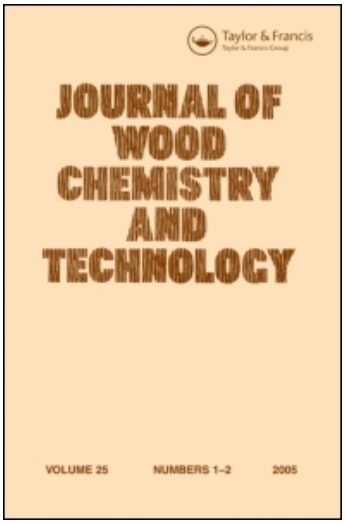

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THE SYNTHESIS AND CHEMICAL STRUCTURES OF TETRAMERIC LIGNIN MODEL COMPOUNDS

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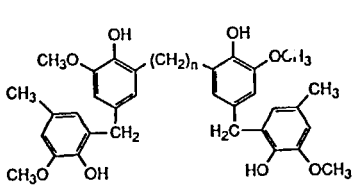
ABSTRACT

In order to study the reaction of high molecular weight residual lignin in pulp with chlorine dioxide, three types of tetrameric lignin model compounds were designed and synthesized. All three tetramers contain diphenylmethane condensation - type structures but **1** also contains a biphenyl structure and **3** contains β-arylether linkages. Synthesis of tetramer **1** involved oxidative coupling of vanillin followed by reduction and condensation with an excess of creosol under alkaline conditions. Tetramer **2** was prepared by the condensation of vanillin with formaldehyde followed by reduction and condensation as for tetramer **1**. Preparation of tetramer **3** was accomplished by condensation of a dimer containing a β-aryl ether linkage with formaldehyde.

INTRODUCTION

Synthetic lignin model compounds containing structural features of residual lignin in pulp are useful for elucidating the chemistry of bleaching. For example, recent studies with a variety of model monomers and dimers have provided valuable information about the nature and properties of products of chlorine dioxide bleaching[1-3] and resulted in the first identification of muconic acids in bleachery effluents[4]. Since the residual lignin present in unbleached pulp has a higher molecular weight, it is important to extend the



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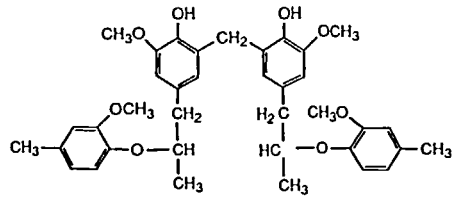
2 n=1



3

FIGURE 1 Structures of tetrameric lignin model compounds

research to trimers and tetramers. A number of synthetic methods have been described for variety of higher molecular weight lignin model compounds[5-8], however, most of the compounds reported have a hydroxyl group on the carbon adjacent to the aromatic ring and as result will be degraded to monomers during bleaching reactions via electrophilic sidechain displacement[9,10]. Even simple β-aryl ethers which do not have oxygen-containing substitutents on either the α or γ-carbons can undergo extensive cleavage during reactions with chlorine[11] and chlorine dioxide[12]. The carbon-carbon linked model dimers used recently avoided the degradation to monomers and gave dimeric muconic acid products which should have characteristics similar to some of the high mass material resulting from chlorine dioxide bleaching[2,3]. In this paper, the synthesis and chemical structures of analogous tetrameric model compounds **1-3** (Figure 1) is reported.

RESULTS AND DISCUSSION

Synthesis of Tetramer 1

The synthesis of tetramer **1** started with commercially available vanillin **4** as shown in Figure 2. Oxidative coupling of vanillin **4** with potassium persulphate gave bivanillin **5**[13]. Reduction of **5** with sodium borohydride was initially carried out in methanol, however, MS (mass spectrometry) showed the product had a molecular weight of 334, 28

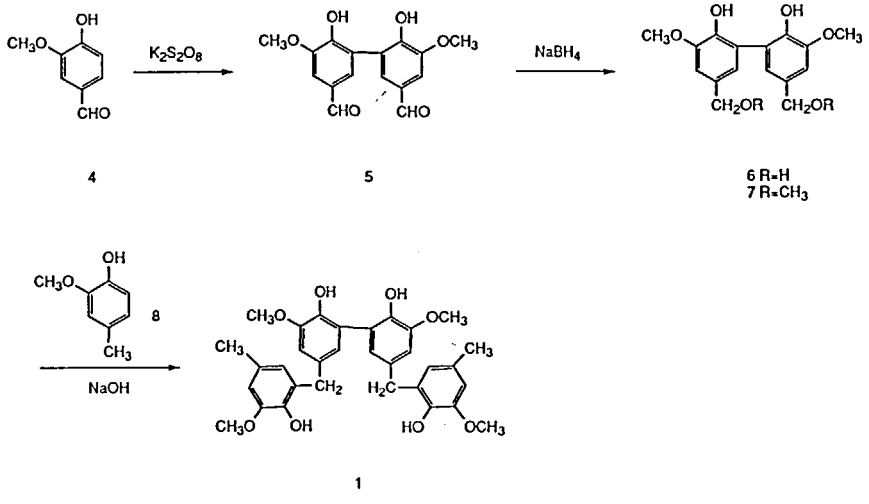


FIGURE 2 Synthetic route for tetramer **1**

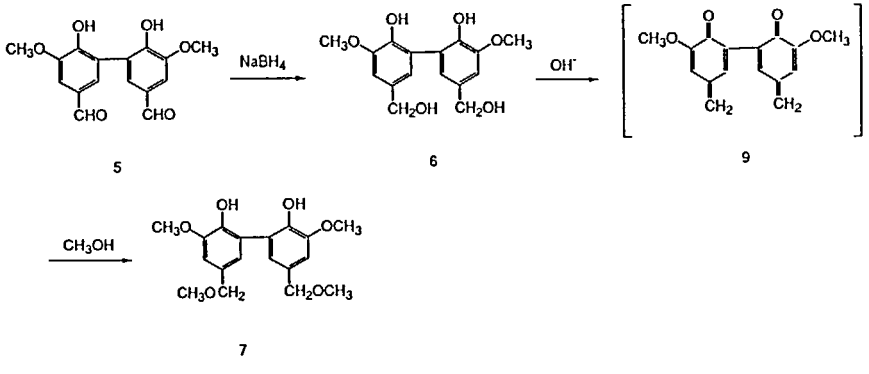


FIGURE 3 Formation of dimeric methylether **8** via quinone methide **9**

mass units higher than that of compound **6** and a peak attributed to methoxy group appeared at 3.39 in the ^1H NMR spectrum. These spectral data suggested that the product was the methylated compound **7** instead of the desired alcohol **6**. Apparently, compound **6** was produced initially but tended to form the quinone methide **9** (Figure 3) in alkaline

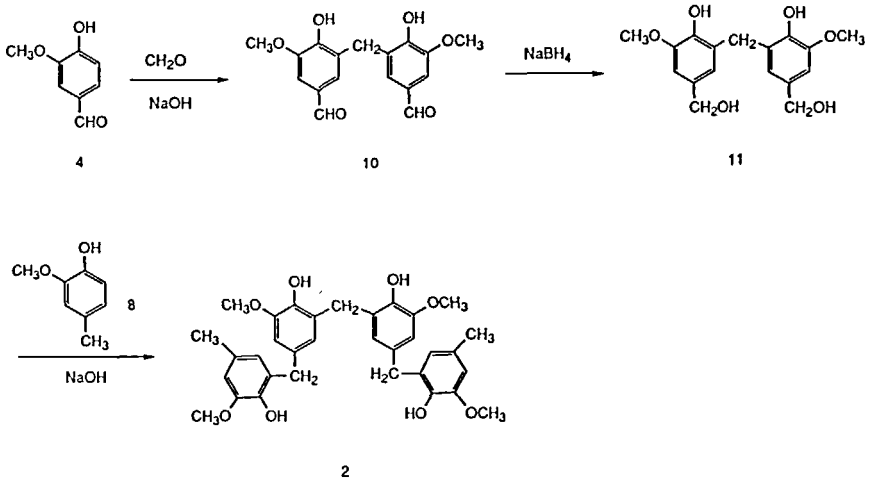


FIGURE 4 Synthetic route for tetramer **2**

media since sodium borohydride is alkaline reducing agent. The methide underwent Michael addition with methanol to form compound **7**. In order to prevent formation of the methylether **7**, a water suspension of **5** was used for reduction. Since compound **6** polymerized even at room temperature under acidic conditions, neutralization of the product with great care at low temperature was required. Reaction of the benzyl alcohol compound **6** with creosol **8** under alkaline conditions gave the desired model tetramer **1**. In order to inhibit the alcohol's self condensation under alkaline conditions, an excess of creosol was used.

Synthesis of Tetramer **2**

Tetramer **2** was prepared by condensation of vanillin **4** with formaldehyde followed by reduction of the product **10** with sodium borohydride and condensation with creosol as described above (Figure 4).

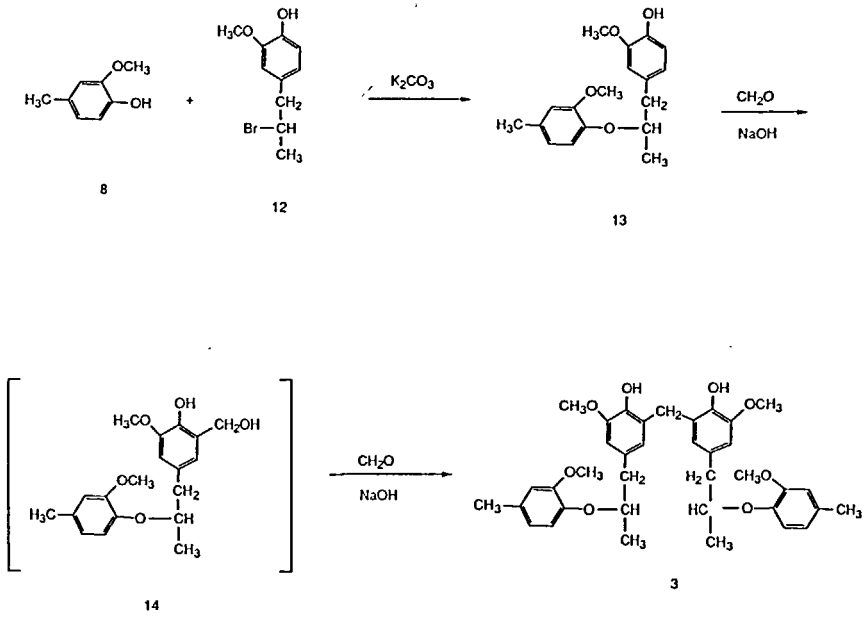


FIGURE 5 Synthetic route for tetramer **3**

Synthesis of Tetramer with β -O-4 linkage **3**

In a previous paper[11], the synthesis of compound **13** (Figure 5) by the condensation of creosol **8** and β-bromodihydroeugenol **12** was reported in 33% yield. Since the low yield was due to intermolecular condensation of the bromocompound with itself, the reaction was improved by adding bromocompound dropwise to creosol solution over 2.5 h, increasing the yield to 65%. Purification of the product **13** by silica column chromatography and crystallization removed the 5% γ-condensation product resulting from the γ-bromoeugenol impurity. Compound **13** was condensed with formaldehyde under alkaline conditions to obtain tetramer **3**. Condensation was time dependent. After 3 h, the major product was the intermediate hydroxymethylated compound **14** which is characterized by a peak at δ 4.74 in ^{1}H NMR spectrum. After 5 h, tetramer **3** was the predominant product.

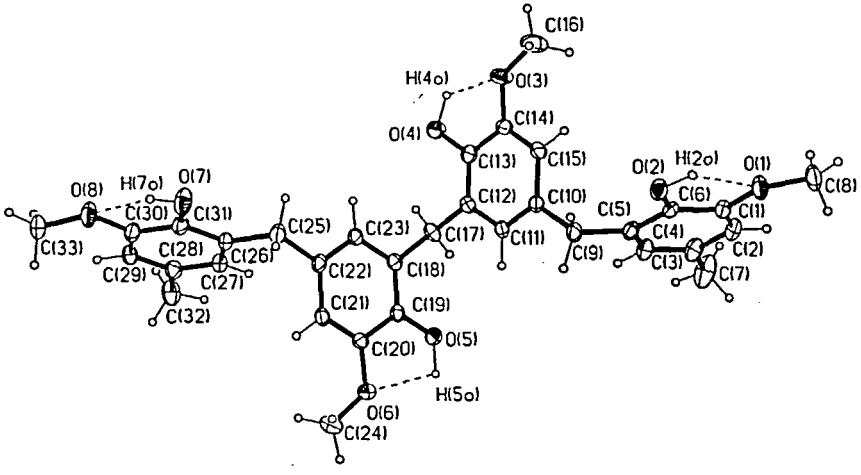


FIGURE 6 X-ray crystallographic analysis of tetramer **1**

The tetrameric lignin model compounds **1** and **2** are useful for the production of synthetic high mass material from bleaching since, by analogy with previous studies on dimers[2,3,11] their oligomeric structure will largely remain intact after reaction with bleaching agents. The resultant tetrameric muconic acids, which would be obtained from reaction with chlorine dioxide and have molecular weights in the range of 700, will be useful for studying the association effects reported for bleached kraft pulp mill effluent constituents[14]. In addition, all three of the models are useful for the study of spectral and other properties, such as hydrogen bonding. Previous studies of the spectral properties of certain dihydroxybiphenyls showed o-methoxyl groups altered the planarity of the compounds in solution due to the formation of intermolecular hydrogen bonds[15]. X-ray crystallographic analysis of tetramers **1** and **2** showed intramolecular H-bonding between the phenolic hydroxyl and adjacent methoxyl groups (Figure 6) and intermolecular H-bonding between hydroxyl and both hydroxyl and methoxyl groups (Figure 7). Therefore, these compounds themselves may show associative effects in solution.

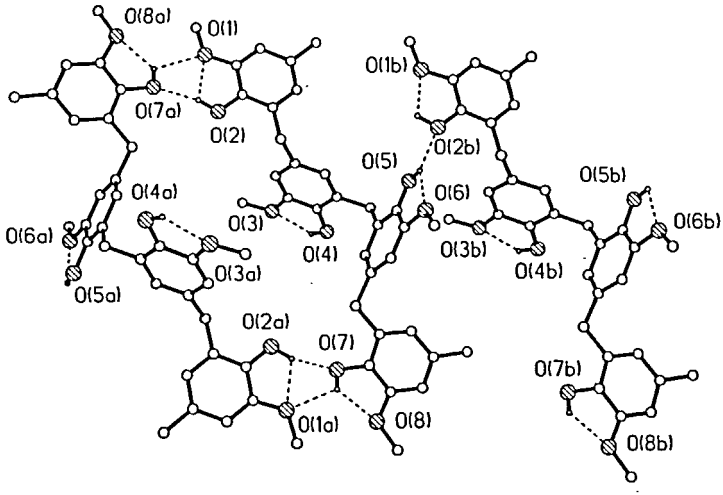


FIGURE 7 X-ray crystallographic analysis of tetramer **1** showing intermolecular H-bonding

EXPERIMENTAL

General

Melting points were determined on a Fisher Johns melting point apparatus and are uncorrected. Silica gel used for normal column chromatography was 80-200 mesh. Purity of products was determined by gas chromatography (GC) (Hewlett Packard 5890 Gas Chromatograph equipped with a 25 m HP-1 capillary column) and/or high performance liquid chromatography (HPLC) (Waters 600E model with 991 Photodiode Array Detector) using Rad-Pak C18, 8 mm x100 mm column in RCM-100 compression module. ^{1}H-NMR and ^{13}C-NMR spectra were recorded in chloroform-d on a Bruker AM-500 (500 MHz) high resolution spectrometer. Signal positions are given in ppm (δ) relative to Me_4Si. Mass spectra (MS) and high resolution mass spectra (HRMS) were recorded on a Fisons 70-250s high resolution mass spectrometer. X-ray crystallographic analyses of **1** and **2** were done using an Enraf-Nonius CAD 4 diffractometer.

2,2'-Dihydroxy-5,5'-dihydroxymethyl-3,3'-dimethoxybiphenyl 6

To a water (250 mL) suspension of compound 5 (15.1g, 0.05 mole), $NaBH_4$ (3.78 g, 0.1 mole) was added slowly over 2h. The mixture was stirred at room temperature for about 3 h until it became clear. The solution was cooled and neutralized with 10% HCl, and the precipitated solid product filtered and washed with water. Recrystallization from ethyl acetate/hexane gave colourless crystals (13.77 g, 90% yield). m.p. 194-195 °C. ^{1}H-NMR: 3.94 (s, 6H, 2 x OCH_3), 4.42 (s, 4H, 2 x OCH_2), 6.11 (s, 2H, 2 x OH), 6.89 (d, J=1.8 Hz, 2H, 2 x ArH), 6.92 (d, J=1.8 Hz, 2H, 2 x ArH). MS m/e (%): 306 (65), 288 (57), 257 (100), 243 (41), 227 (35). HRMS calcd for $C_{16}H_{18}O_6$: 306.110; found: 306.111.

2,2'-Dihydroxy-3,3'-dimethoxy-5,5'-dimethoxymethylbiphenyl 7

Compound 7 was prepared by the procedure described above using CH_3OH as solvent. The product (96% yield) had m.p. 95-97 °C, ^{1}H-NMR: 3.39 (s, 6H, 2 x OCH_3), 3.94 (s, 6H, 2 x OCH_3), 4.42 (s, 4H, 2 x OCH_2), 6.11 (s, 2H, 2 x OH), 6.89 (d, J=1.8 Hz, 2H, 2 x ArH), 6.92 (d, J=1.8 Hz, 2H, 2 x ArH). MS (%): 334 (20), 302 (63), 271 (45), 257 (100). HRMS calcd. for $C_{18}H_{22}O_6$: 334.142; found: 334.143.

3,3'-Dimethoxy-5,5'-di(2-hydroxy-3-methoxy-5-methybenzyl)-1,1'-biphenyl-2,2'-diol 1

To a solution of creosol (8.28 g, 0.06 mole) in 1 N NaOH (0.06 mole), was added compound 6 (3.20 g, 0.01 mole) and the mixture refluxed with stirring for 8 h. The resulting solution was acidified with 10% HCl at 0 °C and the product was extracted with ethyl acetate (3 x 60 mL). The combined extracts were washed successively with 1 M $NaHCO_3$, brine, H_2O, and dried over $MgSO_4$. After evaporation of solvent, the residue was purified by a silica column (hexane:ethyl acetate, 5:2) to give colourless crystals (2.51 g, 46% yield), m.p. 165-167°C. ^{1}H-NMR: 2.23 (s, 6H, 2xCH_3), 3.85 (s, 6H, 2xOCH_3), 3.86 (s, 6H, 2xOCH_3), 3.91 (s, 4H, 2xCH_2), 5.60 (s, 2H, 2xOH), 6.06 (s, 2H, 2xOH), 6.54 (m, 4H, 4xArH), 6.82 (m, 4H, 4xArH). ^{13}C-NMR: 21.1 (CH_3), 35.2

(CH_2), 55.9 (OCH_3), 56.1 (OCH_3), 109.6 111.2, 122.9, 123.6, 124.4, 126.8, 128.8, 132.9, 140.7, 141.0, 146.1, 147.2 (ArH). MS(%): 546 (37), 424 (59), 257 (100), 151 (76). HRMS calcd. for $C_{32}H_{34}O_8$: 546.225; found: 546.223.

Bis(5-formyl-2-hydroxy-3-methoxyphenyl)methane **10**

Into a refluxing mixture of vanillin (30.4 g, 0.2 moles) and 37% formaldehyde (0.12 mole), was added 2 N NaOH (0.24 mole). The resulting solution was refluxed with stirring for 0.5 h. After cooling, it was poured into water (400 mL) and neutralized with 5% HCl. The product was collected by filtration and washed with acetone. The crude product was dissolved in minimum amount of 10% NaOH and diluted with water to 200 mL. Re-acidification with 5% HCl and filtration gave **2** (12.5 g, 41% yield). m.p. 274-276 °C (lit.[16] m.p. 274 °C). HRMS calcd for $C_{17}H_{16}O_6$: 316.095; found: 316.096.

Bis(2-hydroxy-5-hydroxymethyl-3-methoxyphenyl)methane **11**

Into a water (250 mL) suspension of compound **2** (15.1g, 0.05 mole), $NaBH_4$ (3.78 g, 0.1 mole) was added slowly over 2h. The mixture was stirred at room temperature for about 3 h until it became clear. The solution was neutralized with 10% HCl and the precipitated product collected by filtration and washed with water. Crystallization from ethyl acetate/hexane gave colourless crystals (13.5 g, 84% yield); m.p. 141-143°C. ^{1}H-NMR: 3.89 (s, 6H, 2xOCH_3), 3.99(s 2H, Ar_2CH_2), 4.55 (s, 4H, $ArCH_2O$), 6.76 (d, J=1.7Hz, 2H, 2xArH), 6.80 (d, J=1.7, 2H, 2xArH). MS m/e (%): 320 (35), 302 (100), 284 (77), 241 (54), 167 (33), 154 (21). HRMS for $C_{17}H_{20}O_6$: 320.126; found: 320.127.

Bis(2-hydroxy-4-(2'-hydroxy-3'-methoxy-5'-methylbenzyl)-3-methoxyphenyl)methane **2**

Into a solution of creosol (8.28 g, 0.06 mole) in 1 N NaOH (0.06 mole), compound **11** (3.20 g, 0.01 mole) was added and the mixture refluxed with stirring for 8h. The resulting solution was acidified with 10% HCl at 0 °C and the product extracted with ethyl acetate (3 x 60 mL). The combined extracts were washed successively with 1 N

$NaHCO_3$, brine and H_2O, and dried over $MgSO_4$. After evaporation of solvent, the product was purified using a silica column (hexane:ethyl acetate, 5:2) to give colourless crystals (3.05 g, 54% yield), m.p. 167-168°C. ^{1}H-NMR: 2.22 (s, 6H, 2xCH_3), 3.79 (s, 6H, 2xOCH_3), 3.82 (s, 4H, 2xCH_2), 3.85 (s, 6H, 2xOCH_3), 3.90 (s, 2H, CH_2), 5.58 (s, 2H, 2xOH), 5.99 (s, 2H, 2xOH), 6.47 (d, J=1.3Hz, 2H, 2xArH), 6.54 (d, J=1.3Hz, 2H, 2xArH), 6.62 (d, J=2.0Hz, 2H, 2xArH), 6.71 (d, J=1.83Hz, 2xArH). ^{13}C-NMR: 21.1 (CH_3), 29.4 (CH_2), 35.1 (CH_2), 56.0 (OCH_3), 109.5, 109.7, 122.8, 123.0, 126.0, 127.1, 128.7, 132.1, 141.0, 141.2, 146.3, 146.5 (ArH). MS (%): 560 (100), 410 (67), 287 (38), 274 (47), 151 (52), 137 (27). HRMS calcd. for $C_{33}H_{36}O_8$: 560.241; found: 560.242.

1-(4-Hydroxy-3-methoxyphenyl)-2-propanol-(4-methyl-2-methoxyphenyl) ether **13**

The title compound was prepared by a modified procedure[11]. With vigorous stirring, a solution containing β-bromo-(4-hydroxy-3-methoxyphenyl)-propane **12**[17,18] (12.25 g, 0.05 mole) in dried acetone (80 mL) was added dropwise into a refluxing solution of creosol (11.04 g, 0.08 mole) and anhydrous K_2CO_3 (13.8 g) in acetone (150 mL) over 4 h. The reaction was stirred under reflux for another 2 h then cooled to room temperature. The product was filtered and the filtrate was evaporated to dryness. Purification of the residue by a silica column chromatography (hexane:ethyl acetate, 7:3) and recrystallization from ether/hexane gave colourless crystals of **13** (9.2 g, 61%), m.p. 59-60°C, 100% purity by GC. The ^{1}H-NMR spectrum and mp of product were in agreement with those previously reported[11].

1,1'-(4-,4'-dihydroxy-3,3'-methoxy-5,5'-methylenediphenyl)bis(2-(2-methoxy-4-methylphenoxy)propane) **3**

A solution containing compound **13** (3.02 g, 10 mmole), 37% formaldehyde (12 mmole) and 1 N NaOH (12 mmole) was refluxed under argon atmosphere for 12 h. After cooling, the solution was acidified with 10% HCl. The product was extracted with ether

(3x60 mL) and dried over $MgSO_4$. On evaporation of solvent, the residue was purified on a silica gel column to give **10**. ^{1}H-NMR: 1.24 (d, J= 6.2Hz, 6H, 2 x CH_3), 2.27 (s, 6H, 2 x CH_3), 2.66 (q, 4H, 2 x CH), 3.01 (q, 2 x CH), 3.77 (s, 12H, 4 x OCH_3), 3.94 (s, 2H, CH_2), 4.37 (m, 2H, 2 x OCH), 6.08 (s, 2H, 2 x OH), 6.61-6.72 (m, 10H, ArH). ^{13}C-NMR: 14.1 (CH_3), 19.4 (CH_3), 20.9 (CH_2), 29.3 (CH_2), 42.4 (OCH), 55.8 (OCH_3), 110.3, 113.2, 116.5, 120.9, 123.4, 126.1, 129.7, 131.0, 141.6, 145.0, 146.3, 150.2 (ArH). MS (%): 616 (19), 479 (27), 341 (100), 315 (20), 177 (64). HRMS calcd. for $C_{37}H_{44}O_8$: 616.304; found: 616.301. If the reaction was stopped after 3h, the intermediate hydroxymethylated compound **14** could be isolated.

ACKNOWLEGEMENTS

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