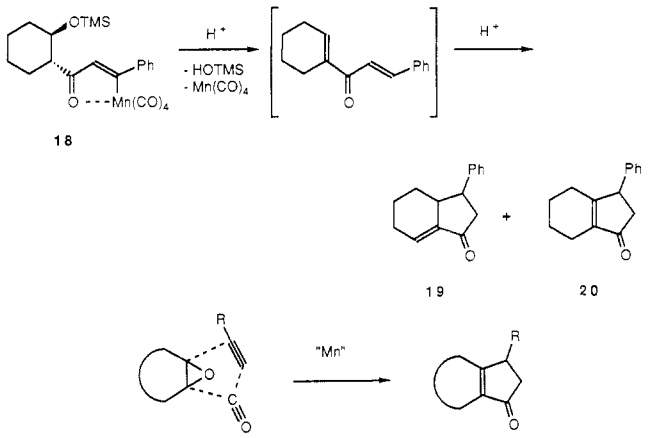
**Scheme IV**




sertion of methyl acrylate at 5 kbar to yield manganacycle **11**.

Alternatively, it was possible to preform the [(silyloxy)alkyl]manganese complex by reacting the epoxide with silylmanganese reagent **7** and then utilize the functionalized alkylmanganese complex for sequential insertion in a separate reaction. For instance, complex **10** was generated and characterized by the treatment of **7** with propylene oxide according to the established protocol.[4] (Silyloxy)manganese complex **10** produced in this manner also underwent sequential insertion to afford manganese complex **11** upon exposure to methyl acrylate at a pressure of 5 kbar. In practice, the simplicity of reagent manipulation and improved yields associated with the in situ procedure made it the method of choice for manganacycle formation.

Epoxide opening by **7** was completely regioselective with monosubstituted epoxides **9** and **12** and afforded adducts arising from attachment of manganese at the less hindered center. Disubstituted epoxide **13**, on the other hand, displayed modest regioselectivity in the reaction with **7**. The major adduct in this case resulted from attack of the metal at the epoxide carbon bearing the methyl group in analogy with the results of Behrens and Sharpless in this system.[7]

Silylmanganese complex **7** is sufficiently oxophilic that it will also cleave less strained ring systems than epoxides. Tetrahydrofuran (Table I, entry 11) and oxetane[4] underwent ring cleavage with **7** to afford the corresponding (silyloxy)manganese pentacarbonyl complexes.

(Silyloxy)manganese complexes resulting from opening of epoxides and tetrahydrofuran by silyl complex **7** were competent to participate in the sequential insertion reaction with either alkenes or alkynes as indicated by the results in the table. They display comparable regioselectivity and stereoselectivity with regard to alkene/alkyne insertion as was observed for simple alkylmanganese pentacarbonyl complexes (see **1**, Scheme I).[3] For example, the in situ opening of tetrahydrofuran by the (trimethylsilyl)manganese complex **7** followed by sequential insertion of methyl acrylate gave unstable manganacycle **14**. An analogous cleavage of tetrahydrofuran by (*tert*-butyldimethylsilyl)manganese pentacarbonyl (**8**)[8] yielded the isolable manganese complex **15** in 55% yield. Manganacycle **16**, the TBS analogue of **14**, was prepared by sequential insertion into **15**.

Manganacycles resulting from sequential insertion of alkenes (entries 1–7, 11, 12; Table I) underwent photoinitiated demetalation by using the established protocol to afford β-hydroxycarbonyl derivatives in moderate yields.[3] The hydroxycarbonyl derivatives arising from demetalation/desilylation of manganacycles **14** and **16**, respectively, cyclized upon exposure to acidic media to give spiroketal lactone **17**.

Acid-catalyzed demetalation of alkyne-derived manganacycles failed to yield the anticipated enone or butenolide derivative; instead, cyclopentenone derivatives were isolated. For example, when manganacycle **18** was subjected to acidic conditions, a mixture of cyclopentenones **19** and **20** (**19**:**20** = 1:2.6) was obtained in 35% yield. Similarly, treatment of manganacycle **21** with acid furnished bicyclic enone **22**. Presumably, the cyclopentenones result from Nazarov cyclization[9] as depicted in Scheme IV involving initial loss of the elements of trialkylsilanol to give a cross-conjugated dienone required for the electrocyclic ring closure. The two-step process of sequential insertion and Nazarov cyclization constitutes a formal cyclopentenone annulation process in which manganese mediates the condensation between an epoxide, carbon monoxide, and an alkyne.

In conclusion, we have demonstrated that the adducts resulting from reaction of (trialkylsilyl)manganese pentacarbonyl complexes with epoxides/cyclic ethers can be utilized for the stereo- and regioselective synthesis of β-hydroxycarbonyl, spiroketal lactone, and cyclopentenone derivatives. The application of this methodology to the total synthesis of natural products will be reported in due course.

**Acknowledgment.** We thank the National Institutes of Health (Grant GM 37014 and AI 23688) for generous financial support. We also thank Dr. Jim Rice for help in obtaining mass spectral data.

(7) Behrens, C. H.; Sharpless, K. B. *J. Org. Chem.* **1985**, *50*, 5696.
(8) Prepared in situ by the reaction of *tert*-butyldimethylsilyl triflate and sodium manganate in pentane at −20 °C.
(9) For a review of the Nazarov cyclization reaction, see: Santelli-Rouvier, C.; Santelli, M. *Synthesis* **1983**, 429. For additional examples of Nazarov cyclization see: (a) Brande, E. A.; Coles, J. A. *J. Chem. Soc.* **1952**, 1430. (b) Hirano, S.; Takagi, S.; Hiyama, T.; Nozaki, H. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 169. (c) Jones, T. K.; Denmark, S. E. *Helv. Chim. Acta* **1983**, *66*, 2377. (d) Jones, T. K.; Denmark, S. E. *Helv. Chim. Acta* **1983**, *66*, 2397.
(10) A description of the high-pressure apparatus can be found in DeShong, P.; Dicken, C. M.; Perez, J. J.; Shoff, R. M. *Org. Prep. Proced. Int.* **1982**, *14*, 369.

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## Cyclopentanoid Synthesis via Directed Cationic Cyclizations. Efficient Generation and Rearrangement of the Intermediate Cyclohexyl Cation

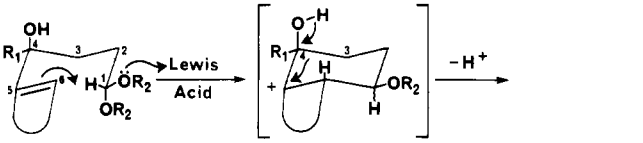
*Summary:* Acyclic acetals in the presence of $SnCl_4$ initiate a cationic cyclization pathway, which is directed to cyclopentanoid ring formation via a pinacol rearrangement step.

*Sir:* Carbocation–olefin cyclizations represent a powerful method to construct 6-membered carbocyclic[1] and 5- to

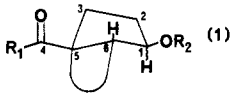
(1) For a recent review, see: Bartlett, P. A. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic: Orlando, 1984; Vol. 3, Chapter 5.

0022-3263/88/1953-4894$01.50/0 

9-membered heterocyclic ring systems.[2,3] In contrast to the rapid developments reported in the oxacyclic field,[3] the direct syntheses of alternate carbocyclic rings remain limited in scope and must rely upon a derived electronic bias to force 5-membered exocyclic ring closure.[1] Our strategy was to take advantage of the preferred endocyclic formation of a cyclohexyl cation[1] and to induce 5-membered ring formation via a pinacol ring contraction step[3c,d,4] (eq 1). If the cyclization of olefin **1** follows the familiar




**1** **2**

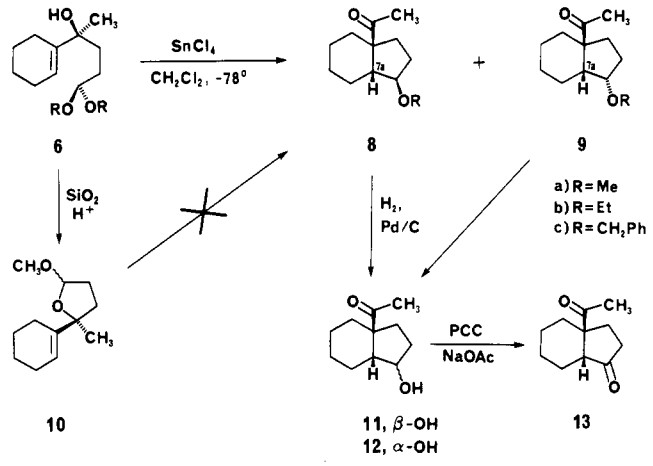


**3** (1)

chairlike antiperiplanar pathway,[1] then the developing carbocation in **2** would adopt a pseudoequatorial position with ideal overlap for a hydroxyl-directed antiperiplanar migration[4] of the C3–C4 ring bond to form cyclopentanoid **3**. In this paper we report that $SnCl_4$-catalyzed reactions of γ-hydroxy-γ-vinylacetals undergo preferential cyclization with the unactivated olefin versus transacetalization, resulting in the formation of cis-fused 3a-acetyl-1-alkoxyperhydroindenes and -pentalenes.[5]

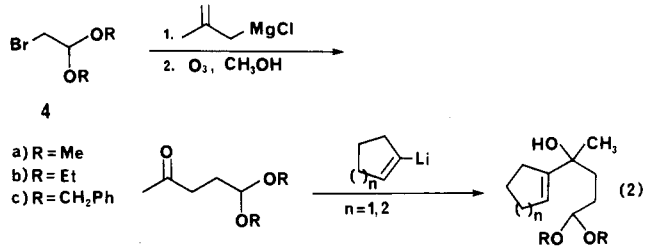
Oxonium cations generated from acyclic acetals have been shown to be useful cyclization initiators for the synthesis of oxacyclic products.[3] Surprisingly, in the carbocyclic area simple acyclic acetals have not been evaluated even though they represent the genesis of all acetal-induced cyclizations.[6] The preparation of acyclic acetal substrates **6**[7] and **7**[7] was readily accomplished by the addition of 1-lithiocyclohexene or 1-lithiocyclopentene[8] to 5,5-dialkoxy-2-pentanones **5**,[7] which were obtained in two steps from the corresponding bromoacetals **4** via a

**Scheme I**




**6** **8** **9** **10** **11**, β-OH **12**, α-OH **13**

Wurtz coupling reaction with methallylmagnesium chloride followed by ozonolysis of the terminal olefin[9,10] (eq 2). These acyclic acetals were not prone to intramolecular transacetalization, and could be readily purified by bulb-to-bulb distillation or by silica gel chromatography.




**4** **5** **6**, n=2 **7**, n=1 (2)

When a 0.03 M solution of dimethyl acetal **6a** in $CH_2Cl_2$ was treated with 1–3 equiv of $SnCl_4$ at −78 °C for 1 h and quenched at this temperature with $Et_3N$ (excess), only unreacted **6a** (>95%) was recovered. Remarkably, transacetalization to cyclic acetal **10**[11] or elimination of the tertiary allylic alcohol was never observed. The addition of excess $SnCl_4$ (4–5 equiv) initiated a facile conversion of **6a** to *cis*-hydroindenes **8a** + **9a**,[7] which were obtained in 40–78% yield (Scheme I). Optimization of the reaction conditions was achieved by employing ~1 equiv of $SnCl_4$ and increasing the dimethyl acetal concentration (~0.11 M), thus after 30 min at −78 °C acetal **6a** provided a 3:2 mixture[12] of *cis*-hydroindenes **8a** + **9a** in 90% isolated yield by simple bulb-to-bulb distillation.[13]

(2) Chamberlin, A. R.; Nguyen, H. D.; Chung, J. Y. L. *J. Org. Chem.* **1984**, *49*, 1682. Speckamp, W. N. *Recl. Trav. Chem. Pays-Bas* **1981**, *100*, 345. Hiemstra, H.; Sno, M. H. A. M.; Vijn, R. J.; Speckamp, W. N. *J. Org. Chem.* **1985**, *50*, 4014 and references therein. Kano, S.; Yokomatsu, T.; Yuasa, Y.; Shibuya, S. *J. Org. Chem.* **1985**, *50*, 3449.

(3) (a) Coppi, L.; Ricci, A.; Taddei, M. *J. Org. Chem.* **1988**, *53*, 911. (b) Perron, F.; Albizati, K. F. *J. Org. Chem.* **1987**, *52*, 4128. (c) Hopkins, M. H.; Overman, L. E. *J. Am. Chem. Soc.* **1987**, *109*, 4748. (d) Herrinton, P. M.; Hopkins, M. H.; Mishra, P.; Brown, M. J.; Overman, L. E. *J. Org. Chem.* **1987**, *52*, 3711. (e) Overman, L. E.; Blumenkopf, T. A.; Castaneda, A.; Thompson, A. S. *J. Am. Chem. Soc.* **1986**, *108*, 3516. (f) Overman, L. E.; Castaneda, A.; Blumenkopf, T. A. *J. Am. Chem. Soc.* **1986**, *108*, 1303. (g) Winstead, R. C.; Simpson, T. H.; Lock, G. A.; Schiavelli, M. D.; Thompson, D. W. *J. Org. Chem.* **1986**, *51*, 275.

(4) For recent examples and leading references, see: Kocovsky, P.; Turecek, F.; Langer, V.; Podlahova, J.; Podlaha, J. *J. Org. Chem.* **1986**, *51*, 4888. Smith, A. B.; Wexler, B. A.; Tu, C.-Y.; Konopelski, J. P. *J. Am. Chem. Soc.* **1985**, *107*, 1308. Heathcock, C. H.; DelMar, E. G.; Graham, S. L. *J. Am. Chem. Soc.* **1982**, *104*, 1907.

(5) Previous investigations in our laboratories on silver(I)-promoted oxy-Cope rearrangements of allylic halides followed this alternate mechanistic pathway, see: Sworin, M.; Lin, K.-C. *J. Org. Chem.* **1987**, *52*, 5640; submitted for publication in *J. Am. Chem. Soc.*

(6) For a discussion of the origins of acetal substrates, see (introductory section): van der Gen, A.; Wiedhaup, K.; Swoboda, J. J.; Dunathan, H. C.; Johnson, W. S. *J. Am. Chem. Soc.* **1973**, *95*, 2656.

(7) All compounds reported were homogeneous by TLC analysis and provided 300-MHz $^1H$ NMR, 75-MHz $^{13}C$ NMR, and IR spectra consistent with the assigned structures. The molecular composition of key compounds was determined by high-resolution mass spectrometry or elemental analysis.

(8) Neumann, H.; Seebach, D. *Chem. Ber.* **1978**, *111*, 2785 and references therein.

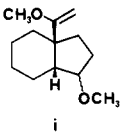
(9) The olefins were prepared via the reported procedure for 5,5-diethoxy-2-methyl-1-pentene. Cf.: Schlosser, M.; Chau, L. V. *Helv. Chim. Acta* **1975**, *58*, 2595.

(10) Ozonolysis was performed at −78 °C in MeOH via the general procedure for 5,5-dimethoxy-2-pentanone (**5a**). Cf.: Odinokov, V. N.; Kukovinets, O. S.; Sakharova, N. I.; Tolstikov, G. A. *Zh. Org. Khim., Eng. Ed.* **1984**, *20*, 1702.

(11) Acetal **10** could be readily prepared by transacetalization with oxalic acid impregnated silica gel. Cf.: Huet, F.; Lechevallier, A.; Pellet, M.; Conia, J. M. *Synthesis* **1978**, 63.

(12) Isomer ratios were determined by capillary GC analysis (15 m × 0.53 mm i.d., 1.5-μm DB-1 film).

(13) In the reverse addition of dimethyl acetal **6a** to $SnCl_4$–$CH_2Cl_2$ we obtained a 90% yield of enol ethers **i**, which could be isolated by bulb-to-bulb distillation.[14] Facile hydrolysis on silica gel or by mild acid-catalyzed hydrolysis conditions provided ketones **8a** + **9a**.

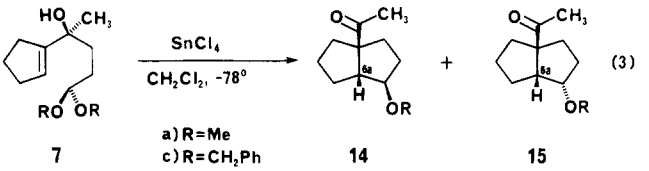


**i**

To examine the possibility that transacetalization of **6a** to cyclic acetal **10**[7,11] was an intermediate step in the cyclization pathway, we subjected acetal **10** to $SnCl_4$ (1 equiv)–MeOH (0.8–1.2 equiv) mixtures in $CH_2Cl_2$ at −78 °C. Only unreacted **10** was obtained in 70–85% yield with no evidence of hydroindenes being detected by $^1H$ NMR and VPC analyses of the crude reaction mixtures. Acetal **10** could not be induced to cyclize under a wide range of reaction conditions,[15] which strongly suggests that the direct cyclization of the Lewis acid mediated oxonium cation of acyclic acetal **6a** initiates the bond-reorganization pathway.

The diethyl **6b** and dibenzyl **6c** acetals also underwent smooth conversion to *cis*-hydroindenes **8** + **9** in 60% and 84% yield, respectively. Since we were unsuccessful in numerous attempts to deprotect the methyl ethers in **8a** and **9a** due to neighboring-group participation of the carbonyl,[16,17] the facile rearrangement of dibenzyl acetal **6c** provided a convenient alternative to the alcohols. Benzyl ethers **8c**[7] and **9c**[7] were readily isolated by chromatographic separation and deprotected by catalytic hydrogenation at 1 atm with 10% Pd/C to give keto alcohols **11**[7] and **12**[7] in >95% yield, respectively. Buffered PCC oxidation of each alcohol provided a single dione **13**[7] in >70% yield. The structural similarity and relative configuration of the 1-alkoxyhydroindenes **8** and **9** were clearly evident from $^{13}C$ NMR spectral data, which exhibited a diagnostic upfield shift (~4.5 ppm) for the C7a resonance of 1α-**9** relative to 1β-**8**.[18-21]

The $SnCl_4$-mediated cyclization of cyclopentene **7a** provided a 2:1 mixture of hydropentalenes **14a** + **15a**[7] in 80% yield after bulb-to-bulb distillation, while dibenzyl acetal **7c** provided essentially a single isomer, 1β-benzyloxy **14c**[7] in 70% yield (eq 3). Stereochemical assignments




7 14 15

were again dictated by the upfield shift of the C6a resonance (Δδ 5.0) in 1α-**15** relative to 1β-**14**.[20]

In summary, we have established that the facile cationic cyclization of oxonium ions generated from acyclic acetals provide an intermediate cyclohexyl cation, which can be directed to the cyclopentanoid ring system via a pinacol rearrangement pathway. The scope, stereochemical criteria, and applications in the natural products area are currently under investigation and will be the subject of future publications.

**Acknowledgment.** We wish to thank Professor L. E. Overman for helpful discussions. NMR spectra were determined with a spectrometer purchased with the assistance of a NSF Instrumentation Grant (CHE-8506671). High-resolution mass spectral determinations were performed by the Midwest Center for Mass Spectrometry, a National Science Foundation Regional Instrumentation Facility.

**Supplementary Material Available:** Spectroscopic data for compounds **6**–**15** and enol ethers i (5 pages). Ordering information is given on any current masthead page.

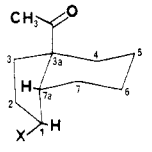
(14) Enamine formation with $SnCl_4$ has been reported, see: Boerth, D. W.; Van-Catledge, F. A. *J. Org. Chem.* **1975**, *40*, 3319. White, W. A.; Weingarten, H. *J. Org. Chem.* **1967**, *32*, 213.

(15) It is likely that the failure of **10** to provide cyclization products reflects the low equilibrium concentration of the oxonium cation formed from Lewis acid mediated opening of the cyclic acetal. An increased stabilization of the initial carbocation could represent an alternate entry to cyclopentanoids, and several systems are currently under investigation.

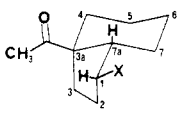
(16) Tardella, P. A.; Campana, F. *Gazz. Chim. Ital.* **1971**, *101* 990. Baddeley, G.; Baylis, E. K.; Heaton, B. G.; Rasburn, J. W. *Proc. Chem. Soc.* **1961**, 451. Baddeley, G.; Heaton, B. G.; Rasburn, J. W. *J. Chem. Soc.* **1961**, 3828 and 3835; **1960**, 4713.

(17) Boron tribromide provided a mixture of 1α-bromohydroindene iii (X = Br) and elimination of MeOH to the $\Delta^{1(7a)}$-hydroindene.

(18) A complete assignment of all $^{13}C$ (and $^1H$) resonances was achieved by 2D-NMR HETCOR and COSY experiments on methoxy ethers **8a** and **9a**, and it was established that C7a, C3, and C7 were all shielded in 1α-iii (X = OMe) by 4.4, 4.2, and 2.7 ppm, respectively. The upfield shift of these resonances reflects a cis-equitorial conformation in 1α-substituted hydroindenes[19] and provides a good correlation with the predicted influence of a 1-hydroxyl group, which can be derived from bicyclo[3.3.0]octane systems,[20] Δδ 5.0, 2.4, 2.6 ppm, respectively.[21]




ii




iii

(19) (a) Lo Cicero, B.; Weisbuch, F.; Dana, G. *J. Org. Chem.* **1981**, *46*, 914. (b) The cis-axial conformation is preferred in most 3a-substituted hydroindenes. For a recent discussion of the substantial discrepancies between calculated and observed equilibrium constants and leading references, see: Peterson, P. E.; Leffew, R. L. B.; Jensen, B. L. *J. Org. Chem.* **1986**, *51*, 1948.

(20) Whitesell, J. K.; Matthews, R. S. *J. Org. Chem.* **1977**, *42*, 3878.

(21) Selective $^1H$ NMR decoupling experiments support the stereochemical assignments, with H1 decoupled ii (X = OMe), 2.39 (apparent t, $J$ = 6 Hz); iii (X = OMe), 2.42 (dd, $J$ = 9, 6 Hz). In conformationally locked *trans*-hydroindenes vicinal couplings of $J$ = 12, 4 Hz are expected, see: Snider, B. B.; Dombroski, M. A. *J. Org. Chem.* **1987**, *52*, 5487.

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