Optically active aromatics possessing helical chirality: one-pot synthesis, optical resolution and crystal structure of 13,14-dimethyldibenzo[*b,j*][4,7]phenanthroline and its dihydro form as a novel chiral building block

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Helical aromatics, 13,14-dimethyldibenzo[*b,j*][4,7]phenanthroline 1 and its dihydro form 2 were synthesized *via* a one-step reaction, resolved into each of the enantiomers by HPLC and their single crystal structures were determined.

The helicity observed in conjugated aromatics is currently attracting considerable attention due to their unique structural features and spectroscopic behaviour, however, this area still remains largely unexplored.[1,2] The chemical properties and functions of these molecules are of particular interest since helical chirality is structurally different from tetrahedral and axis chirality, the properties and functions of which have already been well described. The synthetic complexity, including the multi-step reactions and the chiral resolution, of these aromatics impedes detailed exploration. Here we wish to report a one-pot synthesis, optical resolution and the crystal structure of a helical aromatic, 13,14-dimethyldibenzo[*b,j*][4,7]phenanthroline 1 and its dihydro form 2.[3]

Condensation of *N,N'*-diphenyl-*p*-phenylenediamine (15 mmol) and acetic acid (86 mmol) in the presence of ZnCl$_2$ (15 mmol) as Lewis acid at 200 °C for 5 h gave resinous substances. Soxhlet extraction of the substances with CHCl$_3$ for 12 h and column chromatography (silica gel, CHCl$_3$) of the concentrated extract afforded 1 (56%), together with a small amount of 2 (<1%) and 3 (≪1%) (Scheme 1).[4] Compound 2 can also be quantitatively provided by the reduction of 1 with LiAlH$_4$ in diethyl ether.† ^{1}H NMR (CDCl$_3$) spectra of 1 and 2 showed that the two methyl groups (2.82 and 2.56 ppm for 1 and 2) are equivalent suggesting a symmetric structure. CPK model and molecular simulations using molecular mechanics (MM2) and the molecular orbital method (MOPAC) indicated that the aromatic ring in 1 and 2 is twisted due to the proximity of the two methyl groups giving rise to the left- and right-handed helix forms, a pair of enantiomers (*M*- and *P*-form) (Fig. 1).‡ In fact, the addition of two equivalents of a chiral acid as a shift reagent, *R*-(−)-1,1'-binaphthyl-2,2'-diyl hydrogen phosphate

Scheme 1

1 R = R′ = CH$_3$
3 R = CH$_3$, R′ = H
2
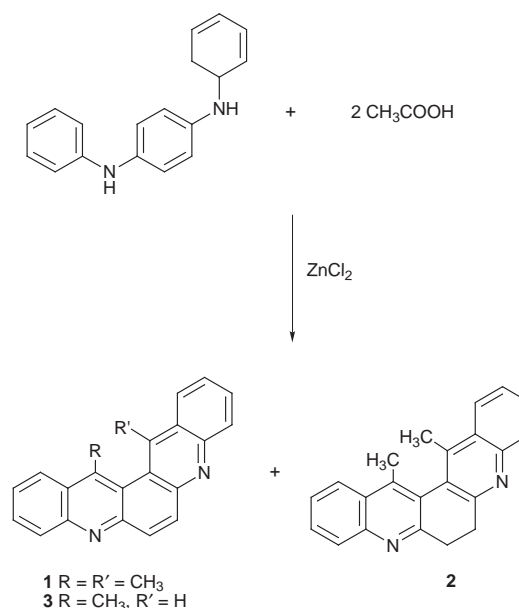
[(−)-4],[5] to 1 in CDCl$_3$ results in the splitting of the methyl resonance into two resonances (2.83 and 2.87 ppm) having the same peak area in the ^{1}H NMR showing that 1 forms a 1:2 complex with (−)-4 giving two diastereomers, (*M*)-1·(4)$_2$ and (*P*)-1·(4)$_2$.§ HPLC analyses with a chiral column (DAICEL, Chiralpack AD) resolved these racemates into the respective enantiomers. However, during separation by HPLC racemization could be observed in 1 but not in 2. The mechanism of the racemization is not clear at present but the tendency to racemize in these aromatics is consistent with the energy barrier of racemization calculated by molecular mechanics; *ca.* 80.2 kJ mol^{-1} and 105.0 kJ mol^{-1} at room temperature for 1 and 2.‡ The respective enantiomers of 2 separated showed a pair of split CD spectra which were mirror images with each other, as illustrated in Fig. 2. The elution band gave the first Cotton effect negative and the second positive, from which the absolute structure of 2 was suggested by the excitation chirality induction method,[6] namely, the first and second eluates could be provisionally assigned as (*M*)-2 and (*P*)-2, respectively.

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† Spectroscopic date for 1: *m/z* (MALDI-TOF) 308 (M$^+$); δ_H(270 MHz, CDCl$_3$, 10 mmol dm^{-3}) 2.82 (6H, s), 7.70 (2H, t, *J* 8.0), 7.85 (2H, t, *J* 8.0), 7.85 (2H, s), 8.23 (2H, w, *J* 8.0), 8.27 (2H, w, *J* 8.0); δ_C(67.5 MHz, CDCl$_3$, 10 mmol dm^{-3}) 19.5 (CH$_3$), 123.2, 124.5, 126.5, 126.7, 129.6, 129.8, 133.7, 142.2, 146.8, 150.5 (aromatic ring); correct CHN analysis. For 2: *m/z* (MALDI-TOF) 310 (M$^+$); δ_H(270 MHz, CDCl$_3$, 10 mmol dm^{-3}) 2.56 (6H, s), 3.1–3.5 (4H, m), 7.59 (2H, t, *J* 8.6), 7.75 (2H, t, *J* 8.6), 8.80 (4H, w, *J* 8.6); δ_C(67.5 MHz, CDCl$_3$, 10 mmol dm^{-3}) 17.5 (CH$_3$), 34.4 (methylene), 124.4, 126.1, 126.3, 127.7, 129.0, 129.5, 141.6, 146.1, 161.7 (aromatic ring); correct CHN analysis. For 3: *m/z* (MALDI-TOF) 294 (M$^+$); δ_H(270 MHz, CDCl$_3$, 10 mmol dm^{-3}) 3.46 (3H, s), 7.6–8.4 (10H), 9.28 (1H, s); δ_C(67.5 MHz, CDCl$_3$, 10 mmol dm^{-3}) 19.8 (CH$_3$), 123–151 (20 resonances, aromatic ring) (*J* values in Hz).

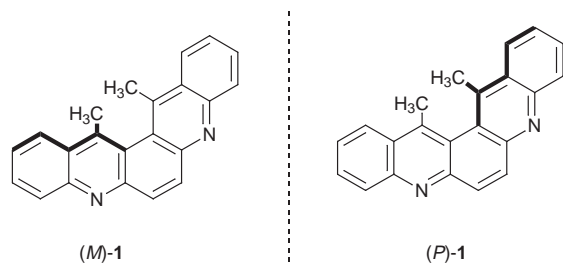‡ CAChe work system including MM2 and MOPAC was utilized for the molecular simulation.

§ The 1:2 stoichiometry was confirmed by the continuous variation (Job's) plots of the concentrations of complexes 1–4 *vs.* mole fraction of 4 (x_{guest}); the maximum occurs at x_{guest} = 0.67. Two molecules of the chiral acid (4) seemed to be bound to two nitrogen atoms in 1 by neutralization or through hydrogen bonds to give the ternary complex.
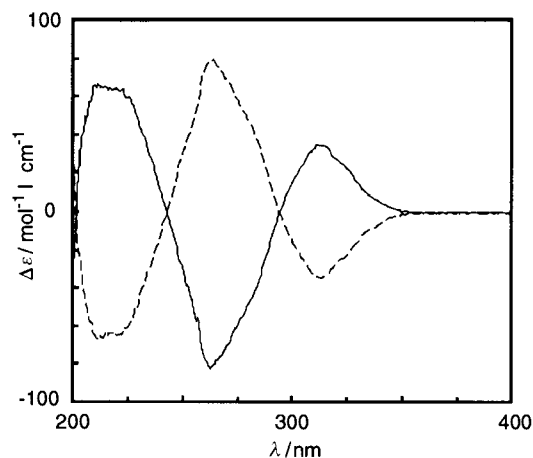
Fig. 1 Mirror image of (*M*)- and (*P*)-**1**

Fig. 2 Circular dichroism spectra of both the first (continuous line) and the second (dashed line) eluates of **2** resolved by chiral HPLC

Fig. 3 ORTEP drawing of (a) **1**, (b) **2**, and (c) **3**. Hydrogen atoms are omitted for clarity.

X-ray analysis of a single crystal of **1** and **2** shows that the aromatic ring is twisted, the interplanar angle between the terminal two benzene rings being about 50° and 60°, respectively [Fig. 3(a), (b)],¶ while [6]helicene has an angle of 58.5°.[7] The observed distance of 2.97 Å and 3.13 Å between two methyl groups in **1** and **2** verified the closed proximity of those groups predicted by the simulation above. In contrast, a single crystal of **3**, which lacks one of the two methyl groups in **1**, shows that the conjugated aromatic ring is flat [Fig. 3 (c)]. The mechanism of formation for **3** is ambiguous but the cleavage of the C–C bond between one of the methyl groups and the aromatic carbon in **1** may take place to relax the distortion on the twisted aromatic ring under the vigorous reaction conditions above. These single crystal analyses clearly indicate that the proximity of the two methyl groups in fact bring about the distortion on the aromatic ring in **1** and **2** to give rise to a pair of enantiomers.

Here we have introduced a very simple one-pot synthetic procedure for aromatics possessing helical chirality, so that **2** may become a more attractive bifunctional chiral building block since both enantiomers are available in large quantities. It is significant that the suitable location of alkyl groups in close proximity in space even on these simple aromatics afforded helical chirality. The helical aromatics presented here might give

a unique chiral environment since these helical molecules are structurally rigid as compared to molecules with tetrahedral and axis chirality which still retain structural flexibility around the single bond(s). A detailed investigation of the spectroscopic and chemical characteristics of these helical aromatics is presently under way in our laboratory.

References

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6 In Fig. 2 the CD bands at 263.5 and 210 nm are first and second Cotton effects, respectively, which are determined by CD and UV–VIS Spectra of **2**. Excitation-coupled CD is based on interacting chromophores, in **2** two quinoline moieties. When the two chromophores are oriented with clockwise movement from front to back the sign of first CD is positive and when anti-clockwise the sign of first CD is negative, see N. Harada and K. Nakanishi, *J. Am. Chem. Soc.*, 1969, **91**, 2989; *Circular Dichroism, Principles and Applications*, ed. K. Nakanishi, N. Berova and R. Woody, VCH Publishers, 1994.
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¶ *Crystal data* for **1**: $C_{22}H_{16}N_2$, $M_r = 308.38$; crystal system monoclinic; $a = 9.3539(8)$, $b = 13.339(1)$, $c = 12.6212(7)$ Å, $\beta = 93.812(6)°$, $V = 1571.3(2)$ Å³, temperature 20.0 °C; space group $P2_1/a$; $Z = 4$; μ(Cu-Kα) = 5.94 cm⁻¹; 2635 ($2\theta_{max} = 120.1°$) measured reflections; 1654 observed reflections with $F_o > 3\sigma(I)$. Final R factor = 0.048 ($R_W = 0.048$). For **2**: $C_{22}H_{18}N_2$, $M_r = 310.40$; crystal system monoclinic; $a = 5.0688(4)$, $b = 22.4999(6)$, $c = 13.9232(6)$ Å, $\beta = 93.771(8)°$, $V = 1584.5(2)$ Å³, temperature 20.0 °C; space group $P2_1/c$; $Z = 4$; μ(Cu-Kα) = 5.90 cm⁻¹; 2747 ($2\theta_{max} = 120.1°$) measured reflections; 1831 observed reflections with $F_o > 3\sigma(I)$. Final R factor = 0.045 ($R_W = 0.046$). For **3**: $C_{21}H_{14}N_2$, $M_r = 294.35$; crystal system orthorhombic; $a = 22.158(3)$, $b = 13.580(2)$, $c = 9.822(1)$ Å, $V = 2955(1)$ Å³, temperature 20.0 °C; space group *Pbca*; $Z = 7$; μ(Cu-Kα) = 5.31 cm⁻¹; 2533 ($2\theta_{max} = 120.1°$) measured reflections; 1335 observed reflections with $F_o > 3\sigma(I)$. Final R factor = 0.108 ($R_W = 0.082$). Full crystallographic details, excluding structure factor tables, have been deposited at the Cambridge Crystallographic Data Centre (CCDC). For details of the deposition scheme, see 'Instructions for Authors', *J. Chem. Soc., Perkin Trans. 1*, available *via* the RSC Web page (http://www.rsc.org/authors). Any request to the CCDC for this material should quote the full literature ci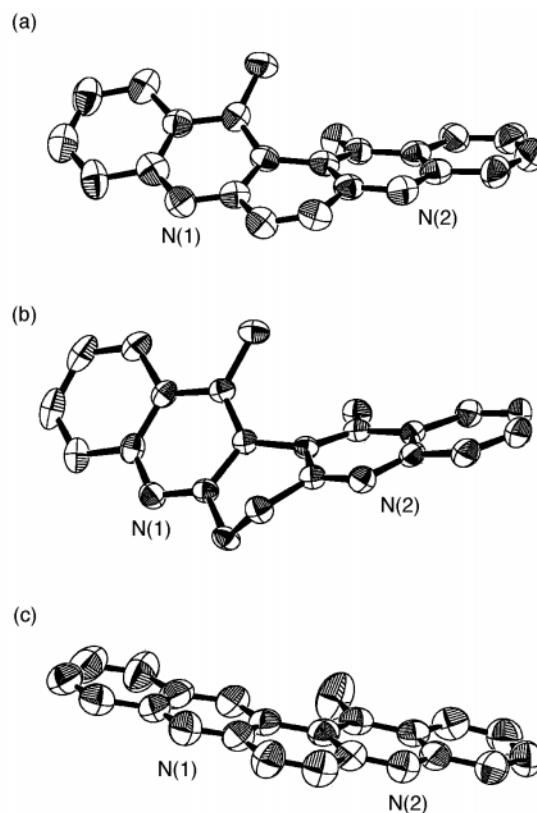tation and the reference number 207/236.