Supporting information attached to article:

A Straightforward and Versatile Synthetic Approach to 1-Azabicyclic Alkaloids

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Index:

- ...Characterization data: S1
- ...¹³C-NMR Spectra: S6

Characterization data:

(*E*)-3-Phenyl-5-(trimethylsilyl)pent-2-en-4-ynal (9b). Prepared from enyne **8b**. Obtained as a brown oil in 85 % yield; bp 80°C (0.1 mmHg), R_f = 0.35 (Hex:EtOAc 10:1) KMnO₄. ¹H-NMR (CDCl₃, 300 MHz): 9.72 (d, ³ J = 8.1; 1H), 7.55-7.44 (m; 5H), 6.50 (d, J = 8.1; 1H), 0.24 (s; 9H). ¹³C-NMR (CDCl₃, 75 MHz): 191.9 (C), 143.1 (C), 134.5 (C), 134.2 (CH), 129.9 (CH), 128.6 (CH), 128.3 (CH), 107.5 (C), 104.0 (C), -0.6 (CH₃). HRMS (EI) calcd for C₁₄H₁₆OSi: 228.0965, found 228.0969.

(*E*)-6-Methyl-8-(trimethylsilyl)octa-1,5-dien-7-yn-4-ol (13a). Prepared from enyne **9a**. Obtained as a colourless oil in 95% yield; R_f = 0.44 (Hex:EtOAc 6:1) KMnO₄. ¹H-NMR (CDCl₃, 300 MHz): 5.89 (d, ³ J = 8.3; 1H), 5.87-5.70 (m; 1H), 5.21-5.11 (m; 2H), 4.45 (d, ³ J = 7.3; 1H), 2.35-2.27 (m; 2H), 1.87-1.81 (m; 1H), 1.85 (s; 3H), 0.25 (s; 9H). ¹³C-NMR (CDCl₃, 75 MHz): 139.5 (CH), 133.6 (CH), 120.2 (C), 118.4 (CH₂), 107.3 (C), 92.1 (C), 67.4 (CH), 41.3 (CH₂), 17.6 (CH₃), -0.1 (CH₃). HRMS (EI) calcd for C₁₂H₂₀OSi-C₃H₅ 167.0523, found 167.0522.

(*E*)-6-Phenyl-8-(trimethylsilyl)octa-1,5-dien-7-yn-4-ol (13b). Prepared from enyne **9b**. Obtained as a colourless oil in 90% yield, R_f = 0.25 (Hex:EtOAc 10:1) KMnO₄. ¹H-NMR (CDCl₃, 300 MHz): 7.46-7.37 (m; 5H), 6.21 (d, ³ J = 9.7; 1H), 5.83-5.71 (m; 1H), 5.22-5.12 (m; 2H), 4.40-4.28 (m; 1H), 2.45-2.31 (m; 2H), 0.21 (s; 9H). ¹³C-NMR (CDCl₃, 75 MHz): 140.1 (C), 136.5 (C), 133.4 (CH), 128.6 (CH),

128.1 (CH), 126.1 (CH), 118.7 (CH₂), 118.3 (C), 105.8 (C), 94.4 (C), 67.3 (CH), 41.6 (CH₂), -0.1 (CH₃). HRMS (EI) calcd for C₁₇H₂₂OSi-C₃H₅ 229.1050, found 229.1040.

((E)-5-Methoxy-3-phenylocta-3,7-dien-1-ynyl)trimethylsilane (15). Prepared from alcohol **13b**. Obtained as a colourless oil in 87% yield; *R_f* = 0.39 (Hex:EtOAc 10:1) KMnO₄. ¹H-NMR (CDCl₃, 300 MHz): 7.46-7.35 (m; 5H), 6.12 (dd, ³*J* = 9.8, ⁴*J* = 1.6; 1H), 5.91-5.79 (m; 1H), 5.21-5.11 (m; 2H), 3.98-3.86 (m; 1H), 3.21 (s; 3H), 2.48-2.35 (m; 2H), 0.25 (s; 9H). ¹³C-NMR (CDCl₃, 75 MHz): 140.5 (C), 139.8 (CH), 136.8 (CH), 133.9 (CH), 128.6 (CH), 128.3 (CH), 127.8 (C), 117.4 (CH₂), 105.7 (C), 94.5 (C), 76.5 (CH₃), 56.1 (CH), 39.5 (CH₂), -0.1 (CH₃). HRMS (EI) calcd for C₁₇H₂₂OSi-C₃H₅: 243.1200, found 243.1194.

N-Methyl-N-((E)-3-methylhepta-1,3,6-trien-2-yl)benzeneamine (18b). Prepared from dienyne **12**. Obtained as a yellowish oil in 52% yield. ¹H-NMR (CDCl₃, 300 MHz): 7.35-7.25 (m; 3H), 7.05-7.01 (m; 2H), 5.95-5.75 (m; 1H), 5.32 (tc, ³*J* = 1.4, ²*J* = 0.9; 1H), 5.15-5.01 (m; 2H), 4.50 (s; 1H), 4.35 (s; 1H), 3.23 (s; 3H), 3.05-2.94 (m; 2H), 1.95 (s; 3H). ¹³C-NMR (CDCl₃, 75 MHz): 155.5 (C), 147.6 (C), 136.7 (CH), 129.7 (CH), 128.4 (CH), 123.2 (CH), 121.7 (CH₂), 115.6 (CH), 114.2 (CH), 97.5 (CH₂), 40.1 (CH₃), 35.1 (CH₂), 23.2 (CH₃).

((E)-7-(N-methylbenzeneamino)-6-methylocta-1,5,7-trien-4-yl acetate (18d). Prepared from dienyne **14**. Obtained as a yellowish oil in 47% yield. ¹H-NMR (CDCl₃, 300 MHz): 7.25-7.18 (m; 2H), 6.85-6.77 (m; 3H), 5.71-5.58 (m; 2H), 5.21-5.07 (m; 3H), 4.95 (s; 1H), 4.71 (s; 1H), 3.12 (s; 3H), 2.31-2.25 (m; 2H), 2.10 (s; 3H), 1.81 (s; 3H). ¹³C-NMR (CDCl₃, 75 MHz): 170.1 (C), 155.2 (C), 148.9 (C), 136.2 (C), 132.8 (CH), 128.5 (CH), 127.4 (CH), 119.4 (CH), 118.1 (CH), 117.8 (CH₂), 102.8 (CH), 70.4 (CH), 40.2 (CH₃), 38.9 (CH₂), 21.0 (CH₃), 15.1 (CH₃).

N-Methyl-N-((E)-3-phenyl-5-methoxyocta-1,3,7-trien-2-yl)benzeneamine (18e). Prepared from dienyne **15**. Obtained as a yellowish oil in 48% yield. ¹H-NMR (CDCl₃, 300 MHz): 7.61-7.11 (m; 5H), 6.93-6.62 (m; 5H), 5.90 (d, ³*J* = 9.6; 1H), 5.86-5.63 (m; 1H), 5.23-5.01 (m; 2H), 4.90 (s; 1H), 4.86 (s; 1H), 3.71-3.62 (m; 1H), 3.21 (s; 3H), 3.10 (s; 3H), 2.48-2.30 (m; 2H). ¹³C-NMR (CDCl₃, 75 MHz): 155.3 (C), 149.8 (C), 149.3 (C), 142.8 (C), 138.6 (CH), 134.7 (CH), 129.7 (CH), 129.1 (CH), 128.9

(CH), 128.3 (CH), 119.3 (CH), 117.6 (CH₂), 112.9 (CH), 106.6 (CH₂), 57.2 (CH₃), 56.3 (CH), 40.6 (CH₂), 31.1 (CH₃).

***N*-Methyl-*N*-((*E*)-3-methyl-5-methoxyhepta-1,3,7-trien-2-yl)benzeneamine (18c).** Prepared from dienyne **17**. Obtained as a yellowish oil in 48% yield. ¹H-NMR (CDCl₃, 300 MHz): 7.22-6.70 (m; 5H), 7.81-7.63 (m; 1H), 5.71 (d, ³*J*=10.7; 1H), 5.16 (dd, ³*J* = 17.3, ²*J* = 1.4; 1H), 5.11 (dd, ³*J* = 10.5, ²*J* = 1.4; 1H), 4.95 (s; 1H), 4.72 (s; 1H), 4.41 (t, ³*J*=6.9; 1H), 3.21 (s; 3H), 3.18 (s; 3H), 1.79 (s; 3H). ¹³C-NMR (CDCl₃, 75 MHz): 156.0 (C), 149.4 (C), 136.3 (CH), 130.1 (CH), 129.7 (C), 129.0 (CH), 127.1 (CH), 120.5 (CH₂), 118.8 (CH), 102.8 (CH₂), 79.3 (CH₃), 56.0 (CH₃), 40.9 (CH), 14.8 (CH₃).

(2*R,3*S**,6*S**)-*N*-Allyl-6-(2-bromophenyl)-3-methyl-2-((*S**)-1-methoxyallyl)piperidin-4-one (21f).** (Major diastereoisomer). Prepared from aminotriene **18c** and imine **19b**. Obtained as a pale yellow oil in 55% yield; *R*_f = 0.23 (Hex:EtOAc 10:1) KMnO₄. ¹H-NMR (CDCl₃, 300 MHz): 7.81 (d, ³*J* = 8; 1H), 7.51 (dd, ³*J* = 8, ⁴*J* = 0.8; 1H), 7.49-7.44 (m; 1H), 7.15-7.10 (m; 1H), 6.10-6.07 (m; 1H), 6.03-5.89 (m; 1H), 5.49-5.12 (m; 3H), 5.05 (d, ³*J* = 16.8; 1H), 4.71 (dd, ³*J*_{aa} = 12.2, ³*J*_{ae} = 3.4; 1H), 3.58-3.49 (m; 1H), 3.23 (s; 3H), 2.83-2.71 (m; 4H), 2.51 (dd, ²*J*_{gem} = 18.0, ³*J*_{ae} = 3.4; 1H), 2.47-1.85 (m; 1H), 1.15 (d, ³*J*=6.8; 3H). ¹³C-NMR (CDCl₃, 75 MHz): 210.2 (C), 142.8 (C), 141.9 (C), 137.4 (CH), 137.0 (CH), 133.8 (CH), 132.5 (CH), 129.4 (CH), 128.0 (CH), 119.2 (CH₂), 117.9 (CH₂), 88.9 (CH), 82.1 (CH₃), 64.8 (CH), 63.9 (CH), 57.8 (CH₂), 45.5 (CH₂), 43.5 (CH), 11.1 (CH₃). HRMS (EI) calcd for C₁₉H₂₄BrNO₂ 377.0990, found 377.0995.

(2*S,5*S**,6*S**)-Ethyl *N*,6-diallyl-5-methyl-4-oxopiperidin-2-carboxylate (21b).** Prepared from aminotriene **18b** and imine **19e**. Obtained as a pale yellow oil in 45% yield; *R*_f = 0.21 (Hex:EtOAc 10:1) KMnO₄. ¹H-NMR (CDCl₃, 300 MHz): 6.01-5.71 (m; 2H), 5.25-5.07 (m; 4H), 4.20 (c, ³*J*=6.1; 2H), 3.85 (dd, ³*J*_{ae} = 4.3, ³*J*_{ee} = 3.5; 1H), 3.52-3.40 (m; 2H), 3.20-3.01 (m; 3H), 2.80-2.68 (m; 1H), 2.58 (dd, ³*J*_{aa} = 13.6, ³*J*_{ae} = 3.5; 1H), 3.13-2.09 (m; 1H), 1.31 (t, *J* = 6.1; 3H), 1.01 (d, ³*J* = 6.8; 3H). ¹³C-NMR (CDCl₃, 75 MHz): 209.4 (C), 172.7 (C), 135.9 (CH), 134.1 (CH), 118.6 (CH₂), 116.6 (CH₂), 62.8 (CH), 61.1 (CH₂), 60.6 (CH), 57.2 (CH₂), 46.4 (CH), 43.7 (CH₂), 35.1 (CH₂), 14.1 (CH₃), 11.2 (CH₃). HRMS (EI) calcd for C₁₅H₂₃NO₃-C₃H₅ : 224.1281, found 224.1279.

(2*S,3*S**,6*S**)-3-Methyl-*N*-(pent-4-enyl)-6-phenyl-2-vinylpiperidin-4-one (21c).** Prepared from aminotriene **18a** and imine **19f**. Obtained as a yellowish oil in 45% yield; R_f = 0.28 (Hex:EtOAc 5:1) KMnO₄. ¹H-NMR (CDCl₃, 300 MHz): 7.42-7.31 (m; 5H), 5.86-5.73 (m; 1H), 5.62-5.43 (m; 1H), 5.29-5.17 (m; 2H), 4.85-4.69 (m; 2H), 3.73 (dd, ³ J_{aa} = 11.7, ³ J_{ae} = 3.1; 1H), 2.96 (dd, ³ J = ³ J' = 9.8, 1H), 2.80-2.63 (m; 2H), 2.60-2.41 (m; 3H), 1.71-1.62 (m; 2H), 1.43-1.24 (m; 2H), 1.03 (d, ³ J = 6.6; 3H). ¹³C-NMR (CDCl₃, 75 MHz): 209.1 (C), 142.2 (C), 139.1 (CH), 138.1 (CH), 128.6 (CH), 127.6 (CH), 127.3 (CH), 117.5 (CH₂), 114.3 (CH₂), 71.8 (CH), 65.5 (CH), 50.6 (CH₂), 49.2 (CH₂), 48.4 (CH), 31.2 (CH₂), 20.4 (CH₂), 11.2 (CH₃). HRMS (EI) calcd for C₁₉H₂₅NO 283.1934, found 283.1934.

(2*S,6*R**)-*N*-Allyl-2-(4-fluorophenyl)-6-((*R*)-1-methoxybut-3-enyl)-1,2,3,6-tetrahydro-5-phenyl-4-(*N*',*N*'-phenylmethylamino)piridine (23a).** Prepared from aminotriene **18e** and imine **19d**. Obtained as a pale yellow oil in 40% yield (major diastereoisomer); R_f = 0.54 (Hex:EtOAc 10:1) KMnO₄. ¹H-NMR (CDCl₃, 300 MHz): 7.51-7.42 (m; 2H), 7.32-7.12 (m; 7H), 7.18-7.00 (m; 2H), 6.82-6.71 (m; 3H), 5.91-5.79 (m; 2H), 5.23-4.90 (m; 4H), 3.70 (s; 1H), 3.25 (s; 3H), 3.19-3.04 (m; 3H), 2.87 (dd, ³ J = 13.4, ³ J = 9.4; 1H), 2.79 (s; 3H), 2.65-2.57 (m; 3H), 2.37 (ddd, ² J_{gem} = 17.3, ³ J = 12, J = 1.5; 1H). ¹³C-NMR (CDCl₃, 75 MHz): 163.9 (C), 159.1 (C), 147.9 (C), 139.3 (C), 139.2 (C), 137.9 (CH), 135.7 (CH), 133.2 (C), 129.0 (CH), 128.7 (CH), 128.5 (CH), 128.2 (CH), 127.5 (CH), 126.8 (CH), 116.9 (CH₂), 116.6 (CH₂), 116.2 (CH), 112.9 (CH), 82.6 (CH), 63.4 (CH₃), 59.0 (CH), 55.0 (CH), 50.4 (CH₂), 37.6 (CH₃), 36.0 (CH₂), 23.5 (CH₂). HRMS (EI) calcd for C₃₂H₃₅FN₂O-C₅H₉O 297.2074, found 297.2086.

(2*S, 6*R**)-*N*-Allyl-2-(4-fluorophenyl)-6-((*S*)-1-methoxybut-3-enyl)-1,2,3,6-tetrahydro-5-phenyl-4-(*N*-methylbenzeneamine)piridine (23b).** Prepared from aminotriene **18e** and imine **19d**. Obtained as a pale yellow oil in 8% yield (minor diastereoisomer); R_f = 0.50 (Hex:EtOAc 10:1) KMnO₄. ¹H-NMR (CDCl₃, 300 MHz): 7.50-7.05 (m; 10H), 6.83-6.70 (m; 4H), 5.95-5.79 (m; 2H), 5.25 (d, ³ J_{trans} = 17.1; 1H), 5.20 (d, ³ J_{cis} = 9.7; 1H), 5.11-5.01 (m; 2H), 4.52 (dd, ³ J = 11.4, ³ J = 4.5; 1H), 3.92 (d, ³ J = 5.4; 1H), 3.59-3.51 (m; 1H), 3.42-3.30 (m; 2H), 3.20 (s; 3H), 3.10-3.01 (m; 1H), 2.95 (d, ³ J = 13.6; J = 7.7; 1H), 2.70 (s; 3H), 2.43-2.36 (m; 2H). ¹³C-NMR (CDCl₃, 75 MHz): 163.3 (C), 160.1 (C), 147.9 (C), 140.4 (C), 138.6 (C), 137.3 (CH), 135.5 (CH), 134.5 (C), 129.1 (CH), 128.8 (CH), 128.7 (CH), 127.1 (CH),

126.4 (CH), 117.1 (CH₂), 116.9 (CH₂), 116.4 (CH), 114.8 (CH), 112.8 (CH), 85.8 (CH), 62.9 (CH₃), 57.8 (CH), 54.5 (CH), 49.9 (CH₂), 37.3 (CH₃), 36.9 (CH₂), 24.6 (CH₂). HRMS (EI) calcd for C₃₂H₃₅FN₂O-C₅H₉O 297.2074, found 297.2085.

(2*S,3*S**,6*S**)-2-Allyl-3-methyl-*N*-(pent-4-enyl)-6-phenylpiperidin-4-one (21d).** Prepared from aminotriene **18b** and imine **19f**. Obtained as a pale yellow oil in 52% yield; *R*_f = 0.34 (Hex:EtOAc 20:1) KMnO₄. ¹H-NMR (CDCl₃, 300 MHz): 7.52-7.43 (m; 5H), 6.12-5.98 (m; 1H), 5.79-5.55 (m; 1H), 5.33-5.21 (m; 2H), 4.95-4.73 (m; 2H), 3.87 (dd, ³*J*_{aa} = 11.5, ³*J*_{ae} = 2.9; 1H), 2.83-2.61 (m; 3H), 2.56-2.40 (m; 3H), 2.23-1.92 (m; 2H), 1.83-1.69 (m; 2H), 1.62-1.50 (m; 1H), 1.46-1.35 (m; 1H), 1.15 (d, ³*J* = 6.8; 3H). ¹³C-NMR (CDCl₃, 75 MHz): 211.5 (C), 143.5 (C), 139.3 (CH), 138.5 (CH), 128.7 (CH), 127.9 (CH), 127.1 (CH), 122.1 (CH₂), 117.5 (CH₂), 66.5 (CH), 65.2 (CH), 63.4 (CH), 52.5 (CH₂), 47.3 (CH₂), 38.5 (CH₂), 35.3 (CH₂), 21.3 (CH), 11.5 (CH₃). HRMS (EI) calcd for C₂₀H₂₇NO-C₃H₅ 256.1695, found 256.1698.

(*S)-1-((2*R**,3*S**,6*S**)-3-Methyl-*N*-(pent-4-enyl)-6-phenyl-4-oxopiperidin-2-yl)but-3-enyl acetate (21g).** (Major diastereoisomer). Prepared from aminotriene **18d** and imine **19f**. Obtained as a pale yellow oil in 50% yield; *R*_f = 0.28 (Hex:EtOAc 3:1) KMnO₄. ¹H-NMR (CDCl₃, 300 MHz): 7.45-7.28 (m; 5H), 5.85-5.61 (m; 2H), 5.22-4.85 (m; 5H), 4.31 (dd, ³*J*_{aa} = 12.5, ³*J*_{ae} = 3.7; 1H), 3.30 (dd, ³*J*_{ae} = 6.5, ³*J*_{ee} = 2.3; 1H), 2.96-2.90 (m; 1H), 2.77 (dd, ²*J*_{gem} = 18.6, ³*J*_{aa} = 12.5; 1H), 2.65-2.45 (m; 3H), 2.33 (s; 3H), 1.83 (s; 3H), 1.82-1.75 (m; 3H), 1.10 (d, ³*J* = 6.8; 3H). ¹³C-NMR (CDCl₃, 75 MHz): 210.6 (C), 170.2 (C), 143.9 (C), 138.9 (CH), 137.8 (CH), 134.2 (CH), 132.1 (CH), 127.4 (CH), 118.7 (CH₂), 117.7 (CH₂), 70.4 (CH), 54.5 (CH₂), 47.9 (CH₂), 44.1 (CH), 38.3 (CH₃), 36.1 (CH₂), 31.2 (CH₂), 25.6 (CH), 22.2 (CH₂), 21.0 (CH), 10.6 (CH₃). HRMS (EI) calcd for C₂₃H₃₁NO₃-C₄H₇ 314.1750, found 314.1759.

¹³C-NMR Spectra

11

12

13a

13b

14

15

16

17

18a

18b

18d

18e

21b

21c

21d

21f

23a

23b

22a

22b

22c

22d

22e

22f

22f

22g

24a

24b