Supporting Information for:

Unprotected Vinyl Aziridines: Facile Synthesis and Cascade Transformations

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Experimental Procedures:

General Information: Chemicals were obtained from Aldrich and Alfa-Aesar. Anhydrous toluene was purchased and used as received. Tetrahydrofuran (THF) was distilled from sodium benzophenone ketyl under argon. Dichloromethane was distilled over calcium hydride under nitrogen. All other solvents were of reagent grade quality. Melting points were obtained on a MelTemp melting-point apparatus and are uncorrected.

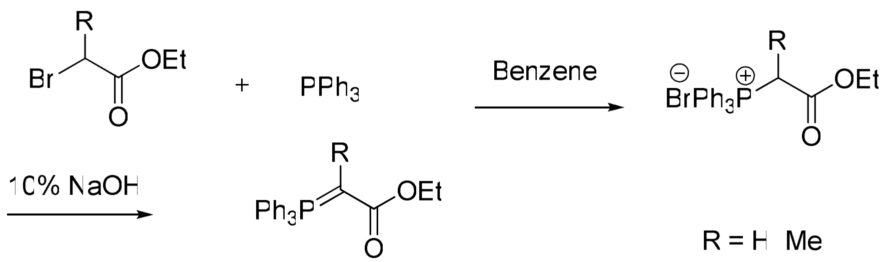
Chromatography: Flash column chromatography was carried out using Silicycle 230- 400 mesh silica gel and thin-layer chromatography (TLC) was performed on Macherey Nagel pre-coated glass backed TLC plates (SIL G/UV254, 0.25 mm) and visualized using a UV lamp (254 nm) or by using either I_2 chamber in case of no UV activity.

Nuclear magnetic resonance spectra: ^{1}H NMR and ^{13}C NMR spectra were recorded on Varian or Mercury 400 MHz spectrometers. ^{1}H NMR spectra were referenced to TMS (0 ppm) and ^{13}C NMR spectra were referenced to $CDCl_3$ (77.2 ppm) or CD_3OD (49.15). Peak multiplicities are designated by the following abbreviations: s, singlet; bs, broad singlet; d, doublet; t, triplet; q, quartet; m, multiplet; dd, doublet of doublets; td, triplet of doublets, dq doublet of quartet; sxt, sextet.

Mass Spectroscopy: High resolution mass spectra were obtained on a VG 70-250S (double focusing) mass spectrometer at 70 eV or on an ABI/Sciex Qstar mass spectrometer with ESI source, MS/MS and accurate mass capabilities.

The amino aldehydes were synthesized using our reported procedure.[1]

Preparation of Stabilized Wittig Salts

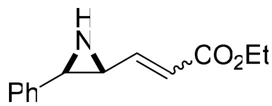


To a solution of triphenylphosphine (7 g, 27.0 mmol) in 30 mL benzene, was added ethyl-2-bromoacetate (3 mL, 27 mmol), and the mixture was heated overnight in pressure tube. The resulting precipitate was collected by filtration and redissolved in a minimal amount of CH_2Cl_2. With stirring, fresh CH_2Cl_2 (50 mL) was added dropwise using a funnel to reprecipitate the product. The precipitate was collected by filtration, and washed with 50 mL CH_2Cl_2. The precipitate was then dissolved in 50 mL CH_2Cl_2, and transferred to a separatory funnel. Aqueous 10% NaOH was added, and the separatory funnel was shaken vigorously to ensure complete mixing. During this step, the CH_2Cl_2 layer developed a bright yellow color, while the aqueous layer became cloudy white. The CH_2Cl_2 layer was collected, dried with $MgSO_4$, filtered, and evaporated to give the desired Wittig reagent as a yellow solid, which could be stored in the dark at room temperature in a closed container.

General procedure for the construction of vinyl aziridines from amino aldehydes:

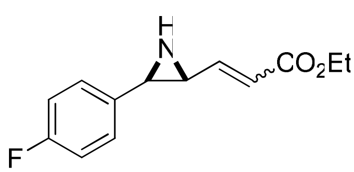
To a solution of the stabilized Wittig reagent (0.22 mmol) in 1 mL TFE (trifluroethanol), aziridine aldehyde (0.1 mmol) was added. The reaction was allowed to stir, until TLC analysis (30% EtOAc/Hexanes) indicated that aziridine aldehyde was fully consumed. Solvent was evaporated, and the residue was redissolved in a small amount of CH_2Cl_2, and loaded onto a silica column. Elution with 30% EtOAc/Hexanes, gave the desired product.

Ethyl 3-(3-phenylaziridin-2-yl)acrylate (3a)



(***E***)**-Ethyl 3-(3-phenylaziridin-2-yl)acrylate;** Yield: 95% (contains20 % of *cis* isomer)**;** Yellow viscous oil; TLC R_f = 0.7 (30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, CD_3OD) δ: 7.34-7.22(m, 5H), 6.64(dd, *J* = 15.6 Hz, 9.6 Hz, 1H), 6.16(d, *J* = 15.2 Hz, 1H), 4.84(HDO, 1H), 4.18(q, *J* = 7.2 Hz, 2H), 3.15 (bs, 1H), 2.68(bs, 1H), 1.27(t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ: 166.4, 147.7, 138.4, 128.4, 127.4, 125.8, 122.1, 60.4, 42.1, 40.7, 13.3 ppm. **(Z)-ethyl 3-(3-phenylaziridin-2-yl)acrylate;** TLC R_f = 0.65 (30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, CD_3OD) δ: 7.34-7.22(m, 5H), 5.94(d, *J* = 11.2 Hz,1H), 5.84(dd, *J* = 11.2 Hz, 9.2 Hz, 1H), 4.84(HDO, 1H), 4.14(q, *J* = 7.2 Hz, 2H), 3.09 (bs, 1H), 2.68(bs, 1H), 1.22(t, *J* = 7.2 Hz, 3H) ppm.

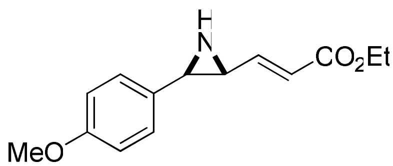
Ethyl 3-(3-(4-fluorophenyl)aziridin-2-yl)acrylate (3b)



(***E***)**-ethyl 3-(3-(4-fluorophenyl)aziridin-2-yl)acrylate;**Yield: 85% (contains20% of *cis* isomer)**;** Viscous oil; TLC R_f = 0.6 (30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, CD_3OD) δ: 7.31-7.25(m, 2H), 7.07-7.01(m, 2H), 6.64 (dd, *J* = 15.6Hz, 9.2 Hz, 1H), 6.16(d, *J* = 15.6 Hz, 1H), 4.84(HDO, 1H), 4.18(q, *J* = 7.2 Hz, 2H), 3.20 (bs, 1H), 2.59 (bs, 1H), 1.27 (t, *J* = 6.8 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ: 166.4, 163.7, 161.3, 147.6, 134.5, 127.7, 122.2, 115.19 (d), 60.4, 42.3, 40.5, 13.3 ppm. **(Z)-ethyl 3-(3-(4-fluorophenyl)aziridin-2-yl)acrylate:** TLC R_f = 0.5 (7:3 hexanes/EtOAc); ^{1}H NMR (400 MHz, CD_3OD) δ: 7.31-7.25(m, 2H), 7.07-7.01(m, 2H), 5.94 (d, *J* = 11.6Hz,1H), 5.83(d, *J* = 11.6 Hz, 9.6 Hz, 1H), 4.84(HDO, 1H), 4.13(q, *J* = 7.2 Hz, 2H), 3.11

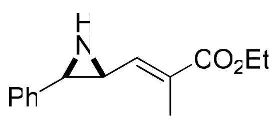
(bs, 1H), 2.59 (bs, 1H), 1.23 (t, *J* = 6.8 Hz, 3H) ppm; HRMS (ESI) $[M]^+$ calcd. For $C_{13}H_{14}FNO_2$ 235.1009 found 235.1008.

(*E*)-Ethyl 3-(3-(4-methoxyphenyl)aziridin-2-yl)acrylate (3c)



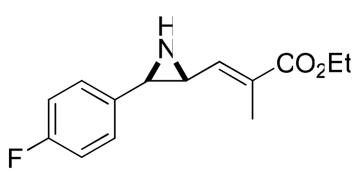
Yield: 65% (containstrace amount of *cis* isomer)**;** Yellow oil; TLC R_f = 0.5 (30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, CD_3OD) δ: 7.19-7.17(m, 2H), 6.88-6.85(m, 2H), 6.63(dd, *J* = 15.6Hz, 8.8 Hz, 1H), 6.15(d, *J* = 15.6 Hz, 1H), 4.84(HDO, 1H), 4.17(q, *J* = 7.2 Hz, 2H), 3.75(s, 3H), 3.15 (bs, 1H), 2.60(bs, 1H), 1.27(t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ: 166.4, 161.2, 147.9, 130.2, 127.1, 121.9, 114.0, 60.4, 54.5, 42.0, 40.8, 13.3 ppm; HRMS (ESI) $[M]^+$ calcd. For $C_{14}H_{17}NO_3$ 247.1208 found 247.1206.

(*E*)-ethyl 2-methyl-3-(3-phenylaziridin-2-yl)acrylate (3d)



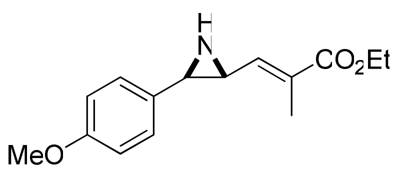
Yield: 95% (containstrace amount of *cis* isomer); Yellow viscous oil; TLC R_f = 0.65 (30% EtOAc /hexanes); ^{1}H NMR (400 MHz, CD_3OD) δ:7.32-7.21(m, 5H), 6.37(dq, *J* = 9.6Hz, 1.2Hz, 1H), 4.83 (HDO, 1H), 4.17(q, *J* = 7.2 Hz, 2H), 3.12(bs, 1H) 2.76(bs, 1H), 1.94(d, *J* = 1.2 Hz, 3H), 1.27(t, *J* = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ:167.7, 140.6, 138.6, 130.1, 128.4, 127.3, 125.8, 60.7, 41.2, 39.5, 13.4, 11.6 HRMS (ESI) $[M+H]^+$ calcd. For $C_{14}H_{18}NO_2$ 232.1332 found 232.1336.

(*E*)-ethyl 3-(3-(4-fluorophenyl)aziridin-2-yl)-2-methylacrylate (3e)



Yield: 80% (contains trace amount of *cis* isomer); Viscous oil; TLC R_f = 0.5 (30% EtOAc/Hexanes); ^{1}H NMR (400 MHz, CD_3OD) δ: 7.31-7.28(m, 2H), 7.06-7.02(m, 2H), 6.37(dq, *J* = 9.6 Hz, 1.2 Hz, 1H), 4.84 (HDO, 1H), 4.18(q, *J* = 7.2 Hz, 2H), 3.19(bs, 1H), 2.67 (bs, 1H), 1.95(d, *J* = 1.2 Hz, 3H), 1.28(t, *J* = 7.2 Hz, 3H). ^{13}C NMR (100 MHz, CD_3OD) δ:167.7, 163.7, 161.3, 140.5, 134.9, 130.2, 127.7, 115.2 (d), 60.7, 40.3, 39.8, 13.4, 11.6; HRMS (ESI) $[M]^+$ calcd. For $C_{14}H_{16}NO_2F$ 249.1165 found 249.1164.

(*E*)-ethyl 3-(3-(4-methoxyphenyl)aziridin-2-yl)-2-methylacrylate(3f)

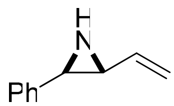


Yield: 63% (contains trace amount of *cis* isomer)**;** Yellow oil; TLC R_f = 0.45 (30% EtOAc/Hexanes);^{1}H NMR (400 MHz, CD_3OD) δ:7.21-7.17(m, 2H), 6.91-6.86(m, 2H), 6.37(dq, *J* = 9.6, 1.2 Hz, 1H), 4.84(HDO, 1H), 4.18(q, *J* = 7.2 Hz, 2H), 3.77(s, 3H), 3.09 (bs, 1H), 2.76(bs, 1H), 1.96(d, *J* = 1.6 Hz, 3H), 1.28(t, 7.2Hz, 3H); ^{13}C NMR (100 MHz, CD_3OD) δ:167.8, 159.5, 140.8, 129.98, 129.1, 126.9, 113.8, 60.7, 54.5, 40.9, 39.2, 13.3, 11.6 ppm. HRMS (ESI) $[M]^+$ calcd. For $C_{15}H_{19}NO_3$ 261.1365 found 261.1360.

General procedure for the construction of unsubstituted vinyl aziridines from amino aldehydes:

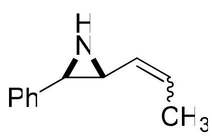
t-BuOK (9.18 mmol, 1M) was added to a stirred suspension of triphenylphosphonium bromide salt (8.16 mmol) in dry THF (20 mL) at 0 °C. The mixture was stirred for 10 min. Afterward, to the resulting red suspension of the ylide, amino aldehyde (2.04 mmol) in THF (5 mL) was added via syringe at room temperature. The mixture was stirred for 1h at that temperature and quenched by the successive addition of a saturated solution of NH_4Cl (10 mL). The suspension was diluted with Et_2O, and the two layers were separated. The aqueous layer was extracted with Et_2O. The combined organic phases were washed with brine, dried with Na_2SO_4, and evaporated under reduced pressure. The resulting residue was purified by flash chromatography on silica gel. Elution with 20 % EtOAc/ Hexanes, delivered the compound.

2-phenyl-3-vinylaziridine (5a)



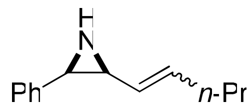
Yield: 86%; Yellow solid at -4 ºC; TLC R_f = 0.6 (7:3 hexanes/EtOAc); ^{1}H NMR (400 MHz, CD_3OD) δ: 7.32-7.19(m, 5H), 5.60(dddd, *J* = 17.2Hz, 10.4Hz, 8.4Hz, 1.6Hz, 1H), 5.38 (ddd, *J* = 17.2Hz, 1.6Hz, 0.4Hz, 1H), 5.16(ddd, 10.4Hz, 1.6Hz, 0.8Hz, 1H),4.85 (HDO, 1H), 2.96(d, *J* = 2.4Hz, 1H), 2.55(d, *J* = 6.4 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ: 139.0, 137.62, 128.31, 127.16, 125.7, 116.1, 43.5, 40 ppm. HRMS (ESI) $[M+H]^+$ calcd. For $C_{10}H_{12}N$ 146.0964 found 146.0971.

2-phenyl-3-(prop-1-enyl)aziridine (5b)



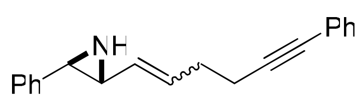
(*Z*) -2-phenyl-3-(prop-1-enyl)aziridine: Yield: 85% (contains 25% of *trans* isomer as inseperable mixture); Yellow oil; TLC R_f = 0.65 (hexanes/ EtOAc); ^{1}H NMR (400 MHz, CD_3OD) δ: 7.30-7.16(m, 5H), 5.71-5.62(m, 1H), 5.08 (ddq, *J* = 12.4 Hz, 8.8 Hz, 1.6 Hz, 1H) 4.85 (HDO, 1H), 2.92 (d, *J* = 2.8Hz, 1H), 2.75(d, *J* = 7.2 Hz, 1H) 1.73 (dd, *J* = 6.8Hz, 1.6 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ: 139.3, 129.5, 128.3, 127.8, 127.1, 125.7, 40.6, 38.5, 12.3 ppm. **(*E*) -2-phenyl-3-(prop-1-enyl)aziridine** ^{1}H NMR (400 MHz, CD_3OD) δ: 7.30-7.16(m, 5H), 5.85-5.78(m, 1H), 5.21 (ddq, *J* = 15.2 Hz, 8.4 Hz, 1.6 Hz, 1H) 4.85 (HDO, 1H), 2.89 (d, *J* = 2.8Hz, 1H), 2.49(d, *J* = 6.0 Hz, 1H), 1.69 (dd, *J* = 6.4Hz, 1.6 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ: 139.3, 130.4, 128.3, 128.2, 127.0, 125.7, 42.97, 40.5, 16.9 ppm. HRMS (ESI) $[M]^+$ calcd. For $C_{11}H_{13}N$ 159.1048 found 159.1045.

2-(pent-1-enyl)-3-phenylaziridine (5c)



(*Z*)-2-(pent-1-enyl)-3-phenylaziridine; Yield 80% (contains 20% of trans isomer as inseparable isomer); Yellow oil; TLC R_f = 0.7 (30% EtOAc/ hexanes); ^{1}H NMR (400 MHz, CD_3OD) δ: 7.32-7.19 (m, 5H), 5.65-5.58(m, 1H), 5.10 (ddt, *J* = 11.2Hz, 8.8 Hz, 1.2 Hz, 1H), 4.85 (HDO, 1H), 2.93(bs, 1H), 2.73(d, *J* = 6.0 Hz 1H), 2.24-2.09(m, 2H), 1.40 (sxt, *J* = 7.6 Hz, 2H), 0.90 (t, *J* = 7.6 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ: 139.3, 133.5, 129.0, 128.3, 127.1, 125.7, 40.7, 38.9, 29.6, 22.6, 12.8 ppm. **(*E*)-2-(pent-1-enyl)-3-phenylaziridine:** ^{1}H NMR (400 MHz, CD_3OD) δ: 7.32-7.19 (m, 5H), 5.85-5.78(m, 1H), 5.22 (ddt, *J* = 13.2 Hz, 8.4 Hz, 1.2 Hz, 1H), 4.85 (HDO, 1H), 2.93 (bs, 1H), 2.52(d, *J* = 8.0 Hz 1H), 2.07-2.01 (m, 2H), 1.40 (sxt, *J* = 7.6 Hz, 2H), 0.90 (t, *J* = 7.6 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ: 139.3, 133.6, 129.5, 128.3, 127.0, 125.7, 43.0, 40.6, 34.4, 22.3, 12.9 ppm. HRMS (ESI) $[M+H]^+$ calcd. For $C_{13}H_{18}N$ 188.1433 found 188.1441.

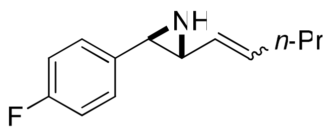
2-phenyl-3-(6-phenylhex-1-en-5-ynyl)aziridine (5d)



(*Z*)-2-phenyl-3-(6-phenylhex-1-en-5-ynyl)aziridine; Yield 70% (contains 10% of trans isomer as inseparable mixture); Viscous oil; TLC R_f = 0.5 (30% EtOAc/ hexanes);^{1}H NMR (400 MHz, CD_3OD) δ: 7.29-7.18(m, 10H), 5.76-5.69(m, 1H), 5.21(dd, *J* = 10.4 Hz, 8.8Hz), 4.83(HDO, 1H), 2.94(bs, 1H), 2.82(d, *J* = 7.24 Hz, 1H), 248-2.46(m, 4H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ: 139.1, 131.8, 131.3, 130.2, 128.3, 128.1, 127.4, 127.1, 125.8, 124.1, 88.8, 80.9, 40.8, 38.7, 27.0, 19.1 **(*E*)- 2-phenyl-3-(6-phenylhex-1-en-5-ynyl)aziridine**: ^{1}H NMR (400 MHz, CD_3OD)

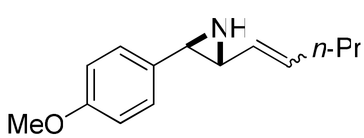
δ: 7.29-7.18(m, 10H), 5.95-5.87(m, 1H), 5.32(ddd, J = 15.2 Hz, 8.4 Hz, 1.2 Hz), 4.83(HDO, 1H), 2.92(bs, 1H), 2.82(d, J = 7.24 Hz, 1H), 236-2.30(m, 4H) ppm. HRMS (ESI) $[M]^+$ calcd. For $C_{20}H_{19}N$ 273.1517 found 273.1524.

2-(4-fluorophenyl)-3-(pent-1-enyl)aziridine (5e)



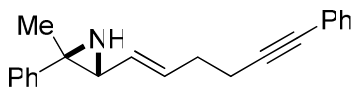
(*Z*)-2-(4-fluorophenyl)-3-(pent-1-enyl)aziridine; Yield 80% (contains 20% of trans isomer as inseparable mixture); Viscous oil; TLC R_f = 0.6 (30% EtOAc/ hexanes)^{1}H NMR (400 MHz, CD_3OD) δ: 7.25-7.20 (m, 2H), 7.04-6.98(m, 2H), 5.65-5.58(m, 1H), 5.07 (ddt, J = 10.4Hz, 9.2 Hz, 1.2 Hz, 1H), 4.83 (HDO, 1H), 2.94(bs, 1H), 2.69(d, J = 8.0 Hz 1H), 2.24-2.09(m, 2H), 1.42 (sxt, J = 7.6 Hz, 2H), 0.90 (t, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ: 163.5, 161.1, 133.6, 129.3, 128.8, 127.5(d), 115.1 (d), 39.9, 38.8, 29.5, 22.6, 12.7ppm. **(*E*)-2-(pent-1-enyl)-3-phenylaziridine:** ^{1}H NMR (400 MHz, CD_3OD) δ: 7.25-7.20 (m, 2H), 7.04-6.98(m, 2H), 5.86-5.79(m, 1H), 5.19 (ddt, J = 15.6 Hz, 8.4 Hz, 1.2 Hz, 1H), 4.85 (HDO, 1H), 2.94 (d, J = 2.0 Hz,1H), 2.49(d, J = 8.0 Hz 1H), 2.06-2.01 (m, 2H), 1.40 (sxt, J = 7.6 Hz, 2H), 0.90 (t, J = 7.6 Hz, 3H) ppm. HRMS (ESI) $[M]^+$ calcd. For $C_{13}H_{16}FN$ 205.1267 found 205.1272.

2-(4-methoxyphenyl)-3-(pent-1-enyl)aziridine(5f)



(*Z*)-2-(pent-1-enyl)-3-phenylaziridine; Yield 65% (containstrace amount of trans isomer); Yellow viscous oil; TLC R_f = 0.75 (30% EtOAc/ hexanes); ^{1}H NMR (400 MHz, CD_3OD) δ: 7.18-7.13 (m, 2H), 6.88-6.85(m, 2H), 5.65-5.59(m, 1H), 5.09 (ddt, J = 10.0Hz, 9.2 Hz, 1.2 Hz, 1H), 4.85 (HDO, 1H), 3.77 (s, 3H), 2.89(d, J = 2.8 Hz, 1H), 2.73(d, J = 9.2 Hz 1H), 2.26-2.11(m, 2H), 1.42 (sxt, J = 7.6 Hz, 2H), 0.92 (t, J = 7.6 Hz, 3H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ: 159.3, 133.3, 131.0, 129.1, 126.8, 113.8, 54.5, 40.4, 38.4, 29.6, 22.6, 12.8 ppm. **(*E*)-2-(pent-1-enyl)-3-phenylaziridine:** ^{1}H NMR (400 MHz, CD_3OD) δ: 7.18-7.13 (m, 2H), 6.88-6.85(m,2H), 5.86-5.79(m, 1H), 5.20 (ddt, *J* = 14.8Hz, 8.4 Hz, 1.2 Hz, 1H), 4.85 (HDO, 1H), 3.76(s, 3H), 2.87(d, *J* = 2.8 Hz, 1H), 2.51(d, *J* = 9.2 Hz 1H), 2.11-2.02(m, 2H), 1.42 (sxt, *J* = 7.6 Hz, 2H), 0.92 (t, *J* = 7.6 Hz, 3H) ppm. HRMS (ESI) $[M]^+$ calcd. For $C_{14}H_{19}NO$ 217.1467 found 217.1469.

(*Z*)-2-methyl-2-phenyl-3-(6-phenylhex-1-en-5-ynyl)aziridine (5g)

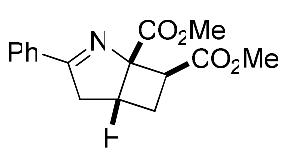


Yield: 65% (contains10% of *trans* isomer); Viscous oil; TLC R_f = 0.45 (7:3 hexanes/EtOAc); ^1H NMR (400 MHz, CD_3OD) δ: 7.35-7.19 (m, 10H), 5.89-5.83(m, 1H), 5.46(dd, *J* = 10.8 Hz, 8.0Hz, 1H), 4.83(HDO, 1H), 2.92(d, *J* = 7.6 Hz, 1H), 256-2.48(m, 4H), 1.49(s, 3 H) ppm; ^{13}C NMR (100 MHz, CD_3OD) δ: 144.4, 133.3, 131.3, 128.4, 128.1, 127.5, 127.3, 126.9, 126.0, 124.1, 88.9, 80.9, 43.7, 41.1, 27.2, 19.9, 19.0 ppm. (HRMS (ESI) $[M+H]^+$ calcd. For $C_{21}H_{22}N$ 288.1746 found 288.1760.

General procedure for the one-pot synthesis of heterobicycles from vinyl aziridines:

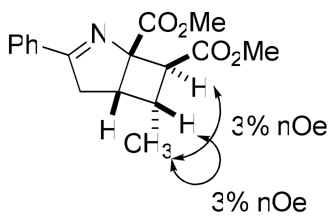
In a flame dried vial equipped with rubber septum attached to a N_2 source and a magnetic stirring bar was added vinyl aziridine (0.068 mmol) dissolved in 750 μL of DMSO-d_6. DMAD (dimethylacetylene dicarboxylate) was added dropwise to the above reaction vial. The resulting mixture was stirred for 3-12 hours, at which point ESI MS showed disappearance of the starting material. The crude NMR showed complete conversion of the cis isomer to the bicyclic compound. A few drops of water was then added and the solution was extracted with diethyl ether three times. The organic layer was concentrated and subjected to flash column chromatography (silica gel; 30% EtOAc/ hexanes) to afford the pure bicyclic compounds.

Dimethyl 3-phenyl-2-aza-bicyclo[3.2.0]hept-2-ene-1,7-dicarboxylate (8a)



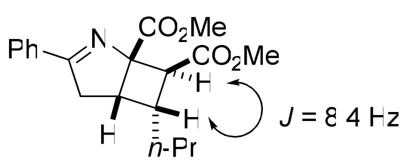
Yield: 70%; White Solid; m.p. 122-125 °C; R_f = 0.4 (7:3 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.95-7.93 (m, 2H), 7.51-7.41 (m, 3H), 3.75(s, 3H), 3.74 (s, 3H), 3.45-3.29(m, 3H), 3.05-2.97(m, 1H), 2.67-2.60 (m, 1H), 1.82-1.75 (m, 1H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 176.3, 173.2, 171.2, 133.9, 131.6, 128.7, 128.7, 85.7, 52.6, 52.2, 49.2, 44.4, 36.8, 26.5 ppm. HRMS (ESI) $[M+H]^+$ calcd. For $C_{16}H_{18}NO_4$ 288.1241 found 288.1246.

Dimethyl 6-methyl-3-phenyl-2-aza-bicyclo[3.2.0]hept-2-ene-1,7-dicarboxylate(8b)



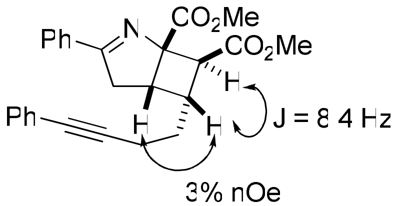
Yield: 68%; Viscous oil; TLC R_f = 0.43 (7:3 hexanes/EtOAc);^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.97-7.94 (m, 2H), 7.50-7.41 (m, 3H), 3.77(s, 3H), 3.72 (s, 3H), 3.39 (dddd, *J* = 13.6 Hz, 9.6 Hz, 4.0 Hz, 0.8 Hz, 1H), 3.25-3.15 (m, 2H), 3.11-3.02(m, 1H), 2.71(dd, *J* = 8.0 Hz, 0.8 Hz, 1H), 1.06 (d, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 176.9, 172.4, 171.6, 133.7, 131.5, 128.7, 128.6, 83.8, 56.5, 52.6, 52.1, 39.7, 36.8, 29.4, 15.8 ppm; HRMS (ESI) $[M+H]^+$ calcd. For $C_{17}H_{20}NO_4$ 302.1386 found 302.1402.

Dimethyl 3-phenyl-6-propyl-2-aza-bicyclo[3.2.0]hept-2-ene-1,7-dicarboxylate(8c)



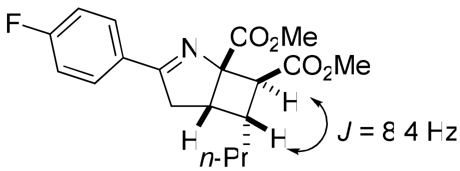
Yield: 75%; Viscous oil; TLC R_f = 0.45 (7:3 hexanes/EtOAc);^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.97-7.94 (m, 2H), 7.51-7.41 (m, 3H), 3.78(s, 3H), 3.71 (s, 3H), 3.37 (dddd, *J* = 11.4, 9.6 Hz,3.6 Hz, 0.8 Hz, 1H), 3.26-3.10(m, 2H), 2.99 -2.91(m, 1H), 2.72(dd, *J* = 8.4 Hz, 0.8 Hz,1H), 1.40-1.22 (m, 4H), 0.89 (t, *J* = 7.6, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ:176.8, 172.4, 171.7, 133.7, 131.5, 128.7, 128.7, 83.8, 55.6, 52.6, 52.1, 39.1, 36.9, 34.1, 32.8, 20.4, 14.1ppm. HRMS (ESI) $[M+H]^+$ calcd. For $C_{19}H_{24}NO_4$ 330.1699 found 330.1716.

Dimethyl 3-phenyl-6-(4-phenylbut-3-ynyl)-2-aza-bicyclo[3.2.0]hept-2-ene-1,7-dicarboxylate (8d)



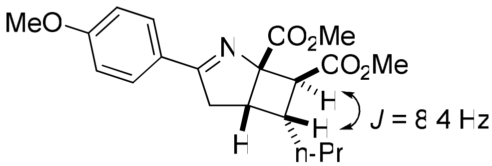
Yield: 85%; Viscous oil; TLC R_f = 0.44 (7:3 hexanes/EtOAc);^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.96-7.92 (m, 2H), 7.50-7.26 (m, 8H), 3.78(s, 3H), 3.70 (s, 3H), 3.45 (ddd, *J* = 8.8 Hz,4.4 Hz, 0.8 Hz 1H), 3.28(dd, *J* = 8.8Hz, 4.4 Hz,1H), 3.15-3.07(m, 1H), 2.83(dd, *J* = 8.4 Hz, 0.8 Hz,1H), 2.42(t, *J* = 7.2 Hz, 2H), 1.81-1.69 (m, 2H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ:176.7, 172.1, 171.6, 133.6, 131.7, 131.6, 128.7, 128.7, 128.4, 127.9, 123.9, 89.2, 83.9, 81.4, 55.4, 52.7, 52.2, 39.4, 37.2, 34.3, 29.7, 17.8 ppm. HRMS (ESI) $[M+H]^+$ calcd. For $C_{25}H_{26}NO_4$ 416.1856 found 416.1872. R_f = 0.44 (7:3 hexanes/EtOAc).

Dimethyl 3-(4-fluorophenyl)-6-propyl-2-aza-bicyclo[3.2.0]hept-2-ene-1,7-dicarboxylate (8e)



Yield: 75%; Viscous oil; TLC R_f = 0.44 (7:3 hexanes/EtOAc);^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.97-7.94 (m, 2H), 7.13-7.08 (m, 2H), 3.77(s, 3H), 3.71 (s, 3H), 3.37 (ddd, *J* = 9.6 Hz,3.6 Hz, 0.8 Hz, 1H), 3.22-3.06(m, 2H), 2.98-2.90 (m, 1H), 2.70(dd, *J* = 8.4 Hz, 0.8 Hz,1H), 1.39-1.21 (m, 4H), 0.89(t, *J* = 7.2 Hz, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ: 175.5, 172.4, 171.7, 166.2, 163.7, 130.8, 130.7, 115.9 (d), 83.8, 55.6, 52.6, 52.1, 39.2, 36.9, 34.1, 32.8, 20.4, 14.1 ppm; HRMS (ESI) $[M]^+$ calcd. For $C_{19}H_{22}FNO_4$ 347.1533 found 347.1536.

Dimethyl 3-(4-methoxyphenyl)-6-propyl-2-aza-bicyclo[3.2.0]hept-2-ene-1,7-dicarboxylate (8f)



Yield: 68%; Yellow viscous oil; TLC R_f = 0.45 (7:3 hexanes/EtOAc); ^{1}H NMR ($CDCl_3$, 400 MHz) δ: 7.91-7.89 (m, 2H), 6.94-6.92 (m, 2H), 3.85(s,3H), 3.76(s, 3H), 3.70 (s, 3H), 3.39 (dddd, J = 11.4 Hz, 9.6 Hz,3.6 Hz, 0.8 Hz, 1H), 3.21-3.06(m, 2H), 2.96 -2.88(m, 1H), 2.70(dd, J = 8.4 Hz, 0.8 Hz,1H), 1.39-1.21(m, 4H), 0.89 (t, J = 7.2, 3H) ppm; ^{13}C NMR ($CDCl_3$, 100 MHz) δ:175.8, 172.4, 171.7, 162.1, 130.2, 126.4, 113.8, 83.6, 55.5, 55.4, 52.4, 51.8, 38.9, 36.6, 33.8, 32.6, 20.2, 13.9 ppm; HRMS (ESI) $[M+H]^+$ calcd. For $C_{20}H_{26}NO_5$ 360.1805 found 360.1817.

Computational details: The Cartesian coordinates (Å) and computed energy values are outlined below. All geometry optimizations and frequency calculations were performed with the B3LYP[1,2] functional implemented in Gaussian 03.[3] The 6-31G+(d,p) basis set was used for all atoms. In addition, opt=verytight and int=ultrafine were used.

Azepine **6a** (zero imaginary frequencies)

Atom	X	Y	Z
C	1.439882	-0.775206	-0.138329
C	1.179503	-2.159337	-0.455252
H	2.066896	-2.78083	-0.385502
N	0.504078	0.192608	-0.160891
C	2.813305	-0.31943	0.156285
C	3.932811	-0.91121	-0.465778
C	3.044429	0.743008	1.055549
C	5.222412	-0.452289	-0.205493
H	3.790123	-1.713427	-1.182354
C	4.336862	1.207663	1.304696
H	2.211974	1.181077	1.599488
C	5.433311	0.612293	0.677516
H	6.066289	-0.918895	-0.705549
H	4.486165	2.022599	2.007137
H	6.439607	0.967676	0.877354
C	0.039618	-2.799027	-0.825034
C	-1.35702,	2.266187	-0.889045
H	0.142129	-3.865846	-1.01379
H	-1.623118	-1.906143	-1.888028
H	-2.059701	-3.079668	-0.676178
C	-0.855934	0.158103	-0.223228
C	-1.584569	-1.104801	0.124706
H	-1.182104	-1.441602	1.090794
C	-1.515213	1.377533	-0.618478
O	-2.722533	1.52562	-0.774237
O	-0.624908	2.41529	-0.811735
C	-3.081226	-0.893983	0.367169
O	-3.968839	-1.369054	-0.307525
O	-3.287388	-0.199713	1.504726
C	-4.658555	0.138719	1.784711
H	-4.63523	0.689783	2.724771
H	-5.054253	0.761958	0.979542
H	-5.2649	-0.765123	1.881697
C	-1.210915	3.677605	-1.167499
H	-0.371591	4.360494	-1.301716
H	-1.783466	3.585505	-2.093404
H	-1.871739	4.033393	-0.372763
H	0.87151	1.142926	-0.200069

```
Zero-point correction=                           0.306451 (Hartree/Particle)
Thermal correction to Energy=                    0.326166
Thermal correction to Enthalpy=                  0.327110
Thermal correction to Gibbs Free Energy=         0.256913
Sum of electronic and zero-point Energies=           -975.314887
Sum of electronic and thermal Energies=              -975.295172
Sum of electronic and thermal Enthalpies=            -975.294228
```

```
Sum of electronic and thermal Free Energies=        -975.364426
```

TS-6a (one imaginary frequency)

Atom	X	Y	Z
C	1.4593834735	-0.2243089499	-0.5935337108
C	1.0929840314	-0.6706817757	-1.8503392183
H	1.8903101233	-0.8808980331	-2.5596929354
N	0.450476501	0.3908915446	0.1270134903
C	2.8188034717	-0.2061252077	-0.0212729342
C	3.9665344351	-0.207479343	-0.8378617982
C	2.9952227821	-0.1636967318	1.3746366134
C	5.2407091491	-0.1688806344	-0.2763290959
H	3.8626812873	-0.2177888594	-1.9178727441
C	4.2740661421	-0.1200465202	1.9345226518
H	2.1251229756	-0.1957741883	2.0231008892
C	5.4025253603	-0.1236051703	1.1131143136
H	6.1115465218	-0.164839037	-0.9255028423
H	4.3853392692	-0.0944610655	3.0147006498
H	6.3973626387	-0.0932629298	1.547337927
C	-0.2541906647	-0.6225625946	-2.3258206673
C	-1.4107881411	-1.4884538368	-1.8460322075
H	-0.3215030701	-0.3621269815	-3.3882388708
H	-2.3440040975	-1.1242158184	-2.2858677788
H	-1.3125056341	-2.5490949147	-2.1197617752
C	-0.8308516263	0.2345396959	-0.3653697212
C	-1.4095538676	-1.183221546	-0.3581263419
H	-0.6805339616	-1.8141332924	0.1658299266
C	-1.7360111788	1.383803231	-0.3271696379
O	-2.9347410105	1.3333554467	-0.5561690426
O	-1.0848090883	2.5470268859	-0.0333132845
C	-2.7344372321	-1.3951074727	0.356750905
O	-3.6791368107	-2.0003526876	-0.1033518584
O	-2.7065328361	-0.8871709627	1.6091920133
C	-3.9294777295	-1.0103922625	2.3598747235
H	-3.7253896788	-0.5496233175	3.3262876911
H	-4.7390416595	-0.487562472	1.845261754
H	-4.1982093783	-2.0624093439	2.4829590456
C	-1.9034577392	3.7299212155	-0.0118047162
H	-1.2280176797	4.5463134977	0.2437070004
H	-2.3549006464	3.8963886536	-0.9928301962
H	-2.6953171342	3.6350755155	0.7352015043
H	0.6806587029	1.266435263	0.5872722786

```
Zero-point correction=                           0.304553 (Hartree/Particle)
Thermal correction to Energy=                    0.323820
Thermal correction to Enthalpy=                  0.324764
Thermal correction to Gibbs Free Energy=         0.255633
Sum of electronic and zero-point Energies=          -975.288526
Sum of electronic and thermal Energies=             -975.269259
Sum of electronic and thermal Enthalpies=           -975.268315
Sum of electronic and thermal Free Energies=        -975.337446
```

imaginary frequency = -395.4741

Bicycle **II** (zero imaginary frequencies)

Atom	X	Y	Z
C	1.5448081633	-0.2559822788	-0.5184135687
C	1.1173760242	-0.8699507665	-1.6451870803
N	0.4821390681	0.306036998	0.2387572854
C	2.9177904221	-0.1500818854	0.0065027964
C	4.0289878101	-0.230047752	-0.8531970957
C	3.144701598	0.0414495823	1.3811361523
C	5.3257903367	-0.1406492798	-0.3506267931
H	3.871165537	-0.3454457544	-1.9211558147
C	4.4450136582	0.1364673186	1.8816457945
H	2.2956705337	0.0921780706	2.055227249
C	5.5403190124	0.0438177967	1.0199126196
H	6.1711059431	-0.2032034453	-1.0300183787
H	4.601104181	0.2778395132	2.9473886254
H	6.5514141197	0.1188614975	1.4093820232
C	-0.3634553042	-0.7003329192	-1.8397890526
C	-1.2951134071	-1.8925702	-1.4763529655
H	-0.6234240038	-0.198345199	-2.7803152954
H	-2.238021612	-1.8693011136	-2.0271016812
H	-0.85760762	-2.8911478146	-1.5505214728
C	-0.7585006546	0.0229708491	-0.4791734818
C	-1.4553297533	-1.3215853604	-0.0481050794
H	-0.7902174748	-1.8055865595	0.6744396218
C	-1.6967568802	1.1964685894	-0.6461285845
O	-2.7950588675	1.1073077947	-1.1570695786
O	-1.173473193	2.3611358934	-0.2076149322
C	-2.8405570926	-1.3151641557	0.5530029762
O	-3.75381794	-2.0330091034	0.2036055857
O	-2.9277086112	-0.4388413591	1.5808468056
C	-4.212970731	-0.3577419549	2.2269717722
H	-4.0948562805	0.3837487586	3.0169299436
H	-4.9760202012	-0.0437422774	1.510815779
H	-4.4899365103	-1.3275784347	2.6471665667
C	-2.0069851296	3.5281874759	-0.3695479721
H	-1.4271101132	4.3556492183	0.0375359557
H	-2.2270606616	3.6906927584	-1.426833248
H	-2.9424301715	3.4013747068	0.1794834364
H	0.608795938	1.2816740689	0.4898604768
H	1.7477736675	-1.4334758668	-2.3218788602

```
Zero-point correction=                           0.305997 (Hartree/Particle)
Thermal correction to Energy=                    0.325451
Thermal correction to Enthalpy=                  0.326395
Thermal correction to Gibbs Free Energy=         0.256252
Sum of electronic and zero-point Energies=           -975.318184
Sum of electronic and thermal Energies=              -975.298730
```

```
 Sum of electronic and thermal Enthalpies=           -975.297786
 Sum of electronic and thermal Free Energies=        -975.367930
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Bicycle **8a** (zero imaginary frequencies)

Atom	X	Y	Z
C	1.4821146514	-0.2729449214	-0.3624834282
C	1.1008953529	-0.9900976278	-1.6573072734
N	0.5002803759	0.2217304873	0.304961097
C	2.880099385	-0.1415232188	0.101020017
C	3.9426472779	-0.6856098452	-0.6394725457
C	3.1674652174	0.5428941019	1.2969938261
C	5.2610256903	-0.5512262445	-0.1972440888
H	3.7461598192	-1.2166072023	-1.5655004675
C	4.4818022785	0.6746410671	1.7368023754
H	2.3441418147	0.9642415368	1.8634933683
C	5.5340752109	0.1279811619	0.9915832702
H	6.071513789	-0.9774806929	-0.7811809491
H	4.6897585132	1.204748614	2.6618157858
H	6.5586956831	0.2321494377	1.3368141479
C	-0.4313861118	-0.9734282053	-1.6154434685
C	-1.153544999	-2.1633228058	-0.9258107214
H	-0.8880930361	-0.6649538543	-2.557610788
H	-2.0436592698	-2.5100782121	-1.4540247533
H	-0.515060328	-3.023495974	-0.702191578
C	-0.7577117736	-0.0619908721	-0.3641851305
C	-1.5067398915	-1.2818791595	0.2981856671
H	-0.9876559001	-1.551255314	1.2230677563
C	-1.5885634594	1.1712076698	-0.6682587434
O	-2.753807727	1.1208404137	-1.0148954314
O	-0.8819117009	2.3112324396	-0.5989791335
C	-2.9803044603	-1.1630391046	0.6306913548
O	-3.8672002851	-1.8199207911	0.1264358417
O	-3.1771181805	-0.2720061812	1.6251152711
C	-4.5495882604	-0.035348259	1.9919377158
H	-4.5123873629	0.6990754219	2.796266401
H	-5.1025179873	0.3560407094	1.134811025
H	-5.0182658811	-0.960740345	2.335314817
C	-1.5975232559	3.5143829185	-0.9420470784
H	-0.8743128387	4.3211054481	-0.8273384025
H	-1.9615616485	3.4619516671	-1.9709982045
H	-2.4452800594	3.6561335166	-0.2677659806
H	1.5065371985	-2.0086642848	-1.6894141051
H	1.5081531594	-0.4567884957	-2.5256174657

```
 Zero-point correction=                           0.305926 (Hartree/Particle)
 Thermal correction to Energy=                    0.325388
 Thermal correction to Enthalpy=                  0.326332
 Thermal correction to Gibbs Free Energy=         0.254769
 Sum of electronic and zero-point Energies=           -975.327164
 Sum of electronic and thermal Energies=              -975.307702
 Sum of electronic and thermal Enthalpies=            -975.306758
 Sum of electronic and thermal Free Energies=         -975.378321
```

References

[1] Hili, R.; Yudin, A. K. *J. Am. Chem. Soc* **2006**, *128*, 14772.
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