## One-Pot Synthesis of α-Amino Phosphonates from Aldehydes Using Lanthanide Triflate as a Catalyst

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## Introduction

In the recent years the synthesis of  $\alpha$ -amino phosphonates has received an increasing amount of attention because they are considered to be structural analogues of the corresponding  $\alpha$ -amino acids and transition state mimics of peptide hydrolysis. In these connections, the utilities of  $\alpha$ -amino phosphonates as peptide mimics,<sup>1</sup> haptens of catalytic antibodies,<sup>2</sup> enzyme inhibitors,<sup>3</sup> and antibiotics and pharmacologic agents<sup>4</sup> are well documented. A variety of synthetic approaches to  $\alpha$ -amino phosphonates are available.<sup>5</sup> Of the methods, the nucleophilic addition reaction of phosphites with imines is one of the most convenient methods, which is usually promoted by an alkali metal alkoxide or an acid.<sup>6</sup> NaOEt has been mainly used for this purpose since the pioneering work of Pudovik<sup>7</sup> and Lewis acids such as SnCl<sub>2</sub>, SnCl<sub>4</sub>, and BF<sub>3</sub>·Et<sub>2</sub>O have also been found to be effective.<sup>8</sup> However, the reaction using these reagents and catalysts resulted in unsatisfactory yields of  $\alpha$ -amino phosphonates. Although later work by Zon demonstrated that the reaction can be strongly promoted by ZnCl<sub>2</sub> or MgBr<sub>2</sub> in high yields,<sup>9</sup> it cannot proceed a one-pot reaction from aldehydes and has to start from imines because the amines and water that exist during imine formation can decompose or deactivate the Lewis acids.

Recently, it was reported that the imines were effectively activated by rare earth metal triflates such as ytterbium triflate (Yb(OTf)<sub>3</sub>) and scandium triflate (Sc- $(OTf)_3)$ .<sup>10</sup> These triflates are stable in water and can be recovered after the reaction are completed and reused.<sup>11</sup> Moreover, they have been used for the activation of nitrogen-containing compounds, which deactivate most Lewis acids. Judging from these unique properties of lanthanide triflates, we planned to use them as a catalyst in the reaction of diethyl phosphite with imines in order to overcome the drawbacks described above.

## **Results and Discussions**

First, benzylideneaniline was treated with diethyl phosphite in the presence of 10 mol %  $Yb(OTf)_3$  in dichloromethane at room temperature. The reaction proceeded smoothly to afford the corresponding  $\alpha$ -amino phosphonate in excellent yield (93%), which showed that  $Yb(OTf)_3$  effectively catalyzes the reaction indeed. However, to our knowledge, many imines are hygroscopic, unstable at high temperature, and difficult to purify by distillation or column chromatography. Thus it is desirable from a synthetic point of view that imines, generated in situ from aldehydes and amines, immediately react with phosphites and afford  $\alpha$ -amino phosphonates in one-pot way.

It was found that the reaction of benzaldehyde, benzylamine, and diethyl phosphite took place smoothly in the presence of 10 mol % Ln(OTf)<sub>3</sub> and 4 Å molecular Sieves or MgSO<sub>4</sub>. Among the lanthanide(III) triflates screened, ytterbium(III) triflate (Yb(OTf)<sub>3</sub>) showed superior catalytic activity, while the yield of the adduct was lower in the presence of lanthanum(III) triflate (La-(OTf)<sub>3</sub>). On the other hand, the reaction proceeded sluggishly in the presence of MgSO<sub>4</sub> without any catalyst, and only a trace amount of product was produced after 12 h. Effect of solvents on the yields of  $\alpha$ -amino phosphonates in the model reaction under the influence of a catalyst amount of Yb(OTf)<sub>3</sub> (10 mol %) are shown in Table 1. Dichloromethane was the best solvent among those tested, such as acetonitrile (71%), tetrahydronfuran (67%), and toluene (30%), which is consistent with solubilities of Yb(OTf)<sub>3</sub> in those solvents. It is worth mentioning that the yield of the  $\alpha$ -amino phosphonate was only 68% when promoted by 120 mol % SnCl<sub>4</sub>, but was improved to 89% in the presence of 10 mol % Yb-(OTf)<sub>3</sub> in dichloromethane.

The reaction of several aldehydes, amines, and diethyl phosphite were examined in the presence of a catalytic amount (10 mol %) of  $Yb(OTf)_3$  and  $MgSO_4$  in dichloromethane, and the results are summarized in Table 2. In all cases, the three-component reaction proceeded smoothly to afford the corresponding  $\alpha$ -amino phospho-

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 Table 1. Effect of Catalysts and Solvents on the

 Reaction of Benzaldehyde, Benzylamine, and Diethyl

 Phosphite

	HOP(OFt)	activator	PhCHNHCH <sub>2</sub> Ph
		MgSO <sub>4</sub> , rt	O=P(OEt)
		CH <sub>2</sub> Cl <sub>2</sub>	4a

entry	solvent	catalyst (10 mol %)	additive	yield (%) <sup>c</sup>
1	$CH_2Cl_2$	None	MgSO <sub>4</sub>	trace
2	$CH_2Cl_2$	La(OTf) <sub>3</sub>	MgSO <sub>4</sub>	34
3	$CH_2Cl_2$	Sm(OTf) <sub>3</sub>	MgSO <sub>4</sub>	56
4	$CH_2Cl_2$	Yb(OTf) <sub>3</sub>	MgSO <sub>4</sub>	89
5	$CH_2Cl_2$	Yb(OTf) <sub>3</sub>	4 Å mol sieves	87
6	THF	Yb(OTf) <sub>3</sub>	MgSO <sub>4</sub>	67
7	CH <sub>3</sub> CN	Yb(OTf) <sub>3</sub>	MgSO <sub>4</sub>	71
8	toluene	Yb(OTf) <sub>3</sub>	MgSO <sub>4</sub>	30
9	$CH_2Cl_2$	SnCl <sub>4</sub> <sup>a</sup>	MgSO <sub>4</sub>	21
10	$CH_2Cl_2$	SnCl <sub>4</sub> <sup>b</sup>	MgSO <sub>4</sub>	68
			-	

 $^a$  Condition: SnCl4 (100 mol %).  $^b$  Condition: SnCl4 (120 mol %).  $^c$  Isolated yield.

 
 Table 2. One-Pot Synthesis of α-Amino Phosphonates from Aldehydes Catalyzed by Yb(OTf)<sub>3</sub>

VI. (0)

RCHO	+ R'CH2NH2 +	HOP(OEt)2	Maso	RCHP(O)(OEt)2NHR'
1	2	3	10 mol%. rt	4

entry	RCHO	R'NH <sub>2</sub>	product	yield (%) <sup>a</sup>
1	benzaldehyde	benzylamine	4 a	89
2	<i>p</i> -anisaldehyde	aniline	4 b	92
3	<i>p</i> -tolualdehyde	aniline	<b>4</b> c	88
4	<i>p</i> -nitrobenzaldehyde	aniline	4 d	93
5	2-furaldehyde	aniline	<b>4</b> e	85
6	cyclohexanecarboxaldehyde	aniline	4 f	71
7	benzaldehyde	<i>n</i> -propylamine	4 g	65
8	benzaldehyde	aniline	4 h	89
9	trans-cinnamaldehyde	aniline	4 i	79
10	C <sub>9</sub> H <sub>19</sub> CHO	benzylamine	4 j	62

<sup>a</sup> Isolated yield.

nates. Aromatic aldehydes provided excellent yields of products, and aliphatic aldehydes afforded phosphonates in moderate yields, which is expected in that aromatic aldehydes have higher reactivity than aliphatic aldehydes. Another important feature of this reaction is that the catalyst can be easily recovered from the aqueous layer after the reaction is completed and can be reused with no loss of yield (see, the following experimental procedure).

Finally, asymmetric reactions using a chiral amine were examined. According to our method a catalytic amount of ytterbium triflate (10 mol %) and anhydrous MgSO<sub>4</sub> were treated at room temperature with an aldehyde and a chiral amine, followed by addition of a dialkyl phosphite. The commercially available (S)-1methoxy-2-phenylethylamine (5a), (S)- $\alpha$ -methylbenzylamine (5b), (S)-1-methoxy-3-methyl-2-butylamine (5c), were chosen as chiral auxiliaries. The diastereoselectivities of the reactions were determined by <sup>31</sup>P-NMR and are listed in Table 3. For benzaldehyde (entry 1 in Table 3), the <sup>31</sup>P-NMR of product showed two resonances at  $\delta$ 24.91 and  $\delta$  24.37 with the integral ratio of 78:22, leading to the % de of 56. The best results were achieved using (S)-1-methoxy-2-phenylethylamine (**5a**), while (S)- $\alpha$ methylbenzylamine (5b) gave low diastereoisomeric excess. To explain the results obtained in the reaction, we suggest the model A transition state in which Yb(OTf)<sub>3</sub> is chelated by the nitrogen and the methoxy group. For chiral amine **5a** and **5c**, it was perhaps that chelate and rigid transition state A existed in the procedure of the reaction, which worked to enhance the diastereoisomeric excess; in sharp contrast, such a transition state A could



not be formed in the case of chiral amine (**5b**), which resulted in the low diastereoisomeric excess.

In summary, lanthanide triflates were found to be efficient catalysts both in the reaction of imines with diethyl phosphite and in one-pot reaction of aldehydes, amines, and phosphite to afford  $\alpha$ -amino phosphonates in good to excellent yields under the mild conditions. Further application of these reactions to asymmetric synthesis is now in progress.

## **Experimental Section**

**General**. CH<sub>2</sub>Cl<sub>2</sub> was distilled from P<sub>2</sub>O<sub>5</sub> under Ar. <sup>1</sup>H NMR spectra were recorded at 300 MHz in CDCl<sub>3</sub> using TMS as internal reference. <sup>31</sup>P NMR (121.4 MHz) was taken in CDCl<sub>3</sub> using 85% H<sub>3</sub>PO<sub>4</sub> as an external standard with broad-band <sup>1</sup>H decoupling. <sup>13</sup>C NMR spectral measurements were performed at 75.4 MHz using CDCl<sub>3</sub> as an internal standard. Benzylideneaniline was prepared from aniline and benzaldehyde.<sup>12</sup> Diethyl phosphite was prepared according to the literature method.<sup>13</sup> Lanthanide(III) triflates were prepared by the reported procedure and dried by heating at 200 °C under reduced pressure prior to use.<sup>14</sup>

The Reaction of Benzylideneaniline with Diethyl Phosphite. Yb(OTf)<sub>3</sub> (0.1 mmol), benzylideneaniline (1 mmol), and diethyl phosphite (1.2 mmol) were mixtured in 5 mL of dichloromethane at 0 °C. After the mixture was stirred for 5 h at room temperature, water was added and the product was extracted with EtOAc. The organic layer was dried with anhydrous Na<sub>2</sub>SO<sub>4</sub> and evaporated to give the crude product. Analytically pure product **4a** was then obtained by column chromatography in 93% yield. α-Amino Phosphate (**4a**). <sup>1</sup>H NMR δ 7.45–7.24 (10 H, m), 4.11–3.53 (7 H, m), 2.95 (1 H, s), 1.27 (3 H, t, J = 7.1 Hz), 1.12 (3 H, t, J = 7.1 Hz), 3<sup>1</sup>P NMR δ 22.9; <sup>13</sup>C NMR δ 146.3 (s, Ph), 136.0 (s, Ph), 130.0 (s, Ph), 129.2 (s, Ph), 128.7 (s, Ph), 128.0 (s, Ph), 118.5 (s, Ph), 114.0 (s, Ph), 77.5 (s, *C*H<sub>2</sub>Ph), 63.4 (s, *OC*H<sub>2</sub>CH<sub>3</sub>), 56.2 (d, CHP, <sup>1</sup> $J_{PC} = 150.8$  Hz), 16.5 (s, *OC*H<sub>2</sub>CH<sub>3</sub>), 16.3 (s, *OC*H<sub>2</sub>CH<sub>3</sub>); HRMS calcd for C<sub>18</sub>H<sub>24</sub>NO<sub>3</sub>P: 333.1494. Found: 333.1483.

A typical experimental procedure is described for one-pot reaction of benzaldehyde, benzylamine, and diethyl phosphite: to a suspension of Yb(OTf)<sub>3</sub> (0.1 mmol) and 4 Å molecular sieves or MgSO<sub>4</sub> (125 mg) in CH<sub>2</sub>Cl<sub>2</sub> (4 mL) were added an aldehyde (1 mmol) in CH<sub>2</sub>Cl<sub>2</sub> (0.5 mL) and an amine (1.1 mmol) in CH<sub>2</sub>-Cl<sub>2</sub> (0.5 mL) at room temperature. The mixture was stirred for 0.5 h at room temperature. Then diethyl phosphite (1 mmol) was added to the sample pot. The mixture was further stirred for 15–30 h, and then CH<sub>2</sub>Cl<sub>2</sub> was removed under reduced pressure. Water was added, and the product was extracted with EtOAc. After the organic layer was dried and evaporated, the crude product was chromatographed on silica gel to afford the  $\alpha$ -amino phosphate **4a** (89% yield). Yb(OTf)<sub>3</sub> can be almost

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Table 3. One-Pot Synthesis of Optical Active  $\alpha$ -Amino Phosphates Catalyzed by Ytterbium Triflate



entry	R	R′NH <sub>2</sub> (5)	<b>6</b> : <b>7</b> <sup><i>a</i></sup>	de, %	yield (%) <sup>b</sup>
1	Ph	(S)-1-phenyl-2-methoxyethylamine	<b>6a:7a</b> , 78:22	56	95
2	Ph	$(S)$ - $\alpha$ -methylbenzylamine	6b:7b, 57:43	14	92
3	Ph	(S)-1-methoxyl-3-methyl-2-butylamine	6c:7c, 74:26	48	82
4	$p-CH_3OC_6H_4$	(S)-1-phenyl-2-methoxyethylamine	6d:7d, 78:22	56	91
5	p-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	(S)-α-methylbenzylamine	6e:7e, 57:43	14	88
6	p-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub>	(S)-1-methoxyl-3-methyl-2-butylamine	6f:7f, 74:26	48	81

<sup>a</sup> The ratio was determined by <sup>31</sup>P NMR. <sup>b</sup> Isolated yields based on aldehydes.

quantitatively recovered from the aqueous layer and can be reused (2nd use, 86% yield).

α-**Amino Phosphate (4b).** <sup>1</sup>H NMR δ 7.40–6.58 (9H, m), 4.71 (1 H, d, <sup>1</sup>J<sub>PH</sub> = 23.8 Hz), 4.14–3.66 (4 H, m), 3.77 (3 H, s), 1.28 (3 H, t, J = 7.0 Hz), 1.14 (3 H, t, J = 7.1 Hz); <sup>31</sup>P NMR δ 23.5; <sup>13</sup>C NMR δ 159.3 (s, Ph), 146.5 (s, Ph), 132.6 (s, Ph), 129.0 (s, Ph), 127.7 (s, Ph), 125.1 (s, Ph), 120.3 (s, Ph), 118.2 (s, Ph), 114.1 (s, Ph), 63.3 (s, OCH<sub>2</sub>CH<sub>3</sub>), 55.4 (d, CHP, <sup>1</sup>J<sub>PC</sub> = 150.8 Hz), 55.6 (s, OMe), 16.4 (s, OCH<sub>2</sub>CH<sub>3</sub>), 16.3 (s, OCH<sub>2</sub>CH<sub>3</sub>); HRMS calcd for C<sub>18</sub>H<sub>24</sub>NO<sub>4</sub>P: 349.1442. Found: 349.1395.

α-Amino Phosphate (4c). <sup>1</sup>H NMR δ 7.36–6.58 (9H, m), 4.73 (1 H, d, <sup>1</sup>J<sub>PH</sub> = 24.1 Hz), 4.14–3.68 (4 H, m), 2.31 (3 H, s), 1.28 (3 H, t, J = 7.1 Hz), 1.13 (3 H, t, J = 7.1 Hz); <sup>31</sup>P NMR δ 23.5; <sup>13</sup>C NMR δ 146.5 (s, Ph), 146.3 (s, Ph), 137.7 (s, Ph), 132.7 (s, Ph), 129.4 (s, Ph), 127.7 (s, Ph), 118.4 (s, Ph), 113.9 (s, Ph), 63.3 (d, OCH<sub>2</sub>CH<sub>3</sub>, <sup>2</sup>J<sub>PC</sub> = 5.1 Hz), 55.8 (d, CHP, <sup>1</sup>J<sub>PC</sub> = 150.8 Hz), 21.2 (s, Me), 16.5 (d, OCH<sub>2</sub>CH<sub>3</sub>, <sup>3</sup>J<sub>PC</sub> = 4.3 Hz), 16.3 (d, OCH<sub>2</sub>CH<sub>3</sub>, <sup>3</sup>J<sub>PC</sub> = 4.6 Hz); HRMS calcd for C<sub>18</sub>H<sub>24</sub>NO<sub>3</sub>P: 333.1494. Found: 333.1529.

α-**Amino Phosphate (4d).** <sup>1</sup>H NMR δ 6.43–7.50 (9 H, m), 5.3 (1 H, m), 3.65–4.6 (4 H, m), 1.07–1.46 (6 H, m); <sup>31</sup>P NMR δ 21.4; <sup>13</sup>C NMR δ 173.8 (s, Ph), 147.7 (s, Ph), 145.6 (s, Ph), 129.4 (s, Ph), 128.9 (s, Ph), 123.8 (s, Ph), 119.6 (s, Ph), 119.3 (s, Ph), 114.1 (s, Ph), 63.8 (s, OCH<sub>2</sub>CH<sub>3</sub>), 50.4 (d, CHP, <sup>1</sup>J<sub>PC</sub> = 159.2 Hz), 16.6 (s, OCH<sub>2</sub>CH<sub>3</sub>), 16.4 (s, OCH<sub>2</sub>CH<sub>3</sub>); HRMS calcd for  $C_{17}H_{21}N_2O_5P$ : 364.1188. Found: 364.1151.

α-**Amino Phosphate (4e).** <sup>1</sup>H NMR δ 7.39–6.33 (8 H, m), 4.90 (1 H, d, <sup>1</sup>*J*<sub>PH</sub> = 23.4 Hz), 4.21–3.84 (4 H, m), 2.95 (1 H, s), 1.30 (3 H, t, *J* = 7.0 Hz), 1.21 (3 H, t, *J* = 7.0 Hz); <sup>31</sup>P NMR δ 20.8; <sup>13</sup>C NMR δ 149.5 (s, Ph), 146.2 (s, furan), 142.6 (s, furan), 129.3 (s, Ph), 119.1 (s, furan), 114.1 (s, Ph), 110.9 (s, Ph), 108.9 (s, furan), 63.5 (s, OCH<sub>2</sub>CH<sub>3</sub>), 50.4 (d, CHPh, <sup>1</sup>*J*<sub>PC</sub> = 159.2 Hz), 16.4 (s, OCH<sub>2</sub>*C*H<sub>3</sub>), 16.0 (s, OCH<sub>2</sub>*C*H<sub>3</sub>); HRMS calcd for C<sub>15</sub>H<sub>20</sub>NO<sub>4</sub>P: 309.1130. Found: 309.1097.

α-**Amino Phosphate (4f).** <sup>1</sup>H NMR δ 7.19–6.63 (5 H, m), 4.14–3.97 (4 H, m), 3.63 (1 H, dd,  ${}^{1}J_{PH} = 19.0$  Hz, J = 2.1 Hz,), 1.89–1.11 (17 H, m); <sup>31</sup>P NMR δ 26.1; <sup>13</sup>C NMR δ 147.8 (s, Ph), 129.7 (s, Ph), 129.3 (s, Ph), 117.8 (s, Ph), 113.2 (s, Ph), 62.6 (s, OCH<sub>2</sub>CH<sub>3</sub>), 56.1 (d, CHP,  ${}^{1}J_{PC} = 150.8$  Hz), 39.9 (s, hexyl), 31.0 (s, hexyl), 29.7 (s, hexyl), 28.3 (s, hexyl), 27.0 (s, hexyl), 22.0 (s, hexyl), 16.4 (s, OCH<sub>2</sub>CH<sub>3</sub>); HRMS calcd for C<sub>17</sub>H<sub>28</sub>NO<sub>3</sub>P: 325.1807. Found: 325.1835.

α-**Amino Phosphate (4g).** <sup>1</sup>H NMR δ 7.5 (5 H, s), 4.0–4.4 (4 H, m), 3.8–3.95 (3H, m), 2.5–2.8 (2 H, m), 1.1–1.7 (9 H, m); <sup>31</sup>P NMR δ 24.1; <sup>13</sup>C NMR δ 135.7 (s, Ph), 132.7 (s, Ph), 129.5 (s, Ph), 129.0 (s, Ph), 63.1 (d, O*C*H<sub>2</sub>CH<sub>3</sub>, <sup>2</sup>*J*<sub>PC</sub> = 7.2 Hz), 60.9 (d, CHP, <sup>1</sup>*J*<sub>PC</sub> = 152.8 Hz), 48.4 (s, *C*H<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>), 29.7 (s, CH<sub>2</sub>*C*H<sub>2</sub>CH<sub>3</sub>), 16.7 (d, OCH<sub>2</sub>*C*H<sub>3</sub>, <sup>3</sup>*J*<sub>PC</sub> = 5.1 Hz), 16.2 (d, OCH<sub>2</sub>*C*H<sub>3</sub>, <sup>3</sup>*J*<sub>PC</sub> = 5.3 Hz), 11.4 (s, CH<sub>2</sub>CH<sub>2</sub>CH<sub>3</sub>); HRMS calcd for C<sub>14</sub>H<sub>24</sub>NO<sub>3</sub>P: 285.1494. Found: 285.1472.

α-**Amino Phosphate (4h)**.<sup>3</sup> <sup>1</sup>H NMR δ 7.48–6.58 (10 H, m), 4.76 (1 H, d,  ${}^{1}J_{\rm PH} = 24.2$  Hz), 4.14–3.67 (4 H, m), 1.28 (3 H, t, J = 7.1 Hz), 1.11 (3 H, t, J = 7.1 Hz);  ${}^{13}$ C NMR δ 139.0 (s, Ph), 135.5 (s, Ph), 128.8 (s, Ph), 128.7 (s, Ph), 128.5 (s, Ph), 128.4 (s, Ph), 128.0 (s, Ph), 127.2 (s, Ph), 63.0 (d, OCH<sub>2</sub>CH<sub>3</sub>,  ${}^{2}J = 7.2$ Hz), 62.9 (d, OCH<sub>2</sub>CH<sub>3</sub>,  ${}^{2}J_{\rm PC} = 7.0$  Hz), 59.5 (d, CHP,  ${}^{1}J_{\rm PC} =$  153.5 Hz), 16.4 (d,  ${}^{3}J_{PC} = 5.5$  Hz, OCH<sub>2</sub>*C*H<sub>3</sub>), 16.2 (d,  ${}^{3}J_{PC} = 5.4$  Hz, OCH<sub>2</sub>*C*H<sub>3</sub>).

α-**Amino Phosphate (4i).** <sup>1</sup>H NMR δ 7.37–6.69 (11 H, m), 6.36–6.18 (1 H, m), 4.47 (1 H, dd, <sup>1</sup>J<sub>PH</sub> = 21.3 Hz, J = 2.1 Hz), 4.22–4.12 (4 H, m), 3.17 (1 H, s), 1.34 ~ 1.26 (6 H, m); <sup>31</sup>P NMR δ 24.1; <sup>13</sup>C NMR δ 146.6 (s, Ph), 146.5 (s, Ph), 136.4 (s, Ph), 133.1 (s, Ph), 133.0 (s, Ph), 129.3 (s, Ph), 127.9 (s, Ph), 126.6 (s, Ph), 123.5 (s, Ph), 118.6 (s, Ph), 113.9 (s, Ph), 63.5 (s, OCH<sub>2</sub>CH<sub>3</sub>), 63.1 (s, OCH<sub>2</sub>CH<sub>3</sub>), 54.1 (d, CHP, <sup>1</sup>J<sub>PC</sub> = 153.4 Hz), 16.5 (s, OCH<sub>2</sub>CH<sub>3</sub>); HRMS calcd for C<sub>19</sub>H<sub>24</sub>NO<sub>3</sub>P: 345.1494. Found: 345.1535.

α-Amino Phosphate (4j). <sup>1</sup>H NMR δ 7.45 (5 H, m), 3.86– 4.4 (7 H, m), 1.1–1.65 (25 H, m); <sup>31</sup>P NMR δ 24.8; <sup>13</sup>C NMR δ 144.4 (s, Ph), 129.8 (s, Ph), 128.7 (s, Ph), 127.7 (s, Ph), 127.1 (s, Ph), 77.5 (s, CH<sub>2</sub>Ph), 61.8 (d, OCH<sub>2</sub>CH<sub>3</sub>, <sup>2</sup>J<sub>PC</sub> = 9.2 Hz), 53.7 (d, CHP, 149.1 Hz) 38.2 (s, C<sub>9</sub>H<sub>19</sub>), 32.3 (s, C<sub>9</sub>H<sub>19</sub>), 31.8 (s, C<sub>9</sub>H<sub>19</sub>), 30.5 (s, C<sub>9</sub>H<sub>19</sub>), 29.7 (s, C<sub>9</sub>H<sub>19</sub>), 29.3 (s, C<sub>9</sub>H<sub>19</sub>), 29.0 (s, C<sub>9</sub>H<sub>19</sub>), 22.7 (s, C<sub>9</sub>H<sub>19</sub>), 16.7 (d, OCH<sub>2</sub>CH<sub>3</sub>, <sup>3</sup>J<sub>PC</sub> = 4.3 Hz), 14.1 (s, C<sub>9</sub>H<sub>19</sub>); HRMS calcd for C<sub>21</sub>H<sub>38</sub>NO<sub>3</sub>P: 382.2511. Found: 382.2484.

α-**Amino Phosphonate (6a**+7**a).** <sup>1</sup>H NMR δ 7.46–7.12 (10 H, m), 4.21–3.58 (6 H, m), 3.84 (3 H, s), 2.25 (1 H, s), 1.42–1.03 (9 H, m); <sup>31</sup>P NMR δ 24.4, 24.9; <sup>13</sup>C NMR δ 128.6 (s, Ph), 127.9 (s, Ph), 127.7 (s, Ph), 62.9 (s,  $OCH_2CH_3$ ), 62.7 (s,  $OCH_2CH_3$ ), 60.8 (s,  $CHCH_2OCH_3$ ), 58.9 (s,  $CH_2OCH_3$ ), 58.4 (s,  $CH_2OCH_3$ ), 58.2 (d, CHP, <sup>1</sup> $J_{PC}$  = 145.1 Hz), 16.5 (s,  $OCH_2CH_3$ ), 16.3 (s,  $OCH_2CH_3$ ); HRMS calcd for C<sub>20</sub>H<sub>28</sub>NO<sub>4</sub>P: 377.1756. Found: 377.1715; the ratio of **6a** to **7a** is 78:22, de: 56%.

α-**Amino Phosphonate (6b**+7**b).** <sup>1</sup>H NMR δ 7.34–7.23 (10 H, m), 4.17–3.89 (5 H, m), 4.10 (1H, d,  ${}^{1}J_{PH} = 23.4$  Hz), 2.96 (1 H, s), 1.32 (3 H, t, J = 7.2 Hz), 1.10 (3 H, t, J = 7.0 Hz); <sup>31</sup>P NMR δ 24.6, 25.1; <sup>13</sup>C NMR δ 128.6 (s, Ph), 128.2 (s, Ph), 127.6 (s, Ph), 127.2 (s, Ph), 63.3 (s, OCH<sub>2</sub>CH<sub>3</sub>), 58.0 (d, CHP,  ${}^{1}J_{PC} = 151.8$  Hz), 56.2 (s, CH(CH<sub>3</sub>)Ph), 21.8 (s, CH(CH<sub>3</sub>)Ph), 16.5 (s, OCH<sub>2</sub>CH<sub>3</sub>), 16.3 (s, OCH<sub>2</sub>CH<sub>3</sub>); HRMS calcd for C<sub>19</sub>H<sub>26</sub>NO<sub>3</sub>P: 347.1650. Found: 347.1651; the ratio of **6b** to **7b** is 57:43, de: 14%.

α-Amino Phosphonate (6c+7c). <sup>1</sup>H NMR δ 7.44–7.26 (5 H, m), 4.34–3.85 (5 H, m), 3.30 (3 H, s), 3.38–3.14 (2 H, m), 2.33 (2 H, m), 1.70–1.66 (1 H, m), 1.32–0.79 (12 H, m); <sup>31</sup>P NMR δ 24.6, 25.5; <sup>13</sup>C NMR δ 145.1 (s, Ph), 129.8 (s, Ph), 128.7 (s, Ph), 127.2 (s, Ph), 127.1 (s, Ph), 62.9 (d, OCH<sub>2</sub>CH<sub>3</sub>, <sup>2</sup>J<sub>PC</sub> = 6.9 Hz), 62.8 (d, OCH<sub>2</sub>CH<sub>3</sub>, <sup>2</sup>J<sub>PC</sub> = 7.5 Hz), 57.4 (d, CHP, <sup>1</sup>J<sub>PC</sub> = 153.4 Hz), 55.3 (s, CH<sub>2</sub>OCH<sub>2</sub>), 54.8 (s, CH<sub>2</sub>OCH<sub>3</sub>), 24.7 (s, CH<sub>2</sub>(CH<sub>3</sub>)<sub>2</sub>), 21.3 (s, CH(CH<sub>3</sub>)<sub>2</sub>), 21.8 (s, CH(CH<sub>3</sub>)<sub>2</sub>) 16.5 (d, <sup>3</sup>J<sub>PC</sub> = 5.5 Hz, OCH<sub>2</sub>CH<sub>3</sub>), 16.3 (d, <sup>3</sup>J<sub>PC</sub> = 5.8 Hz, OCH<sub>2</sub>CH<sub>3</sub>); HRMS calcd for C<sub>17</sub>H<sub>30</sub>NO<sub>4</sub>P: 343.1913. Found: 343.1932; the ratio of **6c** to **7c** is 74:26, de: 48%.

α-**Amino Phosphonate (6d**+7**d).** <sup>1</sup>H NMR δ 7.31–6.81 (9 H, m), 4.13–3.29 (8 H, m), 3.78 (3 H, s), 3.37 (1 H, s), 1.30 (3 H, t, J = 7.1 Hz), 1.15 (3 H, t, J = 7.0 Hz); <sup>31</sup>P NMR δ 24.7, 25.2; <sup>13</sup>C NMR δ 159.3 (s, Ph), 139.6 (s, Ph), 132.2 (s, Ph), 129.0 (s, Ph), 128.5 (s, Ph), 128.2 (s, Ph), 127.9 (s, Ph), 126.8 (s, Ph), 114.0 (s, Ph), 62.7 (d, OCH<sub>2</sub>CH<sub>3</sub>, <sup>2</sup> $J_{PC} = 6.7$  Hz), 59.8 (d, CHP, <sup>1</sup> $J_{PC} =$ 149.4 Hz,), 59.2 (s, OCH<sub>3</sub>), 58.4 (s, *C*HCH<sub>2</sub>OCH<sub>3</sub>), 56.5 (s, *C*H<sub>2</sub>-OCH<sub>2</sub>), 55.5 (s, CH<sub>2</sub>O*C*H<sub>3</sub>), 16.5 (d, <sup>3</sup> $J_{PC} = 5.4$  Hz, OCH<sub>2</sub>*C*H<sub>3</sub>), 16.3 (d,  ${}^{3}J_{PC} = 5.8$  Hz, OCH<sub>2</sub>*C*H<sub>3</sub>); HRMS calcd for C<sub>21</sub>H<sub>30</sub>-NO<sub>5</sub>P: 407.1862. Found: 407.1852; the ratio of **6d**: **7d** is 78: 22, de: 56%.

α-**Amino Phosphonate (6e**+7e). <sup>1</sup>H NMR δ 7.29–6.85 (9 H, m), 4.19–3.78 (6 H, m), 3.79 (3 H, s), 2.95 (1 H, s), 1.33 (3 H, t, J = 7.1 Hz), 1.32 (3 H, d, J = 6.5 Hz), 1.12 (3 H, t, J = 7.1 Hz); <sup>31</sup>P NMR δ 24.9, 25.0; <sup>13</sup>C NMR δ 145.0 (s, Ph), 136.3 (s, Ph), 128.8 (s, Ph), 128.5 (s, Ph), 128.4 (s, Ph), 127.8 (s, Ph), 127.3 (s, Ph), 127.1 (s, Ph), 126.8 (s, Ph), 63.0 (d, OCH<sub>2</sub>CH<sub>3</sub>, <sup>2</sup>J<sub>PC</sub> = 6.8 Hz), 62.9 (d, OCH<sub>2</sub>CH<sub>3</sub>, <sup>2</sup>J<sub>PC</sub> = 7.1 Hz), 58.2 (d, CHP, <sup>1</sup>J<sub>PC</sub> = 151.7 Hz), 55.5 (s, CH(CH<sub>3</sub>)PH), 55.3 (s, OCH<sub>3</sub>), 22.3 (s, CH<sub>3</sub>), 16.5 (d, <sup>3</sup>J<sub>PC</sub> = 5.4 Hz, OCH<sub>2</sub>CH<sub>3</sub>); HRMS calcd for C<sub>20</sub>H<sub>28</sub>NO<sub>4</sub>P: 377.1756. Found: 377.1773; the ratio of **6e** to **7e** is 57:43, de: 14%.

α-Amino Phosphonate (6f+7f).  $^1\rm H$  NMR δ 7.38–6.86 (4 H, m), 4.30–3.85 (5 H, m), 3.81 (3 H, s), 3.32 (3 H, s), 3.40–3.20

(2 H, m), 2.36–2.26 (2 H, m), 1.72 (1 H, m), 1.34–0.81 (12 H, m);  $^{31}$ P NMR  $\delta$  24.6, 25.5; HRMS calcd for C<sub>18</sub>H<sub>32</sub>NO<sub>5</sub>P: 373.2018. Found: 373.1980; the ratio of **6f** to **7f** is 74:26, de: 48%.

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**Supporting Information Available:** IR and mass spectral data and copies of carbon NMR spectra (18 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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