Halogenated Oxabicyclo[3.2.1]octadiene Building Blocks: Elaboration of the Dibromoenone

Phillip M. Pelphrey,[a] Ravi S. Orugunty,[b] Richard J. Helmich,[b] Merle A. Battiste,[b] and Dennis L. Wright*[a]

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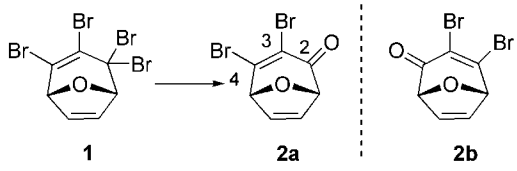
We have been interested in exploiting the highly functionalized oxabicyclo[3.2.1]octadienes that are produced by the cycloaddition of furan and tetrabromocyclopropene as synthetic building blocks. As part of this program, we have prepared non-racemic derivatives of these adducts containing an α,β-dibromoenone moiety embedded in the bicyclic framework. Elaboration of this unit has been realized through substitution and palladium-catalyzed cross-coupling reactions. Formation of bicyclodecenes has also been accomplished by a chromium-nickel-mediated ring closure.

Introduction

Tobey and Law disclosed in 1968 that tetrabromocyclopropene undergoes a facile cycloaddition reaction with furan to generate the halogenated oxabicyclo[3.2.1]octadiene derivative **1** in excellent yield.[1] Over the past several years we have studied the utility of this highly functionalized bicyclic nucleus as a versatile building block and have been interested in using this system in both target-oriented and diversity-oriented manifolds.[2] Recently, we developed a direct route to the chiral enones **2a/b** from **1** involving the resolution of the corresponding tartrate ketals (Scheme 1).[3]



Scheme 1. Bicyclic building blocks containing a dibromoenone.

These enantiomeric building blocks possess an α,β-dibromoenone moiety which should allow for the straightforward introduction of a variety of groups. We have studied the reactivity and selectivity of this uncommon functionality[4] and herein report a range of transformations that can be utilized to elaborate this skeleton.[5]

[a] Department of Chemistry, Dartmouth College, Hanover, NH 03755, USA
Fax: +1-603-646-3946
E-mail: dwright@dartmouth.edu
[b] Department of Chemistry, University of Florida, Gainesville, FL 32611, USA
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Results and Discussion

Functionalization of the β-Bromine by Substitution Reactions: Because of conjugation of the C4 bromide to the carbonyl at C2, it seemed relatively straightforward to selectively exchange this halogen through nucleophilic addition/elimination reactions (Table 1).

We examined a variety of synthetically relevant nucleophiles to effect substitution of this bromide. A vinylogous Finkelstein reaction[6] occurred in excellent yield by heating **2** with sodium iodide in acetone. Morpholine reacted in very high yield to give the vinylogous amide **3b** while cyanide added in much lower yield to give the nitrile **3c**. The lower yield of the nitrile seemed to relate to the instability of **3c**, which is prone to decomposition. The copper-catalyzed addition of organometallic species was also studied as a way to append carbon chains onto the bicyclic enone. Although the Gilman-type cuprate added in very good yield to give **3d**, attempts to add Grignard reagents with substoichiometric copper salts was frustrated by rapid 1,2-addition to the carbonyl group. The ketone in **2** can be regarded as a vinylous acid bromide and appears to be highly reactive. Only with a stoichiometric amount of copper(I) iodide could the acetal derivative **3e** be obtained in reasonable yield. The addition of functionalized units to the enone occurred smoothly utilizing the Knochel conditions,[7] which produced the ester **3f** in very good overall yield.

Functionalization of the β-Bromine by Palladium-Catalyzed Cross-Coupling Reactions: Another attractive strategy for elaborating the dibromoenone found in **2** was to utilize palladium-catalyzed cross-coupling chemistry to substitute this system. Although the literature contained abundant examples of cross-coupling on both α- and β-bromoenones[8] there are few examples with enones containing adjacent reactive groups.[9] Examining a variety of palladium-catalyzed

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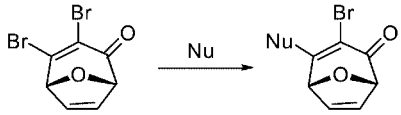
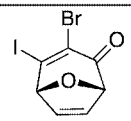
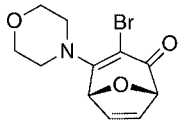
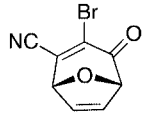
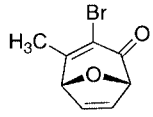
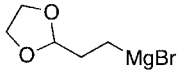
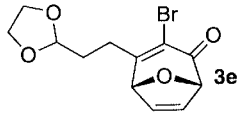
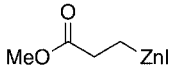
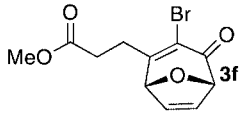
Table 1. Direct substitution of the β-bromide of (±)-**2**.



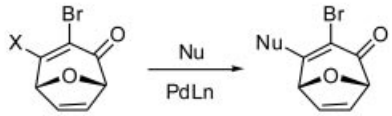
2 **3a–f**

Nucleophiles	Conditions	Product	Yield
NaI	Me_2CO, reflux, 18 h	 **3a**	95%
Morpholine	K_2CO_3, CH_2Cl_2, 25 °C, 1 h	 **3b**	88%
NaCN	DMSO, 25 °C, 30 min	 **3c**	35%
Me_2CuLi	Et_2O, –78 °C	 **3d**	84%
	CuI (1 equiv.), THF	 **3e**	55%
	LiCl, CuCN, BF_3OEt_2, –30 °C	 **3f**	90%

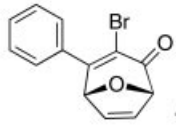
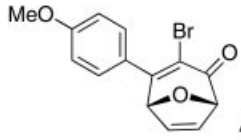
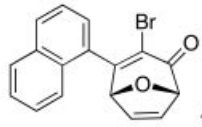
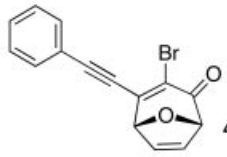
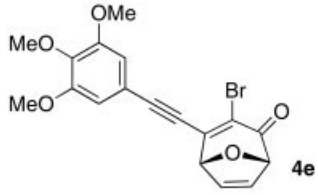
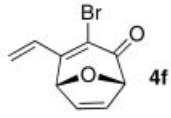
reactions showed that preferential reaction took place at the β position in agreement with the higher reactivity of these moieties in relation to α-haloenone systems (Table 2).

Initial attempts to effect Suzuki cross-coupling with **2** were frustrated by low yields and prolonged reaction times. Standard conditions employing the use of palladium(II) acetate/triphenylphosphane as the source of palladium and potassium phosphate as the base gave essentially only recovered starting materials or after prolonged heating, products of decomposition. Eventually, it was found that the addition of silver salts was critical to obtain high yields of product. Under these conditions, phenyl, 4-methoxyphenyl and naphthylboronic acids were coupled exclusively to the β position to give **4a**–**c**. No coupling at the α position or double coupling was observed in these systems. Attempted Sonagashira coupling under these conditions or with copper additives was unsuccessful, although good yields of the alkyne could be obtained with an amine base present. Installation of a vinyl substituent by a Stille coupling was moderately successful, producing the diene **4f**, while Heck and Negishi couplings were completely unsuccessful even with the more reactive iodide **3a**. Interestingly, the bromide

Table 2. Cross-coupling reactions of (±)-**2**.



2/3a **4a–f**

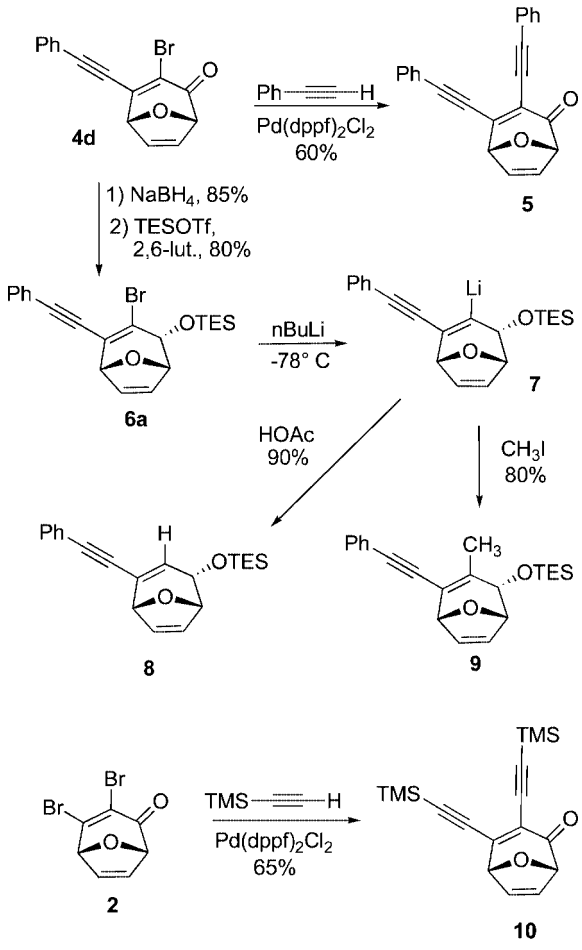
Nucleophile	Conditions	Product	Yield
$PhB(OH)_2$	**A**[a]	 **4a**	80%
4-MeO-$PhB(OH)_2$	**A**[a]	 **4b**	73%
1-naphthylB$(OH)_2$	**A**[a]	 **4c**	78%
phenylacetylene	**A**[a]	no reaction	NA
phenylacetylene	**B**[b]	 **4d**	X = Br (79%) X = I (75%)
(3,4,5-trimethoxyphenyl)acetylene	**B**[b]	 **4e**	X = Br (88%) X = I (87%)
tributylvinylstannane	**C**[c]	 **4f**	X = Br (42%) X = I (30%)
methyl acrylate	**D**[d]	no reaction	NA
2-cyanoethylzinc bromide	**D**[d]	no reaction	NA

[a] Condition **A**: $Pd(OAc)_2$, PPh_3, Et_3N, Ag_2CO_3, MeCN, 25 °C, 12 h. [b] Condition **B**: $Pd(PhCN)_2Cl_2$, CuI, Et_3N, MeCN, 25 °C, 10 min. [c] Condition **C**: $Pd(PhCN)_2Cl_2$, $AsPh_3$, DMF, 25 °C, 30 min. [d] Condition **D**: $Pd(OAc)_2$, PPh_3, Ag_2CO_3, Et_3N, MeCN, 25 °C → reflux.

and iodide showed almost the same reaction profile including rate and product yield in all of the palladium reactions examined. The formation of single regioisomers in the above reactions shows that the β position is significantly more reactive than the α-bromide. To further elaborate these building blocks, a second coupling seemed possible.

Functionalization of the α-Bromine by Metal-Mediated Reactions: Building upon the success of palladium-mediated cross-coupling of the β position, we made attempts to effect a second cross-coupling at the α position (see Scheme 2). To this end, compound **4d** was subjected to a fresh batch of phenylacetylene and palladium. Changing the palladium

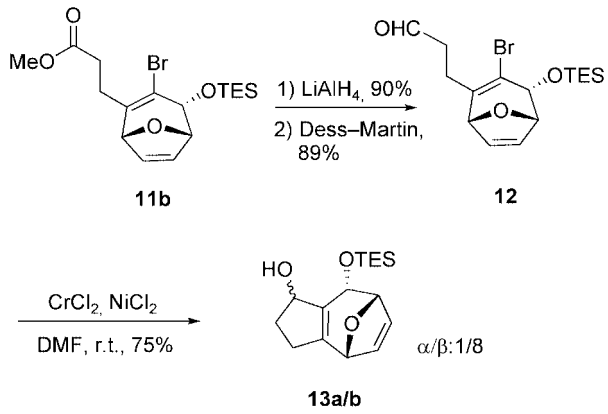
source to a more reactive palladium species effected the desired coupling in good yield. Furthermore, addition of two equivalents of the desired acetylene with dichloro[1,1′-bis(diphenylphosphanyl)ferrocene]palladium(II) and compound **2** gave the bis-coupled product **10** in good yield as the only isolable product. The lower reactivity of these systems has been appreciated,[10] however, effective functionalization of the α position has been accomplished.



Scheme 2. Functionalization of the α-bromide.

To further enhance our strategy of functionalizing the α position, we pursued different metallating protocols (see Scheme 2). Low-temperature metallation of **6a** gave the organolithium **7**, which could be simply protonated with acetic acid to yield the reduced derivative **8** or reacted with electrophiles such as methyl iodide to give the tetrasubstituted olefin **9**. It also proved possible to apply a related metallation of the vinyl bromide to effect a net annulation of the dibromoenone.

Conversion of the previously described **3f** to **11b** by reduction (85%) and silylation (85%) preceded two-step transformation to the unstable aldehyde **12** and a chromium/nickel-promoted ring closure[11] to give the hydroazulene **13a/b** in good overall yield and high diastereoselectivity (Scheme 3).



Scheme 3. Annulation by a Nozaki–Hiyama–Kishi closure .

Conclusions

The direct condensation of furan and tetrabromocyclopropene leads to heavily functionalized synthetic building blocks for seven-membered carbocyclic and five- and six-membered oxacyclic systems. To effectively utilize these building blocks for the preparation of complex molecules, it is important to develop reactions to elaborate the skeleton. We have shown that the dibromoenone unit can be readily derivatized at the β position through a nucleophilic addition/elimination sequence or palladium-mediated cross-coupling reactions. The α-bromide proved equally as reactive towards similar coupling reaction and is amenable to metallation and electrophilic trapping. The application of these building blocks in target and diversity-oriented syntheses is ongoing.

Experimental Section

General: The ^{1}H and ^{13}C spectra were recorded at 500 and 125 MHz, respectively. All melting points are uncorrected. High-resolution mass spectrometry was provided by the University of Illinois Urbana-Champaigne Mass Spectrometry laboratory. All reagents were used directly from commercial sources, unless otherwise stated. All reported yields are the average of at least two independent runs. Compound **2** was prepared according to the literature procedure.[2d]

(1*S*,5*R*)-3-Bromo-4-iodo-8-oxabicylo[3.2.1]octa-3,6-dien-2-one (3a): To a 50 mL round-bottomed flask was added sodium iodide (1.3 g, 8.9 mmol). Acetone (20 mL) was added and the reaction was stirred at 25 °C until all material was dissolved. Compound **2** (1.0 g, 3.6 mmol) was added and the flask placed into a preheated oil bath (60 °C). The reaction was stirred at 60 °C for 18 hours. The flask was removed from the oil bath and cooled to room temperature. The reaction mixture was filtered through a pad of celite. The solvent was removed under reduced pressure and the residue purified by column chromatography (SiO_2, 100 g) using 10% ethyl acetate in hexanes as the eluent to afford **3a** as a white solid (1.12 g, 95%): R_f = 0.51 (hexane/EtOAc, 2:1). M.p. 138–140 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.07 (dd, J = 2.0, 0.7 Hz, 1 H), 6.57 (ddd, J = 5.9, 2.4, 0.5 Hz, 1 H), 5.50 (dd, J = 2.0, 0.7 Hz, 1 H), 5.18 (dd, J = 2.2, 0.7 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 182.8, 138.7, 131.0, 129.5, 127.3, 90.6, 87.1 ppm. IR (thin film,

cm^{-1}): $\tilde{\nu}$ = 3054, 2985, 1706, 1543, 1285, 1175. HRMS: *m*/*z* 325.8444 (calcd. $C_7H_4BrIO_2$, 325.8439).

(1*S*,5*R*)-3-Bromo-4-morpholino-8-oxabicylco[3.2.1]octa-3,6-dien-2-one (3b): To a 25 mL round-bottomed flask was added compound **2** (200 mg, 0.72 mmol). Dichloromethane (10 mL) was added and the reaction was stirred at 25 °C until all material was dissolved. Potassium carbonate (200 mg, 1.43 mmol) was added followed by morpholine (0.125 mL, 1.43 mmol). The reaction mixture was stirred at 25 °C for 1 hour. Water (0.100 mL) was added and the reaction stirred for 30 minutes. The reaction mixture was diluted with dichloromethane (25 mL), washed with saturated sodium hydrogen carbonate (25 mL) and then washed with brine (25 mL). The organics were taken, dried with sodium sulfate and concentrated. The residue was purified by column chromatography (SiO_2, 20 g) using 50% ethyl acetate in hexanes as the eluent to afford **3b** as a white solid (180 mg, 88%): R_f = 0.13 (hexane/EtOAc, 1:1). M.p. 135–137 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.71–6.67 (m, 2 H), 5.47 (d, *J* = 2.0 Hz, 1 H), 5.12 (d, *J* = 2.0 Hz, 1 H), 3.8 (t, *J* = 4.9 Hz, 4 H), 3.66–3.64 (m, 4 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 186.1, 164.2, 136.0, 134.6, 89.6, 87.0, 81.6, 67.3, 50.1 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 3053, 2982, 2919, 2858, 1656, 1547, 1265. HRMS: *m*/*z* 284.9992 (calcd. $C_{11}H_{12}BrNO_3$, 285.0000).

(1*R*,5*S*)-3-Bromo-4-oxo-8-oxabicyclo[3.2.1]octa-2,6-diene-2-carbonitrile (3c): To a 10 mL round-bottomed flask was added dimethyl sulfoxide (2 mL) and sodium cyanide (54 mg, 1.1 mmol). The reaction mixture was heated to 40 °C and stirred until all material was dissolved. The flask was removed and the solution cooled to room temperature. Compound **2** (280 mg, 1.0 mmol) was added and the reaction stirred at 25 °C for 30 minutes. Water (10 mL) was added and the solution extracted with diethyl ether (4 × 20 mL). The combined organics were dried with sodium sulfate and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, 30 g) using 10% ethyl acetate in hexanes as the eluent to afford **3c** as a yellow solid (79 mg, 35%): R_f = 0.42 (hexane/EtOAc, 2:1). M.p. 115–117 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.03 (ddd, *J* = 5.6, 2.0, 0.7 Hz, 1 H), 6.58 (dd, *J* = 5.6, 2.4 Hz, 1 H), 5.34 (d, *J* = 2.0 Hz, 1 H), 5.25 (dd, *J* = 2.2, 0.7 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 182.0, 140.1, 134.4, 130.4, 129.6, 113.5, 87.1, 81.9 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 3054, 2986, 1721, 1572, 1265. HRMS: *m*/*z* 224.9422 (calcd. $C_8H_4BrNO_2$, 224.9425).

(1*S*,5*R*)-3-Bromo-4-methyl-8-oxabicyclo[3.2.1]octa-3,6-dien-2-one (3d): To a 10 mL round-bottomed flask was added copper(I) iodide (82 mg, 0.43 mmol) and ether (2 mL). The suspension was cooled to –78 °C and methyllithium (0.79 mmol) was added dropwise over 5 minutes. The reaction was warmed to –10 °C and stirred for 30 minutes. The resulting cuprate was cooled to –78 °C and a solution of **2** (100 mg, 0.36 mmol) in diethyl ether (2 mL) was added dropwise over 5 minutes. The reaction was stirred at –78 °C for 3 hours. Saturated ammonium chloride (2 mL) was added and the solution allowed to warm to room temperature. The solution was extracted with diethyl ether (3 × 10 mL). The combined organics were dried with sodium sulfate and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, 10 g) using 10% ethyl acetate in hexanes as the eluent to afford the **3d** as a brown semisolid (65 mg, 84%): ^{1}H NMR (300 MHz, $CDCl_3$): δ = 6.92 (dd, *J* = 5.7, 2.1 Hz, 1 H), 6.56 (dd, *J* = 5.2, 2.1 Hz, 1 H), 5.16 (d, *J* = 2.1 Hz, 1 H), 5.12 (d, *J* = 2.1 Hz, 1 H), 2.12 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 185.8, 162.0, 139.4, 131.5, 115.5, 86.8, 84.3, 20.4 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 2980, 1707, 1603, 1240, 1068. HRMS: *m*/*z* 213.9619 (calcd. $C_8H_7BrO_2$, 213.9629).

(1*S*,5*R*)-3-Bromo-4-[2-(1,3-dioxolan-2-yl)ethyl]-8-oxabicylo[3.2.1]-octa-3,6-dien-2-one (3e): To a 10 mL round-bottomed flask was added magnesium turnings (97 mg, 4.0 mmol) and THF (0.900 mL). (Bromoethyl)dioxolane (0.240 mL, 2.0 mmol) in THF (0.900 mL) was added dropwise over 5 minutes. The suspension was stirred at room temperature for 3 hours. The solution was then cooled to –10 °C and copper(I) iodide (381 mg, 2.0 mmol) was added at once. The suspension was stirred at –10 °C for 30 minutes and then cooled to –78 °C. Compound **2** (280 mg, 1.0 mmol) in THF (0.900 mL) was added dropwise over 5 minutes. The solution was stirred at –78 °C for 3 hours. Saturated ammonium chloride (1.0 mL) was added and the solution allowed to warm to room temperature. The solution was extracted with dichloromethane (3 × 5 mL). The combined organics were dried with sodium sulfate and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, 30 g) using 20% ethyl acetate in hexanes as eluent to afford **3e** as a colorless oil (166 mg, 55%): R_f = 0.18 (hexane/EtOAc, 2:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.88 (dd, *J* = 5.6, 1.5 Hz, 1 H), 6.53 (dd, *J* = 5.6, 2.2 Hz, 1 H), 5.22 (d, *J* = 2.0 Hz, 1 H), 5.10 (d, *J* = 1.7 Hz, 1 H), 4.96 (t, *J* = 4.1 Hz, 1 H), 4.04–3.97 (m, 2 H), 3.93–3.88 (m, 2 H), 2.64–2.50 (m, 2 H), 2.16–1.91 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 186.0, 164.7, 140.1, 131.0, 115.5, 103.0, 86.9, 83.3, 65.3, 65.3, 30.1, 28.4 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 2960, 2884, 1703, 1596, 1139. HRMS: *m*/*z* 229.9988 (calcd. $C_{12}H_{13}BrO_4$, 299.9997).

Methyl 3-{(1*R*,5*S*)-3-Bromo-4-oxo-8-oxabicyclo[3.2.1]octa-2,6-dien-2-yl}propanoate (3f): To a 10 mL round-bottomed flask was added lithium chloride (91 mg, 2.1 mmol) and copper(I) cyanide (96 mg, 1.1 mmol). THF (1.0 mL) was added and the solution stirred at 25 °C for 30 minutes. The light green solution was cooled to 0 °C and the organozinc reagent[12] (0.850 mL, 1.1 mmol, 1.26 M) was added. The solution was stirred at 0 °C for 30 minutes and then cooled to –78 °C. BF_3–OEt_2 (0.270 mL, 2.1 mmol) was added, followed by compound **2** (100 mg, 0.36 mmol) in THF (1.0 mL). The solution was warmed to –30 °C and stirred for 3 hours. Saturated ammonium chloride (2.0 mL) and liquid ammonia (aqueous 25%, 0.500 mL) were added and the solution warmed to room temperature and stirred for 30 minutes. The layers were separated and the aqueous layer was extracted with ethyl acetate (3 × 5 mL). The combined organics were washed with brine, dried with sodium sulfate and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, 10 g), using 33% ethyl acetate in hexanes as the eluent to afford **3f** as a white solid (93 mg, 90%): R_f = 0.30 (hexane/EtOAc, 2:1). M.p. 80–82 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.88 (ddd, *J* = 5.6, 2.0, 0.7 Hz, 1 H), 6.51 (dd, *J* = 5.6, 2.2 Hz, 1 H), 5.26 (d, *J* = 2.0 Hz, 1 H), 5.09 (dd, *J* = 2.2, 0.7 Hz, 1 H), 3.72 (s, 3 H), 2.63–2.60 (m, 2 H), 2.79–2.69 (m, 2 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 185.8, 172.5, 163.3, 140.3, 130.8, 116.5, 86.8, 83.7, 52.3, 30.6, 29.4 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 2953, 1735, 1700, 1597, 1438, 1201, 1169. HRMS: *m*/*z* 285.9844 (calcd. $C_{11}H_{11}BrO_4$, 285.9841).

General Procedure for Suzuki Couplings of Arylboronic Acids: In a dry screw-cap tube, acetonitrile (1.0 mL) was degassed. Palladium acetate (8.1 mg, 0.036 mmol), triethylamine (0.018 mL, 0.017 mmol) and triphenylphosphane (37.5 mg, 0.014 mmol) were added and stirred for 15 minutes. To the resulting solution was added **2** (100 mg, 0.36 mmol), boronic acid (0.36 mmol) and silver carbonate (108.4 mg, 0.36 mmol). The solution was stirred overnight at 25 °C. The crude reaction mixture was subjected to Soxhlet extraction using ethyl acetate (25 mL). The crude extract was subjected to column chromatography using 5% ethyl acetate in hexanes to afford the desired products.

(1*S*,5*R*)-3-Bromo-4-phenyl-8-oxabicyclo[3.2.1]octa-3,6-dien-2-one (4a): Compound **2** (50 mg) was subjected to the coupling condi-

tions with phenylboronic acid to afford **4a** (39.8 mg, 80%) as a colorless solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.45 (s, 5 H), 6.96 (dd, J = 5.7, 1.9 Hz, 1 H), 6.62 (dd, J = 5.7, 2.4 Hz, 1 H), 5.46 (d, J = 1.9 Hz, 1 H), 5.20 (d, J = 2.4 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 186.3, 161.1, 140.4, 134.7, 131.1, 130.3, 128.9, 127.9, 114.8, 86.9, 85.2 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 2979, 1699, 1585, 1186, 1072. HRMS: *m/z* 275.9762 (calcd. $C_8H_7BrO_2$, 275.9786).

(1*S*,5*R*)-3-Bromo-4-(4-methoxyphenyl)-8-oxabicyclo[3.2.1]octa-3,6-dien-2-one (4b): Compound **2** (100 mg) was subjected to the coupling conditions with (4-methoxyphenyl)boronic acid to afford **4b** (80 mg, 73%) as a colorless solid; m.p. 122–123 °C. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.50 (d, J = 8.8 Hz, 2 H), 6.98 (d, J = 8.8 Hz, 2 H), 6.92 (dd, J = 5.7, 1.7 Hz, 1 H), 6.60 (dd, J = 5.7, 2.4 Hz, 1 H), 5.49 (d, J = 1.7 Hz, 1 H), 5.18 (d, J = 2.4 Hz, 1 H), 3.86 (s, 3 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 186.4, 161.3, 160.5, 140.3, 131.1, 130.0, 126.6, 114.3, 113.7, 86.9, 85.1, 55.6 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 2974, 2839, 1694, 1604, 1302, 1253, 1179, 1072. HRMS: *m/z* 305.9854 (calcd. $C_{14}H_{11}BrO_3$, 305.9891).

(1*S*,5*R*)-3-Bromo-4-(naphthalen-1-yl)-8-oxabicyclo[3.2.1]octa-3,6-dien-2-one (4c): Compound **2** (100 mg) was subjected to the coupling conditions with 1-napthylboronic acid to afford **4c** (92 mg, 78%) as a colorless solid. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.00–7.86 (m, 5 H), 7.62–7.50(m, 4 H), 7.00 (dd, J = 5.7, 1.9 Hz, 1 H), 6.65 (dd, J = 5.7, 2.4 Hz, 1 H), 5.58 (d, J = 1.9 Hz, 1 H), 5.24 (d, J = 2.4 Hz, 1 H) ppm. ^{13}C NMR (75 MHz, $CDCl_3$): δ = 186.3, 140.5, 133.6, 133.0, 132.0, 131.2, 130.9, 128.8, 128.7, 128.1, 128.1, 127.9, 127.2, 124.8, 87.0, 85.3 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 3057. 2979, 1699, 1575, 1195, 1072; Analysis calcd. for $C_{17}H_{13}BrO_3$: C, 62.41, H, 3.39. Found: C, 62.41, H, 3.25.

General Procedure of the Sonogashira Reaction: To a 10 mL round-bottomed flask was added either **2** (100 mg, 0.36 mmol) or **3a** (100 mg, 0.31 mmol). Acetonitrile (2 mL) was added and the reaction mixture stirred at 25 °C until all material was dissolved. Triethylamine (2 mL) was added followed by copper(I) iodide (0.07 equiv.) and $Pd(PhCN)_2Cl_2$ (0.07 equiv.). The acetylene (1.1 equiv.) was then added and the solution stirred under argon for 10 minutes. The solvent was removed under reduced pressure and the residue was purified by column chromatography.

(1*S*,5*R*)-3-Bromo-4-(2-phenylethynyl)-8-oxabicyclo[3.2.1]octa-3,6-dien-2-one (4d): Compound **2** or **3a** (100 mg) was subjected to the coupling conditions using phenylacetylene. The residue was purified by column chromatography (SiO_2, 10 g) using 15% ethyl acetate in hexanes as eluent to afford **4d** as a yellow oil which solidified upon standing (85 mg, 79% for **2**; 69 mg, 75% for **3a**): R_f = 0.48 (hexane/EtOAc, 2:1). M.p. 86–88 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.59–7.57 (m, 2 H), 7.48–7.44 (m, 1 H), 7.43–7.39 (m, 2 H), 7.01 (ddd, J = 5.6, 2.0, 0.7 Hz, 1 H), 6.58 (dd, J = 5.6, 2.2 Hz, 1 H), 5.35 (d, J = 2.0 Hz, 1 H), 5.20 (dd, J = 2.2, 0.7 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 184.9, 145.7, 140.0, 132.4, 131.0, 130.6, 128.9, 121.6, 120.8, 112.2, 87.2, 84.8, 84.1 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 3054, 2985, 2189, 1698, 1557, 1265, 1194. HRMS: *m/z* 299.9788 (calcd. $C_{15}H_9BrO_2$, 299.9786).

(1*S*,5*R*)-3-Bromo-4-[2-(3,4,5-trimethoxyphenyl)ethynyl]-8-oxabicyclo-[3.2.1]octa-3,6-dien-2-one (4e): Compound **2** or **3a** (100 mg) was subjected to the coupling conditions using (3,4,5-trimethoxyphenyl)acetylene. The residue was purified by column chromatography (SiO_2, 10 g) using 20% ethyl acetate in hexanes as the eluent to afford **4e** as a yellow solid (123 mg, 88% for **2**; 104 mg, 87% for **3a**): R_f = 0.30 (hexane/EtOAc, 2:1). M.p. 145–147 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.01 (dd, J = 5.6, 1.5 Hz, 1 H), 6.79 (s, 2 H), 6.59 (dd, J = 5.6, 2.2 Hz, 1 H), 5.35 (d, J = 2.0 Hz, 1 H), 5.20 (d, J = 2.0 Hz, 1 H), 3.91 (s, 3 H), 3.90 (s, 6 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 184.9, 153.5, 145.6, 139.9, 132.7, 131.0, 128.6, 120.4, 116.4, 112.6, 109.6, 87.2, 84.1, 61.2, 56.4 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 2940, 2184, 1696, 1575, 1501, 1238, 1130. HRMS: *m/z* 390.0095 (calcd. $C_{18}H_{15}BrO_5$, 390.0103).

(1*S*,5*R*)-3-Bromo-4-vinyl-8-oxabicyclo[3.2.1]octa-3,6-dien-2-one (4f): To a 10 mL round-bottomed flask was added either **2** (100 mg, 0.36 mmol) or **3a** (100 mg. 0.31 mmol). DMF (2 mL) was added, followed by $Pd(PhCN)_2Cl_2$ (14 mg, 0.036 mmol for **2**; 12 mg, 0.031 mmol for **3a**) and triphenylarsane (22 mg, 0.072 mmol for **2**; 14 mg, 0.061 mmol for **3a**). The reaction mixture was stirred at 25 °C until all material was dissolved. Vinyltributyltin (0.115 mL, 0.39 mmol for **2**; 0.098 mL, 0.34 mmol for **3a**) was added and the solution stirred at 25 °C for 1 hour. The solvent was removed under reduced pressure and the residue was purified by column chromatography (SiO_2, 10 g) using pentane (100 mL), followed by 10% ethyl acetate in hexanes as eluent to afford **4f** as a yellow solid (34 mg, 42% for **2**; 21 mg, 30% for **3a**): R_f = 0.44 (hexane/EtOAc, 2:1). M.p. 63–65 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.92–6.85 (m, 2 H), 6.53 (dd, J = 5.9, 2.2 Hz, 1 H), 5.79 (d, J = 17.6 Hz, 1 H), 5.73 (d, J = 11.2 Hz, 1 H), 5.59 (d, J = 2.0 Hz, 1 H), 5.17 (dd, J = 2.2, 0.7 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 186.6, 156.1, 139.5, 133.3, 131.4, 124.6, 117.5, 87.2, 80.3 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 3054, 2986, 1697, 1545, 1421, 1265. HRMS: *m/z* 225.9630 (calcd. $C_9H_7BrO_2$, 225.9629).

(1*S*,5*R*)-3,4-Bis(2-phenylethynyl)-8-oxabicyclo[3.2.1]octa-3,6-dien-2-one (5): To a 10 mL round-bottomed flask was added **4d** (205 mg, 0.68 mmol). Acetonitrile (3 mL) was added and the reaction mixture stirred at 25 °C until all material was dissolved. Triethylamine (3 mL) was added followed by copper(I) iodide (9.1 mg, 0.048 mmol) and $Pd(dppf)_2Cl_2$ (39 mg, 0.048 mmol). Phenylacetylene (0.083 mL, 0.75 mmol) was then added and the solution stirred under argon for 1 hour. The solvent was removed under reduced pressure and the residue was purified by column chromatography (SiO_2, 10 g) using 20% ethyl acetate in hexanes as the eluent to afford **5** as a yellow oil (132 mg, 60%): R_f = 0.44 (hexane/EtOAc, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.57–7.55 (m, 4 H), 7.45–7.39 (m, 3 H), 7.36–7.35 (m, 3 H), 6.98 (dd, J = 5.6, 2.0 Hz, 1 H), 6.57 (dd, J = 5.8, 2.2 Hz, 1 H), 5.34 (d, J = 2.0 Hz, 1 H), 5.08 (d, J = 2.2 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 188.16, 146.0, 139.6, 132.3, 132.1, 130.8, 130.4, 129.2, 128.9, 128.6, 122.8, 122.0, 120.5, 112.2, 99.3, 87.1, 85.4, 83.5, 82.9 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 3063, 2980, 2179, 1704, 1543, 1491, 1443, 1364, 1209, 1063. HRMS: *m/z* 322.1000 (calcd. $C_{23}H_{14}O_2$, 322.0994).

(1*S*,2*R*,5*R*)-3-Bromo-4-(2-phenylethynyl)-8-oxabicyclo[3.2.1]octa-3,6-dien-2-ol (6): To a 25 mL round-bottomed flask was added **4d** (200 mg, 0.66 mmol). Methanol (13 mL, 0.05 M) was added and the reaction mixture was stirred at 25 °C until all material was dissolved. Cerium chloride (247 mg, 0.66 mmol) was added and stirred to dissolve. The solution was cooled to –10 °C and sodium borohydride (28 mg, 0.73 mmol) was added. The solution was stirred at –10 °C for 1 hour and quenched with water (2.0 mL). The solution was warmed to room temperature and the solvent removed. The residue was taken up in ethyl acetate (10 mL) and washed with water (5 mL). The aqueous layer was extracted with ethyl acetate (3 × 10 mL). The combined organics were washed with brine, dried with sodium sulfate and concentrated. The residue was purified by column chromatography (SiO_2, 20 g) using 20% ethyl acetate in hexanes as eluent to afford **6** as a colorless oil (170 mg, 85%): R_f = 0.30 (hexane/EtOAc, 2:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.52–7.50 (m, 2 H), 7.39–7.34 (m, 3 H), 6.90 (dd, 6.1, 1.7 Hz, 1 H), 6.24 (dd, J = 6.1, 2.0 Hz, 1 H), 5.26 (dd, J = 6.1,

1.7 Hz, 1 H), 4.92 (d, *J* = 1.7 Hz, 1 H), 4.60 (t, *J* = 5.9 Hz, 1 H), 2.16 (d, *J* = 5.4 Hz, 1 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 141.1, 131.9, 131.5, 129.6, 129.4, 129.3, 128.6, 122.6, 100.0, 84.7, 81.8, 81.1, 68.0 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 3418, 3080, 2967, 2916, 2200, 1307, 1052. HRMS: *m*/*z* 301.9945 (calcud $C_{15}H_{11}BrO_2$, 301.9942).

(1*S*,2*R*,5*R*)-3-Bromo-4-(2-phenylethynyl)-2-triethylsilyloxy-8-oxabicyclo[3.2.1]octa-3,6-diene (6a): To a 10 mL round-bottomed flask was added **6** (130 mg, 0.43 mmol). Dichloromethane (2 mL) was added and the reaction mixture was stirred at 25 °C until all material was dissolved. The solution was cooled to 0 °C and 2,6-lutidine (0.100 mL, 0.86 mmol) was added followed by TESOTf (0.145 mL, 0.64 mmol). The solution was warmed to room temperature overnight. Saturated sodium hydrogen carbonate (5 mL) was added and the layers separated. The aqueous layer was extracted with dichloromethane (3 × 10 mL). The combined organics were dried with sodium sulfate and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, 20 g) using 5% ethyl acetate in hexanes as eluent to afford **6a** as a colorless oil (143 mg, 80%): R_f = 0.52 (hexane/EtOAc, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.50–7.47 (m, 2 H), 7.37–7.32 (m, 3 H), 6.86 (dd, *J* = 5.9, 1.5 Hz, 1 H), 6.20 (dd, *J* = 5.9, 1.7 Hz, 1 H), 5.10 (dd, *J* = 6.1, 1.5 Hz, 1 H), 4.87 (d, *J* = 1.7 Hz, 1 H), 4.60 (d, *J* = 6.1 Hz, 1 H), 1.03 (t, *J* = 7.8 Hz, 9 H), 0.79–0.67 (m, 6 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 140.3, 131.8, 131.1, 130.0, 130.0, 129.0, 128.9, 122.9, 99.3, 85.2, 82.8, 81.7, 68.6, 7.1, 5.1 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 2956, 2911, 2876, 2201, 1339, 1238, 1117. HRMS: *m*/*z* 416.0814 (calcd. $C_{21}H_{25}BrO_2Si$, 416.0807).

(1*S*,2*R*,5*R*)-4-(2-Phenylethynyl)-2-triethylsilyloxy-8-oxabicyclo-[3.2.1]octa-3,6-diene (8): To a dry screw-cap vial, was added **6a** (89 mg, 0.21 mmol). THF (1 mL) was added and the solution was cooled to –78 °C. *n*-Butyllithium (0.174 mL, 0.28 mmol, 1.6 M in pentane) was added and the solution stirred at –78 °C for 1 hour. Acetic acid (0.049 mL, 0.85 mmol) was added and the solution warmed to room temperature. The solution was stirred at 25 °C for 15 min and then diluted with diethyl ether (10 mL). The solution was washed with saturated sodium hydrogen carbonate (5 mL). The aqueous layer was extracted with diethyl ether (2 × 10 mL). The combined organics were washed with brine (5 mL), dried with sodium sulfate and concentrated. The residue was purified by column chromatography (SiO_2, 10 g) using 10% ethyl acetate in hexanes as eluent to afford **8** as a yellow oil that solidified upon standing (65 mg, 90%): R_f = 0.44 (hexane/EtOAc, 2:1). M.p. 80–82 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.46–7.43 (m, 2 H), 7.38–7.34 (m, 3 H), 6.97 (dd, *J* = 5.9, 1.7 Hz, 1 H), 6.16 (dd, *J* = 6.1, 1.7 Hz, 1 H), 5.15 (dd, *J* = 6.1, 1.7 Hz, 1 H), 4.69 (d, *J* = 1.2 Hz, 1 H), 4.51 (dd, *J* = 6.3, 10.0 Hz, 1 H), 1.3 (d, *J* = 10.0 Hz, 1 H), 1.01–0.98 (m, 9 H), 0.92–0.79 (m, 6 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 143.4, 142.8, 139.3, 131.4, 129.4, 128.8, 128.7, 123.2, 98.1, 87.6, 81.8, 81.7, 64.2, 7.9, 3.8 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 2952, 2907, 2873, 2193, 1488, 1236, 1041. HRMS: *m*/*z* 338.1704 (calcd. $C_{21}H_{26}O_2Si$, 338.1702).

(1*S*,2*R*,5*R*)-3-Methyl-4-(2-phenylethynyl)-2-triethylsilyloxy-8-oxabicyclo[3.2.1]octa-3,6-diene (9): To a dry screw-cap vial, was added **6a** (95 mg, 0.23 mmol). THF (1 mL) was added and the solution cooled to –78 °C. *n*-Butyllithium (0.185 mL, 0.30 mmol, 1.6 M in pentane) was added and the solution stirred at –78 °C for 1 hour. Methyl iodide (0.060 mL, 0.91 mmol) was added and the solution warmed to room temperature overnight. The solution was diluted with diethyl ether (10 mL) and washed with water (5 mL). The aqueous layer was extracted with diethyl ether (2 × 10 mL). The combined organics were washed with brine (5 mL), dried with sodium sulfate and concentrated. The residue was purified by column chromatography (SiO_2, 10 g) using 10% ethyl acetate in hexanes as eluent to afford **9** as a yellow oil (64 mg, 80%): R_f = 0.42 (hexane/EtOAc, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.45–7.42 (m, 2 H), 7.37–7.33 (m, 3 H), 6.83 (dd, *J* = 6.1, 1.7 Hz, 1 H), 6.12 (dd, *J* = 6.1, 2.0 Hz, 1 H), 5.33 (dd, *J* = 5.6, 1.7 Hz, 1 H), 4.68 (s, 1 H), 4.09 (d, *J* = 5.6 Hz, 1 H), 3.44 (s, 3 H), 0.98 (t, *J* = 7.8 Hz, 9 H), 0.88–0.72 (m, 6 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 142.5, 140.2, 138.0, 131.4, 129.2, 128.6, 123.5, 97.3, 87.9, 81.6, 79.6, 72.5, 57.5, 7.8, 3.8 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 2952, 2873, 2820, 2200, 1458, 1314, 1190, 1100. HRMS: *m*/*z* 352.1866 (calcd. $C_{22}H_{28}O_2Si$, 352.1859).

(1*S*,5*R*)-3,4-Bis[2-(trimethylsilyl)ethynyl]-8-oxabicyclo[3.2.1]octa-3,6-dien-2-one (10): To a 20 mL round-bottomed flask was added compound **2** (500 mg, 1.79 mmol). Acetonitrile (9 mL) was added and the reaction mixture stirred at 25 °C until all material was dissolved. Triethylamine (9 mL) was added followed by copper(I) iodide (48 mg, 0.25 mmol) and $Pd(dppf)_2Cl_2$ (205 mg, 0.25 mmol). Trimethylsilylacetylene (0.56 mL, 3.93 mmol) was then added and the solution stirred under argon for 1 hour. The solvent was removed under reduced pressure and the residue was purified by column chromatography (SiO_2, 50 g) using 10% ethyl acetate in hexanes as the eluent to afford **10** as a yellow oil (350 mg, 62%): R_f = 0.44 (hexane/EtOAc, 9:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.89 (ddd, *J* = 5.6, 2.0, 0.7 Hz, 1 H), 6.47 (ddd, *J* = 5.6, 2.2, 0.7 Hz, 1 H), 5.15 (dd, *J* = 2.0, 0.5 Hz, 1 H), 4.98 (dd, *J* = 2.2, 0.7 Hz, 1 H), 0.28 (s, 9 H), 0.23 (s, 9 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 187.9, 147.0, 139.5, 130.6, 121.3, 120.0, 105.6, 99.1, 97.5, 87.0, 82.7, 0.08, –0.18 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 2962, 2901, 2254, 2159, 1707, 1540, 1332, 1300, 1252, 1064. HRMS: *m*/*z* 314.1161 (calcd. $C_{17}H_{22}O_2Si_2$, 314.1158).

Methyl 3-[(1*R*,4*R*,5*S*)-3-Bromo-4-triethylsilyloxy-8-oxabicyclo[3.2.1]octa-2,6-dien-2-yl]propanoate (11b): To a flame-dried 50 mL round-bottomed flask, was added compound **3f** (1.10 g, 3.83 mmol). Methanol (30 mL) was added followed by cerium chloride (1.43 g, 3.83 mmol). The solution was cooled to 0 °C. Sodium borohydride (160 mg, 4.21 mmol) was added and the solution stirred at 0 °C for 30 minutes. The reaction was quenched by addition of water (5.0 mL). The solution was warmed to room temperature and the solvent removed. The residue was taken up in ethyl acetate (30 mL) and washed with water (10 mL). The aqueous layer was extracted with ethyl acetate (3 × 20 mL). The combined organics were washed with brine, dried with sodium sulfate and concentrated. The residue was purified by column chromatography (SiO_2, 50 g) using 33% ethyl acetate in hexanes as eluent to afford the alcohol **11a** as a colorless oil (982 mg, 88%): R_f = 0.18 (hexane/EtOAc, 2:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.71 (dd, *J* = 6.1, 1.7 Hz, 1 H), 6.18 (dd, *J* = 6.1, 2.0 Hz, 1 H), 5.15 (dd, *J* = 6.1, 2.0 Hz, 1 H), 4.71 (d, *J* = 1.5 Hz, 1 H), 4.44 (d, *J* = 5.6 Hz, 1 H), 3.70 (s, 3 H), 2.55–2.43 (m, 5 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.0, 144.9, 140.8, 129.4, 122.6, 81.9, 81.3, 68.1, 52.1, 31.5, 28.4 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 3436, 2954, 1737, 1640, 1439, 1367, 1305, 1199, 1055. HRMS: *m*/*z* 288.0005 (calcd. $C_{11}H_{13}BrO_4$, 287.9997).

To a 25 mL round-bottomed flask was added **11a** (982 mg, 3.40 mmol). Dichloromethane (11 mL) was added and the reaction mixture was stirred at 25 °C until all material was dissolved. The solution was cooled to 0 °C and 2,6-lutidine (0.947 mL, 8.15 mmol) was added followed by TESOTf (0.922 mL, 4.08 mmol). The solution was warmed to room temperature overnight. Saturated sodium hydrogen carbonate (5 mL) was added and the layers separated. The aqueous layer was extracted with dichloromethane

(3 × 10 mL). The combined organics were dried with sodium sulfate and concentrated under reduced pressure. The residue was purified by column chromatography (SiO_2, 40 g) using 5% ethyl acetate in hexanes as eluent to afford compoud **11b** as a colorless oil (1.10 g, 80%): R_f = 0.32 (hexane/EtOAc, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.71 (dd, J = 6.1, 1.7 Hz, 1 H), 6.13 (dd, J = 6.1, 2.0 Hz, 1 H), 5.02 (dd, J = 5.9, 2.0 Hz, 1 H), 4.69 (d, J = 1.7 Hz, 1 H), 4.48 (d, J = 5.9 Hz, 1 H), 3.71 (s, 3 H), 2.61–2.42 (m, 4 H), 1.03–1.00 (m, 9 H), 0.75–0.68 (m, 6 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 173.1, 144.5, 140.1, 129.7, 122.6, 82.9, 81.1, 68.8, 52.0, 31.5, 28.6, 7.1, 5.0 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 2954, 2877, 1739, 1438, 1241, 1117. HRMS: m/z 402.0852 (calcd. $C_{17}H_{27}BrO_4Si$, 402.0862).

(1*S*,2*S*,8*R*)-2-Triethylsilyloxy-11-oxatricyclo[6.2.1.0^{3,7}]undeca-3(7),9-dien-4-ol (13a/b): To a 50 mL round-bottomed flask was added lithium aluminum hydride (89 mg, 2.25 mmol). THF (15 mL) was added and the reaction mixture was stirred and cooled to 0 °C. Compound **11b** (860 mg, 2.13 mmol) in THF (5 mL) was added dropwise. After complete addition the reaction was warmed to 25 °C and stirred for 30 minutes. Water (0.500 mL) was added. The solids were filtered off and washed with ethyl acetate (4 × 25 mL). The combined organics were washed with water (10 mL) and brine 10 mL). The organics were dried with anhydrous sodium sulfate, filtered and concentrated to give the crude alcohol as a colorless oil (720 mg, 90%). The crude alcohol was dissolved in dichloromethane (20 mL). Dess–Martin periodinane (1.22 g, 2.88 mmol) was added and the solution stirred at 25 °C for 1 hour. Saturated sodium hydrogen carbonate/saturated sodium thiosulfate (10 mL, 1:1, v/v) was added and the solution stirred for 1 hour. The layers were separated and the organics washed with saturated sodium hydrogen carbonate (10 mL) and water (10 mL). The organics were washed with brine, dried with anhydrous sodium sulfate, and concentrated to give the crude aldehyde **12** as a colorless oil (957 mg, 89%): R_f = 0.18 (hexane/EtOAc, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.81–9.80 (m, 1 H), 6.70 (dd, J = 5.9, 1.7 Hz, 1 H), 6.13 (dd, J = 6.1, 2.0 Hz, 1 H), 5.01 (dd, J = 6.1, 2.0 Hz, 1 H), 4.67 (d, J = 1.7 Hz, 1 H), 4.47 (d, J = 5.9 Hz, 1 H), 2.67–2.64 (m, 2 H), 2.58–2.53 (m, 1 H), 2.46–2.40 (m, 1 H), 1.00 (t, J = 7.8 Hz, 9 H), 0.72–0.67 (m, 6 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 200.9, 144.6, 140.0, 129.7, 122.5, 82.9, 81.1, 68.8, 41.4, 25.8, 7.0, 5.0 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 2955, 2876, 1725, 1459, 1412, 1343, 1240, 1120.

In a glove box was weighed chromium(II) chloride (567 mg, 4.61 mmol) and nickel(II) chloride (6.0 mg, 0.08 mmol). DMF (10.0 mL) was added and the solution stirred at 25 °C for 1 hour. A solution of **12** (200 mg, 0.536 mmol) in DMF (3.0 mL) was added and the flask placed into a preheated oil bath at 45 °C. The solution was heated at 45 °C for 18 hours and cooled to 25 °C. The solution was diluted with hexanes/ethyl acetate (15 mL, 1:1, v:v) and D/L-serinate (10 mL, 1.0 M in satd. $NaHCO_3$) was added dropwise. The reaction was stirred vigorously for 30 min. The layers were separated and the aqueous layer was extracted with hexanes/ethyl acetate (3 × 15 mL, 1:1, v:v). The combined organics were washed with water (10 mL) and brine (10 mL). The organics were dried with anhydrous sodium sulfate, filtered, and concentrated. The residue was purified by column chromatography (SiO_2, 10 g) using 20% ethyl acetate in hexanes as eluent to afford **13a** (13 mg, 8%) and **13b** (105 mg, 67%) as colorless oils: **13a:** R_f = 0.24 (hexane/EtOAc, 4:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.78 (dd, J = 6.1, 1.7 Hz, 1 H), 6.03 (dd, J = 6.1, 2.0 Hz, 1 H), 5.05 (dd, J = 5.9, 2.0 Hz, 1 H), 4.83– 4.81 (m, 1 H), 4.79 (d, J = 6.6 Hz, 1 H), 4.77 (s, 1 H), 2.60–2.54 (m, 1 H), 2.40–2.34 (m, 1 H), 2.12–2.05 (m, 1 H), 1.85–1.80 (m, 1 H), 1.04–1.00 (m, 9 H), 0.74–0.68 (m, 6 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.4, 140.9, 131.9, 128.6, 81.7, 78.3, 78.0, 67.8, 32.3, 30.6, 6.8, 4.9 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 3552, 2953, 2876, 1238, 1077, 1041, 1004. HRMS: m/z 294.1656 (calculated $C_{16}H_{26}O_3Si$, 294.1651). **13b:** R_f = 0.26 (hexane/EtOAc, 2:1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 6.70 (dd, J = 6.1, 1.7 Hz, 1 H), 6.06 (dd, J = 6.1, 2.0 Hz, 1 H), 5.05 (dd, J = 6.1, 2.0 Hz, 1 H), 4.79 (d, J = 6.1 Hz, 1 H), 4.72–4.71 (m, 2 H), 2.65–2.56 (m, 1 H), 2.32–2.24 (m, 2 H), 1.73–1.67 (m, 1 H), 1.00 (t, J = 8.0 Hz, 9 H), 0.72–0.67 (m, 6 H) ppm. ^{13}C NMR (125 MHz, $CDCl_3$): δ = 148.0, 140.2, 135.8, 129.3, 81.4, 78.2, 76.5, 64.0, 33.2, 30.6, 7.0, 4.9 ppm. IR (thin film, cm^{-1}): $\tilde{\nu}$ = 3421, 2953, 2876, 1037. HRMS: m/z 294.1650 (calcd. $C_{16}H_{26}O_3Si$, 294.1651).

Supporting Information: Copies of ^{1}H and ^{13}C spectra for all new compounds are provided and are available via the www; see also the footnote on the first page of this article.

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