Transition Metal Catalyzed Formation and Transformations of allylic N,O-acetals with a focus on olefinic a-amino acids

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CHAPTER 4

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4.1 Introduction

The previous chapter described the formation of cyclic, allylic N,O-acetals via ring-closing metathesis and diastereoselective nucleophilic additions to the corresponding cyclic, allylic N-sulfonyliminium ions. While nucleophilic additions onto N-acyl (1, chart 4.1) and N-sulfonyliminium ions (2) have been extensively described in the literature, only a single report of similar additions onto (cyclic) N-phosphoryliminium ions (3) has appeared by the group of Shono.

Chart 4.1. Different electron poor iminium ions.

In this paper, Shono et al. describe the use of silyl enol ethers in the addition onto cyclic N-phosphoryliminium ions derived from 4 and 5 (eq. 4.1). The yields of the products 6 and 7 were below 50% in both cases. In our view, the choice of the Lewis acid, rather than the reactivity of this particular iminium ion might be responsible for the moderate yields. This was inferred from reports by Kobayashi, who showed that by choosing metal triflates as Lewis acids for the addition of enol ethers, high yields could be obtained without substantial decomposition of the nucleophile.

A reason for the lack of examples of N-phosphoryliminium ions might be the limited access to the required N-phosphoryl-N,O-acetal precursors. An additional reason lies in the use of a phosphoryl-based substituent on the nitrogen, which has obvious drawbacks. Cleavage of a phosphoryl group from the nitrogen is often difficult and was in the initial examples designed to happen through enzymatic (phosphoamidase) splitting of the P-N bond of amidophosphates. Later, a partial answer was found in phosphinamides that were developed as mild acid-cleavable protecting groups for amines and amino acids.
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phosphorus-based protective groups have not found wide applicability, most probably due to the many alternatives present. Despite this drawback, two reasons prompted us to start a short investigation into the use of N-phosphoryliminium ions 3: (i) the low number of representative nucleophilic additions onto such ions and (ii) the easy availability of the precursors through the novel amidopalladation described in chapter 2. Besides, by choosing a chiral phosphoryl moiety, it might be possible to perform both types of additions with diastereoselective induction. This chapter describes the investigations into novel N-phosphoryliminium ion chemistry, meant to be of illustrative value and to give a basis for further investigations.

4.2 Allylglycine derived N-phosphoryliminium ions

A cyclic allylglycine derived precursor was synthesized analogous to the work described in the previous chapter (scheme 4.1). As described earlier, the amidopalladation of 8 with benzyl propadienyl ether proceeded rather well at 60 °C and gave the allylic N,O-acetal 9 in 55% isolated yield.

Scheme 4.1 Synthesis of amidophosphate 12. 

\[ \text{PhO}^- \overset{\text{P} \times \text{PhO}}{\text{P}} \text{CO}_2\text{Me} \]  
\[ \text{PhO}^- \overset{\text{P} \times \text{PhO}}{\text{P}} \text{CO}_2\text{Me} \]  

8  

55%  

\[ \text{PhO}^- \overset{\text{P} \times \text{PhO}}{\text{P}} \text{CO}_2\text{Me} \]  
\[ \text{PhO}^- \overset{\text{P} \times \text{PhO}}{\text{P}} \text{CO}_2\text{Me} \]  

9  

97%  

\[ \text{MesN} \overset{\text{Ph}}{\text{NMes}} \text{CO}_2\text{Me} \]  
\[ \text{MesN} \overset{\text{Ph}}{\text{NMes}} \text{CO}_2\text{Me} \]  

10  

\[ \text{HN} \overset{\text{P} \times \text{PhO}}{\text{P}} \text{CO}_2\text{Me} \]  
\[ \text{HN} \overset{\text{P} \times \text{PhO}}{\text{P}} \text{CO}_2\text{Me} \]  

12  

conditions a or b  

a: 86%  
b: 41%  

Grubbs catalyst 10 turned out to give the highest yield in the ring-closing metathesis of 9. After 6 h in refluxing dichloromethane, this afforded the cyclic N,O-acetal 11 in an almost quantitative yield. The next step would be the addition of a nucleophile to the in situ generated N-phosphoryliminium ion. Allyltrimethylsilane was chosen as the standard silane nucleophile for testing. For these substrates, an excess of the Lewis acid turned out to be 88
higher yielding than a catalytic amount of a metal triflate. In this way, with 3 equiv of both BF$_3$·OEt$_2$ and the nucleophile, olefin 12 was obtained as a single diastereoisomer in 86% yield. In comparison, 2 mol% of Sn(OTf)$_2$ afforded only 41% yield of the same product. Proof for the cis-relationship between the allyl and ester substituent could not be established with 1H NMR experiments, although it was expected that the relative stereochemistry of the product would be cis, similar to the comparable system with the nosyl-protective group (chapter 3).

4.3 Modeling

From the pioneering experiments, it was clear that nucleophilic additions onto $N$-phosphoryliminium ions could be achieved in high yield using silane nucleophiles. This opened up possibilities for the use of a chiral moiety on the phosphorus to induce diastereoselectivity. A BINOL substituted phosphoryl on the nitrogen was thought to be a quick – and not necessarily the best – entry into such a chiral phosphoryl protective group. In order to visualize to a certain extent the influence of the binaphthyl moiety in the transition state conformation, the iminium ion 13 was modeled with MM2 calculations to minimize the energy (fig. 4.1). Thus, one might obtain a better understanding of the conformation of the molecule and the orientation of the binaphthyl moieties.

Figure 4.1 MM2 calculated conformation of the iminium ion 13.

As can be seen from the picture, the six-membered ring is fairly planar, with some distortion. Especially interesting about the minimized configuration is the orientation of one of the naphthyl moieties above the ring. It seems that the chiral binaphthyl moiety is shielding the top face of the iminium ion and therefore might efficiently direct the sense of the nucleophilic attack. Therefore by starting with a rather small cyclic and flat $N,O$-acetal that would give an intermediate iminium ion like 13, the induction during the addition of an incoming nucleophile was expected to be notably.
4.4 Chiral auxiliary induced additions.

First, a saturated cyclic system was studied (scheme 4.2). To synthesize the precursor, racemic 1,1'-bi-2-naphthol was reacted with POCl₃ in the presence of triethylamine at 0 °C. The resulting chloride was treated with aminoacetal 14 in the same pot, to afford the acetal 15 in good yield (63%).

Scheme 4.2 Addition to a saturated five-membered ring system.

This amidophosphat e already cyclized in a quantitative manner upon stirring in chloroform, to give acetal 16 as a 75:25 mixture of diastereoisomers. This ratio also reflects that there is an influence of the chiral auxiliary on the environment of the iminium ion.

With this precursor in hand, the addition of allyltrimethylsilane was studied. By applying BF₃·OEt₂ as the Lewis acid, addition took place in two hours and afforded 17 in 74% yield after isolation. Unfortunately, ³¹P NMR showed a 64:36 mixture of diastereoisomers, which meant even a worsening of the diastereoisomeric ratio compared to 16. Shifting to catalytic Sn(OTf)₂ as the Lewis acid did not improve the ratio and yield (60:40, 52% isolated yield). TFA was used as a protic acid, but this led again to a 64:36 mixture of diastereoisomers in 56% yield.

Nevertheless, the same type of addition was also attempted on unsaturated systems. The unsaturated nitrogen heterocycles were easily available through amidopalladation with benzyl propadienyl ether and the corresponding amidophosphates (scheme 4.3). Again, a one-pot reaction between BINOL, POCl₃ and the unsaturated amines 18 and 19 gave the desired olefinic amidophosphates 20 and 21 in 85 and 89% yield, respectively. The amidopalladation also proceeded in high yields and afforded the ring-closing metathesis precursors 22 and 23 in 89 and 70% yield.
**Scheme 4.3** Synthesis of the cyclic, unsaturated amidophosphate N,O-acetals.

Metathesis using the second-generation Grubbs catalyst provided the unsaturated cyclic N,O-acetals 24 and 25 in 63 and 86% yield. Compound 25 was obtained as a 78:22 mixture of diastereoisomers. Unfortunately, already upon isolation, compound 24 showed decomposition to the pyrrole caused by the facile loss of benzyl alcohol (eq. 4.2).

Because of this, no analytical data of pure 24 could be obtained. Attempts to use 24 in Lewis acid induced additions were therefore not performed. The same phenomenon was observed in the previous chapter for the analogous sulfonamide five-membered ring. The cyclic olefin 25 contained an impurity (up to 15%), which turned out to be inseparable from the desired product using column chromatography.
Addition to the six-membered ring precursor 25 with allyltrimethylsilane proceeded successfully in terms of yield. Standard conditions in dichloromethane at −78 °C afforded the product 27 in 67% isolated yield (eq. 4.3). The most important observation though, was the low diastereoisomeric ratio of 66:34. This ratio was comparable with the additions to the saturated five-membered cycles. Changing the solvent to a more polar and therefore more stabilizing environment (e.g. MeCN) did not influence this ratio.

4.5 Conclusions

It has been shown that the amidopalladation of amidophosphates can be constructively used to synthesize interesting phosphoryl substituted cyclic N,O-acetals. In case of a cyclic unsaturated amino acid, the addition of a nucleophile onto the N-phosphoryliminium ion occurred with complete diastereoselectivity. This indicates that the phosphoryl moiety provides a similar directing behavior as the sulfonyl moiety, although the relative stereochemical outcome could not be established thus far. Furthermore, attempts were made to perform chiral auxiliary induced diastereoselective additions onto N-phosphoryliminium ions, where the chiral induction comes from a chiral moiety on the phosphorus. Despite the somewhat disappointing diastereoselectivity, the method nevertheless represents high yielding additions to N-phosphoryliminium ions. The investigations presented here may therefore well be considered as a starting point for further research.

4.6 Acknowledgements

T. Marcelli is thanked for the initial experiments on the saturated five-membered ring system.

4.7 Experimental section

General remarks, see chapter 2. 4-Aminobutyraldehyde diethyl acetal is commercially available. 3-Butenylamine should be freshly made following the literature procedure. For the compounds 8 and 9, see chapter 2. For diastereoisomerically pure compounds, the carbon-phosphorus coupling constant is given in the $^{13}$C NMR spectra. Otherwise, a listing of all visible lines is given.

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\text{6-Benzyloxy-1-\{(diphenoxyphosphoryl)-1,2,3,6-tetrahydropyridine-2-carboxylic acid methyl ester (11). To a degassed solution of diolefin 9 (0.38 g, 0.749 mmol) in dichloromethane (25 mL) was added catalyst 10 (12 mg, 2 mol%). The solution was refluxed for 6 h and concentrated. The crude oil was purified by column chromatography (pentane/diethyl ether 1:1) to afford 11 and a white solid (~1:1 mixture of...}
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diastereoisomers). Yield 0.349 g (0.73 mmol, 97%). Rf 0.20 (pentane/diethyl ether 1:1); Mp. 72.2-84.5 °C. IR (CHCl3) ν 1026, 1131, 1278, 1491, 1592, 1742, 3045 cm⁻¹; ¹H NMR (400 MHz, CDCl3) both diastereoisomers δ 7.36-7.01 (m, 15H), 6.00-5.93 (m, 1H), 5.85 (d, J = 10.1 Hz, 1H), 5.55-5.49, 5.44-5.41 and 5.32-5.31 (m, 1H), 4.82 (d, J = 11.6 Hz, 0.3H), 4.68-4.53 (m, 2.4H), 4.50-4.41 (m, 0.3H), 3.74 and 3.48 (s, 3H), 2.77-2.62 (m, 1H), 2.38-2.25 (m, 1H); ¹³C NMR (500 MHz, CDCl3) both diastereoisomers δ 171.3, 171.2, 150.7, 150.6, 137.8, 137.5, 129.6, 129.4, 129.3, 128.2, 128.0, 127.8, 127.5, 127.3, 127.2, 127.1, 126.6, 125.6, 125.5, 125.0, 124.9, 124.8, 124.2, 124.1, 120.4, 120.3, 120.2, 120.1, 120.0, 119.9, 119.7, 119.6, 81.6, 81.5, 78.9, 78.6, 69.1, 69.0, 52.5, 52.1, 52.0, 49.8, 49.8, 27.0, 24.0; HRMS (FAB) calcd. for C₂₆H₂₇NO₆P (MH⁺) 480.1576, found 480.1563; Anal. calcd. for C₂₆H₂₇NO₆P: C, 65.13; H, 5.47; N, 2.92; found C, 65.06; H, 5.42; N, 2.85.

6-Allyl-1-(diphenoxyphosphoryl)-1,2,3,6-tetrahydropyridine-2-carboxylic acid methyl ester (12). A solution of N,O-acetal 11 (100 mg, 0.209 mmol) and allyltrimethylsilane (100 μL, 0.63 mmol) in dichloromethane (10 mL) was cooled to -78 °C. BF₃·OEt₂ (80 μL, 0.63 mmol) was added and the solution was stirred while the temperature was allowed to rise slowly to room temperature. After 16 h, H₂O (20 mL) was added, the layers were separated and the aqueous layer was extracted with diethyl ether (2 × 15 mL). The combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated. Column chromatography (pentane/diethyl ether 2:1-0:1) afforded 12 as a colorless oil and as a single isomer. Yield 74 mg (0.179 mmol, 86%). IR (CHCl3) ν 1026, 1135, 1191, 1272, 1491, 1592, 1738, 2953 cm⁻¹; ¹H NMR (400 MHz, CDCl3) 8 7.39-7.32 (m, 8H), 7.29-7.23 (m, 2H), 7.21-7.17 (m, 2H), 5.86-5.80 (m, 3H), 5.12-5.08 (m, 2H), 4.74-4.70 (m, 1H), 4.17-4.16 (m, 1H), 3.67 (s, 3H), 2.65-2.58 (m, 2H), 2.25-2.21 (m, 1H), 2.13-2.10 (m, 1H); ¹³C NMR (500 MHz, CDCl3) 8 172.6, 172.5, 151.1, 151.0, 150.5, 150.5, 134.9, 129.6, 129.5, 126.2, 126.1, 125.0, 124.8, 123.1, 120.4, 120.3, 119.9, 119.9, 117.6, 52.1, 52.1, 40.6, 24.8, 24.8; ³¹P NMR (500 MHz, CDCl3) δ 0.5; HRMS (FAB) calcd. for C₂₂H₂₅NO₅P (MH⁺) 414.1470, found 414.1461.

O,O′-(1,1′Dinaphthyl-2,2′-diyl)-1-(2-ethoxypyrrolidino) phosphat e (16). Similar to the synthesis of 20, BINOL (100 mg, 0.35 mmol) was treated with POCl₃ and 4-aminobutyraldehyde diethyl acetal. Column chromatography (pentane/ethyl acetate 1:1-0:1) afforded the product as a white foam. Yield 0.1072 g (0.22 mmol, 63%). Rf 0.38 (ethyl acetate). ¹H NMR (CDCl3) already showed partial cyclization and therefore the product was dissolved in CHCl₃ and stirred for 6 h. The solvent was evaporated to afford pure 16 (94 mg (0.21 mmol, 96%) as a 75:25 mixture of diastereoisomers. IR (CHCl₃) ν 967, 1060, 1210, 1282, 1465, 1509, 1592, 2979 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) both diastereoisomers: δ 8.06-7.95 (m, 4H), 7.66-7.28 (m, 8H), 5.35 and 5.31 (s, 1H), 4.00-4.93 and 3.53-3.50 (m, 1H), 3.70-3.64 (m, 1H), 3.17-3.15 and 2.96-2.93 (m, 1H), 2.82-2.80 and 2.63-2.61 (m, 1H), 2.03-1.72 (m, 4H), 1.32 and 1.13 (t, J = 7.1 Hz, 3H); ¹³C NMR (500 MHz, CDCl₃) both diastereoisomers: δ 148.4, 148.3, 147.7, 147.6, 146.8, 146.7, 146.6, 146.5, 132.3, 132.2, 131.7, 131.6, 131.3, 131.2, 131.1, 130.9, 130.8, 130.7, 130.6, 128.4, 128.3, 127.2, 127.1, 126.9, 126.7, 126.5, 125.6, 125.5, 125.1, 121.6, 121.3, 121.2, 121.1, 120.1, 120.0, 120.6, 90.7, 89.9, 89.8, 63.3, 63.0, 47.2, 46.5, 33.7, 33.6, 33.2, 33.1, 23.7, 23.6, 23.2, 23.1, 15.2, 15.1; ³¹P NMR (500 MHz, CDCl₃) both diastereoisomers: δ 12.2 (major) and 11.8 (minor).
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**O,O'-(1,1'Dinaphthyl-2,2'-diyl)-1-(2-allylpyrrolidido) phosphate (17).**

Analogous to the procedure for 12, 16 (31 mg, 0.07 mmol) was reacted with allyltrimethylsilane. Column chromatography (pentane/ethyl acetate 2:1-0:1) afforded the product as a white solid (64:36 mixture of diastereoisomers). Yield 23 mg (0.052 mmol, 74%). Rf 0.33 and 0.25 (pentane/ethyl acetate 1:1); Mp. 197.1-198.7 °C. IR (CHCl₃) ν 966, 1073, 1216, 1282, 2977 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) δ 8.06-7.95 (m, 4H), 7.65-7.51 (m, 4H), 7.54-7.43 (m, 4H), 7.35-7.27 (m, 3H), 5.83-5.71 (m, 1H), 5.13-5.00 (m, 2H), 4.07-4.03 (m, 0.6H), 3.93-3.89 (m, 0.4H), 3.07-3.02 (m, 1H), 2.75-2.63 (m, 1H), 2.56-2.52 (m, 0.6H), 2.33-2.27 (m, 0.4H), 1.97-1.86 and 1.78-1.66 (m, 4H); ¹³C NMR (500 MHz, CDCl₃) both diastereoisomers: δ 148.3, 148.2, 148.0, 147.9, 134.9, 134.8, 132.4, 132.3, 131.7, 131.6, 131.3, 131.2, 131.1, 130.6, 128.4, 128.3, 127.2, 126.9, 126.7, 126.5, 125.6, 125.5, 125.4, 121.7, 121.3, 121.2, 121.1, 120.9, 120.8, 117.5, 117.3, 59.5, 59.0, 58.9, 48.1, 40.8, 40.1, 30.4, 30.3, 30.2, 30.1, 25.2, 25.1, 24.8, 24.7; ³¹P NMR (500 MHz, CDCl₃) both diastereoisomers: δ 12.7 (minor) and 12.4 (major); HRMS (FAB) calcd. for C₂₇H₂₄NO₃P: C, 73.46; H, 5.48; N, 3.17, found C, 73.32; H, 5.39; N, 3.11.

**O,O'-(1,1'Dinaphthyl-2,2'-diyl)-N-allylamidophosphat e (20).**

To an iced cold solution of BINOL (200 mg, 0.7 mmol) in dichloromethane (20 mL) was added POCl₃ (66 μL, 0.7 mmol), followed by the addition of Et₃N (0.5 mL, 3.5 mmol). After 0.5 hour allylamine (55 μL, 0.7 mmol) was added and stirring continued for 1 hour at 0 °C, followed by stirring at room temperature for 16 h. H₂O (25 mL) was added and the layers separated. The aqueous layer was extracted with EtOAc (2 x 30 mL) and the combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated. Column chromatography (diethyl ether) afforded the product as a white solid. Yield 1.30 4 g (3.37 mmol, 85%). Rf 0.16 (diethyl ether); IR (CHCl₃) ν 967, 1072, 1229, 1279, 1421, 1465, 1509, 1592, 1731, 3062, 3413 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.02 (d, J = 8.8 Hz, 2H), 8.01 (d, J = 8.8 Hz, 2H), 7.53-7.41 (m, 1H), 7.50 (d, J = 8.8 Hz, 1H), 7.45-7.39 (m, 1H), 7.36-7.26 (m, 3H), 5.87-5.77 (m, 1H), 5.20 (d, J = 17.0 Hz, 1H), 5.10 (d, J = 10.2 Hz, 1H), 3.54-3.45 (m, 2H), 3.23-3.17 (m, NH); ¹³C NMR (400 MHz, CDCl₃) δ 147.3 (d, J = 10.7 Hz, C), 146.4 (d, J = 8.9 Hz, C), 135.2 (d, J = 5.7 Hz, CH), 131.2 (d, J = 1.1 Hz, C), 132.0 (d, J = 1.0 Hz, C), 131.6 (d, J = 1.2 Hz, C), 131.3 (d, J = 1.2 Hz, CH), 130.9 (d, J = 23.6 Hz, CH), 128.3 (d, J = 5.1 Hz, CH), 126.9 (d, J = 20.9 Hz, CH), 126.6 (d, J = 15.3 Hz, CH), 125.5 (d, J = 11.1 Hz, CH), 121.5 (d, J = 2.3 Hz, C), 121.1 (d, J = 2.4 Hz, C), 120.9 (d, J = 2.6 Hz, CH), 120.6 (d, J = 3.0 Hz, CH), 115.8, 44.2; HRMS (FAB) calcd. for C₂₃H₁₉NO₃P: C, 73.46; H, 5.48; N, 3.17, found C, 73.32; H, 5.39; N, 3.11.

**O,O'-(1,1'Dinaphthyl-2,2'-diyl)-N-but-3-enylamido phosphate (21).**

BINOL (1.14 g, 3.98 mmol) was treated with POCl₃ and 3-butenylamine similar as for 20. Column chromatography (diethyl ether) afforded the product as a white foam. Yield 1.427 g (3.56 mmol, 89%). Rf 0.24 (diethyl ether); IR (CHCl₃) ν 817, 873, 967, 1072, 1103, 1229, 1327, 1362, 1413, 1465, 1508, 1591, 1731, 2943, 3063, 3408 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.03-7.96 (m, 2H), 7.91-7.89 (m, 2H), 7.61 (d, J = 8.8 Hz, 1H), 7.50 (d, J = 8.8 Hz, 1H), 7.45-7.39 (m, 3H), 7.33 (d, J = 8.5 Hz, 1H), 7.27-7.19 (m, 2H), 5.70-5.59 (m, 1H), 5.05-5.00 (m, 1H), 3.60-3.53 (m, NH), 2.98-2.86 (m, 2H), 2.21-2.16 (m, 2H); ¹³C NMR (400 MHz, CDCl₃) δ 94.
O,O'-(1,1'Dinaphthyl-2,2'-diyl)-N-(1-benzyloxyallyl)-N-allylamido phosphate (22). To a solution of 20 (1.345 g, 3.47 mmol) and Et₃N (0.725 mL, 5.2 mmol) in MeCN (25 mL) was added Pd(OAc)₂ (39 mg, 0.173 mmol, 5 mol%) and dppp (72 mg, 0.173 mmol) and benzyl propadieny ether (0.535 g, 3.655 mmol). The resulting solution was heated at 60 °C for 16 hours and the solvent was removed in vacuo. The crude oil was purified by column chromatography (diethyl ether) to afford 22 as a colorless oil (~1:1 mixture of diastereoisomers). Yield 1.635 g (3.064 mmol, 89%). Rₜ 0.61 (ethyl acetate).

IR (CHCl₃) ν 967, 1071, 1229, 1272, 1465, 1509, 1592, 1731, 3067 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.07 (d, J = 8.9 Hz, 1H), 7.95-7.91 (m, 1H), 7.81-7.15 (m, 12H), 6.08-6.01 (m, 0.5H), 5.86-5.82 (m, 1H), 5.71-5.29 (m, 3.5H), 4.95-4.87 (m, 2H), 4.75-4.62 (m, 2H), 3.33-3.04 (m, 1.5H), 2.80-2.77 (m, 0.5H), 2.59-2.32 (m, 2H); ¹³C NMR (400 MHz, CDCl₃) δ 148.2, 148.1, 148.0, 147.9, 147.8, 146.4, 146.3, 146.2, 137.9, 137.8, 137.5, 135.6, 135.5, 135.2, 135.1, 134.9, 134.8, 132.3, 132.2, 132.1, 131.7, 131.2, 130.7, 130.6, 128.3, 128.2, 128.1, 127.6, 127.5, 127.4, 127.3, 127.2, 127.1, 126.8, 126.7, 126.6, 126.5, 125.6, 125.5, 121.2, 121.4, 121.1, 121.0, 120.9, 120.8, 120.7, 118.9, 118.6, 118.3, 116.8, 116.4, 86.4, 86.3, 86.0, 85.9, 69.1, 67.0, 45.7, 45.0; HRMS (FAB) calcd. for C₃₃H₂₉NO₄P (MH⁺) 534.1834, found 534.1841.

O,O'-(1,1'Dinaphthyl-2,2'-diyl)-N-(1-benzyloxyallyl)-N-but-3-enylamido phosphate (23). Amidophosphate 21 (1.343 g, 3.35 mmol) was treated with benzyl propadieny ether identical to the procedure for 22. Column chromatography (pentane/diethyl ether 2:1-0:1) afforded diolefin 23 as a colorless oil (~1:1 mixture of diastereoisomers). Yield 1.27 g (2.32 mmol, 70%). Rₜ 0.56 (diethyl ether). ¹H NMR (400 MHz, CDCl₃) δ 8.03 (d, J = 8.5 Hz, 1H), 7.95-7.91 (m, 1H), 7.88 (d, J = 7.8 Hz, 2H), 7.81-7.73 (m, 1H), 7.54-7.15 (m, 12H), 6.08-6.01 (m, 0.5H), 5.86-5.82 (m, 1H), 5.71-5.29 (m, 3.5H), 4.95-4.87 (m, 2H), 4.75-4.62 (m, 2H), 3.33-3.04 (m, 1.5H), 2.80-2.77 (m, 0.5H), 2.59-2.32 (m, 2H); ¹³C NMR (400 MHz, CDCl₃) δ 148.2, 148.1, 148.0, 147.9, 146.5, 146.4, 137.9, 137.5, 135.6, 135.5, 135.2, 135.1, 134.9, 134.8, 132.2, 132.1, 131.7, 131.2, 130.7, 130.6, 128.3, 128.2, 128.1, 127.6, 127.5, 127.4, 127.3, 127.2, 127.1, 126.8, 126.7, 126.6, 126.5, 125.6, 125.5, 121.2, 121.4, 121.1, 121.0, 120.9, 120.8, 120.7, 118.9, 118.6, 118.3, 116.8, 116.4, 86.4, 86.3, 86.0, 85.9, 69.1, 67.0, 45.7, 45.0; HRMS (FAB) calcd. for C₃₄H₃₁NO₄P (MH⁺) 548.1991, found 548.1996.

O,O'-(1,1'Dinaphthyl-2,2'-diyl)-1-(2-benzyloxy-2,5-dihydro-1H-pyrrole) phosphate (24) and O,O'-(1,1'Dinaphthyl-2,2'-diyl)-1H-pyrrole phosphate (26) Diolefin 22 (1.391 g, 2.607 mmol) was subjected to the same conditions as for 11. Column chromatography (pentane/diethyl ether 1:1- pentane/ethyl acetate 1:1) afforded 24 as a foam. Yield 0.826 g (1.633 mmol, 63%). Rₜ 0.39 (ethyl acetate).
Upon isolation the compound already degraded to give the pyrrole 26. R f 0.59 (ethyl acetate). Some data of 26: IR (CHCl₃) ν 972, 1070, 1210, 1308 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ 8.10 (d, J = 8.9 Hz, 1H), 8.00-7.92 (m, 3H), 7.67 (d, J = 8.9 Hz, 1H), 7.56-7.51 (m, 2H), 7.45 (d, J = 8.5 Hz, 1H), 7.39-7.28 (m, 8H), 7.09 (d, J = 8.9 Hz, 1H), 6.74 (q, J = 1.9 Hz, 2H), 6.26-6.24 (m, 2H).

**O,O′-(1,1′Dinaphthyl-2,2′-diyl)-1-(6-benzyloxy-1,2,3,6-tetrahydropyridine) phosphate (25).** Diolein 23 (1.247 g, 2.28 mmol) was subjected to the same conditions as for 11. Column chromatography (pentane/diethyl ether 2:1-0:1) afforded 25 as a foam (78:22 mixture of diastereoisomers). Yield 1.012 g (1.95 mmol, 86% including the inseparable impurity). R f 0.34 & 0.27 (diethyl ether).

¹H NMR (400 MHz, CDCl₃) major diastereoisomer: δ 8.14-8.11 (m, 1H), 8.09-8.01 (m, 3H), 7.76 (d, J = 8.8 Hz, 1H), 7.60-7.24 (m, 12H), 6.08-6.02 (m, 1H), 5.86-5.83 (m, 1H), 5.37-5.34 (m, 1H), 5.14 (d, J = 12.0 Hz, 1H), 4.89 (d, J = 12.0 Hz, 1H), 3.26-3.21 (m, 1H), 3.05-2.99 (m, 1H), 2.32-2.27 (m, 1H), 1.84-1.78 (m, 1H); ¹³C NMR (500 MHz, CDCl₃) δ 147.89 (d, J = 11 Hz, C), 146.4 (d, J = 8.9 Hz, C), 137.9, 137.6, 132.0, 131.6, 131.3, 131.2, 131.1, 130.8, 130.5, 128.9, 128.8, 128.3 (3x), 128.2, 128.2, 128.1, 128.0, 127.8, 127.7, 127.5, 127.4, 127.3, 127.1, 127.0, 126.7, 126.6, 125.6, 125.5, 125.3, 121.1, 121.1, 120.9, 120.7, 79.3, 79.2, 69.8, 69.7, 69.3, 69.2, 37.7, 24.4; ³¹P NMR (500 MHz, CDCl₃) both diastereoisomers: δ 12.7 (major), 12.5 (minor); HRMS (FAB) calcd. for C₃₂H₂₇NO₄P (MH⁺) 520.1678, found 520.1684.

**O,O′-(1,1′Dinaphthyl-2,2′-diyl)-1-(6-allyl-1,2,3,6-tetrahydropyridine) phosphate (27).** A solution of 25 (55 mg, 0.106 mmol) and allyltrimethylsilane (68 µL, 0.42 mmol) in dichloromethane (10 mL) was cooled to −78 °C and BF₃·OEt₂ (53 µL, 0.42 mmol) was added. The resulting mixture was allowed to warm slowly to room temperature in 2 h, after which H₂O (25 mL) was added. The product was extracted with diethyl ether (3 × 15 mL) and the combined organic layers were washed with brine, dried over Na₂SO₄ and concentrated. Column chromatography (pentane/diethyl ether 2:1-0:1) afforded 27 as a solidifying oil (66:34 mixture of diastereoisomers). Yield 32 mg (0.071 mmol, 67%). R f 0.46 (diethyl ether). Mp. 197.6-200.8 °C. IR (CHCl₃) ν 962, 1214, 1231, 1268, 2931 cm⁻¹; ¹H NMR (500 MHz, CDCl₃) both diastereoisomers: δ 8.06-7.95 (m, 4H), 7.63 (d, J = 8.8 Hz, 1H), 7.54-7.26 (m, 7H), 5.94-5.82 (m, 2H), 5.79-5.76 and 5.64-5.61 (m, 1H), 5.20-5.08 (m, 2H), 4.19 and 4.02 (br s, 1H), 3.10-3.00 and 2.88-2.84 (m, 2H), 2.55-2.43 (m, 2H), 2.25-2.24 and 2.11-2.04 (m, 1H), 2.00-1.95 and 1.76-1.72 (m, 1H); ¹³C NMR (400 MHz, CDCl₃) both diastereoisomers: δ 148.3, 148.3, 146.8, 146.7, 134.7, 134.4, 132.4, 132.3, 132.2, 131.8, 131.7, 131.3, 131.2, 131.1, 130.6, 130.5, 128.5, 128.4, 128.1, 127.2, 127.3, 127.2, 126.9, 126.6, 126.5, 125.6, 125.3, 125.0, 121.3, 121.2, 121.1, 120.9, 120.7, 120.6, 117.6, 117.5, 52.5, 52.2, 39.9, 39.7, 38.4, 38.0, 24.9, 24.8; ³¹P NMR (500 MHz, CDCl₃) both diastereoisomers: δ 13.4 (minor), 12.8 (major); HRMS (FAB) calcd. for C₂₈H₂₅NO₃P (MH⁺) 454.1572, found 454.1550; Anal. calcd. for C₂₈H₂₄NO₃P: C, 74.16; H, 5.33; N, 3.09; found C, 74.22; H, 5.30; N, 2.96.
4.8 References and notes
