phenyl H atoms riding) with teXsan (v. 1.7 for SGI workstations), 340 refined parameters, $R(F) = 0.022$ [$I \geq \sigma(I)$], $wR(F^2) = 0.051$, residual electron density: 1.29/−1.31 e Å^{-3}. Data was obtained on an Enraf-Nonius CAD-4 diffractometer. CCDC-185114 (**2**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

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[18] Although 30–35 metallaaromatics are known, most include a second heteroatom (e.g. metallapyridine, metallapyrilium, etc.). Similarly, a majority of the remaining benzene-type structures are η^6-coordinated to a second transition-metal fragment; therefore, only two prior classes, Roper's osmabenzenes and Bleeke's iridabenzenes, are pure metallabenzenes.[9] Compound **2** represents a new, third class.

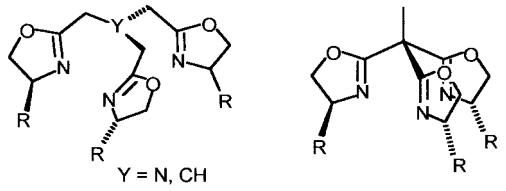
[19] Pt standard: 0.2 M K_2PtCl_4/D_2O ($\delta = -1627$) against K_2PtCl_6; L. S. Hollis, S. J. Lippard, *J. Am. Chem. Soc.* **1983**, *105*, 3494–3503.

A Modular Approach to C_1 and C_3 Chiral N-Tripodal Ligands for Asymmetric Catalysis**

Stéphane Bellemin-Laponnaz and Lutz H. Gade*

In memoriam John Osborn

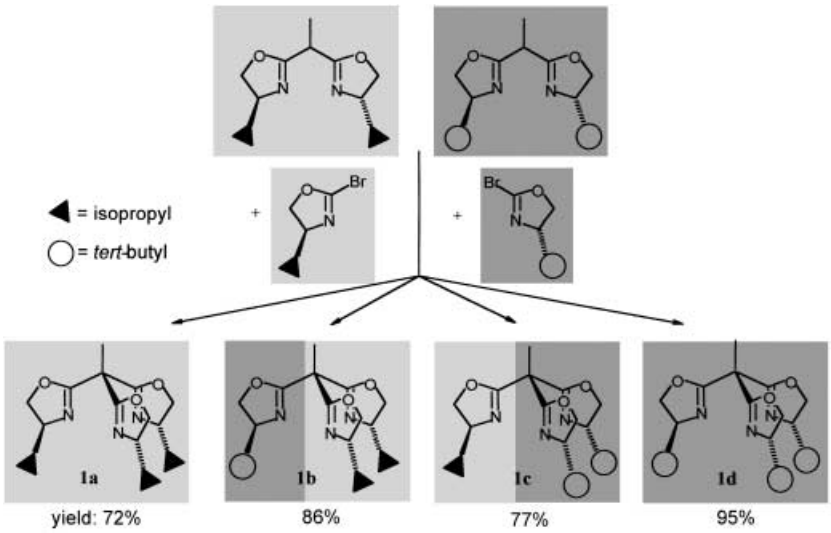
In the development of nitrogen ligand based homogeneous catalysis,[1] oxazoline derivatives have emerged as a paradigmatic class of ligands in asymmetric catalysis.[2,3] Most attention has been centered on mono- or bisoxazoline ligands many of which proved to be highly efficient in a large variety of stereoselective transformations.[4] In contrast, the combination of three oxazolines to form ligands of podand topology, possessing C_1 or C_3 symmetry, has received much less attention. There are several reports of trisoxazoline ligands,[5,6] the most notable example being the $N(CH_2\text{-ox})_3$ and $CH(CH_2\text{-ox})_3$ (ox = 2-oxazolinyl) systems (**I**) developed by Katsuki's group, the copper complexes of which have been employed in asymmetric allylic oxidations.[7] The way these conformationally very flexible trisoxazolines coordinate to the metal centers in the active catalysts remains an



I **II**

open question. However, the access to 1,1,1-tris(oxazolinyl)-methane or -ethane ligands (**II**), which provide a geometry of the metal binding site that is most adapted to tripodal coordination of the metal center and would lead to a relatively rigid and well-defined coordination geometry, proved to be elusive for a long time.[8]

Attempts to synthesize these tripodal ligands by sequential formation of the three oxazoline rings failed due to decarboxylation and related decomposition of the precursors during the formation of the third oxazoline ring. Very recently, we discovered that 1,1,1-tris(oxazolinyl)ethane derivatives may be synthesized by coupling lithiated bisoxazolines with 2-bromooxazolines and reported the achiral 1,1,1-tris[2-(4,4-dimethyl)oxazolinyl]ethane ("trisox-Me_2", **II**).[9] This strategy, which is formally based on a [1+2] condensation scheme of a metalated bisoxazoline[10] with a 2-bromooxazoline[11] has now been used for the synthesis of the first *chiral* tripods and it establishes 2-bromooxazolines as potentially powerful tools in ligand design (Scheme 1).



Scheme 1. Modular assembly of the trisoxazoline ligands **1a**–**1d** by reaction of the metalated bisoxazolines with 2-bromooxazoline derivatives.

Our synthetic method allows the high-yield access to symmetrically substituted derivatives, such as 1,1,1-tris[2-{(*S*)-4-isopropyl}oxazolinyl]ethane (**1a**) or 1,1,1-tris[2-{(*S*)-4-*tert*-butyl}oxazolinyl]ethane (**1d**). Additionally, the synthesis of tripods with mixed substitution patterns, such as **1b** and **1c**, is achieved in excellent yields. This opens up the possibility to approach the synthesis of such polydentate oxazolines in a *modular* way, as displayed in Scheme 1 for the isopropyl/*tert*-butyl couple. From the point of view of ligand design these

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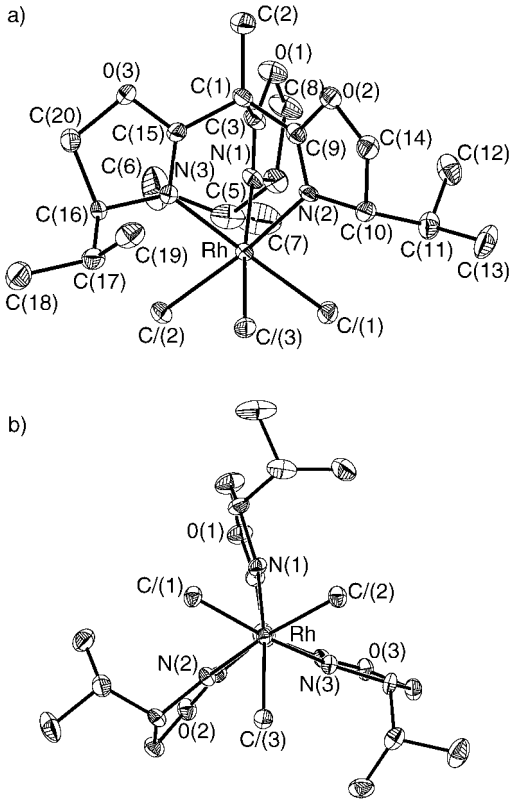


Figure 1. a) Molecular structure of the rhodium complex **2**. Principal bond lengths [Å] and angles [°]: Rh-Cl(1) 2.337(2), Rh-Cl(2) 2.328(2), Rh-Cl(3) 2.315(1), Rh-N(1) 2.066(5), Rh-N(2) 2.063(4), Rh-N(3) 2.066(5), Cl(1)-Rh-Cl(2) 90.32(6), Cl(1)-Rh-Cl(3) 89.35(6), Cl(2)-Rh-Cl(3) 90.45(6), N(1)-Rh-N(2) 85.0(2), N(1)-Rh-N(3) 85.5(2), N(2)-Rh-N(3) 85.4(2). b) View along the virtual threefold molecular axis of **2**.

podands are adapted to non-square-planar coordination geometries in transition metals, including the late elements such as the ubiquitous Cu^{I}/Cu^{II} couple in asymmetric catalysis.

To assess the binding capability of the new trisoxazoline tripods as facially coordinating tridentate ligands, we first chose a transition metal that is less substitutionally labile than copper. Reaction of **1a** with one molar equivalent of $[RhCl_3(H_2O)_3]$ cleanly gave the trisoxazolinerhodium complex [$RhCl_3$-{trisox-(*S*)-*i*Pr)] (**2**), for which the NMR spectroscopic data obtained in solution indicated the expected threefold symmetric structure. An X-ray diffraction study of **2** was carried out to establish the details of the molecular stucture. The view along the threefold molecular axis of the rhodium complex (Figure 1) established the C_3 chirality of the system also in the solid state. The bond lengths and angles within the [2.2.2]bicyclooctane-related ligand cage are within the typical range and confirm the suitability of the ligands **1a**–**1d** for facial coordination.

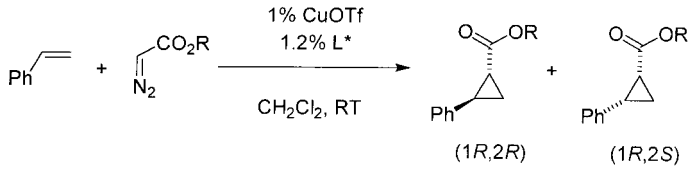
As a first test in copper(I)-based asymmetric catalysis, ligands **1a**–**1d** were employed in the asymmetric cyclopropanation of styrene with ethyl and *tert*-butyl diazoacetate (Table 1).[12] The strong preference for the *trans* diastereomer (80–90%) is similar to results previously obtained with bisoxazoline derivatives.[2a–c,13,14] The stereoselectivity varied with the combination of substituents at the oxazoline ligands and is maximized for the nonsymmetrical ligand **1c**: 85% *ee* for the *cis* diastereomer in the reaction with *tert*-butyl diazoacetate and 86% *ee* for the *trans* diastereomer in the reaction with ethyl diazoacetate. It is notable that in the former conversion the *cis* products are generated with high enantioselectivity, while the trend is reversed for the conversion with ethyl diazoacetate.

As is evident from this first study, the possibility of introducing and combining different substituents at the oxazoline rings within the same tripodal ligand system allows a straightforward access to a large variety of such systems. Moreover, the combination of chiral and achiral units or of oxazoline ligands of opposite absolute configuration within the same ligand system is feasible by this strategy and will provide the foundation for the application of this class of ligands in parallel screening experiments for the optimization of homogeneous catalysts.

Experimental Section

General procedure for the synthesis of the trisoxazolines (given for **1d**): *t*BuLi (1.26 mL, 1.7 M in hexanes, 2.14 mmol) was added dropwise to a solution of 2,2-bis[4-(*S*)-*tert*-butyl-1,3-oxazolinyl]ethane (0.5 g, 1.78 mmol) in anhydrous THF (30 mL) at −78 °C over 10 min. The resulting yellow solution was stirred for an additional 30 min prior to the addition of 1.4 equivalents of 4-(*S*)-*tert*-butyl-2-bromooxazoline. The solution was then stirred at room temperature for one hour, concentrated to about 25 mL and, finally, the Schlenk tube was sealed. The stirred solution was heated at 80 °C for five days. The resulting orange solution was evaporated to dryness; the residue was redissolved with dichloromethane (100 mL) and washed with water (10 mL). The organic extract was dried over Na_2SO_4 and concentrated in vacuo to give a yellow oil. Purification by flash chromatography (EtOAc/MeOH, 50/1) gave the desired product **1d** (0.70 g, 0.69 mmol; 95% yield). Compounds **1a**–**1c** were synthesized accordingly. Yields: **1a** 72%, **1b** 86%, **1c** 77%; see Table 2 for spectroscopic data.

Table 1. Copper(I)-catalyzed asymmetric cyclopropanation of styrene with *tert*-butyl and ethyl diazoacetate using the novel oxazoline tripod ligands.



	R = *t*Bu			R = Et		
L*	*cis*:*trans*	% *ee cis*	% *ee trans*	*cis*:*trans*	% *ee cis*	% *ee trans*
1a	22:78	70	65	29:71	64	67
1b	22:78	72	66	29:71	72	78
1c	23:77	85	81	31:69	81	86
1d	19:81	73	70	31:69	68	70

[a] Styrene (1.0 mmol), diazoacetate (1.2 mmol), $[CuOTf]_2$ (0.005 mmol) and ligand (0.012 mmol). A solution of diazoacetate in CH_2Cl_2 (1.0 mL) was added with a syringe over a period of 8 h to the mixture of styrene and the catalyst in the appropriate solvent (2.0 mL). The resulting solution was stirred for 16 h. The product was purified by flash chromatography. Yields of isolated product are 70–80% (*cis* + *trans*); *ee* values were determined by chiral GC.

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Table 2. Selected spectroscopic data.[a]

1a: ^{1}H NMR: $\delta = 4.26$ (m, 3H), 4.09–3.97 (m, 6H), 1.82 (s, 3H), 1.85–1.74 (m, 3H), 0.91 (d, $J = 6.8$ Hz, 9H); 0.86 ppm (d, $J = 6.8$ Hz, 9H); ^{13}C NMR: $\delta = 164.6$ (C=N), 71.8 (*C*H*i*Pr), 70.6 (CH_2), 44.7 ($C_{quat.}$), 32.3 (*C*H(CH_3)$_2$), 21.3 (CH_3), 18.6 (CH(*C*H$_3$)(CH$_3$)), 17.8 ppm (CH(CH$_3$)(*C*H$_3$)); MS (EI): *m*/*z* (%): 363.2 (1) $[M]^+$, 348.2 (7.6) $[M-CH_3]^+$, 320.2 (100) $[M-CH(CH_3)_2]^+$; $[\alpha]_D^{25} = -88.9°$ ($c = 0.4$, $CHCl_3$).

1b: ^{1}H NMR: $\delta = 4.28$–3.95 (m, 8H), 3.91 (dd, $J = 7.3$ Hz, $J = 10.2$ Hz, 1H), 1.81 (s, 3H), 1.85–1.74 (m, 2H), 0.89 (m, 12H), 0.87 ppm (s, 9H); ^{13}C NMR (75.5 MHz, $CDCl_3$): $\delta = 164.6$, 164.5, 164.4 (C=N), 75.4 (*C*H*t*Bu), 71.7 (2 *C*H*i*Pr), 70.5 (2 CH_2), 69.4 (CH_2), 44.7 ($C_{quat.}$), 33.9 (*C*(CH$_3$)$_3$), 32.3 (2 *C*H(CH$_3$)$_2$), 25.7 (C(*C*H$_3$)$_3$), 21.2 (CH_3), 18.5 (2 CH(*C*H$_3$)(CH$_3$)), 17.8 ppm (2 CH(CH$_3$)(*C*H$_3$)), MS (EI): *m*/*z* (%): 376.3 (1) $[M-H]^+$, 362.3 (8.5) $[M-CH_3]^+$, 334.2 (35) $[M-CH(CH_3)_2]^+$, 320.1 (100) $[M-C(CH_3)_3]^+$; $[\alpha]_D^{25} = -71.0°$ ($c = 0.4$, $CHCl_3$).

1c: ^{1}H NMR: $\delta = 4.27$–3.96 (m, 7H), 3.90 (dd, $J = 7.3$ Hz, $J = 10.1$ Hz, 2H), 1.82 (s, 3H), 1.85–1.74 (m, 1H), 0.89 (m, 6H), 0.87 ppm (s, 18H); ^{13}C NMR: $\delta = 164.6$, 164.4, 164.3 (C=N), 75.4 (2 *C*H*t*Bu), 71.7 (*C*H*i*Pr), 70.4 (CH_2), 69.3 (2 *C*H$_2$), 44.8 ($C_{quat.}$), 33.9 (2 *C*(CH$_3$)$_3$), 32.2 (*C*H(CH$_3$)$_2$), 25.8 (2 C(*C*H$_3$)$_3$), 21.0 (CH_3), 18.5 (CH(*C*H$_3$)(CH$_3$)), 17.8 ppm (CH(CH$_3$)(*C*H$_3$)); MS (EI): *m*/*z* (%): 390.3 (0.5) $[M-H]^+$, 376.2 (7.5) $[M-CH_3]^+$, 348.2 (2) $[M-CH(CH_3)_2]^+$, 334.2 (100) $[M-C(CH_3)_3]^+$; $[\alpha]_D^{25} = -82.8°$ ($c = 0.4$, $CHCl_3$).

1d: ^{1}H NMR: $\delta = 4.27$–4.16 (m, 6H), 3.95 (dd, $J = 7.4$ Hz, $J = 10.1$ Hz, 3H), 1.84 (s, 3H), 0.91 ppm (s, 27H); ^{13}C NMR: $\delta = 164.7$ (C=N), 75.8 (*C*H*t*Bu), 69.7 (CH_2), 45.2 ($C_{quat.}$), 34.3 (*C*(CH$_3$)$_3$), 26.2 (C(*C*H$_3$)$_3$), 21.3 ppm (*C*H$_3$); MS (EI): *m*/*z* (%): 405.2 (0.4) $[M]^+$, 390.3 (8.5) $[M-CH_3]^+$, 348.1 (100) $[M-C(CH_3)_3]^+$; $[\alpha]_D^{25} = -81.0°$ ($c = 0.5$, $CHCl_3$).

2: ^{1}H NMR: $\delta = 5.06$ (m, 3H), 4.75–4.61 (m, 6H), 3.26 (m, 3H), 1.80 (s, 3H), 0.84 (d, $J = 7.3$ Hz, 9H), 0.65 ppm (d, $J = 6.6$ Hz, 9H); ^{13}C NMR: $\delta =$ 166.0 (C=N), 73.7 (*C*H*i*Pr), 68.7 (CH_2), 44.5 ($C_{quat.}$), 27.4 (*C*H(CH$_3$)$_2$), 18.6 (CH(CH$_3$)(*C*H$_3$), 14.3 (CH(*C*H$_3$)(CH$_3$), 11.1 ppm (*C*H$_3$); MS (FAB): *m*/*z* (%): 536.0 ($[M-Cl]^+$, calculated for the most abundant isotopomer: 536.1 amu).

[a] NMR spectra recorded at 300.17 MHz (^{1}H) and 75.48 MHz (^{13}C) in $CDCl_3$. Correct elemental analyses obtained for all compounds.

2: A mixture of the ligand **1a** (116 mg, 0.32 mmol) and $[RhCl_3(H_2O)_3]$ (82 mg, 0.31 mmol) in ethanol (5 mL) was stirred under nitrogen at 50 °C for one hour and then at room temperature for 12 h. The solvent was removed in vacuo and the resulting orange solid was dissolved in chloroform. Filtration over celite, followed by addition of diethyl ether gave orange crystals. Yield: 150 mg, 0.26 mmol; 84 % (see Table 2 for spectroscopic data). X-ray structure analysis of **2**: $C_{20}H_{33}Cl_3N_3O_3Rh \cdot 2\,CHCl_3$, orange, crystal dimensions $0.20 \times 0.16 \times 0.14$ mm, $M_r = 811.52$, orthorhombic, space group $P2_12_12$, $a = 30.2795(1)$, $b = 11;9730(1)$, $c = 9.6101(3)$ Å, $V = 3484.0(1)$ Å^3, $Z = 4$, $\rho_{calcd} = 1.55$ g cm^{-3}, $\mu = 1.208$ mm^{-1}, $F(000) = 1640$, number of data measured: 7998 ($2.5 < \theta < 27.48°$) at 173 K, number of data with $I > 3\sigma(I)$: 3479, number of variables: 343, $R = 0.039$, $Rw = 0.057$, GOF = 1.069, largest peak in final difference: 0.881 e Å^{-3}. The crystal data were collected on a Nonius Kappa CCD diffractometer at −100 °C and transfered to a DEC Alpha workstation; for all subsequent calculations the Nonius OpenMoleN package was used.[15] The structures were solved by using direct methods; absorption corrections were used as part of the scaling procedure of the data reductions. After refinement of the heavy atoms, difference Fourier maps revealed the maxima of residual electron density close to the positions expected for the hydrogen atoms; they were introduced as fixed contributors in the structure factor calculations with fixed coordinates (C–H: 0.95 Å) and isotropic temperature factors ($B(H) = 1.3\,B_{eq}(C)$ Å^2) but not refined. Full-matrix least-square refinements on F^2. A final difference map revealed no significant maxima of electron density. The scattering factor coefficients and the anomalous dispersion coefficients were taken from ref. [16].

CCDC-185098 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/conts/retrieving.html (or from the Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: (+44) 1223-336-033; or deposit@ccdc.cam.ac.uk).

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