Regioselective Functionalization of Sumanene

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Dedicated to Professors Jiro Tsuji and Barry Trost on the occasion of their award winning of the Tetrahedron Prize.

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ABSTRACT

Doubly functionalized dioxosumanene was designed and synthesized to extend π conjugation bi-directionally. Friedel-Crafts double cycloalkylation to sumanene proceeded selectively to give the cycloalkylated compound. This compound was suggested to be the flattened structure as compared to sumanene, which induced the facile bowl-to-bowl inversion. Oxidation of the benzylic position was performed, and then a carbonyl group at the reverse side of the cycloalkylated arene was selectively protected with acetal to afford the doubly functionalized dioxosumanene.

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1. Introduction

Bowl-shaped π -conjugated carbon molecules (geodesic polyarenes,¹ buckybowl,² or π bowls, here we use π bowls) are of fundamental interest due to their unique shape, dynamic behavior such as bowl-to-bowl inversion, and electronic properties derived from the strain and conjugation.³⁻⁸ They can be considered to be another group of key materials in addition to C₆₀ and carbon nanotubes in the curved π -conjugated carbon systems. Further extension of π conjugation in π bowls is expected to lead to various functional materials. Control of bowl-to-bowl inversion will lead to molecular machines and switches.

Corannulene and sumanene (**1**) are representative examples of π bowls, which have the five- and three-fold symmetric structures, respectively. Pentachlorocorannulene **2**⁹ and tetrabromocorannulene **3**¹⁰ are five- and two-fold symmetric halogenated corannulenes, respectively, which can be used as a building block to extend the π conjugation with keeping the symmetry. In fact, it was reported that **2** and **3** were transformed to the further π -conjugation extended compounds.¹¹⁻¹⁹ On the other hand, sumanene (**1**) has three benzylic positions, where substituents can be easily introduced.²⁰⁻²¹ Three-fold symmetric π -conjugation extended sumanene derivatives such as **4** were synthesized before.²² Concerning the aromatic derivatization with

keeping symmetry, there is an issue on regioselective introduction of substituents.²³ Previously, we have reported that the three-fold symmetric hemifullerene derivative **5**, where the regioselectivity of aromatic bromination was problematic.²⁴ Recently, we have reported the improved approach to construct a hemifullerene skeleton via regioselective oxidative cyclization of **4** to form **6**.²² However, bi-directional extension of π conjugation using sumanene (**1**) is still difficult. In this context, we designed molecule **7** as a key building block to extend the π conjugation bi-directionally. Two carbonyl groups are available in this molecule **7**. Wittig reaction and the subsequent oxidative cyclization will lead to the π -conjugation extended bowl-shaped molecules. In order to prevent the formation of undesired isomers in the cyclization, the bulky 1,1,4,4-tetramethyl-1,2,3,4-tetrahydrobenzo moiety²⁵ is introduced at the peripheral arene between two carbonyl groups. Herein, we report the synthesis of **7** via regioselective functionalization. Furthermore, we also would like to report the finding that the introduction of 1,1,4,4-tetramethyl-1,2,3,4-tetrahydrobenzo moiety lowers the activation energy of the bowl-to-bowl inversion.

2. Results and Discussions

2.1. Synthesis

In order to introduce the bulky substituents at the peripheral arene of sumanene (**1**), Friedel-Crafts double cycloalkylation and cycloacylation were investigated. First, 2,2-dimethylmalonyl dichloride and phthaloyl dichloride were employed for the Friedel-Crafts double cycloacylation in the presence of AlCl₃, but the desired compounds were not obtained under these conditions.

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Then, 1,2-bis(chloromethyl)benzene and 1,2-bis(chloromethyl)-4,5-dimethylbenzene were tried for the Friedel-Crafts double cycloalkylation in the presence of AlCl_3 , but these reactions also did not give the favorable results. Use of the 2,4-dichloro-2,4-dimethylpentane and 2,5-dichloro-2,5-dimethylhexane in the presence of AlCl_3 afforded the corresponding double

cycloalkylated products. In the case using the former reagents, the formation of di- and tricycloalkylated products were not suppressed. Finally, the Friedel-Crafts double cycloalkylation proceeded selectively under the conditions using 1.5 equivalents of 2,5-dichloro-2,5-dimethylhexane and 3 equivalents of AlCl_3 in CH_2Cl_2 at 0 °C for 10 min stirring, which was developed after the careful screening of equivalents of each reagent, temperature, time, and solvent. As a result, the desired product **8** was obtained in 95% yield (89% purity, Scheme 1). Dicycloalkylated and a trace amount of tricycloalkylated compounds were observed as side products, which were removed by recycling preparative HPLC with GPC columns.

Benzylic oxidation of **8** was carried out according to the procedure reported for the synthesis of trioxosumanene,²⁶ where $\text{RuCl}_3 \cdot n\text{H}_2\text{O}$ and *t*-BuOOH were employed as oxidants. After screening the conditions (equivalents of each reagent and time), it was found that the desired trioxosumanene **9** was obtained in 46% yield (Scheme 1). There is a dilemma that the low reactivity needs the longer reaction time, which brought the decomposition of **9** (the decomposed products were not determined). This is one of the reasons to explain the low yield of the reaction.

Cyclic acetal formation of **9** was investigated in the presence of protonic acid. Even under the conditions at 140 °C in the presence of large excess amount of ethylene glycol, the undesired multiple acetalization of **9** has never been observed. Only the least hindered carbonyl group was selectively protected to give the desired compound **7** in 49% yield.

Figure 1. (a) Sumanene (**1**) and corannulene. (b) Five- and two-fold symmetric halogenated corannulenes. (c) Three-fold symmetric π conjugation extended sumanene derivatives. (d) Diketone **7** and extension of π conjugation bi-directionally based on sumanene skeleton.

Scheme 1. Synthesis of key building block **7** to extend π conjugation bi-directionally.

2.2. Bowl-to-bowl inversion

Bowl-to-bowl inversion is one of the characteristic dynamic behaviors of small π bowls such as corannulene and sumanene

(1).²⁷⁻²⁸ In our previous study, the activation energy of the bowl-to-bowl inversion of **1** was revealed to be ~20 kcal/mol.²⁹⁻³¹

In order to investigate the bowl-to-bowl inversion barrier of the cycloalkylated sumanene **8** (Figure 2a), variable temperature

Figure 2. (a) Bowl-to-bowl inversion of **7**. (b) Variable temperature ¹H NMR spectroscopy experiments of **7** (400 MHz, 25 to 75 °C in mesitylene-*d*₁₂) and their simulation. The values of $\Delta G^\ddagger$ were calculated on the basis of the equation: $\Delta G^\ddagger = -RT \ln(hk/k_B T)$, in which h is the Planck constant, k is the rate constant, k_B is the Boltzmann constant, and T is the temperature. (c) An optimized structure of **7** on the basis of DFT calculation [B3LYP/6-31G(d,p)].

¹H NMR spectroscopy experiments were carried out (Figure 2b). The ¹H NMR spectrum at 25 °C in mesitylene-*d*₁₂ showed two pair of doublets by germinal coupling for benzylic protons Ha and Hb [δ 4.47 ($J = 18.8 \text{ Hz}$, *exo*-Ha, 2H) and 3.51 ($J = 18.8 \text{ Hz}$, *endo*-Ha, 2H), δ 4.40 ($J = 19.2 \text{ Hz}$, *exo*-Hb, 1H) and 3.07 ($J = 19.2 \text{ Hz}$, *endo*-Hb, 1H)], where *endo*-protons appeared in a relatively higher field due to shielding of the ring current effect from the sumanene skeleton, reversely *exo*-protons appeared in a relatively lower field due to the anti-shielding. These trends are typical as the bowl-shaped sumanene derivatives.⁷⁻⁸ The peak of the *endo*-proton Hb appeared in a higher region compared to Ha, which means that Hb is placed in the environment with the stronger shielding. This might suggest that the bowl structure becomes deeper at the side of Hb. As raising the temperature in the 400 MHz NMR spectra, broadening was observed in the benzylic protons (Figure 2b). The coalescence failed to reach due to the spectrometer limitations. Fitting simulation³² for the peaks (*exo*- and *endo*-Ha) allowed an experimental estimation for the rate constant k . The obtained rate constant k can be converted to the barrier $\Delta G^\ddagger$ using Eyring equation. The estimated $\Delta G^\ddagger$ is about 17.2 kcal mol⁻¹ as shown in Figure 2b. Such fitting simulation for sumanene (**1**) reproduced the inversion barrier of the reported value²⁸⁻²⁹ (about 20 kcal mol⁻¹, see Figure S1 in Supporting Information of reference 33),³³ where the much significant broadening of the peaks in **8** was observed as compared to that in sumanene (**1**). Thus, the bowl-to-bowl inversion of **8** is much faster than that of **1**.

In order to understand the reason, the structure of **8** was optimized based on DFT calculation [B3LYP/6-31G(d,p)] (Figure 2c). The bowl depth was employed to evaluate the curvature. The bowl depth is defined as the distance from the plane of the hub benzene ring. Selected values are shown in Figure 2c. The bowl depth at the cycloalkylated arene is 0.98 Å (carbon A), which is smaller than that for **1** (1.11 Å).²⁰ This flattening accounts for the observed small inversion barrier of **8**. On the other hand, the bowl depth at the reverse side (carbon B) shows the same value as **1**. This can explain the difference of chemical shifts between *endo*-Ha and *endo*-Hb as described above.

3. Conclusion

In summary, doubly functionalized dioxosumanene **7** was designed and synthesized to extend π conjugation bi-directionally. Friedel-Crafts double cycloalkylation of **1** proceeded selectively to give **8**. The cycloalkylated compound **8** was suggested to be the flattened structure as compared to **1**, which induced the facile bowl-to-bowl inversion. Oxidation of the benzylic position was performed, and then a carbonyl group at the reverse side of the cycloalkylated arene was selectively protected as an acetal. Thus-obtained diketone **7** will be useful to synthesize novel bowl-shaped π -conjugated molecule based on sumanene through two-fold symmetric extension of π conjugation.

4. Experimental section

General information

¹H (400 MHz) and ¹³C (100 MHz) NMR spectra were measured on a JEOL JNM-ECS 400 spectrometer. CDCl₃ or CD₂Cl₂ was used as a solvent. The residual CHCl₃ or CHDCl₂ peak ($\delta = 7.26$ or 5.32 ppm) was used as the reference for ¹H NMR, respectively. The CDCl₃ or CD₂Cl₂ peak ($\delta = 77.0$ or 53.8 ppm) was used as the reference for ¹³C NMR, respectively.

Infrared spectra were recorded on a JASCO FT/IR-480plus. Mass spectra were measured on a BRUKER AUTOFLEX III (MALDI-TOF) mass spectrometer. Recycling preparative HPLC was performed with Japan Analytical Industry LC-908 using tandemly arranged GPC columns (JAIGEL-1H and JAIGEL-2H) with chloroform as a solvent. Reagents were purchased from commercial sources and used without further purification.

Synthesis

7,7,10,10-Tetramethyl-6,7,8,9,10,11-hexahydro-3H-as-indaceno[2,1,8,7-defgh]cyclopenta[pqr]tetraphene (**8**)

To a mixture of sumanene (**1**, 60 mg, 0.23 mmol) and AlCl₃ (90 mg, 0.69 mmol) in dry CH₂Cl₂ (6 mL) was added 2,5-dichloro-2,5-dimethylhexane (60 mg, 0.35 mmol) under an argon atmosphere at 0 °C. The reaction mixture was stirred at 0 °C for 10 min. The reaction mixture was filtered through short pad of silica gel and the solvent evaporated *in vacuo* to give **8** [80.4 mg, 0.22 mmol, 95% yield (89% purity)], which was further purified by recycling preparative HPLC to give **8** as a pale yellow solid; mp 79-80 °C (uncorrected); FT-IR (ATR, powder) ν = 2953, 2922, 1460, 1361, 784 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ = 7.12 (d, *J* = 8.0 Hz, 2H), 7.10 (d, *J* = 8.0 Hz, 2H), 4.80 (d, *J* = 19.2 Hz, 2H), 4.71 (d, *J* = 20.0 Hz, 1H), 3.80 (d, *J* = 19.2 Hz, 2H), 3.42 (d, *J* = 19.6 Hz, 1H), 1.77 (m, 4H), 1.56 (s, 6H), 1.32 (s, 6H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ = 148.7, 148.0, 147.92, 147.91, 145.1, 144.7, 142.7, 123.3, 123.0, 44.7, 42.0, 36.9, 36.2, 33.0, 29.8 ppm; HRMS (MALDI TOF) *m/z* [M⁺] calcd for C₂₉H₂₆ 374.2029, found 374.2017.

7,7,10,10-Tetramethyl-7,8,9,10-tetrahydro-3H-as-indaceno[2,1,8,7-defgh]cyclopenta[pqr]tetraphene-3,6,11-trione (**9**)

A mixture of **8** (10 mg, 0.026 mmol), RuCl₃·nH₂O (17 mg), and a 70% aqueous solution of *t*-BuOOH (0.1 mL) in pyridine (0.4 mL) and CH₂Cl₂ (2 mL) was stirred under an argon atmosphere at room temperature for 40 h. The reaction mixture was stirred at 0 °C for 10 min. The reaction mixture was quenched with aqueous saturated Na₂S₂O₃/NaHCO₃ solution. The aqueous layer was extracted with CH₂Cl₂. The combined organic layer was washed with 1M HCl, H₂O, and brine, and then dried with Na₂SO₄, and the solvent evaporated *in vacuo*. The crude product was purified by preparative TLC (hexane/CH₂Cl₂ = 1/3) to give **9** (5.0 mg, 0.012 mmol, 46%) as a red solid; mp 253-254 °C (uncorrected); FT-IR (KBr) ν = 2966, 2925, 2870, 1729, 1717, 1465, 1184, 746 cm⁻¹; ¹H NMR (400 MHz, CDCl₃) δ = 7.37 (t, *J* = 7.6 Hz, 4H), 1.68 (t, *J* = 6.8 Hz, 4H), 1.66 (s, 6H), 1.31 (s, 6H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ = 190.5, 188.9, 153.4, 148.3, 148.0, 145.5, 143.6, 143.2, 140.7, 126.1, 126.0, 36.7, 36.7, 33.1, 25.7 ppm; HRMS (MALDI TOF) *m/z* [M + H⁺] calcd for C₂₉H₂₁O₃ 417.1485, found 417.1503.

7,7,10,10-Tetramethyl-7,8,9,10-tetrahydrospiro[as-indaceno[2,1,8,7-defgh]cyclopenta[pqr]tetraphene-3,2'-[1,3]dioxolane]-6,11-dione (**7**)

A mixture of **9** (6.4 mg, 0.015 mmol) and *p*-toluenesulfonic acid monohydrate (one portion) in dry toluene (0.3 mL) and ethylene glycol (0.3 mL) was stirred under an argon atmosphere at 140 °C for 72 h. The reaction mixture was quenched with aqueous saturated NaHCO₃ solution. The aqueous layer was extracted with CH₂Cl₂. The combined organic layer was washed

with aqueous saturated NaHCO₃ solution and brine, and then dried with Na₂SO₄, and the solvent was evaporated *in vacuo*. The crude product was purified by preparative TLC (hexane/CH₂Cl₂ = 1/3) to give **7** (3.4 mg, 0.074 mmol, 49%) as an orange solid; mp 258-259 °C (uncorrected); FT-IR (KBr) ν = 2957, 2929, 2881, 1717, 1700, 1200, 1081, 734 cm⁻¹; ¹H NMR (400 MHz, CD₂Cl₂) δ = 7.26 (d, *J* = 7.2 Hz, 2H), 7.15 (d, *J* = 7.2 Hz, 2H), 4.44 (td, *J* = 6.4 Hz, 1.2 Hz 2H), 4.36 (td, *J* = 6.4 Hz, 1.2 Hz, 2H), 1.66 (s, 4H), 1.64 (s, 6H), 1.27 (s, 6H) ppm; ¹³C NMR (100 MHz, CD₂Cl₂) δ = 191.3, 155.2, 152.8, 148.6, 145.7, 145.5, 141.4, 141.2, 125.2, 123.6, 117.6, 67.3, 66.1, 37.0, 36.6, 33.0, 25.7 ppm; HRMS (MALDI TOF) *m/z* [M + H⁺] calcd for C₃₁H₂₅O₄ 461.1747, found 461.1757.

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Supplementary data

¹H and ¹³C NMR spectra of **7**, **8**, and **9**. Supplementary data related to this article can be found at <http://dx.doi.org/...>

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***Building block
toward bi-directional extension
of π conjugation***