A New General Method for the Synthesis of Chiral Triarylbismuthines based on the Intramolecular Coordination by a Sulfonyl Group

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Chiral triarylbismuthines **4** are synthesized by the sulfonyl-controlled selective iododearylation of **2**, followed by reaction of the resulting iodobismuthine **3** with aryl Grignard reagents and are resolved into each pair of optical isomers; compounds **4** were readily converted into chiral bismuthines **5** of a more general type by nucleophilic substitution with aryllithium at the bismuth atom centre.

The literature to date contains only one definite report on the synthesis of chiral bismuthines.[1] This class of compounds was first reported by Bras *et al.* in 1983, who carried out the selective bromodearylation of mixed triarylbismuthines $Ar_2Ar'Bi$ with hydrogen bromide to obtain bromobismuthines ArAr'BiBr, which were converted into chiral triarylbismuthines by the reaction with aryl Grignard reagents.[1] This strategy, however, lacks generality as a synthetic tool because bulky aryl ligands such as 2-methylphenyl, 1-naphthyl and mesityl groups are essential for the successful bromodearylation as well as for the stabilization of the bromobismuthines formed. We disclose herein a new method of broad applicability for the synthesis of chiral triarylbismuthines where various aryl groups are tolerated as the ligand for the bismuth atom. In our method, the 2-(*tert*-butylsulfonyl)phenyl group plays an important dual role, in which this group not only blocks further iododearylation of iodobismuthine **3** but works as a preferential leaving group in **4** eventually leading to chiral triarylbismuthines **5**.

The starting bismuthine **2** was easily prepared in 62% yield by the reaction of chlorobis(4-methylphenyl)bismuthine with lithiated *tert*-butyl phenyl sulfone[2] in diethyl ether at −78 °C. Conversion of **2** into chiral bismuthine **4** was accomplished in high yields by selective iododearylation with iodine, followed by treatment of the resulting iodobismuthine **3** with aryl Grignard reagents.

A typical example is exemplified by the synthesis of **4a**: to a well stirred suspension of **2** (588 mg, 1 mmol) in diethyl ether (10 ml) was added dropwise a solution of iodine (254 mg, 1 mmol) in the same solvent (10 ml) under ambient conditions until **2** was completely consumed (checked by TLC). The resulting pale-yellow solution was concentrated *in vacuo* to leave an oily residue, recrystallization of which from benzene–methanol (1 : 5) afforded pure **3** quantitatively as pale-yellow crystals. To a solution of **3** (624 mg, 1 mmol) in tetrahydrofuran (THF, 5 ml) was then added dropwise a solution of 4-chlorophenylmagnesium bromide (*ca.* 1.5 mmol) in the same solvent (5 ml) at room temperature until the pale-yellow colour of the solution of **3** was completely lost and the resulting mixture was stirred for an additional 5 min. Work-up with brine, followed by concentration of the organic layer *in vacuo* afforded an oily residue, which was recrystallized from methanol to give pure **4a** as colourless crystals in 95% yield.

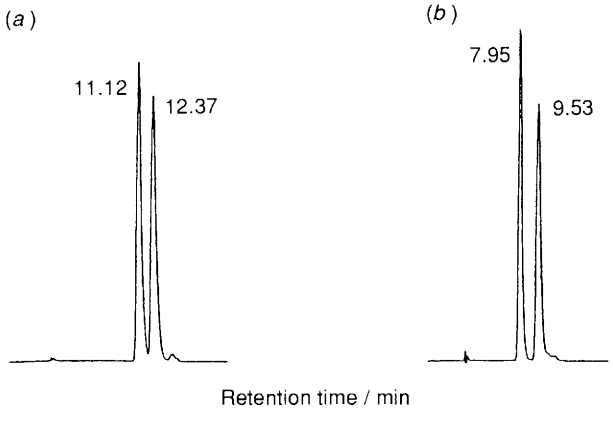


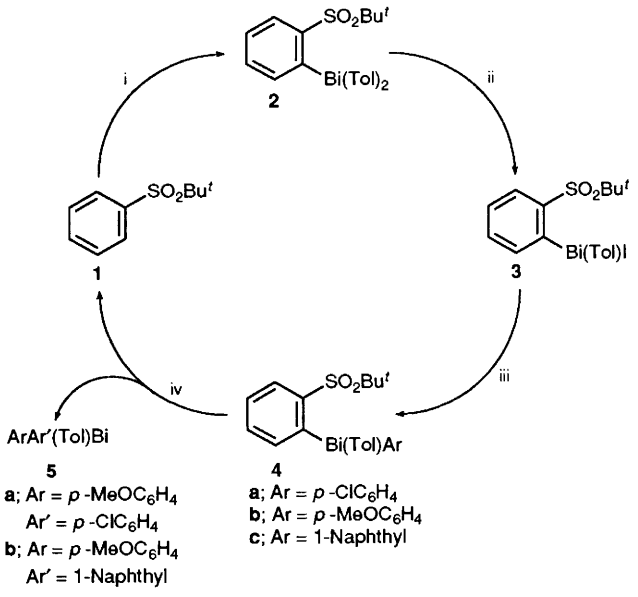
Fig. 1 HPLC resolution of racemic bismuthines **4a** and **4c** on optical columns. Flow rate 1.0 ml min^{-1}, concentration 0.5 mg ml^{-1}, load 5 μl, room temp., detection at 254 nm. (*a*) Compound **4a**, column Chiralcel OD, solvent hexane–Pr^iOH (99 : 1). (*b*) Compound **4c**, column Chiralpak AD, solvent hexane–EtOH (95 : 5).

Unlike ordinary triarylbismuthines which suffer extensive iododearylation with iodine leading to an intractable mixture of many components,[3] the sulfonyl-stabilized bismuthine **2** reacted only with one equivalent of iodine, resulting in the quantitative formation of iodobismuthine **3** along with 4-iodotoluene. The marked difference in reactivity toward molecular iodine may be attributed to the intramolecular interaction between the bismuth atom and one of the sulfonyl oxygen atoms, as has been revealed recently.[4]

Unsymmetrical bismuthines **4** have a chiral bismuth centre and thus the generation of optical activity should be expected. Although the generation of chirality at bismuth atom has been shown indirectly by a spectroscopic approach,[1] no direct evidence has been presented yet. We were successful in resolving racemic bismuthines **4a–c** into each pair of enantiomers on an analytical level by the use of chiral HPLC columns (Fig. 1),† and now the milligram-scale isolation and characterization of some optically pure bismuthines is under way. All the elements beyond bismuth are unstable as nuclides, *i.e.*, radioactive, so our results may be said to have confirmed the heaviest chirality centre that can be reached with safety.

In order to make the present method more broadly applicable to the synthesis of chiral triarylbismuthines with a variety of aryl ligands, the substitution of an aryl group for the 2-(*tert*-butylsulfonyl)phenyl group in **4** was examined. It is known that triarylbismuthines undergo the ligand exchange reaction at the bismuth atom when treated with an appropriate aryllithium reagent.[5] Thus, when **2** (588 mg, 1 mmol) was treated with 4-chlorophenyllithium or 4-methoxyphenyllithium (*ca.* 2 mmol) in THF (10 ml) at −78 °C, selective substitution occurred immediately to form the expected bismuthines, 4-chlorophenylbis(4-methylphenyl)bismuthine and 4-methoxyphenylbis(4-methylphenyl)bismuthine, respectively in 87–95% yields together with *tert*-butyl phenyl sulfone **1**. Encouraged by these results, we applied this transformation to **4b**. As expected, compound **4b** underwent a ligand exchange reaction quite smoothly with 4-chlorophenyllithium and 1-naphthyllithium under the above-mentioned conditions, affording the corresponding chiral bismuthines **5a** and **5b** in 70 and 88% yields, respectively, along with recovered *tert*-butyl phenyl sulfone.[6] These results clearly established the successful introduction of chirality at bismuth atom centre by utilizing

† Chiral HPLC columns, Chiralcel OD, Chiralpak AS and AD recently developed by Daicel Chemical Industries, Ltd, were used for the optical resolution of **4a**, **4b** and **4c**, respectively. However, attempts to resolve sulfonyl-free bismuthines **5a** and **5b** on these chiral columns failed as expected.



Scheme 1 Tol = p-MeC_6H_4 *Reagent and conditions*: i, Bu^nLi, diethyl ether, −78 °C; $(Tol)_2BiCl$; ii, I_2, diethyl ether, room temp.; iii, ArMgBr, THF, room temp.; iv, Ar'Li, THF, −78 °C; H_2O

the intramolecular coordination of a sulfonyl group, which allows the selective iododearylation of **2** into **3** and also the selective aryl ligand exchange of **4** into chiral bismuthines **5**.

The present method provides a simple way for the synthesis of chiral triarylbismuthines difficult to access by conventional methods, thus offering a new entry into the chemistry of chiral organobismuth compounds.

Table 1 Chiral triarylbismuthines obtained[a]

Compound	Ar	Ar'	M.p./°C	Yield (%)[b]
3	—	—	142–144	100
4a	p-ClC_6H_4	—	157–159	95
4b	p-$MeOC_6H_4$	—	155–157	88
4c	1-Naphthyl	—	182–184	98
5a	p-$MeOC_6H_4$	p-ClC_6H_4	118–120	70
5b	p-$MeOC_6H_4$	1-Naphthyl	108–110	88

[a] All compounds are new and gave satisfactory elemental analyses and spectral data. [b] Yields refer to isolated compounds and are not optimized.

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6 P. Bras *et al.* reported that chiral bismuthine **5a** was difficult to synthesize by his method. See ref. (1).