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Synthesis of *m*-terphenyl derivatives for potential use as tectons in crystal engineering☆

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Abstract—Treatment of 4,4-biphenyldiboronic acid with suitably substituted iodo-*m*-terphenyls provide easy access to the precursors for the synthesis of two rigid *m*-terphenyl derivatives bearing, H-bonding groups, for potential use as tectons in crystal engineering.
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1. Introduction

The rational design of molecular solids with desired network topologies is an area of considerable practical applications and interest to chemists and material scientists alike.[1] Organic molecular solids with large and well-defined cavities are expected to find use as molecular sieves, analogous to zeolites. Microporous organic solids capable of selective intracavity incorporation of dienes and dienophiles have shown to promote stereoselective Diels–Alder reactions.[2] Proper alignment of reactants in organic solids via supramolecular assembly have enabled successful realization of unique topochemical reactions.[3] A highly desirable and vigorously sought out goal in the synthesis (construction) of nanoporous molecular solids is the ability to predict the shape and size of the cavities in the solid state structures of organic and organometallic compounds.[4] Crystal engineering, a relatively new area of study, addresses this question by trying to establish a reliable set of rules and paradigms that relate molecular structures of organic and organometallic substances to the crystal (supramolecular)[5] structures of these compounds. A library of weak, but directional, intermolecular interactions have been identified by crystal engineers as the glue that holds the molecular entities in their respective crystal lattice.[5] A knowledge of these weak intermolecular forces, coupled with an understanding of the required directionality and symmetry properties of the functional groups aiding the self-assembly process, has enabled synthetic chemists to prepare suitable tectons (building blocks)[6a] for the construction of molecular solids.[6b–e]

2. Results and discussion

In this communication, we report the synthesis of two rigid *m*-terphenyl derivatives **1** and **2** carrying phenolic and carboxylic acid functional groups. The conventional OH···O hydrogen bonding possible with these functional groups is the most commonly used supramolecular glue in the generation of predictable networks in crystal engineering.[1,5b] The choice of **1** and **2** as potential tectons was guided by the consideration of the following expected structural features of these compounds. The positioning of the functional groups on the outer rings of the top and bottom *m*-terphenyl units of these structures will place these H-bonding functional groups pointing in opposite directions, albeit not orthogonal to each other when R = H as in **1** and **2**. Such H-bonding functional groups, mounted on a conformationally rigid molecular scaffold pointing in opposite directions is likely to favor interaction directionality over close packing in the crystal structures of **1** and **2**. The use of a biphenyl spacer to connect the top and bottom *m*-terphenyl units allows one to tune the angle between the functional groups by introducing bulky *ortho*-substituents (R ≠ H) on the biphenyl spacer. Such a tuning of the angle between the functional groups will also provide a degree of control over the extent of voids in the eventual lattice. Finally, the synthetic approach (Scheme 2, vide infra) allows us to

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Keywords: tectons; *m*-terphenyl derivatives; Suzuki coupling reaction; crystal engineering.

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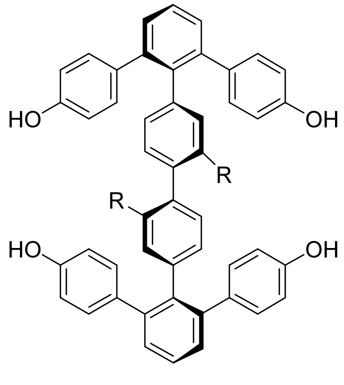
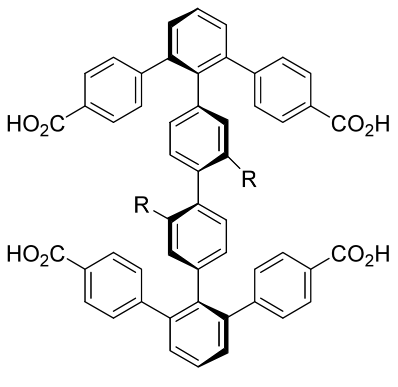
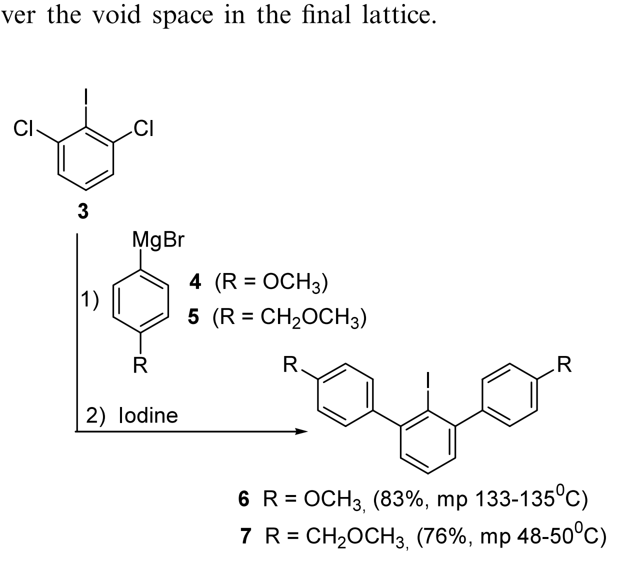


1 (R = H)



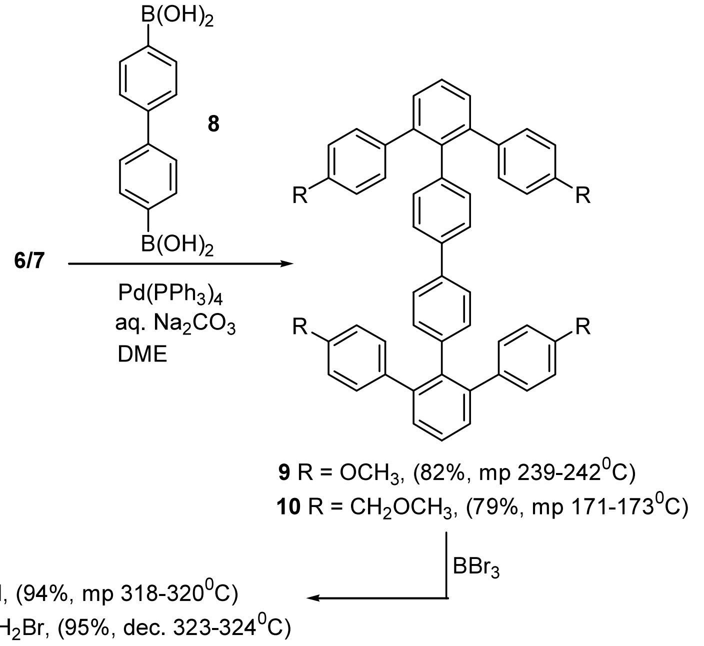
2 (R = H)

use other linear polyphenyls as the spacer between the *m*-terphenyl units allowing another degree of control over the void space in the final lattice.

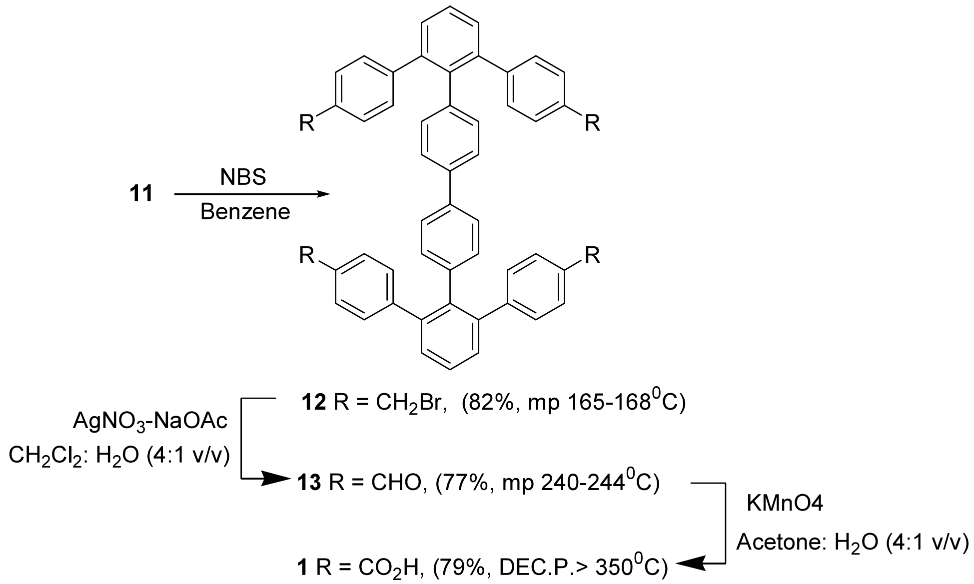


Scheme 1.

Our approach to the synthesis of **1** and **2** relies on Suzuki coupling[7] reactions between appropriately substituted *m*-terphenyl derivatives with 4,4-biphenydiboronic acid (**8**)[8] to mount the *m*-terphenyl caps on the 4,4′ positions of biphenyl, thereby yielding the rigid molecular framework of **1** and **2** (Scheme 2). Hart's tandem aryne generation-nucleophilic capture sequence for the one-pot preparation of *m*-terphenyls[9] was used for the synthesis of 2′-iodo-*m*-terphenyl derivatives, **6** and **7** required in the crucial Suzuki coupling reaction (Scheme 1). Treatment of 2,6-dichloroiodobenzene (**3**) with 3.0 equivalence of 4-methoxyphenylmagnesium bromide (**4**) followed by an iodine quench of the reaction mixture prior to aqueous work-up afforded **6** in 83% yield. The synthesis of **7** was similarly carried out and was isolated in 76% yield by using 3.0 equivalence of 4-methoxymethylphenylmagensium bromide (**5**). Though Suzuki cross-coupling reaction between aryl halides and arylboronic acids has emerged as one of the most reliable protocols for biaryl synthesis, coupling involving sterically demanding substrates (boronioc acid, halide, or both) requires the use of specialized



Scheme 2.



Scheme 3.

catalysts and reaction conditions and the yields are often variable.[10] The sterically demanding nature of halides **6** and **7**, with the iodine site (C2′) flanked by two phenyl rings on the *ortho* carbons, was a concern for us before we attempted the necessary coupling with 4,4-biphenydiboronic acid (**8**). To our surprise, we found that employing the original Suzuki reaction conditions,[11] namely the use of $Pd[P(Ph)_3]_4$ as the catalyst and aq. Na_2CO_3 as the base in the coupling of **6** and **7** with **8**, afforded the coupled products **9** and **10** in 82 and 79% yield, respectively.[12,13] We consider these yields remarkable, as the coupled products **9** and **10** result from a two-fold Suzuki coupling reaction involving sterically demanding aryl halides. Demethylation of **9** using BBr_3 provided the desired tetraphenol, **1**, in 94% yield.[14] Demethylation of **10** provided the expected *tetrakis*-bromomethyl derivative **11**, which we hoped to directly oxidize to the desired tetracarboxylic acid **2**. However, our attempts at this direct oxidation proved difficult with intractable mixture resulting from our oxidation attempts. We were thus forced to adopt a circutous but a sequence of high yielding reactions shown in Scheme 3 to obtain **2**. Benzylic bromination of **11** using excess NBS in benzene yielded the octabromide **12** in 82% yield which was subsequently hydrolyzed to the tetraformyl derivative, **13**, in presence of silver nitrate in $THF–H_2O$ mixture.[15] The final oxidation of **13** to the tetracarboxylic acid derivative, **2**, was easily accomplished with $KMnO_4$ in acetone–water mixture.[16] The precipitation of the product, in essentially pure form upon acidification and decolorization of the reaction mixture, made the product isolation easy. The structures of **1** and **2** are readily discernible from their respective ^1H NMR spectra. Both compounds show two sets of AA′BB′ signals with an intensity ratio of 2:1 in their ^1H NMR spectra for the protons on the outer rings of *m*-terphenyl caps and biphenyl unit respectively. As expected due to the presence of electron donating OH groups, the higher intensity AA′BB′ set in the case of **2** appeared upfield (δ 6.54 and δ 6.84) than the corresponding signals of **1** (δ 7.18 and δ 7.74) which bear electron withdrawing carboxylic acid groups on the outer *m*-terphenyl rings.

In conclusion, we have found an easy route to assemble *m*-terphenyl capped biphenyl derivatives, which by virtue of having suitably positioned H-bonding groups, are likely to find use in crystal engineering as tectons. The ready availability of suitably substituted and functionalized *m*-terphenyls via Hart's one-pot procedure and the ease of coupling of these derivatives with 4,4-biphenyldiboronic acid as demonstrated by the current work should facilitate the synthesis of many structurally analogous derivatives of **1** and **2**. Work on elucidation of solid state structures of **1** and **2** (recrystallized from DMSO) and synthesis of derivatives of **1** and **2** ($R \neq H$) are currently underway in our laboratory.

Acknowledgements

Support of this work by the University Research Council of Western Illinois University and the Petroleum Research Fund of the American Chemical Society (34866-B4) is gratefully acknowledged. We also gratefully acknowledge the support of the National Science Foundation (ILI grant no. DUE –9851569) and Western Illinois University for funding the NMR spectrometer used in this study.

References

1. (a) Desiraju, G. R. *Crystal Engineering, The Design of Organic Solids*; Elsevier: Amsterdam, 1989; (b) Moulton, B.; Zaworotko, M. J. *Chem. Rev.* **2001**, *101*, 1629; (c) Hosseni, M. W.; De Cian, A. *J. Chem. Soc., Chem.*

Commun. **1998**, 727; (d) Wang, X.; Simard, M.; Wuest, J. D. *J. Am. Chem. Soc*. **1994**, *116*, 12119; (e) Aakeröy, C. B. *Acta Crystallogr*. **1997**, *B53*, 569; (f) Rosi, N. L.; Eckert, J.; Eddaoudi, M.; Vodak, D. T.; Kim, J.; O'Keffe, M.; Yaghi, O. M. *Science* **2003**, *300*, 1127.

2. Endo, K.; Koike, T.; Sawaki, T.; Hayashida, O.; Masuda, H.; Aoyama, Y. *J. Am. Chem. Soc*. **1997**, *119*, 4117.
3. (a) MacGillivry, L. R.; Reid, J. L.; Ripmeester, J. A. *J. Am. Chem. Soc*. **2000**, *122*, 7817; (b) Xiao, J.; Yang, M.; Lauher, J. W.; Fowler, F. W. *Angew. Chem., Int. Ed*. **2000**, *39*, 2132.
4. (a) Gavezotti, A. *Acc. Chem. Res*. **1994**, *27*, 309; (b) Schweiber, K. E.; Chin, D. N.; MacDonald, J. C.; Whitesides, G. M. *J. Am. Chem. Soc*. **1996**, *118*, 4018; (c) Klein, C.; Graf, E.; Hosseini, M. W.; De Cian, A.; Fischer, J. *New J. Chem*. **2001**, *25*, 207; (d) Desiraju, G. R. *Nature* **2001**, *412*, 397; (e) Coronado, E.; Galan-Mascaros, J. R.; Gomez-Garcia, C. J.; Laukhin, V. *Nature* **2000**, *408*, 447.
5. (a) Desiraju, G. R. *Angew. Chem., Int. Ed. Engl*. **1995**, *34*, 2311; (b) Aakeröy, C. B.; Beatty, A. M. *Aust. J. Chem*. **2001**, *54*, 409.
6. (a) The term tectons for building blocks in crystal engineering was first suggested by Wuest et al. in: Simard, M.; Su, D.; Wuest, J. D. *J. Am. Chem. Soc*. **1991**, *113*, 4696; (b) Whitesides, G. M.; Mathias, J.-P.; Seto, C. T. *Science* **1991**, 254; (c) Lehn, J.-M.; Mascal, M.; DeCain, A.; Fischer, J. *J. Chem. Soc., Chem. Commun*. **1990**, 479; (d) Aakeröy, C. B.; Beatty, A. M.; Helfrich, B. A. *Angew. Chem., Int. Ed*. **2001**, *40*, 3240; (e) Bhyrappa, P.; Wilson, S. R.; Suslick, K. S. *J. Am. Chem. Soc*. **1997**, *119*, 8492.
7. Miyaura, N.; Suzuki, A. *Chem. Rev*. **1995**, *95*, 2457.
8. Coutts, I. G. C. H.; Goldschmidt, R.; Musgrave, O. S. *J. Chem. Soc. (C)* **1970**, 488.
9. (a) Hart, H.; Harada, H.; Du, C.-J. F. *J. Org. Chem*. **1985**, *50*, 3104; (b) Vinod, T. K.; Hart, H. *J. Org. Chem*. **1990**, *55*, 881.
10. (a) Watanabe, T.; Miyaura, N.; Suzuki, A. *Synlett* **1992**, 207; (b) Littke, A.; Dai, C.; Fu, G. C. *J. Am. Chem. Soc*. **2000**, *122*, 4020; (c) Yin, J.; Rainka, M.; Zhang, X.-X.; Buchwald, S. L. *J. Am. Chem. Soc*. **2002**, *124*, 1162; (d) Griffiths, C.; Leadbeater, N. E. *Tetrahedron Lett*. **2000**, *41*, 2487.
11. Miyaura, N.; Yanagi, T.; Suzuki, A. *Synth. Commun*. **1981**, *11*, 513.
12. For the synthesis of a structurally close analogue of **1** and **2** using an alternate Suzuki coupling approach, See: Chen, T.-S.; Gantzel, P.; Siegel, J. S.; Baldridge, K. K.; English, R. B.; Ho, D. M. *Angew. Chem., Int. Ed*. **1995**, *34*, 2657.
13. **General procedure for the Suzuki coupling reaction between 4,4′-biphenyldiboronic acid (8) and *m*-terphenyl derivatives 6 and 7**: A mixture of 4,4-biphenyldiboronic acid (1.0 mmol) and iodo-*m*-terphenyl **6** or **7** (0.5 mmol) was added to a suspension of $Pd[P(Ph)_3]_4$ (0.06 mmol) in 1,2-dimethoxyethane (20 mL) at rt. The mixture was stirred and to it was added 2.0 mL of 2.0 M aq. Na_2CO_3 and was subsequently maintained at reflux for 12 h. The reaction mixture was then poured in water (50 mL) and extracted with CH_2Cl_2 (2×30 mL). The organic layers were combined, dried $MgSO_4$) and evaporated to obtain a golden yellow oil which was then chromatographed over silica gel using CH_2Cl_2:hexane (2:3, v/v) to give **9** (82%) or **10** (79%). Compound **9**: (mp 239–242°C), IR (KBr) 3000, 2960, 1605, 1512, 1438, 1294, 1245, 1172, 1038, 839, 817, 800 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.75 (s, 12H), 6.79 (AA′BB′, 8H), 6.84 (AA′BB′, 4H), 6.99 (AA′BB′, 8H), 7.01 (AA′BB′, 4H), 7.38 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 158.0, 141.6, 138.6, 137.8, 134.6, 132.0, 131.0, 129.6, 127.3, 125.6, 113.2, 55.2. Compound **10**: (mp 171–173°C), IR (KBr) 2918, 2819, 1580, 1512, 1500, 1438, 1368, 1245, 1101, 823, 798, 760 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$): δ 3.35 (s, 12H), 4.39 (s, 8H), 6.81 (AA′BB′, 4H), 7.08 (m, 20H), 7.40 (m, 6H); ^{13}C NMR (75 MHz, $CDCl_3$): δ 141.8, 141.5, 138.6, 138.3, 137.9, 136.0, 131.9, 130.0, 129.9, 127.2, 125.6, 74.6, 58.2.
14. Data for **1**: White powder (mp 322–324°C), IR (KBr) 3408, 3050, 1654, 1608, 1514, 1450, 1224, 1172, 823, 802, 758 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 6.54 (AA′BB′, 8H), 6.83 (m, 12H), 7.32 (m, 8H), 7.41 (m, 2H), 9.26 (s, 4H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 156.2, 155.6, 142.6, 139.3, 137.3, 133.2, 132.7, 131.2, 128.4, 116.3, 115.0, 114.9; HRMS, calcd for $C_{48}H_{35}O_4$ (MH^+): 675.25354. Found: 675.25283.
15. Vinod, T. K.; Hart, H. *J. Org. Chem*. **1991**, *56*, 5631.
16. Data for **2**: White powder (dec. >350°C), IR (KBr) 3330, 2960, 1691, 1606, 1407, 1226, 1178, 1101, 826, 756 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 6.84 (AA′BB′, 4H), 7.19 (AA′BB′, 8H), 7.32 (AA′BB′, 4H), 7.46 (m, 4H), 7.48 (m, 2H), 7.75 (AA′BB′, 8H); ^{13}C NMR (75 MHz, DMSO-d_6): δ 167.7, 146.4, 141.3, 138.2, 138.1, 136.8, 132.4, 130.6, 130.3, 129.4, 129.1, 128.6, 125.5; HRMS, calcd for $C_{52}H_{35}O_8$ (MH^+): 787.23319. Found 787.23231.