JOC The Journal of Organic Chemistry

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Synthetic Studies toward Polytwistane Hydrocarbon Nanorods

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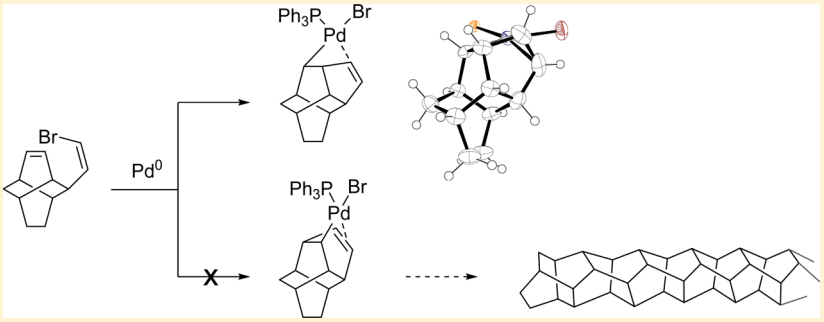
Supporting Information



ABSTRACT: A synthetic strategy toward the intriguing hydrocarbon nanorod polytwistane is outlined. Our approach aims toward the polymerization of acetylene starting from precursors that would provide a helical bias for the formation of polytwistane. Both transition-metal-catalyzed and radical polymerizations were investigated. Two potential initiator molecules were synthesized that could be used for either approach. Although the intended regioselectivities were not observed, unusual organopalladium complexes and numerous compounds with novel carbon skeletons were obtained.

INTRODUCTION

Carbon nanotubes (CNT) feature a variety of attractive mechanical, thermal, and electrical properties.[1] This has led to their use in lightweight composite materials and medical devices and makes them interesting for a range of future applications.[2] The physical properties of CNTs are highly dependent on their geometrical makeup, which is determined by the combination of tube diameter and structural type (armchair vs zigzag vs chiral).[3] These parameters are described commonly by the vectorial indeces (n,m) which indicate how a sheet of graphene would have to be wrapped up to form the corresponding CNT.[4]

Considering the relationship of graphene with graphane,[5] it is interesting to speculate about the relationship of the smallest CNTs with their fully hydrogenated counterparts.[6] As shown in Figure 1, armchair (2,2)-CNT (**1**)[7] corresponds to hydrocarbon nanorod **4**, which was first proposed by Stojkovic et al.[8] Similarly, zigzag (3,0)-CNT **2** corresponds to hydrocarbon nanorod **5**.[8] The smallest possible chiral carbon nanotube, viz. chiral (2,1)-CNT **3**, is related to the recently proposed hydrocarbon nanorod polytwistane (**6**) in the same way.[9] Each of these hydrocarbon nanorods consists of cyclohexane rings locked in distinct conformations. For example, in hydrocarbon **4** all of the rings reside in the boat conformation, whereas in nanorod **5** both boat and chair conformations are present. Polytwistane (**6**) exhibits only D_2-symmetric twist-boat cyclohexanes, thus retaining helical chirality. All of these polymeric structures are isomers of polyacetylene $(C_2H_2)_n$ and display hydrogen atoms and sp^3-hybridized carbon atoms that possess the same chemical environment.[10]

One way to access nanorods **4**–**6** would be to completely hydrogenate the corresponding CNTs **1**–**3**. This has, in fact, been recently studied in order to use CNTs as a material for hydrogen storage.[11] Although these investigations yielded partially hydrogenated CNTs, the products could not be fully characterized.[12]

Several strategies could be imagined to rationally synthesize polytwistane (**6**). The first strategy relies on the polymerization of benzene via Diels–Alder reactions to form laticyclic conjugated polyenes (Scheme 1). These could then be converted to polytwistane (**6**) via N-type cyclizations. A similar pathway was also formulated by Badding and co-workers for the formation of a sp^3-hybridized hydrocarbon nanorod from benzene at very high pressures (20 GPa).[13]

The second approach starts with the polymerization of acetylene to yield the well-known sp^2-hybridized polyacetylene (Scheme 2).[14] This material could then be transformed into polytwistane (**6**) via a two-stage radical olefin polymerization. Indeed, a case of acetylene polymerization has been reported in the literature where partially saturated species were observed.[15]

The third, and more rational, strategy for the synthesis of polytwistane relies on the polymerization of acetylene from an initiator **INR** that carries an alkenyl halide functionality (X = Br, I) (Scheme 3). We envisioned that both transition-metal-catalyzed and radical polymerization of acetylene could afford polytwistane (**6**). In the case of a transition-metal-catalyzed process, the first step would be an oxidative insertion into the

Received: November 17, 2014
Published: December 16, 2014

DOI: 10.1021/jo502618g
J. Org. Chem. 2015, 80, 2042–2055

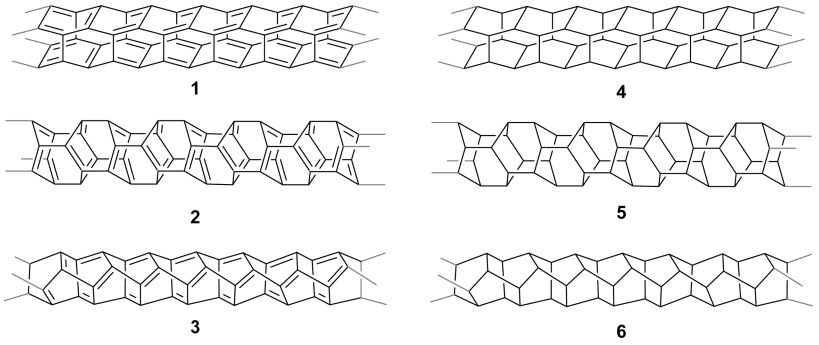
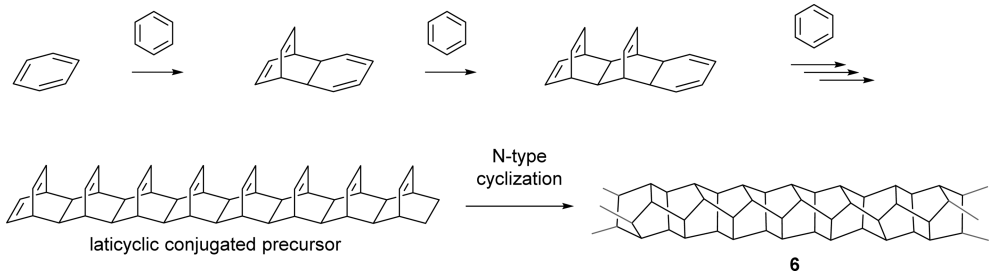
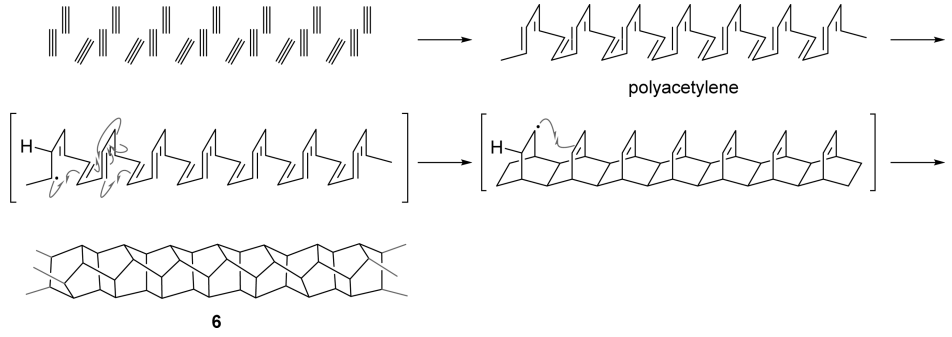


Figure 1. Very small CNTs and their completely hydrogenated equivalents.

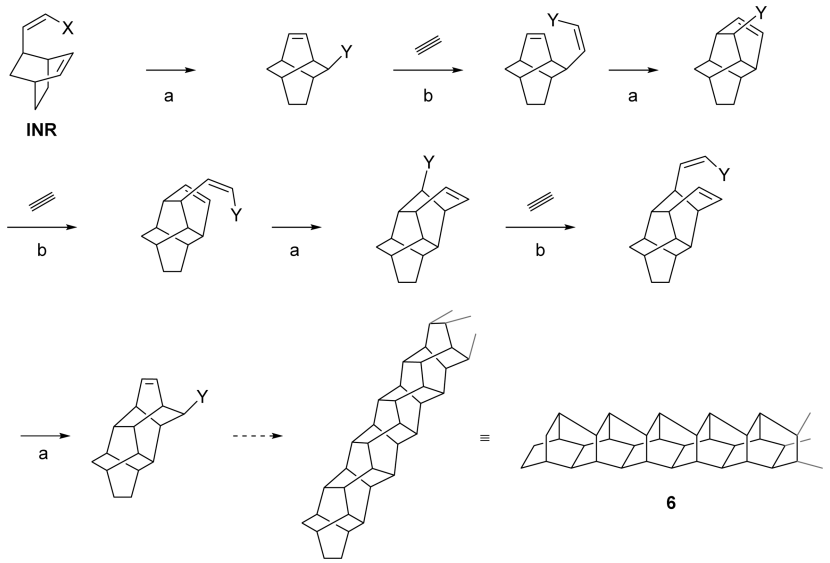
Scheme 1. Proposed Synthesis of Polytwistane (6) via a Diels–Alder Polymerization/N-Type Cyclization Strategy



Scheme 2. Proposed Synthesis of Polytwistane (6) by a Radical Polymerization of Polyacetylene



Scheme 3. Proposed Acetylene Polymerization to Polytwistane (6)[a]



[a]Key: (a) intramolecular cyclization; (b) intermolecular addition. X = Br, I. Y = metal, radical.

DOI: 10.1021/jo502618g
J. Org. Chem. 2015, 80, 2042–2055

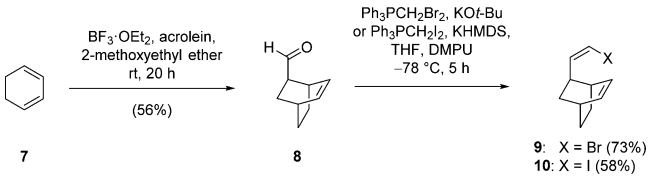
alkenyl halide bond, thereby generating an alkenyl transition metal complex. In a subsequent *intramolecular* carbometalation step, a new six-membered ring would be formed (a). This step is crucial for the outcome of the polymerization as two possible cyclization modes exist. Due to the bicyclic structure of the initiator compound, the desired 6-*endo*-*trig* cyclization has to compete with the undesired 5-*exo*-*trig* cyclization.[16] In the next step, an *intermolecular* carbometalation of an alkyne would occur (b). Alternation of *intra*- and *intermolecular* carbometalation steps of alkenes and acetylene, respectively, would then lead to polytwistane (**6**). In the case of a radical polymerization, the alkenyl halide would be cleaved homolytically and the polymerization would proceed by alternating radical cyclizations (a) and radical additions to acetylene (b).

Herein we describe the syntheses of a bicyclic and a tricyclic initiator molecule corresponding to **INR**. Attempts to achieve both transition-metal-catalyzed and radical cyclizations are discussed.

RESULTS AND DISCUSSION

Synthesis and Cyclization Attempts of Haloalkenylbicyclo[2.2.2]octene. In order to test the feasibility of the proposed polymerization process, the crucial cyclization step was investigated first. For this purpose, the simple initiator molecules **9** and **10** were synthesized (Scheme 4). Addition of

Scheme 4. Synthesis of Bicyclic Initiator Molecules 9 (X = Br) and 10 (X = I)



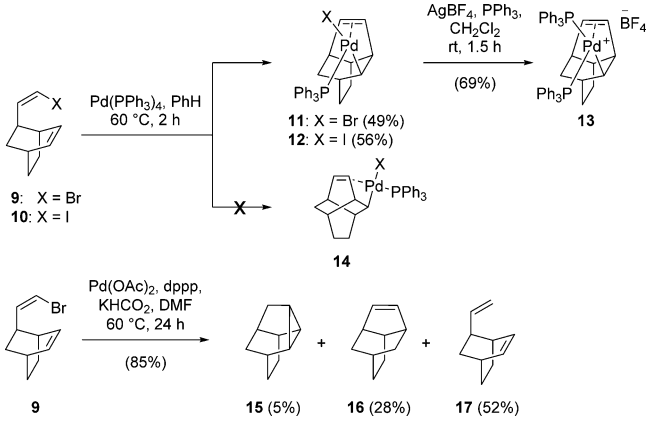
acrolein to cyclohexa-1,3-diene (**7**) afforded the known bicyclo[2.2.2]octenecarbaldehyde **8**,[17] which was converted to (*Z*)-alkenyl bromide **9** or (*Z*)-alkenyl iodide **10** using Stork–Zhao reactions.[18]

With **9** and **10** in hand, the stage was set for the exploration of the first cyclization via oxidative addition to a transition metal followed by migratory insertion. To allow for unambiguous characterization of the cyclization product, the reaction was first carried out using stoichiometric amounts of $Pd(PPh_3)_4$ (Scheme 5). This resulted in the isolation of 5-*exo*-*trig* cyclization products **11** and **12**, the structures of which were confirmed by single-crystal X-ray diffraction. This finding is consistent with the major mode of cyclization reported for similar substrates.[19] In an attempt to change the selectivity of the reversible cyclization by adjusting the electronics, the neutral palladium complex **11** was converted to cationic palladium complex **13** by treatment with $AgBF_4$ and PPh_3. However, upon heating of species **13** no conversion to the desired twistenylpalladium complex **14** was observed.

Efforts to change the selectivity by using catalytic conditions with different palladium species and a variety of hydride sources only gave double cyclization product **15**, 5-*exo*-*trig* cyclization product **16**, and direct reduction product **17**. The same was true for the radical cyclization of **9**, which has been previously described in the literature.[20]

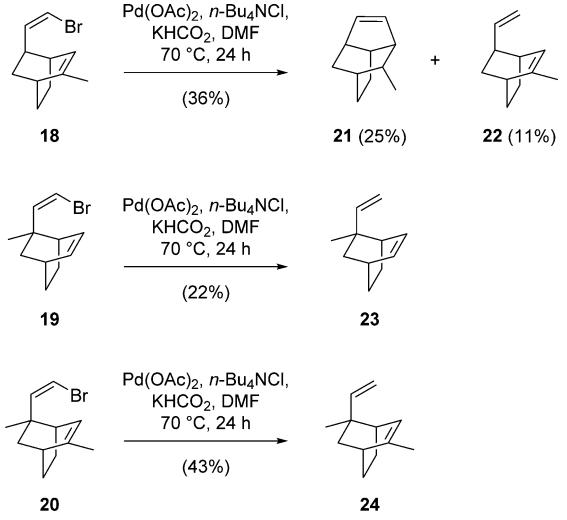
A possible way to influence the steric and electronic parameters of the cyclization reaction could be the introduction

Scheme 5. Exploration of the Cyclization Step on Bicyclic Precursors 9 and 10



of methyl substituents. Therefore, two monomethyl- and one dimethyl-substituted bicyclic cyclization precursors (**18**–**20**) were synthesized. The synthesis was carried out analogously to the preparation of **9** and **10** (see the Supporting Information). Attempts to cyclize **18** using transition-metal catalysis afforded only the undesired 5-*exo*-*trig*-cyclized product **21**, along with the product of direct reduction **22** (Scheme 6). In the case of

Scheme 6. Exploration of the Cyclization Step on Bicyclic Precursors 18–20



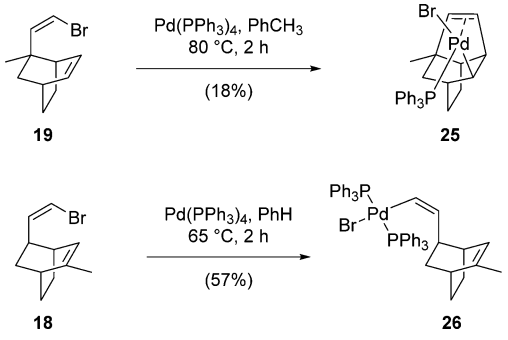
compound **19**, these conditions yielded diene **23**. The same result was also observed in the reaction of alkenyl bromide **20**. Stoichiometric palladation of **19** gave complex **25**, which was characterized by single-crystal X-ray diffraction (Scheme 7). By contrast, in the reaction of its isomer **18** with a stoichiometric amount of Pd(0) the formation of alkenylpalladium complex **26** was observed. This compound is one of the few alkenylpalladium complexes characterized by X-ray crystallography.[21] In no case was the desired 6-*endo*-*trig* product found.

Alkenyl halides **18**–**20** were submitted to radical cyclization conditions as well. As in the case of transition-metal catalysis we observed the formation of **21**, **22**, **23**, and **24**, respectively but could not identify any twistene structures.

Given the reluctance of bicyclo[2.2.2]octenes **9** and **10** to undergo the desired cyclizations, we decided to investigate precursors that contain a twist-boat motif, i.e., twistenes **27** and

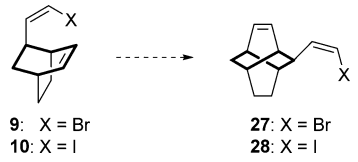
DOI: 10.1021/jo502618g
J. Org. Chem. 2015, 80, 2042–2055

Scheme 7. Stoichiometric Palladation of Alkenyl Bromides 18 and 19



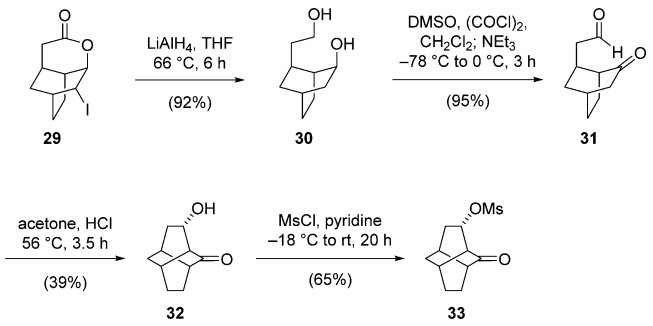
28 (Scheme 8). We reasoned that this modification would provide a helical bias toward the desired *6-endo-trig* cyclization mode.

Scheme 8. Expansion of the Precursor Scaffold To Helically Bias the System



Synthesis and Cyclization Attempts of Haloalkenyltricyclo[4.4.0.0^{3,8}]decene. The next objective was to synthesize an initiator compound that incorporates the twistane skeleton.[22] The synthesis of tricyclic compounds **27** and **28** started with the known iodolactone **29**, which was obtained in six steps from 1,3-cyclohexadiene (**7**), repeating the first steps of Whitlock's twistane synthesis (Scheme 9).[23] Reduction of **29**

Scheme 9. Formation of the Twistane Core by an Aldol Reaction



to diol **30**, followed by Swern oxidation, gave keto aldehyde **31**. Crude **31** could then be directly transformed to keto alcohol **32** in an aldol reaction yielding a separable 2:3 mixture of product and starting material, which could be recycled.[24] Unfortunately, elimination of the secondary alcohol could not be accomplished with standard reagents such as Martin's sulfurane, MsCl/pyridine and Burgess reagent. An X-ray crystal structure of mesylate **33** established the relative configuration of alcohol **32**.

Conversion of **32** to xanthate **34** followed by a subsequent Chugaev elimination was then investigated. However, under the forcing conditions necessary, a retro-Diels–Alder reaction followed by aromatization took place to afford phenol **36** as the major product (Scheme 10).

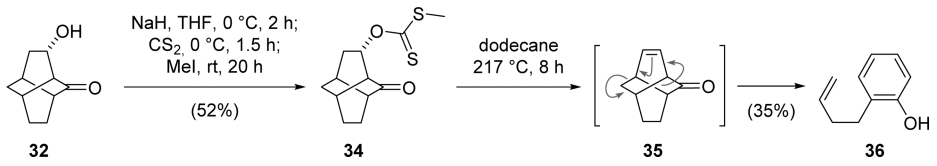
Since elimination reactions were not viable, we decided to introduce the double bond via a ketone. Oxidation of **32** gave diketone **37** which could be selectively converted into enol triflate **38** (Scheme 11). Palladium-catalyzed reduction then gave the desired twistenone **35**.[25] A three-step homologation of **35**, via **39** and **40**, then afforded twistenylcarbaldehyde **41** as a 3:1 mixture of diastereomers in favor of the desired isomer shown.[26] The diastereomers could be separated by column chromatography and the configuration of the desired product was confirmed by single crystal X-ray diffraction after conversion to the corresponding dinitrophenylhydrazone (see the Supporting Information). As in the synthesis of the bicyclo[2.2.2]octene systems, the alkenyl halide handle was established using Stork–Zhao reactions to afford **27** and **28**.[18]

With haloalkenyltwistenes **27** and **28** in hand the crucial cyclization step could be investigated again. The first cyclization attempt was carried out using stoichiometric amounts of $Pd(PPh_3)_4$, in order to facilitate the easy identification of the regiochemistry resulting from the cyclization. Indeed, from the reaction of bromoalkenyltwistene **27** with the Pd(0) source, crystals could be obtained which were suitable for single-crystal X-ray diffraction. Disappointingly, the analysis of the X-ray structure showed that the undesired 5-*exo-trig* cyclization mode was operational to yield isoditwistene palladium complex **42** (Scheme 12 and Figure 2). From the analogous reaction with iodoalkenyltwistene **28** only crystals of $PdI_2(PPh_3)_2$ were obtained. Attempts to thermally isomerize **42** to the desired **43** proved unsuccessful, resulting in decomposition.

Next, we tested the cyclization using reductive transition-metal-catalyzed conditions (Scheme 13). All conditions used only gave cyclopropane **44**, a new hydrocarbon, as the only identifiable product, but failed to deliver the desired ditwistene **45**.

It is well-known that palladium-mediated cyclizations occur predominantly following the *exo* mode for small- to medium-sized rings.[19] It has been argued that reported cases of *endo* cyclizations in such systems actually take place in a sequence of two *exo* cyclizations followed by a rearrangement, and this has been proven for several substrates.[27,28] From three-dimensional models it is obvious that this sequence of reactions is not possible for the present system because of its high rigidity. After 5-*exo-trig* and 3-*exo-trig* cyclizations via **46** and **47** cyclopropane Pd complex **48** would be formed (Scheme 14). The inversion of compound **48** to **49** cannot take place. Therefore, the ensuing rearrangement to ditwistene **50** is not possible and

Scheme 10. Attempt to Introduce the Double Bond by a Chugaev Elimination



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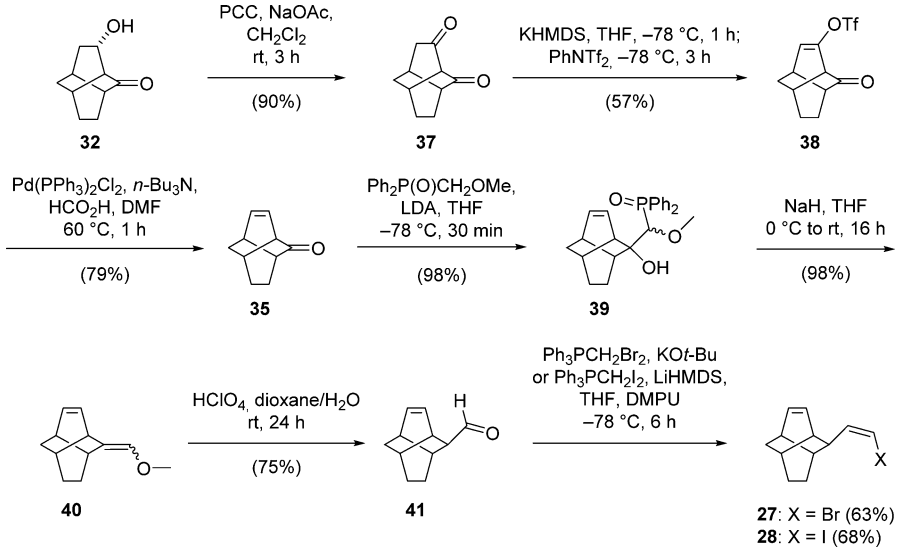
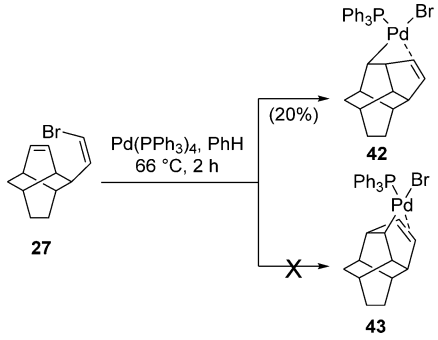
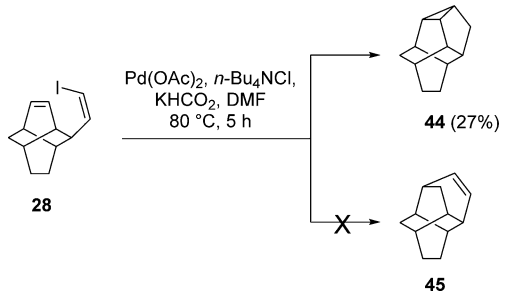
Scheme 11. Synthesis of Haloalkenyltwistenes 27 and 28 from Aldol Product 32



Scheme 12. Palladium-Mediated Cyclization of Bromoalkenyltwistene 27



Scheme 13. Cyclization of Haloalkenyltwistene 28 to Cyclopropane 44 under Reductive Transition-Metal-Catalyzed Conditions



cyclopropane **48** is converted to the corresponding palladium hydride and undergoes reductive elimination as observed in the catalytic reactions.

In parallel to palladium catalysis, the cyclization was investigated employing reductive radical conditions. Again we only obtained cyclopropane **44**, while never observing ditwistene **45** (Scheme 15). Special attention was paid to the concentration of the reaction mixture, as the 5-*exo-trig* vs 6-*endo-trig* selectivity of the radical reaction is reported to be sensitive to this parameter.[29] Even when the reactions were run at very low concentrations to allow for the establishment of the thermodynamic equilibrium, no formation of the desired product **45** could be observed.

In radical chemistry, 5-*exo-trig* cyclizations occur very fast compared to 6-*endo-trig* cyclizations.[29,30] However, in cyclizations involving vinylradicals the product of 5-*exo-trig* cyclization can interconvert to the product of the 6-*endo-trig* cyclization via a cyclopropylcarbinyl radical. Unfortunately, the cyclopropylcarbinyl radical is the only species that is trapped by the tin hydride in our case.

Further attempts to change the cyclization selectivity using among others carbolithiation conditions,[31] atom-transfer-radical-cyclization[32] (Cu^+, Bu_6Sn_2,[33] AIBN[34]) conditions, and

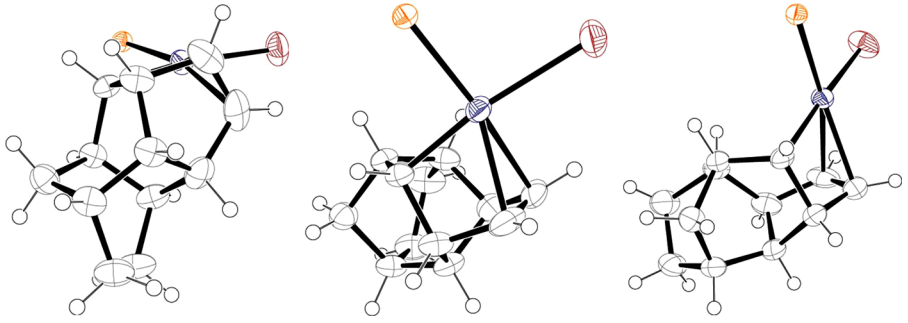


Figure 2. ORTEP plots of the X-ray crystal structure of isoditwistenepalladium bromide **42**. Ellipsoids are scaled to 50% probability except for hydrogens which are of arbitrary size. Phenyl rings are omitted for clarity. Color code: gray = C; black = H; red = Br, navy = Pd; orange = P.

DOI: 10.1021/jo502618g
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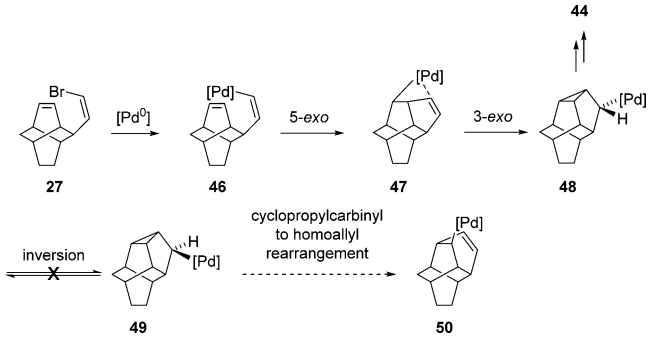
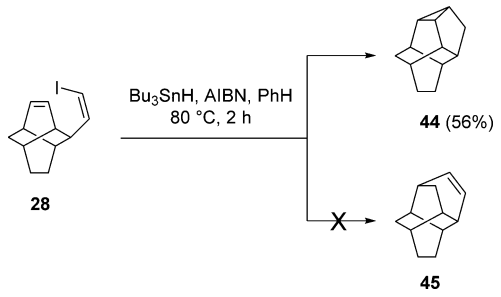
Scheme 14. Mechanism for the Formation of Cyclopropane 45



Scheme 15. Cyclization of Haloalkenyltwistene 29 to Cyclopropane 45 under Reductive Transition-Metal-Catalyzed Conditions



irradiation with different light sources yielded none of the desired product. In an attempt to exploit the thermodynamics in a series of cyclization reactions, the initiator molecules were also submitted to polymerization conditions using an excess of an acetylene derivative. Neither thermal nor photochemical conditions afforded polymeric materials.

Our investigations have led us to conclude that a "rational" approach to synthesizing polytwistane (**6**) from acetylene, as outlined in Scheme 3, is challenging. This does not preclude, however, that polytwistane (**6**) could be synthesized from acetylene under high temperature and/or high pressure conditions. It is also conceivable that fully saturated polytwistane (**6**) could be made from the conducting polymer polyacetylene in its various forms (Scheme 2).[35] Investigations in this direction, as well as attempts to favor a radical polymerization pathway by using substituted alkynes, are currently underway in our laboratories and will be reported in due course. Finally, it should be noted that the hydrocarbon nanorods recently obtained by the Badding group via ultrahigh pressure polymerization of benzene may well contain polytwistane (**6**) or polytwistane substructures.[10,13]

CONCLUSION

A synthetic route toward polytwistane via an initiator-biased acetylene polymerization was explored. Two initiator molecules with different helicities were synthesized. The simpler one exhibits a bicyclo[2.2.2]octene unit wherein a cyclohexane is locked in the boat conformation. In the second initiator molecule, cyclohexane rings are incorporated in the twist-boat conformation. The critical first cyclization step of the proposed polymerization was studied on both systems. The regioselectivity of the Pd-mediated cyclization was elucidated unambiguously by several X-ray analyses of the isolated novel Pd complexes. However, the products were found to be exclusively formed by the undesired 5-*exo* cyclization mode. All efforts to change the selectivity using reductive transition metal catalysis and reductive radical conditions led only to undesired products but provided the X-ray crystal structure of a new alkenylpalladium complex. In addition, a structurally attractive new hydrocarbon has been synthesized (compound **44**).

EXPERIMENTAL SECTION

General Considerations. All reactions, unless stated otherwise, were carried out under a positive pressure of N_2 in flame-dried glassware. Commercial reagents and solvents were used as purchased with the following exceptions. Tetrahydrofuran (THF) and diethyl ether (Et_2O) were predried over $CaCl_2$ and distilled over sodium and benzophenone under a nitrogen atmosphere immediately before use. Dichloromethane (CH_2Cl_2), Et_2O, ethyl acetate (EtOAc), hexanes, and *n*-pentane for flash chromatography and workup were obtained from technical grade by distillation in vacuo prior to use. Hexanes refers to the fraction of petroleum that boils between 40 and 60 °C. All reactions were magnetically stirred and monitored by analytical thin-layer chromatography (TLC) using silica gel 60 F_{254} glass-backed plates. Spots were visualized under UV light (254 nm) or by application of aqueous stains of basic potassium permanganate, ceric ammonium molybdate, anisaldehyde, dinitrophenylhydrazine, or vanillin followed by heating with a heat gun. The statement of drying a combined organic layer includes the removal of the drying agent by filtration and washing of the residue with an appropriate solvent. Flash column chromatography was performed on silica gel 60 (0.040−0.063 mm). Yields refer to chromatographically and spectroscopically pure material. Solutions were concentrated at 30 °C, if not specified otherwise. Nuclear magnetic resonance (NMR) spectra were recorded in $CDCl_3$, DMSO-d_6, or C_6D_6 at 300, 400, and 600 MHz for protons (75, 100, and 150 MHz for carbons). For the measurement of all ^{13}C NMR spectra broadband ^1H decoupling was employed. Chemical shifts (δ) were calibrated using the residual undeuterated solvent as an internal reference and are according to the common convention reported in parts per million (ppm) downfield relative to tetramethylsilane (TMS). The chemical shifts of the reference solvents were defined concurrent with the data from Nudelman and coworkers[36] for $CDCl_3$: 7.26 ppm (^1H NMR) and 77.16 ppm (^{13}C NMR), for DMSO-d_6: 2.50 ppm (^1H NMR) and 39.52 ppm (^{13}C NMR) and for C_6D_6: 7.16 ppm (^1H NMR) and 128.06 ppm (^{13}C NMR). For the designation of multiplicities the following abbreviations were used: s (singlet), d (doublet), t (triplet), br (broad), and m (multiplet) or combinations thereof. Protons and carbons were assigned using 2D spectra (HSQC, COSY, NOESY, HMBC). Infrared (IR) spectra were recorded on an instrument with a Diamond ATR sensor for detection in the range from 4500 to 600 cm^{-1}. Samples were prepared as a film for liquid or neat for solid substances. Data in the experimental part are given in units of cm^{-1}. High-resolution (HRMS) and low-resolution (LRMS) mass spectra were recorded using electron ionization (EI) with a sector field mass spectrometer or electrospray ionization (ESI) with a Fourier transform ion cyclotron resonance mass spectrometer. Here, only the high-resolution mass peak is given, and the used mode of ionization is stated. A graphical overview for the synthesis of methyl-substituted precursors **18**, **19**, and **20** and iodolactone **30** is enclosed in the Supporting Information.

Bicyclo[2.2.2]oct-5-ene-2-*endo*-carbaldehyde (8). To a solution of cyclohexadiene 7 (7.00 mL, 6.01 g, 75.0 mmol, 1.00 equiv) in 2-methoxyethyl ether (75.0 mL) at room temperature were added successively acrolein (25.0 mL, 21.0 g, 375 mmol, 5.00 equiv) and $BF_3 \cdot OEt_2$ (1.39 mL, 1.60 g, 11.3 mmol, 0.150 equiv). The reaction mixture was stirred at room temperature for 20 h. The mixture was diluted with H_2O (90 mL), and the aqueous layer was extracted with Et_2O (3 × 90 mL). The combined organic layer was washed with H_2O (3 × 90 mL), dried (Na_2SO_4) and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, *n*-pentane/Et_2O = 95:5) afforded bicycloaldehyde **8** (5.68 g, 56%) as a colorless oil: R_f = 0.59 (*n*-pentane/Et_2O = 95:5); ^1H NMR (300 MHz, $CDCl_3$) δ = 9.43

DOI: 10.1021/jo502618g
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(d, J = 1.6 Hz, 1H), 6.31 (ddd, J = 8.0, 6.6, 1.2 Hz, 1H), 6.09 (ddd, J = 8.0, 6.4, 1.2 Hz, 1H), 2.98−2.89 (m, 1H), 2.68−2.59 (m, 1H), 2.59−2.50 (m, 1H), 1.77−1.47 (m, 4H), 1.40−1.19 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 204.3, 136.4, 131.0, 51.2, 31.0, 29.5, 27.0, 25.5, 25.1 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2940, 2867, 1721, 1373, 1175, 1159, 1068, 952, 922, 850, 816, 700 cm^{-1}; HRMS (EI) m/z for $C_9H_{12}O^+$ $[M]^+$ calcd 136.0883, found 136.0886.

5-(*endo*-(*Z*)-2-Bromoalkenyl)bicyclo[2.2.2]oct-2-ene (9). To a solution of (bromomethyl)triphenylphosphonium bromide (22.6 g, 51.8 mmol, 1.10 equiv) in THF (214 mL) was added KO-*t*-Bu (5.81 g, 51.8 mmol, 1.10 equiv) at −78 °C. The resulting yellow reaction mixture was stirred at −78 °C for 15 min, after which time DMPU (26.7 mL, 28.4 g, 221 mmol, 4.70 equiv) and aldehyde **8** (6.41 g, 47.1 mmol, 1.00 equiv) were added successively. The mixture was stirred for an additional 4 h at −78 °C, diluted with hexanes (600 mL), and filtered over Celite. The residue was washed with hexanes (600 mL), and the combined filtrates were concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes/EtOAc = 100:1) afforded alkenyl bromide **9** (7.3 g, 73%) as a colorless oil: R_f = 0.69 (hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.38−6.30 (m, 1H), 6.19−6.11 (m, 1H), 5.96 (dd, J = 6.9, 1.0 Hz, 1H), 5.81 (dd, J = 9.0, 6.9 Hz, 1H), 2.91−2.78 (m, 1H), 2.58−2.51 (m, 1H), 2.51−2.44 (m, 1H), 1.93 (ddd, J = 12.5, 9.6, 2.6 Hz, 1H), 1.69−1.57 (m, 1H), 1.54−1.45 (m, 1H), 1.31−1.18 (m, 2H), 1.05−0.94 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 141.7, 135.8, 132.1, 104.7, 38.8, 34.4, 33.8, 29.8, 25.9, 24.5 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2936, 2864, 1616, 1374, 1323, 1290, 1277, 942, 913, 858, 805, 699, 670, 644, 627 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{13}Br^+$ $[M]^+$ calcd 212.0195, found 212.0197.

5-(*endo*-(*Z*)-2-Iodoalkenyl)bicyclo[2.2.2]oct-2-ene (10). To a suspension of (iodomethyl)triphenylphosphonium iodide (4.67 g, 8.80 mmol, 1.10 equiv) in THF (35.0 mL) at 0 °C was added a solution of KHMDS (1.00 M in THF, 8.80 mL, 8.80 mmol, 1.10 equiv). The resulting yellow reaction mixture was stirred at 0 °C for 5 min, after which time the mixture was cooled to −78 °C and DMPU (4.53 mL, 4.82 g, 37.6 mmol, 4.70 equiv) and a solution of aldehyde **8** (1.09 g, 8.00 mmol, 1.00 equiv) in THF (24.0 mL) were added successively. The mixture was stirred for 3 h at −78 °C and was then diluted with hexanes (110 mL) and filtered over Celite. The residue was washed with hexanes (330 mL), and the combined filtrates were concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes/EtOAc = 100:1) afforded alkenyl iodide **10** (1.21 g, 58%) as a colorless oil: R_f = 0.87 (hexanes/EtOAc = 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.37−6.30 (m, 1H), 6.18−6.10 (m, 1H), 5.99 (dd, J = 7.2, 0.8 Hz, 1H), 5.87 (dd, J = 8.7, 7.2 Hz, 1H), 2.71−2.60 (m, 1H), 2.60−2.51 (m, 1H), 2.51−2.43 (m, 1H), 1.94 (ddd, J = 12.4, 9.6 Hz, 2.7 Hz, 1H), 1.70−1.57 (m, 1H), 1.57−1.46 (m, 1H), 1.35−1.16 (m, 2H), 1.00 (dddd, J = 12.4, 4.7, 2.9, 2.9 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 148.0, 135.8, 132.2, 78.9, 43.7, 34.4, 33.5, 29.8, 25.9, 24.5 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2935, 2863, 1604, 1319, 1268, 1238, 912, 857, 801, 712, 699, 660, 636, 610 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{13}I^+$ $[M]^+$ calcd 260.0056, found 260.0064.

Tricyclo[4.3.1.0^{3,7}]dec-4-ene-2-yltriphenylphosphine-palladium(II) Bromide (11). To a solution of $Pd(PPh_3)_4$ (497 mg, 0.430 mmol, 1.00 equiv) in benzene (3.00 mL) was added (*Z*)-alkenyl bromide **9** (91.6 mg, 0.430 mmol, 1.00 equiv) via syringe. The yellow reaction mixture was heated to 65 °C for 2 h. The mixture was allowed to cool to room temperature, and Et_2O (50 mL) was added, precipitating a white solid. The precipitate was filtered off, and the filtrate was allowed to stand. Upon slow evaporation of the solvent the title palladium complex **11** (122 mg, 49%) crystallized in the form of yellow platelets. Crystals suitable for single-crystal X-ray diffraction could be obtained from this mixture: mp 148 °C dec; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.74−7.68 (m, 6H), 7.44−7.36 (m, 9H,), 6.91−6.86 (m, 1H), 6.19−6.15 (m, 1H), 3.13−3.05 (m, 1H), 2.90−2.82 (m, 1H), 2.56−2.49 (m, 1H), 2.21−2.14 (m, 1H), 1.74 (dd, J = 13.0, 8.1 Hz, 1H), 1.60−1.49 (m, 2H), 1.44−1.35 (m, 1H), 1.25−1.22 (m, 1H), 1.02−0.90 (m, 2H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 134.6 (d, J = 12.3 Hz), 133.4 (d, J = 9.8 Hz), 131.2 (d, J = 43.8 Hz), 130.7 (d, J = 2.4 Hz), 128.5 (d, J = 10.4 Hz), 87.0 (d, J = 13.0 Hz), 48.7 (s), 46.3 (s), 41.4 (d, J = 2.4 Hz), 33.1 (s), 31.9 (s), 30.1 (d, J = 5.1 Hz), 26.9 (d, J = 7.9 Hz), 18.1 (s) ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2924, 2857, 1333, 977, 910, 808, 731, 701 cm^{-1}; HRMS (ESI+) m/z for $C_{28}H_{28}PPd^+$ $[M - Br]^+$ calcd 501.0958, found 501.0962.

Tricyclo[4.3.1.0^{3,7}]dec-4-ene-2-yltriphenylphosphine-palladium(II) Iodide (12). To a solution of $Pd(PPh_3)_4$ (497 mg, 0.430 mmol, 1.00 equiv) in benzene (3.00 mL) was added (*Z*)-alkenyl iodide **10** (112 mg, 0.430 mmol, 1.00 equiv). The yellow reaction mixture was heated to 50 °C for 2 h. The mixture was allowed to cool to room temperature, and Et_2O (25 mL) was added, precipitating a white solid. The precipitate was filtered off, and the filtrate was allowed to stand. Upon slow evaporation of the solvent the title palladium complex **12** (150 mg, 56%) crystallized in the form of yellow platelets. Crystals suitable for single-crystal X-ray diffraction could be obtained from this mixture: R_f = 0.49 (hexanes/EtOAc = 3:1); mp 136 °C dec; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.72−7.65 (m, 6H), 7.41−7.36 (m, 9H), 7.20−7.11 (m, 1H), 6.05−5.96 (m, 1H), 3.21−3.11 (m, 1H), 2.87−2.82 (m, 1H), 2.56−2.49 (m, 1H), 2.25−2.18 (m, 1H), 1.71 (dd, J = 13.1, 8.1 Hz, 1H), 1.63−1.50 (m, 2H), 1.46−1.38 (m, 1H), 1.33−1.27 (m, 1H), 1.17−1.07 (m, 1H), 1.00−0.92 (m, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 134.9 (d, J = 12.1 Hz), 131.6 (br s), 131.3 (d, J = 44.0 Hz), 130.7 (d, J = 2.3 Hz), 128.5 (d, J = 10.5 Hz), 84.7 (br s), 48.5 (s), 46.9 (s), 41.2 (s), 32.2 (s), 31.9 (s), 30.5 (s), 28.7 (br s), 18.0 (s) ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2930, 1434, 1090, 998, 981, 758, 743, 703, 694, 688 cm^{-1}; HRMS (ESI+) m/z for $C_{28}H_{28}PPd^+$ $[M - I]^+$ calcd 501.0958, found 501.0959.

Tricyclo[4.3.1.0^{3,7}]dec-4-ene-2-ylbistriphenylphosphine-palladium(II) Tetrafluoroborate (13). A mixture of Pd-complex **11** (79.7 mg, 0.137 mmol, 1.00 equiv), $AgBF_4$ (26.7 mg, 0.137 mmol, 1.00 equiv), and PPh_3 (35.9 mg, 0.137 mmol, 1.00 equiv) in CH_2Cl_2 (15.0 mL) was stirred at room temperature for 1.5 h and was then filtered. Et_2O (15.0 mL) was added to the filtrate, and the mixture was allowed to stand to facilitate crystallization. Silver bromide deposited on the bottom of the flask. The supernatant solution was decanted and concentrated in vacuo. Crystallization of the residue from CH_2Cl_2/Et_2O afforded yellow crystals of complex **13** (80 mg, 69%) that were suitable for single-crystal X-ray diffraction: R_f = 0.43 (CH_2Cl_2/MeOH = 95:5); mp 117 °C dec; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.51−7.44 (m, 6H), 7.43−7.35 (m, 6H), 7.34−7.27 (m, 12H), 7.13−7.07 (m, 6H), 5.99−5.92 (m, 1H), 5.82−5.74 (m, 1H), 3.53−3.43 (m, 1H), 2.73−2.64 (m, 1H), 2.49−2.41 (m, 1H), 2.32−2.22 (m, 1H), 1.97−1.87 (m, 1H), 1.60−1.50 (m, 2H), 1.49−1.40 (m, 1H), 1.40−1.33 (m, 1H), 1.29−1.20 (m, 1H), 0.97−0.86 (m, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 134.3 (d, J = 12.4 Hz), 133.5 (d, J = 12.4 Hz), 131.6 (s), 130.8 (s), 130.4 (d, J = 30.4 Hz), 129.5 (d, J = 30.4 Hz), 129.3 (d, J = 8.6 Hz), 129.1, 129.0 (d, J = 8.6 Hz), 90.0 (br s), 47.8 (s), 47.0 (s), 41.1 (s), 33.1 (s), 31.9 (s), 30.9 (br s), 29.9 (br s), 17.9 (s) ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2926, 1481, 1434, 1094, 1056, 742, 695 cm^{-1}; HRMS (ESI+) m/z for $C_{28}H_{28}PPd^+$ $[M - PPh_3 - BF_4]^+$ calcd 501.0958, found 501.0960.

Cyclization of Alkenyl Bromide 9 with Catalytic Amounts of Palladium. To a round-bottom flask were added $Pd(OAc)_2$ (106 mg, 0.470 mmol 0.100 equiv), 1,3-bis(diphenylphosphino)propane (236 mg, 0.940 mmol, 0.200 equiv), and potassium formate (1.19 g, 14.1 mmol, 3.00 equiv). The flask was evacuated and refilled with argon three times. The salts were dissolved in degassed DMF (250 mL), and alkenyl bromide **9** (1.00 g, 4.70 mmol, 1.00 equiv) was added. The reaction mixture was transferred to a preheated oil bath and stirred at 60 °C for 24 h. During the reaction, the color of the mixture turned from yellow to black. The reaction mixture was allowed to cool to room temperature and was diluted with H_2O (200 mL) and pentane (200 mL), and the resulting mixture was stirred for 15 min at room temperature. The organic layer was separated, and the aqueous layer was extracted with *n*-pentane (3 × 50 mL). The combined organic layer was dried (Na_2SO_4) and concentrated in vacuo (at room temperature). Purification of the residue by flash column chromatography (silica, *n*-pentane) afforded cyclopropane **15** as a colorless solid (33 mg, 5%), isotwistene **16** (196 mg, 28%) as a colorless solid, and vinyl bicyclooctene **17** (400 mg, 52%) as a colorless oil.

Tetracyclo[4.4.0.0^{3,8}.0^{5,7}]decane (15): R_f = 0.88 (hexanes); mp 117−121 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.06−2.01 (m, 1H),

DOI: 10.1021/jo502618g
J. Org. Chem. 2015, 80, 2042−2055

1.97−1.92 (m, 1H), 1.81−1.76 (m, 2H), 1.70−1.64 (m, 1H), 1.63−1.56 (m, 1H), 1.50−1.43 (m, 2H), 1.42−1.35 (m, 1H), 1.29−1.22 (m, 2H), 1.15−1.07 (m, 2H), 0.80−0.74 (m, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 35.6, 33.2, 33.1, 33.0, 27.4, 25.1, 19.6, 18.4, 17.1, 16.3 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2928, 2861, 778, 752, 735 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{14}^+$ $[M]^+$ calcd 134.1090, found 134.1087.

Tricyclo[4.3.1.0^{3,7}]dec-4-ene-Isotwistene (16): R_f = 0.82 (hexanes); mp 96−98 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 6.10−6.07 (m, 2H), 2.29−2.24 (m, 2H), 2.09−2.05 (m, 1H), 1.83−1.77 (m, 3H), 1.58−1.54 (m, 2H), 1.47−1.36 (m, 4H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 140.2, 40.3, 39.4, 29.7, 28.5, 28.4, 19.7 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2924, 2856, 1450, 1345, 966, 907, 819, 785, 726 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{14}^+$ $[M]^+$ calcd 134.1090, found 134.1097.

5-endo-Vinylbicyclo[2.2.2]oct-2-ene (17): R_f = 0.75 (hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.32 (ddd, J = 7.9, 6.6, 1.1 Hz, 1H), 6.22−6.14 (m, 1H), 5.61 (ddd, J = 17.2, 10.1, 8.1 Hz, 1H), 4.92 (ddd, J = 17.2, 2.0, 1.1 Hz, 1H), 4.83 (ddd, J = 10.1, 2.0 Hz, 0.9 Hz, 1H), 2.57−2.51 (m, 1H), 2.51−2.44 (m, 1H), 2.44−2.37 (m, 1H), 1.82 (ddd, J = 12.4, 9.5, 2.7 Hz, 1H), 1.66−1.44 (m, 2H), 1.41−1.23 (m, 2H), 1.16−1.04 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 145.6, 135.0, 132.2, 111.8, 42.6, 35.9, 33.8, 30.0, 26.3, 24.6 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2927, 2861, 994, 906, 857, 819, 727, 708, 676, 668 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{14}^+$ $[M]^+$ calcd 134.1090, found 134.1092.

5-Methylbicyclo[2.2.2]oct-5-ene-2-*endo*-carbaldehyde (S2). To a solution of methylcyclohexadiene **S1**[37] (4.54 mL, 3.77 g, 40.0 mmol, 1.00 equiv) in 2-methoxyethyl ether (20.0 mL) at room temperature were added successively acrolein (4.00 mL, 3.36 g, 60.0 mmol, 1.50 equiv) and $BF_3{\cdot}OEt_2$ (0.740 mL, 0.852 g, 6.00 mmol, 0.300 equiv). The reaction mixture was stirred at room temperature for 20 h. The mixture was diluted with H_2O (50 mL), and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic layer was washed with H_2O (3 × 50 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, *n*-pentane/Et_2O = 95:5) afforded bicycloaldehyde **S2** (3.83 g, 64%) as a colorless oil: R_f = 0.62 (hexanes/EtOAc = 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 9.42 (d, J = 1.6 Hz, 1H), 5.72−5.66 (m, 1H), 2.90−2.82 (m, 1H), 2.54−2.46 (m, 1H), 2.45−2.39 (m, 1H), 1.76 (d, J = 1.7 Hz, 3H), 1.74−1.45 (m, 4H), 1.41−1.22 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 204.6, 145.1, 123.1, 52.0, 35.1, 31.7, 26.7, 26.4, 24.8, 20.3 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 3429, 2935, 2870, 1711, 1452, 1375, 1353, 1176, 1095, 1046, 995, 967, 923 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{14}O^+$ $[M]^+$ calcd 150.1039, found 150.1037.

5-(*endo*-(*Z*)-2-Bromoalkenyl)-2-methylbicyclo[2.2.2]oct-2-ene (18). To a solution of (bromomethyl)triphenylphosphonium bromide (9.59 g, 22.0 mmol, 1.10 equiv) in THF (91.0 mL) at −78 °C was added KO-*t*-Bu (2.47 g, 22.0 mmol, 1.10 equiv). The resulting yellow reaction mixture was stirred at −78 °C for 30 min, after which time DMPU (11.3 mL, 12.0 g, 94.0 mmol, 4.70 equiv) and aldehyde **S2** (3.00 g, 20.0 mmol, 1.00 equiv) were added successively. The mixture was stirred for an additional 3 h at −78 °C and was then diluted with hexanes (300 mL) and filtered over Celite. The residue was washed with hexanes (300 mL), and the combined filtrates were concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes/EtOAc = 1000:1) afforded alkenyl bromide **18** (3.74 g, 82%) as a colorless oil: R_f = 0.73 (hexanes); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.95 (dd, J = 6.8, 0.8 Hz, 1H), 5.81 (dd, J = 8.9, 6.8 Hz, 1H), 5.78−5.73 (m, 1H), 2.87−2.75 (m, 1H), 2.42−2.35 (m, 1H), 2.35−2.30 (m, 1H), 1.91 (ddd, J = 12.5, 9.6, 2.7 Hz, 1H), 1.80 (d, J = 1.7 Hz, 3H), 1.65−1.54 (m, 1H), 1.53−1.43 (m, 1H), 1.32−1.18 (m, 2H), 0.98 (dddd, J = 12.5, 5.0, 2.8, 2.8 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 144.2, 142.0, 124.2, 104.5, 39.6, 35.3, 34.9, 33.4, 26.7, 24.2, 20.4 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2930, 2861, 1443, 1322, 1290, 1277, 981, 940, 912, 854, 808, 799, 707, 663 cm^{-1}; HRMS (EI) m/z for $C_{11}H_{15}Br^+$ $[M]^+$ calcd 226.0352, found 226.0345.

2-Methylbicyclo[2.2.2]oct-5-en-2-*endo*-carbaldehyde (S3). To a solution of cyclohexadiene **7** (3.73 mL, 3.21 g, 40.0 mmol, 2.00 equiv) in 2-methoxyethyl ether (20.0 mL) at room temperature were added successively methacrolein (1.66 mL, 1.40 g, 20.0 mmol, 1.00 equiv) and $BF_3{\cdot}OEt_2$ (0.370 mL, 0.426 g, 3.00 mmol, 0.150 equiv). The reaction mixture was stirred at room temperature for 20 h and was then quenched by addition of K_2HPO_4 (522 mg, 3.00 mmol, 0.150 equiv). The mixture was diluted with H_2O (25 mL), and the aqueous layer was extracted with Et_2O (3 × 30 mL). The combined organic layer was washed with H_2O (3 × 25 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, *n*-pentane/Et_2O = 97:3) afforded bicycloaldehyde **S3** (1.64 g, 54%) as a colorless oil: R_f = 0.53 (hexanes: EtOAc = 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.30 (s, 1H), 6.26−6.19 (m, 2H), 2.62−2.55 (m, 1H), 2.49−2.43 (m, 1H), 2.03−1.96 (m, 1H), 1.92−1.84 (m, 1H), 1.56−1.47 (m, 1H), 1.30−1.10 (m, 6H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 205.7, 135.2, 133.6, 50.0, 36.1, 35.6, 30.6, 25.2, 21.3, 20.3 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2943, 2866, 1721, 1449, 1368, 1074, 1058, 1041, 900, 812, 693, 668 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{14}O^+$ $[M]^+$: calcd 150.1039, found 150.1048.

5-(*endo*-(*Z*)-2-Bromoalkenyl)-5-methylbicyclo[2.2.2]oct-2-ene (19). To a solution of (bromomethyl)triphenylphosphonium bromide (3.48 g, 7.99 mmol, 1.10 equiv) in THF (33.0 mL) at −78 °C was added KO-*t*-Bu (0.896 g, 7.99 mmol, 1.10 equiv). The resulting yellow reaction mixture was stirred at −78 °C for 15 min, after which time DMPU (4.11 mL, 4.37 g, 34.1 mmol, 4.70 equiv) and aldehyde **S3** (1.09 g, 7.26 mmol, 1.00 equiv) were added successively. The mixture was stirred for an additional 3 h at −78 °C and was then diluted with hexanes (200 mL) and filtered over Celite. The residue was washed with hexanes (200 mL), and the combined filtrates were concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes/EtOAc = 100:1) afforded alkenyl bromide **19** (1.27 g, 77%) as a colorless oil: R_f = 0.85 (hexanes/EtOAc = 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.37−6.24 (m, 2H), 6.20 (d, J = 7.6 Hz, 1H), 5.92 (d, J = 7.6 Hz, 1H), 2.57−2.45 (m, 2H), 1.98−1.84 (m, 2H), 1.57 (dd, J = 12.9, 2.4 Hz, 1H), 1.53−1.40 (m, 1H), 1.37 (s, 3H), 1.30−1.05 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 146.9, 135.0, 135.0, 103.8, 45.1, 41.1, 40.2, 31.5, 25.5, 24.4, 20.9 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2940, 2922, 2862, 1608, 1443, 1367, 1312, 911, 811, 746, 702, 692, 671, 641, 615, 566 cm^{-1}; HRMS (EI) m/z for $C_{11}H_{15}^+$ $[M - Br]^+$ calcd 147.1168, found 147.1159.

2,5-Dimethylbicyclo[2.2.2]oct-5-ene-2-*endo*-carbaldehyde (S4). To a solution of methylcyclohexadiene **S1** (2.27 mL, 1.88 g, 20.0 mmol, 1.00 equiv) in 2-methoxyethyl ether (20.0 mL) at room temperature were added successively methacrolein (2.48 mL, 2.10 g, 30.0 mmol, 1.50 equiv) and $BF_3{\cdot}OEt_2$ (0.370 mL, 0.426 g, 3.00 mmol, 0.300 equiv). The reaction mixture was stirred at room temperature for 20 h. The mixture was diluted with H_2O (25 mL), and the aqueous layer was extracted with Et_2O (3 × 25 mL). The combined organic layer was washed with H_2O (3 × 25 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, *n*-pentane/Et_2O = 95:5) afforded bicycloaldehyde **S4** (1.24 g, 38%) as a colorless oil: R_f = 0.44 (*n*-pentane/Et_2O = 95:5); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.30 (s, 1H), 5.82−5.79 (m, 1H), 2.40−2.37 (m, 1H), 2.37−2.34 (m, 1H), 2.02 (ddd, J = 13.0, 3.2, 3.2 Hz, 1H), 1.87 (dddd, J = 12.8, 9.6, 3.1, 3.1 Hz, 1H), 1.73 (d, J = 1.7 Hz, 3H), 1.50 (dddd, J = 12.0, 9.6, 4.7, 2.4 Hz, 1H), 1.26 (ddddd, J = 12.0, 9.9, 3.2, 3.2, 3.1 Hz, 1H), 1.17 (dddd, J = 12.8, 9.9, 4.8, 3.2 Hz, 1H), 1.11 (s, 3H), 1.10 (dd, J = 13.0, 2.4 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 206.0, 144.1, 125.6, 50.6, 36.8, 36.3, 35.1, 25.0, 21.3, 21.0, 20.2 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2930, 2869, 1713, 1447, 1377, 1162, 1103, 1067, 990, 756 cm^{-1}; HRMS (EI) m/z for $C_{11}H_{16}O^+$ $[M]^+$ calcd 164.1196, found 164.1204.

5-(*endo*-(*Z*)-2-Bromoalkenyl)-2,5-dimethylbicyclo[2.2.2]oct-2-ene (20). To a solution of (bromomethyl)triphenylphosphonium bromide (3.60 g, 8.25 mmol, 1.10 equiv) in THF (34.0 mL) at −78 °C was added KO-*t*-Bu (0.926 g, 8.25 mmol, 1.10 equiv). The resulting yellow reaction mixture was stirred at −78 °C for 30 min, after which time DMPU (4.25 mL, 4.52 g, 35.3 mmol, 4.70 equiv) and aldehyde **S4** (1.23 g, 7.50 mmol, 1.00 equiv) were added successively. The mixture was stirred for an additional 3 h at −78 °C and was then diluted with hexanes (600 mL) and filtered over Celite. The residue was washed with hexanes (600 mL), and the combined filtrates were concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes/EtOAc = 1000:1) afforded alkenyl bromide **20** (620 mg, 35%) as a colorless oil: R_f = 0.91 (hexanes/

DOI: 10.1021/jo502618g
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EtOAc = 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.20 (d, J = 7.6 Hz, 1H), 5.94−5.89 (m, 1H), 5.90 (d, J = 7.6 Hz, 1H), 2.39−2.33 (ddd, J = 6.2, 2.9, 2.9 Hz, 1H), 2.33−2.26 (m, 1H), 1.97−1.81 (m, 2H), 1.76 (d, J = 1.7 Hz, 3H), 1.55 (dd, J = 12.9, 2.4 Hz, 1H), 1.44 (dddd, J = 11.7, 9.4, 5.1, 2.9 Hz, 1H), 1.35 (s, 3H), 1.24 (ddddd, J = 11.7, 9.4, 3.2, 3.2, 3.2 Hz, 1H), 1.16−1.03 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 147.2, 143.5, 127.0, 103.6, 44.5, 41.8, 40.7, 37.1, 25.6, 23.9, 21.8, 20.4 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2919, 2861, 1609, 1443, 1373, 1313, 1113, 915, 820, 800, 742, 692 cm^{-1}; HRMS (EI) m/z for $C_{12}H_{17}Br^+$ $[M]^+$ calcd 240.0508, found 240.0515.

Cyclization of Alkenyl Bromide 18 with Catalytic Amounts of Palladium. To a round-bottom flask were added $Pd(OAc)_2$ (12.3 mg, 0.055 mmol, 0.025 equiv), n-Bu_4NCl (611 mg, 2.20 mmol, 1.00 equiv), and potassium formate (555 mg, 6.60 mmol, 3.00 equiv). The flask was evacuated and refilled with argon three times. The salts were dissolved in degassed DMF (132 mL), and alkenyl bromide **18** (0.500 g, 2.20 mmol, 1.00 equiv) was added. The reaction mixture was transferred to a preheated oil bath and stirred at 70 °C for 24 h. During the reaction, the color of the mixture turned from yellow to black. The reaction mixture was allowed to cool to room temperature and was diluted with H_2O (110 mL) and pentane (110 mL), and the resulting mixture was stirred for 15 min at room temperature. The organic layer was separated, and the aqueous layer was extracted with n-pentane (3 × 110 mL). The combined organic layer was dried (Na_2SO_4) and concentrated in vacuo (at room temperature). Purification of the residue by flash column chromatography (silica, n-pentane) afforded methylisotwistene **21** (80 mg, 25%) as a colorless oil and vinyl bicyclooctene **22** (35 mg, 11%) contaminated with methylisotwistene **21** as a colorless oil.

*2-Methyltricyclo[4.3.1.0^{3,7}]dec-4-ene (**21**):* R_f = 0.78 (hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 6.09 (dd, J = 5.7, 3.0 Hz, 1H), 6.07 (dd, J = 5.7, 2.9 Hz, 1H), 2.27−2.23 (m, 1H), 2.08−2.04 (m, 1H), 1.87−1.79 (m, 1H), 1.79−1.74 (m, 3H), 1.70−1.67 (m, 1H), 1.67−1.62 (m, 1H), 1.48−1.44 (m, 2H), 1.31−1.23 (m, 1H), 0.94 (d, J = 7.2 Hz, 3H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 140.5, 139.6, 47.2, 41.0, 38.5, 34.6, 32.6, 31.6, 21.1, 20.7, 19.2 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 3403, 2924, 2864, 1713, 1454, 1404, 1373, 1352, 1266, 1187, 1131, 1104, 1095, 1067, 1041, 1018, 994, 927, 913, 885, 853, 753, 666 cm^{-1}; HRMS (EI) m/z for $C_{11}H_{16}^+$ $[M]^+$ calcd 148.1247, found 148.1243.

*2-Methyl-5-endo-vinylbicyclo[2.2.2]oct-2-ene (**22**):* R_f = 0.68 (hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 5.77−5.74 (m, 1H), 5.56 (ddd, J = 17.2, 10.2, 8.2 Hz, 1H), 4.87 (ddd, J = 17.2, 2.0, 1.1 Hz, 1H), 4.79 (ddd, J = 10.2, 2.0, 0.9 Hz, 1H), 2.37−2.34 (m, 1H), 2.34−2.31 (m, 1H), 2.31−2.28 (m, 1H), 1.79 (d, J = 1.8 Hz, 3H), 1.78−1.74 (m, 1H), 1.57−1.51 (m, 1H), 1.48−1.43 (m, 1H), 1.27−1.21 (m, 2H), 1.08−1.02 (m, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 145.9, 143.3, 124.3, 111.5, 43.4, 36.3, 35.6, 33.5, 27.2, 24.3, 20.3 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2926, 2862, 1710, 1453, 1375, 1356, 1335, 1168, 1102, 1067, 1041, 995, 967, 913, 876, 852, 805, 733 cm^{-1}; HRMS (EI) m/z for $C_{11}H_{16}^+$ $[M]^+$ calcd 148.1247, found 148.1253.

5-Methyl-5-*endo*-vinylbicyclo[2.2.2]oct-2-ene (23). To a round-bottom flask were added $Pd(OAc)_2$ (2.8 mg, 0.013 mmol, 0.025 equiv), n-Bu_4NCl (139 mg, 0.500 mmol, 1.00 equiv), and potassium formate (126 mg, 1.50 mmol, 3.00 equiv). The flask was evacuated and refilled with argon three times. The salts were dissolved in degassed DMF (30.0 mL), and alkenyl bromide **19** (114 mg, 0.500 mmol, 1.00 equiv) was added. The reaction mixture was transferred to a preheated oil bath and stirred at 70 °C for 24 h. During the reaction, the color of the mixture turned from yellow to black. The reaction mixture was allowed to cool to room temperature and was diluted with H_2O (30 mL) and pentane (30 mL) and the resulting mixture was stirred for 15 min at room temperature. The organic layer was separated, and the aqueous layer was extracted with n-pentane (3 × 25 mL). The combined organic layer was dried (Na_2SO_4) and concentrated in vacuo (at room temperature). Purification of the residue by flash column chromatography (silica, n-pentane) afforded vinyl bicyclooctene **23** (16 mg, 22%) as a colorless oil: R_f = 0.74 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.28 (ddd, J = 8.0, 6.5, 1.3 Hz, 1H), 6.17 (ddd, J = 8.0, 6.0, 1.2 Hz, 1H), 5.77 (dd, J = 17.5, 10.8 Hz, 1H), 4.79 (dd, J = 17.5, 1.4 Hz, 1H), 4.78 (dd, J = 10.7, 1.4 Hz, 1H), 2.51 (dddddd, J = 6.0, 3.5, 3.5, 2.2, 2.2, 1.3 Hz, 1H), 2.17 (dddd, J = 6.5, 2.8, 2.8, 1.2 Hz, 1H), 1.91 (dddd, J = 12.7, 9.7, 3.0, 2.8 Hz, 1H), 1.52−1.43 (m, 2H), 1.31−1.20 (m, 2H), 1.15 (s, 3H), 1.16−1.04 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 150.9, 135.7, 132.4, 108.9, 41.0, 40.4, 39.6, 31.1, 27.1, 24.2, 21.8 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2926, 2862, 1634, 1448, 1366, 1005, 904, 886, 816, 810, 731, 716, 689 cm^{-1}; HRMS (EI) m/z for $C_{11}H_{16}^+$ $[M]^+$ calcd 148.1247, found 148.1240.

2,5-Dimethyl-5-*endo*-vinylbicyclo[2.2.2]oct-2-ene (24). To a round-bottom flask were added $Pd(OAc)_2$ (2.8 mg, 0.013 mmol. 0.025 equiv), n-Bu_4NCl (139 mg, 0.500 mmol, 1.00 equiv), and potassium formate (126 mg, 1.50 mmol, 3.00 equiv). The flask was evacuated and refilled with argon three times. The salts were dissolved in degassed DMF (30.0 mL), and alkenyl bromide **20** (121 mg, 0.500 mmol, 1.00 equiv) was added. The reaction mixture was transferred to a preheated oil bath and stirred at 70 °C for 24 h. During the reaction, the color of the mixture turned from yellow to black. The reaction mixture was allowed to cool to room temperature and was diluted with H_2O (30 mL) and pentane (30 mL), and the resulting mixture was stirred for 15 min at room temperature. The organic layer was separated, and the aqueous layer was extracted with n-pentane (3 × 25 mL). The combined organic layer was dried (Na_2SO_4) and concentrated in vacuo (at room temperature). Purification of the residue by flash column chromatography (silica, n-pentane) afforded vinyl bicyclooctene **24** (35 mg, 43%) as a colorless oil: R_f = 0.75 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 5.88−5.85 (ddq, J = 6.7, 2.1, 1.7 Hz, 1H), 5.77 (dd, J = 17.3, 10.9 Hz, 1H), 4.80−4.74 (m, 2H), 2.28 (ddddd, J = 3.8, 3.8, 2.1, 2.1, 2.1 Hz, 1H), 2.06 (ddd, J = 6.7, 2.8, 2.8 Hz, 1H), 1.89 (dddd, J = 12.7, 9.6, 3.0, 3.0 Hz, 1H), 1.76 (d, J = 1.7 Hz, 3H), 1.50−1.41 (m, 2H), 1.31−1.20 (m, 2H), 1.13 (s, 3H), 1.13−1.06 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 151.2, 140.7, 127.7, 108.6, 41.0, 40.6, 40.2, 36.7, 26.9, 23.8, 22.6, 20.2 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2923, 2861, 1446, 906, 887, 733 cm^{-1}; HRMS (EI) m/z for $C_{12}H_{18}^+$ $[M]^+$ calcd 162.1403, found 162.1383.

6-Methyltricyclo[4.3.1.0^{3,7}]dec-4-ene-2-yltriphenylphosphinepalladium(II) Bromide (25). To a solution of $Pd(PPh_3)_4$ (497 mg, 0.430 mmol, 1.00 equiv) in toluene (3.00 mL) was added (*Z*)-alkenyl bromide **19** (97.7 mg, 0.430 mmol, 1.00 equiv) by syringe. The yellow reaction mixture was heated to 80 °C for 2 h. The mixture was allowed to cool to room temperature, and Et_2O (50 mL) was added, precipitating a white solid. The precipitate was filtered off, and the filtrate was allowed to stand. Upon slow evaporation of the solvent, palladium complex **25** (45 mg, 18%) crystallized in the form of yellow platelets. Crystals suitable for single-crystal X-ray diffraction could be obtained from this mixture: mp 158 °C dec; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.75−7.69 (m, 6H), 7.46−7.38 (m, 9H), 6.61−6.56 (m, 1H), 6.15−6.12 (m, 1H), 3.23−3.17 (m, 1H), 3.04 (dd, J = 13.0, 4.1 Hz, 1H), 1.83−1.78 (m, 1H), 1.61−1.52 (m, 1H), 1.47−1.32 (m, 3H), 1.27−1.21 (m, 1H), 1.16 (s, 3H), 0.99−0.89 (m, 2H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 136.9 (d, J = 10.0 Hz), 134.7 (d, J = 12.3 Hz), 131.0 (d, J = 43.9 Hz), 130.7 (d, J = 2.4 Hz), 128.5 (d, J = 10.4 Hz), 85.1 (d, J = 13.3 Hz), 52.6 (s), 50.2 (s), 45.5 (d, J = 2.4 Hz), 41.4 (s), 32.6 (s), 30.3 (d, J = 5.1 Hz), 26.7 (d, J = 7.4 Hz), 23.4 (s), 16.0 (s) ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2361, 2339, 1436, 743, 739, 694, 668 cm^{-1}; HRMS (ESI+) m/z for $C_{29}H_{30}PPd^+$ $[M - Br]^+$ calcd 515.1114, found 515.1117.

(*Z*)-2-(2-Methylbicyclo[2.2.2]oct-2-en-5-*endo*-yl)vinylbis(triphenylphosphine)palladium(II) Bromide (26). To a solution of $Pd(PPh_3)_4$ (994 mg, 0.860 mmol, 1.00 equiv) in benzene (6.00 mL) was added (*Z*)-alkenyl bromide **18** (195 mg, 0.860 mmol, 1.00 equiv) by syringe. The yellow reaction mixture was heated to 65 °C for 2 h. The mixture was allowed to cool to room temperature and Et_2O (50 mL) was added, precipitating a white solid. The precipitate was filtered off, and the filtrate was allowed to stand. Upon slow evaporation of the solvent, palladium complex **26** (290 mg, 57%) crystallized in the form of yellow platelets. Crystals suitable for single-crystal X-ray diffraction could be obtained from this mixture. For NMR analysis the reaction was run in C_6D_6 in a NMR tube resulting in a mixture of starting material and product in the NMR: mp 123 °C dec;^{1}H NMR (400 MHz, C_6D_6): δ = 7.99−7.92 (m, 12H), 7.44 (m, 18H), 5.75 (td, J =

DOI: 10.1021/jo502618g
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10.4, 7.2 Hz, 1H), 5.54 (dq, J = 6.7, 1.7 Hz, 1H), 4.95 (ddt, J = 9.4, 7.3, 4.7 Hz, 1H), 3.07 (dddd, J = 9.4, 9.3, 4.8, 2.0 Hz, 1H), 2.14−2.06 (m, 1H), 2.02−1.94 (m, 1H), 1.88−1.78 (m, 1H), 1.60 (d, J = 1.7 Hz, 3H), 1.57−1.50 (m, 1H), 1.37 (ddd, J = 12.4, 9.3, 2.7 Hz, 1H), 1.32−1.24 (m, 2H), 0.64 (dddd, J = 12.4, 4.8, 2.6, 2.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, C_6D_6): δ = 144.2, 142.7, 137.7, 135.9, 134.3, 134.1, 132.5 (d, J = 44.0 Hz), 125.0, 47.0, 36.2, 36.1, 34.7, 27.8, 24.8, 20.4 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 1478, 1434, 1309, 1262, 1183, 1094, 1027, 998, 751, 741, 703, 689, 677 cm^{-1}; HRMS (ESI+) m/z for $C_{29}H_{30}PPd^+$ [M − PPh_3 − Br]$^+$ calcd 515.1114, found 515.1117.

Methylbicyclo[2.2.2]oct-5-ene-2-*endo*-carboxylate (S5).[38] Within a glovebox, bis(trifluoromethane)sulfonamide (26.4 g, 93.8 mmol, 0.150 equiv) was weighed into a one-necked flask. Allyltrimethylsilane (29.8 mL, 21.4 g, 188 mmol, 0.300 equiv) was added outside of the glovebox at 0 °C with stirring, and stirring was continued at room temperature until the end of gas evolution. The reaction mixture was concentrated for 1 h under high vacuum. The residue was dissolved in toluene (1.25 L), and methyl acrylate (S6.3 mL, 53.8 g, 0.625 mol, 1.00 equiv) and cyclohexadiene **7** (89.4 mL, 75.1 g, 0.938 mol, 1.50 equiv) were added successively at 0 °C to the solution. The reaction mixture was stirred at 0 °C for 3.5 h, after which time 880 mL of a saturated aqueous $NaHCO_3$ solution were added to the violet reaction mixture. The resulting mixture was stirred at room temperature for 1 h during which time it turned yellow. The organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 600 mL). The combined organic layer was dried ($MgSO_4$) and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes/EtOAc = 9:1) afforded bicycloester **S5** as a colorless oil (104 g, 99%): R_f = 0.44 (hexanes/EtOAc = 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.35−6.27 (m, 1H), 6.18−6.11 (m, 1H), 3.63−3.62 (s, 3H), 2.96−2.88 (m, 1H), 2.67−2.56 (m, 2H), 1.79−1.64 (m, 2H), 1.60−1.45 (m, 2H), 1.33−1.19 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 176.1, 135.3, 131.5, 51.8, 42.8, 32.6, 30.0, 29.5, 25.5, 24.5 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2943, 2866, 1733, 1453, 1434, 1374, 1351, 1320, 1235, 1195, 1171, 1081, 1054, 1031, 889, 698 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{14}O_2^+$ [M]$^+$ calcd 166.0994, found 166.0982.

5-*endo*-Hydroxymethylbicyclo[2.2.2]oct-2-ene (S6).[23] To a solution of $LiAlH_4$ (2.50 g, 66.0 mmol, 0.600 equiv) in Et_2O (130 mL) was added dropwise a solution of bicycloester **S5** (18.3 g, 110 mmol, 1.00 equiv) in Et_2O (25.0 mL). After complete addition, the reaction mixture was heated to 35 °C for 16 h and was then cooled to 0 °C. Excess $LiAlH_4$ was hydrolyzed by dropwise addition of H_2O. Rochelle salt was added until a homogeneous solution was obtained. The aqueous layer was extracted with Et_2O (4 × 50 mL), and the combined organic layer was washed with H_2O (75 mL) and brine (75 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes: Et_2O = 2:1) afforded bicyclooctenol **S6** (14.3 g, 94%) as a colorless oil: R_f = 0.44 (hexanes/EtOAc = 1:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 6.27 (ddd, J = 8.0, 6.6, 1.2 Hz, 1H), 6.16−6.09 (m, 1H), 3.28−3.21 (m, 2H), 2.63−2.57 (m, 1H), 2.53−2.45 (m, 1H), 1.93−1.86 (m, 1H), 1.67 (ddd, J = 12.2, 9.5, 2.7 Hz, 1H), 1.55−1.45 (m, 2H), 1.32−1.21 (m, 2H), 0.80−0.70 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 135.2, 131.9, 67.7, 40.7, 31.5, 30.3, 29.9, 26.1, 24.9 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 3315, 2933, 2862, 1463, 1450, 1376, 1049, 1029, 1012, 973, 900, 851, 809, 733, 702 cm^{-1}; HRMS (EI) m/z for $C_9H_{14}O^+$ [M]$^+$ calcd 138.1039, found 138.1048.

5-*endo*-Mesyloxymethylbicyclo[2.2.2]oct-2-ene (S7).[23] To a solution of bicyclic alcohol **S6** (14.4 g, 104 mmol, 1.00 equiv) in pyridine (26.0 mL) at 0 °C was added dropwise MsCl (8.85 mL, 13.1 g, 114 mmol, 1.10 equiv). The resulting reaction mixture was allowed to warm to room temperature and allowed to stand at this temperature for 4 h after which time H_2O (6 mL) was added. The reaction mixture was poured into H_2O (50 mL) and extracted with Et_2O (3 × 75 mL). The combined organic layer was washed with 1 M HCl (100 mL), H_2O (100 mL), and brine (100 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes/EtOAc = 9:1) afforded mesylate **S7** (21.4 g, 95%) as a colorless oil: R_f = 0.19 (hexanes/EtOAc = 9:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 6.33−6.29 (m, 1H), 6.14−6.10 (m, 1H), 3.81−3.79 (m, 2H), 2.98 (s, 3H), 2.65−2.61 (m, 1H), 2.55−2.51 (m, 1H), 2.18−2.11 (m, 1H), 1.72 (ddd, J = 12.6, 9.7, 2.7 Hz, 1H), 1.55−1.47 (m, 2H), 1.33−1.25 (m, 2H), 0.74 (dddd, J = 12.8, 5.3, 3.1, 3.1 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 135.6, 131.2, 73.6, 37.4, 37.4, 31.0, 29.6, 29.6, 25.4, 24.6 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2940, 2866, 1351, 1172, 981, 946, 904, 868, 840, 814, 706 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{16}O_3S^+$ [M]$^+$ calcd 216.0815, found 216.0814.

5-*endo*-Cyanomethylbicyclo[2.2.2]oct-2-ene (S8).[23] Mesylate **S7** (22.5 g, 104 mmol, 1.00 equiv) was dissolved in DMF (46.0 mL), NaCN (11.3 g, 231 mmol, 2.22 equiv) and NaI (0.363 g, 2.42 mmol, 0.023 equiv) were added, and the mixture was heated to 110 °C for 16 h. The reaction mixture was allowed to cool to room temperature and was then poured into H_2O (100 mL). The aqueous layer was extracted with hexanes (3 × 100 mL). The combined organic layer was washed with H_2O (150 mL) and brine (150 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes/Et_2O = 9:1 to 4:1) afforded nitrile **S8** (10.3 g, 67%) as a colorless oil: R_f = 0.41 (hexanes/EtOAc = 9:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 6.33 (ddd, J = 8.0, 6.7, 1.0 Hz, 1H), 6.14−6.10 (m, 1H), 2.59−2.56 (m, 1H), 2.56−2.52 (m, 1H), 2.12−2.04 (m, 3H), 1.88−1.83 (m, 1H), 1.54 (dddd, J = 12.1, 9.8, 4.0, 2.5 Hz, 1H), 1.45 (dddd, J = 12.0, 9.8, 4.2, 2.3 Hz, 1H), 1.34 (dddd, J = 12.1, 12.0, 4.2, 3.4 Hz, 1H), 1.22 (ddddd, J = 12.0, 12.0, 4.0, 3.1, 3.1 Hz, 1H), 0.86−0.81 (m, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 135.9, 130.7, 119.6, 34.9, 34.0, 33.3, 29.9, 25.7, 24.5, 24.1 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2937, 2866, 1425, 1376, 707 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{13}N^+$ [M]$^+$ calcd 147.1043, found 147.1034.

5-*endo*-Carboxymethylbicyclo[2.2.2]oct-2-ene (S9).[23] A mixture of nitrile **S8** (10.3 g, 69.7 mmol, 1.00 equiv) and KOH (7.82 g, 139 mmol, 2.00 equiv) in ethylene glycol (40.0 mL) was heated to 155 °C and stirred at this temperature for 2 h. The reaction mixture was allowed to cool to room temperature, diluted with H_2O (100 mL), and extracted with Et_2O (100 mL). The aqueous layer was acidified (1 m HCl) and extracted with Et_2O (8 × 100 mL). The combined organic layer was washed with H_2O (200 mL) and brine (200 mL), dried (Na_2SO_4), and concentrated in vacuo to afford bicyclic acid **S9** (11.0 g, 95%) as a colorless solid: R_f = 0.16 (hexanes/EtOAc = 9:1); mp 39−41 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 6.31−6.27 (m, 1H), 6.14−6.10 (m, 1H), 2.50−2.46 (m, 1H), 2.45−2.42 (m, 1H), 2.21 (dd, J = 14.4, 7.0 Hz, 1H), 2.18−2.12 (m, 1H), 2.07 (dd, J = 14.4, 7.3 Hz, 1H), 1.83 (ddd, J = 12.5, 9.2, 2.7 Hz, 1H), 1.55 (dddd, J = 12.3, 9.8, 3.9, 2.6 Hz, 1H), 1.45 (dddd, J = 11.8, 9.8, 4.1, 2.3 Hz, 1H), 1.28 (dddd, J = 12.3, 12.1, 4.1, 3.3 Hz, 1H), 1.20 (ddddd, J = 12.1, 11.8, 3.9, 3.1, 3.0 Hz, 1H), 0.84 (dddd, J = 12.5, 4.7, 3.0, 3.0 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 179.6, 135.3, 131.6, 41.9, 34.4, 34.3, 33.8, 30.0, 26.1, 24.3 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 3042, 2935, 1702, 1408, 1294, 1230, 938, 706 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{14}O_2^+$ [M]$^+$ calcd 166.0988, found 166.0990.

Iodolactonization of Carboxylic Acid S9.[23] Carboxylic acid **S9** (16.1 g, 97.0 mmol, 1.00 equiv) was suspended in H_2O (47.0 mL) and dissolved by dropwise addition of cold 50 wt % aqueous NaOH. Solid $NaHCO_3$ was added to saturation, and a solution of I_2 (40.9 g, 161 mmol, 1.66 equiv) and KI (37.5 g, 226 mmol, 2.33 equiv) in H_2O (125 mL) was added. The resulting mixture was stirred at room temperature for 2 h and then decolorized by addition of solid $Na_2S_2O_3$. The layers were separated, and the aqueous layer was extracted with EtOAc (3 × 600 mL). The combined organic layer was washed with 1 N NaOH (450 mL) and brine (450 mL), dried (Na_2SO_4), and concentrated in vacuo. The desired iodolactone **29** (25.9 g, 91%) was obtained as a colorless solid by recrystallization from EtOAc. Purification of the residue after four recrystallizations by flash column chromatography (silica, hexanes/EtOAc = 9:1 to 4:1) afforded rearranged iodolactone **S10** 122 mg, 0.4%) as a colorless solid. Crystals suitable for single-crystal X-ray diffraction could be obtained by recrystallization from EtOAc for both compounds.

6-Iodo-4-oxatricyclo[7.1.1.0^{5,10}]undecan-3-one (S10): R_f = 0.44 (hexanes: EtOAc = 3:1); mp 94−97 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 4.79 (dd, J = 5.6, 3.3 Hz, 1H), 4.56 (ddd, J = 3.3, 3.3, 3.3 Hz, 1H), 2.97−2.87 (m, 2H), 2.60−2.52 (m, 1H), 2.48 (dd, J = 16.8, 2.5 Hz,

DOI: 10.1021/jo502618g
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1H), 2.38 (dd, J = 16.8, 4.0 Hz, 1H), 2.10−2.05 (m, 1H), 2.02 (dddd, J = 15.3, 12.4, 4.7, 3.3 Hz, 1H), 1.85 (dddd, J = 14.6, 12.4, 6.9, 5.1 Hz, 1H), 1.74−1.67 (m, 1H), 1.62−1.55 (m, 1H), 1.45−1.39 (m, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 171.5, 78.2, 32.9, 30.2, 30.0, 28.2, 27.7, 27.1, 23.0, 22.4 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2927, 1735, 1361, 1236, 1228, 1215, 1174, 1146, 1066, 1037, 973 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{13}IO_2^+$ $[M]^+$ calcd 291.9955, found 291.9956.

*2-Iodo-4-oxatricyclo[5.3.1.0^{3,8}]undecan-5-one (**29**):* R_f = 0.39 (hexanes/EtOAc = 3:1); mp 125−127 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 5.03−5.00 (m, 1H), 4.32−4.27 (m, 1H), 2.58 (dd, J = 18.2, 5.4 Hz, 1H), 2.48 (dd, J = 18.2, 1.9 Hz, 1H), 2.20 (ddd, J = 14.1, 11.1, 3.7 Hz, 1H), 2.15−2.08 (m, 1H), 2.01−1.93 (m, 2H), 1.89−1.84 (m, 1H), 1.82−1.74 (m, 2H), 1.54−1.45 (m, 1H), 1.39 (dddd, J = 14.1, 5.1, 2.8, 2.8 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 168.9, 87.1, 39.3, 33.7, 33.2, 32.3, 29.8, 24.5, 21.4, 20.0 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2943, 1718, 1381, 1370, 1353, 1225, 1210, 1179, 1143, 1094, 1056, 1032, 1004, 836 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{13}IO_2^+$ $[M]^+$ calcd 291.9955, found 291.9940.

2-*endo*-Hydroxy-6-*endo*-(2-hydroxyethyl)bicyclo[2.2.2]-octane (30). A suspension of $LiAlH_4$ (9.96 g, 263 mmol, 5.00 equiv) in THF (400 mL) was heated to 66 °C, and a solution of iodolactone **29** (15.3 g, 52.5 mmol, 1.00 equiv) in THF (100 mL) was added over the course of 1.5 h. After complete addition, the reaction mixture was refluxed for an additional 6 h and was then cooled to 0 °C. Rochelle salt was added to provide a homogeneous solution. The reaction mixture was extracted with EtOAc (3 × 400 mL). The combined organic layer was washed with brine (350 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes/EtOAc = 1:1) afforded desired diol **30** (8.26 g, 92%) as a colorless solid. Recrystallization of diol **30** from CH_2Cl_2 afforded crystals suitable for single-crystal X-ray diffraction: R_f = 0.21 (hexanes/EtOAc = 1:1); mp 81−83 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 4.02 (dddd, J = 9.8, 3.5, 3.5, 1.4 Hz, 1H), 3.73 (ddd, J = 10.8, 5.5, 5.5 Hz, 1H), 3.64 (ddd, J = 10.8, 8.1, 5.2 Hz, 1H), 2.39 (br s, 2H), 1.98 (dddd, J = 13.2, 9.8, 3.0, 2.5 Hz, 1H), 1.92 (dddd, J = 13.8, 8.1, 8.0, 5.5 Hz, 1H), 1.86−1.78 (m, 3H), 1.78−1.72 (m, 1H), 1.72−1.68 (m, 1H), (m, 1H), 1.46−1.37 (m, 3H), 1.37−1.30 (m, 1H), 1.24 (dddd, J = 12.2, 5.9, 2.5, 2.5 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 71.3, 62.2, 40.6, 38.2, 34.9, 34.7, 33.1, 25.9, 25.5, 23.6 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 3324, 2925, 2861, 1453, 1378, 1331, 1163, 1102, 1078, 1035, 1002, 948, 928, 874, 846, 752 cm^{-1}; HRMS (ESI−) m/z for $C_{11}H_{19}O_4^-$ $[M + HCO_2^-]^-$ calcd 215.1289, found 215.1289.

2-(2-Oxobicyclo[2.2.2]octan-6-*endo*-yl)acetaldehyde (31). A solution of DMSO (2.30 mL, 2.53 g, 32.4 mmol, 5.40 equiv) in CH_2Cl_2 (16.6 mL) was added dropwise to a solution of oxalyl chloride (7.80 mL, 2 m in CH_2Cl_2, 10.4 g, 15.6 mmol, 2.60 equiv) in CH_2Cl_2 (58.0 mL) at −78 °C. The internal temperature was monitored during the addition to ensure that the temperature did not rise above −50 °C. At −78 °C, a solution of diol **30** (1.02 g, 6.00 mmol, 1.00 equiv) in CH_2Cl_2 (20.0 mL) was added dropwise to the dimethylchlorosulfonium chloride solution, and after complete addition, the mixture was stirred for an additional 1 h at −78 °C. During the addition of the alcohol, precipitation of a white solid was observed to afford an opaque solution. Triethylamine (8.34 mL, 60.0 mmol, 10.0 equiv) was added in one portion, and the reaction was stirred for 10 min at −78 °C during which time the precipitate dissolved again to afford a clear solution. The solution was slowly (30 min) warmed to 0 °C and maintained at 0 °C for 1 h. Upon warming, a white solid again precipitated. The cold solution was partitioned between saturated aqueous $NaHCO_3$ (100 mL) and CH_2Cl_2 (50 mL). The layers were separated, and the aqueous layer was extracted with CH_2Cl_2 (3 × 100 mL). The combined organic layer was washed with brine (100 mL), dried (Na_2SO_4), and concentrated in vacuo. The crude reaction products (0.95 g, 95%) were used without further purification in the next step: R_f = 0.51 (hexanes: EtOAc = 1:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.72−9.70 (dd, J = 1.5, 1.3 Hz, 1H), 2.54 (ddddd, J = 10.4, 8.3, 6.2, 6.1, 2.3 Hz, 1H), 2.45 (ddd, J = 17.7, 6.2, 1.3 Hz, 1H), 2.30 (ddd, J = 17.7, 8.3, 1.5 Hz, 1H), 2.27−2.22 (m, 1H), 2.20−2.07 (m, 4H), 1.93−1.85 (m, 1H), 1.81 (dddd, J = 14.0, 11.3, 5.7, 2.8 Hz, 1H), 1.72−1.59 (m, 2H), 1.08 (dddd, J = 11.4, 5.8, 2.6, 2.8 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 216.5, 200.7, 51.3, 47.5, 45.0, 33.4, 30.5, 28.0, 23.5, 23.1 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2937, 2870, 1716, 1402, 1102 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{14}O_2^+$ $[M]^+$ calcd 166.0988, found 166.0986.

4-*endo*-Hydroxytricyclo[4.4.0.0^{3,8}]decan-2-one (32). To a solution of keto aldehyde **31** (997 mg, 6.00 mmol, 1.00 equiv) in acetone (25.6 mL) was added 1 M HCl (2.40 mL, 2.40 mmol, 0.400 equiv), and the resulting solution was heated to reflux for 3.5 h. After the solution was cooled to 0 °C, $NaHCO_3$ (201 mg, 2.40 mmol, 0.400 equiv) and water (30 mL) were added, and the acetone was removed in vacuo. The residue was extracted with EtOAc (3 × 50 mL), and the combined organic layer was dried (Na_2SO_4) and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes/EtOAc = 3:1 to 1:1) afforded hydroxytwistanone **32** (389 mg, 39%) as a colorless waxy amorphous solid. Significant amounts of starting material (590 mg, 3.55 mmol, ∼55%) could be reisolated and used for another cycle of the aldol reaction: R_f = 0.17 (hexanes: EtOAc = 1:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 4.29 (ddd, J = 8.0, 8.0, 2.0 Hz, 1H), 2.36−2.21 (m, 5H), 1.95−1.87 (m, 1H), 1.85−1.78 (m, 1H), 1.71 (br s, 1H), 1.65−1.58 (m, 1H), 1.58−1.51 (m, 1H), 1.51−1.45 (m, 2H), 1.22−1.16 (m, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 221.0, 70.2, 57.2, 48.5, 37.7, 31.6, 31.0, 25.7, 25.5, 24.5 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 3397, 2937, 2863, 1725, 1325, 1267, 1129, 1091, 1071, 1052, 1040, 1027, 1005, 978, 728 cm^{-1}; HRMS (EI) m/z for $C_{10}H_{14}O_2^+$ $[M]^+$ calcd 166.0988, found 166.0990.

4-*endo*-Mesyloxytricyclo[4.4.0.0^{3,8}]decan-2-one (33). To a solution of keto alcohol **32** (201 mg, 1.21 mmol, 1.00 equiv) in pyridine (10.1 mL) at −18 °C was added methanesulfonyl chloride (0.258 mL, 383 mg, 3.34 mmol, 2.76 equiv). The resulting solution was stirred at room temperature for 20 h and was then diluted with $CHCl_3$ (75 mL). The organic layer was washed with 10% aqueous $CuSO_4$ (5 × 40 mL) and brine (100 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes: EtOAc = 3:1 to 1:1) afforded keto mesylate **33** (193 mg, 65%) as a colorless solid. Recrystallization from EtOAc afforded crystals suitable for single-crystal X-ray diffraction: R_f = 0.21 (hexanes/EtOAc = 1:1); mp 128−130 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 5.22−5.15 (m, 1H), 3.06 (s, 3H), 2.62 (dddd, J = 6.1, 2.2, 1.2, 1.2 Hz, 1H), 2.44−2.38 (m, 2H), 2.39−2.31 (m, 2H), 1.92 (dddd, J = 13.0, 10.0, 9.3, 1.8 Hz, 1H), 1.85 (dddd, J = 13.0, 8.7, 4.4, 0.9 Hz, 1H), 1.66−1.48 (m, 5H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 217.3, 77.8, 53.1, 47.8, 39.3, 34.8, 31.1, 30.9, 25.2, 25.0, 24.8 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2937, 2869, 1722, 1389, 1357, 1225, 1182, 1162, 1100, 1055, 1012 cm^{-1}; HRMS (EI) m/z for $C_{11}H_{16}O_4S^+$ $[M]^+$ calcd 244.0764, found 244.0759.

***S*-Methyl-*O*-(2-oxotricyclo[4.4.0.0^{3,8}]decan-4-yl)carbonodithioate (34).** To a solution of keto alcohol **32** (50.0 mg, 0.300 mmol, 1.00 equiv) in THF (24.0 mL) at 0 °C was added sodium hydride (72.0 mg, 3.00 mmol, 10.0 equiv). The resulting reaction mixture was stirred at 0 °C for 2 h, after which time CS_2 (1.20 mL, 1.51 g, 19.8 mmol, 66.0 equiv) was added, and the mixture was stirred at 0 °C for an additional 1.5 h. Methyl iodide (0.600 mL, 1.37 g, 9.64 mmol, 32.1 equiv) was added, and the solution was allowed to warm to room temperature and stirred at room temperature for 20 h. To the reaction mixture were added successively Et_2O (25 mL) and ice−water (12 mL). The aqueous layer was extracted with Et_2O (3 × 20 mL), and the combined organic layer was washed with brine (50 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes/EtOAc = 9:1) afforded the desired xanthate **34** (40 mg, 52%) as a yellow oil: R_f = 0.17 (hexanes/EtOAc = 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 5.98−5.90 (m, 1H), 2.65−2.58 (m, 1H), 2.50 (s, 3H), 2.46−2.32 (m, 4H), 1.99−1.77 (m, 2H), 1.68−1.42 (m, 5H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 218.5, 214.8, 80.4, 52.5, 48.0, 33.6, 31.0, 31.0, 25.6, 25.2, 25.0, 18.8 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2936, 1735, 1273, 1239, 1224, 1197, 1163, 1146, 1128, 1095, 1071, 1054, 1046, 1031, 1020, 967, 951, 874 cm^{-1}; HRMS (EI) m/z for $C_{12}H_{16}O_2S_2^+$ $[M]^+$ calcd 256.0586, found 256.0589.

2-(But-3-en-1-yl)phenol (36). Xanthate **34** (39.5 mg, 0.154 mmol, 1.00 equiv) was dissolved in dodecane (15.0 mL), and the

DOI: 10.1021/jo502618g
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solution was heated to 217 °C for 8 h. The reaction mixture was allowed to cool to room temperature and was directly purified by flash column chromatography (silica, *n*-pentane/Et_2O = 9:1) to afford only retro-Diels–Alder product **36** (8 mg, 35%) and starting material **34**. Due to the volatility of the compound no complete separation from the solvent was possible: R_f = 0.34 (hexanes/EtOAc = 9:1); ^{1}H NMR (300 MHz, $CDCl_3$) δ = 7.15–7.10 (m, 1H), 7.09–7.05 (m, 1H), 6.90–6.84 (m, 1H), 6.78–6.74 (m, 1H), 5.98–5.83 (m, 1H), 5.12–4.97 (m, 2H), 4.95 (s, 1H), 2.76–2.68 (m, 2H), 2.44–2.33 (m, 2H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 153.7, 138.4, 130.4, 128.0, 127.3, 120.9, 115.4, 115.2, 34.0, 29.8 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 1711, 1362, 1218, 752, 667 cm^{-1}; HRMS (EI) *m*/*z* for $C_{10}H_{12}O^+$ $[M]^+$ calcd 148.0883, found 148.0887.

Tricyclo[4.4.0.0^{3,8}]decane-2,4-dione (37). A mixture of PCC (73.6 g, 342 mmol, 5.00 equiv), sodium acetate (29.4 g, 359 mmol, 5.25 equiv), 4 Å molecular sieves (20 g), and Celite (150 g) was dried under high vacuum at room temperature for 1 h. The solids were suspended in CH_2Cl_2 (400 mL), and to the stirred mixture was added a solution of keto alcohol **32** (11.4 g, 68.3 mmol, 1.00 equiv) in CH_2Cl_2 (500 mL). The resulting mixture was stirred for 3 h at room temperature and was then filtered over a short silica column. The residue was washed with CH_2Cl_2 (2 L), and the combined filtrate was concentrated in vacuo. A second filtration over a silica column gave diketone **37** (10.1 g, 90%) as a colorless solid: R_f = 0.30 (hexanes/EtOAc = 3:1); mp 198–201 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 3.15 (d, *J* = 5.9 Hz, 1H), 2.66–2.61 (m, 1H), 2.57 (dd, *J* = 4.9, 4.9 Hz, 1H), 2.55–2.51 (m, 1H), 2.31 (dd, *J* = 17.4, 4.2 Hz, 1H), 2.20–2.14 (m, 1H), 2.10–2.03 (m, 1H), 1.99 (ddd, *J* = 13.2, 9.1, 4.9 Hz, 1H), 1.89 (ddd, *J* = 13.0, 5.9, 2.8 Hz, 1H), 1.68 (ddd, *J* = 13.3, 9.2, 4.3 Hz, 1H), 1.62–1.55 (m, 1H), 1.49 (dd, *J* = 13.0, 5.7 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 212.3, 206.3, 69.6, 45.7, 45.5, 33.8, 29.3, 28.3, 26.1, 24.9 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2948, 1746, 1716, 1312, 1116, 1060 cm^{-1}; HRMS (EI) *m*/*z* for $C_{10}H_{12}O_2^+$ $[M]^+$ calcd 164.0832, found 164.0831.

2-Oxotricyclo[4.4.0.0^{3,8}]dec-4-en-4-yl Trifluoromethanesulfonate (38). A solution of dione **37** (852 mg, 5.19 mmol, 1.00 equiv) in THF (10.0 mL) was added to a solution of KHMDS (1.14 g, 5.71 mmol, 1.10 equiv) in THF (140 mL) at −78 °C. The resulting mixture was stirred at −78 °C for 1 h and was then transferred to a solution of $PhNTf_2$ (2.13 g, 5.97 mmol, 1.15 equiv) in THF (60.0 mL) at −78 °C. The reaction mixture was stirred at −78 °C for an additional 3 h and was then quenched by addition of saturated aqueous $NaHCO_3$ (50 mL). The organic layer was separated, and the aqueous layer was extracted with Et_2O (3 × 130 mL). The combined organic layer was washed with 10% aqueous NaOH (260 mL), 1 N HCl (260 mL), and brine (2 × 260 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, *n*-pentane/Et_2O = 3:1) afforded enol triflate **38** (875 mg, 57%) as a colorless oil: R_f = 0.12 (hexanes/EtOAc = 9:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 6.31 (dd, *J* = 7.3, 2.5 Hz, 1H), 3.37–3.32 (m, 1H), 3.09 (dddd, *J* = 7.3, 5.4, 5.3, 1.0 Hz, 1H), 2.38–2.31 (m, 1H), 2.11 (dddd, *J* = 5.3, 3.6, 2.2, 1.0 Hz, 1H), 1.94 (dd, *J* = 12.0, 5.4 Hz, 1H), 1.88–1.82 (m, 2H), 1.72 (dddd, *J* = 13.3, 6.6, 4.5, 3.3 Hz, 1H), 1.61 (ddddd, *J* = 13.3, 9.6, 9.6, 1.7, 1.7 Hz, 1H), 1.33 (ddddd, *J* = 12.0, 6.7, 1.8, 1.0, 1.0 Hz, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$) δ = 208.3, 144.0, 125.7, 118.6 (q, *J* = 321.1 Hz), 57.5, 36.6, 33.3, 30.8, 27.7, 25.1, 24.4 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 1746, 1636, 1421, 1244, 1205, 1137, 1087, 1077, 1049, 965, 891, 875, 844, 828, 728, 649, 609 cm^{-1}; HRMS (EI) *m*/*z* for $C_{11}H_{11}F_3O_4S^+$ $[M]^+$ calcd 296.0325, found 296.0317.

Tricyclo[4.4.0.0^{3,8}]dec-4-en-2-one (35). To a mixture of enol triflate **38** (430 mg, 1.45 mmol, 1.00 equiv), *n*-Bu_3N (1.04 mL, 806 mg, 4.35 mmol, 3.00 equiv), and $Pd(PPh_3)Cl_2$ (102 mg, 0.145 mmol, 0.100 equiv) in degassed DMF (20.7 mL) was added formic acid (0.109 mL, 133 mg, 2.90 mmol, 2.00 equiv), and the resulting mixture was stirred at 60 °C for 1 h. The mixture was allowed to cool to room temperature, and H_2O (15 mL) was added. The mixture was extracted with Et_2O (3 × 45 mL), and the combined organic layer was washed with 1 N HCl (2 × 60 mL), saturated aqueous $NaHCO_3$ (60 mL), and brine (2 × 60 mL), dried (Na_2SO_4), and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, *n*-pentane/Et_2O = 4:1) afforded alkene **35** (170 mg, 79%) as a colorless solid: R_f = 0.57 (hexanes: EtOAc = 3:1); mp 150–153 °C; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 6.55 (ddd, *J* = 7.3, 6.0, 0.8 Hz, 1H), 5.92 (ddd, *J* = 7.3, 7.1, 1.9 Hz, 1H), 3.25–3.19 (m, 1H), 2.94–2.87 (m, 1H), 2.09–2.05 (m, 1H), 2.05–2.02 (m, 1H), 1.87 (ddd, *J* = 11.6, 5.7, 1.2 Hz, 1H), 1.85–1.77 (m, 2H), 1.72–1.67 (m, 1H), 1.66–1.59 (m, 1H), 1.22 (ddddd, *J* = 11.6, 6.8, 2.0, 0.9, 0.9 Hz, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 213.8, 140.9, 124.3, 54.9, 38.5, 36.3, 31.0, 27.6, 25.8, 25.1 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2953, 2929, 1731, 702 cm^{-1}; HRMS (EI) *m*/*z* for $C_{10}H_{12}O^+$ $[M]^+$ calcd 148.0883, found 148.0884.

((2-Hydroxytricyclo[4.4.0.0^{3,8}]dec-4-en-2-yl)(methoxy)-methyl)diphenylphosphine Oxide (39). To a solution of diisopropylamine (10.8 mL, 7.71 g, 76.2 mmol, 4.95 equiv) in THF (100 mL) at 0 °C was added *n*-butyllithium (2.75 M in hexanes, 25.5 mL, 70.0 mmol, 4.55 equiv), and the resulting mixture was stirred at 0 °C for 30 min. To the mixture was added a solution of methoxymethyldiphenylphosphine oxide (20.7 g, 84.0 mmol, 5.45 equiv) in THF (150 mL), and the resulting solution was stirred at 0 °C for 15 min and was then cooled to −78 °C. At −78 °C, a solution of ketone **35** (2.28 g, 15.4 mmol, 1.00 equiv) in THF (50.0 mL) was added dropwise, and the resulting mixture was stirred at −78 °C for 30 min. The reaction was quenched by addition of saturated aqueous NH_4Cl and warmed to room temperature, and the aqueous layer was extracted with Et_2O (3 × 200 mL). The combined organic layer was dried (Na_2SO_4) and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes/EtOAc = 1:1) afforded the desired phosphine oxide **39** (5.40 g, 98%) as an inconsequential mixture of diastereomers in the form of a colorless solid. Recrystallization from EtOAc afforded crystals suitable for single-crystal X-ray diffraction: R_f = 0.26 (hexanes/EtOAc = 1:1); mp 113–115 °C; ^{1}H NMR (600 MHz, $CDCl_3$, major isomer) δ = 7.94–7.84 (m, 4H), 7.60–7.42 (m, 6H), 6.28–6.22 (ddd, *J* = 7.5, 6.2, 1.5 Hz, 1H), 5.31 (ddd, *J* = 7.5, 6.4, 1.3 Hz, 1H), 4.51 (d, *J* = 1.4 Hz, 1H), 4.09 (s, 1H), 2.94 (s, 3H), 2.84 (dddd, *J* = 6.4, 6.3, 1.7, 1.5 Hz, 1H), 2.55–2.49 (m, 1H), 2.38–2.31 (m, 1H), 1.86 (ddd, *J* = 12.9, 8.8, 4.4 Hz, 1H), 1.75–1.71 (m, 2H), 1.59–1.55 (m, 1H), 1.53–1.47 (m, 1H), 1.46–1.40 (m, 1H), 0.99–0.94 (m, 1H) ppm; ^{13}C NMR (75 MHz, $CDCl_3$, major isomer) δ = 136.5, 132.4 (d, J_P = 9.0 Hz), 132.0, 131.9, 131.8 (d, J_P = 9.0 Hz), 131.8, 131.4 (d, *J* = 99.6 Hz), 128.8 (d, *J* = 11.4 Hz), 128.2 (d, *J* = 11.4 Hz), 85.4 (d, J_P = 1.9 Hz), 85.3 (d, *J* = 81.2 Hz), 61.5, 44.9, 38.0, 35.6, 29.3 (d, *J* = 7.5 Hz), 26.7, 24.9, 21.0 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2927, 1436, 1182, 1158, 1106, 1085, 1028, 983, 816, 751, 744, 723, 696 cm^{-1}; HRMS (EI) *m*/*z* for $C_{24}H_{27}O_3P^+$ $[M]^+$ calcd 394.1692, found 394.1685.

2-(Methoxymethylene)tricyclo[4.4.0.0^{3,8}]dec-4-ene (40). To a solution of phosphine oxide **39** (3.50 g, 8.87 mmol, 1.00 equiv) in THF (80.0 mL) at 0 °C was added NaH (2.13 g, 88.7 mmol, 10.0 equiv) portionwise. The resulting mixture was stirred at room temperature for 16 h and was then recooled to 0 °C and quenched by addition of H_2O (100 mL). The mixture was extracted with Et_2O (3 × 150 mL), and the combined organic layer was dried (Na_2SO_4) and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, *n*-pentane/Et_2O = 98:2) afforded enol ether **40** (1.54 g, 98%) as an inconsequential mixture of isomers in the form of a colorless oil: R_f = 0.67 (*n*-pentane/Et_2O = 9:1); ^{1}H NMR (600 MHz, $CDCl_3$, major isomer) δ = 6.27 (ddd, *J* = 7.7, 6.2, 1.1 Hz, 1H), 6.10 (ddd, *J* = 7.7, 6.4, 1.4 Hz, 1H), 5.65–5.64 (m, 1H), 3.47 (s, 3H), 2.88–2.82 (m, 1H), 2.71–2.66 (m, 1H), 2.49–2.45 (m, 1H), 1.77 (ddd, *J* = 10.8, 5.3, 1.0 Hz, 1H), 1.72–1.66 (m, 2H), 1.66–1.59 (m, 2H), 1.57–1.51 (m, 1H), 1.07–1.02 (m, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$, major isomer) δ = 136.5, 133.4, 131.7, 128.4, 59.4, 40.5, 35.5, 35.1, 28.2, 26.4, 24.9, 24.5 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2931, 2863, 1698, 1452, 1238, 1224, 1218, 1197, 1178, 1116, 1066, 1026, 980, 834, 820, 798, 787, 772, 758, 682, 662 cm^{-1}; HRMS (EI) *m*/*z* for $C_{12}H_{16}O^+$ $[M]^+$ calcd 176.1196, found 176.1159.

Hydrolysis of Twistene Enol Ether 40. To a solution of enol ether **40** (1.53 g, 8.70 mmol, 1.00 equiv) in 9:1 1,4-dioxane/H_2O (256 mL) was added $HClO_4$ (35 wt % in H_2O, 64.0 mL, 371 mmol, 42.6 equiv), and the resulting mixture was stirred at room temperature for 24 h. The mixture was poured into saturated aqueous $NaHCO_3$ (400

DOI: 10.1021/jo502618g
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mL) and was extracted with Et_2O (3 × 250 mL). The combined organic layer was dried (Na_2SO_4) and concentrated in vacuo. Purification of the residue by flash column chromatography (silica, *n*-pentane/Et_2O = 95:5) afforded *exo*-twistene aldehyde ***exo*-41** (126 mg, 9%) as a colorless oil and *endo*-twistene aldehyde ***endo*-41** (1.06 g, 75%) as a colorless oil.

*Tricyclo[4.4.0.0^{3,8}]dec-4-ene-2-exo-carbaldehyde (**exo-41**:).* R_f = 0.45 (hexanes/EtOAc = 9:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 9.92 (s, 1H), 6.34 (ddd, *J* = 7.9, 6.0, 1.7 Hz, 1H), 6.31 (ddd, *J* = 7.9, 6.0, 1.7 Hz, 1H), 3.11 (dddd, *J* = 6.0, 6.0, 2.2, 1.7 Hz, 1H), 2.73−2.66 (m, 1H), 2.12−2.06 (m, 1H), 1.95 (dd, *J* = 6.2, 2.2 Hz, 1H), 1.80 (dd, *J* = 11.1, 5.5 Hz, 1H), 1.76−1.69 (m, 1H), 1.66−1.56 (m, 3H), 1.36−1.29 (m, 1H), 1.07−1.01 (m, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 204.3, 136.0, 135.3, 61.6, 36.8, 35.1, 34.8, 25.0, 25.0, 23.1, 20.2 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2937, 2881, 1714, 1352, 1092, 1050, 1015, 976, 787, 689 cm^{-1}; HRMS (EI) *m*/*z* for $C_{11}H_{14}O^+$ $[M]^+$ calcd 162.1039, found 162.1034.

*Tricyclo[4.4.0.0^{3,8}]dec-4-ene-2-endo-carbaldehyde (**endo-41**):* R_f = 0.38 (hexanes/EtOAc = 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 9.47 (s, 1H), 6.55 (ddd, *J* = 7.8, 6.6, 1.5 Hz, 1H), 6.11 (ddd, *J* = 7.8, 6.1, 1.5 Hz, 1H), 3.20−3.16 (m, 1H), 2.68 (dd, *J* = 5.3, 0.8 Hz, 1H), 2.64−2.60 (m, 1H), 2.35−2.31 (m, 1H), 1.78−1.63 (m, 5H), 1.62−1.54 (m, 1H), 1.00−0.93 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 203.2, 142.1, 130.1, 58.5, 36.3, 36.0, 34.9, 28.7, 25.4, 24.4, 23.6 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2938, 2871, 1769, 1717, 1358, 1237, 1178, 1112, 1092, 1075, 1056, 1039, 1007, 953, 921, 896, 792, 690 cm^{-1}; HRMS (EI) *m*/*z* for $C_{11}H_{14}O^+$ $[M]^+$ calcd 162.1039, found 162.1045.

Tricyclo[4.4.0.0^{3,8}]dec-4-ene-2-*endo*-carbaldehyde 2,4-Dinitrophenylhydrazone (S11). Dinitrophenylhydrazine (58.5 mg, 0.294 mmol, 0.95 equiv) was dissolved in a mixture of MeOH (4.70 mL) and concentrated HCl (0.30 mL) by slight warming. To this mixture was added aldehyde ***endo*-41** (50.3 mg, 0.310 mmol, 1.00 equiv), and the mixture was stirred at room temperature for 5 min. The resulting orange precipitate was filtered off, washed with MeOH, and dried in vacuo to afford the desired hydrazone **S11** (60 mg, 57%) as an orange solid. Recrystallization from CH_2Cl_2/hexanes afforded crystals suitable for single-crystal X-ray diffraction: R_f = 0.71 (hexanes/EtOAc = 3:1); mp 151 °C dec; ^{1}H NMR (400 MHz, DMSO-d_6) δ = 11.25 (s, 1H), 8.82 (d, *J* = 2.7 Hz, 1H), 8.30 (dd, *J* = 9.7, 2.7 Hz, 1H), 7.79 (d, *J* = 9.7 Hz, 1H), 7.78 (d, *J* = 3.8 Hz, 1H), 6.53 (ddd, *J* = 7.8, 6.5, 1.5 Hz, 1H), 5.94 (ddd, *J* = 7.8, 5.9, 1.2 Hz, 1H), 3.02−2.93 (m, 2H), 2.67−2.60 (m, 1H), 2.09−2.00 (m, 1H), 1.87−1.68 (m, 3H), 1.68−1.55 (m, 3H), 0.97−0.89 (m, 1H) ppm; ^{13}C NMR (100 MHz, DMSO-d_6) δ = 158.7, 144.7, 139.2, 136.2, 129.7, 129.1, 128.5, 123.1, 116.3, 47.2, 37.7, 36.1, 34.0, 28.7, 24.5, 24.2, 23.1 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2944, 1613, 1585, 1518, 1495, 1420, 1321, 1301, 1264, 1220, 1168, 1128, 1067, 1055, 970, 943, 920, 872, 859, 829, 805, 788, 763, 741, 717, 690 cm^{-1}; HRMS (EI) *m*/*z* for $C_{17}H_{18}N_4O_4^+$ $[M]^+$ calcd 342.1323, found 342.1317.

2((*Z*)-2-Bromoalkenyl)tricyclo[4.4.0.0^{3,8}]dec-4-ene (27). To a solution of (bromomethyl)triphenylphosphonium bromide (297 mg, 0.682 mmol, 1.10 equiv) in THF (4.00 mL) at −78 °C was added KO-*t*-Bu (76.5 mg, 0.682 mmol, 1.10 equiv). The resulting yellow reaction mixture was stirred at −78 °C for 15 min, after which time DMPU (0.351 mL, 373 mg, 2.91 mmol, 4.70 equiv) and aldehyde ***endo*-41** (101 mg, 0.620 mmol, 1.00 equiv) in THF (1.00 mL) were added successively. The mixture was stirred for an additional 6 h at −78 °C and was then diluted with *n*-pentane (10 mL) and filtered over Celite. The residue was washed with *n*-pentane (20 mL), and the combined filtrates were concentrated in vacuo. Purification of the residue by flash column chromatography (silica, *n*-pentane) afforded alkenyl bromide **27** (94 mg, 63%) as a colorless oil: R_f = 0.93 (hexanes/EtOAc = 1:1); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 6.48 (ddd, *J* = 7.9, 6.2, 1.5 Hz, 1H), 6.00 (dd, *J* = 7.4, 6.9 Hz, 1H), 5.97−5.94 (m, 2H), 3.12−3.07 (m, 1H), 2.88−2.84 (m, 1H), 2.61−2.57 (m, 1H), 1.92−1.83 (m, 1H), 1.77−1.66 (m, 3H), 1.63−1.57 (m, 2H), 1.49−1.46 (m, 1H), 1.05−0.98 (m, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 140.2, 137.8, 130.5, 105.0, 45.2, 37.9, 37.0, 34.6, 31.5, 25.2, 25.0, 23.8 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2937, 2876, 1298, 1286, 806, 792, 744, 704, 682 cm^{-1}; HRMS (EI) *m*/*z* for $C_{12}H_{15}Br^+$ $[M]^+$ calcd 238.0352, found 238.0346.

2((*Z*)-2-Iodoalkenyl)tricyclo[4.4.0.0^{3,8}]dec-4-ene (28). To a suspension of (iodomethyl)triphenylphosphonium iodide (723 mg, 1.36 mmol, 2.20 equiv) in THF (7.00 mL) at 0 °C was slowly added a solution of NaHMDS (1.00 m in THF, 1.36 mL, 1.36 mmol, 2.20 equiv). The resulting yellow reaction mixture was stirred at 0 °C for 5 min, after which time the reaction mixture was cooled to −78 °C and DMPU (0.702 mL, 747 mg, 5.83 mmol, 9.40 equiv) and a solution of aldehyde ***endo*-41** (101 mg, 0.620 mmol, 1.00 equiv) in THF (3.00 mL) were added. The mixture was stirred at −78 °C for 2 h and was then diluted with *n*-pentane (20 mL). The resulting slurry was filtered over Celite, and the residue was washed with *n*-pentane (50 mL). The combined filtrate was concentrated in vacuo. Purification of the residue by flash column chromatography (silica, hexanes) yielded alkenyl iodide **28** (120 mg, 68%) as a brown oil: R_f = 0.77 (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 6.48 (ddd, *J* = 7.6, 6.1, 1.3 Hz, 1H), 6.09 (dd, *J* = 7.2, 7.2 Hz, 1H), 5.98 (dd, *J* = 7.2, 1.1 Hz, 1H), 5.94 (ddd, *J* = 7.8, 6.1, 1.4 Hz, 1H), 2.94−2.90 (m, 1H), 2.90−2.86 (m, 1H), 2.63−2.58 (m, 1H), 1.92−1.84 (m, 1H), 1.79−1.67 (m, 3H), 1.63−1.57 (m, 2H), 1.51−1.47 (m, 1H), 1.04−0.98 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 146.5, 137.9, 130.6, 79.3, 49.8, 37.8, 37.1, 34.7, 31.3, 25.3, 25.0, 23.7 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2938, 2875, 1277, 1268, 806, 792, 700, 679 cm^{-1}; HRMS (EI) *m*/*z* for $C_{12}H_{15}I^+$ $[M]^+$ calcd 286.0213, found 286.0196.

Tetracyclo[7.2.1.0^{3,8}.0^{5,12}]dodec-10-ene-2-yltriphenylphosphinepalladium(II) Bromide (42). To a solution of $Pd(PPh_3)_4$ (243 mg, 0.210 mmol, 1.00 equiv) in benzene (2.33 mL) was added (*Z*)-vinyl bromide **27** (50.2 mg, 0.210 mmol, 1.00 equiv) via syringe. The yellow reaction mixture was heated to 66 °C for 2 h. The mixture was allowed to cool to room temperature, and Et_2O (5 mL) was added, precipitating a white solid. The precipitate was filtered off, and the filtrate was allowed to stand. Upon slow evaporation of the solvent palladium complex **42** (25 mg, 20%) crystallized in the form of yellow platelets. Crystals suitable for single-crystal X-ray diffraction could be obtained from this mixture: R_f = 0.28 (hexanes/EtOAc = 3:1); mp 126 °C dec; ^{1}H NMR (600 MHz, $CDCl_3$) δ = 7.74−7.68 (m, 6H), 7.46−7.37 (m, 9H), 6.77−6.68 (m, 1H), 6.08−6.01 (m, 1H), 3.21−3.13 (m, 1H), 2.70−2.63 (m, 1H), 2.42−2.35 (m, 1H), 2.25−2.18 (m, 1H), 1.78−1.71 (m, 1H), 1.55−1.41 (m, 4H), 1.31−1.25 (m, 1H), 1.19−1.12 (m, 1H), 1.01−0.92 (m, 1H), 0.83−0.76 (m, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 134.8 (d, *J* = 12.4 Hz), 131.1 (d, *J* = 42.4 Hz), 130.6, 128.5 (d, *J* = 10.4 Hz), 121.5, 89.3, 50.7, 46.1, 45.8, 36.0, 35.7, 33.4, 25.6, 25.1, 24.7 (d, *J* = 6.9 Hz), 24.2 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2918, 2865, 1481, 1435, 1184, 1095, 999, 907, 724, 691 cm^{-1}; HRMS (ESI+) *m*/*z* for $C_{30}H_{30}PPd^+$ $[M - Br]^+$ calcd 527.1114, found 527.1115.

Pentacyclo[6.2.2.0^{2,7}.0^{4,9}.0^{10,11}]dodecane (44). *Method A*: To a round-bottom flask were added $Pd(OAc)_2$ (0.6 mg, 2.50 μmol, 0.025 equiv), *n*-Bu_4NCl (27.8 mg, 100 μmol, 1.00 equiv), and potassium formate (25.2 mg, 300 μmol, 3.00 equiv). The flask was evacuated and refilled with argon three times. The salts were dissolved in degassed DMF (10.0 mL), and alkenyl iodide **28** (28.6 mg, 100 μmol, 1.00 equiv) was added. The reaction mixture was transferred to a preheated oil bath and stirred at 80 °C for 5 h. During the reaction, the color of the mixture turned from yellow to black. The reaction mixture was allowed to cool to room temperature and was diluted with H_2O (25 mL) and pentane (25 mL), and the resulting mixture was stirred for 15 min at room temperature. The organic layer was separated, and the aqueous layer was extracted with *n*-pentane (3 × 25 mL). The combined organic layer was dried (Na_2SO_4) and concentrated in vacuo (at room temperature). Purification of the residue by flash column chromatography (silica, *n*-pentane) afforded cyclopropane **44** (4.3 mg, 27%) as a colorless waxy solid. *Method B*: To a solution of (*Z*)-alkenyl iodide **28** (25.8 mg, 90.0 μmol, 1.00 equiv) and a crystal of AIBN in refluxing benzene (2.00 mL) was added dropwise a solution of Bu_3SnH (40 μL, 43 mg, 148 μmol, 1.70 equiv) and AIBN (1.5 mg, 9.00 μmol, 0.100 equiv) in benzene (8.00 mL). The resulting mixture was heated to 80 °C for 2 h and was then allowed to cool to room temperature. The solvent was removed in vacuo and the residue was purified by flash column chromatography (silica, *n*-pentane) to afford cyclopropane **44** (8.0 mg, 56%) as a colorless waxy solid: R_f = 0.82

DOI: 10.1021/jo502618g
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(hexanes); ^{1}H NMR (600 MHz, $CDCl_3$) δ = 2.19−2.12 (m, 1H), 2.02−1.97 (m, 1H), 1.85−1.80 (m, 1H), 1.75 (dddd, J = 11.4, 6.1, 3.1, 0.9 Hz, 1H), 1.65−1.60 (m, 1H), 1.55−1.52 (m, 1H), 1.52−1.48 (m, 3H), 1.42−1.38 (m, 2H), 1.36−1.32 (m, 1H), 1.30−1.25 (m, 1H), 1.21−1.18 (m, 1H), 1.18−1.15 (m, 1H), 0.87−0.83 (m, 1H) ppm; ^{13}C NMR (150 MHz, $CDCl_3$) δ = 38.2, 37.4, 34.1, 32.9, 31.2, 28.3, 26.1, 26.0, 23.5, 22.5, 18.8, 16.8 ppm; IR (ATR) $\tilde{\nu}_{max}$ = 2954, 2921, 2870, 2858, 1464, 1457, 1376, 1075, 875, 866, 682 cm^{-1}; HRMS (EI) m/z for $C_{12}H_{16}^+$ $[M]^+$ calcd 160.1247, found 160.1249.

■ ASSOCIATED CONTENT

Supporting Information

NMR spectra and crystallographic data, where available, for the synthesized compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

■ ACKNOWLEDGMENTS

We thank Pascal Ellerbrock and Dr. David M. Barber for helpful discussions during the preparation of this manuscript. We thank the Deutsche Forschungsgemeinschaft (SFB 749) for financial support.

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