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INTRAMOLECULAR CYCLOADDITION REACTIONS OF EXOCYCLIC NITRONES

APPLICATION IN THE TOTAL SYNTHESIS OF TERPENES

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Abstract—Exocyclic nitrones smoothly participate in intramolecular cycloaddition reactions to provide bridged and fused polycarbocycles. The exploitation of this methodology in the total syntheses of the sesquiterpenes (±)-7,12-secoishwaran-12-ol (**44**), (±)-hirsutene (**56**), (±)-coriolin (**68**) is also presented.

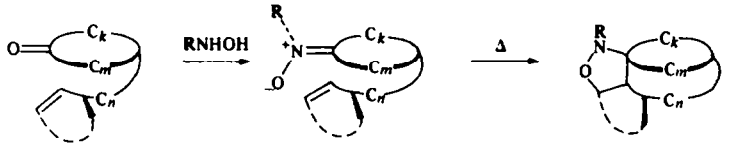
The pioneering effort by LeBel[1] led to a series of papers describing the limitations and considerable potential of intramolecular nitrone–olefin cycloadditions[2] in organic synthesis. The ring constructive power of this reaction is now well appreciated and has been employed by numerous groups[3] in the total synthesis of alkaloids and other nitrogen-containing natural products. Although the amino group is generally regarded as a "higher order" functionality, it can be easily manipulated into other functionalities.[4] We reasoned, therefore, that intramolecular nitrone–olefin cycloadditions might also be of service in the total synthesis of polycyclic terpenes.[5] Our preliminary studies[6] to examine this possibility are described herein with full experimental detail. Moreover, this approach provides an effective solution to the total syntheses of three sesquiterpenes, (±)-7,12-secoishwaran-12-ol (**44**),[7] (±)-hirsutene (**56**),[8a] and (±)-coriolin (68)[8b].

At the outset, we recognized that it would be most advantageous to employ exocyclic nitrones in the intramolecular cycloaddition since bicarbocyclic compounds would necessarily be obtained (Scheme 1). We were somewhat concerned, however, to note that exocyclic nitrones had not been utilized in cycloaddition reactions despite their initial preparation by Exner[9] some 30 years ago. Furthermore, the standard protocol for generating nitrones, condensation of ketones or aldehydes with alkylhydroxylamines, would be expected to give rise to *E*, *Z*-nitrone isomers. In most cases, dipole–olefin orbital overlap is only accessible for the *Z*-nitrone (Scheme 1), although the facile thermal *E*, *Z* equilibration[10] of nitrones would appear to mitigate this concern. With these considerations in mind, we examined the viability of this methodology for the preparation of bridged bicycloalkanes (Scheme 1, $k, m \geqslant 1$).

Preparation of bridged bicycloalkanes

The substrates chosen to test this methodology (cycloalkanones **1**–**13**) are either known compounds or readily available. Indeed, this feature affirms the facility of this strategy. The versatility of this cycloaddition was proved by systematically varying the length and positioning of the alkenyl side chain. It can be readily seen that nitrones with 2-propenyl substrates (entries 1–8) located β to the nitrone carbon cyclize most efficiently and at lower temperatures, typically in refluxing benzene. In all cases, a single diastereomer was isolated as evidenced by the corresponding ^{13}C-NMR spectrum and/or a clear AB pattern characteristic for the oxymethylene protons in the ^{1}H-NMR spectrum. The stereochemistry is assigned to be exo based upon a structural proof for isoxazolidine **14** (*vide infra*) and the expectation that endo transition states would be inaccessible. The yields are not appreciably affected by the nature of the alkyl group on the nitrone nitrogen atom or by the labile β-hydroxyl in cycloalkenol **6** (or the corresponding nitrone, entry 6). However, when serious 1,3 diaxial interactions are encountered in the transition state (entries 4 and 5), higher temperatures are required to effect cyclization and yields are severely attenuated.

The cycloaddition is also successful for nitrones appended with 3-butenyl side chains in the β position (entries 9–11). These reactions are also stereospecific and produce only the exo isomers (entries 9 and 10, *vide infra*). The sensitivity of the exocyclic nitrone cycloaddition to steric and torsional parameters is further apparent in these examples. The yields are lower (for entries 9 and 10) and higher temperatures are required to effect cycloaddition, presumably reflecting destabilizing interactions encountered from a boat-like conformation of the bridging atoms. However, the conformationally restricted nitrone derived from



Scheme 1.

ketone **11** proceeds efficiently to isoxazolidine **24**. It should be noted here that 1-aminoadamantane[11] is a known antiviral compound, and, consequently, this method may prove useful for the preparation of aminoadamantane analogs.

Finally, two additional cycloaddition substrates were examined. If the β-alkenyl side chain is lengthened by an additional methylene (entry 12), then the reaction fails completely. Entries 8 and 13 represent the only cases studied with γ-alkenyl substituted nitrones. The cycloaddition proceeds in satisfactory yield (entry 13) although it is not competitive when cycloaddition with a β-2-propenyl substituent is also possible (entry 8).[12]

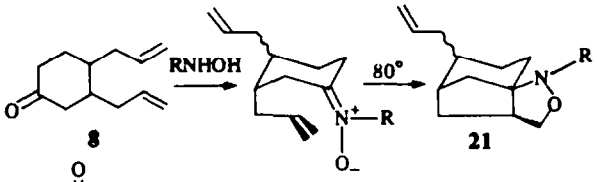
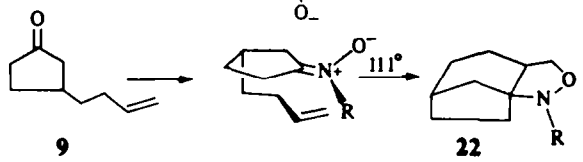
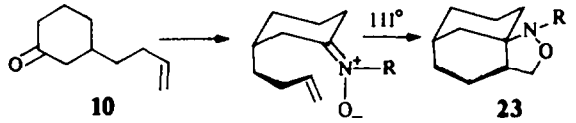
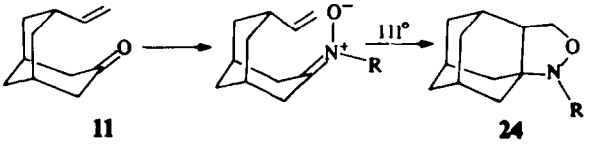
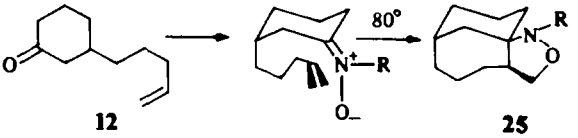
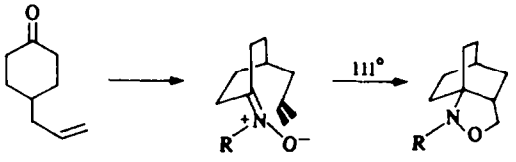
Isoxazolidine transformation studies

With the general success of this methodology now well assured, we concentrated on transforming the bridgehead nitrogen atom of isoxazolidine **14** into a hydrogen or hydroxyl moiety. The motivation for this exercise rested, in part, upon the observation that natural products incorporating the bicyclo[3.2.1] octane substructural unit often occur in pairs differing only by the presence of a bridgehead hydroxyl or hydrogen.[13] Thus, the realization of this goal would set the stage for divergent[14] total syntheses of two bridged bicyclic natural products from a common intermediate.

Table 1. Cyclizations of alkenylcycloalkanones mediated by alkylhydroxylamines

Entry	Temp	R	Yield
1	RNHOH, 80°	Me CH_2Ph Ph	84 100 74
2	80°	Me CH_2Ph	84 82
3	80°	CH_2Ph	94
4	150°	CH_2Ph	8
5	111°	Me	34
6	80°	Me CH_2Ph	66 70
7	80°	CH_2Ph	37

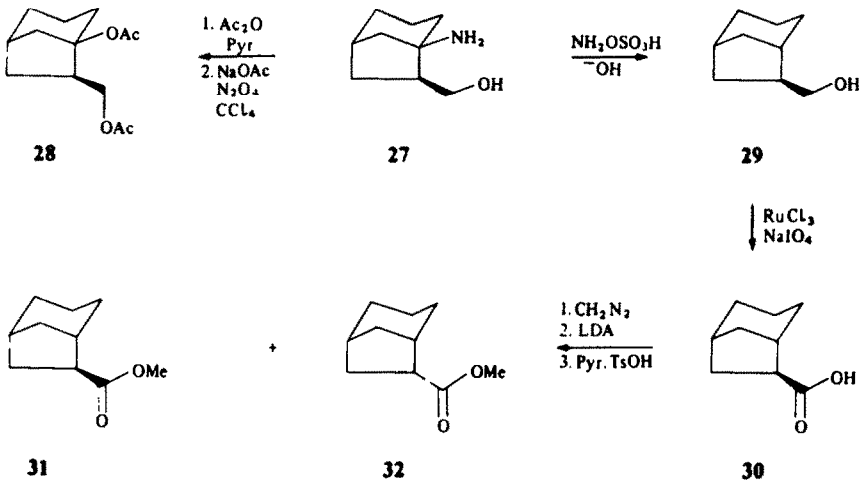
Table 1 *cont.*

Entry	Temp	R	Yield
8		Me CH_2Ph	75 90
9		CH_2Ph	47
10		Me	46
11		Me	81
12		Me	0
13		CH_2Ph	40

The introduction of the bridgehead hydroxyl or equivalent seemed the least problematical since two groups had employed White's methodology[4b] for this purpose in the total syntheses of bridged bicyclic natural products.[15] To this end, scission of both the N—O and N—benzyl bonds in isoxazolidine **14** (Scheme 2) was accomplished by catalytic hydrogenation using Pearlman's catalyst[16] ($Pd(OH)_2$, 1 atm H_2) to provide the amino alcohol **27** (73% after recrystallization). The acetylation of **27** gave an acetoxy acetamide which was deaminated using the procedure of White[4b] to provide the diacetate **28** in 55% overall yield.

The "hydrodeamination" of amino alcohol **27** with hydroxylamine-O-sulfonic acid in aqueous NaOH according to the protocol of Dolduras and Kollonitsch[4c] afforded exo-alcohol **29** (92%). The stereochemical and structural integrity of **29** and, hence, of the parent isoxazolidine **14**, was confirmed upon Sharpless[17] ruthenium tetraoxide catalyzed oxidation to the known exo-bicyclo[3.2.1]octane-6-carboxylic acid (**30**).[18] Furthermore, treatment of the corresponding methyl ester **31** with LDA followed by pyridinium tosylate gave the endo ester **32** and recovered starting material in a ratio of 3 : 1. Separation (HPLC) and treatment of the endo ester **32** with NaOMe in MeOH at 90° in a resealable tube gave complete conversion to exo ester **31**. In addition, the protons α to the carbomethoxy substituents exhibit coupling patterns and chemical shift differences in the ^{1}H-NMR spectra characteristic for similar endo and exo protons in bridged bicyclic systems.[19] Finally, isoxazolidine **22** was similarly processed to exo-bicyclo[3.2.1]octane-2-carboxylic acid (m.p. 47–49°) and the corresponding benzylamine salt (m.p. 139–140°) whose melting points were similar to those reported previously.[20] Thus, all of the stereochemical assignments in Table 1 are secure.

Having shown that the bridgehead nitrogen substituent can be easily exchanged for hydroxyl or hydrogen, we chose to briefly examine its potential for triggering rearrangement or fragmentation of the bridged bicycloalkanes to other carbocyclic systems. Indeed, this is an established tactic in organic synthesis[21] although fragmentation reactions wherein both bridgehead carbons participate in the cleavage



28 **27** **29** **31** **32** **30**

Scheme 2.

process are relatively rare,[22] perhaps due to an inaccessibility of substrates. Consequently, N-methylisoxazolidine **19** was methylated (CH_3I, 60%) and then reduced with zinc in acetic acid[3b] to provide the dimethylamino diol **33** (Scheme 3, 91% yield) which was further methylated to provide the quaternary ammonium salt **34** (67%). The desired Grob fragmentation was found to be easily effected by addition of **34** to excess sodium hydride in THF and refluxing the solution for 2 hr. After silica gel chromatography, the functionalized cycloheptanone **35**, in equilibrium with the cyclic hemiacetal form (7 : 3), was isolated in a yield of 70%. The application of this net one carbon ring expansion sequence (cf. **6** → **35**) in guaianolide[23] total synthesis now merits serious consideration.

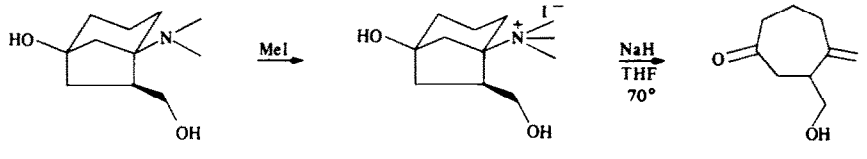
Total synthesis of (±)-7,12-*secoishwaran*-12-*ol* (**44**)

The application of this methodology in natural product synthesis was now of immediate interest. Our target for this objective was (12*S*)-7,12-secoishwaran-12-ol (**44**, Scheme 4), a sesquiterpene recently isolated by Pakrashi *et al.* from *Aristolochia indica* Linn. (Artistolochiaeceae).[7a,b] This compound exhibits 100% interceptive activity and 91.7% anti-implantation activity in mice at a single dose (100 mg kg^{-1}).[7c]

The key step in the projected synthesis was the intramolecular nitrone–olefin cycloaddition of **39** to **40**. Based on the exo preference for cycloaddition in these systems, the methallyl substituted decalone **39b** appeared to be the ideal substrate for cyclization since C-12 of secoishwaranol (**44**) would be introduced with the correct relative asymmetry. However, our previous experimentation with 3-methallylcyclohexanone (entry 4, Table 1) strongly discouraged this choice. Instead, we opted for the allyl substituted decalone **39a**. It was felt that the resulting cycloadduct, **40a**, would serve as a viable precursor to the exocyclic olefin **42** which had previously been converted to secoishwaranol (**44**).[7d]

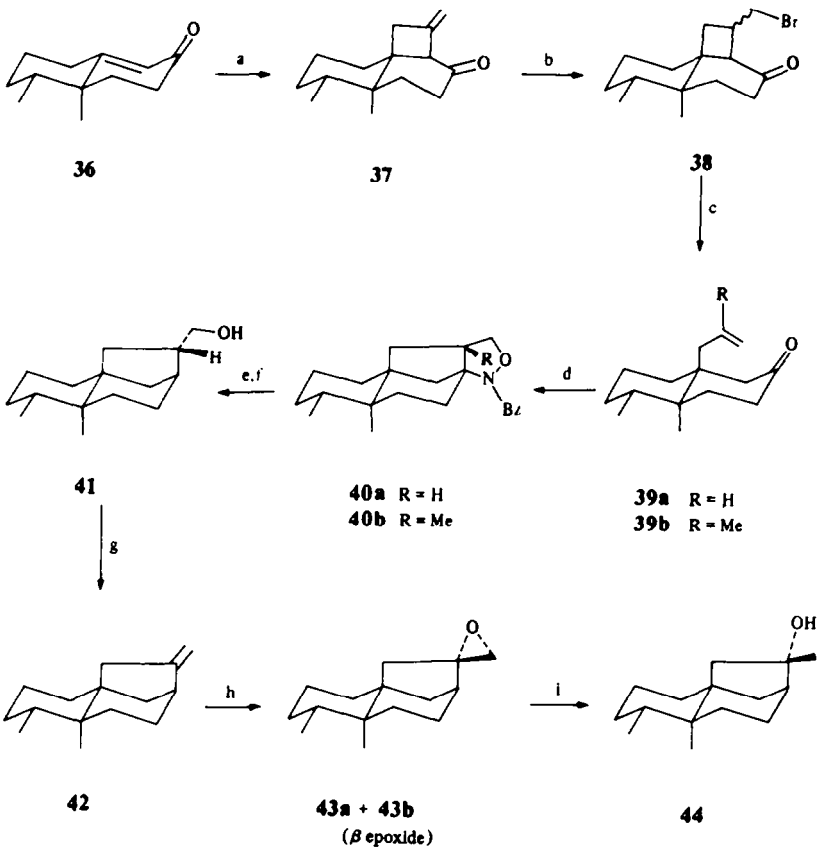
A concise synthesis of cycloaddition substrate **39a** was our initial objective. The conjugate addition of an allylic metal reagent to the known enone **36**[24] is obviously the simplest approach. However, 1,4-addition of diallyl cuprate would be expected to deliver the *cis*-decalone.[25] Furthermore, the stereochemical result obtained upon subjection of **36** to the Sakurai conditions[26] (allyltrimethylsilane, $TiCl_4$) is by no means clear. Nonetheless, we attempted the Sakurai reaction but only recovered the starting enone **36**. We then turned to the known allene-**36** photocycloadduct, **37**,[24] as a precursor to decalone **39a**. The net hydrogenation of the α-keto carbon–vinyl carbon sigma bond was easily accomplished in two steps. Photochemically initiated anti-Markovnikov addition of HBr[27] to olefin **37** gave a mixture of bromides which was immediately subjected to reductive fragmentation by the agency of lithium in ammonia[28] to provide the desired keto olefin (60% overall).

The critical cyclization of **39a** to **40a** proceeded smoothly (80%), provided the nitrone was formed in ethanol (8 hr, reflux) in the presence of a drying agent



33 **34** **35**

Scheme 3.



Scheme 4. (a) allene, *hv*, hexanes; (b) HBr, *hv*, hexanes; (c) Li/NH_3; (d) $C_6H_5CH_2NHOH$, EtOH, Na_2SO_4; (e) H_2, $Pd(OH)_2$, EtOH; (f) NH_2OSO_3H, OH^-, 68% EtOH; (g) ArSeCN, Bu_3P, THF, O_3; (h) MCPBA, CH_2Cl_2, aq $NaHCO_3$; (i) $LiAlH_4$, Et_2O.

(anhydrous Na_2SO_4). Refunctionalization of isoxazolidine **40a** (m.p. 116°) proved uneventful. Thus, catalytic hydrogenation and subsequent "hydrodeamination" gave alcohol **41** (65%) which was dehydrated using the technology of Grieco *et al.*[29] (ArSeCN, Bu_3P, THF; O_3; 65%).

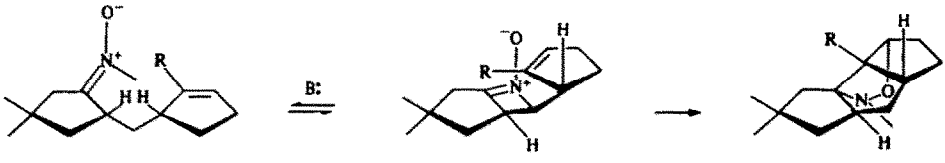
Epoxidation of olefin **42** with mCPBA at 0° for 3 hr gave a mixture of epoxides (7.6:1, 90%). Although the isomeric mixture could be separated by HPLC, it was more convenient to directly submit the mixture to reduction ($LiAlH_4$). After purification by HPLC, crystalline (±)-7,12-secoishwaran-12-ol (m.p. 116–117°, 71%) was obtained which was identical with an authentic sample (TLC, IR, 360 MHz ^{1}H-NMR, ^{13}C-NMR).

Preparation of fused bicycloalkanes

Total synthesis of (±)-*hirsutene* (**56**) *and* (±)-*coriolin* (**68**). The extension of the methodology discussed herein to the preparation of *fused* bicycloalkanes is also conceivable, namely, by intramolecular cycloaddition of an exocyclic nitrone with an α-appended olefinic side chain (cf. Scheme 1; $m = 0, k, n \geqslant 1$). Indeed, Kakisawa and co-workers reported on the feasibility of this proposition,[5d] thereby obviating the necessity for our own preliminary studies. Consequently, we directed our attention to the construction of fused *tricarbocyclic* ring systems mediated by intramolecular nitrone cycloadditions with *cyclo*alkenyl substituents (Scheme 1, dotted lines). Upon examination of the various hypothetical cases, one can quickly surmise that the anti isomer shown in Scheme 1 should have a kinetic advantage toward cyclization. Furthermore, since the internal dipolarophile is connected to the nitrone α carbon, the *syn* and *anti* isomers should be capable of *in situ* base catalyzed interconversion. In essence, this strategy for polycycle construction would permit the joining of two cycloalkanes to create a central, third ring *with important stereochemical consequences.*

Hirsutene (**56**),[8] a linearly fused tricyclopentanoid, represents an attractive target on which to formulate a test of this strategy. Thus, inspection of molecular models reveals that the intramolecular nitrone–olefin cycloaddition is impossible for the *syn* isomer **48** (Scheme 5) but quite feasible for the *anti* isomer **49** (molecular models also indicate that dipole–dipolarophile overlap is more easily accommodated with the *E*-nitrone as shown rather than the *Z*-nitrone. Nevertheless, the same stereoisomer would be produced). Under basic conditions, the *syn*-nitrone **48** should epimerize and also cyclize to the cycloadduct **50** which possesses the correct relative stereochemistry and functionality useful for completion of the hirsutene (**56**) total synthesis.

Our first investigation of this method commenced with the preparation of ketone **47a** (Scheme 6) since it was felt that the corresponding nitrone **49a** (R = H) would have the highest probability of cyclization *vis-à-vis* the more sterically encumbered nitrone **49b** (R = Me). To that end, conjugate addition of allylsilane **46a**[30]

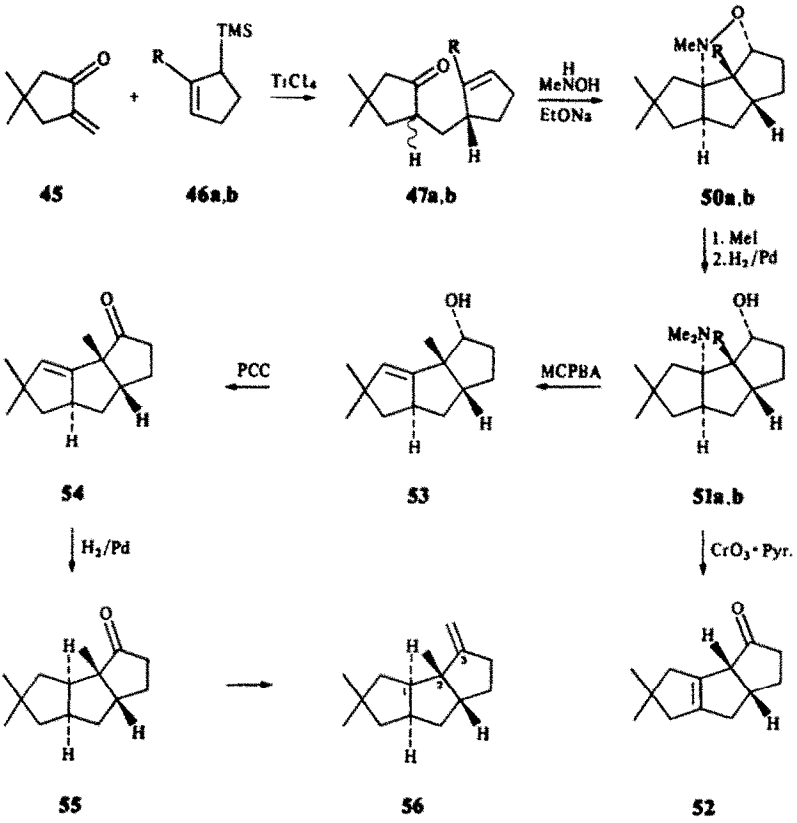


48a,b **49a,b** **50a,b**

a R = H b R = Me

Scheme 5.

to enone **45** (see Experimental) according to the Sakurai protocol[26] rendered the desired cycloaddition substrate **47a** as a mixture of diastereomers (45%, the yield could be substantially improved by modifying this procedure, *vide infra*). We were gratified to discover that the cyclization of ketones **47a** via intermediate nitrones **48a** and **49a** (1.1 equiv MeNHOH · HCl, 3 equiv NaOEt, EtOH, toluene) proceeded smoothly (70%) to afford a single isoxazolidine **50a**. Yields were markedly suppressed when stoichiometric quantities of NaOEt were used which suggests that excess base promotes the desired concomitant α-epimerization. The isoxazolidine **50a** was subjected to a sequence of methylation (CH_3I) and hydrogenation (5% Pd/C, H_2) to furnish the hydroiodide of **51a** (68%). Collins oxidation of this salt directly provided the deconjugated ketone **52**[31] (57%). In principle, ketone **52** is a serviceable intermediate enroute to hirsutene (**56**). However, concurrent experimentation in the methyl series (e.g. **47b**) warranted termination of this less appealing route. In particular, dropwise addition of allylsilane **46b** to enone **45** complexed with $TiCl_4$ gave a mixture of ketones **47b** (2:1 according to the corresponding ^{13}C-NMR spectrum, 36%). In addition, another compound was isolated (40%) which was derived from conjugate addition of the initially formed titanium enolate of **47b** to another equivalent of enone **45**. This troublesome side reaction could be eliminated by inverse addition of enone **45** and $TiCl_4$ to excess allylsilane **46b** (1.5 equiv, CH_2Cl_2, −78°) and provided the diastereomers **47b** in good yield (71%). These isomers were separated by preparative HPLC and each was independently converted to the respective N-methyl nitrone **48b/49b** (1.1 equiv MeNHOH · HCl, 3 equiv NaOEt, EtOH, toluene) and thence to the same cycloadduct **50b** after 36 hr of reflux. When



45 **46a,b** **47a,b** **50a,b**

54 **53** **51a,b**

55 **56** **52**

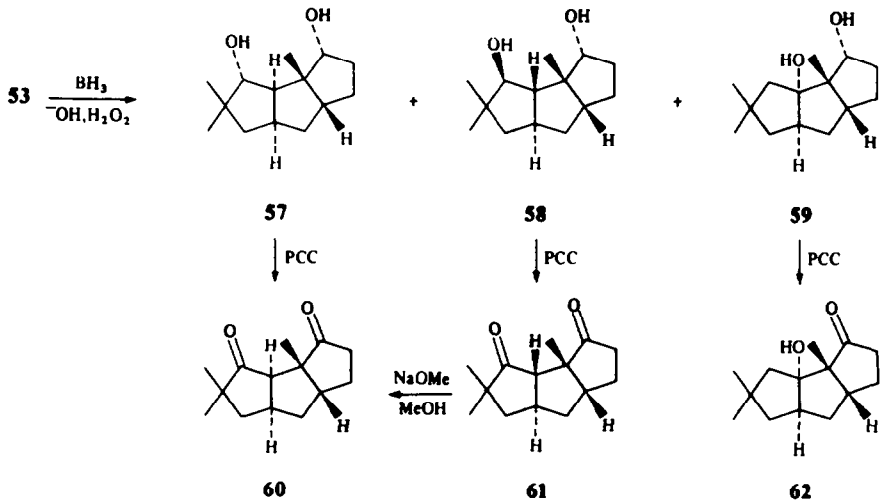
Scheme 6.

stoichiometric quantities of NaOEt were used, the major isomer led to intractable material upon continued heating, whereas the minor isomer rapidly cyclized. It must be deduced, therefore, that the major nitrone isomer is the undesired *syn* isomer **48b**. Obviously, it was more convenient to submit the isomeric mixture of ketones **47b** to the optimized reaction conditions. A 75% yield of isoxazolidine **50b** was obtained after chromatography.

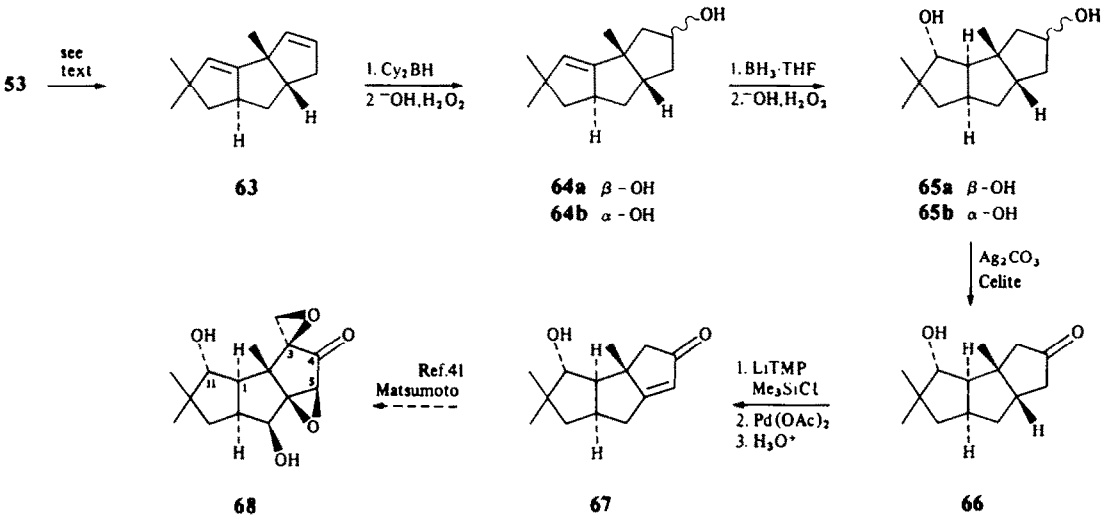
In order to complete the hirsutene synthesis, C-1 of isoxazolidine **50b** must be stereospecifically hydrodeaminated and C-3 must be oxidized to arrive at the ketone **55** (norhirsutene) which has previously been converted to (±)-hirsutene **56**.[32] In the event, methylation (excess CH_3I) of **50b** and subsequent N—O scission (H_2/Pd; NaOH) gave dimethylamino alcohol **51b** (89% overall yield). Cope elimination[4a] of the derived amine oxide (MCPBA, CH_2Cl_2, aq $NaHCO_3$, 50°, 48 hr, 90%) gave a single regioisomer, **53**, and none of the thermodynamically preferred elimination product[31c] with the double bond endocyclic to both rings (>98:2 by ^{13}C-NMR). Experiments are underway to uncover the factor(s) responsible for this surprising regiospecificity. Nonetheless, oxidation of alcohol **53** furnished ketone **54** which was stereospecifically hydrogenated to afford the known ketone **55** (65%) which was identical in all respects (IR, 360 MHz ^1H-NMR, ^{13}C-NMR, m.p.) with an authentic sample and thereby constitutes a formal total synthesis of (±)-hirsutene (**56**).

We next turned our attention to converting alcohol **53** to the antitumor, antibiotic coriolin (**68**) via one of several possible advanced intermediates prepared in previous coriolin syntheses.[8b] The olefin moiety in **53** offers access to the C(11) α-hydroxyl and the *cis*-A,B ring fusion present in coriolin by a hydroboration, oxidation sequence. This strategy had not been exploited in the previous coriolin syntheses and, therefore, deserved investigation. It quickly became apparent that this operation was not straightforward (Scheme 7). Hydroboration of **53** (excess BH_3, 60°, 1 hr) and standard oxidative workup gave a mixture of the three diols **57**, **58**, **59** in a ratio of 1:2:2, respectively. Inspection of molecular models clearly reveals that the alkoxyborane moiety derived from **53** and 1 equiv of borane is positioned to sterically inhibit intermolecular attack by another equivalent of borane on the α face. Therefore, approach by borane on the β face is preferred and ultimately gives rise to the diol **58** despite the formation of the strained *trans*-bicyclo[3.3.0]octane ring system. The formation of diol **59** is most likely a consequence of an intramolecular hydroboration reaction involving the alkoxyborane derivative of **53**.[33] Indeed, when the alcohol **53** was added to 1 equiv of borane, the diol **59** was the major product (**57**:**58**:**59**; 1:1.3:4). The structural assignments for diols **57**–**59** were confirmed by subjecting each to PCC in CH_2Cl_2. Diol **57** afforded the diketone **60** and had a ^1H-NMR spectrum and m.p. similar to those previously reported by Mehta *et al.* in the context of their coriolin (**68**) total synthesis.[34] Oxidation of diol **58** gave the diketone **61** which, upon treatment with catalytic NaOMe in MeOH, rapidly epimerized to the less strained diketone **60**. The diol **59** provided the hydroxy ketone **62**. A carbonyl stretch at 1716 cm^{-1} in the infrared spectrum (in contrast to 1733 cm^{-1} for **60**) and a resonance at δ 4.5 in the NMR spectrum (which disappeared upon addition of D_2O) are indicative of an intramolecular hydrogen bond[35] which would not be possible for an isomer epimeric at the hydroxyl-bearing carbon.

It was clear at this point that the problematical hydroxyl functionality of **53** must be removed and replaced with a much smaller group (i.e. H) in order to effect the desired facial selectivity as well as regioselectivity in the hydroboration reaction. To this end, we examined several methods for dehydrating alcohol **53** to the diene **63**. The corresponding tosylate (TsCl, Pyr) and epimeric bromide (Ph_3PBr_2, CH_2Cl_2) were resistant to elimination (DBU, toluene, reflux). However, diene **63** could be obtained in moderate yield by oxidation of alcohol **53** to ketone **54** (PCC, CH_2Cl_2) which was converted to the corresponding tosylhydrazone and then treated with LDA (5 equiv, 38% overall). A much more satisfactory solution (Scheme 8) involved the preparation of a thionocarbonate from alcohol **53** and O-3,4-dimethylphenyl chlorothiofor-



Scheme 7.



Scheme 8.

mate (1.2 equiv, Pyr)[36] which was then pyrolyzed (220°) with collection of the volatile **63** in a cold trap (70% overall). The hydroboration of diene **63** with dicyclohexylborane (1.5 equiv, 25°) proceeded with complete chemo- and regioselectivity and high stereoselectivity to provide alcohols **64a,b** (14 : 1, 85%) after oxidation (H_2O_2, NaOH). The isomers were separated by HPLC and the major isomer was assigned the β configuration based on the expected preferential attack of Cy_2BH on the convex face of the B, C ring system. Moreover, the resonance for the methine proton on the hydroxylated carbon for **64a** and **64b** appeared as a pentet and heptet, respectively. The analogous proton resonance for regioisomers would show a doublet of doublet or triplet pattern (cf. NMR spectrum of **53**). It was more convenient to use the mixture directly since both stereoisomers are eventually converted to the same intermediate (**66**, *vide infra*).

We were gratified to discover that hydroboration (excess BH_3, 12 hr, 27°) of **64a,b** proceeds both regio- and stereospecifically in the desired sense to deliver, after oxidation, the diols **65a,b** (81%). Moreover, in a labor-saving preparation of **65**, the sequential hydroboration reactions (i.e. **63** → **64** → **65**) were performed in one pot using the crude pyrolysate from the thionocarbonate of **53** (35% overall from **53**, see Experimental). Selective oxidation of the C(4) hydroxyl of diols **65a,b** was easily realized through the agency of Fetizon's reagent[37] (8 equiv, 79°, 1.2 hr) to furnish hydroxy ketone **66** in excellent yield (94%). The corresponding diketone was observed (10%) only when extended reaction periods were employed (4 hr).

In order to complete a formal total synthesis of coriolin (**68**), ketone **66** must be oxidized to enone **67**. An analogous problem was recently encountered and solved by Greene *et al.* in their hirsutic acid total synthesis,[38] namely, oxidation with a mixture of $PdCl_2$ and $Pd(OAc)_2$ in refluxing aqueous dioxane. Unfortunately, subjection of ketone **66** to these conditions gave not only the enone **67** (28% yield based on 75% conversion) but also competing oxidation of the C(11) hydroxyl (6% of the diketone derived from **66** and 17% of the keto enone derived from **67**). Consequently, the hydroxy ketone was converted to a mixture of $\Delta^{3,4}$ and $\Delta^{4,5}$-trimethyl silyl enol ethers (1 : 6, respectively; 5 equiv lithium tetramethylpiperdide, 10 equiv Me_3SiCl) which was then subjected to the Saegusa protocol for oxidation of silyl enol ethers [$Pd(OAc)_2$, CH_3CN][39] followed by hydrolysis of the extraneous trimethylsilyl ether to afford the enone **67** (50% yield overall, 54% based on recovered **66**). Spectra (360 MHz ^{1}H-NMR, IR) of our sample of **67** were identical to those kindly provided by Professor Koreeda.[40] Enone **67** has been previously converted to (±)-coriolin by Matsumoto and co-workers.[41]

Concluding remarks

We have demonstrated that exocyclic nitrones smoothly participate in intramolecular cycloadditions and are of considerable utility in the expeditious and stereospecific assemblage of bridged and fused polycarbocyclic frameworks. The isoxazolidine moiety of these cycloadducts can be efficiently sacrificed for other functionality present in various terpenes. The further development of this strategy and its application in natural product total synthesis is in progress.

EXPERIMENTAL

General methods. 60 MHz ^{1}H-NMR spectra were recorded on a Varian T-60, 90 MHz ^{1}H-NMR spectra were recorded on a Varian EM 390, 200 MHz ^{1}H-NMR spectra were recorded on a Varian XL200, and 360 MHz ^{1}H-NMR spectra were recorded on a Nicolet NMC 360. Data are reported as follows: chemical shifts, in parts per million downfield of internal TMS (number of protons, multiplicity, coupling constants(s)). ^{13}C-NMR spectra were obtained on either a Varian XL100, XL200 or on a Nicolet NMC 360. Chemical shifts are referenced to the central peak of the $CDCl_3$ triplet (77.00 ppm). IR absorption spectra were obtained on a Perkin–Elmer model 283 and were referenced to poly(styrene) (1601 cm^{-1}). High resolution mass spectra were provided by the Midwest Center for Mass Spectrometry, University of Nebraska, Lincoln, Nebraska. Elemental analyses were provided by Galbraith Laboratories,

Inc., Knoxville, Tennessee. M.ps were determined in open Pyrex capillary tubes on a Thomas–Hoover Unimelt apparatus. M.ps and b.ps are uncorrected. Gas chromatography was performed on a Varian Aerograph model 920 with an 8 ft × 1/4 in glass 10% SE-30 on Chromosorb Q conditioned at 210° (Column A) or an 8 ft × 1/4 in glass 10% UCQ982 on Chromosorb Q 80/100 conditioned at 250° (Column B). All high pressure liquid chromatography (HPLC) was performed on a Waters 590 pump equipped with an R401 differential refractometer and a UK6 injector. All chromatography was carried out on E. M. Reagents silica gel (400–230 mesh) according to the method of Still *et al.*,[42] and all TLC on commercial silica gel plates, Analtech Silica HLF 250 m. Solvents were dried by distillation over an appropriate drying agent under a N_2 atmosphere and stored under N_2 over Linde molecular sieves (4 Å). All reactions involving organometallics, air sensitive reagents, and nitrone cycloadditions were carried out in apparatus that was flame dried and cooled under a stream of dry N_2. Evaporation of solvents was performed first at aspirator pressure on a Buchi rotoevaporator and then at *ca* 0.050 mm Hg at room temperature until a constant weight was obtained.

N-*Methylisoxazolidine* **14**. 3-(2-Propenyl)cyclohexanone[26a] (1, 807 mg, 5.84 mmol) was dissolved in 10 ml dry 1:10 MeOH–benzene in a dry 25 ml flask. To this was added freshly distilled methylhydroxylamine[43] (520 mg, 11.6 mmol). The H_2O was azeotropically removed and the reaction refluxed overnight. The solvent was removed and the product isolated by flash column chromatography (75 g, 1:3 EtOAc–pet. ether) yielding 821 mg (84% yield) of a colorless oil. IR (neat) 2930, 2855, 1450, 1340, 1268, 1103, 1038, 990 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 4.05 (1H, br dd, J = 8.4, 8.1 Hz), δ 3.42 (1H, dd, J = 8.1, 4.2 Hz), 2.83–2.30 (2H, m), 2.53 (3H, s), 2.07–1.03 (10H, m); mass spectrum *m/e* (rel intensity) 167 (M^+, 72.14), 150 (9.91), 138 (15.43), 124 (100.00), 110 (7.86), 99 (8.31), 87 (13.10), 79 (8.57). Exact mass calc for $C_{10}H_{17}NO$: 167.1311. Found: 167.1314.

N - *Benzylisoxazolidine* **14**. 3 - (2 - Propenyl)cyclohexanone[26a] (1, 825 mg, 5.97 mmol) was dissolved in dry benzene (20 ml). N-Benzylhydroxylamine[44] (809 mg, 6.57 mmol) was added and the soln heated with azeotropic removal of water followed by an additional 3 hr of reflux. The solvent was removed and the material redissolved in twice its volume in 1:5 EtOAc–pet. ether. The soln was filtered through silica gel and the solvent removed again to give a colorless oil (1.495 g, 100%). IR (neat) 3060, 3030, 2940, 1607, 1497, 1454, 1347, 1272, 1010, 985, 717, and 695 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 90 MHz) δ 7.27 (5H, m), 3.90 (1H, dd, J = 8.3, 7.5 Hz), 3.75 (2H, s), 3.38 (1H, dd, J = 4.5, 8.3 Hz), 2.54 (2H, m), 2.17–1.11 (10H, m); ^{13}C-NMR (25.1 MHz, $CDCl_3$) δ 138.49, 128.49, 128.07, 126.75, 76.73, 73.86, 56.07, 49.25, 37.59, 37.25, 33.37, 31.54, 22.07. (Found: C, 78.72; H, 8.51. Calc for $C_{16}H_{21}NO$: C, 78.91; H, 8.69%.)

N - *Methylisoxazolidine* **15**. 3 - (2 - Propenyl)cycloheptanone[45] (200 mg, 1.31 mmol) was added to 10 ml benzene. Freshly distilled methylhydroxylamine[43] was added and the water was azeotropically removed followed by an additional 8 hr of reflux. The solvent was then removed and the resulting brown oil purified via flash chromatography (20 g silica gel, 1:5 EtOAc–pet. ether) which gave 201 mg (84%) of a light yellow oil. IR (neat) 2920, 2850, 1450, 1260, 1055, 1003, and 988 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 3.87 (1H, br dd, J = 7.5, 7.5 Hz), 3.45 (1H, dd, J = 7.5, 1.5 Hz), 2.80–2.27 (2H, m), 2.55 (3H, s), 2.10–1.10 (12H, m); mass spectrum *m/e* (rel. intensity) 181 (M^+, 51.89), 164 (6.71), 152 (7.82), 140 (21.52), 135 (22.18), 124 (100.00), 112 (21.16), 99 (18.46), 87 (16.05), 70 (23.20). Exact mass calc for $C_{11}H_{19}NO$: 181.1467. Found: 181.1460.

N-*Benzylisoxazolidine* **16**. A soln of **3**[26a] (348 mg, 1.81 mmol) and N-benzylhydroxylamine (243 mg, 1.99 mmol) in 10 ml of benzene was refluxed for 3 hr with azeotropic removal of water. Concentration *in vacuo* followed by purification via flash column chromatography on silica gel (1:20 EtOAc–hexanes) provided a colorless oil (507 mg, 94%). IR (film) 3060, 3030, 2920, 2860, 1495, 1460, 1445, 1345, 1175, 985 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 7.25 (5H, m), 3.88 (1H, dd, J = 9 and 7 Hz), 3.75 (2H, br s), 3.40 (1H, dd, J = 9 and 4 Hz), 2.59 (1H, dddd, J = 15, 8, 6 and 4 Hz), 2.0–1.0 (17H, m); ^{13}C-NMR (90.5 MHz, $CDCl_3$) δ 138.515, 129.515, 127.726, 126.082, 74.216, 55.966, 48.427, 47.227, 47.087, 42.123, 38.553, 29.821, 29.679, 29.294, 29.082, 26.635, 24.084; mass spectrum *m/e* (rel intensity) 297 (99) [M^+], 256 (5), 240 (5), 226 (19), 206 (6), 175 (5), 146 (7), 91 (100), 79 (7), 65 (8), 55 (5). Exact mass calc for $C_{20}H_{27}NO$: 297.2092. Found: 297.2080. (Found: C, 80.61; H, 9.28. Calc for $C_{20}H_{27}NO$: C, 80.76; H, 9.15%.)

N-*Methylisoxazolidine* **19**. Compound **6**[46] (900 mg, 5.84 mmol) was dissolved in 100 ml 1:10 MeOH–benzene followed by freshly distilled methylhydroxylamine[43] (545 mg, 11.6 mmol). The water was azeotropically removed and the mixture refluxed 7 hr. The solvent was then removed and the brown oil purified via flash chromatography (70 g silica gel, 1:5 MeOH–EtOAc) yielding 705 mg (66%) of a colorless oil. IR (neat) 3380 (broad), 2942, 2860, 1448, 1334, 1268, 1123, 1070, and 1000 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 4.02 (1H, dd, J = 7.0, 10.5 Hz), 4.3 (1H, br s, overlapping), 3.48 (1H, br dd, J = 4.5, 7.0 Hz), 2.48 (3H, s), 2.71–0.87 (11H, m); mass spectrum *m/e* (rel intensity) 183 (M^+, 100.00), 166 (55.70), 154 (10.07), 140 (39.89), 124 (25.00), 100 (51.81), and 87 (65.19). Exact mass calc for $C_{10}H_{17}NO_2$: 183.1258. Found: 183.1258.

N-*Benzylisoxazolidine* **20**. Compound **7**[47] (31.6 mg, 0.21 mmol) was dissolved in 4 ml dry benzene in a 10 ml flask fitted with a Dean Stark trap and a condenser. Benzylhydroxylamine[44] (28.3 mg, 0.23 mmol) was added and the mixture was refluxed for 14 hr. The solvent was evaporated and the crude product chromatographed on silica gel (3.5:5 EtOAc–hexanes) to yield 19.5 mg (37%) of a light yellow oil: TLC (EtOAc) R_f = 0.45; IR (CCl_4) 3592 (free OH), 3600–3100 (bonded OH), 3052, 3018, 2931, 1493, 1450, 1325, 1267, 722, 700, 692 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 7.5–7.1 (m, 5H), 5.37 (br s, 1H), 4.37 (d, J = 14 Hz, 1H), 4.23 (d, J = 14 Hz, 1H), 3.84, 3.78 (overlapping d, J *ca* 9 Hz, 2H), 2.3–1.1 (m, 9H); mass spectrum *m/e* (rel intensity) 257 (28.11) [M^+], 240 (7.59), 228 (55.93), 106 (17.14), 91 (100.00), 69 (16.19), 57 (19.33). Exact mass calc for $C_{16}H_{19}NO$: 257.1416. Found: 257.1403.

N-*Benzylisoxazolidine* **21**. *Cis*- and *trans*-**8**[45] (352 mg, 1.98 mmol) was weighed into a 10 ml round bottom flask fitted with a Dean Stark trap and a condenser. Dry benzene and benzylhydroxylamine[44] (268 mg, 2.18 mmol) were added and the soln refluxed for 12 hr. The benzene was removed *in vacuo* and the product purified by chromatography (silica gel, 1:10 EtOAc–hexanes) to yield 509 mg (91%) of a light yellow oil: TLC (2:3 EtOAc–hexanes) R_f = 0.6; IR (neat) 3059, 3024, 2932, 2858, 1639, 1495, 1453, 1156, 985, 722, 695 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 7.47–7.07 (m, 5H), 5.97–5.47 (m, 1H), 5.16–4.77 (m, 2H), 3.95 (dd, J = 8.5, 8.5 Hz, 1H), 3.77 (s, 2H), 3.38 (dd, J = 8.5, 4 Hz, 1H), 2.8–0.8 (m, 13H); mass spectrum *m/e* (rel intensity) 283 (M^+, 42.58), 200 (9.02), 192 (5.18), 175 (6.32), 91 (100.00), 79 (5.18), 65 (6.82). Exact mass calc for $C_{19}H_{25}NO$: 283.1936. Found 283.1929.

N - *Benzylisoxazolidine* **22**. 3 - (3 - Butenyl)cyclopentanone[48] **9** (200 mg, 1.61 mmol) was added to 10 ml of toluene followed by benzylhydroxylamine[44] (257 mg, 2.09 mmol). The water was azeotropically removed and the reaction refluxed for 48 hr. After removing the solvent, the brown oil was purified via flash chromatography (18 g silica gel, 1:5 EtOAc–pet. ether) which afforded 182 mg (47%) of a yellow oil. IR (neat) 3055, 3025, 2930, 2865, 1494, 1451, 1300, 1207, 965, 750, and 688 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 7.27 (5H, m), 4.05 (1H, dd, J = 6.0, 7.5 Hz), 3.80 (2H, s), 3.42 (1H, dd, J = 6.0, 10.5 Hz), 2.67–1.00 (12H, m); ^{13}C-NMR (90.5 MHz, $CDCl_3$) δ 138.490, 129.220, 127.693, 126.105, 76.234, 69.813, 58.975, 47.308, 39.461, 35.249, 31.622, 27.292, 22.470; mass spectrum *m/e* (rel intensity) 243 (21.90) [M^+], 214 (33.89), 170 (4.57), 91 (100), 65 (7.56). Exact mass calc for $C_{16}H_{21}NO$: 243.1624. Found: 243.1618.

N-*Methylisoxazolidine* **23**. Compound **10**[49] (152 mg, 1 mmol) was added to 5 ml toluene followed by freshly distilled methylhydroxylamine[43] (94 mg, 2 mmol). The water was

azeotropically removed and the reaction refluxed for 12 hr. The solvent was removed and the brown oil purified via flash chromatography (75 g silica gel, 1:3 EtOAc–pet. ether) which yielded 83 mg (46%) of a colorless oil. IR (neat) 2958, 2930, 1462, 1260, 1100, 1028, 1015, 800 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 3.99 (1H, dd, J = 7.5, 7.5 Hz), 3.45 (1H, dd, J = 6.8, 7.5 Hz), 2.53 (3H, s), 2.77–0.77 (14H, m); mass spectrum *m/e* (rel intensity) 181 (M^+, 17.29), 152 (5.15), 138 (100.00), 126 (7.86), 110 (3.59), 99 (6.85), 79 (4.64). Exact mass calc for $C_{11}H_{19}NO$: 181.1467. Found: 181.1462.

N-*Methylisoxazolidine* **24**. Ketone **11**[50] (80 mg, 0.49 mmol) was added to a soln of MeNHOH·HCl (74 mg, 0.88 mmol) and NaOMe (48 mg, 0.88 mmol) in MeOH (3 ml). The mixture was refluxed until TLC analysis indicated the absence of **11** (0.5 hr). Toluene was added (6 ml) and the mixture was refluxed using a Dean Stark trap to remove the MeOH. After 2 hr, the solvent was removed *in vacuo* and the residue chromatographed to provide 77 mg of a colorless oil (81%). IR (neat) 2900, 1450, 1090, and 970 cm^{-1}. ^{1}H-NMR (360 MHz, $CHCl_3$, 22°) δ 4.11 (0.5H, t, J = 7.69 Hz), 3.92 (0.5 H, t, J = 7.28 Hz), 3.77 (m, 1H), 2.55 (br s, 3H), 2.54–1.40 (m, 14H). The chemical shift nonequivalence of the oxymethylene protons (δ 4.11 and 3.92) is attributed to slow N inversion.[51] The coalescence temp for these protons is 52° leading to an estimated free energy of activation $\Delta G^{\ddagger} = 15.8$ kcal mol^{-1}.[51a] This value is comparable to the N inversion barrier determined for N-methylisoxoazolidine[51b] in $CHCl_3$ ($\Delta^{\ddagger} = 15.6$ kcal mol^{-1}) and other isoxazolidines.[51c,d] Mass spectrum *m/e* (rel intensity) 193 (M^+, 100.00), 165 (22.96), 136 (97.00), 108 (65.90), 106 (30.01). Exact mass calc for $C_{12}H_{19}NO$: 193.1466. Found: 193.1458. (Found: C, 73.26; H, 9.53. Calc for $C_{12}H_{19}NO$: C, 72.88; H, 9.81%.)

N-*Benzylisoxazolidene* **26**. Compound **13**[52] (100 mg, 0.73 mmol) was added to 5 ml toluene followed by benzylhydroxylamine[44] (117 mg, 0.95 mmol). The water was azeotropically removed and the mixture refluxed for 16 hr. The solvent was removed and the brown oil purified via flash chromatography (7 g silica gel, 1:7 EtOAc–pet. ether) which afforded 71 mg (40%) of a light yellow oil. IR (neat) 2955, 2900, 1440, 1407, 1255, 1015, and 798 cm^{-1}; ^{1}H-NMR (60 MHz, $CDCl_3$) δ 7.40 (5H, m), 4.18 (1H, dd, J = 7.0, 9.2 Hz), 3.85 (2H, s), 3.61 (1H, dd, J = 7.0, 10.0 Hz), 3.00–1.00 (12H, m).

1-*Amino*-7-exo-(*hydroxymethyl*)*bicyclo*[3.2.1]*octane* **27**. Compound **14** (540 mg, 2.22 mmol) was dissolved in 25 ml of 95% EtOH, 0.3 equiv of palladium hydroxide on carbon (20%) was added and the mixture was placed under an atmosphere of H_2. After the H_2 uptake ceased, the mixture was filtered and the solvent removed. After recrystallization from pet. ether–EtOAc, 270 mg (73%) of a white solid was obtained, m.p. 74.5–75.0°. IR ($CHCl_3$) 3320 (broad), 2930, 2850, 1580, 1445, 1122, 1025, 890, and 825 cm^{-1}; ^{1}H-NMR (90 MHz, DMSO-d_6) δ 3.48 (2H, m), 2.80 (3H, br s), 2.30–1.10 (12H, m); mass spectrum *m/e* (rel intensity) 155 (1.78) [M^+], 138 (4.33), 125 (2.55), 112 (24.73), 96 (100.00), 94 (5.49). Exact mass calc for $C_9H_{17}NO$: 155.1310. Found: 155.1309. (Found: C, 69.32; H, 10.86; N, 8.89. Calc for $C_9H_{17}NO$: C, 69.63; H, 11.04; N, 9.02%.)

1-*Acetoxy*-7-*acetoxymethylbicyclo*[3.2.1]*octane* (**28**). The amino alcohol **27** (20 mg, 0.13 mmol) was dissolved in pyridine (1 ml) and Ac_2O was added (0.3 ml, 3.2 mmol). After stirring for 4 hr, the mixture was diluted with water and then ether. The ether layer was separated and washed with 1 M HCl, sat $NaHCO_3$, brine and then dried (Na_2SO_4). Evaporation of the solvent gave N-(7-acetoxymethylbicyclo[3.2.1] octylacetamide as a solid (23 mg, 75%). M.p. 129–131°, ^{1}H-NMR (90 MHz, $CDCl_3$) δ 4.8 (br s, 1H), 3.9 (m, 2H), 2.7–1.0 (m, 14H), 2.0 (s, 3H), 1.9 (s, 3H). The crude amide was dissolved in CCl_4 (1.5 ml) and added to a cold (0°) soln of CCl_4 (0.7 ml) containing NaOAc (45 mg, 0.54 mmol) and N_2O_4 (558 μl of a 0.54 M soln in CCl_4, 0.3 mmol). The soln was warmed to room temp and stirred for 3 hr. The mixture was diluted with ether–hexanes (1:1), washed with sat $NaHCO_3$, brine and dried (Na_2SO_4). Evaporation of the solvent and chromatography (8 g silica gel, EtOAc–hexanes, 5:95) gave 17 mg (55% overall) of a colorless oil. IR (neat) 2920, 1735, 1453, 1360, 1245, 1090, 1032 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 4.05 (1H, dd, J = 11, 6), 3.94 (1H, dd, J = 11, 8), 2.44 (1H, m), 2.21 (1H, m), 2.1–1.2 (16H, m), 2.01 (3H, s), 1.94 (3H, s); E. I. mass spectrum *m/e* (rel intensity) 180 (9), 138 (100), 123 (16), 110 (9), 97 (93), 80 (19), 69 (29), 55 (19); C.I. mass spectrum *m/e* (rel intensity) 241 (28) [M + 1], 181 (91), 149 (100), 133 (4), 121 (13), 103 (53). C.I. exact mass calc for $C_{13}H_{21}O_4$: 241.1440. Found: 241.1431.

exo-6-(*Hydroxymethyl*)*bicyclo*[3.2.1]*octane* **29**. To **27** (155 mg, 1 mmol) was added 5 ml of 2.5 M NaOH which was warmed to 65°. To this soln was added 214 mg (1.0 mmol) of hydroxylamine-O-sulfonic acid and stirred for 40 min. Approximately 3 equiv of hydroxylamine-O-sulfonic acid (339 mg, 3 mmol) was added over the next 1.5 hr and the gas evolution was monitored with a gas buret. When the gas evolution was constant after further additions of the hydroxylamine-O-sulfonic acid, the mixture was acidified with 3 N HCl, extracted with ether (3 × 20 ml), dried ($MgSO_4$), and the solvent removed. Purification via flash chromatography (15 g silica gel, 1:10 EtOAc–hexanes) afforded a colorless oil (129 mg, 92%). IR (neat) 3350 (broad), 2935, 2860, 1265, 1035, 912, 805, and 737 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 3.37 (2H, d, J = 7.50 Hz), 2.30–1.00 (13H, m); mass spectrum *m/e* (rel intensity) 122 (12.90) [$M^+ - H_2O$], 109 (100.00), 93 (19.16), 81 (39.40), 67 (84.03), 55 (36.59). Exact mass calc for C_9H_{14}: 122.1095. Found: 122.1099.

exo-*Bicyclo*[3.2.1]*octane*-6-*carboxylic acid* (**30**). Alcohol **29** (58 mg, 0.42 mmol) was oxidized to the carboxylic acid using the Sharpless[17] oxidation method with $RuCl_3$ affording 60 mg (92%) of a white solid (m.p. 84–85°); IR (neat) 3000 (broad), 2920, 2850, 1695, 1455, 1412, 1298, and 1225 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 9.57 (1H, br s), 2.80–1.10 (13H, m).

Methyl endo- *and* exo-*bicyclo*[3.2.1]*octane* 6-*carboxylate* (**32** and **31**). LDA (0.30 mmol) was prepared in the usual manner and was slowly added to the *exo* ester **31** (50 mg, 0.30 mmol) in 3 ml dry THF at −70°. After the addition was complete, the mixture was stirred for 15 min and then quenched with 150 mg (0.60 mmol) of pyridinium tosylate. The soln was then poured into 1.5 ml cold H_2O and 0.5 ml conc HCl. The aqueous phase was extracted (2 × 10 ml) with ether, washed with sat $NaHCO_3$, sat NaCl, and dried over $MgSO_4$. Comparison of the areas for the *exo* and *endo* methyl proton resonances indicated a 75% conversion to the *endo* isomer. The two esters were separated via prep HPLC (1:49 EtOAc–hexanes, 5 μm Si) and the *endo* isomer eluted first. *Endo* isomer **32**: ^{1}H-NMR (360 MHz, $CDCl_3$), δ 3.63 (3H, s), 2.93 (1H, br ddd, J = 11.7, 6.2, 6.0 Hz), 2.20–1.20 (12H, m); ^{13}C-NMR (90.5 MHz, $CDCl_3$) δ 175.02, 51.22, 47.08, 40.60, 38.75, 34.52, 32.65, 29.86, 28.92, 18.56. *Exo* isomer **31**: ^{1}H-NMR (360 MHz, $CDCl_3$) δ 3.60 (3H, s), 2.66 (1H, br dd, J = 9.0, 5.1 Hz), 2.30–1.00 (12H, m); ^{13}C-NMR (90.5 MHz, $CDCl_3$) δ 177.55, 51.50, 46.30, 40.32, 38.02, 35.50, 33.12, 32.25, 31.82, and 19.13.

5-N,N-*Dimethylamino*-6-(*hydroxymethyl*)*bicyclo*-[3.2.1]*octane*-1-*ol* **33**. N-Methylisoxazolidine **19** (597 mg, 3.26 mmol) was dissolved in 5 ml dry ether and stirred overnight with 30 equiv. (13.9 g, 97.8 mmol) of MeI. The methiodide was isolated via gravity filtration and was washed with dry ether to afford a white solid (621 mg, 60%). ^{1}H-NMR (90 MHz, DMSO-d_6), δ 5.20 (1H, br s), 4.50 (1H, dd, J = 8.4, 9.3 Hz), 4.18 (1H, dd, J = 5.0, 8.4 Hz), 3.40 (6H, s), 2.40–1.40 (11H, m). The methiodide (180 mg, 0.6 mmol) was reduced with activated Zn in AcOH to afford 100 mg (91%) of a colorless oil. ^{1}H-NMR (90 MHz, $CDCl_3$) δ 3.93 (1H, br d, J = 10.5 Hz), 3.90 (2H, brs), 3.45 (1H, br d, J = 10.5 Hz), 2.27 (6H, s), 2.43–1.23 (11H, m).

3-*Methylhydroxy*-4-*methylenecycloheptanone* **35**. The amino diol **33** (100.0 mg, 0.50 mmol) was methylated in refluxing THF (5 ml) containing MeI (2.16 g, 15.2 mmol). Filtration and azeotropic removal of water with dry benzene gave a solid (117 mg, 67%) which was used immediately in the next step. To a dry flask was added 21.6 mg of NaH (50% min oil disp 0.45 mmol) which was washed (3 × 5 ml) with dry hexanes. Dry THF (15 ml) was added followed by 50 mg (0.15 mmol) of the methiodide salt **34**. After heating 2 hr at 70° the reaction was quenched with water, extracted with ether (2 × 40

ml), and dried ($MgSO_4$). The colored oil was purified via flash chromatography (1.0 g silica gel, 20% EtOAc–pet. ether) to give a colorless oil (16 mg, 70%). IR (neat) 3400 (broad), 3070, 2930, 2860, 1702, 1640, 1443, 1063, 1022, and 895 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 4.90 (0.7H, s), 4.80 (0.7H, br s), 4.62 (0.6H v br s), 4.18 (0.3H, dd, J = 7.5, 5.3 Hz), 3.60 (1.7H m), 3.2–1.0 (10H, m); mass spectrum *m/e* (rel intensity) 154 (M^+, 3.33), 124 (100.00), 109 (25.43), 95 (88.50), 85 (16.33), 79 (38.92), 67 (51.80), 55 (52.14). Exact mass calc for $C_9H_{14}O_2$: 154.0994. Found: 154.0986. Silyation (t-$BuMe_2SiCl$, imidazole) gave a silyl ether whose ^{1}H-NMR spectrum was very similar to the spectrum of **35** in the δ 5–3 region except the resonances at δ 4.62 and 4.18 were absent.

Bromoketones **38**. Anhyd HBr was bubbled through a soln of **37** (2.5 g, 11.5 mmol) in 1 l of freshly distilled hexanes while irradiating with a Hanovia 450 W medium-pressure mercury-vapor lamp. The reaction progress was monitored by ^{1}H-NMR until starting material had disappeared (1.5 hr). The resulting cloudy, brown soln was washed several times with sat sodium thiosulfate and dried over $MgSO_4$. After concentration *in vacuo*, the crude product was filtered through a plug of silica gel (1:20 EtOAc–hexanes) to yield 2.5 g of a 2:1 mixture of isomeric bromides (74%). This ratio was confirmed upon purification of a small amount of the crude mixture. Typically, the crude mixture was used in the next step without further purification. ^{1}H-NMR (90 MHz, $CDCl_3$, major isomer) δ 3.40 (1H, dd, J = 9, 6 Hz), 3.2–1.0 (16H, m), 0.75 (3H, d, J = 6 Hz), 0.72 (3H, s); ^{1}H-NMR (90 MHz, $CDCl_3$, minor isomer) δ 3.40 (2H, m), 2.6–1.1 (15H, m), 0.75 (3H, d, J = 6 Hz), 0.65 (3H, s).

trans - 4a,5 - *Dimethyl* - 8a - (2 - *propenyl*) - 2 - *decalone* **39a**. Into a dry 500 ml 3-neck round bottom flask under N_2, fitted with a mechanical stirrer and a dry-ice–acetone condenser was condensed approximately 140 ml of ammonia (freshly distilled from Li). To the flask, cooled to −78°, was added Li (192 mg, 27.7 mmol) which was stirred and allowed to dissolve followed by the addition of 70 ml of dry THF. The crude mixture of bromides **38** (1.65 g, 5.5 mmol) in 10 ml of dry THF was added over a 15 min period. The mixture was stirred at −78° for 1 hr, quenched by the addition of NH_4Cl, and the excess ammonia was evaporated. The soln was then diluted with 100 ml of ether and 40 ml of water. After separation of the two layers, the aqueous layer was extracted three times with 50 ml of ether. The combined organics were washed with brine and dried over $MgSO_4$. Concentration *in vacuo* and purification by flash chromatography on silica gel (1:7 EtOAc–hexanes) afforded 1.0 g of a colorless oil (80%). IR (film) 3070, 2925, 1710, 1635 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 5.65 (1H, m), 5.10 (1H, br s), 4.95 (1H, d, J = 10 Hz), 2.8–1.2 (15H, m), 1.10 (3H, s), 0.85 (3H, d, J = 6 Hz); mass spectrum *m/e* (rel intensity) 220 (1) [M^+], 179 (100), 161 (53), 121 (40), 109 (21), 97 (67), 81 (46), 69 (67), 55 (42). Exact mass calc for $C_{15}H_{24}O$: 220.1827. Found: 220.1845.

N-*Benzylisoxazolidine* **40a**. To a soln of **39a** (250 mg, 1.14 mmol) in 10 ml of dry EtOH under N_2 was added benzylhydroxylamine (278 mg, 2.28 mmol) followed by the addition of anhyd Na_2SO_4 (486 mg, 3.42 mmol). The flask was fitted with a reflux condenser and the soln heated at reflux until analysis by TLC indicated complete product formation (8 hr). Purification by flash column chromatography on silica gel (1:20 EtOAc–hexanes) provided a white crystalline solid which was recrystallized from boiling ether to yield 297 mg (80%) (m.p. 116°). IR (KBr pellet) 3070, 3030, 1600, 1450 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 7.20 (5H, m), 3.95 (1H, dd, J = 7 and 3 Hz), 3.75 (2H, s), 3.40 (1H, dd, J = 7 and 4 Hz), 2.45 (2H, m), 1.9–1.0 (14H, m), 0.83 (3H, s), 0.75 (3H, d, J = 6 Hz); ^{13}C-NMR (90.5 MHz, $CDCl_3$) δ 138.434, 128.565, 128.154, 126.843, 74.111, 56.258, 49.310, 40.697, 38.475, 37.110, 35.273, 35.130, 30.731, 30.010, 23.237, 15.827, 13.509; mass spectrum *m/e* (rel intensity) 325 (32) [M^+], 268 (17), 226 (9), 200 (10), 105 (17), 91 (100). Exact mass calc for $C_{22}H_{31}NO$: 325.2406. Found: 325.2424. (Found: C, 81.48; H, 9.35; N, 4.23. Calc for $C_{22}H_{31}NO$: C, 81.18; H, 9.60; N, 4.30%.)

1 - *Amino* - 4,5 - *dimethyl* - 11 - (*hydroxymethyl*)*tricyclo*[7.2.1.$0^{4,9}$]*dodecane*. To a soln of **40a** (205 mg, 0.63 mmol) in 10 ml of 95% EtOH was added 0.3 equiv of 20% palladium hydroxide on carbon (Pearlman's catalyst).[16] This mixture was then placed under 1 atmosphere of H_2. When TLC analysis indicated a complete reaction, the catalyst was removed by filtration and rinsed with EtOH. Removal of the solvent *in vacuo*, followed by azeotropic removal of water with dry benzene, yielded 149 mg of an off-white solid which was used in the following step without further purification (100%). ^{1}H-NMR (90 MHz, $CDCl_3$) δ 3.36 (2H, m), 2.62 (3H, br s), 2.15 (1H, dd, J = 9 and 3 Hz), 2.04 (1H, dd, J = 9 and 3 Hz), 1.30 (14H, m), 0.72 (3H, s), 0.67 (3H, d, J = 6 Hz); mass spectrum *m/e* (rel intensity) 237 (39) [M^+], 178 (99), 138 (100), 125 (33), 108 (19), 96 (12), 82 (10), 70 (38), 55 (16). Exact mass calc for $C_{15}H_{27}NO$: 237.2093. Found: 237.2094. M.p. decomposed above 150°.

4,5 - *Dimethyl* - 11 - (*hydroxymethyl*)*tricyclo*[7.2.1.$0^{4,9}$]*dodecane* **41**. To the crude amino alcohol from the previous step (52 mg, 0.22 mmol) was added 490 μl of a 1.8 M soln of NaOH in 68% EtOH. The soln was heated to 65° at which time hydroxylamine-O-sulfonic acid (HOS, 58 mg, 0.44 mmol) was added. Stirring and heating were continued and after 45 min, 1 equiv of the NaOH aq (120 μl) was added followed by HOS (29 mg, 0.22 mmol). Similar additions were made three times over a 3 hr period. The evolution of N_2 was monitored through the course of the reaction by means of an inverted buret. It was noted that N_2 evolution ceased after addition of the last portion of HOS. The mixture was poured onto water and ether and the layers were separated. The aqueous layer was extracted with ether three times and the combined organic layers were washed with brine and dried over $MgSO_4$. The solvent was removed *in vacuo* and the resulting oil was purified via flash chromatography on silica gel (1:10 EtOAc–hexanes) to give 32 mg of a colorless oil (65%). IR (film) 3330, 2920, 2850, 1460, 1450, 1380 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 3.37 (2H, d, J = 6 Hz), 2.30 (1H, dd, J = 8 and 3 Hz), 2.00–0.90 (17H, m), 0.84 (3H, s), 0.74 (3H, d, J = 8 Hz); mass spectrum *m/e* (rel intensity) 223 (7) [$M^+ + 1$], 222 (44) [M^+], 191 (100), 163 (75), 149 (16), 133 (25), 121 (32), 107 (54), 95 (45), 93 (92), 81 (99), 67 (48), 55 (58). Exact mass calc for $C_{15}H_{26}O$: 222.1984. Found: 222.1982. (Found: C, 80.88; H, 11.82. Calc for $C_{15}H_{26}O$: C, 81.02; H, 11.79%.)

4,5 - *Dimethyl* - 11 - *methylenetricyclo*[7.2.1.$0^{4,9}$]*dodecane* **42**. To a stirred soln of **41** (64 mg, 0.29 mmol) and *o*-nitrophenyl selenocyanate (82 mg, 0.36 mmol) in dry THF was added dropwise tri-n-butylphosphine (73 mg, 0.36 mmol). The deep-red soln was stirred at room temp for 2 hr at which time analysis by TLC indicated a small amount of starting material. An additional portion of *o*-nitrophenylselenocyanate (66 mg, 0.29 mmol) and tri-n-butylphosphine (59 mg, 0.29 mmol) were added, after 20 min the starting material had disappeared. Removal of solvent and filtration through a silica gel plug (1:4 ether–hexanes) yielded 135 mg of the crude selenide as a bright yellow oil (81%) which was oxidized directly. O_3 was bubbled through a soln of the selenide (47 mg, 0.12 mmol) in CH_2Cl_2 at −78° until a blue color was noted. The soln was then degassed with N_2 followed by the addition of diisopropylamine (24 mg, 0.24 mmol). The mixture was allowed to warm to room temp and the soln was poured onto ether and water, the layers separated and the aqueous phase extracted twice with ether. The combined organic layers were dried over $MgSO_4$. Filtration and evaporation of the solvent yielded an oil which was purified by flash chromatography on silica gel (hexanes) to give 44 mg (65%) of a colorless oil. IR (film) 3060, 2920, 2845, 1655, 1455, 1380, 870 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 4.75 (2H, d, J = 11 Hz), 2.82 (1H, d, J = 17 Hz), 2.55 (1H, br s), 1.84 (1H, d, J = 17 Hz), 1.8–1.0 (13H, m), 0.88 (3H, s), 0.75 (3H, d, J = 6 Hz); mass spectrum *m/e* (rel intensity) 204 (49) [M^+], 189 (100), 161 (64), 147 (34), 133 (55), 119 (43), 105 (73), 91 (72), 79 (53), 67 (25). Exact mass calc for $C_{15}H_{24}$: 204.1878. Found: 204.1877.

Epoxides **43a** *and* **43b**. To a soln of **42** (20 mg, 0.1 mmol) in 3 ml of CH_2Cl_2 at 0° was added 1 ml of a sat $NaHCO_3$ aq followed by the addition of 80% *m*-chloroperbenzoic acid (19

mg, 0.15 mmol). After 3 hr at 0° the organic layer was washed successively with 10% Na_2SO_3 aq and sat $NaHCO_3$ aq and dried over anhyd Na_2SO_4. Evaporation of the solvent yielded 20 mg (90%) of a mixture of isomeric epoxides in a ratio of 7.6:1 (HPLC; 10 mm I.D. × 25 cm 5 μm ultrasphere Si: 5:95 EtOAc–hexanes; 5 ml min^{-1}) which was utilized without purification. IR (film) 3020, 2940, 2860, 1450, 1385, 760 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$, major isomer, retention time 5.4 min) δ 2.88 (1H, d, J = 4.7 Hz), 2.80 (1H, d, J = 4.7 Hz), 2.40 (1H, dd, J = 1.48 and 2.5 Hz), 1.82–1.13 (15H, m), 0.89 (3H, s), 0.76 (3H, d, J = 6.8 Hz); ^{1}H-NMR (360 MHz, $CDCl_3$, minor isomer, retention time 4.6 min) δ 2.85 (1H, d, J = 5.3 Hz), 2.78 (1H, d, J = 5.3 Hz), 2.14 (1H, dd, J = 14.8 and 3.4 Hz), 1.87–1.00 (15H, m), 0.91 (3H, s), 0.78 (3H, d, J = 6.8 Hz); mass spectrum *m/e* (rel intensity) 221 (11) [$M^+ + 1$], 220 (70) [M^+], 205 (27), 177 (18), 163 (26), 149 (19), 135 (29), 122 (100), 105 (56), 91 (77), 81 (75). Exact mass calc for $C_{15}H_{24}O$: 220.1827. Found: 220.1830.

(±)-7,12-*Secoishwaran*-12-*ol*. Reduction of the crude epoxides **43a** and **43b** (14 mg, 0.06 mmol) was accomplished using lithium aluminum hydride (4 mg, 0.10 mmol) in dry ether according to the procedure reported by Pakrashi.[7] Upon completion of the reaction, 100 μl of water, 100 μl of 2.5 M NaOH and 300 μl of water were all added sequentially. The aqueous layer was extracted with ether and dried over Na_2SO_4. The solvent was removed and the mixture purified via HPLC (5 μm ultrasphere Si/10 mm I.D. × 25 cm; 1:9 EtOAc–hexanes; 5 ml min^{-1}) to yield 10 mg of a white solid (retention time 10.2 min, 71%). Recrystallization from acetonitrile gave a highly crystalline material (m.p. = 119°) identical to an authentic sample of (12*S*)-7, 12-secoishwaran-12-ol, kindly provided by Dr Pakrashi. Approximately 1 mg of the C-17 epimer (retention time 3.8 min, 7%) was also obtained. IR (CH_2Cl_2) 3050, 2920, 2850, 1460, 1440, 1420, 1260, 890 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 2.15 (1H, dd, J = 14.6 and 1.3 Hz), 1.75–1.45 (10H, m), 1.35 (3H, s), 1.4–1.0 (6H, m), 0.87 (3H, s), 0.74 (3H, d, J = 6.8 Hz); ^{13}C-NMR (90.5 MHz, $CDCl_3$) δ 13.48, 15.47, 24.10, 24.12, 24.59, 30.68, 32.02, 35.51, 37.61, 38.63, 38.79, 47.98, 48.26, 49.79, 79.99; mass spectrum *m/e* (rel intensity) 222 (9) [M^+], 189 (37), 164 (87), 149 (57), 133 (38), 125 (50), 108 (67), 93 (67), 81 (100), 67 (56). Exact mass calc for $C_{15}H_{26}O$: 222.1984. Found: 222.1983. ^{1}H-NMR (360 MHz, $CDCl_3$, C-12 epimer) δ 2.15 (1H, dd, J = 14.6 and 2.0 Hz), 1.8–0.9 (19H, m), 0.88 (3H, s), 0.76 (3H, d, J = 6.8 Hz).

2-*Methylene*-4,4-*dimethylcyclopentanone* (**45**). To a soln of 2-(tosyloxymethyl)-4,4-dimethylcyclopentan-1-ol (4.62 g, 15.6 mmol) in 30 ml ether at 0° was added DBU (2.80 ml, 18.7 mmol). The white suspension was stirred 30 min at 0°. The mixture was diluted with H_2O and pentane, the layers separated, and the aqueous layer extracted three times with pentane. The combined organic extracts were washed with dilute AcOH, sat $NaHCO_3$ aq, brine, dried over $MgSO_4$, and filtered. The solvent was removed by distillation. Distillation of the crude product (48–50°/5 mm) afforded 1.75 g (90%) of a colorless oil. R_f 0.56 (EtOAc–hexanes, 1:19); IR (neat) 2948, 2886, 2861, 1728, 1638, 1464, 1436, 1409, 1388, 1371, 1308, 1285, 1262, 1220, 1147, 1100, 1088, 970, 943, 918, 906, 899, 749 cm^{-1}; ^{1}H-NMR (90 MHz, $CDCl_3$) δ 5.94 (m, 1H), 5.19 (m, 1H), 2.41 (t, J = 2 Hz, 2H), 2.15 (s, 2H), 1.10 (s, 6H). (Found: C, 77.06; H, 9.96. Calc for $C_8H_{12}O$: C, 77.38; H, 9.74%.)

Preparation of the aforementioned tosylate from methyl 2-oxo-4,4-dimethylcyclopentane carboxylate was accomplished as follows: (1) $HOCH_2CH_2OH$, H^+; (2) $LiAlH_4$, ether; (3) H_3O^+; (4) TsCl, pyridine (70% overall yield).

2-*Methyl*-3-(*trimethylsilyl*)*cyclopentene* (**46b**). To a mixture of N-chlorosuccinimide (16.35 g, 122.4 mmol) in 100 ml dry CH_2Cl_2 at 0° was added dropwise Me_2S (9.6 ml, 130.6 mmol). The mixture was cooled to −20°, and 2-methyl-2-cyclopenten-1-ol (8.0 g, 81.6 mmol) was added gradually over approximately 20 min. The reaction was allowed to warm to 0° and stirred for 2 hr. The mixture was then poured into ice-cold brine and ether in a separatory funnel. The aqueous layer was extracted three times with ether. The combined organics were washed two times with ice-cold brine, dried over $MgSO_4$, and the solvent was removed by distillation. Distillation of the crude product (46–50°/25 mm) afforded 6.86 g (72%) of a rather unstable yellow liquid. ^{1}H-NMR (90 MHz, $CDCl_3$) δ 5.59 (m, 1H), 4.76 (m, 1H), 2.70–1.90 (m, 4H), 1.80 (br s, 3H). A mixture of Mg (2.15 g, 88.3 mmol) and Me_3SiCl (7.5 ml, 58.8 mmol) in 30 ml dry THF was cooled to 0°. A soln of 3-chloro-2-methyl cyclopentene (6.86 g, 58.8 mmol) in 60 ml dry THF was added dropwise over 5 hr. The mixture was allowed to warm to room temp and stirred overnight. The mixture was cooled to 0° and quenched by the dropwise addition of H_2O. The mixture was filtered and washed with pentane. The aqueous phase was extracted three times with pentane. The combined organic extracts were washed with H_2O, brine, dried over $MgSO_4$, filtered, and the solvent was removed. Distillation of the crude material afforded 5.47 g (60%) of a colorless liquid (b.p. 156–160°). ^{1}H-NMR (90 MHz, $CDCl_3$) δ 5.25 (m, 1H), 2.53–1.70 (m, 5H), 1.77 (br s, 3H), 0.18 (s, 9H).

2 - [2 - *Methyl* - 1 - *cyclopentenyl*)*methyl*] - 4,4 - *dimethylcyclopentanone* (**47b**). To a soln of **45** (698 mg, 5.63 mmol) in 17 ml of dry CH_2Cl_2 at −78° was added, dropwise $TiCl_4$ (741 μl, 6.75 mmol). The mixture turns from a deep red color to a yellow ppt upon complete addition of the $TiCl_4$. The mixture was stirred 5 min at −78° and then transferred over a period of 30 min via cannula to a soln of **46b** (1.300 g, 8.44 mmol) in 25 ml dry CH_2Cl_2 at −78° (internal temp did not rise above −65°). The mixture turned to a deep purple color upon the addition of the first drop of complexed enone. The mixture was stirred a further 30 min at −78° and then quenched by pouring directly into a separatory funnel containing cold H_2O and ether. The aqueous layer was extracted three times with ether. The combined organics were washed with brine, dried over $MgSO_4$, filtered, and the solvent was removed affording 1.77 g of crude material. Flash chromatography (100 g silica gel, EtOAc–hexanes, 1:19) gave 821 mg (71%) of a colorless oil. R_f 0.57 (EtOAc–hexanes, 1:9); IR (neat) 3038, 2955, 2933, 2863, 2853, 1741, 1463, 1445, 1406, 1371, 1142, 1020 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 5.33 (br s, 1H), 2.62 (m, 1H), 2.34 (m, 1H), 2.28–1.99 (m, 7H), 1.69 (br s, 3H), 1.53–1.43 (m, 2H), 1.18 (s, 3H), 1.13–1.03 (m, 1H), 1.06 (s, 3H); mass spectrum *m/e* (rel intensity) 206 (3), 125 (8), 112 (24), 95 (100), 81 (34), 79 (42), 67 (9), 55 (15). Exact mass calc for $C_{14}H_{22}O$: 206.1671. Found: 206.1660. The mixture of diastereomers (2.16:1) could be separated only by HPLC (EtOAc–hexanes, 1:19, two ALTEX 5 μm ultrasphere Si 10 mm I.D. × 25 cm columns, flow rate 3.0 ml min^{-1}). Major isomer (retention time 8.5 min): ^{13}C-NMR (50 MHz, $CDCl_3$) δ 143.0, 124.8, 52.8, 47.2, 47.0, 45.4, 34.6, 33.9, 30.9, 30.7, 29.7, 27.7, 15.0; minor isomer (retention time 8.9 min): δ 142.6, 124.7, 53.0, 46.7, 45.9, 44.3, 34.6, 34.1, 30.6, 29.8, 29.5, 27.9, 14.6.

N-*Methyl isoxazolidine* **50b**. To a soln of NaOEt (14.56 mmol) in 40 ml dry EtOH was added $MeNHOH \cdot HCl$ (876 mg, 10.49 mmol) followed by **47b** (1.08 g, 5.24 mmol). The resulting cloudy mixture was refluxed for 24 hr. TLC analysis indicated no starting material present along with some product and nitrone. Most of the EtOH was distilled off and replaced by toluene. The mixture was refluxed with a Dean Stark trap for 24 hr. TLC analysis showed no nitrone remaining (R_f = 0.26, i-PrOH–$CHCl_3$, 1:19). The mixture was diluted with ether and H_2O, transferred to a separatory funnel and extracted three times with ether. The combined organics were washed with brine, dried over $MgSO_4$, filtered, and the solvent was removed. Flash chromatography of the crude product (100 g silica gel, EtOAc–hexanes, 3:17) gave 921 mg (75%) of a colorless oil. R_f 0.47 (EtOAc–hexanes, 1:4). IR (neat) 2946, 2858, 1462, 1453, 1365, 1323, 930, 911, 734 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$, 60°) δ 4.17 (m, 1H), 2.83 (m, 1H), 2.66 (s, 3H), 2.07 (m, 1H), 1.97–1.80 (m, 3H), 1.80–1.64 (m, 4H), 1.58–1.43 (m, 2H), 1.32 (dd, J = 13.27 and 5.84 Hz, 1H), 1.16 (s, 3H), 1.12 (s, 3H), 1.11 (s, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$, 60°) δ 90.0, 52.6, 46.0, 44.2, 44.2, 37.8, 37.7, 31.8, 31.7, 31.7, 30.6, 29.7, 22.7, 18.5; mass spectrum *m/e* (rel intensity) 235 (14), 220 (9), 202 (38), 196 (12), 178 (17), 162 (10), 154 (38), 138 (100), 125 (56), 110 (39), 93 (38), 84 (45), 77 (23), 68 (13), 55 (22). Exact mass calc for $C_{15}H_{25}NO$: 235.1936. Found: 235.1938.

(Found: C, 76.22; H, 10.59. Calc for $C_{15}H_{25}NO$: C, 76.54; H, 10.71%.)

N,N-*Dimethylaminoalcohol* **51b**. To a soln of **50b** (850 mg, 3.62 mmol) in 15 ml dry ether was added MeI (4.5 ml 72.3 mmol). The soln was stirred at room temp for 48 hr. The mixture was filtered, the crude methiodide washed with ether, and dried under vacuum giving 1.24 g (91%) of a white solid melting at 146–147°. IR ($CHCl_3$) 2957, 2867, 2426, 1614, 1461, 1445, 1236, 660 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 4.73 (d, J = 5.79 Hz, 1H), 3.85 (s, 3H), 3.69 (s, 3H), 3.26 (m, 1H), 2.56–2.40 (m, 2H), 2.28–2.00 (m, 2H), 1.96–1.86 (m, 2H), 1.85–1.62 (m, 4H), 1.45 (dd, J = 13.16 and 9.95 Hz, 1H), 1.37 (s, 3H), 1.30 (s, 3H), 1.15 (s, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 102.7, 93.2, 67.1, 55.3, 51.8, 51.0, 49.1, 45.0, 42.8, 38.0, 33.8, 31.4, 30.2, 30.1, 28.0, 21.9.

To a soln of the N,N-dimethylisoxazolidinium iodide (375 mg, 0.99 mmol) in 5 ml EtOH was added 50 mg of 5% Pd on activated charcoal. The mixture was stirred under H_2 at atmospheric pressure for 36 hr. The mixture was filtered and washed with EtOH. The solvent was removed giving the hydroiodide salt, which was taken up in CH_2Cl_2, transferred to a separatory funnel, and washed with dil KOH aq. The layers were separated and the aqueous layer was extracted three times with ether. The combined organic extracts were washed with brine, dried over $MgSO_4$, and filtered. The solvent was removed giving 244 mg (98%) of a colorless oil which was used without further purification. An analytical sample was obtained by chromatography on silica gel, first eluting with EtOAc–hexanes (1:4) and then with MeOH. R_f 0.18 (MeOH); IR (neat) 3200, 2950, 2865, 2828, 2785, 1466, 1386, 1367, 1104, 1020, 1004 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 4.04 (d, J = 6.21 Hz, 1H), 2.69 (dd, J = 11.27 and 9.32 Hz, 1H), 2.35–2.13 (m, 2H), 2.28 (s, 6H), 2.04 (ddd, J = 13.17, 11.22, and 11.22 Hz, 1H), 1.88 (dddd, J = 14.61, 5.25, 9.36, and 1.14 Hz, 1H), 1.83–1.62 (m, 6H), 1.57 (ddd, J = 13.18, 9.94, and 3.24 Hz, 1H), 1.45 (dd, J = 13.48 and 1.50 Hz, 1H), 1.16 (s, 3H), 1.09 (s, 3H), 0.97 (s, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 85.7, 81.7, 61.6, 52.5, 52.0, 49.8, 40.6, 40.5, 40.3, 39.0, 33.4, 31.6, 31.5, 28.3, 24.0; mass spectrum, *m/e* (rel intensity), 251 (11), 249 (18), 236 (19), 219 (10), 206 (8), 192 (58), 178 (16), 162 (22), 152 (100), 138 (58), 124 (22), 106 (22), 93 (23), 85 (16), 79 (19), 67 (10). Exact mass calc for $C_{16}H_{29}NO$: 251.2249. Found: 251.2242. (Found: C, 76.18; H, 11.55. Calc for $C_{16}H_{29}NO$: C, 76.44; H, 11.63%.)

Ketone **52**. To a soln of pyridine (1.23 ml, 15.2 mmol) in 7 ml CH_2Cl_2 was added CrO_3 (759 mg, 7.6 mmol). The mixture was stirred 15 min at room temp, and (300 mg, 1.3 mmol) of the hydroiodide salt of **51a** was added in one portion. The mixture was stirred 15 min at room temp, then diluted with $CHCl_3$ and 1 M NaOH. The aqueous layer was continuously extracted with $CHCl_3$ for 24 hr. The layers were then separated and the solvent was removed. Flash chromatography (1:5 EtOAc–hexanes) afforded 89 mg (57%) of a colorless oil. R_f 0.35 (3:7 EtOAc–hexanes), IR (neat) 2952, 2925, 2866, 1765, 1463, 1406, 1371, 1161, 732 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 2.44–1.75 (m, 9H), 1.55–1.33 (m, 3H), 1.19 (s, 3H), 1.07 (s, 3H); mass spectrum *m/e* (rel intensity) 190 (1), 126 (4), 112 (65), 97 (51), 96 (100), 83 (35), 69 (14), 55 (21). Exact mass calc for $C_{13}H_{18}O$: 190.136. Found: 190.136.

Alcohol **53**. To a mixture of **51b** (251 mg, 1.0 mmol) in a biphasic system of 3 ml CH_2Cl_2 and 3 ml sat $NaHCO_3$ aq at 0° was added MCPBA (223 mg, 1.1 mmol). The mixture was stirred 2 hr at 0°, then warmed to reflux. After 48 hr, the mixture was transferred to a separatory funnel. The layers were separated and the aqueous layer was extracted three times with CH_2Cl_2. The combined organics were washed with sat $NaHCO_3$ aq, brine, and dried over $MgSO_4$. The mixture was filtered and the solvent was removed giving 185 mg (90%) of a colorless oil. IR (neat) 3450, 3020, 2948, 2858, 1455, 1363, 1321, 1095, 1076, 1059, 1028, 1003, 840 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 5.28 (d, J = 2.73 Hz, 1H), 3.75 (t, J = 5.74 Hz, 1H), 3.17 (m, 1H), 2.35 (dd, J = 13.05 and 7.93 Hz, 1H), 1.95–1.80 (m, 3H), 1.67 (dd, J = 12.03 and 7.15 Hz, 1H), 1.63–1.43 (m, 3H), 1.35–1.23 (m, 2H), 1.17 (s, 3H), 1.12 (s, 3H), 1.10 (s, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 155.1, 132.6, 80.9, 54.9, 52.2, 51.6, 51.0, 48.3, 38.2, 35.4, 30.2, 29.6, 28.0, 25.1; mass spectrum *m/e* (rel intensity) 206 (74), 191 (38), 173 (89), 162 (70), 145 (100), 131 (65), 119 (35), 106 (180). Exact mass calc for $C_{14}H_{22}O$: 206.1671. Found: 206.1674. (Found: C, 81.67; H, 10.71. Calc for $C_{14}H_{22}O$: C, 81.50; H, 10.75%.)

Ketone **54**. To a soln of **53** (38 mg, 0.18 mmol) in 2 ml dry CH_2Cl_2 was added PCC (80 mg, 0.37 mmol). The mixture was stirred for 6 hr at room temp. The mixture was then filtered through a silica gel plug, rinsing with CH_2Cl_2. The solvent was removed giving 35 mg (93%) of a colorless oil. An analytical sample was prepared by HPLC (EtOAc–hexanes, 1:9). R_f 0.57 EtOAc–hexanes, 1:4); IR (neat) 3030, 2948, 2856, 1742, 1462, 1455, 1414, 1362, 1069 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 5.29 (d, J = 2.67 Hz, 1H), 3.15 (m, 1H), 2.68 (dd, J = 15.26 and 7.70 Hz, 1H), 2.37 (t, J = 8.18 Hz, 2H), 2.13 (ddd, J = 13.33, 12.33, and 8.06 Hz, 1H), 1.87 (dd, J = 11.90 and 6.85 Hz, 1H), 1.79 (dd, J = 12.31 and 7.32 Hz, 1H), 1.63 (m, 2H), 1.43 (ddd, J = 11.69, 11.69, and 7.77 Hz, 1H), 1.21 (s, 3H), 1.10 (s, 3H), 1.03 (s, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 220.1, 153.1, 131.1, 54.2, 52.6, 51.2, 48.2, 38.4, 37.7, 29.8, 27.1, 26.1, 22.3; mass spectrum *m/e* (rel intensity) 204 (16), 189 (100), 171 (6), 161 (10), 145 (17), 133 (40), 119 (7), 105 (12), 91 (9), 77 (3). Exact mass calc for $C_{14}H_{20}O$: 204.1514. Found: 204.1517. (Found: C, 82.34; H, 9.78. Calc for $C_{14}H_{20}O$: C, 82.30; H, 9.87%.)

Ketone **55**. To a soln of 10 mg (0.049 mmol) of **54** in 1 ml EtOAc was added Pd (5% on activated charcoal, 2 mg). The mixture was stirred under H_2 at atmospheric pressure for 2 hr, filtered, and the solvent removed giving a colorless oil which was purified by HPLC (EtOAc–hexanes, 1:19) giving 7 mg (69%) of a white solid. M.p. 41–43° (recrystallized from hexanes). IR (neat) 2948, 2927, 2862, 1738, 1464 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 2.80 (ddd, J = 10.69, 8.64, and 8.64 Hz, 1H), 2.53 (dddd, J = 17.94, 8.97, 8.97, and 3.46 Hz, 1H), 2.46–2.34 (m, 2H), 2.28 (dddd, J = 17.38, 8.69, and 8.69 Hz, 1H), 2.00 (m, 1H), 1.77–1.55 (m, 2H), 1.48–1.36 (m, 2H), 1.30–0.84 (m, 3H), 1.04 (s, 3H), 0.95 (s, 3H), 0.91 (s, 3H); ^{13}C-NMR (50 MHz, $CDCl_3$) δ 224.7, 59.3, 48.9, 48.8, 46.7, 43.3, 41.8, 41.1, 37.6, 34.2, 29.2, 26.5, 22.4, 17.3; mass spectrum *m/e* (rel intensity) 206 (100), 191 (10), 178 (10), 173 (5), 162 (55), 150 (62), 149 (54), 135 (27), 123 (36), 107 (96), 97 (45), 94 (84), 79 (66), 67 (23). Exact mass calc for $C_{14}H_{22}O$: 206.1671. Found: 206.1681.

Diols **57–59**. To a soln of **53** (30 mg, 0.15 mmol) in 1 ml dry THF at 0° was added dropwise a soln of 1 M $BH_3 \cdot$ THF (0.58 ml, 0.58 mmol). The mixture was then heated at a gentle reflux for 1 hr. The mixture was cooled to 0° and the excess borane quenched with H_2O. The solvent was removed and replaced with DME. A 3 M soln of NaOH (0.25 ml) was added dropwise followed by 30% H_2O_2 (0.25 ml) and the mixture was heated at a gentle reflux for 12 hr. The mixture was cooled, diluted with H_2O and ether, transferred to a separatory funnel, and extracted three times with ether. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and the solvent was removed. HPLC of the crude mixture (EtOAc–hexanes, 2:3) gave a total of 23 mg (71%) of three products. The first compound to elute from the column (R_f 0.55, EtOAc–hexanes, 2:3, 9 mg, colorless oil, 28%) was assigned the structure **59** based on the following spectral data: IR (neat) 3270, 2960, 2863, 1455, 1382, 1198, 1153, 1134, 1087, 1065, 1025, 1007, 970, 960, 907 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 3.92 (d, J = 5.36 Hz, 1H), 2.66–2.57 (m, 1H), 2.12–1.10 (m, 13H), 1.18 (s, 3H), 1.09 (s, 3H), 0.92 (s, 3H). The second compound to elute from the column (R_f 0.38, EtOAc–hexanes, 2:3; 9 mg, 28%; m.p. 154–155°) was assigned the structure **58** based on the following spectral data: IR (KBr pellet) 3310, 2940, 2890, 2852, 1455, 1373, 1073, 1067, 1043, 1002, 944 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 4.17 (d, J = 10.48 Hz, 1H), 4.06 (t, J = 5.67 Hz, 1H), 2.35–2.15 (m, 2H), 2.00–1.80 (m, 2H), 1.75–1.53 (m, 4H), 1.52–1.25 (m, 4H) 1.17 (s, 3H), 1.10–1.04 (m, 1H), 1.08 (s, 3H), 0.97 (s, 3H). The third compound to elute from the column (R_f 0.24, EtOAc–hexanes, 2:3; 5 mg, 15%; m.p. 160–162°) was assigned the structure **57** based on the following spectral data: IR (KBr pellet) 3300, 2948, 2928, 2898, 2855, 1455, 1380, 1088, 1011 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ

3.90(t, J = 7.75 Hz, 1H), 3.56(d, J = 9.20 Hz, 1H), 2.70–2.58(m, 1H), 2.40 (dd, J = 11.52 and 9.20 Hz, 1H), 2.17–2.08 (m, 1H), 2.03–1.93(m, 1H), 1.80–1.50(m, 4H), 1.46–1.25(m, 3H), 1.15(s, 3H), 1.15–0.85 (m, 2H), 1.03 (s, 3H), 0.95 (s, 3H).

Dione **60**. To a soln of **57** (4 mg, 0.018 mmol) in 0.5 ml dry CH_2Cl_2 was added PCC (15 mg, 0.071 mmol). After stirring 1 hr at room temp, the mixture was filtered through a silica gel plug. Removal of the solvent and purification by HPLC (EtOAc–hexanes, 1 : 4) gave 2 mg of **60** as a white solid, m.p. 68–69° (lit.[34] 65–66°). R_f 0.56 (EtOAc–hexanes, 2 : 3); IR (KBr pellet) 2947, 2937, 2860, 1733, 1458, 1380, 1153 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 2.95 (d, J = 8.51 Hz, 1H), 2.78 (ddd, J = 16.02, 8.01, and 8.01 Hz, 1H), 2.49–2.42 (m, 1H), 2.40 (dd, J = 9.95 and 2.79 Hz, 1H), 2.34–2.22 (m, 1H), 2.17–2.04 (m, 1H), 1.94 (ddd, J = 13.00, 8.02, and 1.01 Hz, 1H), 1.87–1.76 (m, 2H), 1.52–1.44 (m, 1H), 1.39 (dd, J = 12.83 and 10.49 Hz, 1H), 1.035 (s, 3H), 1.027 (s, 3H), 1.025 (s, 3H); mass spectrum *m/e* (rel intensity) 220 (28), 164 (19), 149 (5), 136 (14), 135 (8), 118 (5), 111 (7), 94 (23), 93 (40), 92 (14), 91 (12), 81 (10), 80 (100), 79 (32), 77 (18), 65 (6), 55 (6), 53 (9), 51 (5). Exact mass calc for $C_{14}H_{20}O_2$: 220.1463. Found: 220.1457.

Dione **61**. To a soln of **58** (4 mg, 0.018 mmol) in 0.5 ml dry CH_2Cl_2 was added PCC (15 mg, 0.071 mmol). After stirring 1 hr at room temp the mixture was filtered through a silica gel plug. Removal of the solvent gave 3 mg of **61** as an oil. R_f 0.44 (EtOAc–hexanes, 2 : 3); IR (neat) 2947, 2927, 2858, 1738, 1458, 1380, 1202, 1150; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 2.80–2.74 (m, 1H), 2.51–2.39 (m, 1H), 2.28 (dd, J = 18.78 and 9.70 Hz, 1H), 2.22 (dd, J = 9.27 and 4.04 Hz, 1H), 2.20–2.06 (m, 2H), 1.85 (dd, J = 11.88 and 4.73 Hz, 1H), 1.80–1.72 (m, 2H), 1.68–1.60 (m, 1H), 1.42–1.28 (m, 1H), 1.33 (s, 3H), 1.11 (s, 3H), 1.02 (s, 3H). Treatment of a small sample (< 1 mg) of **61** with NaOMe in MeOH for 15 min at room temp gave a product which was identical to **60** by 360 MHz ^{1}H-NMR and TLC.

Hydroxyketone **62**. PCC (19 mg, 0.089 mmol) was added to a soln of **59** (5 mg, 0.022 mmol) in 1 ml CH_2Cl_2. After stirring 2 hr at room temp, the mixture was filtered through a silica gel plug. Removal of the solvent gave 4 mg (80%) of a colorless oil. R_f 0.44 (EtOAc–hexanes, 1 : 4); IR (neat) 3462, 2940, 2919, 2857, 1716, 1458, 1405, 1383, 1310, 1278, 1258, 1150, 1120, 1091, 1050, 1012, 958, 880, 803 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 4.45 (br s, 1H), 2.50–2.24 (m, 3H), 2.09–1.98 (m, 1H), 1.93 (ddd, J = 13.01, 8.38, and 1.35 Hz, 1H), 1.76 (dddd, J = 12.87, 7.49, 3.73, and 1.30 Hz, 1H), 1.68–1.48 (m, 4H), 1.34–1.12 (m, 2H), 1.17 (s, 3H), 1.07 (s, 6H).

Diene **63**. To a soln of **53** (55 mg, 0.27 mmol) in 2 ml dry pyridine at room temp was added O-3,4-dimethylphenyl chlorothioformate (0.065 ml) and the mixture was allowed to stir overnight. Water was added and the mixture was extracted three times with ether. The combined organic extracts were washed two times with 10% HCl, sat $NaHCO_3$ aq, brine, and dried over Na_2SO_4. Removal of the solvent and purification by flash chromatography (10 g silica gel, EtOAc–hexanes, 2 : 98) gave 90 mg (91%) of the thionocarbonate. R_f 0.48 (EtOAc–hexanes, 1 : 19); ^{1}H-NMR (90 MHz, $CDCl_3$) δ 7.10–6.64 (m, 3H), 5.45 (t, J = 3 Hz, 1H), 5.11 (d, J = 3 Hz, 1H), 3.40–3.05 (m, 1H), 2.55–0.75 (m, 9H), 2.23 (br s, 6H), 1.28 (s, 3H), 1.15 (s, 3H), 1.11 (s, 3H). Pyrolysis at 220° for 3 hr at 0.3 Torr gave a mixture (collected in a cold trap at −78°) which was taken up in pentane, washed with 1 M KOH, brine, and dried over Na_2SO_4. Removal of the solvent gave 35 mg (70% overall) of a colorless oil. R_f 0.62 (hexanes); IR (neat) 3034, 2940, 2918, 2848, 1454, 1360, 1332, 846, 748 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 5.58 (m, 1H), 5.32 (m, 1H), 5.00 (d, J = 3 Hz, 1H), 3.20–3.00 (m, 1H), 2.84–2.66 (m, 1H), 2.60–2.44 (m, 1H), 2.18–1.98 (m, 1H), 1.81 (dd, J = 13 and 8 Hz, 1H), 1.64 (dd, J = 13 and 8 Hz, 1H), 1.40–1.15 (m, 2H), 1.19 (s, 3H), 1.06 (s, 3H), 0.99 (s, 3H); mass spectrum *m/e* (rel intensity) 188 (25), 174 (14), 173 (100), 147 (11), 145 (13), 137 (15), 133 (17), 131 (16), 122 (47), 121 (22), 119 (23), 117 (10), 109 (11), 107 (33), 105 (42), 95 (60), 93 (70), 91 (30), 83 (10), 81 (39), 79 (25), 77 (28), 71 (13), 69 (21), 67 (11), 67 (17), 57 (22), 55 (25). Exact mass calc for $C_{14}H_{20}$: 188.1565. Found: 188.1565.

Alcohols **64**. Cyclohexene (98 mg, 1.20 mmol) in 0.5 ml THF was added dropwise to a soln of $BH_3 \cdot THF$ (1 M in THF, 0.60 ml, 0.60 mmol) in 1 ml THF at 0°. After stirring 3 hr at 0°, diene **63** (75 mg, 0.40 mmol) in 0.5 ml THF was added dropwise. The mixture was warmed to room temp and stirred 4 hr. The mixture was cooled to 0° and 3 M NaOH (0.25 ml) was added dropwise followed by 30% H_2O_2 (0.25 ml). The mixture was heated at reflux for 12 hr. After cooling, the mixture was diluted with ether and H_2O, transferred to a separatory funnel, and extracted three times with ether. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and the solvent was removed. Purification of the crude product by flash chromatography (20 g silica gel, EtOAc–hexanes, 1 : 4) gave 69 mg (84%) of a colorless oil identified as a 14 : 1 mixture of the 4-β- and 4-α-isomers of **64**, respectively, which could be separated by HPLC (EtOAc–hexanes, 1 : 4). R_f 0.38 (EtOAc–hexanes, 3 : 7). Major isomer: IR (neat) 3328, 2943, 2918, 2849, 1458, 1360, 1199, 1127, 1066, 1041, 846 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 5.00 (d, J = 2.56 Hz, 1H), 4.37 (p, J = 4.52 Hz, 1H), 3.20–3.07 (m, 1H), 2.57 (dd, J = 16.22 and 8.05 Hz, 1H), 1.97 (dddd, 13.30, 8.93, 4.15, and 1.95 Hz, 1H), 1.83 (dd, J = 11.99 and 7.04 Hz, 1H), 1.80 (d, J = 5.50 Hz, 1H), 1.66 (dd, J = 4.14 and 2.01 Hz, 1H), 1.64–1.56 (m, 3H), 1.31–1.19 (m, 1H), 1.25 (dd, J = 11.85 and 8.14 Hz, 1H), 1.29 (s, 3H), 1.09 (s, 3H), 1.03 (s, 3H); mass spectrum *m/e* (rel intensity) 206 (10), 192 (14), 191 (100), 189 (11), 173 (20), 161 (12), 147 (18), 145 (7), 133 (60), 131 (11), 119 (12), 107 (15), 105 (18), 95 (12), 94 (13), 93 (83), 91 (18), 81 (11), 79 (12), 77 (11), 69 (8), 55 (12). Exact mass calc for $C_{14}H_{22}O$: 206.1671. Found: 206.1671. Minor isomer: ^{1}H-NMR (360 MHz, $CDCl_3$) δ 5.00 (d, J = 2.14 Hz, 1H), 4.16 (h, J = 5.17 Hz, 1H), 3.42–3.30 (m, 1H), 2.30–2.16 (m, 2H), 1.96–1.81 (m, 2H), 1.67 (dd, J = 12.10 and 7.15 Hz, 1H), 1.58 (brs, 1H), 1.48 (dd, J = 12.01 and 10.09 Hz, 1H), 1.41–1.00 (m, 3H), 1.13 (s, 3H), 1.09 (s, 3H), 1.04 (s, 3H); mass spectrum *m/e* (rel intensity) 206 (8), 188 (26), 174 (25), 173 (100), 161 (40), 148 (19), 147 (27), 145 (34), 133 (22), 132 (32), 131 (42), 129 (31), 119 (25), 117 (23), 109 (20), 107 (27), 105 (43). Exact mass calc for $C_{14}H_{22}O$: 206.1671. Found: 206.1672.

Diol **65**. To a soln of the above isomeric mixture of alcohols (68 mg, 0.33 mmol) in 1 ml THF at 0° was added dropwise $BH_3 \cdot THF$ (1 M in THF, 1.32 ml, 1.32 mmol). The mixture was warmed to room temp and stirred for 12 hr. The mixture was cooled to 0° and 3 M NaOH (0.50 ml) was added dropwise followed by 30% H_2O_2 (0.50 ml). The mixture was heated at reflux for 10 hr. After cooling, the mixture was diluted with ether and H_2O, transferred to a separatory funnel, and extracted three times with ether. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and the solvent was removed. Purification of the crude product by flash chromatography (10 g silica gel, EtOAc–hexanes, 7 : 3) gave 60 mg (81%) of a white solid. A sample was recrystallized from hexanes–EtOAc to give the pure β isomer (**65a**, m.p. 111–113°). R_f 0.27 (EtOAc–hexanes, 7 : 3); IR (KBr pellet) 3307, 2927, 2858, 1458, 1437, 1378, 1365, 1345, 1124, 1086, 1070, 1058, 1028 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 4.47 (m, 1H), 3.51 (d, J = 9.28 Hz, 1H), 2.63–2.48 (m, 1H), 2.22 (ddd, J = 15.27, 7.58, and 3.19 Hz, 1H), 2.07 (t, J = 9.55 Hz, 1H), 1.97 (ddd, J = 13.75, 7.10, and 3.25 Hz, 1H), 1.90 (dd, J = 13.93 and 7.27 Hz, 1H), 1.84–1.77 (m, 1H), 1.73 (dd, J = 12.87 and 9.01 Hz, 1H), 1.58 (dd, J = 13.94 and 3.00 Hz, 1H), 1.50–0.83 (m, 5H), 1.30 (s, 3H), 1.00 (s, 3H), 0.87 (s, 3H); mass spectrum *m/e* (rel intensity) 224 (9), 206 (5), 193 (8), 175 (7), 168 (9), 161 (13), 148 (10), 135 (17), 133 (12), 121 (12), 119 (15), 109 (100), 95 (56), 93 (52), 81 (44), 79 (32), 72 (37), 69 (41), 57 (36), 55 (43). Exact mass calc for $C_{14}H_{24}O_2$: 224.1776. Found: 224.1776.

Direct conversion of alcohol **53** *to diol* **65**. To a soln of **53** (295 mg, 1.43 mmol) in 5 ml pyridine at room temp was added O-3,4-dimethylphenyl chlorothioformate (0.345 ml). After stirring 10 hr, H_2O was added and the mixture was extracted three times with ether. The combined organic extracts were washed two times with 10% HCl, sat $NaHCO_3$ aq, brine, dried over Na_2SO_4, and the solvent was removed. Purification by flash chromatography (50 g silica, EtOAc–hexanes, 2 : 98) gave the thionocarbonate as a light yellow oil. Pyrolysis of the

thionocarbonate at 220° for 3 hr at 0.05 Torr gave a mixture (collected in a cold trap at −78°) which was taken up in pentane, washed with 1 M KOH, brine, and dried over Na_2SO_4. Most of the solvent was removed, and the diene was taken up in 3 ml THF. This soln was added dropwise to a mixture of dicyclohexylborane prepared from cyclohexene (304 mg, 3.70 mmol) and BH_3·THF (1.85 ml, 1.85 mmol) in 3 ml THF at 0°. The mixture was warmed to room temp and stirred for 4 hr. The mixture was cooled to 0°, and BH_3·THF (4.94 ml, 4.94 mmol) was added dropwise. The mixture was warmed to room temp and stirred for 12 hr. After cooling to 0°, 3 M NaOH (2.5 ml) was added dropwise followed by 30% H_2O_2 (2.5 ml). The mixture was heated at reflux for 8 hr, cooled, diluted with H_2O and ether, and extracted three times with ether. The combined organic extracts were washed with brine, dried over $MgSO_4$, and the solvent was removed. Purification by flash chromatography (30 g silica, EtOAc–hexanes, 7:3) gave 111 mg of diol **65** as a white solid (35% overall from alcohol **53**).

Hydroxyketone **66**. To a soln of **65** (57 mg, 0.25 mmol) in 7 ml dry benzene was added Ag_2CO_3 on Celite (1.16 g, 2.04 mmol). The mixture was refluxed for 75 min. Cooling, filtration, and removal of the solvent gave 53 mg (94%) of a white solid (m.p. 114–115°). R_f 0.55 (EtOAc–hexanes, 7:3); IR (neat) 3435, 2938, 2927, 2857, 1734, 1459, 1405, 1383, 1368, 1260, 1177, 1090, 916, 737 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 3.53 (d, J = 8.88 Hz, 1H), 2.78–2.65 (m, 1H), 2.44 (dd, J = 18.48 and 7.02 Hz, 1H), 2.40–2.32 (m, 1H), 2.24 (t, J = 9.30, 1H), 2.15 (d, J = 18.31 Hz, 1H), 2.09 (s, 2H), 1.82 (dd, J = 12.78 and 8.99 Hz, 1H), 1.66 (ddd, J = 13.76, 7.72, and 1.55 Hz, 1H), 1.60–1.42 (m, 2H), 1.22 (s, 3H), 1.08–0.98 (m, 1H), 1.02 (s, 3H), 0.90 (s, 3H); mass spectrum *m/e* (rel intensity) 222 (21), 204 (12), 191 (34), 161 (29), 151 (28), 133 (18), 126 (47), 109 (72), 107 (53), 97 (68), 93 (100), 84 (53), 79 (47), 72 (57), 67 (42), 55 (47), 53 (36). Exact mass calc for $C_{14}H_{22}O_2$: 222.1620. Found: 222.1617.

Hydroxyenone **67**. To a soln of 2,2,6,6-tetramethylpiperidine (0.114 ml, 0.68 mmol) in 1 ml dry THF at 0° was added dropwise n-BuLi (1.55 M in hexane, 0.436 ml, 0.68 mmol). The mixture was stirred for 15 min at 0°, then cooled to −78°. Me_3SiCl (0.172 ml, 1.35 mmol) in 0.5 ml THF was added followed by the dropwise addition of a soln of **66** (30 mg, 0.14 mmol) in 1 ml THF. After stirring 5 min at −78°, Et_3N (0.283 ml, 2.03 mmol) was added and the mixture was allowed to slowly warm to room temp. Sat $NaHCO_3$ aq was added and the mixture was diluted with ether, transferred to a separatory funnel, and extracted three times with ether. The combined organic extracts were washed three times with H_2O, brine, dried over Na_2SO_4, and the solvent was removed giving a 6:1 mixture of isomeric silyl enol ethers which was used without further purification. The vinyl proton for the major isomer appeared as a doublet (360 MHz, J = 1.32 Hz, δ 4.46) in the NMR spectrum whereas the corresponding proton for the minor isomer appeared as a broad singlet (δ 4.52). Therefore, the major and minor isomers are the expected $\Delta^{4,5}$ and $\Delta^{3,4}$ isomers, respectively. The mixture of silyl enol ethers in CH_3CN (2 ml) was added dropwise to a mixture of $Pd(OAc)_2$ (34 mg, 0.15 mmol) in dry CH_3CN (2 ml). The mixture was stirred 12 hr at room temperature. The solvent was removed and the residue was taken up in ether and filtered through a silica gel plug. The solvent was removed and the remaining oil was dissolved in a saturated aqueous solution of THF. One drop of 3 N HCl was added and the mixture was stirred 1 hr at room temp. The mixture was diluted with ether and H_2O, transferred to a separatory funnel, and extracted three times with ether. The combined organic extracts were washed with brine, dried over $MgSO_4$, filtered, and the solvent was removed. Purification by HPLC (EtOAc–hexanes, 2:3) gave 15 mg (50% overall from **66**, 54% based on 2 mg recovered **66**) a white solid (m.p. 117–118°, lit.[4i] 120–121°), which was identical in all respects with spectra (IR, 360 MHz ^{1}H-NMR) kindly furnished by Professor Koreeda. R_f 0.17 (EtOAc–hexanes, 2:3); IR (KBr pellet) 3370, 2940, 2932, 2926, 2848, 1695, 1625, 1466, 1431, 1414, 1371, 1365, 1309, 1279, 1258, 1229, 1120, 1091, 1073, 1062, 1038, 850, 825 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 5.70 (d, J = 1.88 Hz, 1H), 3.79 (d, J = 7.84 Hz, 1H), 2.83–2.65 (m, 2H), 2.46 (d, J = 17.59 Hz, 1H), 2.35 (d, J = 17.66 Hz, 1H), 2.25 (ddd, J = 14.54, 8.59, and 1.78 Hz, 1H), 2.16 (dd, J = 11.76 and 8.35 Hz, 1H), 1.92 (dd, J = 12.61 and 7.68 Hz, 1H), 1.30–1.20 (m, 2H), 1.23 (s, 3H), 1.08 (s, 3H), 0.95 (s, 3H); mass spectrum *m/e* (rel intensity) 220 (89), 205 (38), 202 (7), 187 (16), 177 (16), 159 (17), 148 (36), 135 (47), 133 (53), 121 (17), 119 (19), 111 (100), 105 (45), 93 (32), 91 (49), 80 (35), 79 (35), 77 (28), 69 (24), 65 (16), 55 (28), 53 (18). Exact mass calc for $C_{14}H_{20}O_2$: 220.1463. Found: 220.1460.

Hydroxyenone **67**. To a soln of **66** (24 mg, 0.11 mmol) in 1 ml 40% aqueous dioxane was added $PdCl_2$ (27 mg, 0.15 mmol) and $Pd(OAc)_2$ (27 mg, 0.12 mmol). The mixture was heated at reflux for 6 hr. Additional $PdCl_2$ and $Pd(OAc)_2$ (27 mg each) were added and the mixture was refluxed for another 18 hr. The mixture was diluted with ether and H_2O, extracted three times with ether, washed with brine, and dried over $MgSO_4$. Removal of the solvent and purification by HPLC (EtOAc–hexanes, 2:3) gave 6 mg recovered starting material (75% conversion), 5 mg of the desired **67** (28% yield based on recovered **66**), 3 mg of des-3-methylhirsut-5(6)-en-4,11-dione (17% yield based on recovered **66**), R_f 0.54 (EtOAc–hexanes, 7:3); m.p. 112–114°; IR (KBr pellet) 2964, 2949, 2920, 2859, 1724, 1703, 1630, 1466, 1450, 1431, 1416, 1381, 1361, 1313, 1292, 1258, 1243, 1195, 1172, 1115, 1071, 913, 886, 871, 860, 847, 823 cm^{-1}; ^{1}H-NMR (200 MHz, $CDCl_3$) δ 5.79 (d, J = 2 Hz, 1H), 3.16–2.94 (m, 2H), 2.72 (d, J = 10 Hz, 1H), 2.47 (s, 2H), 2.34 (dd, J = 14 and 8 Hz, 1H), 1.74 (m, 1H), 1.03–1.10 (m, 1H), 1.07 (s, 6H), 1.05 (s, 3H); and 1 mg of des-3-methylhirsutane-4, 11-dione (6% yield based on recovered **66**), R_f 0.59 (EtOAc–hexanes, 7:3); m.p. 97–99°; IR (KBr pellet) 2942, 2890, 2854, 1732, 1719, 1465, 1457, 1400, 1262, 1160, 1055, 1009 cm^{-1}; ^{1}H-NMR (360 MHz, $CDCl_3$) δ 2.62–2.30 (m, 3H), 2.18 (d, J = 18.54 Hz, 1H), 2.03 (ddd, J = 13.13, 8.74, and 2.21 Hz, 1H), 1.90 (d, J = 18.46 Hz, 1H), 1.74 (d, J = 13.80 Hz, 1H), 1.71–1.54 (m, 2H), 1.48 (br d, J = 13.85 Hz, 1H), 1.23–1.15 (m, 1H), 1.18 (s, 3H), 1.10 (s, 3H), 1.05 (s, 3H).

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REFERENCES

[1] For an account of this work, see: N. A. Lebel, *Trans. N.Y. Acad. Sci.* **27**, 858 (1965).

[2] For reviews of this intramolecular cycloaddition reaction see: [a]J. J. Tufariello, *Acc. Chem. Res.* **12**, 376 (1979); [b]W. Oppolzer, *Angew. Chem. Int. Ed. Engl.* **16**, 10 (1977); [c]A. Padwa, *Ibid.* **15**, 123 (1976); [d]D. St. C. Black, F. Crozier and V. C. Davis, *Synthesis* 205 (1975)

[3] Some notable examples include the following: [a]luciduline: W. Oppolzer and M. Petrizilka, *Helv. Chim. Acta* **61**, 2755 (1978); [b]cocaine: J. J. Tufariello, G. B. Mullen, J. J. Tegeler, E. J. Trybulski, S. C. Wong and S. A. Ali, *J. Am. Chem. Soc.* **101**, 2435 (1979); [c]chanoclavine: W. Oppolzer and J. I. Grayson, *Helv. Chim. Acta* **63**, 1706 (1980); [d]daunosamine: P. M. Wovkulich and M. R. Uskokovic, *J. Am. Chem. Soc.*

103, 3956 (1981); [c]biotin: E. G. Baggiolini, H. L. Lee, G. Pizzolato and M. R. Uskokovic, *Ibid.* **104**, 6460 (1982).

[4] For example, [a]alkene: A. C. Cope and E. R. Trumbull, *Organic Reactions*, Vol. 11, p. 317. Kreiger, New York (1960); [b]hydroxyl: E. H. White, *J. Am. Chem. Soc.* **77**, 6008 (1955); [c]hydrogen: G. A. Dolduras and J. Kollonitsch, *Ibid.* **100**, 341 (1978); [d]nucleophilic substitution: P. Muller and N. T. M. Phuong, *Tetrahedron Lett.* 4727 (1978).

[5] The preparation of monocyclic terpenes by implementation of this general strategy has been reported. [a]α-Bisabolol: M. A. Schwartz and G. C. Swanson, *J. Org. Chem.* **44**, 953 (1979); [b]α-bisabolol: T. Iwashita, T. Kusumi and H. Kakisawa, *Chem. Lett.* 947 (1979); [c]iridoids: M. Vandewalle, P. Storme and P. Callant, *Bull. Soc. Chim. Belg.* **92**, 1019 (1983); the preparation of the perhydroazulene skeleton has also been accomplished. [d]S. Takahashi, T. Kusami, Y. Sato, Y. Inouyl and H. Kakisawa, *Bull. Chem. Soc. Japan* **54**, 1777 (1981).

[6a] R. L. Funk, L. H. M. Horcher, II, J. U. Daggett and M. M. Hansen, *J. Org. Chem.* **48**, 2632 (1983); [b]R. L. Funk and G. L. Bolton, *Ibid.* **49**, 5021 (1984).

[7a] A. Pakrashi, B. Chakrabarty and A. Dasgupta, *Experientia* **32**, 394 (1976); [b]S. C. Pakrashi, P. P. Ghosh Dastidur, S. Basu and B. Achari, *Phytochemistry* **16**, 1103 (1977); [c]A. Pakrashi and C. Shaha, *Experientia* **33**, 1498 (1977); [d]S. C. Pakrashi, P. P. Ghosh Dastidur, S. Chakrabarty and B. Achari, *J. Org. Chem.* **45**, 4765 (1980).

[8] For a recent compilation of: [a]previous hirsutene total syntheses, see ref. 3 of ref. 6*b*; [b]previous coriolin total syntheses, see: M. Demuth, P. Ritterskamp and K. Schaffner, *Helv. Chim. Acta* **67**, 2023 (1984).

[9] O. Exner, *Coll. Czech. Chem. Commun.* **16**, 258 (1951).

[10a] N. A. LeBel and E. G. Banucci, *J. Org. Chem.* **36**, 2440 (1971); [b]J. Bjorgo, D. R. Boyd and D. C. Neill, *J. Chem. Soc. Chem. Commun.* 478 (1974).

[11] R. C. Fort, Jr., *Adamantane, the Chemistry of Diamond Molecules*, Vol. 5, Chap 7, p. 327. Marcel Dekker, New York (1976).

[12] This structural assignment is based on very similar coupling constants and chemical shift values of the oxymethylene proton resonances for **21** and **14** in contrast to those for **26**.

[13] For example: [a]Giberellins, A_1 and A_4; Kaur-16-en-19-oic acid and stevoil; A. I. Scott and T. K. Devon, *Handbook of Naturally Occurring Compounds*, Vol. II, pp. 226, 236. Academic Press, New York (1972); [b]The aglycones of wedeloside and carboxyatractyloside; P. B. Oelrichs, P. J. Vallely, J. K. Macleod and I. A. S. Lewis, *J. Nat. Prod.* **43**, 414 (1980).

[14] For a recent definition of this term see ref. 5 in: D. L. Boger and C. E. Brotherton, *J. Org. Chem.* **49**, 4050 (1984).

[15a] R. A. Bell, R. E. Ireland and L. N. Mander, *Ibid.* **31**, 2537 (1966); [b]Y. Nakahara, K. Mori and M. Matsui, *Agri. Biol. Chem.* **35**, 918 (1971).

[16] W. M. Pearlman, *Tetrahedron Lett.* **17**, 1663 (1967).

[17] P. H. Carlsen, R. Katsuki, V. S. Martin and K. B. Sharpless, *J. Org. Chem.* **46**, 3936 (1981).

[18] R. M. Moriarty, C. C. Chien and T. B. Adams, *Ibid.* **44**, 2210 (1979). In our hands, the Wolf–Kishner reduction of endo-3-oxobicyclo[3.2.1]octane-6-carboxylic acid proceeded with partial (80%) concomitant epimerization to the exo-acid.

[19] J. L. Marshall and J. R. Walter, *J. Am. Chem. Soc.* **96**, 6358 (1974).

[20] B. C. C. Cantello, J. M. Mellor and G. J. Scholes, *J. Chem. Soc.* 2915 (1971).

[21] For a partial listing, see ref. 2 in ref. 6*a*.

[22] To the best of our knowledge, only adamantane derivatives have been investigated, for example, 1-amino-3-chloro-adamantane. C. A. Grob and W. Schwarz, *Helv. Chim. Acta* **47**, 1870 (1964).

[23] For a review, see: [a]N. H. Fischer, E. J. Oliver and H. D. Fischer, *Fort. Chem. Org. Natur.* **38**, 166 (1979). For synthetic approaches see: [b]G. Posner, K. A. Babiak, G. L. Loomis, W. J. Frazee, R. D. Mittal and I. L. Karle, *J. Am. Chem. Soc.* **102**, 7498 (1980); [c]A. A. Devereese, D. T. De Clercq and M. Vandewalle, *Tetrahedron Lett.* **38**, 4767 (1980); [d]H.-J. Schafer and P. Metz, *Ibid.* **40**, 4067 (1982); [e]J. H. Rigby, *Ibid.* **40**, 1863 (1982).

[24] R. B. Kelly, J. Zamechik and B. A. Beckett, *Can. J. Chem.* **50**, 3455 (1972).

[25] R. E. Ireland, M. I. Dawson, J. Bordner and R. E. Dickerson, *J. Am. Chem. Soc.* **92**, 2568 (1970).

[26a] A. Hosomi and H. Sakurai, *Ibid.* **99**, 1673 (1977). The stereochemistry of the Sakurai reaction with substituted cyclohexenones and cycloheptenones has recently been reported. [b]C. H. Heathcock and T. A. Blumenkopf, *Ibid.* **105**, 2354 (1983).

[27] H. O. House, C. Y. Chu, W. V. Philips, T. S. B. Sayer and C.-C. Yan, *J. Org. Chem.* **42**, 1709 (1977).

[28] The reductive cleavage of γ-bromo ketones has been observed previously. See: [a]K. M. Baker and B. R. Davis, *Tetrahedron* **24**, 1655 (1968); [b]W. Oppolzer, L. Gorrichon and T. G. C. Bird, *Helv. Chim. Acta* **64**, 186 (1981).

[29] P. S. Grieco, S. Gilman and M. Nishizawa, *J. Org. Chem.* **41**, 1485 (1976).

[30] Commercially available from Petrarch Systems, Inc.

[31] Similar isomerizations have been observed previously and attributed to the angle strain inherent in bicyclo[3.3.0]oct-1-ene, see: [a]W. C. Agosta and S. Wolff, *J. Org. Chem.* **40**, 1699 (1975); [b]M. J. Begley, K. Cooper and G. Pattenden, *Tetrahedron* **37**, 4503 (1981); [c]The strain energies of bicyclo[3.3.0]oct-1-ene and bicyclo[3.3.0]oct-1(5)-ene have been calculated by using Allinger's MM1 empirical force field program and are 16.82 and 15.87 kcal mol^{-1} respectively. W. F. Maier and P. V. R. Schleyer, *J. Am. Chem. Soc.* **103**, 1891 (1981).

[32] S. Nozoe, J. Furukawa, U. Sankawa and S. Shibata, *Tetrahedron Lett.* 2795 (1976).

[33] For cyclic hydroboration of dienes, see: W. C. Still and K. P. Darst, *J. Am. Chem. Soc.* **102**, 7385 (1980) and refs therein.

[34] G. Mehta, A. V. Reddy, A. N. Murthy and D. S. Reddy, *J. Chem. Soc. Chem. Commun.* 540 (1982).

[35] H. S. Aaron, *Topics in Stereochemistry* (Edited by N. L. Allinger and E. L. Eliel), Vol. 11, pp. 1–52. Wiley, New York (1979).

[36] H. Gerlach, *J. Chem. Soc. Chem. Commun.* 1215 (1972).

[37] For selective oxidation of steroidal diols with Fetizon's reagent, see: [a]M. Fetizon and M. Golfier, *C.r. Hebd. Seanc. Acad. Sci. Paris* **267** (C), 900 (1968); [b]Sir E. R. H. Jones, G. D. Meakins, J. Pragnell, W. E. Muller and A. L. Wilkins, *J. Chem. Soc. Perkin Trans. I* 2376 (1974).

[38] A. E. Greene, M.-J. Luche and J.-P. Depres, *J. Am. Chem. Soc.* **105**, 2435 (1983).

[39] Y. Ito, T. Hirao and T. Saegusa, *J. Org. Chem.* **43**, 1011 (1978).

[40] M. Koreeda and S. G. Mislanker, *J. Am. Chem. Soc.* **105**, 7203 (1983).

[41a] T. Ito, N. Tomiyoshi, K. Nakamura, S. Azuma, M. Izawa, F. Maruyama, M. Yanagiya, H. Shirahama and T. Matsumoto, *Tetrahedron Lett.* **23**, 1721 (1982); [b]*Idem Tetrahedron* **40**, 241 (1984).

[42] W. C. Still, M. Kahn and A. Mitra, *J. Org. Chem.* **43**, 2923 (1978).

[43] N. A. LeBel, N. D. Ojha, J. R. Menke and R. J. Newland, *Ibid.* **37**, 2896 (1972).

[44] R. F. Borch, M. D. Berstein and H. D. Durst, *J. Am. Chem. Soc.* **93**, 2897 (1971).

[45] Prepared according to the procedure of Sakurai.[26a]

[46] Prepared in 20% yield by addition of 2-propenylmagnesium bromide to the sodium enolate (NaH) of 1,3-cyclohexandione followed by standard aqueous workup.

[47a] Prepared by addition of allenyl lithium[47b] to the sodium enolate (NaH) of 1,3-cyclohexandione; [b]D. Beeker, Z. Harel, M. Nagler and A. Gillon, *J. Org. Chem.* **47**, 3297 (1982).

[48] P. Beslin, R. Bloch and C. Conia, *Bull. Soc. Chim. Fr.* 508 (1969).

[49] P. Beslin and C. Conia, *Ibid.* 483 (1969).

[50] Prepared from 2-adamantanone by the following sequence:

(1) MCPBA, CH_2Cl_2; (2) DIBAL; (3) $Ph_3P{=}CH_2$; (4) PCC.

[51a]J. A. Pople, W. G. Schneider and H. J. Berstein, *High-Resolution Nuclear Magnetic Resonance*, p. 218. McGraw-Hill, New York (1959); [b]F. G. Riddell, *J. Chem. Soc. Chem. Commun.* 1403 (1968); [c]D. L. Griffith and B. L. Olson, *Ibid.* 1683 (1968); [d]M. Raban, F. B. Jones, Jr., E. H. Carlson, E. Banucci and N. A. LeBel, *J. Org. Chem.* **35**, 1496 (1970).

[52]G. Stork and R. L. Danheiser, *J. Org. Chem.* **38**, 1775 (1973).