Electronic supplementary materials *Mendeleev Commun.*, 2019, **29**, 91–93

Trans-etherification of catechol-type benzylic ether with diols as a route to new sterically hindered bis-catechols

Elnara R. Zhiganshina, Maxim V. Arsenyev, Andrey S. Shavyrin, Eugene V. Baranov and Sergey A. Chesnokov

Equipment and materials. The solvents were purified by standard procedures. 4,6-di-*tert*-butyl-3-(methoxymethyl)catechol **1** was synthesized according to the literature [M. V. Arsenyev, E.V. Baranov, M.P. Shurygina, S.A. Chesnokov and G.A. Abakumov, *Mendeleev Commun.*, 2016, **26**, 552.]. Ethylene glycol (Sigma Aldrich), propane-1,3-diol (Fluka), butane-1,4-diol (Sigma Aldrich), pentane-1,5-diol (Sigma Aldrich), hexane-1,6-diol (Sigma Aldrich), diethylene glycol (Sigma Aldrich) were used as purchased. ^{1}H and ^{13}C NMR spectra were recorded on Bruker AV-200. Solvents for NMR were DMSO-d_6 and $CDCl_3$. IR spectra in the 4000-400 cm^{-1} region were recorded on a FMS-1201 spectrophotometer (OOO "Monitoring"). Elemental analysis was carried out on EuroVector EA.

Kinetic experiment. ^{1}H NMR spectroscopy was used to determine the rates of achieving of equilibrium in the ether **1** – hexane-1,6-diol – AcOH-d_4 system. The components of the system (catechol **1** –31.7 mg, hexane-1,6-diol – 7.0 mg and different concentrations of AcOH-d_4 – 0.5, 1.0, 1.5 mol dm^{-3}) were dissolved in a specially purified $CDCl_3$ ($CDCl_3$ was shaken with potassium carbonate to remove HCl/DCl, then filtered). The resulting volume of mixture was 0.6 ml ($[\mathbf{1}]_0$ = 0.2 mol dm^{-3}, $[diol]_0$ = 0.1 mol dm^{-3}). The mixture was placed in a NMR spectrometer tube. The sample was heated at 318 K.

When the reactants were dissolved in $CDCl_3$, an equilibrium was established. The decreasing intensity of signals at 1.33, 1.41 (Bu^t), 3.48 (OMe), 4.91 (CH_2), 6.84 (C_{Ar}–H) ppm (compound **1**) with simultaneous increasing those at 3.44 (MeOD), 1.34 and 1.38 (Bu^t), 4.93 (compounds **4** and **5a**) and at 5.46 ppm (CH_2 of acetate **3)** in ^{1}H NMR spectrum were observed (Figure S1).

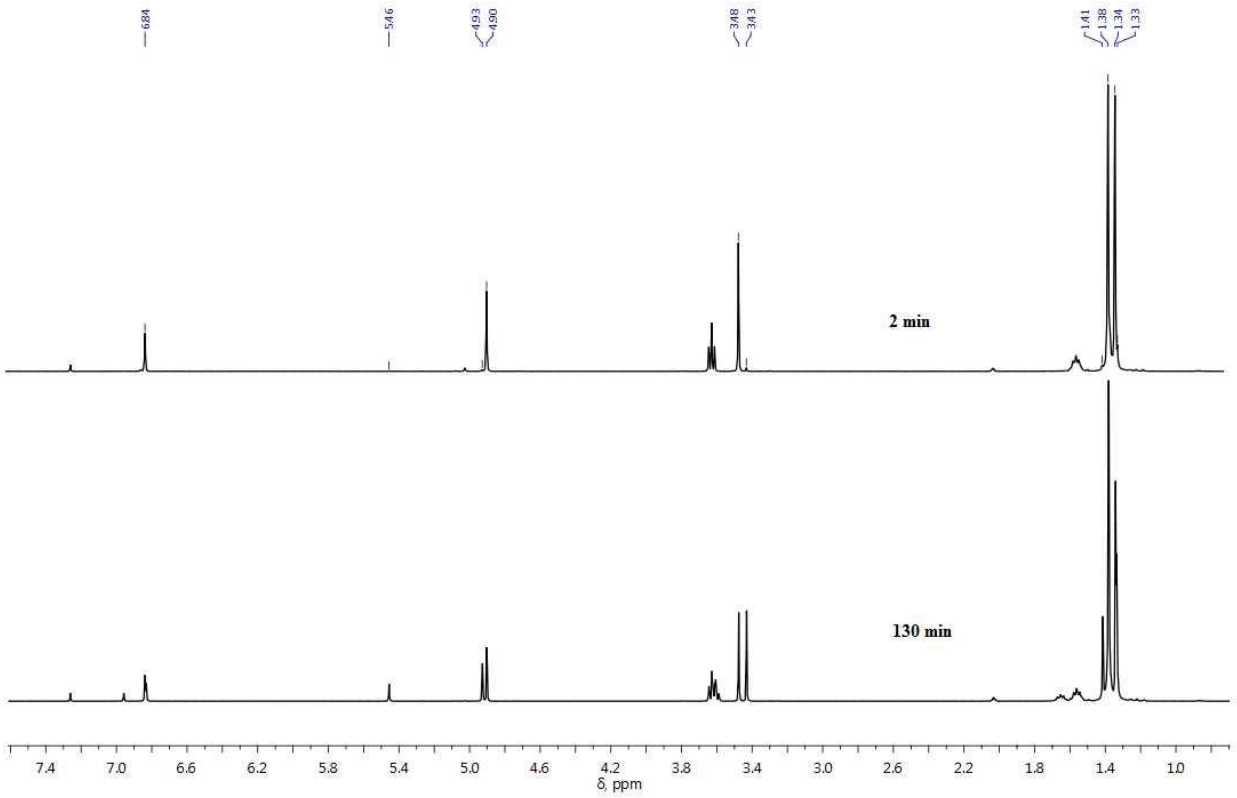


Figure S1. The ^{1}H NMR-spectrum in 2 and 130 minutes after the start of the trans-etherification for catechol **1** – hexane-1,6-diol – AcOH-d_4 (1.5 mol dm^{-3}) system in $CDCl_3$.

The current concentration of catechol **1** at that time was found by the further equation:

$$C(\mathbf{1}), mol\ /l = \frac{I(4.90\ ppm)}{I(4.93\ ppm) + I(4.90\ ppm) + I(5.46\ ppm)} \times [\mathbf{1}]_0$$

The current concentration of compounds **5** and **11** at that time was found by the further equation:

$$C(\mathbf{4} + \mathbf{5}\boldsymbol{a}), mol/l = \frac{I(4.93\ ppm)}{I(4.93\ ppm) + I(4.90\ ppm) + I(5.46\ ppm)} \times [\mathbf{1}]_0$$

I(4.90 ppm) – integral intensity of CH_2 fragment of compound **1**

I(4.93 ppm) - integral intensity of OCH_2 fragment of compounds **4** and **5a**

I(5.46 ppm) - integral intensity of OCH_2 fragment of compound **3**

The current concentration of compound **5a** at that time was found by the further equation:

$$C(\mathbf{5}\boldsymbol{a}), mol/l = \frac{I(5.46\ ppm)}{I(4.93\ ppm) + I(4.90\ ppm) + I(5.46\ ppm)} \times [\mathbf{1}]_0$$

The kinetic curves of the flow rate of compound **1** and the accumulation of products (compounds **3**,**4,** and **5a**) of the trans-etherification reaction are presented in Figure S2.

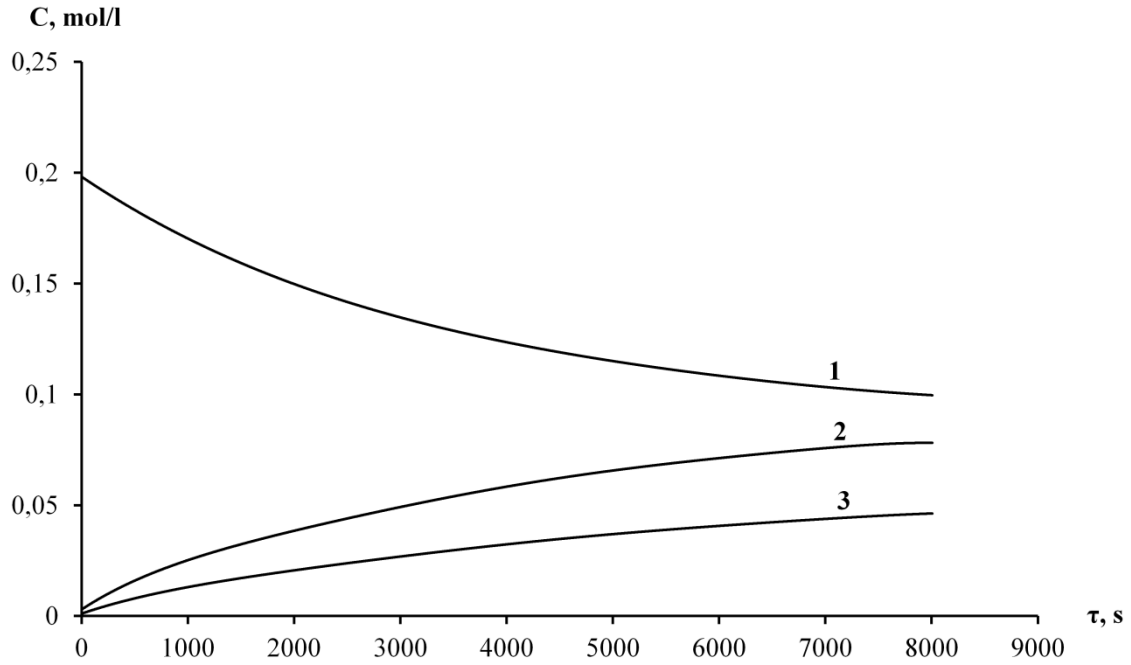


Figure S2. The curves of the changes in the concentration of catechol **1** (1), both **4** and **5a** (2) and **7** (3) during the trans-etherification of catechol **1** with hexane-1,6-diol ($CDCl_3$, 1.5 M AcOH-d_4, 45°C).

The current concentration of methanol at that time was found by the further equation:

$$C(MeOD), mol/l = \frac{I(3.43\ ppm)}{I(3.43\ ppm) + I(3.48\ ppm)} \times [\mathbf{1}]_0$$

The kinetic curves for the accumulation of methanol at various concentrations of AcOH-d_4 are shown in Figure S3.

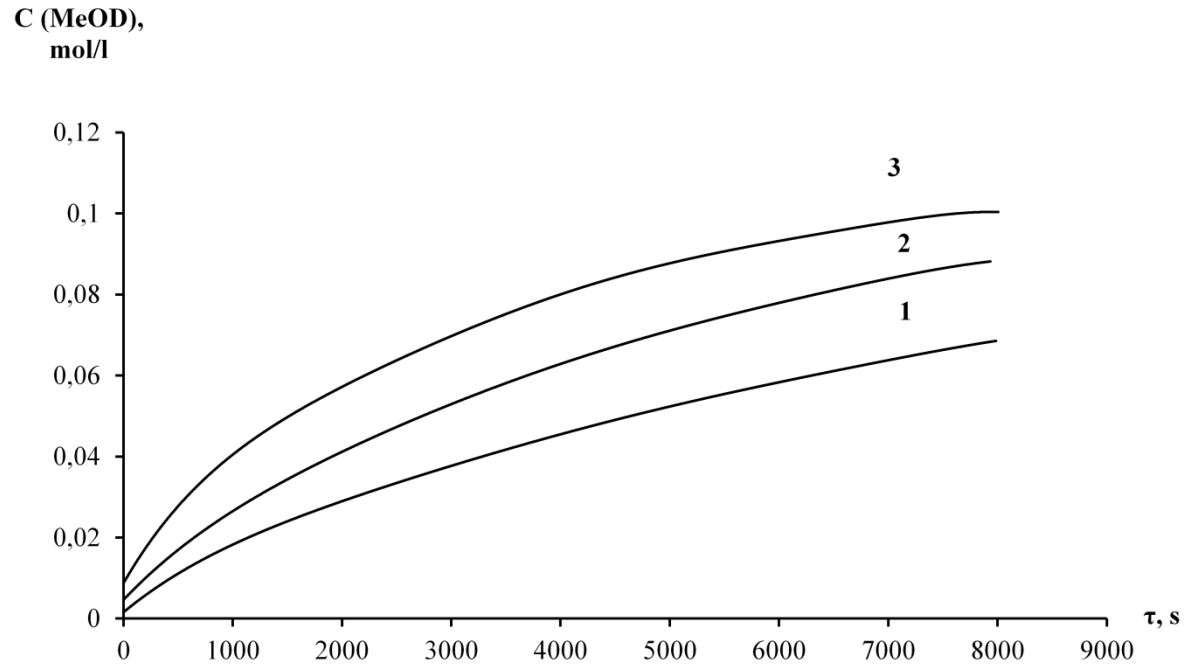
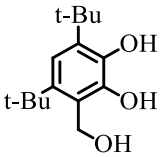


Figure S3. The increase in MeOD concentration in the catechol **1** – hexane-1,6-diol – AcOH-d_4 system ($CDCl_3$, 45°C) during the achieving of equilibrium. Concentrations of AcOH- d_4: 0.5(1), 1.0 (2), 1.5 mol dm^{-3} (3).

4,6-Di-*tert*-butyl-2,3-dihydroxybenzyl alcohol (2)



To a solution of 4,6-di-*tert*-butyl-2,3-dihydroxybenzaldehyde (1 g, 4 mmol), hexane-1,6-diol (0.24 g, 2 mmol) in AcOH (5 ml) with stirring at room temperature, $NaBH_4$ (0.15 g, 4 mmol) was added in portions. Then 20% H_2SO_4 (20 ml) was added dropwise, which caused discoloration of the reaction mixture. The formed precipitate was filtered, washed with water and hexane and dried. The product **2** was isolated as a white powder (0.56 g, 56%), m.p. = 202-204°C. Calculated for: $C_{15}H_{24}O_3$ (%): C, 71.39; H, 9.59. Found (%): C, 71.44; H, 10.01. ^{1}H NMR (200 MHz, $CDCl_3$,): 1.34 (s, 9H, tBu), 1.40 (s, 9H, tBu), 5.08 (s, 2H, CH_2), 5.79 (s, 1H, OH), 6.89 (s, 1H, C_{Ar}-H), 7.10 (s, 1H, OH). ^{13}C NMR (50 MHz, $CDCl_3$, δ, ppm.): 29.48, 32.17, 34.93, 35.35, 68.33, 116.00, 118.92, 134.86, 138.50, 142.08, 144.51. IR (nujol, ν/cm^{-1}):1058, 1220, 1234 (C-O), 3293, 3392, 3465, 3540 (OH).

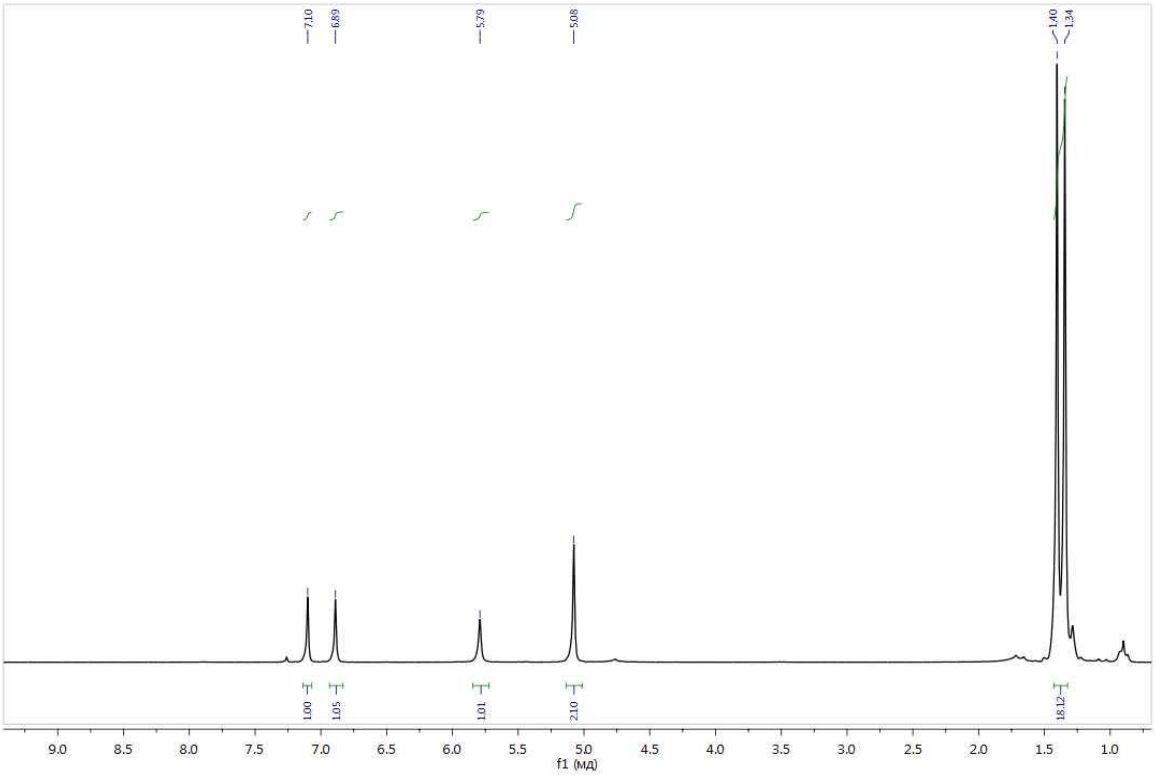


Figure S4. ^{1}H NMR spectrum of 4,6-di-*tert*-butyl-2,3-dihydroxybenzyl alcohol **2** ($CDCl_3$).

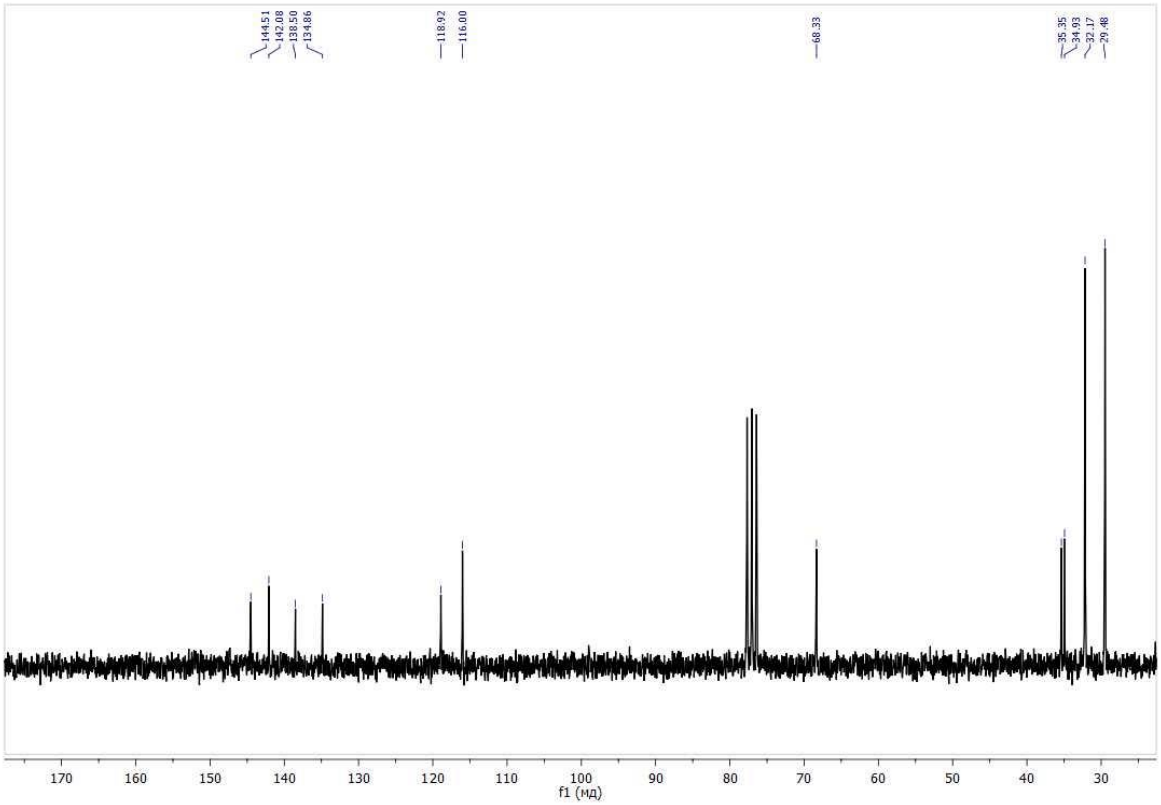
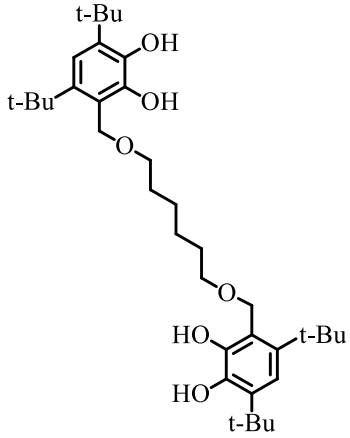


Figure S5. ^{13}C NMR spectrum of 4,6-di-*tert*-butyl-2,3-dihydroxybenzyl alcohol **2** ($CDCl_3$).

The general procedure for the preparation of bis-catechols 5a-f

Diol (2.5 mmol) and methyl ether **1** (1.33 g, 5 mmol) were dissolved in $CHCl_3$ (20 ml) and refluxed for 24 hours with gradual evaporation the mixture to 10 ml. Then the mixture was cooled and the solvent was removed completely. The crude product was recrystallized from *n*-hexane and isolated as white crystalline powders.

3,3'-(Hexane-1,6-diylbis(oxymethylene))bis(4,6-di-*tert*-butylbenzene-1,2-diol) (5a).



Yield 1.18 g (81%), m.p. = 156-158 °C. Calc. for $C_{36}H_{58}O_6$: C, 73.68; H, 9.96. Found (%): C, 73.41; H, 9.87.^{1}H NMR (400 MHz, DMSO, δ, ppm): 1.29 (s, 18H, tBu), 1.29-1.31 (m, 4H, $2CH_2$), 1.32 (s, 18H, tBu), 1.47-1.51 (m, 4H, $2CH_2$), 3.47 (t, 4H, $2CH_2$, J=6.3 Hz), 4.63 (s, 4H,O-CH_2), 6.70 (s, 2H, C_{ar}-H), 7.81 (s, 2H, OH), 7.96 (s, 2H, OH). ^{13}C NMR (d^6-DMSO, 100 MHz, δ, ppm): 26.07, 29.72, 29.90, 32.71, 34.99, 35.62, 66.18, 70.32, 114.96, 122.14, 134.64, 138.46, 142.95, 146.12. IR (nujol, ν/cm^{-1}):1087, 1243, 1264 (C-O), 3040-3340, 3480 (OH).

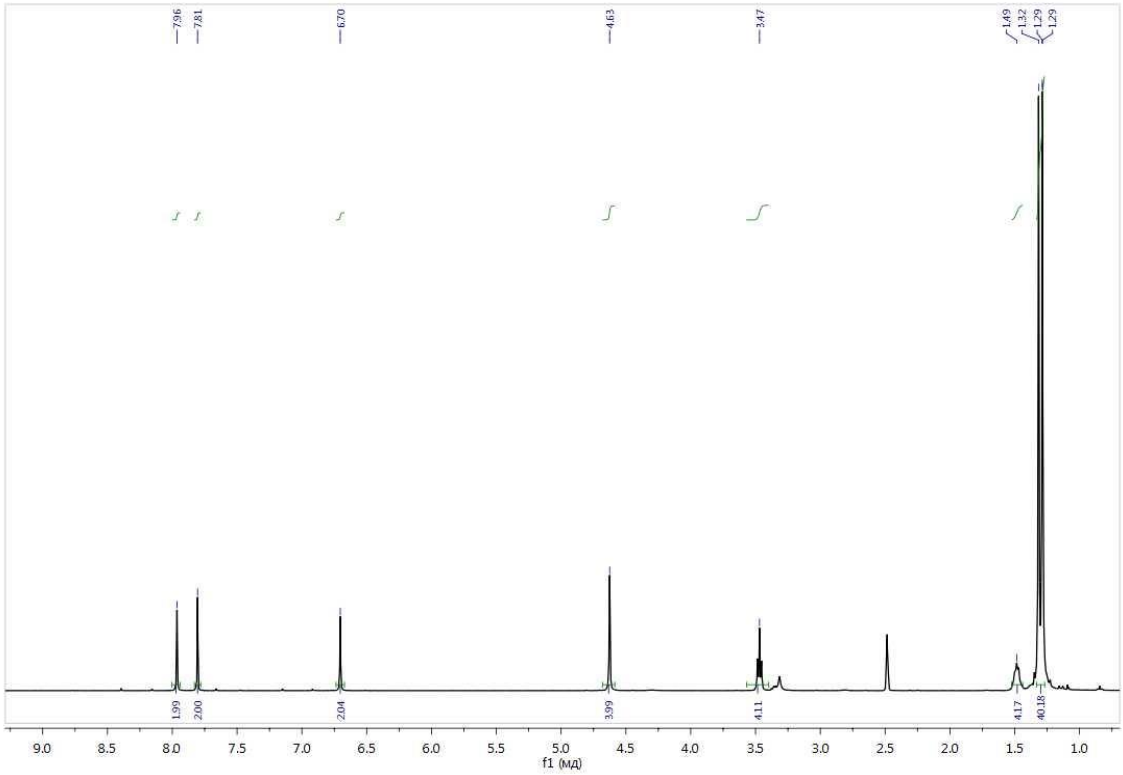


Figure S6. The ^{1}H NMR spectrum of **5a** (DMSO-d_6).

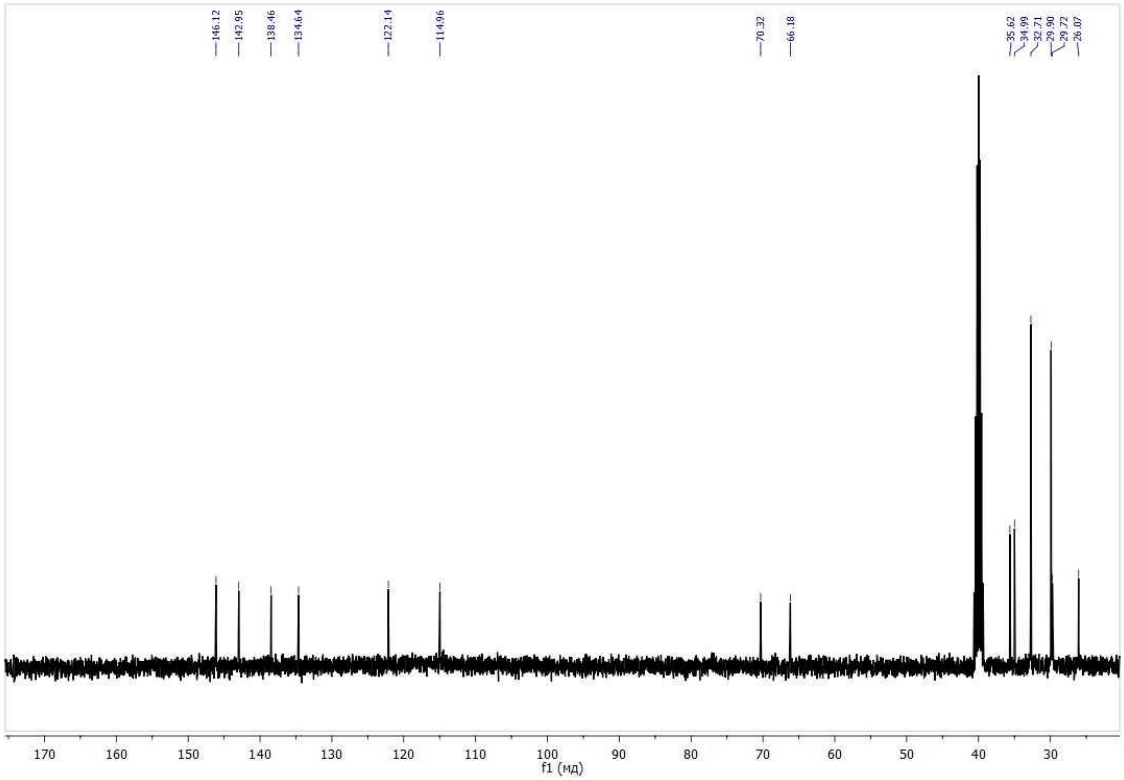
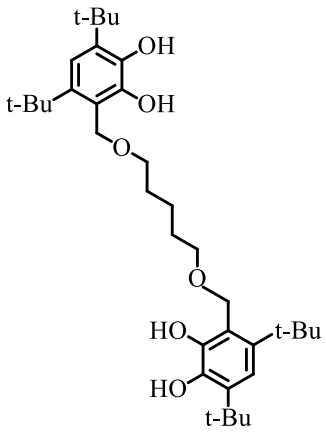


Figure S7. The ^{13}C NMR spectrum of **5a** (DMSO-d_6).

3,3'-(Pentane-1,5-diylbis(oxymethylene))bis(4,6-di-*tert*-butylbenzene-1,2-diol) (5b).



Yield 1.17 g (82%), m.p. = 115-117°C. Calc. for $C_{35}H_{56}O_6$: C, 73.39; H, 9.85. Found (%): C, 73.25; H, 9.78. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.28 (s, 18H, tBu), 1.28-1.30 (m, 2H, CH_2), 1.31 (s, 18H, tBu), 1.47-1.53 (m, 4H, CH_2), 3.47 (t, 4H, $2CH_2$, J=6.3 Hz), 4.62 (s, 4H,O-CH_2), 6.70 (s, 2H, C_{ar}-H), 7.79 (s, 2H, OH), 7.95 (s, 2H, OH). ^{13}C NMR (DMSO-d_6, 100 MHz, δ, ppm.): 23.03, 29.55, 29.89, 32.72, 34.99, 35.62, 66.14, 70.30, 114.96, 122.18, 134.66, 138.50, 142.94, 146.12. IR (nujol, ν/cm^{-1}): 1073, 1242, 1263 (C-O), 3018-3380, 3495(OH).

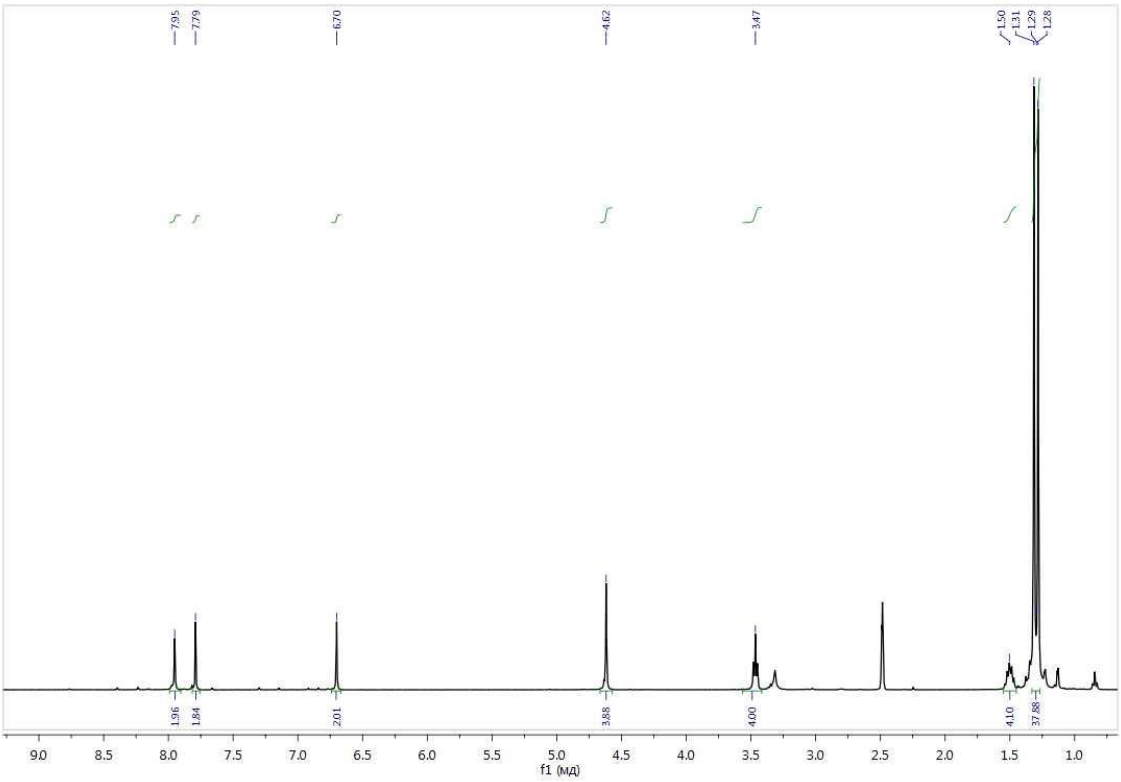


Figure S8. The ^{1}H NMR spectrum of **5b** (DMSO-d_6).

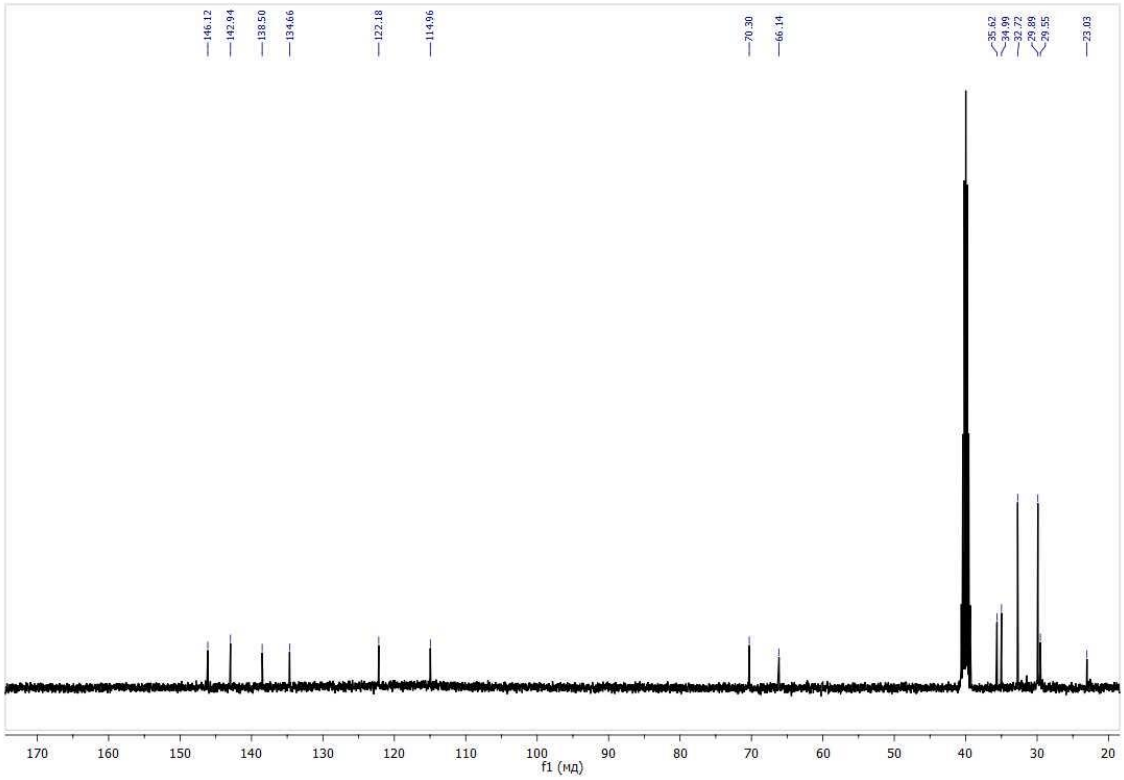
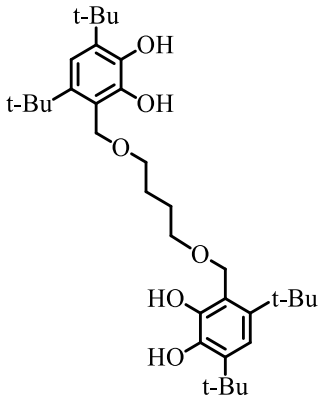


Figure S9. The ^{13}C NMR spectrum of **5b** (DMSO-d_6).

3,3'-((Butane-1,4-diylbis(oxymethylene))bis(4,6-di-*tert*-butylbenzene-1,2-diol) (5c).



Yield 1.19 g (86%), m.p. = 167-169°C. Calc. for $C_{34}H_{54}O_6$: C, 73.08; H, 9.74. Found (%): C, 73.57; H, 9.50. ^1H NMR (400 MHz, DMSO, δ, ppm): 1.28 (s, 18H, tBu), 1.31 (s, 18H, tBu), 1.55 (4H, $2CH_2$), 3.47 (4H, $2CH_2$), 4.62 (s, 4H,O-CH_2), 6.70 (s, 2H, C_{ar}-H), 7.80 (s, 2H, OH), 7.95 (s, 2H, OH). ^{13}C NMR (d^6-DMSO, 100 NMR, δ, ppm): 26.68, 29.90, 32.72, 34.99, 35.62, 66.14, 70.19, 114.95, 122.15, 134.68, 138.49, 142.94, 146.15. IR (nujol, ν/cm^{-1}): 1069, 1261 (C-O), 3000-3300, 3100, 3467 (OH).

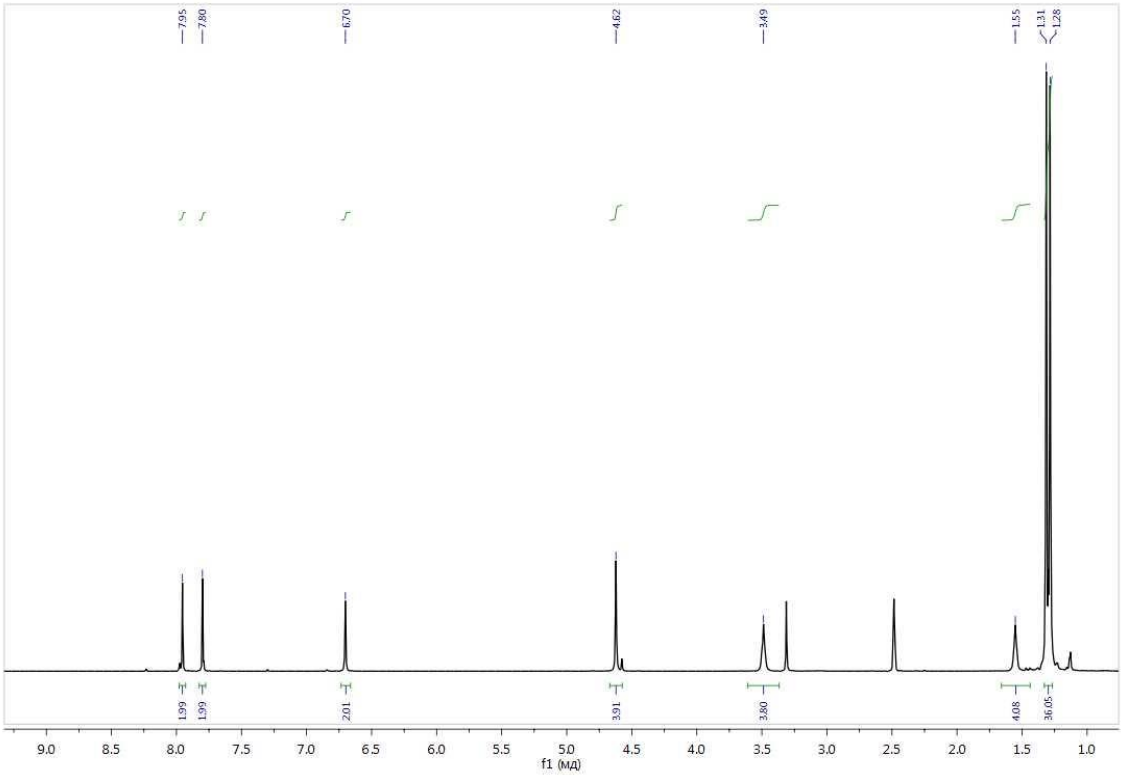


Figure S10. The ^{1}H NMR spectrum of **5c** (DMSO-d_6).

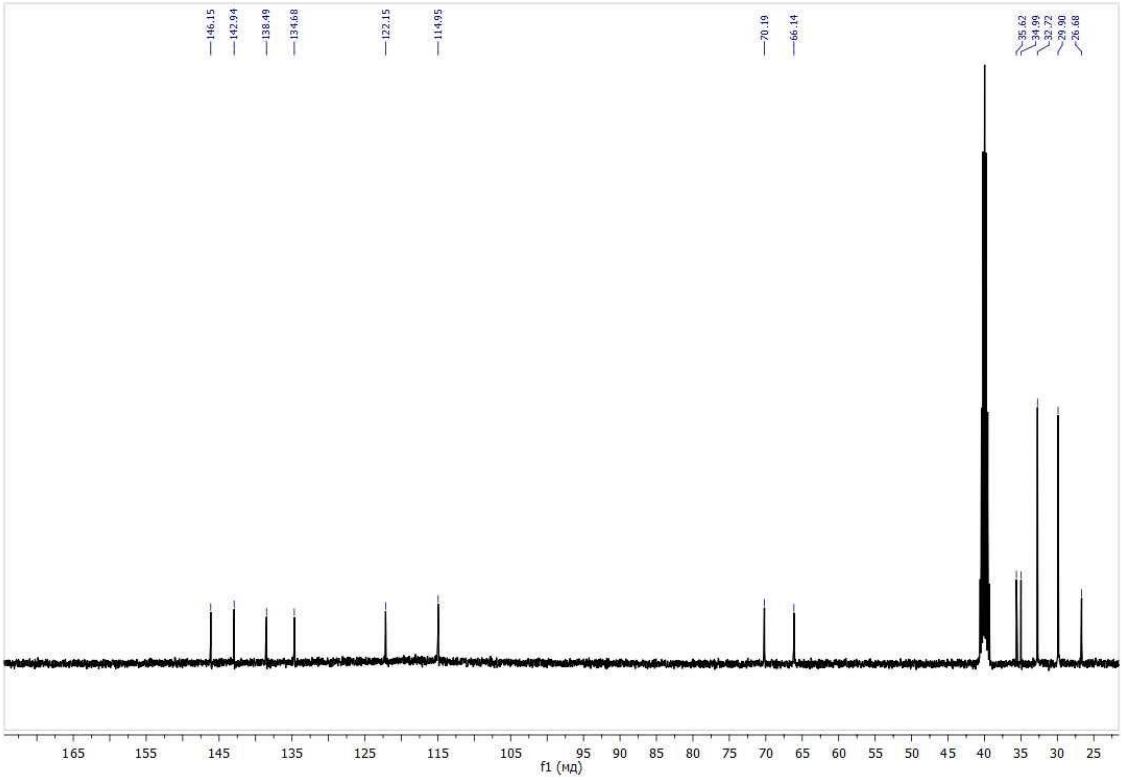
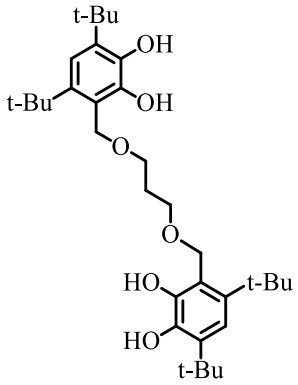


Figure S11. The ^{13}C NMR spectrum of **5c** (DMSO-d_6).

3,3'-((Propane-1,3-diylbis(oxymethylene))bis(4,6-di-*tert*-butylbenzene-1,2-diol) (5d)



Yield 1.18 g (87%), m.p. = 143-145°C. Calc. for $C_{33}H_{52}O_6$: C, 72.76; H, 9.62. Found (%): C, 72.88; H, 9.50. ^{1}H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.29 (s, 18H, tBu), 1.32 (s, 18H, tBu), 1.77 (p, 2H, CH_2, J=6.2 Hz), 3.55 (t, 4H, $2CH_2$, J=6.2 Hz), 4.62 (s, 4H, O-CH_2), 6.71 (s, 2H, C_{ar}-H), 7.77 (s, 2H, OH), 7.94 (s, 2H, OH). ^{13}C NMR (DMSO-d_6, 100 MHz, δ, ppm): 29.90, 30.24, 32.76, 34.99, 35.64, 66.09, 67.80, 114.98, 122.21, 134.71, 138.56, 142.98, 146.13.IR (nujol, ν/cm^{-1}): 1082, 1091, 1261 (C-O), 3294, 3373, 3496 (OH).

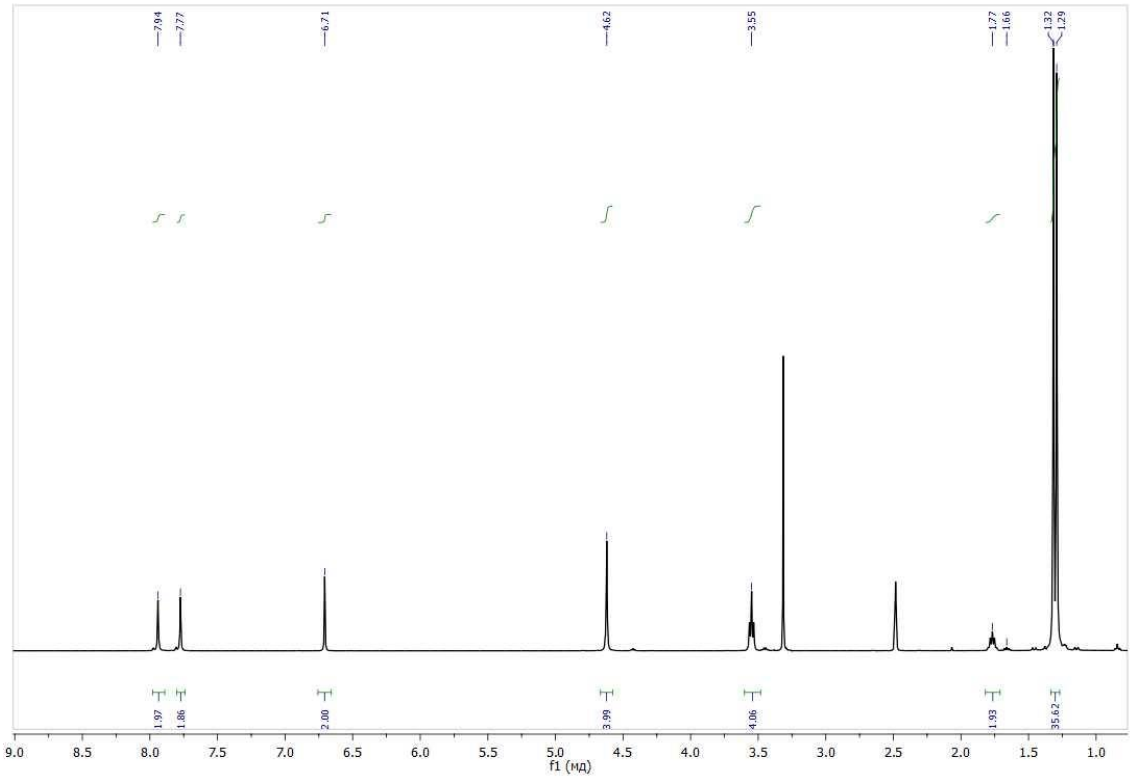


Figure S12. The ^{1}H NMR spectrum of **5d** (DMSO-d_6).

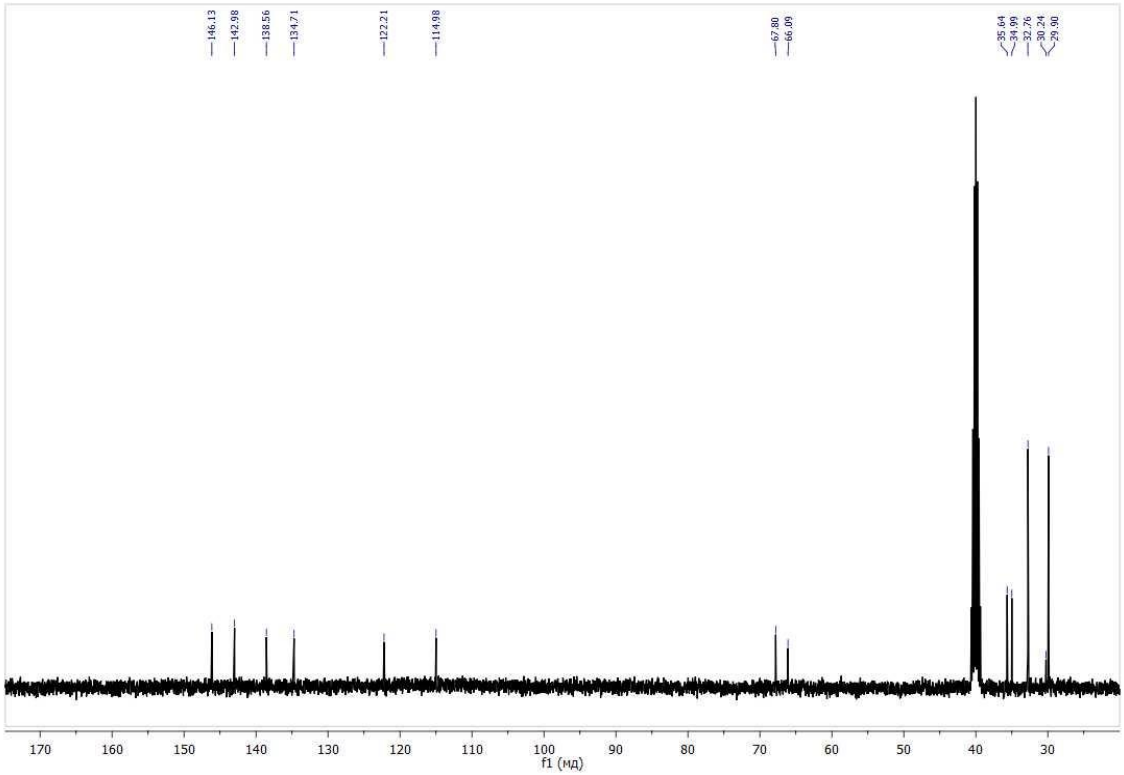
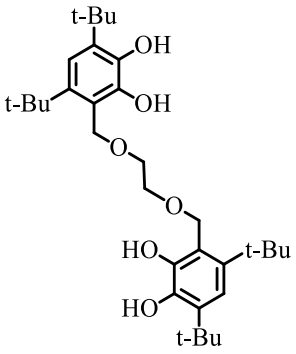


Figure S13. The ^{13}C NMR spectrum of **5d** (DMSO-d_6).

3,3'-(Ethane-1,2-diylbis(oxymethylene)bis(4,6-di-*tert*-butylbenzene-1,2-diol) (5e).



The yield is 1.06 g (80%), m.p. = 173-175°C. Calc. for $C_{32}H_{50}O_6$: C, 72.42; H, 9.50. Found (%): C, 72.32; H, 9.35. ^1H NMR (400 MHz, DMSO-d_6, δ, ppm): 1.28 (s, 18H, tBu), 1.32 (s, 18H, tBu), 3.68 (s, 4H, CH_2), 4.70 (s, 4H,O-CH_2), 6.70 (s, 2H, C_{ar}-H), 7.75 (s, 2H, OH), 7.93 (s, 2H, OH). ^{13}C NMR (d^6-DMSO, 100 MHz, δ, ppm): 29.89, 32.75, 34.99, 35.60, 66.55, 69.78, 114.96, 121.96, 134.67, 134.27, 137.68, 138.48, 142.94, 146.15. IR (nujol, ν/cm^{-1}): 1035, 1260 (C-O), 3434, 3475 (OH).

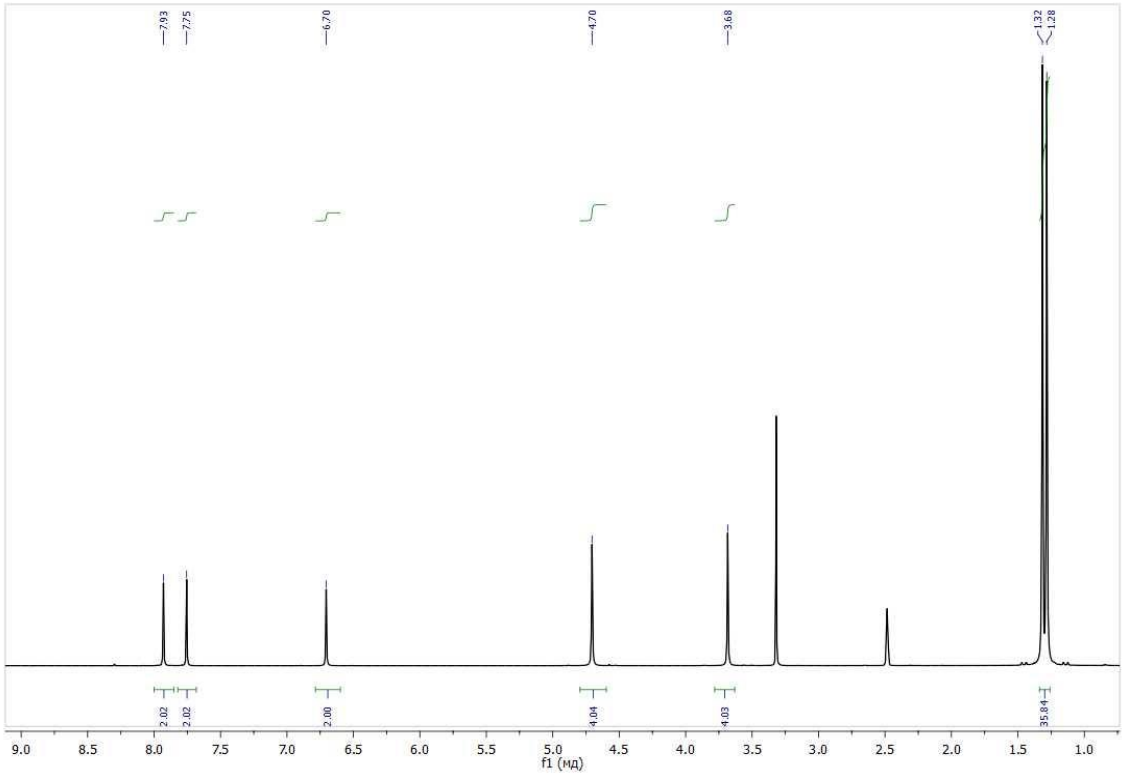


Figure S14. The ^{1}H NMR spectrum of **5e** (DMSO-d_6).

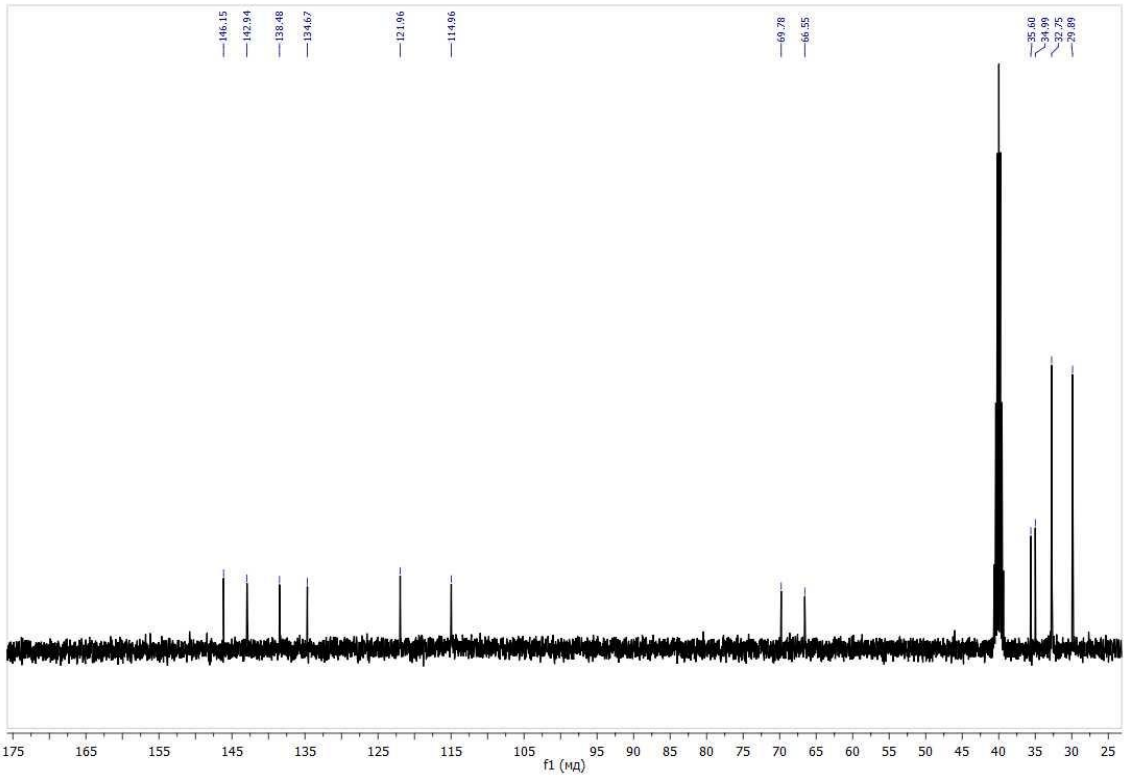
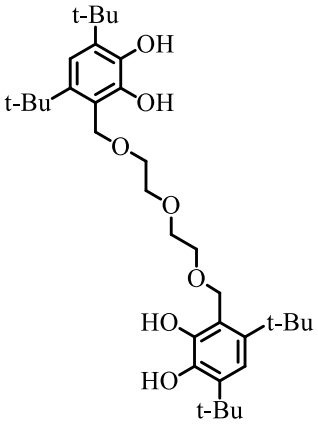


Figure S15. The ^{13}C NMR spectrum of **5e** (DMSO-d_6).

3,3'-[Oxybis(ethane-2,1-diyloxymethylene)]bis(4,6-di-*tert*-butylbenzene-1,2-diol) (5f)



Yield 0.86 g (60%), m.p. = 115-117°C. Calc. for $C_{34}H_{54}O_7$: C, 71.05; H, 9.47. Found (%): C, 71.11; H, 9.56. ^{1}H NMR (400 MHz, DMSO, δ, ppm): 1.28 (s, 18H, tBu), 1.31 (s, 18H, tBu), 3.58 (dd, 4H, $2CH_2$, J=5.7, 3.6 Hz), 3.66 (dd, 4H, $2CH_2$, J=5.7, 3.6 Hz), 4.70 (s, 4H,O-CH_2), 6.69 (s, 2H, C_{ar}-H), 7.80 (s, 2H, OH), 7.92 (s, 2H, OH). ^{13}C NMR (d^6-DMSO, 100 MHz, δ, ppm): 29.86, 32.70, 34.98, 35.56, 66.60, 69.56,70.01, 114.88, 121.83, 134.53, 138.25, 142.94, 146.06. IR (nujol, ν/cm^{-1}): 1071, 1095, 1248 (C-O), 3110- 3500, 3550 (OH).

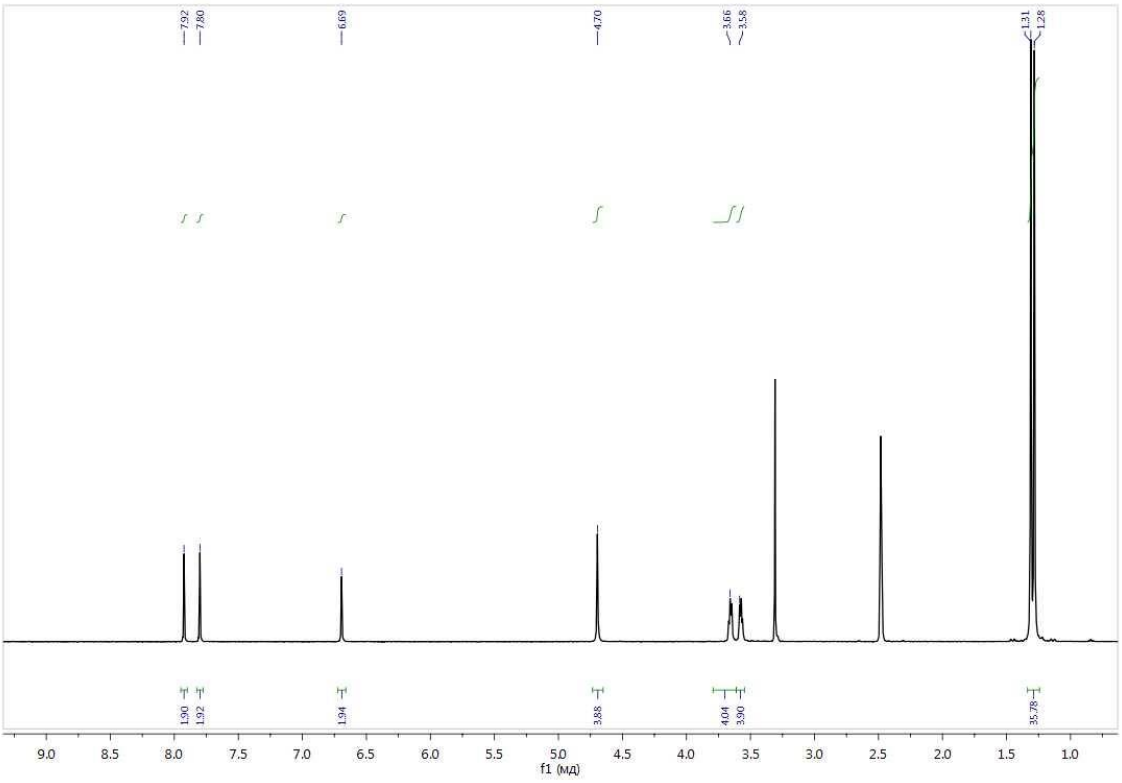


Figure S16. The ^{1}H NMR spectrum of **5f** (DMSO-d_6).

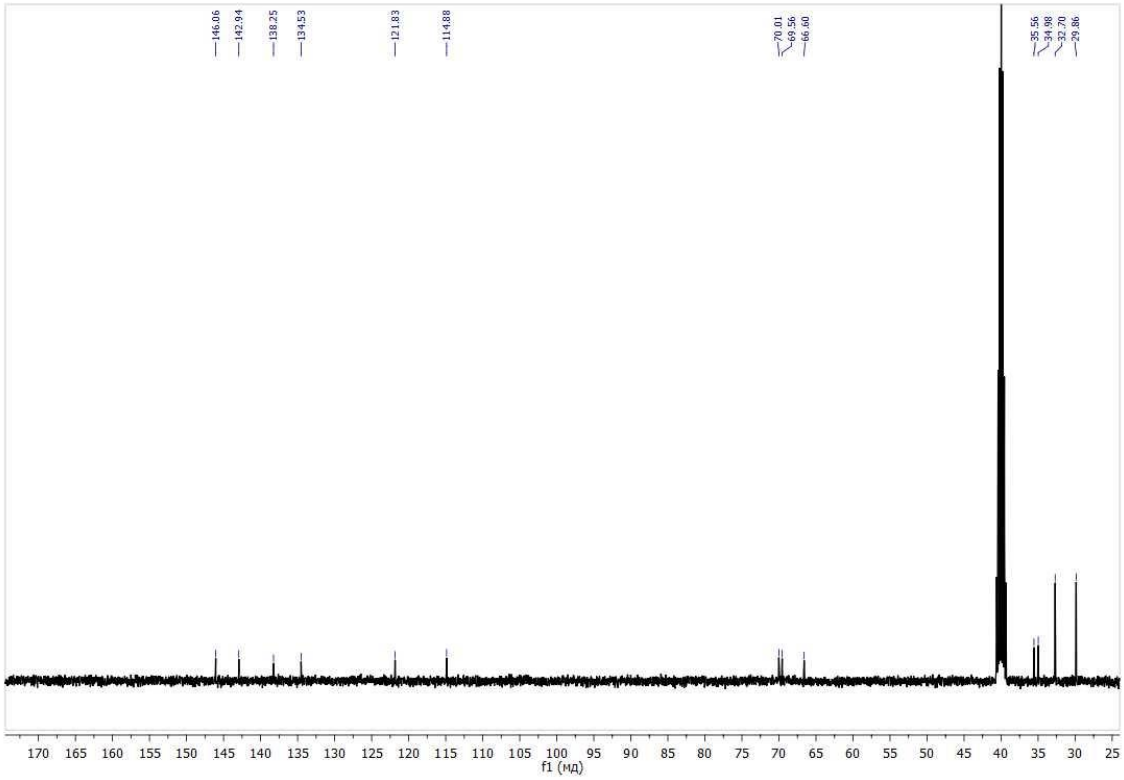
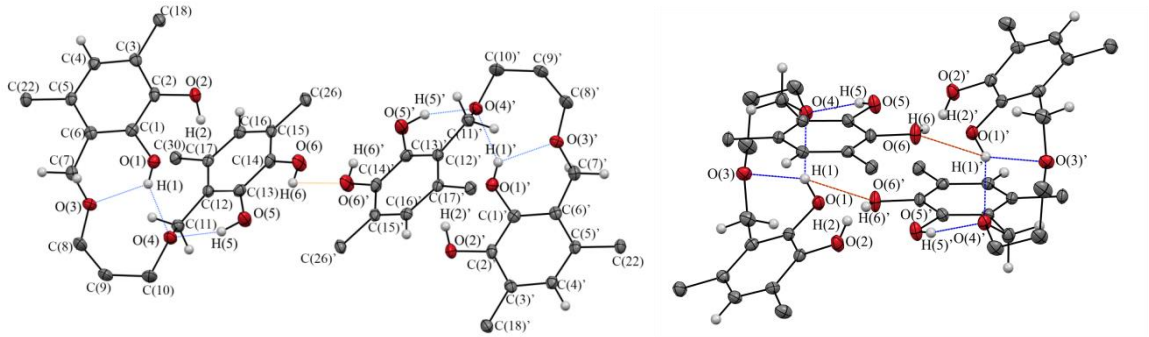


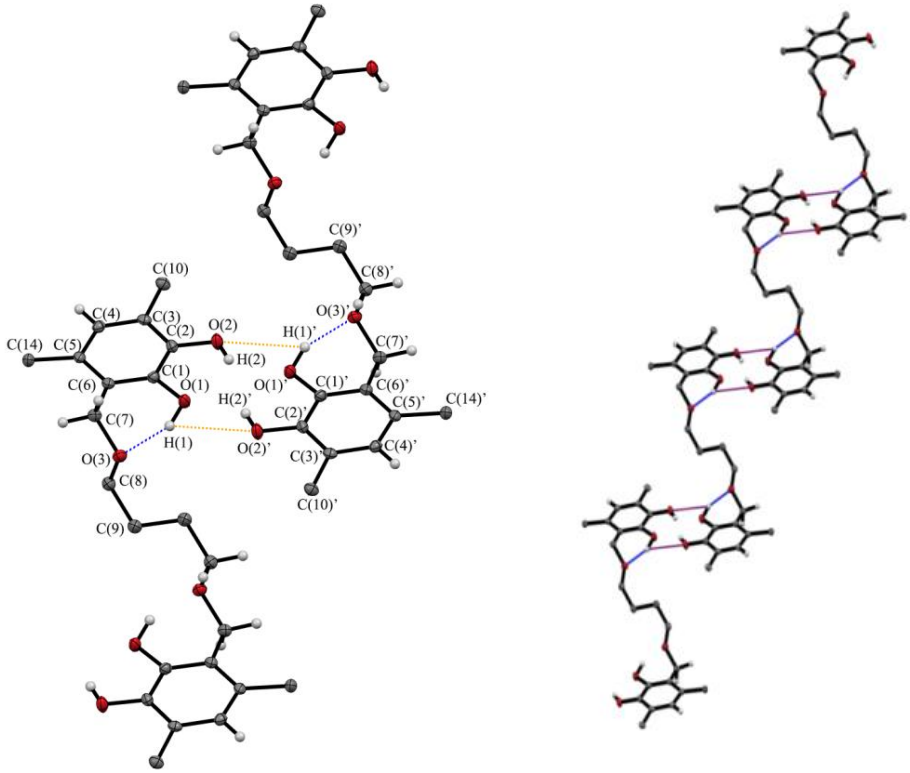
Figure S17. The ^{13}C NMR spectrum of **6f** (DMSO-d_6).

X-Ray diffraction studies

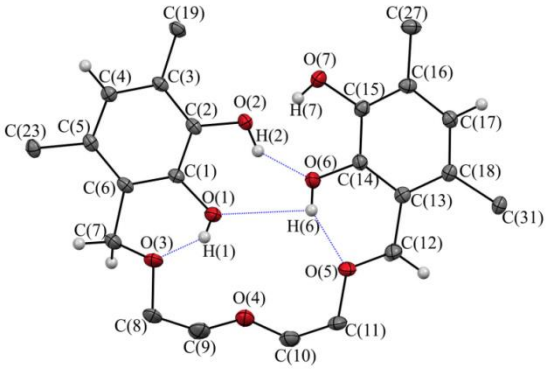
	Compound **5d** $C_{33}H_{52}O_6$	Compound **5c** $C_{34}H_{54}O_6$	Compound **5f** $C_{34}H_{54}O_7$
Formula weight	544.74	558.77	574.77
Crystal system	triclinic	monoclinic	orthorhombic
Space group	P-1	P2(1)/c	P2(1)2(1)2(1)
a (Å)	15.2122(5)	9.5182(7)	10.4399(4)
b (Å)	15.2891(5)	15.4117(9)	11.7539(6)
c (Å)	16.3234(5)	11.1199(8)	27.3482(11)
α (deg)	66.5230(1)		
β (deg)	66.0510(1)	93.932(7)°	
γ (deg)	84.7040(1)		
V (Å^3)	3171.51(18)	1627.36(19)	3355.9(3)
Z	4	2	4
ρ_{calcd} (g/cm^3)	1.141	1.140	1.138
Absorption coefficient (mm^{-1})	0.077	0.076	0.078
F(000)	1192	612	1256
Crystal size (mm^3)	0.37×0.18×0.09	0.30×0.30×0.10	0.40×0.30×0.20
Wavelength, Å	0.71073	0.71073	0.71073
2Θ (deg)	52	52	60.2
Reflections collected	28797	24478	57720
Indep reflections	12420 [R_{int} = 0.0247]	3191 [R_{int} = 0.0429]	9785 [R_{int} = 0.0360]
Final R indices [I>2σ(I)]	R1 = 0.0403	R1 = 0.0401	R1 = 0.0405
R indices (all data)	wR2 = 0.1033	wR2 = 0.1031	wR2 = 0.0967
GOF on F^2	1.038	1.033	1.048
Largest diff. peak and hole (e/ Å^3)	0.238 / -0.227	0.291 / -0.198	0.255 / -0.247



Compound **5d**



Compound **5c**



Compound **5f**

Figure S18. The molecular structures **5c**, **5d** and **5f**. The thermal ellipsoids are given with a 30% probability. Hydrogen atoms (with the exception of OH groups) are not shown for clarity.

The H-bonds for compounds **5d**, **5c** and **5f**

Compound **5d**	
H-bond	**Bond length, Å**
O(1)-H(1)…O(3)	2.23(2), 2.16(2)
O(1)-H(1)…O(4)	2.09(2), 2.00(2)
O(5)-H(5)…O(4)	1.79(2), 1.85(2)
O(6)-H(6)...O(5)	2.04(2), 2.15(2)
O(6)-H(6)…O(6)’	2.29(2)
O(1)’-H(1)’...O(6)	2.94(2)
O(1)-H(1)...O(6)’	2.94(2)
Compound **5c**	
O(1)-H(1)…O(3)	1.77(2)
O(2)-H(2)…O(1)’	2.16(2)
Compound **5f**	
O(2)-H(2)…O(6)	2.21(3)
O(6)-H(6)…O(5)	1.92(3)
O(6)-H(6)…O(1)	2.84
O(1)-H(1)…O(3)	1.86(3)