[Chem. Pharm. Bull. 29(5)1321—1327(1981)]

Heterocycles. X.[1] Syntheses and Absolute Configurations of a Chiral Naphthoquinone Epoxide and Chiral Naphtho[1,2-*c*]isocoumarins

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(Received November 22, 1980)

The (+)-naphthoquinone epoxide (2) has been obtained by the phase-transfer chiral epoxidation of the naphthoquinone (1). Reduction of (+)-2 with sodium borohydride gives the (−)-*cis*-epoxyhydroxy ketone (3) and (−)-*trans*-epoxyhydroxy ketone (4). Further reduction of (−)-3 affords the (−)-*cis*-lactone (5), (−)-*trans*-lactone (6) and (+)-*cis*-epoxydiol (7). Alumina-induced lactonization of (+)-7 yields (−)-6. The 2*S*,3*R* configuration for (+)-2 is deduced from the circular dichroism spectrum. The configurations of the 4-hydroxyl groups in (−)-3 and (−)-4 are determined by the Horeau's method.

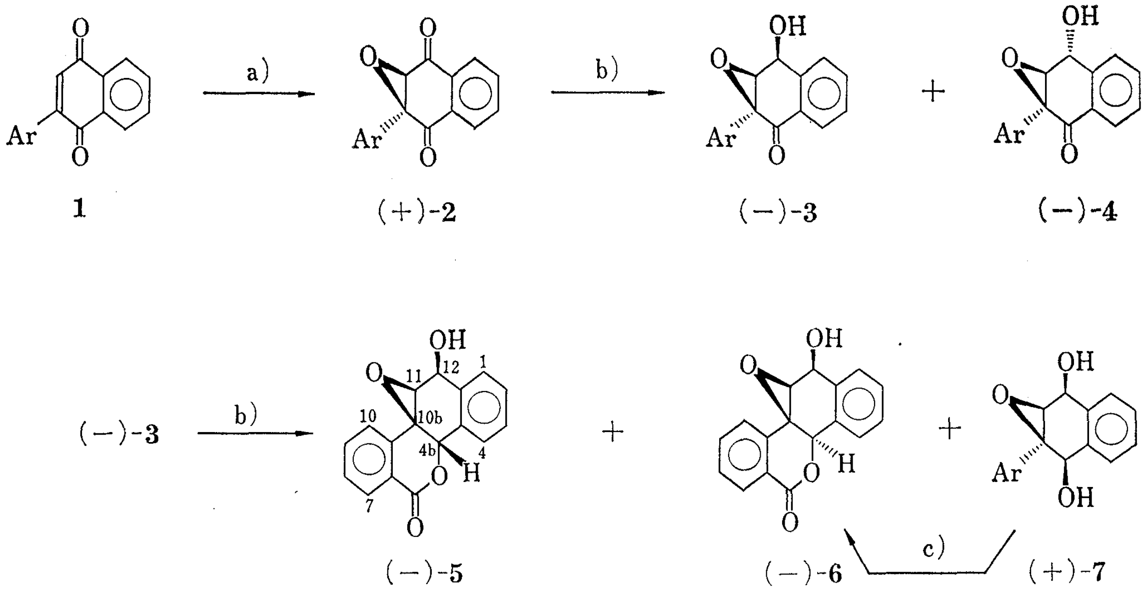
Keywords——naphtho[1,2-*c*]isocoumarin; naphthoquinone epoxide; phase-transfer chiral epoxidation; absolute configuration; circular dichroism; proton magnetic resonance

Although many synthetic methods for benzo[*c*]phenanthridines have been presented, no approach to chiral ones has been attempted. We have previously reported the stereoselective syntheses of benzo[*c*]phenanthridines from the (±)-naphthoquinone epoxide (2) *via* the (±)-*cis*-lactone (5).[2] Thus, if 2 can be obtained in a chiral form, the syntheses of chiral benzo[*c*]phenanthridines should be possible.

Asymmetric epoxidations of enones under phase-transfer conditions in the presence of chiral onium salts as catalysts have been reported.[3] In this connection, we have preliminarily reported the asymmetric epoxidation of the naphthoquinone (1) to chiral 2, and the syntheses of the chiral lactones (5) and (6) from chiral 2.[1] We now wish to report in detail the results obtained by further investigation.

The naphthoquinone (1)[4] was treated with *tert*-butyl hydroperoxide in the presence of 1-benzylquininium chloride (BQC) and sodium hydroxide in toluene. Work-up of the reaction mixture and preparative thin-layer chromatography (prep. TLC) gave (±)-2 in 95% yield. Its enantiomeric excess (ee) (78%) was determined from the proton magnetic resonance (^{1}H NMR) spectrum using tris[3-(heptafluoropropylhydroxymethylene)-(+)-camphorato]europium (III) [Eu(hfc)$_3$] (Fig. 1). Recrystallization from ethanol furnished (+)-2 (100% ee) in 63% yield. On the other hand, the use of aqueous hydrogen peroxide as an oxygen source instead of *tert*-butyl hydroperoxide gave (+)-2 (50% ee) in 89% yield.

Reduction of (+)-2 with sodium borohydride at −50° for 1 hr afforded the (−)-*cis*-epoxyhydroxy ketone (3) (76%), $[\alpha]^{22}_{589}$ −52.0°, and (−)-*trans*-epoxyhydroxy ketone (4) (23%), $[\alpha]^{25}_{589}$ −136.3°. Since one-proton doublets were observed for the 3-protons in (−)-3 and (−)-4 in the ^{1}H NMR spectra, it is evident that the 4-oxo group in (+)-2 was reduced to yield two 4-epimeric alcohols. It is known that the intramolecular hydrogen-bondings between hydroxyl groups and adjacent oxirane oxygen atoms, and between hydroxyl groups and π-bonds in α-tetralols appear at 3580—3520 and 3620—3590 cm^{-1}, respectively, in the infrared (IR) spectra.[5] On the basis of these findings, absorptions at 3520 cm^{-1} observed for (−)-3 and 3587 cm^{-1} for (−)-4 may be assigned to the intramolecular hydrogen-bondings between the 4-hydroxyl group and oxirane oxygen atom, and between the 4-hydroxyl group and π-bond in the benzene moiety, respectively. Since the intramolecular hydrogen-bonding between the *trans*-hydroxyl group and oxirane oxygen atom in the compound in question is impossible, regardless of the conformation of the cyclohexene ring, the configurations of the 4-hydroxyl groups in (−)-3 and (−)-4 are established as *cis* and *trans* with respect to the oxirane rings,



Ar=–$C_6H_4COOMe(o)$

a) *tert*-BuO_2H/BQC/NaOH/toluene. b) $NaBH_4$/MeOH. c) $Al_2O_3/CHCl_3$/MeOH.

Chart 1

respectively, on the basis of these IR data. Reduction of (+)-**2** (50% ee) with sodium borohydride gave (−)-**3** (51% ee)[6] in 70% yield, and its recrystallization from ethanol yielded (−)-**3** (92% ee)[6] in 28% yield.

Further reduction of (−)-**3** with sodium borohydride gave the (−)-*cis*-lactone (**5**) (44%), $[\alpha]^{23}_{589}$ −217.8°, (−)-*trans*-lactone (**6**) (1%), $[\alpha]^{20}_{589}$ −104.0°, and (+)-*cis*-epoxydiol (**7**) (38%), $[\alpha]^{23}_{589}$ +161.4°. The *cis* steroidal conformation of the B/C ring fusion in (−)-**5** was deduced on the basis of a W-path coupling (J=1 Hz) observed between the 4b- and 11-protons in the ^1H NMR spectrum.[7]

Alumina-induced lactonization of (+)-**7** afforded (−)-**6** (74%), which showed a characteristic signal for the 4-proton at δ 7.93 (dd, J=8 and 2 Hz) (**5**: δ 7.43) shifted down-field by an interaction with the 4b-0(5) bond in the ^1H NMR spectrum. The optical purities (100%) of (−)-**5** and (−)-**6** were confirmed by measurement of the ^1H NMR spectra using $Eu(hfc)_3$.

Absolute Configuration

The (+)-Naphthoquinone Epoxide (2)——Wynberg *et al.* have reported that the circular dichroism (CD) spectra correlated with the absolute configurations of 2-alkyl- and 2-phenylnaphthoquinone epoxides and that the compounds with negative Cotton effects between 400 and 340 nm had the 2*R*, 3*S* configurations.[8] The CD spectrum of (+)-**2** showed positive Cotton effects between 400 and 340 nm, suggesting the 2*S*, 3*R* configuration for (+)-**2** by comparison with the CD spectrum of one of the compounds examined by Wynberg *et al.* (Fig. 2).

The (−)-*cis*-Epoxyhydroxy Ketone (3) **and (−)-*trans*-Epoxyhydroxy Ketone** (4)——Horeau has found a novel method to determine the absolute configurations of secondary alcohols, *e.g.* (1) esterification of a chiral alcohol with (±)-2-phenylbutanoic anhydride (**8**), (2) hydrolysis of excess **8** at the end of the reaction, and (3) determination of the rotatory power of 2-phenylbutanoic acid (**9**) thus isolated. The relationship, in general, between the configuration of the alcohol and the sign of **9** is as shown in Chart 2.[9] On application of this method, *R*-(−)-**9** and *S*-(+)-**9** were obtained from (−)-**3** and (−)-**4**, respectively. This result leads to the 4*S* and 4*R* configurations for (−)-**3** and (−)-**4**, respectively. Talking into account the steric relationship of the 4-hydroxyl group and oxirane ring (***vide supra***), the 2*S*, 3*S*, 4*S* configuration for (−)-**3** and the 2*S*, 3*S*, 4*R* configuration for (−)-**4** can be deduced.

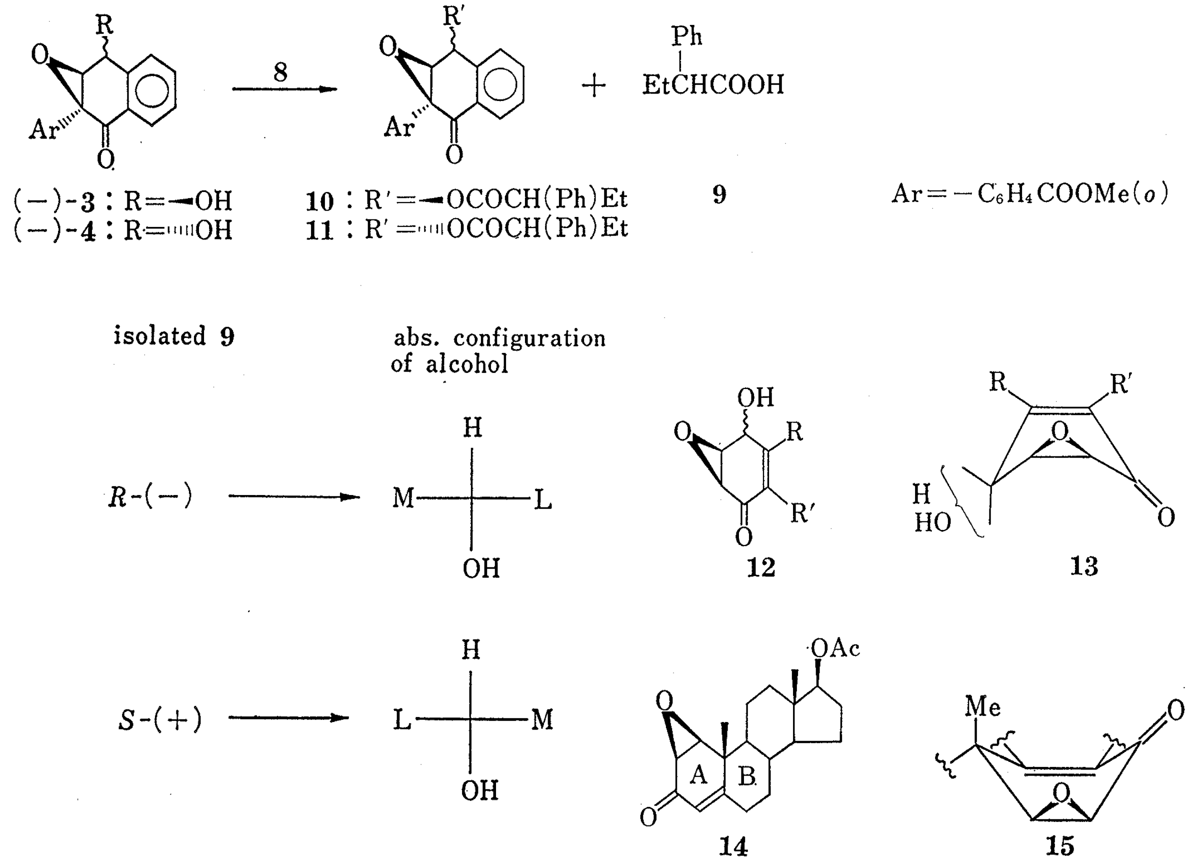


Chart 2

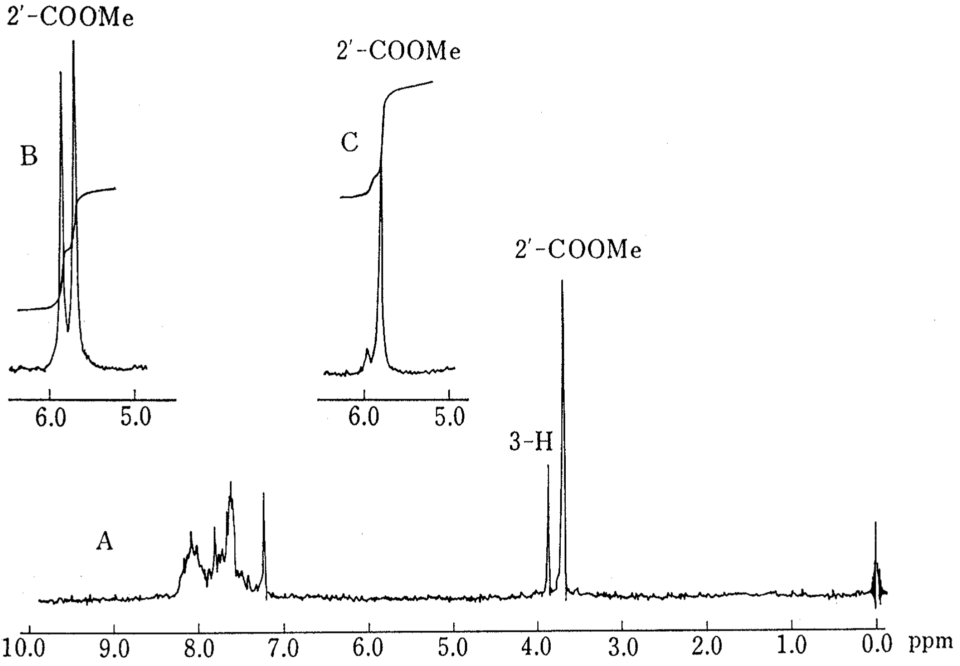


Fig. 1. ^{1}H NMR Spectra of **2** taken on a Hitachi R-24B Spectrometer

A, normal spectrum of (±)-**2** (18 mg, 5.8×10^{-5} mol) in $CDCl_3$ (0.4 ml) at 60 MHz; B, 60 MHz spectrum of (±)-**2** (43 mg, 1.4×10^{-4} mol) in $CDCl_3$ (0.4 ml) containing Eu(hfc)$_3$ (136 mg); C, 60 MHz spectrum of (+)-**2** (78% ee) (40 mg, 1.3×10^{-4} mol) in $CDCl_3$ (0.4 ml) containing Eu(hfc)$_3$ (156 mg).

This conclusion is supported by the correlation of the stereostructure of (+)-**2** with the spatial orientation of the 4-hydroxyl groups in (—)-**3** and (—)-**4**.

It is known that the 2,3-epoxy-4-hydroxycyclohex-5-en-1-one (**12**) has the conformation (**13**), because of the more favorable overlapping between the delocalized electrons of the oxirane ring and π-electrons of the carbonyl group, and that **13** shows a negative Cotton effect at 340—320 nm in the CD spectrum due to the n-π* carbonyl transition.[10] From the coupling constant (2 Hz) observed between the 3- and 4-protons, it can be deduced that the 4-hydroxyl group in (—)-**3** is equatorial in the **13**-type conformation.[11] At present, we have no information on the ring conformation of (—)-**4**. However, although the A ring in the steroid (**14**) exists in the conformation (**15**), the negative Cotton effect, ascribed to the "epoxy ketone partial chromophore," is also observed for **14**.[10] The CD spectra of (—)-**3** and (—)-**4** showed negative Cotton effects at *ca.* 330 nm (Fig. 3). If (—)-**3** and (—)-**4**, which have the benzene moieties instead of the double bonds in **12** and **14**, can be regarded as being similar to **12** and **14** in terms of the CD spectra,[12] both compounds have the same configurations (2*S*, 3*S*) at the 2- and 3-positions, as discussed above.

The (—)-*cis*-Lactone (5), (—)-*trans*-Lactone (6) and (+)-*cis*-Epoxydiol (7)——On the basis of the stereostructure of (—)-**3**, the following assignments can be made. 4b*S*, 10b*R*, 11*S*, 12*S* for (—)-**5**; 4b*R*, 10b*R*, 11*S*, 12*S* for (—)-**6**; 1*R*, 2*R*, 3*S*, 4*S* for (+)-**7**. Interestingly, the CD spectra of (—)-**5** and (—)-**6** appeared to be mirror images (see "Experimental").

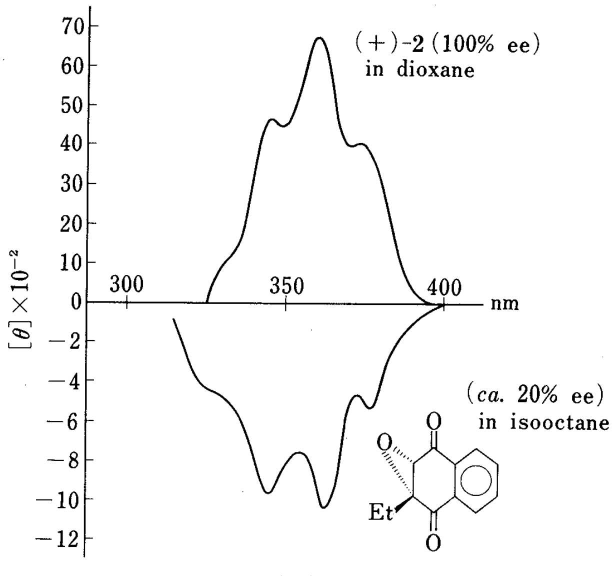


Fig. 2. CD Spectra of (+)-**2** and a Related Compound[8]

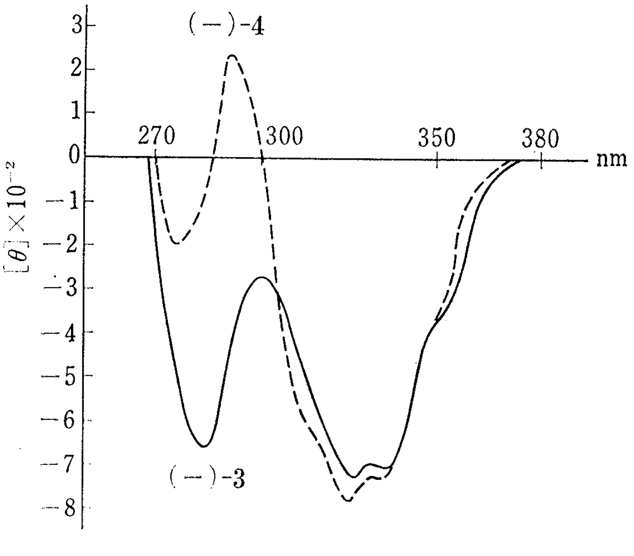


Fig. 3. CD Spectra of (—)-**3** and (—)-**4**(dioxane)

Experimental

Melting points were determined on a micro hot-stage apparatus and are uncorrected. The optical purities of the compounds (**2**—**7**) were estimated by ^{1}H NMR spectroscopy using Eu(hfc)$_3$ and were 100% unless otherwise noted. Optical rotations were taken on a JASCO DPI-181 polarimeter. Spectral data were recorded on the following spectrometers: UV–Hitachi EPS-2U (methanol); CD–JASCO J-20; IR–JASCO IR-G (chloroform) and JASCO DS-701G (hydrogen-bondings); ^{1}H NMR–JEOL JNM PS-100 (100 MHz) (deuteriochloroform); Mass (MS)–JEOL JMS-OIS.

1-Benzylquininium Chloride (BQC)[13]——Quinine trihydrate was dried in a steel desiccator (CaCl$_2$) at 125° overnight, and then recrystallized from anhyd. benzene to afford colorless granules of mp 174—175° with $[\alpha]^{18.5}_{589}$ −121.9° (c=1.0, chloroform).

A solution of benzyl chloride (156 mg) in anhyd. acetone (1.8 ml) was added to a solution of the quinine (402 mg) in anhyd. acetone (20 ml), and the mixture was stirred at 60° for 36 hr. After concentration *in vacuo*, the residue was recrystallized from anhyd. ethanol/anhyd. ether to yield BQC (380 mg, 68%) as light yellow crystals of mp 176—180°, and further recrystallization from the same solvents gave BQC as colorless needles of mp 180—181° with $[\alpha]^{19}_{589}$ −235.5° (c=1.5, water).

(+)-2,3-Dihydro-2,3-epoxy-2-2′-methoxycarbonylphenyl-1,4-naphthoquinone (2)——a) *tert*-Butyl hydroperoxide (75%) (0.4 ml) was added to a stirred mixture of **1** (101 mg), BQC (2.6 mg) and NaOH (27 mg) in toluene (10 ml) with cooling. The mixture was vigorously stirred at 0° for 30 min and then at room temperature for 1 hr. The toluene phase was washed with aq. KI, aq. $Na_2S_2O_3$ and water, then dried over Na_2SO_4. Removal of the solvent *in vacuo*, followed by prep. TLC of the residue (silica gel; benzene/ethyl acetate=20/1, v/v; *Rf* 0.37) gave **2** (101 mg, 95%, 78% ee) as light yellow crystals of mp 135—137° with $[\alpha]_{589}^{23}$ +9.2°, $[\alpha]_{577}^{22}$ +12.5°, $[\alpha]_{546}^{22}$ +20.0° and $[\alpha]_{435}^{22}$ +175.1° (c=1.0, dioxane). Its recrystallization from ethanol yielded **2** (66 mg, 63%, 100% ee) as colorless prisms of mp 140—141.5° with $[\alpha]_{589}^{24}$ +10.5°, $[\alpha]_{577}^{24}$ +13.3°, $[\alpha]_{546}^{24}$ +22.0° and $[\alpha]_{435}^{24}$ +200.3° (c=1.3, dioxane). IR ν_{max} cm^{-1}: 1705, 1700 (C=O and OC=O). UV λ_{max} nm (ε): 348 (shoulder) (141), 302 (1720), 260 (shoulder) (5800), 247 (33400). CD ($c=3.7\times10^{-3}$, dioxane) $[\theta]^{21}$ (nm): 0 (395), +4032 (374.5) (positive maximum), +3990 (371) (negative maximum), +6804 (359.5) (positive maximum), +4452 (349) (negative maximum), +4662 (345) (positive maximum), +1134 (332) (shoulder), 0 (325), −672 (320) (negative maximum), −630 (316.5) (positive maximum), −1008 (308) (negative maximum), −882 (298) (positive maximum), −15455 (264) (negative maximum). ^{1}H NMR δ: 8.19—7.99 (3H, m, aromatic H's), 7.86—7.43 (5H, m, aromatic H's), 3.88 (1H, s, 3-H), 3.71 (3H, s, 2′-COOMe). MS Calcd for $C_{18}H_{12}O_5$: M, 308.068. Found *m/e*: M^+, 308.068.

b) A solution of **1** (200 mg) in toluene (10 ml) was added to a solution of BQC (5.1 mg) and NaOH (51.4 mg) in 30% aq. H_2O_2 (0.62 ml). The mixture was vigorously stirred at room temperature for 4.5 hr. Treatment of the reaction mixture as above afforded **2** (188 mg, 89%, 50% ee) as light yellow crystals of mp 126—137°. Its recrystallization from ethanol gave **2** (45 mg, 21%, 100% ee) as colorless prisms of mp 141—141.5°.

(−)-2,3-Epoxy-*cis*-4-hydroxy-*trans*-2-2′-methoxycarbonylphenyl-α-tetralone (3) **and (−)-2,3-Epoxy-*trans*-4-hydroxy-*trans*-2-2′-methoxycarbonylphenyl-α-tetralone** (4)——a) $NaBH_4$ (50 mg) was added to a solution of (+)-**2** (150 mg) in methanol (50 ml). The mixture was stirred at −50° for 1 hr, and then acetic acid (1 ml) was added. After concentration *in vacuo*, the residue was extracted with ethyl acetate. Work-up gave an oil (160 mg), and prep. TLC (silica gel; benzene/ethyl acetate=10/1, v/v) afforded (−)-**3** (115 mg, 76%) and (−)-**4** (35 mg, 23%) from the zones with *Rf* 0.49 and 0.32, respectively.

The (−)-*cis*-Epoxyhydroxy Ketone (3): Colorless prisms of mp 128.5—130° (from ethanol). IR ν_{max} cm^{-1}: 3520 (OH), 1702 (OC=O and C=O); hydrogen-bonding, 3520 cm^{-1} (ε=117.5) ($c=6.5\times10^{-4}$ mol/l, tetrachloromethane). UV λ_{max} (ε): 336 (shoulder) (58), 280 (shoulder) (2780), 222 (12400), 201 (46500). Optical rotation $[\alpha]^{22}$ (nm): −52.0° (589), −72.0° (577), −94.0° (546), −314.0° (435), −2042.0° (365) (c=0.1, chloroform). CD ($c=1.3\times10^{-3}$, dioxane) $[\theta]^{24.5}$ (nm): 0 (373), −3580 (352) (shoulder), −7021.5 (337) (negative maximum), −6975 (332) (positive maximum), −7300.5 (327) (negative maximum), −2697 (300) (positive maximum), −6603 (284) (negative maximum), 0 (267.5), +7905 (257.5) (positive maximum), 0 (250), −17902.5 (240) (negative maximum), −5580 (228) (positive maximum), −15345 (220) (negative maximum), 0 (214). ^{1}H NMR δ: 8.15 (1H, dd, J=8 and 2 Hz, 8-H),14) 8.04 (1H, dd, J=8 and 2 Hz, 3′-H),14) 7.77—7.41 (6H, m, aromatic H's), 5.22 (1H, dd, J=12 and 2 Hz, 4-H),15) 3.85 (1H, d, J=2 Hz, 3-H), 3.80 (3H, s, 2′-COOMe), 3.68 (1H, d, J=12 Hz, 4-OH).16) MS Calcd for $C_{18}H_{14}O_5$: M, 310.084. Found *m/e*: M^+, 310.084.

The (−)-*trans*-Epoxyhydroxy Ketone (4): A colorless oil. IR ν_{max} cm^{-1}: 3590, 3370 (OH), 1712 (OC=O), 1695 (C=O); hydrogen-bonding, 3587 cm^{-1} (ε=137.7) ($c=1.3\times10^{-3}$ mol/l, tetrachloromethane). UV λ_{max} (ε): 334 (shoulder) (92), 300 (shoulder) (1140), 284 (shoulder) (3180), 240 (14800), 207 (33300), 203 (34600). Optical rotation $[\alpha]^{25}$ (nm): −136.3° (589), −146.4° (577), −174.2° (546), −433.2° (435), −2024.4° (365) (c=0.3, chloroform). CD ($c=1.7\times10^{-3}$, dioxane) $[\theta]^{22}$ (nm): 0 (372), −3647 (351) (shoulder), −7294 (335) (negative maximum), −7257 (332) (positive maximum), −7841 (325) (negative maximum), −6491 (317) (shoulder), 0 (300), +2370 (291.5) (positive maximum), 0 (286), −1969 (277) (negative maximum), 0 (270.5), +15500 (254.5) (positive maximum), 0 (244), −24435 (228) (negative maximum). ^{1}H NMR δ: 8.12 (1H, dd, J=8 and 2 Hz, 8-H),14) 7.95 (1H, dd, J=8 and 2 Hz, 3′-H),14) 7.71 (1H, dt, J=2 and 8 Hz, aromatic H), 7.63—7.29 (5H, m, aromatic H's), 5.35 (1H, br s, W_H 11 Hz, 4-H),15) 3.81 (1H, d, J=3 Hz, 3-H), 3.69 (3H, s, 2′-COOMe), 3.28 (1H, br s, W_H 28 Hz, 4-OH).16) MS Calcd for $C_{18}H_{14}O_5$: M, 310.084. Found: *m/e*: M^+, 310.083.

b) A solution of (+)-**2** (50% ee) (200 mg) and $NaBH_4$ (30 mg) in methanol (100 ml) was stirred at −60° for 1 hr, and then acetic acid (1 ml) was added. Work-up of the reaction mixture and prep. TLC (silica gel; benzene/ethyl acetate=10/1, v/v) gave (−)-**3** (141 mg, 70%, 51% ee) and (−)-**4** (28 mg, 14%). The (−)-*cis*-epoxyhydroxy ketone (3) (100 mg) obtained above was recrystallized from ethanol (1.5 ml).

The First Crystals (50 mg): Colorless prisms of mp 138—139° and 23% ee. Optical rotation $[\alpha]^{24}$ (nm): −20.2° (589), −22.3° (577), −28.0° (546), −96.8° (435), −627.0° (365) (c=1.0, chloroform).

The Second Crystals (40 mg, 28%): Colorless prisms of mp 116—124° and 92% ee. Optical rotation $[\alpha]^{24}$ (nm): −57.3° (589), −62.9° (577), −80.4° (546), −274.7° (435) (c=1.0, chloroform), −1860.0° (365) (c=0.4, chloroform).

(−)-10b,11-Epoxy-*cis*-12-hydroxy-*cis*-4b,10b,11,12-tetrahydronaphtho[1,2-*c*]isocoumarin (5), **(−)-10b,11-Epoxy-*cis*-12-hydroxy-*trans*-4b,10b,11,12-tetrahydronaphtho[1,2-*c*]isocoumarin** (6) **and (+)-1,*cis*-4-Dihydroxy-*cis*-2,3-epoxy-*trans*-2-2′-methoxycarbonylphenyl-1,2,3,4-tetrahydronaphthalene** (7)——$NaBH_4$ (45 mg) was added to a solution of (−)-3 (115 mg) in methanol (50 ml), and the mixture was stirred at −50° for 2 days. After addition of further $NaBH_4$ (20 mg), stirring was continued at −50° for 1 day, and then acetic acid (1 ml) was added. Work-up of the reaction mixture gave an oil (116 mg) which was purified by prep. TLC (silica gel; chloroform/ethyl acetate=10/1, v/v) to afford (−)-**5** (46.1 mg, 44%), *Rf* 0.40, (−)-**6** (0.9 mg, 1%), *Rf* 0.33, and (+)-**7** (43.8 mg, 38%), *Rf* 0.54.

The (−)-*cis*-Lactone (**5**): Colorless leaflets of mp 177—178° (from ethanol). IR ν_{max} cm^{-1}: 3580, 3340 (OH), 1729 (OC=O). UV λ_{max} (ε): 288 (shoulder) (1080), 281 (1140), 234 (7280), 202 (37800). Optical rotation $[\alpha]^{23}$ (nm): −217.8° (589), −225.8° (577), −234.7° (546), −428.4° (435), −659.5° (365) (c=0.2, chloroform). CD ($c=1.8\times10^{-3}$, dioxane) $[\theta]^{24}$ (nm): 0 (303), +8720 (263) (positive maximum), 0 (247.5), −31830 (233.5) (negative maximum), 0 (219.5). ^{1}H NMR δ: 8.12 (1H, dd, J=8 and 2 Hz, 7-H), 7.69 (1H, dt, J=2 and 8 Hz, 9-H),[14] 7.50 (1H, dt, J=2 and 8 Hz, 8-H),[14] 7.43 (4H, s, aromatic H's), 7.39 (1H, dd, J=8 and 2 Hz, 10-H), 5.82 (1H, d, J=1 Hz, 4b-H), 5.14 (1H, br s, W_H 12 Hz, 12-H),[15] 3.6 6(1H, dd, J=2 and 1 Hz, 11-H), 2.46 (1H, d, J=8 Hz, 12-OH).[16] MS Calcd for $C_{17}H_{12}O_4$: M, 280.074. Found *m/e*: M$^+$, 280.074.

The (−)-*trans*-Lactone (**6**): Colorless prisms of mp over 300° (from ethanol). IR ν_{max} cm^{-1}: 3610, 3400 (OH), 1728 (OC=O). UV λ_{max} (ε): 348 (shoulder) (23), 316 (shoulder) (30), 280 (1460), 234 (8630), 204 (37800). Optical rotation $[\alpha]^{20}$ (nm): −104.0° (589), −120.0° (577), −136.0° (546), −264.0° (435), −526.0° (365) (c=0.1, chloroform). CD ($c=1.0\times10^{-3}$, dioxane) $[\theta]^{18}$ (nm): 0 (305), −9744 (260) (negative maximum), 0 (242), +3360 (233)/(positive maximum), 0 (220). ^{1}H NMR δ: 8.31 (1H, dd, J=8 and 2 Hz, 7-H), 7.93 (1H, dd, J=8 and 2 Hz, 4-H), 7.73 (1H, dt, J=2 and 8 Hz, 9- or 8-H), 7.65 (1H, dd, J=8 and 2 Hz, 10-H), 7.54—7.32 (4H, m, aromatic H's), 6.11 (1H, s, 4b-H), 5.37 (1H, br s, W_H 8 Hz, 12-H),[15] 4.49 (1H, d, J=3 Hz, 11-H), 2.21 (1H, d, J=3 Hz, 12-OH).[16] MS Calcd for $C_{17}H_{12}O_4$: M, 280.074. Found: *m/e*: M$^+$, 280.077.

The (+)-*cis*-Epoxydiol (**7**): Colorless prisms of mp 150—151° (from ethanol). IR ν_{max} cm^{-1}: 3580, 3520 (OH), 1709 (OC=O). UV λ_{max} (ε): 277 (1000), 229 (5360), 214 (8630). Optical rotation $[\alpha]^{23}$ (nm): +161.4° (589), +167.0° (577), +195.0° (546), +343.6° (435), +557.9° (365) (c=0.3, chloroform). CD ($c=1.0\times10^{-3}$, dioxane). $[\theta]^{23}$ (nm): 0 (301), −3775 (281.5) (negative maximum), 0 (266) +3837 (252.5) (positive maximum), 0 (243), −4368 (234) (negative maximum), 0 (226). ^{1}H NMR δ: 8.09 (1H, dd, J=8 and 2 Hz, 3′-H), 7.76—7.28 (7H, m, aromatic H's), 5.20 (1H, d, J=11 Hz, 1-H),[17] 5.03 (1H, dd, J=11 and 3 Hz, 4-H),[15] 3.83 (3H, s, 2′-COOMe), 3.59 (1H, d, J=3 Hz, 3-H), 3.54, 2.34 (1H each, d, J=11 Hz, 1- and 4-OH's).[16] MS Calcd for $C_{18}H_{16}O_5-H_2O$: M, 294.089. Found *m/e*: M$^+$, 294.090.

Transformation of (+)-7 to (−)-6——A solution of (+)-**7** (43 mg) in chloroform/methanol (1/1, v/v) (0.8 ml) was left on a column of neutral Al_2O_3 (grade III) (1 g) overnight. Elution with chloroform/methanol (100/1, v/v) afforded crystals (39 mg) which were purified by prep. TLC (silica gel; chloroform/ethyl acetate=5/1, v/v) to give (−)-**6** (28.6 mg, 74%) from the zone with *Rf* 0.54.

Reaction of (−)-3 with the (±)-Anhydride (8)——A solution of **8** (225 mg) in anhyd. pyridine (2 ml) was added to a solution of (−)-**3** (103 mg) in anhyd. pyridine (1 ml), and the mixture was stirred at room temperature for 22 hr. Water (0.5 ml) was added to hydrolyze excess **8**, and the mixture was stirred at room temperature for 2 hr. Neutralization in the presence of benzene (5 ml) and a small amount of phenolphthalein required 0.1 N NaOH (factor=1.001) (11.3 ml): the esterification yield was therefore 100%. The reaction mixture was diluted with water, and the aqueous phase was extracted with benzene. On work-up, the combined benzene extracts gave an oil (167 mg), and prep. TLC (silica gel; benzene/ethyl acetate=10/1, v/v) afforded the ester (**10**) (147 mg, 97%) as a colorless oil. IR ν_{max} cm^{-1}: 1722 (OC=O), 1698 (C=O). MS Calcd for $C_{28}H_{24}O_6$: M, 456.157. Found *m/e*: M$^+$, 456.159. The aqueous phase was acidified with 10% HCl, and then extracted with benzene. Work-up gave **9** (182 mg) as a colorless oil with $[\alpha]^{30}_{589}$ −0.002° (c=8.9, benzene) corresponding to the optical yield (0.15%). The spectral data for isolated **9** were in accord with those for an authentic sample.

Reaction of (−)-4 with the (±)-Anhydride (8)——A solution of **8** (216 mg) in anhyd. pyridine (2 ml) was added to a solution of (−)-**4** (81 mg) in anhyd. pyridine (1 ml), and the mixture was stirred at room temperature for 18 hr. After hydrolysis of excess **8** with water (0.5 ml), it was found that 0.1 N NaOH (factor=1.001) (11.3 ml) was required for neutralization (the esterification yield, 100%). Work-up afforded the ester (**11**) (117 mg, 98%) as a colorless oil. IR ν_{max} cm^{-1}: 1738, 1715 (OC=O), 1698 (C=O). MS Calcd for $C_{28}H_{24}O_6$: M, 456.157. Found: *m/e*: M$^+$, 456.160. In addition **9** (185 mg) was obtained as a colorless oil with $[\alpha]^{30}_{589}$ +0.217° (c=8.9, benzene) corresponding to the optical yield (21%). The spectral data for isolated **9** were in accord with those for an authentic sample.

References and Notes

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14) These assignments may be reversed.

15) On addition of deuterium oxide, this signal changed to a doublet.

16) On addition of deuterium oxide, this signal disappeared.

17) On addition of deuterium oxide, this signal changed to a singlet.