

Chiral Non-Planar Oligophenylenes bridged by Urea Linkage: Synthesis through Intramolecular Direct Arylation, Chiroptical Behavior, and Theoretical Investigation

Koji Takagi,^{[a]*} Yuto Hirano,^[a] Koichiro Mikami,^{[b]*} Shoko Kikkawa,^[c] and Isao Azumaya^[c]

Abstract: The intramolecular direct arylation of N,N'-dihexyl-N-(2bromophenyl)-N'-phenylurea using palladium catalyst gave BPU in 75% yield. Longer terphenyl compound (TPbU) was likewise prepared. Other four conjugated oligomers (BPtU, BPU-1Np, BPU-2Np, and BPU-Ant) were synthesized from BPU in short reaction steps. From the X-ray crystallography, BPtU with the thiourea skeleton was suggested to have a quasi C=N double bond character. Each enantiomer was optically resolved on chiral HPLC to show mirroring Cotton effects and monosignate CD patterns. The enantiomeric excess (e.e.) values were evaluated by HPLC, from which BPU and TPbU exhibited comparable racemization energy barriers ($\Delta G^{\ddagger}_{rac}$ = 23.3 kcal·mol⁻¹ and 23.4 kcal·mol⁻¹). The racemization energy barrier of **BPtU** was considerably high ($\Delta G^{\ddagger}_{rac}$ = 30.1 kcal·mol⁻¹) likely due to the quasi C=N double bond character. On the other hand, **BPU-2Np** and **BPU-Ant** having the π -conjugated system exhibited $\Delta G^{\ddagger}_{rac}$ of 23.8 kcal·mol⁻¹ and 24.0 kcal·mol⁻¹, respectively. These experimental results were well explained by theoretical analyses.

Introduction

Biphenyl compounds bearing an appropriate tether strap adopt the forced non-planar conformation and have the rotation barrier around the sp² carbon-sp² carbon bond of two phenyl rings. Optically active compounds with the axial chirality can be potentially separated by the chiral high performance liquid chromatography (HPLC) and gas chromatography (GC) if the rotation barrier is high enough. Chiral biphenyls have been drawing much attention not only from a viewpoint of general chemistry¹ but also as functional materials including organocatalysts²⁻⁴ and nonlinear optics.⁵ Longer oligo and poly(para-phenylene) derivatives having the same axial chirality are expected to have the persistent helical secondary structure. In contrast to helicences and twistacenes, these so-called Geländer or banister-type oligomers are relatively flexible and exhibit the dynamic motion.⁶ Vögtle and co-workers have propounded the concept of Geländer molecules and prepared bridged terphenyl compounds, in which a pair of enantiomers

[a]	Graduate School of Engineering, Nagoya Institute of Technology Gokiso, Showa, Nagoya, Aichi 466-8555, Japan
	E-mail: takagi.koji@nitech.ac.jp
	http://polysyn.web.nitech.ac.jp
[b]	Sagami Chemical Research Institute
	Hayakawa 2743-1, Ayase, Kanagawa 252-1193, Japan
	E-mail: koichiro.mikami@sagami.or.jp
	http://sagami-
	scri.jp/publics/index/117/&anchor link=page117#page117
[c]	Faculty of Pharmaceutical Sciences. Toho University
L . 1	Miyama 2-2-1 Eunabashi Chiba 274-8510 Janan

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with the helical conformation and one meso form were observed.7 It was found that the chain elongation from biphenyl to terphenyl results in the high rotation value and distinct circular dichroism. Rathore and co-workers have reported a versatile synthesis of a variety of bridged terphenyls from readily available diacetylenic precursors via a simple three-step route.8 Although bulky substituents were installed onto the bridging position, the racemization energy barriers were still low to racemize at room temperature. Recently, true banister oligomers exclusively consisting of two enantiomers (without meso form) were prepared by Mayor and co-workers by utilizing a length mismatch strategy.^{9,10} They also investigated the influence of a tether strap on the helix stability to figure out that the introduction of larger and softer selenium atom reduces the racemization energy barrier.¹¹ As can be seen from these examples, it is important to understand the origin of chirality and the chiral structure-physical properties relationship, and bridged biphenyl compounds are good candidates for predicting the secondary structure of extended helical analogs. Mayor and coworkers have carefully studied the rotation barriers of 4,4'disubstituted torsion-angle-restricted biphenyl cyclophanes with the aid of density functional theory (DFT) calculation for the transition state.12,13

In order to widely investigate the chiral structure-physical properties relationship, the development of new bridged biphenyl compounds is highly desired. There are several methods to prepare biphenyl derivatives with the three-atom bridge, namely, seven-membered rings are fused on the side of biphenyl skeleton.^{14–16} In relation to the framework of our molecules, Kostyanovsky and co-worker have reported the synthesis and HPLC analysis of chiral N.N'-dialkyl-2,2'-biphenylene-N,N'ureas.¹⁷ However, they did not evaluate the racemization energy barriers. During the course of our study on functional conjugated oligomers comprising of the aromatic cyclic triamide structure,^{18–} ²³ we have previously reported that an amide-bridged ladder poly(para-phenylene) with the rigid and planar conformation could be obtained by using the palladium-catalyzed intramolecular direct arylation (Figure 1A).²⁴ More recently, we have systematically prepared lactam-fused π-extended conjugated oligomers by the tandem direct arylation and revealed their potential utility as a n-type field effect transistor material²⁵ as well as flexible optical waveguides/bending mechanofluorochromic materials²⁶ (Figure 1B). The direct arylation is recognized as an alternative to the cross-coupling reaction using organometallic reagents.27-31 Convenient and atom-economic reactions are possible to form biaryl carboncarbon bond linkages without the need of time-consuming preparation of organometallic reagents and the special care for air/moisture sensitive intermediates. The key points of these successful syntheses are based on the fact that N-alkylated benzanilides preferentially adopt a cis conformation (E isomer) with two benzene rings turned into the same direction both in

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Figure 1. (A) Amide-bridged ladder poly(para-phenylene) with the rigid and planar conformation.²⁴ (B) Lactam-fused π -extended conjugated oligomer.^{25,26} (C) Non-planar and urea-bridged conjugated oligomer. Red and blue lines were formed by palladium-catalyzed intramolecular and intermolecular direct arylation, respectively.

solution and solid states.^{32,33} On the other hand, fully *N*-alkylated urea derivatives are also known to adopt similar conformation. in which the aromatic rings are located in close proximity.³⁴⁻³⁷ With these backgrounds in our mind, we came up with the preparation of non-planar and urea-bridged conjugated oligomers by the intramolecular direct arylation (Figure 1C). In contrast to our previous papers, the present intramolecular direct arylation furnishes the seven-membered ring that endows the molecules with chirality. Herein, we report the optimized synthesis of a set of conjugated oligomers with N-alkylated urea and thiourea carrying various π -conjugated segments (Figure 2), the analysis of single crystal X-ray structures, and the evaluation of racemization energy barriers by the HPLC technique and theoretical calculation. Because the C=S bond is longer than the C=O bond and the C-N bond has a double-bond character owing to the small contribution of the thione form,38 the C-N rotation barrier of thiourea should be perturbated. Both the bulkiness of π -conjugated segment appended on the biphenyl framework and this resonance effect would influence the racemization behavior, which are discussed in detail.



Results and Discussion

Synthesis and chiroptical properties of main backbone

Biphenyl derivative bridged by the N,N'-dihexylurea skeleton (BPU) was synthesized in three steps, namely, the reaction of 2bromoaniline with phenyl isocyanate, N-alkylation, and intramolecular cyclization (Scheme 1). We have carried out the palladium-catalyzed direct arylation of N,N'-dihexyl-N-(2bromophenyl)-N'-phenylurea (2) using Pd(OAc)₂, PivOH, and K₂CO₃ in DMAc, where the influence of phosphine ligand and heating method were investigated (Table 1). We have previously demonstrated that the microwave heating is effective for the palladium-catalyzed direct arylation.24 When the ligand-free reaction was performed at 145 °C under the microwave irradiation, the high NMR yield was confirmed after 6 h (Entry 1). The reaction at 120 °C decreased the NMR yield (Entry 2), while the addition of PCy3 HBF4 gave an improved yield even at 100 °C for 6 h (Entry 4). In contrast, the lower NMR yield was observed after 24 h under the similar condition with the oil bath heating (Entry 6), although the detailed reason cannot be discussed at the present moment. In a similar manner, terphenyl derivative bridged by the N,N',N",N"-tetrahexylbisurea skeleton (TPbU) was synthesized albeit in relatively low yield (Scheme 2). We have subsequently obtained biphenyl derivative bridged by the N,N'-dihexylthiourea skeleton (BPtU) from BPU using Lawesson's reagent in toluene at refluxing temperature for 3 h (Scheme 3). In the ¹H-NMR spectrum of **BPU**, the methylene proton signals adjacent to the urea nitrogen atom were separately detected at 3.4 ppm and 4.0 ppm (Figure S1-1), which is most likely ascribed to the diastereotopic environment of methylene protons due to the axial chirality of biphenyl moiety.39 The corresponding proton signals of BPtU were downfield-shifted to be detected at 3.6 ppm and 4.6 ppm. These spectroscopic results are in good accordance with the reported characteristic of urea and thiourea compounds, namely, the small contribution of the thione form in the case of thiourea.⁴⁰ In the IR spectra, the C=O stretching vibration (urea I band) signal of **BPU** at 1672 cm⁻¹ was disappeared in **BPtU**.

Table 1. Palladium-catalyzed direct arylation for preparing BPU. ^[a]					
Entry	Ligand	Temperature/°C ^[b]	Time/h	NMR yield/% ^[c]	
1	-	145 (MW)	6	91	
2	-	120 (MW)	6	20	
3	PCy ₃ ·HBF ₄	145 (MW)	6	90	
4	PCy ₃ ·HBF ₄	100 (MW)	6	89	
5	PCy ₃ ·HBF ₄	80 (MW)	6	74	
6	PCy ₃ ·HBF ₄	100 (OB)	24	33	

[a] Conditions; Pd(OAc)₂ (5.6 mol%), PivOH (42 mol%), K₂CO₃ (3.5 equiv), and PCy₃·HBF₄ (11.2 mol% in Entry 3–6). [b] MW; microwave. OB; oil bath. [c] Calculated from the integral ratio in the ¹H-NMR spectra.

the in-depth discussion about the molecular For conformation and packing structure of synthesized *π*-conjugated oligomers, single crystallographic analyses were carried out. Because the melting temperature of BPU with N-hexyl chains was too low to obtain a single crystal, N-methyl derivative BPU_{Me} was prepared and a colorless crystal was grown by the slow evaporation of the hexane solution. The C=O and CO-N bond lengths are 1.22 Å and 1.38-1.39 Å, respectively (Figure 3). The torsion angle between two phenyl rings (defined by the atoms in cyclic urea) is 39.6°. The crystal packing structure indicates that BPU_{Me} is orthorhombic with a space group of Pbca. One unit cell contains four pairs of two enantiomers (Z = 8) and the enantiomers with the same chirality are aligned along the a axis (Figure S7). A colorless crystal of TPbU was grown by the slow evaporation of the ethanol solution. Although TPbU should contain a pair of enantiomers with the helical conformation and one meso form in solution, only meso form could be crystallized. The C=O bond length (1.22 Å) and CO-N bond length (1.39 Å) as well as the torsion angle between two phenyl rings (41.0°) are almost identical to those of BPUMe. Conformation of TPbU in the single crystal has a center of symmetry on the central benzene ring. The crystal packing structure indicates that TPbU is monoclinic with a space group of $P2_1/c$ and Z = 2. Molecules are aligned along the a axis and the one-dimensional chain architecture along the c axis supported by the C=O···H–C (benzene) hydrogen bonding interaction is observed. Like BPU_{Me}, thiourea compound BPtU_{Me} was prepared to be subjected to the single crystallographic analysis. A colorless crystal was grown by the vapor diffusion method using THF and hexane. Conformation of TPbU in the single crystal has a twofold rotation axis. The C=S and C(=S)-N bond lengths are 1.66 Å and 1.38 Å, respectively. The torsion angle between two phenyl rings (42.1°) is obviously larger than that of BPU_{Me}. The crystal packing structure indicates that BPtU_{Me} is orthorhombic with a space group of Fdd2. One unit cell contains four pairs of two enantiomers (Z = 8) and the enantiomers with the same chirality are aligned along the c axis.



Figure 3. ORTEP representation of BPU_{Me} (CCDC 1883094), TPbU (CCDC 1883095), and $BPtU_{Me}$ (CCDC 1883096) with 50% thermal ellipsoid probability. The purple, red, and orange atoms represent N, O, and S, respectively. Alkyl chains are trimmed for clarity.

Layers with the same chirality are formed along the *a* axis. In all cases, no π - π stacking interactions were observed between neighboring molecules. Although the C(=S)–N bond length of **BPtU**_{Me} is longer than bare S=C(NH₂)₂ (approximately 1.33 Å),⁴¹ **BPtU** would be expected to have a C=N double-bond character in some degree (See theoretical calculation section).

Optically pure two enantiomers of BPU were isolated by using a Daicel CHIRALFLASH IC column with n-hexane/i-PrOH (95/5 in volume ratio) as the mobile phase (See Figure S8 for analytical HPLC chromatogram). Because isolated enantiomers gradually racemize at room temperature (vide infra), CD spectra were collected immediately just after the separation. Figure 4 indicates CD spectra of the first eluent (blue line) and the second eluent (red line) along with UV spectrum (black line), in which each enantiomers exhibit mirroring Cotton effects and monosignate CD patterns. As for the first eluent, the first negative and second positive Cotton effect were observed at 295 nm and 262 nm, respectively, with the zero-crossing point at 281 nm. The CD anisotropy factor ($\Delta \varepsilon / \varepsilon$) at 295 nm was found to be 10^3 gabs = 0.94. The time-dependent density functional theory (TDDFT) calculation was carried out for the enantiomer with a plus (P) configuration around the biphenyl moiety. Although the experimental CD pattern could not be reproduced completely, it was found that the CD sign corresponding to the π - π^* transition band at 291 nm is negative (Figure S17). Accordingly, the first eluent likely has a chiral structure with two benzene rings twisted in a clockwise fashion. On the other hand, in the case of TPbU consisting of three optical isomers, only one enantiomer could be optically resolved (n-hexane/i-PrOH=70/30 as the mobile phase) due to the overlap of HPLC peaks (See Figure S9). The monosignate CD pattern having the peak maximum at 305 nm was observed and the CD anisotropy factor at this wavelength was 10^3 gabs = 3.0. In contrast to BPU, **TPbU** with the longer π -conjugated backbone exhibited a weak but detectable fluorescence emission at 398 nm (Figure S14, Φ = 0.02). The low fluorescence quantum yield might be ascribed to the relatively flexible backbone. In fact, the fluorescence quantum yield was significantly increased (Φ = 0.20) when we measured the emission spectrum in the solid state. Because π - π stacking interaction is not observed between molecules in the crystal state as we described above, the excimer formation can be ignored resulting in the increased fluorescence quantum yield. The optical resolution of racemic BPtU was likewise carried out using n-hexane/i-PrOH (99/1 in volume ratio) as the mobile phase (See Figure S10). In the UV spectrum of BPtU, a weak absorption band was observed at around 350 nm. Although BPtU has a biphenyl segment similar to BPU, the largest CD anisotropy factor (10^3 gabs = 47) among three compounds was observed at 350 nm. The TDDFT calculation indicated that the π - π^* absorption band at 296 nm can be ascribed to the electronic transition not from the highest occupied molecular orbital (HOMO) but from the next highest occupied molecular orbital (HOMO-1). Anyhow, as for the enantiomer with a plus (P) configuration around the biphenyl moiety, the CD sign corresponding to the π - π ^{*} transition band is negative (Figure S18).



Figure 4. CD and UV spectra of BPU (*n*-hexane/*i*-PrOH (95/5 in volume ratio)), TPbU (*n*-hexane/*i*-PrOH (70/30 in volume ratio)), and BPtU (*n*-hexane/*i*-PrOH (99/1 in volume ratio)). Blue line: first eluent, Red line: second eluent.



Figure 5. Decrease of enantiomeric excess (e.e.) value as a function of time for **BPU**, **TPbU**, and **BPtU**. The insets show the linear relationship between ln(e.e.) and time.

Therefore, similar to **BPU**, the first eluent likely has a chiral structure with two benzene rings twisted in a clockwise fashion.

The racemization behavior of BPU was subsequently investigated by monitoring HPLC chromatograms at designated times after the optical resolution (Figure S16). Figure 5 indicates the decrease of enantiomeric excess (e.e.) value as a function of time while keeping the n-hexane/i-PrOH solution (95/5 in volume ratio) at 25 °C. The linear relationship was observed between In(e.e.) and time as depicted in the inset, and the slope gave a racemization rate constant $10^5 k_{rac} = 1.97$. Therefore a racemization energy barrier was calculated as $\Delta G^{\ddagger}_{rac}$ = 23.4 kcal·mol⁻¹. TPbU demonstrated a similar racemization behavior with $10^5 k_{rac} = 2.40$ and $\Delta G^{\ddagger}_{rac} = 23.3 \text{ kcal} \cdot \text{mol}^{-1}$ implying that the elongation of π -conjugated backbone does not affect the rotation barrier around two phenyl rings. Because the racemization of thiourea compound BPtU was very slow at 25 °C, the experiment was carried out at 74 °C. A racemization energy barrier was thus calculated to exhibit $10^5 k_{rac} = 400$ and $\Delta G^{\ddagger}_{rac} =$ 30.1 kcal·mol⁻¹, and +6.7 kcal/mol higher than that of BPU. Závada and co-workers have investigated the synthesis and racemization of axially chiral dilactams to claim that the inversion barriers around phenyl rings are very similar to the parent carbocyclic system and the quasi double bond character of the amide group is the most probable reason.42 Because the C(=S)-N bond in BPtU has a double bond character as deduced by the X-ray crystallography (vide supra), the high rotation barrier around the C(=S)-N bond likely results in the suppressed racemization. This scenario was clearly supported by theoretical investigation (See theoretical calculation section).

Synthesis and chiroptical properties of π -functionalized derivatives

WILEY-VCH We then became interested in the racemization behavior of axially chiral biphenyl derivatives with (bulky) π -conjugated system on the benzene ring. With BPU in our hand, the bromination and Suzuki-Miyaura cross coupling reaction afforded BPU-1Np, BPU-2Np, and BPU-Ant in good yields (Schemes 4-6). In the ¹H-NMR spectra of BPU-1Np and BPU-2Np, the proton signals adjacent to the urea nitrogen atom were observed at around 3.4 and 4.0 ppm, which are almost identical to that of BPU. The corresponding signals of BPU-Ant were shifted to the downfield region (3.7 and 4.3 ppm) probably ascribed to the steric repulsion of anthracene rings and distorted conformation of the urea moiety. Each enantiomer was isolated on chiral HPLC by using a Daicel CHIRALFLASH IC column with an appropriate solvent mixture as the mobile phase (See Figures S11-13). Figure 6 indicates CD spectra of the first eluent (blue line) and the second eluent (red line) along with UV spectrum (black line), in which each enantiomer exhibits the mirroring Cotton effect. Unfortunately, the perfect separation of enantiomers of BPU-1Np was difficult and two CD spectra did not show a complete mirror image. Basically, monosignate CD patterns were observed. The CD anisotropy factors $(\Delta \varepsilon / \varepsilon)$ of BPU-2Np and BPU-Ant were 10³ gabs = 1.09 at 307 nm and 10³ gabs = 0.63 at 391 nm, respectively. BPU-Ant exhibited a fluorescence emission at 408 nm with the vibronic fine structure (Figure S15). The relative fluorescence quantum yield was 0.007, which was very low probably because of the steric repulsion of anthracene rings and the non-radiative decay from the excited state in addition to the relatively flexible BPU backbone. The racemization behavior of BPU-2Np and BPU-Ant were subsequently investigated by monitoring HPLC chromatograms at designated times after the optical resolution. Each solution was kept at 25 °C and the enantiomeric excesses (e.e.) values were determined by the integral ratio of two peaks. Figure 7 indicates the linear relationship between ln(e.e.) and time, and a racemization rate constant was calculated from the slope.



Figure 6. CD and UV spectra of **BPU-1Np** (*n*-hexane/CH₂Cl₂ (66/34 in volume ratio)), **BPU-2Np** (*n*-hexane/THF (88/12 in volume ratio)), and **BPU-Ant** (*n*-hexane/CH₂Cl₂ (27/73 in volume ratio)). Blue line: first eluent, Red line: second eluent.



Figure 7. Linear relationship between ln(e.e.) and time for BPU-2Np, BPU-Ant, and BPU.

Table 2. Summary	of	racemization	rate	constants	and	racemization	energy
barriers. ^[a]							

	$10^5 k_{\rm rac}/{\rm sec^{-1}}$	$\Delta G^{\ddagger}_{\rm rac}/{\rm kcal}\cdot{\rm mol}^{-1}$	Temperature/°C
BPU	1.97	23.4	25
TPbU	2.40	23.3	25
BPtU	0.03	30.3	74
BPU-1Np	NA ^[b]	NA ^[b]	25
BPU-2Np	1.00	23.8	25
BPU-Ant	0.80	24.0	25

[a] Obtained by chiral HPLC analyses. [b] Not available due to imperfect peak separation in HPLC.

Table 2 summarizes racemization rate constants and racemization energy barriers of five non-planar and urea-bridged conjugated oligomers. By introducing the π -conjugated system on the benzene ring, the racemization energy barrier increased as expected. **BPU-2Np** and **BPU-Ant**, however, exhibited a small difference.

Theoretical analyses

The quasi double bond character in **BPtU** at the ground state (**GS1**_(BPtU) and **GS2**_(BPtU)) was supported by theoretical calculations (B3LYP/6-31G(d,p)) (Figure 8). The bond length of C(=X)–N of **BPtU** (X = S) and **BPU** (X = O) were 1.385 Å and 1.399 Å, respectively, and the molecules were significantly deviated from the planer structure nicely reproducing the structures observed in the single-crystal X-ray analysis. The Wiberg Bond Index (WBI) value of C(=S)–N of **BPtU** (1.123) was higher than that of C(=O)–N of **BPU** (1.054) reflecting a quasi C=N double bond character of **BPtU**. Second-order perturbation theory analysis showed that the non-bonding pair of electron localized at the N atom donated the stabilization energy to the π^* orbital of C=S bonding (+57.8 kcal/mol) and C=O bonding (+47.1 kcal/mol), and the stronger secondary orbital interaction would contribute to the quasi double bond character of **BPtU**.

On the contrary to the ground state structures, both of the transition state structures adopted nearly planer conformation. The energy barrier (ΔG^{\ddagger}) of **BPU** and **BPtU** were +23.1 kcal/mol and +28.1 kcal/mol (Figure 8), respectively, indicating that the value of BPtU was 5.0 kcal/mol higher than that of BPU. This was qualitatively in good agreement of the experimental results that the racemization of BPtU is much slower than that of BPU, as described above. Notably, the WBI value of C(=S)-N of BPtU at the transition state was decreased (1.119), although the value of C(=O)-N of BPU was increased (1.069), compared with those ground states. Second-order perturbation theory analysis of BPtU and BPU at the transition states showed that the stabilization energy donated by the non-bonding pair of electron localized at the N atom to the π^* orbital of C=S orbital was also decreased (38.5 kcal/mol), whereas, in the cased of BPU, the value was increased (54.3 kcal/mol).



Figure 8. Theoretical energy diagram of racemization of **BPU** and **BPtU**. Inset; optimized structures of a), b), c) **BPU** and d), e), f) **BPtU** at ground and transition states. The geometries were given by ball and stick type model (atom color: blue = nitrogen, silver = carbon, yellow = S, red = oxygen). **GS** and **TS** stand for ground state and transition state, respectively.

These decrements of WBI and stabilization energy at the transition state of BPtU should be derived from the larger deviation from the planarity of BPtU compared with that of BPU. As provided in Figure S19, the dihedral angle (S=)C-N-C(Me) at transition states of BPtU was -26.311°, and the corresponding value of BPU ((O=)C-N-C(Me)) was -13.171°. The larger deviation from the planarity in BPtU restricts the effective delocalization of the pair of electron on the N atom to the π^* orbital of C=S bonding at BPtU, resulting in the decrement of the value of WBI. Taking these theoretical and experimental viewpoints into consideration, the higher racemization barrier in BPtU than that of BPU should be attributed to two factors; 1) the quasi double bond nature at the C(=S)-N bonding in BPtU stabilizes the ground state geometry, and 2) the deviation from the planarity prevents the stabilization of the transition state. Finally, we theoretically evaluated the racemization energy barrier of BPU-Ant at the same level as BPU (Figure S21). The energy barrier was calculated as 23.8 kcal/mol exhibiting the nearly same energy as BPU. This fact consists with the experimental results, and implies that the substitution at the 4position does not affect the racemization energy barrier significantly.

Conclusions

Optically active biphenyl compounds occupy an important place in the chiral technology and the structure-physical properties relationship is a matter of discussion over the past several decades. In this article, we have prepared non-planar and ureabridged conjugated oligomers by the palladium-catalyzed intramolecular direct arylation and revealed their racemization behaviors with the aid of theoretical calculation. The X-ray crystallographic analyses revealed that the thiourea derivative has a quasi C=N double bond character to result in the increased racemization energy barrier. On the other hand, the elongation of π -conjugation length and the substitution of

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chromophores at the 4-position did not affect the racemization energy barrier significantly. These experimental results were well explained by theoretical analyses. We believe that our present findings can contribute to the design of chiral biphenyl compounds and related longer conjugated oligomers for developing functional chiral materials.

Experimental Section

General information and synthetic procedure for the preparation of precursors are described in the supporting information. The important procedues for obtaining the target compounds and synthetic scheme are provided below.

Synthesis

Biphenylurea (BPU)



Scheme 1

A mixture of 2 (2.0 g, 4.4 mmol), Pd(OAc)₂ (59 mg, 0.24 mmol), PCy3 HBF4 (0.19 g, 0.49 mmol), PivOH (0.20 g, 1.8 mmol), and K₂CO₃ (2.3 g, 15 mmol) in N,N-dimethylacetamide (DMAc, 20 mL) was placed in a microwave vial, which was heated at 100 °C for 6 h. After solvent was removed, CH₂Cl₂ was added and washed with brine, and dried over MgSO₄. After evaporating solvents, the crude product was purified by SiO₂ column chromatography using hexane/ethyl acetate (4/1 in volume) (Rf = 0.53) as an eluent to obtain pale yellow oil BPU in 1.2 g (75% yield). ¹H-NMR (400 MHz, CDCl₃) δ ppm 0.64–0.72 (m, 6H), 0.89-1.07 (br, 12H), 1.27-1.42 (m, 4H), 3.43 (m, 2H), 4.01 (m, 2H), 7.17–7.25 (m, 4H), 7.34–7.40 (m, 2H), 7.48 (dd, J = 7.70, 1.59 Hz, 2H). ¹³C-NMR (101 MHz, CDCl₃) δ ppm 13.81, 22.41, 25.99, 27.49, 31.10, 47.63, 121.43, 124.86, 128.17, 128.20, 134.37, 143.79, 165.54. Anal Calcd for C₂₅H₃₄N₂O·0.25H₂O: C, 78.39%; H, 9.08%; N, 7.31%. Found: C, 78.42%; H, 9.13%; N, 7.33%. IR (liquid film) 1672 cm⁻¹ (C=O).

Terphenylbisurea (TPbU)



A mixture of 4 (1.2 g, 1.4 mmol), Pd(OAc)₂ (37 mg, 0.16 mmol), PCy3·HBF4 (0.12 g, 0.32 mmol), PivOH (0.13 g, 1.2 mmol), and K₂CO₃ (1.4 g, 10 mmol) in DMAc (11 mL) was placed in a microwave vial, which was heated at 100 °C for 6 h. After the solvent was removed, CH₂Cl₂ was added and washed with brine, and dried over MgSO₄. After evaporating solvents, the crude product was purified by SiO₂ column chromatography using hexane/ethyl acetate (4/1 in volume) (Rf = 0.43 and 0.36) as an eluent to obtain colorless solid TPbU as a mixture of diastereomers in 0.30 g (31% yield). Mp: 110.3-112.3 °C. 1H-NMR (400 MHz, CDCl₃) δ ppm 0.62-0.75 (m, 12H), 0.83-1.12 (br, 24H), 1.19-1.53 (m, 8H), 3.38-3.56 (m, 4H), 3.94-4.12 (m, 4H), 7.20–7.31 (m, 4H), 7.37–7.45 (m, 4H), 7.51 (dd, J = 7.70, 1.59 Hz, 2H). ¹³C-NMR (101 MHz,CDCl₃) δ ppm 13.82, 13.87, 13.89, 13.92, 22.41, 22.43, 22.47, 25.90, 25.93, 26.06, 26.08, 27.28, 27.45, 27.49, 27.52, 31.02, 31.07, 31.15, 31.17, 47.41, 47.82, 120.60, 120.76, 121.64, 121.68, 125.02, 125.12, 128.17, 128.59, 133.60, 133.81, 134.09, 134.30, 140.46, 143.55, 143.67, 165.29, 165.36. ¹H- and ¹³C-NMR signals are complex due to the mixture of enantiomers and diastereomer. Anal Calcd for C44H62N4O2; C. 77.83%; H. 9.20%; N. 8.25%; O. 4.71%. Found: C, 77.61%; H, 9.43%; N, 8.21%. IR (ATR) 1658 cm⁻¹ (C=O).

Biphenylthiourea (BPtU)



Scheme 3.

Lawesson's reagent (0.15 g, 0.38 mmol) was added to **BPU** (0.24 g, 0.63 mmol) in toluene (4 mL), and the mixture was heated to reflux for 3 h. After the precipitate was separated by filtration, the solvent was removed. The crude product was purified by SiO₂ column chromatography using hexane/ethyl acetate (4/1 in volume) ($R_f = 0.61$) as an eluent to obtain colorless oil **BPtU** in 0.25 g (67% yield). ¹H-NMR (400 MHz, CDCl₃) δ ppm 0.63–0.71 (m, 6H), 0.79–1.02 (br, 12H), 1.16–1.41 (m, 2H), 1.34 (m, 2H), 3.63 (m, 2H), 4.57 (m, 2H), 7.20 (dd, J = 8.07, 0.98 Hz, 2H), 7.28–7.33 (m, 2H), 7.35–7.40 (m, 2H), 7.49 (dd, *J* = 7.58, 1.71 Hz, 2H). ¹³C-NMR (101 MHz, CDCl₃) δ ppm 13.87, 22.43, 25.82, 27.51, 31.12, 53.24, 122.30, 126.21, 127.75, 128.33, 135.56, 146.01, 199.52. Anal Calcd for C₂₅H₃₄N₂S: C, 76.09%; H, 8.68%; N, 7.10%; S, 8.12%. Found: C, 76.34%; H, 8.73%; N, 7.36%; S, 8.05%.

Biphenylurea with 1-naphthyl group (BPU-1Np)



Scheme 4.

A mixture of ${\bf 5}$ (50 mg, 93 $\mu mol),$ 1-naphthaleneboronic acid (39 mg, 0.22 mmol), Pd(PPh_3)_4 (11 mg, 9.3 $\mu mol),~K_2CO_3$ (0.10 g,

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0.75 mmol) in toluene (11 mL), ethanol (1.4 mL), and water (1.4 mL) was heated at 90 °C for 17 h. After solvents were removed, CH₂Cl₂ and water were added. An aqueous phase was extracted with CH₂Cl₂, and combined organic phase was dried over MgSO₄. After evaporating solvents, the crude product was purified by SiO₂ column chromatography using hexane/ethyl acetate (3/1 in volume) (Rf = 0.58) as an eluent to obtain colorless solid BPU-1Np in 33 mg (56% yield). Mp: 158.1-158.7 °C. ¹H-NMR (400 MHz, CDCl₃) δ ppm 0.70–0.79 (m, 6H), 1.04-1.18 (br, 12H), 1.42-1.55 (m, 4H), 3.58 (m, 2H), 4.16 (m, 2H), 7.33–7.54 (m, 12H), 7.64 (d, J = 1.96 Hz, 2H), 7.81– 7.94 (m, 6H). ¹³C-NMR (101 MHz, CDCl₃) δ ppm 14.01, 22.61, 26.15, 27.59, 31.22, 47.83, 121.39, 125.38, 125.80, 125.85, 126.17, 127.07, 127.84, 128.38, 129.75, 130.02, 131.61, 133.82, 134.13, 137.44, 139.30, 143.05, 165.48. Anal Calcd for C45H46N2O.0.6H2O: C, 84.23%; H, 7.41%; N, 4.37%; O, 3.99%. Found: C, 84.24%; H, 7.54%; N, 4.15%. IR (ATR) 1664 cm⁻¹ (C=O).

Biphenylurea with 2-naphthyl group (BPU-2Np)



Scheme 5.

This compound was prepared in a similar way to that of **BPU-1Np** from **5** and 2-naphthaleneboronic acid as colorless solid in 43% yield. Mp: 213.6–214.2 °C. ¹H-NMR (400 MHz, CDCl₃) δ ppm 0.68 (t, *J* = 6.11 Hz, 6H), 1.05 (br, 12H), 1.44 (m, 4H), 3.54 (m, 2H), 4.09 (m, 2H), 7.35 (d, *J* = 8.56 Hz, 2H), 7.46–7.54 (m, 4H), 7.74–7.83 (m, 4H), 7.84–7.98 (m, 8H), 8.10 (s, 2H). ¹³C-NMR (101 MHz, CDCl₃) δ ppm 13.87, 22.51, 26.15, 27.59, 31.16, 47.76, 122.03, 125.41, 125.73, 126.07, 126.46, 127.13, 127.34, 127.71, 128.20, 128.60, 132.67, 133.71, 134.76, 137.62, 137.86, 143.15, 165.33. Anal Calcd for C₄₅H₄₆N₂O·0.35H₂O: C, 84.83%; H, 7.39%; N, 4.40%; O, 3.39%. Found: C, 84.84%; H, 7.21%; N, 4.34%. IR (ATR) 1651 cm⁻¹ (C=O).

Biphenylurea with anthryl group (BPU-Ant)



Scheme 6.

This compound was prepared in a similar way to that of **BPU-1Np** from **5** and 9-anthraceneboronic acid as colorless solid in 76% yield. Mp: 216.0–218.9°C. ¹H-NMR (400 MHz, CDCl₃) δ ppm 0.78–0.89 (m, 6H), 1.23 (br, 12H), 1.61 (m, 4H), 3.67 (m,

2H), 4.27 (m, 2H), 7.20–7.27 (m, 2H), 7.34 (m, 4H), 7.39–7.50 (m, 6H), 7.53 (d, J = 1.22 Hz, 2H), 7.61 (m, 4H), 7.92–8.05 (m, 4H) 8.44 (s, 2H). 13 C-NMR (101 MHz, CDCl₃) δ ppm 14.14, 22.61, 26.10, 27.61, 31.34, 47.90, 121.68, 125.10, 125.43, 125.64, 126.49, 126.59, 126.79, 128.34, 128.44, 130.27, 130.37, 130.79, 131.22, 131.27, 131.29, 134.20, 135.54, 135.93, 143.30, 165.57. Anal Calcd for C₅₃H₅₀N₂O-2.3H₂O: C, 82.41%; H, 7.13%; N, 3.63%; O, 6.84%. Found: C, 82.47%; H, 6.75%; N, 3.50%. IR (ATR) 1665 cm⁻¹ (C=O).

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Entry for the Table of Contents

FULL PAPER

Axial chirality: Six non-planar and urea-bridged conjugated oligomers were synthesized through palladiumcatalyzed intramolecular direct arylation and their chiroptical properties were investigated in detail.

Key Topic: Axial chirality



Koji Takagi,* Yuto Hirano, Koichiro Mikami,* Shoko Kikkawa, and Isao Azumaya

Page No. – Page No.

Chiral Non-Planar Oligophenylenes bridged by Urea Linkage: Synthesis through Intramolecular Direct Arylation, Chiroptical Behavior, and Theoretical Investigation