ELECTROSYNTHESIS OF OPTICAL ACTIVE DIPEPTIDES FROM MOLYBDENUM NITRIDE COMPLEXES

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Summary

The nitride ligand in the complex *trans*-[Mo(N)Cl(dppe)$_2$] reacts with enantiomeric $ICH_2CONHCH(CH_3)COOCH_3$ to form imide complexes. Sequential nitrogen-carbon and carbon-carbon bond formation, followed by electrochemical Mo-N bond cleavage, defines a pathway to optical active methyl esters of the glycyl-alanine and alanyl-alanine. The key intermediate metallo-nitrogen ylide *trans*-[MoCl(NCHCONHCH(CH$_3$)COOCH$_3$)(dppe)$_2$] has incipient carbanion character at the α-carbon and reacts with methyl iodide to form C-C bonds.

Introduction

The nitride ligand in complexes of the type *trans*-[MX(N)(dppe)$_2$] (X = halide) is nucleophilic and the square-planar {M(dppe)$_2$} assembly is stable[1]. Such nitrides can be synthesized from dinitrogen complexes of the type *trans*-[M(N$_2$)$_2$(dppe)$_2$] by reaction with trimethylsilyl azide [2] or cleavage of the N-N bond after conversion of coordinated dinitrogen to a M^{II} dialkylhydrazide[3].

The nitrides react with protons or other electrophiles to form cationic imides *eg.* *trans*-[MoCl(NCR)(dppe)$_2$]$^+$. The Mo-N bond is electrochemically cleaved in the presence of a weak acid to give the free amine and, under molecular nitrogen, the parent dinitrogen complex is regenerated in reasonable yields[4].

C-H bonds on the α-carbon atom adjacent to the N atom in alkylimides are acidic. For example, a proton can be removed from *trans*-[MoCl(NCH$_2$CH$_3$)(dppe)$_2$]$^+$, to give the ethyleneamide *trans*-[MoCl(NCHCH$_3$)(dppe)$_2$][4].

In this work we report results of the electrochemical reduction of complexes A and B.

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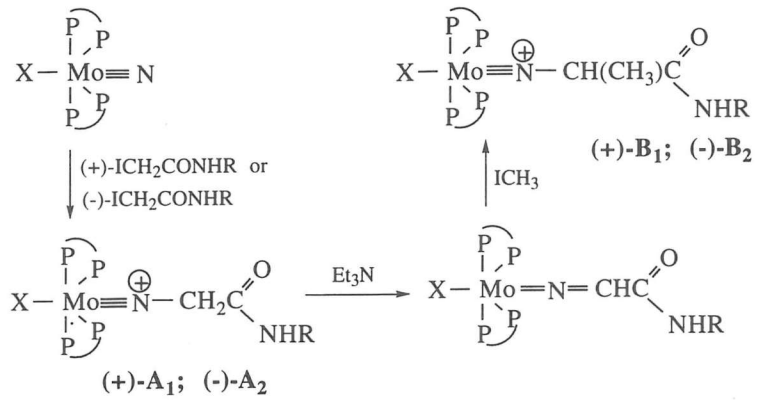
Results and discussion

Scheme 1 outlines the chemical reactions leading to the formation of complexes A_1, A_2, B_1 and B_2.



Scheme 1 - Formation of N-C and C-C bonds by stepwise alkylation, deprotonation and methylation reactions. R represents the $CH(CH_3)COOCH_3$.

Figure 1 shows cyclic voltammograms typical of complexes A and B in thf - 0.1 mol dm^{-3} $[Bu_4N][BF_4]$ at a vitreous carbon-disc electrode. The electrochemical data for complexes A and B is summarized in Table 1.

The reduction of the complexes is irreversible at room temperature but, at moderately low temperatures, the electron-transfer reaction shows partial reversibility. The reduction of the complexes, in the presence of phenol, leads to reversible oxidation peaks assigned to *trans*-$[Mo(N_2)_2(dppe)_2]$ (1) and *trans*-$[MoCl(NCHCONH(CH_3)COOCH_3)(dppe)_2]$ (2) by comparison with authentic samples.

Table 1 - Cyclic voltammetric data of the complexes in thf/$[Bu_4N][BF_4]$ (0.2 mol dm^{-3}) at a carbon-disc electrode.

Complexes	$-E_p$ / V [a]	$-10^{-3}\, I_pc^{-1}v^{-1/2}$ [b]	$-E_p$ / V [a]	ΔE / mV
A_1	2.21	1.1	0.52	65
A_2	2.21	1.2	0.51	60
B_1	2.30	1.2	0.55	60
B_2	2.30	1.2	0.55	65

a - Potential *vs.* fc^+/fc; b - Values in A $mol^{-1}cm\ V^{-1/2}s^{1/2}$, at 0 °C.

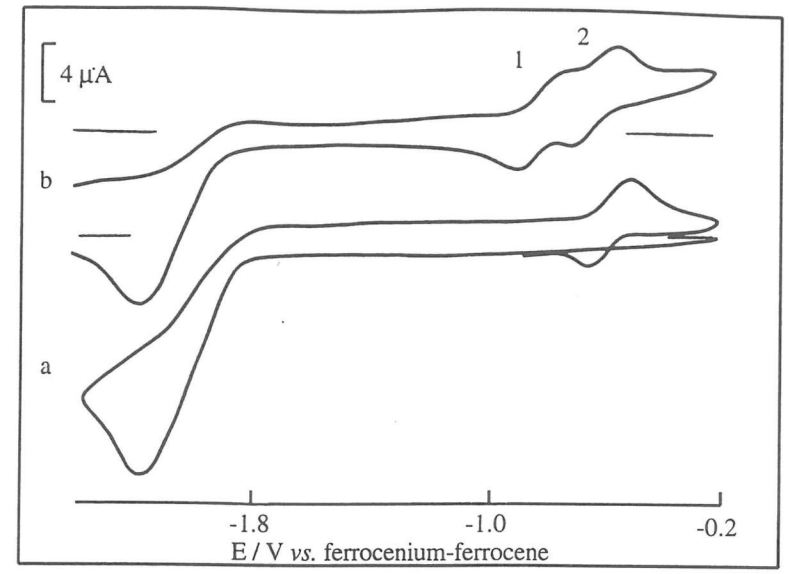


Figure 1 - Cyclic voltammograms of the complex (+)-*trans*-$[MoCl(NCH_2CONH(CH_3)COOCH_3)(dppe)_2]^+$: a) in aprotic medium; b) in presence of phenol showing generation of the *trans*-$[Mo(N_2)_2(dppe)_2]$ (1) and *trans*-$[MoCl(NCHCONH(CH_3)COOCH_3)(dppe)_2]$ (2) after holding the potential at -2.4 V for 30 s. Scan rate 0.1 V s^{-1}.

Controlled-potential electrolysis of the complex (+)-*trans*-$[MoCl(NCH_2CONH(CH_3)COOCH_3)(dppe)_2]^+$ was carried out at - 2.25 V *vs.* fc^+/fc in thf-0.2 mol dm^{-3} $[Bu_4N][BF_4]$ at a mercury-pool cathode, under molecular nitrogen, in presence of phenol. Coulometry showed the consumption of 1.5 F mol^{-1}. Cyclic voltammetry at the end of the electrolysis revealed the formation of two metal products, (+)-*trans*-$[MoCl(NCHCONH(CH_3)COOCH_3)(dppe)_2]$ and *trans*-$[Mo(N_2)_2(dppe)_2]$ in *ca.* 60 and 30 % yields, respectively. The dipeptide esters were identified by infrared spectroscopy and HPLC.

In order to increase the yield an acid stronger than phenol was employed. Controlled-potential electrolysis of the complexes in the presence of acetic acid led to the formation of the corresponding esters. The results are summarized in Table 2. The isolated metal product was identified by infrared spectroscopy and cyclic voltammetry. The optical activity was determined by polarimmetry and the values where compared with literature values[5].

The current against charge plot is typical of type A and B complexes. The current, after some time, assumes values that are higher than expected for a linear decay. This

can by explained in terms of the formation of new active species at a potential more positive than that of the parent imide cation.

In agreement with previous results [6] cyclic voltammetry at the end of electrolysis revealed the formation of the monohydride $[MoH(\eta^2\text{-}O_2CH_3)(dppe)_2]$ and the dihydride $[MoH_2(\eta^2\text{-}O_2CH_3)(dppe)_2]^+$, Figure 2.

Table 2 - Controlled-potential electrolysis of A_1, A_2, B_1 and B_2 complexes in the presence of acetic acid at a mercury-pool cathode.

Complexes	E_p/V [a]	Fmol^{-1}	Products (yields %, $[\alpha]_D^{26}$)[b]	$[\alpha]_D^{26}$
A_1	-2.25	4.2	$[\underline{Mo}H_2(\eta^2\text{-}OOCCH_3)][BPh_4]$ (49)	
			(+)-$NH_2CH_2CONHCH(Me)COOMe$	
			(65. +22.8° ± 2.9°)	+23.5° [c]
A_2	-2.26	4.3	$[\underline{Mo}H_2(\eta^2\text{-}OOCCH_3)][BPh_4]$ (50)	
			(-)-$NH_2CH_2CONHCH(Me)COOMe$	
			(67. -22.3° ± 3.0°)	-23.5° [c]
B_1	-2.35	4.1	$[\underline{Mo}H_2(\eta^2\text{-}OOCCH_3)]BPh_4]$ (47)	
			(+)-$NH_2CH(Me)CONHCH(Me)COOMe$	
			(64. +33.1° ± 3.1°)	+35.0° [d]
B_2	-2.35	4.0	$[\underline{Mo}H_2(\eta^2\text{-}OOCCH_3)][BPh_4]$ (41)	
			(-)-$NH_2CH(Me)CONHCH(Me)COOMe$	
			(67. -32.0° ± 3.5°)	-35.0° [d]

a - Potential *vs.* fc^+/fc; b - Yields determined by HPLC. Values of α obtained from solutions *ca.* 0.2% in $CHCl_3$; c - Values from an authentic sample; d - Values from literature[5].

The specific rotation obtained for the dipeptides isolated from complexes A_1, A_2, B_1 and B_2 are, within experimental error, in agreement with published values for the respective optically pure dipetides [5]. These results give evidence for a stereoselective methylation on the α-carbon of complexes A_1 and A_2, that can be induced by the presence of the second chiral center on the ligand.

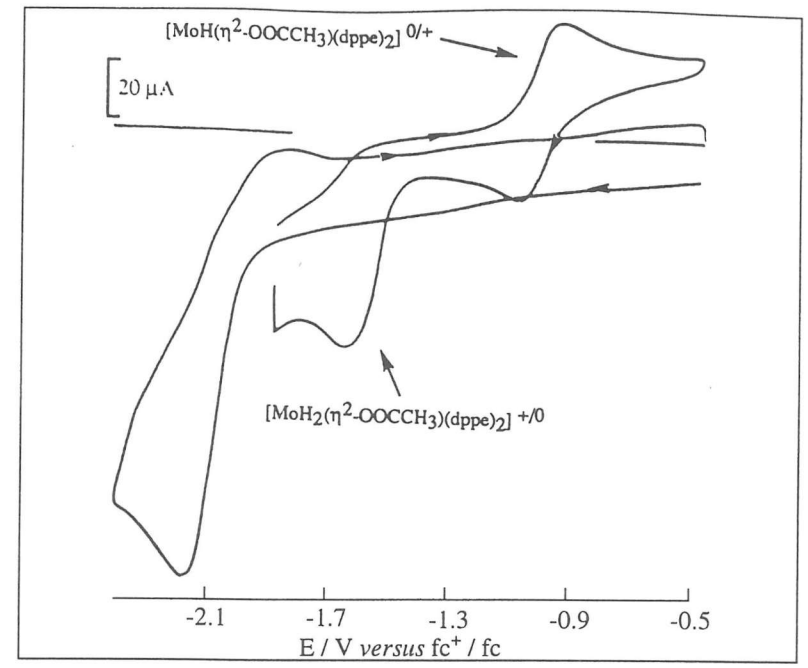


Figure 2 - Cyclic voltammograms of complex A_1 (1.1 mmol dm^{-3}) showing generation of the hydride upon holding the potential at -2.25 V for 2 min. in presence of acetic acid. Recorded in thf/$[Bu_4N][BF_4]$ at a carbon electrode. Scan rate 0.1 V s^{-1}.

Acknowledgments

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