Synthesis and Thermal Behaviors of Hindered Biphenols
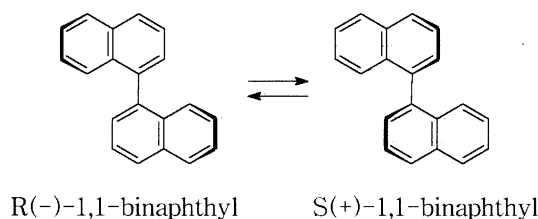
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Received November 13, 1998

The ability of an organic compound to crystallize in several forms is far more frequent than is generally supposed. It has been reported that 1,1'-binaphthyl has two melting points (mp 145 °C and 158 °C) which have been noted two crystalline forms.[1,2] Its dissymmetry is molecular characteristics in nature, and enantiomer interconversion is possible simply by the rotation about the interannular bond without any bond-breaking process. The crystals of 1,1'-binaphthyl resolve via a racemate → melt → eutectic phase transition from $|\alpha|_D$ 1-10° to $|\alpha|_D$ > 200° at 150 °C in the desired positive or negative direction within a few minutes.[3] The hindered biphenols also could exhibit a noncoplanar structure because the substituents in 2,2' positions of biphenols inhibit bond rotation. The noncoplanar structure of hindered biphenol could provide chirality along the 1,1'-biphenyl axis if the rotation barrier is high enough. We here report the synthesis of various hindered biphenols from di and tri-substituted phenols, the thermal behavior of hindered biphenols using differential scanning calorimetry (DSC), as well as the calculated dihedral angles of these biphenols.

R(−)-1,1-binaphthyl   S(+)-1,1-binaphthyl

Experimental Section

^{1}H NMR spectra were taken in CDCl3 solution on a Varian XL-200 instrument, and chemical shifts are given in parts per million downfield from tetramethylsilane as internal standard. Mass spectra were recorded on a ZAB 2F HS spectrometer, ion source 240 °C and 70 eV electron impact, direct inlet: m/z (assignment). Melting points were determined on a Fisher-Johns melting point apparatus. Elemental analyses were performed by Galbraith Laboratories Inc. Pure 2,6-diphenylphenol was supplied by General Electric Company. 1,3-Diphenylacetone and butyronitrile were purchased from Aldrich Chemical Co.. Common reagents, e.g. copper chloride, sodium methoxide, and hydrazine monohydrate (98%) were used without further purification. The reactions were routinely monitored on a Milton Roy HPLC instrument, using a Spherisorb ODS 2 reverse-phase column (250×4.6 mm, 5 mm) with methanol as an eluent at a flow rate of 1.0 mL per minute with a UV detector set at 254 nm

wavelength. Differential scanning calorimetry (DSC) was performed with a Seiko 220 DSC at a heating rate of 10 °C/min with a gas flow rate of 50 mL/min.
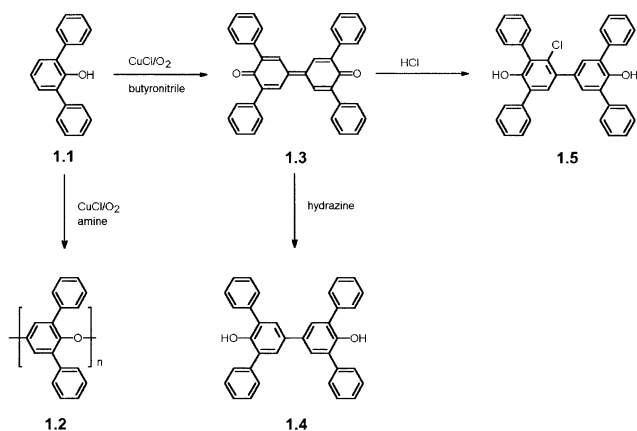
Preparation of 2,2',3,3',5,5'-hexaphenylbiphenyl-4,4-diol (2.4a). Diphenylacetone (11.36 g, 54 mmol), cinnamaldehyde (7.14 g, 54 mmol), and diethylamine (5 mL) were stirred slowly at room temperature. The reaction is exothermic, and the product forms a yellow deposit on the side of the flask. The resulting 2,3,5-triphenylcyclohex-2-enone **2.1a** was recrystallized in ethanol (15.9 g, 91% yield); mp 131-133 °C. The ketone reacted with 5% Pd/C (1 g) on heating to 250 °C for 30 min. After the mixture was allowed to cool, the organics were dissolved in hot ethyl acetate and filtered. The white product crystallized during the cooling to yield 2,3,6-triphenylphenol **2.2a** (69%); mp 164 °C. This phenol was stirred in butyronitrile (50 mL) with CuCl (0.4 g) while bubbling oxygen at 100 °C for 8 h. The reaction mixture was cooled and filtered to remove the catalyst. The filtrate containing a mixture of biphenols **2.4a** and biphenoxy radical **2.3a** was evaporated. The residue was reduced with hydrazine (0.5 mL) in chloroform (50 mL) and acetic acid (10 mL) at reflux temperature until the solution became colorless. The reaction mixture was filtered and the solvent was distilled. The crude product was recrystallized in methanol and chloroform and yielded 65%; mp 248, 259 °C. MS (EI) m/z: 642 (M+). Elemental analysis (%). calculated for $C_{48}H_{34}O_2$: C, 89.69; H, 5.33. Found: C, 89.82; H, 5.76. ^{1}H NMR (200 MHz, CDCl3) δ 5.06 (s, 2 H, OH), 6.96-7.37 (m, 32H, ArH).

2,2'-Dimethyl-3,3',5,5'-tetraphenylbiphenyl-4,4'-diol (2.4b). Dibenzylketone (100 g, 0.48 mol) and acrolein (33.3 g, 0.48 mol) were stirred with diethylamine (50 mL) at room temperature for 3 hrs. The crude residue was purified by Kugelrhor distillation under vacuum at 100 °C and recrystallized from methanol to yield 3-methyl-2,6-diphenylcyclohex-2-enone **2.1b** (101 g, 85%); mp 99-101 °C. This ketone (80 g, 0.32 mol) was dehydrogenated in the presence of 4 g of 5 wt% palladium on carbon catalyst for 20 min at 260 °C. The reaction mixture was cooled and extracted with hot ethanol and the catalyst was removed by filtration. The solvent was evaporated under reduced pressure and the recovered solid was recrystallized from hexane to yield 2,6-diphenyl-3-methylphenol[1] **2.2b** (65.1 g, 83%); mp 130-131 °C. ^{1}H NMR (200 MHz, CDCl3) δ 2.12 (s, 3 H, CH3), 5.01 (s, 1 H, OH), 6.95-7.71 (m, 12 H, ArH). This phenol (50 g, 0.19 mol) was treated with CuCl (3.8 g) and butyronitrile (400 mL). The reaction was heated to 100 °C while bubbling oxygen through for 4 hrs. A white solid precipitated during the

reaction. The heterogeneous solution was cooled and filtered. The precipitate was recrystallized from ethanol and chloroform to yield **2.4b** (44.6 g, 85%); mp 281-283 °C. MS (EI) *m/z*: 518 (M$^+$). Elemental analysis (%), calculated for $C_{38}H_{30}O_2$: C, 88.00; H, 5.83. Found: C, 87.21; H, 5.80. ^1H NMR (200 MHz, CDCl$_3$) δ 1.87 (s, 6 H, methyl), 4.96 (s, 2 H, OH), 7.23-7.63 (m, 22 H, ArH).

Results and Discussion

3,3',5,5'-Tetraphenylbipheny-4,4'-diol **1.4** and 2-chloro-3,3',5,5'-tetraphenylbiphenyl-4,4'-diol **1.5** were prepared by the literature procedures[5,6] (Scheme 1). The oxidative coupling of 2,6-diphenylphenol **1.1** with a CuCl-amine catalyst and oxygen was reported by Hay to yield a high molecular weight poly(phenylene oxide) **1.2** *via* carbon-oxygen coupling.[5-7] However, the corresponding diphenoquinone is obtained by oxidation reaction using a nitrile such as butyronitrile or benzonitrile as the ligand and solvent at 100 °C.[8,9] The diphenoquinone **1.3** can then be reduced to 3,3',5,5'-tetraphenylbiphenol **1.4** in hot chloroform with hydrazine. The diphenoquinone **1.3** has been shown to react with hydrogen chloride to give the chloro-substituted biphenol **1.5** through 1,4 addition.[9] The 2,3,6-triphenylphenol **2.1a** was prepared by the condensation reaction of cinnamaldehyde with dibenzylketone in presence of diethylamine. The product was afforded a mixture of two compounds with very close retention times in the HPLC and approximate peak ratios of 7 to 3 with an overall yield of 96%. The major product was presumably the isomeric cyclohexanone which results from dienol. The resulting cyclohexenone **2.1a** was dehydrogenated with Pd/C at 260 °C to give 2,3,6-triphenylphenol **2.2a**. To prepare the carbon-carbon coupling compound **2.4a** phenol **2.2a** can be oxidatively coupled to highly hindered 2,2',3,3',5,5'-hexaphenylbiphenol **2.4a** with CuCl, oxygen, and butyronitrile. In this case, because of steric hindrance, the central rings cannot be coplanar and presumably the oxidized product exists as a bisphenoxy radical **2.3a** which in contrast to the diphenoquinones[5] is extremely soluble in nonpolar solvents. The 2,6-diphenyl-3-methylphenol **2.2b** has been prepared previously[4] The corresponding biphenol

Scheme 1

Table 1. Thermal Analysis of Biphenols

Bisphenols	First run (°C)	Second run (°C)	Comments
1.4	T$_{exo}$ 154 mp 196	T$_g$ 84	glass state (after first heating)
1.5	mp 210	T$_g$ 93	glass state (after first heating)
2.4a	T$_{exo}$ 171 mp 248, 259	T$_g$ 126 T$_{exo}$ 192 mp 259	two melting points semi-crystalline (after first heating)
2.4b	mp 283	mp 284	crystalline (after first heating)

2.4b was prepared using identical methodology.

We studied the biphenols by a differential scanning calorimetry (DSC) in the range of 25 °C to 320 °C at heating rate of 10 °C/min and the results are summarized in Table 1. Upon heating, different curves can be obtained depending on the history of sample and the speed of the crystal-crystal transformation. A first heat of biphenols **1.4** and **2.4a** shows both endothermic and exothermic peaks while biphenols **1.5** and **2.4b** only show endothermic peaks for their melting points (Figure 1). The exothermic peaks may be explained by crystal to crystal transformation.[2,3] Biphenols **1.4**, **1.5**, and **2.4a** convert to the glassy state when the biphenols are cooled after the first heat, and glass transition temperature of 84 °C, 93 °C, and 126 °C respectively were observed during the second heat (Figure 2). During the second heat, the biphenol **2.4b** showed the same thermogram as in the first heat. Interestingly, biphenol **2.4a** shows two melting points at 248 °C and 259 °C whereas the other biphenols have single melting points. The thermal behavior of biphenol **2.4a** is similar to that of binaphthyl which has two crystalline structures (mp 145 °C and 158 °C) known from X-ray structural analysis.[3,10,11] The low melting form, mp 145 °C, is racemic compound and is optically inactive. The high melting form, mp 158 °C, is an eutectic mixture of individual R and S crystals, and shows optical activity. This unusual solid state reso-
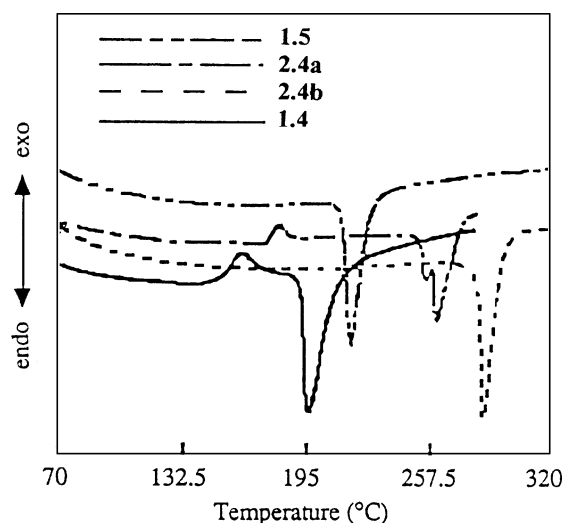
Figure 1. DSC traces (first heating) of biphenols were performed at a heating rate 10 °C/min.
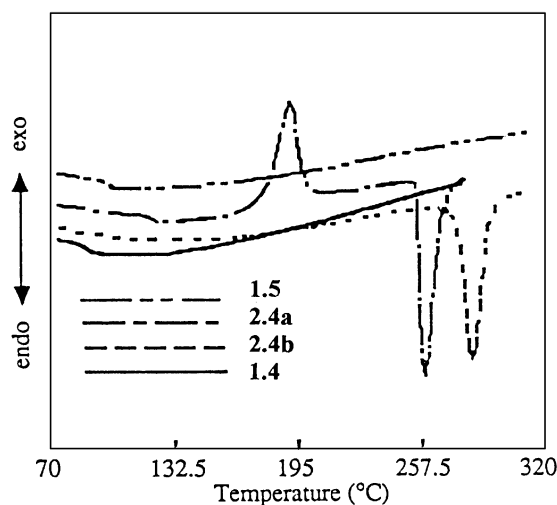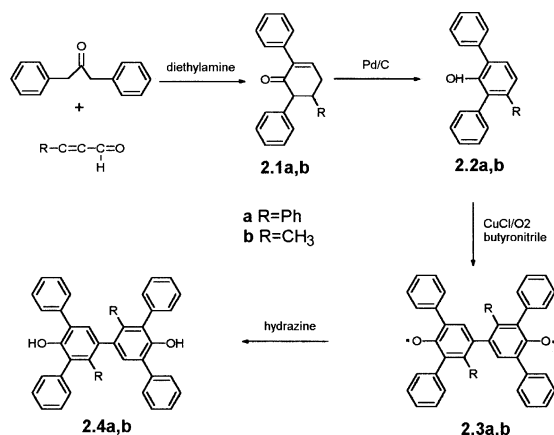
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Figure 2. DSC traces (second heating) of biphenols were performed at a heating rate 10 °C/min.

2.4a-1   2.4a-2

Figure 3. Semiempirical minimum energy structures calculated for 2.4a using Cache work system.

lution is made possible by a phase transformation from a racemic compound (mp 145 °C) to an unequal eutectic mixture (mp 158 °C) of enantiomorphic crystals, with the necessary enantiomer conversion occurring entirely in the solid state. A glass transition temperature of biphenol **2.4a** was observed at 126 °C followed by an exothermic peak at 192 °C, which may be crystal to crystal transformation, and a single melting point at 259 °C.

The effect of substituents at positions 2,2',6,6' on the dihedral angles and the rotational barriers of biphenols is well documented.[12] The dihedral angles in tetra-substituted biphenyls are 90° and rotational barriers are high even when the subtituents are relatively small such as in 2,2'-difluoro-6,6'-dimethoxybiphenyl (E_{rot} ~ 35-39 kcal/mol).[13] Di-substituted biphenyls are much more difficult to resolve because of their lower rotational barriers, which are in the 18-21 kcal/mol range for 2,2'-dibromo, 2,2'-diiodo, and 2,2'-ditrifluoromethyl biphenyl.[14] The dihedral angle for biphenyl is 20° in solution,[15] whereas 2,2'-disubstituted biphenyls in the vapor phase, in solution, and in the crystalline state range from 60° for 2,2'-difluorobiphenyl to 79° for 2,2'-diiodobi-
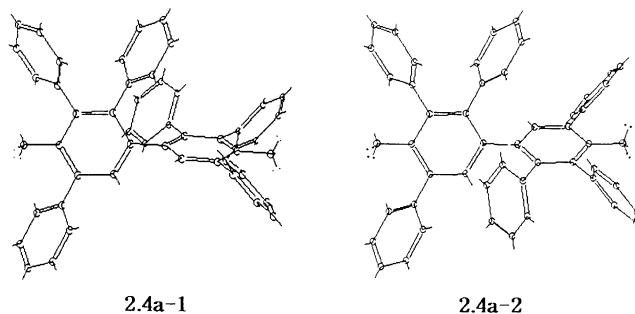
phenyl.[16] Recently, several semiempirical geometry of the 1,1'-binaphthyl derivatives with fixed rotational σ-bond angles were used to estimate barriers to rotation with MNDO and AM1.[17] We have been calculated the molecular models of 3,3',5,5'-tetraphenyl biphenol **1.4** by CHEM 3D Plus™,[18] which shows 12° twisted conformation of the central biphenyl. Molecular models of hindered biphenols, 3-chloro-2,2',6,6'-pentaphenylbiphenol **1.5**, 2,2',3,3',6,6'-hexaphenylbiphenol **2.4a**, and 3,3'-dimethyl-2,2',6,6'-tetraphenylbiphenol **2.4b** were obtained from Cache work system.[19] Dihedral angles of 3,3'-dimethyl-2,2',6,6'-tetra-phenylbiphenol **2.4b** and 3-chloro-2,2',5,5'-tetraphenylbiphenol **1.5** are 75° and 65°, respectively. The noncoplanarity of the biphenyl rings in **2.4a** is associated with interesting feature of phenyl substituents in 2,2' positions and phenyl groups in 2,2'-positions were affected by phenyl substituents in the 3,3',5,5' positions. The two structures of 2,2',3,3',5,5'-hexaphenylbiphenol **2.4a** are shown in Figure 3. The dihedral angles of 2,2',3,3',5,5'-hexaphenylbiphenol **2.4a** are 56° and -67°, which has two different conformations (**2.4a-1**, **2.4a-2**). The 2,2'-diphenyl substituents of **2.4a-1** approximately lie in same side of biphenyl axis and place in parallel face. Presumably, this result may be explained that the π-orbitals of the phenyl substituent in 2 position of biphenol enable a π-interaction with phenyl substituent in 2' position of biphenol.[17] The 2,2'-diphenyl substituents of **2.4a-2** lie in opposite side of biphenyl axis and this twisted arrangement could be possible for providing less steric hindrance conformation between two phenyl substituents.

2.1a,b   2.2a,b

a R=Ph
b R=CH₃

2.4a,b   2.3a,b

Scheme 2

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18. Chem 3D Plus[TM] Version 3.0 is a Molecular Modeling System.

19. The Cache work system uses Allinger's standard MM2.