JOC The Journal of Organic Chemistry

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Synthetic Entry into 1-Phosphono-3-azabicyclo[3.1.0]hexanes

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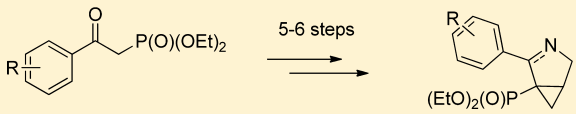
Supporting Information

ABSTRACT: 3-Azabicyclo[3.1.0]hex-2-en-1-yl phosphonates were prepared in a five-step reaction route from β-ketophosphonates. The key steps in this sequence are an atom-transfer radical cyclization and an unforeseen lithium−halogen exchange with *n*-BuLi. The cyclization reaction proceeds with excellent diastereoselectivity. The resulting cyclic imines were reduced, and 3-azabicyclo[3.1.0]hexan-1-yl phosphonates were obtained.



INTRODUCTION

During our ongoing research on the use of heteroatom transfer radical cyclization (HATRC) for the design of phosphonylated heterocycles,[1−4] an unexpected synthesis of diethyl (2-phenyl-3-azabicyclo[3.1.0]hexan-1-yl)phosphonates **1** (Figure 1) has been elaborated. Bicyclic β-aminophosphonates bearing a phosphonate moiety at the bridgehead of the bicyclic structure have only scarcely been reported in literature.[5−8]

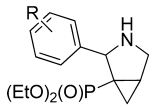


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Figure 1. New azabicyclic phosphonates **1**.

In the class of 3-azabicyclo[3.1.0]hexane scaffolds, no bicycles phosphonylated at the bridgehead have been reported. The carboxylic acid derivatives, on the other hand, which are bioisosters, have been reported in patent literature and exhibit a wide range of therapeutic activities.[9] Amino acid **2** is a bicyclic GABA analogue,[10] while **3** functions as a NK1 antagonist, counteracting emesis in cancer patients receiving chemotherapy (Figure 2).[11] Coupling of the azabicyclic skeleton to larger molecules furnishes antibacterial agents **4**, antihistamines, and $S1P_1$ agonists.[12−14] The synthesis of a library of diethyl (2-phenyl-3-azabicyclo[3.1.0]hexan-1-yl)phosphonates was thus pursued, in view of the interesting biological features of closely related analogues and the lack of literature information regarding this new class of compounds.

RESULTS AND DISCUSSION

Bicyclic β-aminophosphonates **1** were obtained from commercially available substrates in a six-step synthethic pathway. Ten derivatives were prepared starting from differently substituted α-haloacetophenones. These substrates were evaluated for their conversion into the corresponding β-ketophosphonates **5** by a classic Michaelis−Arbuzov reaction with triethyl phosphite. However, these α-haloketones are prone to the Perkow reaction, i.e., phosphite attack across the carbonyl function yielding enol phosphate esters via a zwitterionic intermediate. Electron-withdrawing substituents on the phenyl ring promote the Perkow reaction. In order to avoid formation of these enol phosphates, two literature procedures were applied. α-Haloacetophenones were converted into the corresponding hydrazones. This prevented phosphite attack across the carbonyl function and favored the envisaged Michaelis−Arbuzov reaction (route A).[15] Consecutive hydrolysis delivered the desired β-ketophosphonates **5** in good to excellent yields, as depicted in Table 1.

For α-haloacetophenones with strong electron-withdrawing groups on the phenyl ring (R = 4′-NO_2, 4′-CN), formation of the hydrazones appeared to be troublesome, leading to severe degradation of the reaction products. Hence, a different procedure using the $MgCl_2/Et_3N$ system with diethyl phosphonoacetic acid was evaluated and did cleanly yield the desired electron poor β-ketophosphonates after decarboxylation (route B).[16] Using two different methodologies, we synthesized 10 substituted diethyl (2-oxo-2-phenylethyl)-phosphonates (Table 1). When the purity of the crude reaction product was unsatisfactory, column chromatography was performed since even small impurities caused unproportionally large amounts of side products in the following steps.

Next, diethyl (2-oxo-2-phenylethyl)phosphonates **5a−j** were reacted with allylamine under Dean−Stark conditions, yielding an enamine/imine mixture **6**/**7a−j** in ratios around 80/20 in favor of the enamines (Scheme 1, Table 2). Only one isomer of enamine **6a−j** was formed, whereas the imines **7a−j** were obtained in both their *E* and *Z* forms, the *E* form prevailing (for exact ratios, see Table 2). These β-enaminophosphonates **6** are versatile building blocks and various syntheses of these molecules have accordingly been reported, e.g., the addition of amines to phosphonylated alkynes[17−19] or addition of metalated dialkyl phosphonates to nitriles.[20−23] Furthermore,

Received: May 30, 2013
Published: August 21, 2013

   dx.doi.org/10.1021/jo401185u | *J. Org. Chem.* 2013, 78, 8232−8241

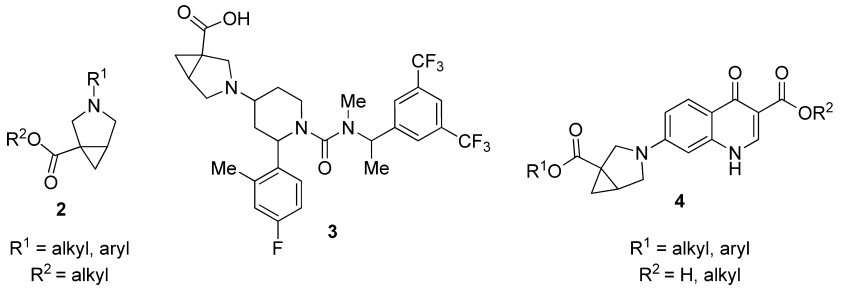


Figure 2. Biologically relevant carboxyl analogues.

Table 1. Yields of *β*-Ketophosphonates 5a–j

entry	R	route	**5** (%)
a	4′-H	A	*a*
b	4′-F	A	50[b]
c	4′-Cl	A	51[b]
d	4′-Br	A	52[b]
e	4′-OMe	A	95[b]
f	4′-Me	A	90
g	4′-Ph	A	99
h	3′-OMe	A	61[b]
i	4′-NO_2	B	51[b]
j	4′-CN	B	50[b]

[a]Commercially available product. [b]After column chromatography.

Table 2. Yields (%) and Conformational Ratios of Enamines/Imines 6/7a–j and *α,α*-Dichlorinated Imines 8a–j

entry	R	yield **6** + **7**	ratio **6**/**7**	ratio *E*/*Z*	yield of **8** (%)
a	4′-H	98	83/17	65/35	95
b	4′-F	89	71/29	53/47	99
c	4′-Cl	80	72/28	51/59	97
d	4′-Br	93	49/51	60/40	82
e	4′-OMe	91	73/27	59/41	92
f	4′-Me	72	74/26	73/27	96
g	4′-Ph	91	82/18	54/46	90
h	3′-OMe	98	84/16	59/41	99
i	4′-NO_2	83	50/50	93/7	42[a]
j	4′-CN	88	51/49	78/22	44[a]

[a]After column chromatography.

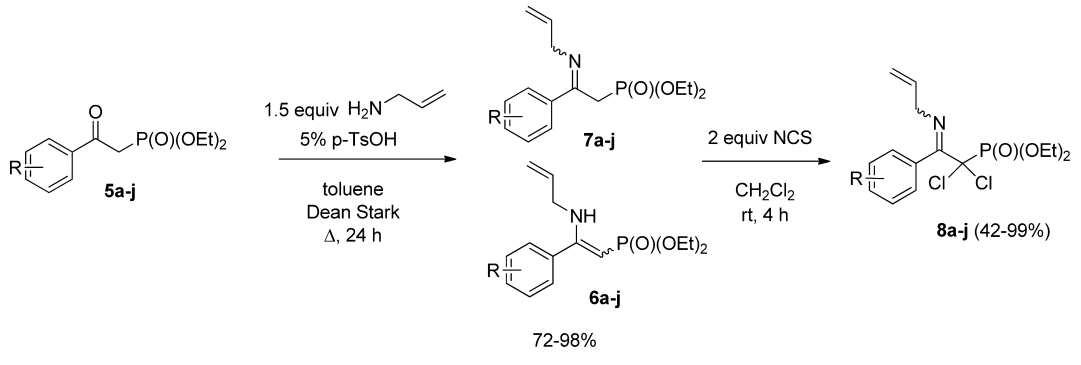
they can be converted into a myriad of acyclic and cyclic compounds, such as 1-aza-1,3-dienes,[22,24,25] 2-pyridones,[23] and pyrazoles.[25] In this work, the enamine/imine mixture was *α,α*-dihalogenated using 2 equiv of *N*-chlorosuccinimide (NCS) furnishing the *α,α*-dichlorinated imines **8a–j** in satisfactory yields and with high purities. No column chromatography was needed except for the derivatives with strong electron-withdrawing groups on the phenyl ring (Table 2).

With a library of *α,α*-dichlorinated imines **8** in hand, a HATRC was performed in order to acquire the 1-pyrrolines **11a–j**.[26] Usually, copper(I) complexes mediate this free-radical ring closure, and their activity can be enhanced by adding ligands that modify solubility and redox potential.[27] The *α,α*-dihalogenated imines **8a–j** were stirred with Cu(I)Cl and *N,N,N′,N′,N″*-pentamethyldiethylenetriamine (PMDTA) as a ligand in CH_2Cl_2 at reflux temperature, and the reaction progress was monitored using HPLC. After all starting material **8a–j** had been consumed (ca. 5 h) and the crude reaction mixture had been subjected to column chromatography, 1-pyrrolines **11a–j** were isolated in satisfactory yields (Scheme 2). Application of other ligating agents such as *N,N,N′,N′*-tetramethylethyelenediamine (TMEDA) gave similar results.

Because of the molecular reorganization caused by the free-radical cyclization process, two stereogenic centers have been introduced into the molecule (Scheme 2, **11a–j**). However, ^{31}P NMR indicated a strong diastereoselectivity. Only one major product peak was present, along with some small signals accounting for the minor enantiomeric pair and a few minor impurities. The diastereoisomeric ratios are all in the range of 90/10 and only the major pair of enantiomers could be obtained in pure form (Table 3).

In order to determine the relative stereochemistry of the 1-pyrrolines **11a–j**, several NMR techniques were applied. A 2D-NOESY experiment displayed no interaction between the phosphonate ethoxy groups and H^3, possibly indicating a *trans* configuration (Figure 3). Furthermore, a heteronuclear 2D-NOESY (HOESY) experiment was performed to determine if any Overhauser effect between the phosphorus atom and H^3

Scheme 1. Formation of *α,α*-Dichlorinated Imines 8a–j



dx.doi.org/10.1021/jo401185u | J. Org. Chem. 2013, 78, 8232–8241

Scheme 2. Mechanism of the HATRC

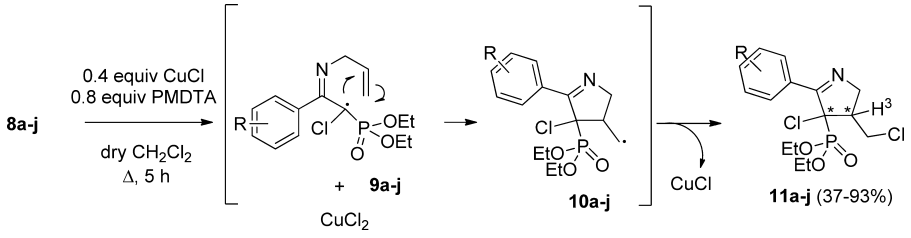


Table 3. Yields (%) after Column Chromatography and Diastereoisomeric Ratios of Crude Reaction Mixtures (Based on ^{31}P NMR)

entry	R	yield of **11** (%)	dr
a	4′-H	93[a]	90/10
b	4′-F	59	92/8
c	4′-Cl	73	90/10
d	4′-Br	43	89/11
e	4′-OMe	45	85/15
f	4′-Me	26	95/5
g	4′-Ph	37	96/4
h	3′-OMe	60	93/7
i	4′-NO_2	23[b]	93/7
j	4′-CN	14[b]	95/5

[a]No column chromatography necessary. [b]After first crystallization; further crystallization proved difficult, so column chromatography was used if necessary.

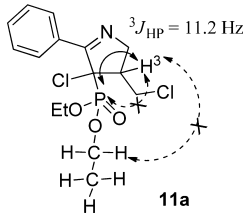


Figure 3. Absence of NOE (dashed arrows) and determination of $^3J_{HP}$ (plain arrow).

could be detected. However, no interaction was observed in this experiment, thereby supporting the result of the previous experiment. Finally, several ^{1}H-undecoupled ^{31}P NMR spectra were recorded with different intensities of decoupling irradiation in order to obtain a clean signal (for details, see the Supporting Information). These experiments proved the coupling constant $^3J_{HP}$ to be 11.2 Hz (Figure 3). Literature values for $^3J_{HP}$ in five-membered rings have been reported as $^3J_{HP,trans}$ = 5.4−6.0 Hz, while $^3J_{HP,cis}$ = 17.2−18.0 Hz.[28] The coupling constant observed in **11** lies in between these two values, rendering the NMR observations inconclusive. In the end, we were able to crystallize two derivatives (**11i**, R = 4′-NO_2 and **11j**, R = 4′-CN). Opposed to the configuration suspected from the NOE NMR experiments, single-crystal X-ray diffraction indicated that the relative stereochemistry is *cis*, with a torsion angle of −37.2(5)° and −33.1(3)° for **11i** and **11j**, respectively, between the phosphorus atom and H^3 (Figure 4). As both compounds **11i** and **11j** crystallized in the centrosymmetric space group $P2_1/c$, both enantiomers are present in the crystal structures.

The origin of this diastereoselectivity most likely lies in steric hindrance caused by the phosphonate's bulky ethoxy substituents, as no other obvious inducing factors are present.

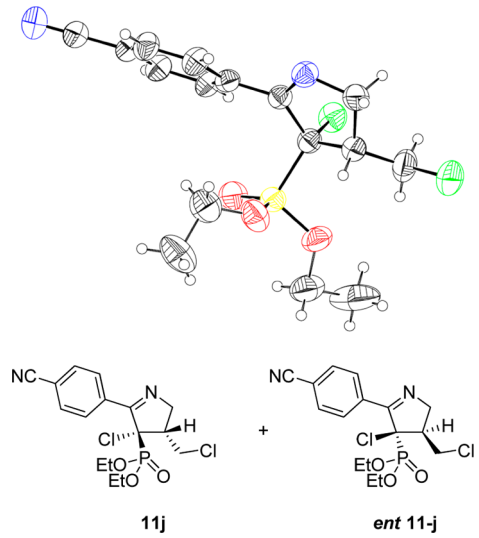


Figure 4. Asymmetric unit of the crystal structure of **11j** showing thermal ellipsoids at the 40% probability level. Both enantiomers are present in the crystal structure. Disorder of the ethoxy groups is omitted for clarity.

Formation of the five-membered ring proceeds through a radical 5-*exo*-*trig* cyclization. In the transition state **9** the allylic methylene carbon is preferentially oriented away from the bulky phosphonate moiety (Scheme 2). In this manner, the energetically most favorable five-membered ring is formed, being the one with least steric hindrance.

With this five-membered ring in hand, the initial goal was to perform a 1,4-dehydrohalogenation reaction in order to produce phosphonylated pyrroles **13** (Scheme 3).[29] Several bases were evaluated. Not surprisingly, weak bases such as triethylamine or potassium carbonate did not engender the desired elimination. Bases of intermediate strength such as KO-*t*-Bu and sodium hydride also failed to do so. The use of LiHMDS yielded some pyrrole **13a**, albeit in very small amounts. In order to achieve complete conversion and to speed up the reaction, *n*-BuLi was employed. However, this resulted in the formation of an unexpected new compound instead of the envisaged pyrrole **13a**. After purification and careful NMR studies, the structure of this new compound was assigned as bicyclic product **14a** (Scheme 3).

The alkyllithium reagent performed a Li−Cl exchange with the tertiary chlorine atom to yield the most stable carbanion **15a−j** (Scheme 4, only one enantiomer shown). This lithiated anion subsequently underwent an intramolecular S_N2 reaction affording bicycle **14a−j**. Conjugation with the imine bond as well as the electron-withdrawing properties of the phosphonate moiety ensure that only the tertiary chlorine is exchanged, and the primary, more accessible one, is left untouched. This hypothesis was proven by the fact that quenching the reaction

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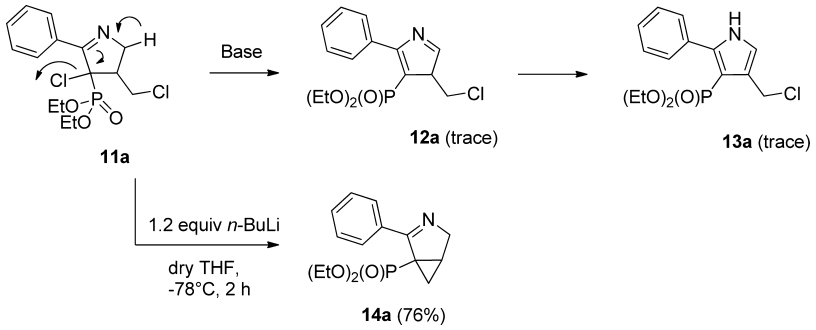
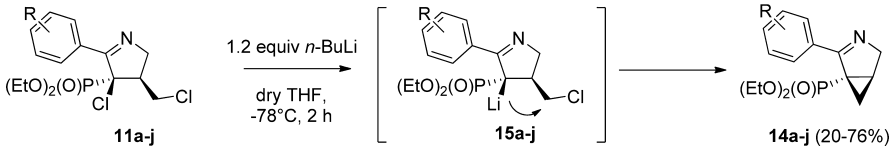
Scheme 3. Attempted Synthesis of Phosphonylated Pyrroles 13a through E2



Scheme 4. Mechanistic Proposal for the Formation of Bicyclic Phosphonates 14a–j (Only One Enantiomer Shown)



with methanol, 5 min after the addition of *n*-BuLi, yielded the same bicyclic product **14a–j**, whereas quenching with acetic acid after the same time interval yielded a mixture of starting material **11a–j**, bicycle **14a–j**, and some monochlorinated compounds. After addition of methanol, lithiated product **15a–j** was quenched by the acidic alcohol proton, but the in situ formed lithium methoxide was basic enough to deprotonate the *β*-imino phosphonate and accomplish the intramolecular ring closure, a process that could not be accomplished by the less basic lithium acetate. If the primary chlorine atom had been exchanged instead, lithium methoxide would not have been able to deprotonate the resulting aliphatic methyl group. This proves that the tertiary chlorine is exchanged after the addition of *n*-BuLi.

The other diastereoisomer of **11a–j**, in which the tertiary chlorine and the chloromethyl group are in a *trans* configuration, is also converted into bicyclic product **14a–j**. In this case, the formation of the three-membered ring is possible by inversion of the stereochemistry via the aza-enolate in order to obtain the necessary configuration for the ring closure. In this manner, we have achieved the unexpected synthesis of diethyl (2-phenyl-3-azabicyclo[3.1.0]hex-2-en-1-yl)phosphonates **14a–j** (Table 4).

Table 4. Yields of Cyclopropanation after Column Chromatography and Reduction

entry	R	yield of **14** (%)	reduction time (h)	yield of **1** (%)
a	4′-H	76	1	84
b	4′-F	49	2	74
c	4′-Cl	33	1	85
d	4′-Br	40[a]		[b]
e	4′-OMe	51	16	92
f	4′-Me	54	16	63
g	4′-Ph	30	24	91
h	3′-OMe	72	24	30[c]
i	4′-NO_2	20	4	81[c]
j	4′-pentanoyl	36	24	60[c]

[a]Inseparable mixture. [b]Reduction was not performed because of unpure starting material. [c]After column chromatography.

In the 4′-Br derivative **11d**, however, the bromine on the phenyl ring was exchanged as well as a tertiary chlorine atom, yielding inseparable mixtures of brominated, chlorinated, and dehalogenated starting materials and cyclopropanated product. Interestingly, lithium–halogen exchange in **11c** (R = 4′-Cl) occurs only on the tertiary chlorine atom and not on the chlorine on the phenyl ring as no dehalogenated products were detected. For **11j** (R = 4′-CN), the simultaneous addition of *n*-BuLi to the nitrile could not be prevented, resulting in a mixture of starting material, cyclopropanated product with the nitrile intact and cyclopropanated product with a pentanoyl substituent **14j** (Figure 5). Therefore, all of **11j** was converted into **14j** by adding an excess of *n*-BuLi.

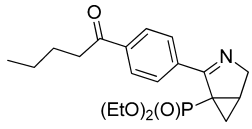


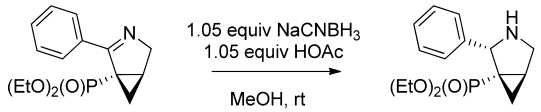
Figure 5. Product after addition of *n*-BuLi to **11j** with loss of the nitrile functional group.

To our surprise, further derivatization of the imine bond proved to be extremely difficult. Hydrolysis in neutral, acidic, or alkaline medium was unsuccessful as well as addition of alkyllithium or Grignard reagents. N-Alkylation using methyl iodide or trimethyloxonium tetrafluoroborate in order to activate the imine bond was not successful, and reduction with $NaBH_4$ or $LiAlH_4$ failed. However, application of equimolar amounts of $NaCNBH_3$ and acetic acid proved to be effective for reduction to the bicyclic pyrrolidine **1a** (Scheme 5, Table 4). Reaction progress was monitored by HPLC (Table 4). The lack of reactivity of **14a–j** may be explained by steric hindrance of the imine bond caused by the bulky ethoxy groups of the phosphonate on one side and a cyclopropane proton on the other side, blocking the antibonding π^*-orbitals. Only the smallest nucleophiles can add, given the imine bond is suitably activated, i.e., by protonation.

Through this reduction, a third stereogenic center was introduced into the molecule with high diastereoselectivity (dr

dx.doi.org/10.1021/jo401185u | J. Org. Chem. 2013, 78, 8232–8241

Scheme 5. Reduction of Imine 14a (Only One Enantiomer Shown)



≥99/1 for all derivatives **1a–j** based on ^{31}P NMR). This observation may again be explained by strong steric hindrance at the imine bond, which forces the hydride to add from the less hindered side of the five-membered ring. This results in a racemic mixture of diethyl (2-phenyl-3-azabicyclo[3.1.0]hexan-1-yl)phosphonates, with the phenyl ring and the phosphonate moiety in a *cis* configuration.

CONCLUSION

A library of 10 azabicyclic phosphonates with a manifold of substituents on the phenyl ring was obtained in five steps. The key steps are two ring-closure reactions of which the first, i.e., the HATRC, displays an excellent diastereoselectivity. The relative stereochemistry of these compounds was confirmed by X-ray analysis. The second ring closure is accomplished through a lithium–chlorine exchange with *n*-BuLi, allowing intramolecular cyclopropanation. The acquired cyclic *β*-imino phosphonates proved very unreactive toward all kinds of nucleophiles, only undergoing a diastereoselective reduction with $NaCNBH_3$ and acetic acid. This step furnishes diethyl (2-phenyl-3-azabicyclo[3.1.0]hexan-1-yl)phosphonates in excellent yields.

EXPERIMENTAL SECTION

Commercially available products were used as received without any purification unless otherwise noted. Column chromatography was performed in a glass column with silica gel (particle size 70–200 μm, pore diameter 60 Å) using mixtures of ethyl acetate (EtOAc) and hexanes. NMR spectra were recorded at 300 MHz (^{1}H), 121 MHz (^{31}P), or 75 MHz (^{13}C) in $CDCl_3$ unless otherwise noted. 2D-NOESY spectra were recorded using a 5 s relaxation delay and a 1.5 s mixing time. Low-resolution mass spectra were obtained with a single quadrupole mass spectrometer (ESI, 70 eV). High-resolution mass spectra were obtained with a time of flight (TOF) mass spectrometer (ESI or APCI). Melting points are uncorrected.

Synthesis of Diethyl (2-Oxo-2-phenylethyl)phosphonates 5a–h. A mixture of substituted 2-chloroacetophenone or 2-bromoacetophenone (1 equiv) and methyl hydrazinecarboxylate (1.05 equiv) was dissolved in toluene (2 mL/mmol) in a round-bottom flask equipped with a Dean–Stark apparatus and heated to reflux temperature for 5 h. Triethyl phosphite was added (1.1 equiv), and the reaction mixture was refluxed for an additional 2 h. The solvent was evaporated in vacuo before the residue was redissolved in a mixture of 20 mL of acetone and 20 mL of 2 M HCl. After 3 h of stirring, the acetone was evaporated in vacuo and the residue was brought to pH 7 with 2 M NaOH before being extracted with CH_2Cl_2 (3 × 20 mL). The combined organic phases were dried over $MgSO_4$ and concentrated in vacuo. If necessary, the product was purified using column chromatography.

Synthesis of Diethyl (2-Oxo-2-phenylethyl)phosphonates 5i,j. A mixture of diethyl phosphonoacetic acid (1 equiv) was dissolved in CH_3CN (2 mL/mmol), $MgCl_2$ (1.2 equiv) and Et_3N (2 equiv) were added, and the reaction mixture was stirred for 2 h at room temperature. Then the suspension was cooled to 0 °C, and the desired acid chloride was dissolved in CH_3CN (1 mL/mmol) and added dropwise to the cooled solution. The reaction was allowed to slowly warm to room temperature overnight. The solvent was removed in vacuo, and the solids were redissolved in 20 mL of CH_2Cl_2 and washed with 20 mL of 2 M HCl. The aqueous phase was extracted with CH_2Cl_2 (3 × 20 mL) and was dried over $MgSO_4$. The solvent was removed in vacuo, and the product was purified using column chromatography.

*Diethyl (2-(4-Cyanophenyl)-2-oxoethyl)phosphonate **5j**.* A 3.00 g (18.12 mmol) sample of commercially available 4-cyanobenzoyl chloride was converted into **5j**. After column chromatography, 2.55 g was obtained (9.06 mmol, 50% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 1.30 (6H, t, *J* = 7.1 Hz), 3.64 (2H, d, $^2J_{HP}$ = 23.1 Hz), 4.15 (4H, dq, $^3J_{HP}$ = 7.4 Hz, *J* = 7.1 Hz), 7.79 (2H, d, *J* = 8.0 Hz), 8.13 (2H, d, *J* = 8.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) *δ*: 16.1 (d, $^3J_{CP}$ = 5.8 Hz), 38.7 (d, $^1J_{CP}$ = 129.2 Hz), 62.7 (d, $^2J_{CP}$ = 5.8 Hz), 116.5, 117.8, 129.4, 132.4, 139.3, 190.9 (d, $^2J_{CP}$ = 5.8 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) *δ*: 19.18. IR (cm^{-1}) ν_{max}: 1019 (P–O), 1051 (P–O), 1248 (P═O), 1685 (C═O), 2232 (C≡N), 2984. MS (ESI, pos): *m*/*z* 282.3/283.0 (M + H$^+$, 100/14). HRMS: *m*/*z* calcd for $C_{13}H_{17}NO_4P$ (M + H)$^+$ 282.0890, found 282.0899. Chromatography: hexanes/EtOAc 2/3, R_f = 0.11.

Synthesis of Diethyl (2-(Allylamino)-2-phenylvinyl)-phosphonates 6a–j and 7a–j. Diethyl (2-oxo-2-phenylethyl)-phosphonates **5a–j** were dissolved in toluene (1 mL/mmol) in a round-bottom flask equipped with a Dean–Stark apparatus. Allylamine (1.5 equiv) and *p*-TsOH (0.05 equiv) were added, and the reaction mixture was heated to reflux temperature and left overnight. The reaction progress was monitored using gas chromatography. After all starting material had been consumed, the solvent was removed in vacuo and the residue was redissolved in diethyl ether and washed with aqueous $NaHCO_3$. The organic phase was extracted with diethyl ether (3 × 20 mL), dried over $MgSO_4$, and concentrated in vacuo.

Synthesis of Diethyl (2-(Allylimino)-1,1-dichloro-2-phenylethyl)phosphonates 8a–j. Diethyl (2-(allylamino)-2-phenylvinyl)phosphonates **6a–j**/**7a–j** were dissolved in CH_2Cl_2 (1 mL/mmol), and *N*-chlorosuccinimide was added (2 equiv). After 4 h, the reaction mixture was poured into 2 M NaOH and extracted (3 × 20 mL CH_2Cl_2). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. If necessary, the residue was purified using column chromatography.

*Diethyl (2-(allylimino)-1,1-dichloro-2-phenylethyl)phosphonate **8a**.* 3.08 g (10.43 mmol) of enamine/imine **6a**/**7a** was converted into 3.61 g of **8a** (9.91 mmol, 95% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 1.37 (6H, t, *J* = 7.2 Hz), 3.86 (2H, d, *J* = 5.3 Hz), 4.27–4.48 (4H, m), 5.10 (1H, dd, $J_{HH,Z}$ = 10.6 Hz, *J* = 1.1 Hz), 5.21 (1H, dd, $J_{HH,E}$ = 17.1 Hz, *J* = 1.4 Hz), 5.90 (1H, ddt, $J_{HH,E}$ = 17.1 Hz, $J_{HH,Z}$ = 10.6 Hz, *J* = 5.3 Hz), 7.31–7.33 (2H, m), 7.43–7.44 (3H, m). ^{13}C NMR (75 MHz, $CDCl_3$) *δ*: 16.5 (d, $^3J_{CP}$ = 5.8 Hz), 55.9, 65.4 (d, $^2J_{CP}$ = 6.9 Hz), 82.0 (d, $^1J_{CP}$ = 176.5 Hz), 116.3, 128.1, 128.9, 129.3, 131.7 (d, $^3J_{CP}$ = 5.8 Hz), 134.3, 166.0. ^{31}P NMR (121 MHz, $CDCl_3$) *δ*: 10.96. IR (cm^{-1}) ν_{max}: 1017 (P–O), 1054 (P–O), 1265 (P═O), 1654, 2982. MS (ESI, pos): *m*/*z* 364.0/365.0/366.0 (M + H$^+$, 100/16/64). HRMS: *m*/*z* calcd for for $C_{15}H_{21}Cl_2NO_3P$ (M + H)$^+$ 364.0631, found 364.0642.

*Diethyl (2-(Allylimino)-1,1-dichloro-2-(4-fluorophenyl)ethyl)-phosphonate **8b**.* 2.42 g (7.72 mmol) of enamine/imine **6b**/**7b** was converted into 2.92 g of **8b** (7.64 mmol, 99% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) *δ*: 1.38 (6H, t, *J* = 7.5 Hz), 3.87 (2H, dt, *J* = 5.3 Hz, *J* = 1.8 Hz), 4.26–4.48 (4H, m), 5.11 (1H, ddd, $J_{HH,Z}$ = 10.5 Hz, *J* = 3.4 Hz, *J* = 1.8 Hz), 5.20 (1H, ddd, $J_{HH,E}$ = 17.3 Hz, *J* = 3.4 Hz, *J* = 1.8 Hz), 5.90 (1H, ddt, $J_{HH,E}$ = 17.3 Hz, $J_{HH,Z}$ = 10.5 Hz, *J* = 5.3 Hz), 7.13 (2H, dd, J_{HF} = 8.5 Hz, *J* = 8.5 Hz), 7.28–7.35 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$) *δ*: 16.5 (d, $^3J_{CP}$ = 5.8 Hz), 55.9, 65.5 (d, $^2J_{CP}$ = 6.9 Hz), 81.9 (d, $^1J_{CP}$ = 176.5 Hz), 115.3 (d, $^2J_{CF}$ = 20.8 Hz), 116.3, 127.6, 131.0 (d, $^3J_{CF}$ = 8.1 Hz), 134.0, 163.1 (d, $^1J_{CF}$ = 249.2 Hz), 165.2. ^{19}F NMR (282 MHz, $CDCl_3$) *δ*: −110.98 to −110.87 (m). ^{31}P NMR (121 MHz, $CDCl_3$) *δ*: 10.76. IR (cm^{-1}) ν_{max}: 1019 (P–O), 1052 (P–O), 1229 (P═O), 1507, 2983. MS (ESI, pos): *m*/*z* 382.0/383.3/384.0 (M + H$^+$, 100/16/64). HRMS: *m*/*z* calcd for $C_{15}H_{20}Cl_2FNO_3P$ (M + H)$^+$ 382.0536, found 382.0540.

*Diethyl (2-(Allylimino)-1,1-dichloro-2-(4-chlorophenyl)ethyl)-phosphonate **8c**.* 0.63 g (1.91 mmol) of enamine/imine **6c**/**7c** was converted into 0.74 g of **8c** (1.85 mmol, 97% yield, yellow oil). ^{1}H

dx.doi.org/10.1021/jo401185u | J. Org. Chem. 2013, 78, 8232–8241

NMR (300 MHz, $CDCl_3$) δ: 1.38 (6H, t, J = 7.5 Hz), 3.85−3.88 (2H, m), 4.26−4.48 (4H, m), 5.11 (1H, ddd, $J_{HH,Z}$ = 10.4 Hz, J = 3.4 Hz, 1.7 Hz), 5.20 (1H, $J_{HH,E}$ = 17.3 Hz, J = 3.4 Hz, J = 1.8 Hz), 5.89 (1H, ddt, $J_{HH,E}$ = 17.3 Hz, $J_{HH,Z}$ = 10.4 Hz, J = 5.2 Hz), 7.26 (2H, d, J = 8.5 Hz), 7.42 (2H, d, J = 8.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.5 (d, $^3J_{CP}$ = 5.8 Hz), 56.0, 65.6 (d, $^2J_{CP}$ = 6.9 Hz), 81.8 (d, $^1J_{CP}$ = 177.0 Hz), 116.5, 128.5, 130.1 (d, $^3J_{CP}$ = 5.8 Hz), 130.4, 134.0, 135.7, 165.1. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 10.65. IR (cm^{-1}) ν_{max}: 1012 (P−O), 1054 (P−O), 1264 (P═O), 1487, 2982. MS (ESI, pos): m/z 398.0/400.0/402.0 (M + H$^+$, 100/97/40). HRMS: m/z calcd for $C_{15}H_{20}Cl_3NO_3P$ (M + H)$^+$ 398.0241, found 398.0246.

Diethyl (2-(Allylimino)-1,1-dichloro-2-(4-bromophenyl)ethyl)-phosphonate ***8d***. 0.67 g (1.80 mmol) of enamine/imine **6d**/**7d** was converted into 0.65 g of **8d** (1.48 mmol, 82% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.38 (6H, t, J = 7.2 Hz), 3.86−3.87 (2H, m), 4.24−4.48 (4H, m), 5.11 (1H, ddd, $J_{HH,Z}$ = 10.2 Hz, J = 3.3 Hz, J = 1.7 Hz), 5.20 (1H, ddd, $J_{HH,E}$ = 17.3 Hz, J = 3.3 Hz, J = 1.7 Hz), 5.90 (1H, ddt, $J_{HH,E}$ = 17.3 Hz, $J_{HH,Z}$ = 10.2 Hz, J = 5.2 Hz), 7.20 (2H, d, J = 8.3 Hz), 7.58 (2H, d, J = 8.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.6 (d, $^3J_{CP}$ = 5.8 Hz), 56.0, 65.7 (d, $^2J_{CP}$ = 6.9 Hz), 81.7 (d, $^1J_{CP}$ = 177.7 Hz), 116.5, 124.0, 130.5, 130.7, 131.5, 134.1, 165.1. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 10.64. IR (cm^{-1}) ν_{max}: 1010 (P−O), 1054 (P−O), 1260 (P═O), 1484, 2982. MS (ESI, pos): m/z 442.0/444.0/446.0 (M + H$^+$, 62/100/45). HRMS: m/z calcd for $C_{15}H_{20}BrCl_2NO_3P$ (M + H)$^+$ 441.9736, found 441.9743.

Diethyl (2-(Allylimino)-1,1-dichloro-2-(4-methoxyphenyl)ethyl)-phosphonate ***8e***. 1.23 g (3.78 mmol) of enamine/imine **6e**/**7e** was converted into 1.37 g **8e** (3.48 mmol, 92% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.38 (6H, t, J = 7.4 Hz), 3.85 (3H, s), 3.89 (2H, dt, J = 5.1 Hz, J = 1.7 Hz), 4.27−4.48 (4H, m), 5.10 (1H, ddd, $J_{HH,Z}$ = 10.5 Hz, J = 3.6 Hz, J = 1.7 Hz), 5.21 (1H, ddd, $J_{HH,E}$ = 17.3 Hz, J = 3.6 Hz, J = 1.7 Hz), 5.91 (1H, ddt, $J_{HH,E}$ = 17.3 Hz, $J_{HH,Z}$ = 10.5 Hz, J = 5.1 Hz), 6.95 (2H, d, J = 8.8 Hz), 7.26 (2H, d, J = 8.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 55.0, 55.5, 65.0 (d, $^2J_{CP}$ = 5.8 Hz), 82.3 (d, $^1J_{CP}$ = 176.5 Hz), 113.3, 115.9, 123.5 (d, $^3J_{CP}$ = 5.8 Hz), 130.1, 134.2, 160.1, 165.9. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 11.12. IR (cm^{-1}) ν_{max}: 1020 (P−O), 1055 (P−O), 1245 (P═O), 1509, 2981. MS: m/z (ESI, pos) 394.3/395.3/396.3 (M + H$^+$, 100/17/64). HRMS: m/z calcd for $C_{16}H_{23}Cl_2NO_4P$ (M + H)$^+$ 394.0736, found 394.0744.

Diethyl (2-(Allylimino)-1,1-dichloro-2-(4-methylphenyl)ethyl)-phosphonate ***8f***. 1.78 g (5.75 mmol) of enamine/imine **6f**/**7f** was converted into 2.09 g **8f** (5.52 mmol, 96% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.37 (6H, t, J = 6.9 Hz), 2.39 (3H, s), 3.87 (2H, dt, J = 5.1 Hz, J = 1.7 Hz), 4.27−4.51 (4H, m), 5.10 (1H, ddd, $J_{HH,Z}$ = 10.4 Hz, J = 3.4 Hz, J = 1.7 Hz), 5.21 (1H, ddd, $J_{HH,E}$ = 17.1 Hz, J = 3.4 Hz, J = 1.7 Hz), 5.90 (1H, ddt, $J_{HH,E}$ = 17.1 Hz, $J_{HH,Z}$ = 10.4 Hz, J = 5.1 Hz), 7.22 (4H, d, J = 2.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.6 (d, $^3J_{CP}$ = 5.8 Hz), 21.5, 55.9, 65.5 (d, $^2J_{CP}$ = 6.9 Hz), 82.2 (d, $^1J_{CP}$ = 176.5 Hz), 116.3, 128.8, 128.9, 134.5, 139.4, 166.3 (d, $^2J_{CP}$ = 2.3 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ: 11.07. IR (cm^{-1}) ν_{max}: 1017 (P−O), 1052(P−O), 1262 (P═O), 1654, 2982. MS (ESI, pos): m/z 378.3/379.3/380.3 (M + H$^+$, 100/18/64). HRMS: m/z calcd for $C_{16}H_{23}Cl_2NO_3P$ (M + H)$^+$ 378.0787, found 378.0795.

Diethyl (2-([1,1′-Biphenyl]-4-yl)-2-(allylimino)-1,1-dichloroethyl)-phosphonate ***8g***. 1.78 g (5.75 mmol) of enamine/imine **6g**/**7g** was converted into 2.09 g of **8g** (5.52 mmol, 90% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.38 (6H, t, J = 7.2 Hz), 3.92 (2H, dt, J = 5.1 Hz, J = 1.8 Hz), 4.28−4.50 (4H, m), 5.12 (1H, ddd, $J_{HH,Z}$ = 10.5 Hz, J = 3.4 Hz, J = 1.8 Hz), 5.24 (1H, ddd, $J_{HH,E}$ = 17.2 Hz, J = 3.4 Hz, J = 1.8 Hz), 5.93 (1J, ddt, $J_{HH,E}$ = 17.2 Hz, $J_{HH,Z}$ = 10.5 Hz, J = 5.1 Hz), 7.35−7.49 (5H, m), 7.57−7.71 (4H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.6 (d, $^3J_{CP}$ = 5.8 Hz), 56.0, 65.6 (d, $^2J_{CP}$ = 6.9 Hz), 82.1 (d, $^1J_{CP}$ = 176.5 Hz), 116.4, 126.8, 127.2, 127.9, 129.0, 129.5, 130.7 (d, $^3J_{CP}$ = 5.8 Hz), 134.4, 140.2, 142.2, 166.0 (d, $^2J_{CP}$ = 2.3 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ: 10.93. IR (cm^{-1}) ν_{max}: 1019 (P−O), 1054 (P−O), 1262 (P═O), 1712, 2982. MS (ESI, pos): m/z 440.3/441.3/442.3 (M + H$^+$, 100/23/64). HRMS: m/z calcd for $C_{21}H_{25}Cl_2NO_3P$ (M + H)$^+$ 440.0944, found 440.0947.

Diethyl (2-(Allylimino)-1,1-dichloro-2-(3-methoxyphenyl)ethyl)-phosphonate ***8h***. 2.01 g (6.18 mmol) of enamine/imine **6h**/**7h** was converted into 2.41 g of **8h** (6.12 mmol, 99% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.38 (6H, t, J = 7.2 Hz), 3.82 (3H, s), 3.88 (2H, dt, J = 5.3 Hz, J = 1.7 Hz), 4.27−4.49 (4H, m), 5.11 (1H, dd, $J_{HH,Z}$ = 10.8 Hz, J = 1.7 Hz), 5.22 (1H, dd, $J_{HH,E}$ = 16.8 Hz, J = 1.7 Hz), 5.91 (1H, ddt, $J_{HH,E}$ = 16.8 Hz, $J_{HH,Z}$ = 10.8 Hz, J = 5.3 Hz), 6.85−6.91 (2H, m), 6.97 (1H, dd, J = 8.1 Hz, J = 2.2 Hz), 7.34 (1H, dd, J = 8.1 Hz, J = 8.1 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.4 (d, $^3J_{CP}$ = 5.8 Hz), 55.2, 55.8, 65.3 (d, $^2J_{CP}$ = 6.9 Hz), 81.7 (d, $^1J_{CP}$ = 177.7 Hz), 114.5, 114.8, 116.1, 121.1, 129.2, 132.8 (d, $^3J_{CP}$ = 5.8 Hz), 134.3, 159.1, 165.7. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 10.96. IR (cm^{-1}) ν_{max}: 1019 (P−O), 1264 (P═O), 1578, 2982. MS (ESI, pos): m/z 394.3/395.3/396.3 (M + H$^+$, 100/16/64). HRMS: m/z calcd for $C_{16}H_{23}Cl_2NO_4P$ (M + H)$^+$ 394.0736, found 394.0743.

Diethyl (2-(Allylimino)-1,1-dichloro-2-(4-nitrophenyl)ethyl)-phosphonate ***8i***. 1.78 g (5.23 mmol) of enamine/imine **6i**/**7i** was converted and purified by column chromatography into 0.90 g **8i** (2.20 mmol, 42% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.39 (6H, t, J = 7.2 Hz), 3.86 (2H, d, J = 5.4 Hz), 4.27−4.49 (4H, m), 5.15 (1H, d, $J_{HH,Z}$ = 11.2 Hz), 5.20 (1H, d, $J_{HH,E}$ = 17.8 Hz), 5.90 (1H, ddt, $J_{HH,E}$ = 17.8 Hz, $J_{HH,E}$ = 11.2 Hz, J = 5.4 Hz), 7.54 (2H, d, J = 8.8 Hz), 8.31 (2H, d, J = 8.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.4 (d, $^3J_{CP}$ = 5.8 Hz), 56.0, 65.7 (d, $^2J_{CP}$ = 6.9 Hz), 81.0 (d, $^1J_{CP}$ = 175.4 Hz), 116.6, 123.2, 130.2, 133.5, 138.2 (d, $^3J_{CP}$ = 5.8 Hz), 148.3, 163.9. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 10.12. IR (cm^{-1}) ν_{max}: 1013 (P−O), 1052 (P−O), 1263 (P═O), 1347 (N−O), 1521 (N−O), 1600, 2980. MS (ESI, pos): m/z 409.0/410.0/411.0 (M + H$^+$, 100/16/64). HRMS: m/z calcd for $C_{15}H_{20}Cl_2N_2O_5P$ (M + H)$^+$ 409.0481, found 409.0492. Chromatography: hexanes/EtOAc 3/2, R_f = 0.11.

Diethyl (2-(Allylimino)-1,1-dichloro-2-(4-cyanophenyl)ethyl)-phosphonate ***8j***. 1.60 g (5.00 mmol) of enamine/imine **6j**/**7j** was converted and purified by column chromatography into 0.86 g **8j** (2.20 mmol, 44% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.38 (6H, t, J = 7.2 Hz), 3.84 (2H, d, J = 5.0 Hz), 4.26−4.48 (4H, m), 5.14 (d, $J_{HH,Z}$ = 11.4 Hz), 5.19 (d, $J_{HH,E}$ = 18.0 Hz), 5.89 (1H, ddt, $J_{HH,E}$ = 18.0 Hz, $J_{HH,Z}$ = 11.4 Hz, J = 5.0 Hz), 7.46 (2H, d, J = 8.3 Hz), 7.74 (2H, d, J = 8.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.4 (d, $^3J_{CP}$ = 5.8 Hz), 55.8, 65.5 (d, $^2J_{CP}$ = 6.9 Hz), 81.0 (d, $^1J_{CP}$ = 176.5 Hz), 113.3, 116.5, 117.9, 129.8, 131.8, 133.6, 136.2 (d, $^3J_{CP}$ = 4.6 Hz), 164.0. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 9.96. IR (cm^{-1}) ν_{max}: 1016 (P−O), 1052 (P−O), 1264 (P═O), 2232 (C≡N), 2984. MS (ESI, pos): m/z 389.0/390.0/391.0 (M + H$^+$, 100/17/64). HRMS: m/z calcd for $C_{16}H_{20}Cl_2N_2O_3P$ (M + H)$^+$ 389.0583, found 389.0597. Chromatography: hexanes/EtOAc 3/2, R_f = 0.10.

Synthesis of Diethyl (4-Chloro-3-(chloromethyl)-5-phenyl-3,4-dihydro-2*H*-pyrrol-4-yl)phosphonates 11a−j. In a round-bottom flame-dried flask and under a N_2-atmosphere were dissolved diethyl (2-(allylimino)-1,1-dichloro-2-phenylethyl)phosphonates **8a−j** in dry CH_2Cl_2 (1 mL/mmol). Cu(I)Cl (0.4 equiv) and *N*,*N*,*N*′,*N*′,*N*″-pentamethyldiethylenetriamine (0.8 equiv) were added, and the reaction mixture was heated to reflux. The reaction progress was monitored using HPLC. After all starting material had been consumed, the reaction mixture was poured into brine and extracted with CH_2Cl_2 (3 × 10 mL). The combined organic phases were washed with water until no more Cu salts were present (blue color of the aqueous phase disappears). The organic layer was dried over $MgSO_4$ and concentrated in vacuo, and the residue was purified by crystallization or column chromatography. Only the major diastereoisomers could be isolated in pure form.

Diethyl (cis-4-Chloro-3-(chloromethyl)-5-phenyl-3,4-dihydro-2H-pyrrol-4-yl)phosphonate ***11a***. 3.42 g (9.39 mmol) of **8a** was converted into **11a**. 3.18 g of product was obtained in a dr of 90/10 (8.73 mmol, 93% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.20 (3H, t, J = 7.2 Hz), 1.28 (3H, t, J = 7.2 Hz), 3.22−3.38 (1H, m), 3.67 (1H, dd, J = 10.7 Hz, J = 10.7 Hz), 3.96−4.23 (6H, m), 4.45 (1H, dd, J = 17.1 Hz, J = 6.6 Hz), 7.36−7.44 (3H, m), 8.02 (2H, d, J = 7.2 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 16.4 (d, $^3J_{CP}$ = 5.8 Hz), 44.2 (d, $^3J_{CP}$ = 2.3 Hz), 48.6, 63.2 (d, $^3J_{CP}$ = 10.4 Hz), 64.3 (d, $^2J_{CP}$ = 6.9 Hz), 64.7 (d, $^2J_{CP}$ = 8.1 Hz), 71.2 (d, $^1J_{CP}$ = 166.1

dx.doi.org/10.1021/jo401185u | J. Org. Chem. 2013, 78, 8232−8241

Hz), 128.0, 129.3, 130.7, 132.8, 169.1 (d, $^2J_{CP}$ = 2.3 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ: 17.11. IR (cm^{-1}) ν_{max}: 1012 (P−O), 1043 (P−O), 1263 (P═O), 1606, 2981. MS (ESI, pos): m/z 364.0/365.0/366.0 (M + H$^+$, 100/16/64). HRMS: m/z calcd for $C_{15}H_{21}Cl_2NO_3P$ (M + H)$^+$ 364.0631, found 364.0636. Chromatography: hexanes/EtOAc 1/1, R_f = 0.4.

Diethyl (cis-4-Chloro-3-(chloromethyl)-5-(4-fluorophenyl)-3,4-dihydro-2H-pyrrol-4-yl)phosphonate ***11b***. 3.00 g (7.82 mmol) of **8b** was converted into **11b**. After column chromatography, 1.77 g of product was obtained in a dr of 92/8 (4.61 mmol, 59% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.20 (3H, t, J = 7.2 Hz), 1.31 (3H, t, J = 7.2 Hz), 3.23−3.36 (1H, m), 3.66 (1H, dd, J = 10.5 Hz, J = 10.5 Hz), 3.96−4.19 (6H, m), 4.43 (1H, ddd, J = 17.1 Hz, J = 7.2 Hz, $^4J_{HP}$ = 1.7 Hz), 7.07 (2H, dd, J = 8.8 Hz, $^3J_{HF}$ = 8.8 Hz), 8.10 (2H, dd, J = 8.8 Hz, $^4J_{FH}$ = 5.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.2 (d, $^3J_{CP}$ = 5.8 Hz), 44.1 (d, $^3J_{CP}$ = 2.3 Hz), 48.4, 63.1 (d, $^3J_{CP}$ = 9.2 Hz), 64.5 (d, $^2J_{CP}$ = 12.1 Hz), 64.6 (d, $^2J_{CP}$ = 12.1 Hz), 71.1 (d, $^2J_{CP}$ = 165.0 Hz), 114.9 (d, $^2J_{CF}$ = 21.9 Hz), 128.7 (d, $^4J_{CF}$ = 3.5 Hz), 131.6 (d, $^3J_{CF}$ = 8.1 Hz), 164.2 (d, $^1J_{CF}$ = 251.22 Hz), 167.7. ^{19}F NMR (282 MHz, $CDCl_3$) δ: −109.43 to −109.32 (m). ^{31}P NMR (121 MHz, $CDCl_3$) δ: 17.08 IR (cm^{-1}) ν_{max}: 1012 (P−O), 1039 (P−O), 1263 (P═O), 1509, 2980. MS (ESI, pos): m/z 382.0/383.0/384.0 (M + H$^+$, 100/17/64). HRMS: m/z calcd for $C_{15}H_{20}Cl_2FNO_3P$ (M + H)$^+$ 382.0536, found 382.0543. Chromatography: hexanes/EtOAc 4/1, R_f = 0.15.

Diethyl (cis-4-Chloro-3-(chloromethyl)-5-(4-chlorophenyl)-3,4-dihydro-2H-pyrrol-4-yl)phosphonate ***11c***. 0.70 g (1.76 mmol) of **8c** was converted into **11c**. After column chromatography, 0.51 g of product was obtained in a dr of 90/10 (1.28 mmol, 73% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.21 (3H, t, J = 7.2 Hz), 1.31 (3H, t, J = 7.2 Hz), 3.22−3.36 (1H, m), 3.65 (1H, dd, J = 10.5 Hz, J = 10.5 Hz), 3.94−4.23 (6H, m), 4.43 (1H, ddd, J = 17.1 Hz, J = 7.2 Hz, $^4J_{HP}$ = 1.7 Hz), 7.37 (2H, d, J = 8.8 Hz), 8.02 (2H, d, J = 8.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 16.4 (d, $^3J_{CP}$ = 4.6 Hz), 44.1 (d, $^3J_{CP}$ = 3.5 Hz), 48.4, 63.2 (d, $^3J_{CP}$ = 9.2 Hz), 64.5 (d, $^2J_{CP}$ = 6.9 Hz), 64.7 (d, $^2J_{CP}$ = 6.9 Hz), 71.1 (d, $^1J_{CP}$ = 165.0 Hz), 128.2, 130.8, 131.0, 136.9, 167.8. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 17.06. IR (cm^{-1}) ν_{max}: 1012 (P−O), 1041 (P−O), 1263 (P═O), 1491, 2982. MS (ESI, pos): m/z 397.0/399.0/401.0 (M + H$^+$, 100/96/31). HRMS: m/z calcd for $C_{15}H_{20}Cl_3NO_3P$ (M + H)$^+$ 398.0241, found 398.0249. Chromatography: hexanes/EtOAc 7/3, R_f = 0.21.

Diethyl (cis-4-Chloro-3-(chloromethyl)-5-(4-bromophenyl)-3,4-dihydro-2H-pyrrol-4-yl)phosphonate ***11d***. 0.65 g (1.47 mmol) of **8d** was converted into **11d**. After column chromatography, 0.28 g of product was obtained in a dr of 89/11 (0.63 mmol, 43% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.12 (3H, t, J = 7.2 Hz), 1.22 (3H, t, J = 7.2 Hz), 3.14−3.27 (1H, m), 3.56 (1H, dd, J = 10.5 Hz, J = 10.5 Hz), 3.88−4.13 (6H, m), 4.33 (1H, ddd, J = 17.2 Hz, J = 7.0 Hz, $^4J_{HP}$ = 1.7 Hz), 7.44 (2H, d, J = 8.8 Hz), 7.88 (2H, d, J = 8.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 16.4 (d, $^3J_{CP}$ = 5.8 Hz), 44.1 (d, $^3J_{CP}$ = 3.5 Hz), 48.4, 63.2 (d, $^3J_{CP}$ = 9.2 Hz), 64.5 (d, $^2J_{CP}$ = 6.9 Hz), 64.7 (d, $^2J_{CP}$ = 6.9 Hz), 71.1 (d, $^1J_{CP}$ = 165.0 Hz), 125.4, 131.0, 131.1, 131.4, 167.8. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 16.97. IR (cm^{-1}) ν_{max}: 1010 (P−O), 1038 (P−O), 1266 (P═O), 1394, 2978. MS (ESI, pos): m/z 442.0/444.0/446.0(M + H$^+$, 62/100/45). HRMS: m/z calcd for $C_{15}H_{20}BrCl_2NO_3P$ (M + H)$^+$ 441.9736, found 441.9737. Chromatography: hexanes/EtOAc 7/3, R_f = 0.19.

Diethyl (cis-4-Chloro-3-(chloromethyl)-5-(4-methoxyphenyl)-3,4-dihydro-2H-pyrrol-4-yl)phosphonate ***11e***. 1.11 g (2.82 mmol) of **8e** was converted into **11e**. After column chromatography, 0.50 g of product was obtained in a dr of 85/15 (1.27 mmol, 45% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.19 (3H, t, J = 7.2 Hz), 1.31 (3H, t, J = 7.2 Hz), 3.21−3.35 (1H, m), 3.64 (1H, dd, J = 10.5 Hz, J = 10.5 Hz), 3.81 (3H, s), 3.91−4.22 (6H, m), 4.39 (1H, ddd, J = 17.1 Hz, J = 7.2 Hz, $^4J_{HP}$ = 1.7 Hz), 6.89 (2H, d, J = 9.4 Hz), 8.08 (2H, d, J = 9.4 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.2 (d, $^3J_{CP}$ = 5.8 Hz), 16.4 (d, $^3J_{CP}$ = 5.8 Hz), 44.3 (d, $^3J_{CP}$ = 3.5 Hz), 48.4, 55.2, 62.8 (d, $^3J_{CP}$ = 9.2 Hz), 64.3 (d, $^2J_{CP}$ = 6.9 Hz), 64.5 (d, $^2J_{CP}$ = 6.9 Hz), 71.1 (d, $^1J_{CP}$ = 163.8 Hz), 113.2, 124.8, 131.0, 161.5, 167.8 (d, $^2J_{CP}$ = 2.3 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ: 17.48. IR (cm^{-1}) ν_{max}: 1012 (P−O), 1177 (P−O), 1252 (P═O), 1513, 1606, 2978. MS (ESI, pos): m/z 394.0/395.0/396.0 (M + H$^+$, 100/18/64). HRMS: m/z calcd for $C_{16}H_{23}Cl_2NO_4P$ (M + H)$^+$ 394.0736, found 394.0740. Chromatography: hexanes/EtOAc 3/2, R_f = 0.23.

Diethyl (cis-4-Chloro-3-(chloromethyl)-5-(4-methylphenyl)-3,4-dihydro-2H-pyrrol-4-yl)phosphonate ***11f***. 1.82 g (4.81 mmol) of **8f** was converted into **11f**. After column chromatography, 0.47 g of product was obtained in a dr of 95/5 (1.25 mmol, 26% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.20 (3H, t, J = 7.2 Hz), 1.30 (3H, t, J = 7.2 Hz), 2.37 (3H, s), 3.19−3.37 (1H, m), 3.65 (1H, dd, J = 10.5 Hz, J = 10.5 Hz), 3.94−4.23 (6H, m), 4.42 (1H, ddd, J = 17.1 Hz, J = 7.2 Hz, $^4J_{HP}$ = 1.7 Hz), 7.19 (2H, d, J = 8.3 Hz), 7.95 (2H, d, J = 8.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 16.5 (d, $^3J_{CP}$ = 5.8 Hz), 21.6, 44.3 (d, $^3J_{CP}$ = 2.3 Hz), 48.5, 63.0 (d, $^3J_{CP}$ = 9.2 Hz), 64.4 (d, $^2J_{CP}$ = 6.9 Hz), 64.7 (d, $^2J_{CP}$ = 6.9 Hz), 71.2 (d, $^1J_{CP}$ = 163.8 Hz), 128.7, 129.3, 129.7, 141.0, 168.8. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 17.36. IR (cm^{-1}) ν_{max}: 1014 (P−O), 1096 (P−O), 1264 (P═O), 1606, 2359, 2981. MS (ESI, pos): m/z 378.3/379.3/380.3 (M + H$^+$, 100/18/64). HRMS: m/z calcd for $C_{16}H_{23}Cl_2NO_3P$ (M + H)$^+$ 378.0787, found 378.0782. Chromatography: hexanes/EtOAc 1/1, R_f = 0.47.

Diethyl (cis-5-([1,1′-Biphenyl]-4-yl)-4-chloro-3-(chloromethyl)-3,4-dihydro-2H-pyrrol-4-yl)phosphonate ***11g***. 1.15 g (2.61 mmol) of **8g** was converted into **11g**. After column chromatography, 0.42 g of product was obtained in a dr of 96/4 (0.97 mmol, 37% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.22 (3H, t, J = 7.0 Hz), 1.31 (3H, t, J = 7.0 Hz), 3.25−3.40 (1H, m), 3.68 (1H, dd, J = 10.5 Hz, J = 10.5 Hz), 4.00−4.21 (6H, m), 4.47 (1H, ddd, J = 17.1 Hz, J = 6.9 Hz, $^4J_{HP}$ = 1.9 Hz), 7.35−7.47 (3H, m), 7.62−7.65 (4H, m), 8.14−8.18 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.4 (d, $^3J_{CP}$ = 5.8 Hz), 16.5 (d, $^3J_{CP}$ = 5.8 Hz), 44.3, 48.5, 63.3 (d, $^3J_{CP}$ = 10.4 Hz), 64.5 (d, $^2J_{CP}$ = 6.9 Hz), 64.7 (d, $^2J_{CP}$ = 6.9 Hz), 71.3 (d, $^1J_{CP}$ = 165.0 Hz), 126.6, 127.2, 127.9, 129.0, 129.9, 131.5, 140.3, 143.3, 168.5 (d, $^2J_{CP}$ = 2.3 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ: 17.27. IR (cm^{-1}) ν_{max}: 1014 (P−O), 1043 (P−O), 1263 (P═O), 1602, 2980. MS (ESI, pos): m/z 440.3/441.3/442.3 (M + H$^+$, 100/23/64). HRMS: m/z calcd for $C_{21}H_{25}Cl_2NO_3P$ (M + H)$^+$ 440.0944, found 440.0949. Chromatography: hexanes/EtOAc 7/3, R_f = 0.29.

Diethyl (cis-4-Chloro-3-(chloromethyl)-5-(3-methoxyphenyl)-3,4-dihydro-2H-pyrrol-4-yl)phosphonate ***11h***. 2.11 g (5.35 mmol) of **8h** was converted into **11h**. After column chromatography, 1.27 g of product was obtained in a dr of 93/7 (3.21 mmol, 60% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.21 (3H, t, J = 7.2 Hz), 1.29 (3H, t, J = 7.2 Hz), 3.24−3.36 (1H, m), 3.66 (1H, dd, J = 10.5 Hz, J = 10.5 Hz), 3.84, 3.96−4.18 (6H, m), 4.45 (1H, dd, J = 17.1 Hz, J = 7.2 Hz), 6.99 (1H, d, J = 8.1 Hz), 7.30 (1H, dd, J = 8.1 Hz, J = 8.1 Hz), 7.63−7.66 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 16.4 (d, $^3J_{CP}$ = 5.8 Hz), 44.2 (d, $^3J_{CP}$ = 2.3 Hz), 48.6, 55.4, 63.1 (d, $^3J_{CP}$ = 10.4 Hz), 64.3 (d, $^2J_{CP}$ = 10.4 Hz), 64.7 (d, $^2J_{CP}$ = 10.4 Hz), 71.2 (d, $^1J_{CP}$ = 165.0 Hz), 114.1, 117.0, 121.7, 129.0, 133.8, 159.1, 168.8. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 17.21. IR (cm^{-1}) ν_{max}: 1013 (P−O), 1263 (P═O), 1578, 2981. MS (ESI, pos): m/z 394.3/395.3/396.3 (M + H$^+$, 100/16/64). HRMS: m/z calcd for $C_{16}H_{23}Cl_2NO_4P$ (M + H)$^+$ 394.0736, found 394.0732. Chromatography: hexanes/EtOAc 3/2, R_f = 0.29.

Diethyl (cis-4-Chloro-3-(chloromethyl)-5-(4-nitrophenyl)-3,4-dihydro-2H-pyrrol-4-yl)phosphonate ***11i***. 0.60 g (1.47 mmol) of **8i** was converted into **11i**. After one crystallization, 0.14 g of product was obtained in a dr of 93/7 (0.34 mmol, 23% yield, orange needles). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.22 (3H, t, J = 7.2 Hz), 1.32 (3H, t, J = 7.2 Hz), 3.25−3.40 (1H, m), 3.67 (1H, dd, J = 10.5 Hz, J = 10.5 Hz), 3.97−4.25 (6H, m), 4.50 (1H, dd, J = 17.6 Hz, J = 7.2 Hz), 8.25 (4H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 16.5 (d, $^3J_{CP}$ = 5.8 Hz), 43.9 (d, $^3J_{CP}$ = 2.3 Hz), 48.4, 63.6 (d, $^3J_{CP}$ = 9.2 Hz), 64.8 (d, $^2J_{CP}$ = 6.9 Hz), 71.1 (d, $^1J_{CP}$ = 163.8 Hz), 123.0, 130.5, 138.5, 149.0, 167.4. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 16.59. IR (cm^{-1}) ν_{max}: 1011 (P−O), 1041 (P−O), 1266 (P═O), 1342 (N−O), 1518 (N−O), 1594, 2980. MS (ESI, pos): m/z 409.0/410.0/411.0 (M + H$^+$, 100/16/64). HRMS: m/z calcd for $C_{15}H_{20}Cl_2N_2O_5P$ (M + H)$^+$ 409.0481, found 409.0483. Melting point range: 108.0−109.0 °C.

dx.doi.org/10.1021/jo401185u | J. Org. Chem. 2013, 78, 8232−8241

Diethyl (cis-4-Chloro-3-(chloromethyl)-5-(4-cyanophenyl)-3,4-dihydro-2H-pyrrol-4-yl)phosphonate ***11j***. 0.85 g (2.18 mmol) of **8j** was converted into **11j**. After one crystallization, 0.12 g of product was obtained in a dr of 95/5 (0.31 mmol, 14% yield, transparent crystals). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.21 (3H, t, J = 7.2 Hz), 1.32 (3H, t, J = 6.9 Hz), 3.24−3.37 (1H, m), 3.66 (1H, dd, J = 10.5 Hz, J = 10.5 Hz), 3.96−4.24 (6H, m), 4.48 (1H, dd, J = 17.6 Hz, J = 7.2 Hz), 7.69 (2H, d, J = 8.3 Hz), 8.19 (2H, d, J = 8.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 16.5 (d, $^3J_{CP}$ = 4.6 Hz), 44.0 (d, $^3J_{CP}$ = 2.3 Hz), 48.4, 63.6 (d, $^3J_{CP}$ = 9.2 Hz), 64.8 (d, $^2J_{CP}$ = 6.9 Hz), 71.1 (d, $^1J_{CP}$ = 166.1 Hz), 114.2, 118.5, 130.1, 131.7, 136.7, 167.6. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 16.67. IR (cm^{-1}) ν_{max}: 1011 (P−O), 1039 (P−O), 1266 (P═O), 2230 (C≡N), 2984. MS (ESI, pos): m/z 389.0/390.0/391.0 (M + H$^+$, 100/17/64). HRMS: m/z calcd for $C_{16}H_{20}Cl_2N_2O_3P$ (M + H)$^+$ 389.0583, found 389.0595. Melting point range: 111.0−112.5 °C.

Synthesis of Diethyl (2-Phenyl-3-azabicyclo[3.1.0]hex-2-en-1-yl)phosphonates 14a−j. In a round-bottom flame-dried flask and under a N_2-atmosphere were dissolved diethyl (*cis*-4-chloro-3-(chloromethyl)-5-phenyl-3,4-dihydro-2*H*-pyrrol-4-yl)phosphonates **11a−j** in dry THF (1 mL/mmol). The solution was cooled to −78 °C, and *n*-BuLi (1.2 equiv, however for **14j** 2.2 equiv was used) was added in a dropwise fashion. The reaction mixture was kept at −78 °C for 2 h and was then slowly warmed to room temperature. Water was added, and the solution was extracted with diethyl ether (3 × 10 mL). After the combined organic layers were dried over $MgSO_4$, the solvent was removed in vacuo and the residue was purified using column chromatography.

Diethyl (2-Phenyl-3-azabicyclo[3.1.0]hex-2-en-1-yl)phosphonate ***14a***. 2.50 g (6.86 mmol) of **11a** was converted into **14a**. After column chromatography, 1.53 g of product was obtained (5.21 mmol, 76% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.84−0.90 (1H, ~q), 1.17 (3H, t, J = 7.2 Hz), 1.20 (3H, t, J = 7.2 Hz), 1.76 (1H, ddd, $^3J_{HP}$ = 14.6 Hz, J = 8.5 Hz, J = 4.7 Hz), 2.58−2.69 (1H, m), 3.91−4.03 (4H, m), 4.10 (2H, ~t), 7.37−7.44 (3H, m), 7.91 (2H, d, J = 6.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.2 (d, $^3J_{CP}$ = 4.6 Hz), 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 19.2, 28.7, 34.0 (d, $^1J_{CP}$ = 199.6 Hz), 61.3 (d, $^3J_{CP}$ = 3.5 Hz), 62.2 (d, $^2J_{CP}$ = 5.8 Hz), 62.4 (d, $^2J_{CP}$ = 6.9 Hz), 128.0, 128.7, 130.5, 134.1, 173.1 (d, $^2J_{CP}$ = 8.1 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ: 22.91. IR (cm^{-1}) ν_{max}: 1022 (P−O), 1049 (P−O), 1247 (P═O), 1596, 2982. MS (ESI, pos): m/z 294.3/295.3 (M + H$^+$, 100/16). HRMS: m/z calcd for $C_{15}H_{21}NO_3P$ (M + H)$^+$ 294.1254, found 294.1264. Chromatography: EtOAc, R_f = 0.06.

Diethyl (2-(4-Fluorophenyl)-3-azabicyclo[3.1.0]hex-2-en-1-yl)-phosphonate ***14b***. 0.18 g (0.47 mmol) of **11b** was converted into **14b**. After column chromatography, 72 mg of product was obtained (0.23 mmol, 49% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.83−0.89 (1H, m), 1.18 (3H, t, J = 7.5 Hz) 1.21 (3H, t, J = 7.5 Hz), 1.75 (1H, ddd, $^3J_{HP}$ = 14.5 Hz, J = 8.4 Hz, J = 4.3 Hz), 2.54−2.69 (1H, m), 3.93−4.05 (4H, m), 4.08 (2H, ~t), 7.09 (2H, dd, J = 8.8 Hz, $^3J_{FH}$ = 8.8 Hz), 7.94 (2H, dd, J = 8.8 Hz, $^4J_{HF}$ = 5.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.3 (d, $^3J_{CP}$ = 5.2 Hz), 16.3 (d, $^3J_{CP}$ = 5.2 Hz), 19.2, 28.9, 33.9 (d, $^1J_{CP}$ = 200.8 Hz), 61.2 (d, $^3J_{CP}$ = 3.5 Hz), 62.3 (d, $^2J_{CP}$ = 5.8 Hz), 62.5 (d, $^2J_{CP}$ = 5.8 Hz), 115.1 (d, $^2J_{CF}$ = 21.9 Hz), 130.3 (d, $^4J_{CF}$ = 2.3 Hz), 130.9 (d, $^3J_{CF}$ = 8.1 Hz), 164.3 (d, $^1J_{CF}$ = 250.4 Hz), 172.0 (d, $^2J_{CP}$ = 8.1 Hz). ^{19}F NMR (282 MHz, $CDCl_3$) δ: −109.92 to −109.82 (m). ^{31}P NMR (121 MHz, $CDCl_3$) δ: 22.83. IR (cm^{-1}) ν_{max}: 1019 (P−O), 1047 (P−O), 1229 (P═O), 1510, 2984. MS (ESI, pos): m/z 312.3/313.3 (M + H$^+$, 100/17). HRMS: m/z calcd for $C_{15}H_{20}FNO_3P$ (M + H)$^+$ 312.1159, found 312.1165. Chromatography: EtOAc, R_f = 0.09.

Diethyl (2-(4-Chlorophenyl)-3-azabicyclo[3.1.0]hex-2-en-1-yl)-phosphonate ***14c***. 0.15 g (0.38 mmol) of **11c** was converted into **14c**. After column chromatography, 41 mg of product was obtained (0.13 mmol, 33% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.81−0.88 (1H, m), 1.18 (3H, t, J = 7.2 Hz), 1.22 (3H, t, J = 7.2 Hz), 1.75 (1H, ddd, $^3J_{HP}$ = 14.5 Hz, J = 8.4 Hz, J = 4.4 Hz), 2.58−2.69 (1H, m), 3.93−4.05 (4H, m), 4.09 (2H, ~t), 7.38 (2H, d, J = 8.5 Hz), 7.87 (2H, d, J = 8.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 16.4 (d, $^3J_{CP}$ = 5.8 Hz), 19.2, 28.9, 33.9 (d, $^1J_{CP}$ = 199.6 Hz), 61.3 (d, $^3J_{CP}$ = 3.5 Hz), 62.4 (d, $^3J_{CP}$ = 5.8 Hz), 62.6 (d, $^3J_{CP}$ = 5.8 Hz), 128.3, 130.2, 132.5, 136.7, 172.1 (d, $^2J_{CP}$ = 8.1 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ: 22.74. IR (cm^{-1}) ν_{max}: 1020 (P−O), 1048 (P−O), 1247 (P═O), 1596, 2984. MS (ESI, pos): m/z 328.3/330.3/329.3 (M + H$^+$, 100/32/17). HRMS: m/z calcd for $C_{15}H_{20}ClNO_3P$ (M + H)$^+$ 328.0864, found 328.0868. Chromatography: EtOAc, R_f = 0.09.

Diethyl (2-(4-Methoxyphenyl)-3-azabicyclo[3.1.0]hex-2-en-1-yl)-phosphonate ***14e***. 1.13 g (2.87 mmol) of **11e** was converted into **14e**. After column chromatography, 0.47 g of product was obtained (1.46 mmol, 51% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.81−0.87 (1H, m), 1.20 (6H, t, J = 7.5 Hz), 1.74 (1H, ddd, $^3J_{HP}$ = 14.6 Hz, J = 8.5 Hz, J = 4.4 Hz), 2.56−2.66 (1H, m), 3.84 (3H, s), 3.93−4.03 (4H, m), 4.06 (2H, m), 6.91 (2H, d, J = 8.8 Hz), 7.91 (2H, d, J = 8.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 15.9 (d, J = 4.6 Hz), 16.0 (d, J = 4.6 Hz), 18.7, 28.5, 33.4 (d, $^1J_{CP}$ = 199.6 Hz), 54.9, 60.5 (d, $^3J_{CP}$ = 3.5 Hz), 61.8 (d, $^2J_{CP}$ = 6.9 Hz), 62.1 (d, $^2J_{CP}$ = 6.9 Hz), 113.0, 126.5, 130.2, 161.2, 171.8 (d, $^2J_{CP}$ = 6.9 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ: 23.26. IR (cm^{-1}) ν_{max}: 1018 (P−O), 1174(P−O), 1249 (P═O), 1514, 1607, 2918, 3429. MS (ESI, pos): m/z 324.3/325.3(M + H$^+$, 100/17). HRMS: m/z calcd for $C_{16}H_{23}NO_4P$ (M + H)$^+$ 324.1359, found 324.1359. Chromatography: EtOAc, R_f = 0.08.

Diethyl (2-(4-Methylphenyl)-3-azabicyclo[3.1.0]hex-2-en-1-yl)-phosphonate ***14f***. 2.70 g (7.14 mmol) of **11f** was converted into **14f**. After column chromatography, 1.18 g of product was obtained (3.86 mmol, 54% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.83−0.88 (1H, m), 1.14−1.26 (6H, m), 1.74 (1H, ddd, $^3J_{HP}$ = 14.3 Hz, J = 8.3 Hz, J = 4.4 Hz), 2.38 (3H, s), 2.61 (1H, m), 3.92−4.04 (4H, m), 4.04−4.12 (2H, m), 7.20 (d, J = 8.0 Hz), 7.82 (d, J = 8.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.2 (d, $^3J_{CP}$ = 5.8 Hz), 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 19.2, 21.5, 28.7, 33.9 (d, $^1J_{CP}$ = 201.9 Hz), 61.1 (d, $^3J_{CP}$ = 3.5 Hz), 62.2 (d, $^2J_{CP}$ = 5.8 Hz), 62.4 (d, $^2J_{CP}$ = 5.8 Hz), 128.7, 131.3, 140.7, 173.0 (d, $^2J_{CP}$ = 8.1 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ: 23.18. IR (cm^{-1}) ν_{max}: 1024 (P−O), 1050(P−O), 1248 (P═O), 1594, 2922. MS (ESI, pos): m/z 308.3/309.3 (M + H$^+$, 100/18). HRMS: m/z calcd for $C_{16}H_{23}NO_3P$ (M + H)$^+$ 308.1410, found 308.1411. Chromatography: EtOAc, R_f = 0.09.

Diethyl (2-([1,1′-Biphenyl]-4-yl)-3-azabicyclo[3.1.0]hex-2-en-1-yl)phosphonate ***14g***. 1.84 g (4.18 mmol) of **11g** was converted into **14g**. After column chromatography, 0.56 g of product was obtained (1.50 mmol, 30% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.85−0.92 (1H, ~q), 1.21 (6H, t, J = 7.6 Hz), 1.78 (1H, ddd, $^3J_{HP}$ = 14.2 Hz, J = 8.9 Hz, J = 4.8 Hz), 2.58−2.71 (1H, m), 3.95−4.07 (4H, m), 4.10−4.13 (2H, ~t), 7.34−7.38 (1H, m), 7.45 (2H, dd, J = 7.3 Hz, J = 7.3 Hz), 7.64 (4H, d, J = 8.3 Hz), 8.01 (2H, d, J = 7.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 16.4 (d, $^3J_{CP}$ = 5.8 Hz), 19.3, 28.8, 33.9 (d, $^1J_{CP}$ = 199.6 Hz), 61.3 (d, $^3J_{CP}$ = 3.5 Hz), 62.3 (d, $^2J_{CP}$ = 5.8 Hz), 62.5 (d, $^2J_{CP}$ = 5.8 Hz), 126.7, 127.2, 127.8, 128.9, 129.3, 133.0, 140.5, 143.2, 172.8 (d, $^2J_{CP}$ = 8.1 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ: 23.02. IR (cm^{-1}) ν_{max}:1021 (P−O), 1045 (P−O), 1246 (P═O), 1594, 2982. MS (ESI, pos): m/z 370.3/371.3 (M + H$^+$, 100/23). HRMS: m/z calcd for $C_{21}H_{25}NO_3P$ (M + H)$^+$ 370.1567, found 370.1563. Chromatography: EtOAc, R_f = 0.10.

Diethyl (2-(3-Methoxyphenyl)-3-azabicyclo[3.1.0]hex-2-en-1-yl)-phosphonate ***14h***. 1.72 g (4.36 mmol) of **11h** was converted into **14h**. After column chromatography, 1.01 g of product was obtained (3.14 mmol, 72% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.86 (1H, ~q), 1.18 (3H, t, J = 7.3 Hz), 1.20 (3H, t, J = 7.3 Hz), 1.75 (1H, ddd, $^3J_{HP}$ = 14.7 Hz, J = 8.4 Hz, J = 4.3 Hz), 2.57−2.69 (1H, m), 3.86 (3H, s), 3.93−4.04 (4H, m), 4.08 (2H, ~t), 6.99 (1H, dd, J = 8.1 Hz, J = 2.8 Hz), 7.31 (1H, dd, J = 8.1 Hz, J = 8.1 Hz), 7.48−7.54 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 19.2, 28.9, 34.0 (d, $^1J_{CP}$ = 200.8 Hz), 55.4, 61.3 (d, $^3J_{CP}$ = 3.5 Hz), 62.2 (d, $^2J_{CP}$ = 6.9 Hz), 62.5 (d, $^2J_{CP}$ = 6.9 Hz), 113.3, 117.1, 121.3, 129.0, 135.3, 152.3, 173.0 (d, $^2J_{CP}$ = 6.9 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ: 22.97. IR (cm^{-1}) ν_{max}: 1018 (P−O), 1238 (P═O), 1327, 1575, 2981. MS (ESI, pos): m/z 324.3/325.3 (M + H$^+$, 100/16). HRMS: m/z calcd for $C_{16}H_{23}NO_4P$ (M + H)$^+$ 324.1359, found 324.1361. Chromatography: EtOAc, R_f = 0.18.

dx.doi.org/10.1021/jo401185u | *J. Org. Chem.* 2013, 78, 8232−8241

*Diethyl (2-(4-Nitrophenyl)-3-azabicyclo[3.1.0]hex-2-en-1-yl)-phosphonate **14i**.* 0.38 g (0.94 mmol) of **11i** was converted into **14i**. After column chromatography, 64 mg of product was obtained (0.19 mmol, 20% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.87−0.93 (1H, m), 1.19 (3H, t, J = 6.9 Hz), 1.23 (3H, t, J = 7.2 Hz), 1.80 (1H, ddd, $^3J_{HP}$ = 13.9 Hz, J = 8.1 Hz, J = 4.3 Hz), 2.69 (1H, m), 3.95−4.08 (4H, m), 4.16 (2H, ∼t), 8.10 (2H, d, J = 8.5 Hz), 8.27 (2H, d, J = 8.5 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 16.3 (d, $^3J_{CP}$ = 5.8 Hz), 16.4 (d, $^3J_{CP}$ = 6.9 Hz), 19.3, 29.0, 34.1 (d, $^1J_{CP}$ = 201.9 Hz), 61.9, 62.5 (d, $^2J_{CP}$ = 5.8 Hz), 62.7 (d, $^2J_{CP}$ = 5.8 Hz), 123.3, 129.8, 139.9, 150.0, 171.5 (d, $^2J_{CP}$ = 9.2 Hz). ^{31}P NMR (121 MHz, $CDCl_3$) δ: 22.17. IR (cm^{-1}) ν_{max}: 1018 (P−O), 1047 (P−O), 1248 (P═O), 1325 (N−O), 1519 (N−O), 1586, 2983. MS (ESI, pos): m/z 339.3/340.3 (M + H$^+$, 100/16). HRMS: m/z calcd for $C_{15}H_{20}N_2O_5P$ (M + H)$^+$ 339.1104, found 339.1114. Chromatography: EtOAc, R_f = 0.21.

*Diethyl (2-(4-Pentanoylphenyl)-3-azabicyclo[3.1.0]hex-2-en-1-yl)phosphonate **14j**.* 0.44 g (1.13 mmol) of **11j** was converted into **14j**. After column chromatography, 0.15 g of product was obtained (0.41 mmol, 36% yield, brown oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.86−0.92 (1H, m), 0.96 (3H, t, J = 7.4 Hz), 1.17 (3H, t, J = 7.3 Hz), 1.21 (3H, t, J = 7.3 Hz), 1.41 (2H, sext, J = 7.4 Hz), 1.73 (2H, quint, J = 7.4 Hz), 1.78−1.83 (1H, m), 2.61−2.71 (1H, m), 2.99 (2H, t, J = 7.4 Hz), 3.92−4.05 (4H, m), 4.14 (2H, d, J = 3.9 Hz), 7.99 (4H, s). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 14.0, 16.3 (d, $^3J_{CP}$ = 6.9 Hz), 16.4 (d, $^3J_{CP}$ = 6.9 Hz), 19.2, 22.5, 26.4, 28.9, 34.1 (d, $^1J_{CP}$ = 200.8 Hz), 38.6, 61.7 (d, $^3J_{CP}$ = 3.5 Hz), 62.4 (d, $^2J_{CP}$ = 5.8 Hz), 62.6 (d, $^2J_{CP}$ = 5.8 Hz), 127.8, 129.0, 138.1, 138.3, 172.5 (d, $^2J_{CP}$ = 9.2 Hz), 200.3. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 22.56. IR (cm^{-1}) ν_{max}: 1024 (P−O), 1249 (P═O), 1684 (C═O), 2931. MS (ESI, pos): m/z 378.3/379.3 (M + H$^+$, 100/16). HRMS: m/z calcd for $C_{20}H_{29}NO_4P$ (M + H)$^+$ 378.1829, found 378.1835. Chromatography: EtOAc, R_f = 0.16.

Synthesis of Diethyl (2-Phenyl-3-azabicyclo[3.1.0]hexan-1-yl)phosphonates 1a−j. Diethyl (2-phenyl-3-azabicyclo[3.1.0]hex-2-en-1-yl)phosphonates **14a−j** were dissolved in MeOH (1 mL/mmol). Then $NaCNBH_3$ (1.05 equiv) and HOAc (1.05 equiv) were added. The reaction progress was monitored using HPLC. After all starting material had been consumed, the reaction mixture was poured into aqueous $NaHCO_3$ and extracted with diethyl ether (3 × 10 mL). The combined organic layers were dried over $MgSO_4$ and concentrated in vacuo. All compounds were obtained in a dr of ≥99/1.

Diethyl ((1S,2S*,5R*)-2-Phenyl-3-azabicyclo[3.1.0]hexan-1-yl)-phosphonate **1a**.* 87 mg (0.32 mmol) of **14a** was converted into **1a**. 79 mg of product was obtained (0.27 mmol, 84% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.00 (3H, t, J = 7.2 Hz), 1.19−1.32 (3H, t, J = 7.2 Hz, 2H, m), 1.97−2.06 (1H, m), 2.09 (1H, br s), 3.16 (2H, s), 3.64−4.05 (4H, m), 4.52 (d, $^3J_{HP}$ = 3.9 Hz), 7.27−7.34 (3H, m), 7.48 (2H, d, J = 6.6 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 8.6, 16.1 (d, $^3J_{CP}$ = 5.8 Hz), 16.5 (d, $^3J_{CP}$ = 5.8 Hz), 24.8, 25.8 (d, $^1J_{CP}$ = 198.5 Hz), 47.7 (d, $^3J_{CP}$ = 3.5 Hz), 61.7 (d, $^2J_{CP}$ = 5.8 Hz), 61.9 (d, $^2J_{CP}$ = 6.9 Hz), 63.0 (d, $^2J_{CP}$ = 10.4 Hz), 127.9, 128.0, 128.2, 139.6. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 28.51. IR (cm^{-1}) ν_{max}: 1019 (P−O), 1056 (P−O), 1234 (P═O), 1366, 2981, 3310. MS (ESI, pos): m/z 296.3/297.3 (M + H$^+$, 100/16). HRMS: m/z calcd for $C_{15}H_{23}NO_3P$ (M + H)$^+$ 296.1410, found 296.1416.

Diethyl ((1S,2S*,5R*)-2-(4-Fluorophenyl)-3-azabicyclo[3.1.0]-hexan-1-yl)phosphonate **1b**.* 0.48 g (1.53 mmol) of **14b** was converted into **1b**. 0.36 g of product was obtained (1.13 mmol, 74% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.02 (3H, t, J = 7.2 Hz), 1.25 (3H, t, J = 7.2 Hz, 2H, m), 1.89−2.01 (1H, m), 2.43 (1H, br s), 3.11 (2H, br s), 3.66−4.04 (4H, m), 4.47 (1H, d, $^3J_{HP}$ = 4.4 Hz), 6.98 (2H, dd, J = 8.6 Hz, $^3J_{HF}$ = 8.6 Hz), 7.45 (2H, dd, J = 8.6 Hz, $^4J_{HF}$ = 5.5). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 8.0, 15.9 (d, $^3J_{CP}$ = 6.9 Hz), 16.3 (d, $^3J_{CP}$ = 6.9 Hz), 24.6, 25.7 (d, J = 198.5 Hz), 47.3 (d, $^3J_{CP}$ = 3.5 Hz), 61.5 (d, J = 6.9 Hz), 61.7 (d, J = 6.9 Hz), 61.9 (d, $^2J_{CP}$ = 10.4 Hz), 114.6 (d, $^2J_{CF}$ = 21.9 Hz), 129.4 (d, $^3J_{CF}$ = 8.1 Hz), 135.6 (d, $^4J_{CF}$ = 2.3 Hz), 162.2 (d, $^1J_{CF}$ = 245.8 Hz). ^{19}F NMR (282 MHz, $CDCl_3$) δ: −115.20 to −115.11. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 28.42. IR (cm^{-1}) ν_{max}: 1021 (P−O), 1058 (P−O), 1231 (P═O), 1508, 2982. MS (ESI, pos): m/z 314.3/315.3 (M + H$^+$, 100/17). HRMS: m/z calcd for $C_{15}H_{22}FNO_3P$ (M + H)$^+$ 314.1316, found 314.1325

Diethyl ((1S,2S*,5R*)-2-(4-Chlorophenyl)-3-azabicyclo[3.1.0]-hexan-1-yl)phosphonate **1c**.* 0.20 g (0.61 mmol) of **14c** was converted into **1c**. 0.17 g of product was obtained (0.52 mmol, 85% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.05 (3H, d, J = 7.2 Hz), 1.11−1.29 (3H, m, 2H, m), 2.00 (1H, m), 2.53 (1H, br s), 3.15 (2H, br s), 3.72−4.05 (4H, m), 4.49 (1H, d, $^3J_{HP}$ = 3.9 Hz), 7.27−7.31 (2H, m), 7.41−7.44 (2H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 8.4, 16.1 (d, $^3J_{CP}$ = 5.8 Hz), 16.5 (d, $^3J_{CP}$ = 5.8 Hz), 24.8, 25.7 (d, $^1J_{CP}$ = 198.5 Hz), 47.5, 61.8 (d, $^3J_{CP}$ = 5.8 Hz), 62.0 (d, $^3J_{CP}$ = 5.8 Hz), 62.1 (d, $^2J_{CP}$ = 11.5 Hz), 128.2, 129.4, 133.4, 138.3. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 28.32. IR (cm^{-1}) ν_{max}: 1014 (P−O), 1021 (P−O), 1232 (P═O), 1491, 2924, 3423. MS (ESI, pos): m/z 330.3/331.3/332.3(M + H$^+$, 100/17/32). HRMS: m/z calcd for $C_{15}H_{22}ClNO_3P$ (M + H)$^+$ 330.1021, found 330.1024.

Diethyl ((1S,2S*,5R*)-2-(4-Methoxyphenyl)-3-azabicyclo[3.1.0]-hexan-1-yl)phosphonate **1e**.* 87 mg (0.27 mmol) of **14e** was converted into **1e**. 81 mg of product was obtained (0.25 mmol, 92% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.03 (3H, t, J = 7.2 Hz), 1.19−1.33 (3H, t, J = 7.2 Hz, 2H, m), 1.96−2.04 (1H, m), 3.15, 3.71−4.09 (4H, m), 3.80 (3H, s), 4.52 (1H, d, $^3J_{HP}$ = 4.4 Hz), 6.86 (2H, d, J = 8.3 Hz), 7.41 (2H, d, J = 8.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 8.6, 16.1 (d, $^3J_{CP}$ = 6.9 Hz), 16.5 (d, $^3J_{CP}$ = 6.9 Hz), 24.3, 25.5 (d, $^1J_{CP}$ = 198.5 Hz), 47.3, 55.3, 61.8 (d, $^2J_{CP}$ = 5.8 Hz), 62.1 (d, $^2J_{CP}$ = 5.8 Hz), 62.5 (d, $^2J_{CP}$ = 11.5 Hz), 113.6, 129.2, 130.6, 159.4. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 27.95. IR (cm^{-1}) ν_{max}: 1019 (P−O), 1177(P−O), 1249 (P═O), 1514, 1607, 2918, 3429. MS (ESI, pos): m/z 326.3/327.3 (M + H$^+$, 100/18). HRMS: m/z calcd for $C_{16}H_{25}NO_4P$ (M + H)$^+$ 326.1516, found 326.1521.

Diethyl ((1S,2S*,5R*)-2-(4-Methylphenyl)-3-azabicyclo[3.1.0]-hexan-1-yl)phosphonate **1f**.* 75 mg (0.24 mmol) of **14f** was converted into **1f**. 47 mg of product was obtained (0.15 mmol, 63% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.03 (3H, t, J = 6.9 Hz), 1.21−1.30 (3H, t, J = 7.2 Hz, 2H, m), 1.91−2.21 (2H, m), 2.33 (3H, s), 3.15 (2H, br s), 3.67−4.05 (4H, m), 4.50 (1H, d, $^3J_{HP}$ = 3.9 Hz), 7.12 (2H, d, J = 8.0 Hz), 7.36 (2H, d, J = 8.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 8.5, 16.1 (d, $^3J_{CP}$ = 6.9 Hz), 16.5 (d, $^3J_{CP}$ = 6.9 Hz), 21.2, 24.9, 25.7 (d, $^1J_{CP}$ = 197.3 Hz), 47.7 (d, $^3J_{CP}$ = 3.5 Hz), 61.7 (d, $^2J_{CP}$ = 6.9 Hz), 61.9 (d, $^2J_{CP}$ = 5.8 Hz), 62.8 (d, $^2J_{CP}$ = 10.4 Hz), 127.8, 128.9, 136.4, 137.5. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 28.62. IR (cm^{-1}) ν_{max}: 1020 (P−O), 1177(P−O), 1236 (P═O), 1443, 2978. MS (ESI, pos): m/z 310.3/311.3 (M + H$^+$, 100/18). HRMS: m/z calcd for $C_{16}H_{25}NO_3P$ (M + H)$^+$ 310.1567, found 310.1569.

Diethyl ((1S,2S*,5R*)-2-([1,1′-Biphenyl]-4-yl)-3-azabicyclo-[3.1.0]hexan-1-yl)phosphonate **1g**.* 0.12 g (0.32 mmol) of **14g** was converted into **1g**. 0.11 g of product was obtained (0.30 mmol, 91% yield, pale yellow solid). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.03 (3H, t, J = 7.2 Hz), 1.28 (3H, t, J = 7.2 Hz, 2H, m), 1.99−2.09 (1H, m), 3.19 (2H, d, J = 1.7 Hz), 3.73−4.14 (4H, m), 4.58 (1H, d, $^3J_{HP}$ = 4.4 Hz), 7.21−7.26 (1H, m), 7.32−7.37 (1H, m), 7.42−7.47 (2H, m), 7.56 (2H, s), 7.56−7.60 (3H, m). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 8.5, 16.1 (d, $^3J_{CP}$ = 6.9 Hz), 16.5 (d, $^3J_{CP}$ = 5.8 Hz), 24.9, 25.9 (d, $^1J_{CP}$ = 198.5 Hz), 47.7 (d, $^3J_{CP}$ = 3.5 Hz), 61.8 (d, $^2J_{CP}$ = 5.8 Hz), 62.0 (d, $^2J_{CP}$ = 5.8 Hz), 62.7 (d, $^2J_{CP}$ = 10.4 Hz), 126.9, 127.1, 127.4, 128.4, 128.9, 138.9, 140.7, 141.0. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 28.59. IR (cm^{-1}) ν_{max}:1017 (P−O), 1052 (P−O), 1233 (P═O), 1484, 2982. MS (ESI, pos): m/z 372.3/373.3 (M + H$^+$, 100/23). HRMS: m/z calcd for $C_{21}H_{27}NO_3P$ (M + H)$^+$ 372.1723, found 372.1718.

Diethyl ((1S,2S*,5R*)-2-(3-Methoxyphenyl)-3-azabicyclo[3.1.0]-hexan-1-yl)phosphonate **1h**.* 88 mg (0.27 mmol) of **14h** was converted into **1h**. After column chromtography 26 mg of product was obtained (0.08 mmol, 30% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.04 (3H, t, J = 7.3 Hz), 1.19−1.29 (3H, t, J = 7.3 Hz, 2H, m), 1.96−2.02 (1H, m), 2.04 (1H, br s), 3.16 (2H, s), 3.69−4.16 (4H, m), 3.81 (3H, s), 4.51 (d, $^3J_{CP}$ = 4.4 Hz), 6.82 (1H, dd, J = 7.8 Hz, J = 4.5 Hz), 7.05−7.09 (2H, m), 7.23 (1H, dd, J = 7.3 Hz, J = 7.3 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 8.6, 16.1 (d, $^3J_{CP}$ = 6.9 Hz), 16.5 (d, $^3J_{CP}$ = 5.8 Hz), 25.0, 25.7 (d, $^1J_{CP}$ = 197.3 Hz), 47.7 (d, $^3J_{CP}$ = 3.5 Hz), 55.3, 61.7 (d, $^2J_{CP}$ = 6.9 Hz), 61.9 (d, $^2J_{CP}$ = 5.8 Hz), 62.9 (d, $^2J_{CP}$ = 10.4 Hz), 113.2, 113.7, 120.2, 129.1, 141.3, 159.5. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 28.53. IR (cm^{-1}) ν_{max}: 1020 (P−O), 1232 (P═O), 1438,

dx.doi.org/10.1021/jo401185u | J. Org. Chem. 2013, 78, 8232−8241

1602, 2981, 3308. MS (ESI, pos): m/z 326.3/327.3 (M + H^+, 100/17). HRMS: m/z calcd for $C_{16}H_{25}NO_4P$ (M + H)$^+$ 326.1516, found 326.1512. Chromatography: EtOAc, R_f = 0.08.

Diethyl ((1S,2S*,5R*)-2-(4-Nitrophenyl)-3-azabicyclo[3.1.0]-hexan-1-yl)phosphonate* ***1i.*** 70 mg (0.21 mmol) of **14i** was converted into **1i**. After column chromtography 58 mg of product was obtained (0.17 mmol, 81% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 1.06 (3H, t, J = 7.2 Hz), 1.13−1.21 (2H, m), 1.28 (3H, t, J = 7.2 Hz), 1.85 (1H, br s), 2.03−2.11 (1H, m), 3.22 (2H, br s), 3.74−4.09 (4H, m), 4.63 (1H, d, $^3J_{HP}$ = 4.4 Hz), 7.69 (2H, d, J = 8.8 Hz), 8.18 (2H, d, J = 8.8 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 8.5, 16.2 (d, $^3J_{CP}$ = 6.9 Hz), 16.5 (d, $^3J_{CP}$ = 6.9 Hz), 25.0, 26.1 (d, $^1J_{CP}$ = 200.8 Hz), 47.4 (d, $^3J_{CP}$ = 3.5 Hz), 61.9 (d, $^2J_{CP}$ = 6.9 Hz), 62.0, 62.1 (d, $^2J_{CP}$ = 6.9 Hz), 123.3, 129.0, 147.6, 147.9. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 27.72. IR (cm^{-1}) ν_{max}: 1023 (P−O), 1238 (P═O), 1347 (N−O), 1520 (N−O), 2982, 3303. MS (ESI, pos): m/z 341.3/342.3 (M + H^+, 100/17). HRMS: m/z calcd for $C_{15}H_{22}N_2O_5P$ (M + H)$^+$ 341.1261, found 341.1265. Chromatography: EtOAc, R_f = 0.07.

Diethyl ((1S,2S*,5R*)-2-(4-Pentanoylphenyl)-3-azabicyclo-[3.1.0]hexan-1-yl)phosphonate* ***1j.*** 51 mg (0.14 mmol) of **14j** was converted into **1j**. After column chromtography 32 mg of product was obtained (0.08 mmol, 60% yield, yellow oil). ^{1}H NMR (300 MHz, $CDCl_3$) δ: 0.95 (3H, t, J = 7.5 Hz), 1.02 (3H, t, J = 7.0 Hz), 1.17−1.29 (3H, t, J = 7.0 Hz, 2H, m), 1.41 (2H, sext, J = 7.5 Hz), 1.71 (2H, quint, J = 7.5 Hz), 1.85 (1H, br s), 1.99−2.09 (1H, m), 2.95 (2H, t, J = 7.5 Hz), 3.19 (2H, s), 3.69−4.07 (4H, m), 4.57 (d, $^3J_{HP}$ = 4.4 Hz), 7.58 (2H, d, J = 8.0 Hz), 7.91 (2H, d, J = 8.0 Hz). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 8.5, 14.0, 16.1 (d, $^3J_{CP}$ = 5.8 Hz), 16.5 (d, $^3J_{CP}$ = 6.9 Hz), 22.6, 24.9, 25.9 (d, $^1J_{CP}$ = 199.6 Hz), 26.7, 38.5, 47.6 (d, $^3J_{CP}$ = 3.5 Hz), 61.8 (d, $^2J_{CP}$ = 5.8 Hz), 62.0 (d, $^2J_{CP}$ = 5.8 Hz), 62.5 (d, $^2J_{CP}$ = 11.5 Hz), 128.0, 128.2, 136.6, 145.2, 200.5. ^{31}P NMR (121 MHz, $CDCl_3$) δ: 28.14. IR (cm^{-1}) ν_{max}: 1025 (P−O), 1238 (P═O), 1681 (C═O), 2931, 3308. MS (ESI, pos): m/z 380.3/381.3 (M + H^+, 100/17). HRMS: m/z calcd for $C_{20}H_{31}NO_4P$ (M + H)$^+$ 380.1985, found 380.1978. Chromatography: EtOAc, R_f = 0.06.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra of new compounds as well as ^{1}H-undecoupled ^{31}P NMR spectra of **11j**; crystallographic data for **11i** and **11j** (CIF). This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank the Research Foundation Flanders (FWO) for financial support. K.V.H. thanks the Hercules Foundation (project AUGE/11/029 "3D-SPACE: 3D Structural Platform Aiming for Chemical Excellence") for funding. Professor Kristof Demeestere and Patrick De Wispelaere are gratefully acknowledged for some urgent analyses.

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