Synthesis, Characterization and Catalytic Activity of Chiral NHC Platinum(II) Pyridine Dihalide Complexes

Romain Pertschi, Delphine Hatey, Patrick Pale, Pierre de Frémont, Aurélien Blanc

om-2019-00850x-Revised

Synthesis, Characterization and Catalytic Activity of Chiral NHC Platinum(II) Pyridine Dihalide Complexes

Romain Pertschi,[ϒ] Delphine Hatey, [ϒ] Patrick Pale,[ϒ]

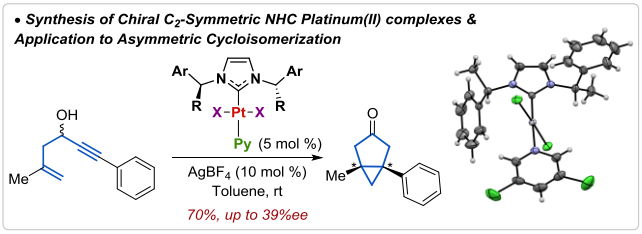
Pierre de Frémont[†*] and Aurélien Blanc,[ϒ*]

[ϒ]*Laboratoire de Synthèse, Réactivité Organique et Catalyse, Institut de Chimie (UMR 7177 CNRS), Université de Strasbourg, 4 rue Blaise Pascal, CS 90032, 67081 Strasbourg, France.*

[†]*Synthèse, Réactivité et Catalyse Organométalliques (UMR 7177 CNRS), Université de Strasbourg, 4 rue Blaise Pascal, CS 90032, 67081 Strasbourg, France.*

RECEIVED DATE

Abstract: *A series of platinum(II) dihalide pyridine complexes bearing chiral C_2-symmetric N-heterocyclic carbene (NHC) ligands [Pt(NHC*)(Py)(Hal)$_2$] was synthesized in a one pot procedure and characterized by NMR spectroscopy and single crystal X-ray diffraction (SC-XRD). The complexes were tested for the asymmetric cycloisomerization of enynol into bicyclo[3.1.0]hexanone and feature an excellent catalytic activity at room temperature along with a modest enantiomeric induction (up to 39%ee).*



Introduction

Platinum and carbenes are intimately linked sharing a long lasting history which started in 1915 with the synthesis of the Chugaev's salt: a platinum(II) complex bearing two acyclic diaminocarbenes.[1] Since, organoplatinum chemistry has always been used to highlight the progresses made on synthetic carbene chemistry, ranging from pioneering works made during the 60s-70's up to the most recent publications. *N*-heterocyclic carbenes (NHCs), a subclass of singlet carbenes also called persistent carbenes, have become extremely popular since the mid 90's to bind late transition metals complexes,[2] and it is no surprise to have plenty of synthetic strategies reported to access NHC platinum complexes.[3,4] Those include the cyclization of platinum isocyanides,[5,6] the addition of isolated carbenes or enetetramines to platinum salts, the reaction of azolium carbene precursors with platinum salts in the presence of bases, or the transmetalation from parent NHC silver(I) complexes.[7] With a NMR active isotope (^{195}Pt NMR; I = ½, isotope abundance = 33.8 %), platinum derivatives and their chemistry can be studied by NMR and ^{195}Pt NMR has been successfully applied for the characterization of complexes or inorganic salts.[8] Platinum has a rich coordination chemistry which covers oxidation states ranging from –II to +VI. With NHCs, the +II oxidation state is mainly studied providing air and moisture stable complexes, with well-defined square planar geometry around the metal, even though NHC platinum(0) and (IV) complexes are also readly accessible.[9,10] Since the discovery of the cisplatin drug, many new NHC platinum(II) complexes are steadily reported and tested for their cytotoxic activities toward cancer cells.[11] However, only few platinum(II) complexes bearing chiral NHC ligands have been reported in the literature and without catalytic applications (Figure 1, top).

In term of homogeneous catalysis, platinum is often outshined by palladium which is more efficient at promoting the well-known and widely applied C–C coupling reactions, despite a surge of the palladium price (since 2016) which makes it currently twice more expensive than platinum.[12] Nevertheless, achiral NHC platinum(II) complexes have proven valuable soft Lewis acids able to catalyze the activation of multiple carbon–carbon bonds

toward electrophilic addition (e.g. cycloisomerization of enynes,[13,14] hydrosilylation,[15,16] hydration of alkynes…).[17,18] However, the more carbophilic gold(I) complexes often proved to be more efficient in such reactions. For these reasons, the development of Pt(II)-catalyzed asymmetric transformations, notably cycloisomerization reactions, are scarce.[19,20] To obtain good enantiomeric excess with NHC platinum(II) catalysts, an additional chiral ligand must be added to the square planar complex such as chiral diphosphine,[21,22] Binepine or Monophos[23,24] developed by the Marinetti et coll. (Figure 1, bottom).

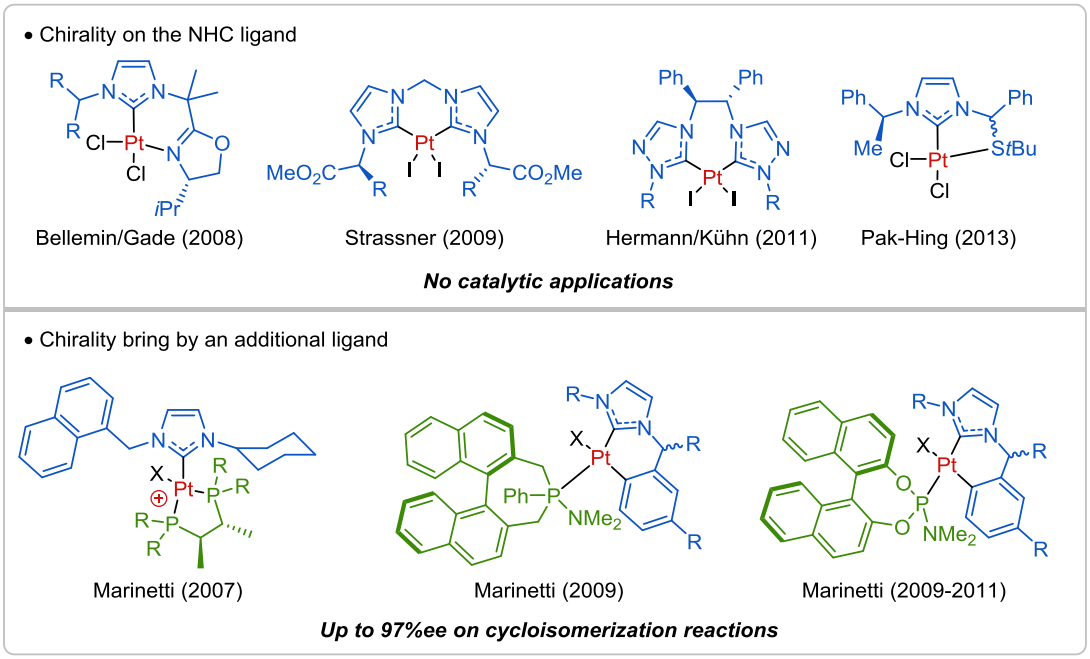


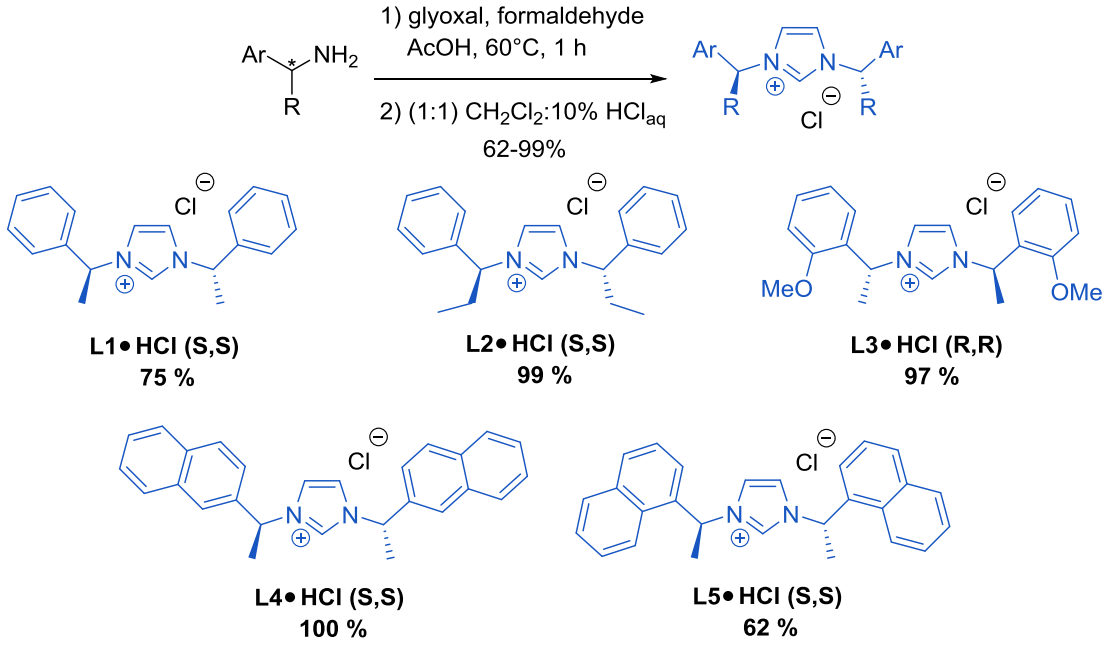
Figure 1: List of reported chiral NHC platinum(II) complexes to date.

Nevertheless, NHC ligands allow for fine-tuning the steric environment around the metal center to create chiral pockets. Most chiral NHCs feature a stereogenic center placed on the *N*,*N*-aryl/alkyl substituents or on the backbone of the heterocycle.[25] Occasionally, axial planar chirality is achieved using bulky *N*-biphenylene arms while planar chirality occurs in the presence of ferrocenes[26] or heterocycles (e.g. morpholine) fused with triazolylidenes.[27]

In this contribution, we report the straightforward synthesis and characterization of a series of unprecedented chiral C_2-symmetric NHC platinum(II) pyridine dihalide complexes. Their catalytic activity was evaluated in asymmetric cycloisomerization.

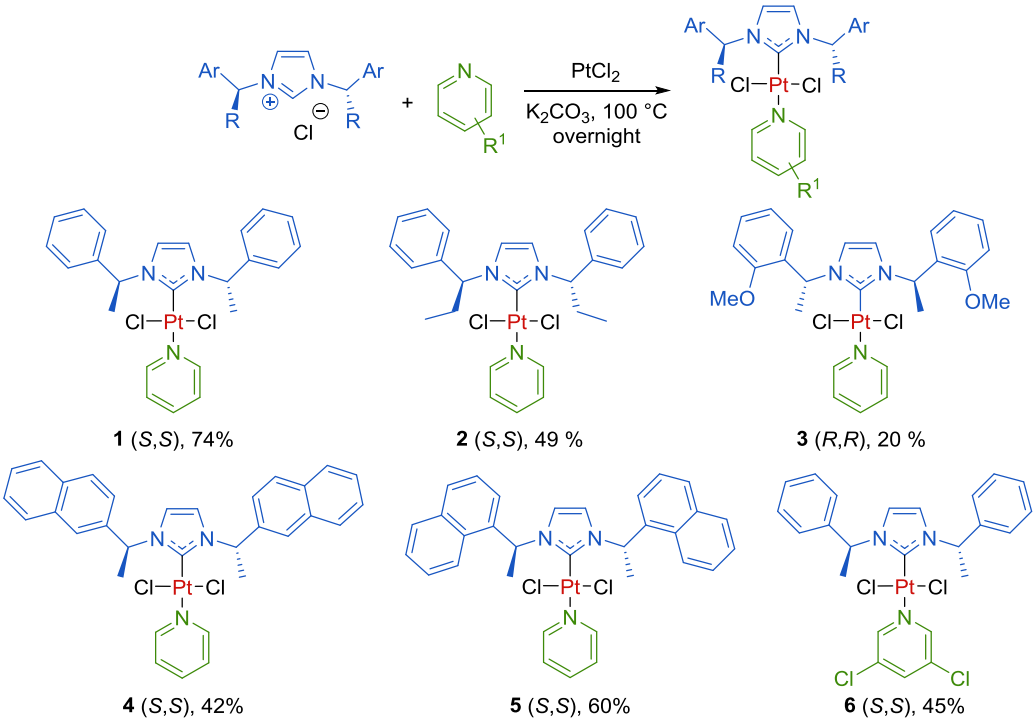
Results and discussion

Ligands and complexes synthesis. A series of ligands was selected so as to bring aryl or alkyl groups of various sizes as close as possible to the platinum center to favor asymmetric induction during the Pt-driven catalytic steps. Representing the simplest model, 2-arylated alkyl amines were used to produce this series of *N*,*N*-disubstituted NHCs. The chiral imidazolium chloride pro-ligands, 1,3-*bis*((S)-1-phenylethyl)-imidazolium chloride (**L1•HCl**),[28] 1,3-*bis*((S)-1-phenylpropyl)-imidazolium chloride (**L2•HCl**),[29] 1,3-bis((S)-1-(2-methoxyphenyl)ethyl)-imidazolium chloride (**L3•HCl**), 1,3-bis((R)-1-(naphthalen-1-yl)ethyl)-imidazolium chloride (**L4•HCl**) and 1,3-bis((S)-1-(naphthalen-2-yl)ethyl)-imidazolium chloride (**L5•HCl**),[30] were readily prepared as previously reported (Scheme 1).



Scheme 1: Synthesis of the pro-ligands [Pt(NHC)(Py)(Cl)$_2$] (**L1-5•HCl**)

The corresponding chiral Pt(II) complexes were conveniently obtained by mixing the imidazolium chloride and platinum dichloride (1equiv.) in hot anhydrous pyridine in the presence of potassium carbonate (10 equiv.). After 12 h, the reaction mixture was filtered over a plug of Celite®, and further purified by column chromatography to afford the corresponding complexes [Pt(NHC)(Py)(Cl)$_2$] (**1-5**), as yellow powder, with yields ranging from 20 to 74% (Scheme 2). It is worth to mention that **1-5** are structurally close from the well-known PEPPSI catalysts based on NHC palladium(II) pyridine complexes.[31,32]

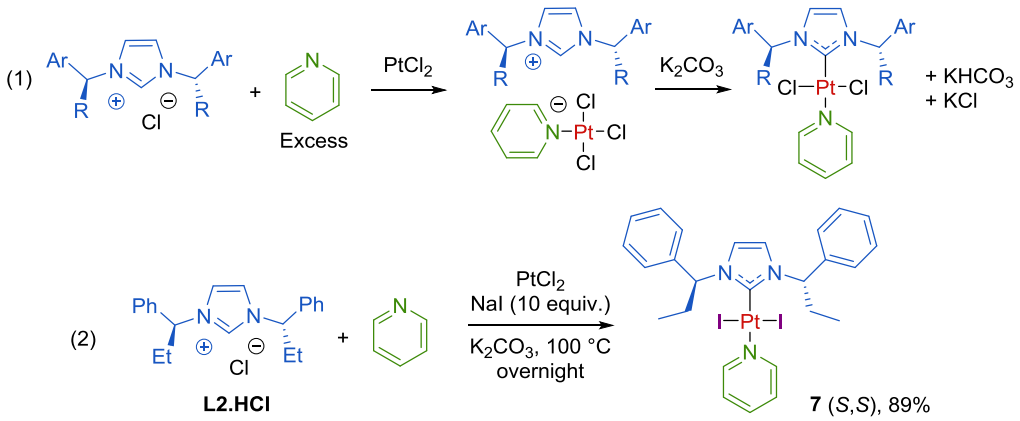


Scheme 2: Synthesis of the complexes [Pt(NHC)(Py)$(Cl)_2$] (**1-6**)

Using (**L3•HPF$_6$**) instead of (**L3•HCl**) failed to provide any NHC platinum complex, while platinum(II) dipyridine dichloride was formed.[33] Nevertheless, the metalation of **L3•HPF$_6$** could be achieved *via* the addition of an excess of halide source such as tetrabutylammonium chloride (1.1 equiv.).

This result strongly suggests that the synthesis of **1-5** requires the initial formation of imidazolium (pyridine)trichloroplatinate intermediates (**L1-5•H{Pt(Py)(Cl)$_3$}**) (Eq. 1, Scheme 3), which is consistent with literature data.[34,35] These intermediates then evolve toward the targeted complexes **1-5** in the presence of potassium carbonate.

With 3,5-dichloropyridine instead of pyridine, the complex [Pt(L1)(^{Cl}Py)$(Cl)_2$] (**6**) was also formed, although in moderate yield (45%), following the protocol used to synthesize **1**. However, the reaction failed employing pyridine-2-carboxylic acid. The complex [Pt(L2)(Py)$(I)_2$] (**7**) was obtained in high yield (89%) from **L2•HCl** in the presence of an excess of sodium iodide using our standard conditions (Eq. 2, Scheme 3).



Scheme 3: Possible pathway for the formation of [Pt(L1)(^{Cl}Py)(Cl)$_2$] (**6**) and synthesis of [Pt(L2)(Py)(I)$_2$] (**7**)

The ^{1}H NMR spectra of **1-7** feature the characteristic absence of the azolium protons from **L1-5•HCl** located above 11 ppm. The *ortho*-protons from the coordinated pyridine feature signals between 8.95 and 9.15 ppm, shifted downfield (from 0.40 to 0.70 ppm) compared to free pyridine. The ^{13}C NMR spectra of **1-7** show carbene signals between 136.0 to 139.5 ppm, in good agreement with the values reported for achiral NHC platinum(II) complexes.[36,37] The presence of platinum carbene bond is also confirmed by ^{195}Pt NMR for **7**, with a signal at -2906.3 ppm, in good agreement with the literature despite a challenging data acquisition.[38] All the so-produced platinum complexes are extremely stable under air and moisture. They are obtained analytically pure (prior catalysis trials) after flash chromatography over silica gel.

Despite many attempts, quality crystals suitable for single crystal X-ray diffraction studies (SC-XRD) could only be grown for **6** and **7**, by slow evaporation of saturated dichloromethane solutions of complexes layered with *n*-heptane. These complexes crystallize respectively in the orthorhombic and monoclinic systems with $P2_12_12_1$ and C*2* Sohncke space groups. The unit cell found for **7** features three independent molecules of complexes per asymmetric unit. As expected, all platinum(II) centers are in a square planar coordination environment with the C–Pt–N angles between 175.0(2) and 177.65(17)°, and the C–Pt–Halogen or N–Pt–Halogen angles are comprised between 88.44(18) and 92.43(18)°. The C–Pt and N–Pt bond lengths are respectively between 1.971(4) - 1.985(6) Å and 2.079(5) - 2.083(4) Å. These values are in the range of those found in other similar NHC and pyridine platinum(II) complexes.[36,39] (Figure 2)

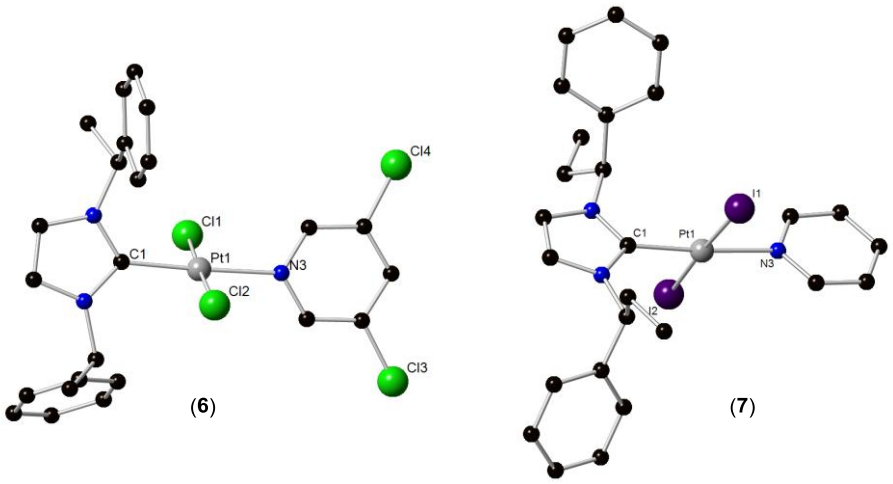
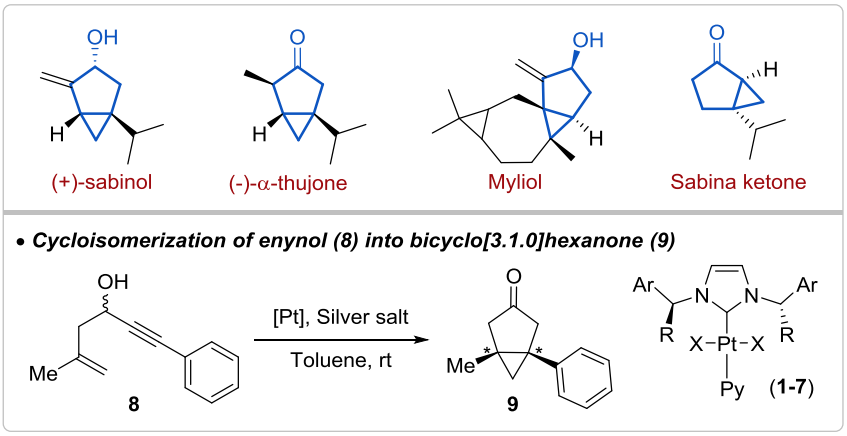


Figure 2: Ball and stick representation of [Pt(L1)(^{Cl}Py)$(Cl)_2$] (**6**) and [Pt(L2)(Py)$(I)_2$] (**7**). Hydrogen atoms have been omitted for clarity.

Catalytic Properties. With these chiral platinum(II) complexes in hand, we applied them to the asymmetric cycloisomerization of 5-methyl-1-phenylhex-5-en-1-yn-3-ol (**8**) to form 1-methyl-5-phenylbicyclo[3.1.0]hexan-3-one (**9**) (Scheme 4, bottom). Such bicyclic scaffold is part of various terpenic natural products such as tabinol or myliol (Scheme 4, top).[40,41] Thus, it is extremely worth to enantioselectively build such bicyclic motif.



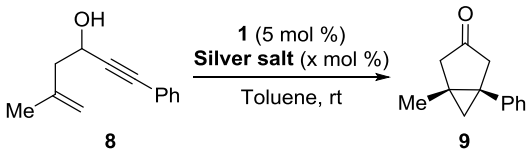
Scheme 4: Selected examples of natural products exhibiting bicyclo[3.1.0]hexanone scaffolds and targeted asymmetric cycloisomerization of the enynol **8**.

The use of silver(I) salts proved mandatory to achieve a catalytic activity (Table 1, entry 1). This suggests that at least one halide has to be removed first from the platinum center to generate a vacant site which can react with **8** to form a π-alkynyl platinum intermediate[18]. The pyridine ligand does not seem labile enough to do so. The role of the silver salt was further studied using complex **1**. At room temperature, in toluene, a

stoichiometric amount of $AgNTf_2$ or $AgBF_4$ relative to platinum complex (**1**, 5 mol %) afforded compound **9** after 12 h with similar yields, 57 and 55% respectively (entries 2 and 3). Despite an interesting catalytic activity compared to other reported platinum catalysts,[24] ees were extremely low (less than 5%). Increasing the amount of $AgNTf_2$ or $AgBF_4$ to 10 mol % was beneficial, providing **9** with higher yields (60 and 70% respectively), after only 4 h (entries 4 and 5). Ees slightly increased up to 18 and 22%. However, reproducibility issue was observed with $AgNTf_2$ leading to unexplained variations of ees from 15 to 22 %. With $AgSbF_6$ and AgOTf at the same loading (10 mol %), no noticeable amelioration could be achieved in term of efficacy (entries 6 and 7). Compound **9** was obtained with 70 and 57 % yields, but ee significantly dropped with the use of $AgSbF_6$ (entry 6 vs 7).

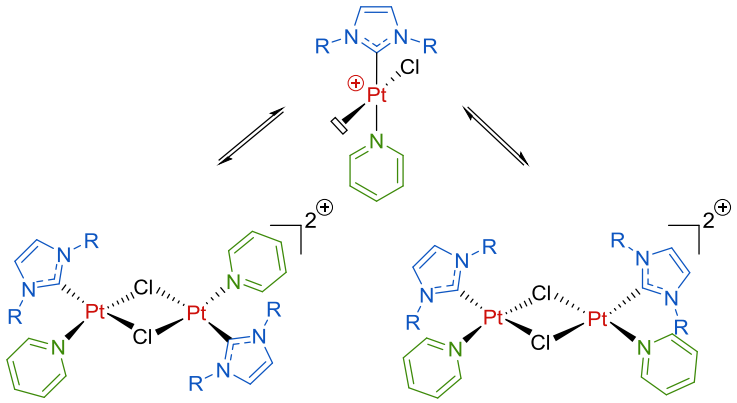
Overall, the presence of anions accepting hydrogen bonds (BF_4^-, OTf^-) seems to enhance the asymmetric induction observed.[42] It is worth noticing that the low to modest ees observed might be related to the formation of transient bridged diplatinum complexes with different geometries and catalytic activities, in equilibrium with the monomeric monochloroplatinum complex (Scheme 5).[43]

Table 1: Summary of the silver(I) salt effect on catalysis.



entry	AgX (mol%)	t (h)	yield[a] of **9** (%)	*ee*[b] (%)
1	-	24	0	-
2	$AgNTf_2$ (5)	12	55	1
3	$AgBF_4$ (5)	12	57	5
4	$AgNTf_2$ (10)	4	60	15-22[c]
5	$AgBF_4$ (10)	4	70	18
6	$AgSbF_6$ (10)	4	57	3
7	AgOTf (10)	4	70	16

[a]Yields calculated by integration of the ^{1}H NMR spectrum of the crude product relative to an internal reference (dimethyl terephtalate). [b]Enantiomeric excess (*ee*) were determined by GC (see supporting information). [c]Unreproducible results.

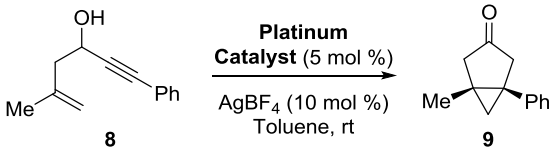


Scheme 5: Formation of cationic bridged diplatinum complexes upon activation with silver

The influence of the NHC and pyridine ligand structure/nature was also studied/evaluated compared to **1**, (Table 2). At room temperature, in toluene, with 10 mol% of $AgBF_4$, complex **2** with a more sterically hindered benzylic position afforded **9** in lower yield (59 % after 9 h vs 70% for **1**), while ee was slightly improved to 22 % (entry 2 vs 1). Complexes **4** or **5** with large aryl groups, respectively 2- or 1-naphtyl, provided **9** with similar or slightly lower yields (66 or 61 % vs 70%) after 6 h, but with similar or improved ees (39 or 15 %), (entries 4 and 5). The better enantioselectivity observed for **4** might come from the favored formation of a π-platinum complex with the pre-oriented 2-naphtyl group which triggered a constrained environment around the platinum center forcing a selective approach and/or orientation of the starting enynol. Compared to **1**, the presence of *ortho*-methoxybenzyl groups appeared detrimental, as complex **3** produced **9** with only 48 % yield and 20 % ee, after 9 h (entry 3).

Complex **6**, similar to **1** but with a *meta*-dichloropyridine ligand, provided **9** with good yield in a rapid reaction (1.5 vs 4 h) but almost without enantioselectivity (2 % ee; entry 6 vs 1). The electro-deficient dichloropyridine used to increase the Lewis acidity of the platinum center led to a complete loss of enantioselectivity, even though the complex **6** was more active. In contrast, the nature of the *trans*-halide ligands had a marginal impact on the catalyst activity, and the diiodide complex **7** provided **9** with 52 % yield and 22 % ee, after 9 h (entry 7).

Table 2: The summary of ligand effect on catalysis.



entry	catalyst	t (h)	yield[a] of **9** (%)	*ee*[b] (%)
1	**1** (*S*,*S*)	4	70	18
2	**2** (*S*,*S*)	9	59	22
3	**3** (*R*,*R*)	9	48	-20
4	**4** (*S*,*S*)	6	66	39
5	**5** (*S*,*S*)	6	61	15
6	**6** (*S*,*S*)	1.5	60	2
7	**7** (*S*,*S*)	9	52	22

[a]Yields calculated by integration of the ^{1}H NMR spectrum of the crude product relative to an internal reference (dimethyl terephtalate). [b]Enantiomeric excess (*ee*) were determined by GC (see supporting information).

Conclusion

A series of chiral NHC platinum(II) dihalide pyridine complexes were synthesized from parent imidazolium salts in the presence of platinum dichloride, pyridine and potassium carbonate, under air condition, using a straightforward one-pot procedure. The yields range from 20 to 79%, being highly dependent from the NHC and pyridine ligand architectures. Upon activation with silver(I) tetrafluoroborate, the complexes were evaluated as catalysts in homogeneous asymmetric cycloisomerization of 5-methyl-1-phenylhex-5-en-1-yn-3-ol. They displayed an interesting catalytic activity at room temperature with yields of formed bicyclohexanone ranging from 48 to 70% after 1.5 to 9 h even though the enantiomeric excesses were rather low ranging from 2 to 39%.

These results proved thus promising considering the simplicity and the straightforward access to the chiral complexes. Work is currently in progress to further tune the various effects (hindrance, π-stacking, etc) the NHC ligands can provide, but also to incorporate a chelating function with hemilabile behavior to create a narrower chiral pocket.

Experimental Section

General considerations

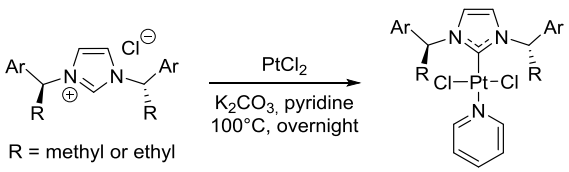
Proton (^{1}H NMR), carbon (^{13}C NMR) and platinum (^{195}Pt NMR) nuclear magnetic resonance spectra were recorded on the following instruments: Bruker AVANCE I – 300 MHz spectrometer, Bruker AVANCE III – 400 MHz spectrometer, and Bruker AVANCE I – 500 MHz spectrometer, respectively. The chemical shifts are given in parts per million (ppm). Data are presented as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintet, sept. = septet, m = multiplet, b = broad), coupling constants (*J*/Hz) and integration. Assignments were determined either based on unambiguous chemical shifts or coupling patterns, or COSY, HSQC, HMBC, NOESY or INADEQUATE experiments were sometimes needed to fully interpret spectra for related compounds. The residual solvent proton (^{1}H) or carbon (^{13}C) resonances were used as references values. For ^{1}H NMR: $CDCl_3$ = 7.26 ppm, CD_2Cl_2 = 5.32 ppm. For $^{13}C\{^{1}H\}$ NMR: $CDCl_3$ = 77.1 ppm, CD_2Cl_2 = 53.8. The signal of K_2PtCl_6 in D_2O was used as reference for ^{195}Pt NMR. IR and IR spectra were recorded neat in the region 4000 - 400 cm^{-1} on a Brucker FTIR ALPHA Spectrometer. Wavelengths of maximum absorbance are quoted in wave numbers (cm^{-1}). Elemental analyses were performed by the "Service de Microanalyses", Université de Strasbourg. For the X-ray diffraction studies, the intensity data were collected at 173(2) K on a Bruker KAPPA APEX II DUO diffractometer. Crystallographic and experimental details for all the structures are summarized in the Supporting Information (See ESI - page S15). The structures were solved by direct methods (SHELXT) and refined by full-matrix least-squares procedures (based on F^2, SHELXL-2014) with anisotropic thermal parameters for all the non-hydrogen atoms.[44] The hydrogen atoms were introduced into geometrically calculated positions (SHELXL-2014 procedures) and refined riding on the corresponding parent atoms. Analytical TLC was carried out on silica gel 60 F254 plates with visualization by ultraviolet light, vanillin, anisaldehyde or $KMnO_4$. Chromatography was carried out using silica gel 60 (40–63 μm). Reagents and solvents were purified using standard methods. Enantiomeric excess were determined by Gas Chromatography (CG) using HP 6850 Series GC System device and LIPODEX®-E, 25 m x 0.25 mm ID (Macherey-Nagel) chiral column. It was programmed with the following sequence: flow = 5.5 $mL.min^{-1}$, 70°C hold 5 min, ramp 9°C/min to 120°C, hold 13 min, ramp 40°C/min to 140°C, hold 1 min. (See ESI - page S11) Anhydrous reactions were carried out in flame-dried glassware and under an argon

atmosphere. Anhydrous CH_2Cl_2, THF, and MeOH were dried by passing through activated alumina under a positive pressure of argon using GlassTechnology GTS100 devices. All other chemicals were used as received, including the starting chiral amines and the platinum dichloride salts bought from Aldrich Company.

Synthesis of the platinum complexes

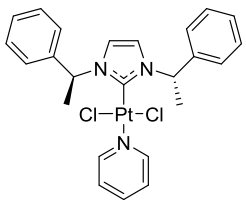
The chiral imidazolium salts **L1-5•HCl** used as pro-ligands were synthesized from the corresponding chiral amines following previously described procedures. (For more details, see S2 in the ESI). The syntheses were set under an atmosphere of argon, using anhydrous pyridine.

General Procedure



In anhydrous pyridine, 1.05 equiv. of chiral imidazolium chloride salt **L1-5•HCl**, 1 equiv. of platinum dichloride salt and 10 equiv. of K_2CO_3 were stirred overnight at 100°C. Then, the excess of pyridine was removed under reduced pressure. Under air atmosphere, the remaining solids were dissolved in CH_2Cl_2 prior filtration through a plug of Celite. The resulting solution was concentrated to afford a solid which was further purified by flash chromatography (SiO_2, CH_2Cl_2/heptane) to yield the desired NHC platinum(II) dichloride complexes analytically pure.

(1,3-Bis((S)-1-phenylethyl)imidazol-2-ylidene) platinum(II) pyridine dichloride (1)

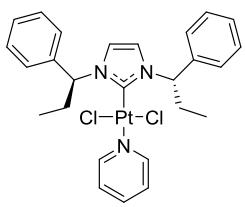


$C_{24}H_{25}Cl_2N_3Pt$
MW: 621.469

Prepared according to **General Procedure** from the imidazolium salt **L1•HCl** (84 mg, 0.269 mmol) and $PtCl_2$ (67.8 mg, 0.255 mmol). Purified by chromatography (SiO_2, 50 to 100% CH_2Cl_2/heptane). **1** was obtained as a pale yellow solid (125.3 mg, 0.202 mmol, **79%**). $\mathbf{R_f}$ = 0.58 (CH_2Cl_2). $\mathbf{[\alpha]_D^{20}}$ = - 189.6° (c = 0.94, CH_2Cl_2). **IR (neat):** 451, 525, 592, 647, 734, 760, 790, 919, 963, 1011, 1027, 1055, 1070, 1115, 1155, 1180, 1210, 1240, 1269, 1287, 1331, 1377, 1427, 1449, 1485, 1497, 1563, 1606, 1967, 2932, 2976, 3030 cm^{-1}. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.95 (d, *J* = 7.1 Hz, 6 H_{CH_3}), 6.55 (s, 2 H_{Im}), 7.12 (q, *J* = 7.1 Hz, 2 H_{CH}), 7.31 (tt, *J* = 1.2, 7.6 Hz, 2 $H_{m\text{-pyr}}$), 7.35 – 7.42 (m, 6 H_{Ar}), 7.60 (d, *J* = 7.7 Hz, 4 H_{Ar}), 7.81 (tt, *J* = 1.7, 7.6 Hz, 1 $H_{p\text{-pyr}}$), 9.11 (dt, *J* = 1.6, 5.1 Hz, 2 $H_{o\text{-pyr}}$). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 20.4 (2 C_{CH_3}), 58.5 (2 C_{CH_2}), 118.4 (2 C_{Im}), 125.0 (2 $C_{m\text{-pyr}}$), 127.8

(4 C_{Ar}), 128.2 (2 C_{Ar}), 128.8 (4 C_{Ar}), 138.1 ($C_{p\text{-pyr}}$), 139.0 ($C_{C\text{-Pt}}$), 139.9 (2 C_{Ar}), 151.6 (2 $C_{o\text{-pyr}}$). **Elemental analysis:** calcd for $C_{24}H_{25}Cl_2N_3Pt$: 6.76 N%, 46.38 %C, 4.05 H%. Found: 6.78 N%, 46.14 %C, 4.06 H%. .

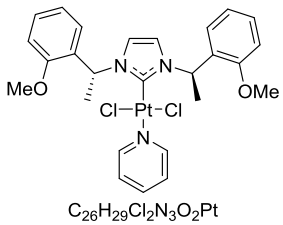
(1,3-Bis((S)-1-phenylpropyl)imidazol-2-ylidene) platinum(II) pyridine dichloride (2)



$C_{26}H_{29}Cl_2N_3Pt$
MW: 649.523

Prepared according to **General Procedure** from the imidazolium salt **L2•HCl** (150 mg, 0.440 mmol) and $PtCl_2$ (111 mg, 0.417 mmol). Purified by chromatography (SiO_2, 50 to 100% CH_2Cl_2/heptane). **2** was obtained as a pale yellow solid (133.7 mg, 0.206 mmol, **49%**). $\mathbf{R_f}$ = 0.58 (CH_2Cl_2). $\mathbf{[\alpha]_D^{20}}$ = - 179.9° (c = 1.01, CH_2Cl_2). **IR (neat):** 452, 521, 647, 691, 724, 760, 806, 846, 915, 930, 1030, 1050, 1070, 1121, 1156, 1177, 1202, 1261, 1354, 1380, 1425, 1449, 1485, 1495, 1565, 1606, 1965, 2037, 2148, 2225, 2875, 2931, 2964, 3030 cm^{-1}. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.06 (t, *J* = 7.4 Hz, 6 H_{CH_3}), 2.24 – 2.46 (m, 4 H_{CH_2}), 6.65 (s, 2 H_{Im}), 6.78 (dd, *J* = 6.4, 9.2 Hz, 2 H_{CH}), 7.31 (dd, *J* = 6.4, 8.3 Hz, 2 $H_{m\text{-pyr}}$), 7.39 (td, *J* = 5.4, 7.5 Hz, 6 H_{Ar}), 7.64 (d, *J* = 7.6 Hz, 4 H_{Ar}), 7.81 (tt, *J* = 1.7, 7.7 Hz, 1 $H_{p\text{-pyr}}$), 9.07 – 9.12 (m, 2 $H_{o\text{-pyr}}$). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 11.5 (2 C_{CH_3}), 27.6 (2 C_{CH_2}), 64.6 (2 C_{CH}), 118.2, (2 C_{Im}) 125.0 (2 $C_{m\text{-pyr}}$), 128.2 (2 C_{Ar}), 128.5 (4 C_{Ar}), 128.9 (4 C_{Ar}), 138.0 ($C_{p\text{-pyr}}$), 138.4 (2 C_{Ar}), 138.9 ($C_{C\text{-Pt}}$), 151.7(2 $C_{o\text{-pyr}}$). **Elemental analysis:** calcd for $C_{26}H_{29}Cl_2N_3Pt$: 6.47 N%, 48.08 %C, 4.50 H%. Found: 6.18 N%, 48.64 %C, 4.68 H%.

(1,3-Bis((R)-1-(2-methoxyphenyl)ethyl)imidazol-2-ylidene) platinum(II) pyridine dichloride (3)

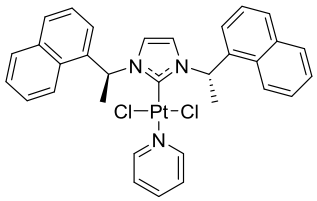


$C_{26}H_{29}Cl_2N_3O_2Pt$
MW: 681.521

Prepared according to **General Procedure** from the imidazolium salt **L3•HCl** (160 mg, 0.43 mmol) and $PtCl_2$ (110 mg, 0.41 mmol). Purified by chromatography (SiO_2, 50% CH_2Cl_2/heptane to 10% Et_2O/CH_2Cl_2). **3** was obtained as a pale yellow solid (56.9 mg, 0.084 mmol, **20%**). $\mathbf{R_f}$ = 0.33 (CH_2Cl_2). $\mathbf{[\alpha]_D^{20}}$ = + 133.6° (c = 0.23, CH_2Cl_2). **IR (neat):** 454, 470, 516, 576, 632, 691, 752, 816, 855, 937, 961, 1026, 1048, 1070, 1114, 1130, 1165, 1183, 1208, 1244, 1288, 1329, 1377, 1424, 1449, 1460, 1492, 1586, 1601, 1743, 1892, 1973, 2005, 2054, 2132, 2182, 2205, 2334, 2835, 2928, 3561, 3672, 3870, 3903 cm^{-1}. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.95 (d, *J* = 7.1 Hz, 6 H_{CH_3}), 3.85 (s, 6 H_{OCH_3}), 6.84 (s, 2 H_{Im}), 6.90 (brd, *J* = 8.1 Hz, 2 H_{Ar}), 6.97 (brt, *J* = 7.4 Hz, 2 H_{Ar}), 7.01 (q, *J* = 7.1 Hz, 2 H_{CH}), 7.30 (td, *J* = 1.7, 7.6 Hz, 2 $H_{m\text{-pyr}}$), 7.33 – 7.38 (m, 2 H_{Ar}), 7.48 (dd, *J* = 1.7, 7.6 Hz, 2 H_{Ar}), 7.77 (tt, *J* = 1.7, 7.6 Hz, 1 $H_{p\text{-pyr}}$), 9.03 (dt, *J* = 1.6, 5.2 Hz, 2 $H_{o\text{-pyr}}$). **^{13}C{^{1}H} NMR (126**

MHz, $CDCl_3$) δ 20.9 (2 C_{CH_3}), 55.5 (2 C_{OCH_3}), 55.6 (2 C_{CH}), 111.3 (2 C_{Ar}), 118.1 (2 C_{Im}), 120.4 (2 $C_{m\text{-pyr}}$), 124.8 (2 C_{Ar}), 128.9 (2 C_{Ar}), 129.1 (2 C_{Ar}), 129.4 (2 C_{Ar}), 137.7 ($C_{p\text{-pyr}}$), 139.1 ($C_{C\text{-Pt}}$), 151.7 (2 $C_{o\text{-pyr}}$), 157.8 ($C_{C\text{-Pt}}$). **Elemental analysis:** calcd for $C_{26}H_{29}Cl_2N_3O_2Pt$: 6.17 N%, 45.82 %C, 4.29 H%. Found: 5.93 N%, 45.63 %C, 4.39 H%.

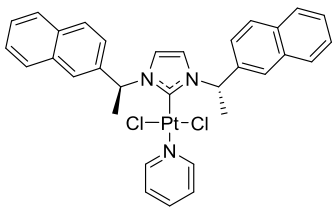
(1,3-Bis((S)-1-(naphthalen-1-yl)ethyl)imidazol-2-ylidene) platinum(II) pyridine dichloride (4)



$C_{32}H_{29}Cl_2N_3Pt$
MW: 721.589

Prepared according to **General Procedure** from the imidazolium salt **L4•HCl** (108.4 mg, 0.263 mmol) and $PtCl_2$ (66.5 mg, 0.25 mmol). Purified by chromatography (SiO_2, 75% CH_2Cl_2/heptane). **4** was obtained as a pale yellow solid (109.5 mg, 0.152 mmol, **61%**). $\mathbf{R_f}$ = 0.65 (CH_2Cl_2). $\mathbf{[\alpha]_D^{20}}$ = - 135.4° (c = 0.25, CH_2Cl_2). **IR (neat):** 416, 434, 471, 507, 524, 559, 648, 690, 736, 760, 805, 851, 868, 956, 999, 1027, 1049, 1070, 1106, 1184, 1214, 1237, 1268, 1313, 1328, 1378, 1419, 1449, 1485, 1510, 1565, 1606, 1819, 1994, 2005, 2073, 2194, 2229, 2922, 3043 cm^{-1}. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 2.20 (d, *J* = 6.9 Hz, 6 H_{CH_3}), 6.36 (s, 2 H_{Im}), 7.35 (ddd, *J* = 1.5, 5.0, 7.6 Hz, 2 $H_{m\text{-pyr}}$), 7.42 (q, *J* = 6.9 Hz, 2H_{CH}), 7.51 (ddd, *J* = 2.2, 4.6, 10.1 Hz, 4 H_{Ar}), 7.61 (ddd, *J* = 1.5, 6.9, 8.5 Hz, 2 H_{Ar}), 7.66 (d, *J* = 7.2 Hz, 2 H_{Ar}), 7.78 (tt, *J* = 1.6, 7.6 Hz, 1 $H_{p\text{-pyr}}$), 7.87 (dd, *J* = 4.3, 8.1 Hz, 4 H_{Ar}), 8.90 – 8.98 (m, 4 $H_{Ar+o\text{-pyr}}$). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 21.8 (2 C_{CH_3}), 55.9 (2 C_{CH}), 118.3 (2 C_{Im}), 124.8 (2 $C_{m\text{-pyr}}$), 124.9 (2 C_{Ar}), 125.1 (2 C_{Ar}), 125.4 (2 C_{Ar}), 126.2 (2 C_{Ar}), 127.3 (2 C_{Ar}), 128.5 (2 C_{Ar}), 129.5 (2 C_{Ar}), 131.7 (2 C_{Ar}), 133.9 (2 C_{Ar}), 135.8 (2 C_{Ar}), 137.9 ($C_{p\text{-pyr}}$), 139.5 ($C_{C\text{-Pt}}$), 151.7 (2 $C_{o\text{-pyr}}$). **Elemental analysis:** calcd for $C_{32}H_{29}Cl_2N_3Pt$: 5.82 N%, 53.26 %C, 4.05 H%. Found: 5.69 N%, 52.95 %C, 4.25 H%.

(1,3-Bis((S)-2-(naphthalen-1-yl)ethyl)imidazol-2-ylidene) platinum(II) pyridine dichloride (5)

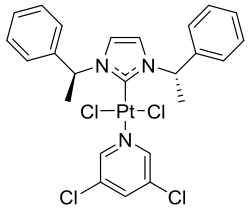


$C_{32}H_{29}Cl_2N_3Pt$
MW: 721,589

Prepared according to **General Procedure** from the imidazolium salt **L5•HCl** (113 mg, 0.274 mmol) and $PtCl_2$ (69.3 mg, 0.26 mmol). Purified by chromatography (SiO_2, 60 to 75% CH_2Cl_2/heptane). **5** was obtained as a pale yellow solid (79.2 mg, 0.110 mmol, **42%**). $\mathbf{R_f}$ = 0.65 (CH_2Cl_2). $\mathbf{[\alpha]_D^{20}}$ = - 231.5° (c = 0.1, CH_2Cl_2). **IR (neat):** 420, 475, 521, 587, 619, 647, 690, 713, 742, 753, 821, 860, 895, 967, 1018, 1033, 1069, 1127, 1191, 1214, 1242, 1271, 1314, 1330, 1379, 1426, 1449, 1485, 1507, 1562, 1605, 1633, 1730, 1917, 2130, 2218, 2924, 2975, 3050 cm^{-1}. **^{1}H NMR (500 MHz,**

$CDCl_3$) δ 2.09 (d, *J* = 7.0 Hz, 6 H_{CH_3}), 6.52 (s, 2 H_{Im}), 7.29 (q, *J* = 6.9 Hz, 2 H_{CH}), 7.38 – 7.44 (m, 2 $H_{m\text{-pyr}}$), 7.46 – 7.55 (m, 4 H_{Ar}), 7.77 (dd, *J* = 1.8, 8.7 Hz, 2 H_{Ar}), 7.79 – 7.87 (m, 5 $H_{Ar+p\text{-pyr}}$), 7.87 – 7.92 (m, 2 H_{Ar}), 8.04 (brs, 2 H_{Ar}), 9.15 (dt, *J* = 1.6, 5.2 Hz, 2 $H_{o\text{-pyr}}$). **$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$)** δ 20.3 (2 C_{CH_3}), 58.7 (2 C_{CH}z), 118.5 (2 C_{Im}), 125.0 (2 $C_{m\text{-pyr}}$), 125.9 (2 C_{Ar}), 126.4 (2 C_{Ar}), 126.5 (2 C_{Ar}), 126.7 (2 C_{Ar}), 127.8 (2 C_{Ar}), 128.4 (2 C_{Ar}), 128.8 (2 C_{Ar}), 133.2 (2 C_{Ar}), 133.2 (2 C_{Ar}), 137.4 (2 C_{Ar}), 138.1 ($C_{p\text{-pyr}}$), 139.2 ($C_{C\text{-Pt}}$), 151.7 (2 $C_{o\text{-pyr}}$). **$^{195}Pt\{^1H\}$ NMR (107 MHz, $CDCl_3$)** δ -2906.3. **Elemental analysis:** calcd for $C_{32}H_{29}Cl_2N_3Pt$: 5.82 N%, 53.26 %C, 4.05 H%. Found: 5.71 N%, 53.29 %C, 4.20 H%.

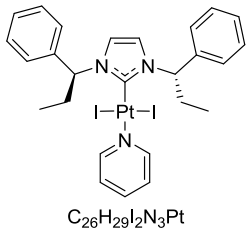
(1,3-Bis((S)-1-phenylethyl)imidazol-2-ylidene) platinum(II) 3,5-dichloropyridine dichloride (6)



$C_{24}H_{23}Cl_4N_3Pt$
MW: 690.353

Prepared according to **General Procedure** from the imidazolium salt **L1•HCl** (103 mg, 0.33 mmol), $PtCl_2$ (80.0 mg, 0.30 mmol) and 3,5-dichloropyridine (1.4 g, 9.5 mmol). Reaction run at 100°C in toluene (*c* = 0.2 M). Purified by chromatography (SiO_2, 50 to 100% CH_2Cl_2/heptane). **6** was obtained as a pale yellow solid (94.0 mg, 0.136 mmol, **45%**). $\mathbf{R_f}$ = 0.78 (CH_2Cl_2). **$[\alpha]_D^{20}$** = - 89° (c = 0.7, CH_2Cl_2). **IR (neat):** 449, 496, 518, 539, 590, 632, 678, 714, 745, 760, 779, 788, 825, 852, 872, 918, 961, 1012, 1029, 1057, 1104, 1122, 1166, 1184, 1218, 1273, 1299, 1335, 1378, 1388, 1421, 1433, 1455, 1497, 1556, 1604, 1699, 1963, 2052, 2187, 2940, 2984, 3068, 3117, 3154 cm^{-1}. **^1H NMR (500 MHz, $CDCl_3$)** δ 1.94 (d, *J* = 7.0 Hz, 6 H_{CH_3}), 6.56 (s, 2 H_{Im}), 7.03 (q, *J* = 7.1 Hz, 2 H_{CH}), 7.29 – 7.36 (m, 2 H_{Ar}), 7.37 – 7.44 (m, 4 H $_{Ar}$), 7.58 (dd, *J* = 1.8, 7.3 Hz, 4 H_{Ar}), 7.86 (t, *J* = 2.1 Hz, 1 $H_{m\text{-pyr}}$), 9.11 (d, *J* = 2.0 Hz, 2 $H_{o\text{-pyr}}$). **$^{13}C\{^1H\}$ NMR (126 MHz, $CDCl_3$)** δ 20.4 (2 C_{CH_3}), 58.7 (2 C_{CH_2}), 118.6 (2 C_{Im}), 127.8 (4 C_{Ar}), 128.3 (2 C_{Ar}), 128.9 (4 C_{Ar}), 133.3($C_{m\text{-pyr}}$), 136.0 ($C_{C\text{-Pt}}$), 137.9 ($C_{p\text{-pyr}}$), 139.7 (2 C_{Ar}), 148.8 (2 $C_{o\text{-pyr}}$). **Elemental analysis:** calcd for $C_{24}H_{23}Cl_4N_3Pt$: 6.09 N%, 41.76 %C, 3.36 H%. Found: 5.82 N%, 41.94 %C, 3.52 H%.

(1,3-Bis((S)-1-phenylpropyl)imidazol-2-ylidene)(pyridine)platinum(II) pyridine diiodide (7)



$C_{26}H_{29}I_2N_3Pt$
MW: 832.432

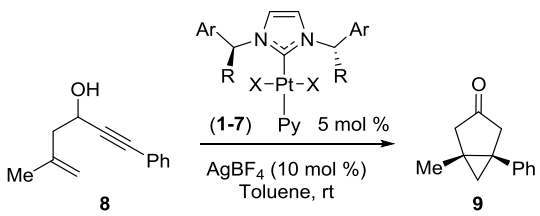
Prepared according to **General Procedure** from the imidazolium salt **L2•HCl** (102.7 mg, 0.3mmol), $PtCl_2$ (73 mg, 0.274 mmol) and NaI (450 mg, 3 mmol). Purified by chromatography (SiO_2, 50% CH_2Cl_2/heptane). **7** was obtained as a yellow solid (203 mg, 0.244 mmol, **89%**). $\mathbf{R_f}$ = 0.83

(CH_2Cl_2). **$[\alpha]_D^{20}$** = - 178.0° (c = 0.1, CH_2Cl_2). **IR (neat):** 415, 454, 520, 605, 630, 647, 710, 723, 758, 805, 846, 914, 928, 973, 1029, 1050, 1069, 1121, 1050, 1069, 1121, 1155, 1176, 1200, 1261, 1323, 1352, 1379, 1423, 1149, 1484, 1495, 1566, 1605, 1722, 1910, 1955, 2149, 2342, 2874, 2931, 2964, 3030, 3060, 3135 cm^{-1}. **^{1}H NMR (500 MHz, $CDCl_3$)** δ 1.03 (t, *J* = 7.4 Hz, 6 H_{CH_3}), 2.15 – 2.29 (m, 2 H_{CH_2}), 2.50 – 2.62 (m, 2 H_{CH_2}), 6.56 (dd, *J* = 4.7, 10.6 Hz, 2 H_{CH}), 6.70 (s, 2 H_{Im}), 7.30 – 7.37 (m, 4 $H_{m\text{-pyr+Ar}}$), 7.37 – 7.44 (m, 4 H_{Ar}), 7.65 – 7.71 (m, 4 H_{Ar}), 7.73 (tt, *J* = 1.6, 7.7 Hz, 1 $H_{p\text{-pyr}}$), 9.09 (dt, *J* = 1.6, 5.1 Hz, 2 $H_{o\text{-pyr}}$). **^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$)** δ 11.5 (2 C_{CH_3}), 27.3 (2 C_{CH_2}), 64.8 (2 C_{CH}), 118.5 (2 C_{Im}), 125.1 (2 $C_{m\text{-pyr}}$), 128.3 (2 C_{Ar}), 128.8 (4 C_{Ar}), 129.0 (4 C_{Ar}), 135.1 ($C_{C\text{-Pt}}$), 137.5($C_{p\text{-pyr}}$), 138.1 (2 C_{Ar}), 154.0 (2 $C_{o\text{-pyr}}$). **Elemental analysis:** calcd for $C_{26}H_{29}I_2N_3Pt$: 5.05 N%, 37.51 %C, 3.51 H%. Found: 5.11 N%, 37.58 %C, 3.64 H%.

Enantioselective cycloisomerization

The model substrate 5-methyl-1-phenylhex-5-en-1-yn-3-ol (**8**) was synthetized following a described procedure (For more details, see S2 in the ESI). The catalytic tests were set under anhydrous conditions.

General Procedure



In toluene, 5 mol% of NHC platinum(II) complex **1-7** (*c* = 0.2 M, relative to the ynol **8**) and 5 to 10 mol% of silver(I) salts were stirred for 15 min. Then, 1equiv. of 5-methyl-1-phenylhex-5-en-1-yn-3-ol (**8**) in toluene (*c* = 0.2 M) was added along with 0.1 to 0.25 equiv. of dimethyl terephthalate, used as internal reference, to monitor the reaction by ^{1}H NMR upon full conversion**.** Once achieved, under air conditions, the toluene was removed under reduced pressure and the crude residue dissolved in CH_2Cl_2 and filtered over au small plug of silica. In order to determine the enantiomeric excess, the crude 1-methyl-5-phenylbicyclo[3.1.0]hexan-3-one (**9**) was dissolvent in CH_2Cl_2 (~1 mg/mL) and analyzed by GC (See Table 2). The retention times of the dimethyl terephthalate was equal to 22.2 min. The retention times for both *cis*-1-methyl-5-phenylbicyclo[3.1.0]hexan-3-one enantiomers were equal to 19.6 min and 20.5 min.

1-Methyl-5-phenylbicyclo[3.1.0]hexan-3-one (9): ^{1}H NMR (300 MHz, $CDCl_3$) δ 0.63 (brd, *J* = 5.8 Hz, 1 H), 1.06 (s, 3 H), 1.24 (dt, *J* = 2.3, 5.1 Hz, 1 H), 2.48 (brd, *J* = 18.9 Hz, 1 H),

2.63 (brd, *J* = 19.0 Hz, 1H), 2.69 (dq, *J* = 1.9, 19.0 Hz, 1 H), 2.85 – 2.99 (m, 1 H), 7.24 – 7.43 (m, 5 H).

Associated content

Supporting information

The NMR spectra of **1-7**, the chromatograms associated with the catalytic trials and the crystal data of **6**, **7** are available. The crystallographic information files (CIF) have been deposited with the CCDC, 12 Union Road, Cambridge, CB2 1EZ, U.K., and can be obtained on request free of charge, by quoting the publication citation and deposition numbers 1955627, 1955628. This material is also available free of charge via the Internet at http://pubs.acs.org.

Author information

Corresponding Authors

*E-mail: defremont@unistra.fr, ablanc@unistra.fr

ORCID

Romain Pertschi: 0000-0002-2561-8689

Patrick Pale: 0000-0002-3924-530X

Pierre de Frémont: 0000-0001-8470-3659

Aurélien Blanc: 0000-0003-4240-3281

Acknowledgment

The Centre National de la Recherche Scientifique (CNRS) and the Ministère de la Recherche are gratefully acknowledged for financial support of this work. R. P. thanks the French Ministry of Research for PhD fellowship.

Notes

The authors declare no competing financial interest.

References

(1) Rouschias, G.; Shaw, B. L. A Revised Structure for Chugaev's Salt $[PtC_8H_{15}N_6]_XCl_X$. *J. Chem. Soc. Chem. Commun.* **1970**, No. 3, 183–183.
(2) Arduengo, A. J.; Harlow, R. L.; Kline, M. A Stable Crystalline Carbene. *J. Am. Chem. Soc.* **1991**, *113* (1), 361–363.
(3) Benhamou, L.; Chardon, E.; Lavigne, G.; Bellemin-Laponnaz, S.; César, V. Synthetic Routes to N-Heterocyclic Carbene Precursors. *Chem. Rev.* **2011**, *111* (4), 2705–2733.
(4) Hashmi, A. S. K.; Lothschütz, C.; Böhling, C.; Hengst, T.; Hubbert, C.; Rominger, F. Carbenes Made Easy: Formation of Unsymmetrically Substituted N-Heterocyclic Carbene Complexes of Palladium(II), Platinum(II) and Gold(I) from Coordinated Isonitriles and Their Catalytic Activity. *Adv. Synth. Catal.* **2010**, *352* (17), 3001–3012.
(5) Riedel, D.; Wurm, T.; Graf, K.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. From Isonitriles to Unsaturated NHC Complexes of Gold, Palladium and Platinum. *Adv. Synth. Catal.* **2015**, *357* (7), 1515–1523.
(6) Tšupova, S.; Rudolph, M.; Rominger, F.; Hashmi, A. S. K. Synthesis and Properties of Hydrazino Amino Acyclic Carbenes of Gold(I), Platinum(II), Palladium(II) and Rhodium(III). *Adv. Synth. Catal.* **2016**, *358* (24), 3999–4005.
(7) de Frémont, P.; Marion, N.; Nolan, S. P. Carbenes: Synthesis, Properties, and Organometallic Chemistry. *Coord. Chem. Rev.* **2009**, *253* (7–8), 862–892.
(8) Still, B. M.; Kumar, P. G. A.; Aldrich-Wright, J. R.; Price, W. S. 195Pt NMR—Theory and Application. *Chem. Soc. Rev.* **2007**, *36* (4), 665–686.
(9) Dierick, S.; Vercruysse, E.; Berthon-Gelloz, G.; Markó, I. E. User-Friendly Platinum Catalysts for the Highly Stereoselective Hydrosilylation of Alkynes and Alkenes. *Chem. - Eur. J.* **2015**, *21* (47), 17073–17078.
(10) Bouché, M.; Bonnefont, A.; Achard, T.; Bellemin-Laponnaz, S. Exploring Diversity in Platinum(IV) N-Heterocyclic Carbene Complexes: Synthesis, Characterization, Reactivity and Biological Evaluation. *Dalton Trans.* **2018**, *47* (33), 11491–11502.

(11) Chardon, E.; Dahm, G.; Guichard, G.; Bellemin-Laponnaz, S. Derivatization of Preformed Platinum N-Heterocyclic Carbene Complexes with Amino Acid and Peptide Ligands and Cytotoxic Activities toward Human Cancer Cells. *Organometallics* **2012**, *31* (21), 7618–7621.
(12) Fortman, G. C.; Nolan, S. P. N-Heterocyclic Carbene (NHC) Ligands and Palladium in Homogeneous Cross-Coupling Catalysis: A Perfect Union. *Chem. Soc. Rev.* **2011**, *40* (10), 5151.
(13) Mamane, V.; Gress, T.; Krause, H.; Fürstner, A. Platinum- and Gold-Catalyzed Cycloisomerization Reactions of Hydroxylated Enynes. *J. Am. Chem. Soc.* **2004**, *126* (28), 8654–8655.
(14) Harrak, Y.; Blaszykowski, C.; Bernard, M.; Cariou, K.; Mainetti, E.; Mouriès, V.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. $PtCl_2$ -Catalyzed Cycloisomerizations of 5-En-1-Yn-3-Ol Systems. *J. Am. Chem. Soc.* **2004**, *126* (28), 8656–8657.
(15) Bernhammer, J. C.; Huynh, H. V. Platinum(II) Complexes with Thioether-Functionalized Benzimidazolin-2-Ylidene Ligands: Synthesis, Structural Characterization, and Application in Hydroelementation Reactions. *Organometallics* **2014**, *33* (1), 172–180.
(16) Hubbert, C.; Breunig, M.; Carroll, K. J.; Rominger, F.; Hashmi, A. S. K. Simple Synthesis of New Mixed Isocyanide-NHC-Platinum(II) Complexes and Their Catalytic Activity. *Aust. J. Chem.* **2014**, *67* (3), 469–474.
(17) Blaszykowski, C.; Harrak, Y.; Gonçalves, M.-H.; Cloarec, J.-M.; Dhimane, A.-L.; Fensterbank, L.; Malacria, M. $PtCl_2$ - Catalyzed Transannular Cycloisomerization of 1,5-Enynes: A New Efficient Regio- and Stereocontrolled Access to Tricyclic Derivatives. *Org. Lett.* **2004**, *6* (21), 3771–3774.
(18) Soriano, E.; Marco-Contelles, J. Theoretical Analysis of the High Versatility in $PtCl_2$ -Mediated Cycloisomerization of Enynes on a Common Mechanistic Basis. *J. Org. Chem.* **2005**, *70* (23), 9345–9353.
(19) Toullec, P. Y.; Chao, C.-M.; Chen, Q.; Gladiali, S.; Genêt, J.-P.; Michelet, V. Enantioselective Platinum-Catalyzed Tandem Hydroarylation - Cycloisomerization of 1,6-Enynes. *Adv. Synth. Catal.* **2008**, *350* (14–15), 2401–2408.
(20) Feducia, J. A.; Campbell, A. N.; Doherty, M. Q.; Gagné, M. R. Modular Catalysts for Diene Cycloisomerization: Rapid and Enantioselective Variants for Bicyclopropane Synthesis. *J. Am. Chem. Soc.* **2006**, *128* (40), 13290–13297.
(21) Brissy, D.; Skander, M.; Retailleau, P.; Marinetti, A. N-Heterocyclic Carbenes in the Synthesis of Axially Chiral Square-Planar Platinum Complexes. *Organometallics* **2007**, *26* (24), 5782–5785.
(22) Brissy, D.; Skander, M.; Jullien, H.; Retailleau, P.; Marinetti, A. Platinum(II) Catalysts for Highly Enantioselective 1,6-Enyne Cycloisomerizations. Synthetic, Structural, and Catalytic Studies. *Org. Lett.* **2009**, *11* (10), 2137–2139.
(23) Jullien, H.; Brissy, D.; Sylvain, R.; Retailleau, P.; Naubron, J.-V.; Gladiali, S.; Marinetti, A. Cyclometalated N-Heterocyclic Carbene-Platinum Catalysts for the Enantioselective Cycloisomerization of Nitrogen-Tethered 1,6-Enynes. *Adv. Synth. Catal.* **2011**, *353* (7), 1109–1124.
(24) Jullien, H.; Brissy, D.; Retailleau, P.; Marinetti, A. Enantioselective Cycloisomerization of 1,5-Enynes Promoted by Cyclometalated NHC-Pt(II)-Monophos Catalysts. *Eur. J. Inorg. Chem.* **2011**, *2011* (33), 5083–5086.
(25) Janssen-Müller, D.; Schlepphorst, C.; Glorius, F. Privileged Chiral N-Heterocyclic Carbene Ligands for Asymmetric Transition-Metal Catalysis. *Chem. Soc. Rev.* **2017**, *46* (16), 4845–4854.

(26) Petrov, A. R.; Derheim, A.; Oetzel, J.; Leibold, M.; Bruhn, C.; Scheerer, S.; Oßwald, S.; Winter, R. F.; Siemeling, U. A Stable Planar-Chiral *N*-Heterocyclic Carbene with a 1,1′-Ferrocenediyl Backbone. *Inorg. Chem.* **2015**, *54* (13), 6657–6670.
(27) Wang, Z.-Y.; Ding, Y.-L.; Wang, G.; Cheng, Y. Chiral N-Heterocyclic Carbene/Lewis Acid Cooperative Catalysis of the Reaction of 2-Aroylvinylcinnamaldehydes: A Switch of the Reaction Pathway by Lewis Acid Activation. *Chem. Commun.* **2016**, *52* (4), 788–791.
(28) Herrmann, W. A.; Goossen, L. J.; Artus, G. R. J.; Köcher, C. Metal Complexes of Chiral Imidazolin-2-Ylidene Ligands. *Organometallics* **1997**, *16* (11), 2472–2477.
(29) Winn, C. L.; Guillen, F.; Pytkowicz, J.; Roland, S.; Mangeney, P.; Alexakis, A. Enantioselective Copper Catalysed 1,4-Conjugate Addition Reactions Using Chiral N-Heterocyclic Carbenes. *J. Organomet. Chem.* **2005**, *690* (24–25), 5672–5695.
(30) Suzuki, Y.; Muramatsu, K.; Yamauchi, K.; Morie, Y.; Sato, M. Chiral N-Heterocyclic Carbenes as Asymmetric Acylation Catalysts. *Tetrahedron* **2006**, *62* (2–3), 302–310.
(31) Nasielski, J.; Hadei, N.; Achonduh, G.; Kantchev, E. A. B.; O'Brien, C. J.; Lough, A.; Organ, M. G. Structure-Activity Relationship Analysis of Pd-PEPPSI Complexes in Cross-Couplings: A Close Inspection of the Catalytic Cycle and the Precatalyst Activation Model. *Chem. - Eur. J.* **2010**, *16* (35), 10844–10853.
(32) Khadra, A.; Mayer, S.; Organ, M. G. Pd-PEPPSI-IPent^{Cl}: A Useful Catalyst for the Coupling of 2-Aminopyridine Derivatives. *Chem. - Eur. J.* **2017**, *23* (13), 3206–3212.
(33) Bolbat, E.; Suarez-Alcantara, K.; Canton, S. E.; Wendt, O. F. Synthesis, Spectroscopic Characterization and Catalytic Activity of Platinum(II) Carbene Complexes. *Inorganica Chim. Acta* **2016**, *445*, 129–133.
(34) Adams, C. J.; Lusi, M.; Mutambi, E. M.; Orpen, A. G. Two-Step Mechanochemical Synthesis of Carbene Complexes of Palladium(II) and Platinum(II). *Cryst. Growth Des.* **2017**, *17* (6), 3151–3155.
(35) Adams, C. J.; Lusi, M.; Mutambi, E. M.; Guy Orpen, A. Two-Step Solid-State Synthesis of PEPPSI-Type Compounds. *Chem. Commun.* **2015**, *51* (47), 9632–9635.
(36) Bouché, M.; Dahm, G.; Maisse-François, A.; Achard, T.; Bellemin-Laponnaz, S. Selective Formation of Cis-N-Heterocyclic Carbene-Pt(II)-Pnictogen Complexes and in Vitro Evaluation of Their Cytotoxic Activities toward Cancer Cells: Selective Formation of Cis-N-Heterocyclic Carbene-Pt(II)-Pnictogen Complexes and in Vitro Evaluation of Their Cytotoxic Activities toward Cancer Cells. *Eur. J. Inorg. Chem.* **2016**, *2016* (17), 2828–2836.
(37) Newman, C. P.; Deeth, R. J.; Clarkson, G. J.; Rourke, J. P. Synthesis of Mixed NHC/L Platinum(II) Complexes: Restricted Rotation of the NHC Group. *Organometallics* **2007**, *26* (25), 6225–6233.
(38) Fantasia, S.; Petersen, J. L.; Jacobsen, H.; Cavallo, L.; Nolan, S. P. Electronic Properties of N-Heterocyclic Carbene (NHC) Ligands: Synthetic, Structural, and Spectroscopic Studies of (NHC) Platinum(II) Complexes. *Organometallics* **2007**, *26* (24), 5880–5889.
(39) Van Beusichem, M.; Farrell, N. Activation of the Trans Geometry in Platinum Antitumor Complexes. Synthesis, Characterization, and Biological Activity of Complexes with the Planar Ligands Pyridine, N-Methylimidazole, Thiazole, and Quinoline. Crystal and Molecular Structure of Trans-Dichlorobis(Thiazole)Platinum(II). *Inorg. Chem.* **1992**, *31* (4), 634–639.
(40) Williams, J. D.; Yazarians, J. A.; Almeyda, C. C.; Anderson, K. A.; Boyce, G. R. Detection of the Previously Unobserved Stereoisomers of Thujone in the Essential Oil and Consumable Products of Sage (*Salvia Officinalis* L.) Using Headspace Solid-Phase Microextraction–Gas Chromatography–Mass Spectrometry. *J. Agric. Food Chem.* **2016**, *64* (21), 4319–4326.

(41) Matsuo, A.; Nozaki, H.; Nakayama, M.; Kushi, Y.; Hayashi, S.; Kamijo, N.; Benešová, V.; Herout, V. X-Ray Crystal and Molecular Structure of the p-Bromobenzoate of (–)-Myliol, a Novel Tetracyclic Sesquiterpene Alcohol from Mylia Taylorii(Liverwort) Containing Two Conjugated Cyclopropane Rings. Revision of a Proposed Structure. *J Chem. Soc. Chem. Commun.* **1976**, No. 24, 1006–1007.
(42) Lu, Z.; Han, J.; Okoromoba, O. E.; Shimizu, N.; Amii, H.; Tormena, C. F.; Hammond, G. B.; Xu, B. Predicting Counterion Effects Using a Gold Affinity Index and a Hydrogen Bonding Basicity Index. *Org. Lett.* **2017**, *19* (21), 5848–5851.
(43) P, S.; Sau, S. C.; Vardhanapu, P. K.; Mandal, S. K. Halo-Bridged Abnormal NHC Palladium(II) Dimer for Catalytic Dehydrogenative Cross-Coupling Reactions of Heteroarenes. *J. Org. Chem.* **2018**, *83* (16), 9403–9411.
(44) Sheldrick, G. M. A Short History of *SHELX*. *Acta Crystallogr. A* **2008**, *64* (1), 112–122.

[ϒ] LSROC, Université de Strasbourg
[†] SRCO, Université de Strasbourg