An indolocarbazole dimer as a new stereodynamic probe for chiral 1,2-diamines

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An indolocarbazole dimer as a new stereodynamic probe for chiral 1,2-diamines

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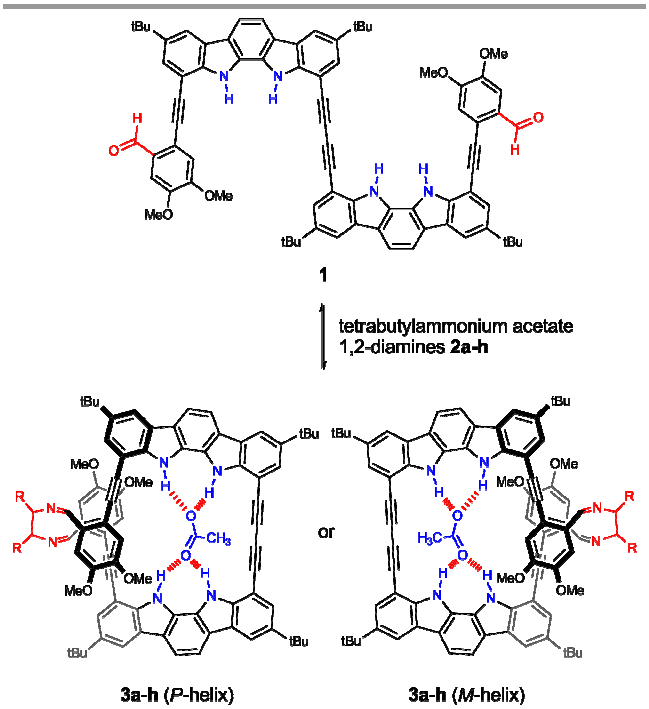
An indolocarbazole dimer that contains aldehyde groups at both ends was prepared by connecting two monomeric units through a rod-like 1,4-butadienyl spacer. Upon mixing with chiral 1,2-diamines at room temperature, the dimer was in-situ converted to the corresponding cyclic diimines in the presence of tetrabutylammonium acetate as a template. The resulting diimines fold to helical conformations of right-handed (*P*) or left-handed (*M*) orientations, depending on the absolute stereochemistries of chiral 1,2-diamines. The patterns and intensities of the CD spectra can be used to determine the absolute configurations and enantiomeric excesses of chiral 1,2-diamines.

Introduction

Chirality is a key feature of chemical entities, from small organic molecules to supramolecular assemblies, and it is at the heart of molecular and supramolecular chemistry. The chirality of small organic molecules in general originates from the configuration of local stereocenters, while the chirality of supramolecular assemblies is often attributed to the global conformation or helicity orientation which is reversible and stereodynamic. Circular dichroism (CD) spectroscopy has been widely used to determine the configurations and enantiomeric excesses (*ee*'s) of chiral molecules.[1] In particular, exiton coupled circular dichroism (ECCD) has been widely implemented for synthetic molecules, so-called stereodynamic probes, that possess two or more interacting chromophores oriented in a twisted array upon interacting with chiral analytes.[2,3] Most small chiral molecules do not have proper chromophores which show strong CD signals in the UV-visible region. These molecules therefore need to interact covalently or noncovalently with some stereodynamic probes that can afford characteristic CD signals for the determination of absolute configurations and *ee*'s of chiral analytes. Several stereodynamic probes for chirality sensing have been described including bisporphyrins,[4] propeller-shaped molecules[5] and aryl ethynyl foldamers,[6] etc.[7]

Recently, we described an indolocarbazole dimer **1** which was able to serve as a stereodynamic probe for chiral α-aminocarboxylates.[8] Upon coupling with ethane-1,2-diamine (**2a**) in the presence of a carboxylate, **1** with two aldehyde groups at ends was converted to the corresponding cyclic diimine **3a** that adopted a helical conformation.[9]



Scheme 1 Molecular structures of probe **1** and cyclic diimines **3a-h** of right (*P*)- and left (*M*)-handed helices.

When achiral acetate was used, two helical conformers were formed in 1:1 ratio. When a chiral α-aminocarboxylate was added instead of acetate, however, one helical complex was predominantly formed exhibiting characteristic CD spectra which allowed us to determine the absolute configurations and enantiomeric excesses (*ee*'s) of α-aminocarboxylates.

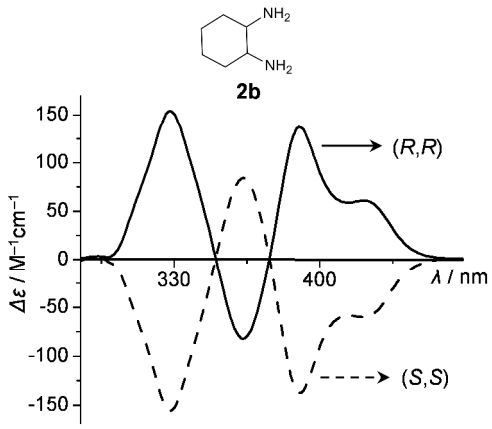


Fig. 1 CD spectra (5.0×10^{-5} M in CH_2Cl_2, 25 °C) of **3b** derived from (*R*,*R*)-**2b** (solid line) and (*S*,*S*)-**2b** (dashed line) (2 equiv) in the presence of tetrabutylammonium acetate (2 equiv).[8]

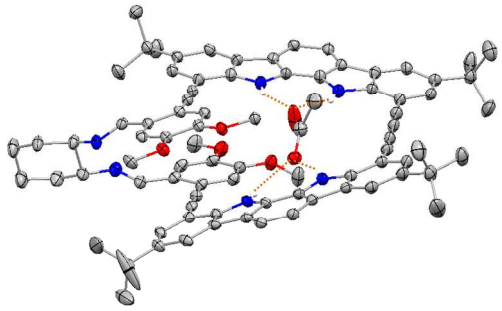


Fig. 2 Crystal structure of **3b** (*P*-helix) complexed with tetrabutylammonium acetate.[8] In the crystal, an oblique location of two indolocarbazole planes forms *P* helix. The acetate anion binds to the internal cavity with the hydrogen bond distances of 2.83~3.16 Å. Countercations and hydrogen atoms except NH protons have been omitted for clarity.

An alternative to induce the helical bias of the cyclic diimine was to replace ethane-1,2-diamine with a chiral 1,2-diamine, as described previously with optically pure cyclohexane-1,2-diamine **2b**. The resulting cyclic diimines, (*R*,*R*)-**3b** and (*S*,*S*)-**3b**, displayed characteristic CD spectra with strong Cotton effects at wavelengths ranging from 300 nm to 460 nm (Fig. 1).[8] The X-ray structure clearly demonstrated that (*R*,*R*)-**3b** was a cyclic diimine with a right-handed (*P*) helicity and the acetate ion was bound to the internal cavity by four NH···O⁻ hydrogen bonds (Fig. 2).[8] In order to demonstrate the scope and generality of this finding, we herein describe the CD spectral behaviours of other cyclic diimines **3c-3h** derived from commercially diamines **2c-2h**. The patterns of the CD spectra strictly depend on the absolute configurations of chiral 1,2-diamines and therefore **1** can be also served as a stereodynamic probe for chiral 1,2-diamines.

Results and Discussion

Probe **1** was synthesized according to the procedures described previously.[8,10] Simple mixing of **1** and 1,2-diamines **2c-2h** afforded the corresponding cyclic diimimes **3c-3h** at room temperature (Fig. 3 and ESI Fig. S1). It should be emphasized that tetrabutylammonium acetate is required as a template for efficient formation of cyclic diimines. As a representative example, the reaction between **1** and 1,2-diphenylethane-1,2-diamine (**2e**) is shown in Fig. 3. As the reaction proceeded, a characteristic ^{1}H NMR signal for imine (CH=N) protons appeared as a singlet around 8.9 ppm at the expense of the aldehyde signal (10.5 ppm, CH=O) in **1**. The reaction was completed within 1 h in the presence of the acetate ion, and one set of ^{1}H NMR signals consistent with the structure of a cyclic diimine **3e** was observed (Fig. 3a). In sharp contrast, the ^{1}H NMR spectrum was highly complicated in the absence of the acetate ion (Fig. 3b, top) possibly due to the formation of side products including acyclic products and higher oligomers.

Next, we examined the CD spectra of cyclic diimimes **3c-3h** which were prepared in-situ from enantiomeric pairs of chiral diamines **2c-2h** (Fig. 4). The general method was as follows. A chiral 1,2-diamine (2 equiv) was added to a CH_2Cl_2 solution of **1** (1 mM) and tetrabutylammonium acetate (~2 equiv) at room temperature. To record the CD spectrum, an aliquot was taken in a vial and diluted with pure CH_2Cl_2 to obtain the concentration of 5.0×10^{-5} M based on probe **1**. The CD spectra remained unchanged after 1 h under these conditions, indicating that the reaction was completed. It should be noted that both chiral diamines **2c-2h** and probe **1** are all CD-silent at wavelengths between 300 nm to 500 nm, and the CD signals of the mixture were attributed solely to the formation of helically twisted cyclic diimines **3c-3h**.

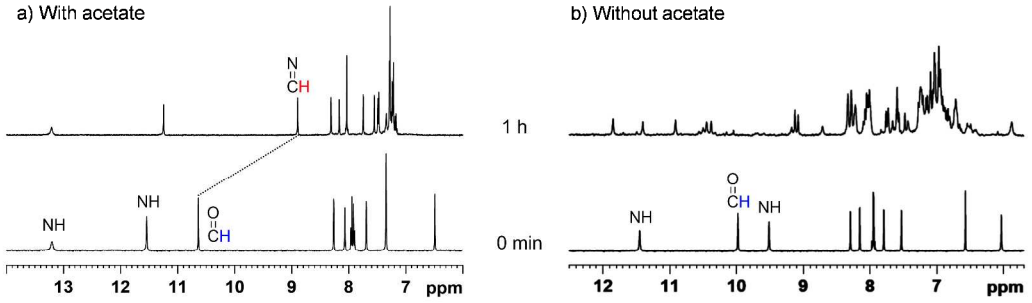


Fig. 3 Time-dependent ^{1}H NMR spectra of probe **1** upon addition of 1,2-diphenylethane-1,2-diamine (**2e,** 2 equiv) a) in the presence of tetrabutylammonium acetate (2equiv) as a template and b) in the absence of tetrabutylammonium acetate. Two NH signals are shifted downfield by Δδ = 1.76 and 1.94 ppm as a result of hydrogen bonding with the acetate ion.

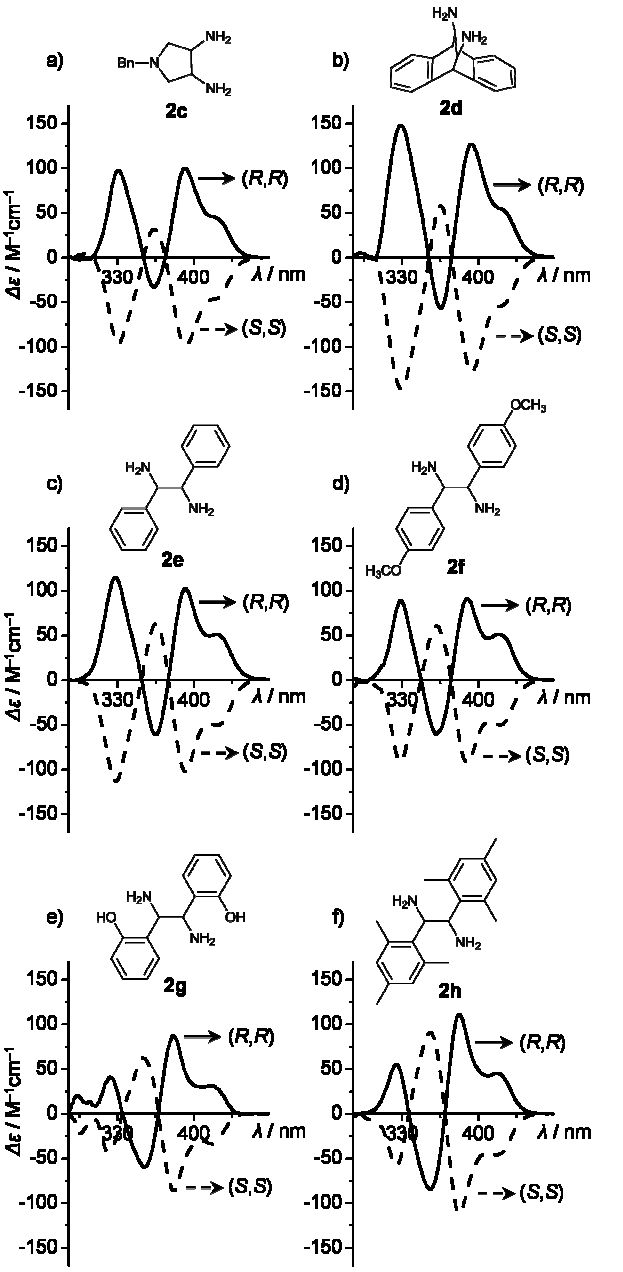


Fig. 4 CD spectra (5.0×10^{-5} M in CH_2Cl_2, 25 °C) of cyclic diimines **3c-3h** resulted from chiral 1,2-diamines **2c-2h** in the presence of tetrabutylammonium acetate (2 equiv).

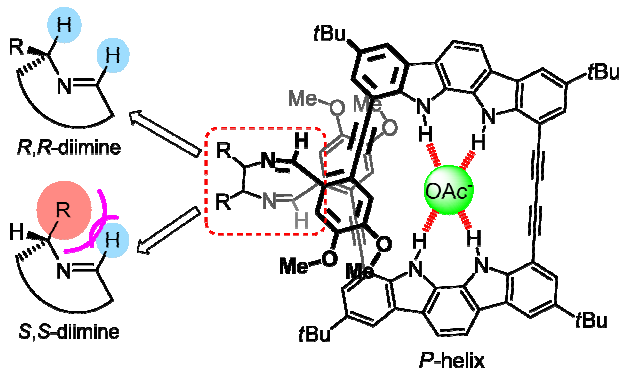


Fig. 5 Schematic representation of allylic 1,3-strain around imine bonds in cyclic diimines **3** of *P*-helices derived from (*R*,*R*)- and (*S*,*S*)-diamines **2**, based on the theoretical calculation.

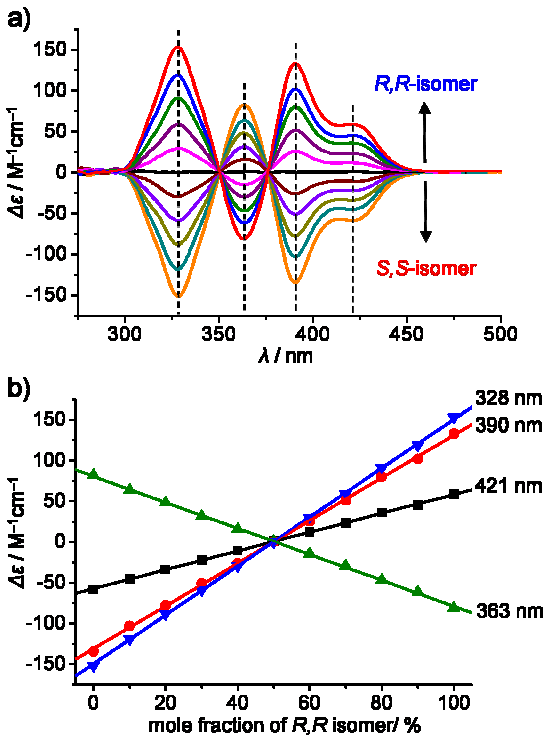


Fig. 6 a) CD spectra (5.0×10^{-5} M in CH_2Cl_2, 25 °C) of **3b** resulted from **2b** with different *ee*'s in the presence of acetate, and b) Obtained *ee* calibration curves at each λ max.

As shown in Fig. 1, (*R*,*R*)-**3b** gave characteristic CD signals with positive Cotton effects at 328, 390, and 421 nm and a negative Cotton effect at 363 nm, while the enantiomer (*S*,*S*)-**3b** yielded a symmetrical, inverted CD spectrum. The identical patterns of CD spectra were observed with all other cyclic diimines **3c-h** (Fig. 4). For examples, diimines (*R*,*R*)-**3c** and (*R*,*R*)-**3d** derived from cyclic diamines (*R*,*R*)-**2c** and (*R*,*R*)-**2d** showed positive Cotton effects at longer wavelengths, while the enantiomers (*S*,*S*)-**3c** and (*S*,*S*)-**3d** displayed negative Cotton effects. In addition, diimines **3e-3h** were derived from acyclic 1,2-diphenylethane-1,2-diamines **2e-2h** with different substituents in the phenyl rings. Diamine **2g** contains a potential hydrogen bonding group OH, while **2h** has sterically demanding dimethyl substituents at the *ortho* positions. Regardless the position and kind of substituents, diimines **3e-3h** gave the identical patterns of CD spectra. All the observations suggest that the CD signals at wavelengths between 300 and 460 nm originate from the exciton coupling of two indolocarbazole chromophores. More importantly, (*R*,*R*)-diimines always exhibit positive Cotton effects at longer

wavelengths while (*S,S*)-diimines show negative Cotton effects. As a result, the absolute stereochemistry of chiral 1,2-diamines can be determined simply by the patterns of Cotton effects in the CD spectra.

Computer modeling studies (Macromodel 9.1,[11] gas phase) were conducted to reveal the origin of helical bias of cyclic diimines. (*R,R*)-Diimines of *P*-helices were found to be more stable than the corresponding *M*-helices mainly because the latter isomers had severe allylic type 1,3-strain[12] around the imine bonds. This strongly distorted the co-planarity of imine and phenyl planes, thus interrupting π-conjugation (Fig. 5). The exciton chirality rule[3] also predicts that (*R,R*)-diimines showing first positive Cotton effects display *P*-helices while the (*S,S*)-diimines with the opposite effects possess *M*-helices. This prediction is consistent with the helical sense found in the X-ray structure of (*R,R*)-diimine **3b** complexed with tetrabutylammonium acetate.[8] Finally, the formation of a cyclic diimine **3b** was conducted with a mixture of two enantiomers (*R,R*)-**2b** and (*S,S*)-**2b** in different ratios. The CD intensities were linearly proportional to the ratio of two enantiomers at any wavelength (R^2 > 0.99) (Fig. 6a, 6b), implying that enantiomeric excesses of chiral 1,2-diamine could be determined based on the CD spectra, in addition to the absolute configurations.

Conclusions

An indolocarbazole dimer that contains two aldehyde units readily reacts with 1,2-diamines to afford the corresponding cyclic diimines that are helically twisted. Owing to the predominant formation of one helical isomer, characteristic CD spectra have been observed. The patterns and intensities of the Cotton effects are consistent with the absolute configurations and enantiomeric excesses of chiral 1,2-diamines. As a consequence, the dimer functions as a stereodynamic probe recognizing the chirality of chiral 1,2-diamines in addition to α-aminocarboxylates described previously.[8]

Experimental

Probe **1** was synthesized according to the procedures described previously,[8] and chiral diamines **2b-h** were all purchased from Aldrich chemical Co. and used without further purification.

Compound 1

M.p. > 297 ºC (dec); ^{1}H NMR (400 MHz, DMSO-d_6): δ = 11.40 (s, 2H; NH), 11.20 (s, 2H; NH), 10.53 (s, 2H), 8.42 (s, 2H), 8.33 (s, 2H), 8.09 (s, 4H), 7.73 (s, 4H), 7.40 (s, 2H), 7.25 (s, 2H), 3.85 (s, 6H), 3.70 (s, 6H), 1.47 ppm (s, 36H); ^{13}C NMR (100 MHz, CD_2Cl_2-d_2): δ = 191.7, 152.7, 147.8, 143.1, 142.2, 140.1, 140.0, 128.2, 126.0, 125.7, 125.6, 124.4, 122.7, 122.6, 121.4, 121.0, 118.5, 117.6, 116.6, 116.1, 114.8, 113.1, 111.5, 105.1, 103.7, 95.1, 91.2, 79.5, 77.9, 55.7, 54.4, 34.8, 34.7, 31.9, 31.7 ppm; IR (KBr): 3404(NH), 2193(C≡C), 1672(C=O) cm^{-1}; MS (MALDI-TOF) [*M*-H]$^+$, 1159.3; Anal. Calcd for $C_{78}H_{70}N_4O_6{\cdot}2H_2O$: C, 78.36; H, 6.24; N, 4.69, Found: C, 78.15; H, 6.34; N, 4.75.

^{1}H NMR and CD measurements of cyclic diimines 3b-h

To a CH_2Cl_2 or CD_2Cl_2 (1~4 mL) of **1**, an aliquot of each stock solution of tetrabutylammonium acetate (2 equiv) and 1,2-diamines (**2b-h**, 2 equiv) were added, and the final concentration of **1** was 1.0 × 10^{-3} M. The solution was allowed for standing at room temperature for 30 min to 1 h, ^{1}H NMR spectra and CD spectra were recorded. For CD spectra, the reaction mixture was diluted with CH_2Cl_2 to afford the concentration of 5.0 × 10^{-5} M based on **1**. CD spectra were recorded at room temperature under the conditions (scanning rate: 500 nm min^{-1}, band width: 1.0 nm, response time: 1.0 sec, accumulations: 2 scans).

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Notes and references

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† Electronic Supplementary Information (ESI) available: NMR studies, Circular dichroism studies and Computer modelling studies. See DOI: 10.1039/b000000x/

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