Tris(2-methoxyphenyl)bismuthane as a Dehydrating Agent with High Template Ability: an Efficient Single-step Synthesis of Macrocyclic Diesters from Diacid Anhydrides and Glycols

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Tris(2-methoxyphenyl)bismuthane works as both a mild dehydrating agent and a good template for macrocyclic ester synthesis; prolonged heating of the bismuthane with a dicarboxylic acid anhydride and a glycol in toluene under reflux afforded the corresponding macrocyclic 1 : 1 diester in moderate to good yields, together with a small amount of a macrocyclic 2 : 2 tetraester.

In spite of being a member of pnictogen family, trivalent organobismuth exhibits a weak Lewis acid nature due to the valence extension ability characteristic of heavy non-metallic elements. There are many reports which describe the coordination of a bismuth atom with the oxygen or nitrogen atoms of ether and amino compounds.[1] However, such a prominent and specific interacting ability of the bismuth atom with lighter heteroatoms has apparently not been utilized in organic synthesis to date. We report herein that tris(2-methoxyphenyl)-bismuthane **1** works as both a mild dehydrating agent[2] and as a good template for the macrocyclic ester synthesis due to its excellent coordinating ability; when heated with compound **1** in toluene under reflux, dicarboxylic acid anhydride and glycol smoothly coupled together to give the corresponding macrocyclic diester in a higher yield than previously reported.[3]

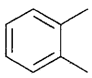
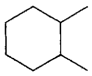
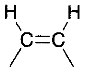
A typical preparation of macrocyclic diesters is as follows: A mixture of phthalic anhydride **2a** (740 mg, 5.0 mmol), tetraethylene glycol **3** (*n* = 3) (970 mg, 5.0 mmol), bismuthane **1** (1.06 g, 2.0 mmol) and dry toluene (10 cm^3) was heated under reflux for 2 d. A white deposit was filtered off and the filtrate was evaporated under reduced pressure to leave a pale yellow oil, which was purified by silica gel column chromatography with 5% MeOH–CH_2Cl_2 as eluent. A 1 : 1 diester **6a** (*n* = 2) was obtained as the major product from the early eluates and a 2 : 2 tetraester **7a** (*n* = 2) as the minor product from the later eluates. The isolated yields of compounds **6a** (*n* = 2) and **7a** (*n* = 2) were 61 and 3% respectively. The results are summarized in Table 1.

Although MS inspection of the crude products revealed the formation of cyclic 2 : 2 tetraesters **7** in every case, only **7a** (*n* = 2, 3), **7c** (*n* = 2) and **7d** (*n* = 2) could be successfully isolated in a pure form. All products were identified by spectral and analytical data.† The macrocyclic 1 : 1 diester and 2 : 2 tetraester structures were confirmed unambiguously by X-ray analyses of **6a** (*n* = 2) and **7a** (*n* = 3), see Figs. 1 and 2.‡

These types of macrocyclic compounds were previously prepared in low yields (1–30%) from the reaction between diacid dichlorides and glylcols by the high dilution method (*ca.* 60 mmol dm^{-3}, 3 d).[3] By using bismuthane **1** as a template, the corresponding macrocyclic diesters could be obtained in much better yields (13–83%) at higher concentrations (*ca.* 500 mmol dm^{-3}).

The initial stage of the macrocyclic formation would be an ordinary reaction between acid anhydride **2** and glycol **3** to give a monoester **4**, which then reacts with the bismuthane **1** to form a key intermediate **5**. In this intermediate, the oxygen atoms of the ethylene glycol moiety coordinate to the bismuth atom,[1a] and subsequently the bismuthane-mediated dehydration occurs intramolecularly to produce the macrocyclic diester **6** (Scheme 1). High-yield formation of macrocyclic compounds even at high concentrations are possible due to the dual role of the bismuthane **1** as the dehydrating agent and the template under the reaction conditions employed.

Table 1 Preparation of macrocyclic di- and tetra-esters

Acid anhydride	X	Polyethylene glycol 3 *n*	Yield (%)[a] (mp/°C) 6		7
2a		2	18	(123–125)	13 (127–128)
		3	61	(94–96)	3 (111–112)
		4	13	(oil)	—[b]
2b		3	60	(oil)	—[b]
		4	56	(oil)	—[b]
2c	–$(CH_2)_3$–	2	20	(oil)	9 (oil)
		3	47	(oil)	—[b]
		4	83	(oil)	—[b]
2d	–$(CH_2)_2$–	2	17	(59–62)	8 (oil)
		3	48	(oil)	—[b]
		4	65	(oil)	—[b]
2e		3	trace (oil)[c]		—[b]

[a] Yields refer to the isolated compounds and were not optimized. [b] Not isolated. [c] Polymeric products were formed.

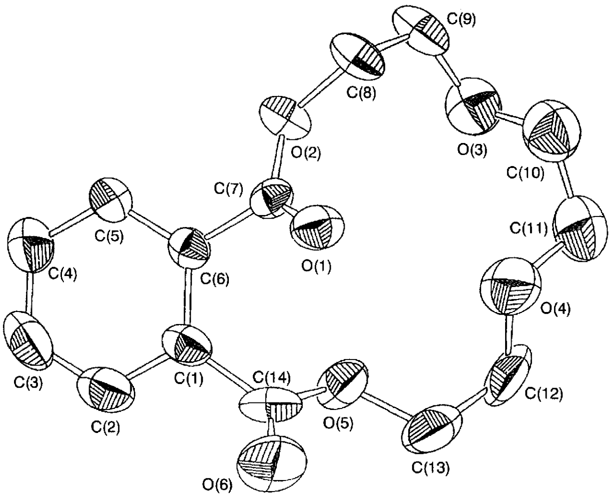


Fig. 1 An ORTEP drawing of macrocyclic 1 : 1 diester **6a** ($n = 2$)

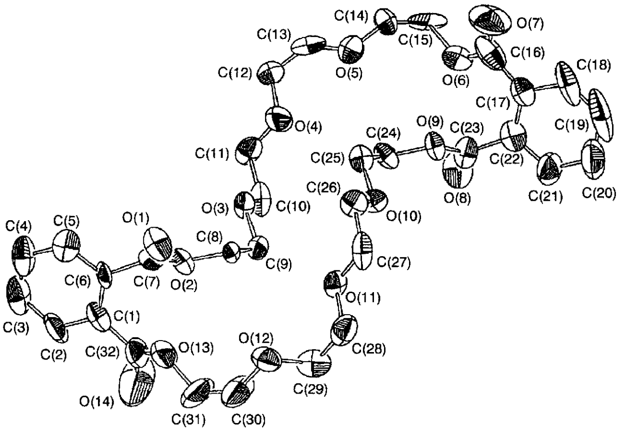
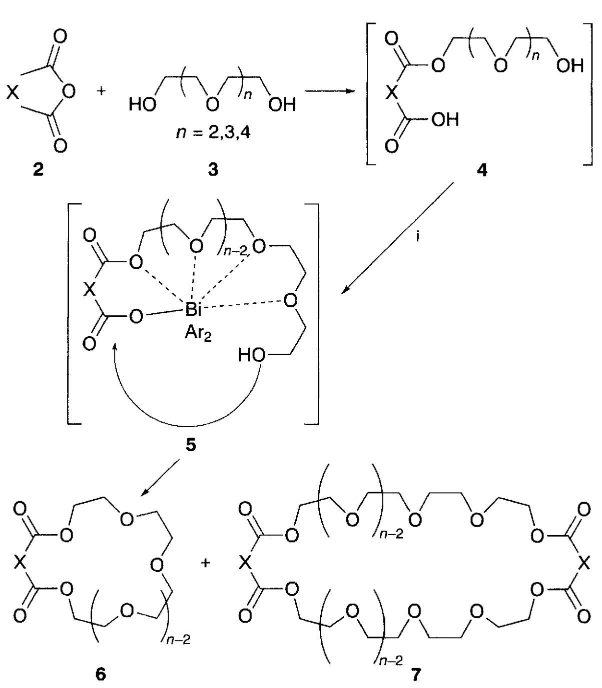


Fig. 2 An ORTEP drawing of macrocyclic 2 : 2 tetraester **7a** ($n = 3$)



Scheme 1 *Reagents and conditions*: i, bismuthane **1**, PhMe, reflux, 2 d

We thank the Ministry of Education, Science and Culture of Japan for financial support of this work by a Grant-in-Aid for Science and Research (No. 05804038).

Received, 10th March 1995; Com. 5/01510C

Footnotes

† *Selected spectroscopic and analytical data* for compound **6a** ($n = 2$); mp 123–125 °C; δ_H (J/Hz) 3.66 (4 H, s), 3.84 (4 H, t, J 4.8), 4.50 (4 H, t, J 4.8) and 7.28 – 7.75 (4 H, m); *m/z* (CI) 281 (8%, M + 1), 237 (8), 193 (54), and 149 (100) (Found: C, 59.7; H, 5.8 $C_{14}H_{16}O_6$ requires C, 60.0; H, 5.8%). For **7a** ($n = 2$); mp 127–128 °C; δ_H (J/Hz) 3.68 (8 H, s), 3.78 (8 H, t, J 5.0), 4.44 (8 H, t, J 5.0) and 7.51–7.74 (8 H, m); *m/z* (CI) 561 (100%, M + 1). **6a** ($n = 3$); mp 94–96 °C; δ_H (J/Hz) 3.66 (8 H, bs), 3.86 (4 H, t, J 6), 4.48 (4 H, t, J 6), 7.53 (2 H, dd, J 3.3 and 5.8) and 7.73 (2 H, dd, J 3.3 and 5.8); δ_C 61.69, 64.72, 68.92, 70.59, 128.98, 131.09 and 167.38; ν_{max} (KBr) cm^{-1} 1710, 1590, 1570 and 1060; *m/z* (CI) 325 (100%, M + 1) (Found: C, 58.6; H, 6.4. $C_{16}H_{20}O_7$ requires C, 59.3; H, 6.2%). For **6a** ($n = 4$); oil; δ_H (J/Hz) 3.64 (4 H, bs), 3.68 (8 H, bs), 3.84 (4 H, t, J 4.9), 4.49 (4 H, t, J 4.9), 7.53 (2 H, dd, J 3.3 and 5.8) and 7.74 (2 H, dd, J 3.3 and 5.8); δ_C 65.07, 68.96, 70.67, 70.79, 128.99, 131.02 and 131.96; *m/z* (CI) 369 (4%, M + 1), 237 (40) and 194 (100). (Found: C, 58.7; H, 6.7. $C_{18}H_{24}O_8$ requires C, 58.7; H, 6.6%). For **6b** ($n = 3$); oil[3]; δ_H (J/Hz) 1.4–2.0 (8 H, m), 2.77 (2 H, m), 3.64 (12 H, bs) and 4.23 (4 H, t, J 6); *m/z* (CI) 331 (18%, M + 1) and 155 (100). For **6b** ($n = 4$); δ_H (J/Hz) 1.4–2.0 (8 H, m), 2.85 (2 H, bs), 3.66 (16 H, bs) and 4.21 (4 H, t, J 4); *m/z* (CI) 375 (10%, M + 1). **6c** ($n = 2$), δ_H (J/Hz) 2.07 (2 H, quintet, J 7.2), 2.42 (4 H, quintet, J 7.2), 3.66 (8 H, bs) and 4.27 (4 H, t, J 6); *m/z* (CI) 247 (100%, M + 1). For **6c** ($n = 3$); oil [lit.,[3] bp 155–157 °C/0.65 Torr], δ_H (J/Hz) 1.94 (2 H, m), 2.40 (4 H, t, J 5), 3.64 (12 H, bs) and 4.24 (4 H, t, J 4.8); ν_{max} (NaCl) cm^{-1} 1710 and 1040; *m/z* (CI) 291 (100%, M + 1). For **6c** ($n = 4$), δ_H (J/Hz) 2.0 (2 H, quintet, J 7), 2.4 (4 H, quintet, J 7), 3.66 (16 H, bs) and 4.25 (4 H, t, J 4.8); *m/z* (CI) 335 (100%, M + 1). For **6d** ($n = 2$); δ_H (J/H$_Z$) 2.66 (4 H, s), 3.66 (8 H, bs) and 4.27 (4 H, t, J 4.8); *m/z* (CI) 233 (100%, M + 1). For **6d** ($n = 3$), δ_H (J/Hz) 2.66 (4 H, s), 3.65 (8 H, bs), 3.68 (4 H, t, J 5) and 4.24 (4 H, t, J 5); ν_{max} (NaCl)/cm^{-1} 1710 and 1040; *m/z* (CI) 277 (100%, M + 1). For **6d** ($n = 4$); δ_H (J/H$_Z$) 2.66 (4 H, s), 3.66 (16 H, bs) and 4.27 (4 H, t, J 4); *m/z* (CI) 321 (100%, M + 1).

‡ *Crystal data* for **6a** ($n = 2$). $C_{14}H_{16}O_6$, $M = 280.28$. Orthorhombic prisms, $a = 14.429(4)$, $b = 11.662(9)$, $c = 8.294(3)$ Å, $V = 1396(2)$ Å^3, space group $Pna2_1$, $Z = 4$, $D_c = 1.334$ g cm^{-3}. Intensity data were recorded on a Rigaku AFC5R diffractometer with graphite-monochromated Mo-Kα radiation and a 12 kW rotating anode generator. Crystal dimensions 0.350 × 0.180 × 0.200 mm. Scans of $(0.68 + 0.30 \tan \theta)°$ were made at a speed of 16.0° min^{-1} (in omega). The final cycle of full-matrix least-squares refinement was based on 751 observed reflections [$I > 3.00\ \sigma(I)$] and 244 variable parameters and converged with unweighted and weighted agreement factors of $R = 0.042$ and $R_w = 0.043$. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.20 and −0.17 e Å^{-3}, respectively. For **7a** ($n = 3$). $C_{32}H_{40}O_{14}$, $M = 648.66$. Monoclinic prisms, $a = 14.404(5)$, $b = 15.436(4)$, $c = 15.982(4)$ Å, $\beta = 114.66(2)$, $V = 3230(2)$ Å^3, space group $P2_1/n$, $Z = 4$, $D_c = 1.334$ g cm^{-3} Scans of $(1.26 + 0.30 \tan \theta)°$ were made at a speed of 16.0° min^{-1} (in omega). The final cycle of full-matrix least-squares refinement was based on 1702 observed reflections [$I > 3.00\ \sigma(I)$] and 415 variable parameters and converged with unweighted and weighted agreement factors of $R = 0.076$ and $R_w = 0.088$. Crystal dimension 0.450 × 0.450 × 0.080 mm. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.36 and −0.27 e Å^{-3}, respectively. Atomic coordinates, bond lengths and angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre. See Information for Authors, Issue No. 1.

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