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Triazole-based P,N ligands : discovery of an enantioselective copper-catalyzed propargylic amination reaction

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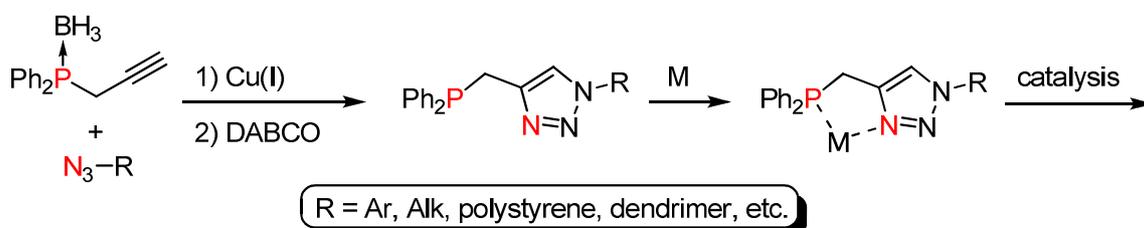
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CHAPTER 2

Concept, Synthesis and Application of ClickPhine P,N Ligands*



ABSTRACT: A novel P,N-type ligand family is disclosed that is easily accessible using the Cu(I)-catalyzed azide-alkyne “click” cycloaddition. A diverse set of ligands was made in just three steps from readily available starting materials to give several homogeneous and a heterogeneous catalyst. Preliminary experiments show the efficacy of these ligands in the Pd-catalyzed allylic alkylation reaction.

* Part of this chapter has been published: Detz, R. J.; Arévalo Heras, S.; de Gelder, R.; van Leeuwen, P. W. N. M.; Hiemstra, H.; Reek, J. N. H.; van Maarseveen, J. H. *Org. Lett.* **2006**, *8*, 3227-3230.

2.1 INTRODUCTION

Transition metal catalysis is increasingly important, because it provides new efficient and sustainable routes for organic synthesis and the production of fine chemicals.¹ Ligand variation is the most powerful tool in transition metal catalysis, and key features of transition metal catalysts such as activity, selectivity, and stability are dictated by the steric and electronic properties of ligands that are coordinated to the metal.² It is therefore no surprise that most effort in the area of catalysis is put into the design of novel ligands. Besides the development of new catalysts by ligand design and combinatorial approaches,³ much research is devoted to catalyst recycling. Various elegant concepts for homogeneous catalyst separation and recycling have been developed⁴ such as the use of ionic liquids,⁵ supercritical fluids,⁶ supported aqueous phase catalysis,⁷ and fluorous phase catalysis.⁸ A widely studied approach to facilitate catalyst-product separation is the attachment of homogeneous catalysts to dendritic,⁹ polymeric organic, inorganic, or hybrid supports.¹⁰ Here the ligand requires a group that enables anchoring to such a support.

Sharpless and co-workers recently introduced click chemistry as a new way of categorizing organic reactions that are modular in nature, highly efficient, mild, and selective and require only simple reaction and workup procedures.¹¹ We anticipated that implementation of a click-reaction in the synthetic scheme of a ligand should automatically lead to a route which is amenable for the synthesis of analogues. In addition, it might also provide a handle to attach the ligand to various supports. We were especially interested in the Cu(I)-catalyzed 1,3-dipolar “click” azide-alkyne cycloaddition,¹² since the resulting 1,4-disubstituted 1,2,3-triazoles can be part of a bidentate P,N-type ligand. P,N ligands represent an important class of ligands that have been applied in various catalytic transformations.¹³ Recently, a triazole-based monophosphine, ClickPhos, was reported showing high activity in the Pd-catalyzed Suzuki-Miyaura coupling and amination reactions of aryl chlorides.¹⁴ Also, the triazole itself has already shown its good metal coordination properties.¹⁵ Surprisingly, the use of triazoles as nitrogen donors in P,N ligands had, as far as we knew, no literature precedent at the start of this research. This novel class of P,N ligands might be attractive because of the easy and highly modular synthetic accessibility, which enables facile tuning of their steric and electronic properties for catalyst optimization (Figure 2.1).

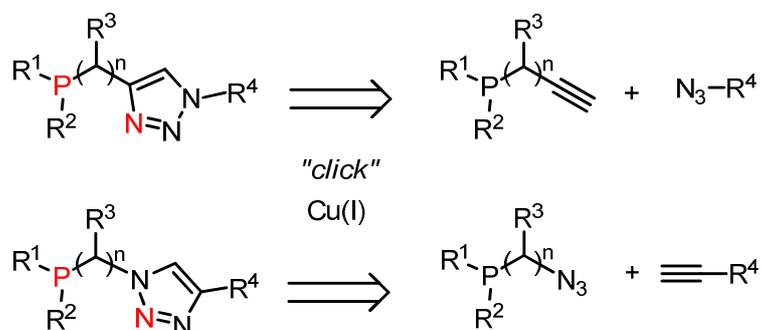
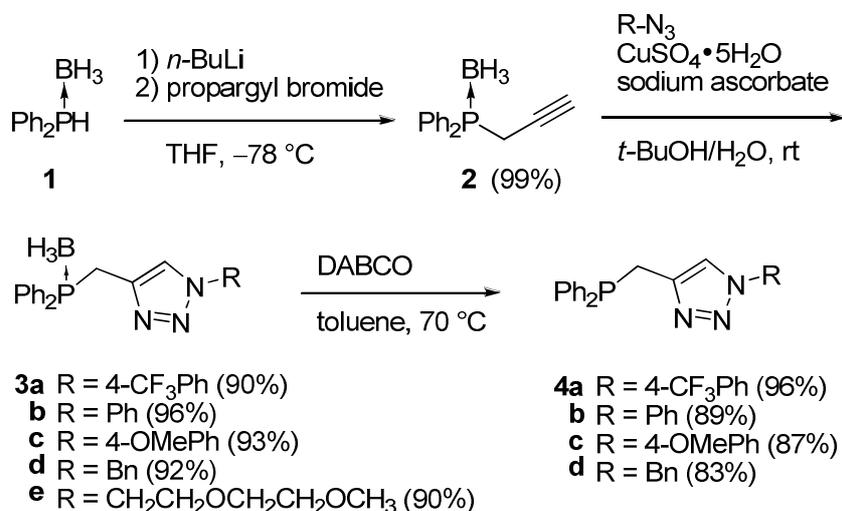


Figure 2.1 P,N ligands obtained by the Cu(I)-catalyzed azide-alkyne cycloaddition reaction

In addition, several commonly used supports have azide or acetylene moieties facilitating a complete system approach including a catalyst-separation step underscoring their versatility. In this chapter, we report the preparation of a series of P,N ligands using click chemistry, and we show that this strategy allows facile immobilization of these ligands on soluble (dendrimers, poly(ethylene glycol)) and insoluble supports (polystyrene resin). Preliminary results show that the palladium catalysts are highly active and regioselective in the allylic alkylation of cinnamyl acetate and that the immobilized catalyst can indeed be recycled.

2.2 LIGAND SYNTHESIS

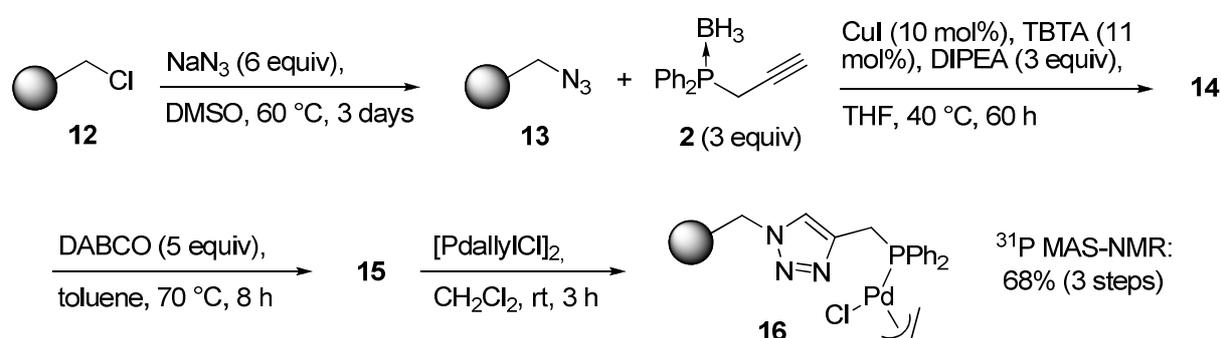
The synthesis of the first ligand commenced with the treatment of commercially available borane-protected diphenylphosphine **1** with *n*-BuLi followed by addition of propargyl bromide providing propynyl phosphine **2** in almost quantitative yield (Scheme 2.1). To prevent allene formation, one equivalent or a small excess of phosphine was used relative to the base. The acetylene moiety was subjected to Cu(I)-catalyzed azide-alkyne cycloaddition providing the P-protected ligand derivatives **3a-e** in high yields. To categorize this new ligand class, we first named it Clickphos, indicating this *phosphine* ligand is obtained by *click* chemistry. Shortly before we published our results, Zhang *et al.* reported the preparation of triazole substituted monophosphines, named ClickPhos.¹⁴ We then decided to name our new ligand class ClickPhine to indicate that *click* chemistry is still *fine* to arrive at *phosphine* ligands. Throughout the sequence, the phosphine was borane-protected to prevent unwanted iminophosphorane formation (Staudinger reaction) during the “click” reaction. The unprotected ClickPhine ligands **4a-d** were obtained after liberation of the phosphine by treatment with a small excess of 1,4-diazabicyclo[2.2.2]octane (DABCO, typically 1.2 equiv) in toluene, which was indicated by a shift of the ³¹P signal (from a very broad signal around 16 ppm due to the P-B coupling, to a sharp singlet around -14 ppm of the liberated phosphine).



Scheme 2.1 Synthesis of ligand derivatives **4**

generation carbosilane dendrimer **9** employing an azide group at the focal point was attached to phosphine **2** using standard click conditions.¹⁷ Deprotection of the phosphine with DABCO gave dendritic ligand **11** in very high yield (Scheme 2.3).

The polystyrene-supported azide was prepared by treatment of Merrifield resin **12** with sodium azide according to literature procedures (Scheme 2.4).¹⁸ The resulting resin **13** was subjected to the Cu(I)-catalyzed cycloaddition with propynylphosphine **2** using tris(benzyltriazolylmethyl)amine (TBTA) as the ligand to accelerate the reaction.¹⁵ The polystyrene-supported ligand complex **16** was obtained after DABCO-mediated phosphine liberation and subsequent complexation with palladium. ³¹P MAS-NMR analysis revealed a yield of 68% of the supported complex. Next to the corresponding phosphine oxide (13%), two minor phosphorus signals (19%) of unidentified species were also detected.



Scheme 2.4 Synthesis of polystyrene-supported complex **14**

2.3 CLICKPHINE COORDINATION

Upon mixing ligands **4a-d** or dendritic ligand **11** with $[\text{Pd}(\text{allyl})\text{Cl}]_2$ in dichloromethane the corresponding neutral metal complexes were formed, according to NMR experiments (Scheme 2.5). The ¹H NMR spectra showed broad signals for the allylic protons (except for the central proton) indicating isomerization via π rotation or π,σ -rearrangement. The ³¹P NMR spectrum showed a broad signal at 20.6 ppm.



Scheme 2.5 Synthesis of palladium complexes

Crystals suitable for X-ray analysis were obtained for complex **17b**, revealing monodentate binding of the ligand (Figure 2.2) with the chloride still coordinated to the palladium.¹⁹ The corresponding cationic palladium-allyl complex was prepared from the palladium chloride by addition of AgBF_4 . The ¹H NMR signal of the triazole proton shifted 0.71 ppm to lower field (from 8.15 to 8.86 ppm) after ion exchange, and the CH_2 group gave rise to an AB pattern

showing that these protons became inequivalent. In addition, the signal in the ^{31}P NMR spectrum shifted from 20.6 to 40.5 ppm and became sharper. These data all point to the formation of a palladium-allyl complex in which the ligand shows bidentate P,N coordination. Unfortunately, all crystallization attempts of these complexes failed.

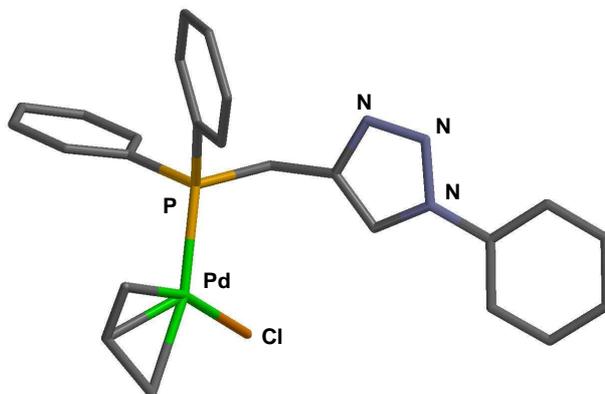


Figure 2.2 X-ray diffraction structure of Pd-complex **17b**. Hydrogen atoms have been omitted for clarity.

2.4 CATALYSIS

Many efforts have been made in enantioselective allylic alkylation with P,N-ligands;²⁰ the subject of regioselectivity has been less studied.²¹ Our initial experiments show that the palladium complexes of the novel ligands described are active in the Pd-catalyzed allylic alkylation of cinnamyl acetate applying the sodium salt of diethyl methylmalonate as nucleophile. The palladium complexes are highly active and selective for the trans product **a** (Table 2.1), and all reactions went to completion after prolonged reaction.

The effect of the bite angle of P,N-type ligands on the selectivity in the palladium-catalyzed allylic alkylation has been studied before, and has demonstrated that large bite angle ligands resulted in preferential formation of the branched product.²² The ligands that are reported here have small bite angles and provide very high selectivities for the linear product (up to 98%).²³ Interestingly, within the small ligand series investigated we already observed a large effect in the reactivity. The catalysts based on ligands **4d** and **11** (the dendritic ligand), with more electron-rich triazole rings, were considerably more active (entries 4 and 5). It was also observed that the cationic palladium complexes generally gave higher initial rates than the neutral analogues. Preliminary experiments with polystyrene-supported catalyst **16** showed that the supported catalyst retained its activity and was easy to recycle. A small decrease in activity upon recycling had to be accepted; the fourth run still gave 54% conversion of the cinnamyl acetate after 1 h reaction time, whereas the first run showed 72% conversion (Table 2.1, entries 6 and 7), which is not uncommon for palladium catalysts.

Table 2.1 Pd-catalyzed allylic alkylation of cinnamyl acetate

entry	ligand	X	conversion ^a (%)		selectivity ^{a,b} (%)	
			35 min.	1 h	a	b
1	4a	BF ₄	55	65	97	3
2	4b	BF ₄	54	68	97	3
3	4c	BF ₄		78	97	3
4	4d	BF ₄	78	90	98	2
5	11	BF ₄	80	91	98	2
6 ^c	15	Cl	64	72	96	4
7 ^{c,d}	15	Cl		54	96	4

^a The conversion of cinnamyl acetate and the regioselectivity were determined by GC using decane as internal standard and in select cases confirmed by NMR. All reactions gave full conversion. ^b No cis product (**c**) was observed. ^c Approximately 2 mol% of catalyst was used and a ratio of 1:0.7 of cinnamyl acetate/Na diethyl methylmalonate. ^d The reaction was carried out with the **15**-Pd complex recovered after 3 previous runs without further addition of [PdallylCl]₂.

2.5 CONCLUSIONS

In conclusion, we have shown the versatility of a new class of P,N ligands which are accessible via the robust Cu(I)-catalyzed alkyne-azide cycloaddition enabling facile tailor made modification for optimization or other (e.g., ligand immobilization) purposes. The efficacy of these ligands is shown for Pd-catalyzed alkylation reactions.

2.6 ACKNOWLEDGEMENTS

Dr. S. Arévalo-Heras is gratefully acknowledged for her contributions to this chapter. Dr. G. Masson is kindly acknowledged for all advice and help during the start of this project. Dr. R. de Gelder (Radboud University Nijmegen) is acknowledged for the crystal structure determinations.

2.7 EXPERIMENTAL SECTION

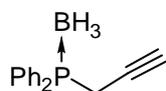
General Remarks. The following general procedures were used in all reactions unless noted otherwise. Oxygen- and moisture-sensitive reactions were carried out using standard Schlenk techniques under a nitrogen or argon atmosphere. Air sensitive liquids and solutions were transferred via a gas-tight syringe or cannula. Reactions were stirred with a teflon-covered magnetic stirring bar. Removal of solvents was accomplished by evaporation on a Buchi rotary evaporator (water bath 40 °C) or directly from the Schlenck using an oil pump. Tetrahydrofuran and diethyl ether were freshly distilled from sodium/benzophenone. Toluene was distilled from sodium. Dry dichloromethane and acetonitrile were freshly distilled from CaH₂. All commercially available reagents were used as received, unless indicated otherwise.

Chromatography. TLC was performed using 250 µm silica gel 60 plates with 254 nm fluorescent indicator. Compounds were visualized by UV, and/or exposure to iodine, KMnO₄, ninhydrine, anisaldehyde, or Cl₂/TDM. *Iodine:* I₂ crystals. *KMnO₄:* KMnO₄ (2.5% w/w) in water. *Ninhydrine:* ninhydrine (630 mg) in ethanol (200 mL). *Anisaldehyde:* solution of anisaldehyde (10 mL), acetic acid (10 mL), and sulfuric acid (6 mL) in ethanol (174 mL). *Cl₂/TDM:* chlorine source is Ca(OCl)₂, TDM solution consists of A:B:C = 30:50:0.75, where A = methylene bis-(4,4'-*N,N'*-dimethylaniline) (TDM) 6.2 g, AcOH 25 mL, H₂O 125 mL; B = KI 12.5 g, H₂O 250 mL; C = ninhydrine 0.6 g, AcOH 20 mL, H₂O 180 mL. The TLC plate was placed for 1 min in a jar filled with at 2 cm layer of Ca(OCl)₂ on the bottom. After blowing off the excess Cl₂ with cold air, the plate was dipped into the TDM solution showing (after heating) the compounds (typically amides) on the plate.

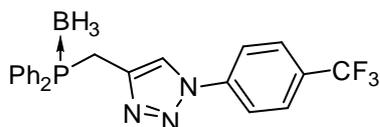
Chromatographic purification refers to flash chromatography using the indicated solvent (mixture) and Biosolve silica gel (0.035-0.070 mm). Analytical HPLC was carried out on reversed phase C₁₈ columns using gradients between 95:5:0.01 (water/acetonitrile/formic acid) and 5:95:0.01. GC analysis of samples obtained during the catalysis were measured on a Shimadzu GC-17A with a BPX35 column and FID detector.

Physical and Spectroscopic Measurements. NMR spectra were recorded in Fourier Transform mode on a Varian Mercury VX (¹H at 300 MHz, ¹³C at 75 MHz, ³¹P at 121 MHz) or a Bruker AV 400 (¹H at 400 MHz, ¹³C at 101 MHz, ³¹P at 162 MHz) or a Varian Unity Inova (¹H at 500 MHz, ¹³C at 126 MHz, ³¹P at 203 MHz) magnetic resonance spectrometer at 25 °C. ³¹P NMR spectra of resins were recorded on the Varian Unity Inova using a Nano-probe (1H {31P} 4 mm PFG Indirect Detection Nano Probe) and Magic angle spinning (MAS) techniques with a spin rate of 3000 Hz. The Nano-probe contains a suspension of the resin beads in d₂-dichloromethane (40 µL). NMR spectra are reported as chemical shifts in parts per million (ppm) relative to the solvent signal and converted to tetramethylsilane scale (CDCl₃: ¹H, 7.26 ppm; ¹³C, 77.16 ppm). ³¹P NMR spectra were calibrated using 85% H₃PO₄ as an external chemical shift reference. Spin multiplicity is described by the following abbreviations: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, and br = broad. Coupling constants (*J*) are reported in Hertz (Hz). ¹³C NMR spectra were recorded with protondecoupling as APT (attached proton test) spectra. Infrared spectra were obtained from CDCl₃ solutions on a NaCl glass plate or from solid KBr on a Bruker IFS 28 Fourier Transform spectrometer (FTIR) and are reported in wavenumbers (cm⁻¹). Fast Atom Bombardment (FAB) mass spectrometry was carried out using a JEOL JMS SX/SX 102A four-sector mass spectrometer, coupled to a JEOL MS-MP9021D/UPD system program. Samples were loaded in a matrix solution (3-

nitrobenzyl alcohol) on a stainless steel probe and bombarded with xenon atoms with an energy of 3 keV. During the high resolution FAB-MS measurements a resolving power of 10,000 (10% valley definition) was used. Melting points were determined on a Wagner & Munz Polytherm A with a Fluke 52 II thermometer.

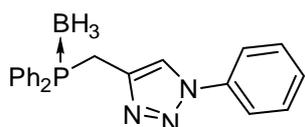


Propargyl(diphenyl)phosphine borane complex (2). To a solution of the commercially available (diphenyl)phosphine borane complex **1** (1.00 g, 5.00 mmol) in THF (19 mL) *n*-BuLi (1.6 M in hexane, 3.13 mL, 5.00 mmol) was added at $-72\text{ }^{\circ}\text{C}$ under nitrogen atmosphere. The solution was stirred for 15 min and propargylbromide (80% in toluene, 0.61 mL, 5.5 mmol) was added, quenching the phosphine anion at $-72\text{ }^{\circ}\text{C}$. The reaction was finished almost directly and after 15 minutes water was added and the solution was warmed to room temperature. The water layer (100 mL) was extracted with EtOAc ($3 \times 50\text{ mL}$) and the combined organic layers were washed with water (80 mL) and brine (80 mL). The organic phase was dried with anhydrous Na_2SO_4 . Evaporation of the solvent gave product **2** (1.17 g, 99%) as a pale yellow oil, which solidified at $-18\text{ }^{\circ}\text{C}$. ^1H NMR (400 MHz); δ (ppm) = 7.78-7.73 (m, 4H of *m*-Ph), 7.55-7.45 (m, 6H of *o,p*-Ph), 3.14 (dd, $J = 2.8\text{ Hz}$, $J_{\text{HP}} = 10.4\text{ Hz}$, 2H, CH_2), 2.08 (m, 1H, acetylene-H), 1.5-0.5 (br, 3H, BH_3); ^{13}C NMR (101 MHz); δ (ppm) = 132.7 (d, $J = 9.5\text{ Hz}$), 131.8 (d, $J = 2.5\text{ Hz}$), 128.9 (d, $J = 10.2\text{ Hz}$), 127.9 (d, $J = 55.5\text{ Hz}$), 75.8 (d, $J = 10.5\text{ Hz}$), 73.0 (d, $J = 6.6\text{ Hz}$), 18.6 (d, $J = 35.4\text{ Hz}$); ^{31}P NMR (162 MHz); δ (ppm) = 18.6 (d, $J = 63.2\text{ Hz}$); FTIR (film, cm^{-1}): 3291 (s), 2383 (s), 1437 (s), 1107 (m), 1059 (s); HRMS (FAB+) m/z : calcd. ($\text{M}^+ - \text{H}$) 237.1004, found 237.1014.



4-((Diphenyl(borane)phosphino)methyl)-1-(4-(trifluoromethyl)phenyl)-1H-1,2,3-triazole (3a). To a mixture of **2** (0.10 g, 0.42 mmol) and 4-trifluoromethylphenylazide (79 mg, 0.42 mmol) in *t*-BuOH (2 mL) a solution of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (1.0 mg, 0.004 mmol) and sodium ascorbate (8.3 mg, 0.042 mmol) in 1 mL water was added. This mixture was stirred at room

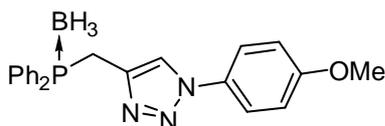
temperature for 22 hours under nitrogen atmosphere. After addition of 10 mL water the aqueous phase was extracted with EtOAc ($3 \times 8\text{ mL}$) and the combined organic layers were washed with water (7 mL) and brine (7 mL). The organic phase was dried with anhydrous Na_2SO_4 . Product **3a** (160 mg, 90%) was obtained after evaporation of the solvent as a white solid. Recrystallization from EtOAc gave in two combined portions the product (157 mg, 88%) as white needles: mp $159\text{--}163\text{ }^{\circ}\text{C}$. ^1H NMR (400 MHz); δ (ppm) = 8.02 (d, $J = 2.1\text{ Hz}$, 1H, triazole-H), 7.83-7.72 (m, 8H), 7.53-7.43 (m, 6H), 3.87 (d, $J_{\text{HP}} = 11.3\text{ Hz}$, 2H, CH_2), 1.6-0.6 (br, 3H, BH_3); ^{13}C NMR (101 MHz); δ (ppm) = 140.3 (d, $J = 2.1\text{ Hz}$), 139.4, 132.5 (d, $J = 9.3\text{ Hz}$), 131.8 (d, $J = 2.3\text{ Hz}$), 130.8 (q, $J = 33.2\text{ Hz}$), 129.1 (d, $J = 10.0\text{ Hz}$), 128.2 (d, $J = 55.4\text{ Hz}$), 127.2 (q, $J = 3.7\text{ Hz}$), 123.6 (q, $J = 272.5\text{ Hz}$), 121.4 (d, $J = 2.9\text{ Hz}$), 120.5, 24.7 (d, $J = 36.3\text{ Hz}$); ^{31}P NMR (162 MHz); δ (ppm) = 16.4 (d, $J = 51.8\text{ Hz}$); FTIR (film, cm^{-1}): 2385 (s), 1616 (w), 1441 (w), 1326 (s), 1171 (m), 1131 (s), 1067 (s), 845 (m).



4-((Diphenyl(borane)phosphino)methyl)-1-phenyl-1H-1,2,3-triazole (3b). To a mixture of **2** (1.19 g, 5.00 mmol) and phenylazide (0.55 mL, 5.0 mmol) in *t*-BuOH (10 mL) and water (8 mL) a solution of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (12.5 mg, 0.050 mmol) in 1 mL water and a sodium ascorbate (99 mg,

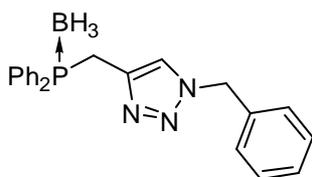
0.50 mmol) solution in 1 mL water were added. This mixture was stirred at room temperature for 2 hours. After addition of 90 mL water the aqueous phase was extracted with EtOAc ($3 \times 40\text{ mL}$) and the combined organic layers were washed with water (60 mL) and brine (60 mL). The organic phase

was dried with anhydrous Na_2SO_4 . Product **3b** (1.72 g, 96%) was obtained after evaporation of the solvent as a solid. Recrystallization from EtOAc with some drops of PE gave the product (1.33 g, 75%) as light yellow needles: mp 125-130 °C. ^1H NMR (400 MHz); δ (ppm) = 7.92 (d, J = 1.7 Hz, 1H, triazole-H), 7.76-7.72 (m, 4H, *m*-Ph-P), 7.64 (d, J = 8.0 Hz, 2H, *m*-Ph-triazole), 7.50-7.41 (m, 8H, *o,p*-Ph), 3.86 (d, J_{HP} = 11.1 Hz, 2H, CH_2), 1.5-0.5 (br, 3H, BH_3); ^{13}C NMR (101 MHz); δ (ppm) = 139.7, 136.9, 132.4 (d, J = 9.3 Hz), 131.6 (d, J = 2.3 Hz), 129.7, 128.9 (d, J = 10.1 Hz), 128.7, 128.2 (d, J = 55.4 Hz), 121.4, 120.4, 24.6 (d, J = 36.2 Hz); ^{31}P NMR (162 MHz); δ (ppm) = 16.3 (d, J = 63.2 Hz); FTIR (film, cm^{-1}); 3058 (m), 2386 (s), 1598 (m), 1501 (s), 1437 (s), 1108 (m), 1060 (s), 1043 (s), 843 (m); HRMS (FAB+) m/z : calcd. (M^+ -H) 356.1488, found 356.1508.



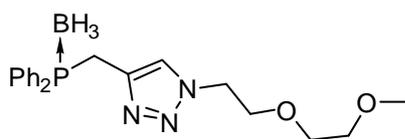
4-((Diphenyl(borane)phosphino)methyl)-1-(4-methoxyphenyl)-1H-1,2,3-triazole (3c). To a mixture of **2** (32 mg, 0.13 mmol) and 4-methoxyphenylazide (20 mg, 0.14 mmol) in *t*-BuOH (0.5 mL) and 3 drops of THF a solution of $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (3.5 mg,

0.014 mmol) and sodium ascorbate (5.5 mg, 0.028 mmol) in 0.5 mL water was added. The acquired brown suspension is stirred at room temperature for 44 hours. After addition of 12 mL water the aqueous phase was extracted with EtOAc (3×7 mL) and the combined organic layers were washed with water (10 mL) and brine (10 mL). The organic phase was dried with anhydrous Na_2SO_4 . Evaporation of solvents afforded product **3c** (48 mg, 93%) as an orange solid containing small quantities of starting materials. Recrystallisation from EtOAc gave the product **3c** (38 mg, 76%) as orange crystals: mp 141-144 °C. ^1H NMR (400 MHz); δ (ppm) = 7.83 (d, J = 1.9 Hz, 1H, triazole-H), 7.76-7.71 (m, 4H), 7.55-7.49 (m, 2H), 7.48-7.42 (m, 6H), 6.99-6.96 (m, 2H), 3.87 (d, J_{HP} = 11.1 Hz, 2H, CH_2), 3.87 (s, 3H, OMe), 1.6-0.6 (br, 3H, BH_3); ^{13}C NMR (126 MHz); δ (ppm) = 159.9, 139.5 (d, J = 2.1 Hz), 132.6 (d, J = 8.9 Hz), 131.7 (d, J = 2.5 Hz), 130.5, 129.1 (d, J = 10.1 Hz), 128.4 (d, J = 55.3 Hz), 122.2, 121.7 (d, J = 2.5 Hz), 114.8, 55.7, 24.8 (d, J = 36.3 Hz); ^{31}P NMR (162 MHz); δ (ppm) = 16.3 (d, J = 61.6 Hz); FTIR (film, cm^{-1}); 3056 (w), 2385 (s), 1517 (s), 1437 (m), 1255 (s), 1037 (m), 836 (m).



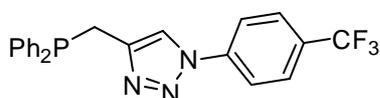
1-Benzyl-4-((diphenyl(borane)phosphino)methyl)-1H-1,2,3-triazole (3d). To a mixture of **2** (0.24 g, 1.0 mmol) and sodium ascorbate (40 mg, 0.20 mmol) in *t*-BuOH/ H_2O (1:1, 4 mL), $\text{CuSO}_4 \cdot 5\text{H}_2\text{O}$ (12 mg, 0.050 mmol) and benzylazide (0.13 mL, 1.0 mmol) were added. This white suspension was stirred at room temperature for 7 hours. After addition of

2 mL water the solvent was removed and the remaining solid was dissolved in EtOAc. This organic layer was washed with water (5 mL) and brine (5 mL) and dried with anhydrous Na_2SO_4 . Product **3d** (340 mg, 92%) was obtained after evaporation of the solvent. Recrystallization from EtOAc gave the product (257 mg, 69%) as yellow crystals: mp 108-112 °C. ^1H NMR (400 MHz); δ (ppm) = 7.69-7.64 (m, 4H), 7.46-7.36 (m, 7H), 7.34-7.32 (m, 3H), 7.12-7.10 (m, 2H), 5.41 (s, 2H), 3.76 (d, J_{HP} = 11.0 Hz, 2H, P- CH_2), 1.5-0.5 (br, 3H, BH_3); ^{13}C NMR (101 MHz); δ (ppm) = 139.5, 134.7, 132.6 (d, J = 9.0 Hz), 131.6 (d, J = 2.3 Hz), 129.2, 128.9 (d, J = 10.2 Hz), 128.7, 128.3 (d, J = 55.3 Hz), 127.9, 123.4, 54.2, 24.8 (d, J = 36.2 Hz); ^{31}P NMR (162 MHz); δ (ppm) = 16.4 (br d, J = 61.6 Hz); FTIR (film, cm^{-1}); 3058 (m), 2378 (s), 1545 (w), 1457 (m), 1435 (s), 1340 (m), 1108 (m), 1063 (s), 1048 (s), 910 (m), 845 (m).



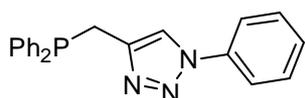
4-((Diphenyl(borane)phosphino)methyl)-1-(2-(2-methoxyethoxy)ethyl)-1H-1,2,3-triazole (3e). Phosphine **2** (60 mg, 0.25 mmol, 1 equiv) was mixed with 1-azido-2-(2-methoxyethoxy)ethane (36.6 mg, 0.25 mmol, 1 equiv) in 3 mL of

THF. CuSO₄ (0.10 equiv) and sodium ascorbate (0.20 equiv) dissolved in 1 mL of water were added to the solution. The reaction mixture was stirred for 12 h at room temperature. Subsequently, the solvent was evaporated and a mixture of CH₂Cl₂/H₂O (10 mL, 1:1) was added. The organic phase was filtered through a pipette packed with MgSO₄. Evaporation of solvent afforded product **3e** in 90% yield (87 mg) as a transparent oil. ¹H NMR (300 MHz); δ (ppm) = 7.74-7.60 (m, 4H, C₆H₅), 7.50-7.34 (m, 7H, C₆H₅ + triazole-H), 4.41 (t, 2H, N-CH₂), 3.77 (d, 2H, P-CH₂), 3.73 (t, 2H, N-CH₂CH₂), 3.46 (AB, 4H, OCH₂CH₂O), 3.33 (t, 3H, CH₃). ¹³C NMR (MHz); δ (ppm) = 138.8 (C_{ipso} triazole), 132.6, 131.7, 129.0 (d, C₆H₅), 128.3 (C_{ipso} C₆H₅), 124.6 (triazole-C), 71.9, 70.8, 69.7 (CH₂O(CH₂)₂O), 59.3 (CH₃), 50.5 (N-CH₂), 24.7 (d, PCH₂). ³¹P NMR (121 MHz); δ (ppm) = 16.6 (br).



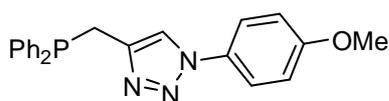
4-((Diphenylphosphino)methyl)-1-(4-(trifluoromethyl)phenyl)-1H-1,2,3-triazole (4a). Under argon atmosphere a solution of **3a** (0.10 g, 0.24 mmol) and DABCO (35 mg, 0.31 mmol) in toluene (4

mL, filtrated over alumina) was stirred at 70 °C. After 4 h the solution was cooled to ambient temperature and purified by filtration over a short silica column (EtOAc) to remove DABCO components. Product **4a** was obtained as a yellow/white powder (93 mg, 96%) after evaporation of solvents. ¹H NMR (400 MHz); δ (ppm) = 7.51 (s, 4H), 7.49-7.46 (m, 4H), 7.43 (d, *J* = 0.7 Hz, 1H, triazole-H), 7.37-7.35 (m, 6H), 3.62 (s, 2H, CH₂); ¹³C NMR (101 MHz); δ (ppm) = 145.2 (d, *J* = 10.4 Hz), 139.4, 137.4 ((d, *J* = 13.9 Hz), 132.8 (d, *J* = 18.9 Hz), 130.5 (q, *J* = 33.0 Hz), 129.1, 128.6 (d, *J* = 6.7 Hz), 127.0 (q, *J* = 3.7 Hz), 123.6 (q, *J* = 272.3 Hz), 120.2, 119.4 (d, *J* = 6.8 Hz), 25.3 (d, *J* = 15.6 Hz); ³¹P NMR (162 MHz); δ (ppm) = -14.1; FTIR (film, cm⁻¹); 1617 (w), 1326 (s), 1169 (m), 1126 (s), 1069 (m), 1041 (m), 844 (m); HRMS (FAB+) *m/z*: calcd. (MH⁺) 412.1190, found 412.1195.



4-((Diphenylphosphino)methyl)-1-phenyl-1H-1,2,3-triazole (4b).

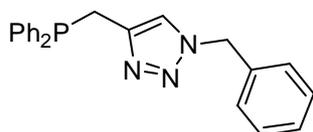
Under argon atmosphere a solution of **3b** (0.20 g, 0.56 mmol) and DABCO (75 mg, 0.67 mmol) in THF (7 mL) was stirred at 67 °C. After 4 h the solution was cooled to ambient temperature and evaporated to dryness. The resulting solid was dissolved in EtOAc and purified by filtration over a short silica column (EtOAc) to remove DABCO components. Product **4b** (170 mg, 89%) was obtained as a white solid after evaporation of solvents. ¹H NMR (400 MHz); δ (ppm) = 7.61-7.59 (m, 2H, *m*-Ph_{triazole}), 7.52-7.35 (m, 14H), 3.61 (s, 2H, CH₂); ¹³C NMR (101 MHz); δ (ppm) = 144.6 (d, *J* = 10.4 Hz), 137.7 (d, *J* = 14.3 Hz), 137.1, 132.8 (d, *J* = 18.8 Hz), 129.6, 129.0, 128.6 (d, *J* = 6.6 Hz), 128.5, 120.3, 119.6 (d, *J* = 6.7 Hz), 25.3 (d, *J* = 15.4 Hz); ³¹P NMR (162 MHz); δ (ppm) = -14.3; FTIR (film, cm⁻¹); 1598 (m), 1500 (s), 1433 (s), 1343 (m), 1234 (m), 1042 (s).



4-((Diphenylphosphino)methyl)-1-(4-methoxyphenyl)-1H-1,2,3-triazole (4c). Under argon atmosphere a solution of **3c** (70

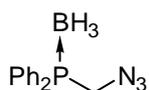
mg, 0.18 mmol) and DABCO (28 mg, 0.25 mmol) in toluene (4 mL, filtrated over alumina) was stirred at 70 °C. After 4 h the solution was cooled to ambient temperature and purified by filtration over a short silica column (EtOAc) to remove DABCO components. Evaporation of solvents gave product **4c** as a yellow/white powder (59 mg, 87%). ¹H

NMR (400 MHz); δ (ppm) = 7.50-7.46 (m, 6H), 7.37-7.34 (m, 6H), 7.31 (m, 1H), 6.97 (m, 1H), 6.96 (m, 1H), 3.84 (s, 3H, OMe), 3.60 (s, 2H, CH₂); ¹³C NMR (101 MHz); δ (ppm) = 159.6, 144.3 (d, J = 10.4 Hz), 137.7 (d, J = 14.1 Hz), 132.8 (d, J = 18.9 Hz), 130.6, 129.0, 128.6 (d, J = 6.6 Hz), 122.0, 119.8 (d, J = 6.7 Hz), 114.7, 55.6, 25.4 (d, J = 15.3 Hz); ³¹P NMR (162 MHz); δ (ppm) = -14.3; FTIR (film, cm⁻¹); 1518 (s), 1434 (w), 1256 (m), 1042 (m), 832 (m); HRMS (FAB+) m/z : calcd. (MH⁺) 374.1422, found 374.1418.



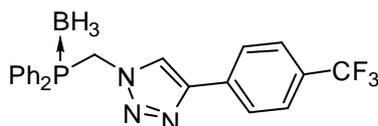
1-Benzyl-4-((diphenylphosphino)methyl)-1H-1,2,3-triazole (4d).

Under argon atmosphere a solution of **3d** (50 mg, 0.13 mmol) and DABCO (23 mg, 0.20 mmol) in toluene (2 mL, filtrated over alumina) was stirred at 70 °C. After 3 h the solution was cooled to ambient temperature and purified by filtration over a short silica column (EtOAc) to remove DABCO components. The white powder obtained after evaporation of solvents was a mixture of product **4d** (39 mg, 83%) and its phosphine oxide (4 mg, 9%, determined by ³¹P NMR). ¹H NMR (400 MHz); δ (ppm) = 7.42-7.27 (m, 13H), 7.14-7.11 (m, 2H), 6.86 (s, 1H), 5.39 (s, 2H), 5.39 (s, 2H), 3.50 (s, 2H); ¹³C NMR (101 MHz); δ (ppm) = 144.3 (d, J = 9.9 Hz), 137.8 (d, J = 14.1 Hz), 134.9, 132.9 (d, J = 18.6 Hz), 129.0 (d, J = 14.4 Hz), 128.68, 128.63, 128.56, 128.0, 121.7 (d, J = 6.4 Hz), 54.1, 25.6 (d, J = 15.1 Hz); ³¹P NMR (162 MHz); δ (ppm) = -14.3; HRMS (FAB+) m/z : calcd. (MH⁺) 358.1473, found 358.1473.



Azidomethyl(diphenyl)phosphine borane complex (6). To a solution of hydroxymethyl(diphenyl)phosphine borane complex¹⁶ (1.02 g, 4.42 mmol) and 2,6-

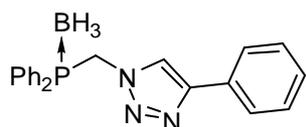
lutidine (0.88 mL, 7.52 mmol) in chloroform (22 mL, filtrated over alumina) at -60 °C Tf₂O (1.26 mL, 7.52 mmol) was added under nitrogen atmosphere. The solution was stirred for 3 hours and tetramethylguanidinium azide (TMGA, 3.0 g, 19 mmol) was added. The mixture was stirred overnight allowing to warm to room temperature. After 24 h saturated aqueous ammonium chloride (100 mL) was added and the mixture was extracted 3 times with CH₂Cl₂ (50 mL). The combined organic layers were washed with water (2 × 50 mL) and brine (50 mL). The water layer (100 mL) was extracted with EtOAc (3 × 70 mL) and the combined organic layers were washed with water (100 mL) and brine (100 mL). The organic phase was dried with anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (PE/EtOAc 9:1) to afford **6** as a pale yellow oil (0.84 g, 74%). ¹H NMR (400 MHz); δ (ppm) = 7.78-7.72 (m, 4H, Ph), 7.59-7.54 (m, 2H, *p*-Ph), 7.52-7.47 (m, 4H, *o*-Ph), 4.04 (d, J_{HP} = 3.4 Hz, 2H, CH₂), 1.5-0.5 (br, 3H, BH₃); ¹³C NMR (126 MHz); δ (ppm) = 132.9 (d, J = 9.3 Hz), 132.2 (d, J = 2.5 Hz), 129.2 (d, J = 10.1 Hz), 126.5 (d, J = 55.3 Hz), 48.6 (d, J = 37.1 Hz); ³¹P NMR (162 MHz); δ (ppm) = 19.8 (d, J = 61.6 Hz); FTIR (film, cm⁻¹); 3058 (w), 2389 (s), 2092 (s), 1437 (s), 1250 (m), 1107 (m), 1061 (s), 858 (w).



1-((Diphenyl(borane)phosphino)methyl)-4-(4-trifluoromethylphenyl)-1H-1,2,3-triazole (7a). Azidomethyl(diphenyl)phosphine borane complex **6** (0.10 g, 0.39 mmol), 4-trifluoromethylphenylacetylene (66 μ L, 0.39 mmol), sodium ascorbate (31 mg, 0.16

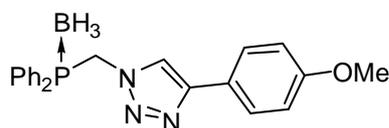
mmol), and CuSO₄·5H₂O (10 mg, 0.039 mmol) were suspended in a mixture of water and *t*-BuOH (2 mL, 1:1). This mixture was stirred at room temperature for 3.5 hours. The white suspension was extracted once with EtOAc (10 mL) and the organic layer was washed two times with H₂O (9 mL). The solution was dried with anhydrous Na₂SO₄ and concentrated under reduced pressure. The residue

was purified by flash chromatography on silica gel (PE/EtOAc 2:1) resulting after evaporation of solvents in compound **7a** as a white solid (118 mg, 71%): mp 124-127 °C. ¹H NMR (400 MHz); δ (ppm) = 7.90 (s, 1H, triazole-H), 7.85 (d, *J* = 8.1 Hz, 2H), 7.75-7.70 (m, 4H), 7.65 (d, *J* = 8.3 Hz, 2H), 7.59-7.54 (m, 2H), 7.51-7.47 (m, 4H), 5.32 (d, *J*_{HP} = 4.1 Hz, 2H, CH₂), 1.6-0.6 (br, 3H, BH₃); ¹³C NMR (101 MHz); δ (ppm) = 146.7, 133.7, 132.9 (d, *J* = 9.8 Hz), 132.6 (d, *J* = 2.5 Hz), 130.3 (q, *J* = 32.4 Hz), 129.4 (d, *J* = 10.4 Hz), 126.01, 125.96 (q, *J* = 3.9 Hz), 125.1 (d, *J* = 55.3 Hz), 124.2 (q, *J* = 272.0 Hz), 122.0, 48.1 (d, *J* = 34.9 Hz); ³¹P NMR (162 MHz); δ (ppm) = 17.9 (br); FTIR (film, cm⁻¹); 3059 (w), 2393 (s), 1622 (w), 1438 (w), 1326 (s), 1167 (m), 1124 (s), 1063 (s), 850 (w).



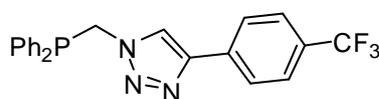
1-((Diphenyl(borane)phosphino)methyl)-4-phenyl-1H-1,2,3-triazole

(7b). To a solution of azidomethyl(diphenyl)phosphine borane complex **6** (0.15 g, 0.59 mmol) in *t*-BuOH (4 mL) phenylacetylene (88 μL, 0.80 mmol) was added, together with a solution of sodium ascorbate (47 mg, 0.24 mmol) in 1 mL water and a solution of CuSO₄·5H₂O (15 mg, 0.059 mmol) in 1 mL water. This mixture was stirred at room temperature for 4 hours under nitrogen atmosphere. The white suspension was extracted once with EtOAc (15 mL) and the organic layer was evaporated to dryness. The residue was purified by flash chromatography on silica gel (first CH₂Cl₂ followed by pure EtOAc) resulting after evaporation of solvents in compound **7b** as a yellow foam (185 mg, 88%): mp 107-111 °C. ¹H NMR (400 MHz); δ (ppm) = 7.77 (s, 1H, triazole-H), 7.75-7.68 (m, 6H, Ph), 7.58-7.29 (m, 9H, Ph), 5.30 (d, *J*_{HP} = 3.9 Hz, 2H, CH₂), 1.6-0.6 (br, 3H, BH₃); ¹³C NMR (101 MHz); δ (ppm) = 148.2, 133.0 (d, *J* = 9.6 Hz), 132.6 (d, *J* = 2.3 Hz), 130.3, 129.5 (d, *J* = 10.3 Hz), 129.0, 128.5, 126.0, 125.3 (d, *J* = 55.4 Hz), 121.2, 48.2 (d, *J* = 34.6 Hz); ³¹P NMR (162 MHz); δ (ppm) = 18.0 (d, *J* = 51.8 Hz); FTIR (film, cm⁻¹); 3059 (w), 2392 (s), 1484 (w), 1437 (s), 1230 (w), 1192 (w), 1108 (m), 1060 (m), 1040 (m), 911 (w), 854 (w).



1-((Diphenyl(borane)phosphino)methyl)-4-(4-methoxyphenyl)-1H-1,2,3-triazole

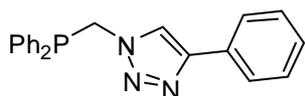
(7c). azidomethyl(diphenyl)phosphine borane complex **6** (0.10 g, 0.39 mmol), 4-methoxyphenylacetylene (54 mg, 0.41 mmol), sodium ascorbate (31 mg, 0.16 mmol), and CuSO₄·5H₂O (10 mg, 0.039 mmol) were suspended in a mixture of water (1.5 mL) and *t*-BuOH (3.0 mL). This mixture was stirred at room temperature for 5 hours. The suspension was extracted once with EtOAc (15 mL) and the organic layer was evaporated to dryness. The residue was purified by flash chromatography on silica gel (gradient EtOAc/PE (1:8 to 1:1)) resulting after evaporation of solvents in compound **7c** as a white solid (106 mg, 70%): mp 132-137 °C. ¹H NMR (400 MHz); δ (ppm) = 7.74-7.63 (m, 7H), 7.57-7.45 (m, 6H), 6.94-6.91 (m, 2H), 5.28 (d, *J*_{HP} = 3.8 Hz, 2H, CH₂), 3.83 (s, 3H, OMe), 1.6-0.6 (br, 3H, BH₃); ¹³C NMR (101 MHz); δ (ppm) = 159.8, 147.9, 132.9 (d, *J* = 9.7 Hz), 132.5 (d, *J* = 2.5 Hz), 129.4 (d, *J* = 10.3 Hz), 127.2, 125.3 (d, *J* = 55.5 Hz), 123.0, 120.3, 114.4, 55.5, 48.1 (d, *J* = 34.7 Hz); ³¹P NMR (162 MHz); δ (ppm) = 18.0 (br); FTIR (film, cm⁻¹); 3054 (w), 2935 (w), 2835 (w), 2390 (s), 1616 (w), 1562 (w), 1496 (s), 1441 (s), 1251 (s), 1065 (m), 1030 (s), 840 (m).



1-((Diphenyl(borane)phosphino)methyl)-4-(4-(trifluoromethyl)phenyl)-1H-1,2,3-triazole

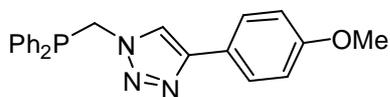
(8a). Under argon atmosphere a solution of borane protected phosphine **7a** (50 mg, 0.12 mmol) and DABCO (16 mg, 0.14 mmol) in dry toluene (2 mL) was stirred at 70 °C. After 2 hours the solution

was cooled to ambient temperature and purified by filtration over a short silica column (toluene as eluent) to remove DABCO components. Evaporation of solvents gave product **8a** as a white solid (42 mg, 86%). ^1H NMR (400 MHz); δ (ppm) = 7.84 (d, 2H, $J = 8.1$ Hz), 7.65 (d, 2H, $J = 8.2$ Hz), 7.61 (s, 1H, triazole-H), 7.48-7.38 (m, 10H), 5.15 (d, $J_{\text{HP}} = 5.2$ Hz, 2H, CH_2); ^{13}C NMR (101 MHz); δ (ppm) = 146.6, 134.4 (d, $J = 12.2$ Hz), 134.1 (d, $J = 1.1$ Hz), 133.1 (d, $J = 19.5$ Hz), 130.0 (q, $J = 32.5$ Hz), 130.0, 129.2 (d, $J = 6.9$ Hz), 125.9-126.0 (s+q, 4C), 124.2 (q, $J = 271.9$ Hz), 120.6 (d, $J = 3.7$ Hz), 50.4 (d, $J = 20.9$ Hz); ^{31}P NMR (162 MHz); δ (ppm) = -13.8; FTIR (film, cm^{-1}); 1621 (w), 1435 (w), 1326 (s), 1166 (m), 1122 (m), 1063 (m), 849 (w); HRMS (FAB+) m/z : calcd. (MH^+) 412.1190, found 412.1195.



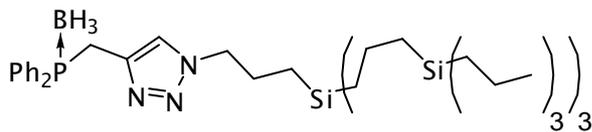
1-((Diphenyl(borane)phosphino)methyl)-4-phenyl-1H-1,2,3-triazole (8b). Under argon atmosphere a solution of borane protected phosphine **7b** (30 mg, 0.085 mmol) and DABCO (18 mg, 0.16 mmol) in toluene (1.5

mL, filtrated over alumina) was stirred at 70 °C. After 5 hours the solution was cooled to ambient temperature and purified by filtration over a short silica column (EtOAc) to remove DABCO components. Evaporation of solvents gave product **8b** as a white solid (20 mg, 69%). Also oxidized material (9 mg, 30%) was recovered as a second fraction. ^1H NMR (400 MHz); δ (ppm) = 7.75-7.73 (m, 2H), 7.57 (s, 1H, triazole-H), 7.48-7.38 (m, 12H), 7.33-7.29 (m, 1H), 5.13 (d, $J_{\text{HP}} = 5.1$ Hz, 2H, CH_2); ^{13}C NMR (101 MHz); δ (ppm) = 148.0, 134.5 (d, $J = 12.4$ Hz), 133.1 (d, $J = 19.2$ Hz), 130.7, 129.9, 129.1 (d, $J = 7.0$ Hz), 128.9, 128.2, 125.8, 119.8 (d, $J = 3.7$ Hz), 50.4 (d, $J = 20.5$ Hz); ^{31}P NMR (162 MHz); δ (ppm) = -14.1; FTIR (film, cm^{-1}); 3053 (m), 1482 (m), 1461 (m), 1434 (s), 1224 (w), 1188 (m), 1096 (m), 1074 (m), 1042 (s), 1026 (m), 914 (w).



1-((Diphenyl(borane)phosphino)methyl)-4-(4-methoxyphenyl)-1H-1,2,3-triazole (8c). Under argon atmosphere a solution of borane protected phosphine **7c** (40 mg, 0.11 mmol) and DABCO

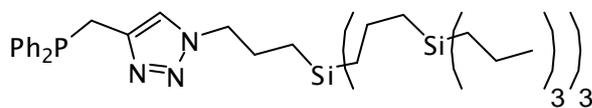
(18 mg, 0.16 mmol) in toluene (1.5 mL, filtrated over alumina) was stirred at 70 °C. After 5 hours the solution was cooled to ambient temperature and purified by filtration over a short silica column (EtOAc) to remove DABCO components. Evaporation of solvents gave product **8c** as a slightly brown/white solid (24 mg, 62%). ^1H NMR (400 MHz); δ (ppm) = 7.68-7.65 (m, 2H), 7.49-7.37 (m, 11H), 6.95-6.91 (m, 2H), 5.11 (d, $J_{\text{HP}} = 5.0$ Hz, 2H, CH_2), 3.82 (s, 3H, OMe); ^{13}C NMR (101 MHz); δ (ppm) = 159.8, 147.8, 134.6 (d, $J = 12.2$ Hz), 133.1 (d, $J = 19.3$ Hz), 130.0, 129.1 (d, $J = 7.0$ Hz), 127.2, 123.2, 119.1 (d, $J = 3.8$ Hz), 114.4, 55.5, 50.6 (d, $J = 20.4$ Hz); ^{31}P NMR (162 MHz); δ (ppm) = -14.2; HRMS (FAB+) m/z : calcd. (MH^+) 374.1422, found 374.1418.



1-((Diphenyl(borane)phosphino)methyl)-4-dend-1H-1,2,3-triazole (10). Phosphine **2** (67 mg, 0.28 mmol, 1.0 equiv) was mixed with dendrimer **9** (200 mg, 0.28 mmol, 1 equiv) in 3 mL of THF.

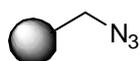
CuSO_4 (0.1 equiv) and sodium ascorbate (0.2 equiv), dissolved in 1 mL of water, were added to the solution. The reaction mixture was stirred for 12 h at room temperature. Subsequently, the solvent was evaporated and a mixture of $\text{Et}_2\text{O}/\text{H}_2\text{O}$ (10 mL, 1:1) was added. The organic phase was filtered through a pipette packed with MgSO_4 . Dendrimer **10** was obtained as a transparent oil in 95% yield (253 mg). ^1H NMR (300 MHz); δ (ppm) = 7.72-7.65 (m, 4H, C_6H_5), 7.45-7.38 (m, 7H, C_6H_5 + triazole-H), 4.17 (t, 2H, N- CH_2), 3.77 (d, 2H, P- CH_2), 1.67 (m, 2H, N- CH_2CH_2), 1.39-1.21 (m, 24H,

CH₂-dend), 0.93 (t, 27H, CH₃), 0.59-0.44 (m, 32H, CH₂-dend). ¹³C NMR (75 MHz); δ (ppm) = 138.8 (C_{ipso} triazole), 132.6, 131.6, 129.0 (d, C₆H₅), 128.3 (C_{ipso} C₆H₅), 123.2 (triazole-C), 53.7 (N-CH₂), 24.9 (d, P-CH₂), 25.6, 18.9, 18.8, 18.0, 17.7, 15.6, 10.0 (dend). ³¹P NMR (121 MHz); δ (ppm) = 16.4 (br).



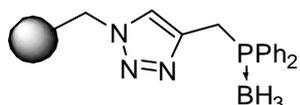
1-((Diphenylphosphino)methyl)-4-dend-1H-1,2,3-triazole (11). A solution of dendrimer **10** (150 mg, 0.16 mmol, 1.0 equiv) and DABCO

(21.3 mg, 0.19 mmol, 1.2 equiv) in toluene (10 mL) was stirred at 70 °C under argon atmosphere. After 3 hours the solvent was removed and the product was purified by filtrating it through a pipette packed with silica using Et₂O as eluent. Dendrimer **11** was obtained as a transparent oil in 95% yield (140.3 mg). ¹H NMR (300 MHz); δ (ppm) = 7.46-7.40 (m, 4H, C₆H₅), 7.35-7.30 (m, 6H, C₆H₅), 6.94 (s, 1H, triazole-H), 4.15 (t, 2H, N-CH₂), 3.51 (d, 2H, P-CH₂), 1.73 (m, 2H, N-CH₂CH₂), 1.39-1.21 (m, 24H, CH₂-dend), 0.95 (t, 27H, CH₃), 0.60-0.40 (m, 32H, CH₂-dend). ¹³C NMR (101 MHz); δ (ppm) = 143.6 (d, *J* = 10.5 Hz, C_{ipso} triazole), 137.9 (d, *J* = 14.2 Hz, C_{ipso} C₆H₅), 132.8 (d, *J* = 18.8 Hz, C₆H₅), 128.8, 128.5 (d, *J* = 18.8 Hz, C₆H₅), 121.1 (d, *J* = 6.7 Hz, triazole-C), 53.6 (N-CH₂), 29.7, 25.4 (d, *J* = 14.1 Hz, P-CH₂), 18.7, 18.6, 17.8, 17.5, 15.6, 9.8 (dend). ³¹P NMR (162 MHz); δ (ppm) = -14.0.



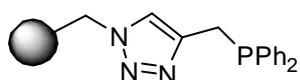
Azidomethyl PS-resin (13). To a suspension of chloromethyl-polystyrene resin (Fluka Merrifield polymer crosslinked with 1% divinylbenzene (DVB); 200-400 mesh; ~0.8

mmol Cl/g; 2.0 g, 1.6 mmol) in DMSO (20 mL) sodium azide (520 mg, 8.0 mmol) was added. The reaction was performed in a scintillation vessel, bubbling nitrogen gas through the resin suspension. The suspension was allowed to react for 3 days at 60 °C. After being cooled to room temperature, the suspension was filtrated and the resin was washed alternatingly with MeOH (5 × 12 mL) and DCM (5 × 12 mL) to give azidomethyl polystyrene **13**. FTIR (KBr, cm⁻¹); 2094 (s).



1-((Diphenyl(borane)phosphino)methyl)-4-PSresin-1H-1,2,3-triazole

(14). Azidomethyl PS-resin **13** (300 mg, 0.8 mmol N₃/g), phosphine **2** (171 mg, 0.72 mmol), CuI (5 mg, 0.024 mmol), TBTA (14 mg, 0.026 mmol) and DIPEA (0.13 mL, 0.72 mmol) were suspended in THF (3 mL). The reaction was run under a nitrogen atmosphere in Radleys Carousel Reaction StationTM using a modified glass reaction tube. The tube was fitted with a glass frit and luer tip to facilitate work-up on the IST VacMaster-20 Sample Processing StationTM. The reaction was gently stirred with a magnetic stirring bar at 40 °C for 20 h. After filtration and washing (same as described below) the resin was reloaded with half the amounts used for the first load to obtain complete conversion of the azide (disappearance of azide signal in FTIR). After 40 h the suspension was filtrated and the resin was washed alternatingly with MeOH (3 × 2 mL), pyridine (3 × 2 mL), and DCM (3 × 2 mL) followed by two additional washing steps with diethyl ether. The resin was dried under vacuum to give “clicked” resin **14** (max. loading 0.67 mmol/g). ³¹P MAS NMR (203 MHz); δ (ppm) = 17.9.



1-((Diphenylphosphino)methyl)-4-PSresin-1H-1,2,3-triazole (15).

Supported ligand **14** (236 mg, 0.67 mmol/g loading) was mixed with DABCO (88.7 mg, 5 equiv) in 10 mL of toluene. The mixture was stirred under a N₂ flow for 8 h at 70 °C. Subsequently, the solvent was removed and the resin was washed with toluene (4 × 7 mL) and dried under vacuum. ³¹P MAS NMR (203 MHz); δ (ppm) = -13.2.

Typical experimental procedure for the preparation of palladium complexes: Ligand **4b** (62 mg, 0.18 mmol, 1.0 equiv) was mixed with [PdallylCl]₂ (33 mg, 0.09 mmol, 0.50 equiv) in 7 mL of CH₂Cl₂. The resulting solution was stirred at room temperature for 45 min under argon affording complex **17b**. To the mixture was added AgBF₄ (35 mg, 0.18 mmol, 1.0 equiv): formation of a precipitate (AgCl) was observed. After 1 h stirring at room temperature the crude mixture was filtered through a pipette packed with Celite. Evaporation of the solvent afforded the cationic Pd complex **18b** as a foamy solid in quantitative yield.

Typical experimental procedure for palladium-catalyzed allylic alkylation: In a schlenck under argon atmosphere cinnamyl acetate (176 mg, 1.0 mmol) was dissolved in THF (10 mL). As internal standard decane (2.0 mmol, 2M in THF) was added. A stocksolution of catalyst was prepared by mixing equimolar quantities of [PdallylCl]₂, and ligand in THF for several minutes, followed, if the cationic complex was used, by addition of AgBF₄. After preparation of the catalyst solution, the proper amount was added to the substrate solution to obtain 0.1 mol% of catalyst relative to the substrate. Simultaneously, the nucleophile, Na diethyl 2-methylmalonate (2.0 equiv), was prepared by deprotonation of diethyl 2-methylmalonate by NaH in THF. After addition of the nucleophile, the reaction mixture (20 mL total) was stirred at 25 °C and followed by GC. GC-samples were prepared by quenching a small amount of the reaction mixture in water and extracting with Et₂O. The organic layer was dried over anhydrous MgSO₄, packed in a pipette, and injected in the GC.

2.8 REFERENCES AND NOTES

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