

## Facile Synthesis of 1,6-Bis(2-furyl)-2,5-bis(2-hydroxy-3-formyl-5-methylbenzyl)-2,5-diazahexane: a New Dinucleating Ligand

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**Abstract:** A convenient three-step preparation of the dinucleating ligand, 1,6-bis(2-furyl)-2,5-bis(2-hydroxy-3-formyl-5-methylbenzyl)-2,5-diazahexane (**3**) starting from 2,6-bis(hydroxymethyl)-4-methylphenol (**4**) is reported. Compound **4** was partially oxidized with preactivated manganese dioxide to form compound **5**, which was converted to 2-hydroxy-3-chloromethyl-5-ethylbenzaldehyde (**6**) with conc.HCl/EtOH. Compound **6** in turn reacted with N,N'-bis (2-furyl)-1,2-diaminoethane (**7**) in the presence of K<sub>2</sub>CO<sub>3</sub> in ethanol to give the title compound **3**. No protecting groups were required in the whole process and the conditions were mild.

**Keywords:** Synthesis, Dinucleating ligand, 2,5-Diazahexane derivative, Partial oxidation, Manganese dioxide.

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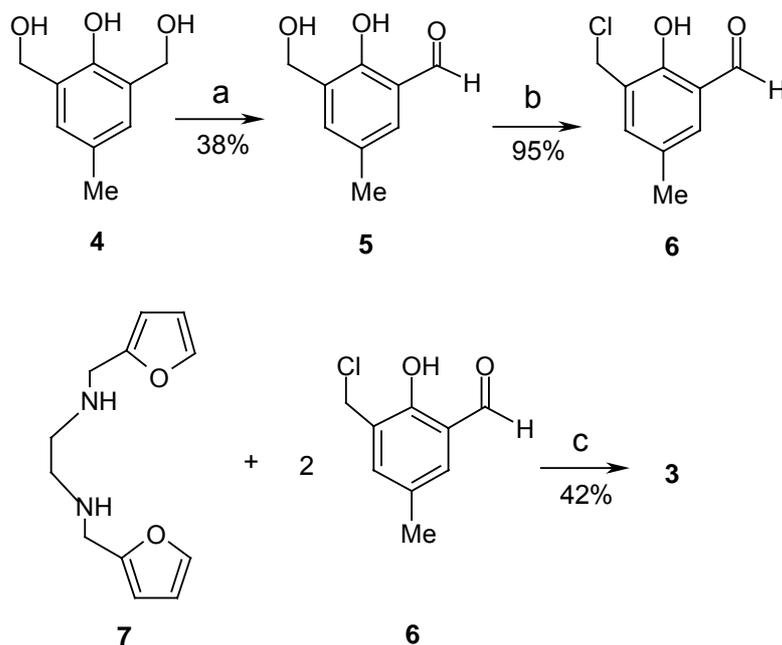


title compound **3** with a yield of 42%. Although the yields of the first and third steps are not as high as those previously reported, mainly because of the reactivity of the phenol derivatives **4** and **6**, the fact that no protecting groups were required makes this method quite attractive in view of the significant simplification of the overall sequence that it represents.

As noted, the previously reported preparation of compound **2**, similar in structure to **3**, involves nine steps [6]. Although the yields of each step in the earlier synthesis were relatively high (ranging from 60% to nearly 100%), thus highlighting both the effectiveness of the use of protecting groups and the elegance of the overall synthetic scheme, the final yield was not as high (about 22%) because of the large number of steps involved. Furthermore, the procedure was cumbersome, requiring some reagents which may be hard to obtain and expensive and some severe reaction conditions. The sequence now presented gave compound **3** in higher yield by a shorter route starting from a common starting material **4**, mainly due to the fact that protecting groups were not used (and consequently did not have to be removed). The reaction conditions were mild too.

In the  $^1\text{H-NMR}$  spectrum of compound **3** the signals belonging to the protons of the phenolic hydroxy groups were broad which showed that the protons were acidic, and suggesting formation of some O-H---N hydrogen bonds. This phenomenon has been observed in some similar systems [10,11] and will be further confirmed by single crystal X-ray diffraction which will be reported elsewhere.

### Scheme I



a).  $\text{MnO}_2/\text{CHCl}_3$ ; b). conc.HCl/EtOH; c).  $\text{K}_2\text{CO}_3/\text{EtOH}$

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## Experimental

### General

Melting points were determined using a WC-1 melting point apparatus.  $^1\text{H-NMR}$  spectra were recorded on Bruker DPX400 spectrometer using TMS as internal reference (chemical shifts reported in  $\delta$  ppm) and IR spectra on a Shimadzu IR435 infrared spectrometer ( $\nu_{\text{max}}$  in  $\text{cm}^{-1}$ ). Elemental analyses were performed on a Carlo-Erba 1106 C, H and N analyzer. 2,6-Bis(hydroxymethyl)-4-methylphenol (**4**) [8] and  $\text{N,N}'$ -bis(2-furyl)-1,2-diaminoethane (**7**) [9] were prepared according to the reported methods. Other reagents were all obtained commercially.  $\text{MnO}_2$  was kept in a muffle oven at a temperature of 300 to 320°C for 12 h until just prior to use.

### 2-Hydroxy-3-hydroxymethyl-5-methylbenzaldehyde (**5**).

This compound was synthesized by a modification of the previously reported method [7]. 2,6-Bis(hydroxymethyl)-4-methylphenol (**4**) (20g, 0.12mol) was placed in a 500 mL flask and stirred with a suspension of  $\text{MnO}_2$  (100g, 1.14mol) in  $\text{CHCl}_3$  (300mL) for 16 h at room temperature. The mixture was filtered and washed with  $\text{CHCl}_3$  for several times until the filtrate became colourless. The solvent was removed and the residue was recrystallized from  $\text{EtOH}/\text{H}_2\text{O}$  (1:3, v:v) to give yellowish needles (yield: 7.6g, 38%). M.p. 72-73° (lit. [7] 75-76°C). Anal. Calc for  $\text{C}_9\text{H}_{10}\text{O}_3$ : C: 65.05%, H: 6.07%; Found: C: 64.66%, H: 5.92%.

### 2-Hydroxy-3-chloromethyl-5-methylbenzaldehyde (**6**).

A solution of compound **5** (5 g, 0.03mol) in alcohol (25 mL) was added dropwise with stirring into a 250 mL flask containing conc.  $\text{HCl}$  (75 mL) placed in a 40°C water bath. The mixture was stirred for about 2 h, then filtered and washed with water until the pH was  $\sim 7$  to give 4.8g (95%) of white needles (m.p. 92-93°C). Anal. Calc. for  $\text{C}_9\text{H}_9\text{O}_2\text{Cl}$ : C: 58.55%, H: 4.91%; Found: C: 58.84%, H: 4.96%;  $^1\text{H-NMR}$  ( $\text{CDCl}_3/400\text{MHz}$ )  $\delta$ : 2.35 (s, 3H), 4.67 (s, 2H), 7.31 (d, 1H), 7.46 (d, 1H), 9.87 (s, 1H), 11.26 (s, 1H). IR (KBr): 1661, 1599, 1469, 875  $\text{cm}^{-1}$ .

### 1,6-Bis(2-furyl)-2,5-bis(2-hydroxy-3-formyl-5-methylbenzyl)-2,5-diazahexane (**3**).

Compound **6** (4.1 g, 0.022mol) in ethanol (80mL) and anhydrous  $\text{K}_2\text{CO}_3$  (5.5 g, 0.04mol) were placed in a 250mL flask, then compound **7** (2.2 g, 0.01mol) in ethanol (20mL) was added dropwise at room temperature. The mixture was stirred for 6 h at 40°C, then quenched and acidified to pH $\sim 2$  with 5% aqueous  $\text{HCl}$ . Most of the solvent was removed by concentration *in vacuo* and the residue was taken up in water (50mL). After filtration the filtrate was taken to pH $\sim 9$  with 1:1 ammonia/water thus forming a yellowish colloidal precipitate. After leaving the mixture standing overnight, the crude product was filtered and washed with water to pH $\sim 7$ . Recrystallization from 95% ethanol gave

compound **3** (2.17 g, 42%) as off-white needles (m.p. 109-110°C). Anal. Calc. for C<sub>30</sub>H<sub>32</sub>N<sub>2</sub>O<sub>6</sub>: C: 69.78%; H: 6.20%; N: 5.43%. Found: C: 69.59%; H: 6.45%; N: 5.44%. <sup>1</sup>H-NMR (CDCl<sub>3</sub>/400MHz) δ: 2.26 (s, 6H), 2.71 (s, 4H), 3.66 (s, 4H), 3.69 (s, 4H), 6.17 (d, 2H), 6.31 (s, 2H), 7.27 (d, 2H), 7.37 (s, 4H), 10.17 (s, 2H), 11.25 (br, 2H). IR (KBr): 2859, 1676, 1605, 1500, 1454, 874 cm<sup>-1</sup>.

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*Sample Availability:* Compounds **3**, **5**, **6**, **7** are available from MDPI and the authors

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