Cycloaddition Routes to Tricyclo[5.4.0^{1,7}.0^{2,9}]undecanes: A Direct Total Synthesis of (+)-Longifolene via an Intramolecular Diels-Alder Strategy†

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Received October 1, 1992

The total synthesis of the sesquiterpene (+)-longifolene (1) by an intramolecular Diels-Alder cycloaddition strategy is described. Addition of methyllithium to the epoxyfulvene 13, derived from cyclopentadiene and 3,4-epoxy-2-butanone, led to an exo-tet cyclization of the resulting cyclopentadienyl anion to generate the spiro[2.4]hepta-4,6-diene alcohol 14. Resolution of this material was effected via its menthyl carbonate derivative 15. Oxidation of the (+)-*R*-alcohol with active MnO_2 afforded the cyclopropyl aldehyde 16 which was condensed with the anion derived from methyl 3-methylcrotonate in the presence of cadmium chloride to generate the unsaturated lactone 20 or the unsaturated ester 18. Microwave heating of the silyl triene 19 effected cycloaddition to the adduct 21. Hydrogenolysis of the alcohol 22 afforded the "sinularene" skeleton 25. Cyclopropane ring cleavage of the derived ketones 23, 30, and the thiocarbonate 27 was examined but only in the Li/NH_3 reduction of 30 was the longifolene skeleton 33 produced as a significant product which unfortunately could not be separated from its isomer 32. Consequently the successful route utilized regiospecific cleavage of the cyclopropane ring in the cyclopentadiene 20 in methanol catalyzed by BF_3·Et_2O to afford the substituted cyclopentadiene lactone(s) 34 (83%). Cyclization proceeded smoothly, in a sealed tube, in toluene, in a microwave oven to afford the single tetracyclic adduct 39 in 97% yield. Double bond hydrogenation and reduction of the lactone with $LiAlH_4$ afforded the substituted longifolene skeleton, and the resulting primary alcohol was acetylated selectively to give 40. Free-radical-mediated replacement of the secondary oxygen functions was accomplished via the phenoxythiocarbonate derivative to afford the methoxy acetate 43. Alternatively the reaction sequence could be modified to convert 39 to 41 to 42 and then to 43. Methoxy cleavage (Me_3SiI) and a second free-radical reaction gave the acetate 44. Pyrolysis of this acetate (525 °C) provided (+)-longifolene (1).

Introduction

Among the bridged-ring sesquiterpenes, longifolene (1, Scheme II) occupies a position of considerable prominence. Its unusual topology intrigued early natural product investigators[1] and the correct structure was eventually established by X-ray analysis.[2] The biosynthesis has also been delineated.[3] In addition, for more than 3 decades the rare tricyclo[5.4.0^{1,7}.0^{2,9}]undecene skeleton has challenged organic chemists and served as a scaffold around which new chemistry has been developed and diverse synthetic strategies investigated. The key carbocyclic bond construction steps employed in the successful total syntheses reported to date are illustrated concisely in Scheme I. Briefly these encompass the in situ conjugation-Michael addition approach of Corey et al.,[4] the intramolecular alkylation-ring expansion route of McMurry and Isser,[5] the acid-catalyzed alkene cyclization of Johnson and co-workers,[6] the [2 + 2] cycloaddition-retro aldol sequence of Oppolzer and Godel,[7] the carbene addition-rearrangement procedure of Schultz and Puig,[8] the camphor-based acetal cyclization-Wagner-Meerwein rearrangement route of Money and Kuo,[9] and recently the fulvene cycloaddition-ring closure-expansion pathway developed by Liu and Ho.[10] Additional synthetic approaches have also received attention but have met with limited success.[11] Among these are several in which an intramolecular Diels-Alder step was contemplated.[12,13]

Synthetic Strategy

Retrosynthetically the double disconnection of longifolene to the substituted cyclopentane framework 2 is synthetically equivalent to the Diels-Alder cycloaddition of a cyclopentadiene precursor of type 3. This [4 + 2] approach to the tricyclo[5.4.0^{1,7}.0^{2,9}]undecene skeleton has

† Dedicated to the memory of Professor Peter Yates, deceased November 16, 1992.

(1) (a) Simonsen, J. L. *J. Chem. Soc.* **1920**, *117*, 578. (b) Simonsen, J. L. *J. Chem. Soc.* **1923**, *123*, 2642. (c) Simonsen, J. L.; Barton, D. H. R. *The Terpenes*; University Press: Cambridge, UK, 1952; Vol. 3, p 92.

(2) (a) Naffa, P.; Ourisson, G. *Chem. Ind.* **1953**, 917. (b) Ourisson, P.; Ourisson, G. *Bull. Soc. Chim. Fr.* **1954**, *21*, 1412. (c) Ourisson, G. *Bull. Soc. Chim. Fr.* **1955**, *22*, 895. (d) Moffett, R. M.; Rogers, D. *Chem. Ind.* **1953**, 916.

(3) Arigoni, D. *Pure Appl. Chem.* **1975**, *41*, 219.

(4) Corey, E. J. Ohno, M.; Mitra, R. B.; Vatakencherry, P. A. *J. Am. Chem. Soc.* **1964**, *86*, 478.

(5) McMurry, J. E.; Isser, S. J. *J. Am. Chem. Soc.* **1972**, *94*, 7132.

(6) Volkmann, R. A.; Andrews, G. C.; Johnson, W. S. *J. Am. Chem. Soc.* **1975** *97*, 4777.

(7) Oppolzer, W.; Godel, T. *Helv. Chim. Acta* **1984**, *67*, 1154.

(8) Schultz, A. G.; Puig, S. *J. Org. Chem.* **1985**, *50*, 915.

(9) Kuo, D. L.; Money, T. *Can. J. Chem.* **1988**, *66*, 1794.

(10) Ho, T. L.; Yeh, W. L.; Yule, J.; Liu, H.-J. *Can. J. Chem.* **1992**, *70*, 1375.

(11) Additional synthetic studies: (a) Scherrer, R. A. Ph.D. Thesis, University of Illinois, 1958; *Diss. Abstr.* **1958**, *19*, 960. (b) Hudak, N. J. Ph.D. Thesis, Cornell University, 1959; *Diss. Abstr.* **1959**, *20*, 79. (c) Napier, R. P. Ph.D. Thesis, University of Rochester, 1964; *Diss. Abstr.* **1964**, *25*, 1577. (d) Grant, J. E., Jr.; Ph.D. Thesis, Pennsylvania State University, 1969; *Diss. Abstr. B.* **1969**, *29*, 3653.

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(13) Glass, R. S.; Herzog, J. D.; Sobczak, R. L. *J. Org. Chem.* **1978**, *43*, 3209.

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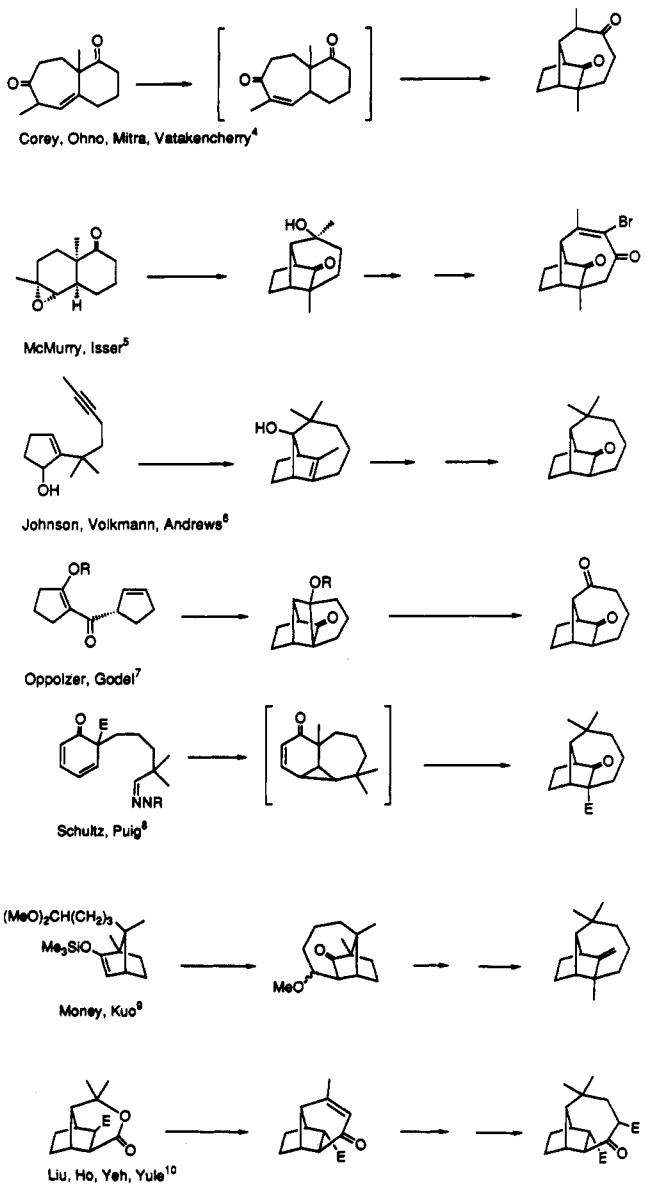
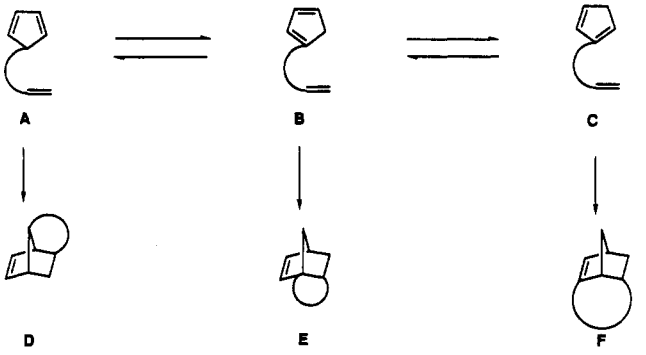
Scheme I



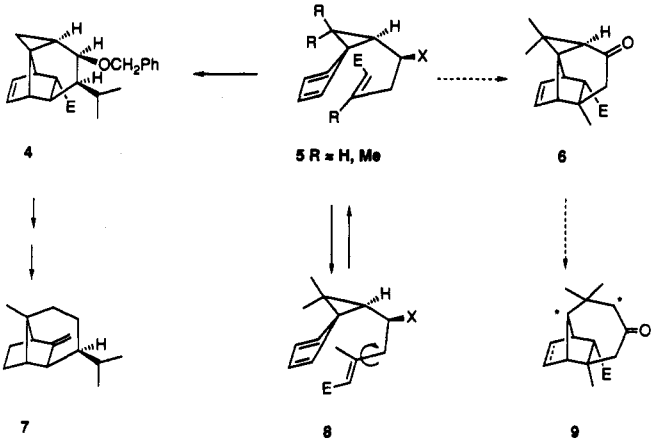
Scheme II

considerable appeal and as such has been widely noted.[12-14] However, as an early approach to longifolene demonstrated (**3**, R = CH_2OH)[12] the propensity of substituted cyclopentadienes to undergo facile 1,5-sigmatropic rearrangement prior to cyclization takes precedence. Thus it is well established that a C_5-substituted cyclopentadiene such as **A** will cyclize preferentially via **B** to systems of type **E** (Scheme III).[12-16] With suitable chain lengths and ester-activated dienophiles, bridgehead olefins such as **F** may also be formed from **C**.[16] In contrast, "brexane type" bridged ring structures corresponding to **D** are formed

Scheme III



Scheme IV



exclusively when two bridging atoms are present,[16-19] although the "homobrexane" product dominated under mild conditions with ester-activated dienophiles and a carbonyl group in the three-carbon bridge.[18] Consequently, for an intramolecular Diels–Alder strategy to succeed as a route to the required cycloheptane–norbornane system, one of the following possibilities should be considered. A "brexane intermediate" could be synthesized and induced to undergo a double ring expansion, however a single ring homologation proved troublesome in a previous longifolene synthesis.[5] The sigmatropic rearrangement could be blocked, but unfortunately blocking the 1,5 migration is not necessarily straightforward since even chlorine migrated prior to cyclization in a related case.[13] More recently an alkyl substituent has been used successfully in a model study directed toward sordaricin.[20] In principle, conditions could be developed where cyclization can compete efficiently with rearrangement as was done for some prostaglandin syntheses.[21] Alternatively it should be possible to build constraints into the dienophile so the desired cyclization is preferred due to the higher energy transition states required in the competing pathways.

An attractive possibility was to employ the cyclopropane moiety present in a spiro[2.4]heptadiene system such as **5** (X = OCH_2Ph, $OSiMe_2{}^tBu$, etc., Scheme IV) to block the normal sigmatropic rearrangement. We have described

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(16) Breiger, G.; Anderson, D. R. *J. Org. Chem.* **1971**, *36*, 243.

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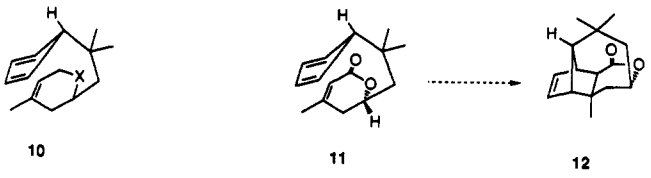
(19) Snowden, R. L. *Tetrahedron* **1986**, *42*, 3277.

(20) Mander, L. N.; Robinson, R. P. *J. Org. Chem.* **1991**, *56*, 3595.

(21) (a) Corey, E. J.; Weinshenker, N. M.; Schaff, T. K.; Huber, W. *J. Am. Chem. Soc.* **1969**, *91*, 5675. (b) Corey, E. J.; Koelliker, U.; Neuffer, J. *J. Am. Chem. Soc.* **1971**, 1489.

Scheme V



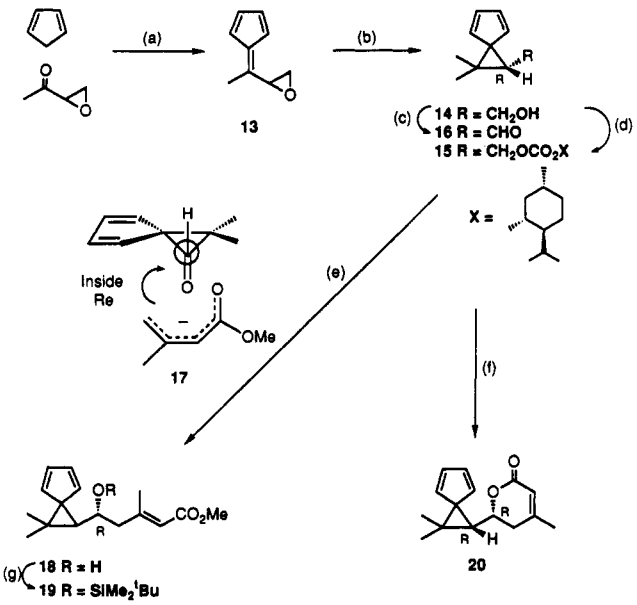
the successful implementation of this strategy for the preparation of the tetracyclic adduct **4** and its conversion by selective cyclopropane bond cleavage into the marine sesquiterpene sinularene (**7**).[22] Earlier investigations indicated that a side-chain alkoxy group (X) was essential to ensure the cycloaddition proceeded.[23] For longifolene this strategy requires, in a retrosynthetic sense, the construction of a bond between the bridge and the neighboring methylene position of a synthon such as **9** (asterisks) to form the tetracyclic ketone **6** prior to double disconnection of the "bicyclo[2.2.1]heptane" nucleus. Thus the triene **5** (R = Me) is a precursor of the adduct **6**, and the oxygen substituent may serve to control the cyclopropane ring opening to generate **9** by analogy with our earlier studies in the normethyl series.[24] In addition, as illustrated, the use of a single enantiomer will allow the chiral cyclopropyl center to control the asymmetric induction in the cycloaddition step since only the rotamer **5** can achieve the required alignment of the diene and dienophile. As illustrated, this geometry is precluded in the rotamer **8**.

Related considerations suggested an additional tactical solution. Molecular models indicated that if the dienophile were constrained to a six-membered ring as illustrated in **10** (Scheme V) then the preferred pathway for intramolecular cycloaddition should lead to a skeleton of type **D**, since as discussed below the other adducts are disfavored. Consequently an activated but cleavable dienophile such as lactone **11** should generate the desired tricyclic carbon nucleus **12** for longifolene directly, and the cyclopentadiene isomers will cease to be a problem. In parallel with the cyclopropane analysis above, the chiral center in the lactone should control the relative configuration during the intramolecular cycloaddition as well as the π-facial selectivity.[25] due to the steric constraints and geometric restrictions within the reacting partners. We wish to report the details[26] of our investigations on these topics which have culminated in a direct total synthesis of (+)-longifolene (**1**).

Results and Discussion

We reported earlier that the condensation of 3,4-epoxy-2-butanone with cyclopentadiene in methanol containing pyrrolidine afforded the fulvene **13** in 86% yield.[27] Addition of methyllithium to **13** generated the cyclopentadienyl anion in situ which cyclized spontaneously in the favored exo-tet manner to the racemic spiro[2.4]hepta-4,6-diene alcohol **14** (65%). In the racemic series this

Scheme VI[a]



[a] Reference 27; MeOH, pyrrolidine, 0 °C, 2 h, 21 °C, 2 h, 86%; (b) reference 27; THF, MeLi, −78–0 °C, 55%; (c) MnO_2/C, CH_2Cl_2, 12 h, 21 °C, 86%; (d) (−)menthol chloroformate, benzene, Et_3N, 21 °C; $LiAlH_4$, THF, 0 °C, 98%; (e) reference 29; LDA, THF, −78 °C, $Me_2C{=}CHCO_2Me$, $CdCl_2$, 30 min; 1 h, −78 °C, 30 min, 0 °C, 73%; (f) LDA, THF, −40 °C, $Me_2C{=}CHCO_2Me$, $CdCl_2$, 30 min; 2 h, 0 °C, 73%; (g) CH_3CN, $^tBuSiMe_2Cl$, $AgClO_4$, 21 °C, 30 min, pyridine, 21 °C, 14 h, 91%.

material was oxidized directly (Swern or MnO_2) to the spiro-aldehyde **16** in a manner analogous to that employed in the normethyl series.[23] In order to obtain the desired enantiomer for (+)-longifolene the alcohol was resolved. It was treated with (−)-menthyl chloroformate (prepared from (−)-menthol and phosgene, toluene, O °C) according to a literature procedure.[28] This allowed chromatographic separation of the diasteromeric carbonate **15** and recovery of the *R*-(+)-isomer of alcohol **14** after $LiAlH_4$ reduction. Oxidation of the primary alcohol with active MnO_2 dispersed on carbon provided the aldehyde **16** (84%).[29]

The most direct synthesis of the required triene would involve the insertion of the dienophilic component in a single step. In order to accomplish this one must control the competing α versus γ condensation with a vinylogous carbanion, a topic that has received considerable attention.[30] The regioselective condensation of resonance-stabilized enolates depends upon several factors including solvation, steric effects and the nature of the counterion. Lithium diisopropylamine at −78 °C generated the enolate **17** and afforded the α product exclusively upon condensation with aldehyde **16**. However, addition of cadmium chloride to the performed enolate resulted in the preferential formation of the γ-substituted thermodynamically more stable product[29] to provide **18** (76%) in which the secondary alcohol was protected as the silyl derivative **19**.

(22) Antczak, K.; Kingston, J. F.; Fallis, A. G.; Hanson, A. *Can. J. Chem.* **1987**, *65*, 114.
(23) Gallacher, G.; Ng, A. S.; Attah-Poku, S. K.; Antczak, K.; Alward, S. J.; Kingston, J. F.; Fallis, A. G. *Can. J. Chem.* **1984**, *62*, 1709.
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(25) Fallis, A. G.; Lu, Y.-F. *Advances in Cycloadditions*; JAI Press: Greenwich, CN, 1993; Vol. 3, in press.
(26) Lei, B.; Fallis, A. G. *J. Am. Chem. Soc.* **1990**, *112*, 4609.
(27) Antczak, K.; Kingston, J. F.; Fallis, A. G. *Can. J. Chem.* **1984**, *62*, 2451.
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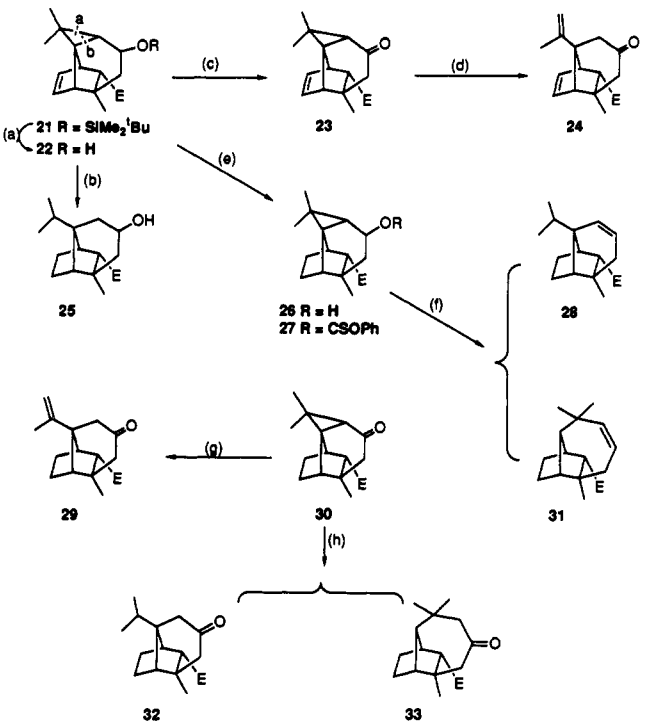
(29) Lei, B.; Fallis, A. G. *Can. J. Chem.* **1991**, *69*, 1450.
(30) (a) Bellassoued, M.; Gaudemar, M.; El Borgi, A.; Baccar, B. *J. Organometal. Chem.* **1985**, *280*, 165. (b) Hudlicky, T.; Natchus, M. G.; Kwart, L. D.; Calwell, B. L. *J. Org. Chem.* **1985**, *50*, 4300. (c) Rice, L. E.; Boston, M. C.; Finklea, H. O.; Suder, B. J.; Frazir, J. O.; Hudlicky, T. *J. Org. Chem.* **1984**, *49*, 1845. (d) Yamamoto, Y.; Hatsuya, S.; Yamada, J. *Chem. Commun.* **1988**, 86. (e) Dugger, R. W.; Heathcock, C. H. *J. Org. Chem.* **1980**, *45*, 1181. (f) Johnson, P. R.; White, J. D. *J. Org. Chem.* **1984**, *49*, 4424. (g) Albaugh-Robertson, P.; Katzenellenbogen, J. A. *J. Org. Chem.* **1983**, *48*, 5288.

Normal silylation methods failed, probably as a consequence of the hindered environment of the alcohol, and thus a procedure in which *tert*-butyldimethylsilyl perchlorate was prepared in situ was employed.[31] Previous experience had demonstrated that a bulky side-chain substituent was required for effective cycloaddition.[22,23] Condensation of the *R*-aldehyde **16** with the anion derived from methyl 3-methylcrotonate (LDA mediated by cadmium chloride, −40–0 °C, 2 h) initially resulted in the γ-substitution product which cyclized spontaneously to the lactone **20** in 73% yield. The crowded environment of the carbonyl center resulted in attack from the less hindered re face (away from the *gem*-dimethyl substituents) to form the C_5(R) enantiomer preferentially (9:1) as illustrated in **17**. In addition, the carbonyl lies in approximately the same plane as the cyclopentadiene and this may allow the delocalized π system of the organocadmium reagent to interact favorably with the π system of the diene.

Initially the cycloaddition of **19** proved challenging and only a 10% yield of the adduct **21** was obtained after 24-h reflux in toluene, while decomposition predominated at higher temperatures. Fortunately microwave heating is often a very useful technique for various thermal transformations.[32] As described in the Experimental Section the triene **19** was heated in a sealed glass tube as a 0.05 M solution in toluene containing 1% molar equiv of hydroquinone for 2 h in a modified, household microwave oven to afford the adduct **21** in 92% yield. It is well established that preferential hydrogenolysis of cyclopropane occurs at the least-substituted bond.[24,33] In the case of **21** the presence of the geminal dimethyl function rendered this prediction uncertain especially as the endo surface of the double bond was more exposed and might influence the orientation on the catalyst. Treatment of **21** at 60 psi with hydrogen and PtO_2 catalyst in ethyl acetate/acetic acid for 24 h saturated the double bond but no significant cyclopropyl ring opening occurred. However, reduction of the alcohol **22** obtained from the adduct by deprotection with fluoride ion resulted in exclusive cleavage of the top bond "a" to afford **25** under these same conditions. Apparently the hydroxyl group assisted the reaction by coordination with the catalyst. Swern oxidation of **22** afforded the cyclopropyl ketone **23**. It was established previously in the normethyl series that chromium(II) salts in DMF(dimethylformamide)/water resulted in exclusive cleavage of the internal ring "b" bond to generate the longifolene skeleton, provided the norbornene double bond was present.[24] In the present case room temperature treatment of **23** with a chromium(II) solution prepared by zinc reduction of chromium(III) sulfate in DMF/H_2O did not result in selective cleavage but instead isomerization to the ring-opened ketone **24** occurred. This was a very facile process and also occurred upon recrystallization of alcohol **22** from ethyl acetate/hexane. Similarly zinc reduction in methanol/acetic acid

Scheme VII[a]



[a] (a) THF, $^nBu_4NF$, 21 °C, 2 h, 75%; (b) EtOAc, PtO_2, H_2, 60 psi, 86%; (c) CH_2Cl_2, DMSO, $Cl_2(CO)_2$, Et_3N, −78–10 °C, 93%; (d) DMF/H_2O, 2:1, Zn, $Cr_2(SO_4)_2 \cdot 15H_2O$, 21 °C, 1 h, 60%; (e) EtOAc, 10% Pd/C, H_2, 10 psi, 10 h, 96%; CH_2Cl_2, ClC(=S)OPh, pyridine, 21 °C, 1 h, 61%; (f) toluene, $^nBu_3SnH$, AIBN, 110 °C, 4 h, 70%; (g) MeOH, Zn, $ZnCl_2$, 65 °C, 14 h, 83%; (h) Li/NH_3, ether, ^tBuOH, −78 °C, 10 min, 97%.

afforded a complex mixture which also contained the isomerization product **24**, in contrast to the normethyl series in which cleavage of cyclpropyl bond "b" occurred preferentially.[24] Hydrogenation of **22** at 20 psi in ethyl acetate with Pd/C catalyst provided the saturated tetracyclic alcohol **26**. Simple α-cyclopropyl radicals are known to undergo rapid ring opening to the homoallyl species.[34] but the direction of cleavage in a complex situation is less clear. Conversion of **26** into the phenoxythiocarbonate **27** was accomplished using the Robins procedure[35] and ring opening effected in refluxing toluene containing azobis(isobutyronitrile) (AIBN) and tributyltin hydride. A 9:1 mixture of the tricyclic olefins **28** and **31** was obtained. Variation of solvent and reaction conditions did not significantly influence the composition of the product mixture, and the desired longifolene skeleton was the minor product. Similarly the thiophenoxy carbonate derived from alcohol **22** was examined but a very complex mixture of products was obtained. Consequently attention was directed to the saturated ketone **30** but as above zinc caused isomerization to **29** rather than the desired ring opening. Previously cyclopropyl ketones lacking the *gem*-dimethyl function provided a 70:30 ratio of bond "a" to bond "b" cleavage with lithium–ammonia reduction, a reaction in which the cyclopropane bond that is the most orthogonal to the carbonyl π system is cleaved preferentially. Molecular models imply there is little difference between the "a" and "b" bonds in **30** and this was confirmed experi-

(31) Barton, T. J.; Tully, C. R. *J. Org. Chem.* **1978**, *43*, 3649.

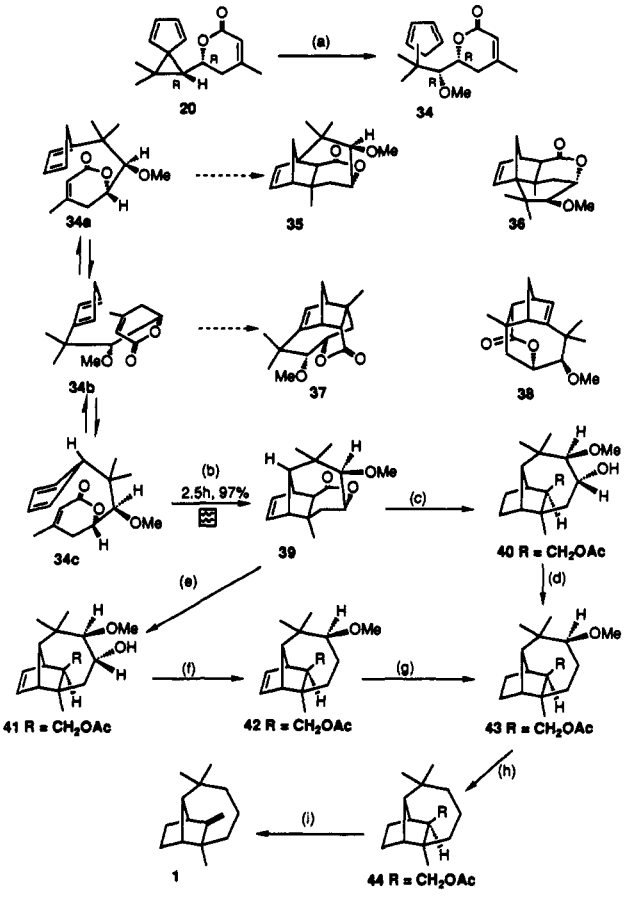
(32) See also (a) Gedye, R.; Smith, F.; Westaway, K.; Ali, H.; Baldisera, L.; Laberge, L.; Rousell, J. *Tetrahedron Lett.* **1986**, *27*, 279. (b) Giguere, R. J.; Bray, T. L.; Duncan, S. M.; Majetich, G. *Tetrahedron Lett.* **1986**, *27*, 4945. (c) Giguere, R. J. *Organic Synthesis: Theory and Applications*; JAI Press: Greenwich, CN, 1989; Vol. 1, pp 103–172. (d) Bose, A. K.; Manhas, M. S.; Ghosh, M.; Shah, M.; Raju, V. S.; Bari, S. S.; Newaz, S. N.; Banik, B. K.; Chaudhary, A. G.; Barakat, K. J. *J. Org. Chem.* **1991**, *56*, 6968.

(33) (a) Altman, J.; Becker, D.; Gingsberg, D.; Loewenthal, H. J. E. *Tetrahedron Lett.* **1967**, 757. (b) Woodworth, C. W.; Buss, V.; Schleyer, P. v. R. *Chem. Commun.* **1968**, 569.

(34) (a) Newcomb, M.; Glenn, A. G. *J. Am. Chem. Soc.* **1989**, *111*, 275. (b) Curran, D. P. *Synthesis* **1988**, 417 and 489.

(35) Robins, M. J.; Wilson, J. S.; Hansske, F. *J. Am. Chem. Soc.* **1983**, *105*, 4059.

Scheme VIII[a]



[a] (a) MeOH, BF_3·Et_2O, 21 °C, 4 h, 83%; (b) toluene, microwave heating, 2.5 h, 97%; (c) EtOAc, 5% Pd/C, H_2, 30 psi, 4 h, 92%; $LiAlH_4$, ether, 0–21 °C, 4 h, 95%, Ac_2O, pyridine, ether, 0 °C, 6 h, 74%; (d) CH_2Cl_2, ClC(=S)OPh, pyridine, 21 °C; toluene, $^nBu_3SnH$, AIBN, 110 °C, 4 h, 71%; (e) ether, $LiAlH_4$, 0–21 °C; Ac_2O, pyridine, ether, 0 °C, 14 h, 74%; (f) CH_2Cl_2, ClC(=S)OPh, pyridine, 21 °C, 3 h, 67%; toluene, $^nBu_3SnH$, AIBN, 110 °C, 6 h, 89%; (g) EtOAc, 5% Pd/C, H_2, 20 psi, 2 h, 97%; (h) CH_2Cl_2, NaI, Me_3SiCl, Et_3N, 21 °C, 1 h; CH_2Cl_2, ClC(=S)OPh, pyridine, 21 °C, 3 h, toluene, $^nBu_3SnH$, AIBN, 110 °C, 5 h, 50%; (i) C_6H_6, 525 °C, flow system, 56%.

mentally as a 1:1 mixture of **32** and **33** resulted. This was the best result but unfortunately the products could not be separated nor could the corresponding tosylhydrazones prepared from the mixture. In view of these practical limitations this approach to longifolene was not feasible and attention was directed toward the strategy outlined in Scheme V.

The cyclopropyl bonds in **20** are strained and polarized, with the negative dipole toward the cyclopentadiene ring, rendering them susceptible to acid-catalyzed cleavage. Consequently, treatment of **20** in methanol containing BF_3·Et_2O at 22 °C resulted in the formal, regiospecific addition of methanol via backside attack to form the $C_5(R)$,$C_1'(R)$-substituted cyclopentadiene **34** (83%) as a mixture of diene isomers (Scheme VIII). In spite of the fact that the Diels–Alder precursor **34** was a single spot on TLC the ^1H NMR spectrum indicated, as expected, that it was a rapidly equilibrating mixture of the isomers **34a**, **34b**, and **34c** due to facile 1,5-sigmatropic rearrangement. In principle **34a** and **34b** may cyclize by addition to either face of the cyclopentadiene to give eight adducts. However, the restricted geometry imposed by the tether and the stereochemistry of the lactone methine center reduce the possibilities to the exo products **35** and **36** from **34a** and the endo structures **37** and **38** from **34b**. Even these are very strained when compared to the single exo adduct **39** that may arise from cyclopentadiene isomer **34c**. Experimentally, the triene **34** was heated in a sealed glass tube in toluene in a microwave oven for 2.5 h to afford a single adduct (97%). This material displayed two olefinic hydrogen signals at δ 6.24 and 6.32 in its ^1H NMR spectrum, data that clearly ruled out the Bredt olefin structures **37** and **38**. In contrast to **39**, adducts **35** and **36** contain two methylene and three quaternary carbons (excluding the carbonyl). The ^{13}C NMR spectrum of the Diels–Alder product displayed a single signal at δ 41.5 due to the ring methylene carbon at C_{13} and only two quaternary carbon signals at 40.4 (C_7 geminal dimethyl) and 56.3 (C_1). These features are only consistent with structure **39** which must have arisen from the exo transition state related to **34c** and excluded the other possible adducts. The arrangement in **34c** is the only geometry that can be readily achieved due to the chirality of C_5 and the restricted rotation which also controls the development of the additional chiral centers in the adduct. This represents the first direct preparation of a cycloheptane in a bridged ring system from a carbocyclic precursor in preference to a cyclohexane bridge.[15,17] However, in this instance, because of the constrained nature of the dienophile, the competing pathways to the cyclohexane systems **35–38** are less favorable. This fact is reflected in the ratios of the energies of these adducts **39/35/36/37/38** (1:7:4.7:3.6:4.1).[36] The twisted nature of **35** is apparent by inspection while its isomer **36**, from addition to the opposite face, has the dimethylcyclohexane unit in a boat conformation which also contains a methyl–hydrogen bowsprit interaction. Thus one may capitalize on these steric features and the symmetry of the diene to generate **39** in both a facially and adduct-specific manner with an enantiopure dienophile constrained in a cleavable six-membered ring.

Selective functional group manipulations were now required to complete the synthesis. Hydrogenation of the double bond (Pd/C, 30 psi, 99%), reduction of the lactone to open the ring ($LiAlH_4$, 96%), and selective acetylation of the resulting primary hydroxyl (Ac_2O, Py, 0 °C, 74%) afforded **40**. Various attempts to remove the ether and/or replace the oxygens in the cycloheptane simultaneously gave complex mixtures necessitating a stepwise sequence. The chiral secondary alcohol having fulfilled its role was thus removed via the phenoxythiocarbonate derivative under free-radical conditions (ClCSOPh, AIBN, nBu_3SnH)[35] to provide **43**. The methyl ether was cleaved with iodotrimethylsilane generated in situ in acetonitrile to which triethylamine was added to avoid concomitant cleavage of the acetate. The resulting alcohol was removed via the phenoxythiocarbonate–tributyltin hydride method to give the tricyclic acetate **44**. An alternative order for the conversion of **39** to **43** was also examined via **41** and **42**, in which hydrogenation (10 psi, 10% Pd/C) was deferred until after hydroxyl removal. Earlier experience had shown that contrary to expectations selenoxide and related eliminations in these bridged ring systems were frequently troublesome.[22] Thus pyrolysis

(36) These relative energies (kcal/mol) were determined using Alchemy II (Tripos Associates Inc., 1699 South Hanley Rd., St. Louis, MO, 63144), based on the MM2 molecular mechanics system of Allinger (Allinger, N.L. *Adv. Phys. Org. Chem.* **1976**, *13*, 1) and a variation of the COSMIC force field (Vinter, J. G.; Davis, A.; Saunders, M. R. *J. Comput.*-Aided *Mol. Des.* **1987**, *1*, 31).

of the acetate 44 in a flow system at 525 °C was employed to provide (+)-longifolene (56%) which was identical with an authentic sample of natural (+)-longifolene by ^{1}H NMR, ^{13}C NMR, infrared, and high resolution mass spectral comparison.

In conclusion, a carefully selected [4 + 2] cycloaddition step, in which competing pathways are energetically unfavorable, has resulted in a direct total synthesis of (+)-longifolene. The sequence required 12 steps from cyclopentadiene in 8.2% overall yield from aldehyde 16. This general strategy in which specific steric constraints are introduced to alter the normal reactivity and reaction preferences of competing pericyclic reactions will be useful for the synthesis of diverse natural product skeletons.

Experimental Section

Melting points were determined in capillary tubes with a Thomas-Hoover Uni-Melt apparatus, or with a Fisher-Johns melting point apparatus, and are uncorrected. Infrared (ir) spectra were recorded on a Perkin-Elmer 783 or 983G infrared spectrophotometer and were calibrated with the 1601-cm^{-1} band of polystyrene film. Proton magnetic resonance spectra (^{1}H NMR) were measured at 80 MHz with a Bruker WP80 spectrometer or at 200 MHz with a Varian Gemini spectrometer or at 300 MHz with a General Electric GN 300 or a Varian XL-300 spectrometer in deuterochloroform. Carbon magnetic resonance spectra (^{13}C NMR) were measured at 50 MHz with a Varian Gemini spectrometer or at 75 MHz with a General Electric GN 300 spectrometer or a Varian XL-300 spectrometer. The residual solvent signal ($CDCl_3$) was used as an internal lock: ^{1}H, δ 7.262; ^{13}C δ 77.00, and chemical shifts are reported in ppm downfield from tetramethylsilane (δ scale) as an internal standard. The number of protons, multiplicity, coupling constants, and proton assignments are indicated in parentheses. Mass spectra were determined on a V. G. Micromass 7070 HS instrument using an ionization energy of 70 eV, or on a Hewlett-Packard 5890A gas chromatograph-5970B mass selective detector equipped with a 12.5-m capillary column (0.2 mm i.d.) coated with cross-linked dimethylsilicone (0.33 μm). Optical rotations were measured using a Perkin-Elmer 241 polarimeter (sodium light, cell length = 10 cm, c = g/100 mL).

Analytical thin-layer chromatography (TLC) employed commercial aluminum sheets precoated (0.2-mm layer) with silica gel 60 F_{254} (E. Merck). Flash column chromatography using E. Merck silica gel 60 (230–400 mesh) was employed for all column chromatography. The purity of all title compounds was judged to be ≥95% as determined by a combination of GC-MS, ^{1}H NMR, and ^{13}C NMR analysis.

Petroleum ether refers to a fraction with boiling range 30–60 °C. Anhydrous diethyl ether (ether), tetrahydrofuran (THF), dimethoxyethane (DME), and dioxane were obtained by distillation from $LiAlH_4$ or potassium/benzophenone. Methanol and absolute ethanol were dried by distillation from magnesium. Dry hexamethylphosphoramide (HMPA), dimethylformamide (DMF), dimethyl sulfoxide (DMSO), and diisopropylamine were prepared by distillation from calcium hydride. Solutions in organic solvents were dried over anhydrous magnesium sulfate and stripped of solvent with a Büchi rotary evaporator connected to a water aspirator. Unless otherwise indicated, all reactions were conducted under an atmosphere of dry nitrogen.

(−)-Menthyl Chloroformate.[28] A solution of (−)-menthol (15.6 g, 0.1 mol, Fisher) and quinoline (14.2 g, 0.11 mol, Aldrich, redistilled) was prepared in toluene (100 mL) and cooled to 0 °C. A stock toluene solution of phosgene (20 g, 0.2 mol) was added dropwise to the solution to slowly form a white precipitate. The mixture was stirred at 0 °C and monitored by TLC until the reaction was complete. The precipitate was removed by filtration and the filtrate was flushed with nitrogen at 21 °C to remove excess phosgene. The flushed solution was transferred to an Erlenmeyer flask and a few grams of calcium carbonate were added as the stabilizer. This (−)-menthyl chloroformate solution (approximately 1 mmol/mL) was stored in the refrigerator until use.

(−)(1*R*′)-(2′,2′-Dimethylspiro[2.4]-hepta-4′,6′-dien-1′-yl)-methyl Menthyl Carbonate (15). The stock solution of (−)-menthyl chloroformate was concentrated and the residue was dissolved in anhydrous benzene to prepare a 0.5 mmol/mL solution. To this solution racemic spiro-alcohol 14[27] (1.32 g, 8.8 mmol) was added dropwise followed by triethylamine (equimolar) in anhydrous benzene (10 mL). The reaction mixture was filtered to remove the resulting precipitate, and the filtrate was concentrated to give a thick brown liquid. This mixture was separated by chromatography (2% ethyl acetate/petroleum ether) to afford 15 (0.65 g, 2 mmol) as a white solid; mp 29–31 °C; ^{1}H NMR (300 MHz) δ 0.79 (d, 3 H, J = 7 Hz, CH_3), 0.91 (t, 6 H, J = 6.5 Hz, isopropyl CH_3), 1.05 (m, 2 H, CH_2), 1.41 (s, 6 H, CH_3-cyclopropane), 1.36–1.46 (m, 2 H, CH_2), 1.66 (m, 2 H, CH_2), 1.94 (m, 1 H, CH), 2.03 (m, 1 H, CH), 2.43 (t, 1 H, J = 7.2 Hz, cyclopropyl H), 4.38 (d, 2 H, J = 7.2 Hz, CH_2O), 4.52 (dt, 1 H, J = 4.4, 10.9 Hz, CHO), 6.25 (m, 2 H, cyclopentadienyl H), 6.45 (m, 1 H, cyclopentadienyl H), 6.53 (m, 1 H, cyclopentadienyl H); ^{13}C NMR δ 158.8, 137.4, 132.5, 131.2, 129.3, 78.4, 66.3, 51.2, 47.0, 40.7, 37.8, 34.1, 33.9, 31.4, 26.8, 26.1, 23.3, 21.9, 20.6, 19.8, 16.3.

Chiral shift reagent, tris[3-(trifluoromethylhydroxymethylene)-(+)-camphorato], europium(III) derivative, was added to a $CDCl_3$ solution (0.5 mL) containing the (−)-menthyl carbonate 15 (6.7 mg, 0.02 mmol) in the following molar ratios (1:1, 1:2, 1:3, 1:4) and ^{1}H NMR spectra were recorded. No new signals were observed, and there was no line broadening except for the isopropyl methyl resonances (δ 0.91) which separated into two doublets.

(+)-(1′*R*)-2′,2′-Dimethyl-1′-(hydroxymethyl)spiro[2.4]-hepta-4′,6′-diene (14). The (−)-menthyl carbonate 15 (3.98 g, 12 mmol) was dissolved in anhydrous THF (50 mL) and cooled to 0 °C with an external ice–water bath. Lithium aluminum hydride (1.14 g, 30 mmol) was added in several small portions. The resulting suspension was allowed to warm slowly to room temperature and stirred until the reaction was complete by TLC. The reaction mixture was cooled to 0 °C and the excess $LiAlH_4$ was destroyed with careful dropwise addition of cold water. The resulting mixture was filtered and the filtrate was neutralized with 5% aqueous hydrochloric acid. This solution was extracted with ether (3 × 25 mL), and the combined extracts were dried, filtered, and concentrated. Chromatography (20% ethyl acetate/petroleum ether) afforded (+)-*R*-spiro-alcohol 14 (1.76 g, 98%); $[\alpha]^{22}$ = +21.4° (c 4.6, $CHCl_3$); IR (film) 3350 (br, OH), 3090, 3060 (HC=C), 1650 (s, C=C) cm^{-1}; ^{1}H NMR (300 MHz) δ 1.41 (s, 3 H, CH_3), 1.43 (s, 3H, CH_3), 1.71 (br s, 1 H, OH), 2.41 (dd, 1 H, J = 7.5, 8.1 Hz, cyclopropyl H), 3.80 (dd, 1 H, J = 8.1, 11.7 Hz, CH_2O), 3.99 (dd, 1 H, J = 7.5, 11.7 Hz, CH_2O), 6.30 (m, 2 H, cyclopentadienyl H), 6.45 (m, 1 H, cyclopentadienyl H), 6.57 (m, 1 H, cyclopentadienyl H); ^{13}C NMR δ 138.4, 133.0, 131.8, 129.2, 62.0, 52.3, 43.4, 35.3, 27.5, 20.4; HRMS (EI) calcd for $C_{10}H_{14}O$ 150.1044, found 150.1032.

(+)(1′*R*)-2′,2′-Dimethylspiro[2.4]hepta-4′,6′-diene-1′-carboxaldehyde (16). The spiro-alcohol 14 (2.25 g, 15 mmol) in dichloromethane (25 mL) was added dropwise to a stirred, refluxing suspension of activated MnO_2/charcoal (40 g) in dichloromethane (250 mL). The mixture was stirred under reflux for 12 h, cooled to 21 °C, filtered through Celite and anhydrous $MgSO_4$, and washed thoroughly with dichloromethane. The combined filtrates were concentrated, and the crude product was purified by chromatography (5% ethyl acetate/petroleum ether) to yield the (+)-*R*-spiro-aldehyde 16 (1.90 g, 86%); $[\alpha]^{22}$ = +23.0° (c 2.9, $CHCl_3$); IR (film) 2825 (H–CO), 2720 (H–CO), 1704 (C=O) cm^{-1}; ^{1}H NMR (300 MHz) δ 1.42 (s, 3 H, CH_3), 1.56 (s, 3 H, CH_3), 2.78 (d, 1 H, J = 6 Hz, cyclopropyl H), 6.17 (m, 1 H, cyclopentadienyl H), 6.53 (m, 2 H, cyclopentadienyl H), 6.60 (m, 1 H, cyclopentadienyl H), 9.56 (d, 1 H, J = 6 Hz, HC=O); ^{13}C NMR δ 198.0, 135.5, 132.4, 131.6, 131.4, 56.8, 49.4, 37.1, 26.8, 20.7. HRMS (EI) calcd for $C_{10}H_{12}O$ 148.0888, found 148.0888.

(+)-(5*R*,1′*R*)-3-Methyl-5-(2′,2′-dimethylspiro[2.4]hepta-4′,6′-dien-1′-yl)-6-oxa-2-cyclohexenone (20). An LDA solution was prepared from diisopropylamine (0.32 mL, 2.3 mmol) and *n*-butyllithium (2.5 M, 0.9 mL, 2.3 mmol, Aldrich) in anhydrous THF (5 mL) at −40 °C, and a solution of methyl 3,3-dimethylacrylate (0.2510 g, 2.2 mmol) in anhydrous THF (2 mL) was added dropwise. After stirring for 20 min, cadmium chloride powder (0.366 g, 2.0 mmol, Aldrich, Gold label, previously ground

in a mortar and dried overnight under vacuum at 110 °C) was added in one portion. The suspension was stirred for 30 min at −40 °C, and a solution of (+)-spiro-aldehyde **16** (0.159 g, 1.1 mmol) in anhydrous THF (5 mL) was added by syringe pump (0.1 mL/min). After the addition was complete, stirring was continued for a further 30 min at −40 °C. The reaction was allowed to warm to 0 °C, stirred for 2 h at 0 °C, and then quenched with saturated aqueous NH_4Cl. The mixture was filtered through Celite, and the filtrate was extracted with ether (2 × 15 mL). The combined organic layers were dried, filtered, and concentrated. Chromatography (15% ethyl acetate/petroleum ether) afforded (+)-triene lactone **20** (0.185 g, 73%) as a colorless liquid and the α-product (0.038 g, 15%). (+)-Triene lactone **20**: $[\alpha]^{22} = +17.7°$ (*c* 3.4, $CHCl_3$); IR (film) 1710 (C=O), 1650 (C=) cm^{-1}; ^1H NMR (200 MHz) δ 1.39 (s, 3 H, CH_3), 1.43 (s, 3 H, CH_3), 1.87 (s, 3 H, CH_3C=C), 1.93 (m, 1 H, axial HCC=C), 2.09 (m, 1 H, eq CHC=C), 2.31 (d, 1 H, *J* = 4.4 Hz, cyclopropyl H), 4.48 (ddd, 1 H, *J* = 4.4, 10.1, 11.1 Hz, HCO), 5.76 (s, 1 H, HC=C), 6.17 (m, 1 H, cyclopentadienyl H), 6.28 (m, 1 H, cyclopentadienyl H), 6.49 (m, 1 H, cyclopentadienyl H), 6.58 (m, 1 H, cyclopentadienyl H); ^{13}C NMR and DEPT δ 164.6 (C=O), 156.0 (C=C), 136.4 (C=CH), 132.3 (C=CH), 131.6 (C=CH), 129.7 (C=CH), 116.8 (C=CH), 76.6 (CH), 51.1 (quaternary C), 42.1 (CH), 35.6 (CH_2), 31.9 (quaternary C), 27.2 (CH_3), 23.0 (CH_3), 20.4 (CH_3); HRMS (EI) calcd for $C_{15}H_{18}O_2$ 230.1302, found 230.1303. Anal. Calcd for $C_{15}H_{18}O_2$: C, 78.21; H, 7.88. Found: C, 78.02; H, 7.69.

5-(*tert*-Butyldimethylsiloxy)-3,3,7-trimethyl-8-(methoxycarbonyl)tetracyclo[5.4.2^{4}.$0^{2,9}$]undecane (21). *tert*-Butyldimethylsilyl chloride (1.3 g, 8.6 mmol, Aldrich) was added to a stirred suspension of silver perchlorate (1.74 g, 8.5 mmol) in anhydrous acetonitrile (25 mL).[31] The resulting white suspension was stirred at 21 °C for 30 min and pyridine (2 mL) was added, followed by a solution of hydroxy ester **18**[29] (1.10 g, 4.2 mmol) in anhydrous acetonitrile (5 mL). The reaction was stirred overnight, diluted with ether (30 mL), and filtered. The filtrate was washed with 5% aqueous $NaHCO_3$, brine, dried, filtered, and concentrated. Chromatography (5% ethyl acetate/petroleum ether) afforded the silyl ether **19** (1.43 g, 91%). An anhydrous toluene solution (25 mL) of **19** (0.618 g, 1.6 mmol) containing hydroquinone (2 mg, Aldrich) was placed in a thick-walled Pyrex pressure tube equipped with a threaded cap which extended through a small hole in the top of the microwave oven, flushed with nitrogen, and sealed. The diameter of the oven opening is less than 3 cm and shielded to minimize microwave leakage. The base of the tube in the microwave oven was surrounded by a beaker of damp vermiculite to facilitate heat transfer. Commercial ovens were used (Toshiba Model ERF-6630C (720 W) at a power setting of 500 W in which the magnetron was tuned to the water frequency (2450 MHz). Reactions were conducted behind a shield in a fume hood. After 2 h the tube was cooled and the solution concentrated and chromatographed (5% ethyl acetate/petroleum ether) to yield the Diels–Alder adduct **21** (0.554 g, 92%): IR (film) 1715 (C=O), 1565 (C=C) cm^{-1}; ^1H NMR (300 MHz) δ −0.23 (s, 3 H, $SiCH_3$), 0.15 (s, 3 H, $SiCH_3$), 0.21 (d, 1 H, *J* = 8.4 Hz, cyclopropyl H), 0.83 (s, 3 H, CH_3), 0.84 (s, 9 H, *tert*-butyl), 1.09 (s, 3 H, CH_3-cyclopropane), 1.16 (s, 4 H, CH_3-cyclopropane, CH_2), 1.95 (dd, 1 H, *J* = 4.2, 11.4 Hz, CH_2, another H hidden in CH_3 peak), 2.42 (m, 2 H, bridgehead CH), 2.90 (d, 1 H, *J* = 8.7 Hz, $HCCO_2Me$), 3.66 (s, 3 H, OCH_3), 3.94 (m, 1 H, HCOTBDMS), 5.89 (m, 1 H, HC=C), 6.17 (m, 1 H, HC=C); ^{13}C NMR δ 175.5 (C=O), 136.6 (C=C), 131.5 (C=C), 71.5 (CH), 65.5 (CH), 56.4 (quaternary C), 51.1 (CH_3), 49.0 (CH_2), 46.2 (CH), 43.8 (CH), 43.4 (quaternary C), 32.4 (CH), 25.6 (3 C, CH_3), 25.0 (quaternary C), 23.7 (CH_3), 22.7 (CH_3), 17.9 (quaternary C), 17.2 (CH_3), −4.6 (CH_3), −5.2 (CH_3); HRMS (EI) calcd for $C_{18}H_{27}O_3Si$ (M^+ − *tert*-butyl) 319.1728, found 319.1726.

5-Hydroxy-3,3,7-trimethyl-8-(methoxycarbonyl)tetracyclo[5.4.$0^{1,7}$.$0^{2,4}$.$0^{2,9}$]-10-undecene (22). Tetra-*n*-butylammonium fluoride (1.0 M in THF, 2.5 mL, 2.5 mmol, Aldrich) was added to a stirred solution of the silyl ether **21** (0.472 g, 1.25 mmol) in anhydrous THF (5 mL). The solution was stirred for 2 h at 21 °C and concentrated. The black residue was dissolved in ether (15 mL) and washed with water (20 mL). The aqueous layer was extracted with ether (10 mL), and the combined organic layers were washed with saturated aqueous NH_4Cl, dried, filtered, and concentrated. The product was purified by chromatography (20% ethyl acetate/petroleum ether) to give 0.245 g (75%) of the tetracyclic alcohol **22**: IR (film) 3440 (OH), 1720 (C=O), 1570 (C=C) cm^{-1}; ^1H NMR (300 MHz) δ 0.23 (d, 1 H, *J* = 8.8 Hz, cyclopropyl H), 0.83 (s, 3 H, CH_3), 1.11 (s, 3 H, CH_3), 1.14 (d, 1 H, *J* = 11.5 Hz, CH_2CHO), 1.17 (s, 3 H, CH_3), 1.95 (dd, 1 H, *J* = 4.1 11.5 Hz, CH_2CHO), 2.03 (br s, 1 H, OH), 2.42 (m, 2 H, CH_2C=C), 2.89 (d, 1 H, *J* = 9 Hz, $CHCO_2Me$), 3.72 (s, 3 H, OCH_3), 4.03 (dd, 1 H, *J* = 8.8, 9 Hz, CHO), 5.88 (m, 1 H, HC=C), 6.16 (m, 1 H, HC=C); ^{13}C NMR δ 175.5, 136.6, 131.8, 70.9, 67.3, 64.7, 56.8, 51.5, 49.0, 46.3, 43.8, 32.0, 25.4, 23.4, 22.6, 17.1; DEPT δ 136.6 (CH), 131.8 (CH), 70.9 (CH), 64.7 (CH), 51.5 (CH_3), 49.0 (CH_2), 46.3 (CH), 43.8 (CH), 32.0 (CH), 23.4 (CH_3), 22.6 (CH_3), 17.1 (CH_3); HRMS (EI) calcd for $C_{16}H_{20}O_2$ ($M^+ - H_2O$) 244.1458, found 244.1462.

4-Hydroxy-2-isopropyl-6-methyl-7-(methoxycarbonyl)-tricyclo[5.3.$0^{1,6}$.$0^{2,8}$]decane (25). Alcohol **22** (0.057 g, 0.2 mmol) was dissolved in ethyl acetate (15 mL) containing PtO_2 (ca. 10 mg, Alfa) in a Parr pressure bottle. Hydrogenation (Parr apparatus, 60 psi) was conducted for 24 h. The mixture was filtered and the filtrate was concentrated to give a yellow solid. Recrystallization (ethyl acetate/hexane) gave the tricyclic alcohol **25** (0.049 g, 86%); IR ($CHCl_3$) 3610, 3450 (OH), 1725 (C=O) cm^{-1}; ^1H NMR (300 MHz) δ 0.81 (d, 3 H, *J* = 6.8 Hz, isopropyl CH_3), 0.90 (d, 3 H, *J* = 6.8 Hz, isopropyl CH_3), 0.96 (s, 3 H, CH_3), 1.00–1.93 (9 H), 2.01 (br s, 1 H, CH), 2.10 (br s, 1 H, OH), 2.22 (d, 1 H, *J* = 9.0 Hz, $CHCO_2Me$), 3.69 (s, 3 H, OCH_3), 4.16 (m, 1 H, CHO); ^{13}C NMR δ 175.6, 70.5, 63.9, 55.0, 51.4, 49.6, 43.7, 41.9, 41.8, 31.3, 27.8, 27.0, 22.6, 20.7, 18.0, 17.4; DEPT δ 70.5 (CH), 63.9 (CH), 51.4 (CH_3), 49.6 (CH_2), 43.7 (CH), 41.8 (CH), 31.3 (CH_2), 27.8 (CH), 27.0 (CH_2), 22.6 (CH_3), 20.7 (CH_2), 18.0 (CH_3), 17.4 (CH_3); HRMS (EI) calcd for $C_{16}H_{24}O_2$ ($M^+ - H_2O$) 248.1770, found 248.1722.

3,3,7-Trimethyl-8-(methoxcarbonyl)tetracyclo-[5.4.$0^{1,7}$.$0^{2,4}$.$0^{2,9}$]-10-undecen-5-one (23). A solution of dimethyl sulfoxide (210 μL, 3.0 mmol, dried over CaH_2) in anhydrous CH_2Cl_2 (2 mL) was added dropwise to a solution of oxalyl chloride (130 μL, 1.5 mmol, Aldrich) in anhydrous CH_2Cl_2 (5 mL) maintained at −78 °C with an external solid CO_2/acetone bath.[37] After stirring for 10 min, alcohol **22** (0.337 g, 1.3 mmol) in anhydrous CH_2Cl_2 (3 mL) was added dropwise. The resulting suspension was stirred for 15 min at −78 °C and triethylamine (0.8 mL, excess) in anhydrous CH_2Cl_2 (2 mL) added dropwise to form a clear yellow solution. The solution was allowed to warm to 0 °C, cold water (15 mL) was added, and the mixture was stirred for 10 min at 0 °C. The resulting mixture was separated and the aqueous layer was extracted with CH_2Cl_2 (10 mL). The combined organic layers were washed with 5% hydrochloric acid (5 mL), 5% aqueous $NaHCO_3$ (5 mL), brine, dried, filtered, and concentrated to afford ketone **23** (0.312 g, 93%), which was recrystallized from ethyl acetate/hexane (0.253 g, 75%): mp 37–38.5 °C; ^1H NMR (300 MHz) δ 0.87 (s, 1 H, cyclopropyl H), 0.90 (s, 3 H, CH_3), 1.12 (s, 3 H, CH_3), 1.16 (s, 3 H, CH_3), 1.30 (d, 1 H, *J* = 12 Hz, *H*CHC=O), 2.13 (dd, 1 H, *J* = 4, 12 Hz, *H*CHC=O), 2.68 (m, 1 H, CHC=C), 2.70 (m, 1 H, CHC=C), 3.58 (s, 1 H, CHC=O), 3.72 (s, 3 H, OCH_3), 6.06 (m, 1 H, HC=C), 6.27 (m, 1 H, HC=C); ^{13}C NMR δ 205.0, 170.7, 136.9, 131.9, 69.9, 57.9, 51.6, 48.3, 47.4, 44.7, 44.6, 35.4, 30.9, 23.1, 22.9, 19.5; HRMS (EI) calcd for $C_{16}H_{20}O_3$ 260.1407, found 260.1420. Anal. Calcd for $C_{16}H_{20}O_3$: C, 73.81; H, 7.75. Found: C, 73.66; H, 7.72.

2-Isopropenyl-6-methyl-7-(methoxycarbonyl)tricyclo-[5.3.$0^{1,6}$.$0^{2,8}$]dec-9-en-4-one (24). Powdered zinc (1.6 g, Aldrich) and $Cr_2(SO_4)_3 \cdot 15H_2O$ (2.35 g, Aldrich) were added in portions to a stirred solution of ketone **23** (0.174 g, 0.67 mmol) in a 2:1 mixture of DMF/H_2O (50 mL) at 21 °C.[24,38] The exothermic reaction formed a deep blue solution containing suspended zinc powder. The mixture was stirred for 1 h at 21 °C, diluted with ether (20 mL), and filtered. The filtrate was separated and the aqueous layer was extracted with ether (15 mL). The combined organic layers were washed with water (20 mL), dried, and concentrated. Chromatography (10% ethyl acetate/petroleum ether) yielded

(37) (a) Omura, K.; Swern, D. *Tetrahedron* **1978**, *34*, 1651. (b) Mancuso, A. J.; Swern, D. *Synthesis* **1981**, 165.

(38) (a) Castro, C. E.; Stephens, R. D.; Moje, S. *J. Am. Chem. Soc.* **1966**, *88*, 4964. (b) House, H. O.; Kinlock, E. F. *J. Org. Chem.* **1974**, *39*, 1173.

24 (0.104 g, 60%): IR (film) 1730 (C=O), 1710 (C=O), 1645 (C=C), 1560 (C=C) cm^{-1}; ^1H NMR (300 MHz) δ 1.04 (s, 3 H, CH_3), 1.13 (m, 1 H, CH_2), 1.62 (m, 1 H, CH_2), 1.65 (s, 3 H, CH_3C=C), 2.47 (m, 1 H, CHC=C), 2.81 (m, 2 H, CH_2C=O), 3.02 (m, 1 H, CHC=C), 3.40 (d, 1 H, J = 1.1 Hz, $CHCO_2Me$), 3.72 (s, 3 H, OCH_3), 4.69 (m, 1 H, CH_2=C), 4.77 (m, 1 H, CH_2=C), 5.97 (m, 1 H, HC=C), 6.17 (m, 1 H, HC=C); ^{13}C NMR δ 205.7, 169.2, 148.0, 137.5, 131.0, 111.8, 68.1, 66.7, 52.1, 50.9, 50.1, 47.4, 41.9, 40.3, 24.4, 21.9; DEPT δ 137.5 (CH), 131.0 (CH), 111.8 (CH_2), 66.1 (CH), 52.1 (CH_3), 50.9 (CH), 50.1 (CH), 47.4 (CH_2), 40.3 (CH_2), 24.4 (CH_3), 21.9 (CH_3); HRMS (EI) calcd for $C_{16}H_{20}O_3$ 260.1407; found 260.1411.

A Cr(II) solution was prepared as follows:[24,38] $Cr_2(SO_4)_3 \cdot 15H_2O$ (5 g) and zinc powder (1.3 g) were mixed in distilled water (30 mL) and the mixture was stirred overnight at room temperature under nitrogen. A clear blue solution of Cr(II)SO_4 (ca. 0.5 M) was obtained by decantation. The Cr(II) solution (2 mL) and zinc powder (0.1 g) were added to a solution of ketone **23** (8 mg, 0.03 mmol) in DMF (6 mL). The reaction was stirred for 36 h at 21 °C and no reaction was observed (GC-MS monitoring). Thus the reaction was refluxed for 12 h, cooled, the mixture was filtered and the filtrate extracted with ether (2 × 15 mL). The combined ether extracts were washed with brine, dried, filtered, and concentrated. Chromatography (5% ethyl acetate/petroleum ether) yielded a single produce (7 mg), whose ^1H NMR spectrum corresponded to the isomerization product **24**.

3,3,7-Trimethyl-8-(methoxycarbonyl)tetracyclo-[5.4.0^{1,7}.0^{2,4}.0^{2,9}]undecan-5-one (30). Ketone **23** (0.221 g, 0.85 mmol) was dissolved in ethyl acetate (10 mL) and 10% Pd/C (ca. 20 mg, Alfa) was suspended in the solution. The hydrogenation was carried out in a Parr apparatus under hydrogen (15 psi) for 12 h. The mixture was filtered through a band of Celite and the filtrate was concentrated to give a yellow solid. Recrystallization (ethyl acetate/hexane) gave the saturated ketone **30** (0.207 g, 93%): mp 37–38 °C; IR ($CHCl_3$) 1732 (C=O), 1715 (C=O) cm^{-1}; ^1H NMR (200 MHz) δ 0.94 (s, 1 H, cyclopropyl H), 1.03 (s, 3 H, CH_3), 1.15 (s, 3 H, CH_3), 1.20 (s, 3 H, CH_3), 1.36 (d, 1 H, J = 12 Hz, *H*CHC=O), 1.75–1.80 (m, 3 H), 1.95–2.15 (m, 4 H), 3.24 (s, 1 H, CHC=O), 3.71 (OCH_3); ^{13}C NMR δ 205.4, 170.1, 72.6, 51.5, 50.6, 47.5, 43.0, 39.9, 33.3, 30.9, 29.0, 22.9, 22.6, 21.4, 19.3. HRMS (EI) calcd for $C_{16}H_{22}O_3$ 262.1563; found 262.1544. Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.24; H, 10.55. Found: C, 73.09; H, 10.44.

2-Isopropyl-6-methyl-7-(methoxycarbonyl)tricyclo-[5.3.0^{1,6}.0^{2,8}]-3-decene (28). Alcohol **22** (0.058 g, 0.22 mmol) was dissolved in ethyl acetate (20 mL), 10% Pd/C (10 mg, Alfa) added, and hydrogenation was conducted in a Parr apparatus under hydrogen (10 psi) for 10 h. The reaction mixture was filtered and the filtrate was concentrated to give the tetracyclic alcohol **26** (0.056 g, 96%). (This product was used directly for the next step, since attempted recrystallization (ethyl acetate/hexane) caused isomerization and cyclopropane ring opening to 4-hydroxy-2-isopropenyl-6-methyl-7-(methoxycarbonyl)tricyclo[5.3.0^{1,6}.0^{2,8}]-decane). IR (film) 3605 (OH), 1725 (C=O), 1640 (C=C) cm^{-1}; ^1H NMR (300 MHz) δ 0.97 (s, 3 H, CH_3), 1.15 (m, 1 H), 1.48 (m, 2 H, CH_2), 1.53 (br s, 2 H, CH_2), 1.73 (s, 3 H, CH_3C=C), 1.66–1.87 (overlap 3 H), 2.01 (br s, 1 H, CH), 2.22 (d, 1 H, J = 8.7 Hz, $CHCO_2Me$), 2.23 (br s, 1 H, OH), 3.69 (s, 3 H, OCH_3), 4.32 (m, 1 H, CHO), 4.71 (m, 2 H, CH_2=C); ^{13}C NMR δ 175.5, 148.4, 109.6, 69.5, 63.5, 56.9, 51.5, 48.7, 43.9, 42.0, 41.7, 38.1, 27.5, 22.5, 21.1, 19.8; DEPT δ 109.2 (CH_2), 69.5 (CH), 63.5 (CH), 48.7 (CH_2), 43.9 (CH), 42.0 (CH), 38.1 (CH_2), 27.5 (CH_2), 22.5 (CH_3), 21.1 (CH_2), 19.8 (CH_3). The hydrogenation product **26** was dissolved in anhydrous dichloromethane (5 mL) and pyridine (65 μL, 0.8 mmol, Aldrich, dried over 3-Å molecular sieves) and phenyl chlorothioformate (53 μL, 0.6 mmol, Aldrich) was added. The yellow solution was stirred for 1 h at 21 °C and concentrated. The residue was dissolved in ether (20 mL) and the ether solution was washed with 5% aqueous HCl (5 mL), 5% aqueous $NaHCO_3$ (5 mL), and brine (10 mL). The organic solution was dried, filtered, and concentrated. The resulting dark oil was passed through a short silica gel column (eluted with 2% ethyl acetate/petroleum ether) to afford thiocarbonate **27** (0.052 g, 61%). A solution of tributyltin hydride (81 μL, 0.3 mmol, Aldrich) and AIBN (5 mg, recrystallized) in anhydrous toluene (5 mL) was added via syringe pump (0.25 mL/h) to a stirred, refluxing toluene solution of the thiocarbonate (0.052 g, 0.13 mmol). After the addition was complete, the reaction mixture was stirred under reflux for a further 4 h, cooled to room temperature, and concentrated to remove the solvent. The residue was applied to the top of a silica gel column (petroleum ether), allowed to sit for several hours, and eluted first with petroleum ether to remove the tin compounds and then with 2% ethyl acetate/petroleum ether to yield 0.026 g (70%) of the ring opened products **28** and **31** (9:1 by GC-MS). **28**: ^1H NMR (300 MHz) δ 0.86 (d, 3 H, J = 6.9 Hz, isopropyl CH_3), 0.92 (d, 3 H, J = 6.9 Hz, isopropyl CH_3), 1.09 (s, 3 H, CH_3), 1.26 (m, 2 H, CH_2), 1.58–1.76 (4 H, CH_2), 1.89 (sextet, 1 H, J = 6.9 Hz, isopropyl H), 2.04 (m, 1 H, CH), 2.23 (m, 1 H, CH), 2.65 (d, 1 H, J = 4.5 Hz, $CHCO_2Me$), 3.65 (s, 3 H, OCH_3), 5.56 (dd, 1 H, J = 4.5, 9.8 Hz, HC=C), 5.90 (d, 1 H, J = 9.8 Hz, HC=C); ^{13}C NMR δ 173.3, 133.2, 123.6, 57.5, 56.8, 51.3, 46.0, 45.8, 44.0, 41.3, 28.8, 26.5, 22.8, 20.3, 19.0, 17.4.

3,3,7-Trimethyl-5-[(phenoxythiocarbonyl)oxy]-8-(methoxycarbonyl)tetracyclo[5.4.0^{1,7}.0^{2,4}.0^{2,9}]-10-undecene. Dry pyridine (160 μL, 2.0 mmol, Aldrich) was added to a stirred solution of tetracyclic alcohol **22** (0.197 g, 0.75 mmol) in anhydrous dichloromethane (5 mL) at 21 °C, followed by phenyl chlorothioformate (118 μL, 0.85 mmol, Aldrich). The resulting yellow solution was stirred for 1 h and concentrated, and the residue was dissolved in ether (20 mL). The ether solution was washed with 5% aqueous HCl (5 mL), 5% aqueous $NaHCO_3$ (5 mL), brine (10 mL), dried, filtered, and concentrated. Radial chromatography (2% ethyl acetate/petroleum ether) afforded the thiocarbonate (0.166 g, 56%): ^1H NMR (300 MHz) δ 0.42 (d, 1 H, J = 8.4 Hz, cyclopropyl H), 0.88 (s, 1 H, CH_3), 1.19 (d, 1 H, J = 11.6 Hz), 1.22 (s, 3 H, CH_3), 2.00 (dd, 1 H, J = 4.2, 11.6 Hz, CH_2), 2.49 (br s, 1 H, CHC=C), 2.54 (m, 1 H, CHC=C), 3.26 (d, 1 H, J = 9 Hz, $CHCO_2Me$), 3.72 (s, 3 H, CH_3), 5.44 (t, 1 H, J = 8.7 Hz, CHO), 5.94 (m, 1 H, HC=C), 6.21 (dd, 1 H, J = 2.7, 5.7 Hz, HC=C), 7.09 (d, 2 H, J = 8.2 Hz, phenyl H), 7.27 (m, 1 H, phenyl H), 7.40 (m, 2 H, phenyl H); ^{13}C NMR δ 193.5, 173.7, 153.4, 136.5, 131.2, 129.4 (2 C), 126.4, 121.9 (2 C), 83.0, 61.3, 56.5, 51.6, 48.5, 46.3, 43.9, 43.8, 29.4, 26.2, 23.4, 22.6, 17.9; LRMS 398 ($C_{23}H_{26}O_4S$, M^+), 366 (M^+ – S), 338 (M^+ – AcOH), 244 (M^+ – PhO(C=S)OH).

2-Isopropenyl-6-methyl-7-(methoxycarbonyl)tricyclo-[5.3.0^{1,6}.0^{2,8}]decan-4-one (29). A methanol (1 mL) solution of ketone **30** (6 mg, 0.02 mmol) was added to a stirred mixture of zinc powder (0.5 g) and zinc chloride (0.5 g) in methanol (5 mL) at room temperature. A few drops of glacial acetic acid were added and the mixture was refluxed with stirring overnight. After cooling to room temperature, the mixture was filtered and the filtrate was extracted with ether (2 × 10 mL). The combined ether layers were washed with 5% aqueous $NaHCO_3$ (5 mL), brine (15 mL), dried, filtered, and concentrated. Chromatography (10% ethyl acetate/petroleum ether) afforded the isomerization product **29** (5 mg, 83%): ^1H NMR (300 MHz) δ 1.11 (s, 3 H, CH_3), 1.07–1.22 (3 H), 1.72 (s, 3 H, CH_3C=C), 1.58–1.89 (3 H), 2.16 (m, 2 H, CH_2), 2.34 (m, 1 H, CH), 2.49 (m, 1 H, CH), 3.10 (br s, 1 H, $CHCO_2Me$), 3.71 (s, 3 H, OCH_3), 4.73 (m, 1 H, HC=C), 4.84 (m, 1 H, HC=C); LRMS 262 ($C_{16}H_{22}O_3$, M^+).

Li/NH_3 Reductive Cyclopropane Ring Opening of Ketone 30.[24] Ammonia was condensed into a flask through a solid CO_2/acetone condenser maintained at −78 °C with an external solid CO_2/acetone bath. Once the liquid ammonia volume was ca. 3 mL, lithium metal (ca. 8 mg) was added to generate a blue solution. A solution of cyclopropylketone **30** (0.209 g, 0.79 mmol) and *tert*-butyl alcohol (0.080 g, 1.1 mmol) in anhydrous ether (10 mL) was added dropwise to the Li/NH_3 solution. After the addition was complete, stirring was continued for 10 min at −78 °C. The reaction was quenched with ammonium chloride, the solid CO_2/acetone bath was removed, the reaction mixture was allowed to warm to 0 °C with an external ice/water bath, and the ammonia was evaporated under a stream of N_2. Water (10 mL) was added, the resulting mixture was separated, and the aqueous layer was extracted with ether (2 × 10 mL). The combined organic layers were washed with saturated aqueous NH_4Cl (20 mL), dried, filtered, and concentrated. Chromatography (5% ethyl acetate/petroleum ether) afforded a pale yellow oil (0.202 g, 97%) consisting of a 1:1 mixture (GC-MS) of the ring opened ketones **32** and **33** which could not be separated.

(5*R*)(1′*R*)-5-(2′-Cyclopentadienyl-1′-methoxy-2′,2′-dimethylethyl)-6-oxa-3-methyl-2-cyclohexenone (34). Boron trif-

luoride etherate (92 μL, 0.75 mmol, Aldrich) was added to a solution of lactone **20** (0.165 g, 0.72 mmol) in absolute methanol (10 mL) at 21 °C. The solution was stirred for 4 h and quenched with 5% aqueous $NaHCO_3$. The mixture was extracted with ether (2 × 25 mL), and the combined extracts were washed with brine, dried, filtered, and concentrated. Chromatography (15% ethyl acetate/petroleum ether) gave the ether **34** (0.157 g, 83%) as a mixture of substituted cyclopentadienes due to rapid 1,5-sigmatropic rearrangement: IR (film) 1730 (C=O), 1575 (C=C) cm^{-1}; ^1H NMR (200 MHz) δ 1.11, 1.12 (s, total 3 H, CH_3), 1.18 (s, 3 H, CH_3), 1.87 (m, 1 H), 1.88 (br s, 3 H, CH_3C=C), 2.24–2.41 (m, 1 H), 2.65 (m, 1 H), 2.87 (m, 1 H), 3.19, 3.20 (s, total 3 H, OCH_3), 5.02 (m, 2 H, CHO), 5.64 (s, 1 H, HC=C), 6.22, 6.34, 6.42, 6.64, 6.68 (m, total 4 H, cyclopentadienyl H).

(1*S*)(2*R*)(5*R*)(6*R*)(8*R*)(9*S*)(12*R*)-1,7,7-Trimethyl-6-methoxy-4-oxatetracyclo[7.3.1.0^{2,9}]-10-tridecen-3-one (39). Cyclopentadiene **34** (0.138 g, 0.6 mmol) and hydroquinone (5 mg) were dissolved in anhydrous toluene (10 mL). The solution was placed in a thick-walled Pyrex pressure tube equipped with a threaded cap which extended through a small hole in the top of the microwave oven, flushed with nitrogen, and sealed. The diameter of the oven opening is less than 3 cm and shielded to minimize microwave leakage. The base of the tube in the microwave oven was surrounded by a beaker of damp vermiculite to facilitate heat transfer. Commercial ovens were used (Toshiba Model ERF-6630C (720 W) at a power setting of 500 W in which the magnetron was tuned to the water frequency (2450 MHz). Reactions were conducted behind a shield in a fume hood. After 2.5 h the tube was cooled, the solution was concentrated, and chromatographed (10% ethyl acetate/petroleum ether) the yield the Diels–Alder adduct **39** (0.134 g, 97%): IR (film) 1725 (C=O), 1575 (C=C) cm^{-1}; ^1H NMR (200 MHz) δ 0.95 (s, 3 H, CH_3), 1.14 (s, 3 H, CH_3), 1.18 (s, 3 H, CH_3), 1.82–2.19 (m, 4 H), 2.53 (s, 1 H, CH_2C=C), 2.72 (s, 1 H, bridge CH_2), 3.11 (s, 4 H, OCH_3, HCO), 4.62 (s, 1 H, HCO), 6.44 (m, 1 H, HC=C), 6.32 (m, 1 H, HC=C); ^{13}C NMR δ 174.9, 138.7, 136.5, 76.3, 74.2, 58.5, 56.3 (quat), 52.9, 51.0, 49.9, 48.5, 41.5, 40.4 (gem, Me), 24.6, 23.6, 23.0; DEPT δ 138.7 (CH), 136.5 (CH), 76.3 (CH), 58.5 (CH), 52.9 (CH), 51.0 (CH), 49.9 (CH), 48.5 (CH_3), 41.5 (CH_2), 24.6 (CH_3), 23.6 (CH_3), 23.0 (CH_3); HRMS (EI) calcd for $C_{15}H_{18}O_2$ ($M^+ - CH_3OH$) 230.1302, found 230.1321. Anal. Calcd for $C_{16}H_{22}O_3$: C, 73.24; H, 10.55. Found: C, 72.95; H, 10.51.

(1*R*)(2*R*)(4*R*)(5*R*)(7*S*)(8*R*)(9*S*)-3,3,7-Trimethyl-4-methoxy-5-hydroxy-8-(acetoxymethyl)tricyclo[5.4.0^{1,7}.0^{2,9}]undecane (40). Tetracyclic lactone **39** (0.079 g, 0.3 mmol) was dissolved in ethyl acetate (10 mL) in a Parr pressure bottle and 55 Pd/C (10 mg) was added. Hydrogenation was conducted in a Parr apparatus (30 psi, hydrogen) for 4 h at room temperature. The resulting mixture was filtered through Celite and the filtrate was concentrated. ^1H NMR indicated the absence of any vinyl hydrogens. This product was dissolved in anhydrous ether (5 mL) and cooled to 0 °C with an external ice/water bath. Lithium aluminum hydride (50 mg, Aldrich) was added to the stirred, cold solution and the reaction was allowed to warm to room temperature and stirred for a further 4 h. The reaction was cooled to 0 °C and quenched with cold water. The mixture was filtered and the filtrate was extracted with ether (2 × 10 mL). The combined extracts were washed with brine, dried, filtered and concentrated. Chromatography (40% ethyl acetate/petroleum ether) yielded 0.065 g (92% from **39**) of the diol; IR (film) 3460 (OH) cm^{-1}; ^1H NMR (200 MHz) δ 0.94 (s, 3 H, CH_3), 1.10 (s, 3 H, CH_3), 1.13 (s, 3 H, CH_3), 1.19–1.85 (m, 9 H, CH_2, CH), 2.10 (br s, 2 H, OH), 3.18 (s, 3 H, OCH_3), 3.73 (m, 2 H, CH_2O), 3.95 (m, 1 H, CHO), 4.60 (s, 1 H, CHO); ^{13}C NMR δ 81.3, 66.1, 63.2, 55.6, 49.2, 48.7, 48.1, 45.7, 44.9, 42.3, 39.7, 31.5, 25.8, 22.9, 21.6, 17.6.

The diol (0.482 g, 1.8 mmol) was dissolved in anhydrous ether (5 mL) and cooled to 0 °C with an external ice/water bath. Pyridine was added (0.3 mL), followed by acetic anhydride (0.2 mL, 2.0 mmol, Aldrich) and the reaction was stirred for 6 h at 0 °C, diluted with ether (20 mL), and then quenched with cold water. The mixture was separated and the aqueous layer was extracted with ether (15 mL). The combined organic extracts were washed with 5% aqueous $NaHCO_3$, brine, dried, filtered, and concentrated. Chromatography (10% ethyl acetate/petroleum ether) afforded 0.072 g (15%) of recovered starting material and 0.413 g (74%) of the hydroxy acetate **40**; IR (film) 3460 (br, OH), 1740 (C=O) cm^{-1}; ^1H NMR (200 MHz) δ 0.77 (s, 3 H, CH_3), 1.24 (s, 3 H, CH_3), 1.27 (s, 3 H, CH_3), 1.40–2.10 (m, 9 H), 2.03 (s, 3 H, CH_3C=O), 2.25 (m, 1 H, C*H*CH_2O), 2.73 (br s, 1 H, OH), 3.20 (s, 3 H, OCH_3), 4.05–4.20 (m, 3 H, CH_2O, CHO), 5.50 (dd, 1 H, J = 7.5, 10 Hz, CHO). Anal. Calcd for $C_{18}H_{30}O4$: C, 69.63; H, 9.75. Found: C, 69.91; H, 9.92.

(1*R*)(2*R*)(4*R*)(7*S*)(8*R*)(9*S*)-3,3,7-Trimethyl-4-methoxy-8-(acetoxymethyl)tricyclo[5.4.0^{1},^{7}.0^{2,9}]undecane (43). Pyridine (0.16 mL, 2.0 mmol) and phenyl chlorothioformate (0.14 mL, 1.0 mmol) were added to a stirred anhydrous dichloromethane solution (5 mL) containing hydroxy acetate **40** (0.202 g, 0.65 mmol) at room temperature. After the reaction was complete (TLC), the solvent was evaporated, the residue was dissolved in ether (30 mL), and the ether solution was washed with 5% aqueous $NaHCO_3$ and brine. This ether solution was dried, filtered, and concentrated. The residue was passed through a short silica gel column with 10% ethyl acetate/petroleum ether as eluant. The product (0.240 g) was dissolved in anhydrous toluene (5 mL). This solution was stirred under reflux and a solution of tributyltin hydride (0.22 mL, 0.8 mmol) containing a catalytic amount of AIBN (6 mg) in anhydrous toluene (2 mL) was added with a syringe pump at a rate of 0.5 mL/h. After the addition was complete, reflux was continued for a further 4 h, and the reaction cooled to room temperature. The solution was concentrated, the product in hexane was applied to the top of a silica gel column, allowed to sit for several hours, and eluted with hexane. Subsequent elution with 5% ethyl acetate/petroleum ether afforded methoxy acetate **43** (0.136 g, 71%); IR (film) 1715 (C=O) cm^{-1}; ^1H NMR (200 MHz) δ 0.83 s, 3 H, CH_3), 1.05 (s, 3 H, CH_3), 1.11 (s, 3 H, CH_3), 1.10–1.40 (m, 8 H, CH_2), 1.56–2.15 (m, 4 H, CH), 2.00 (s, 3 H, CH_3C=O), 2.40 (dd, 1 H, J = 8, 10.5 Hz, CHO), 3.14 (s, 3 H, OCH_3), 3.98 (d, 2 H, J = 8 Hz, CH_2O); ^{13}C NMR δ 171.4, 65.8, 60.0, 49.5, 48.8, 48.4, 47.4, 47.3, 45.9, 37.2, 24.5, 25.6, 24.6, 22.4, 20.8, 17.7. Anal. Calcd $C_{18}H_{30}O_3$: C, 73.41; H, 10.28. Found: C, 73.49; H, 10.27.

Alternatively alkene acetate **42** (0.065 g, 0.22 mmol) was dissolved in ethyl acetate (15 mL) and a catalytic amount (ca. 10 mg) of 5% Pd/C added. Hydrogenation was conducted in a Parr apparatus under H_2 (20 psi) for 2 h. The mixture was filtered through Celite and concentrated. The residue was purified by chromatography (5% ethyl acetate/petroleum ether) to give **43** (0.063 g, 97%).

(1*R*)(2*R*)(4*R*)(5*R*)(7*S*)(8*R*)(9*S*)-3,3,7-Trimethyl-4-methoxy-5-hydroxy-8-(acetoxymethyl)tricyclo[5.4.0^{1,7}.0^{2,9}]-10-undecene (41). Tetracyclic lactone **39** (0.157 g, 0.6 mmol) was dissolved in anhydrous ether (5 mL) and cooled to 0 °C with an external ice/water bath. $LiAlH_4$ (100 mg, excess) was added in several small portions and the resulting suspension was allowed to warm slowly to room temperature. The suspension was stirred until the reaction was complete (TLC), cooled to 0 °C, diluted with ether (15 mL), and quenched with cold water. The resulting mixture was filtered and the filtrate was separated. The aqueous layer was extracted with ether (2 × 15 mL), and organic phases were combined, washed with saturated aqueous NH_4Cl, dried, filtered, and concentrated to give the diol: IR (film) 3410 (br, OH), 3060 (H–C=C), 1585 (C=C) cm^{-1}; ^1H NMR (200 MHz) δ 0.94 (s, 3 H, CH_3), 1.10 (s, 3 H, CH_3), 1.13 (s, 3 H, CH_3), 1.28 (t, 1 H, J = 8 Hz, CH), 1.43 (br s, 1 H, OH), 1.66–1.73 (m, 2 H, CH_2), 1.89 (br s, 1 H, OH), 1.96 (d, 1 H, J = 9.5 Hz, CH), 2.29 (br s, 1 H, CHC=C), 2.39 (br s, 1 H, CHC=C), 3.19 (s, 3 H, OCH_3), 3.77–4.10 (m, 3 H, CH_2O, CHO), 4.56 (s, 1 H, HCO), 5.93 (m, 1 H, HC=C), 6.31 (m, 1 H, HC=C); ^{13}C NMR δ 140.6, 132.8, 66.9, 62.3, 58.4, 53.2, 50.8, 50.4, 49.5, 48.6, 40.0, 38.5, 37.0, 28.4, 22.8, 17.4.

The diol (0.305 g, 1.15 mmol) was dissolved in anhydrous ether (5 mL) and cooled to 0 °C with an external ice/water bath. Pyridine (0.2 mL) was added to this solution, followed by acetic anhydride (0.2 mL, 2.0 mmol, Aldrich). The reaction solution was stirred overnight at 0 °C, diluted with ether (20 mL), and quenched with cold water. The mixture was separated and the aqueous layer was extracted with ether (15 mL). The combined organic extracts were washed with 5% aqueous $NaHCO_3$ and brine, dried, filtered, and concentrated. The product was purified by chromatography (10% ethyl acetate/petroleum ether) to afford 0.261 g (74%) of acetate **41** and 0.077 g (15%) of the diacetate.

Subsequently, the latter material was treated with $LiAlH_4$ to recover the starting material. Acetate 41: IR (film) 3460 (OH), 1740 (C=O), 1560 (C=C) cm^{-1}; ^1H NMR (200 MHz) δ 0.72 (s, 3 H, CH_3), 1.05 (s, 3 H, CH_3), 1.17 (s, 3 H, CH_3), 1.48 (m, 1 H, CH), 1.60–2.10 (m, 3 H), 2.05 (s, 3 H, CH_3C=O), 2.25 (m, 1 H, CHC=C), 2.72 (m, 1 H, CHC=C), 3.08 (br s, 1 H, OH), 3.25 (s, 3 H, OCH_3), 3.35 (d, 1 H, J = 7.5 Hz, CHO), 4.25 (br d, 2 H, CH_2O), 5.52 (m, 1 H, C*H*OH), 5.88 (m, 1 H, HC=C), 6.42 (d, J = 6 Hz, HC=C).

(1*R*)(2*R*)(4*R*)(7*S*)(8*R*)(9*S*)-3,3,7-Trimethyl-4-methoxy-8-(acetoxymethyl)tricyclo[5.4.0^{1,7}.0^{2,9}]-10-undecene (42). Pyridine (0.16 mL, 2 mmol), followed by phenyl chlorothioformate (0.14 mL, 1 mmol, Aldrich), was added to a stirred solution of acetate 41 (0.202 g, 0.65 mmol) in anhydrous CH_2Cl_2 (5 mL) at room temperature. The reaction was stirred for 3 h at room temperature and then concentrated. The residue was extracted with ether (30 mL), and the ether solution was washed with 5% aqueous $NaHCO_3$, brine, dried, filtered, and concentrated. Chromatography (5% ethyl acetate/petroleum ether) gave recovered starting material (0.041 g, 20%) and the thiocarbonate (0.194 g, 67%): IR (film) 1745 (C=O), 1595 (C=C), 1490 (phenyl) cm^{-1}; ^1H NMR (200 MHz) δ 0.77 (s, 3 H, CH_3), 1.24 (s, 3 H, CH_3), 1.27 (s, 3 H, CH_3), 1.54 (m, 2 H, CH_2), 1.70–2.00 (m, 4 H), 2.04 (s, 3 H, CH_3C=O), 2.33 (d, 1 H, J = 7.5 Hz, CHC=C), 2.54 (m, 1 H, CHC=C), 2.79 (br s, 1 H, CHO), 3.20 (s, 3 H, OCH_3), 4.28 (dd, 2 H, J = 3.6, 7.1 Hz, CH_2O), 5.94 (dd, 1 H, J = 2.3, 5.5 Hz, HC=C), 6.07 (dd, 1 H, J = 7.5, 10.1 Hz, CHOC(=S)OPh), 6.35 (d, 1 H, J = 5.9 Hz, HC=C), 7.03 (m, 1 H, phenyl H), 7.06 (m, 1 H, phenyl H), 7.25 (m, 1 H, phenyl H), 7.35 (m, 2 H, phenyl H); ^{13}C NMR δ 194.1, 172.0, 153.5, 138.2, 133.1, 129.5 (2 C), 126.5, 121.9 (2 C), 90.6, 74.9, 64.3, 63.6, 58.4, 55.6, 52.3, 48.9, 48.8, 43.7, 41.1, 23.3, 22.6, 20.9, 20.1.

A solution of tributyltin hydride (0.22 mL, 0.8 mmol, Aldrich) and AIBN (16 mg) in anhydrous toluene (2 mL) was added to a stirred, refluxing solution of the phenoxythiocarbonate (0.140 g, 0.31 mmol) in anhydrous toluene (5 mL) at a rate of 0.5 mL/h with a syringe pump. After the addition was complete, the reaction was stirred under reflux for a further 6 h. It was cooled to room temperature and concentrated. The product in hexane was applied to the top of a silica gel column, allowed to sit for several hours and eluted with hexane. Subsequent elution with 5% ethyl acetate/petroleum ether afforded the acetate 42 (0.0816 g, 89%) as a colorless liquid: IR (film) 3060 (HC=C), 1735 (C=O), 1574 (C=C) cm^{-1}; ^1H NMR (200 MHz) δ 0.66 (s, 3 H, CH_3), 1.10 (s, 3 H, CH_3), 1.16 (s, 3 H, CH_3), 1.31 (m, 2 H, CH_2), 1.56–2.17 (m, 5 H), 2.00 (s, 3 H, CH_3C=O), 2.52 (m, 1 H, CHC=C), 2.70 (br s, 1 H, CHC=C), 3.15 (s, 3 H, OCH_3), 4.04 (d, 2 H, J = 7.3 Hz, CH_2O), 5.91 (dd, 1 H, J = 3, 5.7 Hz, HC=C), 6.35 (d, 1 H, J = 5.7 Hz, HC=C); ^{13}C NMR δ 171.2, 138.9, 133.0, 75.6, 66.5, 66.4, 58.1, 50.8, 49.4, 48.7, 46.4, 43.7, 41.1, 33.7, 23.3, 23.0, 20.7, 18.9. Anal. Calcd for $C_{18}H_{28}O_3$: C, 73.92; H, 9.66. Found: C, 73.70; H, 9.56.

(−)-(1*R*)(2*R*)(7*S*)(8*R*)(9*S*)-3,3,7-Trimethyl-8-(acetoxymethyl)tricyclo[5.4.0^{1,7}.0^{2,9}]undecane (44). Acetate 43 (0.065 g, 0.22 mmol) and sodium iodide (0.045 g, 0.30 mmol) were mixed in anhydrous dichloromethane (5 mL). Triethylamine (56 μL, 0.40 mmol) was added, followed by chlorotrimethysilane (38 μL, 0.30 mmol, Aldrich). After stirring for an hour, the reaction was quenched with saturated aqueous NH_4Cl. The mixture was extracted with dichloromethane (2 × 20 mL), and the combined extracts were washed with 10% aqueous sodium thiosulfate, brine, dried, and concentrated. The resulting alcohol was dissolved in anhydrous dichloromethane (2 mL), and pyridine (32 μL, 0.40 mL, Aldrich, redistilled) was added, followed by phenyl chlorothioformate (42 μL, 0.30 mmol) in anhydrous dichloromethane (1 mL). The reaction was stirred for 3 h at room temperature and concentrated. The residue was dissolved in ether (20 mL), the ether solution washed with water (2 × 20 mL), dried, filtered, and concentrated. Rapid chromatography through a short silica gel column gave the thiocarbonate. It was dissolved in anhydrous toluene (2 mL) and stirred under reflux. A solution of tributyltin hydride (54 μL, 0.2 mmol) and AIBN (5 mg) in anhydrous toluene (2 mL) was added syringe pump at a rate of 0.5 mL/h. After the addition was complete, the solution was refluxed for a further 5 h, cooled to room temperature, and concentrated. The product in hexane was applied to the top of a silica gel column, allowed to sit for several hours, and eluted with hexane. Subsequent elution with 5% ethyl acetate/petroleum ether afforded the acetate 44 (0.029 g, 50% from 43); $[\alpha]^{22}$ = −11.8° (*c* 3.7, $CHCl_3$); IR (film) 1745 (C=O), 1240 (C=O) cm^{-1}; ^1H NMR (200 MHz) δ 0.88 (s, 3 H, CH_3), 0.94 (s, 3 H, CH_3), 1.00–1.65 (m, 13 H, CH_2, CH), 1.95 (m, 1 H, C*H*CH_2O), 2.00 (s, 3 H, CH_3C=O), 4.19 (d, 2 H, J = 7.9 Hz, CH_2O); ^{13}C NMR δ 171.1, 66.2, 64.3, 54.8, 44.9, 44.5, 41.3, 38.9, 36.6, 33.5, 32.7, 32.1, 31.7, 30.8, 24.6, 20.9, 20.8. Exact mass calcd. for $C_{15}H_{24}$ (M^+ − AcOH): 204.1872; found: 204.1884.

(+)-Longifolene (1). A pyrolysis apparatus equipped with a quartz tube filled with quartz-wool was preheated to 525 °C under a flow of nitrogen. A solution of acetate 44 (0.026 g, 0.098 mmol) in anhydrous benzene (2 mL) was added dropwise at a rate that permitted the hot vapor to condense completely in the cold (−78 °C) receiving flask. To neutralize the acetic acid formed during the pyrolysis a small amount of solid $NaHCO_3$ was placed in the receiving flask. Once the reaction solution was added, additional anhydrous benzene (3 mL) was added in the same manner to wash the quartz-wool. The apparatus was cooled to room temperature under nitrogen. The cold receiving flask was removed and warmed to room temperature. Ether (15 mL) was added and the ether solution was filtered into a separatory funnel. The ether solution was washed with saturated aqueous NH_4Cl (15 mL), dried, filtered, and concentrated. The residue was purified by chromatography (petroleum ether) to yield 0.011 g (56%) of (+)-longifolene: $[\alpha]^{22}$ = +47.0° (*c* 1.7, $CHCl_3$), (authentic commercial sample $[\alpha]^{22}$ = +51.2°, *c* 1.9, $CHCl_3$); IR (film) 1658 (C=C) cm^{-1}; ^1H NMR (200 MHz) δ 0.88 (s, 3 H, CH_3), 0.93 (s, 3 H, CH_3), 0.98 (s, 3 H, CH_3), 1.10 (m, 1 H), 1.35–1.70 (m, 10 H), 2.04 (d, 1 H, J = 4 Hz), 2.58 (d, 1 H, J = 5 Hz, CHC=C), 4.45 (s, 1 H, HC=C), 4.71 (s, 1 H, HC=C); ^{13}C NMR δ 168.0, 99.0, 62.0, 47.7, 44.9, 43.8, 43.2, 36.2, 33.4, 30.4, 30.3, 29.9, 29.5, 25.3, 20.9; DEPT δ 99.0 (CH_2), 62.0 (CH), 47.7 (CH), 44.9 (CH), 43.2 (CH_2), 36.2 (CH_2), 30.4 (CH_3), 30.3 (CH_3), 29.9 (CH_3), 29.5 (CH_2), 25.2 (CH_2), 20.9 (CH_2); HRMS (EI) calcd for $C_{15}H_{24}$ 204.1872; found, 204.1870.

Acknowledgment. We are grateful to the University of Ottawa, Memorial University of Newfoundland (where this work was initiated and represents the Ph.D. research of B.L.) and the Natural Sciences and Engineering Research Council of Canada for financial support of this research.

Supplementary Material Available: Copies of ^1H NMR spectra for new compounds, lacking elemental analysis (14 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.