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Absolute Configurations of Novel Axially Dissymmetric 10,10′-Dihydroxy-9,9′-biphenanthryl and Its Related Compounds

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Synopsis. Stereoselective oxidative coupling of 10-hydroxy-1,2,3,4-tetrahydrophenanthrene derived from methyl 3-methoxy-2-naphthoate gave (−)-(*S*)-10,10′-dihydroxy-1,1′,2,2′,3,3′,4,4′-octahydro-9,9′-biphenanthryl which was converted into (+)-(*S*)-10,10′-dimethoxy-9,9′-biphenanthryl assigning the *S* configuration to (−)-10,10′-dihydroxy-9,9′-biphenanthryl.

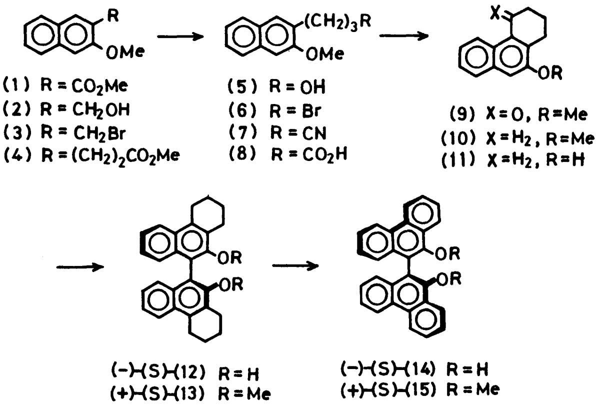
Recently, we found that the novel axially dissymmetric molecule, 10,10′-dihydroxy-9,9′-biphenanthryl (**14**), has been used for synthesis of chiral crown ether with high enantiomer selectivity toward primary amines[1] and enantioselective reduction of ketones.[2] Here we report the determination of the absolute configuration of chiral 10,10′-dihydroxy-9,9′-biphenanthryl (**14**) and its related compounds.

Lithium aluminium hydride reduction of methyl 2-methoxy-3-naphthoate (**1**)[3] furnised the alcohol (**2**) which was converted to the bromide (**3**) with phosphorus tribromide, then submitted to the malonic ester synthesis under usual reaction conditions to afford the ester (**4**) (32.5% yield from **1**). After the side chain of **4** was extended by routine method (*via* cyanide), the resulting acid (**8**) (94% yield from **4**) was cyclized with polyphosphoric acid to yield the expected cyclic ketone (**9**) in 89% yield. Wolff-Kishner reduction of **9** followed by hydrolysis with AcOH–H_2O–concd HCl (10:5:1) gave the naphthol derivative (**11**) (69.7% yield from **9**). Stereoselective oxidative coupling of **11** was carried out using optically active amine-copper(II) complex, which prepared *in situ* by treating (−)-(*S*)-1,2-diphenylethylamine[4] and $Cu(NO_3)_2\cdot3H_2O$ in methanol. The coupling product was purified by recrystallization from benzene to give an optically pure specimen of the binaphthol derivative (−)-(**12**) (79% yield,$[\alpha]_D^{21}$ −29.0° ($CHCl_3$).[5] Comparison of the CD spectra of (−)-**12** with that of authentic (−)-(*S*)-2,2′-dihydroxy-3,3′-dimethyl-1,1′-binaphthyl[7] let us to conclude that these two compounds have the same configuration. Methylation of (−)-(**13**) which was dehydrogenated with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone to give (+)-(*S*)-10,10′-dimethoxy-9,9′-biphenanthryl (**15**) (45% yield from **12**, $[\alpha]_D^{23}$ +26° ($CHCl_3$)). This dextrorotatory compound (**15**) could also be derived from (−)-10,10′-dihydroxy-9,9′-biphenanthryl (**14**)[2] by methylation with methyl *p*-toluenesulfonate. These correlation enable us to assign *S* configurations to (−)-**14** and its related compounds.

Experimental

Melting points are uncorrected. IR, NMR, UV, and CD spectra were recorded on a Hitachi 260-10, a JNM-MH-100, a Hitachi 220A, and a JASCO J-20 spectrometer, respectively.

3-Methoxy-2-naphthaleneethanol (2). A solution of **1** (23.6 g, 0.109 mol) in dry THF (150 ml) was added to a suspension of $LiAlH_4$ (2.5 g, 66 mmol) in dry THF (150 ml). The mixture was refluxed for 8 h with stirred and cooled in an ice-bath. To the chilled reaction mixture was added aq HCl, and extracted with ether. The ether extract was washed with water, dried ($MgSO_4$), concentrated, and recrystallized from benzene, giving 13.9 g (68% yield) of **2**: Mp 72—73 °C; IR (KBr) 3450 cm^{-1} (OH) (Found: C, 75.95; H, 5.79%).



(1) R = CO_2Me
(2) R = CH_2OH
(3) R = CH_2Br
(4) R = $(CH_2)_2CO_2Me$
(5) R = OH
(6) R = Br
(7) R = CN
(8) R = CO_2H
(9) X = O, R = Me
(10) X = H_2, R = Me
(11) X = H_2, R = H
(−)-(S)-(12) R = H
(+)-(S)-(13) R = Me
(−)-(S)-(14) R = H
(+)-(S)-(15) R = Me

2-Bromomethyl-3-methoxynaphthalene (3). To a stirred solution of **2** (11.9 g, 63.4 mmol) in dry ether (150 ml) was added dropwise a solution of phosphorus tribromide (8.6 g, 31.8 mmol) in dry ether (70 ml) at room temperature. The mixture was stirred for further 4 h, and quenched with water (90 ml). After a usual work-up, the crude product was recrystallized from hexane-benzene to give **3** (13 g, 81%), mp 150—151 °C (Found: C, 57.77; H, 4.50%).

Methyl 3-Methoxy-2-naphthalenepropionate (4). The alykylation of malonic ester with **3** (12.3 g, 48 mmol) was carried out according to literature[8] using sodiomalonate (prepared from sodium (1.84 g, 0.08 g-atom), ethyl malonate (21 g, 0.19 mol), and absolute ethanol (28 ml). The resulting diester was saponified by refluxing for 3 h with KOH (30 g) in 80% ethanol (280 ml). After a usual work-up, the resulting dicarboxylic acid (7 g) was decarboxylated by heating at 200 °C for 1 h. The routine esterification of the monocarboxylic acid with methanol and concd H_2SO_4 afforded **4** (6.7 g, 59%): Bp 160—162 °C (0.9 mmHg); IR (film) 1730 cm^{-1} (C=O) (Found: C, 74.01; H, 6.42%).

3-Methoxy-2-naphthalenepropanol (5). Hydride reduction of **4** was carried out followed by the same method as described of **2**, using **4** (6.7 g, 27.5 mmol) and $LiAlH_4$ (0.63 g, 16.5 mmol). The product was distilled to give **5** (5.5 g, 93%): Bp 168—169 °C (0.7 mmHg); IR (film) 3450 cm^{-1} (OH).

2-(3-Bromopropyl)-3-methoxynaphthalene (6). The alcohol (**5**) (5.2 g, 24 mmol) was converted into the bromide (**6**) following the same method as described for **3**. Recrystallization of the product from ethanol afforded **6** (4.1 g, 61%): mp 56—57 °C (Found: C, 60.22; H, 5.39%).

2-(3-Cyanopropyl)-3-methoxynaphthalene (7). A mixture of **6** (3.87 g, 13.9 mmol), KCN (2.55 g, 13.9 mmol), and 80% ethanol (30 ml) was refluxed for 6 h. After removal of the solvent, the reaction mixture was diluted with water and the product was extracted with ether. The etheral extract was dried ($MgSO_4$), concentrated, and recrystallized from methanol, giving 3.0 g (95%) of **7**: Mp 74—75 °C; IR (KBr)

2250 cm^{-1} (C≡N) (Found: C, 79.98; H, 6.78%).

3-Methoxy-2-naphthalenebutyric acid (8). A solution of **7** (2.7 g, 12.2 mmol), KOH (5.4 g, 96 mmol), and 70% ethanol (30 ml) was refluxed for 4 h, and the chilled reaction mixture was quencned with 2M HCl (200 ml) (1 M=1 mol dm^{-3}). The separated product was extracted with chloroform. The extract was dried ($\mathrm{MgSO_4}$), concentrated, and recrystallized from methanol, giving 2.8 g (95%) of **8**: mp 93—94 °C (Found: C, 73.73; H, 6.66%).

10-Methoxy-1,2,3,4-tetrahydro-4-phenanthrenone (9). A solution of **8** (2.55 g, 10.6 mmol) and polyphosphoric acid (40 g) was stirred for 1 h at 60 °C. The hot mixture was poured onto ice-water and the product was extracted with ether. The ether solution was washed with water and dried ($\mathrm{MgSO_4}$). After evaporation of the solvent, the residue was recrystallized from hexane to give **9** (2.13 g, 89%): Mp 83—84 °C; IR (KBr) 1660 cm^{-1} (C=O) (Found: C, 79.73; H, 6.30%).

10-Methoxy-1,2,3,4-tetrahydrophenanthrene (10). Wolff-Kishner reduction of **9** (0.9 g, 4 mmol) using KOH (0.9 g, 16 mmol), 100% hydrazine hydrate (0.8 g, 6 mmol), and diethylene glycol (20 ml) was carried out according to literature[9] to give **10** (0.64 g, 75%). Recrystallization from methanol furnished colorless needles: Mp 72—73 °C (Found: C, 84.84; H, 7.63%).

10-Hydroxy-1,2,3,4-tetrahydrophenanthrene (11). A solution of **10** (0.12 g, 0.57 mmol) in a mixture of 10:5:1 acetic acid, water, and concd HCl (16 ml) was refluxed for 15 h. The mixture poured onto ice-water and the product was extracted with ether. After a usual work-up, the crude product was recrystallized from hexane to give **11** (0.1 g, 93%): Mp 127—128 °C; IR (KBr) 3300 cm^{-1} (OH) (Found: C, 84.72; H, 7.15%).

(−)-10,10′-Dihydroxy-1,1′,2,2′,3,3′,4,4′-octahydro-9,9′-biphenanthryl (12). To a chilled solution (−5 °C) of (−)-(*S*)-diphenylethylamine ($[\alpha]^{23}_{\mathrm{D}}$ −50.8° (EtOH), 99% optical purity[7] (1.3 g, 6.6 mmol) and $\mathrm{Cu(NO_3)_2 \cdot 3H_2O}$ (0.3 g, 1.24 mmol) in methanol (4 ml), was added a solution of **11** (0.12 g, 0.605 mmol) in methanol (1 ml). After stirring at −5 °C for 1 h under $\mathrm{N_2}$, the mixture was quenched with 3% aq HCl (20 ml) and the product was extracted with ether. Work-up followed by recrystallization from benzene gave an optically pure (−)-**12**[5] (93 mg, 79%): Mp 216—218 °C; $[\alpha]^{21}_{\mathrm{D}}$ −30.1° ($\mathrm{CHCl_3}$); IR (KBr) 3520 cm^{-1} (OH); ^{1}H-NMR ($\mathrm{CDCl_3}$) δ=1.76—2.18 (m, 8H), 2.88 (t, 4H), 3.22 (t, 4H), 5.09 (s, 2H), 7.00—7.46 (m, 6H), and 8.00 (d, 2H); UV (MeOH) 285 (log ε 4.13), 295 (4.13), 318 (3.83), and 333 nm (3.92); CD (MeOH) $[\theta]\times 10^{-3}$ (nm) +5.5 (272), −11.4 (296), −6.6 (307), −10.3 (318), −8.2 (324), −8.9 (328), and +2.0 (337); Found: C, 85.35; H, 6.70%. Calcd for $\mathrm{C_{28}H_{26}O_2}$: C, 85.24; H, 6.64%.

(+)-10,10′-Dimethoxy-1,1′,2,2′,3,3′,4,4′-Octahydro-9,9′-biphenanthryl (13). To a boiling suspension of **12** (80 mg, 0.203 mmol), *t*-BuOK (50.2 mg, 0.447 mmol), and dry THF (4 ml) was added a solution of methyl *p*-toluenesulfonate (84 mg, 0.447 mmol) in dry THF (1 ml) under $\mathrm{N_2}$. The reaction mixture was refluxed for further 5 h, cooled in an ice-bath, quenched with water, and extracted with ether. After a usual work-up, the product was recrystallized from benzene to give (+)-**13** (77 mg, 90%): Mp 170—171 °C; $[\alpha]^{19}_{\mathrm{D}}$ +28.9° ($\mathrm{CHCl_3}$); ^{1}H-NMR ($\mathrm{CDCl_3}$) δ=1.71—2.19 (m, 8H), 2.63—3.37 (m, 8H), 3.27 (s, 6H), 7.05—7.35 (m, 6H), and 7.97 (d, 2H) (Found: C, 85.40; H, 7.23%).

(−)-10,10′-Dimethoxy-9,9′-biphenanthryl (15). a) Dehydrogenation of 13: A Solution of **13** (20.5 mg, 0.09 mmol) and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (20.5 mg, 0.09 mmol) in benzene (1 ml) was refluxed for 3 h. Evaporation of the solvent left a solid material which was recrystallized from benzene to give **15** (10 mg, 50%): Mp 251—253 °C; $[\alpha]^{23}_{\mathrm{D}}$ +26.4° ($\mathrm{CHCl_3}$); ^{1}H-NMR ($\mathrm{CDCl_3}$) δ=3.46 (s, 6H), 7.20—7.82 (m, 10H), 8.22—8.36 (m, 2H), and 8.65—8.85 (m, 4H) (Found: C, 87.72; H, 5.67%).

b) Methylation of (−)-14: The same method as described for **13**, using (−)-**14** ($[\alpha]^{23}_{\mathrm{D}}$ −71° ($\mathrm{CHCl_3}$), 98% optical purity)[2] (0.1 g, 0.259 mmol), *t*-BuOK (60 mg, 0.52 mmol), methyl *p*-toluenesulfonate (0.1 g, 0.53 mmol) afforded **15** (70 mg, 65%): mp 251—253 °C; $[\alpha]^{23}_{\mathrm{D}}$ +25.5° ($\mathrm{CHCl_3}$).

References

1) K. Yamamoto, H. Fukushima, Y. Okamoto, K. Hatada, and M. Nakazaki, *J. Chem. Soc., Chem. Commun.*, **1984**, 1111.

2) K. Yamamoto, H. Fukushima, and M. Nakazaki, *J. Chem. Soc., Chem. Commun.*, **1984**, 1490.

3) R. Huisgen and H. Nakaten, *Justus Liebig Ann. Chem.*, **586**, 84 (1954).

4) M. Nakazaki, I. Mita, and N. Toshima, *Bull. Chem. Soc. Jpn.*, **36**, 161 (1963).

5) The optical purity of (−)-**12** was determined by h.p.l.c. analysis with a column packed with (+)-poly (triphenylmethyl methacrylate) (elution with methanol).[6]

6) Y. Okamoto, S. Honda, I. Okamoto, H. Yuki, S. Murata, R. Noyori, and H. Takaya, *J. Am. Chem. Soc.*, **103**, 6971 (1981).

7) R. C. Helgeson, J. M. Timko, P. Moreau, S. C. Peacock, J. M. Mayer, and D. J. Cram, *J. Am. Chem. Soc.*, **96**, 6762 (1974).

8) M. Nakazaki, K. Yamamoto, S. Isoe, and M. Kobayashi, *J. Org. Chem.*, **44**, 2160 (1979).

9) M. Nakazaki, K. Yamamoto, and M. Maeda, *J. Org. Chem.*, **45**, 3229 (1980).