Fragmentation of Alkoxy Radicals and Oxidative Elimination of Alicyclic Iodides†,[1]

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The azaallyl cation-mediated [4 + 3] cycloaddition with spiro[2.4]hepta-4,6-diene by the procedure of Schmid provides the tricyclic cycloadducts of general type **3**. The keto bridge of the cycloadducts **17c**, **21**, and **22** has been cleaved by $PhI(OAc)_2$–I_2 (Suárez cleavage), which involves β-fragmentation of an alkoxy radical, to furnish iodo lactones **19**, **32**, and **30a,b**, respectively. Subsequent oxidation of these alkyl iodides has been investigated to develop a new synthetic route for bridgehead olefins (i.e., **33**) of medium-sized carbocycles.

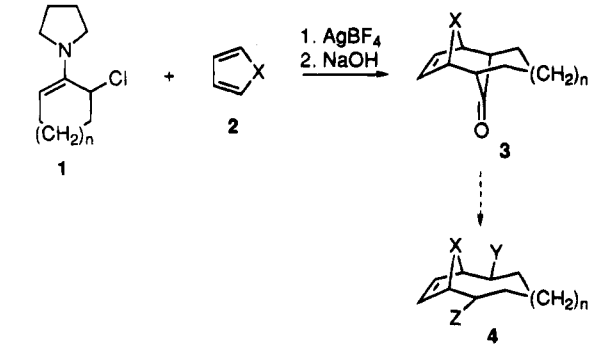
Introduction

As part of our research program directed at developing a new, general method for preparing functionalized medium-sized carbocycles and heterocycles,[1] we have been interested in the cyclic azaallyl [4 + 3] cycloaddition originally discovered by Schmid (Scheme 1).[2,3] The Schmid cycloadduct **3** contains a keto bridge which would be useful not only in providing a suitable functionality for further elaboration, but also in rigidifying the otherwise flexible medium-sized ring. An efficient method for cleavage of the keto bridge to generate the requisite ring system (e.g., **3** → **4**) was, however, central to the successful implementation of the Schmid cycloaddition to natural product synthesis. A practical solution for oxidative cleavage of the keto bridge was recently found by taking advantage of a facile β-fragmentation of an alkoxy radical.[1] Herein we report a full account of an alkoxy radical-mediated β-fragmentation and an oxidative elimination of the resulting alkyl iodides in the preparation of functionalized medium-sized carbocycles.

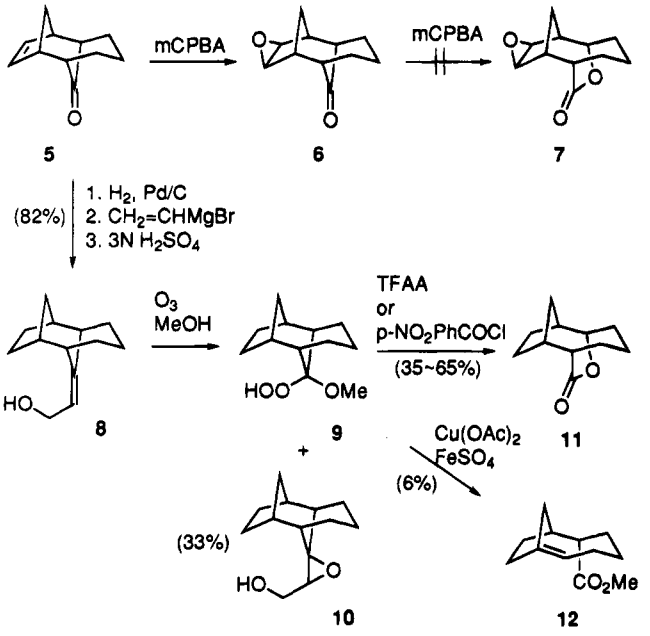
Results and Discussion

Baeyer–Villiger oxidation. Early attempts to convert the cycloadduct **3** to a lactone (*cf.* **7**, Scheme 2) by Baeyer–Villiger oxidation failed.[4] The lack of reactivity at the bridgehead carbonyl group in these compounds can be attributed to its resistance to undergo rehybridization to the sterically demanding sp^3 configuration. For instance, the ketal formation could not be accomplished from ketone **3** under various conditions. A similar behavior was previously noted by White for a structurally related compound.[5] Ultimately, a Baeyer–Villiger-type oxidation was successfully achieved by means of the α-methoxy hydroperoxide **9**, which was readily prepared,

Scheme 1



Scheme 2



along with epoxide **10**, by ozonolysis of olefin **8**. Treatment of **9** with TFAA or *p*-nitrobenzoyl chloride gave the lactone **11** (IR 1730 cm^{-1}) in 35 and 65% overall yield, respectively.[6] Interestingly, when **9** was treated with $Cu(OAc)_2$–$FeSO_4$ in MeOH,[6,7] the bridgehead olefin **12** (IR

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(1) Part 3 in the series "Synthetic Studies toward Taxol". Preliminary communication: Part 2. Oh, J.; Lee, J.; Jin, S.-j.; Cha, J. K. *Tetrahedron Lett.* **1994**, *35*, 3449.

(2) Schmid, R.; Schmid, H. *Helv. Chim. Acta* **1974**, *57*, 1883.

(3) The term "cycloaddition" is used to indicate the overall bonding change rather than to imply a concerted mechanism.

(4) (a) Oh, J.; Choi, J.-R.; Cha, J. K. *J. Org. Chem.* **1992**, *57*, 6664. (b) Choi, J.-R. Ph. D. Thesis, Vanderbilt University, 1993.

(5) White, J. D. In *Strategies and Tactics in Organic Synthesis*; Lindberg, T., Ed.; Academic Press: Orlando, 1984; Chapter 13.

(6) *Cf.* (a) Criegee, R.; Kaspar, R. *Liebigs Ann. Chem.* **1948**, *560*, 127. (b) Schreiber, S. L.; Liew, W.-F. *Tetrahedron Lett.* **1983**, *24*, 2363. (c) Schreiber, S. L. *J. Am. Chem. Soc.* **1980**, *102*, 6163.

(7) (a) Lande, S. S.; Kochi, J. K. *J. Am. Chem. Soc.* **1968**, *90*, 5196. (b) Sheldon, R. A.; Kochi, J. K. *Org. React.* **1972**, *19*, 279.

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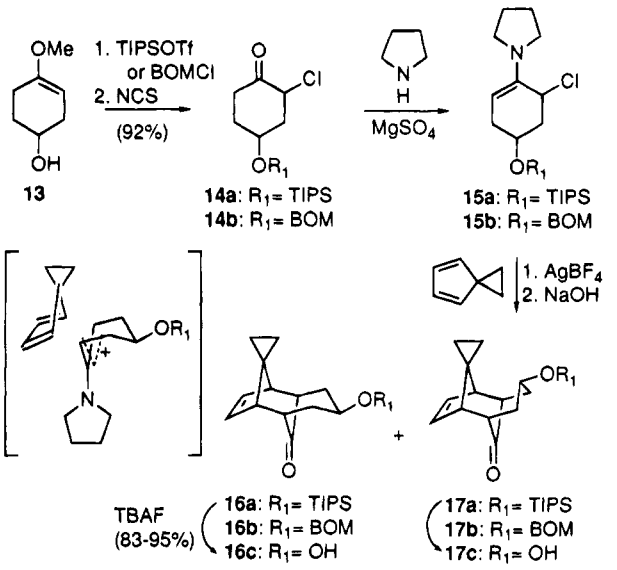
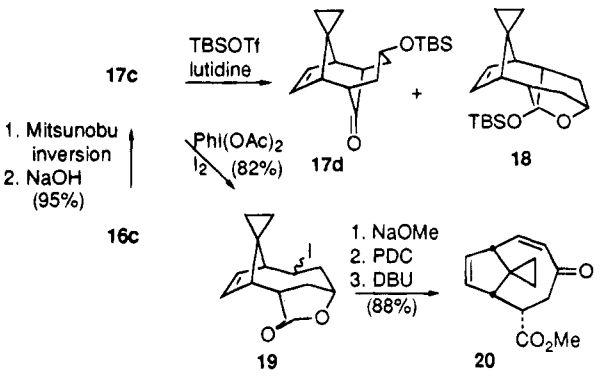
Scheme 3



Scheme 4



1745 cm^{-1}) was isolated in very poor (6%) yield. Structure **12** is consistent with ^1H and ^{13}C NMR spectra; the olefinic proton appears at 5.28 ppm (t, J = 7.5 H, 1 H), while the characteristic carbons appear at 176.3 (s), 145.1 (s) and 121.0 (d) ppm. Although this Criegee rearrangement sequence provides an acceptable solution, we decided to develop a more efficient and convenient method for the pivotal oxidative excision of the keto bridge.

Hydroxy Cycloadducts 16 and 17. We next chose to prepare a hydroxy- or alkoxy-substituted derivative of the cycloadduct **3**. The hydroxy functionality was envisaged to participate in the oxidative cleavage of the keto bridge, as well as provide a source for subsequent functionalization of the B-ring. The requisite starting material for the Schmid cycloaddition, 3-chloro-2-pyrrolidino-5-(triisopropylsiloxy)cyclohexene **15a** (Scheme 3), was prepared in high (~90%) overall yield from readily available 4-methoxy-3-cyclohexenol (**13**);[8] hydroxy protection (TIPS), followed by treatment with NCS gave 2-chloro-4-(triisopropylsiloxy)cyclohexanone (**14a**) as a ~10:1 diastereomeric mixture. Interestingly, this *trans* isomer shows the overwhelming preponderance of the axial orientation for the alkoxy group; the chloro substituent occupies the equatorial position and the alkoxy group axial. This unusual conformational preference was previously noted by Parker.[9] In any event, the ketone **14a** was then converted to the corresponding enamine **15a** by treating with pyrrolidine in the presence of $MgSO_4$.[10] Finally, Schmid cycloaddition of **15a** with spiro[2.4]hepta-4,6-diene gave a 4:1 mixture of cycloadducts **16a** and **17a** in 38–44% overall yield. The major cycloadduct **16a** was shown to possess the *cis* relationship between the cyclopropane moiety and the siloxy group. This stereochemical outcome is most likely a consequence of a boat-shaped azaallyl transition structure with the siloxy substituent in the pseudoequatorial position; such conformation would allow maximum orbital overlap (i.e., axial attack) during the ensuing [4 + 3] cycloaddition. The cycloaddition would also take place in the compact-mode with regard to the diene component.[11] Similarly, use of the BOM-protected derivative **14b** furnished the cycloadducts **16b** and **17b** as a 2:1 diastereomeric mixture (24–27% yield). As expected, the cyclohexane rings in both isomers **16** and **17** adopt a well-defined boat-like and chair-like arrangement, respectively, in which the overall conformation is controlled by the alkoxy group.

Alkoxy radical-induced β-fragmentation. With large quantities of cycloadducts **16** and **17** in hand, our attention was focused on the search for a general and efficient method for excising the keto bridge. We became intrigued with the well-established behavior of an alkoxy radical derived from a hemiketal or a lactol to undergo a facile fragmentation.[12-15] Although **17c** (readily available from desilyation of **17a**) exists largely as the hydroxy ketone, ^1H NMR analysis indicates the presence of a very small (≤10%) amount of the corresponding cyclic hemiketal. Support for the feasibility of this approach was found in an exploratory experiment with the hydroxy protection; silylation of **17c** with TBSOTf gave not only the expected product **17d**, but also the ketal **18** in a 2:1 ratio (95%) (Scheme 4). Indeed, treatment of **17c** with PhI(OAc)$_2$–I_2 (100 W lamp, 40 °C) afforded the iodolactone **19** (IR 1770 cm^{-1}), as a 4:1 diastereomeric mixture, in 76–82% yield. Lactone **19** was then converted to the enone ester **20** (IR 1735, 1680, 1605 cm^{-1}) by standard

(8) Marshall, J. A.; Flynn, G. A. *Synth. Commun.* **1979**, *9*, 123.

(9) (a) Parker, K. A.; Kim, H.-J. *J. Org. Chem.* **1992**, *57*, 752. (b) During silica gel column purification, **14a** undergoes equilibration to give rise to a 4:3 mixture of the two diastereomers, where the *trans* isomer is slightly favored. A similar behavior was also found for 4-(*tert*-butyldimethylsiloxy)- or 4-(benzyloxymethoxy)-substituted 2-chlorocyclohexanone, although the exact ratio of the *trans* isomer to *cis*, after chromatography, is different for each case.

(10) Blazejewski, J. C.; Cantacuzene, D.; Wakselman, C. *Tetrahedron* **1973**, *29*, 4233.

(11) For excellent reviews on the oxyallyl chemistry, see: (a) Noyori, R.; Hayakawa, Y. *Org. React.* **1983**, *29*, 163. (b) Hoffmann, H. M. R. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 1. (c) Mann, J. *Tetrahedron* **1986**, *42*, 4611. (d) Hosomi, A.; Tominaga, Y. In *Comprehensive Organic Synthesis*; Trost, B. M., Fleming, I., Eds.; Pergamon: Oxford, 1991; Vol. 5, Chapter 5.1.

(12) (a) Freire, R.; Marrero, J. J.; Rodríguez, M. S.; Suárez, E. *Tetrahedron Lett.* **1986**, *27*, 383. (b) de Armas, P.; Francisco, C. G.; Suárez, E. *J. Am. Chem. Soc.* **1993**, *115*, 8865 and references cited therein.

(13) For reviews on hypoiodite reactions, see: (a) Heusler, K.; Kalvoda, J. *Angew. Chem., Int. Ed. Engl.* **1964**, *3*, 525. (b) Kalvoda, J.; Heusler, K. *Synthesis* **1971**, 501. With HgO–I_2–*hν*: (c) Akhtar, M.; Barton, D. H. R. *J. Am. Chem. Soc.* **1964**, *86*, 1528. (d) Suginome, H.; Yamada, S. *J. Org. Chem.* **1984**, *49*, 3753. (e) *Idem. Tetrahedron Lett.* **1987**, *28*, 3963. With Pb(OAc)$_4$–I_2: (f) Meystre, C.; Heusler, K.; Kalvoda, J.; Wieland, P.; Anner, G.; Wettstein, A. *Helv. Chim. Acta* **1962**, *45*, 1317. With Hg(OAc)$_2$–I_2: (g) Chen, E. M.; Keefer, R. M.; Andrews, L. J. *J. Am. Chem. Soc.* **1967**, *89*, 428. (h) Georgoulis, C.; Valery, J.-M. *Bull. Soc. Chim. Fr.* **1974**, 178.

(14) For general reviews on polyvalent iodine compounds, see: (a) Varvoglis, A. *Chem. Soc. Rev.* **1981**, *10*, 377. (b) Merkushev, E. B. *Russ. Chem. Rev.* **1987**, *56*, 826. (c) Boguslavskaya, L. S.; Chuvatkin, N. N.; Kartashov, A. V. *Russ. Chem. Rev.* **1988**, *57*, 760. (d) Moriarty, R. M.; Vaid, R. K. *Synthesis* **1990**, 431. (e) Varvoglis, A. In *The Organic Chemistry of Polycoordinated Iodine*; VCH: New York, 1992.

(15) Ogata, Y.; Aoki, K. *J. Am. Chem. Soc.* **1968**, *90*, 6187.

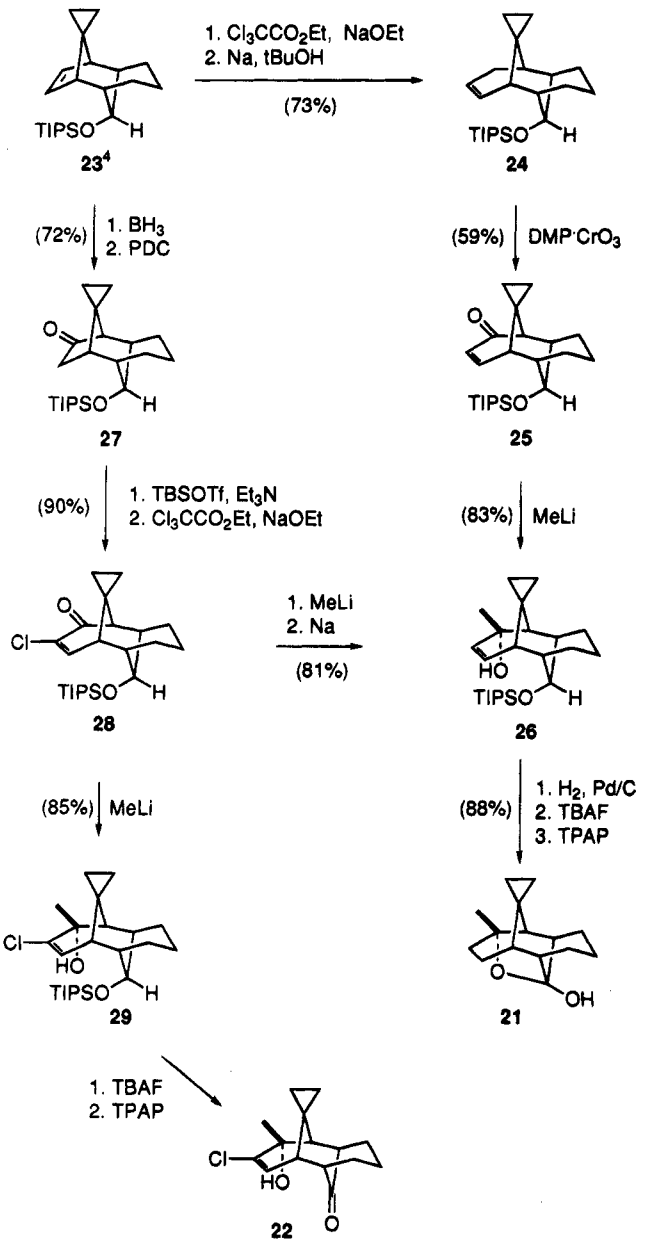
transformations. When a 4:1 mixture of cycloadducts **16a** and **17a** was directly subjected to desilylation and subsequent action of $PhI(OAc)_2-I_2$, the *trans* hydroxy ketone **16c** remained unreacted, whereas **17c** was smoothly converted into **19**. Thus, the Suárez cleavage also provides a practical solution to the otherwise difficult separation of a diastereomeric mixture of the cycloadducts. Although $PhI(OAc)_2-I_2$ had been well-known to generate acetoxy hypoiodite,[14,15] its synthetic potential remained unexplored until recently when Suárez and coworkers reported elegant synthetic applications of the $[PhI(OAc)_2-I_2]$-mediated radical cleavage.[12] In our hands, the Suárez protocol was found to be superior to other related methods.[13]

The requisite inversion of the hydroxy configuration of the major cycloadduct **16c** was then achieved by the Mitsunobu procedure [$iPrO_2CN{=}NCO_2iPr$, p-$NO_2C_6H_4CO_2H$, Ph_3P] and subsequent hydrolysis of the resulting p-nitrobenzoate in 95% overall yield.[16] Our initial concern for steric congestion during the Mitsunobu inversion proved to be unfounded.

As part of our synthetic studies toward taxol, we next examined the Suárez cleavage induced by the hydroxy group preinstalled onto the six-membered A-ring. The requisite substrates **21** and **22** were prepared from the previously prepared silyl ether **23**,[4] as outlined in Scheme 5. The one-carbon ring expansion with dichlorocarbene,[17] followed by dechlorination with Na (tBuOH, THF) and allylic oxidation with $DMP-CrO_3$[18] gave the enone **25** in modest yield. Subsequent treatment with MeLi furnished the tertiary alcohol **26** in 83% yield. Finally, the requisite hydroxy ketone **21** was obtained by hydrogenation (H_2, Pd/C), followed by desilylation and TPAP oxidation.[19] As expected, **21** exists predominantly as the hemiketal shown in Scheme 5. A more efficient route to **26** was later found in a slight modification involving the hydroboration–oxidation sequence of the olefin **23** to produce the ketone **27** in 72% yield. Treatment with TBSOTf and Et_3N gave the corresponding, labile silyl enol ether. The one-carbon ring enlargement was again accomplished in excellent overall yield by the use of dichlorocarbene to furnish the α-chloro ketone **28**. Treatment with MeLi followed by dechlorination with Na (tBuOH, THF) then gave **26** in 81% yield. In a similar manner, the hydroxy α-chloro ketone **22** was also prepared in good overall yield.

As delineated in Scheme 6, the Suárez cleavage of both compounds **21** and **22** took place smoothly to give rise to the corresponding iodo lactones in good yield. In the case of **22**, in competition with the formation of **30a,b** (as a 3:5 diastereomeric mixture, 60%), the direct β-scission of the tertiary alkoxy radical in the A-ring also occurred, followed by ring opening of the resulting cyclopropylcarbinyl radical, to give the bicyclic diketone **31** (12%). Such a bifurcate pathway was completely suppressed in the case of the hemiketal **21**; the iodo lactone **32** was obtained (77%) as a single diastereomer. More interestingly, prolonged exposure under Suárez's reaction conditions resulted in the formation of the bridgehead olefin **33**! No other regioisomeric olefin was found in the reaction mixture. The olefin **33** arises from the further action of Suárez's reagent on the iodo lactone **32**. When pure **32** was resubjected to Suárez's cleavage protocol, the formation of **33** was indeed found to proceed slowly (60% isolation yield, 2 days, 40 °C).

Scheme 5



Oxidation of Alkyl Iodides. Oxidation of alkyl iodides with *m*-CPBA has been postulated to generate the highly labile iodoso intermediates as the initial oxidation products, whose subsequent fate depends on the type of substrate and the solvent, affording the products of R–I bond cleavage by elimination, substitution, α-carbon oxidation or rearrangement (Scheme 7).[14,20-23] The literature results, taken together, sug-

(16) For reviews, see: (a) Mitsunobu, O. *Synthesis* **1981**, 1. (b) Castro, B. R. *Org. React.* **1983**, *29*, 1. (c) Hughes, D. L. *Org. React.* **1992**, *42*, 335.

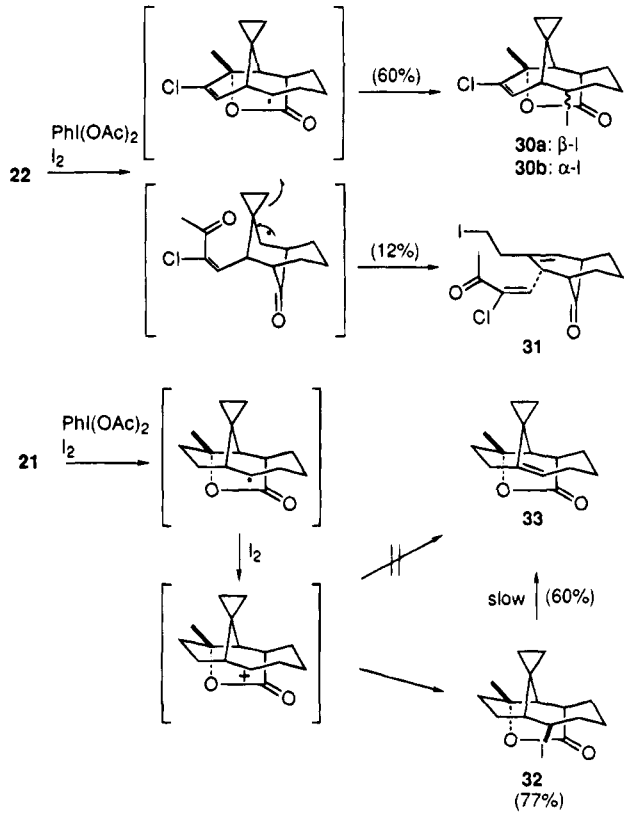
(17) *Cf.* Jefford, C. W.; Gunsher, J.; Hill, D. T.; Brun, P.; Le Gras, J.; Waegell, B. *Organic Syntheses*; Wiley: New York, 1988; Collect. Vol. VI, p 142.

(18) Salmond, W. G.; Barta, M. A.; Havens, J. L. *J. Org. Chem.* **1978**, *43*, 2057.

(19) Griffith, W. P.; Ley, S. V.; Whitcombe, G. P.; White, A. D. *J. Chem. Soc., Chem. Commun.* **1987**, 1625.

(20) (a) Beeley, N. R. A.; Sutherland, J. K. *J. Chem. Soc., Chem. Commun.* **1977**, 321. (b) Reich, H.; Peake, S. L. *J. Am. Chem. Soc.* **1978**, *100*, 4888. (c) Cambie, R. C.; Lindsay, B. G.; Rutledge, P. S.; Woodgate, P. D. *J. Chem. Soc., Chem. Commun.* **1978**, 919. (d) Cambie, R. C.; Chambers, D.; Lindsay, B. G.; Rutledge, P. S.; Woodgate, P. D. *J. Chem. Soc., Perkin Trans. 1* **1980**, 822. (e) Macdonald, T. L.; Narasimhan, N.; Burka, L. T. *J. Am. Chem. Soc.* **1980**, *102*, 7760.

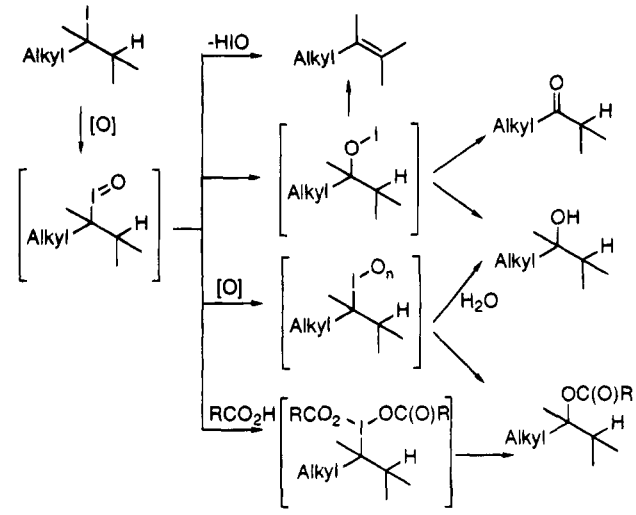
Scheme 6



gest that oxidative elimination of alkyl iodides could represent an excellent method for preparing the hindered olefins from conformationally rigid iodides (i.e., **32** → **33**). The oxidation of alkyl iodides bearing an electron-withdrawing substituent at the α-position has also been shown to provide the α,β-unsaturated compounds in good yield.[20b] Other iodides often give a mixture of products, including substitution/solvolysis products and further reaction products of an initially formed olefin.

We undertook the oxidation of our Suárez cleavage products with a peracid.[20-22] Treatment of **32** with *m*-CPBA (2 equiv) in CH_2Cl_2 gave the epoxide **34** in 59% yield, along with 17% of the epoxy alcohol **35** (Scheme 8). Use of $NaHCO_3$ during *m*-CPBA oxidation suppressed

Scheme 7



the formation of the latter side product, affording **34** in 80% yield, along with a very small (4%) amount of **35**. With *m*-CPBA, the transformation of **32** → **33** is considered as an elimination process of the corresponding iodoso intermediate. This reaction most likely involves a *syn* elimination process (in analogy to amine oxide, sulfoxide, and selenoxide eliminations), although an I → O rearrangement to the hypoiodite intermediate cannot be excluded.[20a,b] Subsequent epoxidation of the initial elimination product **33** appears to be considerably faster than the iodide oxidation of **32**, since epoxide **34** was found to be the major product even when 0.5 equiv of *m*-CPBA was employed. The formation of **35** can best be explained by assuming the intermediacy of the allylic iodide **36**, which would arise from the reaction of hypoiodous acid (IOH) with the olefin **33**. Subsequent oxidation of **36**, followed by [2,3] sigmatropic rearrangement of the resulting allylic iodoso intermediate **37** would then afford the allylic hypoiodite.[22e] The latter undergoes further oxidation or hydrolysis, as well as epoxidation, to give rise to **35**. Sodium bicarbonate is thought to scavenge hypoiodous acid and thus prevent the formation of **36**. Oxidation of the iodide **32** with $PhI(OCOCF_3)_2$–I_2 or $PhI(OCOCF_3)_2$[23b] alone took place in an analogous manner to afford a 1:1.2 mixture of the allylic trifluoroacetates **38** and **39** in 89% yield. The same products were obtained directly from the hemiketal **21** with $PhI(OCOCF_3)_2$–I_2 (Suárez cleavage conditons) in 76% yield. The trifluoroacetates **38** and **39** were further characterized by conversion into the corresponding enones **40** and **41**, respectively, by hydrolysis (NH_3, MeOH) and subsequent Swern oxidation. Furthermore, when the alcohol prepared by hydrolysis (NH_3, MeOH) of **39** was treated with *m*-CPBA, the resulting epoxy alcohol proved to be identical with **35** (vide supra).

When **32** was subjected to the action of NaI in acetone (at reflux) in an attempt to secure the iodo epimer, a mixture of olefins including **33** and **42** was obtained. In passing, we note that oxidative extrusion of the iodide **32** provides a unique solution for the introduction of the hydroxyl group at C-1 in synthetic studies of the taxanes. For example, osmylation (OsO_4, NMO) of the olefin **33** gave smoothly the diol **43** (83%), which was then protected as the acetonide **44**.

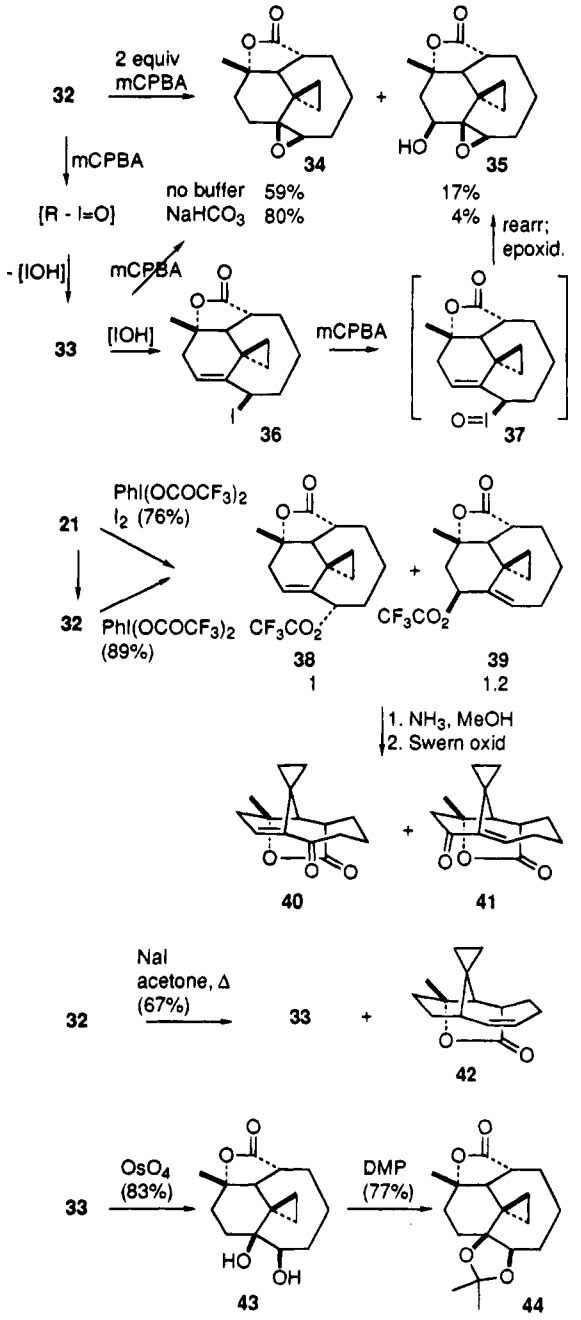
The iodides **19** and **30a,b** failed to react under the conditions of Suárez cleavage.[24] Nonetheless, all of them underwent peracid oxidation.[25] As outlined in

(21) Ogata, Y.; Aoki, K. *J. Org. Chem.* **1969**, *34*, 3974 and 3978.

(22) For other examples of oxidative extrusion of alkyl iodides, see: (a) McCabe, P. H.; de Jenga, C. I.; Stewart, A. *Tetrahedron Lett.* **1981**, *22*, 3679. (b) Morris, D. G.; Shepherd, A. G. *J. Chem. Soc., Chem. Commun.* **1981**, 1250. (c) Greenhouse, R.; Muchowski, J. M. *Can. J. Chem.* **1981**, *59*, 1025. (d) Davidson, R. I.; Kropp, P. J. *J. Org. Chem.* **1982**, *47*, 1904. (e) Yamamoto, S.; Itani, H.; Tsuji, T.; Nagata, W. *J. Am. Chem. Soc.* **1983**, *105*, 2908. (f) Higgins, S. D.; Thomas, C. B. *J. Chem. Soc., Perkin Trans. 1* **1983**, 1483. (g) Citterio, A.; Gandolfi, M.; Giordano, C.; Castaldi, G. *Tetrahedron Lett.* **1985**, *26*, 1665. (h) Eaton, P. E.; Cunkle, G. T. *Tetrahedron Lett.* **1986**, *27*, 6055. (i) Sicinski, R. R.; Szczepek, W. J. *Tetrahedron Lett.* **1987**, *28*, 5729. (j) Holmes, C. P.; Bartlett, P. A. *J. Org. Chem.* **1989**, *54*, 98. (k) Guivisdalsky, P. N.; Bittman, R. *J. Org. Chem.* **1989**, *54*, 4637. (l) Kocovsky, P.; Pour, M. *J. Org. Chem.* **1990**, *55*, 5580. (m) Damon, D. B.; Hoover, D. J. *J. Am. Chem. Soc.* **1990**, *112*, 6439. (n) Knapp, S.; Naughton, A. B. J.; Dhar, T. G. M. *Tetrahedron Lett.* **1992**, *33*, 1025. (o) Maag, H.; Rydzewski, R. M.; McRoberts, M. J.; Crawford-Ruth, D.; Verheyden, J. P. H.; Prisbe, E. J. *J. Med. Chem.* **1992**, *35*, 1440.

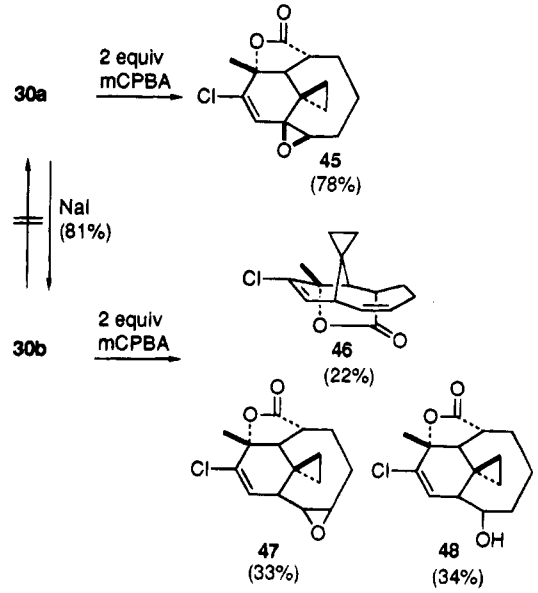
(23) For use of other oxidizing agents, see: aryliodine(III) dicarboxylates: (a) Buddrus, J. *Angew. Chem., Int. Ed. Engl.* **1973**, *12*, 163. (b) Gallos, J.; Varvoglis, A. *J. Chem. Soc., Perkin Trans 1* **1983**, 1999. (c) Boyer, J. H.; Natesh, A. *Synthesis* **1988**, 980. (d) Moriarty, R. M.; Khosrowshahi, J. S. *Synthesis* **1989**, 855; $I(OCOCF_3)_3$: (e) Cech, F.; Lindkeseder, M.; Zbiral, E. *Monatsh. Chem* **1976**, *107*, 1429. (f) Lindkeseder, M.; Zbiral, E. *Liebigs Ann. Chem.* **1977**, 1039. (g) Buddrus, J.; Plettenberg, H. *Chem. Ber.* **1980**, *113*, 1494; RuO_4: (h) Hernández, R.; Melián, D.; Suárez, E. *Synthesis* **1992**, 653.

Scheme 8



Scheme 9, treatment of **30a** with *m*-CPBA (2 equiv) in CH_2Cl_2 gave the epoxide **45** in 78%. On the other hand, *m*-CPBA oxidation of **30b** proceeded more slowly (than that of **30a**) to afford a mixture of products comprising the regioisomeric olefin **46** (22%), epoxide **47** (33%), and alcohol **48** (34%); no attempt has been made to determine the stereochemistry of the latter two products. This remarkably different behavior in the oxidation of iodides can be attributed to the stereoelectronic requirements of *syn* elimination of the iodoso intermediates. Interestingly, treatment of **30a** with NaI in refluxing acetone gave **30b** in 81% yield, while the latter iodide proved to be inert toward displacement. The marked difference in

Scheme 9



reactivity of the two iodides **30a** and **30b** toward S_N2 displacement must stem from the preference for peripheral attack by the nucleophile (i.e., **30a** → **30b**).[26]

Also, recourse was made to X-ray crystallography in order to make the unequivocal stereochemical determination of **30a,b**. While **30a** and **32** were obtained as an oil, crystalline **30b** was suitable for X-ray analysis.[27] The stereochemistry of **32** was then deduced by analogy to **30a,b**, as well as correlation of NMR data.

Conclusion

In summary, we have developed a general synthetic method for functionalized medium-sized carbocycles and heterocycles by tandem application of the Schmid cycloaddition and the Suárez cleavage.[28] Subsequent oxidation of the resulting alkyl iodides provides an efficient route to the bridgehead olefins, which should allow the introduction of additional functional groups. Further synthetic applications in natural product synthesis are currently in progress.

Experimental Section

General. All reactions were conducted under an atmosphere of dry nitrogen and in oven-dried glassware, and concentrations were performed under reduced pressure with a Büchi rotary evaporator. All solvents were purified before use. Ether, tetrahydrofuran, and toluene were distilled from sodium benzophenone ketyl. Methylene chloride was distilled from CaH_2.

NMR spectra were measured on commercially available spectrometers: ^1H at 360 and ^{13}C at 90 MHz. For ^1H spectra tetramethylsilane was used as internal standard. ^{13}C NMR spectra were referenced with the δ 77.0 resonance of $CDCl_3$. Low and high resolution mass spectra were measured as EI.

Melting points are uncorrected. Analytical thin layer chromatography (TLC) was performed by using Merck 60 F_{254} glass plates precoated with a 0.25-mm thickness of silical gel. Column chromatography was performed on kieselgel 60 (70–

(24) *Cf.* Alkyl iodides are known to be inert to a number of oxidizing agents such as ozone, periodate, hydrogen peroxide, and permanganate.[20b] Iodosobenzene also fails to oxidize alkyl iodides.

(25) Oxidation of **19** with *m*-CPBA gave a complex mixture of products, wherein the major reaction pathway appears to be the formation of the corresponding alcohol.

(26) *Cf.* Still, W. C. *J. Am. Chem. Soc.* **1979**, *101*, 2493.

(27) Inquiries concerning X-ray crystallographic analysis should be directed to J.L.A.

(28) Related application of the Suárez's cleavage on the Schmid cycloadduct derived from furan provides a new, conceptually appealing route to oxocane natural products: Kim, H.; Ziani-Cherif, C.; Cha, J. K. Manuscript in preparation.

230 mesh) silical gel. Unless otherwise noted, all compounds purified by chromatography are sufficiently pure (>95% by ^1H analysis) for use in subsequent reactions. Elemental analyses were performed by Atlantic Microlab, GA.

***anti*-10-Hydroxyethylidenetricyclo[4.3.1.1^{2,5}]undecane (8).** To a solution of the ketone **5** (580 mg, 3.58 mmol) in 95% EtOH (20 mL) was added 100 mg of 10% Pd/C, and hydrogenation was carried out at room temperature and under an atmospheric pressure of hydrogen. After 2 h, the solution was filtered through Celite, and the catalyst was washed thoroughly with 95% EtOH. The combined filtrates were concentrated *in vacuo* to give 544 mg (93%) of the dihydro ketone as a white solid: mp 56–58 °C; IR ($CHCl_3$) 1730 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 1.18 (dt, J = 12.6, 3.9 Hz, 1 H), 1.29 (m, 1H), 1.39 (dd, J = 8.6, 2.6 Hz, 2 H), 1.58–1.74 (m, 4 H), 1.99–2.16 (m, 4 H), 2.26 (br s, 1 H), 2.37 (br s, 2 H), 2.55 (br d, J = 12.4 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 18.6, 26.8, 28.0, 30.7, 43.1, 52.2, 221.6.

To a solution of the dihydro ketone (529 mg, 3.23 mmol) in THF (10 mL) was added vinylmagnesium bromide (1 M solution in THF, 9.7 mL) at room temperature. After 6 h, the reaction mixture was quenched with 3 M H_2SO_4. The product was extracted with ether (3 × 30 mL) and concentrated *in vacuo*. The concentrate was then diluted with THF (15 mL) and 3 M H_2SO_4 (15 mL). The resulting mixture was stirred for 72 h at room temperature. The product was extracted with ether (3 × 30 mL), washed with brine, dried over $MgSO_4$, and then concentrated *in vacuo*. The residue was purified by column chromatography using 4:1 hexane–EtOAc to give 460 mg (74%) of the allylic alcohol **8**: IR ($CHCl_3$) 3600–3100 (br) cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 1.0 (d, J = 12.0 Hz, 1 H), 1.19 (m, 1 H), 1.36 (m, 3 H), 1.48 (m, 2 H), 1.60 (m, 1 H), 1.68–1.93 (m, 4 H), 2.10 (m, 3 H), 2.35 (br d, J = 12.0 H, 1 H), 2.63 (br s, 1 H), 4.12 (d, J = 7 Hz, 2 H), 5.42 (t, J = 7 H, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 18.7, 27.6, 27.8, 29.1, 29.6, 30.1, 37.8, 41.9 (2C), 45.5, 58.5, 120.3, 148.1.

***anti*-11-Oxatricyclo[4.3.2.1^{2,5}]dodecan-10-one (11).** A solution of the olefin **8** (182 mg, 0.95 mmol) in 20 mL of MeOH was cooled at −78 °C, and ozone was passed through until the blue color persisted. The solution was purged with nitrogen, allowed to warm to room temperature, and then concentrated *in vacuo* at lower than 20 °C to give a mixture of the α-methoxy hydroperoxide **9** and the epoxide **10**. This crude mixture was dissolved in CH_2Cl_2 (10 mL), and K_2CO_3 (1.0 g) was added at 0 °C. The resulting mixture was stirred for 5 min under nitrogen. After the solution was cooled to −50 °C, TFAA (0.2 mL) was added, and the mixture was then allowed to warm to room temperature and finally stirred for an additional 4 h. The reaction mixture was filtered through Celite, and the salt was washed with CH_2Cl_2. The combined filtrates were washed with brine, dried over $MgSO_4$, and then concentrated *in vacuo*. The residue was purified by column chromatography using 4:1 hexane–EtOAc to give 62 mg (36%) of the lactone **11** as a white solid: mp 57–59 °C; IR ($CHCl_3$) 1730 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 1.22 (m, 1 H), 1.53 (m, 3 H), 1.60–1.98 (m, 7 H), 2.18 (m, 2 H), 2.35 (q, J = 6.6 Hz, 1 H), 3.18 (t, J = 9.3 Hz, 1 H), 4.55 (dd, J = 9.7, 7.2 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 20.8, 23.1, 23.9, 26.7, 26.9, 29.9, 37.1, 41.7, 48.8, 77.7, 176.8. Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.10; H, 8.91.

(6*R,7*R**)-6-Carbomethoxybicyclo[5.2.1]dec-1-ene (12).** A solution of the olefin **8** (90 mg, 0.47 mmol) in 20 mL of MeOH was cooled at −78 °C, and ozone was passed through until the blue color persisted. The solution was purged with nitrogen and allowed to warm to room temperature. Copper acetate (100 mg) was added, followed by 10 drops of a saturated solution of $Fe_2SO_4 \cdot 7H_2O$ in MeOH. The reaction mixture was then stirred for additional 10 min, diluted with ether (10 mL), and then quenched with aqueous 1 N HCl. The aqueous layer was extracted with ether (2 × 10 mL). The combined organic layers were washed with saturated NH_4OH and brine, dried over $MgSO_4$, and concentrated *in vacuo*. The residue was purified by column chromatography using 4:1 hexane–EtOAc to give 32 mg (32%) of the epoxide **10** and 5.5 mg (6%) of the methyl ester **12**: IR ($CHCl_3$) 1740 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 1.56–1.66 (m, 3 H), 1.81 (m, 1 H), 1.87–2.04 (m, 4 H), 2.12 (m, 2 H), 2.30 (d, J = 12.2 Hz, 1 H), 2.40 (m, 2 H), 2.58 (m, 1 H), 3.63 (s, 3 H), 5.28 (t, J = 7.5 H, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 22.2, 23.8, 25.4, 28.3, 32.0, 33.8, 34.1, 51.4, 53.2, 120.1, 145.1, 176.3; DEPT ^{13}C NMR δ (CH or CH_3) 33.8, 51.4, 53.2, 120.1, (CH_2) 22.2, 23.8, 25.4, 28.3, 32.0, 34.1.

2-Chloro-4-(triisopropylsiloxy)cyclohexanone (14a). A solution of **13** (2.00 g, 15.6 mmol) in CH_2Cl_2 (40 mL) were treated sequentially with 2,6-lutidine (3.68 mL, 31.59 mmol) and TIPSOTf (5.18 mL, 19.27 mmol) at 0 °C. The reaction mixture was stirred at rt for 2 h, quenched with water, and then extracted with ether (3 × 100 mL). The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. The concentrate was purified by column chromatography using 5:1 hexane–EtOAc to give 4.16 g (94%) of the corresponding TIPS ether as a light yellow oil.

N-Chlorosuccinimide (2.34 g, 17.56 mmol) was dissolved in a 1:1 mixture of THF and H_2O (60 mL), containing 200 mg (1.46 mmol) of NaOAc. To the resulting solution was added dropwise at 0 °C a solution of the above-mentioned TIPS ether in 10 mL of THF. The reaction mixture was stirred at 0 °C for 2 h and then poured into 30 mL of H_2O, followed by extraction with hexane (3 × 60 mL). The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated *in vacuo* to provide **14a** as ~10:1 mixture of the two diastereomers. The major diastereomer is *trans*; the chloro substituent occupies the equatorial position and the siloxy group axial. The crude product was purified by column chromatography using 5:1 hexane–EtOAc as eluent to afford 4.37 g (98%) of **14a** as a 4:3 diastereomeric mixture: IR (CCl_4) 1736 m^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 1.15 (m, 21 H), 1.66–2.25 (m, 3 H), 2.26–2.75 (m, 3 H), 4.24 (m, 3/7 H), 4.31 (m, 4/7 H), 4.46 (dd, J = 12.3, 6.1 Hz, 3/7 H), 4.78 (dd, J = 11.8, 5.7 Hz, 4/7 H); ^{13}C NMR (90 MHz, $CDCl_3$) major (*trans*) isomer δ 12.1, 18.0, 34.6, 35.7, 45.8, 60.2, 66.4, 202.6; minor (*cis*) isomer δ 11.8, 17.4, 34.0, 35.3, 45.5, 59.6, 65.6, 201.0.

3-Chloro-2-pyrrolidino-5-(triisopropylsiloxy)cyclohexene (15a). To a solution of **14a** (14.65 g, 48.06 mmol) in 120 mL of cyclohexane under a nitrogen atmosphere was added anhydrous $MgSO_4$ (33 g) in one portion. The mixture was cooled to 0 °C with an ice bath, and pyrrolidine (17.09 g, 0.24 mol) was then added dropwise. The reaction suspension was stirred at 0 °C overnight. Magnesium sulfate was removed by filtration through Celite, and the residue was rinsed thoroughly with hexane (3 × 50 mL). The combined filtrates were concentrated *in vacuo* to afford the chloro enamine **15a** as a pale yellow oil (17.2 g, 100%), which was used immediately for the next step without purification: IR (CCl_4) 1640 m^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 1.07 (m, 21 H), 1.72 (m, 1 H), 1.86 (m, 2H), 2.00–2.36 (m, 4 H), 2.55 (ddd, J = 16.6, 6.0, 7.2 Hz, 1 H), 2.71 (m, 1 H), 2.92 (m, 1 H), 3.00 (m, 1 H), 3.19 (m, 1 H), 4.24 (dd, J = 5.4, 2.4 Hz, 1 H), 4.37 (m, 1 H), 4.73 (t, J = 3.1 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 12.3, 18.0, 24.7, 34.3, 34.8, 36.8, 47.4, 56.8, 64.3, 66.4, 95.0, 141.3.

***exo*-8′- and *endo*-8′-(Triisopropylsiloxy)-*anti*-Spiro-{cyclopropane-1,11′-tricyclo[4.3.1.1^{2,5}]undec-3′-en}-10′-one (16a and 17a).** To a suspension of $AgBF_4$ (6.05 g, 31.1 mmol) in anhydrous CH_2Cl_2 (120 mL) under nitrogen and in the dark was added at −78 °C dropwise spiro[2.4]hepta-4,6-diene (5.36 g, 58.2 mmol). To the resulting mixture was added at −78 °C dropwise [via a syringe pump (1 mL/min)] a solution of the crude α-chloro enamine **15a** (9.00 g, 25.1 mmol) in 10 mL of CH_2Cl_2. The reaction mixture was stirred at −78 °C for 4 h and then allowed to warm to rt overnight with vigorous stirring. The precipitate was removed by filtration through Celite and washed with additional CH_2Cl_2. The filtrate was concentrated *in vacuo*, and the concentrate was dissolved in a 1:2 mixture (150 mL) of MeOH and water. Sodium hydroxide (4.0 g, 0.1 mol) was added. The resulting mixture was heated at reflux overnight. After a bulk of methanol was removed *in vacuo*, the aqueous layer was extracted with ether (3 × 50 mL). The combined extracts were washed with 1 N HCl and brine, dried ($MgSO_4$), and concentrated to give the crude product. Purification by column chromatography (10:1 hexane/EtOAc) gave a 4:1 diastereomeric mixture of the cycloadducts **16a** and **17a** (4.0 g, 44%) as white waxy solids. Separation of **16a** and **17a** was achieved by additional purification by column chro-

matography (18:1 hexane/EtOAc). The spectral data of the major product **16a**: R_f = 0.43 (10:1 hexane/EtOAc); IR (CCl_4) 1737 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.15 (dd, J = 7.9, 7.5 Hz, 2 H), 1.05 (m, 21 H), 1.51 (dd, J = 7.9, 7.5 Hz, 2 H), 2.15–2.29 (m, 4 H), 2.37–2.52 (m, 4 H), 3.95 (m, 1 H), 6.25 (s, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 5.2, 12.2 and 12.3 (3 C), 15.4, 17.7, and 18.0 (6 C), 31.1, 34.9, 47.6, 52.0, 64.3, 138.0, 216.9; MS m/e 360 (M^+, 5), 317 (100), 291 (25); HRMS (M^+) 360.2485 calcd for $C_{22}H_{36}O_2Si$, found 360.2460.

The spectral data of the minor product **17a**: R_f = 0.37 (10:1 hexane/EtOAc); IR (CCl_4) 1743 m^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.35 (dd, J = 7.9, 7.5 Hz, 2 H), 0.95–1.11 (m, 21 H), 1.29 (dd, J = 7.9, 7.5 Hz, 2 H), 2.08–2.18 (m, 4 H), 2.41–2.59 (m, 4 H), 4.99 (m, 1 H), 6.29 (s, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 10.8, 12.2, 15.5, 18.0, 32.3, 39.7, 47.9, 51.8, 64.2, 138.6, 216.8; MS m/e 360 (M^+, 5), 317 (55), 169 (90), 143 (100); HRMS (M^+) 360.2485 calcd for $C_{22}H_{36}O_2Si$, found 360.2471.

***exo*-8′-Hydroxy-*anti*-spiro{cyclopropane-1,11′-tricyclo-[4.3.1.1^{2,5}]undec-3′-en}-10′-one (16c).** To a solution of **16a** (2.1 g, 5.8 mmol) in THF (10 mL) were added tetra-*n*-butylammonium fluoride (10 mL of 1.0 M in THF) and 4 Å molecular sieves (500 mg) at 0 °C. The reaction mixture was stirred for 4 h at rt and filtered through Celite. The filtrate was concentrated *in vacuo*. The residue was diluted with EtOAc and 3 N HCl. The aqueous layer was then extracted with EtOAc (2 × 50 mL), and the combined organic layers were dried over $MgSO_4$, filtered, and concentrated *in vacuo*. Purification by column chromatography (1:1 hexane/EtOAc) gave the product **16c** as a white solid (1.0 g, 83%): mp 153–154 °C; IR ($CHCl_3$) 3595, 1725 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.15 (dd, J = 7.9, 7.5 Hz, 2 H), 1.51 (dd, J = 7.9, 7.5 Hz, 2 H), 1.75 (br s, 1 H), 2.18–2.30 (m, 4 H), 2.40–2.52 (m, 4 H), 3.88 (m, 1 H), 6.25 (s, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 5.2, 15.5, 31.1, 33.8, 47.4, 51.9, 64.0, 138.1, 216.2; MS m/e (rel intensity) 204 (M^+, 8), 185 (19), 158 (32), 145 (60), 117 (100); HRMS (M^+) 204.1150 calcd for $C_{13}H_{16}O_2$, found 204.1128.

Mitsunobu Inversion of 16c to *endo*-8′-Hydroxy-*anti*-spiro{cyclopropane-1,11′-tricyclo[4.3.1.1^{2,5}]undec-3′-en}-10′-one (17c). To a solution of alcohol **16c** (780 mg, 3.3 mmol) in THF (20 mL) were added sequentially at 0 °C diisopropyl azodicarboxylate (840 mg, 4.2 mmol), *p*-nitrobenzoic acid (780 mg, 4.7 mmol), and triphenylphosphine (1.2 g, 4.7 mmol). The reaction mixture was allowed to warm to rt and stirred for additional 4 h. After the reaction mixture was concentrated *in vacuo*, the residue was purified by column chromatography (1:10 EtOAc/hexane) to give the *p*-nitrobenzoate of **17c**.

The *p*-nitrobenzoate was dissolved in a 1:1 mixture of MeOH and THF (30 mL), and NaOH (40 mg, 1 mmol) was then added. The reaction mixture was then stirred at rt for 3 h. After the solvents were removed *in vacuo*, purification by column chromatography (1:1 hexane/EtOAc) afforded the desired alcohol **17c** as a white solid (740 mg, 95%): mp 178–180 °C; IR ($CHCl_3$) 3600, 1730 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.30 (dd, J = 7.9, 7.5 Hz, 2 H), 1.32 (dd, J = 7.9, 7.5 Hz, 2 H), 1.63 (br s, 1 H), 2.03 (m, 2 H), 2.16 (m, 2 H), 2.50 (m, 2 H), 2.65 (dd, J = 14.3, 6.9 Hz, 2 H), 4.80 (m, 1 H), 6.28 (s, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 9.7, 15.2, 31.9, 38.5, 48.9, 51.8, 64.1, 138.7, 217.4; MS m/e (rel intensity) 204 (M^+, 13), 161 (37), 145 (43), 117 (100); HRMS (M^+) 204.1150 calcd for $C_{13}H_{16}O_2$, found 204.1157.

TBS Protection of 17c. To a solution of **17c** (19 mg, 0.09 mmol) in CH_2Cl_2 (2 mL) were added sequentially lutidine (30 mg, 0.28 mmol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (30 mg, 0.11 mmol) at 0 °C under N_2. The reaction mixture was stirred for 30 min at 0 °C and then washed successively with aqueous $NaHCO_3$ solution, 3 N HCl, and brine. The organic layer was dried ($MgSO_4$) and concentrated *in vacuo*. The concentrate was purified by prep TLC (18:1 hexane/EtOAc) to give 18 mg (61%) of **17d** and 10 mg (34%) of **18**. The spectral data of **17d**: mp 98–100 °C; IR ($CHCl_3$) 1730 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.01 (s, 6 H), 0.33 (dd, J = 7.9, 7.5 Hz, 2 H), 0.86 (s, 9 H), 1.28 (dd, J = 7.9, 7.5 Hz, 2 H), 2.04 (m, 2 H), 2.13 (br d, J = 3.6 Hz, 2 H), 2.43 (m, 4 H), 4.91 (m, 1 H), 6.27 (br s, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ −4.8, 10.8, 15.3, 17.8, 25.6, 32.2, 39.1, 49.5, 51.6, 64.1, 138.5, 216.5; MS m/e 318 (M^+), 261 (35), 169 (100), 143 (100); HRMS (M^+) 318.2015 calcd for $C_{19}H_{30}O_2Si$, found 318.2021.

The spectral data of **18**: ^1H NMR (360 MHz, $CDCl_3$) δ 0.05 (m, 2 H), 0.10 (s, 6 H), 0.90 (s, 9 H), 1.10 (m, 2 H), 1.85–2.05 (m, 4 H), 2.19 (m, 2 H), 4.25 (m, 1H), 6.18 (m, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ −2.8, 6.0, 15.1, 17.8, 25.8, 29.7, 33.5, 44.2, 47.6, 72.5, 110.1, 137.6.

7β- and 7α-Iodo-*anti*-Spiro{cyclopropane-1,11′-4-oxa-tricyclo[5.2.1.2^{2,5}]dodec-9′-en}-3-one (19). To a solution of the hydroxy ketone **17c** (1.30 g, 6.4 mmol) in a 1:1 mixture of benzene and cyclohexane (300 mL) were added at rt iodine (1.8 g, 7.1 mmol) and iodobenzene diacetate (2.3 g, 7.1 mmol). The reaction mixture was irradiated with one 100 W tungsten filament lamp for 1 h at 40 °C. The mixture was then washed with aqueous $NaHSO_3$ solution and brine and dried over $MgSO_4$. Evaporation of the solvents, followed by purification by column chromatography (4:1 hexane/EtOAc) gave two diastereomeric iodo lactones. The less polar fraction was obtained as a colorless solid (333 mg, 16%): R_f 0.37 (4:1 hexane/EtOAc); mp 111–113 °C dec; IR ($CHCl_3$) 1765 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.47 (m, 1 H), 0.57 (m, 1 H), 0.75 (m, 1 H), 1.75 (m, 1 H), 2.33 (m, 1 H), 2.58 (m, 2 H), 2.67 (m, 1 H), 2.72–2.90 (m, 2 H), 3.28 (d, J = 14.1 Hz, 1 H), 4.82 (m, 1 H), 5.91 (m, 1 H), 6.16 (dd, J = 6.0, 3.3 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 9.9, 17.1, 27.6, 27.8, 29.2, 37.7, 40.7, 48.9, 57.2, 76.9, 134.9, 135.2, 178.7; MS m/e 330 (M^+), 203 (30), 157 (73), 131 (100); HRMS (M^+ − I) 203.1072 calcd for $C_{13}H_{15}O_2$, found 203.1077.

The more polar fraction was obtained as a colorless solid (1.2 g, 57%): R_f 0.29 (4:1 hexane/EtOAc); mp 117–118 °C; IR ($CHCl_3$) 1762 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.64 (m, 2 H), 0.80 (m, 1 H), 1.10 (m, 1 H), 2.24 (m, 1 H), 2.42 (ddd, J = 6.2, 12.9, 1.6 Hz, 1 H), 2.57–2.70 (m, 3 H), 2.90–3.10 (m, 2 H), 4.46 (dd, J = 4.0, 5.0 Hz, 1 H), 4.55 (td, J = 10.0, 3.0 Hz, 1 H), 5.90 (m, 1 H), 6.90 (m, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 8.8, 18.4, 26.4, 30.1, 30.5, 38.0, 44.4, 48.6, 62.6, 77.9, 132.6, 136.0, 177.9; MS m/e 330 (M^+), 203 (50), 157 (75), 131 (100); HRMS (M^+) 330.0072 calcd for $C_{13}H_{15}O_2I$, found 330.0078.

Methyl (1*S,6*R**,7*R**)-4′-Oxo-spiro{cyclopropane-1,10′-bicyclo[5.2.1]deca-2′,8′-diene}-6′-carboxylate (20).** To a solution of **19** (1.10 g, 3.3 mmol) in a 1:2 mixture of MeOH and THF (30 mL) was added NaOMe (3 mg, 0.06 mmol) at rt. After 1 h, the solvents were removed *in vacuo* to afford the corresponding hydroxy methyl ester in quantitative yield. PDC (2.9 g) and 4 Å molecular sieves (2.9 g) were sequentially added at 0 °C to the solution of the crude product in CH_2Cl_2 (20 mL). The resulting mixture was stirred at rt for 3 h, diluted with Et_2O, and filtered through Celite. Evaporation of the solvents *in vacuo* gave the crude iodo ketone as a pale yellow oil. DBU (1.5 g, 10 mmol) was then added to a solution of this crude ketone in THF (10 mL). The reaction mixture was then heated at 70 °C for 2 h. The mixture was cooled to rt and diluted with ether. It was washed successively with water, 3 N HCl, and brine. Finally, the organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. Purification by flash column chromatography (10:1 hexane/EtOAc) gave the enone **20** (670 mg, 88%) as a pale yellow oil: R_f = 0.65 (10:1 hexane/EtOAc); IR ($CHCl_3$) 1735, 1680, 1605 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.50 (m, 2 H), 0.67 (m, 1 H), 0.75 (m, 1 H), 2.39 (m, 1 H), 2.76 (br s, 1H), 2.88 (m, 1 H), 2.94 (m, 1 H), 3.02 (m, 1 H), 3.68 (s, 3 H), 5.80 (m, 1 H), 5.86 (dd, J = 12.3, 1.8 Hz, 1 H), 6.01 (m, 2 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 11.6, 22.6, 28.8, 40.7, 48.0, 51.9, 53.9, 54.2, 130.6, 131.9, 133.1, 137.6, 173.4, 209.6; MS m/e 232 (M^+), 200 (40), 173 (70), 145 (100), 117 (97); HRMS (M^+) 232.1099 calcd for $C_{14}H_{16}O_3$, found 232.1004.

8′-oxo-*endo*-11′-(triisopropylsiloxy)-*anti*-spiro-{cyclopropane-1,10′-tricyclo[5.2.1.1^{2,6}]-undecane} (27). To a solution of the olefin **23** (7.58 g, 21.91 mmol) in 80 mL of anhydrous THF was added dropwise 1 M of BH_3·THF (45.1 mL, 45.1 mmol) at 0 °C under nitrogen. The reaction mixture was stirred for 3 h at the same temperature and then quenched by addition of water (30 mL). To the mixture were added successively 120 mL of EtOH, 110 mL of 2 M NaOH, and 28 mL of 30% H_2O_2 (0.274 mol) at 0 °C. The resulting mixture was allowed to warm to rt and stirred for 3 h. After the volatile solvents were evaporated *in vacuo*, the residue was

then diluted with EtOAc. The aqueous layer was thoroughly extracted with EtOAc. The combined organic layers were dried over $MgSO_4$ and concentrated *in vacuo* to give the crude alcohol.

To a solution of the crude alcohol in 150 mL of anhydrous CH_2Cl_2 were added at room temperature 4 Å molecular sieves (14 g) and PDC (16.5 g, 43.82 mmol) in one portion. The reaction mixture was stirred at rt for 3 h. The mixture was diluted with 150 mL of Et_2O, filtered through Celite, and then concentrated *in vacuo*. The concentrate was purified by column chromatography (15:1 hexane/EtOAc) to afford the ketone **27** as a white solid (5.69 g, 72%): mp 89–92 °C; IR ($CHCl_3$) 1745 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.36 (m, 2 H), 0.98–1.18 (m, 23 H), 1.50–1.62 (m, 2 H), 1.75–1.92 (m, 3 H), 1.98 (m, 2 H), 2.13 (m, 1 H), 2.16–2.35 (m, 3 H), 2.94 (d, J = 17.1 Hz, 1 H), 3.81 (s, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 12.0, 13.4, 13.7, 16.8, 18.0, 25.7, 28.8, 29.5, 39.9, 41.6, 44.9, 45.3, 56.6, 75.2, 215.8; MS *m/e* 362 (M^+, 2), 319 (100), 185 (32), 171 (48), 131 (60); HRMS (M^+) 362.2641 calcd for $C_{22}H_{38}O_2Si$, found 362.2656.

9′-chloro-10′-oxo-12′-*endo*-(triisopropylsiloxy)-*anti*-spiro{cyclopropane-1,10′-tricyclo[5.3.1.1^{2,6}]-8′-dodecene} (28). A solution of the ketone **27** (5.49 g, 15.13 mmol) in anhydrous CH_2Cl_2 (55 mL) was treated sequentially with triethylamine (21.1 mL, 0.151 mol) and *tert*-butyldimethylsilyl trifluoromethanesulfonate (5.9 mL, 25.72 mmol) at 0 °C under nitrogen. The resulting mixture was allowed to warm to rt and stirred for 3 h. After a bulk of the solvents were removed *in vacuo*, the resulting viscous brown residue was dissolved in anhydrous hexane (550 mL). The resulting solution was transferred via a cannula into a 1 L round-bottomed flask for the next step.

Freshly prepared solid NaOMe (16.4 g, 0.303 mmol) was then added, followed by slow addition (3 mL/h, syringe pump) of ethyl trichloroacetate (35 mL, 0.257 mol) at 0 °C under nitrogen. The reaction mixture was allowed to warm to rt and stirred for additional 4 h. The mixture was diluted with water, and the aqueous layer was then extracted with Et_2O. The combined organic layers were dried ($MgSO_4$) and concentrated *in vacuo*. The concentrate was purified by column chromatography (15:1 hexane/EtOAc) to afford the α-chloro enone **28** as a white solid (5.57 g, 90%): mp 99–101 °C; IR ($CHCl_3$) 1696 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.36–0.52 (m, 2 H), 0.93 (m, 2 H), 1.03 (m, 21 H), 1.55 (m, 1 H), 1.64–2.08 (m, 6 H), 2.17–2.33 (m, 2 H), 2.41 (m, 1 H), 3.87 (s, 1 H), 7.20 (d, J = 7.0 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 12.0, 14.3, 17.8, 17.9, 18.6, 22.3, 30.2, 30.3, 37.8, 41.0, 46.4, 56.8, 74.3, 133.9, 149.3, 194.8; MS *m/e* 367 (M^+ – iPr, 57), 365 (M^+ – iPr, 100), 271 (27), 183 (38), 171 (43), 131 (51); HRMS (M^+ – iPr) 367.1674 calcd for $C_{20}H_{30}Cl_{37}O_2Si$, found 367.1679; 365.1704 calcd for $C_{20}H_{30}Cl_{35}O_2Si$, found 365.1701.

10′-Hydroxy-10′-methyl-*endo*-12′-(triisopropylsiloxy)-*anti*-(1*R,2*R**,6*S**,7*S**,10*S**,12*R**)-spiro{cyclopropane-1,-10′-tricyclo[5.3.1.1^{2,6}]-8′-dodecene} (26).** To a solution of **28** (5.57 g, 13.62 mmol) in anhydrous ether was added dropwise a 1.5 M solution of MeLi (55 mL, 81.72 mmol) in Et_2O at 0 °C under nitrogen. After the reaction mixture was stirred for additional 1 h at 0 °C, the reaction was quenched with aqueous saturated NH_4Cl solution. The aqueous layer was extracted with Et_2O, dried ($MgSO_4$), and concentrated *in vacuo*. The concentrate was purified by column chromatography (15:1 hexane/EtOAc) to give the corresponding tertiary alcohol (5.21 g, 90%) as a white solid.

Sodium (2.6 g, 0.11 g atom), followed by *tert*-butyl alcohol (21.2 mL, 0.223 mol) was added to anhydrous THF (50 mL). The resulting mixture was heated at reflux. A solution of the above-mentioned tertiary alcohol (1.90 g, 4.46 mmol) in THF (30 mL) was then added. The reaction mixture was stirred at reflux for additional 24 h, cooled, and filtered through Celite. The filtrate was diluted with ice–water and extracted with Et_2O. The combined organic extracts were dried ($MgSO_4$) and concentrated *in vacuo*. The concentrate was purified by column chromatography (15:1 hexane/EtOAc) to provide the olefin **26** as a colorless oil (1.56 g, 90%): IR (CH_2Cl_2) 3445 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.26 (m, 1 H), 0.63–0.79 (m, 3 H), 1.11 (m, 21 H), 1.17–1.34 (m, 2 H), 1.39 (s, 3 H), 1.42–1.57 (m, 1 H), 1.67–1.80 (m, 2 H), 1.88–2.29 (m, 4 H), 2.60 (m, 1 H), 3.91 (br s, 1 H), 4.46 (br s, 1 H), 5.45 (d, J = 9.6 Hz, 1 H), 5.93 (dd, J = 9.6, 6.2 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 12.2, 13.7, 17.4, 17.7, 18.0, 18.1, 29.8, 31.3, 31.4, 37.4, 40.7, 44.3, 52.7, 73.7, 75.4, 132.5, 136.5; MS *m/e* 347 (M^+ – iPr, 38), 329 (30), 199 (92), 173 (79), 131 (100); HRMS (M^+ – iPr) 347.2406 calcd for $C_{21}H_{35}O_2Si$, found 347.2397.

10′-Hydroxy-10′-methyl-*anti*-(1*R,2*R**,6*S**,7*S**,10*S**)-spiro{cyclopropane-1,10′-tricyclo[5.3.1.1^{2,6}]-8′-dodecen}-12′-one (21).** To a solution of **26** (1.50 g, 3.86 mmol) in 150 mL of MeOH was added 10% Pd/C (0.15 g). The mixture was stirred at rt overnight under an atmosphere of hydrogen and then filtered through Celite. The filtrate was concentrated in *vacuo*. The residue was purified by column chromatography (15:1 hexane/EtOAc) to give the corresponding saturated alcohol as a colorless oil (1.44 g, 95%).

This crude alcohol was dissolved in 75 mL of THF. After the solution was cooled to 0 °C, 4 Å molecular sieves (1.8 g), followed by 1 M tetra-*n*-butylammonium fluoride (7.7 mL, 7.7) mmol) were added. The resulting mixture was then stirred at rt for additional 2 h. The reaction mixture was filtered through Celite, and the filtrate was concentrated *in vacuo*. The concentrate was purified by column chromatography (3:1 hexane/EtOAc) to afford the corresponding diol as a white solid (0.82 g, 95%).

A solution of an aliquot of this diol (0.21 g, 0.89 mmol) in 20 mL of CH_2Cl_2 was treated with 4-methylmorpholine *N*-oxide (0.32 g, 2.67 mmol) and powdered 4 Å molecular sieves (45 mg). Tetrapropylammonium perruthenate (32 mg, 0.09 mmol) was added in one portion at rt. After 1 h, the reaction mixture was filtered through a pad of silica gel and then eluted with EtOAc. The filtrate was concentrated *in vacuo* to furnish the hemiketal **21** as a white solid (0.205 g, 98%): mp 130–132 °C; IR (CH_2Cl_2) 3360, 1710 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.35 (m, 1 H), 0.59 (m, 2 H), 0.75 (m, 1 H), 1.16–1.28 (m, 5 H), 1.42 (m, 1 H), 1.55 (m, 1 H), 1.63–2.23 (m, 10 H), 2.60 (br s, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 13.4, 14.5, 17.9, 22.0, 28.4, 28.6, 28.9, 29.7, 32.5, 41.7, 43.1, 48.4, 55.3, 80.3, 103.5; MS *m/e* 234 (M^+, 29), 176 (100), 164 (93), 145 (66), 135 (81); HRMS (M^+) 234.1620 calcd for $C_{15}H_{22}O_2$, found 234.1598.

9′-Chloro-10′-hydroxy-10′-methyl-*anti*-(1*R,2*R**,6*S**,7*R**,-10*R**)-spiro{cyclopropane-1,10′-tricyclo[5.3.1.1^{2,6}]-8′-dodecen}-12′-one (22).** Following the identical procedure given for the preparation of **21**, treatment of the ketone **28** with MeLi afforded the alcohol **29** in 85% yield. Subsequent deprotection with tetra-*n*-butylammonium fluoride, followed by TPAP oxidation, gave rise to the requisite product **22** in 75% overall yield. Purification by column chromatography (3:1 hexane/EtOAc) gave the hydroxy-ketone **22** as a white solid: mp 138–140 °C; IR ($CHCl_3$) 3460, 1720 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.47 (m,1 H), 0.75 (m, 1 H), 1.04–1.15 (m, 2 H), 1.40–1.65 (m, 4 H), 1.79 (m, 2 H), 2.13–2.33 (m, 6 H), 2.44 (m, 1 H), 3.10 (m, 1 H), 5.98 (d, J = 5.8 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 10.2, 17.0, 18.8, 19.2, 29.1, 30.6, 31.2, 47.2, 49.9, 51.9, 57.5, 75.5, 130.7, 139.1, 220.8; MS *m/e* 231 (M^+ – Cl, 12), 149 (100), 131 (62), 121 (30), 107 (31); HRMS (M^+ – Cl) 231.1385 calcd for $C_{15}H_{19}O_2$, found 231.1384.

Suárez Fragmentation of Hydroxy Ketone (22). To a solution of **22** (0.316 g, 1.184 mmol) in 140 mL of cyclohexane were added sequentially iodobenzene diacetate (0.650 g, 2.013 mmol) and iodine (0.511 g, 2.013 mmol). The resulting reaction mixture was irradiated with one 100 W tungsten lamp for 1 h at 40 °C under nitrogen. The mixture was poured into a 1:1 mixture of ether (100 mL) and aqueous $NaHSO_3$ solution (100 mL). The organic layer was separated, and the aqueous layer was then extracted with ether (2 × 50 mL). The combined organic extracts were washed with brine, dried over $MgSO_4$, and concentrated *in vacuo*. The products were separated by column chromatography (4:1 hexane–EtOAc) to give the two diastereomeric iodo lactones (0.255 g, 55%) [96 mg of **30a** as a white solid and 159 mg of **30b** as a colorless oil], along with the bicyclic diketone **31** (69 mg, 15%) as a colorless oil.

The spectral data of **30a**: IR (CH_2Cl_2) 1766 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.40 (m, 3 H), 0.79 (m, 1 H), 1.58–1.85 (m, 5 H), 1.86–2.09 (m, 3 H), 2.17 (m, 2 H), 2.32 (m, 1 H), 3.05 (m, 1 H), 4.25 (dd, J = 9.6, 4.9 Hz, 1 H), 6.15 (d, J = 6.0

Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 11.0, 16.3, 17.0, 22.1, 25.3, 28.2, 31.1, 32.6, 40.7, 52.7, 53.1, 83.2, 132.0, 135.7, 177.0; MS *m/e* 267 (M^+ − I, 7), 265 (M^+ − I, 21), 237 (12), 201 (35), 185 (40), 165 (37), 153 (85), 141 (66), 129 (90), 115 (100); HRMS (M^+ − I) 265.0995 and 267.0966 calcd for $C_{15}H_{18}O_2Cl$, found 265.0981 and 267.0963.

The spectral data of **30b**: mp 126−130 °C; IR ($CHCl_3$) 1780 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.68 (m, 3 H), 0.99 (m, 1 H), 1.44 (m, 1 H), 1.63−1.81 (m, 5 H), 1.84 (d, J = 10.1 Hz, 1 H), 2.01 (m, 1 H), 2.17 (m, 1 H), 2.50 (m, 2 H), 2.65 (m, 1 H), 4.61 (ddd, J = 12.1, 4.4, 2.9 Hz, 1 H), 6.49 (d, J = 4.0 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 9.3, 16.2, 22.3, 24.5, 25.8, 28.0, 35.7, 41.0, 43.7, 51.9, 54.2, 83.0, 128.0, 136.4, 176.6; MS *m/e* 267 (M^+ − I, 2), 265 (M^+ − I, 6), 201 (69), 153 (100), 129 (57), 117 (58); HRMS (M^+ − I) 265.0995 and 267.0966 calcd for $C_{15}H_{18}O_2Cl$, found 265.0997 and 267.0966.

The spectral data of **31**: IR (CH_2Cl_2) 1723, 1707 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 1.53 (m, 1 H), 1.89 (3 H), 1.97−2.22 (m, 2 H), 2.33 (m, 1 H), 2.44 (s, 3 H), 2.53 (m, 2 H), 2.87 (m, 1 H), 3.26 (m, 1 H), 3.38 (m, 1 H), 4.26 (d, J = 11.1 Hz, 1 H), 5.54 (d, J = 6.0 Hz, 1 H), 5.89 (d, J = 11.1 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 3.4, 17.3, 29.6, 32.9, 35.5, 38.6, 47.3, 48.8, 51.2, 126.8, 129.4, 139.6, 141.5, 196.1, 215.0; MS *m/e* 394 (M^+, 6), 392 (M^+, 17), 267 (8), 265 (21), 239 (26), 237 (71), 159 (56), 145 (62), 131 (90), 117 (93), 105 (100); HRMS (M^+) 392.0040 and 394.0011 calcd for $C_{15}H_{18}O_2ClI$, found 392.0033 and 394.0011.

Suárez Fragmentation of Hemiketal 21. To a solution of the hemiketal **21** (0.237 g, 1.01 mmol) in 120 mL of cyclohexane were added sequentially iodobenzene diacetate (0.488 g, 1.52 mmol) and iodine (0.385 g, 1.52 mmol). The resulting mixture was irradiated with one 100 W tungsten lamp for 1 h at 40 °C under nitrogen. The mixture was poured into a 1:1 mixture of ether (90 mL) and aqueous $Na_2S_2O_3$ solution (90 mL). The organic layer was separated, and the aqueous layer was then extracted with ether. The combined organic extracts were washed with brine, dried ($MgSO_4$), and concentrated *in vacuo*. The concentrate was purified by column chromatography (3:1 hexane−EtOAc) to give the iodo lactone **32** (0.281 g, 77%) as a colorless oil: IR (CH_2Cl_2) 1770 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.29 (m, 1 H), 0.39 (m, 1 H), 0.78 (m, 1 H), 1.10 (m, 1 H), 1.45 (s, 3 H), 1.50−2.12 (m, 10 H), 2.55 (m, 2 H), 2.94 (dt, J = 3.4, 10.7 Hz, 1 H), 4.34 (dt, J = 3.0, 10.4 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 12.5, 16.2, 17.9, 22.4, 25.1, 27.0, 27.8, 32.2, 37.6, 40.6, 42.6, 50.2, 52.0, 84.8, 177.7; MS *m/e* 233 (M^+ − I, 25), 187 (100), 147 (82), 131 (67), 117 (57); HRMS (M^+ − I) 233.1542 calcd for $C_{15}H_{21}O_2$, found 233.1539.

Bridgehead olefin 33. The iodo lactone **32** (61 mg, 0.17 mmol) was resubjected to the Suárez cleavage protocol as described above for **21** for a longer time (~48 h), and 24 mg (60%) of the bridgehead olefin **33** was obtained as a white solid: mp 79−82 °C; IR ($CHCl_3$) 1750 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.38 (m, 1 H), 0.60 (m, 1 H), 0.94 (m, 1 H), 1.15 (m, 1 H), 1.33 (s, 3 H), 1.57−2.48 (m, 11 H), 3.08 (t, J = 9.2 Hz, 1 H), 5.62 (dt, J = 2.0, 8.2 Hz, 1H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 11.0, 12.3, 20.5, 24.3, 26.0, 26.9, 28.3, 28.8, 33.6, 41.5, 58.1, 85.7, 130.0, 136.4, 177.5; MS *m/e* 232 (M^+, 43), 187 (56), 161 (77), 133 (78), 117 (54); HRMS (M^+) 232.1463 calcd for $C_{15}H_{20}O_2$, found 232.1466.

***m*-CPBA oxidation of 32.** To the iodide **32** (48.5 mg 0.135 mmol) dissolved in 8 mL of anhydrous CH_2Cl_2 were added sequentially *m*-CPBA (55%, 85 mg, 0.27 mmol) and solid $NaHCO_3$ (34 mg, 0.4 mmol) at rt. The reaction mixture was stirred at rt for additional 3 h. The reaction was quenched with 8 mL of saturated aqueous $NaHCO_3$ solution. The organic layer was washed with aqueous $NaHCO_3$ solution (3 × 8 mL), dried ($MgSO_4$), and concentrated *in vacuo*. The concentrate was purified by column chromatography (2:1 hexane-EtOAc) to afford 26.8 mg (80%) of the epoxide **34** and 1.2 mg (4%) of the epoxy alcohol **35**. The spectral data of **34**: mp 109−112 °C; IR ($CHCl_3$) 1760 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.34 (m, 1 H), 0.53 (m, 1 H), 0.69 (m, 1 H), 0.98 (m, 1 H), 1.27 (br s, 1 H), 1.48 (s, 3 H), 1.65−1.88 (m, 4 H), 1.89−2.07 (m, 3 H), 2.08−2.31 (m, 3 H), 2.81 (m, 1 H), 3.18 (m, 1 H); MS *m/e* 248 (M^+, 4), 233 (7), 220 (21), 202 (14), 192 (22), 175 (23), 161 (35), 147 (56), 133 (78), 121 (100); HRMS (M^+) 248.1412 calcd for $C_{15}H_{20}O_3$, found 248.1424.

The spectral data of **35**: IR ($CHCl_3$) 3480, 1759 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.38 (m, 1 H), 0.53 (m, 1 H), 0.90 (m, 2 H), 1.39−1.70 (m, 5 H), 1.78 (m, 2 H), 1.88−2.01 (m, 2 H), 2.13−2.29 (m, 3 H), 2.56 (dd, J = 14.1, 6.8 Hz, 1 H), 2.97 (dd, J = 9.3, 5.4 Hz, 1 H), 3.29 (t, J = 9.7 H, 1 H), 3.72 (dd, J = 8.7, 6.8 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 6.9, 8.5, 16.2, 18.9, 23.9, 28.6, 28.9, 39.9, 41.8, 53.4, 61.6, 67.1, 68.6, 84.2, 176.6; MS *m/e* 264 (M^+, 17), 246 (9), 235 (10), 231 (15), 220 (29), 203 (28), 191 (30), 175 (63), 161 (70), 150 (80), 135 (80), 121 (100); HRMS (M^+) 264.1362 calcd for $C_{15}H_{20}O_4$, found 264.1350.

Suárez Cleavage of 21 with $PhI(OCOCF_3)_2$−I_2. To the hemiketal **21** (53 mg, 0.226 mmol) dissolved in 25 mL of cyclohexane were added sequentially $PhI(OCOCF_3)_2$ (243 mg, 0.57 mol) and I_2 (144 mg. 0.57 mmol). The reaction mixture was subjected to a 100 W tungsten lamp, with stirring, for 1 h under nitrogen. The mixture was then diluted with 15 mL of ether (15 mL), washed with saturated aqueous $Na_2S_2O_3$ solution (3 × 20 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The concentrate was purified by preparative TLC (10:1 benzene−ether) to give a mixture of the trifluoroacetates (59 mg, 76%) as white solids. For characterization, a portion of the products was reseparated by preparative TLC (10:1 benzene-ether) to provide **38** (17 mg, 22%) and **39** (21 mg, 27%); MS *m/e* 344 (M^+, 40), 287 (7), 231 (41), 185 (37), 159 (59), 144 (52), 131 (60), 117 (100); HRMS (M^+) 344.1235 calcd for $C_{17}H_{19}O_4F_3$, found 344.1219.

The spectral data of **38**: R_f = 0.24 in 15:1 benzene−ether; IR ($CHCl_3$) 1781, 1761 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.20 (m, 1 H), 0.70 (m, 1 H), 0.79 (m, 1 H), 1.09 (m, 1 H), 1.53 (s, 3 H), 1.68 (m, 2 H), 1.72−1.95 (m, 2 H), 2.01−2.18 (m, 1 H), 2.23−2.43 (m, 2 H), 2.31 (dd, J = 15.0, 3.4 Hz, 1 H), 2.68 (dd, J = 15.0, 7.1 Hz, 1 H), 3.12 (m, 1 H), 5.42 (dd, J = 10.8, 7.6 Hz, 1 H), 6.25 (dd, J = 7.1, 3.4 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 9.5, 11.9, 19.2, 19.7, 27.0, 28.8, 32.6, 37.1, 44.1, 54.6, 82.0, 88.8, 114.5 (m), 136.4, 138.2, 156.7 (m), 177.5.

The spectral data of **39**: R_f = 0.33 in 15:1 benzene−ether; IR ($CHCl_3$) 1780 cm^{-1}, 1760 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.50 (m, 1 H), 0.88 (m, 1 H), 0.98 (m, 1 H), 1.17 (m, 1 H), 1.40 (s, 3 H), 1.75−1.88 (m, 2 H), 1.94−2.29 (m, 4 H), 2.40−2.55 (m, 1 H), 2.42 (dd, J = 14.3, 8.0 Hz, 1 H), 2.78 (dd, J = 14.3, 8.0 Hz, 1 H), 3.15 (t, J = 9.4 Hz, 1 H), 5.50 (t, J = 8.0 Hz, 1 H), 6.28 (t, J = 8.4 Hz, 1 H).

Preparation of Enones 40 and 41 from 38 and 39. A mixture of the two trifluoroacetates **38** and **39** (46.9 mg, 0.136 mmol) was dissolved in MeOH (5 mL), and 5 mL of MeOH presaturated with NH_3 was then added. The resulting mixture was stirred at rt for additional 2 h. Excess NH_3 was removed by passing nitrogen through. After a bulk of the solvent was removed under reduced pressure, the residue was purified by preparative TLC (2:1 hexane−EtOAc) to give the corresponding alcohols (28 mg, 83%) as a colorless oil.

The Swern oxidation of these alcohols was then carried out. To a solution of oxalyl chloride (11.2 μL, 0.13 mmol) in anhydrous CH_2Cl_2 (1 mL) was added dropwise DMSO (11.4 μL, 0.16 mmol) at −78 °C. After the resulting mixture was stirred for additional 15 min, a solution of the alcohols (8.0 mg, 0.03 mmol) in anhydrous CH_2Cl_2 (1 mL) was added. The reaction mixture was then stirred at −78 °C for 40 min, and Et_3N (0.14 μL, 0.966 mmol) was then added. The mixture was allowed to warm to 0 °C, and stirred for additional 5 min at the same temperature. The mixture was poured quickly into a 1:1 mixture of water and CH_2Cl_2 (10 mL). The organic layer was washed with 1 N HCl and then water, dried over $MgSO_4$, and concentrated *in vacuo*. The concentrate was purified by prepartive TLC (1:2 hexane−EtOAc) to afford the corresponding α,β-unsaturated ketones **40** (2.3 mg, 30%) and **41** (3.4 mg, 43%).

The spectral data of **41**: IR ($CHCl_3$) 1758, 1703 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.60 (m, 2 H), 1.18 (m, 1 H), 1.29 (m, 1 H), 1.49 (s, 3 H), 1.58 (m, 1 H), 1.93 (m, 1 H) 2.03 (d, J = 10.1 Hz, 1 H), 2.03−2.18 (m, 3 H), 2.28 (m, 1 H), 2.53 (m, 1 H), 2.82 (d, J = 16.5 Hz, 1 H), 3.21 (d, J = 16.5 Hz, 1 H), 6.68 (t, J = 8.5 Hz, 1 H).

The spectral data of **40**: IR ($CHCl_3$) 1759, 1677 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.45 (m, 1 H), 0.80 (m, 1 H), 1.05 (m, 1 H), 1.20 (m, 1 H), 1.58 (s, 3 H), 1.50–1.61 (m, 1 H), 1.83 (d, J = 11.8 Hz, 1 H), 2.02 (m, 2 H), 2.37 (dd, J = 14.9, 3.6 Hz, 1H), 2.42–2.58 (m, 2 H), 2.79–2.90 (m, 1 H), 2.84 (dd, J = 14.9, 7.2 Hz, 1H), 3.21 (m, 1 H), 6.53 (dd, J = 7.2, 3.6 Hz, 1H).

Sodium Iodide Displacement of 32. To the iodide **32** (48 mg, 0.133 mmol) in 2 mL of acetone (2 mL) was added sodium iodide (200 mg, 1.3 mmol) in one portion. The resulting mixture was heated at reflux for about 2 days. The mixture was concentrated *in vacuo*. The residue was diluted with 4 mL of water, followed by 5 mL of ether. The aqueous layer was then extracted with ether (3 × 5 mL). The combined organic extracts were dried over $MgSO_4$ and concentrated *in vacuo* to give a mixture of the olefins (20.7 mg, 67%), including **33** and **42**.

Osmylation of 33. To the olefin **33** (11.5 mg, 0.0495 mmol) dissolved in a 10:1 mixture of THF–water (3 mL) was added *N*-methylmorpholine *N*-oxide (18 mg, 0.15 mmol) at rt. A catalytic amount of OsO_4 was added, and the resulting mixture turned into dark brown-green. The reaction was completed in 15 min and then quenched with saturated aqueous Na_2SO_3 solution. The resulting mixture was stirred for additional 3 h. After a bulk of THF was removed under reduced pressure, the residue was extracted with ether (3 × 3 mL). The organic extracts were combined, dried ($MgSO_4$), and concentrated *in vacuo*. Purification by preparative TLC (1:1 hexane–EtOAc) afforded the diol **43** (11 mg, 83%).

To a solution of 10.2 mg of the diol **43** thus obtained in 5 mL of 2,2-dimethoxypropane was added a catalytic amount of *p*-toluenesulfonic acid. The mixture was stirred at rt for 1 h, and solid $NaHCO_3$ was added in one portion. Inorganic salts were filtered off, and the filter cake was washed with ether. The combined filtrate was washed with aqueous $NaHCO_3$ solution (5 mL) and then water (5 mL). The organic layer was dried over $MgSO_4$ and concentrated *in vacuo*. Purification by preparative TLC (4:1 hexane–EtOAc) gave the acetonide **44** (9.0 mg, 77%) as a white solid: IR (CH_2Cl_2) 1763 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.05 (m, 1 H), 0.62 (m, 1 H). 1.09 (m, 2 H), 1.28 (s, 3 H), 1.34 (s, 3 H), 1.48 (s, 3 H), 1.57–1.73 (m, 2 H), 1.78–2.28 (m. 9 H), 3.05 (m, 1 H), 3.96 (dd, J = 10.9, 3.5 Hz, 1 H); ^{13}C NMR (90 MHz, $CDCl_3$) δ 11.7, 17.6, 18.8, 20.6, 25.4, 27.2, 28.2, 28.6, 30.6, 32,7, 35.3, 43.5, 53.0, 80.1, 84.6, 85.2, 106.5, 177.9; MS m/e 306 (M^+, 6), 291 (54), 248 (74), 231 (40), 203 (26), 177 (73), 161 (45), 135 (83), 121 (100); HRMS (M^+) 306.1831 calcd for $C_{18}H_{26}O_4$, found 306.1819.

***m*-CPBA Oxidation of 30a.** To the iodide **30a** (9.7 mg) dissolved in 1 mL of CH_2Cl_2 was added $NaHCO_3$ (2.3 mg), followed by *m*-CPBA (55%, 15.5 mg; 2 equiv) at rt under nitrogen. The reaction mixture was stirred for 4.5 h. The reaction was quenched with saturated aqueous $NaHCO_3$ solution (2 mL) and diluted with CH_2Cl_2. The organic layer was washed with aqueous $NaHCO_3$ solution (3 × 5 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The concentrate was purified by preparative TLC (3:1 hexane–EtOAc) to give the epoxide **45** (5.4 mg, 78%) as a pale yellow solid: IR ($CHCl_3$) 1770 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.59 (m, 1 H), 0.79 (m, 1 H), 1.04 (m, 1 H), 1.26 (m, 1 H), 1.66–1.91 (m, 6 H), 1.98–2.19 (m, 4 H), 2.67 (m, 1 H), 2.92 (m, 1 H), 5.80 (s, 1 H).

***m*-CPBA Oxidation of 30b.** To the iodide **30b** (31.5 mg, 0.08 mmol) dissolved in 6 mL of CH_2Cl_2 was added $NaHCO_3$ (13.5 mg), followed by *m*-CPBA (55%, 50.3 mg, 2 equiv) at rt under nitrogen. The reaction mixture was stirred at rt for 24 h. The reaction was quenched with saturated aqueous $NaHCO_3$ solution (2 mL) and diluted with CH_2Cl_2. The organic layer was washed with aqueous $NaHCO_3$ solution (3 × 6 mL), dried over $MgSO_4$, and concentrated *in vacuo*. The concentrate was purified by preparative TLC (3:1 hexane–EtOAc) to furnish three products, **46** (4.7 mg, 22%), **47** (7.4 mg, 33%), and **48** (7.7 mg, 34%). The spectral data of **46**: IR ($CHCl_3$) 1771 cm^{-1}; ^1H NMR (360 MHz, $CDCl_3$) δ 0.54–0.74 (m, 3 H), 0.80 (m, 1 H), 1.73 (s, 3 H), 1.70–1.92 (m, 1 H), 1.98 (d, 1 H), 2.11–2.38 (m, 3 H), 2.51 (m, 1 H), 2.68 (m, 1 H), 5.48 (m, 1 H), 5.88–6.02 (m, 2 H).

Sodium Iodide Displacement of 30a. To a solution of the β-iodide **30a** (9.1 mg) in 1 mL of acetone was added sodium iodide (70 mg, 2 equiv). The reaction mixture was heated at reflux for about 2 days under nitrogen. A bulk of the solvent was evaporated under reduced pressure. The residue was diluted with 4 mL of water and 5 mL of ether. The aqueous layer was extracted with ether (3 × 5 mL). The combined organic extracts were dried over $MgSO_4$, and concentrated *in vacuo*. The concentrate was purified by preparative TLC (3:1 hexane–EtOAc) to afford the α-iodide **30b** (7.4 mg, 81%) as a white solid, which was identical in every aspect to that obtained from the Suárez cleavage of **22** (*vide supra*).

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Supplementary Material Available: Copies of ^1H and ^{13}C NMR spectra of **8**, **11**, **12**, **14a**, **15a**, **16a,c**, **17a,c,d**, **18**, **19**, **21**, **22**, **26-28**, **30a,b**, **31-35**, **38-41**, and **43-46** (61 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.