this oil contains absorptions characteristic of conjugated polyenes.

Hydrolysis of the analogue of V prepared from Er and $DC{\equiv}CC_4H_9$ (175 mg, 0.53 mmol) generates 0.21 mmol of H_2, 0.02 mmol of HD, 0.09 mmol of C_1–C_5 hydrocarbons, 0.06 mmol of 1-hexene, and 0.27 mmol of 1-hexyne. This gives 40% of the theoretical amount of hydride of which 10% is deuteride and 30% of the theoretical amount of C_6H_9.

Catalytic Hydrogenation. In a typical experiment, 0.1 mmol of the compound to be studied is dissolved in 5 mL of toluene (or THF, if the compound is insoluble in toluene) in a 70-mL tube fitted with a greaseless high-vacuum stopcock. 3-Hexyne (1 mL, 9 mmol) is added, and the system is attached to a high-vacuum line. Hydrogen (~750 torr, room temperature) is added, and the solution is magnetically stirred. Approximate hydrogenation rates are obtained by monitoring the drop in hydrogen pressure. Products are analyzed by GC. IV and V are catalytically active in this system, hydrogenating 3-hexyne to greater than 96% *cis*-3-hexene at a rate of 0.002–0.004 turnovers/min. Other products are *trans*-3-hexene, 2%, and hexane, 2%. I and II are not catalytically active under these conditions over a 2 week period.

Acknowledgment. We thank the National Science Foundation for support of this research and the Camille and Henry Dreyfus Foundation for a Teacher-Scholar Grant (to W.J.E.).

Use of Silyloxydienes in Synthesis. Total Syntheses of the Sesquiterpene (±)-Seychellene

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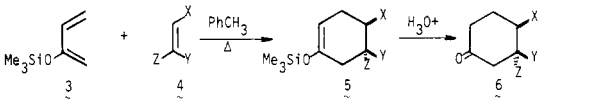
Abstract: 2-Silyloxy-1,3-dienes, e.g., **3**, can be prepared from the corresponding enones and undergo facile Diels–Alder cycloaddition with typical dienophiles. The cyclic enol silyl ethers thus produced, e.g., **5**, can be readily converted into several functionalized ketone derivatives, e.g., **7**. By starting with 2,3-dimethylcyclohex-2-enone (**12**), one can produce rapidly, via the 2-silyloxydiene **13**, bicyclo[2.2.2]octane systems in which the endo isomer **16** generally predominates over the exo isomer **17**. These bicyclo[2.2.2]octane systems permit one to prepare the structurally interesting sesquiterpene (±)-seychellene (**1**) by two general procedures. The methyl vinyl ketone adduct **16b** was converted into a 1:1 mixture of the isomeric bromo ketones **22b** and **23b** which were cyclized to norseychellanone (**2**) and epinorseychellanone (**25**). Conversion of **2** into seychellene (**1**) completed a nonstereoselective 10-step synthesis with an overall yield of 20%. Alternatively, the divinyl ketone adduct **16c** was transformed into the tricyclic dione **26** by a Lewis acid-promoted internal Michael addition in 31% yield. This dione could be converted with a high stereoselectivity (80:20) into a mixture of **2** and **25**. Completion of this route produced seychellene **1** via seven steps in an overall yield of 9%.

Introduction

(–)-Seychellene (**1**), a plant sesquiterpene isolated from patchouli oil, has been often used as a model compound on which to test new general methods of synthesis because of its interesting tricyclic structure.[2-4] Seven syntheses[5-11] have been reported since the pioneering work of Piers in 1969,[5] and several other routes to the substituted tricyclo[5.3.1.$0^{3,8}$]undecane ring system have been described.[12] From the outset of our work in this area, we envisioned a rapid synthesis of the tricyclic system involving essentially only two operations, namely, a Diels–Alder cycloaddition between a 3,4-dimethyl-2-silyloxycyclohexa-1,3-diene (i) and a vinyl ketone (ii) to produce as the major product the adduct iii which would then be converted into the tricyclic system, e.g., norseychellanone (**2**), by an intramolecular cyclization. We now report the full details of our work,[13] including a very much improved procedure for the intramolecular Lewis-acid-catalyzed Michael addition of a silyl enol ether to a vinyl ketone.

Table I. Preparation and Hydrolysis of the Diels–Alder Adducts of 3



3 4 5 6

	X	Y	Z	yield, %	hydrolysis, %
a	COMe	H	H	60	81
b	CO_2Me	H	H	35	99
c	CO_2Me	H	CO_2Me	71	95
d	CO_2Et	H	CO_2Et	77	100
e	CO_2Et	CO_2Et	H	39	*a*

[a] No yield determined.

Results and Discussion

Simple Silyloxydienes.[14] Before beginning the work on seychellene itself, we first investigated the preparation and reactions

(1) Camille and Henry Dreyfus Teacher-Scholar, 1978–83; Fellow of the Alfred P. Sloan Foundation, 1979–81.
(2) Tsubake, N.; Nishimura, K.; Hirose, Y. *Bull. Chem. Soc. Jpn.* **1967**, *40*, 597.
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(5) Piers, E.; de Wall, W.; Britton, R. W. *Chem. Commun.* **1969**, 1069; *J. Am. Chem. Soc.* **1971**, *93*, 5113.
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(8) Fráter, G. *Helv. Chim. Acta* **1974**, *57*, 172; **1979**, *62*, 1893.
(9) Jung, M. E.; McCombs, C. A. *J. Am. Chem. Soc.* **1978**, *100*, 5207.
(10) Yamada, K.; Kyotani, Y.; Manabe, S.; Suzuki, M. *Tetrahedron* **1979**, *35*, 293.
(11) Jung, M. E.; Pan, Y.-G. *Tetrahedron Lett.* **1980**, 3127.
(12) (a) Spitzner, D. *Angew. Chem. Int. Ed. Engl.* **1978**, *17*, 197; *Tetrahedron Lett.* **1978**, 3349. (b) White, K. D.; Reusch, W. *Tetrahedron* **1978**, *34*, 2439.
(13) Preliminary communications; see ref 9 and 11.
(14) (a) Preliminary communication: Jung, M. E.; McCombs, C. A. *Tetrahedron Lett.* **1976**, 2935. (b) See also: Jung, M. E.; McCombs, C. A. *Org. Synth.* **1978**, *58*, 163.

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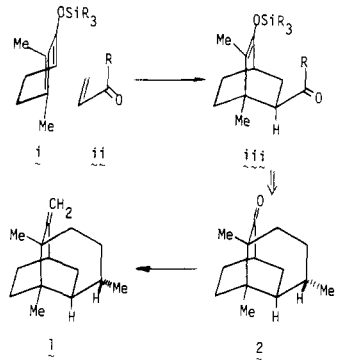
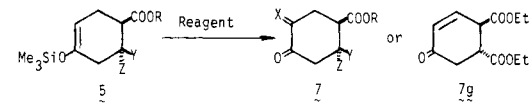


of simple silyloxydienes and their Diels–Alder adducts. This was already an area of wide interest and utility,[15,16] most prominently and elegantly shown in the work of Danishefsky.[15] One of the simplest silyloxydienes, 2-trimethylsilyloxybutadiene (**3**), had been reported in the literature twice[17,18] before we began our work. By a modification in the workup of the usual House procedure[19] for the preparation of silyl enol ethers, we obtained the diene **3** from methyl vinyl ketone in approximately 50% yield. Higher yields (60–65%) can be obtained by forming the anion with lithium diisopropylamide (LDA) in tetrahydrofuran (THF) at −78 °C followed by quenching with trimethylsilyl chloride (TMSCl). The Diels–Alder reactions of **3** with several dienophiles **4a–e** were investigated with the results shown in Table I. The diene proved to be reasonably reactive, giving fair to good yields of the cycloadducts with no serious attempts at optimization. The structures of the adduct **5a–e** were determined by normal spectroscopic techniques including analysis in most cases. They were all hydrolyzed under mild conditions to give the known cyclohexanones **6a–e** in high yields. The regioselectivity of the Diels–Alder reaction of **3** with **4b** was determined by integration of the two methyl singlets in the 100-MHz NMR spectrum to be 98%, 1,4-disubstituted vs. 2% 1,3-disubstituted. The great predominance of the 1,4 isomer over the 1,3 isomer was also indicated by vapor phase chromatography (VPC) although the precise relative amounts were not determined.

In addition, several other known reactions were carried out on the enol silyl ethers **5c,d**, namely, bromination,[20] hydroxylation,[21] aldol condensation,[22] and oxidation.[23] The results of these reactions are shown in Table II. The position of bromination and hydroxylation was determined by examination of the 100-MHz NMR of the products **7a–d**. For example, in **7b** the methine proton of the carbon bearing bromine appeared as a doublet of doublets with coupling constants of 5 and 11 Hz, thus indicating bromination at the position indicated.[24] In the crossed aldol condensation of **5a** with benzaldehyde, we obtained nearly 20% of the bis-aldol product **18** in addition to 80% of the desired aldol product **7e**. The direct oxidation of the silyl enol ether **5b** with

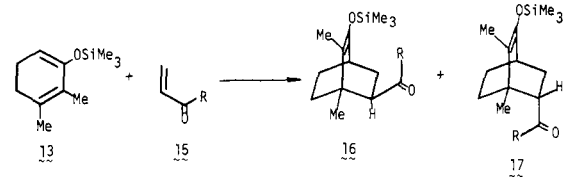
Table II. Reactions of the Adducts 5c–e



	R	Y	Z	reagent	X	yield of 7, %
a	Me	H	CO_2Me	*a*	Br, H	70
b	Et	H	CO_2Et	*b*	Br, H	46
c	Et	CO_2Et	H	*a*	Br, H	56
d	Me	H	CO_2Me	*c*	OH, H	61
e	Me	H	CO_2Me	*d*	PhCH	80
f	Et	H	CO_2Et	*d*	PhCH	65
g	Et	H	CO_2Et	*e*	**7g**	57

[a] Br_2, CCl_4, 25 °C. [b] Br_2, Et_2O, −78 °C. [c] (1) MCPBA, pentane, 0 °C; (2) ion exchange column, MeOH. [d] (1) PhCHO, $TiCl_4$, CH_2Cl_2; (2) 10% HCl or *p*-TsOH. [e] DDQ, PhH, 80 °C.

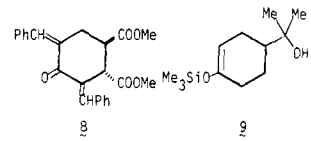
Table III. Diels–Alder Reactions of 13 with Vinyl Ketones 15



	R	conditions	yield, %	ratio 16:17
a	CH_2CH_2OEt	90 °C, 4 d	46	*b*
b	CH_3	80–90 °C, 36 h	79	3:1
c	$CH{=}CH_2$	25 °C, 4 d	94[a]	3:1
d	CH_2CH_2Cl	25 °C, 4 d	75[a]	*b*

[a] Not vigorously purified but used as is for following steps. [b] Not determined.

dichlorodicyanoquinone (DDQ) produced the enone **7g** and thus presents an alternative to the other known routes for production of cyclohexenones via Diels–Alder approaches.[25] However, we were unable to effect simple alkylation of the enolate formed from the silyl enol ether by any of the known mild methods of generation: lithium amide in ammonium,[26] benzyltrimethylammonium fluoride in THF,[27] methyllithium in ethereal solvents.[19,28] In general, only the hydrolysis products or products of incomplete alkylation were obtained. However, with the adducts **5a,b**, treatment with methyllithium afforded in fair yield, after workup with ammonium chloride, the tertiary alcohol **9** in which the silyl



enol ether remained, indicating that in this system reaction of methyllithium with a ketone or ester functionality is more rapid than attack on the trimethylsilyl group.

Synthesis of Seychellene. (i) Cycloaddition. Having demonstrated the ease of preparation and utility of silyl enol ethers, we turned our attention to their application to the synthesis of seychellene. For this purpose, we required the silyl enol ethers **13** or **14**. These were easily prepared in high yield from 2,3-dimethylcyclohexenone,[29] (**12**), itself prepared from 2-methyl-

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(16) (a) Rubottom, G. M.; Krueger, D. S. *Tetrahedron Lett.* **1977**, 611. (b) Ibuka, T.; Mori, Y.; Inubushi, Y. *Ibid.* **1976**, 3169.

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(19) House, H. O.; Gall, M.; Olmstead, H. D. *J. Org. Chem.* **1969**, *34*, 2324.

(20) Hassner, A. *J. Org. Chem.* **1974**, *39*, 1785.

(21) (a) Rubottom, G. M.; Vazquez, M. A.; Pelegrina, D. R. *Tetrahedron Lett.* **1974**, 4319. (b) Brook, A. G.; Macrae, D. M. *J. Organomet. Chem.* **1974**, *77*, C19. (c) Hassner, A.; Reuss, R. H.; Pinnick, H. W. *J. Org. Chem.* **1975**, *40*, 3427.

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(23) Jung, M. E.; Pan, Y.-G.; Rathke, M. W.; Sullivan, D. F.; Woodbury, R. P. *J. Org. Chem.* **1977**, *42*, 3961.

(24) Bromination at the opposite α carbon (via isomerization of the enol silyl ether or via the ketone) would have given a product, the NMR of which would have exhibited a doublet for the methine proton on the carbon bearing bromine.

(25) Danishefsky, S.; Kitahara, T.; Yan, C. F.; Morris, J. *J. Am. Chem. Soc.* **1979**, *101*, 6996. Danishefsky, S.; Yan, C. F.; Singh, R. K.; Gammill, R. B.; McCurry, Jr., P. M.; Fritsch, N.; Clardy, J. *Ibid.* **1979**, *101*, 7001.

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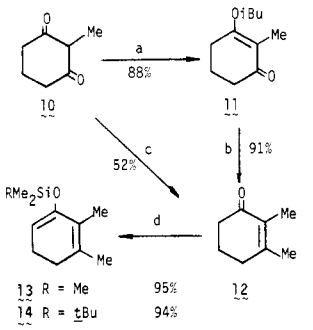
cyclohexane-1,3-dione, (**10**) by either of two methods. The enol ether **11** was prepared by the method of Eschenmoser[30] and converted into **12** by methyllithium addition and acidic hydrolysis.

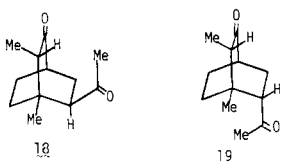


a) iBuOH, pTsOH; b) 1 eq MeLi; H_3O^+; c) 2 eq MeLi; H_3O^+; d) $LiNiPr_2$; RMe_2SiCl

It was also possible to transform **10** directly into **12** by addition of 2 equiv of methyllithium followed by acidic hydrolysis, although the yield is somewhat lower.

Several vinyl ketones dienophiles were envisioned as potentially useful for the synthesis of **1**, namely, β-ethoxyethyl vinyl ketone (**15a**), methyl vinyl ketone (**15b**), divinyl ketone (**15c**), and β-chloroethyl vinyl ketone (**15d**). Their cycloadditions with the silyloxydiene **13** are shown in Table III. Only in the case of **15b** and **15c** was the endo:exo ratio determined. In both cases, the endo isomer was the predominant one, comprising about 75% of the adduct mixture. In the case of **16b**:**17b**, the ratio could be varied somewhat by changing the temperature with higher temperatures favoring the exo isomer. There is also some evidence that the isomers interconvert on heating to above 150 °C. In all cases, we observed no evidence of regiochemical isomers.

The isomer ratio was determined by both VPC and high-field NMR combined with either chemical studies or lanthanide-induced chemical-shift studies. The products from methyl vinyl ketone, **16b**:**17b**, were shown by VPC to be a 3:1 mixture of the two isomers. That the major isomer was the endo product **16b** was indicated by the following. Mild acid hydrolysis of the product mixture **16b**:**17b** afforded dione **18** as the major product with only a small amount of dione **19** present. Base hydrolysis of **16b**:**17b** produced a mixture of **18** and **19** in which the latter predominated. It was shown independently that **18** was isomerized to **19** to a very great extent in base. These results led us to assume that **18** and

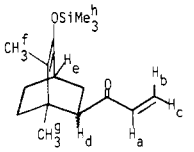


19 are the endo (syn to carbonyl) and exo (anti to carbonyl) isomers, respectively, and that the major isomer in the Diels–Alder reaction is the endo isomer **16b**. However, the correctness of this assignment was not proven until the completion of the synthesis when the synthetic product could be compared with authentic material.

The Diels–Alder adducts **16c**:**17c** from the reaction of **13** with divinyl ketone (**15c**) were formed in a 3:1 ratio, by NMR integration of the 200-MHz NMR spectrum. These isomers could be separated by chromatography on neutral alumina without extensive decomposition, the major isomer being the last eluted. The 200-MHz NMR spectra of the separated isomers are given in Table IV along with the effects of added europium shift reagent. The very substantial differences in the chemical shifts of the two methyl singlets upon addition of the europium shift reagent allows one to assign the endo stereochemistry **16c** to the major isomer. Thus, addition of the shift reagent to the major isomer affects

(30) Eschenmoser, A.; Schreiber, J.; Julia, S. A. *Helv. Chim. Acta* **1953**, *36*, 482.

Table IV. 200-MHz NMR Spectra of **16c** and **17c** and Lanthanide-Induced Chemical Shifts



proton	**16c**	$\Delta\delta^a$	$\Delta\delta^b$	**17c**	$\Delta\delta^a$	$\Delta\delta^b$
H_a	6.36	0.020	0.035	6.42	0.022	0.060
H_b	6.21	0.050	0.092	6.18	0.056	0.150
H_c	5.66	0.040	0.072	5.71	0.083	0.220
H_d	2.72	0.067	0.110	2.79	0.077	0.192
H_e	2.43	0.022	0.038	2.39	0.018	0.034
H_f	1.58	0.024	0.046	1.61	0.019	0.050
H_g	1.10	0.034	0.059	1.06	0.051	0.133
H_h	0.21	0.011	0.017	0.20	0.006	0.016

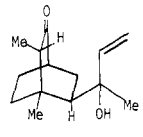
Positive (downfield) chemical shift difference upon addition of [a] 0.05 and [b] 0.5 equiv of $Eu(fod)_3$.

the chemical shifts of the two methyl singlet in a very similar manner (the quaternary methyl is shifted about 30–40% more than the olefinic methyl), as would be expected for the endo isomer (carbonyl cis to olefin), namely, isomer **16c**. However, addition of the shift reagent to the minor isomer causes the quaternary methyl to be shifted more than 2.5 times as much as the olefinic methyl, thus indicating that the carbonyl group lies closer to the quaternary methyl group; i.e., the acyl group must be exo (carbonyl trans to the olefin), namely, isomer **17c**.[31]

(ii) Formation of Tricycloundecane System via Alkylation. Several attempts were made to utilize the β-substituted ethyl ketone adducts[32] **16a,d** for the synthesis of seychellene, e.g., addition of methyllithium to the carbonyl followed by hydrolysis and internal alkylation. However, although promising in some respects, each of these routes met with failure and were not continued. The highest yielding route to seychellene proved to be via the adduct **16b**. The first task was to add two carbon atoms to the ketone of the side chain in **16b** prior to internal alkylation–cyclization. The use of the silyloxydiene in the initial Diels–Alder reaction greatly facilitated this next step since it provided directly a dione monoprotected at the desired carbonyl. However, to our surprise, all attempts at two-carbon functionalization of this ketone by means of the Wittig, Wadsworth-Emmons, or Reformatskii reactions or their variations failed, probably owing to the crowded steric environment of the carbonyl. However, we were successful in adding vinylmagnesium bromide to **16b** to furnish, after aqueous acid workup, the hydroxy ketone **20**. Oxidative rearrangement of **20** with pyridinium chlorochromate gave the enal **21a** which upon dissolving metal reduction afforded complex mixtures of products containing only minor amounts of the alcohols **22a** and **23a**. This result is somewhat surprising in view of the fact that Schmalzl[6] reported the clean and highly stereoselective reduction of a very similar acrylate derivative. With the failure of this direct dissolving metal reduction in our hands, we turned to an alternative, catalytic hydrogenation scheme. Preparation of the allylic alcohol **21e** from **20** could be accomplished by any of several methods, e.g., via the rearranged chloride **21b** or trifluoroacetate **21c**. However, an essentially quantitative yield was obtained by hydrolysis of the acetate **21d** prepared from **20** by treatment with sulfuric acid in acetic acid. Catalytic hydrogenation of the alcohol was always accompanied by hydrogenolysis to give the olefin **24** (the sole product from hydrogenation of the chloride **21b**). However, this could be controlled to a great extent by the use of benzene as the solvent (instead to more polar solvents such as ethyl acetate or ethanol) with rhodium on alumina as the catalyst (in

(31) In the foregoing discussion, we assume that the site of complexation of the shift reagent is the carbonyl group. This assumption is based on analogy to the literature and on the fact that the proton α to the carbonyl (H_d) is greatly shifted in both the endo and exo isomers.

(32) We also prepared the adduct of the *tert*-butyldimethylsilyloxydiene **14** and **15d**, but this also proved of little value for the synthesis of seychellene.



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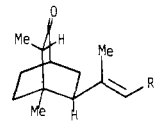
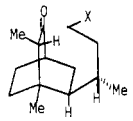
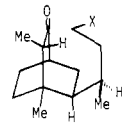


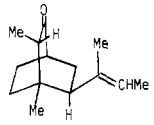
21a R = CHO
21b R = CH_2Cl
21c R = CH_2OCOCF_3
21d R = CH_2OCOCH_3
21e R = CH_2OH



22a X = OH
22b X = Br



23a X = OH
23b X = Br



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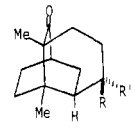
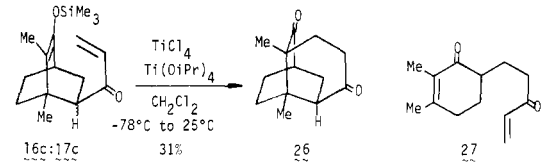


2 R = H R' = Me
25 R = Me R' = H

preference to Pd/C or PtO_2). In this manner an 80% yield of the saturated alcohols **22a**:**23a** could be obtained. However, under all conditions tried, we observed no stereoselectivity in this reaction and obtained an equimolar mixture of the two alcohols **22a** and **23a**. Separation of these isomers at this stage proved difficult and was therefore postponed until after the final ring closure. The alcohols **22a** and **23a** were converted with *N*-bromosuccinimide and triphenylphosphine into the bromides **22b** and **23b** (89%) which were not purified but rather cyclized directly into the ketones **2** and **25** with potassium triphenylmethylide in dimethoxyethane/dimethyl sulfoxide (100%). These isomeric ketones were easily and quantitatively separated by column chromatography and were clearly distinguished by their 200-MHz NMR spectra. Norseychellanone (**2**) was shown to be identical (NMR, IR, TLC) with an authentic sample.[33] The synthesis was completed by reaction of **2** with methyllithium followed by dehydration with thionyl chloride according to the procedure of Piers[5] to give **1** in quantitative yield. Although the synthesis is completely nonstereoselective with regard to the methyl group at C-4, it is fairly short and very high yielding (10 steps, 20% overall yield from 2,3-dimethylcyclohexenone).

(iii) Formation of Tricycloundecane System via Michael Addition. From the outset of this project, it was envisioned that the tricyclic dione **26** would be an extremely useful intermediate for the synthesis of **1**. It was assumed that the two carbonyl groups could be readily differentiated by virtue of their dissimilar steric environments, for example, by their reactivity toward nucleophiles. Since Piers[5] had already demonstrated the diminished reactivity of a carbonyl flanked by a quaternary and a tertiary center, as in norseychellanone (**2**), it appeared likely that the more accessible 4-ketone could be functionalized in the presence of the 11-ketone. This route was very attractive since it seemed likely that one could construct the tricyclic dione system **26** from divinyl ketone **15c** and the dione **13** by two simple operations, namely, cycloaddition followed by Michael addition. This indeed proved to be the case although the overall yields are somewhat lower.

Our initial attempts at the internal Michael addition of the mixture of isomers, **16c** and **17c**, were uniformly discouraging. Under the conditions used by Mukaiyama[21] for the intramolecular silyl enol ether–enone Michael addition, very little cyclization to **26** was observed. The major products were the retro-Michael

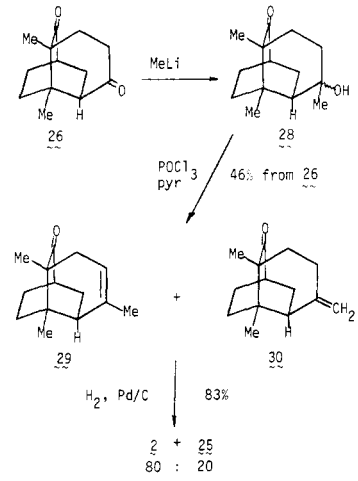


16c:17c 31% 26 27

products, 2,3-dimethyl-6-(3-keto-4-pentenyl)cyclohex-2-enone (**27**) and 2,3-dimethylcyclohexenone (**12**). Lewis acids ($TiCl_4$, $SnCl_4$, $AlCl_3$, BF_3·OEt_2, BF_3, $MgBr_2$) and protic acids (HF, HCl, CF_3CO_2H) under a wide variety of conditions (solvent, temperature, and time) gave only up to 5% of the desired dione **26**. Attempts to generate the enolate ion under basic or neutral conditions ($LiNH_2/NH_3$, Bu_4NF/THF, etc.) also gave poor results. It is clear from these experiments that this bicyclic example of an endo-6-trigonal cyclization[34] is not very favored in contrast to acyclic cases. This is no doubt due to two factors: first, the additional constraints of the bicyclic structural framework make the cyclization resemble more a "disfavored" endo-5-trigonal cyclization than the favored endo-6-trigonal cyclization; second, in only one conformation is the vinyl group of the enone properly aligned for cyclization to occur, while in many conformations the carbonyl group is aligned so that a retro-Michael reaction can take place.

However, in the process of attempting to optimize the yield of **26** in this process, we have made the interesting discovery that the use of a mixture of $TiCl_4$ and $Ti(O\text{-}i\text{-}Pr)_4$ in methylene chloride greatly increases the amount of the dione **26** formed in the reaction at the expense of the retro-Michael products **27** and **12**. The reaction takes several hours to go to completion since the mixture of $TiCl_4$ and $Ti(O\text{-}i\text{-}Pr)_4$ is a much weaker promoter for the silyl enol ether–enone cyclization. Presumably since the reaction is slower, there is more time for the enone unit to achieve the proper conformation for cyclization and the thermodynamically more favorable Michael addition ensues. Thus treatment of the 3:1 mixture of endo and exo isomers, **16c** and **17c**, with 1 mol equiv each of $TiCl_4$ and $Ti(O\text{-}i\text{-}Pr)_4$ in methylene chloride at −78 °C for 3 h, followed by stirring at −40 °C for 2 h and at 25 °C for 12 h, with subsequent workup and silica gel chromatography, afforded a 31% yield of the pure dione **26**. Since only the endo isomer **16c** is undergoing cyclization under these conditions, the yield of the cyclization process itself is over 40%. Thus the key tricyclic dione **26** is available from the diene **13** and divinyl ketone **15c** in only two steps in 29% overall yield.

The synthesis of seychellene was completed as originally planned. Reaction of the dione **26** with methyllithium at −78 °C for 8 h then at 0 °C for 2 h gave a mixture of the two isomeric keto alcohols **28**. This mixture could be isolated in 76% yield but it was found more convenient to dehydrate directly to produce an 85:15 mixture of the endo- and exocyclic olefins, **29** and **30**, respectively, in an overall yield of 46% based on the dione **26**.



26 28 46% from 26 29 30 83% 80 : 20

(33) We are very grateful to Professor E. Piers for a generous sample of (±)-norseychellanone (**2**).

(34) Baldwin, J. E., et al. *Chem. Commun.* **1976**, 734, 736; **1977**, 77, 233.

Direct hydrogenation of the mixture of olefins **29** and **30** furnished an 83% yield of an 80:20 mixture of norseychellanone (**2**) and 4-epinorseychellanone (**25**). Thus, as expected, the postponement of the olefin reduction step until after cyclization greatly improved the stereoselectivity of this hydrogenation in favor of the desired isomer **2** (from 1:1 to 4:1). Application of the Piers procedure[5] afforded (±)-seychellene (**1**) in an overall yield of nearly 9%. While this yield is somewhat lower than the first synthesis, this route is somewhat shorter (7 steps vs. 10 steps for the earlier synthesis) and provides some information on the advantages and disadvantages of the cycloaddition–internal Michael addition approach to tricyclic diones such as **26**.

Experimental Section

General. Melting points were determined on a Büchi capillary melting point apparatus and were uncorrected. Infrared spectra (IR) were recorded on a Perkin-Elmer Model 137 or Model 710B spectrophotometer as a liquid film with polystyrene as standard, in solution, or in a KBr pellet. Spectra taken in a solvent or as a KBr pellet are so labeled. Nuclear magnetic resonance spectra (NMR) were taken on a Varian Model T-60, a Varian Model HA-100, or a Bruker WP-200 spectrometer (for both ^1H and ^{13}C). Spectra taken at the higher fields are labeled 100 MHz and 200 MHz, respectively. The spectra are reported in parts per million downfield from internal tetramethylsilane (nonsilicon-containing samples). For samples containing silicon, chloroform was used as an internal standard.

Mass spectra (MS) were recorded on a Dupont Model 21-491 spectrometer. Ultraviolet spectra (UV) were recorded on a Cary Model 14 ultraviolet spectrophotometer in hexane solution. Analytical vapor phase chromatography (VPC) data were obtained on a Varian Aerograph Model 1200 (FI detector), with the columns and conditions reported in the text.

Microanalyses were performed by the analytical services department at UCLA or by Spang Microanalytical Laboratory, Eagle Harbor, Mich.

High-pressure liquid chromatography experiments were performed on a Waters Associate Prep LC/System 500. For chromatography, the following adsorbents were used: column, Merck silica gel 60 (70–230 mesh); column, Merck alumina active 90 (neutral), activity adjusted with water; preparative layer, Merck silica gel PF-254; thin layer, Merck silica gel G.

Tetrahydrofuran, benzene, and glyme were distilled from sodium and benzophenone, and trimethylsilyl chloride and dichloromethane were distilled from calcium hydride. Dimethylformamide was stored over barium oxide and distilled from calcium hydride. Methyllithium and *n*-butyllithium were purchased from Alfa-Ventron and were titrated periodically when necessary. Other solvents and reagents were purified according to literature methods.

2-Trimethylsilyloxy-1,3-butadiene (3).[14b] An oven-dried, 500-mL, three-necked, round-bottomed flask was fitted with two oven-dried addition funnels and a glass stopper, and placed in an 80–90 °C oil bath. Under an inert atmosphere, methyl vinyl ketone (25.0 g, 0.357 mol) in 25 mL of dimethylformamide (DMF) and chlorotrimethylsilane (43.4 g, 0.400 mol) in 25 mL of DMF were added over 30 min to a magnetically stirred solution of triethylamine (40.5 g, 0.400 mol) in 200 mL of DMF. The reaction gradually darkened from colorless to yellow or dark brown, and supported a white precipitate of triethylamine hydrochloride. The reaction was set up to run overnight, or approximately 14 h. The reaction was cooled to room temperature, filtered, and transferred to a 2-L separatory funnel containing 300 mL of pentane. To this solution was added 1 L of cold 5% sodium bicarbonate solution to facilitate the separation of phases and remove the DMF. The pentane layer was separated and the aqueous layer extracted twice more with 300 mL of pentane. The pentane extracts were combined, washed with 200 mL of cold distilled water, and dried over powdered anhydrous sodium sulfate. The pentane and other volatiles were removed by fractional distillation with a 2-in. steel-wool packed column in a 70 °C oil bath. Using an aspirator vacuum, 20 g (40%) of the product **3** was distilled as a colorless oil, bp 50–55 °C (50 mmHg). On a smaller scale, yields of up to 50% were obtained.

LDA Method. To a solution of lithium diisopropylamide, freshly prepared from 7.9 mL of 1.9 M methyllithium solution and diisopropylamine (1.82 g, 0.018 mol), in 25 mL of tetrahydrofuran (THF) at −78 °C, was added under a nitrogen atmosphere a solution of methyl vinyl ketone (1.05 g, 0.015 mol) in 25 mL of tetrahydrofuran over a 10-min period. After stirring an additional 10 min, the blue THF solution was quenched with chlorotrimethylsilane (1.95 g, 0.018 mol) at −78 °C with immediate precipitation of a white solid and allowed to warm to room temperature. The solution was stirred for 1.5 h and then poured into 50 mL of ether and extracted twice with concd NH_4Cl solution. The ethereal extract was dried over anhydrous sodium sulfate and evaporated in vacuo to give an oil, which was distilled to afford 1.22 g (60%) of the desired butadiene, bp 52–55 °C (50 mmHg): NMR (CCl_4) δ 6.5–4.8 (3 H, m, 12-line ABC vinylic pattern), 4.34 (2 H, bs), 0.33 (9 H, s); IR 3050, 2950, 1620, 1560, 1400, 1360, 1300, 1250, 1060, 1000, 960 920, 880, 850, 750 cm^{-1}; UV λ_{max} 233 nm (ε 6260); MS (*m/e*) 142 (M^+), 127, 85, 75 (base). High resolution mass spectroscopy (*m/e*) 142.0816, calcd for $C_7H_{14}OSi$ 142.0814; 127.0577, calcd for $C_6H_{11}OSi$ 127.0579.

1-Trimethylsilyloxy-4-acetyl-1-cyclohexene (5a). 2-Trimethylsilyloxybutadiene (**3**) (2.32 g, 0.016 mol) and methyl vinyl ketone (1.14 g, 0.16 mol) in 15 mL of toluene were heated to reflux for 45 h under a nitrogen atmosphere. Direct short-path distillation removed toluene and the dimer of methyl vinyl ketone, and afforded 1.72 g (50%) of the adduct **5a** as a colorless oil, bp 115 °C (3 mmHg): NMR (CCl_4) δ 4.74 (1 H, bt, J = 4 Hz), 2.07 (3 H, s), 2.5–1.6 (7 H, m), 0.17 (9 H, s); IR 3030, 1710, 1670, 1360, 1250, 1190, 880, 850, 750 cm^{-1}; MS (*m/e*) 212 (M^+), 197, 169 (base), 127. Anal. Calcd for $C_{11}H_{20}O_2Si$: C, 62.21; H, 9.49. Found: C, 62.32; H, 9.36.

Methyl 4-Trimethylsilyloxy-3-cyclohexenylcarboxylate (5b). 2-Trimethylsilyloxybutadiene (**3**) (4.64 g, 0.032 mol) and methyl acrylate (2.82 g, 0.032 mol) in 15 mL of toluene were heated to reflux for 45 h under a nitrogen atmosphere. Direct short-path distillation removed toluene and unreacted starting materials, and afforded 2.62 g (35%) of the adduct **5b** as a colorless oil, bp 114 °C (3 mmHg): NMR (CCl_4) δ 4.77 (1 H, bt, J = 4 Hz), 3.70 (3 H, s), 2.8–1.7 (7 H, m), 0.25 (9 H, s); NMR (100 MHz, CCl_4) δ 3.70 (3 H, s) 98%, 3.77 (3 H, s) 2% (by NMR integration); IR 3030, 1740, 1670, 1370 cm^{-1}; MS (*m/e*) 228 (M^+), 213, 199, 197, 169 (base). Anal. Calcd for $C_{11}H_{20}O_3Si$: C, 57.85; H, 8.83. Found: C, 58.05; H, 8.89.

Dimethyl *trans*-4-Trimethylsilyloxy-4-cyclohexene-1,2-dicarboxylate (5c). A mixture of 2-trimethylsilyloxy-1,3-butadiene (**3**) (4.7 g, 0.033 mol) and dimethyl fumarate (4.32 g, 0.030 mol) in 30 mL of toluene was heated to reflux for 36 h under a nitrogen atmosphere. After cooling and evaporation of toluene, the residue was distilled to remove unreacted fumarate and to afford 6.13 g (71%) of the adduct **5c** as a colorless oil, bp 115 °C (0.40 mmHg): NMR (CCl_4) δ 4.83 (1 H, m), 3.86 (6 H, s), 3.3–2.7 (2 H, m), 2.7–2.2 (4 H, m), 0.30 (9 H, s); IR 1740, 1670 cm^{-1}; MS (*m/e*): 286 (M^+), 271, 254, 226 (base). High resolution mass spectroscopy (*m/e*) 286.1250, calcd for $C_{13}H_{22}O_5Si$ 286.1236; 226.1023, calcd for $C_{11}H_{18}O_3Si$ 226.1026.

Diethyl *trans*-4-Trimethylsilyloxy-4-cyclohexene-1,2-dicarboxylate (5d). 2-Trimethylsilyloxy-1,3-butadiene (**3**) (9.35 g, 0.066 mol) and diethyl fumarate (5.67 g, 0.033 mol) were heated neat at 130–150 °C for 24 h. Direct short-path distillation afforded a trace of diethyl fumarate and 8.02 g (77%) of the adduct **5d** as a colorless oil, bp 127 °C (0.50 mmHg): NMR (CCl_4) δ 4.70 (1 H, bs), 4.07 (4 H, q, J = 7 Hz), 3.0–2.2 (6 H, m), 1.23 (6 H, t, J = 7 Hz), 0.17 (9 H, s); IR 3030, 1730, 1670 cm^{-1}; MS (*m/e*) 314 (M^+), 299, 268, 240 (base). Anal. Calcd for $C_{15}H_{26}O_5Si$: C, 57.28; H, 8.33. Found: C, 57.47; H, 8.10.

Diethyl *cis*-4-Trimethylsilyloxy-4-cyclohexene-1,2-dicarboxylate (5e). A mixture of 2-trimethylsilyloxy-1,3-butadiene (**3**) (4.64 g, 32.6 mmol) and diethyl maleate (5.63 g, 32.6 mmol) was heated neat at 120 °C for 48 h and at 160 °C for 24 h. Vacuum distillation removed unreacted maleate and afforded 3.97 g (39%) of the adduct **5e**, bp 130 °C (3–4 mmHg): NMR (CCl_4) δ 4.83 (1 H, m), 4.20 (4 H, bq, J = 7 Hz), 3.2–2.0 (6 H, m), 1.33 (6 H, t, J = 7 Hz), 0.20 (9 H, s); IR 1740–1700 (br), 1670 cm^{-1}; MS (*m/e*) 314 (M^+), 299, 264, 240, 167 (base). High resolution mass spectroscopy (*m/e*) 314.1554, calcd for $C_{15}H_{26}O_5Si$ 314.1550; 241.1257, calcd for $C_{12}H_{21}O_3Si$ 241.1260.

4-Acetylcyclohexanone (6a). 1-Trimethylsilyloxy-4-acetyl-1-cyclohexene (**5a**) (0.79 g, 3.7 mmol) was stirred overnight at room temperature with 5 mg of potassium carbonate in 10 mL of methanol. After all the volatile components were removed, the residue was passed through silica gel (20 g) with ether. Evaporation of the ether eluant provided 0.42 g (81%) of the diketone **6a** as a pale yellow oil:[35] NMR (CCl_4) δ 2.08 (3 H, s), 2.8–1.5 (9 H, m); IR 1710 cm^{-1}.

Methyl 4-Cyclohexanonecarboxylate (6b). The silyl enol ether **5b** (0.50 g, 2.2 mmol) was stirred in 10 mL of methanol for 2 h. After evaporation of the volatile components, 0.25 g (99%) of the keto ester **6b** remained as a near-colorless oil:[36] NMR (CCl_4) δ 3.67 (3 H, s), 3.0–1.8 (9 H, m); IR 1740, 1710 cm^{-1}.

Dimethyl *trans*-1,2-Cyclohexan-4-onedicarboxylate (6c). The adduct **5c** (0.67 g, 24 mmol) was dissolved in 20 mL of methanol containing 3 drops of trifluoroacetic acid at room temperature. After 2 h, the hy-

(35) Vig, O. P.; Matta, K. L.; Singh, G.; Raj, I. *J. Indian Chem. Soc.* **1965**, *42*, 581.

(36) (a) House, H. O.; Babad, H.; Toothill, R. B.; Noltes, A. W. *J. Org. Chem.* **1962**, *27*, 4141. (b) Siegel, S.; Komarmy, J. M. *J. Am. Chem. Soc.* **1960**, *82*, 2547.

drolysis was complete as shown by VPC (6 ft × $^1/_8$ in., 10% SE-30 on Chromosorb W, 120 °C) and probably required much less time. In addition, it was observed that neutral methanol hydrolyzes the adduct completely after 24 h at 25 °C (VPC monitoring). After evaporation of the volatiles and distillation of the residual oil, the colorless ketone **6c** crystallized into prisms, mp 61–63 °C, (lit.[37] mp 34–35 °C); NMR (CCl_4) δ 3.73 (3 H, s), 3.72 (3 H, s), 3.4–2.8 (2 H, m), 2.8–2.0 (6 H, m); IR 1730, 1710, 1440 cm^{-1}.

Diethyl *trans*-1,2-Cyclohexan-4-onedicarboxylate (6d). The silyl enol ether **5d** (1.0 g, 3.2 mmol) was stirred for 2 h at room temperature in absolute ethanol containing 10 mg of potassium carbonate. After removing all the volatile components, the residue was eluted through a small amount (5 cm) of silica gel using ether. Evaporation of the eluant provided 0.50 g (65%) as a light yellow oil. With methanol as solvent, the reaction time was reduced, but these conditions also caused complete transesterification. Hydrolysis also occurred using potassium fluoride dihydrate and 18-crown-6 in tetrahydrofuran and gave 0.77 g (100%) of **6d** in 5 h at 25 °C: NMR (CCl_4) δ 4.14 (4 H, 2 q, J = 7 Hz), 3.8–1.7 (8 H, m), 1.33 (6 H, 2 t, J = 7 Hz); IR 1750–1710 cm^{-1} (br); MS (m/e) 242, 197, 196, 169, 168 (base). High resolution mass spectroscopy (m/e) 242.1151, calcd for $C_{12}H_{18}O_5$ 242.1155; 168.0781, calcd for $C_9H_{12}O_3$ 168.0786.

Diethyl *cis*-1,2-Cyclohexan-4-onedicarboxylate (6e). No formal hydrolysis of the silyl enol ether **5e** was ever performed. However, hydrolysis occurred from aqueous acid workup of attempted alkylation reactions. Distillation of the residue from an aqueous workup (Kugelrohr) provided a colorless oil **6e** [oven temp 130 °C (0.2 mmHg)]; lit.[38] bp 96 °C (0.05); NMR (CCl_4) δ 4.17 (2 H, q, J = 8 Hz), 4.14 (2 H, q, J = 8 Hz), 3.3–1.5 (8 H, m), 1.11 (3 H, t, J = 8 Hz), 1.08 (3 H, t, J = 8 Hz); IR 1740–1700 cm^{-1} (br).

Dimethyl 1,2-*trans*-5-Bromocyclohexan-4-one-1,2-dicarboxylate (7a). Bromine (0.28 g, 1.8 mmol) in 10 mL of carbon tetrachloride was added dropwise slowly to a solution of the silyl enol ether **5a** (0.50 g, 1.8 mmol) in 30 mL of carbon tetrachloride at room temperature under a nitrogen atmosphere. After stirring an additional 30 min and evaporation of the solvent, the residual yellow oil was distilled (Kugelrohr) to afford 0.390 g (70%) of a colorless oil [oven temp 115 °C (0.3–0.5 mmHg)] which partially crystallized: NMR (100 MHz, CCl_4) δ 4.6–4.2 (1 H, m), 3.7 (6 H, s), 3.4–2.0 (6 H, m); IR 1740–1700 cm^{-1} (br).

Diethyl 1,2-*trans*-5-Bromocyclohexan-4-one-1,2-dicarboxylate (7b). Bromine (0.25 g, 1.6 mmol) in 5 mL of ether was added dropwise over 15 min to the silyl enol ether **5b** (0.50 g, 1.6 mmol) in 20 mL of ether cooled to −78 °C under a nitrogen atmosphere. (The reaction could also be performed in carbon tetrachloride with stirring at 0 °C). The yellow solution was stirred for 1 h and warmed to room temperature. After evaporation of the volatile components, the brown residue solidified. After two recrystallizations by addition of water to hot absolute ethanol, 0.233 g (46%) of the white crystalline product **7b** was obtained, mp 110–112 °C: NMR (CCl_4) δ 4.63 (1 H, dd, J = 11, 5 Hz), 4.19 (4 H, 2 q, J = 7 Hz), 3.4–1.8 (6 H, m), 1.36 (3 H, t, J = 7 Hz), 1.33 (3 H, t, J = 7 Hz); IR (KBr) 1750–1710 cm^{-1} (br); MS (m/e) 320 (M^+), 291, 275, 246, 241, 214, 140 (base).

Diethyl 1,2-*cis*-5-Bromocyclohexan-4-one-1,2-dicarboxylate (7c). Bromine (0.25 g, 1.6 mmol) in 10 mL of carbon tetrachloride was added dropwise slowly to a carbon tetrachloride solution of the silyl ether **5c** (0.50 g, 1.6 mmol) in order to maintain a colorless solution at room temperature. After addition (45 min), the reaction was stirred for 3 h to ensure complete bromination. After treatment with solid sodium sulfite to remove excess bromine, filtration, and evaporation of the solvent, a yellow oil was obtained. Distillation (Kugelrohr) gave 0.29 g (56%) of the product **7c** as a colorless oil [oven temp 120 °C (0.6 mmHg)]: NMR (CCl_4) δ 4.40 (1 H, dd, J = 5, 3.5 Hz), 4.22 (4 H, 2 q, J = 7 Hz), 3.6–2.0 (7 H, m), 1.38 (3 H, t, J = 7 Hz), 1.33 (3 H, t, J = 7 Hz); IR 1740–1700 cm^{-1} (br).

Dimethyl 1,2-*trans*-5-Hydroxycyclohexan-4-one-1,2-dicarboxylate (7d). To a stirring solution of 85% *m*-chloroperbenzoic acid (0.355 g, 1.8 mmol) in 50 mL of pentane at 0 °C was added a solution of the adduct **5a** (0.50 g, 1.8 mmol) in 25 mL of pentane over 25 min. After stirring for an additional 1 h, the *m*-chlorobenzoic acid was filtered away, the pentane evaporated, and the residue dissolved in 50 mL of methanol. A basic anion-exchange resin in methanol was prepared by treating the chloride form of the resin (Dowex, Ag-1-X8) with NaOH solution (two elutions), rinsing with distilled water (until neutral by litmus), and finally leaching the resin with 200 mL of methanol. The methanol solution of the reaction mixture was eluted through the prepared resin followed by an additional 25 mL of methanol. After evaporation of methanol, the eluent showed complete removal of *m*-chlorobenzoic acid and complete silyl ether hydrolysis. The residual oil was purified by distillation (Kugelrohr) to give 0.246 g (61%) of hydroxy ketone **7d** [oven temp 110 °C (0.7 mmHg)] which crystallized on cooling, mp 117–119 °C: NMR ($CDCl_3$) δ 4.20 (1 H, dd, J = 13, 6 Hz), 3.78 (1 H, s), 3.67 (6 H, s), 3.5–1.6 (6 H, m); IR 3400 (sharp), 3300 (br), 1730–1700 cm^{-1} (br); MS (m/e) 230 (M^+), 198, 154, 126 (base).

Dimethyl 1,2-*trans*-5-Benzylidenecyclohexan-4-one-1,2-dicarboxylate (7e). To a solution of silyl enol ether **5a** (0.50 g, 1.8 mmol) and benzaldehyde (0.36 g, 3.6 mmol) in 30 mL of methylene chloride at room temperature under a nitrogen atmosphere was added titanium tetrachloride (1.00 g, 5.3 mmol). The mixture was then reflux for 1 h, cooled, poured into ether, and extracted with water. The ethereal extract was separated, dried over anhydrous sodium sulfate, and evaporated to give an oil which appeared to be the simple aldol: NMR (CCl_4) δ 5.5 (1 H, m), 5.0–4.0 (1 H, m), 3.70 (6 H, s), 3.4–1.4 (7 H, m); IR 3400, 2950, 1740–1680 (br), 1460, 1250–1150 cm^{-1} (br).

When the reaction was poured into 10% HCl solution, dehydration occurred to give two new products which were separated by dry column chromatography (25 g silica gel) eluting with 5% ethyl acetate in benzene.

Band A (R_f 0.4) provided 0.14 g (20%) of the bis(benzylidene)cyclohexanone **8**: NMR (CCl_4) δ 8.0–7.4 (2 H, m), 7.30 (10 H, bs), 6.10 (1 H, m), 3.67 (3 H, s), 3.42 (3 H, s), 3.8–2.8 (3 H, m); IR 3030, 1740–1680 (br), 1600, 1440, 700 cm^{-1}; MS (m/e) 390 (M^+), 331, 302, 271, 242, 215.

Band B (R_f 0.3) provided 0.42 g (80%) of the benzylidenecyclohexanone **7e**: NMR (CCl_4) δ 7.5–7.1 (6 H, m), 3.67 (3 H, s), 3.64 (3 H, s) 3.6–2.8 (6 H, m); IR 3030, 1750–1680 (br), 1600, 1440, 690 cm^{-1}; MS (m/e) 302 (M^+), 288, 271, 242, 210, 183 (base).

Diethyl 1,2-*trans*-5-Benzylidenecyclohexan-4-one-1,2-dicarboxylate (7f). The silyl enol ether **5b** (0.92 g, 2.9 mmol) in 15 mL of dry methylene chloride was added over 30 min to a red solution of benzaldehyde (0.31 g, 2.9 mmol) and titanium tetrachloride (0.55 g, 2.9 mmol) in 30 mL of methylene chloride at −78 °C. After the resulting yellow suspension was stirred for 30 min. 50 mL of 5% sodium bicarbonate solution was added at −78 °C and the mixture warmed to room temperature. The methylene chloride layer was separated, and the aqueous layer was extracted with 3 × 30 mL of ether. The methylene chloride extract and ether washings were combined, dried over sodium sulfate, and evaporated to afford a yellow oil of the aldol product (IR 3400 cm^{-1}), still containing some benzaldehyde. The aldol was dehydrated using *p*-toluenesulfonic acid in refluxing benzene, and subsequently washed with aqueous potassium carbonate. The oil remaining after evaporation of the benzene was purified by chromatography on silica gel eluting with ether. A homogeneous yellow band was eluted to afford 0.62 g (65%) of the product **7f**: NMR (CCl_4) δ 7.50 (1 H, bs), 7.40 (2 H, m), 7.32 (3 H, bs), 4.06 (4 H, bq, J = 7 Hz), 3.4–1.8 (6 H, m), 1.25 (6 H, bt, J = 7 Hz); IR 3030, 1740–1680, 1600, 860, 750, 700 cm^{-1}.

Diethyl *trans*-3-Cyclohexen-5-one-1,2-dicarboxylate (7g). 2,3-Dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (0.40 g, 1.8 mmol) in 40 mL of benzene was added to a refluxing solution of the diethyl fumarate adduct **5b** in 50 mL of benzene over 30 min, and stirred overnight. The benzene solution was cooled and washed several times with distilled water. The combined aqueous layers were further extracted with ether. The benzene and ethereal extracts were combined and evaporated to give 0.239 g (57%) of a slightly yellow oil, **7g**: NMR (CCl_4) δ 7.7–6.6 (2 H, m), 4.20 (2 H, q, J = 7 Hz), 4.08 (2 H, q, J = 7 Hz), 3.4–1.6 (4 H, m), 1.33 (3 H, t, J = 7 Hz), 1.23 (3 H, t, J = 7 Hz); IR 3030, 2900, 1740–1680 (br), 880, 850, 800–750 (br), 710 cm^{-1}; MS (m/e) 240 (M^+), 214, 213, 212, 196, 168 (base).

4-(1-Hydroxy-1-methylethyl)-1-trimethylsilyloxy-1-cyclohexene (9). From 5a. An ethereal methyllithium solution (1.75 mL of 1.9 M, 3.3 mmol) was added via syringe to a stirred ethereal solution of the adduct **5a** (0.71 g, 3.3 mmol) under a nitrogen atmosphere at −78 °C. The solution immediately turned to yellow and was stirred for 2 h. The reaction mixture was transferred to a separatory funnel and extracted with concd NH_4Cl solution. The ether layer and two additional ether extracts were combined, dried over anhydrous sodium sulfate, and evaporated in vacuo to give 0.68 g of a yellow oil. The oil was distilled (Kugelrohr) but only afforded 0.36 g (47%) of the pure tertiary alcohol **9** [oven temp, 80 °C (0.4–0.7 mmHg)].

From 5b. An ethereal methyllithium solution (1.5 mL of 1.9 M, 2.8 mmol) was added via syringe to a stirred ethereal solution of the adduct **5b** (0.638 g, 2.8 mmol) under a nitrogen atmosphere at −78 °C. After 10 min at −78 °C, methyl iodide (0.60 g, 4.2 mmol) was added in an alkylation attempt. The solution was warmed to room temperature and stirred overnight. After a workup analogous to that described above, 0.40 g of an oil was obtained which was a mixture of starting material and product **9** in a ratio of 73/27 by NMR integration (36% yield): NMR

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(38) McQuillin, F. J.; Ord, W. D.; Simpson, P. L. *J. Chem. Soc., Suppl. No. 1* **1964**, 5526.

(CCl_4) δ 4.80 (1 H, m), 2.18 (1 H, s), 2.3–1.2 (7 H, m), 1.22 (6 H, bs), 0.25 (9 H, s); IR 3400, 2900, 1660, 1600, 1250, 1190, 880, 850 cm^{-1}.

3-Isobutyloxy-2-methyl-2-cyclohexen-1-one (11). The enol ether **11** was prepared by a procedure of Eschenmoser.[30] 2-Methyl-1,3-cyclohexanedione (**10**)[39] (7.1 g, 0.056 mol) was refluxed overnight in 100 mL of benzene containing isobutyl alcohol (15.1 g, 0.20 mol) and 0.25 g of toluenesulfonic acid (hydrate) with azeotropic removal of water (Dean–Stark trap). The benzene solution was cooled to room temperature and extracted with a 5% sodium bicarbonate solution. The aqueous layer was further extracted with 50 mL of ether. The benzene and ether extracts were combined and evaporated to afford 9.65 g (88%) of the isobutyl enol ether **11** after distillation, bp 82 °C (0.06 mmHg). Using 20 g of the dione, 30.2 g of isobutyl alcohol, and 0.50 g of toluenesulfonic acid in refluxing benzene with removal of water, 26.1 g (83%) of the isobutyl enol ether was obtained: NMR (CCl_4) δ 3.67 (2 H, d, J = 6 Hz), 2.6–1.7 (6 H, m), 1.58 (3 H, t, J = 2 Hz), 0.93 (6 H, d, J = 6 Hz); IR 1610, 1360, 1340, 1090 cm^{-1}.

2,3-Dimethyl-2-cyclohexenone (12). The enol ether **11** in 25 mL of ether was added to an ice-cooled solution of methyllithium (48.5 mL of 1.8 M, 0.087 mol) in 80 mL of additional ether over 45 min and stirred for an additional 1.5 h. The reaction mixture was quenched carefully with distilled water, acidified to pH 1 with dilute sulfuric acid, and stirred for 30 min. The two phases were separated and the aqueous layer was extracted with 3 × 30 mL ether. The ether extracts were combined and evaporated to give a yellow oil, which afforded 8.29 g (91%) of the pure cyclohexenone **12** as a colorless oil, bp 76 °C (15 mmHg) [lit.[29a] bp 65 °C (10 mm)].

Alternative Procedure. To a suspension of dione **10** (2.5 g, 2 mmol) in 20 mL of anhydrous ether stirred at 0 °C, 27 mL of methyllithium (1.6 M, 4.4 mmol) was added dropwise. After stirring for 3 h, the solution became clear. The solution was neutralized by the careful addition of cold dilute sulfuric acid. The solution was extracted with 3 × 20 mL of ether, and the organic layer washed with sodium bicarbonate, water, and brine. The organic layer was dried over anhydrous sodium sulfate and evaporated to give a liquid which upon distillation at 45 °C (0.12 mmHg) afforded 1.3 g (52%) of the enone **12**: NMR ($CDCl_3$) δ 2.53–2.11 (6 H, m), 1.91 (3 H, bs), 1.69 (3 H, bs); IR 2900, 1670, 1650, 1380 cm^{-1}.

1,2-Dimethyl-3-trimethylsilyloxy-1,3-cyclohexadiene (13). To a freshly prepared solution of lithium diisopropylamide prepared from diisopropylamine (3.18 g, 0.031 mol) and *n*-butyllithium (0.029 mol) in 30 mL of tetrahydrofuran at 0 °C, was added 2,3-dimethyl-2-cyclohexenone **12** (3.00 g, 0.024 mol) in 30 mL of dry ether. The yellow solution was stirred for 15–30 min and quenched by a fast addition of neat chlorotrimethylsilane (3.94 g, 0.036 mol), with stirring for an additional 1.5 h. The reaction mixture was poured into 50 mL of ether and extracted with dilute $NaHCO_3$ solution. The aqueous layer was separated and further extracted twice with 30 mL of ether. The ether extracts and washings were combined, dried over powdered sodium sulfate, and evaporated. The resulting yellow oil was distilled (Kugelrohr) to give 5.00 g (95%) of the product **13** as a colorless oil [oven temp 60 °C (0.3 mmHg)]; NMR (CCl_4) δ 4.67 (1 H, bs); 2.02 (2 H, bs), 1.99 (2 H, bs), 1.77 (3 H, bs), 1.60 (3 H, bs), 0.17 (9 H, s); IR 3000, 2900, 1640, 1580, 1335, 1240, 1210, 1080, 910, 850, 750 cm^{-1}.

1,2-Dimethyl-3-*tert*-butyldimethylsilyloxy-1,3-cyclohexadiene (14). Lithium diisopropylamide (LDA) was prepared by the reaction of diisopropylamine (9.4 mL, 67 mmol) and *n*-butyllithium (25 mL, 62 mmol) in 100 mL of THF at −78 °C for 30 min. To this pale yellow LDA solution was added dropwise 2,3-dimethylcyclohexenone (**12**) (6.4 g, 52 mmol) in 10 mL of THF at −78 °C. The yellow solution was stirred for 30 min, and then *tert*-butyldimethylchlorosilane (11.7 g, 78 mmol) in 10 mL of THF was added in one portion. The mixture was allowed to warm up to room temperature, then refluxed at 70 °C for 6 h. The cooled solution was poured into a cold saturated sodium bicarbonate solution and extracted with 2 × 50 mL of pentane. The combined organic layers were washed with water and brine, then dried over anhydrous sodium sulfate. The solvent was rotary evaporated and the resulting pale yellow oil was distilled at 90 °C under 0.07 mmHg to give 11.6 g (94%) of **14**: NMR ($CDCl_3$) δ 4.71 (1 H, bs), 2.04–1.90 (4 H, bs), 1.73–1.53 (6 H, bs), 0.92 (9 H, s), 0.06 (6 H, s); IR 2900, 1650, 1600, 1090 cm^{-1}; MS (m/e) 238 (M^+), 181, 179, 124.

1-Ethoxy-4-penten-3-one (15a). The method of Arbuzov[40] was used to prepare this enone. Aluminum chloride (28.0 g, 0.21 mol) was added to an ice-cooled solution of 3-ethoxypropionyl chloride (14.43 g, 0.10 mol) in 80 mL of dichloroethane (distilled from calcium hydride) over a 1-h period to maintain a temperature of 5 °C with vigorous magnetic stirring. The resulting yellow solution was charged with ethylene gas via syringe needle for 6.5 h and stirred overnight without gas flow at room temperature. The reaction mixture was slowly added to cold water to hydrate the aluminum salts, ether was added, and the phases were separated. The aqueous layer was further extracted with 4 × 100 mL of ether. The combined ether extracts were dried over anhydrous sodium sulfate and evaporated to afford 20.56 g (88%) of a brown residue consistent with β-ethoxyethyl β-chloroethyl ketone. This chloro ketone could be purified to a colorless oil by distillation, but only in a 40% yield due to decomposition, bp 70 °C (20 mmHg): NMR (CCl_4) δ 3.7–3.4 (4 H, m), 3.37 (2 H, q, J = 7 Hz), 2.80 (2 H, t, J = 6 Hz), 2.52 (2 H, t, J = 6 Hz), 1.07 (3 H, t, J = 7 Hz); IR 2950, 1700, 1400, 1100 cm^{-1}.

The vinyl ketone **15a** was usually prepared from the crude chloro ketone. A typical procedure is as follows: 3-ethoxypropionyl chloride (19.52 g, 0.14 mol) was treated with aluminum chloride (38.0 g, 0.28 mol) and ethylene gas as previously described. The crude chloro ketone was mixed with potassium acetate (14.0 g, 0.14 mol) in 100 mL of absolute ethanol and heated in an 80 °C oil bath for 20 min. The reaction mixture was cooled to room temperature, and the potassium chloride was filtered away. The ethanol was evaporated with gentle warming and 100 mL of distilled water was added. The aqueous solution was neutralized with sodium bicarbonate until carbon dioxide formation ended and extracted with 3 × 50 mL of chloroform. The chloroform extracts were combined and dried over anhydrous sodium sulfate. The volatile components were removed by evaporation, and distillation of the residual oil afforded 8.36 g (46% overall, two steps) of **15a**, bp 48–50 °C (50 mmHg): NMR (CCl_4) δ 6.4–5.6 (3 H, m 8-line ABC pattern), 3.64 (2 H, t, J = 6 Hz), 3.42 (2 H, q, J = 7 Hz), 2.74 (2 H, t, J = 6 Hz), 1.13 (3 H, t, J = 7 Hz); IR 1700–1680 (br), 1620, 1370, 920, 830 cm^{-1}.

Divinyl Ketone (15c). Distillation of 1,5-dichloro-3-pentanone[41] (1.5 g, 10 mmol) from quinoline (3 g, 23 mmol) at 150 °C under water aspirator pressure afforded 0.84 g (100%) of **15c** as a pale yellow liquid [lit.[41b] bp 30 °C (16 mmHg)]; NMR ($CDCl_3$) δ 6.6–5.63 (6 H, vinyl m); IR 1670, 1610, 1410, 1100, 860 cm^{-1}; MS (m/e) 82 (M^+), 55, 54, 44, 40.

1,2-Dimethyl-3-trimethylsilyloxybicyclo[2.2.2]oct-2-en-6-yl 2-Ethoxyethyl Ketone (16a:17a). The diene **13** (5.38 g, 0.027 mol) and 2-ethoxyethyl vinyl ketone (**15a**) (3.50 g, 0.027 mol) were heated together with hydroquinone in a sealed glass tube at 90 °C for 4 days. The contents were distilled (Kugelrohr) to give 4.04 g (46%) of the product **16a:17a** as a colorless oil [oven temp 110 °C (0.4 mm Hg)] after a small forerun of residual volatiles: NMR (CCl_4) δ 3.48 (2 H, bt, J = 6 Hz), 3.34 (2 H, bq, J = 8 Hz), 2.40 (2 H, t, J = 6 Hz), 2.3–2.0 (2 H, m), 1.92–0.83 (6 H, m), 1.48 (3 H, s), 1.07 (3 H, s), 1.05 (3 H, t, J = 8 Hz), 0.12 (9 H, s); IR 2900, 2830, 1700, 1660, 1245, 1195, 1110, 840 cm^{-1}; MS (m/e) 324 (M^+), 278, 254, 239, 196 (base).

1,2-Dimethyl-3-trimethylsilyloxybicyclo[2.2.2]oct-2-en-6-yl Methyl Ketone (16b). The diene **13** (4.42 g, 0.022 mol) and methyl vinyl ketone (**15b**) (3.90 g, 0.056 mol) were placed in a sealed glass tube with hydroquinone and heated in an 80–90 °C oil bath for 36 h. The contents were transferred to a flask in a Kugelrohr oven from which a forerun of methyl vinyl ketone dimer was removed [oven temp 80 °C (0.7 mmHg)]. Subsequently, 4.66 g (79%) of product **16b** was obtained as a colorless oil [oven temp 80 °C (0.20 mmHg)]: NMR (200 MHz, CCl_4) δ 2.6–1.0 (8 H, m), 1.90 (3 H, s), 1.50 (3 H, s), 1.07 (3 H, s), 0.13 (9 H, s) (the NMR spectrum showed very weak absorptions for the corresponding exo isomers); IR 2950, 1700, 1670, 1240, 840 cm^{-1}; MS (m/e) 266 (M^+), 251, 236, 196 (base).

1,2-Dimethyl-3-trimethylsilyloxybicyclo[2.2.2]oct-2-en-6-yl Vinyl Ketone (16c:17c). The diene **13** (9.3 g, 48 mmol) and divinyl ketone **15c** (3.9 g, 48 mmol) were stirred at room temperature for 4 h. The volatile components [mostly 2,3-dimethylcyclohexenone (**12**) and divinyl ketone (**15c**)] were separated by Kugelrohr distillation. The pale yellow residue weighed 12.4 g (94%) and could be used for the next step synthesis without further purification.

For determination of the stereochemistry of the adducts, the mixture was separated by rapid column chromatography on neutral alumina, eluting with 1:1 hexane/benzene. The minor isomer, **17c**, eluted first (R_f 0.8), with the major isomer, **16c**, eluting last (R_f 0.7).

16c: NMR (200 MHz, $CDCl_3$) δ 6.36 (1 H, dd, J = 17.3, 10.0 Hz), 6.21 (1 H, dd, J = 17.3, 2.0 Hz), 5.66 (1 H, dd, J = 10.0, 2.0 Hz), 2.72 (1 H, dd, J = 9.8, 6.1 Hz), 2.43 (1 H, bt), 2.2–1.3 (6 H, m), 1.58 (3 H, s), 1.10 (3 H, s), 0.21 (9 H, s).

17c: NMR (200 MHz, $CDCl_3$) δ 6.42 (1 H, dd, J = 17.3, 10.3 Hz), 6.18 (1 H, dd, J = 17.3, 1.7 Hz), 5.71 (1 H, dd, J = 10.3, 1.7 Hz), 2.79 (1 H, ddd, J = 9.3, 7.3, 1.8 Hz), 2.39 (1 H, bt, J = 2.7 Hz), 2.2–1.3 (6

(39) 2-Methyl-1,3-cyclohexanedione was prepared from resorcinol. See Newman, M. S.; Mekler, A. B. *J. Am. Chem. Soc.* **1960**, *82*, 4039.

(40) Arbuzov, Y. A.; Klimov, E. M.; Korolev, A. M. *Zh. Obshch. Khim.* **1962**, *32*, 3674, 3681.

(41) (a) Baddeley, G.; Taylor, H. T.; Pickels, W. *J. Chem. Soc.* **1953**, 124. (b) Jones, N.; Taylor, H. T. *Ibid.* **1961**, 1345.

H, m), 1.61 (3 H, s), 1.06 (3 H, s), 0.20 (9 H, s). For effect of added $Eu(fod)_3$ on the NMR spectra, see text. **Mixture**: IR 2900, 1610, 1400, 1220, 1000 cm^{-1}; MS (*m/e*) 278 (M^+), 206, 196 (base). High resolution mass spectroscopy (*m/e*) 266.1700, calcd for $C_{15}H_{26}O_2Si$ 266.1702; 196.1288, calcd for $C_{11}H_{20}OSi$ 196.1284.

1,2-Dimethyl-3-trimethylsilyloxybicyclo[2.2.2]oct-2-en-6-yl 2-Chloroethyl Ketone (16d:17d). The diene **13** (1.4 g, 7.0 mmol) and vinyl ketone **15d**[42] (0.75 g, 6.3 mmol) were stirred at room temperature for 4 days. The volatile components were separated by Kugelrohr distillation to give the pale yellow liquid **16d:17d** (1.5 g, 75%): NMR ($CDCl_3$) δ 3.64 (2 H, t, J = 6 Hz); 2.80 (2 H, t, J = 6 Hz), 2.51–1.67 (8 H, m), 1.51 (3 H, s), 1.02 (3 H, s), 0.06 (9 H, s); IR 3000, 1720, 1650, 1100 cm^{-1}; MS (*m/e*) 314 (M^+), 286, 278, 195.

***endo*-6-Acetyl-1,2-dimethylbicyclo[2.2.2]octan-3-one (18).** The methyl vinyl ketone adduct **16b:17b** (50 mg) was treated with HCl (2% solution), stirred for 10 min, and extracted with 3 × 30 mL of ether. The ether extracts were combined, dried over anhydrous sodium sulfate, and evaporated to give a light yellow oil of the hydrolyzed endo adduct **18**: NMR (CCl_4) δ 2.12 (3 H, s), 2.8–1.1 (9 H, m), 1.11 (3 H, s), 1.00 (3 H, d, J = 7 Hz); IR 2900, 1710, 1450, 1360 cm^{-1}.

***exo*-6-Acetyl-1,2-dimethylbicyclo[2.2.2]octan-3-one (19).** The hydrolyzed endo adduct **18** was mixed with aqueous sodium carbonate; methanol was added until the solution was homogeneous. The mixture was stirred for 30 min and then evaporated in vacuo to remove methanol, and was extracted with 3 × 30 mL of ether. The ether extracts were combined, dried over anhydrous sodium sulfate, and evaporated to afford the hydrolyzed exo adduct **19** as a yellow oil. This compound was also produced by direct treatment of **16b:17b** with aqueous methanolic sodium carbonate for 30 min followed by normal workup (in this case a mixture of **18** and **19** as produced, with **19** greatly predominating): NMR (CCl_4) δ 2.12 (3 H, s), 2.8–1.2 (9 H, m), 0.97 (3 H, d, J = 6 Hz), 0.95 (3 H, s); IR 2900, 1710, 1450, 1360 cm^{-1}; MS (*m/e*) 194 (M^+), 139, 136, 124 (base). High resolution mass spectroscopy (*m/e*) 194.1317, calcd for $C_{12}H_{18}O_2$ 194.1307; 124.0884, calcd for $C_8H_{12}O$ 124.0888.

6-(3-Hydroxy-1-buten-3-yl)-1,2-dimethylbicyclo[2.2.2]octan-3-one (20). The adduct **16b** (3.33 g, 0.125 mol) in 20 mL of tetrahydrofuran solution was added dropwise slowly to a solution of vinylmagnesium bromide prepared from magnesium metal (0.82 g, 0.34 mol) and freshly prepared vinyl bromide in 50 mL of tetrahydrofuran at 0 °C. The reaction mixture was stirred for 2 h, then slowly quenched with water, and acidified to pH 1 with dilute HCl solution. After stirring for an additional 30 min, the two-phase solution was poured into 50 mL of ether and the phases were separated. The aqueous layer was extracted twice more with 25 mL of ether. The ether extracts were combined, dried over anhydrous sodium sulfate, and evaporated to leave a yellow oil of product and hydrolyzed starting material. The hydrolyzed starting material (0.51 g) could be separated by elution through silica gel (60 g) using benzene/10% ethyl acetate and 2.02 g (73%) of the vinyl alcohol **20** could be obtained: NMR (CCl_4) δ 6.4–4.9 (3 H, 12-line vinyl pattern), 2.8–1.4 (10 H, m), 1.27 (3 H, s), 1.03 (3 H, s), 0.96 (3 H, d, J = 7 Hz); IR 3400, 3010, 2900, 1700, 1660, 1450, 1000, 910 cm^{-1}; MS (*m/e*) 204 ($M^+ - 18$), 152, 123 (base). High resolution mass spectroscopy (*m/e*) 204.1512, calcd for $C_{14}H_{20}O$ ($M^+ - H_2O$) 204.1514; 123.0810, calcd for $C_8H_{11}O$ 123.0810.

6-(1-Oxo-2-buten-3-yl)-1,2-dimethylbicyclo[2.2.2]octan-3-one (21a). Pyridinium chlorochromate[43] (0.24 g, 1.2 mmol) was added to the vinyl alcohol **20** (0.12 g, 0.52 mmol) in 20 mL of methylene chloride at room temperature and stirred for 2 h. The reaction was quenched with 30 mL of ether, and the suspended chromium salts were removed by decantation. The supernatant liquid was eluted through a 2-in. column of silica gel and further eluted with 50 mL of ether. The eluent was evaporated to afford 0.098 g (86%) of the unsaturated aldehyde **21a** as a light yellow oil: NMR (CCl_4) δ 10.0 (1 H, d, J = 7 Hz), 5.80 (1 H, bd, J = 7 Hz), 2.18 (3 H, d, J = 1.5 Hz), 2.6–1.4 (9 H, m), 1.02 (3 H, d, J = 7 Hz), 0.88 (3 H, s); IR 2950, 1700, 1650, 1450, 1360, 920, 840 cm^{-1}; MS (*m/e*) 220 (M^+), 205, 202, 187, 124 (base). High resolution mass spectroscopy (*m/e*) 220.1469, calcd for $C_{14}H_{20}O_2$ 220.1463; 124.0892, calcd for C_8H_2O 124.0888.

6-(1-Chloro-2-buten-3-yl)-1,2-dimethylbicyclo[2.2.2]octan-3-one (21b). The vinyl alcohol **20** (0.10 g, 0.45 mmol) was added to a saturated solution of anhydrous hydrogen chloride in 30 mL of chloroform at 0 °C and stirred for 1 h. The chloroform solution was extracted with sodium bicarbonate solution, and the layers were separated. The aqueous layer was further extracted with 30 mL of ether. The chloroform and ether extracts were combined, dried over anhydrous sodium sulfate, and evaporated to afford 0.10 g (92%) of the crude chloride **21b** which needed no further purification: NMR (CCl_4) δ 5.50 (1 H, t, J = 7 Hz), 4.03 (2 H, d, J = 7 Hz), 2.6–1.0 (12 H, m), 1.02 (3 H, d, J = 7 Hz), 0.83 (3 H, s); IR 2950, 1710, 1640, 1460, 1370, 790, 730 cm^{-1}; MS (*m/e*) 242, 240 (M^+), 205, 124 (base). High resolution mass spectroscopy (*m/e*) 240.1286, calcd for $C_{14}H_{21}OCl^{35}$ 240.1281; 124.0892, calcd for $C_8H_{12}O$ 124.0888.

6-(1-Trifluoroacetoxy-2-buten-3-yl)-1,2-dimethylbicyclo[2.2.2]octan-3-one (21c). The trifluoroacetate was prepared by dissolution of the vinyl alcohol **20** in trifluoroacetic acid at 0 °C for 5 min. However, the trifluoroacetate was never isolated, and was easily hydrolyzed during neutralization with sodium bicarbonate.

6-(1-Acetoxy-2-buten-3-yl)-1,2-dimethylbicyclo[2.2.2]octan-3-one (21d) was prepared by addition of one drop of concd sulfuric acid to a solution of the vinyl alcohol **20** (0.10 g, 0.45 mmol) in 10 mL of glacial acetic acid at 10 °C. After 10 min, 15 mL of distilled water was added and the solution was neutralized with solid sodium bicarbonate until carbon dioxide formation ended. This aqueous solution was extracted with 4 × 30 mL of ether. The extracts were combined, dried over anhydrous sodium sulfate, and evaporated to afford 0.12 g (100%) of the acetate **21d**: NMR (CCl_4) δ 5.33 (1 H, t, J = 7 Hz), 4.56 (2 H, d, J = 7 Hz), 2.01 (3 H, s), 2.8–1.4 (15 H, m), 1.02 (3 H, d, J = 7 Hz), 0.83 (3 H, s); IR 2900, 1700–1720 (br), 1450, 1360, 1230, 780, 760 cm^{-1}; MS (*m/e*) 264 (M^+), 204, 189, 124, 122 (base). High resolution mass spectroscopy (*m/e*) 264.1725, calcd for $C_{16}H_{24}O_3$ 264.1725; 122.0730, calcd for $C_8H_{10}O$ 122.0731.

6-(1-Hydroxy-2-buten-3-yl)-1,2-dimethylbicyclo[2.2.2]octan-3-one (21e). Method 1. The crude chloride **21b** was dissolved in 10 mL of dry dioxane and heated in a 60–80 °C oil bath. To this solution was added 10 mL of distilled water and the mixture was stirred for 1.5 h. The resulting solution was poured into 50 mL of ether and extracted with sodium bicarbonate solution (5%). The ether extract was dried over anhydrous sodium sulfate and evaporated to afford the allylic alcohol **21e** plus an unknown impurity. The impurity was removed by column chromatography on silica gel (2.0 g) using benzene/10% ethyl acetate and 48 mg (48%) of the allylic alcohol **21e** was obtained by elution with benzene/25% ethyl acetate.

Method 2. The trifluoroacetate **21c**, which was prepared from the vinyl alcohol **20** (0.050 g, 0.22 mmol) in trifluoroacetic acid, was added to 10 mL of distilled water and neutralized with solid sodium bicarbonate. Within 15–30 min, complete hydrolysis occurred and 44 mg (88%) of the alcohol **21e** could be obtained, but not in pure form.

Method 3. The acetate **21d** (0.180 g, 0.68 mmol) was mixed with excess sodium carbonate and 10 mL of distilled water, and methanol was added until the solution was homogeneous. The reaction mixture was stirred for 1–1.5 h, and the methanol was removed by rotary evaporation. The resulting aqueous layer was extracted with 4 × 30 mL of ether. The ether extracts were combined, dried over anhydrous sodium sulfate, and evaporated to afford 150 mg (100%) of the allylic alcohol **21e**: NMR (CCl_4) δ 5.38 (1 H, t, J = 7 Hz), 4.07 (2 H, d, J = 7 Hz), 2.6–1.2 (13 H, m), 0.97 (3 H, d, J = 7 Hz), 0.80 (3 H, s); IR 3300, 2900, 1710, 1650, 1450, 1000 cm^{-1}; MS (*m/e*) 222 (M^+), 207, 204, 192, 175, 124 (base). High resolution mass spectroscopy (*m/e*) 222.1621, calcd for $C_{14}C_{22}O_2$ 222.1620; 124.0893, calcd for $C_8H_{12}O$ 124.0888.

6-(1-Hydroxy-3-butyl)-1,2-dimethylbicyclo[2.2.2]octan-3-one (22a:23a). The allylic alcohol **21e** (0.10 g, 0.45 mmol) was hydrogenated in 10 mL of benzene containing 30 mg of 5% rhodium on alumina catalyst for 2 days. The catalyst was filtered through a capillary column (3 mm) of silica gel. By elution with additional benzene, the olefin **24** was separated (10%): NMR (CCl_4) δ 5.27 (1 H, m), 2.6–1.4 (15 H, m), 0.98 (3 H, d, J = 7 Hz), 0.77 (3 H, s); IR 2900, 1700 cm^{-1}; MS (*m/e*) 206 (M^+), 191, 149, 124 (base).

By elution with ethyl acetate, 0.080 g (80%) of the desired alcohol was obtained as an equal mixture of diastereomers **22a** and **23a**: NMR (CCl_4) δ 3.54 (2 H, 2 t, J = 7 Hz, equal mixture of **22a** and **23a**), 2.5–1.2 (13 H, m), 1.2–0.70 (9 H, m); IR 3400, 2900, 1700, 1450, 1360 cm^{-1}; MS (*m/e*) 224 (M^+), 206, 151, 124 (base). High resolution mass spectroscopy (*m/e*) 224.1792, calcd for $C_{14}H_{24}O_2$ 224.1777; 124.0887, calcd for $C_8H_{12}O$ 124.0888.

6-(1-Bromo-3-butyl)-1,2-dimethylbicyclo[2.2.2]octan-3-one (22b:23b). A mixture of the alcohols **22a:23a** (0.080 g, 0.36 mmol) and triphenylphosphine (0.104 g, 0.40 mmol) in 15 mL of tetrahydrofuran was mixed with *N*-bromosuccinimide (0.071 g, 0.40 mmol) in 5 mL of tetrahydrofuran at room temperature. Upon addition, a white solid immediately formed and was removed by decantation of the tetrahydrofuran solution. This solution was rotary evaporated to remove tetrahydrofuran, and the remaining residue was eluted through a 6-in. column (1 cm) of silica gel with benzene. After evaporation of benzene, 0.090 g (87%) of the bromide **22b:23b** was obtained. This mixture was used directly and not purified further.

Norseychellanone (2) and 4-Epinorseychellanone (25). The bromides **22b:23b** (20 mg, 0.07 mmol) in 5 mL of dry glyme were added via syringe

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to excess potassium hydride (freshly washed with ligroin or petroleum ether) in a serum-capped flask under nitrogen. Hydrogen evolution began immediately and the solution gradually turned orange over 2 h at room temperature. The excess base was carefully quenched by slow addition of water and acidified with 20 mL of 5% HCl solution. This aqueous solution was extracted with 3 × 30 mL of ether. The ether extracts were combined, dried over anhydrous sodium sulfate, and evaporated to a light yellow oil. The oil was further chromatographed to remove the residual paraffin oil and gave a yellow band which afforded 10 mg (70%) of a 1:1 mixture of norseychellanone (**2**) and 4-epinorseychellanone (**25**).

Alternatively, the bromides **22b**:**23b** (57 mg, 0.20 mmol) in 2 mL of dry glyme were added via syringe to a red solution of tritylpotassium prepared from triphenylmethane (70 mg, 0.20 mmol), excess potassium hydride (freshly washed), and 0.5 mL of dry dimethyl sulfoxide in 3 mL of dry glyme. After addition of the bromide, the red color of the solution immediately disappeared, but the solution was allowed to stand for an additional 30 min. The reaction mixture was quenched and worked up as above, and the resulting yellow oil was chromatographed on silica gel (2.5 g) using benzene to remove the residual paraffin oil. Further elution using benzene/10% ethyl acetate with careful fractionation afforded 20 mg (50%) of norseychellanone (**2**) (R_f 0.35), and 20 mg (50%) of 4-epinorseychellanone (**25**) (R_f 0.25).

Norseychellanone (2): NMR (200 MHz, CCl_4) δ 2.4–1.2 (13 H, m), 0.97 (3 H, s), 0.94 (3 H, s), 0.79 (3 H, d, J = 7 Hz); IR 1705 cm^{-1}.

4-Epinorseychellanone (25): NMR (200 MHz, CCl_4) δ 2.4–1.2 (13 H, m), 1.12 (3 H, d, J = 7 Hz), 1.02 (3 H, s); 0.98 (3 H, s); IR 1705 cm^{-1}.

The norseychellanone produced by this method was identical (200-MHz NMR, IR, TLC) with an authentic sample kindly provided by Dr. E. Piers.[5]

7,8-Dimethyltricyclo[5.3.1.0^{3,8}]undecane-4,11-dione (26). Methylene chloride solutions of $TiCl_4$ and $Ti(O\text{-}i\text{-}Pr)_4$ were prepared separately beforehand, each having a concentration of ca. 0.7 M. To a methylene chloride solution of 1.19 mmol of $TiCl_4$, 10 mL of methylene chloride was added at room temperature under an N_2 atmosphere. The solution was stirred at −78 °C and 1.19 mmol of $Ti(O\text{-}i\text{-}Pr)_4$ in methylene chloride was added dropwise. A methylene chloride solution (2 mL) of 330.8 mg (1.19 mmol) of the silyl enol ether mixture **16c**:**17c** was added dropwise at −78 °C, and kept at −78 °C for about 3 h. The temperature was raised to −40 °C for 2 h and then to room temperature for 12 h. The reaction mixture was poured into aqueous potassium carbonate (15 mL) and was stirred at room temperature for 15 min. A white solid was filtered using Celite and washed with 3 × 10 mL of ether. The organic layer was separated, washed with water and brine, and dried over magnesium sulfate. The solvent was removed under reduced pressure and the residue was separated by silica gel column chromatography using 2:1 hexane:ether as eluent. The first fraction (R_f 0.56) contained 18 mg (7%) of the diene dione **27**: NMR ($CDCl_3$) δ 6.40–5.81 (3 H, m), 2.72 (2 H, t, J = 6 Hz), 2.36 (7 H, bs), 1.89 (3 H, bs), 1.75 (3 H, bs); IR 3100, 1670 cm^{-1}; MS (m/e) 206 (M^+), 188, 136.

The second fraction (R_f 0.43) contained 75 mg (31%) of the desired dione **26**, mp 120 °C: ^1H NMR (200 MHz, $CDCl_3$) δ 2.48–1.59 (12 H, m), 1.10 (3 H, s), 0.87 (3 H, s); ^{13}C NMR (50 MHz, $CDCl_3$) δ 221.4, 213.4, 54.5, 49.5, 41.1, 40.4, 35.0, 32.0, 29.2, 26.3, 23.3, 20.3, 19.4; IR ($CDCl_3$) 2970, 1720 cm^{-1}; MS (m/e) 206 (M^+), 124, 96. Anal. Calcd for $C_{13}H_{18}O_2$: C, 75.69; H, 8.80. Found: C, 75.55; H, 8.84. On occasion these two fractions were preceded by a small amount of 2,3-dimethylcyclohexenone (**12**) (R_f 0.66). This mixture of products could also be separated by HPLC (Waters Prep 500) using 5% ethyl acetate in hexane.

4-Hydroxy-4,7,8-trimethyltricyclo[5.3.1.0^{3,8}]undecan-11-one (28). To a stirred solution of 1.4 M methyllithium (0.6 mL, 0.84 mmol) in 5 mL of anhydrous ether at 0 °C was added via syringe over 5 min the dione **26** (80 mg, 0.38 mmol) in 1.5 mL of anhydrous ether. It was stirred at that temperature for 10 h. The mixture was then slowly poured into a stirred cold saturated ammonium chloride solution. The aqueous layer was extracted with 3 × 20 mL of ether. The combined organic layers were washed with brine and water and then dried over anhydrous sodium sulfate. The solvent was removed at reduced pressure to give a pale yellow oil which could be separated by column chromatography on 10 g of neutral aluminum oxide using ethyl acetate–hexane (1:3) to give 64 mg (76%) of the alcohol **28** as a mixture of two diastereomers. The exact ratio of the two diastereomers was not determined: NMR (200 MHz, $CDCl_3$) δ 2.20–1.18 (13 H, m), 1.15 and 1.14 (total 3 H, bs), 1.10 (3 H, s), 0.96 (3 H, s); IR ($CDCl_3$) 3620, 3500, 2950, 1710 cm^{-1}; MS (m/e) 222 (M^+), 206, 152 (base), 124.

4,7,8-Trimethyltricyclo[5.3.1.0^{3,8}]undec-4-en-11-one (29) and 4-Methylene-7,8-dimethyltricyclo[5.3.1.0^{3,8}]undecan-11-one (30). Into a 25-mL, three-neck, round-bottom flask equipped with a spiral reflux condenser, a nitrogen bubbler, and a magnetic stirring bar was placed freshly distilled phosphorus oxychloride (2 mL, 21 mmol) with stirring. The alcohol **22** (66 mg, 0.3 mmol) in 5 mL of dry pyridine was added dropwise at room temperature. The mixture was then refluxed at 60–90 °C for 4 h. After the mixture was cooled, it was poured into ice water with stirring. The aqueous layer was extracted with 3 × 20 mL of ether and the organic layer was treated with cold 10% HCl, water, and brine and then dried over anhydrous sodium sulfate. The solvent was rotary evaporated to give a clear oil which was chromatographed on 5 g of silica gel using dichloromethane to afford 24 mg (40%) of an 85:15 mixture of endocyclic and exocyclic olefins, **29** and **30**, respectively: NMR (200 MHz, $CDCl_3$) δ 5.13 (0.85 H, bs), 4.61 (0.3 H, bs), 2.40–1.6 (10.3 H, m), 1.59 (2.55 H, bs), 1.00 (2.55 H, s), 0.98 (0.45 H, s), 0.82 (2.55 H, s), 0.80 (0.45 H, s); IR ($CDCl_3$) 2950, 2900, 1720 cm^{-1}; MS (m/e) 204 (M^+, base), 189, 149, 110.

The reaction of 1.5 M methyllithium (0.9 mL, 1.3 mmol) with the dione **26** (0.18 g, 0.87 mmol) was allowed to proceed at −78 °C for 8 h then at 0 °C for 2 h. Careful workup of the mixture as in the procedure for isolation of **28** afforded 0.15 g of yellow oil. To a stirred solution of this crude oil in 1.5 mL of benzene and 1.5 mL of pyridine at 0 °C was added thionyl chloride (0.2 mL, 1.0 mmol) in 1.5 mL of benzene. The resulting solution was stirred for 35 min at 0 °C. The reaction mixture was poured into rapidly stirred ice water and the aqueous solution was extracted with 3 × 20 mL of ether. The combined organic layers were washed with cold 10% HCl, cold sodium bicarbonate solution, and brine. The solution was dried over anhydrous sodium sulfate and the solvent was evaporated to give a colorless liquid. Chromatography of the liquid on 10 g of neutral aluminum oxide using dichloromethane–petroleum ether (2:1) afforded 82 mg (46% overall) of the same 85:15 mixture of olefins **29** and **30** as above.

Norseychellanone (2) and 4-Epinorseychellanone (25). A solution of the mixture of olefins **29** and **30** (13 mg, 0.063 mmol) in 3 mL of 100% ethanol was hydrogenated over 10% palladium on carbon overnight to give 11 mg (83%) of a mixture of **2** and **26**. The ratio of these products was calculated to be 80:20 **2**/**25** by the averaged integration of an expanded 200-MHz ^1H NMR spectrum of the mixture. The products could be separated by chromatography as described above.

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