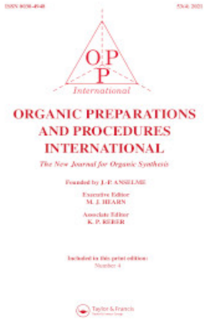

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OPPI BRIEF

A Simple Synthesis of a Pillar[*n*]arene Building Block – 1,4-bis(4-Bromobenzyl)benzene[†]

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Recent years have seen a veritable explosion of activity in the synthesis of "pillar[*n*]arenes"[1] (previously known as "[1_n]paracyclophanes") and their application in the construction of host-guest molecules, supramolecular nanostructures, molecular machines, biological catalysts, and other novel materials. The field has been extensively reviewed,[2–10] and recent work has expanded this exciting new area of supramolecular chemistry.[11–14]

We now describe a two-step synthesis of 1,4-bis(4-bromobenzyl)benzene (**1**) from readily available starting materials (Scheme 1). We previously prepared and utilized this building block in the inaugural synthesis of [1_5]- and [1_6]-paracyclophanes, but without experimental details,[15] and it is the purpose of this paper to provide such details. Monolithiation[16] of 1,4-dibromobenzene (**2**) with *n*-BuLi in THF at −78 °C generated 4-lithiobromobenzene (**3**), which was treated with terephthalaldehyde (**4**) to give diol **5**, presumably as a mixture of diastereomers. Treatment of diol **5** with $NaBH_4$/trifluoroacetic acid[17] gave **1** in high yield.

We believe our method to be superior in terms of yield, simplicity, and cost of starting materials to the procedures of Galun[18] and Stephan,[19] which are shown in Schemes 2 and 3, respectively. Moreover, *ortho* isomers are reported in Stephan's synthesis and are likely to occur in both of Galun's syntheses, but are precluded by our method.

Experimental section

Melting points were obtained on a Thomas-Hoover Mel-Temp capillary apparatus and are uncorrected. Infrared spectra (IR) were recorded on a Perkin-Elmer Model 599 spectrophotometer. Liquids were measured on NaCl plates (neat), while KBr pellets were used for solids. Nuclear Magnetic Resonance spectra (NMR) were recorded on a Perkin-Elmer R-24 or a Varian XL300 spectrometer using TMS as an internal standard. Low resolution mass spectra were obtained with a Finnigan EI-CI gas chromatograph-mass spectrometer, and high-resolution mass spectra were obtained at the NIH Regional Facility at the Massachusetts Institute of Technology. Thin Layer Chromatography (TLC) was carried out on precoated (0.2 mm) Silica Gel 60 F_{254} S

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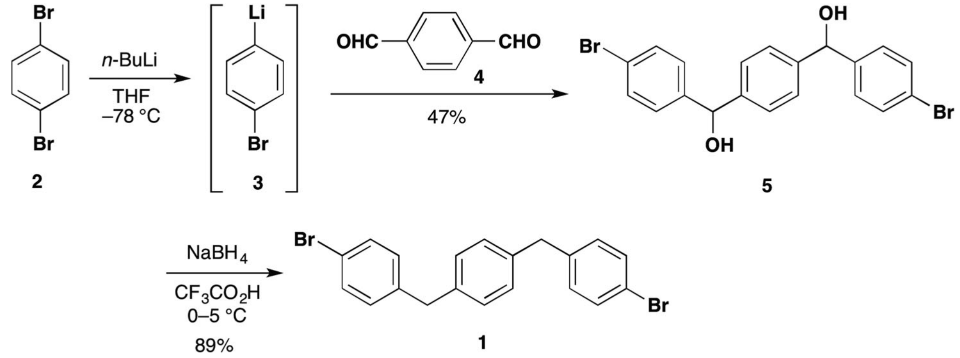
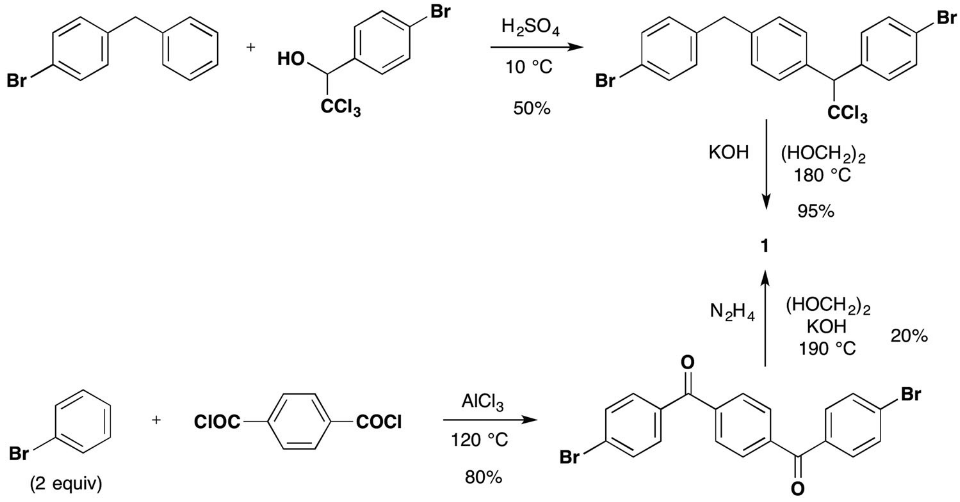
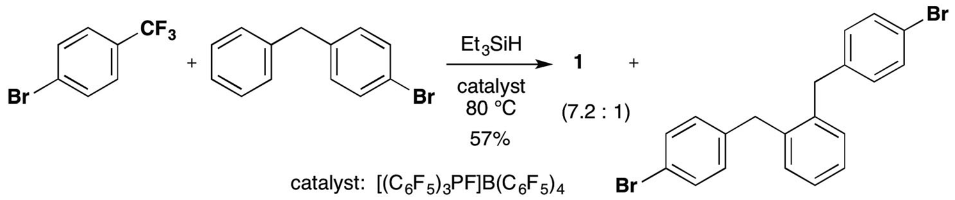
[†]Dedicated to the memory of Max L. Deinzer – climbing partner extraordinaire and a consummate chemist.



Scheme 1. Present synthesis of 1,4-bis(4-bromobenzyl)benzene.



Scheme 2. Two syntheses of 1 by Galun and co-workers.



Scheme 3. Synthesis of 1 by Stephan and co-workers.

plastic sheets. Microanalysis was performed by Atlantic Microlabs, Atlanta, Georgia. Sodium borohydride was obtained from Morton Thiokol and was oven dried at 110 °C before use. Trifluoroacetic acid was provided by Halocarbon, Hackensack, New Jersey, and was distilled before use. Tetrahydrofuran was dried over and distilled from sodium/benzophenone. The *n*-BuLi was purchased from Aldrich and standardized by titration against 2,5-dimethoxylbenzyl alcohol.

1,4-Phenylenebis(4-bromophenylmethanol) (5)

To a magnetically stirred solution of *p*-dibromobenzene (**2**) (1.03 g, 4.36 mmol) in dry THF (15 mL) at –78 °C was added quickly via syringe a solution of *n*-BuLi/hexane (1.52 M, 2.90 mL, 4.41 mmol). The resulting solution was stirred at –78 °C for 5 min, then a solution of terephthalaldehyde (**4**) (0.29 g, 2.2 mmol) in dry THF (10 mL) was added quickly via syringe. The resulting mixture was allowed to warm to 25 °C, stirred at 25 °C for 24 h, then poured into H_2O (75 mL), diluted with brine (100 mL), and extracted with Et_2O (3 x 100 mL). The combined extracts were dried (Na_2SO_4), filtered, and concentrated *in vacuo* to afford a yellow oil (0.84 g). Flash chromatography (2:1 hexane/Et_2O) gave **5** (0.46 g, 47%) as a white solid (presumed mixture of diastereomers) which was recrystallized from hexane/Et_2O: mp 141–142 °C; ^{1}H NMR (acetone-d_6) δ 7.4–7.3 (m, 12H), 5.7 (broad, 2H); ^{13}C NMR (DMSO-d_6) δ 145.0, 143.8, 130.8, 128.3, 126.0, 119.6, 73.3; IR ($CHCl_3$): 3180 cm^{-1} (broad).

Anal. Calcd for $C_{20}H_{16}Br_2O_2$: C, 53.60; H, 3.60; Br, 35.66. Found: C, 54.48; H, 3.92; Br, 36.12. HRMS Calcd for $C_{20}H_{16}Br_2O_2$: 445.9517. Found: 445.9486.

1,4-bis(4-Bromobenzyl)benzene (1)

To trifluoroacetic acid (100 mL) under N_2, magnetically stirred at 0–5 °C was added $NaBH_4$ (15 pellets, 4.5 g, 120 mmol) over 10 min, and the resulting mixture was allowed to warm to 25 °C and stirred at 25 °C for 45 min. To this was added in portions over 2 h a suspension of α,α'-bis(4-bromophenyl)-1,4-benzenedimethanol (**5**) (3.10 g, 6.92 mmol) in CH_2Cl_2 (25 mL). The resulting mixture was stirred at 25 °C for 24 h, then carefully poured into 25% aqueous NaOH (100 mL)/ice chips to make strongly alkaline (pH 11), diluted with brine (200 mL), and extracted with Et_2O (3 x 100 mL). The combined extracts were dried (Na_2SO_4), filtered, and concentrated *in vacuo* to afford **1** (2.55 g, 89%) as a white solid, which was recrystallized from hexane/Et_2O to give colorless needles; mp 121–122.5 °C; (lit.[18] mp 127 °C): ^{1}H NMR ($CDCl_3$) δ 7.3–7.0 (m, 12H), 3.8 (s, 4H); ^{13}C NMR ($CDCl_3$) δ 140.0, 138.3, 131.4, 130.5, 128.9, 119.8, 40.8; MS *m/e* (relative intensity) 418 (M^+, 17), 416 (M^+, 33), 414 (M^+, 16), 337 (12), 335 (12), 247 (100), 245 (99), 166 (66); IR ($CHCl_3$): 2945, 1605, 1085, 1025 cm^{-1}. A reduction of **4** on a 9.5-gram scale gave **1** in 91% yield.

Anal. Calcd for $C_{20}H_{16}Br_2$: C, 57.72; H, 3.88; Br, 38.40. Found: C, 57.48; H, 3.91; Br, 38.48.

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