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One-Pot Synthesis of an Enantiopure N,N,O Scorpionate Ligand Derived from (+)-Camphor

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Dedicated to Professor Horst Kisch on the occasion of his 65th birthday

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A one-pot synthesis of the new enantiopure heteroscorpionate ligand HOPhbpm^{3cam} (**3**) was described. Ligand **3** was obtained in a pyridine-catalysed Peterson rearrangement starting from camphorpyrazole, thionyl chloride, and salicylaldehyde. κ^2- and κ^3-coordination of the ligand was observed, and the ligand was shown to form a tetrahedral zinc complex [Zn-κ^3-(OPhbpm^{3cam})CH$_3$] (**4**) as well as an octahedral rhenium complex [Re-κ^3-(OPhbpm^{3cam})(CO)$_3$] (**6**).

Introduction

During the last decade, various bis(pyrazolyl)methane-based “heteroscorpionate” ligands have been recognised as very versatile ligands for bioinorganic chemistry and organometallics.[1–3] Specifically, several achiral tripodal N,N,O and N,N,S ligands were reported by Carrano and coworkers that can be obtained from 1,1′-carbonylbis(pyrazole) and functionalised aldehydes.[3–5] This cobalt-catalysed reaction, in which CO$_2$ is released, is based on some early reports from the 1970s by Peterson and Thè[6] and was recently modified by Reger to involve aldehyde and 1,1′-sulfinylbis(pyrazole).[7] First applications of group 4 metal complexes bearing these tridentate heteroscorpionate ligands consist of catalytic ethylene and propylene polymerisation.[8]

Results and Discussion

Recently, we reported on a rather simple concept based on prochirality that allows us to synthesise enantiopure facially binding tripod ligands from C_2 symmetric precursors without any additional separation of enantiomers or diastereomers.[9] C_2 symmetry is a feature often used in enantiopure bidentate chelating ligands.[10] In many of these, two identical enantiopure donor groups, Y*, are connected by a tetrahedral bridging atom, for example, an sp^3 carbon atom. Any additional group, Z, at this atom will form a prochiral centre rather than an additional stereocentre (Figure 1).[11]

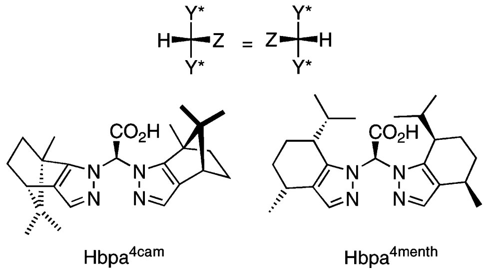

Figure 1. Prochirality in the enantiopure ligands Hbpa^{4cam} and Hbpa^{4menth}.[9]

So far, two examples of enantiopure N,N,O tripod ligands based on this concept were published by our group, namely, bis(camphorpyrazol-1-yl)acetic acid Hbpa^{4cam} and bis(menthylpyrazol-1-yl)acetic acid Hbpa^{4menth} (Figure 1).[9] Other bis(pyrazolyl)methane-derived enantiopure tripod ligands were reported by Otero and coworkers recently.[12] Here we report on a one-step synthesis of an enantiopure N,N,O scorpionate ligand HOPhbpm^{3cam} (**3**) derived from (+)-camphor by using a modified version of the Peterson cobalt rearrangement that does not require the cobalt catalyst.

Camphorpyrazole **1** [i.e. (4*S*,7*R*)-7,8,8-trimethyl-4,5,6,7-tetrahydro-4,7-methano-1(2)H-indazole] is an enantiopure pyrazole derived from the chiral pool that can be obtained easily and in high yield in a two-step synthesis starting from (+)-camphor.[13] Reaction of **1** with phosgene to afford 2,2′-carbonylbis(camphorpyrazole) (**2b**) was previously described in a footnote by Rebek and coworkers.[14]

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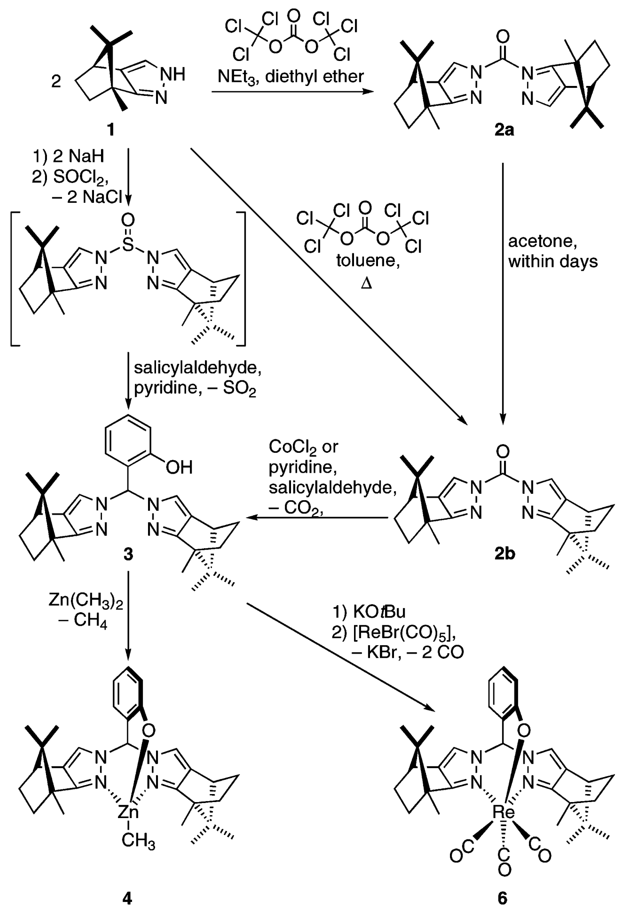
According to a very recent report by Artaud, phosgene can be replaced in such carbonylbis(pyrazole) syntheses by triphosgene.[15] We now found that reaction of **1** with triphosgene and triethylamine first gives the C_1 symmetrical isomer of 1,2′-carbonylbis(camphorpyrazole) (**2a**), which is transformed into the C_2 symmetrical 2,2′-carbonylbis(camphorpyrazole) (**2b**) upon standing in solution within some days (Scheme 1).



Scheme 1. Synthesis of homochiral heteroscorpionato complexes.

A reaction under reflux in toluene or benzene gives only the desired C_2 symmetrical 2,2′-carbonylbis(camphorpyrazole) (**2b**) in very high yield (Scheme 1). An X-ray structure determination of isomer **2b** (Figure 2) allows doubtless differentiation between the two isomers.

Furthermore, only one set of camphorpyrazole signals is observed in the ^{1}H and ^{13}C NMR spectra of **2b**, as to be expected for a C_2 symmetric compound, which is in contrast to the two sets of signals observed in the spectra of **2a**.

To test our concept of "prochirality-based" ligands with a new N,N,O tripod ligand, we then synthesised (*o*-hydroxyphenyl)bis(camphorpyrazol-1-yl)methane HOPhbpm^{3cam} (**3**) by applying the cobalt-catalysed Peterson rearrangement of **2b** with salicylaldehyde.[16] Unfortunately, the yield of this reaction was quite erratic; this observation was also made by various other groups who used the Peterson rearrangement for their syntheses. We thus developed an alternative procedure for this reaction to which we were inspired by a publication of Canty and coworkers.[17] They reported on a coupling of 1,1′-carbonylbis(3,5-dimethylpyrazole) and pyridine-2-aldehyde without any cobalt catalyst.[17] Indeed, a similar reaction of **2b**, pyridine and salicylaldehyde yields the ligand (*o*-hydroxyphenyl)bis(camphorpyrazol-1-yl)methane HOPhbpm^{3cam} (**3**) in reproducible yields up to 70% (Scheme 1) without the use of the cobalt catalyst. The synthetic procedure was modified further by us according to the version of Reger for the Peterson rearrangement, which we mentioned above, involving the aldehyde and 1,1′-sulfinylbispyrazole. Thereby, we finally developed a one-pot synthesis for (*o*-hydroxyphenyl)bis(camphorpyrazol-1-yl)methane HOPhbpm^{3cam} (**3**) starting with the reaction of camphorpyrazole (**1**) with sodium hydride and thionyl chloride. Without any further purification, pyridine and salicylaldehyde were added to the resulting 2,2′-sulfinylbis(camphorpyrazole) to yield ligand **3** in yields up to 60%. After the reaction was scaled up, we were able to obtain up to 7 g of enantiopure ligand **3** in one run. Because of the loss of C_2 symmetry, the two pyrazole donors are no longer spectroscopically equivalent and two sets of signals in the ^{1}H and ^{13}C NMR spectra are exhibited.

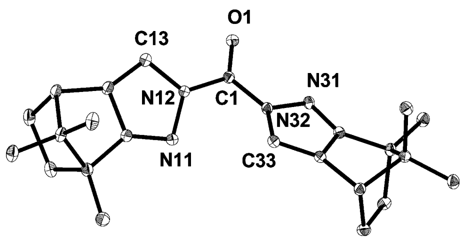


Figure 2. Molecular structure of 2,2′-carbonylbis(camphorpyrazole) (**2b**); thermal ellipsoids are drawn at the 50% probability level; hydrogen atoms are omitted for better clarity. Selected bond lengths [Å] and angles [°]: C1–O1 1.204(2), C1–N32 1.392(3), C1–N12 1.402(3), O1–C1–N32 123.93(19), O1–C1–N12 121.0(2), N32–C1–N12 115.07(18).

Treatment of ligand **3** with dimethylzinc resulted in very pure monomethylzinc complex [Zn(OPhbpm^{3cam})CH$_3$] (**4**) and methane without any formation of bis(ligand) complex [Zn(OPhbpm^{3cam})$_2$]. In the NMR spectra, the methyl group in **4** (^{1}H NMR: δ = –0.60 ppm; ^{13}C NMR: δ = –14.6 ppm) is observed at high field. This agrees well with the complex [Zn(bpa^{Me_2,tBu_2})CH$_3$] reported recently by us and with the sterically hindered (*o*-hydroxyphenyl)bis(pyrazol-1-yl)methane zinc complex published by Carrano and coworkers.[4d,18]

In an attempt to synthesise the chlorido complex [Zn(κ^3-*N*,*N*,*O*-OPhbpm^{3cam})Cl], colourless crystals of [Zn(κ^2-*N*,*N*-HOPhbpm^{3cam})(Cl)$_2$] (**5**) were obtained from an acetonitrile solution.

The molecular structure (Figure 3) clearly shows κ^2-coordination of the ligand, similar to the achiral complex [Zn(κ^2-*N*,*N*-HOPhbdmpzm)(*I*)$_2$] [HOPhbdmpzm: *ortho*-(hydroxyphenyl)bis(dimethylpyrazol-1-yl)methane] recently reported by Carrano and coworkers.[4d] The molecular structure of **5** is proof of the constitution of the HOPhbpm^{3cam} ligand (**3**). It has to be emphasised that in this new ligand the chiral camphorpyrazolyl donors are pointing towards the zinc centre. This is different from our former ligands and makes this ligand a promising candidate for future enantioselective inductions.

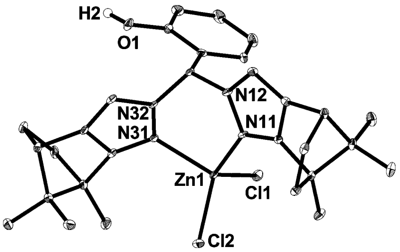


Figure 3. Molecular structure of [Zn(κ^2-*N*,*N*-HOPhbpm^{3cam})(Cl)$_2$] (**5**); thermal ellipsoids are drawn at the 50% probability level; most hydrogen atoms are omitted for better clarity. Selected bond lengths [Å] and angles [°]: Zn–Cl1 2.2267(8), Zn–Cl2 2.2293(7), Zn–N11 2.053(2), Zn–N31 2.089(2), Zn–N31–N32 111.92(16), Zn–N11–N12 122.78(17), N11–Zn–N31 94.20(9), N11–Zn–Cl2 108.64(7), N31–Zn–Cl2 119.39(6), N11–Zn–Cl1 112.42(7), N31–Zn–Cl1 107.79(6), Cl2–Zn–Cl1 113.01(3).

Reaction of K[OPhbpm^{3cam}] with [ReBr(CO)$_5$] resulted in a complex [Re(OPhbpm^{3cam})(CO)$_3$] (**6**). Elemental analysis, FAB MS [M + H]$^+$ peak and, pursuant to C_1 symmetry, three class A carbonyl vibrations at 2018, 1910 and 1881 cm^{-1} indicate κ^3-coordination of the ligand and formation of an octahedral complex.

Conclusions

Chiral modification of the well-established (2-hydroxyphenyl)bis(pyrazol-1-yl)methane ligands leads to the new enantiopure heteroscorpionate ligand (2-hydroxyphenyl)bis(camphorpyrazol-1-yl)methane HOPhbpm^{3cam} (**3**). This ligand provides similar coordination properties as its achiral analogues, which was proven by the synthesis of a tetrahedral monomethylzinc complex and an octahedral tricarbonylrhenium complex. The simple one-pot synthesis, starting from camphorpyrazole, thionyl chloride and salicylaldehyde, should allow broad application of this and related ligands in coordination chemistry, especially because the achiral analogues have already shown their potential for catalytic processes. Furthermore, it is obvious that in the future a broad spectrum of similar homochiral tripod ligands should be accessible by variations of this one-pot synthesis.

Supporting Information (see footnote on the first page of this article): Experimental details and X-ray data for **2b** and **5**.[19]

Acknowledgments

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[16] To avoid extraordinarily long abbreviations, the abbreviation system for Tp and benzopyrazolylborate Tp^{Bo} ligands introduced by Trofimenko was transferred to this manuscript. A superscript of 3 preceding "cam" indicates a 3,4-fusion of the camphor group to the pyrazole. This results in the abbreviation HOPhbpm^{3cam} (**3**). For further details see: S. Trofimenko, *Scorpionates – The Coordination Chemistry of Polypyrazolylborate Ligands*, Imperial College Press, London, **1999**, p. 5.

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[19] Crystallographic data for **2** ($C_{23}H_{30}N_4O$): crystal dimensions $0.50 \times 0.40 \times 0.30$ mm^3, monoclinic space group $P2_1$, a = 6.7212(13) Å, b = 12.544(3) Å, c = 25.060(5) Å, β = 90.32(3)°, V = 2112.7(8) Å^3, Z = 4, $\rho_{calcd.}$ = 1.190 g cm^{-3}, $2\Theta_{max}$ = 58.5°, Mo-K_α radiation, λ = 0.71073 Å, T = 100 K, 28855 reflections

collected, 5896 independent reflections (R_{int} = 0.0834), 5474 reflections used with $I > 2\sigma$, R = 0.0459, wR = 0.1150. Crystallographic data for **5** ($C_{29}H_{36}Cl_2N_4OZn \cdot 2CH_3CN$): crystal dimensions $0.23 \times 0.22 \times 0.18$ mm^3, triclinic space group $P1$, a = 7.7111(3) Å, b = 14.5669(15) Å, c = 15.577(2) Å, α = 80.438(8)°, β = 87.859(6)°, γ = 80.738(5)°, V = 1702.8(3) Å^3, Z = 2, $\rho_{\text{calcd.}}$ = 1.316 g cm^{-3}, $2\Theta_{\max}$ = 59.0°, Mo-K_α radiation, λ = 0.71073 Å, T = 100 K, 44677 reflections collected, 17289 independent reflections (R_{int} = 0.0358), 14660 reflections used with $I > 2\sigma$, R = 0.0334, wR = 0.0734, Flack parameter: 0.020(6). The structures were solved by using direct methods and refined with full-matrix least-squares against F^2 (Siemens SHELX-97).[20] A weighting scheme was applied in the last steps of the refinement with $w = 1/[\sigma^2(F_o^2) + (aP)^2 + bP]$ and $P = [2F_c^2 + \max(F_o^2,0)]/3$. Most hydrogen atoms were included in their calculated positions and refined in a riding model. The phenol proton (**5**) was found and its coordinates were refined isotropically. Pictures were prepared with the program Diamond 2.1e.[21] CCDC-651140 (for **2b**) and -651141 (for **5**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

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