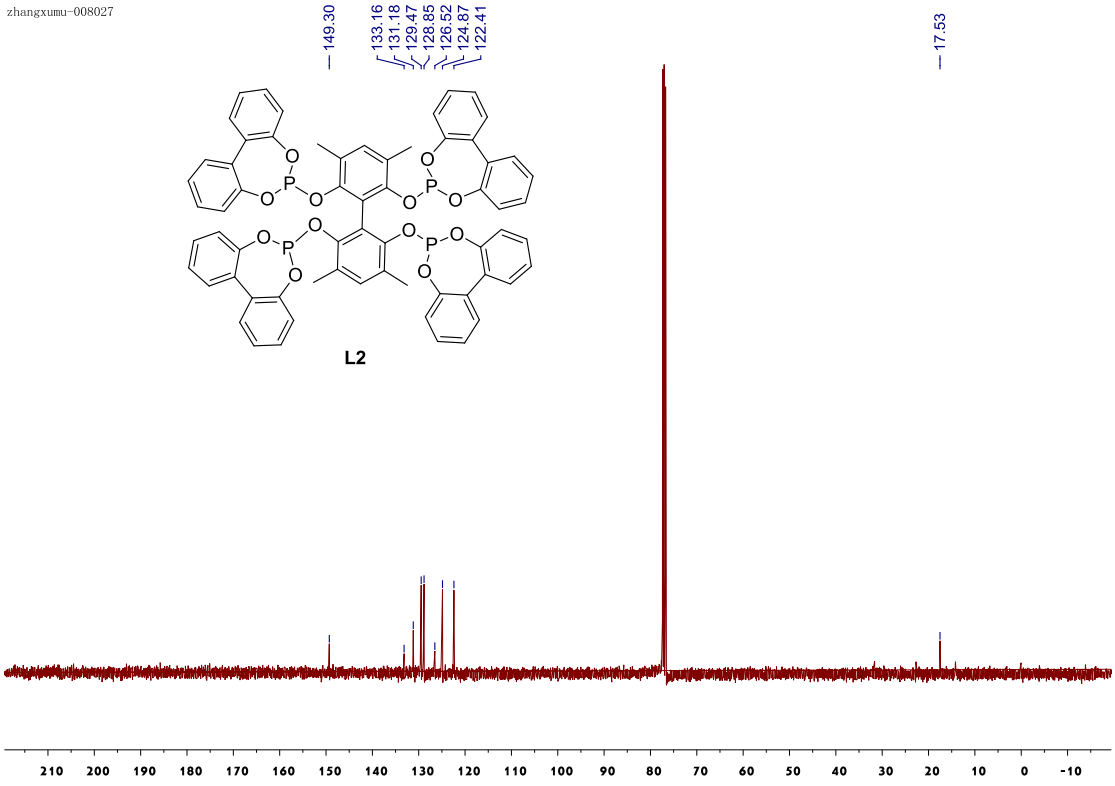
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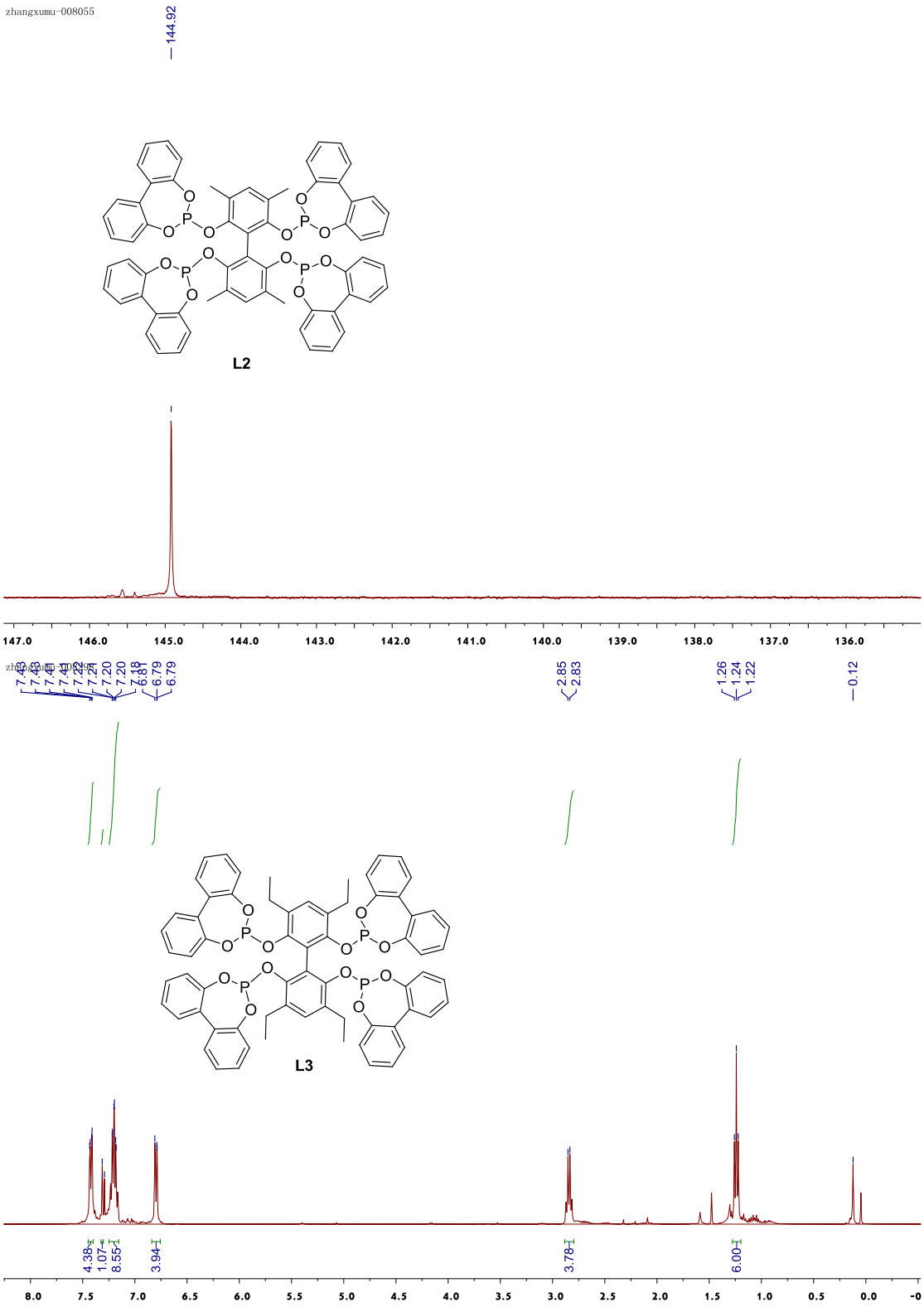
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7.22
7.21
7.20
7.20
7.18
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6.79
6.79
2.85
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1.26
1.24
1.22
0.12
L3
4.38
1.07
8.55
3.94
3.78
6.00
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
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1.0
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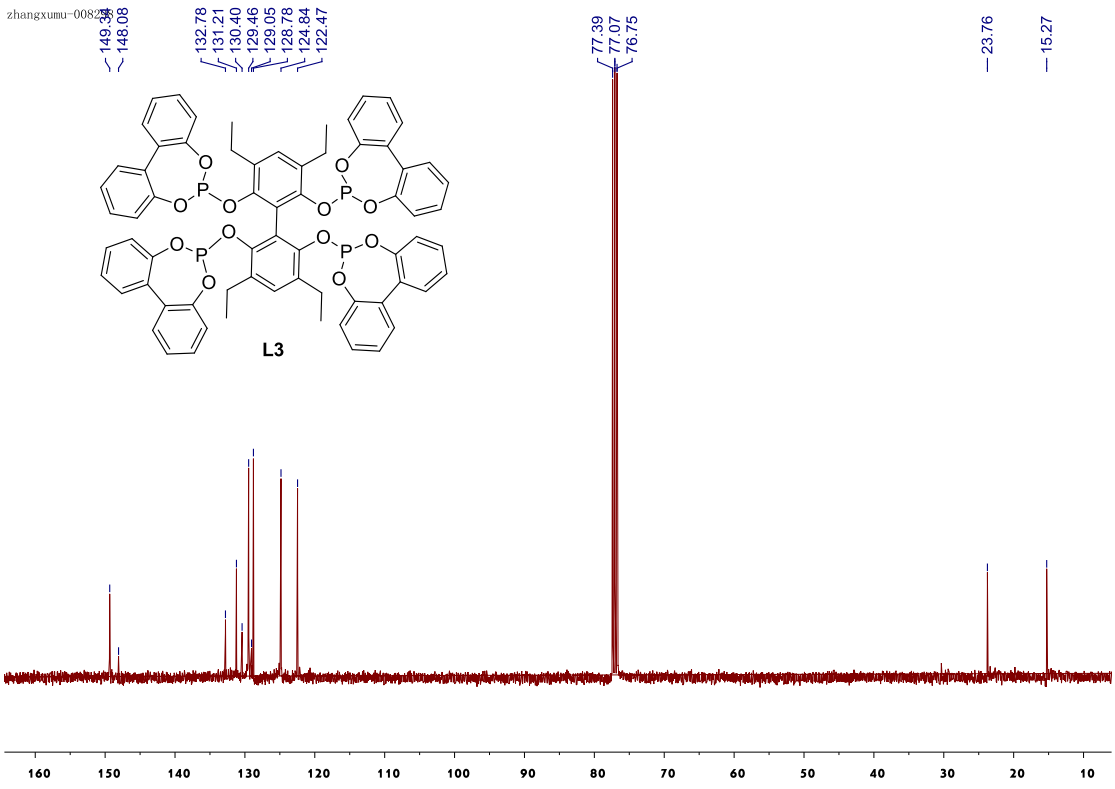
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77.07
76.75
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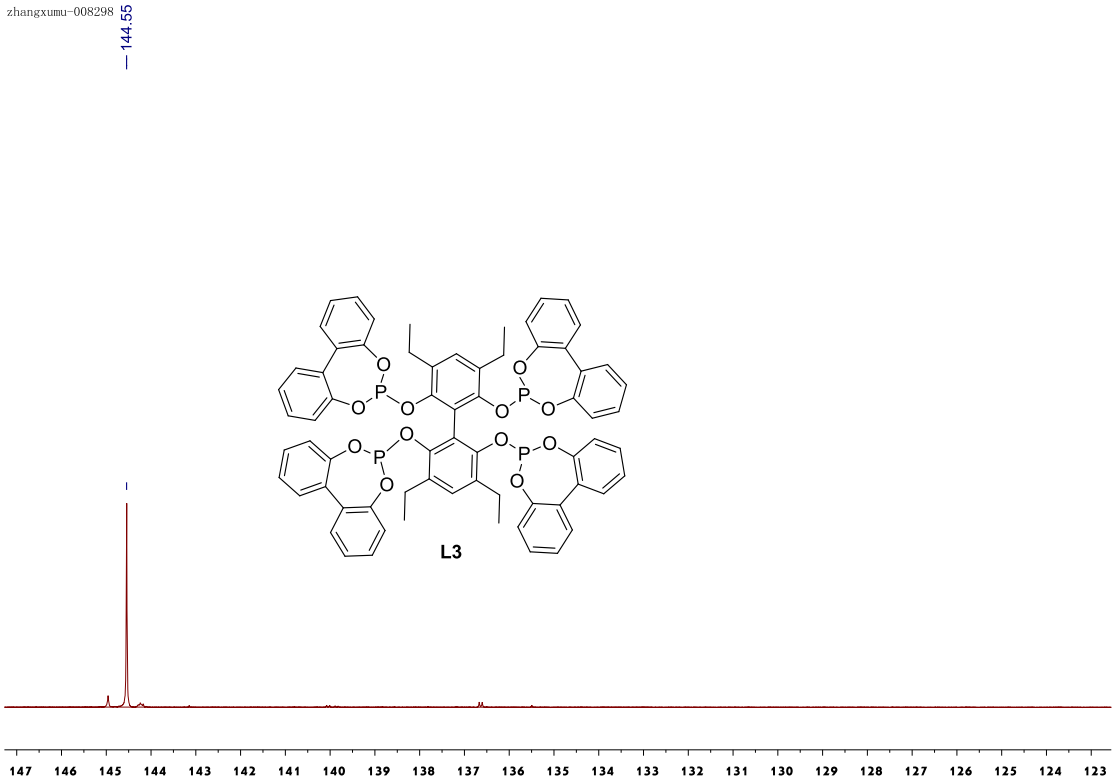
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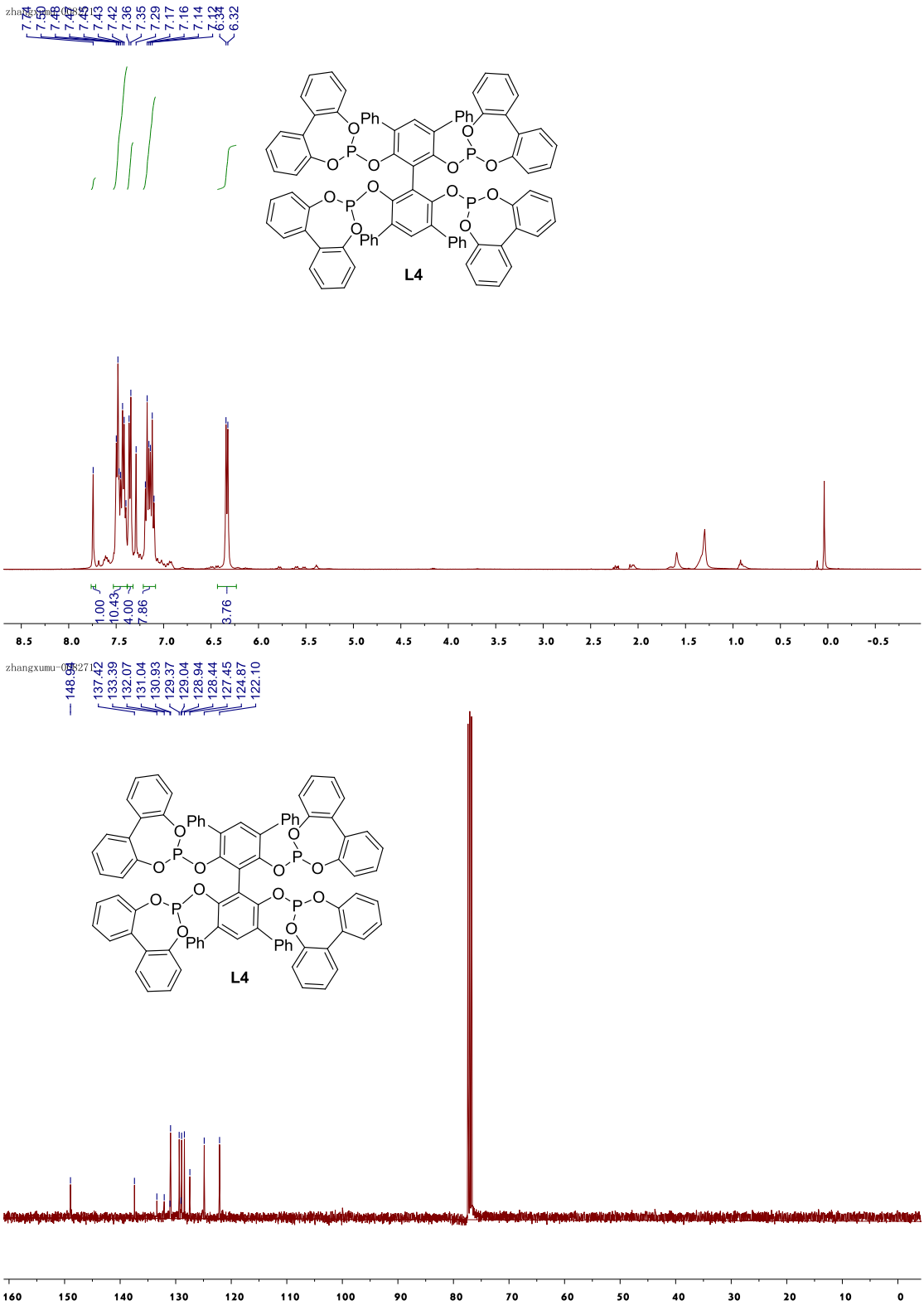
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7.14
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6.32
L4
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10.43
4.00
7.86
3.76
8.5
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3.0
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1.5
1.0
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133.39
132.07
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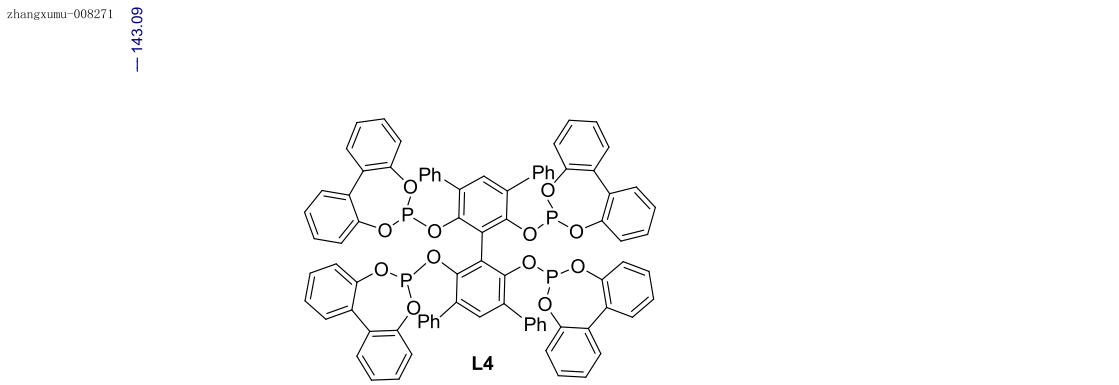
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Ph
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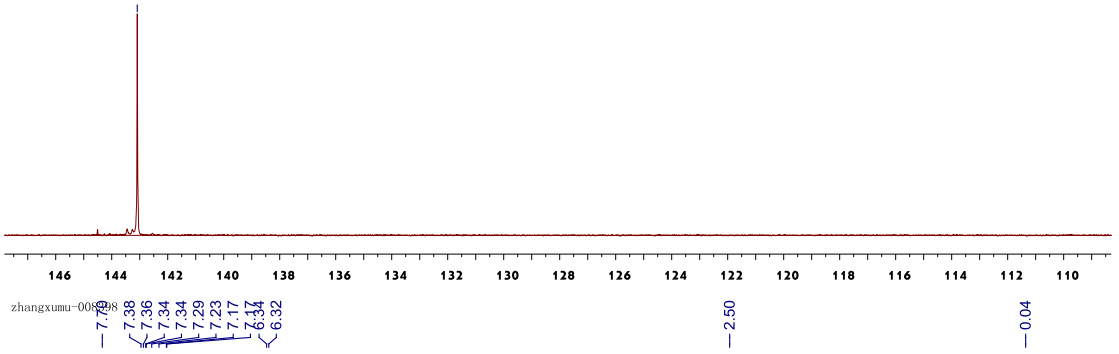
L4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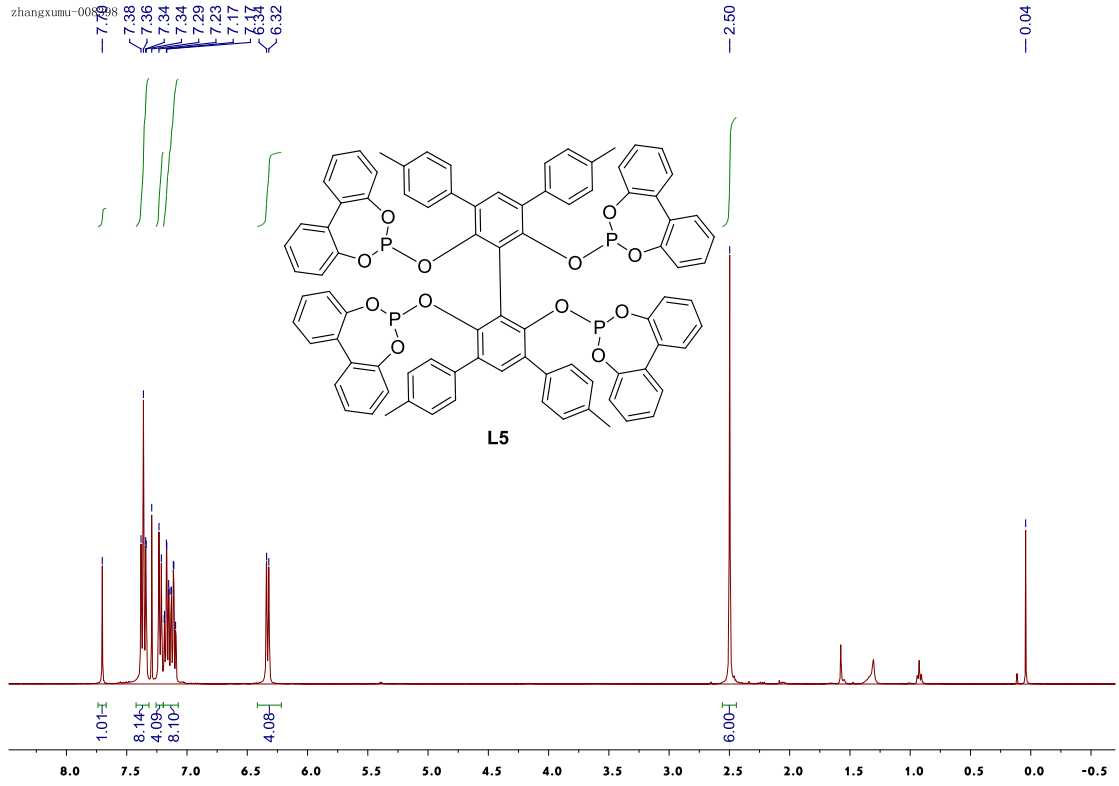
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L5
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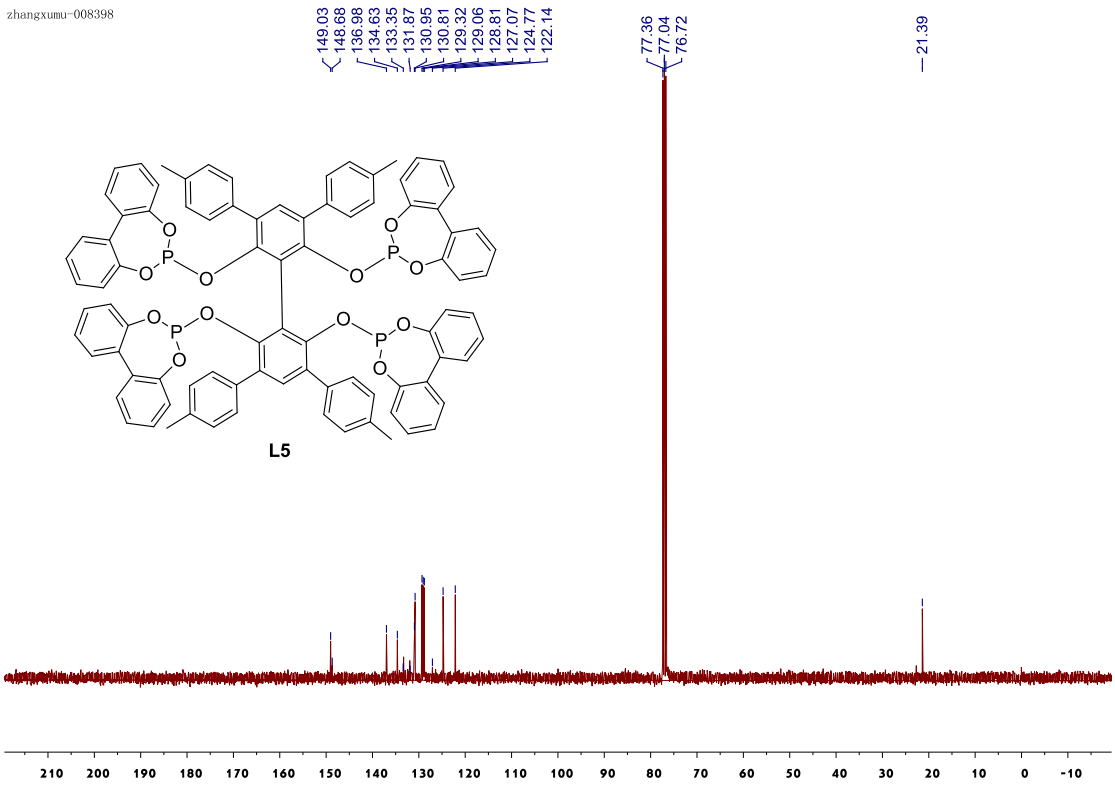
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77.04
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21.39
L5
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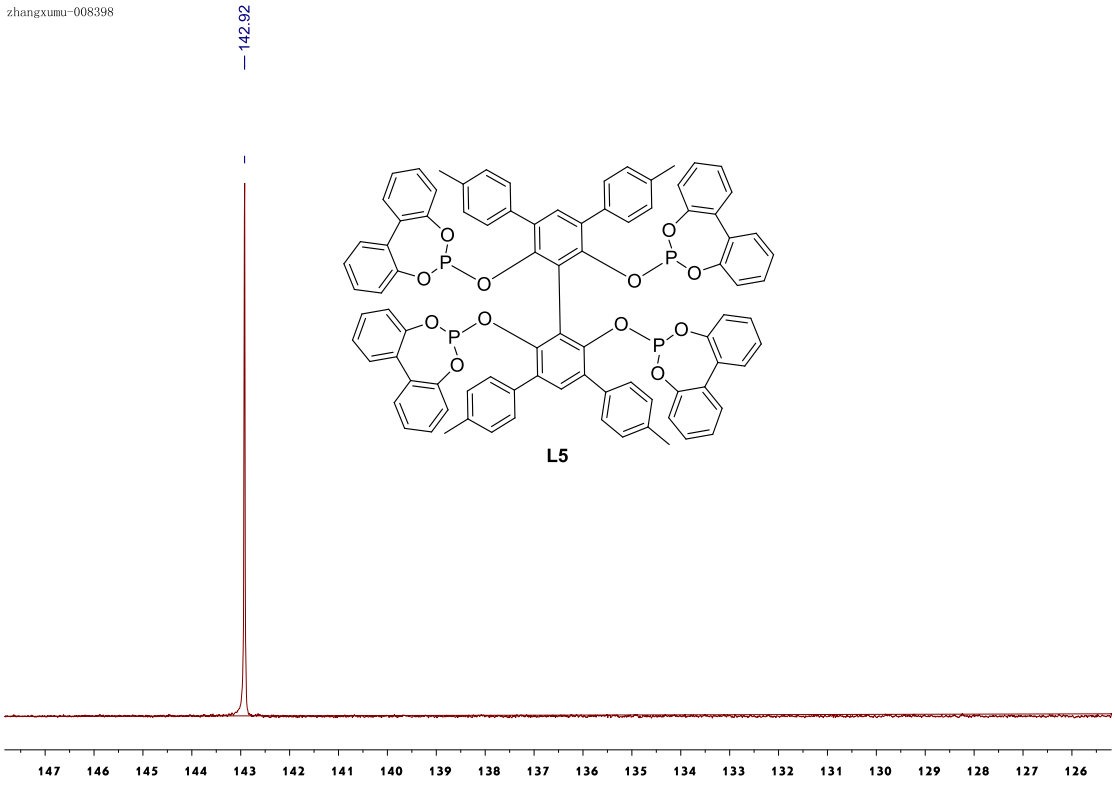
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L5
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5. Reference

[1] H. Kakei, R. Tsuji, T. Ohshima, H. Morimoto, S. Matsunaga, M. Shibasaki, *Chem.-Asian J.*, 2007, **2**, 257-264.

[2] F. Fang, F. Xie, H. Yu, H. Zhang, B. Yang, W. Zhang, *Tetrahedron Letters*, 2009, **50**, 6672-6675.

[3] S. Yu, Y. Chie, Z. Guan, X. Zhang, *Org. Lett.*, 2008, **10**, 3469-3472.

[4] J. Ruchti, E. M. Carreira, *J. Am. Chem. Soc.*, 2014, **136**, 16756-16759.