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## ELECTROCHEMICAL CLEAVAGE OF CHLORO DERIVATIVES OF THE BENZYLOXYCARBONYL GROUP

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### ABSTRACT

The cathodic cleavage of 4-chlorobenzoyloxycarbonyl and 2,4-dichlorobenzoyloxycarbonyl groups from the urethane derivatives of morpholine, at a vitreous carbon cathode in N,N-dimethylformamide is reported.

It is shown by cyclic voltammetry that the derivatives are reduced in the region - 2.4 to - 2.6 V vs SCE; further reduction peaks are observed at more negative potentials.

Controlled potential electrolyses were carried out at a potential just after the first reduction peak and free amine was identified in moderated yields. Hence, the first process is associated with the cleavage of the modified Z groups, but undesired reactions also occur leading to cleavage in other sites of the molecule.

### INTRODUCTION

In peptide synthesis is common to introduce modifications in the aminoacid/peptide molecules in the form of protecting groups, in order to prevent unwanted reactions away from the site where the change is desired.

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Electrochemical methods are known today to be convenient alternatives to deprotect molecules and may offer some advantages when compared to chemical methods. In fact, the control of the potential permits the selectivity between different protecting groups or even between the same group at different sites in the molecule.

Although electrochemical deprotection reactions have been tried for several decades (1), a new interest has appeared in recent years and a range of electrochemically cleaved groups has been investigated (2).

The benzyloxycarbonyl group is the most widely used group in peptide synthesis and it is known that the reduction of benzyloxycarbonyl derivatives of simple amines at vitreous carbon electrodes in DMF only occurs at very negative potentials, approximately - 2.8 V vs SCE and the reaction leads to toluene and free amine in good yields (3). The cleavage reactions have a similar mechanism in aminoacids and peptides (4).

This electrochemical procedure, however, has some severe experimental difficulties related to the reduction of the solvent/electrolyte and of other groups in the molecule which will occur at these negative potentials.

For this reason, attempts were made to design substituted benzyloxycarbonyl groups where the role of the substituent is to shift the reduction potential to much less negative values. The nitrobenzyloxycarbonyl group was investigated (5) and, in aprotic solvents such as DMF, is readily cleaved at about - 1.1 V vs SCE in urethane derivatives of simple amines. Thus, this improvement increases the scope for the use of this protecting group in the synthesis of large molecules. The presence of strong proton donors, however, leads to the reduction of the nitro group, rather than cleavage of the substituted benzyl group, which proves to be an inconvenience in the case of some peptides which would racemise in the basic conditions created by the cathodic reaction.

In the present paper we report the results of another substituted benzyloxycarbonyl group, the chlorobenzyloxycarbonyl and dichlorobenzyloxycarbonyl groups where the chloride is sufficiently electron withdrawing to render the cleavage potential more positive without reduction of the substituents themselves.

## EXPERIMENTAL

The cyclic voltammetry experiments were carried out in a three electrode cell, where the working electrode was a vitreous carbon disc (area = 0.05 cm<sup>2</sup>), the secondary electrode a platinum spiral and the reference electrode the saturated calomel electrode (SCE) which was in a separate compartment linked to the working electrode by a Luggin capillary. The carbon disc used as the working electrode was polished with alumina, washed and dried for each experiment. Coulometry experiments and preparative electrolyses were carried out in a three compartment cell. The catholyte was separated from the anolyte by a glass frit. The reference electrode was the SCE placed in another compartment and was linked to the working electrode by a Luggin capillary. The working electrode was a large carbon disc (area = 4.9 cm<sup>2</sup>), and the secondary electrode was a Pt gauze of a similar area.

Solutions were always de-aerated for several minutes before recording cyclic voltammograms and also during the electrolyses.

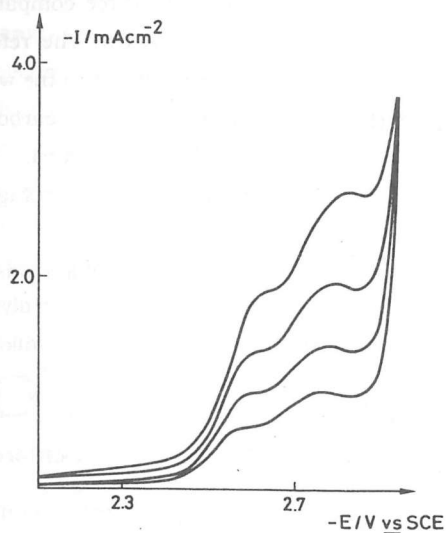
The solvent used in all cases was N,N-dimethylformamide which was dried with MgSO<sub>4</sub> and purified by vacuum distillation. The supporting electrolyte was Bu<sub>4</sub>NBF<sub>4</sub> prepared by mixing aqueous solutions of Bu<sub>4</sub>NHSO<sub>4</sub> and NaBF<sub>4</sub> followed by recrystallization of the product from water. The compounds, Z(Cl)N $\square$ O and Z(Cl<sub>2</sub>)N $\square$ O were prepared by adding a slight excess of chloro and dichlorobenzyloxycarbonyl chloride to HN $\square$ O in ether or ethyl acetate containing triethylamine, extracted and recrystallised.

Product analysis was carried out from the catholyte solution by GLC and by HPLC.

**RESULTS AND DISCUSSION**

Figure 1 shows cyclic voltammograms for the reduction of a solution of  $Z(Cl)N\text{C}_6\text{H}_4\text{O}$   $2 \times 10^{-3} \text{ mol dm}^{-3}$  in DMF/ $\text{Bu}_4\text{NBF}_4$  ( $0.1 \text{ mol dm}^{-3}$ ), at a vitreous carbon electrode.

Two totally irreversible reduction peaks are observed at approximately -2.6 and -2.8 V and the height of the second reduction peak is half that of the first peak.



**Figure 1** - I-E curves for a solution of  $2 \text{ mmol dm}^{-3} Z(Cl)N\text{C}_6\text{H}_4\text{O}$  in  $0.1 \text{ mol dm}^{-3} \text{Bu}_4\text{NBF}_4/\text{DMF}$  at sweep rates of 0.02, 0.05, 0.1 and  $0.2 \text{ Vs}^{-1}$ .

The cyclic voltammetry data extracted for these cyclic voltammograms is presented in table 1. The parameter,  $i_p/cv^{1/2}$  is independent of  $v$ , suggesting that the reaction corresponding to the first peak is diffusion controlled.

Under similar conditions, cyclic voltammograms of chlorotoluene were recorded. They present a totally irreversible peak at a potential close to -2.8 V

indicating that the second peak appearing in the cyclic voltammetry of the urethane derivative is related to the reduction of chlorotoluene, formed in the cleavage of the Z group. The reduction of chlorotoluene probably results in the cleavage of C-Cl bond (6).

**TABLE 1**

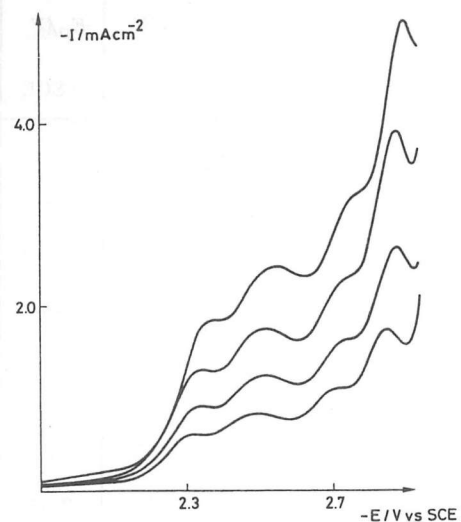
Electrochemical data for the amine derivatives studied.

COMPOUND	$v/\text{Vs}^{-1}$	PEAK 1		PEAK 2	PEAK 3	PEAK 4
		$-E_p/\text{V}$ vs SCE	$i_p/cv^{1/2} *$	$-E_p/\text{V}$ vs SCE	$-E_p/\text{V}$ vs SCE	$-E_p/\text{V}$ vs SCE
$Z(Cl)N\text{C}_6\text{H}_4\text{O}$	0.02	2.56	88	2.76	--	--
	0.05	2.58	89	2.77	--	--
	0.10	2.60	89	2.79	--	--
	0.20	2.62	87	2.82	--	--
$Z(Cl_2)N\text{C}_6\text{H}_4\text{O}$	0.02	2.32	92	2.50	2.72	2.84
	0.05	2.34	85	2.52	2.73	2.87
	0.10	2.35	85	2.52	2.74	2.87
	0.20	2.37	85	2.54	2.76	2.89

\* The units are:  $\text{A mol}^{-1} \text{cm}^3 \text{V}^{-1/2} \text{s}^{1/2}$

Cyclic voltammograms were carried out at different sweep rates for a solution of  $Z(Cl_2)N \begin{array}{c} \square \\ \square \end{array} O$   $2 \times 10^{-3} \text{ mol dm}^{-3}$  in DMF/ $Bu_4NBF_4$  ( $0.1 \text{ mol dm}^{-3}$ ). They are identical to those obtained with the monochloro derivative, although two further peaks are observed, as shown in figure 2. The first peak potential, however, is slightly more positive than that for  $Z(Cl)N \begin{array}{c} \square \\ \square \end{array} O$  as shown in table 1.

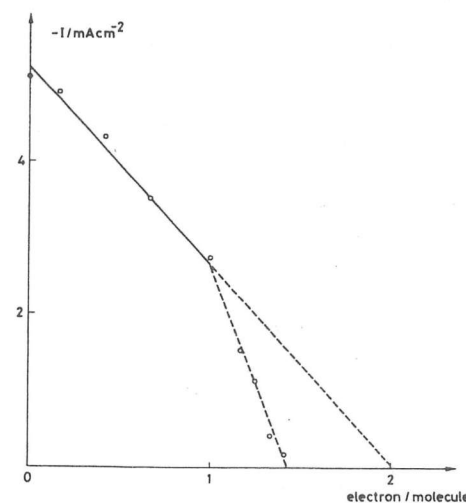
Again, the parameter  $i_p/cv^{1/2}$  is independent of  $v$ , and thus, the reaction corresponding to the first peak is diffusion controlled.



**Figure 2** - I-E curves for a solution of  $2 \text{ mmol dm}^{-3} Z(Cl_2)N \begin{array}{c} \square \\ \square \end{array} O$  in  $0.1 \text{ mol dm}^{-3} Bu_4NBF_4/DMF$  at sweep rates of  $0.02, 0.05, 0.1$  and  $0.2 \text{ Vs}^{-1}$ .

Analysis of the cyclic voltammograms of dichlorotoluene shows two reaction peaks whose potentials almost coincide with those of the second and third peaks of the dichloro derivatives. Hence, they may be related to the reduction of dichlorotoluene (6).

Controlled potential electrolyses have been carried out for the monochloro and dichloro urethane compounds in DMF/ $Bu_4NBF_4$  ( $0.1 \text{ mol dm}^{-3}$ ), at a vitreous carbon electrode, at potentials about  $50 \text{ mV}$  negative to the first reduction peak. In both cases variation of current with charge shows two linear portions with different slopes as exemplified in figure 3, for  $Z(Cl)N \begin{array}{c} \square \\ \square \end{array} O$ . The first region of the curve extrapolated to  $i=0$  corresponds to the number of electrons ( $n$ ) involved per molecule during the initial stages of the electrolysis; the value found was 2. It is observed, however, that the current in the later stages of electrolysis decays more rapidly and the current falls to zero at  $n=1.5$ . For the second derivative coulometric data indicates  $n=1.2$ . Such coulometric data can occur when the electrode passivates or there is a substantial change in the catholyte leading to chemistry of the electroactive species.











**Figure 3** - I-Q curve for controlled potential electrolysis of  $Z(Cl)N \begin{array}{c} \square \\ \square \end{array} O$  ( $20 \text{ mmol dm}^{-3}$  at  $-2.6 \text{ V}$  using a vitreous carbon electrode in DMF +  $Bu_4NBF_4$  ( $0.1 \text{ mol dm}^{-3}$ )).



Table 2 shows the results obtained for the controlled potential electrolysis experiments and contains product yield distribution and coulometry data. In the case of the monochloro derivative, amine was identified as a product with a yield of the order of 50% and chlorotoluene was also detected with a yield of 38%.

TABLE 2

Coulometry and product yield data for the amine derivatives

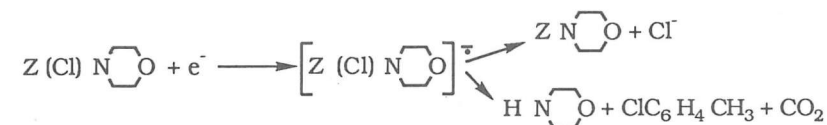
COMPOUND	- Ep / V vs SCE	n	YIELD						
			H N 	C <sub>6</sub> H <sub>5</sub> CH <sub>3</sub>	p-Cl-C <sub>6</sub> H <sub>4</sub> CH <sub>3</sub>	Cl <sub>2</sub> C <sub>6</sub> H <sub>3</sub> CH <sub>3</sub>	Z N 	Z (Cl) N 	Z (Cl <sub>2</sub> ) N 
Z (Cl) N 	2.6	1.5	50%	5%	38%	-	23%	20%	-
Z (Cl <sub>2</sub> ) N 	2.3	1.2	20%	3%	3%	10%	10%	31%	34%

The low yield in free amine may be explained in terms of C-Cl cleavage. In fact, toluene and ZN  have also been identified as products with yields of the order 5% and 23%, respectively. It should be noted that ZN  is not electroactive at the electrolysis potential and when the electrolysis terminated some starting material was still present in the catholyte solution. The current, however, has dropped to values close to zero and, therefore, it was assumed that products of the electrolysis have passivated the surface, preventing the completion of the reaction.

For the dichloro derivative, free amine was detected but only in a yield of 20%, whereas dichlorotoluene was found with a yield of 10%. Again, in this case, Z(Cl)N  was detected as well as low yields of ZN , toluene and chlorotoluene. Also in this case blockage of the electrode surface by passivation was observed since some starting material was found at the end of the electrolysis.

Again, in this case cleavage of C-Cl bonds is responsible for the low value of the yield together with a low value of n.

The C-Cl cleavage may result from either the proximity of the potential for this reaction to the potential of the desired cleavage reaction or it could also result from the competing chemistry:



Thus, although the introduction of chloro in the Z group improves the reduction potential, the desired cleavage only occurs in moderate yields and the tendency seems to be that the more substituted the ring with chloride, the lower the yield.

Attempts to increase the yield in free amine by adding small amounts of a proton donor, such as, acetic acid, methanol, or phenol, were made. In all cases, the experiments totally failed since after the consumption of a very small amount of charge, the current dropped to zero, suggesting strong passivation of the electrode surface.

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## AMBIENT TEMPERATURE LITHIUM BATTERIES WITH LAYER TYPE CATHODES: PERFORMANCE

OF  $TiS_2$  CELLS

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### SUMMARY

A titanium disulphide cathode has been used in a coin cell in which one molar solution of  $LiClO_4$  in propylene carbonate was the electrolyte. The cell was charged and discharged for one hour each at 0.1mA. Cycling between voltage limits of 4 and 1.4 was also carried out.

### INTRODUCTION

The positive electrode material for a secondary lithium cell should have high energy density, stability in the electrolyte, good electrical conductivity and withstand moderate to high rates of discharge. Transition metal chalcogenides have these qualities and hence are being widely used as cathodes in these cells.  $TiS_2$ , a material with layered structure, has good rate capability and a high theoretical specific energy when coupled