

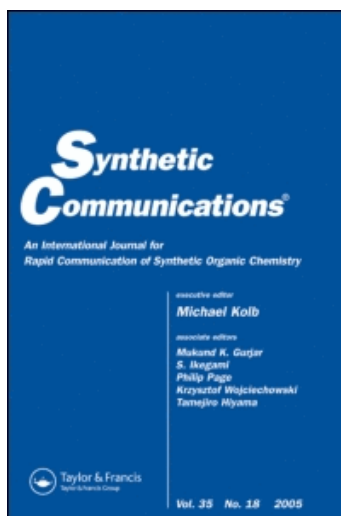
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Tributyltin Hydride-Mediated Synthesis of Bicyclic Carbocycles Initiated by $\text{Et}_3\text{B}/\text{O}_2$

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TRIBUTYLTIN HYDRIDE-MEDIATED SYNTHESIS OF BICYCLIC CARBOCYCLES INITIATED BY Et₃B/O₂

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Synthesis of bicyclic carbocycles involving tributyltin hydride-mediated α -carbonyl radical cyclization reaction at room temperature has been reported.

Keywords: Bicyclic carbocycles; radical cyclization; tributyltin hydride; triethylborane

INTRODUCTION

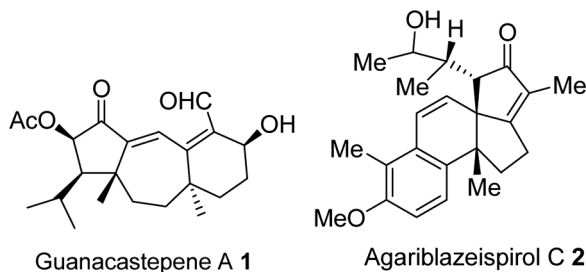
The synthesis of highly functionalized bicyclic systems is an area of continued interest to synthetic chemists because of the existence of these frameworks in many naturally occurring compounds.^[1] The use of triethylborane in air as an initiator of radical-based processes has become increasingly popular in recent years.^[2] Because radical reactions can be initiated by this reagent at ambient temperature, it has found widespread application, particularly in the stereoselective addition of alkyl radicals to double bonds. To widen the scope of this methodology, the α -carbonyl radical cyclization reaction was planned using triethylborane as an initiator. We have recently reported^[3] an efficient synthesis of angularly fused carbocycles via tandem radical cyclization of α -carbonyl radical generated using azobisisobutyronitrile (AIBN) as the radical initiator. Herein, we report the results on the synthesis of bicyclic vinylic ketones, bicyclic skeleton of guanacastepene **1**,^[4] and agariblaizeispirol **C 2**^[5] using Et₃B/O₂^[6] as the radical initiator at room temperature (Scheme 1).

RESULTS AND DISCUSSION

In continuation of our studies to develop a facile and efficient method to synthesize the bicyclic core skeleton of various natural products, the Bu₃SnH-mediated radical cyclization of α -bromo cycloalkanones are initiated. To this end, the CuI-promoted 1,4-addition of 4-(trimethylsilyl)-3-butyne magnesium bromide to 3-methyl-2-cyclohexen-1-one **3** followed by trapping of the resulting enolate with chlorotrimethylsilane (TMSCl) afforded silyl-enol ether **4** in 86% yield, which on

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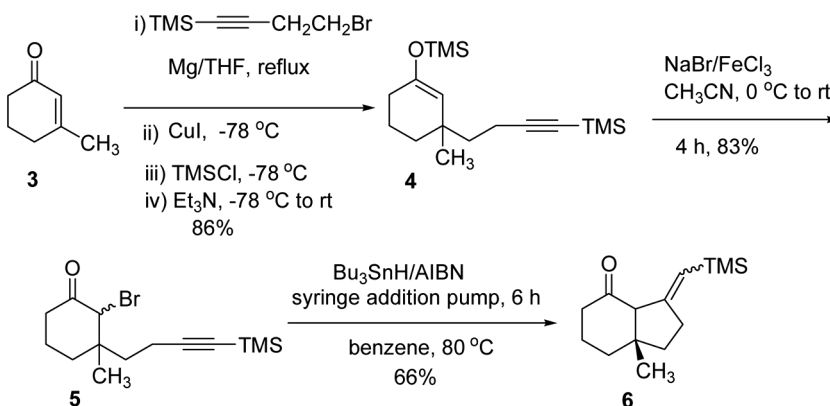
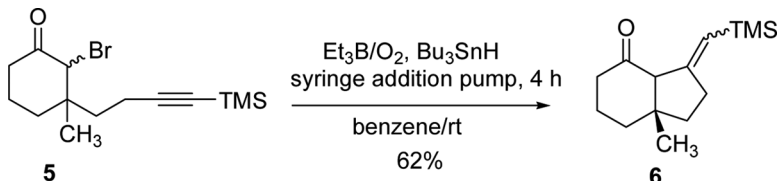
Address correspondence to Arasambattu K. Mohanakrishnan, Department of Organic Chemistry, University of Madras, Guindy Campus, Chennai 600 025, India. E-mail: mohan_67@hotmail.com

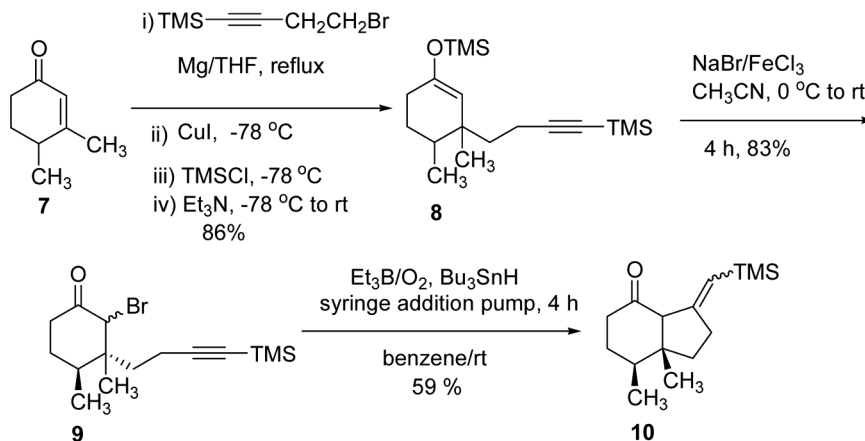


Scheme 1. Natural products containing tricyclic carbocycles.

bromination using $\text{NaBr}/\text{FeCl}_3$ ^[7] delivered bromo compound **5** in good yield. Radical cyclization of **5** was effected by $\text{Bu}_3\text{SnH}/\text{AIBN}$ via syringe addition pump for 6 h in dry benzene at reflux to yield 6–5 bicyclic product **6** in 66% yield (Scheme 2).

During the investigation of radical reactions at room temperature, we have observed bicyclic product formation when $\text{Et}_3\text{B}/\text{O}_2$ was used as the radical initiator. Typically, when bromo compound **5** was treated with tributyltin hydride using $\text{Et}_3\text{B}/\text{O}_2$ as a radical initiator via syringe addition pump for 4 h, it afforded the expected bicyclic product **6** in 62% yield (Scheme 3).

Scheme 2. Preparation of carbocycle **6** using tributyltin hydride and AIBN.Scheme 3. Preparation of carbocycle **6** using tributyltin hydride and triethylborane.

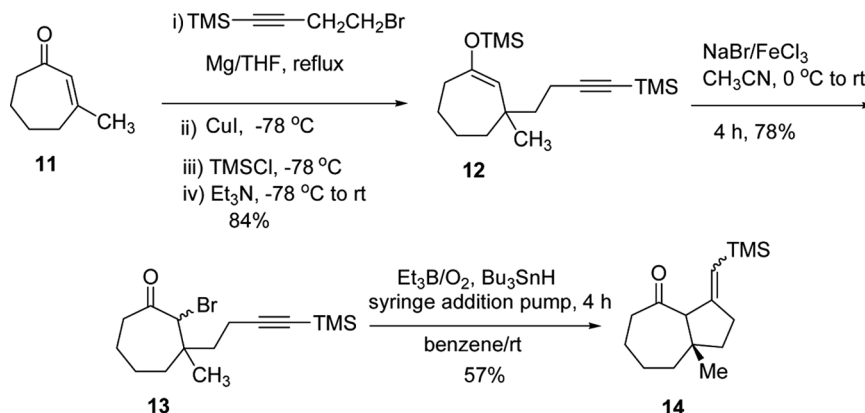


Scheme 4. Preparation of carbocycle 10.

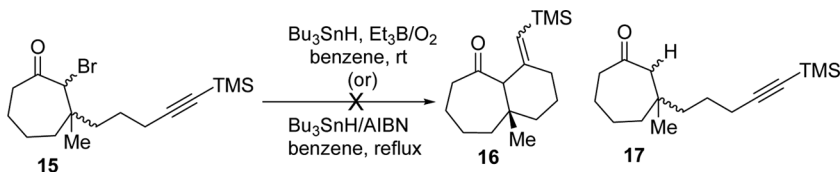
Encouraged by our success on 5-*exo-dig* mode of radical cyclization of **5**, we then examined the similar reaction of bromo compound **9**, which furnished the desired radical cyclized product **10** at room temperature using $\text{Et}_3\text{B/O}_2$ as a radical initiator (Scheme 4).

Having established a method to construct the 6-5 bicyclic system, next we turned our attention to the synthesis of 7-5 bicyclic core unit of guanacastepene. The required enone **11** was prepared using a known procedure.^[8] The CuI -induced 1,4-addition of Grignard reagent to enone **11** followed by bromination using NaBr/FeCl_3 gave the bromo compound **13** in 78% yields. To our delight, upon treatment of bromo compound **13** with tributyltin hydride and $\text{Et}_3\text{B/O}_2$ in benzene via syringe addition pump for 4 h, radical cyclization occurred smoothly to give the 7-5 bicyclic system of guanacastepene **14** in 57% yield (Scheme 5).

Since the natural product, guanacastepene, has a 7-6 bicyclic core, the required α -bromo ketone **15** was prepared using an established procedure.^[9] Surprisingly, the radical cyclizations of bromo compound **15** using tributyltin hydride- $\text{Et}_3\text{B/O}_2$ at

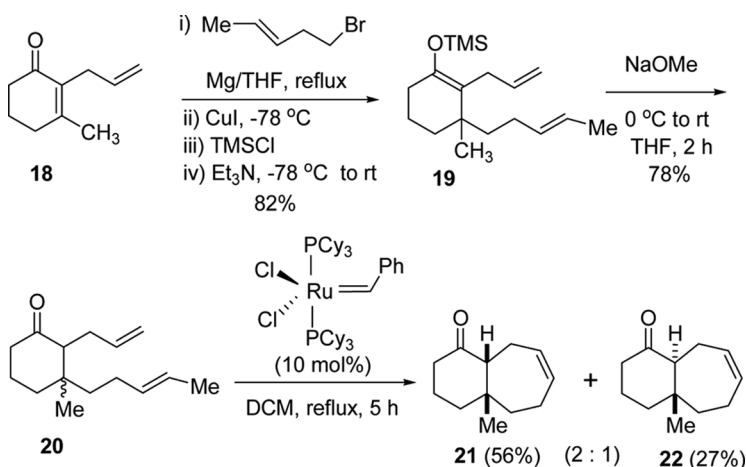


Scheme 5. Preparation of carbocycle 14.

Scheme 6. Attempted preparation of carbocycle **16**.

room temperature or tributyltin hydride–AIBN at reflux were futile. Even though the formation of a six-member ring under radical condition was reported^[10] by Sha et al., in our case in both the conditions the expected radical cyclization product **16** was not at all observed, and only the reduction product **17** was isolated (Scheme 6).

It should be noted that the bromo compounds **5**, **9**, and **13** underwent a smooth radical cyclization at room temperature using $\text{Et}_3\text{B}/\text{O}_2$ as a radical initiator to afford the respective bicyclic compounds in almost comparable yields. However, all attempts to prepare the 7-6 bicyclic system **16** were unsuccessful; only a radical quenched product was obtained. Therefore, we devised another synthetic route for the synthesis of 7-6 bicyclic system using a ring-closing metathesis approach. In recent years, olefin metathesis has emerged as a powerful tool for carbon–carbon bond formation and has enabled the synthesis of rings of different sizes.^[11] The requisite enone **18** was prepared from 1,3-cyclohexanedione and allyl bromide by adopting Stealey et al.'s^[12] procedure. The established CuI-promoted 1,4-addition of enone **18** using the procedure as mentioned afforded the silyl-enol ether **19** in 82% yield. Desilylation of **19** using NaOMe in tetrahydrofuran (THF) at room temperature furnished the keto compound **20** as a pale yellow liquid. Treatment of diene **20** with 10 mol% of Grubb's catalyst I in refluxing dichloromethane (DCM) for 5 h followed by column chromatographic purification furnished 6-7 bicyclic products **21** and **22** (2:1) in 56% and 27% yields, respectively (Scheme 7).

Scheme 7. Preparation of carbocycles **21** and **22**.

In conclusion, we have presented radical cyclization methodology for the synthesis of five- and six-membered bicyclic carbocycles via the intermediacy of α -carbonyl radical generated using tributyltin hydride– $\text{Et}_3\text{B}/\text{O}_2$ at room temperature. The synthesis of 7–6 bicyclic system of guanacastepene was achieved using the ring closing metathesis (RCM) approach. We hope the radical cyclization methodology performed herein at room temperature will be useful in the total synthesis of carbocyclic natural products.

EXPERIMENTAL

All melting points were uncorrected. Reagents were purchased from commercial sources and used as received without purification. Solvents were dried by standard procedures. Column chromatography was carried on silica gel (grade 60, mesh size 230–400, Merck). Infrared (IR) spectra were recorded on a Shimadzu Fourier transform (FT)–IR 8300 instrument. ^1H and ^{13}C NMR spectra were recorded in CDCl_3 using tetramethylsilane (TMS) as an internal standard on a Jeol 400 or 500 spectrometer at 400 and 100 or 125 MHz and on a Bruker-300 instrument at 75 MHz, respectively. Mass spectra were recorded on a Jeol DX 303 HF spectrometer. High-resolution mass analyses were performed using the electrospray ionization (ESI) technique.

Representative Procedure for the Preparation of 4-(Trimethylsilyl)but-3-ynyl)cyclo-hex-1-enyloxy)trimethylsilane (4)

A solution of (4-bromobut-1-ynyl)trimethylsilane (3.71 g, 18.18 mmol) and 1,2-dibromoethane (0.1 mL) in dry THF (10 mL) was added to a stirred suspension of Mg turnings (884 mg, 36.36 mmol) in THF (10 mL) under nitrogen at reflux with a syringe pump (1 h). After the addition, the reaction mixture was heated to reflux for 1 h to ensure the completion of the Grignard formation. It was then diluted with dry THF (30 mL) and cooled to -78°C . CuI (3.46 g, 18.18 mmol) was added. The reaction mixture was stirred for 30 min. 3-Methyl-2-cyclohexen-1-one **3** (800 mg, 7.27 mmol) in dry THF (5 mL) was added dropwise to this mixture, followed by chlorotrimethylsilane (1.1 mL, 8.72 mmol) and triethylamine (1.31 mL, 9.45 mmol). The reaction mixture was warmed to room temperature, stirred for 12 h, and quenched with saturated NaHCO_3 solution (10 mL). The resulting black precipitate was filtered off and washed with hexane (40 mL). The combined organic layer was washed with NaHCO_3 solution (2×20 mL) and dried (K_2CO_3). Filtration followed by removal of solvent gave crude silyl-enol ether **4** as a pale yellow liquid (1.93 g, 86%). Crude product **4** was used for the next step without further purification. IR (KBr): 2175 (alkyne), 1612 (alkene) cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ 4.41 (s, 1H, $-\text{CH}$), 2.24–1.97 (m, 4H, $-\text{CH}_2$), 1.78–1.48 (m, 6H, $-\text{CH}_2$), 0.98 (s, 3H, $-\text{CH}_3$), 0.17 (s, 9H, $-\text{CH}_3$), 0.14 (s, 9H, $-\text{CH}_3$). ^{13}C NMR (CDCl_3 , 100 MHz): δ 138.4, 114.6, 107.3, 84.1, 39.5, 36.7, 35.2, 30.4, 26.8, 19.1, 15.3, 0.62, 0.09. Mass (m/z) % 308 (M^+ , 16), 293 (21), 243 (18), 184 (28), 163 (54), 113 (62), 82 (100).

Representative Procedure for the Preparation of 2-Bromo-3-methyl-3-(4-trimethylsilyl-3-butynyl)-1-cyclohexanone (**5**)

NaBr (535 mg, 5.19 mmol) was added to a solution of FeCl₃ (1.68 g, 10.38 mmol) in acetonitrile (20 mL) and stirred at 0 °C for 15 min. To this, a solution of silyl-enol ether **4** (1.6 g, 5.19 mmol) in acetonitrile (10 mL) was added dropwise at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred for 4 h. It was then quenched (consumption of starting material indicated by TLC) with saturated NH₄Cl solution, and reaction mixture was extracted with Et₂O (2 × 20 mL). The organic layer was separated and washed with saturated Na₂S₂O₃ (2 × 10 mL) solution and water (20 mL) and then dried (Na₂SO₄). Removal of solvent followed by flash-column chromatographic purification (0.5% ethyl acetate in hexane to 1% ethyl acetate in hexane) afforded bromo compound **5** (1.36 g, 83%) as a pale yellow liquid. IR (KBr): 2175 (alkyne), 1710 (CO), cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 4.42 and 4.22 (2s, 1H, -CH), 2.24–2.13 (m, 4H, -CH₂), 1.89–1.76 (m, 2H, -CH₂), 1.72–1.52 (m, 4H, -CH₂), 0.96 and 0.92 (2s, 3H, -CH₃), 0.11 and 0.09 (2s, 9H, -CH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 206.5, 205.3, 107.6, 105.2, 86.5, 85.3, 54.2, 49.1, 46.5, 41.7, 41.2, 36.4, 35.8, 32.4, 32.7, 26.9, 25.2, 21.5, 20.3, 19.1, 15.4, 15.2, 0.13, 0.08. (¹H & ¹³C NMR signals are more because of the diastereomeric mixture.) Mass (*m/z*) % 300 [M - 15]⁺, (13), 298 (13), (25), 284 (21), 223 (35), 175 (23), 134 (54), 82 (100).

Radical Cyclization Using Bu₃SnH/AIBN (7aS*)-Octahydro-7a-methyl-3-((trimethylsilyl)methylene)inden-4-one (**6**)

A solution of Bu₃SnH (0.51 mL, 1.90 mmol) in dry benzene (10 mL) containing AIBN (39 mg, 0.24 mmol) was added dropwise with a syringe pump to a solution of bromo compound **5** (500 mg, 1.59 mmol) in dry benzene (100 mL) under nitrogen at reflux for 6 h. After addition, the reaction mixture was heated at reflux for 1 h to ensure the completion of radical cyclization and then cooled to room temperature. Benzene was removed in vacuo, and the residue was dissolved in Et₂O (20 mL). A saturated KF solution (20 mL) was added. The resulting mixture was stirred at room temperature for 6 h. Then the organic layer was separated and washed with saturated NaHCO₃ solution (2 × 10 mL) followed by brine (2 × 10 mL) and dried (MgSO₄). Removal of solvent followed by flash column chromatographic purification (1% ethyl acetate in hexane to 2% ethyl acetate in hexane) afforded bicyclic product **6** as a viscous liquid (248 mg, 66%). IR (KBr): 1705 (CO), 1613 (alkene) cm⁻¹. ¹H NMR (CDCl₃, 300 MHz): δ 5.84 and 5.27 (2s, 1H, -CH), 2.89 (s, 1H, -CH), 2.52–2.16 (m, 4H, -CH₂), 1.87–1.52 (m, 4H, -CH₂), 1.42–1.25 (m, 2H, -CH₂), 1.10 and 1.05 (2s, 3H, -CH₃), 0.14 and 0.11 (2s, 9H, -CH₃). ¹³C NMR (CDCl₃, 75 MHz): δ 212.8, 212.3, 160.1, 159.6, 123.9, 123.6, 70.9, 65.0, 45.5, 43.3, 42.3, 41.8, 39.3, 38.6, 33.5, 30.6, 27.4, 25.9, 23.6, 22.6, 19.3, 16.9, 0.10, 0.4. (¹H & ¹³C NMR signals are more because of the diastereomeric mixture.) Mass (*m/z*) % 236 (M⁺, 25), 221 (34), 182 (27), 154 (21), 125 (58), 82 (100).

General Procedure for Radical Cyclization Using Bu₃SnH and Et₃B/O₂ (7aS*)Octahydro-7a-methyl-3-((trimethylsilyl)methylene)inden-4-one (6)

A solution of bromo compound **5** (500 mg, 1.59 mmol) in dry benzene (30 mL) was placed in a two-necked flask under oxygen atmosphere. To this, a 1 M solution of Et₃B in THF (1.1 mL, 2.38 mmol) was added, and then oxygen gas was bubbled for 5 min. A solution of Bu₃SnH (0.64 mL, 2.38 mmol) in dry benzene (10 mL) was added via syringe pump over a period of 4 h and stirred at room temperature for additional 1 h. Then the organic layer was separated and washed with saturated NaHCO₃ solution (2 × 10 mL) followed by brine (2 × 10 mL) and dried (MgSO₄). Removal of solvent followed by flash-column chromatographic purification (1% ethyl acetate in hexane to 2% ethyl acetate in hexane) afforded bicyclic product **6** as a viscous liquid (0.23 g, 62%).

3,4-Dimethyl-3-(4-(trimethylsilyl)but-3-ynyl)cyclohex-1-enyl)trimethylsilane (8)

The 1,4-addition was performed using enone **7** (750 mg, 6 mmol), Grignard reagent [prepared from Mg (725 mg, 30.24 mmol), 4-bromo-1-trimethylsilyl-1-butyne (3.1 g, 15.10 mmol)], CuI (2.87 g, 15.1 mmol), TMSCl (0.92 mL, 7.30 mmol), and Et₃N (1.1 mL, 7.86 mmol) following the same procedure as that of **4** to afford crude silyl-enol ether **8** (1.7 g, 86%) as a thick liquid. IR (KBr): 2173 (alkyne) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): 4.50 (s, 1H, -CH), 2.20–1.86 (m, 3H, -CH₂), 1.65–1.50 (m, 4H, -CH₂), 1.42–1.34 (m, 2H, -CH₂), 0.78 (d, *J* = 5.3 Hz, 3H, -CH₃), 0.76 (s, 3H, -CH₃), 0.09 (s, 9H, -CH₃), 0.08 (s, 9H, -CH₃). Mass (*m/z*) %: 322 (M⁺, 15), 307 (24), 274 (19), 231 (34), 73 (100).

(7S*,7aR)-Octahydro-7,7a-dimethyl-3-((trimethylsilyl)methylene)inden-4-one (10)

Radical cyclization of **9** (500 mg, 1.51 mmol) was performed using Bu₃SnH (0.61 mL, 2.27 mmol) and 1 M solution of Et₃B in THF (1.7 mL, 2.27 mmol) following the same procedure as that of **6** to afford bicyclic product **10** (224 mg, 59%) as a viscous liquid. IR (KBr): 1707 (-CO-), 1612 (alkene) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 5.88 and 5.35 (2s, 1H, -CH), 2.94 (s, 1H, -CH), 2.56–2.23 (m, 4H, -CH₂), 1.92–1.37 (m, 5H, -CH₂ & -CH), 1.18 (2d, *J* = 5.3 Hz, 3H, -CH₃), 1.13 and 1.07 (2s, 3H, -CH₃), 0.15 and 0.12 (2s, 9H, -CH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 213.4, 212.8, 161.3, 160.5, 124.6, 123.9, 71.4, 66.2, 45.8, 44.1, 43.5, 42.1, 39.7, 38.3, 34.8, 31.3, 28.2, 26.5, 24.1, 23.8, 20.2, 19.4, 18.7, 17.4, 0.11, 0.05. (¹H & ¹³C NMR signals are more because of the diastereomeric mixture.) Mass (*m/z*) % 250 (M⁺, 25), 235 (28), 220 (38), 185 (22), 163 (24), 136 (43), 82 (100).

Trimethyl(3-methyl-3-(4-(trimethylsilyl)but-3-ynyl)cyclohept-1-enyl)silane (12)

The 1,4-addition was performed using enone **11** (650 mg, 5.24 mmol), Grignard reagent [prepared from Mg (630 mg, 26.20 mmol), 4-bromo-1-trimethylsilyl-1-butyne

(2.68 g, 13.10 mmol)], CuI (2.50 g, 13.10 mmol), TMSCl (0.80 mL, 6.30 mmol), and Et₃N (0.95 mL, 6.81 mmol) following the same procedure as that of **4** to afford crude silyl-enol ether **12** (1.42 g, 84%) as a thick liquid. IR (KBr): 2174 (alkyne), 1616 (alkene) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 4.39 (s, 1H, -CH), 2.34–2.12 (m, 4H, -CH₂), 1.91–1.72 (m, 6H, -CH₂), 1.64–1.48 (m, 2H, -CH₂), 0.96 (s, 3H, -CH₃), 0.18 (s, 9H, -CH₃), 0.13 (s, 9H, -CH₃). ¹³C NMR (125.7 MHz, CDCl₃): δ 126.1, 116.3, 107.5, 85.1, 39.7, 37.5, 36.8, 31.8, 28.4, 26.2, 19.8, 15.2, 0.86, 0.22. MS (EI) *m/z* (%): 322 (M⁺, 16), 307 (11), 226 (29), 198 (14), 158 (23), 73 (100). Crude product **12** was used for the next step without further purification.

2-Bromo-3-methyl-3-(4-trimethylsilyl-3-butynyl)-1-cycloheptanone (**13**)

Bromination using compound **12** (1.30 g, 4.03 mmol), NaBr (415 mg, 4.03 mmol), and FeCl₃ (1.31 g, 8.07 mmol) followed the same procedure as that of **5** to afford the bromo compound **13** (1.03 mg, 78%) as a yellow liquid. IR (KBr): 2173 (alkyne), 1706 (CO) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 4.35 & 4.26 (2s, 1H, -CH), 2.51–2.27 (m, 2H, -CH₂), 2.21–2.07 (m, 4H, -CH₂), 1.92–1.78 (m, 2H, -CH₂), 1.74–1.35 (m, 4H, -CH₂), 0.98 and 0.91 (2s, 3H, -CH₃), 0.16 and 0.12 (2s, 9H, -CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 205.6, 204.8, 108.2, 107.3, 86.3, 85.2, 72.4, 71.7, 71.1, 70.3, 58.5, 54.3, 49.1, 43.2, 38.8, 30.6, 29.7, 28.6, 25.3, 22.2, 19.6, 19.0, 18.5, 17.6, 0.14, 0.09. MS (EI) *m/z* (%): 330 ([M + 2]⁺, 8), 328 (M⁺, 8), 304 (6), 231 (22), 193 (4), 153 (23), 73 (100).

(8aS^{*})-Octahydro-8a-methyl-3-(trimethylsilyl)methyleneazulen-4(5*H*)-one (**14**)

Radical cyclization of **13** (800 mg, 2.43 mmol) was performed using Bu₃SnH (1.1 mL, 3.65 mmol) and 1 *M* solution of Et₃B in THF (2.15 mL, 3.65 mmol) following the same procedure as that of **6** to afford bicyclic product **14** (347 mg, 57%) as a viscous liquid. IR (film) 1701 (CO), 1613 (alkene) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 5.63 & 5.26 (2s, 1H, -CH), 3.54 & 3.30 (2s, 1H, -CH), 2.42–2.38 (m, 4H, -CH₂), 1.72–1.59 (m, 6H, -CH₂), 1.48–1.45 (m, 2H, -CH₂), 1.07 (s, 3H, -CH₃), 0.12 & 0.07 (2s, 9H, -CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 212.3, 212.1, 160.0, 159.5, 123.9, 123.6, 70.9, 65.0, 45.5, 43.3, 42.3, 41.8, 39.3, 38.6, 37.7, 37.5, 34.5, 31.0, 27.5, 23.6, 22.6, 22.5, 19.3, 16.8, 0.36, 0.16. HRMS: calcd. for C₁₅H₂₆OSi 250.1753; found 250.1762.

3-Methyl-3-(5-(trimethylsilyl)pent-4-ynyl)cycloheptanone (**17**)

Radical cyclization of **15** (750 mg, 2.19 mmol) was performed using Bu₃SnH (0.71 mL, 2.68 mmol) and 1 *M* solution of Et₃B in THF following the same procedure as that of **6** to afford radical quenched product as a viscous liquid (0.35 g, 60%). IR (KBr): 2175 (alkyne), 1701 (CO) cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 2.56–2.48 (m, 2H, -CH₂), 2.37–2.21 (m, 2H, -CH₂), 2.15–1.72 (m, 6H, -CH₂), 1.86–1.42 (m, 5H, -CH₂), 1.19 (s, 3H, -CH₃), 0.13 (s, 9H, -CH₃). ¹³C NMR (100 MHz, CDCl₃): δ 210.2, 106.4, 85.3, 55.1, 46.7, 37.5, 34.2, 31.6, 27.5, 25.8, 24.1, 19.4, 15.8, 0.17. HRMS: calcd. for C₁₆H₂₈OSi 264.1909; found 264.1916.

2-Allyl-3-methyl-3-pent-3-enyl)cyclohex-1-enyloxy)trimethyl Silane (19)

The 1,4-addition of 2-allyl-3-methylcyclohex-2-enone **18** (750 mg, 5.0 mmol) was performed using Grignard reagent [prepared from Mg (600 mg, 25.0 mmol), 5-bromopent-2-ene (1.86 g, 12.5 mmol)], CuI (2.38 g, 12.5 mmol), TMSCl (0.76 mL, 6.0 mmol), and Et₃N (0.90 mL, 6.50 mmol) following the same procedure as that of **2** to afford crude silyl-enol ether **19** (1.19 g, 82%) as a thick liquid. ¹H NMR (CDCl₃, 400 MHz): δ 5.81–5.73 (m, 1H, –CH), 5.46–5.40 (m, 2H, –CH₂), 5.11–4.90 (m, 2H, –CH₂), 2.26–1.97 (m, 8H, –CH₂), 1.83–1.67 (m, 4H, –CH₂) 1.61–1.22 (m, 3H, –CH₃), 0.98 (s, 3H, –CH₃), 0.15 (s, 9H, –CH₃). ¹³C-NMR (CDCl₃, 100 MHz): δ 146.3, 144.9, 132.1, 124.6, 121.2, 116.6, 39.2, 34.9, 32.7, 30.2, 27.7, 26.7, 19.1, 18.3, 15.4, 0.24. Mass (m/z) % 292 (M⁺, 31), 248 (25), 184 (34), 142 (46), 93(64), 78 (100). Crude product **15** was used for the next step without further purification.

2-Allyl-3-methyl-3-(pent-3-enyl)cyclohexanone (20)

A solution of silyl-enol ether **19** (0.50 g, 1.71 mmol) in dry THF (15 mL) was added dropwise to the stirred suspension of NaOMe (185 mg, 3.42 mmol) in dry THF (15 mL) at 0 °C. Then it was raised to room temperature and stirred for 2 h. The reaction mixture was quenched by adding ice water (30 mL) and extracted with ether (2 × 15 mL). The combined extracts were washed with brine (2 × 20 mL) and dried (Na₂SO₄). Removal of the solvent followed by flash-column chromatographic purification (silica gel, 2.5% ethyl acetate in hexane) afforded keto compound **20** (294 mg, 78%) as pale yellow liquid. IR (KBr): 1706 (CO), 1632 (alkene) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 5.56–5.51 (m, 1H, –CH), 5.41–5.38 (m, 2H, –CH), 5.16–5.22 (m, 2H, –CH₂), 2.45–2.16 (m, 4H, –CH₂), 2.11–1.81 (m, 5H, –CH₂& –CH), 1.72–1.32 (m, 5H, –CH₂& –CH), 1.12–0.98 (m, 32H, –CH), 0.81 (s, 3H, –CH₃). ¹³C NMR (CDCl₃, 100 MHz): δ 212.5, 133.2, 130.6, 124.7, 118.1, 60.2, 56.4, 42.3, 35.6, 34.2, 31.8, 25.1, 23.4, 17.5, 15.7. Mass (m/z) % 220 (M⁺, 23), 206 (18), 187 (34), 143(54), 84 (100).

(4aS*,9aS*)-2,3,4,4a,5,6,9,9a-Octahydro-4a-methylbenzo(7)annulen-1-one (21 and 22)

The diene **20** (200 mg, 0.91 mmol) was dissolved in DCM (10 mL), and a solution of 10 mol% of Grubbs's first-generation catalyst in dry DCM (5 mL) was slowly added under a nitrogen atmosphere. The resulting solution was refluxed for 5 h. Then, the reaction mixture was filtered, and the solvent was removed under vacuo. The residue was subjected to flash-column chromatographic purification (silica gel; 1.3% ethyl acetate in hexane to 2.5% ethyl acetate in hexane), which furnished the (7-6) bicyclic systems **21** and **22** as viscous liquid.

(Z,4aS,9aR)-2,3,4,4a,5,6,9,9a-Octahydro-4a-methylbenzo[7]annulen-1-one (21)

Yield: 91 mg (56%). IR (KBr): 1710 (CO), 1658 (alkene) cm⁻¹. ¹H NMR (CDCl₃, 400 MHz): δ 5.69–5.62 (m, 2H, –CH), 2.44–2.41 (m, 1H, –CH),

2.34–2.27 (m, 2H, $-\text{CH}_2$), 2.25–2.10 (m, 4H, $-\text{CH}_2$), 2.04–1.80 (m, 2H, $-\text{CH}_2$), 1.79–1.73 (m, 2H, $-\text{CH}_2$), 1.54–1.39 (m, 2H, $-\text{CH}_2$), 0.78 (s, 3H, $-\text{CH}_3$). ^{13}C NMR (CDCl_3 , 100 MHz): δ 213.1, 132.0, 130.2, 57.3, 41.7, 39.6, 35.7, 27.2, 25.2, 23.4, 22.7, 18.4. Mass (m/z) % 178 (M^+ , 12), 163 (22), 119 (38), 107 (25), 93 (26), 81 (48), 79 (100).

**(Z,4aS,9aS)-2,3,4,4a,5,6,9a-Octahydro-4a-methylbenzo[7]
annulen-1-one (22)**

Yield: 43 mg (27%). IR (KBr): 1708 (CO), 1661 (alkene) cm^{-1} . ^1H NMR (CDCl_3 , 400 MHz): δ 5.60–5.58 (m, 2H, $-\text{CH}$), 2.47–2.43 (m, 1H, $-\text{CH}$), 2.39–2.36 (m, 2H, $-\text{CH}_2$), 2.25–2.10 (m, 4H, $-\text{CH}_2$), 1.96–1.87 (m, 2H, $-\text{CH}_2$), 1.85–1.66 (m, 2H, $-\text{CH}_2$), 1.43–1.30 (m, 2H, $-\text{CH}_2$), 0.93 (s, 3H, $-\text{CH}_3$). ^{13}C NMR (CDCl_3 , 100 MHz): δ 214.1, 131.4, 128.8, 59.2, 39.8, 39.6, 35.7, 27.2, 25.3, 23.1, 21.8.

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