Designer cyclopalladated-amine catalysts for the asymmetric Claisen rearrangement

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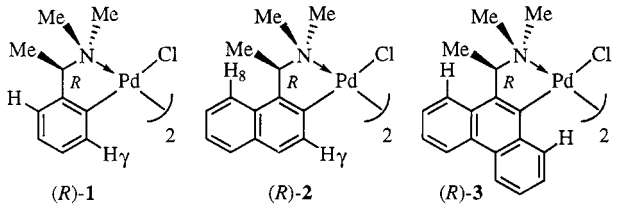
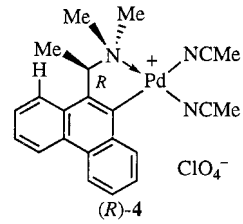
The novel ortho-metallated complex (*R*,*R*)-di-μ-chlorobis{9-[(1-dimethylamino)ethyl]-10-phenanthrenyl-*C*,*N*}dipalladium has been prepared and found to be a significantly better catalyst than its phenyl and naphthylamine analogues for the asymmetric Claisen rearrangement of a non-activated allyl imidate.

Over the past decade, chiral cyclopalladated-amine complexes have contributed significantly to many aspects of synthetic stereochemistry.[1] They have been frequently used as efficient resolving agents for chiral ligands, clear and reliable references for the NMR assignment of unknown absolute stereochemistry in solution, sensitive chiral shift reagents for the determination of optical purities, activators for the asymmetric carbon–carbon bond formation and as chiral templates for the synthesis of functionalized P-chiral phosphines. Surprisingly, these easily accessible square-planar organometallic complexes have not been used in any catalytic asymmetric transformations. Here, we present the systematic application of three analogous cyclopalladated-amine complexes **1**–**3** for the asymmetric Claisen rearrangement. Similar to the Diels–Alder reaction, Claisen rearrangement is an efficient and elegant method for asymmetric carbon–carbon bond formation.[2]



Both enantiomeric forms of complexes **1** and **2** are well documented. The optically active forms of the new phenanthrylamine ligand for complex **3** were obtained by optical resolution using *O*,*O*′-dibenzoyltartaric acid as the resolving agent. Thus, both the (*R*)-(+)- and (*S*)-(−)-forms of α-(9-phenanthryl)ethylamine were obtained as white solids in 60–70% yields, mp 79–81 °C, $[\alpha]_D$ ±44.0 (*c* = 0.5, CH_2Cl_2). The ortho-metallated complex (*R*)-**3** was prepared from the (*R*)-(+)-phenanthrylamine and $[Pd(MeCN)_4](ClO_4)_2$ in the presence of Et_3N followed by the treatment with an excess of NH_4Cl. The dimeric complex was obtained as pale yellow needles (60%), $[\alpha)_D$ −393 (*c* = 0.6, CH_2Cl_2). However, single crystals of (*R*)-**3** that are suitable for structural analysis could not be produced. In an effort to determine the absolute stereochemistry of the phenanthrylamine ligand, (*R*)-**3** was converted quantitatively to the perchlorate salt (*R*)-**4** by treatment of the dimeric complex with silver perchlorate in acetonitrile, $[\alpha]_D$ −198 (*c* = 0.5, CH_2Cl_2). X-Ray structural analysis of the highly crystalline cationic complex (*R*)-**4** was achieved (Fig. 1).† Similar to that observed in (*R*)-**2**,[1] the X-ray analysis of the phenanthrylamine complex reveals that the methyl group at the *R*-chiral carbon centre is located at the axial position. The geometry at palladium is distorted square planar with *cis* angles ranging between



80.2(2) and 96.4(2)°, the most acute being associated with the five-membered chelate ring which has a distinctly folded conformation with C(14) and C(15) lying 0.61 and 1.04 Å respectively out of the coordination plane. The palladium coordination distances are unexceptional, though the Pd–N bond *trans* to carbon is significantly longer than those *trans* to nitrogen. The phenanthrylene ring has a slightly twisted conformation, with deviations from planarity of up to 0.07 Å; the palladium atom lies 0.35 Å from this plane.

To compare the efficiency of the three analogous complexes on the Claisen rearrangement, an electronically non-activated allyl imidate was selected (Scheme 1). All the rearrangement processes were carried out at the optimum temperature of 20 °C in the presence of a palladium catalyst (10 mol%). Interestingly, while all three dimeric catalysts gave the corresponding amide efficiently, the cationic complex (*R*)-**4** could not catalyse the rearrangement. Apparently an electronically neutral Pd(II) species is required for this catalytic process. Furthermore, in

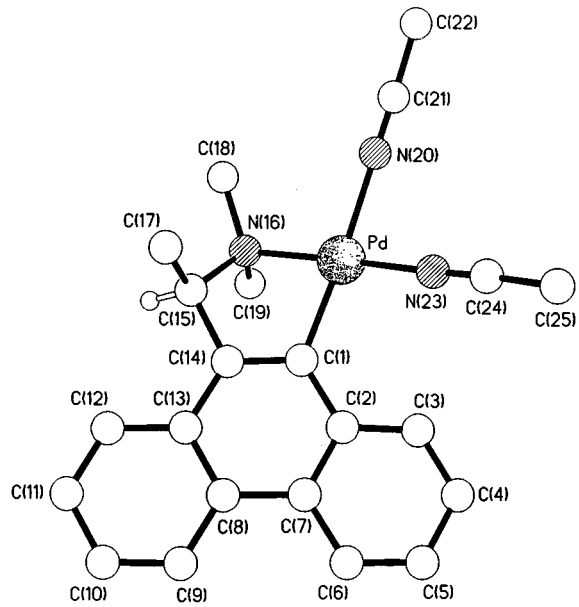
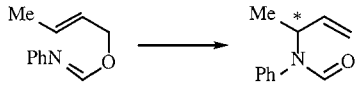


Fig. 1 Molecular structure and absolute stereochemistry of the complex cation (*R*)-**4**. Selected bond lengths (Å) and angles (°); Pd–C(1) 2.000(4), Pd–N(16) 2.062(4), Pd–N(20) 2.126(5), Pd–N(23) 2.023(4); C(1)–Pd–N(16) 80.2(2), C(1)–Pd–N(20) 176.2(2), C(1)–Pd–N(23) 96.3(2), N(16)–Pd–N(20) 96.4(2), N(16)–Pd–N(23) 172.0(2), N(20)–Pd–N(23) 86.9(2).

terms of stereoselectivities, it is obvious that (*R*)-**3** is the best asymmetric catalyst among the three studied. When benzene was used as the solvent, (*R*)-**3** produced the chiral amide with 79% ee.‡ Under the same reaction conditions, however, only 4% ee could be achieved by both (*R*)-**1** and (*R*)-**2**. These catalytic results are indeed in agreement with our expectations, based on the well established stereoelectronic features of complexes **1** and **2**. The five-membered organometallic ring in complex (*R*)-**1** is stereochemically non-rigid and the chiral chelate adopts both the δ and λ conformations in the solid state and these ring chiralities are inter-convertable in solution. In complex (*R*)-**2**, however, there is a strong steric inter-locking force operating between the methyl group at the chiral carbon centre and the neighbouring H(8) of the naphthylenyl ring.[1,3] Thus the δ conformation is secured in the skew organometallic ring in (*R*)-**2** and cannot be inverted into the λ form, even at elevated temperatures. Thus the stereochemistry of the naphthylamine moiety is expected to be transmit *via* the prochiral NMe groups and the H_γ proton onto the neighbouring coordination sites without any fluctuation. The X-ray analysis of (*R*)-**4** and the 2D ^{1}H ROSEY NMR studies of (*R*)-**3** and (*R*)-**4** in $CDCl_3$ confirmed that similar stereochemical inter-locking forces are operating within the palladium–phenanthrylamine chelates. In terms of electronic directing effects, it is well established that in both (*R*)-**1** and (*R*)-**2**, the Pd–Cl bonds which are located *trans* to the π-accepting aromatic carbon are stable and inert.[1,4] In contrast, the Pd–Cl bonds that are *trans* to the σ-donating nitrogen are kinetically labile. As the donor atoms in all three complexes are similar, we therefore expect that the Pd–Cl bonds in (*R*)-**3** to exhibit similar kinetic stabilities as their counterparts in (*R*)-**1** and (*R*)-**2**. Undoubtedly the labile chloro ligands in these chiral complexes provide the catalytic sites for the asymmetric Claisen rearrangements. It is noted that the stereochemical environment of the catalytic sites in (*R*)-**1** and (*R*)-**2** are controlled only by the projecting H_γ protons. However, the influence exerted by these H_γ protons is less than that of the extended aromatic ring in (*R*)-**3** as the protons are small and further away from the site. Currently we are investigating the absolute stereochemistry of the Claisen rearrangement products. In addition synthesis of analogous optically active chrysenylamine complexes and further studies of the asymmetric Claisen rearrangements involving activated allyl imidates are currently in progress.



Catalyst	Solvent	*T*/°C	Enantiomer	ee(%)
(*R*)-**1**	CH_2Cl_2	20	(−)	10
(*R*)-**2**	CH_2Cl_2	20	(−)	13
(*R*)-**3**	CH_2Cl_2	20	(−)	67
(*R*)-**4**	CH_2Cl_2	20	NR	—
(*R*)-**1**	C_6H_6	20	(−)	4
(*R*)-**2**	C_6H_6	20	(+)	4
(*R*)-**3**	C_6H_6	20	(−)	79
(*R*)-**4**	C_6H_6	20	NR	–

Scheme 1 NR = no reaction.

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Notes and references

† *Crystal data* for (*R*)-**4**: $C_{22}H_{24}N_3O_4ClPd\cdot0.25H_2O$, M = 540.8, monoclinic, space group $P2_1$ (no. 4), a = 12.399(2), b = 7.601(1), c = 13.098(1) Å, β = 108.60(1)°, V = 1169.8(2) Å^3, Z = 2, D_c = 1.535 g cm^{-3}, μ(Mo-Kα) = 9.41 cm^{-1}, F(000) = 549. A pale yellow prism with dimensions 0.61 × 0.39 × 0.21 mm was used for diffraction studies. A total of 2879 independent reflections were measured on a Siemens P4/PC diffractometer with Mo-Kα radiation (graphite monochromator) using ω-scans. All the non-hydrogen atoms were refined anisotropically. Full-matrix least-squares refinement based on F^2 with absorption corrected data gave R_1 = 0.032, wR_2 = 0.077. The absolute stereochemistry was determined unambiguously by a combination of *R*-factor tests (R_1^+ = 0.0269, R_1^- = 0.0327) and by use of the Flack parameter [x^+ = −0.01(3), x^- = +0.99(3)] using a data set collected on the same crystal with Cu-Kα radiation (with the exception of those associated with the chirality assignment, the data and derived parameters given are for the Mo-Kα data set as it has a higher data to parameter ratio). CCDC 182/1470. See http://www.rsc.org/suppdata/cc/1999/2435/ for crystallographic files in .cif format.

‡ Determined by HPLC using a perfunctionalized cyclodextrin column eluted with 2% Pr^{i}OH–*n*-hexane.[5]

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