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# ABSOLUTE CONFIGURATIONS OF ENANTIOMERIC K-REGION *CIS*-5,6-DIHYDRODIOLS OF 12-METHYLBENZ[*A*]ANTHRACENE AND 7-BROMO-12-METHYLBENZ[*A*]ANTHRACENE

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ABSTRACT: The absolute configurations of enantiomeric 7-bromo-12-methylbenz[*a*]anthracene *cis*-5,6-dihydrodiols (3) were determined by exciton chirality circular dichroism method. The absolute configurations of enantiomeric 12-methylbenz[*a*]anthracene *cis*-5,6-dihydrodiols (1) were determined by debromination of enantiomeric 3 of known absolute stereochemistry.

The hydroxyl groups of K-region *trans*-dihydrodiols of polycyclic aromatic hydrocarbons (PAHs) can assume either a quasidiequatorial or a quasidiaxial conformation.[1] The absolute configurations of enantiomeric *trans*-dihydrodiols of either conformation can be determined by the exciton chirality circular dichroism (CD) method.[2,3] In the absence of steric and/or electronic constraints, each of the two hydroxyl groups of *cis*-dihydrodiols of PAHs (e.g., 12-methylbenz[*a*]anthracene (12-methyl-BA) *cis*-5,6-dihydrodiol, 1) adopts either a quasiaxial or a quasiequatorial conformation. Because of this dual conformational possibility, the absolute configuration of enantiomeric *cis*-dihydrodiols such as 1 cannot be determined by the exciton chirality CD method (see below).

When an alkyl or a halo substituent is present at a *peri* position (e.g., the 7-substituent in 7,12-dimethyl-BA, 2 and in 7-bromo-12-methyl-BA, 3), the hydroxyl group *peri* to the substituent is forced to adopt a quasiaxial conformation due to either steric hindrance (e.g., 2)[3] or electronic repulsion (e.g., 3)[4-6] imposed by the *peri* substituent. The hydroxyl group distant to the *peri* substituent adopts a quasiequatorial conformation. The absolute configuration of enantiomeric *cis*-dihydrodiols that have a locked conformation (such as 2)[7] can thus be determined by the exciton chirality CD method.[2,8]

Recently chiral columns (see Table 1 for definition of the columns used in this study) have been employed to resolve enantiomers of a large number of mono-ols and diols of PAHs.[8-12] Enantiomers of 1, 2, and 3 can be resolved by at least three of the four chiral columns tested (Table 1). The establishment of absolute configuration-elution order relationship of the CSP-HPLC resolved enantiomers will greatly enhance our understanding of the chiral recognition mechanisms responsible for enantiomeric separations.

The CD spectrum of the enantiomeric 1 more strongly retained by (*S*)-DNBL-I (Table 1) is shown in Fig. 1A. This enantiomer was converted to a *bis-p-N,N*-dimethylaminobenzoate by reac-

Table 1. CSP-HPLC Resolution of K-region *cis*-Dihydrodiol Enantiomers of 12-Methyl-BA, 7-Bromo-12-methyl-BA, and 7,12-Dimethyl-BA.[a]

| Dihydrodiol | CSP[b] | Rt[c] | RV[d] |
|---|---|---|---|
| 12-methyl-BA | (*R*)-DNBPG-I | 23.5 (5*R*,6*S*) | 1.6 |
| *cis*-5,6-dihydrodiol (1)[e] | (*R*)-DNBPG-C | 15.6 (5*R*,6*S*) | 1.2 |
| (5e,6a & 5a,6e)[f] | (*S*)-DNBL-I | 20.4 (5*S*,6*R*) | 3.3 |
| | (*S*)-DNBL-C | 12.5 (5*S*,6*R*) | 2.2 |
| 7,12-dimethyl-BA[g] | (*R*)-DNBPG-I | 16.0 (5*S*,6*R*) | 1.0 |
| *cis*-5,6-dihydrodiol (2) | (*R*)-DNBPG-C | 11.6 (5*S*,6*R*) | 1.3 |
| (5e,6a) | (*S*)-DNBL-I | 17.7 (5*S*,6*R*) | 1.9 |
| | (*S*)-DNBL-C | 9.1 (5*S*,6*R*) | 0.5 |
| 7-bromo-12-methyl-BA | (*R*)-DNBPG-I | 20.9 | 0 |
| *cis*-5,6-dihydrodiol (3) | (*R*)-DNBPG-C | 13.8 (5*S*,6*R*) | 1.0 |
| (5e,6a) | (*S*)-DNBL-I | 17.2 (5*S*,6*R*) | 2.1 |
| | (*S*)-DNBL-C | 10.6 (5*S*,6*R*) | 0.5 |

[a] The enantiomers were resolved with HPLC columns (4.6 mm i.d. x 25 cm; Regis Chemical Co., Morton Grove, IL) packed with an (*R*)-*N*-(3,5-dinitrobenzoyl)phenylglycine either ionically bonded ((*R*)-DNBPG-I) or covalently bonded ((*R*)-DNBPG-C) and an (*S*)-*N*-(3,5-dinitrobenzoyl)leucine either ionically bonded ((*S*)-DNBL-I) or covalently bonded ((*S*)-DNBL-C) to spherical particles of 5 micrometer diameter of γ-aminopropylsilanized silica.[15,16] HPLC was performed using a Waters Associates (Milford, MA) liquid chromatograph consisting of a Model 6000A solvent delivery system, a Model M45 solvent delivery system, a Model 660 solvent programmer, and a Model 440 absorbance (254 nm) detector. Samples were injected via a Valco model N60 loop injector (Valco, Houston, TX). Separation of enantiomeric dihydrodiols was achieved isocratically with a flow rate of 2 ml/min using premixed solvents of 10% (v/v) of ethanol/acetonitrile (2:1, v/v) in hexane at ambient temperature.

[b] Chiral stationary phases (CSP) are defined above.

[c] Retention time (Rt) of the more strongly retained enantiomer. The absolute configurations of the more retained dihydrodiol enantiomers are indicated in parentheses.

[d] Resolution value (RV) = $2(V_2-V_1)/(W_2+W_1)$, where V is retention volume and W is peak width at base. The void time was 1.2 min.

[e] $\epsilon_{268}$ = 41800 $cm^{-1}M^{-1}$ (methanol); $[\alpha]_D^{24}$ +97 (*c* 0.54 mg/ml, methanol) for the 5*S*,6*R* enantiomer and -83 (*c* 0.62 mg/ml, methanol) for the 5*R*,6*S* enantiomer.

[f] Conformation of the hydroxyl group is indicated by a (quasiaxial) and e (quasiequatorial) in parenthesis.

[g] Resolution[11] and absolute configuration[8] of enantiomers were reported earlier and are included for comparison.

tion with *p-N,N*-dimethylaminobenzoyl chloride.[2,8] The CD spectrum of the dibenzoate (Fig. 1A) has a positive CD band with a maximum at 305 nm owing to the dipole-dipole interactions between the two benzoate groups. However, the expected exciton splitting with either a positive or a negative CD band at around 324 nm[2,8] was not observed. The lack of exciton chirality splitting is probably due to the dual conformations (quasiaxial and quasiequatorial) of both $C_5$-O and $C_6$-O bonds of 1. When the conformations of $C_5$-O and $C_6$-O bonds of *cis*-dihydrodiols such as 2 are restricted in one of two possibilities, an exciton splitting was observed in the CD spectrum of its *bis-p-N,N*-dimethylaminobenzoate derivative.[8]

Since the absolute configuration of an enantiomeric 1 could not be determined by the exciton chirality CD method, a novel approach was taken to elucidate the absolute configuration of an enantiomeric *cis*-dihydrodiol of 1. 7-Bromo-12-methyl-BA *cis*-5,6-dihydrodiol (3) was synthesized from 7-bromo-12-methyl-BA by reaction with $OsO_4$.[13] Since 3 has a locked conformation (5-quasiequatorial-6-quasiaxial)[7], the absolute configuration of an enantiomeric 3 can be determined by the exciton chirality CD method.[2,8] The bromo group of 3 can be removed by hydrogenolysis (tetrahydrofuran, $H_2/PtO_2$, 1 atm, 2 hrs).[4-6] Thus an enantiomeric 3 can be converted to an enantiomeric 1 with the absolute configuration unchanged. Hence the absolute configuration of an enantiomeric *cis*-dihydrodiol of 1 can be determined.

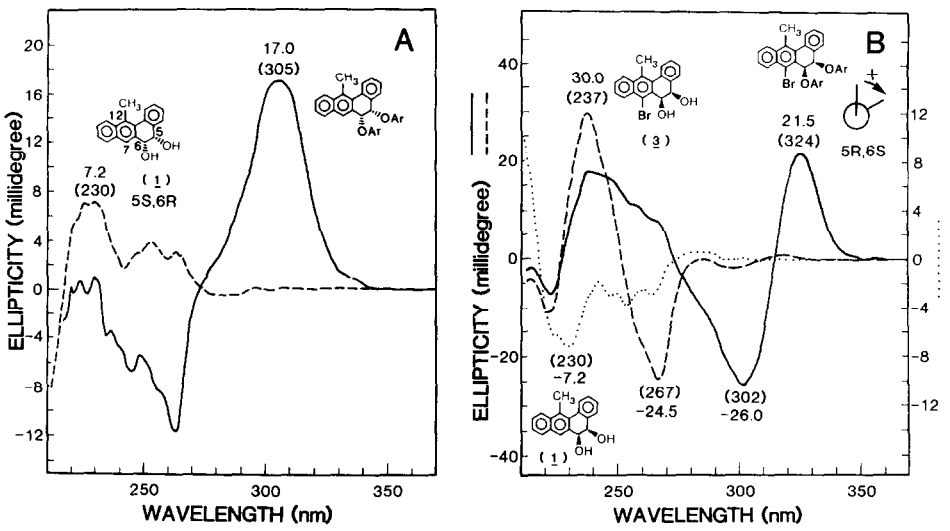


Figure 1. (A) CD spectra of an enantiomeric 1 (----, $\epsilon_{max}$ 265 nm) more strongly retained by (*S*)-DNBL-I and its *bis-p-N,N*-dimethylaminobenzoate (____, $\epsilon_{max}$ 310 nm). (B) CD spectra of an enantiomeric 3 (----, $\epsilon_{max}$ 268 nm) less strongly retained by (*S*)-DNBL-I, its *bis-p-N,N*-dimethylaminobenzoate (____, $\epsilon_{max}$ 313 nm), and its hydrogenolysis product (....., $\epsilon_{max}$ 265 nm). Ar = *p-N,N*-dimethylaminobenzoyl. CD spectra were obtained using a JASCO model 500A spectropolarimeter equipped with a DP-500 data processor.

The enantiomeric 3 less strongly retained by (*S*)-DNBL-I was converted to a *bis-p-N,N*-dimethylaminobenzoate by reaction with *p-N,N*-dimethylaminobenzoyl chloride.[2,8] The dibenzoate was purified by reversed-phase HPLC.[3,6,8] The CD spectrum of the *bis-p-N,N*-dimethylaminobenzoate (Fig. 1B) showed a positive CD band with an ellipticity ($\Phi_{324}/A_{313}$)[8] of +21.5 millidegrees due to the interacting transition moments of the benzoates. This positive CD chirality spectrum indicates that the enantiomeric 3 less strongly retained by (*S*)-DNBL-I has a 5*R*,6*S* absolute stereochemistry.[2] This 7-bromo-12-methyl-BA (5*R*,6*S*)-dihydrodiol was converted to a 12-methyl-BA (5*R*,6*S*)-dihydrodiol by catalytic hydrogenolysis (57% yield).[14] Analysis of the hydrogenolysis product with an (*S*)-DNBL-I column indicated that racemization did not occur. The CD spectrum of the hydrogenolysis product (Fig. 1B) indicates that it is a mirror image to that of an enantiomeric 1 which is more strongly retained by (*S*)-DNBL-I column (Fig. 1A and Table 1). These procedures thus established that 12-methyl-BA (5*R*,6*S*)-dihydrodiol is more strongly retained by both ionically and covalently bonded (*R*)-DNBPG columns and is less strongly retained by both ionically and covalently bonded (*S*)-DNBL columns. This study also established the relationship between the absolute configurations and CD spectra of enantiomeric 1 and 3.

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