A General Route to 4-Imidazolyl Containing Multidentate Ligands for Biomimetic Studies

(Supporting Information)

James P. Collman*, Min Zhong , and Zhong Wang

Department of Chemistry, Stanford University, Stanford, California 94305-5080

Materials and methods. All reagents were used as supplied commercially unless otherwise noted. Compound **5g** was synthesized according to literature procedure[1]. All melting points were determined on MEL-TEMP and are uncorrected. IR and ^{1}H NMR spectra were recorded on Mattson Infinity 60AR and Varian XL-400 instruments respectively. Mass spectra were due by University of California, San Francisco Mass Spectrometry Facility.

Synthesis and characterization

Methyl 1-(2-methoxyphenyl)-2-imidazolecarboxylate (5h) : It was synthesized according to literature procedure[1,2] from imidazole sodium salt and 2-iodoanisole. Yield 40%; m. p 104-106 ° C; IR (KBr): 1718 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 7.42 (td, J= 1.6, 7.9 Hz), 7.27 (s, 1H), 7.23 (dd, J= 1.8, 5.5Hz, 1H), 7.09 (s, 1H), 6.99-7.04 (m, 2H), 3.81 (s, 3H), 3.73 (s, 3H) ppm; EIMS (m/e): 232, 201, 173(100), 144, 92, 77, 68, 59; HRMS : calcd. for $C_{12}H_{12}N_2O_3$ 232.0847, found, 232.0850.

Methyl 1-(2-nitrophenyl)-4-imidazolecarboxylate (5i) : It was synthesized according to literature procedure[3] from 2-fluoronitrobenzene and methyl 4-imidazolecarboxylate. Yield 85%; m. p 172-174 °C; IR (KBr): 1699 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 8.09 (d, J= 8.0 Hz, 1H), 7.78 (t, J= 8.0 Hz, 1H), 7.76 (s, 1H), 7.74 (s, 1H), 7.69 (t, J= 8.0 Hz, 1H), 7.52 (d, J= 8.0 Hz, 1H), 3.89 (s, 3H) ppm; EIMS (m/e): 248, 230, 216, 160, 134, 105(100), 78; HRMS : calcd. for $C_{11}H_9N_3O_4$ 247.0593, found, 247.0594.

General Procedure for Addition Reaction: To a 0.25 M solution of 1-trityl-4-iodoimidazole in dry CH_2Cl_2 was added a 3.0 M solution of EtMgBr (1.0 eq.) in diethyl ether at rt under N_2 . After stirring at rt for 2 hrs, the ester (0.45 eq. for **7a-d**, **7f-i** , 0.30 eq. for **7e** and 0.22 eq. for **8**) was

added to the reaction system and the resulting mixture was stirred at rt for 24-48 hrs. The reaction was quenched by addition of several drops of methanol, and then the mixture was concentrated and the residue was subject to chromatography on silica gel using CH_2Cl_2/hexanes (saturated with ammonia gas) as the eluent.

Bis(1-trityl-4-imidazolyl)phenylcarbinol (7a) : yield 73%; m. p 104-106 °C; IR (KBr): 3446 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.39 (d, J= 7.1 Hz, 2H), 7.32 (s, 2H), 7.24-7.28 (m, 19H), 7.23 (d, J=1.6 Hz, 2H), 7.07 (dd, J= 1.6, 7.9 Hz, 12H), 6.74 (d, J=1.4 Hz, 2H) ppm; ESIMS : m/e = 725.4 $M+H^+$ for $C_{51}H_{40}N_4O$.

Bis(1-trityl-4-imidazolyl)-4-methoxyphenylcarbinol (7b) : yield 56%; m. p 118-120 °C; IR (KBr): 3429 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.18-7.30 (m, 20H), 7.06 (dd, J= 1.4, 7.9 Hz, 12H), 6.75 (d, J= 8.8 Hz, 2H), 6.72 (d, J=1.4 Hz, 2H), 3.73 (s, 3H) ppm; ESIMS : m/e = 755.4 $M+H^+$ for $C_{52}H_{42}N_4O_2$.

Bis(1-trityl-4-imidazolyl)-4-nitrophenylcarbinol (7c) : yield 79%; m. p 172-174 °C; IR (KBr): 3429 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.09 (dd, J= 1.9, 8.9 Hz, 2H), 7.62 (dd, J= 2.0, 9.0 Hz, 2H), 7.39 (d, J= 7.1 Hz, 2H), 7.24-7.33 (m, 20H), 7.04-7.06 (m, 12H), 6.81 (d, J=1.4 Hz, 2H) ppm; ESIMS : m/e = 770.4 $M+H^+$ for $C_{51}H_{39}N_5O_3$.

Di(1-trityl-4-imidazolyl)methanol (7d) : yield 67%; m. p 178-180 °C; IR (KBr): 3429 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.34 (d, J=1.4 Hz, 2H), 7.23-7.30 (m, 18H), 7.06 (dd, J= 1.4, 8.0 Hz, 12H), 6.71 (d, J=1.4 Hz, 2H), 5.76 (s, 1H) ppm; ESIMS : m/e = 649.4 $M+H^+$ for $C_{45}H_{36}N_4O$.

Tris(1-trityl-4-imidazolyl)carbinol (7e): yield 40%; m. p 128-130 °C; IR (KBr): 3438 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.20-7.26 (m, 27H), 7.06 (d, J= 7.3 Hz, 18H), 6.80 (s, 3H) ppm; ESIMS : m/e = 957.4 $M+H^+$ for $C_{67}H_{52}N_6O$.

Bis(1-trityl-4-imidazolyl)-2-pyridylcarbinol (7f) : yield 54%; m. p 208-210 °C (dec.); IR (KBr): 3345 cm^{-1}; ^1H NMR ($CDCl_3$): δ 8.48 (dd, J= 0.9, 8.5 Hz, 1H), 7.65-7.72 (m, 2H), 7.20-7.30 (m, 20H), 7.15-7.19 (m, 1H), 7.05 (d, J= 7.0 Hz, 12H), 6.91 (s, 2H) ppm; ESIMS : m/e = 726.4 $M+H^+$ for $C_{50}H_{39}N_5O$.

Bis(1-trityl-4-imidazolyl)-2-(1-methylimidazol)ylcarbinol (7g) : yield 52%; m. p 116-118 °C ; IR (KBr): 3406 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.30 (d, J= 1.4 Hz, 2H), 7.21-7.29 (m, 18H), 7.07 (dd, J= 1.3, 8.2 Hz, 12H), 6.92 (s, 1H), 6.80 (d, J= 1.4 Hz, 2H), 6.76 (s, 1H), 3.41 (s, 3H) ppm; ESIMS : m/e = 729.4 $M+H^+$ for $C_{49}H_{40}N_6O$.

Bis(1-trityl-4-imidazolyl)-2-(1-(2-methoxyphenyl)imidazol)ylcarbinol (7h) : yield 65%; m. p 120-122 °C ; IR (KBr): 3433 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.17-7.28 (m, 21H), 7.11 (d, J= 7.6 Hz,

1H), 7.06 (s, 1H), 6.99 (d, J= 7.1 Hz, 12 H), 6.80 (s, 1H), 6.67 (d, J= 7.6Hz, 1H), 6.63 (s, 2H), 3.60 (s, 3H) ppm; ESIMS : m/e = 821.4 $M+H^+$ for $C_{55}H_{44}N_6O_2$.

Bis(1-trityl-4-imidazolyl)-2-(1-(2-nitrophenyl)imidazol)ylcarbinol (7i) : yield 44%; m. p 136-138 °C ; IR (KBr): 3419 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.91 (dd, J= 1.3, 8.1 Hz, 1H), 7.63 (td, J= 1.4, 7.8 Hz, 1H), 7.51 (dd, J= 1.4, 8.0 Hz, 1H), 7.49 (d, J= 1.4 Hz, 1H), 7.42 (dd, J= 1.2, 7.9 Hz, 1H), 7.30 (d, J= 1.5 Hz, 1H), 7.20-7.24 (m, 18H), 7.06-7.08 (m, 12H), 7.00 (d, J= 1.5 Hz, 1H), 6.86 (d, J= 1.4 Hz, 2H) ppm; ESIMS : m/e = 836.2 $M+H^+$ for $C_{54}H_{41}N_7O_3$.

α,α,α',α'-Tetrakis(1-trityl-4-imidazolyl)-2,6-pyridinedimethanol (8) : yield 48%; m. p 148-150 °C ; IR (KBr): 3383 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.65 (dd, J= 6.7, 8.5 Hz, 1H), 7.56-7.58 (m, 2H), 7.19-7.26 (m, 40H), 7.04-7.06 (m, 24H), 6.90 (s, 4H) ppm; ESIMS : m/e = 1372.6 $M+H^+$ for $C_{95}H_{73}N_9O_2$.

Tris(4(5)-imidazolyl)carbinol trifluoroacetic acid salt (10) : A solution of tris(1-trityl-4-imidazolyl)carbinol in 85% aq. TFA was refluxed for 4hrs, and the resulting mixture was concentrated and the residue was added into distilled water. Subsequently, the suspension was filtered and the filtrate was concentrated and dried *in vacuo* over P_2O_5. yield 65%; IR (KBr): 3413, 1676 cm^{-1}; ^1H NMR (D_2O): δ 8.64 (s, 3H), 7.33 (s, 3H) ppm; ESIMS : m/e = 231.0 $M+H^+$ for $C_{10}H_{10}N_6O$.

References

1. Bachtiar, C.; Smith, E. H. *J. Chem. Soc. Perkin Trans. 1*, **1994**, 239.
2. Cozzi, P.; Carganico, G.; Fusar, D.; Grossoni, M.; Menichincheri, M.; Pinciroli, V.; Tonani, R.; Vaghi, F.; Salvati, P. *J. Med. Chem.*, **1993**, *36*, 2964
3. Davey, D. D.; Erhardt, P. W.; Cantor, E. H.; Greenberg, S. S.; Ingebretsen, W. R.; Wiggins, J. *J. Med. Chem.*, **1991**, *34*, 2671