

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

Koji YAMAMOTO,* Hitoshi FUKUSHIMA, Hiroya YUMIOKA, and Masao NAKAZAKI

Department of Chemistry, Faculty of Engineering Science, Osaka University, Toyonaka, Osaka 560

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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.

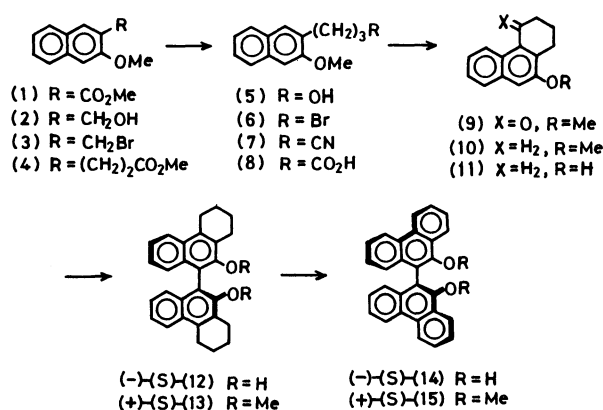
Recently, we found that the novel axially dissymmetric molecule, 10,10'-dihydroxy-9,9'-biphenanthryl (**14**), has been used for synthesis of chiral crown ether with high enantiomer selectivity toward primary amines¹⁾ and enantioselective reduction of ketones.²⁾ Here we report the determination of the 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⁾ furnished 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–H₂O–conc'd 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-diphenylethylamine⁴⁾ and Cu(NO₃)₂·3H₂O in methanol. The coupling product was purified by recrystallization from benzene to give an optically pure specimen of the binaphthol derivative (–)-(12) (79% yield, $[\alpha]_D^{25}$ –29.0° (CHCl₃).⁵⁾ Comparison of the CD spectra of (–)-**12** with that of authentic (–)-(S)-2,2'-dihydroxy-3,3'-dimethyl-1,1'-binaphthyl⁷⁾ 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**, $[\alpha]_D^{25}$ +26° (CHCl₃)). 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 LiAlH₄ (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 (MgSO₄), 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%).

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 alkylation of malonic ester with **3** (12.3 g, 48 mmol) was carried out according to literature⁸⁾ 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 conc'd H₂SO₄ 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 LiAlH₄ (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 ether extract was dried (MgSO₄), concentrated, and recrystallized from methanol, giving 3.0 g (95%) of **7**: Mp 74–75°C; IR (KBr)

2250 cm^{-1} ($\text{C}\equiv\text{N}$) (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 quenched with 2M HCl (200 ml) (1 M=1 mol dm^{-3}). The separated product was extracted with chloroform. The extract was dried (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 (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} ($\text{C}=\text{O}$) (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 literature⁹ 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 ($[\alpha]_D^{25}$ –50.8° (EtOH), 99% optical purity)⁷ (1.3 g, 6.6 mmol) and $\text{Cu}(\text{NO}_3)_2 \cdot 3\text{H}_2\text{O}$ (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 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; $[\alpha]_D^{21}$ –30.1° (CHCl_3); IR (KBr) 3520 cm^{-1} (OH); $^1\text{H-NMR}$ (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 $\text{C}_{28}\text{H}_{26}\text{O}_2$: C, 85.24; H, 6.64%.

(+)-10,10'-Dimethoxy-1,1',2,2',3,3',4,4'-Octahydro-9,9'-biphen-

anthryl (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 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; $[\alpha]_D^{19}$ +28.9° (CHCl_3); $^1\text{H-NMR}$ (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; $[\alpha]_D^{23}$ +26.4° (CHCl_3); $^1\text{H-NMR}$ (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** ($[\alpha]_D^{23}$ –71° (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; $[\alpha]_D^{23}$ +25.5° (CHCl_3).

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