$PtCl_2$-Mediated Cyclopropane Opening: A Mechanistic Study

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The platinum-mediated cyclopropane opening of [4 + 2 + 2] homo Diels–Alder cycloadducts has been probed through deuterium-labeling studies. The location of the deuterium in the olefinic products strongly supports an α-elimination mechanism that proceeds through a platinum carbene intermediate. Kinetic isotopic effects provide additional insights into the reaction mechanism, lending support to the platinum carbene formation as the rate-determining step.

Introduction

The cobalt-catalyzed [4 + 2 + 2] homo Diels–Alder (HDA) reaction of norbornadienes with butadienes holds considerable potential for development into a valuable synthetic tool since this simple reaction can quickly lead to various bi- and tricyclic ring systems upon selective opening of the initial tetracyclic adduct **1** (Figure 1).[1] For example, Pt-promoted cyclopropane cleavage of the C2−C3 bond,[2] employing Zeise's dimer, leads to the tricyclic olefin **2** (route A).[3] With subsequent ozonolysis, the perhydroazulene core **4**, found in many natural products including the abundant guaianolide and pseudoguaianolide classes of sesquiterpenes,[4] as well as the dolastane and neodolastane class of diterpenes,[5] can be produced in three key steps (HDA, Pt−cyclopropane opening, ozonolysis). Alternatively, hydroxyl-directed Pt insertion into the C2−C4 or C3−C4 bond (X = OH) yields tricyclo[5.4.0.$0^{3,7}$]undecan-5-ones **3**.[6] Baeyer–Villiger oxidation and reduction then produces bicyclo[4.2.1]nonanes **5**, the basic ring system of longifolene as well as the antitumor mediterraneols[7] (route B).

Platinum-mediated cyclopropane openings, mainly using Zeise's dimer,[8] have been known for a long time.[9] A drawback of earlier work, which focused primarily on the novelty of the chemistry, not its synthetic applications, was the requirement of stoichiometric platinum.[8,10] Over the years, applications of Zeise's dimer opening to oxycyclopropanes in substoichiometric amounts (≤5 mol %),[11] as well as improved Pt-catalytic systems that require lower loading (5 mol %),[12] have been reported. Although considerable advancements have been made in this field, the reaction mechanism itself remains controversial.[8]

We recently reported a simple $PtCl_2$-based catalytic system for the cyclopropane opening of [4 + 2 + 2] cycloadducts such as **6**:[12] treatment with $PtCl_2$ (5 mol %) and tris(pentafluorophenyl)phosphine (10 mol %) led to the alkene **7** in excellent yield (Scheme 1). We now report a mechanistic study of this Pt-catalyzed alkene formation from deuterium-labeled precursors that allows for the elucidation of the mechanism of the rearrangement.

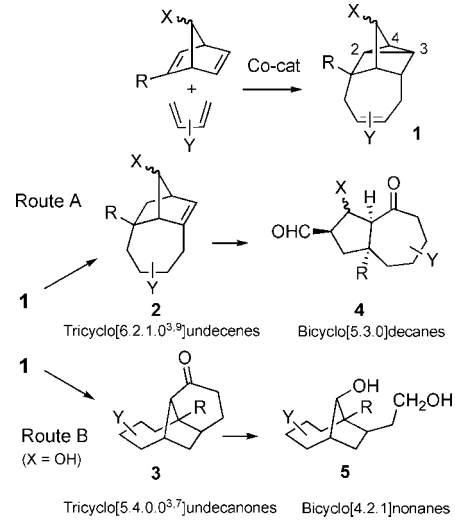

Figure 1. [4 + 2 + 2] HDA strategy toward bicyclo[5.3.0]decanes and bicyclo[4.2.1]nonanes.

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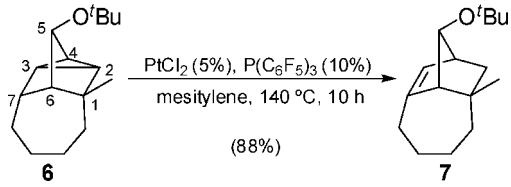
Scheme 1. $PtCl_2$-Promoted Cyclopropane Opening of 6



While the first step toward the formation of the alkene **7** most likely begins with the insertion of Pt(II) into the cyclopropane yielding a platinacyclobutane, formally a Pt(IV) species,[8] alkene formation from this intermediate, the most intriguing and challenging facet of this reaction, remains unresolved. Three mechanistic variants have been hypothesized in the past.[13]

In 2001, we proposed the rather cumbersome endocyclic β-elimination mechanism for the Zeise's dimer-promoted cyclopropane opening of **6** depicted in Figure 2,[3b] based on earlier deuterium-labeling studies by Jennings.[14] According to this proposal, after Pt insertion to form platina(IV)cyclobutane **8**, an endocyclic β-hydride elimination from C4, followed by reductive elimination, produces the transient,[15] Pt(II)-stabilized anti-Bredt alkene[16] **9**-*endo* with the original H4 hydrogen becoming the *endo*-H2 via Pt mediation. Migration of the platinum to the *exo* face gives **9**-*exo*, which subsequently isomerizes to the π-allyl complex **10** via H7 transfer to the platinum. Completion of the Pt-mediated hydrogen transposition to C4 leads to olefin−Pt(II) complex **11**, and alkene **7** is finally formed after Pt decomplexation. This pathway clearly suffers from poor orbital alignment in the initial transfer of the H4 hydrogen to the platinum unless assisted by an external hydrogen transfer agent such as base or proceeding by a hydride tunneling mechanism.[17]

Another β-elimination mechanism is more straightforward, consisting of only three basic steps[18] (Figure 3). The first step is, again, the addition of the platinum into the C2−C3 bond to form the platina(IV)cyclobutane **8**. An exocyclic β-elimination from C7 follows, leading to the olefinic hydridoplatinum(IV) intermediate **12**, and the alkene **7** is formed after reductive elimination. This pathway recalls features of the classic E_2 elimination for alkene formation in organic chemistry, but still suffers poor orbital alignment for hydride β-elimination onto the platinum and would again likely require the intervention of a hydrogen transfer agent.

A third mechanism, referred to as the "α-elimination mechanism", is characterized by an α-elimination followed by

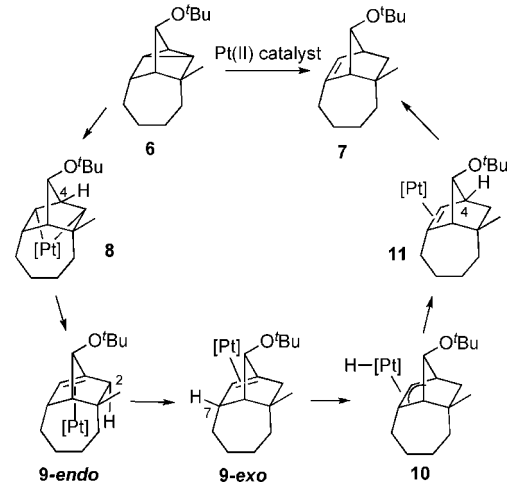


Figure 2. "Endocyclic β-elimination" mechanism.

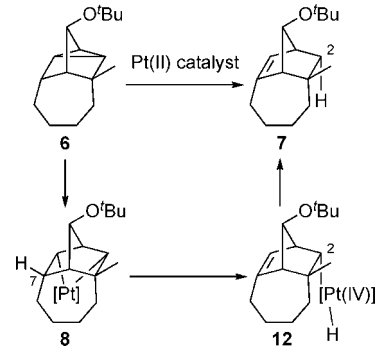


Figure 3. "Exocyclic β-elimination" mechanism.

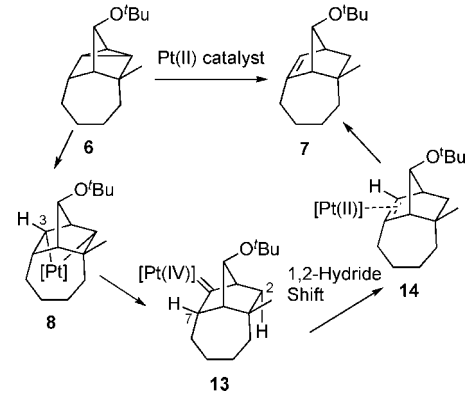


Figure 4. "α-Elimination" mechanism: Puddephatt rearrangement.

rearrangement as described some time ago by Puddephatt[8,19] following deuterium-labeling studies and supported by later labeling studies by Jennings[20] (Figure 4). Beginning with platina(IV)cyclobutane **8**, α-hydride transfer from C3 to the platinum leads to the platinum(IV) carbene **13**,[21] which could

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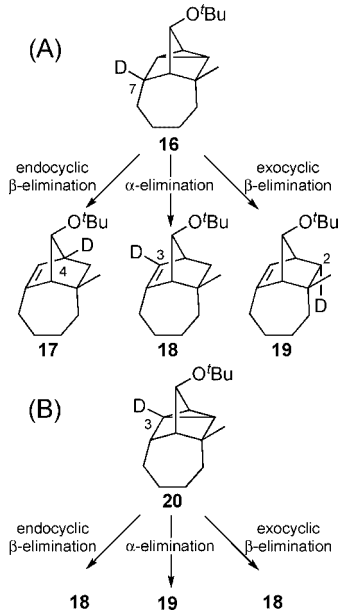

Figure 5. Use of deuterium-labeled precursors to distinguish the mechanisms. (A) Predicted products from cyclopropane opening of 7-deutero adduct **16**. (B) Predicted products from cyclopropane opening of 3-deutero adduct **20**.

be stabilized by addition of the phosphine to form an ylide.[22] A 1,2-hydride shift then leads to the platinum(II)-alkene **14**,[23] which gives **7** after decomplexation. A 1,3-hydride shift of H7 to the platinum, forming an alkenyl Pt(IV) intermediate, followed by reductive elimination would also be a possible pathway from **13** to **14**.

To resolve this mechanistic issue, deuterium-labeled substrates, which would lead to different products depending on the pathway followed, were prepared. Past deuterium-labeling studies on similar cyclopropane openings have supported both α- and endocylic *β*-elimination pathways.[13,14,18,19] An unambiguous solution to differentiate these three mechanisms would start with C7-deuterated HDA cycloadduct **16** since the "endocyclic *β*-elimination", the "α-elimination", and the "exocyclic *β*-elimination" routes would yield different alkenes **17**, **18**, and **19** bearing deuterium atoms in the C4, C3 or C2 *endo* position, respectively (Figure 5). In the same way, C3-deuterated **20** could single out the "α-elimination" mechanism since it would lead to olefin **19**, while the two *β*-elimination mechanisms would both give **18**.

Results and Discussion

Monodeuterated regioisomers **16** and **20** were prepared from 7-*tert*-butoxynorbornadiene[24] (**21**, Scheme 2). Treatment of **21** with Schlosser's base,[1b] then quenching with 1,2-diiodoethane,[25] afforded the desired *syn*-2-iodo-7-*tert*-butoxynorbornadiene **22** in 94% yield. Hydroboration of the least hindered double bond in **22** with 9-BBN[6] gave a 2.3:1 mixture of regioisomers **23a** and **23b**, which were easily separated by column chromatography. Negishi coupling of iodo alcohol **23a** with Me_2Zn in the presence of $Pd(PPh_3)_4$ afforded the methylated norbornadiene **24** in 88% yield.[26] Vinyl triflate **25** was obtained after PCC oxidation and treatment of the resulting ketone with KHMDS, with subsequent enolate quench by *N*-phenyltrifluoromethanesulfonimide.[27] Reduction of **25** with tributyltin deuteride in the presence of $Pd(PPh_3)_4$[28] gave the desired deuterated norbornadiene **26** in 98% yield and with near-complete deuterium incorporation (>95%) as determined by ^{1}H NMR. The same synthetic sequence was also applied to regioisomer **23b** to produce **27** in 65% yield over the analogous four steps. Both **26** and **27** proved to be very volatile.

Deuterium-labeled norbornadienes **26** and **27** were then both reacted with 1,3-butadiene in the presence of the cobalt catalyst to form the resulting [4 + 2 + 2] homo Diels–Alder cycloadducts (Scheme 3).[1b,c] Hydrogenation of the resulting double bond in the cycloadducts produced the desired compounds **16** and **20** in 60% yield (two steps).

Deuterated cycloadduct **16** was then subjected to the cyclopropane opening.[12] Upon treatment with $PtCl_2$ (10 mol %) and tris(pentafluorophenyl)phosphine (20 mol %) in mesitylene, olefin **18** was obtained in 83% yield as a single deuterated isomer. The ^{1}H and ^{13}C spectra, upon comparison with those of the corresponding nondeuterated olefin **7**,[29] led to the immediate observation that the deuterium atom was located at C3 in the ring-opened product **18** (Scheme 3). This result eliminates the two *β*-elimination pathways and strongly supports the "α-elimination" mechanism. To confirm this result, the C3 deuterium-labeled regioisomer **20** was also reacted with the Pt catalyst, and after a noticeably more sluggish reaction, the C2-deuterated olefin **19** was obtained, as expected following the "α-elimination" pathway.

Intrigued by the difference in the rates of reaction between the two monodeuterated compounds **16** and **20**, a kinetic comparison with the nondeuterated analogue **6** was conducted (Figure 6).[30] The relative rates of olefin formation for **7** and **19** revealed an isotope effect, $k_H/k_D = 5.44$ (Table 1). This ratio indicates a primary isotope effect and suggests that the rate-determining step is most likely the α-hydride transfer (**8** to **13** in Figure 3). The rate of formation of **7** and **18** was compared as well and showed a much smaller kinetic isotope effect ($k_H/k_D = 1.54$), which is consistent with a relatively large secondary isotope effect.[31] Larger secondary isotope effects have been reported in cases where significant *σ*-donation into an adjacent developing carbocationic center occurs in the transition state of the rate-determining step.[32] The large secondary isotope effect observed here is likely a consequence of considerable *σ*-donation from C7-H/C7-D into the developing electron-deficient center at C3 during the hydride transfer to the platinum enhanced by the rigid orientation of C7-H/C7-D bonds *syn* periplanar to the

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(29) ^{1}H and ^{13}C spectra for the nondeuterated olefin **7** can be found in the Supporting Information.
(30) For the kinetic study, the appearance of alkene and disappearance of the starting material was monitored via NMR through the H5 resonance (from 3.55 ppm in the starting material to 3.36 ppm for the alkene product).
(31) The usual range for secondary isotope effect is $k_H/k_D = 0.7–1.5$. Carey, F. A.; Sundberg, R. J. *Advanced Organic Chemistry, Part A: Structure and Mechanisms*, 4th ed.; Kluwer/Plenum: New York, 2000; p 223.
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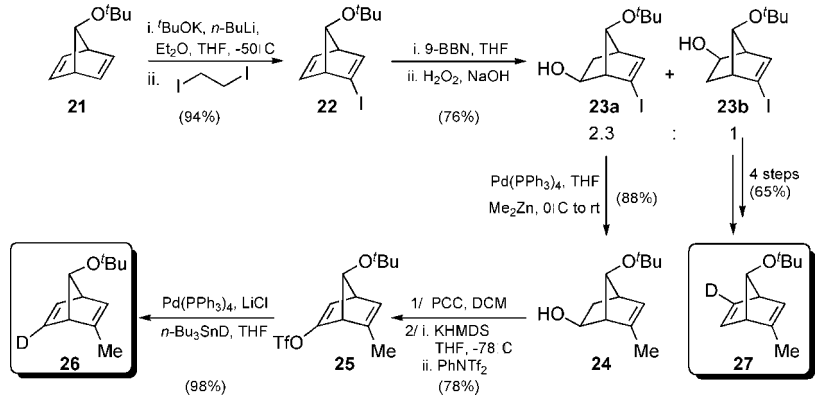
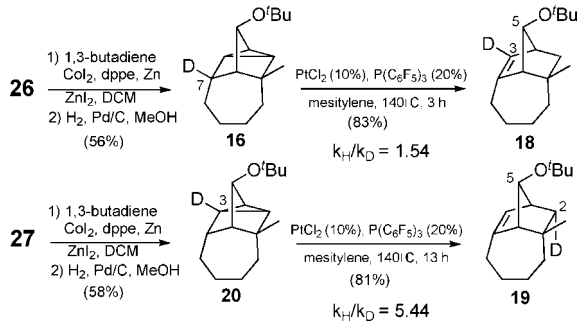
Scheme 2. Synthesis of Monodeuterated Norbornadienes 26 and 27



Scheme 3. Formation of Deuterated Alkenes 18 and 19; Confirmation of "α-Elimination" Mechanism



developing positive charge, and as such further supports the proposed α-elimination mechanism.[33] Since the H7/D7 secondary isotope effect is not as large as the primary isotope effect observed for H3/D3, the 1,2-hydride shift from C7 to C3 is not thought to be concerted with the α-elimination. Such a sequence would bypass the formal platinum carbene **13** shown in Figure 4, proceeding through hydridoplatinum intermediate **15** (Figure 7).

To further support these observed isotope effects, the C1,C2-dideuterated cycloadduct **33** was synthesized using a strategy similar to that applied to the preparation of **16** and **20**. Starting from norbornadiene **21**, hydroboration and PCC oxidation of the resulting alcohol furnished ketone **28** (Scheme 4). Refluxing the latter in D_2O in the presence of potassium carbonate allowed for the clean introduction of deuterium at C3. Dideuterated norbornadiene **31** was then obtained in two steps (formation of the triflate **30** and subsequent reduction with tributyltin deuteride

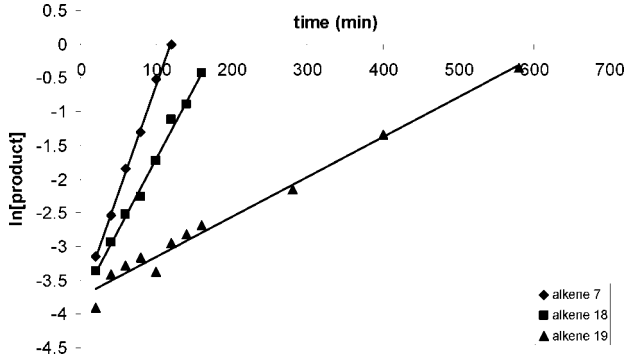


Figure 6. Kinetics for the formation of alkenes **7**, **18**, and **19** via Pt-catalyzed cyclopropane opening. Reactions were run at 140 °C in mesitylene-d_{12} (conc 0.1 M), with 10 mol % Pt-catalyst system, monitored by ^{1}H NMR.

Table 1. Kinetic Isotope Effects in the Formation of Alkenes 7, 18, and 19[a]

alkene	k_H/k_D
monodeuterated alkene **18**	1.54
monodeuterated alkene **19**	5.44

[a] Average of duplicate runs. Reactions were monitored via ^{1}H NMR observation of the H5 hydrogen resonance (shifting from 3.55 ppm in the starting cycloadduct to 3.36 ppm for the alkene product).

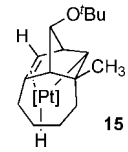
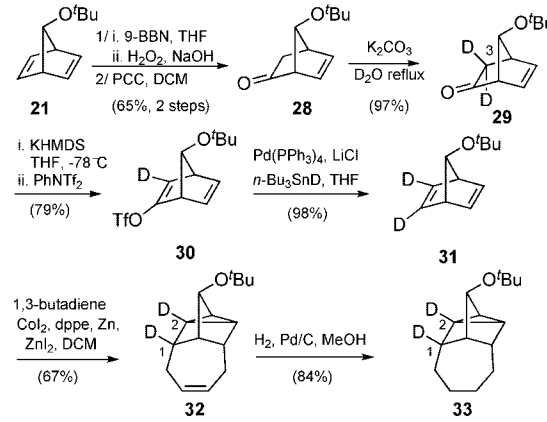


Figure 7. Intermediate **15** that would result from a concerted α-elimination/1,2-hydride shift process.

Scheme 4. Synthesis of Dideuterated HDA-Cycloadduct 33

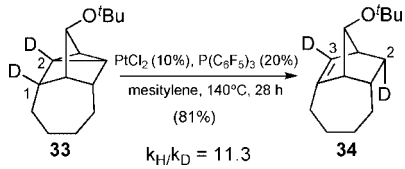


in the presence of $Pd(PPh_3)_4$, 77% yield, two steps). Dideuterated norbornadiene **31** was then subjected to the [4 + 2 + 2] homo Diels–Alder reaction with 1,3-butadiene in the presence of the cobalt catalyst.[1b,c] Hydrogenation of the resulting double bond in the cycloadduct produced the desired cycloadduct **33** in 56% yield (two steps).

Compound **33** was then subjected to $PtCl_2$-mediated cyclopropane opening. The expected C2,C3-dideuterated olefin **34** was obtained in agreement with the α-elimination mechanism, and a $k_H/k_D = 11.3$ was observed, consistent with combined primary and secondary isotope effects (Scheme 5).

In summary, the mechanism of the Pt-catalyzed isomerization of [4 + 2 + 2] homo Diels–Alder cycloadducts has been probed through deuterium-labeling studies. These studies point to an α-elimination pathway proceeding through a platinum carbene

Scheme 5. Formation of Dideuterated Alkene 33



intermediate. Deuterium isotope effects indicate that the α-elimination is the rate-determining step of the isomerization. Trapping of the carbene intermediate as well as application of this isomerization in synthesis are under study and will be reported in due course.

Experimental Section

General Information. All reactions were carried out in oven- (105 °C) or flame-dried glassware under an argon atmosphere employing standard techniques in handling air-sensitive materials. All solvents were reagent grade. Tetrahydrofuran (THF) was freshly distilled from sodium/benzophenone under argon immediately prior to use. Dichloromethane and mesitylene were freshly distilled from calcium hydride immediately prior to use. Lithium chloride was purchased from Aldrich and sublimed prior to use. All other reagents were used as supplied. The sealed glass vessels used for the low boiling point reactants were Ace heavy-walled tubes with Teflon plugs, designated as "pressure tube" in the text. 1,3-Butadiene was transferred as a liquid trapped at −78 °C (bp −5 °C) via cannula. Flash chromatography was performed with silica gel 60 (particle size 0.032–0.063 mm) supplied by Sorbent Technologies. Melting points were determined on a capillary melting point apparatus and are uncorrected. Hydrogen NMR spectra were recorded using an internal deuterium lock at ambient temperature on a Varian 400 MHz spectrometer (93.94 kG). An internal reference of δ H 7.24 (residual $CHCl_3$) was used for $CDCl_3$. Exchangeable protons (OH) were confirmed by addition of D_2O. Data are presented as follows: chemical shift (in ppm on the δ scale relative to $\delta_{TMS} = 0.00$), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, quint = quintuplet, m = multiplet, br = broad), coupling constant (*J*/Hz) and integration. Resonances that are either partially or fully obscured are denoted "overlap". Carbon-13 NMR spectra were recorded on a Varian 300 MHz spectrometer (70.50 kG). An internal reference of δ C 77.20 was used for $CDCl_3$ (center line of $CDCl_3$ triplet). Infrared spectra were recorded on a Nexus 670 FTIR spectrophotometer; the samples were prepared by depositing a solution of the sample on the NaCl plate in an appropriate, volatile solvent (typically $CHCl_3$) followed by evaporation of the solvent. High-resolution mass spectra (HRMS) were recorded on a Finnegan MAT-90 spectrometer using chemical ionization mode (CI) and NH_3 as the reagent gas at 140 eV.

***syn*-7-*tert*-Butoxy-2-iodobicyclo[2.2.1]hepta-2,5-diene (22).** To a flamed-dried round-bottom flask containing potassium *tert*-butoxide (820 mg, 7.3 mmol) dissolved in anhydrous Et_2O (30 mL) was added 7-*tert*-butoxynorbornadiene[34] (**21**, 1.0 g, 6.1 mmol). After cooling to −50 °C a solution of *n*-BuLi (3.3 mL, 7.3 mmol) in hexanes was added over 1 h at −50 °C, then the temperature was allowed to rise to −30 °C. Subsequently, THF (8 mL) was added at −30 °C, and the mixture was stirred at this temperature for 1 h. Finally, 1,2-diiodoethane (3.4 g, 12.2 mmol) dissolved in THF (6 mL) was added at once, and the reaction mixture was stirred at −30 °C for one more hour. The temperature was allowed to rise to 0 °C, then the reaction was quenched by the addition of a saturated solution of aqueous NH_4Cl (20 mL). The crude mixture was diluted with Et_2O (10 mL), and the separated organic layer was washed with water (3 × 30 mL) and brine (30 mL), then dried over Na_2SO_4. After removal of the solvent in vacuo, the residue was purified by flash chromatography (petroleum ether/Et_2O, 90/10) to give **22** (R_f 0.73; 1.66 g; 94% yield) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.82 (ddd, J = 3.3, 1.0, 1.0 Hz, 1H), 6.70 (ddd, J = 5.6, 3.3, 1.0 Hz, 1H), 6.58 (ddd, J = 5.6, 3.3, 1.0 Hz, 1H), 3.75 (dd, J = 2.5, 1.8 Hz,1H), 3.44 (m, 1H), 3.33 (m, 1H) 1.17 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 142.5, 138.48, 138.45, 103.8, 99.7, 74.0, 66.5, 57.9, 28.5 (3C); CIMS *m*/*z* (%) 204 (100), 86 (78); HRMS (CI, NH_3) *m*/*z* 291.0221 ([M + 1]$^+$, 3%), calcd for $C_{11}H_{16}IO$ 291.0246.

***anti*-7-*tert*-Butoxy-6-iodobicyclo[2.2.1]hept-5-en-*exo*-2-ol (23a) and *anti*-7-*tert*-Butoxy-5-iodobicyclo[2.2.1]hept-5-en-*exo*-2-ol (23b).** To a solution of *syn*-7-*tert*-butoxy-2-iodobicyclo[2.2.1]hepta-2,5-diene (**22**, 410 mg, 1.41 mmol) in THF (2.3 mL) under Ar was added 9-borabicyclo[3.3.1]nonane (9-BBN, 0.5 M in THF, 2.3 mL) at rt. The reaction was sonicated in an ultrasound bath at rt for 3 h, then stirred for 12 h. After cooling the solution to 0 °C in an ice bath, an aqueous solution of NaOH (2.5 M, 5.5 mL) was added, followed by the dropwise addition of 30% H_2O_2 (4.1 mL). The mixture was allowed to warm to rt and stirred for 1 h, then neutralized with 3 M HCl. The mixture was extracted with Et_2O (3 × 10 mL), the combined organic layers were washed with brine (3 × 10 mL), dried over Na_2SO_4, and filtered, and the solvent was removed in vacuo. The ^{1}H NMR spectrum of this crude reaction product showed a 2.3:1 mixture of regioisomers (**23a**:**23b**). The regioisomers were purified by flash chromatography (petroleum ether/Et_2O, 60/40). The regioisomers were distinguished from the coupling sequences as delineated in H,H-COSY spectra. *anti*-7-*tert*-Butoxy-6-iodobicyclo[2.2.1]hept-5-en-*exo*-2-ol **23a** (major isomer) was obtained as a white solid (R_f 0.61; 230 mg, 53% yield) along with *anti*-7-*tert*-butoxy-5-iodobicyclo[2.2.1]hept-5-en-*exo*-2-ol **23b** (minor isomer) (R_f 0.56; 103 mg, 23% yield) as a colorless oil. *anti*-7-*tert*-Butoxy-6-iodobicyclo[2.2.1]hept-5-en-*exo*-2-ol (**23a**): mp 74–78 °C; IR (NaCl) 3409, 2970, 1155, 1046, 820 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.51 (d, J = 3.2 Hz, 1H), 4.16 (br s, 1H), 3.84 (dd, J = 7.8, 2.7 Hz, 1H), 2.77 (br s, 1H), 2.61 (br s, 1H), 1.71 (dd, J = 12.7, 7.8 Hz, 1H), 1.68 (br s, OH), 1.41 (ddd, J = 12.7, 3.2, 2.7 Hz, 1H), 1.18 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 144.1, 91.2, 86.2, 74.1, 69.9, 65.9, 48.8, 34.9, 28.5 (3C); CIMS *m*/*z* (%) 309 ([M + 1]$^+$, 3), 308 ([M]$^+$, 3), 252 (34), 234 (88), 205 (87), 57 (100); HRMS (CI, NH_3) *m*/*z* 309.0328 ([M + H]$^+$, 3%), calcd for $C_{11}H_{18}IO_2$ 309.0351. *anti*-7-*tert*-Butoxy-5-iodobicyclo[2.2.1]hept-5-en-*exo*-2-ol (**23b**): IR (NaCl) 3397, 2969, 1158, 1095, 1019 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.27 (d, J = 3.2 Hz, 1H), 4.20 (br s, 1H), 3.81 (ddd, J = 7.6, 2.6, 2.6 Hz, 1H), 2.78 (br s, 1H), 2.57 (br s, 1H), 1.67 (dd, J = 13.0, 7.6 Hz, 1H), 1.64 (s, OH), 1.35 (ddd, J = 13.0, 3.2, 2.6 Hz, 1H), 1.16 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 137.2, 98.9, 85.9, 74.1, 70.4, 58.1, 57.7, 33.7, 28.5 (3C); CIMS *m*/*z* (%) 309 ([M + 1]$^+$, 4), 234 (18), 205 (11), 57 (100); HRMS (CI, NH_3) *m*/*z* 309.0377 ([M + 1]$^+$, 4%), calcd for $C_{11}H_{18}IO_2$ 309.0351.

***anti*-7-*tert*-Butoxy-6-methylbicyclo[2.2.1]hept-5-en-*exo*-2-ol (24).** To a flamed-dried round-bottom flask containing palladium tetrakis(triphenylphosphine) (88 mg, 0.076 mmol) was added *anti*-7-*tert*-butoxy-6-iodobicyclo[2.2.1]hept-5-en-*exo*-2-ol **23a** (238 mg, 0.77 mmol) dissolved in THF (8.3 mL). The solution was cooled to 0 °C in an ice bath, and dimethylzinc (1.2 M in toluene, 0.969 mL) was added dropwise. The mixture was allowed to warm to rt and stirred for 10 h, then the reaction was quenched with brine (5 mL). The mixture was diluted with Et_2O (5 mL), and the organic layer was washed with brine (3 × 5 mL) and dried over Na_2SO_4. After removal of the solvent in vacuo, the residue was purified by flash chromatography (petroleum ether/Et_2O, 60/40) to give *anti*-

(33) One of the largest secondary isotope effects observed was 2.35, with significant σ-donation contribution to carbocation formation from more than one C-H/D in an acyclic system: Shiner, V. J., Jr. *J. Am. Chem. Soc.* **1953**, *75*, 2925.

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7-*tert*-butoxy-6-methylbicyclo[2.2.1]hept-5-en-*exo*-2-ol **24** (R_f 0.51; 130 mg; 88% yield) as a white solid: mp 54–55 °C; IR (NaCl) 3400, 2970, 1160 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.65 (br s, 1H), 4.21 (br s, 1H), 3.77 (ddd, J = 7.8, 3.0, 2.5 Hz, 1H), 2.59 (br s, 1H), 2.40 (br s, 1H), 1.74 (s, 3H), 1.66 (dd, J = 12.3, 7.8 Hz, 1H), 1.57 (d, J = 3.0 Hz, OH), 1.40 (ddd, J = 12.3, 3.0, 2.5 Hz, 1H), 1.16 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.2, 128.5, 86.3, 73.6, 70.8, 60.1, 46.8, 37.0, 28.6 (3C), 15.9; CIMS *m*/*z* (%) 219 ([M + Na]$^+$, 100), 123 (45), 109 (14); HRMS (CI, NH_3) *m*/*z* 197.1546 ([M + 1]$^+$, 2%), calcd for $C_{12}H_{21}O_2$ 197.1541.

***anti*-7-*tert*-Butoxy-5-methylbicyclo[2.2.1]hept-5-en-*exo*-2-ol.** *anti*-7-*tert*-Butoxy-5-methylbicyclo[2.2.1]hept-5-en-*exo*-2-ol was prepared following the preceding procedure for **24**, beginning with *anti*-7-*tert*-butoxy-5-iodobicyclo[2.2.1]hept-5-en-*exo*-2-ol (**23b**, 86 mg, 0.278 mmol). Purification by flash chromatography (petroleum ether/Et_2O, 60/40) gave *anti*-7-*tert*-butoxy-5-methylbicyclo[2.2.1]hept-5-en-*exo*-2-ol (R_f 0.51; 130 mg; 89% yield) as a viscous yellow liquid: IR (NaCl) 3407, 2969, 1158, 1020 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.40 (br s, 1H), 4.20 (br s, 1H), 3.74 (br d, J = 7.8 Hz, 1H), 2.54 (br s, 1H), 2.39 (br s, 1H), 1.74 (s, 3H), 1.62 (br s, OH), 1.57 (dd, J = 12.6, 7.8 Hz, 1H), 1.36 (ddd, J = 12.6, 2.9, 2.9 Hz, 1H), 1.16 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.3, 121.4, 85.9, 73.6, 72.3, 56.2, 50.6, 34.1, 28.6 (3C), 16.2; CIMS *m*/*z* (%) 219 ([M + Na]$^+$, 93), 197 ([M + 1]$^+$, 3), 123 (18), 69 (100), 57 (17); HRMS (CI, NH_3) *m*/*z* 197.1549 ([M + 1]$^+$, 2%), calcd for $C_{12}H_{21}O_2$ 197.1541.

***anti*-7-*tert*-Butoxy-6-methylbicyclo[2.2.1]hept-5-en-2-one.** To a suspension of PCC (122 mg, 0.56 mmol) in CH_2Cl_2 (5 mL) at rt was added *anti*-7-*tert*-butoxy-6-methylbicyclo[2.2.1]hept-5-en-*exo*-2-ol (**24**, 93 mg, 0.47 mmol). The reaction was stirred under Ar at rt for 4 h, then passed through a silica plug, eluting with CH_2Cl_2 (3 × 5 mL) to remove inorganic salts. The solvent was removed in vacuo, and the residue was purified by flash chromatography (petroleum ether/Et_2O, 80/20) to give *anti*-7-*tert*-butoxy-6-methylbicyclo[2.2.1]hept-5-en-2-one (R_f 0.42; 79 mg; 86% yield) as a white solid: mp 48–50 °C; IR (NaCl) 2973, 1743, 1125 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.00 (br s, 1H), 4.19 (br s, 1H), 2.97 (br m, 1H), 2.85 (br s, 1H), 1.98 (d, J = 1.9 Hz, 2H), 1.74 (d, J = 1.6 Hz, 3H), 1.15 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 211.5, 135.8, 131.8, 89.3, 74.3, 67.6, 46.9, 39.2, 28.5 (3C), 16.1; CIMS *m*/*z* (%) 217 ([M + Na]$^+$, 14), 138 (38), 69 (62), 57 (14); HRMS (CI, NH_3) *m*/*z* 195.1385 ([M + 1]$^+$, 6%), calcd for $C_{12}H_{19}O_2$ 195.1385.

***anti*-7-*tert*-Butoxy-5-methylbicyclo[2.2.1]hept-5-en-2-one.** The ketone was prepared following the preceding procedure, with PCC (80 mg, 0.37 mmol) in CH_2Cl_2 (4 mL) and *anti*-7-*tert*-butoxy-5-methylbicyclo[2.2.1]hept-5-en-*exo*-2-ol (60 mg, 0.31 mmol). Purification by flash chromatography (petroleum ether/Et_2O, 80/20) gave *anti*-7-*tert*-butoxy-5-methylbicyclo[2.2.1]hept-5-en-2-one (R_f 0.42; 51 mg; 86% yield) as a white solid: mp 73–75 °C; IR (NaCl) 2972, 1727, 1124 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.42 (br s, 1H), 4.13 (br s, 1H), 3.01 (br m, 1H), 2.75 (br s, 1H), 2.01 (dd, J = 17.1, 3.4 Hz, 1H), 1.90 (dd, J = 17.1, 1.6 Hz, 1H), 1.86 (s, 3H), 1.16 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.7, 150.1, 116.7, 88.3, 74.4, 63.1, 51.4, 38.0, 28.5 (3C), 16.7; CIMS *m*/*z* (%) 195 ([M + 1]$^+$, 1), 69 (27); HRMS (CI, NH_3) *m*/*z* 195.1379 ([M + 1]$^+$, 1%), calcd for $C_{12}H_{19}O_2$ 195.1385.

***anti*-7-*tert*-Butoxy-6-methylbicyclo[2.2.1]hepta-2,5-dien-2-yl trifluoromethane sulfonate (25).** To a solution of *anti*-7-*tert*-butoxy-6-methylbicyclo[2.2.1]hept-5-en-2-one (196 mg, 1.01 mmol) in anhydrous THF (5 mL) was added dropwise a KHMDS solution (0.5 M in toluene, 2.6 mL) at −78 °C under Ar. The reaction mixture was stirred for 2 h at −78 °C, then the temperature was allowed to warm to 0 °C, and *N*-phenyltrifluoromethanesulfonimide ($PhNTf_2$, 431 mg, 1.21 mmol), dissolved in anhydrous THF (1 mL), was added. The solution was stirred at rt for 10 h, then quenched with a saturated aqueous solution of $NaHCO_3$(3 mL). The crude mixture was diluted with Et_2O (10 mL), and the organic layer was washed with water (3 × 10 mL) and brine (10 mL) and dried over Na_2SO_4. After removal of the solvent in vacuo, the residue was purified by flash chromatography (petroleum ether/EtOAc, 90/10) to give *anti*-7-*tert*-butoxy-6-methylbicyclo[2.2.1]hepta-2,5-dien-2-yl trifluoromethanesulfonate **25** (R_f 0.61; 290 mg; 88% yield) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.20 (dd, J = 4.0, 2.4 Hz, 1H), 6.08 (m, 1H), 4.08 (br s, 1H), 3.26 (br m, 1H), 3.06 (br s, 1H), 1.94 (d, J = 2.0 Hz, 3H), 1.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.6, 146.6, 129.3, 123.5, 118.8 (q, $^1J_{CF}$ = 318 Hz), 103.3, 74.5, 61.4, 53.8, 28.5 (3C), 16.8; CIMS *m*/*z* (%) 253 (100), 105 (29), 91 (99), 69 (36), 57 (90); HRMS (CI, NH_3) *m*/*z* 327.0875 ([M + 1]$^+$, 2%), calcd for $C_{13}H_{18}F_3O_4S$ 327.0877.

***anti*-7-*tert*-Butoxy-5-methylbicyclo[2.2.1]hepta-2,5-dien-2-yl Trifluoromethanesulfonate.** The triflate was prepared following the preceding procedure, beginning with *anti*-7-*tert*-butoxy-5-methylbicyclo[2.2.1]hept-5-en-2-one (50 mg, 0.257 mmol), KHMDS (0.5 M in toluene, 0.672 mL), THF (1.5 mL), and $PhNTf_2$ (0.111 mg, 0.310 mmol). Purification by flash chromatography (petroleum ether/EtOAc, 90/10) gave *anti*-7-*tert*-butoxy-5-methylbicyclo[2.2.1]hepta-2,5-dien-2-yl trifluoromethanesulfonate (R_f 0.61; 73 mg; 88% yield) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.19 (dd, J = 4.1, 1.6 Hz, 1H), 6.04 (br s, 1H), 4.05 (br s, 1 H), 3.23 (br s, 1H), 3.03 (br s, 1H), 1.88 (d, J = 1.6 Hz, 3H), 1.13 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 163.4, 149.6, 125.8, 121.9, 118.7 (q, $^1J_{CF}$ = 318 Hz), 102.6, 74.5, 58.7, 57.0, 28.4 (3C), 17.2; CIMS *m*/*z* (%) 327 ([M]$^+$, 19), 271 (43), 270 (64), 253 (100); HRMS (CI, NH_3) *m*/*z* 327.0896 ([M + 1]$^+$, 19%), calcd for $C_{13}H_{18}F_3O_4S$ 327.0877.

***syn*-7-*tert*-Butoxy-6-deutero-2-methylbicyclo[2.2.1]hept-2,5-diene (26).** To a flamed-dried round-bottom flask under argon were added $Pd(PPh_3)_4$ (9 mg, 7.8 × 10^{-3} mmol), freshly sublimed LiCl (23 mg, 0.55 mmol), and anhydrous THF (0.5 mL). The mixture was stirred for 5 min at rt, then *anti*-7-*tert*-butoxy-6-methylbicyclo[2.2.1]hepta-2,5-dien-2-yl trifluoromethanesulfonate (**25**, 60 mg, 0.18 mmol) dissolved in anhydrous THF (0.5 mL) was added, immediately followed by *n*-Bu_3SnD (0.065 mL, 0.24 mmol). The reaction mixture was stirred for 2 h under Ar, then quenched with 10% ammonia solution (NH_4OH, 1 mL). The mixture was diluted with Et_2O (3 mL), and the separated organic layer was washed with brine (3 × 3 mL) and dried over Na_2SO_4. After removal of the solvent in vacuo, the residue was purified by flash chromatography (pentane/Et_2O, 95/5) to give **26** (R_f 0.53; 32 mg; 98% yield) as a volatile colorless oil, which was taken on to the next step without further purification.^{1}H NMR (400 MHz, $CDCl_3$, unpurified **26**) δ 6.60 (d, J = 3.6 Hz, 1H), 5.95 (m, 1H), 3.69 (br s, 1H), 3.24 (m, 1H), 3.01 (br s, 1H), 1.86 (d, J = 2.0 Hz, 3H), 1.18 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, unpurified **26**) δ 148.5, 140.4, 127.9, 103.1, 73.5, 60.3, 55.5, 28.6 (3C), 17.5, C6 not observed, appears at δ 138.9 in nondeuterated compound. For spectroscopic data of the nondeuterated analogue, see ref 3a.

***syn*-7-*tert*-Butoxy-5-deutero-2-methylbicyclo[2.2.1]hept-2,5-diene (27).** The norbornadiene **27** was prepared following the preceding procedure for **26**, beginning with *anti*-7-*tert*-butoxy-5-methylbicyclo[2.2.1]hepta-2,5-dien-2-yl trifluoromethanesulfonate (50 mg, 0.153 mmol), $Pd(PPh_3)_4$ (7 mg, 6.1 × 10^{-3} mmol), LiCl (20 mg, 0.45 mmol), and anhydrous THF (0.35 mL). Purification by flash chromatography (pentane/Et_2O, 95/5) gave **27** (R_f 0.53; 27 mg; 97% yield) as a volatile colorless oil which was used in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$, unpurified **27**) δ 6.65 (d, J = 2.8 Hz, 1H), 5.96 (br s, 1H), 3.71 (br s, 1H), 3.25 (br s, 1H), 3.02 (br s, 1H), 1.87 (s, 3H), 1.18 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$, unpurified **27**) δ 148.4, 140.3 (t, $^1J_{CD}$ = 26 Hz), 139.0, 127.9, 103.1, 73.5, 60.3, 55.4, 28.6 (3C), 17.5. For spectroscopic data of the nondeuterated analogue, see ref 3a.

***syn*-5-*tert*-Butoxy-7-deutero-1-methyltetracyclo[5.4.0.0^{2,4}0^{3,7}]-undec-9-ene.** To a flamed-dried 15 mL pressure tube under argon was added 1,2-bis(diphenylphosphino)ethane (dppe, 132 mg, 0.334 mmol) followed by CoI_2 (70 mg, 0.223 mmol) and CH_2Cl_2 (2.3 mL). To this dark brown mixture were added sequentially ZnI_2 (178 mg, 0.558 mmol), Zn (36 mg, 0.558 mmol), and **26** (200 mg, 1.12 mmol). The solution was cooled to −78 °C, and 1,3-butadiene (182 mg, 3.36 mmol) was added via cannula. The pressure tube was immediately capped and allowed to warm to rt. The dark brown cloudy solution was stirred at rt for 20 h, then the crude mixture was passed through a silica gel plug, eluting with CH_2Cl_2 (3 × 2 mL) to remove the catalyst. The solvent was removed in vacuo and the residue partially purified by flash chromatography (hexanes/EtOAc, 90/10) to give the cycloadduct as a colorless oil (R_f = 0.7; 151 mg; 62% yield). This partially purified cycloadduct was used in the next step without further purification. ^{1}H NMR (400 MHz, $CDCl_3$, unpurified product) δ 5.61 (m, 1H), 5.54 (m, 1H), 3.54 (br s, 1H), 2.29 (br d, J = 16.6 Hz, 1H), 2.22 (br m, 2H), 2.10 (dd, J = 16.6, 8.4 Hz, 1H), 1.35 (s, 3H), 1.35 (overlap, 1H), 1.17 (s, 9H), 1.04 (d, J = 4.7 Hz, 1H), 1.00 (d, J = 4.7 Hz, 1H), 0.90 (d, J = 4.7 Hz, 1H). For spectroscopic data of the nondeuterated analogue, see ref 3a.

***syn*-5-*tert*-Butoxy-3-deutero-1-methyltetracyclo[5.4.0.0^{2,4}0^{3,7}]-undec-9-ene.** This cycloadduct was prepared following the preceding procedure, beginning with dppe (133 mg, 0.334 mmol), CoI_2 (70 mg, 0.223 mmol), CH_2Cl_2 (2.3 mL), ZnI_2 (178 mg, 0.558 mmol), Zn (36 mg, 0.558 mmol), **27** (209 mg, 1.13 mmol), and 1,3-butadiene (182 mg, 3.36 mmol). Purification by flash chromatography (hexanes/EtOAc, 90/10) gave *syn*-5-*tert*-butoxy-3-deutero-1-methyltetracyclo[5.4.0.0^{2,4}0^{3,7}]undec-9-ene as a colorless oil (R_f = 0.7; 150 mg; 60% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.62 (m, 1H), 5.55 (m, 1H), 3.54 (br s, 1H), 2.29 (br d, J = 16.6 Hz, 1H), 2.22 (br m, 2H), 2.10 (dd, J = 16.6, 8.1 Hz, 1H), 1.77 (dd, J = 4.5, 4.0 Hz, 1H), 1.35 (s, 3H), 1.35 (overlap, 1H), 1.17 (s, 9H), 1.04 (d, J = 4.7 Hz, 1H), 1.00 (d, J = 4.7 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 129.7, 128.0, 80.5, 73.5, 51.7, 44.3, 39.9, 39.8, 30.4, 28.6 (3C), 25.4, 21.8, 16.4, C3 not observed, appears at δ 16.8 in nondeuterated compound; CIMS m/z (%) 123 (100), 57 (41); HRMS (CI, NH_3) m/z 234.1974 ([M + H]$^+$, 1%), calcd for $C_{16}H_{24}DO$ 234.1968. For spectroscopic data of the nondeuterated analogue, see ref 3a.

***syn*-5-*tert*-Butoxy-7-deutero-1-methyltetracyclo[5.4.0.0^{2,4}0^{3,7}]-undecane (16).** A mixture of *syn*-5-*tert*-butoxy-7-deutero-1-methyltetracyclo[5.4.0.0^{2,4}0^{3,7}]undec-9-ene (151 mg, 0.689 mmol) and Pd−C (10% Pd on activated carbon, 86 mg, 0.070 mmol) in MeOH (13 mL) was kept under a H_2 atmosphere (balloon, 1 atm) at rt for 5 h with stirring. The reaction mixture was then passed through a short silica gel plug, eluting with MeOH (3 × 10 mL) to remove the catalyst. The solvent was removed in vacuo and the residue purified by flash chromatography (hexanes/EtOAc, 90/10) to give **16** as a colorless oil (R_f = 0.7; 137 mg; 89% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.55 (br s, 1H), 1.65–1.73 (overlap, 2H), 1.38–1.60 (overlap, 7H), 1.32 (s, 3H), 1.17 (s, 9H), 1.01–1.03 (overlap, 2H), 0.97 (br dd, J = 5.1, 4.5 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 81.6, 73.8, 48.5, 47.5, 42.9, 42.6 (t, $^1J_{CD}$ = 15.0 Hz), 31.4, 29.0 (3C), 27.6, 26.5, 26.0, 23.2, 20.1, 16.7; CIMS m/z (%) 178 (70), 163 (15), 162 (100), 145 (51); HRMS (CI, NH_3) m/z 236.2126 ([M + H]$^+$, 2%), calcd for $C_{16}H_{26}DO$ 236.2124. For spectroscopic data of the nondeuterated analogue, see ref 3b.

***syn*-5-*tert*-Butoxy-3-deutero-1-methyltetracyclo[5.4.0.0^{2,4}0^{3,7}]-undecane (20).** Dihydrocycloadduct **20** was prepared following the preceding procedure for **16**, beginning with *syn*-5-*tert*-butoxy-3-deutero-1-methyltetracyclo[5.4.0.0^{2,4}0^{3,7}]undec-9-ene (77 mg, 0.351 mmol), MeOH (7 mL), and Pd−C (10% Pd on activated carbon, 36 mg, 0.035 mmol). Purification by flash chromatography (hexanes/EtOAc, 20:1) gave **20** as a colorless oil (R_f = 0.5; 74 mg; 96% yield): ^{1}H NMR (400 MHz, $CDCl_3$, unpurified **20**) δ 3.54 (br s, 1H), 1.66–1.78 (overlap, 3H), 1.38–1.60 (overlap, 7H), 1.32 (s, 3H), 1.17 (s, 9H), 1.01–1.03 (overlap, 2H). For spectroscopic data of the nondeuterated analogue, see ref 3b.

10-*tert*-Butoxy-2-deutero-*syn*-8-methyltricyclo[6.2.1.0^{3,9}]undec-2-ene (18). To a solution of $PtCl_2$ (3 mg, 0.011 mmol) in anhydrous mesitylene (1.0 mL) under Ar were added tris-pentafluorophenylphosphine (12 mg, 0.026 mmol) and **16** (25 mg, 0.113 mmol). The reaction was stirred for 12 h at 140 °C, then allowed to cool to rt. The solution was filtered through a short plug of silica gel, eluting with CH_2Cl_2 (6 mL) to remove the catalyst. Then the solvent was removed in vacuo and the residue was purified by flash chromatography (hexanes/EtOAc, 95/5) to give **18** (R_f = 0.7; 25 mg; 83% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.36 (br s, 1H), 2.40 (br s, 1H), 2.13–2.26 (overlap, 2H), 1.99 (dd, J = 1.6, 1.6 Hz, 1H), 1.74 (dd, J = 11.0, 3.5 Hz, 1H), 1.63 (m, 1H), 1.50 (m, 1H), 1.30–1.44 (overlap, 3H), 1.29 (s, 3H), 1.22 (m, 1H), 1.14 (s, 9H), 0.96 (d, J = 11.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.4, 84.5, 73.3, 58.9, 47.8, 47.4, 40.3, 39.7, 30.9, 30.1, 28.5 (3C), 27.7, 23.4, C2 not observed, appears at δ 125.1 in nondeuterated compound; CIMS m/z (%) 179 (100), 162 (37), 57 (22); HRMS (CI, NH_3) m/z 236.2117 ([M + 1]$^+$, 2%), calcd for $C_{16}H_{26}DO$ 236.2124. For spectroscopic data of the nondeuterated analogue, see ref 3b.

***syn*-10-*tert*-Butoxy-11-*endo*-deutero-8-methyltricyclo[6.2.1.0^{3,9}]undec-2-ene (19).** Undecane **19** was prepared following the preceding procedure, beginning with $PtCl_2$ (7 mg, 0.027 mmol), tris-pentafluorophenylphosphine (29 mg, 0.054 mmol), and **20** (60 mg, 0.269 mmol) in mesitylene (2.8 mL). Purification by flash chromatography (hexanes/EtOAc, 20/1) gave **19** (R_f = 0.6; 48 mg; 81% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.47 (br s, 1H), 3.35 (br s, 1H), 2.39 (br s, 1H), 2.13–2.25 (overlap, 2H), 1.98 (br s, 1H), 1.71 (br s, 1H), 1.60 (m, 1H), 1.48 (m, 1H), 1.30–1.44 (overlap, 3H), 1.29 (s, 3H), 1.22 (m, 1H), 1.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 147.6, 125.1, 84.5, 73.3, 58.9, 47.8, 47.3, 40.2 (t, $^1J_{CD}$= 20.3 Hz), 39.7, 31.0, 30.1, 28.5 (3C), 27.7, 23.4; CIMS m/z (%) 178 (100), 162 (81), 145 (88), 57 (99); HRMS (CI, NH_3) m/z 236.2103 ([M + 1]$^+$, 2%), calcd for $C_{16}H_{26}DO$ 236.2124. For spectroscopic data of the nondeuterated analogue, see ref 3b.

***anti*-7-*tert*-Butoxy-3,3-dideuterobicyclo[2.2.1]hept-5-en-2-one (29).** To a flask containing the nondeuterated ketone[6] (500 mg, 2.8 mmol), D_2O (27 mL) and potassium carbonate (460 mg, 3.3 mmol) were added and the reaction mixture was refluxed for 3 h. After cooling to rt, the mixture was extracted with Et_2O (3 × 30 mL), and the combined organic layers were washed with brine (100 mL), dried over Na_2SO_4, filtered, and concentrated in vacuo. The residue was purified by flash chromatography (petroleum ether/Et_2O, 8/1) to give **29** (R_f 0.3; 588 mg, 97% yield) as a white solid: mp 67–69 °C; IR (NaCl) 2973, 2876, 2231, 2177, 1734, 1363, 1237, 1130, 1105, 910, 722 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.49 (dd, J = 5.7, 2.6 Hz, 1H), 5.96 (dddd, J= 5.7, 3.3, 1.1, 1.1 Hz, 1H), 4.22 (br s, 1H), 3.08–3.10 (overlap, 2H), 1.17 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 210.2, 139.0, 124.9, 89.1, 73.9, 62.3, 46.5, 37.1 (q, $^1J_{CD}$ = 20.6 Hz), 27.9 (3C); CIMS m/z (%) 131 (72), 126 (65), 97 (100); HRMS (CI, NH_3) m/z 183.1368 ([M + 1]$^+$, 100%), calcd for $C_{11}H_{15}D_2O_2$ 183.1352. For spectroscopic data of the nondeuterated analogue, see ref 1c.

***anti*-7-*tert*-Butoxy-3-deuterobicyclo[2.2.1]hepta-2,5-dien-2-yl Trifluoromethanesulfonate (30).** To a solution of *anti*-7-*tert*-butoxy-3,3-dideuterobicyclo[2.2.1]hept-5-en-2-one **29** (229 mg, 1.26 mmol) in anhydrous THF (6 mL) was added dropwise a KHMDS solution (0.5 M in toluene, 3.2 mL, 1.59 mmol) at −78 °C under Ar. The reaction mixture was stirred for 2 h at −78 °C, then the temperature was allowed to warm to 0 °C, and *N*-phenyltrifluoromethanesulfonimide (495 mg, 1.38 mmol), dissolved in anhydrous THF (1 mL), was added. The solution was stirred at rt for 10 h, then quenched with a saturated aqueous solution of $NaHCO_3$ (3

mL). The crude mixture was diluted with Et_2O (10 mL), and the organic layer was washed with water (3 × 10 mL) and brine (10 mL) and dried over Na_2SO_4. After removal of the solvent in vacuo, the residue was purified by flash chromatography (petroleum ether/EtOAc, 95/5) to give **30** (R_f 0.34; 312 mg; 79% yield) as a yellow oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.66 (br s, 2H), 4.12 (br s, 1 H), 3.41 (br s, 1H), 3.35 (br s, 1H), 1.14 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 162.9, 138.4, 135.5, 122.7 (t, $^1J_{CD}$ = 27.2 Hz), 118.7 (q, $^1J_{CF}$ = 317.9 Hz), 104.1, 74.7, 56.9, 54.1, 28.3 (3C); CIMS *m/z* (%) 314 (7), 257 (22), 240 (100); HRMS (CI, NH_3) *m/z* 314.0803 ([M + 1]$^+$, 7%), calcd for $C_{12}H_{15}DF_3O_4S$ 314.0783. For spectroscopic data of the nondeuterated analogue, see ref 1c.

***anti*-7-*tert*-Butoxy-2,3-dideuterobicyclo[2.2.1]hept-2,5-diene (31).** To a flamed-dried flask under argon were added $Pd(PPh_3)_4$ (18 mg, 0.16 mmol), freshly sublimed LiCl (102 mg, 2.4 mmol), and anhydrous THF (1.5 mL). The mixture was stirred for 5 min at rt, then *anti*-7-*tert*-butoxy-3-deuterobicyclo[2.2.1]hepta-2,5-dien-2-yl trifluoromethanesulfonate (**30**, 250 mg, 0.80 mmol) dissolved in anhydrous THF (0.5 mL) was added, immediately followed by *n*-Bu_3SnD (0.220 mL, 0.80 mmol). The reaction mixture was stirred for 2 h under Ar, then quenched with 10% ammonia solution (NH_4OH, 1 mL). The mixture was diluted with Et_2O (5 mL), and the organic layer was washed with brine (3 × 5 mL) and dried over Na_2SO_4. After removal of the solvent in vacuo, the residue was purified by flash chromatography (petroleum ether/Et_2O, 95/5) to give **31** (R_f 0.53; 130 mg; 98% yield) as a volatile colorless oil, which was used in the next step without purification. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.56 (m, 2H), 3.75 (br s, 1H), 3.37 (m, 2H), 1.12 (s, 9H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 139.6 (t, $^1J_{CD}$ = 27 Hz, 2C), 137.5 (2C), 104.6, 73.7, 55.6 (2C), 28.5 (3C); CIMS *m/z* (%) 167 ([M + 1]$^+$, 94), 57 (80); HRMS (CI, NH_3) *m/z* 167.1418 ([M + 1]$^+$, 24%), calcd for $C_{11}H_{15}D_2O$ 167.1403. For spectroscopic data of the nondeuterated analogue, see ref 3a.

***anti*-5-*tert*-Butoxy-1,2-dideuterotetracyclo[5.4.0.0^{2,4}0^{3,7}]undec-9-ene (32).** To a flamed-dried 15 mL pressure tube under argon was added dppe (45 mg, 0.112 mmol) followed by CoI_2 (17 mg, 0.056 mmol) and CH_2Cl_2 (2.5 mL). To this dark brown mixture were added sequentially ZnI_2 (143 mg, 0.448 mmol), Zn (29 mg, 0.448 mmol), and *anti*-7-*tert*-butoxy-2,3-dideuterobicyclo[2.2.1]hept-2,5-diene (**31**, 186 mg, 1.12 mmol). The solution was cooled to −78 °C, and 1,3-butadiene (182 mg, 3.36 mmol) was added via cannula. The pressure tube was immediately capped and allowed to warm to rt. The dark brown cloudy solution was stirred at rt for 20 h, then the crude mixture was passed through a silica gel plug to remove the catalyst. The solvent was removed in vacuo and the residue purified by flash chromatography (hexanes/EtOAc, 20/1) to give *anti*-5-*tert*-butoxy-3,7-dideuterotetracyclo[5.4.0.0^{2,4}0^{3,7}]undec-9-ene as a colorless oil (R_f = 0.3; 165 mg; 67% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.53 (dddd, J = 11.6, 7.6, 2.6, 2.4 Hz, 1H), 5.45 (dddd, J = 11.6 8.0, 2.8, 2.0 Hz, 1H), 3.61 (br s, 1H), 2.40–2.46 (overlap, 2H), 2.26 (dd, J = 17.2, 7.0 Hz, 2H), 2.18 (br d, J = 17.2, 1H), 1.55 (br s, 1H), 1.18 (s, 9H), 1.04 (d, J = 5.0 Hz, 1H), 0.98 (d, J = 5.0 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 128.3, 127.0, 78.5, 73.3, 47.1, 38.1 (t, $^1J_{CD}$ = 20.3 Hz), 37.3, 31.2, 30.3, 28.8 (3C), 16.7, 15.2, the resonance for C2 not observed clearly due to overlap, this signal appears at δ 16.9 in nondeuterated compound; CIMS *m/z* (%) 221.2 ([M + 1]$^+$, 2), 167.2 (32), 147.1 (100), 146.1 (36); HRMS (CI, NH_3) *m/z* 221.1874 ([M + 1]$^+$, 2%), calcd for $C_{15}H_{21}D_2O$ 221.1895. For spectroscopic data of the nondeuterated analogue, see ref 3a.

***anti*-5-*tert*-Butoxy-1,2-dideutero-tetracyclo[5.4.0.0^{2,4}0^{3,7}]undecane (33).** A mixture of *anti*-5-*tert*-butoxy-3,7-dideuterotetracyclo[5.4.0.0^{2,4}0^{3,7}]undec-9-ene (**32**, 165 mg, 0.748 mmol) and Pd−C (10% Pd on activated carbon, 92 mg, 0.075 mmol) in MeOH (15 mL) was kept under a H_2 atmosphere (balloon, 1 atm) at rt for 5 h with stirring. The reaction mixture was then passed through a short silica gel plug, eluting with MeOH (3 × 10 mL) to remove the catalyst. The solvent was removed in vacuo and the residue purified by flash chromatography (hexanes/EtOAc, 20/1) to give **33** as a colorless oil (R_f = 0.5; 140 mg; 84% yield): ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.56 (br s, 1H), 2.47 (br s, 1H), 1.75 (m, 1H), 1.67 (br s, 1H), 1.43–1.61 (overlap, 5H), 1.23–1.33 (overlap, 2H), 1.17 (s, 9H), 1.04 (d, J = 5 Hz, 1H), 0.92 (d, J = 5.1 Hz, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 78.8, 73.2, 43.7, 40.6 (t, $^1J_{CD}$ = 19.3 Hz), 39.5, 31.5, 30.6, 28.8 (3C), 26.74, 26.69, 19.1 (t, $^1J_{CD}$= 26.3 Hz), 17.0, 16.6; CIMS *m/z* (%) 223.2 ([M + 1]$^+$, 5), 222.2 ([M]$^+$, 17), 165 (100); HRMS (CI, NH_3) *m/z* 223.2043 ([M + 1]$^+$, 100%), calcd for $C_{15}H_{23}D_2O$ 223.2029. For spectroscopic data of the nondeuterated analogue, see ref 3a.

***anti*-10-*tert*-Butoxy-2,11-*endo*-dideuterotricyclo[6.2.1.0^{3,9}]undec-2-ene (34).** To a solution of $PtCl_2$ (7 mg, 0.027 mmol) in anhydrous mesitylene (2.8 mL) under Ar was added tris-pentafluorophenylphosphine (29 mg, 0.054 mmol) and **33** (60 mg, 0.269 mmol). The reaction was stirred for 16 h at 140 °C then allowed to cool to rt. The solution was filtered through a short plug of silica gel, eluting with CH_2Cl_2 (6 mL) to remove the catalyst. The solvent was removed in vacuo, and the residue was purified by flash chromatography (hexanes/EtOAc, 20/1) to give **34** (R_f = 0.6; 48 mg; 81% yield) as a colorless oil: ^{1}H NMR (400 MHz, $CDCl_3$) δ 3.34 (br s, 1H), 2.46 (br m, 1H), 2.28–2.32 (overlap, 3H), 1.93–2.02 (overlap, 2H), 1.74 (br ddd, J = 14.4, 7.4, 7.4 Hz, 1H), 1.64 (dddd, J = 14.8, 5.6, 2.5, 2.5 Hz, 1H), 1.49 (dddd, J = 14.8, 6.0, 2.8, 2.0 Hz, 1H), 1.15–1.31 (overlap, 2H), 1.13 (s, 9H), 1.03–1.09 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 143.9, 128.8 (t, $^1J_{CD}$= 24.8 Hz), 83.0, 73.1, 52.8, 46.4, 34.5, 31.8, 31.2 (t, $^1J_{CD}$= 24.7 Hz), 30.6, 28.8 (3C), 27.8, 21.5. CIMS *m/z* (%) 223.2 ([M + 1]$^+$, 3), 222.2 ([M]$^+$, 16), 166 (100), 165 (41), 57 (37); HRMS (CI, NH_3) *m/z* 222.1942 ([M]$^+$, 11%), calcd for $C_{15}H_{22}D_2O$ 222.1953. For spectroscopic data of the nondeuterated analogue, see ref 3a.

Kinetic Studies. All kinetic experiments were performed in duplicate, with both monodeuterated compounds **16** and **20** and nondeuterated compound **6** run side by side in each run. A stock solution of $PtCl_2$ in mesitylene-d_{12} was prepared as follow: $PtCl_2$ (4 mg, 0.015 mmol) was placed in a round-bottom flask and mesitylene-d_{12} (1.6 mL) was added. The mixture was warmed to 100 °C for 20 min to ensure dissolution of $PtCl_2$. Compound **16**(9 mg, 0.04 mmol) was placed in a NMR tube followed by tris-pentafluorophenylphosphine (4 mg, 0.08 mmol) and the stock solution containing $PtCl_2$ (0.4 mL). The NMR tube was then capped and heated to 135 °C. An NMR spectrum was recorded every 20 min for the first 3 h and then every hour. The appearance of alkene and disappearance of the starting material was monitored via NMR through the H5 peak (from 3.55 ppm in the starting material to 3.36 ppm for the alkene product).

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Supporting Information Available: Kinetic data for individual experiments of isotope effects and ^{1}H and ^{13}C NMR spectra for all new compounds. This information is available free of charge via the Internet at http://pubs.acs.org.

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