Supporting Information

Efficient Synthesis of Highly Enantoienriched $\Delta^1$-Pyrrolines

Diana I. S. P. Resende, Samuel Guieu, Cristina G. Olivaa, and Artur M. S. Silva

Department of Chemistry, QOPNA, University of Aveiro, 3810-193 Aveiro, Portugal.
Department of Chemistry, CICECO, University of Aveiro, 3810-193 Aveiro, Portugal.
Actual address: Medicinal Chemistry Section, Experimental Therapeutics Programme, CNIO (Spanish National Cancer Research Centre), Madrid, Spain.

artur.silva@ua.pt

Table of contents

1. General.............................................................................................................................. S1
   Remarks............................................................................................................................. S1
2. General procedure for enantioselective addition of nitromethane to cinnamylideneacetophenone 1g. Synthesis of 3g............................................................... S2
3. General procedure for the synthesis of $\Delta^1$-pyrrolines 4a—h............................................. S2
4. Single-Crystal X-ray diffraction......................................................................................... S7
5. References........................................................................................................................ S8
6. NMR spectra of the synthesized products......................................................................... S9

General Methods: Melting points were determined on a BUCHI Melting point apparatus and are uncorrected. $^1$H and $^{13}$C NMR spectra were recorded on Bruker 300 or 500 [300.13 MHz ($^1$H), 75.47 MHz ($^{13}$C)] spectrometers with TMS as internal reference. Data for $^1$H NMR are recorded as follows: chemical shift (δ, ppm), multiplicity [s (singlet), d (doublet), t (triplet), q (quartet) and m (multiplet)], coupling constant (J, Hz) and integration. Data for $^{13}$C NMR are reported in terms of chemical shift (δ, ppm). Unequivocal $^1$H assignments were made with aid of 2D COSY ($^1$H/$^1$H), while $^{13}$C assignments were made on the basis of 2D HSQC ($^1$H/$^{13}$C) and HMBC experiments. Elemental analyses were obtained with a Carlo Erba 1108 CHNS analyser. High resolution mass spectra analysis (HRMS-ESI) were performed on a microTOF (focus) mass spectrometer (Bruker Daltonics, Bremen, Germany). Ions were generated using an Apollo II (ESI) source. Ionization was achieved by electrospray, using a voltage of 4500 V applied to the needle, and a counter voltage between 100 and 150 V applied to the capillary. Silica gel 60 F254 (Merck) was used for TLC, and the spots were detected with UV light (254 nm). Flash column chromatography was carried out on silica gel 60 (Merck).
Materials: Methanol (I₂/Mg) and THF (sodium/benzophenone) were distilled prior to use. Fe (powder) was purchased from Sigma-Aldrich and activated in a 20% HCl aqueous solution. 1,5-Diarylpent-2,4-dien-1-one 1g and (R,E)-1,5-diphenyl-3-(nitromethyl)-5-pent-4-en-1-ones (R,E)-3a-f and (R,E)-3h were prepared as described in literature.

2. General procedure for enantioselective addition of nitromethane to cinnamylideneacetophenone 1g. Synthesis of 3g.

1,5-Diarylpent-2,4-dien-1-one 1g (0.179 mmol) and thiourea catalyst 2 (32.0 mg, 0.054 mmol) were dissolved in 0.3 M solution of nitromethane (0.60 mL) under nitrogen atmosphere. The mixture was stirred for 7 days at room temperature. The resulting solution was evaporated and purified by column chromatography eluting with hexane/AcOEt (9/1). Finally the residues were crystallized from hexane/AcOEt to get the desired compound 3g.

(R,E)-3-(Nitromethyl)-1-(4-nitrophenyl)-5-phenylpent-4-en-1-one 3g: Yield: 84%; orange solid; mp 110-113°C. ¹H NMR (300 MHz, CDCl₃): δ 8.33 (d, J 8.9 Hz, 2H, H-2, H-5), 8.11 (d, J 8.9 Hz, 2H, H-3', H-5'), 7.35-7.22 (m, 5H, H-2'', H-5'', H-3'', H-4', H-4''), 6.60 (d, J 15.9 Hz, 1H, H-5), 6.15 (dd, J 15.9 Hz and 8.6 Hz, 1H, H-4), 4.71 (ABX, J 12.2 and 6.3 Hz, 1H, H-1'''), 4.65 (ABX, J 12.2 and 6.7 Hz, 1H, H-1'''), 3.82-3.70 (m, 1H, H-3), 3.40 (ABX, J 16.9 and 5.5 Hz, 1H, H-2), 3.32 (ABX, J 16.9 and 5.4 Hz, 1H, H-2) ppm. ¹³C NMR (75.47 MHz, CDCl₃, 20°C): δ 195.6 (C-1), 150.6 (C-4'), 140.7 (C-1'), 135.9 (C-1'''), 133.9 (C-5), 129.1 (C-5), 128.6 (C-2', H-6'), 128.2 (C-3'', H-5''), 126.4 (C-4'), 125.7 (C-2', H-6''), 124.0 (C-4), 78.5 (C-1'''), 40.9 (C-2), 37.1 (C-3) ppm.

3. General procedure for enantioselective synthesis of A¹-pyrrolines 4a-h. (R,E)-1,5-Diaryl-3-(nitromethyl)-5-pent-4-en-1-ones 3a-h (0.31 mmol) were dissolved in a mixture of THF/CH₂OH (2:1, 6 mL) and then it was successively added acetic acid (4.98 mmol) and Fe (14.0 mmol) at room temperature. The resulting mixture was heated at 65°C for 15 h under nitrogen atmosphere. After cooling down to room temperature, the reaction mixture was filtrated through Celite, rinsed with AcOEt. The whole mixture was washed with sat. NaHCO₃ aq., brine, dried over Na₂SO₄ and concentrated under reduced pressure. The resulting residue was purified by column chromatography eluting with hexane/AcOEt (8/2). Finally the residues were crystallized from hexane/AcOEt to get the desired compounds 4a-h.

It was also performed an experiment using the racemic 1,5-diaryl-3-(nitromethyl)-5-pent-4-en-1-one 3a to validate the formation of a single enantiomer when using the enantiopure substrate.
**2-Phenyl-4-styryl-\(\Lambda^1\)-pyrrole:** Yield: 83%; brown oil. HPLC (\(i\)-propanol/hexane = 10/90, flow rate 0.7 mL/min, \(\lambda = 254\) nm), retention time of \((R)\)-4a 10.77 minutes, retention time of \((S)\)-4a 12.72 minutes.

![Structural diagram of 2-Phenyl-4-styryl-\(\Lambda^1\)-pyrrole](image)


\((R,E)\)-2-Phenyl-4-styryl-\(\Lambda^1\)-pyrrole 4a: Yield: 72%; brown oil. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.85 (dd, \(J = 7.0\) and 2.3 Hz, 2H, H-2’,6’), 7.45-7.19 (m, 8H, H-3’,5’, H-4’, H-2’”,6’”, H-3’”,5’”, H-4’”), 6.47 (d, \(J = 15.8\) Hz, 1H, H-\(\beta\)), 6.24 (dd, \(J = 15.8\) and 7.9 Hz, 1H, H-\(\alpha\)), 4.33 (dd, \(J = 15.6\) and 7.2 Hz, 2H, H-5), 3.90 (dd, \(J = 15.6\) and 5.1 Hz, 1H, H-5), 3.36-3.19 (m, 2H, H-3, H-4), 2.97-2.81 (m, 1H, H-3) ppm. \(^{13}\)C NMR (75 MHz, CDCl\(_3\)): \(\delta\) 172.7 (C-2), 137.1 (C-1’”), 134.2 (C-1’), 132.2 (C-\(\alpha\)), 130.5 (C-4’), 129.9 (C-\(\beta\)), 128.5 (C-3’,5’,C-3’”,5’”), 127.5 (C-2’,6’), 127.2 (C-4’”), 126.0 (C-2’”,6’”), 67.2 (C-5), 41.8 (C-3), 41.3 (C-4) ppm. HRMS (ESI\(^+\)): calcd. for \([\text{C}_{19}\text{H}_{17}\text{N+H}]^+\) 248.1434, found 248.1433. HPLC (\(i\)-propanol/hexane = 10/90, flow rate 0.7 mL/min, \(\lambda = 254\) nm), retention time of \((R)\)-4a 10.90 minutes (\(ee = 99\%\)).

![Structural diagram of (R,E)-2-Phenyl-4-styryl-\(\Lambda^1\)-pyrrole 4a](image)

\((R,E)\)-2-(4-Methylphenyl)-4-styryl-\(\Lambda^1\)-pyrrole 4b: Yield: 83%; brown solid; mp = 68-69°C. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.73 (d, \(J = 8.0\) Hz, 2H, H-2’,6’), 7.34 (d, \(J = 7.1\) Hz, 2H, H-2’”,6”’), 7.29 (t, \(J = 8.0\) Hz, 2H, H-3’,5’), 7.24-7.19 (m, 3H, H-3’”,5’”, H-4’”), 6.44 (d, \(J = 15.7\) Hz, 1H, H-\(\beta\)), 6.23 (dd, \(J = 15.7\) and 8.3 Hz, 1H, H-\(\alpha\)), 4.32-4.27 (m, 1H, H-5), 3.89-3.84 (m, 1H, H-5), 3.27-3.19 (m, 2H, H-3, H-4), 2.87-2.81 (m, 1H, H-3), 2.37 (s, 3H, CH\(_3\)) ppm. \(^{13}\)C NMR (75.47 MHz, CDCl\(_3\)): \(\delta\) 172.6 (C-2), 140.7 (C-4’), 137.0 (C-1’”), 132.2 (C-\(\alpha\)), 131.5 (C-1’), 129.8 (C-\(\beta\)), 129.1 (C-3’,5’”), 128.4 (C-3’,5’), 127.5 (C-2’,6’), 127.1 (C-4’”), 126.0 (C-2’”,6’”), 67.0 (C-5), 41.7 (C-3), 41.2 (C-4), 21.3 (CH\(_3\)) ppm. HRMS (ESI\(^+\)): calcd. for \([\text{C}_{19}\text{H}_{19}\text{N+H}]^+\) 262.1590, found 262.1588. HPLC (\(i\)-propanol/hexane = 10/90, flow rate 0.7 mL/min, \(\lambda = 254\) nm), retention time of \((R)\)-4b 19.77 minutes (\(ee = 99\%\)).

![Structural diagram of (R,E)-2-(4-Methylphenyl)-4-styryl-\(\Lambda^1\)-pyrrole 4b](image)

\((R,E)\)-2-(4-Methoxyphenyl)-4-styryl-\(\Lambda^1\)-pyrrole 4c: Yield: 73%; brown solid; mp 87-89°C. \(^1\)H NMR (300 MHz, CDCl\(_3\)): \(\delta\) 7.79 (d, \(J = 8.9\) Hz, 2H, H-2’’,6’’), 7.34 (d, \(J = 7.4\) Hz, 2H, H-2’”,6””), 7.29 (t, \(J = 7.4\) Hz, 2H, H-3’,5’”), 7.20 (t, \(J = 7.4\) Hz, 1H, H-4’”), 6.92 (d, \(J = 8.9\) Hz, 2H, H-3’,5’”), 6.45 (d, \(J = 15.7\) Hz, 1H, H-\(\beta\)), 6.23 (dd, \(J = 15.7\) and 8.3 Hz, 1H, H-\(\alpha\)), 4.30-4.25 (m, 1H, H-5), 3.89-3.83 (m, 1H, H-5), 3.83 (s, 3H, OCH\(_3\)), 3.30-3.18 (m, 2H, H-3, H-4), 2.87-2.80 (m, 1H, H-3) ppm. \(^{13}\)C NMR (75.47 MHz, CDCl\(_3\)): \(\delta\) 172.0 (C-2), 161.4 (C-4’”), 137.0 (C-1’”), 132.3 (C-\(\alpha\)), 129.8 (C-\(\beta\)), 129.1 (C-2’,6’), 128.5 (C-3”,5’”), 127.1
(C-4”), 127.0 (C-1’), 126.0 (C-2”,6”), 113.7 (C-3’,5’), 66.9 (C-5), 55.2 (OCH3), 41.7 (C-3),
41.3 (C-4) ppm. HRMS (ESI⁺): calcd. for [C18H10NO+H]⁺ 278.1539, found 278.1537. HPLC (i-
propanol/hexane = 10/90, flow rate 0.7 mL/min, λ = 254 nm), retention time of (R)-4c 12.64 minutes (ee = 99%).

(R,E)-2-(4-Chlorophenyl)-4- styryl-λ¹-pyrrole 4d: Yield: 49%; orange solid; mp 118-119°C.

1H NMR (300 MHz, CDCl3): δ 7.77 (d, J 8.5 Hz, 2H, H-2’,6’),
7.41-7.19 (m, 7H, H-3’,5’, H-2”,6”, H-3”’,5”’, H-4”), 6.46 (d, J
15.7 Hz, 1H, H-β), 6.23 (dd, J 15.7 and 8.1 Hz, 1H, H-α), 4.32
(dd, J 16.8 and 7.5 Hz, 1H, H-5), 3.89 (dd, J 16.8 and 5.1 Hz, 1H, H-5), 3.33-3.18 (m, 2H, H-3, H-4), 2.89-2.82 (m, 1H, H-3) ppm. 13C NMR (75.47 MHz, CDCl3): δ 171.6 (C-2), 137.0 (C-
1”), 136.5 (C-4”), 132.7 (C-1”), 131.9 (C-α), 130.1 (C-β), 128.8 (C-2”,6”), 128.7 (C-3’,5’),
128.5 (C-3”’,5”’), 127.3 (C-4”), 126.0 (C-2”,6”), 67.3 (C-5), 41.8 (C-3), 41.4 (C-4) ppm.
HRMS (ESI⁺): calcd. for [C18H10ClN+H]⁺ 282.1044, found 282.1042. Caled. HPLC (i-
propanol/hexane = 10/90, flow rate 0.7 mL/min, λ = 254 nm), retention time of (R)-4d 11.85 minutes (ee = 99%).

(R,E)-2-(4-Bromophenyl)-4- styryl-λ¹-pyrrole 4e: Yield: 44%; salmon solid; mp 110-111°C.

1H NMR (300 MHz, CDCl3): δ 7.71 (d, J 8.6 Hz, 2H, H-2’,6’), 7.55
(d, J 8.6 Hz, 2H, H-3’,5’), 7.37-7.18 (m, 5H, H-2”,6”, H-3”’,5”’,
H-4”), 6.46 (d, J 15.8 Hz, 1H, H-β), 6.23 (dd, J 15.8 and 8.2 Hz,
1H, H-α), 4.38-4.24 (m, 1H, H-5), 3.94-3.82 (m, 1H, H-5), 3.38-3.16 (m, 2H, H-3, H-4), 2.92-
2.79 (m, 1H, H-3) ppm. 13C NMR (75.47 MHz, CDCl3): δ 171.8 (C-2), 137.0 (C-1”), 133.2 (C-
4”), 132.0 (C-α), 131.7 (C-3’,5’), 130.2 (C-β), 129.1 (C-2”,6”), 128.6 (C-3”’,5”’), 127.4 (C-4”),
126.1 (C-2”,6”), 125.1 (C-1”), 67.4 (C-5), 41.8 (C-3), 41.4 (C-4) ppm. HRMS (ESI⁺): calcd.
for [C18H10BrN+H]⁺ 326.0539, found 326.0537. HPLC (i-propanol/hexane = 10/90, flow rate
0.7 mL/min, λ = 254 nm), retention time of (R)-4e 13.07 minutes (ee = 99%).

(R,E)-2-(4-Fluorophenyl)-4- styryl-λ¹-pyrrole 4f: Yield: 67%; beige solid; mp 103-104°C.

1H NMR (300 MHz, CDCl3): δ 7.84 (dd, J 8.7 and 5.5 Hz, 2H, H-
2”,6”), 7.37-7.20 (m, 5H, H-2”,6”, H-3”’,5”’, H-4”), 7.11 (t, J 8.7
Hz, 2H, H-3’,5’), 6.47 (d, J 15.7 Hz, 1H, H-β), 6.24 (dd, J 15.7 and
8.2 Hz, 1H, H-α), 4.32 (dd, J 16.3 and 7.3 Hz, 1H, H-5), 3.89 (dd, J 16.3 and 4.4 Hz, 1H, H-5),
3.44-3.14 (m, 2H, H-3, H-4), 2.99-2.71 (m, 1H, H-3) ppm. 13C NMR (75.47 MHz, CDCl3): δ
171.5 (C-2), 164.2 (d, J 250.6 Hz, C-4”), 137.0 (C-1”), 132.1 (C-α), 130.6 (d, J 3.2 Hz, C-1’),
130.0 (C-β), 129.6 (d, J 8.6 Hz, C-2”,6”), 128.6 (C-3”’,5”’), 127.3 (C-4”), 126.1 (C-2”,6”),
115.5 (d, J 21.7 Hz, C-3’,5’), 67.3 (C-5), 41.9 (C-3), 41.5 (C-4) ppm. HRMS (ESI⁺): calcd.
for [C18H16FN+H]⁺ 266.1339, found 266.1338. HPLC (i-propanol/hexane = 10/90, flow rate 0.7
mL/min, λ = 254 nm), retention time of (R)-4f 11.48 minutes, retention time of (S)-4f 13.17 minutes (ee = 96%).

(R,E)-2-(4-Aminophenyl)-4-styryl-Λ^1-pyrrole 4g: Yield: 40%; orange solid; mp 153-156°C. \(^1H\) NMR (300 MHz, CDCl\(_3\)): δ 7.66 (d, J 8.4 Hz, 2H, H-2',6'), 7.36-7.18 (m, 5H, H-2'',6'', H-3''',5'''', H-4''), 6.66 (d, J 8.4 Hz, 2H, H-3',5') ppm. \(^13C\) NMR (75.47 MHz, CDCl\(_3\)): δ 172.5 (C-2), 148.9 (C-4'), 137.2 (C-1'''), 132.5 (C-α), 129.9 (C-β), 129.4 (C-2',6'), 128.6 (C-3''',5''''), 127.2 (C-4''), 126.1 (C-2'',6''), 124.5 (C-1'), 114.5 (C-3',5'), 66.6 (C-5), 41.7 (C-3), 41.3 (C-4) ppm. HRMS (ESI\(^+\)): calcd. for [C\(_{18}\)H\(_{19}\)N\(_2\)+] 263.1543, found 263.1542.

(R,E)-4-(p-Methoxystyryl)-2-phenyl-Λ^1-pyrrole 4h: Yield: 38%; orange solid; mp 74-76°C. \(^1H\) NMR (300 MHz, CDCl\(_3\)): δ 7.84 (d, J 7.3 Hz, 2H, H-2',6'), 7.50-7.35 (m, 3H, H-3',5', H-4'), 7.29 (d, J 8.4 Hz, 2H, H-2'',6'') ppm. \(^13C\) NMR (75.47 MHz, CDCl\(_3\)): δ 172.6 (C-2), 158.8 (C-4''), 134.1 (C-1''), 130.3 (C-4'), 129.9 (C-α), 129.7 (C-1'''), 129.2 (C-β), 128.3 (C-3',5'), 127.4 (C-2',6'), 127.0 (C-2'',6''), 113.8 (C-3''',5''''), 67.2 (C-5), 55.1 (OCH\(_3\)), 41.8 (C-3), 41.2 (C-4) ppm. HRMS (ESI\(^+\)): calcd. for [C\(_{19}\)H\(_{19}\)NO+H\(^+\)] 278.1539, found 278.1538. HPLC (i-propanol/hexane = 10/90, flow rate 0.7 mL/min, λ = 254 nm), retention time of (R)-4h 15.71 minutes (ee = 99%).

(R,E)-2-Phenyl-4-styryl-Λ^1-pyrrole-1-oxide 5a: Yield: 8%; brown oil. \(^1H\) NMR (300 MHz, CDCl\(_3\)): δ 8.35 (d, J 8.6 Hz, 2H, H-2',6'), 7.54-7.19 (m, 8H, H-3',5', H-4', H-2'',6'', H-3''',5'''', H-4'') ppm. \(^13C\) NMR (75.47 MHz, CDCl\(_3\)): δ 136.3 (C-1'''), 133.9 (C-β), 130.5, 129.1 (C-α), 128.7 (C-Ar), 128.5 (C-Ar), 127.9, 127.3 (C-2',6'), 126.3 (C-Ar), 69.6 (C-5), 37.9 (C-3), 34.5 (C-4) ppm. HRMS (ESI\(^+\)): calcd. for [C\(_{19}\)H\(_{19}\)NO+H\(^+\)] 264.1383, found 264.1381.

(R,E)-2-(4-Methylphenyl)-4-styryl-Λ^1-pyrrole-1-oxide 5b: Yield: 6%; brown oil. \(^1H\) NMR (300 MHz, CDCl\(_3\)): δ 8.25 (d, J 8.1 Hz, 2H, H-2',6'), 7.35-7.26 (m, 8H, H-3',5', H-4', H-2'',6'', H-3''',5'''', H-4'') ppm. \(^13C\) NMR (75.47 MHz, CDCl\(_3\)): δ 135.2, 128.7 (C-Ar), 128.5 (C-Ar), 127.9, 127.3 (C-2',6'), 126.3 (C-Ar), 69.6 (C-5), 37.9 (C-3), 34.5 (C-4) ppm. HRMS (ESI\(^+\)): calcd. for [C\(_{19}\)H\(_{19}\)NO+H\(^+\)] 264.1383, found 264.1381.
1H, H-5), 4.20-4.13 (m, 1H, H-5), 3.50-3.36 (m, 2H, H-4, H-3), 3.13-3.01 (m, 1H, H-3), 2.40 (s, 3H, \( \text{CH}_3 \)). \(^{13}\text{C}\) NMR (75.47 MHz, CDCl\(_3\)): Due to the low quantity of the obtained product it was not possible to perform further studies. HRMS (ESI\(^+\)): calcd. for \([\text{C}_{19}\text{H}_{16}\text{NO}+\text{H}]^+\) 278.1539, found 278.1538.

\(^{(R,E)}\)2-(4-Methoxyphenyl)-4-styryl-\(^1\text{A}\)-pyrrole-1-oxide \(5c\): Yield: 11%; brown oil. \(^1\text{H}\) NMR (300 MHz, CDCl\(_3\)):

\(^{13}\text{C}\) NMR (300 MHz, CDCl\(_3\)): \( \delta \) 8.35 (d, \( J \) 8.6 Hz, 2H, H-2',6'), 7.54-7.19 (m, 8H, H-Ar), 6.97 (d, \( J \) 8.7 Hz, 2H, H-Ar), 6.55 (d, \( J \) 15.7 Hz, 1H, H-\( \beta \)), 6.25 (dd, \( J \) 15.7 and 7.6 Hz, 1H, H-\( \alpha \)), 4.43-4.37 (m, 1H, H-5), 4.19-4.12 (m, 1H, H-5), 3.87 (s, 3H, \( \text{CH}_3 \)), 3.50-3.35 (m, 2H, H-4, H-3), 3.11-3.03 (m, 1H, H-3) ppm. \(^{13}\text{C}\) NMR (75.47 MHz, CDCl\(_3\)): Due to the low quantity of the obtained product it was not possible to perform further studies. HRMS (ESI\(^+\)): calcd. for \([\text{C}_{19}\text{H}_{16}\text{NO}+\text{H}]^+\) 294.1489, found 294.1489.

\(^{(R,E)}\)2-(4-Chlorophenyl)-4-styryl-\(^1\text{A}\)-pyrrole-1-oxide \(5d\): Yield: 5%; brown oil. \(^1\text{H}\) NMR (300 MHz, CDCl\(_3\)):

\(^{13}\text{C}\) NMR (300 MHz, CDCl\(_3\)): \( \delta \) 8.31 (d, \( J \) 8.7 Hz, 2H, H-2',6'), 7.48-7.26 (m, 7H, H-3',5', H-2'',6''), 7.35-7.57 (m, 2H, H-3'',5''), 7.28-7.24 (m, 1H, H-4''), 6.55 (d, \( J \) 15.7 Hz, 1H, H-\( \beta \)), 6.24 (dd, \( J \) 15.7 and 8.1 Hz, 1H, H-\( \alpha \)), 4.43-4.37 (m, 1H, H-5), 3.20-4.13 (m, 1H, H-5), 3.49-3.38 (m, 2H, H-4, H-3), 3.11-3.01 (m, 1H, H-3) ppm. \(^{13}\text{C}\) NMR (75.47 MHz, CDCl\(_3\)): Due to the low quantity of the obtained product it was not possible to perform further studies. HRMS (ESI\(^+\)): calcd. for \([\text{C}_{18}\text{H}_{16}\text{ClNO}+\text{H}]^+\) 298.0993, found 298.0993.

\(^{(R,E)}\)2-(4-Bromophenyl)-4-styryl-\(^1\text{A}\)-pyrrole-1-oxide \(5e\): Yield: 9%; brown oil. \(^1\text{H}\) NMR (300 MHz, CDCl\(_3\)):

\(^{13}\text{C}\) NMR (300 MHz, CDCl\(_3\)): \( \delta \) 8.24 (d, \( J \) 8.8 Hz, 2H, H-2',6'), 7.59 (d, \( J \) 8.8 Hz, 2H, H-3',5'), 7.37 (dd, \( J \) 8.3 and 1.3 Hz, 2H, H-2'',6''), 7.35-7.31 (m, 2H, H-3'',5''), 7.28-7.24 (m, 1H, H-4''), 6.55 (d, \( J \) 15.7 Hz, 1H, H-\( \beta \)), 6.24 (dd, \( J \) 15.7 and 8.1 Hz, 1H, H-\( \alpha \)), 4.43-4.37 (m, 1H, H-5), 3.20-4.13 (m, 1H, H-5), 3.49-3.38 (m, 2H, H-4, H-3), 3.11-3.01 (m, 1H, H-3) ppm. \(^{13}\text{C}\) NMR (75.47 MHz, CDCl\(_3\)): Due to the low quantity of the obtained product it was not possible to perform further studies. HRMS (ESI\(^+\)): calcd. for \([\text{C}_{18}\text{H}_{16}\text{BrNO}+\text{H}]^+\) 342.0488, found 342.0487.

\(^{(R,E)}\)2-(4-Fluorophenyl)-4-styryl-\(^1\text{A}\)-pyrrole-1-oxide \(5f\): Yield: 6%; brown oil. \(^1\text{H}\) NMR (300 MHz, CDCl\(_3\)):

\(^{13}\text{C}\) NMR (300 MHz, CDCl\(_3\)): \( \delta \) 8.39 (d, \( J \) 8.8 Hz, 2H, H-2',6'), 7.38-7.24 (m, 5H, H-2'',6'', H-3'',5'', H-4''), 7.14 (t, \( J \) 8.8 Hz, 2H, H-3',5'), 6.55 (d, \( J \) 15.8 Hz, 1H, H-\( \beta \)), 6.24 (dd, \( J \) 15.8 and 8.2 Hz, 1H, H-\( \alpha \)), 4.41 (dd, \( J \) 13.5 and 8.9 Hz, 1H, H-5), 4.17 (dd, \( J \) 13.5 and 6.4 Hz, 1H, H-5), 3.52-3.36 (m, 2H, H-3, H-4), 3.08 (d, \( J \) 11.7 Hz, 1H, H-3) ppm. \(^{13}\text{C}\) NMR (75.47 MHz, CDCl\(_3\)): Due to the low quantity
of the obtained product it was not possible to perform further studies. HRMS (ESI⁺): calcd. for [C₁₈H₁₃FNO⁺H⁺] 282.1289, found 282.1287.

(R,E)-2-(4-Aminophenyl)-3-(nitromethyl)-5-phenylpent-4-en-1-one 3i: Yield: 57%; orange solid; mp 153-154°C. ¹H NMR (300 MHz, CDCl₃): δ 7.80 (d, J 8.6 Hz, 2H, H-2’,6’), 7.44-7.14 (m, 5H, H-2”,6”, H-3”,5”), H-4”), 6.65 (d, J 8.6 Hz, 2H, H-3’,5’), 6.56 (d, J 15.9 Hz, 1H, H-5), 6.17 (dd, J 15.9 and 8.6 Hz, 1H, H-4), 4.72 (dd, J 12.1 and 5.6 Hz, 1H, H-1’’’’), 4.58 (dd, J 12.1 and 7.7 Hz, 1H, H-1’’’’’), 4.17 (br s, 2H, NH₂), 3.84-3.53 (m, 1H, H-3), 3.18 (d, J 6.6 Hz, 2H, H-2) ppm. ¹³C NMR (75.47 MHz, CDCl₃): δ 194.9 (C-1), 151.5 (C-4’), 136.3 (C-1’’), 133.1 (C-β), 130.6 (C-2’,6’), 128.5 (C-3”,5”), 127.8 (C-4”), 126.9 (C-1’, C-4), 126.4 (C-2”,6”), 113.8 (C-3’,5’), 79.0 (C-1’’”), 39.6 (C-2), 37.6 (C-3) ppm. HRMS (ESI⁺): calcd. for [C₁₈H₁₃N₂O₃+H⁺] 311.1390, found 311.1389.

(R,E)-4-(p-Methoxystyryl)-2-phenyl-L¹-pyrroline-1-oxide 5h: Yield: 4%; Brown oil. ¹H NMR (300 MHz, CDCl₃): δ 8.34 (dd, J 8.6 and 4.5 Hz, 2H, H-2’,6’), 7.47-7.20 (m, 5H, H-Ar), 6.86 (d, J 8.4 Hz, 2H, H-3”,5”), 6.49 (d, J 15.6 Hz, 1H, H-β), 6.11 (dd, J 15.6 and 8.1 Hz, 1H, H-α), 4.47-4.35 (m, 1H, H-5), 4.23-4.12 (m, 1H, H-5), 3.82 (s, 3H, OCH₃), 3.53-3.33 (m, 2H, H-4, H-3), 3.16-3.01 (m 1H, H-3) ppm. ¹³C NMR (75.47 MHz, CDCl₃): Due to the low quantity of the obtained product it was not possible to perform further studies. HRMS (ESI⁺): calcd. for [C₁₀H₁₀NO₂+H⁺] 294.1489, found 294.1488.

4. Single-Crystal X-ray Diffraction

Single-crystals with block shape of compound 4d and with flake shape of compound 4e were manually selected from the crystallization vial. A suitable single-crystal was mounted on a glass fiber with the help of silicon grease. Data were collected at 180(2) K on a Bruker X8 Kappa APEX II charge-coupled device (CCD) area-detector diffractometer (Mo Kα graphite-monochromated radiation, λ = 0.71073 Å) controlled by the APEX2 software package, and equipped with an Oxford Cryosystems Series 700 cryostream monitored remotely using the software interface Cryopad. Images were processed using the software package SAINT+, and data were corrected for absorption by the multi-scan semi-empirical method implemented in SADABS. The structure was solved using the direct methods algorithm implemented in SHELXS-97, which allowed the immediate location of the majority of the atoms. All remaining non-hydrogen atoms were located from difference Fourier maps calculated from
successive full-matrix least squares refinement cycles on $F^2$ using SHELXL-97.$^{8,10}$ All non-hydrogen atoms were successfully refined using anisotropic displacement parameters.

Hydrogen atoms bound to carbon were located at their idealized positions using appropriate HFIX instructions in SHELXL (43 for the aromatic and vinylic, 23 for the $-\text{CH}_2-$ moieties and 13 for the chiral tertiary carbon atoms) and included in subsequent refinement cycles in riding-motion approximation with isotropic thermal displacements parameters ($U_{eq}$) fixed at 1.2 times $U_{eq}$ of the atom to which they are attached.

Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication No. CCDC-1033064-1033065. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 2EZ, U.K. FAX: (+44) 1223 336033. E-mail: deposit@ccdc.cam.ac.uk.

5. References
(2) Oliva, C. G.; Silva, A. M. S.; Paz, F. A. A.; Cavaleiro, J. A. S. Synlett 2010, 1123.
(6) SAINT+, Data Integration Engine v. 7.23a © 1997-2005, Bruker AXS, Madison, Wisconsin, USA.
(7) G. M. Sheldrick, SADABS v.2.01, Bruker/Siemens Area Detector Absorption Correction Program 1998, Bruker AXS, Madison, Wisconsin, USA.
6. NMR spectra of the synthesized products

<table>
<thead>
<tr>
<th>Peak</th>
<th>R. Time</th>
<th>Area</th>
<th>Area (%)</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>10.77</td>
<td>13568355</td>
<td>49%</td>
<td>0</td>
</tr>
<tr>
<td>2</td>
<td>12.72</td>
<td>13732279</td>
<td>51%</td>
<td></td>
</tr>
</tbody>
</table>

Solvant: i-propanol / Hexane (10/90)
Flow rate: 0.7 mL/min, $\lambda = 254$ nm

S9
Peak | R. | Area | Area ee (%)
---|---|---|---
1 | 19.77 | 44609304 | 100 >99

Solvent: i-propanol /Hexane (10/90)
Flow rate: 0.7 mL/min, λ = 254 nm
Peak | R. Time | Area 1 | Area 2 | ee % (%)
--- | --- | --- | --- | ---
1   | 12.64 | 13737694 | 100 | >99

Solvent: t-propanol / Hexane (10/90)
Flow rate: 0.7 mL/min, λ = 254 nm
Peak | R. Time | Area | % ee (%)
--- | ---- | ---- | ---- |
1 | 11.85 | 16702285 | 100 >99

Solvent: 2-propanol /Hexane (10/90)
Flow rate: 0.7 mL/min, λ = 254 nm
Solvent: i-propanol / Hexane (10/90)
Flow rate: 0.7 mL/min, \( \lambda = 254 \) nm

<table>
<thead>
<tr>
<th>Peak</th>
<th>R.</th>
<th>Area</th>
<th>Area %</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>13.07</td>
<td>13899625</td>
<td>100</td>
<td>&gt;99</td>
</tr>
</tbody>
</table>

Peak R. Area Area ee (%) Time
<table>
<thead>
<tr>
<th>Peak</th>
<th>R. Time</th>
<th>Area</th>
<th>Area %</th>
<th>ee (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>11.48</td>
<td>18312538</td>
<td>96</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>13.17</td>
<td>402143</td>
<td>4</td>
<td>96</td>
</tr>
</tbody>
</table>

Solvent: i-propanol / Hexane (10/90)
Flow rate: 0.7 mL/min, λ = 254 nm
Peak | R. | Area | Area % | ee (%)  
---|---|---|---|---
I | 15.71 | 9972484 | 100 | >99

Solvent: i-propanol / Hexane (10/90)
Flow rate: 0.7 mL/min, λ = 254 nm