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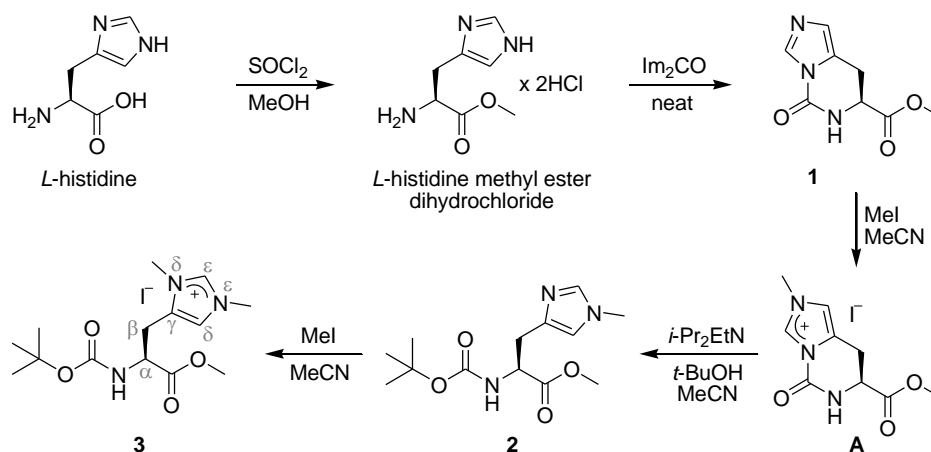
Stereospecific Synthesis and Catalytic Activity of *L*-Histidylidene Metal Complexes

Angèle Monney, Elisabetta Alberico, Yannick Ortin, Helge Müller-Bunz, Serafino Gladiali and Martin Albrecht*

Experimental procedures

General comments

L-Histidine methyl ester dihydrochloride,^{S1} compound **2**,^{S2} complex **8**,^{S3} (*S*)-Ph-binepine,^{S4} [Rh(cod)Cl]₂^{S5} and [Ir(Cp*)Cl]₂^{S6} were prepared according to literature procedures. All other reagents are commercially available and were used as received. Unless specified otherwise, NMR spectra were recorded at 30 °C on Varian spectrometers at the frequencies indicated. Chemical shifts (δ in ppm, coupling constants *J* in Hz) were referenced to residual solvent resonances. Assignments are based on homo- and heteronuclear shift correlation spectroscopy and comparison with related compounds. Elemental analyses were performed by the Microanalytical Laboratory at University College Dublin (Ireland).



Scheme S1 Synthesis of the optically pure histidine-based ligand precursor **3**.

Synthesis of **1**

The synthesis of compound **1** has been described using a mechanical stirrer.^{S2} In our hands, a maximum yield of 55% was obtained. Here we report the synthesis of **1** using a ball mill.

Two 20 cm³ steel vessels were each charged with *L*-histidine methyl ester dihydrochloride (2.00 g, 8.26 mmol), 1,1'-carbonyldiimidazole (1.47 g, 9.09 mmol) and a steel ball bearing and shaken with a Retsch MM200 mixer mill for 50–60 min at 30 Hz. The crude mixture was hydrolysed with H₂O (50 mL) and extracted with CH₂Cl₂ (6 × 30 mL). The organic phase was dried over MgSO₄ and the solvent was removed under reduced pressure. The resulting white solid was precipitated using CH₂Cl₂/Et₂O and dried under high vacuum (1.55 g, 48%). An analytically pure sample (white needles) was obtained by recrystallisation from hot toluene at 4 °C.

¹H NMR (400 MHz, CD₃OD) δ 8.13 (s, 1H, NCHN), 6.80 (s, 1H, NCHCN), 4.42–4.39 (m, 1H, CHCH₂), 3.67 (s, 3H, CH₃), 3.29–3.27 (m, 2H, CHCH₂), NH not resolved; ¹³C{¹H}NMR (100 MHz, CD₃OD) δ 172.3 (C=O), 149.9 (C=O), 136.0 (NCHN), 126.6 (NCHCN), 126.3 (NCHCN), 53.7 (CHCH₂), 53.4 (CH₃), 23.7 (CHCH₂); Elem. anal. calcd. for C₈H₉N₃O₃ (195.18): C 49.23, H 4.65, N 21.43; found: C 49.20, H 4.54, N 21.32; [α]_D²⁰ = +46 (c = 1 in MeOH).

Synthesis of **A**

This compound has been published^{S2} but no experimental and analytical data were given.

To a solution of **1** (5.92 g, 30.35 mmol) in MeCN (120 mL) was added MeI (3.78 mL, 60.70 mmol) and the mixture was stirred at reflux for 15 h. The volatiles were removed under reduced pressure in a well-ventilated fume hood. The residue was dissolved in a minimum of hot MeOH and precipitated with Et₂O. The product was filtered, washed several times with Et₂O and dried under high vacuum to give an off-white solid (9.78 g, 96%). Analytically pure sample (white crystals) was obtained by recrystallisation from hot MeOH at 4 °C.

¹H NMR (500 MHz, CD₃OD) δ 7.52 (s, 1H, NCHCN), 4.65 (t, ³J_{HH} = 5.3 Hz, 1H, CHCH₂), 3.99 (s, 3H, NCH₃), 3.77 (s, 3H, COOCH₃), 3.48–3.46 (m, 2H, CHCH₂), NCHN and NH not resolved; ¹³C{¹H}NMR (125 MHz, CD₃OD) δ 171.4 (C=O), 145.8 (C=O), 135.8 (NCHN), 130.1 (NCHCN), 121.9 (NCHCN), 53.8 (COOCH₃), 53.3 (CHCH₂), 37.4 (NCH₃), 23.0 (CHCH₂); Elem. anal. calcd. for C₉H₁₂IN₃O₃ (337.11): C 32.07, H 3.59, N 12.46; found: C 31.99, H 3.41, N 12.23; [α]_D²⁰ = +45 (c = 1 in MeOH).

Synthesis of 3

To a solution of **2** (2.73 g, 9.64 mmol) in MeCN (100 mL) was added MeI (3.0 mL, 48 mmol) and the mixture was stirred at 40 °C for 16 h. The volatiles were removed under reduced pressure in a well-ventilated fume hood and the residue was purified by flash chromatography (SiO₂, CH₂Cl₂/MeOH 95:5) to give the desired product as a hygroscopic off-white solid (3.97 g, 97%).

¹H NMR (500 MHz, CD₃OD) δ 8.96 (s, 1H, C_εH), 7.44 (s, 1H, C_δH), 4.54-4.51 (m, 1H, C_αH), 3.94 (s, 3H, NCH₃), 3.92 (s, 3H, NCH₃), 3.79 (s, 3H, COOCH₃), 3.34 (dd, ²J_{HH} = 15.9 Hz, ³J_{HH} = 5.0 Hz, 1H, C_βH₂), 3.15 (dd, ²J_{HH} = 15.9 Hz, ³J_{HH} = 9.3 Hz, 1H, C_βH₂), 1.43 (s, 9H, C(CH₃)₃), NH not resolved; ¹³C{¹H}NMR (125 MHz, CD₃OD) δ 172.4 (COOCH₃), 157.5 (NHCOO), 138.2 (C_εH), 133.2 (C_γ), 123.0 (C_δH), 80.9 (C(CH₃)₃), 53.33 (COOCH₃), 53.25 (C_αH), 36.8 (NCH₃), 34.5 (NCH₃), 28.6 (C(CH₃)₃), 26.9 (C_βH₂); *m/z* (HRMS, ESI⁺) found 298.1771 ([M – Γ]⁺), C₁₄H₂₄N₃O₄ requires 298.1767; Elem. anal. calcd. for C₁₄H₂₄IN₃O₄ (425.26): C 39.54, H 5.69, N 9.88; found: C 39.42, H 5.54, N 9.59; [α]_D²⁰ = –16 (c = 1 in MeOH).

X-ray crystallography

Crystal data were collected using an Oxford Diffraction SuperNova A diffractometer fitted with an Atlas detector (Mo–K α radiation, 0.71073 Å). A three-fold redundant dataset was collected, assuming that the Friedel pairs are not equivalent. An analytical absorption correction based on the shape of the crystal was performed.^{S7} The structure was solved by direct methods using the program SHELXS-97 and refined by full matrix least squares on F² with SHELXL-97.^{S8} The hydrogen atoms were included in calculated positions and treated as riding atoms using SHELXL-97 default parameters. All non-hydrogen atoms were refined anisotropically. Further details on data collection and refinement are summarised in Table S1. Crystallographic data (excluding structure factors) have been deposited with the Cambridge Crystallographic Centre as supplementary publication no. CCDC 870836. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk].

Table S1 Crystal data and structure refinement for complex *rac-4*.

CCDC no.	870836
Molecular formula	$C_{24}H_{38}N_3O_4Cl_2Ir \times 2 CH_2Cl_2$
Formula weight	865.53
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system	Triclinic
Space group	P-1 (#2)
Unit cell dimensions	$a = 8.4640(2) \text{ \AA}$ $\alpha = 74.079(3)^\circ$ $b = 12.6916(4) \text{ \AA}$ $\beta = 85.089(2)^\circ$ $c = 17.2532(5) \text{ \AA}$ $\gamma = 70.787(3)^\circ$
Volume	$1682.98(8) \text{ \AA}^3$
Z	2
Density (calculated)	1.708 g cm^{-3}
Absorption coefficient	4.478 mm^{-1}
F(000)	860
Crystal size	$0.267 \times 0.194 \times 0.163 \text{ mm}^3$
Reflections collected	43921
Independent reflections	8591 [R(int) = 0.0533]
Absorption correction	Analytical
Max. and min. transmission	0.606 and 0.506
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8591 / 0 / 372
Goodness-of-fit on F^2	1.068
Final R indices [$I > 2\sigma(I)$]	R1 = 0.0276, wR2 = 0.0479
R indices (all data)	R1 = 0.0358, wR2 = 0.0514
Largest diff. peak and hole	1.027 and $-0.920 \text{ e \AA}^{-3}$

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