Synthesis of Tricyclic β-Methylene Spiro Lactones Related to Bakkenolides by Successive Radical Cyclization−High Pressure Diels−Alder Reactions

Thomas G. Back,* Patricia L. Gladstone, and Masood Parvez

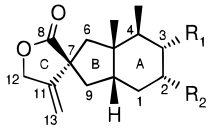
Department of Chemistry, University of Calgary, Calgary, Alberta, Canada T2N 1N4

Received January 17, 1996[⊗]

The synthesis of some novel bakkenolides and their epi-spiro analogues was achieved by a new approach. Photolysis of allyl 1-(phenylseleno)-2-oxocyclopentanecarboxylates **7**-**9** afforded the corresponding spiro lactones **10**-**12** by radical cyclization via group transfer of the phenylseleno group. Selenoxide elimination of **11** and **12** produced the corresponding β-methylene lactones **14** and **15**. Diels−Alder cycloaddition of lactone **11** with piperylene failed at ambient pressure, but proceeded in generally good yield in the presence of various Lewis acids at pressures of ca. 16 kbar, to give mixtures of β-exo, α-endo, and β-endo cycloadducts **19**, **21**, and **23**, respectively. The preponderance of endo products **21** and **23**, formed via highly hindered, but more compact, transition states was attributed to the high pressure and resulted in *trans*-dimethyl configurations of the products. The facial selectivity was dependent upon the Lewis acids, and the greatest α:β ratio was observed with catalysts of the type $TiCl_2(OR)_2$. Epimerization of the C-4 methyl group in **21** and **23** to furnish the corresponding *cis*-dimethyl analogues was achieved via exo-epoxidation, regioselective reduction, oxidation to the corresponding 3-keto derivatives, and base-catalyzed equilibration, thereby affording (±)-3,6-dioxobakkenolide-A (**39**) and its epi-spiro derivative **28**, respectively. When the radical cyclization step was performed subsequent to the Diels−Alder cycloaddition by photolysis of perhydrindane **43**, only the epi-spiro product **44** was obtained.

The bakkenolides (fukinanolides) comprise a relatively rare class of naturally-occurring β-methylene spiro lactones that are thought to be biogenetically related to the eremophilanolides.[1] Bakkenolide-A (**1**) was first isolated from the buds of *Petasites japonicus*[1b] while homogynolides-A (**2**) and -B (**3**) were obtained from extracts of the plant *Homogyne alpina*.[1c] Some members of the bakkenolide family have been reported to display antitumor activity[2] and to act as insect antifeedants.[3] Their biological activity and unusual architecture have prompted several recent synthetic approaches to **1**-**3**[4] and to related analogues.[5]

We wish to report the synthesis of several tricyclic β-methylene spiro lactones related to the bakkenolides and their epi-spiro counterparts by means of tandem radical cyclizations to generate the spiro lactone moiety, and high pressure Diels−Alder reactions for annulation of the A-ring. Our general approach by this route is shown retrosynthetically in Scheme 1.



1 Bakkenolide A; $R_1 = R_2 = H$

2 Homogynolide A; $R_1 = H$; R_2 =

3 Homogynolide B; R_1 =

; $R_2 = H$

Results and Discussion

Radical cyclizations are proving increasingly useful in organic synthesis.[6] Recently, Curran[7] and Byers[8] have independently shown that radicals derived from the homolytic cleavage of α-seleno active methylene compounds undergo group transfer additions to unsaturated substrates. Scheme 2 illustrates an intramolecular

[⊗] Abstract published in *Advance ACS Abstracts,* May 1, 1996.

(1) (a) For a review, see: Fischer, N. H.; Olivier, E. J.; Fischer, H. D. In *Progress in the Chemistry of Organic Natural Products*; Herz, W.; Grisebach, H.; Kirby, G. W., Eds.; Springer-Verlag: Wien, 1979; Volume 38, pp 257−264. (b) Abe, N.; Onoda, R.; Shirahata, K.; Kato, T.; Woods, M.C.; Kitahara, Y. *Tetrahedron Lett.* **1968**, 369. (c) Harmatha, J.; Samek, Z.; Synáčková, M.; Novotný, L.; Herout, V.; Šorm, F.; *Collect. Czech. Chem. Commun.* **1976**, *41*, 2047.

(2) (a) Jamieson, G. R.; Reid, E. H.; Turner, B. P.; Jamieson, A. T. *Phytochem.* **1976**, *15*, 1713. (b) Kano, K.; Hayashi, K.; Mitsuhashi, H. *Chem. Pharm. Bull.* **1982**, *30*, 1198.

(3) Nawrot, J.; Bloszyk, E.; Harmatha, J.; Novotný, L.; Drozdz, B. *Acta Entomol. Bohemoslov.* **1986**, *83*, 327; via *Chem. Abstr.* **1987**, *106*, 48926r.

(4) Bakkenolide-A: (a) Srikrishna, A.; Reddy, T. J.; Nagaraju, S.; Sattigeri, J. A. *Tetrahedron Lett.* **1994**, *35*, 7841. (b) Greene, A. E.; Coelho, F.; Deprés, J.-P.; Brocksom, T. J. *Tetrahedron Lett.* **1988**, *29*, 5661. (c) Greene, A. E.; Deprés, J.-P.; Coelho, F.; Brocksom, T. J. *J. Org. Chem.* **1985**, *50*, 3943. (d) Evans, D. A.; Sims, C. L.; Andrews, G. C. *J. Am. Chem. Soc.* **1977**, *99*, 5453. (e) Hayashi, K.; Nakamura, H.; Mitsuhashi, H. *Chem. Pharm. Bull.* **1973**, *21*, 2806. Homogynolide-A: (f) Mori, K.; Matsushima, Y. *Synthesis* **1995**, 845. (g) Hartmann, B.; Kanazawa, A. M.; Deprés, J.-P.; Greene, A. E. *Tetrahedron Lett.* **1993**, *34*, 3875. (h) Hartmann, B.; Kanazawa, A. M.; Deprés, J.-P.; Greene, A. E. *Tetrahedron Lett.* **1991**, *32*, 767. Homogynolide-B: (i) Srikrishna, A.; Nagaraju, S.; Venkateswarlu, S. *Tetrahedron Lett.* **1994**, *35*, 429. (j) Coelho, F.; Deprés, J.-P.; Brocksom, T. J.; Greene, A. E. *Tetrahedron Lett.* **1989**, *30*, 565.

(5) (a) Srikrishna, A.; Viswajanani, R.; Sattigeri, J. A. *J. Chem. Soc., Chem. Commun.* **1995**, 469. (b) Srikrishna, A.; Nagaraju, S.; Sharma, G. V. R. *J. Chem. Soc., Chem. Commun.* **1993**, 285. (c) Hartmann, B.; Deprés, J.-P.; Greene, A. E. *Tetrahedron Lett.* **1993**, *34*, 1487.

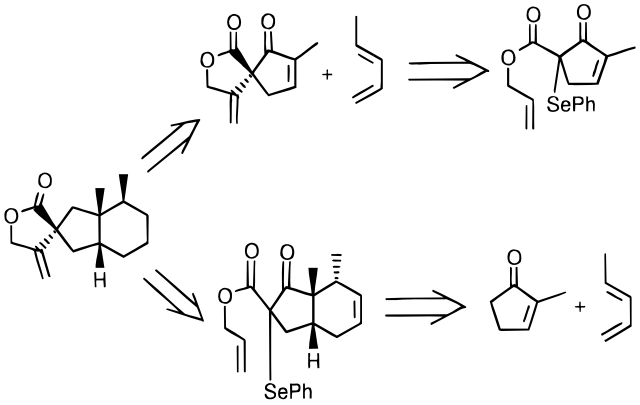
(6) For reviews of radical cyclizations, see: (a) Giese, B. *Radicals in Organic Synthesis: Formation of Carbon-Carbon Bonds*; Pergamon Press: Oxford, 1986. (b) Jasperse, C. P.; Curran, D. P.; Fevig, T. L. *Chem. Rev.* **1991**, *91*, 1237. (c) Curran, D. P. *Synthesis* **1988**, 417 and *Ibid.* 489. (d) Ramaiah, M. *Tetrahedron* **1987**, *43*, 3541. (e) Hart, D. J. *Science* **1984**, *223*, 883.

(7) (a) Curran, D. P.; Eichenberger, E.; Collis, M.; Roepel, M. G.; Thoma, G. *J. Am. Chem. Soc.* **1994**, *116*, 4279. (b) Curran, D. P.; Thoma, G. *J. Am. Chem. Soc.* **1992**, *114*, 4436.

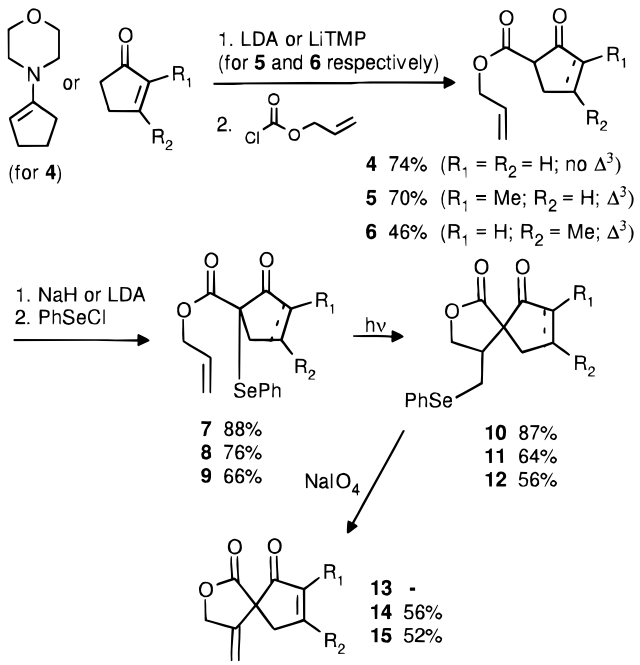
(8) (a) Byers, J. H.; Thissell, J. G.; Thomas, M. A. *Tetrahedron Lett.* **1995**, *36*, 6403. (b) Byers, J. H.; Lane, G. C. *J. Org. Chem.* **1993**, *58*, 3355. (c) Byers, J. H.; Harper, B. C. *Tetrahedron Lett.* **1992**, *33*, 6953. (d) Byers, H. J.; Gleason, T. G.; Knight, K. S. *J. Chem. Soc., Chem. Commun.* **1991**, 354. (e) Byers, J. H.; Lane, G. C. *Tetrahedron Lett.* **1990**, *31*, 5697.

S0022-3263(96)00111-9 CCC: $12.00

Scheme 1



Scheme 2



variation of this process, whereby the corresponding spiro lactone is obtained by photolysis of an appropriately substituted allyl α-phenylseleno-β-keto ester.[9,10] Moreover, the presence of the (phenylseleno)methyl group in the product permits the introduction of the exocyclic β-methylene moiety by means of a subsequent selenoxide elimination. Thus, the morpholine enamine of cyclopentanone, or the kinetic enolates of 2-methyl- or 3-methylcyclopent-2-enone, were acylated with allyl chloroformate to provide **4**-**6** and then selenenylated[11] with benzeneselenenyl chloride to afford **7**-**9**. Irradiation for several hours with UV light at 254 nm in benzene, or for ca. 1 h with a 275 Watt sunlamp, resulted in ring-closure to give spiro lactones **10**-**12**, formed as pairs of diastereomers in the ratio of >20:1, 5:1 and 10:1, respectively. Oxidation and selenoxide elimination of either the pure major diastereomers of **11** or **12**, or of the mixtures of isomers, then afforded the desired products **14** or **15**, respectively. Attempts to induce cyclization of allyl β-keto ester **4** with electrophilic selenium reagents,[12,13] and of its α-phenylseleno derivative **7** with Lewis acids,[14] to furnish lactone **10** were unsuccessful.

The Diels−Alder cycloaddition[15] of the enone moiety of spiro lactone **11** with piperylene was then investigated. The desired regiochemistry (vicinal methyl substituents) was expected on the basis of frontier MO considerations[16] and precedents.[17] Moreover, we anticipated that the orthogonal nature of the spiro ring system would favor the formation of the much less sterically congested exo transition states **16** and **18** (Scheme 3), which afford the required *cis*-dimethyl diastereomers **17** and **19**, respectively. Endo approach of the diene toward the α or β side of the enone moiety via transition states **20** and **22** is hindered by the phenylselenomethyl group (or the exocyclic methylene moiety if selenoxide elimination precedes cycloaddition) and the lactone carbonyl oxygen atom, respectively. An endo attack would produce the corresponding *trans*-dimethyl analogues **21** and **23**. Furthermore, the facial selectivity of the Diels−Alder reaction determines the configuration at the spiro center relative to the other stereocenters.[18] Attack via the α-face of the enone (transition states **16** and **20**) affords the same spiro configuration (products **17** and **21**) as found in the natural bakkenolides, whereas attack via the β-face (transition states **18** and **22**) leads to the epi-spiro series (products **19** and **23**). Although steric hindrance by the (phenylseleno)methyl substituent of the α-face appears to be greater than that by the lactone carbonyl group of the β-face, we expected that some control of the α:β ratio should be possible by inclusion of appropriate Lewis acid catalysts. In particular, bidentate oxophilic Lewis acids capable of coordinating with both the lactone and ketone carbonyl oxygen atoms should increase steric hindrance toward β-attack, thereby rendering approach from the α-side of the dienophile relatively more facile.

The attempted cycloaddition of the pure major diastereomer of **11** with piperylene failed to proceed even

(9) Preliminary communication: Back, T. G.; Gladstone, P. L. *Synlett* **1993**, 699.

(10) The term radical spirocyclization has recently been employed to describe the formation of other spiro structures by radical reactions: (a) Clive, D. L. J.; Tao, Y.; Khodabocus, A.; Wu, Y.-J.; Angoh, A. G.; Bennett, S. M.; Boddy, C. N.; Bordeleau, L.; Kellner, D.; Kleiner, G.; Middleton, D. S.; Nichols, C. J.; Richardson, S. R.; Vernon, P. G. *J. Am. Chem. Soc.* **1994**, *116*, 11275. (b) Clive, D. L. J.; Angoh, A. G.; Bennett, S. M. *J. Org. Chem.* **1987**, *52*, 1339.

(11) (a) Reich, H .J.; Renga, J. M.; Reich, I. L. *J. Org. Chem.* **1974**, *39*, 2133. (b) Reich, H. J.; Renga, J. M.; Reich, I. L. *J. Am. Chem. Soc.* **1975**, *97*, 5434.

(12) For reviews of cyclizations mediated by electrophilic selenium compounds, see: (a) Nicolaou, K. C.; Petasis, N. A.; Claremon, D. A. In *Organoselenium Chemistry*; Liotta, D., Ed.; Wiley: New York, 1987; Chapter 2. (b) Paulmier, C. In *Selenium Reagents and Intermediates in Organic Synthesis*; Pergamon Press: Oxford, 1986; Chapter 8. (c) Back, T. G. In *The Chemistry of Organic Selenium and Tellurium Compounds*; Patai, S., Ed.; Wiley: Chichester, 1987; Volume 2, Chapter 3.

(13) For examples of cyclizations of unsaturated β-dicarbonyl compounds with selenium electrophiles, see (a) Ley, S. V.; Murray, P. J.; Palmer, B. D. *Tetrahedron* **1985**, *41*, 4765. (b) Ley, S. V.; Lygo, B.; Molines, H. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2403. (c) Ley, S. V.; Murray, P. J. *J. Chem. Soc., Chem. Commun.* **1982**, 1252. (d) Ley, S. V.; Lygo, B.; Molines, H.; Morton, J. A. *J. Chem. Soc., Chem. Commun.* **1982**, 1251. (e) Jackson, W. P.; Ley, S. V.; Morton, J. A. *J. Chem. Soc., Chem. Commun.* **1980**, 1028. (f) Jackson, W. P.; Ley, S. V.; Whittle, A. J. *J. Chem. Soc., Chem. Commun.* **1980**, 1173. (g) Alderdice, M.; Weiler, L. *Can. J. Chem.* **1981**, *59*, 2239.

(14) Jackson, W. P.; Ley, S. V.; Morton, J. A. *Tetrahedron Lett.* **1981**, *22*, 1981.

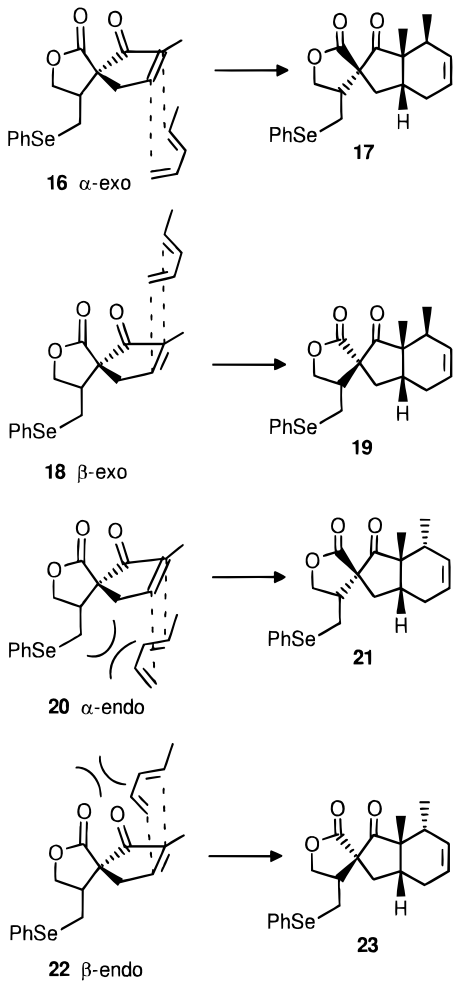
(15) For general reviews, see: (a) Carruthers, W. *Cycloaddition Reactions in Organic Synthesis*; Pergamon Press: Oxford, 1990. (b) Oppolzer, W. In *Comprehensive Organic Synthesis*, Trost, B. M., Ed.; Pergamon Press: Oxford, 1991; Volume 5, Chapter 4.1.

(16) Fleming, I. *Frontier Orbitals and Organic Chemical Reactions;* Wiley: Chichester, 1976; Chapter 4.

(17) For example, 2-methylcyclopent-2-enone reacts with piperylene to afford the vicinal dimethyl regioisomer with high selectivity: Fringuelli, F.; Pizzo, F.; Taticchi, A.; Halls, T. D. J.; Wenkert, E. *J. Org. Chem.* **1982**, *47*, 5056.

(18) For a review of the facial selectivity of Diels−Alder reactions, see: Fallis, A. G.; Lu, Y.-F. *Adv. Cycloaddit.* **1993**, *3*, 1.

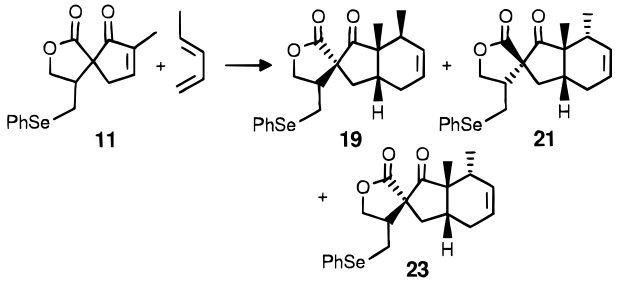
Scheme 3



after prolonged heating in benzene at 200 °C in a sealed tube. Similarly, catalysis of the reaction with a variety of Lewis acids[19] (ZnI_2, $TiCl_4$, $TiCl_2(O\text{-}i\text{-}Pr)_2$, $AlCl_3$, $SnCl_4$, $BF_3{\cdot}OEt_2$, etc.) failed to promote the reaction, as did the use of aqueous LiCl[20] or ethereal $LiClO_4$.[21] We then turned our efforts toward the use of high pressure. Since the Diels–Alder reaction is characterized by a negative volume of activation (ΔV^*), the application of pressure facilitates transformation of the reactants into the relatively more compact transition state, thereby lowering the activation energy of the process. Moreover, ΔV for the overall process is also negative, thus making the process thermodynamically, as well as kinetically, favorable.[22]

The results of the high pressure (ca. 16 kbar) experiments are shown in Table 1. The uncatalyzed reaction in entry 1 afforded 41% of recovered starting material, as well as two products identified as **19** and **23**. The same two products were obtained in a similar ratio, but in higher yield in the presence of ZnI_2 (entry 2). The

Table 1: Products of High Pressure Diels–Alder Reactions of 11 with Piperylene[a,b]



entry	catalyst (equiv)	combined yield, %	ratio of **19**:**21**:**23**
1[c]	none	34	40:0:60
2	ZnI_2 (1.41)	76	40:0:60
3	$AlCl_3$ (0.49)	83	61:6:33
4[d]	$MeAlCl_2$ (0.13)	49	61:8:31
5	$BF_3{-}OEt_2$ (0.55)	90	51:10:39
6	$Eu(fod)_3$ (0.20)	76	33:15:52
7[d,e]	$SnCl_4$ (0.55)	48	44:22:34
8	$TiCl_4$ (0.62)	82	46:28:26
9[f]	$TiCl_2(Oi\text{-}Pr)_2$ (0.61)	78	45:25:30
10	$TiCl_2$–TADDOL (87)	87	31:35:34

[a] Reactions were performed in CH_2Cl_2 at room temperature with excess diene for 1 or 2 days. [b] Pressures of 15.5–16.6 kbar were employed. [c] Unreacted **11** was recovered (41%). [d] Substantial polymerization of the diene was observed. [e] Unreacted **11** was recovered (12%). [f] Unreacted **11** was recovered (16%).

Lewis acids in entries 3–10 afforded a third cycloadduct **21** in addition to **19** and **23**. The fourth possible stereoisomer **17** was not produced in significant amounts in any of the cycloadditions in Table 1. Unequivocal evidence for the assigned structures of the products **19**, **21**, and **23** was obtained by their further transformations, and ultimately by X-ray crystallography of products derived from them (*vide infra*).

These results indicate that *β*-attack predominates in all of the examples studied, leading to the preferential formation of the epi-spiro products **19** and **23**. Cycloadduct **21**, the sole observed product of α-attack, was formed in greatest amounts when tin- or titanium-containing Lewis acids were employed, and it was the most abundant product in entry 10, with $TiCl_2$–TADDOL [i.e. $TiCl_2(OR)_2$ where $(OR)_2$ = (2*R*,3*R*)-2,3-*O*-(1-phenylethylidene)-1,1,4,4-tetraphenyl-1,2,3,4-butanetetrol] as the catalyst.[23] The relative extent of α vs *β* approach was therefore enhanced by the use of a relatively bulky, oxophilic, bidentate Lewis acid such as the latter, but even in that case *β*-attack was still the dominant pathway. A possible explanation for the preponderance of *β*-attack is that the phenylseleno group adopts the preferred conformation in **11a** that places it directly under the C=C bond of the enone moiety, thereby blocking the α-face of the dienophile. This could be the result of stabilizing interactions between the aromatic and enone *π*-systems, and because this relatively compact conformation is favored at high pressures. In order to circumvent this effect, attempts were made to employ the exocyclic olefin **14** instead of the selenide **11** in the high pressure Diels–Alder reactions. Unfortunately, **14** af-

(19) For a review of the enhancement of Diels–Alder reactions with Lewis acids and by other methods, see: Pindur, U.; Lutz, G.; Otto, C. *Chem. Rev.* **1993**, *93*, 741.

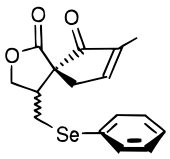
(20) Breslow, R. *Acc. Chem. Res.* **1991**, *24*, 159.

(21) Grieco, P. A.; Nunes, J. J.; Gaul, M. D. *J. Am. Chem. Soc.* **1990**, *112*, 4595.

(22) For reviews of high pressure Diels–Alder reactions, see: (a) Ibata, T. In *Organic Synthesis at High Pressures*, Matsumoto, K.; Acheson, R. M., Eds.; Wiley: New York, 1991; Chapter 9. (b) Jenner, G. In *Organic High Pressure Chemistry*; Le Noble, W. J., Ed.; Elsevier: Amsterdam, 1988; Chapter 6. (c) Jurczak, J. *Ibid.*, Chapter 11. (d) Van Eldik, R.; Asano, T.; Le Noble, W. J. *Chem. Rev.* **1989**, *89*, 549. (e) Matsumoto, K.; Sera, A. *Synthesis* **1985**, 999.

(23) Since the catalyst itself is homochiral in this example, it raises the possibility of enantioselective cycloaddition by kinetic resolution of the racemic dienophile. This is not the focus of the present work, however, and this aspect was not investigated further. For a review of Ti–TADDOL complexes and related compounds, see: Duthaler, R. O.; Hafner, A. *Chem. Rev.* **1992**, *92*, 807.

forded more complex product mixtures and considerably lower yields of the corresponding cycloadducts with a variety of Lewis acids, despite the less encumbered approach to the α-face.



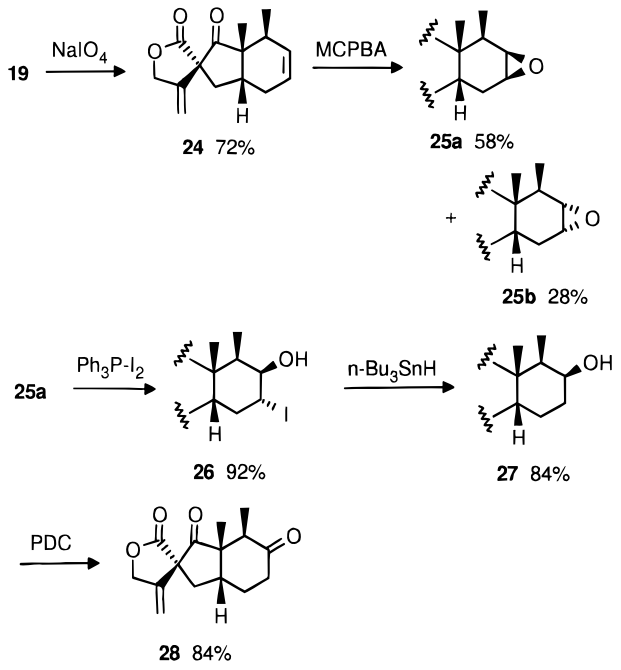
11a

It is also of interest to note that products **21** and **23** were produced via the highly crowded endo transition states **20** and **22**, respectively. Their combined yields are greater than that of the expected exo addition product **19** in all of the entries in the Table except 3−5. This too is attributed to the high pressures employed in these experiments, where steric effects are more easily overcome and the more compact endo transition states compete more favorably with their exo counterparts than at ambient pressures.[24]

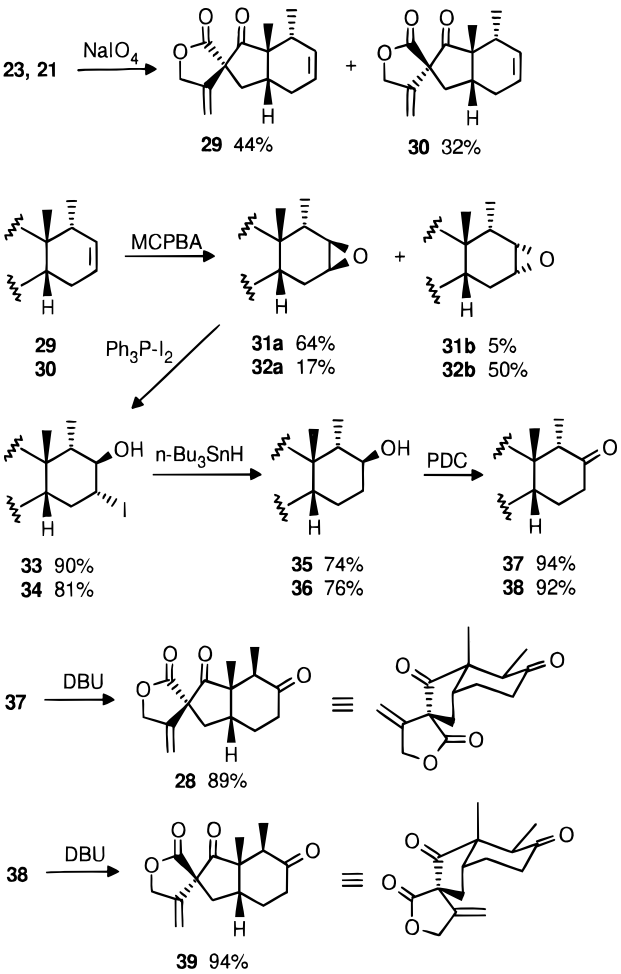
The *trans*-dimethyl orientation in products **21** and **23** requires an additional protocol for epimerizing the A-ring methyl substituent in order to obtain the *cis*-dimethyl configuration of the bakkenolides. The following further transformations of cycloadducts **19**, **21**, and **23** were therefore performed in order to establish their structures and, in the case of **21** and **23**, to epimerize the A-ring methyl group. Product **19** was easily separated from the other cycloadducts by chromatography, whereas **21** and **23** could not be separated from each other. The yields shown in Table 1 are therefore the combined isolated yields of products **19**, **21**, and **23**, and their indicated ratios were obtained by NMR integration. The separation of **21** and **23** was achieved at a later stage. Compound **19** was subjected to selenoxide elimination to afford diene **24**. Chemo- and stereoselective epoxidation of the cyclohexene double bond from the exo side produced the β-epoxide **25a** as the major product. Trans-diaxial opening[25] of the latter epoxide with triphenylphosphine−iodine[26,27] afforded the iodohydrin **26** with excellent regio- and stereoselectivity. Further conversion into the ketone **28** via **27** was achieved as shown in Scheme 4. The structure of **28** was unequivocally established by X-ray crystallography.[28]

The mixture of cycloadducts **21** and **23** was subjected to selenoxide elimination to afford the more easily separated dienes **30** and **29**, respectively (Scheme 5).

Scheme 4



Scheme 5



Compound **29** was then subjected to the same protocol as diene **24** to provide ketone **37** as shown in Scheme 5. Finally, treatment of **37** with DBU resulted in the epimerization of the A-ring methyl group from the axial to the equatorial position to afford the *cis*-dimethyl isomer **28**, identical in all respects to that produced via

(24) In several other examples studied, increased pressure also enhanced the amount of endo vs exo addition, although to a relatively small degree. Seguchi, K.; Sera, A.; Maruyama, K. *Tetrahedron Lett.* **1973**, 1585.

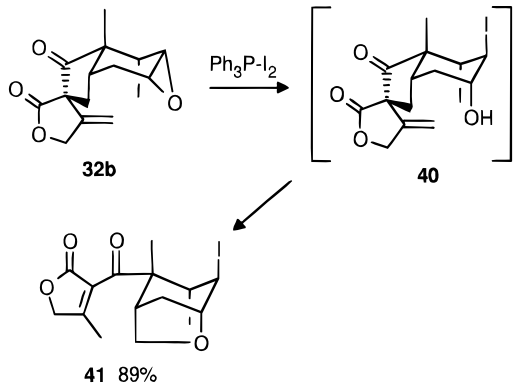
(25) (a) The opening of cyclohexene epoxides is subject to the Fürst-Plattner rule: Fürst, A.; Plattner, P. A. *Abstracts of Papers of the 12th International Congress of Pure and Applied Chemistry* 1951, IUPAC: New York, p 409; via Eliel, E. L.; Wilen, S. H.; Mander, L. N. *Stereochemistry of Organic Compounds*; Wiley: New York, 1994; p 730. (b) For a discussion of the stereoelectronic effects underlying the Fürst−Plattner rule, see Deslongchamps, P. In *Stereoelectronic Effects in Organic Chemistry*; Pergamon Press: Oxford, 1983; Chapter 5.

(26) Palumbo, G.; Ferreri, C.; Caputo, R. *Tetrahedron Lett.* **1983**, *24*, 1307.

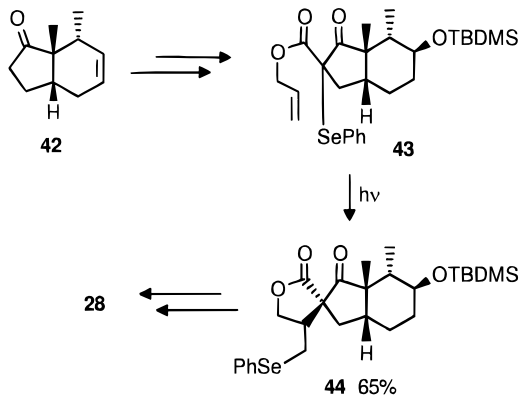
(27) Other attempts to reduce the epoxide with hydride reducing agents, or with Se or Te nucleophiles, followed by reductive deselenization/detellurization, proved less effective.

(28) The authors have deposited atomic coordinates for structures **28** and **39** 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, U.K.

Scheme 6



Scheme 7



Scheme 4 and identified by X-ray crystallography. The greater stability of the *cis*-dimethyl isomer **28** vs its *trans*-dimethyl analogue **37** was in accordance with predictions based upon molecular modeling,[29] which indicated that the latter was 9.25 kJ/mol higher in energy than the former. These experiments confirm that the cycloadducts **19** and **23** both possess the epi-spiro configuration, and that **19** is the *cis*- and **23** the *trans*-dimethyl diastereomer.

The remaining diene **30** was similarly converted into the corresponding ketone **38**, as illustrated in Scheme 5. Treatment of **38** with DBU again effected epimerization of the A-ring methyl group to afford (±)-3,6-dioxobakkenolide-A (**39**), with the same relative stereochemistry at all four chiral centers as the naturally-occurring bakkenolides **1**-**3**. The identity of this product was also verified by X-ray crystallography.[28]

The predominant formation of the endo-epoxide **32b** from the peracid oxidation of diene **30** is in unexpected contrast to the exo-epoxides formed preferentially from the epi-spiro diene analogues **24** and **29** and remains puzzling. We also investigated the treatment of the major product **32b** with triphenylphosphine−iodine, with the expectation of obtaining the diaxial iodohydrin regioisomer **40**. Instead, the cyclic ether **41** was isolated in high yield, indicating that the iodohydrin, which can be detected by TLC in the early stages of the reaction, undergoes intramolecular attack by the hydroxyl group upon C-9, with displacement of a highly stabilized enolate leaving group (Scheme 6).

We also attempted to perform the key cyclization steps (radical cyclization and Diels−Alder reaction) in reverse order, in order to observe whether the spiro center would be formed with normal or epi-spiro stereochemistry. Recently, Srikrishna et al.,[4a,i,k,l] demonstrated that radical spirocyclizations of acetals of propargyl alcohol and α-bromoperhydrindane aldehydes proceed predominantly from the endo side of the bicyclic precursor to afford the relative spiro configuration associated with the natural bakkenolides. Thus, the reaction of 2-methylcyclopent-2-enone with piperylene provided the known *trans*-dimethyl cycloadduct **42**,[17] which underwent hydroboration, silylation, acylation with allyl cyanoformate,[30] and selenenylation to afford product **43** (Scheme 7). Radical cyclization, followed by our standard protocol for the epimerization of the A-ring methyl group, afforded the same product **28**, as obtained via Scheme 4. The radical cyclization therefore occurred via the exo side of the bicyclic precursor, producing the epi-spiro configuration almost exclusively, in contrast to the results of Srikrishna et al.

Conclusion

The photoinduced radical cyclization of allyl α-(phenylseleno)-β-keto esters **7**-**9** provides a convenient approach to spiro lactones **10**-**12**, and their β-methylene derivatives **14** and **15** after selenoxide elimination. The further annulation of **11** by means of a Diels−Alder reaction with piperylene failed at ambient pressure, but proceeded at 16 kbar in the presence of Lewis acids. The products **19**, **21**, and **23** were formed by β-exo, α-endo, and β-endo transition states **18**, **20**, and **22**, respectively. Although some control over the α:β ratio was possible through appropriate choice of Lewis acid catalyst, β-attack upon the dienophile predominated and resulted in the epi-spiro configuration. The observation of substantial amounts of the two endo products, which lead to *trans*-dimethyl diastereomers, is noteworthy in that the transition states required for their formation are highly hindered. The base-catalyzed *trans*- to *cis*-dimethyl epimerization of the 3-keto derivatives **38** and **37** afforded the novel analogue (±)-3,6-dioxobakkenolide-A (**39**), with the same relative configuration at all four stereocenters as the natural bakkenolides and its epi-spiro counterpart **28**, respectively.

Experimental Section

Photolyses were carried out in a Rayonet RMR-500 reactor equipped with four 254 nm lamps or by means of a 275 Watt sunlamp. The high pressure Diels−Alder reactions were performed in a Harwood Model DJ-320/42 cylindrical pressure vessel. The samples, in 1 mL plastic syringes, were placed in the cylinder, which was filled with Coleman camp fuel, and pressure was applied with a piston powered by a hydraulic ram. ^{1}H- and ^{13}C-NMR spectra were taken at 200 and 50 MHz, respectively, unless otherwise noted. Elemental analyses and mass spectra were obtained by Ms. D. Fox and Ms. Q. Wu at the University of Calgary.

The following reagents were prepared by literature methods: allyl cyanoformate,[30c] $TiCl_2(Oi\text{-}Pr)_2$,[31] and $TiCl_2$−TAD-

(29) Molecular modeling was carried out with MacroModel version 3.5a, Columbia University, 1992. Local energy minima were calculated with the MM2 force field, and the global minimum energy conformations were determined by Monte Carlo searches using 1000 structures within 50 kJ/mol of the global minimum.

(30) (a) Allyl cyanoformate proved a superior reagent to allyl carbonate or allyl chloroformate in this case, but was inferior to allyl chloroformate for the acylations shown in Scheme 2. (b) The use of methyl cyanoformate for the acylation of ketone enolates has been previously reported: Mander, L. N.; Sethi, S. P. *Tetrahedron Lett.* **1983**, *24*, 5425. (c) Allyl cyanoformate was prepared by the method of: Donnelly, D. M. X.; Finet, J.-P.; Rattigan, B. A. *J. Chem. Soc., Perkin Trans. 1* **1993**, 1729.

DOL.[32] *m*-Chloroperbenzoic acid was purified by washing with a pH 7.5 phosphate buffer[33] and was assumed to be 100% pure. Piperylene was used as a mixture of *cis* and *trans* isomers (30:70 by NMR integration).[34] The bicyclic keto olefin **42** was prepared by the method of Fringuelli and Wenkert *et al.*[17] Other reagents were obtained from commercial sources and purified as required by standard methods. Flash chromatography was performed using silica gel as the adsorbent.

Allyl 2-Oxocyclopentanecarboxylate (4). β-Keto ester **4** was prepared from allyl chloroformate and 4-(1-cyclopenten-1-yl)morpholine by the general procedure of Stork.[35] The crude product was purified by chromatography with 15% ethyl acetate−hexanes to afford 74% of **4** as a colorless oil: IR (film) 1755, 1726, 1705, 1649, 1242, 1117 cm^{-1}; ^{1}H-NMR δ 6.01−5.81 (m, 1 H), 5.39−5.20 (m, 2 H), 4.68−4.61 (m, 2 H), 3.18 (t, J = 9.1 Hz, 1 H), 2.39−2.22 (m, 4 H), 2.22−2.05 (m, 1 H), 2.00−1.78 (m, 1 H); ^{13}C-NMR δ 212.0, 169.0, 131.7, 118.4, 65.8, 54.7, 38.0, 27.4, 20.9; mass spectrum, *m*/*z* (relative intensity, %) 168 (M^+, 7), 143 (16), 111 (36), 99 (19), 83 (18), 69 (11), 55 (85), 41 (100). Exact mass calcd for $C_9H_{12}O_3$: 168.0786. Found: 168.0786.

Allyl 1-(Phenylseleno)-2-oxocyclopentanecarboxylate (7). Compound **7** was prepared by the general procedure of Reich.[11] Oil-free sodium hydride (115 mg, 4.79 mmol) in 5 mL of dry THF under an argon atmosphere was cooled to 0 °C. A solution of β-keto ester **4** (502 mg, 2.99 mmol) in 5 mL of dry THF was added, followed after 30 min by benzeneselenenyl chloride (610 mg, 3.19 mmol) in 5 mL of dry THF. After an additional 15 min, the reaction was quenched with water, diluted with ether-pentane (1:1), washed with saturated $NaHCO_3$ solution, and dried ($MgSO_4$), and the solvent was evaporated. Chromatography with 15% ethyl acetate−hexanes afforded 846 mg (88%) of **7** as a yellow oil: IR (film) 1751, 1728, 1246, 1138, 988 cm^{-1}; ^{1}H-NMR δ 7.66−7.60 (m, 2 H), 7.45−7.27 (m, 3 H), 5.99−5.80 (m, 1 H), 5.39−5.21 (m, 2 H), 4.67−4.63 (m, 2 H), 2.58−2.22 (m, 3 H), 2.15−1.90 (m, 3 H); ^{13}C-NMR δ 207.2, 169.2, 137.6, 131.4, 129.8, 129.0, 126.4, 118.7, 66.4, 58.7, 36.9, 34.1, 19.0; mass spectrum, *m*/*z* (relative intensity, %) 324 (M^+, ^{80}Se, 27), 266 (6), 184 (7), 157 (27), 111 (21), 77 (21), 55 (80), 41 (100). Exact mass calcd for $C_{15}H_{16}O_3$Se: 324.0266. Found: 324.0263. This product was used in the next step without further purification.

4-[(Phenylseleno)methyl]-2-oxaspiro[4.4]nonane-1,6-dione (10). A solution of ester **7** (351 mg, 1.08 mmol) in 20 mL of benzene in a Pyrex vessel was irradiated at 254 nm for 7 h, the solvent was evaporated, and the crude product was chromatographed (elution with 15% ethyl acetate−hexanes) to afford 305 mg (87%) of **10** as one diastereomer, in the form of a yellow oil: IR (film) 1773, 1730, 1202, 1103, 1022, 743 cm^{-1}; ^{1}H-NMR δ 7.53−7.45 (m, 2 H), 7.34−7.26 (m, 3 H), 4.43 (dd, J = 8.6, 8.1 Hz, 1 H), 4.23 (dd, J = 10.3, 8.8 Hz, 1 H), 3.11−2.87 (m, 2 H), 2.81−2.18 (m, 4 H), 2.17−1.96 (m, 2 H); ^{13}C-NMR δ 213.4, 174.8, 133.3, 129.4, 128.2, 127.9, 71.1, 60.3, 45.7, 39.5, 32.7, 24.1, 20.1; mass spectrum, *m*/*z* (relative intensity, %) 324 (M^+, ^{80}Se, 23), 197 (7), 167 (100), 91 (28), 81 (53), 77 (29), 55 (27), 41 (40). Anal. Calcd for $C_{15}H_{16}O_3$Se: C, 55.73; H, 4.99. Found: C, 55.57; H, 4.80.

A comparable yield of the same product was obtained when the reactant was irradiated in benzene in a water-cooled vessel with a sunlamp for ca. 1 h.

Products **5** and **6** were prepared by treatment of 2- or 3-methylcyclopent-2-enone with LDA or LiTMP, respectively, in THF at −78 °C, followed by allyl chloroformate. Their subsequent selenenylations and cyclizations were performed as in the case of **4**. The selenoxide eliminations of **11** and **12** to afford **14** and **15**, respectively, were carried out with sodium metaperiodate in THF−methanol−water (20:7:3) at room temperature. Experimental details for compounds **8**, **9**, **11**, **12**, **14**, and **15** were described earlier.[9]

High Pressure Diels−Alder Reactions of 11 with Piperylene. See Table 1. Typical procedure (entry 9): A mixture of the pure major diastereomer of spiro lactone **11** (800 mg, 2.38 mmol), piperylene (1.00 mL, 10.0 mmol), and dichlorodiisopropoxytitanium (341 mg, 1.44 mmol) in 1.0 mL of dry dichloromethane was taken up into six 1 mL plastic syringes. The syringes were subjected to a pressure of 16 kbars for 24 h, their contents were combined, diluted with ether, and washed with water, and the solvent was evaporated. The crude material was chromatographed with dichloromethane to afford three fractions. The first contained 337 mg (35%) of 2,3-dehydro-11,13-dihydro-6-oxo-13-(phenylseleno)-7-epibakkenolide-A (**19**) as a yellow oil: IR (film) 1769, 1725, 1195, 1022, 754 cm^{-1}; ^{1}H-NMR δ 7.53−7.46 (m, 2 H), 7.34−7.27 (m, 3 H), 5.62−5.34 (m, 2 H), 4.48−4.36 (m, 1 H), 4.30−4.20 (m, 1 H), 3.08−2.98 (m, 1 H), 2.90−2.67 (m, 2 H), 2.60−2.47 (m, 2 H), 2.40−2.20 (m, 1 H), 2.20−2.05 (m, 1 H), 2.05−1.90 (m, 1 H), 1.78 (dd, J = 13.1, 6.5 Hz, 1 H), 0.94 (s, 3 H), 0.85 (d, J = 7.3 Hz, 3 H); mass spectrum, *m*/*z* (relative intensity, %) 404 (M^+, ^{80}Se, 58), 247 (75), 179 (45), 108 (100), 91 (72), 41 (38). Exact mass calcd for $C_{21}H_{24}O_3$Se: 404.0894. Found: 404.0866. The second fraction contained 414 mg (43%) of a mixture of **21** and **23**, in the ratio of 5:6 (NMR integration) as a yellow oil. The separation of these compounds was more conveniently achieved after selenoxide elimination (*vide infra*). The third fraction contained 128 mg (16%) of starting material **11**.

2,3-Dehydro-6-oxo-7-epibakkenolide-A (24). A solution of sodium metaperiodate (250 mg, 1.17 mmol) in 1.5 mL of water and 3.5 mL of methanol was added to a solution of lactone **19** (229 mg, 0.567 mmol) in 10 mL of THF. The mixture was stirred at room temperature for 40 h, diluted with ether, washed with water, and dried ($MgSO_4$), and the solvent was evaporated. Chromatography with 10% ethyl acetate−hexanes afforded 100 mg (72%) of **24** as a colorless oil: IR (film) 1772, 1731, 1666, 1160, 1101, 1021 cm^{-1}; ^{1}H-NMR δ 5.78−5.57 (m, 1 H), 5.44−5.38 (m, 1 H), 5.20−4.95 (m, 3 H), 4.78 (dt, J = 12.2, 1.9 Hz, 1 H), 2.70−2.34 (m, superimposed on t at 2.54, J = 12.4 Hz, total 2 H), 2.34−2.14 (m, 2 H), 2.14−2.08 (m, 2 H), 0.99 (s, 3 H), 0.87 (d, J = 7.3 Hz, 3 H); ^{13}C-NMR (100 MHz) δ 209.2, 174.7, 145.6, 129.1, 122.3, 107.0, 71.4, 61.1, 50.4, 40.0, 35.1, 25.6, 23.9, 14.9, 14.3; mass spectrum, *m*/*z* (relative intensity, %) 246 (M^+, 2), 218 (16), 203 (16), 111 (78), 108 (100), 93 (68), 91 (39), 77 (24). Anal. calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.16; H, 7.61.

2β,3β-Epoxy-6-oxo-7-epibakkenolide-A (25a) and 2α,3α-Epoxy-6-oxo-7-epibakkenolide-A (25b). A solution of diene **24** (95 mg, 0.39 mmol) and mCPBA (70 mg, 0.41 mmol) in 7 mL of dichloromethane was stirred at room temperature for 24 h. The reaction mixture was diluted with ether, washed with saturated $NaHCO_3$ solution, and dried ($MgSO_4$), and the solvent was evaporated. Chromatography with 20% ethyl acetate−hexanes gave two fractions. The first contained 59 mg (58%) of **25a** as a white solid: mp 101−104.5 °C (from ethyl acetate−hexanes); IR (film) 1771, 1731, 1667, 1164, 1025, 907 cm^{-1}; ^{1}H-NMR δ 5.10−4.99 (m, 3 H), 4.81−4.73 (m, 1 H), 3.22 (t, J = 4.8 Hz, 1 H), 3.16−3.13 (m, 1 H), 2.59−2.31 (m, 3 H), 2.27−1.93 (m, 3 H), 1.11 (s, 3 H), 1.06 (d, J = 7.1 Hz, 3 H); ^{13}C-NMR δ 209.1, 174.7, 145.3, 107.1, 71.5, 60.7, 57.1, 50.9, 49.8, 39.0, 35.8, 24.8, 23.5, 16.5, 12.2; mass spectrum, *m*/*z* (relative intensity, %) 262 (M^+, 5), 201 (15), 171 (41), 157 (35), 124 (39), 111 (94), 109 (64), 106 (100), 95 (49), 91 (49), 41 (39). Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.27; H, 7.13.

The second fraction contained 28 mg (28%) of **25b** as a white solid: mp 94−98.5 °C; IR (film) 1774, 1731, 1669, 1163, 1021, 906 cm^{-1}; ^{1}H-NMR δ 5.10−5.03 (m, 3 H), 4.79−4.71 (m, 1 H), 3.24−3.18 (m, 1 H), 2.88 (dd, J = 4.1, 1.6 Hz, 1 H), 2.73−2.31 (m, 2 H), 2.28−2.05 (m, 4 H), 1.03 (s, superimposed on d at δ 1.03, J = 7.4 Hz, total 6 H); ^{13}C-NMR (100 MHz) δ 209.4, 173.9, 145.6, 106.8, 71.2, 61.5, 54.3, 50.7, 50.0, 38.4, 35.5, 28.9, 23.9, 18.3, 13.1; mass spectrum, *m*/*z* (relative intensity, %) 262 (M^+, 1), 201 (4), 171 (9), 111 (33), 106 (56), 85 (80), 83 (100), 47

(31) Dijkgraaf, C.; Rousseau, J. P. G. *Spectrochim. Acta* **1968**, *24A*, 1213.

(32) Narasaka, K.; Iwasawa, N.; Inoue, M.; Yamada, T.; Nakashima, M.; Sugimori, J. *J. Am. Chem. Soc.* **1989**, *111*, 5340.

(33) Schwartz, N. N.; Blumbergs, J. H. *J. Org. Chem.* **1964**, *29*, 1976.

(34) Typically, the more reactive *trans* isomer of piperylene reacts selectively when a *cis*,*trans* mixture is employed in normal Diels−Alder reactions. The use of pure *trans*-piperylene in several experiments at high pressure conferred no advantage over the mixture.

(35) Stork, G.; Brizzolara, A.; Landesman, H.; Szmuszkovicz, J.; Terrell, R. *J. Am. Chem. Soc.* **1963**, *85*, 207.

(42), 41 (29). Exact mass calcd for $C_{15}H_{18}O_4$: 262.1205. Found: 262.1199.

3β-Hydroxy-2α-iodo-6-oxo-7-epibakkenolide-A (26). Triphenylphosphine (44 mg, 0.17 mmol) was added to a solution of iodine (41 mg, 0.16 mmol) in 2 mL of dry dichloromethane, followed by a solution of epoxide **25a** (39 mg, 0.15 mmol) in 2 mL of dry dichloromethane. The reaction was stirred at room temperature for 5 min, diluted with ether, washed with saturated $NaHCO_3$ solution, and dried ($MgSO_4$), and the solvent was evaporated. The crude material was chromatographed with 20% ethyl acetate−hexanes to afford 53 mg (92%) of iodohydrin **26** as a white solid: mp 153−156 °C; IR (film) 3542, 1770, 1728, 1667, 1161, 1018, 754 cm^{-1}; ^{1}H-NMR δ 5.23−5.20 (m, 2 H), 4.82−4.76 (m, 2 H), 4.31 (ddd, J = 10.5, 10.5, 5.0 Hz, 1 H), 3.52 (dd, J = 9.7, 3.9 Hz, 1 H), 2.82−2.53 (m, 2 H), 2.53−2.23 (m, 5 H), 1.14 (s, 3 H), 0.99 (d, J = 7.3 Hz, 3 H); ^{13}C-NMR (100 MHz) δ 210.8, 174.0, 144.4, 107.9, 74.9, 71.5, 61.1, 56.0, 40.1, 39.5, 35.7, 34.4, 31.5, 21.9, 8.4; mass spectrum, m/z (relative intensity, %) 390 (M^+, 2), 362 (1), 263 (11), 217 (59), 171 (10), 124 (13), 111 (100), 108 (47), 106 (73), 91 (36), 41 (25). Exact mass calcd for $C_{15}H_{19}IO_4$: 390.0324. Found: 390.0340.

3β-Hydroxy-6-oxo-7-epibakkenolide-A (27). A solution of iodohydrin **26** (42 mg, 0.11 mmol) and tributyltin hydride (0.030 mL, 0.11 mmol) in 2 mL of degassed dry benzene was refluxed under argon for 3 h, the solvent was evaporated, and the crude material was chromatographed (elution with 40% ethyl acetate−hexanes), yielding 24 mg (84%) of **27** as a white solid: IR (film) 3524, 1764, 1724, 1668, 1165, 1026, 911 cm^{-1}; ^{1}H-NMR δ 5.11−5.02 (m, 3 H), 4.83−4.75 (m, 1 H), 3.94−3.88 (m, 1 H), 2.78 (t, J = 13.2 Hz, 1 H), 2.43−1.70 (m, 8 H), 1.25 (s, 3 H), 0.94 (d, J = 7.1 Hz, 3 H); mass spectrum, m/z (relative intensity, %) 264 (M^+, 2), 218 (36), 173 (34), 112 (83), 111 (96), 108 (100), 106 (43), 93 (63), 41 (55). This material was used without further purification in the next step.

3,6-Dioxo-7-epibakkenolide-A (28). Alcohol **27** was oxidized by the general procedure of Corey and Schmidt.[36] A mixture of **27** (24 mg, 0.091 mmol) and PDC (53 mg, 0.14 mmol) in 2 mL of dry dichloromethane was stirred at room temperature for 20 h, the reaction mixture was diluted with ether, washed with 5% HCl and saturated $NaHCO_3$ solution, and dried ($MgSO_4$), and the solvent was evaporated. Chromatography with 40% ethyl acetate−hexanes afforded 20 mg (84%) of **28** as a white solid: mp 126.5−128.5 °C (from absolute ethanol); IR (film) 1773, 1719, 1669, 1165, 1010, 907 cm^{-1}; ^{1}H-NMR δ 5.19−5.07 (m, 3 H), 4.90−4.82 (m, 1 H), 3.15−3.04 (m, 2 H), 2.79−2.62 (m, 1 H), 2.43−2.17 (m, 5 H), 1.00 (s, 3 H), 0.86 (d, J = 6.6 Hz, 3 H); ^{13}C-NMR δ 209.2, 207.9, 174.6, 145.2, 107.5, 71.7, 61.9, 57.7, 41.9, 41.5, 36.8, 33.2, 26.2, 15.9, 7.1; mass spectrum, m/z (relative intensity, %) 262 (M^+, 17), 234 (8), 124 (100), 109 (37), 82 (48), 67 (49), 55 (40), 41 (42). Exact mass calcd for $C_{15}H_{18}O_4$: 262.1205. Found: 262.1211.

2,3-Dehydro-6-oxo-4,7-diepibakkenolide-A (29) and 2,3-Dehydro-6-oxo-4-epibakkenolide-A (30). A solution of sodium metaperiodate (236 mg, 1.11 mmol) in 1.2 mL of water and 2.8 mL of methanol was added to the mixture of lactones **21** and **23** (216 mg, 0.535 mmol), prepared by the high pressure Diels−Alder reaction described above, in 8 mL of THF. The mixture was stirred at room temperature for 28 h, diluted with ether, washed with water, and dried ($MgSO_4$), and the solvent was evaporated. Chromatography with 10% ethyl acetate−hexanes gave two fractions. The first contained 42 mg (32%; based on the total amount of starting materials **21** and **23**) of **30** as a colorless oil: IR (film) 1773, 1730, 1669, 1149, 1019, 756 cm^{-1}; ^{1}H-NMR δ 5.81−5.64 (m, 2 H), 5.18−5.12 (m, 2 H), 5.10−4.97 (m, 1 H), 4.83−4.73 (m, 1 H), 2.90−2.74 (m, 1 H), 2.52−2.37 (m, 1 H), 2.30 (dd, J = 13.3, 7.2 Hz, 1 H), 2.18−1.91 (m, superimposed on t at δ 1.97, J = 12.7 Hz, total 3 H), 1.20 (s, 3 H), 0.93 (d, J = 7.6 Hz, 3 H); ^{13}C-NMR (100 MHz) δ 215.0, 174.3, 142.5, 131.4, 124.3, 108.3, 72.1, 62.6, 52.1, 37.7, 36.2, 35.5, 26.5, 25.5, 19.8; mass spectrum, m/z (relative intensity, %) 246 (M^+, 2), 218 (10), 203 (24), 111 (91), 108 (100), 93 (74). Anal. calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.01; H, 7.53.

(36) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* **1979**, 399.

The second fraction contained 58 mg (44%; based on the total amount of starting materials **21** and **23**) of **29** as a colorless oil: IR (film) 1773, 1729, 1667, 1292, 1162, 1019, 908 cm^1; ^{1}H-NMR δ 5.73−5.72 (m, 2 H), 5.19−5.09 (m, 2 H), 4.99 (dt, J = 12.4, 2.5 Hz, 1 H), 4.72 (dt, J = 12.3, 1.5 Hz, 1 H), 2.57−2.30 (m, 3 H), 2.30−2.02 (m, 3 H), 1.21 (s, 3 H), 1.00 (d, J = 7.6 Hz, 3 H); ^{13}C-NMR δ 213.8, 173.0, 145.3, 131.5, 123.2, 107.0, 70.6, 62.6, 51.9, 40.0, 37.0, 36.3, 27.7, 25.7, 18.4; mass spectrum, m/z (relative intensity, %) 246 (M^+, 3), 218 (12), 203 (23), 112 (67), 111 (95), 108 (100), 93 (80), 91 (37), 77 (23). Anal. Calcd for $C_{15}H_{18}O_3$: C, 73.15; H, 7.37. Found: C, 73.08; H, 7.59.

2β,3β-Epoxy-6-oxo-4,7-diepibakkenolide-A (31a) and 2α,3α-Epoxy-6-oxo-4,7-diepibakkenolide-A (31b). A solution of diene **29** (108 mg, 0.439 mmol) and mCPBA (80 mg, 0.46 mmol) in 7 mL of dichloromethane was stirred at room temperature for 24 h, the reaction mixture was diluted with ether, washed with saturated $NaHCO_3$ solution, and dried ($MgSO_4$), and the solvent was evaporated. The crude material was chromatographed with 20% ethyl acetate−hexanes to afford two fractions. The first contained 74 mg (64%) of **31a** as a white solid: mp 130−132 °C (from ethyl acetate−hexanes); IR (film) 1771, 1724, 1668, 1164, 910, 756 cm^{-1}; ^{1}H-NMR δ 5.14−5.11 (m, 2 H), 4.99 (dt, J = 12.6, 2.5 Hz, 1 H), 4.75 (dt, J = 12.6, 1.6 Hz, 1 H), 3.24−3.20 (m, 1 H), 3.11 (t, J = 3.9 Hz, 1 H), 2.62−2.18 (m, 5 H), 2.17−2.05 (m, 1 H), 1.34 (s, 3 H), 0.96 (d, J = 7.3 Hz, 3 H); ^{13}C-NMR (100 MHz) δ 215.2, 173.6, 144.9, 107.6, 70.8, 62.4, 55.1, 51.2, 49.9, 37.5, 36.4, 35.9, 30.8, 28.7, 15.1; mass spectrum, m/z (relative intensity, %) 262 (M^+, 3), 201 (8), 171 (18), 157 (19), 111 (36), 106 (100), 91 (36), 41 (39). Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.37; H, 6.93.

The second fraction contained 6 mg (5%) of a colorless oil, tentatively identified as crude **31b**: ^{1}H-NMR δ 5.11−5.04 (m, 3 H), 4.83−4.72 (m, 1 H), 3.27−3.15 (m, 1 H), 2.89 (dd, J = 4.1, 1.6 Hz, 1 H), 2.74−2.03 (m, 6 H), 1.04 (s, superimposed on d at δ 1.04, J = 7.4 Hz, total 6 H).

3β-Hydroxy-2α-iodo-6-oxo-4,7-diepibakkenolide-A (33). Epoxide **31a** (42 mg, 0.16 mmol) was converted into the iodohydrin **33** by the same procedure used for the preparation of **26**. Chromatography with 20% ethyl-acetate−hexanes afforded 57 mg (90%) of **33** as a white solid: mp 184−187.5 °C; IR (film) 3540, 1771, 1727, 1666, 1160, 1017, 910, 754 cm^{-1}; ^{1}H-NMR δ 5.24−5.21 (m, 2 H), 5.05 (dt, J = 12.2, 2.4 Hz, 1 H), 4.77 (dt, J = 12.2, 1.3 Hz, 1 H), 4.06 (ddd, J = 12.7, 10.0, 4.3 Hz, 1 H), 3.35 (t, J = 9.8 Hz, 1 H), 2.86−2.38 (m, 4 H), 2.17−2.04 (m, 2 H), 1.60−1.49 (m, 1 H), 1.43 (d, J = 6.3 Hz, 3 H), 1.34 (s, 3 H); ^{13}C-NMR δ 209.8, 174.1, 143.9, 108.2, 76.5, 71.4, 61.7, 55.0, 45.5, 44.4, 41.3, 39.9, 31.0, 23.9, 11.4; mass spectrum, m/z (relative intensity, %) 390 (M^+, 3) 362 (5), 263 (11), 217 (54), 171 (22), 124 (36), 111 (100), 106 (90), 95 (45), 91 (44), 41 (46). Exact mass calcd for $C_{15}H_{19}IO_4$: 390.0324. Found: 390.0290.

3β-Hydroxy-6-oxo-4,7-diepibakkenolide-A (35). Iodohydrin **33** (36 mg, 0.092 mmol) was reduced to alcohol **35** by the same procedure used for the preparation of **27**. Chromatography with 40% ethyl acetate−hexanes, afforded 18 mg (74%) of **35** as a white solid: mp 135−138 °C (from ethyl acetate−hexanes); IR (film) 3425, 1776, 1730, 1668, 1176, 1103, 1016, 756 cm^{-1}; ^{1}H-NMR δ 5.23−5.18 (m, 2 H), 5.02 (dt, J = 12.2, 2.4 Hz, 1 H), 4.75 (dt, J = 12.1, 1.4 Hz, 1 H), 3.35 (ddd, J = 9.7, 9.7, 3.4 Hz, 1 H), 2.42 (dd, J = 14.2, 6.7 Hz, 1 H), 2.17 (dd, J = 14.2, 2.4 Hz, 1 H), 2.04−1.81 (m, 5 H), 1.80−1.65 (br s, 1 H), 1.52−1.36 (m, 1 H), 1.35 (s, 3 H), 1.28 (d, J = 6.8 Hz, 3 H); ^{13}C-NMR δ 211.3, 174.3, 144.6, 107.7, 72.0, 71.2, 62.1, 54.6, 46.6, 42.1, 32.5, 32.3, 27.1, 24.9, 11.4; mass spectrum, m/z (relative intensity, %) 264 (M^+, 3), 236 (6), 218 (18), 203 (25), 173 (21), 112 (83), 111 (53), 108 (100), 93 (54), 82 (23), 67 (26), 55 (17), 41 (34). Anal. Calcd for $C_{15}H_{20}O_4$: C, 68.16; H, 7.63. Found: C, 67.78; H, 7.88.

3,6-Dioxo-4,7-diepibakkenolide-A (37). Alcohol **35** (76 mg, 0.29 mmol) was oxidized with PDC as in the preparation of **28**. Chromatography with 50% ethyl acetate−hexanes afforded 71 mg (94%) of **37** as a white solid: mp 122−124.5 °C; IR (film) 1775, 1729, 1713, 1668, 1170, 1108, 1018, 911 cm^{-1}; ^{1}H-NMR δ 5.24−5.17 (m, 2 H), 4.98 (dt, J = 12.6, 2.5

Hz, 1 H), 4.77 (dt, J = 12.5, 1.6 Hz, 1 H), 2.65−2.26 (m, 7 H), 2.18−2.08 (m, 1 H), 1.30 (s, 3 H), 1.15 (d, J = 7.4 Hz, 3 H); ^{13}C-NMR δ 212.2, 211.5, 173.3, 144.7, 107.9, 70.6, 63.0, 53.8, 50.9, 40.6, 35.3, 35.1, 29.0, 25.9, 13.2; mass spectrum, m/z (relative intensity, %) 262 (M^+, 16), 234 (17), 124 (100), 105 (67), 82 (82), 67 (69), 57 (64), 41 (75). Exact mass calcd for $C_{15}H_{18}O_4$: 262.1205. Found: 262.1208.

Epimerization of Ketone 37. A solution of ketone **37** (51 mg, 0.20 mmol) and DBU (0.060 mL, 0.40 mmol) in 1 mL of dry dichloromethane was stirred at room temperature for 5 h. The reaction mixture was diluted with ether, washed with 5% HCl and saturated $NaHCO_3$ solutions, and dried ($MgSO_4$), and the solvent was evaporated. The crude product was purified by chromatography (elution with 50% ethyl acetate−hexanes) to afford 46 mg (89%) of **28**, identical to the sample obtained from the oxidation of alcohol **27**.

2β,3β-Epoxy-6-oxo-4-epibakkenolide-A (32a) and 2α,3α-Epoxy-6-oxo-4-epibakkenolide-A (32b). A solution of diene **30** (111 mg, 0.451 mmol) and mCPBA (77 mg, 0.45 mmol) in 12 mL of dichloromethane was stirred at room temperature for 28 h, the reaction mixture was diluted with ether, washed with saturated $NaHCO_3$ solution, and dried ($MgSO_4$), and the solvent was evaporated. The crude product was chromatographed with 20% ethyl acetate−hexanes to afford two fractions. The first contained 59 mg (50%) of **32b** as a white solid: mp 147.5−150 °C (from ethyl acetate−hexanes); IR (film) 1770, 1728, 1671, 1158, 1018 cm^{-1}; ^{1}H-NMR δ 5.34−5.31 (m, 1 H), 5.25−5.23 (m, 1 H), 5.13 (dt, J = 12.3, 2.6 Hz, 1 H), 4.78 (dt, J = 12.3, 1.7 Hz, 1 H), 3.30 (t, J = 3.5 Hz, 1 H), 3.01 (dd, J = 4.5, 1.4 Hz, 1 H), 2.70−2.47 (m, 2 H), 2.30−2.05 (m, 4 H), 1.30 (d, J = 7.5 Hz, 3 H), 1.25 (s, 3 H); ^{13}C-NMR δ 213.2, 175.2, 143.9, 108.8, 72.1, 62.9, 55.4, 51.9, 49.5, 38.1, 38.0, 36.8, 26.7, 26.3, 15.4; mass spectrum, m/z (relative intensity, %) 262 (M^+, 2), 201 (8), 171 (19), 157 (16), 111 (48), 106 (100), 93 (46), 41 (37). Anal. calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.44; H, 6.98.

The second fraction contained 20 mg (17%) of **32a** as a white solid: mp 160.5−162 °C (from ethyl acetate−hexanes); IR (film) 1761, 1726, 1676, 1152, 756 cm^{-1}; ^{1}H-NMR δ 5.23−5.20 (m, 1 H), 5.12 (dt, J = 12.4, 2.6 Hz, 1 H), 5.02−5.00 (m, 1 H), 4.81 (dt, J =12.4, 1.8 Hz, 1 H), 3.24−3.22 (m, 1 H), 3.14 (t, J = 3.8 Hz, 1 H), 2.75−2.50 (m, 3 H), 2.40−2.20 (m, 1 H), 1.90−1.75 (m, 2 H), 1.39 (s, 3 H), 0.94 (d, J = 7.3 Hz, 3 H); ^{13}C-NMR δ 215.3, 173.9, 143.4, 108.1, 71.9, 62.0, 55.4, 51.4, 49.7, 38.0, 35.2, 34.5, 29.0, 28.4, 16.0; mass spectrum, m/z (relative intensity, %) 262 (M^+, 5), 216 (7), 201 (15), 171 (32), 157 (31), 111 (81), 106 (100), 91 (81), 41 (80). Anal. Calcd for $C_{15}H_{18}O_4$: C, 68.69; H, 6.92. Found: C, 68.68; H, 6.99.

3β-Hydroxy-2α-iodo-6-oxo-4-epibakkenolide-A (34). Epoxide **32a** (25 mg, 0.095 mmol) was converted into the iodohydrin **34** by the same procedure used for the preparation of **26**. Chromatography with 20% ethyl acetate−hexanes yielded 30 mg (81%) of iodohydrin **34** as a white solid: IR (film) 3515, 1771, 1732, 1667, 1156, 1006, 754 cm^{-1}; ^{1}H-NMR δ 5.29−5.14 (m, 3 H), 4.75 (d, J = 12.3 Hz, 1 H). 4.15−4.02 (m, 1 H), 3.34 (dt, J = 10.0, 2.6 Hz, 1 H), 3.00 (dd, J = 14.6, 6.6 Hz, 1 H), 2.64 (dt, J = 12.5, 3.6 Hz, 1 H), 2.36 (d, J = 2.9 Hz, 1 H), 2.15−2.04 (m, 1 H), 1.95 (d, J = 12.8 Hz, 1 H), 1.80 (d, J = 14.6 Hz, 1 H), 1.70−1.52 (m, 1 H), 1.46 (s, 3 H), 1.43 (d, J = 6.6 Hz, 3 H); ^{13}C-NMR δ 209.4, 173.4, 144.7, 109.0, 77.1, 72.1, 61.5, 56.3, 45.3, 44.2, 43.5, 39.4, 32.0, 21.3, 11.5; mass spectrum, m/z (relative intensity, %) 390 (M^+, 4) 362 (7), 263 (6), 217 (55), 171 (24), 111 (82), 106 (100), 91 (50), 57 (14), 41 (43). Exact mass calcd for $C_{15}H_{19}IO_4$: 390.0324. Found: 390.0331.

3β-Hydroxy-6-oxo-4-epibakkenolide-A (36). Iodohydrin **34** (27 mg, 0.069 mmol) was reduced to alcohol **36** by the same procedure used for the preparation of **27**. Chromatography with 40% ethyl acetate−hexanes afforded 14 mg (76%) of **36** as a white solid: IR (film) 3445, 1770, 1730, 1666, 1284, 1015, 754 cm^{-1}; ^{1}H-NMR (400 MHz) δ 5.22−5.13 (m, 3 H), 4.74−4.71 (m, 1 H), 3.29 (dt, J = 9.8, 3.7 Hz, 1 H), 2.93 (dd, J = 14.3, 6.9 Hz, 1 H), 2.06−1.91 (m, 3 H), 1.80 (dd, J = 14.3, 1.7 Hz, 1 H), 1.70−1.50 (m, 1 H), 1.47 (s, 3 H), 1.45−1.20 (m, 3 H), 1.30 (d, J = 7.0 Hz, 3 H); ^{13}C-NMR (100 MHz) δ 211.0, 173.8, 145.0, 108.6, 72.3, 72.0, 61.8, 55.9, 46.5, 41.7, 33.0, 32.9, 29.2, 22.2, 11.3; mass spectrum, m/z (relative intensity, %) 264 (M^+, 5), 236 (9), 218 (27), 203 (46), 173 (37), 112 (92), 108 (100), 93 (75), 41 (70). Exact mass calcd for $C_{15}H_{20}O_4$: 264.1362. Found: 264.1385. The product could not be further separated from a small amount of tin-containing byproducts and so was used in the next step without further purification.

3,6-Dioxo-4-epibakkenolide-A (38). Alcohol **36** (14 mg, 0.053 mmol) was oxidized with PDC as in the preparation of **28.** Chromatography with 40% ethyl acetate−hexanes afforded 13 mg (92%) of **38** as a white solid: IR (film) 1768, 1732, 1706, 1667, 1163, 1021 cm^{-1}; ^{1}H-NMR (400 MHz) δ 5.19−5.14 (m, 1 H), 5.08 (dt, J = 12.7, 2.6 Hz, 1 H), 4.97−4.95 (m, 1 H), 4.82 (dt, J = 12.7, 1.7 Hz, 1 H), 2.89−2.82 (m, 1 H), 2.64−2.40 (m, 5 H), 2.09−2.02 (m, 1 H), 1.87 (dd, J = 14.2, 11.1 Hz, 1 H), 1.38 (s, 3 H), 1.05 (d, J = 7.1 Hz, 3 H); ^{13}C-NMR (100 MHz) δ 212.9, 212.6, 173.0, 143.1, 108.8, 72.1, 61.9, 55.1, 49.9, 39.5, 35.9, 34.0, 26.5, 23.7, 11.1; mass spectrum, m/z (relative intensity, %) 262 (M^+, 8), 234 (10), 124 (100), 106 (45), 82 (50), 67 (35), 55 (29), 41 (33). Exact mass calcd for $C_{15}H_{18}O_4$: 262.1205. Found: 262.1196. The product partly epimerized during chromatography and so was used in the next step without further purification.

3,6-Dioxobakkenolide-A (39). A solution of ketone **38** (13 mg, 0.048 mmol) and DBU (0.020 mL, 0.13 mmol) in 1 mL of dry dichloromethane was stirred at room temperature for 3 h. The reaction mixture was diluted with ether, washed with 5% HCl and saturated $NaHCO_3$ solutions, and dried ($MgSO_4$), and the solvent was evaporated. Chromatography with 40% ethyl acetate−hexanes afforded 12 mg (94%) of **39** as a white solid: mp 202−203 °C (from absolute ethanol); IR (film) 1758, 1716, 1659, 1216, 1149, 1017 cm^{-1}; ^{1}H-NMR (400 MHz) δ 5.28 (dd, J = 3.7, 1.7 Hz, 1 H), 5.17−5.12 (m, 2 H), 4.91−4.88 (m, 1 H), 2.75−2.70 (m, 1 H), 2.70−2.39 (m, 5 H), 2.30−2.16 (m, 2 H), 1.02 (s, 3 H), 0.92 (d, J = 6.7 Hz, 3 H); ^{13}C-NMR (100 MHz) δ 209.3, 208.9, 174.1, 144.3, 107.9, 71.9, 61.7, 56.5, 43.1, 40.0, 37.0, 32.4, 26.0, 16.0, 7.3; mass spectrum, m/z (relative intensity, %) 262 (M^+, 4), 234 (5), 124 (100), 82 (38), 67 (30), 55 (29), 41 (32). Exact mass calcd for $C_{15}H_{18}O_4$: 262.1205. Found: 262.1200.

Anomalous Reaction of Epoxide 32b with Triphenylphosphine−Iodine. Triphenylphosphine (32 mg, 0.12 mmol) was added to a solution of iodine (30 mg, 0.12 mmol) in 1.5 mL of dry dichloromethane, followed by epoxide **32b** (28 mg, 0.11 mmol) in 1.5 mL of dry dichloromethane. The reaction mixture was stirred at room temperature for 5 min, diluted with ether, washed with saturated $NaHCO_3$ solution, and dried ($MgSO_4$), and the solvent was evaporated. Chromatography with 20% ethyl acetate−hexanes afforded 38 mg (89%) of **41** as a white solid: mp 186−189 °C; IR (film) 1758, 1735, 1676, 1219, 1065, 932, 752 cm^{-1}; ^{1}H-NMR δ 4.66 (d, J = 0.5 Hz, 2 H), 4.50−4.44 (m, 1 H), 4.35 (d, J = 4.1 Hz, 1 H), 2.96 (dd, J = 14.1, 7.1 Hz, 1 H), 2.65−2.55 (m, 1 H), 2.50−2.30 (m, 1 H), 2.12−1.88 (m, superimposed on d at δ 1.98, J = 0.8 Hz, total 6 H), 1.23 (s, 3 H), 1.08 (d, J = 7.1 Hz, 3 H); ^{13}C-NMR δ 178.0, 174.2, 158.5, 124.4, 83.9, 72.6, 50.0, 44.0, 37.6, 36.2, 24.4, 23.1, 14.8, 13.5, 12.4; mass spectrum, m/z (relative intensity, %) 390 (M^+, 2), 263 (87), 217 (100), 91 (77), 83 (77), 55 (67), 41 (72). Exact mass calcd for $C_{15}H_{19}IO_4$: 390.0324. Found: 390.0310.

Preparation of Allyl 4β-*tert*-Butyldimethylsilyloxy-5α,6β-dimethyl-7-oxo-8-phenylseleno-*cis*-bicyclo[4.3.0]-nonane-8-carboxylate (43) from Keto Olefin 42. A 1 M solution of borane−THF complex in THF (6.70 mL, 6.70 mmol) was added to a solution of **42** (1.01 g, 6.17 mmol) in 10 mL of dry THF at 0 °C under argon, and the reaction mixture was warmed to room temperature and stirred for 15 min. Then, 3.50 mL of a 3 M NaOH solution were added cautiously, followed by 3.50 mL of 30% hydrogen peroxide, and the mixture was stirred for 1 h. It was diluted with water and extracted with ether, the ether extracts were washed with saturated $NaHCO_3$ solution and dried ($MgSO_4$), and the solvent was evaporated. The crude products were separated by chromatography (elution with 30% ethyl acetate−hexanes), yielding two fractions. The first contained 353 mg (31%) of crude 4β-hydroxy-5α,6β-dimethyl-*cis*-bicyclo[4.3.0]nonan-7-one as a colorless oil. It was employed in the next step without

further purification. The second fraction contained 385 mg (34%) of a compound tentatively identified as the 3β-hydroxy regioisomer, obtained as a colorless oil.

The crude 4β-hydroxy isomer (350 mg, 1.92 mmol) was silylated with *tert*-butyldimethylsilyl chloride by the general method of Corey and Venkateswarlu,[37] to afford 357 mg (63%) of 4β-(*tert*-butyldimethylsilyloxy)-5α,6β-dimethyl-*cis*-bicyclo-[4.3.0]nonan-7-one as a colorless oil after chromatography. This product (280 mg, 0.947 mmol) in 4 mL of dry THF was added to LDA (1.21 mmol) in 4 mL of dry THF at −78 °C , and the solution was stirred for 10 min, followed by addition of allyl cyanoformate (143 mg, 1.29 mmol) in 4 mL of dry THF. The reaction mixture was stirred for another 30 min, quenched with saturated NH_4Cl solution, diluted with ether, washed with $NaHCO_3$ solution, and dried ($MgSO_4$), and the solvent was evaporated. Chromatography with 2% ethyl acetate−hexanes provided 147 mg (40%) of an unseparated mixture of two diastereomers of allyl 4β-(*tert*-butyldimethylsilyloxy)-5α,6β-dimethyl-7-oxo-*cis*-bicyclo[4.3.0]nonane-8-carboxylate in the ratio of 4:1, as a colorless oil.

The above product (330 mg, 0.868 mmol) was selenenylated as in the preparation of **7**-**9**. Chromatography afforded 400 mg (86%) of an unseparated mixture of two diastereomers of **43** in the ratio of 2:1, as a yellow oil: IR (film) 1752, 1722, 1250, 1211, 1081, 836, 774 cm^{-1}; ^{1}H-NMR δ 7.67−7.57 (m, 2 H), 7.42−7.26 (m, 3 H), 6.00−5.70 (m, 1 H), 5.39−5.19 (m, 2 H), 4.65−4.50 (m, 2 H), 3.58−3.46 (m, 1 H), 2.27−1.50 (m, 7H); other signals attributed to the major diastereomer: δ 2.46−2.34 (m, 1 H), 1.48 (s, 3 H), 0.95 (d, J = 7.6 Hz, 3 H), 0.89 (s, 9 H), 0.03 (s, 3 H), 0.02 (s, 3 H); other signals attributed to the minor diastereomer: δ 2.78−2.68 (m, 1 H), 1.24 (d, J = 7.1 Hz, 3 H), 1.16 (s, 3 H), 0.91 (s, 9 H), 0.11 (s, 3 H), 0.08 (s, 3 H); mass spectrum, m/z (relative intensity, %) 536 (M^+, ^{80}Se, 6), 479 (11), 323 (42), 265 (20), 237 (17), 75 (100), 73 (46), 41 (44). Anal. Calcd for $C_{27}H_{40}O_4SeSi$: C, 60.54; H, 7.53. Found: C, 60.22; H, 7.27.

3β-*tert*-Butyldimethylsilyloxy-11,13-dihydro-6-oxo-13-(phenylseleno)-4,7-diepibakkenolide-A (44). Allyl ester **43** (814 mg, 1.52 mmol) in 40 mL of degassed benzene under argon was irradiated with a 275 W sunlamp for 20 min, during which time the reaction mixture refluxed. The solvent was evaporated, and the crude material was chromatographed (elution with 5% ethyl acetate−hexanes), to afford 528 mg (65%) of an unseparated mixture of two diastereomers of **44** in the ratio of 3:1, as a yellow oil: IR (film) 1768, 1723, 1253, 1102, 1081, 1023, 838, 775 cm^{-1}; ^{1}H-NMR signals attributed to the major diastereomer: δ 7.52−7.46 (m, 2 H), 7.34−7.26 (m, 3 H), 4.45−4.38 (m, 1 H), 4.37−4.26 (m, 1 H), 3.56 (ddd, J = 6.2, 6.2, 2.8 Hz, 1 H), 3.18−3.04 (m, 1 H), 2.77−2.53 (m, 2 H), 2.36 (dd, J = 13.0, 7.6 Hz, 1 H), 2.06−1.71 (m, 4 H), 1.70−1.57 (m, 1 H), 1.38−1.29 (m, 1 H), 1.25 (s, 3 H), 1.03 (d, J = 7.5 Hz, 3 H), 0.88 (s, 9 H), 0.04 (s, 6 H); signals assigned to the minor diastereomer: δ 4.75−4.60 (m, 2 H), 3.32 (ddd, J = 8.6, 8.6, 3.3 Hz, 1 H), 1.13 (d, J = 7.3 Hz, 3 H), 1.09 (s, 3 H), 0.87 (s, 9 H), 0.00 (s, 6 H); mass spectrum, m/z (relative intensity, %) 536 (M^+, ^{80}Se, 0.6), 479 (58), 314 (29), 157 (44), 149 (76), 77 (53), 75 (100), 73 (52), 57 (51), 41 (54). Anal. calcd for $C_{27}H_{40}O_4SeSi$: C, 60.54; H, 7.53. Found: C, 60.50; H, 7.33.

Conversion of Spiro Lactone 44 into 3,6-Dioxo-7-epibakkenolide-A (28). Acetic acid (6 mL) and water (2 mL) were added to a solution of **44** (176 mg, 0.328 mmol) in 2 mL of THF, and the mixture was stirred at room temperature for 48 h. The mixture was diluted with ether, washed with saturated $NaHCO_3$ solution, and dried ($MgSO_4$), and the solvent was evaporated. Chromatography with 40% ethyl acetate−hexanes gave 114 mg (82%) of an unseparated mixture of two diastereomers of the desilylated product 11,13-dihydro-3β-hydroxy-6-oxo-13-(phenylseleno)-4,7-diepibakkenolide-A in the ratio of 3:1, as a yellow oil.

A solution of sodium metaperiodate (246 mg, 1.15 mmol) in 1.2 mL of water and 2.8 mL of methanol was added to the above mixture of stereoisomers (235 mg, 0.560 mmol) in 8 mL of THF. The mixture was stirred at room temperature for 28 h, diluted with ether, washed with water, and dried ($MgSO_4$), and the solvent was evaporated. The residue was chromatographed (elution with 50% ethyl acetate−hexanes) to afford 97 mg (66%) of **35**, identical to the product obtained from the reduction of iodohydrin **33**. The conversion of **35** into **28** via **37** was described earlier (Scheme 5).

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada (NSERC) for financial support. P.L.G. gratefully acknowledges receipt of an NSERC Postgraduate Scholarship, a Province of Alberta Graduate Scholarship, and an award from IODE. We thank Professor B. A. Keay for providing access to the high pressure reactor used in these experiments and to members of his group (Dr. S. Maddaford, Dr. I. Hunt, and Mr. M. Mouck) for technical assistance with this apparatus.

Supporting Information Available: ORTEP diagrams of compounds **28** and **39**, and the ^{1}H- and ^{13}C-NMR spectra of compounds **4**, **7**, **19**, **25b**, **26**, **28**, **33**, **34**, **36**−**39**, and **41** (28 pages). This material is contained in libraries on microfiche, immediately follows this article in the microform version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO960111+

(37) Corey, E. J.; Venkateswarlu, A. *J. Am. Chem. Soc.* **1972**, *94*, 6190.