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ALKALI METAL ION EXTRACTION USING LARIAT ETHERS POSSESSING A CHROMOGENIC GROUP

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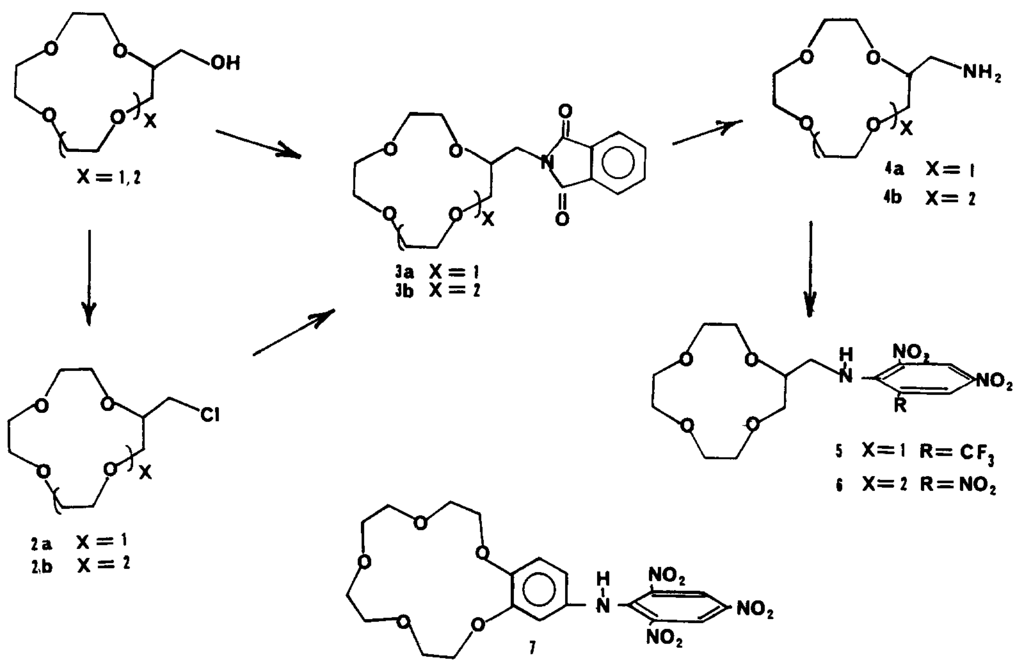
ABSTRACT - Chromogenic lariat ethers have been prepared which show improved extraction of alkali metals compared to their benzo analogues.

Crown ethers have developed in an attempt to mimic the complexation behavior toward alkali metals of naturally occurring macrocycles such as valinomycin, nonactin, and enniatin A. The ability to selectively complex alkali metals is governed by structural features inherent to the molecule in addition to the charge and diameter of the metal(1). Measurement of the extent and selectivity of complexation has been accomplished using ion-pairing(2), electrochemical(3), and calorimetric techniques(4). The incorporation of chromogenic tags within the framework of the crown ether has proved useful for the determination of K^+ in blood serum(5). Presented is a synthetic route to chromogenic lariat ethers possessing a monobasic amine accompanied by alkali metal ion extraction data in $CHCl_3/H_2O$ extraction systems.

The synthetic route is depicted in Figure 1. Hydroxymethyl crown ethers were prepared as described in the literature(6). Chloromethyl-12-crown-4 2a and chloromethyl-15-crown-5 2b were prepared by refluxing 1 with equimolar amounts of C_5H_5N and $SOCl_2$ in C_6H_6 for 8 hours. The product was vacuum distilled; 2a bp. 94-99°C @ 0.25mm Hg, 80% yield and ^1H NMR δ 3.4-3.9(s); 2b bp. 113-125°C @ 0.25mm Hg, 80% yield and ^1H NMR δ 3.4-3.9(s). The chloromethyl crown ethers 2 in DMF were refluxed with potassium phthalimide for seven hours. The DMF was evaporated and the residue dissolved in 100ml of water. This mixture was extracted with $CHCl_3$; 3a yield 88 %, ^1H NMR δ 3.4-3.9(s 21 H), δ 7.6-7.9(d 4 H); 3b yield 90%, ^1H NMR δ 3.4-3.9(s 17 H), δ 7.6-7.9(D 4 H).



Alternatively, one can proceed to the amine by treatment of 1 with equimolar amounts of diethylazodicarboxylate, triphenylphosphine, phthalimide, and the appropriate hydroxymethyl crown ether in 300ml of freshly distilled THF. This mixture is allowed to react for 10 hours at room temperature. This reaction produced the same phthalimidomethyl crown ethers 3 in 70% yields with one less synthetic step.

The aminomethyl crown ether hydrochlorides were then prepared from the phthalimidomethyl crown ethers 3 by hydrolysis with hydrazine hydrate. This reaction employed a 15 fold excess of 100% hydrazine hydrate which was added to 20ml of methanol containing the phthalimidomethyl crown ether. This mixture was refluxed for 1 hour after which the methanol was removed and the residue refluxed with 20ml of concentrated HCl for 1 hour. The crystalline products were isolated; 4a m.p. 122-126°C, yield 85%, ^{1}H NMR δ 2.9-3.1 (m 2 H), δ 3.4-3.9 (s 15 H), $C_9H_{20}NO_4Cl$: 44.72%C, 8.29%H, 5.80%N, 14.70%Cl. Found 44.04%C, 8.28%H, 6.2%N, 14.80%Cl. 4b m.p. 163-168°C, yield 87%, ^{1}H NMR δ 2.9-3.1 (m 2 H), δ 3.4-3.9 (S 19 H), $C_{11}H_{24}NO_5Cl$: Calc. 46.20% C, 8.47%H, 4.90%N, 12.43%Cl. Found: 46.59%C, 8.28%H, 4.73%N, 12.11%Cl.

The aminomethyl crown ether hydrochlorides 4 were dissolved in 25ml of THF with an equimolar amount of NaOH. After 30 minutes, another equivalent of NaOH and an equimolar amount of the chlorinated chromophore was added. This mixture was allowed to react for 1 hour. After the THF was removed and water added to the residue, the chromogenic lariat crown ether was recovered by extraction with $CHCl_3$. Yellow powders were recovered in about 60% yields and were recrystallized in ethanol. Compound 5: m.p. 86-88°C, ^1H NMR δ 2.9-3.1 (m 2 H), δ 3.4-3.9 (s 15 H), δ 9.0-9.1 (s 2 H), δ 9.6-9.8 (s 1 H). $C_{17}H_{25}N_4O_{11}Cl$: Calc. 41.09%C, 5.07%H, 11.27%N. Found 41.81%C, 5.48%H, 11.28%N. Compound 6: m.p. 187-188°C, δ 2.9-3.1 (m 2 H), δ 3.4-3.9 (s 19 H), δ 9.0-9.1 (s 12 H), δ 9.6-9.8 (s 1 H). $C_{16}H_{2}0F_3N_3O_8$: Calc. 43.74%C, 4.58%H, 12.97%F, 9.56%N. Found 43.80%C, 4.61%H, 13.0%F, 9.43%N.

The behavior of chromogenic crown ether-alkali metal complexes can be described by their extraction constants(7). The extractions were performed using 5ml of 0.1-0.001M alkali chloride solution and 5ml Of 10^{-3}M chromogenic lariat crown ether in a 1M triethylamine in chloroform solution. Table 1 lists the pK_{ext} of 5 and 6 along with those of the benzocrown ether analogue of 7 for alkali metals. The alkyl chromogenic crown ethers (5 and 6) exhibited better overall extraction of alkali metals. This could be in

Table 1. pK EXTRACTION CONSTANTS FOR ALKALI METAL IONS[a]

	Li^+	Na^+	K^+	Rb^+	Cs^+
7[b]	---	~10	7.55	8.5	10.4
5[c]	7.4	6.19	5.86	6.5	7.64
6	7.1	7.41	6.1	8.0	7.3

a. $H_2O/CHCl_3$ (1.0 M triethylamine); b. from ref #7; c. calc for 1:2 metal-ligand complex with the exception of Li^+ using equations in ref #7.

part due to the removal of the benzene ring to give the molecule a more lipophilic character and better aqueous solubility. Also, the charge separation of the complexed ligand was smaller than in the case of 7. A tight ion-pair or chelate type interaction between the anion and metal should improve extraction. Although the improvement in extraction efficiency was beneficial, the reduced selectivity of the reagents could present problems in some samples such as blood or plasma. The alkyl reagents also differ in that Li^+ was extracted. It is interesting to note that the 15-crown-5 molecule (6) extracted Li^+ better than the 12-crown-4 chromophore 5. This may be due to the complexation of $Li^+ \cdot H_2O$ which has a larger diameter and would better meet the cavity/cation diameter constraints on complexation.

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