# MODIFIED CROWN ETHER CATALYSTS. 4. CLEAVAGE OF MACROCYCLIC ETHERS BY EATON'S REAGENT (METHANESULFONIC ACID/PHOSPHOROUS PENTOXIDE)[1]

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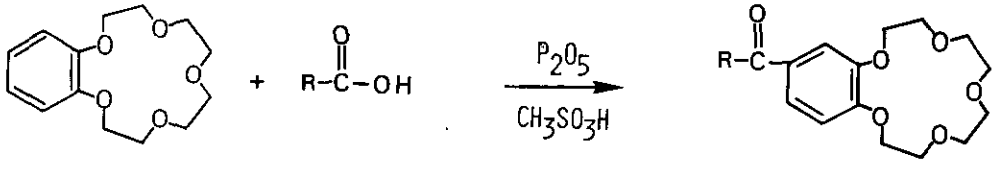
Abstract - Eaton's reagent (methanesulfonic acid/phosphorous pentoxide) is a superior media for the acylation of benzo crown ether compounds. Benzo-15-crown-5 was cleaved in Eaton's reagent to form methansulfonate esters of the glycol cleavage products. A comparison of the NMR spectrum of the cleavage products with those of some of the possible products showed that the aliphatic glycols formed the major portion of the cleavage products.

We have been interested in forming substituted crown ethers[2-4] and in their use as phase transfer agents.[1] We observed that Eaton's reagent,[5] a solution of methanesulfonic acid in phosphorous pentoxide, was a convenient medium for the acylation of benzo crown ethers with carboxylic acids.[2,3] The exact acylation mechanism using Eaton's reagent is unknown, however, Eaton did demonstrate that




methanesulfonic anhydride was easily isolated from the reagent.[5]

The acylation of dibenzo-18-crown-6 and dibenzo-24-crown-8 in Eaton's reagent gave particularly good yields of the bis(acylbenzo)crown ether (85-95%). Reactions with dibenzo-24-crown-8, however, gave a considerable amount of byproduct when the reaction was carried out at 50°C. The acylation of benzo-15-crown-5 in Eaton's reagent gave a considerable amount of byproduct, even when carried out at room temperature. The byproducts from these reactions were separated and found to contain both carboxylate (IR, 1740 $cm^{-1}$) and sulfonate (IR, 1350 and 1170 $cm^{-1}$) ester functions.

To further understand the nature of the byproducts from these acylation reactions, we have studied

the cleavage of benzo-15-crown-5 in Eaton's reagent. The NMR spectrum of the resulting reaction mixture exhibited more than ten signals attributable to the methyl hydrogens of methanesulfonate esters (δ 3.2-3.3). This large number of signals indicates the macrocycle was cleaved in several places. Interestingly, less than 10% of the total peak area can be attributed to aromatic methanesulfonate esters (δ 3.26-3.30).[6] Figure 1 illustrates the possible bis methanesulfonate ester cleavage products.

In an attempt to determine the exact nature of the cleavage products, we prepared five (1,2,8,12 and 13) of the possible products. These compounds were then used to help identify the major peaks in the NMR spectrum of the reaction mixture. In a cleavage reaction run for 18 hours, the NMR peaks attributable to aromatic methanesulfonate esters (1 and 2 for example) amounted to 8% of the total while those attributed directly to 8, 12 and 13 amounted to over 50% of the total. The major com-

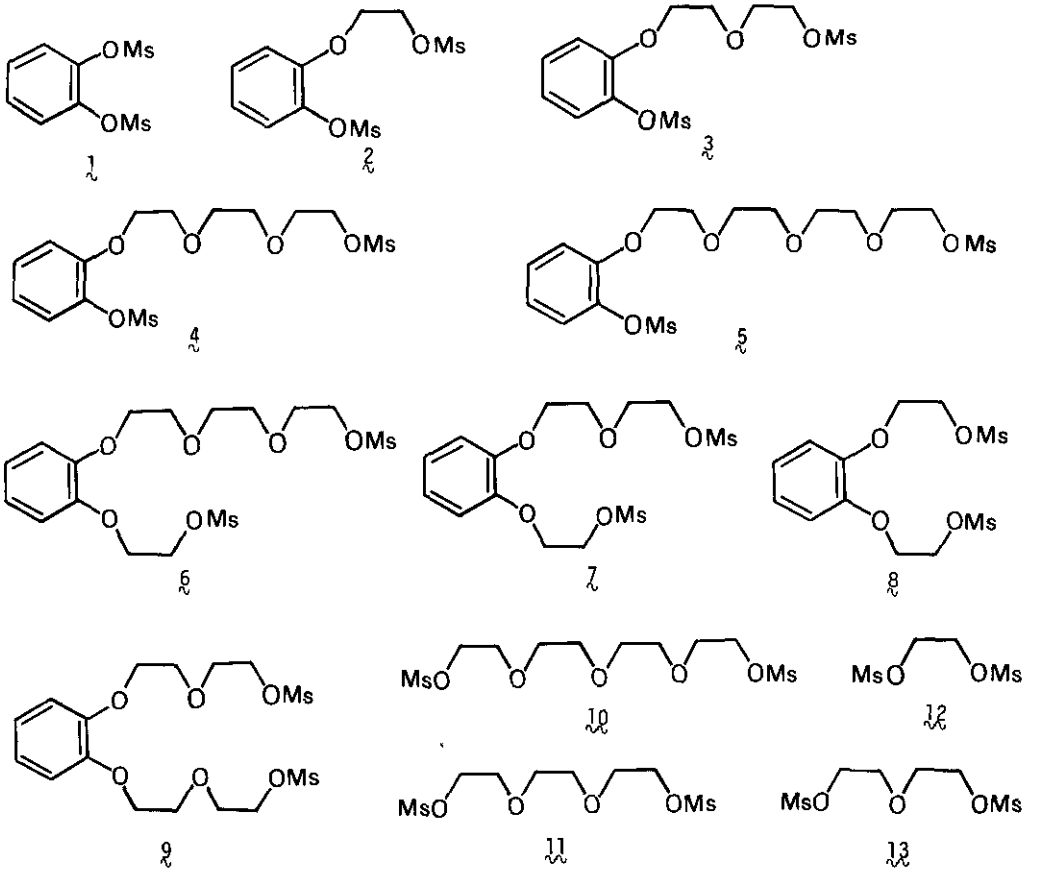



Figure 1. Cleavage Products (Ms = $CH_3SO_2$)

ponent appeared to be 1,2-ethane bis methanesulfonate (13). In a reaction run for over 4 months, the aromatic methanesulfonate ester portion of the NMR spectrum was only 12% of the total integral for methyl hydrogens indicating again that the cleavage must be occurring at the aliphatic ether positions. Secondary cleavage of the initial cleavage products produces the ethylene and diethylene glycol derivatives 12 and 13. Cleavage by methanesulfonic acid, which can occur in some circumstances,[7] did not occur under our reaction conditions. The benzo-15-crown-5 compound used in these studies was found to be contaminated with a small amount (~ 5%) of diol. Treatment of the benzo-15-crown-5 compound with methanesulfonyl chloride gave a mixture which exhibited both the methyl hydrogens of aromatic and aliphatic methanesulfonate esters. Based on the method of formation for this crown compound,[8] we believe the bis methanesulfonate ester product of the glycol contaminant to be compound 5. The small amount of this contaminant, however, accounts for only about one third of the aromatic methanesulfonate ester found in the cleavage product.

We believe the active cleaving agent in Eaton's reagent is methanesulfonic anhydride which is known to be present.[5] Karger and Mazur have reported that treatment of tetrahydrofuran with methanesulfonic anhydride gave the corresponding bis methanesulfonate ester of 1,4-butanediol.[9] When tetrahydrofuran was treated with the mixed acetic methanesulfonic anhydride, the mixed acetate and methanesulfonate ester of 1,4-butanediol was formed.[9] They also reported that anisole gave only methoxyacetophenone products when treated with the mixed acetic methanesulfonic anhydride.[10] Their results closely parallel our results with Eaton's reagent wherein we observed both cleavage of aliphatic ethers and acylation of the aromatic ring in the presence of carboxylic acids.[2,3] The consistency of these results strongly suggests that the acylating agent in the mixture of Eaton's reagent and carboxylic acids is the mixed carboxylic methanesulfonic anhydride.

*Sulfonic anhydride and mixed carboxylic sulfonic anhydrides are unstable and are therefore very* difficult to prepare and store. Eaton's reagent, which is extremely easy to prepare and can be stored indefinately,[11] is thus a superior medium for the cleavage of aliphatic ethers to form the methanesulfonate esters. The addition of carboxylic acids to Eaton's reagent is likewise a superior method to acylate phenyl ethers.[2,3]

## EXPERIMENTAL

All NMR spectra were obtained with a Varian EM 390 spectrometer. All infrared spectra were obtained with a Beckman Acculab II spectrophotometer. Melting points are uncorrected and were obtained with a Thomas-Hoover apparatus. Elemental analyses were obtained from M-H-W Laboratories, Phoenix, Arizona.

Starting Materials. Benzo-15-crown-5 was purchased from Parish Chemical Company. The bis methanesulfonate esters were prepared as follows: A solution of 0.0065 moles of the appropriate dihydroxy compound and 4.2 g of freshly distilled triethylamine in 25 ml of $CH_2Cl_2$ was cooled as 4.6 g (0.040 mol) of methanesulfonyl chloride was added. The reaction was stirred for 10 min at room temperature

and poured into 50 mL of water. The organic layer was dried over sodium sulfate and the solvent was evaporated to give the crude bis methanesulfonate ester. The following esters were prepared:

Catechol dimethanesulfonate (1) recrystallized from chloroform; mp, 103-105°; NMR(δ), 2.26 (s, 6H) and 7.35 (d, 4H); Anal. Calcd for $C_8H_{10}S_2O_6$: C, 36.09; H, 3.79. Found: C, 36.36; H, 3.97.

2-(2-Methylsulfonatoethyl)phenyl methanesulfonate, (2); recrystallized from dichloromethane; mp, 93-94°; NMR(δ), 3.16 (s,3), 3.26 (s, 3), 4.22 (m, 2), 4.55 (m. 2), 7.1 (m, 4); Anal. Calcd for $C_{10}H_{14}S_2O_7$: C, 38.70; H, 4.55. Found: C, 38.54; H, 4.55.

1,2-Bis(2-methanesulfonatoethoxy)benzene (8); mp 134-136°C.

Diethylene glycol dimethanesulfonate (12); mp, 54-55° (lit,[12] 54-55°).

1,2-Ethane dimethanesulfonate (13); oil (lit,[13] mp 43-45°).

Cleavage of benzo-15-crown-5 with Eaton's reagent. A mixture of 1 g of benzo-15-crown-5 and 20 mL of Eaton's reagent[2,5] was stirred overnight. The dark red mixture was poured into 50 mL of water and extracted with two 25 mL portions of $CH_2Cl_2$. The organic solvent was evaporated to leave a viscous oily residue. The infrared spectrum showed strong bands at 1350 and 1170 $cm^{-1}$ (sulfonate esters). The NMR spectrum showed more than ten sharp singlets of varying intensity between δ 3.21 and 3.26 (methane sulfonate esters). The NMR spectra of the reaction mixture with added amounts of each of compounds 1,2,8,12 and 13 indicated that each of these compounds was present.

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