July, 1987] © 1987 The Chemical Society of Japan Bull. Chem. Soc. Jpn., 60, 2463—2473 (1987) 2463

Synthesis of (Diethoxyphosphoryl)acetonitrile Oxide and Its Cycloaddition to Olefins. Synthetic Applications to 3,5-Disubstituted 2-Isoxazolines

Otohiko Tsuge,* Shuji Kanemasa, Hiroyuki Suga, and Norihiko Nakagawa
Institute of Advanced Material Study, and Department of Molecular Science and Technology,
Interdisciplinary Graduate School of Engineering Sciences, Kyushu University,
Kasugakoen, Kasuga 816

(Received February 5, 1987)

(Diethoxyphosphoryl)acetonitrile oxide undergoes regioselective cycloaddition to olefins leading to 3-[(diethoxyphosphoryl)methyl]-2-isoxazolines or -isoxazole. The phosphorus-stabilized carbanions generated by deprotonation of the cycloadducts can be utilized for the condensation with carbonyl compounds, alkylation, and oxidation with oxygen to provide 3,5-disubstituted 2-isoxazolines as useful synthetic building blocks. Raney nickel hydrogenolysis of 3-[(diethoxyphosphoryl)methyl]-2-isoxazolines gives β-hydroxy-β'-phosphoryl ketones bearing a variety of functional groups, which can be further converted into α,β-unsaturated β'-phosphoryl ketones.

High synthetic versatility of isoxazoles and 2-isoxazolines is based on their potentiality as flexible synthetic equivalents of 1,3-diketones, β-hydroxy ketones, γ-amino alcohols, α,β-unsaturated ketones, and other related functions.[1] One of the most general preparation methods of these heterocycles is regioselective cycloaddition of nitrile oxides.[2] Use of monosubstituted acetylenes or olefins furnishes isoxazoles or 2-isoxazolines bearing a 5-substituent. As nitrile oxides undergo smooth cycloadditions to electron-poor to -rich dipolarophiles,[3] a wide variety of substituents may be introduced at the 5-position by the regioselective cycloaddition route. Accordingly it is soon realized that these cycloadducts will become synthetically versatile building blocks which involve masked complex functionalities.[4]

From this point of view, a functionalized nitrile oxide must be important because the cycloaddition reaction of this 1,3-dipole produces isoxazoles or 2-isoxazolines with this newly added functionality which can be then utilized to introduce these heterocycles as talent synthetic blocks into other molecules.[5] We recently started our project on the synthetic applications of a phosphorus-functionalized nitrile oxide, (diethoxyphosphoryl)acetonitrile oxide (**1**).

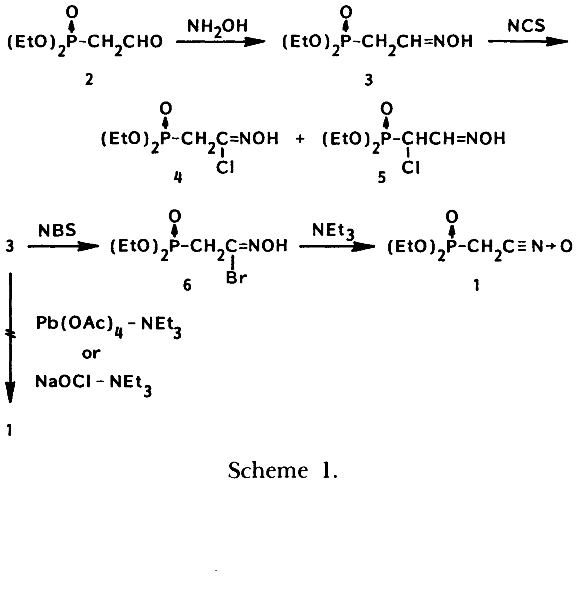
The present report describes the first preparation of **1** and some examples of its synthetic applications: Regioselective cycloaddition of **1** to monosubstituted olefins leading to 2-isoxazolines or isoxazole; reactions of the phosphorus-stabilized carbanions with electrophiles; reductive cleavage of the heterocycles on Raney Ni.[6]

Results and Discussion

Among several preparation methods of nitrile oxides,[7] the halogenation and dehydrohalogenation sequence of aldoximes as well as the direct oxidation method was applied to *N*-[2-(diethoxyphosphoryl)-ethylidene]hydroxylamine (**3**) because **3** is available in large quantities from bromoacetaldehyde diethyl acetal and triethyl phosphite. Thus, known (diethoxyphosphoryl)acetaldehyde (**2**)[8] was prepared by Arbuzov reaction of the acetal and further converted into oxime **3** in 95% yield (a 3 : 4 mixture of syn and anti forms).

The direct oxidative conversion of aldoxime **3** into nitrile oxide **1** was unsuccessful: Both the reaction of **3** with lead tetraacetate/triethylamine[7c] and the treatment of **3** with sodium hypochlorite/triethylamine,[7b] both in dichloromethane solution, failed in the generation of nitrile oxide **1**. Complex mixture of many products was only formed.

The chlorination and dehydrochlorination method[7d] was next applied. When **3** was treated with *N*-chlorosuccinimide (NCS) in DMF, chlorination took place not only at the oxime carbon but also at the adjacent methylene carbon to give a mixture of *N*-[1-chloro-2-(diethoxyphosphoryl)ethylidene]hydroxylamine (**4**) and its isomer **5** (Scheme 1). Both combined yield (**4**+**5**) and isomer ratio were found to depend upon the reaction temperature as shown in Table 1. Although the desired chloro oxime **4** could be separated from **5** through column chromatography over silica gel, the maximum yield of isolated **4** was only less than 50% even under the optimum conditions



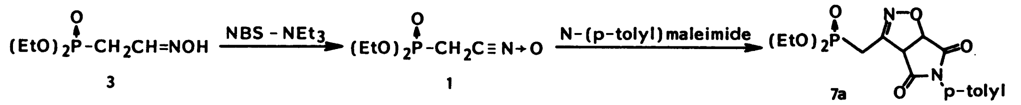
Scheme 1.

Table 1. Chlorination of Oxime **3** with NCS Leading to **4** and **5**[a]

Run	Reaction condition		Total yield/%[b]	Isomer ratio (**4**:**5**)[c]
	Addition of NCS	Reaction with NCS		
1	0 °C, 5 min	rt, 5 h	60	1:1
2	0 °C, 5 min	0 °C, 1 h	71	10:3
3	−15 °C, 5 min	−15 °C, 30 min	34	17:7
4	0 °C, 40 min	0 °C, 2 h	71	16:3

a) Carried out in DMF with 1 equiv amount of NCS. b) Yield of the isolated mixture of **4** and **5** based on **3**. c) Determined by ^{1}H NMR spectrum of the mixture of **4** and **5**.

Table 2. Generation of Nitrile Oxide **1** and Its Trapping with *N*-(*p*-Tolyl)maleimide[a]



Run	Reaction with NBS		NEt$_3$ (equiv)[c]	Cycloaddition[b] time/h	Yield of **7a**/%[d]
	NBS (equiv)	Condition[e]			
1	1	0 °C, 30 min	1	15	54
2	1	−20 °C, 5 min then 0 °C, 30 min	1	12	63
3	1	−20 °C, 1 h then 0 °C, 30 min	1	12	67
4	2	−20 °C, 5 min then 0 °C, 30 min	1	21	71
5	2	0 °C, 30 min	2	21	41
6	2	−20 °C, 1 h then 0 °C, 30 min	1	18	80

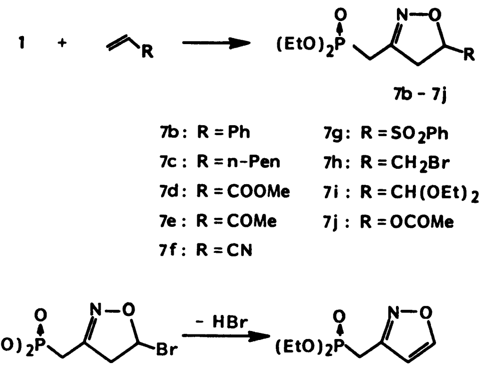
a) Carried out in DMF. b) Reaction temperature; room temperature. c) After the reaction with NBS was over, a mixture of *N*-(*p*-tolyl)maleimide and triethylamine was added. d) Yield of isolated **7a** based on **3**. e) NBS in DMF was added to **3** in a period of 5 min.

(Run 4, total yield: 71%; **4** : **5** = 16 : 3) to let us discard this chlorination route.

An alternative is bromination of oxime **3**. Thus, **3** was treated with *N*-bromosuccinimide (NBS) in DMF according to the Steven's method.[7d] As bromo oxime **6** was not isolable, **6** was in situ dehydrobrominated with triethylamine. The nitrile oxide **1** generated was trapped by *N*-(*p*-tolyl)maleimide as cycloadduct **7a** (Table 2). It should be noted that all procedures for the bromination of **3**, the dehydrobromination of **6**, and the cycloaddition trapping could be conveniently carried out in one flask.

When oxime **3** was treated with two equivalents of NBS at −20 °C in a period of 5 min and then one equivalent of triethylamine at room temperature (run 6 of Table 2), the desired nitrile oxide **1** was generated in an excellent yield and successfully captured by *N*-(*p*-tolyl)maleimide to give **7a** in 80% yield.

Cycloadditions of nitrile oxide **1** with a variety of olefins were next investigated. Under similar conditions, **1** underwent smooth cycloadditions to such a wide variety of olefins as electron-poor olefins (*N*-(*p*-tolyl)maleimide, methyl acrylate, 3-buten-2-one, acrylonitrile, phenyl vinyl sulfone), an electron-rich olefin (vinyl acetate), and nonactivated olefins (styrene, 1-heptene, 3-bromopropene, 3,3-diethoxypropene) all in regioselective manners to give 5-substituted 3-[(diethoxyphosphoryl)methyl]-2-isoxazolines **7a**—**j** (Scheme 2 and Table 3). Better yields of **7** were generally obtained if more than 1 equivalent amount of dipolarophiles was employed. Accordingly some of low-boiling or volatile olefins were used as much as 5 equivalents. The reaction of **1** with bromoethene pro-



Scheme 2.

Table 3. Cycloaddition of Nitrile Oxide **1** to Olefins[a)]

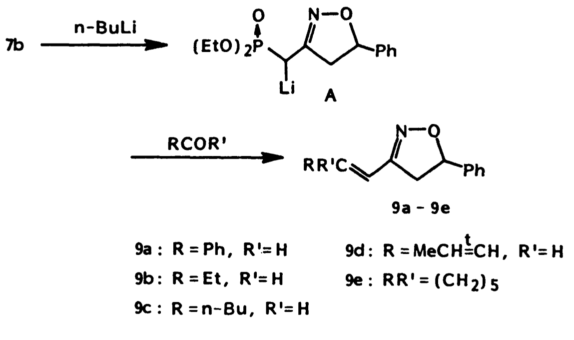
Olefin (equiv)	Time/h[b)]	Product	Yield/%[c)]
N-(*p*-Tolyl)maleimide (1)	18	**7a**	80
Styrene (5)	18	**7b**	81
1-Heptene (5)	18	**7c**	75
Methyl acrylate (1)	18	**7d**	84
3-Buten-2-one (2)	48	**7e**	70
Acrylonitrile (5)	27	**7f**	77
Phenyl vinyl sulfone (1)	18	**7g**	25
3-Bromopropene (5)	18	**7h**	62
3,3-Diethoxypropene (5)	18	**7i**	54
Vinyl acetate (5)	18	**7j**	73

a) Carried out in DMF. b) Bromo oxime **6** was first generated by treatment of oxime **3** with NBS (2 equiv) at −20 °C for 1 h and then 0 °C for 30 min. A mixture of olefin and triethylamine (1 equiv) was added. The mixture was stirred at room temperature for the reaction time listed in this table. c) Yield of isolated cycloadduct **7** based on **3**.

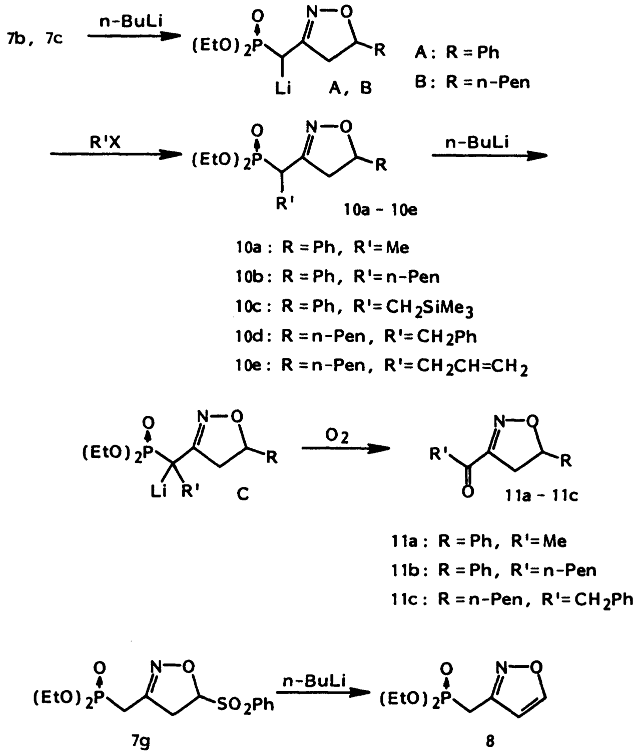
duced 3-[(diethoxyphosphoryl)methy]isoxazole (**8**) in 47% yield by the elimination of hydrogen bromide of the initial cycloadduct, 5-bromo-3-[(diethoxyphosphoryl)methyl]-2-isoxazoline (**7k**).

Regioselective deprotonation of 3-alkyl-2-isoxazolines is quite difficult. Thus, it is known that 3-methyl-5-phenyl-2-isoxazoline can be deprotonated, at a low temperature, with LDA both at the 3-methyl group (exo) and the 4-position (endo).[9] At an elevated temperature the endo carbanion causes a ring opening via a β-elimination leading to α,β-unsaturated ketone. The regioselectivity depends upon the substituents[10] as well as the polarity of reaction solvent.[11] Although a few successful cases of the trapping of exo carbanions have been recently reported,[12] the exclusive utilization of exo carbanion is still difficult. The phosphorus-functionalized 2-isoxazolines **7** are expected to generate stable phosphoryl-stabilized carbanions.

The 2-isoxazoline **7b** as a representative was first treated with butyllithium at −78 °C in THF. The resulting yellow carbanion **A** is so highly stabilized that it can servive even at room temperature. It was then treated with carbonyl compounds at room temperature to succeed in reacting with aromatic, aliphatic, α,β-unsaturated aldehydes, and a ketone to give 3-(1-alkenyl)-2-isoxazolines **9a**—**e** (Scheme 3 and Table 4). The Horner-Emmons olefination products **9** were mostly E-isomers as expected. The carbanions derived from 2-isoxazolines **7d** and **7e** which carry a carbonyl group failed in reacting with aldehydes.[13]



Scheme 3.



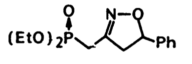
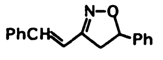
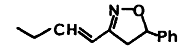
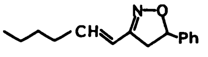
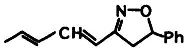
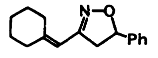
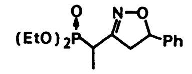
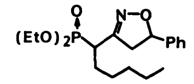
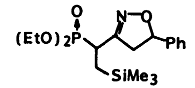
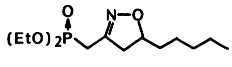
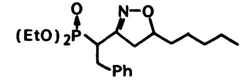
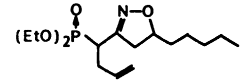
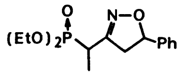
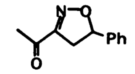
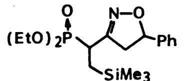
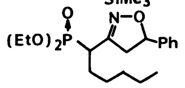
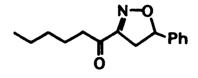
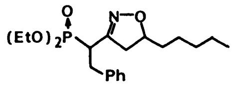
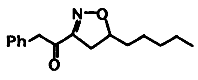
Scheme 4.

Under similar conditions, the above carbanion **A** as well as **B** which was derived from 5-alkyl-2-isoxazoline **7c** by deprotonation reacted with alkyl halides to give 3-(1-phosphorylalkyl)-2-isoxazolines **10a** — **e** in good yields (Scheme 4 and Table 4). Alkyl iodides (methyl, pentyl, and trimethylsilylmethyl iodides) were sufficiently reactive toward **A** or **B**. Although activated bromides such as benzyl and 2-propenyl bromides are exceptions, less reactive alkyl bromides such as pentyl and 1-methylpropyl bromides were recovered intact.

The 3-(1-phosphorylalkyl)-2-isoxazolines **10** thus prepared could be again deprotonated with butyllithium at the same carbon to generate carbanions **C**. These anions **C** were oxidized with dry oxygen gas at −78 °C to furnish 3-(1-oxoalkyl)-2-isoxazolines **11a**—**c** (Scheme 4 and Table 4). The silylmethyl-substituted 2-isoxazoline **10c** led to desilylated ketone **11a** which was also accessible from **10a**.

When the cycloadduct **7g** obtained from the cycloaddition to phenyl vinyl sulfone was treated with butyllithium, deprotonation took place at the 4-position causing the elimination of benzenesulfinic acid

Table 4. Reaction of 2-Isoxazolines **7** and **10** with Electrophiles[a)]

2-Isoxazoline	Electrophile	Temp/°C	Time/h	Product	Yield/%[b)]
 **7b**	PhCHO	rt	12.5	 **9a**	99$^{c)}$
7b	EtCHO	rt	12.5	 **9b**	75$^{d)}$
7b	*n*-BuCHO	rt	16	 **9c**	66$^{e)}$
7b	MeCH$\overset{t}{=}$CHCHO	rt	17	 **9d**	81$^{c)}$
7b	Cyclohexanone	rt	16	 **9e**	94
7b	MeI	rt	17	 **10a**	80
7b	*n*-PenI	rt	11	 **10b**	72
7b	Me_3SiCH_2I	rt	15	 **10c**	70
 **7c**	$PhCH_2Br$	rt	15	 **10d**	75
7c	$CH_2=CHCH_2Br$	rt	15.5	 **10e**	91
 **10a**	Oxygen	−78	1	 **11a**	70$^{f)}$
 **10c**	Oxygen	−78	1	**11a**	78$^{g)}$
 **10b**	Oxygen	−78	1	 **11b**	83$^{h)}$
 **10d**	Oxygen	−78	1	 **11c**	57$^{i)}$

a) Carbanions **A**—**C** were first generated by the action of butyllithium in THF at −78 °C and the reactions with electrophiles were followed under the conditions shown above. b) Yield of isolated product. c) E only (^{1}H NMR). d) E:Z=75:25 (GLC). e) E:Z=72:28 (GLC). f) Recovered **10a**: 16%. g) Recovered **10c**: 12%. h) Recovered **10b**: 15%. i) Recovered **10d**: 39%.

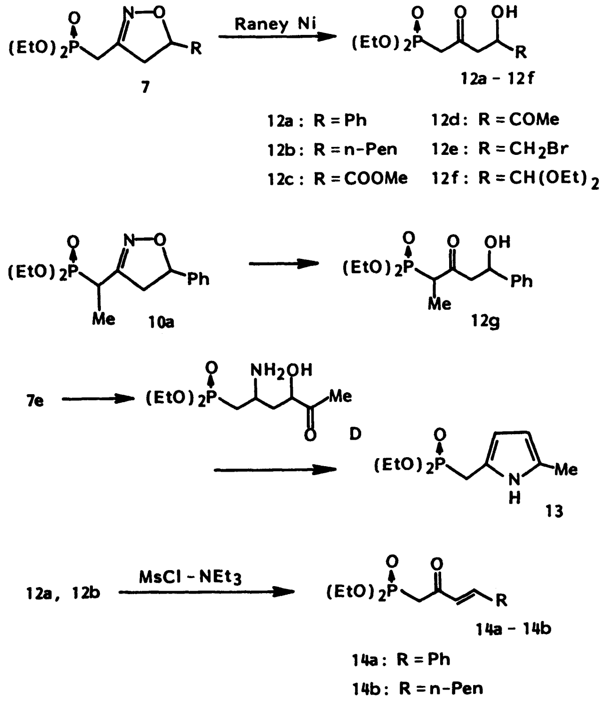
to give 3-phosphorylmethyl-2-isoxazole **8** whose formation was already mentioned above.

The phosphoryl moiety of **7** was found to servive on the reductive N-O bond fission and the subsequent hydrolysis. Thus, 3-phosphorylmethyl-2-isoxazolines **7** bearing a variety of substituents at the 5-position were hydrogenated on Raney-Ni (W-2) in aqueous ethanol in the presence of acetic acid or boric acid to give good yields of *β*-hydroxy ketones **12a** — **f** bearing phosphoryl and R moieties (Scheme 5). Such functional groups as ester, ketone, halogen, and acetal are also safe under the conditions of hydrogenolysis. Instability of **12d** may arise from its 1,4-dicarbonyl or *α*-hydroxy ketone structure.[14)]

Although the Raney Ni reduction of **7e** in H_3BO_3-H_2O gave *β*-hydroxy ketone **12d** as described above, a similar reduction in AcOH-H_2O procuced 2-methyl-5-[(diethoxyphosphoryl)methyl]pyrrole (**13**) in a fair yield. The intermediary *β*-hydroxy imine, initially formed by the N-O bond reduction of 2-isoxazoline **7e**, was presumably overreduced to lead to 4-amino-2-hydroxy ketone intermediate **D** whose intramolecular dehydration gave **13**.

The alkylated derivative **10a** prepared above by methylation of the phosphorus-stabilized carbanion **A** was similarly converted into 1-phosphorylethyl 2-hydroxyalkyl ketone **12g** (Scheme 5).

The phosphorus-functionalized *β*-hydroxy ketones **12** could be further converted into phosphorus-functionalized *α*,*β*-unsaturated ketones **14a** and **14b**



Scheme 5.

in quantitative yields through the initial mesylation with methanesulfonyl chloride and triethylamine and the subsequent chromatography over silica gel (Scheme 5).

Synthetic utilization of the phosphoryl moiety of the compounds newly prepared herein is now under progress. The results will be soon published elsewhere.

Experimental

General. Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. IR spectra were taken with a JASCO IRA-1 or a JASCO A-702 spectrometer. ^{1}H NMR spectra were recorded on a Hitachi R-40 (90 MHz) or a JEOL FX-100 instrument (100 MHz) and ^{13}C NMR on a JEOL FX-100 spectrometer at 25.05 MHz. Chemical shifts are expressed in parts per million downfield from tetramethylsilane as an internal standard. Mass spectra were measured with a JEOL-01SG-2 spectrometer at 70 eV of ionization energy. High resolution mass spectra were obtained on the same instrument. Elemental analyses were performed on a Hitachi 026 CHN analyzer. Thin-layer chromatography (TLC) was accomplished on 0.2 mm precoated plates of silica gel 60 F-254 (Merck). Visualization was made with ultraviolet light (254 and 365 nm), iodine, molybdophosphoric acid (5% in ethanol), or *p*-anisaldehyde (5% in ethanol containing 5% of sulfuric acid). For preparative column chromatography, Wakogel C-200, C-300 (Wako), and Silicagel 60 (Merck) were employed. Flash chromatography was carried out on an EYELA EF-10 apparatus using a column (20 × 180 mm) packed with Silicagel 60 (Merck, size: 0.04 — 0.063 mm). Preparative high performance liquid chromatography (HPLC) was performed on a Kusano KHLC-201 apparatus with a UV-detector Uvilog-III using a column (22 × 300 mm) packed with silica gel (Wakogel LC-50H). Gas liquid chromatography (GLC) was accomplished on a Yanaco G-2800 gas chromatograph (Yanagimoto) with an ionization flame detector using a glass column (SE-30, 3 × 2000 mm) or a glass capillary column (Silicone GE, SE-30, 0.25 × 5000 mm). Micro vacuum distillation was carried out on a Sibata GTO-250R Kugelrohr distilling apparatus. Solvents were evaporated with a Tokyo Rikakikai rotary evaporator type-V at about 50 °C unless otherwise stated.

***N*-[2-(Diethoxyphosphoryl)ethylidene]hydroxylamine (3).** To a solution of aldehyde **2**[8] (0.5 g, 2.78 mmol) in ethanol (5 ml) was added an aqueous hydroxylamine hydrochloride (0.386 g, 5.56 mmol in 2 ml of water). The mixture was stirred at room temperature for 11.5 h, poured into water (50 ml), and extracted with dichloromethane (25 ml × 2). The combined extracts were dried over magnesiun sulfate and evaporated in vacuo to give **3** (0.513 g, 95%) as a 3 : 4 mixture of syn and anti isomers, which was purified through a column chromatography (silica gel/ethyl acetate): Colorless liquid; IR (neat) 3200, 1600, and 1240 cm^{-1}; ^{1}H NMR (CDCl$_3$) $\delta=1.30$ (6H, t, $J=7.0$ Hz, OEt), 2.77 (3/7 × 1H, dd, $J=6.3$ and 21.8 (HP) Hz, CH$_2$ (syn)), 3.04 (4/7 × 1H, dd, $J=6.0$ and 22.0 (HP) Hz, CH$_2$ (anti)), 4.12 (4H, dq, $J=7.0$ and 7.5 (HP) Hz, OEt), 6.75 (4/7 × 1H, dt, $J=6.0$ and 5.0 (HP) Hz, CH=N (anti)), 7.35 (3/7 × 1H, dt, $J=6.3$ and 5.0 (HP) Hz, CH=N (syn)), and 10.10 (1H, br, OH); ^{13}C NMR (CDCl$_3$) $\delta=16.32$ (qd, $J_{cp}=7.4$ Hz, OEt), 23.56 (td, $J_{cp}=139.7$ Hz, OEt (anti)), 28.18 (td, $J_{cp}=141.2$ Hz, OEt (syn)), 62.62 (td, $J_{cp}=7.4$ Hz, CH$_2$), 140.74 (dd, $J_{cp}=7.4$ Hz, CH=N (anti)), and 142.27(dd, $J_{cp}=10.3$ Hz, CH=N (syn)); MS (rel intensity, %) 195 (M$^+$, 13), 167 (17), 139 (39), 122 (49), 111 (25), 109 (56), 104 (19), 99 (64), 96 (23), 93 (32), 82 (27), 81 (base peak), and 65 (72). HRMS Found: *m/z* 195.0603. Calcd for $C_6H_{14}NO_4P$: M, 195.0660.

Reaction of Oxime 3 with NCS Leading to 4 and 5. A mixture of **3** (1 mmol) and NCS (1 mmol) in DMF (1 ml) was stirred under the conditions shown in Table 1. The mixture was poured into water (20 ml) and extracted with diethyl ether (20 ml × 2). The combined extracts were washed with water, dried over magnesium sulfate, and evaporated in vacuo. The residue was chromatographed over silica gel. The fraction eluted with hexane-ethyl acetate (1 : 2 v/v) gave *N*-[1-chloro-2-(diethoxyphosphoryl)-ethylidene]hydroxylamine (**4**) and with hexane-ethyl acetate (1 : 5 v/v) *N*-[2-chloro-2-(diethoxyphosphoryl)ethylidene]-hydroxylamine (**5**). Results obtained under several conditions are listed in Table 1. Both **4** and **5** are too labile to be highly purified as analytical samples.

4: Yellow liquid; IR (neat) 3200, 1625, 1220, 1020, and 800 cm^{-1}; ^{1}H NMR (CDCl$_3$) $\delta=1.31$ (6H, t, $J=7.0$ Hz, OEt), 3.06 (2H, d, $J=21.0$ (HP) Hz, CH$_2$P), 4.10 (4H, qd, $J=7.0$ and 7.5 (HP)Hz, OEt), and 10.66 (1H, br, OH); MS *m/z* (rel intensity, %) 229 (M$^+$, 4), 138 (11), 137 (16), 122 (21), 109 (51), 104 (19), 91 (21), 81 (86), 77 (18), 65 (42), and 43 (base peak).

5 (A 7 : 5 mixture of syn- and anti-isomers): Pale yellow liquid; IR (neat) 3200, 1625, 1240, and 1020 cm^{-1}; ^{1}H NMR (CDCl$_3$) $\delta=1.34$ (6H, t, $J=7.0$ Hz, OEt), 4.23 (4H, qd, $J=7.0$ and 7.4 (HP) Hz, OEt), 4.61 (7/12 × 1H, dd, $J=8.5$ and 13.0 (HP) Hz, CH (syn)), 5.42 (5/12 × 1H, dd, $J=8.0$ and

13.0 (HP) Hz, CH (anti)), 6.77 (5/12×1H, dd, *J*=8.0 and 3.0 (HP) Hz, CH=N (anti)), and 7.38 (7/12×1H, dd, *J*=8.5 and 4.0 (HP) Hz, CH=N (syn)); ^{13}C NMR ($\mathrm{CDCl_3}$) δ= 16.38 (qd, J_{cp}=6.1 Hz, OEt), 40.89 (dd, J_{cp}=159.9 Hz, OEt (anti)), 48.83 (dd, J_{cp} = 163.6 Hz, OEt (syn)), 64.74 (td, J_{cp}=7.3 Hz, CH), 142.26 (dd, J_{cp}=3.7 Hz, CH=N (anti)), and 143.89 (dd, J_{cp}=2.4 Hz, CH=N (syn)); MS *m/z* (rel intensity, %) 229 (M$^+$, 8), 130 (10), 127 (14), 109 (61), 99 (33), 91 (27), 81 (56), 73 (14), 65 (69), and 43 (base peak).

General Procedure for the Generation of Nitrile Oxide 1 and Its Cycloaddition to Olefins Leading to 7a—j. To a solution of oxime **3** (0.195 g, 1 mmol) in dry DMF (2 ml) was added NBS (0.356 g, 2 mmol in 2 ml of DMF) at −20 °C. The mixture was stirred at the same temperature for 1 h and then at 0 °C for 30 min. A mixture of triethylamine (0.101 g, 1 mmol) and an olefin (1 to 5 mmol) in dry diethyl ether (2 ml) was added. The mixture was stirred at room temperature, poured into water (20 ml), and extracted with dichloromethane (20 ml × 2) or diethyl ether (20 ml × 2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel to give cycloadduct **7**. The eluents used are as follows: **7a**, **7b**, **7d**, and **7j**: ethyl acetate; **7c**, **7e**, **7f**, **7g**, **7h**, and **7i**: hexane-ethyl acetate (1 : 5 v/v). The yields of **7**, the amounts of olefin used, and the reaction times are summarized in Table 3. The reaction with *N*-(*p*-tolyl)maleimide under various conditions is shown in Table 2.

7a: Colorless prisms (diethyl ether); mp 88—89 °C; IR (KBr) 1720, 1240, and 1020 cm^{-1}; ^{1}H NMR ($\mathrm{CDCl_3}$) δ= 1.32 (6H, t, *J*=7.0 Hz, OEt), 2.34 (3H, s, *p*-Me), 3.00 (1H, d, *J*= 15.5 (gem) and 22.5 (HP) Hz, one of $\mathrm{CH_2P}$), 4.13 (1H, d, *J*= 15.5 (gem) and 21.0 (HP) Hz, the other of $\mathrm{CH_2P}$), 4.14 (4H, qd, *J*= 7.0 and 7.3 (HP) Hz, OEt), 4.75 (1H, dd, *J*=9.5 and 4.0 (HP) Hz, 3a-H), 5.43 (1H, d, *J*= 9.5 Hz, 6a-H), and 7.0—7.3 (4H, m, Ar); ^{13}C NMR ($\mathrm{CDCl_3}$) δ=16.35 (qd, J_{cp}=5.9 Hz, OEt), 21.23 (q, *p*-Me), 24.35 (td, J_{cp}= 138.3 Hz, $\mathrm{CH_2P}$), 52.82 (d, 3a-C), 63.18 (td, J_{cp}= 5.9 Hz, OEt), 79.77 (d, 6a-C), 126.24 (d), 128.54 (s), 130.07 (d), 139.48 (s), 148.54 (d, J_{cp} = 8.8 Hz, 3-C), 170.67, and 171.95 (each s, CON); MS *m/z*(rel intensity, %) 380 (M$^+$, 3), 353 (18), 352 (90), 246 (base peak), 218 (46), 190 (67), 133 (72), 132 (46), 109 (60), 107 (28), 105 (22), 104 (39), 91 (34), 81 (68), 78 (24), and 77 (26). Found: C, 53.86; H, 5.61; N, 7.46%. Calcd for $\mathrm{C_{17}H_{21}N_2O_6P}$: C, 53.67; H, 5.57; N, 7.37%.

7b: Pale yellow liquid; IR (neat) 1620, 1250, 1020, and 825 cm^{-1}; ^{1}H NMR ($\mathrm{CDCl_3}$) δ=1.2—1.4 (6H, m, OEt), 2.98 (2H, d, *J*= 21.8 (HP) Hz, $\mathrm{CH_2P}$), 3.07 (1H, ddd, *J*=17.5 (gem), 8.0, and 4.2 (HP) Hz, one of 4-H), 3.50 (1H, ddd, *J*= 17.5 (gem), 10.8, and 4.2(HP) Hz, the other of 4-H), 3.9—4.3 (4H, m, OEt), 5.56 (1H, dd, *J*= 10.8 and 8.0 Hz, 5-H), and 7.28 (5H, s, Ph); ^{13}C NMR ($\mathrm{CDCl_3}$) δ=16.38 (qd, J_{cp}=6.1 Hz, OEt), 26.24 (td, J_{cp}=140.4 Hz, $\mathrm{CH_2P}$), 45.26 (t, 4-C). 62.62 (td, J_{cp}= 6.1 Hz, OEt), 82.37 (d, 5-C), 126.02, 128.32, 128.51 (each d), 141.06 (s), and 151.27 (d, J_{cp}=9.8 Hz, 3-C); MS *m/z* (rel intensity, %) 297 (M$^+$, 2), 109 (16), 105 (11), 104 (13), 81 (15), 77 (19), and 43 (base peak). HRMS Found: *m/z* 297.1120. Calcd for $\mathrm{C_{14}H_{20}NO_4P}$: M, 297.1128.

7c: Pale yellow liquid; IR (neat) 1630, 1260, 1025, and 825 cm^{-1}; ^{1}H NMR ($\mathrm{CDCl_3}$) δ= 0.88 (3H, t, *J*=7.0 Hz, *n*-Pen), 1.1—1.8 (8H, m, *n*-Pen), 1.33 (6H, t, *J*=7.0 Hz, OEt), 2.72 (1H, ddd, *J*=17.0 (gem), 8.2, and 4.2 (HP) Hz, one of 4-H), 2.93 (2H, d, *J*=21.5 (HP) Hz, $\mathrm{CH_2P}$), 3.14 (1H, ddd, *J*= 17.0 (gem), 10.0, and 4.2 (HP) Hz, the other of 4-H), 4.12 (4H, qd, *J*=7.0 and 7.5 (HP) Hz, OEt), and 4.52 (1H, m, 5-H); ^{13}C NMR ($\mathrm{CDCl_3}$) δ= 14.00 (q), 16.41 (qd, J_{cp}= 5.8 Hz, OEt), 22.59, 25.06 (each t), 26.41 (td, J_{cp}=141.2 Hz, $\mathrm{CH_2P}$), 31.71, 35.12 (each t), 42.36 (t, 4-C), 62.59 (td, J_{cp}= 5.8 Hz, OEt), 81.42 (d, 5-C), and 151.48 (d, J_{cp}=8.8 Hz, 3-C); MS *m/z*(rel intensity, %) 291 (M$^+$, 8), 220 (base peak), 192 (28), 164 (43), 146 (10), 109 (14), 81 (17), and 44 (29). HRMS Found: *m/z* 291.1587. Calcd for $\mathrm{C_{13}H_{26}NO_4P}$: M, 291.1598.

7d: Pale yellow liquid; IR (neat) 1730, 1620, 1220, 1020, and 825 cm^{-1}; ^{1}H NMR ($\mathrm{CDCl_3}$) δ=1.33 (6H, t, *J*=7.0 Hz, OEt), 2.98 (2H, d, *J*=21.5 (HP) Hz, $\mathrm{CH_2P}$), 3.39 (2H, dd, *J*=9.0 and 4.0 (HP) Hz, 4-H), 3.76 (3H, s, COOMe), 4.13 (4H, qd, *J*= 7.0 and 7.4 (HP) Hz, OEt), and 5.04 (1H, t, *J* = 9.0 Hz, 5-H); ^{13}C NMR ($\mathrm{CDCl_3}$) δ=16.35 (qd, J_{cp}= 5.9Hz, OEt), 25.83 (td, J_{cp}= 141.2 Hz, $\mathrm{CH_2P}$), 41.24 (t, 4-C), 52.77 (q, COOMe), 62.80 (td, J_{cp}=7.4 Hz, OEt), 77.77 (d, 5-C), 151.48 (d, J_{cp} = 8.8 Hz, 3-C), and 170.77 (s, COOMe); MS *m/z* (rel intensity, %) 220 (M$^+$ −COOMe, 52), 192 (28), 164 (92), 146 (44), 109 (49), 91 (16), 83 (20), 82 (19), 81 (80), 65 (40), 59 (base peak), and 54 (89). Found: C, 43.25; H, 6.26; N, 4.74%. Calcd for $\mathrm{C_{10}H_{18}NO_6P}$: C, 43.01; H, 6.50; N, 5.02%.

7e: Pale yellow liquid; IR (neat) 1725, 1625, 1250, 1025, and 800 cm^{-1} ^{1}H NMR ($\mathrm{CDCl_3}$) δ=1.33 (6H, t, *J*= 7.0 Hz, OEt), 2.27 (3H, s, COMe), 2.96 (2H, d, *J*=21.5 (HP) Hz, $\mathrm{CH_2P}$), 3.1—3.5 (2H, m, 4-H), 4.13 (4H, qd, *J*=7.0 and 7.5 (HP) Hz, OEt), and 4.90 (1H, dd, *J*= 10.0 and 8.0 Hz, 5-H); ^{13}C NMR ($\mathrm{CDCl_3}$) δ=16.41 (qd, J_{cp}=5.9 Hz, OEt), 25.97 (td, J_{cp}= 139.7 Hz, $\mathrm{CH_2P}$), 26.12 (q, COMe), 39.71 (t, 4-C), 62.77 (td, J_{cp}=5.9 Hz, OEt), 84.18 (d, 5-C), 152.07 (d, J_{cp} = 8.8 Hz, 3-C), and 207.37 (s, COMe); MS *m/z* (rel intensity, %) 220 (M$^+$ −COMe, 54), 192 (25), 164 (base peak), 152 (18), 146 (30), 125 (15), and 42 (43). Satisfactory elemental analysis was not obtained because of its hygroscopic property.

7f: Pale yellow liquid; IR (neat) 2230, 1625, 1250, 1025, and 800 cm^{-1}; ^{1}H NMR ($\mathrm{CDCl_3}$) δ= 1.35 (6H, t, *J*= 7.0 Hz, OEt), 3.01 (2H, d, *J*=22.0 (HP) Hz, $\mathrm{CH_2P}$), 3.2—3.7 (2H, m, 4-H), 4.15 (4H, qd, *J*=7.0 and 7.6 (HP) Hz, OEt), and 5.27 (1H, dd, *J*= 9.0 and 7.2 Hz, 4-H); ^{13}C NMR ($\mathrm{CDCl_3}$) δ= 16.35 (qd, J_{cp}=5.9 Hz, OEt), 25.71 (td, J_{cp}= 141.2 Hz, $\mathrm{CH_2P}$), 43.24 (t, 4-C), 63.03 (td, J_{cp}=7.3 Hz, OEt), 66.59 (d, 5-C), 117.30 (s, CN), and 152.33 (d, J_{cp}= 10.3 Hz, 3-C); MS *m/z* (rel intensity, %) 246 (M$^+$, 62), 220 (17), 218 (35), 192 (17), 190 (58), 164 (40), 146 (40), 122 (47), 109 (67), 108 (21), 97 (19), 96 (45), 83 (88), 82 (23), 81 (base peak), 79 (20), 64 (45), and 54 (63). HRMS Found: *m/z* 246.0745. Calcd for $\mathrm{C_9H_{15}N_2O_4P}$: M, 246.0768.

7g: Colorless prisms (benzene-hexane); mp 108—110 °C; IR (KBr) 1590, 1300, 1250, 1150, 1020, and 810 cm^{-1}; ^{1}H NMR ($\mathrm{CDCl_3}$) δ=1.32 (6H, t, *J*= 7.0 Hz, OEt), 2.71 (1H, dd, *J*= 17.5 (gem) and 21.5 (HP) Hz, one of $\mathrm{CH_2P}$), 3.10 (1H, dd, *J*= 17.5 (gem) and 20.5 (HP) Hz, the other of $\mathrm{CH_2P}$), 3.3—3.9 (2H, m, 4-H), 4.12 (4H, qd, *J*=7.0 and 7.5 (HP) Hz, OEt), 5.42 (1H, dd, *J*=10.0 and 6.0 Hz, 5-H), and 7.4—8.0 (5H, m, Ar); ^{13}C NMR ($\mathrm{CDCl_3}$) δ=16.35 (qd, J_{cp}=5.9 Hz, OEt), 25.62 (td, J_{cp}=141.2 Hz, $\mathrm{CH_2P}$), 39.00 (t, 4-C), 62.95 (td, J_{cp}=5.9 Hz, OEt), 93.18 (d, 5-C), 129.48, 129.83, 134.72 (each d), 135.60 (s), and 152.75 (d, J_{cp}=10.3 Hz, 3-C); MS m/z (rel intensity, %) 220 (M$^+$, 78), 192 (36), 164 (base peak), 146 (36), and 76 (32). Found: C, 46.42; H, 5.58; N, 3.89%. Calcd for $C_{14}H_{20}NO_6PS$: C, 46.54; H, 5.58; N, 3.88%.

7h: Pale yellow liquid; IR (neat) 1625, 1250, 1020, and 825 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.33 (6H, t, J=7.0 Hz, OEt), 2.93 (2H, d, J=21.8 (HP) Hz, CH$_2$P), 2.9—3.6 (4H, m, 4-H and CH$_2$Br), 4.13 (4H, qd, J=7.0 and 7.4 (HP) Hz, OEt), and 4.84 (1H, m, 5-H); ^{13}C NMR (CDCl$_3$) δ= 16.41 (qd, J_{cp} = 5.9 Hz, OEt), 26.15 (td, J_{cp}=139.7 Hz, CH$_2$P), 33.24 (t, CH$_2$Br), 41.82 (t, 4-C), 62.74 (td, J_{cp} = 5.9 Hz, OEt), 79.60 (d, 5-C), and 151.51 (d, J_{cp}=10.3 Hz, 3-C); MS m/z (rel intensity, %) 314 (M$^+$, 1), 220 (base peak), 192 (26), 164 (65), and 146 (17). HRMS Found: m/z 313.0055. Calcd for $C_9H_{17}NO_4BrP$: M, 313.0078.

7i: Pale yellow liquid; IR (neat) 1675, 1250, 1025, and 830 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.1—1.3 (6H, m, OEt), 1.33 (6H, t, J=7.0 Hz, OEt), 2.93 (2H, d, J=22.0 (HP) Hz, CH$_2$P), 2.9—3.3 (2H, m, 4-H), 3.4—3.9 (4H, m, OEt), 4.14 (4H, qd, J=7.0 and 7.5 (HP) Hz, OEt), and 4.3—4.7 (2H, m, 5-H and CH); ^{13}C NMR (CDCl$_3$) δ= 14.65 (q, OEt), 15.71 (qd, J_{cp}=5.9 Hz, OEt), 25.41 (td, J_{cp}=141.2 Hz, CH$_2$P), 37.83 (t, 4-C), 61.83 (td, J_{cp}=5.9 Hz, OEt), 62.53, 63.48 (each t, OEt), 80.48 (d, 5-C), 101.65 (d, CH(OEt)$_2$), and 151.16 (d, J_{cp}=10.3 Hz, 3-C); MS m/z (rel intensity, %) 278 (M$^+$−OEt, 9), 103 (base peak), 75 (45), and 47 (27), Satisfactory elemental analysis was not available because of its hygroscopic property.

7j: Pale yellow liquid; IR (neat) 1750, 1230, 1020, and 825 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ= 1.34 (6H, t, J = 7.0 Hz, OEt), 2.04 (3H, s, COMe), 2.9—3.6 (2H, m, 4-H), 3.05 (2H, d, J=22.0 (HP) Hz, CH$_2$P), 4.15 (4H, qd, J=7.0 and 7.5 (HP) Hz, OEt), and 6.64 (1H, dd, J=6.2 and 2.0 Hz, 5-H); ^{13}C NMR (CDCl$_3$) δ=16.41 (qd, J_{cp}=5.9 Hz, OEt), 21.00 (q, COMe), 25.83 (td, J_{cp}=141.2 Hz, CH$_2$P), 43.53 (t, 4-C), 62.83 (td, J_{cp} = 5.9 Hz, OEt), 96.01 (d, 5-C), 152.89 (d, J_{cp}=8.8 Hz, 3-C), and 169.83 (s, OCOMe); MS m/z(rel intensity, %), 220 (M$^+$−OCOMe, base peak), 209 (39), 192 (40), 164 (78), 146 (24), 83 (21), 81 (28), 64 (20), 54 (23), and 44 (75). Found: C, 42.93; H, 6.57; N, 5.08%. Calcd for $C_{10}H_{18}NO_6P$: C, 43.01; H, 6.50; N, 5.02%.

Reaction of Nitrile Oxide 1 with Bromoethene Leading to 8. To a solution of oxime **3** (0.39 g, 2 mmol) in dry DMF (4 ml) was added at −20 °C NBS (0.712 g, 4 mmol in 4 ml of DMF) in a period of 5 min. The mixture was stirred at −20 °C for 1 h, at 0 °C for 30 min, and then again cooled to −20 °C. Dry diethyl ether (4 ml) and triethylamine (0.28 ml, 2 mmol in 4 ml of diethyl ether) were added. After bromoethene (5 ml, 71 mmol) was added, the resulting mixture was stirred at room temperature for 18 h, poured into ice water, and extracted with dichloromethane (100 ml × 2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using hexane-ethyl acetate (3 : 1 v/v) to give **8** (0.205 g, 47%): Colorless liquid; IR (neat) 1650, 1565, 1250, 1020, and 800 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.30 (6H, t, J=7.0 Hz, OEt), 3.27 (2H, d, J=20.8 (HP) Hz, CH$_2$P), 4.09 (4H, qd, J= 7.0 and 7.4 (HP) Hz, OEt), 6.45 (1H, t, J= 1.5 Hz, 4-H), and 8.36 (1H, dd, J= 1.5 and 0.8 Hz, 5-H); ^{13}C NMR (CDCl$_3$) δ= 16.35 (qd, J_{cp}=5.9 Hz, OEt), 24.47 (td, J_{cp}= 141.2 Hz, CH$_2$P), 62.68 (td, J_{cp}= 7.3 Hz, OEt), 105.36 (d, 4-C), 159.07 (d, 5-C), and 155.12 (d, J_{cp}=6.8 Hz, 3-C); MS m/z (rel intensity, %) 219 (M$^+$, 92), 192 (31), 176 (28), 174 (34), 164 (67), 163 (31), 149 (37), 148 (25), 146 (70), 112 (23), 111 (20), 110 (67), 83 (base peak), 82 (48), 81 (53), 65 (30), and 55 (35). HRMS Found: m/z 219.0658. Calcd for $C_8H_{14}NO_4P$: M, 219.0660.

General Procedure for the Horner Emmons Olefination of 7b Leading to 9a—e. To a solution of isoxazoline **7b** (1 mmol) in dry THF (3 ml) was added butyllithium (1.6 M[†] in hexane, 0.66 ml, 1.06 mmol) at −78 °C under nitrogen. After 1 h an aldehyde or a ketone (1 mmol) was added. The mixture was stirred under the conditions shown in Table 4, poured into ice water (30 ml), and extracted with dichloromethane (20 ml × 2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was crystallized or chromatographed over silica gel by using the following eluent: **9a**: crystallization; **9b** and **9d**: hexane-ethyl acetate (20 : 1 v/v); **9c** and **9e**: hexane-ethly acetate (30 : 1 v/v). All the results are summarized in Table 4.

9a: Colorless needles (diethyl ether-hexane); mp 109—111 °C; IR (KBr) 1600 and 950 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=3.10 (1H, ddd, J= 16.5 (gem), 8.5, and 0.7 Hz, one of 4-H), 3.54 (1H, ddd, J= 16.5 (gem), 10.8, and 0.7 Hz, the other of 4-H), 5.59 (1H, dd, J= 10.8 and 8.5 Hz, 5-H), 6.64 (1H, d, J=16.0 Hz, CH=), 7.07 (1H, d, J=16.0 Hz, CHPh), and 7.2—7.4 (10H, m, Ph); ^{13}C NMR (CDCl$_3$) δ= 41.65 (t, 4-C), 82.76 (d, 5-C), 117.96 (d, CH=), 126.02, 127.14, 128.41, 128.91, 129.00, 135.88 (s), 136.81 (d), 141.02 (s), and 157.52 (s, 3-C); MS m/z (rel intensity, %) 249 (M$^+$, 10), 248 (18), 143 (20), 130 (23), 128 (20), 115 (81), 105 (23), 104 (43), 103 (42), 102 (25), 91 (55), 89 (30), 78 (45), 77 (base peak), 76 (19), and 65 (25). Found: C, 82.00; H, 6.21; N, 5.66%. Calcd for $C_{17}H_{15}NO$: C, 81.90; H, 6.21; N, 5.62%.

9b (A 75 : 25 mixture of E- and Z-isomers): Pale yellow liquid; IR (neat) 1640, 1610, and 970 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.01 (2/9×3H, t, J=7.5 Hz, Et (Z)), 1.03 (7/9×3H, t, J= 7.0 Hz, Et (E)), 2.18 (2H, m, Et), 2.97 (7/9×1H, dd. J= 16.5 (gem) and 8.5 Hz, one of 4-H (E)), 3.07 (2/9×1H, dd, J= 16.5 (gem) and 8.5 Hz, one of 4-H (Z)), 3.46 (7/9×1H, dd, J=16.5 (gem) and 11.0 Hz, the other of 4-H (E)), 3.55 (2/9×1H, dd, J= 16.5 (gem) and 11.0 Hz, the other of 4-H (Z)), 5.53 (1H, dd, J=11.0 and 8.5 Hz, 5-H), 5.7—6.5 (2H, m, CH=CH), and 7.26 (5H, s, Ph); ^{13}C NMR (CDCl$_3$) δ=12.84 (q, Et (E)), 14.06 (q, Et (Z)), 22.90 (t, Et (Z)), 25.92 (t, Et (E)), 42.09 (t, 4-C (E)), 45.36 (t, 4-C (Z)), 82.13 (d, 5-C (E)), 82.32 (d, 5-C (Z)), 117.19, 119.14, 125.97, 128.22, 128.80, 141.21, 142.04 (each d), 155.71 (s, 3-C (Z)), and 157.23 (s, 3-C (E)); MS m/z (rel intensity, %) 201 (M$^+$, 6), 129 (22), 128 (39), 127 (17), 115 (36), 105 (30), 104 (63), 91 (39), 78 (76), 77 (base peak), and 65 (30). Found: C, 77.65; H, 7.52; N, 6.93%. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51; N, 6.96%.

9c (A 72 : 28 mixture of E- and Z-isomers): Colorless liquid; IR (neat) 1640, 1600, and 960 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ= 0.89 (3H, m, *n*-Bu), 1.1—1.6 (4H, m, *n*-Bu), 2.0—2.4 (2H, m, *n*-Bu), 2.98 (7/10×1H, dd, J= 16.5 (gem) and 8.5 Hz, one of 4-H (E)), 3.07 (3/10×1H, dd, J= 16.5 and 8.5 Hz, one of 4-H (Z)), 3.46 (7/10×1H, dd, J=16.5 (gem) and

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[†] 1M=1 mol dm^{-3}.

11.0 Hz, the other of 4-H (E)), 3.56 (3/10×1H, dd, J=16.5 (gem) and 11.0 Hz, the other of 4-H (Z)), 5.53 (1H, dd, J=11.0 and 8.5 Hz, 5-H), 5.6−6.5 (2H, m, CH=CH), and 7.26 (5H, s, Ph); ^{13}C NMR (CDCl$_3$) δ=13.82 (q), 22.18, 29.29, 30.83, 31.71, 32.59, 42.12, 45.42 (each t), 82.12 (d, 5-C (E)), 82.36 (d, 5-C (Z)), 117.71, 120.07, 126.01, 128.25, 128.83, 139.83, 140.72 (each d), 141.30, 155.78 (s, 3-C (Z)), and 157.19 (s, 3-C (E)); MS m/z (rel intensity, %) 229 (M$^+$, 36), 212 (17), 200 (25), 168 (17), 129 (18), 128 (20), 115 (25), 105 (20), 104 (base peak), 103 (23), 91 (43), 78 (36), 77 (49), and 51 (30). Found: C, 78.28; H, 8.37; N, 6.12%. Calcd for $C_{15}H_{19}NO$: C, 78.56; H, 8.35; N, 6.11%.

9d: Colorless prisms (diethyl ether-hexane); mp 62—64 °C; IR (KBr) 1650, 1625, and 975 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.76 (3H, d, J=6.0 Hz, Me), 2.96 (1H, dd, J=16.5 (gem and 8.5 Hz, one of 4-H), 3.43 (1H, dd, J=16.5 (gem) and 11.0 Hz, the other of 4-H), 5.50 (1H, dd, J=11.0 and 8.5 Hz, 5-H), 5.6—6.6 (3H, m, CH=), and 7.24 (5H, s, Ph); ^{13}C NMR (CDCl$_3$) δ=18.41 (q, Me), 41.70 (t, 4-C), 82.42 (d, 5-C), 118.71, 126.01, 128.25, 128.83, 131.13, 134.48, 137.42 (each d), 141.13 (s), and 157.42 (s, 3-C); MS m/z (rel intensity, %) 213 (M$^+$, 30), 198 (base peak), 180 (25), 115 (19), 105 (18), 104 (46), 103 (26), 91 (36), 78 (39), 77 (68), and 65 (26). Found: C, 78.73; H, 7.05; N, 6.71%. Calcd for $C_{14}H_{15}NO$: C, 78.84; H, 7.09; N, 6.57%.

9e: Colorless needles (hexane); mp 82—84 °C; IR (KBr) 1640 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.54 (6H, m, *c*-Hex), 2.15, 2.41 (each 2H, m, *c*-Hex), 2.99 (1H, dd, J=16.5 (gem) and 8.5 Hz, one of 4-H), 3.50 (1H, dd, J=16.5 (gem) and 11.0 Hz, the other of 4-H), 5.47 (1H, dd, J=11.0 and 8.5 Hz, 5-H), 5.83 (1H, s, CH=), and 7.24 (5H, s, Ph); ^{13}C NMR (CDCl$_3$) δ=26.27, 27.78, 28.56, 30.81, 38.28, 45.90 (each t), 81.88 (d, 5-C), 111.18 (d, CH=), 125.93, 128.12, 128.76 (each d), 141.50, 151.56 (each s), and 155.71 (s, 3-C); MS m/z (rel intensity, %) 241 (M$^+$, 21), 224 (18), 135 (25), 134 (base peak), 128 (24), 107 (31), 106 (42), 105 (27), 104 (55), 103 (30), 91 (76), 79 (43), 78 (50), 77 (84), 67 (28), and 65 (41). Found: C, 79.52; H, 7.90; N, 5.94%. Calcd for $C_{16}H_{19}NO$: C, 79.63; H, 7.94; N, 5.80%.

Genearl Procedure for the Alkylation of 7b, 7c Leading to 10a—e. To a solution of isoxazoline **7b** or **7c** (1 mmol) in dry THF (3 ml) was added butyllithium (1.6M in hexane, 0.62 ml, 0.989 mmol) at −78 °C under nitrogen. After 1 h, an alkyl halide (2 mmol) was added. The mixture was stirred at −78 °C for 1 h, at 0 °C for 1 h, and then at room temperature for the time shown in Table 4. Ice water (30 ml) was added and the mixture was extracted with dichloromethane (20 ml × 2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using the following eluent: **10a**: hexane-ethyl acetate (1 : 5 v/v); **10b**, **10c**, **10d**: hexane-ethyl acetate (1 : 1 v/v); **10e**: hexane-ethyl aceate (2 : 3 v/v). All alkylated isoxazolines **10** were mixtures of two diastereoisomers. The results are summarized in Table 4.

10a: Pale yellow liquid; IR (neat) 1600, 1250, 1020, and 800 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.2—1.6 (9H, m, OEt and Me), 2.8—3.7 (3H, m, CH and 4-H), 3.8—4.3 (4H, m, OEt), 5.55 (1H, dd, J=11.0 and 8.5 Hz, 5-H), and 7.27 (5H, s, Ph); ^{13}C NMR (CDCl$_3$) δ=12.35 (qd, J_{cp}=5.9 Hz, Me), 16.41 (qd, J_{cp}=5.9 Hz, OEt), 32.30, 32.47, (each dd, J_{cp}=141.2 Hz, CH), 43.71, 44.00 (each t), 62.69 (d, J_{cp}=7.4 Hz, 4-C), 82.24 (d, 5-C), 126.10, 128.30, 128.83 (each d), 141.13, 141.24 (each s), and 156.19 (d, J_{cp}=8.9 Hz, 3-C); MS m/z (rel intensity, %) 311 (M$^+$, 62), 310 (base peak), 248 (28), 234 (41), 220 (14), 206 (21), 178 (34), 156 (25), 129 (21), 128 (23), 109 (29), 105 (23), 104 (49), 103 (23), 91 (25), 81 (34), 78 (20), and 77 (31). HRMS Found: m/z 311.1268. Calcd for $C_{15}H_{22}NO_4P$: M, 311.1285.

10b: Pale yellow liquid; IR (neat) 1610, 1250, 1025, and 830 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=0.83, 0.89 (3H, each t, *n*-Pen), 1.1—2.1 (8H, m, *n*-Pen), 1.26 (6H, m, OEt), 2.7—3.7 (3H, m, 4-H and CH), 3.8—4.3 (4H, m, OEt), 5.56, 5.59 (1H, each dd, J=10.5 and 8.0 Hz, 5-H), and 7.27 (5H, s, Ph); ^{13}C NMR (CDCl$_3$) δ=13.87, 13.96 (each q, *n*-Pen), 16.38 (qd, J_{cp}=6.1 Hz, OEt), 22.31, 26.37, 26.56, 27.10, 27.29, 27.69, 27.88, 31.10, 31.25 (each t), 37.70 (dd, J_{cp}=139.2 Hz, CH), 43.21, 43.66 (each t), 62.35 (td, J_{cp}=4.7 Hz, 4-C), 62.57 (td, J_{cp}=6.1 Hz, 4-C), 81.98 (d, 5-C), 125.78, 126.02, 128.22, 128.80 (each d), 141.30 (s), and 155.13 (d, J_{cp}=7.3 Hz, 3-C); MS m/z (rel intensity, %) 367 (M$^+$, 53), 366 (66), 290 (19), 230 (24), 137 (31), 128 (21), 109 (base peak), 105 (33), 104 (43), 91 (35), 81 (68), 78 (20), and 77 (41). HRMS Found: m/z 367.1904. Calcd for $C_{19}H_{30}NO_4P$: M, 367. 1911.

10c: Pale yellow liquid; IR (neat) 1600, 1250, 1025, 850 and 800 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=0.02, 0.07 (9H, each s, SiMe$_3$), 1.0—1.4 (8H, m, OEt and CH$_2$SiMe$_3$), 2.8—3.6 (3H, m, 4-H and CH), 3.9—4.3 (4H, m, OEt), 5.53 (1H, dd, J=11.0 and 8.0 Hz, 5-H), and 7.28 (5H, s, Ph); ^{13}C NMR (CDCl$_3$) δ=−1.37 (q, SiMe$_3$), 13.38 (t, CH$_2$SiMe$_3$), 16.38 (qd, J_{cp}=6.1 Hz, OEt), 33.50 (dd, J_{cp}=139.1 Hz, CH), 33.72 (dd, J_{cp}=137.9 Hz, CH), 43.41, 43.90 (each t), 62.50 (td, J_{cp}=7.3 Hz, 4-C), 62.60 (td, J_{cp}=7.3 Hz, 4-C), 82.22 (dd, J_{cp}=7.3 Hz, 5-C), 126.07, 128.22, 128.76 (each d), 140.72, 141.30 (each s), 155.95 (d, J_{cp}=9.8 Hz, 3-C), and 156.32 (d, J_{cp}=8.5 Hz, 3-C); MS m/z (rel intensity, %) 383 (M$^+$, base peak), 382 (72), 368 (29), 156 (19), and 73 (46). HRMS Found: m/z 383.1654. Calcd for $C_{18}H_{30}NO_4PSi$: M, 383.1680.

10d: Pale yellow liquid; IR (neat) 1600, 1250, 1025, and 800 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=0.85 (3H, t, *n*-Pen), 1.1—1.7 (8H, m, *n*-Pen), 1.30 (6H, t, J=7.0 Hz, OEt), 2.3—3.7 (5H, m, 4-H, CH, and CH$_2$Ph), 4.11 (4H, qd, J=7.0 and 7.5 (HP) Hz, OEt), 4.40 (1H, m, 5-H), and 7.17 (5H, s, Ph); ^{13}C NMR (CDCl$_3$) δ=13.96 (q, *n*-Pen), 16.43 (qd, J_{cp}=6.2 Hz, OEt), 22.51, 24.91, 31.60, 32.76, 34.72, 34.91 (each t), 39.09 (dd, J_{cp}=137.9 Hz, CH), 39.38 (dd, J_{cp}=137.9 Hz, CH), 40.77, 41.02 (each t), 62.77 (td, J_{cp}=6.7 Hz, 4-C), 81.09 (d, 5-C), 126.96, 128.76 (each d), 137.74, 138.37 (each s), and 154.64 (d, J_{cp}=6.6 Hz, 3-C); MS m/z (rel intensity, %) 381 (M$^+$, 15), 311 (19), 310 (base peak), 254 (23), 91 (29), and 43 (45). HRMS Found: m/z 381.2062. Calcd for $C_{20}H_{32}NO_4P$: M, 381.2067.

10e: Colorless liquid; IR (neat) 1640, 1250, 1025, 980, and 800 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=0.89 (3H, t, *n*-Pen), 1.1—1.9 (8H, m, *n*-Pen), 1.33 (6H, t, J=7.0 Hz, OEt), 2.3—3.4 (5H, m, 4-H, CH, and CH$_2$CH=CH$_2$), 4.12 (4H, qd, J=7.0 and 7.4 (HP) Hz, OEt), 4.52 (1H, m, 5-H), 5.05 (1H, dd, J=10.0 and 1.7 Hz, one of =CH$_2$), 5.09 (1H, dd, J=17.5 and 1.7 Hz, the other of =CH$_2$), and 5.70 (1H, m, CH=); ^{13}C NMR (CDCl$_3$) δ=14.00 (q, *n*-Pen), 16.47 (qd, J_{cp}=5.9 Hz, OEt), 22.59, 25.07, 25.18, 30.88, 31.00, 31.71, 35.06 (each t), 37.56 (dd, J_{cp}=139.7 Hz, CH), 40.36 (t), 62.71 (td,

J_{cp}=5.9 Hz, 4-C), 81.12 (d, 5-C), 117.54 (t, =CH_2), 134.77 (dd, J_{cp} = 17.6 Hz, CH=), and 154.98 (d, J_{cp} = 7.3 Hz, 3-C); MS *m/z* (rel intensity, %) 331 (M^+, 6), 260 (34), 204 (20), 109 (21), 94 (29), 93 (21), 91 (24), 82 (23), 81 (52), 80 (24), 79 (25), and 43 (base peak). HRMS Found: *m/z* 311.1902. Calcd for $C_{16}H_{30}NO_4P$: M, 311.1911.

General Procedure for Oxidation of the Carbanions Derived from 10a—d Leading to 3-(1-Oxoalkyl)-2-isoxazolines 11a — c. Butyllithium (1.6 M in hexane, 0.63 ml, 1 mmol) was added, at −78 °C under nitrogen, to the solution of isoxazoline **10** (1 mmol) in dry THF (5 ml) and stirred for 1 h. Dry oxygen was slowly bubbled into this solution for 1 h at the same temperature. The mixture was poured into ice water (20 ml) and extracted with dichloromethane (20 ml × 2). The combined extracts were dried over magnesiun sulfate and evaporated in vacuo. The residue was chromatographed over silica gel with the following eluent: **11a**: hexane-ethyl acetate (10 : 1 v/v); **11b**, **11c**: hexane-ethyl acetate (20 : 1 v/v). Unreacted **10** was recovered from the fraction eluted with ethyl acetate. The results are listed in Table 4.

11a: Colorless liquid; IR (neat) 1680 and 1575 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 2.52 (3H, s, COMe), 3.09 (1H, dd, *J* = 17.7 (gem) and 9.0 Hz, one of 4-H), 3.53 (1H, dd, *J* = 17.7 (gem) and 11.5 Hz, the other of 4-H), 5.73 (1H, dd, *J* = 11.5 and 9.0 Hz, 5-H), and 7.31 (5H, s, Ph); ^{13}C NMR ($CDCl_3$) δ = 26.71 (q, COMe), 39.77 (t, 4-C), 85.59 (d, 5-C), 126.01, 128.77, 129.01 (each d), 139.78 (s), 158.06 (s, 3-C), and 193.19 (s, COMe); MS *m/z* (rel intensity, %) 189 (M^+, 3), 115 (17), 105 (15), 104 (13), 78 (17), 77 (38), 51 (32), and 43 (base peak). Found: C, 69.90; H, 5.93; N, 7.37%. Calcd for $C_{11}H_{11}NO_2$: C, 69.83; H, 5.86; N, 7.40%.

11b: Colorless needles (hexane); mp 43—44 °C; IR (KBr) 1660 and 1560 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.89 (3H, t, *n*-Pen), 1.1—1.9 (6H, m, *n*-Pen), 2.90 (2H, t, *J* = 7.0 Hz, *n*-Pen), 3.07 (1H, dd, *J* = 17.8 (gem) and 9.0 Hz, one of 4-H), 3.51 (1H, dd, *J* = 17.8 (gem) and 11.2 Hz, the other of 4-H), 5.69 (1H, dd, *J* = 11.2 and 9.0 Hz, 5-H), and 7.27 (5H, s, Ph); ^{13}C NMR ($CDCl_3$) δ = 13.88 (q, *n*-Pen), 22.41, 23.71, 31.36, 39.30, 40.00 (each t), 85.24 (d, 5-C), 126.01, 128.71, 129.01 (each d), 139.89 (s), 157.59 (s, 3-C), and 196.02 (s, CO); MS *m/z* (rel intensity, %) 245 (M^+, base peak), 244 (24), 228 (43), 129 (21), 128 (16), 115 (20), 105 (19), 104 (83), 99 (49), 91 (20), 76 (26), and 71 (35). Found: C, 73.57; H, 7.85; N, 5.78%. Calcd for $C_{15}H_{19}NO_2$: C, 73.44; H, 7.81; N, 5.71%.

11c: Colorless prisms (hexane); mp 33—34 °C; IR (KBr) 1680 and 1580 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.88 (3H, t, *J* = 7.0 Hz, *n*-Pen), 1.2—1.8 (8H, m, *n*-Pen), 2.67 (1H, dd, *J* = 17.5 (gem) and 9.0 Hz, one of 4-H), 3.10 (1H, dd, *J* = 17.5 (gem) and 10.5 Hz, the other of 4-H), 4.13 (2H, s, CH_2Ph), 4.67 (1H, m, 5-H), and 7.22 (5H, s, Ph); ^{13}C NMR ($CDCl_3$) δ = 13.94 (q, *n*-Pen), 22.47, 24.88, 31.53, 35.18, 36.89, 45.65 (each t), 85.06 (d, 5-C), 127.19, 128.72, 129.89 (each d), 133.90 (s), 157.95 (s, 3-C), and 193.07 (s, CO); MS *m/z* (rel intensity, %) 259 (M^+, 71), 258 (base peak), 168 (38), 91 (89), and 65 (11). Found; C, 74.31; H, 8.26; N, 5.65%. Calcd for $C_{16}H_{21}NO_2$: C, 74.10; H, 8.16; N, 5.40%.

Reaction of 7k with Butyllithium Leading to 8. Butyllithium (1.6 M in hexane, 0.23 ml, 0.37 mmol) was slowly added, at −78 °C under nitrogen, to the solution of isoxazoline **7k** (0.133 g, 0.37 mmol) in dry THF (2 ml). After 1 h at −78 °C, pentyl iodide (0.146 g, 0.74 mmol) was added. The mixture was stirred at 0 °C for 1 h, at room temperature for 12 h, and then poured into ice water. The product was extracted with dichloromethane (30 ml × 2). The combined extracts were dried over magnesium sulfate and evaporated in vacuo. The residue was chromatographed over silica gel by using hexane-ethyl acetate (1 : 5 v/v) to give **8** (0.059 g, 73%) which was characterized above.

General Procedure for the Raney Ni Hydrogenolysis of 7 or 10a Leading to 12a—g. The following two procedures were applied: A mixture of **7** or **10a** (1 mmol), Raney Ni (W-2, suspension in ethanol, 1 ml), acetic acid (0.5 ml), and water (0.5 ml) in ethanol (5 ml) -Method A- or a mixture of **7** or **10a** (1 mmol), Raney Ni (1 ml), boric acid (0.13 g, 2 mmol), and water (1 ml) in ethanol (5 ml) -Method B- was stirred under an atmosphere of hydrogen (1 atm) at room temperature. The insoluble materials were removed off by filteration through celite 545 and the filtrate was evaporated in vacuo. The residue was dissolved in dichloromethane (20 ml). The solution was washed with water, dried over magnesium sulfate, and evaporated in vacuo to give **12**. The methods applied, the reaction times, the yields of **12**, and the purification methods are as follows: **12a**: B, 12 h, 80%, a silica-gel chromatography with ethyl acetate; **12b**: B, 13 h, 91%, a silica-gel chromatography with ethyl acetate; **12c**: B, 13 h, 63%, a silica-gel chromatography with ethyl acetate; **12d**: B, 13 h, 63%, decomposed in a silica-gel column; **12e**: A, 20 h, 77%, a silica-gel chromatography with hexane-ethyl acetate (5 : 1 v/v); **12f**: B, 13 h, 88%, a silica-gel chromatography with ethyl acetate. **12g**: B, 12 h, 73%, a silica-gel chromatography ethyl acetate.

12a: Colorless liquid: IR (neat) 3360, 1710, 1240, 1020, and 790 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 1.28 (6H, t, *J* = 7.0 Hz, OEt), 2.7—3.2 (2H, m, $COCH_2$), 3.08 (2H, d, *J* = 23.0 (HP) Hz, CH_2P), 3.8—4.3 (1H, br, OH), 4.08 (4H, qd, *J* = 7.0 and 7.5 (HP) Hz, OEt), 5.12 (1H, dd, *J* = 8.0 and 4.5 Hz, CHPh), and 7.0 − 7.5 (5H, m, Ph); ^{13}C NMR ($CDCl_3$) δ = 16.29 (qd, J_{cp} = 5.9 Hz, OEt), 43.06 (td, J_{cp} = 126.5 Hz, CH_2P), 53.06 (t, $COCH_2$), 62.83 (td, J_{cp} = 5.9 Hz, OEt), 69.95 (d, CH), 125.95, 127.77, 128.65 (each d), 143.48 (s), and 202.02 (d, J_{cp} = 5.9 Hz, CO); MS *m/z* (rel intensity, %) 300 (M^+, 1), 125 (14), 123 (20), 109 (37), 107 (33), 105 (29), 97 (20), 96 (22), 81 (48), 79 (84), 78 (33), and 77 (base peak). HRMS Found: *m/z* 300.1121. Calcd for $C_{14}H_{21}O_5P$: M, 300.1125.

12b: Colorless liquid IR (neat) 3400, 1710, 1240, 1025, and 790 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ = 0.88 (3H, t, *J* = 6.0 Hz, *n*-Pen), 1.33 (6H, t, *J* = 7.0 Hz, OEt), 1.1 — 1.7 (8H, m, *n*-Pen), 2.72 (2H, d, *J* = 6.0 Hz, $COCH_2$), 3.16 (2H, d, *J* = 22.5 (HP) Hz, CH_2P), 3.82 (1H, br, OH), 4.04 (1H, m, CH), and 4.13 (4H, qd, *J* = 7.0 and 7.5 (HP) Hz, OEt); ^{13}C NMR ($CDCl_3$) δ = 14.06 (q, *n*-Pen), 16.29 (qd, J_{cp} = 5.9 Hz, OEt), 22.65, 25.24, 31.83, 37.00 (each t), 43.00 (d, J_{cp} = 126.5 Hz, CH_2P), 51.36 (t), 62.77 (td, J_{cp} = 5.9 Hz, OEt), 67.77 (d, CH), and 202.89 (d, J_{cp} = 5.9 Hz, CO); MS *m/z* (rel intensity, %) 294 (M^+, 3), 223 (base peak), 195 (33), 194 (42), 179 (19), 167 (17), 152 (18), 139 (19), 125 (20), 123 (25), and 97 (16). HRMS Found: *m/z* 294.1546. Calcd for $C_{13}H_{27}O_5P$: M, 294.1595.

12c: Colorless liquid; IR (neat) 3340, 1730, 1710, 1240, 1020, 970, and 790 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.33 (6H, d, J=7.0 Hz, OEt), 3.10 (2H, d, J=5.0 Hz, COCH$_2$), 3.15 (2H, d, J=22.5 (HP) Hz, CH$_2$P), 3.73 (3H, s, COOMe), 4.13 (4H, qd, J=7.0 and 7.5 (HP) Hz, OEt), 4.51 (1H, t, J=5.0 Hz, CH), and 4.65 (1H, s, OH); ^{13}C NMR (CDCl$_3$) δ=16.30 (qd, $J_{\rm cp}$=5.9 Hz, OEt), 42.80 (td, $J_{\rm cp}$=128.0 Hz, CH$_2$P), 47.71 (t, COCH$_2$), 52.42 (q, COOMe), 62.89 (td, $J_{\rm cp}$=5.9 Hz, OEt), 66.89 (d, CH), 174.19 (s, COOMe), and 199.89 (d, $J_{\rm cp}$=5.9 Hz, CO); MS *m/z* (rel intensity, %) 282 (M$^+$, 2), 223 (base peak), 195 (16), 194 (22), 179 (29), 152 (21), 151 (23), 139 (21), 125 (34), and 123 (54). HRMS Found: *m/z* 282.0864. Calcd for C$_{10}$H$_{19}$O$_7$P: M, 282.0867.

12d: Labile colorless liquid; ^{1}H NMR (CDCl$_3$) δ=1.33 (6H, J=7.0 Hz, OEt), 2.25 (3H, s, COMe), 3.06 (2H, dd, J=6.2 and 4.2 Hz, COCH$_2$), 3.15 (2H, d, J=22.6 (HP) Hz, CH$_2$P), 4.13 (4H, qd, J=7.0 and 7.4 (HP) Hz, OEt), 4.37 (1H, dd, J=6.2 and 4.2 Hz, CH), and 4.34 (1H, br, OH); ^{13}C NMR (CDCl$_3$) δ=16.32 (qd, $J_{\rm cp}$=7.4 Hz, CH$_2$P), 25.53 (q, COMe), 42.97 (td, $J_{\rm cp}$=125.0 Hz, OEt), 47.12 (t, COCH$_2$), 62.98 (td, $J_{\rm cp}$=8.3 Hz, OEt), 73.53 (d, CH), 200.37 (d, $J_{\rm cp}$=5.9 Hz, CO), and 209.72 (s, COMe); MS*m/z* (rel intensity, %) 223 (M$^+$−COMe, 77), 195 (26), 179 (22), 167 (26), 152 (34), 151 (26), 139 (48), 125 (40), 123 (73), 121 (20), 109 (23), 97 (33), and 43 (base peak). This compound was too labile to be purified as an authentic sample.

12e: Colorless liquid; IR (neat) 3400, 1700, 1240, 1025, and 800 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.33 (6H, t, J=7.0 Hz, OEt), 2.93 (2H, d, J=6.0 Hz, CH$_2$Br), 3.16 (2H, d, J=22.5 (HP) Hz, CH$_2$P), 3.46 (2H, d, J=5.0 Hz, COCH$_2$), 3.72 (1H, s, OH), 4.12 (4H, qd, J=7.0 and 7.3 (HP) Hz, OEt), and 4.24 (1H, tt, J=6.0 and 5.0 Hz, CH); ^{13}C NMR (CDCl$_3$) δ=16.30 (qd, $J_{\rm cp}$=5.9 Hz, OEt), 37.82 (t, CH$_2$Br), 43.03 (td, $J_{\rm cp}$=128.0 Hz, CH$_2$P), 48.94 (t, COCH$_2$), 62.95 (td, $J_{\rm cp}$=5.9 Hz, OEt), 67.01 (d, CH), and 201.19 (d, $J_{\rm cp}$=5.9 Hz, CO); MS *m/z* (rel intensity, %) 319, 317 (M$^+$, 17), 223 (base peak), 219 (47), 195 (23), 194 (60), 179 (40), 167 (22), 163 (19), 151 (33), 139 (34), 125 (36), 123 (59), 109 (32), 97 (26), and 80 (41). Found: C, 33.87; H, 5.65%. Calcd for C$_9$H$_{18}$O$_5$BrP: C, 34.09; H, 5.72%.

12f: Colorless liquid; IR (neat) 3370, 1710, 1245, 1025, and 965 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.1—1.4 (12H, m, OEt), 2.79 (2H, d, J=5.8 Hz, COCH$_2$), 3.12 (2H, d, J=21.6 (HP) Hz, CH$_2$P), 3.20 (1H, br, OH), 3.4—3.8 (4H, m, OEt), 3.9—4.2 (1H, m, CH), 4.07 (4H, qd, J=7.0 and 7.5 (HP) Hz, OEt), and 4.30 (1H, d, J=5.8 Hz, CH(OEt)$_2$); ^{13}C NMR (CDCl$_3$) δ=15.35 (q, OEt), 16.29 (qd, $J_{\rm cp}$=5.9 Hz, OEt), 43.15 (td, $J_{\rm cp}$=128.0 Hz, CH$_2$P), 46.06 (t, COCH$_2$), 62.65 (td, $J_{\rm cp}$=5.9 Hz, OEt), 63.36, 64.00 (each t, OEt), 68.77 (d, CHOH), 104.36 (d, CH(OEt)$_2$), and 201.60 (s, CO); MS *m/z* (rel intensity, %) 281 (M$^+$-OEt), 223 (16), 179 (7), 152 (6), 123 (9), 104 (6), 103 (base peak), 75 (31), and 47 (21). Found: C, 47.85; H, 8.24%. Calcd for C$_{13}$H$_{27}$O$_7$P: C, 47.85; H, 8.44%.

12g (A mixture of two diastereomers): Pale yellow liquid; IR (neat) 3360, 1710, 1240, 1020, and 790 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.26 (6H, t, J=7.0 Hz, OEt), 1.4—1.5 (3H, m, Me), 2.8—3.6 (3H, m, CH$_2$CO and CH), 4.04 (4H, qd, J=7.0 and 8.0 (HP) Hz, OEt), 5.12 (1H, dd, J=7.0 and 5.0 Hz, CHPh), and 7.1—7.5 (5H, m, Ph); ^{13}C NMR (CDCl$_3$) δ=10.24 (q, Me), 16.00 (qd, $J_{\rm cp}$=5.9 Hz, OEt), 46.65, 47.12 (each td, $J_{\rm cp}$=126.5 Hz, CH$_2$P), 52.12, 52.89 (each d), 62.30 (td, $J_{\rm cp}$=5.9 Hz, OEt), 69.59, 69.89 (each d, CHPh), 125.60, 127.13, 128.13 (each d), 143.78 (s), 204.87, and 205.34 (each d, $J_{\rm cp}$=4.4 Hz, CO); MS *m/z*(rel intensity, %) 314 (M$^+$, 4), 208 (16), 190 (23), 180 (32), 166 (28), 139 (21), 138 (29), 137 (26), 123 (30), 109 (79), 107 (47), 105 (52), 103 (24), 91 (26), 81 (68), 79 (86), 78 (30), 77 (base peak), 51 (24), and 43 (22). HRMS Found: *m/z* 314.1276. Calcd for C$_{15}$H$_{23}$O$_5$P: M, 314.1282.

2-[(Diethoxyphosphoryl)methyl]-5-methylpyrrole (13). The Raney Ni reduction of **7e** (0.270 g, 1.03 mmol) was carried out for 19 h according to the method A mentioned above and followed by the usual work-up and the column chromatography over silica gel (hexane-ethyl acetate (1 : 1 v/v)) to give **13** (0.056 g, 24%): Pale yellow liquid; IR (neat) 3220, 1590, 1225, 1020, and 790 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.24 (6H, t, J=7.0 Hz, OEt), 2.17 (3H, d, J=1.5 Hz, Me), 3.11 (2H, d, J=20.0 (HP) Hz, CH$_2$P), 4.00 (4H, qd, J=7.0 and 14.0 (HP) Hz, OEt), 5.6—5.9 (2H, m, 3- and 5-H), and 8.90 (1H, br, s, NH); ^{13}C NMR (CDCl$_3$) δ=13.00 (q, Me), 16.41 (qd, $J_{\rm cp}$=5.3 Hz, OEt), 25.88 (td, $J_{\rm cp}$=141.2 Hz, CH$_2$P), 62.50 (td, $J_{\rm cp}$=7.4 Hz, OEt), 106.02 (d, 4-C), 108.33 (dd, $J_{\rm cp}$=10.3 Hz, 3-C), 118.89 (d, $J_{\rm cp}$=11.8 Hz, 2-C), and 128.33 (s, 5-C); MS *m/z* (rel intensity, %) 231 (M$^+$, 6), 95 (15), 94 (base peak), and 93 (12). HRMS Found: *m/z* 231.1019. Calcd for C$_{10}$H$_{18}$NO$_3$P: M, 231.1023.

General Procedure for the Dehydration of Hydroxy Ketones 12a, 12b Leading to 14a, 14b. To a solution of **12** (1 mmol) and triethylamine (0.3 g, 3 mmol) in dichloromethane (5 ml) was added dropwise methanesulfonyl chloride (0.14 g, 1.2 mmol) at −20 °C. The mixture was stirred at −20 °C for 0.5 h and at room temperature for 1 h. Ice water (20 ml) was added and the product was extracted with diethyl ether (20 ml × 2). The combined extracts were washed with 1 M hydrochloric acid (20 ml), aqueous sodium hydrogencarbonate (20 ml), and water (20 ml × 2). After dried over magnesium sulfate, the solvent was evaporated in vacuo. The residue was chromatographed over silica gel by using hexane-ethyl acetate (1 : 5 v/v).

14a: Yield 87%; pale yellow liquid; IR (neat) 1650, 1600, 1240, 1020, and 790 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=1.30 (6H, t, J=7.0 Hz, OEt), 3.30 (2H, d, J=23.0 (HP) Hz, CH$_2$P), 4.14 (4H, qd, J=7.0 and 8.0 (HP) Hz, OEt), 6.84 (1H, d, J=16.0 Hz, CH=), 7.60 (1H, d, J=16.0 Hz, CH=), and 7.2—7.6 (5H, m, Ph); ^{13}C NMR (CDCl$_3$) δ=16.29 (qd, $J_{\rm cp}$=5.9 Hz, OEt), 40.97 (td, $J_{\rm cp}$=128.0 Hz, CH$_2$P), 62.68 (td, $J_{\rm cp}$=7.4 Hz, OEt), 125.95, 128.77, 129.13, 131.01 (each d), 134.06 (s), 144.89 (d), and 191.30 (d, $J_{\rm cp}$=5.9 Hz, CO); MS *m/z* (rel intensity, %) 282 (M$^+$, 31), 253 (14), 224 (66), 197 (96), 180 (47), 179 (base peak), 169 (35), 152 (62), 151 (70), 144 (49), 131 (32), 125 (43), 123 (88), 109 (44), 97 (24), 88 (38), and 81 (38). HRMS Found: *m/z* 282.1019. Calcd for C$_{14}$H$_{19}$O$_4$P: M, 282.1020.

14b: Yield 93%; pale yellow liquid; IR (neat) 1690, 1660, 1250, 1025, 960, and 790 cm^{-1}; ^{1}H NMR (CDCl$_3$) δ=0.89 (3H, t, J=6.0 Hz, *n*-Pen), 1.1—1.7 (6H, m, *n*-Pen), 1.32 (6H, t, J=7.0 Hz, OEt), 2.24 (2H, q, J=7.0 Hz, *n*-Pen), 3.20 (2H, d, J=22.0 (HP) Hz, CH$_2$P), 4.13 (4H, qd, J=7.0 and 7.5 (HP) Hz, OEt), 6.20 (1H, dt, J=15.0, 1.0, and 1.0 Hz, CH=), and 6.94 (1H, dt, J=15.0, 7.0, and 7.0 Hz, CH=); ^{13}C NMR (CDCl$_3$) δ=13.94 (q, *n*-Pen), 16.35 (qd, $J_{\rm cp}$=5.9 Hz, OEt), 22.41, 27.71, 31.41, 32.59 (each t), 40.18 (tq, $J_{\rm cp}$=129.4 Hz, CH$_2$P), 62.59 (td, $J_{\rm cp}$=5.9 Hz, OEt), 130.25, 150.72 (each d), and 191.57 (d, $J_{cp}=7.4$ Hz, CO); MS m/z (rel intensity, %) 276 (M^+, 6), 244 (73), 173 (40), 136 (24), 121 (base peak), 81 (23), 65 (70), and 55 (30). HRMS Found: m/z 276.1487. Calcd for $C_{13}H_{25}O_4P$: M, 276.1489.

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