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Ortho-Silylated Derivatives of Tetrakis(2-hydroxyphenyl)ethene: A Sterically Isolated Structural Model for Oxo-Surface Binding Domains

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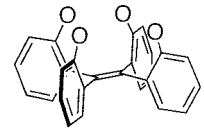
ABSTRACT

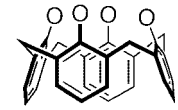
The introduction of sterically isolating *ortho*-trialkylsilyl, -aryldialkylsilyl, and -diarylalkylsilyl substituents onto the structurally preorganized tetrakis(2-hydroxyphenyl)ethene ligand framework has been accomplished by a 4-fold retro-Brook rearrangement. Installation of the most sterically demanding silyl substituents required the development of an iterative procedure, involving successive double silylation/metalation/migration sequences without the isolation of intermediates. This system was designed to function as a soluble structural model for the planar binding domains of heterogeneous "oxo-surfaces" of silica and alumina supports.

Structurally preorganized polydentate organic ligands provide metal coordination domains appropriate for a range of applications in catalysis, supramolecular chemistry, and materials science. Covalent and conformational constraints engineered into the ligand can predispose the nucleation of unusual and reactive coordination arrays inaccessible using conventional ligand designs.

The tetrakis(2-hydroxyphenyl)ethene ligand system[1] (**I**) is a differentially constrained analogue of the more familiar calix[4]arene structural class (**II**).[2] Despite considerable steric congestion, the ligand retains a significant degree of conformational mobility, undergoing rapid (but presumably correlated[3]) rotation at room temperature. In contrast to the calixarene macrocycle, the relatively rigid ethylene core of the tetrakis(2-hydroxyphenyl)ethene ligand inhibits inward collapse, promoting the assembly of bridged polymetallic coordination arrays over lower nuclearity chelated structures.[4]



I



II

The conformation that situates the four aryloxy rings perpendicular to the ethylene plane and the four oxygen residues in the same hemisphere, as shown in structure **I**, provides a roughly square planar arrangement of the aryloxy binding sites and a coordination environment that models the "oxo-surface" of standard heterogeneous metal oxide supports such as silica and alumina. The relatively acidic phenolic hydroxy groups are only marginally less acidic than

(1) (a) Verkerk, U. H.; Fujita, M.; Dzwiniel, T. L.; McDonald, R.; Stryker, J. M. *J. Am. Chem. Soc.* **2002**, *124*, 9988–9989. (b) Fujita, M.; Qi, G.; Verkerk, U. H.; Dzwiniel, T. L.; McDonald, R.; Stryker, J. M. *Org. Lett.* **2004**, *6*, 2653–2656. Improved synthesis: (c) Chung, M.-K.; Qi, G.; Stryker, J. M. *Org. Lett.* **2006**, *8*, 1491–1494. (d) Chung, M.-K.; Fancy, P.; Stryker, J. M. *Can. J. Chem.* **2006**, *84*, 1250–1253.

(2) Gutsche, C. D. *Calixarenes Revisited*; Royal Society of Chemistry: Cambridge, England, 1998, and references therein.

(3) Mislow, K. *Acc. Chem. Res.* **1976**, *9*, 26–33, and references therein.

(4) (a) Floriani, C. *Chem.−Eur. J.* **1999**, *5*, 19–23. and references therein. (b) Giannini, L.; Guillemot, G.; Solari, E.; Floriani, C.; Re, N.; Chiesi-Villa, A.; Rizzoli, C. *J. Am. Chem. Soc.* **1999**, *121*, 2797–2807.

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many surface silanol residues, and the rotational flexibility allows for the accommodation of a range of main group and transition metal elements.

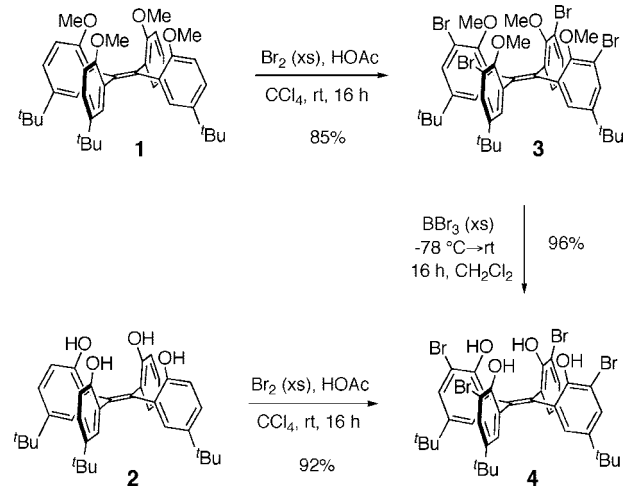
For applications to catalysis, steric isolation of the binding sites is essential to directing metal coordination, inhibiting intermolecular aggregation, and the formation of sandwich structures lacking surface-like character.[5] To this point, however, the largest substituent that has been successfully installed adjacent to the hydroxy functionality is the *n*-propyl group, which was introduced by a 4-fold Claisen rearrangement of tetrakis(2-allyloxyphenyl)ethene followed by standard catalytic hydrogenation.[1a] While this classical procedure is highly efficient (>80% overall starting from the unsubstituted ligand), the introduction of sterically larger *ortho*-substituents with equal efficiency represents a substantial synthetic challenge.[6]

In this communication, we report the use of the retro-Brook rearrangement[7] for the simultaneous installation of four trialkylsilyl or aryldialkylsilyl substituents onto the tetrakis(2-hydroxphenyl)ethene ligand framework. Under optimized conditions, this intramolecular 1,3-migration reaction can be conducted on a substantial scale and proceeds in remarkably high yields. The resulting tetrakis(2-hydroxy-3-silylphenyl)ethene derivatives have been characterized both spectroscopically and, for the trimethylsilyl derivative, by X-ray crystallography.[8]

Application of the retro-Brook rearrangement to the tetrakis(2-hydroxphenyl)ethene structural class requires efficient halogenation *ortho* to the phenoxy residues. To avoid issues of regioselectivity,[9] the synthesis begins with derivatives bearing 5-*tert*-butyl substituents in each arene residue.[1a,c] These compounds are prepared in high yield on a multigram scale via the McMurry olefination of bis(5-*tert*-butyl-2-methoxyphenyl)methanone.[1c,10]

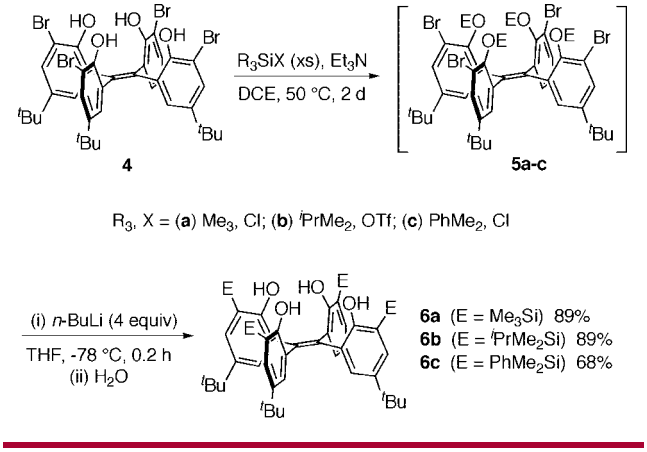
Bromination of either tetrakis(5-*tert*-butyl-2-methoxyphenyl)ethene **1** or tetrakis(5-*tert*-butyl-2-hydroxyphenyl)ethene **2** proceeds under conventional conditions,[11,12] giving tetrakis(3-bromo-5-*tert*-butyl-2-methoxyphenyl)ethene **3** or tetrakis(3-bromo-5-*tert*-butyl-2-hydroxyphenyl)ethene **4**, respectively, cleanly and in high yield (Scheme 1). Despite the dense functionality, NMR spectroscopic analysis at room temperature reveals no evidence of restricted rotation in either system.

Scheme 1



The retro-Brook sequence is initiated by exhaustive *O*-silylation (Scheme 2). For sterically small silyl derivatives, the simple chlorosilane is sufficiently reactive to provide quantitative conversion. Reactions using the more hindered silyl derivatives, however, require the use of the corresponding silyl triflate reagents for optimal conversion.[13] The

Scheme 2



(5) Verkerk, U. H.; McDonald, R.; Stryker, J. M. *Can. J. Chem.* **2005**, *83*, 922–928.

(6) The introduction of *tert*-butyl substituents to either tetrakis(2-hydroxyphenyl)ethene or tetrakis(5-*tert*-butyl-2-hydroxyphenyl)ethene via Friedel-Crafts alkylation using a range of standard synthetic procedures invariably produces intractable mixtures of *tert*-butylated products and cannot be driven to completion.

(7) (a) Brook, A. G. *Acc. Chem. Res.* **1974**, *7*, 77–83. (b) Wright, A.; West, R. *J. Am. Chem. Soc.* **1974**, *96*, 3214–3222, and 3227−3232. (c) Linderman, R. J.; Ghannam, A. *J. Am. Chem. Soc.* **1990**, *112*, 2392–2398. Review: (d) Moser, W. H. *Tetrahedron* **2001**, *57*, 2065−2084. Phenolic cases: (e) Simchen, G.; Pfetschinger, J. *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 428–429. (f) Billedeau, R. J.; Sibi, M. P.; Snieckus, V. *Teterahedron Lett.* **1983**, *24*, 4515–4518. (g) Maruoka, K.; Itoh, T.; Araki, Y.; Shirasaka, T.; Yamamoto, H. *Bull. Soc. Chem. Jpn.* **1988**, *61*, 2975–2976. (h) Thadani, A. N.; Huang, Y.; Rawal, V. H. *Org. Lett.* **2007**, *9*, 3873–3876.

(8) Detailed experimental procedures and complete characterization data are provided as Supporting Information.

(9) None of the methodologies reported for selective *ortho*-bromination of 4-unsubstituted phenols was sufficiently selective for adaptation to this substrate. See, for example: (a) Posner, G. H.; Canella, K. A. *J. Am. Chem. Soc.* **1985**, *107*, 2571–2573. (b) Beak, P.; Brown, R. A. *J. Org. Chem.* **1977**, *42*, 1823–1824.

(10) Chung, M.-K.; Stryker, J. M. *Inorg. Synth.*, in press.

(11) Majetich, G.; Hicks, R.; Reister, S. *J. Org. Chem.* **1997**, *62*, 4321–4326.

(12) (a) Despite a previous report,[12b] the bromination of **2** using a Br_2/DMSO reagent was neither clean nor reproducible upon scale-up. In addition, a procedure reported for the bromination of **1** was not adaptable to large scale. (b) Verkerk, U. Ph.D Dissertation, 2002.

(13) (a) ^{t}BuMe$_2$SiOTf: Corey, E. J.; Cho, H.; Rucker, C.; Hua, D.-H. *Tetrahedron Lett.* **1981**, *22*, 3455–3458. (b) ^{i}PrMe$_2$SiOTf: Olah, G. A.; Laali, K.; Farooq, O. *Organometallics* **1984**, *3*, 1337−1340. (c) Ph$_2$MeSiOTf; Uhlig, W. *J. Organomet. Chem.* **1993**, *452*, 29–32.

intermediate silyloxy derivatives **5a**−**c**, homogeneous by analytical TLC analysis, were isolated by filtration through a short column of silica gel but not further purified or characterized.

Metalation of the silyloxy compounds **5a**−**c** with *n*-BuLi at low temperature initiates the 4-fold retro-Brook rearrangement, providing the corresponding tetrakis(5-*tert*-butyl-2-hydroxy-3-silylphenyl)ethenes **6a**−**c** in excellent overall yield. The *ortho*-silylated compounds were obtained as amorphous white solids after isolation and purification by chromatography on silica gel. Despite the markedly increased steric bulk, the silyl derivatives showed no evidence for restricted rotation at room temperature by NMR spectroscopy. At low temperature, however, ^{1}H NMR spectroscopy of **6a** (−60 °C, toluene-d_8) revealed a complex mixture of static rotational isomers but no obvious energetic bias toward any one conformation.

Although resistant to crystallization, single crystals of the trimethylsilyl derivative **6a** were obtained as colorless blocks by slowly cooling a hot benzene solution. The solid state structure was determined by X-ray crystallography (Figure 1),[8] revealing a conformational preference for the rotational

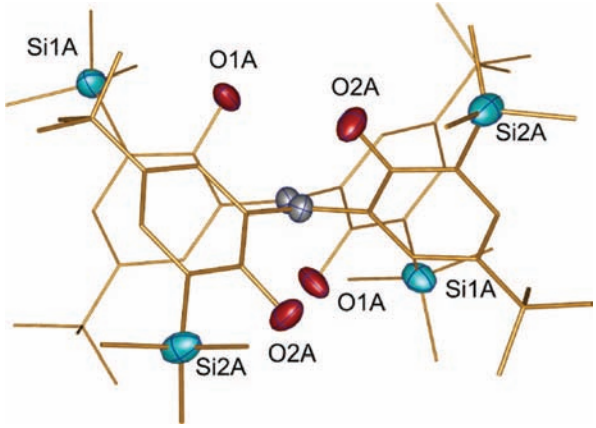
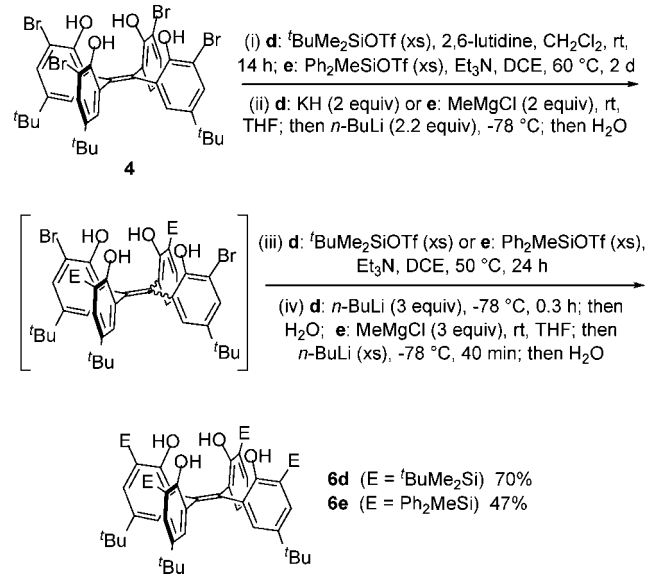


Figure 1. Solid state molecular structure of tetrakis(5-*tert*-butyl-2-hydroxy-3-trimethylsilylphenyl)ethene **6a**. All hydrogen atoms have been omitted for clarity. Thermal ellipsoids are shown at the 20% probability level. Nonbonding distance between O1A and O2A: 5.560 Å. Final residuals: $R_1 = 0.0586$. w$R_2 = 0.1741$.

isomer that places the two hydroxy groups from mutually *trans*-phenolic residues on opposite faces of the ethylene plane. In contrast to the unsubstituted tetrakis(2-hydroxyphenyl)ethene,[1a] neither intramolecular nor intermolecular hydrogen bonding is observed for the sterically isolated functionality. In the absence of self-association, the observed solid state conformation is, presumably, that which minimizes the net molecular dipole for the system.

Perhaps unsurprisingly, exhaustive *O*-silylation is problematic for sterically larger silanes. After considerable optimization, however, an iterative protocol has been developed that allows for the efficient preparation of tetrakis(*ortho*-silylated) compounds bearing very large silyl functionalities. In this procedure, an initial nonspecific bis(silylation) reaction

Scheme 3



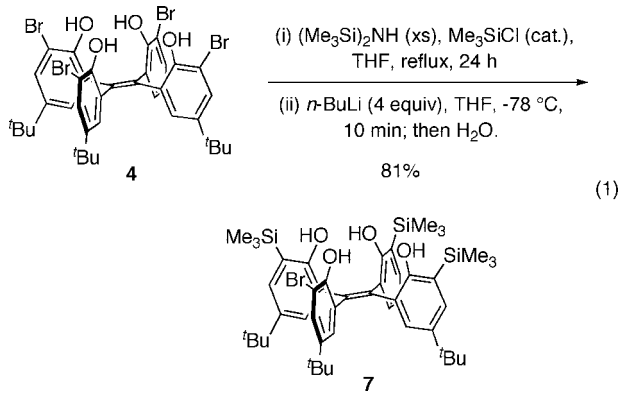
is conducted under relatively mild conditions (Scheme 3). After deprotonating the remaining free phenolic residues using a nonmetallating base (KH or MeMgCl), the retro-Brook rearrangement at the silylated sites is triggered by the addition of *n*-BuLi (2 equiv) at low temperature, followed by a water quench. Without purification, the partial silylation/migration protocol is then repeated, providing the *ortho*-silylated products **6d**,**e** in very reasonable overall yields.

Under these conditions, the intial double metal/halogen exchange reaction is highly selective for the silyloxy sites, leaving intact the arylbromide functionality adjacent to the remaining alkoxide residues. The "preemptive" deprotonation of the nonsilylated phenols is a precautionary measure designed to avoid competitive metalation and destructive protonation at nonsilylated phenolic residues. This step provides only a marginal improvement in the yield of the *tert*-butyldimethylsilyl derivative **6d** but raises substantially the yield of the methyldiphenylsilylated product **6e**. This suggests that only in the latter case does the metal/halogen exchange reaction become competitive with the deprotonation of unsilylated phenols, leading to some nonproductive quenching of metallated intermediates.

It is equally noteworthy that the second iteration of the silylation is highly selective for the remaining bromide-bearing residues: no evidence for competitive silylation of the presumably more sterically encumbered *ortho*-silylated phenols is observed. The attenuated yield obtained for the methyldiphenylsilyl derivative can be tentatively ascribed to the reversible nature of the retro-Brook rearrangement for electron-deficient silanes,[7d] suggesting a natural electronic limit to the scope of this methodology.

The extension of the *ortho*-silylation protocol to partial substitution of the ligand periphery addresses the synthesis of differentially functionalized derivatives, which further enhances the potential for applications development. To this end, we report that the silylation of tetrakis(3-bromo-5-*tert*-

butyl-2-hydroxyphenyl)ethene **4** in the presence of excess hexamethyldisilazane[14] proceeds selectively to the tris(trimethylsilylated) derivative. Without purification, treatment of this intermediate with excess *n*-BuLi leads to the isolation of the tristrimethylsilylated product **7** (81%), accompanied by a minor amount of tetrakis(5-*tert*-butyl-2-hydroxy-3-trimethylsilylphenyl)ethene **6a** (6%) (eq 1). Further investigation of selective partial silylation reactions is in progress.



(1)

The high efficiency of this *ortho*-silylation protocol offers considerable promise for developing applications of this polydentate ligand system in catalysis and supramolecular chemistry. The use of this soluble platform to model the coordination chemistry and catalytic reactions mediated by polymetallic arrays coordinated to heterogeneous supports will be reported in due course.

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Supporting Information Available: Experimental procedures and complete characterization data for all new compounds and details of the X-ray crystallography for compound **6a**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(14) Gautret, P.; El-Ghammarti, S.; Legrand, A.; Couturier, D.; Rigo, B. *Synth. Commun.* **1996**, *26*, 707–713.