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STEREOCHEMICAL STUDIES–VIII*

UNEQUIVOCAL DETERMINATION OF THE ABSOLUTE CONFIGURATION IN BIARYL SYSTEMS

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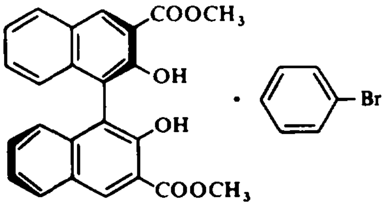
Abstract – According to the reaction sequences shown in Figs 1–5, the absolute configuration of optically active biaryl derivatives such as biphenyl, binaphthyl, bianthryl and bianthroaquinonyl have been clearly established, based on the standard compound (R)-(+)-I, in the binaphthyl system, whose absolute configuration was unequivocally determined by the anomalous X-ray diffraction method.

AMONG THE optically active compounds known, some possess inherently dissymmetric molecules, not containing any asymmetric atoms, the optical activity of restricted biaryl systems have been observed since the early 1920s. and to date many stereochemical investigations[1] concerning these compounds have been vigorously carried out. In addition. various kinds of optically active biaryl compounds have recently been found in nature.[2]

As almost all of the methods used to correlate the absolute configurations of molecules with asymmetric atoms, by their nature, cannot be used to determine the absolute configurations in these systems directly, the methods[3] described below have been used to solve this problem.

(i) Asymmetric transformation methods:
  (a) Relationships between stereochemical structures of alkaloids.[4]
  (b) Asymmetric Meerwein-Ponndorf-Verley reductions.[5]
  (c) Extensions to Prelog's rule.[5]
(ii) Optical property methods containing CD and ORD.[6]
(iii) Thermal analysis methods[7] (only intercorrelations between biaryl systems).

Recently. after long investigation the absolute configuration of (+)-2.2'-dihydroxy-1.1'-binaphthyl-3,3'-dicarboxylic acid dimethyl ester (I) bromobenzene solvate was proved unequivocally to be the (*R*)-configuration by the method of anomalous X-ray



R-(+)-I

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* Part VII: H. Mizuno, S. Terashima, and S. Yamada, *Chem. Pharm. Bull. (Tokyo)*, **19**, 227 (1971).

diffraction in our laboratories.[8] and also, the absolute configurations in some other biaryl systems were rigorously determined by their chemical correlations with the standard reference, (*R*)-(+)-I.[9]

This paper details these chemical correlations between biaryl systems.

Chemical correlations between binaphthyl systems

As the absolute configuration of one standard compound, (+)-I. in the binaphthyl system has been shown to be of the (*R*)-series by X-ray study. the absolute configurations of some other derivatives in the same system have now been correlated chemically only by chemical modifications of their substituents as shown in Figs 1 and 2.

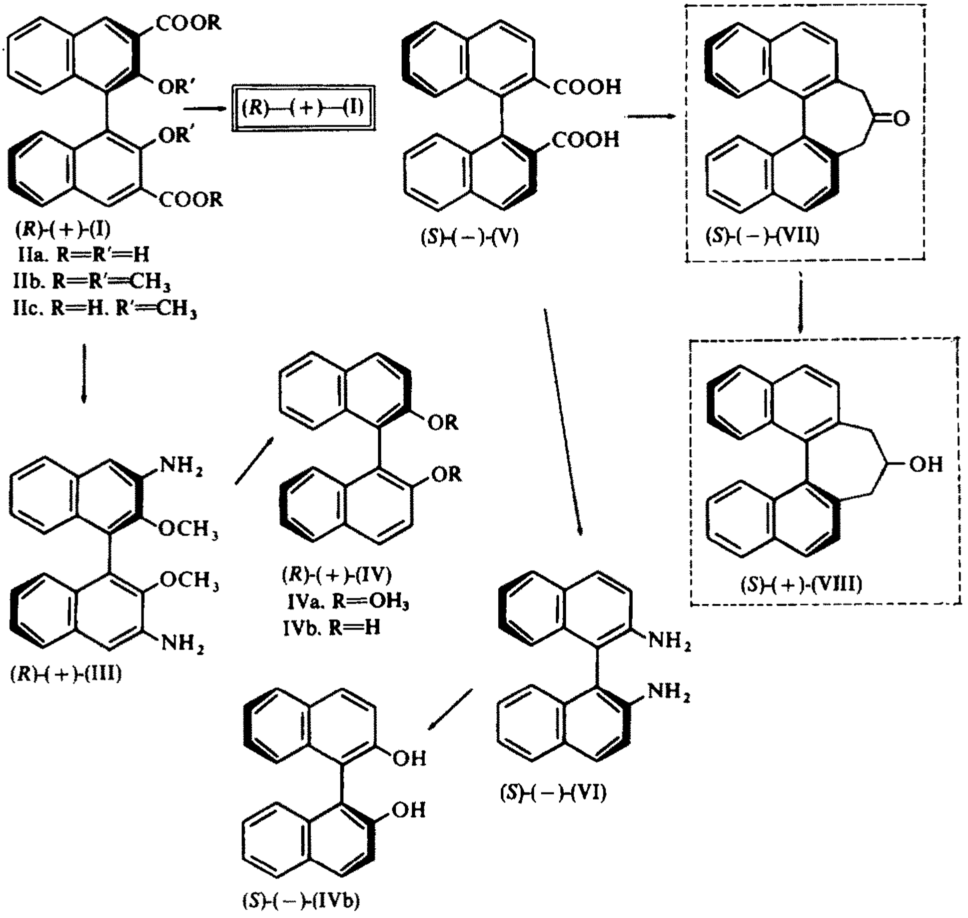

Fig 1[*]

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[*] For Figs 1–5 the molecules surrounded in the double, the single, and the dot-lined frames are the key compounds whose absolute configurations were determined by the direct X-ray diffraction methods, by chemical correlations with the standard references, and only by stereochemical transformation methods respectively.

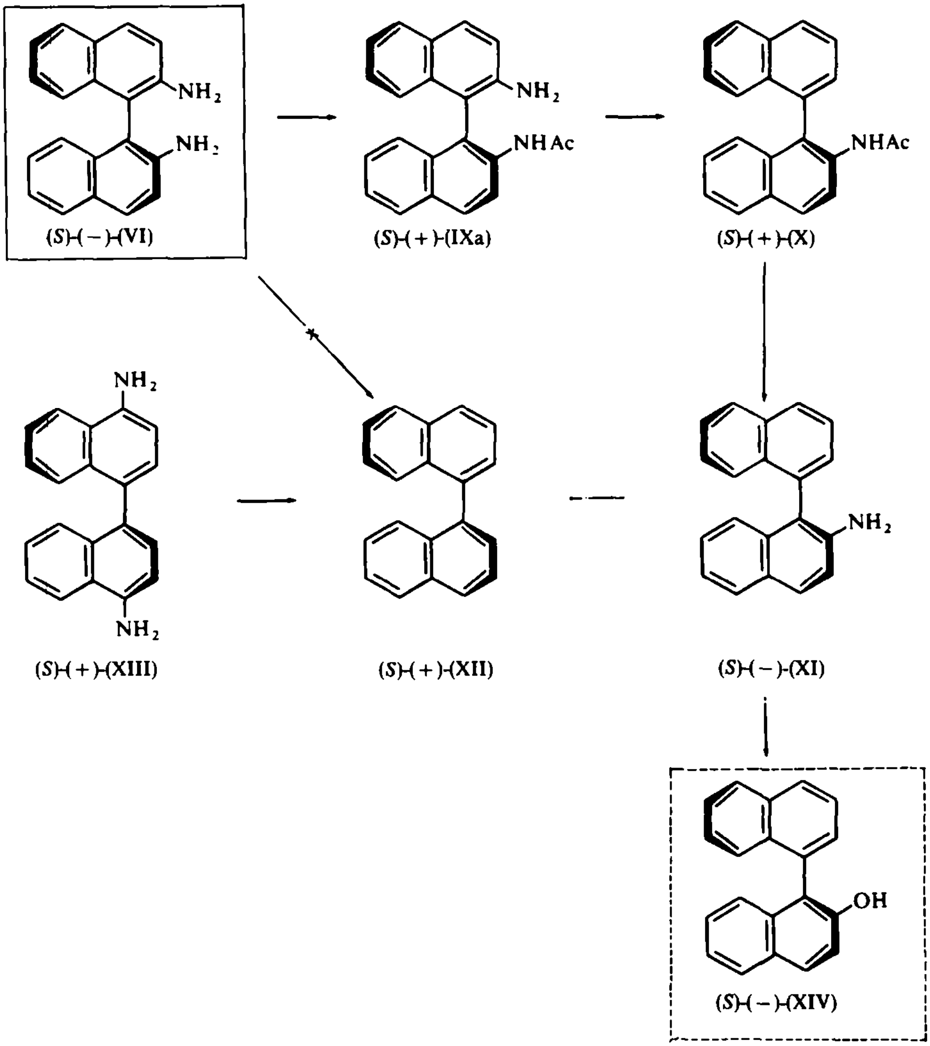

Fig 2*

Treatment of (*R*)-(+)-IIa, correlated with the standard (*R*)-(+)-I. with CH_2N_2 in a mixture of ether and MeOH gave the tetramethyl derivative (*R*)-(+)-IIb. which was hydrolyzed to the dicarboxylic acid (*R*)-(+)-IIc with methanolic KOH. The resulting carboxylic acid was submitted to Curtius rearrangement by way of the acid chloride and acid azide to afford the (*R*)-(+)-diamine (III), which. after reductive deamination of its tetrazotised solution by cold hypophosphorous acid. was demethylated with BBr_3 in cold CH_2Cl_2 to yield the (*R*)-(+)-diol (IVb). While, the transformation of the other diamine, (−)-VI, correlated to the (−)-dicarboxylic acid (V) by K. Mislow *et al.*,[10] to the diol (IVb), was accomplished by treatment of its tetrazotised solution with hot dilute H_2SO_4. The diol (IVb) so obtained was negative rotatory, so the absolute configurations of (−)-V and (−)-VI were proved to be of the (*S*)-configuration in accordance with Mislow's proposal by the asymmetric transformation methods[5] regarding both (*S*)-(−)-VII and (*S*)-(+)-VIII.

An attempt to synthesize optically active 1,1′-binaphthyl (XII), the simplest model in the binaphthyl system, from the diamine (VI) was reported unsuccessfully by F. Bell *et al.*,[11], later A. S. Cooke *et al.* succeeded in obtaining it by the reductive deamination of optically active XIII without any discussion about the absolute configuration.[12] In our report, the absolute configuration of the (+)-1,1′-binaphthyl (XII) has been clearly established to be the (*S*)-configuration according to the sequence in Fig. 2. Monoacetyl derivative (*S*)-(+)-IXa prepared from (*S*)-(−)-VI by means of Ac_2O and pyridine was deaminated with HNO_2 and hypophosphorous acid to give, after hydrolysis, the monoamine (*S*)-(−)-XI. The stepwise deamination of (*S*)-(−)-XI by the same procedure as above yielded the crude (*S*)-(+)-XII, purified through chromatography on alumina to afford the pure (*S*)-(+)-XII, Besides. the thermal decomposition of the borofluoride of the diazotised monoamine (*S*)-(−)-XI in glacial AcOH gave, after hydrolysis in basic aqueous solution, the optically active phenolic compound (*S*)-(−)-XIV, proposed to belong to the (S)-configuration by J. A. Berson *et al.*[5] Consequently, the proposals regarding the determination of the absolute configurations in the binaphthyl system by asymmetric transformation methods were proved to be completely correct by these chemical correlations.

Chemical correlations between the binaphthyl system and other biaryl systems

No attempts at chemical correlations between different biaryl systems, including aromatic ring formations or decompositions, have been carried out in spite of the inconvenicnece of individual determinations of the absolute configurations in each biaryl system. The first chemical intercorrelations between different biaryl systems are reported in this article, and at the same time, the absolute configurations in biphenyl. bianthryl and bianthraquinonyl systems have been determined unequivocally, based on the standard reference (*R*)-(+)-I.

A chemical correlation between the binaphthyl and biphenyl systems has been shown in Fig. 3. The optically active (−)-XVIII, obtained from the resolved dicarboxylic acid (−)-XVI according to the literature,[13] was treated with ethanolic HCl, followed by LAH reduction, to give the diol (−)-(XIX), which was converted to the dibromide with PBr_3, then submitted to the malonic ester synthesis under the usual reaction conditions to afford the dicarboxylic acid (−)-(XX). The Friedel-Crafts reaction of the acid chloride prepared from (−)-XX yielded the expected cyclic diketone (−)-(XXI), which was reduced with LAH in ether, converted to the dibromide with PBr_3 in benzene and then to the tetrabromide with NBS in CCl_4, and dehydrobrominated with KOAc to afford a binaphthyl derivative (−)-(XXII) after purification through chromatography on silica-gel. As the absolute configuration of the positive rotatory 2,2′-dimethyl-1,1′-binaphthyl, (+)-(XXII), has been already established to be the (*S*)-configuration by chemical correlation of (*S*)-(−)-V[10], the absolute configuration of the negative compound, (−)-XXII, was proved to belong to the (*R*)-configuration, and thus the absolute configurations of the biphenyl derivatives, (−)-XVI, (+)-XVII, (−)-XVIII, (−)-XIX, (−)-XX and a tetralone derivative (−)-XXI were demonstrated respectively to belong to the (*R*)-configuration.[14]

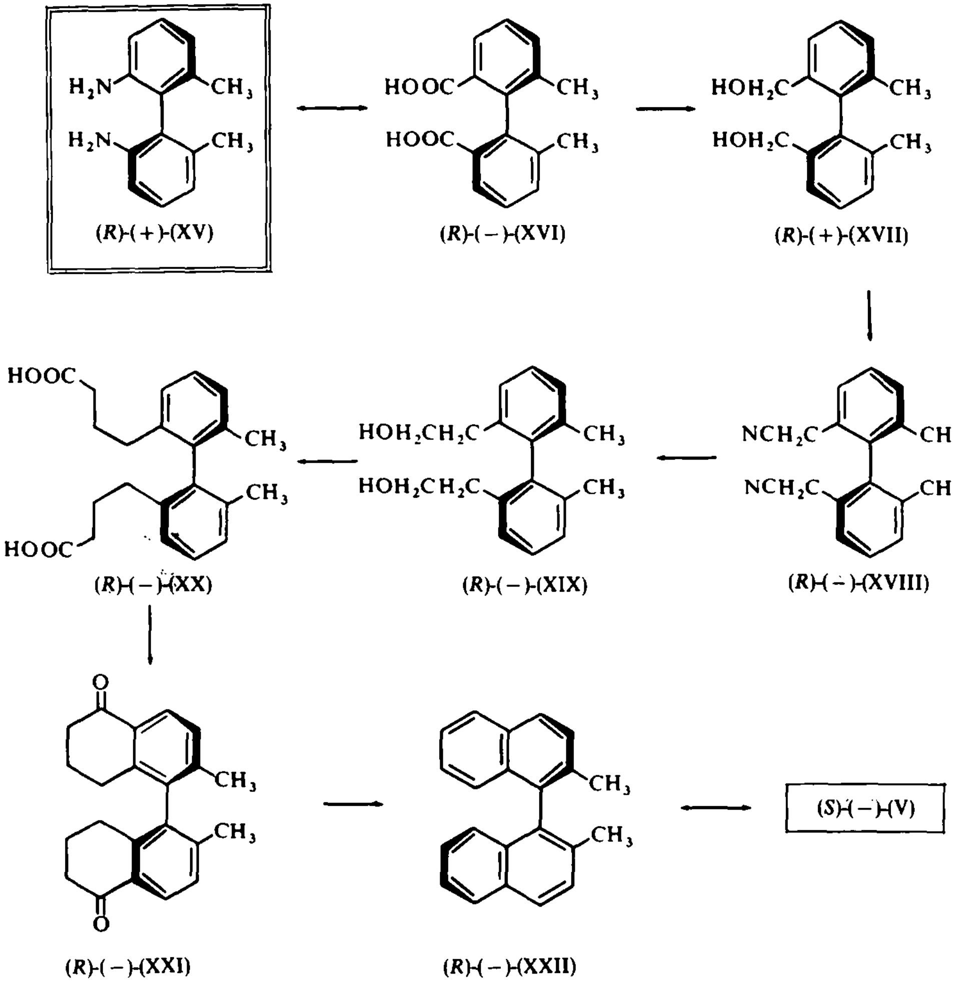

Fig 3

A chemical correlation between biphenyl and bianthraquinonyl is also shown in Fig. 4.

The reaction of the resolved dicarboxylic acid, (S)-(+)-XVI, with *ortho*-tolyl lithium yielded the (S)-(–)-ditoluoyl derivative (XXIII), which was converted to the (S)-(+)-2,2′-dimethyl-1,1′-bianthraquinonyl (XXV) by the oxidation of the (S)-(–)-XXIII with $KMnO_4$, followed by dehydration with conc. H_2SO_4.

Furthermore, the first chemical correlation[11, 15] between the bianthryl and bianthraquinonyl systems was undertaken as shown in Fig. 5.

Reduction of the dibromide, (–)-(XXVII), derived from the dicarboxylic acid (–)-(XXVI) according to the literature,[18] with LAH, yielded (–)-2,2′-dimethyl-1,1′-bianthryl, (–)-(XXVIII), which was oxidized with $NaClO_3$ accompanied by a small amount

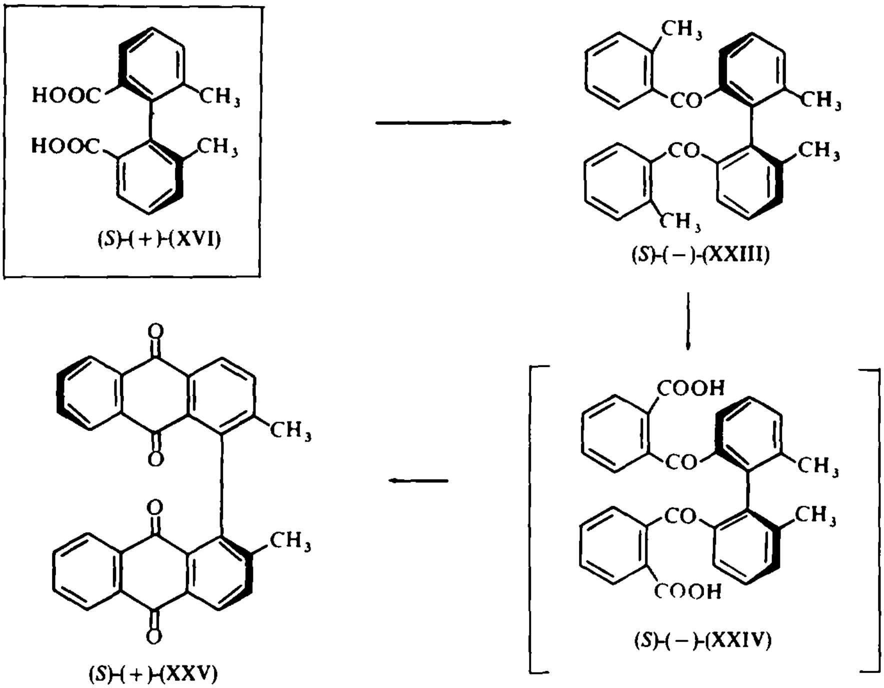
HOOC
CH$_3$
HOOC
CH$_3$
(S)-(+)-(XVI)
CH$_3$
CO
CH$_3$
CO
CH$_3$
CH$_3$
(S)-(−)-(XXIII)
COOH
CO
CH$_3$
CO
CH$_3$
COOH
(S)-(−)-(XXIV)
O
CH$_3$
O
O
CH$_3$
O
(S)-(+)-(XXV)

FIG 4

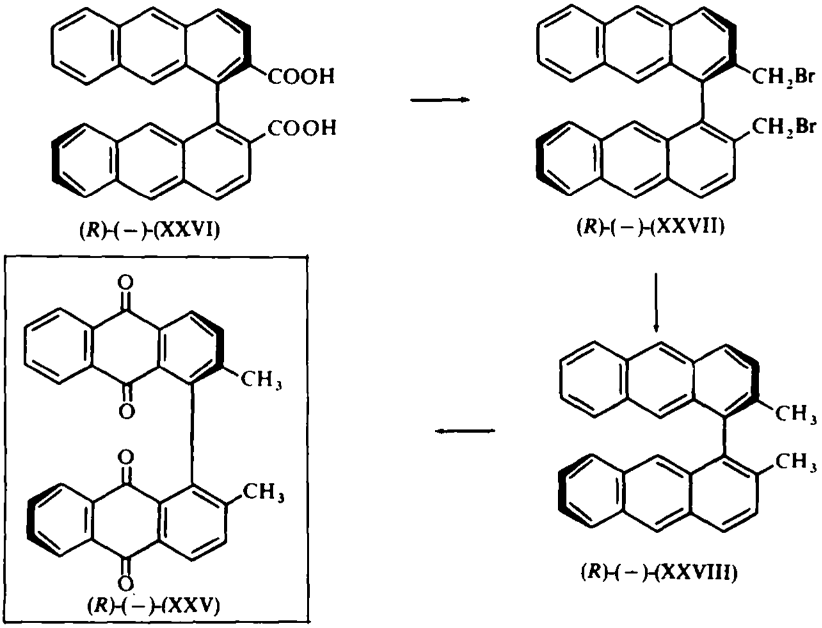
COOH
COOH
(R)-(−)-(XXVI)
CH$_2$Br
CH$_2$Br
(R)-(−)-(XXVII)
CH$_3$
CH$_3$
(R)-(−)-(XXVIII)
O
CH$_3$
O
O
CH$_3$
O
(R)-(−)-(XXV)

FIG 5

of vanadium pentoxide to afford (–)-XXV. The absolute configuration of (–)-XXV has been determined to be the (*R*) configuration as described above, *i.e.*, the absolute configurations of (–)-XXVI, (–)-XXVII and (–)-XXVIII were found to belong to the (*R*)-configuration.

EXPERIMENTAL

(R)-(+)-2,2′-*Dimethoxy*-1,1′-*binaphthalene*-3,3′-*dicarboxylic acid dimethyl ester* (IIb). A solution of CH_2N_2 (*ca.* 2·8 g) in ether (100 ml) was added slowly to a stirred solution of 500 mg of the acid (+)-(IIa), $[\alpha]_D^{26}$ + 176°, resolved through its brucine salt[16] in a mixture of MeOH (100 ml) and ether (100 ml). The mixture was allowed to stand at room temp. for two days, evaporated to dryness *in vacuo*, and redissolved in ether (100 ml). The ethereal solution was washed with two 50 ml portions of 5% NaOH aq and water, dried (Na_2SO_4) and evaporated to dryness to give 460 mg (80%) of the tetramethyl compound $[\alpha]_D^{23}$ + 43 (*c* = 1·0, THF), which could not be recrystallized; IR spectrum ($CHCl_3$): 1725, 1620 and 1590 cm^{-1}; NMR ($CDCl_3$): τ 1·45 (s, 2H), 1·95–2·90 (m, 8H), 6·00 (s, 6H) and 6·50 (s, 6H).

(*R*)-(+)-2,2′-*Dimethoxy*-1,1′-*binaphthalene*-3,3′-*dicarboxylic acid* (IIc). A solution of the above tetramethyl compound, (+)-(IIb) in 10% methanolic KOH (100 ml) was refluxed on a water bath for 90 min. After evaporation of MeOH, water (100 ml) was added, extracted with two 50 ml portions of ether, and acidified with conc. HCl to give a white precipitate, collected and washed with water. Recrystallization from C_6H_6 gave 470 mg (88%) of the pure dicarboxylic acid, m.p. 228–229°, $[\alpha]_D^{23}$ + 48·5° (*c* = 1·0, THF). (Calcd. for $C_{24}H_{18}O_6$: C, 71·63; H, 4·51. Found: C, 71·75; H, 4·77%).

(*R*)-(+)-3,3′-*Diamino*-2,2′-*dimethoxy*-1,1′-*binaphthyl* (III). A mixture of the (+)-dicarboxylic acid (IIc) (201 mg) and $SOCl_2$ (10 ml) was refluxed for 2 hr and excess $SOCl_2$ evaporated to give a slightly yellow caramel. A solution of NaN_3 (200 mg) in water (0·5 ml) was added dropwise to a stirred solution of the above acid chloride in dry acetone (9 ml). After 15 min at room temp., water (18 ml) was added to the mixture on an ice bath to form a yellow viscous oil, which was extracted with two 20 ml portions of C_6H_6, the C_6H_6 layers were dried (Na_2SO_4). Gas evolution was observed as the C_6H_6 soln was refluxed for one hr., 50% aqueous KOH (20 ml) was introduced, and refluxing was continued for another one hr. The aqueous layer was separated, *ca.* 5N HCl (40 ml) was added to the organic layer, and the mixture was warmed on a water bath for 15 min. The aqueous layer was separated, after filtration made alkaline with conc. NH_4OH, extracted with three 50 ml portions of $CHCl_3$, dried over Na_2SO_4, and evaporated to dryness *in vacuo* to afford 130 mg (76%) of (+)-3,3′-diamino-2,2′-dimethoxy-1,1′-binaphthyl (III), m.p. 95–97°, $[\alpha]_D^{25}$ + 9·3°(*c* = 0·64, THF). Recrystallization of the hydrochloride from benzene-ether gave colorless needles, m.p. 235–236°. (Calcd. for $C_{22}H_{22}N_2O_2Cl_2$: C, 63·31; H, 5·31; N, 6·71. Found: C, 63·50; H, 5·37; N, 6·73%).

(*R*)-(+)-2,2′-*Dimethoxy*-1,1′-*binaphthyl* (IVa). (+)-3,3′-Diamino-2,2′-dimethoxy-1,1′-binaphthyl (III) (550 mg) in 5N HCl (50 ml) were tetrazotised with $NaNO_2$ (230 mg) in H_2O (2 ml), and poured, with stirring, into 32% aqueous hypophosphorus acid (150 ml), below 5°. After 3 days at 7–8°, an orange precipitate was extracted with benzene. The benzene layer was washed with 5% NaOH aq. 5% HCl and water. dried (Na_2SO_4), and evaporated to dryness *in vacuo* to give, after chromatography (silica gel-C_6H_6) and recrystallization from C_6H_6–haxane, 221 mg (44%) of (+)-2,2′-dimethoxy-1,1′-binaphthyl (IVa), m.p. 184–185°, $[\alpha]_D^{21}$ + 79·5° (*c* = 1·0, THF). (Calc. for $C_{22}H_{18}O_2$: C, 84·05; H, 5·77. Found: C, 83·90, H, 5·87%).

(*R*)-(+)-2,2′-*Dihydroxy*-1,1′-*binaphthyl* (IVb). After treatment of (+)-2,2′-dimethoxy-1,1′-binaphthyl (IVa). (200 mg) in CH_2Cl_2 (40 ml) with BBr_3 (500 mg) at –80° for 30 min. the mixture was allowed to stand at room temp. for 1 hr. poured into ice-water (40 ml) and extracted with CH_2Cl_2. The organic layer was extracted with two 20 ml portions of 10% NaOH aq. the combined extracts were acidified with 5% HCl to afford a white precipitate, recrystallized from aqueous EtOH to give 132 mg (72%) of (+)-2,2′-dihydroxy-1,1′-binaphthyl (IVb), m.p. 199–201°, $[\alpha]_D^{26}$ + 43·0° (*c* = 0·9, THF). (Calc. for $C_{20}H_{14}O_2$: C, 83·90; H, 4·93. Found: C, 83·88; H, 4·95%).

(*S*)-(–)-2,2′-*Dihydroxy*-1,1′-*binaphthyl* (IVb). (–)-2,2′-Diamino-1,1′-binaphthyl (VI) (284 mg), $[\alpha]_D^{25}$ – 95·5° (optical purity 52%), synthesized and resolved as described in the literature.[17] in a mixture of 1 ml of conc. H_2SO_4 and 5 ml water. were tetrazotised with $NaNO_2$(140 mg) in water (2 ml) with cooling on an ice bath. and then added dropwisely to a refluxing mixture of conc. H_2SO_4 (2 ml) and water (10 ml). The mixture was refluxed for an additional 5 min then immediately cooled on an ice bath, and extracted with ether (70 ml). After washing with water, the ethereal solution was extracted with three 20 ml portions of 5% NaOH aq: the aqueous layer was acidified with 10% HCl aq and reextracted with ether (70 ml). The ethereal solution was washed with water, dried (Na_2SO_4), evaporated to dryness and chromatographed (silica gel.

acetone-C_6H_6 1:6). The combined fractions were evaporated to give 11 mg (3·9%) of the desired diol, (−)-(IVb), m.p. 190–193°, $[\alpha]_D^{24}$ − 19·0° (c = 0·2, THF) after recrystallization from aqueous EtOH. (Calc. for $C_{20}H_{14}O_2$: C, 83·90· H. 4·93. Found: C, 83·74; H. 5·12%). The IR spectra (KBr pellet) of (R)-(+)-IVb and (S)-(−)-IVb were identical.

(S)-(+)-2-*Acetamido-2'-amino-1,1'-binaphthyl* (IXa) and (S)-(+)-2 2'-*diacetamido-1 1'-binaphthyl* (IXb). To a solution of 2·13 g of the (−)-diamine (VI), $[\alpha]_D^{25}$ − 95·5°, in dry benzene (75 ml) was added Ac_2O ml (0·9) and dry pyridine (1·0 ml). The mixture was allowed to stand at room temp. overnight to give, after washing with C_6H_6, 690 mg (25%) of (+)-2,2'-diacetamido-1,1'-binaphthyl (IXb) as colorless prisms, m.p. 226–7° (C_6H_6), $[\alpha]_D^{25}$ +10·8° (c = 1·0, THF). The combined C_6H_6 fractions of the filtrate and washing were evaporated to dryness *in vacuo* and chromatographed (silica gel, acetone-C_6H_6 1:4) to afford three compounds: the first was starting material (26%). The second was 901 mg (37%) of the desired monoacetyl derivative, (+)-(IXa), m.p. 236–9° (C_6H_6), $[\alpha]_D^{25}$ + 9·6° (c = 1·0, THF) and, the third, 193 mg (7%) of the diacetyl derivative (IXb), obtained in 32% total yield. (Calc. for $C_{22}H_{18}ON_2$ (monoacetyl derivative): C, 80·95; H, 5·56; N, 8·58. Found: C, 81·07; H, 5·53; N, 8·31%; Calc. for $C_{24}H_{20}O_2N_2$ (diacetyl derivative): C, 78·24; H, 5·47; N. 7·60. Found: C, 78·12; H, 5·41; N, 7·51%).

(S)-(+)-2-*Acetamido-1,1'-binaphthyl* (X). To a chilled solution of 990 mg of (+)-2-acetamido-2'-amino-1,1'-binaphthyl (IXa) in 5N HCl (100 ml) was added. dropwise, a solution of $NaNO_2$ (210 mg) in 1·8 ml of water. The resulting diazotised solution was poured into a mixture of 48% hypophosphorous acid (200 ml) and water (100 ml), allowed to stand overnight at 7–8°, and extracted with C_6H_6 (350 ml). The organic layer was washed with two 100 ml portions of 5% NaOH aq, 5% HCl. three 100 ml portions of water and dried over Na_2SO_4. Removal of solvent *in vacuo* gave 746 mg (81%) of crude (+)-2-acetamido-1,1'-binaphthyl (X), recrystallized from aqueous MeOH to yield colorless prisms, m.p. 169–172°, $[\alpha]_D^{25}$ +8·5° (c = 1·0, THF). (Calc. for $C_{22}H_{19}ON$: C. 84·86; H. 5·50; N. 4·50. Found: C, 84·84; H, 5·66; N, 4·63%).

(S)-(−)-2-*Amino-1,1'-binaphthyl* (XI). A solution of 671 mg of the above monoacetamido derivative (X) in a mixture of conc. HCl (10 ml) and dioxane (20 ml) was heated on a water bath under reflux for one hr., after dilution with water-(200 ml)-made alkaline by addition of a sufficient amount of 10% NaOH aq. and then extracted with C_6H_6 (350 ml). The C_6H_6 layer was washed with water, dried over Na_2SO_4, and evaporated to dryness *in vacuo* to give 546 mg (84%) of (−)-2-amino-1,1'-binaphthyl, decolorized by chromatography (alumina, acetone-C_6H_6 1:4), and recrystallized from aqueous MeOH as colorless needles, m.p. 189–190°, $[\alpha]_D^{25}$ −51·4° (c = 1·0, THF). (Calc. for $C_{20}H_{15}N$: C, 89·18; H, 5·61; N, 5·20. Found: C, 89·35; H, 5·76; N, 5·19%).

(S)-(+)-1,1'-*Binaphthyl* (XII). 135 mg of (−)-2-amino-1,1'-binaphthyl (XI) in 5N HCl (10 ml) were diazotised with $NaNO_2$ (35 mg) in water (0·3 ml), and poured, while stirring, into 32% aqueous hypophosphorous acid (60 ml) at 0°. The mixture was maintained at 0° for one hr, and extracted with C_6H_6 (70 ml). The C_6H_6 layer was washed with two 20 ml portions of cold 5% NaOH aq., two 20 ml portions of cold 5% HCl, three 20 ml portions of ice-water, dried ($MgSO_4$), and evaporated to dryness *in vacuo* below 10° to leave a slightly brown solid, purified by chromatography (alumina at 0°, C_6H_6-hexane 1:1) to give 105 mg (83%) of crude 1,1'-binaphthyl (XII). Rapid recrystallization from light petroleum-ether yielded a pale yellow powder, m.p. 153–4°,[14] $[\alpha]_D^{19}$ +104° (c = 1·0, THF). (Calc. for $C_{20}H_{14}$: C, 94·45; H, 5·55. Found: C, 94·58; H, 5·69%).

(S)-(−)-2-*Hydroxy-1,1'-binaphthyl* (XIV). The diazotised solution, prepared from 135 mg of (−)-monoamine as above, was poured into 42% aqueous borofluoride acid (20 ml) a large amount of yellow precipitate formed, collected and dried over P_2O_5. The dried borofluoride was suspended in glacial AcOH (10 ml), decomposed on a boiling water bath until evolution of N_2 ceased, and evaporated to dryness under reduced pressure. The residue was dissolved in water (10 ml), made alkaline with Na_2CO_3, and extracted with two 20 ml portions of ether. The ethereal solution was dried ($MgSO_4$), evaporated to dryness, and chromatographed (silica gel, hexane-C_6H_6 1:2) to give 67 mg (39%) of pale yellow oil (XIII). The IR spectrum (cap.) showed the expected carbonyl peak at 1770 cm^{-1}, NMR spectrum ($CDCl_3$) exhibited bands at 1·95–3·00 (m, 13H) and 8·33 (s, 3H), which suggested compound XIII to be the acetate of 2-hydroxy-1,1'-binaphthyl (XIV). A solution of this acetate in 5% methanolic KOH (10 ml) was refluxed on a water bath for 30 min, and, after evaporation of the MeOH, water (10 ml) was added to the residue to dissolve it completely, acidified with 5 ml of 10% HCl, and extracted with two 20 ml portions of C_6H_6. The C_6H_6 layer was washed with sat. $NaHCO_3$ aq. and water, dried (Na_2SO_4), and evaporated *in vacuo* to afford 52 mg (39%) of colorless oil, easily recrystallized from aqueous MeOH as needles. m.p. 87–8°,* $[\alpha]_D^{20}$ −2·9° (c = 1·0. THF). (Calc. for $C_{20}H_{14}O$: C. 88·86; H, 5·22. Found: C, 89·15; H, 5·35%).

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* The difference between the m.ps in the literature and in this work was amended in the kindly private communication by J. A. Berson.

(R)-(−)-*6,6′-Dimethyl-2,2′-bis-(1-hydroxyethyl)-biphenyl* (XIX). Dry HCl gas was introduced into a solution of 1·4 g of (−)-6.6′-dimethyl-2,2′-bis-(cyanomethyl)-biphenyl (XVIII) $[\alpha]_D^{20}$ −15° (optical purity 75%), prepared from the carboxylic acid (XVI) by way of the diol (XVII)[13] in abs. EtOH (100 ml) and saturated under cooling on an ice bath. The solution was left overnight at room temp. and heated to reflux on a water bath for two hr. After addition of water (2 ml), the solution was refluxed for 1 hr, then evaporated to dryness *in vacuo*. The residue, after addition of water (50 ml), was extracted with ether (200 ml); the ethereal solution was washed with water, dried ($MgSO_4$) and evaporated under reduced pressure to leave 1·7 g (89%) of crude ester, whose IR spectrum exhibited a band at 1740 cm^{-1} (C = O). The ester in dry ether (20 ml) was added dropwise to a solution of 1·5 LAH in dry ether (45 ml), and the mixture was heated under reflux for 30 min. After decomposition of excess LAH by addition of dilute HCl, the ethereal layer was separated and the aqueous layer was extracted with ether. The combined ether solutions, were washed successively with 10% HCl, 10% Na_2CO_3 aq and water, dried (Na_2SO_4), and evaporated to give 1·1 g (76%) of pale yellow oil, recrystallized from C_6H_6-hexane as colorless prisms, m.p. 109–110°, $[\alpha]_D^{21}$ − 25° (*c* = 1·0, THF). (Calc. for $C_{18}H_{22}O_2$; C, 79·96; H, 8·20. Found: C, 79·92; H, 8·30%).

(R)-(−)-*6,6′-Dimethyl-1,1′-biphenyl-2,2′-bis-(butyric acid)* (XX). A solution of 1·5 g of PBr_3 in benzene (2 ml) was added dropwise to a 65° solution of 1·08 g of the diol (XIX) in dry benzene (10 ml). The mixture was heated under reflux for one hr, and, after cooling, water (10 ml) were introduced, with stirring, to decompose excess PBr_3. The C_6H_6 layer separated was washed with water dried (Na_2SO_4), and evaporated to leave 1·6 g of pale yellow oil. which was dissolved in dry ether (3 ml), and added to a solution of 460 mg of Na and 3·84 g of diethyl malonate in abs. EtOH (30 ml). The mixture was refluxed for 3 hr, after addition of water (120 ml) and extracted with ether (200 ml). The organic layer was washed with 10% HCl and sat. NaCl aq. dried ($MgSO_4$) and evaporated to leave a pale yellow oil, purified through chromatography (silica gel, acetone-C_6H_6 1:1) to give 750 mg (33%) of colorless oil; NMR spectrum ($CDCl_3$), exhibiting bands at τ2·80 (s. 6H), 5·90 (q. 8H) 6·75 (m, 2H), 7·80–8·30 (m 8H) 8·11 (s, 6H), and 8·80 (t, 12H), suggested the desired tetraester derivative. The tetraester was dissolved in EtOH (50 ml) with KOH (5·0 g), and hydrolyzed under reflux for four hr. After evaporation of EtOH, the residue was dissolved in water (50 ml), washed with ether, acidified with 10% HCl and extracted with ether (100 ml). The ethereal layer was washed with water, dried ($MgSO_4$), and evaporated to give an oily product, which was decarboxylated by heating (130–160°) on an oil bath for 3 min to afford 410 mg (29%) of waxy solid, $[\alpha]_D^{20}$ −20° (*c* = 1·0, THF), resisting crystallization; NMR spectrum bands at τ1·30 (s, 2H), 2·89 (s, 6H), 7·50–8·30 (m, 12H) and 8·14 (s, 6H), indicating the expected dicarboxylic acid (XX).

(*R*)-(−)-*5,5′-bis-(6-Methyltetralone-1)* (XXI). A mixture of 340 mg of the (−) -dicarboxylic acid (XX) and $SOCl_2$ (1·0 ml) was refluxed on a warm bath for 30 min. Removal of excess $SOCl_2$ gave a pale yellow residue, which was dissolved in dry CS_2 (10 ml) and reacted with anhyd. $AlCl_3$ (500 mg) under reflux for 30 min. After cooling, ice (5 g) and conc. HCl (5 ml) were added and the mixture extracted with C_6H_6 (70 ml). The C_6H_6 layer was washed with water, dried (Na_2SO_4), and evaporated to afford, after purification through chromatography (silica gel, acetone-C_6H_6 1:10) 198 mg (64%) of pale yellow oil (XXI). $[\alpha]_D^{20}$ − 9·0° (*c* = 1·0, THF); IR spectrum: 1670 cm^{-1}; NMR spectrum: τ2·02 (d, 2H), 2·70 (d, 2H), 7·20–8·20 (m, 12H), 8·05 (s, 6H). The 2,4-dinitrophenylhydrazone from EtOAc in a form of red powder, decomp. 285–9°. (Calc. for $C_{34}H_{30}O_8N_8$: C, 60·17; H, 4·46; N, 16·51. Found: C, 60·20; H, 4·35; N. 16·20%).

(*R*)-(−)-*2,2′-Dimethyl-1,1′-binaphthyl* (XXII). A solution of 180 mg of the above diketone (XXI) in dry ether (3 ml) was treated with a stirred solution of 200 mg of LAH in dry ether (10 ml) for 15 min under reflux. The excess LAH was decomposed by addition of water, and acidified with HCl. The ethereal layer was separated, and the aqueous layer extracted with two 10 ml portions of ether; the combined organic layers were washed with water, dried ($MgSO_4$) and evaporated to leave 174 mg of colorless caramel. This was dissolved in hot benzene (4 ml), reacted under reflux with PBr_3 (300 mg) in benzene (2 ml) for 30 min. The mixture was cooled in an ice bath, water (10 ml) added, extracted with 20 ml of C_6H_6, dried (Na_2SO_4), and evaporated under reduced pressure to leave 190 mg of yellow oil. This oil in CCl_4 (14 ml) was brominated by reaction with 200 mg of N-bromosuccinimide (benzoyl peroxide initiated) under reflux for 30 min. then treated with 3·0 g of KOAc and 1·0 ml of glacial AcOH, with stirring, for another 30 min. under reflux. After cooling, the mixture was poured into water (40 ml) with 2·0 g NaOH, and extracted with ether (80 ml). The ethereal layer was washed with water and dried ($MgSO_4$). Removal ov solvent gave 62 mg (39%) 2,2′-dimethyl-1,1′-binaphthyl (XXII), m.p. 66–7°,[6] $[\alpha]_D^{20}$ −7·0° (*c* = 0·5, EtOH), after purification through chromatography (silica gel. hexane) and recrystallization from aqueous EtOH. (Calc. for $C_{30}H_{22}$: C. 95·37; H, 6·43. Found: C, 93·40; H, 6·40%).

(*S*)-(−)-*2,2′-Dimethyl-6,6′-di-(o-toluoyl)-biphenyl* (XXIII). A solution of the (+)-6,6′-dimethyl-2,2′-

diphenic acid (XVI), $[\alpha]_D^{20}$ + 24° (c = 1·0, MeOH) in dry ether (10 ml), synthesized and resolved according to the literature,[13a] was treated with *o*-tolyl lithium, prepared from 4·1 g of bromobenzene and 340 mg of Li in 50 ml of ether, under N_2 with reflux for 5 hr. After cooling 20 ml of water and 30 ml of dil. HCl were added with stirring. The ethereal layer was separated and the aqueous layer extracted with two 25 ml portions of ether; the combined ethereal solutions were washed with three 20 ml portions of 10% NaOH aq and of water, dried (Na_2SO_4), and evaporated to give, after purification through chromatography (silica gel, C_6H_6), 172 mg (21%)of yellow oil, recrystallized from aqueous EtOH to yield pure diketone (XXIII), m.p. 78–81 , $[\alpha]_D^{19}$ −17·4° (c=1·0, THF). (Calc. for $C_{30}H_{26}O_2$: C. 86·09; H, 6·26. Found: C, 85·86; H, 6·22%).

(*S*)-(+)-*2,2′-Dimethyl-1,1′-bianthraquinonyl* (XXV). 170 mg of the (−)-diketone (XXIII) in pyridine (7 ml) and 10 ml of 2% NaOH aq were oxidized with 1·0 g of $KMnO_4$ under reflux for 30 min. After cooling, the mixture was acidified with 10% H_2SO_4, treated with $NaHSO_3$ until the precipitated MnO_2 disappeared and extracted with ether (200 ml). The ethereal solution was extracted with 10% NaOH aq, and the aqueous extract acidified with dil. HCl and re-extracted with ether (100 ml). The organic layer was washed with water, dried ($MgSO_4$), and evaporated to leave crude dicarboxylic acid (XXIV), which was dissolved in 5 ml of 20% fuming H_2SO_4 and heated to 80–90° for 90 min. The mixture was cooled and diluted with ice-water, (50 ml), and extracted with 1:2 ether-THF (200 ml). The organic layer was washed with three 15 ml portions of 10% NaOH aq and sat. NaCl, dried ($MgSO_4$), and evaporated to afford, after recrystallization from hexane and *o*-dichlorobenzene, 30 mg (17%) of 2,2′-cimethyl-1,1′-bianthraquinonyl, m.p. >300°, $[\alpha]_D^{19}$ +180° (c=0·1, THF). (Calc. for $C_{30}H_{18}O_4$: C, 81·43; H, 4·10. Found: C, 81·45; H, 4·08%).

(*R*)-(−)-*2,2′-Dimethyl-1,1′-bianthryl* (XXVIII). A solution of 300 mg of dibromide (XXVII), $[\alpha]_D^{20}$ −102° (optical purity 52%), prepared from the (−)-dicarboxylic acid (XXVI) according to the literature,[18] in dry ether (20 ml) was added to a stirred solution of 1·0 g of LAH in dry ether (25 ml). The mixture was heated under reflux for 2 hr, cooled in an ice bath, and decomposed with 20 ml of 10% HCl. The ethereal layer was separated and the aqueous layer extracted with two 25 ml portions of ether; the combined ethereal layers were washed with sat. NaCl, dried ($MgSO_4$) and evaporated to dryness to leave a yellow solid, which, after purification through chromatography (silica gel, C_6H_6-hexane 1:1), was recrystallized from hexane to give 180 mg of 2,2′-dimethyl-1,1-bianthryl, m.p. 155–7°, $[\alpha]_D^{20}$ − 284° (c = 1·0, THF). (Calc. for $C_{30}H_{22}$: C, 94·20; H, 5·80. Found: C, 94·16; H, 6·09%).

(*R*)-(−)-*2,2′-Dimethyl-1,1′-bianthraquinonyl* (XXV). To a solution of 150 mg of the above (−)-bianthryl derivative (XXVIII) in glacial AcOH (40 ml) was added 1·5 g of $NaClO_3$ 10 mg of vanadium pentoxide and 8 ml of 2% H_2SO_4. The mixture was heated under reflux for 2 hr, and, after cooling, diluted with water (80 ml) to afford a yellow precipitate, which was washed with water, dried over P_2O_5, and chromatographed (silica gel, C_6H_6) to give, after recrystallization from a mixture of hexane and *o*-dichlorobenzene, 145 mg (83%) of bianthraquinonyl derivative (XXV) m.p. > 300°, $[\alpha]_D^{10}$ − 163° (c = 0·5, THF). (Calc. for $C_{30}G_{18}O_4$; C, 81·43; H, 4·10. Found: C, 81·19; H, 4·02%).

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