Fabian Thomas, Dominik Steden, Alexander Eith, Alexander Hoffmann and Sonja Herres-Pawlis

Chiral bis(pyrazolyl)methane copper(l) complexes and their application in nitrene transfer reactions

https://doi.org/10.1515/znb-2021-0140
Received September 14, 2021; accepted October 7, 2021; published online October 29, 2021

Abstract: In this study, chiral bis(pyrazolyl)methane copper(I) acetonitrile complexes were applied to generate two novel terminal copper tosyl nitrene complexes with the nitrene generating agent SPhINTs in dichloromethane at low temperatures. The syntheses of the chiral bis(pyrazolyl) methane ligands are based on pulegone and camphor, members of the natural chiral pool. The chiral copper(I) acetonitrile complexes were applied as catalysts in the copper nitrene mediated aziridination reaction of different styrene derivatives and the C–H amination of various substrates. The reactions afforded good yields, but low enantioselectivity under mild conditions. The nitrene species have been characterized with UV/Vis and EPR spectroscopy and the products of the decay by ESI mass spectrometry.

Keywords: asymmetric catalysis; aziridination; copper; N-donor ligands; terminal nitrenes.

Dedicated to: Professor Richard Dronskowski of the RWTH Aachen on the occasion of his 60th birthday.

1 Introduction

Nitrogen-containing motifs are found in a variety of synthetically [1], biologically [2] and pharmaceutically [3] relevant molecules. In biologically and pharmacologically active molecules, asymmetric amines are of high interest [4, 5]. Nitrogen-containing motifs are achieved by direct functionalization of unreactive C–H bonds with high atom efficiency [6–9]. This can be approached synthetically by inserting a metal-bound nitrene into a C–H bond [10, 11] and a variety of suitable metals and ligands can be used [12–16]. Due to their low cost, low toxicity and good environmental compatibility copper complexes were studied extensively. Reaction protocols for catalytic C–H aminations [17–24], N-group transfer [17, 25–38] and asymmetric aziridination [39–45] were developed, while also asymmetric cobalt-catalyzed C–H amination reactions [46] were developed. For these copper-catalyzed reactions the key intermediates have been proposed to be copper nitrene complexes based on experimental [43, 47] and theoretical [17, 23, 37, 48–52] investigations.

Essential for the reactivity is the presence of terminal copper nitrene complexes, which mediate the reactivity [17, 18, 23, 37, 38, 43, 47–54]. In the literature only a limited number of stable copper nitrene complexes are presented (Figure 1). Pioneer work on copper nitrene complexes was carried out by the Warren group, who reported the molecular structure of different μ-nitrene-bridged dicopper complexes stabilized by anionic NacNac ligands. Catalytic reactivity is observed due to the dissociation of the dimetallic complex into a terminal copper nitrene complex [47, 55, 56]. The catalytic reactivity of this system was further investigated and various nitrene generating agents and substrates were successfully applied [24, 57]. The Ray group reported stable copper nitrene complexes coordinated by neutral amine ligands. These can be stabilized by incorporation into an azamacrocycle [58] or by the addition of scandium(III) triflate [59, 60]. While the latter copper nitrene complex can be generated from azides and iminiodanimane, the iminiodanimane nitrene complexes tend to give a tautomeric copper imidyl form [61]. The Bertrand group presented stable copper nitrenes synthesized from a metal free phosphonitrene. The phosphonitrene can coordinate in different stoichiometries and forms a μ-nitrene-bridged, a terminal nitrene and a twofold coordinated species [62]. In contrast to those singlet copper nitrene complexes, the Betley group reported a terminal copper nitrene complex in the triplet state stabilized by...
a sterically demanding dipyrrol ligand. The complex was characterized using XAS and NMR spectroscopy and multi-reference calculations of a truncated system. Furthermore, it was shown that the nitrene complex is capable of mediating catalytic aziridination and C–H amination reactions [63]. In previous work, our group presented a series of terminal singlet bis(pyrazolyl)methane copper nitrene complexes. These nitrene complexes were stabilized and characterized at low temperature. It was shown that the ligand design of the used bis(pyrazolyl)-methane ligands is crucial for the stability and the reactivity of the copper nitrene complexes. Additionally, protocols for aziridination reactions and C–Hamination of different substrate classes under mild conditions were developed. Furthermore, the mechanism of the aziridination was studied theoretically and experimentally. It could be shown that the aziridination of styrene mainly follows a singlet pathway [64, 65].

Herein, heteroscorpionate ligands of the bis(pyrazolyl)-methane family were used. This ligand family was chosen because it was shown in the past that these ligands can be tailor-made for a variety of applications [66]. This includes a tyrosinase-like catalytic phenol hydroxylation [67–70], the oxidation of benzylalcohols with modified microgels [71], a palladium-free Sonogashira cross coupling [72, 73] and the asymmetric cyclopropanation of styrene [74–76].

2 Results and discussion

2.1 Synthesis and characterization of ligands and copper complexes

Three novel bis(pyrazolyl)methane ligands were synthesized. Two of the ligands are based on molecules of the chiral pool, namely on a modified pulegone moiety (HC(PulPz)2Py, L1) or on a camphor moiety (HC(CamPz)2Py, L2). In contrast, the third ligand has sterically demanding groups on the pyridine and on the pyrazolyl units (HC(BuPz)2(6-CO2MePy), L3, Figure 2) but no chiral information.

The ligands L1 and L2 were synthesized to study the influence of the steric demand of different pyrazolyl units whereas in L3 the influence of a sterically demanding pyrazolyl unit and a substituted pyridine unit were evaluated. All three bis(pyrazolyl)methane ligands were synthesized by a modified Peterson rearrangement [77]. Therefore, the used pyrazole was deprotonated by sodium hydride in THF. In the next step thionyl chloride was added to form a bis(pyrazolyl)-sulfonyl species. This species is rearranged by cobalt(II) chloride and an aldehyde to the ligand. For the ligands L1 (73%) and L3 (59%) high yields were obtained, while for L2 only a yield of 26% was observed. By adding [Cu(MeCN)4]PF6 to the ligand solution, the copper(I) acetonitrile complexes were obtained and isolated for all three ligands (C1: [CuL1(MeCN)]PF6, C2: [CuL2(MeCN)]PF6, C3: [CuL3(MeCN)]PF6, Figure 3). The complex C2 is not stable in pure acetonitrile or in acetonitrile-free solution, whereas the formation of the dinuclear complex C4 ([CuL2]2(PF6)2, Figure 3) is observable thanks to a color change from pale yellow to intense yellow.
The instability of \( C_2 \) in solution also limited the scale of the synthesis of \( C_2 \). The equilibrium of both complexes in a solution can be pushed to \( C_2 \) by the addition of 10 equivalents of acetonitrile in relation to \( C_2 \). For further application, \( C_2 \) was synthesized in situ from dissolved \( C_4 \) by the addition of 20 equivalents of acetonitrile to a dichloromethane solution of \( C_4 \). Starting from a solution of \( C_4 \), the formation of \( C_2 \) can also be observed by a change of the electrochemical properties (Table S1, Supplementary material available online; see the link given at the end of the paper) and the differences in the NMR spectra (Figure S8). For both complexes an irreversible one electron transfer is observed in the CV measurements. Furthermore, it is noticeable that the potential of \( C_2 \) (630 mV) is lower than for \( C_4 \) (1230 mV). Of the four novel copper(I) complexes three could be analyzed with single crystal X-ray diffraction. The cations of the three complexes are shown in Figure 4 (ellipsoid plots: see Figure S6), key bond lengths and angles are presented in Table 1 and the crystallographic details are given in Table S6 (SI). In \( C_3 \), four independent molecules are found in the asymmetric unit with equal (within the standard deviation) or very similar bond lengths and angles. Therefore, only the bond lengths and angles of one copper complex are given in Table 1 (for the other independent molecules: see Table S7). The torsion angle between the pyridine group and the carbonyl group varies between \(-16.7(1)^\circ\) and \(156.3(1)^\circ\) (see Table S7). In the three copper(I) complexes \( C_1 \), \( C_3 \) and \( C_4 \), the copper ion is distorted tetrahedrally coordinated. In \( C_1 \) and \( C_3 \), the copper ion is coordinated by the two N-donor atoms of the pyrazolyl units, the N-donor of the pyridine unit and the N-donor of the coordinating acetonitrile molecule. The bond length of the pyridinyl N-donor in \( C_3 \) is elongated in comparison to \( C_1 \) due to the different electronic influence of the substituted pyridinyl unit [67]. In \( C_4 \) each copper ion is coordinated by a pyridine and a pyrazolyl unit from one ligand and a pyrazolyl unit from the second ligand. The N-donor of the pyridinyl unit acts as bridge between both copper ions.

The complex \( C_1 \) can be compared with different bis(pyrazolyl)methane complexes with different substituted pyrazolyl units, for example with phenyl [65], tert-butyl [64] or CF\(_3\) [64] substituted pyrazolyl units. It is observed that the nature of the substitution of the pyrazolyl unit leads to slightly different pyrazolyl copper bond lengths, which are the same within the 3\( \sigma \) error margin (\( C_1 \): 2.046(4) Å, 2.100(5) Å, \[Cu(PhPz)_2Py\]([MeCN])PF\(_6\): 2.066(3) Å, 2.067(3) Å, \[Cu\{HC(\text{t}BuPz)2Py\}([MeCN])PF\(_6\): 2.056(2) Å, 2.107(2) Å, \[Cu\{HC(CF\(_3\)Pz)2Py\}([MeCN])HCPF\(_6\): 2.089(6) Å, 2.093(5) Å).

Complex \( C_3 \) can be compared to the literature known complex \[Cu\{HC(\text{t}BuPz)2Py\}([MeCN])PF\(_6\) [64]. The copper pyridinyl bond length is elongated in \( C_3 \) compared to the reference complex (2.088(3) Å), indicating that through the introduction of the methyl ester group the donor strength is lowered. This effect was also reported for the complex \[Cu\{HC(BuPz)2(4-CO\(_2\)MePy)}Br] [67], were the methyl ester group is in a different position on the pyridinyl ring. A comparison between this complex (2.153(3) Å) and \( C_3 \) is difficult, due to the coordinating bromido anion.

When the dinuclear complex \( C_4 \) is compared to the dinuclear complex \[Cu\(_2\{(Ph\_Pz)2MeIm\}2\](PF\(_6\))\(_2\) [65] it is observed that the Cu–Cu bond length (2.568(1) Å: \( C_4 \):...
2.2 Synthesis and characterization of the copper nitrene complexes

Two novel chiral copper nitrene complexes were generated from the copper(I) acetonitrile complex and SPhINTs (2-(tert-butyl-sulfonyl)(p-toluenesulfonyliminoido)benzene) in dichloromethane at low temperature. The reaction is shown in Figure 5 (top) on the example of C2. For both nitrene complexes a $\tau$-coordination of the nitrene fragment is assumed, due to observations with previously investigated bis(pyrazolyl)methane nitrene complexes [64, 65]. The reaction is indicated by a color change from colorless to an intense green and was monitored by UV/Vis spectroscopy. For C1 the formation of a nitrene complex $\{\text{CuI}_{\text{L1}}\}(\text{NTs})$ can be observed at $\sim$80 °C. The formation of the nitrene complex $\{\text{CuII}_{\text{L2}}\}(\text{NTs})$ from C2 needs higher temperature and a slow reaction between the copper(I) complex and SPhINTs can be observed at $\sim$63 °C. In contrast, for the complexes C3 and C4 no formation of a stable nitrene complex could be observed. The nitrene formation starting from C1 and C2 is indicated in the UV/Vis spectra by two characteristic bands for terminal bis(pyrazolyl)methane copper nitrene complexes: one strong transition ($\epsilon \approx 4000–7000$ L mol$^{-1}$ cm$^{-1}$) at about 410–420 nm and a weak transition ($\epsilon \approx 500–1000$ L mol$^{-1}$ cm$^{-1}$) at about 620–650 nm (Figure 5, bottom) [64, 65].

The herein reported copper nitrene complexes have been characterized with previously established UV/Vis experiments for bis(pyrazolyl)methane copper nitrene...
complexes [64, 65]. This was achieved by a titration of \(^{5}\text{PhINTs}\) against the copper(I) acetonitrile complex at low temperature (Figure S3). For the complex C1 the maximum in absorption was achieved after the addition of 1.0 equiv. of \(^{5}\text{PhINTs}\), while for the complex C2 the absorption maximum was reached after the addition of 0.8 equivalent. This observation results from the slow reaction between \(^{5}\text{PhINTs}\) and C2 and the low stability of \(^{5}\text{PhINTs}\) in solution. The formation of a nitrene from C2 has further been confirmed by the observation of \([\text{N}2-\text{H}]^+\) and \([\text{N}2+\text{H}]^+\) in the ESI mass spectrum of the decayed species (Figure S7 [SI]) while in the ESI mass spectrum of the decay products of \(\text{NIPF}_6\) only \([\text{CuL}]^+\) was observed. The decay species can be the product of an intra or inter molecular H atom abstraction or addition [64]. The H atom addition is assumed on the nitrene nitrogen atom, while the abstraction can take place in the apical position or on the substituent of the pyrazolyl unit. The nitrene species \(\text{NIPF}_6\) and \(\text{N2PF}_6\) are terminal copper nitrene complexes analogous to those presented in our previous publications [64, 65].

The thermal stability of both chiral copper nitrene complexes was investigated. The nitrenes were generated at \(-80^\circ\text{C}\) for \(\text{NIPF}_6\) or \(-63^\circ\text{C}\) for \(\text{N2PF}_6\) and the decay was observed at \(-42^\circ\text{C}\) by UV/Vis spectroscopy. Both copper nitrene complexes decay to a species with a blue shifted absorption maximum (\(\text{NIPF}_6\) by about 30 nm, \(\text{N2PF}_6\) by about 50 nm) but with a significantly lower extinction coefficient. The half-life time was determined as 2 min for \(\text{NIPF}_6\) and 21 min for \(\text{N2PF}_6\) (Table S2). For both nitrenes a decay with neither first nor second order was observed (Figure S4). This shows that the decay of the nitrene species is due to different reactions, as observed previously for bis(pyrazolyl)methane copper nitrene complexes [65]. Compared to other bis(pyrazolyl)methane copper nitrene complexes the stability of the two chiral nitrene complexes is low [64, 65]. One reason for the low stability is that there are aliphatic hydrogen atoms in close contact to the nitrene moiety, which can be easily abstracted by the nitrene moiety. For example, the half-life time for the nitrene \([\text{Cu}(\text{HC(BuPz)}_2\text{Py})(\text{NTs})]^+\) is 38 min while for the nitrene \([\text{Cu}(\text{HC(PhPz)}_2\text{Py})(\text{NTs})]^+\) a half-life time of 50 min is observed. Due to the nature of the ligands, the bond dissociation energy of C–H bonds of the tert-butyl group in \(\text{NIPF}_6\) is smaller compared to that of the C–H bonds of the methyl group in \(\text{N2PF}_6\) leading to a lower half-life time.

In the next step, the yield of the nitrene generation was determined. One way to estimate the yield is by oxidizing ferrocene to ferrocenium. Ferrocenium has a characteristic UV/Vis band at 624 nm with an extinction coefficient of 507 L mol\(^{-1}\) cm\(^{-1}\). The Lambert–Beer law allows to calculate the yield from the measured absorption [64, 65]. For the copper nitrene complexes \(\text{NIPF}_6\) and \(\text{N2PF}_6\) a yield of 50% is obtained (Figure S5 and Table S3). In comparison to literature data [64, 65] for known bis(pyrazolyl)methane copper nitrene complexes (\(Y = 71–95\%\)) the yield of the present nitrene complexes is lower. The low stability of \(\text{NIPF}_6\) and the slow formation reaction of \(\text{N2PF}_6\) lead to side reactions and thus lower yields of nitrene.

The spin state of the two chiral nitrene copper complexes was determined using EPR spectroscopy (Figures S1 and S2). The observed EPR spectra of the nitrene sample and the decayed species are very similar. This indicates an EPR silent nitrene species and a copper(II) decay species. Further investigation of the spin state by the Evans NMR method was not possible because of the low stability of \(\text{NIPF}_6\), the necessary addition of acetonitrile and the slow generation of \(\text{N2PF}_6\). Therefore, in accordance with results for previous bis(pyrazolyl)methane copper nitrene complexes [64, 65] a singlet spin state is assumed for \(\text{NIPF}_6\) and \(\text{N2PF}_6\).

\subsection{2.3 Catalytic aziridination}

With both chiral copper acetonitrile complexes C1 and in situ formed C2, the aziridination of different styrene derivatives was performed. Different 4-substituted as well as \(\beta\)-substituted styrene derivatives were applied as substrates (Scheme 1, Table 2, Table S4).

The catalytic aziridination reactions were performed at room temperature with PhINTs as nitrene generating agent analogous to the previously applied protocol [64, 65]. For the aziridination to \(\beta\)-substituted styrene derivatives the expected behavior [17] was observed that starting from the trans derivatives leads to pure trans products. In contrast, from the cis derivative a mixture of both isomers is obtained.

Both catalysts have an overall good activity in the aziridination of styrene derivatives. While for C1 a racemic product is obtained, for C2 a slightly enantio-enriched

\begin{center}
\textbf{Scheme 1: Aziridination of styrene derivatives.}
\end{center}
product is obtained. The enantiomeric excess can be increased by adding a sterically demanding group in the β-position of the substrate, decreasing the reaction temperature from room temperature to 0 °C or the introduction of an electron withdrawing or donating group into the substrate. For the conversion of stilbene, the highest enantiomeric excess was achieved with 30 (Table 2).

In comparison to other bis(pyrazolyl)methane copper nitrene complexes [64, 65] the activity of C1 and C2 is in the same range. It is remarkable that for β-substituted styrene derivatives a higher fraction of trans product is obtained starting from the cis substrate than previously reported. This indicates that an aromatically substituted pyrazolyl unit leads to a transition state with a higher singlet contribution than aliphatically substituted pyrazolyl units. Furthermore, for C1 a higher fraction of trans product is observed than for C2. This indicates a higher triplet contribution to the mechanism, which can be one reason for the difference in the observed enantiomeric excess for both catalysts. In comparison to other chiral copper complexes it can be observed that for styrene higher yields (63%) and enantiomeric excess (89%) are achievable by the use of bis(oxazoline) ligands [39].

### 2.4 Catalytic C–H amination

With all four copper(I) complexes, the C–H amination of different substrates was performed. Beside the prochiral substrates ethylbenzene, bibenzyl and neopentyl benzene, also cyclohexane and toluene were applied (Scheme 2, Table 3, Table S5).

The catalytic C–H aminations were performed at room temperature with 5PhINTs as nitrene generating agent analogously to known protocols [64, 65]. For the amination of benzylic substrates it was observed, that the amination occurs selectively in the benzylic position.

### Scheme 2: C–H amination of different substrates.

The C–H amination reactions of ethylbenzene with C3 and C4 lead to a low or no conversion of the substrate. As the complex C4 shows a low solubility in chlorobenzene, the reaction was also performed in dichloromethane with the same result (Table S5 [SI]). With C1 as catalyst good yields were obtained for cyclohexane, toluene and ethylbenzene, but the conversion of ethylbenzene led to a racemic product. For the application of C2 as catalyst, DCM was used as solvent, because the solubility of C2 in chlorobenzene is low. When isolated as well as in situ formed C2 was used, higher yields (25 and 7%) for the isolated complex and a higher enantiomeric excess (10 and 4) were obtained. Therefore, it can be concluded that the addition of acetonitrile to C4 to yield C2 decreases the reactivity for the application in C–H amination reactions, but not for aziridination reactions. By lowering the reaction temperature, the enantiomeric excess can be increased for the in situ formed complex from 4 to 10. For the other substrates only a trace amount of product was observed.

In comparison to other bis(pyrazolyl)methane copper nitrene complexes [64, 65] the activity of C1 is in the same range, while the necessary change of the solvent and the addition of acetonitrile lowers the activity of C2 significantly. Other ligands, for example guanidines, lead to a higher activity for the C–H amination reactions [17]. A

### Table 2: Yields of the aziridination of different styrene derivatives with C1 and in situ formed C2 at room temperature (enantiomeric excess), (cis/trans).

|        | C1 (%) | C2 (%) |
|--------|--------|--------|
| Styrene | 16     | 55 (4) |
| 4-Cl-CF3-styrene | 46     | 52 (10) |
| 4-NO2-styrene | 52     | 58 (8)  |
| cis-methylstyrene | 39 (33/67) | 49 (57/43) |
| trans-methylstyrene | 38     | 55 (8)  |
| cis-stilbene | –      | 24 (49/51) |
| trans-stilbene | –      | 13 (30)  |

Yields were determined using 1H NMR spectroscopy with nitromethane as internal standard.

### Table 3: Yields of the C–H amination of different substrates with C1 and in situ formed C2 at room temperature (enantiomeric excess).

|        | C1 (%) | C2 (%) |
|--------|--------|--------|
| Cyclohexane | 38     | 7      |
| Toluene | 56     | 8      |
| Ethylbenzene | 43     | 7 (4)  |
| Bibenzyl | –      | Traces |
| Neopentyl benzene | –      | Traces |

Yields were determined using 1H NMR spectroscopy with nitromethane as internal standard.
variety of different metal complexes were applied as catalyst for the nitrene mediated asymmetric C–H amination [79]. However, no chiral copper complexes were found for the nitrene mediated asymmetric C–H amination reaction and only a few examples [80] are presented for other asymmetric C–H amination reactions.

3 Conclusions

In this study, two novel terminal, chiral bis(pyrazolyl)methane copper tosyl nitrene complexes have been synthesized and characterized in terms of their stoichiometry, yield, thermal stability, reactivity, and spectroscopic features using UV/Vis and EPR spectroscopy. The ligand design was varied regarding different aspects, and three novel bis(pyrazolyl)methane ligands were prepared which have different chiral pyrazolyl units or substituents on the pyridinyl group, with the chiral pyrazolyl units based on pulegone and camphor. With these ligands four copper(I) complexes were obtained. Two of these four copper(I) complexes were successfully applied to the synthesis of two novel nitrene complexes. Furthermore, it was shown that with the two novel chiral copper nitrene complexes aziridinations of styrene derivatives can be carried out with good yields and C–H aminations are also possible under mild reaction conditions. It was shown that with the camphor-based ligand enantiomerically enriched products are achieved with an enantiomeric excess of up to 30, while the pulegone-based ligand only gives racemic products. As asymmetric copper-mediated C–H aminations are rare, the approach presented here is a first step for the development of more enantioselective catalysts.

4 Experimental section

4.1 General

All manipulations were carried out under nitrogen atmosphere. Nitrogen was dried by passage through P2O5. All solvents used were dried and degassed by standard literature procedures [81] prior to use. All chemicals were purchased from commercial suppliers and used without further purification. Ferrocene was sublimed prior to use. Molecular sieves (3 Å) were activated under vacuum at 220 °C for 20 h.

The starting materials (4R,7S)-7-(tert-butyl)-4-methyl-4,5,6,7-tetrahydro-2H-indazole (PulPz) [82], (4S,7R)-7,8,8-trimethyl-4,5,6,7-tetrahydro-2H-4,7-methanoindazole (CamPz) [82], [Cu(MeCN)4]PF6 [83], (2-tert-butylsulfonyl)(p-toluenesulfonfonyl)liminioiodo-benzene (PhINTs) [59], (2-tert-butylsulfonyl)(diacetoxioido)benzene [84] and (p-toluenesulfonfonyl)liminioiodobenzene (PhINTs) [85] were synthesized according to literature.

NMR spectra were recorded on a Bruker Avance III HD 400 or a Bruker Avance II 400 spectrometer at 25 °C. 1H and 13C[1]H NMR signals are given relative to the deuterated solvents as an internal standard. Chemical shifts were assigned with the use of two-dimensional NMR experiments (COSY, HSQC, HMBC). The enantiomeric excess was determined by 1H NMR with the help of [Eu(hfc)]3 in CD3OD. NMR data of the ligands and complexes were deposited as original data in the repository Chemotion [86] and are published under an Open Access model. The link is given in the analytical description. FT-IR spectra were recorded on a Shimadzu IRTracer 100 using a CsI beam splitter in combination with an ATR unit (Quest model from Specac utilising a robust monolithic crystalline diamond) in a resolution of 2 cm⁻¹. ESI mass spectra were obtained with a ThermoFisher Scientific LTQ Orbitrap XL. The source voltage was 4.49 kV and the capillary temperature was 299.54 °C. The tube lens voltage was set between 110 and 130 V. UV/Vis spectra were recorded with a Cary 60 spectrophotometer from Agilent Technologies connected via a Cary 50 fiber optic coupler in combination with a fibre-optic quartz glass immersion probe (Hellma, 1 mm) in a customized Schlenk measurement cell. Thin layer chromatography sheets were received from Machery-Nagel with a layer thickness of 0.20 mm and a pre-coating of a fluorescent indicator. Column chromatography was performed with Geduran silica gel 60 (40–63 μm) from Merck or with alumina B, activity Super I from MP Biomedicals. EPR spectra were recorded at 77 K on a Miniscope MS 600 from Magnetech with a microwave frequency of 9.4 GHz. The concentration of the measured frozen solution was 10 mM regarding the copper concentration. The B0 field was adjusted to 325 mT with a range of 160 mT (245–405 mT) and a sweep time of 60 s. Further parameters were adjusted as follows: sweep = 0.100 s, NOPs = 4096, gain mantissa = 5, gain exponent = 1 and MWattenu. = 10. The obtained EPR spectra were simulated using the comprehensive software packet EasySpin (version 5.2.28) [87]. The cyclic voltammetric measurements were performed at room temperature with a Metrohm Autolab PGSTAT 101 potentiostat with a three-electrode arrangement with a Pt disc working electrode (1 mm diameter), an Ag wire pseudo reference electrode and a glassy-carbon counter electrode under inert conditions. The samples were prepared with a 0.5–1.0 mM concentration of analyte and 0.1 M NBut4PF6 as supporting electrolyte in dichloromethane. Ferrocene was added as internal standard after each measurement. All potentials are referenced relative to the FeC/Fe⁺ couple. The cyclic voltammograms were measured with sweep rates of 20, 50, 100 and 200 mV s⁻¹.

The crystallographic data for C1, C3 and C4 is presented in Table S6 in the Supplementary material. The data of C1, C3 and C4 was collected with a Bruker D8 goniometer with APEX CCD detector using an Incoatec microsource with MoKα radiation (λ = 0.71073 Å). Temperature control was achieved with an Oxford Cryostream 700. Crystals were mounted with grease on glass fibers and data were collected at T = 100 K in ω-scan mode. Data were collected with SMART [88], integrated with SAINT [88] and corrected for absorption by multi-scan methods with SADABS [88].

The structure was solved by direct and conventional Fourier methods and all non-hydrogen atoms were refined anisotropically with full-matrix least-squares based on F² [XPREP [89], SHELXS [90], SHELXT [91], SHELXL [92], and SHELXL [93]]. Hydrogen atoms were derived from different Fourier maps and placed at idealized positions, riding on their parent C atoms, with isotropic displacement parameters Uiso(H) = 1.2Ueq(C) and 1.5Ueq(C methyl). All methyl groups were allowed to rotate but not to tip. The asymmetric unit of C4 features two large voids, each characterized by a volume of ca. 394 Å³ and an electron content of ca. 102
electrons, in good agreement with the requirements for two molecules of disordered pentane per void. As no model with atomic resolution for the co-crystallized solvent molecules could be derived, their contribution of the structure factors was taken into account with the SQUEEZE procedure as incorporated in PLATON [94, 95].

Full crystallographic data for C1, C3 and C4 have been deposited with the Cambridge Crystallographic Data Centre as supplementary.

Additional information on the NMR of the target compound including original data files is available via Chemotion Repository: https://dx.doi.org/10.14272/NWKTUCNDIPMMKM-TZYAJKAJSAN.1

### 4.2 Synthesis and characterization

#### 4.2.1 Synthesis of (4R,4’R,7R,7’S)-2,2’-(pyridin-2-ylmethylene)bis(7-(tert-butyl)-4-methyl-4,5,6,7-tetrahydro-2H-indazole) (HC(PulPz)2Py) (L1): PulPz (4.000 g, 20.8 mmol, 2 equiv.) was added gradually to a suspension of NaH (0.513 g, 21.3 mmol, 2 equiv.) in THF (50 mL) at 0 °C. After stirring at 0 °C until no more gas formation was observed, approximated 30 min, SOCl2 (0.76 mL, 10.4 mmol, 1 equiv.) was added dropwise. After stirring at 0 °C for 30 and 45 min at room temperature, picolinaldehyde (0.99 mL, 10.4 mmol, 1 equiv.) and CoCl2 (0.130 g, 1.0 mmol, 10 mol%) were added and the reaction mixture was reacted overnight. The residue was purified by silica gel column chromatography (iso-hexane/ethyl acetate, 8/5, Rf = 0.70) to give HC(PulPz)2Py (3.61 g, 7.6 mmol, 73%) as a light yellowish oil.

#### 4.2.2 Synthesis of methyl 6-(bis(3-(tert-butyl)-1H-pyrazol-1-yl)methyl) picolinate (HC(BuPz)(6-CO2MePy)) (L3): The Ligand L3 was synthesized analogous to L1. 3-tert-butylpyrazole (1.504 g, 12.11 mmol, 2 equiv.) and 6-formyl-2-pyridinecarboxylate (1.000 g, 6.82 mmol, 7,8,8-trimethyl-4,5,6,7-tetrahydro-2H-4,7-methanoindazole) (HC(CamPz)2Py) (L2): The Ligand L2 was synthesized analogous to L1.

### HRMS (HRMS) (EI-ESI, MeOH): m/z (found): 464.2795 (100%), 465.2832 (29%), 466.2867 (6%), m/z (calc.) = 464.2792 (100%), 15Na12C14H18N5+ (465.2837 (30%), 15Na12C14H18N5+ (466.2873 (4%), 15Na12C14H18N5+ (4%) 15Na12C14H18N5+). – IR (ATR, neat), ν (cm−1): 2965 (s), 2865 (w), 1590 (m), 1572 (w), 1485 (w), 1472 (m), 1457 (w), 1437 (m), 1418 (w), 1385 (m), 1376 (s), 1366 (w), 1342 (w), 1284 (m), 1277 (vs), 1268 (m), 1238 (w), 1227 (w), 1210 (w), 1181 (m), 1141 (m), 1102 (s), 1107 (vw), 1093 (w), 1085 (w), 1050 (vw), 998 (w), 969 (w), 963 (w), 950 (w), 909 (w), 881 (m), 862 (w), 816 (w), 805 (m), 793 (vs), 771 (vs), 748 (m), 718 (w), 698 (m), 667 (m), 640 (w), 620 (v), 610 (w), 570 (w).

Additional information on the NMR of the target compound including original data files is available via Chemotion Repository: https://dx.doi.org/10.14272/KXRYDZCNHUCBC-SJWRFNRESAN.1
6.1 mmol, 1 equiv.) were used in THF (20 mL). The reaction mixture was refluxed for 24 h. The residue was purified by silica gel column chromatography (isoo-hexane/ethyl acetate, 7:3, Rf = 0.56) to give HC(BuPz)2Py·(6-CO2MePy) (1.41 g, 3.6 mmol, 59%) as a colorless solid.

Chemical formula: C32H46CuF6N6P. Molecular mass: 723.27 g mol⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ = 8.65 (d, J = 4.8 Hz, H-1, H-1), 7.94 (m, H-2, H-3, H-4), 7.61 (d, J = 4.8 Hz, 2H, H-7), 7.49 (m, 2H, H-2, H-6), 2.66 (t, J = 8.0 Hz, 2H, H-13), 2.50 (m, 3H, H-18), 1.90 (m, 2H, H-12), 1.84 (m, 2H, H-11), 1.67 (m, 2H, H-12), 1.08 (2 x s, 6H, H-14), 0.96 (m, 2H, H-11), 0.82 (2 x s, 18H, H-16) ppm. – ¹³C (¹H) NMR (CDCl₃, 100 MHz): δ = 154.6 (C-5), 153.5 (C-8), 152.6 (C-17), 149.3 (C-1), 139.9 (C-3), 128.5 (C-7), 126.9 (C-9), 125.8 (C-2), 125.4 (C-4), 73.0 (d, C-6), 43.1 (d, C-13), 36.3 (d, C-15), 32.9 (d, C-11), 28.6 (d, C-16), 27.9 (d, C-8), 25.0 (d, C-12), 21.3 (d, C-14), 3.4 (C-18) ppm. Note: The doublets are due to the asymmetry of the pyrazolyl units, therefore no J couplings are given. – ¹⁹F (¹H) NMR (CDCl₃, 377 MHz): δ = −73.1 (d, J = 711 Hz) ppm. – ³¹P (¹H) NMR (CDCl₃, 162 MHz): δ = 144.1 (sept, J = 715 Hz) ppm. – HRMS ([M]+): m/z (calculated): 356.2807 (100%), 357.2838 (35%), 358.2830 (44%), 359.2821 (14%); m/z (found): 356.2807 (100%), 357.2838 (35%), 358.2830 (44%), 359.2821 (14%). Additional information on the NMR of the target compound including original data files is available via Chemotion Repository: https://dx.doi.org/10.14272/IOWUBGJSYWBQTK-SPFGKSOKSAN.1

4.2.5 Synthesis of [Cu(HC(CamPz)₂Py)(MeCN)]PF₆ (C2): A solution of HC(CamPz)₂Py (22.1 mg, 0.05 mmol, 1 equiv.) in THF (2 mL) was added slowly dropwise to a solution of [Cu(MeCN)]PF₆ (18.6 mg, 0.05 mmol, 1 equiv.) in THF (2 mL). The solution was stirred for 10 min. Diethyl ether (15 mL) was added and a precipitate formed, which was collected by filtration and washed with diethyl ether to yield [Cu(HC(CamPz)₂Py)(MeCN)]PF₆ (29.7 mg, 0.04 mmol, 80%).

A low concentration and a very slow addition of the ligand solution is necessary to avoid the formation of a [CuL₁(PF₆)] coordination motif. The formation of the title compound is implicated by a pale yellowish color of the solution and a precipitate, while the formation of a [CuL₁(PF₆)] coordination motif is implicated by an intense yellow color of the solution. Trials to scale up the reaction were not successful. When the title compound is dissolved the formation of a [CuL₂(PF₆)] coordination motif can be observed, which can be reversed by the dropwise addition of about 10–20 equiv. of acetonitrile to the solution. The adduct of too much acetonitrile leads to the formation of [Cu(MeCN)]PF₆, this is implicated by a complete loss of color to the solution.

This complex was additionally synthesized in situ from C4. Acetonitrile (0.26 mL, 5 mmol, 20 equiv.) was added to a solution of C4 (325 mg, 0.25 mmol, 1 equiv.) in DCM (1 mL) at room temperature. The reaction mixture was stirred for 10 min.
Chemical formula: $C_{24}H_{32}CuF_6N_6O_2P$. Molecular mass: 645.07 g mol$^{-1}$. 

4.2.6 Synthesis of $[\text{Cu}_2\{\text{HC(CamPz)}_2\text{Py}\}](\text{PF}_6)_2$ (C4): A solution of $[\text{HC(BuPz)}_2(6\text{-CO}_2\text{MePy})]$ (22.1 mg, 0.05 mmol, 1 equiv.) in acetonitrile (0.5 mL) was added to a solution of $[\text{Cu}(\text{MeCN})]_2\text{PF}_6$ (18.6 mg, 0.05 mmol, 1 equiv.) in acetonitrile (0.5 mL). The solution was stirred overnight. Hexane (4 mL) was added and the precipitate formed, which was collected by filtration and washed with hexane to yield $[\text{Cu}_2\{\text{HC(CamPz)}_2\text{Py}\}](\text{PF}_6)_2$ (26.3 mg, 0.02 mmol, 80%).

The reaction can also be performed with DCM and THF as solvent. Crystals suitable for single crystal X-ray diffraction were obtained from a concentrated solution of $[\text{Cu}_2\{\text{HC(CamPz)}_2\text{Py}\}](\text{PF}_6)_2$ in DCM, which was layered with n-hexane. 

A high concentration is beneficial to avoid the formation of a $\text{CuL(MeCN)}\text{PF}_6$ coordination motif, which may occur as an impurity.

Chemical formula: $C_{20}H_{29}CuF_2N_2P_2$. Molecular mass: 1300.27 g mol$^{-1}$. 

4.2.7 Synthesis of $[\text{Cu}_2\{\text{HC(CamPz)}_2\text{Py}\}](\text{PF}_6)_2$ (C4): A solution of $[\text{HC(CamPz)}_2]$ (22.1 mg, 0.05 mmol, 1 equiv.) in acetonitrile (0.5 mL) was added to a solution of $[\text{Cu}(\text{MeCN})]_2\text{PF}_6$ (18.6 mg, 0.05 mmol, 1 equiv.) in acetonitrile (0.5 mL). The solution was stirred overnight. Hexane (4 mL) was added and the precipitate formed, which was collected by filtration and washed with hexane to yield $[\text{Cu}_2\{\text{HC(CamPz)}_2\text{Py}\}](\text{PF}_6)_2$ (26.3 mg, 0.02 mmol, 80%).

The reaction can also be performed with DCM and THF as solvent. Crystals suitable for single crystal X-ray diffraction were obtained from a concentrated solution of $[\text{Cu}_2\{\text{HC(CamPz)}_2\text{Py}\}](\text{PF}_6)_2$ in DCM, which was layered with n-hexane. 

A high concentration is beneficial to avoid the formation of a $\text{CuL(MeCN)}\text{PF}_6$ coordination motif, which may occur as an impurity.

Chemical formula: $C_{20}H_{29}CuF_2N_2P_2$. Molecular mass: 1300.27 g mol$^{-1}$.
were removed in vacuo. The residues were dissolved in CDCl₃/MeNO₂ (1 mL, 10 mL/20 µL) and filtered. The yields were determined by ¹H NMR spectroscopy.

5 Supporting information

The experimental and simulated EPR spectra of NIPF₆ and N₂PF₆, the UV/Vis spectra of the UV/Vis experiments of NIPF₆ and N₂PF₆, the mass spectra of the decay species of N₂PF₆, an overview over all catalytic reactions, the CV data of C₁–C₄, all NMR spectra and an overview over the crystallographic data are given as supplementary material available online (https://doi.org/10.1515/znb-2021-0140).

Author contributions: All the authors have accepted responsibility for the entire content of this submitted manuscript and approved submission.

Research funding: Financial support by the Deutsche Forschungsgemeinschaft in the framework of the SFB 985 (Subproject A1) is gratefully acknowledged.

Conflict of interest statement: The authors declare no conflicts of interest regarding this article.

References

1. Collet F., Dodd R. H., Dauban P. Chem. Commun. 2009, 5061–5074; https://doi.org/10.1039/b905820f.
2. Hili R., Yudin A. K. Nat. Chem. Biol. 2006, 2, 284–287.
3. Roughley S. D., Jordan A. M. J. Med. Chem. 2011, 54, 3451–3479.
4. Abdine R. A. A., Hedouin G., Colobert F., Wencel-Delord J. ACS Catal. 2021, 11, 25–247.
5. Sutin L., Andersson S., Bergquist L., Castro V. M., Danielsson E., James S., Henriksson M., Johansson L., Kaiser C., Fyhrén K., Williams M. Bioorg. Med. Chem. Lett 2007, 4837–4840; https://doi.org/10.1016/j.bmcl.2007.06.054.
6. Bergman R. G. Nature 2007, 446, 391–393.
7. Davies H. M. L., Morton D. J. Org. Chem. 2016, 81, 343–350.
8. Tzouras N. V., Stamatakopoulos I. K., Papastavrou A. T., Liori A. A., Vougioukalakis G. C. Coord. Chem. Rev. 2017, 343, 25–139.
9. Hartwig J. F. Nature 2008, 455, 314–322.
10. Davies H. M. L., Manning J. R. Nature 2008, 451, 417–424.
11. Roizen J. L., Harvey M. E., Du Bois J. Acc. Chem. Res. 2012, 45, 911–922.
12. Iovan D. A., Betley T. J. Am. Chem. Soc. 2016, 138, 1893–1993.
13. Kuijpers R. F., van der Vlugt J. I., Schneider S., Bruin B. Chem. Eur. J. 2017, 23, 13819–13829.
14. Scamp R. F., Scheffer B., Schomaker J. M. Chem. Commun. 2019, 55, 7362–7365.
15. Rey-Rodriguez R., Grelier G., Habert L., Retailleau P., Darses B., Gillaizeau I., Dauban P. J. Org. Chem. 2017, 82, 11897–11902.
16. Dequirez G., Pons V., Dauban P. Angew. Chem. Int. Ed. 2012, 51, 7384–7395.
70. Hoffmann A., Citek C., Binder S., Gooss A., Rübben M., Troeppner O., Ivanović-Burmazović I., Wasinger E. C., Stack T. D. P., Herres-Pawlis S. Angew. Chem. Int. Ed. 2013, 52, 5398–5401.
71. Schäfer D., Fink F., Kleinschmidt D., Keisers K., Thomas F., Hoffmann A., Pich A., Herres-Pawlis S. Chem. Commun. 2020, 56, 5601–5604.
72. Moegling J., Benischke A. D., Hammann J. M., Vepřek N. A., Zoller F., Rendenbach B., Hoffmann A., Sievers H., Schuster M., Knochel P., Herres-Pawlis S. Eur. J. Org Chem. 2015, 2015, 7475–7483.
73. Mertens M. A. S., Thomas F., Nöth M., Moegling J., El-Awaad I., Sauer D. F., Dhoke G. V., Xu W., Pich A., Herres-Pawlis S., Schwaneberg U. Eur. J. Org Chem. 2019, 2019, 6341–6346.
74. Elfllein J., Platzmann F., Burzlaff N. Eur. J. Inorg. Chem. 2007, 2007, 5173–5176.
75. Godau T., Bleifuss S. M., Müller A. L., Roth T., Hoffmann S., Heinemann F. W., Burzlaff N. Dalton Trans. 2011, 6547–6554; https://doi.org/10.1039/cdt10032g.
76. Godau T., Platzmann F., Heinemann F. W., Burzlaff N. Dalton Trans. 2009, 254–255; https://doi.org/10.1039/b819596j.
77. Hoffmann A., Flörke U., Schürmann M., Herres-Pawlis S. Eur. J. Org Chem. 2010, 2010, 4136–4144.
78. Yang L., Powell D. R., Houser R. P. Dalton Trans. 2007, 955–964; https://doi.org/10.1039/c001702b.
79. Hayashi H., Uchida T. Eur. J. Org. Chem. 2020, 2020, 909–916.
80. Murru S., Mokar B. D., Bista R., Harakat D., Le Bras J., Fronczek F., Nicholas K. M., Srivastava R. S. Org. Chem. Front. 2021, 8, 3228–3237.
81. Leonard J., Lygo B., Procter G. Praxis der organischen Chemie; Ein Handbuch, VCH: Weinheim, 1996.
82. LeCloux D. D., Tokar C. J., Osawa M., Houser R. P., Keyes M. C., Tolman W. B. Organometallics 1994, 13, 2855–2866.
83. Kubas G. J., Monzyk B., Crumbliss A. L. Inorg. Synth. 1990, 90–91.
84. Macikenas D., Skrzypczak-Jankun E., Protasiewicz J. D. J. Am. Chem. Soc. 2011, 133, 4151.
85. Yamada Y., Yamamoto T., Okawara M. Chem. Lett. 1975, 4, 361–362.
86. Tremouilhac P., Lin C.-L., Huang P.-C., Huang Y.-C., Nguyen A., Jung N., Bach F., Ulrich R., Neumair B., Streit A., Bräse S. Angew. Chem. Int. Ed. 2020, 59, 22771–22778.
87. Stoll S., Schweiger A. J. Magn. Reson. 2006, 178, 42–55.
88. SMART (version 5.631), SAINT (version 8.37A) and SADABS (version 2008/1); Bruker AXS Inc.: Madison, Wisconsin (USA), 2008.
89. XPREP (version 5.1); Bruker AXS Inc.: Madison, Wisconsin (USA), 1997.
90. Sheldrick G. M. Acta Crystallogr. 2008, A64, 112.
91. Sheldrick G. M. Acta Crystallogr. 2015, A71, 3–8.
92. Sheldrick G. M. Acta Crystallogr. 2015, C71, 3–8.
93. Hübschle C. B., Sheldrick G. M., Dittrich B. J. Appl. Crystallogr. 2011, 44, 1281–1284.
94. Spek A. L. PLATON, A Multipurpose Crystallographic Tool; Utrecht University: Utrecht (The Netherlands), 2008.
95. Spek A. L. Acta Crystallogr. 2015, C71, 9–18.

Supplementary Material: The online version of this article offers supplementary material (https://doi.org/10.1515/znb-2021-0140).