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Expeditious synthesis of TADDOL-derived phosphoramidite and phosphonite ligands

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Dedicated to Professor Henri Kagan on the occasion of his 80th birthday

ABSTRACT

A simple and reliable protocol for the synthesis of TADDOL-derived monodentate ligands is reported. The reaction of the requisite TADDOL with PCl_3 is immediately followed by the treatment of the crude intermediate with both nitrogen and carbon nucleophiles. Several previously unknown or difficult-to-make phosphoramidite and phosphonite ligands **L1**–**L3** and **L4**–**L9** were accessed using this novel procedure.

1. Introduction

Chiral monodentate phosphorus ligands attracted considerable interest in recent years.[1] These ligands challenged the supremacy of bidentate ligands in asymmetric transition metal catalysis.[2] Privileged monodentate ligands are often based on chiral BINOL or TADDOL backbones (Fig. 1), which are combined with a phosphorus(III) reagent and a carbon or heteroatom substituent in a modular way.[3–5] The modular assembly predestines these ligands for systematic screenings, and that makes general protocols for their rapid synthesis highly desirable.

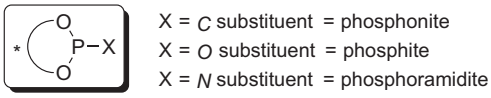

Figure 1. Chiral monodentate phosphorus ligands.

We recently reported a kinetic resolution through catalytic asymmetric, dehydrogenative Si–O coupling of donor-functionalized alcohols and achiral silanes.[6] This enantioselective Si–O coupling is catalyzed by a Cu–H complex decorated with a single monodentate phosphorus ligand in the stereochemistry-determining step. The ligand identification required extensive screening for which a straightforward protocol for the synthesis was needed. Herein we report a robust and reliable procedure for the time-saving preparation of several TADDOL-derived phosphoramidites and phosphonites. We have exclusively focused on new ligands in this work, except for **L5** (cf. entry 5, Table 1). Ligand **L5** emerged as the ideal ligand in the enantioselective Si–O coupling, and hence we also report a gram scale synthesis herein.

2. Results and discussion

There are many protocols in the literature describing the synthesis of phosphorus ligands derived from TADDOL.[7] A generally applicable method is still missing though, and this is particularly true for sterically congested ligands. Our aim was to find conditions that would allow for the rapid assembly of both phosphoramidites and phosphonites decorated with electron-donating as well as electron-withdrawing groups in addition to sterically demanding substituents. The general procedure is shown in Table 1. The TADDOLs **I** used in these syntheses were prepared according to the literature.[8]

The synthesis began with the reaction of TADDOL **I** with PCl_3 and *N*-methylmorpholine as base in toluene; *N*-methylmorpholine appears to be superior to Et_3N (often used in other protocols) as the yields obtained were considerably higher in several cases. The reaction mixture was filtered under argon at −78 °C to remove as much of the salt as possible. After a solvent change from toluene to THF, the resulting intermediate **II** was either added to a freshly prepared solution of a lithium amide or treated with an organolithium compound. The reaction mixture was usually kept at room temperature for 2 h, before it was concentrated to a small volume and submitted directly to flash column chromatography on deactivated silica gel (cyclohexane/Et_3N mixtures as eluent). The ligands were obtained as white or pale-yellow solids. This protocol gives the ligands in moderate to excellent yields in a few hours.

The ligands synthesized by this method are shown in Table 1. Ligands **L1** and **L2** were substituted with a sterically demanding 2,2,6,6-tetramethylpiperidinyl (TMP) group at phosphorus (Table 1, entries 1 and 2). To the best of our knowledge, no such TMP-substituted TADDOL-based phosphoramidite had been reported so far.[9] We were able to obtain crystals of **L1** suitable for X-ray analysis (Fig. 2). Its molecular structure in the single crystal reveals that the environment around the phosphorus atom is indeed sterically crowded. The steric hindrance is even more pronounced in ligand

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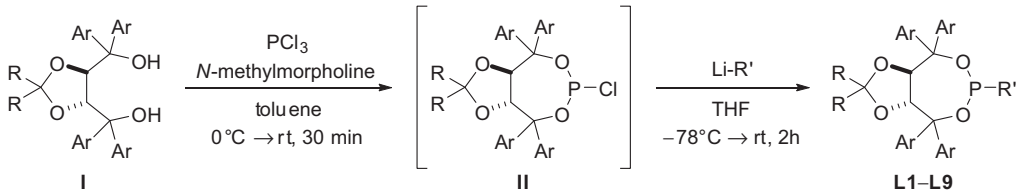
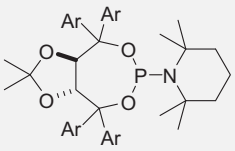
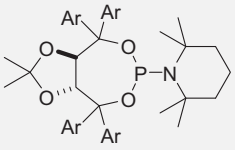
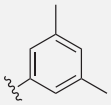
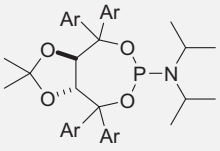
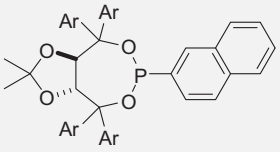
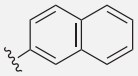
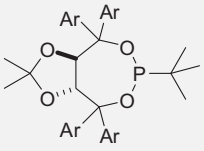
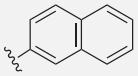
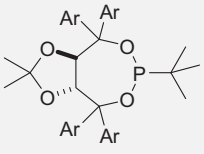
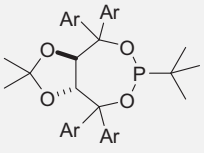
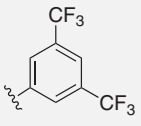
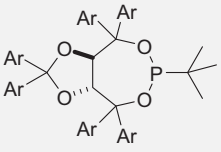
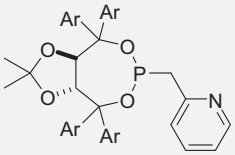
Table 1
Preparation of phosphoramidites and phosphonites with a TADDOL backbone



Entry	Compound	Ligand	Ar	Yield (%)
1	**L1**			50
2	**L2**			20
3	**L3**			73 (lit: 27%)[7c]
4	**L4**			62 (lit: 45%)[3a]
5	**L5**			78 (lit: 66%)[6]
6	**L6**			69
7	**L7**			22
8	**L8**			86
9	**L9**			26

L2, with xylyl instead of phenyl moieties in the TADDOL backbone. This might also account for the rather poor chemical yield (20% as compared to 50%).

Phosphoramidite **L3**[7b] (Table 1, entry 3), phosphonites **L4**[3a], and **L5**[6] (Table 1, entries 4 and 5) have been published previously, but the yields obtained with our method are substantially higher. Li-

gand **L5** was prepared on a gram scale in 78% yield. Ligand **L6** is the first phosphonite derived from tetra-*o*-tolyl-substituted TADDOL (Table 1, entry 6), and **L7** is an unprecedented octa-CF_3-substituted TADDOL derivative (Table 1, entry 7). Ligand **L8** is a hexaphenyl-substituted TADDOL ligand (Table 1, entry 8) and **L9** is substituted with a picolyl moiety, providing another Lewis basic coordination site.

3. Conclusion

In conclusion, we elaborated a general, time-saving method for the preparation of TADDOL-derived phosphoramidites and phosphonites, easily applicable to almost any TADDOL.

4. Experimental

4.1. General

Reagents were obtained from commercial sources and were used without further purification unless otherwise noted. All reactions were performed in flame-dried glassware under a static pressure of argon. Liquids and solutions were transferred with syringes. Solvents were dried prior to use following standard procedures (tetrahydrofuran and toluene). Technical grade cyclohexane for chromatography was distilled before use. Analytical thin layer chromatography was performed on Silica Gel 60 F_{254} glass plates by *Merck* using the indicated solvents. ^{1}H, ^{13}C, ^{31}P and ^{19}F NMR spectra were recorded in C_6D_6 or toluene-d_8 on *Bruker* AV 300 and AV 400 instruments. Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, m = multiplet, br = broad), coupling constants (Hz), and integration. Infrared spectra were recorded on a *Digilab* Excalibur Series FTS 4000 spectrophotometer. Optical rotations were measured on a *Perkin–Elmer* 341 polarimeter. Melting points (Mp) were measured with a Thompson Scientific apparatus and are not corrected. High resolution mass spectrometry (HRMS) as well as elemental analysis was performed by the analytical facility at the Organisch-Chemisches Institut of the Universität Münster.

4.2. General procedure for the preparation of TADDOL-derived phosphoramidites and phosphonites

To an ice-cold solution of PCl_3 (1.0 equiv) in toluene (0.4 M) was added a solution of TADDOL **I** (1.0 equiv) and freshly distilled *N*-methylmorpholine (2.0 equiv) in toluene (0.2 M based on **I**). The resulting suspension was stirred at rt for 30 min, cooled to −78 °C, and filtered under argon. The solvent of the filtrate was removed under reduced pressure and the pale-yellow residue was dissolved in THF (0.3 M). The solution was cooled to −78 °C and added dropwise to the lithium amide (1.0 equiv) in THF (for phosphoramidites) or the appropriate organolithium solution (1.0 equiv) was added to the dissolved crude intermediate **II** (for phosphonites). After stirring for an additional 2 h at rt, the mixture was concentrated to a slurry and subjected directly to flash column chromatography on silica gel using cyclohexane/Et_3N mixtures as eluent. Ligands **L1**–**L9** were obtained as white or pale-yellow solids.

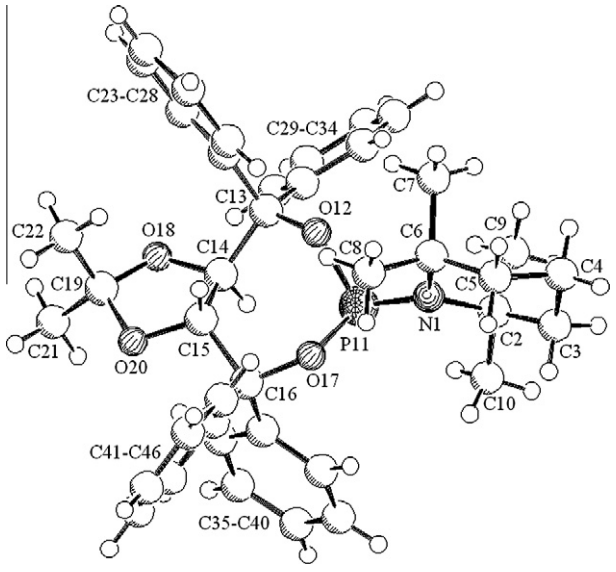


Figure 2. Molecular structure of phosphoramidite **L1**.

4.3. (1*R*,7*R*)-4-(2,2,6,6-Tetramethylpiperidin-1-yl)-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]-decane L1

According to the general procedure, a solution of [(4*R*,5*R*)-2,2-dimethyl-1,3-dioxolan-4,5-diyl]bis(diphenylmethanol)[10] (250 mg, 0.536 mmol) and *N*-methylmorpholine (108 mg, 1.07 mmol) in toluene (2 mL) was added to an ice-cold solution of PCl_3 (73.6 mg, 0.536 mmol) in toluene (1 mL). The resulting suspension was stirred for 30 min at rt, cooled to −78 °C, and filtered under argon. The solvents of the filtrate were removed under reduced pressure. The pale-yellow residue was dissolved in THF (2 mL) and added dropwise to a solution of lithium tetramethylpiperidide in THF [prepared by the addition of methyl lithium (1.6 M in Et_2O, 0.335 mL, 0.536 mmol) to a solution of 2,2,6,6-tetramethylpiperidine (75.7 mg, 0.536 mmol) in THF (2 mL) at −78 °C followed by warming to 0 °C] at −78 °C. The solution was maintained at rt for 2 h and concentrated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (cyclohexane/Et_3N 97:3), yielding **L1** as a white solid (170 mg, 50%). Crystals suitable for X-ray diffraction were obtained from a methanol/ethylacetate (1:1) solution. R_f = 0.39 (cyclohexane–*tert*-butylmethylether 97:3). Mp 250–252 °C. ^{1}H NMR (400 MHz, C_6D_6): δ 0.33 (s, 3H), 0.85–2.25 (m, 18H), 1.39 (s, 3H), 5.28 (d, J = 8.6 Hz, 1H), 5.88 (dd, J = 8.6, 4.2 Hz, 1H), 6.94–7.24 (m, 12H), 7.74–7.91 (m, 6H), 8.13–8.18 (m, 2H) ppm. ^{13}C NMR (100 MHz, C_6D_6): δ 17.6, 25.2, 28.0, 32.5 (m), 42.6 (m), 56.7, 82.7 (d, J_{C-P} = 27.8 Hz), 83.1 (d, J_{C-P} = 5.5 Hz), 83.5 (d, J_{C-P} = 3.9 Hz), 83.8 (d, J_{C-P} = 14.4 Hz), 111.6, 127.3–128.3 (m), 129.6, 129.7, 130.0, 142.9 (d, J_{C-P} = 2.1 Hz), 143.7 (d, J_{C-P} = 1.3 Hz), 147.3 (d, J_{C-P} = 3.0 Hz), 148.0 ppm. ^{31}P NMR (121 MHz, C_6D_6) δ 156.5 ppm. IR (ATR): 1447 (w), 1031 (s), 736 (s), 696 (s) cm^{-1}. HRMS (ESI) calcd for $C_{40}H_{46}NO_4PNa$ ([M+Na]$^+$): 658.3057. Found: 658.3067. Anal. Calcd for $C_{40}H_{46}NO_4P$ (635.77): C, 75.57; H, 7.29; N, 2.20. Found: C, 75.44; H, 7.15; N, 2.09. $[\alpha]_D^{20} = -102$ (c 0.985, $CHCl_3$).

4.4. (1*R*,7*R*)-4-(2,2,6,6-Tetramethylpiperidin-1-yl)-9,9-dimethyl-2,2,6,6-tetrakis(3,5-dimethylphenyl)-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane L2

According to the general procedure, a solution of [(4*R*,5*R*)-2,2-dimethyl-1,3-dioxolan-4,5-diyl]bis{bis[(3,5-dimethylphenyl)-methanol]}[11] (673 mg, 1.16 mmol) and *N*-methylmorpholine (241 mg, 2.38 mmol) in toluene (5 mL) was added to an ice-cold solution of PCl_3 (159 mg, 1.16 mmol) in toluene (3 mL). The resulting suspension was stirred at rt for 30 min, cooled to −78 °C, and filtered under argon. The solvents of the filtrate were removed under reduced pressure. The pale-yellow residue was dissolved in THF (4 mL) and then added dropwise to a solution of lithium tetramethylpiperidide in THF [prepared by the addition of *n*-butyl lithium (2.5 M in hexanes, 0.465 mL, 1.16 mmol) to a solution of 2,2,6,6-tetramethylpiperidine (164 mg, 1.16 mmol) in THF (4 mL)

at −78 °C followed by warming to 0 °C] at −78 °C. The solution was maintained at rt for 2 h and concentrated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (cyclohexane/Et_3N 95:5), yielding an off-white solid, which was recrystallized from a methanol/ethylacetate (1:1) solution to obtain **L2** as colorless crystals (175 mg, 20%). R_f = 0.18 (cyclohexane–*tert*-butylmethylether 97:3). Mp 221 °C. ^{1}H NMR (300 MHz, C_6D_6): δ 0.44 (s, 3H), 1.07–1.68 (m, 12H), 1.62 (s, 3H), 2.04 (s, 6H), 2.05–2.26 (m, 6H), 2.11 (s, 6H), 2.16 (s, 6H), 2.19 (s, 6H), 5.36 (d, J = 8.6 Hz, 1H), 5.93 (dd, J = 8.6, 4.1 Hz, 1H), 6.69 (m, 3H), 6.79 (m, 1H), 7.56 (m, 2H), 7.63 (m, 2H), 7.68 (m, 2H), 8.01 (m, 2H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ 17.8, 21.5, 21.6, 21.7, 21.7, 25.5, 28.3, 32.5 (m), 43.2 (m), 56.8, 82.8 (d, J_{C-P} = 6.7 Hz), 83.4 (d, J_{C-P} = 27.8 Hz), 84.0 (d, J_{C-P} = 13.8 Hz), 84.6 (d, J_{C-P} = 3.6 Hz), 111.4, 126.1, 126.4, 127.4–128.4 (m), 129.0, 129.1, 129.4, 129.5, 136.6, 136.9, 137.0, 137.4, 143.1 (d, J_{C-P} = 2.0 Hz), 143.4 (d, J_{C-P} = 1.2 Hz), 147.4 (d, J_{C-P} = 3.2 Hz), 148.5. ^{31}P NMR (121 MHz, C_6D_6) δ 156.4 ppm. IR (ATR): 1458 (w), 1041 (s), 854 (s), 779 (s) cm^{-1}. HRMS (ESI) calcd for $C_{48}H_{62}NO_4PH$ ([M+H]$^+$): 748.4489. Found: 748.4484. Anal. Calcd for $C_{48}H_{62}NO_4P$ (747.98): C, 77.08; H, 8.35; N, 1.87. Found: C, 77.48; H, 8.62; N, 1.62. $[\alpha]_D^{20} = -80.1$ (*c* 1.03, $CHCl_3$).

4.5. (1*R*,7*R*)-4-(Diisopropylamino)-9,9-dimethyl-2,2,6,6-tetraphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane L3

According to the general procedure, a solution of [(4*R*,5*R*)-2,2-dimethyl-1,3-dioxolan-4,5-diyl]bis(diphenylmethanol)[10] (600 mg, 1.29 mmol) and *N*-methylmorpholine (260 mg, 2.57 mmol) in toluene (5 mL) was added to an ice-cold solution of PCl_3 (177 mg, 1.29 mmol) in toluene (3 mL). The resulting suspension was stirred for 30 min at rt, cooled to −78 °C, and filtered under argon. The solvents of the filtrate were removed under reduced pressure. The pale-yellow residue was dissolved in THF (4 mL) and then added dropwise to a solution of LDA in THF [prepared by the addition of methyl lithium (1.6 M in Et_2O, 0.804 mL, 1.29 mmol) to a solution of diisopropylamine (143 mg, 1.41 mmol) in THF (4 mL) at −78 °C followed by warming to 0 °C] at −78 °C. The solution was maintained at rt for 2 h and concentrated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (cyclohexane/Et_3N 95:5), yielding **L3** as a white solid (479 mg, 73%). R_f = 0.29 (cyclohexane–*tert*-butylmethylether 97:3). Mp 173–175 °C. ^{1}H NMR (300 MHz, C_6D_6): δ 0.32 (s, 3H), 1.15 (d, J = 6.8 Hz, 6H), 1.20 (d, J = 6.8 Hz, 6H), 1.40 (s, 3H), 3.96 (m, 2H), 5.11 (d, J = 8.6 Hz, 1H), 5.73 (dd, J = 8.6, 3.9 Hz, 1H), 6.93–7.25 (m, 12H), 7.72–7.78 (m, 2H), 7.82–7.92 (m, 4H), 8.11–8.17 (m, 2H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ 24.2 (d, J_{C-P} = 7.2 Hz), 24.4 (d, J_{C-P} = 6.9 Hz), 25.3, 27.9, 44.5 (d, J_{C-P} = 14.3 Hz), 81.6 (d, J_{C-P} = 2.9 Hz), 81.8 (d, J_{C-P} = 10.6 Hz), 83.1 (d, J_{C-P} = 22.2 Hz), 83.8 (d, J_{C-P} = 3.7 Hz), 111.5, 127.3–128.4 (m), 129.3, 129.4, 130.0, 142.7 (d, J_{C-P} = 1.8 Hz), 143.5 (d, J_{C-P} = 1.3 Hz), 147.2 (d, J_{C-P} = 2.6 Hz), 148.2. ^{31}P NMR (121 MHz, C_6D_6) δ 141.1 ppm. IR (ATR): 1447 (w), 1049 (s), 733 (s), 696 (s) cm^{-1}. HRMS (ESI) calcd for $C_{37}H_{42}NO_4PH$ ([M+H]$^+$): 596.2924. Found: 596.2922. Anal. Calcd for $C_{37}H_{42}NO_4P$ (595.71): C, 74.60; H, 7.11; N, 2.35. Found: C, 74.53; H, 7.04; N, 2.10. $[\alpha]_D^{20} = -96.2$ (*c* 1.00, $CHCl_3$).

4.6. (1*R*,7*R*)-9,9-Dimethyl-2,2,4,6,6-penta(naphthalen-2-yl)-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane L4

According to the general procedure, a solution of [(4*R*,5*R*)-2,2-dimethyl-1,3-dioxolan-4,5-diyl]bis(dinaphthalen-2-ylmethanol)[12] (1.00 g, 1.50 mmol) and *N*-methylmorpholine (303 mg, 3.00 mmol) in toluene (6 mL) was added to an ice-cold solution of PCl_3 (206 mg, 1.50 mmol) in toluene (6 mL). The resulting suspension was stirred for 30 min at rt, cooled to −78 °C, and filtered under argon. The solvents of the filtrate were removed under reduced pressure. The pale-yellow residue was dissolved in THF (6 mL) and a solution of 2-naphthyl lithium in THF [prepared by the addition of *n*-butyl lithium (2.5 M in hexanes, 0.600 mL, 1.15 mmol) to a solution of 2-naphthyl bromide (311 mg, 1.15 mmol) in THF (6 mL) at −78 °C] was added dropwise at −78 °C. The solution was maintained at rt for 2 h and concentrated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (cyclohexane/Et_3N 95:5), yielding **L4** as a white solid (765 mg, 62%). R_f = 0.18 (cyclohexane–*tert*-butylmethylether 97:3). Mp 180 °C (decomp.). ^{1}H NMR (300 MHz, C_6D_6): δ 0.28 (s, 3H), 1.65 (s, 3H), 5.81 (d, J = 8.6 Hz, 1H), 6.70 (dd, J = 8.6, 4.9 Hz, 1H), 7.00–7.30 (m, 9H), 7.39–7.69 (m, 14H), 7.78–7.82 (m, 1H), 7.86 (dd, J = 8.6, 1.5 Hz, 2H), 8.03 (dd, J = 8.7, 1.6 Hz, 1H), 8.17 (ddd, J = 8.8, 8.8, 1.8 Hz, 2H), 8.47–8.61 (m, 4H), 8.70 (d, J = 1.3 Hz, 1H), 9.21 (d, J = 0.9 Hz, 1H). ^{13}C NMR (75 MHz, C_6D_6): δ 25.5, 27.2, 28.2, 83.7 (d, J_{C-P} = 20.6 Hz), 83.8 (d, J_{C-P} = 3.6 Hz), 84.6 (d, J_{C-P} = 7.6 Hz), 85.0 (d, J_{C-P} = 4.1 Hz), 112.5, 125.9–129.3 (m), 132.2, 132.6, 133.4–133.6 (m), 135.4, 139.2 (d, J_{C-P} = 20.6 Hz), 139.5 (d, J_{C-P} = 1.9 Hz), 139.9 (d, J_{C-P} = 1.5 Hz), 143.9 (d, J_{C-P} = 3.6 Hz), 144.6 ppm. ^{31}P NMR (121 MHz, C_6D_6) δ 159.1 ppm. IR (ATR): 3055 (m), 2924 (m), 1506 (m), 1027 (s), 879 (s), 858 (s), 756 (s). HRMS (ESI) calcd for $C_{57}H_{43}O_4PNa$ ([M+Na]$^+$): 845.2791. Found: 845.2794. $[\alpha]_D^{20} = -109$ (*c* 0.305, $CHCl_3$).

4.7. (1*R*,7*R*)-4-*tert*-Butyl-9,9-dimethyl-2,2,6,6-tetra(naphthalen-2-yl)-3,5,8,10-tetraoxa-4-phosphabicyclo-[5.3.0]decane L5

According to the general procedure, a solution of [(4*R*,5*R*)-2,2-dimethyl-1,3-dioxolan-4,5-diyl]bis(dinaphthalen-2-ylmethanol)[12] (2.57 g, 3.85 mmol) and *N*-methylmorpholine (779 mg, 7.70 mmol) in toluene (20 mL) was added to an ice-cold solution of PCl_3 (529 mg, 3.85 mmol) in toluene (10 mL). The resulting suspension was stirred for 30 min at rt, cooled to −78 °C, and filtered under argon. The solvents of the filtrate were removed under reduced pressure. The pale-yellow residue was dissolved in THF (25 mL) and *tert*-butyl lithium (1.9 M in *n*-pentane, 2.07 mL, 3.85 mmol) was added dropwise at −78 °C. The solution was maintained at rt for 2 h and concentrated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (cyclohexane/Et_3N 4:1), yielding **L5** as a pale-yellow solid (2.22 g, 78%). R_f = 0.15 (cyclohexane–*tert*-butylmethylether 97:3). Mp 130 °C (decomp.). ^{1}H NMR (300 MHz, C_6D_6): δ 0.18 (s, 3H), 1.38 (d, J = 12.8 Hz, 9H), 1.63 (s, 3H), 5.51 (d, J = 8.6 Hz, 1H), 6.50 (dd, J = 8.6, 4.9 Hz, 1H), 7.05–7.74 (m, 20H), 7.82–7.94 (m, 2H), 8.08 (m, 2H), 8.35 (m, 1H), 8.48 (s, 1H), 8.58 (m, 1H), 9.10 (m, 1H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ 24.1 (d, J_{C-P} = 16.4 Hz), 25.4, 28.2, 35.4 (d, J_{C-P} = 13.2 Hz), 82.8 (d, J_{C-P} = 2.2 Hz), 83.0 (d, J_{C-P} = 23.5 Hz), 83.9 (d, J_{C-P} = 5.4 Hz), 84.9 (d, J_{C-P} = 3.6 Hz), 112.0, 126.2, 126.3, 126.3, 126.4, 126.5, 126.5, 126.5, 126.6, 126.7, 127.1, 127.1, 127.7–128.5 (m), 128.9–129.3 (m), 133.1, 133.2, 133.3, 133.4, 133.6, 140.3 (m), 144.4, 144.4 ppm. ^{31}P NMR (121 MHz, C_6D_6) δ 172.0 ppm. IR (ATR): 2926 (m), 1032 (m), 802 (s), 741 (s) cm^{-1}. HRMS (ESI) calcd for $C_{51}H_{45}O_4PH$ ([M+H]$^+$): 753.3131. Found: 753.3128. Anal. Calcd for $C_{51}H_{45}O_4P$ (752.87): C, 81.36; H, 6.02. Found: C, 81.68; H, 5.99. $[\alpha]_D^{20} = -95.2$ (*c* 1.05, $CHCl_3$).

4.8. (1*R*,7*R*)-4-*tert*-Butyl-9,9-dimethyl-2,2,6,6-tetra-(*o*-tolyl)-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane L6

According to the general procedure, a solution of [(4*R*,5*R*)-2,2-dimethyl-1,3-dioxolan-4,5-diyl]bis(*o*-tolylmethanol)[13] (599 mg, 1.15 mmol) and *N*-methylmorpholine (232 mg, 2.29 mmol) in toluene (4 mL) was added to an ice-cold solution of PCl_3 (158 mg, 1.15 mmol) in toluene (4 mL). The resulting suspension was stirred for 30 min at rt, cooled to −78 °C, and filtered under argon. The

solvents of the filtrate were removed under reduced pressure. The pale-yellow residue was dissolved in THF (8 mL) and *tert*-butyl lithium (1.75 M in *n*-pentane, 0.66 mL, 1.15 mmol) was added dropwise at −78 °C. The solution was maintained at rt for 2 h and concentrated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (cyclohexane/Et_3N 95:5), yielding **L6** as a white solid (484 mg, 69%). R_f = 0.28 (cyclohexane–*tert*-butylmethylether 97:3). Mp 125 °C (decomp.). Presumably due to hindered C–C bond rotation of the four *o*-tolyl groups, the signals in the NMR spectra are broadened.[14] ^{1}H NMR (300 MHz, C_6D_6): δ 0.15 (br s, 3H), 0.89–1.13 (m, 9H), 1.51 (br s, 3H), 1.79–2.14 (m, 12H), 5.02–6.33 (m, 1H), 6.71–7.45 (m, 13H), 8.06–8.97 (m, 4H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ 22.5, 22.7, 23.3, 23.6, 24.5 (d, J_{C-P} = 17.3 Hz), 25.6, 28.6, 34.8 (d, J_{C-P} = 13.7 Hz), 82.2, 82.4, 82.6, 83.2, 83.3, 88.3 (d, J_{C-P} = 3.8 Hz), 111.7, 125.4, 126.4, 126.5, 126.7, 127.2, 127.5, 127.8, 128.7, 129.2, 130.0, 132.9, 133.1, 133.4, 133.7, 137.7, 139.0, 139.8, 139.9, 140.4, 141.4, 144.0, 145.9 ppm. ^{31}P NMR (121 MHz, C_6D_6) δ 167.6 ppm (two additional minor signals at 173.6 and 184.0 ppm that might be assigned to rotamers were detected). IR (ATR): 2923 (m), 2360 (m), 1457 (s), 1215 (s), 998 (s) cm^{-1}. HRMS (ESI) calcd for $C_{39}H_{45}O_4PH$ ([M+H]$^+$): 609.3128. Found: 609.3137. Anal. Calcd for $C_{39}H_{45}O_4P$ (608.75): C, 76.95; H, 7.45. Found: C, 77.07; H, 7.71. $[\alpha]_D^{20} = -89.7$ (*c* 1.00, $CHCl_3$).

4.9. (1*R*,7*R*)-4-*tert*-Butyl-9,9-dimethyl-2,2,6,6-tetrakis[3,5-bis(trifluoromethyl)phenyl]-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane L7

According to the general procedure, a solution of [(4*R*,5*R*)-2,2-dimethyl-1,3-dioxolan-4,5-diyl]bis{bis[3,5-bis(trifluoromethyl)phenyl]methanol}[15] (1.04 g, 1.03 mmol) and *N*-methylmorpholine (208 mg, 2.06 mmol) in toluene (15 mL) was added to an ice-cold solution of PCl_3 (141 mg, 1.03 mmol) in toluene (10 mL). The resulting suspension was stirred for 30 min at rt, cooled to −78 °C, and filtered under argon. The precipitate was washed thoroughly with THF (3 × 10 mL). The solvents of the combined filtrates were removed under reduced pressure. The residue was dissolved in THF (30 mL) and *tert*-butyl lithium (1.75 M in *n*-pentane, 0.590 mL, 1.03 mmol) was added dropwise at −78 °C. The solution was maintained at rt for 2 h and concentrated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (cyclohexane/Et_3N 95:5), yielding **L7** as a pale-yellow solid (246 mg, 22%). This phosphonite appeared to be quite sensitive toward air and moisture as compared to the other ligands. R_f = 0.58 (cyclohexane–*tert*-butylmethylether 97:3). Mp 68–70 °C. ^{1}H NMR (300 MHz, toluene-d_8): δ 0.05 (s, 3H), 1.10 (d, *J* = 12.6 Hz, 9H), 1.34 (s, 3H), 4.51 (d, *J* = 8.9 Hz, 1H), 5.50 (dd, *J* = 8.9, 4.6 Hz, 1H), 7.60 (m, 2H), 7.64 (m, 2H), 8.04 (m, 2H), 8.09 (m, 2H), 8.25 (m, 2H), 8.50 (m, 2H) ppm. ^{13}C NMR (75 MHz, toluene-d_8): δ 23.0 (d, J_{C-P} = 15.9 Hz), 24.3, 26.6, 35.5 (d, J_{C-P} = 13.2 Hz), 80.5 (d, J_{C-P} = 3.3 Hz), 82.0 (d, J_{C-P} = 22.8 Hz), 82.4 (d, J_{C-P} = 4.6 Hz), 84.5 (d, J_{C-P} = 3.9 Hz), 113.3, 121.5–123.3 (m), 125.2–125.3 (m), 127.1 (m), 127.5 (m), 128.9–129.4 (m), 131.4–133.5 (m), 142.8, 142.8 (d, J_{C-P} = 1.9 Hz), 146.7 (d, J_{C-P} = 3.1 Hz), 147.2 ppm. ^{19}F NMR (282 MHz, toluene-d_8) δ −63.3 (s, 6F), −63.3 (s, 6F), −63.2 (s, 6F), −63.1 (s, 6F) ppm. ^{31}P NMR (121 MHz, toluene-d_8) δ 177.2 ppm. IR (ATR): 1373 (m), 1122 (s), 902 (s) cm^{-1}. HRMS (ESI) calcd for $C_{43}H_{29}F_{24}O_4PH$ ([M+H]$^+$): 1097.1493. Found: 1097.1482. $[\alpha]_D^{20} = -38.4$ (*c* 0.645, $CHCl_3$).

4.10. (1*R*,7*R*)-4-*tert*-Butyl-2,2,6,6,9,9-hexaphenyl-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane L8

According to the general procedure, a solution of [(4*R*,5*R*)-2,2-diphenyl-1,3-dioxolan-4,5-diyl]bis(diphenylmethanol)[16] (484 mg, 0.820 mmol) and *N*-methylmorpholine (166 mg, 1.64 mmol) in toluene (4 mL) was added to an ice-cold solution of PCl_3 (113 mg, 0.820 mmol) in toluene (4 mL). The resulting suspension was stirred for 30 min at rt, cooled to −78 °C, and filtered under argon. The solvents of the filtrate were removed under reduced pressure. The pale-yellow residue was dissolved in THF (8 mL) and *tert*-butyl lithium (1.9 M in *n*-pentane, 0.430 mL, 0.820 mmol) was added dropwise at −78 °C. The solution was maintained at rt for 2 h and concentrated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (cyclohexane/Et_3N 95:5), yielding **L8** as a white solid (477 mg, 86%). R_f = 0.18 (cyclohexane–*tert*-butylmethylether 97:3). Mp 115 °C. ^{1}H NMR (300 MHz, C_6D_6): δ 1.17 (d, *J* = 12.8 Hz, 9H), 5.35 (d, *J* = 8.9 Hz, 1H), 6.36 (dd, *J* = 8.9, 4.3 Hz, 1H), 6.61–6.81 (m, 8H), 6.93–7.21 (m, 12H), 7.47 (m, 2H), 7.72 (m, 2H), 7.82–7.94 (m, 6H). ^{13}C NMR (75 MHz, C_6D_6): δ 24.0 (d, J_{C-P} = 16.2 Hz), 35.2 (d, J_{C-P} = 12.9 Hz), 82.1 (d, J_{C-P} = 3.7 Hz), 83.4 (d, J_{C-P} = 5.4 Hz), 84.3 (d, J_{C-P} = 22.6 Hz), 86.4 (d, J_{C-P} = 4.0 Hz), 122.2, 125.5, 126.1, 127.2–129.5 (m), 141.9 (d, J_{C-P} = 1.7 Hz), 142.4 (d, J_{C-P} = 1.9 Hz), 144.4, 147.2 (d, J_{C-P} = 3.4 Hz), 147.4 ppm. ^{31}P NMR (121 MHz, C_6D_6) δ 171.5 ppm. IR (ATR): 2922 (m), 1447 (m), 1221 (m), 982 (s), 810 (s), 737 (s) cm^{-1}. Anal. Calcd for $C_{45}H_{41}O_4P$ (522.57): C, 79.86; H, 6.11. Found: C, 79.96; H, 6.14. $[\alpha]_D^{20} = +28.4$ (*c* 0.295, $CHCl_3$).

4.11. (1*R*,7*R*)-9,9-Dimethyl-2,2,6,6-tetraphenyl-4-(7-picolyl)-3,5,8,10-tetraoxa-4-phosphabicyclo[5.3.0]decane L9

According to the general procedure, a solution of [(4*R*,5*R*)-2,2-dimethyl-1,3-dioxolan-4,5-diyl]bis(diphenylmethanol)[10] (933 mg, 2.00 mmol) and *N*-methylmorpholine (405 mg, 4.00 mmol) in toluene (6 mL) was added to an ice-cold solution of PCl_3 (275 mg, 2.00 mmol) in toluene (6 mL). The resulting suspension was stirred for 30 min at rt, cooled to −78 °C, and filtered under argon. The solvents of the filtrate were removed under reduced pressure. The pale-yellow residue was dissolved in THF (6 mL) and a solution of 7-picolyl lithium in THF [prepared by the addition of LDA (1.0 M in THF, 2.00 mL, 2.00 mmol) to a solution of 2-picoline (186 mg, 2.00 mmol) in THF (4 mL) at −78 °C] was added dropwise at −78 °C. The solution was maintained at rt for 2 h and concentrated under reduced pressure. The residue was subjected to flash column chromatography on silica gel (cyclohexane/Et_3N 95:5), yielding **L9** as a white solid (306 mg, 26%). R_f = 0.18 (cyclohexane–*tert*-butylmethylether 97:3). Mp 215 °C (decomp.). ^{1}H NMR (300 MHz, C_6D_6): δ 0.23 (s, 3H), 1.42 (s, 3H), 3.53 (d, *J* = 5.9 Hz, 2H), 5.08 (d, *J* = 8.6 Hz, 1H), 5.87 (dd, *J* = 8.6, 4.3 Hz, 1H), 6.61 (m, 1H), 6.91–7.08 (m, 11H), 7.11–7.21 (m, 3H), 7.53–7.62 (m, 4H), 7.73–7.78 (m, 2H), 8.00–8.05 (m, 2H), 8.41–8.45 (m, 1H) ppm. ^{13}C NMR (75 MHz, C_6D_6): δ 25.0, 27.2, 27.9, 46.9 (d, J_{C-P} = 23.0 Hz), 82.0 (d, J_{C-P} = 2.9 Hz), 83.3 (d, J_{C-P} = 23.4 Hz), 83.5 (d, J_{C-P} = 7.2 Hz), 84.4 (d, J_{C-P} = 4.2 Hz), 111.7, 120.9 (d, J_{C-P} = 2.1 Hz), 124.7 (d, J_{C-P} = 4.2 Hz), 127.4–128.5 (m), 129.1 (d, J_{C-P} = 4.0 Hz), 129.9, 142.0 (d, J_{C-P} = 1.5 Hz), 142.5 (d, J_{C-P} = 1.1 Hz), 146.8, 147.3, 149.8 (d, J_{C-P} = 1.0 Hz), 155.5 (d, J_{C-P} = 5.2 Hz) ppm. ^{31}P NMR (121 MHz, C_6D_6) δ 173.0 ppm. IR (ATR): 2361 (s), 2342 (s), 1448 (m), 1034 (s), 877 (s), 805 (s), 791 (s), 740 (s) cm^{-1}. HRMS (ESI) calcd for $C_{37}H_{34}NO_4PH$ ([M+H]$^+$): 588.2298. Found: 588.2297. Anal. Calcd for $C_{37}H_{34}NO_4P$ (587.64): C, 75.62; H, 5.83; N, 2.38. Found: C, 75.82; H, 5.84; N, 2.43. $[\alpha]_D^{20} = -118$ (*c* 0.430, $CHCl_3$).

4.12. X-ray data

4.12.1. General information

Data set was collected with a Nonius KappaCCD diffractometer. Programs used: data collection COLLECT (Nonius B.V., 1998), data

reduction DENZO-SMN,[17a] absorption correction DENZO,[17b] structure solution SHELXS-97,[17c] structure refinement SHELXL-97,[17d] graphics SCHAKAL (E. Keller, Universität Freiburg, 1997).

CCDC 761360 **L1** 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].

4.12.2. X-ray crystal structure analysis of L1

Formula $C_{40}H_{46}NO_4P$, $M = 635.75$, colorless crystal $0.30 \times 0.25 \times 0.15$ mm, $a = 10.8981(5)$, $b = 9.4572(4)$, $c = 16.8058(9)$ Å, $\beta = 90.507(2)$, $V = 1732.03(14)$ Å^3, $\rho_{calcd} = 1.219$ g cm^{-3}, $\mu = 1.027$ mm^{-1}, empirical absorption correction ($0.748 \leqslant T \leqslant 0.861$), $Z = 2$, monoclinic, space group $P2_1$ (No. 4), $\lambda = 1.54178$ Å, $T = 223(2)$ K, ω and φ scans, 9157 reflections collected ($\pm h$, $\pm k$, $\pm l$), [$(\sin\theta)/\lambda$] = 0.60 Å^{-1}, 4624 independent ($R_{int} = 0.034$) and 4528 observed reflections [$I \geqslant 2\sigma(I)$], 422 refined parameters, $R = 0.036$, $wR^2 = 0.097$, Flack parameter 0.04(2), max. (min.) residual electron density 0.22 (−0.32) e Å^{-3}, hydrogen atoms calculated and refined as riding atoms.

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