

Figure 2 - Comparison between the experimental data (■) and a simulated voltammogram with $k_1 = 1.5 \text{ s}^{-1}$ and k_2 as infinity.

Although the general agreement between the experimental and the simulated cyclic voltammograms is evident, there are still some discrepancies, namely involving the cathodic peak current for the fluoride complex. This conceivably can be corrected by improving the original scheme and is currently under investigation.

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THE CATHODIC CLEAVAGE OF SOME PROTECTING GROUPS FROM AMINE AND THIOL DERIVATIVES

M.D. Geraldo and M.J. Medeiros

Centro de Química Pura e Aplicada, Universidade do Minho, Largo do Paço

4719 Braga Codex, Portugal

The large molecule synthesis is totally dependent on the use and removal of protecting groups from amine and carboxylic acid groups and also sometimes from alcohols and thiols [1].

Electrochemical methods are known today to be convenient alternatives to deprotect molecules, because the control of the potential permits the selectivity between different protecting groups or even between the same group at different sites in the molecule. Thus, we have been concerned with the study of electrocleavage of some groups of interest for protection during the synthesis [2-5].

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, aminoacids and peptides at vitreous carbon electrodes in *N,N*-dimethylformamide (DMF) only occurs at very negative potentials, approximately -2.8 V vs SCE.

This electrochemical procedure, however, has some experimental difficulties due to the very 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.

In this paper we present the results obtained in the study of the cathodic cleavage of 4-chlorobenzyloxycarbonyl and 2,4-dichlorobenzyloxycarbonyl groups from the urethane derivatives of morpholine and of 4-picolyl group from thioethers at a vitreous

carbon electrode in N,N-dimethylformamide (DMF).

I-E curves were recorded at a vitreous carbon disc electrode in DMF/Bu₄NBF₄ (0.1 mol dm⁻³) for 4-chlorobenzoyloxycarbonyl and 2,4-dichlorobenzoyloxycarbonyl derivatives of morpholine.

In the case of chlorobenzoyloxycarbonyl amide, we observe two totally irreversible reduction processes, as shown in figure 1.

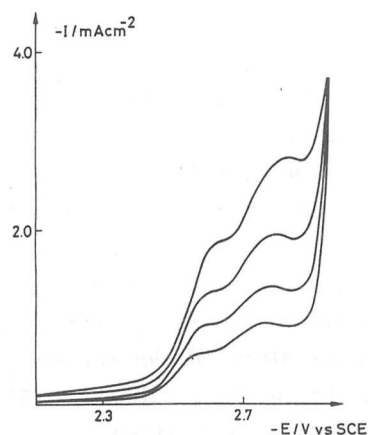


Figure 1 - I-E curves for a solution of 2 mmol dm⁻³ Z(Cl)N-morpholine in 0.1 mol dm⁻³ Bu₄NBF₄/DMF at sweep rates of 0.02, 0.05, 0.1 and 0.2 Vs⁻¹.

Moreover, the current function, for the first reduction peak, $I_p/v^{1/2c}$, is independent of the potential scan rate confirming that the reduction becomes mass transport controlled beyond the peak.

For the dichlorobenzoyloxycarbonyl derivative we observe four totally irreversible reduction peaks (figure 2).

Again, in this case the current function for the first peak, $I_p/v^{1/2c}$, is independent of the potential scan rate, and thus, the reaction is diffusion controlled.

Controlled potential coulometry was carried with each of the two derivatives in DMF/Bu₄NBF₄; the cathode was again vitreous

carbon and the applied potentials were about 50 mV negative to the first reduction peaks.

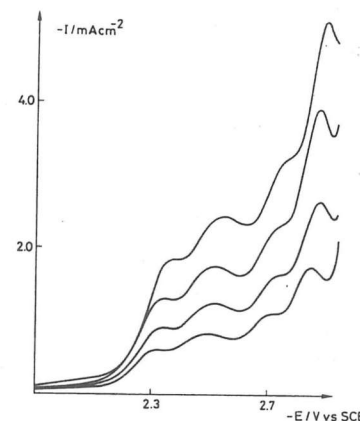


Figure 2 - I-E curves for a solution of 2 mmol dm⁻³ Z(Cl₂)N-morpholine in 0.1 mol dm⁻³ Bu₄NBF₄/DMF at sweep rates of 0.02, 0.05, 0.1 and 0.2 Vs⁻¹.

For each urethane derivative, a plot of the current *versus* charge passed shows two linear portions with different slopes. The first region of the curve extrapolated to $i=0$ corresponds to the number of electrons involved per molecule during the initial stages of the electrolysis, and the value found was two. In the later stages of electrolysis, however, the current decays more rapidly and the current falls to zero at different n for each derivative as shown in table 1.

Table 1 also shows the product yields obtained by GLC and HPLC.

In both cases, the low yield in free amine may be explained in terms of C-Cl cleavage. On the other hand, at the end of electrolysis some starting material was found in the catholyte solution.

It is likely that the products of the electrolysis have

passivated the surface, preventing the completion of the reaction because the current has dropped to values close to zero. This fact is, also, responsible for the low value of n .

Thus, although the introduction of chloro in the Z group improves the reduction potential, the desired reaction only occurs in moderate yields.

We also report here the cleavage of 4-picolyyl group from thioethers at a vitreous carbon electrode in DMF.

Figure 3 shows a cyclic voltammogram for 4-picolylphenylthioether in DMF/ Bu_4NBF_4 .

Three irreversible reduction peaks are observed; the first reduction peak appears at - 2.19 V vs SCE and its current intensity is proportional to the square root of the potential scan rate, suggesting that the reaction is diffusion controlled.

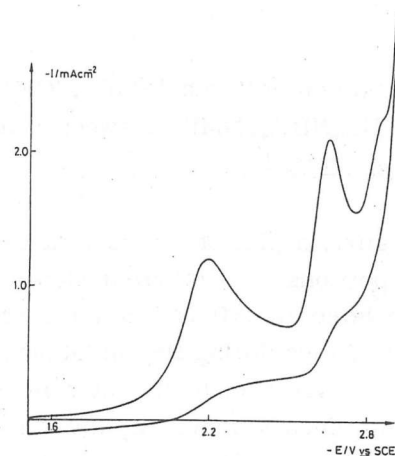


Figure 3 - Cyclic voltammogram for a 2×10^{-3} mol dm^{-3} solution of 4-picolylphenylthioether in DMF/ Bu_4NBF_4 (0.1 mol dm^{-3}) at a vitreous carbon electrode and at the scan rate 0.1 V s^{-1} .

Further cyclic voltammograms were recorded for 4-picolylphenylthioether in DMF with NaClO_4 or NaBr as the electrolyte and also with $\text{NaClO}_4 + 5\% \text{ H}_2\text{O}$. In the potential range of

TABLE 1

Coulometry and product yield data for the amine derivatives

COMPOUND	- E_p / V vs SCE	n	YIELD	
			Product	Yield (%)
Z (Cl) <chem>N1CCOCC1</chem>	2.6	1.5	<chem>N1CCOCC1</chem>	50%
Z (Cl ₂) <chem>N1CCOCC1</chem>	2.3	1.2	<chem>N1CCOCC1</chem>	20%
			<chem>C6H5CH3</chem>	5%
			<chem>p-Cl-C6H4CH3</chem>	38%
			<chem>Cl2C6H3CH3</chem>	-
			<chem>Z N1CCOCC1</chem>	23%
			<chem>Z (Cl) N1CCOCC1</chem>	20%
			<chem>Z (Cl2) N1CCOCC1</chem>	-
				10%
				31%
				34%

the first reduction peak, the voltammogram is unaltered.

Controlled potential electrolysis have been carried out for the 4-picolyphenylthioether in DMF/ Bu_4NBF_4 at just 50 mV after the first reduction peak.

A plot of the current *versus* charge passed during the electrolysis was linear and the number of electrons involved per molecule of starting material was equal to 2.

In this case, thiophenol was identified as a product with a yield of the the order of 85%.

Almost identical data was obtained in DMF/ $\text{NaClO}_4 \cdot \text{H}_2\text{O}$. This medium has the advantages that the water will mediate the strongly basic conditions created during the electrolysis and that the sodium salt is readily separated from products by water extraction.

Thus, the cleavage by cathodic reduction of the picolyl group occurs in high yields and in a convenient potential range, which may well make it a very suitable protecting group of the thiol function.

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THE EFFECT OF ELECTROLYTE CONCENTRATION ON THE BEHAVIOUR OF ELECTROCHEMICAL SYSTEMS

M.F. Bento, M.J. Medeiros, M.I. Montenegro, M.A. Queirós

*Centro de Química Pura e Aplicada da Universidade do Minho
Largo do Paço, 4719 Braga Codex, Portugal*

and D. Pletcher

*Department of Chemistry, The University, Southampton, SO9 5NH,
UK.*

The electrochemical techniques usually employ high concentrations of electrolyte because i) it lowers the solution resistance, which is particularly high in many organic solvents, ii) its presence supresses the migration current. This is, however, a disadvantage of electrochemistry when compared with spectroscopic techniques, such as NMR, ESR, etc., whose measurements have no equivalent requirement for addition of electrolyte. In fact, the addition of an electrolyte limits the usefulness of voltammetric studies in thermodynamics, kinetics and analytical investigations. Therefore, it would be highly desirable if electrochemical studies could be carried out in the absence of electrolyte.

Recent developments in microelectrodes design, instrumentation and theory have shown that many new possibilities are open for electrochemical science. In particular, this has been demonstrated by voltammetric studies in solutions containing low concentrations of electrolyte[1], in the absence of electrolyte[2], in glasses[3] and in solvents with very low dielectric constant[4].

In this work we report preliminary results of an investigation of the effect of the electrolyte concentration on the reduction of nitrotoluene in N,N-dimethylformamide at gold microdiscs.