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6π-Electrocyclization of Azahexa-1,3,5-trienes: A New Entry to a Regiospecific Synthesis of 3-Aryl(heteroaryl)pyridines

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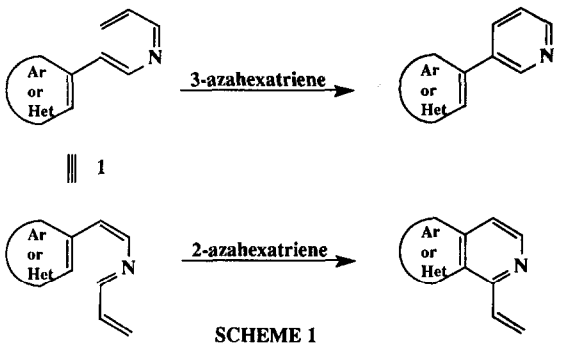
Abstract.- Aza Wittig reaction of iminophosphoranes derived from ethyl α-azido-β-aryl(pyrazolyl)propenoates with α,β-unsaturated aldehydes leads to aldimines which by heating undergo electrocyclic ring-closure through the 3-azahexa-1,3,5-triene moiety to give 3-aryl(pyrazolyl)pyridines in a completely regiospecific fashion. However, iminophosphoranes derived from ethyl α-azido-β-furyl(thienyl)propenoates furnish a mixture (1.2:1 ratio) of the corresponding furo- or thieno-pyridine(2-azahexa-1,3,5-triene electrocyclization product) and 3-furyl(thienyl)pyridine(3-azahexa-1,3,5-triene electrocyclization product).

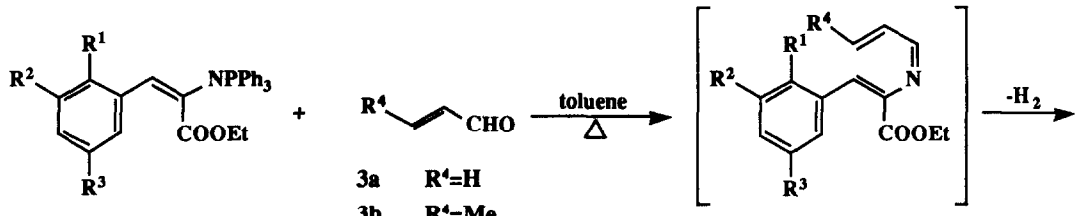
In the course of our studies directed toward the synthesis of fused nitrogen-containing heterocycles based on heterocyclization reactions of heterocumulenes, we have reported a pyrido annelation procedure so-called tandem aza Wittig/ electrocyclization strategy based on the thermally induced 6π-electrocyclization of formal 2-azahexa-1,3,5-trienes bearing a cumulated double bond at one end, available by aza Wittig-type reaction of β-aryl(heteroaryl)vinyl iminophosphoranes with isocyanates, isothiocyanates, ketenes, carbon dioxide, and carbon disulfide. This methodology allows the *c*-fusion of a pyridine ring both onto a preformed heterocyclic ring e.g. furan, thiophene[1], indole[2], pyrazole[3], pyridine[4] and aromatic rings[5]. A slight modification of this methodology, which involves the aza Wittig reaction of those above mentioned iminophosphoranes with aliphatic, aromatic or heteroaromatic aldehydes, has been applied to prepare the carbon skeleton of some alkaloids of valuable biological interest



SCHEME 1

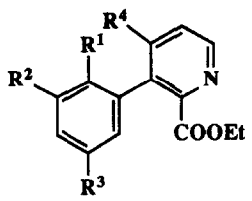
such as eudistomins A and M, lavendamycin[6], and the genotoxic heterocyclic amine[7] Trp-P-2. An important extension of this methodology, which significantly could expand the scope of the method, would be to employ α,β-unsaturated aldehydes in this reaction. Thus, the aza Wittig reaction of β-aryl(heteroaryl)vinyl iminophosphoranes with α,β-unsaturated aldehydes would give rise to azahexa-1,3,5-triene systems type **1**, which could undergo electrocyclic ring-closure through either the 3-azahexa-1,3,5-triene moiety or the 2-azahexa-1,3,5-triene moiety involving the aromatic or heteroaromatic ring as a 2π-component, to give 3-aryl(heteroaryl)pyridines or *c*-fused pyridine derivatives (Scheme 1).

β-Arylvinyliminophosphoranes **2**, readily available from aromatic aldehydes by sequential treatment with ethyl azidoacetate and triphenylphosphine, react with several α,β-unsaturated aldehydes **3** in toluene at reflux temperature and then at 160°C in a sealed tube for 24 h to produce directly 3-arylpyridines **5** in a completely regiospecific fashion. No products derived from the electrocyclic ring-closure across the 2-azahexa-1,3,5-triene moiety are observed. When the reaction is carried out in nitrobenzene at reflux temperature for a short period of time (3 h), compounds **5** are isolated after chromatographic purification in similar yields, except for compounds **5** (R^4=aryl) which are isolated in higher yields (53-75%).



2a $R^1=R^2=R^3=H$
2b $R^1=R^2=CH_3O$, $R^3=H$
2c $R^1=R^2=CH_3O$, $R^3=Br$

3a $R^4=H$
3b $R^4=Me$
3c $R^4=Ph$
3d $R^4=2\text{-}H_3CO\text{-}C_6H_4$
3e $R^4=2\text{-}O_2N\text{-}C_6H_4$

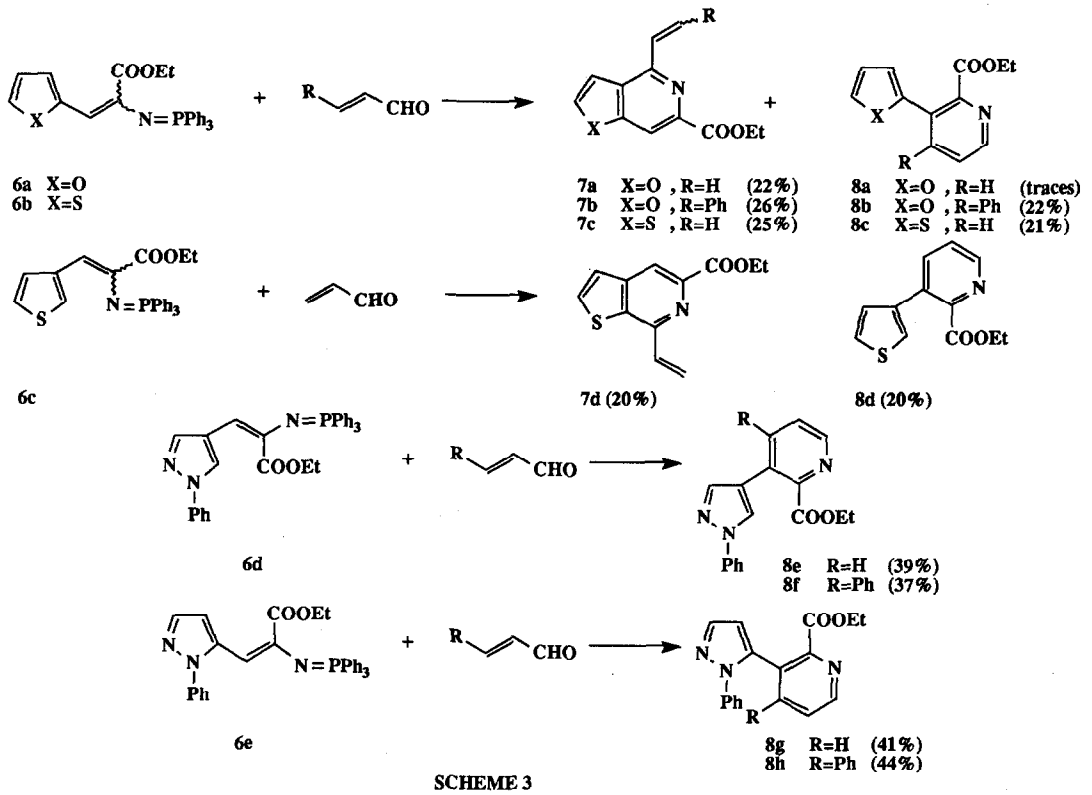


5a $R^1=R^2=R^3=R^4=H$
5b $R^1=R^2=R^3=H$, $R^4=Me$
5c $R^1=R^2=R^3=H$, $R^4=Ph$
5d $R^1=R^2=R^3=H$, $R^4=2\text{-}H_3CO\text{-}C_6H_4$
5e $R^1=R^2=R^3=H$, $R^4=2\text{-}O_2N\text{-}C_6H_4$
5f $R^1=R^2=CH_3O$, $R^3=R^4=H$
5g $R^1=R^2=CH_3O$, $R^3=H$, $R^4=Ph$
5h $R^1=R^2=CH_3O$, $R^3=Br$, $R^4=H$
5i $R^1=R^2=CH_3O$, $R^3=Br$, $R^4=Ph$

SCHEME 2

The conversion **2**+**3** → **5** can be rationalized in terms of an initial aza Wittig reaction to give the azahexa-1,3,5-triene intermediate **4** which undergoes electrocyclic ring-closure, further dehydrogenation under the reaction conditions of the resulting dihydropyridine[8] furnishes **5** (Scheme 2). Examples in Scheme 2 suggest that this reaction

seems to be quite general in nature. The ready availability of 3-arylpyridines possesing either electron-withdrawing or electron-donating substituents in the benzene ring is exemplified by entries **5d** and **5e**. In spite of the numerous synthetic methods available for 2- and 4-arylpyridines methodology for the 3-arylpyridines is scarce[9]. This synthesis is competitive with the previously reported synthesis of 3-arylpyridines based on either coupling reaction of 3-bromopyridines with aryl boronic acids under the Suzuki´s conditions[10], which seems to be limited to arylboronic acids with only one ortho substituent, or inverse electron demand Diels-Alder cycloaddition reactions of 1,2,4-triazines with enamines[11].



SCHEME 3

With a good synthesis of 3-arylpyridines available, we turned our attention to the formation of 3-heteroarylpyridines. Thus, the readily available β-heteroarylvinyl iminophosphoranes[1] **6a-b** were submitted to react with α,β-unsaturated aldehydes under the aforementioned reaction conditions. In each instance, two products were isolated in 1.2:1 ratio after chromatographic separation. Both two are formed from the precursor aza Wittig product, a formal azahexa-1,3,5-triene system, which undergoes cyclization through a non regiospecific pathway to give furo- or thieno[3,2-c]pyridines **7** (2-azahexa-1,3,5-triene electrocyclization product) and the corresponding 3-heteroarylpyridine **8** (3-azahexa-1,3,5-triene electrocyclization product). Similar results were obtained when the iminophosphorane **6c** was used. In this case thieno[2,3-c]pyridine **7d** (20%) and 3-(3-thienyl)pyridine **8d** (20%) were formed (Scheme 3).

On the other hand, β-heteroarylvinyl iminophosphoranes **6d** and **6e** derived from the pyrazole ring react with α,β-unsaturated aldehydes to provide 3-pyrazolylpyridines **8e-h** in moderate yields as the only reaction products (Scheme 3). This results are in accord with the fact that the pyrazole ring fails to undergo pericyclic reactions under conditions similar to those in which other heterocyclic compounds will react[12]. Only under the influence of high temperature and pressure vinylpyrazoles react with electron deficient dienophiles to give [4+2] cycloaddition products[13].

The present study demostrates that the tandem aza Wittig/ electrocyclic ring-closure is a viable alternative to the methods previously reported for the preparation of 3-arylpyridines. Our approach is simple, direct and leads from aromatic aldehydes to the key intermediates β-arylvinyl iminophosphoranes, which undergo aza Wittig reaction with α,β-unsaturated aldehydes and further cyclization in good yields.

EXPERIMENTAL

All melting points were determined on a Kofler hot-plate melting point apparatus and are uncorrected. IR spectra were obtained as Nujol emulsions on a Nicolet FT-5DX spectrophotometer. NMR spectra were recorded on a Bruker AC-200 (200 MHz) or a Varian Unity 300 (300 MHz). Electron-impact mass spectra were carried out on a Hewlett-Packard 5993C spectrometer at an ionization potential of 70 eV. Microanalyses were performed on a Perkin-Elmer 240 C instrument.

Materials. Iminophosphoranes **6a-c**[1] and **6d-e**[3] were prepared as described in the literature.

General Procedure for the Preparation of Iminophosphoranes 2.

To a well-stirred solution containing sodium (0.76 g, 33 mmol) in anhydrous ethanol (10 ml), a solution of ethyl azidoacetate (4.3 g, 33 mmol) in anhydrous ethanol (3 ml) and the corresponding aromatic aldehyde (8.25 mmol) were added dropwise at -5°C under nitrogen. The reaction mixture was allowed to warm to room temperature and was then stirred for 15 h. After this, it was poured into aqueous 30% ammonium chloride (30 ml) and the formed solid was separated by filtration, washed with water (3x10 ml), air-dried, and chromatographed on a silicagel column eluting with ethyl acetate/ n-hexane (1:3) to give corresponding ethyl α-azido-β-arylpropenoate.

To a solution of triphenylphosphine (1.20 g, 5.17 mmol) in dry dichloromethane (15 ml), a solution of the appropriate ethyl α-azido-β-arylpropenoate (5.17 mmol) in the same solvent (10 ml) was added dropwise at 0°C under nitrogen. The reaction mixture was stirred at room temperature for 8 h. The solvent was removed under reduced pressure at 35°C and the residual material was recrystallized from dichloromethane/ n-hexane (1:1) to give **2**.

Compound 2a: (90%), m.p. 149°C (colourless prisms); (Found: C, 76.92; H, 5.62; N, 3.28. $C_{29}H_{26}NO_2P$ requires: C, 77.15; H, 5.80; N, 3.10); i.r. (Nujol) 1693, 1412, 1228, 1201 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 0.98 (t, 3H, J=7.1

Hz), 3.85 (q, 2H, J=7.1 Hz), 6.77 (d, 1H, $^4J_{P-H}$=6.6 Hz, H_β), 7.12 (tt, 1H, J=7.2, 1.1 Hz, H_p), 7.26 (t, 2H, J=7.1 Hz, H_m), 7.36-7.50 (m, 9H, PPh_3 H_m+H_p), 7.73 (ddd, 6H, $^3J_{P-H}$=12.1, 7.7, 1.8 Hz, PPh_3 H_o), 8.13 (d, 2H, J=7.3 Hz, H_o); ^{13}C n.m.r. δ ($CDCl_3$):14.1 (CH_3), 60.8 (CH_2), 116.6 ($^3J_{P-C}$=18.3 Hz, C_β), 125.7 (C_p), 127.8 (C_m), 128.2 ($^2J_{P-C}$=12.1 Hz, PPh_3 C_m), 129.4 (C_o), 131.0 ($^4J_{P-C}$=2.4 Hz, PPh_3 C_p), 132.4 ($^3J_{P-C}$=9.8 Hz, PPh_3 C_o), 132.8 ($^1J_{P-C}$=103.3 Hz, PPh_3 C_i), 136.3 ($^2J_{P-C}$=6.1 Hz, C_α), 138.2 (C_i), 167.9 ($^3J_{P-C}$=6.8 Hz, C=O); m/z (%) 451 (M^+, 7), 201 (100).

Compound 2b: (85%), m.p. 125°C (colourless prisms); (Found: C, 72.99; H, 6.06; N, 2.51. $C_{31}H_{30}NO_4P$ requires: C, 72.79; H, 5.91; N, 2.74); i.r. (Nujol) 1695, 1425, 1406, 1207 cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 0.98 (t, 3H, J=7.1 Hz, CH_3), 3.81-3.91 (m, 8H, CH_2+2xOCH_3), 6.74 (d, 1H, J=8.1 Hz, H_p), 6.95 (t, 1H, J=8.0 Hz, H_m), 7.07 (d, 1H, $^4J_{P-H}$=6.6 Hz, H_β), 7.35-7.42 (m, 9H, PPh_3 H_m+H_p), 7.68-7.78 (dd, 6H, $^3J_{P-H}$=15.2, 8.2 Hz, PPh_3 H_o), 8.62 (d, 1H, J=8.1 Hz, H_o); ^{13}C n.m.r. δ ($CDCl_3$):14.0 (CH_3), 55.8 (OCH_3), 60.6 (CH_2), 60.8 (OCH_3), 109.4 ($^3J_{P-C}$=24.5 Hz, C_β), 110.2 (C_p), 122.7 (C_o), 123.0 (C_m), 128.1 ($^3J_{P-C}$=12.1 Hz, PPh_3 C_m), 130.9 (PPh_3 C_p), 131.9 (C_i), 132.4 ($^2J_{P-C}$=9.7 Hz, PPh_3 C_o), 132.7 ($^1J_{P-C}$=103.8 Hz, PPh_3 C_i), 136.9 ($^2J_{P-C}$=14.5 Hz, C_α), 146.5 (q, C_o), 152.2 (q, C_m), 166.0 ($^3J_{P-C}$=7.1 Hz, C=O); m/z (%) 511 (M^+, 64), 183 (100).

Compound 2c: (80%), m.p. 140°C (colourless prisms); (Found: C, 63.17; H, 4.75; N, 2.43. $C_{31}H_{29}BrNO_4P$ requires: C, 63.06; H, 4.95; N, 2.37); i.r. (Nujol) 1705, 1574, 1427, 1209 cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 0.98 (t, 3H, J=7.1 Hz, CH_3), 3.79-3.90 (m, 8H, CH_2+2xOCH_3), 6.85 (d, 1H, J=2.3 Hz, H_p), 6.92 (d, 1H, $^4J_{P-H}$=7.4 Hz, H_β), 7.36-7.50 (m, 9H, PPh_3 H_m+H_p), 7.73 (ddd, 6H, $^3J_{P-H}$=12.1, 6.2, 2.3 Hz, PPh_3 H_o), 9.09 (d, 1H, J=2.3 Hz, H_o); ^{13}C n.m.r. δ ($CDCl_3$):13.9 (CH_3), 56.0 (OCH_3), 60.6 (OCH_3), 60.6 (CH_2), 106.8 ($^3J_{P-C}$=20.4 Hz, C_β), 113.2 (C_p), 116.2 (q, C_m), 124.8 (C_o), 128.3 ($^3J_{P-C}$=12.2 Hz, PPh_3 C_m), 131.0 ($^4J_{P-C}$=2.8 Hz, PPh_3 C_p), 132.4 ($^2J_{P-C}$=9.8 Hz, PPh_3 C_o), 132.7 ($^1J_{P-C}$=101.8 Hz, PPh_3 C_i), 134.0 (C_i), 138.4 ($^2J_{P-C}$=6.8 Hz, C_α), 145.4 (q, C_o), 152.9 (q, C_m), 167.7 ($^3J_{P-C}$=7.6 Hz, C=O); m/z (%) 591 (M^+, 14), 589 (M^+, 9), 262 (100).

General Procedure for the Preparation of 3-Arylpyridines 5.

A mixture of iminophosphorane **2** (2 mmol), aldehyde **3** (4 mmol) and dry toluene (30 ml) was stirred at reflux temperature for 1 h and was then heated in a glass sealed tube at 160°C for 24 h. After cooling, the solvent was removed under reduced pressure and the residual material was chromatographed on a silica gel column eluting with diethyl ether to give **5** which were obtained as crystalline solids after recrystallization from diethyl ether/ n-hexane (1:1).

Compound 5a: (53%), m.p. 111°C (yellow prisms); (Found: C, 74.18; H, 5.53; N, 5.90. $C_{14}H_{13}NO_2$ requires: C, 73.99; H, 5.77; N, 6.16); i.r. (Nujol) 1732, 1269, 1200 cm^{-1}; ^{1}H n.m.r. δ ($CDCl_3$): 1.00 (t, 3H, J=7.2 Hz), 4.11 (q, 2H, J=7.2 Hz), 7.22-7.37 (m, 6H, aromatics),7.65 (dd, 1H, J=7.9, 1.6 Hz, H-4), 8.57 (dd, 1H, J=4.7, 1.6 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 13.8 (CH_3), 61.7 (CH_2), 125.2 (C-5), 128.1 (CH), 128.3 (2xCH), 128.5 (2xCH), 137.3 (q), 138.3 (C-3), 138.5 (C-4), 148.1 (C-6), 149.0 (C-2), 166.9 (C=O); m/z (%) 277 (M^+, 6), 127 (100).

Compound 5b: (30%), m.p. 160°C (yellow prisms); (Found: C, 74.88; H, 6.08; N, 5.94. $C_{15}H_{15}NO_2$ requires: C, 74.67; H, 6.27; N, 5.81); i.r. (Nujol) 1734, 1307, 1177 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 0.94 (t, 3H, J=7.2 Hz), 2.09 (s, 3H, Ar-CH_3), 4.02 (q, 2H, J=7.2 Hz), 7.10-7.40 (m, 6H, aromatics), 8.46 (d, 1H, J=4.9 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 13.7 (CH_3), 20.1 (Ar-CH_3), 61.3 (CH_2), 126.7 (C-5), 127.8 (CH), 128.3 (2xCH), 128.9 (2xCH), 136.9 (q), 137.0 (C-3), 147.1 (C-4), 148.0 (C-6), 149.8 (C-2), 166.8 (C=O); m/z (%) 241 (M^+, 2), 168 (100).

Compound 5c: (42%), m.p. 120°C (colourless prisms); (Found: C, 79.34; H, 5.88; N, 4.45. $C_{20}H_{17}NO_2$ requires: C, 79.19; H, 5.65; N, 4.62); i.r. (Nujol) 1732, 1315, 1178 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 0.96 (t, 3H, J=7.2 Hz), 4.07 (q, 2H, J=7.1 Hz), 7.15-7.18 (m, 10H, aromatics), 7.42 (d, 1H, J=5.0 Hz, H-5), 8.64 (d, 1H, J=5.0 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 13.7 (CH_3), 61.8 (CH_2), 126.3 (C-5), 127.8 (CH), 128.0 (2xCH), 128.1 (CH), 128.2 (2xCH),129.3 (2xCH), 129.9 (2xCH), 135.0 (C-3), 136.0 (q), 137.8 (q), 147.7 (C-6), 150.4 (C-4), 150.9 (C-2), 166.6 (C=O); m/z (%) 303 (M^+, 2), 230 (100).

Compound 5d: (53%), m.p. 126°C (colourless prisms); (Found: C, 75.77; H, 5.51; N, 4.36. $C_{21}H_{19}NO_3$ requires: C, 75.66; H, 5.74; N, 4.20); i.r. (Nujol) 1729, 1318, 1178 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 0.93 (t,3H, J=7.1 Hz), 3.34 (s, 3H, OCH_3), 4.04 (q, 2H, J=7.5 Hz), 6.59 (d, 1H, J=8.4 Hz), 6.78 (t, 1H, J=7.5 Hz), 6.93 (dd, 1H, J=7.7, 1.5 Hz), 6.97-7.09 (m, 5H, aromatics), 7.14 (td, 1H, J=8.0, 1.6 Hz), 7.30 (d, 1H, J=5.1 Hz, H-5), 8.57 (d, 1H, J=5.1 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 13.7 (CH_3), 54.9 (OCH_3), 61.5 (CH_2), 110.5 (CH), 120.3 (CH),126.9 (C-5), 127.2 (q), 127.2 (CH), 127.3 (2xCH), 129.2 (2xCH),129.7 (CH), 130.6 (CH), 136.0 (C-3), 136.9 (q), 147.8 (C-6), 147.9 (C-4), 150.4 (C-2), 155.8 (q),167.4 (C=O); m/z (%) 333 (M^+, 12), 260 (64), 51 (100).

Compound 5e: (45%), m.p. 99°C (colourless prisms); (Found: C, 69.15; H, 4.84; N, 7.82. $C_{20}H_{16}N_2O_4$ requires: C, 68.96; H, 4.63; N, 8.04); i.r. (Nujol) 1732, 1518, 1350, 1184 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 0.98 (t, 3H, J=7.2 Hz), 4.09 (q, 2H, J=7.2 Hz), 6.96-7.05 (m, 2H, aromatics), 7.14-7.23 (m, 4H, aromatics), 7.33 (d, 1H, J=5.1 Hz, H-5), 7.39 (td, 1H, J=7.8, 1.5 Hz), 7.51 (td, 1H, J=7.5, 1.4 Hz), 7.84 (dd, 1H, J=8.1, 1.2 Hz), 8.69 (d, 1H, J=5.1 Hz, H-6); ^{13}C n.m.r. δ($CDCl_3$): 13.7 (CH_3), 61.7 (CH_2), 124.6 (CH), 124.8 (C-5), 127.8 (CH), 127.8 (2xCH), 129.3 (CH), 129.3 (2xCH), 132.1 (CH), 133.0 (CH), 133.6 (q), 135.0 (C-3), 135.4 (q), 147.8 (q), 147.9 (C-4), 148.3 (C-6), 150.3 (C-2), 166.5 (C=O); m/z (%) 348 (M^+, 5), 230 (100).

Compound 5f: (50%), m.p. 71°C (colourless prisms); (Found: C, 66.72; H, 6.20; N, 4.73. $C_{16}H_{17}NO_4$ requires: C, 66.89; H, 5.96; N, 4.88); i.r. (Nujol) 1730, 1317, 1265, 1134 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.11 (t, 3H, J=7.1 Hz), 3.50 (s, 3H, OCH_3), 3.86 (s, 3H, OCH_3), 4.20 (q, 2H, J=7.1 Hz), 6.77 (dd, 1H, J=7.7, 1.7 Hz), 6.93 (dd, 1H, J=8.3, 1.5 Hz), 7.07 (t, 1H, J=7.9 Hz), 7.43 (dd, 1H, J=7.9, 4.8 Hz, H-5), 7.73 (dd, 1H, J=7.9, 1.6 Hz, H-4), 8.65 (dd, 1H, J=4.9, 1.6 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 13.7 (CH_3), 55.8 (OCH_3), 60.3 (OCH_3), 61.3 (CH_2), 112.5 (CH), 121.7 (CH), 124.0 (CH), 125.0 (C-5), 133.0 (q), 134.1 (C-3), 139.5 (C-4), 146.1 (q), 148.1 (C-6), 148.9 (C-2), 152.6 (q), 166.5 (C=O); m/z (%) 287 (M^+, 14), 214 (100).

Compound 5g: (45%), (oil); (Found: C, 72.54; H, 5.58; N, 4.08. $C_{22}H_{21}NO_4$ requires: C, 72.71; H, 5.82; N, 3.85); i.r. (Nujol) 1734, 1267, 1182 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.02 (t, 3H, J=7.2 Hz), 3.41 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 4.10 (q, 2H, J=7.3 Hz), 6.60 (dd, 1H, J=8.4, 1.7 Hz), 6.77 (dd, 1H, J=8.4, 1.6 Hz), 6.86 (t, 1H, J=7.9 Hz), 7.04-7.07 (m, 2H), 7.11-7.15 (m, 3H), 7.39 (d, 1H, J=5.0 Hz, H-5), 8.64 (d, 1H, J=5.0 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 13.7 (CH_3), 55.6 (OCH_3), 59.9 (OCH_3), 61.3 (CH_2), 112.6 (CH), 122.8(CH), 123.1 (CH), 126.0 (C-5), 127.8 (2xCH), 127.8 (CH), 128.6 (2xCH), 130.5 (q), 131.9 (C-3), 138.2 (q), 142.2 (q), 148.0 (C-6), 150.0 (C-2), 151.0 (C-4), 152.2 (q), 166.4 (C=O); m/z (%) 363 (M^+, 33), 290 (100).

Compound 5h: (53%), m.p. 115°C (colourless prisms); (Found: C, 52.29; H, 4.61; N, 3.61. $C_{16}H_{16}BrNO_4$ requires: C, 52.45; H, 4.40; N, 3.84); i.r. (Nujol) 1732, 1298, 1097 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.14 (t, 3H, J=7.0 Hz), 3.43 (s, 3H, OCH_3), 3.81 (s, 3H, OCH_3), 4.20 (q, 2H, J=7.1 Hz), 6.89 (s, 1H), 7.00 (s, 1H), 7.41 (m, 1H, H-5), 7.65 (d, 1H, J=7.8 Hz, H-4), 8.63 (d, 1H, J=4.4 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 13.9 (CH_3), 56.1 (OCH_3), 60.4 (OCH_3), 61.6 (CH_2), 115.8 (CH), 116.2 (q), 124.1(CH), 125.2 (C-5), 132.9 (q), 134.4 (C-3), 139.3 (C-4), 145.1(q), 148.5 (C-6), 148.6 (C-2), 153.2 (q), 165.8 (C=O); m/z (%) 367 (M^+, 36), 365 (M^+, 40), 294 (86), 292 (100).

Compound 5i: (40%), m.p. 157°C (colourless prisms); (Found: C, 59.55; H, 4.81; N, 3.03. $C_{22}H_{20}BrNO_4$ requires: C, 59.74; H, 4.58; N, 3.17); i.r. (Nujol) 1730, 1319, 1188 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.18 (t, 3H, J=7.1 Hz), 3.46 (s, 3H, OCH_3), 3.77 (s, 3H, OCH_3), 4.24 (q, 2H, J=7.1 Hz), 6.84 (d, 1H, J=2.0 Hz), 6.95 (d, 1H, J=2.1 Hz), 7.11-7.16 (m, 2H), 7.24-7.27 (m, 3H), 7.45 (d, 1H, J=4.9 Hz, H-5), 8.72 (d, 1H, J=5.0 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 14.0 (CH_3), 56.0 (OCH_3), 60.2 (OCH_3), 61.7 (CH_2), 115.4 (q), 115.9 (CH), 125.4(CH), 126.3 (C-5), 128.1 (2xCH), 128.1 (CH), 128.7 (2xCH), 130.7 (q), 132.3 (C-3), 138.1 (q), 145.7(q), 148.8 (C-6), 150.1 (C-2), 151.0 (C-4), 153.0 (q), 166.3 (C=O); m/z (%) 443 (M^+, 83), 441 (M^+, 86), 370 (85), 368 (100).

Reaction of Iminophosphoranes 6a-c with α,β-Unsaturated Aldehydes: General Procedure.

A solution of the appropriate iminophosphorane **6a-c** (2.5 mmol), and the α,β-unsaturated aldehyde (5 mmol) in dry toluene (30 ml) was heated at 160°C in a glass sealed tube for 24 h. After cooling, the solvent was removed under reduced pressure and the residual material was chromatographed on a silica gel column eluting with ethyl acetate/ n-hexane (1:2) to give **7** (R_f=0.42) and **8** (R_f=0.26).

Compound 7a: (22%), (oil); (Found: C, 66.56; H, 4.87; N, 6.64. $C_{12}H_{11}NO_3$ requires: C, 66.35; H, 5.10; N, 6.45); i.r. (Nujol) 1731, 1314, 1231 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.37 (t, 3H, J=7.1 Hz), 4.41 (q, 2H, J=7.1 Hz), 5.64 (dd, 1H, J=11.0, 1.2 Hz), 6.37 (dd, 1H, J=17.4, 1.2 Hz), 6.96 (dd, 1H, J=2.1, 0.9 Hz, H-3), 7.07 (dd, 1H, J=17.4, 11.1 Hz), 7.44 (d, 1H, J=2.4 Hz, H-2), 8.10 (d, 1H, J=0.9 Hz, H-7); ^{13}C n.m.r. δ ($CDCl_3$): 14.3 (CH_3), 61.9 (CH_2), 105.1 (C-3), 108.1 (C-7), 121.6 (CH_2), 124.7 (C-3a), 134.3 (CH), 143.2 (C-6), 148.1 (C-2), 150.1 (C-4), 160.2 (C-1a), 165.4 (C=O); m/z (%) 217 (M^+, 17), 145 (100).

Compound 7b: (26%), m.p.=116°C (yellow prisms from diethyl ether/ n-hexane 1:1); (Found: C, 73.86; H,

4.92; N, 5.02. $C_{18}H_{15}NO_3$ requires: C, 73.71; H, 5.16; N, 4.78); i.r. (Nujol) 1734, 1307, 1223, 1199 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.48 (t, 3H, J=7.2 Hz), 4.52 (q, 2H, J=7.1 Hz), 7.12 (t, 1H, J=1.1 Hz, H-3), 7.34 (t, 1H, J=7.1 Hz), 7.39 (t, 2H, J=7.2 Hz), 7.48 (d, 1H, J=16.2 Hz), 7.64 (d, 2H, J=7.2 Hz), 7.82 (d, 1H, J=2.1 Hz, H-2), 7.91 (d, 1H, J=16.4 Hz), 8.16 (s, 1H, H-7); ^{13}C n.m.r. δ ($CDCl_3$): 14.4 (CH_3), 61.9 (CH_2), 105.1 (C-3), 107.7 (C-7), 124.7 (CH), 125.0 (C-3a), 127.3 (2xCH), 128.7 (CH), 128.8 (2xCH), 135.7 (CH), 136.3 (q), 143.5 (C-6), 147.9 (C-2), 150.0 (C-4), 160.1 (C-1a), 165.5 (C=O); m/z (%) 293 (M^+, 39), 219 (100).

Compound 7c: (25%), (oil); (Found: C, 61.53; H, 4.94; N, 6.18. $C_{12}H_{11}NO_2S$ requires: C, 61.78; H, 4.75; N, 6.00); i.r. (Nujol) 1732, 1271, 1215, 1020 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.37 (t, 3H, J=7.1 Hz), 4.41 (q, 2H, J=7.1 Hz), 5.72 (dd, 1H, J=11.0, 0.7 Hz), 6.48 (dd, 1H, J=17.3, 0.7 Hz), 7.09 (dd, 1H, J=17.5, 11.2 Hz), 7.39 (d, 1H, J=5.4 Hz, H-3), 7.69 (d, 1H, J=5.6 Hz, H-2), 8.37(s, 1H, H-7); ^{13}C n.m.r. δ ($CDCl_3$): 14.3 (CH_3), 61.8 (CH_2), 119.0 (C-7), 122.2 (CH_2), 124.1 (C-2), 132.5 (C-3), 135.0 (CH), 142.4 (C-3a), 142.7 (C-6), 146.3 (C-1a), 150.4 (C-4), 165.9 (C=O); m/z (%) 233 (M^+, 4), 161 (100).

Compound 7d: (20%), (oil); (Found: C, 61.59; H, 4.99; N, 6.23. $C_{12}H_{11}NO_2S$ requires: C, 61.78; H, 4.75; N, 6.00); i.r. (Nujol) 1732, 1298, 1107 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.39 (t, 3H, J=7.2 Hz), 4.42 (q, 2H, J=7.2 Hz), 5.67 (dd, 1H, J=10.8,1.4 Hz), 6.56 (dd, 1H, J=17.1, 1.6 Hz), 7.24 (dd, 1H, J=17.4, 10.8 Hz), 7.59 (d, 1H, J=5.3 Hz, H-3), 7.65 (d, 1H, J=5.3 Hz, H-2), 8.50 (s, 1H, H-4); ^{13}C n.m.r. δ ($CDCl_3$): 14.4 (CH_3), 61.8 (CH_2), 118.6 (C-4), 121.8 (C-2), 122.3 (CH_2), 130.6 (C-3), 133.1 (CH), 141.4 (C-3a), 143.4 (C-5), 148.3 (C-1a), 150.9 (C-7), 165.7 (C=O); m/z (%) 233 (M^+, 6), 161 (100).

Compound 8b: (22%), (oil); (Found: C, 73.52; H, 5.41; N, 4.62. $C_{18}H_{15}NO_3$ requires: C, 73.71; H, 5.16; N, 4.78); i.r. (Nujol) 1737, 1316, 1181 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.26 (t, 3H, J=7.2 Hz), 4.32 (q, 2H, J=7.2 Hz), 6.01 (d, 1H, J=3.3 Hz), 6.31 (m, 1H), 7.15-7.51 (m, 7H, aromatics), 8.57 (d, 1H, J=4.8 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 14.0 (CH_3), 61.8 (CH_2), 111.2 (CH), 111.5 (CH), 124.2 (q), 126.0 (C-5), 128.3 (2xCH), 128.3 (2xCH), 128.3 (CH), 138.1 (C-3), 142.6 (CH), 147.9 (C-4), 148.8 (C-6), 150.4 (C-2), 151.3 (q), 166.9 (C=O); m/z (%) 293 (M^+, 14), 221 (100).

Compound 8c: (21%), (oil); (Found: C, 61.99; H, 4.51; N, 6.23. $C_{12}H_{11}NO_2S$ requires: C, 61.78; H, 4.75; N, 6.00); i.r. (Nujol) 1727, 1300, 1138, 1107 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.17 (t, 3H, J=7.1 Hz), 4.20 (q, 2H, J=7.2 Hz), 7.09 (dd, 1H, J=4.9, 1.3 Hz), 7.28-7.45 (m, 3H, aromatics), 7.38 (dd, 1H, J=8.0, 1.5 Hz, H-4), 8.57 (d, 1H, J=4.6 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 13.9 (CH_3), 61.8 (CH_2), 123.5 (CH), 125.0 (C-5), 126.0 (CH), 127.9 (CH), 131.6 (C-3), 138.0 (C-4), 138.2 (q), 148.0 (C-6), 149.2 (C-2), 167.0 (C=O); m/z (%) 233 (M^+, 3), 161 (100).

Compound 8d: (20%), (oil); (Found: C, 61.98; H, 4.92; N, 5.75. $C_{12}H_{11}NO_2S$ requires: C, 61.78; H, 4.75; N, 6.00); i.r. (Nujol) 1734, 1300, 1105 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.16 (t, 3H, J=7.1 Hz), 4.24 (q, 2H, J=7.2 Hz), 6.99-7.07 (m, 2H), 7.31-7.38 (m, 2H), 7.76 (dd, 1H, J=7.8, 1.3 Hz, H-4), 8.54 (dd, 1H, J=4.8, 1.4 Hz, H-6); ^{13}C n.m.r.

δ ($CDCl_3$): 13.6 (CH_3), 61.8 (CH_2), 124.8 (C-5), 127.0 (CH), 127.2 (CH), 127.6 (CH), 129.4 (C-3), 138.4 (C-4), 138.6 (q), 148.3 (C-6), 149.6 (C-2), 166.8 (C=O); m/z (%) 233 (M^+, 6), 161 (100).

General Procedure for the Preparation of 3-Pyrazolylpyridines 8e-h.

These compounds were prepared starting from iminophosphoranes **6d** and **6e** and α,β-unsaturated aldehydes using the same procedure as described for the preparation of compounds **5**.

Compound 8e: (39%), (oil); (Found: C, 69.83; H, 4.95; N, 14.54. $C_{17}H_{15}N_3O_2$ requires: C, 69.61; H, 5.16; N, 14.33); i.r. (Nujol) 1730, 1504, 1300 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.34 (t, 3H, J=7.2 Hz), 4.40 (q, 2H, J=7.1 Hz), 7.33 (t, 1H, J=7.5 Hz), 7.44-7.51 (m, 3H), 7.82 (d, 2H, J=8.0 Hz), 7.85 (s, 1H), 7.87 (dd, 1H, J=7.9, 1.5 Hz, H-4), 8.18 (s, 1H), 8.62 (dd, 1H, J=4.7, 1.6 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 14.1 (CH_3), 62.2 (CH_2), 119.2 (2xCH), 119.8 (q), 125.4 (C-5), 126.2 (CH), 127.0 (CH), 127.4 (C-3), 129.6 (2xCH), 138.1 (C-4), 139.8(q), 140.5 (CH), 147.4 (C-6), 148.3 (C-2), 165.8 (C=O); m/z (%) 293 (M^+, 17), 220 (100).

Compound 8f: (37%), m.p. 163°C (colourless prisms); (Found: C, 74.91; H, 5.02; N, 11.18. $C_{23}H_{19}N_3O_2$ requires: C, 74.78; H, 5.18; N, 11.37); i.r. (Nujol) 1730, 1508, 1182, 954 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.21 (t, 3H, J=7.1 Hz), 4.30 (q, 2H, J=7.1 Hz), 7.18-7.55 (m, 12H, aromatics), 7.66 (s, 1H), 8.63 (d, 1H, J=4.8 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 14.0 (CH_3), 62.0 (CH_2), 117.5 (q), 118.9 (2xCH), 124.7 (C-3), 125.9 (C-5), 126.8 (CH), 128.4 (CH), 128.5 (2xCH), 129.0 (2xCH), 129.5 (2xCH), 138.2 (q), 139.7(q), 141.5 (CH), 148.0 (C-6), 150.6 (C-4), 151.6 (C-2), 167.5 (C=O); m/z (%) 369 (M^+, 38), 296 (100).

Compound 8g: (41%), (oil),; (Found: C, 69.48; H, 4.95; N, 14.57. $C_{17}H_{15}N_3O_2$ requires: C, 69.61; H, 5.16; N, 14.33); i.r. (Nujol) 1730, 1500, 1300 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.15 (t, 3H, J=7.1 Hz), 4.14 (q, 2H, J=7.1 Hz), 6.48 (d, 1H, J=1.8 Hz), 7.24-7.28 (m, 5H, aromatics), 7.41 (dd, 1H, J=7.8, 4.7 Hz, H-5), 7.64 (dd, 1H, J=8.0, 1.7 Hz, H-4), 7.75 (d, 1H, J=1.8 Hz), 8.68 (dd, 1H, J=4.8, 1.5 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 13.7 (CH_3), 61.8 (CH_2), 108.7 (CH), 124.3 (2xCH), 125.2 (C-5), 127.2 (CH), 127.3 (C-3), 128.9 (2xCH), 138.7 (q), 139.1 (q), 139.2 (C-4), 140.1 (CH), 148.9 (C-2), 149.3 (C-6), 165.2 (C=O); m/z (%) 293 (M^+, 10), 220 (100).

Compound 8h: (44%), (oil); (Found: C, 74.62; H, 5.41; N, 11.48. $C_{23}H_{19}N_3O_2$ requires: C, 74.78; H, 5.18; N, 11.37); i.r. (Nujol) 1739, 1502, 1182 cm^{-1}; ^1H n.m.r. δ ($CDCl_3$): 1.07 (t, 3H, J=7.1 Hz), 4.18 (q, 2H, J=7.2 Hz), 6.46 (d, 1H, J=2.1 Hz), 6.50 (d, 2H, J=7.2 Hz), 6.66 (d, 2H, J=7.2 Hz), 6.92-7.03 (m, 4H, aromatics), 7.14 (t, 2H, J=7.5 Hz), 7.17 (d, 1H, J=4.8 Hz, H-5), 7.60 (d, 1H, J=1.8 Hz), 8.61 (d, 1H, J=4.8 Hz, H-6); ^{13}C n.m.r. δ ($CDCl_3$): 13.8 (CH_3), 62.0 (CH_2), 110.3 (CH), 123.6 (2xCH), 124.0 (C-3), 125.8 (C-5), 126.8 (CH), 127.9 (2xCH), 128.2 (2xCH), 128.2 (CH), 128.4 (2xCH), 136.6 (q), 136.8 (q), 139.1 (q), 140.0 (CH), 150.0(C-6), 150.5 (C-4), 151.8 (C-2), 166.6 (C=O); m/z (%) 369 (M^+, 35), 296 (100).

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