Synthesis and Structure of Optically Active 1,12-Diethyl- and 1,12-Diisopropylbenzo[*c*]phenanthrenes: An Isopropyl Group Can Be Smaller than a Methyl Group

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1,12-Diethyl- and 1,12-diisopropylbenzo[*c*]phenanthrene-5,8-dicarboxylic acids were synthesized, and resolved. The dihedral angles formed by the A and D rings increased in the order of diisopropyl < diethyl < dimethyl as indicated by X-ray analysis, which showed that the strain decreased with the increase of the bulkiness at the 1,12-groups.

Helicenes are a group of chiral compounds possessing a nonplanar *o*-condensed polycyclic aromatic ring system.[1] If a series of helicenes with different pitches could be provided by the modification of their molecular structures, the properties of helical compounds can be better understood and fine-tuned. The effect of substituents on strain was compared in a series of 4,5-disubstituted phenanthrenes by experiments and calculations.[2,3] The following orders of the 4,5-substituent were obtained regarding the dihedral angle between the A and C rings, dihydro < difluoro < dimethyl < dichloro;[2] dihydro < dimethyl < diisopropyl < di(*t*-butyl).[3] The orders of the strain are in accordance with the bulkiness of the substituents. These compounds, however, generally racemize in solution at room temperature, and may not be suitable to study the effect of pitch. Thiaheterohelicenes with different substituents at the terminal benzene rings were compared.[4–7] It was shown that, in the solid state, the dihedral angles of the terminal benzenes changed depending on the structure of the bridged moiety, which connected the terminal benzenes.[5] Since the angle considerably changed by inclusion complexation, thiaheterohelicenes appear to possess a flexile structure.[6] A systematic study is needed to provide a series of optically active helicenes with different pitches.

1,12-Dimethylbenzo[*c*]phenanthrene is one of the configurationally stable helicenes, and their chirality is generated by the repulsion between the 1,12-dimethyl groups. Unlike 4,5-dimethylphenanthrenes, 1,12-dimethylbenzo[*c*]phenanthrenes do not racemize even at higher temperatures. In addition, this all-carbon helicene possesses a rigid structure as inferred by the invariable dihedral angles formed by the average plane of the A and D rings: (*P*)-1,12-Dimethylbenzo[*c*]phenanthrene-5,8-dicarboxylic acid bis(*l*-camphorsultam) amide (*P*)-**7**,[8] 47.9°; (*M*)-1,12-dimethylbenzo[*c*]phenanthrene-5,8-di(methylamine) dihydrochloride,[9] 46.99°; (±)-1,12-dimethylbenzo[*c*]phenanthrene-5,8-di(methylamine) dihydrochloride,[9] 47.03°. It was therefore considered interesting to modify the helical structure by substituting the 1,12-dimethyl group with other groups. Synthesized in this study are 1,12-diethylbenzo[*c*]phenanthrene and 1,12-diisopropylbenzo[*c*]phenanthrenes: Racemic 5,8-dinitriles (±)-**17** and (±)-**18**; 5,8-dicarboxylic acids (±)-**2** and (±)-**3**; optically pure 5,8-dimethanols (*P*)-**5**, (*M*)-**5**, (*P*)-**6**, and (*M*)-**6**; biscamphorsultams (*P*)-**8**, (*P*)-**9**, and (*M*)-**10** (Chart 1). The structures were compared with the 1,12-dimethyl derivatives: dinitrile (±)-**19**, dicarboxylic acid (±)-**1**, dimethanol (*P*)-**4**, and biscamphorsultam (*P*)-**7**.[8] Contrary to the expectation that replacing the 1,12-dimethyl group with diethyl and diisopropyl groups would increase the strain of the helicene ring system, the diisopropyl derivative was less strained than the dimethyl derivative.

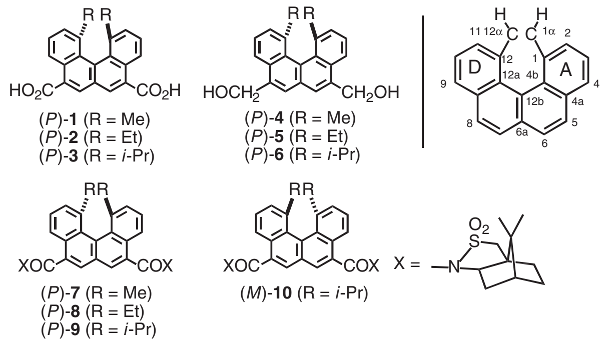
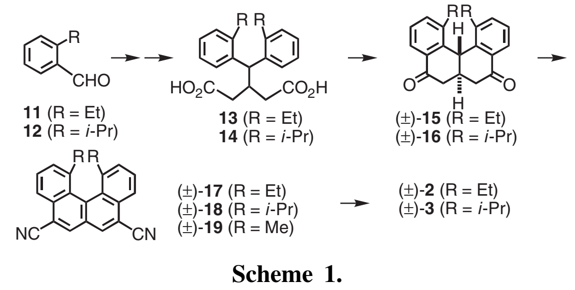


Chart 1.

The dicarboxylic acids (±)-**2** and (±)-**3** were synthesized employing the same method[8] with (±)-**1** starting from *o*-ethylaniline **11** and *o*-isopropylaniline **12**, respectively (Scheme 1). A diacid **13**, which was obtained from **11** in 5 steps, was treated with polyphosphoric acid giving a diketone (±)-**15** in 70% yield. The same reaction of another diacid **14**, synthesized from **12**, gave (±)-**16** (43%), which was accompanied by substantial deisopropylation (40%). The side reaction may be ascribed to the increased steric repulsions and/or cation stabilization of isopropyl group. Cyanation and aromatization of (±)-**15** and (±)-**16** gave 5,8-dinitriles (±)-**17** and (±)-**18**, respectively, which were hydrolyzed to provide (±)-**2** and (±)-**3**. Diethyl derivative (±)-**2** was resolved as brucine salt. Optically pure (*P*)-**2** was converted to biscamphorsultam (*P*)-**8** to determine the absolute configuration by X-ray analysis,[10,11] and was transformed to 5,8-dimetha-



Scheme 1.

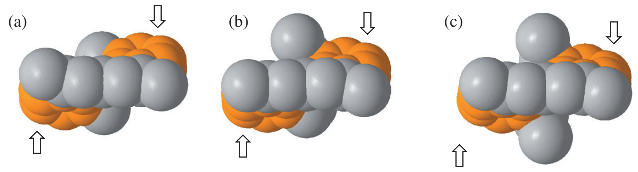


Figure 1. X-ray structures of biscamphorsultams (*P*)-**7** (a), (*P*)-**8** (b), and (*P*)-**9** (c): shown in orange are the A and D ring, in which the arrows indicate the increased volume of the helicene moiety.

nol (*P*)-**5** by lithium aluminum hydride reduction. Diisopropyl derivative (±)-**3** was converted to biscamphorsultams (*P*)-**9** and (*M*)-**10**, which were chromatographically separated. The compound (*P*)-**9** was subjected to X-ray analysis to determine the absolute configuration.[10,11] The chiral auxiliaries of (*P*)-**9** and (*M*)-**10** were removed by reduction giving enantiomeric (*P*)-**6** and (*M*)-**6**, respectively.

The X-ray structures (*P*)-**8** and (*P*)-**9** were compared with (*P*)-**7**.[11] Two distinct methyl groups are present in (*P*)-**9**, out-of-plane and in-plane methyls, and the rotation of isopropyl group is restricted. Notable are the bottom views (Figures 1a–1c). The A and D rings of the benzo[*c*]phenanthrene moiety colored orange were larger in (*P*)-**7** compared to (*P*)-**9** as indicated by the arrows. In order to confirm this qualitatively, the dihedral angles obtained by the average plane of the A and D rings at the benzo[*c*]phenanthrene ring were compared: (*P*)-**7**, 47.9(1)°;[8] (*P*)-**8**, 45.2(1)°; (*P*)-**9**, 41.8(2)°. The dihedral angles of the related compounds were reported: benzo[*c*]phenanthrene, 26.68° and 1,4-dimethylbenzo[*c*]phenanthrene, 36.65°.[12] It is reasonable that the angle increases as the number of 1,12-methyl groups increases. However, as shown in this study, the decrease of the angle in the 1,12-diethyl and 1,12-diisopropyl derivatives is unusual, and is reverse to the well-accepted bulkiness of the substituent. *The dimethyl group exerts more hindrance than the diisopropyl group on the strain of 1,12-disubstituted benzo[c]phenanthrene.*

The UV spectra of dinitriles (±)-**17**, (±)-**18**, and (±)-**19** were compared (Figure 2a). The $\lambda_{\max}$ at ca. 300 nm attributable to π–π^* transition shifted to longer wavelengths as the 1,12-substituent changes from dimethyl to diisopropyl: (±)-**19**, 308 nm, (±)-**17**, 312 nm, and (±)-**18**, 317 nm. Such trend in the UV spectra was also observed with the racemic 5,8-dicarboxylic acids (±)-**1**, (±)-**2**, and (±)-**3**[11] and optically active 5,8-dimethanols (*P*)-**4**, (*P*)-**5**, and (*P*)-**6** (Figure 2b).[11] A stronger Cotton effect at ca. 300 nm was observed for (*P*)-**6** than for (*P*)-**4** (Figure 2c).

The steric effect of substituent is an important concept in organic chemistry, and it is well established that an isopropyl group is larger than a methyl group. The concept has been qualitatively discussed using, for example, the *A* values,[13] E_s values,[14] or $I^{X\text{–}H}$ values.[15] It was noticed in several occasions that isopropyl group can behave as a slightly larger substituent compared to a methyl group, which was explained by the rotation directing the proton to the hindered site.[3,12] However, described in the present study is a reverse to this rule.

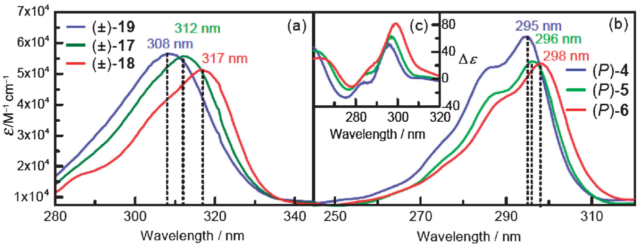


Figure 2. (a) UV spectra of (±)-**17**, (±)-**18**, and (±)-**19** (2.0×10^{-5} mol/L, 25 °C) in chloroform. (b) UV (2.0×10^{-5} mol/L, 25 °C), and (c) CD (5.0×10^{-5} mol/L, 25 °C) spectra of (*P*)-**4**, (*P*)-**5**, and (*P*)-**6** in methanol.

The rotation of the *C*(1α)–*C*(1) bond in (*P*)-**9** is restricted, whereas the methyl group in (*P*)-**7** can freely rotate. The antiperiplanar arrangements of the *C*(1α)–*H* bond and *C*(12α)–*H* bond in (*P*)-**9** appear to have contributed to decrease repulsions of the isopropyl group, torsion angle *H*–*C*(12α)···*C*(1α)–*H*: 158.8(5)° for (*P*)-**9**. The reduced mobility of the isopropyl group minimized the steric repulsion, and have decreased the formal size of the isopropyl group compared to the methyl group. Since the discussions of *A* values or E_s values treat the free rotating groups, the inhibition of the rotation would provide different conclusions.

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10 Crystallographic data reported in this manuscript have been deposited with Cambridge Crystallographic Data Center as supplementary publication No. CCDC-625074 ((*P*)-**8**) and 625075 ((*P*)-**9**).

11 See Supporting Information, being available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.

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