Synthesis of (formylferrocenyl)bismuthanes. A way to control the stereochemistry at the chiral bismuth centre using hypervalent bond formation and planar chirality of ferrocene

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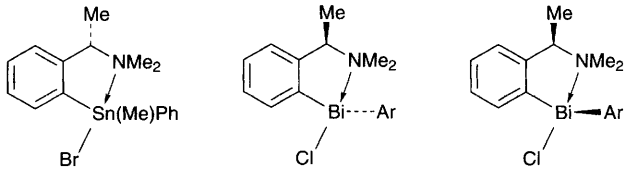
Induction of chirality at a bismuth centre is found to occur with exclusive stereoselectivity by using planar chirality of ferrocene as a chiral auxiliary.

Optical resolution of a compound having a chiral bismuth atom, the heaviest stable element in nature, is an important issue for us. Initially, we demonstrated the possibility of resolution of racemic triarylbismuthanes by means of analytical HPLC.[1] To date, however, the selective synthetic method of the optically pure triarylbismuthane has not been developed. Then, we succeeded in asymmetric induction at a bismuth centre using the (*R*)-1-(dimethylamino)ethyl group as an auxiliary chiral ligand that was effective in the isolation of diastereomerically pure tin compound **1**.[2] In contrast to tin compound **1**,[3] optical resolution was not successful. Thus, the diastereomeric chlorobismuthanes **2a**,**b**, each being stabilized by a hypervalent bond, were yielded as an equilibrium mixture in solution (77 : 23 in $CDCl_3$). The replacement of a phenyl group with a bulkier 1-naphthyl group, such as in **3**, did not markedly raise the diastereomeric ratio (78 : 22 for **3**). An X-ray analysis, furthermore, revealed that chlorobismuthanes **2a**, **b** form *cis*/*trans* pairing crystals in a ratio of 1 : 1.[4]



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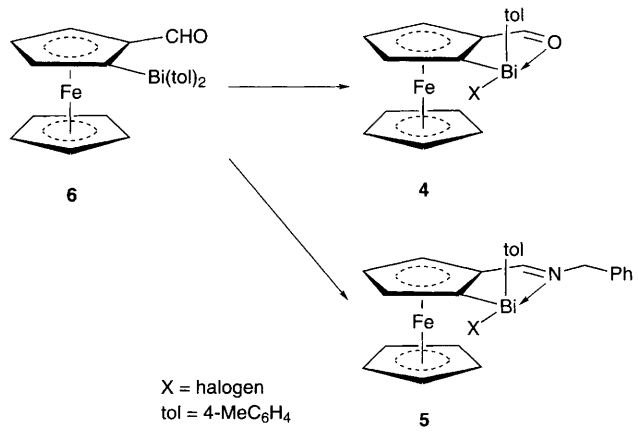
2a; Ar = Ph
3a; Ar = 1-Naphthyl

2b; Ar = Ph
3b; Ar = 1-Naphthyl

Outstanding structural features of each isomer **2a** and **b** are a smaller angle [95.6(7)° (**2a**), 98.0(8)° (**2b**)][4] constituted by two carbons of the ligands and a bismuth atom than that of the corresponding angle [114.8(4)–127.8(3)°][3] of **1** and an axial position of benzylic methyl group. A loss of the repulsion between the benzylic methyl group and the equatorial substituent (Ph) observed in **1** is considered to cause the comparable values between those of **2** and **3**. If the skeletal benzene ring could be replaced by a ferrocene ring, such as in **4** or **5**, the small angle Bi–C (*ca.* 93°)[2,5] should enhance the repulsive interaction between the *endo* aromatic substituent and the ferrocene moiety, leading to the high *exo* stereoselectivty (Scheme 1).[6] In addition, to the best of our knowledge, few examples associated with ferrocene bonded directly to a bismuth atom have appeared in organic bismuth chemistry.[7]

Although Kagan and coworkers have recently reported an elegant diastereoselective ortholithiation of ferrocenyl acetal,[8] this method is not applicable to the synthesis of **6** because deprotection of the acetal functionality by acidic hydrolysis would lead to concomitant cleavage of the bismuth–carbon bonds. Hence, we initially utilized the ortholithiation directed by a protective lithium α-amino alkoxide, which was successfully conducted by Comins *et al.* in benzaldehydes.[9] Thus, lithiated lithium α-amino alkoxide was prepared from the addition of Bu^nLi at 0 °C to a mixture of lithium *N*-methylpiperazide and **7**, and the resultant suspension was quenched with chlorobis(4-methylphenyl)bismuthane to give **8** as the sole product.[10] Replacement of *N*-methylpiperazine by *N*,*N*,*N*′-trimethylethylenediamine afforded **9** (8%) together with **6** (3%) and **8** (16%). Under forced conditions **9** was predominantly obtained together with small amounts of **6** and **8**. After many attempts, finally, the selective synthesis of **6** was achieved *via* an addition of chlorotrimethylsilane to a solution of lithium α-amino alkoxide from *N*,*N*,*N*′-trimethylethylenediamine and further lithiation by Bu^tLi at −78 °C in diethyl ether.† The formation of **6** is reasonably explained to proceed *via* site-selective lithiation of silyl α-amino alkoxide as illustrated in Scheme 2. A loss of the repulsion between two anions generated on the oxygen atom and the adjacent carbon atom is considered responsible for this desired lithiation.[10].

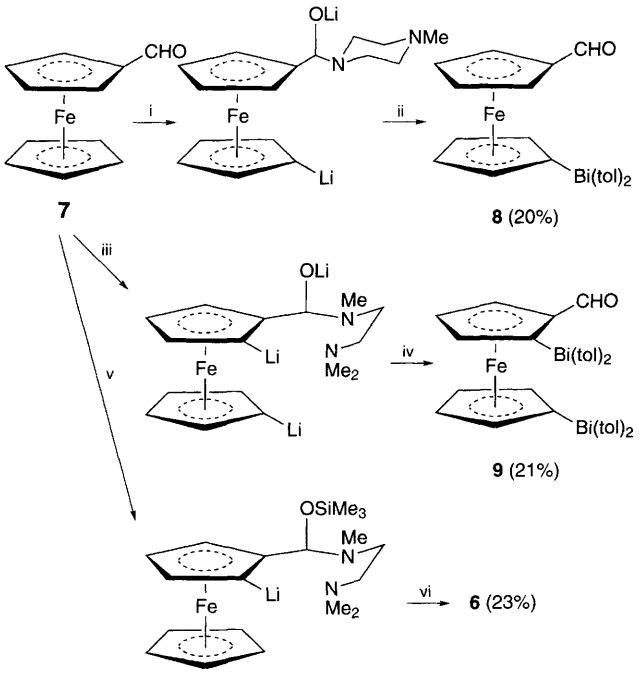
Conversion to chiral halogenobismuthanes **4** was carried out with the procedure developed by us.[5b] In contrast to the case of benzaldehyde,[5b] **4** was unstable and decomposed under isolation conditions. The halogenobismuthane, however, could be isolated as **5**, after transformation of the carbonyl group into the imino group (Scheme 3). The stability of **5** is ascribable to the longer length of the C=N double bond relative to C=O atoms. In the ^1H NMR spectrum of **5**, only one set of signals of a single diastereomer were present and the proton signals of the unsubstituted cyclopentadienyl ring did not undergo any upfield shift.‡ Taking the small C–Bi–C angle in **2** into account, this should undoubtedly indicate the *exo* configuration of the tolyl group, since the ring current effect of this group in *endo* configuration would be large on these protons.[11]§ The marked downfield shift of a one-proton signal of **5a**,**b** (δ 5.19, 5.27 respectively) shows the close proximity of the proton to the halogen atom,[5a] since the formation of the hypervalent bond compels nitrogen, bismuth, and halogen atoms to be coplanar with the cyclopentadienyl ring. The shift of imino stretching to



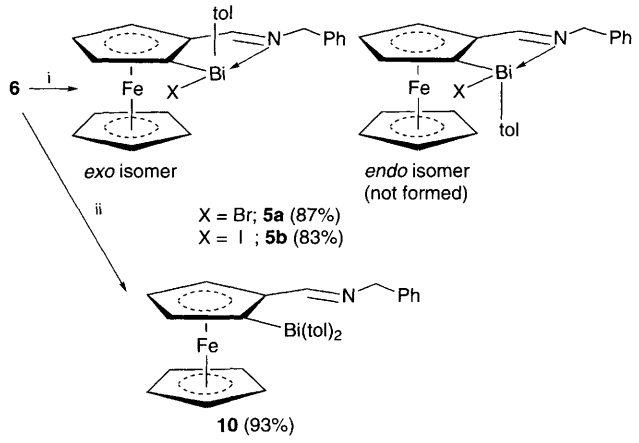
Scheme 1

a lower wavenumber region by 30 cm^{-1} compared with **10** is consistent with hypervalent bond formation.[5b]

In conclusion we have found reaction conditions to introduce bismuth selectively into formylferrocene. Furthermore, the planar chirality was shown to yield exclusively a diastereomerically pure isomer, in which chirality at the bismuth was induced by hypervalent bond formation.



Scheme 2 *Reagents and conditions*: i, lithium *N*-methylpiperazide (2 equiv.), Et_2O, 0 °C, 15 min; Bu^nLi (2 equiv.), 0 °C, 1 h; ii, $(tol)_2BiCl$ (1.5 equiv.), 0 °C, 15 min; brine; iii, $Me_2N(CH_2)_2NMeLi$ (2 equiv.), Et_2O, 0 °C, 15 min; Bu^nLi (3 equiv.), 0 °C, then reflux, 3 h; iv, $(tol)_2BiCl$ (2 equiv.), 0 °C, 15 min; brine; v, $Me_2N(CH_2)_2NMeLi$ (2 equiv.), Et_2O, 0 °C, 15 min, then $SiMe_3Cl$ (1 equiv.), room temp., 1 h; Bu^tLi (2 equiv.), −78 °C, 30 min; vi, $(tol)_2BiCl$ (1.5 equiv.), −78 °C, 15 min; brine, 0 °C



Scheme 3 *Reagents and conditions*: i, $BF_3{\cdot}OEt_2$ (1 equiv.), C_6H_6, 10 °C, then $PhCH_2NH_2$ (1.5 equiv.); NaX (aq.); ii, $PhCH_2NH_2$ (3 equiv.), 4 Å molecular sieves, C_6H_6, reflux, 5 h

Footnotes

† The new compounds **5**, **6**, **8** and **9** were fully characterized by spectroscopic data and elemental analyses. *Selected data* for **6**, mp 149–151 °C, ^1H NMR ($CDCl_3$) δ 2.28 (3 H, s, Me), 2.35 (3 H, s, Me), 4.20 (5 H, s, C_5H_5), 4.32 (1 H, m, C_5H_3), 4.66 (1 H, m, C_5H_3), 4.83 (1 H, m, C_5H_3), 7.15 (2 H, d, J_{AB} 7.3, MeAr H), 7.24 (2 H, d, J_{AB} 7.3, MeAr H), 7.59 (2 H, d, J_{AB} 7.3, MeAr H), 7.76 (2 H, d, J_{AB} 7.3, MeAr H), 10.05 (1 H, s, CHO); $\nu_{max.}$ (KBr)/cm^{-1} 1660 (C=O); UV–VIS ($CHCl_3$): $\lambda_{max.}$ 462 nm (ε 580 dm^3 mol^{-1} cm^{-1}), 342 (1350). For **8**, mp 102–104 °C, ^1H NMR ($CDCl_3$) δ 2.33 (6 H, s, Me), 4.21 (2 H, m, C_5H_4), 4.43 (2 H, m, C_5H_4), 4.47 (2 H, m, C_5H_4), 4.70 (2 H, m, C_5H_4), 7.20 (4 H, d, J_{AB} 7.9, MeAr H), 7.65 (4 H, d, J_{AB} 7.9, MeAr H), 9.82 (1 H, s, CHO); $\nu_{max.}$ (KBr)/cm^{-1} 1665 (C=O); UV–VIS ($CHCl_3$): $\lambda_{max.}$ 462 nm (630 dm^3 mol^{-1} cm^{-1}), 344 (1700). For **9**, mp 120–122 °C, ^1H NMR ($CDCl_3$) δ 2.27 (3 H, s, Me), 2.31 (3 H, s, Me), 2.32 (3 H, s, Me), 2.36 (3 H, s, Me), 4.11 (1 H, m, Fc H), 4.21 (1 H, m, Fc H), 4.27–4.29 (2 H, m, Fc H), 4.39–4.45 (2 H, m, Fc H), 4.70 (1 H, m, Fc H), 7.11–7.26 (8 H, m, MeAr H), 7.55–7.60 (6 H, m, MeAr H), 7.74 (2 H, d, J_{AB} 7.3, MeAr H), 9.86 (1 H, s, CHO); $\nu_{max.}$ (KBr)/cm^{-1} 1670 (C=O); UV–VIS ($CHCl_3$): $\lambda_{max.}$ 466 nm (ε 570 dm^3 mol^{-1} cm^{-1}), 344(sh) (1765). For **5a**, mp 190–192 °C (decomp.), ^1H NMR ($CDCl_3$) δ 2.26 (3 H, s, Me), 4.25 (5 H, s, C_5H_5), 4.44 (1 H, d, J_{AB} 14.0, CH_2), 4.54 (1 H, d, J_{AB} 14.0, CH_2), 4.67 (1 H, m, C_5H_3), 4.76 (1 H, m, C_5H_3), 5.19 (1 H, m, C_5H_3), 7.15–7.38 (7 H, m, Ar H), 7.99 (2 H, d, J_{AB} 7.3, MeAr H), 8.70 (1 H, s, CHN); $\nu_{max.}$ (KBr)/cm^{-1} 1610 (C=N).

‡ The chemical shift of these protons is δ 4.25, which is comparable to that of the parent imine derived from formylferrocene and benzylamine (δ 4.17).[11a]

§ Such a ring current effect is observed in the cyclopalladated complex of ferrocenylimine, where one of the phenyl groups of a triphenylphosphine ligand lies *endo* to the ferrocenyl iron. The proton signals of the unsubstituted cyclopentadienyl ring (δ 3.67) suffer from the upfield shift by 0.5 as compared with those of the parent imine (δ 4.17).[11a,b]

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