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Phenyl-(2-pyridyl)-(3-pyridyl)-(4-pyridyl)methane: Synthesis, Chiroptical Properties, and Theoretical Calculation of Its Absolute Configuration

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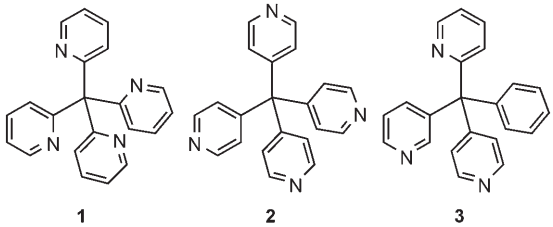
Abstract: The title compound, a prototypical chiral molecule based on a tetraarylmethane framework, has been synthesized in five steps from (2-pyridyl)-(3-pyridyl)ketone. X-ray crystallographic analysis revealed the tetraarylmethane framework of the molecule but did not determine the positions of the nitrogen atoms because the crystal is a racemic compound and the aryl groups are disordered in the crystal. The optical resolution of the title compound was achieved by chiral HPLC with a Chiralcel OD column. The CD spectra of the two fractions in acetonitrile exhibited opposite signs as expected for a pair of enantiomers. Their CD spectra are changed in 2 M HCl due to protonation. The calculated CD curve for the target molecule based on time-dependent density functional theory (TDDFT) reproduces the experimental result very well, thus suggesting that the first eluted fraction is the *R* isomer in terms of absolute configuration.

Keywords: chirality · circular dichroism · configuration determination · density functional calculations · tetraarylmethane

Introduction

A number of chiral molecules based on various topological motifs have been synthesized to elucidate the relationship between molecular structure and chiroptical properties. Nonplanar aromatic compounds[1] (helicenes,[2] corannulene derivatives,[3] and cyclophanes[4]), macrocycles,[5] mechanically interlocked molecules[6] (catenanes,[7] rotaxanes,[8] knots,[9] and pretzelanes[10]), and fullerenes[11] have attracted considerable attention with respect to molecular chirality. We recently reported the synthesis and properties of tetrakis(2-pyridyl)methane (**1**)[12] and tetrakis(4-pyridyl)methane (**2**)[13] as novel tetrahedral, tetradentate bridging ligands (Scheme 1). In the course of our studies, we designed phenyl-(2-pyridyl)-(3-pyridyl)-(4-pyridyl)methane (**3**) as a prototype of a chiral molecule based on a tetraarylmethane framework. Although compound **3** has three pyridyl rings on the same carbon atom, it does not have any symmetry elements and is inherently a chiral molecule. However, the four aryl groups on the central carbon atom are quite similar to one another; three CH units in tetraphenylmethane are asymmetrically replaced by nitrogen atoms. Wynberg and co-workers reported chiral tetraalkylmethane deriva-



Scheme 1. Symmetrical tetrapyridylmethanes (**1** and **2**) and a chiral molecule based on the tetraarylmethane framework (**3**).

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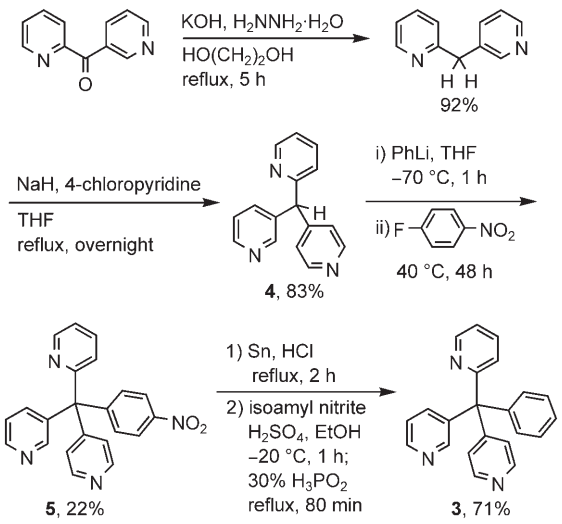
tives in which the polarizabilities of the four alkyl groups on the asymmetric carbon atom are almost equal.[14] Although they stated that these chiral tetraalkylmethanes exhibited undetectable or very small specific rotation, the CD spectra for these compounds were not presented. We are interested in the chiroptical properties of **3** that originate from the subtle differences in the aryl groups, and we report herein the synthesis and chiroptical properties of **3**. A theoretical approach to the assignment of the absolute configuration of **3** is also presented. To our knowledge, although there are a few chiral tetraphenylmethane derivatives known so far,[15] this is the first report about chiroptical properties and a theoretical approach for the determination of the absolute configuration of a tetraarylmethane-based chiral molecule.

Results and Discussion

The synthesis of **3** is illustrated in Scheme 2. In studies on the synthesis of tetrapyridylmethanes, it was found that halopyridines rarely gave the corresponding tetrapyridylmethanes by nucleophilic substitution with tris(4-pyridyl)methyl anions. Hence, we planned to synthesize **3** from (2-pyridyl)-(3-pyridyl)-(4-pyridyl)methane (**4**) and a halobenzene derivative. The key compound **4** was synthesized by the procedure used for tris(4-pyridyl)methane. Wolff–Kishner reduction of (2-pyridyl)-(3-pyridyl)ketone[16] gave the corresponding dipyridylmethane in good yield. Aromatic nucleophilic substitution of 4-chloropyridine with dipyridylmethyl anion gave **4**, which is also a chiral molecule. Deprotonation of **4** with PhLi followed by treatment with 4-fluoronitrobenzene gave the desired tetraarylmethane derivative **5** in 22% yield. Removal of the nitro group by reduction followed by a diazotization–reduction protocol afforded the target chiral molecule **3** in 71% yield. As expected, compound **3** is a stable colorless crystalline compound. The high solubility of **3** in a variety of common organic solvents facilitated the investigation of its properties.



Scheme 2. Synthesis of **3**.

Although the ^{1}H NMR spectrum of **3** is very complicated, each signal is assignable and consistent with the structure of **3** (see Supporting Information, Figure S1). There are 17 signals in the aromatic region in the ^{13}C NMR spectrum of **3**, which also correspond to the structure of **3** in a dynamic regime characterized by fast rotation of the aryl groups. This observation is consistent with the ^{1}H NMR spectra of **1** and **2**, in which no restricted rotation of pyridyl groups was observed at 30 °C. The ^{13}C chemical shift of the central carbon atom (Cα) was observed at 64.7 ppm. Compared with those of the related tetraarylmethanes (**1**: 72.4; **2**: 63.6; Ph_4C: 64.9; $(2\text{-Py})_3C(4\text{-Py})$: 70.0 ppm), this value is similar to that of Ph_4C as a result of the superposition of the effect of each substituent. Full assignment of the ^{1}H and ^{13}C NMR spectra was achieved by the acquisition of heteronuclear multiple-quantum correlation (HMQC) and heteronuclear multiple-bond correlation (HMBC) spectra (see Supporting Information, Figures S1–S5).

Fortunately, the enantiomeric pair of **3** was resolved by chiral HPLC with a Chiralcel OD column (Figure 1); however, the resolution of the intermediates **4** and **5** has not yet been achieved. The electronic CD spectra of the two fractions in acetonitrile (Figure 2, top) show a typical pattern of paired enantiomers, that is, they are mirror images of each other.

The structure of **3** was confirmed by X-ray crystallographic analysis (see Supporting Information, Figure S6).[17] Single crystals of **3** were obtained from a solution of the racemic mixture of **3** in chloroform by vapor diffusion with pentane. Although the tetraarylmethane framework was successfully revealed, the nitrogen atoms could not be assigned; the asymmetric unit was only half of a molecule, and there were no specific features for the reflection intensity, the bond lengths or angles of the six-membered rings, or the packing diagram. When a single crystal of **3** was analyzed by chiral HPLC, equal amounts of the enantiomers were found to be contained in a single crystal. Therefore, the obtained single crystal of **3** turned out to be a racemic compound. The uncertainty of the nitrogen atoms is attributed to the inconsistent distribution of the enantiomeric mixture in the crystal, the conformational disorder of the aryl groups, and the rotational disorder of the 2- and 3-pyridyl groups.

Besides the chiroptical properties of **3**, we are also interested in the chiroptical properties of **6**, the triprotonated form of **3** (Scheme 3). As benzene and pyridinium ion have

Abstract in Japanese:

テトラアリールメタンを基盤とするキラル分子として表題化合物を合成した。表題化合物はキラル HPLC で光学分割でき、各フラクションのCDスペクトルは典型的なミラーイメージを与えた。時間依存密度汎関数 (TDDFT) 法を用いて絶対配置の決定を行い、キラル HPLC で先に溶出するエナンチオマーを*R*-体と決定した。

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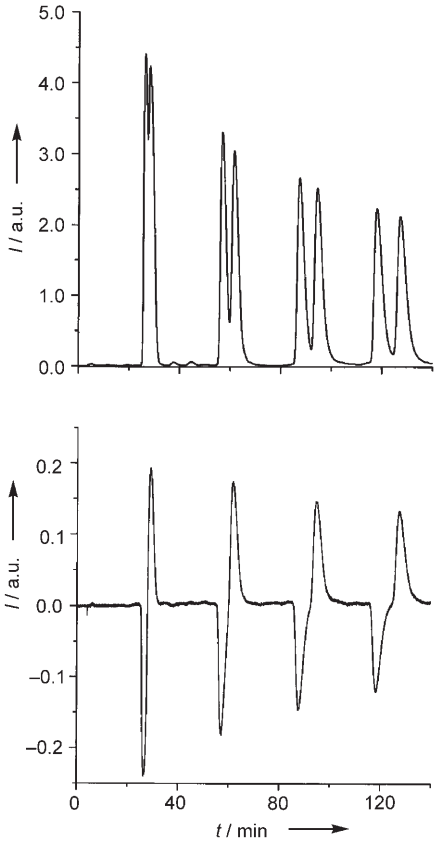


Figure 1. Chromatogram for the enantiomeric separation of **3**. Top: UV detection ($\lambda = 275$ nm). Bottom: CD detection ($\lambda = 275$ nm). Column: Chiralcel OD, eluent: hexane/ethanol = 90:10, flow rate: 1.0 mL min^{-1}, temperature: 25 °C. After four cycles, the two enantiomers were well-resolved.

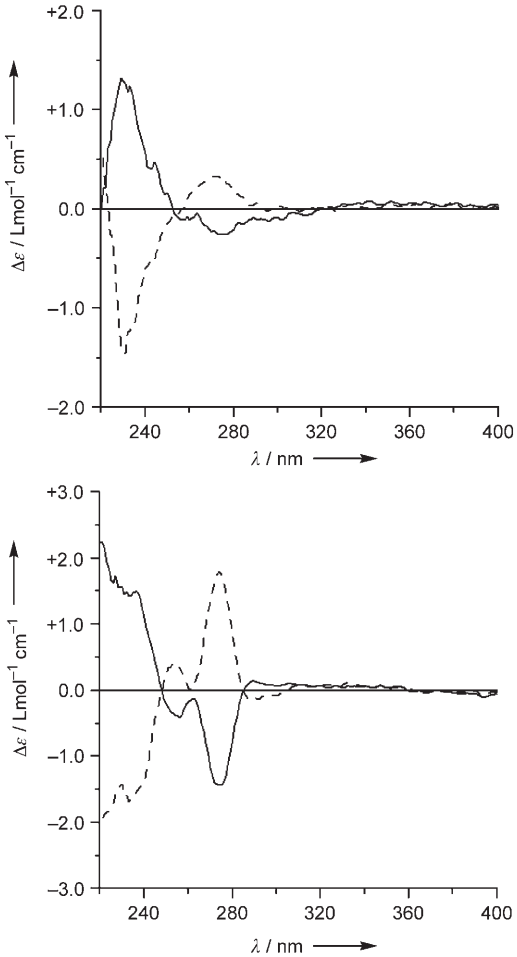
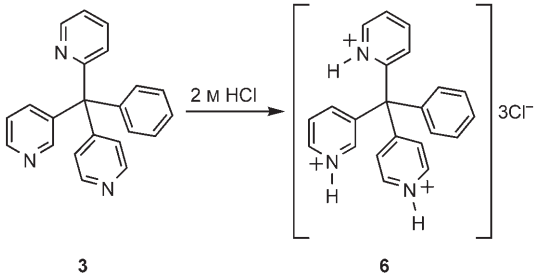


Figure 2. CD spectra of the enantiomeric pair of **3**. Top: in acetonitrile. Bottom: in 2 M HCl. The curves of the first and second eluted fractions are plotted as solid and dashed lines, respectively.

isoelectronic structures, all four aryl groups in **6** are isoelectronic. As shown in Figure 2 (bottom), the CD spectrum of each enantiomer of **3** in 2 M HCl is considerably different from that in acetonitrile, although the mirror-image character is maintained. It is likely that both the electronic structure and the conformational population of **3** are changed by triprotonation.

To determine the absolute configuration of **3**, we applied a quantum-mechanical method to calculate the electronic CD curve for comparison with the experimental ones.[18] The calculations were performed on structures of **3** with the *R* configuration. At first, a molecular-mechanics conformational analysis was carried out with MMFF94S[19] to give 12 stable conformations within the energy range 3 kcal mol^{-1}, which correspond to the various rotamers around the four C–aryl bonds. Each of the obtained conformers was further optimized with the density functional theory (DFT) method at the B3LYP[20]/6-31G(d)[21] level (their structures are shown in the Supporting Information, Figure S7). The relative populations of these 12 conformers at 298 K were then evaluated by the Boltzmann equation at that temperature (see Supporting Information, Table S1) and employed in the following CD estimation.



3 **6**

Scheme 3. Triprotonation of **3**.

The rotational strengths of the lowest 24 excited states for each conformer were calculated with the time-dependent density functional theory (TDDFT) method[22] by employing the B3LYP functional[20] with the TZVP[23] basis set of triple-zeta split-valence quality. The CD spectra computed for the various conformers (see Supporting Information, Figures S8 and S9) exhibited great variation in terms of band positions, intensities, and signs, due to the superimposition of many individual rotational strengths; on the contrary, the calculated UV/Vis spectra did not differ as much, in

keeping with the superior sensitivity of CD to the molecular conformation. The twelve calculated CD curves were Boltzmann-weighted and summed to afford the average curve in Figure 3.[18c] As a result, the calculated CD spectrum for

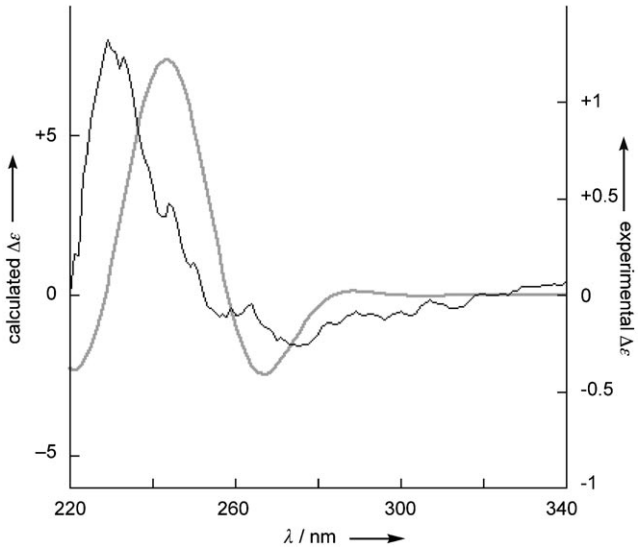


Figure 3. Boltzmann-weighted average calculated CD curve for (*R*)-**3** at the TDB3LYP/6-31G(d) level (gray) and experimental CD spectrum for the first eluted enantiomer (black).

(*R*)-**3** has a negative peak at 267 nm and a stronger positive one at 243 nm, which reproduce the experimental result very well in terms of wavelength and relative intensity of the bands (Figure 3); the overall shape of the calculated CD spectrum was not sign-reversed or drastically changed by reasonable modification of the conditions of the calculation (see Experimental Section). By comparison of the calculated and experimental CD curves, this output suggests that the first eluted fraction of **3** is the *R* isomer in terms of absolute configuration.

Conclusions

We have synthesized phenyl-(2-pyridyl)-(3-pyridyl)-(4-pyridyl)methane **3** as a prototype of tetraarylmethane-based chiral molecules. The optical resolution of **3** was achieved by chiral HPLC, which was confirmed by CD spectroscopy. TDDFT calculations for **3** show that the first eluted fraction has the absolute configuration *R*. The determination of the absolute configuration by X-ray crystallographic analysis of a diastereomeric salt, N-methylation and N-oxidation, as well as the formation of metal complexes will be further examined for **3**.

Experimental Section

General

Melting points were obtained on a Yanako MP 500D apparatus and are uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a JEOL EX-270 (270 MHz) or JEOL LA-500 (500 MHz) spectrometer. Chemical shifts were recorded in units of parts per million downfield from tetramethylsilane as an internal standard, and all coupling constants are reported in hertz. Electronic spectra were recorded in CH_2Cl_2 on a JASCO V-570 spectrophotometer. CD spectra were recorded on a JASCO J-720W spectropolarimeter. Mass spectra were recorded with a Shimadzu GCMS-QP5050 spectrometer by the EI method. Chiral HPLC was performed on a JASCO PU-2080/CO-2060/UV-2075/CD-2095 chromatograph with a Daicel Chiralcel OD column. Elemental analysis was performed at the Elemental Analysis Center at the Faculty of Science, Osaka University. Commercially available reagents and solvents were purified and dried when necessary.

Syntheses

(2-Pyridyl)-(3-pyridyl)methane: (2-Pyridyl)-(3-pyridyl)ketone[16] (6.80 g, 36.9 mmol), KOH (4.87 g), and ethylene glycol (110 mL) were placed in a 300-mL round-bottomed flask. This mixture was gently warmed to dissolve the ketone and the KOH. After cooling, hydrazine hydrate (3.58 mL, 73.8 mmol) was added, and the reaction mixture was heated under reflux for 5 h. The reaction mixture was cooled, diluted with water (160 mL), and extracted with chloroform (100 mL) five times. The combined organic layers were washed with water and dried over anhydrous sodium sulfate. After filtration to remove sodium sulfate, the filtrate was concentrated and dried under vacuum. The residue was purified by distillation under reduced pressure to afford (2-pyridyl)-(3-pyridyl)methane (5.82 g, 92%) as pale-yellow liquid. B.p.: 142–143 °C (0.8 mmHg); ^{1}H NMR (270 MHz, $CDCl_3$) δ = 8.57–8.54 (m, 2H, 2-Py 6-H, 3-Py 2-H), 8.47 (dd, J = 4.9, 1.6 Hz, 1H, 3-Py 6-H), 7.63–7.56 (m, 2H, 2-Py 4-H, 3-Py 4-H), 7.22 (ddd, J = 8.0, 4.7, 0.9 Hz, 2H, 2-Py 5-H), 7.16–7.11 (m, 2H, 2-Py 3-H, 3-Py 5-H), 4.15 ppm (s, 2H, CH_2); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 159.3, 150.0, 149.3, 147.6, 136.5, 136.2, 134.8, 123.2, 122.8, 121.4, 41.7 ppm; MS (EI): *m*/*z* (%) = 170 (16) $[M]^+$, 169 (100) $[M-H]^+$; elemental analysis: calcd (%) for $C_{11}H_{10}N_2$: C 77.62, H 5.92, N 16.46 (this compound is hygroscopic; calcd (%) for $C_{11}H_{10}N_2 \cdot 0.05H_2O$: C 77.21, H 5.95, N 16.37); found: C 77.21, H 5.92, N 16.37.

(2-pyridyl)-(3-pyridyl)-(4-pyridyl)methane (**4**): 4-Chloropyridine hydrochloride (7.1 g, 47.3 mmol) was neutralized by adding aqueous NH_3 (14%, 120 mL). The solution was extracted thrice with diethyl ether (30 mL). The combined organic layers were dried over NaOH pellets. After decantation, the solution of 4-chloropyridine was concentrated to give an ethereal solution ($\approx$10 mL) of 4-chloropyridine. (Complete evaporation of solvent caused the decomposition of 4-chloropyridine.) THF (15 mL) was added, and diethyl ether was removed by distillation. A solution of (2-pyridyl)-(3-pyridyl)methane (4.0 g, 23.5 mmol) in THF (15 mL) was added to a suspension of NaH (2.81 g, 60% oil dispersion, 70.3 mmol) in THF (40 mL) at 0 °C. The mixture was stirred for an additional 30 min at 0 °C. A freshly prepared solution of 4-chloropyridine in THF was added dropwise to the mixture over 10 min. The reaction mixture was stirred for 3 h at room temperature, then heated under reflux for 17 h. The reaction, which produced a reddish-brown suspension, was carefully quenched by addition of water (100 mL) at 0 °C. The reaction mixture was extracted with chloroform (100 mL) five times. The combined organic layers were dried over anhydrous sodium sulfate. After filtration and concentration, the residue was purified by column chromatography on alumina (50 g; EtOAC) to give **4** (4.79 g, 83%) as colorless crystals. M.p.: 66–68 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 8.62 (ddd, J = 4.9, 1.9, 0.8 Hz, 1H, 2-Py 6-H), 8.54 (dd, J = 4.3, 1.6 Hz, 2H, 4-Py 2,6-H), 8.53–8.49 (m, 2H, 3-Py 2,6-H), 7.67 (td, J = 7.7, 1.9 Hz, 1H, 2-Py 4-H), 7.56 (dddd, J = 8.0, 2.3, 1.8, 0.7 Hz, 1H, 3-Py 4-H), 7.26 (ddd, J = 8.1, 4.9, 0.8 Hz, 1H, 3-Py 5-H), 7.21 (ddd, J = 7.6, 4.9, 1.1 Hz, 1H, 2-Py 5-H), 7.15 (dt, J = 7.8, 0.8 Hz, 1H, 2-Py 3-H), 7.11 ppm (ddd, J = 4.3, 1.6, 0.7 Hz, 2H, 4-Py 3,5-H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 159.9, 150.3, 150.3, 149.8, 149.7, 148.2, 136.7, 136.5, 136.4, 124.0, 123.5, 123.3, 122.1, 56.0 ppm; MS (EI): *m*/*z* (%) = 247 (45) $[M]^+$, 246 (100) $[M-H]^+$, 169 (18) $[M-C_5H_4N]^+$; elemental analysis: calcd (%) for $C_{16}H_{13}N_3 \cdot 0.25H_2O$: C 76.32, H 5.40, N 16.69; found: C 76.28, H 5.15, N 16.56 (this compound is highly hygroscopic).

(4-Nitrophenyl)-(2-pyridyl)-(3-pyridyl)-(4-pyridyl)methane (**5**): A solution of PhLi (0.91 M) in butylether (1.6 mL, 1.46 mmol) was added to a

solution of **4** (360 mg, 1.46 mmol) in THF (30 mL) at −70 °C under nitrogen atmosphere. The reaction mixture was stirred for an additional hour at −70 °C. A solution of 4-fluoronitrobenzene (1.03 g, 7.3 mmol) in THF (10 mL) was added dropwise at −70 °C. The reaction mixture was allowed to warm to room temperature and then heated at 40 °C for 48 h. After it was cooled, the reaction mixture was diluted with water (50 mL) and extracted with chloroform (50 mL) five times. The combined organic layers were washed with water and dried over anhydrous sodium sulfate. After filtration and concentration, the residue was purified by column chromatography on alumina (50 g; EtOAc then EtOAc/methanol = 100:3 *v*/*v*) to afford **5** (133 mg, 22 %) as pale-yellow solid. M.p.: 178–179 °C; ^{1}H NMR (270 MHz, $CDCl_3$) δ = 8.64 (ddd, J = 4.9, 1.9, 1.1 Hz, 1H, 2-Py 6-H), 8.57 (dd, J = 4.6, 1.6 Hz, 2H, 4-Py 2,6-H), 8.53 (dd, J = 4.6, 1.6 Hz, 1H, 3-Py 6-H), 8.46 (dd, J = 2.7, 0.8 Hz, 1H, 3-Py 2-H), 8.18–8.13 (AA′BB′, 2H, Ph 3,5-H), 7.68 (ddd, J = 8.1, 7.6, 2.2 Hz, 1H, 2-Py 4-H), 7.54 (ddd, J = 8.2, 2.6, 1.5 Hz, 1H, 3-Py 4-H), 7.41–7.36 (AA′BB′, 2H, Ph 2,6-H), 7.26 (ddd, J = 8.1, 4.6, 0.8 Hz, 1H, 3-Py 5-H), 7.23 (ddd, J = 7.6, 4.9, 1.1 Hz, 1H, 2-Py 5-H), 7.19 (dt, J = 8.1, 1.1 Hz, 1H, 2-Py 3-H), 7.13 ppm (dd, J = 4.6, 1.6 Hz, 2H, 4-Py 3,5-H); ^{13}C NMR (67.8 MHz, $CDCl_3$) δ = 161.6, 152.8, 151.6, 150.9, 149.6, 149.0, 147.9, 146.4, 139.4, 136.5, 131.4, 125.1, 124.9, 123.0, 122.8, 122.0, 64.7 ppm; MS (EI): *m*/*z* (%) = 368 (100) $[M]^+$, 367 (98) $[M-H]^+$, 321 (25) $[M-HNO_2]^+$, 290 (13) $[M-C_5H_4N]^+$, 246 (21) $[M-C_6H_4NO_2]^+$; elemental analysis: calcd (%) for $C_{22}H_{16}N_4O_2$: C 71.73, H 4.38, N 15.21; found: C 71.60, H 4.46, N 14.86.

Phenyl-(2-pyridyl)-(3-pyridyl)-(4-pyridyl)methane (**3**): Conc. HCl (15 mL) was added dropwise to a mixture of **5** (655 mg, 1.78 mmol) and tin powder (3.0 g, 25 mmol) at 0 °C. The reaction mixture was heated under reflux for 2 h. The resulting yellow solution was alkalized with NaOH (10 %) at 0 °C. A white precipitate ($Sn(OH)_2$) appeared, which was removed by filtration and washed with chloroform. The filtrate was extracted with chloroform (50 mL) thrice, and the combined organic layers were dried over anhydrous sodium sulfate. Filtration and concentration gave crude (4-aminophenyl)-(2-pyridyl)-(3-pyridyl)-(4-pyridyl)-methane as a light-pink solid. This compound was used for the next step without further purification. Conc. H_2SO_4 (0.75 mL) was added to a suspension of (4-aminophenyl)-(2-pyridyl)-(3-pyridyl)-(4-pyridyl)methane (214 mg, 0.58 mmol) in ethanol (5 mL). Isoamyl nitrite (0.45 mL, 3.3 mmol) was added dropwise to the resulting yellow solution at −20 °C. The reaction mixture was stirred for an additional hour at −20 °C. H_3PO_2 (30 %, 2.2 mL) was added at −20 °C, and the reaction mixture was heated under reflux for 80 min. After it was cooled, the reaction mixture was diluted with water (50 mL) and washed with hexane to remove unreacted isoamyl nitrite. The aqueous layer was alkalized with NaOH (10 %) and then extracted with chloroform (100 mL) five times. The combined organic layers were dried over anhydrous sodium sulfate. After filtration and evaporation, the residue was purified by column chromatography on alumina (40 g; EtOAc/methanol = 20:1 *v*/*v*) to give **3** (145 mg, 71 %) as colorless crystals. M.p.: 208–210 °C; UV/Vis (acetonitrile): λ_{max} (log ε) = 260 nm (3.92 $M^{-1}cm^{-1}$); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.63 (ddd, J = 4.5, 2.0, 1.0 Hz, 1H, 2-Py 6-H), 8.53 (dd, J = 4.5, 1.5 Hz, 2H, 4-Py 2,6-H), 8.49–8.48 (m, 2H, 3-Py 2,6-H), 7.63 (ddd, J = 8.0, 7.5, 2.0 Hz, 1H, 2-Py 4-H), 7.59 (ddd, J = 8.0, 2.5, 1.5 Hz, 1H, 3-Py 4-H), 7.33–7.25 (m, 3H, Ph *meta*,*para*-H), 7.24 (ddd, J = 8.5, 4.5, 1.0 Hz, 1H, 3-Py 5-H), 7.20 (dt, J = 8.5, 1.0 Hz, 1H, 2-Py 3-H), 7.19 (ddd, J = 7.5, 5.0, 1.0 Hz, 1H, 2-Py 5-H), 7.17 (dd, J = 4.5, 1.5 Hz, 2H, 4-Py 3,5-H), 7.13–7.11 ppm (m, 2H, Ph *ortho*-H); ^{13}C NMR (125 MHz, $CDCl_3$) δ = 163.1, 154.3, 152.3, 149.5, 148.9, 147.5, 143.9, 140.7, 138.1, 136.3, 130.6, 128.3, 127.1, 125.8, 125.3, 122.6, 121.7, 64.7 ppm; MS (EI): *m*/*z* (%) = 323 (99) $[M]^+$, 322 (100) $[M-H]^+$, 245 (30) $[M-C_5H_4N]^+$, 244 (37) $[M-C_5H_5N]^+$; elemental analysis: calcd (%) for $C_{22}H_{17}N_3$: C 81.71, H 5.30, N 12.99; found: C 81.47, H 5.31, N 12.95.

Computations

All calculations were performed either on a Linux computer or on the grid server at the Media Information Center of Hiroshima University. Conformational analysis was performed by CONFLEX5[24] with the MMFF94S[19] force field, in which starting structures selected from a set within 50 kcal mol^{-1} were converged by applying systematic structural deviations.[25] Besides the 12 adopted conformers, two more conformations were found but excluded as their energies were far outside the range of 3 kcal mol^{-1}. The same 12 conformers found by the above analysis were also afforded by a Monte Carlo search with MMFF run with the Spartan 06 program (Wavefunction, Inc., Irvine, CA, 2006).

DFT calculations were run with the Gaussian 03 program.[26] Geometry optimization of the 12 conformers found by MMFF94S was performed at the B3LYP/6-31G(d) level.[20,21] For each input structure thus obtained, the first 24 excited states were computed with TDB3LYP/TZVP.[20,23] For the conformers that contributed to a greater extent to the average UV/Vis/CD spectra, we verified that all the 24 computed transitions involve virtual orbitals with negative eigenvalues and have energies (5.47–5.55 eV) well below the computed ionization potential (6.6–6.8 eV).[27] The impact of other functionals and basis sets was also tested on a few representative conformers by employing the PBE0[28] hybrid functional and the augmented double-zeta valence-quality-plus polarization functions basis set ADZP.[29] Both PBE0/TZVP and B3LYP/ADZP gave results very similar to those of B3LYP/TZVP. The dipole-length (DL) gauge formulation for the rotational strengths was considered in view of faster convergence toward the basis-set limit;[30] dipole-velocity values differed from DL ones within 15 % for most transitions with TZVP, and within 5 % with ADZP. All rotational strengths obtained from the calculations were converted into Gaussian-type curves by adopting a band of σ 20 nm width, and were summed to afford the calculated CD curve for each conformer (shown in the Supporting Information, Figures S9 and S10). Variation of σ values between 18 and 22 nm did not greatly affect the appearance of the Boltzmann-weighted average spectrum (see Supporting Information, Figure S11).

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[17] Crystal data for **3**: $C_{22}H_{17}N_3$, $M_r = 323.40$, orthorhombic, $P2_12_12$ (No. 18), $a = 7.676(8)$, $b = 14.65(1)$, $c = 7.334(5)$ Å, $V = 824(2)$ Å^3, $Z = 2$, $D_{calcd} = 1.302$ g cm^{-3}, $T = 200$ K, total reflections collected = 7874, unique reflections = 1889 ($R_{int} = 0.057$), final R factor = 0.053 ($R_w = 0.146$ for all data) for 1362 reflections ($I > 2\sigma(I)$), GOF = 1.05. The structure was solved by direct methods and refined by full-matrix least squares by using the SHELXL-97 program. Unfortunately, as the assignment of nitrogen atoms could not be achieved, the structure was solved as tetraphenylmethane. An ORTEP drawing of **3** is shown in the Supporting Information. CCDC-634542 (**3**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre at www.ccdc.cam.ac.uk/data_request/cif.

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