Unusual Reactivity of (Vinylimino)phosphoranes and Their Utility in the Preparation of Pyridine and Dihydropyridine Derivatives

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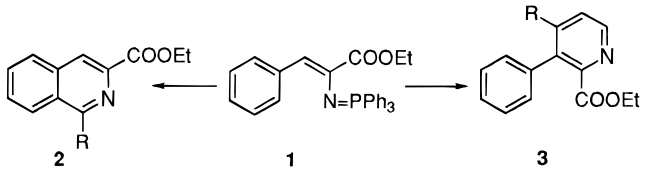
New reactions of (vinylimino)phosphoranes with aldehydes involving an initial nucleophilic attack of the β-carbon atom of the vinyl side chain on the carbonyl carbon atom are reported. Iminophosphorane **4** derived from ethyl β-azidoacrylate reacts with substituted cinnamyl aldehydes to give a mixture of 2-arylpyridine and 4-styryldihydropyridine derivatives, whereas the reaction with substituted benzaldehydes provides 4-aryldihydropyridine derivatives. However, the iminophosphorane **16** derived from the diethyl azidofumarate reacts with cinnamyl aldehydes through the expected aza-Wittig fashion to give 4-arylpyridine derivatives after dehydrogenation of the resulting dihydropyridine.

The utility of (vinylimino)phosphoranes as useful building blocks for the synthesis of azaheterocycles has been demonstrated convincingly.[1] (Vinylimino)phosphoranes may be considered to be an equivalent of an enamine and to contain two nucleophilic centers at the β-carbon atom of the vinyl side chain and the nitrogen atom of the iminophosphorane portion. Thus (vinylimino)phosphoranes undergo a single-step annulation with compounds containing two electrophilic centers such as α,β-unsaturated ketones,[2] α,β-unsaturated aldehydes,[3] and related Michael acceptors[4] to give several types of nitrogen-containing heterocycles. This kind of conversion takes place through two pathways: (i) a Michael type addition followed by proton transfer to generate an intermediate iminophosphorane which then undergoes an intramolecular aza-Wittig reaction and (ii) aza-Wittig reaction leading to an intermediate azahexatriene which then undergoes a thermal 6π-electrocyclization.[5] In this sense, (vinylimino)phosphoranes of type **1** reacted with aliphatic, aromatic, and heteroaromatic aldehydes to give the corresponding 2-azahexatriene, which underwent electrocyclic ring-closure followed by dehydrogenation to give pyridines[6] or isoquinoline derivatives[7] **2**. However, the reaction with α,β-unsaturated aldehydes provided 3-arylpyridines **3** in a completely regioselective fashion.[8]

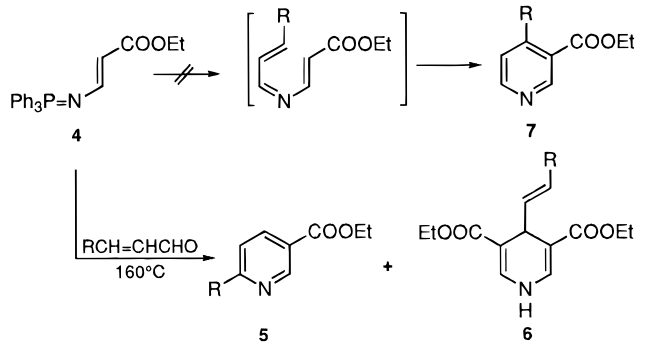
We wish to report therein that the behavior of the (vinylimino)phosphorane **4**, bearing an ethoxycarbonyl group at the position β toward aldehydes is completely different from those previously reported for unsubstituted (vinylimino)phosphoranes and even for the closely related (vinylimino)phosphorane **1**.



Results and Discussion

(Vinylimino)phosphorane **4** was readily prepared in 79% yield by Staudinger reaction of ethyl β-azidoacrylate[9] with triphenylphosphine at room temperature. In the ^{1}H-NMR spectrum the chemical shifts of the vinylic protons and the vicinal H−H coupling constant ($^3J_{H-H}$ = 12.6 Hz) suggested that both protons were relatively *trans*.[10] Compound **4** reacted with α,β-unsaturated aldehydes in *o*-xylene at 160 °C, in the presence of palladium on charcoal, in a sealed tube to give a mixture of pyridine **5** and dihydropyridine **6**, instead of the expected pyridine **7** (Scheme 1). From the reaction with

Scheme 1



acrolein, only the pyridine **5e** (R = H) was isolated in moderate yield. In the ^{1}H NMR spectra, the observed H-3/H-4 coupling constant ($^3J_{H-H}$ = 8.1−8.4 Hz) clearly

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Scheme 2

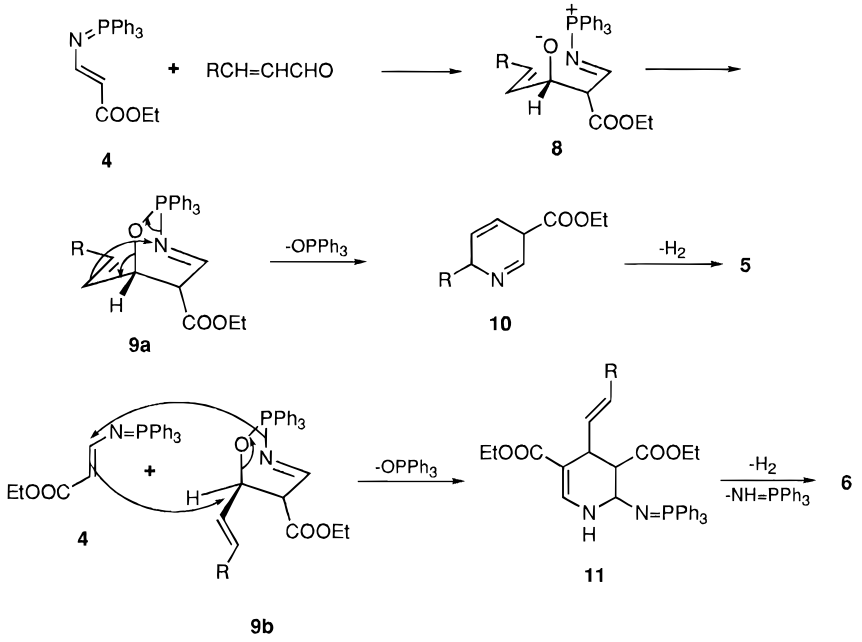

Table 1. Pyridines 5 and Dihydropyridine Derivatives 6

compound	R	yield (%)
5a	C_6H_5	33
5b	4-ClC_6H_4	30
5c	2-$O_2NC_6H_4$	30
5d	2-$H_3COC_6H_4$	31
5e	H	42
6a	C_6H_5	44
6b	4-ClC_6H_4	40
6c	2-$O_2NC_6H_4$	46
6d	2-$H_3COC_6H_4$	38

confirms the proposed 2-aryl-substituted pyridine **5** and rule out the isomeric 4-substituted pyridine **7**.

These findings are in clear contrast with the recently reported behavior of this kind of (vinylimino)phosphoranes toward carbonyl compounds, such as ethyl glyoxalate, diethyl ketomalonate, and pyruvonitrile, to give 2-azadienes.[11]

Formation of compounds **5** and **6** could be rationalized in terms of an initial addition of the β-carbon atom of the iminophosphorane **4** to the carbonyl carbon atom of the α,β-unsaturated aldehyde to give the betaine **8**, which cyclized to give the isomeric 1,2,5-oxaazaphosphane **9** (Scheme 2). The *endo* isomer **9a** underwent intramolecular cyclization with concomitant elimination of triphenylphosphine oxide to give the dihydropyridine **10**, which was dehydrogenated under reaction conditions to give **5**. Regiospecific attack of a second molecule of the iminophosphorane **4** on the *exo* isomer **9b** with loss of triphenylphosphine oxide provided the tetrahydropyridine **11**. Subsequent elimination of triphenylphosphinimine afforded the dihydropyridine **6**, which was surprisingly stable under the reaction conditions.

Dihydropyridines were also formed from the reaction of iminophosphorane **4** with the aromatic aldehydes. In this case, dihydropyridines **12** were prepared in moderate yields (40−43%), as the only reaction product, under the above-mentioned conditions. Likewise, the closely related (vinylimino)phosphorane **13** reacted with aromatic aldehydes for a longer period of time afforded the fused dihydropyridines **14** (36−44%).

Scheme 3

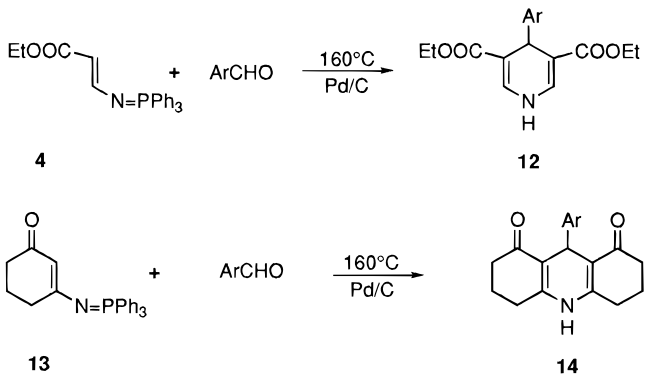

Table 2. 4-Aryldihydropyridine Derivatives 12 and 14

compound	R	yield (%)
12a	4-$H_3CC_6H_4$	43
12b	4-ClC_6H_4	40
12c	4-$H_3COC_6H_4$	40
12d	3-$H_3COC_6H_4$	41
14a	4-$H_3CC_6H_4$	44
14b	4-ClC_6H_4	43
14c	4-$H_3COC_6H_4$	38
14d	3-$H_3COC_6H_4$	36

Formation of dihydropyridines **12** and **14** (Scheme 3) could follow a pathway similar to the conversion **9** → **6**. As it has been mentioned before, dihydropyridines **6** and **12** are stable under thermal conditions; however, when they were exposed to sunlight for 324 h, the corresponding pyridines were obtained in almost quantitative yields.

Keeping in mind, that the reactivity of (vinylimino)-phosphoranes bearing an ethoxycarbonyl group as substituent strongly depends on the relative position of the substituents on the vinylic chain, we have turned our attention to the preparation and synthetic applications of this type of (vinylimino)phosphorane bearing two ethoxycarbonyl groups at the two different positions of the vinylic chain. Diethyl fumarate was treated sequen-

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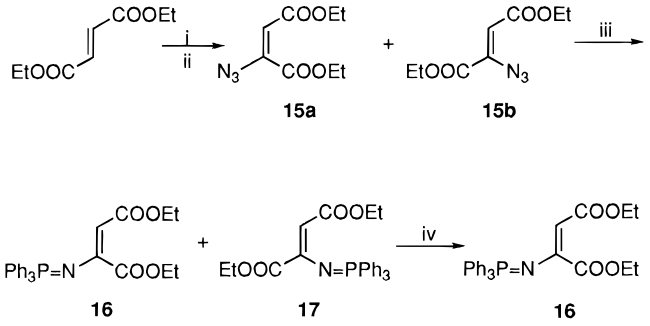
Scheme 4



Reagents and Conditions: i) ICl, NaN_3, acetonitrile; ii) Et_3N, acetone; iii) PPh_3, rt: iv) Recrystallization from CH_2Cl_2/Et_2O

Scheme 5

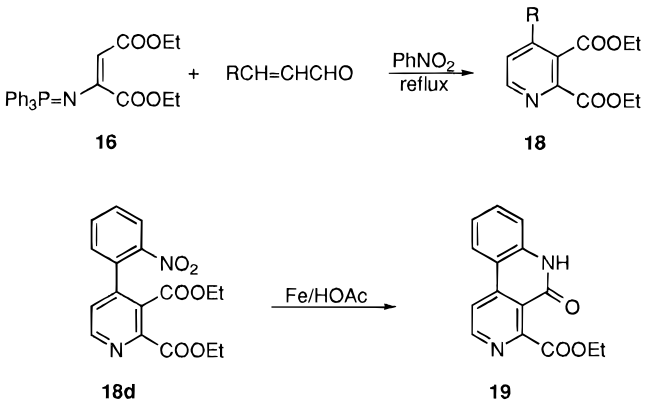


Table 3. 4-Arylpyridines 18

compound	R	yield (%)
18a	C_6H_5	38
18b	2-$H_3COC_6H_4$	40
18c	4-ClC_6H_4	36
18d	2-$O_2NC_6H_4$	37

tially with iodine monochloride/sodium azide[12] and triethylamine to give a mixture of vinyl azides **15** in 60% yield, which were converted into the corresponding iminophosphoranes **16** and **17** by reaction with triphenylphosphine (Scheme 4).

All attempts to separate the iminophosphoranes by columm chromatography were unsuccessful, and only the corresponding amines were obtained. However, (vinylimino)phosphorane **16** was obtained from the mixture in pure state (70%) by crystallization. The *E* configuration of compound **16** was assigned by means of a NOE difference experiment. Thus, irradiation of the *o*-phenyl proton signals of the iminophosphorane portion induced a 36% enhancement of the vinylic proton signal.

Reaction of (vinylimino)phosphorane **16** with α,β-unsaturated aldehydes in nitrobenzene at reflux temperature for 8 h gives directly 4-arylpyridines **18** (Scheme 5) in moderate yields (36−40%). The conversion **16** → **18** can be rationalized in terms of an initial aza-Wittig reaction to give an azahexatriene as an intermediate, which undergoes ring-closure and further dehydrogenation under the reaction conditions.

Reduction of compound **18d** with Fe/HOAc directly gave the benzo[*c*][2,7]naphthyridinone **19** in 74% yield. Some related derivatives of this ring system, which have been utilized as key intermediates in the synthesis of the marine alkaloid amphimedine,[13] have been prepared recently by Pd-catalyzed Suzuki[14] or Stille[15] cross-coupling reaction followed by cyclization.

These results show a detailed picture of the reactivity of (vinylimino)phosphoranes bearing ethoxycarbonyl groups as substituents toward several kind of aldehydes. Several trends have surfaced from this study. First, when both functionalities are placed at the same carbon atom, the reaction takes place via an aza-Wittig process. Second, when they are placed on different carbon atoms, the reaction is initiated by nucleophilic attack of the β-carbon atom of the vinylic side chain on the carbonyl group (charge-controlled reaction). And third, when the two ethoxycarbonyl groups are placed on different carbon atoms, the reaction takes place via an aza-Wittig process to give a 3-azahexatriene moiety, which undergoes electrocyclic ring-closure to give the pyridine ring after dehydrogenation.

This unprecedented behavior of (vinylimino)phosphoranes toward aldehydes opens a new way to the preparation of a wide variety of functionalized pyridines and dihydropyridines.

Experimental Section

All melting points were determined on a Kofler hot-plate melting point apparatus and are uncorrected. IR spectra were obtained as Nujol emulsions or films on a Nicolet Impact 400 spectrophotometer. NMR spectra were recorded on a Bruker AC200 (200 MHz) or a Varian Unity 300 (300 MHz). Mass spectra were recorded on a Hewlett-Packard 5993C spectrometer. Microanalyses were performed on a Perkin Elmer 240C instrument.

Preparation of (*E*)-3-[(Triphenylphosphoranylidene)-amino]propenoic Acid Ethyl Ester (4). To a solution of ethyl β-azidoacrylate (1.0 g, 7.1 mmol) in dry Et_2O (20 mL) cooled at 0 °C was added Ph_3P (1.86 g, 7.1 mmol). The mixture was stirred at room temperature for 6 h, and the separated solid was collected by filtration and recrystallized from dichloromethane/Et_2O/*n*-hexane (1:1:3) to give **4** in 79% yield; mp 118−124 °C, colorless prisms; ^{1}H-NMR ($CDCl_3$) δ 1.20 (t, 3H, J = 7.1 Hz), 4.07 (q, 2H, J = 7.1 Hz), 5.42 (dd, 1H, J = 12.6,1.1 Hz), 7.46−7.66 (m, 15H), 7.95 (dd, 1H, J = 27.5, 12.3 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.6, 58.5, 99.4 (J = 29.2 Hz), 127.7 (J = 99.2 Hz), 128.9 (J = 12.1 Hz), 132.6 (J = 2.6 Hz), 132.7 (J = 9.6 Hz), 157.5 (J = 2.6 Hz), 170.8; EI MS *m*/*z* (%): 375 (M^+, 25), 183 (100). Anal Calcd for $C_{23}H_{22}NO_2P$: C, 73.59; H, 5.91; N, 3.73. Found: C, 73.71; H, 5.75; N, 3.92.

General Procedure for the Preparation of Pyridines 5 and Dihydropyridines 6. A mixture of vinyliminophosphorane **4** (0.75 g, 2 mmol), the appropiate α,β-unsaturated aldehyde (2 mmol), and palladium on charcoal (0.053 g) in dry *o*-xylene (35 mL) was treated at 160 °C in a sealed tube for 24 h. After cooling, the mixture was filtered and the filtrate concentrated to dryness. The crude product was chromatographed on a silica gel column using ethyl acetate/dichloromethane (1:7) as eluent to give the pyridine **5** and the dihydropyridine **6**, which were recrystallized from dichloromethane/Et_2O/*n*-hexane (1:2:1).

2-Phenyl-5-(ethoxycarbonyl)pyridine (5a): 33% yield; mp 51−53 °C, colorless prisms; ^{1}H-NMR ($CDCl_3$) δ 1.42 (t, 3H, J = 7.1 Hz), 4.43 (q, 2H, J = 7.1 Hz), 7.47−7.51 (m, 3H), 7.80 (d, 1H, J = 8.3 Hz), 8.03−8.08 (m, 2H), 8.34 (dd, 1H, J = 8.4, 2.1 Hz), 9.29 (d, 1H, J = 1.9 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.3, 61.4, 119.8, 124.5, 127.4, 128.9, 129.9, 137.9, 138.4, 151.0,

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160.8, 165.4; EI MS *m*/*z* (%): 227 (M^+, 25), 182 (100). Anal. Calcd for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 74.20; H, 5.96; N, 6.02.

2-(4-Chlorophenyl)-5-(ethoxycarbonyl)pyridine (5b): 30% yield; mp 122−124 °C, colorless prisms; ^{1}H-NMR ($CDCl_3$) δ 1.43 (t, 3H, J = 7.1 Hz), 4.43 (q, 2H, J = 7.2 Hz), 7.47 (d, 2H, J = 8.4 Hz), 7.77 (dd, 1H, J = 8.4, 0.6 Hz), 8.01 (d, 2H, J = 8.7 Hz), 8.34 (dd, 1H, J = 8.3, 2.3 Hz), 9.27 (dd, 1H, J = 1.8, 0.6 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.4, 61.5, 119.6, 124.8, 128.6, 129.2, 136.2, 136.8, 138.0, 151.0, 159.5, 165.3; EI MS *m*/*z* (%): 263 (M^+ + 2, 6), 261 (M^+, 17), 216 (100). Anal. Calcd for $C_{14}H_{12}ClNO_2$: C, 64.25; H, 4.62; N, 5.35. Found: C, 64.11; H, 4.73; N, 5.11.

2-(2-Nitrophenyl)-5-(ethoxycarbonyl)pyridine (5c): 30% yield; mp 113−115 °C, colorless prisms; ^{1}H-NMR ($CDCl_3$) δ 1.42 (t, 3H, J = 7.1 Hz), 4.43 (q, 2H, J = 7.2 Hz), 7.55−7.71 (m, 4H), 7.92 (d, 1H, J = 7.8 Hz), 8.39 (dd, 1H, J = 8.1, 2.1 Hz), 9.23 (dd, 1H, J = 1.5, 0.9 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.2, 61.5, 122.2, 124.5, 125.3, 129.8, 131.1, 132.6, 134.5, 137.9, 149.1, 150.7, 159.1, 164.9; EI MS *m*/*z* (%): 272 (M^+, 18), 170 (100). Anal. Calcd for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.44; N, 10.29. Found: C, 61.59; H, 4.63; N, 10.53.

2-(2-Methoxyphenyl)-5-(ethoxycarbonyl)pyridine (5d): 31% yield; mp 51−52 °C, colorless prisms; ^{1}H-NMR ($CDCl_3$) δ 1.41 (t, 3H, J = 7.1 Hz), 3.86 (s, 3H), 4.42 (q, 2H, J = 7.2 Hz), 7.01 (d, 1H, J = 8.3 Hz), 7.09 (td, 1H, J = 7.5, 0.9 Hz), 7.41 (td, 1H, J = 8.3, 1.3 Hz), 7.86 (dd, 1H, J = 7.7, 1.8 Hz), 7.95 (dd, 1H, J = 8.4, 0.7 Hz), 8.29 (dd, 1H, J = 8.3, 2.1 Hz), 9.29 (dd, 1H, J = 1.9, 0.5 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.3, 55.6, 61.2, 111.5, 121.1, 124.0, 124.5, 128.1, 130.8, 131.3, 136.6, 150.5, 157.2, 159.7, 165.5; EI MS *m*/*z* (%): 257 (M^+, 33), 152 (100). Anal. Calcd for $C_{15}H_{15}NO_3$: C, 70.02; H, 5.88; N, 5.44. Found: C, 70.26; H, 5.75; N, 5.22.

3-(Ethoxycarbonyl)pyridine (5e): 42% yield; oil; ^{1}H-NMR ($CDCl_3$) δ 1.42 (t, 3H, J = 7.1 Hz), 4.42 (q, 2H, J = 7.2 Hz), 7.40 (ddd, 1H, J = 8.2, 4.9, 0.7 Hz), 8.31 (dt, 1H, J = 8.0, 2.0 Hz), 8.78 (dd, 1H, J = 4.9, 1.7 Hz), 9.24 (d, 1H, J = 2.0 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.3, 61.5, 123.3, 126.4, 137.1, 151.0, 153.4, 165.4; EI MS *m*/*z* (%): 151 (M^+, 28), 122 (100). Anal. Calcd for $C_8H_9NO_2$: C, 63.57; H, 6.00; N, 9.27. Found: C, 63.34; H, 6.15; N, 9.15.

1,4-Dihydro-4-[(*E*)-2-phenylethenyl]-3,5-bis(ethoxycarbonyl)pyridine (6a): 44% yield; mp 132−135 °C, colorless prisms; ^{1}H-NMR ($CDCl_3$) δ 1.26 (t, 6H, J = 7.1 Hz), 4.18 (m, 4H), 4.54 (m, 1H), 6.28−6.30 (m, 2H), 6.74−6.89 (m, 1H), 7.15-7.35 (m, 7H); ^{13}C-NMR ($CDCl_3$) δ 14.4, 34.0, 60.1, 106.2, 126.3, 127.1, 128.4, 129.7, 132.2, 134.6, 137.5, 167.3; EI MS *m*/*z* (%): 327 (M^+, 4), 224 (100). Anal. Calcd for $C_{19}H_{21}NO_4$: C, 69.71; H, 6.47; N, 4.28. Found: C, 69.49; H, 6.71; N, 4.19.

1,4-Dihydro-4-[(*E*)-2-(4-chlorophenyl)ethenyl]-3,5-bis-(ethoxycarbonyl)pyridine (6b): 40% yield, oil; ^{1}H-NMR ($CDCl_3$) δ 1.19 (t, 6H, J = 7.1 Hz), 4.03−4.19 (m, 4H), 4.46−4.49 (m, 1H), 6.10−6.28 (m, 2H), 6.60−6.71 (m, 1H), 7.10−7.19 (m, 4H), 7.21 (2H, d, J = 5.3 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.4, 34.0, 60.2, 106.0, 127.5, 128.4, 128.5, 132.6, 132.8, 134.6, 136.0, 167.2; EI MS *m*/*z* (%): 363 (M^+ + 2, 16), 361 (M^+, 46), 332 (100). Anal. Calcd for $C_{19}H_{20}ClNO_4$: C, 63.07; H, 5.29; N, 3.87. Found: C, 62.95; H, 5.42; N, 4.08.

1,4-Dihydro-4-[(*E*)-2-(2-nitrophenyl)ethenyl]-3,5-bis-(ethoxycarbonyl)pyridine (6c): 46% yield; mp 131−134 °C, colorless prisms; ^{1}H-NMR ($CDCl_3$) δ 1.29 (t, 6H, J = 7.1 Hz), 4.22 (q, 4H), 4.61 (d, 1H, J = 5.9 Hz), 6.36 (dd, 1H, J = 16.4, 5.9 Hz), 6.75 (d, 1H, J = 15.9 Hz), 7.00 (t, 1H, J = 5.0 Hz), 7.32 (tt, 1H, J = 8.9, 1.5 Hz), 7.37 (d, 2H, J = 5.4 Hz), 7.50 (td, 1H, J = 7.9, 1.2 Hz), 7.56 (dd, 1H, J = 7.9, 2.0 Hz), 7.88 (dd, 1H, J = 8.6, 0.9 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.4, 34.1, 60.3, 105.8, 124.4, 125.6, 127.6, 128.8, 133.0, 133.6, 135.0, 137.8, 147.6, 167.1; EI MS *m*/*z* (%): 372 (M^+, 2), 168 (100). Anal. Calcd for $C_{19}H_{20}N_2O_6$: C, 61.29; H, 5.41; N, 7.52. Found: C, 61.14; H, 5.54; N, 7.64.

1,4-Dihydro-4-[(*E*)-2-(2-methoxyphenyl)ethenyl]-3,5-bis(ethoxycarbonyl)pyridine (6d): 38% yield; mp 116−121 °C, colorless prisms; ^{1}H-NMR ($CDCl_3$) δ 1.27 (t, 6H, J = 7.1 Hz), 3.78 (s, 1H), 4.18 (m, 4H), 4.55 (d, 1H, J = 6.5 Hz), 6.27 (dd, 1H, J = 16.1, 6.5 Hz), 6.55 (t, 1H, J = 5.0 Hz), 6.66 (d, 1H, J = 16.1 Hz), 6.79−6.90 (m, 2H), 7.15 (td, 1H, J = 7.7, 1.5 Hz), 7.28 (d, 2H, J = 5.4 Hz), 7.39 (dd, 1H, J = 7.6, 1.5 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.4, 34.4, 55.5, 60.1, 106.7, 110.9, 120.6, 124.5, 126.6, 126.7, 128.1, 132.7, 134.3, 156.6, 167.3; EI MS *m*/*z* (%): 357 (M^+, 22), 168 (100). Anal. Calcd for $C_{20}H_{23}NO_5$: C, 67.21; H, 6.49; N, 3.92. Found: C, 67.33; H, 6.64; N, 3.69.

General Procedure for the Preparation of Dihydropyridines 12 and 14. A mixture of the appropriate (vinyliminо)phosphorane **4** or **13** (2 mmol), the corresponding aromatic aldehyde (2 mmol), and palladium on charcoal (0.056 g) in dry *o*-xylene (35 mL) was treated at 160 °C in a sealed tube for 24 h (for compounds **12**) or 48 h (for compounds **14**). After cooling, the mixture was filtered and from the filtrate the solvent was removed under reduced pressure. The residual material was chromatographed on a silica gel columm using ethyl acetate/*n*-hexane (1:2) as eluent to give the dihydropyridine **12** or **14**, respectively.

1,4-Dihydro-4-(4-methylphenyl)-3,5-bis(ethoxycarbonyl)pyridine (12a): 43% yield; oil; ^{1}H-NMR ($CDCl_3$) δ 1.11 (t, 6H, J = 7.1 Hz), 2.19 (s, 3H), 3.90−4.07 (m, 4H), 4.76 (s, 1H), 6.97 (d, 2H, J = 8.0 Hz), 6.99−7.05 (m, 1H), 7.14 (d, 2H, J = 7.5 Hz), 7.17 (d, 2H, J = 5.1 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.2, 21.0, 37.1, 60.0, 106.1, 128.1, 128.7, 133.9, 135.6, 144.2, 167.4; EI MS *m*/*z* (%): 315 (M^+, 6), 224 (100). Anal. Calcd for $C_{18}H_{21}NO_4$: C, 68.55; H, 6.71; N, 4.44. Found: C, 68.68; H, 6.54; N, 4.68.

1,4-Dihydro-4-(4-chlorophenyl)-3,5-bis(ethoxycarbonyl)pyridine (12b): 40% yield; oil; ^{1}H-NMR ($CDCl_3$) δ 1.19 (t, 6H, J = 6.9 Hz), 3.99−4.16 (m, 4H), 4.87 (s, 1H), 7.05−7.19 (m, 1H), 7.21 (d, 2H, J = 8.4 Hz), 7.27 (d, 2H, J = 8.4 Hz), 7.30 (d, 2H, J = 5.4 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.2, 37.2, 60.2, 107.8, 128.1, 129.7, 132.1, 134.0, 145.5, 167.1; EI MS *m*/*z* (%): 337 (M^+ + 2, 14), 335 (M^+, 48), 224 (100). Anal. Calcd for $C_{17}H_{18}ClNO_4$: C, 60.81; H, 5.40; N, 4.17. Found: C, 60.99; H, 5.45; N, 4.04.

1,4-Dihydro-4-(4-methoxyphenyl)-3,5-bis(ethoxycarbonyl)pyridine (12c): 40% yield; mp 125−128 °C, yellow prisms; ^{1}H-NMR ($CDCl_3$) δ 1.12 (t, 6H, J = 7.1 Hz), 3.66 (s, 3H), 3.88−4.12 (m, 4H), 4.75 (s, 1H), 6.71 (d, 2H, J = 8.7 Hz), 6.80−6.91 (m, 1H), 7.17 (d, 2H, J = 8.3 Hz), 7.20 (d, 2H, J = 5.1 Hz); ^{13}C-NMR ($CDCl_3$) δ 14.2, 36.7, 55.1, 60.0, 108.4, 113.3, 129.2, 133.7, 139.6, 158.1, 167.4; EI MS *m*/*z* (%): 331 (M^+, 5), 224 (100). Anal. Calcd for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.15; H, 6.57; N, 4.31.

1,4-Dihydro-4-(3-methoxyphenyl)-3,5-bis(ethoxycarbonyl)pyridine (12d): 40% yield; mp 135−138 °C, colorless prisms; ^{1}H-NMR ($CDCl_3$) δ 1.08 (t, 6H, J = 7.1 Hz), 3.76 (s, 3H), 3.83−4.07 (m, 4H), 5.14 (s, 1H), 6.72−6.81 (m, 3H), 7.05 (td, 1H, J = 7.8, 1.7 Hz), 7.18−7.23 (m, 3H); ^{13}C-NMR ($CDCl_3$) δ 14.2, 32.4, 55.6, 59.8, 107.9, 110.8, 120.3, 127.6, 131.1, 134.4, 135.6, 157.1, 167.6; EI MS *m*/*z* (%): 331 (M^+, 13), 302 (100). Anal. Calcd for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.15; H, 6.62; N, 4.12.

3,4,6,7,9,10-Hexahydro-9-(4-methylphenyl)-1,8(2*H*,5*H*)-acridinedione (14a): 44% yield; mp 280 °C, decomposed, colorless prisms; ^{1}H-NMR (DMSO-d_6) δ 1.72−1.99 (m, 4H), 2.11−2.25 (m, 4H), 2.43−2.58 (m, 4H) 4.86 (s, 1H), 6.94 (d, 2H, J = 8.1 Hz), 7.02 (d, 2H, J = 8.1 Hz), 9.40 (s, 1H); ^{13}C-NMR (DMSO-d_6) δ 20.5, 20.8, 26.3, 31.6, 36.8, 112.6, 127.3, 128.2, 134.2, 144.2, 151.0, 194.6; EI MS *m*/*z* (%): 307 (M^+, 24), 216 (100). Anal. Calcd for $C_{20}H_{21}NO_2$: C, 78.15; H, 6.89; N, 4.56. Found: C, 78.28; H, 7.04; N, 4.35.

3,4,6,7,9,10-Hexahydro-9-(4-chlorophenyl)-1,8(2*H*,5*H*)-acridinedione (14b): 43% yield; mp 280 °C, decomposed, colorless prisms; ^{1}H-NMR (DMSO-d_6) δ 1.74−1.97 (m, 4H), 2.17−2.20 (m, 4H), 2.51−2.54 (m, 4H) 4.89 (s, 1H), 7.16 (d, 2H, J = 7.5 Hz), 7.22 (d, 2H, J = 7.5 Hz), 9.49 (s, 1H); ^{13}C-NMR (DMSO-d_6) δ 20.7, 26.3, 31.9, 36.7, 112.0, 127.6, 129.3, 129.9, 146.2, 151.4, 194.7; EI MS *m*/*z* (%): 329 (M^+ + 2, 8), 327 (M^+, 22), 216 (100). Anal. Calcd for $C_{19}H_{17}ClNO_2$: C, 69.83; H, 5.24; N, 4.29. Found: C, 69.68; H, 5.42; N, 4.11.

3,4,6,7,9,10-Hexahydro-9-(4-methoxyphenyl)-1,8(2*H*,5*H*)-acridinedione (14c): 38% yield; mp 280 °C, decomposed, colorless prisms; ^{1}H-NMR (DMSO-d_6) δ 1.70−1.84 (m, 2H), 1.85−1.97 (m, 2H), 2.17−2.22 (m, 4H), 2.49−2.51 (m, 4H), 3.66 (s, 3H), 4.84 (s, 1H), 6.71 (d, 2H, J = 8.7 Hz), 7.04 (d, 2H, J =

8.7 Hz), 9.40 (s, 1H); ^{13}C-NMR (DMSO-d_6) δ 21.0, 26.5, 31.4, 37.0, 55.0, 112.9, 113.3, 128.5, 139.9, 151.2, 157.3, 194.9; EI MS m/z (%): 323 (M^+, 17), 216 (100). Anal. Calcd for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. Found: C, 74.33; H, 6.64; N, 4.44.

3,4,6,7,9,10-Hexahydro-9-(3-methoxyphenyl)-1,8(2*H*,5*H*)-acridinedione (14d): 36% yield; mp 280 °C, decomposed, yellow prisms; ^{1}H-NMR (DMSO-d_6) δ 1.70−1.99 (m, 4H), 2.18−2.24 (m, 4H), 2.50−2.51 (m, 4H), 3.66 (s, 3H), 4.90 (s, 1H), 6.60−6.74 (m, 3H), 7.08 (t, 1H, J = 7.6 Hz), 9.46 (s, 1H); ^{13}C-NMR (DMSO-d_6) δ 20.8, 26.3, 31.9, 36.8, 54.7, 110.2, 112.3, 113.8, 119.7, 128.7, 148.8, 151.3, 158.8, 194.8; EI MS m/z (%): 323 (M^+, 100), 216 (82). Anal. Calcd for $C_{20}H_{21}NO_3$: C, 74.28; H, 6.55; N, 4.33. Found: C, 74.11; H, 6.46; N, 4.53.

Preparation of (*E*)-[(Triphenylphosphoranylidene)-amino]butenedioic Acid Diethyl Ester (16). To a stirred slurry of sodium azide (15.0 g, 0.25 mol) in dry acetonitrile (100 mL) at −10 °C under nitrogen was added iodine monochloride (18.3 g, 0.113 mmol) over a period of 20 min. The reaction mixture was stirred for an additional 10 min, and diethyl fumarate (17.218 g, 0.1 mol) was added, allowed to warm to room temperature, and stirred for 20 h. The resultant solution was poured into water (250 mL) and extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with 5% sodium thiosulfate (150 mL) and brine (4 × 225 mL) and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure at room temperature, the residual material was dissolved in acetone (200 mL), and triethylamine (10.117 g, 0.1 mol) was added. The resultant mixture was stirred at room temperature for 24 h and then poured into water (20 mL) and extracted with Et_2O (3 × 100 mL). The combined organic layers were washed with brine (2 × 100 mL) and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure at room temperature, and the residual material was chromatographed on a silica gel column with dichloromethane/*n*-hexane (1:1) as eluent to give a mixture of vinyl azides **15a** and **15b**.

To a solution of Ph_3P (3.075g, 11.7 mmol) in dry dichloromethane (20 mL) was added a solution of the vinyl azide **15** (2.5 g, 11.7 mmol) in the same solvent (10 mL) dropwise at room temperature under nitrogen. The reaction mixture was stirred at room temperature for 2 h. The solvent was removed under reduced pressure, and the crude product was found to be a mixture of (vinylimino)phosphoranes **16** and **17** from which iminophosphorane **16** was isolated in 69% yield in pure state by recrystallization from dichloromethane/Et_2O (1:1): mp 132−134 °C, colorless prisms; ^{1}H-NMR ($CDCl_3$) δ 1.15 (t, 3H, J = 7.2 Hz), 1.25 (t, 3H, J = 7.2 Hz), 4.01 (q, 2H, J = 7.1 Hz), 4.03 (q, 2H, J = 7.1 Hz), 4.82 (d, 1H, J = 0.6 Hz), 7.43−7.49 (m, 6H), 7.52−7.58 (m, 3H), 7.68−7.75 (m, 6H); ^{13}C-NMR ($CDCl_3$) δ 13.8, 14.4, 58.8, 60.8, 95.6 (J = 16.1 Hz), 128.4 (J = 100.7 Hz), 128.7 (J = 12.5 Hz), 132.6 (J = 2.5 Hz), 132.6 (J = 10.1 Hz), 159.2 (J = 4.0 Hz), 167.8 (J = 1.1 Hz), 168.6 (J = 23.7 Hz); EI MS m/z (%): 447 (M^+, 2), 201 (100). Anal. Calcd for $C_{26}H_{26}NO_4P$: C, 69.79; H, 5.86; N, 3.13. Found: C, 69.65; H, 6.05; N, 3.30.

General Procedure for the Preparation of 4-Arylpyridines 18. A solution of the (vinylimino)phosphorane **16** (0.5 g, 1.12 mmol) and the appropriate α,β-unsaturated aldehyde (1.12 mmol) in nitrobenzene (5 mL) was heated at reflux temperature for 8 h. After cooling, the solvent was removed under reduced pressure and the residual material was chromatographed on a silica gel column with ethyl acetate/*n*-hexane (1:3) as eluent to give **18** which was purified by recrystallization from ethyl acetate/Et_2O/*n*-hexane (1:1:1).

4-Phenyl-2,3-bis(ethoxycarbonyl)pyridine (18a): 38% yield; mp 82−83 °C, colorless prisms; ^{1}H-NMR ($CDCl_3$) δ 1.08 (t, 3H, J = 7.2 Hz), 1.44 (t, 3H, J = 6.9 Hz), 4.19 (q, 2H, J = 7.2 Hz), 4.48 (q, 2H, J = 7.1 Hz), 7.38−7.46 (m, 5H), 7.48 (d, 1H, J = 5.1 Hz), 8.78 (d, 1H, J = 4.8 Hz); ^{13}C-NMR ($CDCl_3$) δ 13.7, 14.2, 61.8, 62.5, 127.0, 128.2, 128.6, 129.1, 131.0, 137.0, 146.0, 149.2, 149.8, 164.8, 167.0; EI MS m/z (%): 299 (M^+, 3), 155 (100). Anal Calcd for $C_{17}H_{17}NO_4$: C, 68.22; H, 5.73; N, 4.68. Found: C, 68.01; H, 5.87; N, 4.89.

4-(2-Methoxyphenyl)-2,3-bis(ethoxycarbonyl)pyridine (18b): 36% yield; mp 75−79 °C, colorless prisms; ^{1}H-NMR ($CDCl_3$) δ 1.03 (t, 3H, J = 6.9 Hz), 1.41 (t, 3H, J = 7.2 Hz), 3.72 (s, 3H), 4.10 (q, 2H, J = 7.1 Hz), 4.44 (q, 2H, J = 7.2 Hz), 6.93 (d, 1H, J = 8.1 Hz), 6.99 (td, 1H, J = 7.5, 0.9 Hz), 7.18 (dd, 1H, J = 7.5, 2.1 Hz), 7.38 (td, 1H, J = 7.5, 1.8 Hz), 7.42 (d, 1H, J = 5.1 Hz), 8.72 (d, 1H, J = 4.8 Hz); ^{13}C-NMR ($CDCl_3$) δ 13.6, 14.2, 55.4, 61.4, 62.3, 110.8, 120.6, 125.8, 128.0, 130.1, 130.5, 130.9, 146.7, 147.1, 149.5, 156.1, 165.3, 166.6; EI MS m/z (%): 329 (M^+, 15), 256 (100). Anal. Calcd for $C_{18}H_{19}NO_5$: C, 65.64; H, 5.82; N, 4.25. Found: C, 65.73; H, 5.95; N, 4.11.

4-(4-Chlorophenyl)-2,3-bis(ethoxycarbonyl)pyridine (18c): 36% yield; mp 80−82 °C, colorless prisms; ^{1}H-NMR ($CDCl_3$) δ 1.14 (t, 3H, J = 7.1 Hz), 1.44 (t, 3H, J = 6.9 Hz), 4.22 (q, 2H, J = 7.2 Hz), 4.48 (q, 2H, J = 7.1 Hz), 7.34 (d, 2H, J = 9.0 Hz), 7.43 (d, 2H, J = 8.7 Hz), 7.45 (d, 1H, J = 5.1 Hz), 8.79 (d, 1H, J = 5.1 Hz); ^{13}C-NMR ($CDCl_3$) δ 13.7, 14.2, 61.9, 62.5, 126.7, 128.9, 129.6, 130.8, 135.3, 135.4, 146.1, 147.8, 149.8, 164.6, 166.8; EI MS m/z (%): 335 (M^+ + 2, 4), 333 (M^+, 11), 189 (100). Anal. Calcd for $C_{17}H_{16}ClNO_4$: C, 61.18; H, 4.83; N, 4.20. Found: C, 60.95; H, 5.01; N, 4.33.

4-(2-Nitrophenyl)-2,3-bis(ethoxycarbonyl)pyridine (18d): 37% yield; mp 116−118 °C, colorless prisms; ^{1}H-NMR ($CDCl_3$) δ 1.03 (t, 3H, J = 7.2 Hz), 1.43 (t, 3H, J = 7.2 Hz), 4.07 (dq, 2H, J = 7.2 Hz, 4.5 Hz), 4.47 (q, 2H, J = 7.2 Hz), 7.34 (dd, 1H, J = 7.2Hz, 1.5 Hz), 7.42 (d, 1H, J = 5.1 Hz), 7.64 (td, 1H, J = 7.7 Hz, 1.8 Hz), 7.71 (td, 1H, J = 7.5 Hz, 1.5 Hz), 8.19 (dd, 1H, J = 7.5 Hz, 1.4 Hz), 8.83 (d, 1H, J = 4.8 Hz); ^{13}C-NMR ($CDCl_3$) δ 13.6, 14.2, 62.0, 62.6, 124.8, 126.0, 129.5, 130.1, 131.5, 132.0, 133.2, 146.7, 146.8, 147.7, 149.9, 164.7, 165.9; EI MS m/z (%):271 (22), 224 (100), 192 (81), 182 (41). Anal. Calcd for $C_{17}H_{16}N_2O_6$: C, 59.30; H, 4.68; N, 8.14. Found: C, 59.09; H, 4.86; N, 8.30.

4-(Ethoxycarbonyl)benzo[*c*][2,7]naphthyridin-5-one (5): A mixture of **18d** (0.193 g, 0.56 mmol), acetone (10 mL), acetic acid (1 mL), water (1 mL), and powdered iron (0.36 g) was refluxed for 1 h and then dichloromethane (10 mL) was added. The resultant suspension was filtered, and a saturated solution of sodium carbonate (5 mL) was added to the filtrate. The organic layer was separated and dried over anhydrous magnesium sulfate. The solvent was removed under reduced pressure, and the crude product was recrystallized acetonitrile to give **5** in 74% yield: mp 280−283 °C, colorless prisms; ^{1}H-NMR (DMSO-d_6) δ 1.33 (t, 3H, J = 7.1 Hz), 4.24 (q, 2H, J = 7.1 Hz), 7.35 (t, 1H, J = 8.1Hz), 7.42 (d, 1H, J = 8.7 Hz), 7.66 (d, 1H, J = 7.6 Hz), 8.50 (d, 1H, J = 8.1 Hz), 8.56 (d, 1H, J = 5.6 Hz), 8.78 (d, 1H, J = 5.5 Hz), 12.01 (s, 1H); ^{13}C-NMR (DMSO-d_6) δ 13.9, 61.1, 115.3, 116.5, 117.0, 117.3, 122.8, 124.6, 132.4, 138.2, 142.0, 150.9, 153.6, 158.9, 167.1; EI MS m/z (%): 268 (23), 223 (46), 196 (100). Anal. Calcd for $C_{15}H_{12}N_2O_3$: C, 67.16; H, 4.51; N, 10.44. Found: C, 67.40; H, 4.35; N, 10.67.

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