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Dedicated to Professor Ionel Haiduc
on the occasion of his 65th birthday

AN IMPROVED SYNTHESIS OF 1,7-DIOXA-4,10-DIAZACYCLODODECANE

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ABSTRACT. An improved method for preparation of 1,7-dioxa-4,10diaza-cyclododecane is described.

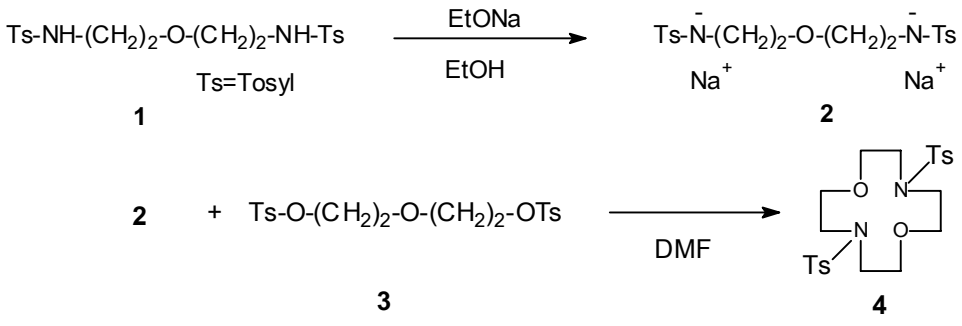
INTRODUCTION

There is a continuing interest in the preparation of diazacoronards which have important uses as macrocyclic molecular receptors as well as being valuable intermediates for the synthesis of cryptands and related compounds[1].The title compound was obtained by classical procedures by reaction of the sodium salt of N,N'-ditosyl-2,2'-diaminodiethyl ether with diethyl glycol ditosylate by Richmon-Atkins method [2,3], α,ω-dicarboxylate esters or with dicarboxylyl dichlorides[4-6]. A similar method uses *o*-carbamoylbenzenesulfonyl group, derived from saccharin, as the nitrogen atom protecting group [7]. N,N'-Ditosyl-2,2'-diaminodiethylether and corresponding dibromide ether were used as starting materials in phase transfer catalysis procedure[8-10].

Taking into consideration the accessibility of starting material, the yields and the work-up of the crude reaction product the more attractive way to obtain compound **1** is Richmon-Atkins method.

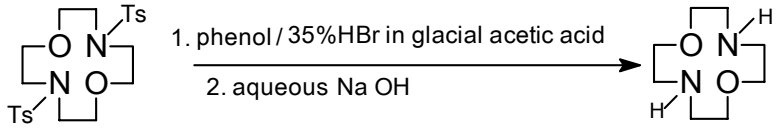
RESULTS AND DISCUSSION

Ambel and Dall[3] applied Richmond-Atkins procedure according to the following reaction scheme:



By adding to the disodium salt of N,N'-ditosyl-2,2'diaminodiethyl ether in DMF, the DMF solution of diethyl glycol ditosylate at 100 ^{0}C for 12 h, they obtained compound **4** with 87 %. Preparing this compound by this procedure we noticed that working at 120^{0}C the reaction time can be reduced at 2.5 h and the yield was almost quantitative.

Compound **4** was detosylated by gentle heating in 35% solution of anhydrous hydrogen bromide in glacial acetic solution in presence of phenol:



4 **5**

In conclusion with succeeded to improve the previous method of Ambell and Dall[2] obtaining compound **1** in a shorter reaction time, improved yield and a very simple work-up of the reaction product (see experimental).

EXPERIMENTAL

N,N'-Ditosyl-1,7dioxa-4,10-diazacyclododecane. The compound **1** [2] (0.025 mmol) was suspended in dry ethanol (20 mL) and warmed. To this hot suspension a solution of sodium (1.15 g, 0.05 mol) in dry ethanol (30 mL) was added. The mixture was then refluxed for about 20 min and the solvent evaporated under reduced pressure. The dry residue of the sodium salt **2** was then dissolved in DMF (180 mL) and heated at 120^0. A solution of diethyl glycol ditosylate **3** (0.025 mol) in DMF (50 mL) was added over a period of 2 h, keeping the temperature at 120^{0}C. Subsequently the reaction mixture was maintained at the same temperature for 30 min more. Then, after cooling, water was added (250 mL) and the precipitate collected and refluxed in ethanol (50 mL). The ethanolic mixture was filtered hot and the precipitate washed with cold ethanol when compound **4** was obtained almost quantitatively. M.p.= 202-203 (lit. m.p.[2]= 203-204).

^{1}H-NMR ($CDCl_3$), δ : 2.44 (s, 6H, CH_3), 3.25(t, J= 4.5, 8H, CH_2-NH), 3.77 (t, J= 4.8, 8H, CH_2-O), 7.34 (d, J=8.7, 4H), 7.72 (d, J= 8.1 4H). ^{13}C-NMR ($CDCl_3$), δ : 21.46, 50.83, 70. 06, 127.35, 129.72, 135.24, 143. 45.

1,7,-Dioxa-4,10-diazacyclododecane. A mixture of 0.005 mole of the compound **4** and 2 g of phenol in 20 g of 35 % solution of anhydrous hydrogen bromide in glacial acetic acid was stirred at 50 ^{0}C for 24 h. The solution was poured into 700 ml of anhydrous ether and the hydrobromide was extracted with a LiOH aqueous solution. The basic solution was acidulated

and extracted with chloroform (5x50 mL). The combined extracts were dried over anhydrous magnesium sulfate, solvent evaporated *in vacuo* and residue extracted with boiling hexane. After evaporation of the solvent the pure reaction product was obtained. Yield 80%. M.p. = 82-84 (lit. m.p.[2] = 82-84).

^{1}H-NMR ($CDCl_3$), δ : 2.42 (s, 2H, NH), 2.77 (8H, CH_2N), 3. 70 (8H, CH_2O)

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