Supporting Information

Solid-Phase Asymmetric Synthesis of 2*H*-Azirines Derived from Phosphine Oxides. Ring Opening of Azirines with Carboxylic Acids

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General Methods. Solvents for extraction and chromatography were technical grade. All solvents used in reactions were freshly distilled from appropriate drying agents before use: CH₂Cl₂ (P₂O₅); *n*-hexane and diethyl ether (sodium benzophenone ketyl); ethyl acetate (K₂CO₃); CHCl₃ (P₂O₅); toluene (CaH₂); dioxane (Na, benzophenone). All other reagents were recrystallized or distilled as necessary. All reactions were performed under an atmosphere of dry nitrogen. Analytical TLC was performed with silica gel 60 F₂₅₄ plates. Visualization was accomplished by UV light and KMnO₄ solution. Flash chromatography was carried out using silica gel 60 (230–400 mesh). Melting points are uncorrected. ¹H (300 MHz), ¹³C (75 MHz) and ³¹P NMR (120 MHz) spectra were recorded using tetramethylsilane (TMS) (0.00 ppm) or chloroform (7.26 ppm) as an internal reference in CDCl₃ or D₂O solutions for ¹H

NMR spectra or chloroform (77.0 ppm) as an internal reference in CDCl₃ solutions for ¹³C NMR, and phosphoric acid (85%) for ³¹P NMR spectra. Chemical shifts (δ) are given in ppm; multiplicities are indicated by s (singlet), d (doublet), dd (double-doublet), t (triplet), q (quadruplet) or m (multiplet). Coupling constants (J) are reported in hertz. Low-resolution mass spectra (MS) were obtained at 50–70 eV by electron impact (EI) or chemical ionization (CI). Data are reported in the form m/z (intensity relative to base = 100). Infrared spectra (IR) were taken on a IRFT spectrometer, and were obtained as solids in KBr or as neat oils in NaCl. Peaks are reported in cm⁻¹. $[\alpha]_D^{20}$ were taken on a polarimeter using a Na/HaI lamp. Oximes **1a,b**,¹⁷ morpholinomethyl polystyrene resin **2b**,³¹ and 2*H*-azirine-2-phosphonates **11**^{18a} were synthesized according to literature procedures.

General procedure for the preparation of polymer-supported amines (2c) and (2d). A suspension of Merrifield resin (4 mmol, 1 mmol of Cl/g resin, 4 g) in DMF (32 ml) was treated with (*S*)-(+)-2-(methoxymethyl)pyrrolidine or (*R*)-(-)-2-(methoxymethyl)pyrrolidine³² (16 mmol, 2 ml). The resulting mixture was shaken at 65 °C for 18 h under N₂ atmosphere and then allowed to stand at room temperature 24 h. After cooling to room temperature, the resin was filtered and washed successively with MeOH, DMF, MeOH, CH₂Cl₂, MeOH, CH₂Cl₂, MeOH, AcOEt, and pentane. The resulting polymer-supported amine, was dried at 20 °C under vacuum, for 12 h and stored in tightly sealed bottles.

(*R*)-(-)-2-(methoxymethyl)pyrrolidinomethyl polystyrene resin (2d). IR (KBr) 2805 (OMe st), 1109 (C-O-C st) cm⁻¹; Anal. Found C, 90.55; H, 8.23; N, 1.57.

General procedure for the synthesis of 2*H*-azirine-2-phosphine oxides (3). To a suspension of resin-supported amine **2a-c** (*ca.* 0.5 mmol, 1.1 equiv) in benzene (8.0 ml) was added tosyl oxime **1** (0.45 mmol, 1 equiv). The mixture was shaken at 50 °C for 3 to 4 days under N₂ atmosphere after

which time the polymer was filtered and washed with CH₂Cl₂ (5 ml), Et₂O (5 ml), CH₂Cl₂ (5 ml) and Et₂O (5 ml). The filtrate was evaporated under vacuum. Purification of the crude product by flash-chromatography (silica gel AcOEt-hexanes 4:1) afforded an oil which was precipitated with Et₂O and recrystallized from AcOEt-hexanes to yield compounds **3**. Resin-supported amines **2a-c** were recovered by washing successively with MeOH, TEA, CH₂Cl₂, MeOH, TEA, CH₂Cl₂, MeOH, TEA, and CH₂Cl₂.

(3-Ethyl-2H-azirin-2-yl)phosphine oxide (3b). (A) As described in the general procedure, 106.5 mg (88%) was obtained as a white solid from (*E*)- and (*Z*)-2-(*N*-*p*-toluenesulfonyloximino)butyldiphenylphosphine oxide **1b** and resin-supported amine **2a**. (B) As described in the general procedure, 79.9 mg (66%) was obtained as a white solid from (*E*)- and (*Z*)-2-(*N*-*p*-toluenesulfonyloximino)butyldiphenylphosphine oxide **1b** and resin-supported amine **2b**: mp 61-62 °C; ¹H NMR (CDCl₃) δ 7.89-7.29 (m, 10H), 2.67 (dq, ³J_{HH} = 7.5 Hz, ⁴J_{PH} = 4.0 Hz, 2H), 2.22 (d, ²J_{PH} = 36.3 Hz, 1H), 1.12 (t, ³J_{HH} = 7.5 Hz, 3H) ppm; ¹³C NMR (CDCl₃) δ 166.7 (d, ²J_{PC} = 3.0 Hz), 133.2-128.0 (m), 27.5 (d, ¹J_{PC} = 112.3 Hz), 21.4, 8.1 ppm; ³¹P NMR (CDCl₃) δ 29.4 ppm; IR (KBr) 3045, 1732, 1434, 1175 cm⁻¹; MS (CI) *m/z* 270 (M⁺ + 1, 100), 201 (P(O)Ph₂⁺, 6); Anal. Calcd for C₁₆H₁₆NOP: C, 71.37; H, 5.99; N, 5.20. Found C, 71.43; H, 6.01; N, 5.19.

(-)-(R)-(3-Ethyl-2H-azirin-2-yl)phosphine oxide (3b). As described in the general procedure, 78.7 mg (65%) was obtained as a white solid from (*E*)- and (*Z*)-2-(*N*-*p*-toluenesulfonyloximino)butyldiphenylphosphine oxide **1b** and resin-supported amine **2c**, ee 37%; [α]_D²⁰ -21.8. For spectroscopic data see above.

(+)-(S)-(3-Methyl-2H-azirin-2-yl)phosphine oxide (3a). As described in the general procedure, 68.9 mg (60%) was obtained as a white solid from (*E*)- and (*Z*)-2-(*N*-*p*-

toluenesulfonyloximino)propyldiphenylphosphine oxide **1a** and resin-supported amine **2d**, ee 37%; $[\alpha]_D^{20} +14.0$. For spectroscopic data see experimental section.

(+)-(S)-(3-Ethyl-2H-azirin-2-yl)phosphine oxide (3b). As described in the general procedure, 107.7 mg (89%) was obtained as a white solid from (*E*)- and (*Z*)-2-(*N*-*p*-toluenesulfonyloximino)butyldiphenylphosphine oxide **1b** and resin-supported amine **2c**, ee 15%; $[\alpha]_D^{20} +14.5$. For spectroscopic data see above.

General procedure for the synthesis of α -ketamides derived from phosphine oxides (5). Method A: to a $-80\text{ }^{\circ}\text{C}$ solution of 2*H*-azirine **3** (5 mmol) in THF (5 ml), was added a solution of carboxylic acid **4** (15 mmol) in THF (5 ml) under nitrogen atmosphere. Then, the mixture was allowed to warm to room temperature and was stirred for 1 to 4 days. The solvent was evaporated under vacuum, and the crude product was purified by flash-chromatography (silica gel AcOEt). Method B: the carboxylic acid **4** (5.5 mmol) was added under nitrogen atmosphere and at room temperature to 2*H*-azirine **3** (5 mmol) without solvent. The mixture was stirred for 12 to 20 h and then, the crude residue was crystallized from diethyl ether to yield products **5** as white solids.

***N*-[1-(Diphenylphosphinoyl)-2-oxopropyl]benzamide (5ab)**. (1.22 g, 65%) obtained as a white solid from 2*H*-azirine **3a** (1.28 g, 5 mmol) and benzoic acid **4b** (1.83 g, 15 mmol) as described in the general procedure method A: mp 125-126 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 8.06-7.26 (m, 15H), 7.17 (d, $^3J_{\text{HH}} = 8.7\text{ Hz}$, 1H), 6.00 (dd, $^2J_{\text{PH}} = 11.6\text{ Hz}$, $^3J_{\text{HH}} = 8.7\text{ Hz}$, 1H), 2.27 (s, 3H) ppm.; ^{13}C NMR (CDCl_3) δ 200.9, 166.9, 133.0-127.0 (m), 61.2 (d, $^1J_{\text{PC}} = 64.5\text{ Hz}$), 30.1 ppm; ^{31}P NMR (CDCl_3) δ 31.7 ppm; IR (KBr) 3204, 3052, 3022, 1724, 1643 cm^{-1} ; MS (CI) m/z 378 ($\text{M}^+ + 1$, 3), 201 ($\text{P}(\text{O})\text{Ph}_2^+$, 80); Anal. Calcd for $\text{C}_{22}\text{H}_{20}\text{NO}_3\text{P}$: C, 70.02; H, 5.34; N, 3.71. Found C, 69.78; H, 5.32; N, 3.72.

***N*-[1-(Diphenylphosphinoyl)-2-oxopropyl]-2-methoxyacetamide (5ac).** (1.16 g, 67%) obtained as a white solid from 2*H*-azirine **3a** (1.28 g, 5 mmol) and methoxyacetic acid **4c** (0.42 g, 5 mmol) as described in the general procedure method B: mp 146-147 °C; ¹H NMR (CDCl₃) δ 7.96-7.40 (m, 11H), 5.85 (dd, ²*J*_{PH} = 12.3 Hz, ³*J*_{HH} = 9.5 Hz, 1H), 3.75 (d, ²*J*_{HHgem} = 15.3 Hz, 1H), 3.55 (d, ²*J*_{HHgem} = 15.3 Hz, 1H), 3.21 (s, 3H), 2.20 (s, 3H) ppm; ¹³C NMR (CDCl₃) δ 200.1, 169.1(d, ³*J*_{PC} = 3.5 Hz), 132.8-128.5 (m), 71.4, 60.1 (d, ¹*J*_{PC} = 63.9 Hz), 59.2, 30.0 ppm; ³¹P NMR (CDCl₃) δ 31.0 ppm; IR (KBr) 3190, 3050, 1726, 1660 cm⁻¹; MS (EI) *m/z* 345 (M⁺ + 5), 201 (P(O)Ph₂⁺, 100); Anal. Calcd for C₁₈H₂₀NO₄P: C, 62.60; H, 5.84; N, 4.06. Found C, 62.77; H, 5.86; N, 4.06.

***N*-[1-(Diphenylphosphinoyl)-2-oxopropyl]acrilamide (5ad).** (1.23 g, 75%) obtained as a white solid from 2*H*-azirine **3a** (1.28 g, 5 mmol) and acrylic acid (0.36 g, 5 mmol) as described in the general procedure method B: mp 190-191 °C; ¹H NMR (CDCl₃) δ 7.59-7.39 (m, 10H), 7.15 (d, ³*J*_{HH} = 9.3 Hz, 1H), 6.12 (m, 2H), 5.90 (dd, ²*J*_{PH} = 11.4 Hz, ³*J*_{HH} = 9.3 Hz, 1H), 5.58 (dd, ²*J*_{HHgem} = 2.1 Hz, ³*J*_{HHcis} = 9.6 Hz, 1H), 2.17 (s, 3H) ppm; ¹³C NMR (CDCl₃) δ 200.9, 164.9 (d, ³*J*_{PC} = 4.0 Hz), 132.9-128.1 (m), 127.9, 60.6 (d, ¹*J*_{PC} = 64.9 Hz), 29.9 ppm; ³¹P NMR (CDCl₃) δ 31.4 ppm; IR (KBr) 3222, 3045, 1721, 1662 cm⁻¹; MS (EI) *m/z* 327 (M⁺ + 8), 201 (P(O)Ph₂⁺, 100); Anal. Calcd for C₁₈H₁₈NO₃P: C, 66.05; H, 5.54; N, 4.28. Found C, 66.27; H, 5.56; N, 4.27.

Hept-6-enoic acid [1-diphenylphosphinoyl]-2-oxopropyl]amide (5ae). (1.24 g, 65%) obtained as a white solid from 2*H*-azirine **3a** (1.28 g, 5 mmol) and 6-heptenoic acid **4e** (0.44 g, 5 mmol) as described in the general procedure method B: mp 133-134 °C; ¹H NMR (CDCl₃) δ 7.95-7.45 (m, 10H), 6.94 (d, ³*J*_{HH} = 9.6 Hz, 1H), 5.86 (dd, ²*J*_{PH} = 10.8 Hz, ³*J*_{HH} = 9.6 Hz, 1H), 5.66 (m, 1H), 4.91(m, 2H), 2.12 (s, 3H), 2.10-1.88 (m, 4H), 1.37 (m, 2H), 1.17 (m, 2H) ppm; ¹³C NMR (CDCl₃) δ 200.9, 172.6, 138.2, 132.8-128.6 (m), 114.7, 60.5 (d, ¹*J*_{PC} = 65.4 Hz), 35.9, 32.3, 29.8, 28.1, 24.7 ppm; ³¹P NMR

(CDCl₃) δ 31.8 ppm; IR (KBr) 3185, 1713, 1653 cm⁻¹; MS (EI) m/z 384 (M⁺ + 1, 36), 201 (P(O)Ph₂⁺, 19); Anal. Calcd for C₂₂H₂₆NO₃P: C, 68.92; H, 6.83; N, 3.65. Found C, 68.77; H, 6.81; N, 3.64.

***N*-[1-(Diphenylphosphinoyl)-2-oxobutyl]benzamide (5bb).** (1.17 g, 60%) obtained as a white solid from 2*H*-azirine **3b** (1.35 g, 5 mmol) and benzoic acid **4b** (1.83 g, 15 mmol) as described in the general procedure method A: mp 187-188 °C; ¹H NMR (CDCl₃) δ 7.98-7.28 (m, 15H), 7.16 (d, ³*J*_{HH} = 8.4 Hz, 1H), 5.99 (dd, ²*J*_{PH} = 11.1 Hz, ³*J*_{HH} = 8.8 Hz, 1H), 2.68 (dq, ³*J*_{HH} = 7.2 Hz, ²*J*_{HHgem} = 14.5 Hz, 1H), 2.43 (dq, ³*J*_{HH} = 7.2 Hz, ²*J*_{HHgem} = 14.5 Hz, 1H), 0.94 (t, ³*J*_{HH} = 7.2 Hz, 3H) ppm.; ¹³C NMR (CDCl₃) δ 203.9, 166.8 (d, ³*J*_{PC} = 4.0 Hz), 133.2-127.0 (m), 60.3 (d, ¹*J*_{PC} = 65.0 Hz), 36.1, 7.2; ³¹P NMR (CDCl₃) δ 31.9 ppm; IR (KBr) 3224, 3058, 3018, 1725, 1646 cm⁻¹; MS (CI) m/z 392 (M⁺ + 1, 5), 201 (P(O)Ph₂⁺, 78); Anal. Calcd for C₂₃H₂₂NO₃P: C, 70.58; H, 5.67; N, 3.58. Found C, 70.45; H, 5.65; N, 3.59.

***N*-[1-(Diphenylphosphinoyl)-2-oxobutyl]malonamic acid (5bf).** (1.06 g, 57%), obtained as a white solid from 2*H*-azirine **3b** (1.35 g, 5 mmol) and malonic acid **4f** (1.56 g, 15 mmol) as described in the general procedure method A: mp 94-95 °C; ¹H NMR (CDCl₃) δ 8.99 (d, ³*J*_{HH} = 9.5 Hz, 1H), 8.10-7.26 (m, 10H), 5.93 (dd, ²*J*_{PH} = 9.5 Hz, ³*J*_{HH} = 9.4 Hz, 1H), 3.16 (dd, ⁴*J*_{HH} = 18.0 Hz, ²*J*_{HHgem} = 46.3 Hz, 2H), 2.45 (m, ³*J*_{HH} = 7.6 Hz, 2H), 0.86 (t, ³*J*_{HH} = 6.8 Hz, 3H) ppm.; ¹³C NMR (CDCl₃) δ 203.2, 170.6 (d, ³*J*_{PC} = 4.5 Hz), 166.1, 132.9-125.1 (m), 59.5 (d, ¹*J*_{PC} = 69.0 Hz), 40.4, 34.9, 7.1; ³¹P NMR (CDCl₃) δ = 34.4 ppm; IR (KBr) 3496, 3423, 3025, 1752, 1706, 1643 cm⁻¹; MS (CI) m/z 374 (M⁺ + 1, 4), 313 (M⁺ – CH₃COOH, 20), 201 (P(O)Ph₂⁺, 25); Anal. Calcd for C₁₉H₂₀NO₅P: C, 61.12; H, 5.40; N, 3.75. Found C, 61.26; H, 5.42; N, 3.74.

General procedure for synthesis of *N*-[1-(Diphenylphosphinoyl)-2-oxobutyl]malonamic acid methyl ester (5bg). To a solution of *N*-[1-(diphenylphosphinoyl)-2-oxobutyl]malonamic acid **5bf** (1.86 g, 5 mmol), in MeOH was added thionyl chloride (0.72 ml, 10 mmol) under nitrogen atmosphere

and with continuous stirring. The mixture is heated at MeOH reflux for 4 h. Then, the solvent is concentrated under vacuum, the subsequent residue is diluted in CH_2Cl_2 and washed three times with water. The organic layer is dried over anhydrous magnesium sulfate, filtered and concentrated under pressure. The crude residue was purified by flash-chromatography (silica gel AcOEt/hexanes) affording compound **5bg** (1.30 g, 67%): mp 156-157 °C; ^1H NMR (CDCl_3) δ 7.95-7.48 (m, 10H), 5.85 (dd, $^2J_{\text{PH}} = 12.7$ Hz, $^3J_{\text{HH}} = 9.2, 8.8$ Hz, 1H), 3.67 (s, 3H), 3.14 (dd, $^4J_{\text{HH}} = 17.0$ Hz, $^2J_{\text{HHgem}} = 30.3$ Hz, 2H), 2.74 (dq, $^3J_{\text{HH}} = 7.3$ Hz, $^2J_{\text{HHgem}} = 18.7$ Hz, 1H), 2.46 (dq, $^3J_{\text{HH}} = 7.0$ Hz, $^2J_{\text{HHgem}} = 18.6$ Hz, 1H), 0.97 (t, $^3J_{\text{HH}} = 7.2$ Hz, 3H) ppm.; ^{13}C NMR (CDCl_3) δ 203.7, 168.1, 165.1 (d, $^3J_{\text{PC}} = 5.0$ Hz), 132.6-128.1 (m), 59.9 (d, $^1J_{\text{PC}} = 66.5$ Hz), 52.2, 41.3, 35.4, 7.0 ppm; ^{31}P NMR (CDCl_3) δ 31.4 ppm; IR (KBr) 3237, 3018, 1739, 1719, 1672 cm^{-1} ; MS (CI) m/z 389 ($\text{M}^+ + 2$, 37), 388 ($\text{M}^+ + 1$, 100); Anal. Calcd for $\text{C}_{20}\text{H}_{22}\text{NO}_3\text{P}$: C, 62.01; H, 5.72; N, 3.62. Found C, 61.85; H, 5.70; N, 3.63.

General procedure for the preparation of oxazoles (8). To a room temperature solution of triphenyl phosphine (1.70 g, 6.5 mmol) and hexachloroethane (1.54 g, 6.5 mmol) in THF (20 ml) was added a solution of α -ketamide **5** (5 mmol) in THF (5 ml) under nitrogen atmosphere. The mixture was stirred at room temperature for 5 minutes. After that, triethylamine (2.10 ml, 15 mmol) was dropped for 10 minutes. The mixture was heated at THF reflux for 20 h. The solvent was evaporated under vacuum and the residue was diluted with water and extracted with CH_2Cl_2 . The organic layers were dried over anhydrous magnesium sulfate, filtered and concentrated under vacuum. The crude residue was purified by flash-chromatography (silica gel AcOEt).

4-(Diphenylphosphinoyl)-5-methyl-2-phenyloxazole (8ab). (1.42 g, 79%) obtained as a white solid from α -ketamide **5ab** (1.89 g, 5 mmol) as described in the general procedure: mp 134-135 °C; ^1H NMR (CDCl_3) δ 7.96-7.35 (m, 15H), 2.65 (d, $^4J_{\text{PH}} = 1.9$ Hz, 3H) ppm; ^{13}C NMR (CDCl_3) δ 160.7 (d, $^3J_{\text{PC}} = 18.9$ Hz), 159.0 (d, $^2J_{\text{PC}} = 27.0$ Hz), 133.8-126.5 (m), 11.9 ppm; ^{31}P NMR (CDCl_3) δ 18.9 ppm; IR

(KBr) 3070, 1780, 1590, 1187 cm^{-1} ; MS (EI) m/z 359 (M^+ , 56); Anal. Calcd for $\text{C}_{22}\text{H}_{18}\text{NO}_2\text{P}$: C, 73.53; H, 5.05; N, 3.90. Found C, 73.43; H, 5.06; N, 3.91.

4-(Diphenylphosphinoyl)-2-methoxymethyl-5-methyloxazole (8ac). (1.14 g, 70%) obtained as a white solid from α -ketamide **5ac** (1.73 g, 5 mmol) as described in the general procedure: mp 113-114 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 7.86-7.39 (m, 10H), 4.46 (s, 2H), 3.40 (s, 3H), 2.61 (d, $^4J_{\text{PH}} = 2.1$ Hz, 3H) ppm; ^{13}C NMR (CDCl_3) δ 160.1 (d, $^2J_{\text{PC}} = 26.7$ Hz), 159.7 (d, $^3J_{\text{PC}} = 17.6$ Hz), 133.6-128.3 (m), 126.7 (d, $^1J_{\text{PC}} = 145.0$ Hz), 66.1, 58.9, 11.8 ppm; ^{31}P NMR (CDCl_3) δ 19.1 ppm; IR (KBr) 3070, 1780, 1600, 1198 cm^{-1} ; MS (EI) m/z 327 (M^+ , 100); Anal. Calcd for $\text{C}_{18}\text{H}_{18}\text{NO}_3\text{P}$: C, 66.05; H, 5.54; N, 4.28. Found C, 66.00; H, 5.52; N, 4.29.

4-(Diphenylphosphinoyl)-5-methyl-2-vinyloxazole (8ad). (0.91 g, 59%) obtained as a white solid from α -ketamide **5ad** (1.64 g, 5 mmol) as described in the general procedure: mp 100-101 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 7.86-7.38 (m, 10H), 6.50 (dd, $^3J_{\text{HHcis}} = 11.1$ Hz, $^3J_{\text{HHtrans}} = 17.7$ Hz, 1H), 6.10 (dd, $^2J_{\text{HHcis}} = 0.9$ Hz, $^3J_{\text{HHtrans}} = 17.7$ Hz, 1H), 5.58 (dd, $^2J_{\text{HHgem}} = 0.9$ Hz, $^3J_{\text{HHcis}} = 11.1$ Hz, 1H), 2.61 (d, $^4J_{\text{PH}} = 2.1$ Hz, 3H) ppm; ^{13}C NMR (CDCl_3) δ 159.9 (d, $^3J_{\text{PC}} = 18.2$ Hz), 158.9 (d, $^2J_{\text{PC}} = 26.7$ Hz), 133.4-128.3 (m), 126.4 (d, $^1J_{\text{PC}} = 145.0$ Hz), 123.0, 122.4, 11.7 ppm; ^{31}P NMR (CDCl_3) δ 18.9 ppm; IR (KBr) 3065, 1750, 1600, 1180 cm^{-1} ; MS (CI) m/z 310 ($\text{M}^+ + 1$, 26); Anal. Calcd for $\text{C}_{18}\text{H}_{16}\text{NO}_2\text{P}$: C, 69.90; H, 5.21; N, 4.53. Found C, 69.75; H, 5.19; N, 4.55.

4-(Diphenylphosphinoyl)-2-hex-5-enyl-5-methyloxazole (8ae). (1.61 g, 88%) obtained as a white solid from α -ketamide **5ae** (1.92 g, 5 mmol) as described in the general procedure: mp 77-78 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 7.89-7.41 (m, 10H), 5.78 (m, 1H), 4.98 (m, 2H), 2.73 (t, $^3J_{\text{HH}} = 7.5$ Hz, 2H), 2.58 (d, $^4J_{\text{PH}} = 2.1$ Hz, 3H), 2.12 (dt, $^3J_{\text{HH}} = 7.5$ Hz, $^3J_{\text{HH}} = 7.5$ Hz, 2H), 1.75 (tt, $^3J_{\text{HH}} = 7.5$ Hz, $^3J_{\text{HH}} = 7.5$ Hz, 2H),

1.44 (tt, $^3J_{\text{HH}} = 7.5$ Hz, $^3J_{\text{HH}} = 7.5$ Hz, 2H) ppm; ^{13}C NMR (CDCl_3) δ 163.8 (d, $^3J_{\text{PC}} = 17.6$ Hz), 158.6 (d, $^2J_{\text{PC}} = 26.7$ Hz), 138.3, 133.9-128.3 (m), 126.0 (d, $^1J_{\text{PC}} = 145.0$ Hz), 114.7, 29.6, 28.2, 27.7, 26.3, 11.6 ppm; ^{31}P NMR (CDCl_3) δ 18.3 ppm; IR (KBr) 3070, 1686, 1600, 1195 cm^{-1} ; MS (EI) m/z 365 (M^+ , 100); Anal. Calcd for $\text{C}_{22}\text{H}_{24}\text{NO}_2\text{P}$: C, 72.31; H, 6.62; N, 3.83. Found C, 72.51; H, 6.60; N, 3.82.

4-(Diphenylphosphinoyl)-5-ethyl-2-phenyloxazole (8bb). (1.23 g, 66%) obtained as a white solid from α -ketamide **5bb** (1.96 g, 5 mmol) as described in the general procedure. mp 164-165 $^{\circ}\text{C}$; ^1H NMR (CDCl_3) δ 7.96-7.35 (m, 15H), 3.10 (dq, $^4J_{\text{PH}} = 1.4$ Hz, $^3J_{\text{HH}} = 7.6$ Hz, 2H), 1.25 (t, $^3J_{\text{HH}} = 7.6$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 163.9 (d, $^2J_{\text{PC}} = 26.7$ Hz), 160.7 (d, $^3J_{\text{PC}} = 18.1$ Hz), 134.0-126.2 (m), 19.5, 13.0; ^{31}P NMR (CDCl_3) δ 18.4 ppm; IR (KBr) 3059, 1819, 1580, 1440, 1188, 1110 cm^{-1} ; MS (EI) m/z 373 (M^+ , 100); Anal. Calcd for $\text{C}_{23}\text{H}_{20}\text{NO}_2\text{P}$: C, 73.98; H, 5.40; N, 3.75. Found C, 73.70; H, 5.38; N, 3.76.

[4-(Diphenylphosphinoyl)-5-ethyl-oxazol-2-yl]acetic acid methyl ester (8bg). (1.07 g, 58%) obtained as a colorless syrup from α -ketamide **5bg** (1.94 g, 5 mmol) as described in the general method: Rf 0.52 (AcOEt); ^1H NMR (CDCl_3) δ 7.86-7.41 (m, 15H), 3.83 (s, 2H), 3.74 (s, 3H), 3.07 (q, $^3J_{\text{HH}} = 7.6$ Hz, 2H), 1.23 (t, $^3J_{\text{HH}} = 7.5$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 167.6, 164.8 (d, $^2J_{\text{PC}} = 26.7$ Hz), 156.3 (d, $^3J_{\text{PC}} = 18.6$ Hz), 133.6-125.3 (m), 52.5, 34.2, 19.3, 12.7; ^{31}P NMR (CDCl_3) δ 18.8 ppm; IR (NaCl) 3065, 1745, 1586, 1434, 1195, 1122 cm^{-1} ; MS (EI) m/z 369 (M^+ , 100); Anal. Calcd for $\text{C}_{20}\text{H}_{20}\text{NO}_4\text{P}$: C, 65.04; H, 5.46; N, 3.79. Found C, 65.10; H, 5.48; N, 3.80.

General procedure for synthesis of α -ketamides derived from phosphonates (12). The carboxylic acid **4** (7.5 mmol) was added to 2*H*-azirinephosphonate **11** (5 mmol) without solvent, under nitrogen atmosphere, at room temperature, and with continuous stirring. The mixture was heated at 70 $^{\circ}\text{C}$ for 2

h. Then, the crude residue was purified by flash-chromatography (silica gel AcOEt/hexanes) affording α -ketamides **12** and a small proportion (15–20%) of pyrazine phosphonates.³⁰

Diethyl (1-benzoylamino-2-oxopropyl)phosphonate (12ab). (0.97 g, 62%) obtained as a white solid from 2*H*-azirinephosphonate **11a** (0.96 g, 5 mmol) and benzoic acid **4b** (0.92 g, 7.5 mmol) as described in the general procedure: mp 45-46 °C; ¹H NMR (CDCl₃) δ 7.71-7.29 (m, 5H), 7.02 (d, ³*J*_{HH} = 7.9 Hz, 1H), 5.39 (dd, ²*J*_{PH} = 23.3 Hz, ³*J*_{HH} = 8.3 Hz, 1H), 4.07 (m, 4H), 2.35 (s, 3H), 1.19 (m, 6H) ppm; ¹³C NMR (CDCl₃) δ 199.7, 166.6 (d, ³*J*_{PC} = 5.4 Hz), 133.3-127.1 (m), 63.6 (d, ²*J*_{PC} = 6.5 Hz), 58.4 (d, ¹*J*_{PC} = 141.0 Hz), 29.0, 16.2 ppm; ³¹P NMR (CDCl₃) δ 20.0 ppm; IR (KBr) 3238, 3065, 2986, 1713, 1660 cm⁻¹; MS (CI) *m/z* 313 (*M*⁺ + 1, 3), 271 (*M*⁺ – CH₂CO, 37); Anal. Calcd for C₁₄H₂₀NO₃P: C, 53.67; H, 6.43; N, 4.47. Found C, 53.80; H, 6.45; N, 4.45.

Diethyl (1-benzoylamino-2-oxobutyl)phosphonate (12bb). (1.28 g, 78%) obtained as a white solid from 2*H*-azirinephosphonate **11b** (0.96 g, 5 mmol) and benzoic acid **4b** (0.92 g, 7.5 mmol) as described in the general procedure: mp 53-54 °C; ¹H NMR (CDCl₃) δ 8.04-7.36 (m, 6H), 5.51 (dd, ²*J*_{PH} = 22.9 Hz, ³*J*_{HH} = 8.4 Hz, 1H), 4.15 (m, 4H), 2.94 (dq, ³*J*_{HH} = 7.2 Hz, ²*J*_{HHgem} = 14.5 Hz, 1H), 2.62 (dq, ³*J*_{HH} = 7.2 Hz, ²*J*_{HHgem} = 14.5 Hz, 1H), 1.25 (m, 6H), 1.06 (t, ³*J*_{HH} = 7.2 Hz, 3H) ppm; ¹³C NMR (CDCl₃) δ 203.0, 166.8 (d, ³*J*_{PC} = 5.0 Hz), 133.2-127.2 (m), 63.5 (d, ²*J*_{PC} = 6.1 Hz), 57.5 (d, ¹*J*_{PC} = 143.6 Hz), 34.9, 16.3, 7.5 ppm; ³¹P NMR (CDCl₃) δ 16.8 ppm; IR (KBr) 3317, 3066, 1725, 1662 cm⁻¹; MS (CI) *m/z* 328 (*M*⁺ + 1, 12), 190 (*M*⁺ – P(O)(OEt)₂, 27), 105 (PhCO⁺, 74) Anal. Calcd for C₁₅H₂₂NO₃P: C, 55.04; H, 6.77; N, 4.28. Found C, 55.09; H, 6.74; N, 4.28.

General procedure for the preparation of diethyl (2,4-dialkylloxazol-4-yl)phosphonates (13). To a room temperature solution of triphenyl phosphine (1.70 g, 6.5 mmol) and hexachloroethane (1.54 g,

6.5 mmol) in toluene (20 ml), was added a solution of α -ketamide **12** (5 mmol) in toluene (5 ml) under nitrogen atmosphere. The mixture was stirred at that temperature for 5 minutes. After that, triethylamine (2.10 ml, 15 mmol) was dropped for 10 minutes. The subsequent mixture was heated at toluene reflux for 20 h. The solvent was evaporated under vacuum and the residue was purified by precipitating in cold ethyl ether. The organic layers were concentrated under vacuum and the subsequent residue was grinded with cold water and filtered. The aqueous layer was concentrated affording compounds **13** as colorless oils.

Diethyl (5-methyl-2-phenyl-oxazol-4-yl) phosphonate (13ab). (0.86 g 58%) obtained as a colorless oil from α -ketamide **12ab** (1.56 g, 5 mmol) as described in the general procedure. Rf 0.60 (AcOEt); ^1H NMR (CDCl_3) δ 7.96-7.21 (m, 5H), 4.08 (q, $^3J_{\text{HH}} = 7.8$ Hz, 4H), 2.53 (d, $^4J_{\text{PH}} = 2.1$ Hz, 3H), 1.24 (t, $^3J_{\text{HH}} = 7.0$ Hz, 6H); ^{13}C NMR (CDCl_3) δ 160.6 (d, $^3J_{\text{PC}} = 22.2$ Hz), 158.20 (d, $^2J_{\text{PC}} = 39.8$ Hz), 130.3-123.4 (m), 62.2 (d, $^2J_{\text{PC}} = 5.5$ Hz), 15.9 (d, $^3J_{\text{PC}} = 6.6$ Hz), 11.2; ^{31}P NMR (CDCl_3) δ 9.7 ppm; IR (NaCl) 3025, 2952, 1750, 1593, 1447, 1024, 956 cm^{-1} ; MS (EI) m/z 295 (M^+ , 45); Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{NO}_4\text{P}$: C, 56.95; H, 6.14; N, 4.74. Found C, 56.80; H, 6.12; N, 4.73.

Diethyl (5-ethyl-2-phenyl-oxazol-4-yl) phosphonate (13bb). (0.96 g, 62%) obtained as a colorless oil from α -ketamide **12bb** (1.60 g, 5 mmol) as described in the general method. Rf 0.61 (AcOEt); ^1H NMR (CDCl_3) δ 8.07-7.42 (m, 5H), 4.14 (m, 4H), 3.09 (dq, $^4J_{\text{PH}} = 1.8$ Hz, $^3J_{\text{HH}} = 7.5$ Hz 2H), 1.36 (t, $^3J_{\text{HH}} = 7.0$ Hz, 6H), 1.33 (t, $^3J_{\text{HH}} = 7.6$ Hz, 3H); ^{13}C NMR (CDCl_3) δ 163.4 (d, $^2J_{\text{PC}} = 39.8$ Hz), 160.9 (d, $^3J_{\text{PC}} = 22.6$ Hz), 128.7-123.0 (m), 62.5 (d, $^2J_{\text{PC}} = 5.5$ Hz), 19.2, 16.2 (d, $^3J_{\text{PC}} = 6.5$ Hz), 12.8; ^{31}P NMR (CDCl_3) δ 9.8 ppm; IR (NaCl) 3065, 2979, 2932, 1724, 1580, 1447, 1162, 1029, 970 cm^{-1} ; MS (EI) m/z 309 (M^+ , 70); Anal. Calcd for $\text{C}_{15}\text{H}_{20}\text{NO}_4\text{P}$: C, 58.25; H, 6.52; N, 4.53. Found C, 58.34; H, 6.54; N, 4.51.

References and Notes

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