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ELECTROCHEMICAL REDUCTION OF COMPLEX SULFONAMIDES : A CATHODIC SYNTHESIS OF AZA AND AZA-OXA LIGANDS

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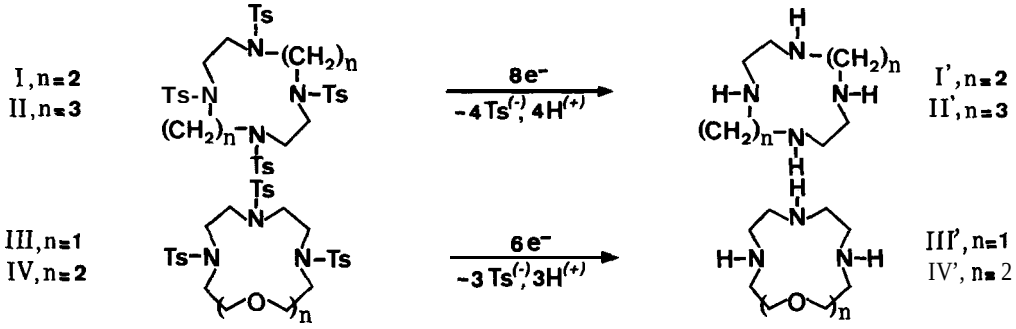
Recent reports on interesting properties of multiheteromacrocycles and specially their tendency to complex with metals have prompted us to examine a synthetic route to poly-aza and poly-oxa-aza-cycloalkanes, which was generally carried out via macrocyclic polysulfonamides [1-5]. The last step in this synthesis is the removal of the tosyl groups, Such a removal can be achieved electrochemically and we wish here to report the successful cathodic cleavage of N-S bonds in the poly -p-toluenesulfonamides according to the general scheme :



The electrochemical reduction of these substrates can be carried out by using two methods : the direct reduction in solvent-electrolyte couples such as DMF - $R_4N^+X^-$ or acetonitrile-$R_4N^+X^-$, and/or the indirect reduction by some well chosen electrogenerated anion radicals [7-11]. This second method allows the use of alkali metal salts as supporting electrolytes, in dipolar aprotic solvents, when the primary electron source is the mercury cathode.

In the case of macrocyclic polysulfonamides, such as I-V, table 1 shows that the electrochemical deprotection is feasible often in good yield, when indirect reduction using the pyrene anion radical as reducing reagent is performed. Similar results were found with direct electrolyses, although with a more problematic work up.

Experimental

a) Indirect reduction

Reductions are performed in an H-cell with a mercury pool (area : 7 cm^2) as cathode. Counter electrode : graphite rod. Volume of catholyte : 70 ml Solvent : dry DMF. Electrolyte : Li ClO_4 0.2M.

The mass of substrate reduced by this way is 1.5g in the presence of 100 mg of pyrene. The chosen fixed potential corresponds to the redox potential of pyrene. Reduction is stopped when the red colour of the pyrene anion radical appears. The course of the reduction can also be followed by means of cyclic voltammetry as shown in figure 1 (decrease of catalytic current at the level of the reversible step of pyrene).

This reduction can also be achieved in a constant current electrolysis, with pyrene or other suitable mediators (e.g. stilbene, anthracene).

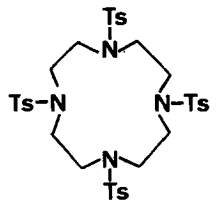
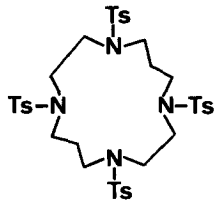
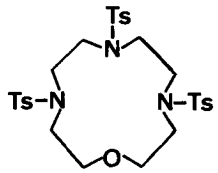
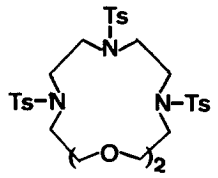
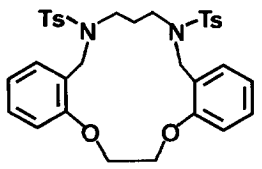
b) Direct reduction

In principle , a direct reduction of I-V is possible. However in this case tetraalkylammonium salts must be used as supporting electrolyte and some disturbances are often brought about by the presence, during the work up, of amines, produced by Hoffmann degradation of the salts, difficult to separate from the product mixture. Nevertheless, this type of reduction can be achieved in the same conditions as previously described using 1 g to 1.5 g of sulfonamides in DMF-nBu_4NClO_4 0.1 M on a mercury pool at a fixed potential (-1.80V).

Discussion

It is worth shortly discussing here the mechanism of the cleavage of (I) and explaining why reduction must be carried out in a rather weakly acidic solvent. In fact, the amines produced after cleavage of 1, 2, 3 and 4 N-S bonds are increasingly more basic and can produce, through the conjugate acid[12] a catalytic hydrogen evolution. Figure 2 illustrates this fact : a large increase in the peak current is induced by adding some proton donor. We checked that, in a basic solvent (DMF or DMSO), good current yields, in macroscale electrolyses, are exclusively observed in the total absence of proton donor.

Table 1. Indirect preparative electrolysis of some macrocyclic polysulfonamides by electrogenerated pyrene-anion-radical. Supporting electrolyte : Li ClO_4 0.2M in aprotic DMF. Working electrode : mercury pool. [a] vs Ag/AgI/I^- 0.1 M. [b] After a possible methylation of the catholyte solution by CH_3I. [c] Isolated in the form of tripicrate (m.p.). [d] Coulometric results of direct reduction at -1.8 V, in DMF nBu_4NClO_4 0.2M, on mercury electrode.

	Substrates	Potential of electrolysis E(V)[a]	Number of F. mol.$^{-1}$	Products [b] (% of conversion)
I		-1.50	8.10 8.30[d]	1,4,7,10-tetra-aza-cyclododecane m.p. 34-35°C (52) p-$CH_3C_6H_4SO_2$-CH_3 (96)
II		-1.50	8.08 8.10[d]	1,4,8,10-tetra-aza-cyclotetradecane m.p. 185-186°C (85) p-$CH_3C_6H_4SO_2$-CH_3 (95)
III		-1.55	5.95 6.08[d]	1-oxa-4,7,10-tri-aza-cyclododecane m.p. 237-240 C (26)[c] p-$CH_3C_6H_4SO_2$-CH_3 (96)
IV		-1.55	5.85 6.15[d]	1,4-di-oxa-7,10,13-tri-aza-cyclopentadecane m.p. 215-218°C (43)[c] p-$CH_3C_6H_4SO_2$-CH_3 (94)
V		-1.56	4.11 4.05[d]	Dibenzo-1,4-di-oxa-8.di-aza-cyclopentadeca-5,14-diene. m.p. 139-140°C (92) p-$CH_3C_6H_4SO_2$-CH_3 (96)

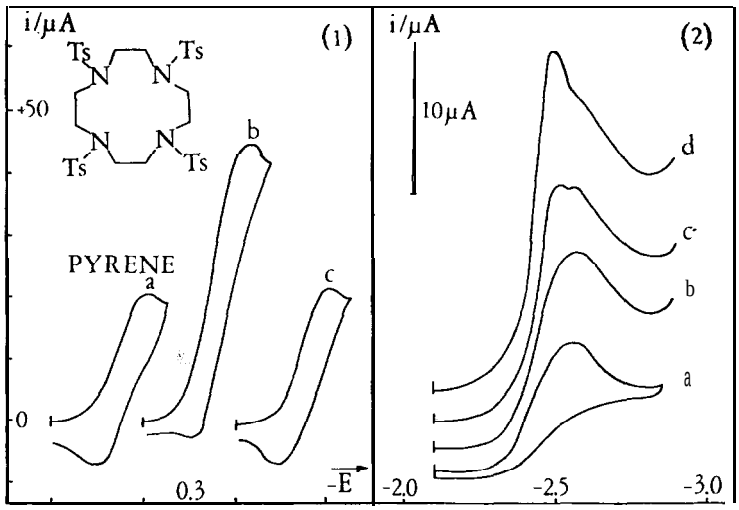


Figure 1 : Cyclic voltammograms at a stationnary mercury electrode of pyrene (5.10^{-3}M) in the presence of (I) ;x= ((I))s/(pyrene)s, before and after coulometry at -1.54V. (a) x = 0 ; (b) x = 10 ; (c) after consumption of 8.2 F. Moi!Supporting-electrolyte : $LiClO_4$ 0.2M in aprotic DMF. Sweep rate : 10 mV. s^{-1}. In the three cases the starting potential is -1.30V.

Figure 2 : Cyclic voltammograms at a stationnary mercury electrode of (I) in the presence of phenol ; m = (phenol)s/((I))s. Concentration of (I) : 10^{-3}M. (a) m =0 (b) m = 5 ;(c) m = 7 ;(d) m =8. Medium : acetonitrile-nBu_4NI 0.1M. Sweep rate : 100 mV.s^{-1}.

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