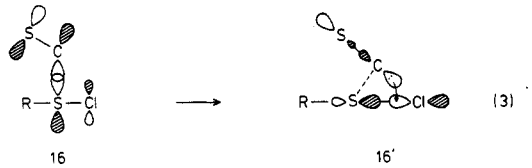

16 16' (3)

of CS into the sulfur–chlorine bonds of S_2Cl_2 and RSCl[4,5,19] are readily understood.

The frontier orbitals of thiols are somewhat similar to the frontier orbitals of the sulfenyl chlorides and insertion of CS into the sulfur–hydrogen bond should, therefore, be possible. There are, however, some significant differences. The sulfur in the thiol has, contrary to the sulfur atoms in **11** and **12**, a net negative atomic charge which might lead to a lowering (although it is very small) of the reactivity toward CS. Furthermore, the LUMO of the thiol lies higher in energy than the LUMOs of **11** and **12**, thus increasing the energy gap between this LUMO and the filled σ orbital of CS (cf. Figures 1 and 4). This energy gap reduces the rate of the insertion (eq 3). As a result of these considerations the thiols should be less reactive toward CS than, e.g., **11** and **12**, and, indeed, this prediction fits nicely with the experimental result. CS does react with thiols but very sluggishly under the standard conditions.[5c] The primary insertion products are unstable so that only secondary products are obtained in very low yield.[19]

The picture that emerges from the analysis of primary amines is very similar to the result of the analysis of the thiols. The main difference is the significantly larger net negative atomic charge on nitrogen compared to the sulfur in thiols. The reactivity of primary amines toward CS should, therefore, be comparable to the reactivity of thiols, and the experimental results are in complete accord with the prediction. The resulting stable thioformamides are obtained in very low yield.

(19) M. P. Kramer, Ph.D. Thesis, Kansas State University, 1985.

Secondary amines, however, are very reactive toward CS. The resulting stable thioformamides are obtained in high yields[5a] and the only limiting factor seems to be the steric bulk of the R groups in R_2NH. The observed difference in reactivity between primary and secondary amines can be traced to the HOMO energy of the amines: Secondary amines have generally a higher HOMO energy than primary[20] amines and should then according to the perturbation theory[8] be expected to be more reactive toward electrophiles than primary amines.

Alcohols have very low-lying HOMO orbitals and, furthermore, a significant amount of net negative atomic charge on oxygen. The reactivity of alcohols toward CS should, therefore, be very low which is in accord with the experimental results. No reactions between CS and alcohols have been observed and alcohols have been used as solvents in several CS reactions.[4b]

Conclusion

The analysis presented here shows that the frontier orbital approach, combined with the electrostatic interaction approach, gives a satisfactory coherent explanation of the reactivity of CS. This analysis can also be useful for future choices of substrates for CS. The ideal substrate should have an energetically high-lying HOMO orbital of a symmetry which allows overlap with the empty p orbital of CS, and the major part of the electron density of this HOMO orbital should be located on the atom which is attacked by CS. This specific atom should also have a net positive atomic charge and not be sterically hindered. A further requirement for a successful reaction is that there has to be a pathway from the initially formed transition state, e.g., **16**, to a chemically possible product.

(20) See, e.g., the ionization potentials ($\simeq$–HOMO energy) for secondary and primary amines in: *Handbook of Chemistry and Physics*, 55th ed.; CRC: Boca Raton, FL, 1974.

Stereospecific Skeletal Rearrangement Reactions in Bridgehead-Substituted Bicyclo[2.2.2] Systems under Neutral Conditions

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General and stereospecific pinacolic-type rearrangement reactions of vicinal methoxy mesylates under neutral conditions have been developed for the construction of functionalized bicyclo[3.2.1]octanes. For instance, *exo*-5,5-dimethyl-1-methoxy-6-[(methylsulfonyl)oxy]bicyclo[2.2.2]oct-2-ene rearranged to 8,8-dimethylbicyclo-[3.2.1]oct-6-en-2-one when treated with NaI in DMF. The tolerance of various functional groups to these reaction conditions was demonstrated in the transformation of the C ring of thebaine to the corresponding bicyclo-[3.2.1]octenone. The quadrone skeleton (ABC rings) was also constructed by utilizing this pinacol-type rearrangement reaction.

Introduction

Our interest in functionalized bicyclo[3.2.1]octene systems stemming from our synthetic work directed toward the taxane diterpenes,[1] exemplified by taxol (**1**),[1b] prompted us to investigate a mild and effective skeletal rearrangement reaction of 1-methoxybicyclo[2.2.2]octenes. Scheme I outlines the retrosynthetic plan for the synthesis of the taxane ring system.

The pinacolic-type rearrangement of vicinal *cis*-glycol monotosylates[2] would provide a method to prepare bicy-

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(1) (a) For a recent review, see: Miller, R. W. *J. Nat. Prod.* **1980**, *43*, 425. (b) Isolation and structure of taxol: Wani, M. C.; Taylor, H. L.; Wall, M. E.; Coggon, P.; McPhail, A. T. *J. Am. Chem. Soc.* **1971**, *93*, 2325. For approaches to the synthesis of taxanes: (c) Holton, R. A. *J. Am. Chem. Soc.* **1984**, *106*, 5731. (d) Sakan, K.; Craven, B. M. *J. Am. Chem. Soc.* **1983**, *105*, 3732. (e) Brown, P. A.; Jenkins, P. R.; Fawcett, J.; Russell, D. R. *J. Chem. Soc., Chem. Commun.* **1984**, 253. (f) Shea, K. J.; David, P. D. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 419. (g) Martin, S. F.; White, J. B.; Wagner, R. *J. Org. Chem.* **1982**, *47*, 3190. (h) Trost, B. M.; Hiemstra, H. *J. Am. Chem. Soc.* **1982**, *104*, 886.

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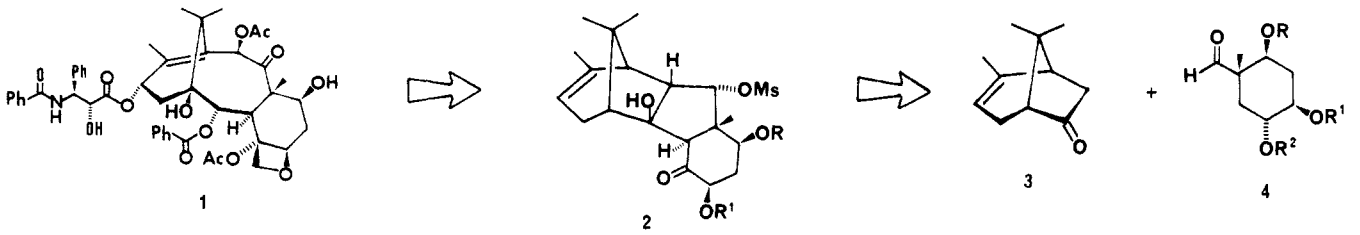
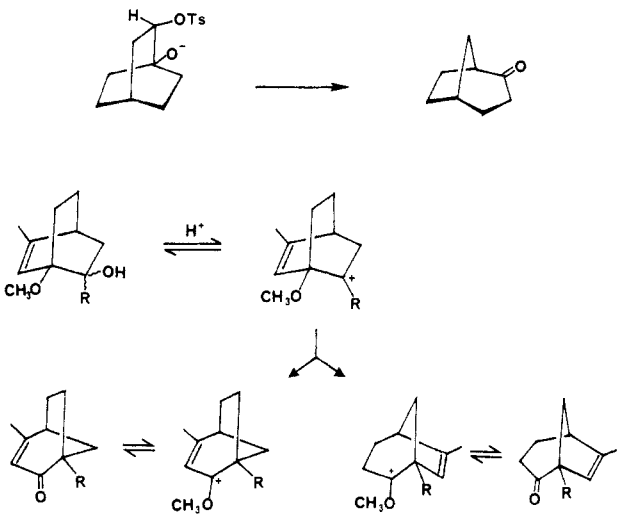
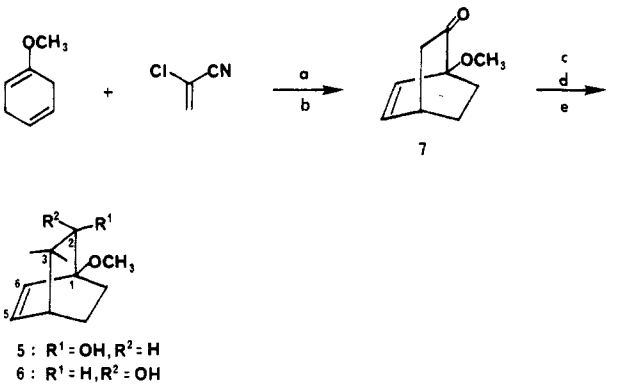
Scheme I. Retrosynthesis



Scheme II



Scheme III[a]



5 : R^1 = OH, R^2 = H
6 : R^1 = H, R^2 = OH

[a] (a) Benzene, reflux; (b) $Na_2S \cdot 9H_2O$, EtOH, reflux; (c) LDA, CH_3I, THF, HMPA; (d) LDA, CH_3I, THF, HMPA; (e) $LiAlH_4$, ether, 0 °C.

clo[3.2.1]octanes from bicyclo[2.2.2]octanes (Scheme II). This process, however, requires a bridgehead hydroxy group that is not easily obtained. Pinacol-type rearrangement reactions have also been explored in acidic media[3] such as *p*-toluenesulfonic acid in AcOH under elevated temperatures or conditions that generate carbocations (Scheme II). Many acid-labile functional groups will not tolerate these conditions. Herein, we report a general and stereospecific pinacolic-type rearrangement of vicinal methoxy mesylates under neutral conditions for the construction of functionalized bicyclo[3.2.1]octanes from the corresponding bicyclo[2.2.2]octanes.

Results and Discussion

I. Rearrangement Reactions of 2-Hydroxy-1-methoxybicyclo[2.2.2]oct-5-ene and Its Methanesulfonate Ester. The starting material for the preparation of the required bicyclo[2.2.2]octenes **5** and **6** is the previously unreported α,α-dimethyl derivative of ketone **7** (Scheme III). The two methyl groups at C-3 position are present in every member of the taxane diterpenes. This α,α-dimethyl derivative of ketone **7** was prepared by the sequence of reactions: (i) [4 + 2] cycloaddition of 1-methoxy-1,4-cyclohexadiene and 2-chloroacrylonitrile in benzene reflux for 10 h (70% yield);[3a] (ii) hydrolysis of the resulting α-chloro cyanide with $Na_2S \cdot 9H_2O$ in refluxing ethanol[4] for 9 h (50% yield); (iii) monomethylation of ketone **7** with 1 equiv of lithium diisopropylamide (LDA) in THF at −78 °C followed by CH_3I in hexamethylphosphoramide (HMPA); and (iv) second methylation of the resulting monomethylated ketone under the same conditions as above (75% yield in two steps). The α,α-dimethyl derivative of ketone **7** was unreactive toward most reducing agents, including K-Selectride (Aldrich), $LiAl(O\text{-}t\text{-}Bu)_3H$, and Dibal-H. It was finally reduced with 1 equiv of lithium aluminium hydride (LAH) in ether at 0 °C for 3 h, producing 95% yield of the isomeric alcohols exo, **5**, and endo, **6** (55:45), each being isolated by column chromatography.

Attempts to demethylate the C-1 methoxy of **5** or **6** to diol **9** or **11** with various standard reagents (e.g., Me_3SiI in CH_2Cl_2,[5a] or 48% HBr in AcOH with heat,[5b] or $BF_3 \cdot Et_2O$, CH_3CH_2SH, 25 °C[5c]) failed. Only starting alcohol **5** or **6** and a mixture of byproducts were obtained. However, when exo alcohol **5** was treated with 2 equiv of BBr_3 in CH_2Cl_2 at −78 °C for 2 min followed by 10 equiv of ethanethiol and 15 equiv of 4-(dimethylamino)pyridine (DMAP) at −78 °C for 1 h, and then 25 °C for 3 h, 37% of bicyclo[3.2.1]octenone **8**, 27% of the diol **9**, and 20% of enol thioether **10** were isolated (Scheme IV).

Under identical conditions, endo alcohol **6** afforded only the diol **11** in 83% yield (Scheme IV). Apparently the migratory aptitude of the alkenyl carbon is greater than that of the alkyl carbon. The rearrangement of **11** could be effected by treating diol **11** with 1.1 equiv of *p*-toluenesulfonyl chloride in pyridine at room temperature for 24 h (87% isolated yield) followed by 1 equiv of NaH

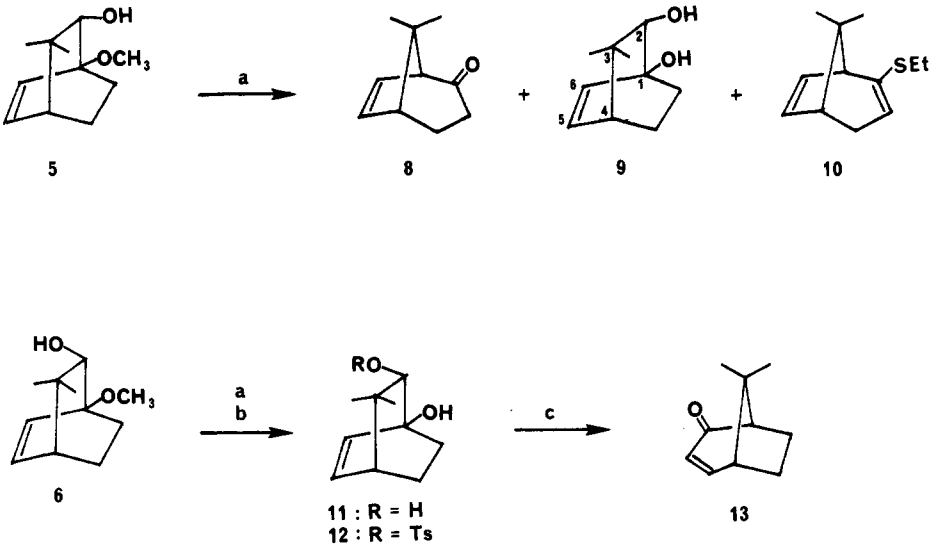
(2) (a) Bartlett, P. D.; Rosenwald, R. H. *J. Am. Chem. Soc.* **1934**, *56*, 1990. (b) Bates, R. B.; Buchi, G.; Matsuura, T.; Shaffer, R. R. *Ibid.* **1960**, *82*, 2327. (c) Corey, E. J.; Ohno, M.; Vatakencherry, P. A.; Mitra, R. B. *Ibid.* **1961**, *83*, 1251. (d) Wendler, N. L. *Tetrahedron* **1960**, *11*, 213. (e) Mazur, Y.; Nussim, M. *J. Am. Chem. Soc.* **1961**, *83*, 3911. (f) Paukstelis, J. V.; Kao, J.-L. *Tetrahedron Lett.* **1970**, 3691. (g) Paukstelis, J. V.; Macharia, B. W. *Tetrahedron* **1973**, 1955; *J. Org. Chem.* **1973**, *38*, 646.

(3) (a) Quaseem, M. A.; Othman, A. A.; Rogers, N. A. J. *Tetrahedron* **1968**, *24*, 4535. (b) Monti, S. A.; Chen, S.-C.; Yang, Y.-L.; Yuan, S.-S.; Bourgeois, O. P. *J. Org. Chem.* **1978**, *43*, 4062. (c) Monti, S. A.; Chen, S.-C. *Ibid.* **1979**, *44*, 1170. (d) Monti, S. A.; Yang, Y.-L. *Ibid.* **1979**, *44*, 897. (e) Monti, S. A.; Dean, T. R. *Ibid.* **1982**, *47*, 2679. (f) Pramod, K.; Subba Rao, G. S. R. *J. Chem. Soc., Chem. Commun.* **1982**, 762. (g) Wender, P. A.; Wolanin, D. J. *J. Org. Chem.* **1985**, *50*, 4418.

(4) (a) Evans, D. A.; Scott, W. L.; Truesdale, L. K. *Tetrahedron Lett.* **1972**, 121. (b) Madge, N.; Holmes, A. B. *J. Chem. Soc., Chem. Commun.* **1980**, 956.

(5) (a) Jung, M. E.; Luster, M. A. *J. Org. Chem.* **1977**, *42*, 3761. (b) Callahan, F. M.; Anderson, G. W.; Paul, R.; Zimmerman, J. E. *J. Am. Chem. Soc.* **1963**, *85*, 201. (c) Node, M.; Hori, H.; Fujita, E. *J. Chem. Soc., Perkin Trans. 1* **1976**, 2237.

Scheme IV[a]



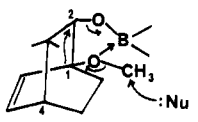
[a] (a) (i) 2 equiv of BBr_3, CH_2Cl_2, −78 °C, 3 min; (ii) 10 equiv of EtSH, 15 equiv of DMAP, −78 °C, 1 h, 25 °C, 3 h; (b) TsCl, pyridine, 25 °C, 24 h; (c) NaH, DME, 25 °C, 2 h.

in 1,2-dimethoxyethane (DME) at room temperature for 2 h to produce conjugated enone **13** (64% yield).

The stereochemistry of the C-2 OH groups in alcohols **9** and **11** was established by proton–proton NOE-difference spectroscopy.[6]

Since enol thioether **10** was formed during the rearrangement reaction of **5** (Scheme IV), the absence of ethanethiol improved the yield of ketone **8**, (65% yield), which was obtained directly by treating exo alcohol **5** with 2 equiv of BBr_3 in CH_2Cl_2 at −78 °C followed by the addition of 15 equiv of DMAP at −30 °C and then warming the reaction to room temperature for 3 h; 31% of the starting alcohol **5** was recovered.

A hypothetical working scheme proposed to account for this rearrangement at low temperature (−30 °C to room temperature) under basic conditions (excess of DMAP) involves the chelation of the oxygen atoms at C-1 and C-2 by boron (structure **14**) followed by attack at the C-1



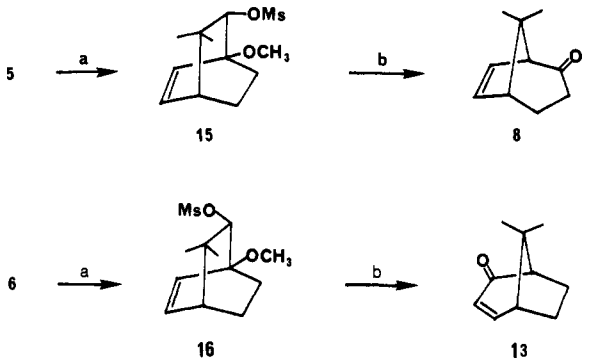
14

methoxy carbon by a nucleophile (e.g., DMAP) to induce the migration of the C-6 carbon (from C-1 to C-2). The attack of a migrating carbon stereospecifically occurs from the side opposite the leaving group.

This hypothesis encouraged us to prepare the corresponding mesylate **15** by treating alcohol **5** with 1.2 equiv of methanesulfonyl chloride and 3 equiv of triethylamine in ether at room temperature for 24 h (85% yield). Rearrangement of **15** was induced with 10 equiv of NaI in *N,N*-dimethylformamide (DMF) at 70 °C for 10 h to provide 82% yield of ketone **8** (Scheme V).

Similarly, mesylate **16** (obtained in 80% yield from the mesylation of endo alcohol **6** with methanesulfonyl chloride

Scheme V[a]



[a] (a) CH_3SO_2Cl, Et_3N, ether, 25 °C, 24 h; (b) 10 equiv of NaI, DMF.

and triethylamine) also underwent stereospecific rearrangement when treated with NaI in DMF to produce conjugated enone **13** in 90% yield (Scheme V).

This two-step, mild, and stereospecific transformation constitutes a general route for the rearrangement of functionalized bicyclo[2.2.2]octanes to bicyclo[3.2.1]octanes. It is worth noting that the *exo*- and the *endo*-bicyclo[2.2.2]octenol (**5** and **6**) each gave only a single rearrangement product, **8** and **13**, respectively, under these conditions, while previous investigators reported the isolation of two isomers, analogues of **8** and **13** from an *endo*-bicyclo[2.2.2]octenol, analogous to **6**, under acidic conditions.[3a]

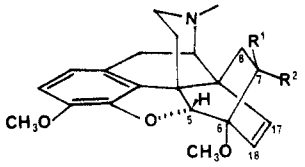
II. Rearrangement of the [4 + 2] Adduct 17 Derived from Thebaine (18). To further demonstrate the generality of this rearrangement and tolerance of various functional groups to these reaction conditions, we examine the Diels–Alder adduct **17** from thebaine (**18**).

Thebaine (**18**) was heated with 2 equiv of 2-chloroacrylonitrile in benzene at 170 °C in a sealed tube for 2 h to give 98% yield of a mixture of endo and exo adducts (**17a** and **17b**) in a ratio of 2:1. These two isomeric adducts were separated by column chromatography.

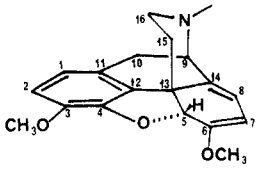
Hydrolysis of these α-chloro nitriles **17a** and **17b** to ketone **19** was effected by the reported method[7] with

(6) The percentages of NOE for alcohols **9** and **11** were observed as the following. **9**: 12% for C-3 *endo*-methyl and C-2 H; 5% for C-3 *endo*-methyl and C-5 H; 2% for C-3 *exo*-methyl and C-2 H; and 1.5% for C-3 *exo*-methyl and C-5 H. **11**: 11% for C-3 *exo*-methyl and C-2 H; 1.5% for C-3 *exo*-methyl and C-5 H; 5% for C-3 *endo*-methyl and C-5 H; and 1.5% for C-3 *endo*-methyl and C-2 H.

(7) Lewis, J. W.; Readhead, M. J.; Smith, A. C. B. *J. Med. Chem.* **1973**, *16*, 9.

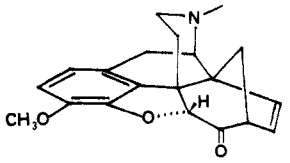


17a : R^1 = Cl, R^2 = CN
17b : R^1 = CN, R^2 = Cl
19 : R^1 = R^2 = O
20 : R^1 = OH, R^2 = H
21 : R^1 = OMs, R^2 = H



18

aqueous NaOH in ethanol under reflux for 16 h. Stereoselective reduction of **19** with K-Selectride in THF at room temperature for 3 h furnished alcohol **20** in 90% yield. Mesylation of alcohol **20** with 5 equiv of methanesulfonyl chloride and 15 equiv of triethylamine in CH_2Cl_2 at room temperature for 10 h provided mesylate **21** in 65% yield and 13% of recovered alcohol **20**. As expected, mesylate **21** rearranged by reacting with NaI (10 equiv) in DMF at 75 °C for 15 h, affording 60% yield of ketone **22** after chromatographic purification.



22

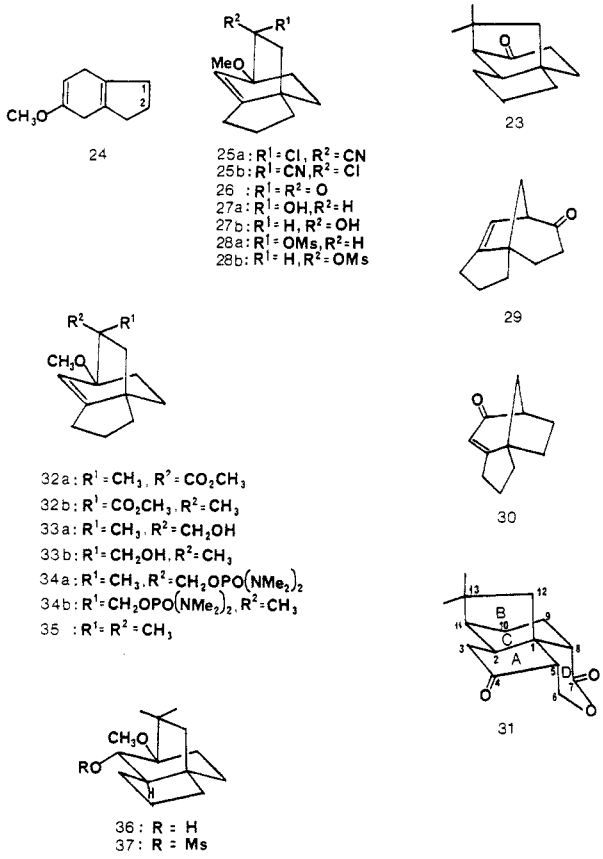
This sequence of reactions provides a novel class of thebaine derivatives. Modification of ring C of thebaine has been shown to produce the most significant influence on the pharmacological responses associated with this class of potent analgesics.[8]

Under an acidic medium (TsOH AcOH, Δ)[3] mesylate **21** decomposed to many products, but ketone **22** was not among them.

III. Rearrangement of Derivatives of 5-Methoxyindan. Synthesis of the Quadrone Skeleton (23). Tricyclic (substituted on the double bond; C-3 or **25**) systems[3f] were also subjected to the rearrangement conditions. Birch reduction[9] of 5-methoxyindan with lithium in ether–NH_3(l)–*t*-BuOH at −35 °C for 2 h provided diene **24** in 93% yield. Diels–Alder reaction of diene **24** with 2 equiv of 2-chloroacrylonitrile in benzene at 210 °C in a sealed tube gave 80% yield of a mixture of endo adduct **25a** and exo adduct **25b** (2:1). Treatment of **25a** and **25b** with 3 equiv of $Na_2S{\cdot}9H_2O$ in ethanol under reflux for 24 h produced an 80% yield of ketone **26**. Reduction of **26** with 1.5 equiv of lithium aluminium hydride in ether at room temperature for 1 h gave a 23% yield of exo alcohol **27a** and a 69% yield of endo alcohol **27b**, each being isolated by column chromatography (Chart I).

The same proportion of exo and endo alcohols (**27a** and **27b**) was obtained when **26** was treated with 2.0 equiv of $NaBH_4$ in ethanol at room temperature. Subba Rao et al.[3f] reported obtaining exo/endo alcohols in a 1:1 ratio from a similar ketone treated this way. The reported exo/endo assignments are derived from the ^1H NMR chemical shifts of *H*–C–OH. The chemical shift of *H*–C–OH assigned to exo alcohol **27a** (δ 3.80) is slightly upfield from that assigned to endo alcohol **27b** (δ 3.90), the higher field signal being associated with the shielding provided by the double

Chart I



24

25a: R^1 = Cl, R^2 = CN
25b: R^1 = CN, R^2 = Cl
26 : R^1 = R^2 = O
27a: R^1 = OH, R^2 = H
27b: R^1 = H, R^2 = OH
28a: R^1 = OMs, R^2 = H
28b: R^1 = H, R^2 = OMs

23

29

30

31

32a: R^1 = CH_3, R^2 = CO_2CH_3
32b: R^1 = CO_2CH_3, R^2 = CH_3
33a: R^1 = CH_3, R^2 = CH_2OH
33b: R^1 = CH_2OH, R^2 = CH_3
34a: R^1 = CH_3, R^2 = $CH_2OPO(NMe_2)_2$
34b: R^1 = $CH_2OPO(NMe_2)_2$, R^2 = CH_3
35 : R^1 = R^2 = CH_3

36 : R = H
37 : R = Ms

bond. A similar chemical shift difference was observed in the spectra of alcohols **5** and **6**; in this case the stereochemistry was elucidated by proton–proton NOE-difference spectroscopy[6] (vide supra). Furthermore, only endo alcohol **27b** provided conjugated enone **30** exclusively.

Endo alcohol **27b** was converted into the rearranged conjugated enone **30** in 80% yield by a two-step sequence: (1) mesylation with 1.5 equiv of methanesulfonyl chloride and 3 equiv of triethylamine in CH_2Cl_2 at 25 °C for 1 h and (2) treatment with 10 equiv of NaI in DMF at 90 °C for 2 h.

However, when *exo* alcohol **27a** was allowed to react with methanesulfonyl chloride under the same conditions as those of **27b**, only the rearranged nonconjugated enone **29** was isolated (65% yield). While the expected initial product, mesylate **28a**, was not detected, it reasonably could have undergone rapid rearrangement into ketone **29** under the mesylation conditions. An attempt to isolate the corresponding 2-propanesulfonate, by treating **27a** with 1.5 equiv of 2-propanesulfonyl chloride–3.0 equiv of Et_3N in ether also failed. Again, only ketone **29** was isolated. It should be noted that our findings regarding this rapid rearrangement of the alkanesulfonate derivatives of exo alcohol **27a** contrast with the report of the isolation of the exo tosylate derivative of similar structure by Subba Rao.[3f]

Treatment of alcohols **27a** and/or **27b** with *p*-toluenesulfonic acid in acetic acid or BBr_3 in CH_2Cl_2 at −78 °C followed by DMAP provided a mixture of cationic rearrangement products, the reaction being initiated presumably through protonation at the double bond to generate the tertiary carbocation (C-3a). 3a,5-Ethano-8-hydroxy-5-methoxy-2,3,3a,4,5,6-hexahydro-1*H*-indene was isolated and identified as one of the cationic rearrangement products.

(8) (a) For a recent review, see: Casy, A. F.; Parfitt, R. T. *Opioid Analgesics Chemistry and Receptors*; Plenum Press: New York, 1986; pp 69–84. (b) Bentley, K. W.; Burton, M.; Uff, B. C. *J. Med. Chem.* **1984**, *27*, 1276.

(9) For a review, see: Birch, A. J.; Subba Rao, G. S. R. *Adv. Org. Chem.* **1972**, *8*, 1.

The structural resemblance of **25** and quadrone (**31**)[10] prompted us to investigate the construction of the quadrone skeleton **23**.

Quadrone (**31**) was isolated[10a,b] as a metabolite of *Aspergillus terreus* and exhibited significant antitumor activity. Migration of C-13 from carbon 10 to carbon 11 would provide the basic ABC rings.

[4 + 2] cycloaddition of diene **24** with methyl methacrylate in benzene at 240 °C for 5 h in a sealed tube gave 79% yield of adducts **32a** and **32b** (1.2:1). A mixture of **32a** and **32b** was transformed to the dimethyl intermediate **35** by the sequence of reactions: (i) reduction with 3 equiv of lithium aluminum hydride in ether at 25 °C for 3 h (96% yield); (ii) phosphorylation with 1.5 equiv of *N,N,N',N'*-tetramethylphosphorodiamidic chloride–3 equiv of Et_3N–2 equiv of DMAP in toluene (5 mL/g) at 60 °C for 24 h (86% yield); and (iii) deoxyphosphorylation[11] with 10 equiv of lithium–4 equiv of *t*-BuOH in $EtNH_2$–THF under reflux (10 °C) for 1 h (78% yield of **35** and 18% recovery of alcohol **33**).

Hydroboration of olefin **35** [3 equiv of BH_3·THF (1 M) at 25 °C for 24 h, 50 °C for 24 h, followed by 1 N NaOH and 30% H_2O_2 at 25 °C] afforded 93% yield of a single alcohol, **36**. The *gem*-dimethyl at C-13 shields the endo face of **35**, so that borane attacks the double bond exclusively from the exo face. The C-11 leaving group is thus antiperiplanar to C-12–C-13. Mesylation of **36** with MsCl–Et_3N in CH_2Cl_2 at 25 °C provided **37** (87% yield).

A single-crystal X-ray structure determination of alcohol **36** firmly established the relative stereochemistry at C-1, C-2, C-10, and C-11. The crystals are triclinic, space group $P\bar{1}$. Full-matrix refinement with anisotropic for non-hydrogen and isotropic for hydrogen gave a final *R* of 0.055.

Rearrangement of mesylate **37** with 10 equiv of NaI in DMF at 100 °C for 1 h furnished the quadrone skeleton **23** in 65% yield. With proper appendages at C-1 and C-2 of 5-methoxyindan, the total synthesis of quadrone can be realized, and this is currently underway.

Conclusions

1. A mild, general, and stereospecific pinacolic-type rearrangement reaction has been developed for the construction of various bicyclo[3.2.1]octane systems from bicyclo[2.2.2]octanes.

2. The migratory aptitude of the alkenyl carbon (sp^2 carbon) is greater than that of the alkyl carbon (sp^3 carbon).

3. Utilization of this mild rearrangement reaction in the modification of ring C of thebaine provided a novel class of thebaine derivatives.

4. The quadrone skeleton (ABC rings) was also synthesized by employing this rearrangement reaction.

Experimental Section

General Methods. Proton magnetic resonance spectra were obtained in deuteriochloroform on Bruker WM-400 (400 MHz in ^1H and 100 MHz in ^{13}C) spectrometer and are reported in ppm (δ units) downfield of internal tetramethylsilane (Me_4Si). Infrared spectra were recorded on a Perkin-Elmer 1330 spectrophotometer. Mass spectra were determined on a Finnigan 4000 automated gas chromatograph/EI–CI mass spectrometer. High resolution MS were performed by Dr. Sadahiko Iguchi of Ono Pharmaceutical Co., Japan. Microanalyses were carried out by the MicAnal Organic Microanalysis, Tucson, AZ. Samples for microanalysis were purified by recrystallization, distillation, or, for oils, by rechromatography with extensive drying of the sample under vacuum (<0.01 mm). Optical rotations were measured on a Perkin-Elmer 241 polarimeter. The solvents used in most of the experiments were dried and distilled under argon. Flash chromatography was performed by using Davisil silica gel, grade 643 (200–425 mesh). E. Merk pre-coated TLC plates, silica gel 60 F-254, were used in preparative thin layer chromatography.

1-Methoxybicyclo[2.2.2]oct-5-en-2-one (7). A solution of 24.2 g (0.22 mol) of 1-methoxy-1,4-cyclohexadiene and 28.0 g (0.31 mol) of 2-chloroacrylonitrile in benzene was heated under reflux for 15 h. The solvent was removed, and the residue was distilled under vacuum to give 30.35 g (70% yield) of 6-chloro-6-cyano-1-methoxybicyclo[2.2.2]oct-2-ene: bp 116–119 °C/0.1 mm [The ^1H NMR spectrum of this oil indicated it was a mixture of endo and exo cyanide in a ratio of 3:1]; IR (Nujol) 2240, 1610; ^1H NMR ($CDCl_3$) δ 6.49 (dd, J = 10 Hz, 7.5 Hz, 1 H, =CH of *exo*-CN), 6.37 (dd, J = 9.5 Hz, 7.5 Hz, 1 H, =CH of *endo*-CN), 6.36 (d, J = 10 Hz, 1 H, =CH of *exo*-CN), 6.22 (d, J = 9.5 Hz, 1 H, =CH of *endo*-CN), 3.51 (s, 3 H, OCH_3 of *endo*-CN), 3.49 (s, 3 H, OCH_3 of *exo*-CN), 1.4–2.7 (m, 7 H); ^{13}C NMR ($CDCl_3$) δ 136.69 (d, CH= of *exo*-CN), 133.93 (d, CH= of *endo*-CN), 131.39 (d, CH= of *exo*-CN), 130.13 (d, CH= of *endo*-CN), 120.0 (s, CN of *exo*-CN), 119.5 (s, CN of *endo*-CN), 80.7 (s, CO of *exo*-CN), 77.0 (s, CO of *endo*-CN), 61.7 (s, CCl of *exo*-CN), 61.5 (s, CCl of *endo*-CN), 52.4 (d, *C*HC=C), 46.9 (q, OCH_3 of *endo*-CN), 46.7 (q, OCH_3 of *exo*-CN), 29.5 (t, CH_2), 24.7 (t, CH_2 of *endo*-CN), 24.6 (t, CH_2 of *endo*-CN), 24.5 (t, CH_2 of *exo*-CN), 21.9 (t, CH_2 of *endo*-CN).

This mixture of endo and exo cyanide was used in the next reaction. However, pure endo cyanide could be obtained by recrystallization of the mixture from petroleum ether to give white crystals, mp 75–77 °C. ^1H and ^{13}C NMR spectra of these crystals showed them to be pure endo cyanide.

A solution of 33.0 g (0.165 mol) of 6-chloro-6-cyano-1-methoxybicyclo[2.2.2]oct-2-ene and 79.0 g (0.33 mol) of $Na_2S·9H_2O$ in 250 mL of ethanol was heated under reflux for 14 h. The solution was poured into H_2O and extracted three times with ether. The combined extracts were washed with saturated aqueous NH_4Cl solution, H_2O, and brine. The organic layer was dried ($MgSO_4$), concentrated, and distilled under reduced pressure to give 12.54 g (50% yield) of **7**: bp 80 °C/1 mm; IR (neat) 1720, 1660; ^1H NMR ($CDCl_3$) δ 6.48 (dd, J = 8.7 Hz, 6.4 Hz, 1 H, =CH), 6.27 (d, J = 8.7 Hz, 1 H, =CH), 3.53 (s, 3 H, OCH_3), 2.98 (m, 1 H, CH), 2.13 (m, 2 H, CH_2C=O), 1.5–1.9 (m, 4 H, CH_2); ^{13}C NMR ($CDCl_3$) δ 209.8 (s, C=O), 135.8 (d, CH=), 129.8 (d, CH=), 84.7 (s, C—O), 53.2 (q, OCH_3), 40.4 (d, CH), 31.7 (t, CH_2), 26.8 (t, CH_2), 25.3 (t, CH_2).

***exo*-3,3-Dimethyl-1-methoxybicyclo[2.2.2]oct-5-en-2-ol (5) and *endo*-3,3-Dimethyl-1-methoxybicyclo[2.2.2]oct-5-en-2-ol (6).** To a solution of 4.0 g (24 mmol) of ketone **7** in 10 mL of THF at −78 °C under argon was added a solution of 26.4 mL (0.0264 M) of lithium diisopropylamide (LDA) in THF (prepared from diisopropylamine and *n*-butyllithium in THF at −30 °C for 15 min) via cannula. The solution was stirred at −78 °C for 30 min, and 4.2 mL (24 mmol) of hexamethylphosphoramide (HMPA) was added, followed by 1.62 mL (26 mmol) of CH_3I. The reaction mixture was stirred an additional of 20 min at −78 °C and 15 min at 25 °C and poured into 100 mL of aqueous NH_4Cl. The mixture was extracted with ether three times and the combined ether layers were washed with H_2O and brine. The organic layer was dried ($MgSO_4$) and concentrated to dryness; the ^1H NMR spectrum of the resulting oil showed it to consist of 80% of the monomethylated ketone and 20% of the starting ketone **7**. Without purification, this oil was subjected to the same reaction conditions as described above. The resulting crude product was column chromatographed on silica gel to give 2.8 g (60% yield) of 3,3-dimethyl-1-methoxybicyclo[2.2.2]oct-5-en-2-one as an oil: ^1H NMR ($CDCl_3$) δ 6.48 (dd, J = 8.5 Hz, 6.5 Hz, 1 H, =CH), 6.14 (d, J = 8.5 Hz, 1 H, =CH), 3.50 (s, 3 H, OCH_3), 2.50 (m, 1 H,

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CH), 2.0 (m, 1 H, -CH_2-), 1.8 (m, 1 H, -CH_2-), 1.72 (m, 1 H, -CH_2-), 1.60 (m, 1 H, -CH_2-), 1.11 (s, 3 H, CH_3), 1.06 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 213.94 (s, C=O), 137.29 (d, CH=), 127.92 (d, =CH), 84.58 (s, $COCH_3$), 53.16 (q, CH_3O), 43.34 (d, CH), 30.83 [s, $C(CH_3)_2$], 27.39 (t, CH_2), 26.04 (q, CH_3), 24.42 (t, CH_2), 21.65 (q, CH_3).

To a solution of 3.0 g (16.7 mmol) of the above ketone in 50 mL of ether at 0 °C under argon was added 0.63 g (16.7 mmol) of lithium aluminium hydride. The reaction mixture was stirred at 0 °C for 3 h prior to the addition of wet ether and aqueous NH_4Cl. The mixture was extracted with ether three times, and the combined organic layers were washed with 1 N HCl, $NaHCO_3$ solution, and brine and dried ($MgSO_4$). The organic layer was concentrated and column chromatographed on silica gel to give 1.60 g (53% yield) of exo alcohol **5** and 1.40 g (47% yield) of endo alcohol **6**.

5: IR (neat) 3400, 1620; ^1H NMR ($CDCl_3$) δ 6.27 (dd, J = 8.8 Hz, 6.3 Hz, 1 H, =CH), 6.14 (d, J = 8.8 Hz, 1 H, CH=), 3.37 (s, 3 H, CH_3O), 3.29 (d, J = 1.7 Hz, 1 H, HCO), 2.08 (s, 1 H, OH), 1.99 (m, 1 H, CH), 1.90 (m, 1 H, CH_2), 1.80 (m, 1 H, CH_2), 1.14–1.27 (m, 2 H, CH_2), 0.99 (s, 3 H, CH_3), 0.93 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 135.6 (d, =CH), 129.7 (d, =CH), 81.3 (s, $COCH_3$), 77.0 (d, HCO), 51.1 (q, OCH_3), 42.3 (d, CH), 36.0 [s, $C(CH_3)_2$], 32.4 (q, CH_3), 22.7 (q, CH_3), 22.2 (t, CH_2), 18.7 (t, CH_2); mass spectrum, m/z 182.1 (M^+).

6: IR (neat) 3350, 1620; ^1H NMR ($CDCl_3$) δ 6.40 (dd, J = 8.6 Hz, 6.6 Hz, 1 H, =CH), 6.0 (d, J = 8.6 Hz, 1 H, =CH), 3.46 (d, J = 2.7 Hz, 1 H, HCO), 3.37 (s, 3 H, OCH_3), 2.1 (d, J = 2.7 Hz, 1 H, OH), 1.9 (m, CH), 1.6–1.2 (m, 4 H, CH_2), 1.1 (s, 3 H, CH_3), 0.9 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 135.9 (d, CH=), 129.2 (d, =CH), 81.2 (s, $COCH_3$), 80.6 (d, COH), 50.5 (q, OCH_3), 42.8 (d, CH), 40.6 [s, $C(CH_3)_2$], 29.7, (t, CH_2), 24.2 (t, CH_2), 23.9 (q, CH_3), 21.9 (q, CH_3); mass spectrum, m/z 182.1 (M^+).

Reaction of Alcohol 5 with BBr_3–EtSH–DMAP. To a solution of 0.28 g (1.5 mmol) of exo alcohol **5** in 3 mL of CH_2Cl_2 at −78 °C under argon was added a solution of 3 mmol of BBr_3 in 3 mL of CH_2Cl_2 dropwise, followed by 1 mL (13.5 mmol) of CH_3CH_2SH and a solution of 1 g (8.2 mmol) of 4-(dimethylamino)pyridine (DMAP) in 2 mL of CH_2Cl_2. The solution was stirred at −78 °C for 1 h and 25 °C for 3 h and then poured into aqueous NH_4Cl solution. The mixture was extracted three times with ether, and the combined extracts were washed with H_2O and brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 84 mg (37.3% yield) of 8,8-dimethylbicyclo-[3.2.1]oct-6-en-2-one (**8**), 67 mg (27% yield) of *exo*-3,3-dimethylbicyclo[2.2.2]oct-5-ene-1,2-diol (**9**), and 59 mg (20.3% yield) of 2-(ethylthio)-8,8-dimethylbicyclo[3.2.1]octa-2,6-diene (**10**).

8: IR (neat) 1730, 1630; ^1H NMR ($CDCl_3$) δ 6.1 (dd, J = 5.8 Hz, 2.9 Hz, 1 H, =CH), 5.9 (dd, J = 5.8 Hz, 3 Hz, 1 H, =CH), 2.6 (d, J = 3 Hz, 1 H, CH-C=O), 2.5 (m, 1 H, *exo*-CH_2C=O), 2.3 (m, 1 H, CHC=C), 2.1 (dd, J = 18 Hz, 7.7 Hz, *endo*-CH_2C=O), 1.9 (m, 1 H, CH_2), 1.6 (m, 1 H, CH_2), 1.1 (s, 3 H, CH_3), 1.0 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 211.0 (s, C=O), 138.0 (d, =CH), 131.0 (d, CH=), 66.4 (d, CHC=O), 48.9 [s, $C(CH_3)_2$], 48.0 (d, CHC=), 33.4 (t, CH_2C=O), 26.4 (q, CH_3), 21.4 (q, CH_3), 21.3 (t, CH_2); HRMS calcd for $C_{10}H_{14}O$ 150.1041, found 150.1060. Anal. Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.39. Found: C, 79.71; H, 9.25.

9: IR (neat) 3400, 1620; ^1H NMR ($CDCl_3$) δ 6.18 (dd, J = 10 Hz, 6 Hz, 1 H, CH=), 6.01 (d, J = 10 Hz, 1 H, CH=), 3.2 (s, 1 H, CH-O), 2.01 (s, 2 H, OH), 1.8–1.9 (m, 2 H, CH_2), 1.1–1.25 (m, 2 H, CH_2), 0.98 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 134.2 (d, CH=), 133.7 (d, CH=), 79.8 (s, COH), 76.02 (d, CHOH), 42.4 (d, CH), 36.15 [s, $C(CH_3)_2$], 32.3 (t, CH_2), 23.0 (t, CH_2), 22.8 (q, CH_3), 22.51 (q, CH_3). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.45; H, 9.37.

10: IR (neat) 1640, 1620; ^1H NMR ($CDCl_3$) δ 6.22 (dd, J = 8 Hz, 4 Hz, 1 H, CH=), 5.68 (dd, J = 8 Hz, 3.5 Hz, 1 H, CH=), 5.05 (dd, J = 2.5 Hz, 1 H, SC=CH), 2.64 (q, J = 7.4 Hz, CH_2S), 2.32 (m, 1 H, CHC=CS), 2.19 (s, 1 H, =CCHC=), 2.08 (br s, 1 H, =CCH), 1.88 (dd, J = 18 Hz, 3 Hz, 1 H, CHC=CS), 1.25 (t, J = 7.4 Hz, 3 H, CH_3), 1.11 (s, 3 H, CH_3), 1.07 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 139.2 (d, CH=), 138.0 (s, =CS), 131.7 (d, CH=), 117.1 (d, CH=CS), 55.0 (d, =CCH-C=), 47.0 (d, CHC=), 44.8 [s, $C(CH_3)_2$], 28.1 (t, SCH_2), 27.2 (q, CH_3), 25.1 (t, CH_2), 20.9 (q, CH_3), 13.9 (q, CH_3); HRMS calcd for $C_{12}H_{18}S$ 194.2004, found 194.2027.

Reaction of Alcohol 5 with BBr_3–DMAP. To a solution of 1.60 g (8.8 mmol) of exo alcohol **5** in 30 mL of CH_2Cl_2 at −78 °C under argon was added a solution of 17.6 mmol of BBr_3 in 18 mL of CH_2Cl_2 dropwise. The solution was stirred at −78 °C for 1 h and −30 °C for 1 h, and a solution of 6.9 g (56 mmol) of DMAP in 30 mL of CH_2Cl_2 was added. The cooling bath was removed and the solution was stirred at 25 °C for 3 h. The reaction mixture was poured into a solution of 4 g of citric acid in 20 mL of H_2O and stirred for 30 min. The mixture was extracted with ether three times, and the combined extracts were washed with 1 N HCl, aqueous $NaHCO_3$, and brine, and dried ($MgSO_4$). After the solvent was removed under vacuum, the resulting oil was column chromatographed on silica gel to give 0.86 g (65% yield) of ketone **8** and 0.5 g (31% recovery) of starting alcohol **5**.

Reaction of Endo Alcohol 6 with BBr_3–EtSH–DMAP. Endo alcohol **6** was subjected to the same reaction conditions described above for the reaction of alcohol **5** with BBr_3–EtSH–DMAP. *endo*-3,3-Dimethylbicyclo[2.2.2]oct-5-ene-1,2-diol (**11**) (83% yield) was isolated after column chromatography: IR (neat) 3400, 1620; ^1H NMR ($CDCl_3$) δ 6.38 (dd, J = 10 Hz, 6 Hz, 1 H, CH=), 5.93 (d, J = 10 Hz, 1 H, CH=), 3.28 (d, J = 6 Hz, 1 H, CHO), 2.82 (br s, 1 H, OH), 2.06 (m, 1 H, CHC=), 1.86 (m, 1 H, CH_2), 1.61 (s, 1 H, OH), 1.4–1.58 (m, 3 H, CH_2), 1.11 (s, 3 H, CH_3), 0.90 (s, 3 H, CH_3). Anal. Calcd for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.28; H, 9.71.

***endo*-5,5-Dimethyl-6-[[(4-methylphenyl)sulfonyl]oxy]bicyclo[2.2.2]oct-2-en-1-ol (12).** A solution of 85 mg (0.6 mmol) of endo diol **11**, 0.13 g (0.7 mmol) of *p*-toluenesulfonyl chloride, and 1 mL of pyridine was stirred under argon at 25 °C for 24 h. The reaction mixture was diluted with ether, washed with H_2O, aqueous $CuSO_4$, and brine, dried ($MgSO_4$), and concentrated to give 0.14 g (87% yield) of tosylate **12**: IR (neat) 3400, 1620, 1350, 1170; ^1H NMR ($CDCl_3$) δ 7.8 (d, J = 10 Hz, 2 H, Ar *o*-Hs), 7.34 (d, J = 10 Hz, 2 H, Ar *m*-Hs), 6.28 (dd, J = 10 Hz, 6 Hz, 1 H, CH=), 5.90 (d, J = 10 Hz, 1 H, =CH), 4.28 (s, 1 H, $CHOSO_2$), 2.47 (s, 3 H, *p*-CH_3), 2.09 (m, 1 H, =CCH), 1.82 (m, 1 H, CH_2), 1.4–1.6 (m, 2 H, CH_2), 1.2 (m, 1 H, CH_2), 1.06 (s, 3 H, CH_3), 0.82 (s, 3 H, CH_3). Anal. Calcd for $C_{17}H_{22}O_4S$: C, 63.33; H, 6.88. Found: C, 63.19; H, 6.97.

8,8-Dimethylbicyclo[3.2.1]oct-3-en-2-one (13). To a solution of 0.14 g (0.43 mmol) of tosylate **12** in 1 mL of 1,2-dimethoxyethane (DME) was added 50 mg (1 mmol) of NaH (50% dispersion in oil), and the mixture was stirred at 25 °C for 2 h. The mixture was diluted with ether, washed with H_2O and brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 42 mg (64% yield) of enone **13** as an oil: IR (neat) 1700, 1600; ^1H NMR ($CDCl_3$) δ 7.11 (dd, J = 10 Hz, 6.7 Hz, 1 H, =CH), 5.95 (dd, J = 10 Hz, 2 Hz, 1 H, O=CCH=), 2.4–2.1 (m, 4 H), 1.4–1.6 (m, 2 H), 1.10 (s, 3 H, CH_3), 1.0 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 204 (s, C=O), 155 (d, =CH), 127.7 (d, =CH), 60.4 (d, CHC=O), 48.4 [s, $C(CH_3)_2$], 47.4 (d, CH), 28.4 (t, CH_2), 26.0 (t, CH_2), 23.6 (q, CH_3), 20.9 (q, CH_3). Anal. Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.39. Found: C, 79.81; H, 9.53.

***exo*-5,5-Dimethyl-1-methoxy-6-[(methylsulfonyl)oxy]bicyclo[2.2.2]-2-octene (15).** To a solution of 0.5 g (2.7 mmol) of exo alcohol **5** in 10 mL of ether at 0 °C under argon were added 2 mL of Et_3N and 0.65 g (5.6 mmol) of methanesulfonyl chloride. The mixture was stirred at 25 °C for 24 h, then poured into H_2O, and extracted with ether three times. The combined ether extract was washed with 1 N HCl, aqueous $NaHCO_3$, and brine, dried ($MgSO_4$), and concentrated to give 0.6 g (85% yield) of mesylate **15**: IR (neat) 1620, 1370, 1190; ^1H NMR ($CDCl_3$) δ 6.40 (dd, J = 10 Hz, 6.8 Hz, 1 H, =CH), 6.14 (d, J = 10 Hz, 1 H, =CH), 4.18 (d, J = 2.5 Hz, 1 H, $CHOSO_2$), 3.40 (s, 3 H, CH_3O), 3.08 (s, 3 H, CH_3S), 2.1 (m, 1 H, CH), 2.0 (m, 1 H, CH_2), 1.8 (m, 1 H, CH_2), 1.4 (m, 1 H, CH_2), 1.2 (m, 1 H, CH_2), 1.1 (s, 3 H, CH_3), 1.0 (s, 3 H, CH_3). Anal. Calcd for $C_{12}H_{20}O_4S$: C, 55.36; H, 7.74. Found: C, 55.41; H, 7.71.

Rearrangement Reaction of Mesylate 15 with NaI. A solution of 0.6 g (2.3 mmol) of mesylate **15** and 1.7 g (11.5 mmol) in 20 mL of *N,N*-dimethylformamide (DMF) under argon was stirred and heated to 70 °C for 10 h. The solution was poured into H_2O and the mixture extracted three times with ether. The combined extracts were washed with H_2O twice and then with brine, dried ($MgSO_4$), concentrated, and column chromatographed to give 0.283 g (82% yield) of ketone **8**.

***endo*-5,5-Dimethyl-1-methoxy-6-[(methylsulfonyl)oxy]-bicyclo[2.2.2]-2-octene (16).** To a solution of 1.0 g (5.5 mmol) of endo alcohol **6** and 2.4 mL (16.5 mmol) of triethylamine in 20 mL of CH_2Cl_2 at 0 °C under argon was added 0.95 g (8.25 mmol) of methanesulfonyl chloride. The mixture was stirred at 25 °C for 24 h and then poured into H_2O and the mixture extracted three times with ether. The combined extracts were washed with 0.5 N HCl, aqueous $NaHCO_3$, and brine, dried ($MgSO_4$), concentrated, and column chromatographed to give 1.144 g (80% yield) of mesylate **16**: IR (neat) 1620, 1355, 1175; ^1H NMR ($CDCl_3$) δ 6.41 (dd, J = 8.7 Hz, 6.6 Hz, 1 H, =CH), 6.08 (d, J = 8.7 Hz, 1 H, =CH), 4.33 (s, 1 H, CHOS), 3.37 (s, 3 H, OCH_3), 3.05 (s, 3 H, CH_3S), 2.13 (m, 1 H), 1.89 (m, 1 H), 1.69 (td, J = 12.4 Hz, 2.6 Hz, 1 H), 1.4 (m, 1 H), 1.18 (m, 1 H), 1.16 (s, 3 H, CH_3), 0.95 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 135.98 (d, =CH), 127.94 (d, =CH), 91.24 (d, CHOS), 79.0 (s, CO), 50.97 (q, OCH_3), 42.12 (q, CH_3), 41.11 (s, CCH_3), 38.23 (d, CHC=), 28.36 (q, CH_3), 25.91 (q, CH_3), 23.54 (t), 21.56 (t).

Reaction of Mesylate 16 with NaI. Formation of Enone 13. A solution of 0.30 g (1.15 mmol) of mesylate **16** and 1.73 g (11.5 mmol) of NaI in 20 mL of DMF was heated at 90 °C for 12 h under argon. The solution was poured into H_2O and extracted three times with ether. The combined extracts were washed with H_2O and brine, dried ($MgSO_4$), concentrated, and column chromatographed to give 0.155 g (90% yield) of enone **13**.

7-Chloro-7-cyano-6,14-*endo*-ethenotetrahydrothebaine (17a and 17b).[12] The reported procedure[12] wass modified by heating a solution of 2.0 g (6.4 mmol) of thebaine (**18**) and 1.12 g (0.0128 mol) of 2-chloroacrylonitrile in 20 mL of benzene in a sealed tube for 2 h at 170 °C. The solution was concentrated and column chromatographed to give 1.7 g (65% yield) of endo cyanide **17a** and 0.84 g (33% yield) of exo cyanide **17b**.

17a: mp 172–173 °C (lit.[12] mp 172–174 °C); IR (CH_2Cl_2) 2304, 1625, 1600; ^1H ($CDCl_3$) δ 6.66 (d, J = 8 Hz, 1 H, CH Ar), 6.57 (d, J = 8 Hz, 1 H, CH Ar), 5.86 (dd, J = 9 Hz, 1.5 Hz, 1 H, CH=), 5.61 (d, J = 9 Hz, 1 H, =CH), 5.06 (d, J = 1.5 Hz, 1 H, CHO), 3.88 (d, J = 14.8 Hz, 1 H, CH_2N), 3.84 (s, 3 H, OCH_3 Ar), 3.83 (s, 3 H, OCH_3), 3.23 (d, J = 18.6 Hz, 1 H, CHN), 3.18 (d, J = 6.6 Hz, 1 H, CHN), 2.56 (dd, J = 12 Hz, 5 Hz, 1 H, CHAr), 2.4–2.5 (m, 2 H, CH_2), 2.35 (s, 3 H, CH_3N), 2.23 (dt, J = 13 Hz, 5.5 Hz, 1 H, CH), 2.05 (d, J = 14.8 Hz, 1 H, CH_2N), 1.98 (dd, J = 13 Hz, 2.5 Hz, 1 H, CH); ^{13}C NMR ($CDCl_3$) δ 147.4 (s), 142.2 (s), 136.8 (d), 133.8 (s), 127.4 (s), 124.9 (d), 120.1 (d), 119.1 (s, CN), 114.4 (d), 91.7 (d), 82.2 (s), 59.5 (q, OCH_3), 58.6 (s), 56.8 (q, OCH_3), 54.9 (d), 46.7 (s), 45.5 (t), 45.1 (t), 43.4 (q, NCH_3), 42.8 (s), 32.2 (t), 22.3 (t).

17b: ^1H NMR ($CDCl_3$) δ 6.65 (d, J = 8 Hz, 1 H, CH Ar), 6.56 (d, J = 8 Hz, 1 H, CH Ar), 6.05 (d, J = 9 Hz, 1 H, CH=), 5.72 (d, J = 9 Hz, 1 H, =CH), 5.17 (s, 1 H, CHO), 3.85 (s, 3 H, OCH_3 Ar) 3.83 (s, 3 H, OCH_3), 3.45 (d, J = 14.7 Hz, 1 H, CH_2N), 3.23 (d, J = 18 Hz, 1 H, CHN), 3.20 (d, J = 5.4 Hz, 1 H, CH Ar), 2.6–2.3 (m, 5 H), 2.35 (s, 3 H, NCH_3), 1.83 (d, J = 10.9 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 147.4 (s), 142.3 (s), 139.9 (d), 133.9 (s), 127.4 (s), 125.8 (d), 120.0 (d), 119.2 (s, CN), 114.4 (d), 91.6 (d), 82.2 (s), 61.7 (s), 59.5 (q, OCH_3), 56.8 (q, OCH_3), 55.7 (d), 45.5 (t), 45.2 (t), 44.8 (s), 43.4 (q, NCH_3), 42.8 (s), 32.1 (t), 22.3 (t).

6,14-*endo*-Etheno-7-oxotetrahydrothebaine (19).[7] A mixture of **17a** and **17b** was allowed to react with aqueous NaOH–EtOH at 95 °C for 14 h as in the reported procedure,[7] providing ketone **19** (65% yield) as white crystal: mp 192–194 °C (lit.[7] mp 190–192 °C); IR (Nujol) 1730; ^1H NMR ($CDCl_3$) δ 6.65 (d, J = 8 Hz, 1 H, CH Ar), 6.59 (d, J = 8 Hz, 1 H, CH Ar), 5.89 (d, J = 9 Hz, 1 H, =CH), 5.69 (d, J = 9 Hz, 1 H, CH=), 4.67 (s, 1 H, CHO), 3.83 (s, 3 H, OCH_3 Ar), 3.63 (s, 3 H, OCH_3), 3.31 (d, J = 7 Hz, 1 H, CHN), 3.23 (d, J = 19 Hz, 2 H, CHN), 2.6–2.4 (m, 3 H), 2.38 (s, 3 H, NCH_3), 2.17 (d, J = 19 Hz, 1 H, CHN), 2.06 (dt, J = 13 Hz, 6 Hz, 1 H), 1.87 (dd, J = 13 Hz, 2.5 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 208.0 (s, C=O), 148.2 (s), 142.2 (s), 138.8 (d), 133.6 (s), 127.6 (s), 124.4 (d), 119.8 (d), 113.5 (d), 90.9 (d, CHO), 88.3 (s, CO), 59.5 (d, CHN), 56.4 (q, OCH_3), 53.9 (q, OCH_3), 47.7 (s), 45.4 (s), 43.7 (t), 43.5 (t), 39.0 (q, NCH_3), 32.0 (t), 21.8 (t).

6,14-*endo*-Etheno-7α-hydroxytetrahydrothebaine (20). To a solution of 0.35 g (1 mmol) of ketone **19** in 4 mL of THF at 0 °C under argon was added 2.5 mL (2.5 mmol) of potassium tri-*sec*-butylborohydride (K-Selectride, 1 M in THF), and the solution was stirred at 25 °C for 3 h. The solution was poured into aqueous NH_4Cl and extracted three times with CH_2Cl_2. The combined extracts were washed with brine, dried (Na_2SO_4), concentrated, and column chromatographed to give 0.32 g (90% yield) of a single alcohol, **20**; mp 166–167 °C; $[\alpha]^{23}_D$ –212.5° (c 3.85, CH_2Cl_2); IR (Nujol) 3400, 1625, 1620; ^1H NMR ($CDCl_3$) δ 6.61 (d, J = 8.1 Hz, 1 H, CH Ar), 6.50 (d, J = 8.1 Hz, 1 H, CH Ar), 5.87 (d, J = 8.9 Hz, 1 H, =CH), 5.50 (d, J = 8.9 Hz, 1 H, CH=), 5.02 (d, J = 1.3 Hz, CHO), 3.95 (dd, J = 9.8 Hz, 2.3 Hz, 1 H, CHOH), 3.81 (s, 3 H, OCH_3 Ar), 3.59 (s, 3 H, OCH_3), 3.20 (d, J = 18.5 Hz, 1 H, CHN), 3.13 (d, J = 6.5 Hz, 1 H), 2.36–2.60 (m, 5 H), 2.35 (s, 3 H, NCH_3), 1.73 (m, 2 H); ^{13}C NMR ($CDCl_3$) δ 148.5 (s), 142.1 (s), 138.5 (d), 136.5 (s), 128.1 (s), 125.4 (d), 119.1 (d), 113.7 (d), 93.5 (d, CHO), 83.0 (s, CO), 71.82 (d, CHOH), 65.86 (q, CH_3O), 60.24 (q, OCH_3), 56.81 (d, CHN), 53.65 (s), 45.67 (t), 43.69 (t), 43.38 (s), 32.84 (t), 30.89 (q, NCH_3), 22.21 (t). Anal. Calcd for $C_{21}H_{25}NO_4$: C, 70.96; H, 7.09; N, 3.94. Found: C, 70.63; H, 6.73; N, 3.99.

6,14-*endo*-Etheno-7α-[(methylsulfonyl)oxy]tetrahydrothebaine (21). To a solution of 0.4 g (1.1 mmol) of alcohol **20** in 5 mL of CH_2Cl_2 at 0 °C under argon were added 1.6 mL (11 mmol) of triethylamine and 0.38 g (3.3 mmol) of methanesulfonyl chloride. The mixture was stirred at 25 °C for 12 h, then poured into H_2O, and extracted three times with CH_2Cl_2. The combined extracts were washed with brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 0.31 g (65% yield) of mesylate **21** and 0.050 g (13% recovery) of starting alcohol **20**.

21: $[\alpha]^{23}_D$ –122.1° (c 2.9, CH_2Cl_2); IR (neat) 1625, 1600, 1370, 1190; ^1H NMR ($CDCl_3$) δ 6.62 (d, J = 8.1 Hz, 1 H, CH Ar), 6.52 (d, J = 8.1 Hz, 1 H, Ar o-CH to methoxy), 5.84 (d, J = 8.8 Hz, 1 H, =CH), 5.57 (d, J = 8.8 Hz, 1 H, CH=), 4.91 (d, J = 1.4 Hz, CHO), 4.82 (d, J = 9.8 Hz, 1 H, $CHOSO_2$), 3.80 (s, 3 H, OCH_3 Ar), 3.59 (s, 3 H, OCH_3), 3.18 (d, J = 11.9 Hz, 1 H), 3.13 (d, J = 2.5 Hz, 1 H), 3.12 (s, 3 H, CH_3S), 2.88 (d, J = 8.0 Hz, 1 H), 2.34–2.60 (m, 4 H), 2.33 (s, 3 H, CH_3N), 1.95 (dd, J = 11 Hz, 7 Hz, 1 H), 1.76 (d, J = 8 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 148.11 (s, Ar), 142.11 (s, Ar), 139.84 (d), 134.25 (s, Ar), 128.0 (s, Ar), 124.25 (d), 119.49 (d), 113.80 (d), 91.82 (d, CHO), 81.28 (s, CO), 81.0 (d), 59.69 (d), 56.73 (q), 53.49 (q), 46.70 (s), 45.41 (t), 43.50 (q), 43.13 (s), 38.66 (q), 36.61 (t), 31.12 (t), 22.26 (t).

Rearrangement Reaction of Mesylate 21 with NaI–DMF. Formation of Ketone 22. A solution of 0.17 g (0.39 mmol) of mesylate **21** and 0.5 g (3.9 mmol) of NaI in 10 mL of DMF was heated at 75 °C for 15 h under argon. The solution was cooled, poured into H_2O, and extracted three times with CH_2Cl_2. The combined extract was washed with brine, dried (Na_2SO_4), concentrated, and column chromatographed on silica gel to give 0.076 g (60% yield) of ketone **22**: $[\alpha]^{23}_D$ +75.3° (c 1.1, CH_2Cl_2); IR (neat) 1730, 1625, 1600; ^1H NMR ($CDCl_3$) δ 6.72 (d, J = 8.1 Hz, 1 H, m-CH), 6.66 (d, J = 8.1 Hz, 1 H, o-CH), 5.68 (dd, J = 5.5 Hz, 3.4 Hz, CH=), 5.13 (d, J = 5.5 Hz, 1 H, =CH), 4.55 (s, 1 H, CHO), 3.84 (s, 3 H, OCH_3 Ar), 3.33 (d, J = 3.4 Hz, 1 H, CHC=O), 3.28 (d, J = 12 Hz, 1 H), 3.18 (d, J = 6.8 Hz, 1 H), 2.77 (d, J = 11.7 Hz, 1 H), 2.41 (s, 3 H, CH_3N), 2.23–2.61 (m, 4 H), 2.18 (dd, J = 4.2 Hz, J = 2.2 Hz, 1 H), 1.85 (dd, J = 3.7 Hz, J = 2.2 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 197.68 (s, C=O), 145.12 (s, Ar), 142.83 (d), 142.35 (s, Ar), 132.36 (s, Ar), 129.97 (d), 127.64 (s, Ar), 120.22 (d), 114.28 (d), 91.44 (d, CHO), 60.91 (d, CHC=O), 56.71 (q, OCH_3), 55.77 (d, CHN), 52.45 (s), 43.91 (s), 43.52 (q, NCH_3), 45.43 (t), 37.81 (t), 36.69 (t), 23.49 (t). Anal. Calcd for $C_{20}H_{21}O_3N$: C, 74.28; H, 6.55; N, 4.33. Found: C, 73.97; H, 6.30; N, 4.17.

5-Methoxy-2,3,4,7-tetrahydro-1*H*-indene (24). To a cold (–35 °C) solution of 8.0 g (0.054 mol) of 5-methoxyindan, 80 mL of ether, and 80 mL of t-BuOH in 200 mL of liquid NH_3 under argon was added 2.0 g (0.286 mol) of lithium wire. The mixture was refluxed (–35 °C) for 2 h, and 50 mL of aqueous NH_4Cl solution was added carefully. The NH_3 was allowed to evaporate at 25 °C, and the reaction mixture was diluted with H_2O and extracted with ether three times. The combined extracts were washed with H_2O and brine, dried ($MgSO_4$), and concentrated to give 7.29 g (90% yield) of diene **24**: ^1H NMR ($CDCl_3$) δ 4.69 (br s, 1 H, =CH), 3.57 (s, 3 H, OCH_3), 2.72 (m, 4 H), 2.30 (m, 4 H), 1.92 (quintet, J = 6.8 Hz, 2 H). Anal. Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.39. Found: C, 79.81; H, 9.50.

(12) Lewis, J. W.; Readhead, M. J.; Selby, I. A.; Smith, A. C. B.; Young, C. A. *J. Chem. Soc. C* **1971**, 1158.

8-Chloro-8-cyano-5,7a-ethano-5-methoxy-2,3,5,6,7,7a-hexahydro-1*H*-indene (25a, 25b). A solution of 2.0 g (0.013 mol) of diene **24** and 2.3 g (0.027 mol) of 2-chloroacrylonitrile in 20 mL of benzene was heated in a sealed tube at 210 °C for 4 h. The solution was cooled, concentrated, and column chromatographed on silica gel to give 2.45 g (80% yield) of a mixture of **25a** and **25b** (ratio of 2:1; determined by ^{1}H NMR): IR (Nujol) 2240, 1620; ^{1}H NMR ($CDCl_3$) δ 6.05 (s, 1 H, =CH of **25b**), 5.88 (s, 1 H, =CH of **25a**), 3.51 (s, 3 H, OCH_3 of **25a**), 3.50 (s, 3 H, OCH_3 of **25b**), 2.68 (d, J = 14.4 Hz, 1 H), 2.4 (m, 3 H), 2.30 (d, J = 3 Hz, 1 H), 2.0–1.7 (m, 7 H), 1.33 (m, 1 H); ^{13}C NMR ($CDCl_3$) δ **25a** 152.81 (s, =C), 119.78 (s, CN), 117.18 (d, =CH), 82.51 (s, CO), 62.90 (s, CCl), 52.54 (t), 51.73 (q, OCH_3), 43.76 (s), 35.15 (t), 30.38 (t), 30.0 (t), 26.50 (t), 25.91 (t); ^{13}C NMR ($CDCl_3$) δ **25b** 156.04 (s, =C), 120.19 (s, CN), 118.32 (d, =CH), 82.40 (s, CO), 62.87 (CCl), 52.46 (t), 51.41 (q, OCH_3), 43.92 (s), 35.22 (t), 30.47 (t), 30.04 (t), 25.95 (t), 23.86 (t). Anal. Calcd for $C_{13}H_{16}ClNO$: C, 65.68; H, 6.78. Found: C, 65.63; H, 6.97.

5,7a-Ethano-5-methoxy-8-oxo-2,3,5,6,7,7a-hexahydro-1*H*-indene (26). A solution of 9.2 g (0.0387 mol) of **25a** and **25b** and 18.6 g (0.077 mol) of $Na_2S{\cdot}9H_2O$ in 100 mL of ethanol was heated under reflux for 24 h. The solution was poured into 0.5 N HCl and extracted three times with ether. The combined extracts were washed with $NaHCO_3$, H_2O, and brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 5.95 g (80% yield) of ketone **26** as an oil: IR (neat) 1730, 1620; ^{1}H NMR ($CDCl_3$) δ 5.88 (s, 1 H, =CH), 3.51 (s, 3 H, OCH_3), 2.3–2.5 (m, 2 H), 2.20 (d, J = 18 Hz, 1 H), 2.0–1.7 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 210.38 (s, C=O), 155.56 (s, =C), 116.17 (d, =CH), 52.98 (s), 45.19 (q, OCH_3), 37.47 (t), 35.51 (t), 30.61 (t), 30.30 (t), 27.72 (t), 25.85 (t).

5,7a-Ethano-8-hydroxy-5-methoxy-2,3,5,6,7,7a-hexahydro-1*H*-indene (27a, 27b). To a solution of 4.07 g (0.021 mol) of ketone **26** in 50 mL of ether at 0 °C under argon was added 1.14 g (0.030 mol) of lithium aluminium hydride. The mixture was stirred at 0 °C for 1 h and 25 °C for 2 h, and aqueous NH_4Cl was slowly added to the reaction mixture. The mixture was extracted with ether three times, and the combined extracts were washed with H_2O and brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 0.937 g (23% yield) of exo alcohol **27a** (less polar) and 2.81 g (69% yield) of endo alcohol **27b** (more polar).

27a: IR (neat) 3400, 1620; ^{1}H NMR ($CDCl_3$) δ 5.84 (s, 1 H, =CH), 3.80 (dt, J = 10 Hz, 3 Hz, 1 H, CHO), 3.37 (s, 3 H, OCH_3), 2.4–2.2 (m, 3 H), 2.0 (td, J = 11 Hz, 5 Hz, 1 H), 1.8–1.2 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 153.79 (s, C=), 118.1 (d, =CH), 82.44 (s, CO), 71.58 (d, COH), 51.31 (q, OCH_3), 43.76 (s, *C*C=), 39.98 (t), 36.12 (t), 31.40 (t), 30.38 (t), 26.15 (t), 23.07 (t). Anal. Calcd for $C_{12}H_{18}O_2$: C, 74.19; H, 9.34. Found: C, 74.01; H, 9.62.

27b: ^{1}H NMR ($CDCl_3$) δ 5.77 (s, 1 H, =CH), 3.90 (dd, J = 8 Hz, 1 Hz, 1 H, CHO), 3.40 (s, 3 H, OCH_3), 2.5–2.2 (m, 2 H), 2.19 (s, 1 H, OH), 2.02 (dd, J = 13 Hz, 8 Hz, 1 H), 1.8–1.1 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 152.94 (s, C=), 117.01 (d, =CH), 82.12 (s, CO), 73.08 (d, COH), 51.06 (q, OCH_3), 43.53 (s, *C*C=), 42.70 (t), 35.88 (t), 31.41 (t), 30.42 (t), 26.17 (t), 26.06 (t).

5,7a-Ethano-5-methoxy-8-[(methylsulfonyl)oxy]-2,3,5,6,7,7a-hexahydro-1*H*-indene (28b). To a solution of 1.0 g (5.15 mmol) of alcohol **28b** in 2.2 mL (15.5 mmol) of triethylamine and 10 mL of CH_2Cl_2 at 0 °C under argon was added 0.6 mL (7.73 mmol) of methanesulfonyl chloride. The mixture was stirred at 25 °C for 3 h, poured into aqueous NH_4Cl, and extracted three times with ether. The combined extracts were washed with 0.5 N HCl, aqueous $NaHCO_3$, H_2O, and brine, dried ($MgSO_4$), concentrated, and column chromatographed to give 1.26 g (90% yield) of mesylate **28b**: IR (neat) 1620, 1355, 1175; ^{1}H NMR ($CDCl_3$) δ 5.80 (s, 1 H, =CH), 4.84 (dd, J = 9 Hz, 1.5 Hz, 1 H, CHO), 3.39 (s, 3 H, OCH_3), 3.05 (s, 3 H, CH_3S), 2.4 (m, 2 H), 2.22 (dd, J = 12 Hz, 7 Hz, 1 H), 1.7–1.1 (m, 9 H); ^{13}C NMR ($CDCl_3$) δ 152.94 (s, =C), 116.83 (d, =CH), 83.86 (d, CHO), 80.08 (s, CO), 51.16 (q, OCH_3), 43.39 (s, *C*C=), 42.12 (t), 38.52 (t), 35.45 (t), 30.83 (t), 30.40 (t), 26.06 (t, q, 2C). Anal. Calcd for $C_{13}H_{20}O_4S$: C, 57.33; H, 7.40. Found: C, 57.51; H, 7.13.

7-Oxotricyclo[6.2.1.0^{1,5}]-5-undecene (30). A solution of 0.6 g (2.2 mmol) of mesylate **28b** and 3.3 g (2.2 mmol) of NaI in 20 mL of DMF was heated at 90 °C for 2 h under argon. The solution was cooled, poured into H_2O, and extracted three times with ether. The combined extracts were washed with H_2O twice and brine, dried ($MgSO_4$), concentrated, and column chromatographed to give 0.32 g (90% yield) of enone **30**: IR (neat) 1700, 1600; ^{1}H NMR ($CDCl_3$) δ 5.71 (s, 1 H, =CH), 2.9 (m, 1 H, CHC=O), 2.7–1.5 (m, 12 H); ^{13}C NMR ($CDCl_3$) δ 204.13 (s, C=O), 180.46 (s, =C), 118.95 (d, =CH), 53.55 (s, *C*C=), 50.44 (d, *C*HC=O), 44.22 (t), 35.29 (t), 34.70 (t), 32.05 (t), 25.74 (t), 24.58 (t). Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: C, 81.12; H, 8.91.

Reaction of Alcohol 27a with Methanesulfonyl Chloride. Formation of 8-Oxotricyclo[5.3.1.0^{1,5}]-5-undecene (29). To a solution of 0.48 g (2.47 mmol) of exo alcohol **27a** and 1.1 mL (7.4 mmol) of triethylamine in 20 mL of CH_2Cl_2 at 0 °C under argon was added 0.424 g (3.7 mmol) of methanesulfonyl chloride. The mixture was stirred at 25 °C for 2 h, then poured into H_2O, and extracted three times with ether. The combined extracts were washed with 0.5 N HCl, aqueous $NaHCO_3$, and brine, dried ($MgSO_4$), concentrated, and column chromatographed to give 0.26 g (65% yield) of ketone **29**: IR (neat) 1730, 1630; ^{1}H NMR ($CDCl_3$) δ 5.46 (dt, J = 2.8 Hz, 1 H, =CH), 3.15 (t, J = 3.9 Hz, 1 H, =CCHC=O), 2.75 (ddd, J = 17.6 Hz, 8.6 Hz, 8.2 Hz, 1 H, CHC=O), 2.4–1.6 (m, 11 H); ^{13}C NMR ($CDCl_3$) δ 211.27 (s, C=O), 161.42 (s, =C), 117.79 (d, =CH), 61.48 (d, *C*HC=O), 55.67 (s, *C*C=), 48.50 (t), 34.84 (t), 33.83 (t), 29.30 (t), 27.86 (t), 24.02 (t). Anal. Calcd for $C_{11}H_{14}O$: C, 81.44; H, 8.70. Found: 81.21; H, 8.35.

5,7a-Ethano-5-methoxy-8-(methoxycarbonyl)-8-methyl-2,3,5,6,7,7a-hexahydro-1*H*-indene (32a, 32b). A solution of 4.69 g (0.031 mol) of diene **24** and 6.2 g (0.062 mL) of methyl methacrylate in 10 mL of benzene was heated at 250 °C in a sealed tube for 3 days. The solution was cooled, concentrated, and column chromatographed to give 2.80 g (36% yield; less polar) of **32b** and 3.36 g (43% yield; more polar) of **32a**.

32a: IR (neat) 1750, 1620; ^{1}H NMR ($CDCl_3$) δ 6.01 (s, 1 H, =CH), 3.61 (s, 3 H, CO_2CH_3), 3.34 (s, 3 H, OCH_3), 2.2–2.4 (m, 3 H), 1.9–1.6 (m, 9 H), 1.35 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 177.23 (s, C=O), 149.86 (s, C=), 120.95 (d, CH=), 82.48 (s, CO), 51.72 (q, OCH_3), 51.63 (q, OCH_3), 51.33 (s, *C*C=O), 47.48 (t), 43.91 (s, *C*C=), 36.41 (t), 30.41 (t), 30.19 (t), 26.18 (t), 25.89 (t), 21.55 (q, CH_3). Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.77; H, 8.81.

32b: ^{1}H NMR ($CDCl_3$) δ 5.92 (s, 1 H, =CH), 3.69 (s, 3 H, CO_2CH_3), 3.31 (s, 3 H, OCH_3), 2.38 (d, J = 12 Hz, 1 H), 2.33 (td, J = 7 Hz, 2 Hz, 2 H), 1.9–1.6 (m, 7 H), 1.2 (m, 1 H), 1.12 (s, 3 H, CH_3), 0.88 (dd, J = 12 Hz, 3.7 Hz, 1 H); ^{13}C NMR ($CDCl_3$) δ 2.63 (s, C=O), 150.94 (s, =C), 120.39 (d, =CH), 83.21 (s, CO), 52.14 (s, *C*C=), 51.77 (q, OCH_3), 51.63 (q, OCH_3), 46.17 (t), 43.74 (s, *C*C=O), 36.23 (t), 30.48 (t), 30.34 (t), 26.56 (t), 26.12 (t), 23.26 (q, CH_3). Anal. Calcd for $C_{15}H_{22}O_3$: C, 71.97; H, 8.86. Found: C, 71.91; H, 8.95.

5,7a-Ethano-8-(hydroxymethyl)-5-methoxy-8-methyl-2,3,5,6,7,7a-hexahydro-1*H*-indene (33a, 33b). A mixture of 3.10 g (0.0124 mol) of a mixture of **32a** and **32b** and 1.41 g (0.0372 mol) of lithium aluminium hydride in 100 mL of ether was stirred at 25 °C for 2 h under argon. The reaction mixture was quenched by adding aqueous NH_4Cl carefully and then H_2O and extracted three times with ether. The combined extracts were washed with H_2O and brine, dried ($MgSO_4$), and concentrated to give 2.64 g (96% yield) of alcohols **33a** and **33b**: IR (neat) 3400, 1620; ^{1}H NMR δ 6.01 (s, 1 H, =CH, **33a**), 5.95 (s, 1 H, =CH, **33b**), 3.88 (dd, J = 10.5 Hz, 2 H, CH_2O, **33b**), 3.62 (dd, J = 10.5 Hz, 2 H, CH_2O, **33a**), 3.35 (s, 3 H, OCH_3 of **33a** and **33b**), 2.84 (t, J = 10.4 Hz, 1 H), 2.31 (m, 2 H), 1.8–1.0 (m, 9 H), 1.22 (s, 3 H, CH_3 of **33a** and **33b**); ^{13}C NMR ($CDCl_3$) δ **33a** 149.99 (s, C=), 120.91 (d, CH=), 85.88 (s, CO), 72.56 (t, CH_2O), 71.54 (q, CH_3O), 51.13 (s, *C*C=), 46.57 (t), 43.37 (s, *C*CH_3), 36.24 (t), 30.57 (t), 30.25 (t), 26.10 (t), 25.84 (t), 22.69 (q, CH_3); ^{13}C NMR ($CDCl_3$) δ **33b** 150.83 (s, =C), 120.45 (d, =CH), 86.18 (s, CO), 72.25 (t, CH_2O), 70.96 (q, CH_3O), 51.00 (s, *C*C=), 45.99 (t), 43.01 (s, *C*CH_3), 36.31 (t), 30.21 (t), 29.62 (t), 26.06 (t), 25.62 (t), 21.0 (q, CH_3); mass spectrum (EI), m/z 222 (M^+). Anal. Calcd for $C_{14}H_{22}O_2$: C, 75.63; H, 9.97. Found: C, 75.71; H, 9.90.

5,7a-Ethano-5-methoxy-8-methyl-8-[(*N*,*N*,*N*′,*N*′-tetramethylphosphorodiamidoyl)oxy]-2,3,5,6,7,7a-hexahydro-1*H*-indene (34a, 34b). To a solution of 1.37 g (6.17 mmol) of alcohols **33a** and **33b**, 2.7 mL (18.5 mmol) of triethylamine, and 0.376 g (3.1 mmol) of 4-(dimethylamino)pyridine in 10 mL of toluene

under argon was added 1.37 mL (9 mmol) of *N,N,N',N'*-tetramethylphosphorodiamidic chloride. The mixture was stirred at 60 °C for 14 h, diluted with H_2O, and extracted three times with CH_2Cl_2. The combined extracts were washed with 0.5 N HCl, aqueous $NaHCO_3$, H_2O, and brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 1.889 g (86% yield) of **34a** and **34b** as an oil: IR (neat) 1650, 1450, 1290, 990; ^1H NMR ($CDCl_3$) δ 5.95 (s, 1 H, =CH, **34a**), 5.90 (s, 1 H, =CH, **34b**), 3.92 (dd, J = 9.2 Hz, 4 Hz, 1 H, CH_2OP, **34a**), 3.86 (dd, J = 9.2 Hz, 4 Hz, 1 H, CH_2OP, **34a**), 3.77 (dd, J = 9.2 Hz, 4 Hz, 1 H, CH_2OP, **34b**), 3.61 (dd, 1 H, J = 9.2 Hz, 4 Hz, 1 H, CH_2OP, **34b**), 3.28 (s, 3 H, OCH_3, **34a**), 3.27 (s, 3 H, OCH_3, **34b**), 2.68 (s, 3 H, NCH_3, **34a**), 2.67 (s, 3 H, NCH_3, **34a**), 2.654 (s, 3 H, NCH_3, **34a**), 2.64 (s, 3 H, NCH_3, **34a**), 2.650 (s, 3 H, NCH_3, **34b**), 2.628 (s, 3 H, NCH_3, **34b**), 2.626 (s, 3 H, NCH_3, **34b**), 2.60 (s, 3 H, NCH_3, **34b**), 2.3 (m, 2 H), 1.8–1.2 (m, 11 H), 1.13 (s, 3 H, CH_3, **34b**), 0.89 (s, 3 H, CH_3, **34a**); ^{13}C NMR ($CDCl_3$) δ **34a** 150.42 (s, =C), 121.50 (d, =CH), 82.50 (s, CO), 71.06 (t, CH_2OP), 51.36 (s, *C*C=), 45.5 (t), 45.35 (q, OCH_3), 43.64 (s, *C*CH_3), 36.69 (q, NCH_3), 36.61 (q, NCH_3), 36.60 (t), 30.41 (t), 30.22 (t), 26.16 (t), 25.53 (t), 22.72 (q, CH_3); ^{13}C NMR ($CDCl_3$) δ **34b** 150.56 (s, C=), 120.70 (d, =CH), 82.0 (s, CO), 71.84 (t, CH_2OP), 51.23 (s, *C*C=), 45.51 (t), 44.72 (q, OCH_3), 43.84 (s, *C*CH_3), 36.73 (q, NCH_3), 36.66 (q, NCH_3), 36.59 (t), 30.52 (t), 30.22 (t), 30.21 (t), 25.83 (t), 20.65 (q, CH_3).

8,8-Dimethyl-5,7a-ethano-5-methoxy-2,3,5,6,7,7a-hexahydro-1*H*-indene (35). To a cold (−10 °C) solution of 0.34 g (48 mmol) of lithium wire in 30 mL of ethylamine under argon was added a solution of 1.703 g (0.0048 mol) of **34a** and **34b** in 1.8 mL of *t*-BuOH and 6 mL of THF. The solution was stirred at 16 °C for 1.5 h, and aqueous NH_4Cl was added carefully. Ethylamine was allowed to evaporate at room temperature, and the mixture was diluted with H_2O and extracted three times with hexane. The combined extracts were washed with 0.5 N HCl, aqueous $NaHCO_3$, and brine, dried ($MgSO_4$), concentrated, and column chromatographed to give 0.77 g (78% yield) of olefin **35** and 0.19 g (18% yield) of alcohols **33a** and **33b**.

35: IR (neat) 1640; ^1H NMR ($CDCl_3$) δ 5.93 (s, 1 H, =CH), 3.31 (s, 3 H, OCH_3), 2.3 (m, 2 H, CH_2C=), 1.8–1.1 (m, 10 H), 1.01 (s, 3 H, CH_3), 0.79 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 149.71 (s, =C), 121.45 (s, =CH), 83.33 (s, CO), 51.51 (s, *C*C=), 51.08 (q, OCH_3), 50.70 (t), 36.69 (t), 35.83 (s), 30.91 (t), 30.40 (t), 27.97 (t), 26.18 (t), 25.86 (q, CH_3), 25.64 (q, CH_3). Anal. Calcd for $C_{14}H_{22}O$: C, 81.50; H, 10.75. Found: C, 81.62; H, 10.71.

8,8-Dimethyl-5,7a-ethano-4β-hydroxy-5-methoxyoctahydro-1*H*-indene (36). A solution of 1.0 g (4.85 mmol) in 10 mL (9.7 mmol) of borane in THF (1 M solution) under argon was stirred at 25 °C for 24 h and 50 °C for 24 h. To the cold (0 °C) reaction solution were added 15 mL of 1 N NaOH and 10 mL of 30% H_2O_2. The solution was stirred at 25 °C for 20 min, diluted with aqueous NaCl, and extracted with ether three times. The combined extracts were washed with H_2O and brine, dried ($MgSO_4$), concentrated, and column chromatographed to give 1.01 g (93% yield) of alcohol **36** as white crystals: mp 54–55 °C; IR (Nujol) 3500; ^1H NMR ($CDCl_3$) δ 3.81 (dd, J = 6 Hz, 1.6 Hz, 1 H, CHO), 3.42 (s, 3 H, OCH_3), 2.44 (s, 1 H, OH), 2.15–1.2 (m, 13 H), 1.14 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) 81.0 (s, CO), 74.76 (d, CHOH), 53.89 (d), 52.35 (q, OCH_3), 46.64 (t), 40.5 (s), 36.14 (t), 35.6 (s), 32.77 (t), 28.82 (t), 28.36 (t), 25.91 (t), 23.20 (q, CH_3), 17.97 (q, CH_3); mass spectrum (EI), m/z 224 (M^+).

8,8-Dimethyl-5,7a-ethano-5-methoxy-4β-[(methylsulfonyl)oxy]octahydro-1*H*-indene (37). To a solution of 1.23 g (5.49 mmol) of alcohol **36** and 3.2 mL (22 mmol) of triethylamine in 20 mL of CH_2Cl_2 under argon at 0 °C was added 1.26 g (11 mmol) of methanesulfonyl chloride. The mixture was stirred at 25 °C for 1 h, poured into H_2O, and extracted three times with ether. The combined extracts were washed with 0.5 N HCl, aqueous $NaHCO_3$, and brine, dried ($MgSO_4$), concentrated, and column chromatographed on silica gel to give 1.44 g (87% yield) of white solid: mp 97–98 °C; IR (Nujol) 1355, 1175; ^1H NMR ($CDCl_3$) δ 4.72 (dd, J = 5.2 Hz, 1.7 Hz, 1 H, CHOS), 3.40 (s, 3 H, OCH_3), 3.03 (s, 3 H, CH_3S), 2.2–1.2 (m, 13 H), 1.07 (s, 3 H, CH_3), 1.00 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 88.27 (d, $CHOSO_2$), 78.63 (s, CO), 53.46 (d, CH), 52.79 (q, OCH_3), 45.11 (t), 40.49 (s), 37.80 (t), 36.75 (s), 35.79 (t), 32.27 (t), 27.77 (t), 27.06 (t), 26.00 (q, CH_3S), 22.51 (q, CH_3), 18.84 (q, CH_3). Anal. Calcd for $C_{15}H_{26}O_4S$: C, 59.57; H, 8.67. Found: C, 59.50; H, 8.73.

8,8-Dimethyl-4,7a-ethano-5-oxooctahydro-1*H*-indene (23). A solution of 0.36 g (1.19 mmol) of mesylate **37** and 1.79 g (11.9 mmol) of NaI in 20 mL of DMF under argon was heated at 100 °C for 1.5 h. The solution was cooled, poured into H_2O, and extracted three times with ether. The combined extract was washed with H_2O twice and brine, dried ($MgSO_4$), concentrated, and column chromatographed to give 0.149 g (65% yield) of ketone **23** and 42 mg (17% yield) of olefin **35**.

23: IR (neat) 1730; ^1H NMR ($CDCl_3$) δ 2.4 (m, 3 H), 2.0–1.4 (m, 11 H), 1.22 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3); ^{13}C NMR ($CDCl_3$) δ 213.5 (s, C=O), 68.41 (d), 54.92 (d), 53.62 (s), 50.07 (t), 41.9 (s), 36.77 (t), 36.14 (t), 35.70 (t), 32.90 (t), 27.97 (t), 27.88 (q, CH_3), 25.33 (q, CH_3); mass spectrum (EI), m/z 192 (M^+), 177 (M^+ − 15), 149, 135, 121, 107, 93, 85. Anal. Calcd for $C_{13}H_{20}O$: C, 81.20; H, 10.48. Found: C, 81.27; H, 10.40.

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Supplementary Material Available: Fractional coordinates and equivalent isotropic thermal parameters (Table I), anisotropic thermal parameters (Table II), bond distances and bond angles (Tables III and IV), and torsion angles (Table V) (16 pages); F_o and F_c lists for alcohol **36** (20 pages). Ordering information is given on any current masthead page.