Synthesis of New Lariat Ethers Containing Polycyclic Phenols and Heterocyclic Aromatic Compound on Graphite Surface via Mannich Reaction

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Synthesis of novel lariat ethers containing polycyclic phenols and heterocyclic aromatic compound using graphite via Mannich reaction are herein described. For this purpose N-(methoxymethyl) azacrown ether was synthesized in nearly quantitative yield. The reaction of N-(methoxymethyl) azacrown ether with polycyclic phenols and heterocyclic aromatic compound was performed in 10-20 min in the presence of graphite. The graphite powder can be reused up to five times after simple washing with acetone.

Keywords: Azacrown ether, Mannich reaction, Graphite, Solvent less

INTRODUCTION

The Mannich reaction is one of the most useful synthetic methods for functionalizing azacrown ethers with proton-ionizable phenol groups [1]. Phenolic sidearms have been extensively used to enhance the stability of the macrocyclic ligand for selected metal ions. The sidearms are often composed of UV-active or fluorophoric proton-ionizable materials that allow an analytical determination of certain cations by spectrophotometric methods [2].

The present study is a continuation of our efforts to develop simple and general methods for the preparation of new lariat ethers. A key element of this research is the incorporation of additional proton-ionizable ligating units with chromophoric and fluorophoric abilities onto ion-selective macrocycles to provide changes in properties of the azacrown ether upon metal ion binding while maintaining or improving the ion selectivities of the macrocycle [3,4].

We have previously shown that new lariat ethers can be prepared by the reaction of azacrown ether, phenols and paraformaldehyde on solid supported (CaO and graphite) [5,6]. In continuation of our interest in Mannich base synthesis, in peculiar on solid supports, we now described new method to the aminoalkylation of polycyclic and heterocyclic aromatic compounds.

EXPERIMENTAL

Instrumentation, Analyses and Starting Materials

NMR spectra were recorded on a Bruker Avance DPX-250 (1H NMR 250 MHz and 13C NMR 62.9 MHz) spectrometer in pure deuterated solvents with tetramethylsilane as an internal standard. IR spectra were obtained using a Shimadzu FT-IR 8300 spectrophotometer. Mass spectra were determined on a Shimadzu GCMS-QP 1000 EX instruments at 70 or 20 ev. Melting points were determined in open capillary tubes in a Büchi-535 circulating oil melting point apparatus. The purity
Synthesis of 1,2-Phenylenedioxy Diacetic Acid (1)

To the mixture of catechol (11 g, 0.1 mol), and chloroacetic acid (28.4 g, 0.3 mol) at 90 °C on a water-bath, a mixture of NaOH 33% (W/V) (48 g, in 97.5 ml water) was added dropwise. The mixture was stirred at 90 °C for 2 h, and after cooling to room temperature, the solution was kept in ice bath. Then concentrated HCl was added dropwise. The mixture was stirred at 90 °C for 2 h, and after cooling to room temperature, the solution was kept in ice bath. Then concentrated HCl was added dropwise to the solution with stirring. The mixture was allowed to warm to room temperature and the solution was filtered and the white precipitates were washed with cold water. Crystallization of the residue from hot water afforded white solid of 1,2-phenylenedioxy diacetic acid (2.26 g, 0.01 mol), ethanol (75 ml) and concentrated sulfuric acid (0.1 ml) were refluxed with stirring for 12 h. The ethanol was removed in vaccum and the residue was dissolved in CHCl3 (100 ml). The organic layer was washed with saturated sodium bicarbonate solution (2 × 100 ml), and water (2 × 100 ml), dried (anhydrous calcium chloride) and CHCl3 was removed under reduced pressure to give 2 as a yellow oil (90% yield). IR (CH2Cl2): 750.3(m), 1068.5(m), 1186.1(s), 1595(s), 1759(s), 2981.7(w), 3066.6(m) cm⁻¹. ¹H NMR (CDCl3, 250 MHz): δ = 1.28 (t, 6H), 3.56 (q, 4H), 4.48 (s, 2H), 6.29-6.39 (m, 2H), 7.21-7.25 (m, 4H), 7.42 (s, 2H). ¹³C NMR (CDCl3, 62.9 MHz): δ = 14.5, 26.0, 112.7, 121.9, 146.4, 167.6. Mass m/z (%): 295(M++2, 0.9), 294 (M ++1, 2.9), 293 (M +, 5.4), 155(11.7), 147(13.9), 135(15.2), 123(100), 107(38.7), 81(52.7), 64(43.4), 43(25.7).

2-(2-Chloro-2-oxoethoxy)phenoxy]acetyl chloride (2a).

[2-(Carboxymethoxy)phenoxy]acetic acid (5.65 g, 0.025 mol) was heated in thionyl chloride (50 ml) for 4 h at 50-60 °C. The thionyl chloride was evaporated at low temperature and residue was recrystallized from petroleum ether to give 2a as a white cream solid in 85% (5.4 g) yield. m.p.: 161-162 °C. IR (KBr): 575(m), 756(s), 822(m), 1053(s), 1123(m), 1265(s), 1427(w), 1512(s), 1543(m), 1593(w), 1686(vs), 2843(m), 3414(s), 3450(s). Mass m/z (%): 295(M++2, 0.9), 294 (M ++1, 2.9), 293 (M +, 5.4), 225(50.6), 180(10.5), 167(17.3), 150(14.9), 121(17.7), 85(33.6), 69(78.7), 56(78.4), 43(100).

7-(Methoxymethyl)-5,6,7,8,9,10-Hexahydro-2H,11,13,4,7,10-benzodioxatriaza cyclo pentadec-3,11(4H,12H)-dione (3).

Azacrown ether (3) was obtained in quantitative yield. m.p.: 161-162 °C. IR (KBr): 575(m), 756(s), 822(m), 1053(s), 1123(m), 1265(s), 1427(w), 1512(s), 1543(m), 1593(w), 1686(vs), 2843(m), 3414(s). Mass m/z (%): 307(-OME, 0.3), 306(15.7), 305(7.0), 194(12.0), 293(2.6), 225(18.1), 180(10.5), 167(17.3), 150(14.9), 121(17.7), 85(33.6), 69(78.7), 56(78.4), 43(100).


Ethyl 2-[2-(Ethoxy-2-oxoethoxy)phenoxy]acetate (2b), 1,2-Phenylenedioxy diacetic acid (2.26 g, 0.01 mol), ethanol (75 ml) and concentrated sulfuric acid (0.1 ml) were refluxed with stirring for 12 h. The ethanol was removed in vaccum and the residue from hot water afforded white solid of azacrown ether 3 in 80% yield. Decomposed in 233 °C.

5,6,7,8,9,10-Hexahydro-2H-1,13,4,7,10-benzodioxatriaza cyclo pentadec-3,11(4H,12H)-dione (4).

Azacrown ether 4 (5 mmol) was added to solution of paraformaldehyde (6 mmol) in 75 ml of dry CH2OH. The mixture was stirred at room temperature for 24 h. CH2OH was evaporated under vacuum at 40 °C. N-(Methoxymethyl) azacrown ether 4 was obtained in quantitative yield. m.p.: 161-162 °C. IR (KBr): 575(m), 756(s), 822(m), 1053(s), 1123(m), 1265(s), 1427(w), 1512(s), 1543(m), 1593(w), 1686(vs), 2843(m), 3414(s), 3450(s). Mass m/z (%): 307(-OME, 0.3), 306(16.8), 305(7.0), 194(12.0), 293(2.6), 225(18.1), 180(10.5), 167(17.3), 150(14.9), 121(17.7), 85(33.6), 69(78.7), 56(78.4), 43(100).