Pergamon

*Tetrahedron Letters*, Vol. 37, No. 37, pp. 6701-6704, 1996

0040-4039/96 $15.00 + 0.00

PII: S0040-4039(96)01469-4

# Oxidation and Chiral Recognition of Amino Esters by Dioxoruthenium(VI) Porphyrins : Synthesis of New Imino ester Ru (II) Complexes.

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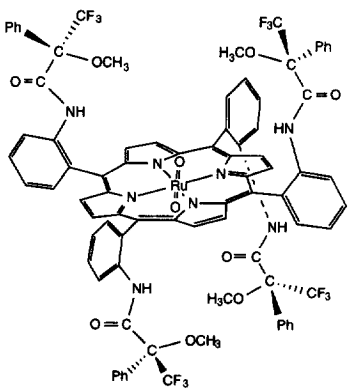
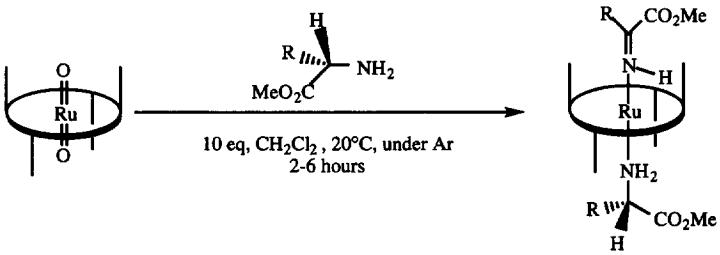
**Abstract:** Oxidation and chiral recognition of racemic amino esters by dioxoruthenium (VI) picket-fence complex bearing optically active α-methoxy-α-(trifluoromethyl) phenylacetyl residues on both sides of the porphyrin plane (αβαβ isomer) lead to the formation of mixed-ligated imino ester/amino ester Ru(II) complexes. Copyright © 1996 Elsevier Science Ltd

Amine oxidations are important in the metabolism of both naturally occuring amines and xenobiotics[1]. During the oxidative deamination of amino-acids, imino-acids are often postulated as the intermediates. Few syntheses of imino acidato metal complexes have been reported[2] and the chelation to a metal ion seems essential to stabilize the imino acidate moiety against hydrolysis[3]. We wish to report herein the synthesis and characterization of imino ester complexes of Ru(II) porphyrins from oxidation of racemic α-amino esters by dioxoruthenium (VI) picket-fence complex $[Ru^{VI}(\mathbf{L})(O)_2]$ **1** (αβαβ isomer)[4] { **L** = 5,10,15,20-tetrakis[o-(2-methoxy-2-phenyl-3,3,3-trifluoro-propanoyl amino)phenyl]porphyrin} (scheme 1). So far as we are able to determine, they are the first examples of imine ruthenium porphyrin complexes which have been isolated and characterized.




Scheme 1 : αβαβ $Ru^{VI}(\mathbf{L})(O)_2$

Our interest in the stereochemical oxidation of organic substrates using optically active trans-dioxoruthenium(VI) porphyrins[4] has prompted us to investigate the reactivity of amino acids towards these chiral complexes. The reaction of L-alanine methyl ester (10 equiv.) with optically active trans-dioxoruthenium(VI) **1** in dry dichloromethane at room temperature under argon is moderately rapid as shown by visible spectroscopy by the progressive appearance of a new spectrum with maxima at 408 and 506 nm. The reaction is complete in 2 hours and the complex **2** (scheme 2) can be isolated with 55% yield, after TLC purification on silica gel using ether-hexane (1:1) as eluent. The IR spectrum of **2** lacked the band at 823 $cm^{-1}$ due to ruthenium-oxo bonds, and the $^1H$ NMR spectrum showed resonances characteristic of a diamagnetic metalloporphyrin with two different axial ligands: one alanine methyl ester and one ligand with a methyl group located in proximity of the porphyrin as shown by its upfield shift due to the ring current. This methyl appears as a singlet. According to the $^1H$ NMR spectrum, the elemental analysis and the mass spectrum (FAB+; m/e=1842,4519 ($M^+$)), this axial ligand should have the formula $C_4H_7NO_2$. The $^1H$ NMR spectrum (absence of doublet for the upfield methyl for this ligand) suggests the presence of an α-imino ester group which is confirmed by a similar synthesis, using glycine methyl ester instead of alanine methyl ester and compound **1** as oxidant. In this case, the $^1H$ NMR spectrum showed two doublets (J =20 Hz) at 4.5 (NH) and 2.57 ppm (CH) characteristic of the presence of the dehydro amino ester **3**.




| | R |
|---|---|
| **2** | $CH_3$ |
| **3** | H |
| **4a, 4b** | $CH(CH_3)_2$ |
| **5** | $CH_2CH(CH_3)_2$ |
| **6** | $CH_2Ph$ |

Scheme 2

Similar mixed-ligated ketimine/amino esters Ru (II) complexes were also obtained with L-valine methyl ester **4a** (55 % yield), L-leucine methyl ester **5** (44 % yield) and L-phenylalanine methyl ester **6** (50 % yield), using **1** as oxidant. For the purpose of chiral recognition, oxidation of racemic valine methyl ester (10 equiv.) was also tested, using previous experimental conditions, yielding two isomers **4a** and **4b**, in the ratio 65/35, which can be separated by TLC on silica gel using ether-hexane (1:3) as eluent. To confirm the stereochemical identity of the second isomer, the same reaction was carried out with pure D-valine methyl ester enantiomer, leading to **4b**. Moreover, exchange of pure complex **4b** with pure L-valine methyl ester in dichloromethane (15 equiv) leads to the formation of **4a** in a nearly quantitative yield (25°C, 10 h). Thus the Ru-ketimine bond is stronger than the Ru-amino ester bond. However the ketimine ligand is displaced in dichloromethane at room temperature by addition of a large excess (20 equiv.) of benzylmethylphenylphosphine to **4a**, leading to Ru(L)[P(Me)(Phe)(Benzyl)]$_2$[4]. The data for representative compounds are mentioned in reference section[5].

The synthetic pathway may involve imido complexes of Ru (VI) and/or Ru(IV) as intermediates. Stable alkylimido complexes of metalloporphyrins have been recently reported as a new class of ligands for osmium (VI) and ruthenium (VI) porphyrins[6]. The details of the mechanism and the nature of the intermediates are under study.

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5. All new compounds show convenient spectroscopic and analytical data. All NMR spectra were recorded on a Bruker AC 300P spectrometer in $CDCl_3$ at 300 MHz ($^1H$), 282 MHz ($^{19}F$). Visible spectra were measured in dichloromethane.

   Selected spectroscopic data :

   for **2**, $^1H$: δ -6.14 (d, 1H, J=11Hz, NH), -4.48 (t, 1H, J=10Hz, NH), -2.12 (m, 1H, *CH), -1.45 (s, 3H, $CH_3$ imine), -1.16 (d, 3H, J=7Hz, $CH_3$ amine), 3.54 (s, 1H, NH), 2.70 (s, 3H, $CO_2CH_3$ amine), 2.93 (s, 3H, $CO_2CH_3$ imine), 1.99 (s, 3H, OMe). 2,43 (s, 3H, OMe), 6.95, 7.08 (2d, 8H, J=8Hz, o-H Ph picket), 7.12-7.23 (m, 12H, m-H and p-H Ph picket), 7.41, 7.47 (2t, 4H, J=7Hz, H-5 meso-Ph), 7.69-7.76 (m, 8H, H-4, H-6 meso-Ph), 8.79, 8.88 (2d, 4H, J=8Hz, H-3 meso-Ph), 7.79, 7.88, 8.03, 8.09 (4d, 8H, H-pyrrole), 8.44, 8.93 (2s, 4H, NHCO). $^{19}F$: δ -70.37, -71.06 (2s, 4 $CF_3$). VIS($CH_2CL_2$): $\lambda_{max}$/nm 408(soret) , 506 , 599. IR (KBr): ν/cm$^{-1}$, 3371(br), 1709, 1584, 1522, 1447, 1262.

   For **3**, $^1H$: δ -5.44, -5.29 (2m, 2H, $NH_2$), -1.78 (m, 2H, $CH_2$), 2.57 ( d, 1H, J=20Hz, CH=), 4.5 (d, 1H, J=20Hz, NH=), 2.79 (s, 3H, $CO_2Me$ amine), 2.85 (s, 3H, $CO_2Me$ imine). $^{19}F$: δ -70.42 (s, 2 $CF_3$), -70.93 (s, 2 $CF_3$). VIS($CH_2CL_2$): $\lambda_{max}$ / nm 406(soret), 505, 595. IR (KBr): ν/cm$^{-1}$, 3370(br), 1712, 1581, 1523, 1447, 1262.

   For **4a**, $^1H$: δ -6.01 (d, 1H, J=10Hz, NH), -4.67 (t, 1H, J=10Hz, NH), -2.69 (m, 1H, *CH), -2.52 ( sept, 1H, J=7Hz, CH-iPr), -1.09, -0.81 (2d, 6H, J=7Hz, $CH_3$-iPr), -1.0, -0.66 (2d,

6H, J=7Hz, $CH_3$-iPr), -0.47 (m, 1H, CH-iPr), 2.44 (s, 3H, $CO_2$Me amine), 2.97 (s, 3H, $CO_2$Me imine), 3.52 (s, 1H, NH). $^{19}$F: δ -70.02 (s, 2 $CF_3$), -70.08 (s, 2 $CF_3$). VIS($CH_2CL_2$): $\lambda_{max}$ / nm 409(soret), 507, 605. IR (KBr): ν/cm$^{-1}$, 3380(br), 1720, 1580, 1520, 1443, 1262.

For **4b**, $^1$H: δ -6.15 (d, 1H, J=10Hz, NH), -4.96 (t, 1H, J=10Hz, NH), -2.67 (m, 1H, *CH), -2.53 ( sept, 1H, J=7Hz, CH-iPr), -1.25, -1.08 (2d, 6H, J=7Hz, $CH_3$-iPr), -0.98, -0.69 (2d, 6H, J=7Hz, $CH_3$-iPr), -0.34 (m, 1H, CH-iPr), 2.70 (s, 3H, $CO_2$Me amine), 2.96 (s, 3H, $CO_2$Me imine), 3.46 (s, 1H, NH). $^{19}$F: δ -69.11 (s, 2 $CF_3$), -70.21 (s, 2 $CF_3$). VIS($CH_2CL_2$): $\lambda_{max}$ / nm 409(soret), 507, 605. IR (KBr): ν/cm$^{-1}$, 3380(br), 1720, 1580, 1520, 1443, 1262.

For **5**, $^1$H: δ -6.15 (d, 1H, J=11Hz, NH), -4.73 (t, 1H, J=11Hz, NH), -2.34 (m, 1H, *CH), -1.25, -1.7 (2m, 2H, $CH_2$), -0.87, -1.39 (2m, 2H, $CH_2$), -0.48, -0.98 (2d, 6H, J=7Hz, $CH_3$-iPr), -0.17 (2d, 6H, $CH_3$-iPr), 2.42 (s, 3H, $CO_2$Me amine), 2.96 (s, 3H, $CO_2$Me imine), 3.70 (s, 1H, NH). $^{19}$F: δ -69.70 (s, 2 $CF_3$), -69.91 (br s, 2 $CF_3$). VIS($CH_2CL_2$): $\lambda_{max}$ / nm 410(soret), 508, 606. IR (KBr): ν/cm$^{-1}$, 3380(br), 1710, 1582, 1520, 1445, 1262.

For **6**, $^1$H: δ -5.77 (d, 1H, J=11Hz, NH), -4.65 (t, 1H, J=10Hz, NH), -2.08 (m, 1H, *CH), -0.19 (s, 2H, $CH_2$), 0.31 (m, 2H, $CH_2$), 2.50 (s, 3H, $CO_2$Me amine), 2.73 (s, 3H, $CO_2$Me imine), 3.92 (s, 1H, NH), 4.70 (d, 2H, J=7Hz, o-H Ph), 5.35 (d, 2H, J=7Hz, o-H Ph), 6.56, 6.75, 6.93 (m, 6H, m-H,p-H Ph). $^{19}$F: δ -69.67 (s, 2 $CF_3$), -69.95 (br s, 2 $CF_3$). VIS($CH_2CL_2$): $\lambda_{max}$ / nm 409(soret), 508, 599. IR (KBr): ν/cm$^{-1}$, 3420(br), 1750, 1710, 1580, 1520, 1450, 1262.

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(*Received in France* 26 *June* 1996; *accepted* 24 *July* 1996)