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Simple synthesis of non-symmetric 1,4-dialkoxybenzenes *via* 4-alkoxyphenols

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Abstract: A three steps synthesis of non-symmetric 1,4-dialkoxybenzenes starting from 4-hydroxybenzaldehydes was described. At first step 4-alkoxyphneols were alkylated to give 4-alkoxybenzaldehydes. At the second step 4-alkoxybenzaldehydes were submitted to a Baeyer-Villiger oxidation with 30% H_2O_2 to afford 4-alkoxyphenols. At the last step 4-alkoxyphenols were secondly alkylated to give the title compounds.

Keywords: 4-alkoxyphenols**;** 1,4-dialkoxybenzenes**;** monomer; PPV; synthesis.

1. Introduction

Both 4-alkoxyphenols and 1,4-dialkoxybenzenes are important raw materials for the industry. Several simple 4-alkoxyphenols, for instance 4-methoxyphenol and 4-benzyloxyphenol, are of high interest because of their biological activity[1]. For example, 4-methoxyphenol serves as an antioxidant, a polymerization inhibitor, a stabilizer of photosensitive materials, or as an intermediate in the pharmaceutical industry.[1] It is also an active ingredient in topical drugs used for skin depigmentation (Mequinol).[2] Also 4-benzyloxyphenol is used in cosmetics and medicine (Monobenzone)[3] or as a starting material for syntheses of new azo dyes for polyesters.[4]

Symmetrical 1,4-dialkoxybenzenes (e.g., 1,4-dimethoxy and 1,4-diethoxy) are mainly used as dyestuff intermediates and pharmaceutical intermediates as well as in production of perfumes and soaps.[5] 1,4-Dialkoxybenzenes are also widely used as starting materials in synthesis of conducting polymers characterized by low band gaps.[6,7] It was discovered already twenty five years ago that polymers having a conjugated system of multiple bonds can find applications in light emitting devices.[8-13] That discovery stimulated intensive research on PPV-type (Poly-Phenylene-Vinylene) polymers. Syntheses and properties of such polymers have been still widely investigated[14-23] as active laser components, photovoltaic devices, light emitters, transistors, photodetectors and photodiodes. As a result of easy preparation

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of symmetric 1,4-dialkoxybenzenes through exhaustive *O*-alkylation of hydroquinone, overwhelming number of PPV-type polymers contain core of such type. The analogue polymers bearing two different alkyl substituents are much rarer since the access to the corresponding non-symmetric 1,4-dialkoxybenzenes is still difficult.

Effective mono-*O*-alkylation of hydroquinone is limited to the synthesis of 4-methoxy, 4-ethoxy- and 4-benzyloxyphenol. 4-Alkoxyphenols with longer alkyl chain and the same non-symmetric 1,4-dialkoxybenzenes with two longer but different alkyl chains are rather difficult to obtain. Recently interest on PPV-type and PPP-type Poly(*P*-Phenylene) polymers based on non-symmetric 1,4-dialkoxybenzenes has been significantly increasing. [19, 21, 23-30] Some polymers based on 1-alkoxy-4-methoxybenzene are already commercially available e. g., MEH-PPV, MDMO-PPV and their analogues depicted in Fig. 1.

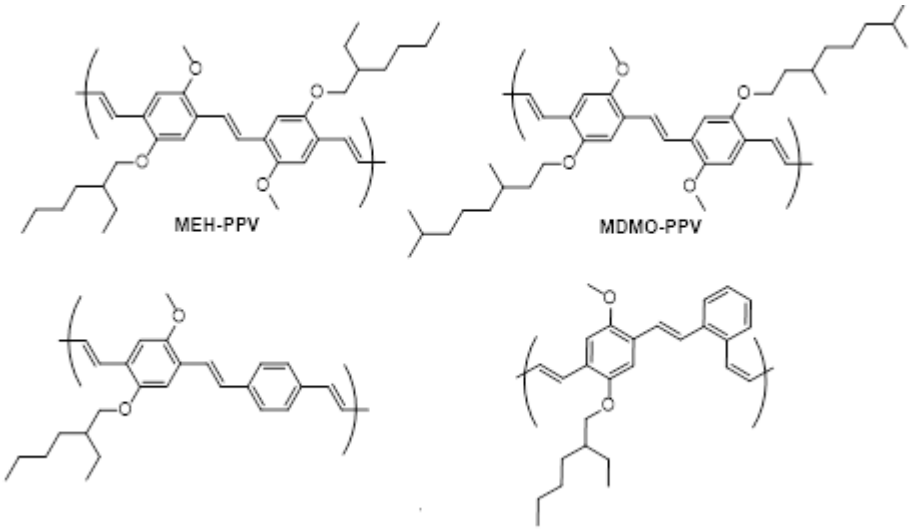


Figure 1. Non-symmetrical 1,4-dialkoxybenzene derived PPV-polymers

Similar polymers with 1,4-dialkoxybenzene core containing two different longer alkoxy substituents have been synthesized only few times due to difficulties in preparing starting dialkoxybenzenes.

Many of PPV-type polymers comprises electron rich 1,4-dialkoxybenzene core connected *via* a carbon-carbon double bond with five-membered heteroarenes such as furan,[29] tiophene,[15-18] selenophene[20] or even tellurophene.[30] Such polymers are preferably obtained by using electrochemical methods. According to our best knowledge, electro-polymerization of monomers containing non-symmetrical 1,4-dialkoxybenzene and five-membered heteroarene fragments connected by C=C bonds has not been investigated since the pioneering works of Lacaze and co-workers published in 1991[31] though through the next twenty five years that paper was cited over a dozen times. The mentioned substitution pattern provides sufficient solubility of polymers, while diversity of alkoxy groups in a starting monomer improves electropolymerization process by reducing the negative luminescence quenching of polymers, which may reasoned by too strong intermolecular π-π interactions in too orderly solid layers of electropolymerization products. As already mentioned, the main problem that limits broaden electrochemical studies on PPV-type polymers with broken symmetry of the central core is lack of general, efficient and simple method for synthesis of non-symmetrical 1,4-dialkoxybenzenes containing both longer alkyl chains.

In general, two possible approaches to the preparation of non-symmetrical 1,4-dialkoxybenzenes **2** can be considered as outlined in Figure 2. In both cases 4-alkoxyphenol **1** is an intermediate.

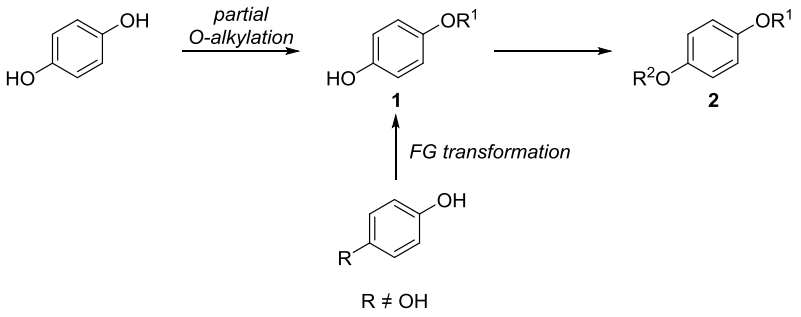


Figure 2. Possible strategies for synthesis of non-symmetrical 1,4-dialkoxybenzenes **2**

Partial *O*-alkylation of hydroquinone, realized *via* Williamson reaction allows, in practice, for effective preparation of *O*-methoxy, *O*-ethoxy or *O*-benzyloxyphenols only. *O*-Alkylation of hydroquinone using longer-chain alkyl halides provides predominately symmetrical 1,4-dialkoxybenzenes and unreacted hydroquinone along with traces of the 4-alkoxyphenols. Yields of 4-alkoxyphenols decrease with the increase of length of an alkylation agent as well as with increase of its bond order due to competitive elimination reaction. The complementary to Williamson reaction is *O*-alkylation of hydroquinone with alcohols under acidic conditions exemplified by high yielding procedures for preparation of 4-methoxyphenol with the use of zeolites[32] or heteropolyacids on montmorillonite.[33] An application of these procedures for synthesis of 4-alkoxyphenols with longer alkyl chain have not been checked. The recently published[34] preparation of 4-methoxyphenol, through the alkylation of hydroquinone with methanol in the presence of small amounts of sodium nitrate(III) and sulfuric acid is also suitable for hydroquinone *O*-alkylation with other alcohols. Unfortunately, the introduction of longer alkyl groups requires a significant elongation of reaction time and may decrease of product yield. For example, the replacement of methanol by butanol as an alkylating agent of hydroquinone, resulted in elongation of the reaction time seventy two times.[34] Preparation of 4-alkoxyphenols with alkyl chains longer than butyl by this method was not described.

The alternate approach to the synthesis of 4-alkoxyphenols and non-symmetrical 1,4-dialkoxybenzenes assumes use of phenol bearing substituent at the C-4 that differ from the hydroxyl group and can be readily converted into hydroxyl group at the further synthesis steps. For example, 4-alkoxyphenols may be obtained from 4-acyloxyphenols[35, 36] (Figure 3). Next, 4-acyloxyphenols can be subjected *O*-alkylation reaction to provide 1-acyloxy-4-alkoxybenzenes which, after hydrolysis, would give desired 4-alkoxyphenols (Figure 3).

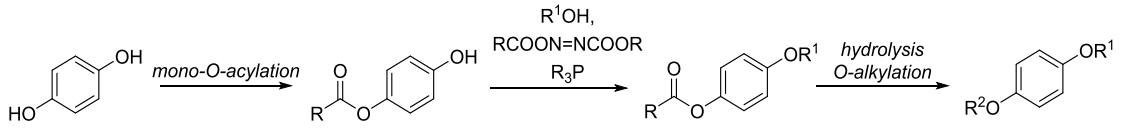


Figure 3. Synthesis of non-symmetrical 1,4-dialkoxybenzenes *via* 4-acyloxyphenols

Since 4-acyloxyphenols are sensitive to acids and bases, it is more suitable to perform the *O*-alkylation process under Mitsunobu conditions[37] in polar organic solvents e.g. in dimethylformamide. Although, Mitsunobu reaction proceeds under favorable mild and inert conditions[37], its considerable disadvantage is the high cost of reagents, low atom-economy and necessity of removal of large amount of by-products such as phosphine oxide and dicarboxylhydrazine derivatives. These reasons, makes preparation of 4-alkoxyphenols with the use of Mitsunobu strategy unattractive for industry, therefore it is limited to special cases.

For example, Merlo and co-workers[35] applied this approach to preparation of 1-benzyloxy-4-(2'-methyl-1'-butyloxy)benzene.

Interesting solution could be use of 4-aminophenol, as an easily available starting compound. Selective acylation of the amino group, followed by *O*-alkylation and hydrolysis should provide the corresponding 4-alkoxyaniline. The diazotization of the latter one with subsequent denitrification of the forming diazonium salt would result in formation of desired 4-alkoxyphenol (Figure 4).

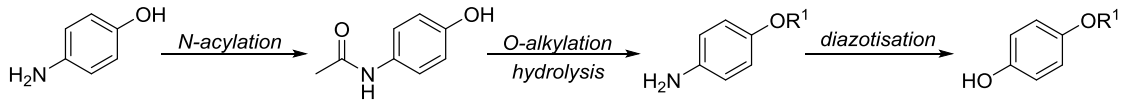
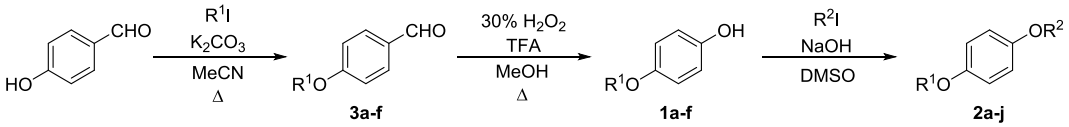


Figure 4. Synthesis of 4-alkoxyphenols from 4-aminophenols

In practice, only the steps of *O*-acetylation and *O*-alkylation of the resulting 4-hydroxyacetanilide occur with high yields, as it was demonstrated by Glatzhofer and co-workers[38] who converted 4-methoxyacetanilide directly to 4-methoxyphenyl acetate. We tested the approach presented in Figure 4, however, low yields and difficulties in purification of intermediates practically excluded 4-aminophenol as a starting reagent in the general synthesis of 4-alkoxyphenols containing longer alkyl substituents. In this manuscript, we present a new protocol for efficient preparation of asymmetric 1,4-dialkoxyphenols.

2. Results and discussion

During the search of alternative methods for preparation of 4-alkoxyphenols and further non-symmetrical 1,4-dialkoxybenzenes, we considered use of 4-hydroxybenzaldehyde as a starting material (Figure 5). It was assumed that it *O*-alkylation followed by Baeyer-Villiger rearrangement[39] should provide 4-alkoxyphenyl formates easily hydrolysable to desired 4-alkoxyphenols (**1**), direct precursors of target non-symmetrical 1,4-dialkoxybenzenes (**2**) (Figure 5).



1a R^1 = Et, 91%
1b R^1 = *i*-Pr, 83%
1c R^1 = *n*-Bu, 70%
1d R^1 = *n*-C_6H_{13}, 65%
1e R^1 = *n*-C_8H_{17}, 65%
1f R^1 = *n*-$C_{12}H_{25}$, 60%

2a R^1= Et, R^2 = *i*-Pr, 91% (from **1a**), 77% (from **1b**)
2b R^1= *i*-Pr, R^2 = *n*-Bu, 86%
2c R^1= *n*-Bu, R^2 = *n*-C_8H_{17}, 81% (from **1c**), 79% (from **1e**)
2d R^1= *n*-C_6H_{13}, R^2 = *n*-C_8H_{17}, 80% (from **1d**), 68% (form **1e**)
2e R^1= *n*-C_8H_{13}, R^2 = *n*-Pr, 85%
2f R^1= *n*-$C_{12}H_{25}$, R^2 = *n*-C_6H_{13}, 87% (from **1d**), 87% (form **1f**)
2g R^1= Et, R^2 = *n*-C_6H_{13}, 90%
2h R^1= Et, R^2 = *n*-C_8H_{17}, 85% (from **1a**), 95% (from **1e**)
2i R^1= Et, R^2 = *n*-$C_{12}H_{25}$, 92%
2j R^1= *n*-C_8H_{13}, R^2 = *i*-Pr, 47%

Figure 5. Synthesis of 4-alkoxyphenols and non-symmetrical 1,4-dialkoxybenzenes from 4-hydroxybenzaldehyde

Initial *O*-alkylation of 4-hydroxybenzaldehyde was performed by using a slightly modified procedure reported by Brun and Etemad-Moghadam.[40] Less active bromides were replaced by iodides, what led to higher yields of products **3** (Figure 5). The transformation of aldehydes **3a-f** into the corresponding phenols **1a-f** *via* Baeyer-Villiger reaction was conducted by using modified procedure reported by Matsumoto and co-workers.[41] The selected procedure

of Baeyer-Villiger rearrangement is particularly attractive since under those conditions also the subsequent acid hydrolysis of intermediate 4-alkoxyphenyl formate proceeds to afford 4-alkoxyphenols. For purifications of 4-alkoxyphenols with a longer alkyl chain (**1c-f**), a simple and rapid precipitation of the products by introducing the post-reaction mixture into ice water was applied instead of the chromatography. The obtained solid 4-alkoxyphenols **1** were then recrystallized from cyclohexane. Five 4-alkoxyphenols with unbranched alkyl groups (**1a**, **1c-f**) and 4-isopropyloxyphenol (**1b**) were synthesized in yields of 60-90% (Figure 5). The resulting 4-alkoxyphenols (**1a-f**) were *O*-alkylated with alkyl iodides in DMSO in the presence of NaOH following the procedure reported by Johnston and Rose.[42] Advantage of this procedure is no need for anhydrous solvent. We have obtained ten 1,4-dialkoxybenzenes **2a-j** with yields of 65-95%, eight of which hitherto not described in the literature **2a-e, 2h-j** (compounds **2f** and **2g** are known and were described in the literature[46, 47]). Five compounds, namely, 1-ethoxy-4-isopropyloxybenzene (**2a**), 1-butyloxy-4-octyloxybenzene (**2c**), 1-hexyloxy-4-octyloxybenzene (**2d**), 1-dodecyloxy-4-hexyloxybenzene (**2f**), and 1-ethoxy-4-octyloxybenzene (**2h**), were prepared by two ways which differed in the order of introduction of alkyl substituents. Both the reactions led to products with identical properties.

3. Experimental Section

The melting points (not corrected) were determined with a Boetius HMK apparatus or with an open capillary. ^{1}H and ^{13}C spectra were recorded on a Varian XL-300 (300 MHz for ^{1}H and 75 MHz for ^{13}C) in DMSO-d_6 or $CDCl_3$ and with TMS as the internal reference. The chemical shifts (δ) are reported in parts per million and the coupling constants (*J*) in hertz. HRMS (ESI) spectra were recorded on a Xevo G2 QTof (Waters Corporation) spectrometer. Elemental analyses (EA) using a 2400 Series II CHNS/O Elemental Analyzer were performed only for new non-symmetric dialkoxybenzenes; other purified compounds were characterized by m.p., NMR and sometimes IR spectra.

3.1 Synthesis of 4-alkoxyphenols from 4-alkoxybenzaldehydes, general procedure:

To a stirred solution of 4-alkoxybenzaldehyde (10.0 mmol) in methanol (15 mL) a solution of 30% H_2O_2 (4.6 mL, 1.53 g, 45.0 mmol) was added dropwise. Next, trifluoroacetic acid (0.11 g, 1.0 mmol) was added slowly. The reaction mixture was heated then to 40-45 ^{o}C and maintained that temperature for 4 hours. The progress of the reaction was monitored by thin layer chromatography. Then the post-reaction mixture was cooled to room temperature and poured into water (100 mL). An excess of hydrogen peroxide was destroyed by sodium bisulfite and the solution was neutralized with sodium bicarbonate. The neutral solution was extracted with diethyl ether (3×25 mL). The combined extracts were dried over anhydrous $MgSO_4$ and then solvents were evaporated using a rotatory evaporator. The residue was chromatographed on silica gel by using chloroform as the eluent. The obtained solid products were additionally recrystallized from a mixture of hexane-dichloromethane by slow evaporation of the solvents (In case of **1c**, **1d** and **1e** after pouring the mixture into water, the precipitate was collected by filtration, dried over P_2O_5 and crystallized from cyclohexane).

3.1.1. 4-Ethyloxyphenol **(1a):** Yield 91%, white needles, m.p. 64-66 °C (lit.[43] 64-67 ^{o}C); ^{1}H NMR δ_H 6.68-6.74 (m, 4H), 5.33 (br. s, 1H), 3.97 (q, $^{3}J_{HH}$ 7.0 Hz, 2H), 1.38 (t, $^{3}J_{HH}$ 7.0 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 153.0, 149.6, 116.2, 115.8, 64.4, 15.0.

3.1.2. 4-Isopropopyloxyphenol **(1b)**: Yield 83%, thick yellowish liquid (commercial, but no data available in the literature except lit.[44] b.p. 117 ^{o}C/4 mm Hg). ^{1}H NMR δ_H 6.68-6.74 (m, 4H), 4.90 (br. s, 1H), 4.40 (sept., $^{3}J_{HH}$ 6.0 Hz, 1H), 1.30 (d, $^{3}J_{HH}$ 6.0 Hz, 6H). ^{13}C NMR δ_C 152.1, 150.0, 118.1, 116.4, 71.6, 22.4.

3.1.3. 4-Butyloxyphenol **(1c):** Yield 70%, white solid flakes, m. p. 63.5-64.0 °C (lit.[44] 63.0-64.0 °C); ^{1}H NMR δ_H 6.70-6.78 (m, 4H), 4.64 (br. s, 1H), 3.90 (t, $^{3}J_{HH}$ 6.6 Hz, 2H), 1.70-1.80

(m, 2H), 1.42-1.52 (m, 2H), 0.96 (t, $^3J_{HH}$ 7.3 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 153.3, 149.6, 116.2, 115.8, 68.7, 31.5, 19.3, 14.0.

3.1.4. 4-Hexyloxyphenol **(1d):** Yield 65%, white solid flakes, m. p. 44.5-46.5 °C (lit.[44] 44 °C); ^{1}H NMR δ_H 6.73-6.77 (m, 4H), 4.74 (br. s, 1H), 3.89 (t, $^3J_{HH}$ 6.6 Hz, 2H), 1.68-1.81 (m, 2H), 1.25-1.51 (m, 6H), 0.90 (t, $^3J_{HH}$ 6.9 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 153.4, 149.5, 116.1, 115.8, 68.9, 31.7, 29.5, 25.9, 22.7, 14.2.

3.1.5. 4-Octyloxyphenol **(1e):** Yield 65%, white solid flakes, m. p. 59.5-60.5 °C (lit.[44] 60.0-61.0 °C); ^{1}H NMR δ_H 6.72-6.79 (m, 4H), 4.43 (br. s, 1H), 3.89 (t, $^3J_{HH}$ 6.6 Hz, 2H), 1.71-1.78 (m, 2H), 1.15-1.50 (m, 10H), 0.84-0.93 (m, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 153.2, 149.3, 116.0, 115.7, 68.8, 31.8, 29.4, 29.2, 26.0, 22.6, 14.1.

3.1.6. 4-Dodecyloxyphenol **(1f):** Yield 60%, white solid, m. p. 73-75 °C (lit.[45] 74-75 °C); ^{1}H NMR δ_H 6.73-6.80 (m, 4H), 4.62 (br. s, 1H), 3.89 (t, $^3J_{HH}$ 6.6 Hz, 2H), 1.68-1.81 (m, 2H), 1.20-1.52 (m, 18H), 0.88 (t, $^3J_{HH}$ 6.7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ: 153.32, 149.26, 115.95, 115.58, 68.71, 31.90, 29.66, 29.63, 29.59, 29.56, 29.42, 29.36, 29.33, 26.05, 22.67, 14.10.

3.2. Synthesis of non-symmetrical 1,4-dialkoxybenzenes. General procedure:
4-Alkoxyphenol (5.0 mmol) and powdered sodium hydroxide (0.3 g, 7.5 mmol) were mixed in DMSO (20 mL) under nitrogen atmosphere for 10 min. Then alkyl iodide (5.3 mmol) was added dropwise with stirring. Precipitations were observed during the course of reaction. The stirring was continued for 1-5 h; the progress of the reaction was monitored by TLC. Water (70 mL) was added to the reaction mixture and then precipitated solids were separated by filtration, rinsed with water and dried on air. Crude products were chromatographed on silica gel using hexane and then dichloromethane as eluents. In a case when oil, instead of a solid, separated after the addition of water, post-reaction mixture was extracted with hexane (3x20 mL), combined extracts were rinsed with water and dried over $MgSO_4$. A resulting solution was evaporated and the residue was flash-chromatographed using the same eluents as before.

3.2.1. 1-Ethoxy-4-isopropyloxybenzene **(2a):** Yield 91% (starting from **1a**) and 77% (starting from **1b**), yellowish oil. ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.71 (s, 4H), 4.29 (sept., $^3J_{HH}$ 6.0 Hz, 1H), 3.84 (q, $^3J_{HH}$ 7.0 Hz, 2H), 1.27 (t, $^3J_{HH}$ 7.0 Hz, 3H), 1.19 (d, $^3J_{HH}$ 6.0 Hz, 6H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 153.0, 151.7, 117.2, 115.2, 70.6, 63.7, 22.0, 14.8. HRMS (ESI) Calc. for $C_{11}H_{16}O_2$+H^+ *m/z* 181.1223; Found *m/z* 181.1219

3.2.2. 1-Butyloxy-4-isopropyloxybenzene **(2b):** Yield 86% (starting from **1b**), yellowish oil; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.81 (s, 4H), 4.40 (sept., $^3J_{HH}$ 6.0 Hz, 1H), 3.90 (t, $^3J_{HH}$ 7.2 Hz, 2H), 1.73 (pent., $^3J_{HH}$ 7.2 Hz, 2H), 1.46 (sext., $^3J_{HH}$ 7.2 Hz, 2H), 1.29 (d, $^3J_{HH}$ 6.0 Hz, 6H), 0.96 (t, $^3J_{HH}$ 7.2 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C 153.3, 151.6, 117.3, 115.2, 70.7, 68.1, 31.4, 22.0, 19.2, 13.8. HRMS (ESI) Calc. for $C_{13}H_{20}O_2$+H^+ *m/z* 209.1536; Found *m/z* 209.1536.

3.2.3. 1-Butyloxy-4-octyloxybenzene **(2c)**: Yield 81% (starting from **1c**) and 79% (starting from **1e**); white plates; m. p. 36.0-36.5 °C; ^{1}H NMR δ_H 6.81 (s, 4H), 3.85-3.93 (m, 4H), 1.65-1.80 (m, 4H), 1.20-1.60 (m, 12H), 0.97 (t, $^3J_{HH}$ 7.3 Hz, 3H), 0.86-0.90 (m, 3H). ^{13}C NMR δ_C 153.39, 115.58, 68.86, 68.52, 31.97, 31.63, 29.57, 29.54, 29.40, 26.23, 22.80, 19.41, 14.23, 14.00; Anal. calc. for $C_{18}H_{30}O_2$ (%): C 77.64, H 10.67; Found: C 77.78, H 10.81.

3.2.4. 1-Hexyloxy-4-octyloxybenzene **(2d):** Yield 80% (starting from **1d**) and 68% (starting from **1e**); white plates; m. p. 38.0-38.5 °C. ^{1}H NMR δ_H 6.81 (s, 4H), 3.89 (t, $^3J_{HH}$ 6.6 Hz, 4H), 1.70-1.82 (m, 4H), 1.15-1.50(m, 16H), 0.86-0.93 (m, 6H). ^{13}C NMR δ_C 153.23, 115.43, 68.60, 31.82, 31.62, 29.42, 29.38, 29.24, 26.07, 25.74, 22.65, 22.60, 14.07, 14.01. HRMS (ESI) Calc. for $C_{20}H_{34}O_2$+Na^+ *m/z* 329.2451; Found *m/z* 329.2464. Anal. calc. for $C_{20}H_{32}O_2$ (%): C 78.38, H 11.18; Found C 78.80, H 11.20.

3.2.5. 1-Octyloxy-4-propyloxybenzene **(2e):** Yield 65% (starting from **1e**), white plates, m. p. 36.5-37.5 °C; ^{1}H NMR δ_H 6.81 (s, 4H), 3.87 (m, 4H), 1.72-1.79 (m, 4H), 1.10-1.52. (m, 10H), 1.02 (t, $^{3}J_{HH}$ 7.3 Hz, 3H), 0.82-0.94 (m, 3H). ^{13}C NMR δ_C 153.21, 153.18, 115.37, 70.14, 68.63, 31.84, 29.41, 29.40, 29.27, 26.09, 22.70, 22.68, 14.11, 10.78. Anal. calc. for $C_{17}H_{28}O_2$ (%): C 77.22, H 10.67; Found: C 77.09, H 10.77.

3.2.6. 1-Dodecyloxy-4-hexyloxybenzene **(2f):** Yield 87% (starting from **1d**), 87% (starting from **1f**); white slightly waxy solid, m. p. was not determined; ^{1}H NMR δ_H 6.82 (s, 4H), 3.90 (t, $^{3}J_{HH}$ 6.60 Hz, 4H), 1.69-1.81 (m, 4H), 1.20-1.50 (m, 24H), 0.85-0.95 (m, 6H). ^{13}C NMR δ_C 153.16, 115.34, 68.62, 31.91, 31.61, 29.65, 29.62, 29.58, 29.41, 29.38, 29.34, 26.04, 25.74, 22.68, 22.62, 14.11, 14.04. HRMS (ESI) Calc. for $C_{24}H_{42}O_2$+Na^+ *m/z* 385.3077; Found *m/z* 385.3086. Anal. calc. for for $C_{24}H_{42}O_2$ (%): C 79.50, H 11.68; Found: C 79.74, H 11.88.

3.2.7. 1-Ethoxy-4-hexyloxybenzene **(2g):** Yield 90% (starting from **1a**), white solid, m.p. 36.0-39.0 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.85 (s, 4H), 3.99 (q, $^{3}J_{HH}$ 7.0 Hz, 2H), 3.92 (t, $^{3}J_{HH}$ 6.6 Hz, 2H), 1.74-1.82 (m, 2H), 1.28-1.54 (m, 6H), 1.41 (t, $^{3}J_{HH}$ 7.0 Hz, 3H), 0.94 (t, $^{3}J_{HH}$ 6.8 Hz, 3H). ^{13}C-NMR (75 MHz, $CDCl_3$) δ_C 153.2, 152.9, 115.3, 68.5, 63.9, 31.6, 29.3, 25.7, 22.6, 14.9, 14.0. HRMS (ESI) Calc. for $C_{14}H_{22}O_2$+H^+ *m/z* 223.1693; Found *m/z* 223.1684.

*3.2.8. 1-Ethoxy-4-octyloxybenzene***(2h):** Yield 85% (starting form **1a**), 95% (starting from **1e**); white plates; m. p. 34.5-35.5°C; ^{1}H NMR δ_H 6.81 (s, 4H), 3.97 (q, $^{3}J_{HH}$ 7.0 Hz, 2H), 3.89 (t, $^{3}J_{HH}$ 6.6 Hz, 2H), 1.70-1.78 (m, 2H), 1.11-1.50 (m, 10H), 0.83-0.92 (m, 6H). ^{13}C NMR δ_C 153.3, 152.9, 115.4, 68.6, 63.9, 31.8, 29.4, 29.3, 26.1, 22.7, 14.9, 14.1. Anal. calc. for $C_{16}H_{26}O_2$ (%): C 76.75, H 10.47; Found: C 76.90, H 10.35.

3.2.9. 1-dodecyloxy-4-ethoxybenzene **(2i):** Yield 92% (starting from **1a**), white crystalline solid, m.p. 51.0-52.5 °C; ^{1}H NMR (300 MHz, $CDCl_3$) δ_H 6.83 (s, 4H), 3.98 (q, $^{3}J_{HH}$ 7.0 Hz, 2H), 3.90 (t, $^{3}J_{HH}$ 6.6 Hz, 2H), 1.71-1.81 (m, 2H), 1.39 (t, *J* = 7,0 Hz, 3H), 1.21-1.50 (m, 18H), 0.89 (t, *J* = 6,7 Hz, 3H). ^{13}C NMR (75 MHz, $CDCl_3$) δ_C 153.20, 152.90, 115.33, 68.59, 63.95, 31.94, 29.65, 29.62, 29.59, 29.58, 29.41, 29.38, 29.34, 26.04, 22.68, 14.94, 14.11. HRMS (ESI) Calc. for $C_{20}H_{34}O_2$+H^+ *m/z* 307.2632; Found *m/z* 307.2637.

3.2.10. 1-isopropyloxy-4-octyloxybenzene **(2j):** Yield 47%, colorless oil; ^{1}H NMR δ_H 6.81 (br. s, 4H), 4.40 (m, 1H), 3.89 (t, $^{3}J_{HH}$ 6.6 Hz, 2H), 1.72-1.79 (m, 2H), 1.10.-1.52 (m, 16H), 0.86-0.91 (m, 3H). ^{13}C NMR δ_C 153.42, 151.78, 117.46, 115.36, 70.93, 68.59, 31.85, 29.43, 29.41, 29.28, 26.09, 22.68, 22.16, 14.20. Anal. calc. for $C_{17}H_{28}O_2$ (%): C 77.22, H 10.67; Found: C 77.35, H 10.86.

5. Conclusion

In conclusion, a series of 4-alkoxyphenols **1(a-f**) and non-symmetric 1,4-dialkoxybenzenes **2(a-j**) were prepared from 4-hydroxybenzaldehyde. The obtained dialkoxybenzenes can be potentially applied to the synthesis of dialkoxyterephthalaldehydes[48] useful staring materials for PPV-type polymers.

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