Stereochemistry of Epoxidation of Some Caryophyllenols

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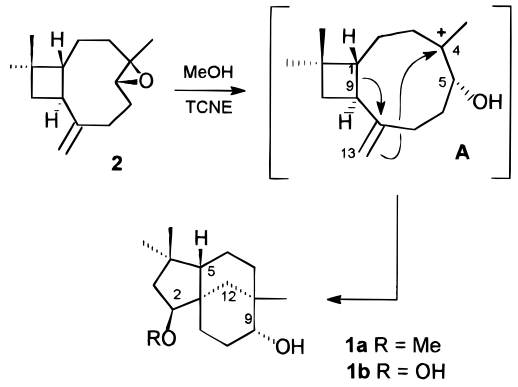
Epoxidation of the caryophyllene allylic alcohols **3**−**5** by *tert*-butyl hydroperoxide/vanadyl acetylacetonate afforded the epoxides **6a**, **7**, and **8**, respectively. The tetracyanoethylene-catalyzed solvolysis shed some light on the stereochemistry of epoxidation. Formation of trans epoxides by syn epoxidation is a consequence of the conformational flexibility of the nine-membered ring, which places the alcohol at C-5 close to the α-face of the *endo*-alkene in **4** and close to the *β*-face in **3** and **5**.

Methoxyclovanol (**1a**) (Scheme 1) is an inhibitor of the growth of the plant pathogen, *Botrytis cinerea*, an organism that causes serious losses of commercial crops. Compound **1**, at 100 ppm dose, shows a growth inhibition[1] of 66% after 3 days assay. There is a structural analogy between this inhibitor and the phytotoxic metabolites of the botrydial series. In order to examine the scope of this analogy, we required some substituted clovanes. Compounds with the clovane skeleton are formed by the cyclization of caryophyllene and its derivatives.[2] We have recently explored the cyclization of caryophyllene 4*β*,5α-oxide to clovanes using the mild catalysis of tetracyanoethylene [TCNE].[3] In this paper, we report the preparation and cyclization of some hydroxycaryophyllene oxides, which sheds some light on the consequences of the variable conformations of the nine-membered ring of caryophyllene.

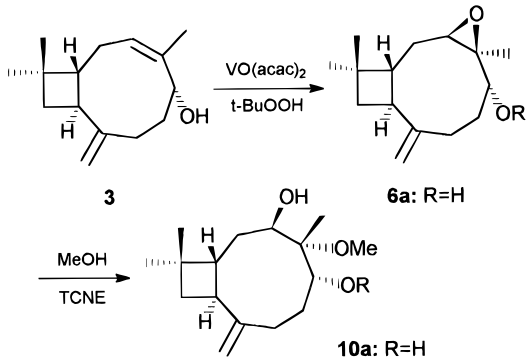
The cyclization to a clovane may be initiated by the formation of a carbocation at C-4 of caryophyllene. In prior work,[11a] and in our earlier study[3] this was achieved by the cleavage of caryophyllene 4*β*,5α-oxide (**2**) (Scheme 1). However, in principle, this carbocation may also be formed by cleavage of 3,4- or 4,12-epoxides. The starting materials for the preparation of these epoxides were the hydroxy-alkenes **3**−**5** which were prepared from caryophyllene 4*β*,5α-oxide (**2**).[3]

The conformational mobility of the *trans*-cyclononene ring of caryophyllene is reflected by the formation of two *trans*-epoxides on epoxidation with peroxy acid.[4] The stereoselective epoxidation of allyl alcohols with *tert*-butyl hydroperoxide and vanadyl acetonylacetonate is a well-established process[5] although the prediction of the stereochemical outcome in this series was ambiguous. The cleavage reactions with tetracyanoethylene however facilitated the determination of the stereochemistry of the epoxides.

Scheme 1



Scheme 2



The epoxidation reactions of **3**−**5** with *tert*-butyl hydroperoxide and vanadyl acetonylacetonate proceeded smoothly in each case to give a single epoxide (**6a**, **7**,[6] and **8**) (Schemes 2−4). Epoxidation of **5** with *m*-chloroperbenzoic acid gave a poor yield of **8**. The epoxides **6a** and **8** from the 5α-alcohols were interrelated by reduction with lithium aluminum hydride to form the same secondary, tertiary alcohol **9**[6] (Scheme 5). The TCNE-catalyzed cleavage of the epoxides **6a** and **6b** was studied under various conditions. Treatment of the alcohol **6a** with TCNE in methanol gave the methyl ether **10a** (Scheme 2), while the acetate **6b** gave a separable mixture of the alcohol **10a** and the acetate **10b** (Scheme 6). Treatment of the acetate **6b** with TCNE in acetone containing lithium bromide or hydroxylamine hydrochlo-

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(1) Vincent, J. M. *Nature* **1927**, *159*, 850.
(2) (a) Guha, P. C. *Indian Chem. Soc.* **1953**, *30*, 82. (b) Barton, D. H. R. *Rec. Chem. Prog.* **1954**, *15*, 19. (c) Nickon, A. *Perfum. Essent. Oil. Rec.* **1954**, *45*, 149.
(3) Collado, I. G.; Hanson, J. R.; Macías-Sánchez, A. J. *Tetrahedron* **1996**, *52*, 7961.
(4) Warnhoff, E. W.; Srinivasan, V. *Can. J. Chem.* **1973**, *51*, 3955.
(5) (a) Sharpless, K. B.; Verhoeven, T. R. *Aldrichim. Acta* **1979**, *12*, 63. (b) Ziegler, F. E.; Jaynes, B. H.; Saindane, M. *Tetrahedron Lett.* **1985**, *26*, 3307. (c) Marino, J. P.; de la Pradilla, R. F.; Laborde, E. *J. Org. Chem.* **1987**, *52*, 4898.
(6) Hermann, H.; Tezuka, Y,; Kikuchi, T.; Supriyatna, S. *Chem. Pharm. Bull.* **1994**, *42*, 138.

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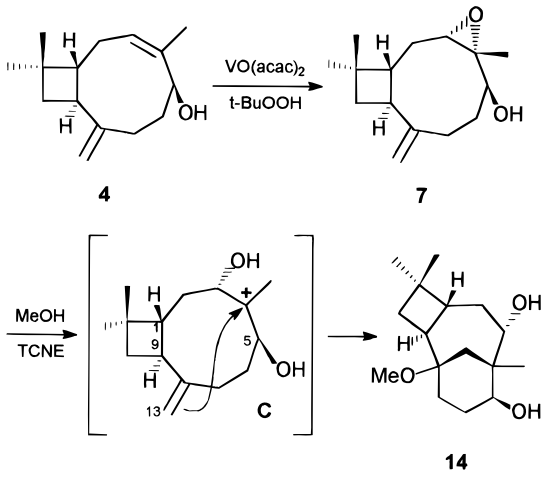
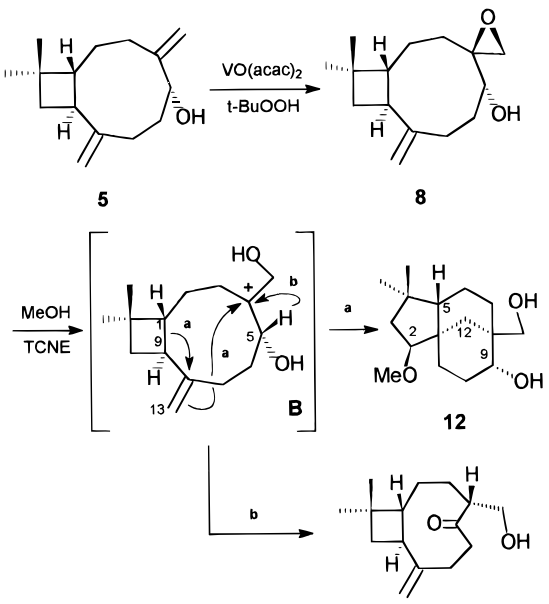
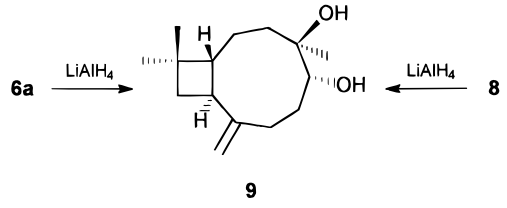
Scheme 3



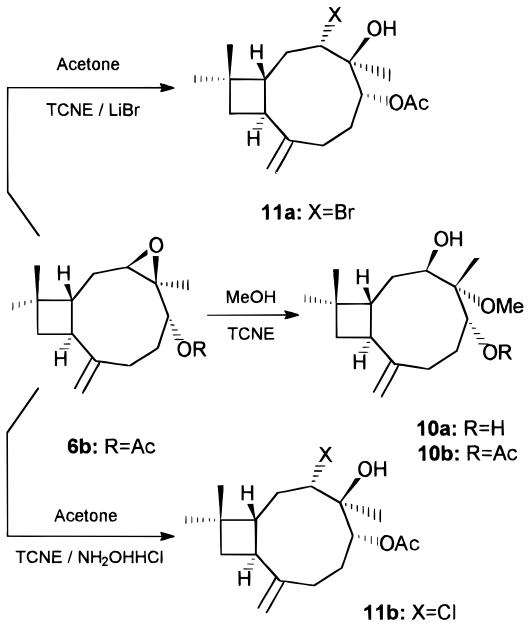
Scheme 4



Scheme 5



Scheme 6



ride gave the bromo (**11a**) and chloro (**11b**) compounds (Scheme 6). The stereochemistry of the chloro compound **11b** was established by X-ray crystallography.[12] This in turn served to establish the stereochemistry of the epoxides **6a** and **6b** and the 4(12) epoxide **8**, with which it had been interrelated. The structure and stereochemistry of the methyl ethers **10a** and **10b** then followed from the known stereo- and regiochemistry of TCNE-catalyzed reactions, and it was confirmed on the basis of several NOE effects that were observed. The (3*R*,4*R*,5*R*) stereochemistry for compound **10a** was established by NOE effects between H-9α and H-3α, H-1*β* and H-5*β*, and H-5*β* and CH_3-12*β*, respectively.

Reaction of the epoxide **8** with TCNE in methanol (see Scheme 4) gave the methoxyclovanediol **12** as the major product. This was identified by its ^{1}H NMR spectrum, which showed signals at δ_H 3.30−3.40 (CH(OMe)), 3.36 (OMe), 3.30−3.40 and 3.58 (CH_2OH) and 3.66 (CH(OH)). These data were very similar to those of the known clovanediol **1b**.[6] A series of NOE and 2D COSY experiments led to a full assignment of the ^{1}H NMR spectrum and were fully consistent with the stereochemistry.

The ketone **13** was obtained as a second product. An NOE enhancement between H-1*β* and H-4*β* established the stereochemistry at C-4. This stereochemistry implied a 1,2 hydride shift on the *β*-face of the molecule, and consequently, a concerted mechanism in the genesis of **13** was excluded. In order to accommodate the experimental results, a carbocationic intermediate **B**, which could adopt an appropriate conformation for a 1,2 hydride shift on the *β*-face of the molecule, is proposed (Scheme 4).

In order to obtain additional support for this hypothesis, the stability of the conformations of intermediate **B**, keeping a *β* disposition of the exocyclic double bond, was studied. A semiempirical calculation[7] of the most favored conformation[8] of intermediate **B** shows that the preferred 1,2-H shift between C-5 and C-4 would generate (4*R*) stereochemistry in compound **13** (see Figure 1).

Treatment of the epoxide **7** with TCNE in methanol (see Scheme 3) gave the methoxycaryolanediol **14**, the stereochemistry of which was established by X-ray crystallography. This in turn served to establish the stereochemistry of the starting epoxide.

These results may be rationalized as follows. The conformational flexibility of the nine-membered ring allows both of the epimeric substituents at C-5 to adopt an exo orientation. These are shown in the Figure 2.[9] These place the alcohol close to the α-face of the alkene

(7) Stewart, J. J. P. *J. Comput. Chem.* **1989**, *10*, 209 and 221. Molecular orbital calculations were carried out using the PM3 Hamiltonian as implemented in MOPAC 6.0.

(8) The most stable conformation (PM3 parametrization) of compound **8** shows a value of 59.7° for the dihedral angle formed by atoms α, *β*, *γ*, and *δ*. On the other hand, there is an energy minimum for dihedral angle value of 45° in intermediate **B** (see Figure 1). So, it seems reasonable to consider the conformation shown in Figure 1 as the preferred structure for a 1,2 H shift in intermediate **B**.

(9) Most stable conformers for exo-C-5 substituent were calculated using the MOPAC 6.0 program (ref 7). Calculated heats of formation of the appropriate conformations of compounds **3**−**5** were −36.512, −41.685, and −29.202 kcal/mol, respectively.

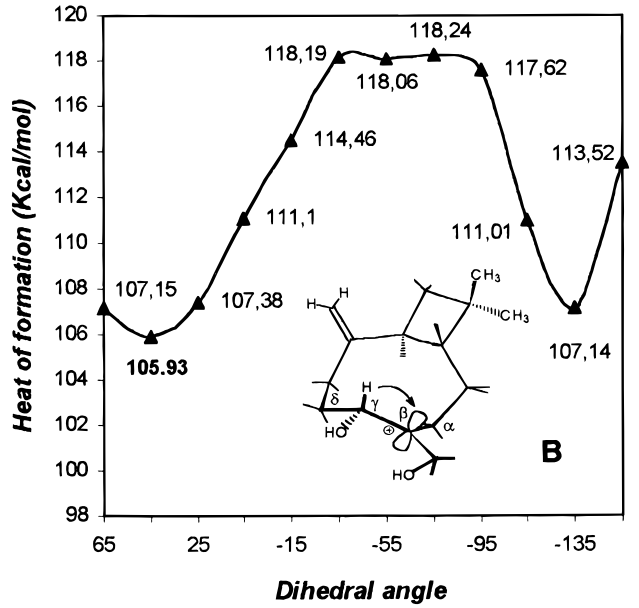


Figure 1. Energy profile of conformers of intermediate B (Scheme 4), via variation of dihedral angle $\alpha\beta\gamma\delta$, using PM3 calculations.

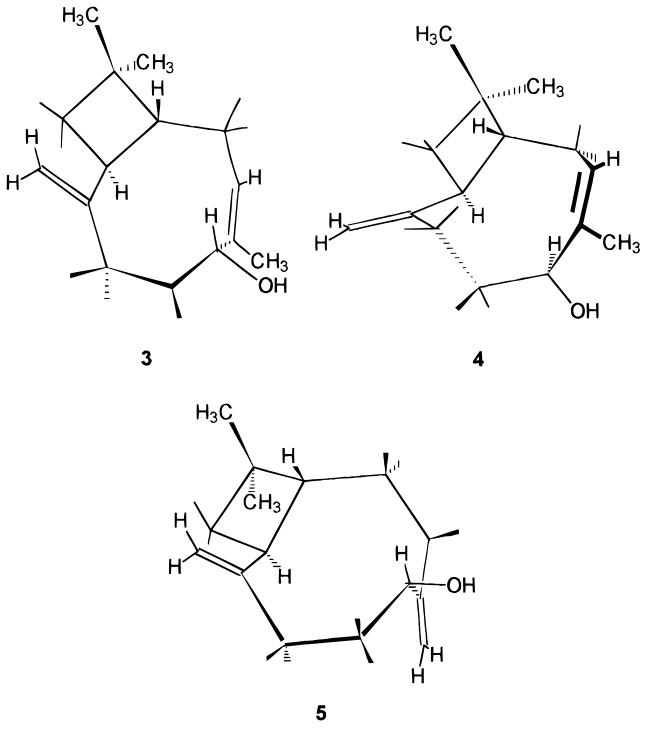


Figure 2. Most stable conformers for the *exo*-C-5 substituent for compounds **3**−**5**.

in **4** and to the β-face in **3** and **5**. This accounts for a syn epoxidation by the *tert*-butyl hydroperoxide/vanadyl acetylacetonate reagent, generating epoxides with stereochemistry trans in regard to the hydroxyl group. The epoxide **8** has been prepared previously, but the stereochemistry at C-4 was incorrectly assigned.[10] The formation of a caryolane (**14**) from **7** and a clovane (**12**) from **8** is also in accord with the stereochemistry for the epoxides. Intermediate **B** (Scheme 4), derived from compound **8**, is probably similar in conformation to the intermediate **A** (Scheme 1), produced from caryophyllene 4β,5α-oxide (**2**), and both gave clovane products. However, intermediate **C**, derived from compound **7** (Scheme 3), can undergo initial C13−C4 ring closure, but the C1−C9 ring bond is not properly aligned with the developing p-orbital at C8 to allow facile ring expansion, generating the caryolane product **14**. On the other hand, compounds **6a** and **6b** did not give any cyclization products when they were reacted under TCNE-catalyzed reaction conditions because of the restriction in the mobility of the 9-membered ring, induced by the epoxide between C-3 and C-4. Furthermore, cyclization of compounds **6a** or **6b** to the caryolane skeleton would require a (4*S*) stereochemistry for the oxirane ring and a movement of the exocyclic double bond over the β face of the 9-membered ring, in order to attack the electron-deficient C-4 position.[11]

(10) Hoffmann, H. M. R.; Vogt, U. *Synlett* **1990**, 581.

Experimental Section

General Methods. Melting points are uncorrected. TLC was performed on Merck Kieselgel 60 F_{254}, 0.2 mm thick. Silica gel (Merck) was used for column chromatography. Purification by HPLC was accomplished using a Si gel column (Hibar 60, 7 μm, 1 cm wide, 25 cm long).

General Procedure for the Stereoselective Epoxidation of Compounds 3 and 4. An 80% solution of *tert*-butyl hydroperoxide (1.1 mol equiv) was added to a solution of the compound (1 mol equiv) and vanadyl acetylacetonate (0.1 mol equiv) (see below) in refluxing benzene (10 mL) over a period of 5 min. The initially pale green solution turned deep red as the *t*-BuOOH was added. The reaction was monitored by TLC and judged complete after 1 h at reflux. During this time, the deep red color turned to brown and then to light green.

The reaction mixture was cooled to 25 °C, and the benzene layer was washed, first with a 40% solution of sodium bisulfite and then with brine. The solvent was dried over Na_2SO_4 and evaporated under vacuum. The crude reaction product was purified by column chromatography on silica gel, with increasing gradients of ethyl acetate in petroleum ether, giving **6a** and **7** (see yields below). Physical data for compound **7** were identical to those described in ref 6.

compd	mg of $VO(acac)_2$	mL of *t*-BuOOH	product (yield, %)
3 (56 mg)	7	0.04	**6a** (25)
4 (40 mg)	5	0.03	**7** (23)

(3*R*,4*R*,5*R*)-5-Hydroxycaryophyll-8(13)-ene 3,4-epoxide (6a): oil; $[\alpha]^{25}_D$ −3 (*c* 0.65 $CHCl_3$); IR ν_{max} (neat, KBr) cm^{-1} 3445, 3075, 1636; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.98 (s, 3H, H-15β), 1.05 (s, 3H, H-14α), 1.30 (s, 3H, H-12α), 1.70−1.90 (3H, H-6, H-6′, H-2β), 1.61 (dd, 1H, $J_{9\alpha-10\beta}$ = 10.4 Hz, $J_{10\alpha-10\beta}$ = 10.4 Hz, H-10β),), 1.73 (dd, 1H, $J_{10\alpha-10\beta}$ = 10.4 Hz, $J_{10\alpha-9\alpha}$ = 8.9 Hz, H-10α), 1.85 (ddd, 1H, $J_{1\beta-2\beta}$ = 3.0 Hz, $J_{1\beta-2\alpha}$ = 4.0 Hz, $J_{1\beta-9\alpha}$ = 8.9 Hz, H-1β), 1.99 (m, 1H, H-7α), 2.03 (ddd, 1H, $J_{2\alpha-3\alpha}$ = 5.0 Hz, $J_{1\beta-2\alpha}$ = 4.0 Hz, $J_{2\alpha-2\beta}$ = 8.0 Hz, H-2α), 2.29 (ddd, 1H, *J* = 8.4 Hz, 13.2 Hz, 4.5 Hz, H-7β), 2.51 (ddd, 1H, $J_{1\beta-9\alpha}$ = 8.9 Hz, $J_{10\alpha-9\alpha}$ = 8.9 Hz, $J_{9\alpha-10\beta}$ = 10.4 Hz, H-9α), 3.06 (dd, 1H, $J_{2\alpha-3\alpha}$ = 5.0 Hz, $J_{3\alpha-2\beta}$ = 5.0 Hz, H-3α), 3.61 (dd, 1H, $J_{5\beta-6}$ = 9.9 Hz, $J_{5\beta-6'}$ = 3.9 Hz, H-5β), 4.77 (s, 1H, H-13), 4.84 (s, 1H, H-13′); ^{13}C NMR ($CDCl_3$, 50 MHz) (see Table 1, Supporting Information); EIMS *m*/*z* (rel intensity) 221 (1.5) [M^+ − 15], 218 (0.4) [$M^+ - H_2O$], 203 (4) [M^+ − 15 - H_2O], 185 (3), 149 (13), 147 (22), 136 (26), 125 (43), 123 (85), 120 (57), 109 (82), 107 (69), 105 (62), 96 (70) 95 (90), 93 (90), 91 (87), 81 (81), 79 (92), 71 (100); HREIMS 236.177 ($C_{15}H_{24}O_2$ requires 236.177).

(4*S*,5*R*)-5-Hydroxycaryophyll-8(13)-ene 4,12-Epoxide (8). An 80% solution of *tert*-butyl hydroperoxide (1.1 mol

(11) (a) Tkachev, A. V. *Chem. Nat. Compd.* **1987**, 393 (Translation of Tkachev, A. V. *Khim. Prir Soedin* **1987**, 475). (b) Edamura, F. Y.; Nickon, A. *J. Org. Chem.* **1970**, *35*, 1509. (c) Nickon, A.; Edamura, F. Y.; Iwadare, T.; Matsuo, K.; McGuire, F. J.; Roberts, J. S. *J. Am. Chem. Soc.* **1968**, *90*, 4196.

(12) The author has deposited atomic coordinates for **11b** and **14** with the Cambridge Crystallographic Data Centre. The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK.

equiv) was added to a solution of the compound **5** (309 mg) and vanadyl acetylacetonate (37 mg) in refluxing benzene (15 mL) over a period of 5 min. The initially pale green solution turned deep red as the *t*-BuOOH was added. The reaction was monitored by TLC and judged complete after 1 h at reflux. During this time, the deep red color turned to brown and then to light green.

The reaction mixture was cooled to 25 °C, and the benzene layer was washed, first with a 40% solution of sodium bisulfite and then with brine. The solvent was dried over Na_2SO_4 and evaporated under vacuum. The crude reaction product was purified by column chromatography on silica gel, with increasing gradients of ethyl acetate in petroleum ether, giving compound **8** (105 mg) (33%): mp 50−51 °C; $[\alpha]^{25}_D$ −10 (*c* 1.85 $CHCl_3$); IR ν_{max} (neat, KBr) cm^{-1} 3386, 1639; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.98 (s, 3H, H-14α), 0.99 (s, 3H, H-15*β*), 1.67 (brdd, 1H, $J_{1\beta-9\alpha}$ = 9.8 Hz, $J_{1\beta-2\alpha}$ = 9.8 Hz, H-1*β*), 1.78 (dddd, 1H, $J_{6\beta-6\alpha}$ = 10.0 Hz, $J_{6\beta-7\alpha}$ = 4.5 Hz, $J_{6\beta-7\beta}$ = 5.1 Hz, $J_{6\beta-5\beta}$ = 5.0 Hz, H-6*β*), 1.40−1.80 (6H, H-10, H-10′, H-2, H-2′, H-3, H-3′), 1.84 (dddd, 1H, $J_{6\beta-6\alpha}$ = 10.0 Hz, $J_{6\beta-7\beta}$ = 10.0 Hz, $J_{6\alpha-5\beta}$ = 5.0 Hz, $J_{6\alpha-7\alpha}$ = 10.0 Hz, H-6α), 2.06 (ddd, 1H, $J_{7\alpha-7\beta}$ = 12.0 Hz, $J_{7\alpha-6\alpha}$ = 10.0 Hz, $J_{7\alpha-6\beta}$ = 4.5 Hz, H-7α), 2.42 (ddd, 1H, $J_{9\alpha-1\beta}$ = 9.8 Hz, $J_{9\alpha-10\alpha}$ = 9.8 Hz, $J_{9\alpha-10\beta}$ = 9.8 Hz, H-9α), 2.45 (ddd, 1H, $J_{7\alpha-7\beta}$ = 12.0 Hz, $J_{7\beta-6\alpha}$ = 10.0 Hz, $J_{7\beta-6\beta}$ = 5.1 Hz, H-7*β*), 2.63 (d, 1H, $J_{12-12'}$ = 4.7 Hz, H-12), 2.94 (d, 1H, $J_{12-12'}$ = 4.7 Hz, H-12′), 3.82 (dd, 1H, $J_{5\beta-6\beta}$ = 5.0 Hz, $J_{5\beta-6\alpha}$ = 5.0 Hz, H-5*β*), 4.92 (s, 2H, H-13, H-13′); ^{13}C NMR ($CDCl_3$, 50 MHz) (see Table 1, Supporting Information); EIMS *m*/*z* 236 (2.1) [M^+], 221 (4) [$M^+ - 15$], 203 (6) [$M^+ - 15 - H_2O$], 187 (8), 175 (8), 161 (12), 149 (35), 135 (42), 121 (46), 109 (48), 107 (70), 95 (70) 93 (100), 91 (77), 81 (71), 79 (88); HREIMS 236.177 ($C_{15}H_{24}O_2$ requires 236.177).

(4*R*,5*R*)-4,5-Dihydroxycaryophyll-8(13)-ene (9). Compounds **6a** and **8**, dissolved in diethyl ether (5 mL), were treated for 24 h with an excess of lithium aluminum hydride. Then, H_2O (10 mL) was slowly added, and the reaction mixture was extracted with diethyl ether. The organic layer was washed with brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a crude reaction product that was purified by column chromatography on silica gel, with increasing gradients of ethyl acetate in petroleum ether, giving compound **9.** Compound **6a** (14 mg) yielded 12 mg (85%) of **9**. Compound **8** (30 mg) yielded 25 mg (82%) of **9**: mp 46−47 °C; $[\alpha]^{25}_D$ −30 (*c* 1.27 $CHCl_3$); IR ν_{max} (neat, KBr) cm^{-1} 3392, 3077, 1640; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.96 (s, 3H, H-14α), 0.98 (s, 3H, H-15*β*), 1.12 (s, 3H, H-12α), 1.31 (m, 1H, H-2α), 1.53 (dd, 1H, $J_{2-3\beta}$ = 8.0 Hz, $J_{3\beta-3\alpha}$ = 15.0 Hz, H-3*β*), 1.58 (dd, 1H, $J_{10\beta-10\alpha}$ = 10.4 Hz, $J_{10\beta-9\alpha}$ = 8.0 Hz, H-10α), 1.60 (m, 1H, H-6*β*) 1.62 (ddd, 1H, $J_{1\beta-2\beta}$ = 3.2 Hz, $J_{1\beta-2\alpha}$ = $J_{1\beta-9\alpha}$ = 10.0 Hz, H-1*β*), 1.67 (m, 1H, H-2*β*), 1.72 (m, 1H, H-6α), 1.73 (t, 1H, $J_{10\beta-1\beta}$ = $J_{10\beta-9\alpha}$ = 10.4 Hz, H-10*β*), 1.91 (ddd, 1H, $J_{3\beta-3\alpha}$ = 15.0 Hz, $J_{3\alpha-2\beta}$ = 11.3 Hz, $J_{3\alpha-2\alpha}$ = 1.5 Hz, H-3α), 2.05 (ddd, 1H, $J_{7\alpha-7\beta}$ = 13.2 Hz, $J_{7\alpha-6\alpha}$ = 3.6 Hz, $J_{7\alpha-6\beta}$ = 8.9 Hz, H-7α), 2.27 (brs, 1H, OH), 2.35 (q, 1H, $J_{9\alpha-10\alpha}$ = $J_{9\alpha-10\beta}$ = $J_{9\alpha-1\beta}$ = 10.0 H-9α), 2.41 (ddd, 1H, $J_{7\beta-7\alpha}$ = 13.2 Hz, $J_{7\beta-6\alpha}$ = 4.4 Hz, $J_{7\beta-6\beta}$ = 9.2 Hz, H-7*β*), 3.57 (t, 1H, $J_{5\beta-6\beta}$ = $J_{5\beta-6\alpha}$ = 5.3 Hz, H-5*β*) 4.90 (s, 1H, H-13), 4.92 (s, 1H, H-13′); ^{13}C NMR ($CDCl_3$, 50 MHz) (see Table 1, Supporting Information); EIMS *m*/*z* 239 (2) [$M^+ + H^+$], 238 (2.6) [M^+], 223 (9) [$M^+ - 15$], 221 (37) [$M^+ + H^+ - H_2O$], 205 (12) [$M^+ - 15 - H_2O$], 203 (52) [$M^+ + H^+ - 2H_2O$], 195 (8), 177 (26), 162 (17), 149 (26), 147 (28), 123 (33), 121 (50), 109 (100); HREIMS 238.192 ($C_{15}H_{26}O_2$ requires 238.193).

(3*R*,4*R*,5*R*)-3,5-Dihydroxy-4-methoxycaryophyll-8(13)-ene (10a). Compound **6a** (370 mg), dissolved in methanol (15 mL), was treated with 0.1 mol equiv of TCNE (20 mg). After 24 h, the solvent was evaporated under vacuum. The resulting gum was redissolved in ethyl acetate and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a crude reaction product that was purified by column chromatography on silica gel, with increasing gradients of ethyl acetate in petroleum ether, giving 60 mg of compound **10a** (14%); oil; $[\alpha]^{25}_D$ −40 (*c* 0.45 $CHCl_3$); IR ν_{max} (neat, KBr) cm^{-1} 3443, 3077, 1636; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.00 (s, 6H, H-14α, H-15*β*), 1.28 (s, 3H, H-12*β*), 1.49 (ddd, 1H, $J_{2\beta-2\alpha}$ = 13.0 Hz, $J_{2\beta-3\alpha}$ = 10.8 Hz, $J_{2\beta-1\beta}$ = 10.8 Hz, H-2*β*), 1.60 (dddd, 1H, $J_{6\beta-6\alpha}$ = 14.0 Hz, $J_{6\beta-7\alpha}$ = 12.6 Hz, $J_{6\beta-7\beta}$ = 7.0 Hz, $J_{6\beta-5\beta}$ = 3.2 Hz, H-6*β*), 1.61 (dd, 1H, $J_{10\alpha-10\beta}$ = 10.6 Hz, $J_{10\alpha-9\alpha}$ = 8.8 Hz, H-10α), 1.65 (ddd, 1H, $J_{1\beta-2\beta}$ = 4.0 Hz, $J_{1\beta-9\alpha}$ = 8.8 Hz, $J_{1\beta-2\alpha}$ = 13.0 Hz, H-1*β*), 1.73 (dd, 1H, $J_{10\alpha-10\beta}$ = 10.6 Hz, $J_{10\beta-9\alpha}$ = 8.8 Hz, H-10*β*), 1.76 (ddd, 1H, $J_{2\alpha-2\beta}$ = 13.0 Hz, $J_{2\alpha-1\beta}$ = 13.0 Hz, $J_{2\alpha-3\alpha}$ = 4.0 Hz, H-2α), 1.93 (ddd, 1H, $J_{7\alpha-7\beta}$ = 13.0 Hz, $J_{7\alpha-6\beta}$ = 12.6 Hz, $J_{7\alpha-6a}$ = 4.8 H-6α), 2.24 (dddd, 1H, $J_{6\alpha-6\beta}$ = 14.0 Hz, $J_{6\alpha-5\beta}$ = 9.0 Hz, $J_{6\alpha-7\alpha}$ = 4.8 Hz, $J_{6\alpha-7\beta}$ = 4.3 Hz, H-6α), 2.35 (ddd, 1H, $J_{9\alpha-1\beta}$ = 8.8 Hz, $J_{9\alpha-10\beta}$ = 8.8 Hz, $J_{9\alpha-10\alpha}$ = 8.8 Hz, H-9α), 2.48 (ddd, 1H, $J_{7\beta-7\alpha}$ = 13.0 Hz, $J_{7\beta-6\alpha}$ = 4.3 Hz, $J_{7\beta-6\alpha}$ = 4.3 Hz, $J_{7\beta-6\beta}$ = 7.0 Hz, H-7*β*), 3.47 (s, 3H, OMe), 3.65 (dd, 1H, $J_{5\beta-6\beta}$ = 3.2 Hz, $J_{5\beta-6\alpha}$ = 9.0 Hz, H-5*β*), 3.88 (dd, 1H, $J_{3\alpha-2\alpha}$ = 4.0 Hz, $J_{3\alpha-2\beta}$ = 10.8 Hz, H-3α), 4.87 (s, 2H, H-13, H-13′); ^{13}C NMR ($CDCl_3$, 50 MHz) (see Table 1, Supporting Information); EIMS *m*/*z* 268 (7) [M^+], 250 (0.1) [$M^+ - H_2O$], 236 (0.5) [M^+ − MeOH], 218 (1.4) [$M^+ - H_2O$ − MeOH], 167 (12), 125 (18), 107 (18), 101 (47), 88 (51), 85 (89), 81 (47), 79 (45), 69 (45), 67 (33), 59 (100); HREIMS 268.204 ($C_{16}H_{28}O_3$ requires 268.204).

(3*R*,4*R*,5*R*)-5-Acetoxycaryophyll-8(13)-ene 3,4-Epoxide (6b). Compound **6a** (60 mg), dissolved in dry pyridine (2 mL), was treated with excess acetic anhydride. After 24 h ethyl acetate (50 mL) was added, and the mixture was washed twice with 2 N hydrochloric acid (50 mL). The organic layer was washed with brine and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a crude reaction product that was purified by column chromatography on silica gel, with increasing gradients of ethyl acetate in petroleum ether, giving 56 mg of compound **6b** (79%); oil; $[\alpha]^{25}_D$ −16 (*c* 0.74 $CHCl_3$); IR ν_{max} (neat, KBr) cm^{-1} 1739, 1244, 3075, 1640; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.00 (s, 3H, H-15*β*), 1.07 (s, 3H, H-14α), 1.34 (s, 3H, H-12α), 1.65 (t, 1H, $J_{9\alpha-10\beta}$ = $J_{10\alpha-10\beta}$ = 10.4 Hz, H-10*β*), 1.77 (m, 1H, H-10), 1.78−1.85 (3H, H-6, H-6′, H-2), 1.96 (dt, 1H, $J_{1\beta-2}$ = $J_{1\beta-2'}$ = 6.0 Hz, $J_{1\beta-9\alpha}$ = 10.4 Hz, H-1*β*), 2.03−2.10 (2H, H-7, H-2′), 2.05 (s, 3H, −Oac), 2.28 (ddd, 1H, $J_{7'-7}$ = 13.8 Hz, $J_{7'-6}$ = 8.2 Hz, $J_{7'-6'}$ = 3.4 Hz, H-7′), 2.57 (brq, 1H, $J_{1\beta-9\alpha}$ = $J_{10\alpha-9\alpha}$ = $J_{9\alpha-10\beta}$ = 10.4 Hz, H-9α), 3.00 (dd, 1H, $J_{2-3\alpha}$ = 4.8 Hz, $J_{3\alpha-2'}$ = 7.2 Hz, H-3α), 4.74 (s, 1H, H-13′), 4.75 (dd, 1H, $J_{5\beta-6}$ = 9.7 Hz, $J_{5\beta-6'}$ = 3.6 Hz, H-5*β*), 4.80 (s, 1H, H-13′); ^{13}C NMR ($CDCl_3$, 50 MHz) (see Table 1, Supporting Information); EIMS *m*/*z* (rel intensity) 278 (0.2) [M^+], 263 (0.2) [$M^+ - 15$], 236 (0.6) [$M^+ - 42$], 218 (2) [M^+ − AcOH], 203 (4) [$M^+ - 15$ − AcOH], 185 (5), 175 (8), 161 (7), 147 (17), 133 (22), 125 (87); HREIMS 219.176 ($C_{15}H_{23}O$ requires 219.175).

(3*R*,4*S*,5*R*)-5-Acetoxy-3-hydroxy-4-methoxycaryophyll-8(13)-ene (10b). Compound **6b** (28 mg), dissolved methanol (4 mL), was treated with 0.2 mol equiv of TCNE (3 mg). After 72 h, the solvent was evaporated under vacuum. The resulting gum was redissolved in ethyl acetate and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a crude reaction product that was purified by column chromatography on silica gel, with increasing gradients of ethyl acetate in petroleum ether, to give the starting material (9 mg), compound **10a** (9.2 mg) (50%), and compound **10b** (3.9 mg) (18%): mp 73−75 °C; $[\alpha]^{25}_D$ −36 (*c* 0.19 $CHCl_3$); IR ν_{max} (neat, KBr) cm^{-1} 3466, 1741, 1240, 1656; ^1H NMR ($CDCl_3$, 400 MHz) δ 1.01 (s, 3H, H-14α), 1.03 (s, 3H, H-15*β*), 1.11 (s, 3H, H-12α), 1.48−1.58 (2H, H-2*β*, H-6*β*), 1.62 (dd, 1H, $J_{9\alpha-10\alpha}$ = 7.6 Hz, $J_{10\alpha-10\beta}$ = 10.5 Hz, H-10α), 1.77 (ddd, 1H, $J_{2\alpha-2\beta}$ = 13.0 Hz, $J_{2\alpha-1\beta}$ = 13.0 Hz, $J_{2\alpha-3\alpha}$ = 2.2 Hz, H-2α), 1.79 (dd, 1H, $J_{10\alpha-10\beta}$ = $J_{10\beta-9\alpha}$ = 10.5 Hz, H-10*β*), 1.90 (ddd, 1H, $J_{1\beta-2\alpha}$ = 13.0 Hz, $J_{1\beta-9\alpha}$ = 10.5 Hz, $J_{1\beta-2\beta}$ = 4.8 Hz, H-1*β*), 1.96 (ddd, 1H, $J_{7\alpha-7\beta}$ = 13.0 Hz, $J_{7\alpha-6\beta}$ = 12.6 Hz, $J_{7\alpha-6\alpha}$ = 4.8 Hz, H-7α), 2.05 (s, 3H, −OAc), 2.24 (dddd, 1H, $J_{6\alpha-6\beta}$ = 14.0 Hz, $J_{6\alpha-5\beta}$ = 9.1 Hz, $J_{6\alpha-7\alpha}$ = 4.8 Hz, $J_{6\alpha-7\beta}$ = 4.3 Hz, H-6α), 2.35−2.48 (2H, H-9α, H-7*β*), 2.74 (s, 1H, −OH), 3.42 (s, 3H, −OMe), 3.85 (dd, 1H, $J_{2\alpha-3\alpha}$ = 2.2 Hz, $J_{3\alpha-2\beta}$ = 11.0 Hz, H-3α), 4.87 (s, 1H, H-13), 4.95 (s, 1H, H-13′), 5.08 (dd, 1H, $J_{5\beta-6\beta}$ = 2.8 Hz, $J_{5\beta-6\alpha}$ = 9.1 Hz, H-5*β*); ^{13}C NMR ($CDCl_3$, 50 MHz) (see Table 1, Supporting Information); EIMS *m*/*z* (rel intensity) 311 (4) [$M^+ + H^+$], 310 (5) [M^+], 279 (24) [M^+ − MeOH], 250 (10) [M^+ − AcOH], 218 (27) [M^+ − AcOH − MeOH], 201 (20) [M^+ − AcOH − MeOH − H_2O], 189 (14), 175 (18), 152 (39), 150 (42), 149 (33), 120 (44), 119 (50), 100 (23), 85 (80), 84 (100); HREIMS 310.215 ($C_{18}H_{30}O_4$ requires 310.214).

(3*S*,4*S*,5*R*)-5-Acetoxy-3-bromo-4-hydroxycaryophyll-8(13)-ene (11a) and (3*S*,4*S*,5*R*)-5-Acetoxy-3-chloro-4-hydroxycaryophyll-8(13)-ene (11b). Compound **6b** was dissolved in acetone (10 mL), and LiBr or $NH_2OH{\cdot}HCl$ was added (see below). Then a catalytic amount of TCNE was added, and

the reaction mixture was stirred for 24 h. Once the reaction was complete (TLC control), the solvent was evaporated under vacuum. The resulting gum was redissolved in ethyl acetate and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a crude reaction product that was purified by column chromatography on silica gel, with increasing gradients of ethyl acetate in petroleum ether (see reaction conditions, products, and yields below).

6b (mg)	reagent (mol equiv)	product (mg, yield, %)
116	TCNE (0.2) + LiBr (5)	**11a** (76, 51)
109	TCNE (0.2) + NH_2OH−cdtHCl (1.1)	**11b** (63, 53)

Compound 11a: mp 97−99 °C; $[\alpha]^{25}_D$ −10 (*c* 1.07 $CHCl_3$); IR ν_{max} (neat, KBr) cm^{-1} 3510, 3081, 1644, 1746, 1235; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.98 (s, 3H, H-14α), 1.02 (s, 3H, H-15*β*), 1.30 (s, 3H, H-12α), 1.29 (t, 1H, $J_{10\alpha-9\alpha} = J_{10\alpha-10\beta} = 10.1$ Hz, H-10α), 1.58 (brt, 1H, $J_{1\beta-9\alpha} = J_{1\beta-2\alpha} = 8.0$ Hz, H-1*β*), 1.62−1.76 (2H, H-6, H-6′), 1.81 (t, 1H, $J_{10\beta-10\alpha} = J_{10\beta-9\alpha} = 10.1$ Hz, H-10*β*), 2.07 (s, 3H, −OAc), 2.08−2.18 (3H, H-7, H-7′, H-2α), 2.29 (brd, 1H, $J_{2\alpha-2\beta} = 16.4$ Hz, H-2*β*), 2.41 (brdt, 1H, $J_{9\alpha-1\beta} = 8.0$ Hz, $J_{9\alpha-10\alpha} = J_{9\alpha-10\beta} = 10.1$ Hz, H-9α), 4.16 (d, 1H, $J_{3\beta-2\alpha} = 10.4$ Hz, H-3*β*), 4.76 (d, 1H, $J_{5\beta-6\alpha} = 7.9$ Hz, H-5*β*), 4.91 (s, 1H, H-13), 5.00 (s, 1H, H-13′); ^{13}C NMR ($CDCl_3$, 50 MHz) (see Table 2, Supporting Information); EIMS *m*/*z* 361 (0.1) [$M^+ + H^+ + 2$], 359 (0.1) [$M^+ + H^+$], 343 (0.7) [$M^+ + H^+ + 2 - H_2O$], 341 (0.7) [$M^+ + H^+ - H_2O$], 299 (0.6) [$M^+ + H^+$ − AcOH], 301 (0.6) [$M^+ + H^+ + 2$ − AcOH], 279 (0.3) [$M^+ + H^+$ − HBr], 261 (0.5) [$M^+ + H^+ - H_2O$ − HBr], 219 (8) [$M^+ + H^+$ − AcOH − HBr], 201 (17) [$M^+ + H^+ - H_2O$ − HBr − AcOH], 181 (3), 163 (8), 145 (11), 125 (34), 95 (18), 93 (22), 81 (20), 69 (21), 55 (16), 43 (100); HREIMS 341.115 ($C_{17}H_{26}O_2Br$ requires 341.112).

Compound 11b. Mp 103−105 °C, $[\alpha]^{25}_D$ −24 (*c* 0.89 $CHCl_3$); IR ν_{max} (neat, KBr) cm^{-1} 3526, 3080, 1642, 1727, 1236; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.97 (s, 3H, H-14α), 1.02 (s, 3H, H-15*β*), 1.27 (s, 3H, H-12α), 1.57 (dd, 1H, $J_{10\alpha-9\alpha} = 8.1$ Hz, $J_{10\alpha-10\beta} = 10.5$ Hz, H-10α), 1.60 (brt, 1H, $J_{1\beta-9\alpha} = J_{1\beta-2\alpha} = 8.1$ Hz, H-1*β*), 1.64−1.78 (2H, H-6, H-6′), 1.82 (t, 1H, $J_{10\beta-10\alpha} = J_{10\beta-9\alpha} = 10.5$ Hz, H-10*β*), 1.94−2.04 (2H, H-2, H-2′), 2.07 (s, 3H, −Oac), 2.09−2.18 (2H, H-7, H-7′), 2.41 (dt, 1H, $J_{9\alpha-10\alpha} = J_{9\alpha-1\beta} = 8.1$ Hz, $J_{9\alpha-10\beta} = 10.5$ Hz, H-9α), 3.96 (dd, 1H, $J_{3\beta-2\alpha} = 10.2$ Hz, $J_{3\beta-2\beta} = 2.2$ Hz, H-3*β*), 4.74 (dd, 1H, $J_{5\beta-6\alpha} = 7.9$ Hz, $J_{5\beta-6\beta} = 1.1$ Hz, H-5*β*), 4.91 (s, 1H, H-13′), 5.00 (s, 1H, H-13); ^{13}C NMR ($CDCl_3$, 50 MHz) (see Table 2, Supporting Information); EIMS *m*/*z* 256 (0.3) [$M^+ + 2$ − AcOH], 254 (0.9) [M^+ − AcOH], 219 (2) [M^+ − AcOH − HCl], 201 (2) [$M^+ - H_2O$ − HCl − AcOH], 175 (3), 163 (4), 145 (5), 137 (7), 125 (44), 109 (13), 95 (16), 93 (20), 79 (21), 69 (27), 55 (16), 43 (100); HREIMS 314.166 ($C_{17}H_{27}O_3Cl$ requires 314.165).

(2*S*,9*R*)-2-Methoxyclovane-9,15-diol (12) and (4*R*)-12-Hydroxy-5-ketocaryophyll-8(13)-ene (13). Compound **8** (49 mg), dissolved in methanol (10 mL), was treated with 0.1 mol equiv of TCNE (3 mg). After 24 h the solvent was evaporated under vacuum. The resulting gum was redissolved in ethyl acetate and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a crude reaction product that was purified by column chromatography on silica gel, with increasing gradients of ethyl acetate in petroleum ether, giving **12** (23 mg) (41%) and **13** (14 mg) (28%).

Compound 12: mp 52−53 °C; $[\alpha]^{25}_D$ −2 (*c* 0.78 $CHCl_3$); IR ν_{max} (neat, KBr) cm^{-1} 3386; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.83 (s, 3H, H-13α), 0.95 (d, 1H, $J_{12\beta-12\alpha} = 12.8$ Hz, H-12*β*), 1.02 (s, 3H, H-14*β*), 1.08 (brd, 1H, $J = 13.2$ Hz, H-11), 1.10−1.30 (4H, H-6,H-6', H-7,H-7′), 1.39 (m, 1H, H-5*β*), 1.44 (dd, 1H, $J_{3\beta-3\alpha} = 11.1$ Hz, $J_{3\beta-2\alpha} = 14.3$ Hz, H-3*β*), 1.54 (brd, 1H, $J = 13.4$ Hz, H-10*β*), 1.72 (dd, 1H, $J_{3\alpha-3\beta} = 11.1$ Hz, $J_{3\alpha-2\alpha} = 5.8$ Hz, H-3α), 1.76 (ddd, 1H, $J = 13.5, 13.5, 4.7$ Hz, H-10α), 2.00 (d, 1H, $J_{12\alpha-12\beta} = 12.8$ Hz, H-12α), 2.55 (brs, 1H, −OH), 2.98 (brs, 1H, −OH), 3.36 (s, 3H, −OMe), 3.30−3.40 (2H, H-2α,H-15), 3.58 (d, 1H, H-15′), 3.66 (brs, 1H, H-9*β*); ^1H NMR (C_6D_6, 400 MHz) δ 0.78 (ddd, 1H, $J_{7\beta-7\alpha} = 14.5$ Hz, $J = 9.4, 2.0$ Hz, H-7*β*), 0.85 (s, 3H, H-13α), 0.98 (d, 1H, $J_{12\beta-12\alpha} = 12.8$ Hz, H-12*β*), 1.09 (s, 3H, H-14*β*), 1.10−1.20 (3H, H-6,H-6′,H-7α), 1.27 (m, 1H, H-11*β*), 1.42 (dd, 1H, $J_{5\beta-6\alpha} = 12.2$ Hz, $J_{5\beta-6\beta} = 5.4$ Hz, H-5*β*), 1.58 (m, 1H, H-10α), 1.60 (dd, 1H, $J_{3\beta-3\alpha} = 11.1$ Hz, $J_{3\beta-2\alpha} = 10.0$ Hz, H-3*β*), 1.74 (dd, 1H, $J_{3\alpha-3\beta} = 11.1$ Hz, $J_{3\alpha-2\alpha} = 5.6$ Hz, H-3α), 1.82 (m, 1H, H-10*β*), 2.18 (ddd, 1H, $J = 13.6, 13.6, 4.8$ Hz, H-11α), 2.24 (d, 1H, $J_{12\alpha-12\beta} = 12.8$ Hz, H-12α), 3.34 (s, 3H, −OMe), 3.35 (dd, 1H, $J_{15-15'} = 10.7$ Hz, $J = 4.3$ Hz, H-15), 3.39 (dd, 1H, $J_{3\beta-2\alpha} = 10.0$ Hz, $J_{3\alpha-2\alpha} = 5.6$ Hz, H-2α), 3.59 (dd, 1H, $J_{15'-15} = 10.7$ Hz, $J = 2.3$ Hz, H-15′); ^{13}C NMR ($CDCl_3$, 50 MHz) (see Table 2, Supporting Information); EIMS *m*/*z* 268 (0.22) [M^+], 267 (0.6) [$M^+ - 1$], 250 (13) [$M^+ - H_2O$], 235 (8) [$M^+ - 15$ - H_2O], 219 (11), 218 (37), 200 (26), 185 (23), 161 (100); HREIMS 268.204 ($C_{16}H_{28}O_3$ requires 268.203).

Compound 13: oil; $[\alpha]^{25}_D$ −11 (*c* 0.47 $CHCl_3$); IR ν_{max} (neat, KBr) cm^{-1} 3450, 1703, 3077, 1636; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.92 (s, 3H, H-14α), 0.96 (s, 3H, H-15*β*), 1.29 (dddd, 1H, $J_{2\alpha-1\beta} = 10.0$ Hz, $J_{2\alpha-3\beta} = 10.0$ Hz, $J_{2\alpha-2\beta} = 14.7$ Hz, $J_{2\alpha-3\alpha} = 3.1$ Hz, H-2α), 1.44 (dddd, 1H, $J_{2\beta-3\alpha} = 8.4$ Hz, $J_{2\alpha-3\beta} = 14.7$ Hz, $J_{2\beta-1\beta} = 3.2$ Hz, $J_{2\beta-3\beta} = 3.2$ Hz, H-2*β*), 1.51 (m, 1H, H-3*β*), 1.52 (ddd, 1H, $J_{1\beta-2\beta} = 3.2$ Hz, $J_{1\beta-2\alpha} = 10.0$ Hz, $J_{1\beta-9\alpha} = 10.0$ Hz, H-1*β*), 1.57 (dd, 1H, $J_{10\beta-10\alpha} = 10.4$ Hz, $J_{10\beta-9\alpha} = 10.0$ Hz, H-10*β*), 1.68 (dd, 1H, $J_{10\alpha-10\beta} = 10.4$ Hz, $J_{10\alpha-9\alpha} = 8.2$ Hz, H-10α), 1.81 (dddd, 1H, $J_{3\alpha-2\alpha} = 3.1$ Hz, $J_{3\alpha-4\beta} = 10.0$ Hz, $J_{3\alpha-3\beta} = 14.6$ Hz, $J_{3\alpha-2\beta} = 8.4$ Hz, H-3α), 2.23 (ddd, 1H, $J_{9\alpha-10\alpha} = 8.2$ Hz, $J_{9\alpha-1\beta} = 10.0$ Hz, $J_{9\alpha-10\beta} = 10.0$ Hz, H-9α), 2.38−2.68 (4H, H-6, H-6′, H-7, H-7′), 2.82 (ddd, 1H, $J_{4\beta-12'} = 8.0$ Hz, $J_{4\beta-12} = 5.0$ Hz, $J_{4\beta-3\alpha} = 10.0$ Hz, H-4*β*), 3.57 (dd, 1H, $J_{12'-12} = 11.2$ Hz, $J_{12-4\beta} = 5.0$ Hz, H-12), 3.83 (dd, 1H, $J_{12'-12} = 11.2$ Hz, $J_{12'-4\beta} = 8.0$ Hz, H-12′), 4.94 (s, 2H, H-13, H-13′); ^{13}C NMR ($CDCl_3$, 50 MHz) (see Table 2, Supporting Information); EIMS *m*/*z* 236 (2) [M^+], 221 (3) [$M^+ - 15$], 218 (3) [$M^+ - H_2O$], 203 (4) [$M^+ - 15 - H_2O$], 187 (5), 175 (5), 163 (5), 162 (5) 154 (21), 136 (13), 130 (16), 123 (31), 95 (27) 93 (48), 82 (66), 79 (100); HREIMS 236.176 ($C_{15}H_{24}O_2$ requires 236.177).

(7*S*,9*S*)-1-Methoxycaryolane-7,9-diol (14). Compound **7** (13 mg), dissolved in methanol (4 mL), was treated with 0.2 mol equiv of TCNE (2 mg). After 24 h, the solvent was evaporated under vacuum. The resulting gum was redissolved in ethyl acetate and dried over anhydrous Na_2SO_4. Evaporation of the solvent afforded a crude reaction product that was purified by column chromatography on silica gel, with increasing gradients of ethyl acetate in petroleum ether, giving **14** (6 mg) (45%): mp 158−159 °C; $[\alpha]^{25}_D$ +9 (*c* 0.23 $CHCl_3$); IR ν_{max} (neat, KBr) cm^{-1} 3311; ^1H NMR ($CDCl_3$, 400 MHz) δ 0.99 (s, 3H, *H-13α), 1.08 (s, 3H, *H-14*β*), 1.47 (d, 1H, $J_{12-12'} = 13.7$ Hz, H-12), 1.54 (m, 1H, H-11α), 1.55 (m, 1H, H-6α), 1.57 (d, 1H, $J_{12'-12} = 13.7$ Hz, H-12′), 1.61 (t, 1H, $J_{3\beta-3\alpha} = J_{3\beta-2\alpha} = 9.9$ Hz, H-3*β*), 1.62−1.68 (2H, H-10, H-10′), 1.69 (m, 1H, H-5*β*), 1.77 (t, 1H, $J_{3\beta-3\alpha} = J_{3\beta-2\alpha} = 9.9$ Hz, H-3α), 1.86 (t, 1H, $J_{11\beta-11\alpha} = J_{11\beta-10\beta} = 9.4$ Hz, H-11α), 1.87 (ddd, 1H, $J_{6\beta-6\alpha} = 12.5$ Hz, $J_{6\beta-7\beta} = 6.4$ Hz, $J_{6\beta-5\beta} = 2.1$ Hz, H-6*β*), 1.88 (m, 1H, H-2α), 3.08 (s, 3H, −OMe), 3.47 (dd, 1H, $J_{7\beta-6\beta} = 6.4$ Hz, $J_{7\beta-6\alpha} = 9.7$ Hz, H-7*β*), 4.20 (dd, 1H, $J_{9\alpha-10\alpha} = 3.4$ Hz, $J_{9\alpha-10\beta} = 11.8$ Hz, H-9α); ^{13}C NMR ($CDCl_3$, 50 MHz) (see Table 2, Supporting Information); EIMS *m*/*z* 269 (0.2) [$M^+ + H^+$], 268 (0.3) [M^+], 251 (7) [$M^+ + H^+ - H_2O$], 218 (5) [M^+ − MeOH − H_2O], 209 (35), 192 (24), 191 (20), 177 (22), 153 (13), 141 (100); HREIMS 250.192 ($C_{16}H_{26}O_2$ requires 250.193).

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Supporting Information Available: Copies of ^1H NMR and ^{13}C NMR spectra and tables of ^{13}C NMR data for compounds **6a**, **6b**, **8**, **9**, **10a**, **10b**, **11a**, **11b**, **12**, **13**, and **14**. Copy of ^1H NMR of the previously reported [6] compound **7**. ORTEP drawings for compounds **11b** and **14** (27 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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