# Lewis Acid Catalyzed Synthesis of N-Protected Diphenyl 1-Aminoalkylphosphonates

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**Abstract:** Diphenyl α-aminomethylphosphonates are prepared in good yields using a Lewis acid catalyzed Birum–Oleksyszyn reaction. This approach enlarges the scope of this reaction, allowing the use of aldehydes and ketones and the use of acid-labile groups in the synthesis of mono-and disubstituted diphenyl 1-aminoalkylphosphonates.

**Key words:** diphenyl 1-aminoalkylphosphonates, carbamates, Lewis acid, aldehydes, ketones

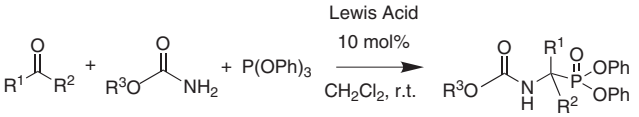
The synthesis of mono- and disubstituted diphenyl α-aminomethylphosphonates is accomplished in good yield using benzyl- or *tert*-butyl carbamate, an aldehyde or a ketone and triphenyl phosphite in the presence of a Lewis acid.

Diphenyl 1-aminoalkylphosphonates are generally synthesized using the Birum–Oleksyszyn reaction.[1] We use the name 'Birum–Oleksyszyn reaction' for the condensation of an aldehyde, benzyl carbamate and triphenyl phosphite in which a Z-protected diphenyl aminoalkylphosphonate is formed. The term 'Oleksyszyn reaction' has been used in the past to designate the synthesis of aminoalkane phosphonates from benzyl carbamate, an aldehyde and phosphorous trichloride. The name 'Birum reaction' has been used to describe the condensation reaction of a urea derivative, an aldehyde and triphenyl phosphate.[2] This reaction is part of a larger spectrum of reactions in which the α-aminophosphonate function is formed by the addition of a trivalent phosphorus nucleophile to an imine carbon or an imine equivalent (e.g. pyrroline trimer or oxazolidine). Most of these synthetic methodologies have been directed toward the synthesis of free aminophosphonic acids or alkyl esters.[3]

The Birum–Oleksyszyn reaction is a simple and direct route to diphenyl 1-aminoalkylphosphonates. In a typical one-pot protocol, an aldehyde, benzyl carbamate and triphenyl phosphite are stirred in glacial acetic acid at 80 °C. After completion of the reaction, acetic acid is removed and the compound is precipitated from cold methanol. In spite of the remarkably simple reaction protocol, which has been used invariantly since it was first published, there are still some problems associated with it. The first drawback consists of the rather modest yields (typically 35–55%), together with the formation (often >20%) of α-hydroxyphosphonates. A second limitation is that the reaction conditions are incompatible with some starting materials or products containing acid labile protecting groups. Finally, the Birum–Oleksyszyn reaction works only for aldehydes. Finding a variant that also works for ketones and that is compatible with acid labile functional groups would greatly broaden the scope of accessible products. These compounds are very interesting probes in biochemistry and medicinal chemistry as they selectively inhibit, depending on the N-substituent, various serine proteases.[4]

The use of Lewis acids instead of acetic acid in the Birum–Oleksyszyn reaction has been poorly documented. Birum mentioned the possibility to initiate the analogous condensation reaction of urea, aldehydes and triphenyl phosphite using $BF_3$.[2] Hudson et al. used $BF_3$ etherate in toluene at 85–90 °C, but did not isolate the diphenyl esters. After hydrolysis in situ, the presence of α-hydroxyphosphonic acids as by-products of the reaction was compared with the usual acetic acid procedure and no difference was found.[5]A few papers report the use of Lewis acids as catalysts in the synthesis of dialkyl aminoalkylphosphonates, but these approaches are not applicable for diphenyl esters.[6]

We found that a Lewis acid such as $ZnCl_2$ effectively promoted the Birum–Oleksyszyn condensation at room temperature. Optimal conditions for the Lewis acid were found to be 10 mol% in dichloromethane (Scheme 1). At 5 mol%, the reaction afforded the same yield but required longer reaction times.




**Scheme 1** Synthesis of diphenyl 1-aminoalkylphosphonic acids. $R^1$ = H, alkyl, aryl, aralkyl; $R^2$ = alkyl, aryl, aralkenyl, aralkyl; $R^1$–$R^2$ = cycloalkyl; $R^3$ = benzyl, *tert*-butyl.

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**Table 1** Lewis Acid Catalyzed Birum–Oleksyszyn Reaction

| Entry and Product No. | Carbonyl Compound | $R^3$ | Lewis Acid | Reaction Time | Yield (%)[a] |
|---|---|---|---|---|---|
| **1** | benzaldehyde | Bn | $TiCl_4$ | 20 min | 87 |
| **1a** | benzaldehyde | Bn | $ZnCl_2$ | 140 min | 86 |
| **2** | *trans*-cinnamaldehyde | Bn | $SnCl_4$ | 70 min | 94 |
| **3** | dimethylaminobenzaldehyde | Bn | $BF_3{\cdot}Et_2O$ | 120 min | 74 |
| **4** | 3-phenylpropionaldehyde | Bn | $Cu(OTf)_2$ | 120 min | 91 |
| **5** | piperonal | Bn | $TiCl_4$ | 120 min | 91 |
| **6** | *N*-Boc-*p*-aminobenzaldehyde | Bn | $Cu(OTf)_2$ | 240 min | 68 |
| **7** | benzaldehyde | *t*-Bu | $TiCl_4$ | 30 min | 81 |
| **8** | *trans*-cinnamaldehyde | *t*-Bu | $SnCl_4$ | 70 min | 82 |
| **9** | cyclohexylaldehyde | *t*-Bu | $SnCl_4$ | 70 min | 88 |
| **10** | 3-methylbutyraldehyde | *t*-Bu | $Cu(OTf)_2$ | 120 min | 84 |
| **11** | piperonal | *t*-Bu | $Cu(OTf)_2$ | 100 min | 87 |
| **12** | acetophenone | Bn | $Cu(OTf)_2$ | 48 h | 44 |
| **13** | cyclohexanone | Bn | $Cu(OTf)_2$ | 36 h | 72 |
| **14** | pentan-2-one | Bn | $Cu(OTf)_2$ | 48 h | 69 |
| **15** | phenylacetone | Bn | $Cu(OTf)_2$ | 48 h | 64 |

[a] Isolated yield.

To further validate the concept of using Lewis acids in the Birum–Oleksyszyn reaction, a range of aldehydes and ketones, triphenyl phosphite and benzyl- and *tert*-butyl carbamates were subjected to different Lewis acids. Results are summarized in Table 1. Excellent yields were obtained in the reactions between benzyl carbamate and aldehydes (entries 1–6) and only traces of α-hydroxyphosphonates were found. There was a remarkable difference in the reaction time. Not completely surprising, these results roughly reflect the relative acidities of the different Lewis acids used. Protected 1-aminoalkylphosphonates usually precipitate from a methanol solution.

Noteworthy is the good yield when using an aldehyde containing the acid labile Boc-protecting group (entry 6). The stability of Boc-groups is confirmed by the use of *tert*-butyl carbamate (entries 7–11). Although not very pronounced, the product yields obtained are somewhat lower than with benzyl carbamate. Steric factors might be invoked to explain these observations. No deprotected product was detected when a Boc-group was present. The Boc-protected compounds however did not show the tendency to precipitate from methanol and had to be purified using chromatographic techniques.

The direct access to Boc-protected compounds might be of use for the transformation of more complex aldehydes, containing functional groups that are not resistant toward HBr or hydrogenolysis (cleavage conditions for the Z-group) or in cases where the specific introduction of a Boc group is part of a protecting group strategy.

To the best of our knowledge, the use of ketones instead of aldehydes in the Birum–Oleksyszyn reaction, which would yield α,α-disubstituted diphenyl 1-aminoalkylphosphonates, has never been described. The condensation of acetophenone, benzyl carbamate and triphenyl phosphite in acetic acid at 80 °C did not provide any target product after 48 hours.

Based on the results for the Birum–Oleksyszyn condensation with aldehydes, a Lewis acid promoted reaction was investigated for ketones. Again, there was little influence of the used catalyst on the yield of the reaction. Different ketones (entries 12–15) were subjected to the Lewis acid catalyzed Birum–Oleksyszyn reaction. The aminophosphonates indeed turned out to have formed in reasonable yields but longer reaction times were required. Yields were lower than those obtained with aldehydes. Ketone-derived compounds did not show the tendency to precipitate from a cold methanolic solution and had to be purified using chromatographic techniques. The synthesis of the free aminophosphonic acid diphenyl esters is not described, with Z- or Boc protecting groups being easily removed by well known procedures.[4]

The mechanism of this reaction has not been investigated in detail. We suppose that after reaction of the carbonyl

compound with the carbamate, the acylimine intermediate is attacked by triphenyl phosphite with the formation of a phosphonium intermediate[5,6e]and that both reactions are catalyzed by the Lewis acid. Reaction with water affords the target compound.

In summary, Lewis acid catalysis efficiently promotes the Birum–Oleksyszyn reaction. The yields obtained from these reactions are significantly higher compared to the yields obtained using the usual protocol (heating in acetic acid). Aldehydes with acid labile Boc groups can now be used without difficulties and *tert*-butyl carbamate can be used as a reaction partner. Lewis acid catalysis also extends the scope of the Birum–Oleksyszyn reaction, allowing ketones to be transformed into the corresponding diphenyl 1-aminoalkylphosphonates.

$^1$H NMR and $^{31}$P NMR spectra were recorded on a Bruker Avance DRX-400 spectrometer (400 MHz) and a Jeol Eclipse 300 FT NMR Spectrometer (109 MHz), respectively, using TMS for $^1$H NMR and phosphoric acid for $^{31}$P NMR. ES Mass spectra were obtained on a Bruker Esquire 3000 plus mass spectrometer. Column chromatography was performed on silica gel 60 (220–440 mesh) from Fluka Chemie. TLC was performed on precoated silica gel plates (Polygram® SIL G/UV$_{254}$). Reagents and starting materials were from Acros Organics and were used without purification.

**Reaction of Aldehydes with Benzyl Carbamate; General Procedure**

Aldehyde (1.2 mmol), benzyl carbamate (1 mmol) and $P(OPh)_3$ (1 mmol) were dissolved in well dried anhyd $CH_2Cl_2$ (2 mL). The Lewis acid (10 mol%) was added in one portion. $BF_3{\cdot}Et_2O$, $TiCl_4$ and $SnCl_4$ were added as 1 M solution in anhyd $CH_2Cl_2$; $Cu(OTf)_2$ was added as such. This mixture was stirred at r.t., until TLC analysis showed the complete consumption of benzyl carbamate. Then $CH_2Cl_2$ was evaporated and the residue dissolved in MeOH (10 mL). The product was precipitated from this solution by storing at –20 °C for 3–6 h, followed by the collection of the precipitate by filtration. Recrystallization was carried out by dissolving the product in $CHCl_3$ (2 mL), concentrating the $CHCl_3$ under reduced pressure, and adding MeOH (8 mL) to the residue. This solution was then stored at –20 °C for 3–6 h, the precipitated product filtered off and dried under reduced pressure (Table 1).

**Reaction of Aldehydes and Ketones with *tert*-Butyl Carbamate; General Procedure**

Aldehyde (1.2 mmol), *tert*-butyl carbamate (1 mmol) and $P(OPh)_3$ (1 mmol) were dissolved in $CH_2Cl_2$ (2 mL). The Lewis acid (10 mol%) was added in one portion. This mixture was stirred at r.t. until TLC analysis showed the complete consumption of carbamate. The oily residue was then adsorbed onto silica gel and chromatographed using hexanes–EtOAc (2:1) (Table 1).

**Diphenyl [(Benzyloxycarbonyl)amino](phenyl)methylphosphonate (1)[1a,7]**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 5.05–5.22 (m, 2 H, $CH_2OC$), 5.5–5.69 (m, 1 H, CHP), 6.81–6.98 (br s, 1 H, NH), 6.78–6.89 (m, 2 $H_{arom}$), 7.05–7.43 (m, 16 $H_{arom}$) 7.41–7.58 (m, 2 $H_{arom}$).

MS (ESI): *m*/*z* = 488 ($M^+$ + 1), 511 ($M^+$ + Na).

**Diphenyl (2*E*)-1-{[(Benzyloxy)carbonyl]amino}-3-phenylprop-2-enylphosphonate (2)**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 5.15 (AB system, 2 H, *J* = 12 Hz, $CH_2OC$), 5.21–5.35 (br m, 1 H, NCHP), 5.57 (br d, 1 H, *J* = 7.6 Hz, NH), 6.31 (ddd, 1 H, *J* = 6.2, 12.4, 16 Hz, =CH), 6.70–6.78 (dd, 1 H, *J* = 3.6, 16 Hz, =CH), 7.09–7.38 (m, 20 $H_{arom}$).

$^{31}$P NMR ($CDCl_3$, 109 MHz): δ = 14.32.

MS (ESI): *m*/*z* = 500 ($M^+$ + 1), 523 ($M^+$ + Na).

Anal. Calcd for $C_{29}H_{26}NO_5P$ (499): C, 69.73; H, 5.21; N, 2.80. Found: C, 69.81; H, 5.44; N, 2.97.

**Diphenyl {[(Benzyloxy)carbonyl]amino}[4-(dimethylamino)phenyl]methylphosphonate (3)**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 2.94 (s, 6 H, 2 $CH_3$), 5.09 (AB system, 2 H, *J* = 12.4 Hz, $CH_2OC$), 5.47 (dd, 1 H, *J* = 9.6 Hz, NCHP), 5.72 (br d, 1 H, *J* = 8 Hz, NH), 6.69 (d, 2 $H_{arom}$, *J* = 8.4 Hz), 6.88 (d, 2 $H_{arom}$, *J* = 8.8 Hz), 7.06–7.37 (m, 15 $H_{arom}$).

$^{31}$P NMR ($CDCl_3$, 109 MHz): δ = 15.17.

MS (ESI): *m*/*z* = 517 ($M^+$ + 1), 539 ($M^+$ + 1).

Anal Calcd for $C_{29}H_{29}N_2O_5P$ (516): C, 67.44; H, 5.62; N, 5.42. Found: C, 66.86; H, 5.59; N, 5.44.

**Diphenyl 1-{[(Benzyloxy)carbonyl]amino}-3-phenylpropylphosphonate (4)**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 2.00–2.23 (br m, 1 H, $CH_2$), 2.32–2.45 (br m, 1 H, $CH_2$), 2.69–2.82 (br m, 1 H, $CH_2$), 2.84–2.94 (br m, 1 H, $CH_2$), 4.47–4.58 (m, 1 H, NCHP), 5.08–5.18 (m, 3 H, NH + $CH_2OC$), 7.00–7.39 (m, 20 $H_{arom}$).

$^{31}$P NMR ($CDCl_3$, 109 MHz): δ = 17.89.

MS (ESI): *m*/*z* = 502 ($M^+$ + 1), 524 ($M^+$ + Na).

Anal Calcd for $C_{29}H_{28}NO_5P$ (501): C, 69.46; H, 5.58; N, 2.79. Found: C, 69.47; H, 5.93; N, 2.97.

**Diphenyl 1,3-Benzodioxol-5-yl-{[(benzyloxy)carbonyl]aminomethylphosphonate (5)**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 5.09 (AB system, 2 H, *J* = 12.2 Hz, $CH_2OC$), 5.46 (dd, 1 H, *J* = 9.2, 9.6 Hz, NCHP), 5.84 (br d, 1 H, *J* = 6 Hz, NH), 5.93 (s, 2 H, $OCH_2O$), 6.76 (d, 1 $H_{arom}$, *J* = 7.6 Hz), 6.89–6.99 (m, 4 $H_{arom}$), 7.06–7.37 (m, 13 $H_{arom}$).

$^{31}$P NMR ($CDCl_3$, 109 MHz): δ = 14.32.

MS (ESI): *m*/*z* = 518 ($M^+$ +1), 540 ($M^+$ + Na).

Anal Calcd for $C_{28}H_{24}NO_7P$ (517): C, 64.99; H, 4.64; N, 2.70. Found: C, 65.05; H, 4.60; N, 2.86.

**Diphenyl {[(Benzyloxy)carbonyl]amino}[4-(*tert*-butoxycarbonyl)aminophenyl]methylphosphonate (6)**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 1.52 (s, 9 H, *t*-$C_4H_9$), 5.09 (AB system, 2 H, *J* = 12 Hz, $CH_2OC$), 5.51 (dd, 1 H, *J* = 10, 14 Hz, NCHP), 5.77 (br d, 1 H, *J* = 7.2 Hz, NH), 6.50 (br s, 1 H, NHBoc), 6.89 (d, 2 $H_{arom}$, *J* = 8.4 Hz), 7.05–7.44 (m, 17 $H_{arom}$).

$^{31}$P NMR ($CDCl_3$, 109 MHz): δ = 14.48.

MS (ESI): *m*/*z* = 589 ($M^+$ + 1), 611 ($M^+$ + Na).

Anal Calcd for $C_{32}H_{33}N_2O_7P$ (588): C, 65.30; H, 5.61; N, 4.76. Found: C, 65.07; H, 5.91; N, 4.87.

**Diphenyl [(*tert*-Butoxycarbonyl)amino](phenyl)methylphosphonate (7)**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 1.42 (s, 9 H, *t*-$C_4H_9$), 5.47–5.69 (br m, 2 H, NCHP + NH), 6.87 (d, 2 $H_{arom}$, *J* = 8.0 Hz), 7.07–7.39 (m, 11 $H_{arom}$) 7.41–7.48 (m, 2 $H_{arom}$).

$^{31}$P NMR ($CDCl_3$, 109 MHz): δ = 15.03.

MS (ESI): *m*/*z* = 440 ($M^+$ + 1), 462 ($M^+$ + Na).

Anal Calcd for $C_{24}H_{26}NO_5P$ (439): C, 65.60; H, 5.92; N, 3.19. Found: C, 65.46; H, 6.06; N, 3.32.

**Diphenyl (2*E*)-1-[(*tert*-Butoxycarbonyl)amino]-3-phenylprop-2-enylphosphonate (8)**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 1.46 (s, 9 H, *t*-$C_4H_9$), 5.23 (br s, 2 H, NCHP + NH), 6.32 (ddd, 1 H, *J* = 6, 12, 16 Hz, =CH), 6.74 (dd, 1 H, *J* = 4.4, 16 Hz, =CH), 7.13–7.38 (m, 15 $H_{arom}$).

$^{31}$P NMR ($CDCl_3$, 109 MHz): δ = 14.89.

MS (ESI): *m*/*z* = 466 ($M^+$ + 1), 488 ($M^+$ + Na).

Anal Calcd for $C_{26}H_{28}NO_5P$ (465): C, 67.10; H, 6.02; N, 3.01. Found: C, 67.43; H, 6.12; N, 3.26.

**Diphenyl [(*tert*-Butoxycarbonyl)amino](cyclohexyl)methylphosphonate (9)**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 1.08–1.37 (m, 6 H, 3 $CH_2$), 1.44 (s, 9 H, *t*-$C_4H_9$), 1.62–1.89 (m, 3 H, $CH_2$ + CH), 1.97–2.08 (m, 2 H, $CH_2$), 4.36 (2 dd, 1 H, *J* = 10.8 Hz, NCHP), 4.97 (dd, 1 H, *J* = 8.4, 10.8 Hz, NH), 7.11–7.23 (m, 6 $H_{arom}$), 7.26–7.37 (m, 4 $H_{arom}$).

$^{31}$P NMR ($CDCl_3$, 109 MHz): δ = 18.45.

MS (ESI): *m*/*z* = 446 ($M^+$ + 1), 468 ($M^+$ + Na).

Anal Calcd for $C_{24}H_{32}NO_5P$ (445): C, 64.72; H, 7.19; N, 3.15. Found: C, 64.96; H, 7.23; N, 3.33.

**Diphenyl 1-[(*tert*-Butoxycarbonyl)amino]-3-methylbutylphosphonate (10)**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 0.94–1.01 (m, 6 H, 2 $CH_3$), 1.43 (s, 9 H, *t*-$C_4H_9$), 1.66–1.89 (m, 3 H, CH + $CH_2$), 4.45–4.58 (m, 1 H, NCHP), 4.80 (d, 1 H, *J* = 10.4 Hz, NH), 7.12–7.22 (m, 6 $H_{arom}$), 7.26–7.35 (m, 4 $H_{arom}$).

$^{31}$P NMR (109 MHz, $CDCl_3$): δ = 19.44.

MS (ESI): *m*/*z* = 420 ($M^+$ + 1), 442 ($M^+$ + Na).

Anal Calcd for $C_{22}H_{30}NO_5P$ (419): C, 63.00; H, 7.16; N, 3.34. Found: C, 63.06; H, 7.23; N, 3.48.

**Diphenyl 1,3-Benzodioxol-5-yl-[(*tert*-butoxycarbonyl)amino]methylphosphonate (11)**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 1.41 (s, 9 H, *t*-$C_4H_9$), 5.42 (dd, 1 H, *J* = 8.8, 9.2 Hz, NCHP), 5.69–5.79 (br m, 1 H, NH), 5.93 (s, 2 H, $OCH_2O$), 6.77 (d, 1 $H_{arom}$, *J* = 8 Hz), 6.92–7.00 (m, 4 $H_{arom}$), 7.08–7.33 (m, 8 $H_{arom}$).

$^{31}$P NMR ($CDCl_3$, 109 MHz): δ = 14.90.

MS (ESI): *m*/*z* = 484 ($M^+$ + 1), 506 ($M^+$ + Na).

Anal. Calcd for $C_{25}H_{26}NO_7P$ (483): C, 62.11; H, 5.38; N, 2.89. Found: C, 62.15; H, 5.39; N, 3.12.

**Diphenyl 1-{[(Benzyloxy)carbonyl]amino}-1-phenylethylphosphonate (12)**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 2.34 (d, 3 H, *J* = 17.6 Hz, $CH_3$), 5.07 (br s, 2 H, $CH_2OC$), 6.13 (d, 1 H, *J* = 11.2 Hz, NH), 6.80–7.62 (m, 20 $H_{arom}$).

$^{31}$P NMR ($CDCl_3$, 109 MHz): δ = 17.22.

MS (ESI): *m*/*z* = 488 ($M^+$ + 1), 510 ($M^+$ + Na).

Anal Calcd for $C_{28}H_{26}NO_5P$ (487.48): C, 68.99; H, 5.38; N, 2.87. Found: C, 69.28; H, 5.38; N, 3.00.

**Diphenyl 1-{[(Benzyloxy)carbonyl]amino}cyclohexylphosphonate (13)**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 1.50–1.80 (m, 6 H, 3 $CH_2$), 1.88–1.99 (m, 2 H, $CH_2$), 2.54–2.66 (br s, 2 H, $CH_2$), 4.90 (br s, 1 H, NH), 5.08 (br s, 2 H, $CH_2OC$), 7.07–7.18 (m, 6 $H_{arom}$), 7.20–7.28 (m, 4 $H_{arom}$), 7.29–7.38 (m, 5 $H_{arom}$).

$^{31}$P NMR ($CDCl_3$, 109 MHz): δ = 19.67.

MS (ESI): *m*/*z* = 466 ($M^+$ + 1), 488 ($M^+$ + Na).

Anal. Calcd for $C_{26}H_{28}NO_5P$ (465.48): C, 67.09; H, 6.06; N, 3.01. Found: C, 67.03; H, 6.15; N, 3.09.

**Diphenyl 1-{[(Benzyloxy)carbonyl]amino}-1-methylbutylphosphonate (14)**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 0.90–1.00 (m, 3 H, $CH_3$), 1.47–1.58 (br m, 2 H, $CH_2$), 1.81 (d, 3 H, *J* = 17.6 Hz, $CH_3$), 1.93–2.05 (m, 1 H, $CH_2$), 2.19–2.31 (m, 1 H, $CH_2$), 5.06 (br s, 3 H, $CH_2OC$ + NH), 7.09–7.33 (m, 15 $H_{arom}$).

$^{31}$P NMR ($CDCl_3$, 109 MHz): δ = 20.63.

MS (ESI): *m*/*z* = 454 ($M^+$ + 1), 476 ($M^+$ + Na).

Anal. Calcd for $C_{25}H_{28}NO_5P$ (453.47): C, 66.22; H, 6.22; N, 3.09. Found: C, 66.04; H, 6.33; N, 3.16.

**Diphenyl 1-Benzyl-1-{[(benzyloxy)carbonyl]amino}ethylphosphonate (15)**

$^1$H NMR ($CDCl_3$, 400 MHz): δ = 1.72 (d, 3 H, *J* = 17.2 Hz, $CH_3$), 3.15–3.23 (m, 1 H, $CH_2$), 3.75–3.82 (m, 1 H, $CH_2$), 4.98 (br s, 1 H, NH), 5.09 (br s, 2 H, $CH_2OC$), 7.05–7.35 (m, 20 $H_{arom}$).

$^{31}$P NMR ($CDCl_3$, 109 MHz): δ = 19.86.

MS (ESI): *m*/*z* = 502 ($M^+$ + 1), 524 ($M^+$ + Na).

Anal. Calcd for $C_{29}H_{28}NO_5P$ (501.51): C, 69.45; H, 5.63; N, 2.79. Found: C, 69.20; H, 5.64; N, 2.58.

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