

# Salicylaldehyde Derivatives as Building Blocks in the Synthesis of Useful Open Chain and Macrocyclic Crown Compounds

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The conversion of salicylaldehyde and its derivatives into new useful polyethers with bis-terminal functional groups, crown diamides and crown ethers is described.

Much attention has been directed to the supramolecular chemistry of crown compounds owing to their diverse applications in many fields. The introduction of an amide linkage in the polyether ring modifies the binding properties of crown compounds in favour of alkaline earth cations with respect to alkali metal ions.<sup>15–20</sup> Also, some polyether diamides and crown diamides showed interesting applications in cation selective electrodes.<sup>25a–f</sup> Moreover, open chain crown compounds with suitable end groups have interesting applications and some of them were shown to form stable crystalline complexes with various metal cations.<sup>26–29</sup>

In continuation of our recent<sup>20,45</sup> interest in synthesizing macrocyclic crown compounds and their precursors starting from salicylaldehyde and its derivatives, we describe here an easy access towards a number of polyethers with terminal bis-functional groups, crown diamides and crown ethers.

The starting bis(chloromethyl) derivatives **7a–f** and the naphtho analogue **15** were prepared from salicylaldehyde (**1**) *o*-hydroxybenzyl alcohols **9a–c** and 2-hydroxynaphthaldehyde (**11**) as outlined in Scheme A. Thus, alkylation of the appropriate salicylaldehyde derivatives **1**, **2a,b** with the appropriate dihalo compounds gave the corresponding bis(carbonyl)ethers, **5a–c** which underwent NaBH<sub>4</sub> reduction to give the corresponding bis(hydroxymethyl) derivatives **6a,d,b**, respectively. The latter were alternatively prepared from the appropriate *o*-hydroxybenzyl alcohol derivatives **9a–c**. The bis(hydroxymethyl)naphthyl derivative **14** was similarly prepared from 2-hydroxynaphthaldehyde. The bis(hydroxymethyl)ethers **6a–f**, **14** were converted into the corresponding bis(chloromethyl) derivatives **7a–f**, **15** upon treatment with SOCl<sub>2</sub> in chloroform.

Interestingly, we found that during attempted crystallization of **7a,h,j**, **15** from alcohols, alcoholysis took place and the corresponding bis(alkoxymethyl) derivatives **16c–e** and **21** were obtained, respectively. The syntheses of the bis(ethoxymethyl) derivatives **16a,b,f** were achieved upon treatment of **7a,b,k** with sodium ethoxide in refluxing ethanol after 24 h. This is due to the decreased reactivity caused by the electron withdrawing effect of the arylazo and chloro groups as shown in Scheme B.

Nucleophilic attack on **7a–k** with phenoxides, secondary amines and potassium formate gave the corresponding bis-(functionalized)polyether derivatives **18a–i**, **19a–e**, **20a–d**. Similarly, compound **18i** was converted to the diol **18g** then to the corresponding bis(chloromethyl) derivative **18k** which was reacted with **17d** to give the extended  $\alpha,\omega$ -bis(carbonyl)-ether **18l**.

Also, nucleophilic reaction of the appropriate bis-phenoxides **25a,b**, **28** with **7a–f** gave the corresponding macrocyclic 23,24-crown-diamides **26a–g** and 23-crown-6 derivatives **29a–c**.

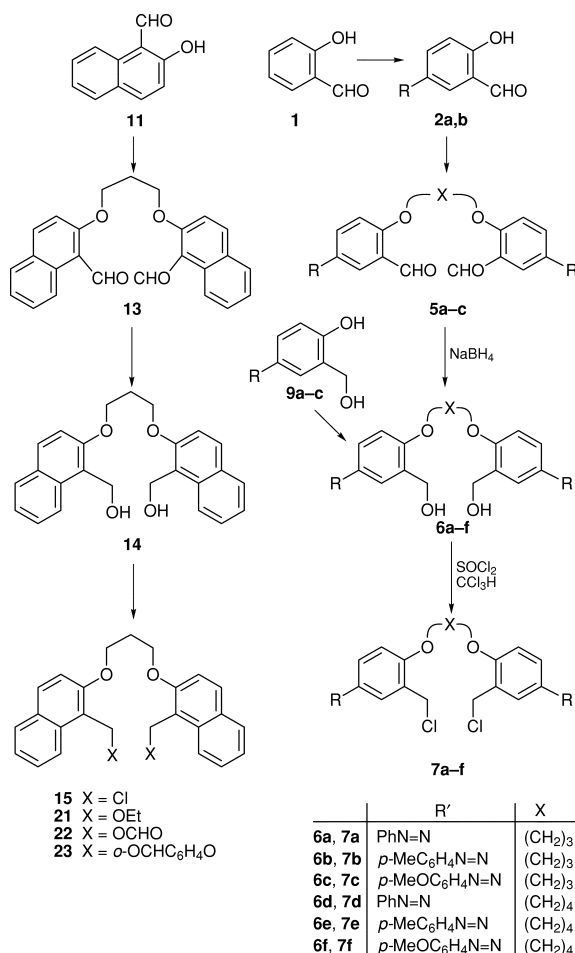
Techniques used: <sup>1</sup>H and <sup>13</sup>C NMR and MS

Schemes: 5    References: 50

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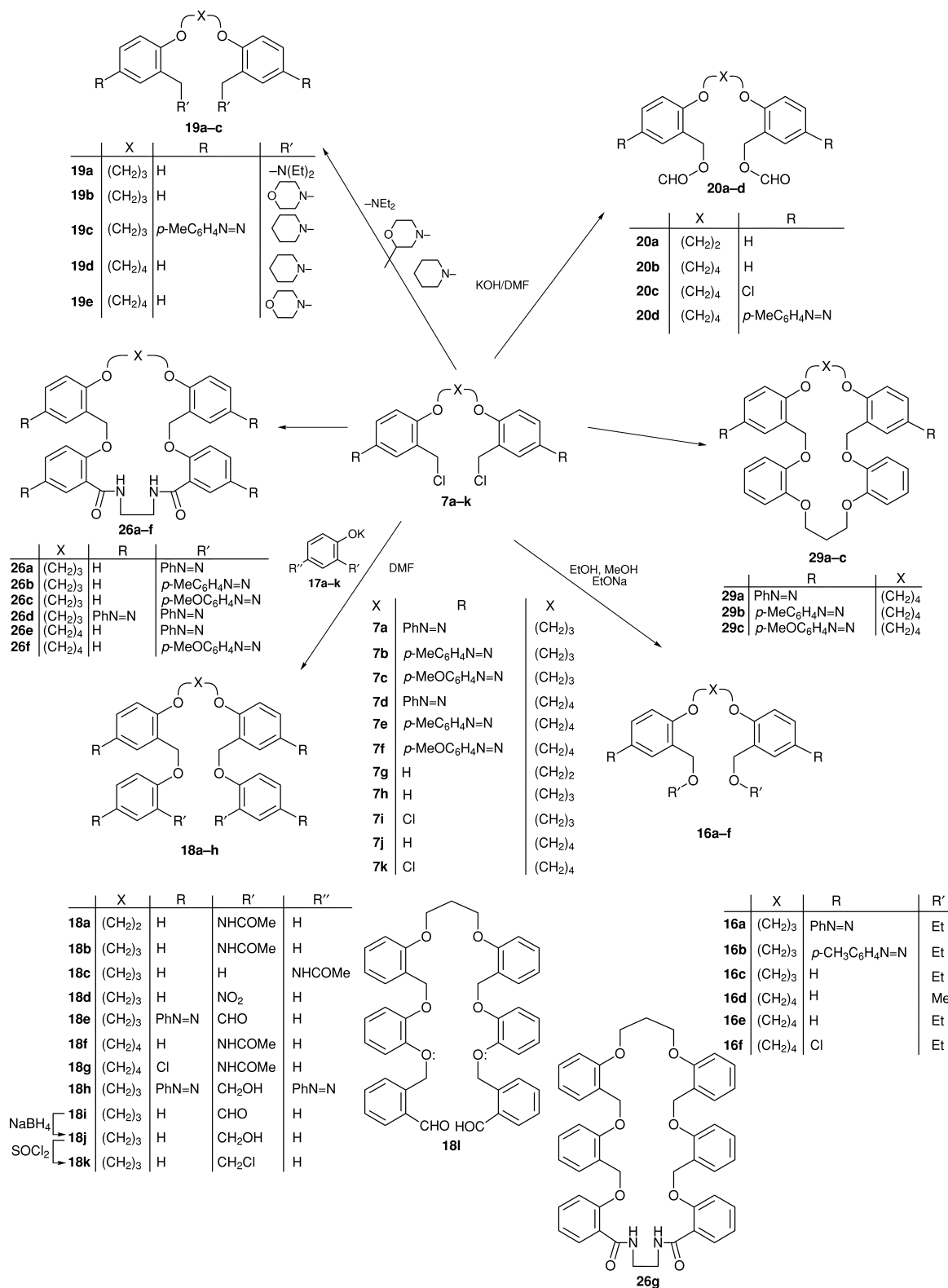
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Scheme A

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Scheme B

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