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A chiral bis-*N*-oxide isoelectronic with Jacobsen's salen ligand

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Abstract

A chiral bis-*N*-oxide as a tetradentate ligand for various transition metals is introduced. A Cu(II)-complex is fully characterized including its X-ray structure and the corresponding Cu(I)-complex proved to be an active catalyst for asymmetric cyclopropanation. © 1999 Elsevier Science Ltd. All rights reserved.

1. Introduction

Since epoxides are valuable building blocks for organic synthesis, the asymmetric epoxidation of olefins is of special importance. For several years the Sharpless epoxidation, although restricted to allylic alcohols, was the most important route to chiral epoxides.[1,2] In 1990, Jacobsen[3] and Katsuki[4] reported that chiral manganese salen complexes[5] are capable of catalyzing the asymmetric epoxidation of unfunctionalized olefins. In particular, the easily accessible[6] ligand **1b** (R=*tert*-butyl) introduced by Jacobsen became popular and turned out to be equally useful for other asymmetric transformations such as the cobalt catalyzed hydrolytic kinetic resolution of terminal epoxides,[7a,b] the manganese catalyzed formation of α-hydroxy ketones from silyl enol ethers,[7c,d] the titanium catalyzed addition[7e–g] of TMSCN to arylaldehydes, the chromium catalyzed addition[7h–k] of TMSCN to epoxides, the cobalt catalyzed addition[7l] of carboxylic acids to epoxides, the chromium catalyzed hetero-Diels–Alder reaction[7m] and the aluminum catalyzed addition[7n] of HCN to imines. Salen ligands similar to **1** have been applied for asymmetric aziridination.[8]

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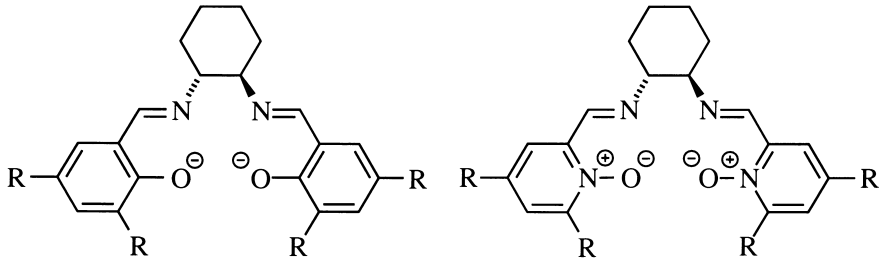


1 **a**: R = H **2**

b: R = $C(CH_3)_3$

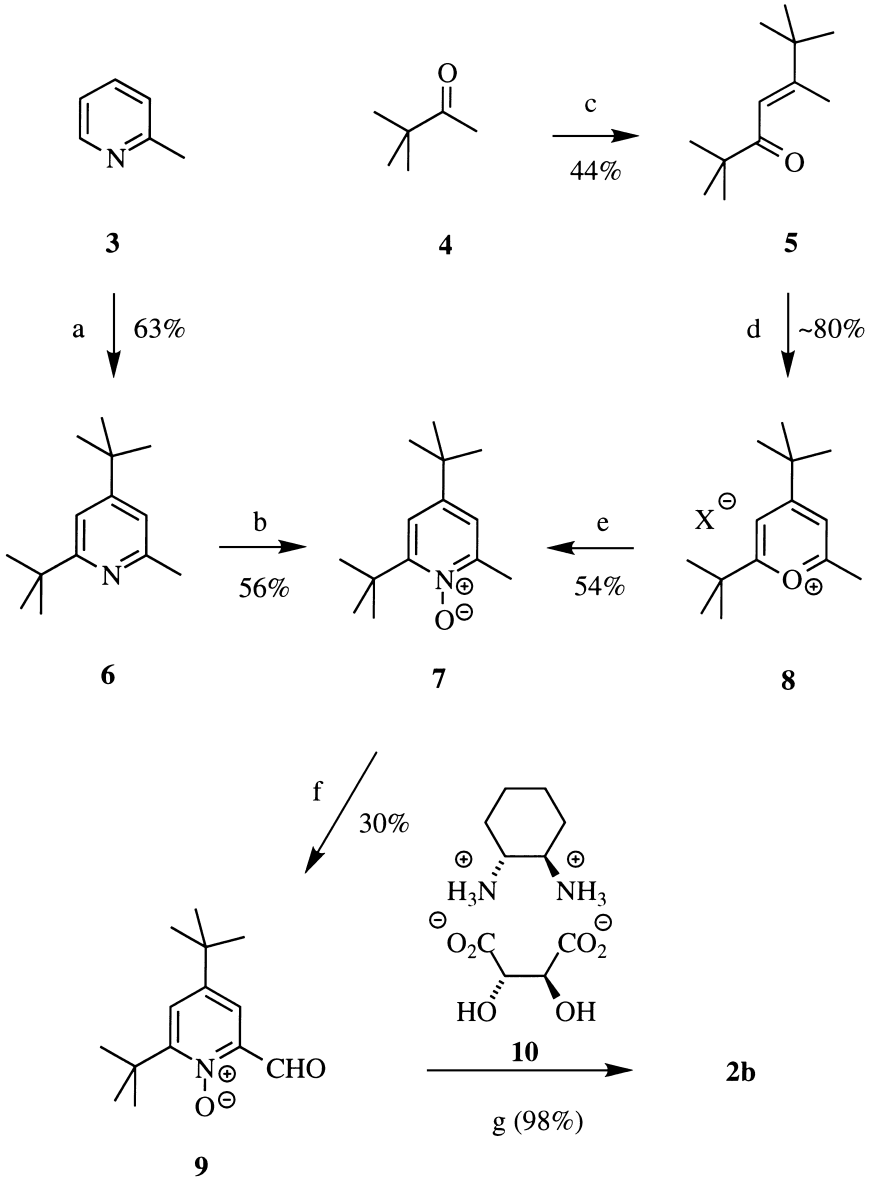
Considering the multitude of opportunities offered by salen ligands we envisioned that structurally related bis-*N*-oxides of type **2** deserved some attention. In addition chiral *N*-oxides recently turned out to be valuable catalysts themselves, useful for the enantioselective addition[9a] of allyltrichlorosilanes to aldehydes and for the enantioselective reduction[9b] of ketones. Since the name salen ligand obviously derives from salicylaldehyde and **2** is based on the *N*-oxide of picolinaldehyde we proposed the general expression 'picolinoxen ligands' for type **2** structures. While tetradentate salen ligands of type **1** are negatively charged their isoelectronic[10] and likewise tetradentate counterparts **2** are formally neutral. Therefore it was anticipated that despite the structural similarity of these ligands their transition metal complexes should behave fundamentally differently: for instance, **1** regularly substitutes two halide, carboxylate or similar anions while complexing an appropriate transition metal salt. In contrast, in the case of **2** these formally negatively charged ligands should stay at the metal centre, blocking potential coordination sides. Thus, catalytic active complexes of **2** should generally have a lower oxidation state than those of **1** or have to be of cationic nature.

2. Results and discussion

For the synthesis of **2b** (R=*tert*-butyl) we have developed two independent routes (Scheme 1). Starting from 2-picoline **3** the *tert*-butyl groups were introduced by the reaction with an excess of *tert*-butyllithium, by analogy to the known derivatization of other pyridines.[11] Presumably the first *tert*-butyl group was introduced in 4-position since 4-*tert*-butyl-2-methylpyridine is the only by-product detected. This approach to **6** with a 63% yield is clearly superior to the elegant but inefficient transition metal catalyzed formation from *tert*-butylacetylene and acetonitrile (3.4% yield reported).[12] The attempted shortcut to **7** via reaction of 2-picolin-*N*-oxide with an excess of *tert*-butyllithium failed: the *N*-oxide was reduced during the reaction and again **6** and 4-*tert*-butyl-2-methylpyridine were the observed products.

Difficulties with the *N*-oxidation of sterically hindered pyridines are known from the literature;[13] therefore it is not surprising that hydrogen peroxide and dimethyldioxirane failed to react with **6**. With a small excess of *m*-chloroperbenzoic acid (mCPBA) less than 1% conversion was observed after 4 days at room temperature according to the ^{1}H NMR of the crude product. Surprisingly, with 7 equivalents of mCPBA up to 56% yield of *N*-oxide **7** was obtained in a much shorter reaction time.

This first route has two significant drawbacks: the excess of *tert*-butyllithium applied in the first step is relatively expensive and the success of the oxidation step is hampered by the rather difficult purification of **7**: the large excess of mCPBA and the corresponding benzoic acid afford a chromatographic separation of **7** on silica gel, which turned out to be somewhat unreliable; in several runs separation was sometimes incomplete and the yield of pure **7** dropped to about 10%. On the other hand, the purity of **7** proved to



Scheme 1. Reaction conditions: (a) 5 equiv. *tert*-butyllithium, from −78°C (1 h) to reflux temperature (2.5 h); (b) 7 equiv. *m*-chloroperbenzoic acid, room temperature, 26 h; (c) 4 equiv. potassium *tert*-butoxide, neat, 200°C, 4 h; (d) acetic anhydride, boron trifluoride diethyl etherate, reflux, 3 min; (e) 5 equiv. hydroxylamine hydrochloride, 22 equiv. NaOAc, AcOH, reflux, 1.5 h; (f) 1.2 equiv. SeO_2, pyridine, reflux, 19 h; (g) 0.5 equiv. **10**, 3 equiv. K_2CO_3, $EtOH/H_2O$, reflux, 3 h

be essential for the success of the next step in the synthesis of **2b**. Therefore we developed a second independent route to **7** in analogy to the procedure for 2,4,6-tris-*tert*-butylpyridin-*N*-oxide by Weber and Rohn.[13] Aldol-condensation of methyl-*tert*-butylketone **4** leads to the α,β-unsaturated ketone **5**,[14] which cyclizes with acetic anhydride on treatment with boron trifluoride to give a mixture of pyrylium salts **8** (see Experimental).[15]

Compound **8** was directly subjected to condensation with hydroxylamine hydrochloride and the desired *N*-oxide **7** was isolated in a 43% overall yield over two steps. The aldehyde function was introduced by

Table 1
Change in colour during complexation reaction of equimolar amounts of metal salts MX_n with ligand **2b** (91 μmol in 2 ml solvent)

MX_n	solvent	initial colour	temp.,time	final colour
$Pd(OAc)_2$	$CHCl_3$	orange	20 °C	purple
Na_2PdCl_4	CH_3OH	brown	40 °C, 5 min	red; yellow solid after 1 h
$PtCl_2$	CH_3OH	black suspension	65 °C,1 h	red + yellow solid
CuCl	MeOH	colourless	65 °C, 2 h	green
CuBr	MeOH	colourless	20 °C	red, but green after 12 h
$Cu(NO_3)_2*3H_2O$	MeOH	blue	65 °C, 4 h	dark green
$CuCl_2$	MeOH	green	20 °C	dark green
$CoCl_2*6H_2O$	MeOH	red	65 °C, 2 h	brown
$Co(NO_3)_2*6H_2O$	MeOH	red	65 °C, 2 h	brown
$CrCl_3*6H_2O$	MeOH	green	65 °C, 2 h	green
$Cr(NO_3)_2*9H_2O$	MeOH	green	65 °C, 2 h	brown
$VOSO_4*5H_2O$	MeOH	blue	20 °C, 5 min	green + yellow solid
$Zn(OAc)_2*2H_2O$	MeOH	colourless	20 °C	slightly yellow
$FeCl_2*4H_2O$	MeOH	yellow	20 °C	dark blue
$AgBF_4$	MeOH	slightly yellow	20 °C	intensive yellow
$LaCl_3*7H_2O$	MeOH	colourless	65 °C, 14 h	yellow
$La(NO_3)_3*6H_2O$	MeOH	colourless	65 °C, 4 h	yellow
$GaCl_3$	THF	colourless	60 °C	yellow

an oxidation with selenium dioxide (73% yield based on recovered starting material). The subsequent double condensation with the ammonium salt **10**[16] as the final step in the synthesis of the bis-*N*-oxide ligand **2b** proceeded almost quantitatively.

The tetradentate ligand **2b** interacted with various transition metal salts as qualitatively indicated by the change in colour (see Table 1).[17] A freshly prepared stoichiometric mixture of **2b** with Na_2PdCl_2 in methanol-d_4 showed a significant downfield shift of the aryl hydrogens in the ^1H NMR spectrum ($\Delta\delta$ up to 0.96 ppm, Fig. 1), being in accord with structure **11.1**. Due to the smooth decomposition in solution at room temperature to give a rather insoluble yellow solid we could not isolate this palladium complex. With copper(II) nitrate we obtained complex **11.2** as dark green crystals, unsuitable for measuring NMR because of paramagnetism spectra, but suitable for X-ray structure analysis (Fig. 2):[18] **11.2** crystallizes in the monoclinic space group C2 with six formula units per unit cell. The crystal contains two independent $[C_{34}H_{52}N_4O_2Cu]^{2+}$ complex cations with square-planar *cis*-CuO_2N_2 coordination sites. One of the two independent $[C_{34}H_{52}N_4O_2Cu]^{2+}$ complex cations was situated on a twofold rotation axis and binds two monodentate nitrate anions normal to the CuO_2N_2 plane (Fig. 2a; Cu–O: 2.63(1) Å) resulting in neutral $[C_{34}H_{52}N_4O_2Cu][NO_3]_2$ molecules. The other one forms dimeric $[(C_{34}H_{52}N_4O_2Cu)_2(l\text{-}NO_3)(NO_3)_2]^+$ cations with a nitrate anion as a bridging ligand (Cu–O: 2.55(2) (2×) Å) and two terminally bonded nitrate groups (Fig. 2b; Cu–O: 2.47(2) Å).

In order to demonstrate the catalytic activity of transition metal complexes of ligand **2b** we chose the

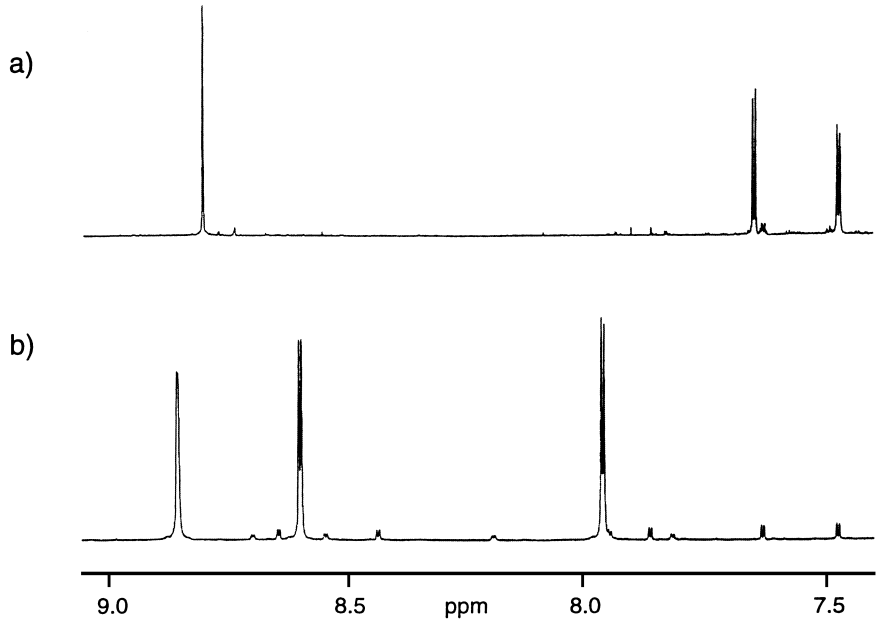
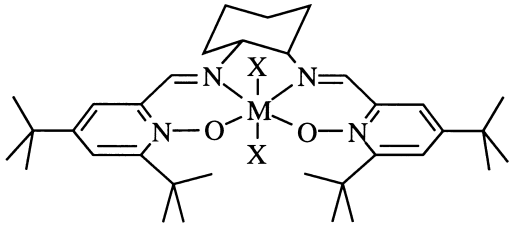


Figure 1. ^{1}H NMR spectra in methanol-d_4: (a) of ligand **2b**, (b) of ligand **2b** with an equimolar amount of Na_2PdCl_4

cyclopropanation of styrene **12** with diazoacetic acid ester **13** as the model reaction (Scheme 2).[19] While no asymmetric induction was observed with cobalt, palladium and rhodium acetate, copper(I) chloride led to a small but significant enantioselectivity (21% ee for *cis*-**14**). A similar result was achieved with copper(II) complex **11.2** after in situ reduction as indicated by the change in colour from green to purple.



11.1 (M = Pd, X = Cl)
11.2 (M = Cu, X = NO_3)

Catalytic activity of other transition metal complexes of **2b** with special emphasis on low oxidation states are currently being investigated. We are also extending the concept of replacing the phenolate moieties of appropriate chiral ligands by *N*-oxide units to other examples such as the structural analogy of 1,1′-binaphthol[20] and 1,1′-biisoquinoline-bis-*N*-oxide.

3. Experimental

3.1. General

Mp (uncorrected): Reichert Thermovar. IR: Perkin–Elmer 983. UV: Perkin–Elmer 554. NMR: Bruker DRX 500, Bruker WM 300; ^{1}H NMR spectra (500 MHz or 300 MHz) were recorded in $CDCl_3$ with TMS

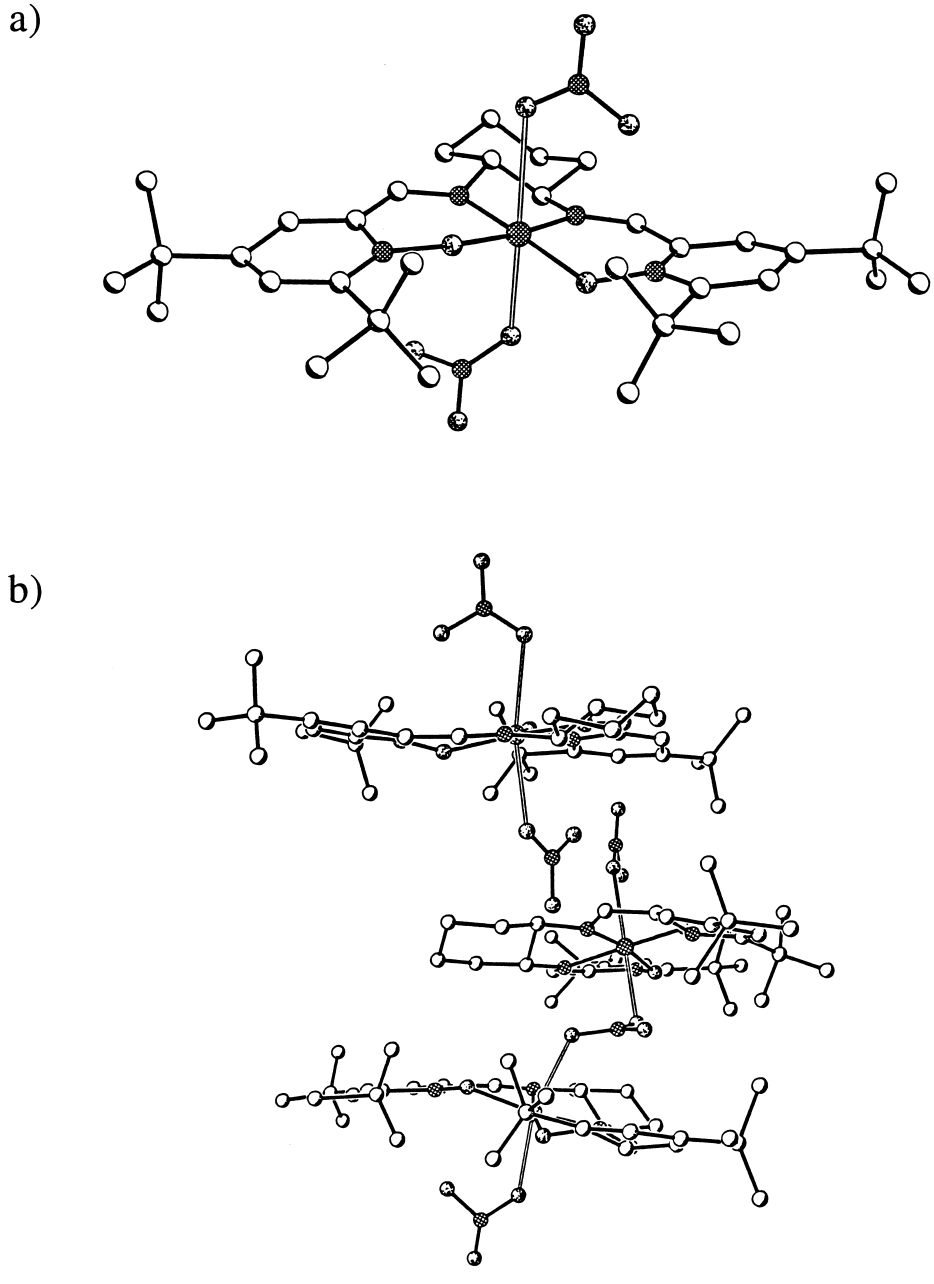
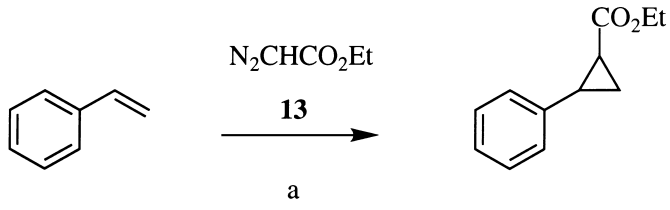


Figure 2. Perspective views of the crystal structure of copper complex **11.2**: (a) C_2-symmetric part, (b) part of the elemental cell with three copper centres and one bridging nitrate ligand

as the internal standard. ^{13}C NMR spectra (125.8 MHz or 75.5 MHz) were measured by using $CDCl_3$ as the solvent and as the internal standard. MS: MAT 311A (70 eV). For analytical TLC precoated plastic sheets POLYGRAM SIL G/UV254 from Macherey–Nagel were used.



12 **14** (20%), cis/trans: 45/55 (21 and 15%ee)

Scheme 2. Reaction conditions: (a) 7 equiv. **13**, 1.7 mol% CuCl, 3.5 mol% **2**, neat, room temperature, 2.5 h

3.2. 2,4-Di-tert-butyl-6-methylpyridine **6**

To 4.66 g (50.0 mmol) of 2-methylpyridine in 60 ml of dry *n*-heptane 156 ml of a 1.6 M solution of *tert*-butyllithium (250 mmol) in *n*-pentane were added at −78°C and stirring was continued at this temperature for 1 h. The *n*-pentane fraction was distilled off, the reaction mixture was heated to reflux temperature for 2.5 h and after cooling to room temperature hydrolyzed dropwise with 40 ml of 2-propanol followed by 60 ml of water. The water layer was extracted three times with 50 ml of *n*-pentane, the combined organic layer dried with $MgSO_4$ and the solvent was evaporated. The residue was fractionated by flash chromatography; TLC (silica, petroleum ether:methyl-*tert*-butyl ether 3:1): R_f=0.86 (**6**), 0.25.

First fraction (R_f=0.86): 6.44 g (63%) of **6** as a colourless solid with mp 28°C. IR (film): ν=2956 cm^{-1} (s), 2870 (s), 1599 (s), 1559 (m), 1478 (m), 1408 (m), 1361 (m), 1319 (w), 1254 (w), 1232 (w), 1202 (w), 1171 (w), 1035 (w), 940 (w), 894 (w), 864 (w), 759 (w). ^{1}H NMR (500 MHz): δ=1.29 (s, 9H), 1.35 (s, 9H), 2.51 (s, 3H), 6.92 (d, *J*=1.6 Hz, 1H), 7.11 (d, *J*=1.6 Hz, 1H). ^{13}C NMR (75.5 MHz): δ=24.92 (q, CH_3), 30.41 (q, $C(CH_3)_3$), 30.74 (q, $C(CH_3)_3$), 34.64 (s), 37.36 (s), 112.50 (d), 117.02 (d), 156.73 (s), 159.83 (s), 168.45 (s). MS (70 eV; 130°C); *m/z* (%): 205 (51) [M^+], 204 (61), 191 (15), 190 (100), 175 (21), 163 (62), 160 (13), 149 (26). $C_{14}H_{23}N$ (205.1): calcd C 81.88, H 11.30, N 6.82; found C 81.88, H 11.26, N 6.76.

Second fraction (R_f=0.25): 1.15 g (15%) of 4-*tert*-butyl-2-methylpyridine as a yellow oil, whose ^{1}H NMR spectrum is in accord with published data.[21] ^{1}H NMR (300 MHz): δ=1.29 (s, 9H), 1.54 (s, 3H), 7.07 (dd, *J*=5.3 Hz, 1H), 7.32 (s, 1H), 8.39 (d, *J*=5.3 Hz, 1H).

3.3. 2,4-Di-tert-butyl-6-methyl-pyridin-N-oxide **7** from substituted pyridine **6**

To 5.13 g (25.0 mmol) 2,4-di-*tert*-butyl-6-methylpyridine **6** in 600 ml of $CHCl_3$ 29.5 g (163 mmol) of 85% *m*-chloroperbenzoic acid were added under stirring at room temperature and after 2 h another 2.24 g (12.3 mmol) of *m*-chloroperbenzoic acid. Stirring was continued for 24 h and 100 ml of a saturated aqueous solution of sodium hydrogen carbonate were added. The water layer was extracted twice with 50 ml of $CHCl_3$, the combined organic layer was dried with $MgSO_4$ and the solvent was evaporated. The residue was fractionated by flash chromatography; TLC (silica, ethyl acetate:triethylamine 4:1): R_f=0.93 (**6**), 0.69 (**7**), 0.00–0.17.

The first fraction was eluted with petroleum ether:methyl-*tert*-butyl ether (80:1): 1.54 g (30%) of starting material **6**.

The second fraction was eluted with ethyl acetate: 3.10 g (56% yield, or 80% based on recovered starting material) of *N*-oxide **7** as a colourless solid with mp 62°C. IR (KBr): ν=3423 cm^{-1} (w), 2998 (w), 2966 (s), 2870 (m), 1763 (w), 1618 (w), 1550 (w), 1535 (w), 1474 (m), 1420 (m), 1399 (m), 1378 (m), 1368 (m), 1351 (m), 1308 (m), 1264 (m), 1239 (s), 1218 (m), 1167 (w), 1042 (w), 943 (w), 928 (w),

910 (w), 890 (w), 877 (w), 826 (w), 805 (w), 752 (w), 741 (w), 652 (w), 634 (w). ^{1}H NMR (300 MHz): δ=1.30 (s, 9H), 1.54 (s, 9H), 2.51 (s, 3H), 7.12 (d, *J*=2.8 Hz, 1H), 7.21 (d, *J*=2.8 Hz, 1H). ^{13}C NMR (75.5 MHz): δ=18.99 (q, *C*H$_3$), 27.47 (q, C(*C*H$_3$)$_3$), 30.69 (q, C(*C*H$_3$)$_3$), 34.47 (s), 36.55 (s), 118.13 (d), 121.25 (d), 148.40 (s), 149.43 (s), 156.64 (s). MS (70 eV; 45°C); *m/z* (%): 221 (30) [M$^+$], 210 (21), 206 (30), 204 (31), 189 (22), 188 (14), 179 (100), 174 (26), 164 (20), 162 (24), 148 (14), 141 (17), 139 (51), 111 (15). $C_{14}H_{23}NO$ (221.2): calcd C 75.96, H 10.48, N 6.33; found C 75.84, H 10.48, N 6.25.

*3.4. 2,2,5,6,6-Pentamethyl-hept-4-en-3-one **5***

A mixture of 36.0 g (321 mmol) of potassium *tert*-butoxide and 11 ml (78.5 mmol) of 3,3-dimethyl-2-butanone **4** was heated for 4 h at 200°C. After cooling to room temperature the reaction mixture was hydrolyzed with 100 ml of 1 M sulfuric acid and the water layer (pH 4) was extracted twice with 100 ml of diethyl ether. The combined organic layer was dried with $MgSO_4$, the solvent was evaporated and the residue distilled: First fraction: 4.93 g (56%) starting material **4** with bp 106°C. Second fraction: 6.30 g (44%) of condensation product **5** with bp 85°C/11 mbar (lit.[14b]: bp 43–45°C/0.33 mbar). ^{1}H NMR (300 MHz): δ=1.12 (s, 9H), 1.15 (s, 9H), 2.06 (d, *J*=1.2 Hz, 3H), 6.38 (d, *J*=1.2 Hz).

3.5. 2,4-Di-tert-*butyl-6-methylpyrylium salt **8***

To a solution of 6.30 g (34.6 mmol) of α,β-unsaturated ketone **4** in 22 ml acetic anhydride 12.0 ml (91.6 mmol) of boron trifluoride diethyletherate were added and the resulting mixture was heated at 100°C bath temperature for 3 min. After cooling to room temperature the reaction mixture was mixed with 400 ml of diethyl ether, the ether layer was decanted and the residue was dried for 5 h at 0.24 mbar to give 8.13 g of a dark brown oil. We do not agree with the article which claims, but did not prove, that exclusively the tetrafluoroborate is formed by this procedure;[15] at least some acetate should be present. However, the ^{1}H NMR spectrum proves that the pyrylium salt **8** is pure enough for further transformations and the yield is estimated to be about 80%. ^{1}H NMR signals of the pyrylium cation (300 MHz, $CDCl_3$): δ=1.36 (s, 9H), 1.45 (s, 9H), 2.88 (s, 3H), 7.66 (d, *J*=1.7 Hz, 1H), 7.82 (d, *J*=1.7 Hz, 1H).

3.6. 2,4-Di-tert-*butyl-6-methyl-pyridin*-N-*oxide **7** from pyrylium salt **8***

To a solution of 2.34 g (33.7 mmol) of hydroxylamine hydrochloride and of 12.9 g (136 mmol) sodium acetate trihydrate in 55 ml of acetic acid at reflux was added a solution of 1.81 g (6.14 mmol) of **8** in 10 ml of acetic acid within 5 min. After stirring for 1.5 h at reflux temperature about 40 ml of the acetic acid were distilled off at 40°C/20 mbar. 130 ml of water was added to the residue and the pH adjusted to 10 with solid sodium hydroxide. The water layer was extracted three times with 100 ml of $CHCl_3$, the combined organic layer was dried with $MgSO_4$ and the solvent was evaporated to give 733 mg (54%) of *N*-oxide **7** (characterization: see above).

3.7. 4,6-Di-tert-*butyl 2-pyridincarboxaldehyde*-N-*oxide **9***

A mixture of 2.62 g (11.9 mmol) of *N*-oxide **7** and of 1.58 g (14.3 mmol) selenium dioxide in 10 ml of pyridine was heated under reflux for 19 h. Solid material was filtered off, the filtrate concentrated in vacuo (0.24 mbar) and the residual oil extracted four times with 50 ml of hot toluene. TLC (silica, petroleum ether:methyl-*tert*-butyl ether 2:1): R_f=0.54 (**7**), 0.11 (**9**). By flash chromatography with petroleum ether:methyl-*tert*-butyl ether (80:1) 1.54 g (59%) of recovered **7** were obtained as the first fraction.

Second fraction: 842 mg (30% yield, or 73% based on recovered starting material) of carboxaldehyde **9** as yellow solid with mp 115°C. IR (KBr): ν=2971 cm^{-1} (m), 2923 (w), 2876 (w), 1768 (w), 1688 (s), 1612 (w), 1482 (w), 1441 (w), 1402 (m), 1386 (w), 1367 (m), 1292 (w), 1269 (w), 1253 (s), 1231 (w), 1150 (m), 1117 (w), 1027 (w), 946 (w), 932 (w), 893 (w), 835 (w), 818 (w), 755 (w), 691 (w), 644 (w). ^{1}H NMR (300 MHz): δ=1.33 (s, 9H), 1.55 (s, 9H), 7.50 (d, *J*=3.0 Hz, 1H), 7.67 (d, *J*=3.0 Hz, 1H), 10.66 (s, 1H). ^{13}C NMR (75.5 MHz): δ=27.12 (q), 30.49 (q), 34.83 (s), 36.42 (s), 120.51 (d), 124.62 (d), 144.29 (s), 148.64 (s), 157.77 (s), 187.68 (d). MS (70 eV; 45°C); *m/z* (%): 235 (14) [M^+], 220 (56), 219 (11), 218 (35), 216 (10), 208 (13), 204 (22), 203 (22), 202 (18), 193 (10), 191 (11), 190 (55), 189 (10), 188 (40), 178 (17), 177 (100), 176 (10), 175 (10), 174 (19), 162 (40), 160 (17), 149 (15), 148 (27), 147 (14), 134 (39), 133 (11), 132 (14), 121 (16), 118 (10), 117 (12), 107 (12), 91 (18), 77 (13), 65 (11), 59 (13), 57 (53), 41 (31), 39 (11). $C_{14}H_{21}NO_2$ (235.3): calcd C 71.46, H 8.99, N 5.95; found C 71.39, H 8.97, N 5.88.

*3.8. (1*R,*2*R*)*-N,N′*-Bis(4,6-di*-tert-*butyl-1-oxypyridin-2-yl-methylen)-1,2-diaminocyclohexane **2b***

To a mixture of 810 mg (3.07 mmol) of (1*R*,2*R*)-(−)-1,2-diammoniumcyclohexane mono-L-(+)-tartrate **10**, 897 mg (9.94 mmol) K_2CO_3, 5 ml of water and 12 ml of ethanol at 80°C a solution of 1.45 g (6.14 mmol) of carboxaldehyde **9** in 20 ml of ethanol was added within 45 min. After refluxing for 3 h the reaction mixture was concentrated to about half of its volume and extracted four times with 20 ml of diethyl ether. The combined organic layer was dried with Na_2SO_4 and the solvent removed in vacuo to give 1.65 g (98%) of bis-*N*-oxide ligand **2b** as a yellow solid, according to the ^{1}H NMR spectrum with sufficient purity for complexation studies. An analytically pure sample with mp 200°C and $[\alpha]_D^{27}$ +55.7 ($CHCl_3$, c=0.544 g/100 ml) was obtained by flash-chromatography (silica, ethyl acetate:triethylamine 8:1, R_f=0.87). IR (KBr): ν=3419 cm^{-1} (w), 2961 (s), 2864 (w), 1634 (w), 1613 (w), 1539 (w), 1478 (m), 1405 (m), 1385 (w), 1365 (w), 1285 (w), 1245 (s), 1204 (w), 1158 (w), 1026 (w), 934 (w), 885 (w), 829 (w), 751 (w), 692 (w), 646 (w). UV–vis (acetonitrile): λ_{max} (lg ε)=201 nm (4.35, sh), 243 (4.64), 286 (4.24), 354 (3.52). ^{1}H NMR (300 MHz, $CDCl_3$): δ=1.21 (s, 18H), 1.21–1.91 (m, 8H), 1.48 (s, 18H), 3.55–3.58 (m, 2H), 7.23 (d, *J*=2.9 Hz, 2H), 7.57 (d, *J*=2.9 Hz, 2H), 8.88 (s, 2H). ^{1}H NMR (300 MHz, CD_3OD): δ=1.29 (s, 18H), 1.48 (s, 18H), 0.80–2.00 (m, 8H), 3.61 (m, 2H), 7.47 (d, *J*=2.9 Hz, 2H), 7.64 (d, *J*=2.9 Hz, 2H), 8.80 (s, 2H). ^{13}C NMR (75.5 MHz): δ=24.34 ppm (t), 27.31 (q), 30.51 (q), 32.54 (t), 34.59 (s), 36.36 (s), 74.14 (d), 119.66 (d), 121.33 (d), 145.93 (s) 148.42 (s), 155.14 (d), 156.52 (s). MS (L-SIMS pos., matrix: 3-nitrobenzylic alcohol); *m/z* (%): 588 (5) [M+K]$^+$, 587 (11), 571 (35), 566 (7), 565 (16), 555 (5), 551 (8), 550 (38), 549 (100) [M^+], 548 (7), 547 (13), 534 (5), 533 (12), 532 (12), 531 (33), 516 (15), 515 (34), 513 (13), 499 (10). $C_{34}H_{52}N_4O_2$ (548.8): calcd C 74.41, H 9.55, N 10.21; found C 74.32, H 9.52, N 9.97.

*3.9. Complexation of copper(II) nitrate with bis-*N*-oxide ligand **2b***

To 22.0 mg (91 μmol) of copper(II) nitrate trihydrate in 1 ml of methanol 50.0 mg (91 μmol) of ligand **2b** in 1 ml of methanol were added under stirring and the resulting dark green solution was heated under reflux for 4 h. After cooling to room temperature and carefully adding 0.5 ml diethyl ether for crystalization 45 mg (66%) of copper complex **11.2** (monohydrate) as dark green plates with mp 230–234°C and $[\alpha]_D^{23}$=+343.6 ($CHCl_3$, c=0.012 g/100 ml) were obtained. IR (KBr): ν=3433 (w), 2961 (m), 2870 (m), 1667 (w), 1616 (w), 1383 (s), 1239 (m), 1216 (m), 1192 (m), 1029 (w), 933 (w), 890 (w), 863 (w), 829 (m), 809 (w), 747 (w), 655 (w), 606 (w). UV–vis (MeOH): λ_{max} (lg ε)=201 nm (6.03), 245 (5.71, sh), 256 (5.82), 263 (5.69), 280 (5.17 sh), 327 (4.61 sh), 431 (4.07). MS (L-SIMS, matrix:

3-nitrobenzylic alcohol); *m/z* (%): 673 $[M-NO_3]^+$, 611 $[M-2NO_3]^+$, 549 $C_{34}H_{52}CuO_8N_6$ (736.4): calcd C 55.46, H 7.12, N 11.41; $C_{34}H_{52}CuO_8N_6 \cdot H_2O$ (754.4): calcd C 54.13, H 7.22, N 11.14; found C 54.05, H 7.20, N 11.08.

Crystal structure determination:[18] a single crystal of the title compound was mounted on top of a glass capillary with silicone grease and cooled down to 150 K with a cold nitrogen stream of the cooling device of a Siemens P4RA four-circle diffractometer equipped with a rotating anode tube and a graphite monochromator. Accurate cell dimensions were determined at 150 K from the setting angles of 18 centred reflections with $20<2\theta<30°$. Integrated intensities were collected by the ω-scan technique with scan rates varying from 6 to 30°/min and a total scan range of 1.4°. During data collection, the intensity of a standard reflection, monitored every 199 reflections, as well as the intensity profiles indicated stable measuring conditions. In total, 5598 reflections were collected. The intensity data were corrected for Lorentz, polarization and absorption effects.

Solution and refinement of the structure: the structure was solved by direct methods and subsequent difference Fourier synthesis in the monoclinic space group C2. After anisotropic refinement of this model (SHELXL97), H atoms were added on idealized positions with the exception of the H_2O molecules. One common isotropic temperature factor was refined for the otherwise riding H atoms. The final refinement converged to $R1=0.0891$ for 2993 observed reflections ($I>2\sigma(I)$) and $wR2=0.3033$ for all reflections.

*3.10. Complex formation of Na_2PdCl_4 with bis-*N*-oxide ligand **2b***

To 13.4 mg (46 μmol) of Na_2PdCl_4 in 1 ml of tetradeuteromethanol 25.5 mg (46 μmol) of ligand **2b** in 1 ml of tetradeuteromethanol were added under stirring and the resulting red solution was heated at 40°C for 5 min. ^1H NMR (500 MHz, CD_3OD): δ=1.46 (s, 18H), 1.66 (s, 18H), 0.85–2.10 (m, 8H), 4.15 (m, 2H), 7.96 (d, *J*=2.8 Hz, 2H), 8.60 (d, *J*=2.7 Hz, 2H), 8.85 (s, 2H).

3.11. Experiment for the enantioselective cyclopropanation of styrene with diazoacetic acid ethyl ester

A mixture of 135 mg (246 μmol) of ligand **2b**, 12.2 mg (123 μmol) CuCl and 740 mg (7.11 mmol) of styrene **12** was stirred at room temperature under N_2 for 5 min. Diazoacetic acid ethyl ester (1.04 g, 9.12 mmol) was added within 30 min and stirring was continued for 2 h. By distillation at 80°C/0.24 mbar 270 mg (20%) of cyclopropanation product **14** was obtained; according to GC on a cyclodextrin column the *cis*:*trans* ratio is 45:55 and the enantiomeric excess 21% and 15%, respectively.

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