First synthesis and properties of dendritic Bi_n-bismuthanes

Hitomi Suzuki,* Haruto Kurata and Yoshihiro Matano

Department of Chemistry, Graduate School of Science, Kyoto University, Sakyo-ku, Kyoto 606-01, Japan

Directed tris-ortholithiation of tris[2-(diethylaminosulfonyl)phenyl]bismuthane 1 with *tert*-butyllithium followed by treatment with 3 equiv. of bis[2-(diethylaminosulfonyl)phenyl]bismuth iodide 2a gives a symmetrically branched Bi_4-bismuthane 5a, which, on a similar treatment, is converted in a one-pot synthesis into a highly branched Bi_{10}-bismuthane 6a.

Owing to excellent contrast density of bismuth toward X-rays of short wavelength, the synthesis of water-soluble non-ionic organobismuth compounds represents an interesting area of research in pursuit of iodine-free positive X-ray contrast agents. High bismuth content (m/m %) is a prerequisite for such a purpose and the incorporation of multiple bismuth atoms into a molecule is a straightforward approach to this. However, the literature to date contains no report of the synthesis of organobismuth compounds bearing more than two bismuth atoms in the molecule. Several tetraorganyldibismuthanes ($\mathrm{R_2BiBiR_2}$) are known,[1] but they are quite sensitive to air and light and difficult to handle. During the course of our effort to synthesize polybismuth compounds, we came across a simple one-pot method for introducing three diarylbismuthyl units directly into the three aromatic rings of a triarylbismuthane and this methodology has now enabled us to gain easy access to highly branched aromatic polybismuth compounds. Herein we report the first synthesis of dendrimer-type aromatic polybismuth compounds bearing up to ten bismuth atoms in a single molecule,[2] utilizing the directed ortholithiation of triarylbismuthanes bearing a sulfonamide function at the *ortho* position of each aromatic ring.

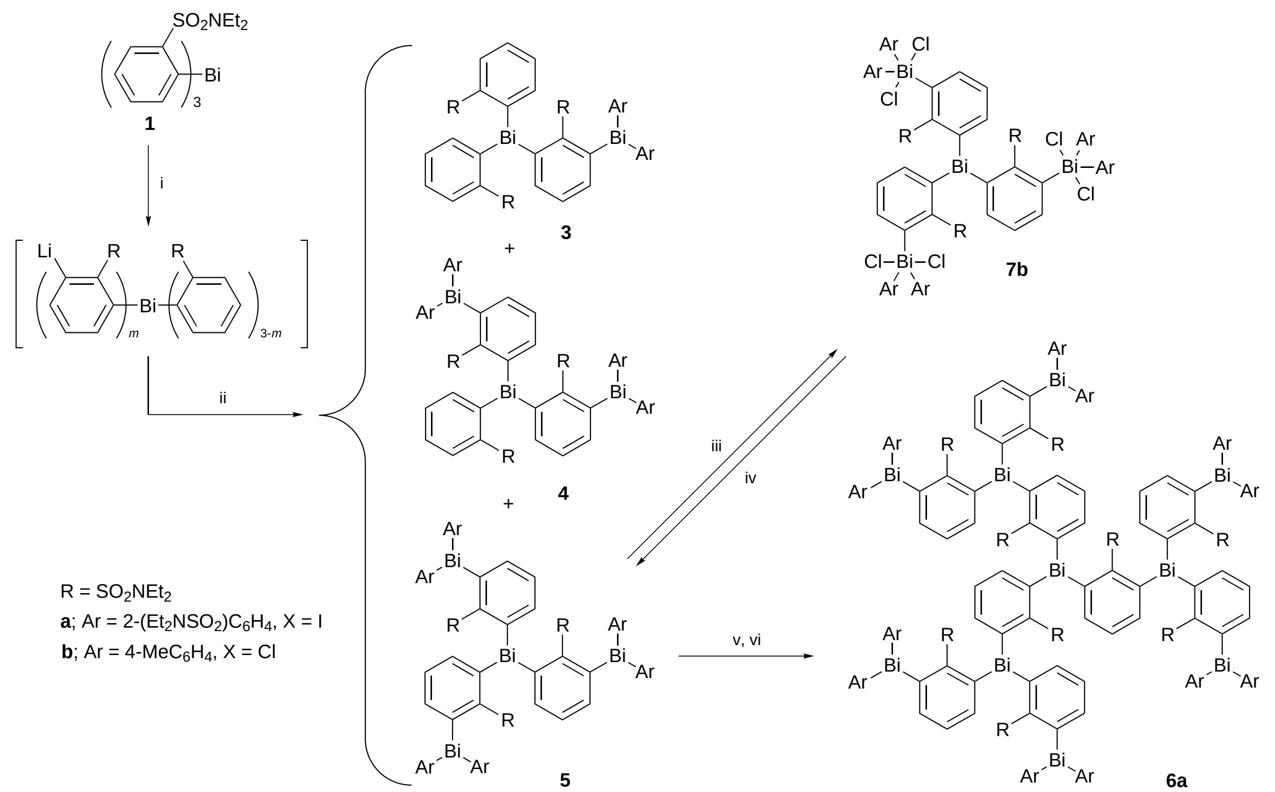
Since the sulfonamide group is a good directing group in the ortholithiation of arenes,[3] tris[2-(diethylaminosulfonyl)phenyl]bismuthane[4] **1** was chosen as the starting material for water-soluble neutral polybismuth compounds. This bismuthane was synthesized by the ortholithiation of *N,N*-diethylbenzenesulfonamide with butyllithium followed by treatment with 1/3 $\mathrm{BiCl_3}$ in THF at −78 °C. Compound **1** contains acidic protons *ortho* to the sulfonyl group on the three aromatic rings, so it can be further lithiated in the presence of an excess of an alkyllithium. When compound **1** was lithiated with 1.1 equiv. of *tert*-butyllithium in THF at −78 °C for 1 h and then treated with 1 equiv. of bis[2-(diethylaminosulfonyl)phenyl]bismuth iodide[5] **2a**, Bi_2-bismuthane **3a** and Bi_3-bismuthane **4a** were obtained in 37 and 18% yields, respectively, together with 25% of recovered starting material **1**, where Bi_n-bismuthane represents a bismuthane bearing *n* bismuth atoms in one molecule (Table 1, entry 1). When 3.3 equiv. of *tert*-butyllithium was used under appropriate conditions, a symmetrically branched Bi_4-bismuthane **5a** was obtained as the main product. The yields of these bismuthanes varied considerably depending on the temperatures employed; compound **5a** was obtained in moderate and good isolated yield when the reaction mixture was warmed to −20 and 0 °C before iodide **2a** was added (entries 3 and 4, respectively), whereas Bi_4-bismuthane **5a** was not formed at all when bismuthane **1** was reacted with *tert*-butyllithium followed by iodide **2a** at −78 °C (entry 2). These results suggest that the tris-ortholithiation of compound **1** was the crucial step for the formation of a dendrimer-type Bi_4-bismuthane **5a** and that it did not proceed to completion at −78 °C. An isomeric linear Bi_4-bismuthane was not formed under the conditions employed. When bis(4-methylphenyl)bismuth chloride[4] **2b** was used in place of iodide **2a**, tolyl-substituted analogues **3b**, **4b** and **5b** were obtained in 2, 6 and 11% isolated yields, respectively (entry 5). Three of four bismuth atoms in Bi_4-bismuthane **5b** readily underwent oxidative chlorination with an excess of sulfuryl chloride in $\mathrm{CH_2Cl_2}$ at room temp. to give a hexachloride **7b** in 55% yield, in which the central bismuth atom is intact, while the outer three bismuth atoms are oxidized to $\mathrm{Bi^V}$ (Scheme 1). The reduction of hexachloride **7b** with saturated aqueous $\mathrm{Na_2S_2O_3}$ smoothly regenerated the original Bi_4-bismuthane **5b** in 92% yield. All Bi_n-bismuthanes **3a,b**, **4a,b** and **5a,b** and hexachloride **7b** obtained were characterized by NMR and MALDI-TOF mass spectroscopies as well as by elemental analyses.

Bi_4-bismuthane **5a** bears acidic protons at the positions *ortho* to the sulfonamide group in the six outer aromatic rings. This structural advantage enabled us to extend the present methodology further, making access possible to a highly branched dendrimer-type Bi_{10}-bismuthane **6a**. Thus, treatment of Bi_4-bismuthane **5a** with 6.6 equiv. of *tert*-butyllithium in THF at 0 °C for 1 h followed by the addition of 6 equiv. of iodide **2a** at −78 °C afforded a crude Bi_{10}-bismuthane **6a** in *ca.* 20% yield, accompanied by small amounts of Bi_8- and Bi_9-congeners. The Bi_{10}-dendrimer **6a**, isolated by gel permeation chromatography and further purified by column chromatography on silica gel, is a white powder which begins to decompose above 180 °C without melting. It is readily soluble in dichloromethane and chloroform, but insoluble in methanol and ethanol. Its MALDI-TOF mass spectrum showed a $(\mathrm{M + Na})^+$ peak at *m/z* 6558.1 (calc; 6561.9). In its $^{13}\mathrm{C}$ NMR spectrum, three distinct sets of $^{13}\mathrm{C}$ absorptions were observed for non-equivalent ethyl groups at δ 41.8, 40.3 and 40.0 for methylene carbons and at δ 14.1, 13.0 and 12.7 for methyl carbons, respectively. Simple NMR peak patterns observed suggest a high molecular symmetry in accord with the dendritic structure of bismuthane **6a**. In the sense of atomic mass of a key element involved, the dendrimer **6a** represents the heaviest example of dendrimers so far reported. Attempts to elucidate the molecular geometry of compound **5a** by X-ray analysis have so far met with failure owing to the rapid efflorescence of the specimen crystals in air.

Table 1 Reaction of lithiated bismuthane **1** with halides **2**

		Conditions for step i		Yield (%)^a			
Entry	Halide	$\mathrm{Bu^tLi}$ (equiv.)	T/°C	**1**	**3**	**4**	**5**
1	**2a**	1.1	−78	25	37	18	0
2	**2a**	3.3	−78	9	7	31	0
3	**2a**	3.3	−78 to −20	4	9	11	13
4	**2a**	3.3	−78 to 0	6	2	8	49
5	**2b**	3.3	−78 to 0	2	2	6	11

^{a} Based on total bismuth (**1** + **2**) employed.



R = $\mathrm{SO_2NEt_2}$
a; Ar = 2-$(\mathrm{Et_2NSO_2})\mathrm{C_6H_4}$, X = I
b; Ar = 4-$\mathrm{MeC_6H_4}$, X = Cl

Scheme 1 *Reagents and conditions*: i, $\mathrm{Bu^tLi}$, THF, −78 to *ca*. 0 °C, 1 h; ii, $\mathrm{Ar_2BiX}$ **2**, −78 °C to room temp.; iii, $\mathrm{SO_2Cl_2}$ (3.5 equiv.), $\mathrm{CH_2Cl_2}$, room temp., 3 h, 55%; iv, $\mathrm{Na_2S_2O_3}$ (aq), $\mathrm{CH_2Cl_2}$, room temp., 1 h, 92%; v, $\mathrm{Bu^tLi}$ (6.6 equiv.), THF, −78 to 0 °C, 1 h; vi, $\mathrm{Ar_2BiI}$ **2a** (6 equiv.), −78 °C to room temp.

Footnotes and References

* E-mail: suzuki@kuchem.kyoto-u.ac.jp

† Selected data for **5a**: mp 162–164 °C (Found: C, 39.63; H, 4.61; N, 4.50. $\mathrm{C_{90}H_{123}Bi_4N_9O_{18}S_9}$ requires C, 39.40; H, 4.52; N, 4.59%); δ_H (200 MHz, $\mathrm{CDCl_3}$) 7.97 (6 H, d, *J* 7.6 Hz), 7.89 (3 H, d, *J* 7.3 Hz), 7.80 (3 H, d, *J* 7.3 Hz), 7.67 (6 H, d, *J* 7.6 Hz), 7.45 (6 H, t, *J* 7.6 Hz), 7.30 (6 H, t, *J* 7.6 Hz), 7.16 (3 H, t, *J* 7.3 Hz), 3.27 (36 H, q, *J* 6.6 Hz), 1.13 (54 H, t, *J* 6.6 Hz); MALDI-TOF, *m/z* 2766.2 ([M + Na]$^+$ requires 2766.5). For **5b**: mp 110–112 °C (Found: C, 43.03; H, 4.00; N, 2.03. $\mathrm{C_{72}H_{81}Bi_4N_3O_6S_3}$ requires C, 42.88; H, 4.05; N, 2.08%); δ_H ($\mathrm{CDCl_3}$) 8.11 (3 H, dd, *J* 7.3, 1.2 Hz), 7.85 (3 H, dd, *J* 7.3, 1.2 Hz), 7.58 (12 H, d, *J* 7.8 Hz), 7.3–7.1 (15 H, m), 3.22 (12 H, q, *J* 7.0 Hz), 2.30 (18 H, s), 1.01 (18 H, t, *J* 7.0 Hz); MALDI-TOF, *m/z* 2039.6 ([M + Na]$^+$ requires 2039.6). For **7b**: mp 156–157 °C (Found: C, 38.55; H, 3.62; N, 1.90. $\mathrm{C_{72}H_{81}Bi_4Cl_6N_3O_6S_3}$ requires C, 38.79; H, 3.66; N, 1.88%); δ_H ($\mathrm{CDCl_3}$) 8.5–8.3 (12 H, m), 7.87 (3 H, d, *J* 7.0 Hz), 7.79 (3 H, d, *J* 7.0 Hz), 7.63 (3 H, t, *J* 7.0 Hz), 7.5–7.3 (12 H, m), 3.34 (12 H, q, *J* 7.2 Hz), 2.42, 2.37 (18 H, two s), 1.02 (18 H, t, *J* 7.2 Hz); MALDI-TOF, *m/z* 2252.2 ([M + Na]$^+$ requires 2252.3). For **6a**: (Found: C, 38.72; H, 4.40; N, 4.62. $\mathrm{C_{210}H_{285}Bi_{10}N_{21}O_{42}S_{21}}$ requires C, 38.57; H, 4.39; N, 4.50%); δ_H ($\mathrm{CDCl_3}$) 8.0–7.8 (21 H, m), 7.8–7.7 (9 H, m), 7.7–7.6 (12 H, m), 7.5–7.2 (24 H, m), 7.2–7.1 (9 H, m), 3.26 (84 H, br q), 1.12 (126 H, br t); δ_C (200 MHz $\mathrm{CDCl_3}$) 178.6, 175.5, 174.3, 147.1, 144.4, 140.8, 139.9, 138.3, 135.2, 129.3, 127.8, 41.8, 40.3, 40.0, 14.1, 13.0, 12.7.

‡ *General procedure*: To a solution of bismuthane **1** (0.42 g, 0.5 mmol) in THF (7 ml) was added *tert*-butyllithium (*n*-pentane solution; 1.9 M × 0.29 ml, 0.55 mmol) at −78 °C. After stirring for 1 h at this temperature, a THF solution (5 ml) of iodide **2a** (0.38 g, 0.5 mmol) was added. The reaction mixture was allowed gradually to warm to room temp. and quenched with brine. The aqueous phase was extracted twice with ethyl acetate, and the combined extracts were dried over $\mathrm{MgSO_4}$, and evaporated under reduced pressure to leave a white solid, which was chromatographed on silica gel using hexane–ethyl acetate as the eluent to give bismuthane **1**, $\mathrm{Bi_2}$-bismuthane **3a** and $\mathrm{Bi_3}$-bismuthane **4a** in this elution order in 25, 37 and 18% isolated yields, respectively.

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