

Short Note

# 2-Hydroxy-3-octyloxybenzaldehyde

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**Abstract:** Herein, we report the chromatography-free synthesis of 2-hydroxy-3-octyloxybenzaldehyde by the alkylation of 2,3-dihydroxybenzaldehyde as a promising precursor for new SalEn-type complexes with transition metals. The structure of the product is elucidated by means of  $^1\text{H}$  and  $^{13}\text{C}$ -NMR spectra, high-resolution mass spectrometry with electrospray ionization (ESI-HRMS) and Fourier-transform infrared spectroscopy (FTIR).

**Keywords:** 2-hydroxy-3-octylbenzaldehyde; alkylation; SalEn precursor; Schiff base



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## 1. Introduction

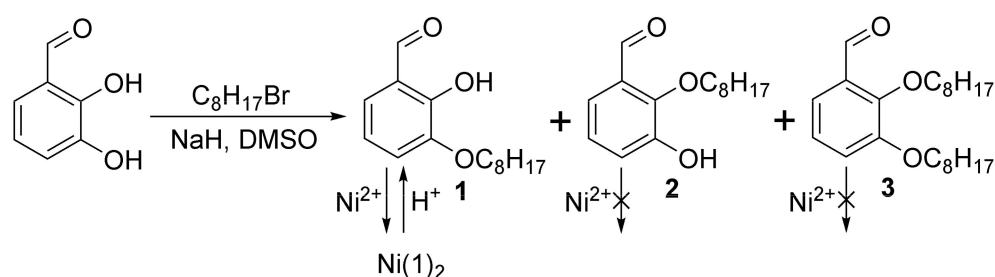
Polymeric complexes of transition metals with SalEn-type ligands represent a family of materials with a wide range of potential applications in energy storage [1–4], (photo) electrocatalysis [5–9], and chemical and biological sensing [10–12]. One of the key benefits of the SalEn-type coordination materials is the ability to fine tune the functional properties by varying the substituents of the ligand. Long alkyl chains attached to the ligand of NiSalen polymer may decrease the phase transition temperature of this material, which may allow the development of temperature-sensitive materials with low trigger temperature and increased electrochemical stability. NiSalen complexes are usually synthesized from the 3-substituted salicylaldehyde; thus, 2-hydroxy-3-octyloxybenzaldehyde was considered as a precursor for the preparation of NiSalEn-bearing octyl chains [13–16]. In addition, the 2-hydroxy-3-octyloxybenzaldehyde is a promising material in the field of biomedicine, since alkyl-substituted salicylic acids are actively used as selective ligands of the cannabinoid CB2 receptor and are also an intermediate product of salviandic acid, which has a therapeutic effect in coronary heart disease [17–19].

In the framework of the development of thermoresistant and temperature-switchable conductive polymers, here, we present the synthesis and characterization of a new NiSalen precursor, 2-hydroxy-3-octyloxybenzaldehyde, obtained by direct alkylation of 2,3-dihydroxybenzaldehyde with octyl bromide for further targeted modification of polymer structures. The alkylation of 2,3-dihydroxybenzaldehyde proceeds with low selectivity, resulting in a mixture of mono- and bis-alkylated products, which are usually separated chromatographically. To avoid the time- and material-consuming chromatographic separation, we developed an alternative isolation route via the template approach with the complexation of the target product. Ni (II) was chosen as a templating ion for its known ability for the complexation of the salicylaldehydes and the low solubility of the resulting complexes. The structure of the product was elucidated by means of  $^1\text{H}$  and  $^{13}\text{C}$ -NMR spectroscopy, high-resolution mass spectrometry with electrospray ionization (ESI-HRMS) and Fourier-transform infrared spectroscopy (FTIR).

## 2. Results

In this study, 2-hydroxy-3-octyloxybenzaldehyde was obtained by alkylation of 2,3-dihydroxybenzaldehyde with octyl bromide using a modified method [17]. The synthetic route

for the target compound is outlined in Scheme 1. The alkylation of 2,3-dihydroxybenzaldehyde affords a mixture of 3- and 2-alkylated isomers, **1** and **2**, respectively, along with 2,3-dialkylated product **3**, which are normally separated using flash chromatography. NMR yields of **1** and **3** in crude reaction mixture were found to be 18% and 21%, respectively (Figure S5). However, the separation of these products with close  $R_f$  values is quite difficult, especially for large loadings. To avoid the chromatographic separation, we proposed a chemical method for the isolation of product **1** based on differences in reactivity. Namely, only product **1** is able to form a stable complex with  $\text{Ni}^{2+}$  due to the presence of salicylaldehyde's chelating functionality, while **2** and **3** are inert to this ion. Treatment of the reaction mixture with nickel acetate after simple workup led to the precipitation of the greenish-yellow Ni complex of **1**. The free ligand **1** was then released from the isolated complex by hydrolysis with 20% aqueous  $\text{H}_2\text{SO}_4$ .



**Scheme 1.** Synthesis of **1** and its isolation via the nickel complex.

The  $^1\text{H}$ -NMR spectrum of the product (Figure S1) shows a set of 2-hydroxy-3-octylbenzaldehyde-related signals: phenolic and aldehyde singlets at 10.99 and 9.92 ppm, respectively, a typical pattern of 1,2,3-trisubstituted aromatics with two doublets at 7.17 and 7.12 ppm, along with a triplet at 6.94 ppm. The alkoxy group chain is represented by a triplet at 4.05, attributed to the  $\alpha$ -methylene group, a pseudo-triplet at 1.86, a large multiplet around 1.60–1.20 and a methyl triplet at 0.89.

The  $^{13}\text{C}$ -NMR spectrum (Figure S2) contains a complete set of signals: a carbonyl at 196.6, an aryl set at 152.1, 147.9, 124.7, 121.1, 119.7, 119.6 and eight signals from the octyloxy group at 69.7, 31.9, 29.5, 29.3, 29.3, 26.1, 22.8 and 14.2. The exact mass of the  $[\text{M} - \text{H}]^-$  ion, determined by ESI-HRMS in negative mode (Figure S3), was found to be 249.1495 (249.1496 as calcd. for  $\text{C}_{15}\text{H}_{21}\text{O}_3^-$ ). The FTIR spectrum recorded in KBr (Figure S4) contained a characteristic  $\text{C} = \text{O}$  vibration at  $1659\text{ cm}^{-1}$ .

Herein, we report the direct alkylation of 2,3-dihydroxybenzaldehyde with octyl bromide, which affords a valuable precursor for new SalEn-type complexes with transition metals. The resulting compound may be used further in electrocatalytic and photoelectrochemical reactions and also act as a promising material for creating energy storage devices.

### 3. Materials and Methods

#### 3.1. General Considerations

All chemicals used in the synthesis were of “reagent-grade” purity and were purchased from local suppliers. Moreover, 2,3-dihydroxybenzaldehyde was sublimed twice at 1 Pa prior to use. DMSO was distilled over  $\text{CaH}_2$  and stored over  $4\text{ \AA}$  molecular sieves prior to use. The progression of the reaction was monitored by TLC, using  $\text{SiO}_2$  sheets with a fluorescent indicator F254. The Fourier-transform infrared spectra were recorded on a Shimadzu IRAffinity-1 FTIR spectrophotometer (Shimadzu Europa GmbH, Kyoto, Japan) in KBr pellets. The  $^1\text{H}$  and  $^{13}\text{C}$ -NMR spectra were acquired on a Bruker Avance 400 spectrometer (Bruker Analytische Messtechnik GmbH, Rheinstetten, Germany) at 400 and 101 MHz, respectively, using  $\text{CDCl}_3$  as the solvent. The HRMS spectrum was recorded using electrospray ionization on a Bruker microTOF apparatus (Bruker Analytische Messtechnik GmbH, Rheinstetten, Germany) in negative mode. All the spectra of the products can be found in the Supplementary Materials.

### 3.2. Synthesis of 2-Hydroxy-3-octyloxybenzaldehyde

A suspension of NaH (60% dispersion in mineral oil; 0.3 g, 12.5 mmol) in dry DMSO (12.5 mL) was stirred in a cold water bath for 15 min under argon. To the suspension, a solution of 2,3-dihydroxybenzaldehyde (0.69 g, 5 mmol) in dry DMSO (2.5 mL) was added dropwise and the mixture was stirred for another 1 h. Then, 1-bromooctane (0.97 g, 5 mmol) was added in one portion; the color of the solution changed from brown to dark green. The reaction was stirred overnight at room temperature, poured into cold water (60 mL), acidified with 1 M HCl to pH 3 and extracted with petroleum ether. The organic phase was extracted with 1% sodium hydroxide; the aqueous phase was acidified with 1 M HCl to pH 3, then extracted again with petroleum ether, dried over Na<sub>2</sub>SO<sub>4</sub> and evaporated in vacuo.

The resulting residue (0.7 g) was dissolved in EtOH (5 mL); then, a solution of Ni(OAc)<sub>2</sub>·4H<sub>2</sub>O (200 mg, 0.81 mmol) in warm EtOH (~2 mL) was added. The mixture was stirred for 30 min at 80 °C. The resulting yellow–green precipitate was filtered, dried and treated with 20% aqueous H<sub>2</sub>SO<sub>4</sub> with the addition of EtOH (2 mL). The resulting mixture was extracted with PE. The organic layer was washed with 1 M NaHCO<sub>3</sub> (10 mL), dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>, evaporated, dried in vacuo and crystallized in a fridge. The yield was 0.136 g (10.9%).

<sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>) δ, ppm: 10.99 (s, 1H), 9.92 (s, 1H), 7.17 (dd, *J* = 7.9, 1.5 Hz, 1H), 7.11 (dd, *J* = 8.0, 1.5 Hz, 1H), 6.94 (t, *J* = 7.9 Hz, 1H), 4.05 (t, *J* = 6.7 Hz, 2H), 1.85 (t, *J* = 14.8 Hz, 2H), 1.6–1.2 (m, 10H), 0.89 (t, 3H). <sup>13</sup>C-NMR (101 MHz, CDCl<sub>3</sub>) δ, ppm: 196.6, 152.1, 147.9, 124.7, 121.1, 119.7, 119.6, 69.7, 31.9, 29.5, 29.3, 26.1, 22.8, 14.2. FTIR (KBr)  $\bar{\nu}$ , cm<sup>-1</sup>: 2800–3000 (C–H, O–H), 1659 (C = O). HRMS (ESI) *m/z* [M – H]<sup>-</sup> calcd. for C<sub>15</sub>H<sub>21</sub>O<sub>3</sub><sup>-</sup> 249.1496, found 249.1495.

**Supplementary Materials:** The following are available online: <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectral analysis, HRMS and FTIR data for 2-hydroxy-3-octylbenzaldehyde and <sup>1</sup>H-NMR spectrum of the crude reaction mixture. Figure S1: <sup>1</sup>H-NMR spectrum of **1**, CDCl<sub>3</sub>, 400 MHz. Figure S2: <sup>13</sup>C-NMR spectrum of **1**, CDCl<sub>3</sub>, 400 MHz. Figure S3: ESI-HRMS spectrum of **1**. Figure S4: FTIR spectrum of **1**, KBr. Figure S5: <sup>1</sup>H NMR spectrum of reaction mixture with C<sub>2</sub>H<sub>4</sub>Br<sub>2</sub> additive, CDCl<sub>3</sub>, 400 MHz.

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**Conflicts of Interest:** The authors declare no conflict of interest. The funders had no role in the design of the study; in the collection, analyses, or interpretation of data; in the writing of the manuscript, or in the decision to publish the results.

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