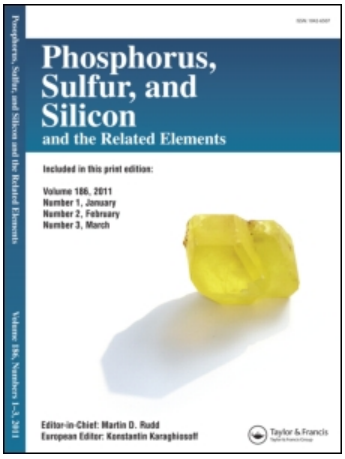

Phosphorus, Sulfur, and Silicon and the Related Elements
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713618290

SYNTHESIS OF DIALKYL (PYRROLIDIN-2-YL)-PHOSPHONATES BY MERCURIC ACETATE PROMOTED CYCLIZATION OF α-AMINOALKENYLPHOSPHONATES. REGIO AND STEREOCHEMICAL ASPECTS

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To cite this Article Roubaud, Valérie , Moigne, Franois Le , Mercier, Anne and Tordo, Paul(1994) 'SYNTHESIS OF DIALKYL (PYRROLIDIN-2-YL)-PHOSPHONATES BY MERCURIC ACETATE PROMOTED CYCLIZATION OF α-AMINOALKENYLPHOSPHONATES. REGIO AND STEREOCHEMICAL ASPECTS', Phosphorus, Sulfur, and Silicon and the Related Elements, 86: 1, 39 — 54
To link to this Article: DOI: 10.1080/10426509408018386
URL: http://dx.doi.org/10.1080/10426509408018386

Phosphorus, Sulfur, and Silicon, 1994, Vol. 86, pp. 39–54
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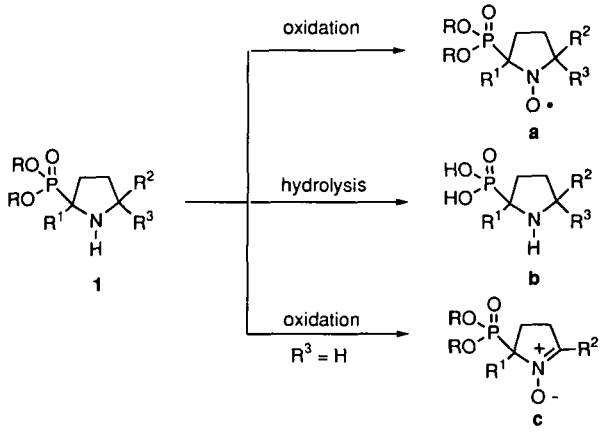
(Received December 30, 1993; in final form January 11, 1994)

A new series of dialkyl(pyrrolidin-2-yl)phosphonates was synthesized by regiospecific intramolecular aminomercuration of α-amino alkenylphosphonates followed by sodium borohydride reduction. The formation of dialkyl (2,5-dialkyl pyrrolidin-2-yl) and dialkyl (5-alkyl pyrrolidin-2-yl)phosphonates was stereoselective and the stereochemistry of diastereomers was assigned using X-ray analysis and ^{1}H, ^{13}C and ^{31}P-NMR data. EPR evidence for the production of free radicals during the borohydride reduction of the intermediate organomercurials was achieved by spin-trapping experiments.

Key words: Pyrrolidin-2-yl phosphonates; α-aminophosphonates; aminomercuration; mercuric acetate; radical-mediated reduction; EPR.

INTRODUCTION

α-Phosphorylated pyrrolidines can be transformed into a variety of molecules (Scheme 1) such as stable β-phosphorylated pyrrolidinoxyl radicals[1,2] **a**, phosphorus analogs



SCHEME 1

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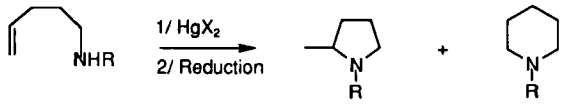
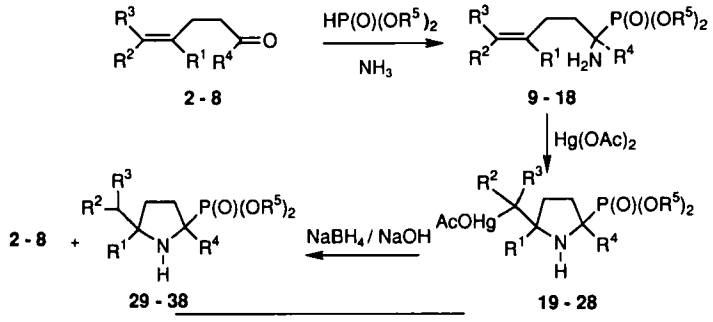
of proline[3] **b** or α-phosphorylated pyrrolin-1-oxides[4,5] **c**, a new class of efficient scavengers of oxygen-derived free radicals. All these compounds have interesting applications in different fields.[6–8]

While different syntheses of α-phosphorylated pyrrolidines have been previously described,[3,9] to the best of our knowledge, no general approach to these compounds



SCHEME 2



carbonyl compounds	R^1	R^2	R^3	R^4
2	H	H	H	H
3*	H	n-C_5H_{11}	H	H
4	H	H	H	CH_3
5**	H	CH_3	H	CH_3
6**	CH_3	CH_3	H	CH_3
7	CH_3	H	H	CH_3
8	H	CH_3	CH_3	CH_3

* trans isomer

** cis / trans mixture

Amino -phosphonates	Organo -mercurials	Pyrrolidinyl derivatives	R^1	R^2	R^3	R^4	R^5
9	**19**	**29**	H	H	H	H	C_2H_5
10	**20**	**30**	H	n-C_5H_{11}	H	H	C_2H_5
11	**21**	**31**	H	H	H	CH_3	C_2H_5
12	**22**	**32**	H	CH_3	H	CH_3	C_2H_5
13	**23**	**33**	CH_3	CH_3	H	CH_3	C_2H_5
14[1]	**24**	**34**[1]	CH_3	H	H	CH_3	C_2H_5
15[27]	**25**	**35**[27]	H	CH_3	CH_3	CH_3	C_2H_5
16	**26**	**36**	H	n-C_5H_{11}	H	H	$CH(CH_3)_2$
17	**27**	**37**	H	H	H	CH_3	$CH(CH_3)_2$
18	**28**	**38**	H	CH_3	H	CH_3	$CH(CH_3)_2$

SCHEME 3

exists. Our interest in new stable β-phosphorylated aminoxyl radicals and α-phosphorylated pyrrolin-1-oxides faced us with the need to develop a general synthetic route to α-phosphorylated pyrrolidines **1**.

Intramolecular aminomercuration[1,2,10–26] of alkenylamines is a useful approach to substituted heterocyclic amines and this reaction has been particularly applied to the synthesis of substituted pyrrolidines and piperidines. Usually, the reaction is regiospecific but the aminomercuration-demercuration sequence applied to δ-alkenylamines can lead both to five and six-membered rings[10,15,23] (Scheme 2).

The stereochemical selectivity of these reactions is more difficult to predict and was shown to strongly depend on experimental conditions.[20,22,24–26]

In the present paper, we report the synthesis of a series of α-amino alkenylphosphonates and their transformation to α-phosphorylated pyrrolidines via an aminomercuration-demercuration sequence (Scheme 3). We will also discuss the regio and stereoselectivity of this original approach to α-phosphorylated pyrrolidines.

RESULTS AND DISCUSSION

Synthesis

Bubbling ammonia into solutions of γ-alkenyl aldehydes or ketones (**2–8**) in dialkylphosphites gave the corresponding α-amino alkenylphosphonates (**9–18**) (Table I) in reasonable yields (50–70%) from the γ-ethylenic ketones but in rather poor yields (10–30%) from aldehydes. Cyclization of the α-amino alkenylphosphonates to the pyrrolidin-2-yl phosphonates **29–38** was carried out by intramolecular aminomercuration, followed by reduction of the intermediate organomercurial (Scheme 3). The influence of the experimental conditions was investigated on compound **11**, and the different experimental procedures (A–G) are given in Table II.[28]

TABLE I

Synthesis of α-amino alkenylphosphonates by reaction of γ-alkenyl ketones or aldehydes with ammonia and dialkylphosphites

Compounds	Phosphites	Products	Yields (%)
2	$HP(O)(OEt)_2$	**9**	30
3	"	**10**	15
4	"	**11**	67
5	"	**12**	50
6	"	**13**	54
7	"	**14**[1]	70
8	"	**15**[27]	70
3	$HP(O)(O\textit{i}\text{-}Pr)_2$	**16**	10
4	"	**17**	40
5	"	**18**	42

^{1}H- and ^{31}P-NMR monitoring of the aminomercuration step showed that the transformation of **11** to the corresponding organomercurial was total, whatever the experimental conditions. Reduction of the intermediate organomercurial **21** with sodium borohydride gave then a mixture of the expected diastereomeric pyrrolidin-2-yl phosphonates **31a,b** together with variable amounts of the starting amino-phosphonate **11**. The conversion ratio ([**31**]/[**11**] + [**31**]) (Table II) was shown to depend on the experimental procedure and changed from 66% (B) to 100% (F); however, procedure F led to a mixture of **31a,b** (91%) and of a dialkyl mercury compound **39** (9%) (Scheme 4).

All the procedures A–G led regiospecifically to the diastereomers **31a,b** with different diastereomeric ratio (Table II). Finally, procedures A and E were shown to be the best compromises to obtain pure samples of **31a,b** and were thus applied to all the series of α-aminoalkenyl phosphonates. The results obtained are shown in Table III.

All the cyclizations were regiospecific and gave only the pyrrolidinic phosphonates **29–38a,b**, with 17 to 86% conversion ratio, except for compound **33** which was not obtained. As shown in Table III, the best conversion ratios and the highest stereoselectivities were obtained using the E procedure.

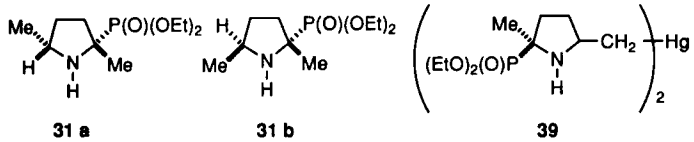
Formation of free radicals during sodium borohydride reduction of organomercurials is well documented[29–31] and easily accounts for the formation of the

TABLE II

Comparative results of A–G cyclization procedures of α-amino alkenyl phosphonate **11**

Procedures[i]	Products	Conversion ratios[j] (%)	a/b[j] (%)
A	**31 a,b**	74	30/70
B	"	66	30/70
C	"	68	30/70
D	"	83	20/80
E	"	86	17/83
F	**31 a,b**[k] + **39**[l]	100	23/77
G	"	83	15/85

i : A: $Hg(OAc)_2$ (1 eq), $NaBH_4$ (1 mol eq), H_2O/ THF; B: under N_2, $Hg(OAc)_2$ (1 eq), $NaBH_4$ (1 mol eq) in H_2O/ THF; C: $Hg(OAc)_2$ (1 eq) (reverse addition), $NaBH_4$ (1 mol eq) in H_2O/ THF; D: $Hg(OAc)_2$ (1 eq), $NaBH_4$ (1 mol eq) in CH_2Cl_2; E: $Hg(OAc)_2$ (1 eq), $NaBH_4$ (1 mol eq), Benzyltriethyl ammonium chloride (3.5 eq) in CH_2Cl_2; F: $Hg(OAc)_2$ (2 eq), $NaBH_4$ (2 mol eq) in H_2O/ THF; G: $Hg(OAc)_2$ (1 eq), $NaBH_4$ (1 mol eq), Benzyltriethyl ammonium chloride (3.5 eq) in acetone.*j* : Based on ^{1}H and ^{31}P-NMR of the crude mixtures. *k* : 91%; *l* : 9%.



31 a **31 b** **39**

SCHEME 4

TABLE III

Results of cyclization of α-amino alkenylphosphonates **9–18**, following procedures A or E

Compounds	Products	Conversion(%) ratios A	E	Diastereomeric ratios a/b A	E
9	**29**	39	58	33/66	20/80
10	**30**	42	73	23/77	14/86
11	**31**	74	86	30/70	17/83
12	**32**	25	55	30/70	18/82
13	**33**	0	0	-	-
14	**34**	-	72	-	-
15	**35**	17	37	45/55	28/72
16	**36**	47	80	23/77	10/90
17	**37**	64	63	31/69	25/75
18	**38**	19	57	50/50	32/78

Experimental procedures: A: $Hg(OAc)_2$ (1 eq), $NaBH_4$ (1 mol eq), in water / THF; E: $Hg(OAc)_2$ (1 eq), benzyltriethylammonium chloride (3.5 eq), $NaBH_4$ (1 mol eq) in CH_2Cl_2.

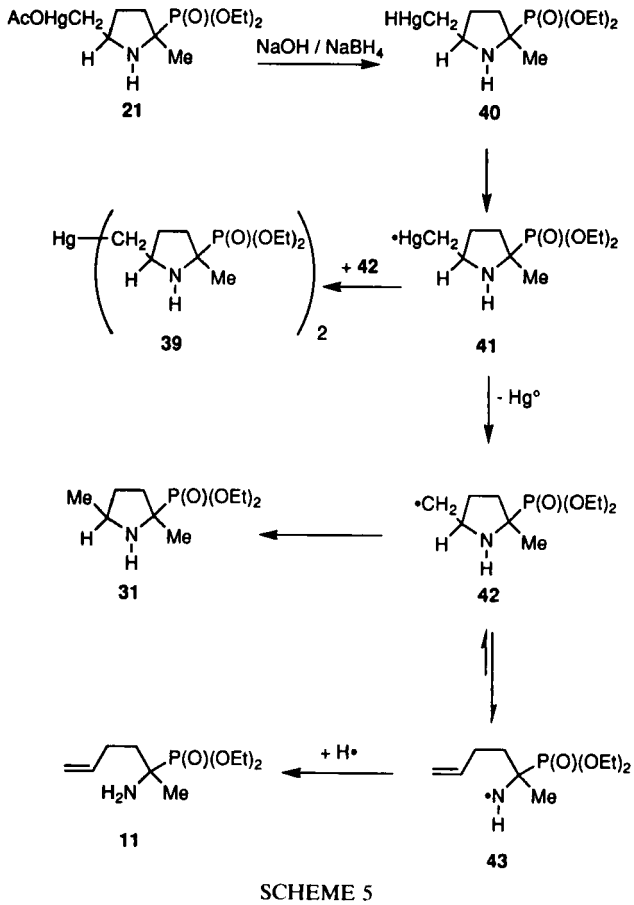
dialkyl mercury compound **39** (Scheme 5).[32] On the other hand, the formation of a significant amount of **11** during the reduction of the intermediate organomercurial **21** can rationalized assuming a β-scission of the alkyl radical **42** to give a primary aminyl radical **43** which rapidly abstracts a hydrogen atom. This β-scission corresponds to the reverse reaction of the intramolecular addition of a neutral aminyl radical on a carbon-carbon double bond. In the case of N-alkyl aminyl radical,[33] this reverse reaction was shown to have a kinetic of $1 \pm 0.1\ 10^4\ s^{-1}$ at 50°C while the cyclization was shown to have a kinetic of $3.5 \pm 0.3\ 10^3\ s^{-1}$ at the same temperature.

The formation of free radicals during the reduction of the organomercurials **21**, **23**, **25** was supported by spin-trapping experiments (Scheme 6). The pentamethoxynitrosobenzene[34] was used as scavenger and the EPR characteristics of the observed spin adducts **46–48** are listed in Table IV.

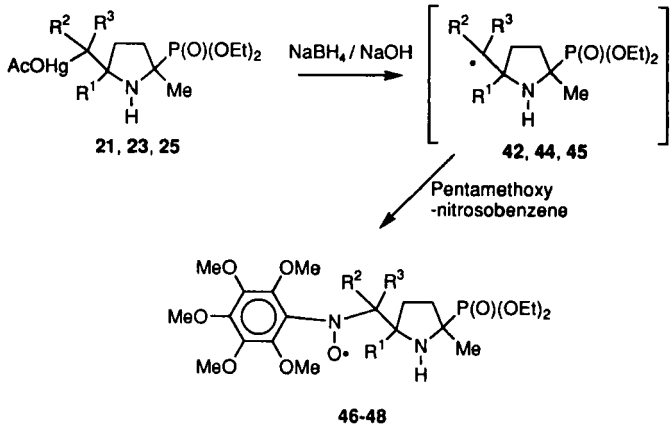
These experiments were carried out in methylene chloride under argon. No EPR signal was observed unless the appropriate amount of $NaBH_4$/NaOH solution was added to the solution containing the organomercurial and the spin trap. Only the alkyl radicals **42**, **44**, **45** were trapped and no spin-adduct from primary aminyl radical was detected. Arylnitroso compounds are known to trap alkyl radicals very efficiently[35] (with rate constants in the range of $10^7\ mol^{-1}\ s^{-1}$). This explains the fact that we did not trap aminyl species.

NMR and Stereochemical Studies

Pure **37a** (minor isomer) was isolated by successive crystallizations in n-pentane (−20°) and X-ray analysis (Figure 1) showed a trans stereochemistry of the two methyl groups.



SCHEME 5



21, 42, 46 : $R^1 = R^2 = R^3 = H$
23, 44, 47 : $R^1 = R^2 = Me$, $R^3 = H$
25, 45, 48 : $R^1 = H$, $R^2 = R^3 = Me$

SCHEME 6

TABLE IV

EPR characteristics of pentamethoxynitrosobenzene spin-adducts **46–48** formed during the sodium borohydride reduction of organomercurials **21**, **23**, **25**

Adducts	a_H (G)	a_N (G)	g
46	7.10 10.89	13.07	2.0061
47	2.51	12.85	2.0061
48		13.66	2.0061

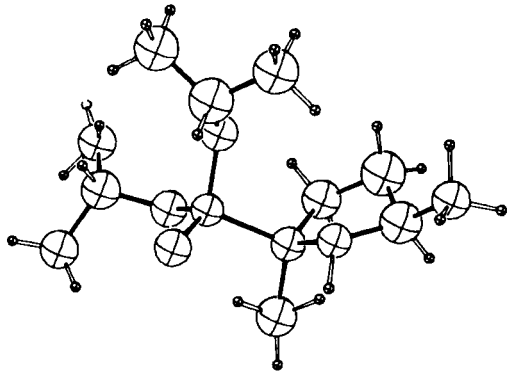
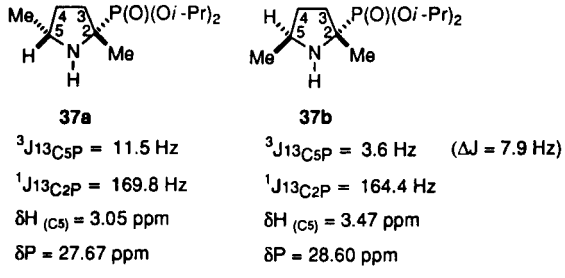


FIGURE 1 X-ray structure of diastereomer **37a**.



37a

$^3J_{13C5P}$ = 11.5 Hz

$^1J_{13C2P}$ = 169.8 Hz

$\delta H_{(C5)}$ = 3.05 ppm

δP = 27.67 ppm

37b

$^3J_{13C5P}$ = 3.6 Hz (ΔJ = 7.9 Hz)

$^1J_{13C2P}$ = 164.4 Hz

$\delta H_{(C5)}$ = 3.47 ppm

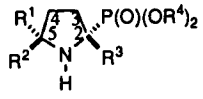
δP = 28.60 ppm

SCHEME 7

Diastereomers **37a** and **37b** (Scheme 7) showed significant differences in their ^1H, ^{13}C and ^{31}P-NMR data (Table V). Particularly striking is the difference between the $^3J13_{C5P}$ values (ΔJ = 7.9 Hz). Similar differences were found for the diastereomeric mixtures of 2,2,5-trisubstituted (**31a,b**, **32a,b**, **38a,b**) as well as for those of 2,5-disubstituted (**29a,b**, **30a,b**, **36a,b**) pyrrolidinic compounds (Table V). In the 2,2,5-trisubstituted series, these data allowed us to conclude that the major

TABLE V

^1H, ^{13}C and ^{31}P-NMR (C_6D_6, δ (ppm), J (Hz)) comparative data of the diastereomers of dialkyl (2,5-disubstituted) and 2,2,5-trisubstituted (pyrrolidin-2-yl) phosphonates



Products	R^1	R^2	R^3	R^4	$^1J_{13C2P}$	$^3J_{13C5P}$	$\delta H_{(C5)}$	$\delta^{31}P$
31a	Me	H	Me	Et	169.3	11.1	3.10	28.84
31b	H	Me	Me	Et	162.2	3.0	3.43	29.36
32a	Et	H	Me	Et	168.6	10.4	2.91	28.81
32b	H	Et	Me	Et	160.3	3.9	3.25	30.13
37a	Me	H	Me	*i*-Pr	169.8	11.5	3.05	27.67
37b	H	Me	Me	*i*-Pr	164.4	3.6	3.47	28.60
38a	Et	H	Me	*i*-Pr	166.6	10.2	3.09	27.45
38b	H	Et	Me	*i*-Pr	161.3	3.2	3.30	28.59
29a	Me	H	H	Et	166.8	15.5	2.81	27.09
29b	H	Me	H	Et	164.1	7.1	3.29	28.03
30a	Hexyl	H	H	Et	167.2	14.6	2.76	27.03
30b	H	Hexyl	H	Et	161.7	7.2	3.14	27.76
36a	Hexyl	H	H	*i*-Pr	168.6	15.4	2.70	25.54
36b	H	Hexyl	H	*i*-Pr	163.4	7.3	3.18	26.43

products **31b**, **32b** and **38b**, like **37b**, have the 2,5-alkyl groups in a cis configuration, while the dialkoxyphosphoryl group and the 5-alkyl group stand in a trans configuration. In the same way, for 2,5-disubstituted compounds, a trans configuration was assigned to the major diastereomers **29b**, **30b**, **36b**.

^{199}Hg, ^{31}P and ^1H-NMR of different organo mercurials indicated that the stereoselectivity is the same before and after sodium borohydride reduction (Table VI). On the other hand, ^{13}C-NMR showed us that the diastereomers of the organomercurial **27** present a similar difference in the $^3J13_{C5P}$ values.[36]

Concerning the cyclization of δ-alkenyl carbamates to 2,5-disubstituted pyrrolidinic compounds, Harding[37] reported that the stereoselectivity (majority of the trans isomer) of the reaction is under kinetic control and that equilibration into the thermodynamic products can be achieved through the ammonium form of the organomercuric intermediate. Furthermore, during the synthesis of 2,5-disubstituted N-alkyl pyrrolidines by intramolecular aminomercuration, Tokuda[22] observed that, under homogeneous conditions, the trans diastereomer was the major product, while the cis diastereomer was preferentially formed in heterogeneous medium;

TABLE VI

Diastereomeric ratios, before and after the reduction step, determined by ^{31}P or $^{199}Hg(*)$-NMR. (Cyclization solvent: *i*: THF/water, *ii*: methylene chloride)

organo -mercurials	reduced products	a/b ratios non reduced	reduced
20a,b	**30a,b**	*i* 22/78	*i* 23/77
		ii 11/89	*ii* 14/86
21a,b	**31a,b**	*i* 20/80	*i* 30/70
		ii 15/85	*ii* 17/83
23a,b	**33a,b**	*ii* 12/88	–
27a,b	**37a,b**	*ii* 16/84	*ii* 25/75
		ii 23/77*	

these results were interpreted by Orena[38] in terms of kinetic control for the former, and thermodynamic control for the latter.

When we monitored our experiments by ^1H-NMR, we never detected the protonated form of the mercurated pyrrolidines. On the other hand, the cyclizations were carried out in homogeneous conditions and it is then reasonable to assume that the major components **31b**, **32b**, **35b**, **37b**, **38b** (2,5,5-trisubstituted) and **29b**, **30b**, **36b** (2,5-disubstituted) would be the kinetic products; this would imply that, in the transition state, the (1-3) interactions between alkyl and phosphorylated substituents are greater than between the two alkyl groups.

In summary, we developed the synthesis of a new series of dialkyl (pyrrolidin-2-yl) phosphonates from α-amino alkenylphosphonates via a regiospecific and stereoselective aminomercuration-demercuration sequence. X-ray and NMR analysis allowed us to attribute the stereochemistry for all the series. EPR evidence for the formation of alkyl radicals during the borohydride demercuration step was obtained by spin-trapping experiments.

EXPERIMENTAL

General Comments. NMR spectra were performed on a Bruker AC 100 (^1H, 100 MHz; ^{31}P, 40.53 MHz; ^{13}C 25.18 MHz), a Bruker AC 200 (^1H, 200 MHz; ^{13}C, 50.32 MHz) and a Bruker AM 400 X (^1H, 400 MHz; ^{13}C, 100.61 MHz; ^{199}Hg, 71.66 MHz) spectrometers. IR absorptions were recorded on a Mattson 1000 Series FTIR spectrometer. Preparative TLC were performed on Merck Kieselgel 60 F254 plates. Elemental analyses were determined in the University of Aix-Marseille III. Mass spectra and HRMS were realized in the University of Rennes. Previously described alkenyl ketones and alkenyl aldehydes were prepared and characterized according to the following references: **2**,[39] **5**,[2b,40] **6**[2b,41]; commercially available **3**, **4** and dialkylphosphites were purchased from Aldrich.

Aminophosphorylation of Alkenyl Ketones and Alkenyl Aldehydes, Typical Procedure.

Ammonia was bubbled for 15 mn into the alkenyl carbonyl compound (52 mmol). At room temperature, the phosphite (57 mmol) was added. The mixture was then stirred, with ammonia, at 50–60°C. The progress of the reaction was monitored by ^1H and ^{31}P NMR. In some cases, a precipitate was observed, which was dissolved by addition of ethanol. The mixture was acidified with diluted (5%) hydrochloric acid and washed several times with ether, to remove residual starting materials. The aqueous layer was

poured over sodium hydroxide, extracted with ether; the organic layer was dried over magnesium sulfate. Filtration and removal of the solvent gave the alkenyl aminophosphonate.

Diethyl (1-aminopent-4-enyl) phosphonate (**9**). Yield 30%. ^{1}H-NMR (100 MHz, $CDCl_3$) δ 1.35 (t, J = 7.0 Hz, 6H, 2 CH_3CH_2O), 1.2–2.5 (m, 6H, NH_2, 2 CH_2), 3.00 (td, J = 10.6 Hz, J = 3.1 Hz, 1H,*CH), 4.16 (qt, J = 7.0 Hz, 4H, 2OCH_2), 5.10 (m, 2H, 2 CH=), 5.80 (m, 1H, CH=). ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ 28.17. ^{13}C-NMR (50.32 MHz, C_6D_6) δ 16.86 and 16.96 (2 OCH_2CH_3), 30.54 (d, J = 7.1 Hz, CH_2), 31.43 (CH_2), 48.82 (d, J = 149.2 Hz, CHP), 61.03 (d, J = 6.6 Hz, OCH_2CH_3), 62.24 (d, J = 6.3 Hz, OCH_2CH_3), 115.64 (CH=), 138.53 (CH_2=). IR (CCl_4) 3439, 1549, 1252, 1098, 1032 and 1005 cm^{-1}.

Diethyl (1-aminodec-4-enyl) phosphonate (**10**). Purification by preparative TLC over silica gel eluting with (6:4 v/v) pentane/acetone, afforded pure **10** in 15% yield. ^{1}H-NMR (100 MHz, $CDCl_3$) δ 0.75 (t, J = 5.5 Hz, 3H, CH_3CH_2), 1–2.5 (m, 14H, NH_2, 6 CH_2), 1.30 (t, J = 7.1 Hz, 6H, 2 CH_3CH_2O), 2.85 (td, J = 9.6 Hz, J = 3.2 Hz, 1H,*CH), 4.02 (qt, J = 7.1 Hz, 4H, 2OCH_2), 5.31 (m, 2H, 2 CH=). ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ 28.86. ^{13}C-NMR (50.32 MHz, $CDCl_3$) δ 13.76 ($CH_3(CH_2)_4$), 16.11 (d, J = 6.1 Hz, 2CH_3CH_2O), 22.23 (CH_2), 28.72 (d, J = 13.7 Hz, CH_2—C=), 28.91 (CH_2), 30.75 (CH_2), 31.09 (CH_2CP), 32.25 (CH_2), 47.62 (d, J = 148.9 Hz, CHP), 61.58 (d, J = 7.6 Hz, OCH_2CH_3), 61.68 (d, J = 7.5 Hz, OCH_2CH_3), 128.29 and 131.44 (2CH=). IR (CCl_4) 3393, 1457, 1241, 1163, 1056 and 1030 cm^{-1}. Anal. Calcd for $C_{14}H_{30}NO_3P$: C, 57.72; H, 10.38; N, 4.81. Found: C, 57.65; H, 10.30; N, 4.81%.

Diethyl (2-aminohex-5-en-2-yl) phosphonate (**11**). Yield 67%. ^{1}H-NMR (100 MHz, $CDCl_3$) δ 1.3 (d, J = 16.1 Hz, 3H, CH_3), 1.4 (t, J = 7.1 Hz, 6H, 2 CH_3), 1.5–2.5 (m, 6H, 2 CH_2, NH_2), 4.2 (qt, J = 7.1 Hz, 4H, 2 OCH_2), 5.1 (m, 2H, CH=CH), 5.8 (m, 1H, CH=CH). ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ 30.05. ^{13}C-NMR (25.18 MHz, $CDCl_3$) δ 16.41 (d, J = 5.3 Hz, 2 OCH_2CH_3), 22.01 (d, J = 2.4 Hz, CH_3CP), 27.05 (d, J = 7.6 Hz, =C—CH_2), 36.38 (d, J = 3.9 Hz, CH_2—C—P), 51.56 (d, J = 147.3 Hz, C—P), 62.15 (d, J = 7.6 Hz, 2OCH_2CH_3), 114.45 (CH_2=), 138.33 (=CH). IR (neat) 3360, 1670, 1230, 1170, 1040 and 1010 cm^{-1}. Picrate salt: Anal. Calcd for $C_{16}H_{25}N_4O_9P$: C, 41.38; H, 5.42; N, 12.06. Found: C, 41.79; H, 5.46; N, 12.12%. mp 160°C.

Diethyl (2-aminohept-5-en-2-yl) phosphonate (**12**). Yield: 50%. ^{1}H-NMR (100 MHz, $CDCl_3$) δ 1.30 (d, J = 16.0 Hz, 3H, CH_3C*P), 1.35 (t, J = 7.1 Hz, 6H, 2CH_3CH_2O), 1.61 (d, J = 4.9 Hz, 3H, CH_3CH=), 1.7–2.7 (m, 6H, 2CH_2, NH_2), 4.15 (qt, J = 7.1 Hz, 4H, 2 OCH_2), 5.4 (m, 2H, 2 CH=CH) ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ 30.60. ^{13}C-NMR (25.18 MHz, $CDCl_3$) δ 12.07 (CH_3—C=), 15.97 (d, J = 5.3 Hz, 2 OCH_2CH_3), 17.26 (CH_3—C=), 20.00 and 25.30 (2d, J = 7.6 Hz, CH_2—C=), 21.58 (d, J = 2.1 Hz, CH_3—C—P), 36.59 (d, J = 3.6 Hz, CH_2—C—P), 51.29 (d, J = 146.4 Hz, C—P), 61.78 (d, J = 8.0 Hz, 2 OCH_2CH_3), 123.61, 124.41, 129.54 and 130.41. (2 CH=). IR (neat) 3340, 1630, 1235, 1170, 1060 and 1040 cm^{-1}. Picrate salt: Anal. Calcd for $C_{17}H_{27}N_4O_{10}P$: C, 42.67; H, 5.69; N, 11.71. Found: C, 42.96; H, 5.67; N, 11.70%. mp 154°C.

Diethyl (2-amino-5-methylhept-5-en-2-yl) phosphonate (**13**). Yield: 54%. ^{1}H-NMR (400 MHz, $CDCl_3$) δ 1.29 (d, J = 16.1 Hz, 3H, CH_3C*P), 1.34 (t, J = 7.1 Hz, 6H, 2 CH_3CH_2O), 1.57 (dd, J = 1.4 Hz, J = 6.7 Hz, 3H, CH_3CH=), 1.68 (m, 3H, CH_3C=), 1.50–2.40 (m, 6H, 2 CH_2, NH_2), 4.16 (qt, J = 7.1 Hz, 4H, 2 OCH_2CH_3), 5.21 (m, 1H, HC=C). ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ 30.66. ^{13}C-NMR (25.18 MHz, $CDCl_3$) δ 12.77 (CH_3—C=), 16.26 (d, J = 5.3 Hz, 2 OCH_2CH_3), 21.85 (d, J = 2.2 Hz, CH_3—C—P), 22.99 (CH_3—C=), 24.61 (d, J = 7.0 Hz, CH_2—C=), 35.24 (d, J = 3.9 Hz, CH_2—C—P), 51.55 (d, J = 146.5 Hz, C*P), 61.92 and 61.98 (2d, J = 7.9 Hz, 2 OCH_2CH_3), 118.89 (CH=), 135.31 (C=CH). IR (neat) 3350, 1670, 1230, 1170, 1060 and 1040 cm^{-1}. Anal. Calcd for $C_{12}H_{26}NO_3P$: C, 54.73; H, 9.95; N, 5.32. Found: C, 54.66; H, 9.95; N, 5.49%.

Diisopropyl (1-aminodec-4-enyl) phosphonate (**16**). Purification by preparative TLC over silica gel eluting with (7:3 v/v) pentane/acetone, afforded 10% of pure **16**. ^{1}H-NMR (100 MHz, $CDCl_3$) δ 0.88 (t, J = 6.6 Hz, 3H, CH_3CH_2), 1.2–2.6 (m, 14H, NH_2, 6 CH_2), 1.32 (d, J = 6.2 Hz, 12H, 4 CH_3CHO), 2.80 (td, J = 9.6 Hz, J = 3.6 Hz, 1H, *CH), 4.75 (m, 2H, 2 OCH), 5.43 (m, 2H, 2 CH=). ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ 28.38. ^{13}C-NMR (100.61 MHz, C_6D_6) δ 14.24 ($CH_3(CH_2)_4$), 22.88 (CH_2), 24.03 (2d, J = 4.8 Hz, $OCHCH_3$), 24.13 (d, J = 3.9 Hz, $OCHCH_3$), 24.17 (d, J = 3.5 Hz, $OCHCH_3$), 29.43 (d, J = 13.3 Hz, CH_2—C=), 29.60 and 31.72 (CH_2), 31.95 (CH_2—C*), 32.95 (CH_2), 48.95 (d, J = 149.9 Hz, C*—P), 70.04 (d, J = 7.0 Hz, OCH), 70.13 (d, J = 11.1 Hz, OCH), 129.70 and 131.62 (CH=). IR (neat) 3390, 1460, 1246, 1164, 1056 and 1030 cm^{-1}. Anal. Calcd for $C_{14}H_{30}NO_3P$: C, 60.16; H, 10.64; N, 4.38. Found: C, 59.65; H, 10.69; N, 4.38%.

Diisopropyl (2-aminohex-5-en-2-yl) phosphonate (**17**). Yield: 40%. ^{1}H-NMR (100 MHz, $CDCl_3$) δ 1.2 (d, J = 16.1 Hz, 3H, CH_3), 1.3 (d, J = 6.1 Hz, 12H, 4 CH_3CHO), 1.4–2.5 (m, 6H, NH_2, 2 CH_2), 4.7 (m, 2H, 2 OC*H*), 4.95 (m, 2H, 2 C*H*=CH), 5.8 (m, 2H, 2 C*H*=CH). ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ 28.61. ^{13}C-NMR (100.61 MHz, C_6D_6) δ 23.89 (d, J = 4.3 Hz, $OCHCH_3$), 23.93 (d, J = 3.3 Hz, $OCHCH_3$), 24.17 (d, J = 2.8 Hz, $OCHCH_3$), 24.28 (d, J = 3.4 Hz, $OCHCH_3$), 27.71 (d, J = 8.1 Hz, CH_2CH=), 37.23 (d, J = 4.4 Hz, CH_2C*P), 51.71 (d, J = 148.9 Hz, C*P), 70.13 (d, J = 7.8 Hz, OCH), 70.35 (d, J = 7.8 Hz, OCH), 114.44 (CH_2=), 139.33 (CH=). IR (neat) 3300, 1640, 1235, 1190, 1020 and 1000 cm^{-1}. Picrate salt: Anal. Calcd for $C_{18}H_{29}N_4O_{10}P$: C, 43.90; H, 11.38; N, 5.93. Found: C, 43.84; H, 11.29; N, 5.93%. mp 159°C.

Diisopropyl (2-aminohept-5-en-2-yl) phosphonate (**18**). Yield: 42% ^{1}H-NMR (100 MHz, $CDCl_3$) δ 1.25 (d, J = 16.1 Hz, 3H, CH_3C*P), 1.33 (d, J = 6.2 Hz, 12H, 4 CH_3CHO), 1.62 (d, J = 5.5 Hz, 3H, CH_3CH=), 1.70–2.75 (m, 6H, 2 CH_2, NH_2), 4.70 (m, 2H, 2 OC*H*), 5.45 (m, 2H, 2 C*H*=CH). ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ 29.27. ^{13}C-NMR (100.61 MHz, C_6D_6) δ 12.80 and 18.06 (CH_3—C=), 21.08 (d, J = 7.3 Hz, CH_2—C=), 22.63 (d, J = 1.5 Hz, CH_3—C*), 23.88 (d, J = 3.4 Hz, CH_3CHO), 23.93 (d, J = 3.2 Hz, CH_3CHO), 24.17 (d, J = 3.1 Hz, CH_3CHO), 24.24 (d, J = 2.9 Hz, CH_3CHO), 26.50 (d, J = 8.0 Hz, CH_2—C=), 37.89 (d, J = 4.0 Hz, CH_2C*P), 51.85 (d, J = 148.9 Hz, C*P), 70.10 (d, J = 8.3 Hz, OCH), 70.28 (d, J = 8.2 Hz, OCH), 124.16, 124.93, 130.95 and 131.87 (2CH=). IR (CCl_4) 3350, 1457, 1230, 1170, 1060 and 1040 cm^{-1}. HRMS: Calcd for $C_{13}H_{28}NO_3P$: 277.1806. Found: 277.1795. MS m/e 112 (M^+—P(O)(O*i*—Pr)$_2$, 100%).

Synthesis of (Pyrrolidin-2-yl) Phosphonates (**29–38**)*; Aminomercuration/Reduction Procedures.*

A: At room temperature, a suspension of mercuric acetate (4.2 mmol) in water/THF (20 ml, 1:1 v/v) was slowly added to the alkenyl aminophosphonate (4.2 mmol). After the end of addition, the reaction mixture was stirred for 10 mn; sodium borohydride (4.2 mmol) in 10% aqueous sodium hydroxide solution (2 ml) was then added. After 1 hour, the mixture was saturated with sodium chloride, extracted with ether and dried over sodium sulfate. Filtration and removal of the solvent afforded the crude pyrrolidinyl phosphonates. **B**: The reaction was performed under inert atmosphere. At room temperature, mercuric acetate (4.2 mmol) was slowly added to a solution of the alkenyl aminophosphonate (4.2 mmol) in water/THF (20 ml, 1:1 v/v) and the mixture stirred over 1 day. Then, sodium borohydride (4.2 mmol) in 10% aqueous sodium hydroxide solution (2 ml) was added and, after 3 hours, a saturated aqueous sodium carbonate solution was added. Usual work-up was performed as described for A. **C**: The reaction was carried out as described for A, but the solution of the alkenyl aminophosphonate was added to the suspension of mercuric acetate in water/THF. **D**: At room temperature, mercuric acetate (4.2 mmol) in methylene chloride (20 ml) was slowly added to the alkenyl aminophosphonate (4.2 mmol). After 10 mn, sodium borohydride (4.2 mmol) in 10% aqueous sodium hydroxide solution (2 ml) was added. After 1 hour, the mixture was saturated with sodium chloride, extracted with methylene chloride and dried over sodium sulfate. Usual work-up was as described before. **E**: The aminomercuration was performed as described for D; the resulting organomercurial was poured over a solution of benzyltriethylammonium chloride (14.7 mmol) in water (20 ml), before addition of the sodium borohydride solution. **F**: At room temperature, mercuric acetate (8.4 mmol) in water/THF (20 ml, 1:1 v/v) was slowly added to the alkenyl aminophosphonate (4.2 mmol). The mixture was then stirred for 1 hour; a white precipitate was formed. Sodium borohydride (8.4 mmol) in 10% aqueous sodium hydroxide solution was added. Work-up was done as described for A. **G**: Experimental conditions were those reported for E, but using acetone instead of methylene chloride as solvent. Before reduction, acetone was removed under reduced pressure and the residue diluted in methylene chloride for usual work-up.

The yields given below were obtained according to the E procedure.

Diethyl (5-methyl pyrrolidin-2-yl)phosphonate (**29a,b**). The crude product was purified by preparative TLC over silica gel eluting with 3:4 v/v pentane/acetone to give **29a,b** (20%). ^{1}H-NMR (400 MHz, C_6D_6) δ 0.95[a] (d, J = 6.3 Hz, 3H, CH_3), 1.01[b] (d, J = 6, 2 Hz, 3H, CH_3), 1.08 (t, J = 7.1 Hz, 3H, CH_3CH_2O), 1.09 (t, J = 7.1 Hz, 3H, CH_3), 1.1–2.1 (m, 5H, N*H*, 2 CH_2), 3.22 (m, 1H, *C*H*), 3.40 (m, 1H, *C*H*), 4.02 (m, 4H, 2 OCH_2). ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ **29a**: 27.09, **29b**: 28.03. ^{13}C-NMR (100.61 MHz, C_6D_6) δ **29a**: 16.62 (d, J = 4.8 Hz, 2 OCH_2CH_3), 21.04 (CH_3CH), 27.00 (d, J = 2.9 Hz, CH_2), 33.45 (d, J = 8.7 Hz, CH_2), 54.86 (d, J = 166.8 Hz, CHP), 55.48 (d, J = 15.5 Hz, $CHCH_3$), 61.83 (d, J = 6.9 Hz, OCH_2CH_3), 62.43 (d, J = 7.0 Hz, OCH_2CH_3), **29b**: 16.63 (d, J = 4.8 Hz, 2 OCH_2CH_3), 20.63 (CH_3CH), 27.45 (CH_2), 34.54 (d, J = 5.9 Hz, CH_2), 54.09 (d, J = 164.1 Hz, CHP), 54.92 (d, J = 7.1 Hz, $CHCH_3$), 61.96 (d, J = 6.9 Hz, OCH_2CH_3) 61.96 (d, J = 6.2 Hz, OCH_2CH_3), 62.09 (d, J = 6.9 Hz, OCH_2CH_3), 62.43 (d, J = 7.0 Hz, OCH_2CH_3). IR (CCl_4) (**29a,b**) 3360, 1244, 1177, 1053 and 1028. HRMS: Calcd for $C_9H_{20}NO_3P$: 221.1181. Found: 221.1185. MS m/e

88 (M^+—$P(O)(OEt)_2$, 100%).
a:: **29b**; *b*: **29a**.

Diethyl (5-hexyl pyrrolidin-2-yl) phosphonate (**30a,b**). The crude product was purified by preparative TLC over silica gel eluting with 7:3 v/v pentane/acetone to give **30a,b** (38%). ^{1}H-NMR (400 MHz, C_6D_6) δ 0.88 (t, J = 6.2 Hz, 3H, CH_3), 1.0–2.5 (m, 15H, N*H*, 7 CH_2), 1.32 (t, J = 7.1 Hz, 6H, 2 CH_3CH_2O), 3.1 (m, 1H, **CH*), 3.4 (m, 1H, **CH*), 4.15 (qt, J = 7.1 Hz, 4H, 2 OCH_2). ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ **30a**: 27.03, **30b**: 27.76. ^{13}C-NMR (50.32 MHz, C_6D_6) δ **30a**: 14.25 ($CH_3(CH_2)_5$), 16.72 (d, J = 4.5 Hz, 2 OCH_2CH_3), 21.55, 29.60, 31.72, 31.92 and 36.52 ($5CH_2$), 33.59 (d, J = 2.6 Hz, CH_2), 34.65 (d, J = 2.6 Hz, CH_2), 58.43 (d, J = 167.2 Hz, *C*HP), 60.22 (d, J = 14.6 Hz, $CH(CH_2)_5$), 61.92 (d, J = 7.0 Hz, 2 OCH_2CH_3). **30b**: 14.28 ($CH_3(CH_2)_5$), 16.72 (d, J = 4.5 Hz, 2 OCH_2CH_3), 22.97, 27.39, 27.60, 29.84 and 36.52 (5 CH_2), 32.45 (CH_2), 33.01 (d, J = 6.1 Hz, CH_2), 54.23 (d, J = 161.7 Hz, *C**P), 59.60 (d, J = 7.2 Hz, $CH(CH_2)_5$), 61.92 (d, J = 7.0 Hz, 2 OCH_2CH_3). IR (neat) (**30a,b**) 3312, 1236, 1163, 1056 and 1029 cm^{-1}. Anal. Calcd for $C_{14}H_{30}NO_3P$: C, 57.72; H, 10.38; N, 4.81. Found: C, 57.60; H, 9.90; N, 5.21%.

Diethyl (2,5-dimethyl pyrrolidin-2-yl) phosphonate (**30a,b**). Crystallization in pentane at −20°C afforded 25% of **31a,b**. ^{1}H-NMR (400 MHz, C_6D_6) δ 0.95[a] (d, J = 6.2 Hz, CH_3), 1.03[b] (d, J = 6.1 Hz, CH_3), 1.082[a] (t, J = 7.1 Hz, CH_3CH_2O), 1.086[b] (t, J = 7.1 Hz, CH_3CH_2O), 1.091[a] (t, J = 7.0 Hz, CH_3CH_2O), 1.11[b] (t, J = 6.8 Hz, CH_3CH_2O), 1.29[b] (d, J = 15.3 Hz, CH_3), 1.34[a] (d, J = 15.1 Hz, CH_3), 1.35–148 (m, 3H, N*H*, 2 CH_2), 1.60[b] (m, 1H, CH_2), 1.81[a] (m, 1H, CH_2), 2.41 (m, 1H, CH_2), 3.10[b] (m, 1H, C*H*), 3.43[a] (m, 1H, C*H*), 4.06 (m, 4H, 2 OCH_2). ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ **31a**: 28.84, **31b**: 29.96. ^{13}C-NMR (100.61 MHz, C_6D_6) **31a**: δ 16.72 (d, J = 4.6 Hz, 2 CH_3CH_2O), 21.63 (CH_3CH), 24.65 (d, J = 7.4 Hz, CH_3CP), 34.14, 35.59 ($2CH_2$), 53.17 (d, J = 11.0 Hz, $CHCH_3$), 60.81 (d, J = 169.3 Hz, *C**P), 61.05 (d, J = 7.7 Hz, OCH_2), 62.92 (d, J = 7.1 Hz, OCH_2). **31b**: 16.72 (d, J = 4.6 Hz, $2CH_3CH_2O$), 21.57 (CH_3CH), 25.95 (d, J = 6.6 Hz, CH_3CP), 34.14 (d, J = 3.5 Hz, CH_2), 35.16 (d, J = 2.7 Hz, CH_2), 55.55 (d, J = 3.0 Hz, $CHCH_3$), 60.21 (d, J = 162.2 Hz, *C**P), 61.85 (d, J = 7.2 Hz, OCH_2), 62.08 (d, J = 7.2 Hz, OCH_2). IR (CCl_4) (**31a,b**) 3390, 1246, 1164, 1056 and 1030 cm^{-1}. Picrate salt: Anal. Calcd for $C_{16}H_{25}N_4O_{10}P$: C, 41.40; H, 5.43; N, 12.07. Found: C, 41.36; H, 5.52; N, 12.04%.
a: **31b**; *b*: **31a**.

Diethyl (5-ethyl-2-methyl pyrrolidin-2-yl) phosphonate (**32a,b**). The crude product was purified by preparative TLC over silica gel eluting with 1:1 v/v pentane/acetone to give **32a,b** (18%). ^{1}H-NMR (400 MHz, $CDCl_3$) δ 0.82[b] (t, J = 7.4 Hz, CH_3CH_2), 0.84[a] (t, J = 7.5 Hz, CH_3CH_2), 1.108[b] (t, J = 7.1 Hz, 3H, CH_3CH_2O), 1.112[a] (t, J = 7.1 Hz, 3H, CH_3CH_2O), 1.32[b] (d, J = 15.4 Hz, CH_3CP), 1.35[a] (d, J = 15.0 Hz, CH_3CP), 1.40–1.65 (m, 3H, N*H*, CH_2), 1.75[b] (m, CH_2), 1.85[a] (m, CH_2), 2.35 (m, 2H, CH_2), 2.91[b] (m, C*H*), 3.25[a] (m, C*H*), 4.15 (m, 4H, 2 OCH_2). ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ **32a**: 28.81, **32b**: 30.13. ^{13}C-NMR (100.61 MHz, C_6D_6) **32a**: δ 14.02 (CH_3CH_2), 16.70 (d, J = 4.2 Hz, 2 OCH_2CH_3), 24.53 (d, J = 7.9 Hz, CH_3CP), 29.73 (CH_3CH_2), 31.76 (CH_2), 35.07 (CH_2), 59.63 (d, J = 10.4 Hz, CHC_2H_5), 59.80 (d, J = 168.6 Hz, *C**P), 62.09 (d, J = 7.5 Hz, OCH_2CH_3), 63.02 (d, J = 7.2 Hz, OCH_2CH_3). **32b**: 11.54 (CH_3CH_2), 16.70 (d, J = 4.2 Hz, 2 OCH_2CH_3), 25.90 (d, J = 7.5 Hz, CH_3CP), 29.73 (CH_3CH_2), 31.64 (d, J = 3.9 Hz, CH_2), 34.58 (d, J = 3.4 Hz, CH_2), 59.93 (d, J = 160.3 Hz, *C**P), 61.72 (d, J = 3.9 Hz, CHC_2H_5), 62.02 (d, J = 7.5 Hz, OCH_2CH_3), 62.09 (d, J = 7.5 Hz, OCH_2CH_3). IR (neat) (**32a,b**) 3370, 1239, 1164, 1055 and 1028 cm^{-1}. MS m/e 112 (M^+—)
a: **32b**; *b*: **32a**.

Diisopropyl (5-hexyl pyrrolidin-2-yl) phosphonate (**36a,b**). The crude product was purified by preparative TLC over silica gel eluting with 6:4 v/v pentane/acetone to give **36a,b** (42%). ^{1}H-NMR (100 MHz, $CDCl_3$) δ 0.88 (t, J = 6.1 Hz, 3H, CH_3), 1.0–2.5 (m, 15H, N*H*, 7 CH_2), 1.33 (d, J = 6.0 Hz, 12H, 4 CH_3), 3.21 (m, 1H, **CH*), 3.40 (m, 1H, **CH*), 4.74 (m, 2H, 2O*CH*). ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ **36a**: 25.54, **36b**: 26.43. ^{13}C-NMR (50.32 MHz, C_6D_6) δ **36a**: 14.05 ($CH_3(CH_2)_5$), 22.68 (CH_2), 24.34 (d, J = 4.5 Hz, 2 CH_3CHO), 24.67 (d, J = 4.2 Hz, 2 CH_3CHO), 26.62, 27.37, 29.39 and 29.68 (4 CH_2), 31.63 (d, J = 10.0 Hz, CH_2), 36.49 (CH_2), 55.09 (d, J = 168.6 Hz, *C**HP), 60.63 (d, J = 15.4 Hz, $C^*H(CH_2)_5$. **36b**: 14.09 ($CH_3(CH_2)_5$, 22.79 (CH_2), 24.44 (d, J = 4.8 Hz, 2 CH_3CHO), 24.60 (d, J = 3.2 Hz, 2 CH_3CHO), 27.22, 27.37, 29.61 and 31.98 (4 CH_2), 32.74 (d, J = 6.6 Hz, CH_2), 36.37 (CH_2), 54.36 (d, J = 163.4 Hz, *C**HP), 59.31 (d, J = 7.3 Hz, $C^*H(CH_2)_5$), 70.28 (d, J = 7.5 Hz, 2 $OCH(CH_3)_2$). IR (neat) (**36a,b**) 3305, 1234, 1177, 1007 and 987 cm^{-1}. Anal. Calcd for $C_{16}H_{34}NO_3P$: C, 60.16; H, 10.73; N, 4.38. Found: C, 60.18; H, 11.09; N, 4.82%.

Diisopropyl (2,5-dimethyl pyrrolidin-2-yl) phosphonate (**37a,b**). Crystallization in pentane at −20°C afforded 30% of **37a,b**. ^{1}H-NMR (400 MHz, C_6D_6) δ 0.93[a] (d, J = 6.1 Hz, 3H, CH_3C^*H), 1.03[b] (d, J

= 6.1 Hz, 3H, CH_3C^*H), 1.19 (d, J = 6.2 Hz, 3H, CH_3CHO), 1.21 (d, J = 6.2 Hz, 3H, CH_3CHO), 1.220 (d, J = 6.2 Hz, 3H, CH_3CHO), 1.222 (d, J = 6.2 Hz, 3H, CH_3CHO), 1.30[b] (d, J = 15.2 Hz, 3H, CH_3C^*P), 1.32[a] (d, J = 15.2 Hz, 3H, CH_3C^*P), 1.35–1.5 (m, 3H, N*H*, 2 CH_2), 1.61[b] (m, 1H, 1 CH_2), 1.78[a] (m, 1H, CH_2), 2.37 (m, 1H, CH_2), 3.05[b] (m, 1H, C*H*), 3.47[a] (m, 1H, C*H*), 4.74 (m, 2H, 2 OC*H*). ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ **37a**: 27.67, **37b**: 28.60. ^{13}C-NMR (100.61 MHz, C_6D_6) δ **37a**: 21.48 (CH_3CH), 24.02 (d, J = 4.8 Hz, CH_3CHO), 24.06 (d, J = 3.9 Hz, CH_3CHO) 24.28 (d, J = 4.5 Hz, CH_3CHO), 24.46 (d, J = 4.0 Hz, CH_3CHO), 24.65 (d, J = 6.64 Hz, C^*CH_3P), 34.11 (d, J = 6.2 Hz, CH_2), 35.48 (CH_2), 53.18 (d, J = 11.5 Hz, $CHCH_3$), 59.93 (d, J = 169.8 Hz, C^*P), 69.52 (d, J = 6.9 Hz, OCH), 70.33 (d, J = 7.5 Hz, OCH). **37b**: 21.60 (CH_3CH), 24.02 (d, J = 4.8 Hz, CH_3CHO), 24.06 (d, J = 3.9 Hz, CH_3CHO), 24.30 (d, J = 3.1 Hz, CH_3CHO), 24.39 (d, J = 2.9 Hz, CH_3CHO), 26.14 (d, J = 6.5 Hz, C^*CH_3P), 34.23 (d, J = 2.6 Hz, CH_2), 35.15 (d, J = 2.9 Hz, CH_2), 55.56 (d, J = 3.6 Hz, $CHCH_3$), 60.21 (d, J = 164.4 Hz, C^*P), 69.74 (d, J = 7.6 Hz, OCH), 70.02 (d, J = 7.2 Hz, OCH). IR (CCl_4) (**37a,b**) 3410, 1253, 1177, 1006 and 984 cm^{-1}.
a: **37b**; *b*: **37a**.

Diisopropyl (5-ethyl-2-methyl pyrrolidin-2-yl) phosphonate (**38a,b**). The crude product was purified by preparative TLC over silica gel eluting with 8:2 v/v pentane/acetone to give **38a,b** (15%). ^{1}H-NMR (200 MHz, C_6D_6) δ 0.73[a] (t, J = 7.3 Hz, CH_3CH_2), 0.75[b] (t, J = 7.4 Hz, CH_3CH_2), 0.90 (d, J = 6.1 Hz, 3H, CH_3CHO), 1.11 (d, J = 6.2 Hz, 3H, CH_3CHO), 1.13 (d, J = 6.1 Hz, 6H, 2 CH_3CHO), 1.32 (d, J = 7 Hz, 12H, 4 CH_3), 1.32 (d, J = 16 Hz, 6H, 2 CH_3), 1.40–2.85 (m, 5H, 2 CH_2, NH_2), 3.09[b] (m, $CHCH_2$), 3.30[a] (m, $CHCH_2$), 4.74 (m, 2H, 2 OC*H*). ^{31}P-NMR (40.53, $CDCl_3$) δ **38a**: 27.45, **38b**: 28.59. ^{13}C-NMR (50.32 MHz, C_6D_6) δ **38a**: 14.22 (CH_3CH_2), 24.02, 24.06, 24.36 and 24.36 (4 CH_3CHO), 25.66 (d, J = 6.1 Hz, C^*CH_3P), 30.20 (CH_3CH_2), 31.94 (CH_2), 34.65 (CH_2), 59.89 (d, J = 10.2 Hz, CHC_2H_5), 59.26 (d, J = 166.6 Hz, C^*HP), 70.40 (d, J = 7.1 Hz, OCH), 70.65 (d, J = 7.0 Hz, OCH). **38b**: 11.62 (CH_3CH_2), 24.02, 24.06 and 24.36 (4 CH_3CHO), 26.05 (d, J = 6.42 Hz, C^*CH_3P), 30.02 (CH_3CH_2), 31.79 and 34.73 (2 CH_2), 59.86 (d, J = 161.3 Hz, C^*HP), 61.90 (d, J = 3.2 Hz, CHC_2H_5), 70.00 (d, J = 8.0 Hz, OCH), 70.12 (d, J = 8.0 Hz, OCH). IR (CCl_4) (**38a,b**) 3410, 1241, 1178, 1003 and 982 cm^{-1}.

Mercurated product (**39**). ^{1}H-NMR (100 MHz, $CDCl_3$) δ 1.42 (t, J = 7.1 Hz, 12H, 4 CH_3), 1.51 (d, J = 15.4 Hz, 6H, 2CH_3), 1.7–2.8 (m, 14H, 2N*H*, 6CH_2), 4.0 (m, 2H, 2C*H*), 4.3 (qt, J = 7.1 Hz, 8H, 4 OCH_2). ^{31}P-NMR (40.53 MHz, $CDCl_3$) δ 29.90. Anal. Calcd for $C_{20}H_{42}N_2HgO_6P_2$: C, 35.90; H, 6.62; N, 4.18. Found: C, 35.63; H, 6.53; N, 4.15%.

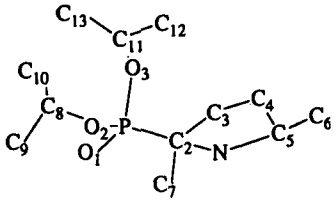
X-ray analysis of **37a**. A pure sample of **37a** was obtained by successive recrystallizations of a mixture of **37a** and **37b** in pentane at −20°C. Then slow crystallization in heptane at 20°C afforded orthorhombic crystals for an X-ray structure analysis. The molecular structure of **37a** is shown in Figure 1, the crystallographic data are given in Table VII and the bond lengths and bond angles are summarized in Table VIII.

TABLE VII
Crystallographic data of **37a**

Crystallographic data	
Formula	$C_{12}H_{26}NO_3P$
Molecular weight (g)	263.32
Crystalline system, space group	orthorombic, P_{bca}
Cell parameters (a:b:c) (Å)	10.098(3): 18.902(4): 16.710(3)
Volume (Å^3)	3189.5
Z	8
Calculated density (g.cm^{-3})	1.097
Absorption coeff.(cm^{-1})	1.653
F_{000}	1152
Crystal size (mm)	0.3 x 0.4 x 0.3
number of variables	154
R	0.05831
R_w	0.05834

TABLE VIII

Bond lengths and bond angles of **37a**



Bond lengths (Å)

P - O (1)	1.456 (3)	N - C (2)	1.479 (6)	C (5) - C (6)	1.511 (9)
P - O (2)	1.576 (3)	N - C (5)	1.462 (6)	C (8) - C (9)	1.492 (9)
P - O (3)	1.569 (3)	C (2) - C (3)	1.563 (7)	C (8) - C (10)	1.491 (8)
P - C (2)	1.804 (5)	C (2) - C (7)	1.532 (7)	C (11) - C (12)	1.42 (1)
O (2) - C (8)	1.451 (6)	C (3) - C (4)	1.516 (7)	C (11) - C (13)	1.423 (9)
O (3) - C (11)	1.453 (7)	C (4) - C (5)	1.502 (7)		

Bond angles (°)

O (1) -P - O (2)	114.9 (2)	P - C (2) - N	104.9 (3)
O (1) -P - O (3)	113.5 (2)	P - C (2) - C (3)	109.9 (3)
O (2) -P - O (3)	103.4 (2)	N - C (2) - C (3)	104.4 (3)
O (2) -P - C (2)	101.2 (2)	N - C (2) - C (7)	113.2 (4)
O (3) -P - C (2)	107.4 (2)	C (3) - C (2) - C (7)	111.8 (4)
P - O(2) - C (8)	120.2 (3)	C (2) - C (3) - C (4)	105.1 (4)
P - O(3) - C (11)	122.2 (3)	C (3) - C (4) - C (5)	104.5 (5)
C (2) - N - C (5)	107.4 (4)	N - C (5) - C (4)	103.2 (4)
N - C (5) - C (6)	111.1 (4)	O (3) - C (11) - C (12)	110.5 (5)
C (4) - C (2) - C (7)	117.1 (5)	O (3) - C (11) - C (13)	110.1 (6)
O (2) - C (8) - C (9)	108.5 (4)	C (12) - C (11) - C (13)	112.7 (6)
O (2) - C (8) - C (10)	107.5 (4)		
C (9) - C (8) - C (10)	112.5 (5)		

^{31}*P-NMR of organomercurials* **20**, **21**, **23** *and* **27** (**a**,**b**). (40.53 MHz, CD_2Cl_2) **20**: δ 29.92 (**a**, 19%) and 26.82 (**b**, 81%). **21**: δ 30.95 (**a**, 15%) and 32.10 (**b**, 85%). **23**: 29.19 (**a**, 15%) and 29.89 (**b**, 85%). **27**: δ 29.12 (**a**, 14%) and 29.62 (**b**, 86%).

^{199}*Hg-NMR of organomercurials* **27**(**a**,**b**). ^{199}Hg NMR (71.66 MHz, CD_2Cl_2) δ −1243 (**27a**, 23%) and −1218 (**27b**, 77%).

^{1}*H-NMR (200 MHz) shift experiments on diastereomeric mixture of organomercurials* **27**(**a**,**b**). Variations of the ^{1}H-NMR chemical shift values of the signals from CH_3C_2P (**I**) and C_5H (II) were studied in the following conditions: in CD_2Cl_2: δ 1.25 (I) and 3.60 (II); in CD_2Cl_2 and trifluoroacetic acid: δ 1.46 (I) and 3.92 (II); in CD_2Cl_2 and pyridine δ 1.25 (I) and 3.60 (II).

Spin-Trapping Experiments

Under inert atmosphere, organomercurials **21**, **23** and **25** (8.51 mmol) were prepared according to the D procedure. Pentamethoxynitrosobenzene (10^{-2} mmol) was added before the reduction step. The formation of spin adducts **46**–**48** was monitored by EPR; no signal was detected before addition of the sodium borohydride solution.

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36. ^{13}C-NMR (CD_2Cl_2) (δ, $^3J13_{C5P}$): mercuric intermediate **27a**: 57.92, 9.1 Hz (minor isomer), **27b**:

60.69, 2.7 Hz (major isomer); reduced pyrrolidinyl phosphonate **37a**: 53.43, 11.6 Hz, **37b**: 56.00, 4.6 Hz.
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