An Efficient One-Pot Synthesis of New Polyfunctional Phosphorus Acid Amphiphiles

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Keywords: Phosphorus acid amphiphiles / (α-Aminoalkyl)phosphonic acids / Carboxyalkyl (α-aminoalkyl)phosphonic acid monoesters / Spirophosphorane / Pudovik reaction

The addition reaction between the P–H bond of tetraoxyspirophosphoranes **1**–**2** and long-chain imines **3a–h** (decyl, dodecyl, tetradecyl, hexadecyl, octadecyl, and oleyl imines) occurs instantaneously at room temperature. It is diastereoselective, and quantitatively leads to the corresponding (α-aminoalkyl)spirophosphoranes **4a–h** and **5e**. The influence of the pentacoordinated phosphorus atom on the stereoselectivity of the Pudovik reaction might be attributed to the involvement of the rigid spirophosphoranide (P^V) intermediate in the addition reaction. Selective and one-pot hydrolysis of these P–C bond spirophosphoranes readily proceeds either at room temperature in the presence of moist solvents to give the corresponding carboxyalkyl (α-aminoalkyl)phosphonic acid monoesters **6a–h** and **7e**, or the reaction may be carried out in the presence of 20% aqueous hydrochloric acid under reflux, to afford the free (α-aminoalkyl)phosphonic acid amphiphiles **8a–h** in high yields. In contrast to their sodium salts, these single- and double-chained free and monoester phosphonic acid amphiphiles exist as zwitterions and are not soluble in water.

Introduction

The phosphorus analogs of α-aminocarboxylic acids, (α-aminoalkyl)phosphorus acids (phosphonic acids, esters, and salts) have attracted significant attention owing to their synthetic and biological value as both agrochemical (herbicides, pesticides, growth regulator in plants) and medicinal (antibiotics, antivirals, enzyme inhibitors) products with broad applications.[1−3] Platinum complexes with phosphonocarboxylate ligands show promising antitumor activity.[4] Their usefulness as corrosion inhibitors[5] and as flame-retardants for some polymers[6] has also been described. The metal-ion-coordinating properties of (aminoalkyl)phosphonic acids were looked at more intensively in recent years, to arrive at a better understanding of their biological activity (inhibition of metalloenzymes, metabolic regulation, etc.).[7] Thus, there has been increasing activity in the study of the chemistry of phosphonates,[8] and the development of new methodologies for their preparation is still of great interest.

The bioactivity of these compounds is known to be strongly dependent on their absolute configurations, and numerous methods, including diastereomeric[9] and chemoenzymatic[10] resolutions and asymmetric synthesis,[11−14] are available for the synthesis of optically pure aminophosphonic acids. Of the various methods for the preparation of (α-aminoalkyl)phosphonic acids, the most general route is the Pudovik addition of dialkylphosphonate to a Schiff base, followed by hydrolytic or reductive cleavage of diester precursors.[15] In contrast, the synthesis of their monoesters is more delicate, and requires partial hydrolytic or nonhydrolytic cleavage of diester precursors, partial esterification of phosphonic diacids, or oxidation of α-aminophosphinic acid precursors.[16]

We have continued our investigations into the reactivity of the P−H-labile phosphorus derivatives[17][18] and the synthesis of new α-functionalized phosphorus amphiphiles,[19] and we wish to report here the reactivity of spirophosphoranes towards long-chain imines, and their one-pot and selective hydrolysis to result in (α-aminoalkyl)phosphorus acid amphiphiles.

The presence of hydrophobic substituents is expected to widen their application field, because their coordinating and biological properties should be enhanced by the coexistence of hydrophilic and hydrophobic groups in one molecule. Long-chain phosphonate esters were therefore evaluated as enhancers of the transdermal penetration of drugs,[20] and as new ionic membrane carriers for the transport of metal ions or amino acids through lipophilic membranes in biological systems.[21] Benzylaminophosphonic acids were reported to be potent inhibitors of human prostatic acid phosphatase; their affinity for the enzyme-active site was attributed to their highly hydrophobic character.[3c] Metal phosphonates are also able to form layered compounds with magnetic and electronic properties, which may be modulated by interlayer interactions through the choice of the organic moieties and the inclusion of suitable functional groups.[22]

Results and Discussion

Spirophosphoranes with a P−H-labile bond are well documented as useful models for mimicking the pentacoordinate transition states or intermediates in phosphate ester hydrolysis.[23] It is already known that tetraoxyspirophos-

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  1434−193X/00/0202−281 $ 17.50+.50/0

phoranes that bear a P−H bond are reactive towards alkynes,[24] imines,[25] enamines,[26] and aldehydes.[27] However, their use as chiral reagents in the development of new stereoselective methods is rarer. The asymmetric addition reaction between a tricyclic chiral phosphorane and an activated carbonyl compound leads to rearranged alkoxyphosphoranes with high stereoselectivity.[28] More recently, the synthetic utility of spirooxyphosphoranyl C anions as valuable intermediates in Horner−Emmons olefination chemistry was reported.[29]

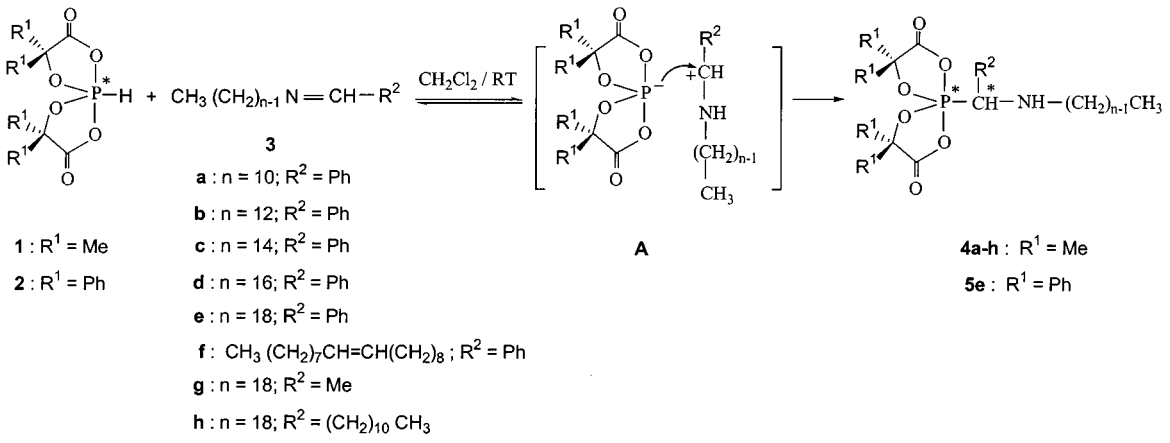
For this work, we selected the tetraoxyspirophosphoranes **1**−**2**, whose two mixed anhydride functions [C(O)−O−P] are highly electron-withdrawing and are more apicophilic than the ethereal P−O−C oxygen atoms are; this ensures a strong preference for the axial orientation of the carboxy groups in the trigonal bipyramidal arrangement of substituents attached to phosphorus.[23][30] As a consequence, the spirophosphoranes **1**−**2**: (i) are made up of a smaller number of stereoisomers, due to the high barrier of the stereomutation process, (ii) have phosphorus atoms that are more Lewis acidic, and (iii) have P−H bonds with enhanced acidity.[30−32] Moreover, **1**−**2** exhibit a strong preference for the spirophosphoranide (P^V) substructure **A** (Scheme 1) in basic media (e.g., DMF/Et_3N). This is in contrast to the spirophosphoranes derived from substituted glycols (methylene group in lieu of carbonyl), for which the tautomeric P^{III}/P^V chain-ring equilibria, involving the migration of a proton, are greatly favor of the tricoordinated form (P^{III}).[23][33] Consequently, the rigidity of the P^V substructure of **1**−**2**, added to the strong acidity of the P−H bond [pK_{DMF} (**1**) = 4.0][30] should allow stereoselective condensation with prochiral imines **3a**−**h**.

The nonplanarity of spirophosphoranes **1**−**2** results in their chirality, with the phosphorus atom as a stereogenic center.[34] The ^{31}P NMR spectra of **1**−**2** contain a single high-field signal with a large coupling constant [**1** (R^1 = Me): ^{31}P δ = −50.4; $^1J_{PH}$ = 920 Hz; **2** (R^1 = Ph): ^{31}P δ = −50.5; $^1J_{PH}$ = 917 Hz], characteristic of pentacoordinated phosphorus compounds and corresponding to a racemic mixture.

The addition reaction of equimolar amounts of spirophosphorane **1**−**2** to long-chain imines **3a**−**h** in anhydrous dichloromethane occurs instantaneously at room temperature, and stereoselectively and quantitatively gives the (α-aminoalkyl)spirophosphoranes **4a**−**h** and **5e,** which contain a P*−C* bond. The high selectivity of the reaction results from the asymmetric induction during the formation of the P−C bond (Scheme 1).

The spirophosphoranes **4a**−**h** and **5e**, containing a P−C bond, have two stereogenic centers: (1) the pentacoordinated phosphorus atom and (2) the carbon bonded to the phosphorus atom; these compounds exist as two diastereomeric pairs of enantiomers (Table 1). The ^{31}P NMR spectra of the two diastereomers of **4a**−**h** and **5e** are characterized by two high-field signals at approximately δ = −31 ($^2J_{PH}$ ≈ 25 Hz), confirming the preservation of the (P^V) substructure. The signals of the two diastereomers are separated by approximately 1 ppm. The major isomer, with the larger $^2J_{PH}$ coupling constant, is the most deshielded one. Replacement of the phenyl by an aliphatic alkyl group (R^2 = Me, undecyl) causes deshielding of the ^{31}P signal by approximately 5 ppm. The chemical shift of the carbon atom adjacent to the phosphorus atom (^{13}C δ ≈ 67) and the coupling constant ($^1J_{CP}$ ≈ 190 Hz) are consistent with the presence of an (α-aminoalkyl)spirophosphorane moiety. The methine proton resonance appears in most cases as a doublet at approximately δ = 4−5 ($^2J_{HP}$ ≈ 25 Hz). ^{31}P-, ^{13}C-, and ^1H NMR analysis show that the two diastereomers are present in most cases. Their relative ratios, determined by ^{31}P NMR spectroscopy, are nearly identical to the values obtained from ^1H NMR data (Table 1).

The diastereoselectivity of the addition reaction is dependent on the nature of the α-substituent of the phosphorus atom, since for R^2 = Ph, and regardless of the length of the long-chain (n = 10−18), the diastereomeric excess is high (**4a**−**f**: 90:10 ≥ ratio ≥ 80:20). In contrast, substitution by methyl instead of phenyl results in decreasing diastereoselectivity of the reaction (**4g**: ratio = 65:35). This can be attributed to: (i) the steric hindrance of the phenyl group during the addition reaction, promoting the preferential attack of



Scheme 1. Diastereoselective synthesis of the P−C-bond (α-aminoalkyl)spirophosphoranes

Table 1. Diastereomeric ratio of (α-aminoalkyl)spirophosphoranes **4**, isolated yields of phosphonic acid monoesters **6** and phosphonic acids **8**, and their characteristic NMR parameters

Compd.	R^1	R^2	$CH_3(CH_2)_{n-1}$	(%)[a,b]	^{31}P: δ ($^2J_{PH}$)[c]	^{13}C: δ ($^1J_{CP}$)[d]	^1H: δ ($^2J_{HP}$)[d]
4a−f	Me	Ph	$n = 10-18$	80−90[a]	−31 (25)	67 (190)	4.4 (25)
				10−20[a]	−33 (21)	69 (180)	4.5 (21)
4g	Me	Me	$n = 18$	65[a]	−25.9 (24)	58 (194)	3.3 (m)
				35[a]	−26.2 (m)	62 (184)	
6a−h	Me	Ph	$n = 10-18$	74−96[b]	9 (17)	62 (146)	4.7 (17)
6g	Me	Me	$n = 18$	80[b]	12 (15)	52 (150)	3.3 (m)
8a−h	−	Ph	$n = 10-18$	66−92[b]	12 (17)	62 (137)	4.6 (17)
8g	−	Me	$n = 18$	79[b]	15 (m)	53 (140)	3.5 (m)

[a] Diastereomeric ratio of **4a−f** and **4g** determined by ^{31}P and ^1H NMR analysis of the reaction mixture (the accuracy of the measurements is within ±5%). − [b] Isolated yields of the phosphonic acid monoesters **6** and phosphonic acids **8**. − [c] ^{31}P NMR spectra of the reaction mixture in $CDCl_3$; *J* in Hz. − [d] ^{13}C and ^1H NMR data of the methine group α to the phosphorus atom, measured in $CDCl_3$ for **4** and in CD_3COOD for **6** and **8**; *J* in Hz.

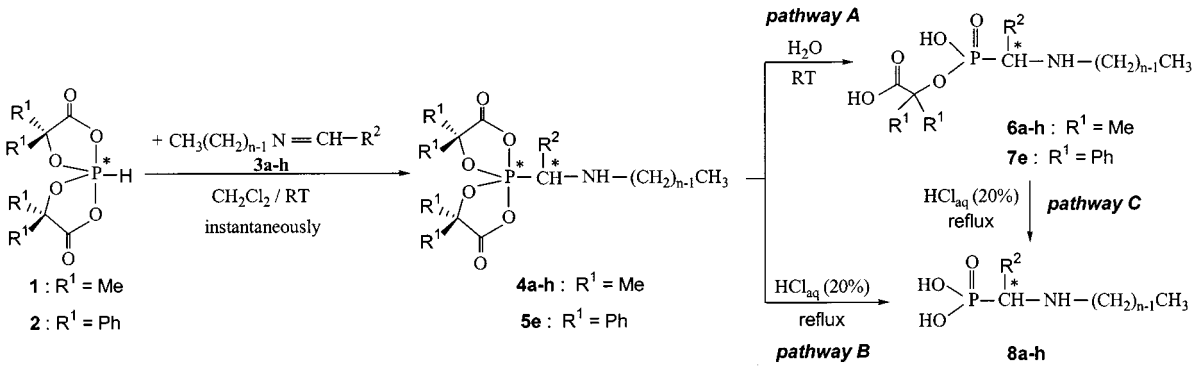
1 upon one face of the imine, (ii) the inductive effect of the phenyl group which enhances the electrophilic character of the imine′s carbon atom towards nucleophilic attack of **1**, and (iii) the *syn*/*anti* isomerism of the imine (the ^1H NMR spectra of **3g** shows the presence of two isomers, whereas no isomerism is observed for the imines **3a−f** derived from benzaldehyde).

To account for the high diastereofacial selectivity of the spirophosphorane addition to the Shiff base, we propose a reaction mechanism proceeding through the spirophosphoranide intermediate **A**, followed by the nucleophilic attack of this pentacoordinated anion at the electrophilic carbon atom of imine to afford the (α-aminoalkyl) spirophosphoranes **4a−e** and **5e**. The rigidity of the spirophosphoranide intermediate is the decisive stereochemical factor (Scheme 1). Moreover, the reaction occurs instantaneously at room temperature, and avoids the reversibility of the addition reaction observed for other spirophosphoranes.[25]

The (α-aminoalkyl)spirophosphoranes **4a−h** and **5e** are stable in solution and under argon for one week; they can be readily and selectively transformed, in situ, at room temperature in the presence of moist solvents, e.g., acetonitrile/water, and in good yields, into carboxyalkyl (α-aminoalkyl)-phosphonic acid monoesters **6a−h** and **7e** (Scheme 2, pathway A).

The (α-aminoalkyl)phosphonic acid monoesters **6−7** have only one stereogenic center (α-carbon atom). They exist as a pair of enantiomers indistinguishable by NMR analysis. Their ^{31}P NMR spectra are characterized by chemical shifts around δ = 8; this shows that the P nucleus is deshielded by approximately 40 ppm relative to that of **4a−h** and **5e**. This is consistent with the conversion of a pentacoordinated phosphorus atom into a tetracoordinated phosphorus atom (Table 1). As for (α-aminoalkyl)spirophosphoranes, their ^{31}P chemical shift is sensitive to the nature of the α-substituent, since for alkyl substituents (R^2 = Me, undecyl) instead of phenyl, a shielding of the phosphorus nucleus by approximately 3−4 ppm takes place. The chemical shift of the α-carbon ($\delta(^{13}C) \approx 62$) does not change significantly [$\Delta\delta(^{13}C) \approx 5$ ppm], but the coupling with phosphorus ($^1J_{CP} \approx 145$ Hz) is smaller, by about 45 Hz, than that of (α-aminoalkyl)spirophosphoranes **4a−h** and **5e**. We observed the same chemical shift for the methine proton in **6−7** (related to **4−5**), but the coupling constant $^2J_{HP} \approx 18$ Hz decreased by approximately 7 Hz. The ^1H NMR spectra of **6a−h** show that the methyl groups of the monoesters′s lateral chain are nonequivalent due to the asymmetric center.

The reaction of spirophosphoranes **1−2** with imines, followed by the in situ hydrolysis of the (α-aminoalkyl)spirophosphorane intermediates, is therefore general, and can be applied to long-chain imines derived from aromatic and aliphatic aldehydes and long-chain amines. This affords polyfunctional phosphonic acid monoesters bearing α-amino



Scheme 2. Selective and one-pot synthesis of free or monoester (α-aminoalkyl)phosphonic acid amphiphiles from P−H-bond spirophosphorane and long-chain imines

and β-carboxylic acid groups. Apart from their several applications,[1][5] complexes of these monoesters with metals are characterized by their limited oligomerization ability, in contrast to aminophosphonic acids and their diesters that, in the presence of transition metal ions, have the disadvantage of polymerizing.[16a]

Moreover, it has recently been demonstrated that the good crosslinking ability of phosphonocarboxylic acids for cellulose is related to the presence of a β-COOH function.[35]

The synthesis of (α-aminoalkyl)phosphonic acids **8a−h** can be achieved either by one-pot hydrolysis of **4a−h** and **5e** in the presence of 20% aqueous hydrochloric acid under reflux for 10 h (Scheme 2, pathway B), or by hydrolysis of carboxyalkyl (α-aminoalkyl)phosphonic acid monoesters **6a−h** and **7e** under the same conditions (Scheme 2, pathway C). Both methods afford **8** as a crystalline white powder in good yields. The ^{31}P chemical shifts of **8** exhibit slight deshielding of the ^{31}P nucleus with respect to monoesters **6−7** [$\Delta\delta(^{31}P) \approx 5$] whereas no noticeable variations are observed for ^{1}H and ^{13}C NMR spectra except for a decrease in the coupling constant $\Delta^{1}J_{CP} \approx 10$ Hz.

The phosphonic acid monoesters **6−7** and the free phosphonic acids **8** are not soluble in water and, to a great extent, precipitate from the reaction mixture during the reaction. These acids probably exist as zwitterions with three titratable protons: a strongly dissociated proton (P−OH) and two weakly dissociated ones (COOH and NH). In contrast, their sodium salts, obtained from cationic exchange resins, are soluble in water, and their ^{31}P chemical shifts show, as expected, a weak deshielding [$\Delta\delta(^{31}P) \approx 5$] compared to the acid precursors.

As in amino- and hydroxy-substituted phosphonic acid compounds,[2b,19,36] the ^{31}P chemical shifts of the carboxyalkyl (α-aminoalkyl)phosphonic acid monoesters **6−7** and the free (α-aminoalkyl)phosphonic acids **8** are strongly dependent on the pH of the solution. The insolubility of the long-chain (α-aminoalkyl)phosphorus acids in water, DMF, or DMSO prevents the determination of their p*K* values. Thus, the measurements are realized from the water-soluble **6e** disodium salt in distilled water ($c = 0.35$ M, pH = 10.8). Addition of concentrated sodium hydroxide solution or hydrochloric acid to this solution led to pH values of 13 and 7.5, respectively. For more acidic solutions it is not possible to determine the pH accurately since the product precipitates. An increase of the pH of the solution (about 10 pH units) causes a deshielding of the phosphorus nucleus by approximately 7 ppm without significant modification of the $^{2}J_{PH}$ coupling constants (Table 2).

Table 2. Influence of pH on the $\delta^{31}P$ and $^{2}J_{PH}$ (Hz) values of the (α-aminoalkyl)phosphonic acid monoester **6e** in water, at 20 °C ($c = 0.35$ M)

pH	δ (^{31}P)	$^{2}J_{PH}$ (Hz)
1.7[a]	8.7	17.2
7.5	10.9	br. m
10.8	12.7	20.6
13.0	16.5	19.3

[a] **6e** in 20% aqueous acetic acid.

Conclusion

In conclusion, the diastereoselective, instantaneous, and quantitative addition of spirophosphoranes **1−2** to long-chain imines, followed by selective one-pot hydrolysis of the (α-aminoalkyl)spirophosphorane intermediates, provides a novel, direct, and efficient route for the nearly quantitative synthesis of a new series of single-chain and double-chain phosphonic acid amphiphiles as free acids or as carboxyalkyl monoesters. Our study shows that the pentacoordinated phosphorus atom is able to exert a strong influence on the stereochemistry of carbon−phosphorus bond formation in the Pudovik reaction, due to the involvement of the spirophosphoranide (P^{V}) intermediate. The spirophosphoranic substructure can be considered to be a chiral auxiliary: it induces asymmetry and is then removed by being converted into tetracoordinated phosphonic acid derivatives. Owing to its easy implementation, this method has broad synthetic utility, and we are currently investigating the enantioselective version of the addition of chiral spirophosphoranes to imines, our main aim being the synthesis of optically pure phosphorus analogs of amino acids. The aggregation behavior of these new α-functionalized amphiphiles is under investigation.

Experimental Section

General: Spectra were recorded with the following instruments: IR spectra: Perkin−Elmer IRFT 1600; ^{1}H, ^{13}C and ^{31}P spectra: Bruker AC80, AC200 or 250WM; mass spectra by chemical ionization (DCI/NH_3 or DCI/CH_4) or positive FAB modes: Nermag R10−10H. − Elemental analyses were performed by the Microanalytical Service Laboratory of the "Laboratoire de Chimie de Coordination" of Toulouse. − Long-chain amines (C_{10}−C_{18}), benzaldehyde, acetaldehyde, dodecylaldehyde, phosphorus trichloride, 2-hydroxyisobutyric acid, benzilic acid (Aldrich), and oleylamine (Acros) were used as received without further purification. Dichloromethane, reagent grade product, was maintained over 4 Å molecular sieves and stored in a dark bottle protected from moisture. − The spirophosphoranes **1−2** were prepared according to the procedure already described.[31]

General Procedure for the Synthesis of Schiff Bases (3a−h): Equimolar amounts of amine and aldehyde in anhydrous dichloromethane were stirred at 40 °C for 6 h in the presence of 3 Å molecular sieves. The heterogeneous mixture was centrifuged, the organic phase was separated, then evaporated to dryness, and dried under vacuum.

***N*-(Benzylidene)decylimine (3a):** Yield: 95% (yellow oil).[37] − ^{1}H NMR (80.13 MHz, $CDCl_3$): δ = 8.26 (s, 1 H), 7.79−7.34 (m, 5 H), 3.61 (t, $^{3}J_{HH} = 6.5$ Hz, 2 H), 1.71 (m, 2 H), 1.29 (m, 14 H), 0.89 (t, $^{3}J_{HH} = 5.3$ Hz, 3 H). − ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 160.72 (s), 136.38 (s), 130.45−128.05 (m), 61.86 (s), 31.96−22.74 (m), 14.18 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1647.7 (C=N), 1580.5 (C=C). − MS (DCI/NH_3); *m/z*: 246 $(M + 1)^{+}$.

***N*-(Benzylidene)dodecylimine (3b):** Yield: 91% (yellow oil).[38] − ^{1}H NMR (80.13 MHz, $CDCl_3$): δ = 8.26 (s, 1 H), 7.75−7.34 (m, 5 H), 3.61 (t, $^3J_{HH}$ = 6.7 Hz, 2 H), 1.69 (m, 2 H), 1.26 (m, 18 H), 0.90 (t, $^3J_{HH}$ = 5.3 Hz, 3 H). − ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 160.63 (s), 136.43 (s), 130.41−128.05 (m), 61.86 (s), 32.00−22.75 (m), 14.17 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1645.9 (C=N), 1579.7 (C=C). − MS (DCI/NH_3); *m*/*z*: 274 (M + 1)$^+$.

***N*-(Benzylidene)tetradecylimine (3c):** Yield: 93% (yellow oil). − ^{1}H NMR (250.13 MHz, $CDCl_3$): δ = 8.26 (s, 1 H), 7.76−7.38 (m, 5 H), 3.62 (t, $^3J_{HH}$ = 7.0 Hz, 2 H), 1.72 (m, 2 H), 1.28 (m, 22 H), 0.91 (t, $^3J_{HH}$ = 6.1 Hz, 3 H). − ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 160.61 (s), 136.42 (s), 131.41 (s), 128.55 (s), 128.05 (s), 61.99 (s), 32.02−22.78 (m), 14.20 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1647.6 (C=N), 1537.7 (C=C). − MS (DCI/NH_3); *m*/*z*: 302 (M + 1)$^+$.

***N*-(Benzylidene)hexadecylimine (3d):** Yield: 96%. − M.p. 27−28°C (pale yellow solid).[39] − ^{1}H NMR (80.13 MHz, $CDCl_3$): δ = 8.26 (s, 1 H), 7.90−7.34 (m, 5 H), 3.60 (t, $^3J_{HH}$ = 6.5 Hz, 2 H), 1.70 (m, 2 H), 1.26 (m, 26 H), 0.89 (t, $^3J_{HH}$ = 5.3 Hz, 3 H). − ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 160.67 (s), 136.42 (s), 130.42−128.04 (m), 61.86 (s), 31.98−22.74 (m), 14.16 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1647.2 (C=N), 1580.5 (C=C). − MS (DCI/NH_3); *m*/*z*: 330 (M + 1)$^+$.

***N*-(Benzylidene)octadecylimine (3e):** Yield: 93%. − M.p. 34−36°C (pale yellow solid).[40] − ^{1}H NMR (80.13 MHz, $CDCl_3$): δ = 8.26 (s, 1 H), 7.69−7.34 (m, 5 H), 3.60 (t, $^3J_{HH}$ = 6.7 Hz, 2 H), 1.69 (m, 2 H), 1.25 (m, 30 H), 0.88 (t, $^3J_{HH}$ = 5.0 Hz, 3 H). − ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 160.74 (s), 136.37 (s), 130.45 (s), 128.58 (s), 128.03 (s), 61.87 (s), 31.96−22.73 (m), 14.16 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1642.9 (C=N), 1580.5 (C=C). − MS (DCI/NH_3); *m*/*z*: 358 (M + 1)$^+$.

***N*-(Benzylidene)oleylimine (3f):** Yield: 96% (yellow oil). − ^{1}H NMR (250.13 MHz, $CDCl_3$): δ = 8.26 (s, 1 H), 7.76−7.38 (m, 5 H), 5.39−5.35 (m, 2 H), 3.62 (t, $^3J_{HH}$ = 6.0 Hz, 2 H), 2.03 (m, 4 H), 1.72 (m, 2 H), 1.29 (m, 22 H), 0.91 (t, $^3J_{HH}$ = 6.8 Hz, 3 H). − ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 160.60 (s), 136.43 (s), 130.40−128.05 (m), 61.83 (s), 32.67−22.62 (m), 14.16 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1647.0 (C=N), 1579.6 (C=C). − MS (DCI/NH_3); *m*/*z*: 356 (M + 1)$^+$.

***N*-(Ethylidene)octadecylimine (3g):** Yield: 86%. − M.p. 39−42°C (orange solid). − ^{1}H NMR (80.13 MHz, $CDCl_3$): δ = 7.65 (q, $^3J_{HH}$ = 4.8 Hz, 1 H), 3.32 (t, $^3J_{HH}$ = 5.9 Hz, 2 H), 1.91 (d, $^3J_{HH}$ = 4.7 Hz, 3 H), 1.24 (m, 32 H), 0.86 (t, $^3J_{HH}$ = 5.1 Hz, 3 H). − ^{13}C NMR (50.32 MHz, $CDCl_3$): δ = 162.75 (s, minor product,*syn*), 160.31 (s, main product, *anti*), 61.70 (s, *syn*), 61.47 (s,*anti*), 31.99−22.76 (m), 22.24 (s, *anti*), 20.73 (s, *syn*), 14.19 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1673.2 (C=N). − MS (DCI/NH_3); *m*/*z*: 296 (M + 1)$^+$.

***N*-(Dodecylidene)octadecylimine (3h):** Yield: 86% (pale yellow solid). − ^{1}H NMR (80.13 MHz, $CDCl_3$): δ = 8.50 (s, 1 H), 3.32 (t, $^3J_{HH}$ = 6.6 Hz, 2 H), 1.50 (m, 2 H), 1.24 (m, 50 H), 0.86 (t, $^3J_{HH}$ = 5.8 Hz, 6 H). − ^{13}C NMR (50.32 MHz, $CDCl_3$): δ = 164.70 (s), 61.46 (s), 42.08−22.71 (m), 14.11 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 1666.7 (C=N). − MS (DCI/NH_3); *m*/*z*: 436 (M + 1)$^+$.

General Procedure for the Synthesis of (α-Aminoalkyl)spirophosphoranes 4a−h and 5e: The reaction was carried out under argon. The imines **3a−h** (10 mmol) in anhydrous dichloromethane (10 mL) were added dropwise to a stirred solution of spirophosphorane **1−2** (10 mmol) in anhydrous dichloromethane (20 mL) at room temperature. The progress of the reaction was monitored by ^{31}P NMR analysis. The addition reaction occurred instantaneously, and afforded (α-aminoalkyl)spirophosphoranes **4a−h** and **5e** in quantitative yields. In spite of their stability in solution under argon during several days, all attempts to purify them failed due to their decomposition into tetracoordinated phosphorus compounds. In order to characterize these P^V−C bond spirophosphoranes, the reaction was then carried out directly in an NMR tube in deuterated solvent under argon. The imines **3a−h** (0.3 mmol) in $CDCl_3$ (0.5 mL) were added to a solution of spirophosphorane **1−2** (0.3 mmol) in $CDCl_3$ (0.5 mL) at room temperature. (α-Aminoalkyl)spirophosphoranes **4a−h** and **5e** were instantaneously and quantitatively formed and characterized by ^{31}P, ^{1}H, and ^{13}C NMR analysis.

***P*-(α-Decylaminobenzyl)spirophosphorane 4a:** ^{31}P NMR (81.01 MHz, $CDCl_3$): δ = −31.28 (d, $^2J_{PH}$ = 25.2 Hz, 90%), −32.63 (d, $^2J_{PH}$ = 20.8 Hz, 10%). − ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 7.33 (m, 5 H), 4.55 (d, $^2J_{HP}$ = 21.4 Hz, 1 H, 13%), 4.38 (d, $^2J_{HP}$ = 25.0 Hz, 1 H, 87%), 2.39 (m, 2 H), 1.58 (d, $^3J_{HH}$ = 2.3 Hz, 1 H, NH), 1.46 (s, 6 H), 1.34 (m, 2 H), 1.18 (m, 14 H), 1.05 (s, 6 H), 0.83 (t, $^3J_{HH}$ = 6.4 Hz, 3 H). − ^{13}C NMR (50.32 MHz, $CDCl_3$): δ = 172.57 (s), 135.27 (s), 130.05−128.36 (m), 81.00 (s), 68.83 (d, $^1J_{CP}$ = 180.0 Hz, minor isomer), 67.42 (d, $^1J_{CP}$ = 190.9 Hz, major isomer), 47.62 (d, $^3J_{CP}$ = 24.3 Hz), 31.89−22.69 (m), 26.36 (s), 23.50 (s), 14.15 (s).

***P*-(α-Dodecylaminobenzyl)spirophosphorane 4b:** ^{31}P NMR (81.01 MHz, $CDCl_3$): δ = −31.48 (d, $^2J_{PH}$ = 24.8 Hz, 90%); −32.82 (d, $^2J_{PH}$ = 21.7 Hz, 10%). − ^{1}H NMR (80.13 MHz, $CDCl_3$): δ = 7.35−7.23 (m, 5 H), 4.38 (d, $^2J_{HP}$ = 25.0 Hz, 1 H), 2.42 (m, 2 H), 1.47 (m, 7 H), 1.22 (m, 20 H), 1.07 (s, 6 H), 0.85 (m, 3 H). − ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 172.40 (s), 135.27 (s), 129.22−127.93 (m), 80.88 (s), 69.49 (d, $^1J_{CP}$ = 170.0 Hz, minor isomer), 67.40 (d, $^1J_{CP}$ = 190.4 Hz, major isomer), 47.56 (d, $^3J_{CP}$ = 24.5 Hz), 31.83−22.62 (m), 27.02 (s), 23.33 (s), 14.15 (s).

***P*-(α-Tetradecylaminobenzyl)spirophosphorane 4c:** ^{31}P NMR (81.01 MHz, $CDCl_3$): δ = −31.39 (d, $^2J_{PH}$ = 25.0 Hz, 95%); −33.18 (d, $^2J_{PH}$ = 19.9 Hz, 5%). − ^{1}H NMR (80.13 MHz, $CDCl_3$): δ = 7.34 (m, 5 H), 4.38 (d, $^2J_{HP}$ = 24.8 Hz, 1 H), 2.41 (m, 2 H), 1.46 (s, 6 H), 1.20 (m, 25 H), 1.06 (s, 6 H), 0.84 (t, $^3J_{HH}$ = 4.3 Hz, 3 H). − ^{13}C NMR (50.32 MHz, $CDCl_3$): δ = 172.55 (s), 135.24 (s), 129.31−128.63 (m), 81.03 (s), 68.45 (d, $^1J_{CP}$ = 188.7 Hz, minor isomer), 67.35 (d, $^1J_{CP}$ = 190.9 Hz, major isomer), 47.58 (d, $^3J_{CP}$ = 24.2 Hz), 31.93−22.70 (m), 26.34 (s), 23.48 (s), 14.16 (s).

***P*-(α-Hexadecylaminobenzyl)spirophosphorane 4d:** ^{31}P NMR (81.01 MHz, $CDCl_3$): δ = −31.28 (d, $^2J_{PH}$ = 24.9 Hz, 90%); −33.63 (d, $^2J_{PH}$ = 23.1 Hz, 10%). − ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 7.40−7.32 (m, 5 H), 4.56 (d, $^2J_{HP}$ = 21.0 Hz, 1 H, 15%), 4.39 (d, $^2J_{HP}$ = 24.9 Hz, 1 H, 85%), 2.40 (m, 2 H), 1.48 (s, 6 H), 1.23 (m, 29 H), 1.07 (s, 6 H), 0.85 (t, $^3J_{HH}$ = 6.7 Hz, 3 H). − ^{13}C NMR (50.32 MHz, $CDCl_3$): δ = 172.66 (s), 135.33 (s), 129.31−127.95 (m), 81.08 (s), 69.21 (d, $^1J_{CP}$ = 184.5 Hz, minor isomer), 67.44 (d, $^1J_{CP}$ = 190.9 Hz, major isomer), 47.65 (d, $^3J_{CP}$ = 24.2 Hz), 31.97−22.74 (m), 26.38 (s), 23.36 (s), 14.19 (s).

***P*-(α-Octadecylaminobenzyl)spirophosphorane 4e:** ^{31}P NMR (81.01 MHz, $CDCl_3$): δ = −31.37 (d, $^2J_{PH}$ = 24.7 Hz, 80%); −33.15 (d, $^2J_{PH}$ = 18.2 Hz, 20%). − ^{1}H NMR (80.13 MHz, $CDCl_3$): δ = 7.36 (m, 5 H), 4.39 (d, $^2J_{HP}$ = 24.8 Hz, 1 H), 2.43 (m, 2 H), 1.57 (m, 7 H), 1.22 (m, 32 H), 1.06 (s, 6 H), 0.84 (t, $^3J_{HH}$ = 6.6 Hz, 3 H). − ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 172.51 (s), 135.21 (s), 129.24−128.62 (m), 80.99 (s), 68.91 (d, $^1J_{CP}$ = 181.6 Hz, minor isomer), 67.39 (d, $^1J_{CP}$ = 190.9 Hz, major isomer), 47.58 (d, $^3J_{CP}$ = 24.6 Hz), 31.90−22.67 (m), 26.23 (s), 23.45 (s), 14.10 (s).

***P*-(α-Oleylaminobenzyl)spirophosphorane 4f:** ^{31}P NMR (81.01 MHz, $CDCl_3$): δ = −31.31 (d, $^2J_{PH}$ = 24.9 Hz, 75%);

−32.63 (d, $^2J_{PH}$ = 21.1 Hz, 25%). − ^{1}H NMR (250.13 MHz, $CDCl_3$): δ = 7.38−7.33 (m, 5 H), 5.32 (m, 2 H), 4.55 (d, $^2J_{HP}$ = 23.4 Hz, 1 H, 20%), 4.39 (d, $^2J_{HP}$ = 24.9 Hz, 1 H, 80%), 2.40 (m, 2 H), 1.97 (m, 4 H), 1.47 (s, 6 H), 1.42 (s, 1 H),1.23 (m, 24 H), 1.07 (s, 6 H), 0.85 (t, $^3J_{HH}$ = 6.8 Hz, 3 H). − ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 172.53 (s), 135.33 (s), 130.35−127.95 (m), 80.99 (s), 68.97 (d, $^1J_{CP}$ = 181.1 Hz, minor isomer), 67.45 (d, $^1J_{CP}$ = 190.9 Hz, major isomer), 47.60 (d, $^3J_{CP}$ = 24.2 Hz), 32.60−22.55 (m), 26.32 (s), 23.46 (s), 14.11 (s).

***P*-(α-Octadecylaminoethyl)spirophosphorane 4g:** ^{31}P NMR (81.01 MHz, $CDCl_3$): δ = −25.90 (dq, $^2J_{PH}$ = 23.8 Hz, $^3J_{PH}$ = 12.3 Hz, 65%); −26.20 (m, 35%). − ^{1}H NMR (80.13 MHz, $CDCl_3$): δ = 3.56−3.07 (m, 1 H), 2.65 (m, 2 H), 2.05 (m, 2 H), 1.58 (m, 12 H), 1.55 (m, 3 H), 1.21 (m, 31 H), 0.83 (t, $^3J_{HH}$ = 5.7 Hz, 3 H). − ^{13}C NMR (50.32 MHz, $CDCl_3$): δ = 172.75 (s), 81.23 (s), 62.04 (d, $^1J_{CP}$ = 183.9 Hz, minor isomer), 58.29 (d, $^1J_{CP}$ = 194.2 Hz, major isomer), 48.64 (s), 32.69−22.70 (m), 26.33 (s), 24.16 (s), 16.12 (s), 14.14 (s).

***P*-(α-Octadecylaminododecyl)spirophosphorane 4h:** ^{31}P NMR (81.01 MHz, $CDCl_3$): δ = −25.94 (d, $^2J_{PH}$ = 24.8 Hz, 80%); −29.74 (d, $^2J_{PH}$ = 23.2 Hz, 20%). − ^{1}H NMR (80.13 MHz, $CDCl_3$): δ = 3.48−3.01 (m, 1 H), 2.65 (m, 2 H), 1.57 (m, 12 H), 1.22 (m, 43 H), 0.84 (t, $^3J_{HH}$ = 5.4 Hz, 6 H). − ^{13}C NMR (50.32 MHz, $CDCl_3$): δ = 172.85 (s), 80.86 (s), 65.52 (d, $^1J_{CP}$ = 151.0 Hz, minor isomer), 63.75 (d, $^1J_{CP}$ = 187.9 Hz, major isomer), 49.63 (d, $^3J_{CP}$ = 14.1 Hz), 34.44−22.72 (m), 26.24 (s), 24.09 (s), 14.15 (s).

***P*-(α-Octadecylaminobenzyl)spirophosphorane 5e:** ^{31}P NMR (81.01 MHz, $CDCl_3$): δ = −29.65 (d, $^2J_{PH}$ = 23.2 Hz, 85%); −31.51 (d, $^2J_{PH}$ = 21.5 Hz, 15%). − ^{1}H NMR (200.13 MHz, $CDCl_3$): δ = 7.39−7.02 (m, 25 H), 4.49 (d, $^2J_{HP}$ = 23.4 Hz, 1 H), 2.19 (m, 2 H), 1.77 (m, 2 H), 1.28 (m, 30 H), 0.90 (t, $^3J_{HH}$ = 6.8 Hz, 3 H). − ^{13}C NMR (50.32 MHz, $CDCl_3$): δ = 168.73 (s), 142.66−134.10 (m), 129.37−125.91 (m), 87.12 (s), 68.00 (d, $^1J_{CP}$ = 181.2 Hz, minor isomer), 67.20 (d, $^1J_{CP}$ = 189.5 Hz, major isomer), 48.34 (d, $^3J_{CP}$ = 23.1 Hz), 32.01−22.78 (m), 14.23 (s).

General Procedure for the Synthesis of Carboxyalkyl (α-Aminoalkyl)-phosphonic Acid Monoesters 6a−h and 7e: Imine **3a−h** (10 mmol) in anhydrous dichloromethane (10 mL) was added dropwise to a stirred solution of spirophosphorane **1**−**2** (10 mmol) in anhydrous dichloromethane (20 mL) at room temperature under argon. The mixture was stirred for 5 min at room temperature and then concentrated to dryness. The residue was treated by acetonitrile/distilled water, 1:1 (50 mL). The precipitate, immediately formed after addition, was collected by filtration, washed several times with acetonitrile, recrystallized from ethanol, and then dried under vacuum to give a white powder.

Carboxyisobutyl α-Decylaminobenzylphosphonic Acid Monoester (6a): Yield: 87%. − M.p. 173−174°C (from ethanol); ^{31}P NMR (81.01 MHz, CD_3COOD): δ = 8.60 (d, $^2J_{PH}$ = 17.5 Hz). − ^{1}H NMR (250.13 MHz, CD_3COOD): δ = 7.60−7.43 (m, 5 H), 4.71 (d, $^2J_{HP}$ = 17.8 Hz, 1 H), 2.96 (m, 2 H), 1.79 (m, 2 H), 1.64 (s, 3 H), 1.58 (s, 3 H), 1.29 (m, 15 H), 0.91 (t, $^3J_{HH}$ = 6.2 Hz, 3 H). − ^{13}C NMR (62.90 MHz, CD_3COOD): δ = 179.71 (s), 131.13 (s), 130.29−129.59 (m), 81.29 (s), 61.60 (d, $^1J_{CP}$ = 146.2 Hz), 47.86 (s), 32.48−23.20 (m), 27.65 (s), 26.72 (s), 14.16 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3433.3 (broad, OH, NH), 2529.3 (P−OH), 1725.0 (C=O), 1637.3 (C=C), 1192.3 (P=O), 1073.7 (O=P−O). − MS (Glycerol, FAB > 0); *m*/*z*: 414 (M + 1)$^+$. − $C_{21}H_{36}NO_5P$ (413.47): calcd. C 61.00, H 8.78, N 3.39; found C 60.96, H 8.79, N 3.32.

Carboxyisobutyl α-Dodecylaminobenzylphosphonic Acid Monoester (6b): Yield: 74%. − M.p. 173−175°C (from ethanol). − ^{31}P NMR (81.01 MHz, CD_3COOD): δ = 8.62 (d, $^2J_{PH}$ = 16.8 Hz). − ^{1}H NMR (250.13 MHz, CD_3COOD): δ = 7.59−7.42 (m, 5 H), 4.74 (d, $^2J_{HP}$ = 17.9 Hz, 1 H), 2.94 (m, 2 H), 1.80 (m, 2 H), 1.63 (s, 3 H), 1.46 (s, 3 H), 1.29 (m, 19 H), 0.91 (t, $^3J_{HH}$ = 6.6 Hz, 3 H). − ^{13}C NMR (62.90 MHz, CD_3COOD): δ = 179.19 (s), 130.99 (s), 130.91−129.57 (m), 80.84 (s), 61.82 (d, $^1J_{CP}$ = 146.3 Hz), 47.93 (s), 32.50−23.19 (m), 27.36 (s), 26.43 (s), 14.09 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3417.4 (broad, OH, NH), 2368.4 (P−OH), 1724.7 (C=O), 1632.2 (C=C), 1168.3 (P=O), 1067.2 (O=P−O). − MS (MNBA, FAB > 0); *m*/*z*: 442 (M + 1)$^+$. − $C_{23}H_{40}NO_5P$ (441.53): calcd. C 62.56, H 9.13, N 3.17; found C 62.56, H 9.48, N, 3.04.

Carboxyisobutyl α-Tetradecylaminobenzylphosphonic Acid Monoester (6c): Yield: 96%. − M.p. 166−167°C (from ethanol). − ^{31}P NMR (81.01 MHz, CD_3COOD): δ = 8.56 (d, $^2J_{PH}$ = 16.4 Hz). − ^{1}H NMR (250.13 MHz, CD_3COOD): δ = 7.57−7.42 (m, 5 H), 4.73 (d, $^2J_{HP}$ = 17.8 Hz, 1 H), 2.97 (m, 2 H), 1.78 (m, 2 H), 1.62 (s, 3 H), 1.47 (s, 3 H), 1.29 (m, 23 H), 0.91 (t, $^3J_{HH}$ = 5.7 Hz, 3 H). − ^{13}C NMR (62.90 MHz, CD_3COOD): δ = 179.53 (s), 131.03 (s), 130.17−129.56 (m), 81.43 (s), 61.70 (d, $^1J_{CP}$ = 146.1 Hz), 47.89 (s), 32.52−23.20 (m), 27.51 (s), 26.48 (s), 14.10 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3430.2 (broad, OH, NH), 2362.6 (P−OH), 1727.6 (C=O), 1635.0 (C=C), 1169.0 (P=O), 1068.1 (O=P−O). − MS (MNBA, FAB > 0); *m*/*z*: 470 (M + 1)$^+$. − $C_{25}H_{44}NO_5P$ (469.58): calcd. C 63.94, H 9.44, N 2.81; found C 64.13, H 9.63, N 2.95.

Carboxyisobutyl α-Hexadecylaminobenzylphosphonic Acid Monoester (6d): Yield: 88%. − M.p. 172−173°C (from ethanol). − ^{31}P NMR (81.01 MHz, CD_3COOD): δ = 8.62 (d, $^2J_{PH}$ = 16.1 Hz). − ^{1}H NMR (250.13 MHz, CD_3COOD): δ = 7.59−7.43 (m, 5 H), 4.74 (d, $^2J_{HP}$ = 17.6 Hz, 1 H), 2.96 (m, 2 H), 1.77 (m, 2 H), 1.63 (s, 3 H), 1.50 (s, 3 H), 1.31 (m, 27 H), 0.91 (t, $^3J_{HH}$ = 6.6 Hz, 3 H). − ^{13}C NMR (62.90 MHz, CD_3COOD): δ = 178.80 (s), 130.27 (s), 129.83−129.56 (m), 81.1 (s), 61.60 (d, $^1J_{CP}$ = 147.6 Hz), 47.92 (s), 32.52−23.21 (m), 27.53 (s), 26.83 (s), 14.14 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3422.2 (broad, OH, NH), 2359.4 (P−OH), 1724.5 (C=O), 1607.9 (C=C), 1172.6 (P=O), 1082.4 (O=P−O). − MS (Glycerol, FAB > 0); *m*/*z*: 498 (M + 1)$^+$. − $C_{27}H_{48}NO_5P$ (497.63): calcd. C 65.16, H 9.72, N 2.81; found C 65.35, H 9.88, N 2.83.

Carboxyisobutyl α-Octadecylaminobenzylphosphonic Acid Monoester (6e): Yield: 90%. − M.p. 173−175°C (from ethanol). − ^{31}P NMR (81.01 MHz, CD_3COOD): δ = 8.67 (d, $^2J_{PH}$ = 17.2 Hz). − ^{1}H NMR (250.13 MHz, CD_3COOD): δ = 7.57−7.43 (m, 5 H), 4.70 (d, $^2J_{HP}$ = 17.0 Hz, 1 H), 2.97 (m, 2 H), 1.78 (m, 2 H), 1.62 (m, 3 H), 1.49 (m, 3 H), 1.30 (m, 31 H), 0.91 (m, 3 H). − ^{13}C NMR (62.90 MHz, CD_3COOD): δ = 179.87 (s), 131.06 (s), 130.25−129.57 (m), 80.97 (s), 61.79 (d, $^1J_{CP}$ = 145.7 Hz), 47.81 (s), 32.55−23.23 (m), 27.52 (s), 26.50 (s), 14.16 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3440.7 (broad, OH, NH), 1727.1 (C=O), 1635.9 (C=C), 1169.8 (P=O), 1068.2 (O=P−O). − MS (MNBA, FAB > 0); *m*/*z*: 526 (M + 1)$^+$. − $C_{29}H_{52}NO_5P$ (525.68): calcd. C 66.26, H 9.97, N 2.66; found C 66.12, H 10.25, N 2.64.

Carboxyisobutyl α-Oleylaminobenzylphosphonic Acid Monoester (6f): Yield: 91%. − M.p. 169−171°C (from ethanol). − ^{31}P NMR (81.01 MHz, $CDCl_3$): δ = 8.64 (m). − ^{1}H NMR (250.13 MHz, $CDCl_3$): δ = 7.59−7.43 (m, 5 H), 5.37 (m, 2 H), 4.67 (d, $^2J_{HP}$ = 17.0 Hz, 1 H), 2.98 (m, 2 H), 2.05 (m, 4 H), 1.76 (m, 2 H), 1.62 (s, 3 H), 1.52 (s, 3 H), 1.30 (m, 25 H), 0.91 (t, $^3J_{HH}$ = 6.8 Hz, 3 H). − ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 172.00 (s), 130.60 (s), 130.55−129.60 (m), 81.33 (s), 61.80 (d, $^1J_{CP}$ = 147.2 Hz), 47.00 (s), 33.12−23.22 (m), 27.64 (s), 26.00 (s), 14.17 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3418.6 (broad, OH, NH), 2362.8 (P−OH), 1726.4 (C=O), 1635.8 (C=C), 1169.6 (P=O), 1068.5 (O=P−O). − MS (Glycerol,

FAB > 0); *m/z*: 524 $(M + 1)^+$. − $C_{29}H_{50}NO_5P$ (523.67): calcd C 66.51, H 9.62, N 2.67; found C 66.79, H 9.33, N 2.64.

Carboxyisobutyl α-Octadecylaminoethylphosphonic Acid Monoester (6g): Yield: 80%. − M.p. 139−140°C (from ethanol). − ^{31}P NMR (81.01 MHz, $CDCl_3$): δ = 11.96 (dd, $^2J_{PH} = {}^3J_{PH} = 14.8$ Hz). − ^1H NMR (250.13 MHz, $CDCl_3$): δ = 9.99 (m, 1 H), 7.88 (m, 1 H), 3.29 (m, 1 H), 2.85 (m, 2 H), 1.75 (m, 2 H), 1.66 (s, 3 H), 1.48 (s, 3 H), 1.45 (m, $^3J_{HH} = 7.1$ Hz, 3 H), 1.23 (m, 31 H), 0.86 (t, $^3J_{HH} = 6.4$ Hz, 3 H). − ^{13}C NMR (62.90 MHz, $CDCl_3$): δ = 178.11 (s), 78.78 (s), 51.60 (d, $^1J_{CP} = 151.0$ Hz), 46.30 (s), 31.98−22.75 (m), 28.30 (s), 26.60 (s), 14.18 (s), 11.33 (d, $^2J_{CP} = 7.0$ Hz). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3422.2 (broad, OH, NH), 2503.9 (P−OH), 1731.6 (C=O), 1180.5 (P=O), 1060.0 (O=P−O). − MS (DCI/NH_3); *m/z*: 464 $(M + 1)^+$. − $C_{24}H_{50}NO_5P$ (463.62): calcd C 62.17, H 10.87, N 3.02; found C 62.09, H 10.83, N 3.00.

Carboxyisobutyl α-Octadecylaminododecylphosphonic Acid Monoester (6h): Yield: 93%. − M.p. 147−150°C (from dichloromethane). − ^{31}P NMR (81.01 MHz, $CDCl_3$ and two drops of CD_3COOD): δ = 9.46 (dt, $^2J_{PH} = {}^3J_{PH} = 16.0$ Hz). − ^1H NMR (250.13 MHz, $CDCl_3$ and two drops of CD_3COOD): δ = 3.10 (m, 1 H), 2.76 (m, 2 H), 1.70 (m, 5 H), 1.48 (s, 3 H), 1.25 (m, 51 H), 0.88 (t, $^3J_{HH} = 6.6$ Hz, 6 H). − ^{13}C NMR (50.32 MHz, $CDCl_3$ and two drops of CD_3COOD): δ = 178.76 (s), 79.82 (s), 56.10 (d, $^1J_{CP} = 147.8$ Hz), 47.08 (s), 31.94−22.71 (m), 27.86 (s), 14.11 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3480.7 (broad, OH, NH), 2500.5 (P−OH), 1720.4 (C=O), 1177.0 (P=O), 1066.8 (O=P−O). − MS (Glycerol, FAB > 0); *m/z*: 604 $(M + 1)^+$. − $C_{34}H_{70}NO_5P$ (603.88): calcd. C 67.62, H 11.68, N 2.32; found C 67.33, H 11.62, N 2.29.

Carboxybenzil α-Octadecylaminobenzylphosphonic Acid Monoester (7e): Yield: 78%. − M.p. 125−128°C (from diethyl ether). − ^{31}P NMR (81.01 MHz, $CDCl_3$): δ = 7.62 (m). − ^1H NMR (80.13 MHz, $CDCl_3$): δ = 7.51−7.28 (m, 15 H), 4.30 (d, $^2J_{HP} = 16.8$ Hz, 1 H), 2.50 (m, 2 H), 1.86 (m, 3 H), 1.30 (m, 30 H), 0.93 (t, $^3J_{HH} = 6.4$ Hz, 3 H). − ^{13}C NMR (50.32 MHz, $CDCl_3$): δ = 176.92 (s), 142.96−130.11 (m), 129.32−127.60 (m), 86.68 (s), 60.78 (d, $^1J_{CP} = 138.8$ Hz), 48.38 (s), 31.96−22.72 (m), 14.11 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3411.1 (broad, OH, NH), 2464.2 (P−OH), 1711.5 (C=O), 1601.4 (C=C), 1172.6 (P=O), 1071.4 (O=P−O). − MS (DCI/NH_3); *m/z*: 649 $(M)^+$.

General Procedure for the Synthesis of (α-Aminoalkyl)phosphonic Acids 8a−h: Their synthesis can be accomplished either by acid hydrolysis of (α-aminoalkyl)phosphonocarboxylic acids **6a−h** and **7e** (Method A), or by one-pot acid hydrolysis of the reaction mixture (Method B). − **Method A:** (α-Aminoalkyl)phosphonocarboxylic acids **6a−h** and **7e** (1.1 mmol) in 20% aqueous hydrochloric acid (7 mL) were heated under reflux for 5−10 h. The progress of the reaction was monitored by ^{31}P NMR analysis. The mixture was then allowed to cool to room temperature. The mixture was concentrated under vacuum. The precipitate was collected by filtration and washed several times with distilled water, methanol, and diethyl ether. The white solid was recrystallized from ethanol, 2-propanol, or butanol if necessary, then dried under vacuum. − **Method B:** The reaction mixture obtained from spirophosphorane **1−2** (3.9 mmol) and imine **3a−h** (3.9 mmol), in anhydrous dichloromethane (20 mL) at room temperature under stirring for 5−10 min, was concentrated in vacuo. To the residue was added 20% aqueous hydrochloric acid (25 mL), with stirring; the mixture was heated under reflux for 5−10 h. After cooling to room temperature, the mixture was worked up as described for Method A.

(α-Decylaminobenzyl)phosphonic Acid (8a): Yield: 92%. − M.p. 214−216°C (from ethanol). − ^{31}P NMR (81.01 MHz, CD_3COOD): δ = 11.79 (d, $^2J_{PH} = 16.3$ Hz). − ^1H NMR (200.13 MHz, CD_3COOD): δ = 7.53−7.41 (m, 5 H), 4.64 (d, $^2J_{HP} = 17.2$ Hz, 1 H), 2.94 (m, 2 H), 1.79 (m, 2 H), 1.28 (m, 15 H), 0.90 (t, $^3J_{HH} = 6.7$ Hz, 3 H). − ^{13}C NMR (50.32 MHz, CD_3COOD): δ = 131.09 (s), 131.00−129.74 (m), 61.81 (d, $^1J_{CP} = 136.8$ Hz), 48.10 (s), 32.58−23.31 (m), 14.23 (s); IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3404.8 (broad, OH, NH), 2288.0 (P−OH), 1608.3 (C=C), 1173.1 (P=O), 1082.6 (O=P−O). − MS (DCI/NH_3); *m/z*: 328 $(M + 1)^+$. − $C_{17}H_{30}NO_3P$ (327.39): calcd. C 62.37, H 9.24, N 4.28; found C 61.81, H 9.31, N 4.11.

(α-Dodecylaminobenzyl)phosphonic Acid (8b): Yield: 83%. − M.p. 225−227°C (from butanol). − ^{31}P NMR (81.01 MHz, CD_3COOD): δ = 12.05 (d, $^2J_{PH} = 16.7$ Hz). − ^1H NMR (250.13 MHz, CD_3COOD): δ = 7.56−7.42 (m, 5 H), 4.66 (d, $^2J_{HP} = 17.4$ Hz, 1 H), 2.95 (m, 2 H), 1.79 (m, 2 H), 1.29 (m, 19 H), 0.91 (t, $^3J_{HH} = 6.1$ Hz, 3 H). − ^{13}C NMR (62.90 MHz, CD_3COOD): δ = 130.84 (s), 130.77−129.66 (m), 61.70 (d, $^1J_{CP} = 137.4$ Hz), 47.94 (s), 32.51−23.20 (m), 14.10 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3495.4 (broad, OH, NH), 2367.5 (P−OH), 1608.3 (C=C), 1172.3 (P=O), 1082.6 (O=P−O). − MS (MNBA, FAB > 0); *m/z*: 356 $(M + 1)^+$. − $C_{19}H_{34}NO_3P$ (355.44): calcd. C 64.18, H 9.64, N 3.94; found C 63.40, H 9.72, N 3.79.

(α-Tetradecylaminobenzyl)phosphonic Acid (8c): Yield: 67%. − M.p. 213−216°C. − ^{31}P NMR (81.01 MHz, CD_3COOD): δ = 10.90 (m). − ^1H NMR (250.13 MHz, CD_3COOD): δ = 7.55−7.41 (m, 5 H), 4.54 (d, $^2J_{HP} = 17.2$ Hz, 1 H), 2.94 (m, 2 H), 1.76 (m, 2 H), 1.30 (m, 23 H), 0.91 (t, $^3J_{HH} = 6.4$ Hz, 3 H). − ^{13}C NMR (62.90 MHz, CD_3COOD): δ = 130.78 (s), 130.03−129.54 (m), 61.85 (d, $^1J_{CP} = 137.1$ Hz), 47.86 (s), 32.52−23.21 (m), 14.12 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3395.4 (broad, OH, NH), 2317.8 (P−OH), 1609.1 (C=C), 1173.5 (P=O), 1082.8 (O=P−O). − MS (Glycerol, FAB >0); *m/z*: 384 $(M + 1)^+$. − $C_{21}H_{38}NO_3P$ (383.49): calcd. C 65.77, H 9.99, N 3.65; found C 65.78, H 10.16, N 3.60.

(α-Hexadecylaminobenzyl)phosphonic Acid (8d): Yield: 80%. − M.p. 214−216°C (from butanol). − ^{31}P NMR (81.01 MHz, CD_3COOD): δ = 12.11 (d, $^2J_{PH} = 17.2$ Hz, 1 H). − ^1H NMR (250.13 MHz, CD_3COOD): δ = 7.55−7.41 (m, 5 H), 4.65 (d, $^2J_{HP} = 17.3$ Hz, 1 H), 2.94 (m, 2 H), 1.79 (m, 2 H), 1.30 (m, 27 H), 0.91 (t, $^3J_{HH} = 6.7$ Hz, 3 H). − ^{13}C NMR (62.90 MHz, CD_3COOD): δ = 130.83 (s), 130.75−129.65 (m), 61.70 (d, $^1J_{CP} = 137.7$ Hz), 48.05 (s), 32.52−23.20 (m), 14.09 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3430.4 (broad, OH, NH), 2359.4 (P−OH), 1607.9 (C=C), 1172.6 (P=O), 1082.4 (O=P−O). − MS (MNBA, FAB > 0); *m/z*: 412 $(M + 1)^+$. − $C_{23}H_{42}NO_3P$ (411.54): calcd. C 67.12, H 10.29, N 3.40; found C 67.20, H 10.47, N 3.38.

(α-Octadecylaminobenzyl)phosphonic Acid (8e): Yield: 78%. − M.p. 215−217°C (from 2-propanol). − ^{31}P NMR (81.01 MHz, CD_3COOD): δ = 10.98 (m). − ^1H NMR (250.13 MHz, CD_3COOD): δ = 7.54−7.40 (m, 5 H), 4.55 (d, $^2J_{HP} = 17.0$ Hz, 1 H), 2.92 (m, 2 H), 1.76 (m, 2 H), 1.31 (m, 31 H), 0.91 (t, $^3J_{HH} = 6.6$ Hz, 3 H). − ^{13}C NMR (50.32 MHz, $CDCl_3$ and two drops of CD_3COOD): δ = 131.50 (s), 128.96−128.76 (m), 61.72 (d, $^1J_{CP} = 137.6$ Hz), 47.30 (s), 31.92−22.68 (m), 14.07 (s). − IR (KBr, cm^{-1}): $\tilde{\nu}$ = 3422.5 (broad, OH, NH), 2364.7 (P−OH), 1606.8 (C=C), 1169.8 (P=O), 1069.1 (O=P−O). − MS (DCI/NH_3); *m/z*: 440 $(M + 1)^+$. − $C_{25}H_{46}NO_3P$ (439.60): calcd. C 68.30, H 10.55, N 3.19; found C 68.61, H 10.24, N 2.99.

(α-Oleylaminobenzyl)phosphonic Acid (8f): Yield: 66%. − M.p. 212−214°C (from ethanol). − ^{31}P NMR (81.01 MHz, $CDCl_3$ and two drops of CD_3COOD): δ = 10.06 (d, $^2J_{PH} = 15.7$ Hz). − ^1H NMR (80.13 MHz, $CDCl_3$ and two drops of CD_3COOD): δ = 7.29 (m, 5 H), 5.23 (m, 2 H), 4.32 (d, $^2J_{HP} = 17.0$ Hz, 1 H), 2.65 (m, 2 H), 1.91 (m, 4 H), 1.57 (m, 2 H), 1.16 (m, 23 H), 0.77 (t, $^3J_{HH} =$

5.2 Hz, 3 H). – ^{13}C NMR (50.32 MHz, $CDCl_3$ and two drops of CD_3COOD): δ = 131.08 (s), 130.66–129.82 (m), 61.74 (d, $^1J_{CP}$ = 137.0 Hz), 48.01 (s), 33.21–23.33 (m), 14.29 (s). – IR (KBr, cm^{-1}): ṽ = 3392.9 (broad, OH, NH), 2323.8 (P–OH), 1609.5 (C=C), 1173.3 (P=O), 1080.9 (O=P–O). – MS (DCI/NH_3); *m/z*: 438 (M + 1)$^+$. – $C_{25}H_{44}NO_3P$ (437.58): calcd. C 68.62, H 10.14, N 3.20; found C 68.69, H 10.18, N 3.09.

(α-Octadecylaminoethyl)phosphonic Acid (8g): Yield: 79%. – 190°C (decomposition). – ^{31}P NMR (81.01 MHz, CD_3COOD): δ = 15.30 (m). – ^{1}H NMR (200.13 MHz, CD_3COOD): δ = 3.49 (m, 1 H), 3.17 (m, 2 H), 1.78 (m, 2 H), 1.32 (m, 33 H), 0.91 (t, $^3J_{HH}$ = 6.3 Hz, 3 H). – ^{13}C NMR (50.32 MHz, CD_3COOD): δ = 52.90 (d, $^1J_{CP}$ = 141.5 Hz), 47.17 (s), 32.67–23.36 (m), 14.27 (s), 11.50 (s). – IR (KBr, cm^{-1}): ṽ = 3422.2 (broad, OH, NH), 1173.3 (P=O), 1080.7 (O=P–O). – MS (DCI/NH_3); *m/z*: 378 (M + 1)$^+$. – $C_{20}H_{44}NO_3P$ (377.53): calcd. C 63.63, H 11.75, N 3.71; found C 63.39, H 12.19, N 3.61.

(α-Octadecylaminododecyl)phosphonic Acid (8h): Yield: 92%. – M.p. 193–195°C. – ^{31}P NMR (81.01 MHz, $CDCl_3$ and two drops of CD_3COOD): δ = 13.97 (d, $^2J_{PH}$ = 15.7 Hz). – ^{1}H NMR (80.13 MHz, $CDCl_3$ and two drops of CD_3COOD): δ = 3.02 (m, 3 H), 1.44 (m, 2 H), 1.18 (m, 51 H), 0.79 (t, $^3J_{HH}$ = 5.7 Hz, 6 H). – ^{13}C NMR (50.32 MHz, $CDCl_3$ and two drops of CD_3COOD): δ = 55.80 (d, $^1J_{CP}$ = 141.0 Hz), 46.54 (s), 31.85–22.60 (m), 13.91 (s). – IR (KBr, cm^{-1}): ṽ = 3391.5 (broad, OH, NH), 2360.1 (P–OH), 1179.2 (P=O), 1078.2 (O=P–O). – MS (DCI/NH_3); *m/z*: 518 (M + 1)$^+$. – $C_{30}H_{64}NO_3P$ (517.79): calcd. C 69.59, H 12.46, N 2.70; found C 69.63, H 12.40, N 2.64.

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Received June 18, 1999
[O99374]