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Ready Access to the Echinopines Skeleton via Gold(I)-Catalyzed Alkoxycyclizations of Enynes

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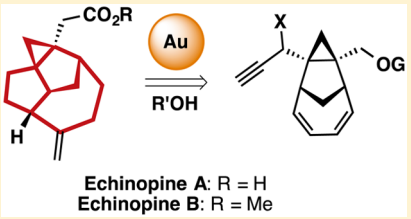
Supporting Information

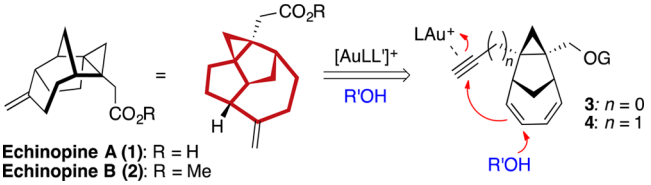
ABSTRACT: The [3,5,5,7] tetracyclic skeleton of echinopines has been stereoselectively accessed through a gold(I)-catalyzed alkoxycyclization of cyclopropyl-tethered 1,6-enynes. The key bicyclo[4.2.1]nonane core of the enyne precursors was readily assembled by means of a Co-catalyzed [6 + 2] cycloaddition. Furthermore, the attempted alkoxycyclization of 1,5-enyne substrates revealed an uncovered cyclopropyl rearrangement that gives rise to [3,6,5,7] tetracyclic structures.



INTRODUCTION

Echinopines A and B (**1** and **2**) were isolated in 2008 from the roots of *Echinops spinosus* and feature an unprecedented [3,5,5,7]-membered-ring tetracyclic skeleton (Scheme 1), which probably originates biosynthetically from a guaiane precursor.[1] This complex carbon framework holds five contiguous stereogenic centers, two of them being adjacent quaternary stereocenters. Despite the fact that no biological activity has been reported to date for **1** and **2**, the unique architecture of these sesquiterpenes has constituted an appealing challenge for the synthetic community and several syntheses of echinopines have been accomplished to date.[2−7] The key feature in all these syntheses is the establishment of the unique [3,5,5,7] skeleton, and to this aim conceptually very different ring-forming sequences have been successfully established.[8] However, the assembly of the complex polycyclic framework of the echinopines skeleton is not easily addressed by conventional methods, as evidenced by the lengthy existing syntheses, and it is in most of the cases delayed to one of the last steps of the sequence.

Scheme 1. Strategy for the Gold-Catalyzed Synthesis of the Skeleton of Echinopines

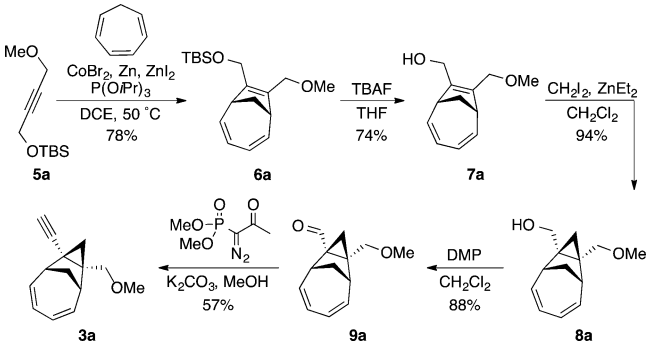


Gold(I) catalysis constitutes a powerful tool for the construction of complex polycyclic architectures from relatively simple enyne substrates under mild reaction conditions.[9−12] A concise synthesis of the complex polycyclic framework of the echinopines skeleton could easily provide access to structural analogues for further evaluation of their biological properties. In this context, we envisioned a gold(I)-catalyzed alkoxycyclization of cyclopropyl-tethered tricyclic 1,5- (**3**) or 1,6-enynes (**4**) as the key step for the ready access to the tetracyclic skeleton of echinopines via 5-endo or 5-exo cyclization, respectively (Scheme 1).[13−16] This transformation would stereoselectively lead to echinopine-based tetracyclic products bearing different groups suited for further functionalization.

RESULTS AND DISCUSSION

Our approach for the synthesis of tricyclic enynes **3** and **4** relied on a cobalt-catalyzed [6 + 2] cycloaddition between cycloheptatriene and an internal alkyne as the key step to build the bicyclo[4.2.1]nonane core.[17,18] Thus, orthogonally protected diol **5a** afforded cycloadduct **6a**, which upon monodeprotection and cyclopropanation of the tetrasubstituted olefin from the less sterically hindered face gave rise to tricyclic compound **8a** (Scheme 2). Oxidation of the primary alcohol and subsequent homologation employing the Ohira−Bestmann reagent provided 1,5-enyne **3a**.

Scheme 2. Synthesis of Tricyclic 1,5-Enyne 3a



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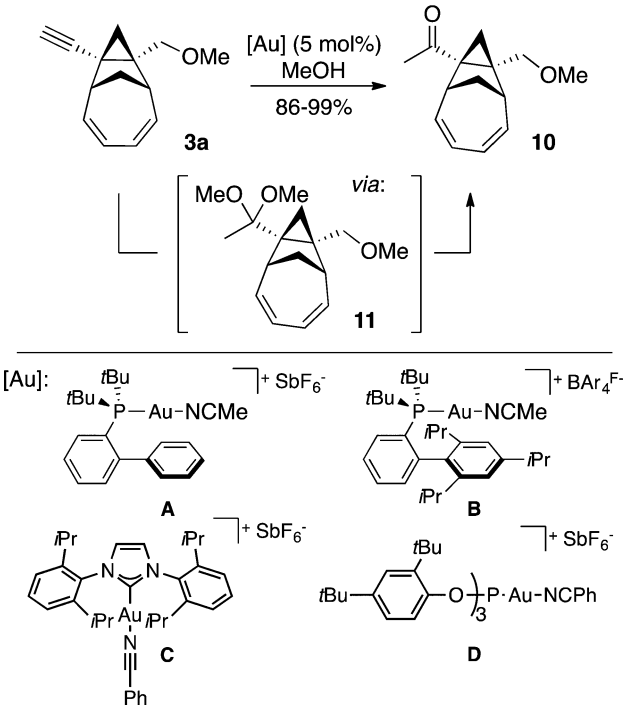
Initial attempts to perform the alkoxycyclization of **3a** with methanol as the external nucleophile in the presence of different cationic gold(I) complexes **A**–**D** only provided methyl ketone **10** as a result of the formal hydration of the terminal alkyne (Scheme 3).[19−22] Moreover, when the reaction

Scheme 3. Formal Hydration of 3a

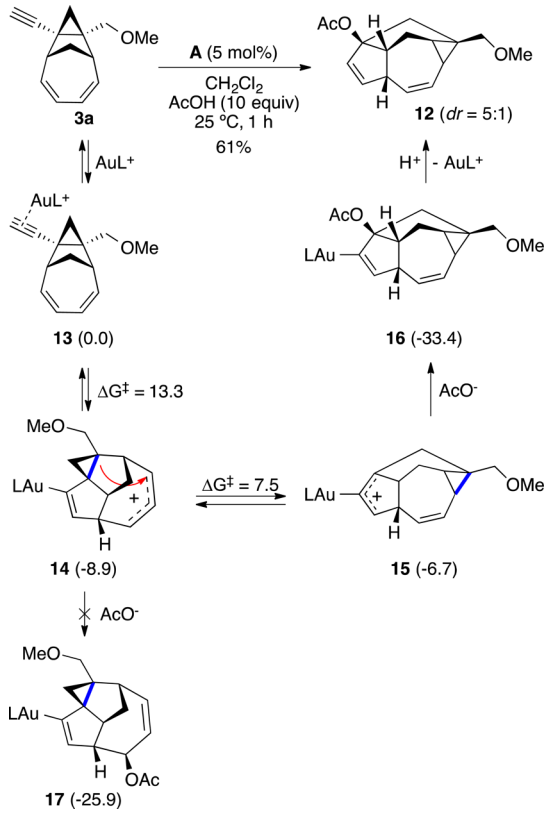


was performed under strictly anhydrous conditions, the corresponding dimethyl acetal **11** could be isolated, which rapidly decomposed to **10** under ambient conditions, thus demonstrating that the addition of methanol to the terminal alkyne of **3a** is favored over the attack of the alkene moiety. Similar results were obtained when other alcohols were employed as the external nucleophiles.

The use of carbonucleophiles such as indole, 1,3-diketones, and electron-rich benzenes only resulted in the recovery of unreacted **3a**. Nevertheless, when the reaction of **3a** was performed with commercially available gold(I) complex **A** in the presence of acetic acid, complete conversion of **3a** was achieved in 1 h, leading to the formation of rearranged product **12** in up to 61% yield (Scheme 4). A closer mechanistic inspection of this transformation suggested that the gold(I)-catalyzed reaction initially forms intermediate **14** that rearranges to form allyl cation **15**, which is trapped by acetic acid. DFT calculations indicated that the formation of intermediate **16** that leads to **12** is thermodynamically favored over the formation of **17**, which is predicted to be the driving force for the rearrangement to take place. This result further illustrates the influence of the cyclopropane functionality on the reaction pathways followed in the gold(I)-catalyzed cyclizations of cyclopropane-tethered 1,5-enynes[23] and underscores the propensity of the strained tetracyclic system of echinopines to undergo rearrangements.[6]

In order to unequivocally ensure the structure of **12**, the acetate moiety was cleaved to form alcohol **18**, which was converted into the corresponding crystalline *p*-nitrobenzoate derivative **19**, whose structure was confirmed by X-ray

Scheme 4. Gold-Catalyzed Rearrangement of 3a[a]



[a]Values in parentheses correspond to relative free energies in kcal mol^{-1} (M06/6-31G(d) (C, H, P, O) and SDD (Au), solvent = CH_2Cl_2). L = PMe_3.

diffraction (Scheme 5).[24] In addition, a related system having one of the double bonds reduced was also examined with the aim of promoting a rearrangement toward the echinopine skeleton on the basis of the higher stability of carbocation **24** over **22** predicted by DFT calculations. Thus, **18** could be selectively hydrogenated in the presence of Crabtree's catalyst to give **20**, which was converted into tertiary carbocation **22** via triflate **21**. Nonetheless, the rearranged product was not observed and only nonrearranged elimination product **23** was isolated under different reaction conditions.

The synthesis of the homologous 1,6-enyne **4a** commenced with the cobalt-catalyzed [6 + 2] cycloaddition between cycloheptatriene and alkyne **25** followed by treatment with *N*-iodosuccinimide, which afforded vinyl iodide **27** (Scheme 6). Kumada cross-coupling of **27** with (3-(trimethylsilyl)prop-2-yn-1-yl)magnesium bromide furnished **28**, which was treated with HF·py to give allylic alcohol **29**. Cyclopropanation of the tetrasubstituted olefin followed by deprotection of the terminal alkyne and protection of the primary alcohol gave rise to tricyclic 1,6-enyne **4a**. However, all attempts to perform the alkoxycyclization of **4a** in the presence of different gold(I) complexes provided only traces of the cyclized tetracyclic product and resulted in the formation of methyl ketone **31** as the major product.

Aldehydes **9a**,**b**[25] were next employed as the platform to access a series of tricyclic 1,6-enynes featuring different functionalities at the propargylic position. Thus, the addition of ethynylmagnesium bromide provided **4b**,**c** as single diastereoisomers and their alkoxycyclization was investigated

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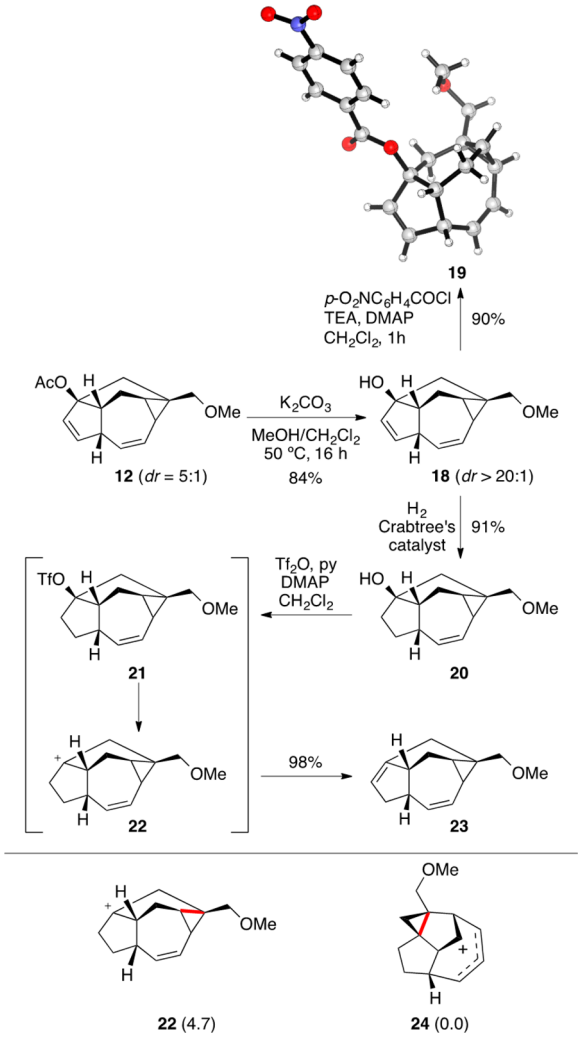
Scheme 5. Synthesis of 23 from Acetate 12 and CYLview Depiction of the X-ray Crystal Structure of 19[a]



[a]Values in parentheses correspond to relative free energies in kcal mol^{-1} (M06/6-31G(d), solvent = CH_2Cl_2).

using methanol as the external nucleophile in the presence of a series of gold(I) complexes spanning a range of electrophilicities. The desired alkoxycyclization products could only be detected from the reactions carried out in the presence of phosphine–gold(I) complexes, whereas gold(I) complexes bearing NHC and phosphite ligands gave complex mixtures.[26] Cationic gold(I) complex **B** provided the best results, and the use of the alcohol as the solvent proved to be optimal for the alkoxycyclization of enynes **4b,c** to afford regio- and stereoselectively tetracyclic products **32a–c**, which feature the [3,5,5,7] tetracyclic skeleton of echinopines (Scheme 7). While the reaction of **4b** with methanol provided **32a** as a single regioisomer, the analogous reaction of **4c** gave rise to a 5:1 mixture of regioisomers. Nonetheless, changing the external nucleophile from methanol to allyl alcohol in the reaction of **4c** resulted in the exclusive formation of **32c** as the sole isomer. The structure of tetracycles **32a–c** could be confirmed from the X-ray crystal structure of **32a**.[24]

Interestingly, the propargylic alcohol of enynes **4b,c** was substituted by a second molecule of alcohol in the gold(I)-catalyzed cyclization process. In order to elucidate the order of events in this transformation, the closely related system **34** in which the 1,3-diene had been reduced to the corresponding alkane was submitted to the optimized reaction conditions for the gold(I)-catalyzed alkoxycyclization (Scheme 8). However, after 2 h only hydroxyketone **35** and unreacted **34** were detected from the crude mixture and no substitution of the propargylic alcohol was observed.[26] This result supports a catalytic cycle in which the propargylic alcohol in **4b,c** is eliminated after the cyclization of the enyne by the attack of a molecule of methanol to intermediate **36**, which generates α,β-unsaturated gold(I) carbene intermediate **37**.[27] The attack of a second molecule of alcohol to **37** forms **38**, which releases tetracycles **32** by protodeauration (Scheme 9).

Ketoenynes **4d,e** were also prepared by direct oxidation of **4b,c**, and their alkoxycyclization under the optimized reaction conditions provided mixtures of the two possible regioisomeric products **39a′,b′** and **39a″,b″**,[28] which could be separated by preparative chromatography (Scheme 10). Water could also be used as the external nucleophile to afford inseparable mixtures of regioisomeric allylic alcohols **39c′,d′/39c″,d″** in moderate yields.

CONCLUSION

In summary, the [3,5,5,7] tetracyclic core of echinopines can be readily accessed through the gold(I)-catalyzed alkoxycyclization of tricyclic cyclopropyl-tethered 1,6-enynes bearing an O functionality at the propargylic position, giving access to functionalized echinopine analogues as single stereoisomers. Furthermore, the cyclization of 1,5-enyne **3a** uncovered an unexpected migration of the cyclopropane functionality, thus providing access to the complex natural-product-like [3,6,5,7] tetracycle **12**.

EXPERIMENTAL SECTION

General Remarks. Chemicals and solvents for chromatography were used as received. Solvents used in reactions under an inert atmosphere were dried by passing through an activated alumina column on a solvent purification system. Analytical thin-layer chromatography was carried out using TLC-aluminum sheets with 0.2 mm of silica gel (Merck FG254) with UV light as the visualizing agent or an acidic solution of vanillin in ethanol as the developing agent. Purifications by chromatography were carried out using flash grade silica gel (SDS Chromatogel 60 ACC, 40–60 mm). Preparative TLC was performed on 20 cm × 20 cm silica gel plates. Organic solutions were concentrated under reduced pressure on a rotary evaporator. NMR spectra were recorded at 298 K on 300, 400, and 500 MHz devices. ^{1}H and ^{13}C chemical shifts (δ) are given in ppm relative to TMS, and coupling constants (J) in Hz. Mass spectra were recorded employing TOF mass analyzers (ESI, APCI). Melting points were determined by observation of the fusion of the solids placed in a capillary, through a magnifying glass. Crystal structure determinations were carried out using a diffractometer equipped with an APPEX 2 4K CCD area detector, an FR591 rotating anode with Mo Kα radiation, Montel mirrors as the monochromator, and a Kryoflex low temperature device (T = −173 °C). Full-sphere data collection was used with ω and φ scans. Programs used: data collection APEX-2, data reduction Bruker Saint V/.60A, and absorption correction SADABS. Structure solution and refinement: crustal structure solution was achieved using direct methods as implemented in SHELXTL and visualized using the program XP. Missing atoms were subsequently located from difference Fourier synthesis and added to the atom list. Least-squares refinement on F^2 using all measured intensities was carried out using the program SHELXTL. All non-hydrogen atoms were refined including anisotropic displacement parameters.

***tert*-Butyl((4-methoxybut-2-yn-1-yl)oxy)dimethylsilane (5a).** NaH (60% in mineral oil, 1.89 g, 47.2 mmol) was added to a solution of 4-((*tert*-butyldimethylsilyl)oxy)but-2-yn-1-ol[29] (8.60 g, 42.9 mmol)

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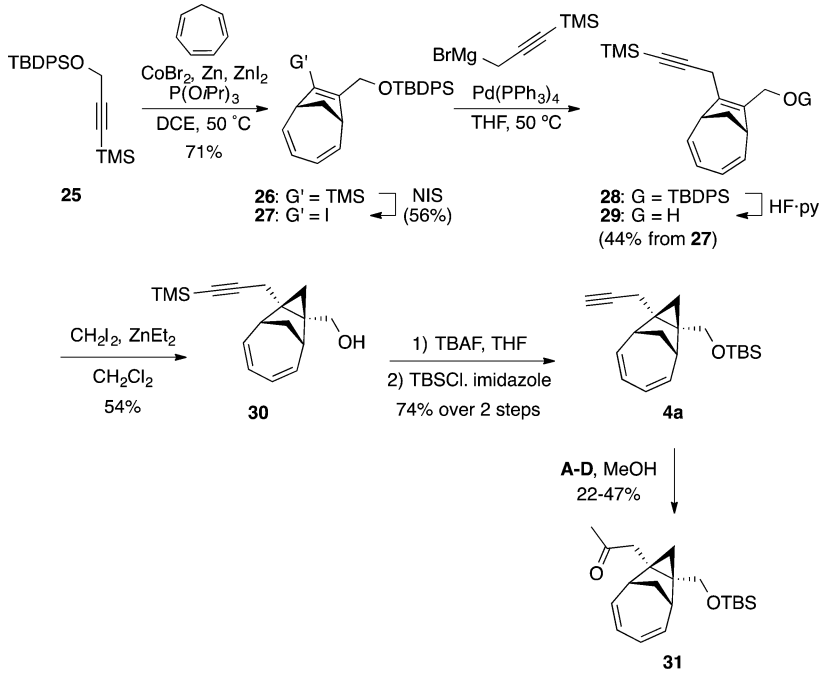
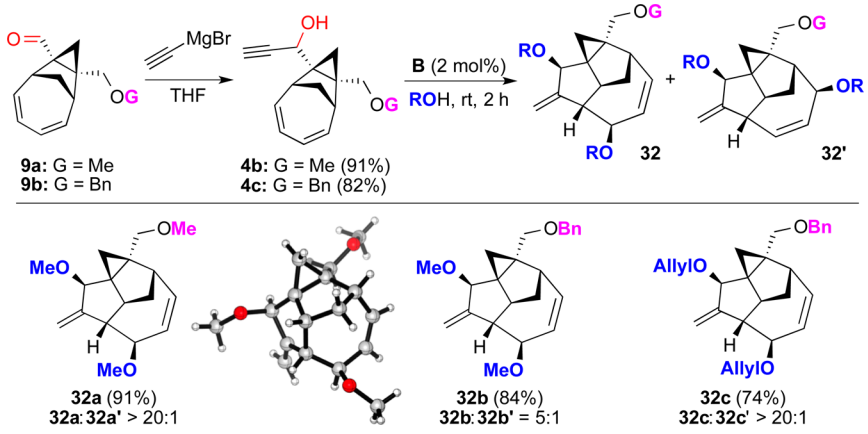
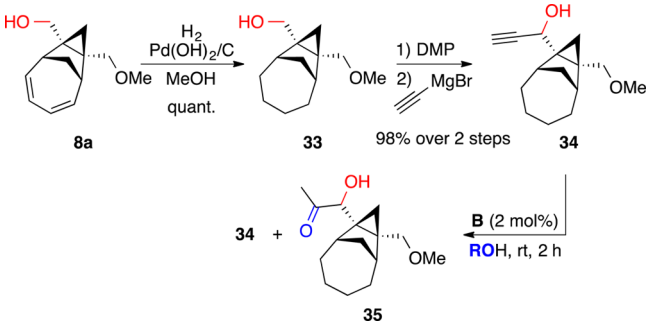
Scheme 6. Synthesis and Formal Hydration of Tricyclic 1,6-Enyne 4a



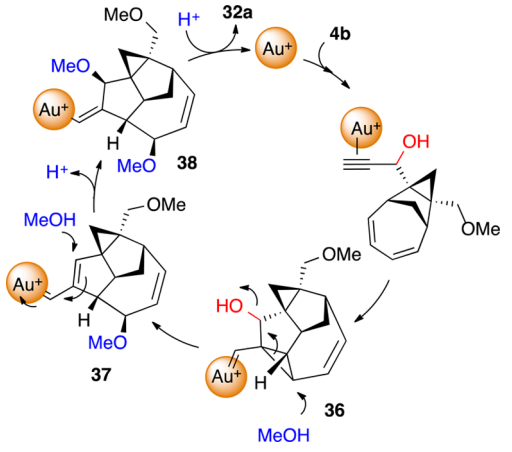
Scheme 7. Synthesis and Alkoxycyclization of 4b,c and CYLview Depiction of the X-ray Crystal Structure of 32a



Scheme 8. Synthesis of 34 and Gold(I)-Catalyzed Reaction under the Optimized Alkoxycyclization Reaction Conditions



Scheme 9. Catalytic Cycle for the Alkoxycyclization of 4b,c



in anhydrous THF (210 mL) under argon at 0 °C. The resulting suspension was stirred for 30 min, and then methyl iodide (3.2 mL, 51.5 mmol) was slowly added. The reaction mixture was warmed to room temperature and then stirred for 1.5 h. After it was diluted with Et_2O (100 mL), the mixture was washed with a saturated solution of NH_4Cl (150 mL) and water (150 mL), the aqueous layers were extracted with Et_2O (2 × 100 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The product was obtained after purification by flash

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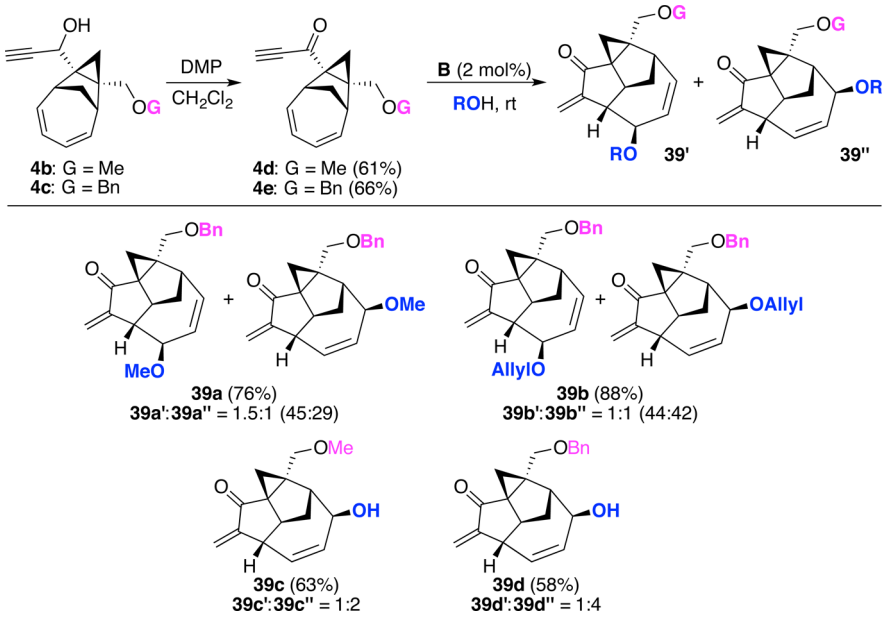
Scheme 10. Synthesis and Alkoxycyclization of 4d,e



chromatography (cyclohexane/EtOAc 95/5) as a clear oil (8.00 g, 37.3 mmol, yield 87%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.38 (t, J = 1.8 Hz, 2H), 4.15 (t, J = 1.8 Hz, 2H), 3.40 (s, 3H), 0.93 (s, 9H), 0.14 (s, 6H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 85.1, 80.6, 60.0, 57.6, 51.7, 25.8, 18.3, −5.2. HRMS (ESI+): m/z calcd for $C_{11}H_{22}NaO_2Si$ [M + Na]$^+$, 237.1281; found, 237.1278.

Synthesis of 6. $CoBr_2$ (306.1 mg, 1.40 mmol), Zn (366.1 mg, 5.60 mmol), and ZnI_2 (1.79 g, 5.60 mmol) were suspended in anhydrous 1,2-dichloroethane (20 mL) under argon. Then $P(OiPr)_3$ (0.69 mL, 2.80 mmol) was added, followed by cycloheptatriene (4.36 mL, 41.98 mmol) and a solution of **5**[30] (27.99 mmol) in dry 1,2-dichloroethane (8 mL). The resulting mixture was stirred at 50 °C for 16 h and then filtered through a pad of Celite and concentrated under reduced pressure. Purification of the resulting crude by flash chromatography (cyclohexane/EtOAc 1/0 to 95/5) afforded compounds **6**.

tert-Butyl(((1R,6S*)-8-(methoxymethyl)bicyclo[4.2.1]nona-2,4,7-trien-7-yl)methoxy)dimethylsilane (**6a**).* Pale yellow oil (6.69 g, 21.83 mmol, yield 78%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.29−6.11 (m, 2H), 5.84−5.74 (m, 2H), 4.35 (d, J = 13.1 Hz, 1H), 4.23 (d, J = 13.1 Hz, 1H), 4.12 (d, J = 12.3 Hz, 1H), 3.92 (d, J = 12.3 Hz, 1H), 3.41 (t, J = 7.1 Hz, 1H), 3.32 (d, J = 7.1 Hz, 1H), 3.27 (s, 3H), 2.29−2.17 (m, 1H), 1.61 (d, J = 11.6 Hz, 1H), 0.93 (s, 9H), 0.08 (s, 3H), 0.07 (s, 3H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 139.8, 139.8, 138.4, 132.1, 124.3, 124.2, 66.2, 57.8, 57.2, 45.4, 44.7, 30.0, 25.9, 18.4, −5.3, −5.4. HRMS (ESI+): m/z calcd for $C_{18}H_{30}NaO_2Si$ [M + Na]$^+$, 329.1907; found, 329.1904.

(((1R,6S*)-8-((Benzyloxy)methyl)bicyclo[4.2.1]nona-2,4,7-trien-7-yl)methoxy) (tert-butyl)dimethylsilane (**6b**).* Colorless oil (5.89 g, 15.39 mmol, yield 55%). ^{1}H NMR (300 MHz, $CDCl_3$): δ 7.40−7.29 (m, 5H), 6.26−6.14 (m, 2H), 5.84−5.74 (m, 2H), 4.48 (d, J = 11.8 Hz, 1H), 4.41 (d, J = 11.9 Hz, 1H), 4.32 (d, J = 13.0 Hz, 1H), 4.20 (d, J = 12.6 Hz, 2H), 4.04 (d, J = 12.4 Hz, 1H), 3.43 (t, J = 7.1 Hz, 1H), 3.37 (t, J = 7.1 Hz, 1H), 2.25 (dt, J = 12.7, 6.7 Hz, 1H), 1.62 (d, J = 11.4 Hz, 1H), 0.92 (s, 9H), 0.07 (s, 3H), 0.07 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 139.9, 139.8, 138.5, 138.5, 132.1, 128.3, 127.8, 127.5, 124.3, 124.3, 71.7, 63.7, 57.2, 45.5, 44.7, 30.0, 25.9, 18.4, −5.3, −5.4. HRMS (ESI+): m/z calcd for $C_{24}H_{34}NaO_2Si$ [M + Na]$^+$, 405.2220; found, 405.2230.

Synthesis of 7. TBAF (1.0 M in THF, 22.8 mL, 22.8 mmol) was added to a solution of **6** (11.4 mmol) in anhydrous THF (200 mL) at 0 °C under argon. The mixture was stirred at room temperature for 2 h and then diluted with Et_2O (100 mL) and washed with saturated solution of NH_4Cl (150 mL) and water (150 mL). The aqueous layers were extracted with Et_2O (2 × 100 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/EtOAc 7/3) afforded products **7**.

((1R,6S*)-8-(Methoxymethyl)bicyclo[4.2.1]nona-2,4,7-trien-7-yl)methanol (**7a**).* Colorless oil (1.62 g, 8.4 mmol, yield 74%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.30−6.14 (m, 2H), 5.89−5.78 (m, 2H), 4.30 (dd, J = 13.2, 6.3 Hz, 1H), 4.24 (dd, J = 13.2, 4.9 Hz, 1H), 4.17 (d, J = 12.6 Hz, 1H), 4.00 (d, J = 12.4 Hz, 1H), 3.38−3.26 (m, 2H), 3.32 (s, 3H), 2.26 (dtt, J = 11.5, 6.8, 1.3 Hz, 1H), 1.95 (t, J = 5.7 Hz, 1H), 1.61 (d, J = 11.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 139.3, 139.3, 137.6, 133.3, 124.6, 125,6, 66.6, 58.1, 57.6, 45.7, 45.7, 30.0. HRMS (ESI+): m/z calcd for $C_{12}H_{16}NaO_2$ [M + Na]$^+$, 215.1043; found, 215.1042.

((1R,6S*)-8-((Benzyloxy)methyl)bicyclo[4.2.1]nona-2,4,7-trien-7-yl)methanol (**7b**).* Colorless oil (2.29 g, 8.55 mmol, yield 75%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.41−7.30 (m, 5H), 6.28−6.16 (m, 2H), 5.86−5.84 (m, 1H), 5.84−5.81 (m, 1H), 4.52 (d, J = 11.8 Hz, 1H), 4.46 (d, J = 11.8 Hz, 1H), 4.31−4.19 (m, 3H), 4.11 (d, J = 12.5 Hz, 1H), 3.35 (t, J = 7.0 Hz, 2H), 2.27 (dtt, J = 11.5, 6.8, 1.2 Hz, 1H), 1.76 (s, 1H), 1.63 (d, J = 11.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 139.4, 139.4, 138.1, 137.7, 133.5, 128.4, 127.8, 127.7, 124.6, 124.6, 72.2, 63.9, 57.5, 45.7, 45.7, 30.0. HRMS (ESI+): m/z calcd for $C_{18}H_{20}NaO_2$ [M + Na]$^+$, 291.1356; found, 291.1365.

Synthesis of 8. Diiodomethane (0.61 mL, 7.57 mmol) and $ZnEt_2$ (1.0 M in hexanes, 15.75 mL, 15.75 mmol) were added to a solution of **7** (6.30 mmol) in anhydrous CH_2Cl_2 (210 mL) at 0 °C. The resulting mixture was warmed to room temperature and stirred until TLC analysis showed complete disappearance of the starting material (5−12 h). The reaction mixture was quenched by the slow addition of a saturated aqueous Na/K-tartrate solution (100 mL), and after it was stirred for 30 min the organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (100 mL), and the combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/EtOAc 7/3) afforded products **8**.

((1R,6S*,7R*,9S*)-9-(Methoxymethyl)tricyclo[4.3.1.0^{7,9}]deca-2,4-dien-7-yl)methanol (**8a**).* Colorless oil (1.22 g, 5.92 mmol, yield 94%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.11−6.00 (m, 2H), 5.85−5.74 (m, 2H), 4.01 (dd, J = 10.0, 1.2 Hz, 1H), 3.84 (d, J = 11.7 Hz, 1H), 3.67 (d, J = 11.7 Hz, 1H), 3.38 (s, 3H), 3.10 (d, J = 10.0 Hz, 1H), 2.86−2.78 (m, 2H), 2.01 (dtt, J = 12.8, 6.3, 1.3 Hz, 1H), 1.78 (d, J = 13.1 Hz, 1H), 1.73 (d, J = 13.0 Hz, 1H), 0.81 (d, J = 5.6 Hz, 1H), 0.26 (d, J = 5.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.3, 136.5, 125.9, 125.0, 73.4, 64.2, 58.8, 42.1, 42.0, 41.4, 39.6, 26.6, 14.4. HRMS

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(ESI+): m/z calcd for $C_{13}H_{18}NaO_2$ $[M + Na]^+$, 229.1199; found, 229.1207.

((1R,6S*,7R*,9S*)-9-((Benzyloxy)methyl)tricyclo[4.3.1.0^{7,9}]deca-2,4-dien-7-yl)methanol (**8b**).* Colorless oil (1.53 g, 5.42 mmol, yield 86%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39−7.33 (m, 4H), 7.32−7.29 (m, 1H), 6.10−6.04 (m, 1H), 6.01−5.95 (m, 1H), 5.81−5.70 (m, 2H), 4.59 (d, J = 12.1 Hz, 1H), 4.52 (d, J = 12.1 Hz, 1H), 4.08 (dd, J = 10.0, 1.2 Hz, 1H), 3.82 (dd, J = 11.7, 7.0 Hz, 1H), 3.63 (d, J = 11.6 Hz, 1H), 3.21 (d, J = 10.0 Hz, 1H), 2.87 (t, J = 6.2 Hz, 1H), 2.81 (t, J = 6.2 Hz, 1H), 2.01 (dtt, J = 12.8, 6.3, 1.3 Hz, 1H), 1.79 (d, J = 13.0 Hz, 1H), 1.68 (s, 1H), 0.83 (d, J = 5.6 Hz, 1H), 0.26 (d, J = 5.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 138.5, 137.3, 136.5, 128.4, 127.7, 127.6, 125.9, 125.0, 72.9, 70.9, 64.3, 42.1, 42.1, 41.5, 39.7, 26.6, 14.6. HRMS (ESI+): m/z calcd for $C_{19}H_{22}NaO_2$ $[M + Na]^+$, 305.1512; found, 305.1517.

Synthesis of 9. Dess−Martin periodinane (2.67 g, 6.30 mmol) was added to a solution of **8** (4.85 mmol) in CH_2Cl_2 (50 mL). After the addition of 1 drop of water the resulting suspension was stirred at room temperature for 1 h and then washed with a 1/1 mixture of a saturated solution of $Na_2S_2O_3$/Na_2CO_3 (40 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The product was obtained after purification by flash chromatography (cyclohexane/EtOAc 7/3).

(1R,6S*,7R*,9S*)-9-(Methoxymethyl)tricyclo[4.3.1.0^{7,9}]deca-2,4-diene-7-carbaldehyde (**9a**).* Colorless oil (871.7 mg, 4.27 mmol, yield 88%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.39 (s, 1H), 6.31 (ddq, J = 11.4, 7.5, 1.0 Hz, 1H), 5.99 (ddq, J = 12.3, 7.5, 1.0 Hz, 1H), 5.79 (ddd, J = 11.4, 7.4, 0.9 Hz, 1H), 5.72 (ddd, J = 12.3, 7.4, 0.8 Hz, 1H), 3.95 (dd, J = 9.9, 1.4 Hz, 1H), 3.40 (s, 3H), 3.35 (d, J = 9.9 Hz, 1H), 3.00−2.95 (m, 1H), 2.88 (t, J = 7.0 Hz, 1H), 2.05 (dtt, J = 12.9, 6.4, 1.3 Hz, 1H), 1.91 (d, J = 13.2 Hz, 1H), 1.25 (d, J = 5.8 Hz, 1H), 1.19 (dd, J = 5.8, 1.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 200.0, 136.6, 134.8, 125.7, 124.5, 71.5, 58.9, 51.8, 46.0, 41.3, 39.4, 26.5, 17.5. HRMS (ESI+): m/z calcd for $C_{13}H_{16}NaO_2$ $[M + Na]^+$, 227.1043; found, 227.1040.

(1R,6S*,7R*,9S*)-9-((Benzyloxy)methyl)tricyclo[4.3.1.0^{7,9}]deca-2,4-diene-7-carbaldehyde (**9b**).* Colorless oil (1.06 g, 3.78 mmol, yield 78%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.36 (s, 1H), 7.42−7.34 (m, 4H), 7.34−7.29 (m, 1H), 6.33−6.27 (m, 1H), 5.97−5.89 (m, 1H), 5.78−5.67 (m, 2H), 4.60 (d, J = 11.9 Hz, 1H), 4.52 (d, J = 11.9 Hz, 1H), 4.04 (dd, J = 9.9, 1.3 Hz, 1H), 3.48 (d, J = 9.8 Hz, 1H), 2.97 (dd, J = 7.5, 6.3 Hz, 1H), 2.93 (t, J = 7.0 Hz, 1H), 2.06 (dtt, J = 12.9, 6.4, 1.3 Hz, 1H), 1.91 (d, J = 13.2 Hz, 1H), 1.26 (d, J = 5.8 Hz, 1H), 1.21 (dd, J = 5.9, 1.3 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 199.9, 138.2, 136.6, 134.8, 128.4, 127.7, 125.7, 124.4, 73.2, 69.2, 51.9, 46.1, 41.4, 39.4, 26.4, 17.7. HRMS (ESI+): m/z calcd for $C_{19}H_{20}NaO_2$ $[M + Na]^+$, 303.1356; found, 303.1361.

(1R*,6S*,7S*,9S*)-7-Ethynyl-9-(methoxymethyl)tricyclo-[4.3.1.0^{7,9}]deca-2,4-diene (3a). Ohira−Bestmann reagent (790 mg, 4.98 mmol) and K_2CO_3 (947.3 mg, 6.85 mmol) were sequentially added to a solution of **9a** (700 mg, 3.43 mmol) in MeOH (34 mL), and the resulting mixture was stirred at room temperature for 16 h. Then the volatiles were removed under reduced pressure and the residue was dissolved in EtOAc (30 mL) and washed with water (30 mL) and brine (30 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/EtOAc 85/15) afforded the product as a colorless oil (391.6 mg, 1.96 mmol, yield 57%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.09−5.96 (m, 2H), 5.85−5.78 (m, 2H), 4.09 (dd, J = 10.2, 1.6 Hz, 1H), 3.40 (s, 3H), 3.10 (d, J = 10.2 Hz, 1H), 2.82 (dd, J = 6.7, 5.2 Hz, 1H), 2.80 (dd, J = 6.4, 5.3 Hz, 1H), 2.00−1.92 (m, 1H), 1.98 (s, 1H), 1.85 (dd, J = 13.2, 0.6 Hz, 1H), 0.98 (dd, J = 5.7, 1.6 Hz, 1H), 0.57 (d, J = 5.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 136.5, 135.6, 125.6, 125.0, 84.5, 74.2, 67.3, 58.8, 42.3, 40.6, 40.5, 30.0, 26.7, 17.2. HRMS (APCI+): m/z calcd for $C_{14}H_{17}O$ $[M + H]^+$, 201.1274; found, 201.1271.

1-((1R*,6S*,7R*,9S*)-9-(Methoxymethyl)tricyclo[4.3.1.0^{7,9}]-deca-2,4-dien-7-yl)ethan-1-one (10). To a solution of **3a** (20.0 mg, 0.1 mmol) in MeOH (1 mL) was added gold(I) complex **B**[31] (7.9 mg, 0.005 mmol), and the resulting mixture was stirred at room temperature for 2 h. The reaction was quenched by the addition of 1 drop of Et_3N, and the volatiles were removed under reduced pressure. Purification by column chromatography (cyclohexane/EtOAc 8/2) afforded the product as a colorless oil (21.6 mg, 0.099 mmol, yield 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.12−6.02 (m, 2H), 5.82−5.70 (m, 2H), 3.96 (dd, J = 10.2, 1.4 Hz, 1H), 3.66 (d, J = 10.2 Hz, 1H), 3.40 (s, 3H), 3.03 (dd, J = 7.4, 6.5 Hz, 1H), 2.86 (dd, J = 7.4, 6.4 Hz, 1H), 2.29 (s, 3H), 2.05 (dddd, J = 13.0, 6.5, 5.1, 1.4 Hz, 1H), 1.82 (d, J = 13.2 Hz, 1H), 1.11 (dd, J = 5.0, 1.4 Hz, 1H), 0.83 (d, J = 5.0 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 207.9, 136.5, 135.5, 124.9, 124.9, 72.1, 58.8, 49.4, 44.3, 41.3, 40.9, 31.5, 25.9, 20.8. HRMS (ESI+): m/z calcd for $C_{14}H_{18}NaO_2$ $[M + Na]^+$, 241.1199; found, 241.1193.

Isolation of the Acetal Intermediate (1R,6S*,7R*,9S*)-7-(1,1-Dimethoxyethyl)-9-(methoxymethyl)tricyclo[4.3.1.0^{7,9}]deca-2,4-diene (**11**).* Inside a glovebox, **3a** (20 mg, 0.1 mmol) was dissolved in anhydrous and degassed CH_2Cl_2 (1 mL) and then anhydrous MeOH (41 μL, 1 mmol) and gold(I) complex **B** (7.9 mg, 0.005 mmol) were sequentially added. The resulting mixture was stirred at room temperature for 30 min and then quenched by the addition of 1 drop of Et_3N. After removal of the volatiles under reduced pressure, filtration through a pad of basic Al_2O_3 afforded the product as an unstable colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$): δ 6.10−5.99 (m, 2H), 5.80−5.64 (m, 2H), 3.89 (dd, J = 9.6, 1.4 Hz, 1H), 3.40 (s, 3H), 3.36 (d, J = 9.5 Hz, 1H), 3.20 (s, 3H), 3.04 (s, 3H), 2.83 (t, J = 6.7 Hz, 1H), 2.73 (dd, J = 7.7, 6.6 Hz, 1H), 2.06 (dt, J = 12.8, 6.4 Hz, 1H), 1.75 (d, J = 13.0 Hz, 1H), 1.40 (s, 3H), 0.80 (d, J = 5.1 Hz, 1H), 0.63 (dd, J = 5.1, 1.3 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 138.4, 136.5, 125.4, 124.4, 100.7, 72.5, 58.8, 48.8, 48.0, 42.3, 42.1, 29.7, 27.4, 23.2, 17.6, 12.1. HRMS could not be obtained due to decomposition to **10**.

(1R*,1aR*,3R*,5aR*)-1-(Methoxymethyl)-1,1a,2,2a,5a,7a-hexahydro-3*H*-1,3-methanocyclopropa[*f*]azulen-3-yl Acetate (12). Gold(I) complex **A** (38.6 mg, 0.05 mmol) was added to a solution of **3a** (200.3 mg, 1 mmol) and AcOH (0.57 mL, 10 mmol) in CH_2Cl_2 (10 mL), and the resulting mixture was stirred at room temperature for 1 h. The reaction was quenched by the addition of 1 drop of Et_3N, and the volatiles were removed under reduced pressure. Purification by column chromatography (cyclohexane/EtOAc 95/5 to 8/2) afforded the product as a colorless oil (158.8 mg, 0.61 mmol, dr = 5:1, yield 61%). Data for the major isomer are as follows. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.53 (dt, J = 6.0, 0.9 Hz, 1H), 5.74 (dd, J = 5.9, 3.1 Hz, 1H), 5.62 (ddd, J = 12.5, 7.9, 2.0 Hz, 1H), 5.28 (ddd, J = 12.4, 4.3, 1.4 Hz, 1H), 3.32 (s, 3H), 3.29 (d, J = 10.0 Hz, 1H), 3.12 (d, J = 10.0 Hz, 1H), 3.03−2.97 (m, 1H), 2.70 (dd, J = 16.8, 1.5 Hz, 1H), 2.48−2.42 (m, 1H), 2.33 (ddd, J = 14.5, 7.4, 5.1 Hz, 1H), 2.06 (s, 3H), 2.05 (d, J = 14.6 Hz, 1H), 1.65 (d, J = 11.2 Hz, 1H), 1.39−1.34 (m, 1H), 1.19 (t, J = 8.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 170.6, 137.6, 133.4, 126.8, 123.5, 85.9, 81.4, 58.1, 47.4, 42.8, 31.7, 28.1, 24.5, 22.1, 21.7, 19.1. HRMS (ESI+): m/z calcd for $C_{16}H_{20}NaO_3$ $[M + Na]^+$, 283.1305; found, 283.1307.

(1R*,1aR*,3R*,5aR*)-1-(Methoxymethyl)-1,1a,2,2a,5a,7a-hexahydro-3*H*-1,3-methanocyclopropa[*f*]azulen-3-ol (18). K_2CO_3 (253.9 mg, 1.92 mmol) was added to a solution of **12** (100 mg, 0.38 mmol) in a 1/1 mixture of CH_2Cl_2 and MeOH (4 mL), and the resulting mixture was stirred at 50 °C for 16 h. After the mixture was cooled to room temperature, the volatiles were removed under reduced pressure and the resulting crude was purified by column chromatography (cyclohexane/EtOAc 7/3 to 1/1) to give the product as a colorless oil (69.7 mg, 0.32 mmol, dr > 20:1, yield 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.00 (dt, J = 5.8, 0.9 Hz, 1H), 5.68 (dd, J = 5.8, 3.2 Hz, 1H), 5.61 (ddd, J = 12.5, 7.9, 2.0 Hz, 1H), 5.29 (ddd, J = 12.4, 4.3, 1.4 Hz, 1H), 3.35 (s, 3H), 3.31 (d, J = 9.8 Hz, 1H), 3.15 (d, J = 9.8 Hz, 1H), 3.06−2.97 (m, 1H), 2.37 (ddd, J = 14.5, 7.4, 5.2 Hz, 1H), 2.19 (dd, J = 15.9, 1.5 Hz, 1H), 2.11 (t, J = 7.1 Hz, 1H), 2.02 (d, J = 14.6 Hz, 1H), 1.78 (s, 1H), 1.68 (d, J = 15.9 Hz, 1H), 1.36 (ddd, J = 9.0, 5.4, 1.3 Hz, 1H), 1.19 (t, J = 8.4 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.4, 132.6, 127.1, 123.3, 81.8, 77.9, 58.4, 48.8, 45.7, 35.0, 28.3, 24.6, 21.7, 18.9. HRMS (ESI+): m/z calcd for $C_{14}H_{18}NaO_2$ $[M + Na]^+$, 241.1199; found, 241.1205.

(1R*,1aR*,3R*,5aR*)-1-(Methoxymethyl)-1,1a,2,2a,5a,7a-hexahydro-3*H*-1,3-methanocyclopropa[*f*]azulen-3-yl 4-Nitro-

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benzoate (19). 4-Nitrobenzoyl chloride (30.6 mg, 0.16 mmol) was added to a solution of **18** (30 mg, 0.14 mmol), Et_3N (38 μL, 0.27 mmol), and DMAP (1.2 mg, 0.01 mmol) in anhydrous CH_2Cl_2 (3 mL), and the mixture was stirred at room temperature for 1 h and then washed with H_2O (2 × 5 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by column chromatography (cyclohexane/EtOAc 9/1) afforded the product as a white solid (51.3 mg, 0.14 mmol, yield quantitative). Mp: 136−138 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 8.32−8.29 (m, 2H), 8.24−8.20 (m, 2H), 6.63 (dt, *J* = 5.9, 0.9 Hz, 1H), 5.84 (dd, *J* = 5.9, 3.1 Hz, 1H), 5.68 (ddd, *J* = 12.5, 8.0, 2.1 Hz, 1H), 5.34 (ddd, *J* = 12.4, 4.2, 1.1 Hz, 1H), 3.32 (d, *J* = 10.0 Hz, 1H), 3.25 (s, 3H), 3.12−3.09 (m, 1H), 3.11 (d, *J* = 10.0 Hz, 1H), 2.84 (dd, *J* = 16.9, 1.6 Hz, 1H), 2.73−2.68 (m, 1H), 2.43 (ddd, *J* = 14.7, 7.4, 5.2 Hz, 1H), 2.16 (d, *J* = 14.7 Hz, 1H), 1.80 (d, *J* = 16.8 Hz, 1H), 1.44 (dd, *J* = 8.9, 5.2 Hz, 1H), 1.29−1.23 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 163.9, 150.4, 137.0, 136.9, 134.0, 130.6, 126.7, 123.7, 123.5, 88.0, 81.3, 58.2, 47.5, 42.7, 32.0, 28.1, 24.5, 21.7, 19.3. HRMS (ESI+): *m*/*z* calcd for $C_{21}H_{21}NNaO_5$ $[M + Na]^+$, 390.1312; found, 390.1315.

(1*R,1a*R**,3*S**,5a*S**)-1-(Methoxymethyl)-1,1a,2,2a,4,5,5a,7a-octahydro-3*H*-1,3-methanocyclopropa[*f*]azulen-3-ol (20).** A round-bottom flask containing a solution of **18** (50 mg, 0.23 mmol) and Crabtree's catalyst (3.7 mg, 0.0046 mmol) in anhydrous MeOH (3 mL) was evacuated and back-filled with H_2 (repeated three times). The resulting mixture was stirred at room temperature for 1 h, then the volatiles were removed under reduced pressure, and the crude waqs purified by column chromatography (cyclohexane/EtOAc 1/1) to afford the product as a yellow oil (46.0 mg, 0.21 mmol, yield 91%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.47−5.36 (m, 2H), 3.41−3.33 (m, 1H), 3.37 (s, 3H), 2.99 (d, *J* = 9.3 Hz, 1H), 2.54−2.46 (m, 1H), 2.29−2.20 (m, 1H), 2.06−1.96 (m, 1H), 1.95−1.85 (m, 4H), 1.77−1.58 (m, 4H), 1.38−1.24 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 135.6, 120.0, 82.0, 74.6, 58.7, 43.5, 40.1, 38.6, 31.5, 29.3, 24.2, 22.4, 21.4, 18.4. HRMS (ESI+): *m*/*z* calcd for $C_{14}H_{20}NaO_2$ $[M + Na]^+$, 243.1356; found, 243.1355.

(1*R,1a*R**,5a*S**)-1-(Methoxymethyl)-1a,2,2a,5,5a,7a-hexahydro-1*H*-1,3-methanocyclopropa[*f*]azulene (23).** Tf_2O (37 μL, 0.22 mmol) was slowly added to a solution of **20** (40 mg, 0.18 mmol), pyridine (29 μL, 0.36 mmol), and DMAP (2.2 mg, 0.018 mmol) in anhydrous CH_2Cl_2 (2 mL) at 0 °C. The reaction mixture was warmed to room temperature and after stirring for 1 h was quenched by the addition of H_2O (2 mL). The organic layer was separated, dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by column chromatography (cyclohexane/EtOAc 98/2) afforded the product as a yellow oil (35.6 mg, 0.18 mmol, yield 98%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.51 (bs, 1H), 5.44 (ddd, *J* = 12.4, 7.3, 1.7 Hz, 1H), 5.40−5.34 (m, 1H), 3.63 (d, *J* = 9.9 Hz, 1H), 3.40 (s, 3H), 3.28 (d, *J* = 9.9 Hz, 1H), 2.55−2.49 (m, 1H), 2.27−2.11 (m, 5H), 2.05−2.00 (m, 1H), 1.77−1.73 (m, 1H), 1.72−1.65 (m, 1H), 1.56 (t, *J* = 8.1, 7.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 147.9, 134.1, 121.3, 118.1, 79.6, 58.6, 44.1, 38.5, 36.7, 33.8, 30.8, 27.9, 27.8, 21.0. HRMS (ESI+): *m*/*z* calcd for $C_{14}H_{18}NaO$ $[M + Na]^+$, 225.1250; found, 225.1243.

***tert*-Butyldiphenyl(((1*R**,6*S**)-8-(trimethylsilyl)bicyclo[4.2.1]nona-2,4,7-trien-7-yl)methoxy)silane (26).** $CoBr_2$ (238.6 mg, 1.09 mmol), Zn (285.4 mg, 4.36 mmol), and ZnI_2 (1.39 g, 4.36 mmol) were suspended in anhydrous 1,2-dichloroethane (35 mL) under argon. Then $P(O^iPr)_3$ (0.54 mL, 2.18 mmol) was added, followed by cycloheptatriene (3.40 mL, 32.73 mmol) and a solution of **25**[32] (8.00 g, 21.82 mmol) in anhydrous 1,2-dichloroethane (9 mL). The resulting mixture was stirred at 50 °C for 30 h and then filtered through a short pad of silica gel and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/EtOAc 1/0 to 95/5) afforded the product as a colorless oil (7.10 g, 15.49 mmol, yield 71%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.74−7.68 (m, 4H), 7.48−7.39 (m, 6H), 6.16−6.10 (m, 1H), 6.09−6.03 (m, 1H), 5.83−5.72 (m, 2H), 4.43 (d, *J* = 12.8 Hz, 1H), 4.23 (d, *J* = 12.7 Hz, 1H), 3.69 (t, *J* = 7.2 Hz, 1H), 3.14 (t, *J* = 7.0 Hz, 1H), 2.14 (dtt, *J* = 11.4, 6.7, 1.2 Hz, 1H), 1.56 (d, *J* = 11.4 Hz, 1H), 1.11 (s, 9H), 0.01 (s, 9H). ^{13}C NMR (75 MHz, $CDCl_3$): δ 147.7, 139.2, 138.9, 135.7, 135.7, 135.6, 133.7, 133.7, 133.2, 129.6, 127.6, 127.6, 124.3, 123.5, 60.4, 48.5, 46.4, 30.8, 26.9, 19.3, 0.4. HRMS (ESI+): *m*/*z* calcd for $C_{29}H_{38}NaOSi_2$ $[M + Na]^+$, 481.2353; found, 481.2378.

***tert*-Butyl(((1*R**,6*S**)-8-iodobicyclo[4.2.1]nona-2,4,7-trien-7-yl)methoxy)diphenylsilane (27).** *N*-Iodosuccinimide (2.35 g, 10.45 mmol) was added to a solution of **26** (4.00 g, 8.72 mmol) in anhydrous CH_3CN (87 mL) under argon in darkness, and the resulting mixture was stirred at room temperature for 16 h. The reaction was quenched by the addition of a saturated solution of $Na_2S_2O_3$ (50 mL) and the product extracted with EtOAc (3 × 60 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/EtOAc 95/5) afforded the product as a pale yellow oil (2.52 g, 4.88 mmol, yield 56%).[33] ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.73−7.66 (m, 4H), 7.48−7.38 (m, 6H), 6.20 (ddq, *J* = 11.2, 7.2, 1.1 Hz, 1H), 6.11 (ddq, *J* = 11.2, 7.3, 1.0 Hz, 1H), 5.95 (ddd, *J* = 11.1, 7.5, 0.9 Hz, 1H), 5.86 (ddd, *J* = 11.0, 7.4, 0.9 Hz, 1H), 4.35 (d, *J* = 13.6, 0.8 Hz, 1H), 4.17 (d, *J* = 13.5 Hz, 1H), 3.50 (t, *J* = 7.0 Hz, 1H), 3.25 (t, *J* = 7.0 Hz, 1H), 2.31 (dtt, *J* = 11.3, 6.8, 1.2 Hz, 1H), 1.62 (d, *J* = 11.4 Hz, 1H), 1.10 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.7, 139.1, 138.1, 135.6, 135.6, 133.4, 133.4, 129.7, 127.7, 125.4, 124.9, 84.5, 63.0, 52.9, 44.1, 30.8, 26.9, 19.3. HRMS (ESI+): *m*/*z* calcd for $C_{26}H_{29}INaOSi$ $[M + Na]^+$, 535.0925; found, 535.0919.

((1*R,6*S**)-8-(3-(Trimethylsilyl)prop-2-yn-1-yl)bicyclo[4.2.1]nona-2,4,7-trien-7-yl)methanol (29).** A dry two-neck round-bottom flask equipped with a condenser was charged with activated magnesium tunings (583 mg, 24.0 mmol) that were covered with anhydrous THF (100 mL). Dibromoethane (0.1 mL) was added, followed by trimethylsilylpropargyl bromide (2.0 mL, 12.12 mmol). The reaction mixture was heated at 50 °C for 1 h and then cooled to room temperature and transferred via cannula to a second two-neck round-bottom flask containing a solution of **27** (1.23 g, 2.40 mmol) and $Pd(PPh_3)_4$ (138.7 mg, 0.12 mmol) in anhydrous THF (30 mL). The resulting mixture was stirred at 50 °C for 2 h and then cooled to room temperature, poured on brine (100 mL), and extracted with Et_2O (2 × 100 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/EtOAc 95/5) afforded **28** as a yellow oil that was directly taken to the next step due to its low stability. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72−7.67 (m, 4H), 7.47−7.36 (m, 6H), 6.27−6.18 (m, 1H), 6.17−6.09 (m, 1H), 5.83−5.71 (m, 2H), 4.33 (d, *J* = 12.8 Hz, 1H), 4.20 (d, *J* = 13.0 Hz, 1H), 3.42 (t, *J* = 7.0 Hz, 1H), 3.36 (t, *J* = 7.0 Hz, 1H), 2.95 (d, *J* = 19.4 Hz, 1H), 2.85 (d, *J* = 18.6 Hz, 1H), 2.26 (dtt, *J* = 11.3, 6.7, 1.2 Hz, 1H), 1.61 (d, *J* = 11.3 Hz, 1H), 1.08 (s, 9H), 0.16 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 140.2, 139.7, 135.6, 135.6, 135.0, 133.7, 133.6, 129.9, 129.6, 129.6, 127.7, 127.7, 124.4, 124.1, 104.8, 85.0, 58.5, 46.6, 45.0, 30.3, 26.8, 19.2, 17.2, 0.1. To a solution of **28** (646.0 mg, 1.30 mmol) in THF (12 mL) in a Teflon flask was added HF·py (70% weight, 0.31 mL, 12.1 mmol), and the resulting mixture was stirred at room temperature for 16 h. The reaction was quenched by the slow addition of a saturated solution of $NaHCO_3$ (10 mL), and the product was extracted with Et_2O (2 × 10 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/EtOAc 8/2) afforded the product as a yellow oil (528.1 mg, 1.06 mmol, yield over two steps 44%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.31−6.19 (m, 2H), 5.87−5.78 (m, 2H), 4.29 (d, *J* = 12.7 Hz, 1H), 4.19 (d, *J* = 12.7 Hz, 1H), 3.37 (d, *J* = 7.2 Hz, 1H), 3.34 (d, *J* = 7.2 Hz, 1H), 3.17 (d, *J* = 19.3 Hz, 1H), 3.11 (d, *J* = 19.1 Hz, 1H), 2.27 (dtt, *J* = 11.4, 6.7, 1.2 Hz, 1H), 1.61 (d, *J* = 11.4 Hz, 1H), 0.18 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 139.8, 139.4, 135.1, 131.5, 124.7, 124.5, 104.4, 85.4, 57.3, 46.7, 45.4, 30.1, 17.2, 0.0. HRMS (ESI+): *m*/*z* calcd for $C_{16}H_{22}NaOSi$ $[M + Na]^+$, 281.1332; found, 281.1322.

((1*R,6*S**,7*R**,9*S**)-9-(3-(Trimethylsilyl)prop-2-yn-1-yl)-tricyclo[4.3.1.0^{7,9}]deca-2,4-dien-7-yl)methanol (30).** To a solution of **29** (430 mg, 1.66 mmol) in anhydrous CH_2Cl_2 (83 mL) were sequentially added CH_2I_2 (0.15 mL, 1.99 mmol) and $ZnEt_2$ (1.0 M in hexanes, 4.15 mL, 4.15 mmol), and the resulting solution was stirred at room temperature for 3 h. The reaction mixture was quenched by the

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slow addition of a saturated aqueous Na/K-tartrate solution (100 mL), and after the mixture was stirred for 30 min, the organic layer was separated, the aqueous layer was extracted with CH_2Cl_2 (100 mL), and the combined organic phases were dried over $MgSO_4$ and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/EtOAc 8/2) afforded the product as a pale yellow oil (378.0 mg, 1.39 mmol, yield 84%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.11−6.00 (m, 2H), 5.84−5.70 (m, 2H), 3.92 (d, J = 11.6 Hz, 1H), 3.57 (d, J = 11.5 Hz, 1H), 2.89 (dd, J = 17.3, 0.8 Hz, 1H), 2.85−2.75 (m, 2H), 2.07 (d, J = 17.3 Hz, 1H), 1.99 (ddd, J = 12.8, 7.0, 5.7 Hz, 1H), 1.74 (d, J = 13.1 Hz, 1H), 1.50 (s, 1H), 0.74 (d, J = 5.7 Hz, 1H), 0.18 (s, 10H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 136.9, 136.5, 125.7, 125.3, 105.4, 85.8, 64.0, 43.1, 42.3, 41.4, 38.9, 26.2, 21.0, 14.3, 0.1. HRMS (ESI+): m/z calcd for $C_{17}H_{24}NaOSi$ $[M + Na]^+$, 295.1489; found, 295.1482.

***tert*-Butyldimethyl(((1*R**,6*S**,7*R**,9*R**)-9-(prop-2-yn-1-yl)-tricyclo[4.3.1.0^{7,9}]deca-2,4-dien-7-yl)methoxy)silane (4a).** TBAF (1.0 M solution in THF, 1.53 mL, 1.53 mmol) was added to a solution of **30** (378.1 mg, 1.39 mmol) in THF (14 mL) at 0 °C, and the resulting solution was warmed to room temperature and stirred for 15 min. Then the mixture was poured on brine (30 mL) and the product was extracted with Et_2O (2 × 20 mL). The combined organic layers were dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by flash chromatography (cyclohexane/EtOAc 8/2) afforded ((1*R**,6*S**,7*R**,9*R**)-9-(prop-2-yn-1-yl)tricyclo-[4.3.1.0^{7,9}]deca-2,4-dien-7-yl)methanol (**30′**) as a colorless oil (222.7 mg, 1.11 mmol, yield 80%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.12−6.03 (m, 2H), 5.84−5.76 (m, 2H), 3.91 (d, J = 11.6 Hz, 1H), 3.60 (d, J = 11.6 Hz, 1H), 2.91 (ddd, J = 17.1, 2.7, 0.9 Hz, 1H), 2.84 (td, J = 6.8, 4.0 Hz, 2H), 2.04 (t, J = 2.7 Hz, 1H), 2.03−1.95 (m, 2H), 1.75 (d, J = 13.1 Hz, 1H), 1.53 (s, 1H), 0.76 (d, J = 5.7 Hz, 1H), 0.17 (d, J = 5.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 136.9, 136.4, 125.8, 125.3, 82.8, 69.1, 64.1, 42.8, 42.3, 41.6, 38.8, 26.1, 19.7, 14.3. HRMS (APCI +): m/z calcd for $C_{14}H_{17}O$ $[M + H]^+$, 201.1274; found, 201.1266. TBSCl (165.6 mg, 1.10 mmol) and imidazole (136.2 mg, 2.00 mmol) were added to a solution of **30′** (200.3 mg, 1.00 mmol) in CH_2Cl_2 (10 mL), and the mixture was stirred at room temperature for 1 h. Then it was washed with H_2O (10 mL) and brine (10 mL) and the organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. Purification by column chromatography (cyclohexane) afforded the product as a colorless oil (314.4 mg, 0.99 mmol, yield 99%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.06−5.92 (m, 2H), 5.79−5.69 (m, 2H), 4.08 (dd, J = 10.4, 1.1 Hz, 1H), 3.37 (d, J = 10.4 Hz, 1H), 2.85−2.73 (m, 3H), 2.04−1.94 (m, 3H), 1.72 (d, J = 13.0 Hz, 1H), 0.91 (s, 9H), 0.71 (d, J = 5.6 Hz, 1H), 0.22 (d, J = 5.7 Hz, 1H), 0.06 (s, 3H), 0.04 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 136.8, 136.4, 125.3, 124.9, 83.2, 68.8, 63.0, 43.1, 42.4, 41.5, 38.3, 26.0, 25.9, 19.1, 18.3, 13.6, −5.2, −5.4. HRMS (ESI+): m/z calcd for $C_{20}H_{30}NaOSi$ $[M + Na]^+$, 337.1958; found, 337.1945.

1-((1*R,6*S**,7*R**,9*S**)-9-(((*tert*-Butyldimethylsilyl)oxy)-methyl)tricyclo[4.3.1.0^{7,9}]deca-2,4-dien-7-yl)propan-2-one (31).** Gold(I) complex (0.002 mmol) was added to a solution of **4a** (0.1 mmol) in MeOH (1 mL), and the resulting mixture was stirred at room temperature for 2 h before the addition of 1 drop of Et_3N. Then the volatiles were removed under reduced pressure, and purification by column chromatography afforded the product in 22−47% yield. ^{1}H NMR (400 MHz, $CDCl_3$): δ 5.98−5.83 (m, 2H), 5.77−5.69 (m, 2H), 4.09 (d, J = 10.6 Hz, 1H), 3.37 (d, J = 10.4 Hz, 1H), 3.01 (d, J = 16.1 Hz, 1H), 2.76 (t, J = 7.2 Hz, 1H), 2.73 (t, J = 6.7 Hz, 1H), 2.18 (s, 3H), 2.14 (d, J = 16.0 Hz, 1H), 2.04−1.95 (m, 1H), 1.71 (d, J = 13.0 Hz, 1H), 0.91 (s, 9H), 0.79 (d, J = 5.7 Hz, 1H), 0.21 (d, J = 5.7 Hz, 1H), 0.06 (s, 3H), 0.06 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 208.9, 136.6, 136.5, 125.2, 125.1, 63.1, 43.7, 42.9, 41.8, 41.0, 35.6, 30.2, 26.4, 25.9, 18.3, 13.9, −5.2, −5.4. HRMS (ESI+): m/z calcd for $C_{20}H_{32}NaO_2Si$ $[M + Na]^+$, 355.2064; found, 355.2056.

Synthesis of 4b,c. Ethynylmagnesium bromide (0.5 M in THF, 8.07 mL, 4.04 mmol) was added to a solution of **9** (3.67 mmol) in anhydrous THF (37 mL) at 0 °C. After it was stirred at room temperature for 30 min, the reaction mixture was diluted with Et_2O (15 mL) and quenched by the addition of saturated NH_4Cl aqueous solution (50 mL). The aqueous layer was extracted with Et_2O (2 × 40 mL), the combined organic phases were dried over $MgSO_4$, filtered, and concentrated under reduced pressure, and the resulting crude was purified by column chromatography (cyclohexane/EtOAc 7/3).

1-((1R,6S*,7R*,9S*)-9-(Methoxymethyl)tricyclo[4.3.1.0^{7,9}]deca-2,4-dien-7-yl)prop-2-yn-1-ol (**4b**).* Pale yellow solid (769.2 mg, 3.34 mmol, yield 91%). Mp: 82−84 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.10−5.99 (m, 2H), 5.84−5.72 (m, 2H), 4.94 (s, 1H), 3.87 (dd, J = 10.1, 0.7 Hz, 1H), 3.68 (d, J = 10.1 Hz, 1H), 3.37 (s, 3H), 2.97 (s, 1H), 2.82 (dd, J = 7.1, 6.2 Hz, 1H), 2.76 (dd, J = 7.1, 6.2 Hz, 1H), 2.54 (d, J = 2.2 Hz, 1H), 2.12−2.03 (m, 1H), 1.76 (d, J = 13.0 Hz, 1H), 0.76 (d, J = 5.9 Hz, 1H), 0.74 (d, J = 6.1 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 137.2, 136.0, 126.2, 125.0, 84.0, 73.5, 72.0, 61.1, 58.7, 43.8, 43.3, 43.0, 40.2, 26.3, 10.6. HRMS (APCI+): m/z calcd for $C_{15}H_{18}NaO_2$ $[M + Na]^+$, 253.1199; found, 253.1211.

1-((1R,6S*,7R*,9S*)-9-((Benzyloxy)methyl)tricyclo[4.3.1.0^{7,9}]-deca-2,4-dien-7-yl)prop-2-yn-1-ol (**4c**).* Colorless oil (923.0 mg, 3.01 mmol, yield 82%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39−7.33 (m, 4H), 7.33−7.29 (m, 1H), 6.06 (dd, J = 10.7, 7.5 Hz, 1H), 6.00 (dd, J = 9.7, 7.5 Hz, 1H), 5.80 (ddd, J = 11.3, 7.4, 0.9 Hz, 1H), 5.74 (ddd, J = 11.2, 7.4, 0.9 Hz, 1H), 4.95 (dd, J = 4.0, 2.2 Hz, 1H), 4.60 (d, J = 11.9 Hz, 1H), 4.51 (d, J = 11.9 Hz, 1H), 3.97 (d, J = 10.2 Hz, 1H), 3.80 (d, J = 10.2 Hz, 1H), 2.89 (d, J = 4.1 Hz, 1H), 2.85−2.79 (m, 2H), 2.51 (d, J = 2.2 Hz, 1H), 2.08 (dtt, J = 12.8, 6.3, 1.3 Hz, 1H), 1.77 (d, J = 13.1 Hz, 1H), 0.79−0.75 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 138.1, 137.3, 136.0, 128.4, 127.7, 127.6, 126.3, 125.0, 83.9, 73.6, 73.0, 69.7, 61.2, 43.8, 43.3, 43.0, 40.3, 26.4, 11.0. HRMS (ESI+): m/z calcd for $C_{21}H_{22}NaO_2$ $[M + Na]^+$, 329.1512; found, 329.1518.

Gold-Catalyzed Cyclization of 1,6-Enynes 4b,c. Gold(I) complex **B** (3.1 mg, 0.002 mmol) was added to a solution of **4b,c** (0.1 mmol) in ROH (1 mL), and the resulting suspension was stirred at room temperature for 2 h before the addition of 1 drop of Et_3N. Then the volatiles were removed under reduced pressure and the resulting crude was purified by column chromatography to afford tetracycles **32**.

(1aR,2S*,3aS*,4S*,6R*,6aS*,7R*)-6,7-Dimethoxy-1a-(methoxymethyl)-5-methylene-1,1a,2,3,3a,4,5,6-octahydro-2,4-prop[1]-enocyclopropa[c]pentalene (**32a**).* Purification: pentane/CH_2Cl_2 9/1. White solid (25.1 mg, yield 91%). **32a**:**32a′** > 20:1. Mp: 95−97 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 6.12 (ddd, J = 11.6, 6.8, 1.5 Hz, 1H), 5.76 (ddd, J = 11.6, 7.3, 0.6 Hz, 1H), 5.17 (d, J = 2.9 Hz, 1H), 5.04 (d, J = 2.4 Hz, 1H), 3.98 (dd, J = 7.3, 3.7 Hz, 1H), 3.70 (dd, J = 9.8, 1.6 Hz, 1H), 3.47 (s, 1H), 3.41 (s, 3H), 3.36 (s, 3H), 3.36−3.29 (m, 1H), 3.33 (s, 3H), 2.90 (dd, J = 9.7, 6.6 Hz, 1H), 2.84−2.80 (m, 2H), 2.50 (d, J = 13.7 Hz, 1H), 1.42 (dtd, J = 13.6, 6.7, 1.6 Hz, 1H), 1.12 (dd, J = 5.8, 1.6 Hz, 1H), 1.08 (d, J = 5.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 151.2, 140.2, 127.6, 110.9, 85.7, 80.8, 74.1, 58.7, 56.6, 55.6, 45.9, 45.6, 42.8, 40.9, 36.1, 30.3, 16.0. HRMS (ESI+): m/z calcd for $C_{17}H_{24}NaO_3$ $[M + Na]^+$, 299.1618; found, 299.1626. *Note*: this reaction could be scaled up to obtain 400 mg of **32a** without any decrease in yield or selectivity. X-ray-quality single crystals were obtained by slow evaporation of a solution of **32a** in CH_2Cl_2 at 5 °C.

(1aR,2S*,3aS*,4S*,6R*,6aS*,7R*)-1a-((Benzyloxy)methyl)-6,7-dimethoxy-5-methylene-1,1a,2,3,3a,4,5,6-octahydro-2,4-prop[1]-enocyclopropa[c]pentalene (**32b**).* Purification: cyclohexane/EtOAc 1/0 to 95/5. Colorless oil (29.6 mg, yield 84%). **32b**:**32b′** = 5:1. Data for the major isomer are as follows. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.40−7.34 (m, 4H), 7.33−7.29 (m, 1H), 6.09 (ddd, J = 11.6, 6.7, 1.5 Hz, 1H), 5.72 (ddd, J = 11.6, 7.3, 0.6 Hz, 1H), 5.15 (d, J = 2.9 Hz, 1H), 5.03 (d, J = 2.4 Hz, 1H), 4.57 (d, J = 12.1 Hz, 1H), 4.52 (d, J = 12.1 Hz, 1H), 3.97 (dd, J = 7.3, 3.7 Hz, 1H), 3.78 (dd, J = 9.8, 1.5 Hz, 1H), 3.45 (d, J = 1.2 Hz, 1H), 3.41 (s, 3H), 3.32 (s, 1H), 3.32 (s, 3H), 2.96 (d, J = 9.8 Hz, 1H), 2.91 (dd, J = 10.0, 6.3 Hz, 1H), 2.87 (t, J = 6.9 Hz, 1H), 2.51 (d, J = 13.7 Hz, 1H), 1.47−1.40 (m, 1H), 1.14 (dd, J = 5.8, 1.5 Hz, 1H), 1.10 (d, J = 5.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 151.2, 140.2, 138.5, 128.4, 128.4, 127.6, 127.6, 110.9, 85.7, 80.8, 72.7, 71.5, 56.6, 55.6, 46.0, 45.7, 42.9, 41.0, 36.3, 30.3, 16.1. HRMS (ESI+): m/z calcd for $C_{23}H_{28}NaO_3$ $[M + Na]^+$, 375.1931; found, 375.1925.

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(1aR,2S*,3aS*,4S*,6R*,6aS*,7R*)-6,7-Bis(allyloxy)-1a-((benzyloxy)methyl)-5-methylene-1,1a,2,3,3a,4,5,6-octahydro-2,4-prop[1]enocyclopropa[c]pentalene (**32c**).* Purification: cyclohexane/EtOAc 1/0 to 95/5. White solid (30.0 mg, yield 84%). **32c**:**32c**′ > 20:1. Mp: 138−140 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39−7.34 (m, 4H), 7.33−7.29 (m, 1H), 6.07 (ddd, J = 11.6, 6.8, 1.5 Hz, 1H), 6.01−5.88 (m, 2H), 5.69 (ddd, J = 11.6, 7.3, 0.6 Hz, 1H), 5.31 (dq, J = 17.2, 1.7 Hz, 1H), 5.26 (dq, J = 17.2, 1.7 Hz, 1H), 5.20 (dq, J = 10.4, 1.8 Hz, 1H), 5.17 (dq, J = 10.2, 1.9 Hz, 1H), 5.13 (d, J = 2.9 Hz, 1H), 4.99 (d, J = 2.4 Hz, 1H), 4.56 (d, J = 12.1 Hz, 1H), 4.51 (d, J = 12.1 Hz, 1H), 4.13 (dd, J = 7.4, 3.8 Hz, 1H), 4.09 (dt, J = 5.5, 1.5 Hz, 1H), 4.08 (dt, J = 5.7, 1.5 Hz, 1H), 4.05 (dq, J = 5.7, 1.6 Hz, 1H), 3.97 (ddt, J = 12.7, 6.0, 1.4 Hz, 1H), 3.77 (dd, J = 9.8, 1.5 Hz, 1H), 3.65 (s, 1H), 3.34 (dq, J = 9.5, 3.0 Hz, 1H), 2.96 (d, J = 6.3 Hz, 1H), 2.94 (d, J = 6.4 Hz, 1H), 2.87 (t, J = 6.7 Hz, 1H), 2.57 (d, J = 13.7 Hz, 1H), 1.48−1.42 (m, 1H), 1.16 (dd, J = 5.8, 1.5 Hz, 1H), 1.09 (d, J = 5.8 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 151.8, 140.1, 138.5, 135.4, 135.3, 128.4, 127.8, 127.6, 127.6, 116.9, 116.8, 110.8, 83.2, 78.2, 72.7, 71.5, 69.7, 68.5, 46.3, 45.7, 42.9, 41.1, 36.3, 30.3, 16.3. HRMS (ESI+): m/z calcd for $C_{27}H_{32}NaO_3$ $[M + Na]^+$, 427.2244; found, 427.2227.

((1*R,6*S**,7*S**,9*R**)-9-(Methoxymethyl)tricyclo[4.3.1.0^{7,9}]-decan-7-yl)methanol (33).** A round-bottom flask containing a solution of **8a** (200 mg, 0.97 mmol) and $Pd(OH)_2/C$ (20 wt %, 28.1 mg, 0.048 mmol) in anhydrous MeOH (10 mL) was evacuated and back-filled with H_2 (repeated three times). The resulting mixture was stirred at room temperature for 4 h, and then the volatiles were removed under reduced pressure and the crude was purified by column chromatography (cyclohexane/EtOAc 1/1) to afford the product as a colorless oil (204.0 mg, 0.97 mmol, yield quantitative). ^{1}H NMR (400 MHz, $CDCl_3$): δ 4.02 (dd, J = 11.6, 1.1 Hz, 1H), 3.79 (dd, J = 10.2, 1.0 Hz, 1H), 3.48 (d, J = 11.6 Hz, 1H), 3.37 (s, 3H), 3.27 (d, J = 10.1 Hz, 1H), 2.43−1.36 (m, 2H), 2.01−1.93 (m, 1H), 1.91−1.82 (m, 1H), 1.70−1.34 (m, 9H), 0.88 (dt, J = 4.7, 1.1 Hz, 1H), 0.52 (d, J = 4.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 73.6, 63.4, 58.8, 40.4, 39.8, 36.3, 34.7, 29.1, 29.1, 28.9, 25.1, 24.8, 18.4. HRMS (ESI+): m/z calcd for $C_{13}H_{22}NaO_2$ $[M + Na]^+$, 233.1512; found, 233.1511.

(*R)-1-((1*R**,6*S**,7*S**,9*R**)-9-(Methoxymethyl)tricyclo-[4.3.1.0^{7,9}]decan-7-yl)prop-2-yn-1-ol (34).** Dess−Martin periodinane (524.3 mg, 1.24 mmol) was added to a solution of **33** (200 mg, 0.95 mmol) in CH_2Cl_2 (10 mL). After the addition of 1 drop of water the resulting suspension was stirred at room temperature for 15 min and then washed with a 1/1 mixture of saturated solution of $Na_2S_2O_3$/Na_2CO_3 (20 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The product (**33**′) was obtained after filtration through a pad of silica gel as a colorless oil and directly submitted to the next step. ^{1}H NMR (500 MHz, $CDCl_3$): δ 9.44 (s, 1H), 3.86 (dd, J = 10.2, 1.3 Hz, 1H), 3.54 (d, J = 10.2 Hz, 1H), 3.39 (s, 3H), 2.66 (ddd, J = 7.3, 4.4, 2.7 Hz, 1H), 2.51−2.41 (m, 2H), 1.97−1.88 (m, 1H), 1.64−1.40 (m, 9H), 1.37 (dd, J = 4.9, 1.3 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 200.7, 71.6, 58.9, 45.5, 43.1, 39.5, 38.1, 30.2, 29.6, 27.8, 25.5, 24.3, 23.4. Ethynylmagnesium bromide (0.5 M in THF, 2.01 mL, 1.00 mmol) was added to a solution of aldehyde **33**′ (190 mg, 0.91 mmol) in anhydrous THF (9 mL) at 0 °C. After it was stirred at room temperature for 30 min, the reaction mixture was diluted with Et_2O (15 mL) and quenched by the addition of saturated NH_4Cl aqueous solution (50 mL). The aqueous layer was extracted with Et_2O (2 × 40 mL), the combined organic phases were dried over $MgSO_4$, filtered, and concentrated under reduced pressure, and the resulting crude was purified by column chromatography (cyclohexane/EtOAc 7/3) to afford **34** as a colorless oil (208.9 mg, 0.89 mmol, yield over two steps 98%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 4.87 (dd, J = 5.2, 2.2 Hz, 1H), 3.81 (d, J = 10.4 Hz, 1H), 3.70 (d, J = 10.3 Hz, 1H), 3.48 (d, J = 5.3 Hz, 1H), 3.36 (s, 3H), 2.51 (d, J = 2.2 Hz, 1H), 2.42 (ddd, J = 7.7, 5.3, 2.4 Hz, 1H), 2.31 (ddd, J = 7.8, 6.1, 1.9 Hz, 1H), 2.08−2.01 (m, 1H), 1.86−1.79 (m, 1H), 1.78−1.71 (m, 1H), 1.70−1.61 (m, 1H), 1.57−1.42 (m, 4H), 1.40−1.32 (m, 2H), 0.94 (d, J = 4.7 Hz, 1H), 0.82 (d, J = 4.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 84.5, 74.0, 72.8, 61.1, 58.4, 42.1, 41.5, 38.7, 35.8, 29.6, 29.1, 29.0, 25.2, 24.5, 16.4. HRMS (ESI+): m/z calcd for $C_{15}H_{22}NaO_2$ $[M + Na]^+$, 257.1512; found, 257.1514.

Synthesis of 4d,e. Dess-Martin periodinane (478.8 mg, 1.13 mmol) was added to a solution of **4b,c** (0.87 mmol) in CH_2Cl_2 (9 mL). After the addition of 1 drop of water, the resulting suspension was stirred at room temperature for 1 h and then washed with a 1/1 mixture of a saturated solution of $Na_2S_2O_3$/Na_2CO_3 (40 mL). The organic layer was dried over $MgSO_4$, filtered, and concentrated under reduced pressure. The product was obtained after purification by flash chromatography (cyclohexane/EtOAc 7/3).

1-((1R,6S*,7R*,9S*)-9-(Methoxymethyl)tricyclo[4.3.1.0^{7,9}]deca-2,4-dien-7-yl)prop-2-yn-1-one (**4d**).* Yellow oil (121.2 mg, 0.53 mmol, yield 61%). ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.32 (ddd, J = 11.4, 7.4, 1.1 Hz, 1H), 6.02 (ddd, J = 11.2, 7.7, 0.9 Hz, 1H), 5.79 (ddd, J = 11.5, 7.4, 0.8 Hz, 1H), 5.70 (ddd, J = 11.4, 7.4, 0.8 Hz, 1H), 4.02 (dd, J = 10.1, 1.5 Hz, 1H), 3.82 (d, J = 10.1 Hz, 1H), 3.42 (s, 3H), 3.26 (s, 1H), 3.12−3.06 (m, 1H), 2.91 (t, J = 7.0 Hz, 1H), 2.06−1.98 (m, 1H), 1.85 (dd, J = 13.2, 0.6 Hz, 1H), 1.34 (dd, J = 5.5, 1.4 Hz, 1H), 1.26 (d, J = 5.5 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 185.7, 136.9, 134.8, 125.5, 124.1, 82.0, 79.1, 71.4, 58.8, 52.3, 45.5, 41.7, 40.4, 25.6, 22.5. HRMS (ESI+): m/z calcd for $C_{15}H_{16}NaO_2$ $[M + Na]^+$, 251.1043; found, 251.1035.

1-((1R,6S*,7R*,9S*)-9-((Benzyloxy)methyl)tricyclo[4.3.1.0^{7,9}]-deca-2,4-dien-7-yl)prop-2-yn-1-one (**4e**).* Yellow oil (174.9 mg, 0.57 mmol, yield 66%). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42−7.34 (m, 4H), 7.34−7.29 (m, 1H), 6.32 (ddq, J = 11.3, 7.6, 0.7 Hz, 1H), 5.97 (ddq, J = 11.4, 7.5, 1.0 Hz, 1H), 5.75 (ddd, J = 11.3, 7.4, 0.8 Hz, 1H), 5.67 (ddd, J = 11.4, 7.3, 0.8 Hz, 1H), 4.61 (d, J = 11.9 Hz, 1H), 4.58 (d, J = 12.0 Hz, 1H), 4.10 (dd, J = 10.1, 1.5 Hz, 1H), 3.95 (d, J = 10.0 Hz, 1H), 3.11 (s, 1H), 3.07 (t, J = 7.1 Hz, 1H), 2.98 (t, J = 7.0 Hz, 1H), 2.02 (dtt, J = 13.0, 6.4, 1.3 Hz, 1H), 1.85 (d, J = 14.0 Hz, 1H), 1.35 (dd, J = 5.6, 1.4 Hz, 1H), 1.27 (d, J = 5.6 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 185.7, 138.5, 137.0, 134.7, 128.4, 127.8, 127.6, 125.5, 124.0, 81.7, 79.2, 73.0, 68.9, 52.6, 45.7, 41.8, 40.4, 25.5, 22.5. HRMS (ESI+): m/z calcd for $C_{21}H_{20}NaO_2$ $[M + Na]^+$, 327.1356; found, 327.1363.

Gold-Catalyzed Cyclizations of 1,6-Enynes 4d,e. Gold(I) complex **B** (3.1 mg, 0.002 mmol)[31] was added to a solution of **4d,e** (0.1 mmol) in ROH (1 mL) or a 2/1 dioxane/H_2O mixture (2 mL), and the resulting suspension was stirred at room temperature for the appointed time before the addition of 1 drop of Et_3N. Then the volatiles were removed under reduced pressure and purification by preparative TLC afforded the tetracyclic products **39**′/**39**″.

(1aR,2S*,3aS*,4S*,6aS*,7R*)-1a-((Benzyloxy)methyl)-7-methoxy-5-methylene-1a,2,3,3a,4,5-hexahydro-2,4-prop[1]-enocyclopropa[c]pentalen-6(1H)-one (**39a**′).* General procedure starting from **4e** and methanol. Reaction time: 1 h. Purification: cyclohexane/EtOAc 95/5 (eluted three times). White solid (15.1 mg, yield 45%). Mp: 59−61 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.28 (m, 5H), 6.14−6.07 (m, 2H), 5.72 (dd, J = 11.8, 7.2 Hz, 1H), 5.33 (dd, J = 2.2, 0.6 Hz, 1H), 4.58 (d, J = 11.9 Hz, 1H), 4.44 (d, J = 12.0 Hz, 1H), 3.82 (ddd, J = 7.3, 3.1, 0.7 Hz, 1H), 3.68 (dd, J = 10.0, 1.9 Hz, 1H), 3.54−3.48 (m, 1H), 3.44 (s, 3H), 3.07 (d, J = 9.9 Hz, 1H), 3.03 (t, J = 6.6 Hz, 1H), 2.89 (dd, J = 9.3, 7.2 Hz, 1H), 2.74 (d, J = 13.9 Hz, 1H), 1.87 (d, J = 5.7 Hz, 1H), 1.68 (dtd, J = 13.9, 6.9, 1.7 Hz, 1H), 1.52 (dd, J = 5.8, 1.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 201.7, 147.6, 140.4, 138.3, 128.4, 127.7, 127.7, 127.1, 118.0, 82.7, 73.1, 70.5, 56.6, 52.7, 47.3, 45.6, 42.4, 42.0, 31.5, 22.4. HRMS (ESI+): m/z calcd for $C_{22}H_{24}NaO_3$ $[M + Na]^+$, 359.1618; found, 359.1617.

(1aR,2R*,3aS*,4S*,6aS*,9S*)-1a-((Benzyloxy)methyl)-9-methoxy-5-methylene-1a,2,3,3a,4,5-hexahydro-4,2-prop[1]-enocyclopropa[c]pentalen-6(1H)-one (**39a**″).* General procedure starting from **4e** and methanol. Reaction time: 1 h. Purification: cyclohexane/EtOAc 95/5 (eluted three times). White solid (9.7 mg, yield 29%). Mp: 70−72 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40−7.29 (m, 5H), 5.92 (dd, J = 1.4, 0.7 Hz, 1H), 5.43 (ddt, J = 12.8, 4.7, 1.9 Hz, 1H), 5.34 (ddd, J = 12.9, 4.9, 0.9 Hz, 1H), 5.28 (dd, J = 1.3, 0.7 Hz, 1H), 4.60 (d, J = 11.9 Hz, 1H), 4.41 (d, J = 11.9 Hz, 1H), 3.90 (t, J = 4.0 Hz, 1H), 3.60 (t, J = 6.3 Hz, 1H), 3.52 (dd, J = 10.4, 1.8 Hz, 1H), 3.38 (s, 3H), 3.17 (d, J = 10.4 Hz, 1H), 2.83 (dt, J = 8.0, 2.6 Hz, 1H), 2.76 (t, J = 7.4 Hz, 1H), 2.29 (d, J = 14.4 Hz, 1H), 1.77 (d, J =

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5.4 Hz, 1H), 1.68−1.61 (m, 1H), 1.34 (dd, J = 5.5, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 202.1, 149.7, 138.1, 131.5, 128.4, 127.9, 127.8, 124.1, 115.5, 78.2, 73.1, 69.3, 56.9, 47.5, 47.1, 44.8, 43.6, 43.2, 26.7, 21.0. HRMS (ESI+): m/z calcd for $C_{22}H_{24}NaO_3$ $[M + Na]^+$, 359.1618; found, 359.1616.

(1aR,2S*,3aS*,4S*,6aS*,7R*)-7-(Allyloxy)-1a-((benzyloxy)-methyl)-5-methylene-1a,2,3,3a,4,5-hexahydro-2,4-prop[1]-enocyclopropa[c]pentalen-6(1H)-one (**39b′**).* General procedure starting from **4e** and allyl alcohol. Reaction time: 1.5 h. Purification: cyclohexane/EtOAc 95/5 (eluted three times). White solid (15.9 mg, yield 44%). Mp: 44−46 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39−7.28 (m, 5H), 6.13−6.07 (m, 2H), 5.98 (ddt, J = 17.2, 10.3, 5.6 Hz, 1H), 5.68 (dd, J = 11.7, 7.3 Hz, 1H), 5.34 (dq, J = 17.1, 1.4 Hz, 1H), 5.31−5.29 (m, 1H), 5.23 (dq, J = 10.4, 1.4 Hz, 1H), 4.58 (d, J = 11.9 Hz, 1H), 4.44 (d, J = 11.8 Hz, 1H), 4.15 (ddt, J = 12.6, 5.5, 1.5 Hz, 1H), 4.07 (ddt, J = 12.6, 5.7, 1.4 Hz, 1H), 3.97 (ddd, J = 7.3, 3.1, 0.6 Hz, 1H), 3.68 (dd, J = 10.0, 1.8 Hz, 1H), 3.50 (dq, J = 9.2, 2.5 Hz, 1H), 3.06 (d, J = 10.0 Hz, 1H), 3.06 (t, J = 6.7 Hz, 1H), 2.90 (dd, J = 9.3, 7.2 Hz, 1H), 2.80 (d, J = 13.9 Hz, 1H), 1.86 (d, J = 5.7 Hz, 1H), 1.69 (dtd, J = 13.9, 6.9, 1.7 Hz, 1H), 1.52 (dd, J = 5.7, 1.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 201.7, 147.7, 140.3, 138.3, 135.1, 128.4, 127.7, 127.7, 127.3, 118.0, 117.2, 80.1, 73.1, 70.5, 69.7, 52.8, 47.3, 46.0, 42.4, 42.0, 31.6, 22.4. HRMS (ESI+): m/z calcd for $C_{24}H_{26}NaO_3$ $[M + Na]^+$, 385.1774; found, 385.1780.

(1aR,2R*,3aS*,4S*,6aS*,9S*)-9-(Allyloxy)-1a-((benzyloxy)-methyl)-5-methylene-1a,2,3,3a,4,5-hexahydro-4,2-prop[1]-enocyclopropa[c]pentalen-6(1H)-one (**39b″**).* General procedure starting from **4e** and allyl alcohol. Reaction time: 1.5 h. Purification: cyclohexane/EtOAc 95/5 (eluted three times). White solid (15.1 mg, yield 42%). Mp: 67−69 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39−7.29 (m, 5H), 6.00−5.86 (m, 1H), 5.93−5.91 (m, 1H), 5.42 (ddt, J = 12.8, 4.6, 1.8 Hz, 1H), 5.37−5.31 (m, 1H), 5.29−5.27 (m, 1H), 5.28 (dq, J = 17.2, 1.6 Hz, 1H), 5.18 (dq, J = 10.3, 1.4 Hz, 1H), 4.57 (d, J = 11.8 Hz, 1H), 4.41 (d, J = 11.8 Hz, 1H), 4.13−4.04 (m, 2H), 3.99 (ddt, J = 12.8, 5.8, 1.4 Hz, 1H), 3.61 (t, J = 6.0 Hz, 1H), 3.52 (dd, J = 10.4, 1.8 Hz, 1H), 3.16 (d, J = 10.4 Hz, 1H), 2.84−2.79 (m, 1H), 2.77 (td, J = 7.1, 1.1 Hz, 1H), 2.36 (d, J = 14.4 Hz, 1H), 1.77 (d, J = 5.4 Hz, 1H), 1.71−1.59 (m, 1H), 1.33 (dd, J = 5.4, 1.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 202.1, 149.7, 138.1, 135.1, 131.5, 128.4, 127.9, 127.7, 124.5, 117.0, 115.5, 76.0, 73.2, 70.2, 69.5, 47.4, 47.1, 44.9, 43.8, 43.6, 26.8, 21.0. HRMS (ESI+): m/z calcd for $C_{24}H_{26}NaO_3$ $[M + Na]^+$, 385.1774; found, 385.1780.

(1aR,2S*,3aS*,4S*,6aS*,7R*)-7-Hydroxy-1a-(methoxymethyl)-5-methylene-1a,2,3,3a,4,5-hexahydro-2,4-prop[1]enocyclopropa-[c]pentalen-6(1H)-one (**39c′**) and (1aR*,2R*,3aS*,4S*,6aS*,9S*)-9-hydroxy-1a-(methoxymethyl)-5-methylene-1a,2,3,3a,4,5-hexahydro-4,2-prop[1]enocyclopropa[c]pentalen-6(1H)-one (**39c″**).* General procedure starting from **4d** and water. Reaction time: 3 h. Purification: cyclohexane/EtOAc 6/4 (eluted twice). Colorless oil (15.5 mg, yield 63%). **39c′**:**39c″** = 1:2. ^{1}H NMR (400 MHz, $CDCl_3$): **39c′**, δ 6.17 (ddd, J = 11.6, 6.8, 1.6 Hz, 1H), 6.11 (dd, J = 2.5, 0.6 Hz, 1H), 5.82 (dd, J = 11.6, 7.3 Hz, 1H), 5.40−5.32 (m, 1H), 4.38 (dd, J = 7.3, 3.1 Hz, 1H), 3.59 (dd, J = 10.1, 1.9 Hz, 1H), 3.47 (dd, J = 9.3, 2.7 Hz, 1H), 3.35 (s, 3H), 3.05−2.91 (m, 2H), 2.93 (d, J = 10.1 Hz, 1H), 2.75 (d, J = 14.2 Hz, 1H), 1.86 (d, J = 5.7 Hz, 1H), 1.79−1.66 (m, 1H), 1.50 (dd, J = 5.8, 1.9 Hz, 1H); **39c″**, δ 5.94 (dd, J = 1.4, 0.6 Hz, 1H), 5.49 (ddt, J = 12.7, 4.9, 2.0 Hz, 1H), 5.39−5.33 (m, 1H), 5.30 (dd, J = 1.4, 0.6 Hz, 1H), 4.57 (t, J = 4.1 Hz, 1H), 3.62 (t, J = 6.6 Hz, 1H), 3.45 (dd, J = 10.5, 1.8 Hz, 1H), 3.33 (s, 3H), 3.03 (d, J = 10.5 Hz, 1H), 2.79 (td, J = 7.2, 1.2 Hz, 1H), 2.67 (dt, J = 8.0, 2.7 Hz, 1H), 2.30 (d, J = 14.5 Hz, 1H), 1.76 (d, J = 5.5 Hz, 1H), 1.74−1.64 (m, 1H), 1.32 (dd, J = 5.5, 1.8 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): **39c′** + **39c″**, δ 202.0, 201.6, 149.4, 147.5, 139.8, 131.2, 129.2, 126.0, 118.4, 115.7, 74.5, 72.8, 71.7, 69.0, 58.9, 58.8, 52.3, 48.2, 47.4, 47.2, 46.7, 44.7, 43.5, 42.3, 41.9, 32.1, 29.7, 26.4, 21.9, 20.9. HRMS (ESI+): m/z calcd for $C_{15}H_{18}NaO_3$ $[M + Na]^+$, 269.1148; found, 269.1139.

(1aR,2S*,3aS*,4S*,6aS*,7R*)-1a-((Benzyloxy)methyl)-7-hydroxy-5-methylene-1a,2,3,3a,4,5-hexahydro-2,4-prop[1]-enocyclopropa[c]pentalen-6(1H)-one (**39d′**) and (1aR*,2R*,3aS*,4S*,6aS*,9S*)-1a-((benzyloxy)methyl)-9-hydroxy-5-methylene-1a,2,3,3a,4,5-hexahydro-4,2-prop[1]enocyclopropa[c]pentalen-6(1H)-one (**39d″**).* General procedure starting from **4e** and water. Reaction time: 5 h. Purification: cyclohexane/EtOAc 6/4 (eluted twice). Colorless oil (18.6 mg, yield 58%). **39d′**:**39d″** = 1:4. ^{1}H NMR (500 MHz, $CDCl_3$): **39d′** δ 7.38−7.31 (m, 5H), 6.10 (dd, J = 2.5, 0.6 Hz, 1H), 6.08 (ddd, J = 11.6, 6.9, 1.6 Hz, 1H), 5.76 (dd, J = 11.7, 7.3 Hz, 1H), 5.38−5.31 (m, 1H), 4.56 (d, J = 11.9 Hz, 1H), 4.44 (d, J = 11.9 Hz, 1H), 4.38−4.34 (m, 1H), 3.68 (dd, J = 10.0, 1.8 Hz, 1H), 3.47 (dq, J = 9.2, 2.1 Hz, 1H), 3.08 (d, J = 9.8 Hz, 1H), 3.05 (d, J = 6.7 Hz, 1H), 2.96 (dd, J = 9.1, 7.2 Hz, 1H), 2.74 (d, J = 14.1 Hz, 1H), 1.87 (d, J = 5.8 Hz, 1H), 1.79−1.74 (m, 1H), 1.52 (dd, J = 5.7, 1.8 Hz, 1H); **39d″**, δ 7.39−7.29 (m, 6H), 5.94 (dd, J = 1.4, 0.6 Hz, 1H), 5.42 (ddt, J = 12.7, 4.7, 1.9 Hz, 1H), 5.34 (ddt, J = 12.7, 5.2, 0.9 Hz, 1H), 5.29 (dd, J = 1.3, 0.6 Hz, 1H), 4.55 (d, J = 12.0 Hz, 1H), 4.52 (s, 1H), 4.43 (d, J = 11.8 Hz, 1H), 3.64−3.59 (m, 1H), 3.53 (dd, J = 10.5, 1.7 Hz, 1H), 3.20 (d, J = 10.5 Hz, 1H), 2.82−2.77 (m, 1H), 2.73−2.69 (m, 1H), 2.29 (d, J = 14.5 Hz, 1H), 1.77 (d, J = 5.4 Hz, 1H), 1.69 (dddd, J = 14.8, 8.3, 7.1, 1.5 Hz, 1H), 1.34 (dd, J = 5.5, 1.7 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): **39d′** + **39d″**, δ 201.9, 149.4, 139.9, 138.0, 131.1, 129.8, 128.4, 128.4, 127.8, 127.74, 127.7, 127.7, 127.7, 126.1, 118.3, 115.7, 74.5, 73.2, 73.1, 70.5, 69.5, 69.1, 52.5, 48.2, 47.4, 47.3, 46.8, 45.0, 43.5, 42.4, 42.0, 32.1, 26.4, 22.1, 21.0 (2 peaks missing due to overlapping). HRMS (ESI+): m/z calcd for $C_{21}H_{22}NaO_3$ $[M + Na]^+$, 345.1461; found, 345.1459.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.joc.6b01607.

Spectral data for all new compounds and Cartesian coordinates of the optimized structures (PDF)
X-ray crystallography data for compound **19** (CIF)
X-ray crystallography data for compound **32a** (CIF)

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Notes

The authors declare no competing financial interest.

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(24) CCDC 1489805 (**19**) and CCDC 1489806 (**32a**) contain supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.
(25) Aldehydes **9b,c** were prepared following a route analogous to that for the preparation of **9a** shown in Scheme 2. See the Experimental Section.
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(33) This product decomposes under ambient conditions and therefore either was directly used in the next step or was stored under argon in darkness at −5 °C.

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