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Copper-catalyzed asymmetric addition of Et_2Zn to 2-cyclohexen-1-one and 2-carbamoyloxy-2-cyclohexen-1-one with phosphoramidite, phosphite, and bidentate phosphite–oxazoline ligands

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ABSTRACT

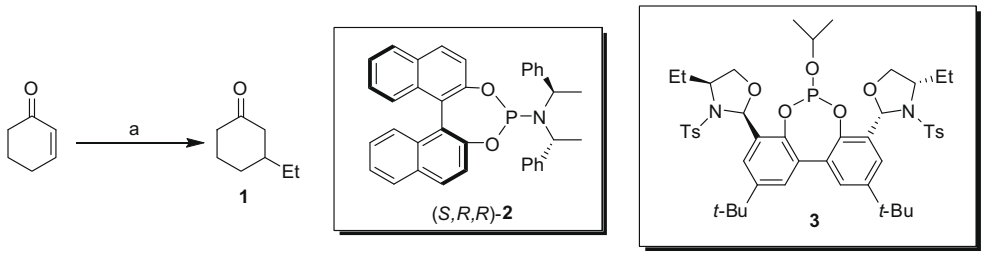
New biphenol-backboned phosphite–oxazoline bidentate ligands were synthesized and applied in the copper-catalyzed asymmetric conjugate additions on 2-cyclohexen-1-one with Et_2Zn. In these reactions, the non-chiral oxazoline unit has demonstrated significant impact on the enantioselectivity. 2-Carbamoyloxy-2-cyclohexen-1-one is a new α-oxygenated cyclic enone substrate and was synthesized and applied to the aforementioned addition with certain phosphoramidite, phosphite, and the new bidentate ligands. Good ee has been obtained on this substrate.

1. Introduction

With the contribution from many research groups,[1] copper-catalyzed asymmetric conjugate addition (ACA) of organozinc reagent to cyclic enone has become a well-established model reaction (Scheme 1). With phosphoramidite ligand (*S,R,R*)-**2** discovered by Feringa et al.,[1h,1i] excellent ee (>98%) has been achieved. However, diversity of both ligands and substrates for this reaction is relatively low. We tried to develop this reaction from both aspects. Recently, we have reported that biphenol-backboned *tropos*-phosphite ligands (e.g., compound **3**) induce good ee for this model reaction.[2] Based on these phosphite ligands, we have synthesized some bidentate ligands by adding a non-chiral oxazoline module. The new phosphite–oxazoline bidentate ligands were applied to the model ACA shown in Scheme 1. The non-chiral oxazoline module has displayed significant impact on the asymmetric induction. Also, we have developed 2-oxygenated 2-cyclohexen-1-one as a new α-oxygenated cyclic enone substrate for the aforementioned reaction shown in Scheme 1, copper-catalyzed ACA of Et_2Zn was realized for this new substrate and a good ee was obtained. Herein we disclose those preliminary results.

2. Results and discussion

Bidentate ligands are highly useful in metal-catalyzed asymmetric synthesis.[3] In particular, phosphite–oxazoline ligands have been proven to be useful in copper-catalyzed asymmetric conjugate additions with Et_2Zn, and they sometimes offer better ee than their mono-phosphite counterparts.[1a,b,4] Two reasons might account for this: (a) the bidentate ligand may offer a better chiral environment by adding more chelating points; or (b) phosphite–oxazoline ligand may fall into the category of hemilabile hybrid ligand,[5] which



Scheme 1. Reagents and conditions: (a) Et_2Zn, toluene, cat. $Cu(OTf)_2$, ligand, −40 °C, 16 h.

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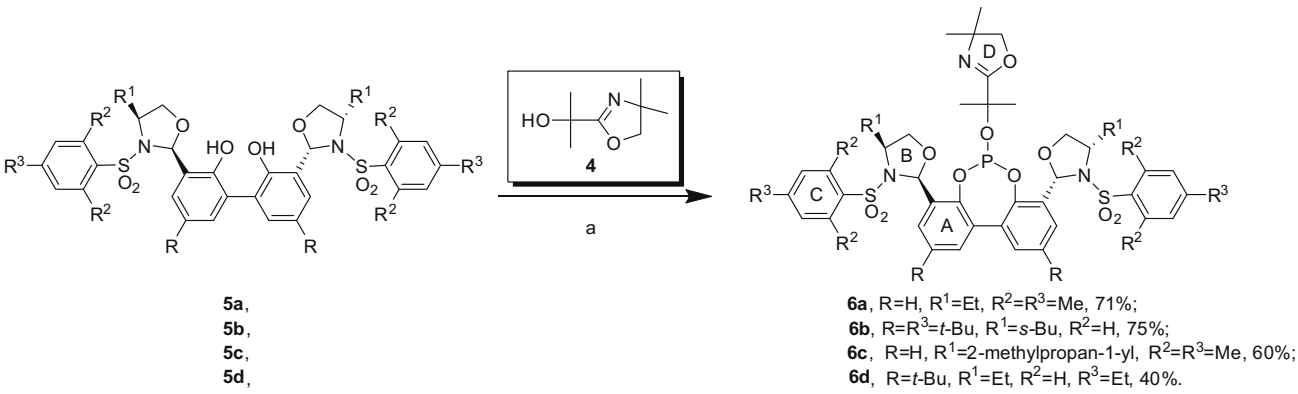
behaves differently compared to common bidentate ligands. Hence, it is reasonable to develop some new phosphite–oxazoline bidentate ligands based on our biphenol-derived phosphite ligands.

Following this idea, we chose the non-chiral alcohol **4** to construct the oxazoline module. Biphenols **5a–d** were condensed with PCl_3 and were then coupled with the oxazoline module **4**[6] to yield the target ligands **6a–d** (Scheme 2). Compounds **6a–d** are quite polar and basic. The mobile phase for their separation by silica gel chromatography requires Me_2NEt as an additive for a complete washing-off.



Scheme 2. Reagents and conditions: (a) PCl_3, TEA, toluene, 90 °C, 16 h, then compound **4**, 90 °C, overnight. The designations of R–R^3 for the substituents and A–D for the rings are used in the Experimental for assigning the NMR data.

The single crystal of compound **6c** was obtained from diethyl ether and *n*-pentane, analyzed with X-ray and is illustrated in Figure 1.[7]

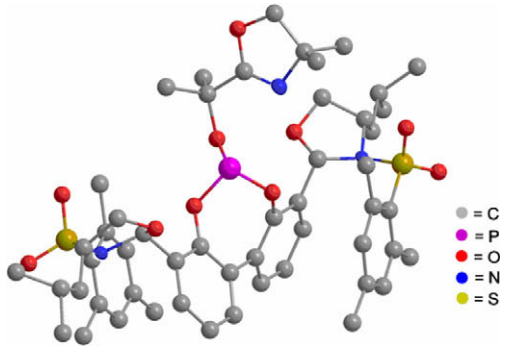


Figure 1. Crystal structure of compound **6c**. Hydrogens are omitted in the image.

New ligands **6a–d** were subjected to the model ACA shown in Scheme 1 and the resulting ees are listed out in Table 1. Compared to the optimized phosphite ligand **3**,[2] the new bidentate ligands **6a–d** produced a lower ee. In particular, compound **6d**, which has biphenol modules that are identical to those of ligand **3**, gave lowest ee among all examples. A more interesting fact is the following: the biphenol module on ligands **6a–d** originated from homologous amino alcohols; however, after being connected with a non-chiral oxazoline module, ligands **6b** and **6c** yielded reversed enantioselectivity compared to ligands **3**, **6a**, and **6d**. All the results clearly indicated the great impact of the non-chiral oxazoline module on the asymmetric induction.

Table 1
Ligands applied to the model reaction shown in Scheme 1

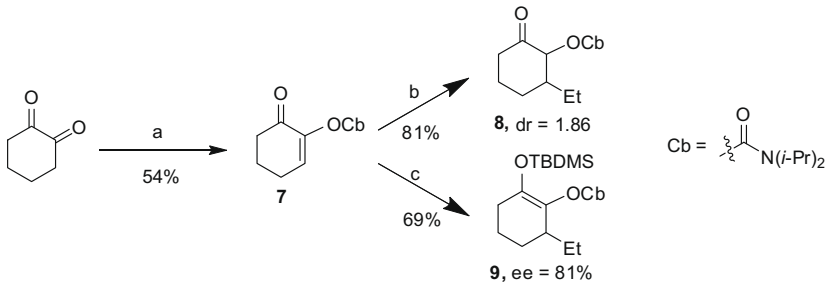
Entry	Ligand	Yield[a]	ee[b] (%)
1[c]	**3**	Quant.	+83
2	**6a**	Quant.	+16
3	**6b**	87%	−37
4	**6c**	Quant.	−23
5	**6d**	95%	+11

[a] GC yield.
[b] Measured by chiral GC on a Supelco α-Dex 225, 30 m × 0.32 mm column; symbol '+' denotes (*R*:*S*), '−' denotes (*S*:*R*).
[c] Data in this entry were published before.[2]

To extend the scope for the model reaction shown in Scheme 1, we have synthesized 2-carbamoyloxy-2-cyclohexen-1-one **7** as a new substrate (Scheme 3). To the best of our knowledge, this is the first α-oxygenated cyclic enone that undergoes copper-catalyzed ACA with organozinc reagents. Compound **7** was readily prepared by condensing 1,2-cyclohexandione and CbCl. Moderate yield was obtained probably due to the decomposition of the unstable starting material at room temperature or with the strong base. With Et_2Zn, compound **7** undergoes copper-catalyzed conjugate addition to yield compound **8**. Although this reaction is significantly accelerated by phosphoramidite (*S,R,R*)-**2**,[1a] it is still slower than the model ACA shown in Scheme 1, and hence has to be performed at −25 °C for a good yield. With phosphoramidite ligand (*S,R,R*)-**2**, 81% yield was observed after an overnight reaction. Unfortunately, we were not able to resolve compound **8** completely by chiral GC or chiral HPLC, probably due to its high polarity. However, we found that the ACA intermediate of compound **7** and Et_2Zn, which should be a pair of enantiomers, can be quenched by TBDMSOTf in situ to yield compound **9**.[8] Compound **9** was readily resolved by chiral HPLC, and it brought us the chiral information of the ACA step.

It is worth mentioning that employing a stable OCb protection is advantageous compared to simple ester protection or even other carbamates for the 2-oxygen. A less stable 2-O-protection may partially migrate when the metalated enol is formed as the intermediate of the ACA. In fact this undesired reaction was observed with 2-O-$CONPh_2$ protection.[9] However, with 2-OCb protection, no migration was detected.

As demonstrated in Scheme 3 and Table 2, ligand (*S,R,R*)-**2** produced an ee of 81% (>98% ee was achieved for the model reaction shown in Scheme 1 with this ligand) and a moderate yield for the conversion from compound **7** to **9**, while the ligand (*S,S,S*)-**2** produced practically the same ee of 82% (75% ee was achieved for the model reaction shown in Scheme 1 with (*S,S,S*)-**2**[10]) and a similar yield. This indicated a significant influence of the binaphthalene module on the asymmetric induction,[11] since the matched or mismatched bis(1-phenylethyl)amine module on ligands **2** had little effect on the asymmetric induction. Our phosphite ligand **3** has induced moderate ee (50%) and yield. The newly synthesized bidentate ligands **6a–d** gave no noticeable ee for the conversion of substrate **7** to compound **9**. The fact that ligand **3** failed to in-



Scheme 3. Reagents and conditions: (a) NaH, THF, CbCl, rt; (b) −25 °C overnight, $Cu(OTf)_2$, Et_2Zn, ligand (*S,R,R*)-**2**, toluene; (c) −25 °C overnight, $Cu(OTf)_2$, Et_2Zn, ligand (*S,R,R*)-**2**, toluene, then TBDMSOTf, rt, 4 h. Compound **9** was resolved by chiral HPLC on a Nucleosil 100-5 Chiral-2 (Macherey-Nagel) column.

duce a good ee as it does for the model reaction shown in Scheme 1, is probably because of its high steric hindrance on the *ortho*-position of the biphenol backbone, which exhibits, synergistically with the bulky 2-OCb substitution on the substrate, negative effects on the coordination with copper and the asymmetric induction. This presumption is supported by the early investigations on ACA with biphenol-backboned ligands from the group of Alexakis.[12] For the same reason, the more sterically hindered ligands **6a–d**, gave no noticeable ee for this substrate **7**.

Table 2
Asymmetric induction for the conversion from compound **7** to compound **9**

Entry	Ligand	Yield[a] (%)	ee[b] (%)
1	(*S,R,R*)-**2**	67	81
2	(*S,S,S*)-**2**	69	82
3	**3**	63	50
4	**6a**	61	<5
5	**6b**	59	<5
6	**6c**	60	<5
7	**6d**	55	<5

[a] Isolated yield.
[b] Measured by chiral HPLC on a Nucleosil 100-5 Chiral-2 (Macherey-Nagel) column. Absolute stereochemistry of product **9** was not assigned.

The enantioenriched products **8** and **9**, with three contiguous substituents on the six-membered ring, can serve as potential building blocks for complex structures.

3. Conclusions

In summary, based on our biphenol-backboned *tropos*-phosphite ligands, by incorporating a non-chiral oxazoline module, we have prepared four new phosphite–oxazoline bidentate ligands. These ligands were applied to the copper-catalyzed ACA onto 2-cyclohexen-1-one with Et_2Zn. Although lower ees were obtained compared to those obtained with their parent phosphite monodentate ligands and the phosphoramidite ligands discovered by Feringa et al., the non-chiral oxazoline module has demonstrated its significant impact on the asymmetric induction. In addition, we have invented 2-carbamoyloxy-2-cyclohexen-1-one as a new α-oxygenated substrate for the above-mentioned ACA. Phosphoramidite, phosphite, and the new phosphite–oxazoline bidentate ligands were applied with this new substrate. Good ee has been achieved with phosphoramidite ligands **2** discovered by Feringa et al. The enantioenriched products **8** and **9** can serve as potential building blocks for complex structures.

4. Experimental

4.1. General

All solvents were dried and purified prior to use: Et_2O was distilled from sodium with benzophenone as indicator, toluene was distilled from sodium, and THF was distilled from potassium. For low temperatures reactions, a *Julabo* FT902 kryostat and an acetone bath were used. All moisture-sensitive reactions were performed under Ar (ca. +1.3 bar) in heating-gun (500–600 °C)/vacuum-dried glassware sealed with a rubber septum. Medium pressure liquid chromatography (MPLC) was performed on *Merck* 60 Silica Gel (40–60 μm, 230–400 mesh ASTM), and monitored by thin layer chromatography (TLC) on *Merck* 60 F254 TLC-plates. NMR data were collected on a *Bruker* AV 300, an AV 400, an ARX 400, a *Varian* Inova 500 or a Unity Plus 600. Spectra from solutions in $CDCl_3$ (δ_C = 77.0 ppm) are calibrated relative to $SiMe_4$ (δ_H = 0.00 ppm). IR data were collected on a *Varian* 3100 Excalibur Series with *Specac* Golden Gate Single Reflection ATR. Mass data were collected on a *Bruker* MicroTof (ESI). Optical rotation data were collected on a *Perkin Elmer* 341 or 241. Melting point (not corrected) was measured on a *Stuart Scientific* SMP3. Elemental analyses were performed on an *Elementar-Analysensysteme* Vario EL III. GC data were collected on an *Agilent* 6890. Non-chiral GC was performed on a 30 m × 0.32 mm HP-5 column (GC condition: 1.5 mL × min^{-1} H_2; starting at 50 °C, 10 °C × min^{-1} to 300 °C, 15 min at 300 °C). HPLC data were collected with a *Knauer* Smartline PDA detector 2600, a Pump 1000, an Autosampler 3900, and a Manager 5000.

4.2. 3-Ethylcyclohexanone 1

A mixture of $Cu(OTf)_2$ (2 mg, 0.0055 mmol, 2.5% equiv) and the ligand (0.0055 mmol, 2.5% equiv) in 1 mL of toluene was stirred at rt for 1 h. Then 2-cyclohexen-1-one (21 mg in 1 mL toluene, 0.22 mmol) was added dropwise. The mixture was cooled to −40 °C, followed by addition of 1 M Et_2Zn in hexane (0.27 mL, 0.27 mmol, 1.2 equiv) and was stirred at this temperature for 16 h. 1 M HCOOH solution in MeOH (0.3 mL) was added to quench the reaction. Internal standard MeOPh (9 mg) was then added. The mixture was passed through a short pad of silica gel, which was then washed several times by Et_2O. Combined organic phases were evaporated (not less than 150 mbar/45 °C) and the residue was purified by MPLC (*n*-pentane/diethyl ether = 20:1 to 10:1 to 5:1 to 1:1) to yield the product or was directly analyzed by chiral GC. Analyses match the reported data.[13] Chiral GC: Supelco α-Dex 225, 30 m × 0.32 mm, 50 °C; $t_{(MeOPh)}$ = 22.0 min, $t_{(2\text{-cyclohexen-1-one})}$ = 57.6 min, $t_{(R)\text{-}\mathbf{1}}$ = 78.9 min, $t_{(S)\text{-}\mathbf{1}}$ = 83.7 min.

4.3. 2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)propan-2-ol 4

2-Hydroxy-2-methylpropanoic acid (3.12 g, 3.0 mmol) and 2-amino-2-methyl-1-propanol (2.67 g, 3.0 mmol) were suspended in 400 mL of xylene (mixture of regioisomers) and were refluxed for 20 h with continuous separation of water. The resulting mixture was directly purified by MPLC (*n*-pentane/diethyl ether = 5:1 to 2:1 to 1:1 to 1:2) to yield the product as a white solid (990 mg, 0.63 mmol, 21%). The product can be further purified by sublimation at 45 °C and 10 mbar to give colorless crystals. mp

60–62 °C (crystals from sublimation). R_f = 0.07 (ethyl acetate/cyclohexane = 1:2). t_R = 5.2 min (HP-5). IR ($\tilde{\nu}$/cm^{-1}, ATR): 3396 (br), 2975 (s), 2934 (m), 2895 (m), 1662 (s), 1464 (s), 1119 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 3.95 (s, 2H, O–C*H*$_2$–C(Me)$_2$–N), 3.19 (s, 1H, OH), 1.37 (s, 6H, (*Me*)$_2$C–OH), 1.21 (s, 6H, O–CH$_2$–C(*Me*)$_2$–N). ^{1}H NMR matches the reported data.[6] ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 170.73 (O–C=N), 80.41 (O–*C*H$_2$–C(Me)$_2$–N), 68.62 ((Me)$_2$–*C*–OH), 66.94 (O–CH$_2$–*C*(Me)$_2$–N), 28.18 (2C, O–CH$_2$–C(*Me*)$_2$–N), 27.72 (2C, (*Me*)$_2$C–OH). HRMS (ESI+) calcd for $C_8H_{15}NO_2H^+$ = 158.1181, $C_8H_{15}NO_2Na^+$ = 180.1000, found $[M+H]^+$ = 158.1180, $[M+Na]^+$ = 180.0999.

4.4. General procedure for the syntheses of ligands 6a–d

One of the diols **5a**–**d** (0.1 mmol, 1.0 equiv) and triethylamine (0.33 mmol, 3.3 equiv) were mixed in 3 mL of toluene, and this was followed by addition of PCl_3 (1.0 mmol, 1.0 equiv) at rt. The reaction mixture was then stirred at 90 °C for 16 h, before the oxazoline module **4** (1.2 mmol, 1.2 equiv) was added. The resulting mixture was further stirred overnight at 90 °C, and was directly subjected to MPLC separation (*n*-pentane/diethyl ether = 10:1 to 5:1 to 2:1 to 1:1 to 1:2 to 1:5, all the eluents contain 5% v/v Me_2-NEt) to yield the product **6a**–**d**.

4.4.1. (2*S*,2′*S*,4*S*,4′*S*)-2,2′-[6-(2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl)propan-2-yloxy)dibenzo-[*d*,*f*][1,3,2]dioxaphosphepine-4,8-diyl]bis[4-ethyl-3-(mesitylsulfonyl)oxazolidine] 6a

Compound was obtained as a white foam, yield: 71%. R_f = 0.15 (ethyl acetate/cyclohexane = 1:2). $[\alpha]_D^{20} = -38.2$ (*c* 0.50, $CHCl_3$). IR ($\tilde{\nu}$/cm^{-1}, ATR): 2971 (s), 2938 (m), 2877 (m), 1666 (m), 1604 (m), 1454 (s), 1316 (s), 1157 (s), 969 (s), 889 (s), 677 (s). For the subscripts and superscripts used in the following NMR data, see Scheme 2. ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.33–7.29 (m, 2H, H$_A$), 6.99–6.88 (m, 4H, H$_A$), 6.44 (s, 2H, H$_C$), 6.33 (s, 2H, H$_C$), 6.22 (s, 1H, O–C*H*–N$_B$), 6.13 (s, 1H, O–C*H*–N$_B$), 4.20–3.91 (m, 8H, H$_{B\ and\ D}$), 2.44 (s, 6H, CH$_{3C}$), 2.40 (s, 6H, CH$_{3C}$), 2.02–1.95 (m, 2H, CH$_{2R^1}$), 1.95 (s, 3H, CH$_{3C}$), 1.86 (s, 3H, CH$_{3C}$), 1.84–1.69 (m, 2H, CH$_{2R^1}$), 1.61 (s, 3H, O–C(C*H*$_3$)$_{2D}$), 1.60 (s, 3H, O–C(C*H*$_3$)$_{2D}$), 1.28 (s, 6H, CH$_{3D}$), 0.99–0.92 (m, 6H, CH$_{3R^1}$). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 166.98 (O–C=N$_D$), 147.92 (C$_A$), 146.99 (C$_A$), 142.76 (C$_C$), 142.59 (C$_C$), 140.75 (2C, C$_C$), 140.57 (2C, C$_C$), 131.52 (2C, C$_C$), 131.21(2C, C$_C$), 130.49 (C$_C$), 130.14 (C$_C$), 130.02 (C$_A$), 129.98 (2C, C$_A$), 129.88 (2C, C$_A$), 129.55 (C$_A$), 128.08 (C$_A$), 128.74 (C$_A$), 124.00 (C$_A$), 123.62 (C$_A$), 87.18 (O–*C*H–N$_B$), 87.12 (O–*C*H–N$_B$), 79.83 (O–*C*H$_2$–C(Me)$_{2D}$), 75.83 (O–*C*H$_2$–C(Me)$_{2D}$), 70.92 (O–*C*H$_2$–CHEt$_B$), 70.53 (O–*C*H$_2$–CHEt$_B$), 67.87 (O–CH$_2$–*C*(Me)$_{2D}$), 59.61 (O–CH$_2$–*C*HEt$_B$), 59.16 (O–CH$_2$–*C*HEt$_B$), 27.73 (2C, CH$_{2R^1}$), 28.15–28.01 (4C, O–C(*C*H$_3$)$_{2D}$ and O–CH$_2$–C(*C*H$_3$)$_{2D}$), 23.09 (2C, CH$_{3C}$), 23.01 (2C, CH$_{3C}$), 20.87 (CH$_{3C}$), 20.82 (CH$_{3C}$), 11.01 (CH$_{3R^1}$), 10.96 (CH$_{3R^1}$). ^{31}P NMR (121.5 MHz, $CDCl_3$): δ/ppm = 151.6. HRMS (ESI+) calcd for $C_{48}H_{60}N_3O_{10}PS_2H^+$ = 934.3536, $C_{48}H_{60}N_3O_{10}PS_2Na^+$ = 956.3355, found $[M+H]^+$ = 934.3519, $[M+Na]^+$ = 956.3344.

4.4.2. (2*S*,2′*S*,4*S*,4′*S*)-2,2′-[2,10-Di-*tert*-butyl-6-(2-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)propan-2-yloxy)dibenzo[*d*,*f*][1,3,2]dioxaphosphepine-4,8-diyl]bis[4-*sec*-butyl-3-(4-*tert*-butylphenylsulfonyl)oxazolidine] 6b

Compound was obtained as a white foam, yield: 75%. R_f = 0.41 (ethyl acetate/cyclohexane = 1:2). $[\alpha]_D^{20} = -3.4$ (*c* 0.50, $CHCl_3$). IR ($\tilde{\nu}$/cm^{-1}, ATR): 2964 (s), 2873 (m), 1662 (m), 1595 (m), 1477 (s), 1354 (s), 1169 (s), 1088 (s), 909 (s), 730 (s), 643 (s). For the subscripts and superscripts used in the following NMR data, see Scheme 2. ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.68 (d, *J* = 8.6 Hz, 2H, H$_C$), 7.65 (d, *J* = 8.6 Hz, 2H, H$_C$), 7.58 (d, *J* = 2.4 Hz, 1H, H$_A$), 7.41 (d, *J* = 2.4 Hz, 1H, H$_A$), 7.37 (d, *J* = 8.6 Hz, 2H, H$_C$), 7.29 (d, *J* = 8.6 Hz, 2H, H$_C$), 7.27 (m, 1H, H$_A$), 7.18 (m, 1H, H$_A$), 6.26 (s, 1H, O–C*H*–N$_B$), 6.13 (s, 1H, O–C*H*–N$_B$), 3.99–3.86 (m, 2H, O–C*H*$_2$–CH-*s*-Bu$_B$), 3.90–3.70 (m, 4H, O–C*H*$_2$–CH-*s*-Bu$_B$ and O–C*H*$_2$–C(Me)$_{2D}$), 3.44–3.40 (m, 2H, O–CH$_2$–C*H*-*s*-Bu $_B$), 1.96–1.79 (m, 6H, CH$_{R^1}$ and CH$_{2R^1}$), 1.50 (s, 3H, O–C(C*H*$_3$)$_{2D}$), 1.49 (s, 3H, HO–C(C*H*$_3$)$_{2D}$), 1.26–1.19 (m, 36H, *t*-Bu), 1.19–1.17 (m, 6H, CH$_{3D}$), 1.00–0.92 (m, 12H, Me$_{R^1}$). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 165.94 (O–C=N$_D$), 155.81 (C$_C$), 155.53 (C$_C$), 146.20 (C$_A$), 145.66 (C$_A$), 145.21 (C$_A$), 145.13 (C$_A$), 144.10 (C$_A$), 144.07 (C$_A$), 133.38 (C$_C$), 133.33 (C$_C$), 128.16 (C$_A$), 128.00 (C$_A$), 127.22 (2C, C$_C$), 127.14 (2C, C$_C$), 127.07 (C$_A$), 126.31 (C$_A$), 124.97 (2C, C$_C$), 124.71 (2C, C$_C$), 124.27 (C$_A$), 124.00 (C$_A$), 88.02 (O–*C*H–N$_B$), 87.05 (O–*C*H–N$_B$), 78.41 (O–*C*H$_2$–C(Me)$_{2D}$), 74.47 (O–*C*(CH$_3$)$_{2D}$), 67.70 (O–*C*H$_2$–CH-*s*-Bu$_B$), 67.51 (O–*C*H$_2$–CH-*s*-Bu$_B$), 66.61 (O–CH$_2$–*C*(Me)$_{2D}$), 63.80 (O–CH$_2$–*C*H-*s*-Bu$_B$), 63.09 (O–CH$_2$–*C*H-*s*-Bu$_B$), 37.17 (CH$_{R^1}$), 36.45 (CH$_{R^1}$), 34.10 (*t*-Bu), 34.06 (*t*-Bu), 33.64 (*t*-Bu), 33.45 (*t*-Bu), 30.41 (4C, *t*-Bu), 30.38 (4C, *t*-Bu), 30.03 (4C, *t*-Bu), 27.01 (*C*H$_{3D}$), 26.97 (*C*H$_{3D}$), 26.91 (HO–C(*C*H$_3$)$_{2D}$), 26.72 (HO–C(*C*H$_3$)$_{2D}$), 25.45 (CH$_{2R^1}$), 25.21 (CH$_{2R^1}$), 14.36 (Me$_{R^1}$), 14.27 (Me$_{R^1}$), 10.86 (Me$_{R^1}$), 10.68 (Me$_{R^1}$). ^{31}P NMR (121.5 MHz, $CDCl_3$): δ/ppm = 151.2. HRMS (ESI+) calcd for $C_{62}H_{88}N_3O_{10}PS_2H^+$ = 1130.5727, $C_{62}H_{88}N_3O_{10}PS_2Na^+$ = 1152.5546, found $[M+H]^+$ = 1130.5719, $[M+Na]^+$ = 1152.5532.

4.4.3. (2*S*,2′*S*,4*S*,4′*S*)-2,2′-[6-(2-(4,4-Dimethyl-4,5-dihydrooxazol-2-yl) propan-2-yloxy)dibenzo-[*d*,*f*][1,3,2]dioxaphosphepine-4,8-diyl]bis[4-isobutyl-3-(mesitylsulfonyl)oxazolidine] 6c

Compound was obtained as a white foam (60%) which can be recrystallized from diethyl ether and *n*-petane. Mp 177–180 °C (diethyl ether and *n*-pentane). R_f = 0.27 (ethyl acetate/cyclohexane = 1:2). $[\alpha]_D^{20} = +30.2$ (*c* 0.50, $CHCl_3$). IR ($\tilde{\nu}$/cm^{-1}, ATR): 2959 (s), 2936 (m), 2871 (m), 1663 (m), 1604 (m), 1453 (s), 1313 (s), 1154 (s), 971 (s), 888 (s), 729 (s). For the subscripts and superscripts used in the following NMR data, see Scheme 2. ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.35–7.31 (m, 2H, H$_A$), 7.05–6.93 (m, 4H, H$_A$), 6.49 (s, 2H, H$_C$), 6.38 (s, 2H, H$_C$), 6.27 (s, 1H, O–C*H*–N$_B$), 6.16 (s, 1H, O–C*H*–N$_B$), 4.31–4.19 (m, 2H, O–CH$_2$–C*H*–N$_B$), 4.13–3.85 (m, 6H, O–C*H*$_2$–CH–N$_B$ and O–C*H*$_2$–C(Me)$_{2D}$), 2.46 (s, 6H, CH$_{3C}$), 2.41 (s, 6H, CH$_{3C}$), 1.98 (s, 3H, CH$_{3C}$), 1.90 (s, 3H, CH$_{3C}$), 1.78–1.71 (m, 2H, CH$_{R^1}$), 1.70–1.60 (m, 4H, CH$_{R^1}$), 1.62 (s, 3H, O–C(C*H*$_3$)$_{2D}$), 1.60 (s, 3H, O–C(C*H*$_3$)$_{2D}$), 1.28 (s, 6H, CH$_{3D}$), 0.94–0.88 (m, 12H, Me$_{R^1}$). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 166.01 (O–C=N$_D$), 146.97 (C$_A$), 146.08 (C$_A$), 141.81 (C$_C$), 141.62 (C$_C$), 139.75 (2C, C$_C$), 139.61 (2C, C$_C$), 130.56 (2C, C$_C$), 130.25 (2C, C$_C$), 129.61 (C$_C$), 129.29 (C$_C$), 129.11 (C$_A$), 129.05 (2C, C$_A$), 128.68 (2C, C$_A$), 128.64 (C$_A$), 127.09 (C$_A$), 126.74 (C$_A$), 122.97 (C$_A$), 122.62 (C$_A$), 85.95 (O–*C*H–N$_B$), 85.86 (O–*C*H–N$_B$), 79.55 (O–*C*H$_2$–C(Me)$_{2D}$), 78.81 (HO–*C*(CH$_3$)$_{2D}$), 70.41 (O–*C*H$_2$–CHN$_B$), 70.14 (O–*C*H$_2$–CHN$_B$), 66.86 (O–CH$_2$–*C*(Me)$_{2D}$), 55.76 (O–CH$_2$–*C*HN$_B$), 55.20 (O–CH$_2$–*C*HN$_B$), 42.93 (CH$_{2R^1}$), 42.56 (CH$_{2R^1}$), 27.20–26.99 (4C, HO–C(*C*H$_3$)$_{2D}$ and O–CH$_2$–C(*C*H$_3$)$_{2D}$), 26.67 (CH$_{R^1}$), 24.76 (CH$_{R^1}$), 22.11 (2C, Me$_{R^1}$), 22.01 (4C, CH$_{3C}$), 20.76 (2C, Me$_{R^1}$), 19.86 (CH$_{3C}$), 19.82(CH$_{3C}$). ^{31}P NMR (121.5 MHz, $CDCl_3$): δ/ppm = 151.8. HRMS (ESI+) calcd for $C_{52}H_{68}N_3O_{10}PS_2H^+$ = 990.4162, $C_{52}H_{68}N_3O_{10}PS_2Na^+$ = 1012.3981, found $[M+H]^+$ = 990.4133, $[M+Na]^+$ = 1012.3942. $C_{52}H_{68}N_3O_{10}PS_2$ (990.21): C 63.07, H 6.92, N 4.24. Found: C 63.15, H 7.03, N 4.06.

4.4.4. (2*S*,2′*S*,4*S*,4′*S*)-2,2′-[2,10-Di-*tert*-butyl-6-(2-(4,4-dimethyl-4,5-dihydrooxazol-2-yl)propan-2-yloxy)dibenzo[*d*,*f*][1,3,2] dioxaphosphepine-4,8-diyl]bis[4-ethyl-3-tosyloxazolidine] 6d

Compound was obtained as a white foam, yield: 40%. R_f = 0.12 (ethyl acetate/cyclohexane = 1:2). $[\alpha]_D^{20} = +3.3$ (*c* 0.50, $CHCl_3$). IR ($\tilde{\nu}$/cm^{-1}, ATR): 2965 (s), 2935 (m), 2905 (m), 2872 (m), 1662 (m), 1598 (m), 1463 (s), 1353 (s), 1165 (s), 1124 (s), 1094 (s), 971 (s), 911 (s), 881 (s), 867 (s), 729 (s), 666 (s), 596 (s). For the subscripts and superscripts used in the following NMR data, see Scheme 2. ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm = 7.77 (d, *J* = 8.4 Hz, 2H, H$_C$), 7.70 (d,

J = 8.1 Hz, 2H, H_C), 7.63 (d, J = 2.5 Hz, 1H, H_A), 7.50 (d, J = 2.5 Hz, 1H, H_A), 7.38 (d, J = 2.5 Hz, 1H, H_A), 7.31 (d, J = 2.5 Hz, 1H, H_A), 7.28 (d, J = 8.4 Hz, 2H, H_C), 7.19 (d, J = 8.1 Hz, 2H, H_C), 6.47 (s, 1H, O–C*H*–N_B), 6.25 (s, 1H, O–C*H*–N_B), 3.99–3.95 (m, 1H, O–CH_2–C*H*Et_B), 3.94–3.89 (m, 2H, O–C*H*$_2$–$CHEt_B$ and O–CH_2–C*H*Et_B), 3.88–3.86 (m, 2H, O–C*H*$_2$–$C(Me)_{2D}$), 3.76–3.60 (m, 3H, O–C*H*$_2$–$CHEt_B$), 2.42 (s, 3H, CH_{3C}), 2.38 (s, 3H, CH_{3C}), 2.17–2.08 (m, 1H, CH_{2R^1}), 2.08–2.01 (m, 1H, CH_{2R^1}), 1.91–1.83 (m, 1H, CH_{2R^1}), 1.79–1.69 (m, 1H, CH_{2R^1}), 1.62 (s, 3H, HO–C(C*H*$_3$)$_{2D}$), 1.61 (s, 3H, HO–C(C*H*$_3$)$_{2D}$), 1.37 (s, 9H, *t*-Bu), 1.34 (s, 9H, *t*-Bu), 1.27 (s, 3H, CH_{3D}), 1.26 (s, 3H, CH_{3D}), 1.11 (t, J = 7.4 Hz, 3H, CH_{3R^1}), 1.07 (t, J = 7.5 Hz, 3H, CH_{3R^1}). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm = 167.05 (O–C=N_D), 147.08 (C_A), 146.83 (C_A), 145.99 (C_A), 145.26 (C_A), 143.74 (C_C), 143.45 (C_C), 134.98 (C_C), 134.85 (C_C), 131.76 (C_A), 130.42 (C_A), 129.71 (2C, C_C), 129.42 (2C, C_C), 129.13 (2C, C_A), 128.19 (2C, C_C) 128.05 (2C, C_C), 128.02 (C_A), 127.50 (C_A), 125.09 (C_A), 125.03 (C_A), 88.92 (O–*C*H–N_B), 87.80 (O–*C*H–N_B), 79.39 O–CH_2–C(Me)$_{2D}$), 75.54 (O–*C*(C*H*$_3$)$_{2D}$), 70.32 (O–*C*H$_2$–$CHEt_D$), 70.24 (O–*C*H$_2$–$CHEt_B$), 67.57 (O–CH_2–*C*(Me)$_{2D}$), 61.54 (O–CH_2–*C*HEt_B), 60.80 (O–CH_2–*C*HEt_B), 34.66 (*t*-Bu), 34.51 (*t*-Bu), 31.44 (3 C, *t*-Bu), 31.36 (3 C, *t*-Bu), 28.19 (CH_{2R^1}), 27.96 (*C*H$_{3D}$), 27.91 (*C*H$_{3D}$), 27.75 (O–C(*C*H$_3$)$_{2D}$), 27.69 (O–C(*C*H$_3$)$_{2D}$), 27.49 (CH_{2R^1}), 21.54 (2C, CH_{3C}), 10.85 (CH_{3R^1}), 10.67 (CH_{3R^1}). ^{31}P NMR (121.5 MHz, $CDCl_3$): δ/ppm = 151.5. HRMS (ESI+) calcd for $C_{52}H_{68}N_3O_{10}PS_2H^+$ = 990.4162, $C_{52}H_{68}N_3O_{10}PS_2Na^+$ = 1012.3981, found $[M+H]^+$ = 990.4147, $[M+Na]^+$ = 1012.3956. Anal. Calcd for $C_{52}H_{68}N_3O_{10}PS_2$ (990.21): C, 63.07; H, 6.92; N, 4.24. Found: C, 62.84; H, 6.79; N, 4.04.

4.5. 6-Oxocyclohex-1-enyl *N,N*-diisopropylcarbamate 7

At first, NaH (600 mg, 60% in oil, 15 mmol, 1.5 equiv) was suspended in 40 mL of THF and cooled with an ice bath. To this suspension, a solution of 1,2-cyclohexanedione (1.12 g, 10 mmol) in 40 mL of THF was added dropwise. The reaction mixture was then warmed to rt, followed by addition of CbCl (2460 mg, 15 mmol, 1.5 equiv). The resulting suspension was stirred at rt for 4 h. 2 N HCl (30 mL) was added to quench the reaction. Water phase was separated and extracted several times with diethyl ether. Combined organic layers were washed with 2 N HCl, satd aq $NaHCO_3$, and brine in turn and were evaporated to dryness. The residue was purified by MPLC (*n*-pentane/diethyl ether = 10:1 to 5:1 to 1:1 to 1:2) to yield the product as a yellow oil (1.29 g, 5.4 mmol, 54%) which turns into solid upon storage at +4 °C. R_f = 0.28 (ethyl acetate/cyclohexane = 1:2). t_R = 14.6 min (HP-5). IR ($\tilde{\nu}$/cm^{-1}, ATR): 3036 (m), 2969 (s), 2935 (s), 2875 (m), 2837 (m), 1711 (s), 1689 (s), 1652 (m), 1433 (s), 1369 (s), 1312 (s), 1292 (s), 1140 (s), 1108 (s), 1044 (s), 903 (s), 630 (s), 605 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm 6.50 (t, J = 4.4 Hz, 1H, CH=), 3.91–3.84 (m, 2H, Cb), 2.49–2.46 (m, 2H, CH_2), 2.44–2.40 (m, 2H, CH_2), 1.99 (dt, J = 6.1 Hz, 12.4 Hz, 2H, CH_2), 1.20 (d, J = 6.7 Hz, 12H, Cb). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm 192.88 (C=O), 153.03 (C=O), 145.49 (CbOC=), 134.99 (CH=), 46.54 (Cb), 46.51 (Cb), 38.27 (CH_2), 24.84 (CH_2), 22.71 (CH_2), 21.17 (2C, Cb), 20.36 (2C, Cb). HRMS (ESI+) calcd for $C_{13}H_{21}NO_3Na^+$ = 262.1419, found $[M+Na]^+$ = 262.1408. Anal. Calcd for $C_{13}H_{21}NO_3$ (239.31): C, 65.25; H, 8.84; N, 5.65. Found: C, 64.98; H, 8.60; N, 5.56.

4.6. 2-Ethyl-6-oxocyclohexyl *N,N*-diisopropylcarbamate 8

A mixture of $Cu(OTf)_2$ (2 mg, 0.0055 mmol, 2.5% equiv) and the ligand (*S,R,R*)-**2** (3 mg, 0.0055 mmol, 2.5% equiv) in toluene (1 mL) was stirred at rt for 1 h. Then the starting material **7** (53 mg in 1 mL of toluene, 0.22 mmol) was added dropwise. The mixture was cooled to −25 °C, followed by addition of 1 M Et_2Zn in hexane (0.27 mL, 0.27 mmol, 1.2 equiv) and was stirred at this temperature for 16 h. Then, 1 M HCOOH solution in MeOH (0.3 mL) was added to quench the reaction. The quenched mixture was passed through a short pad of silica gel, which was then washed several times by Et_2O. Combined organic phases were evaporated and the residue was purified by MPLC (*n*-pentane/diethyl ether = 20:1 to 10:1 to 5:1 to 1:1) to yield the product **8** (48 mg, 0.18 mmol, 81%) as a colorless oil. R_f = 0.33 (ethyl acetate/cyclohexane = 1:2). t_R = 15.1 min (major), 15.5 (minor) (HP-5) (dr = 1.86:1). $[\alpha]_D^{20} = -18.9$ (produced with (*S,R,R*)-2, as the 1.86:1 diastereomeric mixture, *c* 1.0, $CHCl_3$). IR ($\tilde{\nu}$/cm^{-1}, ATR): 2966 (s), 2935 (s), 2874 (m), 1733 (s), 1687 (s), 1434 (s), 1368 (s), 1293 (s), 1215 (s), 1134 (s), 1089 (s), 1048 (s), 632 (s), 609 (s). NMR data were recorded from the diastereomeric mixture and were resolved separately as following. NMR of major diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm 4.95 (d, J = 11.8 Hz, 1H, CH–OCb), 4.10–3.95 (m, 1H, Cb), 3.94–3.77 (m, 1H, Cb), 2.47–2.32 (m, 2H, CH_{2ring}), 2.08–2.00 (m, 2H, CH_{2ring}), 1.80–1.77 (m, 1H, CH–Et), 1.75–1.68 (m, 1H, CH_{2Et}), 1.64–1.44 (m, 2H, CH_{2ring}), 1.37–1.32 (m, 1H, CH_{2Et}), 1.31–1.15 (m, 12H, Cb), 0.93 (t, J = 7.5 Hz, 3H, Me_{Et}). ^{13}C–NMR (100 MHz, $CDCl_3$): δ/ppm 205.90 (C=O), 154.90 (C=O), 80.36 (CH–OCb), 46.38 (Cb), 45.67 (Cb), 45.67 (*C*H–Et), 40.43 (CH_{2ring}), 28.94 (CH_{2ring}), 25.66 (CH_{2ring}), 25.33 (CH_{2Et}), 21.73 (CH_{3Cb}), 21.26 (CH_{3Cb}), 20.51 (CH_{3Cb}), 20.33 (CH_{3Cb}), 10.53 (Me_{Et}). NMR of minor diastereoisomer: ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm 5.15 (d, J = 4.8 Hz, 1H, CH–OCb), 4.10–3.95 (m, 1H, Cb), 3.94–3.77 (m, 1H, Cb), 2.47–2.32 (m, 2H, CH_{2ring}), 2.20–2.15 (m, 1H, CH–Et), 1.92–1.77 (m, 2H, CH_{2ring}), 1.64–1.54 (m, 1H, CH_{2Et}), 1.51–1.44 (m, 2H, CH_{2ring}), 1.31–1.15 (m, 12H, Cb), 1.19–1.15 (m, 1H, CH_{2Et}), 0.90 (t, J = 7.5 Hz, 3H, Me_{Et}). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm 206.80 (C=O), 154.60 (C=O), 79.98 (CH–OCb), 46.38 (Cb), 45.67 (Cb), 43.91 (*C*H–Et), 39.80 (CH_{2ring}), 26.01 (CH_{2ring}), 22.83 (CH_{2ring}), 21.73 (CH_{3Cb}), 21.26 (CH_{3Cb}), 20.51 (CH_{3Cb}), 20.33 (CH_{3Cb}), 20.33 (CH_{2Et}), 11.37 (Me_{Et}). HRMS (ESI+) calcd for $C_{15}H_{27}NO_3Na^+$ = 292.1889, found $[M+Na]^+$ = 292.1883. Anal. Calcd for $C_{15}H_{27}NO_3$ (269.38): C, 66.88; H, 10.10; N, 5.20. Found: C, 66.92; H, 10.00; N, 5.38.

4.7. 2-(*tert*-Butyldimethylsilyloxy)-6-ethylcyclohex-1-enyl *N,N*-diisopropylcarbamate 9

A mixture of $Cu(OTf)_2$ (2 mg, 0.0055 mmol, 2.5% equiv) and the ligand (0.0055 mmol, 2.5% equiv) in 1 mL of toluene was stirred at rt for 1 h. Then the starting material **7** (53 mg in 1 mL of toluene, 0.22 mmol) was added dropwise. The mixture was cooled to −25 °C, followed by addition of 1 M Et_2Zn in hexane (0.27 mL, 0.27 mmol, 1.2 equiv) and was stirred at this temperature for 16 h. Then TBDMSOTf (143 mg, 0.54 mmol, 2.4 equiv) was added and the reaction mixture was warmed to rt. After being stirred at rt for 4 h, the reaction mixture was quenched by satd aq $NaHCO_3$ solution. The water phase was separated and extracted with diethyl ether. Each batch of the organic washings was passed through a short silica gel column (the same column for all batches). Combined organic phases were evaporated and the residue was purified by MPLC (*n*-pentane/diethyl ether = 40:1 to 30:1 to 20:1 to 10:1) to yield the product **9** (yields are described in Table 2) as a colorless oil. R_f = 0.63 (ethyl acetate/cyclohexane = 1:2). t_R = 18.1 min (HP-5). chiral-HPLC: Nucleosil 100-5 Chiral-2 (Macherey-Nagel), isopropanol/*n*-hexane = 1:2000, 0.6 mL/min, 41 min, 45 min. $[\alpha]_D^{20} = +19.0$ (produced with (*S,S,S*)-2, ee = 82%, *c* 1.0, $CHCl_3$). IR ($\tilde{\nu}$/cm^{-1}, ATR): 2961 (s), 2931 (s), 2859 (s), 1708 (s), 1429 (s), 1361 (s), 1314 (s), 1212 (s), 1114 (s), 1045 (s), 939 (s), 836 (s), 781 (s), 632 (s). ^{1}H NMR (400 MHz, $CDCl_3$): δ/ppm 4.26–4.17 (m, 1H, Cb), 3.73–3.65 (m, 1H, Cb), 2.44–2.37 (m, 1H, *C*H–Et), 2.17–2.14 (m, 2H, CH_2-3), 1.79–1.76 (m, 1H, CH_2-5), 1.72–1.62 (m, 2H, CH_2-4) 1.59–1.56 (m, 1H, CH_{2Et}), 1.47–1.41 (m, 1H, CH_2-5), 1.32–1.29 (m, 6H, Cb), 1.28–1.26 (m, 1H, CH_{2Et}), 1.23–1.21 (m, 6H, Cb), 0.93–0.92 (m, 9H, *t*-Bu), 0.89 (t, J = 7.5 Hz,

3H, Me_{Et}), 0.15 (s, 3H, Si–CH_3), 0.14 (s, 3H, Si–CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ/ppm 152.44 (C=O), 138.92 (C=*C*–OSi), 133.11 (C=*C*–OCb), 46.74 (Cb), 45.46 (Cb), 37.83 (*C*H–Et), 30.18 (CH_2-3), 27.33 (CH_2-5), 25.80 (3 C, $Me_{t\text{-}Bu}$), 24.86 (*C*$H_{2,Et}$), 21.33 (Cb), 20.96 (Cb), 20.74 (Cb), 20.52 (Cb), 20.40 (CH_2-4), 18.13 ($C_{q,t\text{-}Bu}$), 11.36 (Me_{Et}). HRMS (ESI+) calcd for $C_{21}H_{41}NO_3Si$-Na^+ = 406.2753, found $[M+Na]^+$ = 406.2753. Anal. Calcd for $C_{21}H_{41}NO_3Si$ (383.64): C, 65.75; H, 10.77; N 3.65. Found: C, 65.49; H, 10.89; N, 3.63.

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References

1. Examples using phosphite ligands: (a) Alexakis, A.; Vastra, J.; Burton, J.; Benhaim, C.; Mangeney, P. *Tetrahedron Lett.* **1998**, 7869–7872; (b) Alexakis, A.; Benhaim, C.; Fournioux, X.; van den Heuvel, A.; Leveque, J. M.; March, S.; Rosset, S. *Synlett* **1999**, 1811–1813; Using phosphite–oxazoline ligands: (c) Knöbel, A. K. H.; Escher, I. H.; Pfaltz, A. *Tetrahedron* **2000**, *56*, 2879–2888; (d) Escher, I. H.; Pfaltz, A. *Synlett* **1997**, 1429–1431; Using phosphonite ligands: (e) Reetz, M.; Gosberg, A.; Goddard, R.; Kyung, S. H. *Chem. Commun.* **1998**, 2077–2078; Using phosphine ligands (f) Yamanoi, Y.; Imamoto, T. *J. Org. Chem.* **1999**, *64*, 2988–2989; (g) Morimoto, T.; Yamaguchi, Y.; Suzuki, M.; Saitoh, A. *Tetrahedron Lett.* **2000**, 10025–10029; Using phosphoramidte ligands: (h) Feringa, B. L.; Pineschi, M.; Arnold, L. A.; Imbos, R.; de Vries, A. H. M. *Angew. Chem., Int. Ed.* **1997**, *36*, 2620–2623; (i) Feringa, B. L. *Acc. Chem. Res.* **2000**, *33*, 346–353; Using non-phosphorous ligands: (j) Chataignier, I.; Gennari, C.; Piarulli, U.; Ceccarelli, S. *Angew. Chem., Int. Ed.* **2000**, *39*, 916–918; For a general review, see: (k) Alexakis, A.; Bäckvall, J. E.; Krause, N.; Pàmies, O.; Diéguez, M. *Chem. Rev.* **2008**, *108*, 2796–2823.
2. Wünnemann, S.; Fröhlich, R.; Hoppe, D. *Org. Lett.* **2006**, *8*, 2455–2458.
3. Several excellent reviews: (a) Breit, B. *Angew. Chem., Int. Ed.* **2005**, *44*, 6816–6825; (b) Guiry, P. J.; Saunders, C. P. *Adv. Synth. Catal.* **2004**, *346*, 497–537; (c) van Leeuwen, P. W. N. M.; Kamer, P. C. J.; Reek, J. N. H.; Dierkes, P. *Chem. Rev.* **2000**, *100*, 2741–2770.
4. For a review, see: McManus, H. A.; Guiry, P. J. *Chem. Rev.* **2004**, *104*, 4151–4202. and references therein.
5. (a) Bonnaventure, I.; Charette, A. B. *J. Org. Chem.* **2008**, *73*, 6330–6340; For review, see: (b) Bassetti, M. *Eur. J. Inorg. Chem.* **2006**, 4473–4482.
6. Pridgen, L. N.; Miller, G. *J. Heterocycl. Chem.* **1983**, *20*, 1223–1230.
7. X-ray crystal structure analysis for compound **6c**: formula $C_{52}H_{68}N_3O_{10}PS_2$, M = 990.18, colorless crystal 0.15 × 0.10 × 0.04 mm, a = 8.7952(4), b = 10.8509(5), c = 27.7865(14) Å, β = 94.857(2)°, V = 2642.3(2) Å^3, ρ_{calc} = 1.245 g cm^{-3}, μ = 1.673 mm^{-1}, empirical absorption correction ($0.788 \leqslant T \leqslant 0.936$), Z = 2, monoclinic, space group $P2_1$ (No. 4), λ = 1.54178 Å, T = 223 K, ω and φ scans, 20,350 reflections collected (±h, ±k, ±l), [(sinθ)/λ] = 0.60 Å^{-1}, 7136 independent (R_{int} = 0.077) and 5863 observed reflections [$I \geqslant 2\sigma(I)$], 627 refined parameters, R = 0.058, wR^2 = 0.162, Flack parameter 0.00(2), max. residual electron density 0.22 (−0.27) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms. Data set was collected with a Nonius KappaCCD diffractometer. Programs used: data collection COLLECT (Nonius B.V., 1998), data reduction Denzo-SMN (Otwinowski, Z.; Minor, W. *Methods Enzymol.*, **1997**, *276*, 307–326), absorption correction Denzo (Otwinowski, Z.; Borek, D.; Majewski, W.; Minor, W. *Acta Crystallogr., Sect. A.* **2003**, *59*, 228–234), structure solution SHELXS-97 (Sheldrick, G. M. *Acta Crystallogr., Sect. A* **1990**, *46*, 467–473), structure refinement SHELXL-97 (Sheldrick, G. M. Universität Göttingen, 1997), graphics Mopict (Brüggemann, M. Universität Münster, 2001). CCDC 719443 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge at www.ccdc.cam.ac.uk/conts/retrieving.html [or from the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ, UK; fax: (internat.) +44(1223)336-033, E-mail: deposit@ccdc.cam.ac.uk].
8. Knopff, O.; Alexakis, A. *Org. Lett.* **2002**, *4*, 3835–3837.
9. Unpublished results in this group.
10. Alexakis, A.; Rosset, S.; Allamand, J.; March, S.; Guillen, F.; Benhaim, C. *Synlett* **2001**, 1375–1378.
11. Review (a) Muñiz, K.; Bolm, C. *Chem. Eur. J.* **2000**, *6*, 2309–2316; (b) Zhang, S. Y.; Girard, C.; Kagan, B. *Tetrahedron: Asymmetry* **1995**, *6*, 2637–2640.
12. Alexakis, A.; Polet, D.; Rosset, S.; March, S. *J. Org. Chem.* **2004**, *69*, 5660–5667.
13. Shi, M.; Wang, C.-J.; Zhang, W. *Chem. Eur. J.* **2004**, *10*, 5507–5516.