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Practical Multigram Synthesis of 3,3,3',3'-Tetramethyl-1,1'-spirobisindane-5,5'-diamino-6,6'-diol

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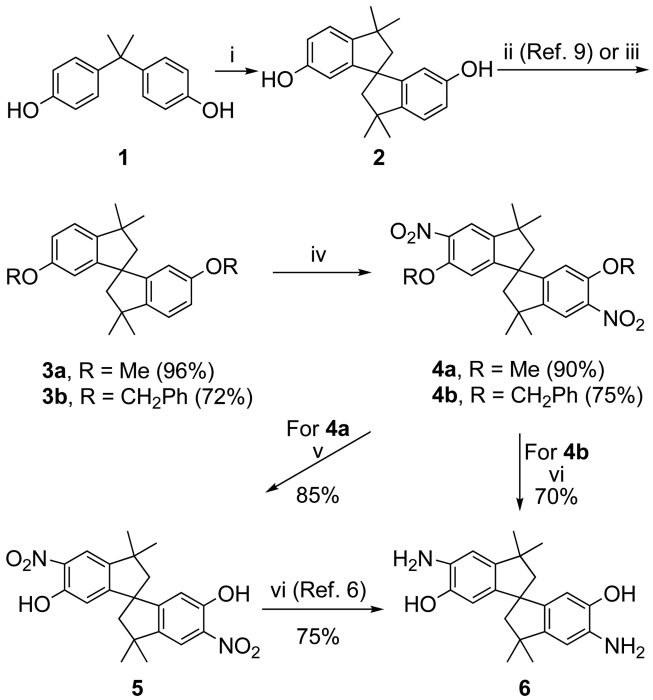
Polymers of intrinsic microporosity (PIMs)[1-4] containing 1,1'-spirobisindane building blocks as subunits are very attractive for the construction of gas separation membranes.[5] PIMs possess a fused-ring, ladder-type structure interrupted by sites of contortion. These structural features prevent the polymer from packing space efficiently in the solid state, leading to its high free volume and microporosity. Recently, thermally rearranged polybenzoxazole polymers[6] and hydroxyl-functionalized polyimides[7] with a spirobisindane moiety have been developed. One of the key monomers is 3,3,3',3'-tetramethyl-1,1'-spirobisindane-5,5'-diamino-6,6'-diol (**6**) as shown in Scheme 1. A few known synthetic methods of **6** are a direct nitration of 3,3,3',3'-tetramethyl-1,1'-spirobisindane-6,6'-diol (**2**) with nitric acid followed by reduction using HCO_2NH_4/Pd-C, $NH_2NH_2{\cdot}H_2O$/Pd-C and $SnCl_2$/conc·HCl.[6-8] The critical drawback of this method is that several nitro-substituted regioisomers are produced. So this method requires tedious chromatographic isolation and suffers from a low yield. Rajamohanan and co-workers have reported that nitration of the *O*-methylated spirobisindane compound **3a** with HNO_3-H_2SO_4 in acetic acid afforded the 5-nitro substituted spirobisindane **4a** in excellent yield.[9] They demonstrated the utility of inherently rigid building blocks such as 1,1'-spirobisindane for generating conformationally ordered synthetic oligomers after conversion of nitro group into amino group followed by acylation of several acid chlorides.

At first, we carried out demethylation of known **4a** with boron tribromide in dichloromethane at 0-5 °C and the spirobisindanediol **5** was produced in a 85% yield. Reduction of **5** with Pd-C and hydrazine hydrate in refluxing ethanol resulted in 3,3,3',3'-tetramethyl-1,1'-spirobisindane-5,5'-diamino-6,6'-diol (**6**) in 75% yield.[10] But, the above-described method requires engagement of BBr_3, which makes this method expensive and environmentally less friendly. From the economic and ecological point of view, it would be great if nitration is occurred selectively and both reduction and dealkylation are proceeded simultaneously. Herein, we describe a facile and multigram scale synthesis of **6** by the *O*-benzylation, nitration and concomitant reduction and debenzylation from readily available spiro-bisindanediol **2**. Using this easy-to-operate method, without tedious isolation and chromatographic procedures, we have been able to make **6** in quantities up to ten grams by an efficient single crystallization protocol.

The starting material 3,3,3',3'-tetramethyl-1.1'-spirobisindane-6,6'-diol (**2**) was prepared by the skeletal rearrangement of bisphenol A (**1**) in excess methansulfonic acid following the earlier reported procedure.[11] *O*-Benzylation of **2** with benzyl chloride in the presence of K_2CO_3 in acetonitrile at reflux temperature for 8 h benzyloxyspirobisindane **3b** was produced in 72% yield. Isolation of the product was simple. The reaction mixture was poured into water, extracted with dichloromethane, dried ($MgSO_4$) and evaporated under reduced pressure. The resulting white solid was filtered with petroleum ether afforded pure **3b**. Nitration of **3b**



Scheme 1. Reagents and Conditions: (i) CH_3SO_3H, rt, 48 h; (ii) Me_2SO_4, K_2CO_3, acetone, reflux, 8 h; (iii) $PhCH_2Cl$, K_2CO_3, CH_3CN, reflux, 8 h; (iv) AcOH, HNO_3, H_2SO_4, 0 °C → rt, 4 h; (v) BBr_3, CH_2CH_2, 0-5 °C, 1 h; (vi) $NH_2NH_2{\cdot}H_2O$, Pd-C, EtOH, reflux, 8 h.

with nitric acid in the presence of sulfuric acid for 5 h was proceeded smoothly on activated indane aromatic ring selectively giving **4b** in 75% yield. Again, the isolation procedure was remarkably simple and similar to that of **3b** except filtering with ethyl ether. On concomitant reduction and debenzylation of **4b** with hydrazine hydrate and 10% Pd-C in refluxing ethanol for 8 h, spirobisindanediaminodiol **6** was produced in 70% yield by the simple precipitation and filtration. The overall yield of **6** from **2** through the compounds **3b** and **4b** is 38%.

In summary, this work discloses an easy-to-handle and chromatography-free synthetic method that can furnish the valuable monomer 3,3,3',3'-tetramethyl-1,1'-spirobisindane-5,5'-diamino-6,6'-diol (**6**) in multigram quantities.

Experimental Section

Spirobisindane derivatives **2**,[11] **3a**, and **4a**[9] were prepared according to the procedures reported in the literatures.

6,6'-Dibenzyloxy-3,3,3',3'-tetramethyl-1,1'-spirobisindane (3b). A mixture of spirobisindanediol **2** (9.24 g, 30 mmol), benzyl chloride (11.3 g, 90 mmol) and K_2CO_3 (12.4 g, 90 mmol) in CH_3CN (120 mL) was stirred at reflux temperature for 8 h. The reaction mixture was poured into water, extracted with CH_2Cl_2 (3 × 100 mL), and dried over $MgSO_4$. The solvent was evaporated under reduced pressure. The resulting solid was filtered with petroleum ether to produce pure **3b** (10.5 g, 72%) as a white solid. mp 184-185 °C; IR (KBr) 1601, 1484, 1358, 1014 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.33 (s, 6H, two CH_3), 1.37 (s, 6H, two CH_3), 2.25 (d, J = 12.9 Hz, 2H, CH_2), 2.35 (d, J = 13.2 Hz, 2H, CH_2), 4.92 (s, 4H, CH_2Ph), 6.43 (d, J = 2.3 Hz, 2H, aromatic), 6.87 (dd, J = 8.2 and 2.3 Hz, 2H, aromatic), 7.08 (d, J = 8.5 Hz, 2H, aromatic), 7.27-7.39 (m, 10H, two Ph); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.5, 31.8, 42.9, 57.8, 59.6, 70.1, 110.2, 114.0, 122.4, 127.6, 127.8, 128.4, 137.1, 144.9, 151.9, 158.5. Anal. Calcd for $C_{35}H_{36}O_2$: C, 86.03; H, 7.43. Found: C, 85.85; H, 7.29.

6,6'-Dibenzyloxy-3,3,3',3'-tetramethyl-5,5'-dinitro-1,1'-spirobisindane (4b). To a chilled mixture (0 °C) of glacial acetic acid (130 mL), 60% HNO_3 (24.8 mL, 360 mmol), and 97% H_2SO_4 (16.0 mL, 300 mmol), dibenzyloxyspirobisindane **3b** (14.6 g, 30 mmol) were slowly added. The reaction mixture was stirred for 5 min at 0 °C and then at room temperature for 5 h. The reaction mixture was poured into ice water and the precipate was filtered off. The crude product was dissolved in CH_2Cl_2, dried over $MgSO_4$, and evaporated under reduced pressure. The resulting solid was filtered with Et_2O to produce pure **4b** (13.0 g, 75%) as a slightly yellowish solid. mp 175-178 °C; IR (KBr) 1616, 1580, 1521, 1347, 1289 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 1.35 (s, 6H, two CH_3), 1.40 (s, 6H, two CH_3), 2.17 (d, J = 13.2 Hz, 2H, CH_2), 2.38 (d, J = 13.5 Hz, 2H, CH_2), 4.98 (two d, J = 12.3 Hz, 4H, CH_2Ph), 6.31 (s, 2H, aromatic), 7.21-7.34 (m, 10H, two Ph), 7.66 (s, 2H, aromatic); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.1, 31.4, 43.4, 58.4, 58.8, 71.0, 110.4, 119.5, 126.9, 128.1, 128.6, 135.4, 140.1, 144.5, 151.8, 155.5. Anal. Calcd for $C_{35}H_{34}N_2O_6$: C, 72.65; H, 5.92; N, 4.84. Found: C, 72.53; H, 5.81; N, 4.98.

3,3,3',3'-Tetramethyl-1,1'-spirobisindane-5,5'-dinitro-6,6'-diol (5). To a chilled (0-5 °C) solution of **4a** (8.52 g, 20 mmol) in CH_2Cl_2 was added BBr_3 (5.8 mL, 60 mmol) dropwise manner. The reaction mixture was stirred at same temperature for 1 h. The mixture was poured into cold saturated aq. $NaHCO_3$ solution (500 mL), and extracted with CH_2Cl_2 (200 mL × 3). The combined organic layers were dried ($MgSO_4$) and the solvent was evaporated under reduced pressure. The resulting solid was filtered with Et_2O-petroleum ether to produce pure **5** (6.77 g, 85%) as a yellow solid. mp 238-241 °C;[8] ^1H NMR (300 MHz, $CDCl_3$) δ 1.37 (s, 6H, two CH_3), 1.44 (s, 6H, two CH_3), 2.28 (d, J = 13.2 Hz, 2H, CH_2), 2.42 (d, J = 13.2 Hz, 2H, CH_2), 6.54 (s, 2H, aromatic), 7.92 (s, 2H, aromatic), 10.61 (s, 2H, OH); ^{13}C NMR (75 MHz, $CDCl_3$) δ 30.1, 31.6, 43.4, 58.2, 58.7, 114.8, 118.7, 133.6, 145.1, 155.3, 160.5.

3,3,3',3'-Tetramethyl-1,1'-spirobisindane-5,5'-diamino-6,6'-diol (6). To a stirred suspension of **4b** (11.6 g, 20 mmol) and 10% Pd-C (638 mg, 0.6 mmol) in refluxing ethanol (300 mL) was added $NH_2NH_2{\cdot}H_2O$ (19.4 mL, 400 mmol) dropwise manner. After stirring at reflux temperature for 8 h, the reaction mixture was filtered with celite and washed with EtOH (20 mL). The organic phase was poured into water and the precipitate was filtered off and dried to give pure **6** (4.73 g, 70%) as a white solid. mp 262-265 °C; IR (KBr) 3492, 3376, 3285, 1616, 1506, 1322 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) δ 1.20 (s, 6H, two CH_3), 1.25 (s, 6H, two CH_3), 1.97 (d, J = 12.6 Hz, 2H, CH_2), 2.14 (d, J = 12.6 Hz, 2H, CH_2), 4.31 (s, 4H, NH_2), 6.04 (s, 2H, aromatic), 6.37 (s, 2H, aromatic), 8.65 (s, 2H, OH); ^{13}C NMR (75 MHz, DMSO-d_6) δ 30.7, 31.7, 42.3, 56.2, 59.7, 107.0, 109.1, 135.5, 138.7, 142.2, 143.8.

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