Supplementary Information

Stereospecific photochemical ring expansion of lithiated benzamides

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General methods for the amide cyclisation–photochemical rearrangement

The extended enolate (generally deep red-orange in colour) was formed by one of the following three methods.

Method A: Formation of the cyclic enolate with LDA (method of Clayden, Menet and Mansfield)¹

The benzamide (1 mmol) in THF (10 ml) was added at 0 °C to a solution of freshly prepared LDA (1.3 eq.) in THF (5 ml). The reaction was allowed to warm to ambient temperature over 2 h, and cooled to –78 °C.

*Method B: Formation of the cyclic enolate with *t*-BuLi (method of Clayden, Knowles and Menet)²*

tert-Buli (3 equiv) was added to a solution of the amide (1 mmol) in THF (15 ml) at –78°C dropwise. The resulting solution was allowed to warm to 0°C over 30 mins and cooled to –78°C.

*Method C: Formation of the cyclic enolate with LDA *t*-BuLi–HMPA (method of Ahmed, Clayden and Yasin)³*

tert-Buli (1.3 equiv) was added dropwise to a solution of the amide (1 mmol) in THF (15 ml) and HMPA (3 equiv.) at –78°C. The resulting solution was stirred overnight at –78°C.

The enolate thus formed was placed under a 500W tungsten filament halogen security lamp obtained from a local hardware store (B&Q IQ series 2193LO). Irradiation was continued at –78 °C for 3 h. Saturated ammonium chloride solution was added, the layers separated and the aqueous layer was extracted with dichloromethane (x 3). The combined organic fractions were washed with brine, dried (MgSO₄) and evaporated to yield a crude product, which was purified by flash chromatography.⁴

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3-Phenylcyclohepta-1,4,6-trienecarboxylic acid *tert*-butylamide 5. Amide **1** (0.201 g, 0.94 mmol) was cyclised by Method C and irradiated. Purification by flash chromatography, eluting with 5:1 petrol-EtOAc,

afforded the title compound **5** as a white solid (0.144 g, 72 %). Mp = 111-113 °C; Found C 80.56 %, H, 7.64 %, N 4.98 %, C₁₈H₂₁NO requires C 80.86 %, H 7.92 %, N 5.24 %; m/z (CI) 268 (M+H⁺, 100 %); δ_{H} (300 MHz, CDCl₃) 7.5-7.2 (5H, m, PhH), 7.12 (1H, d, *J* 11.5, H7), 6.88 (1H, dd, *J* 11, 5.5, H6), 6.30 (1H, m, H5), 5.98 (1H, d, *J* 6, H2), 5.60 (1H, b, NH), 5.54 (1H, dd, *J* 9, 5.5, H4), 2.77 (1H, t, *J* 6, H3), 1.40 (9H, s, *tert*-butyl); δ_{C} (75 MHz, CDCl₃) 166.9, 142.7, 133.4, 132.1, 128.7, 128.0, 127.5, 127.3, 126.9, 126.3, 125.1, 51.4, 44.5, 28.7; ν_{max} (film)/cm⁻¹ 3330 (NH), 1640 (C=O), 1527 (C=C).

8a

N-(tert-Butyl)-2-methoxy-7-phenylbicyclo[4.1.0]hepta-2,4-diene-1-carboxamide 8a. Amide **6a** (0.502 g, 1.68 mmol) was cyclised by Method A and irradiated. Purification by flash chromatography, eluting with 5:1 petrol-EtOAc, afforded the title compound **8a** as a yellow oil (0.40 g, 80 %). *R*_f = 0.15; Found M⁺ 297.1729; C₁₉H₂₃NO₂ requires *M*, 297.1729; m/z (CI) 298 (M+H⁺, 100 %), 266 (M-MeO, 60 %), 193 (40 %); δ_{H} (300 MHz, C₆D₆) 7.2-7.0 (6H, m, PhH, H7), 6.85 (1H, b, NH), 6.00 (1H, ddd, *J* 6.5, 5, 1, H4), 5.76 (1H, d, *J* 5, H3), 5.36 (1H, dd, *J* 7, 4, H5), 3.18 (3H, s, MeO), 2.94 (1H, t, *J* 5, H6), 1.35 (9H, s, *tert*-butyl); δ_{C} (75 MHz, C₆D₆) 163.7, 158.2, 142.9, 135.5, 129.0, 127.0, 125.8, 124.3, 107.6, 102.7, 54.7, 50.8, 45.5, 28.8, 28.5; ν_{max} (film)/cm⁻¹ 3350 (NH), 1646 (C=O), 1600 (C=C), 1553 (C=C).

8d

N-(tert-Butyl)-2,4-dimethoxy-7-phenylbicyclo[4.1.0]hepta-2,4-diene-1-carboxamide 8d. Amide **6d** (0.203 g, 0.61 mmol) was cyclised by Method A and irradiated. Purification by flash chromatography on alumina, eluting with 10:1 petrol-EtOAc afforded the title compound **8d** as white foam (0.066 g, 33 %). *R*_f = 0.13. Found C 73.17 %, H 7.78 %, N 4.25 %, C₂₀H₂₅NO₃ requires C 73.37 %, H 7.70 %, N 4.28 %; m/z (CI) 328 (M+H⁺, 100 %), 238 (30 %), 58 (60 %); δ_{H} (300 MHz, CDCl₃) 7.4-7.2 (5H, m, PhH), 7.14 (1H, b, NH), 5.73 (1H, dd, *J* 6.5, 3.5, H5), 5.67 (1H, s, H3), 3.82 (4H, m, MeO2, H7), 3.64 (3H, s, MeO4), 2.51 (1H, t, *J* 6.5, H6), 1.42 (9H, s, *tert*-butyl); δ_{C} (75 MHz, CDCl₃) 164.2, 158.8, 156.9, 142.3, 128.4, 128.0, 127.0, 126.3, 97.5, 55.8, 55.5, 50.8, 35.6, 30.7, 28.8, 28.6; ν_{max} (film)/cm⁻¹ 3390 (NH), 1648 (C=O), 1530 (C=C).

Cyclised but unrearranged product **A**¹ was also recovered (0.11 g, 60 %).

N-(tert-Butyl)-5-methoxy-3-methyl-7-phenylbicyclo[4.1.0]hepta-2,4-diene-2-carboxamide 8h. Amide **6h** (0.25 g, 0.80 mmol) was cyclised by method A and irradiated. Purification by flash chromatography, eluting with 4:1 petrol-EtOAc, afforded the title compound **8h** as a white solid (0.12 g, 48 %). $R_f = 0.21$. Mp = 147-149 °C. Found M^+ 311.1886; $C_{20}H_{25}NO_2$ requires M , 311.1885; m/z (EI) 312 ($M+H^+$, 100 %), 239 (80 %); δ_H (300 MHz, $CDCl_3$) 7.4-7.2 (5H, m, PhH), 5.65 (1H, s, H4), 5.22 (1H, b, NH), 4.24 (1H, b, H1), 3.63 (3H, s, MeO), 3.48 (1H, b, H6), 2.21 (1H, t, J 5, H7), 2.14 (3H, s, CH_3), 1.39 (9H, s, *tert*-Butyl); δ_C (75 MHz, $CDCl_3$) 168.6, 158.1, 142.8, 135.8, 128.9, 126.9, 126.5, 112 (b), 55.9, 51.7, 43.9, 32.0 (b), 29.1, 21.7; ν_{max} (film)/ cm^{-1} 3390 (NH), 1665 (C=O).

2,5-Dimethoxy-7-phenyl-cyclohepta-1,3,5-trienecarboxylic acid tert-butylamide 9f. Amide **6f** (0.206 g, 0.63 mmol) was cyclised by method A and irradiated. Purification by flash chromatography, eluting with 1:1 petrol-EtOAc, afforded the title compound **9f** (0.061 g, 24 %). Found: C, 72.94 %; H, 7.89 %, N, 4.25 %; $C_{20}H_{24}NO_3$ requires C, 73.37 %; H, 7.70 %; N, 4.28 %; δ_H (300 MHz, $CDCl_3$) 7.3 (5H, m, PhH), 6.85 (1H, d, J 8.5, H6), 6.01 (1H, d, J 7, H3), 5.33 (1H, d, J 7, H4); 3.66 (3H, s, MeO), 3.60 (3H, s, MeO), 3.75 (1H, d, J 8.5, H7), 1.43 (9H, s, *tert*-butyl); δ_C (75 MHz, $CDCl_3$) 164.2, 152.2, 137.6, 132.6, 128.8, 127.7, 107.8, 94.1, 56.4, 56.1, 50.9, 47.6, 28.7; ν_{max} (film)/ cm^{-1} 3395 (NH), 1638 (C=O).

Cyclised but unrearranged compound **B** was also recovered (0.145 g, 74 %).

10c

N-(tert-Butyl)-5-methoxy-7-phenylbicyclo[4.1.0]hepta-2,4-diene-2-carboxamide 10c. Amide **6c** (0.50 g, 1.68 mmol) was cyclised by method A and irradiated. Purification by flash chromatography, eluting with 4:1 petrol-EtOAc, afforded the title compound **10c** as a white solid (0.36 g, 73 %). R_f = 0.16; Mp = 148-150 °C; Found C 76.65 %, H 7.89 %, N 4.72 %; $C_{19}H_{23}NO_2$ requires C 76.73 %, H 7.80 %, N 4.71 %; m/z (CI) 298 ($M + H^+$, 100 %), 208 (50 %); δ_H (300 MHz, $CDCl_3$) 7.4-7.1 (5H, m, PhH), 6.78 (1H, d, J 8, H4), 5.63 (1H, b, NH), 5.42 (1H, dd, J 8, 1.5, H3), 3.69 (3H, s, OMe), 3.47 (1H, t, J 5, H1), 2.87 (1H, t, J 5, H6), 1.73 (1H, t, J 5, H7), 1.41 (9H, s, *tert*-Butyl); δ_C (75 MHz, C_6D_6) 165.8, 160.9, 141.6, 128.4-125.9 (Ar, C=C), 99.3, 54.9, 54.2, 50.4, 46.7, 28.4, 26.0; ν_{max} (film)/ cm^{-1} 3350 (NH), 1646 (C=O), 1600 (C=C), 1553 (C=C).

Alternatively, amide **6c** (0.50 g, 1.68 mmol) was cyclised by method A but with lithium amide **C**⁵ in the place of LDA, and irradiated. Purification by flash chromatography, eluting with 4:1 petrol-EtOAc, afforded the title compound **10c** as a white solid (0.34 g, 69 %). Analytical HPLC (Regis Whelk O1), eluting with IPA–hexane (30:70), showed it to consist of a 12.9:87.1 mixture of two enantiomers with retention times 10.98 and 20.92 min respectively (ee = 75 %). $[\alpha]_D^{25} = +25.8$ (c = 0.96 in $CHCl_3$).

10e

5,6-Dimethoxy-7-phenyl-bicyclo[4.1.0]hepta-2,4-diene-2-carboxylic acid tert-butylamide 10e. Amide **6e** (0.21 g, 0.64 mmol) was cyclised by method A and irradiated. Purification by flash chromatography, eluting with 3:2 petrol-EtOAc, afforded the title compound **10e** as a yellow solid (0.16 g, 75 %). R_f = 0.22. Mp = 91-93 °C. Found C 73.16 %, H 7.83 %, N 4.25 %; $C_{20}H_{25}NO_3$ requires C 73.37 %, H 7.70 %, N 4.28 %; m/z (CI) 328 ($M+H^+$, 100 %); δ_H (300 MHz, $CDCl_3$) 7.3-7.1 (5H, m, PhH), 6.52 (1H, dd, J 8, 1, H4), 5.70 (1H, b, NH), 5.29 (1H, d, J 8, H3), 3.79 (3H, s, MeO5), 3.41 (3H, s, MeO6), 3.31 (1H, dd, J 9, 1, H7), 2.55 (1H, d, J 9, H8), 1.48 (9H, s, *tert*-butyl); δ_C (75 MHz, C_6D_6) 165.7, 155.9, 150.8, 135.6, 129.2, 126.3, 124.0, 100.8, 56.9, 55.7, 51.1(b), 50.6, 29.4, 28.5; ν_{max} (film)/ cm^{-1} 3378 (NH), 1647 (C=O), 1618 (C=C), 1522.

11b

4-Methoxy-3-phenyl-cyclohepta-1,4,6-trienecarboxylic acid tert-butylamide 11b. Amide **6b** (0.5 g, 1.68 mmol) was cyclised by method C and irradiated. Purification by flash chromatography, eluting with 4:1 petrol-EtOAc, afforded the title compound **11b** as a white solid (0.32 g, 63 %). $R_f = 0.18$. Found M^+ 297.1734; $C_{19}H_{23}NO_2$ requires M , 297.1729; m/z (CI) 298 ($M+H^+$, 100 %), 213 (20 %), 74 ($(CH_3)_3CNHCO$, 50 %); δ_H (300 MHz, $CDCl_3$) 7.4-7.2 (5H, m, PhH), 6.58 (2H, d, J 3, H6, H7), 6.28 (1H, d, J 8, H2), 5.69 (1H, b, NH), 5.53 (1H, t, J 3.5, H5), 3.71 (1H, d, J 8, H3), 3.67 (3H, s, MeO), 1.43 (9H, s, tert-butyl); δ_C (75 MHz, $CDCl_3$) 167.2, 155.0, 137.9, 135.4, 130.0, 128.4, 127.8, 126.6, 125.4, 120.9, 97.0, 56.5, 51.4, 47.7, 28.7; ν_{max} (film)/ cm^{-1} 3430 (NH), 1645 (C=O).

11b'

5-Oxo-6-phenyl-cyclohepta-1,3,6-trienecarboxylic acid tert-butylamide 11b'. Amide **6b** (0.25 g, 0.84 mmol) was cyclised and irradiated in the same way, and conc HCl (1 ml) was added to a solution of the crude cycloheptadiene **11b** in THF. After stirring for 4 h, water was added to the reaction, and the layers were separated. The standard work-up gave a crude product which was purified by flash chromatography, eluting with 1:1 petrol-EtOAc to afford the title compound **11b'** as a yellow oil (0.13 g, 54 %). $R_f = 0.11$. Found M^+ 281.1411; $C_{18}H_{19}NO_2$ requires M , 281.1415; m/z (CI) 282 ($M+H^+$, 100 %); δ_H (300 MHz, $CDCl_3$) 7.76 (1H, d, J 1.5 Hz, H2), 7.4 (8H, m, ArH, H3, H4, H7), 5.85 (1H, b, NH), 1.48 (9H, s, *t*-butyl); δ_C (75 MHz, $CDCl_3$) 186.0, 167.5, 151.9, 143.3, 141.8, 139.1, 134.3, 133.8, 130.2, 129.1, 128.6, 128.1, 52.2, 28.6; ν_{max} (film)/ cm^{-1} 3300 (NH), 1654 (C=O), 1624, 1541.

11c

N-(tert-Butyl)-5-oxo-3-phenyl-1,6-cycloheptadiene-1-carboxamide 11c. Norcaradiene **10c** (0.36 g, 1.21 mmol) was dissolved in THF and treated with a solution of 2 M HCl. Work-up as above gave ketone **11c** as a colourless oil (0.34 g, 100%). δ_H (300 MHz, $CDCl_3$) 7.5-7.2 (5H, m, PhH), 7.12 (1H, d, J 12.5, H7) 6.99 (1H, d, J 5, H2), 6.35 (1H, d, J 12.5, H6), 5.71 (1H, b, NH), 3.93 (1H, dd, J 12.5, 4.5, H3), 3.17 (1H, dd, J 16.5, 13, H_a4), 2.90 (1H, d, J 16.5, H_b4), 1.43 (9H, s, *tert*-Butyl); δ_C (75 MHz, $CDCl_3$) 199.4, 166.9, 145.6, 142.6, 135.9, 135.5, 132.5, 129.4, 127.7, 127.4, 52.1, 50.1, 40.2, 28.9.

Purification by flash chromatography, eluting with 4:1 petrol-EtOAc, led to rearrangement to **N-(tert-Butyl)-4-oxo-6-phenyl-1,5-cycloheptadiene-1-carboxamide D** as a brown oil (0.34 g, 100 %). Found M^+

283.1577; $C_{18}H_{21}NO_2$ requires M , 283.1572; m/z (CI) 284 ($M+H^+$, 100 %), 242 (35 %), 74 (90 %); δ_H (300 MHz, $CDCl_3$) 7.35 (5H, m, PhH), 6.73 (1H, t, J 6.0, H2), 6.67 (1H, s, H5), 3.24 (2H, s, H6), 3.14 (2H, d, J 6, H3), 1.36 (9H, s, *tert*-Butyl); δ_C (75 MHz, $CDCl_3$) 210.0, 166.0, 141.0, 139.3, 138.4, 129.4, 129.0, 128.6, 126.5, 122.9, 52.0, 49.2, 44.6, 29.0. ν_{max} (film)/ cm^{-1} 3367 (NH), 1719 (C=O), 1647 (C=O), 1524.

N-(*tert*-Butyl)-2-hydroxy-4-oxo-6-phenyl-1,5-cycloheptadiene-1-carboxamide 11d. Conc. HCl (1 ml) was added to a solution of norcaradiene **8d** (0.091 g, 0.27 mmol) in THF. After stirring for 4 h, water was added and the layers were separated. The aqueous layer was extracted with ether. The combined organic fractions were dried over $MgSO_4$ and evaporated under reduced pressure to give a crude product. Purification by flash chromatography, eluting with 1:1 petrol-EtOAc, afforded the title compound **11d** as a colourless oil (0.052 g, 63 %). R_f = 0.12. Found M^+ 299.1523; $C_{18}H_{21}NO_3$ requires M , 299.1521; m/z (CI) 300 ($M+H^+$, 100 %); δ_H (300 MHz, $CDCl_3$) 7.3-7.1 (5H, m, PhH), 6.22 (1H, s, H5), 5.20 (1H, b, NH), 3.41 (1H, s, H3), 3.19 (1H, s, H7), 1.24 (9H, s, *tert*-butyl); δ_C (75 MHz, $CDCl_3$) 206.1, 171.3, 167.9, 140.8, 134.2, 128.6, 127.9, 126.0, 120.2, 102.9, 52.0, 50.2, 48.3, 28.9; ν_{max} (film)/ cm^{-1} 3368 (NH+OH), 1718 (C=O), 1667, 1616 (C=O), 1593 (C=O).

7-Methyl-3-phenyl-cyclohepta-1,4,6-trienecarboxylic acid tert-butylamide 11g. Amide **6g** (0.204 g, 0.70 mmol) was cyclised by method A and irradiated. Purification by flash chromatography, eluting with 5:1 petrol-EtOAc, afforded the title compound **11g** as a white solid (0.156 g, 76 %). R_f = 0.3. M_p = 67-69 °C. Found M^+ 281.1780; $C_{19}H_{23}NO$ requires M , 281.1780; m/z (CI) 282 ($M+H^+$, 100 %); δ_H (300 MHz, $CDCl_3$) 7.03 (5H, m, PhH), 6.68 (1H, d, J 5.5, H6), 6.20 (1H, dd, J 9, 6, H4), 5.70 (1H, d, J 6.5, H2), 5.53 (1H, dd, J 9, 5, H5), 5.48 (1H, b, NH), 2.83 (1H, t, J 5.5, H3); δ_C (75 MHz, $CDCl_3$) 168.3, 143.1, 136.9-126.8 (Ar, C=C), 125.3, 51.5, 44.5, 28.6, 22.2; ν_{max} (film)/ cm^{-1} 3300 (NH), 1642 (C=O).

11h

5-Methoxy-7-methyl-3-phenyl-cyclohepta-1,4,6-triene carboxylic acid isopropylamide 11h. 2 M HCl (5 ml) was added to a solution of morcaradiene **8h** (0.12 g, 0.38 mmol) in THF (5 ml). After stirring for 4 h, water was added and the layers were separated. The aqueous layer was extracted with ether. The combined organic fractions were dried over MgSO₄ and evaporated under reduced pressure to give a crude product. Purification by flash chromatography, eluting with 4:1 petrol-EtOAc afforded the title compound **11h** as a brown oil (0.119 g, 99 %). δ_{H} (300 MHz, CDCl₃) 7.5-7.2 (5H, m, PhH), 6.68 (1H, d, *J* 7.5, H2), 6.25 (1H, m, H6), 6.18 (1H, d, *J* 6.5, NH), 5.49 (1H, dd, *J* 9, 5, H4), 3.85 (3H, s, MeO), 2.89 (1H, m, H3), 1.51 (3H, s, CH₃); 1.43 (9H, s, *tert*-butyl); δ_{C} (75 MHz, CDCl₃) 164.4, 157.7, 142.8, 135.4, 129.3, 129.0, 127.9, 127.0, 125.8, 124.5, 107.7, 55.5, 51.3, 45.3, 29.0, 28.8; ν_{max} (film)/cm⁻¹ 3395 (NH), 1665 (C=O), 1529 (C=C).

(-)-16c

2-Isopropylamino-1-(2-methoxyphenyl)-2-phenylpropan-1-one. Amide (+)-**13c** (0.66 g, 2.21 mmol) in THF (60 ml) was cyclised according to method B and irradiated. Flash chromatography, eluting with 3:1 petrol-EtOAc, gave the title compound **(-)-16c** (0.43g, 70%) as a yellow oil, *R*_f [1:1 petrol-EtOAc] 0.54; Found *M*⁺ 298.1813; C₁₉H₂₃NO₂ requires *M* 298.1807. ν_{max} (film)/cm⁻¹ 3400 (NH), 2965 (CH), 1696 (C=O); δ_{H} (300 MHz, CDCl₃) 7.50-7.26 (6H, m, ArH + H7), 6.84 (1H, d, *J* 8, H9), 6.73 (1H, dd, *J* 8, 7, H8), 6.48 (1H, dd, *J* 7, 2, H6), 3.67 (3H, s, OMe), 2.75 (1H, septet, *J* 6, H3), 1.72 (3H, s, H5), 1.01 (3H, d, *J* 6, H1/2), 0.97 (3H, d, *J* = 6, H1/2); δ_{C} (75 MHz, CDCl₃) 206.6, 156.2, 142.2, 130.8, 129.2, 128.2, 128.1, 127.1, 126.8, 119.9, 111.0, 69.9, 55.2, 44.0, 25.8, 25.3, 23.4; *m/z* (CI) 298 (*M* + H⁺, 100%). [α]_D²² (CHCl₃) = -38.5. (*c* = 1.36, CHCl₃).

(-)-17a

5-Methoxy-7-methyl-7-phenyl-bicyclo[4.1.0]hepta-2,4-diene-2-carboxylic acid (1-phenyl-ethyl)-amide 17a.

Amide **13a** (0.25 g, 0.70 mmol) was cyclised by method B and irradiated. Purification by flash chromatography, eluting with 4:1 petrol-EtOAc, afforded the title compound (–)-**17a** as a white solid (0.13 g, 52 %). $R_f = 0.16$. Found M^+ 359.1898; $C_{24}H_{25}NO_2$ requires M , 359.1885; m/z (CI) 360 ($M+H^+$, 5 %), 207 ($M-C_6H_5CHCH_3NHCO$, 100 %); δ_H (300 MHz, C_6D_6) 7.29 (2H, d, J 8, PhH), 7.21 (2H, d, J 7.5, PhH), 7.04 (6H, m, PhH), 6.51 (1H, d, J 6.5, H3), 5.97 (1H, b, NH), 5.42 (1H, m, $CHCH_3$), 4.62 (1H, d, J 7, H4), 3.11 (3H, s, MeO), 2.77 (1H, d, J 9, H1), 2.28 (1H, d, J 9, H6), 1.29 (3H, d, J 7, CH_3CH), 1.50 (3H, s, CH_3); δ_C (75 MHz, C_6D_6) 166.4, 161.2, 144.5, 131.6-126.4 (Ar), 121.9, 113.7, 93.1, 55.1, 54.7, 48.9, 33.9, 33.7, 26.1, 21.8; ν_{max} (film)/ cm^{-1} 3333 (NH), 1648 (C=O), 1602 (Ar), 1555 (C=C). $[\alpha]_D^{21} = -49$ ($c = 1.27$ in $CHCl_3$).

17e

5-Methoxy-7-methyl-7-phenyl-bicyclo[4.1.0]hepta-2,4-diene-2-carboxylic acid isopropyl-amide 17e.

Amide (±)-**13e** (0.2 g, 0.67 mmol) was cyclised by method B and irradiated. Purification by flash chromatography, eluting with 4:1 petrol-EtOAc, afforded the title compound (±)-**17e** as a colourless oil (0.188 g, 94 %). Analytical HPLC (Regis Whelk O1), eluting with IPA and hexane (30:70), showed it to consist of a 1:1 mixture of two enantiomers with retention times 9.97 and 15.03 min respectively; Found M^+ 297.1726; $C_{19}H_{23}NO_2$ requires M , 297.1728; m/z ($M+H^+$, 100 %), 194 (30 %); δ_H (300 MHz, $CDCl_3$) 7.4-7.1 (5H, m, PhH), 6.68 (1H, d, J 7, H3), 5.71, (1H, d, J 7.5, NH), 5.06 (1H, d, J 7, H4), 4.24 (1H, s, J 6.5, $CH(CH_3)_2$), 3.71 (3H, s, MeO), 2.69 (1H, dd, J 9, 1, H1), 2.39 (1H, dd, J 9, 1, H6), 1.24 (9H, m, CH_3); δ_C (75 MHz, $CDCl_3$) 166.8, 161.1, 144.5, 128.4, 128.2, 127.9, 126.2, 121.1, 113.7, 93.0, 55.6, 41.4, 33.9, 33.2, 28.8, 22.90, 22.88; ν_{max} (film)/ cm^{-1} 3322 (NH), 1647 (C=O), 1605 (Ar), 1557 (C=C).

Enantiomerically pure amide **13e** (0.5 g, 1.68 mmol) was treated in the same way. Purification by flash chromatography afforded the title compound (+)-**17e** as a colourless oil (0.47 g, 94 %) $[\alpha]_D^{21.5} = +38.3$ ($c = 1.7$ in $CHCl_3$); Analytical HPLC (Regis Whelk O1), eluting with IPA and hexane (30:70), showed only the enantiomer with retention time 14.45 min (ee = >99 %).

17f

3,5-Dimethoxy-7-methyl-7-phenylbicyclo[4.1.0]hepta-2,4-diene-2-carboxylic acid isopropylamide 17f.

Amide **13f** (0.55 g, 1.53 mmol) in THF (30 ml) was cyclised by method C, replacing HMPA with DMPU. Purification by flash chromatography, eluting with 2:1 petrol-EtOAc, gave the title compound **17f** (0.02 g, 20%) as an orange oil, R_f [2:1 petrol-EtOAc] 0.56; Found M^+ 327.1836; $C_{20}H_{25}NO_3$ requires M^+ 327.1834. $\nu_{\max}$ (film)/ cm^{-1} 3399 (NH), 2967 (CH), 1646 (C=O); δ_H (300 MHz, $CDCl_3$) 7.4-7.1 (5H, m, ArH), 4.97 (1H, bs, H4), 4.22 (1H, m, H10), 3.75 (3H, s, OMe), 3.45 (3H, bs, OMe), 3.19 (1H, d, $J = 9$, H6), 2.26 (1H, d, $J = 9$, H8), 1.27 (3H, s, H10), 1.23 (3H, d, $J = 7$, i Pr), 1.19 (3H, d, $J = 7$, i Pr); δ_C (75 MHz, $CDCl_3$) 166.3, 164.1, 157.0, 129.7, 128.8, 128.5, 128.2, 127.6, 127.4, 126.3, 90.0, 56.2, 41.2, 35.6, 34.6, 23.4, 23.3; m/z (CI) 328 ($M + H^+$, 100%). $[\alpha]_D^{25} = -12.3$ ($c = 1.14$ in $CHCl_3$).

Comparison of the HPLC trace (Whelk O1; 70:30 hexane:*i*-PrOH) with that of the product of cyclising ($\pm$)-**13f** (two enantiomers, retention times 11.34 and 17.35 min.) indicated an ee of 92%.

17i

5,7-Dimethyl-7-phenylbicyclo[4.1.0]hepta-2,4-diene-2-carboxylic acid isopropylamide 17i. Amide **13i** (0.024 g, 0.083 mmol) was cyclised by method B. Purification by column chromatography, eluting with 4:1 petrol-EtOAc, gave the title compound **17i** (0.02 g, 85%) as a yellow oil, R_f [2:1 petrol-EtOAc] 0.39; Found M^+ 281.1778; $C_{19}H_{23}NO$ requires M^+ 281.1780. $\nu_{\max}$ (film)/ cm^{-1} 3323 (NH), 2971 (CH), 1613 (C=O); δ_H (300 MHz, $CDCl_3$) 7.3-7.1 (5H, m, ArH), 6.45 (1H, d, $J = 7$, H1), 5.78 (1H, d, $J = 7$, H2), 5.62 (1H, b, NH), 4.14 (1H, septet, $J = 7$, H7), 3.10 (1H, d, $J = 7$, H4), 2.64 (1H, d, $J = 7$, H5), 2.00 (3H, s, H3), 1.14 (6H, d, $J = 7$, H9), 1.14 (3H, s, H6); δ_C (75 MHz, $CDCl_3$) 167.3, 145.3, 139.1, 129-126 (ArC), 121.1, 51.9, 48.3, 41.7, 24.0, 23.0, 21.3, 20.5, 19.8; m/z (CI) 282 ($M+H^+$, 100%); $[\alpha]_D^{23} = -20.4$ ($c = 1.32$, $CHCl_3$)

Comparison of the HPLC trace (Whelk O1; 70:30 hexane:*i*-PrOH) with that of the product of cyclising ($\pm$)-**13i** (two enantiomers, retention times 7.17 and 12.25 min.) indicated an ee of 86%.

(-)-18b

3-Methyl-(3R)-3-phenyl-cyclohepta-1,4,6-trienecarboxylic acid isopropylamide 18b. Amide **13b** (0.201 g, 0.75 mmol) was cyclised by method B and irradiated. Purification by flash chromatography, eluting with 10:1 petrol-EtOAc, afforded the title compound **18b** as a yellow oil (0.161 g, 80 %). R_f = 0.17. Found M^+ 267.11628; $C_{18}H_{21}NO$ requires M , 267.11623; m/z (CI) 268 ($M+H^+$, 100 %); δ_H (300 MHz, $CDCl_3$) 7.6-7.0 (5H, m, PhH), 6.63 (1H, m, H7), 6.32 (2H, m, H6, H5), 5.67 (1H, b, NH), 5.23 (1H, d, J 3.5, H2), 4.74 (1H, m, H4), 4.22 (1H, s, J 6.5, $CH(CH_3)_2$), 1.52 (3H, s, CH_3), 1.25 (6H, d, J 6.5, $(CH_3)_2$); δ_C (75 MHz, $CDCl_3$) 167.2, 145.5, 131.8, 129.0, 127.4, 127.1, 127.0, 126.4, 126.1, 125.9, 105.1, 41.8, 35.4, 28.6, 22.8, 22.7; ν_{max} (film)/ cm^{-1} 3312 (NH), 1638 (C=O), 1529 (C=C); $[\alpha]_D^{23} = -84.6$ ($c = 1.49$ in $CHCl_3$).

18d

4-Methoxy-3-methyl-3-phenylcyclohepta-1,4,6-triene carboxylic acid N-isopropylamide 18d. Amide **13d** (0.10 g, 0.34 mmol) was cyclised by method B and irradiated. Purification by column chromatography (3:1 petrol-EtOAc) gave the title compound **18d** (0.02 g, 20%) as a white solid, R_f [1:1 petrol-EtOAc] 0.35; mp = 160 °C (decomp.). Found M^+ 297.1733; $C_{19}H_{23}NO_2$ requires M^+ 297.1729. ν_{max} (film)/ cm^{-1} 3333 (NH), 2971 (CH), 1637 (C=O); δ_H (300 MHz, $CDCl_3$) 7.14-6.95 (5H, m, ArH), 6.25 (2H, m, H5+6), 6.17 (1H, s, H2), 5.64 (1H, bd, $J = 7$, NH), 5.55 (1H, d, $J = 6$, H7), 4.18 (1H, septet, $J = 7$, H9), 3.75 (3H, s, OMe), 1.64 (3H, s, H8), 1.21 (3H, d, $J = 7$, i Pr), 1.19 (3H, d, $J = 7$, i Pr); δ_C (75 MHz, $CDCl_3$) 167.1, 158.7, 144.9, 133.5, 131.7, 129.4, 126.8, 125.9, 125.7, 119.9, 97.9, 56.8, 48.3, 41.8, 29.4, 22.7; m/z (CI) 298 ($M + H^+$, 100%). $[\alpha]_D^{25} = +90.6$ ($c = 0.53$ in $CHCl_3$).

Comparison of the HPLC trace (Whelk O1; 70:30 hexane:*i*-PrOH) with that of the product of cyclising ($\pm$)-**13d** (two enantiomers, retention times 33.01 and 35.30 min.) indicated an ee of 90%.

18e

(3S)-3-Methyl-5-oxo-(3S)-3-phenylcyclohepta-1,6-dienecarboxylic acid isopropylamide 18e. Norcaradiene **17e** (0.15 g, 0.5 mmol) was treated with a 2M aqueous solution of HCl. Purification by flash chromatography, eluting with 4:1 petrol-EtOAc afforded the title compound **18e** as a yellow oil (0.142 g, 99 %). Found M^+ 283.1576; $C_{19}H_{23}NO_2$ requires M , 283.1572; m/z (CI) 284 ($M+H^+$, 100 %), 196 (20 %); δ_H

(300 MHz, CDCl₃) 7.20 (5H, m, PhH), 7.0 (1H, s, H₂), 6.85 (1H, d, *J* 12.5, H₇), 5.99 (1H, d, *J* 12.5, H₆), 5.61 (1H, bd, *J* 6.5, NH), 4.11 (1H, sept, *J* 6.5, CH(CH₃)₂), 3.15 (1H, d, *J* 15.5, H_a4), 2.89 (1H, d, *J* 15.5, H_b4), 1.48 (3H, s, CH₃), 1.18 (3H, d, *J* 6.5, CH₃), 1.16 (3H, d, *J* 6.5, CH₃); δ_C (75 MHz, CDCl₃) 198.4, 167.0, 150.3, 143.5, 134.4, 133.6, 132.4, 128.6, 127.0, 125.7, 54.6, 42.2, 40.3, 29.6, 22.6; ν_{max} (film)/cm⁻¹ 3310 (NH), 1644 (C=O); [α]_D²⁴ = +35 (c = 1.13 in CHCl₃).

(-)-18g

3,7 Dimethyl-3-phenylcyclohepta-1,4,6-trienecarboxylic acid isopropylamide 18g. Amide **13g** (0.062 g, 0.174 mmol) was cyclised by method B and irradiated. Purification by column chromatography (6:1 petroleum ether: ethyl acetate) gave the title compound (0.030 g, 49%) as a colourless oil, R_f [6:1 petrol-EtOAc] 0.12; Found M⁺ 281.1776; C₁₉H₂₃NO requires M⁺ 281.1780. ν_{max} (film)/cm⁻¹ 3294 (NH), 2971 (CH), 1638 (C=O); δ_H (300 MHz, CDCl₃) 7.3-6.9 (5H, m, ArH), 6.00 (1H, d, *J* = 8, H₁), 5.96 (1H, s, H₄), 5.31 (1H, b, NH), 5.14 (1H, d, *J* = 3, H₃), 4.70 (1H, dd, *J* = 8, 3, H₂), 4.19 (1H, sp, *J* = 7, H₅), 1.88 (3H, s, H₆), 1.35 (3H, s, H₇), 0.89 (3H, d, *J* = 7, ⁱPr), 0.87 (3H, d, *J* = 7, ⁱPr); δ_C (75 MHz, CDCl₃) 168.9, 146.8, 135.2, 134.5, 130.5, 127.7, 127.0, 126.5, 126.1, 41.9, 37.4, 29.3, 23.0, 23.0, 21.4; *m/z* (CI) 281 (M, 100%); [α]_D²² = -33.7 (c = 1.02, CHCl₃)

Comparison of the HPLC trace (Whelk O1; 70:30 hexane:*i*-PrOH) with that of the product of cyclising (±)-**13g** (two enantiomers, retention times 5.63 and 6.68 min.) indicated an ee of 80%.

18h

3,4 Dimethyl-3-phenylcyclohepta-1,4,6-trienecarboxylic acid isopropylamide 18h. Amide **13h** (0.122 g, 0.433 mmol) was cyclised by method B and irradiated. Purification by column chromatography, eluting with 4:1 petrol-EtOAc, gave the target material (48.7 mg, 40%) as a colourless oil, R_f [2:1 petrol-EtOAc] 0.36; ν_{max} (film)/cm⁻¹ 3313 (NH), 2972 (CH), 1639 (C=O); δ_H (300 MHz, CDCl₃) 7.1-7.0 (5H, m, ArH), 6.48 (1H, t, *J* = 5, H₂), 6.26 (2H, d, *J* = 6, H₁+3), 5.85 (1H, s, H₄), 5.68 (1H, d, *J* = 6, NH), 4.20 (1H, septet, *J* = 7, H₇), 2.13 (3H, s, H₅), 1.64 (3H, s, H₆), 1.24 (3H, d, *J* = 7, ⁱPr); δ_C (75 MHz, CDCl₃) 167.5, 146.3, 132-123

(ArC), 42.1, 30.2, 24.4, 23.1, 23.0, 21.8; $[\alpha]_{\text{D}}$ (CHCl_3) = -19.7 ; m/z (CI) 282 ($\text{M}+\text{H}^+$, 100%). Found M^+ 281.1779; $\text{C}_{19}\text{H}_{23}\text{NO}$ requires M^+ 281.1780; $[\alpha]_{\text{D}}^{22} = -19.7$ ($c = 1.42$, CHCl_3)

Comparison of the HPLC trace (Whelk O1; 70:30 hexane:*i*-PrOH) with that of the product of cyclising ($\pm$)-**13g** (two enantiomers, retention times 6.02 and 7.43 min.) indicated an ee of 92%.

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