Supporting Information
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Supporting Information

Stereoselective Intramolecular Carbene C–H Insertion Catalyzed by Rhodium(III) Porphyrin Complexes

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General Experimental Section

All reactions were performed using the standard Schlenk technique under a nitrogen atmosphere. Reagents were obtained commercially and were used without further purification unless indicated otherwise. The free base porphyrins H2TTP,1 H2TDCPP,2 H2TMP2 and H2TTPPP3 were synthesized by the literature methods. Toluene and THF were freshly distilled from Na/benzophenone under an Ar atmosphere. CH2Cl2 was freshly distilled from CaH2 under an Ar atmosphere. Flash chromatography was performed on a silica gel (Merck Kiesegel 60 F254 230-400 mesh) or alumina (Merck 90 active neutral 70-230 mesh ASTM) column. 1H and 13C-NMR spectra were recorded on a Bruker DPX-300, AV-400 or DRX-500 spectrometer. Chemical shifts (δ, ppm) were determined with TMS as internal reference. UV-visible spectra were obtained on a Perkin-Elmer Lambda 19 spectrophotometer. Mass spectra were obtained on a Finnigan LCQ quadrupole ion trap (ESI), Finnigan MAT 95 (EI and FAB) mass spectrometer.
General Procedure for Synthesis of [Rh(Por)Me]4

A mixture of H2Por (100 mg) and [Rh(CO)2Cl]2 (100 mg) in toluene (30 mL) was heated under reflux. The reaction was monitored by UV-vis spectrometry for the complete disappearance of the Q-band of H2Por. After completion of reaction, toluene was removed by vacuum distillation. [RhIII(Por)Cl] complex was purified by column chromatography using neutral alumina with CH2Cl2 as eluent as a red fraction.

[RhIII(Por)Cl] was dissolved in degassed ethanol. Addition of NaBH4 (14 mg) in 1M NaOH (4 mL) to the solution under N2 led to a color change from red to reddish brown, indicating the formation of [RhI(Por)] anion. The resulting solution was then stirred at room temperature for 30 min. Addition of CH3I (0.2 mL) led to the formation of a light red precipitate, which was collected by filtration followed by purification by flash column chromatography on silica gel using CH2Cl2 as the eluent. The red solid characterized as [RhIII(Por)Me] was obtained in 67–72% yield.

Characterization of Rhodium(III) Porphyrin Complexes

[RhIII(TTP)Me]5 UV-vis/CH2Cl2 \( \lambda_{\text{max}}/\text{nm} \) (\( \log \varepsilon/\text{dm}^3\text{mol}^{-1}\text{cm}^{-1} \)): 413 (5.29), 521 (4.52). \( ^1\text{H NMR (300 MHz, CDCl}_3 \delta 8.72 \text{ (s, 8H), 8.08–7.99 \text{ (m, 8H), 7.53 \text{ (d, } J = 8.0 \text{ Hz, 8H), 2.70 \text{ (s, 12H), -5.82 \text{ (d, } J = 2.9 \text{ Hz, 3H). MS (FAB) m/z 786 (M}^+)} \).

[RhIII(TDCPP)Me] UV-vis/CH2Cl2 \( \lambda_{\text{max}}/\text{nm} \) (\( \log \varepsilon/\text{dm}^3\text{mol}^{-1}\text{cm}^{-1} \)): 412 (5.27), 525 (4.38), 552 (4.18). \( ^1\text{H NMR (300 MHz, CDCl}_3 \delta 8.67 \text{ (s, 8H), 7.80–7.67 \text{ (m, 12H), -5.63 \text{ (d, } J = 2.9 \text{ Hz, 3H). MS (FAB) m/z 1006 (M}^+)} \).

[RhIII(TMP)Me]4 UV-vis/CH2Cl2 \( \lambda_{\text{max}}/\text{nm} \) (\( \log \varepsilon/\text{dm}^3\text{mol}^{-1}\text{cm}^{-1} \)): 425 (5.01), 537 (4.14), 569 (1.26). \( ^1\text{H NMR (300 MHz, CDCl}_3 \delta 8.62 \text{ (s, 8H), 2.62 \text{ (s, 12H), 2.08 \text{ (s, 12H), 1.74 \text{ (s, 12H), -2.94 \text{ (d, } J = 2.6 \text{ Hz, 3H). MS (FAB) m/z 898 (M}^+)} \).

[RhIII(TTPPP)CH3]6 THF was used as solvent in the reductive alkylation step with NaBH4 / CH3I. UV-vis/CH2Cl2 \( \lambda_{\text{max}}/\text{nm} \) (\( \log \varepsilon/\text{dm}^3\text{mol}^{-1}\text{cm}^{-1} \)): 434 (5.17), 539 (4.13). \( ^1\text{H NMR (400 MHz, CDCl}_3 \delta 8.45 \text{ (s, 8H), 7.95–7.90 \text{ (m, 16H), 7.86 \text{ (d, } J = 2.1 \text{ Hz, 4H), 7.57 \text{ (t, } J = 7.2 \text{ Hz, 10H), 7.48–7.46 \text{ (m, 6H), 7.01 \text{ (d, } J = 8.4 \text{ Hz, 8H), 6.48–6.45 \text{ (m, 16H), 6.13 \text{ (t, } J = 7.7 \text{ Hz, 8H), -7.13 \text{ (d, } J = 2.8 \text{ Hz, 3H). MS (FAB) m/z 1645 (M}^+)} \).
General Procedure for Preparation of $\alpha$-Diazoacetamides$^{7,8}$

To a mixture of malonic acid ethyl esters (10 mmol) and $p$-ABSA (15 mmol) in anhydrous acetonitrile (20 mL), DBU (15 mmol) was added dropwise. The resulting mixture was stirred at room temperature, and the reaction was monitored by TLC (20% EtOAc-hexanes mixture). Upon complete consumption of the starting materials, the reaction mixture was diluted with 20 mL distilled water, followed by extraction with diethyl ether. After washing with 10% NaHCO$_3$ solution and brine, the combined organic extracts were dried over MgSO$_4$ and concentrated to ca. 2 mL under reduced pressure. The residue was purified by flash chromatography (10–15% EtOAc-hexanes) to afford the $\alpha$-diazoacetamides.

General Procedure for Rhodium(III) Porphyrin-Catalyzed Formation of $\beta$-Lactam 2 from $\alpha$-Diazoacetamides 1

Diazo ester 1 (0.1 mmol) dissolved in toluene (5 mL) was added to a toluene solution (5 mL) containing [Rh(Por)Me] (1 mol%) under N$_2$ atmosphere. The reaction mixture was refluxed until the starting diazo ester was completely consumed. The mixture was concentrated under reduced pressure, and the residue was purified by flash chromatography using $n$-hexane/ethyl acetate as the eluent to obtain the lactams 2.
General procedure for rhodium(III) porphyrin-catalyzed formation of γ-lactam 3 from α-diazoacetamides 1

Diazo ester 1 (0.1 mmol) dissolved in toluene (5 mL) was added to a toluene solution (5 mL) containing [Rh(TTP)Me] (1 mol%) under N₂ atmosphere. The reaction mixture was refluxed until the starting diazo ester was completely consumed. The mixture was concentrated under reduced pressure, and the residue was purified by flash chromatography using n-hexane/ethyl acetate as the eluent to obtain the lactams 3.
Literature References for 2(3H)-indolinones 3e–3f, and 3k

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\begin{array}{c|c}
\text{MeO} & (a) \text{Choi, M. K.-W.; Yu, W.-Y.; Che, C.-M.} \text{ Org. Lett. 2005, 7, 1081.} \\
\text{3e} & (b) \text{Choi, M. K.-W.; Yu, W.-Y.; So, M.-H.; Zhou, C.-Y.; Deng, Q.-H.; Che, C.-M. Chem. Asian J. 2008, 3, 1256.} \\
\text{3f} & \text{MeO} \\
\text{CH}_2\text{CH}_2\text{Ph} & \text{Choi, M. K.-W.; Yu, W.-Y.; Che, C.-M. Org. Lett. 2005, 7, 1081.} \\
\text{3k} & \\
\end{array}
\]

Literature References for \(\gamma\)-lactams 4g and 4j

\[
\begin{array}{c|c}
\text{Ph} & \text{Choi, M. K.-W.; Yu, W.-Y.; Che, C.-M. Org. Lett. 2005, 7, 1081.} \\
\text{CO}_2\text{Et} & \text{4g} \\
\text{Bn} & \\
\text{Ph} & (a) \text{Padwa, A.; Austin, D. J.; Price, A. T.; Semones, M. A.; Doyle, M. P.; Protopopova, M. N.; Winchester, W. R.; Tran, A. J. Am. Chem. Soc. 1993, 115, 8669.} \\
\text{CO}_2\text{Et} & (b) \text{Choi, M. K.-W.; Yu, W.-Y.; Che, C.-M. Org. Lett. 2005, 7, 1081.} \\
\text{rBu} & \text{4j} \\
\end{array}
\]
Characterization of β-lactams 2f, 2(3H)-indolinones 3l, and γ-lactams 4h–4i, 4k–4n

**N-\((p\)-Nitrophenyl\)-trans-2-phenyl-3-(ethoxycarbonyl)-azetidine-4-one (2f)** Yellow oil. \(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 8.15 (d, \(J = 5.1\) Hz, 2H), 7.43–7.37 (m, 7H), 5.41 (d, \(J = 2.8\) Hz, 1H), 4.31 (q, \(J = 7.1\) Hz, 2H) 3.65 (d, \(J = 2.8\) Hz, 1H). 1.34 (t, \(J = 7.1\) Hz, 3H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 168.2, 161.8, 137.8, 134.6, 129.6, 129.5, 128.6, 126.1, 125.2, 117.1, 64.1, 62.5, 58.3, 14.1. EIMS m/z 340 (M\(^+\)). HRMS (EI) for C\(_{18}\)H\(_{16}\)N\(_2\)O\(_5\), calcd. 340.1059, found 340.1065.

**N-Pentyl-trans-3-(ethoxycarbonyl)-4-propyl-pyrrolidine-2-one (4h)** Colorless oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 4.24 (m, 2H), 3.53 (m, 1H), 3.15–3.11 (m, 2H), 2.98(m, 1H), 2.70 (m, 1H), 1.58 (m, 1H), 1.45 (m, 2H) 1.31–1.25 (m, 7H), 1.24 (m, 1H), 0.94–0.85 (m, 9H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 169.4, 168.3, 61.5, 55.5, 52.1, 52.0, 48.9, 49.0, 36.3, 33.0, 26.9, 20.4, 16.8, 14.0, 11.2. EIMS m/z 269 (M\(^+\)). HRMS (EI) for C\(_{19}\)H\(_{18}\)N\(_2\)O\(_5\), calcd. 269.1991, found 269.1992.

**N-Ethyl-3-(ethoxycarbonyl)-pyrrolidine-2-one (4i)** Yellow oil. \(^1\)H NMR (400 MHz, CDCl\(_3\)) \(\delta\) 4.22 (q, \(J = 7.1\) Hz, 2H), 3.53–3.50 (m, 1H), 3.43–3.33 (m, 4H), 2.40–2.24 (m, 2H), 1.31 (t, \(J = 7.1\) Hz, 3H), 1.14 (t, \(J = 7.3\) Hz, 3H). \(^13\)C NMR (100 MHz, CDCl\(_3\)) \(\delta\) 170.5, 169.4, 61.5, 48.7, 45.0, 37.6, 22.3, 14.1, 12.3. EIMS m/z 185 (M\(^+\)). HRMS (EI) for C\(_9\)H\(_{15}\)NO\(_3\), calcd. 185.1052, found 185.1048.
**N-(p-Methoxyphenyl)-trans-3-(ethoxycarbonyl)-4-phenyl-pyrrolidine-2-one (4k)** White solid. 

$^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 7.53 (d, $J = 6.7$ Hz, 2H), 7.39–7.26 (m, 5H), 6.91 (d, $J = 6.7$ Hz, 2H), 4.31–4.21 (m, 2H), 4.18 (d, $J = 8.5$ Hz, 1H), 4.09 (q, $J = 8.4$ Hz, 1H), 3.87 (t, $J = 8.6$ Hz, 1H), 3.80 (s, 3H), 1.29 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 170.0, 168.2, 157.3, 139.6, 136.8, 129.1, 127.7, 127.0, 126.7, 114.2, 61.9, 57.1, 55.5, 54.2, 41.3, 14.2. EIMS $m/z$ 339 (M$^+$). HRMS (EI) for C$_{20}$H$_{21}$NO$_4$, calcd. 339.1471, found 339.1469.

**N-(p-Nitrophenyl)-trans-3-(ethoxycarbonyl)-4-phenyl-pyrrolidine-2-one (4l)** White solid. $^{1}$H NMR (400 MHz, CDCl$_3$) $\delta$ 8.27 (d, $J = 9.3$ Hz, 2H), 7.86 (d, $J = 9.3$ Hz, 2H), 7.41–7.11 (m, 5H), 4.35–4.31 (m, 4H), 4.26–4.17 (m, 1H), 3.97 (d, $J = 9.1$ Hz, 1H), 3.93–3.86 (m, 1H), 1.31 (t, $J = 7.1$ Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 168.5, 168.2, 142.3, 134.2, 129.2, 128.0, 126.8, 124.7, 119.1, 117.1, 62.1, 57.0, 53.4, 40.9, 14.0. EIMS $m/z$ 354 (M$^+$). HRMS (EI) for C$_{19}$H$_{18}$N$_2$O$_5$, calcd. 354.1216, found 354.1211.

**N-Phenethyl-5-nitro-1,3-dihydro-indol-2-one (3l)** Yellow oil. $^{1}$H NMR (500 MHz, CDCl$_3$) $\delta$ 8.18 (d, $J = 8.7$ Hz, 1H), 8.12 (s, 1H), 7.30–7.18 (m, 5H), 6.70 (d, $J = 8.7$ Hz, 1H), 3.99 (t, $J = 7.3$ Hz, 2H), 3.59 (s, 2H), 2.98 (t, $J = 7.5$ Hz, 2H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 174.6, 150.2, 143.0, 137.6, 128.8, 128.7, 127.0, 125.2, 124.9, 120.3, 107.7, 42.1, 35.2, 33.8. EIMS $m/z$ 282 (M$^+$). HRMS (EI) for C$_{17}$H$_{17}$NO$_2$, calcd. 282.1004, found 282.1005.
3,3-Dimethyl-5-oxo-7-phenyl-tetrahydro-pyrrolo[1,2-c]oxazole-6-carboxylic acid ethyl ester (4m) Colorless oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.37–7.22 (m, 5H), 4.30–4.23 (m, 2H), 4.21–4.14 (m, 2H), 4.04 (d, $J$ = 11.9 Hz, 1H), 3.84 (dd, $J$ = 11.8, 8.7 Hz, 1H), 3.76 (t, $J$ = 8.6 Hz, 1H), 1.72 (s, 3H), 1.50 (s, 3H), 1.27 (t, $J$ = 7.1 Hz, 3H). $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 168.5, 165.3, 137.5, 129.1, 127.9, 127.1, 92.2, 69.1, 65.1, 61.8, 60.9, 48.8, 26.6, 23.8, 14.1. ESI-MS $m/z$ 304 ([M+1]$^+$).

6-Acetyl-3,3-dimethyl-7-phenyl-tetrahydro-pyrrolo[1,2-c]oxazol-5-one (4n) Yellow oil. $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.35–7.21 (m, 5H), 4.28–4.24 (m, 1H), 4.18–4.13 (m, 2H), 3.90 (dd, $J$ = 11.2, 8.7 Hz, 1H), 3.68 (t, $J$ = 8.7 Hz, 1H), 2.39 (s, 3H), 1.68 (s, 3H), 1.52 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 202.2, 165.3, 138.4, 129.1, 127.7, 127.3, 92.1, 69.3, 67.5, 64.8, 45.5, 31.1, 26.6, 23.8; EIMS $m/z$ 273 (M$^+$); HRMS (EI) for C$_{16}$H$_{19}$NO$_3$, calcd. 273.1365, found 273.1364.
NOESY spectrum of \textit{trans}-4m

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\includegraphics[width=0.5\textwidth]{spectrum.png}
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$^1$H and $^{13}$C NMR spectra of $\beta$-lactams 2f, 2(3H)-indolinones 3l, and $\gamma$-lactams 4h–4i, 4k–4n
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References