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Catalytic asymmetric hydrogenation using [2.2]paracyclophane based chiral 1,2,3-triazol-5-ylidene-Pd complex under ambient conditions and 1 atmosphere of H_2

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Chiral 1,2,3-triazol-5-ylidene-Pd complexes with planar chiral [2.2]paracyclophane wing tip group have been synthesized and structurally characterized. The complex with a labile acetonitrile co-ligand is an excellent catalyst for chemoselective hydrogenation of alkynes and alkene and enantioselective hydrogenation of prochiral alkenes at ambient conditions and 1.0 atmosphere of H_2.

Catalytic enantioselective transformations (CET) mediated by *N*-heterocyclic carbenes (NHCs)[1-4] and their transition metal complexes[5-9] have gained importance in asymmetric organic synthesis.[10-14] Compared to the conventional phosphane ligands, chiral NHC ligands are relatively easier to synthesize by appending a suitable chiral auxiliary group to the *N*-heterocycle scaffold.[1,2,4,15-17] Mono substituted [2.2]paracyclophane (PC) derivatives are planar chiral and they are configurationally very robust.[18-21] Several NHC-metal complexes bearing chiral PC wing tip groups have been reported and their utility in CET has been demonstrated.[22-26] The vast majority of these belong to imidazol-2-ylidene-metal (normal NHC-metal) complexes. PC based chiral mesoionic carbene (MIC)-metal complexes are unknown and hence their potential as catalyst for CET remains unexplored. In particular the application of MIC-Pd complexes for catalytic asymmetric hydrogenation (CAH)[27], a transformation of high industrial importance, has not been investigated. Earlier reports of CAH using NHC-metal complexes involved Ir[28-36], Rh[37-39] and Ru[40] metals and generally at high pressures of H_2. Herein we report the design, synthesis and structural characterization of PC based 1,2,3-triazol-5-ylidene-Pd complexes.[5,41-42] Application of these complexes as catalysts for chemoselective hydrogenation of substituted alkenes and alkynes and for the CAH of prochiral alkenes at 1.0 atm of H_2 has been investigated. Structures of complexes **1** and **2** are shown in Scheme 1 and were readily synthesized from the corresponding triazolium iodide **3** in both racemic (*rac*) and enantio pure (S_p) forms. Compound **3** was synthesized in five steps from [2.2]paracyclophane (ESI). Treatment of **3** with silver oxide[43-45] gave the corresponding silver complex **4** which was characterized by NMR and HRMS data. Reaction of **4** with $PdCl_2(MeCN)_2$ in refluxing acetonitrile yielded **1** in 91% yield.

Scheme 1. Synthesis of NHC complexes **1** and **2** from *rac*-**3** and S_p-**3**.

Further, treatment of **1** with PPh_3 gave complex **2**. Structures of **1, 2** and **3** were confirmed by spectroscopic and single crystal XRD data. In both the complexes the geometry around Pd atom is distorted square planar (Figure 1). However, the stereochemistry of the two chlorine atoms around Pd in **1** is *trans* and that of **2** is *cis*. Also the

orientation of the triazolylidene-$PdCl_2$ unit with respect to the PC scaffold is very different in these complexes (Figure 1).

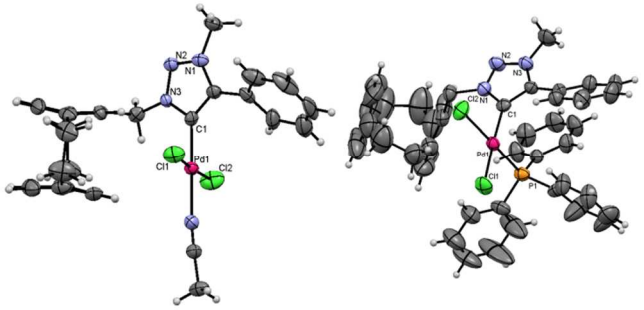
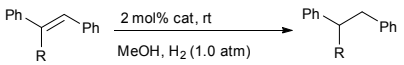


Figure 1. Ellipsoid (50% probability) representation of the structures of complexes S_p-**1** (left) and *rac*-**2** (right) in the crystal.

Complexes *rac*-**1** and *rac*-**2** (racemic form) were screened as catalysts for the hydrogenation of *E*-stilbene. The reactions were carried out in methanol at room temperature (30-35 ^oC) with 2 mol% catalyst loading under 1.0 atm of H_2 (795 mm Hg of H_2). With complex **1** as the catalyst the reaction mixture turned from yellow to black and *E*-stilbene was converted to 1,2-diphenylethane within 7 h in quantitative yield (Scheme 2). With complex **2** the reaction mixture remained yellow throughout and no reaction was observed over 24 h. With *E*-1,2-diphenylpropene as the substrate the reaction was complete to give 1,2-diphenylpropane in 20 h with **1** and no reaction was observed with **2**. Hydrogenation of *E*-stilbene did not occur with complex **1** in the presence of 4 mol% of Ph_3P indicating inhibition of the reaction in the presence of Ph_3P due to the formation of complex **2**. This is in sharp contrast to the stabilization of the catalytically active NHC-Rh species by Ph_3P reported in literature.[38] The difference in the reactivity between **1** and **2** can be attributed to the lability of acetonitrile ligand in **1** compared to the triphenylphosphane in **2**. Also the Pd atom in **2** is sterically more hindered than that in **1** thus reducing the catalytic activity of the former compared to the latter. The visual color changes observed in case of **1** and the lack of it in case of **2** indicates the formation of active catalyst from **1** and not from **2**. Control experiments clearly revealed that **2** could be recovered quantitatively after workup of the reaction. The apparent catalytic turnover number (TON) after 13 consecutive cycles of hydrogenation of *trans*-stilbene with **1** in MeOH was 640 and the overall yield of 1,2-diphenylethane was 98%. Hydrogenation of stilbene did not proceed in CH_2Cl_2, THF and CH_3CN when either **1** or **2** was used as the catalyst. Thus, a combination of **1** as the catalyst and MeOH as solvent under 1.0 atm of H_2 at room temperature was found to be most effective for the catalytic hydrogenation of alkenes and alkynes.

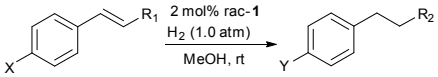


cat = rac-**1**, R = H, 7 h, 100%; R = Me, 20 h, 98%
cat = rac-**2**, R = H and Me, upto 48 h, 0%

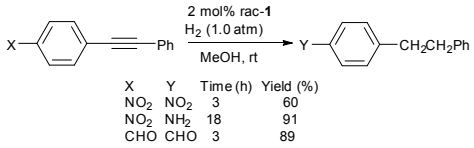
Scheme 2. Comparison of catalytic activities of **1** and **2**

Complex **1** was screened for the hydrogenation of a variety of alkenes and alkynes to establish its reactivity and chemoselectivity. The results are summarized in Table 1 and Scheme 3.

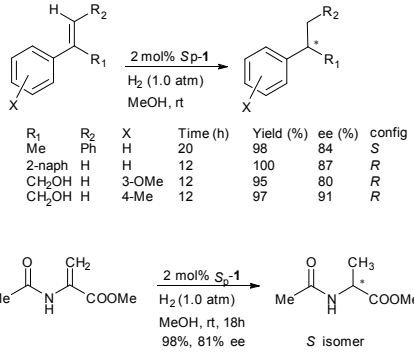
Table 1. Hydrogenation of styrene derivatives



	R_1	X	R_2	Y	Time (h)	Yield (%)
1	Ph	H	Ph	H	7	100
2	CO_2H	H	CO_2Me	H	8	100
3	CO_2Me	H	CO_2Me	H	8	100
4	CHO	H	CH_2OH	H	8	100
5	CO_2H	CHO	CO_2Me	CHO	8	95
6	COMe	H	COMe	H	8	90
7	COPh	H	COPh	H	8	97
8	Ph	NO_2	Ph	NO_2	8	76
9	Ph	NO_2	Ph	NH_2	18	88
10	COPh	NO_2	COPh	NO_2	5	70
11	COPh	NO_2	COPh	NH_2	18	90



Scheme 3. Hydrogenation of tolan derivatives



Scheme 4. CAH of prochiral alkenes

Cinnamaldehyde was quantitatively converted to cinnamyl alcohol (entry 4). Aromatic aldehyde was not reduced to the corresponding alcohol under the reaction conditions (entry 5 and Scheme 3). Benzalacetone and benzalacetophenone were reduced to the corresponding saturated ketones leaving the keto group intact (entry 6 and 7). Alkenes can be selectively reduced in the presence of nitro groups. Thus 4-nitrostilbene and 4-nitrobenzalacetophenone were first reduced to 1-(4-nitrophenyl)-2-phenylethane and 3-(4-nitrophenyl)-1-phenylpropan-1-one (entry 8 and 10), respectively, which were further reduced to 1-(4-aminophenyl)-2-phenylethane and 3-(4-aminophenyl)-1-phenylpropan-1-one, respectively, upon prolonged hydrogenation (entry 9 and 11). Similarly 4-nitrotolan was first reduced to 1-(4-nitrophenyl)-2-phenylethane in 60% isolated yield. Prolonged hydrogenation led to the formation of 1-(4-aminophenyl)-2-phenylethane in 91% isolated yield (scheme 3). The supposed intermediate, namely 4-nitrostilbene was not observed by TLC and NMR analysis of the reaction mixture at various stages of the reaction. Thus C-C double and triple bonds were reduced much faster than the nitro group. Cinnamic acid and methyl cinnamate were reduced to methyl 3-phenylpropionate (entry 2 and 3). Under the reaction conditions acids were converted to the corresponding methyl esters in MeOH. CAH of prochiral alkenes shown in Scheme 4 using S_p-1 gave excellent yields and good enantioselectivities of the corresponding alkanes. 1,1-Disubstituted alkenes reacted faster than trisubstituted alkenes. Assignment of absolute configuration of the products is based on correlation of the observed optical rotation with the literature (ESI).[46-47] Methyl α-acetamidoacrylate was

hydrogenated to the corresponding saturated ester with 81% ee and in near quantitative yield.

Conclusions

PC based chiral 1,2,3-triazol-5-ylidene-Pd complexes **1** and **2** were synthesized and structurally characterized by single crystal XRD. While complex **1** showed excellent activity towards catalytic hydrogenation of alkenes and alkynes, no reaction was observed with **2** under identical conditions. Strong coordination of PPh_3 compared to acetonitrile and steric hindrance could be responsible for the difference in reactivity between these two complexes for catalytic hydrogenation. For the hydrogenation of *E*-stilbene **1** was found to be active up to 13 cycles with a TON of 640. Enantiopure S_p-**1** was found to be an excellent catalyst for the CAH of prochiral alkenes in near quantitative yields and good enantioselectivity. Further investigations on the synthetic utility of these Pd complexes are in progress. *Finally it is noteworthy that Pd instead of Ir and Rh as metal for hydrogenation and that hydrogenation is carried out at ambient conditions and at 1.0 atm of H_2.*

Notes and references

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Electronic Supplementary Information (ESI) available: [Synthesis and characterization data of all compounds and CIF files of complexes **1** and **2**.]. See DOI: 10.1039/c000000x/

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