type of calculations: (i) extension of the basis set does not lead to drastic changes in the optimized geometrical parameters characterizing the most important structures. For instance, if EE and EF structures are reoptimized by 4-31G calculations followed by 3 × 3 CI, their energies are only 1.3 (EE) and 1.9 (EF) kcal/mol lower than those gotten by using the geometries optimized with method I (STO-3G + 3 × 3 CI); (ii) whatever the point on the potential energy surface, the most important configurations in the correlated wave function are by far those involved in the limited 3 × 3 CI. Both these factors lead us to think that the use of the rather crude method I as a first approach is a reasonable compromise between the need for qualitatively correct results and the cost of calculations. From a quantitative point of view, calculations of type II, which include a large part of correlation effect, are necessary to be confident in the numerical values used to discuss the reaction mechanisms.

Registry No. Oxirane, 75-21-8.

A New Route to Functionalized *trans*-Hydrindenones

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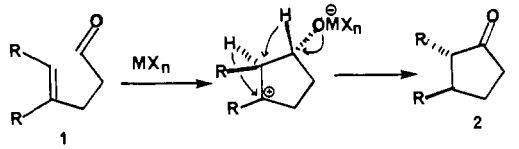
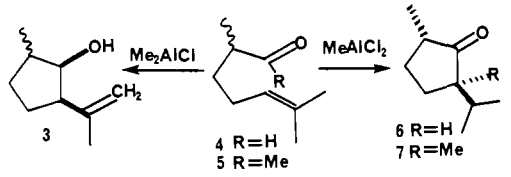
Abstract: $MeAlCl_2$-initiated cyclization of dienone **12** provides the functionalized trans-fused hydrindenone **15** in 50% yield. Ketone **15**, which is now readily available in three steps from hydrocinnamic acid via this novel cyclopentanone synthesis, has been converted to **27** and **30**, thus completing a formal total synthesis of 11-oxo steroids.

Introduction

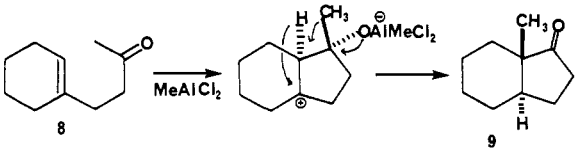
One of the challenging problems in steroid synthesis is the construction of the trans-fused CD ring systems present in most steroids.[1] An examination of Lewis-acid-initiated cyclization of unsaturated carbonyl compounds has led us to a new solution to this problem. Treatment of aldehyde **1** (R = H or alkyl) with a Lewis acid leads to the cyclopentanone **2**.[2,3] We have examined the Lewis-acid-initiated cyclization of **4**.[4] Depending on the strength and amount of Lewis acid, either ene adduct **3**[5] or cyclopentanone **6** can be obtained selectively. $MeAlCl_2$ (1–2 equiv) converts **4** to **6** at −78 °C and converts the ketone **5** to cyclopentanone **7** in 60% yield at 0 °C. We therefore chose to investigate the cyclization of methyl ketones related to aldehyde **1** as a route to trans-fused hydrindanones.





Treatment of the methyl ketone **8**[6] with 2 equiv of $MeAlCl_2$ in CH_2Cl_2 at 25 °C for 24 h leads to the trans-fused hydrindanone **9** in moderate yield. The stereochemistry of **9** is established by the absorption of the methyl group in the NMR spectrum (δ 0.88) which is 0.15 ppm upfield from that of the cis isomer.[7]

The harsh conditions required for this cyclization appeared likely to limit its generality and preclude its application to more highly functionalized systems. We were therefore gratified by the successful cyclization of the unstable dienone **12** to the hydrindenone **15** which is reported here.



Results and Discussion

Birch reduction (Na/NH_3, CH_3OH, −78 to −33 °C)[8] of hydrocinnamic acid (**10**) gives a 60:40 mixture of **11** and **10**. This mixture of acids cannot be separated chromatographically. Iodolactonization (I_2, $NaHCO_3$) of this mixture converts **11** to lactone **13** which is separated from **10** by base extraction of **10**.[8] Treatment of lactone **13** with Zn in acetic acid regenerates **11** (40% overall yield) which is converted to methyl ketone **12** (82% yield) by treatment with 2 equiv of methyllithium.[9] Separation of **10** and **11** is not necessary, since, on treatment with methyllithium, **10** is converted to 4-phenyl-2-butanone which can be separated easily from **15** after cyclization.

The cyclization of **12** to **15** proved to be very sensitive to reaction conditions. Treatment of **12** (0.3 M in CH_2Cl_2 containing 2.7% BHT) with 1.1 equiv of 1.40 M $MeAlCl_2$ in heptane in a sealed tube under N_2 for 2 h at 90 °C gives 15 in 47–53% yield.[10] Small amounts of 4-phenyl-2-butanone (~10%) and polymer account for the remainder of the material. The survival of the sensitive dihydrobenzene moiety indicates the versatility of the cyclopentanone synthesis. Although other Lewis acids were not in-

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(4) (a) Karras, M.; Snider, B. B. *J. Am. Chem. Soc.* **1980**, *102*, 7951. (b) Snider, B. B.; Karras, M.; Price, R. T.; Rodini, D. J. *J. Org. Chem.* **1982**, *47*, 4538.
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(10) The amount of Lewis acid used is not critical. However use of <1 equiv leads to complex mixtures since uncomplexed ketone can abstract a proton from the zwitterionic intermediate. Similarly, use of >2 equiv leads to complex mixtures. $MeAlCl_2$ disproportionates in the presence of a deficiency of base. The active species may be the $AlCl_3$–ketone complex with Me_2AlCl acting as proton scavenger. The presence of traces of water or oxygen has a very deleterious effect on the reaction.

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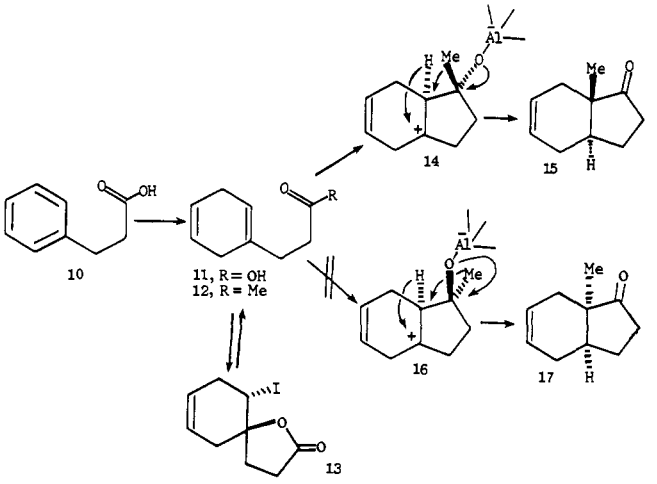
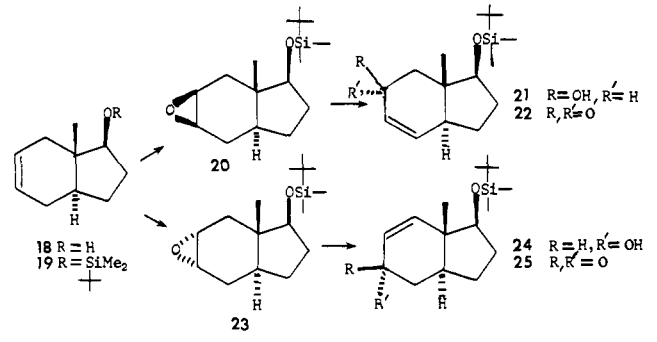


vestigated, $MeAlCl_2$ is probably close to optimal since it is a very strong Lewis acid and a proton scavenger.

Cyclization of **12** can give zwitterionic intermediates **14** and **16** which will undergo hydride and methyl shifts to give **15** and **17**, respectively. It is tempting to explain the virtually exclusive formation of **15** by invoking a preference for concerted hydride and methyl shifts. However, we have established in related systems that hydride shifts are not concerted.[11] Formation of **14** should be preferred since the oxygen–$MeAlCl_2$ complex is bulkier than the methyl group. This may not be significant since zwitterion formation is probably reversible[11] with the initial hydride shift being the rate-determining step.

With **15** now available in three steps from hydrocinnamic acid, its utility as an intermediate for steroid synthesis was briefly explored. Reduction of **15** with sodium borohydride gives **18** (100% yield); *tert*-butyldimethylsilylation[12] of **18** gives **19** (95% yield). The conversion of **19** to **21** and **24** follows procedures developed for 2-cholestene, a molecule with similar steric constraints. Treatment of **19** with *N*-iodosuccinimide in formic acid,[13] followed by saponification and cyclization (K_2CO_3, MeOH),[13] gives a 89% yield of a 9:1 mixture of **20** and **23**. The stereochemistry of the epoxides is established by the chemical shift of the methyl group. In these, and related systems,[14] the methyl group of the β-epoxide absorbs 0.08 ppm downfield. Epoxide **20** is converted to allylic alcohol **21** by Sharpless' procedure ($PhSe^-$, then H_2O_2, Δ)[15] in 45% yield. Oxidation of **21** with buffered pyridinium chlorochromate (PCC)[16] gives enone **22**,[17] mp 35.0–36.0 °C, in 100% yield. Similarly, treatment of **19** with *m*-chloroperbenzoic acid gives **23** in 90% yield which was converted to **25** in 71% yield as described above for the conversion of **20** to **22**.



(11) Snider, B. B.; Rodini, D. J.; Van Straten, J. *J. Am. Chem. Soc.* **1980**, *102*, 5872.
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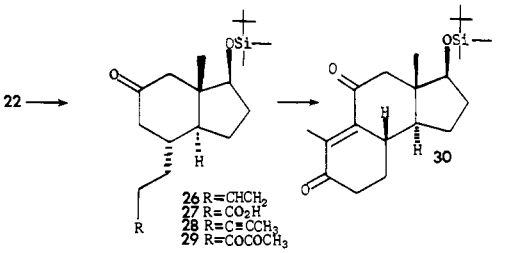
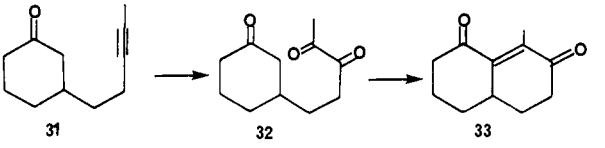
(14) Tori, K.; Komeno, T.; Nakagawa, T. *J. Org. Chem.* **1964**, *29*, 1136.
(15) Sharpless, K. B.; Lauer, R. F. *J. Am. Chem. Soc.* **1973**, *95*, 2697.
(16) Corey, E. J.; Suggs, J. W. *Tetrahedron Lett.* **1975**, 2647.
(17) MnO_2 oxidation gave a mixture of **22** and the cis isomer.

Addition of cuprates to cyclohexenones usually introduces an axial substituent. Stork and Spiess have shown that cuprate additions to *trans*-10-methyl-Δ^3-octal-2-one introduces an equatorial substituent.[18] Addition of the cuprate[19] prepared from 3-butenylmagnesium bromide and $CuI \cdot Me_2S$ to **22** gives a 46% yield of **26**. Oxidation of **26** (RuO_2–$NaIO_4$,[20] then Jones' oxidation) gives acid **27** in 50% yield which is identical with an authentic sample[21] by chromatographic and spectroscopic comparison. Acid **27** has been converted to 11-oxo steroids by a short, elegant route by Stork, Clark, and Shiner.[21]



Enedione **30** (protected as the *tert*-butyl ether) is a key intermediate in a second route to 11-oxo steroids developed by Stork and Logusch.[22] It appeared to be readily accessible from **22** via the conjugate addition of the 3-pentynyl group, oxidation of the triple bond to the dione, and aldol reaction. Since the aldol reaction could give rise to a five- or six-membered ring, model studies were carried out with 2-cyclohexenone. Conjugate addition of the reagent prepared from 3-pentynylmagnesium bromide and $CuI \cdot BF_3$[23] to 2-cyclohexenone gives a 48% yield of **31**. Oxidation of **31** by potassium permanganate in buffered acetone[24] gives diketone **32** (89% yield) which cyclizes to **33** in 79% yield on treatment with dilute aqueous NaOH for 2 h. Polar intermediates are observed by TLC at shorter reaction times. The selective formation of the six-membered ring product is the desired, but unexpected, result of this aldol reaction. One possible explanation is rapid, reversible cyclization followed by a slower dehydration which favors the six-membered ring.

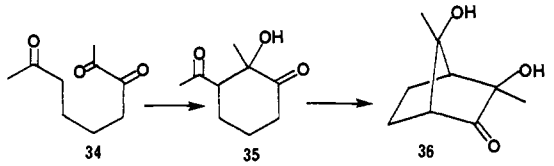


Application of this route to **22** proceeds analogously. Conjugate addition of the reagent prepared from 3-pentynylmagnesium bromide and $CuI \cdot BF_3$[23] to **22** gives a 53% yield (76% based on recovered **22**) of **28**. Oxidation of **28** by potassium permanganate in buffered acetone[24] gives diketone **29** (87% yield) which was cyclized to **30** (73% yield) by treatment with NaOH in aqueous EtOH. The spectral data for **30** corresponds closely to that reported for the *tert*-butyl ether.[22]

The above three-step procedure is a potentially general, new annelation for the conversion of cycloalkenones to annelated en-

(18) Stork, G.; Spiess, E. J., Columbia University, unpublished results. Spiess, E. J. Ph.D. Thesis, Columbia University, 1980. The stereochemistry of **26–29** follows from the chemical shift of the methyl group since introduction of an equatorial methyl group into the octalone results in a 0.09-ppm upfield shift, while an axial methyl group causes a 0.02-ppm downfield shift of the quaternary methyl group.
(19) House, H. O.;Chu, C.-Y.; Wilkins, J. M.; Umen, M. J. *J. Org. Chem.* **1975**, *40*, 1460.
(20) Carlsen, P. H. J.; Katsuki, T.; Martin, V. S.; Sharpless, K. B. *J. Org. Chem.* **1981**, *46*, 3936.
(21) We wish to thank Professor Stork for providing an authentic sample of **27**. (a) Stork, G.; Clark, G.; Shiner, C. S. *J. Am. Chem. Soc.* **1981**, *103*, 4948. (b) Stork, G.; Sherman D. H. *Ibid.* **1982**, *104*, 3758.
(22) (a) Stork, G.; Logusch, E. *J. Am. Chem. Soc.* **1980**, *102*, 1218, 1219. (b) Stork, G.; Winkler, J. D.; Shiner, C. S. *Ibid.* **1982**, *104*, 3767. Logusch, E. W. Ph.D. Thesis, Columbia University, 1979.
(23) (a) Yamamoto, Y.; Maruyama, K. *J. Am. Chem. Soc.* **1978**, *100*, 3240. (b) Schostarez, H.; Paquette, L. A. *Tetrahedron* **1981**, *37*, 4431.
(24) Srinivasan, N. S.; Lee, D. G. *J. Org. Chem.* **1979**, *44*, 1574.

ediones.[25] Unfortunately, the reaction takes a different course with acyclic systems. Treatment of **34** with KOH in methanol gives a low yield of a compound tentatively identified as **36**. The NMR spectrum shows two high-field methyl groups (δ 1.43, 1.60), and the IR spectrum shows a ketone stretch at high frequency (1765 cm^{-1}). Ketone **36** can be formed by two sequential aldol reactions. The first aldol reaction gives **35**. The second aldol reaction can occur in this case, but not in those cases discussed above, owing to the flexibility of the monocyclic intermediate.



34 35 36

Conclusion

We have established that this Lewis-acid-initiated synthesis of cyclopentanones tolerates sensitive functionality and that the products can be converted to useful intermediates for steroid synthesis. Application of this method to the synthesis of other ring systems and development of more general syntheses of the required γ,δ-unsaturated ketones is in progress.

Experimental Section

NMR spectra were taken on Perkin-Elmer R-32, Varian EM390, and Bruker WH-90 spectrometers. IR spectra were recorded on a Perkin-Elmer 683 spectrometer. Mass spectra were recorded on a DuPont 21-490 spectrometer. GC analyses were carried out on a 10 ft × $^1/_4$ in., 10% carbowax 20M on Chromosorb PNAW column at a flow rate of 50 mL/min. CH_2Cl_2 was dried by distillation from CaH_2. Combustion analyses were performed by Galbraith Laboratories.

Me_2AlCl (1.14 M in heptane) and $MeAlCl_2$ (1.40 M in heptane) were obtained from Texas Alkyls, Inc. $MeAlCl_2$ was also made by adding 18.1 mL of 1.14 M (14.6% w/w) Me_2AlCl in heptane (20.4 mmol) to 2.72 g of $AlCl_3$ (20.4 mmol) under N_2.[26] The mixture was heated at 80 °C until all the $AlCl_3$ dissolved. Dry heptane (17.6 g) was added to give a solution which was 13.9% w/w $MeAlCl_2$ in heptane. The density was determined to be 0.75 g/mL. Therefore the concentration is 0.92 M.

Starting Materials. 4-(1-Cyclohexenyl)-2-butanone (**8**) was made by a previously reported procedure.[6] 3-Pentyn-1-yl bromide was prepared from the alcohol by tosylation and displacement of the tosylate with LiBr.[27] 2,3,8-Nonanetrione (**34**) was synthesized as follows. 5-Hexyn-1-ol was converted to the dianion with butyllithium and treated with 1 equiv of methyl iodide and then tosyl chloride to give 5-heptyn-1-yl tosylate. This was converted to the iodide (NaI, acetone) which was coupled with 1-ethoxyvinyllithium in TMF/HMPA[28] to give 2-ethoxy-1-nonen-7-yne. Acid hydrolysis gave the ketone which was oxidized ($KMnO_4$ in buffered acetone[24]) to give **34**.

Cyclization of 8. A solution of 0.500 g (3.29 mmol) of **8** in 20 mL of CH_2Cl_2 at 0 °C under nitrogen was treated with $MeAlCl_2$ (7.1 mL of 0.92 M in heptane, 6.5 mmol). The solution was stirred for 24 h at 25 °C and worked up to give 0.458 g of crude product which was shown by NMR and GC to be ~60% **9** along with several minor components. Chromatography of 0.273 g of this material on silica gel (9:1 pentane–ether) gave 83 mg (28%) of pure **9**: NMR ($CDCl_3$) δ 0.87 (s, 3); ^{13}C NMR ($CDCl_3$) δ 47.5, 45.8, 35.3, 32.0, 26.2, 25.5, 24.2, 20.9, 12.6; IR (neat) 1740 cm^{-1}; MS *m/e* (rel intensity) 152 (M^+, 15), 110 (11), 109 (11), 108 (18), 97 (15), 96 (39), 95 (23), 81 (100), 68 (33), 67 (54). The ^1H NMR and mass spectral data are in agreement with those reported for the trans isomer.[7,29]

1,4-Cyclohexadienepropanoic acid (11). A 1-L three-necked flask was fitted with a mechanical stirrer, a Dewar condenser and a stopcock adapter connected to a nitrogen line. The flask was flame-dried under nitrogen flow and cooled to −78 °C. Ammonia (500 mL) was distilled from sodium into the flask. Hydrocinnamic acid (**10**) (3.0 g, 20 mmol) and methanol (100 mL) were added to the cooled solution which was stirred until all of the acid had dissolved. Small pieces of cleaned sodium (24.0 g) were added to the cooled solution (−78 °C) over the course of 2 h. An additional 19.0 g of sodium was added (1 h) while the solution was allowed to warm to reflux. Methanol (50 mL) was added to facilitate stirring. Sodium (12 g) was added over the course of 1 h. The reaction was quenched by cautious addition of 10 g of NH_4Cl. The condenser was removed and the ammonia allowed to evaporate under a stream of nitrogen. After 8 h all the ammonia had evaporated; 300 mL of methanol was added to ensure destruction of any excess sodium. The methanol was removed at reduced pressure. The remaining white solid was dissolved in 500 mL of water and carefully acidified to pH 6 with hydrochloric acid. The aqueous solution was extracted three times with 250 mL of ether. The ether layers were combined and extracted three times with saturated $NaHCO_3$ solution. The combined aqueous layers were carefully acidified and extracted with several portions of ether. The combined ether extracts were washed with brine, treated with 0.20 g of BHT, dried (Na_2SO_4), and evaporated to give 1.827 g of crude product which NMR indicated to be a 60:40 mixture of **11**–**10**.

A portion of the preceding mixture (1.727 g) was dissolved in a solution of 2.5 g of $NaHCO_3$ in 50 mL of water. Iodine (1.75 g, 6.9 mmol) was added and the solution was stirred for 15 min. Ether (30 mL) was added and the resulting two-phase mixture was stirred for 1 h. The ether layer was removed, diluted to 80 mL, washed with 10% $NaHSO_3$ and brine, and dried (Na_2SO_4). Evaporation of the solvent gave 2.180 g (7.84 mmol) of **13** as an orange oil: NMR ($CDCl_3$) 5.63 (m, 2), 4.51 (dd, 1, J = 8.0, 6.6 Hz), 3.07–2.00 (m, 8); IR (neat) 3090, 1780, 1655 cm^{-1}.

A solution of **13** (2.10 g, 7.55 mmol) in 30 mL of acetic acid was added to a rapidly stirred suspension of Zn powder (1.48 g, 3.0 equiv) in 30 mL of acetic acid which was cooled in a water bath. An exothermic reaction ensued. After 15 min the mixture was diluted with 200 mL of water and extracted three times with 100 mL of ether. The combined ether extracts were washed with water and saturated $NaHCO_3$ solution. The combined aqueous layers were acidified with 10% hydrochloric acid and extracted three times with 50 mL of ether. The combined ether extracts were washed with water and brine, dried (Na_2SO_4), and evaporated to give 1.15 g (100% from **13**, 38% from **10**) of **11** which contained less than 1% of **10**, mp 48 °C: NMR ($CDCl_3$) δ 8.40 (br s, 1), 5.61 (br s, 2, $W_{1/2}$ = 4 Hz), 5.49 (br s, 1 $W_{1/2}$ = 7 Hz), 2.75 (br s, 4, $W_{1/2}$ = 5 Hz), 2.53–2.27 (m, 4).

4-(1,4-Cyclohexadienyl)-2-butanone (12). Acid **11** (1.0 g, 6.6 mmol) was carefully dried and dissolved under nitrogen in 150 mL of THF in a 500-mL, flame-dried, three-necked flask with addition funnel. The solution was cooled to 0 °C. Methyllithium (9.0 mL of 1.5 M, 13.5 mmol, 2.03 equiv) was added dropwise over 20 min. The solution became cloudy and then homogeneous again. The solution was allowed to warm to 25 °C over 1 h. The reaction mixture was slowly transferred via cannula under positive nitrogen pressure to a rapidly stirred solution of 40 mL of acetic acid in 120 mL of ethyl acetate. The resultant mixture was treated with 200 mL of ether and washed with water (5×), sodium bicarbonate solution (3×), water, and brine. The ether layer was dried (Na_2SO_4) and evaporated to give 0.809 g (5.38 mmol, 82%) of ketone **12** as a light-yellow, air-sensitive oil: NMR ($CDCl_3$) δ 5.67 (br s, 2, $W_{1/2}$ = 4 Hz), 5.40 (br s, 1, $W_{1/2}$ = 6 Hz), 2.62 (br s, 4, $W_{1/2}$ = 5 Hz), 2.58–2.45 (m, 2), 2.33–2.17 (m, 2), 2.13 (s, 3); IR (neat) 3020, 1710, 1645 cm^{-1}; GC (150 °C) t_R 25.2 min (4-phenyl-2-butanone, t_R 4 min).

Cyclization of 12 to 15. A 25-mL reselable tube with screw-type Teflon stopcock and side arm was equipped with a stirring bar and a septum on the side arm. The tube was carefully flame-dried under vacuum and filled with nitrogen via a syring needle connected to a vacuum manifold. Ketone **12** (0.500 g, 3.33 mmol) and BHT (20 mg, 0.09 mmol, 2.7 mol %) were dissolved in 12 mL of CH_2Cl_2 and added via syringe. Nitrogen was bubbled through the solution for 15 min. $MeAlCl_2$ (2.65 mL of 1.40 M in heptane, 3.7 mmol, 1.1 equiv) was added. The tube was sealed and heated at 90–93 °C for 135 min. The tube was cooled and the contents poured into 40 mL of water. 10% Hydrochloric acid (10 mL) was added to dissolve the precipitated alumina. The organic layer was removed and the aqueous layer was extracted with two 20-mL portions of CH_2Cl_2. The combined organic layers were washed with brine, dried (Na_2SO_4), and evaporated in vacuo to give 0.550 g of crude product which NMR and GC indicated to be ~60% **15**. Chromatography on silica gel (9:1 hexane–ether) gave 0.2645 g (53%) of pure **15**: NMR ($CDCl_3$) δ 5.67 (br s, 1), 5.64 (br s, 1), 2.65–1.90 (m, 9), 0.87 (s, 3); ^{13}C NMR ($CDCl_3$) δ 220.8, 125.9, 125.2, 45.8, 41.0, 35.4, 33.4, 27.7, 24.1, 13.1; IR (neat) 3015, 1740, 1635 cm^{-1}; GC (150 °C) t_R 15.8 min. Anal. Calcd for $C_{10}H_{14}O$: C, 79.96; H, 9.39. Found: C, 79.91; H, 9.42.

Reduction of Ketone 15. A solution of 1.237 g (8.23 mmol) of **15** in 50 mL of ethanol was treated with 0.17 g (4.5 mmol, 2.2 equiv) of

(25) For a related annelation procedure to make five-membered ring enediones, see: Danishefsky, S.; Zamboni, R.; Kahn, M.; Etheredge, S. J. *J. Am. Chem. Soc.* **1981**, *103*, 3460.

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$NaBH_4$ in 5 mL of ethanol. The solution was stirred for 4 h and worked up to give 1.269 g (101%) of **18** as white crystals. An analytical sample was prepared by preparative GC: mp 59.5–60.0 °C; NMR ($CDCl_3$) δ 5.66 (br s, 1), 5.64 (br s, 1), 3.78 (dd, 1, $J \simeq 9$, 9 Hz), 2.30–1.30 (m, 10), 0.73 (s, 3); IR (neat) 3360, 3020, 1640 cm^{-1}. Anal. Calcd for $C_{10}H_{16}O$: C, 78.90; H, 10.59. Found: C, 79.01; H, 10.61.

Protection of Alcohol 18. A solution of 1.26 g (8.34 mmol) of **18** in 25 mL of anhydrous DMF was treated with 3.0 g (44 mmol) of imidazole and 3.4 g (22.6 mmol) of *tert*-butyldimethylsilyl chloride. The reaction was stirred for 12 h at 25 °C and worked up to give 2.380 g (108%) of crude **19**. Chromatography on silica gel (6:1 hexane–ether) gave 2.082 g (7.81 mmol, 95%) of pure **19**: NMR ($CDCl_3$) δ 5.65 (br s, 1), 5.62 (br s, 1), 3.69 (dd, 1, $J \simeq 8$, 8 Hz), 2.3–1.2 (m, 9), 0.92 (s, 9), 0.73 (s, 3), 0.04 (s, 6); GC (170 °C) t_R 10.2 min. Anal. Calcd for $C_{16}H_{30}OSi$: C, 72.11; H, 11.35. Found: C, 72.27; H, 11.34.

Preparation of β-Epoxide 20. Silyl ether **19** (1.0 g, 3.75 mmol) was dissolved in 50 mL of chloroform which had been dried by filtration through alumina. *N*-Iodosuccinimide (1.20 g, 4.9 mmol, 1.3 equiv) and formic acid (0.400 g of 88%, ~7.5 mmol, 2.0 equiv) were added. The resultant solution was stirred 13.5 h. An additional 0.30 g of *N*-iodosuccinimide and 0.05 g of formic acid were added and the solution was stirred for 10 h. The reaction mixture was washed with 100 mL of water, 100 mL of saturated bisulfite solution, 100 mL of water, and 100 mL of brine, dried (Na_2SO_4), and evaporated to give the iodoformate as a thick yellow oil. *Note: β-iodoformates are reported to be explosive and should be handled with caution.*[13]

The crude iodoformate was dissolved in 150 mL of methanol, and 28 g of K_2CO_3 was added. An exothermic reaction occurred. After 12 h, the reaction was filtered to remove excess K_2CO_3 and evaporated in vacuo. The residue was taken up in 100 mL of ether which was washed with water, sodium bisulfite solution, and brine, dried (Na_2SO_4), and evaporated in vacuo to give 0.989 g (93%) of a 19:2:1 mixture of **20**, **23**, and **19** as indicated by GC analysis. An analytical sample of **20** was prepared by preparative GC: NMR ($CDCl_3$) δ 3.52 (dd, 1, $J \simeq 8$, 8 Hz), 3.10 (br s, 1), 3.06 (br s, 1), 2.15 (d, 1, $J = 15$ Hz), 2.05–1.15 (m, 8), 0.87 (s, 9), 0.80 (s, 3), 0.05 (s, 6); GC (170 °C) t_R 37.9 min. Anal. Calcd for $C_{16}H_{30}O_2Si$: C, 68.03; H, 10.70. Found: C, 68.27; H, 10.92.

Preparation of Allylic Alcohol 21. Diphenyl diselenide (0.66 g, 2.11 mmol, 1.2 eq) in 10 mL of EtOH was placed in a two-necked 100-mL flask equipped with stirring bar, reflux condenser, and inlet tube with septum. A solution of 0.40 g (10.6 mmol) of $NaBH_4$ in 20 mL of EtOH was added. The solution was stirred for 30 min and treated with 0.967 g (3.42 mmol) of crude β-epoxide **20** in 6 mL of EtOH. The solution was heated at reflux under N_2 for 2 h, cooled to 0 °C, and treated with 15 mL of THF. A total of 5 mL of 30% H_2O_2 was added to the cooled solution in 0.5-mL portions over 40 min. The solution was stirred for 24 h at 25 °C and heated at reflux for 8 h. Normal workup and chromatography on silica gel (4:1 hexane–ether) gave 0.089 g (9%) of recovered β-epoxide **20**, 0.111 g (11%) of a saturated ketone, and 0.402 g (42%) of alcohol **21**: NMR ($CDCl_3$) δ 5.72 (s, 2), 4.31 (m, 1), 3.65 (dd, 1, J = 8, 8 Hz), 2.12–1.38 (m, 8), 0.89 (s, 9), 0.86 (s, 3), 0.06 (s, 6); IR (neat) 3350 cm^{-1}. An analytical sample was prepared by evaporative distillation (120 °C, 0.10 torr). Anal. Calcd for $C_{16}H_{30}O_2Si$: C, 68.03; H, 10.70. Found: C, 67.87; H, 10.56.

The data for the saturated ketone are: NMR ($CDCl_3$) δ 3.79 (dd, 1, J = 8, 8 Hz), 2.48–1.18 (m, 11), 0.89 (s, 9), 0.70 (s, 3), 0.04 (s, 6); IR (neat) 1710 cm^{-1}. The compound is probably 3aβ-methyl-3β-*tert*-butyldimethylsilyloxy-1,2,3,3aβ,4,6,7,7aα-octahydroinden-5-one.

Preparation of Ketone 22. Pyridinium chlorochromate (0.130 g, 0.60 mmol, 1.7 equiv) was added to a suspension of sodium acetate (0.040 g, 0.49 mmol, 1.4 equiv) in a solution of alcohol **21** (0.100 g, 0.35 mmol) in 10 mL of CH_2Cl_2. The mixture was stirred for 70 min, diluted with 10 mL of ether, and filtered through alternate layers of Florisil and Celite. The filter pad was washed with 20 mL of ether and the combined filtrate was evaporated in vacuo to give 0.104 g (105%) of crude **22** which was used without purification. An analytical sample was prepared by evaporative distillation (100 °C, 10 torr): mp 35–36 °C; NMR ($CDCl_3$) δ 6.78 (dd, 1, J = 10, 2 Hz), 5.92 (dd, 1, J = 10, 3 Hz), 3.89 (dd, 1, J = 8, 8 Hz), 2.72–1.19 (m, 7), 0.91 (s, 9), 0.84 (s, 3), 0.05 (s, 6); IR (neat) 3030, 1675 cm^{-1}. Anal. Calcd for $C_{16}H_{28}O_2Si$: C, 68.52; H, 10.06. Found: C, 68.68; H, 10.00.

Oxidation of **21** with MnO_2 gave a ~1:1 mixture of **22** and the cis isomer as determined by analysis of the NMR spectrum. The data for the cis isomer are: NMR ($CDCl_3$) δ 7.02 (br d, 1, J = 10 Hz), 5.82 (dd, 1, J = 10, 3 Hz), 4.13 (dd, 1, J = 8, 8 Hz), 1.03 (s, 3).

Epoxidation of 19. A solution of alkene **19** (0.100 g, 0.375 mmol) in 10 mL of 1,2-dichloroethane was treated with 5 mg of BHT and 0.100 g of *m*-chloroperbenzoic acid (80%, 0.464 mmol, 1.24 equiv) and heated at 60 °C under nitrogen for 70 h. Normal workup gave 0.106 g (100%) of α-epoxide **23**: NMR ($CDCl_3$) δ 3.53 (dd, 1, J = 8, 8 Hz), 3.12 (m, 2), 2.15–1.14 (m, 9), 0.88 (s, 9), 0.70 (s, 3), 0.05 (s, 6); GC (170 °C) t_R 33.6 min. Anal. Calcd for $C_{16}H_{30}O_2Si$: C, 68.03; H, 10.70. Found: C, 68.12; H, 10.82.

Preparation of Allylic Alcohol 24. α-Epoxide **23** (100 mg, 0.354 mmol) was converted to allylic alcohol **24** as previously described for the conversion of **20** to **21**. Chromatography on silica gel (5:1 hexane–ether) gave 0.071 g (71%) of **24**: NMR ($CDCl_3$) δ 6.08 (d, 1, J = 10 Hz), 5.57 (dd, 1, J = 10, 4 Hz), 4.21 (br dd, 1, J = 4, 4 Hz), 3.77 (dd, 1, J = 9, 6 Hz), 2.09–1.16 (m, 8), 0.90 (s, 9), 0.75 (s, 3), 0.05 (s, 6). An analytical sample was prepared by evaporative distillation (120 °C, 0.1 torr). Anal. Calcd for $C_{16}H_{30}O_2Si$: C, 68.03; H, 10.70. Found: C, 68.24; H, 10.90.

Oxidation of Alcohol 24. Oxidation of **24** (0.071 g, 0.251 mmol) as described for **21** gave 0.059 g (84%) of pure **25**. An analytical sample was prepared by evaporative distillation (100 °C, 0.1 torr): NMR ($CDCl_3$) δ 6.10 (d, 1, J = 10 Hz), 5.80 (d, 1, J = 10 Hz), 3.85 (dd, 1, J = 8, 8 Hz), 2.48–1.30 (m, 9), 0.95 (s, 3), 0.90 (s, 9), 0.06 (s, 6); IR (neat) 1680, 1600 cm^{-1}. Anal. Calcd for $C_{16}H_{28}O_2Si$: C, 68.52; H, 10.06. Found: C, 68.61; H, 10.14.

Preparation of 26. A 1.0 M solution of 3-buten-1-ylmagnesium bromide in THF was prepared from 2.03 g of 4-bromo-1-butene and 0.42 g of magnesium with enough THF to make 15 mL of solution. The Grignard reagent (1.14 mL, 1.14 mmol) was added dropwise over 3 min to a solution of 0.108 g (0.57 mmol) of cuprous iodide in 5 mL of dimethyl sulfide and 5 mL of THF at −78 °C. The resulting pale orange solution was stirred 10 min at −78 °C and treated with 0.100 g (0.356 mmol) of enone **22** in 2 mL of THF over 5 min. The solution slowly became green. The solution was warmed to 25 °C over 8 h and worked up to give 0.130 g of crude product. Chromatography on silica gel (10:1 hexane–ether) gave 0.055 g (46%) of **26**: NMR ($CDCl_3$) δ 5.72 (m, 1), 4.98 (br d, 1, J = 18 Hz), 4.95 (br d, 1, J = 10 Hz), 3.77 (dd, 1, J = 8, 8 Hz), 2.62–1.1 (m, 14), 0.89 (s), 0.70 (s, 3), 0.05 (s, 6); ^{13}C NMR ($CDCl_3$) δ 211.3, 138.1, 114.7, 80.0, 53.3, 48.4, 46.8, 46.4, 35.7, 33.7, 31.0, 30.3, 25.7, 23.2, 12.2, 5.0; IR (neat) 3080, 1710, 1640 cm^{-1}. Anal. Calcd for $C_{20}H_{36}O_2Si$: C, 71.37; H, 10.78. Found: C, 71.29; H, 10.90.

Preparation of 27. A solution of 0.048 g of **26** in 1 mL of CCl_4 and 1 mL of CH_3CN was treated with 1.5 mL of water, 0.180 g of sodium periodate, and 1 mg of ruthenium dioxide hydrate and then stirred for 6 days at 25 °C. The solution was extracted with three portions of CH_2Cl_2 which was filtered through Celite and evaporated to give 0.053 g of a mixture of acid and aldehyde. The mixture was dissolved in 5 mL of acetone, and 0.1 mL of Jones' reagent (26.72 g of CrO_3 in 23 mL of H_2SO_4 diluted to 100 mL with water) was added. The solution was stirred for 1 h, diluted with 20 mL of water, and extracted with three portions of CH_2Cl_2 which was filtered through Celite and evaporated to give 0.045 g of crude acid. Chromatography on silica gel (ethyl acetate) gave 0.026 g (52%) of pure **27** as white crystals: mp 118–120 °C; NMR ($CDCl_3$) 3.70 (dd, 1, J = 8, 8 Hz), 2.6–1.22 (m, 14), 0.82 (s, 9), 0.77 (s, 3), 0.05 (s, 6); the 270-MHz NMR spectrum was superposable on that of an authentic sample;[21] ^{13}C NMR ($CDCl_3$) δ 211.0, 178.7, 80.0, 53.2, 48.3, 46.8, 46.1, 35.9, 30.9, 29.2, 25.7, 23.2, 18.0, 12.2, −4.4; IR (KBr) 2950, 2930, 2890, 2855, 3100–2500, 1705, 1700, 1470, 1460, 1415, 1265, 1255, 1220, 1140, 1100, 1060, 1015, 895, 840, 780 cm^{-1}; the IR spectrum was superposable on that of an authentic sample.[21]

Preparation of 31. A slurry of 0.380 g (2.0 mmol) of CuI in 5 mL of THF at −78 °C was treated with 4.0 mL of a 1 M solution of 3-pentyn-1-ylmagnesium bromide in THF. The resulting deep brown solution was stirred for 10 min and treated with 0.25 mL (2.0 mmol) of $BF_3 \cdot Et_2O$. The solution was stirred for 30 min at −78 °C and then treated with a solution of 0.193 g (2.0 mmol) of 2-cyclohexenone in 5 mL of THF over 4 h at −78 °C. The mixture was stirred for 1 h at −78 °C and allowed to warm to 25 °C over 5 h. Normal workup gave 0.272 g of crude **31**. Chromatography on silica gel (6:1 hexane–ether) gave 0.159 g (48%) of pure **31**: NMR ($CDCl_3$) δ 2.52–1.22 (m, 13), 1.75 (t, 3, J = 1 Hz). Anal. Calcd for $C_{11}H_{16}O$: C, 80.44; H, 9.82. Found: C, 80.48; H, 7.93.

Preparation of Trione 32. Alkynone **31** (0.025 g, 0.15 mmol) was dissolved in 5 mL of acetone and 2 mL of a buffer solution prepared from 0.10 g of $NaHCO_3$, 1.0 g of $MgSO_4$, and 20 mL of water. $KMnO_4$ (0.10 g, 0.6 mmol) was added in portions over 5 h to the stirred solution. Normal workup gave 0.027 g (89%) of **32**: NMR ($CDCl_3$) δ 2.75 (t, 2, J = 7 Hz) 2.45–1.25 (m, 11), 2.33 (s, 3); IR (neat) 2930, 2860, 1710, 1450, 1420, 1360, 1230 cm^{-1}.

Cyclization of Trione 32. The crude trione **32** (0.026 g, 0.136 mmol) was dissolved in 15 mL of 0.05 M aqueous NaOH. The solution was stirred for 2 h at 25 °C and extracted with three 30-mL portions of CH_2Cl_2. The organic layer was dried (Na_2SO_4) and evaporated to give 0.053 g of crude product. Thin layer chromatography on silica gel (1:1 hexane–ether) gave 0.018 g (74%) of enedione **33**: NMR ($CDCl_3$) δ 2.65–1.20 (m, 11), 1.87 (d, 3, J = 2.3 Hz); IR (neat) 2940, 2860, 1710, 1680, 1440, 1265, 1135, 1110, 800, cm^{-1}; UV max (EtOH) 256 nm (ε 3550), 203. The data are identical with those previously reported.[22c]

Preparation of 28. A slurry of 0.204 g (1.07 mmol) of CuI in 5 mL of THF at −78 °C was treated with 1.10 mL of a 1.0 M solution of 3-pentyn-1-ylmagnesium bromide in THF. The resulting gray solution was treated with 0.132 mL (1.07 mmol) of $BF_3{\cdot}Et_2O$ over a period of 30 min. The resulting orange solution at −78 °C was treated with 0.080 g (0.285 mmol) of enone **22** in 5 mL of THF in small protions over 6 h. The reaction was warmed slowly to 25 °C over 4 h. Normal workup gave 0.1281 (128%) of crude product. Chromatography on silica gel (6:1 hexane–ether) gave 0.055 g (55%, 76% based on recovered **22**) of **28** and 0.022 g (27%) of recovered **22**.

The data for **28** are: NMR ($CDCl_3$) δ 3.78 (dd, 1, J = 9, 9 Hz), 2.85–1.19 (m, 14), 1.77 (t, 3, J = 1 Hz), 0.88 (s, 9), 0.71 (s, 3), 0.05 (s, 6); IR (neat) 1710 cm^{-1}. An analytical sample was prepared by evaporative distillation (120 °C, 0.1 torr). Anal. Calcd for $C_{21}H_{36}O_2Si$: C, 72.35; H, 10.41. Found: C, 72.07; H, 10.35.

Oxidation of 28. Oxidation of **28** as described above for **31** gave 0.022 g (87%) of **29**: NMR ($CDCl_3$) 3.78 (dd, 1, J = 7, 7 Hz), 2.73 (m, 2), 2.58–1.15 (m, 12), 2.34 (s, 3), 0.88 (s, 9), 0.71 (s, 3), 0.04 (s, 6); IR (neat) 1715 cm^{-1}.

Cyclization of 29. A stirred solution of 0.022 g of diketone in 3 mL of EtOH was treated with 5 drops of 3 M aqueous NaOH. The solution was stirred for 20 min, diluted with water (20 mL), and acidified to pH 7 with dilute hydrochloric acid. The solution was extracted with three portions of CH_2Cl_2 which was dried (Na_2SO_4) and evaporated at reduced pressure to give 0.019 g of crude **30**. Chromatography on silica gel (4:1 hexane–ether) gave 0.012 g (59%) of **30** as white crystals: mp 94.0–95.5 °C; NMR ($CDCl_3$) 3.75 (m, 1), 2.75–1.15 (m, 12), 1.88 (d, 3, J = 2.3 Hz), 0.88 (s, 9), 0.81 (s, 3), 0.06 (s, 6); IR (CCl_4) 2960, 2930, 2860, 1685, 1470, 1460, 1255, 1140, 1110, 840 cm^{-1}; UV max (EtOH) 258 nm (ϵ 4880), 204. The data correspond closely to those of the corresponding *tert*-butyl ether.[22c]

Cyclization of Trione 34. Three drops of 10% aqueous potassium hydroxide solution was added to a solution of trione **34** (29 mg, 0.17 mmol) in MeOH (1 mL). The solution was stirred for 20 min and evaporated in vacuo. The residue was taken up in ether which was filtered through Na_2SO_4 and evaporated to give 16.4 mg of crude product which was ~50% **36**. Chromatography on silica gel (2:1 pentane–ether) gave 4.0 mg (14%) of a pure compound tentatively identified as **36**: NMR ($CDCl_3$) δ 1.60 (s, 3), 1.43 (s, 3); IR (CCl_4) 3600, 1765 cm^{-1}.

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Registry No. 8, 69245-96-1; **9**, 17428-83-0; **10**, 501-52-0; **11**, 85029-28-3; **12**, 85029-29-4; **13**, 85029-30-7; **15**, 85029-31-8; **18**, 85048-00-6; **19**, 85029-32-9; **20**, 85029-33-0; **21**, 85029-34-1; **22**, 85029-35-2; *cis*-**22**, 85029-48-7; **23**, 85081-51-2; **24**, 85029-36-3; **25**, 85029-37-4; **26**, 85029-38-5; **27**, 85081-52-3; **27** (aldehyde), 85029-49-8; **28**, 85029-39-6; **29**, 85029-40-9; **30**, 85029-41-0; **31**, 85029-42-1; **32**, 85029-43-2; **33**, 73922-20-0; **34**, 85029-44-3; **36**, 85029-45-4; 5-hexyn-1-ol, 928-90-5; 5-heptyn-1-yl tosylate, 70396-17-7; 5-heptyn-1-yl iodide, 70396-14-4; 1-ethoxyvinyllithium, 40207-59-8; 2-ethoxy-1-nonen-7-yne, 85029-46-5; 7-nonyn-2-one, 85029-47-6; 4-phenyl-2-butanone, 2550-26-7; 4-bromo-1-butene, 5162-44-7; 2-cyclohexenone, 930-68-7; 3-pentyn-1-yl bromide, 18719-27-2.

Chromyl Complexes in the Direct Epoxidation of Alkenes

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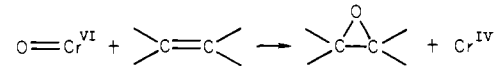
Abstract: Alkenes such as (*E*)- and (*Z*)-β-methylstyrene are converted stereospecifically by dinitratodioxochromium(VI), or chromyl nitrate, to the corresponding epoxide with high selectivities in aprotic media under rather mild conditions. The presence of the cosolvents, *N*,*N*-dimethylformamide (DMF), acetone, pyridine, etc., is critical for effective epoxidation with this reagent. In DMF and pyridine, the epoxide remains generally intact, but in acetone it is transformed to the corresponding alkene ketal which can also be isolated in high yields. The rates of oxidation are evaluated by the competition method, and the relative reactivities of various alkenes toward chromyl nitrate are found to generally parallel those previously determined for other chromyl reagents such as chromic acid, chromyl acetate, and chromyl chloride. Under optimum conditions for epoxidation, chromyl nitrate effects exclusive oxidation of 1,2-diphenylethanol to deoxybenzoin, which is uncontaminated by the usual cleavage products benzaldehyde and benzyl alcohol. Since the latter is known to derive from chromium(IV) intermediates, we conclude that the active species in chromyl epoxidation is oxochromium(V) formed in situ by the prior one-electron oxidation of solvent. The latter is in accord with the efficient transfer of the oxygen atom from macrocyclic oxochromium(V) species previously observed by Groves and co-workers. The ESR spectra of the transient chromium(V) intermediates derived from chromyl nitrate and chromyl acetate by reduction with cosolvent are reported.

Introduction

Chromium(VI) complexes have been extensively used as oxidants in a wide variety of both inorganic and organic systems.[1-4] The presence of at least one oxo–chromium bond, i.e., O=Cr, is the most common feature in such high-valent complexes.[5] Chemical reactivity is frequently centered around this functionality, and the possibility of effecting a direct transfer of the oxygen atom to a donor such as an olefin, e.g.,



represents a synthetically attractive goal and a theoretically challenging transformation.[6,7] Indeed, the oxidation of olefins by various chromium(VI) comlexes has a particularly long and interesting history revolving around the epoxide which has been suspected as the prime intermediate. Although there are some sporadic instances of the isolation of epoxides from the chromi-

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