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Novel *meta*-Selective Friedel–Crafts Acylation of Phenylsilsesquioxane

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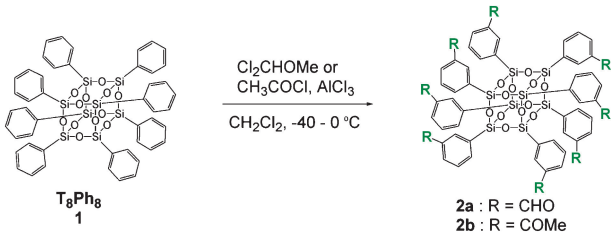
The Friedel–Crafts acylation of octaphenylsilsesquioxane (T_8Ph_8) (**1**) with Cl_2CHOCH_3 or CH_3COCl at low temperature followed by subsequent hydrolysis provided the octakis(*m*-acylphenyl)octasilsesquioxanes ($T_8(C_6H_4R\text{-}m)_8$); R = CHO (**2a**) and R = $COCH_3$ (**2b**) in high yields. The remarkable *meta*-selectivity of **2a** and **2b** in more than 99:1 and 93:7 *meta*/*para* ratios was confirmed by ^{1}H NMR and X-ray analyses, and further elucidated via theoretical calculations.

Polyhedral oligomeric silsesquioxanes (POSSs)[1a] represented by the formula $(RSiO_{3/2})_n$ (n = 6, 8, 10, 12, ...) have been intriguing the scientific community for over half a century. The octahedral octasilsesquioxanes (T_8), having a cubic Si_8O_{12} cage with a variety of functional groups attached to each silicon vertex, are of especially significant importance due to their highly symmetric rigid framework and multifunctionality. These functionalized octasilsesquioxanes (T_8) have shown great potential for many applications such as supports for transition-metal catalysts,[1b] liquid crystals,[1c] dendrimers,[1d–1f] and network solids.[1g] Because of this wide variety of potential applications, the need for a variety of functionalized silsesquioxanes has increased.

Functionalization of octasilsesquioxanes (T_8) has generally been achieved via either hydrosilylation of octahydridosilsesquioxane (T_8H_8),[2] the Heck coupling and cross-metathesis of octavinylsilsesquioxane ($T_8(CH{=}CH_2)_8$),[3] or substitution or cross coupling of octabenzyl- and octaarylsilsesquioxanes ($T_8(C_6H_4X)_8$, X = CH_2I and I).[4] An alternative pathway to functionalized octasilsesquioxanes (T_8) was demonstrated by the electrophilic substitution of octaphenylsilsesquioxane (T_8Ph_8) to give $T_8(C_6H_4R)_8$ (R = NO_2, Br, and SO_3H).[5,6] However, electrophilic substitution often gives limited substitutional selectivity. For example, nitration of T_8Ph_8 in fuming nitric acid gives a 20:65:15 *ortho*:*meta*:*para* mixture of $T_8(C_6H_4NO_2)_8$. Bromination of T_8Ph_8 gives a 20:15:65 *ortho*:*meta*:*para* mixture of $T_8(C_6H_4Br)_8$,[5b] although iodination of T_8Ph_8 with ICl at −40 °C gives $T_8(C_6H_4I\text{-}p)_8$ with >93% *para*-substitution.[4b] Here we have found a novel *meta*-selective Friedel–Crafts formylation, as well as the acylation of T_8Ph_8 (**1**), toward a goal of the functionalization of silsesquioxane by acyl groups, as shown in Scheme 1.

In the first experiment, Cl_2CHOCH_3 (6.0 mmol) in ca. 10-mL CH_2Cl_2 was added dropwise into a ca. 30-mL CH_2Cl_2 solution of octaphenylsilsesquioxane (**1**) (T_8Ph_8, 4.0 mmol based on Ph groups) and $AlCl_3$ (4.0 mmol). After 2 h of stirring at 0 °C, subsequent hydrolysis provided a mixture of formylated products $T_8(C_6H_4CHO)_n(Ph)_{8-n}$ (n = 1–8), as shown in Table 1 (Run 1 and Scheme 1). The 96:4 *meta*/*para* ratio of the formylated products was determined by ^{1}H NMR integration of the formyl proton at around 10.0 ppm.[6] When the temperature was reduced from 0 to −40 °C, this high *meta*/*para* ratio further increased to more than 99:1 (Run 2 in Table 1). However, both yields were still low (21% and 41% yields determined by ^{1}H NMR) as evidenced by recovered SiPh groups observed in the ^{1}H NMR spectra of the crude mixtures.[6] In order to improve the yields, larger amounts of Cl_2CHOCH_3 and $AlCl_3$ were used at the same temperature (−40 °C), as shown in Table 1 (Runs 3 and 4). The use of 2.0 equivalents of Cl_2CHOCH_3 and 4.0 equivalents of $AlCl_3$ resulted in 86% yield, and octakis(*m*-formylphenyl)octasilsesquioxane (**2a**) was obtained in 70% isolated yield (>99:1 *meta*/*para*) by column chromatography.[6] In the ^{1}H NMR spectrum of **2a**, the spin-coupling pattern of the aromatic protons at 8.34 (s), 8.03 (d), 8.01 (d), and 7.61 (t) ppm confirmed assignment of the *meta*-substituted structure.[6] Crystallization of **2a** from mixed solvent of chloroform and hexane gave crystals suitable for X-ray analysis, which disclosed eight *meta*-formyl groups attached to each vertex of the T_8 cage, as shown in Figure 1a.[6]



Scheme 1. *meta*-Selective acylation of T_8Ph_8.

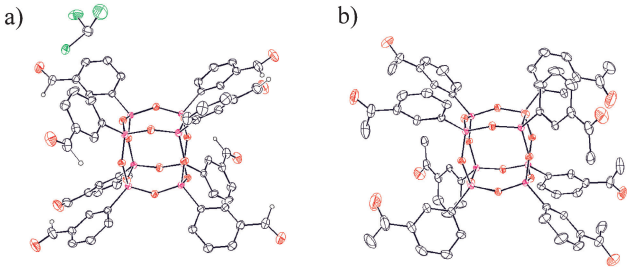


Figure 1. X-ray structures of (a) **2a**·$CHCl_3$ and (b) **2b**. All ellipsoids are shown at the 30% probability level. Hydrogen atoms are omitted for clarity except for the formyl proton in **2a**.

The acetylation of T_8Ph_8 (**1**) was also carried out using CH_3COCl, giving a mixture of acetylated products $T_8(C_6H_4COCH_3)_n(Ph)_{8-n}$ (n = 1–8). The results are summarized in Table 1 (Runs 5–8 and Scheme 1). The *meta*/*para* ratio was determined by ^{1}H NMR integration of the acetyl methyl protons at around 2.5 ppm.[6] Although the use of the optimized formylation reaction conditions gives a high *meta*/*para* ratio (>99:1), the yield is unacceptably low, as shown in Table 1 (Run 5). When the reaction temperature was raised from −40 °C

Table 1. Acylation condition and yields of **2a** and **2b**

Run	Reagent	(equiv)[a]	$AlCl_3$[a]	Temp/°C	Time/h	*meta*/*para*	Conversion[b]
1	Cl_2CHOMe (**2a**)	1.5	1.0	0	2	96/4	21.0
2		1.5	1.0	−40	4	>99/1	41.0
3		2.0	2.0	−40	4	>99/1	76.5
4		2.0	4.0	−40	4	>99/1	86.8 (70.3)[c]
5	CH_3COCl (**2b**)	2.0	4.0	−40	4	>99/1	5.7
6		2.0	4.0	−20	4	98/2	50.9
7		4.0	4.0	0	4	92/8	90.4 (72.9)[c]
8		4.0	4.0	0	16	93/7	99.5 (90.2)[c]

[a]Based on Ph group. [b]Yields of acylated phenyl groups determined by ^{1}H NMR. [c]Isolated yields of $T_8(C_6H_4R)_8$ (R = CHO and $COCH_3$).

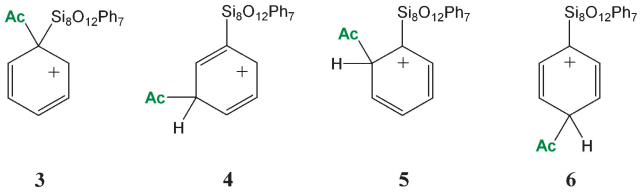


Figure 2. σ-Complexes for the acetylation reaction of T_8Ph_8.

to −20 to 0 °C, the yield increased from 5% to 50% to 90% (Runs 6 and 7). Finally, elongation of reaction time from 4 and 16 h led the acetylated product in 99% yield (Run 8). Even at 0 °C, the *meta*/*para* ratio (93:7) was slightly decreased. Purification of the acetylated products by column chromatography gave pure octakis(*m*-acetylphenyl)octasilsesquioxane (**2b**) in 90% isolated yield. Similar to **2a**, the ^{1}H NMR showed aromatic protons at 8.38 (s), 8.07 (d), 8.00 (d), and 7.53 (t) ppm,[6] and X-ray analysis revealed that substitution of each of the eight phenyl groups of the T_8 cage occurred at the *meta*-position, as shown in Figure 1b.[6]

Although a few alternative studies of *meta*-functionalization have been reported recently,[7] no *meta*-substitution via traditional Friedel–Crafts reaction has been discussed. In order to understand the *meta*-selectivity, four different methods were used to calculate the charge density for the aromatic rings in the T_8Ph_8 and related phenylsilanes such as $PhSiMe_3$, $PhSiCl_3$, and $PhSi(OMe)_3$.[6] All calculations show the highest negative charge at the *ipso*-position, and the second highest at the *meta*-position from the silyl-substituent.[6] When the acyl cation cannot attack the *ipso*-position sterically and electronically to afford the σ-complex **3**, the reaction occurs at the *meta*-position to give **4** (Figure 2), a trend which has precedents.[6] Thus, the σ-complex **4** derived from *meta* attack of the acyl cation is stabilized by σ–π conjugation compared to other σ-complexes **5** and **6** derived from *ortho*- and *para* attack leading exclusively to *meta*-substitution (Figure 2).[8]

In conclusion, a unique *meta*-selective Friedel–Crafts formylation and acetylation of octaphenylsilsesquioxane (T_8Ph_8) has been accomplished. The reasons for the *meta*-selectivity are understood in terms of the charge density of the aromatic ring as well as stabilization of the σ-complex intermediate.

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8 In contrast to the charge-controlled reaction of a hard elecrophile such as $ClCHOCH_3^+$, CH_3CO^+, and NO_2^+, soft electrophile such as Br^+ and I^+ probably undergo a frontier orbital controlled reaction to affored *ortho*, *para*-selectivity. Summary of regio selectivity of electrophilic aromatic substitution to phenylsilanes is also involving Supporting Information.[6]

