

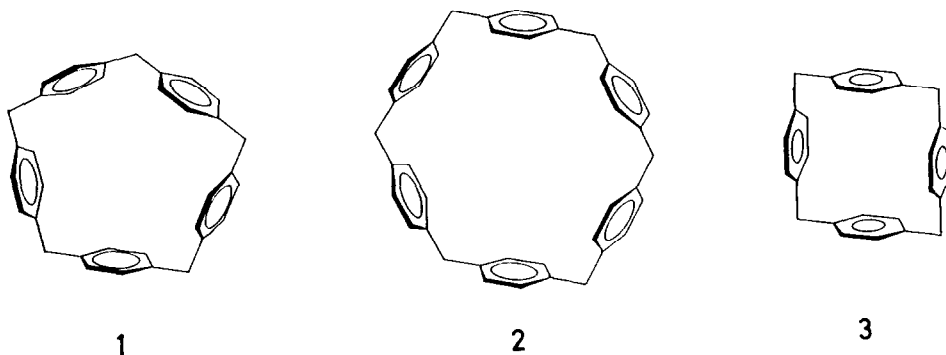
[1.1.1.1.1]PARACYCLOPHANE AND [1.1.1.1.1.1]PARACYCLOPHANE

Gordon W. Gribble* and Charles F. Nutaitis

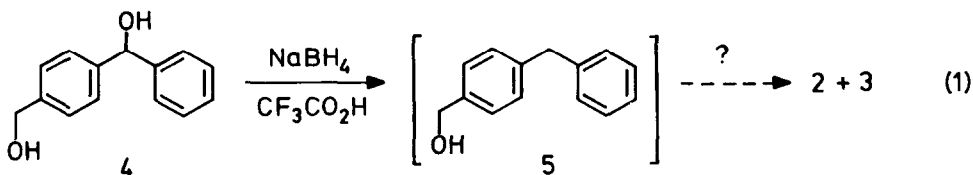
Department of Chemistry, Dartmouth College, Hanover, New Hampshire 03755

Summary: The first syntheses of [1.1.1.1.1]paracyclophane (1) and [1.1.1.1.1.1]paracyclophane (2) are described, featuring a trifluoroacetic acid promoted Friedel-Crafts cycloalkylation as the final step.

We wish to report the first syntheses of [1.1.1.1.1]paracyclophane (1) ([1₅]PCP) and [1.1.1.1.1.1]paracyclophane (2) ([1₆]PCP). During the course of our work, there was reported¹ the synthesis of [1.1.1.1]paracyclophane (3), the first example of this class of paracyclophanes.

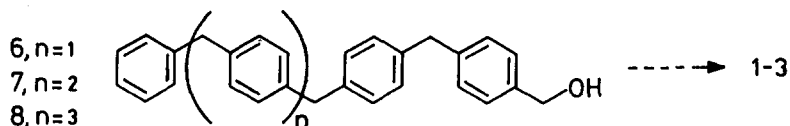


Several years ago, during a study² of the reduction of di- and triarylmethanols to di- and triarylmethanes with sodium borohydride (NaBH_4) in trifluoroacetic acid (TFA), we attempted the selective reduction of 4-(hydroxymethyl)diphenylmethanol (4) shown in Eqn. 1. Instead of the anticipated² 4-(hydroxymethyl)diphenylmethane (5), this reaction produced a mixture of products which, from ¹H NMR spectroscopy and mass spectrometry, appeared to contain the novel [1₆]PCP (2) and perhaps [1₄]PCP (3), which would arise from a Friedel-Crafts cyclooligomerization of the initially formed 5. Subsequent model studies revealed that TFA, in fact, is an excellent medium for promoting the Friedel-Crafts alkylation of arenes (ie., benzene, toluene) with benzyl alcohol and related alcohols.³

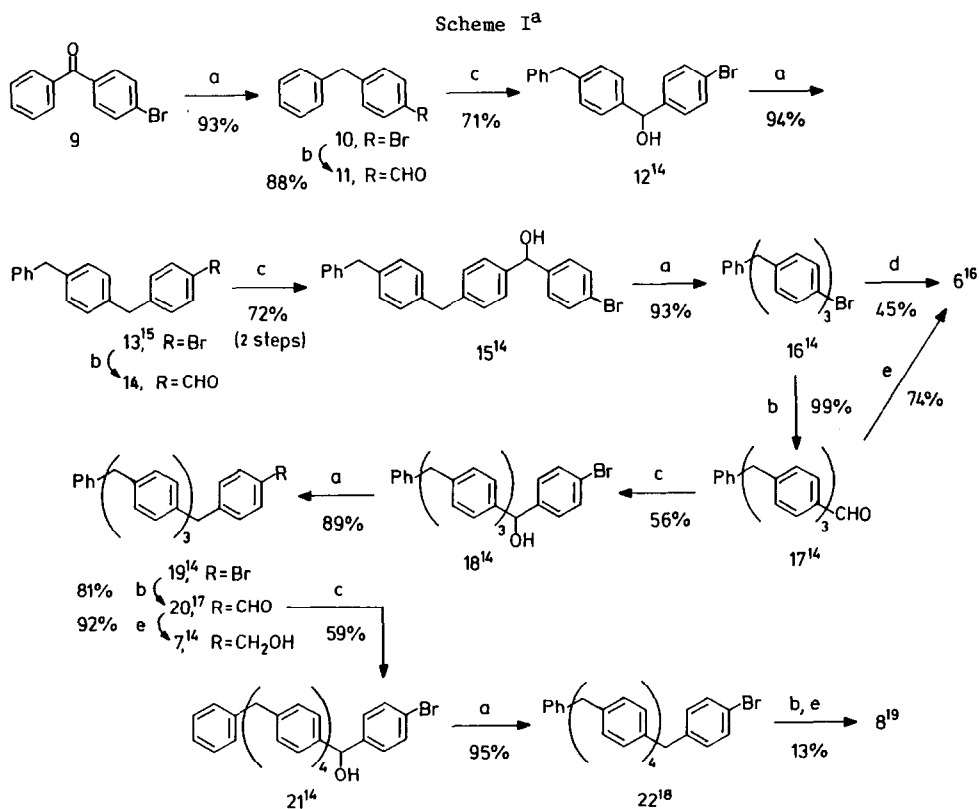


These observations, coupled with the fact that, despite the enormous cyclophane literature,⁴ no examples of $[1_n]$ paracyclophanes were known,⁵⁻⁷ prompted us to pursue the present project. Moreover, it is possible that Cannizzaro⁸ prepared $[1_n]$ PCPs as early as 1854 during his studies on the acid-promoted polymerization of benzyl alcohol and derivatives. Indeed, hydrocarbons with the empirical formula $(C_7H_6)_n$ have been alluded to many times in the ensuing years.^{9,10}

Our approach to the synthesis of $[1_n]$ PCPs, while simultaneously answering the question posed in Eqn. 1, was to prepare alcohols 6-8 and study their cyclization reactions in TFA.



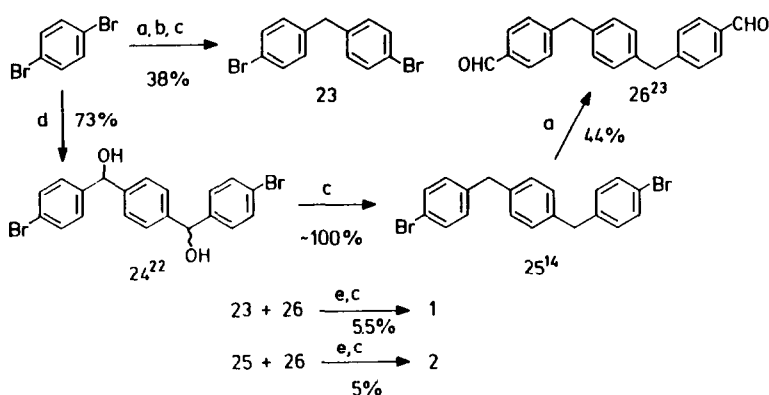
The preparation of 6-8 is summarized in Scheme I. Starting with 4-bromobenzophenone (9) (Aldrich Chem. Co.) and utilizing a repetitive three-step benzyl group homologation methodology, we synthesized 6-8 in straightforward fashion. Unfortunately, the final step in the synthesis of 8 proceeds very poorly.



^a a: $NaBH_4/TFA$ ^{2,11}; b: $n-BuLi/N$ -formylpiperidine¹²; c: 4-lithiobromobenzene/THF¹³; d: $n-BuLi$ /paraformaldehyde; e: $NaBH_4/CH_2Cl_2$, EtOH.

Slow addition of a solution of 6 in CH_2Cl_2 to refluxing TFA gives, after workup and preparative TLC, a mixture of products²⁰ none of which can be identified as $[1_4]\text{PCP}$ (3). Molecular models indicate that such a Friedel-Crafts cycloalkylation transition state would be prohibitively strained and the failure of 6 to cyclize to 3 is not surprising.

However, similar treatment of 7 with TFA gives a mixture of products from which can be isolated by prep TLC $[1_5]\text{PCP}$ (1) in 3% yield.²¹ This colorless powdery material (mp 316-318°C dec) displays the expected two singlets in the ^1H NMR spectrum, δ 3.75 and 6.95 ppm (ratio 1:2), and three signals in the proton-decoupled ^{13}C NMR spectrum, δ 43.7, 128.5, and 139.2 ppm. These data as well as the IR, UV, and mass spectrum are similar to those reported¹ for $[1_4]\text{PCP}$ (3).²⁴ The structure of 1 is confirmed by the high resolution mass spectrum which shows M^+ at m/e 450.2369 (calcd for $\text{C}_{35}\text{H}_{30}$, 450.2347). Likewise, exposure of 8 to TFA gives after prep TLC $[1_6]\text{PCP}$ (2) in 31% yield.²¹ This colorless compound (mp 230°C dec) exhibits two singlets in the ^1H NMR spectrum (δ 3.85 and 7.0 ppm) in the ratio 1:2, and three signals in the proton-decoupled ^{13}C NMR spectrum (δ 41.0, 128.8, and 138.6 ppm). The IR, UV, and mass spectrum are consistent with the structure of 2 and similar to the spectra observed for 1.²⁴ The high resolution mass spectrum shows M^+ at m/e 540.2814 (calcd for $\text{C}_{42}\text{H}_{36}$, 540.2817), confirming the structure of 2. The higher yield of 2 presumably reflects a less strained transition state for cyclization than that leading to 1 (CPK and Dreiding models). Neither 1 nor 2 appears to exhibit charge-transfer interaction between rings as is the case with 3 (UV spectrum),¹ although CPK molecular models indicate that the "face" conformation should be favored for all three PCPs. In an attempt to obtain greater amounts of 1 and 2, we pursued the convergent routes shown in Scheme II. Although both 1 and 2 can be obtained in this fashion, the dismal yields obtained thus far in the final step preclude a study of the π -complexing²⁵ properties of $[1_5]\text{PCP}$ and $[1_6]\text{PCP}$.

Scheme II^a

^a a: *sec*-BuLi/THF/*N*-formylpiperidine; b: 4-lithiobromobenzene/CuI; c: NaBH_4 /TFA; d: *sec*-BuLi/*p*-diformylbenzene; e: *n*-BuLi (2 equiv)/THF.

Finally, examination of the crude reaction product from Eqn. 1 indeed revealed the presence of $[1_6]\text{PCP}$ (2) by direct comparison with pure material synthesized herein.

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References and Notes

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7. For the synthesis of sulfur and oxygen bridged analogues, see (a) M.L. Kaplan and W.D. Reents, Jr., *Tetrahedron Lett.*, **23**, 373 (1982); (b) J. Franke and F. Vögtle, *ibid.*, **25**, 3445 (1984); (c) M.L. Kaplan, W.D. Reents, Jr., and C.S. Day, *Cryst. Struct. Comm.*, **11**, 1751 (1982).
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9. For a summary of the early work in this area, see R.L. Shriner and A. Berger, *J. Org. Chem.*, **6** 305 (1941). These workers reported the isolation of an isomer of 1,2,3,4,5,6-hexaphenylcyclohexane from the reaction of benzyl alcohol and boric oxide. That this material is actually 2 is an intriguing possibility.
10. For allusion to the possibility of forming cyclooligomers in the polymerization of benzyl halides, see T. Yamamoto and A. Yamamoto, *Chem. Lett.*, 353 (1977).
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12. G.A. Olah and M. Arvanaghi, *Angew. Chem. Int. Ed.*, **20**, 878 (1981).
13. H. Gilman, W. Langham, and F.W. Moore, *J. Am. Chem. Soc.*, **62**, 2327 (1940). We find that the use of *sec*-butyllithium/THF with *p*-dibromobenzene is superior to *n*-butyllithium.
14. This compound gave an elemental analysis within the following limits: C, ±0.40; H, ±0.24; Br, ±0.30 (if present); and exhibited ¹H and ¹³C NMR, IR, and mass spectra consistent with their proposed structures. The following melting points were observed: 12, mp 96.5-98°C; 15, mp 90-91°C; 16, mp 74-76°C; 17, mp 83-85°C; 18, mp 110-112°C; 19, mp 118-119°C; 7, mp 152-154°C; 21, mp 138-140°C; 25, mp 121-122.5°C.
15. This compound gave satisfactory spectral data (¹H and ¹³C NMR, IR, high resolution mass).
16. This compound (mp 128-129°C) gave satisfactory spectral data (¹H and ¹³C NMR, IR, high resolution mass).
17. This compound (mp 116-118°C) gave satisfactory spectral data (¹H and ¹³C NMR, IR, mass).
18. This compound (mp 142-144°C) gave satisfactory spectral data (¹H and ¹³C NMR, IR, mass) and the following elemental analysis: Calcd for C₄₁H₃₅Br: C, 81.04; H, 5.81; Br, 13.15. Found: C, 80.59; H, 5.76; Br, 13.64.
19. This compound gave a satisfactory low resolution mass spectrum.
20. These products are tentatively identified as 4,4'-dibenzylidiphenylmethane, the trifluoroacetate of 6, and two trifluoroacetyl derivatives of 4,4'-dibenzylidiphenylmethane.
21. The only other product identified is the trifluoroacetate derivative of the starting alcohol. The majority of the material appears to be polymer.
22. This compound (mp 141-142°C) gave satisfactory spectral data (¹H and ¹³C NMR, IR) including a high resolution mass spectrum.
23. This compound (mp 102-104°C) gave satisfactory spectral data (¹H and ¹³C NMR, IR, mass).
24. For example, the UV spectra of 1 (262, 268, 276 nm) and 2 (261, 267, 276 nm) are virtually identical to that of 4,4'-bis(*p*-tolylmethyl)benzene, 1 and the mass spectra of 1 (m/e 450 (M⁺, 18), 278 (23), 194 (28), 179 (100), 165 (46), 146 (21), 105 (22), 91 (75) and 2 (m/e 540 (M⁺, 24), 283 (3), 270 (7), 255 (6), 193 (4), 179 (100), 165 (23), 104 (18), 91 (29)) show similar fragmentation patterns to those of 3.
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