

Axial structures of biphenyl compounds linked by diethyl ether chains

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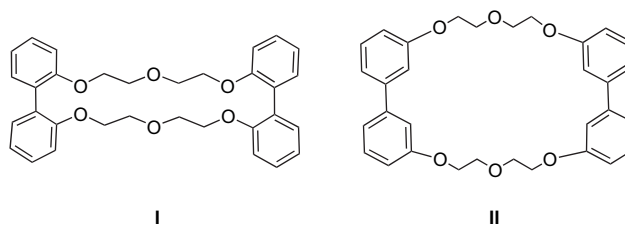
Abstract—Two simple biphenyl compounds, **I** and **II**, linked by diethyl ether chains have been synthesized. These biphenyl compounds are able to respectively rotate about an internal axis. From X-ray analyses, it was found that the 2,2'-linked biphenyl compound **I** can transmit the same axial chirality of the biphenyl backbones through the diethyl ether chains. On the other hand, in the 3,3'-linked biphenyl compound **II**, the opposite axial chirality of the biphenyl backbones is transmitted.

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1. Introduction

It is known that biphenyl compounds have an internal rotation axis. It is possible to control the rotation about this internal axis by introducing substitutions into appropriate positions of the biphenyl backbone.¹ It is also possible to control the axial chirality of the biphenyl backbone by the steric and electronic effects of the substituents.² A diethyl ether chain has been used both as a molecular binding site and as a connecting unit in wire-like molecules.³ A biphenyl derivative joined by diethyl ether chains has been reported previously;⁴ however, no direct information concerning the structure was given.

We report here the considerably high overall yield synthesis of two simple biphenyl compounds, **I** and **II**, linked by diethyl ether chains by using a novel synthetic route, and the crystal structure as well as the chiral transfer of the biphenyl backbone in these compounds.



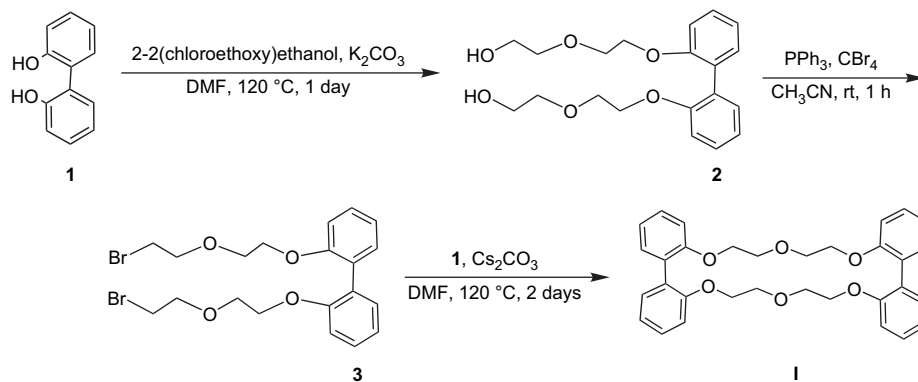
Biphenyl compound **I** has two diethyl ether chains in the 2,2'-positions of the biphenyl backbone. Biphenyl compound **II** is connected by two diethyl ether chains in the 3,3'-positions of the biphenyl backbone. The crystal structures of these compounds provide important information on axial structures of biphenyl derivatives in polymer and macromolecular chemistry.

2. Results and discussion

Although the synthesis of compound **I** has been previously reported, the overall yield from the starting compound was very low (7%).⁵ In this work, we attempted a novel synthesis of compound **I** via biphenyl derivative **3** (Scheme 1). As a result, compound **I** could be obtained in three steps in 38% overall yield from 2,2'-biphenol (**1**).

Keywords: Axial chirality; Biphenyl; Chiral transfer; Crystal; Diethyl ether chain.

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Scheme 1. Synthesis of compound **I**.

Novel compound **II** was synthesized from 3,3'-biphenol via the same synthetic route as compound **I** (Scheme 2) in 30% overall yield.

In order to study the transmission of structural information from the biphenyl backbone through the diethyl ether chains, the crystal structures of these compounds were studied by X-ray crystallography. The crystallization of compound **I** from an acetone solution produced good colorless crystals. From X-ray analysis, the space group of this crystal is $P\bar{1}$. In crystal **I**, there are two independent molecules, **I(A)** and **I(B)**, in an asymmetric unit. Inclusion of solvent molecules was not observed. In Figure 1, both (*R,R*)-**I(A)** and (*R,R*)-**I(B)** molecules are demonstrated. The torsion angles of the two biphenyl units are 60.36 and 67.55° in **I(A)**, and 59.74 and 65.70° in **I(B)**, respectively. In each molecule, the absolute configuration (axial chirality) of the two biphenyl units is identical.

I(A) and **I(B)** molecules form column structures along the *a*-axis of crystal **I** (Fig. 2). One column is composed of (*R,R*)-**I(A)** (Fig. 2a, indicated in orange) and (*S,S*)-**I(A)** (Fig. 2, indicated in red) molecules. These two molecules are alternately arranged along the *a*-axis (Fig. 2a) and are connected by both intermolecular π - π and CH- π interactions. The π - π interaction (3.7 Å) is observed between the benzene ring in (*R,R*)-**I(A)** and the benzene ring in

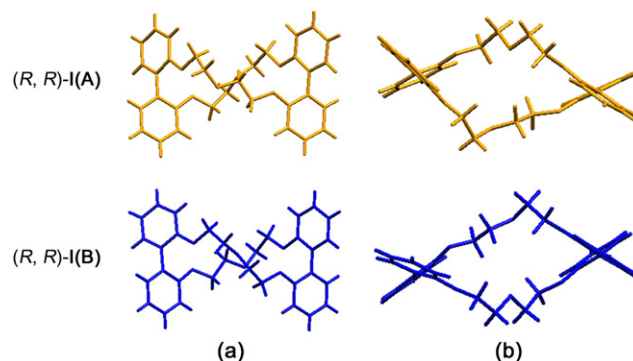
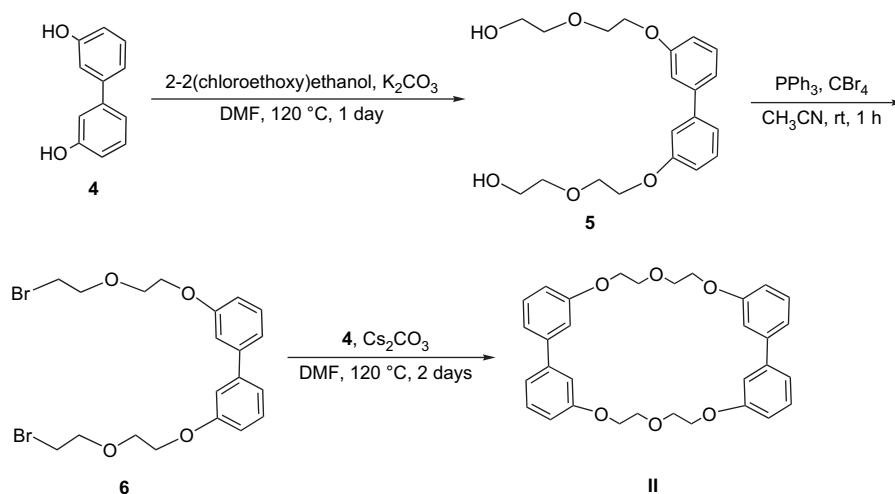


Figure 1. Crystal structures of (*R,R*)-**I(A)** and (*R,R*)-**I(B)** molecules. (a) View from the side of the biphenyl unit. (b) View down the internal axis of the biphenyl unit.

(*S,S*)-**I(A)** (Fig. 2a, indicated by blue arrows). Moreover, a CH- π interaction (2.96 Å) is also observed between the benzene ring in the biphenyl unit and a proton of the diethyl ether chain (Fig. 2a, indicated by red arrows). Similar to **I(A)**, in the column structure of **I(B)**, (*R,R*)-**I(B)** (Fig. 2b, indicated in blue) and (*S,S*)-**I(B)** (Fig. 2b, indicated in green) molecules are connected by both π - π and CH- π interactions. The π - π interaction (3.8 Å) is shown between the benzene rings in (*R,R*)-**I(B)** and (*S,S*)-**I(B)** (Fig. 2b, indicated by blue arrows). The CH- π interaction (2.93 Å) is shown



Scheme 2. Synthesis of compound **II**.

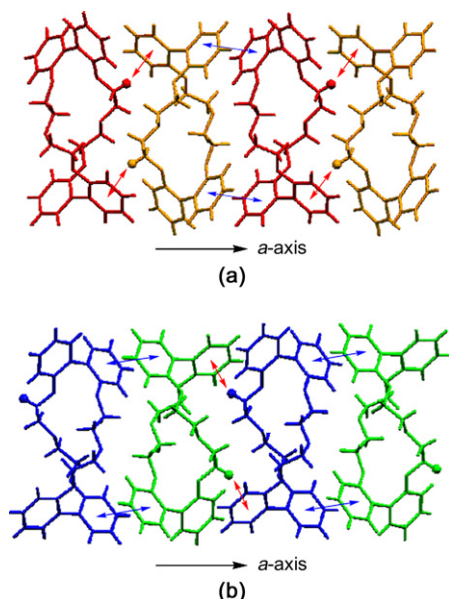


Figure 2. π - π and CH- π interactions in column structures. Blue and red arrows indicate π - π and CH- π interactions, respectively. (a) Column structure of **I(A)**. (*R,R*)-**I(A)** and (*S,S*)-**I(A)** are shown in orange and red, respectively. (b) Column structure of **I(B)**. (*R,R*)-**I(B)** and (*S,S*)-**I(B)** are shown in blue and green, respectively.

between the benzene ring in a biphenyl unit and a proton of the diethyl ether chain (Fig. 2b, indicated by red arrows).

Crystal **I** is formed by self-assembly of these columns. Each column of **I(A)** and **I(B)** interacts by four CH- π interactions per molecule along the *b*-axis (Fig. 3, indicated by red arrows). These distances are 2.89, 2.92, 2.93, and 2.95 Å. However, there is no interaction in the direction of the *c*-axis. It is thought that the absolute configuration of the two biphenyl units on one molecule is the same due to a synergistic effect of the π - π and CH- π interactions.

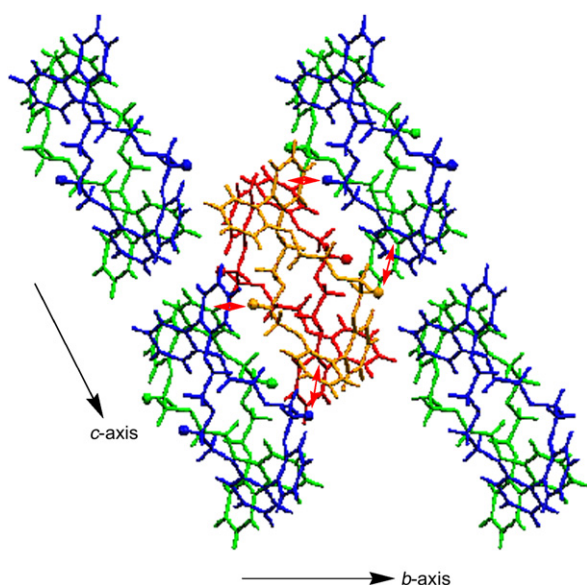


Figure 3. Molecular packing structure of **I** observed along the *a*-axis. Red arrows indicate CH- π interactions of (*R,R*)-**I(A)**.

In order to study the influence of the binding position of the diethyl ether chain, the crystal structure of compound **II** was studied by X-ray crystallography. Good colorless crystals (*R,S*)-**II** were obtained from an acetone solution. The structure of crystal (*R,S*)-**II** is shown in Figure 4. The space group of this crystal is $P2_1/c$. Inclusion of solvent molecules is also not observed in this crystal. A major difference from crystal **I** is that there is only one independent molecule in crystal (*R,S*)-**II**. The torsion angles of the two biphenyl units are the same (45.75°), but the absolute configuration (axial chirality) of the two biphenyl units is different. In other words, this molecule adopts a *meso*-conformation in the solid state.

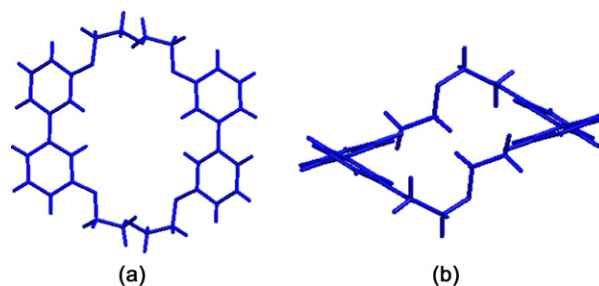


Figure 4. Crystal structures of (*R,S*)-**II**. (a) View from the side of the biphenyl unit. (b) View down the internal axis of the biphenyl unit.

Column structures are formed along the *a*-axis in this crystal as well (Fig. 5). Although a clear π - π interaction between the benzene rings is not observed, two kinds of intermolecular CH- π interactions (2.80 and 2.93 Å) are observed between the benzene ring in a biphenyl unit and a proton of the diethyl ether chain in the column (Fig. 5, indicated by red and green arrows, respectively).

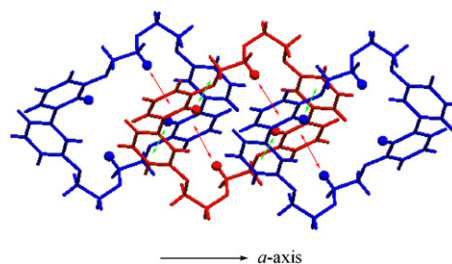


Figure 5. Two kinds of CH- π interactions in column structures of (*R,S*)-**II** indicated by green and red arrows (2.93 and 2.80 Å, respectively).

Each column interacts via eight positions per molecule by two kinds of CH- π interactions along the *b*- and *c*-axes (2.72 and 2.76 Å, respectively) (Fig. 6, indicated by red and green arrows, respectively).

In crystal (*R,S*)-**II**, a clear π - π interaction is not observed. It is thought that this lack of interaction is the cause of the difference in the absolute configuration between the two biphenyl units in compounds **I** and **II**.

The axial chirality of compounds **I** and **II** may be determined in a cyclization process. Then, the flexibility of the biphenyl backbones in the two compounds was examined by theoretical calculations.⁶ The energy barriers to the biphenyl *R*-*S* inversion for compounds **I** and **II** were calculated as 13.4

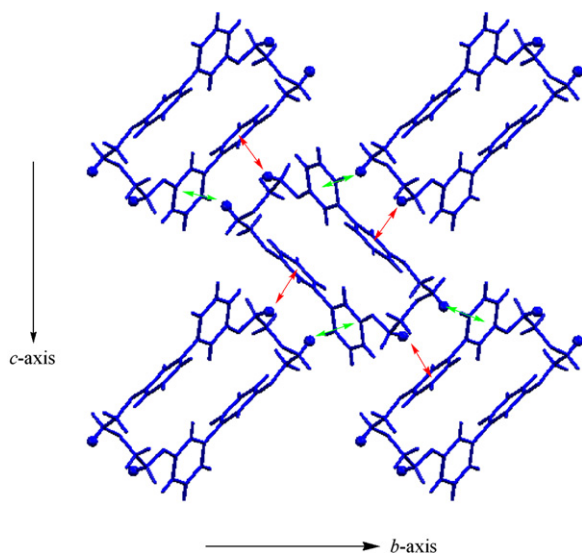


Figure 6. Molecular packing structure of (*R,S*)-**II**. Green and red arrows indicate CH– π interactions (2.76 and 2.72 Å, respectively) between column structures of (*R,S*)-**II**. View down the *a*-axis.

and 2.7 kcal/mol, respectively. These values can be compared with the experimentally observed energy barrier of 23.5 kcal/mol for the racemization of 1,1'-binaphthyl, which is known to proceed rapidly even at room temperature.⁷ The biphenyl backbones of compounds **I** and **II** would be rotatable in solutions. This result also suggests that the cause of the difference in the absolute configuration between the two biphenyl units in compounds **I** and **II** is mainly various intra- and intermolecular interactions.

3. Conclusion

We have synthesized two simple biphenyl compounds, **I** and **II**, having biphenyl backbones and diethyl ether chains in good yields. From X-ray analyses, the absolute configuration (axial chirality) of the biphenyl units is the same in compound **I**. This result suggests that the absolute configuration of the biphenyl units is transferred throughout the diethyl ether chains. On the other hand, in compound **II**, the absolute configuration (axial chirality) of the biphenyl units is different, suggesting that the opposite absolute configuration of the biphenyl unit is transferred. It is expected that this study will be useful for structural analysis of polymeric biphenyl derivatives.

4. Experimental

4.1. General

4.1.1. 2,2'-Bis(5-hydroxy-3-oxa-1-pentylloxy)-1,1'-biphenyl (2). 2,2'-Biphenol (**1**) (0.9 g, 4.8 mmol) was dissolved in dimethylformamide (DMF) (20 mL) and potassium carbonate (3.5 g, 25 mmol) and 2-(2-chloroethoxy)ethanol (2.6 mL, 25 mmol) were added. The resulting solution was heated at 120 °C under argon atmosphere overnight. The suspension was filtered and the solvent was removed under vacuum. The crude product was flash chromatographed through silica gel column (hexane/ethyl acetate 3:7) to

afford 1.8 g of **2** as a yellow oil (98% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.33 (dd, *J*=8.1, 2.1 Hz, 2H), 7.25 (dd, *J*=7.2, 1.8 Hz, 2H), 7.02 (d, *J*=7.2 Hz, 2H), 6.97 (d, *J*=8.1 Hz, 2H), 4.06 (t, *J*=2.7 Hz, 4H), 3.76 (s, 2H), 3.67 (t, *J*=2.7 Hz, 4H), 3.62 (t, *J*=2.7 Hz, 4H), 3.47 (t, *J*=2.7 Hz, 4H). HRMS (EI) *m/z* 362.1718, calcd for C₂₀H₂₆O₆ 362.1729.

4.1.2. 2,2'-Bis(5-bromo-3-oxa-1-pentylloxy)-1,1'-biphenyl (3). Compound **2** (2.3 g, 6.3 mmol) and triphenylphosphine (5.0 g, 19 mmol) were dissolved in dry acetonitrile (CH₃CN) (50 mL) and carbon tetrabromide (6.3 g, 19 mmol) was added. The resulting solution was stirred under argon atmosphere at room temperature for 1 h. The suspension was filtered and the solvent was removed under vacuum. The crude product was flash chromatographed through silica gel column (hexane/ethyl acetate 4:1) to afford 2.4 g of **3** as a yellow oil (78% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.32 (dd, *J*=7.8, 1.8 Hz, 2H), 7.27 (dd, *J*=7.5, 1.5 Hz, 2H), 7.02 (d, *J*=7.5 Hz, 2H), 6.95 (d, *J*=7.8 Hz, 2H), 4.08 (t, *J*=4.8 Hz, 4H), 3.72 (t, *J*=4.8 Hz, 4H), 3.60 (t, *J*=6.0 Hz, 4H), 3.27 (t, *J*=6.0 Hz, 4H). HRMS (EI) *m/z* 486.0035, calcd for C₂₀H₂₄O₄Br₂ 486.0041.

4.1.3. 3,3'-Bis(5-hydroxy-3-oxa-1-pentylloxy)-1,1'-biphenyl (5). 3,3'-Biphenol (**4**) (0.9 g, 4.8 mmol) was dissolved in DMF (25 mL) and potassium carbonate (3.1 g, 23 mmol) and 2-(2-chloroethoxy)ethanol (2.4 mL, 23 mmol) were added. The resulting solution was heated at 120 °C under argon atmosphere overnight. The suspension was filtered and the solvent was removed under vacuum. The crude product was flash chromatographed through silica gel column (ethyl acetate) to afford 1.6 g of **5** as a yellow oil (99% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.35 (t, *J*=8.1 Hz, 2H), 7.18 (m, 4H), 6.91 (m, 2H), 4.87 (s, 2H), 4.21 (m, 4H), 3.90 (m, 4H), 3.78 (m, 4H), 3.70 (m, 4H). HRMS (EI) *m/z* 362.1718, calcd for C₂₀H₂₆O₆ 362.1729.

4.1.4. 3,3'-Bis(5-bromo-3-oxa-1-pentylloxy)-1,1'-biphenyl (6). A compound **5** (1.4 g, 3.9 mmol) and triphenylphosphine (2.9 g, 11 mmol) were dissolved in dry CH₃CN (5 mL) and carbon tetrabromide (3.7 g, 11 mmol) was added. The resulting solution was stirred under argon atmosphere at room temperature for 1 h. The suspension was filtered and the solvent was removed under vacuum. The crude product was flash chromatographed through silica gel column (hexane/ethyl acetate 4:1) to afford 1.1 g of **6** as a yellow oil (78% yield). ¹H NMR (300 MHz, CDCl₃) δ 7.33 (d, *J*=7.8 Hz, 2H), 7.18 (dd, *J*=7.8, 2.7 Hz, 2H), 7.14 (s, 2H), 6.91 (dd, *J*=7.8, 2.7 Hz, 2H), 4.21 (t, *J*=4.8 Hz, 4H), 3.93–3.89 (m, 8H), 3.51 (t, *J*=4.8 Hz, 4H). HRMS (EI) *m/z* 486.0035, calcd for C₂₀H₂₄O₄Br₂ 486.0041.

4.1.5. Bis-2,2'-biphenyl-22-crown-6 (I). Compound **1** (186 mg, 1.00 mmol) and cesium carbonate (717 mg, 2.20 mmol) were dissolved in dry DMF (100 mL) at 60–65 °C under argon atmosphere. Then a solution of compound **3** (486 mg, 1.00 mmol) in dry DMF (30 mL) was added dropwise for a period of 16 h with a syringe pump. The resulting solution was stirred under argon atmosphere at 120 °C for 2 days. The suspension was filtered and the solvent was removed under vacuum. The crude product was flash chromatographed through silica gel column

(benzene/ethyl acetate 9:1) to afford 225 mg of **I** as colorless needle crystals (50% yield). Mp 166–168 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.32 (dd, *J*=8.1, 1.8 Hz, 4H), 7.20 (d, *J*=8.1 Hz, 4H), 7.01 (dd, *J*=8.1, 1.8 Hz, 4H), 6.85 (d, *J*=8.1 Hz, 4H), 4.09–3.90 (m, 8H), 3.62–3.47 (m, 8H). HRMS (EI) *m/z* 512.2166, calcd for C₃₂H₃₂O₆ 512.2199. Anal. Calcd (%) for C₃₂H₃₂O₆·0.3H₂O: C, 74.20; H, 6.34. Found: C, 74.20; H, 6.23. Crystallographic data: C₃₂H₃₂O₆, triclinic, space group P $\bar{1}$, *a*=13.2357(15), *b*=14.8562(16), *c*=15.5916(17) Å, α =62.256(2)°, β =77.302(2)°, γ =77.049(2)°, *V*=2620.5(5) Å³, *Z*=4, *D*_c=1.299 g cm⁻³, μ (Mo K α)=0.089 mm⁻¹, 16,472 reflections measured, 11,708 unique, final *R*(*F*²)=0.0565 using 7303 reflections with *I*>2.0 σ (*I*), *R*(all data)=0.1053, *T*=110(2) K. CCDC 624827.

4.1.6. Bis-3,3'-biphenyl-26-crown-6 (II). Compound **4** (150 mg, 0.81 mmol) and cesium carbonate (587 mg, 1.80 mmol) were dissolved in dry DMF (150 mL) at 60–65 °C under argon atmosphere. Then a solution of compound **6** (389 mg, 0.80 mmol) in dry DMF (30 mL) was added dropwise for a period of 16 h with a syringe pump. The resulting solution was stirred under argon atmosphere at 120 °C for 2 days. The suspension was filtered and the solvent was removed under vacuum. The crude product was flash chromatographed through silica gel column (benzene/ethyl acetate 95:5) to afford 160 mg of **II** as colorless plate crystals (39% yield). Mp 173–174 °C. ¹H NMR (300 MHz, CDCl₃) δ 7.29 (d, *J*=7.8 Hz, 4H), 7.20 (d, *J*=2.4 Hz, 4H), 7.17 (d, *J*=7.8 Hz, 4H), 6.87 (dd, *J*=7.8, 2.4 Hz, 4H), 4.24 (t, *J*=4.5 Hz, 8H), 3.97 (t, *J*=4.5 Hz, 8H). HRMS (FAB⁺) *m/z* 512.2186, calcd for C₃₂H₃₂O₆ 512.2199. Anal. Calcd (%) for C₃₂H₃₂O₆·0.3H₂O: C, 74.20; H, 6.34. Found: C, 74.38; H, 6.23. Crystallographic data: C₃₂H₃₂O₆, monoclinic, space group *P*2₁/*c*, *a*=6.4148(7), *b*=14.3765(16), *c*=14.4950(16) Å, β =95.244(2)°, *V*=1331.2(3) Å³, *Z*=2, *D*_c=1.279 g cm⁻³, μ (Mo K α)=0.088 mm⁻¹, 8196 reflections measured, 3131 unique, final *R*(*F*²)=0.0574 using 2513 reflections with *I*>2.0 σ (*I*), *R*(all data)=0.0724, *T*=110(2) K. CCDC 624826.

4.2. Crystallization of biphenyl compounds

Biphenyl compound **I** or **II** (10 mg, 0.020 mmol) was dissolved in acetone (2 mL). After 2–3 days, colorless crystals **I** or **II** were deposited and collected.

4.3. X-ray crystallographic study

X-ray diffraction data for single crystals were collected on BRUKER APEX diffractometer. The crystal structures were solved by direct methods and refined by full-matrix

least-squares using SHELX97. The diagrams were prepared using PLATON.

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