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Synthesis of Distorted 1,8,13-TrisilyI-9-hydroxytriptycenes via Triple Cycloaddition of Ynolates to 3-SilyIbenzynes

Tatsuro Yoshinaga,^[a] Takumi Fujiwara,^[a] Takayuki Iwata,^[b] and Mitsuru Shindo*^[b]

Abstract: 1,8,13-Trialkyl(aryl)silyl-9-hydroxytriptycenes (trisilyltriptycenes) were synthesized via the triple addition of ynolates and 3-silylbenzynes with high regioselectivity. Benzene rings in the resulting triptycenes were highly distorted where the dihedral angles between the substituents were as high as 35°. The distortion energy induced step-by-step halogenation reactions to yield halogenated triptycenes, including chiral triptycenes. The 1,8,13-trihalogenated triptycenes were then converted to 1,8,13-functionalized triptycenes.

Triptycene is a rigid and symmetric propeller shaped organic molecule with a bicylo[2.2.2]octatriene skeleton.¹ Because of these special properties, triptycenes have been used as basic units of host molecules in the field of molecular recognition,² supramolecular chemistry,³ macromolecules,⁴ material sciences,⁵ and metal ligands⁶. However, functionalized triptycenes are not easily obtained because major synthetic methods for triptycenes are limited to cycloaddition of benzyne⁷ or benzoquinone⁸ to anthracenes. Thus, it is difficult to prepare these starting materials with specific substituents. This synthetic limitation is a critical drawback for syntheses of functionalized designed triptycenes.

Recently, we developed a sequential triple addition reaction of ynolates⁹ to arynes to form triptycenes, where three arynes are formally condensed to an ynolate, along with cleavage of the triple bond in one pot (Scheme 1(a)).¹⁰ When substituted arynes are used as a substrate, functionalized and/or pre-functionalized triptycenes can be prepared. In a previous report, we also described the selective synthesis of 1,8,13-trimethoxytriptycenes (X = OMe) using 3-methoxybenzyne, highlighting the secondary orbital interactions as a major controlling factor of the selectivity in addition to the inductive effect¹¹ and distortion model.¹² It should be noted that the 1, 8, and 13-positions are located on the same plane (blue triangle in Scheme 1(b)) and the substituents at these positions are oriented vertically from the plane. Although this unique structure could be used as a platform for functionalized triptycenes,¹³ efficient synthetic methods for this type of triptycene have rarely been reported. This triple addition method can be applied to the short-step synthesis of functionalized triptycenes.

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Silylarenes are frequently used as powerful synthetic tools in synthetic organic chemistry because their silyl groups can be converted into other substituents. If silylarynes could be applied to the triple addition, the resulting triptycenes would be useful as precursors for functionalized triptycenes. However, these silylarynes have not only been used in a few organic syntheses.^{14,15} Herein, we report the selective synthesis of highly distorted 1,8,13-trisilyltriptycenes via reaction of ynolates and 3-silylbenzynes, and their subsequent conversion into 1,8,13-substituted triptycenes (Scheme 1(b)).





Scheme 1. Triple cycloaddition reaction of benzynes to ynolates.

The readily available 1-fluoro-2-trimethylsilyl(TMS)benzene 2^{16} was selected as a precursor for 3-trimethylsilylbenzyne because it can be prepared using simple methods (ortholithiation followed by β -elimination). In addition, this synthesis can be achieved without generation of reactive side products such as alkyl halides. Initially, we examined the reaction of an ynolate, prepared via double lithium-halogen exchange of dibromoester 1^{17} with 3-trimethylsilylbenzyne,¹⁸ prepared by the addition of *sec*-BuLi, which would be better than labile *tert*-BuLi or less reactive *n*-BuLi, to **2** at -20 °C. After 1 h, the reaction was worked up,

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yielding a small amount of tris(TMS)-substituted triptycene **3aa** among many side products (Table 1, entry 1). Therefore, we decided to optimize the reaction conditions. After screening the addition time and temperature (entries 2–5), the relatively slow addition of *sec*-BuLi at 0 °C yielded the best result, providing 42% tris-TMS-triptycene **3aa** (entry 4). Remarkably, the "all-*syn*" product was the most abundant, with three trimethylsilyl groups positioned at C1, C8, and C13, all of which were oriented on the same side of the hydroxy group at C9, as illustrated in **3aa**. No other isomers were detected, as they would be generated in small amounts if at all. Major side products were oligomers of arenes, derived from arynes. Thus, this reaction could be used for highly regioselective synthesis.

Table 1. Synthesis of tris(TMS)-substituted triptycene 3aa.

Me Br Br 1	t-BuLi (4.0 equiv) THF -78 °C to 0 °C	SiMe 2a (6.0 equiv)	sec-BuLi (5.0 equiv) over t min T °C, 1 h Me	Me ₃ Si Me ₃ Si Me ₃ Si Me ₃ Si Me ₃ Si Me ₃ Si
Entry	Т		t (min)	Yield (%)
1	-20 °C		5	23
2	0°0		3	27
3	0 °C		30	39
4	0 °C		60	42 ^[a]
5	rt		3	0

[a] 10 mmol scale, 5.0 equiv of **2a** was used.

This **3aa** product contained three sets of sterically crowded trimethylsilyl groups densely packed on the face of the rigid structure of triptycene. X-ray crystal structure analysis of **3aa** indicated that the dihedral angle of Si-C1-C9a-C9 was 21.7° and the internal angles of benzene were 115.2° and 123.4°, showing pronounced distortion (Figure 1, Table 2). This is likely due to the steric congestion between the TMS groups because, in contrast, the benzene rings of the 1,8,13-non-substituted triptycenes exhibited negligible distortion, with dihedral angles of <5°.¹⁹



Figure 1. X-ray crystallographic analysis of 3aa (a) upper view, (b) side view.

Encouraged by this result, we synthesized triptycenes with more sterically hindered silyl groups via triple addition reaction.

As shown in Table 2, we successfully isolated ethyldimethylsilyl-(3b), dimethylphenyl- (3c), tert-butyldimethylsilyl- (3d) and methyldiphenylsilyl- (3e) triptycenes with high regioselectivity in good to moderate yields as major products. Furthermore, the extremely sterically congested triethylsilyl-(**3f**) and triisopropylsilyl- (3g) triptycenes were obtained. According to the X-ray crystal structures of these products, all prepared triptycenes were highly distorted because of the non-planar phenyl groups and dissymmetrical hexagons. Particularly, the most distorted triptycene 3g exhibited a maximum Si-C1-C9a-C9 dihedral angle of 35.4°. The C2-C1-C9a bond angles (a) of the benzene rings were 111.7-115.2°, approximately 5% smaller than that of benzene, while the C1-C2-C3 bond angles (f) were 123.0-126.0°, approximately 5% wider than those of the less distorted triptycenes (5C-Br and 9,10-dimethyltriptycene¹⁹ in Table 2) and benzene. The C1-C2, C1-C9a, and C9a-C4a bond lengths in the benzene rings were 1.40–1.41 Å, slightly longer than 1.39 Å in benzene but similar to that of a non-substituted triptycene (see SI). These structural analyses indicated the highly distorted character of the prepared benzene rings. The distances between O and Si atoms were 3.05-3.32 Å, less than the sum of the van der Waals radii of the two atoms (1.52 Å (O) + 2.10 Å (Si) = 3.62 A) suggesting a penta-coordinate silicon character.

 Table 2. Synthesis and selected crystal structure data of the prepared trisilyltriptycenes (see also SI).

Me + SiR₃ Sec-BuLi (5.0 equiv) \overline{HF} $0 \degree \text{C}, 1 \text{ h}$ $R_3 \text{Si}$ $R_3 \text{Si}$

SiR ₃	Yield	Si-O	Dihedral	Bond angles [°]
(3)	(%)	[Å]	angles [°]	a f
SiMe₃ (3aa)	42	3.08	21.7	115.2, 123.4,
SiMe₂Et (3b)	39	3.14 3.14 3.24	19.3 19.3 0	115.2, 123.6 115.2, 123.6 114.8, 123.7
SiMe₂Ph (3c)	13	3.06 3.11 3.12	20.9 24.4 26.9	115.1, 123.3 115.1, 123.0 115.2, 123.1
SiMe₂ <i>t</i> -Bu (3d)	50	3.29 3.29 <u>3.29</u> 3.20	23.7 15.0 20.1 13.4	114.8, 124.0 114.2, 125.3 115.5, 123.2 111.7, 126.0
		3.23 3.32	18.0 15.5	114.9, 123.9 115.4, 123.7
SiMePh₂ (3e)	21	3.13 3.14 3.19	18.2 15.8 12.2	115.6, 123.1 115.5, 122.8 115.2, 123.7
SiEt ₃ (3f)	52	3.05 3.13 <u>3.17</u> 3.08 3.19	16.5 16.2 29.5 31.9 30.7	114.3, 124.2 115.1, 124.0 115.3, 123.5 115.0, 123.5 115.2, 123.1
		3.29 3.21	18.4 35.4	114.8, 124.2
Si(<i>i</i> -Pr) ₃ (3g)	2	3.21 3.27	29.0 34.7	114.8, 123.4 114.8, 123.2
Br (5C-Br)ª	-	-	6.74 6.74 0	121.3, 120.1 121.3, 120.1 121.5, 119.4
9 10-diMe ^b			0.35	119.8 120.5

3 Si-O distance

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^[a]Discussed below. ^[b]X-ray crystallographic data was obtained from CCDC246642.

Ynolates with various substituents were subjected to triple addition to 3-trismethylsilylbenzyne (Table 3). The primary alkyl group-substituted ynolates afforded triptycenes **3ab–ad** as major products (entries 1–3). In contrast, the triple addition using secondary and tertiary alkyl and aryl-substituted ynolates did not afford the corresponding triptycenes, but instead anthrones **4a–c**, intermediates of the triple addition, were isolated (entries 4–6). The structures were determined by X-ray crystallographic analyses (see SI). This is the first report of the successful isolation of the intermediates in this sequential reaction. The steric hindrance of substituents in addition of silyl groups suppressed the third cycloaddition of benzyne, supporting our proposed mechanism.

Table 3. Synthesis of triptycenes or anthracenones using substituted ynolates.



Although the observed steric hindrance might have been expected to inhibit their reactivity, instead we envisioned that the strain energy may actually enhance the reactivity of these triptycenes. Gratifyingly, this latter scenario proved to be the case. Hence, because the halogenation reaction of silvlarenes is wellknown, we examined the halogenation of the silvl-triptycenes to create a platform for functionalization. As shown in Table 4, halogenation reactions smoothly proceeded and by controlling the stoichiometry of N-chlorosuccinimide (NCS), efficient and selective synthesis of mono-, di-, and trichlorotriptycenes from 3aa was achieved (entries 1-3). Selective bromination was accomplished in a similar manner (entries 4-6). Notably, since mono-bromination of 3aa proceeded at room temperature or lower, the first halogenation was much faster than the second and third, although 3aa was more sterically hindered than the monobromo- and dibromo 5A and 5B. This distinctive reactivity difference (3aa > 5A > 5B) due to steric hindrance indicates the release of distortion as a driving force for the reaction. In contrast to chlorination and bromination, iodination with ICI was less selective, likely because of the higher reagent reactivity.

To exploit this step-by-step halogenation approach, three halogens were introduced to the triptycene, as shown in Scheme 2. The successive chlorination, bromination, and iodination of **3aa** afforded 1-bromo-8-chloro-13-iodotriptycene **7** in satisfactory yield, which could be further improved by a chromatography-free

procedure (see SI) to 55%. This product represents a useful platform for functional 1,8,13-trisubstituted-triptycenes and chiral triptycenes with chiral centers at C9 and C10.

The tri-halogenated triptycenes could be easily functionalized (Scheme 3). The tribromo triptycene **5C-Br** were subjected to Suzuki-Miyaura coupling with arylboronic acid and vinylbnonic acid ester, affording triaryl and triviny-triptycenes (**8** and **10**), respectively. In addition, Sonogashira coupling was conducted to afford trialkynyltriptycenes (**9**) in good yield.

Table 4. The selective halogenation of trisilyltriptycene 3aa.



^[a]Addition in two portions. ^[b]Addition in three portions.



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Scheme 2. Synthesis of chiral triptycene with chloro, bromo, and iodo substituents.

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The regioselectivity of the addition of the ynolate and other nucleophiles to 3-silylbenzyne can be elucidated by the steric effect rather than - I effect, according to Tokiwa and Akai.²⁰ The sterically bulky nucleophiles tended to attack at C1, while C2 became electronically positive owing to its silicon substituent. However, secondary orbital interactions and/or Si-O (ynolate) interactions could not be dismissed because stronger driving forces should be a prerequisite for producing these highly distorted products with high regioselectivity.

In summary, we successfully synthesized distorted 1,8,13trisilyltriptycenes with high regioselectivity via ynolate-aryne triple addition. The distortion of aromatic rings induced the step-by-step halogenation reactions to afford selective halogenated triptycenes including chiral triptycenes, which represent a useful platform for constructing functionalized triptycenes. Theoretical calculations for the regioselectivity and synthetic applications are underway.



Scheme 3. Coupling reactions of tribromotriptycene 5C-Br.

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Keywords: triptycene • ynolate• distortion • aryne • regioselectivity

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