Novel Optically Active 7,7′-Bridged-1,1′-biisoquinolines and their Chelation to Rhodium(I) Ion

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Optically pure 7,7′-ethylenedioxy-1,1′-biisoquinoline **2** and the 7,7′-(5-methoxy-*m*-xylylenedioxy) analogue **3** are prepared; their chelation to rhodium(I) takes place with complete retention when (*R*)-(−)-**3** is treated with [RhCl(cod)]$_2$ to give [Rh{(*R*)-(−)-**3**}(cod)]$^+$, while a similar reaction of (+)-**2** gives a racemic complex [Rh(**2**)(cod)]$^+$; both Rh^I complexes are structurally characterized by an X-ray diffraction study.

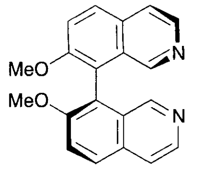
Recent advances in asymmetric catalysis with chiral transition metal compounds[1] have aroused interest in chelating ligands incorporating axially dissymmetric heteroaromatic compounds with two nitrogen atoms. Although a number of 3,3′-annulated 2,2′-bipyridines[2] and 2,2′-biquinolines[3] have been prepared and some shown to be conformationally stable in free and/or in their octahedral Ru^{II} complexes, optically active analogues of this type are completely unknown. Previously, we reported the synthesis of optically active 7,7′-dimethoxy-8,8′-biisoquinoline **1** and its rhodium(I) complex [Rh$_2${μ-(+)-**1**}$_2$(cod)$_2$]$^{2+}$, where the biisoquinoline coordinates as a bridging ligand rather than a chelating one owing to its inherent non-coplanarity of two isoquinoline rings.[4]

One of the factors determining the coordination modes of non-coplanar biisoquinolines as bridging or chelating ligands may be the distance between the nitrogen and pivotal carbon atoms. Thus, 7,7′-disubstituted-1,1′-biisoquinolines with a shorter N–C distance than the 8,8′-analogue are expected to chelate Rh^I. Here, we report the preparation of novel optically active 7,7′-ethylenedioxy- and -(5-methoxy-*m*-xylylenedioxy)-1,1′-biisoquinolines **2** and **3**, respectively. The latter coordinates to Rh^I as a chelating ligand with retention to give optically active [Rh(**3**)(cod)]$^+$ **5**, while the former gives racemic [Rh(**2**)(cod)]$^+$ **4**.

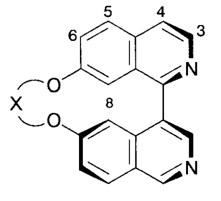
1-Chloro-7-hydroxyisoquinoline **6** (mp 202–204 °C) was prepared by *N*-oxidation of 7-methoxyisoquinoline[5] and chlorination of the resulting isoquinoline *N*-oxide with phosphorus oxychloride followed by demethylation with boron tribromide (42% overall yield).† The termolecular condensation of 1,2-dibromoethane with **6** (2 equiv.) was carried out in DMF with caesium carbonate to give the biisoquinoline dichloride **7** (mp 177–179 °C, 34%). Lithiation of **7** with n-butyllithium in THF followed by halogenation (iodine) gave the diiodide **8** (mp 202–204 °C, 72%). Intramolecular Ullmann coupling of **8** with activated copper powder[6] in DMF yielded **2** (mp 257–259 °C, 28%).† Compound **3** (mp 226–227 °C) was prepared as for **2** starting from the biisoquinoline dichloride **9** obtained by condensation of **6** with 3,5-bis(bromomethyl)anisole[7] (17.5% overall yield) (Scheme 1). Optical resolution of both (±)-**2** and (±)-**3** was achieved by HPLC [cellulose tris(3,5-dimethylphenylcarbamate) on silica gel],[8] elution with hexane–ethanol (7 : 3) afforded optically pure (−)-**2**, (+)-**2**, (−)-**3** and (+)-**3** with [α]$^{24}_{D}$ (CHCl$_3$) −161, +163, −80 and +82, respectively. Optical stability of (−)-**2** and (−)-**3** was examined by monitoring thermal racemization with polarimetry. The former racemizes at 78 °C in ethanol with a halflife of 64 min ($\Delta G^{\ddagger}$ 26 kcal mol^{-1}) (1 cal = 4.184 J), while the latter proved to be optically stable; showing no change in optical rotation after refluxing in EtOH (24 h).

The preparation of an optically active rhodium(I) complex of enantiometrically pure **2** was unsuccessful owing to its optical instability. Thus, treatment of (+)-**2** with [RhCl(cod)]$_2$ in methanol at room temp. and subsequent addition of AgClO$_4$ gives the racemic complex **4** [mp 240 °C (decomp.), dark-red needles, 65% yield]. The racemization may be ascribed to the conformational lability of the free and coordinated biisoquinoline. The latter is shown by the temperature dependence of the diastereoisotopic ethylene proton signals; two multiplets observed at δ 4.66 and 4.86 at room temp. coalesced to broad peak at δ 4.7 at 95 °C. In contrast, a similar reaction of (+)-**3** and (−)-**3** with more rigid conformation proceeds with retention to afford optically active rhodium(I) complex **5** [mp 245 °C (decomp.) 61–65% yield] as dark-red needles [(S)-(+)-**5**, [α]$^{24}_{D}$ (CHCl$_3$) +24.6; (*R*)-(−)-**5**, [α]$^{24}_{D}$ (CHCl$_3$) −25.0]. The chelate coordination of the biisoquinolines in **4** and (*R*)-(−)-**5** and absolute configuration of the latter are unambiguously determined by an X-ray structural study. (Figs. 1 and 2.)‡

The geometry about the Rh atom of **4** and (*R*)-(−)-**5** is essentially planar with the dihedral angle of the Rh–N(2)–N(12) and Rh–*c*–*c*′ plane of 7.0 and 2.9°, where *c* and *c*′ represent the midpoint of the coordinated olefinic bonds of cod, respectively. The ^{1}H NMR spectra of **4** and (*R*-(−)-**5** indicate that both cations have a strict twofold symmetry axis in solution. The former also assumes approximately C_2 symmetry in the crystal, while the latter loses axial symmetry owing to an asymmetric disposition of the 7,7′-bridged group. The Rh–N distance [mean 2.097(9) Å] and N–Rh–N angle [78.0(4)°] of **4** are comparable with the respective values [2.113(18) Å, 78.3(7)°] of (*R*)-(−)-**5**. Optimum chelation of bipyridines and biquinolines to metal is known to be attained when two aromatic rings are coplanar. This conformation is not possible for the present 1,1′-biisoquinolines with the 7,7′-bridging group. Indeed, the dihedral angle between two pyridine rings is 30.5 and 34.2° for **4** and (*R*)-(−)-**5**, respectively. The long span between the 7 and

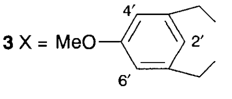


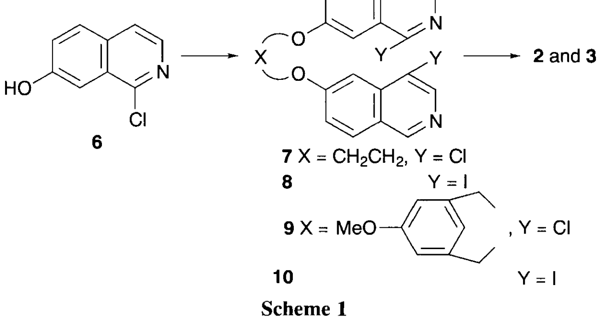
1



2 X = CH$_2$CH$_2$

3 X =





Scheme 1

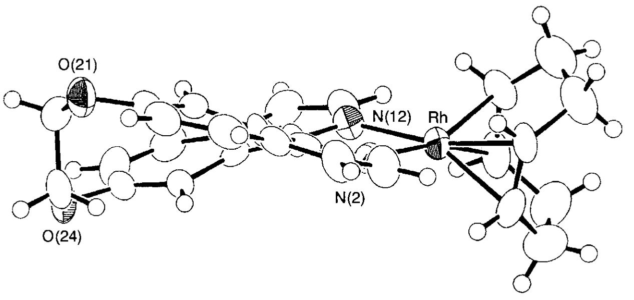


Fig. 1 View of the cation of **4**. Selected bond distances (Å) and angles (°) Rh–N(2) 2.103(9), Rh–N(12) 2.090(9), Rh–C(25) 2.16(1), Rh–C(26) 2.13(1), Rh–C(29) 2.15(1), Rh–C(30) 2.16(1), C(25)–C(26) 1.39(2), C(29)–C(30) 1.38(2); N(2)–Rh–N(12) 78.0(4), N(2)–Rh–C(25) 163.7(5), N(2)–Rh–C(26) 157.6(4), N(2)–Rh–C(29) 98.4(4), N(2)–Rh–C(30) 95.8(5), N(12)–Rh–C(25) 96.7(4), N(12)–Rh–C(26) 97.6(4), N(12)–Rh–C(29) 166.9(5), N(12)–Rh–C(30) 154.7(5), C(25)–Rh–C(26) 37.7(4), C(29)–Rh–C(30) 37.4(5).

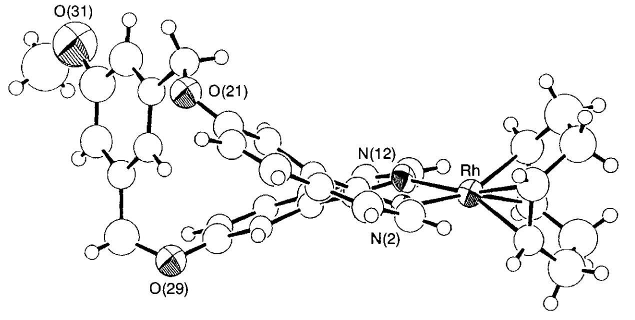


Fig. 2 View of the cation of (*R*)-(−)-**5**. Selected bond distances (Å) and angles (°) Rh–N(2) 2.121(18), Rh–N(12) 2.104(18), Rh–C(33) 2.18(3), Rh–C(34) 2.13(3), Rh–C(37) 2.17(3), Rh–C(38) 2.18(3), C(33)–C(34) 1.41(3), C(37)–C(38) 1.38(4); N(2)–Rh–N(12) 78.3(7), N(2)–Rh–C(33) 162.2(8), N(2)–Rh–C(34) 158.1(9), N(2)–Rh–C(37) 97.2(9), N(2)–Rh–C(38) 95.2(8), N(12)–Rh–C(33) 97.1(8), N(12)–Rh–C(34) 94.4(9), N(12)–Rh–C(37) 163.4(8), N(12)–Rh–C(38) 158.2(9), C(33)–Rh–C(34) 38(1), C(37)–Rh–C(38) 37.1(9).

7′-positions of the biisoquinoline in (*R*)-(−)-**5** is reflected in the large dihedral angle. Remarkably, the isoquinoline rings in the latter also deviate from planarity by bending outward at the fused C–C bonds as shown by the large dihedral angle (48.7°) between two benzene rings compared with that of two pyridines. Such a deviation is not observed for **4**, the corresponding angle (30.3°) is comparable with that of two pyridines. Despite the extensive development of asymmetric hydrogenation and C–C coupling reactions catalysed by chiral transition metal complexes, asymmetric oxidation reaction still remains to be explored.[10] This is probably due to the rarity of suitable chiral ligands stable to oxidation. In view of the stability to oxidation and racemization in both free and coordinated states, **3** may serve as a potential chiral ligand in metal-catalysed asymmetric oxidation.

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Footnotes

† Satisfactory analytical and spectroscopic data have been obtained for all new compounds. *Selected data* for **2**: ^{1}H NMR (100 MHz, CD_3NO_2) δ 4.16 (m, 2H, CH_2), 4.62 (m, 2H, CH_2), 7.49 (dd, *J* 1.8, 9.4 Hz, 2H, H^6), 7.80 (d, *J* 1.8 Hz, 2H, H^8), 7.92 (d, *J* 9.4 Hz, 2H, H^5), 8.01 (d, *J* 5.6 Hz, 2H, H^4), 8.94 (d, *J* 5.6 Hz, 2H, H^3); For **3**: ^{1}H NMR (270 MHz, CD_3NO_2) δ 3.71 (s, 3H, OMe), 5.22 and 5.34 (d, *J* 13.2 Hz, 4H, CH_2), 6.63 (d, *J* 2.0 Hz, 2H, $H^{4'}$, $H^{6'}$), 6.71 (d, *J* 2.0 Hz, 1H, $H^{2'}$), 6.80 (d, *J* 2.5 Hz, 2H, H^8), 7.43 (dd, *J* 2.5, 9.0 Hz, 2H, H^6), 7.70 (d, *J* 5.6 Hz, 2H, H^4), 7.85 (d, *J* 9.0 Hz, 2H, H^5), 8.62 (d, *J* 5.6 Hz, 2H, H^3). For **4**: ^{1}H NMR (100 MHz, CD_3NO_2) δ 1.88–3.12 (m, 8H, CH_2), 4.40–4.64 (m, 4H, =CH), 4.66 and 4.86 (br d, 4H, CH_2), 7.59 (dd, *J* 1.8, 9.1 Hz, 2H, H^6), 7.84 (dd, J_{Rh-H^3} 1.3, *J* 6.1 Hz, 2H, H^3), 8.03 (d, *J* 2.0, 9.1 Hz, 2H, H^5), 8.09 (d, *J* 6.1 Hz, 2H, H^4), 8.14 (d, *J* 1.8 Hz, 2H, H^8). For (*R*)-(−)-**5**: ^{1}H NMR (270 MHz, CD_3NO_2) δ 1.85 (m, 2H, CH_2), 2.33 (m, 4H, CH_2), 3.77 (s, 3H, OMe), 4.58 (m, 2H, =CH), 4.75 (m, 2H, =CH), 5.22 and 5.35 (d, *J* 15.0 Hz, 4H, CH_2), 6.60 (d, *J* 2.0 Hz, 2H, $H^{4'}$, $H^{6'}$), 6.90 (d, *J* 2.0 Hz, 1H, $H^{2'}$), 6.96 (d, *J* 1.9 Hz, 2H, H^8), 7.62 (d, *J* 6.5 Hz, 2H, H^5), 7.80 (dd, *J* 1.9, 6.5 Hz, 2H, H^6), 7.97 (d, *J* 4.0 Hz, 2H, H^4), 8.06 (dd, J_{Rh-H^3} 1.0, *J* 4.0 Hz, 2H, H^3); UV–VIS (MeOH) λ_{max}/nm 255(sh) (43200), 402 (10950), 535 (515); CD (MeOH) for (+)-**5** [θ] (nm) +108740 (277), +14370 (350), +290 (414), −2520 (447), +1360 (496).

‡ The structures of **4** and (*R*)-(−)-**5** were solved by Patterson methods and refined by full-matrix least-squares techniques of intensity data collected on a Rigaku AFC-5R diffractometer using grafite-monochromated Mo-Kα radiation (λ = 0.7107 Å).

Crystal data for **4**: $C_{28}H_{26}ClN_2O_6Rh\cdot(CH_3)_2CO$, M = 683.0, monoclinic, $P2_1/a$, a = 20.028(16), b = 12.677(5), c = 11.251(10) Å, β = 94.09(8)°, V = 2849(6) Å^3, Z = 4, D_c = 1.592 g cm^{-3}, μ(Mo-Kα) = 7.33 cm^{-1}, $F(000)$ = 1400, final $R(R_w)$ = 0.060 (0.050) for 2077 intensities [$I > 2.5\sigma(I)$] and 379 variables.

Crystal data for (*R*)-(−)-**5**: $C_{35}H_{32}ClN_2O_7Rh\cdot 2CHCl_3$, M = 969.8, orthorhombic, $P2_12_12_1$, a = 16.834(8), b = 25.971(9), c = 8.994(8) Å, V = 3932(8) Å^3, Z = 4, D_c = 1.638 g cm^{-3}, μ(Mo-Kα) = 9.56 cm^{-1}, $F(000)$ = 1960, final $R(R_w)$ = 0.0694 (0.0548) for 1342 intensities [$I > 2.0\sigma(I)$] and 252 variables. The possibility of the alternative (*S*)-enantiomer is ruled out on the basis of significance tests on the *R*-factor,[9] the final $R(R_w)$ factors being 0.0703(0.0556).

Atomic coordinates, bond lengths and angles, and thermal parameters for both compounds have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

References

1 *Asymmetric Synthesis*, ed. J. D. Morrison, Academic, Orlando, 1985.
2 R. P. Thummel and F. Lefoulon, *Inorg. Chem.*, 1987, **26**, 675; R. P. Thummel, F. Lefoulon and J. D. Korp, *Inorg. Chem.*, 1987, **26**, 2370.
3 R. P. Thummel, F. Lefoulon and R. Mahadevan, *J. Org. Chem.*, 1985, **50**, 3824; J. Rebek, Jr., T. Costello and R. Wattley, *J. Am. Chem. Soc.*, 1985, **107**, 7487.
4 K. Yamamoto, K. Watanabe, H. Chikamatsu, Y. Okamoto and T. Yoshida, *J. Chem. Soc. Chem. Commun.*, 1987, 807.
5 von P. Fritsch, *Liebigs Ann. Chem.*, 1985, **286**, 1.
6 R. C. Fuson and E. A. Cleveland, *Org. Synth.*, 1955, Coll. Vol. III, 339.
7 E. Weber and F. Vögtle, *Chem. Ber.*, 1976, **109**, 1803.
8 Y. Okamoto, M. Kawashima and K. Hatada, *J. Chromatogr.*, 1986, **363**, 173.
9 W. C. Hamilton, *Acta Crystallogr.*, 1965, **18**, 502; D. Roger, *Acta Crystallogr. Sect. A*, 1981, **37**, 734.
10 *Catalytic Asymmetric Synthesis*, ed. I. Ojima, VCH, New York, 1993; *Asymmetric Catalysis in Organic Synthesis*, ed. R. Noyori, Wiley, New York, 1993.