Supporting Information for:

Electrophilic Activation of Alkynes for Enyne Cycloisomerization Reactions with In Situ Generated Early/Late Heterobimetallic Pt–Ti Catalysts

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I. General Information

All reactions were carried out in oven-dried glassware with magnetic stirring, unless otherwise indicated. Reactions requiring a moisture-free environment were conducted in a nitrogen atmosphere glove box (Innovative Technology, PureLab HE system, double glove box). Solvents were taken from dry solvent system and stored under molecular sieves. Hexanes were distilled with Calcium hydride. Analytical thin-layer chromatography was performed with 0.25 mm coated commercial silica gel plates (E. Merck, DC-Plastikfolien, kieselgel 60 F254). Flash Chromatography was performed with EM Science silica gel (0.040-0.063µm grade) Phosphorous nuclear magnetic resonance (^{31}P NMR) data were acquired on an Inova 300 (300 MHz). Proton nuclear magnetic resonance (^{1}H NMR) data were acquired on an Inova 300 (300 MHz) or on an Inova-500 (500 MHz) spectrometer. Chemical shifts are reported in delta (δ) units, in parts per million (ppm) downfield from the deuterium signal of the NMR solvent. Carbon-13 nuclear magnetic resonance (^{13}C-NMR) data were acquired on an Inova 500 at 125 MHz. Signals are reported as follows: s (singlet), d (doublet), t (triplet), q (quartet), dd (doublet of doublets), qd (quartet of doublets), brs (broad singlet), m (multiplet). Coupling constants are reported in hertz (Hz). Chemical shifts are reported in ppm relative to the deuterium signal of the NMR solvent. Mass spectral data were obtained using ESI techniques (Agilent, 6210 TOF).

II. Synthesis of Trichlorotitanium N-tert-butyl(diphenylphosphino)amide

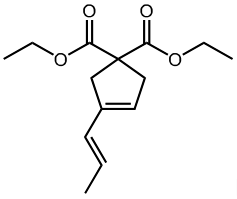
In a Schlenk tube, 2.594g N-tert-butyl-1,1-diphenylphosphanamine (10.038 mmol, 1.1 eq) was dissolved in 2 mL dry Et_2O. Then 16 mL dry hexanes were added. 1 mL $TiCl_4$ (9.12 mmol, 1 eq) was added and the reaction vessel was sealed. The reaction was heated to 90 ºC for 3 hours. The warm reaction was brought into the glovebox, and filtered through a fritted funnel and placed in the fridge (-30 °C) immediately. The product is afforded as dark red crystals. 0.66g. 17.5% yield. Spectra matched previously reported spectra.[1]

III. Experimental Procedures:

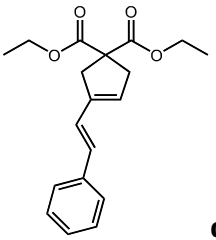
Ligand Screen from Table 1

In a glovebox, 52 mg (0.206 mmol) of substrate was added to a 3 dram vial with 8.42 mg trichlorotitanium N-tert-butyl(diphenylphosphino)amide (0.0206 mmol, 10 mol %), 5.48 mg $PtCl_2$ (0.0206 mmol, 10 mol %) and 1 mL toluene. The reaction was stirred and monitored by NMR. At the indicated time (see table 1), a small aliquot was taken from the reaction, diluted in $CDCl_3$ and the conversion was determined by ^{1}H NMR.

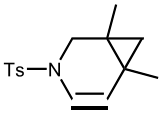
General Procedure I: Enyne cycloisomerization



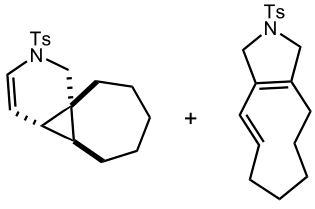
D**iethyl (*E*)-3-(prop-1-en-1-yl)cyclopent-3-ene-1,1-dicarboxylate(2a)**: In a glovebox, 10 mg (0.040 mmol) **1a** was added to a 25 mL vial with 1.6 mg trichlorotitanium N-tert-butyl(diphenylphosphino)amide (0.0040 mmol, 10 mol %), 1 mg $PtCl_2$ (0.0040 mmol, 10 mol%) and 0.2 mL toluene. The reaction was stirred and monitored by NMR. Reaction went to completion in 2 hours. Upon completion, the reaction was filtered through a small silica plug in aplug and the silica washed with 20:1 hexanes:ethyl acetate (5 ml). The product was isolated as a colorless oil (10 mg, >99% yield). Spectra matched previously reported values.[2]



diethyl (E)-3-styrylcyclopent-3-ene-1,1-dicarboxylate(2b): Synthesized according to general procedure I using 64.76 mg **1b** (0.206 mmol), 5.48 mg $PtCl_2$ (0.0206 mmol, 10 mol %), 8.43 mg trichlorotitanium N-tert-butyl(diphenylphosphino)amide (0.206 mmol, 10 mol%) and 1 mL toluene. Product isolated as a colorless oil: 38.4 mg (58% yield). Spectra matches previously reported spectra.[2]

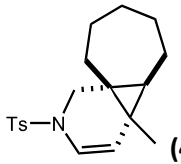


1,6-dimethyl-3-tosyl-3-azabicyclo[4.1.0]hept-4-ene(2c): Synthesized according to general procedure I with 57 mg (.206 mmol) **1c**, 8.42 mg trichlorotitanium N-tert-butyl(diphenylphosphino)amide (0.0206 mmol, 10 mol %), 5.48 mg $PtCl_2$ (0.0206 mmol, 10 mol %), and 1 mL toluene. Completed in 48 hours. At 36 hours 86% conversion was observed. Upon completion of the reaction, the mixture was filtered through a small plug of silica gel and eluted with 20:1 hexxanes:ethyl acetate to provide 57 mg recovered of the product as a colorless oil (99 % yield). Spectra matches previously reported spectra.[4]

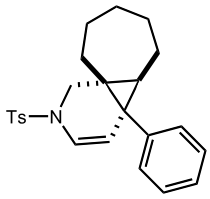


2-tosyl-1,2,3,4,4a,5,6,7-octahydrocyclopenta[f]isoindole(2d) and **(4aR,4bS,9aR)-2-tosyl-2,4a,4b,5,6,7,8,9-octahydro-1H-cyclohepta[1,3]cyclopropa[1,2-c]pyridine(7):** When conducted according to general procedure 1, the product was isolated as a 1:1.3 mixture of diene in 96% total yield. Reaction performed using 65 mg **1d** (.206 mmol), 5.48 mg $PtCl_2$ (0.0206 mmol, 10 mol %), 8.42 mg trichlorotitanium N-tert-butyl(diphenylphosphino)amide (0.0206 mmol, 10 mol %) and 1 mL toluene. Completed in 5

hours and purified on a column of silica gel with 20:1 hexanes:ethyl acetate to give 27 mg of **2d** (41% yield) and 36 mg **7** (55% yield); 96% combined isolated yield.



(4aR,4bS,9aR)-4a-methyl-2-tosyl-2,4a,4b,5,6,7,8,9-octahydro-1H-cyclohepta[1,3]cyclopropa[1,2-c]pyridine(2e): Synthesized according to general procedure I with 68.3mg **1e** (.206 mmol), 5.48 mg $PtCl_2$ (0.0206 mmol, 10 mol %), 8.42 mg trichlorotitanium N-tert-butyl(diphenylphosphino)amide (0.0206 mmol, 10 mol %) and 1 mL toluene. Completed in 18 hours. 59.3 mg recovered. 87% isolated yield. IR (film): υ = 1048.3, 1097.6, 1167.9, 1716.29, 2987.95; ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.66 (d, J=8.05 Hz, 2H), 7.34 (d, J=8.06 Hz, 2H), 6.25 (d, J=7.93 Hz, 1H), 5.23 (d, J=7.93 Hz, 1H), 3.99 (d, J=11.59 Hz, 1H), 2.60 (d, J=11.59 Hz, 1H), 2.43 (s, 3H), 1.87 (m, 1H), 1.71 (m, 5H), 1.37 (m, 3H), 1.06 (m, 1H), 0.70 (m, 1H); ^{13}C-NMR (500 MHz, $CDCl_3$): δ (ppm) = 14.0, 21.5, 23.0, 25.6, 26.7, 28.3, 28.5, 32.5, 33.3, 37.3, 46.1, 119.7, 120.4, 127.0, 129.7, 135.1,143.5; (M+H) calculated: 332.1771, found 332.1606.



(4aR,4bS,9aR)-4a-phenyl-2-tosyl-2,4a,4b,5,6,7,8,9-octahydro-1H-cyclohepta[1,3]cyclopropa[1,2-c]pyridine(2f): Synthesized according to general procedure I with 81 mg **1f** (0.206 mmol), 5.48 mg $PtCl_2$ (0.0206mmol), 8.42 mg trichlorotitanium N-tert-butyl(diphenylphosphino)amide (0.0206 mmol, 10 mol %), and 1 mL toluene. 65 mg recovered. Completed in 19 hours. 80% isolated yield. IR (film): υ = 1048.7, 1100.2, 1170.9, 1710.1, 2956.9; ^{1}H-NMR (500 MHz, $CDCl_3$): δ (ppm) = 7.73 (d, J=8.17 Hz, 2H), 7.38 (d, J=7.93 Hz, 2H), 7.25 (m, 3H), 7.0 (d, J= 7.08 Hz, 2H), 6.28 (d, J=7.93 Hz, 1H), 5.24 (d, J=7.93 Hz, 1H), 4.17 (d, j=11.84 Hz, 1H), 2.87 (d, J=11.72 Hz, 1H), 2.46 (s, 3H), 1.95 (m, 1H), 1.91 (m, 1H), 1.71 (m, 3H), 1.48 (q, 1H), 1.08 (m, 3H), 0.95 (m, 1H), 0.86 (m, 1H); ^{13}C-NMR (500 MHz, $CDCl_3$): δ (ppm) = 21.6, 26.3, 28.0, 28.2, 30.6, 31.5, 35.0, 35.3, 39.1, 46.3, 119.1, 120.0, 126.5, 127.1, 128.5, 129.8, 131.2, 135.2, 139.8, 143.7; (M+H) calculated: 394.1936, found 394.1762.

Table 3 Product Selectivity Studies:

Table 3, Entry 7: In a 3 dram vial is placed 29.3mg of **1d**, (0.092 mmol), 2.2 mg $Pt(COD)_2Cl_2$ (0.0046 mmol, 5 mol %) and 3.2 mg (0.0046 mmol, 5 mol %) **4** and 1 mL $CDCl_3$. Reaction was heated to 35 °C. The reaction is monitored by ^{1}H NMR and went to completion in 24 hours. ^{1}H NMR of the crude reaction mixture showed a 10:1 ratio of cyclopropane:diene products. The reaction mixture was loaded directly loaded onto a column of silica gel and eluted with 20:1 hexanes:ethyl acetate. The product was isolated as a colorless oil (24 mg of **2d,** 4 mg of **7**. 96% yield total). Spectra matched previously reported values.[3]

IV. ^{31}P NMR Sudies:

When Ligand **5** (2 equivalents) is mixed with $PtCl_2$ in either toluene or $CHCl_3$, trace amounts of a new signal at ~72 ppm is observed (low solubility of $PtCl_2$). When the same experiment is conducted with more soluble $Pt(cod)Cl_2$, the same peak at 72.7 ppm is initially observed (Figure S1), which slowly converts to a new signal at 30.97 ppm after extended

reaction times (1 week, Figure S2). Importantly, these new peaks contain Pt satelites, indicating the formation of new Pt-P complexes. These peaks are different from the free phosphinoamide (*t*BuNPPh$_2$)TiCl$_3$ ligand **5** (-11.0 ppm, Figure S3), the peak for free phosphinoamide ligand **6** (22.0 ppm, Figure S4) and the peaks formed when Pt(cod)Cl$_2$ is mixed with phosphinoamide ligand **6** (Figure S5). Efforts to isolate either of these intermediates via crystallization have been unsuccessful to date.

Figure S1. ^{31}P NMR mixture of (tBuNPPh$_2$)TiCl$_3$ and Pt(cod)Cl$_2$ after 12 h reaction time (in C_6D_6).

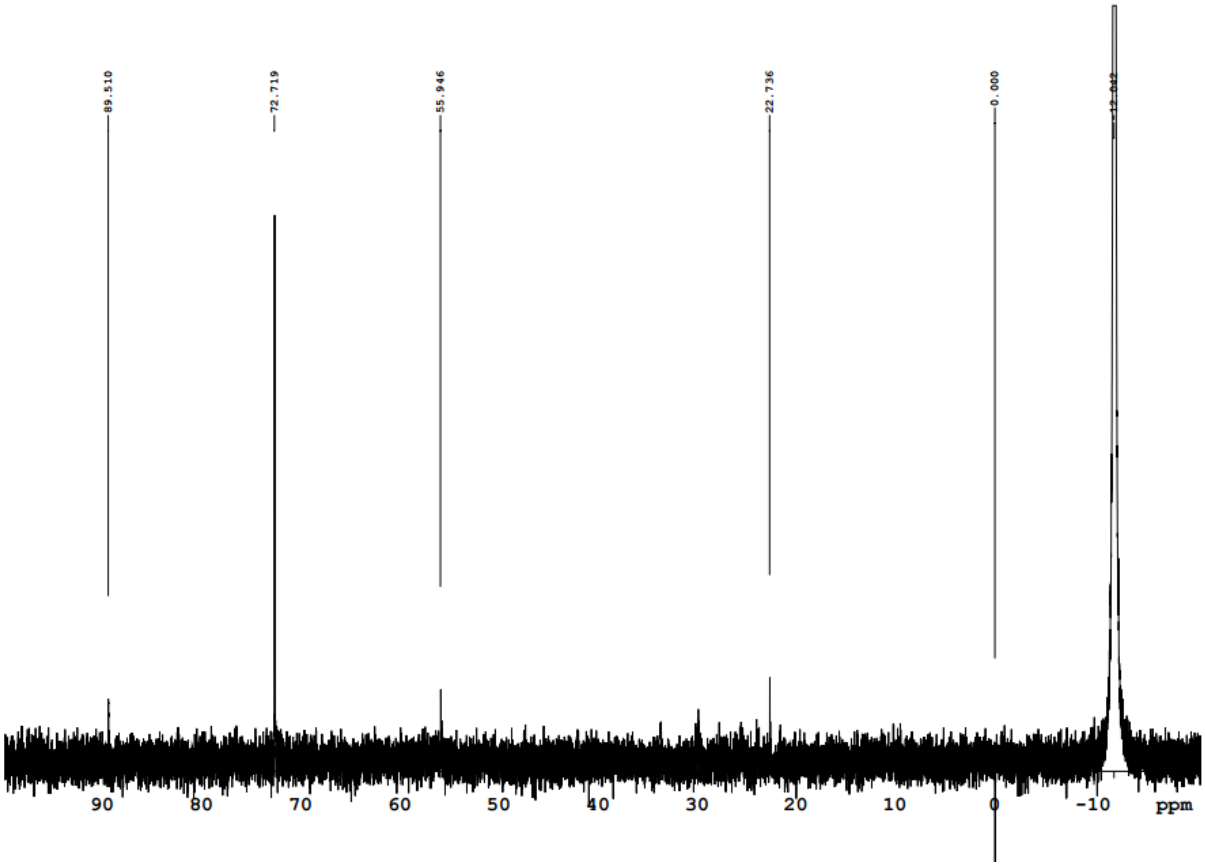


Figure S2. ^{31}P NMR mixture of $(tBuNPPh_2)TiCl_3$ and $Pt(cod)Cl_2$ after 7 days reaction time (in $CDCl_3$).

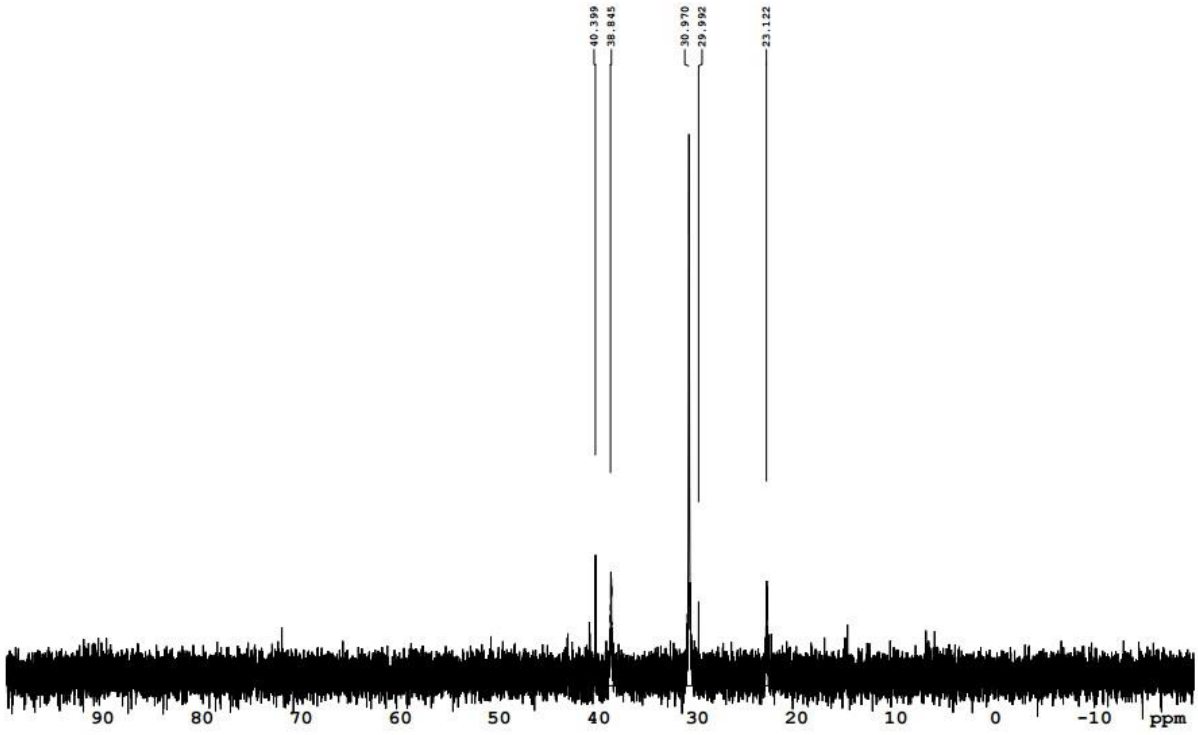


Figure S3. ^{31}P NMR spectrum of $(tBuNPPh_2)TiCl_3$ (in $CDCl_3$).

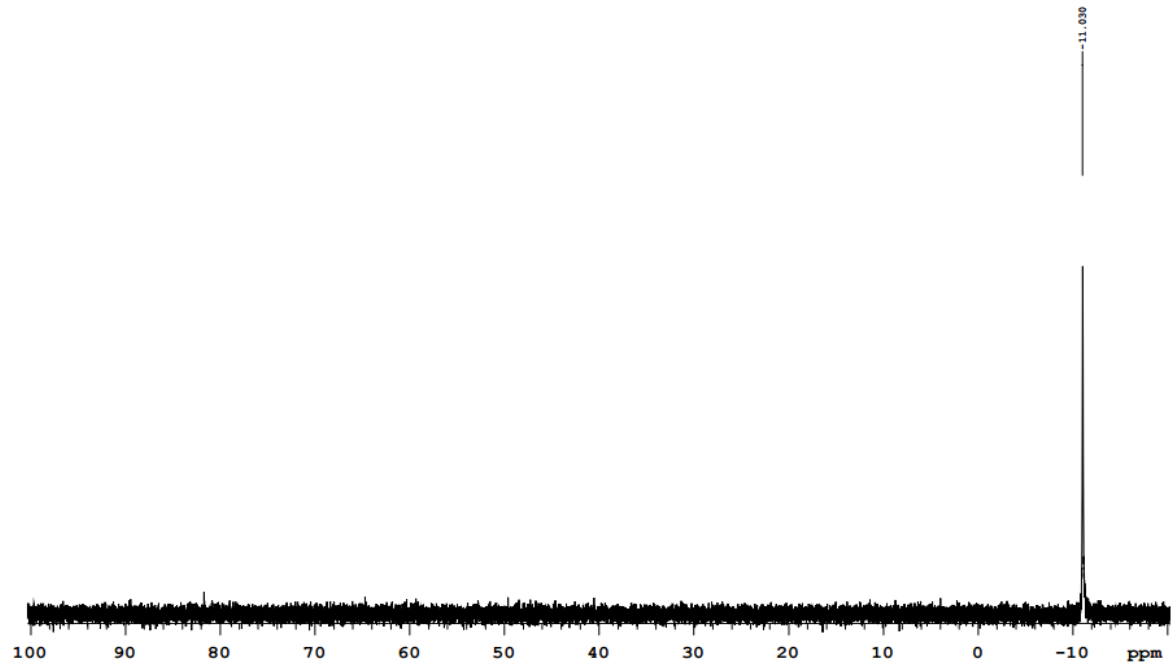


Figure S4. Ligand 6 (*t*BuNHPPh2) in $CDCl_3$.

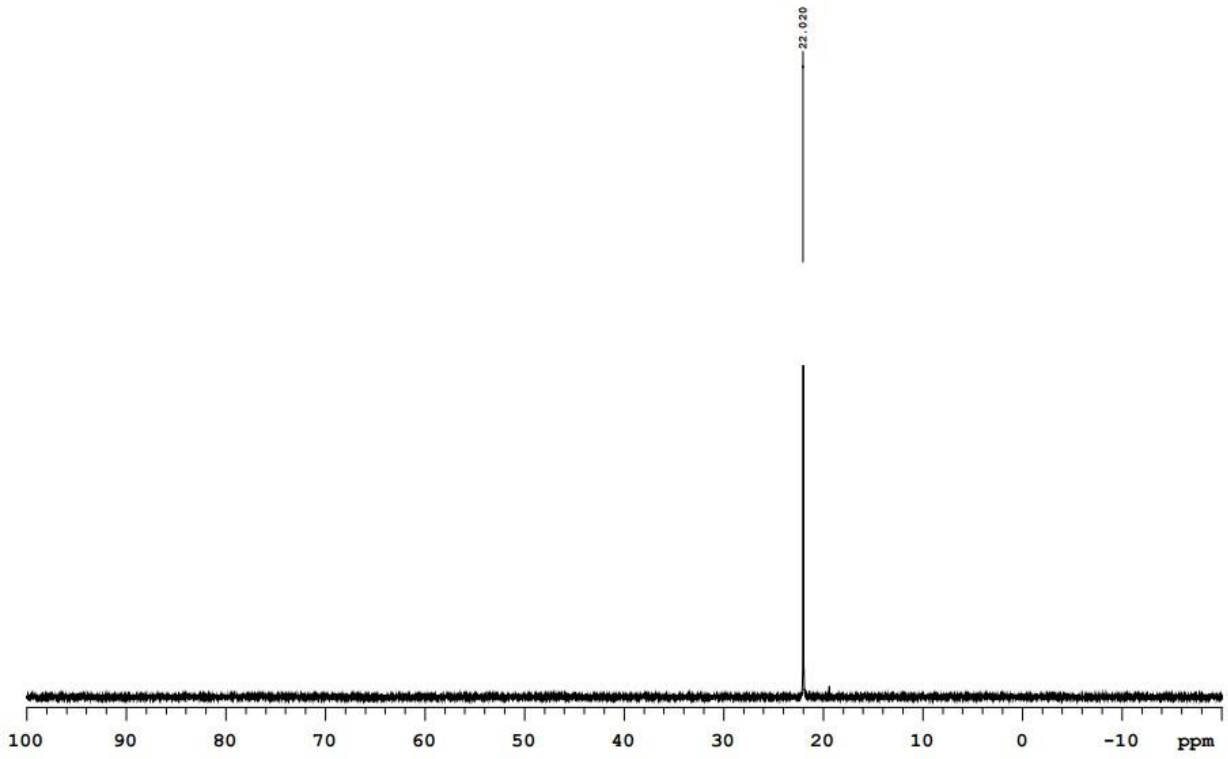
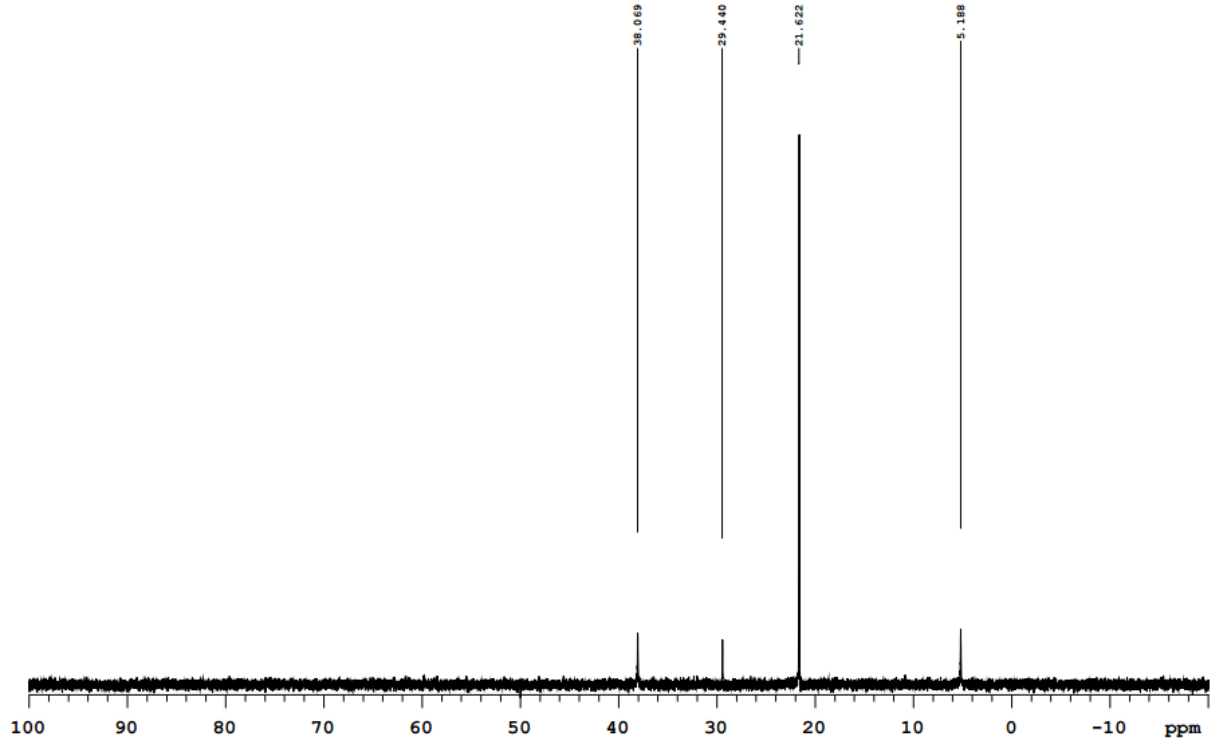
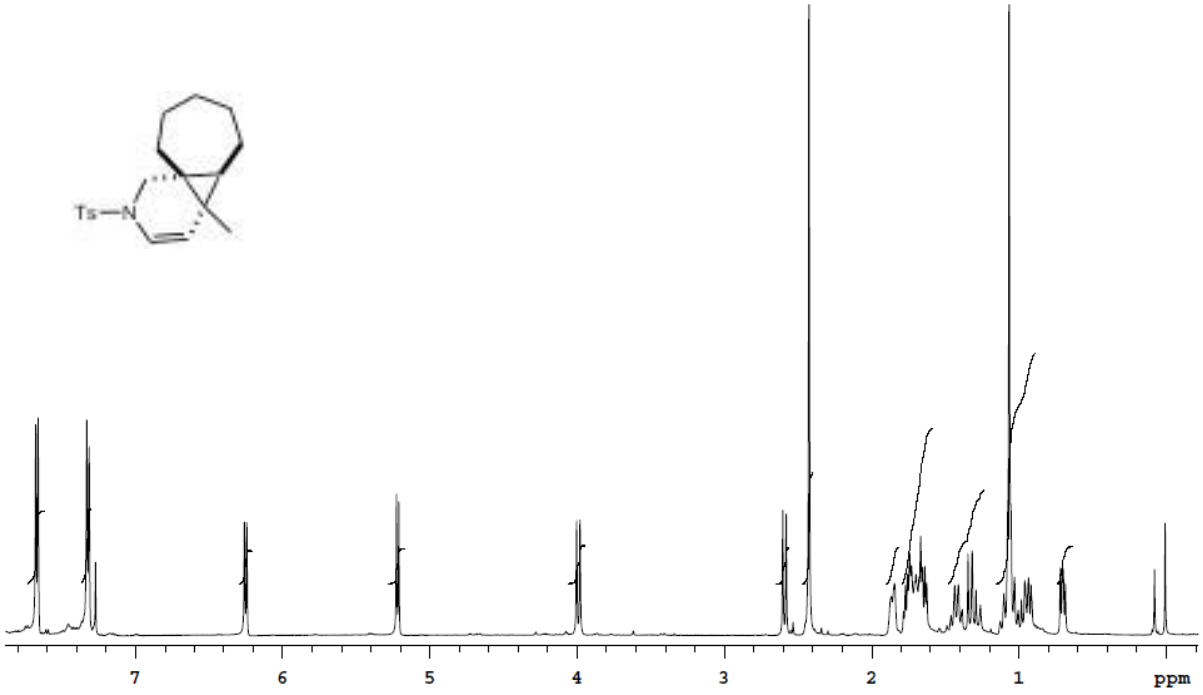


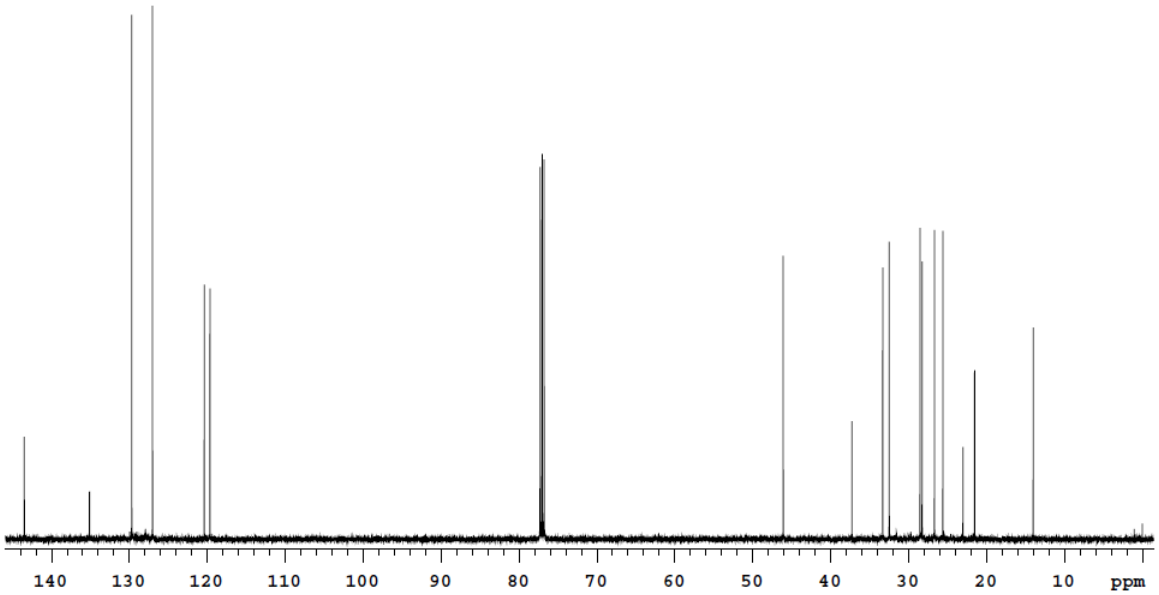
Figure S5. ^{31}P NMR mixture of $tBuNHPPh_2$ (**6**) and $Pt(cod)Cl_2$ after 24 h reaction time (in $CDCl_3$).



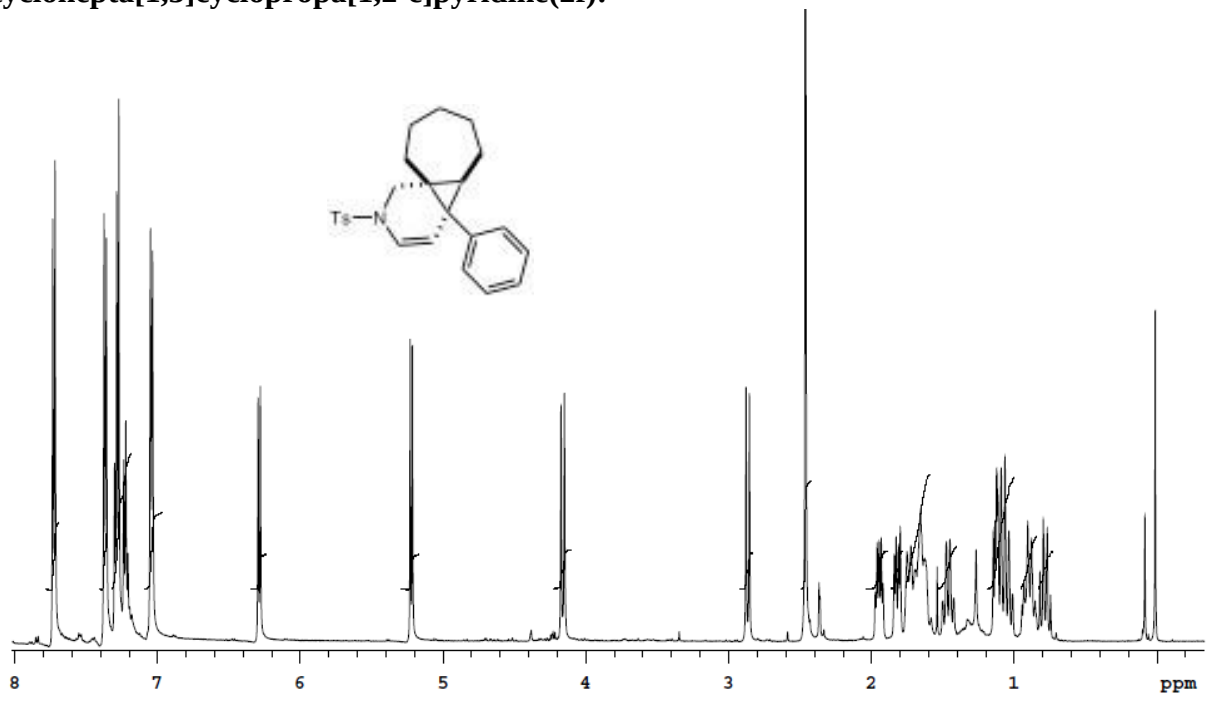
V. Spectral Images for new compounds.

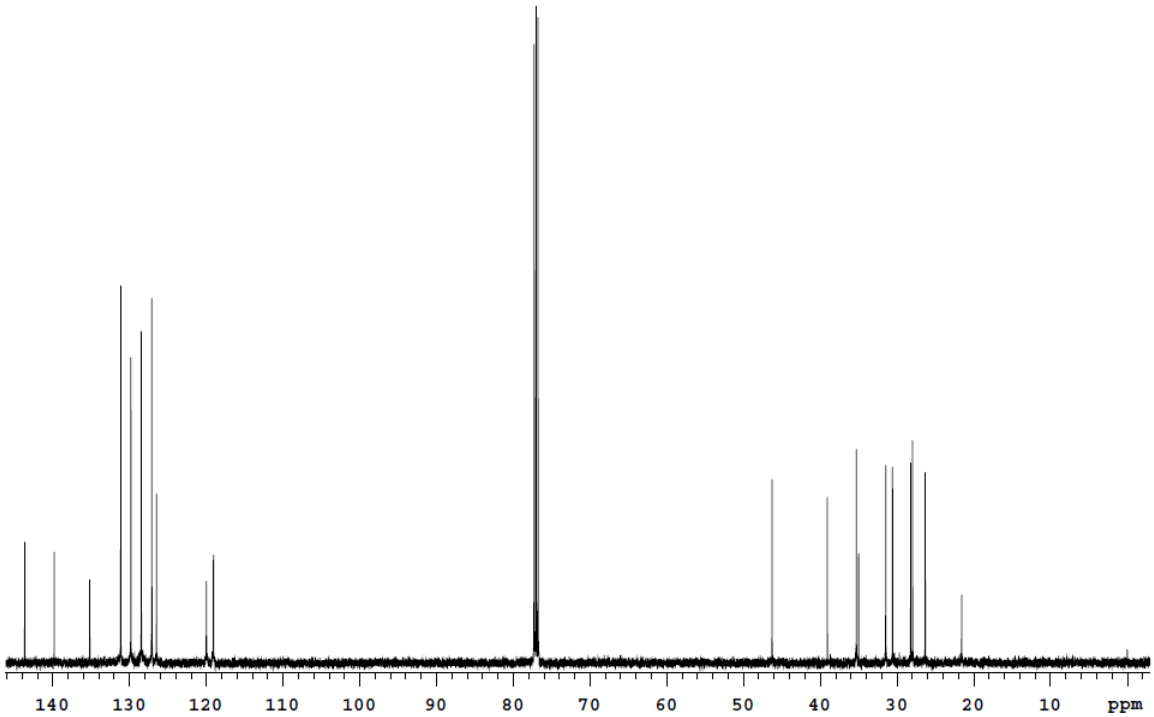
(4aR,4bS,9aR)-4a-methyl-2-tosyl-2,4a,4b,5,6,7,8,9-octahydro-1H-cyclohepta[1,3]cyclopropa[1,2-c]pyridine(2e):





(4aR,4bS,9aR)-4a-phenyl-2-tosyl-2,4a,4b,5,6,7,8,9-octahydro-1H-cyclohepta[1,3]cyclopropa[1,2-c]pyridine(2f):





VI. References:

1. Walker, W. K.; Anderson, D. L.; Stokes, R. W.; Smith, S. J.; Michaelis, D. J. *Org. Lett.* **2015** *17* (3), 752-755
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4. Fürstner, A.; Stelzer, F.; Szillat H. *J. Am. Chem. Soc.* **2001** *123* (48), 11863-11869