New ruthenium metathesis catalysts with chelating indenylidene ligands: synthesis, characterization and reactivity

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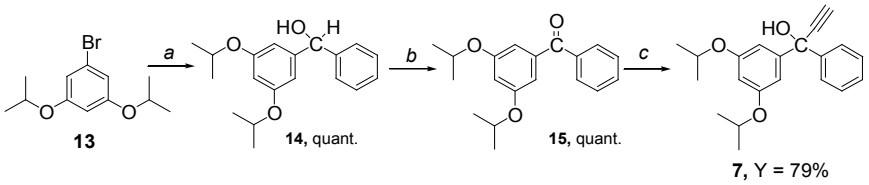
1) General informations

All reactions were carried out under an inert atmosphere of argon using Schlenck tube techniques. Solvents were freshly distilled and dried prior to use according to classical procedures: over CaH_2 for dichloromethane, Na for toluene, THF and diethyl ether were distilled from sodium benzophenone ketyl. 3,5-Dimethoxybenzaldehyde, 1,3,5-trimethoxybenzene, (trimethylsilyl)acetylene, 2,6-difluorobenzaldehyde, 3-hydroxybenzaldehyde, N^1-methylethane-1,2-diamine, 2-bromo-1,3,5-trimethylbenzene, methyl oleate, and dimethyl carbonate were purchased from Alfa Aesar; manganese (IV) oxide (activated) and PCy_3 (20% solution in toluene) – from Strem Chemicals; Celite®545, BBr_3 (1M solution in CH_2Cl_2), benzaldehyde, CuCl – from Acros organics; 1-bromo-3,5-dimethoxybenzene, 2,6-dimethylbenzaldehyde, diethyldiallyl malonate from Sigma-Aldrich. DCPD was purchased from Sigma-Aldrich and distilled prior to use, all other commercial compounds were used as received. $RuCl_2(PPh_3)_3$,[1] diethylallyl(2-methylallyl)malonate,[2] diethyldi(2-methylallyl)malonate,[2] diethyl prop-2-en-1-yl(prop-2-yn-1-yl)propanedioate,[3] 1-allyloxy-1,1-diphenyl-2-propyne,[4] diallyl tosylamide[5] were synthesized according to previously reported procedures. Column chromatography was performed using Merck silica gel 60 (40-63 μm). ^1H, ^{13}C and ^{31}P NMR spectra were recorded on Bruker avance 300 MHz and 500 MHz spectrometers. Chemical shifts are reported in ppm from tetramethylsilane with the solvent resonance as an internal standard for ^1H and ^{13}C, and from 85% H_3PO_4 – for ^{31}P. Gas chromatography analyses were performed on a Shimadzu GC-2014 gas chromatograph with internal calibration. GCMS analyses were performed on a Shimadzu QP2010S apparatus. HRMS analyses were performed on WATERS Q-TOF 2 or Micromass Zab Spec Tof.

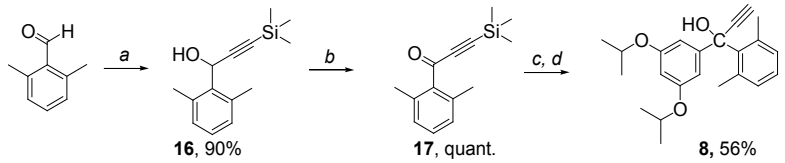
2) Synthesis of the propargylic alcohols 7, 8 and 9

Compound **7** was prepared in good yields in three steps according to Scheme 1.



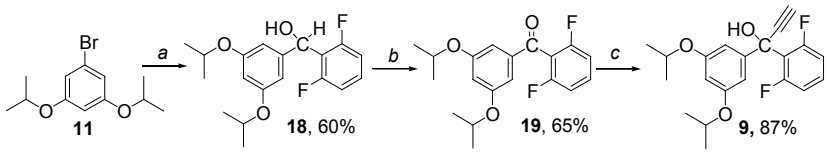
Scheme 1 Synthesis of the propargylic alcohol **7**: *a*) *t*BuLi, Et_2O, -78°C, PhCHO. *b*) MnO_2, CH_2Cl_2, r.t. *c*) C_2H_2, *n*BuLi, THF, -78°C.

By contrast, the propargylic alcohol **8** could not be prepared by the same procedure. Here the alkyne moiety must be introduced in the very first step of the synthesis providing **16** in 90% yield (Scheme 2). Quantitative oxidation by MnO_2 followed by arylation and desilylation led to **8** obtained in 56% yield (2 steps).



Scheme 2 Synthesis of the propargylic alcohol **8** : *a*) *n*BuLi, THF, -78°C, trimethylsilyl acetylene. *b*) MnO_2, CH_2Cl_2, r.t. *c*) *t*BuLi, **13**, Et_2O, -78°C. *d*) K_2CO_3, MeOH.

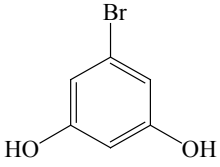
Finally, the synthesis of **9** also required some procedure adaptation as the MnO_2 oxidation did not proceed with **18**. The greener catalytic acceptorless dehydrogenation[6] was thus employed for the preparation of **19** obtained in 65% yield. Final alkynylation furnished the propargylic alcohol **9** in 87% yield (Scheme 3).



Scheme 3 Synthesis of the propargylic alcohol **9** : *a*) *t*BuLi, Et_2O, -78°C, 2,6-difluorobenzaldehyde. *b*) $[RuCl_2(p\text{-cymene})]_2$, PPh_3, LiOH, toluene, reflux. *c*) C_2H_2, *n*BuLi, THF, -78°C.

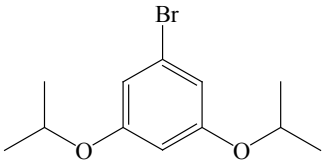
3) Experimental procedures

1-Bromo-3,5-dihydroxybenzene



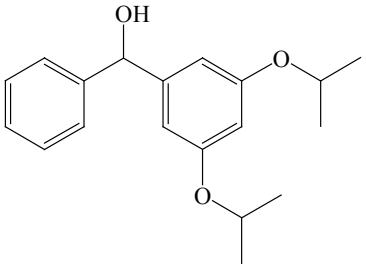
To a stirred solution of 1-bromo-3,5-dimethoxybenzene (2.0 g, 9.2 mmol) in dry CH_2Cl_2 (75 mL) under argon was added dropwise at -78ºC a solution of BBr_3 (3.5 eq, 32.2 mL). The brown reaction mixture was allowed to warm to r.t. and stirred for two days at r.t. During this period a yellow-brown precipitate formed. The mixture was hydrolyzed by careful addition of water (50 mL) and the precipitate was dissolved by the addition of diethyl ether (300 mL). The organic layer was separated and the water layer was washed twice with diethyl ether (2×100 mL). Organic extracts were combined, dried under anhydrous Na_2SO_4, filtered, and concentrated under vacuum to give a brown solid of crude product (1.74 g). According to ^1H this crude product was pure enough to be engaged in the next step without any further purification. ^1H NMR (200 MHz, CD_3OD): δ 6.44 (bs, 2H, CH), 6.20 (bs, 1H, CH). ^{13}C NMR: δ 161.1, 124.3, 109.4, 100.9. ESI $[M+H]^+$ found, 273.0489; calculated, 273.04902.

1-Bromo-3,5-diisopropoxybenzene 13



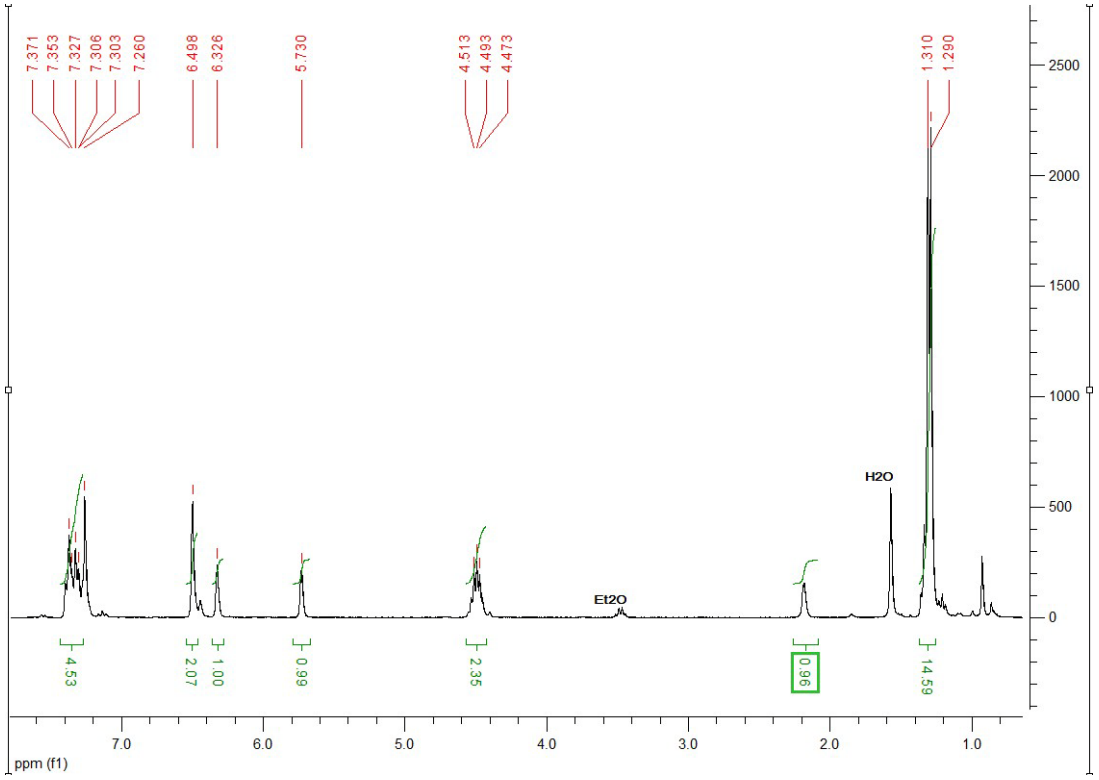
To a solution of 1-Bromo-3,5-dihydroxybenzene (1.74 g, 9.2 mmol) in acetone (100 mL) were added anhydrous K_2CO_3 (4 eq, 5.09 g, 36.8 mmol) and 2-bromopropane (4 eq, 3.5 mL). The resulting suspension was refluxed and the reaction progress was monitored by TLC until completion. The solvent was evaporated under *vacuo*, water was added, and the product was extracted with CH_2Cl_2. The organic layer was washed with water followed by brine, dried under anhydrous Na_2SO_4, filtrated and concentrated under *vacuo*. The crude product was purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 10/1) to afford **13** (2.15 g, 86%) as a colorless oil. ^1H NMR (200 MHz, $CDCl_3$): δ 6.64 (d, 1.8 Hz, 2H, CH), 6.37 (bs, 1H, CH), 4.49 (hept, J = 6.0 Hz, 2H, CH), 1.34 (d, J = 6.0 Hz, 12H, CH_3). ^{13}C NMR: δ 159.9, 123.3, 111.7, 103.3, 70.7, 22.4. Elemental analysis calculated for $C_{12}H_{17}O_2Br$: C, 52.76; H, 6.27; experimental: C, 52.25; H, 6.24. HRMS ESI $[M+H]^+$ calculated 273.0490, measured, 273.0489.

(3,5-Diisopropoxyphenyl)-(phenyl)-methanol 14

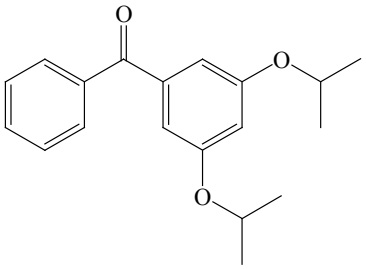


t-BuLi (2.2 eq, 3.16 mmol) was added dropwise at -78ºC to a solution of 1-bromo-3,5-diisopropoxybenzene **13** (1.1 eq, 432 mg, 1.58 mmol) in dry diethyl ether (10 mL). The yellow reaction mixture was stirred for 3 h at -78ºC and benzaldehyde (1 eq, 153 mg, 1.44 mmol) in dry diethyl ether was added. The resulting mixture was stirred for 1 h at -78ºC, and then overnight at r.t. The crude mixture was quenched by addition of saturated NH_4Cl and diluted with diethyl ether. The organic layer was washed with water and brine, and then dried with

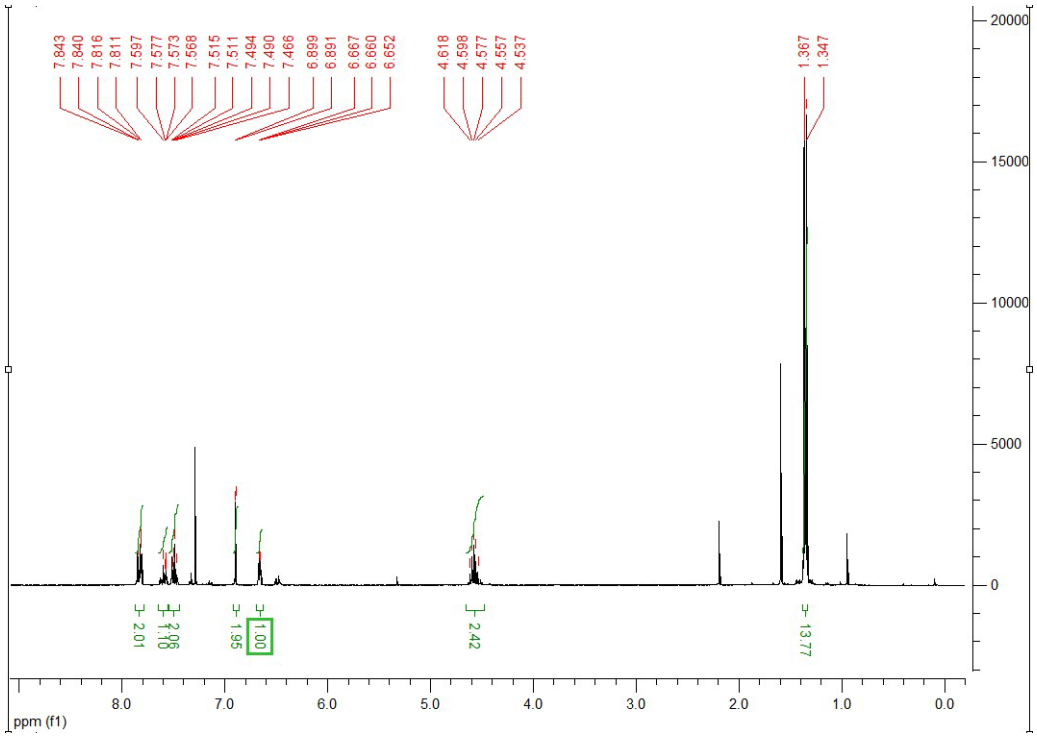
anhydrous Na_2SO_4, filtered, and concentrated under *vacuo*. **14** was obtained in quantitative yield (420 mg) as colorless oil and engaged in the next step without any further purification. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.42-7.30 (m, 5H, CH), 6.52 (bs, 2H, CH), 6.34 (bs, 1H, CH), 5.75 (bs, 1H, CH), 4.51 (hept, 6.0 Hz, 2H), 2.20 (bs, 1H, OH), 1.33 (d, 6 Hz, 12H, CH_3).



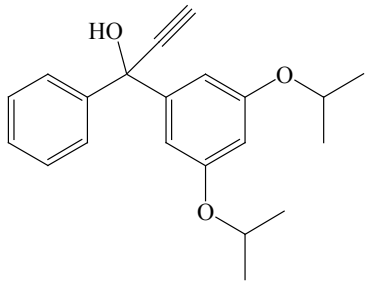
(3,5-Diisopropoxyphenyl)(phenyl)methanone 15



A solution of **14** (0.40 g, 1.33 mmol) and activated MnO_2 (10 eq, 1.16 g, 13.3 mmol) in dry CH_2Cl_2 (35 mL) was stirred at r.t. for 30h. The reaction progress was monitored by TLC. If necessary, 2 eq. of MnO_2 were added and the reaction strirred for a few hours until full conversion of **14**. After reaction completion, MnO_2 was filtered through a pad of Celite and washed with CH_2Cl_2. The solvent was evaporated under reduced pressure. The pure product was obtained in quantitative yield (0.38 g) as colorless oil and used without further purification. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.84-7.81 (m, 2H, CH), 7.63-7.46 (m, 3H, CH), 6.90 (d, 2,4 Hz, 2H, CH), 6.66 (m, 1H, CH), 4.58 (hept, 6.0 Hz, 2H, CH), 1.36 (d, 6.0 Hz, 12H, CH_3). ^{13}C NMR: δ 196.5, 158.8, 139.4, 137.7, 132.3, 129.9, 128.2, 109.6, 108.2, 70.3, 22.1, 21.9.

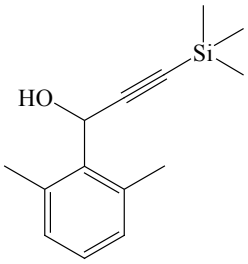


1-(3,5-Diisopropoxyphenyl)-1-phenylprop-2-yn-1-ol 7.



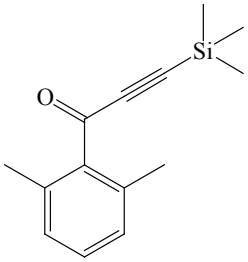
Acetylene (4.5 eq, 5.66 mmol, 130 mL) was dissolved in 20 mL of dry THF at -78ºC before dropwise addition of *n*-BuLi (1.2 eq, 1.51 mmol). The reaction mixture was stirred for 1 h at -78ºC and **15** (1 eq, 0.38 g, 1.26 mmol) dissolved in dry THF (10 mL) was added. The resulting mixture was stirred for 1 h at -78ºC and 1 h at r.t. The crude mixture was quenched by addition of 1N HCl (25 mL). The organic layer was separated and the water layer was extracted twice with diethyl ether. Organic layers were combined, washed with brine, dried under anhydrous Na_2SO_4, filtered, and concentrated under *vacuo*. The crude product was purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 10/1) to afford **7** as a colorless oil (0.37 g, 79%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.64-7.61 (m, 2H, CH), 7.37-7.28 (m, 3H, CH), 6.75 (d, 2.1 Hz, 2H, CH), 6.36 (m, 1H, CH), 4.51 (hept, 2H, J = 6.0 Hz, CH), 2.87 (s, 1H, CH), 2.79 (bs, 1H, OH), 1.31 (d, 12H, J = 6.0 Hz, CH_3). ^{13}C NMR: δ 158.89, 146.62, 144.20, 128.24, 127.82, 125.88, 105.95, 102.86, 86.34, 75.29, 74.29, 69.86, 22.03, 22.00. Elemental analysis calculated for $C_{21}H_{24}O_3$: C, 77.75; H, 7.46; experimental C, 77.62; H, 7.73. HRMS ESI $[M+Na]^+$ measured: 347.1622; calculated: 347.16231.

1-(2,6-dimethylphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol 16

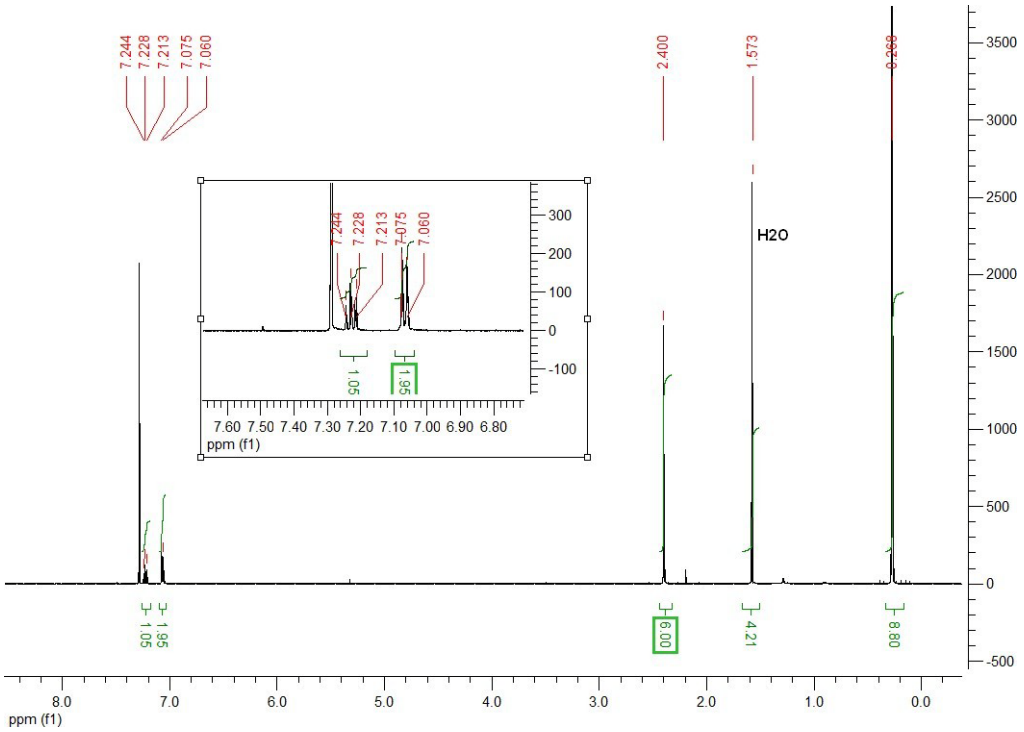


n-BuLi (1.2 eq, 13.1 mmol) was added at -78ºC to a solution of trimethylsilyl acetylene (1.2 eq, 13.1 mmol, 1.8 mL) in 45 mL of dry THF and the reaction mixture was stirred for 1 h at -78ºC. 2,6-dimethylbenzaldehyde (1 eq, 1.46 g, 10.8 mmol) in dry THF (10 mL) was then added and the resulting mixture stirred for 1 h at -78ºC and allowed to warm up to r.t. for 20 h. The crude mixture was quenched by addition of 1N HCl (30 mL). The organic layer was separated and the water layer was extracted twice with diethyl ether. Organic layers were combined, washed with brine, dried under anhydrous Na_2SO_4, filtered, and concentrated under *vacuo*. The crude product was purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 10/1) to afford a yellow oil (2.24 g, 90% yield). ^{1}H NMR (300 MHz, $CDCl_3$): 7.18-7.03 (m, 3H, CH), 5.93 (s, 1H), 2.55 (s, 6H, CH_3), 2.05 (bs, 1H, OH), 0.18 (s, 9H, CH_3). ^{13}C NMR (75 MHz, CDCl3): 136.8, 136.1, 129.24, 128.2, 104.7, 90.9, 60.9, 20.4, -0.2. Elemental analysis calculated for $C_{14}H_{20}OSi$: C, 72.36; H, 8.67; experimental C, 72.94; H, 8.80. HRMS ESI $[M+Na]^+$ experimental, 255.1184; calculated, 255.1181.

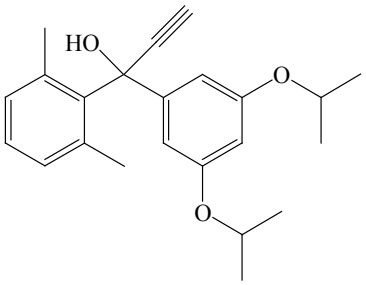
1-(2,6-dimethylphenyl)-3-(trimethylsilyl)prop-2-yn-1-one 17



A solution of **16** (0.55 g, 2.37 mmol) and activated MnO_2 (10 eq, 2 g, 23.7 mmol) in dry CH_2Cl_2 (75 mL) was stirred at r.t. for about 30h. The reaction progress was monitored by TLC. If necessary, 2 eq. of MnO_2 were added and the reaction strirred for a few hours until full conversion of **16**. After reaction completion, MnO_2 was filtered through a pad of celite and washed with CH_2Cl_2. The solvent was evaporated under reduced pressure. The pure product was obtained in quantitative yield (0.53 g) as a yellow oil and used without any further purification. ^{1}H NMR (500,13 MHz, $CDCl_3$): δ 7.23 (t, 7.5 Hz, 1H, CH), 7.07 (d, 7.5 Hz, 2H, CH), 2.40 (s, 6H, CH_3), 0.27 (s, 9H, CH_3).



1-(3,5-Diisopropoxyphenyl)-1-(2,6-dimethylphenyl)prop-2-yn-1-ol 8

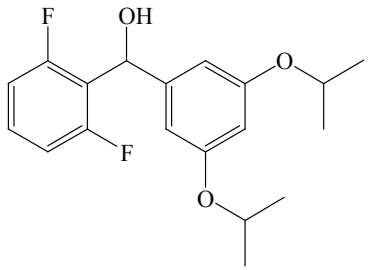


t-BuLi (2 eq, 4.2 mmol) was added dropwise at -78ºC to a solution of 1-bromo-3,5-diisopropoxybenzene **13** (1 eq, 0.58 g, 2.1 mmol) in 20 mL of dry diethyl ether. The yellow reaction mixture was stirred for 3 h at -78ºC before addition of **17** (1.1 eq, 0.53 g, 2.3 mmol) dissolved in dry diethyl ether. The resulting mixture was stirred overnight at r.t. The crude mixture was quenched by addition of saturated NH_4Cl and diluted with diethyl ether. The organic layer was washed with water and brine, and then dried with anhydrous Na_2SO_4, filtered, and concentrated under *vacuo*. 1-(3,5-diisopropoxyphenyl)-1-(2,6-dimethylphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol was obtained in quantitative yield (0.89 g) and used without further purification. ^{1}H NMR (200 MHz, $CDCl_3$): 7.11-6.98 (m, 3H), 6.65 (bs, 2H, CH), 6.38 (s, 1H, CH), 4.47 (hept, 6.0 Hz, 2H, CH), 2.42 (s, 6H, CH_3), 2.27 (s, 1H, OH), 1.31 (m, 12H, CH_3), 0.23 (s, 9H, CH_3). ^{13}C NMR: δ 159.2, 147.6, 137.4, 130.9, 127.5, 108.1, 106.4, 103.6, 70.1, 24.3, 22.3, 22.2, 0.0.

Anhydrous K_2CO_3 (0.1 eq, 0.03g, 0.2 mmol) was added to a solution of 1-(3,5-diisopropoxyphenyl)-1-(2,6-dimethylphenyl)-3-(trimethylsilyl)prop-2-yn-1-ol (0.88 g, 2.0 mmol) in methanol (10 mL). After stirring for 3 h at r.t., the resulting mixture was concentrated under *vacuo*, diluted with CH_2Cl_2 (20 mL) and washed with Na_2CO_3 solution (20 mL). The organic layer was then dried with $MgSO_4$, filtered, and concentrated under

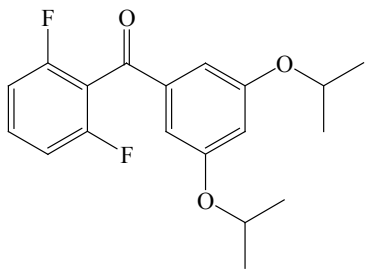
vacuo. The crude product was purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 10/1) to afford **8** as a white solid (0.39 g, 56% for 3 steps). ^{1}H NMR (300 MHz, $CDCl_3$): 7.12-7.07 (m, 1H, CH), 7.01 (d, 7.5 Hz, 2H, CH), 6.66 (d, 2.4 Hz, 2H, CH), 6.39 (d, 2.4 Hz, 1H, CH), 4.47 (hept, 6.0 Hz, 2H, CH), 2.87 (s, 1H, CH), 2.51 (bs, 1H, OH), 2.41 (s, 6H, CH_3), 1.31 (d, 6.0 Hz, 6H, CH_3), 1.29 (d, 6.0 Hz, 6H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): 159.1, 147.3, 138.9, 137.1, 130.7, 127.2, 106.3, 103.2, 86.0, 76.7, 75.4, 69.9, 24.0, 21.9(7), 21.9(3). Elemental analysis calculated for $C_{23}H_{28}O_3$: C: 78.38, H: 8.01; measured: C: 77.95, H:8.10. HRMS ESI $[M+Na]^+$ experimental: 375.1930; calculated, 375.1930(6).

(2,6-Difluorophenyl)(3,5-diisopropoxyphenyl)methanol 18



t-BuLi (2.2 eq, 0.88 mmol) was added dropwise at -78ºC to a solution of 1-bromo-3,5-diisopropoxybenzene **13** (0.11 g, 0.4 mmol) in dry diethyl ether (20 mL). The yellow reaction mixture was stirred for 3 h at -78ºC before addition of 2,6-difluorobenzaldehyde (0.06 g, 0.4 mmol) dissolved in dry diethyl ether was added. The resulting mixture was stirred for 1 h at -78ºC, and then for 4 h at r.t. The crude mixture was quenched by addition of saturated NH_4Cl and diluted with diethyl ether. The organic layer was washed with water and brine, and then dried with anhydrous Na_2SO_4, filtered, and concentrated under *vacuo*. The crude product was purified by flash column chromatography (silica gel, petroleum ether/EtOAc = 10/1) to afford a colorless oil (0.08 g, 60% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.21-7.14 (m, 1H, CH), 6.90 (t, 8.4 Hz, 2H, CH), 6.43 (m, 2H), 6.35 (d, 1H), 6.26 (t, 2.4 Hz, 1H), 6.06 (d, 8.8 Hz, 1H, OH), 4.43 (hept, 6.0 Hz, 2H, CH), 2.61 (dt, 9.2 Hz, 2.4 Hz, 1H, CH), 1.24 (d, 6H, 6.0 Hz, CH_3), 1.23 (d, 6H, 6.0 Hz, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): 160.1 (dd, 246.9 Hz, 8.2 Hz, CF), 158.4 (C), 143.8 (C), 128.7 (t, 10.6 Hz, CH), 119.3 (t, 16.4 Hz, C), 111.1 (dd, 25.8 Hz, 6.6 Hz, CH), 104.6 (CH), 101.9 (CH), 69.9 (CH), 66.9 (t, 3.4 Hz, CH), 21.3 (CH_3), 21.2 (CH_3). ESI $[M+Na]^+$ experimental, 359.1427; calculated, 359.14292.

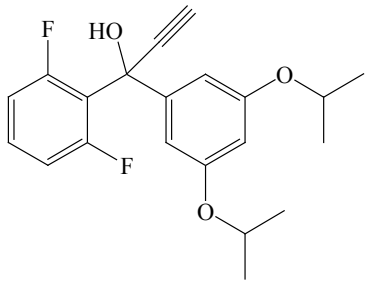
(2,6-Difluorophenyl)(3,5-diisopropoxyphenyl)methanone) 19



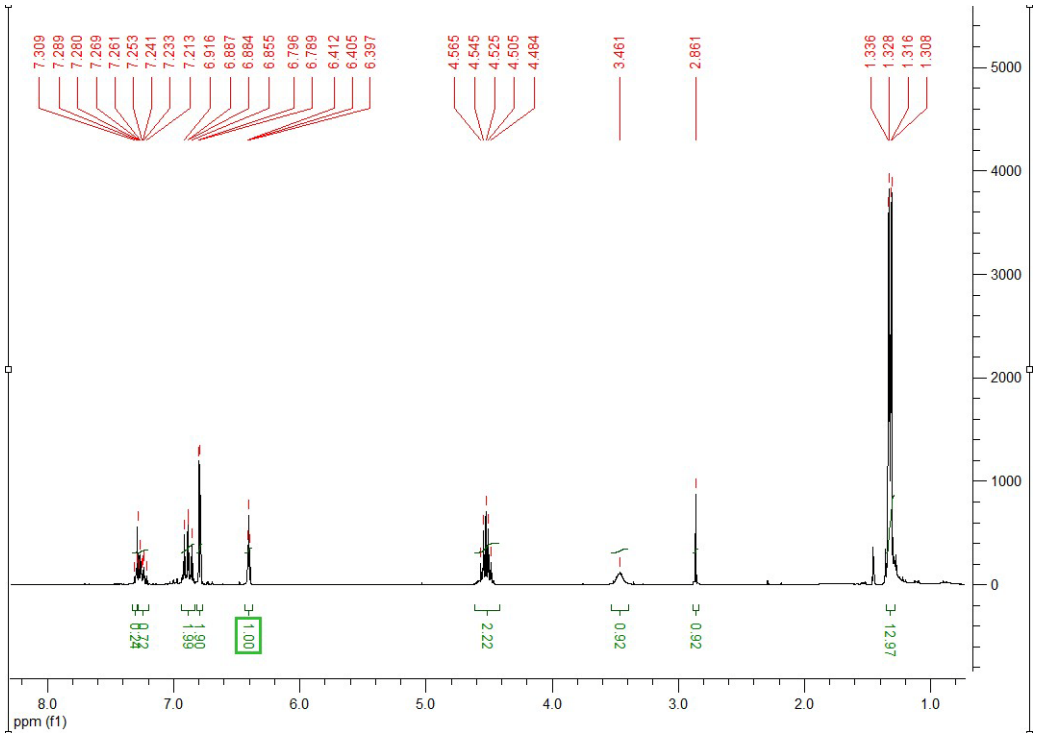
18 (185 mg, 0.55 mmol), PPh_3 (20 mol%, 29 mg, 0.11 mmol), LiOH (15 mol%, 2 mg, 0.083 mmol), and $[RuCl_2(p\text{-cymene})]_2$ (10 mol%, 33.6 mg, 0.055 mmol) were dissolved in dry toluene (5 mL) and refluxed for 2 days. The mixture was concentrated under *vacuo* and the crude was purified by column chromatography (silica

gel, petroleum ether/EtOAc = 20/1) to afford **19** as a colorless oil (120 mg, 65% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.47-7.41 (m, 1H), 7.03-6.96 (m, 4H), 6.68 (bs, 1H), 4.57 (hept, 6.0 Hz, 2H), 1.35 (m, 12H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): 188.8, 159.7 (dd, 251.5, 7.6 Hz, CF), 159.3 (C), 138.7 (C), 131.7 (t, 9.8 Hz, CH), 117.2 (t, 22.0 Hz, C), 111.8 (dd, 19.5 Hz, 5.6 Hz, CH), 109.7 (CH), 70.3 (CH), 21.9 (CH_3). HRMS ESI $[M+Na]^+$ experimental: 357.1278; calculated, 357.1278.

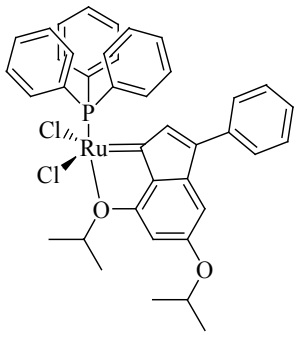
1-(2,6-Difluorophenyl)-1-(3,5-diisopropoxyphenyl)prop-2-yn-1-ol 9



n-BuLi (1.2 eq, 0.158 mmol) was added at -78ºC to a solution of acetylene (4.5 eq, 0.592 mmol, 13 mL) in 10 mL of dry THF and the reaction mixture was stirred for 1 h at -78ºC. **19** (1 eq, 44 mg, 0.132 mmol) in dry THF (5 mL) was then added. The resulting mixture was stirred for 1 h at -78ºC and then overnight at r.t. The crude mixture was quenched by addition of 1N HCl (10 mL). The organic layer was separated and the water layer was extracted twice with diethyl ether. Organic layers were combined, washed with brine, dried under anhydrous Na_2SO_4, filtered, and concentrated under *vacuo* to afford **9** as colorless oil (41 mg, 87 % yield) of good enough purity. **9** was engaged in the next step without any further purification. ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.30-7.21 (m, 1H, CH), 6.89 (m, 2H, CH), 6.79 (d, 2.1 Hz, 2H, CH), 6.40 (t, 2.1 Hz, 1H, CH), 4.52 (hept, 6.0 Hz, 2H, CH), 3.45 (bs, 1H, OH), 2.86 (s, 1H, CH), 1.32 (d, 6.0 Hz, 6H, CH_3), 1.31 (d, 6.0 Hz, 6H, CH_3). HRMS ESI $[M+Na]^+$ experimental, 383.1435; calculated, 383.1434.



Preparation of complex 10

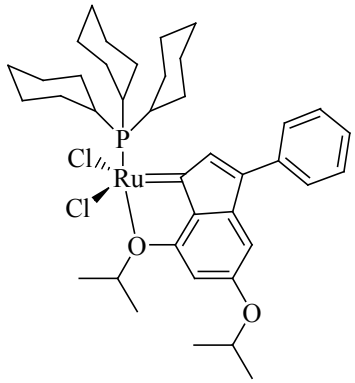


A Schlenk tube under argon was charged with $RuCl_2(PPh_3)_3$ (145 mg, 0.151 mmol), propargylic alcohol **7** (1.1 eq, 54 mg, 0.166 mmol), CuCl (2.5 eq, 38 mg, 0.378 mmol), and DMC (5 mL). The resulting mixture was stirred at 70ºC under argon for 3 h. A white powder of $[CuClPPh_3]_4$ precipitated upon cooling the reaction mixture to room temperature. The crude product was extracted from the precipitate by cannula filtration under argon. After solvent evaporation under *vacuo* the red-brown residue was purified by flash column chromatography (CH_2Cl_2). **10** was obtained as a red-brown powder (42 mg, 38 %).

Complex **10** can also be prepared following the previously reported procedure i. e. After 3 h refluxing in THF and solvent evaporation, the residue was dissolved in CH_2Cl_2, and CuCl (5.0 eq) was added. The reaction mixture was stirred for 2 h at r.t., yielding **10** in 50 % after column chromatography purification. Crystallization of this complex by slow diffusion of hexane in CH_2Cl_2 provided crystals suitable for X-Ray characterization.

^{1}H NMR (500.13 MHz, CD_2Cl_2): δ 7.56-7.39 (m, 20H, CH), 6.84 (d, 1.5 Hz, 1H, CH), 6.60 (d, 1.5 Hz, 1H, CH), 6.53 (s, 1H), 5.21 (dhept, 6.3 Hz, J_{H-P}= 2.0 Hz, 1H), 4.67 (hept, 6.0 Hz, 1H), 1.80 (d, 6.3 Hz, 6H, CH_3), 1.41 (d, 6.0 Hz, 6 H, CH_3). ^{13}C NMR (125.77 MHz): δ 259.6 (d, J_{C-P} = 16.4 Hz), 161.5, 152.6, 141.4, 135.4, 135.3, 135.2, 134.9 (br), 130.8, 129.2, 128.7, 128.3 (br), 128.2, 126.8, 102.9, 99.3, 74.9, 71.2, 22.3, 21.8. ^{31}P NMR (121.5 MHz, CD_2Cl_2): δ 63.4 (s, PPh_3). Elemental analysis calculated for $C_{39}H_{37}Cl_2O_2PRu$: C, 63.24; H, 5.04; experimental: C, 63.08; H, 5.27.

Preparation of complex 2

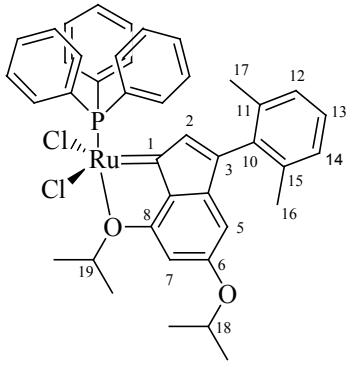


PCy_3 (2 eq, 0.183 mmol) was added to a solution of complex **10** (68 mg, 0.092 mmol) in dry CH_2Cl_2 (5 mL) at 0°C and the resulting mixture was stirred for 2.5 h at r.t. under argon. After solvent evaporation under *vacuo* the dark-brown residue was purified by column chromatography (pentane to CH_2Cl_2). **2** was obtained as a brown powder (26 mg, 38 %).

1 step synthesis in DMC. A Schlenk tube with a magnetic stirring bar under argon was charged with $RuCl_2(PPh_3)_3$ (104 mg, 0.109 mmol), propargylic alcohol **7** (1.1 eq, 39 mg, 0.120 mmol), CuCl (2.5 eq, 27 mg, 0.273 mmol), and DMC (5 mL). The resulting mixture was stirred at 70ºC under argon for 3 h. A white powder of $[CuClPPh_3]_4$ precipitated upon cooling the reaction mixture to room temperature. The crude product was extracted from the precipitate by cannula filtration under argon. PCy_3 (3 eq, 0.327 mmol) was added to the reaction mixture at 0°C and the resulting solution was stirred for 5 h at r.t. under argon and the solvent was removed under *vacuo*. The dark-brown residue was purified by column chromatography (pentane to CH_2Cl_2). **2** was obtained as a brown powder (20 mg, 24 %).

^{1}H NMR (500.13 MHz, CD_2Cl_2): δ 7.85 (dd, 8.1 Hz, 1.5 Hz, 2H), 7.60 (m, 1H), 7.52 (t, 7.5 Hz, 2H), 6.96 (s, 1H), 6.80 (d, 7.5 Hz, 1H), 6.51 (d, 1.5 Hz, 1H), 5.07 (dhept, 6.3 Hz, J_{H-P}= 2.0 Hz, 1H), 4.65 (hept, 6.0 Hz, 1H), 2.38 (bs, 3H), 2.30-1.33 (m, 30H), 1.74 (d, 6.3 Hz, 6 H, CH_3), 1.39 (d, 6.0 Hz, 6H, CH_3). ^{13}C NMR (125.77 MHz): δ 256.9 (d, J_{C-P} = 14.0 Hz), 160.8, 151.8, 140.1, 136.3, 135.6, 129.4, 128.7, 126.7, 102.0, 99.4, 74.0, 71.0, 35.6, 30.7, 29.7, 27.9, 27.8, 26.4, 22.1, 21.7. ^{31}P NMR (121.5 MHz, CD_2Cl_2): 66.9 (s, PCy_3). Elemental analysis calculated for $C_{39}H_{55}Cl_2O_2PRu$: C, 61.73; H, 7.31; experimental: C, 61.58; H, 7.25.

Preparation of complex 11

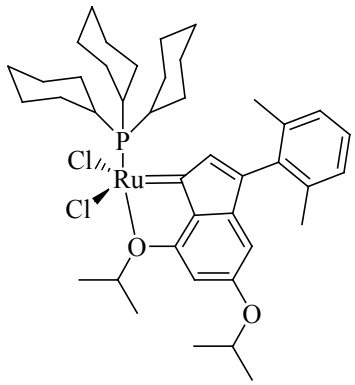


A Schlenk tube equipped with a magnetic stirring bar was charged under argon with $RuCl_2(PPh_3)_3$ (148 mg, 0.154 mmol). DMC (5 mL) and propargylic alcohol **8** were introduced and the resulting mixture was stirred at 70ºC under argon for 3 h. The complex precipitated from the solution during the reaction. After cooling down the red powder was filtrated by cannula under argon, the solid was washed 2 times with dry pentane (2×5 mL) and then dried under *vacuo*. Pure complex **11** was obtained as a red-brown powder (70 mg, 61 %).

Complex **11** can also be prepared in 56% yield following the previously reported procedure (CuCl (5.0 eq), refluxing in THF). Crystallization of this complex by slow diffusion of hexane in CH_2Cl_2 provided crystals suitable for X-Ray characterization.

^{1}H NMR (500.13 MHz, CD_2Cl_2): 7.65-7.39 (m, 15H, CH), 7.20 (t, 7.5 Hz, 1H, CH^{13}), 7.08 (d, 7.5 Hz, 2H, $CH^{12,14}$), 6.56 (d, 1.5 Hz, 1H, CH^7), 6.38 (s, 1H, CH^2), 6.19 (d, 1.5 Hz, 1H, CH^5), 5.2 (heptd, 6.2 Hz, 1.8 Hz, 1H, CH^{19}), 4.6 (hept, 6.0 Hz, 1H, CH^{18}), 2.15 (s, 6H, CH_3), 1.81 (d, 6.2 Hz, 6H, CH_3), 1.34 (d, 6.0 Hz, CH_3). ^{13}C NMR (125.77 MHz): δ 261.9 (d, 16.4 Hz, C-1), 161.8, 152.6, 141.8, 137.1 (d, 4.4 Hz, C-2), 136.4, 135.1, 134.7 (br), 134.1, 130.7, 128.3 (br), 127.8, 127.2, 127.1, 101.4 (C-5), 99.4 (C-7), 74.7 (C-19), 71.0 (C-18), 22.4, 21.7, 20.4. ^{31}P NMR (121.5 MHz, CD_2Cl_2): 64.8 (s, PPh_3). Elemental analysis calculated for $C_{44}H_{47}Cl_2O_5PRu$ + 1 DMC: C, 61.54; H, 5.52; found, C, 61.45; H, 4.99.

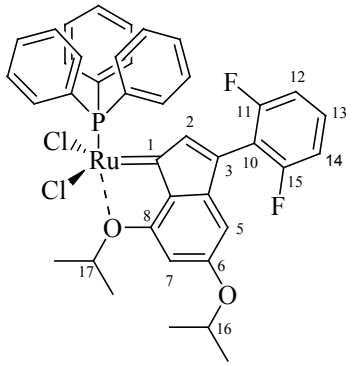
Preparation of complex 3



PCy_3 (2 eq, 0.24 mmol) was added to a solution of complex **11** (93 mg, 0.12 mmol) in dry CH_2Cl_2 (5 mL) at 0°C and the resulting mixture was stirred for 2-5 h at r.t. under argon. The solvent was removed under *vacuo*. The dark-brown residue was purified by column chromatography (pentane to CH_2Cl_2). **3** was obtained as a

brown powder (56 mg, 60%). Crystallization of this complex by slow diffusion of hexane in THF provided crystals suitable for X-Ray characterization. ^{1}H NMR (500.13 MHz, CD_2Cl_2): δ 7.27 (t, 7.5 Hz, 1H), 7.16 (d, 7.5 Hz, 2H), 6.76 (s, 1H), 6.45 (s, 1H), 6.13 (s, 1H), 5.03 (hept, *J* = 6.2 Hz, 1H), 4.52 (hept, 6.0 Hz, 1H), 2.38-1.29 (bs, 33H), 2.23 (s, 6H), 1.76 (d, 6.2 Hz, 6H, CH_3), 1.33 (d, 6.0 Hz, 6 H, CH_3). ^{13}C NMR (125.77 MHz): δ 259.0 (d, 14.2 Hz), 161.3, 151.9, 140.2, 137.6, 136.9, 134.9, 134.7, 127.8, 127.2, 100.5, 99.3, 73.9, 70.8, 30.7 (bs), 27.7 (bs), 26.4, 22.3, 21.7, 20.2. ^{31}P NMR (121.5 MHz, CD_2Cl_2): 69.4 (s, PCy_3). HRMS ESI $[M+]^+$ experimental, 786.2693; calculated, 786.26732.

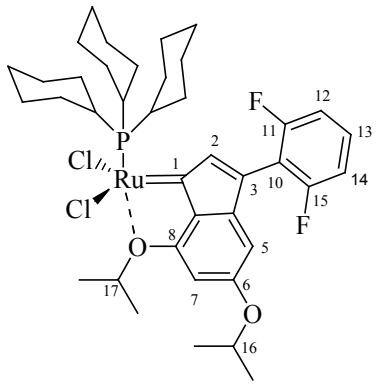
Preparation of complex 12



A Schlenk tube with a magnetic stirring bar under argon was charged with $RuCl_2(PPh_3)_3$ (96 mg, 0.10 mmol), propargylic alcohol **9** (1.0 eq, 36 mg, 0.10 mmol), CuCl (2.5 eq, 25 mg, 0.25 mmol), and DMC (5 mL). The resulting mixture was stirred at 70ºC under argon for 3 h. After cooling down, a white powder of $[CuClPPh_3]_4$ precipitated from the mixture. The crude product **12** was extracted from the precipitate by cannula filtration under argon. An aliquat was taken for ^{31}P NMR characterization and the rest of the solution was used for the next step.

^{31}P NMR (121.5 MHz, CD_2Cl_2): δ 63.0 (s, PPh_3).

Preparation of complex **4**



PCy_3 (2 eq, 0.20 mmol) was added to the solution of complex **12** in DMC at 0°C and the resulting mixture was stirred for 2-5 h at r.t. under argon. CuCl (2.5 eq, 0.25 mmol) was the added and the mixture was stirred for 2 h at r.t. The crude product was extracted from the white precipitate of $CuCl{\times}PPh_3$ and $CuCl{\times}PCy_3$ by cannula

filtration. The solvent was removed under *vacuo*, and the dark-brown residue was purified by column chromatography (CH_2Cl_2). Complex **4** was obtained as a brown powder (40 mg, 50 % after 2 steps).
^{1}H NMR (500 MHz, CD_2Cl_2): δ 7.55-7.50 (m, 1H, CH), 7.09 (t, 2H, CH), 7.03 (s, 1H, CH), 6.53 (d, 1H, CH), 6.47 (d, 1H, CH), 5.08-5.03 (hept, 1H, CH), 4.63-4.58 (hept, J = 6.0 Hz, 1H, CH), 2.38-1.29 (m, 33H, 3×Cy), 1.74 (d, J = 6.0 Hz, 6H, CH_3), 1.37 (d, 6H, J = 6.0 Hz, CH_3). ^{13}C NMR (125.77 MHz): δ 255.3 (d, $J_{C\text{-}P}$ = 14.0 Hz), 161.0, 160.2, 158.2, 151.6, 139.6, 135.8, 130.0, 128.0, 127.5, 112.4, 112.2, 101.7, 99.5, 74.1, 70.9, 30.7, 27.8, 26.4, 22.2, 21.8. ^{31}P NMR (121.5 MHz, CD_2Cl_2): 66.7 (s, PCy_3). $C_{39}H_{53}Cl_2F_2O_2PRu$: calculated, C, 58.94; H, 6.72; found, C, 58.79; H, 6.97.

4) References

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