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Communications

Enantiomerically Pure Copper(I) and Zinc(II) Complexes of a Novel C_3-Symmetric Polypyrazole Ligand

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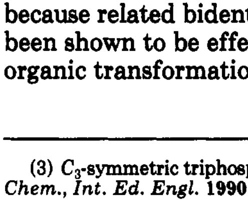
Summary: We report the synthesis and characterization of the first enantiomerically pure C_3-symmetric polypyrazole ligand, tris[(4*S*,7*R*)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-2-indazolyl]phosphine oxide (OP(camphpz)$_3$, **2**). The new optically active complexes $[(\eta^3\text{-}\mathbf{2})\mathrm{Cu(CH_3CN)}]\mathrm{BF_4}$ (**3**), $[(\eta^3\text{-}\mathbf{2})\mathrm{Cu(X)}]$ (X = Cl (**4**), X = O_3SCF_3 (**5**)), and $[(\eta^2\text{-}\mathbf{2})\text{-}\mathrm{ZnCl_2}]$ (**6**) were prepared. Complex **3** catalyzed the cyclopropanation of styrene with ethyl and 2,6-di-*tert*-butyl-4-methylphenyl diazoacetates with ee's of up to 60%.

Bidentate optically active ligands containing a 2-fold rotation axis are well-established auxiliaries for metal-promoted enantioselective reactions.[1] Structural features cited to be responsible for the stereodifferentiating ability exhibited by complexes of this class of ligands include the close proximity of asymmetric ligand components to substrate binding sites on the metal atom and rotational symmetry-controlled limits on possible diastereomeric transition states. Tridentate ligands with higher order rotational symmetry[2,3] (C_3) may be even better at promoting asymmetric reactions, since greater steric interactions may result from the presence of three stereogenic centers in a metal complex rather than two and because there is the potential for rendering binding sites in complexes with higher coordination numbers (i.e., octahedral) symmetry-equivalent. To test this idea[3] experimentally, we have begun to prepare C_3-symmetric tridentate ligands that contain pyrazolyl donors with strategically placed stereogenic centers (structure A). Polypyrazole molecules were chosen for study because they are well-established ligands in organometallic and bioinorganic chemistry[4] and because related bidentate N-donor chelates recently have been shown to be effective auxiliaries in metal-catalyzed organic transformations.[1g,5,6] In this communication we



X = B, P, C, or N-centered fragment
R* = enantiomerically pure substituent

A

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(1) Reviews: (a) Whitesell, J. K. *Chem. Rev.* **1989**, *89*, 1581–1590. (b) Noyori, R.; Kitamura, M. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Springer-Verlag: Berlin, Heidelberg, Germany, 1989; Vol. 5, pp 114–198. (c) Ojima, I.; Clos, N.; Bastos, C. *Tetrahedron* **1989**, *45*, 6901–6939. (d) Brunner, H. *Top. Stereochem.* **1988**, *18*, 129–247. (e) Blystone, S. *Chem. Rev.* **1989**, *89*, 1663–1679. (f) Bosnich, B.; Fryzuk, M. D. *Top. Stereochem.* **1981**, *15*, 119–154. (g) Pfaltz, A. In *Modern Synthetic Methods*; Scheffold, R., Ed.; Springer-Verlag: Berlin, 1989; Vol. 5, pp 198–248. (h) Kagan, H. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: Orlando, FL, 1985; Vol. 5, pp 1–39.

(2) Monophosphines with C_3 symmetry: (a) Bolm, C.; Davis, W. M.; Halterman, R. L.; Sharpless, K. B. *Angew. Chem., Int. Ed. Engl.* **1988**, *27*, 835. (b) Bolm, C.; Sharpless, K. B. *Tetrahedron Lett.* **1988**, *29*, 5101–5104. (c) Bogdanovic, B.; Henc, B.; Meister, B.; Pauling, H.; Wilke, G. *Angew. Chem., Int. Ed. Engl.* **1972**, *11*, 1023–1024. A D_4-symmetric porphyrin: (d) Halterman, R. L.; Jan, S.-T. *J. Org. Chem.* **1991**, *56*, 5253–5254.

(3) C_3-symmetric triphosphines: (a) Burk, M. J.; Harlow, R. L. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1462–1464. (b) Burk, M. J.; Feaster, J. E.; Harlow, R. L. *Tetrahedron: Asymmetry* **1991**, *2*, 569–592. (c) Ward, T. R.; Venanzi, L. M.; Albinati, A.; Lianza, F.; Gerfin, T.; Gramlich, V.; Tombo, G. M. R. *Helv. Chim. Acta* **1991**, *74*, 983–988.

(4) Leading references for ligands that are B-centered: (a) Trofimenko, S. *Prog. Inorg. Chem.* **1986**, *34*, 115–210. (b) Shaver, A. In *Comprehensive Coordination Chemistry*; Wilkinson, G., Gillard, R. D., McCleverty, J. A., Eds.; Pergamon Press: Oxford, U.K., 1987; Vol. 2, pp 245–259. P-centered: (c) Joshi, V. S.; Kale, V. K.; Sathe, K. M.; Sarkar, A.; Tavale, S. S.; Suresh, C. G. *Organometallics* **1991**, *10*, 2898–2902. N-centered: (d) Sorrell, T. N.; Jameson, D. L. *Inorg. Chem.* **1982**, *21*, 1014–1019.

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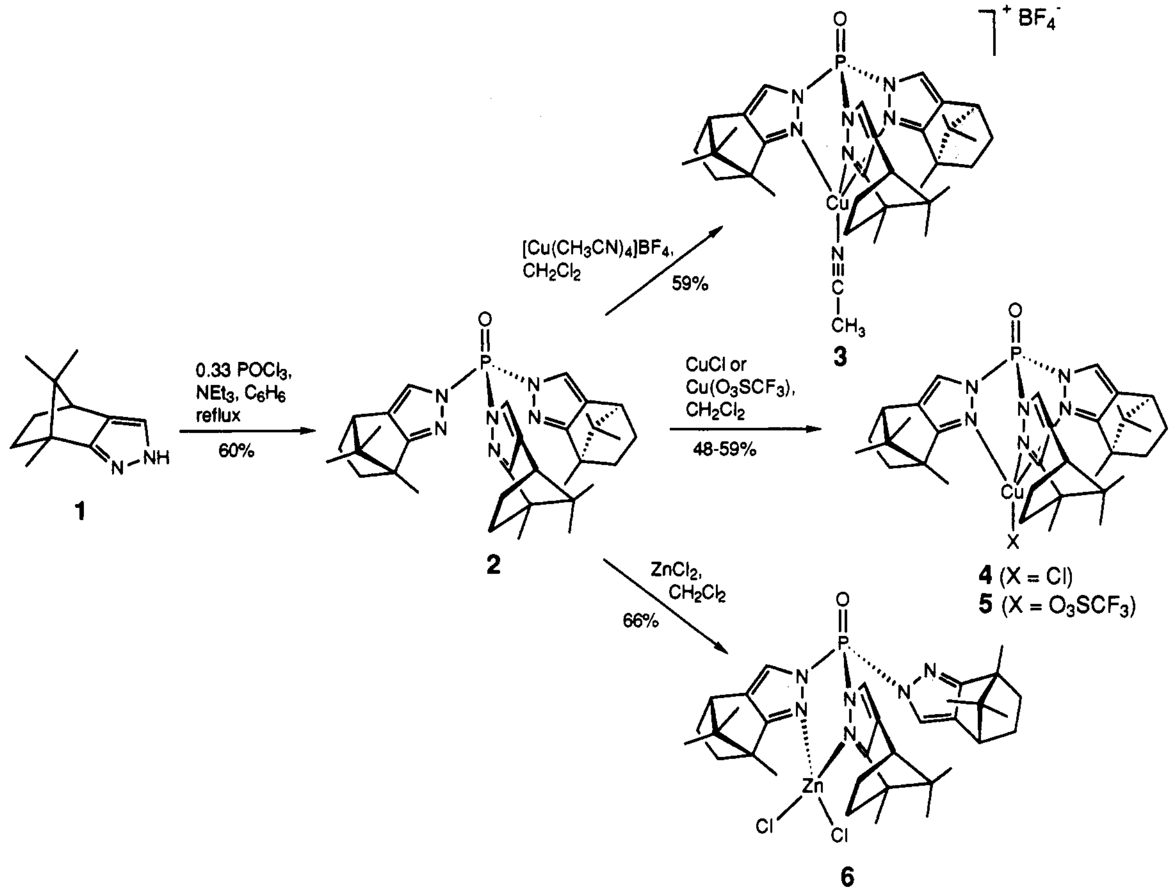
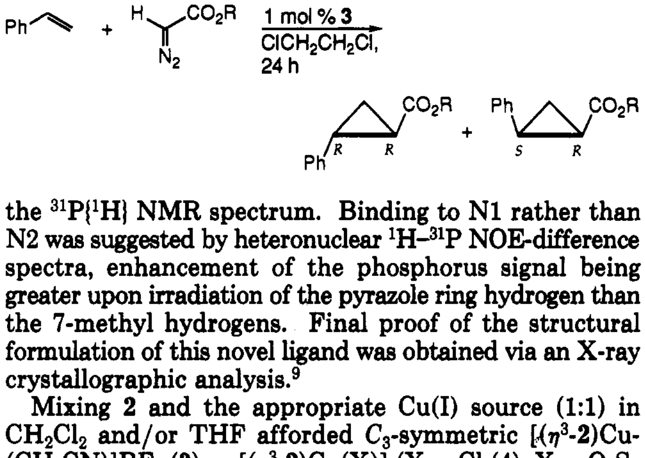
Scheme I



report the synthesis of the first such C_3-symmetric optically active polypyrazole ligand and its complexes with Cu(I) and Zn(II), as well as a preliminary demonstration of their use in asymmetric catalysis.

Ligand **2** (Scheme I) was obtained upon treatment of the camphor–pyrazole **1**[6a,c] with NEt$_3$ and OPCl$_3$ (0.33 equiv) in refluxing benzene (20 h, 60%).[7] In contrast to the lack of differentiation between the nitrogen atoms observed in previously reported functionalization reactions of **1**,[6a,8] spectroscopic data for **2** indicated regioselective bonding of each pyrazole to phosphorus via N1. Thus, the presence of three camphor–pyrazoles linked identically to a single O=P unit was evident from the single set of camphor–pyrazole resonances in the ^{1}H and ^{13}C NMR spectra and a lone resonance at −14.5 ppm (vs H$_3$PO$_4$) in the ^{31}P{^{1}H} NMR spectrum. Binding to N1 rather than N2 was suggested by heteronuclear ^{1}H–^{31}P NOE-difference spectra, enhancement of the phosphorus signal being greater upon irradiation of the pyrazole ring hydrogen than the 7-methyl hydrogens. Final proof of the structural formulation of this novel ligand was obtained via an X-ray crystallographic analysis.[9]

Scheme II



Mixing **2** and the appropriate Cu(I) source (1:1) in CH$_2$Cl$_2$ and/or THF afforded C_3-symmetric [(η^3-**2**)Cu(CH$_3$CN)]BF$_4$ (**3**) or [(η^3-**2**)Cu(X)] (X = Cl (**4**), X = O$_3$SCF$_3$ (**5**)), which were identified by analytical and spectroscopic methods (Scheme I).[7] A single set of camphor–pyrazole resonances in the ^{1}H and ^{13}C NMR spectra of **3**–**5** was consistent with the presence of 3-fold rotational symmetry in the complexes, and retention of the connectivity of the N1 atom of each pyrazole ring to the central phosphorus atom was confirmed by heteronuclear NOE-difference spectroscopic results for **3** analogous to those obtained for **2**. Reaction of **2** with ZnCl$_2$, on the other hand, resulted in bidentate coordination to afford pseudotetrahedral (η^2-**2**)ZnCl$_2$ (**6**), as indicated by NMR

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[5] (a) Bolm, C. *Angew. Chem., Int. Ed. Engl.* **1991**, *30*, 542–543. (b) Bolm, C.; Zehnder, M.; Bur, D. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 205–207. (c) Evans, D. A.; Woerpel, K. A.; Hinman, M. M.; Faul, M. M. *J. Am. Chem. Soc.* **1991**, *113*, 726–728. (d) Corey, E. J.; Imai, N.; Zhang, H.-Y. *J. Am. Chem. Soc.* **1991**, *113*, 728–729. (e) Nishiyama, H.; Sakaguchi, H.; Nakamura, T.; Horihata, M.; Kondo, M.; Itoh, K. *Organometallics* **1989**, *8*, 846–848. (f) Nishiyama, H.; Kondo, M.; Nakamura, T.; Itoh, K. *Organometallics* **1991**, *10*, 500–508. (g) Fritschi, H.; Leutenegger, U.; Pfaltz, A. *Helv. Chim. Acta* **1988**, *71*, 1553–1565. (h) Fritschi, H.; Leutenegger, U.; Siegmann, K.; Pfaltz, A.; Keller, W.; Kratky, C. *Helv. Chim. Acta* **1988**, *71*, 1541–1552. (i) Matt, P. v.; Pfaltz, A. *Tetrahedron: Asymmetry* **1991**, *2*, 691–700. (j) Leutenegger, U.; Umbricht, G.; Fahrni, C.; Matt, P. v.; Pfaltz, A. *Tetrahedron* **1992**, *48*, 2143–2156. (k) Lowenthal, R. E.; Masamune, S. *Tetrahedron Lett.* **1991**, *32*, 7373–7376. (l) Ahn, K.-H.; Klassen, R. B.; Lippard, S. J. *Organometallics* **1990**, *9*, 3178–3181.

[6] Optically active pyrazoles: (a) Watson, A. A.; House, D. A.; Steel, P. J. *J. Org. Chem.* **1991**, *56*, 4072–4074 and references therein. (b) Brunner, H.; Scheck, T. *Chem. Ber.* **1992**, *125*, 701–709. (c) Nagai, S.-I.; Oda, N.; Ito, I. *Yakugaku Zasshi* **1979**, *99*, 699–704.

[7] Syntheses and analytical and spectroscopic data for all new compounds are presented in the supplementary material.

[8] In attempts to prepare KHB(camphpz)$_3$ by thermolysis of **2** with KBH$_4$, we obtained a mixture of products, presumably derived from linkage of both N1 and N2 to boron (^{1}H NMR).

[9] X-ray data for **2**, C$_{33}$H$_{45}$N$_6$OP, M_r 572.73, space group $P2_1$ (No. 4) at 24 °C: a = 6.841 (4) Å, b = 18.657 (8) Å, c = 12.633 (4) Å, β = 103.62 (4)°, V = 1567 (2) Å^3, Z = 2. For 2564 unique, observed reflections with $I > 2\sigma(I)$ and 369 variable parameters R = 0.052 and R_w = 0.057. Full tables of positional and thermal parameters, as well as bond lengths and angles, are reported in the supplementary material.

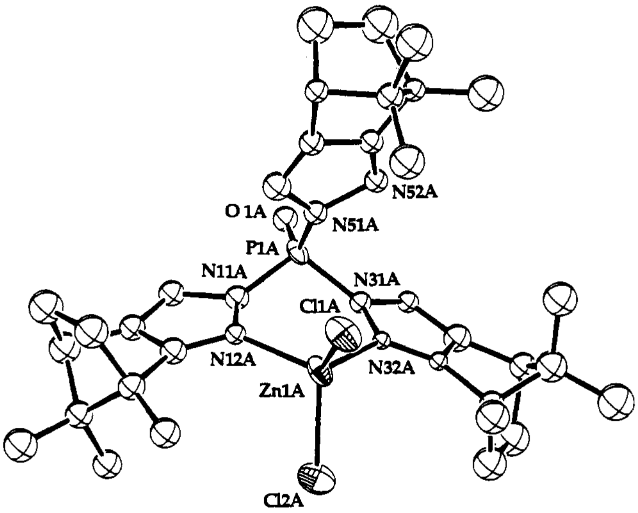

Figure 1. ORTEP drawing of one of the independent molecules of 6·$2CH_2Cl_2$ showing 60% probability thermal ellipsoids (Zn, Cl, and P anisotropic, the remaining isotropic) and atom labels for all non-hydrogen atoms (excluding CH_2Cl_2 solvate molecules; atom labels for carbon atoms omitted for clarity). Selected interatomic distances (Å) and angles (deg) are as follows: Zn1A–Cl1A, 2.221 (5); Zn1A–Cl2A, 2.234 (6); Zn1A–N12A, 2.04 (2); Zn1A–N32A, 2.04 (2); P1A–O1A, 1.42 (1); P1A–NA (average), 1.66 (2); Cl1A–Zn1A–Cl2A, 116.9 (2); Cl1A–Zn1A–N12A, 111.8 (4); Cl1A–Zn1A–N32A, 114.6 (4); Cl2A–Zn1A–N12A, 108.0 (4); Cl2A–Zn1A–N32A, 104.2 (4), N12A–Zn1A–N32A, 99.5 (6).

spectroscopy and a preliminary X-ray crystal structure determination (Figure 1).[10] Not surprisingly,[11] variable-temperature ^1H NMR data obtained for 6 revealed that exchange of coordinated and free pyrazolyl rings occurred in solution ($\Delta G^{\ddagger}$ = 11.9 (2) kcal mol^{-1}).

In a first attempt to assess the propensity of the C_3-symmetric species to effect enantioselective reactions, we examined the cyclopropanation of styrene with ethyl and 2,6-di-*tert*-butyl-4-methylphenyl diazoacetates, reactions known to be catalyzed by Cu(I) reagents possessing N-donor ligands.[5c,g–j,12] After high catalytic efficiency was first demonstrated with its similarly sterically hindered yet achiral analog [(η^3-(*t*-Bupz)$_3$PO)Cu(CH_3CN)]BF_4 (7; 75% yield of a 1.6:1 mixture of trans (anti) and cis (syn) cyclopropanes with 1.0 mol % Cu(I) complex), stereoselectivities were assessed by using optically pure 3 as catalyst (Scheme II, Table I). We note from our initial runs that (a) % ee's exhibit only a moderate temperature dependence and (b) an increase in the trans (anti)/cis (syn) ratio and a dramatic decrease in % ee occur upon using the sterically hindered aryl diazo ester.[13] Although moderate, the observed ee's for the cis (syn) product of up to 60% are promising indications of useful applications of the new ligand and its 3-fold-symmetric complexes toward asymmetric synthesis. In future work we will explore such applications, as well as the design and synthesis of new members of the class of ligands represented by structure A that contain central atoms and stereogenic centers complementary to those within the camphor-based system described herein.

Table I. Results of Catalysis by 3 of Cyclopropanation of Styrene with Diazo Esters RO_2CCHN_2 (See Scheme II)

R	temp, °C	yield, %	trans (anti)/ cis (syn) ratio	% ee trans (anti)/ cis (syn)[a]
Et	22	52	0.8	31/51
Et	0	64	0.6	37/57
Et	−78	48	0.6	40/60
BHT[b]	22	94[c]	23[d]	10[e]/···

[a] Enantiomeric excesses and the indicated absolute configurations (Scheme II) of the major stereoisomers were determined by GC and NMR analyses, respectively, of diastereomeric amides prepared from (*S*)-(−)-α-methylbenzylamine according to a published procedure.[5c] [b] 2,6-Di-*tert*-butyl-4-methylphenyl.[13] [c] 3 mol % catalyst. [d] After $LiAlH_4$ reduction to the corresponding cyclopropylcarbinol.[5c] [e] Determined via ^{19}F NMR analysis of the Mosher ester.

Acknowledgment. We thank Professor Doyle Britton for his work on the X-ray crystal structure determinations as well as the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the University of Minnesota for financial support.

Supplementary Material Available: Text giving synthetic procedures and analytical and spectroscopic data for 2–7, an ORTEP drawing of 2, and tables of bond lengths and angles as well as atomic positional and thermal parameters for 2 and 6·$2CH_2Cl_2$ (51 pages). Ordering information is given on any current masthead page.

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[10] (a) The preliminary X-ray crystal structure of chiral 6·$2CH_2Cl_2$ was found to be pseudocentrosymmetric,[10b] and solution and refinement in space group *P*1 was only possible by using the following procedure. The Zn, Cl, P, and pyrazolyl ring atoms were located by using the space group $P\bar{1}$, but the camphor ring atoms were obscured by the pseudosymmetry. A rigid group for the camphor unit (including two C atoms of the pyrazolyl ring) was constructed by averaging the bond distances and angles of the three independent camphor–pyrazole groups in the X-ray structure of 2. Placement of the rigid group in the six positions of the two molecules of 6 in the unit cell was followed by refinement in *P*1 with group constraints in place but individual *B*(eq) values for all atoms. X-ray data for 6·$2CH_2Cl_2$, $C_{35}H_{49}Cl_8N_6OPZn$, M_r 878.88, space group *P*1 (No. 1) at −101 °C: a = 11.768 (8) Å, b = 12.451 (4) Å, c = 15.43 (1) Å, α = 108.00 (4)°, β = 102.84 (5)°, γ = 95.31 (4)°, V = 2065 (5) Å^3, Z = 2. For 3412 unique, observed reflections with $I > 2\sigma(I)$ and 334 variable parameters R = 0.064 and R_w = 0.079. Full tables of positional and thermal parameters, as well as bond lengths and angles, for both independent molecules in the unit cell are reported in the supplementary material. (b) For a related case, see: Wallix, J. D.; Dunitz, J. D. *Acta Crystallogr., Sect. C* **1988**, *44*, 1037–1039.

[11] See, for example: Reger, D. L.; Huff, M. F.; Rheingold, A. L.; Haggerty, B. S. *J. Am. Chem. Soc.* **1992**, *114*, 579–584.

[12] Doyle, M. P. *Chem. Rev.* **1986**, *86*, 919–939.

[13] Doyle, M. P.; Bagheri, V.; Wandless, T. J.; Harn, N. K.; Brinker, D. A.; Eagle, C. T.; Loh, K.-L. *J. Am. Chem. Soc.* **1990**, *112*, 1906–1912.