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First Synthesis of 1,1,4,4-Tetrakis(2-hydroxyphenyl)-butane Type Compounds from Condensation of *p*-Substituted Phenol Derivatives with 2,5-Dimethoxytetrahydrofuran in Trifluoroacetic Acid†

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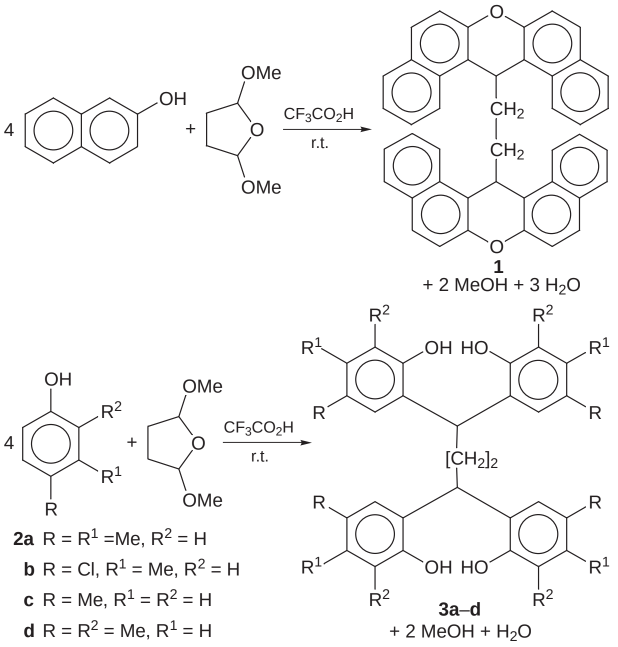
Condensation reactions of 2,5-dimethoxytetrahydrofuran with *p*-substituted phenols and 2-naphthol in trifluoroacetic acid produce 1,1,4,4-tetrakis(2-hydroxyphenyl)butane type compounds and 1,2-bis(1,3-dibenzo[*a,j*]xanthyl)ethane in good yields.

Acetals, known as very reactive intermediates in synthetic organic chemistry, have been used for many reactions where an aldehyde derivative was needed.[1,2] Some of the dialdehydes and especially their synthetic equivalents are interesting reactive precursors in organic chemistry and are considered as useful starting materials for the preparation of the thermally stable polymers.[9,11] 2,5-Dimethoxytetrahydrofuran as a very reactive protected dialdehyde has been used as a cyclization reagent for the preparation of heterocyclic ring compounds.[12–15] Condensation of 2-naphthol with 2,5-dimethoxytetrahydrofuran in the presence of *p*-toluenesulfonic acid as catalyst with the formation of 1,2-bis(1,3-dibenzo[*a,j*]xanthyl)ethane **1** in 42% yield was also reported.[16]

In continuation of our research on the synthesis of thermally stable polymers from new polymerizable monomers and condensation of diphenols with dialdehydes[11,17–19] we needed to synthesise some model compounds from the condensation of phenols with 2,5-dimethoxytetrahydrofuran. We therefore applied the reported method for condensation of 2-naphthol and 2,5-dimethoxytetrahydrofuran to different phenols under the same conditions. We observed that this method can not be applied to phenolic compounds and the yields of the reactions were found to be very low (< 10%). We therefore decided to develop a new synthetic method for condensation of *p*-substituted phenolic compounds with 2,5-dimethoxytetrahydrofuran. We have reported the possibility of using trifluoroacetic acid as a suitable medium for the condensation of phenols with malonaldehydetetramethyl acetal.[20] We now disclose the first synthesis of 1,1,4,4-tetrakis(2-hydroxyphenyl)butane type compounds from the condensation of phenols with 2,5-dimethoxytetrahydrofuran using trifluoroacetic acid as both solvent and catalyst.

The condensations of *p*-substituted phenols **2a**–**d** with 2,5-dimethoxytetrahydrofuran in trifluoroacetic acid were examined. The reactions were found to be efficient and the compounds **3a**–**d** were obtained in good yields (Table 1).

We also applied our method to the condensation of 2-naphthol and 2,5-dimethoxytetrahydrofuran and the yield of compound **1** was increased to 61%. In this reaction we also observed the intramolecular elimination of water from two hydroxy groups as reported earlier.[16] The absence of intramolecular elimination of water from two hydroxy groups in compounds **3a**–**d** could be due to the structural differences and rigidity between phenol and naphthol moieties in the products. The condensation of unsubstituted phenols with 2,5-dimethoxytetrahydrofuran in trifluoroacetic acid produces insoluble resins.



Scheme 1

The structure of all compounds **3a**–**d** were deduced from their IR, ^1H, ^{13}C NMR and Mass spectral data. The IR spectra show a very broad strong absorption bands in the region 3200–3650 cm^{-1}, which are characteristic for the hydroxy groups. Undoubtedly, this broadening is the result of intramolecular hydrogen bonding. The ^1H NMR spectra show a multiplet in the region δ 1.7–1.8 assigned to the methylene, a multiplet in the region δ 4.3–4.8 assigned to the methine protons and also a singlet in the

Table 1 Condensation of phenolic compounds **2a**–**d** and 2-naphthol with 2,5-dimethoxytetrahydrofuran in trifluoroacetic acid

Substrate	Reaction time[a]/h	Product/Yield(%)[b]	Mp/°C
2-Naphthol	5	**1** (61)	299–300
2a	3.5	**3a** (79)	>300
2b	4	**3b** (76)	>300
2c	4	**3c** (74)	>300
2d	6	**3d** (68)	>300

[a] All of the reactions were carried out at room temperature.
[b] Isolated yield.

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region δ 8.5–9.5 assigned to the hydroxy groups. These multiplicities are the result of virtual coupling, as observed for **1** and related compounds.[16,21] The ^{13}C NMR spectra show two aliphatic resonances for the methylene in the region δ 32–34.2 and methine carbons at δ 36–37.2, respectively, consistent with the overall mirror symmetry.

From the viewpoint of facile one-pot synthesis of the new title compounds from readily available starting materials and the possibility of applying this method to phenols and naphthols, the present method is expected to be very useful for this type of transformation in organic synthesis.

Experimental

Melting points were determined with a Buchi 535 melting point apparatus. UV spectra were recorded on a Pharmacia Biotech Ultraspec 3000 model 80-2106-20 spectrometer, IR spectra on a Perkin-Elmer IR-157-G spectrophotometer, ^{1}H and ^{13}C NMR spectra on a 250 MHz Bruker Avance DPX-250 spectrometer using tetramethylsilane (TMS) as an internal standard and mass spectra with a GCMS-Trio 1000 (Fisons) at 70 eV. 2,5-Dimethoxytetrahydrofuran and other chemicals were obtained from Merck.

General Procedure.—Phenolic compounds **2a**–**d** or 2-naphthol (100 mmol), 2,5-dimethoxytetrahydrofuran (3.2 ml, 25 mmol) and trifluoroacetic acid (10–20 ml) were allowed to stand for 3.5 to 6 h at room temperature. The reaction mixture solidified. After addition of acetic acid (20–30 ml), the crude product was collected by filtration and washed with water. The products were further purified by recrystallization.

1,2-*Bis*(1,3-*dibenzo*[a,j]*xanthyl*)*ethane* **1**. White solid, mp 299–300 °C (from pyridine) (lit.,[16] 300 °C), yield 61% (Found: C,89.2; H,4.71. $C_{33}H_{30}O_2$ requires C, 89.5; H, 5%); UV ($CHCl_3$) λ 251 nm (log $\epsilon = 5.24$); ν_{max} (KBr) 3058 m, 2952 w, 1615 s, 1585 s, 1452 s, 1397 s, 1250 s, 1235 s, 1070 s, 952 s, 805 s, cm^{-1}; δ_H (250 MHz, $CDCl_3$) 1.85(m, 4 H, CH_2), 5.21(m, 2H, CH), 6.99–7.79 (m, 24 H, Ar); δ_C (62.9 MHz, $CDCl_3$) 28.88 (CH_2), 30.66 (CH), 115.31, 116.8, 121.95, 123.66, 126.29, 128.17, 128.57, 129.5, 130.53, 130.75 and 149.56 (ArC); *m/z* (EI) 590 (M$^+$, 1.4), 308 (1.9), 282 (17.7), 281 (100) and 252 (15.5%).

1,1,4,4-*Tetrakis*(2-*hydroxy*-4,5-*dimethylphenyl*)*butane* **3a**. White solid, mp > 300 °C (from CH_3OH-H_2O; 4/1, v/v), yield 79% (Found: C, 79.96; H, 7.69. $C_{18}H_{21}O_2$ requires C, 80.29; H, 7.8%); UV (CH_3OH) λ 215 ($\log\epsilon = 5.21$), 286 nm ($\log\epsilon$ 4.75); ν_{max} (KBr) 3250–3500 br) s, 3015 w, 2935 w, 1615 m, 1570 w, 1495 s, 1455 s, 1405 s, 1265 s, 1185 s, 1075 m, 845 s cm^{-1}; δ_H (250 MHz, DMSO-d_6) 1.74 (m, 4H, CH_2), 2.02(s, br, 12H, CH_3), 2.04 (s, br, 12H, CH_3), 4.38 (m, 2H, CH), 6.48 (s, 4H, Ar), 6.68 (s, 4H, Ar), 8.7 (s, 4H, OH); δ_C (62.9 MHz, DMSO-d_6) 19.13 (CH_3), 19.45 (CH_3), 33.29 (CH_2), 36 (CH), 116.64, 125.76, 128.75, 129.2, 133.75 and 152.57 (ArC); *m/z* (EI) 538 (M$^+$, 2), 268 (1.9), 255 (100), 237 (6.4), 194 (3.6), 179 (3.9) and 135 (12.5%).

1,1,4,4-*Tetrakis*(5-*chloro*-2-*hydroxy*-4-*methylphenyl*)*butane* **3b**. White solid, mp > 300 °C (from CH_3OH-H_2O; 5/1, v/v), yield 76% (Found: C, 61.64; H, 4.74. $C_{16}H_{15}Cl_2O_2$ requires C, 61.94; H, 4.84%); UV (CH_3OH) λ 211 ($\log\epsilon = 5.25$), 287 nm ($\log\epsilon = 4.8$); ν_{max} (KBr) 3200–3520 (br) s, 3010 w, 2940 w, 1615 m, 1490 s, 1450 m, 1395 s, 1255 m, 1155 s, 1025 s, 875 m, cm^{-1}; δ_H (250 MHz, DMSO-d_6) 1.77 (m, 4H, CH_2), 2.17(s, 12H, CH_3), 4.4 (m, 2H, CH), 6.67 (s, 4H, Ar), 6.9 (s, 4H, Ar), 9.4 (s, 4H, OH); δ_C (62.9 MHz, DMSO-d_6) 19.63 $(CH)_3$, 32.15 (CH_2), 37.1 (CH), 117.9, 122.75, 128.3, 130.4, 133.6 and 154 (ArC); *m/z* (EI) 622 (M$^+ + 2$, 2), 621(M$^+$+1, 1.2), 620 (M$^+$, 2.8), 308(2.8), 297(66), 296(12.8), 295(100), 237(6.1) and 135 (100%).

1,1,4,4-*Tetrakis*(2-*hydroxy*-5-*methylphenyl*)butane **3c**. White solid, mp > 300 °C (from CH_3OH-H_2O; 5/1, v/v), yield 74%; UV (CH_3OH) λ 221.5 ($\log\epsilon = 5.28$), 284 nm ($\log\epsilon = 4.83$); ν_{max} (KBr) 3200–3550 br), s, 3025 w, 2930 m, 1610 m, 1495 s, 1455 m, 1380 m, 1250 s, 1095 s, 1035 m, 815 s, cm^{-1}; δ_H (250 MHz, DMSO-d_6) 1.8 (m, 4H, CH_2), 1.95 (s, 12H, CH_3), 4.47 (m, 2H, CH), 6.6 (m, 12H, Ar), 8.9 (s, 4H, OH); δ_C (62.9 MHz, DMSO-d_6) 20.87 (CH_3), 32.7 (CH_2), 36.17 (CH), 115.2, 117.8, 127, 128.3, 130 and 152.8 (ArC); *m/z* (EI) 482 (M$^+$, 2.4), 238 (1.5), 225 (100), 207 (4.5), 164 (3.5), 149 (4) and 107 (11%).

1,1,4,4-*Tetrakis*(2-*hydroxy*-3,5-*dimethylphenyl*)*butane* **3d**. White solid, mp > 300 °C (from $C_2H_5OH-H_2O$; 5/1, v/v), yield 68%; UV (CH_3OH) λ 210 ($\log\epsilon = 5.12$), 276 nm ($\log\epsilon = 4.25$); ν_{max} (KBr) 3200–3500 (br), s, 3010 w, 2940 w, 1620 m, 1565 w, 1490 s, 1450 s, 1330 s, 1270 s, 1175 s, 1060 m, 840 s, cm^{-1}; δ_H (250 MHz, DMSO-d_6) 1.79 m, 4H, CH_2), 2.1 (s, br, 12H, CH_3), 2.21 (s, br, 12H, CH_3), 4.42 (m, 2H, CH), 6.4-6.75 (m, 8H, Ar), 8.65 (s, 4H, OH); δ_C (62.9 MHz, DMSO-d_6) 18.7 and 21.65 (CH_3), 34.15 (CH_2), 37.5 (CH), 119.5, 128.2, 131.3, 134.2, 136.5 and 153.1 (ArC); *m/z* (EI) 538 (M$^+$, 1.9), 267 (1.5), 255 (100), 194 (3.5), 179 (3.6), 159 (3.5) and 135 (11%).

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