Studies on Lewis Acid-Mediated Intramolecular Cyclization Reactions of Allene–Ene Systems

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The Lewis acid-mediated reactions of allene–ene compounds, derived from 3-methylcitronellal or dimethyl malonate, were carried out using various Lewis acids such as ethylaluminum dichloride, diethylaluminum chloride, titanium chloride, zinc chloride etherate, or boron trifluoride etherate, affording unexpectedly intramolecular [2+2]cycloaddition products under some particular reaction conditions without any formation of intramolecular ene reaction products.

Key words allene; [2+2]cycloaddition; Lewis acid; allene–ene system; intramolecular cycloaddition

Allene compounds have received much attention so far in regard to their unique chemical reactivity and specific stereochemical behavior, which arises from the structural characteristics of allenes; thus have been widely employed as a carbon three unit in organic synthesis.[1—11] Currently, much interest is being focused on the transition metal- or Lewis acid-catalyzed reactions of allenes, and our attention is paid to the use of the chirality of allenes in asymmetric synthesis,[12,13] especially with transition metal catalysts.[14,15] We describe in this report our recent works on allene chemistry, in particular, the unprecedented intramolecular [2+2]cycloaddition reactions[16—21] of inactivated allene and ene functionality by the assistance of Lewis acids. A paper concerning Lewis acid-mediated [2+2]cycloaddition reactions of activated allenes (conjugated allenic esters) has appeared,[22] however there has been no intramolecular Lewis acid-mediated [2+2] cycloaddition of simple allenes and enes.[23]

Previously, we reported Lewis acid-catalyzed asymmetric intramolecular ene reactions of 1,7-diene systems bearing a chiral sulfinyl group as a chiral electrophile. Further detailed studies on these reactions reveal that the mode of the cyclization depends on the activity of the electrophilic functional groups in the dienophiles and on the Lewis acid used.[24] Therefore we have taken much interest in the mode of cyclization of allene–ene systems, namely ene, hetero Diels–Alder, and/or [2+2]cycloaddition reactions, by the assistance of Lewis acids.

Allene–ene systems were constructed in the following way. Lithium or magnesium acetylides of **2a**—**c** attacked aldehyde in 3-methylcitronellal (**1**) derived from citral to give propargylic alcohol derivatives **3a**—**c** in excellent yields (83—96%). The corresponding acetates **4a**—**c** of the alcohols were reacted with methyl- or phenylmagnesium bromide in the presence of copper(I) iodide to afford allenyl compounds **5a**—**d** in fairly good yields.

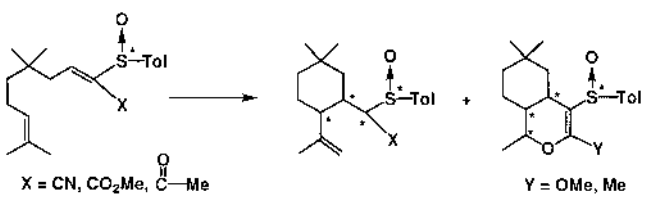

Chart 1

Allenylmalonate was prepared in the usual way. An allenenyl part **14** was prepared starting from 1,3-propanediol (**6**). The selective monosilylation of the diol[25] with *tert*-butyldiphenylchlorosilane (TBDPSCl), followed by Swern oxidation, gave 3-(*tert*-butyldiphenylsilyloxy)propanal (**8**). The addition of 1-propynylmagnesium bromide to the aldehyde in **8** afforded a propargylic alcohol derivative **9** in good yield. The acetate **10** of the alcohol **9** was reacted with methylmagnesium bromide in the presence of copper(I) iodide to furnish allene **11** in 90% yield. Removal of the silyl group in **11** by treatment with tetrabutylammonium fluoride (TBAF), followed by tosylation with TsCl-triethylamine and iodination of the tosylate **13** with NaI, gave 5-methyl-3,4-hexadienyl iodide (**14**).

Alkylation of dimethyl malonate with 3-methyl-2-butenyl bromide was carried out in the presence of sodium hydride to produce dimethyl (3-methyl-2-butenyl)propanedioate (**15**)[26] in 89% yield. The reaction of **15** with allenyl iodide **14** using sodium hydride as a base gave an allene–ene compound, dimethyl (3-methyl-2-butenyl)(5-methyl-3,4-hexadienyl)propanedioate (**16**), in 47% yield.

Studies on Lewis acid-mediated cyclization reactions of the allenyl compounds **5a**—**d** were undertaken under various reaction conditions using typical Lewis acids such as ethylaluminum dichloride ($EtAlCl_2$), diethylaluminum chloride (Et_2AlCl), titanium tetrachloride ($TiCl_4$), boron trifluoride etherate ($BF_3 \cdot OEt_2$), zinc chloride etherate ($ZnCl_2 \cdot OEt_2$), and zinc bromide ($ZnBr_2$). Upon treatment with $EtAlCl_2$ (1.5

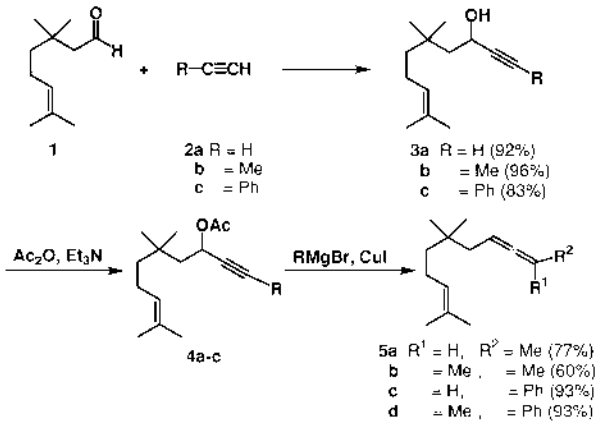

Chart 2

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or 3.0 eq) at −78 °C, the allenyl compound **5b** unexpectedly underwent a [2+2]cycloaddition reaction to give 8-isopropylidene-3,3,7,7-tetramethylbicyclo[4.2.0] octane (**17**) in a fairly good yield, as listed is Table 1.

However, polymerization occurred upon treatment with $EtAlCl_2$ (1.5 eq) at 0 °C, whereas the reaction using weaker acids, $ZnBr_2$ or $BF_3 \cdot OEt_2$ (3.0 eq), at room temperature recovered the starting material.

Thus, the reactions of **5b** with more acidic Lewis acids under milder reaction conditions gave a [2+2]cyclization product, whereas the reactions under more severe reaction conditions (at a much higher reaction temperature) resulted in polymerization of the starting material, or the reactions with weaker acids provided no cyclization product with recovery of the starting material.

Lewis acid-mediated reactions of other allene–ene compounds **5a**,**c**, and **d** provided no cycloaddition product, presumably due to the high reactivity of the allenyl system **5a** resulting in polymerization, the lability of the allene **5c** leading to decomposition, and the inaccessibility of **5d** by steric hindrance recovering the starting material.

Similarly, the Lewis acid-mediated reactions of another allenyl compound **16** provided the corresponding [2+2]cycloaddition product, dimethyl 8,8-dimethyl-7-isopropylidenebicyclo[4.2.0]octane-3,3-dicarboxylate (**18**) in considerably good yield, as shown in Table 1; however, the reactions were dependent upon the Lewis acids employed, much different from that of **5**.

Upon treatment with more weakly acidic Lewis acids such as $TiCl_4$, $ZnCl_2 \cdot OEt_2$, or $BF_3 \cdot OEt_2$ at room temperature (r.t.), the allene–ene compound **16** was converted into a [2+2]cycloaddition product **18** in 87, 77, and 92% yield, respectively. In contrast to the previous cases mentioned above, upon mediation with more acidic Lewis acids (3.0 eq) such as $EtAlCl_2$ (0 °C), Et_2AlCl (r.t.) or $ZnBr_2$ (r.t.), the allene–ene compound **16** underwent no desired cycloaddition, recovering the starting material. Upon treatment of **16** with stronger Lewis acid ($EtAlCl_2$) at r.t., however, polymerization occurred.

The results thus obtained are rationalized as follows. One of the π-bonds in the allenes **5b** and **16** is activated by the assistance of the Lewis acid used, generating more cationic β-carbon centers, and the intramolecular ene parts in **5b** and **16** attack the cationic β-carbon of the allenes to give [2+2]cycloaddition products **17** and **18**. The existence of a quarternary carbon close to the reaction center (allene) in **5b** makes the activation by the Lewis acid sterically rather inaccessible, compared with the case of **16**. However, in the case of the 1,7-allene–ene system **16** bearing ester groups, the preference of coordination of the ester carbonyl groups to the more acidic Lewis acids provides large steric interference by the two methoxy groups of the esters owing to the conformational fixation resulting from the coordination, thus giving the recovered starting material without any cycloaddition product. With weaker acids, insufficient coordination of the two ester carbonyl groups allows steric access from the allene to the ene part, giving a [2+2]cycloaddition product.

In conclusion, the [2+2]cycloaddition reactions of 1,7-allene–ene systems were largely dependent upon the acidity of the Lewis acid used and the reaction temperature. The simple 1,7-allene–ene compound **5b** without any functional group underwent a [2+2]cycloaddition reaction upon treatment with more acidic Lewis acid ($EtAlCl_2$) at milder reaction conditions (at −78 °C) in dichloromethane, however, poly-

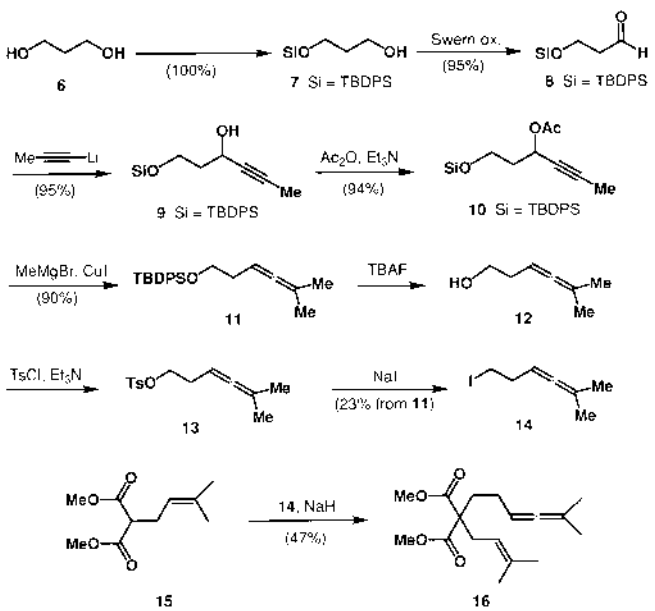

Chart 3

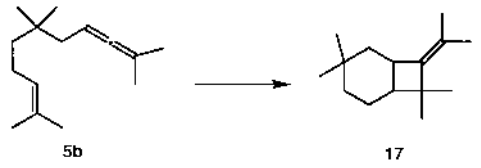

Chart 4

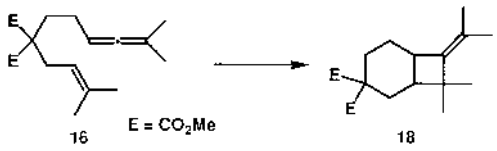

Chart 5

Table 1. Studies on Lewis Acid-Mediated Reactions of Allene–Ene Systems

Substrate	Lewis acid (eq)	Solvent	Reaction temp. (°C)	Reaction time (h)	Product yield (%)
5b	$EtAlCl_2$ (1.5)	CH_2Cl_2	−78	0.5	82 (**17**)
5b	$EtAlCl_2$ (3.0)	CH_2Cl_2	−78	1	93 (**17**)
5b	Et_2AlCl (1.5)	Toluene	−78	1	79 (**17**)
16	$TiCl_4$ (3.0)	CH_2Cl_2	r.t.	22	87 (**18**)
16	$ZnCl_2 \cdot OEt_2$ (3.0)	CH_2Cl_2	r.t.	24	77 (**18**)
16	$BF_3 \cdot OEt_2$ (7.0)	CH_2Cl_2	r.t.	23	92 (**18**)

merization occurred at a higher reaction temperature (0 °C). On the other hand, the 1,7-allene–ene system **16** bearing ester groups gave a [2+2]cycloaddition product upon treatment with rather weaker acids (3.0—7.0 eq) such as $TiCl_4$, $ZnCl_2 \cdot OEt_2$, and $BF_3 \cdot OEt_2$ at r.t., whereas with more acidic Lewis acids (3.0 eq) such as $EtAlCl_2$ (0 °C), Et_2AlCl (r.t.), and $ZnBr_2$ (r.t.), no reaction occurred with recovery of the starting material.

Experimental

Infrared (IR) spectra were obtained in the indicated state with a JASCO DR-81 fourier-transform IR spectrometer. NMR spectra were determined in the indicated solvent with a JEOL EX-270 (^{1}H-NMR; 270 MHz) high-resolution NMR spectrometer; chemical shifts are given in ppm from tetramethylsilane as an internal standard. Splitting patterns are designated as s: singlet, br s: broad singlet, d: doublet, dd: double of doublet, dt: triple of doublet, t: triplet, tt: triple of triplet, tq: quartet of triplet, m: multiplet. Mass spectra were taken on a JEOL JMS-DX 303/JMA-DA 5000 system. Flash column chromatography was performed with Merck Silica gel 60 (230—400 mesh).

5,5,9-Trimethyl-8-decen-1-yn-3-ol (3a) A 0.5 M tetrahydrofuran (THF) solution of ethynylmagnesium bromide (16.4 ml, 8.21 mmol) was added at 0 °C to a solution of 3,3,7-trimethyl-6-octen-1-al (**1**) (920 mg, 5.48 mmol) in THF (10 ml), and the reaction mixture was stirred at the same temperature for 30 min, then at room temperature for 5 h. The reaction mixture was diluted with ether and the solution was washed with 20% aqueous NH_4Cl and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1 : 4) to give **3a** (978 mg, 92% yield).

The reaction of **1** (2.29 g, 13.63 mmol) with 0.5 M THF solution of 1-propynylmagnesium bromide (40.9 ml, 20.45 mmol) was carried out using the same procedure as described above to give 2,6,6-trimethyl-2-undecen-9-yn-8-ol (**3b**) (2.71 g, 96% yield).

3a: IR (neat, cm^{-1}): 3380 (alcohol), 3310 (acetylene), 2260 (acetylene), 1630 (olefin). ^{1}H-NMR ($CDCl_3$) δ: 1.00 (6H, s, $C(CH_3)_2$), 1.08—1.52 (4H, m, $(CH_2)_2$), 1.61, 1.68 (6H, s, s, $C=C(CH_3)_2$), 1.78 (1H, s, C≡CH), 2.38 (1H, br s, OH), 2.65 (2H, d, J=2.0 Hz, $C\underline{H}_2CHOH$), 4.42 (1H, br s, $C\underline{H}OH$), 5.09 (1H, m, CH=C). MS *m/z*: 194 (M^+). Exact mass determination: 194.1671 (Calcd $C_{13}H_{22}O$: 194.1671).

3b: IR (neat, cm^{-1}): 3380 (alcohol), 2230 (acetylene), 1650 (olefin). ^{1}H-NMR ($CDCl_3$) δ: 0.95 (6H, s, $C(CH_3)_2$), 1.05—1.42 (4H, m, $(CH_2)_2$), 1.59, 1.65 (6H, s, s, $C=C(CH_3)_2$), 1.67 (2H, d, J=5.4 Hz, $C\underline{H}_2CHOH$), 1.78 (3H, d, J=2.1 Hz, $C\equiv CCH_3$), 2.11 (1H, br s, OH), 4.31 (1H, br s, $C\underline{H}OH$), 4.96 (1H, m, CH=C). MS *m/z*: 208 (M^+). Exact mass determination: 208.1779 (Calcd $C_{14}H_{24}O$: 208.1827).

1-Phenyl-5,5,9-trimethyl-8-decen-1-yn-3-ol (3c) A 1.54 M hexane solution of *n*-butyllithium (2.1 ml, 3.21 mmol) was added at −78 °C to a solution of phenylacetylene (0.41 ml, 3.75 mmol) in THF (10 ml), and the reaction mixture was stirred at the same temperature for 30 min. A solution of **1** (450 mg, 2.68 mmol) in THF (10 ml) was added to the above solution, and the reaction mixture was stirred at −78 °C for 1 h, quenched by the addition of saturated aqueous NH_4Cl at the same temperature, and then stirred for an additional hour. The reaction mixture was gradually warmed to room temperature and diluted with ether, and the solution was washed with saturated aqueous NH_4Cl and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1 : 8) to give **3c** (598 mg, 83% yield).

3c: IR (neat, cm^{-1}): 3340 (alcohol), 2260 (acetylene), 1650 (olefin), 1590 (aromatic). ^{1}H-NMR ($CDCl_3$) δ: 1.02 (6H, s, $C(CH_3)_2$), 1.12—1.47 (4H, m, $(CH_2)_2$), 1.60, 1.67 (6H, s, s, $C=C(CH_3)_2$), 1.81 (2H, d, J=6.4 Hz, $C\underline{H}_2CHOH$), 2.27 (1H, br s, OH), 4.67 (1H, t, J=6.5 Hz, $C\underline{H}OH$), 5.09 (1H, m, CH=C), 7.03—7.55 (5H, m, C_6H_5). MS *m/z*: 270 (M^+). Exact mass determination: 270.2076 (Calcd $C_{19}H_{26}O$: 270.1984).

3-Acetoxy-5,5,9-trimethyl-8-decen-1-yne (4a) Acetic anhydride (0.71 ml, 7.50 mmol) was added to a solution of **3a** (970 mg, 5.00 mmol) and triethylamine (2.1 ml, 15.00 mmol) in dichloromethane (10 ml) at room temperature. 4-Dimethylaminopyridine (30 mg, 0.25 mmol) was added to the above solution, and the reaction mixture was stirred at room temperature for 12 h. The reaction mixture was diluted with ether and the solution was washed with water and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1 : 9) to give **4a** (1.15 g, 98% yield).

The reaction of **3b** (2.71 g, 13.03 mmol) or **3c** (590 mg, 2.19 mmol) was carried out using the same procedure as described above to give 4-acetoxy-6,6,10-trimethyl-9-undecen-2-yne (**4b**) (3.15 g, 97% yield) or 3-acetoxy-1-phenyl-5,5,9-trimethyl-8-decen-1-yne (**4c**) (626 mg, 92% yield), respectively.

4a: IR (neat, cm^{-1}): 3280 (acetylene), 2250 (acetylene), 1740 (ester), 1660 (olefin). ^{1}H-NMR ($CDCl_3$) δ: 0.97 (6H, s, $C(CH_3)_2$), 1.06—1.44 (4H, m, $(CH_2)_2$), 1.63, 1.68 (6H, s, s, $C=C(CH_3)_2$), 1.81 (2H, d, J=6.3 Hz, $C\underline{H}_2CHO$), 2.05 (3H, s, $COCH_3$), 2.45 (1H, d, J=1.9 Hz, C≡CH), 5.07 (1H, m, CH=C), 5.42 (1H, dt, J=6.5, 2.0 Hz, CHO). MS *m/z*: 236 (M^+). Exact mass determination: 236.1799 (Calcd $C_{15}H_{24}O_2$: 236.1776).

4b: IR (neat, cm^{-1}): 2250 (acetylene), 1740 (ester), 1670 (olefin). ^{1}H-NMR ($CDCl_3$) δ: 0.95 (6H, s, $C(CH_3)_2$), 1.05—1.43 (4H, m, $(CH_2)_2$), 1.62, 1.70 (6H, s, s, $C=(CH_3)_2$), 1.77—1.93 (5H, m, $C\underline{H}_2CHC\equiv CC\underline{H}_3$), 2.04 (3H, s, $COCH_3$), 5.08 (1H, m, CH=C), 5.41 (1H, tq, J=6.2, 1.9 Hz, CHO). MS *m/z*: 250 (M^+). Exact mass determination: 250.1967 (Calcd $C_{16}H_{26}O_2$: 250.1933).

4c: IR (neat, cm^{-1}): 2220 (acetylene), 1740 (ester), 1660 (olefin), 1590 (aromatic). ^{1}H-NMR ($CDCl_3$) δ: 1.01 (6H, s, $C(CH_3)_2$), 1.12—1.49 (4H, m, $(CH_2)_2$), 1.62, 1.68 (6H, s, s, $C=C(CH_3)_2$), 1.90 (2H, d, J=6.7 Hz, $C\underline{H}_2CHO$), 2.07 (3H, s, CH_3CO), 5.09 (1H, m, CH=C), 5.70 (1H, t, J=6.6 Hz, CHO), 7.03—7.58 (5H, m, C_6H_5). MS *m/z*: 312 (M^+). Exact mass determination: 312.2122 (Calcd $C_{21}H_{28}O_2$: 312.2090).

2,6,6-Trimethyl-2,8,9-undecatriene (5a) A 3.0 M ether solution of methylmagnesium bromide (9.75 ml, 29.24 mmol) was added at −78 °C to a suspension of copper(I) iodide (2.78 g, 14.62 mmol) and lithium chloride (620 mg, 14.62 mmol) in THF (30 ml), and the reaction mixture was stirred at the same temperature for 1 h. A solution of **4a** (1.15 g, 4.87 mmol) in THF (20 ml) was added to the above solution, and the reaction mixture was stirred at −78 °C for 4 h. The reaction mixture was gradually warmed to −20 °C, quenched by the addition of saturated aqueous NH_4Cl at the same temperature and stirred for an additional hour. The reaction mixture was allowed to warm to room temperature and was diluted with ether, then the solution was washed with saturated aqueous NH_4Cl and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (hexane) to give **5a** (720 mg, 77% yield).

The reaction of **4b** (3.10 g, 12.40 mmol) or **4c** (600 mg, 1.92 mmol) with Me_2CuLi was carried out using the same procedure as described above to give 2,6,6,10-tetramethyl-2,3,9-undecatriene (**5b**) (1.53 g, 60% yield) or 2-phenyl-6,6,10-trimethyl-2,3,9-undecatriene (**5d**) (478 mg, 93% yield), respectively, and the reaction of **4a** (1.35 g, 5.72 mmol) with Ph_2CuLi was carried out using the same procedure as described above to give 1-phenyl-5,5,9-trimethyl-1,2,8-decatriene (**5c**) (1.35 g, 93% yield).

5a: IR (neat, cm^{-1}): 1950 (allene), 1660 (olefin). ^{1}H-NMR ($CDCl_3$) δ: 0.90 (6H, s, $C(CH_3)_2$), 1.05—1.52 (4H, m, $(CH_2)_2$), 1.62, 1.68 (6H, s, s, $C=C(CH_3)_2$), 1.78—2.23 (5H, m, $C\underline{H}_2CH=C=CHC\underline{H}_3$), 4.42—4.75 (1H, m, $C\underline{H}CH_3$), 4.77—5.30 (2H, m, $CH_2C\underline{H}=C\times2$). MS *m/z*: 192 ($M^+$). Exact mass determination: 192.1801 (Calcd $C_{14}H_{24}$: 192.1878).

5b: IR (neat, cm^{-1}): 1970 (allene), 1650 (olefin). ^{1}H-NMR ($CDCl_3$) δ: 0.88 (6H, s, $C(CH_3)_2$), 1.02—1.42 (4H, m, $(CH_2)_2$), 1.53—1.77 (12H, m, $C=C(CH_3)_2\times2$), 1.86 (2H, d, J=7.9 Hz, $CH_2C=C=C$), 4.63—5.27 (2H, m, $CH=C\times2$). MS *m/z*: 206 (M^+). Exact mass determination: 206.2030 (Calcd $C_{15}H_{26}$: 206.2034).

5c: IR (neat, cm^{-1}): 1950 (allene), 1660 (olefin), 1600 (aromatic). ^{1}H-NMR ($CDCl_3$) δ: 0.97 (6H, s, $C(CH_3)_2$), 1.08—1.45 (4H, m, $(CH_2)_2$), 1.58, 1.68 (6H, s, s, $C=C(CH_3)_2$), 2.05 (2H, dd, J=7.7, 2.3 Hz, $CC\underline{H}_2CH$), 5.08 (1H, m, $C\underline{H}=C(CH_3)_2$), 5.47 (1H, dt, J=7.8, 3.7 Hz, $CH_2C\underline{H}=C=CH$), 5.93—6.17 (1H, m, $C\underline{H}C_6H_5$), 7.00—7.67 (5H, m, C_6H_5). MS *m/z*: 254 (M^+). Exact mass determination: 254.1939 (Calcd $C_{19}H_{26}$: 254.2034).

5d: IR (neat, cm^{-1}): 1950 (allene), 1670 (olefin), 1600 (aromatic). ^{1}H-NMR ($CDCl_3$) δ: 0.94 (6H, s, $C(CH_3)_2$), 1.07—1.52 (4H, m, $(CH_2)_2$), 1.59, 1.67 (6H, s, s, $CH=C(C\underline{H}_3)_2$), 2.00 (2H, d, J=5.5 Hz, $C\underline{H}_2CH=C=C$), 2.08 (3H, s, $C=C=CCH_3$), 4.91—5.70 (2H, m, $CH=C\times2$), 7.03—7.58 (5H, m, C_6H_5). MS *m/z*: 268 (M^+). Exact mass determination: 268.2139 (Calcd $C_{20}H_{28}$: 268.2191).

3-(*tert*-Butyldiphenylsilyloxy)-1-propanol (7) A 50 ml two-necked flask equipped with a septum inlet and a magnetic stirring bar, and containing sodium hydride (50% oil dispersion; 630 mg, 13.14 mmol) was flushed with argon, and maintained under a positive pressure of argon. THF (10 ml) and a solution of 1,3-propandiol (**6**) (1.00 g, 13.14 mmol) in THF (10 ml) were added to the above flask. The reaction mixture was stirred at room temperature for 1 h. A solution of TBDPSCl (3.68 g, 13.14 mmol) in THF (10 ml)

was added to the above solution at 0 °C, and the mixture was stirred at 0 °C for 2 h. The reaction mixture was allowed to warm to room temperature, was diluted with ether, then the solution was washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1 : 1) to give **7** (4.13 g, 100% yield).

7: IR (neat, cm^{-1}): 3260 (alcohol), 1580 (aromatic). ^{1}H-NMR ($CDCl_3$) δ: 1.03 (9H, s, $C(CH_3)_3$), 1.77 (2H, tt, J=5.7, 5.7 Hz, $CH_2C\underline{H}_2CH_2$), 2.33 (1H, m, OH), 3.58—3.92 (4H, m, $C\underline{H}_2CH_2C\underline{H}_2$), 7.04—7.65 (10H, m, $C_6H_5\times2$). MS *m/z*: 314 (M^+). Exact mass determination: 314.1731 (Calcd $C_{19}H_{26}O_2Si$: 314.1702).

3-(*tert*-Butyldiphenylsilyloxy)-1-propanal (8) A solution of dimethyl sulfoxide (0.68 ml, 9.54 mmol) in dichloromethane (10 ml) was added to a solution of oxalyl chloride (0.42 ml, 4.77 mmol) in dichloromethane (10 ml) at −78 °C. After the mixture was stirred for 30 min, a solution of **7** (1.00 g, 3.18 mmol) in dichloromethane (10 ml) was added to the above solution at −78 °C, and the mixture was stirred at the same temperature for 1 h. Triethylamine (4.0 ml, 28.62 mmol) was then added to the reaction mixture, which was gradually warmed to room temperature. The reaction mixture was washed with water and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1 : 4) to give **8** (948 mg, 95% yield).

8: IR (neat, cm^{-1}): 1720 (aldehyde), 1580 (aromatic). ^{1}H-NMR ($CDCl_3$) δ: 1.04 (9H, s, $C(CH_3)_3$), 2.57 (2H, dt, J=5.8, 1.8 Hz, CH_2CO), 4.00 (2H, t, J=5.8 Hz, CH_2O), 7.16—7.81 (10H, m, $C_6H_5\times2$), 9.75 (1H, t, J=1.8 Hz, CHO). MS *m/z*: 312 (M^+). Exact mass determination: 312.1499 (Calcd $C_{19}H_{24}O_2Si$: 312.1546).

1-(*tert*-Butyldiphenylsilyloxy)-4-hexyn-3-ol (9) A 0.5 M THF solution of 1-propynylmagnesium bromide (19.2 ml, 9.60 mmol) was added at 0 °C to a solution of **8** (2.00 g, 6.40 mmol) in THF (19.2 ml), and the reaction mixture was stirred at room temperature for 3.5 h. The reaction mixture was diluted with ether, and the solution was washed with 20% aqueous NH_4Cl and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1 : 2) to give **9** (2.14 g, 95% yield).

9: IR (neat, cm^{-1}): 3400 (alcohol), 2240 (acetylene), 1590 (aromatic). ^{1}H-NMR ($CDCl_3$) δ: 1.07 (9H, s, $C(CH_3)_3$), 1.62—2.17 (5H, m, $C\underline{H}_2CHC{\equiv}CC\underline{H}_3$), 3.05 (1H, d, J=5.6 Hz, OH), 3.87 (2H, t, J=5.2 Hz, CH_2O), 4.65 (1H, br s, $C\underline{H}OH$), 7.12—7.82 (10H, m, $C_6H_5\times2$). MS *m/z*: 352 (M^+). Exact mass determination: 352.1812 (Calcd $C_{22}H_{28}O_2Si$: 352.1859).

3-Acetoxy-1-(*tert*-butyldiphenylsilyloxy)-4-hexyne (10) Acetic anhydride (0.63 ml, 6.70 mmol) was added to a solution of **9** (1.57 g, 4.47 mmol) and triethylamine (1.87 ml, 13.40 mmol) in dichloromethane (15 ml) at room temperature. 4-Dimethylaminopyridine (27 mg, 0.22 mmol) was added to the above solution, and the reaction mixture was stirred at room temperature for 6 h. The reaction mixture was diluted with ether and the solution was washed with saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1 : 9) to give **10** (1.66 g, 94% yield).

10: IR (neat, cm^{-1}): 2250 (acetylene), 1740 (ester), 1590 (aromatic). ^{1}H-NMR ($CDCl_3$) δ: 1.07 (9H, s, $C(CH_3)_3$), 1.79 (3H, d, J=1.9 Hz, $CH_3C{\equiv}C$), 1.88—2.21 (5H, m, $C\underline{H}_2CHOCOC\underline{H}_3$), 3.77 (2H, t, J=6.0 Hz, OCH_2), 5.56 (1H, tq, J=6.8, 2.2 Hz, CHOCO), 7.12—7.81 (5H, m, C_6H_5). MS *m/z*: 394 (M^+). Exact mass determination: 394.1959 (Calcd $C_{24}H_{30}O_3Si$: 394.1964).

1-(*tert*-Butyldiphenylsilyloxy)-5-methyl-3,4-hexadiene (11) A 3.0 M ether solution of methylmagnesium bromide (4.20 ml, 12.62 mmol) was added at −78 °C to a suspension of copper(I) iodide (1.2 g, 6.31 mmol) in THF (43 ml), and the reaction mixture was stirred at −78 °C for 1 h. A solution of **10** (1.66 g, 4.21 mmol) in THF (20 ml) was added to the above solution, and the reaction mixture was stirred at −78 °C for 2 h. The reaction mixture was gradually warmed to −10 °C, and quenched by the addition of 20% aqueous NH_4Cl at the same temperature and stirred for an additional hour. The reaction mixture was allowed to warm to room temperature and was diluted with ether, then the solution was washed with 20% aqueous NH_4Cl and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1 : 9) to give **11** (1.32 g, 90% yield).

11: IR (neat, cm^{-1}): 1970 (allene), 1590 (aromatic). ^{1}H-NMR ($CDCl_3$) δ: 1.07 (9H, s, $C(CH_3)_3$), 1.63 (6H, d, J=2.7 Hz, $C{=}C(CH_3)_2$), 2.21 (2H, dt, J=7.1, 6.8 Hz, $C\underline{H}_2CH{=}C$), 3.70 (2H, t, J=6.7 Hz, OCH_2), 4.70—5.15 (1H, m, CH=C), 7.07—7.82 (10H, m, $C_6H_5\times2$). MS *m/z*: 350 (M^+). Exact mass determination: 350.2017 (Calcd $C_{23}H_{30}OSi$: 350.2066).

1-Iodo-5-methyl-3,4-hexadiene (14) A 1.0 M THF solution of TBAF (6.9 ml, 6.90 mmol) was added at room temperature to a solution of **11** (1.21 g, 3.451 mmol) in THF (10 ml) and the reaction mixture was stirred at the same temperature for 2 h. The reaction mixture was diluted with ether, then the solution was washed with water and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product of 5-methy-3,4-hexadien-1-ol (**12**) was used in the next step without further purification. TsCl (990 mg, 5.18 mmol) was added to a solution of the crude alcohol **12** obtained above and triethylamine (1.4 ml, 10.04 mmol) in dichloromethane (10 ml) at 0 °C. 4-Dimethylaminopyridine (21 mg, 0.17 mmol) was added to the above solution, and the reaction mixture was stirred at 0 °C for 1 h and then at room temperature for 12 h. The reaction mixture was diluted with ether, and the solution was washed with water and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product of 2-methy-6-(*p*-toluenesulfonyloxy)-2,3-hexadiene (**13**) was used in the next step without further purification. A crude product **13** obtained above was dissolved in acetone (30 ml), then NaI (1.4 ml, 34.51 mmol) was added at room temperature. The reaction mixture was stirred at room temperature for 21 h, then filtered. The filtrate was concentrated *in vacuo*. The crude product was subjected to flash column chromatography (hexane) to give **14** (174 mg, 23% yield from **11**).

14: IR (neat, cm^{-1}): 1970 (allene). ^{1}H-NMR ($CDCl_3$) δ: 1.68 (6H, d, J=2.3 Hz, $C(CH_3)_2$), 2.45 (2H, dt, J=7.5, 6.9 Hz, $C\underline{H}_2CH_2I$), 3.15 (2H, t, J=7.0 Hz, CH_2I), 4.62—5.18 (1H, m, CH=C=C). MS *m/z*: 222 (M^+). Exact mass determination: 221.9961 (Calcd $C_7H_{11}I$: 221.9906).

Dimethyl (3-Methyl-2-butenyl)(5-methyl-3,4-hexadienyl)propanedioate (16) A 50 ml two-necked flask equipped with a septum inlet and a magnetic stirring bar, and containing sodium hydride (50% oil dispersion; 49 mg, 1.03 mmol) was flushed with argon, and maintained under a positive pressure of argon. THF (5 ml) and a solution of dimethyl (3-methyl-2-butenyl)propanedioate (**15**) (206 mg, 1.03 mmol) in THF (10 ml) were added to the above solution at 0 °C, and the reaction mixture was stirred at room temperature for 30 min. A solution of **14** (190 mg, 0.86 mmol) in THF (10 ml) was added to the above solution at 0 °C, and the mixture was stirred at room temperature for 48 h. The reaction mixture was diluted with ether, then the solution was washed with water and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1 : 9) to give **16** (118 g, 47% yield).

16: IR (neat, cm^{-1}): 1970 (allene), 1740 (ester), 1670 (olefin). ^{1}H-NMR ($CDCl_3$) δ: 0.87—1.24 (12H, m, $C{=}C(CH_3)_2\times2$), 1.80—1.99 (4H, m, $(CH_2)_2$), 2.60 (2H, d, J=7.1 Hz, $C\underline{H}_2CH$), 3.78 (6H, s, $C(CO_2CH_3)_2$), 4.71—5.14 (2H, m, CH=C×2). MS *m/z*: 294 (M^+). Exact mass determination: 294.1876 (Calcd $C_{17}H_{26}O_4$: 294.1831).

Lewis Acid–Mediated Intramolecular Cyclization Reactions of 5b. General Procedure A dry 25 ml two-necked flask equipped with a septum inlet and a magnetic stirring bar was flushed with argon and maintained under a positive pressure of argon. A 1.0 M hexane solution of Lewis acid was added at −78 °C to a solution of **5b** (100 mg, 0.49 mmol) in solvent (10 ml). The reaction mixture was stirred under the conditions listed in Table 1, then diluted with ether; the solution was then washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (hexane) to give 8-(1-methylethylidene)-3,3,7,7-tetramethylbicyclo[4.2.0]octane (**17**). The yields of the product are summarized in Table 1.

17: IR (neat, cm^{-1}): 1680 (olefin). ^{1}H-NMR ($CDCl_3$) δ: 0.87—1.00 (12H, m, $C(CH_3)_2\times2$), 1.07—1.27 (6H, m, $CH_2\times3$), 1.29—1.46 (2H, m, CH×2), 1.54 (6H, s, $C{=}C(CH_3)_2$). MS *m/z*: 206 (M^+). Exact mass determination: 206.2055 (Calcd $C_{15}H_{26}$: 206.2034).

Lewis Acid–Mediated Intramolecular Cyclization Reactions of 16. General Procedure A dry 15 ml two-necked flask equipped with a septum inlet and a magnetic stirring bar was flushed with argon and maintained under a positive pressure of argon. A solution of Lewis acid in dichloromethane (1 ml) was added at 0 °C to a solution of **16** (30 mg, 0.10 mmol) in dichloromethane (2 ml). The reaction mixture was stirred under the conditions listed in Table 1, then diluted with ether; the solution was then washed with saturated aqueous $NaHCO_3$ and saturated aqueous NaCl, dried over anhydrous $MgSO_4$, and concentrated *in vacuo*. The crude product was subjected to flash column chromatography (ether–hexane, 1 : 9) to give dimethyl [8,8-dimethyl-7-(1-methylethylidene)bicyclo[4.2.0]octane] 3,3-dicarboxylate (**18**). The yields of the product are summarized in Table 1.

18: IR (neat, cm^{-1}): 1740 (ester), 1680 (olefin). ^{1}H-NMR ($CDCl_3$) δ: 0.92—1.05 (8H, m, $C(CH_3)_2$, $CH_2C\underline{H}_2CH$), 1.13—1.40 (2H, m, CH×2),

1.58 (6H, s, $C{=}C(CH_3)_2$), 1.80—2.55 (4H, m, $C(CH_2)_2$), 3.73 (6H, s, $C(CO_2CH_3)_2$). MS *m/z*: 294 (M^+). Exact mass determination: 294.1863 (Calcd $C_{17}H_{26}O_4$: 294.1831).

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