Stereoselective Access to the Basic Skeleton of Tetracyclic Diterpenes via a Sequence of Consecutive [3 + 2], [2 + 2 + 2], and [4 + 2] Cycloaddition Reactions

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Benzocyclobutenes **9a**, **9b**, **23**, and **24**, prepared from 1,5-hexadiyne in good yields in a sequence involving [3 + 2] annelation and [2 + 2 + 2] cycloaddition reactions, underwent an intramolecular [4 + 2] reaction to afford the basic skeleton of tetracyclic diterpenes phyllocladane and kaurane. The factors governing the stereochemistry of the Diels-Alder reaction have been elucidated. A carbonyl group at C_{12} favored the kaurane stereochemistry (58:42) whereas acetal or silylether functions at that same position led to a highly (97:3) or totally stereoselective formation of the phyllocladane ring system.

Introduction

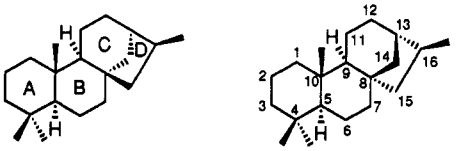
The bridged bicyclic C/D ring structure is common to several members of the tetracyclic diterpenes. This substituted bicyclo[3.2.1]octane is present in the phyllocladane, kaurane, and gibbane families.[1] There is a wide distribution of natural compounds belonging to these groups and displaying important biological activities.[2] For example, the *ent*-kaurane group plays a fundamental role as biosynthetic precursor of the plant growth hormone gibberellins.[3]

Inspection of phyllocladane and kaurane molecules 1 and 2 (Chart I) reveals the presence of a *trans-anti-trans* perhydrophenanthrene system in 1 and a *trans-anti-cis* one in 2. These two families differ only by the stereochemistry of the B/C ring junction, and they naturally occur in both optical forms.

As a consequence, many synthetic approaches leading to these diterpenoids have been reported.[4] In most cases, the D ring was built in the last stage starting from a tricyclic intermediate. Some notable exceptions are the syntheses of (±)-hibaol by Kametani,[5] gibberellin A_1 by Mander,[6] and (±) cafestol,[7a] (±) kaweol,[7b] and (±) atractyligenin[7c] by Corey. In the latter achievement, a complete stereoselective cyclization allowing the simultaneous elaboration of the rings B and D was developed.

For our purposes we were interested in the quest for a stereoselective approach to both families, using a common synthetic pathway based upon a sequence of three consecutive cycloaddition reactions. Our strategy, retrosynthetically depicted in Scheme I, featured a combination of very powerful transition metal catalyzed annelation reactions: Trost's palladium-assisted [3 + 2] cycloaddition,[8] Vollhardt's [2 + 2 + 2] cobalt-catalyzed cyclotrimerization[9] of bis(trimethylsilyl)ethyne with α,ω-diynes, and finally, an intramolecular [4 + 2] cycloaddition reaction of an orthoquinodimethane which was first investigated by Kametani.[5] In this former synthesis, a thiobutylmethylene group was introduced to provide both a blocking group and a dienophile portion but afforded only the basic skeleton of the phyllocladane family.

Chart I



(±) PHYLLOCLADANE 1 (±) KAURANE 2

This synthetic sequence deserves various comments: the cobalt-mediated cocyclization will take place between bis(trimethylsilyl)ethyne (btmse) and an enediyne having a methylenecyclopentane unit which up to now has never been tested yet in such a reaction. Then, the consecutive intramolecular [4 + 2] cycloaddition reaction will then afford the basic skeleton of the tetracyclic diterpenes kaurane (β-H_9) and/or phyllocladane (α-H_9). In order to keep all the potentialities of these two reactions which would allow the formation of five C-C bonds possibly in a one-pot process, the introduction of the methylenecyclopentane unit was envisioned *via* a [3 + 2] cycloaddition reaction between a trimethylenemethane stabilized as a π-allylpalladium complex and an electron-deficient alkene receptor.

In connection with the fundamental problem of stereochemistry, we have to consider that the orthoquinodimethane involved in the [4 + 2] cycloaddition process will react only *via* the *E*-configuration,[10] indicating that the absolute configuration at C_9 is without significance; therefore, the absolute stereochemistry of the final compounds is directly associated with the enantioselective

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(1) (a) Devon, T. K.; Scott, A. I. *Handbook of Naturally Occuring Compounds*; Academic Press: New York, 1972; Vol. II. (b) Anderson, A. B.; McCrindle, R.; Turnbull, J. K. *Can. J. Chem.* **1975**, *53*, 1181.

(2) Hanson, J. R. *Nat. Prod. Rep.* **1988**, *3*, 211 and references cited therein.

(3) Beale, M. H.; McMillian, J. *Nat. Prod. Rep.* **1988**, *3*, 248 and references cited therein.

(4) Goldsmith, D. *The Total Synthesis of Natural Products*; John Wiley: New York, 1992; Vol. 8, pp 101-174.

(5) Kametani, T.; Suzuki, K.; Nemoto, H.; Fukumoto, K. *J. Org. Chem.* **1979**, *44*, 1036.

(6) Lombardo, L.; Mander, L. N.; Turner, J. V. *J. Am. Chem. Soc.* **1979**, *102*, 6626.

(7) (a) Corey, E. J.; Wess, G.; Xiang, Y. B.; Singh, A. K. *J. Am. Chem. Soc.* **1987**, *109*, 4717. (b) Corey, E. J.; Xiang, Y. B. *Tetrahedron Lett.* **1987**, 5403. (c) Singh, A. K.; Bakshi, R. K.; Corey, E. J. *J. Am. Chem. Soc.* **1987**, *109*, 6187.

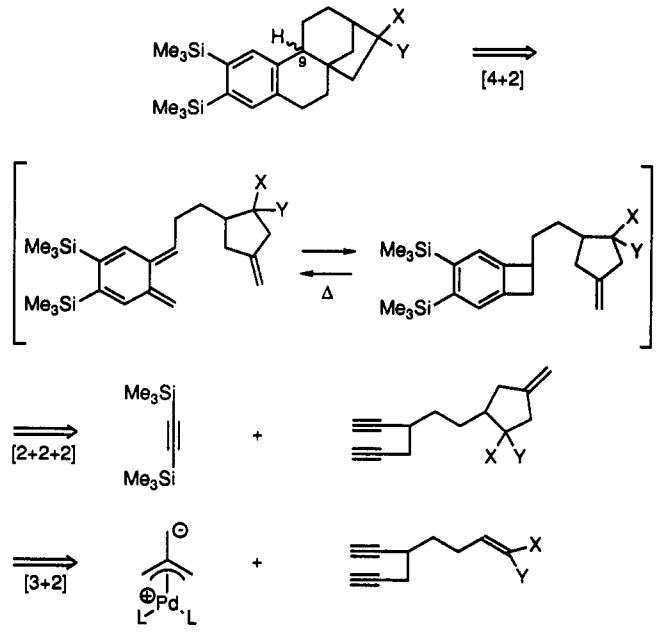
(8) Trost, B. M. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1.

(9) Vollhardt, K. P. C. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 539.

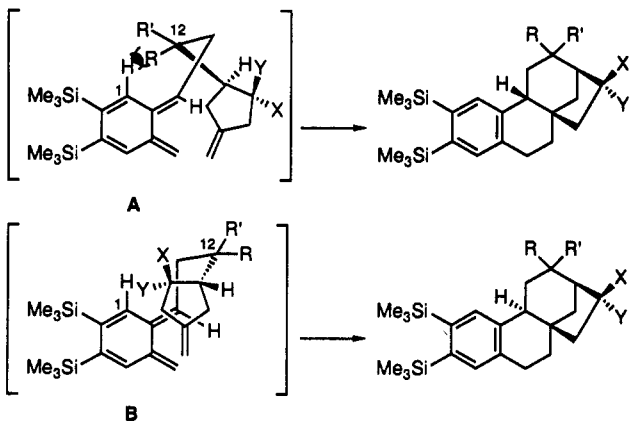
(10) Oppolzer, W. *Synthesis* **1978**, 793.

0022-3263/93/1958-4298$04.00/0

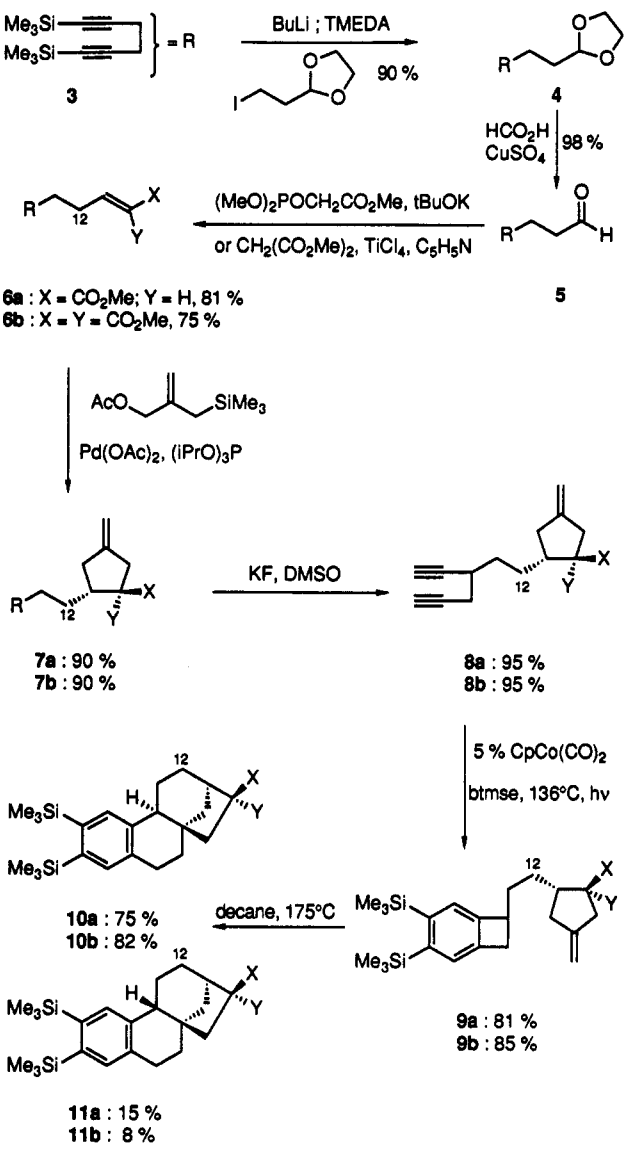
Scheme I



Scheme II



Scheme III



construction of the methylenecyclopentane.[11] Furthermore and directly related to the initial problem of relative stereochemistry due to the rigidity created by the presence of the cyclopentane in the tether between the orthoquinodimethane and the dienophile, only two transition states representing the best orbital overlapping are possible (Scheme II). In both cases, there is a "chairlike" arrangement of the carbon chain leading to the ring C.

The dienophile can approach either by the bottom (**A**) or by the top (**B**) sides of the plane defined by the orthoquinodimethane. In **A**, a nonbonding interaction between H_1 and R exists; this transition state will deliver the kaurane skeleton. In **B**, the nonbonding interaction H_1–R does not exist but a steric interaction between the two established rings will appear, therefore providing a new route to phyllocladane skeleton.

In this paper, we report full details of our synthetic efforts toward the total stereoselective construction of a variously functionalized phyllocladane basic framework.

(11) For this purpose, we have shown that substituted homochiral vinyl sulfoxides are good partners in the [3 + 2] annelation reaction: Chaigne, F.; Gotteland, J. P.; Malacria, M. *Tetrahedron Lett.* **1989**, *30*, 1803.

Results and Discussion

In order to validate the feasibility of our strategy and to gain a better understanding of the factors governing the stereoselectivity of the [4 + 2] cycloaddition process, we first examined the behavior of the acyclic diyne esters **8a** and **8b**. Their straightforward and efficient preparation is outlined in Scheme III.[12]

1,5-Hexadiyne was converted quantitatively into 1,6-bis(trimethylsilyl)-1,5-hexadiyne (**3**).[13] Alkylation of its lithio derivative with 3-iodopropanal ethylene acetal[14] provided compound **4** which was subsequently hydrolyzed with formic acid[15] to yield the aldehyde **5**. A Wittig–Horner[16a] or a Knoevenagel condensation[16b] achieved the preparation of **6a** and **6b**, respectively. These compounds were cyclized through the action of 2 equiv of [2-(ace-

(12) (a) Gotteland, J. P.; Malacria, M. *Tetrahedron Lett.* **1989**, 2541. (b) *Comprehensive Organic Synthesis*: Pergamon Press: Oxford, 1991; Vol. 5, p 312.

(13) Auderset, P. C.; Dreiding, A. S.; Gesing, E. R. F. *Synth. Commun.* **1983**, *13*, 881.

(14) Larson, G. L.; Klesse, R. *J. Org. Chem.* **1985**, *50*, 3627.

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(16) (a) Trost, B. M.; Lynch, J.; Renaut, P.; Steinnan, D. H. *J. Am. Chem. Soc.* **1986**, *108*, 284. (b) Lehnert, W. *Tetrahedron Lett.* **1970**, 4723.

toxymethyl)-3-allyl]trimethylsilane, 5 mol % of palladium-(II) acetate, and 20 mol % of triisopropyl phosphite in refluxing tetrahydrofuran to afford the substituted methylenecyclopentane adducts **7a** and **7b** in excellent yields and in a complete diastereoselective manner for **7a**. Protodesilylation of the cycloadducts occured uneventfully to give **8a** and **8b** in nearly quantitative yields.

Our initial attempts of [2 + 2 + 2] cycloaddition reactions were conducted according to the regular protocol.[17] The reaction seemed to proceed perfectly, but much to our surprise, we obtained a 1:1 mixture of two inseparable benzocyclobutenes in which the double bond had migrated in the endocyclic position. Control experiments showed that no double-bond migration occured when the enediyne was refluxed in bis(trimethylsilyl)ethyne under irradiation for 24 h in the absence of the cobalt catalyst. We anticipated that new cobalt species resulting from the partial decomposition of the catalyst due to a too long reaction time were at the origin of this migration.

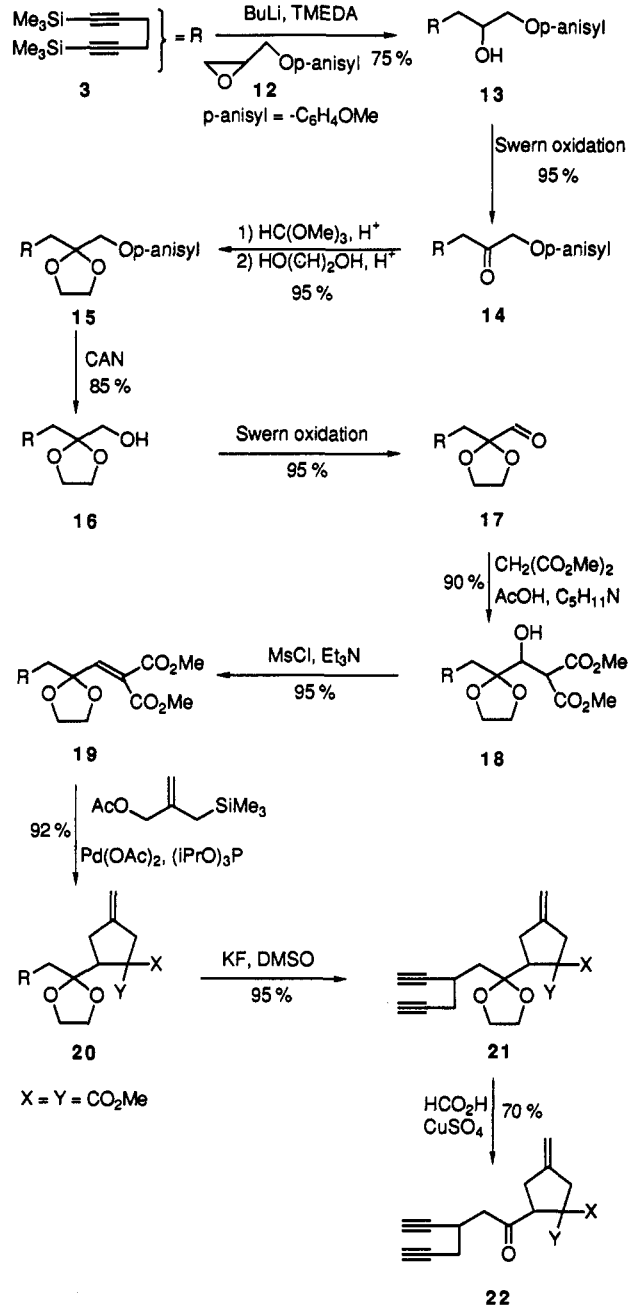
Gratifyingly, exposure of **8a** and **8b** to a catalytic amount of (η^5-cyclopentadienyl)cobalt dicarbonyl ($CpCo(CO)_2$) in boiling bis(trimethylsilyl)ethyne and irradiation for only 30–45 min furnished the benzocyclobutenes **9a** and **9b**, respectively, in high yields. Thermolysis of **9a** and **9b** in refluxing decane ended the preparation of the tetracyclic compounds **10** and **11** in a diastereoselective manner (5:1 and 10:1, respectively). The overall yields to **10a** and **10b** from commercially available 1,5-hexadiyne were 40% and 38%, respectively, for the eight-step sequence.

The major isomer **10b** and the minor one **11b** were separated by flash column chromatography on silica gel. Elucidation of these structures entailed a combination of spectroscopic and X-ray crystallographic techniques. Proton chemical shifts and coupling constants of **10b** were fully assigned by COSY and decoupling experiments. NOESY analysis indicated a NOE effect for H_9–H_7 and H_9–H_{14}, establishing a *trans* B/C ring junction configuration characteristic of the phyllocladane skeleton. Finally, the assigned structure of **10b** was unambiguously confirmed by a single X-ray analysis.[18] Although the isomers **10a** and **11a** were not separated by flash column chromatography, the stereochemistry of **10a** was assigned by elucidation of the ^{13}C-NMR spectrum of the mixture which showed chemical shifts of the major component similar to those of **10b**.

As noted earlier (Scheme II), the diastereoselectivity observed in favor of the phyllocladane formation can be attributed to the severe H_1–H_{12} nonbonding interaction in the transition state **A** leading to the kaurane skeleton. Whereas, the interaction between the two established rings which exists in approach **B** is without significant influence on the stereochemical course of the reaction.

Having secured a straightforward access to the diterpenes framework, we turned our attention to changing the stereoselectivity of the reaction. Therefore, we examined the influence of a C_{12} carbonyl, acetal,[19] and silyl ether group. We thought that the presence of a carbonyl substituent would decrease, at least partially, this unfavorable nonbonding interaction and consequently increase the ratio of kaurane type framework. *A contrario*, the presence of an acetal should improve the stereoselective access to the phyllocladane family.

Scheme IV



The requisite diynes **21** and **22** were obtained as described in Scheme IV. The regioselective opening of commercially available epoxide **12** with the lithio derivative of **3** provided alcohol **13**, which was cleanly oxidized[20] to ketone **14**. Generation of the dimethyl acetal followed by transacetalization[21] with ethylene glycol gave acetal **15** whose *p*-anisyl group was removed[22] to furnish primary alcohol **16**. The following Swern oxidation[20] afforded aldehyde **17**. Knoevenagel condensation[16b] of **17** with dimethyl malonate, under conditions (3 Å molecular sieves)

(17) Halterman, R. L.; Nguyen, N. H.; Vollhardt, K. P. C. *J. Am. Chem. Soc.* **1985**, *107*, 1379. Exposure of the diyne to refluxing btmse with simultaneous irradiation in presence of a catalytic amount of $CpCo(CO)_2$ over 4 h.

(18) Gotteland, J. P.; Malacria, M.; Faure, A. *Acta Crystallogr.* **1990**, *C-46*, 1271.

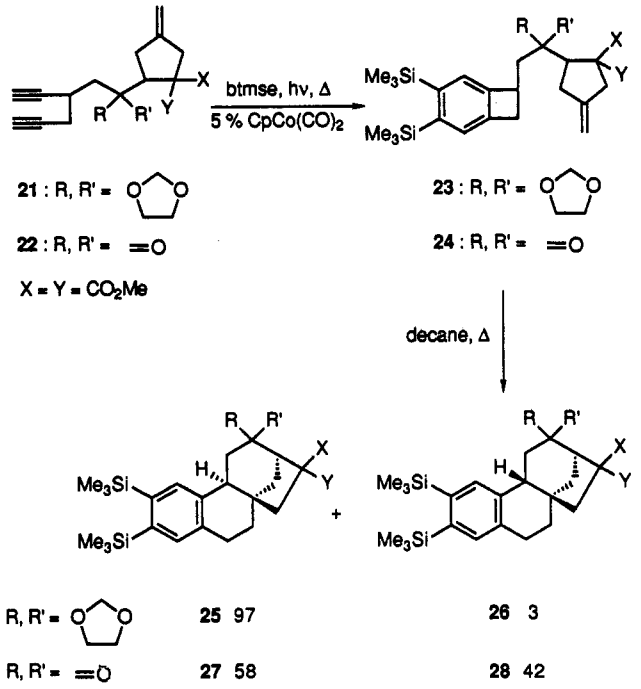
(19) Gotteland, J. P.; Malacria, M. *Synlett* **1990**, 667.

(20) Mancuso, A. J.; Swern, D. *J. Org. Chem.* **1978**, *43*, 165.

(21) Nemoto, H.; Fujita, S.; Nagai, N.; Fukumoto, K.; Kametani, T. *J. Am. Chem. Soc.* **1988**, *110*, 2931.

(22) (a) Fukuyama, T.; Laird, A. A.; Hotchkiss, L. M. *Tetrahedron Lett.* **1985**, 6291. (b) Petitou, M.; Duchaussoy, P.; Choay, J. *Tetrahedron Lett.* **1988**, 1389.

Scheme V



designed to prevent a deprotection of the acetal, produced hydroxy ester **18**. Surprisingly, dehydration did not spontaneously take place but was readily performed in the presence of mesyl chloride and triethylamine to yield the desired diester **19**.

The adduct **20** was obtained in 92% isolated yield as a 1:3 mixture of diastereoisomers, according to a Trost procedure described earlier. Removal of the trimethylsilyl groups gave **21**, which was deprotected to ketone **22**. Cooligomerization of enediynes **21** and **22** with bis(trimethylsilyl)ethyne catalyzed by $CpCo(CO)_2$ afforded benzocyclobutenes **23** and **24** (Scheme V) as a 1:3 mixture of two diastereoisomers (confirming the ratio of the [3 + 2] annelation). Each couple of diastereoisomers **23(a+b)** or **24(a+b)** were not necessary separated as they gave the same orthoquinodimethane intermediate in the [4 + 2] cycloaddition. Thermolysis of **23** provided the precursor of the phyllocladane skeleton with high stereoselectivity (**25:26** = 97:3), whereas **24** gave a more statistical mixture (**27:28** = 58:42).

These results agree with the dramatic influence of the nonbonding interaction between H_1 and the substituents at the sp^3-hybridized C_{12}. By introducing at C_{12} bulkier substituents than hydrogen, the nonbonding interaction increased. On the other hand, the presence of an sp^2 carbon partially suppresses this interaction, the ratio 58:42 meaning that the two transition states have almost the same energy level.

The influence of this severe nonbonding interaction was unambiguously confirmed by studying the stereochemical outcome of the reaction of both silyl ethers diastereoisomers. As anticipated in the case of the *unlike* stereoisomer[23] where the repulsive interaction between the aromatic hydrogen and the bulky silicon substituent is maximum allowed the exclusive formation of the phyllocladane type compound, whereas the *like* isomer delivered a mixture of phyllocladane–kaurane skeletons in a ratio very close to what we have previously observed for the cyclization of **9a** and **9b**.

(23) Prelog, V.; Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 654.

Conclusion

In this paper, we have described a rapid construction of tetracyclic systems belonging to the phyllocladane and kaurane families. This concise strategy can be viewed as an illustration of the very high performance of transition metal catalysis applied to the synthesis of complex organic molecules.

This sequence of three consecutive cycloaddition reactions allowed the formation of 7 C–C bonds in a totally controlled regio-, chemo-, and stereoselective manner, starting from an acyclic enediyne system. The efficiency of our methodology has been demonstrated by the stereoselective preparation of several functionalized phyllocladane-based frameworks. Finally, factors governing the stereoselectivity in the intramolecular Diels–Alder reaction have been clearly elucidated.

Efforts in our laboratories are currently devoted to the inversion of the stereoselectivity to eventually provide the kaurane structure.

Experimental Section[24]

2-[(Trimethylsilyl)ethynyl]-6-(trimethylsilyl)-5-hexyn-1-one Ethylene Acetal (4). To a stirred solution of 1,6-[bis(trimethylsilyl)]-1,5-hexadiyne (10 g, 45 mmol) and *N,N,N',N'*-tetramethylethylenediamine (TMEDA) (6.8 mL, 45 mmol) in dry THF (50 mL) at −78 °C was added *n*-butyllithium (1.6 M in hexanes, 28.2 mL, 45 mmol). The reaction mixture was slowly warmed to 0 °C over 4 h. The solution was then cooled to −78 °C, and a freshly prepared solution of 2-(iodo-1-ethyl)-1,3-dioxolane[14] (13.34 g, 85 mmol) in THF (50 mL) was added dropwise over 30 min. After being stirred for another 10 min, the temperature was increased to 0 °C.

The reaction mixture was diluted with ether (300 mL) and poured onto a saturated solution of NH_4Cl (100 mL). The organic layer was washed successively with a saturated solution of $CuSO_4$ (100 mL), water (100 mL), and brine (2 × 100 mL) and then dried over $MgSO_4$. The solvent was removed under vacuum and the residue purified by flash chromatography (petroleum ether–ether (9:1)) to yield **4** (13.1 g; 90%): ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.95 (1H, t, J = 4.5 Hz), 3.94–3.75 (4H, m, A_2B_2), 2.60–2.48 (1H, m), 2.40 (1H, dd, J = 16.8, 6.2 Hz), 2.30 (1H, dd, J = 16.8, 7.5 Hz), 1.92–1.45 (4H, m), 0.25 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 108.0, 104.2, 104.1, 86.5, 86.4, 64.9, 32.0, 31.3, 28.1, 26.1, 0.2, 0.1; IR (neat) 2960, 2880, 2180, 1250, 1150, 845, 760 cm^{-1}; MS (*m/z*) 322, 133, 99, 73, 46. Anal. Calcd for $C_{17}H_{30}O_2Si_2$: C, 63.29; H, 9.37. Found: C, 62.98; H, 9.46.

4-[(Trimethylsilyl)ethynyl]-7-(trimethylsilyl)-6-heptyn-1-al (5). A solution of **4** (12g, 37.2 mmol) and formic acid (55 mL, 40 equiv) dried over anhydrous copper(II) sulfate in petroleum ether (20 mL) was stirred at room temperature for 90 min.

The reaction mixture was diluted with hexane (350 mL) and neutralized by the addition of anhydrous Na_2CO_3. The organic layer was washed successively with a saturated solution of

(24) **General.** Melting points were measured on a Büchi B-510 apparatus and are uncorrected. ^{1}H-NMR spectra were taken on 80-MHz Bruker WP80, 200-MHz Bruker AC 200, 300-MHz Bruker AM 300, 350-MHz Cameca 350, 400-MHz Bruker AM 400, and 500-MHz Bruker AM 500 spectrometers. ^{13}C-NMR spectra were recorded on 50-MHz Bruker AC 200 and 75.5-MHz Bruker AM 300 instruments. Chemical shifts are reported in ppm referenced to the residual proton resonances of the solvents. Infrared (IR) spectra were recorded by using a Perkin-Elmer 298 spectrophotometer. Mass spectra (MS) were obtained on a Nermag R10-10S spectrometer. Elemental analyses were carried out on a C,H,N elemental analyser. Thin-layer chromatography (TLC) was performed on Merck silica gel 60F-254. Silica gel 60 (35–70 μm) Amicon was used for column chromatography using Still's method.[25]

(25) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

$NaHCO_3$ (2 × 100 mL) and brine (2 × 50 mL), dried over $MgSO_4$, and concentrated. The residue was filtered on alumina (activity III: 5% H_2O) affording **5** (10.15 g; 98%): ^{1}H-NMR (300 MHz, $CDCl_3$) δ 8.45 (1H, t, J = 1.3 Hz), 2.65–2.5 (3H, m), 2.45 (1H, dd, J = 16.8, 6.2 Hz), 2.35 (1H, dd, J = 16.8, 7.5 Hz), 2.18–1.92 (1H, m), 1.82–1.70 (1H, m), 0.25 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 201.8, 107.1, 103.6, 87.5, 86.6, 41.5, 31.6, 26.0, 0.2; IR (neat) 2920, 2720, 2180, 1730, 1250, 845, 760 cm^{-1}; MS (*m/z*) 278, 147, 133, 96, 83, 73, 59, 45.

Methyl 6-[2-(Trimethylsilyl)ethynyl]-9-(trimethylsilyl)-2-nonen-8-ynoate (6a). To a solution of potassium *tert*-butoxide (8 g, 71.2 mmol) in THF (90 mL) at 0 °C was added dropwise trimethyl phosphonoacetate (12.7 mL, 78.3 mmol). After being stirred at 0 °C for 90 min the reaction mixture was cooled to −78 °C, and a solution of aldehyde **5** (10 g, 35.6 mmol) in THF (60 mL) was added over 15 min. The mixture was allowed to warm to 0 °C (2 h). The reaction mixture was extracted with ether, washed with a saturated solution of NH_4Cl (3 × 100 mL) and brine (100 mL), dried over $MgSO_4$, and concentrated. The residue was flash chromatographed (petroleum ether–ether (9:1)) affording **6a-*Z*** (720 mg; 6%) and **6a-*E*** (9.6 g; 81%). **6a-*Z***: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.25 (1H, dt, J = 11.2, 7.7 Hz), 5.80 (1H, dt, J = 11.2, 1.5 Hz), 3.60 (3H, s), 2.81 (2H, qd, J = 7.7, 1.5 Hz), 2.60–2.56 (1H, m), 2.46 (1H, dd, J = 16.7, 5.6 Hz), 2.38 (1H, dd, J = 16.7, 7.7 Hz), 1.79–1.70 (1H, m), 1.69–1.58 (1H, m), 0.25 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 167.6, 150.5, 120.8, 108.9, 105.0, 87.6, 87.4, 51.9, 34.0, 32.8, 27.7, 26.9, 1.0; IR (neat) 3050, 2180, 1730, 1655, 1250, 845, 760 cm^{-1}. **6a-*E***: ^{1}H-NMR (350 MHz, $CDCl_3$) δ 6.83 (1H, dt, J = 15.5, 6.9 Hz), 5.71 (1H, dt, J = 15.5, 1.3 Hz), 3.60 (3H, s), 2.48–2.38 (1H, m), 2.31 (1H, dd, J = 16.7, 5.6 Hz), 2.19 (1H, dd, J = 16.7, 7.7 Hz), 2.29–2.10 (2H, m), 1.68–1.57 (1H, m), 1.55–1.39 (1H, m), 0.25 (18H, s); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 167.0, 148.6, 121.4, 107.5, 103.6, 87.0, 86.7, 51.4, 33.0, 31.5, 29.9, 26.0, 0.2; IR (neat) 3050, 2180, 1730, 1655, 1250, 845, 760 cm^{-1}; MS (*m/z*) 334, 319, 261, 109, 89, 83, 73, 59, 45. Anal. Calcd for $C_{18}H_{30}O_2Si_2$: C, 64.61; H, 9.04. Found: C, 64.77; H, 9.09.

Dimethyl 4-(2-Trimethylsilyl)-7-(trimethylsilyl)-6-heptynylidenepropanedioate (6b). Titanium tetrachloride (1.0 M in CH_2Cl_2, 18 mL, 18 mmol) was added dropwise at 0 °C to THF (15 mL) and stirred for a few minutes during which time a yellow precipitate appeared. Then solutions of dimethyl malonate (1.2 g 9 mmol) and aldehyde **5** (2.5 g, 9 mmol) in THF (6 mL) were added. After the mixture was stirred for 10 min at 0 °C, a solution of pyridine (2.9 mL, 36 mmol) in THF (12 mL) was added by a syring pump over 90 min. The reaction mixture was stirred at 0 °C for 6 h and 22 h further at room temperature. The solution was then partitioned between ether (200 mL) and water (120 mL). The aqueous phase was extracted with ether (100 mL), and the combined organic layers were washed with brine, dried over $MgSO_4$, and concentrated. The residue was purified by flash chromatography (petroleum ether–ether (9:1)) to give the α,β-unsaturated diester **6b** (2.65 g, 75%): ^{1}H-NMR (350 MHz, $CDCl_3$) δ 7.04 (1H, t, J = 7.8 Hz), 3.81 (3H, s), 3.76 (3H, s), 2.62–2.50 (1H, m), 2.48–2.29 (2H, m), 2.44 (1H, dd, J = 16.8, 5.7 Hz), 2.34 (1H, dd, J = 16.8, 7.7 Hz), 1.83–1.57 (2H, m), 0.13 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 167.2, 165.7, 149.4, 128.4, 107.3, 103.6, 87.2, 86.8, 52.3, 52.2, 32.2, 31.8, 27.6, 25.9, 0.1; MS (*m/z*) 392, 377, 145, 89, 83, 73, 59; IR (neat) 2880, 2180, 1740, 1645, 1250, 845, 760 cm^{-1}. Anal. Calcd for $C_{20}H_{32}O_4Si_2$: C, 61.18; H, 8.22. Found: C, 60.83; H, 8.12.

4-[2-(Trimethylsilyl)ethynyl]-1-(4-methoxyphenoxy)-7-(trimethylsilyl)-6-heptynyl-2-ol (13). To a solution of 1,6-[bis(trimethylsilyl)]-1,5-hexadiyne (**3**) (10 g, 45 mmol) and TMEDA (6.8 mL, 45 mmol) in THF (60 mL) at −78 °C was added n-butyllithium (1.6 M in hexanes, 28.2 mL, 45 mmol). The reaction mixture was stirred until the temperature reached 0 °C (4 h) and then cooled to −78 °C, and a solution of 2,3-epoxypropyl 4-methoxyphenyl ether (10.5 g, 58.5 mmol) in THF (70 mL) was added over 1 h. The mixture was stirred at −78 °C for an additionnal 30 min, warmed to 0 °C, and diluted with ether (350 mL). The organic layer was washed with brine (150 mL), dried over Na_2SO_4, and concentrated. Purification by flash chromatography (petroleum ether–ether (9:1)) furnished **13** (13.6 g, 75%) as a mixture of inseparable diastereoisomers (GC and ^{1}H-NMR indicated a 60/40 mixture): ^{1}H-NMR (350 MHz, $CDCl_3$) δ 6.84 (8H, m, A_2B_2), 4.30–4.15 (2H, m), 4.05–3.80 (4H, m), 3.75 (6H, m), 2.92–2.85 (1H, m), 2.80–2.70 (1H, m), 2.55–2.38 (2H, m), 2.02–1.92 (2H, m), 1.90–1.75 (2H, m), 1.70–1.58 (2H, m), 0.15 (36H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 154.0, 152.7, 115.6, 115.5, 108.0, 107.7, 103.8, 103.7, 87.4, 87.0, 86.9, 86.7, 72.9, 72.1, 68.8, 68.3, 55.7, 37.4, 37.3, 29.0, 28.7, 26.4, 26.0, 0.03; IR (neat) 3070, 2180, 1510, 1250, 845, 760 cm^{-1}; MS (*m/z*) 402, 147, 124, 109, 83, 73, 45. Anal. Calcd for $C_{22}H_{34}O_3Si_2$: C, 65.61; H, 8.51. Found: C, 65.38; H, 8.51.

4-[2-(Trimethylsilyl)ethynyl]-1-(4-methoxyphenoxy)-7-(trimethylsilyl)-6-heptyn-2-one (14). A solution of dimethyl sulfoxide (4.6 mL, 60 mmol) in CH_2Cl_2 (48 mL) was added dropwise at −78 °C to a solution of oxalyl chloride (3.2 mL, 36 mmol) in CH_2Cl_2 (47 mL). After 5 min a solution of **13** (12 g, 30 mol) in CH_2Cl_2 (40 mL) was added over 10 min. After the solution was stirred at −78 °C for 15 min, triethylamine (20.9 mL, 150 mmol) was added. The reaction mixture was warmed to room temperature, diluted with CH_2Cl_2 (200 mL), and hydrolyzed with 5% HCl (100 mL). The organic layer was washed with brine (3 × 150 mL), dried on $MgSO_4$, and concentrated. Flash chromatography (petroleum ether–ether (8:2)) afforded **14** (11.4 g, 95%): ^{1}H-NMR (350 MHz, $CDCl_3$) δ 6.82 (4H, s), 4.55 (2H, s), 3.75 (3H, s), 3.15 (1H, m), 2.91 (1H, dd, J = 16.9, 2.2 Hz), 2.82 (1H, dd, J = 16.9, 7.7 Hz), 2.51 (1H, dd, J = 16.9, 5.8 Hz), 2.43 (1H, dd, J = 16.9, 7.0 Hz), 0.13 (9H, s), 0.12 (9H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 205.2, 154.5, 151.9, 115.5, 114.7, 106.8, 103.1, 87.4, 86.6, 73.9, 55.6, 42.7, 26.9, 25.6, −0.02; IR (neat) 3060, 3040, 2180, 1730, 1510, 1250, 1230, 845, 760 cm^{-1}; MS (*m/z*) 400, 139, 124, 77, 73, 59, 45. Anal. Calcd for $C_{22}H_{32}O_3Si_2$: C, 65.95; H, 8.05. Found: C, 65.71; H, 8.12.

4-[2-(Trimethylsilyl)ethynyl]-1-(4-methoxyphenoxy)-7-(trimethylsilyl)-6-heptynone 2-Ethylene Acetal (15). (a) To a solution of ketone **14** (10 g, 25 mmol) in methanol (150 mL) in the presence of a catalytic amount of (±)-10-camphorsulfonic acid (290 mg, 1.25 mmol) was added trimethyl orthoformate (10.9 mL, 100 mmol). After being stirred at room temperature for 30 h, the reaction mixture was diluted with ether (350 mL) and poured onto water (150 mL). The organic phase was washed with a saturated solution of sodium hydrogen carbonate (150 mL) and brine (2 × 100 mL), dried on $MgSO_4$, and concentrated. The crude product was used in the next step without purification.

(b) A solution of the dimethyl acetal (11 g, 24.6 mmol), freshly prepared, ethylene glycol (6.9 mL, 123 mmol), and (±)-10-camphorsulfonic acid (280 mg, 1.23 mmol) in toluene (300 mL) was heated at reflux with a Dean-Stark apparatus for 4 h. The solution was cooled, and toluene was evaporated. The residue was diluted with ether (200 mL) and neutralized with a saturated solution of $NaHCO_3$ (50 mL). The organic layer was washed with brine (3 × 50 mL), dried on Na_2SO_4, and concentrated. The residue was quickly purified by flash chromatography (petroleum ether–ether (8:2)) to yield **15** (9.8 g, 90%): ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.87–6.78 (4H, m, A_2B_2), 4.04 (4H, s), 3.96 (2H, s), 3.75 (3H, s), 2.88–2.83 (1H, m), 2.52 (1H, dd, J = 16.7, 6.3 Hz), 2.45 (1H, dd, J = 16.7, 7.1 Hz), 2.15 (1H, dd, J = 14.3, 8.1 Hz), 2.08 (1H, dd, J = 14.3, 5.3 Hz), 0.15 (9H, s), 0.09 (9H, s)); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 154.0, 153.0, 115.5, 114.5, 108.7, 108.6, 104.2, 86.3, 85.7, 71.0, 65.5, 65.4, 55.7, 38.8, 27.4, 27.0, 0.08, 0.01; IR (neat) 3060, 3040, 2180, 1510, 1250, 1230, 1065, 845, 760 cm^{-1}; MS (*m/z*) 444, 307, 195, 123, 109, 95, 73, 59, 43. Anal. Calcd for $C_{24}H_{36}O_4Si_2$: C, 64.82; H, 8.16. Found: C, 64.59; H, 8.12.

2-(Ethylenedioxy)-4-[2-(trimethylsilyl)ethynyl]-7-(trimethylsilyl)-6-heptyn-1-ol (16). Ceric ammonium nitrate (CAN) (27.4 g, 50 mmol) was added to a cooled solution (0 °C) of **15** (9 g, 20 mmol) in a mixture of 4/1 acetonitrile–water (500 mL). After being stirred for 10 min at 0 °C, the reaction mixture was diluted with ether (400 mL). The organic layer was washed successively with saturated solutions of NH_4Cl (150 mL), $NaHCO_3$ (8 × 150 mL), and brine (150 mL), dried on Na_2SO_4, and concentrated. The residue was flash chromatographed (petroleum ether–ether (6:4)) yielding **16** (5.75 g, 85%): ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.00–3.96 (4H, m, A_2B_2), 3.66–3.56 (2H,m, AB), 2.76–2.69 (1H, m), 2.46 (1H, dd, J = 16.8, 6.1 Hz), 2.37 (1H, dd, J = 16.8, 7.6 Hz), 2.00 (1H, dd, J = 14.4, 8.0 Hz), 1.93 (1H, dd, J = 14.4, 5.2 Hz), 0.12 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 109.5, 108.9, 104.0, 86.5, 85.9, 65.3, 65.0, 38.5, 27.3, 26.9, 0.02; IR (neat) 3460, 2180, 1250, 1065, 1045, 845, 760 cm^{-1}; MS (*m/z*) 338,

307, 195, 103, 73, 45, 31. Anal. Calcd for $C_{17}H_{30}O_3Si_2$: C, 60.30; H, 8.93. Found: C, 60.00; H, 9.02.

3-(Ethylenedioxy)-5-[2-(trimethylsilyl)ethynyl]-8-(trimethylsilyl)-7-octynal (17) was prepared using the procedure described for 14. Aldehyde 17 (5.10 g, 95%) was fairly unstable on alumina and was used without further purification. ^{1}H-NMR (300 MHz, $CDCl_3$) δ 9.45 (1H, s), 4.11–3.92 (4H, m, A_2B_2), 2.86–2.79 (1H, m), 2.48 (1H, dd, J = 16.8, 6.1 Hz), 2.43 (1H, dd, J = 16.8, 7.0 Hz), 2.20 (1H, dd, J = 14.2, 9.4 Hz), 2.07 (1H, dd, J = 14.2, 4.7 Hz), 0.15 (9H, s), 0.13 (9H, s); IR (neat) 2820, 2180, 1750, 1250, 1065, 1045, 845, 760 cm^{-1}; MS (m/z) 336, 307, 195, 101, 73, 45.

Dimethyl [2-(Ethylenedioxy)-4-[2-(trimethylsilyl)ethynyl]-1-hydroxy-7-(trimethylsilyl)-6-heptynyl]propanedioate (18). To a solution of aldehyde 17 (5 g, 15 mmol) and dimethyl malonate (2.2 g, 16.5 mmol) in CH_2Cl_2 (45 mL) in the presence of 4-Å molecular sieves at 0 °C was added piperidine (1.48 mL, 15 mmol). After being stirred at 0 °C for 15 min, acetic acid (0.86 mL, 15 mmol) was added dropwise. The reaction mixture was stirred at 0 °C for an additional 1 h and 15 h at room temperature and then partitioned between CH_2Cl_2 (200 mL) and water (200 mL). The organic layer was washed with brine (100 mL), dried over Na_2SO_4, and concentrated. Flash chromatography (petroleum ether–ether (6:4)) afforded 18 (6.3 g, 90%) as a mixture of two inseparable diastereoisomers (300-MHz ^{1}H-NMR spectrum revealed a ratio of 55:45): ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.58 (1H, t, J = 7.2 Hz), 4.37 (1H, t, J = 6.9 Hz), 4.05–3.95 (4H, m, A_2B_2), 3.71 (3H, s), 3.70 (3H, s), 3.68 (3H, s), 3.67 (3H, s), 3.61 (1H, d, J = 6.9 Hz), 3.57 (1H, d, J = 7.2 Hz), 3.48 (1H, d, J = 7.2 Hz), 3.46 (1H, d, J = 6.9 Hz), 2.77–2.65 (1H, m), 2.49–2.29 (2H,m), 2.17–2.09 (1H, m), 1.94–1.85 (1H, m), 0.09 (18H, s), 0.08 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 169.2, 169.0, 167.6, 167.5, 110.0, 108.6, 108.4, 103.0, 86.4, 85.9, 85.3, 73.2, 72.6, 65.2, 65.0, 64.7, 52.6, 52.5, 52.4, 52.1, 36.8, 36.5, 27.1, 27.0, 26.8, 26.5, –0.05, –0.06; IR (neat) 2180, 1770, 1745, 1250, 1065, 1045, 845, 760 cm^{-1}; MS (m/z) 468, 307, 195, 101, 83, 73, 59, 45. Anal. Calcd for $C_{22}H_{36}O_7Si_2$: C, 56.38; H, 7.74. Found: C, 56.45; H, 7.80.

Dimethyl [2-(Ethylenedioxy)-4-[2-(trimethylsilyl)ethynyl]-7-(trimethylsilyl)-6-heptynylidene]propanedioate (19). To a –20 °C cooled solution of hydroxy exter 18 (6.1 g, 13 mmol) and triethylamine (12.7 g, 91 mmol) in CH_2Cl_2 (60 mL) was added dropwise methanesulfonyl chloride (1.3 mL, 19.5 mmol). The reaction mixture was stirred at –20 °C for 5 min and an additional 1 h at room temperature and diluted with CH_2Cl_2 (200 mL). The organic layer was washed with a saturated solution of NH_4Cl (3 × 150 mL) and brine (100 mL), dried over Na_2SO_4, and concentrated. Purification of the residue by flash chromatography (petroleum ether–ether (8:2)) yielded 19 (5.6 g, 95%): ^{1}H-NMR (300 MHz, $CDCl_3$) δ 6.76 (1H, s), 3.90–3.80 (4H, m, A_2B_2), 3.73 (3H, s), 3.70 (3H, s), 2.80–2.70 (1H, m), 2.39 (2H, d, J = 6.4 Hz), 2.06 (1H, dd, J = 14.2, 7.3 Hz), 1.99 (1H, dd, J = 14.2, 5.8 Hz), 0.07 (9H, s), 0.04 (9H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 166.1, 163.5, 144.7, 128.5, 108.2, 107.1, 103.9, 86.4, 86.0, 65.1, 65.0, 52.6, 52.3, 41.4, 26.9, 26.6, 0.1; IR (neat) 2180, 1735, 1660, 1250, 1065, 1045, 845, 760 cm^{-1}; MS (m/z) 450, 435, 215, 89, 73, 59. Anal. Calcd for $C_{22}H_{34}O_6Si_2$: C, 58.63; H, 7.60. Found: C, 58.43; H, 7.62.

[3 + 2] Annelation Reaction. General Procedure. A flame-dried flask was charged under argon with palladium(II) acetate (340 mg, 1.5 mmol) and triisopropyl phosphite (1.5 mL, 6 mmol). The reaction mixture was stirred until the catalyst was completely dissolved. Then, a 1 M solution of α,β-unsaturated ester (15 mmol) in THF and a 1.5 M solution of 2-[(trimethylsilyl)methyl]-2-propen-1-yl acetate (30 mmol) in THF were added, and the resulting mixture was heated at reflux until the TLC indicated that starting material had been consumed. After cooling and evaporation of the volatiles, the crude material was flash chromatographed affording the methylenecyclopentane adducts.

7a: 5.25 g, 90%; GC analysis indicated a 1:1 mixture of two inseparable diastereoisomers; ^{1}H-NMR (350 MHz, $CDCl_3$) δ 4.85 (2H, br s), 3.69 (3H, s), 2.65–2.53 (3H, m), 2.52–2.29 (4H, m), 2.27–2.10 (1H, m), 2.03–1.90 (1H, m), 1.80–1.25 (4H, m), 0.25 (18H, s); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 175.8, 175.7, 149.2, 149.1, 109.5, 109.4, 106.2, 104.2, 104.1, 86.4, 86.3, 86.2, 51.6, 50.1, 49.9, 43.7, 43.5, 40.0, 39.7, 36.9, 36.8, 32.1, 32.0, 31.9, 31.8, 31.5, 25.9, 25.8, 0.2; IR (neat) 3080, 2180, 1745, 1655, 1250, 845, 760 cm^{-1}; MS (m/z) 388, 373, 91, 89, 79, 73, 59. Anal. Calcd for $C_{22}H_{32}O_2Si_2$: C, 67.98; H, 9.34. Found: C, 67.68; H, 9.39.

7b: 2.05 g, 90%; GC indicated a 1:1 mixture of two inseparable diastereoisomers; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.89 (2H, br s), 3.71 (6H, s), 2.62–2.16 (8H, m), 1.73–1.43 (4H, m), 0.12 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 172.3, 171.3, 147.2, 108.7, 108.5, 107.0, 104.4, 104.3, 86.6, 86.5, 86.4, 63.3, 63.2, 52.7, 52.3, 45.3, 45.0, 40.7, 37.4, 37.2, 32.5, 32.4, 32.3, 32.1, 28.6, 28.5, 26.2, 25.9, 0.3, 0.2; IR (neat) 3080, 2180, 1740, 1660, 1250, 845, 760 cm^{-1}; MS (m/z) 446, 91, 89, 73, 59. Anal. Calcd for $C_{24}H_{38}O_4Si_2$: C, 64.53; H, 8.57. Found: C, 64.55; H, 8.61.

20: 1:3 mixture of two diastereoisomers **20a** (1.7 g, 28%) and **20b** (3.9 g, 64%) was obtained. **20a**: white solid; mp 56–57 °C; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.87 (1H, br s), 4.84 (1H, br s), 3.97–3.85 (4H, m A_2B_2), 3.70 (3H, s), 3.67 (3H, s), 3.38 (1H, dd, J = 8.4, 5,1 Hz), 3.28 (1H, br d, J = 16.5 Hz), 2.78–2.55 (4H, m), 2.50 (1H, dd, J = 16.7, 5.5 Hz), 2.37 (1H, dd, J = 16.7, 8.0Hz), 2.05 (1H, dd, J = 14.5, 4.2 Hz), 1.88 (1H, dd, J = 14.5, 8.4 Hz), 0.12 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 172.2, 170.0, 147.0, 111.1, 109.0, 106.7, 104.2, 86.3, 84.8, 65.0, 63.9, 61.4, 52.7, 52.0, 49.9, 41.5, 38.2, 34.0, 27.5, 26.7, 0.1. **20b**: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.86 (2H, br s), 3.90–3.80 (4H, m, A_2B_2), 3.70 (3H, s), 3.68 (1H, m), 3.65 (3H, s), 3.28 (1H, dq, J = 16.5, 2.0 Hz), 2.78–2.57 (3H, m), 2.63 (1H, dq, J = 16.5, 2.0 Hz), 2.50 (1H, dd, J = 16.7, 5.5 Hz), 2.33 (1H, dd, J = 16.7, 8.0 Hz), 1.94 (1H, dd, J = 14.5, 3.8 Hz), 1.84 (1H, dd, J = 14.5, 8.9 Hz), 0.14 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 172.2, 170.5, 147.3, 111,2, 108.5, 106.3, 104.3, 86.3, 85.9, 64.9, 63.7, 61.0, 52.6, 51.9, 49.2, 42.0, 38.4, 34.0, 27.5, 26.9, 0.1; **20a + 20b**: IR (neat) 3080, 2180, 1735, 1670, 1250, 1065, 1045, 845, 760 cm^{-1}; MS (m/z) 504, 307, 269, 209, 195, 89, 73, 59, 45. Anal. Calcd for $C_{26}H_{40}O_6Si_2$: C, 61.87; H, 7.99. Found: C, 62.09; H, 7.89.

Deprotection of Acetylenic Functions. General Procedure. To a solution of potassium fluoride dihydrate (10 equiv) in DMSO was added a solution of bis(trimethylsilyl) compound in DMSO. After being stirred at room temperature for 2 h, the reaction mixture was filtered and diluted with ether. The organic layer was washed with brine, dried over Na_2SO_4, and concentrated. Purification of the crude material by flash chromatography (petroleum ether–ether (8:2)) afforded the deprotected compounds.

8a: 96%; two diastereoisomers with the same ratio as **7a**; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.85 (2H, br s), 3.69 (3H, s), 2.70–2.30 (7H, m), 2.27–2.16 (1H, m), 2.13 (1H, d, J = 1.8 Hz), 2.11 (1H, d, J = 1.8 Hz), 2.04 (1H, m), 2.00–1.93 (1H, m), 1.80–1.25 (4H, m); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 176.5, 176.0, 149.0, 106.5, 86.1, 86.0, 81.6, 81.5, 70.4, 70.3, 70.2, 51.7, 50.1, 49.9, 43.5, 39.0, 38.8, 36.9, 32.0, 31.9, 31.8, 30.9, 30.8, 24.6, 24.5; IR (neat) 3300, 3080, 2120, 1745, 1655, 880 cm^{-1}; MS m/z 244, 185, 169, 155, 129, 119, 105, 91, 79, 39. Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.45; H, 8.16.

8b: 95%; two diastereoisomers with the same ratio as **7b**; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.89 (2H, br s), 3.73 (3H, s), 3.72 (3H, s), 2.73–2.34 (1H, d, J = 2.5 Hz), 2.13 (1H,d, J = 2.5 Hz), 2.06 (1H, m), 1.84–1.47 (4H, m); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 172.0, 171.1, 147.0, 106.9, 85.7, 85.5, 81.4, 81.3, 70.4, 70.3, 63.0, 52.5, 52.2, 46.2, 45.9, 40.7, 40.6, 37.3, 37.0, 32.4, 32.3, 30.9, 30.8, 28.5, 28.4, 24.7, 24.3; IR (neat) 3300, 3080, 2120, 1740, 1660, 1270, 890 cm^{-1}; MS (m/z) 302, 183, 167, 155, 143, 129, 115, 105, 92, 91, 79, 77, 59, 39. Anal. Calcd for $C_{18}H_{22}O_4$: C, 71.52; H, 7.34. Found: C, 71.32; H, 7.31.

21: 95%; mixture of two inseparable diastereoisomers; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.84 (4H, br s), 3.90 (8H, m, A_2B_2), 3.78 (3H, s), 3.77 (3H, s), 3.65 (3H, s), 3.63 (3H, s), 3.52 (1H, dd, J = 8.4, 5.5 Hz), 3.32 (1H, dd, J = 8.3, 6.0 Hz), 3.29–3.20 (2H, m), 2.75–2.32 (12H, m), 2.16–1.90 (8H, m); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 172.4, 172.3, 170.4, 170.3, 147.0, 146.8, 111.3, 111.2, 106.9, 106.8, 86.5, 86.3, 81.6, 81.5, 70.3, 70.2, 69.8, 69.2, 65.8, 65.5, 64.8, 64.3, 61.3, 61.2, 52.8, 52.3, 52.2, 50.5, 49.4, 41.8, 41.6, 38.5, 38.2, 34.2, 34.1, 26.1, 26.0, 25.5, 25.4; IR (neat) 3300, 3080, 2120, 1735, 1670, 1270, 1065, 1045, 890 cm^{-1}; MS (m/z) 360, 269, 209, 163, 123, 79, 67, 59, 39. Anal. Calcd for $C_{20}H_{24}O_6$: C, 66.35; H, 6.71. Found: C, 66.40; H, 6.68.

Methyl 2-(3-Ethynyl-1-oxo-5-hexynyl)-1-(methoxycarbonyl)-4-methylidenecyclopentanecarboxylate (22). To a solution of diyne acetal 21 (1 g, 2.77 mmol) in a mixture of CH_2Cl_2

(2 mL) and hexane (6 mL) was added dropwise formic acid (3 mL, 80 mmol). After being stirred 1 h at room temperature, the reaction mixture was diluted with hexane (230 mL) and neutralized with potassium carbonate. The resulting organic layer was washed with a saturated solution of $NaHCO_3$ (100 mL) and brine (2 × 100 mL), dried over K_2CO_3, and concentrated. The residue was purified by flash chromatography (petroleum ether–ether (7:3)) affording **22** (610 mg, 70%) as a mixture of inseparable diastereoisomers: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 4.95–4.92 (2H, m), 3.76 (3H, s), 3.75–3.71 (1H, m), 3.69 (3H, s), 3.30–3.23 (1H, m), 3.15–3.07 (1H, m), 3.03–2.78 (4H, m), 2.68–2.58 (1H, m), 2.51–2.39 (2H, m), 2.14 (1H, d, J = 2.5 Hz), 2.10–2.08 (1H, m); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 206.6, 171.3, 170.2, 145.3, 145.2, 108.4, 108.3, 84.8, 80.7, 70.9, 70.8, 70.0, 69.9, 62.6, 62.5, 55.9, 55.8, 53.2, 52.7, 45.6, 45.3, 40.5, 40.4, 34.9, 34.5, 25.6, 25.3, 23.7, 23.6; IR (neat) 3300, 3080, 2120, 1770–1720, 1670, 890 cm^{-1}; MS (m/z) 316, 257, 225, 137, 119, 91, 79, 77, 67, 59. Anal. Calcd for $C_{18}H_{20}O_5$: C, 68.34; H, 6.37. Found: C, 68.05; H, 6.38.

[2 + 2 + 2] Cycloaddition Reactions. General Procedure. The reactions were carried out under argon in a flame-dried flask, and all the solutions were degassed by three freeze–pump–thaw cycles. A solution of the diyne (1 mmol) and $CpCo(CO)_2$ (25 μL, 0.2 mmol) in degassed bis(trimethylsilyl)ethyne (5 mL) was added dropwise over 20 min to a boiling degassed solution of btmse (10 mL) and $CpCo(CO)_2$ (12.5 μL, 0.1 mmol). Light from a projector lamp (ELW, 300 W, 25% of its power) was directed at the reaction mixture during the addition. After the mixture was boiled and irradiated for an additional 30 min, the solvent was removed by vacuum transfer. The crude residue was purified by flash chromatography to give the benzocyclobutenes.

9a: 270 mg, 80%; 1:1 mixture of inseparable diastereoisomers; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.42 (1H, br s), 7.40 (1H, br s), 4.86 (2H, s), 3.70 (3H, s), 3.50–3.41(1H, m), 3.35 (1H, dd, J = 13.9, 5.4Hz), 2.74 (1H, d, J = 13.9 Hz), 2.68–2.49 (4H, m), 2.27–2.23 (1H, m), 2.04–1.95 (1H, m), 1.74–1.61 (3H, m), 1.45–1.39 (1H, m), 0.36 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 175.8, 149.5, 149.2, 144.7, 144.1, 143.8, 143.7, 129.6, 129.5, 128.3, 106.2, 51.7, 50.1, 50.0, 44.3, 44.2, 44.0, 43.8, 39.1, 38.9, 37.0, 36.9, 36.7, 36.6, 33.2, 33.1, 32.6, 32.5, 2.38; IR (neat) 3080, 2960, 1745,1670, 1260, 845, 760 cm^{-1}; MS (m/z) 414, 399, 187, 89, 73, 59, 45. Anal. Calcd for $C_{24}H_{38}O_2Si_2$: C, 69.51; H, 9.24. Found: C, 69.31; H, 9.29.

9b: 400 mg, 85%; 1:1 mixture of inseparable diastereoisomers; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.44 (2H, br s), 4.91 (2H, br s), 3.76 (3H, s), 3.74 (3H, s), 3.54–3.46 (1H, m), 3.40–3.31 (1H, m), 3.15 (1H, d, J = 17.4 Hz), 2.86–2.62 (4H, m), 2.27–2.22 (1H, m), 1.83–1.71 (3H, m), 1.35–1.25 (1H, m), 0.38 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 169.8, 169.7, 168.9, 168.8, 147.1, 144.8, 144.7, 142.4, 141.7, 141.3, 127.2, 127.1, 126.0, 125.9, 104.6, 104.5, 60.8, 60.6, 50.1, 49.8, 43.0, 42.8, 41.8, 41.7, 38.3, 38.1, 34.8, 34.4, 34.2, 34.1, 30.7, 30.6, 27.5, 27.3, 24; IR (neat) 3080, 2960, 1730, 1670, 1260, 845, 760 cm^{-1}; MS (m/z) 472, 457, 187, 161, 89, 73, 59. Anal. Calcd for $C_{26}H_{40}O_4Si_2$: C, 66.05; H, 8.53. Found: C, 65.75; H, 8.65.

23: 350 mg, 80%; 3:7 mixture of diastereoisomers **23a**:**23b**. **23a**: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.45 (1H, s), 7.40 (1H, br s), 4.90 (1H, s), 4.87 (1H, br s), 3.96–3.88 (4H, m, A_2B_2), 3.72 (3H, s), 3.71 (3H, s), 3.69–3.60 (1H, m), 3.45 (1H, dd, J = 8.2, 4.5 Hz), 3.39 (1H, dd, J = 14.3, 5.3 Hz), 3.32 (1H, d, J = 17.3 Hz), 2.86 (3H, dd, J = 14.3, 2.3 Hz), 2.72 (1H, d, J = 17.3 Hz), 2.71–2.55 (2H, m), 2.14 (1H, dd, J = 14.5, 7.0 Hz), 2.05 (1H, dd, J = 14.5, 7.5 Hz), 0.35 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 171.2, 170.9, 149.5, 147.0, 145.1, 145.0, 144.5, 129.3, 129.0, 112.0, 107.0, 64.9, 64.3, 61.5, 52.6, 51.6, 50.0, 41.5, 39.4, 38.2, 36.8, 34.4, 2.4. **23b**: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.48 (1H, br s), 7.41 (1H, br s), 4.89 (1H, br s), 4.87 (1H br s), 4.04–3.90 (4H, m, A_2B_2), 3.72 (3H, s), 3.70 (3H, s), 3.69–3.61 (1H, m), 3.46 (1H, dd, J = 8.0, 4.7 Hz), 3.35 (1H, dd, J = 14.3, 5.4 Hz), 3.31 (1H, d, J = 17.2 Hz), 2.89 (1H, dd, J = 14.3, 2.6 Hz), 2.74 (1H, d, J = 17.2 Hz), 2.68–2.57 (2H, m), 2.15 (1H, dd, J = 14.5, 7.3 Hz), 2.08 (1H, dd, J = 14.5, 7.0 Hz), 0.36 (18 H, s); ^{13}C-NMR, (75.5 MHz, $CDCl_3$) δ 172.4, 170.5, 149.3, 147.1, 144.7, 144.2, 144.1, 129.3, 129.1, 112.1, 106.9, 65.2, 64.4, 61.5, 52.8, 52.2, 50.4, 41.5, 39.2, 38.6, 37.2, 34.3, 2.4. **23a + 23b**: IR (neat) 3080, 3040, 1740, 1670, 1570, 1260, 845, 760 cm^{-1}; MS (m/z) 530, 333, 269, 209, 83, 73, 59, 45, 29.

24: 580 mg, 75%; 3:7 mixture of diastereoisomers **24a**:**24b**. **24a**: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.48 (1H, br s), 7.45 (1H, br s), 4.98 (1H, br s), 4.93 (1H, br s), 3.95–3.76 (2H, m), 3.77 (3H, s), 3.71 (3H, s), 3.48 (1H, dd, J = 14.3, 5.2 Hz), 3.33 (1H, d, J = 17.0 Hz), 3.05 (1H, dd, J = 17.3, 7.3 Hz), 2.95 (1H, dd, J = 17.3, 8.0 Hz), 2.95–2.76 (3H, m), 2.61 (1H, dd, J = 16.8, 4.4 Hz), 0.38 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 208.8, 171.6, 170.5, 148.3, 145.7, 145.5, 144.8, 143.6, 129.7, 129.1, 108.5, 62.7, 56.1, 53.3, 52.9, 46.5, 40.7, 39.2, 39.1, 35.3, 2.57. **24b**: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.47 (1H, br s), 7.44 (1H, br s), 4.98 (1H, br s), 4.93 (1H, br s), 3.91–3.72 (2H, m), 3.77 (3H, s), 3.73 (3H, s), 3.49 (1H, dd, J = 14.3, 5.1 Hz), 3.34 (1H, d, J = 17.0 Hz), 3.06 (1H, dd, J = 17.3, 7.5 Hz), 2.97 (1H, dd, J = 17.3, 7.2 Hz), 2.92–2.72 (3H, m), 2.61 (1H, dd, J = 16.8, 4.2 Hz), 0.37 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 208.8, 171.7, 170.6, 148.5, 145.7, 145.5, 144.8, 143.7, 129.7, 128.9, 108.4, 62.8, 56.0, 53.3, 52.9, 46.7, 40.8, 38.8, 36.9, 35.2, 2.6. **24a + 24b**: IR (neat) 3080, 3040, 1770–1720, 1670, 1570, 1260, 1090, 845, 760 cm^{-1}; MS (m/z) 486, 289, 225, 159, 137, 89, 73, 59, 45, 28.

[4 + 2] Cycloaddition Reaction. General Procedure. The reactions were carried out under argon in a flame-dried flask and the solutions were degassed by bubbling argon during 30 min.

A degassed solution of the benzocyclobutene (1 mmol) in decane (20 mL) was heated at reflux until TLC indicated that starting material had been consumed. The solvent was removed by vacuum transfer. The crude residue was purified by flash chromatography to afford the tertracyclic compounds.

10a/11a: 225 mg, 90%. The 300-MHz ^{1}H-NMR spectrum revealed a ratio **10a**/**11a** = 5/1. **10a**: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.58 (1H, s), 7.39 (1H, s), 3.70 (3H, s), 2.84–2.32 (6H, m), 2.05–1.60 (6H, m), 1.50–1.28 (3H, m), 0.38 (18H, s); ^{13}C-NMR (75.MHz, $CDCl_3$) δ 177.4, 142.5, 142.3, 138.9, 135.9, 135.8, 133.7, 51.7, 46.7, 45.0, 44.9, 44.3, 40.5, 34.2, 33.7, 32.4, 27.6, 25.3, 2.0, 1.9. **11a**: ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.67 (1H, s), 7.41 (1H, s), 3.71 (3H, s), 2.84–2.32 (6H, m), 2.05–1.60 (6H, m), 1.50–1.28 (3H, m), 0.38 (18H, s); ^{13}C-NMR (75.5.MHz, $CDCl_3$) δ 177.6, 142.3, 142.2, 138.2, 136.7, 136.6, 132.3, 51.4, 46.4, 44.3, 43.6, 41.7, 40.6, 36.2, 34.5, 28.6, 28.3, 21.4, 2.0, 1.9. **10a + 11a**: IR (neat) 3040, 3000, 2860, 1730, 1580, 1540, 1430, 1250, 860 cm^{-1}; MS (m/z) 414, 399, 87, 84, 73, 59, 45. Anal. Calcd for $C_{24}H_{37}O_2Si_2$: C, 69.67; H, 9.01. Found: C, 69.47; H, 8.97.

10b: 245 mg, 82%; white solid; mp 156–157 °C; ^{1}H-NMR (400 MHz, $CDCl_3$) δ 7.52 (1H, br s), 7.34 (1H, br s), 3.71 (3H, s), 3.69 (3H, s), 2.88 (1H, m), 2.83 (1H, m), 2.76 (1H, m), 2.70 (1H, dd, J = 12.5, 5.5 Hz), 2.50 (1H, dd, J = 14.8, 2.3 Hz), 2.31 (1H, ddd, J = 13.8, 5.7, 5.5 Hz), 1.97 (1H, ddd, J = 11.5, 4.7, 2.1 Hz), 1.89 (1H, m), 1.82 (1H, td, J = 12.7, 6.2 Hz), 1.73 (1H, tdd, J = 12.5, 5.7, 3.0 Hz), 1.64 (1H, d, J = 14.8 Hz), 1.61 (1H, ddd, J = 12.7, 5.3, 2.1 Hz), 1.52 (1H, dd, J = 11.5, 2.3 Hz), 1.41 (1H, dtd, J = 13.8, 12.5, 5.9 Hz), 0.35 (9H, s), 0.34 (9H, s); ^{13}C-NMR (75.5.MHz, $CDCl_3$) δ 173.2, 170.8, 142.6, 142.3, 138.6, 136.2, 135.5, 133.9, 63.2, 52.5, 52.4, 46.5, 45.5, 42.7, 42.3, 37.4, 34.5, 28.9, 27.4, 24.9, 2.0, 1.9.

11b: 25 mg, 8%; white foam; ^{1}H-NMR (300 MHz, $CDCl_3$) δ 7.62 (1H, br s), 7.32 (1H, br s), 3.78 (3H, s), 3.73 (3H, s), 2.86–2.74 (6H, m), 2.28 (1H, m), 2.05–1.80 (3H, m), 1.68–1.38 (4H, m), 0.35 (18H, s); ^{13}C-NMR (75.5.MHz, $CDCl_3$) δ 173.3, 171.3, 142.5, 142.4, 138.3, 136.6, 136.5, 132.5, 62.8, 52.7, 52.6, 45.0, 44.6, 43.4, 42.5, 37.7, 34.9, 28.2, 25.4, 20.9, 2.0, 1.9. **10b + 11b**: IR ($CHCl_3$) 3040, 3000, 2860, 1730, 1540, 1430, 1250, 1150, 860, 840 cm^{-1}. Anal. Calcd for $C_{26}H_{40}O_4Si_2$: C, 66.05; H, 8.53. Found: C, 65.78; H, 8.60.

25: 223 mg, 80%; white solid; mp 206 °C; ^{1}H-NMR (500 MHz, C_6D_6) δ 7.74 (1H, br s), 3.50–3.42 (4H, m, A_2B_2), 3.45 (3H, s), 3.39 (1H, d, J = 4.6 Hz), 3.32 (3H, s), 3.08 (1H, dd, J = 14.8, 2.2 Hz), 3.06 (1H, dd, J = 12.5, 5.8 Hz), 2.70 (1H, ddd, J = 14.0, 5.8, 1.5 Hz), 2.63 (1H, m), 2.57 (1H, dd, J = 14.0, 12.5 Hz), 2.53 (1H, dd, J = 17.0, 5.8 Hz), 2.19 (1H, dd, J = 12.0, 2.2 Hz), 2.08 (1H, dd, J = 12.0, 4.6 Hz), 1.89 (1H, d, J = 14.8 Hz), 1.65 (1H, td, J = 13.0, 5.8 Hz), 1.34 (1H, ddd, J = 13.0, 5.7, 1.6 Hz), 0.40 (9H, s), 0.30 (9H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 173.2, 170.3, 142.9, 142.6, 137.6, 136.2, 135.3, 133.7, 109.7, 64.4, 63.9, 61.1, 52.8, 52.3, 49.7, 43.3, 43.2, 41.9, 36.7, 35.4, 33.7, 27.4, 2.0, 1.9; IR ($CHCl_3$) 3040, 3000, 2860, 1730, 1430, 1250, 860 cm^{-1}; MS (m/z) 530, 515, 444, 333, 229, 89, 73, 59, 45. Anal. Calcd for $C_{28}H_{46}O_6Si_2$: C, 63.36; H, 7.98. Found: C, 63.07; H, 7.94.

26: 7 mg, 2%; white foam; ^{1}H-NMR (500 MHz, C_6D_6) δ 7.87 (1H, br s), 7.44 (1H, br s), 3.54 (3H, s), 3.38 (3H, s), 3.30 (1H, d, J = 4.8 Hz), 3.28–3.23 (4H, m, A_2B_2), 3.20 (1H, dd, J = 14.8, 2.0

Hz), 2.83 (1H, dd, J = 15.4, 8.1 Hz), 2.77–2.71 (2H, m), 2.59–2.54 (2H, m), 2.26 (1H, d, J = 12.2 Hz), 2.00 (1H, d, J = 14.8 Hz), 1.76 (1H, ddd, J = 12.2, 4.8, 1.8 Hz), 1.66 (1H, td, J = 13.0, 6.3 Hz), 1.30 (1H, m), 0.44 (9H, s), 0.37 (9H, s).

27: 140 mg, 46%; white solid; mp 180 °C; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.39 (1H, br s), 7.33 (1H, br s), 3.75 (3H, s), 3.64 (3H, s), 3.32 (1H, d, J = 4.6 Hz), 3.11 (1H, ddd, J = 15.5, 6.4, 1.1 Hz), 2.98 (1H, dd, J = 12.3, 6.4 Hz), 2.93–2.83 (2H, AA'BB'), 2.45 (1H, d, J = 14.8 Hz), 2.32 (1H, dd, J = 14.8, 1.9 Hz), 2.29 (1H, dd, J = 15.5, 12.3 Hz), 2.11 (1H, dd, J = 12.7, 4.6 Hz), 1.87–1.84 (2H, AA'BB'), 1.75 (1H, dd, J = 12.7, 1.9 Hz), 0.35 (9H, s), 0.31 (9H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 208.0, 171.2, 170.2, 143.7, 143.6, 136.9, 136.2, 134.5, 133.3, 62.1, 58.1, 53.4, 53.1, 45.5, 43.7, 42.7, 41.4, 36.2, 33.0, 27.5, 1.9. Anal. Calcd for $C_{26}H_{38}O_5Si_2$: C, 64.16; H, 7.87. Found: C, 64.33; H, 7.96.

28: 100 mg, 34%; white solid; mp 150–152 °C; ^{1}H-NMR (500 MHz, $CDCl_3$) δ 7.48 (1H, br s), 7.35 (1H, br s), 3.75 (3H, s), 3.72 (3H, s), 3.29 (1H, d, J = 4.6 Hz), 3.19 (1H, t, J = 5.6 Hz), 2.88–2.86 (2H, m), 2.83 (1H, m), 2.77 (1H, m), 2.75 (1H, dd, J = 14.8, 2.0 Hz), 2.40 (1H, q, J = 14.8 Hz), 1.99 (1H, td, J = 13.0, 6.1 Hz), 1.92 (1H, dd, J = 12.8, 2.0 Hz), 1.87 (1H, ddd, J = 12.8, 4.2, 1.8 Hz), 1.78 (1H, ddd, J = 13.0, 5.5, 2.5 Hz), 0.32 (18H, s); ^{13}C-NMR (75.5 MHz, $CDCl_3$) δ 208.5, 171.4, 170.6, 143.4, 143.3, 137.4, 136.3, 135.2, 134.2, 62.4, 57.8, 53.3, 53.2, 45.9, 44.5, 43.4, 40.8, 36.2, 33.7, 27.8, 1.9. Anal. Calcd for $C_{26}H_{38}O_5Si_2$: C, 64.16; H, 7.87. Found: C, 64.44; H, 7.98. **27** + **28**: IR ($CHCl_3$) 3040, 3000, 2860, 1730, 1720, 1430, 1250, 860, 845 cm^{-1}; MS (m/z) 486, 471, 455, 145, 89, 73, 59, 28, 18.

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