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Ring-closing metathesis for the synthesis of a molecular gyrotop†

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Macrocage molecules with a bridged phenylene rotor have been synthesized as molecular gyrotops, whose cages were constructed by ring-closing metathesis (RCM) of bis(trialkenylsilyl)benzenes. An analysis of the yields of the products in the RCM reaction under various temperature conditions revealed that the desired cage, *i.e.*, a molecular gyrotop, was produced in good yield under reflux, indicating that the cage is a thermodynamically controlled product.

Macrocage molecules with a bridged phenylene have been widely investigated as molecular gyroscopes and gyrotops, because the phenylene can rotate rapidly inside the molecular cage even in the crystalline state.[1–5] Recently, we reported the synthesis of crystalline molecular gyrotops and gyroscopes, such as compound **1** containing a phenylene rotor encased by three long alkyl spokes, that showed novel functions due to the dynamic states of the molecules with the rapid rotation of the rotor (Fig. 1).[4,5]

It is well known that one of the most useful methods for the synthesis of such macrocages is ring-closing metathesis (RCM) of alkenyl compounds (*cf.* Scheme 1).[6] In particular, there are many reports on the synthesis of functional molecules as well as natural products by RCM using Grubbs' catalysts.[3,4,6,7] The cage of compound **1** was synthesized by RCM of 1,4-bis(tris-7-octenyl)silylbenzene followed by hydrogenation of the unsaturated cage.[4c] However, the optimal conditions for the synthesis of macrocage compounds, such as molecular gyrotop **1**, have not yet been determined. In this report, we

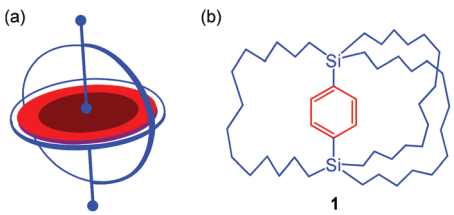
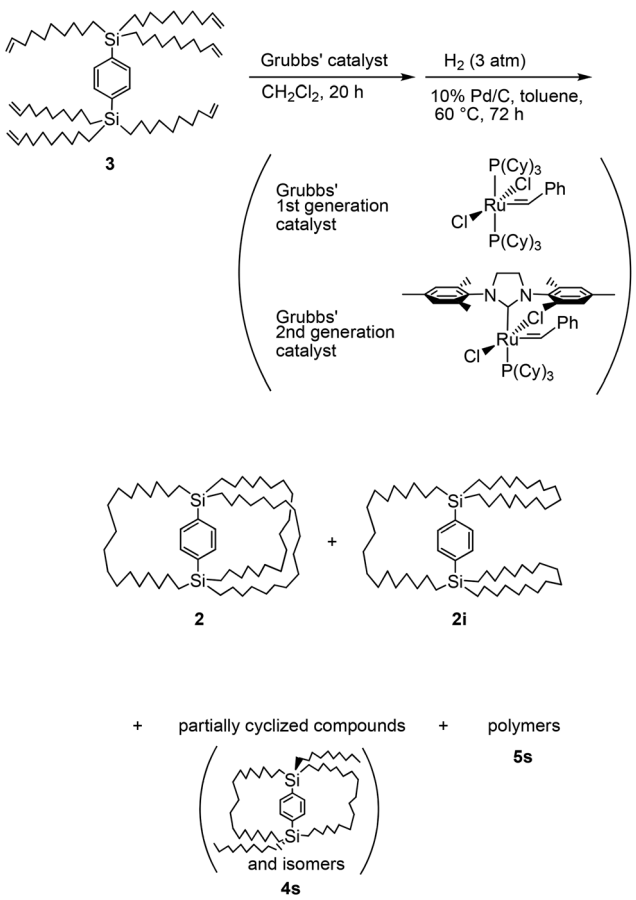


Fig. 1 (a) Schematic representation of a gyrotop and (b) structural formula of molecular gyrotop **1**.



Scheme 1 Synthesis of molecular gyrotop **2**.

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wish to find out the optimal conditions for the synthesis of a novel molecular gyrotop **2**, which has longer side chains (C18-chains) in the cage than **1** (C14-chain). The molecular gyrotop **2** was synthesized by RCM of 1,4-bis(tris-9-decenyl)silylbenzene (**3**) (Scheme 1). Because a non-caged isomer **2i** was also formed in this reaction, the ratio of the formed products can be analyzed both experimentally and statistically (a non-caged isomer was not obtained in the synthesis of **1**[4c]). In addition, we also characterized the structures of the cage **2** and the isomer **2i** by single crystal X-ray diffraction analysis.

The procedure for the synthesis of molecular gyrotop **2** by RCM is similar to the synthesis of **1** and is described as follows:[4] dichloromethane (300 mL) and Grubbs' catalyst (0.02 g, 0.02 mmol) were added to a 500 mL three-necked flask, which was kept at 40 °C, 20 °C, and 0 °C, respectively, as shown in Table 1. A dichloromethane solution (200 mL) of **3** (0.300 g, 0.3 mmol) was added dropwise to the solution with stirring over 12 h. Under these conditions, **3** was present under highly dilute conditions in the solution, thereby preventing the intermolecular RCM reaction. During the reaction, the catalyst (0.02 g, 0.06 mmol) was added into the flask two times (every 2 h) in order to avoid deactivation of the catalyst. The mixture was further stirred for another 8 h. The volatile materials were removed *in vacuo*, and the benzene-soluble fraction was treated with flash column chromatography (silica gel, benzene as the eluent) to remove the metal catalysts. Then, 3 atm of hydrogen gas was introduced into a toluene (5 mL) solution of the reaction mixture in the presence of 10% Pd/C (0.03 g) in an autoclave, and the mixture was allowed to stand for 72 h at 60 °C. After the excess H_2 gas had been released, the mixture was filtered to remove the Pd/C catalyst. The volatile materials were removed *in vacuo*. The crude products were obtained quantitatively. The mixture was then subjected to preparative recycling gel permeation chromatography (GPC), a type of size exclusion chromatography. The fractions containing polymeric products (**5s**, retention time (r.t.) = 30–40 min), a partially cyclized mixture (**4s**, r.t. = 43.0 min), the cage (**2**, r.t. = 44.7 min), and its isomer (**2i**, r.t. = 44.2 min) were collected during the 1st, 8th, 28th, and 28th cycle, respectively (Fig. 2). Interestingly, the starting compound **3** was not recovered under any of the reaction conditions. Yields of the products under various conditions are summarized in Table 1.

Table 1 Optimization of the reaction conditions for the synthesis of molecular gyrotop **2** by RCM reaction

	Condition		Isolated yield (%)			
Entry	Catalyst	T^c/°C	**2**	**2i**	**4s**	**5s**[d]
1	[a]	40	23	39	0	38
2	[a]	20	12	12	13	63
3	[a]	0	7.7	5.8	17	70
4	[b]	40	6.7	2.8	14	76
5	[b]	20	3.7	1.0	16	79

[a] Grubbs' 1st generation catalyst. [b] Grubbs' 2nd generation catalyst. [c] Reaction temperature. [d] Based on the monomer conversion.

Structures of the cage (**2**) and the isomer (**2i**) were identified using ^{1}H NMR, ^{29}Si NMR, and ^{13}C NMR spectroscopy, and elemental analysis. ^{1}H and ^{13}C NMR spectra of **2** in chloroform solution show that the three alkyl chains are identical within the NMR time scale (pseudo D_3 symmetry), indicating rapid rotation of the phenylene inside the cage. The recrystallization of **2** from a mixture of tetrahydrofuran (THF) and methanol (MeOH) (4 : 1 v/v) afforded single crystals, whose structures were determined using X-ray diffraction (Fig. 3(a)). The phenylene ring was effectively surrounded by three alkyl chains in the structure of **2** even though the cage structure is slightly deformed from a sphere. The slight deformation arises because the length of the side chains in the cage of **2** is long for the phenylene rotor. On the other hand, the ^{1}H and ^{13}C NMR spectra of **2i** in chloroform solution show that two of the three alkyl chains are identical, reflecting the symmetry (pseudo C_{2v}) of the structure. A single crystal of the isomer **2i** was also obtained by recrystallization from chloroform. Fig. 3 (b) shows the molecular structure of **2i**, as determined by X-ray crystallography. As expected, two kinds of octadecyl chains were observed; one kind is connected to two different silicons, whereas the other kind is connected to the same silicon atoms. The structure of the partially cyclized mixture (**4s**) was identified by its retention time on the GPC (similar to **2** and **2i**) and ^{1}H NMR spectroscopy (Fig. S9 in ESI†). The spectrum showed signals corresponding to terminal methyls (δ 0.87,

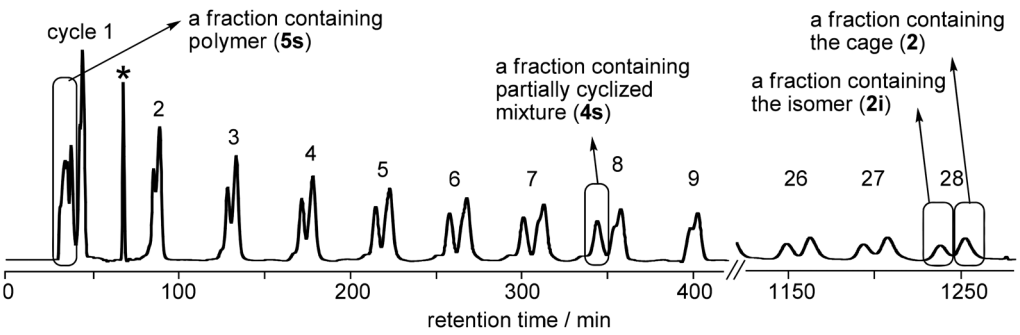

Fig. 2 Representative recycling GPC chart (refractive index detector) of the reaction mixture in RCM reactions (entry 3 in Table 1). The asterisk indicates residual solvents (*e.g.* benzene as the column eluent), and the fraction was collected here.

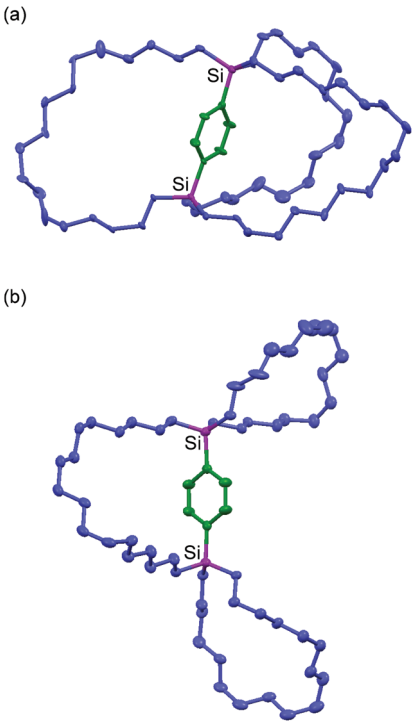

Fig. 3 Molecular structure of (a) the molecular gyrotop **2** and (b) the isomer **2i**, as determined by X-ray crystallography (ORTEP, 30% thermal ellipsoid probability). Hydrogen atoms are omitted for clarity.

triplet, 6H), methylenes (δ 0.75, multiplet, 12H (adjacent to silicons), δ 1.1–1.4, multiplet, 96H), and several aromatic signals (δ 7.41–7.45, several signals, total 4H). Unfortunately, further purification of the mixture was unsuccessful.

Additionally, the stereochemistry of alkene junctions formed by RCM reactions for the synthesis of **2** and **2i** was investigated before hydrogenation reaction. In contrast to the result that only (*E*,*E*,*E*)-cage was obtained before hydrogenation in the synthesis of **1**,[4d] formation of a complex mixture that includes both *E* and *Z* junctions was confirmed by ^{1}H NMR spectra (Fig. S12†) in the synthesis of **2** and **2i**. Because of the overlapping of the signals of olefinic protons in the NMR spectra, the ratio of *E*/*Z* in the mixture could not be determined. This result indicates that *E*/*Z* selectivity of alkene junctions in RCM is not controllable generally.

The statistical formation ratio of the monomeric products (**2**, **2i**, and **4s**) in this RCM based on probability theory can be analyzed as shown in Fig. 4 although this analysis ignores the intermolecular RCM reaction. The statistical analysis revealed the yields of the cage and the isomer to be 20% and 60%, respectively, and the formation ratio of **2** to **2i** to be 0.3.

However experimentally determined formation ratios using Grubbs' 1st generation catalyst were 0.59 at 40 °C (entry 1 in Table 1), 1.0 at 20 °C (entry 2), and 1.3 at 0 °C (entry 3). These results indicate that the formation of the cage is more enhanced than that expected by statistical analysis (0.3). A similar phenomenon was observed in the synthesis of **1** (only the cage compound **1** was produced and the isomer is not

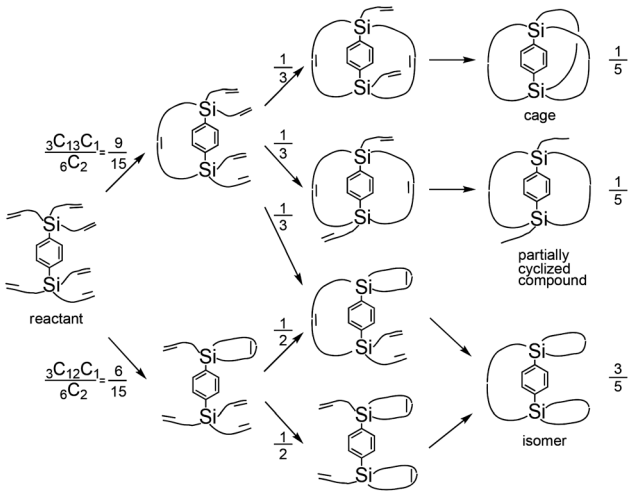

Fig. 4 Statistical analysis of the formation of the cage **2** and the isomer **2i**.

obtained[4c]). Since the formation of a partially cyclized mixture (**4s**) was observed in the reaction at low temperature (20 °C (entry 2) and 0 °C (entry 3)), a high temperature is necessary for the reaction to proceed to completion. The yields of both **2** and **2i** increased with temperature, indicating that they are thermodynamically controlled products. On the other hand, the yield of the polymers increased with decreasing temperature, indicating that the polymers are kinetically controlled products because polymerization is entropically unfavorable. Entries 4 and 5 in Table 1 show the results obtained using Grubbs' 2nd generation catalyst. Although this catalyst is more stable than the 1st generation catalyst, the yield of the desired cage is low. Therefore, the 2nd generation catalyst is not suitable for the synthesis of molecular gyrotops.

Conclusion

We investigated the RCM reaction of 1,4-bis(tri-ω-decenyl)silylbenzene (**3**) for the synthesis of a molecular gyrotop (**2**). The structures of the cage compound **2** and its structural isomers **2i** were determined by single crystal X-ray diffraction. The reaction conditions for the synthesis of molecular gyrotop **2** by RCM were optimized, and the desired cage **2** was found to be a thermodynamically controlled product. The reaction of **3** with Grubbs' 1st generation catalyst under reflux in dichloromethane was determined to be optimal for the synthesis of **2**.

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