Supporting Information

N-Heterocyclic Carbene-Catalyzed Highly Enantioselective Synthesis of Substituted Dihydropyranopyrazolones

Han-Ming Zhang, Hui Lv and Song Ye*

Beijing National Laboratory for Molecular Sciences, Key Laboratory of Molecular Recognition and Function, Institute of Chemistry, Chinese Academy of Sciences, Beijing 100190, China
songye@iccas.ac.cn

Table of Contents

Part I General Information ........................................................................................................2

Part II Experimental part ........................................................................................................3

1. Materials .............................................................................................................................3

2. Annulation of α-chloroaldehydes and pyrazolone-derived oxodienes ................................3

3. References ..........................................................................................................................16

Part III NMR Spectra ............................................................................................................17

Part IV HPLC Spectra ............................................................................................................37
Part I General Information

Unless otherwise indicated, all reactions were carried out under N₂ atmosphere in oven-dried glassware with magnetic stirring. Anhydrous THF and toluene were distilled from sodium and benzophenone. Anhydrous CH₂Cl₂ was distilled from CaH₂. Column chromatograph was performed on silica gel 200–300 mesh. All ¹H NMR (300 MHz), ¹³C NMR (75 MHz) spectra were recorded on a Bruker-DMX 300 spectrometer in CDCl₃, with tetramethylsilane as an internal standard and reported in parts per million (ppm, δ). ¹H NMR Spectroscopy splitting patterns were designated as singlet (s), doublet (d), triplet (t). Splitting patterns that could not be interpreted or easily visualized were designated as multiplet (m) or broad (br). Infrared spectra were recorded on a JASCO FT/IR-480 spectrophotometer and reported as wave number (cm⁻¹). Optical rotations were measured on Perkin Elmer/Model-343 digital polarimeter operating at the sodium D line with a 100 mm path cell, and are reported as follows: [α]₀T(concentration (g/100 mL), solvent).
Part II Experimental part

1. Materials

Both arylideneypyrazolone\(^1\) and \(\alpha\)-chloraldehydes\(^2\) were prepared according to literature methods.

2. Annulation of \(\alpha\)-chloraldehydes and Pyrazolone-derived oxodienes

![Diagram](https://example.com/diagram.png)

Typical procedure.

To an oven-dried 50 mL Schlenk tube equipped with a stir bar was charged with trazolium salt 5b (12.38 mg, 0.03 mmol). This tube was closed with a septum, evacuated, and back-filled with argon. To this mixture was added freshly distilled DCM (3 mL) and Et\(_3\)N (51 \(\mu\)L, 0.36 mmol), then stirred for 30 minutes at room temperature. Then Chloraldehyde 1 (75.8mg, 0.45 mmol), pyrazolone-derived oxodienes 2 (81.9mg, 0.3 mmol) was added. The reaction was stirred at room temperature until full consumption of compound 2. The solvent was removed under reduced pressure and the residue was purified by chromatography on silica gel (ethyl
acetate/petroleum ether, typically 1/25) to give the desired product.

Racemic samples for the standard of chiral HPLC spectra were prepared using the triazolium salts S1 as the catalyst.

![Chemical structure of S1](image)

(4S,5S)-5-benzyl-3-methyl-1,4-diphenyl-4,5-dihydropyrano[2,3-c]pyrazol-6(1H)-one (3a)

Yield: 113.6 mg (96%), white solid. mp 188-192 °C; R_f = 0.38 (petroleum ether/ethyl acetate, 5:1); [α]_D^{25} +224.3 (c 1.0, CH₂Cl₂), HPLC analysis: >99% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 95:5, 0.6 mL/min, 254 nm, 12.9min(minor), 18.0min (major)]; ¹H NMR (300 MHz, CDCl₃) δ 7.75 (d, J = 8.1 Hz, 2H), 7.43 (t, J = 7.5 Hz, 2H), 7.34-7.25 (m, 7H), 7.10 (d, J = 6.9 Hz, 2H), 7.01 (d, J = 6.6 Hz, 2H), 3.93 (d, J = 6.9 Hz, 1H), 3.53-3.46 (m, 1H), 3.28 (dd, J = 4.8 Hz, J = 14.7 Hz, 1H ), 2.50 (dd, J = 9.3 Hz, J = 14.4 Hz, 1H), 2.05 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 168.5, 146.2, 145.4, 138.6, 138.1, 137.8, 129.3, 129.2, 129.1, 128.7, 127.9, 127.8, 126.9, 126.6, 120.8, 102.4, 46.8, 38.2, 33.2, 12.5; IR (KBr) ν 2950, 1754, 1563, 1162, 1058, 754; HRMS (ESI) m/z: [M+H]⁺ for C₂₆H₂₂N₂O₂, 395.1754, Found 395.1751
(4S,5S)-5-benzyl-3-methyl-1-phenyl-4-p-tolyl-4,5-dihydropyrano[2,3-c]pyrazol-6(1H)-one (3b)

Yield: 115.3 mg (94%), white solid. mp 130-132 °C; Rf = 0.45 (petroleum ether/ethyl acetate, 5:1); [α]D[^25] +244.8 (c 1.00, CH2Cl2), HPLC analysis: 99% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 95:5, 0.6 mL/min, 254 nm, 12.5 min (minor), 17.1 min (major)]; 1H NMR (300 MHz, CDCl3) δ 7.66 (t, J = 1.2 Hz, 2H), 7.34 (d, J = 1.5 Hz, 2H), 7.22-7.15 (m, 4H), 7.03 (d, J = 4.2 Hz, 4H), 6.82 (t, J = 1.5 Hz, 2H), 3.82 (t, J = 1.5 Hz, 1H), 3.38 (dd, J = 1.8 Hz, J = 4.2 Hz, 1H), 3.17 (dd, J = 1.8 Hz, J = 15.0 Hz, 1H), 2.46-2.36 (m, 1H), 2.24 (s, 3H), 1.96 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 168.6, 146.2, 145.4, 138.3, 137.8, 137.5, 135.5, 129.8, 129.3, 129.2, 128.7, 127.8, 126.8, 126.5, 126.0, 102.6, 46.9, 37.8, 33.2, 21.2, 12.5; IR (KBr) ν 2990, 1785, 1502, 1100, 1074, 776; HRMS (ESI) m/z: [M+H]^+ for C27H24N2O2, 409.1910, Found 409.1907.
(4S,5S)-5-benzyl-4-(4-methoxyphenyl)-3-methyl-1-phenyl-4,5-dihydropyrano[2,3-c]pyrazol-6(1H)-one  (3c)

Yield: 119.6 mg (94%), white solid. mp 142-143 °C; Rf = 0.25 (petroleum ether/ethyl acetate, 5:1 ); [α]D25 +234.2 (c 0.50, CH2Cl2), HPLC analysis: 98% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 95:5, 0.6 mL/min, 254 nm, 17.8 min (minor), 27.7 min (major)]; 1H NMR (300 MHz, CDCl3) δ 7.76 (d, J = 7.8 Hz, 2H), 7.44 (t, J = 7.5 Hz, 2H), 7.35-7.25 (m, 4H), δ 7.13 (d, J = 7.2 Hz, 2H ), 6.93 (d, J = 8.4 Hz, 2H), 6.85 (d, J = 8.4 Hz, 2H), 3.90 (d, J = 6.9 Hz, 1H), 3.80 (s, 3H), 3.49 (dd, J = 5.7 Hz, J = 14.4, 1H), 3.28 (dd, J = 4.5 Hz, J = 14.4 Hz, 1H ), 2.52 (dd, J = 9.6 Hz, J = 14.7 Hz, 1H), 2.06 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 168.6, 159.2, 146.2, 145.4, 138.2, 137.8, 130.5, 129.3, 129.2, 129.0, 128.7, 126.8, 126.5, 120.8, 114.5, 102.7, 55.4, 47.0, 37.4, 33.2, 12.5; IR (KBr) ν 3443, 1786, 1612, 1066, 802; HRMS (ESI) m/z: [M+H]+ for C27H24N2O3 , 425.1860, Found 425.1857.

(4S,5S)-5-benzyl-4-(4-fluorophenyl)-3-methyl-1-phenyl-4,5-dihydropyrano[2,3-c]pyrazol-6(1H)-one (3d)

Yield: 112.6 mg (91%), white solid. mp 111-112 °C; Rf = 0.31 (petroleum ether/ethyl acetate, 5:1 ); [α]D25 +204.0 (c 0.8, CH2Cl2), HPLC analysis: 99% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 95:5, 0.6 mL/min, 254
nm, 12.0 min (minor), 16.6 min (major)); $^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.74 (d, $J$ = 8.1 Hz, 2H), 7.44 (t, $J$ = 7.5 Hz, 2H), 7.35-7.24 (m, 4H), 7.10 (d, $J$ = 6.9 Hz, 2H), 7.04-6.96 (m, 4H), 3.93 (d, $J$ = 6.9 Hz, 1H), 3.55-3.48 (m, 1H), 3.28 (dd, $J$ = 5.1 Hz, J = 15.0, 1H), 2.47 (dd, $J$ = 9.6 Hz, $J$ = 14.7 Hz, 1H), 2.05 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 168.3, 162.3 ($J$ = 245.3), 146.2, 145.3, 137.8, 137.7, 134.3 ($J$ = 3.0), 129.6, 129.5, 129.3, 128.8, 126.8 ($J$ = 22.5), 120.8, 116.1 ($J$ = 21.8), 102.2, 46.7, 37.4, 33.1, 12.5; IR (KBr) ν 3447, 1618, 1509, 1066, 1015, 796; HRMS (ESI) m/z: [M$^+$H]$^+$ for C$_{26}$H$_{21}$FN$_2$O$_2$, 413.1660, Found 413.1656.

(4S,5S)-5-benzyl-4-(4-chlorophenyl)-3-methyl-1-phenyl-4,5-dihydropyran[2,3-c]pyrazol-6(1H)-one (3e)

Yield: 114.5 mg (89%), white solid. mp 134-136 °C; $R_f$ = 0.30 (petroleum ether/ethyl acetate, 5:1); [$\alpha$]$_D^{25}$ +230.0 (c 0.16, CH$_2$Cl$_2$), HPLC analysis: >99% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 95:5, 0.6 mL/min, 254 nm, 12.6 min (minor), 18.6 min (major)]; $^1$H NMR (75 MHz, CDCl$_3$) $\delta$ 7.74 (d, $J$ = 8.1 Hz, 2H), 7.45 (d, $J$ = 7.8 Hz, 2H), 7.33-7.24 (m, 6H), 7.09 (d, $J$ = 6.9 Hz, 2H), 6.93 (d, $J$ = 8.4 Hz, 2H), 3.92 (d, $J$ = 6.6 Hz, 1H), 3.55-3.45 (m, 1H), 3.29 (dd, $J$ = 5.1 Hz, $J$ = 15.0 Hz, 1H), 2.47 (dd, $J$ = 9.6 Hz, $J$ = 14.7 Hz, 1H), 2.04 (s, 3H); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 168.1, 146.2, 145.3, 137.8, 137.7, 137.1, 133.7, 129.4,
129.3, 129.1, 128.8, 128.6, 127.0, 126.7, 120.8, 101.9, 46.5, 37.6, 33.1, 12.5; IR (KBr) v 2992, 1788, 1612, 1513, 1094, 802; HRMS (ESI) m/z: [M+H]+ for C26H21ClN2O2 , 429.1364, Found 429.1362.

(4S,5S)-5-benzyl-4-(4-bromophenyl)-3-methyl-1-phenyl-4,5-dihydropyrano[2,3-c]pyrazol-6(1H)-one (3f)

Yield: 127.5 mg (90%), white solid. mp 113-114 °C; Rf = 0.30 (petroleum ether/ethyl acetate, 5:1); [α]D25 +104.2 (c 1.1, CH2Cl2), HPLC analysis: 98% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 95:5, 0.6 mL/min, 254 nm, 13.3 min (minor), 19.6 min (major)]; 1H NMR (300 MHz, CDCl3) δ 7.73 (d, J = 7.8 Hz, 2H), 7.42 (t, J = 7.5 Hz, 4H), 7.31-7.23 (m, 4H), 7.08 (d, J = 6.9 Hz, 2H), 6.86 (d, J = 6.9 Hz, 2H), 3.89 (d, J = 6.6 Hz, 1H), 3.54-3.47 (m, 1H), 3.28 (dd, J = 4.5 Hz, J = 14.7 Hz, 1H), 2.46 (dd, J = 9.6 Hz, J = 14.7 Hz, 1H ), 2.03 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 168.1, 146.2, 145.2, 137.7, 137.6, 137.5, 132.3, 129.6, 129.3, 129.1, 128.8, 127.0, 126.7, 121.8, 120.8, 101.8, 46.4, 37.6, 33.1, 12.5; IR (KBr) ν 3448, 1636, 1016, 801, 472; HRMS (ESI) m/z: [M+H]+ for C26H21BrN2O2 , 473.0859, Found 473.0853.
4-((4S,5S)-5-benzyl-3-methyl-6-oxo-1-phenyl-1,4,5,6-tetrahydropyrano[2,3-c]pyrazol-4-yl)benzonitrile (3g)

Yield: 113.2 mg (90%), white solid. mp 120-121 °C; Rf = 0.18 (petroleum ether/ethyl acetate, 5:1); [α]D25 +227.8 (c 1.0, CH2Cl2), HPLC analysis: 91% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 90:10, 0.6 mL/min, 254 nm, 24.8 min (minor), 29.6 min (major)]; 1H NMR (300 MHz, CDCl3) δ 7.74 (d, J = 8.1 Hz, 2H), 7.63 (d, J = 8.1 Hz, 2H), 7.45 (t, J = 7.5 Hz, 2H), 7.36-7.27 (m, 4H), 7.09 (t, J = 8.4 Hz, 4H), 4.01 (d, J = 14.3 Hz, 1H), 3.62-3.55 (m, 1H), 3.32 (dd, J = 4.8 Hz, J = 14.7 Hz, 1H), 2.42 (dd, J = 9.6 Hz, J = 14.7 Hz, 1H), 2.04 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 167.7, 146.2, 145.1, 144.0, 137.5, 137.2, 132.9, 129.3, 128.9, 128.8, 128.7, 127.1, 126.8, 120.8, 118.3, 111.9, 101.0, 46.0, 38.1, 33.1, 12.4; IR (KBr) ν 3490, 1754, 1582, 1166, 805; HRMS (ESI) m/z: [M+H]+ for C27H21N3O2 , 420.1707, Found. 420.1712.
Yield: 116.3 mg (95%), white solid. mp 123-124 °C; R_f = 0.45 (petroleum ether/ethyl acetate, 5:1 ); [α]_D^25 +151.2 (c 0.50, CH₂Cl₂), HPLC analysis: >99% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 95:5, 0.6 mL/min, 254 nm, 10.2 min (minor), 13.9 min (major)]; ^1_H NMR (300 MHz, CDCl₃) δ 7.76 (d, J = 7.8 Hz, 2H), 7.46 (t, J = 5.7 Hz, 2H), 7.41-7.18 (m, 5H), 7.10 (t, J = 6.9 Hz, 3H), 6.79 (t, J = 5.7 Hz, 2H), 3.90 (d, J = 6.9 Hz, 1H), 3.52-3.45 (m, 1H), 3.26 (dd, J = 5.1 Hz, J = 14.7 Hz, 1H ), 2.50 (dd, J = 9.0 Hz, J = 14.7 Hz, 1H), 2.06 (s, 3H ); ^13_C NMR (75 MHz, CDCl₃) δ 168.5, 146.2, 145.4, 138.8, 138.4, 138.2, 129.3, 129.2, 128.9, 128.6, 128.5, 126.8, 126.5, 125.0, 120.8, 102.4, 46.7, 38.2, 33.2, 21.6, 12.5; IR (KBr) ν 2962, 1787, 1494, 1262, 1066, 797; HRMS (ESI) m/z: [M+H]^+ for C₂₇H₂₄N₂O₂ , 409.1910, Found 409.1907.

(4S,5S)-5-benzyl-4-(3-methoxyphenyl)-3-methyl-1-phenyl-4,5-dihydropyrano[2,3-c]pyrazol-6(1H)-one  (3i)

Yield: 119.6 mg (94%), white solid. mp 127-128 °C; R_f = 0.30 (petroleum ether/ethyl acetate, 5:1 ); [α]_D^25 +178.3 (c 0.3, CH₂Cl₂), HPLC analysis: >99% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 95:5, 0.6 mL/min, 254 nm, 10.4 min (minor), 14.9 min (major)]; ^1_H NMR (300 MHz, CDCl₃) δ 7.75 (d, J = 8.4 Hz, 2H), 7.44 (t, J = 15.3 Hz, 2H), 7.34-7.20 (m, 5H), 7.12 (t, J = 17.1 Hz, 3H),
6.79 (t, J = 8.1, 2H), 3.84 (d, J = 6.6 Hz, 1H), 3.52-3.45 (m, 1H), 3.27 (dd, J = 4.8 Hz, J = 14.7 Hz, 1H), 2.47 (dd, J = 9.3 Hz, J = 14.7 Hz, 1H), 2.31 (s, 3H), 2.06 (s, 3H);

13C NMR (75 MHz, CDCl3) δ 168.6 146.3, 146.5, 138.8, 138.4, 138.3, 137.9, 129.4, 129.2, 129.0, 128.7, 128.5, 126.9, 126.6, 125.1, 120.8, 102.5, 46.8, 38.2, 33.2, 21.6, 12.6; IR (KBr) ν 2929, 1787, 1492, 1066, 799, 697; HRMS (ESI) m/z: [M +H]+ for C27H24N2O3 , 425.1860, Found 425.1858.

(4S,5S)-5-benzyl-4-(3-chlorophenyl)-3-methyl-1-phenyl-4,5-dihydropyrano[2,3-c]pyrazol-6(1H)-one (3j)

Yield: 109.4  (85%), white solid. mp 151-153 °C; Rf = 0.32 (petroleum ether/ethyl acetate, 5:1 ); [α]D25 +174.0 (c 0.2, CH2Cl2), HPLC analysis: 99% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 95:5, 0.6 mL/min, 254 nm, 11.5 min (minor), 16.2 min (major)]; 1H NMR (300 MHz, CDCl3) δ 7.75 (d, J = 8.1 Hz, 2H), 7.45 (t, J = 7.8 Hz, 2H), 7.37-7.26 (m, 6H), 7.10 (d, J = 6.9 Hz, 2H), 6.96 (s, 1H), 6.90-6.87 (m, 1H), 3.91 (d, J = 6.9 Hz, 1H), 3.56-3.51 (m, 1H ), 3.31 (dd, J = 4.8 Hz, J = 14.7 Hz, 1H), 2.47 (dd, J = 9.6 Hz, J = 14.7 Hz, 1H), 2.06 (s, 3H); 13C NMR (75 MHz, CDCl3) δ 168.0, 146.2, 145.3, 140.5, 137.7, 134.9, 130.5, 129.5, 129.4, 129.1, 128.8, 128.3, 128.2, 127.0, 126.7, 125.9, 120.9, 101.6, 46.4, 37.8, 33.2, 12.6; IR (KBr) ν 3726, 1790, 1514, 1017, 799; HRMS (ESI) m/z: [M^+H]⁺ for
C_{26}H_{21}ClN_{2}O_{2}, 429.1364, Found 429.1361.

(4S,5S)-5-benzyl-4-(2-chlorophenyl)-3-methyl-1-phenyl-4,5-dihydropyrano[2,3-c]pyrazol-6(1H)-one (3k)

Yield: 106.8 mg (83%), white solid. mp 158-161°C; R_{f} = 0.36 (petroleum ether/ethyl acetate, 5:1); [\alpha]_{D}^{25} = -53.0 (c 0.2, CH_{2}Cl_{2}), HPLC analysis: 99% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 95:5, 0.6 mL/min, 254 nm, 11.4 min (minor), 12.8 min (major)]; \textsuperscript{1}H NMR (300 MHz, CDCl_{3}) \delta 7.79 (d, J = 7.8 Hz, 2H), 7.48 (t, J = 7.8 Hz, 2H), 7.38-7.19 (m, 6H), 7.18 (t, J = 3.9 Hz, 3H), 6.92 (dd, J = 1.8 Hz, J = 6.6 Hz, 1H), 4.46 (d, J = 2.7 Hz, 1H), 3.33-3.28 (m, 1H), 3.16 (dd, J = 6.9 Hz, J = 13.5 Hz, 1H), 2.98 (dd, J = 8.4 Hz, J = 13.5 Hz, 1H), 2.04 (s, 3H); \textsuperscript{13}C NMR (75 MHz, CDCl_{3}) \delta 167.5, 147.1, 146.7, 138.0, 137.8, 136.7, 133.4, 130.3, 129.4, 129.3, 129.1, 128.8, 128.4, 127.7, 127.5, 126.7, 120.8, 97.1, 49.3, 37.9, 35.5, 12.6; IR (KBr) ν 2962, 1793, 1513, 1261, 1097, 799; HRMS (ESI) m/z: [M\textsuperscript{+}H\textsuperscript{+}] for C_{26}H_{21}ClN_{2}O_{2}, 429.1364, Found 429.1360.
**(4R,5S)-5-benzyl-3-methyl-4-(naphthalen-1-yl)-1-phenyl-4,5-dihydropyrano[2,3-c]pyrazol-6(1H)-one** (3l)

Typical procedure but with 0.1 equiv. Cs₂CO₃ and 1.4 equiv. Et₃N used. Yield: 109.3 mg (82%), white solid. mp 171-173 °C; Rᵣ = 0.38 (petroleum ether/ethyl acetate, 5:1 ); [α]ᵣ²⁵ +4.2 (c 1.7, CH₂Cl₂), HPLC analysis: >99% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 98:2, 0.5 mL/min, 254 nm, 18.8 min (minor), 19.8 min (major)];¹H NMR (300 MHz, CDCl₃) δ 7.91-7.87 (m, 2H), 7.81 (d, J = 8.1 Hz, 1H), 7.67 (d, J = 8.2 Hz, 1H), 7.67-7.38 (m, 6H), 7.30-7.17 (m, 5H), 7.04 (d, J = 7.2 Hz, 1H), 6.97 (d, J = 8.7 Hz, 1H), 4.73 (s, 1H), 3.37-3.31 (m, 1H), 3.21 (dd, J = 4.8 Hz, J = 13.2 Hz, 1H), 2.95 (dd, J = 10.5 Hz, J = 13.2 Hz, 1H), 2.05 (s, 3H);¹³C NMR (75 MHz, CDCl₃) δ 167.8, 147.4, 146.9, 137.9, 136.9, 135.9, 134.3, 130.4, 129.7, 129.4, 129.3, 129.1, 128.4, 127.4, 126.6, 126.4, 125.8, 125.6, 124.5, 122.1, 120.7, 97.4, 50.4, 37.7, 33.1, 12.6; IR (KBr) ν 3450, 2962, 1790, 1513, 1107, 1015, 801; HRMS (ESI) m/z: M+Calc. for C₃₀H₂₄N₂O₂ , 445.1901, Found 445.1905.

**(4S,5S)-5-hexyl-3-methyl-1,4-diphenyl-4,5-dihydropyrano[2,3-c]pyrazol-6(1H)-one** (3m)

Yield: 95.5 mg (82%), colorless oil; Rᵣ = 0.38 (petroleum ether/ethyl acetate, 5:1 ); [α]ᵣ²⁵ +249.8 (c 5.2, CH₂Cl₂), HPLC analysis: 99% ee [Daicel CHIRALPAK AD-H
column, 20 °C, 254 nm hexane/i-PrOH = 98:2, 0.5 mL/min, 254 nm, 14.5 min (minor), 20.1 min (major)]; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.77 (d, \(J = 7.5\) Hz, 2H), 7.43 (t, \(J = 7.5\) Hz, 2H), 7.40-7.20 (m, 4H), 7.08 (t, \(J = 1.5\) Hz, 2H), 4.09 (d, \(J = 6.9\) Hz, 1H), 3.03 (dd, \(J = 6.9\) Hz, \(J = 13.5\) Hz, 1H), 2.13 (s, 3H), 1.79-1.70 (m, 1H), 1.46 (q, \(J = 6.9\) Hz, 2H), 1.30-1.17 (m, 8H), 0.86 (t, \(J = 8.3\) Hz, 3H); \(^1\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 168.7, 146.5, 145.4, 138.7, 129.2, 129.0, 127.6, 127.5, 126.4, 120.7, 102.2, 45.3, 38.8, 31.6, 29.1, 27.4, 27.1, 22.6, 14.1, 12.5; IR (KBr) \(\nu\) 2926, 1793, 1599, 1493, 1023, 756; HRMS (ESI) m/z: [M+H]\(^+\) for C\(_{25}\)H\(_{28}\)N\(_2\)O\(_2\), 389.2224, Found 389.2221.

\(\text{O} \quad \text{Ph} \quad \text{N} \quad \text{N} \quad \text{O} \quad \text{n-C}_9\text{H}_{19}\)

(4S,5S)-5-decyl-3-methyl-1,4-diphenyl-4,5-dihydropyrano[2,3-c]pyrazol-6(1\(H\))-one (3n)

Yield: 110.6 mg (83%), colorless oil; \(R_f = 0.38\) (petroleum ether/ethyl acetate, 5:1); \([\alpha]_D^{25}\) +214.3 (c 5.1, CH\(_2\)Cl\(_2\)), HPLC analysis: >99% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 98:2, 0.5 mL/min, 254 nm, 10.9 min (minor), 14.6 min (major)]; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.77 (d, \(J = 7.8\) Hz, 2H), 7.44 (t, \(J = 7.8\) Hz, 2H), 7.32-7.21 (m, 4H), 7.09 (t, \(J = 1.5\) Hz, 2H), 4.10 (d, \(J = 6.9\) Hz, 1H), 3.04 (dd, \(J = 6.9\) Hz, \(J = 13.2\) Hz, 1H), 2.13 (s, 3H), 1.82-1.71 (m, 1H), 1.44 (s, 2H), 1.25 (s, 16 H), 0.88 (t, \(J = 6.6\) Hz, 3H); \(^1\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 168.7, 146.5, 145.4, 138.7, 137.9, 129.3, 129.1, 127.7, 127.6, 126.5, 120.8, 102.2, 45.4, 38.8,
32.0, 29.7, 29.6, 29.5, 29.4, 27.4, 27.2, 22.8, 14.2, 12.6; IR (KBr) ν 2923, 1792, 1599, 1493, 1047, 690; HRMS (ESI) m/z: [M+H]+ for C29H36N2O2 , 445.6242, Found 445.2846.

(4S,5S)-5-decyl-3-methyl-1-phenyl-4-p-tolyl-4,5-dihydropyrano[2,3-c]pyrazol-6(1H)-one (3o)

Yield: 114.1 mg (83%), colorless oil; Rf = 0.45 (petroleum ether/ethyl acetate, 5:1 ); [α]D25 +211.7 (c 5.2, CH2Cl2), HPLC analysis: >99% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 98:2, 0.5 mL/min, 254 nm, 9.4 min (minor), 10.6 min (major)]; 1H NMR (300 MHz, CDCl3) δ 7.78 (dd, J = 1.2 Hz, J = 3.0 Hz, 2H), 7.45-7.40 (m, 2H), 7.28-7.23 (m, 1H), 7.08 (d, J = 7.8 Hz, 2H), 6.96 (d, J = 8.1, 2H), 4.06 (d, J = 6.9 Hz, 1H), 3.01 (dd, J = 7.2 Hz, J = 13.5 Hz, 1H), 2.29 (s, 3H), 2.12 (s, 3H), 1.80-1.70 (m, 1H), 1.43 (t, J = 6.9 Hz, 2H), 1.19 (t, J = 11.7 Hz, 16H ), 0.88 (t, J = 6.6 Hz, 3H); 13C NMR (75 MHz, CDCl3) δ 168.8, 146.5, 145.3, 137.9, 137.3, 135.6, 129.7, 129.3, 127.2, 126.4, 120.7, 102.4, 45.4, 38.3, 32.0, 29.6, 29.5, 29.4, 29.3, 27.3, 27.2, 22.7, 21.1, 14.2, 12.5; IR (KBr) ν 2924, 1792, 1599, 1492, 1049, 756; HRMS (ESI) m/z: [M+H]+ for C30H38N2O2 , 459.3001, Found 459.3003.
(4S,5S)-4-(4-chlorophenyl)-5-decyl-3-methyl-1-phenyl-4,5-dihydropyrano[2,3-c]pyrazol-6(1H)-one \((3p)\)

Yield: 119.1 mg (83%), colorless oil; \(R_f=0.42\) (petroleum ether/ethyl acetate, 5:1); \([\alpha]_D^{25} +214.5\) (c 4.8, CH\(_2\)Cl\(_2\)), HPLC analysis: 98% ee [Daicel CHIRALPAK AD-H column, 20 °C, 254 nm hexane/i-PrOH = 98:2, 0.5 mL/min, 254 nm, 11.9 min (minor), 13.9 min (major)]; \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 7.78 (d, \(J = 8.1\) Hz, 2H), 7.47 (t, \(J = 7.8\) Hz, 2H), 7.33-7.29 (m, 3H), 7.04 (d, \(J = 8.4\) Hz, 2H), 4.11 (d, \(J = 6.9\) Hz, 1H), 3.01 (dd, \(J = 6.9\) Hz, \(J = 13.5\) Hz, 1H), 2.14 (s, 3H), 1.84-1.73 (m, 1H ), 1.46 (t, \(J = 7.2\) Hz, 2H), 1.28 (s, 16H), 0.91 (t, \(J = 6.3\) Hz, 3H ); \(^{13}\)C NMR (75 MHz, CDCl\(_3\)) \(\delta\) 168.4, 146.5, 145.3, 137.8, 137.3, 133.6, 129.4, 129.3, 129.0, 126.6, 120.8, 101.7, 45.3, 38.2, 32.0, 29.7, 29.6, 29.5, 27.4, 27.2, 22.8, 14.2, 12.6; IR (KBr) ν 2924, 1792, 1492, 1050, 756; HRMS (ESI) m/z: [M+H]\(^+\) for \(C_{29}H_{35}ClN_2O_2\), 479.2460, Found 479.2458.

3. References


Part III NMR Spectra

![NMR Spectra Diagram]

**NAME**: zhm-755-2

**EXPN**: 11

**PROCNO**: 1

**Date**: 20130126

**Time**: 16.07

**INSTRUM**: spect

**PROBHD**: 5 mm DUL 13C-1

**PULPROG**: zg30

**TD**: 65536

**SOLVENT**: CDCl3

**NS**: 8

**DS**: 0

**SWH**: 8992.806 Hz

**FIDRES**: 0.137219 Hz

**AQ**: 3.6438515 sec

**RG**: 71.8

**D**: [additional NMR parameters here]

---

**NAME**: zhm-755-2

**EXPN**: 11

**PROCNO**: 1

**Date**: 20130126

**Time**: 16.11

**INSTRUM**: spect

**PROBHD**: 5 mm DUL 13C-1

**PULPROG**: zgpg30

**TD**: 65536

**SOLVENT**: CDCl3

**NS**: 49

**DS**: 4

**SWH**: 17985.611 Hz

**FIDRES**: 0.274439 Hz

**AQ**: 1.8219508 sec

**RG**: 3251

**D**: [additional NMR parameters here]

---

**NAME**: zhm-755-2

**EXPN**: 11

**PROCNO**: 1

**Date**: 20130126

**Time**: 16.11

**INSTRUM**: spect

**PROBHD**: 5 mm DUL 13C-1

**PULPROG**: zgpg30

**TD**: 65536

**SOLVENT**: CDCl3

**NS**: 49

**DS**: 4

**SWH**: 17985.611 Hz

**FIDRES**: 0.274439 Hz

**AQ**: 1.8219508 sec

**RG**: 3251

**D**: [additional NMR parameters here]
<table>
<thead>
<tr>
<th>ppm</th>
<th>9</th>
<th>8</th>
<th>7</th>
<th>6</th>
<th>5</th>
<th>4</th>
<th>3</th>
<th>2</th>
<th>1</th>
<th>0</th>
</tr>
</thead>
<tbody>
<tr>
<td>12.56</td>
<td>14.22</td>
<td>22.78</td>
<td>27.19</td>
<td>27.38</td>
<td>29.41</td>
<td>29.45</td>
<td>29.61</td>
<td>29.65</td>
<td>32.00</td>
<td>38.79</td>
</tr>
</tbody>
</table>

**Diagram with Molecular Structure:**

- **NAME:** zhm-826-b
- **EXPNO:** 10
- **PROCNO:** 1
- **Date:** 20130323
- **Time:** 16.19
- **INSTRUM:** spect
- **PROBHD:** 5 mm DUL 13C-1
- **POLPROG:** zg30
- **TD:** 32768
- **SOLVENT:** CDCl3
- **NS:** 9
- **DS:** 0
- **SWH:** 6172.839 Hz
- **FIDRES:** 0.188380 Hz
- **AQ:** 2.6542580 sec
- **RG:** 35.9
- **D:** 81.000 usec
- **D:** 6.50 usec
- **TE:** 296.0 K
- **D1:** 1.00000000 sec

---

**For CHANNEL f1:**

- **NUC1:** 1H
- **P1:** 10.30 usec
- **PL1:** 3.00 dB
- **SFO1:** 300.1318534 MHz
- **SI:** 32768
- **SF:** 300.1300099 MHz
- **WDW:** EM
- **SSB:** 0
- **LB:** 0.30 Hz
- **PC:** 1.00

---

**For CHANNEL f2:**

- **CPDPRG:** waltz16
- **NUC2:** 1H
- **PCD2:** 100.00 usec
- **PL2:** 3.00 dB
- **PL12:** 22.74 dB
- **PL13:** 23.00 dB
- **SFO2:** 300.1312005 MHz
- **SI:** 32768
- **SF:** 75.4677428 MHz
- **WDW:** EM
- **SSB:** 0
- **LB:** 1.00 Hz
- **PC:** 1.40
Part IV HPLC Spectra
Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry
This journal is © The Royal Society of Chemistry 2013
n-C9H19

3n

Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry
This journal is © The Royal Society of Chemistry 2013