Tetrahedron 126 (2022) 133041

Contents lists available at ScienceDirect

Tetrahedron

journal homepage: www.elsevier.com/locate/tet

A symmetry-driven approach toward the total synthesis of dodecahedrane

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ARTICLE INFO

Article history:
Received 5 August 2022
Received in revised form
4 September 2022
Accepted 13 September 2022
Available online 21 September 2022

This article is dedicated to Professor John Wood, a mentor, a friend, and a giant in the field of total synthesis.

Keywords:
Total synthesis
Polyene cyclization
Platonic hydrocarbon
Metathesis

ABSTRACT

Herein, we describe our progress toward the total synthesis of dodecahedrane, a complex and highly symmetrical hydrocarbon that bears twelve fused rings arranged in a cage-like architecture. Central to our approach is a late-stage [2+2+2+2+2] polyene cyclization cascade, which is expected to construct five new bonds and ten new rings in a single transformation. Toward this end, we describe efforts to synthesize key monomeric fragments, along with successful dimerization studies using a pinacol coupling approach. Subsequent studies include an attempted olefin metathesis rearrangement cascade in addition to a successful intramolecular photochemical [2+2] reaction. Although attempts to elaborate the photocycloaddition product were unsuccessful, our studies provide access to complex dimeric scaffolds and are expected to help guide our future total synthesis studies.

1. Introduction

Achieving access to complex, sp^3-rich molecules has grown increasingly desirable in the discovery of new drug molecules [1]. Indeed, the escalating complexity of targets in the pharmaceutical and agrochemical industries has highlighted the need for new synthetic approaches that rapidly build molecular complexity [2]. Toward this end, the total synthesis of molecules with high three-dimensional character can serve to inform the development of new synthetic strategies and inspire new approaches. Dodecahedrane (**1**, Fig. 1) represents a particularly compelling target, bearing a highly symmetrical and sp^3-rich carbon skeleton that harbors twelve fused rings arranged in a cage-like structure [3]. Indeed, dodecahedrane **1** has long fascinated scientists and was even regarded as the "Mount Everest of Alicyclic Chemistry" due to its extraordinary architecture [3d,4]. From a synthetic standpoint, dodecahedrane **1** poses notable synthetic challenges. Although **1** is not chiral, its synthesis requires that the relative stereochemistry at each sp^3 center is carefully orchestrated, such that all twenty hydrogen atoms are arranged *syn* to one another. In addition to its twelve fused rings and unique symmetry, the lack of polarizable functional groups in the molecule complicates retrosynthetic logic, which traditionally relies on identifying combinations of positively and negatively charged synthons [5]. With these challenges in mind, dodecahedrane **1** offers exciting opportunities for the development of new synthetic methodologies and strategies. Moreover, despite the limited quantities of dodecahedrane **1** accessed to date, experimental [6], as well as theoretical [7], studies of **1** and its derivatives demonstrate that it may hold promise in the fields of polymer chemistry and materials science.

The compelling structure of dodecahedrane **1** has prompted several research groups to engage in efforts to achieve its synthesis. Beginning in 1964, the Woodward group proposed a dimerization of triquinacene as a means to synthesize **1** [8]. Nearly two decades later, in 1982, the first total synthesis of dodecahedrane **1** was accomplished by Paquette and co-workers in 23 synthetic operations [4,9]. In 1987, Prinzbach disclosed a route to **1** from its constitutional isomer pagodane that was subsequently optimized to give dodecahedrane **1** in a total of 20 steps [10]. Although no synthetic reports of dodecahedrane **1** have been described over the past two decades, these early efforts highlight the value of pursuing unnatural hydrocarbons as a means to push our understanding of molecular reactivity [11]. Intrigued by the structure of

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https://doi.org/10.1016/j.tet.2022.133041
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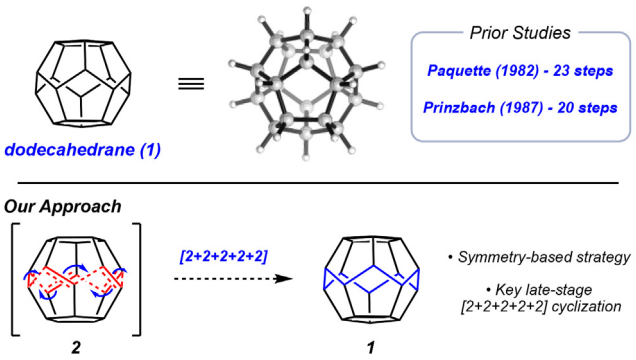

Figure 1. The structure of dodecahedrane **1** and overview of current approach.

dodecahedrane **1**, we are pursuing a concise synthesis of **1** that relies on a symmetry-based disconnection. Our envisioned strategy hinges on a late-stage [2+2+2+2+2] polyene cyclization (**2** → **1**) that should provide valuable insights into molecular reactivity.

2. Results and discussion

A brief retrosynthetic analysis for dodecahedrane **1** is depicted in (Fig. 2). From a retrosynthetic perspective, we view the molecule as having all-*syn* cyclopentyl rings at the northern and the southern faces, with these rings connected via ten central sp^3 carbons that are attached to one another. We envision the central ten-membered ring (highlighted in blue) could be derived from pentaene **3**. In the forward sense, **3** would undergo a thermodynamically favorable [2+2+2+2+2] polyene cyclization reaction, via a transition structure such as **2** [12]. Interestingly, in this proposed transformation, which could plausibly be achieved thermally, photochemically, or via the use of π-Lewis acids, one of the five olefins in **3** would serve as both the initiation point and terminus of cyclization. Although this parent transformation is unknown, a variety of polyene cyclizations [13] and [2+2+2] reactions have been reported, including the hexadehydro-Diels–Alder reaction, which is similarly driven by favorable thermodynamics [14].

We envision that **3** could be accessed through the phased construction of its five alkenes from the coupling and elaboration of appropriately decorated all-*syn* cyclopentane units, conceptually shown as **4**. In particular, we envisioned that pentaene **3** could be derived from tetracycle **5** through ring-closing metathesis. **5** would in turn be constructed from **6** through olefin installation, and the latter could be traced back to bis(norbornene) **7** by means of metathesis isomerization and functional group manipulations. Importantly, the two norbornene fragments of **7** would be covalently linked to one another to enable intramolecular reactivity, and the hydrogens of the two cyclopentane units (blue) would be oriented *syn* relative to each other. It is expected that **7** could be derived from generalized cyclopentyl monomers **8** via dimer formation.

A major challenge in our total synthesis studies of dodecahedrane **1** involved the preparation of a dimeric fragment of the type **7** shown in (Fig. 2). Ultimately, we were able to devise a short route to such a dimer using the sequence shown in (Fig. 3). First, we prepared known norbornene derivative **9**, which is available from cyclopentanone in three synthetic steps (Fig. 3) [15]. Elaboration of ketal **9** to norbornyl ketone **10** was achieved through an additional 3-step sequence. Specifically, the anhydride in **9** was reduced to yield the corresponding diol, which was then silylated. Subsequent $BF_3 \cdot Et_2O$-mediated deketalization afforded **10** in 22% yield over three steps [15]. To date, over 25 g of ketone **10** have been prepared. With ketone **10** in hand, efforts were undertaken to achieve the desired homocoupling to generate dimer **11**. Following extensive optimization [16], a SmI_2-mediated pinacol coupling was found to reliably generate dimer **11** in 43% yield, thus forming a highly

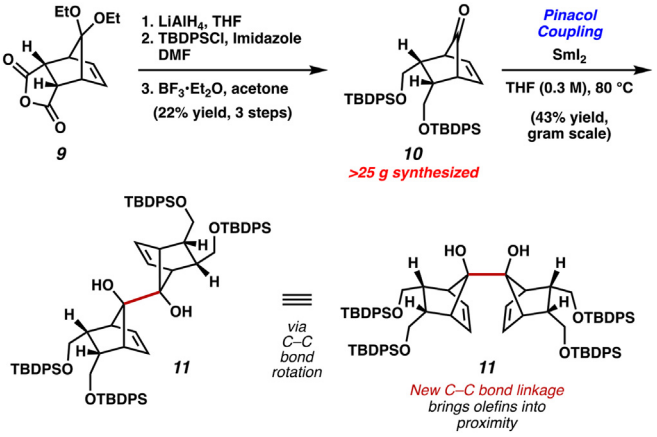

Figure 3. Forward synthesis of **11** enabled by a key SmI_2-mediated pinacol coupling.

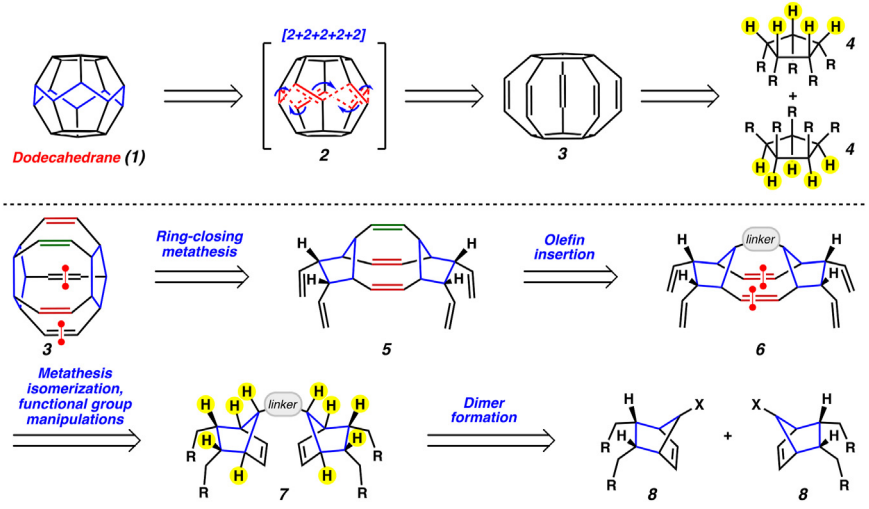

Figure 2. Retrosynthetic analysis of dodecahedrane **1**.

congested C–C bond with complete facial selectivity [17]. It was found that high reaction concentration (0.3 M) was critical to promoting dimerization over reduction. Additionally, this step could be executed on gram scale. Strategically, the direct C–C linkage (highlighted in red) of **11** joining the two norbornene fragments was anticipated to bring the two olefins into proximity for the later C–C bond-forming steps.

With access to gram quantities of **11**, we were poised to engage in efforts to form two of the key remaining C–C bonds of dodecahedrane **1**. In particular, we sought to leverage olefin metathesis to construct two key olefins. First, the vicinal alcohols in diol **11** were protected as methyl ethers using MeI and NaH to generate protected bis(alkene) **12** in 89% yield (Fig. 4). With **12** in hand, we evaluated a variety of metathesis catalysts and reaction conditions to achieve the desired metathesis isomerization[16], including Mo-based Schrock-type alkylidene catalysts, Ru-based Grubbs-type alkylidene catalysts, as well as various solvents and temperatures [18]. Whereas analogous strain-release driven metathesis isomerizations of norbornenes have been shown to be highly efficient in the context of complex molecule synthesis, no such reactions have yet been described using tethered norbornene species such as **12** [19]. However, exhaustive efforts to access **13** ultimately proved fruitless, and recovered starting material was observed in nearly all cases. Removal of the TBDPS groups was also performed to alleviate steric congestion, but proved ineffective in enabling the metathesis rearrangement.

We hypothesized that difficulties in this transformation (**12** → **13**) could be ascribed to the freely rotating nature of the two norbornyl fragments about the central C–C σ-bond, leading to the two olefins residing distant from one another. To evaluate this hypothesis, we sought to lock the vicinal diol moiety into a rigid conformation, which would force the two olefins into closer proximity. In particular, diol **11** was treated with tosic acid in acetone to give conformationally rigid acetonide **14** in 22% yield. Unfortunately, metathesis isomerization of this substrate to provide **15** also proved challenging. It was concluded from these results that the high level of steric congestion in these systems, specifically surrounding the alkene of each norbornene, prevents the large metathesis catalysts from engaging with the substrate.

With these results in mind, and considering the close proximity of the two olefins in the locked conformation found in **14**, we pursued an alternative [2+2]/retro-[2+2] approach from **14** (Fig. 4). The first step, photochemical [2+2] cycloaddition of **14**, was successfully achieved via irradiation with 254 nm light, delivering cyclobutane product **16**. Acetone was identified as an ideal solvent for this transformation, which is attributed to its well-documented role as a triplet sensitizer [20]. Notably, this transformation reliably occurs in quantitative yield in only 20 min, allowing for efficient construction of the two desired C–C bonds. The success of this transformation was found to be a direct result of the spatial proximity of the olefins enforced by the installation of the acetonide, as photolysis of derivatives lacking a cyclic protecting group on the diol uniformly failed to react. Notably, this highly efficient photocycloaddition leads to the fully diastereoselective formation of four new contiguous stereocenters, which highlights the rapid generation of structural and stereochemical complexity enabled by [2+2] photocycloadditions.

With **16** in hand, we then pursued a retro-[2+2] reaction, which would serve to rupture the cyclobutane ring and generate diene **15**. However, despite evaluation of a variety of thermal and catalyst-mediated conditions [16], the carbon skeleton remained unreactive and only degradation of the peripheral functional groups was observed. Efforts toward the elaboration of **16** are currently underway in our laboratory. If successful, these efforts would provide access to **3** and set the stage for the key [2+2+2+2+2] polyene cyclization.

3. Conclusions

We have detailed an ambitious plan to synthesize dodecahedrane **1**, as well as reported ongoing experimental efforts toward this end. Central to our symmetry-driven approach is a late-stage polyene cyclization cascade that is expected to form five new bonds and ten new rings, wherein one of the olefins serves as both the initiation point and terminus of the cyclization. Thus far, we have synthesized advanced intermediates bearing key

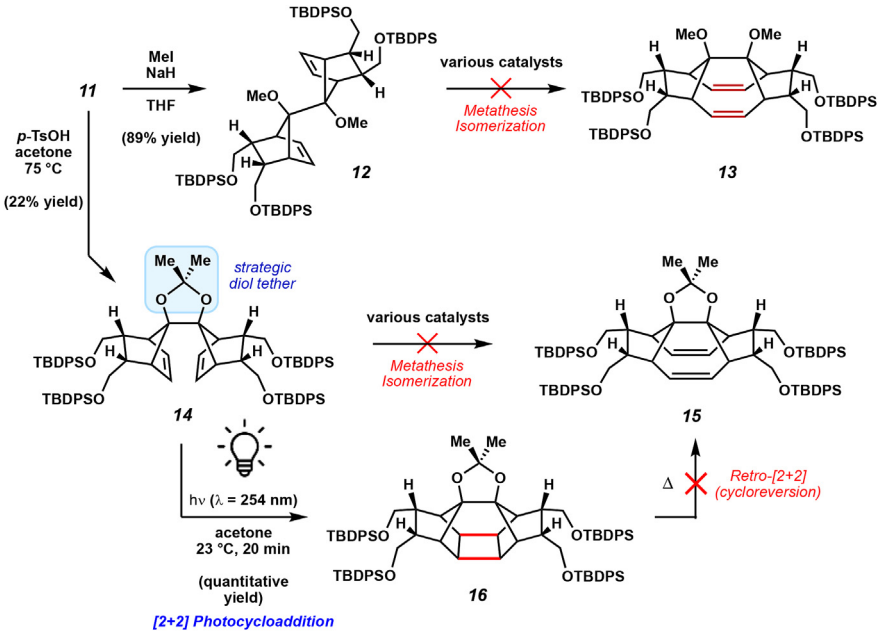

Figure 4. Metathesis studies and an intermolecular [2 + 2] cycloaddition approach.

carbon–carbon bonds present in the carbon skeleton of dodecahedrane **1**. Our current approach features a diastereoselective pinacol coupling to unite two complex, hindered norbornene fragments. Metathesis isomerization reactions of this bis-norbornene dimer were evaluated, but ultimately proved unsuccessful; however, an alternative photochemical [2+2] cycloaddition enabled by conformational restriction was found to be highly efficient, generating two more of the C–C bonds present in dodecahedrane **1**. Ongoing efforts are directed toward elaborating photocycloadduct **16** to pentaene **3** in order to evaluate the key polyene cyclization. Ultimately, these studies are expected to provide access to dodecahedrane **1** in a concise manner and provide new synthetic tools to inform future studies in the area of complex molecule synthesis.

4. Experimental section

4.1. Materials and methods

Unless stated otherwise, reactions were conducted in flame-dried glassware under an atmosphere of nitrogen and commercially obtained reagents were used as received. Anhydrous solvents were either freshly distilled or passed through activated alumina columns, unless otherwise stated. Acetone and THF were further dried over activated 3 Å Mol Sieves for >24 h before use. Prior to use, toluene was purified by distillation over CaH_2 and taken through five freeze-pump-thaw cycles. $LiAlH_4$ (2.0 M in THF), boron trifluoride diethyl etherate ($BF_3{\cdot}Et_2O$), 1,2-diiodoethane (further purified by washing with a saturated aqueous sodium thiosulfate solution), and sodium hydride were obtained from Sigma-Aldrich. *Tert*-Butyldiphenylchlorosilane (TBDPSCl) and *p*-toluenesulfonic acid monohydrate (*p*-TsOH) were obtained from Oakwood Chemical, Inc. Imidazole was obtained from Acros Organics. Samarium metal (powder, 40 mesh) was obtained from Strem Chemicals, Inc. Iodomethane (stabilized) was obtained from Spectrum Chemical Mfg. Corp. Ethylenediaminetetraacetic acid disodium salt dihydrate (EDTA) was obtained from Combi-Blocks. Reaction temperatures were controlled using an IKAmag temperature modulator, and unless stated otherwise, performed at room temperature (approximately 23 °C). [2 + 2] cycloaddition reactions were conducted in a Rayonet RPR-100 photoreactor equipped with eight 14-W lamps (λ = 254 nm). Thin-layer chromatography (TLC) was conducted with EMD gel 60 F_{254} pre-coated plates (0.25 mm for analytical chromatography and 0.50 mm for preparative chromatography) and visualized using a combination of UV and potassium permanganate staining techniques. Silicycle Siliaflash P60 (particle size 40–63 μm) was used for flash column chromatography. ^{1}H NMR and 2-D NOESY spectra were recorded on Bruker spectrometers (at 400 and 500 MHz) and are reported relative to residual solvent signals. Data for ^{1}H NMR spectra are reported as follows: chemical shift (δ ppm), multiplicity, coupling constant (Hz), integration. Data for ^{13}C NMR are reported in terms of chemical shift (125 MHz). DART-MS spectra were collected on a Thermo Exactive Plus MSD (Thermo Scientific) equipped with an ID-CUBE ion source and a Vapur Interface (IonSense Inc.). Both the source and MSD were controlled by Excalibur software version 3.0. The analyte was spotted onto OpenSpot sampling cards (IonSense Inc.) using $CHCl_3$ as the solvent. Ionization was accomplished using UHP He plasma with no additional ionization agents. The mass calibration was carried out using Pierce LTQ Velos ESI (+) and (−) Ion calibration solutions (Thermo Fisher Scientific).

4.2. Experimental procedures

Note: An experimental procedure for the synthesis of ketal **9** has been published, and spectral data match those previously reported [15].

Ketone **10**. A 500 mL round bottom flask equipped with a magnetic stir bar was charged with **9** (7.84 g, 31.1 mmol, 1.0 equiv) and then purged with N_2 for 5 min. Next, THF (100 mL, 0.3 M) was added, and stirring began at 23 °C. The mixture was then cooled to 0 °C. At 0 °C, $LiAlH_4$ (2.0 M in THF, 42.2 mL, 84.4 mmol, 2.72 equiv) was added slowly (5 drops/sec) to the vigorously stirring reaction mixture. Following complete addition, the ice bath was removed and the reaction was left to stir and warm to 23 °C. Next, the flask was fitted with a flame-dried air condenser and the reaction mixture was heated to 70 °C.

After stirring at 70 °C for 2 h, the reaction was removed from heat, and subsequently cooled to 0 °C. At 0 °C, EtOAc (15 mL) was added dropwise across 5 min to quench any unreacted $LiAlH_4$. Following complete addition, the ice bath was removed, and the reaction mixture was warmed to 23 °C. Saturated aqueous EDTA (150 mL) was added, and the resultant mixture was left to stir vigorously for 1 h at 23 °C. This mixture was then transferred to a separatory funnel with EtOAc (100 mL), brine (100 mL), and deionized H_2O (100 mL). The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 100 mL). The organic layers were combined, washed with brine (150 mL), dried over Na_2SO_4, and filtered before the volatiles were removed under reduced pressure. The crude material was then dissolved in EtOAc (10 mL), loaded onto a silica gel plug (3 × 4 cm contained in a fritted funnel), and eluted with EtOAc (1.5 L). The volatiles were again removed under reduced pressure. The resulting crude material was used in the subsequent step without further purification.

To a flask containing a magnetic stir bar and the crude material from the prior step was added DMF (89 mL, 0.2 M). Stirring was started, and the resultant solution was subsequently cooled to 0 °C. Next, imidazole (6.1 g, 89 mmol, 5.0 equiv) and TBDPSCl (12.3 g, 44.7 mmol, 2.0 equiv) were added, the ice bath was removed, and the reaction mixture was allowed to warm to 23 °C while stirring.

After stirring at 23 °C for 42 h, HCl (30 mL, 1.0 M in H_2O) was added to the reaction mixture, and the resulting slurry was transferred to a separatory funnel with EtOAc (50 mL). The layers were separated and the aqueous layer was extracted with EtOAc (3 × 75 mL). The combined organic layers were washed sequentially with saturated aqueous $NaHCO_3$ (50 mL), brine (50 mL), and deionized H_2O (3 × 50 mL), before being dried over Na_2SO_4, and filtered. The volatiles were removed under reduced pressure, and the resulting crude residue was purified by flash chromatography (49:1 hexanes:EtOAc) to yield the disilylated product (7.91 g, 11.0 mmol) as a colorless oil.

To a flame-dried flask containing a magnetic stir bar and the purified product from the prior step was added acetone (16 mL), and stirring began at 23 °C. The solution was then further diluted by the addition of acetone (76 mL, 0.12 M final concentration). $BF_3{\bullet}Et_2O$ (1.4 mL, 11 mmol, 1.0 equiv) was then added dropwise to the stirring reaction mixture. Next, the flask was fitted with a flame-dried air condenser, and the reaction mixture was heated to 60 °C for 1.5 h.

After 1.5 h, the reaction was removed from heat, cooled to 23 °C, and the volatiles were removed under reduced pressure. The resulting crude residue was purified by flash chromatography (49:1 hexanes:EtOAc). Subsequently, the purified material was recrystallized from *n*-heptane to yield ketone **10** (4.48 g, 22% yield, over three steps) as a white solid. Ketone **10**: mp 108.3–110.2 °C; R_f 0.27 (18:1:1 hexanes:benzene:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58–7.50 (m, 8H), 7.40–7.30 (m, 12H), 6.19 (t, J = 2.2, 2H), 3.61 (dd, J = 10.4, 5.7, 2H), 3.35–3.26 (m, 2H), 3.06 (br s, 2H), 2.73–2.64 (br m, 2H), 0.98 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$): δ 204.8, 135.7, 135.6, 133.58, 133.55, 131.7, 129.9, 129.8, 127.9, 127.8, 61.9, 50.9, 40.4,

26.9, 19.2; IR (film): 3070, 2933, 2858, 1787, 1428, 1112 cm^{-1}; HRMS–APCI (*m/z*) $[M + H]^+$ calcd for $C_{41}H_{49}O_3Si_2^+$, 645.32147; found, 645.32122.

Dimer **11**. A flame-dried Schlenk flask equipped with a magnetic stir bar was purged with N_2 for 10 min and then taken into a nitrogen-filled glovebox. In the glovebox, the flask was charged with samarium metal (1.17 g, 7.81 mmol, 1.1 equiv). The flask was then removed from the glovebox and placed under N_2.

Next, a scintillation vial equipped with a magnetic stir bar was flame-dried under reduced pressure and cooled to 23 °C under N_2. To this vial was added 1,2-diiodoethane (2.0 g, 7.1 mmol, 1.0 equiv) and the vial was purged with N_2 for 2 min. Next, THF (8.35 mL, 0.85 M) was added and the resulting mixture was stirred for 2 min at 23 °C. This solution was then added dropwise (1 drop/sec) to the Schlenk flask containing the samarium. Following complete addition, the resultant suspension was stirred for 1 h at 23 °C, generating a dark blue solution of SmI_2 (assumed 0.85 M).

To a separate Schlenk flask equipped with a magnetic stir bar was added ketone 10 (0.84 g, 1.3 mmol, 1.0 equiv), and the system was flushed with N_2 for 5 min. Next, the freshly prepared solution of SmI_2 (0.85 M in THF, 4.6 mL, 3.9 mmol, 3.0 equiv) was added. The reaction was then heated to 80 °C with vigorous stirring for 20 h.

After 20 h, the reaction mixture was removed from heat and cooled to 23 °C. Next, the reaction was quenched by the addition of saturated aqueous $Na_2S_2O_3$ (2 mL) and diluted with EtOAc (2 mL). The resultant heterogeneous mixture was stirred vigorously at 23 °C for 10 min. The layers were then separated and the aqueous layer was extracted with EtOAc (3 × 2 mL). The organic layers were then combined, washed with brine (3 mL), dried over Na_2SO_4, and filtered. The volatiles were removed under reduced pressure, and the resulting crude residue was purified by flash chromatography (45:4:1 → 18:1:1 hexanes:benzene:EtOAc) to yield dimer **11** (0.36 g, 43% yield) as a white foam. Dimer **11**: R_f 0.11 (18:1:1 hexanes:benzene:EtOAc); ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60–7.53 (m, 16H), 7.40–7.28 (m, 24H), 5.52 (br t, J = 1.9, 4H), 3.56 (dd, J = 9.7, 6.1, 4H), 3.25 (m, 4H), 2.82 (br m, 4H), 2.62 (br s, 4H), 2.33 (s, 2H), 0.97 (s, 36H); ^{13}C NMR (125 MHz, $CDCl_3$, 14 of 15 signals observed): δ 135.6, 135.5, 133.98, 133.95, 132.6, 129.5, 129.4, 127.6, 93.9, 62.7, 52.5, 43.4, 26.9, 19.2; IR (film): 3557, 3070, 2930, 2856, 1111, 701 cm^{-1}; HRMS-APCI (*m/z*) $[M + H]^+$ calcd for $C_{82}H_{99}O_6Si_4^+$, 1291.65132; found 1291.65244.

Methylated Dimer **12**. To a 20 mL scintillation vial equipped with a magnetic stir bar were added NaH (60% dispersion in mineral oil, 157 mg, 3.93 mmol, 12.0 equiv) and **11** (423 mg, 0.33 mmol, 1.0 equiv), and the system was flushed with N_2 for 5 min. Next, THF (6.5 mL, 0.05 M) and MeI (205 μL, 3.28 mmol, 10.0 equiv) were added sequentially in single portions. The septa cap was then replaced under a stream of N_2 with a Teflon-lined screw cap, and the reaction mixture was transferred to an Al-block preheated to 85 °C, where it was stirred for 18 h. After 18 h, the reaction was removed from heat and cooled to 23 °C. The reaction was then diluted with EtOAc (2 mL) and quenched with saturated aqueous NH_4Cl (3 mL). This heterogeneous mixture was stirred vigorously at 23 °C for 3 min. Next, the mixture was diluted with deionized H_2O (20 mL) and EtOAc (20 mL), the layers were separated, and the aqueous layer was extracted with EtOAc (4 × 20 mL). The organic layers were combined, dried over Na_2SO_4, and filtered. The volatiles were removed under reduced pressure, and the resulting crude residue was purified by flash chromatography (95:4:1 hexanes:benzene:EtOAc → 45:4:1 hexanes:benzene:EtOAc) to afford methylated dimer **12** (386 mg, 89% yield) as a white foam. Methylated dimer **12**: R_f 0.32 (18:1:1 hexanes:benzene:EtOAc); ^{1}H NMR (500 MHz, C_6D_6, 70 °C): δ 7.77–7.70 (m, 16H), 7.23–7.17 (m, 24H), 5.74–5.63 (m, 4H), 3.88–3.76 (m, 4H), 3.58–3.50 (m, 4H), 3.33 (br s, 6H), 3.17 (br s, 4H), 2.99–2.90 (m, 4H), 1.39 (s, 36H); ^{13}C NMR (125 MHz, C_6D_6, 12 of 16 signals observed): δ 135.7, 135.6, 134.1.132.8, 129.54, 129.53, 101.1, 77.3, 63.4, 53.2, 26.8, 19.1; IR (film): 3070, 2931, 2857, 1428, 1112 cm^{-1}; HRMS–APCI (*m/z*) $[M + H]^+$ calcd for $C_{84}H_{103}O_6Si_4^+$, 1319.68262; found, 1319.69068.

Acetonide **14**. To a 250 mL round bottom flask equipped with a magnetic stir bar was added *p*-toluenesulfonic acid monohydrate (74 mg, 0.39 mmol, 50 mol%) and dissolved in acetone (30 mL). **11** (1.0 g, 0.77 mmol, 1.0 equiv) was then added as a solution in acetone (6.7 mL), and the flask was topped with a reflux condenser and placed under N_2. The reaction was then heated to 75 °C and stirred for 18 h. After 18 h, the reaction was removed from heat and allowed to cool to 23 °C. The volatiles were removed under reduced pressure, and the resulting crude residue was purified by flash chromatography (hexanes → 50:1 hexanes:EtOAc → 20:1 hexanes:EtOAc) to afford acetonide **14** (226 mg, 22% yield) as an off-white foam. Acetonide **14**: R_f 0.53 (9:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.58 (dd, J = 15.1, 6.9, 16H), 7.43–7.35 (m, 8H), 7.35–7.27 (m, 16H), 5.46 (s, 4H), 3.56 (dd, J = 9.8, 5.1, 4H), 3.25 (dd, J = 10.7, 8.9, 4H), 2.85 (br s, 4H), 2.57 (s, 4H), 1.45 (s, 6H), 0.98 (s, 36H); ^{13}C NMR (125 MHz, $CDCl_3$, 16 of 17 signals observed): δ 135.73, 135.65, 134.2, 134.1, 131.9, 129.6, 129.5, 127.7, 105.1, 98.4, 63.0, 49.9, 43.4, 28.7, 27.0, 19.3; IR (film): 3070, 2931, 2857, 1428, 1111, 1068, 700 cm^{-1}; HRMS–APCI (*m/z*) $[M + H]^+$ calcd for $C_{85}H_{103}O_6Si_4^+$, 1331.68262; found, 1331.69446.

Cyclobutane **16**. A solution of **14** (19.7 mg, 14.8 μmol, 1.0 equiv) in acetone (2.0 mL, 7.4 mM) was transferred to a 2 mL quartz tube equipped with a magnetic stir bar. The solution was sparged with N_2 for 10 min. The vial was then sealed and transferred into a Rayonet RPR-100 photoreactor, where it was irradiated with 254 nm light at 23 °C for 20 min. After 20 min, the reaction was removed from the photobox, and the volatiles were removed under reduced pressure to afford cyclobutane **16** (19.8 mg, quantitative yield) as a clear oil. Cyclobutane **16**: R_f 0.48 (9:1 hexanes:EtOAc); ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.55 (dd, J = 15.3, 7.1, 16H), 7.40–7.27 (m, 24H), 3.75 (dd, J = 9.7, 6.1, 4H), 3.41 (t, J = 8.7, 4H), 2.70 (s, 4H), 2.19 (s, 4H), 1.94 (s, 4H), 1.58 (s, 6H), 0.92 (s, 36H); ^{13}C NMR (125 MHz, $CDCl_3$, 16 of 17 signals observed): δ 135.7, 135.6, 134.01, 133.97, 129.61, 129.57, 127.7, 107.7, 90.8, 61.5, 42.4, 39.8, 32.9, 27.8, 26.9, 19.2; IR (film): 3072, 2929, 2856, 1428, 1112 cm^{-1}; HRMS–APCI (*m/z*) $[M + H]^+$ calcd for $C_{85}H_{103}O_6Si_4^+$, 1331.68262; found, 1331.69389. Note: acetone does not need to be anhydrous for this reaction, but degassing is important.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Neil Garg reports financial support was provided by National Science Foundation.

Data availability

No data was used for the research described in the article.

Acknowledgments

The authors thank the NSF (CHE-1900178 for N.K.G., DGE-1144087 for J.E.D., and DGE-1144087 for B.J.S.), the Foote Family (for J.V.C. and J.E.D.), and the UCLA Graduate Division (Dissertation Year Fellowship to J.V.C) for financial support. These studies were supported by shared instrumentation grants from the NSF (CHE-1048804) and the National Center for Research Resources (S10RR025631). The authors acknowledge Melissa Ramirez (UCLA) for assistance with computations.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tet.2022.133041.

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