An Efficient Approach to the Stereocontrolled Synthesis of Enamides.

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Supporting Information.

Index

Experimental Procedures	1
NMR Data	7

General Information. All reactions were performed in oven-dried glassware under an inert argon atmosphere unless otherwise stated. Anhydrous DMF was purchased from Aldrich Chemical Co. Tetrahydrofuran (THF), diethyl ether, and dichloromethane (DCM) were purified through a Pure Solv 400-5MD solvent purification system (Innovative Technology, Inc). All reagents were used as received, unless otherwise stated. Solvents were evaporated under reduced pressure at 40 °C using a Buchi Rotavapor.

IR spectra were recorded as thin films on NaCl plates using a Jasco FT/IR 4100 Fourier Transform spectrometer. Only significant absorptions ($\nu_{\max}$) are reported in wavenumbers (cm^{-1}) with the following abbreviations used to describe absorption intensity: w, weak; m, medium; s, strong and br, broad.

Proton magnetic resonance spectra (^1H -NMR) were recorded at 400MHz using a Bruker DPX Avance400 instrument. Chemical shifts (δ_{H}) are reported in parts per million (ppm), and are referenced to the residual solvent peak. The order of citation in parentheses is (1) number of equivalent nuclei (by integration), (2) multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet, br = broad), and (3) coupling constant (J) quoted in Hertz to the nearest 0.5Hz. Carbon magnetic resonance spectra (^{13}C) were recorded at 100MHz using a Bruker DPX Avance400 instrument. Chemical shifts (δ_{C}) are quoted in parts per million (ppm) and are referenced to the appropriate solvent peak.

High resolution mass spectra were recorded on a JEOL JMS-700 spectrometer by electrospray ionisation mass spectrometer operating at a resolution of 15000 full widths at half height.

Flash chromatography was performed using silica gel (Apollo Scientific Silica Gel 60, 40-63 micron) as the stationary phase. TLC was performed on aluminium sheets pre-coated with silica (Merck Silica Gel 60 F₂₅₄). The plates were visualised by the quenching of UV fluorescence ($\lambda_{\max}$ 254nm) and/or by staining with either anisaldehyde, potassium permanganate or iodine followed by heating.

Representative Procedures.

General Procedure for the Synthesis of Lactam Derived *N*-Formyl Imides **9, **9a**, **9b**, **9c**, **9d**, and **9e**.** A mixture of formic acid (0.1 mol) and acetic acid (0.1 mol) was heated under argon at 55 °C for 3 hours. The neat lactam (**8-8e**) (0.01 mmol) was then added, and the resulting reaction mixture stirred at 60 °C for 15 hours. The reaction solution was then cooled to room temperature and the excess mixed anhydride removed under vacuum (10 mbar). The resulting crude product was then suspended in ethyl acetate (10 mL) and the resulting solution filtered through a plug of neutral alumina to afford the desired lactam derived *n*-formyl imides **9**, **9a**, **9b**, **9c**, **9d**, and **9e**.

2-Oxo-azetidine-1-carbaldehyde, **9a**.

^1H NMR (400MHz, CDCl_3) δ 8.60 (1H, s), 3.60 (2H, m), 3.10 (2H, m). ^{13}C NMR (100MHz, CDCl_3) δ 166.0, 156.3, 22.1, 20.5. IR $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 2981 (s), 1830 (s), 1652(s). HRMS calcd for $\text{C}_4\text{H}_5\text{O}_2\text{N}$ (M^+): 99.0320. Found 99.0321.

2-Oxo-pyrrolidine-1-carbaldehyde, **9b**.

^1H NMR (400MHz, CDCl_3) δ 9.01 (1H, s), 3.67 (2H, td, $J = 7.3, 0.8$ Hz), 2.54 (2H, t, $J = 7.9$ Hz), 2.07 (2H, m). ^{13}C NMR (100MHz, CDCl_3) δ 176.8, 160.3, 42.1, 32.2, 17.8. IR $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 2905 (s), 1750 (s), 1698 (s), 1351 (s), 1300 (m). HRMS calcd for $\text{C}_5\text{H}_7\text{O}_2\text{N}$ (M^+): 113.0477. Found 113.0479.

2-Oxo-piperidine-1-carbaldehyde, **9**:

^1H NMR (400MHz, CDCl_3) δ : 9.42 (1H, s), 3.55 (2H, bs), 2.55 (2H, bm), 1.80 (4H, bm). ^{13}C NMR (100MHz, CDCl_3) δ : 173.2, 162.8, 41.6, 33.3, 21.7, 19.9. IR $\nu_{\max}(\text{film})/\text{cm}^{-1}$ 2958 (s), 1690 (s), 1717 (s). HRMS calcd for $\text{C}_6\text{H}_{10}\text{O}_2\text{N}$ ($\text{M}+\text{H}^+$): 128.0712. Found 128.0710.

2-Oxo-azepane-1-carbaldehyde, 9c.

^1H NMR (400MHz, CDCl_3) δ : 9.41 (1H, s), 3.81 (2H, m), 2.70 (2H, m), 1.81 (4H, m), 1.71 (2H, m). ^{13}C NMR (100MHz, CDCl_3) δ : 178.1, 162.2, 40.2, 38.3, 29.6, 28.6, 23.6. IR ν_{max} (film)/ cm^{-1} 2986 (s), 1700 (s), 1695 (s). HRMS calcd for $\text{C}_7\text{H}_{12}\text{O}_2\text{N}$ ($\text{M}+\text{H}^+$): 142.0868. Found 142.0870.

2-Oxo-azocane-1-carbaldehyde, 9d.

^1H NMR (400MHz, CDCl_3) δ : 9.39 (1H, s), 3.77 (2H, m), 2.59 (2H, m), 1.85 (2H, m), 1.65 (2H, m), 1.50 (2H, m), 1.45 (2H, m). ^{13}C NMR (100MHz, CDCl_3) δ : 178.3, 162.6, 40.5, 35.0, 29.0, 28.6, 25.8, 24.3. IR ν_{max} (film)/ cm^{-1} 2935 (s), 1652 (s), 1635 (s). HRMS calcd for $\text{C}_8\text{H}_{14}\text{O}_2\text{N}$ ($\text{M}+\text{H}^+$): 156.1025. Found 156.1024.

2-Oxo-azonane-1-carbaldehyde, 9e.

^1H NMR (400MHz, CDCl_3) δ : 9.35 (1H, s), 3.75 (2H, m), 2.61 (2H, m), 1.84 (2H, m), 1.65 (2H, m), 1.55 (2H, m), 1.47 (4H, m). ^{13}C NMR (100MHz, CDCl_3) δ : 178.8, 162.9, 42.3, 36.2, 28.1, 27.1, 25.1 (2C's), 22.5. IR ν_{max} (film)/ cm^{-1} 2932 (s), 1695 (s), 1635 (s). HRMS calcd for $\text{C}_9\text{H}_{16}\text{O}_2\text{N}$ ($\text{M}+\text{H}^+$): 170.1181. Found 170.1182.

General Procedure for the Synthesis of Lactam Derived Enamides 10, 10a, 10b, 10c, 10d and 10e. A solution of the lactam derived *n*-formyl imide (**9-9e**) (1.0 mmol) in benzene (10 mL) was treated with ethoxycarbonylmethylene triphenylphosphorane (3.0 mmol) and the resulting homogeneous mixture heated to 80°C for 18 hours. Once the reaction was complete by TLC analysis, the solvent was then removed *in vacuo* to generate a semi-solid crude residue. Purification of the crude product by flash column chromatography (silica gel, 30% EtOAc in 40-60 petroleum ether) proceeded to generate the desired lactam derived *E*-enamides **10, 10a, 10b, 10c, 10d** and **10e** as a single double bond isomer in each case.

(E)-3-(2-Oxo-azetidin-1-yl)-acrylic acid ethyl ester, 10a.

^1H NMR (400MHz, CDCl_3) δ : 7.65 (1H, d, $J = 14.0$ Hz), 5.20 (1H, d, $J = 14.0$ Hz), 4.12 (2H, q, $J = 7.1$ Hz), 3.45 (2H, t, $J = 4.9$ Hz), 3.09 (2H, t, $J = 4.9$ Hz), 1.20 (3H, t, $J = 7.1$ Hz). ^{13}C NMR (100MHz, CDCl_3) δ : 166.9, 164.9, 134.9, 100.0, 60.3, 38.8, 37.3, 14.3. IR ν_{max} (film)/ cm^{-1} 2983 (s), 1774 (s), 1701 (s), 1632 (s), 1178 (s). HRMS calcd for $\text{C}_8\text{H}_{11}\text{O}_3\text{N}$ (M^+): 169.0739. Found 169.0738.

(E)-3-(2-Oxo-pyrrolidin-1-yl)-acrylic acid ethyl ester, 10b.

^1H NMR (400MHz, CDCl_3) δ : 8.04 (1H, d, $J = 14.3$ Hz), 5.14 (1H, d, $J = 14.2$ Hz), 4.13 (2H, q, $J = 7.1$ Hz), 3.49 (2H, t, $J = 7.2$ Hz), 2.49 (2H, t, $J = 7.9$ Hz), 2.1 (2H, appq, $J = 7.5$ Hz), 1.23 (3H, t, $J = 7.1$ Hz). ^{13}C NMR (100MHz, CDCl_3) δ : 174.2, 167.1, 137.2, 100.8, 60.2, 44.9, 30.9, 17.4, 14.3. IR ν_{max} (film)/ cm^{-1} 2981 (s), 1728 (s), 1699 (s), 1630 (m), 1260 (m), 1159 (m). HRMS calcd for $\text{C}_9\text{H}_{13}\text{O}_3\text{N}$ (M^+): 183.0895. Found 183.0888.

(E)-3-(2-Oxo-piperidin-1-yl)-acrylic acid ethyl ester, 10.

^1H NMR (400MHz, CDCl_3) δ : 8.65 (1H, d, $J = 14.5$ Hz), 5.30 (1H, d, $J = 14.5$ Hz), 4.25 (2H, q, $J = 7.1$ Hz), 3.45 (2H, t, $J = 6.1$ Hz), 2.60 (2H, t, $J = 6.7$ Hz), 1.88 (2H, m), 1.78 (2H, m), 1.30 (3H, t, $J = 7.1$ Hz). ^{13}C NMR (100MHz, CDCl_3) δ : 169.5, 167.4, 140.7, 100.0, 60.1, 45.6, 33.1, 22.4, 20.2, 14.4. IR ν_{max} (film)/ cm^{-1} 2957 (s), 1708 (s), 1683 (s), 1622 (s), 1255 (s), 1159 (m). HRMS calcd for $\text{C}_{10}\text{H}_{15}\text{O}_3\text{N}$ (M^+): 197.1052. Found 197.1050.

(E)-3-(2-Oxo-azepan-1-yl)-acrylic acid ethyl ester, 10c.

¹H NMR (400MHz, CDCl₃) δ: 8.39 (1H, d, *J* = 14.5 Hz), 5.22 (1H, d, *J* = 14.4 Hz), 4.15 (2H, q, *J* = 7.1 Hz), 3.55 (2H, m), 2.64 (2H, m), 1.70 (6H, m), 1.25 (3H, t, *J* = 7.06 Hz). ¹³C NMR (100MHz, CDCl₃) δ: 174.8, 167.7, 140.7, 98.8, 60.0, 45.4, 37.0, 29.1, 27.2, 23.4, 14.3. IR ν_{max}(film)/cm⁻¹ 2936 (s), 1706 (s), 1684 (s), 1621 (s), 1173 (s), 1148 (m). HRMS calcd for C₁₁H₁₇O₃N (M⁺): 211.1208. Found 211.1207.

(E)-3-(2-Oxo-azocan-1-yl)-acrylic acid ethyl ester, 10d.

¹H NMR (400MHz, CDCl₃) δ: 8.45 (1H, d, *J* = 14.6 Hz), 5.25 (1H, d, *J* = 14.6 Hz), 4.15 (2H, q, *J* = 7.1 Hz), 3.75 (2H, m), 2.60 (2H, m), 1.80 (2H, m), 1.65 (2H, m), 1.50 (2H, m), 1.40 (2H, m), 1.22 (3H, t, *J* = 7.1 Hz). ¹³C NMR (100MHz, CDCl₃) δ: 174.6, 167.6, 139.6, 100.2, 60.1, 44.0, 34.5, 29.0, 27.2, 26.1, 24.0, 14.4. IR ν_{max}(film)/cm⁻¹ 2935 (s), 1702 (s), 1678 (s), 1621 (s), 1130 (s). HRMS calcd for C₁₂H₁₉O₃N (M⁺): 225.1365. Found 225.1364.

(E)-3-(2-Oxo-azonan-1-yl)-acrylic acid ethyl ester, 10e.

¹H NMR (400MHz, CDCl₃) δ: 8.45 (1H, d, *J* = 14.6 Hz), 5.21 (1H, d, *J* = 14.6 Hz), 4.14 (2H, q, *J* = 7.1 Hz), 3.74 (2H, m), 2.50 (2H, m), 1.80 (2H, m), 1.70 (2H, m), 1.50 (2H, m), 1.40 (4H, m), 1.25 (3H, t, *J* = 7.1 Hz). ¹³C NMR (100MHz, CDCl₃) δ: 175.5, 167.6, 140.0, 100.3, 60.1, 45.7, 35.2, 28.1, 25.3, 25.2, 25.1, 22.2, 14.4. IR ν_{max}(film)/cm⁻¹ 2931 (s), 1703 (s), 1676 (s), 1620 (s), 1155 (m). HRMS calcd for C₁₃H₂₁O₃N (M⁺): 239.1521. Found 239.1524.

General Procedure for the Synthesis of *N*-Formyl Imides 12a, 12b, and 12c. A solution of the acyclic amide (**11a-11c**) (1 mmol) in anhydrous THF (10 mL) was cooled to 0 °C before being treated with *n*-BuLi (1.1 mmol, 1.6 M solution in hexanes). The reaction was then stirred at 0 °C for 5 minutes before being treated with *N*-formylbenzotriazole (1.2 mmol).¹ The resulting mixture was then allowed to warm up to room temperature and then stirred for a further 2 hours. The reaction was diluted with *t*-butylmethyl ether (10 mL), and quenched with a saturated aq. NaHCO₃ solution (10 mL). The aqueous phase was then extracted with diethyl ether (3 x 20 mL) and the combined organic layers dried over Na₂SO₄. The solvent was removed under vacuum to afford the crude product, which was then purified by flash column chromatography (silica gel, 10% to 20% ethyl acetate in 40-60 petroleum ether) to afford the desired *N*-formyl imides (**12a-12c**).

***N*-Formylbenzamide, 12a:**

¹H NMR (400MHz, CDCl₃) δ: 10.36 (1H, bd, *J* = 7.7 Hz), 9.33 (1H, d, *J* = 9.5 Hz), 7.91 (2H, m), 7.56 (1H, m), 7.46 (2H, m). ¹³C NMR (100MHz, CDCl₃) δ: 165.8, 164.1, 132.9, 130.0, 128.0, 127.1. IR ν_{max}(film)/cm⁻¹ 3414 (m), 1728 (s), 1683 (s), 1463 (s), 1364 (m), 1252 (s), 1208 (s). HRMS calcd for C₈H₇O₂N (M⁺): 149.0477. Found 149.0474.

***N*-Formylnicotinamide, 12b.**

¹H NMR (400MHz, CDCl₃) δ: 10.3 (1H, bs), 9.26 (1H, d, *J* = 10.6 Hz), 8.58 (1H, dm, *J* = 4.8 Hz), 8.19 (1H, dm, *J* = 7.8 Hz), 7.89 (1H, td, *J* = 7.7, 1.7 Hz), 7.53 (1H, ddd, *J* = 7.6, 4.7, 1.1 Hz). ¹³C NMR (100MHz, CDCl₃) δ: 164.4, 161.8, 148.7, 147.1, 137.8, 128.1, 123.3. IR ν_{max}(film)/cm⁻¹ 3347 (s), 2926 (s), 1736 (s), 1697 (s), 1462 (m), 1367 (s), 1183 (m). HRMS calcd for C₇H₆O₂N₂ (M⁺): 150.0427. Found 150.0429.

¹ Katritzky, A. R.; Chang, H.-X.; Yang, B. *Synthesis*, **1995**, 503.

***N*-Formyl-(*R*)-2,2,5,5-tetramethyl-[1,3]dioxane-4-carboxylic acid amide, 12c.**

¹H NMR (400MHz, CDCl₃) δ: 9.08 (1H, d, *J* = 10.4 Hz), 8.80 (1H, bs), 4.12 (1H, s), 3.65 (1H, d, *J* = 11.8 Hz), 3.27 (1H, d, *J* = 11.8 Hz), 1.41 (3H, s), 1.39 (3H, s), 0.99 (3H, s), 0.98 (3H, s). ¹³C NMR (100MHz, CDCl₃) δ: 170.6, 161.4, 99.7, 77.0, 71.1, 33.3, 29.3, 21.7, 18.9, 18.6. IR ν_{max}(film)/cm⁻¹ 3383 (s), 2994 (s), 1744 (s), 1699 (s), 1459 (s), 1096 (m). HRMS calcd for C₁₀H₁₈O₄N (M+H⁺): 216.1236. Found 216.1233. [α]_D +48.0 (c = 1.4, CHCl₃).

General Procedure for the Synthesis of Acyclic Enamides (13a-13c). A solution of *n*-formyl imide (12a-12c) (1.0 mmol) in benzene (10 mL) was treated with ethoxycarbonylmethylene triphenylphosphorane (3.0 mmol) and the resulting mixture heated to 95 °C for 19 hours. Upon reaction completion as indicated by TLC analysis, the solvent was removed under vacuum. The crude residue was then purified by flash column chromatography (silica gel, 10% to 30% EtOAc in 40-60 petroleum ether) to afford the desired enamides (13a-13c).

(*Z*)-3-Benzoylamino-acrylic acid ethyl ester, 13a (*cis*).

¹H NMR (400MHz, CDCl₃) δ: 11.5 (1H, bs), 7.90 (2H, m), 7.68 (1H, dd, *J* = 9.1, 8.8 Hz), 7.53 (1H, m), 7.44 (2H, m), 5.20 (1H, d, *J* = 8.8 Hz), 4.17 (2H, q, *J* = 7.1 Hz), 1.27 (3H, t, *J* = 7.1 Hz). ¹³C NMR (100MHz, CDCl₃) δ: 169.6, 164.5, 138.8, 132.9, 132.2, 128.9, 127.7, 97.2, 60.3, 14.3. IR ν_{max}(film)/cm⁻¹ 3337 (s), 2985 (s), 1679 (s), 1627 (s), 1396 (m), 1381 (m), 1210 (m), 739 (s). HRMS calcd for C₁₂H₁₃O₃N (M⁺): 219.0895. Found 219.0898.

(*E*)-3-Benzoylamino-acrylic acid ethyl ester, 13a (*trans*).

¹H NMR (400MHz, CDCl₃) δ: 8.28 (1H, dd, *J* = 14.1, 11.8 Hz), 8.08 (1H, bd, *J* = 11.8 Hz), 7.88 (2H, m), 7.64 (1H, m), 7.54 (2H, m), 5.65 (1H, d, *J* = 14.1 Hz), 4.25 (2H, q, *J* = 7.1 Hz), 1.33 (3H, t, *J* = 7.1 Hz). ¹³C NMR (100MHz, CDCl₃) δ: 167.3, 164.9, 137.9, 132.9, 132.3, 128.9, 127.5, 102.5, 60.3, 14.4. IR ν_{max}(film)/cm⁻¹ 3400 (s), 2993 (s), 1694 (s), 1639 (s), 1095 (m), 1051 (m), 908 (s). HRMS calcd for C₁₂H₁₃O₃N (M⁺): 219.0895. Found 219.0897.

(*Z*)-3-[(Pyridine-3-carbonyl)-amino]-acrylic acid ethyl ester, 13b (*cis*).

¹H NMR (400MHz, CDCl₃) δ: 12.35 (1H, bs), 8.67 (1H, dm, *J* = 4.7 Hz), 8.18 (1H, dt, *J* = 7.8, 1.0 Hz), 7.83 (1H, td, *J* = 7.7, 1.7 Hz), 7.60 (1H, dd, *J* = 11.9, 8.9 Hz), 7.44 (1H, ddd, *J* = 7.6, 4.7, 1.2 Hz), 5.22 (1H, d, *J* = 8.8 Hz), 4.21 (2H, q, *J* = 7.2 Hz), 1.28 (3H, t, *J* = 7.17 Hz). ¹³C NMR (100MHz, CDCl₃) δ: 168.6, 162.9, 148.9, 148.5, 137.5, 137.0, 127.2, 123.3, 98.4, 60.3, 14.4. IR ν_{max}(film)/cm⁻¹ 3424 (s), 2985 (s), 1688 (s), 1625 (s), 1204 (m), 735 (s). HRMS calcd for C₁₁H₁₂O₃N₂ (M⁺): 220.0848. Found 220.0850.

(*E*)-3-[(Pyridine-3-carbonyl)-amino]-acrylic acid ethyl ester, 13b (*trans*).

¹H NMR (400MHz, CDCl₃) δ: 10.05 (1H, bd, *J* = 10.4 Hz), 8.66 (1H, dm, *J* = 4.8 Hz), 8.29 (1H, dm, *J* = 7.8 Hz), 8.22 (1H, dd, *J* = 14.2, 12.2 Hz), 7.95 (1H, td, *J* = 7.7, 1.7 Hz), 7.57 (1H, ddd, *J* = 7.6, 4.8, 1.2 Hz), 5.76 (1H, d, *J* = 14.2 Hz), 4.26 (2H, q, *J* = 7.1 Hz), 1.35 (3H, t, *J* = 7.12 Hz). ¹³C NMR (100MHz, CDCl₃) δ: 167.3, 162.2, 148.4, 147.9, 137.8, 136.8, 127.39, 123.1, 103.3, 60.25, 14.40. IR ν_{max}(film)/cm⁻¹ 3274 (s), 2971 (s), 1694 (s), 1637 (s), 1498 (s), 1150 (m). HRMS calcd for C₁₁H₁₂O₃N₂ (M⁺): 220.0848. Found 220.0847.

(Z)-3-(((R)-2,2,5,5-Tetramethyl-[1,3]dioxane-4-carbonyl)-amino)-acrylic acid ethyl ester, 13c (cis).

¹H NMR (400MHz, CDCl₃) δ: 11.05 (1H, bs), 7.36 (1H, dd, *J* = 11.8, 8.9 Hz), 5.10 (1H, d, *J* = 8.9 Hz), 4.14 (1H, s), 4.13 (2H, q, *J* = 7.4 Hz), 3.66 (1H, d, *J* = 11.7 Hz), 3.26 (1H, d, *J* = 11.7 Hz), 1.52 (3H, s), 1.40 (3H, s), 1.23 (3H, t, *J* = 7.2 Hz), 0.98 (3H, s), 0.97 (3H, s). ¹³C NMR (100MHz, CDCl₃) δ: 168.7, 168.2, 135.9, 99.3, 98.1, 76.7, 71.3, 60.1, 33.3, 29.3, 21.9, 19.0, 18.6, 14.3. IR $\nu_{\max}$ (film)/cm⁻¹ 3402 (s), 2992 (s), 1690 (s), 1629 (s), 1197 (s), 731 (s). HRMS calcd for C₁₄H₂₃O₅N (M⁺): 285.1576. Found 285.1574.

(E)-3-(((R)-2,2,5,5-Tetramethyl-[1,3]dioxane-4-carbonyl)-amino)-acrylic acid ethyl ester, 13c (trans).

¹H NMR (400MHz, CDCl₃) δ: 8.35 (1H, bd, *J* = 11.8 Hz), 7.91 (1H, dd, *J* = 11.9, 14.2 Hz), 5.25 (1H, d, *J* = 14.2 Hz), 4.13 (1H, s), 4.12 (2H, q, *J* = 7.1 Hz), 3.65 (1H, d, *J* = 11.8 Hz), 3.25 (1H, d, *J* = 11.8 Hz), 1.44 (3H, s), 1.38 (3H, s), 1.21 (3H, t, *J* = 7.1 Hz), 0.98 (3H, s), 0.94 (3H, s). ¹³C NMR (100MHz, CDCl₃) δ: 166.9, 166.1, 134.8, 102.1, 98.5, 77.2, 70.2, 59.1, 32.3, 28.4, 20.8, 17.8, 17.6, 13.3. IR $\nu_{\max}$ (film)/cm⁻¹ 3399 (s), 2993 (s), 1716 (s), 1639 (s), 910 (s), 733 (m). HRMS calcd for C₁₄H₂₃O₅N (M⁺): 285.1576. Found 285.1572. [α]_D +45.6 (c = 0.5, CHCl₃).

General Procedure for the Synthesis of Acyclic Methyl-Enamides (14a-14c). A solution of *n*-formyl imide (**12a-12c**) (1.0 mmol) in benzene (10 mL) was treated with 1-carbethoxyethylidene triphenylphosphorane (3.0 mmol) and the resulting mixture heated to 95 °C for 19 hours. Upon reaction completion as indicated by TLC analysis, the solvent was removed under vacuum. The crude residue was then purified by flash column chromatography (silica gel, 10% to 30% EtOAc in 40-60 petroleum ether) to afford the desired enamides **16c**, **17c** and **18c**.

(Z)-3-Benzoylamino-2-methyl-acrylic acid ethyl ester, 14a (cis).

¹H NMR (400MHz, CDCl₃) δ: 11.40 (1H, d, *J* = 10.8 Hz), 7.87 (2H, m), 7.56 (1H, dd, *J* = 10.9, 1.2 Hz), 7.49 (1H, m), 7.42 (2H, m), 4.20 (2H, q, *J* = 7.1 Hz), 1.85 (3H, d, *J* = 1.3 Hz), 1.29 (3H, t, *J* = 7.1 Hz). ¹³C NMR (100MHz, CDCl₃) δ: 169.0, 168.1, 134.3, 132.3, 131.6, 127.8, 126.5, 104.6, 59.6, 16.3, 13.2.

(E)-3-Benzoylamino-2-methyl-acrylic acid ethyl ester, 14a (trans).

¹H NMR (400MHz, CDCl₃) δ: 8.19 (1H, bd, *J* = 11.7 Hz), 8.10 (1H, dd, *J* = 11.6, 1.2 Hz), 7.73 (2H, m), 7.45 (1H, m), 7.34 (2H, m), 4.09 (2H, q, *J* = 7.14 Hz), 1.82 (3H, d, *J* = 1.3 Hz), 1.20 (3H, t, *J* = 7.1 Hz). ¹³C NMR (100MHz, CDCl₃) δ: 168.1, 164.5, 132.8, 132.7, 131.9, 128.9, 127.3, 109.0, 60.6, 14.4, 10.8. IR $\nu_{\max}$ (film)/cm⁻¹ 3335 (s), 2983 (s), 1684 (s), 1649 (s), 1267 (m), 1133 (s). HRMS calcd for C₁₃H₁₅O₃N (M⁺): 233.1052. Found 233.1053.

(Z)-2-Methyl-3-[(pyridine-3-carbonyl)-amino]-acrylic acid ethyl ester, 14b (cis).

¹H NMR (400MHz, CDCl₃) δ: 8.64 (1H, dm, *J* = 4.8 Hz), 8.17 (1H, dt, *J* = 7.8, 1.1 Hz), 7.82 (1H, td, *J* = 7.7, 1.7 Hz), 7.49 (1H, dq, *J* = 11.8, 1.3 Hz), 7.41 (1H, ddd, *J* = 7.6, 4.7, 1.1 Hz), 4.25 (2H, q, *J* = 7.2 Hz), 1.87 (3H, d, *J* = 1.3 Hz), 1.20 (3H, t, *J* = 7.1 Hz). ¹³C NMR (100MHz, CDCl₃) δ: 167.9, 161.3, 147.9, 147.8, 136.3, 132.4, 125.8, 122.1, 105.9, 59.5, 15.5, 13.3. IR $\nu_{\max}$ (film)/cm⁻¹ 3391 (s), 2963 (s), 1694 (s), 1632 (s), 996 (s). HRMS calcd for C₁₂H₁₄O₃N₂ (M⁺): 234.1004. Found 234.1007.

(E)-2-Methyl-3-[(pyridine-3-carbonyl)-amino]-acrylic acid ethyl ester, 14b (*trans*).

¹H NMR (400MHz, CDCl₃) δ: 9.87 (1H, d, *J* = 12.4 Hz), 8.52 (1H, dm, *J* = 4.8 Hz), 8.14 (1H, dm, *J* = 7.8 Hz), 8.06 (1H, dq *J* = 12.5, 1.3 Hz), 7.82 (1H, td, *J* = 7.7, 1.6 Hz), 7.45 (1H, ddd, *J* = 7.6, 4.7, 1.2 Hz), 4.15 (2H, q, *J* = 7.1 Hz), 1.89 (3H, d, *J* = 1.4 Hz), 1.22 (3H, t, *J* = 7.1 Hz). ¹³C NMR (100MHz, CDCl₃) δ: 168.2, 161.7, 148.4, 148.3, 137.7, 131.05, 127.2, 123.0, 109.9, 60.52, 14.43, 10.84. IR ν_{max}(film)/cm⁻¹ 3367 (s), 2986 (s), 1692 (s), 1652 (s), 1498 (s), 1265 (m). HRMS calcd for C₁₂H₁₄O₃N₂ (M⁺): 234.1004. Found 234.1006.

(Z)-2-Methyl-3-[(*R*)-2,2,5,5-tetramethyl-[1,3]dioxane-4-carbonyl)-amino]-acrylic acid ethyl ester, 14c (*cis*).

¹H NMR (400MHz, CDCl₃) δ: 10.9 (1H, bd, *J* = 12.4 Hz), 7.26 (1H, dd, *J* = 11.5, 1.3 Hz), 4.18 (2H, qd, *J* = 7.2, 1.4 Hz), 4.13 (1H, s), 3.66 (1H, d, *J* = 11.7 Hz), 3.26 (1H, d, *J* = 11.7 Hz), 1.79 (3H, d, *J* = 1.3 Hz), 1.51 (3H, s), 1.39 (3H, s), 1.25 (3H, t, *J* = 7.1 Hz), 0.98 (3H, s), 0.96 (3H, s). ¹³C NMR (100MHz, CDCl₃) δ: 167.6, 167.3, 131.3, 105.5, 98.2, 75.7, 70.4, 60.1, 32.2, 28.4, 20.9, 18.0, 17.6, 15.4, 13.4.

(E)-2-Methyl-3-[(*R*)-2,2,5,5-tetramethyl-[1,3]dioxane-4-carbonyl)-amino]-acrylic acid ethyl ester, 14c (*trans*).

¹H NMR (400MHz, CDCl₃) δ: 8.25 (1H, bd, *J* = 12.3), 7.86 (1H, dq, *J* = 12.3, 1.4 Hz), 4.14 (1H, s), 4.10 (2H, qd, *J* = 7.2, 1.2 Hz), 3.64 (1H, d, *J* = 11.8 Hz), 3.22 (1H, d, *J* = 11.8 Hz), 1.71 (3H, d, *J* = 1.4 Hz), 1.41 (3H, s), 1.39 (3H, s), 1.25 (3H, t, *J* = 7.1 Hz), 0.97 (3H, s), 0.91 (3H, s). ¹³C NMR (100MHz, CDCl₃) δ: 168.0, 167.4, 130.1, 109.2, 99.3, 77.2, 71.2, 60.5, 33.2, 29.4, 21.8, 18.8, 18.6, 14.38, 10.4. IR ν_{max}(film)/cm⁻¹ 3410 (s), 2992 (s), 1695 (s), 1652 (s). HRMS calcd for C₁₅H₂₅O₅N (M⁺): 299.1733. Found 1735. [α]_D +40.7 (c = 1.1, CHCl₃).

2-Oxo-azetidine-1-carbaldehyde, 9a.

User - Matthew Villa
MV2-10Apure 4 members
PROTON CDCl3 u matvil 49

User - Matthew Villa
MV2-10Apure 4 members
C13CPD_A3.q1a CDCl3 u matvil 49

2-Oxo-pyrrolidine-1-carbaldehyde, 9b.

User - Matthew Villa
C13CPD_A3.q1a CDCl₃ u matvil 30

2-Oxo-piperidine-1-carbaldehyde, 9.

2-Oxo-azepane-1-carbaldehyde, 9c.

2-Oxo-azocane-1-carbaldehyde, 9d.

2-Oxo-azonane-1-carbaldehyde, 9e.

(E)-3-(2-Oxo-azetidin-1-yl)-acrylic acid ethyl ester, 10a.

(E)-3-(2-Oxo-pyrrolidin-1-yl)-acrylic acid ethyl ester, 10b.

(E)-3-(2-Oxo-piperidin-1-yl)-acrylic acid ethyl ester, 10.

(E)-3-(2-Oxo-azepan-1-yl)-acrylic acid ethyl ester, 10c.

(E)-3-(2-Oxo-azocan-1-yl)-acrylic acid ethyl ester, 10d.

(E)-3-(2-Oxo-azonan-1-yl)-acrylic acid ethyl ester, 10e.

N-Formylbenzamide, 12a.

(Z)-3-Benzoylamino-acrylic acid ethyl ester, 13a (*cis*).

(E)-3-Benzoylamino-acrylic acid ethyl ester, 13a (*trans*).

(Z)-3-Benzoylamino-2-methyl-acrylic acid ethyl ester, 14a (*cis*).

(E)-3-Benzoylamino-2-methyl-acrylic acid ethyl ester, 14a (*trans*).

***N*-Formylnicotinamide, 12b.**

(Z)-3-[(Pyridine-3-carbonyl)-amino]-acrylic acid ethyl ester, 13b (*cis*).

(E)-3-[(Pyridine-3-carbonyl)-amino]-acrylic acid ethyl ester, 13b (*trans*).

(Z)-2-Methyl-3-[(pyridine-3-carbonyl)-amino]-acrylic acid ethyl ester, 14b (*cis*).

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MV2-88Bpe2
PROTON CDCl3 u matvil 32

(E)-2-Methyl-3-[(pyridine-3-carbonyl)-amino]-acrylic acid ethyl ester, 14b (trans).

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MV2-88Bps3
PROTON CDCl3 v matvil 26

168.220
161.734
148.411
148.323
137.772
131.050
127.224
123.014
108.899

77.386
77.070
76.752

60.519

14.435
10.835

User - Matthew Villa
MV2-88Bps3
C13CFD_A3.gia CDCl3 v matvil 7

***N*-Formyl-2,2,5,5-(*R*)-tetramethyl-[1,3]dioxane-4-carboxylic acid amide, 12c.**

(Z)-3-(((R)-2,2,5,5-Tetramethyl-[1,3]dioxane-4-carbonyl)-amino)-acrylic acid ethyl ester, 13c
(*cis*).

(E)-3-[(R)-2,2,5,5-Tetramethyl-[1,3]dioxane-4-carbonyl)-amino]-acrylic acid ethyl ester, 13c (trans).

(Z)-2-Methyl-3-[(*R*)-2,2,5,5-tetramethyl-[1,3]dioxane-4-carbonyl]-amino]-acrylic acid ethyl ester, 14c (*cis*).

(*E*)-2-Methyl-3-[(*R*)-2,2,5,5-tetramethyl-[1,3]dioxane-4-carbonyl)-amino]-acrylic acid ethyl ester, 14c (*trans*).