Inclusion Properties of Acyclic Phenol–Formaldehyde Oligomer Analogs Containing 2,2′-Dihydroxybiphenyl or 2,2′-Dihydroxy-1,1′-binaphthyl Unit

Tyo SONE,* Yoshitomo KOBORI, Yuji ANDO, and Yoshihiro OHBA
Department of Materials Science and Engineering, Faculty of Engineering, Yamagata University, Yonezawa 992
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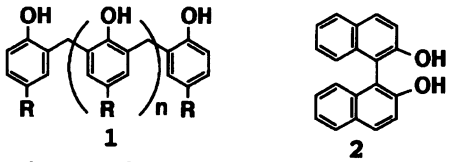
Synopsis. Acyclic phenol–formaldehyde tetramer and hexamer analogs containing 2,2′-dihydroxybiphenyl or 2,2′-dihydroxy-1,1′-binaphthyl unit as a central building block were synthesized. The tetramer analogs preferentially formed crystalline inclusion complexes with aromatic guests as the parent *p*-*t*-butylphenol–formaldehyde tetramer; those with the binaphthol unit were superior for complexation.

We recently reported that acyclic *p*-substituted phenol–formaldehyde oligomers **1** (Scheme 1; n=2—4) with methylene bridges ortho to phenolic OH groups could form crystalline inclusion complexes with a variety of organic compounds.[1a] The structural variations in the number of phenol units, the *p*-substituent of phenol, or the replacement of the methylene bridge(s) by other(s) such as sulfur[1b] and C=O[1c] markedly affect the inclusion behavior. Another feature of interest is that the oligomers undergo conformational changes in the inclusion of the guest molecules, as revealed by an X-ray structural study;[1d] the methylene bridges in the molecules apparently play a role in the inclusion. As an extension of the study, we synthesized an analog of **1a** which lacked the central methylene bridge in the molecule of **1a** and its 2,2′-dihydroxy-1,1′-binaphthyl analogs, and investigated their inclusion abilities towards liquid organic compounds by a recrystallization method. 2,2′-Dihydroxy-1,1′-binaphthyl (**2**) has itself been known as a versatile inclusion host.[2,3] Besides, the optically resolved **2** are effective in optical resolution of some classes of racemic compounds.[2b,3]

The target compounds were prepared via the routes shown in Scheme 2. The *p*-*t*-butylphenol-formaldehyde tetramer analog **5** containing 2,2′-dihydroxybiphenyl unit was obtained by the reaction of 5,5′-di-*t*-butyl-3,3′-bis(chloromethyl)-2,2′-dimethoxybiphenyl (**3**) with *p*-*t*-butylphenol in the presence of *p*-toluenesulfonic acid (TsOH), followed by ether-cleavage of the resultant methyl ether **4**. On the other hand, the compounds **8a**, **8b**, and **9**, with central 2,2′-dihydroxy-1,1′-binaphthyl unit corresponding to the tetramer (**1**; n=2) and the hexamer (**1**; n=4), were synthesized by the TsOH-catalyzed reactions of 2,2′-dihydroxy-3,3′-bis(hydroxymethyl)-1,1′-binaphthyl (**7**) with *p*-*t*-butylphenol, *p*-cresol, or 4,4′-di-*t*-butyl-2,2′-methylenediphenol (**1**; n=0, R=*t*−Bu), respectively. The attempt at acid-catalyzed condensation of **2** with 4-*t*-butyl-2-(hydroxymethyl)phenol to obtain **8a** was unsuccessful.



1

1a: n=2, R=t-Bu
1b: n=2, R=Me

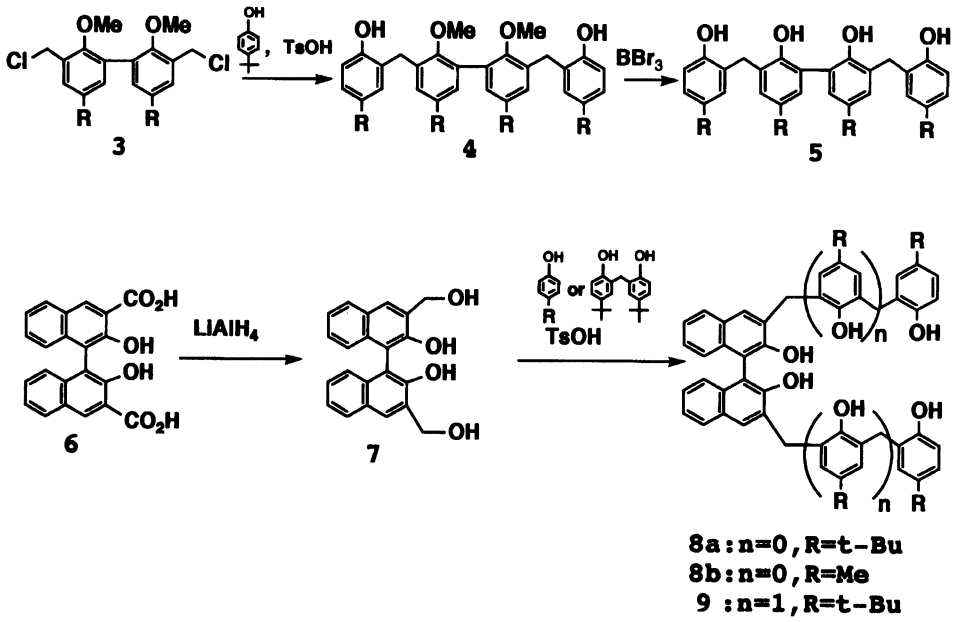
2

Scheme 1.

The synthesized compounds show OH stretching bands in the 3250—3380 cm^{-1} region in their IR spectra (KBr disk), indicative of somewhat weaker hydrogen bonding between the OH groups in their molecules than in the parent oligomers, which exhibit the bands at around 3250 cm^{-1}.[1a] Interestingly, the $ArCH_2Ar$ methylene protons of the binaphthol compounds, **8** and **9**, in the ^1H NMR spectra ($CDCl_3$; 270 MHz) appeared as a pair of doublets, while those of the parent tetramer **1a**[4] and the biphenol compound **5** appeared as singlets. This suggests that the binaphthol compounds are conformationally less flexible even in the solution at room temperature.

The inclusion behavior of the prospective hosts **5**, **8a**, **8b**, and **9**, was examined towards liquid organic guests (Table 1). The biphenol derivative **5** which lacked the central methylene bridge in the parent tetramer **1a** showed moderate inclusion behavior; **5** was less effective than the parent tetramer **1a**, but instead had a tendency to complex methanol and ethanol. The host–guest ratios (H:G) in its complexes with the aromatic guests are 1:1, while it is 2:1 in most of the similar complexes of **1a**, indicating an essential difference in the complexation mode between the two. The methyl ether **4** has no inclusion ability towards the guests examined, which demonstrates the importance of the presence of four adjacent phenolic OH groups for the construction of an inclusion lattice in the molecule of **5**.

The binaphthol derivatives, **8a** and **8b**, also behaved as hosts, and were similar to the tetramer **1a** in guest selectivity. The most remarkable feature of the two hosts is that they preferentially form complexes with aromatic guests but not with the simple alcohols and acetone. The results show the binaphthol hosts form complexes with the guests mainly via van der Waals interactions. This presents a striking contrast to the inclusion behavior of the basic component **2**[2,3] or phenolic hosts[5] which preferably include molecules capable of forming hydrogen bonds, but are ineffective to aromatic guests. The binaphthyl hosts, **8a** and **8b**, are superior to the biphenol host **5** in the inclusion of aromatic guests. This may be ascribable to the increase in



Scheme 2.

Table 1. Crystalline Inclusion Complexes of 2,2′-Dihydroxybiphenyl and 2,2′-Dihydroxy-1,1′-binaphthyl Hosts

Guest (G)	Host (H)							
	4	**5**	**8a**	**8b**	**9**	**1a**[b]	**1b**[b]	**2**
	(H : G)							
Cyclohexane	–	–	–	2 : 1	–	1 : 2	–	–
Methanol	–	+	–	–	–	–	–	1 : 2[c]
								–[d]
Ethanol	–	+	–	–	–	–	–	–[d]
Acetone	–	–	–	–	–	–	–	–[d]
								1 : 1[c]
Dioxane	–	1 : 1	1 : 1	1 : 1	–	2 : 1	1 : 1	1 : 2[c]
								1 : 1[d]
Dichloromethane	–	2 : 1	1 : 1	1 : 1	–	–	2 : 1	–
Benzene	–	–	1 : 2	1 : 1	–	2 : 1	2 : 1	–[d]
Toluene	–	–	2 : 1	1 : 1	–	1 : 1	–	–
Ethybenzene		–	2 : 1			–		–
Butylbenzene		–	–			–		–
o-Xylene	–	1 : 1	2 : 1	+	–	2 : 1	–	–
m-Xylene	–	–	2 : 1	1 : 1	–	2 : 1	–	–
p-Xylene	–	1 : 1	2 : 1	1 : 1	–	2 : 1	–	–
Mesitylene		–	–			–		–
Bromobenzene		1 : 1	2 : 1			1 : 1		–
1-Methylnaphthalene		2 : 1	2 : 1			1 : 1		–
1-Bromonaphthalene		–	2 : 1			1 : 1		–

a) – host-guest complex does not form. + host-guest ratio is not clear.
b) See Ref. 1a. c) See Ref. 2b. d) See Ref. 3.

the nonpolar surface area by enlargements of the basic skeleton by an extra aromatic ring, which strengthens the van der Waals forces in the host-guest interactions.

The compound **9**, an analogue to the phenol–formaldehyde hexamer (**1**; n=4), shows no inclusion properties at all, reflecting the earlier observation that the parent hexamer is decidedly inferior to the tetramer.[1a)]

The results obtained here indicate that the central methylene bridge in the phenol–formalaldehyde oligomers is not essential for the construction of the inclusion lattices.

It also became apparent that a slight structural modification produces a complete change in the inclusion mode. Thus, **8a** involving terminal *p*-*t*-butylphenols

forms complexes with the aromatic guests with the H : G ratio of 2 : 1, while **8b** consisting of *p*-cresols forms 1 : 1 complexes. Further, in spite of the difference in the inclusion mode, thermal stabilities of their benzene complexes which were evaluated from their thermal dissociation rates are very similar; the enthalpy of activation, $\Delta H^{\neq}$, was 113.5 kJ mol^{-1} for the **8a** complex and 118.7 kJ mol^{-1} for the **8b** complex, the values being comparable to those of the benzene complexes (H : G = 2 : 1) of the parent tetramers, **1a** and **1b** (123 and 110.0 kJ mol^{-1}, respectively).[1a)]

Experimental

All melting points are uncorrected. NMR spectra were obtained on a JEOL JNM-EX270 (270 MHz) spectrometer using TMS as an internal reference. IR and mass spectra (70 eV) were recorded on a Hitachi EPI-S2 and on a Hitachi UMU-6MG spectrometer, respectively. TG/DTA curves were recorded on a Seiko TG/DTA30 instrument with a heating rate of 10 °C min^{-1} under air stream.

5, 5′-Di-*t*-butyl-3, 3′-bis(5-*t*-butylsalicyl)-2, 2′-dimethoxybiphenyl (4). A mixture of 5,5′-di-*t*-butyl-3, 3′-bis(chloromethyl)-2,2′-dimethoxybiphenyl (**3**; 3.5 g, 10.7 mmol),[6)] *p*-*t*-butylphenol (40.3 g, 0.27 mol), *p*-TsOH (0.2 g, 1.2 mmol), and toluene (70 ml) was stirred at 100 °C for 25 h. Excess *p*-*t*-butylphenol and the solvent were removed by steam distillation. The residual mass was recrystallized from a mixture of hexane and benzene to afford **4** (3.5 g, 65%): Colorless powder, mp 197—198 °C; IR (KBr) 3400, 2970, 2900, 2870, 1480, 1280, 1240, and 1010 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.29 (18H, s), 1.31 (18H, s), 3.49 (6H, s), 3.93 (4H, s), 6.82 (2H, d, J=8.6 Hz), 7.14 (2H, dd, J=2.6 and 8.6 Hz), 7.2—7.3 (4H, m), and 7.33 (2H, d, J=2.6 Hz); MS m/z 650 (M^+, 30%). Found: C, 80. 98; H, 9.18%. Calcd for $C_{44}H_{58}O_4$: C, 81.18; H, 8.98%.

5,5′-Di-*t*-butyl-3,3′-bis(5-*t*-butylsalicyl)-2,2′-dihydroxybiphenyl (5). A solution of boron tribromide (2.0 g, 8 mmol) in CH_2Cl_2 (65 ml) was added to an ice-cooled solution of **4** (1.0 g, 1.5 mmol) in CH_2Cl_2 (55 ml) during a period of 25 min with stirring. After stirring at room temperature for 90 min, the mixture was poured onto ice-water. The organic layer was separated and the aqueous layer was extracted with CH_2Cl_2 (100 ml). The combined CH_2Cl_2 solution was washed with saturated NaCl solution, dried, and concentrated. The residue was recrystallized from hexane to give **5** (0.9 g, 94%): Colorless powder, mp 207—209 °C; IR (KBr) 3300, 2970, 2900, 2870, 1480, and 1280 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.29 (18H, s), 1.30 (18H, s), 3.96 (4H, s), 6.74 (2H, d, J=8.3 Hz), 7.00 (2H, br s), 7.10 (2H, dd, J=2.6 and 8.3 Hz), 7.11 (2H, d, J=2.6 Hz), 7.33 (2H, d, J=2.6 Hz), 7.37 (2H, d, J=2.6 Hz), and 7.56 (2H, br s); MS m/z 622 (M^+, 49%). Found: C, 80.72; H, 8.77%. Calcd for $C_{42}H_{54}O_4$: C, 80.99; H, 8.74%.

2,2′-Dihydroxy-3,3′-bis(hydroxymethyl)-1,1′-binaphthyl (7). A solution of 3,3′-dicarboxy-2,2′-dihydroxy-1,1′-binaphthyl (**6**)[7)] (3.8 g, 0.01 mol) in dry tetrahydrofuran (THF; 50 ml) was added over a 1 h period to a suspension of $LiAlH_4$ (3.0 g, 0.08 mol) in the boiling THF (80 ml). The mixture was refluxed for 3.5 h and then cooled. Aqueous HCl solution (20%; 40 ml) was added to the mixture and the THF layer was separated. The aqueous layer was extracted twice with ether. The combined organic layers were washed with saturated NaCl solution and dried. Evaporation of the solvents, followed by recrystallization of the residual mass from THF, yielded **7** (2.64 g, 75%): Yellow crystals, mp 193—195 °C (lit,[7)] 192—195 °C).

3,3′-Bis(5-*t*-butylsalicyl)-2,2′-dihydroxy-1,1′-binaphthyl (8a). A mixture of **7** (2.1 g, 6.06 mmol), *p*-*t*-butylphenol (18 g, 0.12 mol), *p*-TsOH (0.1 g, 0.6 mmol), and benzene (150 ml) was refluxed with stirring for 6 h; the water produced during the reaction was removed by azeotropic distillation using a Dean–Stark condenser. Work-up as described for the preparation of **5** and column chromatography (Merck, silica gel 60; AcOEt/hexane=1 : 3) of the raw product gave **8a** (2.2 g, 60%): Colorless powder, mp 175—176 °C (cyclohexane); IR (KBr) 3380, 3070, 2970, 1510, 1230, and 1210 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.32 (18H, s), 4.17 and 4.19 (2H, d, J=15.2 Hz each), 5.70 (2H, br s), 6.05 (2H, br s), 6.78 (2H, d, J=8.6 Hz), 7.06 (2H, d, J=8.2 Hz), 7.16 (2H, dd, J=2.3 and 8.6 Hz), 7.20—7.35 (4H, m), 7.37 (2H, d, J=2.3 Hz), 7.83 (2H, d, J=7.9 Hz), and 7.88 (2H, s); MS m/z 610 (M^+, 31%). Found: C, 82.04; H, 7.12%. Calcd for $C_{42}H_{42}O_4$: C, 82.59; H, 6.93%.

3,3′-Bis(5-methylsalicyl)-2,2′-dihydroxy-1,1′-binaphthyl (8b). Prepared by the reaction of **7** with *p*-cresol analogously to the preparation of **8a**. Yield, 43%. Colorless needless, mp 156—157 °C (cyclohexane); IR (KBr) 3380, 1510, 1430, 1330, and 1220 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=2.29 (6H, s), 4.13 and 4.15 (2H, d, J=10.5 Hz each), 5.69 (2H, s), 6.04 (2H, s), 6.73 (2H, d, J=8.4 Hz), 6.94 (2H, dd, J=1.9 and 8.4 Hz), 7.04 (2H, d, J=8.4 Hz), 7.16 (2H, d, J=1.9 Hz), 7.20—7.40 (4H, m), 7.83 (2H, d, J=7.8 Hz), and 7.89 (2H, s); MS m/z 526 (M^+, 57%). Found: C, 82.02; H, 5.84%. Calcd for $C_{36}H_{30}O_4$: C, 82.11; H, 5.74%.

3,3′-Bis[5-*t*-butyl-3-(5-*t*-butylsalicyl)-2-hydroxybenzyl]-2,2′-dihydroxyl-1,1′-binaphthyl (9). Prepared by the reaction of **7** with 4,4′-di-*t*-butyl-2,2′-methylenediphenol (**1**; n=0, R=*t*-Bu)[8)] analogously to the preparation of **8a**. Yield, 31%. Colorless powder, mp 225—226 °C (cyclohexane); IR (KBr) 3250, 2900, 1510, 1480, 1350, 1270, 1240, 1120, and 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ=1.25 (18H, s), 1.33 (18H, s), 3.84 and 3.96 (2H, d, J=13.7 Hz each), 4.00 and 4.36 (2H, d, J=14.8 Hz each), 6.72 (2H, d, J=8.6 Hz), 6.80 (2H, br s), 7.00 (2H, d, J=8.2 Hz), 7.05 (2H, dd, J=2.6 and 8.6 Hz), 7.15—7.30 (8H, m), 7.33 (2H, d, J=2.6 Hz), 7.57 (2H, br s), 7.83 (2H, d, J=7.6 Hz), 7.90 (2H, s), and 8.30 (2H, br s); MS m/z 934 (M^+, 41%). Found: C, 82.02; H, 7.35%. Calcd for $C_{64}H_{70}O_6$: C, 82.19; H, 7.54%.

Preparation of Inclusion Complex. The prospective host was recrystallized using a minimum amount of organic solvent (guest). The precipitates were collected by filtration and dried overnight at ambient temperature. The host–guest ratio was determined by means of ^{1}H NMR spectroscopy.

Evaluation of Thermal Stability of Inclusion Complex. The weight-decreasing rate of a complex was measured from the TG-DTA curve, using Al_2O_3 as a reference. The programmed temperature was raised at a rate of 10 °C min^{-1} up to each temperature. Based on the rate constants thus obtained, the $\Delta H^{\neq}$ values were calculated by a least-squares method.

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