Stereochemical Consequences of 6- and 8-Substitution in Reactions of Bicyclo[4.2.0]octan-7-ones[1,†]

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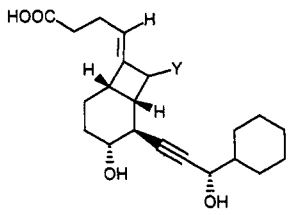
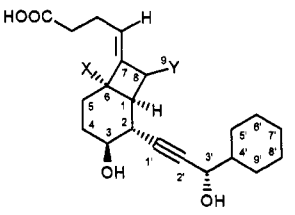
Reduction (zinc/copper couple) of each epimer of 8-chloro-8-methylbicyclo[4.2.0]oct-2-en-7-one (**6** and **7**) gives the same product mixture containing 95% of the 8-*endo*-methyl compound **8**. Ketalization of **8** catalyzed by TMSOTf gives the *endo*-methyl cyclic ethylene ketal **10** at −78 °C and the *exo*-methyl epimer **11** (90:10) at 25 °C, in contrast to β-naphthalenesulfonic acid- catalyzed reactions. Wittig olefination of *both* the functionalized 8-*endo*- and 8-*exo*-methyl ketones gives only the 8-*endo*-methyl olefin, whereas introduction of a 6-methoxy or 6-methyl substituent favors the 8-*exo* configuration. A rationale for these observations is proposed.

We recently described[2–5] the synthesis of the bicyclo[4.2.0]octanes **1** and **2** as stable mimics of the natural antithrombotic agent prostacyclin. In the course of this work, we became interested in the effect of substitution at the 6- and 8-positions[3–5] of the bicyclo[4.2.0]octane ring on the biological activity of these compounds and found that substitution at the 8-position significantly affected both the profile and intrinsic activity of the molecule.[3] We therefore sought to prepare the individual 8-*exo*- and 8-*endo*-methyl isomers of compounds having different substituents at the 6-position. In the course of this work, we found some interesting stereochemical consequences in reactions leading to **3** and **4** and in particular have found remarkable effects of the 6- and 8-substituents on the Wittig reactions used to convert bicyclic ketones to final products.



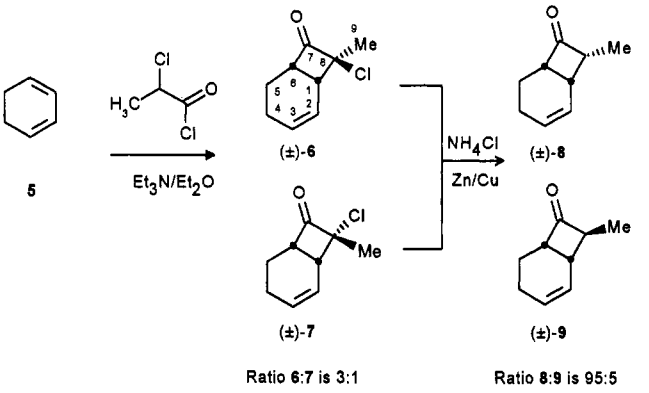
1 Y = H
3 Y = Me



2 X = OMe, Me Y = H
4 X = H, OMe, Me Y = Me

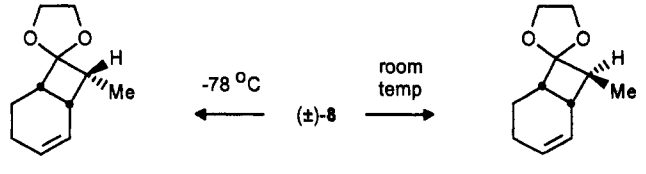
We initially set out to prepare the isomeric 8-methylbicyclo[4.2.0]octanones **8** and **9** for further elaboration to final products by our previous route[2] (Scheme 1). Reaction of 1,3-cyclohexadiene **5** with 2-chloropropionyl chloride and Et_3N in ether gave a separable mixture of 8-*endo*- and 8-*exo*-methyl chloro ketones **6** and **7** in a ratio of 3:1. However, separate reduction of each isomer with zinc/copper couple gave the same mixture of products consisting of 95% 8-*endo*-methyl ketone **8** and 5% of 8-*exo*-methyl ketone **9**. The structures of ketones **8** and **9** were confirmed by ^{13}C NMR spectroscopy and GC/MS (*vide infra*).

Scheme 1



The ratio of products obtained by ketalization of the purified 8-*endo*-methyl ketone **8** proved to be sensitive to the reaction conditions and temperature. Reaction with ethylene glycol and β-naphthalenesulfonic acid in refluxing benzene gave 8-*endo*-methyl ketal **10** (15%), the epimeric 8-*exo*-methyl ketal **11** (25%), and unreacted ketone **8** (60%), as estimated by ^1H NMR spectroscopy and GC/MS. When the reaction was repeated at a higher temperature in refluxing heptane, all the ketone **8** was consumed, giving a mixture of 65% of the epimeric 8-*exo*-methyl ketal **11** and only 35% of the desired 8-*endo*-methyl ketal **10**. These results suggest that the 8-*exo*-methyl ketal **11** is thermodynamically more stable.

In an attempt to obtain a diastereomerically pure ketal, the ketalization was repeated using 1,2-bis[(trimethylsilyl)oxy]ethane in CH_2Cl_2 with trimethylsilyl trifluoromethanesulfonate as catalyst[6] at −78 °C. Under these conditions, very little epimerization (about 3%) occurred, giving



(±)-10 (±)-11

8-*endo*-methyl ketal **10** in 89% yield. Furthermore, it was noticed that as the reaction temperature was raised from

† Dedicated to Dr. John A. Edwards on the occasion of his retirement from Syntex Research.

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(1) Contribution No. 882 from the Institute of Organic Chemistry.

(2) Kluge, A. F.; Kertesz, D. J.; O'Yang, C.; Wu, H. Y. *J. Org. Chem.* **1987**, *52*, 2860–8.

(3) Kluge, A. F.; Wu, H. Y. U. S. Patent 4,678,805, 1987.

(4) Wu, H. Y.; Kurz, W. U. S. Patent 4,735,966, 1988.

(5) O'Yang, C.; Kurz, W.; Walker, K. A. M.; Wu, H. Y. U. S. Patent 4,983,627, 1991.

(6) Tsunoda, T.; Suzuki, M.; Noyori, R. *Tetrahedron Lett.* **1980**, *21*, 1357.

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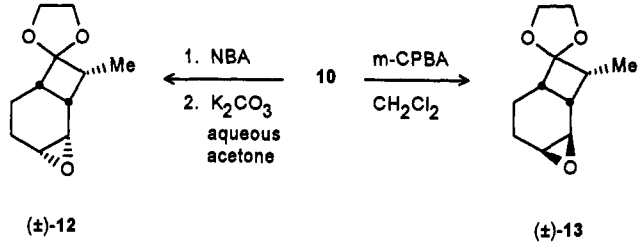
-78 °C to room temperature, the 8-*endo*-methyl ketal **10** gradually and almost completely (90%) epimerized to the 8-*exo*-methyl ketal **11**. Thus, use of 1,2-bis[(trimethylsilyl)oxy]ethane in CH_2Cl_2 with the appropriate choice of temperature permits preparation of either the 8-*exo*- or 8-*endo*-methyl isomer.

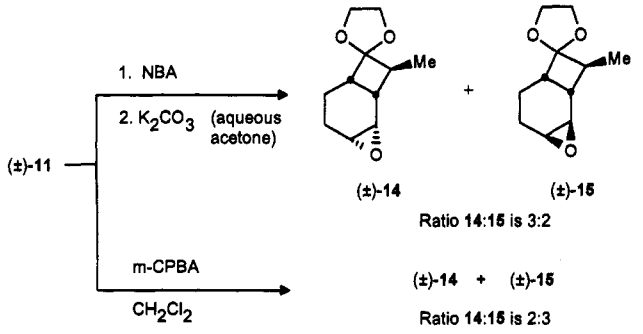
Having obtained isomers **10** and **11**, it seemed that conversion to the epimeric final products would be routine. Introduction of the lower side chain with the correct stereochemistry required formation of an *endo* epoxide in the cyclohexane ring. Epoxidation of the 8-*endo*-methyl ketal **10** with *N*-bromoacetamide (NBA) and K_2CO_3 gave the desired 2,3-*endo*-epoxide **12** exclusively, whereas use of *m*-CPBA in CH_2Cl_2 at room temperature gave only the undesired 2,3-*exo*-epoxide **13**. In contrast, reaction of



(±)-12 (±)-13

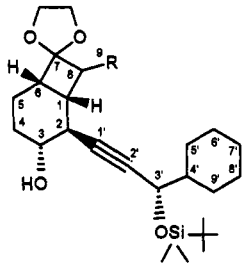
8-*exo*-methyl ketal **11** with NBA/K_2CO_3 gave a separable mixture of the desired *endo*-epoxide **14** (60%) and *exo*-epoxide **15** (40%), whereas reaction with *m*-CPBA gave 40% of the *endo*-epoxide **14** and 60% of **15** as determined by analysis of the ^1H and ^{13}C NMR spectra (Scheme 2).

Scheme 2



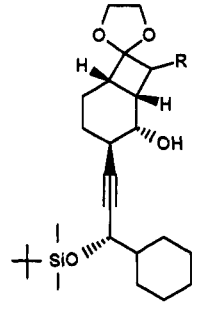
The assignments of the configuration of the C8-methyl group on the cyclobutane ring[7-10] were based on the ^{13}C NMR data. The ^{13}C NMR chemical shift of the C8-Me resonance is shifted upfield when the methyl group is *cis* to the six-membered ring and downfield in the *trans* isomer due to steric compression.[7] This general rule has been observed in other four-membered ring model compounds such as *cis*- and *trans*-1,2-dimethylcyclobutane[8] and *cis*- and *trans*-2,3-dimethyloxetanes[9] as well as in three-, five- and six-membered rings.[10] This same rationale was used to assign the configurations of the four isomers of the epoxide analogues (compounds **12–15**). NOE difference spectra were run on the final carbacyclin products (**52–55**) to confirm these initial assignments as well as the *E*/*Z* configuration of the side chain.

Addition of the lower side chain as described previously[2] by reaction of epoxide **12** with the chiral lithium acetylide in the presence of BF_3·Et_2O gave regioisomers **16** + **17** and **20** + **21** in a ratio of 10:1. Chromatography and further



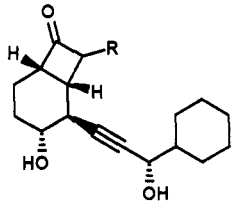
16 R = Me (endo) **17** R = Me (endo)

18 R = Me (exo) **19** R = Me (exo)



20 R = Me (endo) **21** R = Me (endo)

22 R = Me (exo) **23** R = Me (exo)



24 R = Me (endo) **25** R = Me (endo)

26 R = Me (exo) **27** R = Me (exo)

treatment of **16** + **17** with dicobalt octacarbonyl in ether followed by separation and cleavage with ceric ammonium nitrate gave the pure enantiomers **16** and **17** (Scheme 3).

Similar treatment of the mixture of *endo*-epoxide **14** and *exo*-epoxide **15** (ratio of 3:2) from Scheme 2 with BF_3·Et_2O and the lithium acetylide gave compounds **18** + **19** as the major and **22** + **23** as the minor product. Pure enantiomers **18** and **19** were derived from the mixture as above. Acid hydrolysis of compounds **16–19** gave ketones **24–27**, respectively.

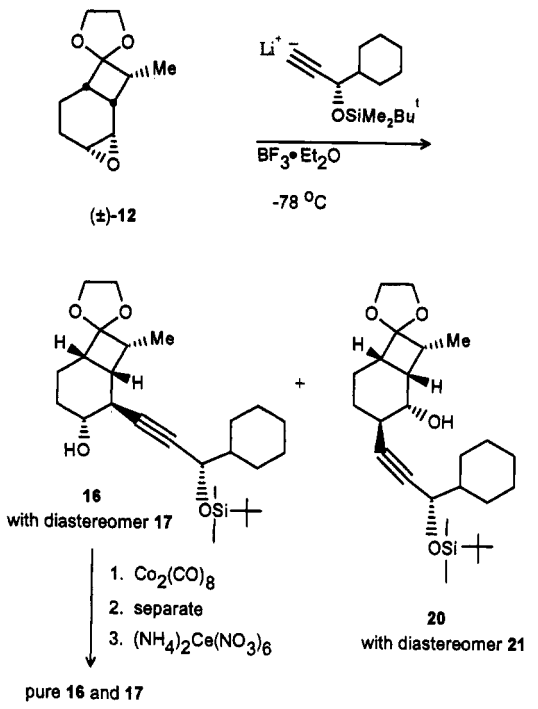
The stage now seemed set for preparing both the target *exo*- and *endo*-isomers of compounds **3** and **4** (X = H) and their acid side-chain homologs. Wittig reaction of 8-*endo*-methyl ketone **24** with ylides **28** and **29** gave the expected 8-*endo*-methyl products **30** and **31**, and **34** and **35**.

$Ph_3P{=}CH(CH_2)_nCOO^-Na^+$

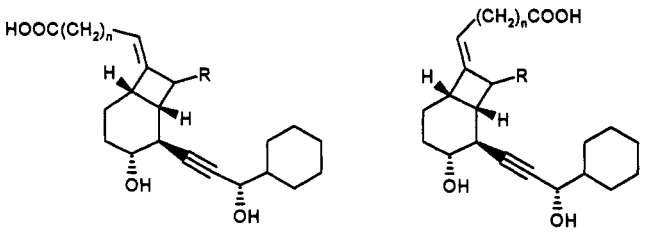
28 n = 2
29 n = 3

(7) Levy, G. C.; Nelson, G. L. In *Carbon-13 Nuclear Magnetic Resonance for Chemists*; Wiley-Interscience: 1972; p 24 and 43–44.
(8) *Sadtler Standard Carbon-13 NMR Spectra Collection*, NMR 25245 and NMR 25246.
(9) Eliel, E. L.; Pietrusiewicz, K. M. In *Topics in Carbon-13 NMR Spectroscopy*; Levy, G. C., Ed.; Wiley-Interscience: New York, 1979; Vol. 3, p 178.
(10) Rol, N. C.; Clague, A. D. *Org. Magn. Reson.* **1981**, *16*, 187. Christl, M.; Reich, H. J.; Roberts, J. D. *J. Am. Chem. Soc.* **1971**, *93*, 3463. Dalling, D. K.; Grant, D. M.; Chaney, B. V. *J. Am. Chem. Soc.* **1967**, *89*, 5315.

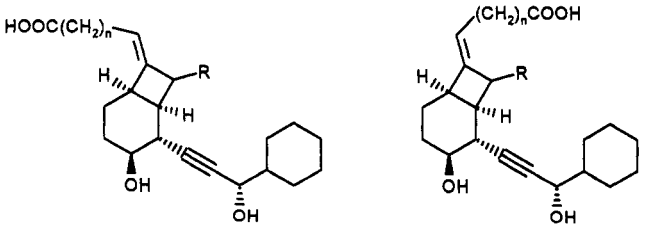
Scheme 3



However, to our surprise, under the same conditions, the 8-*exo*-methyl ketone **26** gave *the same endo*-methyl products **30**, **31**, **34**, and **35**, with none of the *exo*-methyl compounds (**32**, **33**, **36**, and **37**) isolated. The *ent-epi* 8-*endo*-methyl ketone **25** and 8-*exo*-methyl ketone **27** behaved similarly giving 8-*endo*-methyl analogs **38**, **39**, **42**, and **43**. The structural assignments were based on the



30	R = ,,,CH3	(endo)	n = 2	**31**
32	R = ◢CH3	(exo)	n = 2	**33**
34	R = ,,,CH3	(endo)	n = 3	**35**
36	R = ◢CH3	(exo)	n = 3	**37**



38	R = ◢CH3	(endo)	n = 2	**39**
40	R = ,,,CH3	(exo)	n = 2	**41**
42	R = ◢CH3	(endo)	n = 3	**43**
44	R = ,,,CH3	(exo)	n = 3	**45**

^1H and ^{13}C NMR and NOE difference spectra (Table 1). Apparently the 8-*exo*-methyl group restricts the preferred

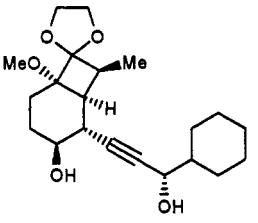
Table 1. Nuclear Overhauser Enhancements

compound	resonance saturated	NOE observed
30[a]	C_8-Me	=CH (no enhancements on H-1 and H-6)
31	C_8-Me	=CHCH_2, H-8
	H-6	H-8, H-1
	H-8	C_8-Me, H-1, H-6

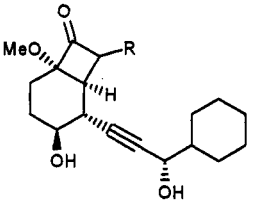
[a] The H-8 and H-6 resonances are only separated by 0.10 ppm, making observation of the enhancement between them impossible.

exo approach of the bulky triphenylphosphorane to the carbonyl group. We believe that base-catalyzed equilibration of the 8-*exo*-methyl ketone to a mixture containing the 8-*endo* methyl isomer, and conversion of the latter to product, is faster than the Wittig reaction of the starting ketone. As the more reactive 8-*endo* methyl isomer is removed by reaction, further equilibration eventually leads to exclusive formation of 8-*endo*-methyl olefin. Although base-catalyzed equilibration of the pure 8-*endo*-methyl ketone **24** may take place simultaneously with the Wittig reaction, it too eventually gives rise to only the 8-*endo*-methyl olefin by selection of the 8-*endo* isomer. Thus despite the preparation of isomerically pure precursors, the same stereochemically pure product could presumably have been obtained from a mixture of *exo* and *endo* ketones.

In stark contrast to the above observations, a different outcome is seen in the Wittig reaction when the 8-substituent is accompanied by one at the 6-position. Hydrolysis of ketal **46**[4] (dilute H_2SO_4/acetonitrile/60 °C)

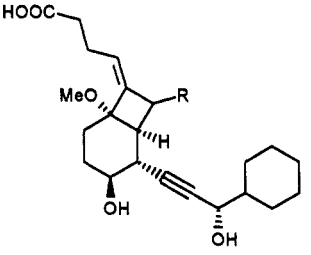


46



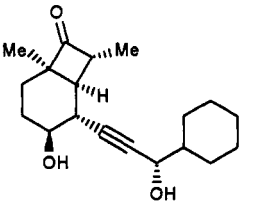
47 R = ◢CH3

48 R = ,,,CH3

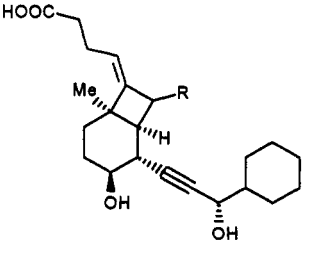


49 R = ,,,CH3

50 R = ◢CH3

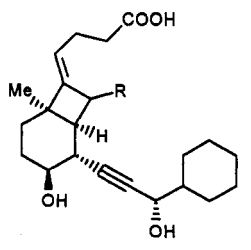


51



52 R = ,,,CH3

53 R = ◢CH3



54 R = ,,,CH3

55 R = ◢CH3

Table 2. Nuclear Overhauser Enhancements

compound	resonance saturated	NOE observed
49	=CH	C_8-Me, =CHCH_2, H-8
	C_8-Me	=CH, H-8, H-1
	C_6-OMe	H-1

Table 3. Nuclear Overhauser Enhancements

compound	resonance saturated	NOE observed
52	=CH	C_8-Me, =CHCH_2, H-8
	H-2	
	C_8-Me	H-1, H-8, =CH
	C_6-Me	H-1
53	=CH	C_8-Me
	C_8-Me	H-2, H-8, =CH
54	H-8	H-2, C_8-Me
	C_8-Me	H-8, H-1
	C_6-Me	=CH, H-1
55	H-1	C_6-Me, H-8, H-3
	C_8-Me	H-2, H-8

caused some epimerization giving 8-*endo*-methyl ketone **47** containing 20% of 8-*exo*-methyl ketone **48**. Further epimerization was observed during purification on silica gel. When **47** and **48** were separately subjected to the Wittig reaction, again each gave the same product. In this case, however, 8-*exo*-methyl compound **49** rather than the 8-*endo* compound **50** was the sole product! The structural assignment was confirmed by NOE experiments (Table 2). It would appear that the presence of a 6-MeO substituent now prevents *exo* attack by the phosphorane, which is forced to react from the more hindered face. In this case, the 8-*exo*-methyl isomer is removed from the equilibrium as that least hindered to *endo*-attack, giving the *exo*-methyl olefin **49**.

In view of these two opposing results, we were interested in the effect a smaller 6-methyl substituent might have. The Wittig reaction of 8-*exo*-methyl ketone **51**[5] gave two *Z* isomers, 8-*exo*-methyl compound **52** and 8-*endo*-methyl compound **53** in a ratio of 6:1, with trace amounts of the corresponding *E* isomers **54** and **55**. The structures of **52–55** were confirmed by ^{1}H NMR, ^{13}C NMR, and NOE experiments (Table 3). It would therefore appear that this represents an intermediate case, such that reaction of the phosphorane takes place largely, but not exclusively, from the endo face.

We have thus shown that the stereochemistry of 8-methylbicyclo[4.2.0]octan-7-one derivatives can be controlled during ketalization (and hydrolysis) to give either the *exo* or *endo* isomer; however, Wittig reactions of the stereochemically pure 8-methyl ketones give common products determined by the substituent at C-6.

The PGI_2 analogs inhibited ADP-induced aggregation[11] of human platelets *in vitro* with the following activities, relative to PGE_1 = 1.0: **30**, 3.9; **31**, 3.5; **34**, 0.4; **35**, 0.2; **38**, 2; **39**, 0.006; **42**, 0.05; **43**, 0.001; **49**, 147; **52**, 23; **53**, 4.5; **54**, 0.07; **55**, 0.11.

Experimental Section

General. All reactions were performed under argon. Melting points are uncorrected. Thin-layer chromatograms were run on glass supported silica gel 60 plates (0.25-mm layer, F-254, E. Merck). Flash chromatography[12] was performed with 40–63 mm silica gel 60 (E. Merck). ^{1}H and ^{13}C NMR spectra were measured on a Bruker WM-300 instrument as $CDCl_3$ solutions referenced to internal $SiMe_4$. Heteronuclear single frequency decoupling experiments and the attached proton test (APT)[13] were used to assign the ^{13}C NMR spectra. Tetrahydrofuran (THF) was freshly distilled from sodium and benzophenone.

8-*exo*-Chloro-8-*endo*-methyl[4.2.0]oct-2-en-7-one (6) and 8-*endo*-Chloro-8-*exo*-methylbicyclo[4.2.0]oct-2-en-7-one (7). A refluxing mixture of cyclohexadiene (50.0 g, 624 mmol) and 2-chloropropionyl chloride (58.4 g, 460 mmol) in ether (400 mL) under nitrogen was treated dropwise with triethylamine (46.7 g, 460 mmol) in ether (300 mL) over 3 h. The mixture was stirred at room temperature for 20 h and then filtered, and the filtrate was washed with brine, 1 *N* HCl and saturated $NaHCO_3$ and dried (Na_2SO_4). The solvent was removed under reduced pressure and the residue distilled to give a mixture of the 8-*exo*-methyl and 8-*endo*-methyl isomers (57.8 g). Chromatography on silica gel, eluting with hexane/CH_2Cl_2 (1:1) gave **6** (40 g, 51%) as an oil: IR (neat) 1778 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.50 (s, 3 H, H-9), 1.50, 2.00 (2 m, 2 H, H-5), 2.00 (m, 2 H, H-4), 3.14 (ddd, 1 H, J = 1.3, 3.0, 5.8 Hz, H-1), 4.14 (m, 1 H, H-6), 5.87 (bd, 1 H, J = 9.2 Hz, H-2), 6.01 (m, 1 H, H-3); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 18.71 (t, C-5), 19.38 (q, C-9), 21.34 (t, C-4), 40.40 (d, C-1), 54.69 (d, C-6), 77.19 (s, C-8), 124.19 (d, C-2), 131.76 (d, C-3), 206.01 (s, C-7); MS *m/z* 170 (M$^+$). Anal. Calcd for $C_9H_{11}ClO$: C, 63.35; H, 6.50; Cl, 20.78. Found: C, 63.41; H, 6.51; Cl, 20.82; and **7** (12.0 g, 15.3%) as an oil: IR (neat) 1778 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.60, 2.08 (2 m, 2 H, H-5), 1.82 (s, 3 H, H-9), 2.08 (m, 2 H, H-4), 2.96 (m, 1 H, H-1), 3.74 (ddd, 1 H, J = 3.2, 6.0, 9.4 Hz, H-6), 5.83 (dm, 1 H, J = 9.9 Hz, H-2), 6.00 (bddd, 1 H, J = 5.4, 5.4, 9.9 Hz, H-3); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 18.98 (t, C-5), 20.98 (t, C-4), 26.41 (q, C-9), 38.01 (d, C-1), 52.40 (d, C-6). 76.04 (s, C-8), 124.63 (d, C-2), 130.29 (d, C-3), 206.58 (s, C-7); MS *m/z* 170 (M$^+$). Anal. Calcd for $C_9H_{11}ClO$: C, 63.35; H, 6.50; Cl, 20.78. Found: C, 63.10; H, 6.55; Cl, 20.90.

8-*endo*-Methylbicyclo[4.2.0]oct-2-en-7-one (8). To a mixture of **6** (40.0 g, 234 mmol) and NH_4Cl (60.0 g, 1122 mmol) in ethanol (250 mL) at room temperature was added zinc/copper couple (40 g) in portions. The mixture was stirred at room temperature for 3 h, diluted with ether, and filtered. The filtrate was washed with brine and dried (Na_2SO_4), and the solvent was removed under reduced pressure. The residue was purified by chromatography on silica gel, eluting with hexane–CH_2Cl_2 (1:1) to give **8** as an oil (25.9 g, 83%), containing 5% of **9**.

8: IR (neat) 1770 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.99 (d, 3 H, J = 7.3 Hz, H-9), 1.50, 2.00 (2 m, 2 H, H-5), 2.00 (m, 2 H, H-4), 3.02 (bdd, 1 H, J = 9.8, 9.8 Hz, H-1), 3.41 (ddq, 1 H, J = 2.2, 7.3, 9.8 Hz, H-8), 3.60 (m, 1 H, H-6) 5.76 (bd, 1 H, J = 9.9 Hz, H-2) 5.95 (m, 1 H, H-3); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 8.90 (q, C-9), 18.64 (t, C-5), 21.46 (t, C-4), 27.78 (d, C-1), 55.40 (d, C-6), 55.54 (d, C-8), 125.62 (d, C-2), 130.29 (d, C-3), 214.08 (s, C-7); MS *m/z* 136 (M$^+$). Anal. Calcd for $C_9H_{12}O$: C 79.37; H, 8.88. Found: C, 79.29; H, 8.88.

9 (as a mixture with **8**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.26 (d, 3 H, J = 7.3 Hz, H-9).

Spiro[8-*endo*-methylbicyclo[4.2.0]oct-2-ene-7,2′-(1′,3′-dioxolane)] (10). A mixture of **8** (680 mg, 5.0 mmol) and 1,2-bis[(trimethylsilyl)oxy]ethane (2.1 g, 10.2 mmol) was cooled to −78 °C under N_2, and Me_3SiOTf (40 μL, 0.2 mmol) was added in portions (4 × 10 μL). The reaction mixture was stirred for a total of 16 h at −78 °C and then quenched by addition of excess pyridine. The mixture was then poured into saturated aqueous $NaHCO_3$ and extracted with ether. Evaporation of the solvent under reduced pressure and chromatography of the residue on silica gel, eluting with 5% acetone/hexane, gave **10** (800 mg, 89%) as an oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.90 (d, 3 H, J = 7.0 Hz, H-9), 1.55, 1.73 (2 m, 2 H, H-5), 1.80, 2.27 (2 m, 2 H, H-4), 2.58 (m, 1 H, H-1), 2.70 (m, 1 H, H-8), 2.78 (m, 1 H, H-6), 3.82 (m, 4 H, ketal), 5.64 (bd, 1 H, J = 9.2 Hz, H-2), 5.94 (m, 1 H, H-3); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 9.68 (q, C-9), 19.40 (t, C-5), 21.93 (t, C-4), 27.34 (d, C-1), 42.68 (d, C-6), 43.07 (d, C-8), 63.51, 65.47 (2 t, ketal), 111.40 (s, C-7), 125.62 (d, C-2), 129.61 (d, C-3); MS *m/z* 180 (M$^+$). Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.20; H, 9.00.

Spiro[8-*exo*-methylbicyclo[4.2.0]oct-2-ene-7,2′-(1′,3′-dioxolane)] (11). Following the procedure for **10** above at room temperature instead of −78 °C gave **11** as an oil: ^{1}H NMR ($CDCl_3$,

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(12) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(13) Patt, S. L.; Schoolery, J. N. *J. Magn. Reson.* **1982**, *46*, 535.

300 MHz) δ 1.05 (d, 3 H, J = 7.0 Hz, H-9), 1.60–2.10 (2 m, 4 H, H-4, H-5), 2.04 (m, 1 H, H-1), 2.40 (dq, 1 H, J = 7.0, 9.2 Hz, H-8), 2.53 (m, 1 H, H-6), 3.89 (m, 4 H, ketal), 5.81 (m, 2 H, H-2, H-3); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.76 (q, C-9), 20.79 (t, C-4), 22.08 (t, C-5), 32.83 (d, C-1), 42.44 (d, C-6), 48.39 (d, C-8), 63.89, 64.51 (2 t, ketal), 109.29 (s, C-7), 127.88 (d, C-2), 128.54 (d, C-3); MS *m/z* 181 (MH^+). Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.21; H, 8.97.

(1*S,2*S**,4*R**,7*S**)-Spiro[3-oxa-9-*endo*-methyltricyclo-[5.2.0.0^{2,4}]nonane-8,2′-(1′,3′-dioxolane)] (12).** To a stirred solution of **10** (5.0 g, 27.8 mmol) in acetone (40 mL) and water (20 mL) at 0 °C was added *N*-bromoacetamide (4.70 g, 34.1 mmol) over 1 h. This mixture was stirred at room temperature for 20 h and then treated with K_2CO_3 (12.4 g, 89.7 mmol), and the resulting mixture was stirred at room temperature for 2 days. The mixture was saturated with sodium chloride and extracted with ether (4 × 150 mL), and the combined extracts were washed with saturated NaCl solution (100 mL) and dried (Na_2SO_4). Removal of the solvent under reduced pressure and chromatography of the residue on silica gel eluting with 25% acetone/hexane gave **12** (3.07 g, 15.7 mmol, 56.3%) as an oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.23 (d, 3 H, J = 7.6 Hz, H-9), 1.30, 2.03 (2 m, 2 H, H-4), 1.65 (ddd, 1 H, J = 4.5, 13.2, 13.2 Hz, H-5β), 1.90 (m, 1 H, H-5α), 2.47 (ddd, 1H, J = 2.6, 9.8, 10.0 Hz, H-1), 2.55 (m, 1 H, H-6), 2.92 (ddq, J = 2.1, 7.6, 9.8 Hz, H-8), 3.11 (m, 2 H, H-2, H-3), 3.85 (m, 4 H, ketal); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 10.29 (q, C-9), 14.75 (t, C-5), 21.76 (t, C-4), 26.70 (d, C-1), 41.39 (d, C-6), 44.61 (d, C-8), 49.62 (d, C-2), 51.19 (d, C-3), 63.46 and 65.26 (2 t, ketal), 109.78 (s, C-7); HRMS *m/z* exact mass calcd for $C_{11}H_{16}O_3$ 196.109945, found 196.110809.

(1*S,2*R**,4*S**,7*S**)-Spiro[3-oxa-9-*endo*-methyltricyclo-[5.2.0.0^{2,4}]nonane-8,2′-(1′,3′-dioxolane)] (13).** *m*-CPBA (85%, 136 mg, 0.67 mmol) was added to a solution of **10** (100 mg, 0.56 mmol) in CH_2Cl_2 (2 mL) at room temperature and the mixture was stirred for 5 h. The organic phase was washed with saturated $NaHCO_3$ (3 mL) and the aqueous phase reextracted with CH_2Cl_2 (5 mL). The organic phases were combined, dried (Na_2SO_4), and evaporated. The residual oil was purified by flash chromatography (hexane/acetone 4:1) to give **13** (86 mg, 78.6%) as an oil: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.03 (d, 3 H, J = 7.3 Hz, H-9), 1.40, 1.57 (2 m, 2 H, H-4), 1.92, 2.33 (2 m, 2 H, H-5), 2.52 (m, 2 H, H-1, H-6), 2.82 (m, 1 H, H-8), 3.07 (d, 1 H, J = 4.1 Hz, H-2), 3.27 (m, 1 H, H-3), 3.90 (m, 4 H, ketal); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 8.90 (q, C-9), 16.10 (t, C-5), 20.76 (t, C-4), 25.85 (d, C-1), 40.31 (d, C-6), 41.59 (d, C-8), 52.04 (d, C-2), 53.99 (d, C-3), 63.81 and 65.55 (2 t, ketal), 111.46 (s, C-7); HRMS *m/z* exact mass calcd for $C_{11}H_{16}O_3$ 196.109945, found 196.110809. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.41; H, 8.34.

(1*S,2*S**,4*R**,7*S**)-Spiro[3-oxa-9-*exo*-methyltricyclo-[5.2.0.0^{2,4}]nonane-8,2′-[1′,3′-dioxolane)] (14) and (1*S**,2*R**,4*S**,7*S**)-Spiro[3-oxa-9-*exo*-methyltricyclo[5.2.0.0^{2,4}]-nonane-8,2′-(1′,3′-dioxolane)] (15).** The reaction of **11** using conditions described above for **12** gave **14** and **15** in a ratio of 3:2. Reaction of **11** using conditions as for **13** gave **14** and **15** in a ratio of 2:3.

14 (as mixture with **15**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.07 (d, 3 H, J = 7.0 Hz, H-9), 2.96 (bdq, 1 H, J = 7.0, 9.5 Hz, H-8), 3.12 (dd, 1 H, J = 4.2, 4.2 Hz, H-2), 3.21 (bdd, 1 H, J = 3.4, 4.2 Hz, H-3), 3.85 (m, 4 H, ketal); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.09 (q, C-9), 15.78 (t, C-5), 21.97 (t, C-4), 31.09 (d, C-1), 41.16 (d, C-6), 42.74 (d, C-8), 50.96 (d, C-2), 52.48 (d, C-3), 63.96 and 64.58 (2 t, ketal), 109.69 (s, C-7).

15 (as mixture with **14**): ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.11 (d, 3 H, J = 7.2 Hz, H-9); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 14.02 (q, C-9), 16.22 (t, C-5), 21.16 (t, C-4), 31.33 (d, C-1), 39.63 (d, C-6), 43.91 (d, C-8), 52.78 (d, C-2), 53.20 (d, C-3), 64.02 and 64.52 (2 t, ketal), 108.81 (s, C-7).

14 + 15: ms *m/z* 196 (M^+). Anal. Calcd for $C_{11}H_{16}O_2$: C, 67.32; H, 8.22. Found: C, 67.24; H, 8.25.

Mixture of (3′*S*,1*S*,2*S*,3*R*,6*S*)-spiro[2-[3′-[(*tert*-butyldimethylsilyl)oxy]-3′-cyclohexylprop-1′-ynyl]-3-hydroxy-8-*endo*-methylbicyclo[4.2.0]octane-7,2″-(1″,3″-dioxolane)] (16) and (3′*S*,1*R*,2*R*,3*S*,6*R*)-spiro[2-[3′-[(*tert*-butyldimethylsilyl)oxy]-3′-cyclohexylprop-1′-ynyl]-3-hydroxy-8-*endo*-methylbicyclo[4.2.0]octan-7,2″-(1″,3″-dioxolane)] (17). To a mixture of (*S*)-3-[(*tert*-butyldimethylsilyl)oxy]-3-cyclohexyl-1-propyne (6.45 g, 25.5 mmol) in THF (48 mL) at 0 °C under argon was added over 20 min *n*-BuLi (1.37 M, 15.96 mL, 21.9 mmol) in hexane. The resulting solution was cooled to −78 °C and treated with stirring with **12** (3.6 g, 18.4 mmol) in THF (18 mL) followed by $BF_3{\cdot}Et_2O$ (2.26 mL, 18.4 mmol) dropwise over 25 min. After addition of saturated Na_2SO_4 solution (25 mL), the mixture was warmed to room temperature and extracted thoroughly with EtOAc. The combined extracts were dried (Na_2SO_4) and concentrated *in vacuo*, and the oily residue was purified by flash chromatography on silica gel using 2% acetone/CH_2Cl_2 to give regioisomers **16 + 17** (4.6 g, 55.8%) and **20 + 21** (0.4 g, 4.8%) as oils.

16 + 17: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.08 (s, 3 H, SiMe), 0.11 (s, 3 H, SiMe), 0.90 (s, 9 H, Si*t*Bu), 1.01 (d, 3 H, J = 7.0 Hz, H-9), 2.16 (m, 1 H, H-1), 2.38 (m, 1 H, OH), 2.50 (bdd, 1 H, J = 8.2, 8.2 Hz, H-6), 2.65 (m, 2 H, H-2, H-8), 3.37 (ddd, 1 H, J = 2.2, 10.5, 10.5 Hz, H-3), 3.90 (m, 4 H, ketal), 4.08 (m, 1H, H-3′); HRMS *m/z* exact mass calcd for $C_{26}H_{44}SiO_4$ 391.230464, found 391.229665.

20 + 21: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.08 (s, 3 H, SiMe), 0.10 (s, 3 H, SiMe), 0.90 (s, 9 H, Si*t*Bu), 1.24 (d, 3 H, J = 7.6 Hz, H-9), 2.57 (m, 2 H, H-1, H-6), 2.70 (m, 1 H, H-3), 2.78 (dq, 1 H, J = 4.5, 7.6 Hz, H-8), 3.47 (d, 1 H, J = 7.0 Hz, OH), 3.93 (m, 1 H, H-2), 3.93 (m, 4 H, ketal), 4.06 (dd, 1 H, J = 1.4, 6.3 Hz, H-3′). Anal. Calcd for $C_{26}H_{44}SiO_4$: C, 69.60; H, 9.88. Found: C, 69.30; H, 9.91.

Separation of 16 and 17. The diastereomeric mixture **16 + 17** (4.5 g, 10.0 mmol) in ether (200 mL) was treated with dicobalt octacarbonyl (5.1 g, 14.9 mmol), and the resulting solution was stirred at 23 °C for 2 h. The mixture was diluted with ether (200 mL) and filtered, and the filtrate was concentrated to an oil. Purification by flash chromatography using 12% EtOAc/hexane gave two components: A (high R_f) and B (low R_f). Component A (2.7 g) was dissolved in acetone/water (9:1) (150 mL), to which was added ceric ammonium nitrate (10.1 g, 18.4 mmol). After 2 min this mixture was diluted with water (200 mL) and the product isolated by extraction with ether. After drying and evaporation there was obtained **16** (1.5 g, 33.3%) as an oil. Similarly, component B (3.1 g) was converted to **17** (1.62 g, 36.0%).

16: $[\alpha]^{25}_D$ −9.5° (*c* 0.31, MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.08 (s, 3 H, SiMe), 0.11 (s, 3 H, SiMe), 0.90 (s, 9 H, Si*t*Bu), 1.01 (d, 3H, J = 7.1 Hz, H-9), 2.17 (m, 1 H, H-1), 2.37 (bd, 1 H, J = 1.3 Hz, OH), 2.50 (bdd, 1 H, J = 8.0, 8.0 Hz, H-6), 2.66 (m, 2 H, H-2, H-8), 3.36 (ddd, 1 H, J = 3.6, 10.3, 10.3 Hz, H-3), 3.90 (m, 4 H, ketal), 4.08 (dd, 1 H, J = 1.6, 6.2 Hz, H-3′); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −5.01 q, -4.36 q ($SiMe_2$), 8.01 (q, C-9), 18.27 (s, SiC), 20.70 (t, C-5), 25.84 (q, *t*-Bu), 26.05 (t, C-6′, C-8′), 26.61 (t, C-7′), 27.68 t, 28.79 t (C-5′, C-9′), 29.57 (t, C-4), 35.47 (d, C-1), 36.18 (d, C-2), 41.55 (d, C-6), 43.04 (d, C-8), 45.18 (d, C-4′), 64.31, 65.57 (2 t, ketal), 67.83 (d, C-3′), 71.96 (d, C-3), 84.31 (s, C-2′), 85.93 (s, C-1′), 112.17 (s, C-7). Anal. Calcd for $C_{26}H_{44}SiO_4$: C, 69.60; H, 9.88. Found: C, 69.52; H, 9.95.

17: $[\alpha]^{25}_D$ −59.6° (*c* 0.74, MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.09 (s, 3 H, SiMe), 0.12 (s, 3 H, SiMe), 0.90 (s, 9 H, Si*t*Bu), 1.01 (d, 3 H, J = 7.1 Hz, H-9), 2.16 (m, 1 H, H-1), 2.36 (bs, 1 H, OH), 2.49 (bdd, 1 H, J = 7.9, 7.9 Hz, H-6), 2.65 (m, 2 H, H-2, H-8), 3.36 (ddd, 1 H, J = 3.4, 10.4, 10.4 Hz, H-3), 3.92 (m, 4 H, ketal), 4.09 (dd, 1 H, J = 1.4, 6.2 Hz, H-3′); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.99 q, −4.37 q ($SiMe_2$), 8.00 (q, C-9), 18.28 (s, SiC), 20.67 (t, C-5), 25.85 (q, *t*-Bu), 26.06 (t, C-6′, C-8′), 26.60 (t, C-7′), 28.69 t, 28.74 t (C-5′, C-9′), 29.56 (t, C-4), 35.43 (d, C-1), 36.12 (d, C-2), 41.55 (d, C-6), 43.04 (d, C-8), 45.20 (d, C-4′), 64.30, 65.57 (2 t, ketal), 67.85 (d, C-3′), 71.91 (d, C-3), 84.27 (s, C-2′), 85.98 (s, C-1′), 112.17 (s, C-7); MS *m/z* 447 [$(M - H)^+$]. Anal. Calcd for $C_{26}H_{44}SiO_4$: C, 69.60; H, 9.88. Found: C, 69.35; H, 9.94.

(3′*S*,1*S*,2*S*,3*R*,6*S*)-Spiro[2-[3′-[(*tert*-butyldimethylsilyl)-oxy]-3′-cyclohexylprop-1′-ynyl]-3-hydroxy-8-*exo*-methylbicyclo[4.2.0]octane-7,2″-(1″,3″-dioxolane)] (18) and (3′*S*,1*R*,2*R*,3*S*,6*R*)-Spiro[2-[3-[(*tert*-butyldimethylsilyl)oxy]-3′-cyclohexylprop-1′-ynyl]-3-hydroxy-8-*exo*-methylbicyclo-[4.2.0]octane-7,2″-(1″,3″-dioxolane)] (19). **12** was replaced with 8-*exo*-methyl isomers **14 + 15**, and the regioisomers **18 + 19** (45.6%) and **22 + 23** (7.5%) were prepared as above.

18 + 19: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.09 (s, 3 H, SiMe), 0.12 (s, 3 H, SiMe), 0.90 (s, 9 H, Si*t*Bu), 1.11 (d, 3H, J = 7.2 Hz, H-9), 2.29 (dq, 1 H, J = 3.0, 7.2 Hz, H-8), 2.61 (ddd, 1 H, J = 1.7, 8.8, 8.8 Hz, H-2), 2.69 (ddd, 1 H, J = 3.2, 8.0, 8.8 Hz, H-6), 3.42 (dddd, 1 H, J = 2.2, 4.0, 10.0, 10.0 Hz, H-3), 3.85 (m, 4 H, ketal), 4.09 (dd, 1 H, J = 1.7, 6.3 Hz, H-3′); ^{13}C NMR ($CDCl_3$, 75.5 MHz), δ

−4.96, −4.31 (2q, $SiMe_2$), 14.97 (q, C-9), 18.30 (s, SiC), 19.49 (t, C-5), 25.87 (q, *t*-Bu), 26.05 (t, C-6′, C-8′), 26.61 (t, C-7′), 28.69 and 28.80 (2 t, C-5′,C-9′), 29.37 (t, C-4), 38.98 (d, C-1), 40.15 (d, C-6), 40.73 (d, C-2), 45.16 (d, C-4′), 47.28 (d, C-8), 64.05, 64.19 (2 t, ketal), 67.86 (d, C-3′), 71.27 (d, C-3), 84.25 (s, C-2′), 84.31 (s, C-1′), 110.60 (s, C-7); MS *m/z* 447 (M^+ − H). Anal. Calcd for $C_{26}H_{44}SiO_4$: C, 69.60; H, 9.88. Found: C, 69.44; H, 9.72.

22 + 23: ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.09 (s, 3 H, SiMe), 0.12 (s, 3 H, SiMe), 0.91 (s, 9 H, Si*t*Bu), 1.12 (d, 3 H, *J* = 7.3 Hz, H-9), 2.18 (m, 1 H, H-3), 2.23 (nm, 1 H, OH), 2.42 (dq, 1 H, *J* = 3.6, 7.3 Hz, H-8), 2.87 (ddd, 1 H, *J* = 3.0, 9.6, 9.6 Hz, H-6), 3.73 (dd, 1 H, *J* = 8.5, 8.7 Hz, H-2), 3.85 (m, 4 H, ketal), 4.09 (dd, 1 H, *J* = 1.9, 6.4 Hz, H-3′); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ −4.99 q, −4.34 q ($SiMe_2$), 14.83 (q, C-9), 18.30 (s, SiC), 19.99 (t, C-5), 25.88 (q, *t*-Bu), 26.06 (t, C-6′, C-8′), 26.59 (t, C-7′), 27.96 (t, C-4), 28.74 and 28.78 (2 t, C-5′, C-9′), 35.95 (d, C-3), 40.15 (d, C-1), 41.46 (d, C-6), 45.11 (d, C-4′), 46.75 (d, C-8), 64.15, 64.19 (2 t, ketal), 67.87 (d, C-3′), 75.73 (d, C-3), 84.10 (s, C-2′), 84.11 (s, C-1′), 110.79 (s, C-7); HRMS *m/z* exact mass calcd for $C_{26}H_{44}SiO_4$ 391.230464, found 391.229665.

Separation of 18 and 19. Replacing the diastereomeric mixture **16** + **17** with the 8-*exo*-methylisomers **18** + **19** and following the procedure above gave:

18 (32.4%): $[\alpha]^{25}_D$ −7.2° (*c* 0.5, MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.09 (s, 3 H, SiMe), 0.12 (s, 3 H, SiMe), 0.90 (s, 9 H, Si*t*-Bu), 1.11 (d, 3 H, *J* = 7.3 Hz, H-9), 2.29 (dq, 1 H, *J* = 7.3, 9.8 Hz, H-8), 2.61 (ddd, 1 H, *J* = 1.8, 10.0, 10.0 Hz, H-2), 2.70 (m, 1 H, H-6), 3.40 (ddd, 1 H, *J* = 2.0, 9.8, 9.8 Hz, H-3), 3.85 (m, 4 H, ketal), 4.10 (dd, 1 H, *J* = 1.8, 6.3 Hz, H-3′); MS *m/z* 391 (M − C_4H_9)$^+$. Anal. Calcd for $C_{26}H_{44}SiO_4$·0.5H_2O: C, 68.23; H, 9.91. Found: C, 68.32, H, 9.88.

19 (36.4%): $[\alpha]^{25}_D$ −43.6° (*c* 0.44, MeOH); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 0.09 (s, 3 H, SiMe), 0.12 (s, 3 H, SiMe), 0.90 (s, 9 H, Si*t*Bu), 1.11 (d, 3H, *J* = 7.3 Hz, H-9), 2.28 (dq, 1 H, *J* = 7.3, 9.8 Hz, H-8), 2.61 (ddd, 1 H, *J* = 1.8, 10.0, 10.0 Hz, H-2), 2.70 (m, 1 H, H-6), 3.41 (ddd, 1 H, *J* = 2.0, 9.8, 9.8 Hz, H-3), 3.85 (m, 4 H, ketal), 4.10 (dd, 1 H, *J* = 1.8, 6.3 Hz, H-3′); MS *m/z* 391 (M − C_4H_9)$^+$. Anal. Calcd for $C_{26}H_{44}SiO_4$: C, 69.60; H, 9.88. Found: C, 69.39; H, 10.19.

(3′*S*,1*S*,2*S*,3*R*,6*S*)-2-(3′-Hydroxy-3′-cyclohexylprop-1′-ynyl)-3-hydroxy-8-*endo*-methylbicyclo[4.2.0]octane-7-one (24). A solution of **16** (110 mg, 0.25 mmol), acetonitrile (3 mL), and 2 *N* sulfuric acid (1.5 mL) was stirred at room temperature for 16 h. The reaction was quenched by neutralization with aqueous $NaHCO_3$ and the mixture was extracted with diethyl ether. The extracts were dried ($MgSO_4$) and evaporated to dryness, and the residue was purified by short column silica gel chromatography. Elution with ethyl acetate/hexane (7:3) gave **24** (58 mg, 82%): mp 140–142 °C; $[\alpha]^{25}_D$ +72.6° (*c* 0.35, $CHCl_3$); IR (KBr) 1770 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18 (d, 3 H, *J* = 7.1 Hz, H-9), 2.05 (ddd, 1 H, *J* = 1.6, 9.8, 10.4 Hz, H-2), 2.19 (d, 1 H, *J* = 5.3 Hz, OH), 2.64 (ddd, 1 H, *J* = 9.8, 9.8, 9.8 Hz, H-1), 2.65 (bs, 1 H, OH), 3.29 (bdd, 1 H, *J* = 7.7, 7.7 Hz, H-6), 3.50 (m, 2 H, H-3, H-8), 4.18 (ddd, 1 H, *J* = 1.6, 5.3, 6.0 Hz, H-3′); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 7.97 (q, C-9), 19.56 (t, C-5), 25.90 and 25.92 (2 t, C-6′, C-8′), 26.48 (t, C-7′), 28.19 and 28.20 (2 t, C-5′, C-9′), 30.10 (t, C-4), 34.21 (d, C-1), 38.27 (d, C-2), 44.37 (d, C-4′), 54.31 (d, C-6), 55.97 (d, C-8), 67.27 (d, C-3′), 71.15 (d, C-3), 84.09 (s, C-2′), 85.68 (s, C-1′), 208.40 (s, C-7); MS *m/z* 272 (M^+ − H_2O). Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.82, H, 9.22.

(3′*S*,1*R*,2*R*,3*S*,6*R*)-2-(3′-Hydroxy-3′-cyclohexylprop-1′-ynyl)-3-hydroxy-8-*endo*-methylbicyclo[4.2.0]octan-7-one (25). Replacing **16** with **17** as above gave **25** (83%) as an oil: $[\alpha]^{28}_D$ −54.4° (*c* 0.4, $CHCl_3$); IR (neat) 1770 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.18 (d, 3 H, *J* = 7.1 Hz, H-9), 2.05 (ddd, 1 H, *J* = 1.7, 9.7, 10.5 Hz, H-2), 2.51 (bs, 1 H, OH), 2.65 (ddd, 1 H, *J* = 9.7, 9.7, 9.7 Hz, H-1), 3.29 (bdd, 1 H, *J* = 7.8, 7.8 Hz, H-6), 3.50 (m, 2 H, H-3, H-8), 4.20 (nm, 1 H, H-3′); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 7.97 (q, C-9), 19.54 (t, C-5), 25.90 (t, C-6′, C-8′), 26.47 (t, C-7′), 28.23 and 28.75 (2 t, C-5′, C-9′), 29.98 (t, C-4), 34.20 (d, C-1), 38.31 (d, C-2), 44.36 (d, C-4′), 54.35 (d, C-6), 55.97 (d, C-8), 67.27 (d, C-3′), 71.13 (d, C-3), 84.29 (s, C-2′), 85.56 (s, C-1′), 208.29 (s, C-7); HRMS *m/z* exact mass calcd for $C_{18}H_{26}O_3$ 272.177630, found 272.176635. Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.73; H, 9.34.

(3′*S*,1*S*,2*S*,3*R*,6*S*)-2-(3′-Hydroxy-3′-cyclohexylprop-1′-ynyl)-3-hydroxy-8-*exo*-methylbicylo[4.2.0]octan-7-one (26). Replacing **16** by **18** as above gave **26** (85%): mp 125–128 °C; $[\alpha]^{25}_D$ +36.5° (*c* 0.35, $CHCl_3$); IR (KBr) 1770 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.34 (d, 3 H, *J* = 7.6 Hz, H-9), 1.93 (d, 1 H, *J* = 5.3 Hz, OH), 2.23 (m, 2 H, H-1, H-2), 2.33 (d, 1 H, *J* = 2.0 Hz, OH), 3.05 (m, 1 H, H-8), 3.52 (m, 2 H, H-3, H-6), 4.19 (bdd, 1 H, *J* = 5.3, 5.7 Hz, H-3′); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 15.90 (q, C-9), 19.09 (t, C-5), 25.88 and 25.91 (2 t, C-6′, C-8′), 26.47 (t, C-7′), 28.21 and 28.79 (2 t, C-5′, C-9′), 29.70 (t, C-4), 37.68 (d, C-2), 41.77 (d, C-1), 44.36 (d, C-4′), 53.85 (d, C-6), 60.69 (d, C-8), 67.32 (d, C-3′), 70.66 (d, C-3), 84.14 (s, C-2′), 85.31 (s, C-1′), 211.93 (s, C-7); MS *m/z* 290 (M^+). Anal. Calcd for $C_{18}H_{26}O_3$: C, 74.45; H, 9.02. Found: C, 74.73; H, 9.34.

(3′*S*,1*R*,2*R*,3*S*,6*R*)-2-(3′-Hydroxy-3′-cyclohexylprop-1′-ynyl)-3-hydroxy-8-*exo*-methylbicylo[4.2.0]octane-7-one (27). Replacing **16** with **19** as above gave **27** (86%) as a gum: $[\alpha]^{25}_D$ −25.7° (*c* 0.43, $CHCl_3$); IR (neat) 1770 cm^{-1} (C=O); ^{1}H NMR ($CDCl_3$, 300 MHz), δ 1.34 (d, 3 H, *J* = 7.6 Hz, H-9), 2.23 (m, 2 H, H-1, H-2), 3.04 (m, 1 H, H-8), 3.52 (m, 2 H, H-3, H-6), 4.20 (bd, 1 H, *J* = 5.7 Hz, H-3′); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 15.89 (q, C-9), 19.08 (t, C-5), 25.91 (t, C-6′, C-8′), 26.48 (t, C-7′), 28.20 and 28.77 (2 t, C-5′, C-9′), 29.71 (t, C-4), 37.69 (d, C-2), 41.75 (d, C-1), 44.36 (d, C-4′), 53.83 (d, C-6), 60.70 (d, C-8), 67.30 (d, C-3′), 70.69 (d, C-3), 84.11 (s, C-2′), 85.33 (s, C-1′), 211.94 (s, C-7); HRMS calcd for $C_{18}H_{26}O_3$ *m/z* 290.188195, found 290.188002.

(*Z*)-(3′*S*,1*S*,2*S*,3*R*,6*S*)-4-[2-(3′-Hydroxy-3′-cyclohexylprop-1′ynyl)-3-hydroxy-8-*endo*-methylbicyclo[4.2.0]oct-7-ylidene]-butanoic Acid (30) and (*E*)-(3′*S*,1*S*,2*S*,3*R*,6*S*)-4-[2-(3′-Hydroxy-3′-cyclohexylprop-1′-ynyl)-3-hydroxy-8-*endo*-methylbicyclo[4.2.0]oct-7-ylidene]butanoic Acid (31). A stock solution of dimsyl sodium was prepared by dissolving NaH (0.6 g of 50% dispersion in mineral oil; 12.5 mmol) in DMSO (10 mL) at 65 °C under nitrogen. To a stirred slurry of (3-carboxypropyl)-triphenylphosphonium bromide (1.13 g, 2.6 mmol) in DMSO (5 mL) under nitrogen was added the above stock solution (4.0 mL, 5.0 mmol). After 20 min at 23 °C, a solution of **24** (180 mg, 0.62 mmol) in DMSO (1 mL) was added in one portion. After 4 h at 23 °C the mixture was poured into 5% Na_2CO_3 solution (15 mL), washed with ethyl acetate (2 × 30 mL), and then acidified with concd HCl. The aqueous layer was extracted with ether (3 × 50 mL) and the combined extract was concentrated to 20 mL and kept at −20 °C for 2 h. The resulting precipitate was filtered off and discarded. Evaporation of the filtrate gave an oil (300 mg) which was purified by silica gel flash chromatography eluting with AcOH/EtOAc/hexane (0.25:75:25) to give an oil (230 mg). Further purification by flash chromatography eluting with AcOH/methanol/dichloromethane (0.2:5.3:94.5) gave **30** and **31**.

First eluted was **31** (73 mg, 32.6%): $[\alpha]^{25}_D$ +101.5° (*c* 0.41, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.29 (d, 3 H, *J* = 7 Hz, 8α*Me*), 2.30* (1 H, H-1β), 2.40* (2 H, =CHCH_2), 2.75 (m, 1 H, H-6), 3.12 (m, 1 H, H-8), 3.39 (ddd, 1 H, *J* = 3.6, 6 Hz, H-3), 4.16 (dd, 1 H, *J* = 2, 6 Hz, H-3′), 4.99 (m, 1 H, =C*H*) (*obscured by other resonances); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.25 (q, C-9), 22.19 (t, C-5), 22.94 (t, CH_2CH=), 25.92 (t, C-6′ or C-8′), 25.98 (t, C-6′ or C-8′), 26.53 (t, C-7′), 28.07 (t, C-5′ or C-9′), 28.78 (t, C-5′ or C-9′), 28.84 (t, C-4), 35.01 (t, *C*H_2COO), 36.45 (d, C-2), 39.21 (d, C-6), 41.42 (d, C-1), 41.75 (d, C-8), 44.21 (d, C-4′), 67.32 (d, C-3′), 71.91 (d, C-3), 82.51 (s, C-1′), 87.81 (s, C-2′), 116.06 (d, =CH), 145.51 (s, C-7), 177.10 (s, COOH); MS *m/z* 342 (M^+ − H_2O). Anal. Calcd for $C_{22}H_{32}O_4$·0.5H_2O: C, 71.51; H, 9.00. Found: C 71.49; H, 9.12.

The second eluted was **30** (36 mg, 16%): mp 46–51 °C; $[\alpha]^{25}_D$ +103.1° (*c* 0.37, $CHCl_3$); ^{1}H NMR ($CDCl_3$, 300 MHz) δ 1.04 (d, 3 H, *J* = 6.9 Hz, 8α*Me*), 2.35* (3 H, =CHCH_2, H-1), 2.91 (m, 1 H, H-8), 3.01 (m, 1 H, H-6), 3.45 (ddd, 1 H, J = 3, 6, 6 Hz, H-3), 4.15 (dd, 1 H, *J* = 2, 6 Hz, H-3′), 5.05 (m, 1 H, =C*H*); ^{13}C NMR ($CDCl_3$, 75.5MHz) δ 11.92 (q, C-9), 22.84 (t, C-5), 23.77 (t, CH_2-CH=), 25.94 (t, C-6′, C-8′), 25.97 (t, C-7′), 28.11 (t, C-5′ or C-9′), 28.80 (t, C-5′ or C-9′), 29.84 (t, C-4), 34.63 (t, *C*H_2COO), 36.38 (d, C-2), 39.70 (d, C-6), 40.61 (d, C-1), 40.96 (d, C-8), 44.37 (d, C-4′), 67.30 (d, C-3′), 71.93 (d, C-3), 82.84 (s, C-1′), 87.35 (s, C-2′), 116.47 (d, CH=), 146.56 (s, C-7), 176.78 (s, COOH); MS *m/z* 342 (M^+ − H_2O). Anal. Calcd for $C_{22}H_{32}O_4$: C, 73.30; H, 8.95. Found: C 73.30; H, 9.16.

(*Z*)-(3′*S*,1*S*,2*S*,3*R*,6*S*)-4-[2-(3′-Hydroxy-3′-cyclohexylprop-1′ynyl)-3-hydroxy-8-*endo*-methylbicyclo[4.2.0]oct-7-ylidene]-pentanoic Acid (34) and (*E*)-(3′*S*,1*S*,2*S*,3*R*,6*S*)-4-[2-(3′-Hydroxy-3′-cyclohexylprop-1′-ynyl)-3-hydroxy-8-*endo*-methylbicyclo[4.2.0]oct-7-ylidene]pentanoic Acid (35). Prepared from **29** as above; first eluted was **35** (24.4%): mp 36–41 °C; $[\alpha]^{25}_D$ +82.9° (*c* 0.27, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.25 (d, 3 H, *J* = 7.7 Hz, H-8αMe), 1.53 (m, 1 H, H-4′), 2.10 (m, 2 H, =CHC*H*$_2$), 2.36 (t, 2 H, *J* = 7.1 Hz, C*H*$_2$COOH), 2.38 (m, 1 H, H-2), 2.67 (nm, 1 H, H-6), 3.15 (bdq, 1 H, *J* = 6.6, 7.0 Hz, H-6), 3.39 (ddd, 1 H, *J* = 1.5, 9.3, 9.3 Hz, H-3), 4.15 (dd, 1 H, *J* = 1.8, 6.0 Hz, H-3′), 5.01 (bt, 1 H, *J* = 7.8 Hz, =C*H*); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.55 (q, C-9), 22.15 (t, C-5), 25.32 (t, $CH_2CH_2CH_2$), 25.88 (t, C-6′ or C-8′), 26.47 (t, C-7′), 26.52 (t, CH_2CH=), 28.09 (t, C-5′ or C-9′), 28.76 (t, C-5′ or C-9′), 28.94 (t, C-4), 33.35 (t, CH_2COO), 36.67 (d, C-2), 38.99 (d, C-6), 41.13 (d, C-8), 41.39 (d, C-1), 44.29 (d, C-4′), 64.26 (d, C-3′), 71.73 (d, C-3), 82.98 (s, C-1′), 87.38 (s, C-2′), 117.21 (d, =CH), 145.30 (s, C-7), 178.27 (s, COOH); MS *m*/*z* 356 ($M^+ - H_2O$). Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.50. Found: C, 73.87; H, 9.42.

The second eluted was **34** (29.1%): mp 31–38 °C; $[\alpha]^{25}_D$ +107.6° (*c* 0.25, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.05 (d, 3 H, *J* = 6.8 Hz, H-8αMe), 1.54 (m, 1 H, H-4′), 2.08 (m, 2 H, C*H*CH=), 2.35 (m, 2 H, C*H*$_2$COOH), 2.35 (m, 1H, H-2), 2.92 (bdq, 1 H, *J* = 6.6, 6.8 Hz, H-8), 3.01 (nm, 1H, H-6), 3.40 (ddd, 1 H, *J* = 3.6, 9.4, 9.4 Hz, H-3), 4.14 (dd ,1 H, *J* = 1.9, 4.6 Hz, H-3′), 5.03 (bt, 1 H, *J* = 7.2 Hz, C*H*=); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 11.95 (q, C-9), 23.84 (t, C-5), 25.21 (t, $CH_2CH_2CH_2$), 25.93 (t, C-6′ or C-8′), 25.95 (t, C-6′ or C-8′), 26.40 (t, C*H*$_2$CH=), 26.51 (t, C-7′), 28.12 (t, C-5′ or C-9′), 28.77 (t, C-5′ or C-9′), 29.94 (t, C-4), 33.29 (t, C*H*$_2$COOH), 36.38 (d, C-2), 39.63 (d, C-8), 40.65 (d, C-1), 40.92 (d, C-6), 44.38 (d, C-4′), 67.31(d, C-3′), 71.91 (d, C-3), 82.90 (s, C-1′), 87.31 (s, C-2′), 117.34 (d, CH=), 146.07 (s, C-7), 178.41 (s, COOH); MS *m*/*z* 356 ($M^+ - H_2O$). Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C,73.71; H, 9.16.

Replacing **24** with **25** as above gave **(*Z*)-(3′*S*,1*R*,2*R*,3*S*,6*R*)-4-[2-(3′-hydroxy-3′-cyclohexylprop-1′-ynyl)-3-hydroxy-8-*endo*-methylbicyclo[4.2.0]oct-7-ylidene]butanoic Acid (38)** (15.1%): mp 50–56 °C; $[\alpha]^{25}_D$ −106.9° (*c* 0.12, $CHCl_3$); ^1H and ^{13}C NMR are identical to **30**; MS *m*/*z* 342 ($M^+ - H_2O$); HRMS exact mass calcd for ($M^+ - H_2O$) 342.219496, found 342.218989. Anal. Calcd for $C_{22}H_{32}O_4 \cdot 0.6H_2O$: C, 71.17; H, 9.01. Found: C, 71.03; H, 9.08.

(*E*)-(3′*S*,1*R*,2*R*,3*S*,6*R*)-4-[2-(3′-Hydroxy-3′-cyclohexylprop-1′-ynyl)-3-hydroxy-8-*endo*-methylbicyclo[4.2.0]oct-7-ylidene]-butanoic acid (39) (31%): gum; $[\alpha]^{25}_D$ −93.8° (*c* 0.37, $CHCl_3$); ^1H and ^{13}C NMR are identical to **31**; MS *m*/*z* 342 ($M^+ - H_2O$). Anal. Calcd for $C_{22}H_{32}O_4 \cdot 1.75H_2O$: C, 67.40; H, 9.13. Found: C, 67.01; H, 8.87.

(*Z*)-(3′*S*,1*R*,2*R*,3*S*,6*R*)-4-[2-(3′-Hydroxy-3′-cyclohexylprop-1′-ynyl)-3-hydroxy-8-*endo*-methylbicyclo[4.2.0]oct-7-ylidene]-pentanoic acid (42) (31%): gum; $[\alpha]^{25}_D$ −90.8° (*c* 0.19; $CHCl_3$); ^1H and ^{13}C NMR are identical to **34**; MS *m*/*z* 356 ($M^+ - H_2O$). Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 73.83; H, 9.18.

(*E*)-(3′*S*,1*R*,2*R*,3*S*,6*R*)-4-[2-(3′-Hydroxy-3′-cyclohexylprop-1′-ynyl)-3-hydroxy-8-*endo*-methylbicyclo[4.2.0]oct-7-ylidene]-pentanoic acid (43) (24%): $[\alpha]^{25}_D$ −71.9° (*c* 0.42, $CHCl_3$); ^1H and ^{13}C NMR are identical to **35**; MS *m*/*z* 356 ($M^+ - H_2O$); HRMS exact mass calcd for $C_{23}H_{34}O_4$ 374.245711, found 374.243208. Anal. Calcd for $C_{23}H_{34}O_4 \cdot 0.1H_2O$: C, 73.41; H, 9.16. Found: C, 73.03, H, 9.51.

(*Z*)-(3′*S*,1*S*,2*R*,3*S*,6*S*)-4-[2-(3′-Hydroxy-3′-cyclohexylprop-1′-ynyl)-3-hydroxy-6-methoxy-8-*endo*-methylbicyclo[4.2.0]-oct-7-ylidene]butanoic Acid (49). Replacing **28** with **47** or **48**, following the procedure for **30** and **31**, and performing the reaction at 60 °C instead of room temperature gave **49** (27.4%): foam; $[\alpha]^{25}_D$ +15° (*c* 0.27, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.14 (d, 3 H, *J* = 6.7 Hz, 8αMe), 2.27 (dd, 1H, *J* = 7.2, 6.8 Hz, H-1), 2.3–2.5 (bm, 4 H, =CHC*H*$_2$C*H*$_2$COOH), 2.48* (1 H, H-8), 2.56 (ddd, 1 H, *J* = 7.2, 7.2, 1.5 Hz, H-2), 3.25 (s, 3 H, C6-OMe), 3.89 (ddd, 1 H, *J* = 7.2, 5.5, 5.3 Hz, H-3), 4.15 (dd, 1H, *J* = 5.9, 1.5 Hz, H-3′), 5.23 (bt, 1 H, *J* = 6.0 Hz, =C*H*) (*obscured by other resonances); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 17.68 (q, 8αMe), 23.05 (t, C-5), 25.60 (t, =CHCH$_2$), 25.90 (t, C-6′), 26.44 (t, C-7′), 28.66 (t, C-4), 34.23 (t, C*H*$_2$COOH), 35.71 (d, C-2), 36.88 (d, C-8), 44.27 (d, C-4′), 45.14 (d, C-1), 50.89 (q, OMe), 67.25 (d, C-3′), 69.11 (d, C-3), 81.13 (s, C-6), 82.77 (s, C-2′), 86.57 (s, C-1′), 119.01 (d, =CH), 147.05 (s, C-7), 177.61 (s, COOH); MS *m*/*z* 372 ($M^+ - H_2O$); HRMS exact mass calcd for ($M^+ - H_2O$) 372.230061, found 372.227861.

(*Z*)-(3′*S*,1*S*,2*R*,3*S*,6*S*)-4-[2-(3′-Hydroxy-3′-cyclohexylprop-1′-ynyl)-3-hydroxy-6-methyl-8-*exo*-methylbicyclo[4.2.0]oct-7-ylidene]butanoic Acid (52), (*E*)-(3′*S*,1*S*,2*R*,3*S*,6*S*)-4-[2-(3′-Hydroxy-3′-cylohexylprop-1′-ynyl)-3-hydroxy-6-methyl-8-*exo*-methylbicyclo[4.2.0]oct-7-ylidene]butanoic Acid (54), (*Z*)-(3′*S*,1*S*,2*R*,3*S*,6*S*)-4-[2-(3′-Hydroxy-3′-cyclohexylprop-1′-ynyl)-3-hydroxy-6-methyl-8-*endo*-methylbicyclo[4.2.0]oct-7-ylidene]butanoic Acid (53), and (*E*)-(3′*S*,1*S*,2*R*,3*S*,6*S*)-4-[2-(3′-Hydroxy-3′-cyclohexylprop-1′-ynyl)-3-hydroxy-6-methyl-8-*endo*-methylbicyclo[4.2.0]oct-7-ylidene]butanoic Acid (55). Replacing **28** with **51** (900 mg scale) and performing the reaction at 55 °C instead of room temperature, following the procedure of **30** gave **52–55**. HPLC purification eluting with 8% 2-propanol in hexane with 0.1% H_2O gave, in order of elution:

55: an oil (7 mg, 0.6%); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.17 (s, 3 H, C-6 Me), 1.28 (d, 3 H, *J* = 7.1 Hz, C-8 Me), 1.53 (m, 1 H, H-4′), 1.99 (dd, 1 H, *J* = 10.1, 7.9 Hz, H-1), 2.1–2.5 (m, 4 H, =CHC*H*$_2$CH$_2$COOH), 2.39 (ddd, 1 H, H-2), 3.43* (2 H, H-8, H-3), 4.23 (dd, 1 H, *J* = 6.0, 1.8 Hz, H-3′), 5.00 (m, 1 H, =C*H*); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 13.55 (q, C-8 Me), 23.18 (t, C-5), 25.91 (t, C-6′, C-8′), 26.48 (t, C-7′), 28.14, 28.71 (2 t, C-5′, C-9′), 28.71 (q, C-6 Me), 29.36 (t, C-4), 31.14 (t, =CHC*H*$_2$), 34.83 (t, C*H*$_2$-COOH), 36.75 (d, C-2), 39.05 (d, C-8), 43.21 (s, C-6), 44.26 (d, C-4′), 47.16 (d, C-1), 67.19 (d, C-3′), 71.50 (d, C-3), 82.67 (s, C-1′), 87.87 (s, C-2′), 116.42 (d, =CH), 149.96 (s, C-7), 175.63 (s, COOH); MS *m*/*z* 374 (M^+); HRMS exact mass calcd 374.24511, found 374.245422.

54: an oil (19 mg, 1.7%); $[\alpha]^{25}_D$ −67.3° (*c* 0.37, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.17 (s, 3 H, C-6 Me), 1.31 (d, 3 H, *J* = 7.2 Hz, C-8 Me), 1.52 (m, 1 H, C-4′), 1.58 (dd, 1 H, *J* = 8.5, 4.8 Hz, H-1), 2.30 (m, 4 H, =CHC*H*$_2$C*H*$_2$), 2.43 (ddd, 1 H, *J* = 8.5, 8.5, 1.6 Hz, H-2), 2.84 (dq, 1 H, H-8), 3.68 (m, 1 H, H-3), 4.18 (dd, 1 H, *J* = 5.8, 1.6 Hz, H-3′), 5.11 (bt, 1 H, *J* = 6.2 Hz, =CH); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 20.26 (q, C-8 Me), 23.11 (t, C-5), 25.92 (t, C-6′, C-8′), 26.47 (t, C-7′), 27.19 (q, C-6 Me), 27.88 (t, =CHC*H*$_2$), 28.08, 28.72 (t, C-5′, C-9′), 30.40 (t, C-4), 34.45 (t, C*H*$_2$COOH), 39.45 (d, C-2), 41.75 (d, C-8), 41.95 (s, C-6), 44.27 (d, C-4′), 49.86 (d, C-1), 67.27 (d, C-3′), 70.32 (d, C-3), 82.44 (s, C-1′), 87.35 (s, C-2′), 117.33 (d, =CH), 153.09 (s, C-7), 177.45 (s, COOH); MS *m*/*z* 356 ($M^+ - H_2O$); HRMS exact mass calcd for $C_{23}H_{34}O_4$ 374.245697, found 374.244324.

53 (79 mg, 7.1%): an oil; $[\alpha]^{25}_D$ −62.6° (*c* 0.30, $CHCl_3$); ^1H NMR ($CDCl_3$ 300 MHz) δ 1.08 (d, 3 H, *J* = 6.9 Hz, C-8Me), 1.26 (s, 3 H, C-6Me), 1.52 (m, 1 H, H-4′), 1.91 (dd, 1 H, *J* = 10.9, 8.4 Hz, H-1), 2.35 (m, 4 H, =CHC*H*$_2$C*H*$_2$), 2.37 (ddd, 1 H, *J* = 10.9, 10.9, 1.7 Hz, H-2), 3.19 (dq, 1 H, *J* = 6.9, 8.4 Hz, H-8), 3.56 (m, 1 H, H-3), 4.16 (dd, 1 H, *J* = 6.0, 1.7 Hz, H-3′), 5.01 (dt, 1 H, *J* = 7.2, 2.3 Hz, =CH); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 12.44 (q, C-8 Me), 23.03 (t, C-5), 25.92 (t, C-6′), 26.47 (t, C-7′), 27.18 (q, C-6 Me), 28.14, 28.71 (t, C-5′, C-9′), 29.31 (t, C-4), 31.30 (t, =CHCH2), 34.65 (t, C*H*$_2$COOH), 36.05 (d, C-2), 37.02 (d, C-8), 44.31 (d, C-4′), 45.26 (s, C-6), 46.05 (d, C-1), 67.26 (d, C-3′), 71.60 (d, C-3), 82.79 (s, C-1′), 87.57 (s, C-2′), 117.02 (d, =CH), 151.37 (s, C-7), 176.97 (s, COOH); MS *m*/*z* 374 (M^+); HRMS calcd for $C_{23}H_{34}O_4$ 374.245711, found 374.245026. Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 73.88; H, 9.35.

52 (512 mg, 46.3%): an oil; $[\alpha]^{25}_D$ −30.9° (*c* 0.57, $CHCl_3$); ^1H NMR ($CDCl_3$, 300 MHz) δ 1.16 (d, 3 H, *J* = 7.0 Hz, C-8 Me), 1.28 (s, 3 H, C-6 Me), 1.52 (dd, 1 H, *J* = 8.3, 5.5 Hz, H-1), 1.53 (m, 1 H, H-4′), 2.51 (ddd, 1 H, *J* = 8.3, 8.3, 1.9 Hz, H-2), 2.69 (dq, 1 H, *J* = 7.0, 5.5 Hz, H-8), 3.80 (m, 1 H, H-3), 4.16 (dd, *J* = 5.9, 1.9 Hz, H-3′), 5.02 (dt, 1 H, *J* = 6.9, 2.1 Hz, =CH); ^{13}C NMR ($CDCl_3$, 75.5 MHz) δ 19.71 (q, C-8Me), 23.52 (t, C-5), 25.88 (t, C-6′), 26.18 (q, C-6Me), 26.46 (t, C-7′), 26.74 (t, =CHC*H*$_2$), 28.06, 28.72 (t, C-5′, C-9′), 28.46 (t, C-4), 34.68 (t, C*H*$_2$COOH), 37.84 (d, C-2), 40.57 (C-8), 42.97 (s, C-6), 44.34 (d, C-4′), 49.64 (d, C-1), 67.28 (d, C-3′), 69.40 (dq, C-3), 82.58 (s, C-1′), 87.12 (s, C-2′), 117.95 (d, =CH), 153.42 (s, C-7), 177.14 (s, COOH); HRMS exact mass calcd for $C_{23}H_{34}O_4$ 374.245697, found 374.244690. Anal. Calcd for $C_{23}H_{34}O_4$: C, 73.76; H, 9.15. Found: C, 74.05; H, 9.26.