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Generation of chirality in 4,4′-azopyridine by co-crystallization with optically active dicarboxylic acids

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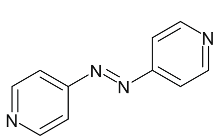
A B S T R A C T

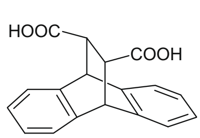
The co-crystals of *anti*-4,4′-azopyridine **apy** with optically active 9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboxylic acid **1** and *trans*-1,2-cyclohexanedicarboxylic acid **2** were prepared and their solid state CD spectra were measured. The positive Cotton effect sign, corresponding to the lowest energy n–π* transition, was correlated with the *M* helicity of the twisted Ar–N=N chromophore. The absolute sense of the twist of the guest **apy** molecule was deduced from the X-ray structures of the (*S,S*)-**1**·**apy** and (*S,S*)-**2**·**apy** complexes.

1. Introduction

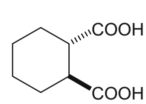
A phenomenon of induced optical activity arises when an achiral guest molecule is complexed by a chiral host. The guest becomes optically active due to a dissymmetry created by a chiral environment or generation of an excess population of two rapidly interconverting chiral conformers.[1] An asymmetric perturbation of the chromophore leads to induced circular dichroism (ICD), whose magnitude depends on the mutual arrangement of the host and guest molecules.[2] Optical activity can be induced upon dissolution of an achiral solute in a chiral solvent or by inclusion complexation of an achiral guest in the cavity of a chiral host. One well-known example is ICD observed in symmetric cyclohexanones, benzophenone, or azo dyes upon complexation with cyclodextrins.[3,4] Solid state CD measurements of crystalline inclusion complexes in combination with X-ray studies have recently emerged as an exceptionally useful technique for the elucidation of the mechanisms of induction of optical activity.[5,6] In particular, crystal lattices of naturally occurring cholic and deoxycholic acids are able to accommodate many types of organic guest molecules that make them versatile hosts for ICD studies.[6] Recently, we have shown that the *anti*-azobenzene trapped in the crystal lattices of these bile acids exhibits strong CD in the region of the n–π* electronic transition.[7]



apy

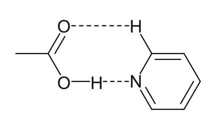


(*R,R*)-**1**



(*S,S*)-**2**

Azo dyes, particularly azobenzene, undergo a photoinduced *syn*–*anti* isomerization that is responsible for their potential application in optical switches and sensors, reversible data storage,[8] photoresponsive supramolecular systems,[9] or liquid crystalline polymers.[10] Control of supramolecular chirality is often a decisive factor in molecular recognition, assembly, or catalysis. In this context, we explored the new possibility of inducing optical activity by using supramolecular hydrogen-bonded assemblies of *anti*-4,4′-azopyridine **apy** with optically active dicarboxylic acids **1** and **2**. The motivation for this study was that the pyridine unit can form a stable cyclic hydrogen bond motif **I**.[11] Herein, we report X-ray studies of the co-crystals **1** and **2** with **apy** and their solid state CD spectra.



I

2. Results and discussion

The reported procedures for the asymmetric synthesis or chiral resolution of **1** are rather elaborate and suffer from low yields.[12] We found that the racemic acid **1** can be easily resolved to its enantiomers via the use of the diastereomeric cinchonine salt. Acid **2** was resolved with quinine according to the literature method.[13] Diffraction quality co-crystals of **apy** with optically active dicarboxylic acids **1** and **2** were grown from ethanol at ambient temperature using a 1:1 molar ratio of components. The X-ray structure of the complex (*S,S*)-**1**·**apy** revealed that the crystals (space group $P2_12_12_1$) are built of polymeric zig-zag chains with the alternating component molecules connected by strong O–H···N hydrogen

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bonds (Fig. 1). A non-planar arrangement of the pyridine ring and the carboxyl group forming two different dihedral angles of 27.4(3)° and 80.4(2)° prevents them from the additional weak C–H···O interactions. The **apy** molecule adopts a propeller geometry due to a significant twisting of the pyridine rings from the CN=N planes, as shown by the C=C–N=N torsion angles of −17.4(8)° and −18.1(7)°, whereas the azo chromophore is only slightly distorted from planarity [the C–N=N–C torsion angle is 172.9(4)°] (Fig. 2).

The UV–vis spectrum of **apy** taken in cyclohexane closely resembles that of *anti*-azobenzene and is characterized by a weak absorption at 458 nm (ε 260), corresponding to the forbidden n–π^* transition, and a strong one near 288 nm (ε 21,300), that can be assigned to the allowed π–π^* transition.[14,15] However, in contrast to azobenzene both bands are structureless.

The CD curves of the enantiomeric complexes (*S*,*S*)-**1**·**apy** and (*R*,*R*)-**1**·**apy** taken in KBr disks are perfect mirror images of each other which indicates the opposite helicity of the guest **apy** molecules (Fig. 3). A relatively strong Cotton effect near 500 nm and a weaker one at 364 nm can be assigned to the n–π^* and π–π^* excitations, respectively. There is a significant red-shift of both bands in the solid state CD spectra of **1**·**apy** with respect to the solution UV–vis spectrum. This might be due to the twisting of the azo chromophore in the solid state as shown by the X-ray structure. In contrast, the strong n–π^* Cotton effect exhibited by (*S*,*S*)-**2**·**apy** having a planar azo group almost perfectly matches the corresponding absorption band (Fig. 4). The observed positive sign of the long-wavelength CD band can be correlated with the *M* helicity of the skewed aryl–N=N system of the guest **apy** molecule revealed by the crystal structures of both complexes. This behavior is very similar to that shown by the *anti*-azobenzene complexes with bile acids.[7] The inherent chirality of the twisted aryl–N=N systems in both classes of the above-mentioned adducts leads to the strong magnitude of the observed n–π^* Cotton effects that contrasts with relatively weak Cotton effects reported for the induced CD spectra of the cyclodextrin complexes with azo dyes.[4]

3. Conclusion

In conclusion, the co-crystallization with optically active dicarboxylic acids leading to the formation of polymeric hydrogen-bonded assemblies is an effective method of inducing optical activity in *anti*-4,4′-azopyridine **apy**. The observed strong Cotton effect in the region of the n–π^* transition results from twisting of the guest molecule. The helicity of the guest molecules can either be assigned by X-ray crystallography or be deduced from the solid state CD measurements.

4. Experimental

Racemic acid **1** was prepared by Diels–Alder synthesis following the literature method.[16] Compound (*S*,*S*)-**2** was obtained by resolution of the racemate with quinine according to the reported procedure.[13] The solid state CD spectra were taken with freshly prepared KBr disks and recorded with a Jasco J-715 dichrograph. A mixture of 2–5 mg of the sample and 250 mg of dried KBr was ground and formed into a disk having a thickness of 0.5 mm and a radius of 15 mm. The disk was rotated around the optical axis and the CD recordings were made for several positions in order to check for reproducibility of the spectra. The UV–vis spectra were measured with a Unicam SP-300 spectrophotometer.

4.1. Resolution of 9,10-dihydro-9,10-ethanoanthracene-11,12-dicarboxylic acid, 1

Racemic acid **1** (5.6 g, 19 mmol) and cinchonine (5.6 g, 19 mmol) were dissolved in a hot mixture of ethanol (10 mL) and ethyl acetate (25 mL). The precipitated crystals were filtered and washed with ethyl acetate to obtain 5.2 g of the salt. The filtrate was evaporated to dryness and treated with aqueous KOH. The precipitated cinchonine was filtered and washed with water. The combined filtrates were acidified with concd hydrochloric acid and extracted with diethyl ether (3 × 30 mL). The organic layer

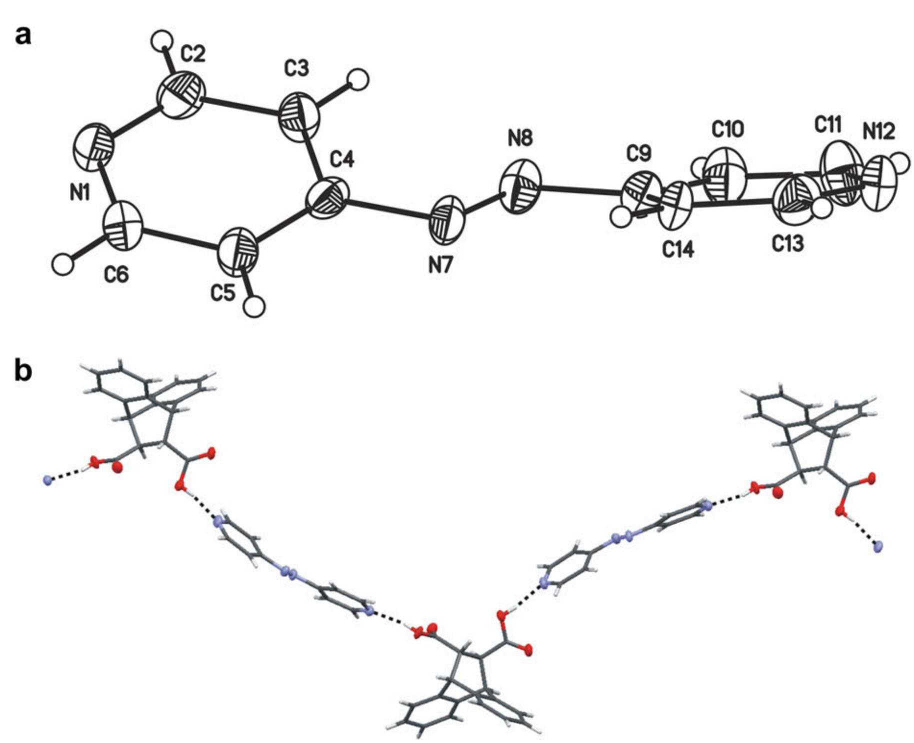

Figure 1. (a) The molecule of *anti*-4,4′-azopyridine in the (*S*,*S*)-**1**·**apy** complex and (b) the chain composed of the alternating hydrogen-bonded (*S*,*S*)-**1** and **apy** molecules.

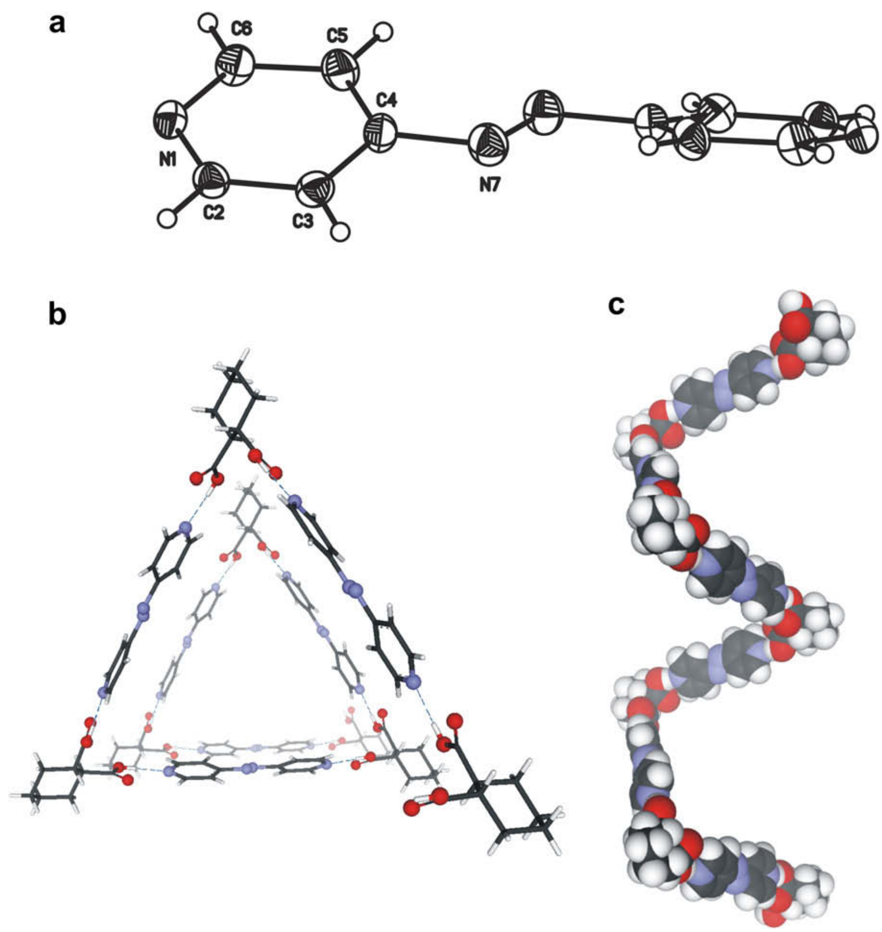

Figure 2. (a) The molecule of *anti*-4,4′-azopyridine in the (*S*,*S*)-**2**·**apy** complex, (b) and (c) the left-handed helix formed by hydrogen-bonded (*S*,*S*)-**2** and **apy** molecules.

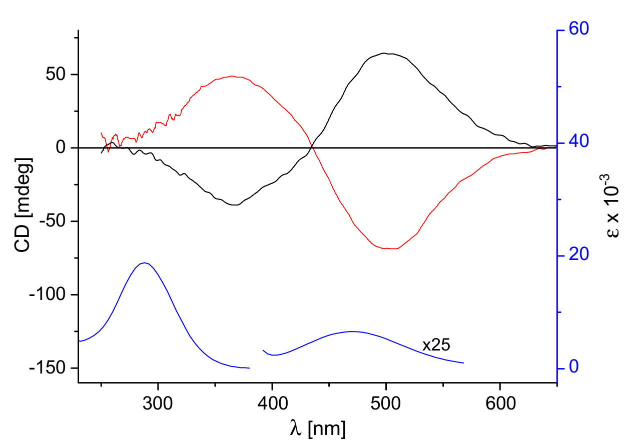

Figure 3. Solid state CD spectra of the (*S*,*S*)-**1**·**apy** and (*R*,*R*)-**1**·**apy** complexes taken in KBr disks (black and red line, respectively) and UV–vis spectrum of **apy** measured in cyclohexane (blue line).

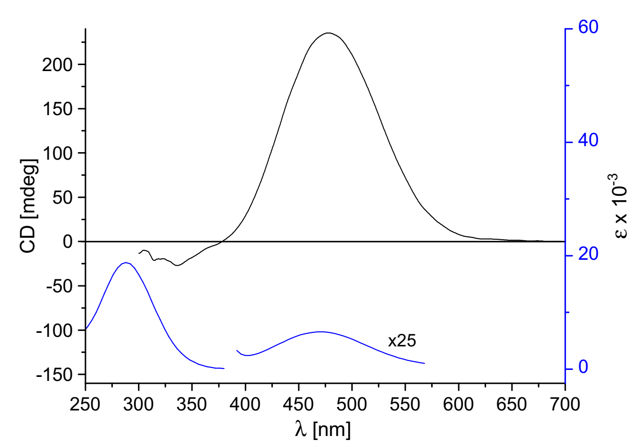

Figure 4. Solid state CD spectrum of (1*S*,2*S*)-**2**·**apy** taken in KBr disk and UV–vis spectrum of **apy** measured in cyclohexane (blue line).

was dried (Na_2SO_4) and concentrated in vacuo, and after the addition of hexane the product, 2.45 g, was crystallized; mp 225–226 °C (lit.[12a] mp 226–227 °C); $[\alpha]_D^{22} = +8.3$ (*c* 3, MeOH) [lit.[12c] $[\alpha]_D^{22} = +7.7$ (*c* 1.164, MeOH); ee 97%; lit.[12a] $[\alpha]_D = +7.9$ (*c* 0.795, MeOH)].

The crystalline salt was treated with dil. hydrochloric acid and extracted with diethyl ether (3 × 30 mL). The extract after work-up as described above gave 2.5 g of the product; mp 225–226 °C (lit.[12a] mp 226–227 °C); $[\alpha]_D^{22} = -9.2$ (*c* 4, MeOH) [lit.[12c] $[\alpha]_D^{22} = -7.6$ (*c* 1.574, MeOH); ee 96%].

4.2. X-ray structure analysis

Diffraction data were collected with a KM4CCD diffractometer. The crystal structures were solved by direct methods with SHELXS97[17] and refined by full-matrix least-squares with SHELXL97.[17]

All H atoms were positioned geometrically. In the absence of significant anomalous scattering, Friedel pairs were merged. All structural drawings were prepared with the program Mercury[18] or ORTEP-III for Windows.[19]

Crystal data for $C_{18}H_{14}O_4 \cdot C_{10}H_8N_4$ [(*S*,*S*)-**1**·**apy**], $M = 478.50$, orthorhombic, space group $P2_12_12_1$, $a = 8.2928(3)$, $b = 8.8548(4)$, $c = 32.8862(12)$ Å, $V = 2414.87(17)$ Å^3, $T = 105$ K, $Z = 4$, $\rho_x = 1.316$ g cm^{-3}, μ(Mo Kα) = 0.090 mm^{-1}, $\lambda = 0.71073$ Å, 21,382 reflections measured, 2452 unique ($R_{int} = 0.0447$). Final residuals for 325 parameters were $R_1 = 0.0662$, $wR_2 = 0.1801$ for 2177 reflections with $I > 2\sigma(I)$, and $R_1 = 0.0734$, $wR_2 = 0.1842$ for all data.

Crystal data for $C_8H_{12}O_4 \cdot C_{10}H_8N_4$ [(*S*,*S*)-**2**·**apy**], $M = 356.38$, trigonal, space group $P3_221$, $a = b = 7.4951(3)$, $c = 28.4287(14)$ Å, $V = 1383.06(10)$ Å^3, $T = 130$ K, $Z = 3$, $\rho_x = 1.284$ g cm^{-3}, μ(Mo Kα) = 0.093 mm^{-1}, $\lambda = 0.71073$ Å, 6184 reflections measured, 1146 unique ($R_{int} = 0.0256$). Final residuals for 118 parameters were $R_1 = 0.0307$, $wR_2 = 0.0807$ for 1019 reflections with $I > 2\sigma(I)$, and $R_1 = 0.0370$, $wR_2 = 0.0845$ for all data.

Crystallographic data (excluding structure factors) for the structures in this paper have been deposited with the Cambridge Crystallographic Data Center as supplementary publication numbers CCDC 724085 and 724086. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44(0)-1223-336033 or e-mail: deposit@ccdc.cam.ac.uk].

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