New chiral ligands bearing two *N*-heterocyclic carbene moieties at a dioxolane backbone. Gold, palladium and rhodium complexes as enantioselective catalysts†

Avelina Arnanz,[a] Camino González-Arellano,[a] Alberto Juan,[b] Gonzalo Villaverde,[b] Avelino Corma,[c] Marta Iglesias*[a] and Félix Sánchez*[b]

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***Bis*carbene ligands with two imidazolin-2-ylidene moieties at a chiral dioxolane backbone were used as ligands for gold, rhodium and palladium complexes. All new complexes showed varying degrees of enantioselectivity toward hydrogenation of prochiral alkenes with ees up to 95%.**

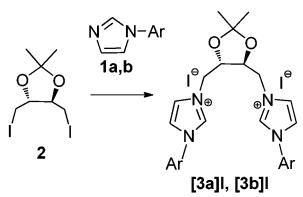
The creation of an asymmetric environment around a metallic centre in order to accommodate the partners of an organic transformation, allows enantioselectivity induction in catalytic processes.[1] A classical approach to achieve this goal is the use of enantiomerically pure ligands containing donor atoms (mainly nitrogen and phosphorus) with a defined symmetry.[2] The backbone is one of the key aspects to take into account in the design of chiral ligands. Keeping this idea in mind, we have worked with a family of ligands containing a chiral dioxolane backbone. Transition metal complexes supported by ligands bearing *N*-heterocyclic carbene (NHC) groups are emerging as effective catalysts for enantioselective and non-stereospecific organic transformations.[3] The attraction of this ligand design[4] and catalysis is straightforward: NHC supported complexes have the potential to promote any reaction catalyzed by traditional tertiary phosphine- and phosphite-based catalysts.[5] While the promise of similar reactivity is inviting, the hope of increased efficiency, lower toxicity, air stability, and electronic and structural diversity[6] makes NHCs a logical and smart choice for exploration. The popular and highly successful motif of chelating diphosphorus-based ligands, particularly chiral versions, prompted our investigation into chiral di-NHC ligands. These ligands often display significant advantages over the analogous phosphine-containing compounds.[7] Few ligands have been synthesized thus far, and the available structural diversity for NHCs is low in comparison to established phosphorus systems.

In catalytic systems, NHCs have been shown to prevent the formation of elemental metal, a problem often associated with weak ligand–metal interactions.[8] The literature abounds with examples of chiral monodentate carbene complexes designed for asymmetric synthesis,[9] but, until recently, C_2-symmetric bidentate carbene complexes were scarce.[10] In a recent paper a comprehensive list was presented describing the synthesis of all chiral di-NHC ligands and complexes reported to date, including pertinent catalytic and structural features.[11]

Thus far, there have been few reports regarding the use of chiral NHC-metal complexes in asymmetric catalysis.[12] To date, the best enantioselectivities for any reaction featuring a catalyst with a bidentate chiral di-NHC ancillary ligand were reported by Shi *et al.*[10b] (binapthyl-*bis*-NHC–Rh). The complex is an excellent precatalyst for the enantioselective hydrosilation of methyl ketones. Marshal *et al.*[10a] capitalized on naturally derived tartaric acid to form ligands containing *trans*-2,2-dimethyl-1,3-dioxolane and were able to form Pd(II) complexes featuring *cis*-chelate orientation. Machado and Dorta have synthesized the analogous chiral diimidazole version but do not report metalation attempts or catalysis.[13]

Mindful of this, we began the synthesis of stable C_2-symmetric diimidazolidinylidene ligands bridged by a *trans*-2,2-dimethyl-1,3-dioxolane backbone to use as phosphine substitutes in catalytic asymmetric transformations. We prepared different chelated gold, rhodium and palladium complexes to see how the carbene substituent affects the catalytic activity. These complexes were screened for catalytic activity in the hydrogenation of prochiral alkenes.

The manipulation of L-tartaric acid using modified described methods[14] gave access to (4*R*,5*R*)-*bis*(iodomethyl)-2,2-dimethyl-1,3-dioxolane (**2**), which, when heated with 1-arylimidazoles **1a,b**;[15] produced quantitative yields of the salts **[3a]I**, **[3b]I** as light yellow solids (Scheme 1). These syntheses have been performed by an adaptation of a



a: Ar = 2,4,6-trimethylphenyl, b: Ar = 2,6-diisopropylphenyl

Scheme 1 Synthesis of chiral *bis*-NHC ligand precursor.

[a] *Instituto de Ciencia de Materiales de Madrid, CSIC, C/Sor Juana Inés de la Cruz 3, Cantoblanco, 28049 Madrid, Spain. E-mail: marta.iglesias@icmm.csic.es; Fax: (+)34 (91)3720623; Tel: (+)34 (91)3349000*
[b] *Instituto de Química Orgánica General, CSIC. C/ Juan de la Cierva, 3, 28006 Madrid, Spain. E-mail: felix-iqo@icmm.csic.es; Fax: (+)34 (91)5644853; Tel: (+)34 (91)5622900*
[c] *Instituto de Tecnología Química, CSIC-UPV. Avda de los Naranjos, s/n, 46022 Valencia, Spain. E-mail: acorma@itq.upv.es; Fax: (+)34 (96)3877809; Tel: (+)34 (96)3877800*

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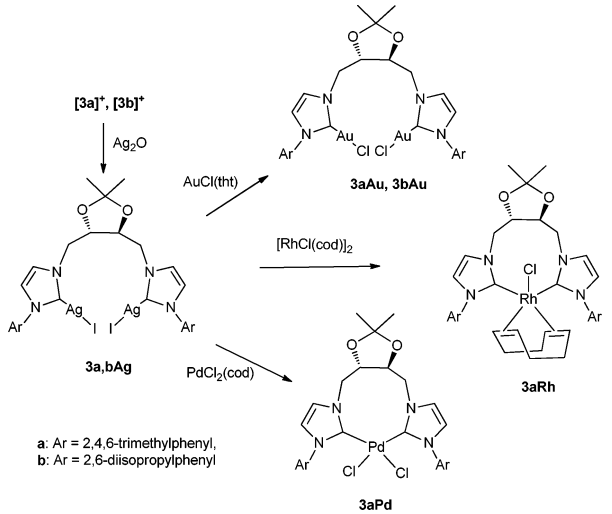

Scheme 2 Synthesis of *bis*-NHC-complexes

procedure described previously.[10f,13] The imidazolium carbon (N-*C*H=N) appears at 137.42 ppm (**[3a]I**) and 137.90 (**[3b]I**).

It is well known that silver(I) oxide is a suitable metal salt for the synthesis of the corresponding carbene complexes. The treatment of the imidazolium iodide salts (**[3a]I**, **[3b]I**) with Ag_2O yielded the silver complexes (**4*S*,5*S*)-3a,3bAg**. The formation of the carbene complexes **3a,3bAg** was established by a weak peak below δ 174 ppm in each ^{13}C-{^1H} NMR spectrum which was assigned to the *C*-imidazol-2-ylidene (carbene) carbon, and by the absence of the downfield peak for the 2*H*-imidazolium proton in each ^1H NMR spectrum (below δ 9.7 ppm). (Scheme 2).

As Ag–NHC bonds are quite weak[16] the silver complexes could then be used as carbene transfer reagents to gold, palladium and rhodium according to Lin *et al.*[17] The reaction of the silver complexes with AuCl(tht) (tht = tetrahydrothiophene), $[RhCl(cod)]_2$ and $[PdCl_2(cod)]$ (cod = 2,5-cyclooctadiene) yielded the respective complexes (**4*S*,5*S*)-3aAu**, **3bAu**, **3aRh**, **3aPd**, (Scheme 2) in >80% yield along with the formation of AgI precipitate.

The ESI spectrum for (**3aAu**) shows a peak at m/z = 927 which corresponds to the loss of one chloride (m/z = 1011 for (**3bAu**)). FT IR spectra show a strong band at 328–331 cm^{-1} assigned to the ν(Au–Cl) vibration. ^{13}C NMR spectra show all resonances shifted as compared to the uncoordinated ligand with the diagnostic gold-bound (N*C*N–Au) peak at 177.1 ppm (**3aAu**) or 173.9 ppm (**3bAu**).

The ^1H NMR spectrum of [RhCl(cod)(**3a**)] (**3aRh**) shows the resonance due to the cod protons significantly broadened due to fluxionality of the complex. The mesityl rings undergo restricted rotation about the N–C bond as evidenced by the presence of two distinct resonances in the ^1H NMR spectrum for each of the *o*-methyl groups and each of the *m*-protons on the mesityl ring. The (N*C*N–Rh) signal appears at δ = 179.8 ppm in the ^{13}C NMR spectrum. The monomolecular structure is confirmed by the intense MS molecular peak 745 (M^+).

The ^1H-NMR spectrum of [$PdCl_2$(**3a**)] (**3aPd**) shows one signal set of a symmetric species. In the ^{13}C NMR spectrum

Table 1 Hydrogenation of (*E*)-diethyl 2-*R*-succinates with *bis*-NHC and diphosphine catalysts[a,c]

Entry	Catalyst	R	TOF[b]	ee (%)
1	**3aRh**	Methylene	258	10 (*S*)
2	**3aRh**	Benzylidene	16	99 (*S*)
3	**3aRh**	Naphthylmethylene[d]	10	>95 (*S*)
4	**DIOP-Rh**	Methylene	579	20 (*S*)
5	**DIOP-Rh**	Benzylidene	28	99 (*S*)
6	**3aPd**	Methylene	45	5 (*S*)
7	**3aPd**	Benzylidene	17	98 (*S*)
8	**3aPd**	Naphthylmethylene[d]	2	>95 (*S*)
9	**DIOP-Pd**	Methylene	119	11 (*S*)
10	**DIOP-Pd**	Benzylidene	35	97 (*S*)
11	**3aAu**	Methylene	2000	15 (*S*)
12	**3aAu**	Benzylidene	1250	90 (*S*)
13	**3aAu**	Naphthylmethylene[d]	150	95 (*S*)
14	**3bAu**	Methylene	210	25 (*S*)
15	**3bAu**	Benzylidene	50	85 (*S*)
16	**3bAu**	Naphthylmethylene[d]	5	90 (*S*)
17	**3a(OPNB)Au**	Methylene	120	25 (*S*)
18	**3a(OPNB)Au**	Benzylidene	15	90 (*S*)
19	**3a(OPNB)Au**	Naphthylmethylene[d]	0.5	93 (*S*)
20	**DIOP-Au**	Benzylidene	45	98 (*S*)
21	**Duphos-Au**	Benzylidene	906	80 (*S*)[21]

[a] Ethanol, 4 atm. H_2, 40 °C, cat.: 0.5 mol%. [b] TOF: h^{-1} (calculated at maximum rate). [c] HPLC (Chiralcel AD-H, λ: 230 nm, hexane/iPrOH: 98/2, Chiralcel OD, λ: 250 nm, hexane/iPrOH: 95/5). [d] 60 °C, 4 atm. H_2.

formation of the carbene complex is indicated by a carbene signal at 175.0 ppm, which is comparable to the chemical shift observed in other *trans*-[$PdCl_2$(*bis*(NHC))] complexes.[18] Cationic complexes were generated by halide abstraction *via* addition of $AgPF_6$ in a CH_2Cl_2–water solvent system.

The problem in (NHC)M-catalyzed hydrogenation is the tendency for NHC reductive elimination to the imidazolium salt $[NHC–H]^+$. Not surprisingly, there is to date only a single example of enantioselective alkene hydrogenation using chiral monodentate NHC complexes.[19] *Bis*-NHC ligands are expected to be resilient to reductive elimination but only one report of hydrogenation of alkenes has been described.[12f] The efficiency of gold-, palladium- and rhodium-complexes as catalysts for the asymmetric hydrogenation of different alkenes (diethyl itaconate, (*E*)-diethyl 2-benzylidenesuccinate, and (*E*)-diethyl 2-naphthylmethylenesuccinate) was investigated (Table 1). All complexes showed significant activities. In the hydrogenation of (*E*)-diethyl 2-benzylidenesuccinate up to 99% ee was obtained with the rhodium catalyst. Palladium and gold complexes also yielded good enantioselectivity (Table 1).

For comparison purposes, we obtained the rhodium and palladium complexes with the diphosphine (*R*,*R*)-DIOP as ligand ((*R*,*R*)-DIOP = (4*R*,5*R*)-4,5-*bis*(diphenylphosphinomethyl)-2,2-dimethyldioxolane) which has the same skeleton as the *bis*carbene ligand studied in this paper). The reactivity is slightly higher with the diphosphine Rh-complex ($[Rh(cod)(DIOP)]^+$), however the enantioselectivity was similar in the case of succinates with greater steric hindrance. The palladium complex $[Pd(cod)(DIOP)]^{2+}$ and cationic gold complex ($\{[Au(benzonitrile)]_2(R,R)\text{-DIOP}\}^{2+}$)[20] activities and enantioselectivities were similar to those obtained with the

corresponding derivative *bis*(NHC)-complex (**3aAu**). These results are similar to that obtained when freshly prepared $[(AuCl)_2((R,R)$-Me-Duphos$)]$[21] was the catalyst with the difference that the **3aAu** complex is stable for at least 3 months and is easier to synthesize and manipulate.

To extend the scope of the complexes as catalysts we have used (*Z*)-α-ethyl benzamidocinnamate as a substrate with the result that the catalytic activity for **3aRh** is good (TOF = 35 h^{-1}) but the enantiomeric excess is marginal (<10%). The $[Rh(cod)(DIOP)]^+$ gives an ee of 15% (TOF = 264 h^{-1}) and the palladium complex decomposes in the reaction medium under the same conditions.

An important fact is to check is how the catalyst activity varies over time; it was found that the carbene complex maintains its activity for at least three months, however the activity for the $[Rh(cod)(DIOP)]^+$ complex decreases over a week (Fig. S2†).

As can be seen from Table 1, the complex **3bAu**, which contains a 2,6-diisopropylphenyl on the NHC donor, had much slower reaction rates. These results indicate that the bulky substituents severely limit the activity of the catalysts. This effect is most probably due to the inhibition of substrate coordination due to steric interaction with the bulky isopropyl substituent. Dramatic decrease of reactivity was also founded when the chlorine was substituted by OPNB (4-nitrobenzoate), **[Au(OPNB)]$_2$((*S*,*S*)-3a)]**, probably due to increased steric hindrance.

In summary, we report the synthesis of gold, palladium and rhodium complexes bound to a chiral dioxolane ligand bearing two NHC moieties. To the best of our knowledge, this is the first example of the use of chiral *bis*(NHC)–metal catalysts in asymmetric hydrogenation with high enantioselectivity. These *N*-heterocyclic carbenes represent a class of ligands that can be used in place of phosphine ligands in transition-metal catalysis, which provide more effective metal complexes owing to their stability to air and moisture.

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