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A Versatile Preparation of Geländer-Type *p*-Terphenyls from a Readily Available Diacetylenic Precursor

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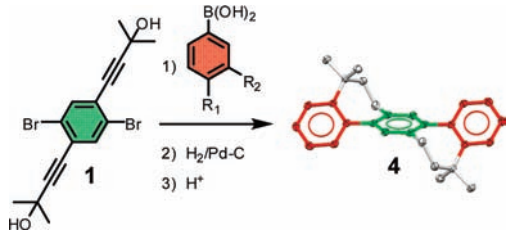
ABSTRACT



A series of doubly bridged *p*-terphenyls (4) have been synthesized utilizing a facile three-step synthesis starting from the readily available diacetylenic precursor (1) in excellent overall yields, and their structures were confirmed by $^{1}H/^{13}C$ NMR spectroscopy as well as by X-ray crystallography. The racemization barrier between the meso and chiral atropisomers of one of the derivatives of 4 was found to be ~12 kcal/mol by variable-temperature NMR spectroscopy. The versatility of the protocol developed herein was further demonstrated by the preparation of a quadruply bridged penta-*p*-phenylene derivative.

The doubly bridged *p*-terphenyls are helical ribbon-shaped molecules which have been coined the name "Geländer" owing to the similarity of the their shape with the banister of a spiral staircase, i.e., Figure 1.[1]

The helical biaryls, such as binaphthyls and biphenyls, have found widespread use as chiral ligands in modern asymmetric catalysis.[2] Although a multistep synthesis of Geländer-type terphenyls has been reported by Vögtle and co-workers,[1a] their potential either in asymmetric catalysis or for materials' applications, thus far, remains unexplored. The lack of applications of such doubly bridged *p*-terphenyls as well as bridged biphenyls may, in part, arise owing to the unavailability of a simple general synthesis.[3]

Figure 1. Showing the similarity of the shape of doubly bridged *p*-terphenyl with the helical ribbons and the banister of a helical staircase.

Herein, we report a versatile synthesis of a variety of doubly bridged *p*-terphenyls from a readily available diacetylenic precursor via a simple three-step route which involves high-yielding reactions, such as Suzuki coupling, catalytic hydrogenation, and intramolecular Friedel−Crafts alkylation (see Scheme 2). Various doubly bridged terphenyls, obtained in excellent overall yields, were characterized

(1) (a) Kiupel, B.; Niederalt, C.; Nieger, M.; Grimme, S.; Vogtle, F. *Angew. Chem., Int. Ed.* **1998**, *37*, 3031–3034. (b) Grimme, S.; Harren, J.; Sobanski, A.; Vogtle, F. *Eur. J. Org. Chem.* **1998**, *149*, 1–1509. (c) Also see :Hill, D. J.; Mio, M. J.; Prince, R. B.; Hughes, T. S.; Moore, J. S. *Chem. Rev.* **2001**, *101*, 3893–4011.

(2) (a) Koěovský, P.; Vyskoěil, S.; Smrèina, M. *Chem. Rev.* **2003**, *103*, 3213–3245. (b) Jeulin, S.; de Paule, S. D.; Ratovelomanana-Vidal, V.; Genêt, J.-P.; Champion, N.; Dellis, P. *Proc. Natl. Acad. Sci. U.S.A.* **2004**, *101*, 5799–5804. (c) Vachon, J.; Perollier, C.; Monchaud, D.; Marsol, C.; Ditrich, K.; Lacour, J. *J. Org. Chem.* **2005**, *70*, 5903–5911. (d) Goncalves-Farbos, M.-H.; Vial, L.; Lacour, J. *Chem. Commun.* **2008**, 829–831, and references cited therein.

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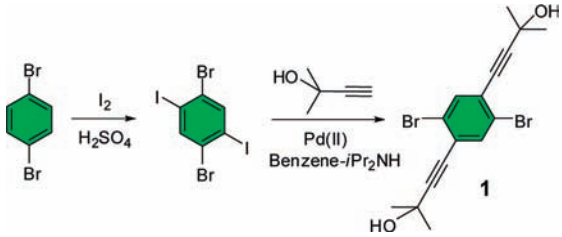
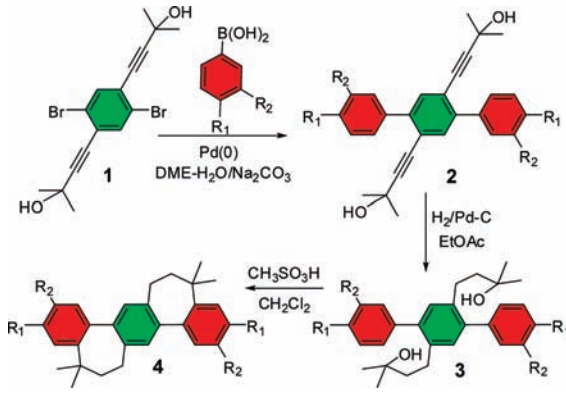
Scheme 1. Synthesis of Diacetylenic Precursor **1** for the Preparation of Geländer-Type *p*-Terphenyls



Scheme 2. Three-Step Synthetic Protocol for the Preparation of Geländer-Type *p*-Terphenyls from Diacetylenic Precursor **1**

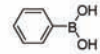
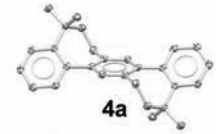
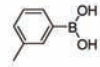
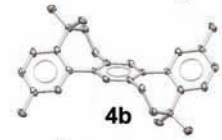
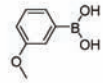
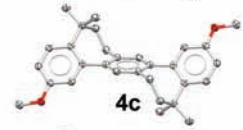
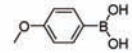
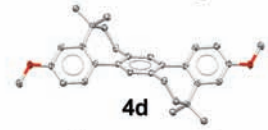
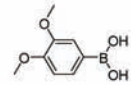
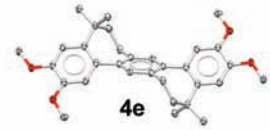
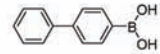
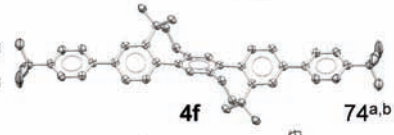
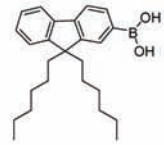
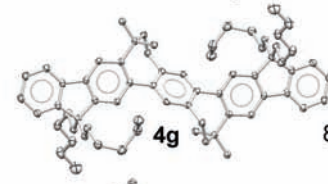
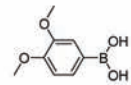
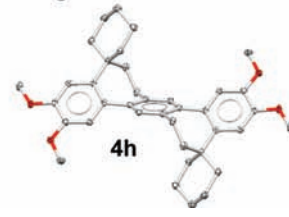


by NMR spectroscopy and by X-ray crystallography. Moreover, it is shown that these doubly bridged *p*-terphenyls, similar to the singly bridged biphenyls,[4] undergo a ready racemization at room temperature as probed by variable-temperature ^{1}H NMR spectroscopy and by DFT calculations. The details of these preliminary findings are described herein.

Thus, the common diacetylenic precursor **1** for the synthesis of doubly bridged *p*-terphenyls was easily obtained in excellent yield via a standard Sonogashira coupling[5] of the readily available 1,4-dibromo-2,5-diiodo-benzene[6] and 2-methyl-3-butyn-2-ol, i.e., Scheme 1.

Syntheses of the various doubly bridged *p*-terphenyls from **1** were accomplished via a three-step route as follows. Thus, a standard Suzuki coupling[7] of the diacetylenic precursor **1** with various aryl boronic acids (see Table 1) in the presence of a Pd(0) catalyst afforded the diacetylenic *p*-terphenyls (**2**), which in most cases were easily purified by a simple filtration

Table 1. Molecular Structures of Various Doubly Bridged *p*-Terphenyls Obtained by X-Ray Crystallography and Their Overall Yields in Three Steps

boronic Acid	product	%yield in 3 steps
	 **4a**	80[a]
	 **4b**	76
	 **4c**	85
	 **4d**	72[a]
	 **4e**	95
	 **4f**	74[a,b]
	 **4g**	80[c]
	 **4h**	94

[a] Yields include both the doubly bridged *p*-terphenyls **4** and the centrally cyclized isomer **5** (vide infra); i.e., **4a/5a**: 83:17; **4d/5d**: 38:62; **4f/5f**: 58:42. [b] **4f** did not afford single crystals, and thus a *tert*-butyl derivative was prepared by a reaction of **4f** with *tert*-butyl chloride and a catalytic amount of $FeCl_3$ (see Supporting Information).[9] [c] A single crystal of **4g** contained a 1:1 mixture of meso (shown) and d/l mixture (see text).

over a short pad of silica gel using a hexane/ethyl acetate mixture as the eluent. The resulting diacetylenic *p*-terphenyls (**2**) were then subjected to catalytic hydrogenation in ethyl acetate in the presence of 10% palladium on activated carbon as the catalyst. The resulting reduced terphenyls

(3) (a) Griffin, G. W.; Horn, K. A. *Org. Prep. Proc. Int.* **1985**, *17*, 187–190. (b) Muellen, K.; Heinz, W.; Klaemer, F. G.; Roth, W. R.; Kindermann, I.; Adamczak, O.; Wette, M.; Lex, J. *Chem. Ber.* **1990**, *123*, 2349–2371. (c) Pomerantz, M.; Dassanayake, N. L.; McManus, T. R.; Reynolds, C. H. *J. Org. Chem.* **1984**, *49*, 4029–4032.

(4) (a) Jaime, C.; Font, J. *J. Org. Chem.* **1990**, *55*, 2637–2644. (b) Mislow, K.; Glass, M. A. W.; Hopps, H. B.; Simon, E.; Wahl, G. H., Jr. *J. Am. Chem. Soc.* **1964**, *86*, 1710–1733.

(5) Sonogashira, K. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 3, pp 521−548.

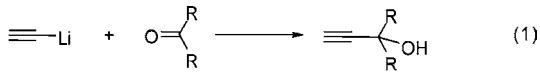
(6) 1,4-Dibromo-2,5-diiodobenzene is commercially available and can also be easily prepared from 1,4-dibromobenzene. See: Chanteau, S. H.; Tour, J. M. *J. Org. Chem.* **2003**, *68*, 8750–8766.

(7) (a) Suzuki, A. *Chem. Commun.* **2005**, 4759−4763. (b) Hassan, J.; Sevignon, M.; Gozzi, C.; Schulz, E.; Lemaire, M. *Chem. Rev.* **2002**, *102*, 1359–1469, and references therein.

(**3**) were then treated with methanesulfonic acid in dichloromethane at room temperature to afford the doubly bridged *p*-terphenyls via two facile intramolecular Friedel−Crafts cyclizations[8] (Scheme 2).

With the use of the protocol developed in Scheme 2, a variety of doubly bridged *p*-terphenyls were prepared in excellent overall yields (see Table 1) and their structures were established by $^{1}H/^{13}C$ NMR spectroscopy and further confirmed by X-ray crystallography (see Table 1).

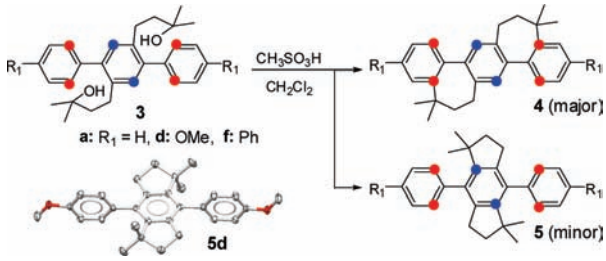
It is noteworthy that the use of 1-ethynyl-1-cyclohexanol instead of 2-methyl-3-butyn-2-ol (in Scheme 1) easily allows for the preparation of a biscyclohexyl derivative **4h** instead of the corresponding tetramethyl derivative **4e** (see Table 1 and Supporting Information for additional details). As such, the preparation of **4h** also demonstrates that the bridge substituents (i.e., dimethyl and cylohexyl in **4e** and **4h**, respectively) can be easily varied by employing an appropriate acetylenic tertiary alcohol, which, in turn, can be readily prepared by a reaction of the acetylene monoanion with the corresponding ketone, e.g., eq 1.



(1)

As shown in Scheme 3, the final step of the synthesis of the doubly bridged *p*-terphenyls (**4**) required that the

Scheme 3. Intramolecular Friedel−Crafts Cyclizations Leading to Seven-Membered vs Five-Membered Isomers



Friedel−Crafts cyclization must occur at the terminal aryls producing a pair of entropically less accessible seven-membered carbocycles. Indeed, the substrates which contained an activating para-substituent (i.e., at carbon 3) on the terminal aryls (i.e., **3b**, **3c**, **3e**, **3g**, and **3h**) exclusively produced the doubly bridged *p*-terphenyls (**4**), without contamination from the products (i.e., **5**, Scheme 3) formed via an alternative Friedel−Crafts cyclization onto the central aromatic ring producing the entropically favored five-membered carbocycles (i.e., Scheme 3).

Expectedly, in the case of *p*-terphenyl substrates (i.e., **3a**, **3d**, and **3f**), which do not contain an activating substituent at carbon 3 of the terminal aryl groups, the Friedel−Crafts cyclization also produced significant amounts of bisindano products (i.e., **5a**, **5d**, and **5f**) where the cyclization occurred at the central aromatic ring (see Scheme 3 and Table 1). Furthermore, the structure of a representative bisindano product (i.e., **5d**) was confirmed by X-ray crystallography (see Scheme 3).

To further confirm that the preferential formation of doubly bridged *p*-terphenyls (**4**), containing seven-membered carbocycles in Scheme 3, did not occur via an acid-catalyzed rearrangement of **5** to **4** or vice versa, samples of both **4a** and **5a** were subjected to the same acidic conditions employed for the Friedel−Crafts intramolecular cyclizations, and the course of the reactions was monitored by ^{1}H NMR spectroscopy over several days. Under these conditions, both **4** and **5** showed no signs of interconversion as judged by the ^{1}H NMR spectroscopic analysis of the aliquots after 3 and 6 days.

The DFT calculations at the B3LYP/6-31G* level[10] showed that two atropisomers of the doubly bridged *p*-terphenyls, i.e., the chiral syn atropoisomer (C_2) or the achiral anti (meso) astropoisomer (C_i), are almost isoenergentic (see Figure 2).

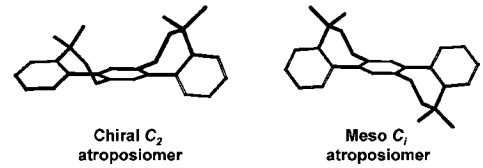


Figure 2. Structures of the two almost isoenergetic atropisomers of the doubly bridged *p*-terphenyl **4a** as obtained by DFT calculations at the B3LYP/6-31G* level.[10]

Interestingly, however, in the solid state almost all doubly bridged *p*-terphenyls showed the presence of only the centrosymmetric anti (meso) conformer with the dihedral angles between the central and peripheral aryl rings varying only in a very narrow range, i.e., 45.6−49.5°, as determined by X-ray crystallography (see Table 1). The exception is the fluoranyl-containing **4g** which contained a 1:1 mixture of both syn and anti atropisomers in a single crystal, i.e., the meso and chiral atropisomers (see Figure 3). The cocrystallization of both syn and anti conformers may, in part, arise owing to the fact that each half of the *syn*-**4g** was structurally identical to that of the *anti*-**4g** (see Figure 3) with the dihedral angles of 47.6 and 46.9° between the central aryl and fluoranyl rings.

The low activation barriers for the interconversion between the (isoenergetic) syn and anti conformers of the various doubly bridged *p*-terphenyls was apparent by the presence of broadened methyl signals in their ^{1}H NMR spectra at ambient temperatures (see Supporting Information and Figure 4).

Variable-temperature ^{1}H NMR spectroscopy of a representative doubly bridged *p*-terphenyl (**4e**) in dichloromethane-d_2 over a temperature range of +20 to −90 °C showed that

(8) Compare: Rathore, R.; Abdelwahed, S. H.; Guzei, I. A. *J. Am. Chem. Soc.* **2003**, *125*, 8712.

(9) Rathore, R.; Burns, C. L. *J. Org. Chem.* **2003**, *68*, 4071–4074.

(10) The DFT calculations were performed using Spartan 10.

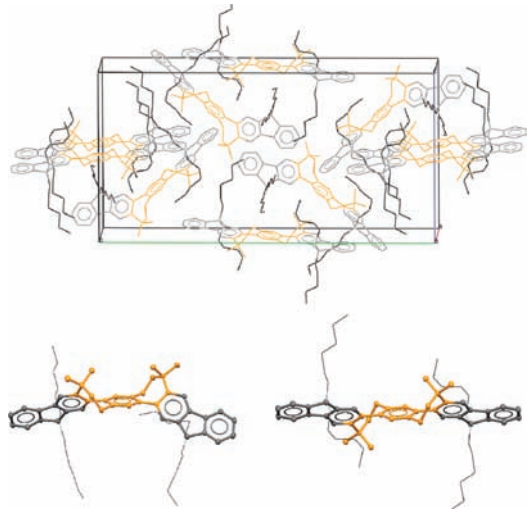


Figure 3. Isoenergetic conformers of **4g** obtained within a single crystalline sample.

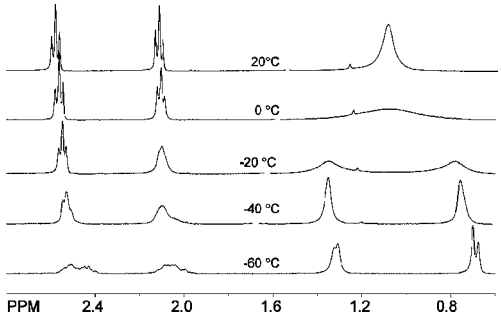


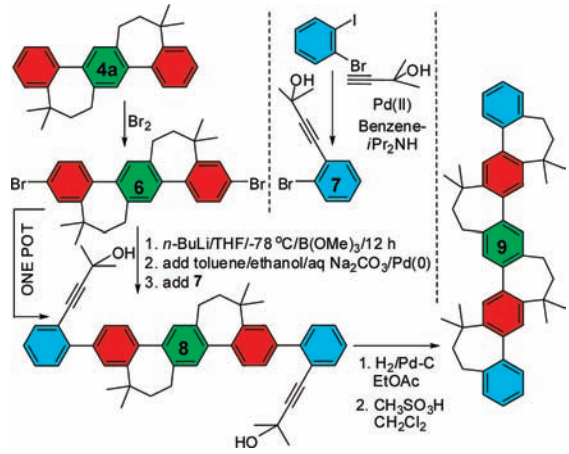
Figure 4. ^{1}H NMR spectra of the aliphatic region of *p*-terphenyl **4e** which show that the broadened signal (at ~1.1 ppm) due to four methyl groups splits into two sets of signals at ~−60 °C.

the interchange between the two isoenergetic conformers can be frozen at ~−60 °C, and the activation energy for the interchange into syn and anti conformers[11] was estimated to be $E_a \sim 12$ kcal mol^{-1} by line-shape analysis of the signals in the variable-temperature ^{1}H NMR spectra in Figure 4 (see additional details in the Supporting Information).

A substitution of the methyl groups in *p*-terphenyl **4e** with the cyclohexyl groups (i.e., **4h**) did not change the activation barrier (i.e., E_a ~11 kcal mol^{-1}) significantly for the interconversion between the two atropisomers. The broadened signals attributed to the cyclohexyl moiety, the methoxy peaks, and the aromatic peaks of **4h** resolved into two sets of signals at low temperatures (see Supporting Information for VT ^{1}H NMR spectra of **4h**).

The versatility of the synthetic protocol in Schemes 1 and 2 for the preparation of various doubly bridged *p*-terphenyls was readily extended for the preparation of a higher poly-*p*-phenylene homologue with fixed dihedral angles.[12] For example, a quadruply bridged penta-*p*-phenylene **9** was obtained in good overall yield by a one-pot Suzuki coupling of the dibromo derivative **6** with monoacetylenic precursor **7** to afford **8** followed by a simple hydrogenation and a reaction with methanesulfonic acid (Scheme 4). The dibromo derivative **6** was, in turn, obtained by a bromination of **4a**, while **7** was prepared by Sonogashira coupling according to Scheme 1.

Scheme 4. Preparation of Quadruply Bridged Penta-*p*-phenylene



In summary, we have developed a facile synthesis of the doubly bridged *p*-terphenyls from the readily available diacetylenic precursor (**1**) via three high-yielding synthetic steps. In most cases, the X-ray crystal structure analysis showed that the achiral (meso) atropoisomer preferentially crystallizes with the exception of **4g** whose crystalline samples contained both the achiral and chiral atropisomers within the same crystal. It was also shown by variable-temperature ^{1}H NMR spectroscopy that the interchange between the two atropisomers can be prevented at low temperatures. A successful synthesis of quadruply bridged penta-*p*-phenylene **9** was also accomplished which further demonstrates the versatility of the synthetic protocol in Schemes 1 and 2. The preparation of other higher homologues of bridged poly-*p*-phenylenes and the study of their optoelectronic properties is in progress and will be presented in due course.[12]

Acknowledgment. We thank the National Science Foundation (CHE-0848871) for financial support.

Supporting Information Available: Synthetic details, ^{1}H/^{13}C NMR data of various compounds, X-ray data, and VT ^{1}H NMR data. This material is available free of charge via the Internet at http://pubs.acs.org.

OL901938F

(11) Franco, G.; Alberti, A.; Guerra, M.; Seconi, G.; Vivarelli, P. Compare. *J. Chem. Soc., Perkin Trans. 2* **1976**, 173–178, and references cited therein.

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