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Absolute Stereochemistry of 1-(9-Phenanthryl)-2-naphthoic Acid as Determined by CD and X-Ray Methods

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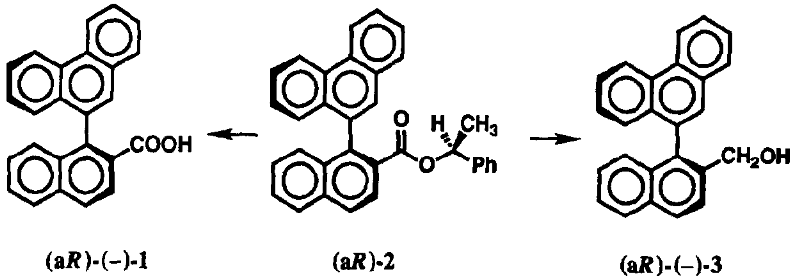
Abstract: 1-(9-Phenanthryl)-2-naphthoic acid (**1**) is optically resolved as the (1*S*,2*R*,4*R*)-(–)-2,10-camphorsultam amide (**5**) by HPLC. The absolute stereochemistry of acid (+)-**1** is determined to be (a*S*) by CD and X-ray studies.

Recently one group of the authors reported the practical and convenient asymmetric synthesis of 1,1'-binaphthyl-2-carboxylates.[1] In the studies, 1-(9-phenanthryl)-2-naphthoic acid (**1**) was also enantioselectively synthesized by the reaction of 9-phenanthrylmagnesium bromide with (*S*)-α-methylbenzyl 1-methoxy-2-naphthoate to give (*S*)-α-methylbenzyl 1-(9-phenanthryl)-2-naphthoate (**2**) in 49 % de.[1] The resolution of the diastereomeric mixture **2** by HPLC on silica gel and subsequent reduction of the major fraction with $LiAlH_4$ gave optically pure (–)-1-(9-phenanthryl)-2-naphthalenemethanol (**3**): $[\alpha]_D^{15}$ –90 (c 0.188, CH_3OH). The alkaline hydrolysis of the diastereomeric mixture **2** afforded the acid (–)-**1**: $[\alpha]_D^{25}$ –22 (c 0.992, THF). The absolute configuration of (–)-**1** was empirically determined to be (a*S*) on the basis of ^1H NMR studies of ester **2**.[1a] We report here that the absolute stereochemistry of acid (–)-**1** should be revised.



(a*R*)-(–)-1 **(a*R*)-2** **(a*R*)-(–)-3**

As shown in Figure 1, the CD spectrum of alcohol (–)-**3** shows a more complex pattern than typical exciton Cotton effects observed for chiral 1,1'-binaphthyl compounds. Since it is not clear which CD band is the first Cotton effect, the CD exciton chirality method[2] is not simply applicable to (–)-**3** which consists of phenanthrene and naphthalene chromophores. However, by comparison of the UV spectrum of **3** with that of phenanthrene, the UV band at 255.0 nm is assigned to the phenanthrene ^1B_b transition with a long axis polarization (Figure 1). The band at 226.6 nm is similarly assignable to the naphthalene ${}^1B_b$ transition. Therefore, it is concluded that the negative and positive CD Cotton effects at 246 nm ($\Delta\varepsilon$ −26.8) and 226 nm ($\Delta\varepsilon$ +139) are the first and second Cotton effects due to the exciton interaction between phenanthrene and naphthalene chromophores, respectively. This interpretation leads to the negative exciton chirality between two long axes of phenanthrene and naphthalene moieties, which corresponds to the (a*R*) configuration of the aromatic moiety (Figure 1). The absolute configurations of alcohol (−)-**3** and acid (−)-**1** were thus determined to be (a*R*), respectively. This conclusion is in conflict with the previously assigned absolute configuration

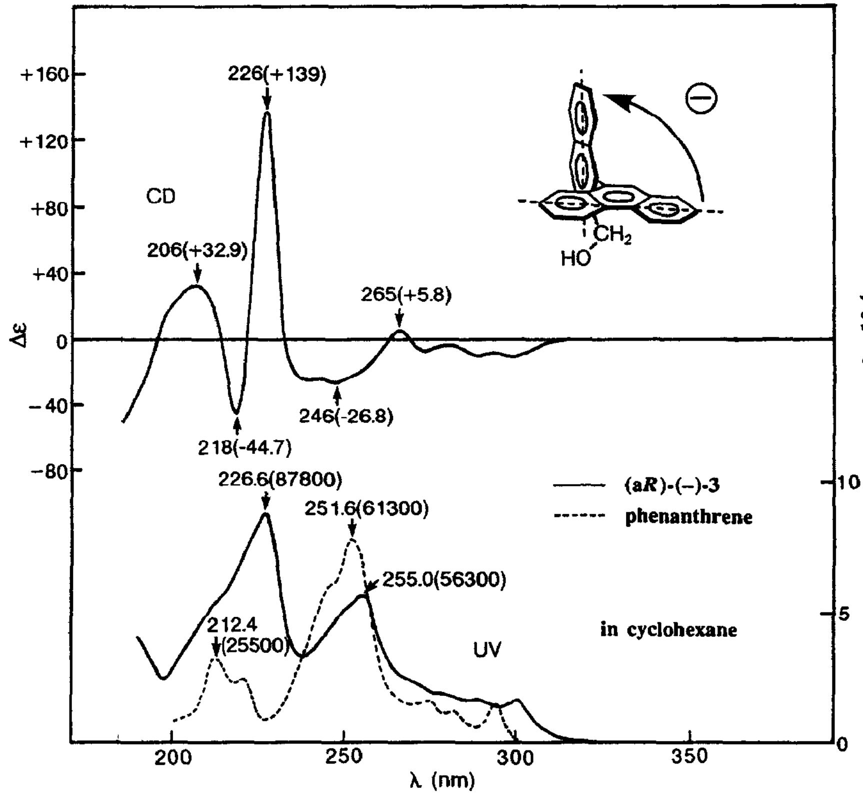
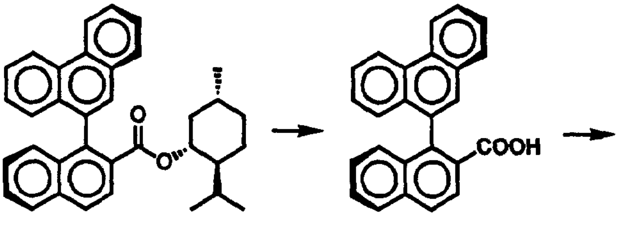


Figure 1. CD and UV spectra of alcohol (a*R*)-(−)-3

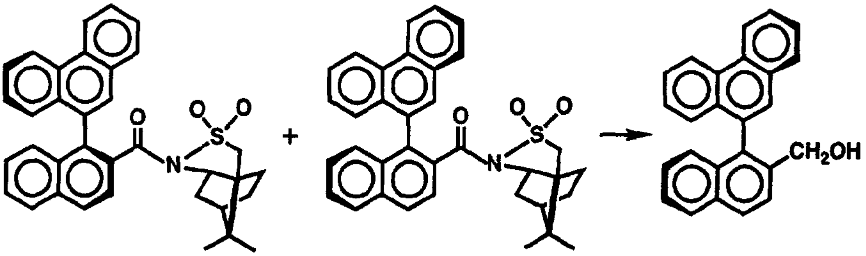
based on the ${}^1H$ NMR studies of ester **2**.[1a] Which assignment is correct? The determination by the CD method has the weak point that the observed CD spectrum of alcohol **3** does not show an ideal exciton split CD pattern. To confirm the absolute configuration determined by the CD method, we next carried out the X-ray crystallographic structure analysis.

Recently we reported that (1*S*,2*R*,4*R*)-(−)-2,10-camphorsultam was very useful as a chiral probe for optical resolution and X-ray crystallographic determination of the absolute stereochemistry of various carboxylic acids.[3,4] This camphorsultam method was applied to acid **1**. The coupling reaction of (1*R*,3*R*,4*S*)-

menthyl 1-((1*R*,3*R*,4*S*)-menthyloxy)-2-naphthoate with 9-phenanthrylmagnesium bromide gave (1*R*,3*R*,4*S*)-menthyl 1-(9-phenanthryl)-2-naphthoate (**4**), which was hydrolyzed to afford acid (+)-**1**: $[\alpha]_D^{17}$ +36.2 (c 1.30, THF), 61 % ee.[1,5] Acid chloride of (+)-**1** (61 % ee) was allowed to react with the anion of (1*S*,2*R*,4*R*)-(–)-2,10-camphorsultam generated with sodium hydride. The diastereomeric mixture of amides formed was separated by HPLC on silica gel (hexane/EtOAc 4:1). Amide (–)-**5a** was obtained as a major diastereomer from the first-eluted fraction: amorphous solid, $[\alpha]_D^{24}$ –71.8 (c 1.88, $CHCl_3$). Reduction of amide (–)-**5a** with $LiAlH_4$ yielded alcohol (+)-**3**: amorphous solid, $[\alpha]_D^{21}$ +97.3 (c 1.20, CH_3OH).



(a*S*)-4 **(a*S*)-(+)-1**



(a*R*)-(–)-5b (minor) **(a*S*)-(–)-5a (major)** **(a*S*)-(+)-3**

The second-eluted fraction of HPLC was evaporated to give amide (–)-**5b** as a minor diastereomer. The solid material of (–)-**5b** was crystallized from ethyl acetate to afford prisms (mp 231.0-232.0 °C; $[\alpha]_D^{24}$ –165 (c 1.19, $CHCl_3$)), which were subjected to X-ray crystallographic analysis: crystal dimension, 0.27 × 0.14 × 0.08; formula, $C_{35}H_{31}NO_3S$; formula weight, 545.69; crystal system, orthorhombic; space group $P2_12_12_1$; a = 10.815 (1) Å, b = 24.189 (3) Å, c = 10.538 (1) Å, vol = 2756.9 (5) $Å^3$; Z = 4; ρ(calcd) = 1.315 g/cm^3; ρ(obsd) = 1.315 g/cm^3 determined by flotation using a CCl_4/hexane solution; Cu K_α (1.541 78 Å); graphite crystal monochromator; linear absorption coefficient, 12.967 cm^{-1}; temperature 20 °C; θ–2θ scan; 2θ scan limits, 2-130°; no indication of standard reflection decay during data collection; independent reflections $F_0 > 3.0\ \sigma(F_0)$, 1878. The crystal structure was solved by the direct method, and all hydrogen atoms were placed at ideal positions. Block diagonal least-squares refinement of positional and thermal parameters, including anomalous scattering factors, led to the final convergence with R = 0.0563 for the (a*R*) absolute configuration, while R = 0.0590 for the mirror image structure. The absolute stereochemistry of amide (–)-**5b** was thus determined as shown in Figure 2. The (a*R*) configuration of (–)-**5b** was also assigned by use of the (1*S*,2*R*, 4*R*)-(–)-2,10-camphorsultam part as an internal reference of the absolute configuration.

From the chemical conversion and X-ray results described above, the absolute configurations of acid **1** and related compounds are now determined as follows: (a*S*)-(+)-1-(9-phenanthryl)-2-naphthoic acid **1**, (a*S*)-(+)-1-(9-phenanthryl)-2-naphthalenemethanol **3**, and diastereomeric amide (a*S*)-(–)-**5a**. It should be noted that the empirical method^{1a} for determination of the absolute configuration on the basis of ^{1}H NMR chemical shift data leads to a wrong configuration in this case.^{6}

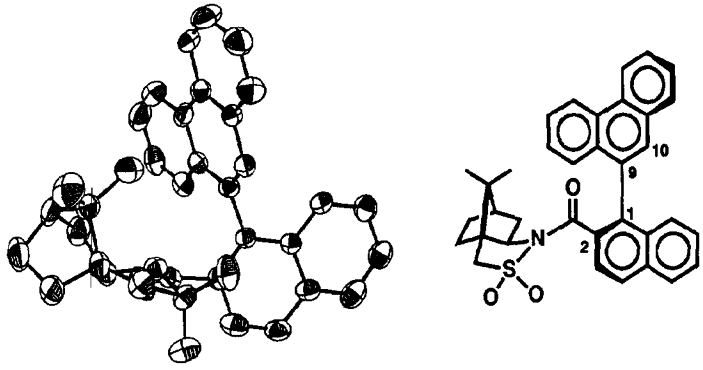


Figure 2. ORTEP drawing of amide (a*R*)-(–)-5b (minor): dihedral angle (2-1-9-10), +113°

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References and Notes

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5. The enantiomeric excess of acid (+)-1 was determined by the HPLC analysis of its methyl ester (Pirkle column, hexane/2-propanol 99:1).
6. It was found that the ^{1}H NMR spectra of (*S*)-α-methylbenzyl esters of binaphthyl- and bianthryl-carboxylic acids with the P-helicity showed the secondary methyl proton signal at lower field than those of esters with the M-helicity: ref. 1a. The case of 1-(9-phenanthryl)-2-naphthoic acid **1**, however, deviates from this tendency; the methyl protons of the (*S*)-α-methylbenzyl ester of (a*S*)-(+)-acid **1** with the M-helicity resonate at δ 0.59, while those of the ester of (–)-acid **1** with the P-helicity at δ 0.46. The deviation may be due to the conformational change and/or the anisotropic effect caused by the extra benzene moiety of the phenanthrene group.