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A novel and efficient chiral palladium–phosphinooxazolidine catalyst for the enantioselective Diels–Alder reaction†

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Easily prepared, chiral cationic palladium(II)–phosphinooxazolidine complexes are described which give excellent enantioselectivity (up to 98% ee) in the Diels–Alder reaction of cyclopentadiene with a range of acyl-1,3-oxazolidin-2-one dienophiles.

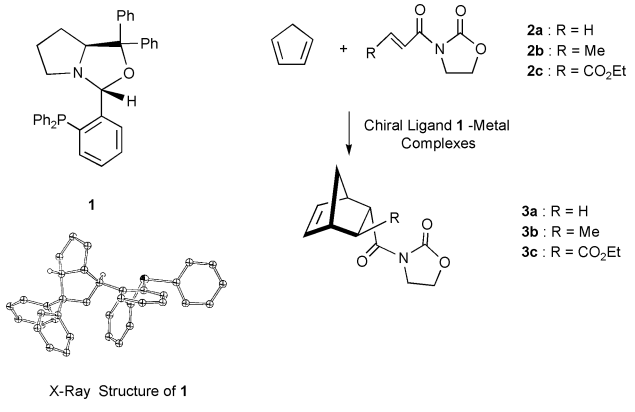
We have recently disclosed the Pd-complex of the novel chiral phosphinooxazolidine (POZ) ligand **1** (Scheme 1) as an effective catalyst for the asymmetric allylic alkylation reaction (96% ee).[1] Of great utility here is the fact that either enantiomeric form of the chiral ligand **1** can be readily obtained from the reaction of commercially available (*R*)- or (*S*)-1,1-diphenyl(2-pyrrolidinyl)methanol with 2-(diphenylphosphino)benzaldehyde. To further demonstrate the utility of **1** as a chiral catalyst, we have now examined the versatility of **1** to the asymmetric Diels–Alder (DA) reaction.[2] Although several efficient DA-catalysts[3] have been developed, for example the copper complexes of chiral oxazoline-based ligands[4] or the cationic palladium complexes of chiral BINAP ligands,[5] most catalytic systems have the disadvantage that they only work effectively within a specific range of substrates. As a significant advance in this area, Evans *et al*. have reported bis(oxazoline)Cu(II) complexes which display high enantioselectivity in the DA reactions of cyclopentadiene with various imide dienophiles.[6]

Herein, we report that the readily accessible cationic Pd(II)–POZ complex **6c** invokes excellent enantioselectivity (98% ee) in all cases for the DA reaction of cyclopentadiene with imide dienophiles, namely the acryloyl-, crotonyl- and fumaroyl-1,3-oxazolidin-2-ones (**2a–c**). In addition, we reveal the stereochemistry of ligand **1**, which until now has remained uncertain by NMR methods,[1] and show the unique structures of the $PdCl_2$–phosphinooxazolidine complexes **4a** and **5** by single crystal X-ray diffraction.‡

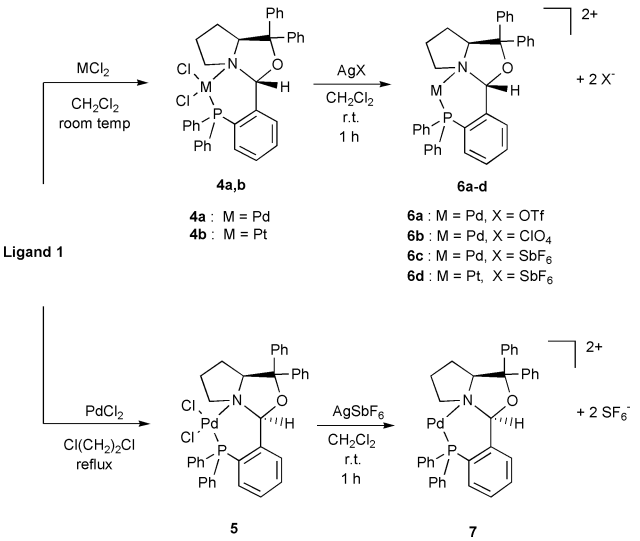
The requisite chiral $PdCl_2$–POZ complexes were prepared in a convenient and efficient manner by the reaction of **1** (1 equiv.) with $PdCl_2$ (1 equiv.) in 1,2-dichloroethane (Scheme 2). Depending on the reaction temperature, this reaction afforded either the *N*,*O*-acetal epimer **4a** or its counterpart **5**; at room temperature the complex **4a** formed in 95% yield, which bears the same stereochemistry as ligand **1**, while under reflux the epimeric complex **5** was formed in 90% yield. This stereochemical outcome was confirmed by examination of the X-ray structures of **4a** and **5** (Fig. 1). Both complexes adopt a square-planar geometry with the palladium being coordinated to the nitrogen and phosphorous atoms of POZ, however the coordination of **4a** is considerably distorted from planarity, as shown by the dihedral angle of 10.2° between plane (N–Pd–Cl2) and plane (P–Pd–Cl1), whereas complex **5** adopts a coplanar coordination. Collectively these results indicate that **5** is more thermodynamically stable than **4a**.

For the catalytic asymmetric version of the DA reaction, we first tested the reaction of the acryloyl-1,3-oxazolidin-2-one **2a** with cyclopentadiene in the presence of 10 mol% of catalyst **4a** at −45 °C, however the reaction only generated the DA adduct **3a** in a low chemical isolated yield (45%) and almost no enantioselectivity was observed. To increase the reactivity of **4a** we next examined the effects of various counterions. The cationic catalyst of **6a** with a triflate counterion was prepared by the reaction of **4a** (1 equiv.) with AgOTf (2 equiv.) in dry CH_2Cl_2 at rt for 1 h under argon (Scheme 2). Similarly, the catalysts **6b** and **6c** were also prepared with their respective perchlorate and hexafluoroantimonate counterions. As summarized in Table 1, the DA reactions of cyclopentadiene (4 equiv.) with **2a** (1 equiv.) by using the catalysts **6a–c** (10 mol%) were then examined in dry CH_2Cl_2 to give the DA adduct **3a**; the absolute configuration of **3a** (2*R*) was determined on the basis of the optical rotations given in the literature.[7]

The reaction catalyzed by the triflate complex **6a** gave the DA adduct **3a** in 52% isolated yield and with moderate *endo*



Scheme 1



Scheme 2

† Electronic supplementary information (ESI) available: experimental details. See http://www.rsc.org/suppdata/cc/b2/b201625g/

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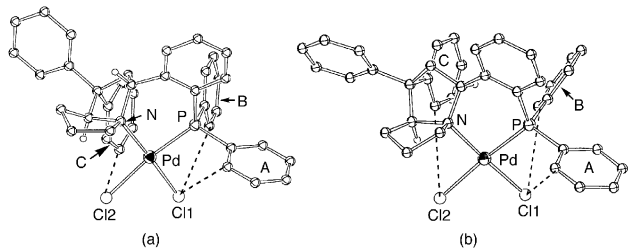

Fig. 1 X-Ray structures of **4a** and **5**. In both crystals, two independent molecules exist, having essentially the same structure. The following structural parameters are averaged; for **4a**, Pd–Cl1 = 2.291(3), Pd–Cl2 = 2.383(3), Pd–P = 2.223(3), Pd–N = 2.102(8) Å, Cl1–Pd–Cl2 = 89.0(1), Cl1–Pd–P = 87.0(1), Cl2–Pd–N = 89.2(2), P–Pd–N = 95.7(2)°; for **5**, Pd–Cl1 = 2.288(1), Pd–Cl2 = 2.371(1), Pd–P = 2.242(1), Pd–N = 2.099(4) Å, Cl1–Pd–Cl2 = 89.55(5), Cl1–Pd–P = 85.38(5), Cl2–Pd–N = 93.47(9), P–Pd–N = 91.76(9)°. Maximum deviations from least squares planes of the Pd coordination atoms are 0.195 Å in **4a** and 0.045 Å in **5**. The dihedral angles between the two planes N–Pd–Cl2 and P–Pd–Cl1 are 10.2° in **4a** and 1.5° in **5**. The shortest non-bonding atom distances between Cl atoms and phenyl carbons are Cl1–C (phenyl A) = 3.58, Cl1–C (phenyl B) = 3.50, Cl2–C (phenyl C) = 3.89Å in **4a** and Cl1–C(phenyl A) = 3.75, Cl1–C(phenyl B) = 3.62, Cl2–C(phenyl C) = 4.11 Å in **5**.

Table 1 Enantioselective DA reactions of cyclopentadiene with dienophiles **2a–c**

Entry	Dieno-phile	Catalyst (mol%)	Temp (time)	Yield (%)[a]	*endo*/*exo*[b]	ee (%)[c] (config.)
1	**2a**	**6a** (10)	−45 °C (45 h)	52 (**3a**)	86:14	74 (2*R*)
2	**2a**	**6b** (10)	−45 °C (20 h)	97 (**3a**)	94:6	93 (2*R*)
3	**2a**	**6c** (10)	−45 °C (24 h)	96 (**3a**)	97:3	98 (2*R*)
4	**2a**	**6c** (5)	−50 °C (22 h)	94 (**3a**)	97:3	97 (2*R*)
5	**2a**	**6c** (2.5)	−35 °C (24 h)	82 (**3a**)	95:5	96 (2*R*)
6	**2a**	**6c** (1)	−45 °C (48 h)	76 (**3a**)	97:3	94 (2*R*)
7	**2a**	**6c** (0.5)	−45 °C (48 h)	62 (**3a**)	96:4	90 (2*R*)
8	**2a**	**6d** (10)	−45 °C (90 h)	37 (**3a**)	95:5	0
9	**2a**	**7** (5)	−45 °C (24 h)	55 (**3a**)	94:6	55 (2*R*)
10	**2b**	**6c** (5)	−35 °C (36 h)	73 (**3b**)	96:4	98 (2*R*)
11	**2c**	**6c** (5)	−45 °C (24 h)	95 (**3c**)	94:6	98 (2*S*)[d]

[a] Isolated yields. [b] *Endo*/*exo* ratios were determined by HPLC or ^{1}H NMR. [c] Ee of *endo* isomers were determined by chiral HPLC using a Daicel OD-H column (**3a**:0.5 mL min^{-1}, hexane:propan-2-ol = 90:10, **3b**: 0.5 mL min^{-1}, hexane:ethanol = 95:5). [d] After conversion to the corresponding iodolactone (I_2, KI, $NaHCO_3$, yield 63%), the absolute configuration was determined by comparison with known optical rotation of **3c** $[\alpha]_D^{20}$ + 39.1 (*c* 3.3; $CHCl_3$); lit.[4], $[\alpha]_D^{23}$ −39.2 (*c* 4.65; $CHCl_3$).

enantioselectivity (74% ee; entry 1). However, by using the perchlorate (**6b**) or the antimonate complex (**6c**), the reaction was found not only to be more rapid but also gave high conversions and enantioselectivities (93% ee; entry 2 and 98% ee; entry 3). Next, we examined the effect of reducing the molar ratio of the superior antimonate catalyst **6c**. The use of 5 mol% and 2.5 mol% of **6c** gave equally satisfactory results in terms of chemical yields and enantioselectivities (5 mol%, 87% yield, 97% ee; entry 4, and 2.5 mol%, 82% yield, 96% ee; entry 5). Further, at low catalytic loadings the reactions also gave good enantioselectivities (1 mol%, 94% ee; entries 6 and 0.5 mol%, 90% ee; entry 7).

To test the nature of the metal, we prepared and examined the use of the Pt(II)–POZ complex **6d**, but both the chemical yield and enantioselectivity were poor (37% yield, 0% ee; entry 8). We also tested the catalytic ability of the alternative antimonate complex **7**, which was derived from the isomeric complex **5**, but again this did not work as effectively as **6c** (55% ee; entry 9). This latter observation can likely be explained by the difference in steric congestion about the structures of the intermediates that are derived by the imide dienophile (**3a**) associating with the complexes of **6c** and **7**. As indicated in Fig. 1, the X-ray structures of **4a** and **5** reveal that the spaces between the two Cl atoms and the three encumbering phenyl rings are as a whole smaller in **4a** (3.58, 3.50, and 3.89 Å) than in **5** (3.75, 3.62, and 4.11 Å). Although the exact structures of the reactive intermediates are a matter of speculation, these results suggest that the facial attack of cyclopentadiene onto an imide-complexed dienophile would be expected to proceed more stereoselectively in **6c** than in **7**.

Finally, we examined the DA reactions of the crotonoyl-1,3-oxazolidin-2-one **2b** and fumaroyl-1,3-oxazolidin-2-one **2c**. By using 5 mol% of the superior chiral catalyst **6c** with the antimonate counterion, the reaction proceeded smoothly to give the desired DA adducts **3b** and **3c** in good isolated yields and in excellent enantioselectivities (73% yield, 98% ee in **3b**; entry 10 and 95% yield, 98% ee in **3c**; entry 11). Notwithstanding the work of Evans *et al*., it should be noted that **2b** and **2c** are notoriously difficult to obtain in such high efficiencies.[6]

In summary, we have developed readily prepared cationic Pd(II)–POZ complexes to catalyze the DA reaction of cyclopentadiene with a range of 1,3-oxazolidin-2-one dienophiles. Both the reactivity and enantioselectivity were found to be profoundly influenced by the counterion, with the hexafluoroantimonate complex **6c** giving superior results. Mechanistically, it is interesting that the use of the epimeric POZ ligand **5** gave a low enantioselectivity. Most significantly, the reactions proceeded efficiently even at low molar ratios of catalyst **6c**, and enantioselectivity up to 98% ee for all the dienophiles of **2a–c** could be achieved. Further studies to examine the scope and limitations of our catalytic version of the asymmetric DA reaction are now in progress.

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Notes and references

‡ *Crystal data*: **1**, $C_{36}H_{32}ONP$; M_W = 525.63, orthorhombic, space group $P2_12_12_1$(#19); a = 9.472(7), b = 17.00(1), c = 18.07(2) Å, V = 2908(4) Å^3; Z = 4, D_c = 1.203 g cm^{-3}, μ(Mo-Kα) = 0.123 mm^{-1}, T = 150 K, final R and R_w are 0.104 and 0.123 for 1113 observed data [$Io > 3\sigma(Io)$], GOF = 2.81. For **4a**, MF = $2(C_{36}H_{32}ONPPdCl_2)$-$(CHCl_3)0.5(CHCl_3)0.5(H_2O)$; M_W = 1593.94, orthorhombic, $P2_12_12_1$(#19); a = 10.641(3), b = 18.805(5), c = 34.692(9) Å, V = 6942(3) Å^3; Z = 4, D_c = 1.525 g cm^{-3}, μ(Mo-Kα) = 0.940 mm^{-1}, T = 150 K, final R and R_w are 0.052 and 0.061 for 7688 observed data [$Io > 3\sigma(Io)$], GOF = 1.09, Flack parameter = 0.00(5). For **5**, $2(C_{36}H_{32}ONPPdCl_2)2(CHCl_3)$; M_W = 1644.63, triclinic P_1(#1),; a = 10.841(3), b = 12.860(3), c = 13.625(3) Å, α = 100.916(4), β = 96.331(3), γ = 104.576(3)°, V = 1780.0(8) Å^3; Z = 1, D_c = 1.534 g cm^{-3}, μ(Mo-Kα) = 0.973 mm^{-1}, T = 173 K, final R and R_w are 0.031 and 0.033 for 10276 observed data [$Io > 4\sigma(Io)$], GOF = 0.920, Flack parameter = −0.01(2).

The structure of **1** could not be refined fully but only isotropically for non-hydrogen atoms because of the small sizes of crystal, giving a relatively high R value and GOF. CCDC 180368–180370. See http://www.rsc.org/suppdata/cc/b2/b201625g/ for crystallographic files in .cif format.

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