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AN EFFECTIVE AND MILD ELECTROCATALYTIC PROCEDURE FOR THE REMOVAL OF 1,3-DITHIANE PROTECTING GROUPS[1]

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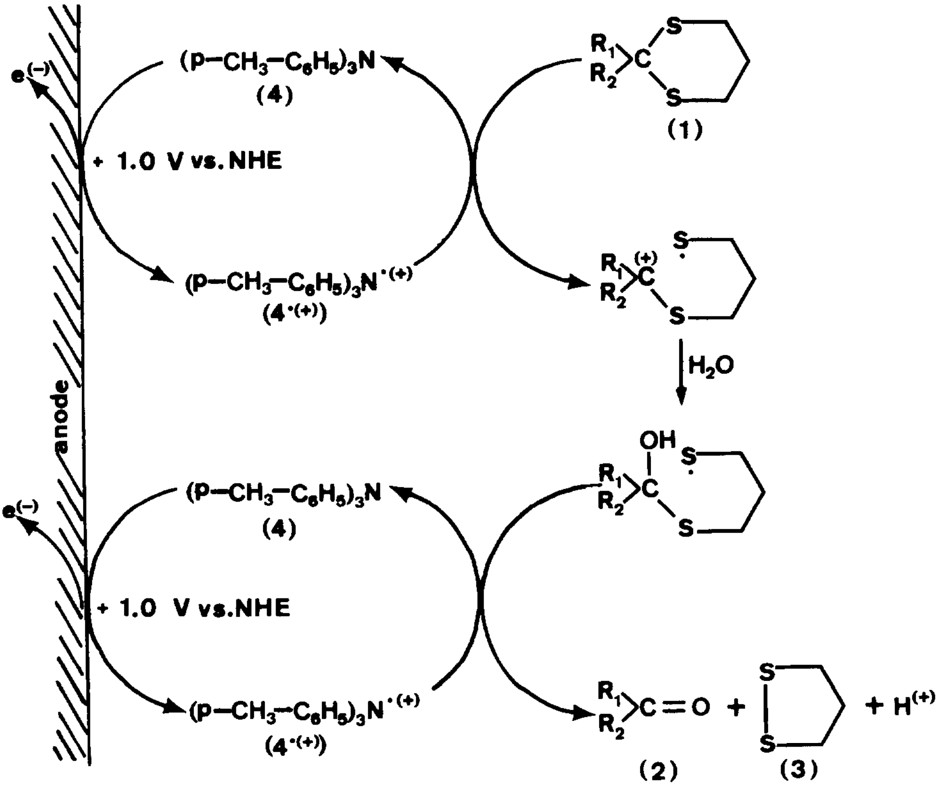
Summary: The 1,3-dithiane protecting group can effectively be removed by indirect electrochemical oxidation under extremely mild conditions, if catalytic amounts of tris(p-tolyl)amine are used as homogeneous electron transfer agents.

We wish to report on a very effective new oxidative method for the removal of 1,3-dithiane protecting groups which is superior to known oxidative procedures[2,3] because of its taking place under extremely mild conditions besides giving almost quantitative yields.

This method is based on the principle of electrochemical oxidations against the standard potential gradient[4,5] using electrochemically generated homogeneous electron transfer agents. This procedure has already been realized in several cases of synthetic interest in a very similar manner[5-10]. As shown in the reaction scheme, the electron transfer agent tris(p-tolyl)-amine (**4**) is oxidized at + 1.0 V vs. the Normal Hydrogen Electrode (NHE) to form the cation radical ($\mathbf{4}^{\cdot+}$). $\mathbf{4}^{\cdot+}$ then undergoes homogeneous electron transfer with the dithiane (**1**). As **1** has an oxidation potential which is 300 mV more positive than the one of **4** the electron transfer equilibrium favourably lies on the side of $\mathbf{4}^{\cdot+}$. The fast carbon-sulfur bond cleavage is shifting the equilibrium to the product side. Hydrolysis and a second oxidation step then lead to the deprotected carbonyl compound. Presence of $NaHCO_3$ is necessary to accelerate the reaction. The acetonitrile must contain small amounts of water[12] to be able to hydrolize the intermediate carbenium ion. Loss of the tris(p-tolyl)amine catalyst has not been detected indicating a long catalytic chain. Passivation of the electrode has never been observed. Therefore periodic pulsing of the anode potential is unnecessary in contrast to the direct anodic oxidation[3]. The results are given in the table.

Scheme:



If the electrochemical generation respectively regeneration of the electron transfer agent is not desired, the stable and crystalline dark blue tris-(p-tolyl)ammoniumyl hexachloroantimonate, easily prepared from the amine and $SbCl_5$[11], can be used in stoichiometric amounts with similar results in acetonitrile solution containing $NaHCO_3$. In the same way the tris(p-bromophenyl)amine cation radical hexachloroantimonate can be used as homogeneous electron transfer agent giving excellent yields. In this case, however, one has to sacrifice the advantage of low potential oxidation, as the tris(p-bromophenyl)amine has a 300 mV more positive oxidation potential as compared with **4**. On the other hand, the reaction rate is accelerated.

The more difficultly oxidizable 1,3-dithiolanes(oxidation potential 300 mV more positive than **1**) undergo reaction with the electrochemically

Table: Indirect anodic cleavage of dithianes using tris(p-tolyl)amine as electron transfer agent

Dithiane (1)		Carbonyl Compound (2)
R_1	R_2	Yield (%)
C_6H_5-	CH_3-	95^a
$-(CH_2)_5-$		95^a
$n-C_3H_7-$	$n-C_6H_{13}$	85^a
$n-C_8H_{17}-$	$H-$	97^b
$n-C_8H_{17}-$	$C_2H_5O-\underset{O}{\underset{\|}{C}}-$	70^c

[a] Yield determined by GLC.
[b] Yield determined by isolation as O-methyloxime.
[c] Yield determined by distillation. Reaction taking place at lower rate because of the higher oxidation potential of the dithiane. For faster rates tris-(p-bromophenyl)amine can be used as electron transfer agent.

generated cation radical of tris(p-bromophenyl)amine as electron transfer agent. In the case of the 1,3-dithiolane of acetophenone the cleavage product could be obtained in 70 % yield. Again the redox potential of the substrate is 300 mV more positive than the one of the electron transfer agent. In this case, however, a polymeric sulfur compound is formed which deposits onto the walls of the cell as well as onto the electrode leading to decreasing currents. One should be able to avoid this problem by using molar amounts of the cation radical salt.

<u>Indirect electrochemical removal of 1,3-dithiane protecting groups;</u>
2.5 mmol of 1 and 143 mg (0.5 mmol) of 4 dissolved in 100 ml moist acetonitrile[12] (0.2 M $LiClO_4$) containing 1 g (12 mmol) $NaHCO_3$ are electrolized in a divided cell (Pt-anode; Pt-cathode; 20°C) at a controlled potential of + 0.5 V <u>vs</u>. $Ag/AgNO_3$(0.1 M)-reference electrode until total turnover is achieved(GLC-control). For work up the acetonitrile solution is poured into 300 ml water. The mixture is three times extracted with ether. Product yields are determined by GLC or by isolation via bulb-to-bulb distillation.

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[12] Acetonitrile containing 10 mmol water.

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