solvolysis of **1**. The minor product is assigned as 2,5-dimethyl-5-methoxy-4-isopropylidenehexan-3-one (**15**): ir 5.91, 6.10, 7.95, 8.55, 9.35 (strong), and 10.5 μ; nmr τ 8.93 (d, 6, J = 7 Hz), 8.71 (s, 6), 8.42 (s, 3), 8.12 (s, 3), 7.38 (septet, 1, J = 7 Hz), and 6.94 (s, 3).

Rearrangement of 1 with Sodium Methoxide.—To a solution of 1.9 g of metallic sodium in 50 ml of anhydrous methanol was added dropwise a solution of 0.50 g of **1** in 5 ml of methanol. After heating to reflux for 18 hr, the mixture was poured into 100 ml of water and extracted with four 25-ml portions of pentane. The combined pentane extracts were washed with saturated sodium chloride solution and dried. Removal of the solvent by flash evaporation gave 0.38 g of crude oil. Glpc analysis showed three major products as 36, 48, and 8% of the volatile reaction product. No other product amounted to more than 1%. The products were purified by glpc.

The first component (36%) was identified as 2,5-dimethyl-4-isopropyl-1,4-hexadien-3-one (**16**): ir (neat) 6.02, 6.14, and 10.69 μ; nmr τ 9.03 (d, 6, J = Hz, $CH(CH_3)_2$, 8.51 (s, 3), 8.26 (s, 3), 8.15 (m, 3, $H_2C{=}CCH_3$), 7.92 (septet, 1, $CH(CH_3)_2$), and 4.2 (m, 2, $C{=}CH_2$); uv max (hexane) 215 nm (ϵ 2050) and 255 (190). The mass spectrum of **16** shows a molecular ion at m/e 166.

Anal. Calcd for $C_{11}H_{18}O$: C, 79.46; H, 10.91. Found: C, 79.43; H, 10.76.

The second product was identified as 2-isopropylidene-3,3,4,4-tetramethylcyclobutanone (**2**) by comparison with an authentic sample.[4]

The third product was identified as 2,5-dimethyl-4-isopropyl-2-methoxyhex-4-en-3-one (**17**): ir 5.94, 6.09, 8.35, 8.65, and 9.35 μ; nmr τ 8.71 (s, 6, $C(CH_3)_2$), 8.48 (s, 3), 8.29 (s, 3), 7.35 (septet, 1, J = 7.0 Hz, $CH(CH_3)_2$), 9.05 (d, 6, J = 7.0 Hz, $CH(CH_3)_2$), and 6.78 (s, 3, OCH_3). The mass spectrum of **17** shows a molecular ion at m/e 198.

Anal. Calcd for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.72; H, 11.07.

Rearrangement of 1 with *tert*-Butoxide in Benzene.—To a mixture of 1.2 g of potassium *tert*-butoxide and 70 ml of benzene was added a solution of 0.58 g of **1** in 10 ml of benzene. After heating to reflux for 6 hr, the mixture was shaken with 100 ml of water, the layers were separated, and the aqueous layer was extracted with 50 ml of benzene. The benzene layers were combined and dried. Removal of the solvent by flash evaporation gave 0.53 g of crude product. Glpc collection gave three compounds as 7, 10, and 83% of the volatile reaction product.

The first compounds was identified as starting material **1**; the second compound was shown to be ketone **8**. The major product was a new compound assigned as 1-isopropenyl-2-(1-methyl-1-hydroxyethyl)-3,3-dimethylcyclopropene (**19**): ir 2.71, 2.82, 3.20, 5.47, 6.20, and 11.20 μ; nmr τ 8.78 (s, 6, $C(CH_3)_2$), 8.60 (s, 6, $C(CH_3)_2OH$), 8.06 (m, 3, $H_2C{=}CCH_3$), 7.06 (s, 1, OH), 4.91 (m, 2, $C{=}CH_2$); uv max (hexane) 242 nm (ϵ 4475). The mass spectrum of **19** shows a molecular ion at 166.1358 (calcd for $C_{11}H_{18}O$, 166.1358). Similar results were obtained when *tert*-butyl alcohol was used as solvent in place of benzene.

Rearrangement of 1 with Lithium Diethylamide.—To a predried flask were added 50 ml of anhydrous ether, 0.16 g of anhydrous diethylamine, and 1.5 ml of 1.6 N n-butyllithium solution in hexane. The resulting solution was stirred for 30 min under a nitrogen atmosphere, 0.25 g of **1** in 5 ml of ether was added dropwise, and the resulting solution was refluxed for 18 hr. The reaction mixture was poured into 100 ml of water, the layers were separated, and the aqueous layer was washed with 25 ml of ether. The combined ethereal solutions were dried and the ether was removed by flash evaporation to give 0.22 g of crude product. Glpc analysis showed three major components as 11, 57, and 28% of the reaction product. Glpc collection and comparison with known samples showed these to be unreacted epoxide **1**, ketone **8**, and cyclopropenol **19**, respectively. This reaction was repeated under identical conditions on several occasions with varying percentages of **8** (57–90%) and **19** (39–10%) observed.

A second reaction was followed closely by removing aliquots and analyzing by glpc. All of the **1** was gone after 2 hr when the ratio of **8**:**19** was 59:41. Subsequent work-up gave a 75:25 ratio of these same two materials in good yield.

Acid-Catalyzed Rearrangement of 19.—To an 87-mg sample of **19**, in 75 ml of glacial acetic acid, was added 9 drops of concentrated sulfuric acid, and the resulting mixture was stirred for 4 hr, poured into 200 ml of water, and extracted with five 25-ml portions of pentane. The pentane extracts were washed with two 25-ml portions of saturated sodium bicarbonate solution and dried. The solvent was removed by flash evaporation to give 82 mg of crude product. Two products were isolated by preparative glpc as 66 and 34% of the volatile reaction product. The major material was shown to be ketone **18**, and the minor product was the enol acetate of ketone **8** as established by glpc isolation and comparison with authentic materials.[4]

Hydrogenation of 16.—A solution of 50 mg of **16** in 24 ml of methanol was hydrogenated at atmospheric pressure using 30% palladium on charcoal as catalyst. After the uptake of 2 mol of hydrogen, the resulting mixture was filtered to remove the catalyst and the filtrate was poured into 100 ml of water and extracted several times with 25-ml portions of pentane. The pentane extracts were combined and dried. After removal of the solvent, a single product was isolated in almost quantitative yield. Ketone **18** was shown to be 2,5-dimethyl-4-isopropylhex-3-one by comparison with an authentic sample.[4]

Registry No.—**1**, 15448-69-8; **3**, 28054-75-3; **4**, 28054-76-4; **5**, 28054-77-5; **6**, 28054-78-6; **7**, 28054-79-7; **15**, 28054-80-0; **16**, 28054-81-1; **17**, 28054-82-2; **19**, 28054-83-3.

Reductive Elimination of Epoxides to Olefins with Zinc–Copper Couple

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A new direct and single-step reductive elimination of epoxides to olefins by treatment with zinc–copper couple in ethanol is described. The scope and stereochemistry of the reaction have been studied with epoxides of sesquiterpenes, steroids, styrene, stilbenes, and octenes. The reaction has been compared with reductive elimination of epoxides with the Cr^{II}–ethylenediamine complex.

In the course of structural studies of sesquiterpene lactones from *Eupatorium rotundifolium*,[1] an attempt was made to dehydrochlorinate eupachloroxin (**1**) to eupatundin (**2**) with zinc–copper couple in boiling ethanol.[2] The desired product was not obtained, but treatment for 3 days resulted primarily in reductive elimination of the 3,4 epoxide to yield eupachlorin (**3**) as the principal isolable product. Treatment for 4 days resulted in reductive elimination of the epoxide *and* dehydrochlorination to give deoxyeuparotin (**4**) in 31% yield.

(1) S. M. Kupchan, J. E. Kelsey, M. Maruyama, and J. M. Cassady, *Tetrahedron Lett.*, 3517 (1968); S. M. Kupchan, J. E. Kelsey, M. Maruyama, J. M. Cassady, J. C. Hemingway, and J. R. Knox, *J. Org. Chem.*, **34**, 3876 (1969).

(2) J. Elks, G. H. Phillipps, T. Walker, and L. J. Wyman, *J. Chem. Soc.*, 3440 (1956).

TABLE I

REDUCTIVE ELIMINATION OF SESQUITERPENE, STEROID, STYRENE, AND STILBENE OXIDES

Starting material	Reaction time	Product isolated (% yield)
Eupachloroxin (1)	3 days	Eupachlorin (3, 28)
1	4 days	Deoxyeuparotin (4, 31)
Euparotin (5)	3 days	4 (75)
Euparotin acetate (6)	3 days	Deoxyeuparotin acetate (7, 20) + 4 (25)
Eupatundin (2)	5 days	4 (9) + 2 (recovery, 8)
Eupatoroxin (8)	5 days	4 (15) + 2 (27)
10-*epi*-Eupatoroxin (9)	5 days	4 (10) + 2 (10)
Elephantopin (10)	3 days	Deoxydihydroelephantopin (11, 63)
2β,3β-Oxido-22a-5α-spirostan-12-one (12)	10 hr	22a-5α-Spirost-2-en-12-one (13, 88)
16α,17α-Oxido-3α-acetoxy-16β-methyl-5β-pregnane-11,12-dione (14)	2 days	3α-Acetoxy-16-methyl-5β-pregn-16-ene-11,12-dione (15, 75)
Cholesterol α-oxide (16)	3 days	Cholesterol (17, 68)
3α-Acetoxy-11β,12β-oxido-5β-pregnan-20-one (18)	8 days	3α-Acetoxy-11β,12β-oxido-5β-pregnan-20-ol (19, 58) + starting material (18, 9)
Styrene oxide	4 hr	Styrene (90) + ethylbenzene (4)
Styrene oxide	6 hr	Styrene (47) + ethylbenzene (47)
cis-Stilbene oxide	6 hr	*cis*-Stilbene (13) + *trans*-stilbene (80)
trans-Stilbene oxide	6 hr	*trans*-Stilbene (95)

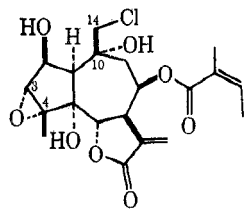
Zinc–copper couple is widely used as a reagent for abstraction of halogen atoms,[3] but our results appear to be the first reported one-step reductive eliminations with zinc–copper couple of an epoxide and a chlorohydrin to yield the corresponding olefins.

To explore the scope of the reductive elimination of epoxides, several other sesquiterpene lactone epoxides[1,4] and steroid epoxides[5] were treated in the same manner. In general, a mixture of the epoxide, zinc–copper couple, and ethanol was heated under reflux for several days. The results are summarized in Table I.

Reductive elimination of the C-3,4 epoxide in eupachloroxin (1) proceeded more rapidly than the dehydrochlorination at C-10,14. However, diepoxides **8** and **9** yielded deoxyeuparotin (4) and eupatundin (2), in which the epoxide at C-3,4 remained intact. The less sterically hindered epoxide at C-10,14 of the sesquiterpenes thus appears to be more reactive than the epoxide at C-3,4. In the case of the steroid derivatives, the epoxide at C-2,3 was most reactive and that at C-11,12, which is sterically hindered, was not reduced. Apparently, styrene oxide was first reduced to styrene and saturation of the terminal double bond followed to give ethylbenzene as a final product. Saturation of the terminal double bond was also observed in the case of elephantopin.

Cis–trans isomerization was not observed when *cis*- or *trans*-stilbene was treated with zinc–copper couple under the same reaction conditions. To explore further the stereochemistry of the reaction, several octene oxides[6] were reduced (Table II). In a typical experiment, a mixture of 2-*cis*-octene oxide, zinc–copper couple, and ethanol was heated in a sealed tube at 140° for 2 days.

The product from 1-octene oxide was *n*-octane, presumably formed *via* epoxide elimination and saturation of the terminal double bond, as observed earlier. Accordingly, zinc–copper treatment of 1-octene yielded *n*-octane in 12% yield. In contrast to the stilbene oxides, reductive elimination of octene epoxides gave mixtures



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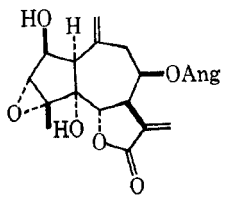

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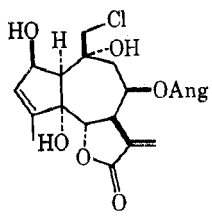

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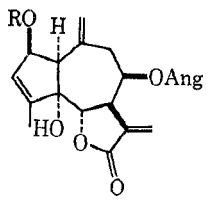
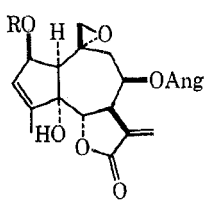
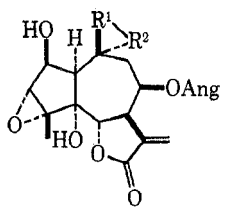


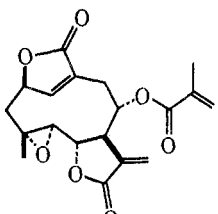
4, R = H
7, R = Ac



5, R = H
6, R = Ac



8, $R^1 = CH_2$; $R^2 = O$
9, $R^1 = O$; $R^2 = CH_2$



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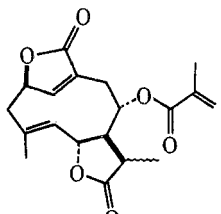

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(3) C. R. Noller, "Organic Syntheses," Collect. Vol. II, Wiley, New York, N. Y., 1943, p 184; T. F. Corbin, R. C. Halm, and H. Shechter, *Org. Syn.*, **44**, 30 (1964).

(4) S. M. Kupchan, J. C. Hemingway, J. M. Cassady, J. R. Knox, A. T. McPhail, and G. A. Sim, *J. Amer. Chem. Soc.*, **89**, 467 (1967); S. M. Kupchan, Y. Aynehchi, J. M. Cassady, A. T. McPhail, G. A. Sim, H. K. Schnoes, and A. L. Burlingame, *ibid.*, **88**, 3674 (1966).

(5) The authors acknowledge with thanks the generosity of Dr. D. Taub, Merck & Co. Inc., in supplying samples of steroid oxides.

(6) J. W. Cornforth, R. H. Cornforth, and K. K. Mathew, *J. Chem. Soc.*, 112 (1959).

TABLE II

REDUCTIVE ELIMINATION OF OCTENE OXIDES

Starting material	Total yield, %	Product (ratio)
1-Octene oxide	25	*n*-Octane
2-*cis*-Octene oxide	8	4-*cis*-Octene (67) + 2-*trans*-octene (33)
2-*trans*-Octene oxide	13	2-*cis*-Octene (39) + 2-*trans*-octene (61)
3-*cis*-Octene oxide	8	3-*cis*-Octene (54) + 3-*trans*-octene (46)
3-*trans*-Octene oxide	33	3-*cis*-Octene (18) + 3-*trans*-octene (82)
4-*cis*-Octene oxide	16	4-*cis*-Octene (55) + 4-*trans*-octene (45)
4-*trans*-Octene oxide	82	4-*cis*-Octene (11) + 4-*trans*-octene (89)

stilbene oxides proceeded rapidly at room temperature, reduction of the epoxides of the octenes and of cholesterol proceeded very slowly under the conditions described earlier.[7] The latter compounds were reduced most effectively at 90° in 4.5–5 hr.

No cis–trans isomerization or saturation of double bonds in olefins with Cr^{II}(en) complex was observed. Both *cis*- and *trans*-stilbene oxides gave mixtures of *cis*- and *trans*-stilbenes in which the trans isomer predominated. The products from *cis*- and *trans*-octene oxides were mixtures of *cis*- and *trans*-octenes, and there appeared to be no stereoselectivity in this reaction. In contrast, limited stereoselectivity *was* observed in the zinc–copper couple reductive eliminations of *cis*- and *trans*-octene oxides.[8]

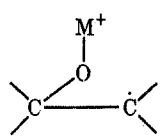
TABLE III

RESULTS OF Cr^{II}(en) REDUCTION

Starting material	Conditions	Product	Yield, %	Isomer ratio—Cis	Isomer ratio—Trans
cis-Stilbene oxide	Room temp, 20 hr	*cis*- and *trans*-stilbenes	80	10	90
trans-Stilbene oxide	Room temp, 20 hr	*cis*- and *trans*-stilbenes	96	7	93
1-Octene oxide	90°, 4.5 hr	1-Octene	49		
2-*cis*-Octene oxide	90°, 4.5 hr	2-*cis*- and -*trans*-octenes	46	62	38
2-*trans*-Octene oxide	90°, 4.5 hr	2-*cis*- and -*trans*-octenes	56	57	43
3-*cis*-Octene oxide	90°, 4.5 hr	3-*cis*- and -*trans*-octenes	43	55	45
3-*trans*-Octene oxide	90°, 4.5 hr	3-*cis*- and -*trans*-octenes	54	52	48
4-*cis*-Octene oxide	90°, 4.5 hr	4-*cis*- and -*trans*-octenes	42	53	47
4-*trans*-Octene oxide	90°, 4.5 hr	4-*cis*- and -*trans*-octenes	52	53	47
Cholesterol α-oxide	90°, 5 hr	Cholesterol	39		

of *cis*- and *trans*-octenes. *cis*-Octenes predominated among the products from *cis*-epoxides and *trans*-octenes predominated from *trans*-epoxides. When *cis*-2-octene was treated under the same conditions, the product, in quantitative yield, was a mixture of 7% of *n*-octane, 80% of 2-*cis*-octene, and 13% of 2-*trans*-octene. 2-*trans*-Octene gave a mixture of 3% of *n*-octane, 7% of 2-*cis*-octene, and 90% of 2-*trans*-octene, in quantitative yield. Some cis–trans isomerization of olefins appears to occur under the reaction conditions.

The zinc–copper couple reductive elimination reaction is presumed to proceed *via* C–O bond cleavage to a radical like **20**. The observed limited stereoselectivity



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in the reduction of octene oxides suggests that the rate of C–C bond rotation in the intermediate may be comparable to the rate of formation of the olefin.

While this work was in progress, the reductive elimination of three epoxides to olefins with Cr^{II}–ethylenediamine complex [Cr^{II}(en)] was reported.[7] To compare this reaction with zinc–copper couple reductive elimination, the reduction of epoxides of stilbenes, octenes, and cholesterol with Cr^{II}(en) complex was carried out (Table III). Whereas reduction of the

(7) J. K. Kochi, D. M. Singleton, and L. J. Andrews, *Tetrahedron*, **24**, 3503 (1968).

Experimental Section

Melting points were determined on a Thomas-Hoover capillary melting point apparatus and are corrected. Values of $[\alpha]_D$ were determined on a Zeiss-Winkel polarimeter and have been approximated to the nearest degree. Ultraviolet absorption spectra were determined on a Coleman Hitachi EPS-3T recording spectrophotometer. Infrared absorption spectra were determined on a Beckman Model 9 recording spectrophotometer. Nmr spectra were determined on Varian A-60 spectrometer. Vapor phase chromatography was carried out on F & M Model 770, 700, and Varian Aerograph Model 1860-1 gas chromatographs. Thin layer chromatography (tlc) was carried out on precoated silica gel and precoated alumina (Brinkmann) plates. Microanalyses were carried out by Spang Microanalytical Laboratory, Ann Arbor, Mich. Petroleum ether refers to the fraction of bp 35–40°. Silica gel refers to silica gel, Merck, 0.05–0.2 mm for column chromatography. Previously known products showed melting points within 2° of the reported values and were identified by mixture melting point, mixture tlc, and ir and nmr spectral comparison with authentic material.

Zinc–Copper Couple Reduction of Eupachloroxin (1). **A.**—A mixture of eupachloroxin (**1**, 20 mg), zinc–copper couple prepared from zinc dust (800 mg), and ethanol (8 ml) was heated under reflux for 3 days. The precipitate was filtered off and the solution was evaporated *in vacuo* to give an oil, which was chromatographed on a silica gel (20 g) column. Elution with chloroform, acetone, and ethanol (85:15:1 vol) gave a crystalline fraction (11 mg). Rechromatography on silica gel (15 g) gave crystals (6 mg), which were recrystallized from methanol to give pure eupachlorin (**3**, 4 mg, 28%).

B.—Eupachloroxin (**1**, 80 mg) was reduced in the same way for 4 days. The product was separated by tlc on silica gel ($CHCl_3$–EtOH 19:1) to give crystals[9] (21 mg, 31%) which were re-

(8) After completion of this work, reductive elimination of epoxides to olefins with magnesium bromide and magnesium amalgam was reported: F. Bertini, P. Grasselli, G. Zubiani, and G. Cainelli, *Chem. Commun.*, 144 (1970).

(9) The homogeneity of crystalline products for which yields are cited was shown to be higher than 90% by nmr spectroscopy.

crystallized from acetone to yield deoxyeuparotin (4), identical with the product from euparotin (5).

Zinc–Copper Couple Reduction of Euparotin (5).—Euparotin (5, 44 mg) was reduced in the same way for 3 days. The product was chromatographed on silica gel (30 g) and elution with chloroform, acetone, and ethanol (85:15:1 vol) gave crystals (32 mg, 75%). Recrystallization from acetone gave deoxyeuparotin (4): mp 200–204°; $[\alpha]^{26}D$ −138.8° (*c* 0.36, MeOH); uv end (MeOH) 210 mμ (ε 18,600); ir (KBr) 5.88 and 5.66 μ.

Anal. Calcd for $C_{20}H_{24}O_6$: C, 66.65; H, 6.71. Found: C, 66.77; H, 6.92.

Zinc–Copper Couple Reduction of Euparotin Acetate (6).—Euparotin acetate (6, 100 mg) was reduced in the same way for 3 days. The product was separated by tlc on silica gel to give high R_f noncrystalline material (25 mg, 25%) and low R_f crystals (18 mg, 20%). The high R_f amorphous material was a homogeneous solid (tlc) and the ir spectrum was identical with that of deoxyeuparotin acetate [Calcd for $C_{22}H_{26}O_7$: mol wt, 446. Found: mol wt (mass spectrum), 446] prepared by acetylation of deoxyeuparotin (4) with acetic anhydride in pyridine. The low R_f crystals were recrystallized from aqueous acetone to give deoxyeuparotin (4, 8 mg).

Zinc–Copper Couple Reduction of Eupatundin (2).—Eupatundin (2, 100 mg) was reduced in the same way for 5 days. The product was separated by tlc on alumina to give high R_f crystals (9 mg, 9%) and low R_f crystals (8 mg, 8%). Recrystallization of the high R_f material from aqueous acetone gave deoxyeuparotin (4, 2 mg). Recrystallization of the low R_f product from a mixture of chloroform, benzene, and petroleum ether gave eupatundin (2, 2 mg).

Zinc–Copper Couple Reduction of Eupatoroxin (8).—Eupatoroxin (8, 100 mg) was reduced in the same way for 5 days. The product was separated by tlc on alumina to give high R_f crystals (14 mg, 15%) and low R_f crystals (26 mg, 27%). Recrystallization of the high R_f product from acetone gave deoxyeuparotin (4, 4 mg). Recrystallization of the low R_f product from a mixture of chloroform, benzene, and petroleum ether gave eupatundin (2, 13 mg).

Zinc–Copper Couple Reduction of 10-Epi-eupatoroxin (9).—10-Epi-eupatoroxin (9, 100 mg) was reduced in the same way for 5 days. The product was separated by tlc on alumina to give high R_f crystals (10 mg, 10%) and low R_f crystals (10 mg, 10%). Recrystallization of the high R_f product from aqueous acetone gave deoxyeuparotin (4, 2 mg). Recrystallization of the low R_f product from a mixture of chloroform, benzene, and petroleum ether gave eupatundin (2, 2 mg).

Zinc–Copper Couple Reduction of Elephantopin (10).—A mixture of elephantopin (10, 300 mg), zinc–copper couple prepared from zinc dust (12 g), and ethanol (150 ml) was heated under reflux for 3 days. The product (280 mg) was chromatographed on acid-washed alumina (100 g, Merck) with alcohol-free chloroform to give homogeneous (tlc, 220 mg) material. Recrystallization from ethanol gave colorless needles of deoxydihydroelephantopin (11, 180 mg, 63%): mp 212–216° dec; $[\alpha]^{22}D$ +13.8° (*c* 1.2, acetone); uv end (MeOH) 210 mμ (ε 17,600); ir (KBr) 5.57, 5.73, 5.82, and 5.84 μ.

Anal. Calcd for $C_{19}H_{22}O_6$: C, 65.88; H, 6.43; mol wt, 346. Found: C, 65.89; H, 5.88; mol wt (mass spectrum), 346.

Zinc–Copper Couple Reduction of 2β,3β-Oxido-22a-5α-spirostan-12-one[10] (12).—2β,3β-Oxido-22a-5α-spirostan-12-one (12, 95 mg) was reduced in the same way for 10 hr. The product (90 mg) was chromatographed on silica gel (30 g) with chloroform containing 1% acetone to give crystals (88 mg, 88%). Recrystallization from ethanol gave 22a-5α-spirost-2-en-12-one[10] (13).

Zinc–Copper Couple Reduction of 16α,17α-Oxido-3α-acetoxy-16β-methyl-5β-pregnane-11,12-dione[11] (14).—16α,17α-Oxido-3α-acetoxy-16β-methyl-5β-pregnane-11,12-dione (14, 100 mg) was reduced in the same way for 2 days. The product was chromatographed on silica gel (50 g) with chloroform, acetone, and ethanol (98:2:0.5 vol) to give crystals (72 mg, 75%). Recrystallization from ethanol gave 3α-acetoxy-16-methyl-5β-pregn-16-ene-11,12-dione (15, 33 mg): mp 167–168.5°; $[\alpha]^{26}D$ +69.5° (*c* 1.90, $CHCl_3$); ir (KBr) 5.75, 5.88, 6.06 μ.

Anal. Calcd for $C_{24}H_{34}O_4$: C, 74.57; H, 8.87; mol wt, 386. Found: C, 74.53; H, 8.96; mol wt (mass spectrum), 386.

(10) H. L. Slates and N. L. Wendler, *J. Amer. Chem. Soc.*, **78**, 3749 (1956).

(11) D. Taub, N. L. Wendler, and R. D. Hoffsommer, Jr., U. S. Patent 3,309,272 (1967); *Chem. Abstr.*, **67**, 3196n (1967).

Zinc–Copper Couple Reduction of Cholesterol α-Oxide (16).—Cholesterol α-oxide (16, 200 mg) was reduced in the same way for 3 days. The product was purified by tlc on silica gel to give crystals (125 mg, 68%). Recrystallization from ethanol gave cholesterol (17, 100 mg).

Zinc–Copper Couple Reduction of 3α-Acetoxy-11β,12β-oxido-5β-pregnan-20-one[12] (18).—3α-Acetoxy-11β,12β-oxido-5β-pregnan-20-one (18, 100 mg) was reduced in the same way for 8 days. The product was chromatographed on silica gel to give starting material (9 mg, 9%) and product (60 mg, 58%), which was recrystallized from petroleum ether to give 3α-acetoxy-11β,12β-oxido-5β-pregnan-20-ol (19, 18 mg): mp 149–151°; $[\alpha]^{26}D$ +14.5° (*c* 1.35, $CHCl_3$); ir (KBr) 2.86, 5.84 μ.

Anal. Calcd for $C_{23}H_{36}O_4$: C, 73.36; H, 9.64; mol wt, 376. Found: C, 73.79; H, 9.53; mol wt (mass spectrum), 376.

Zinc–Copper Couple Reduction of Styrene Oxide. A.—A mixture of styrene oxide (500 mg), zinc–copper couple prepared from zinc dust (8 g), and ethanol (50 ml) was heated under reflux for 4 hr. The precipitate was filtered off, water (20 ml) was added, and the solution was extracted with petroleum ether (15 ml, three times). The combined petroleum ether extract was washed with $CaCl_2$ solution and NaCl solution, and dried (Na_2SO_4). The solution was distilled through a Vigreux column to yield a mixture of styrene (388 mg, 90%) and ethylbenzene (17 mg, 4%). The products were analyzed by vpc with an SE-30 column at 64°.

B.—The reaction was carried out for 6 hr in the same way to give a mixture of styrene (203 mg, 47%) and ethylbenzene (212 mg, 47%).

Zinc–Copper Couple Reduction of Octene Oxides or Octene.—A mixture of octene oxide (1 g, or octene, 1 g), zinc–copper couple prepared from zinc dust (6 g), and ethanol (20 ml) was heated in a sealed tube at 140° for 2 days. After the precipitate was filtered off, the solution was diluted with water (20 ml) and extracted with petroleum ether (15 ml, three times). The combined petroleum ether extract was washed with $CaCl_2$ solution and NaCl solution, dried (Na_2SO_4), and distilled through a Vigreux column. No octene was detected in the distillate. The residue was analyzed by vpc by comparison with standard mixtures of the products with an SE-30 column to determine yield and a β,β-oxydipropionitrile column to determine the ratio of cis and trans isomers.

Zinc–Copper Couple Reduction of Stilbene Oxides.—A mixture of stilbene oxide (196 mg), zinc–copper couple prepared from zinc dust (4 g), and ethanol (50 ml) was heated under reflux for 6 hr. After the precipitate was filtered off, the solution was evaporated to dryness *in vacuo*. The ratio of *cis*- and *trans*-stilbenes in the product was determined by nmr spectroscopy.

Preparation of Cr^{II} Solution.—Chromium pellets (8 g) were treated with concentrated HCl (10 ml) until the reaction began. The pellets were washed well with water and added to water (60 ml) covered with purified nitrogen. Perchloric acid (60%, 30 ml) was added and the mixture was allowed to stand at room temperature under an atmosphere of purified nitrogen. The reagent was ready for use after 2 days.

Cr^{II}(en) Reduction of Stilbene Oxides.—To a mixture of stilbene oxide (100 mg) and dimethylformamide (30 ml) under purified nitrogen, Cr^{II} solution (3 ml) and ethylenediamine (0.1 ml) were added, and the solution was allowed to stand for 20 hr at room temperature. The solution was poured into 2 *N* HCl (20 ml) and the solution was extracted with petroleum ether. The extract was washed with water, dried (Na_2SO_4), and evaporated to give a mixture of stilbenes. The ratio of cis and trans isomers in the product was determined by nmr spectroscopy.

Cr^{II}(en) Reduction of Octene Oxide.—To a mixture of dimethylformamide (30 ml) and octene oxide (100 mg) under purified nitrogen, Cr^{II} solution (3 ml) and ethylenediamine (0.15 ml) were added and the solution was heated at 90° for 4.5 hr. The solution was poured into 2 *N* HCl (20 ml) and separated into two equal portions. One was extracted with petroleum ether (2 ml) after addition of *n*-nonane (50 mg) as a standard, and the petroleum ether extract was analyzed by vpc with an SE-30 column to determine the yield of octenes. The other portion of the aqueous solution was extracted with petroleum ether (2 ml) and analyzed by vpc with a β,β-oxydipropionitrile column to determine the ratio of cis and trans isomers.

(12) P. L. Julian, and A. Magnani, U. S. Patent 2,944,052 (1960); *Chem. Abstr.*, **55**, 1710e (1961).

Cr^{II}(en) Reduction of Cholesterol α-Oxide.—To a solution of cholesterol α-oxide (100 mg) in dimethylformamide (30 ml) under purified nitrogen, Cr^{II} solution (3 ml) and ethylenediamine (0.15 ml) were added. The solution was kept at 90° for 5 hr and then poured into 2 *N* HCl (20 ml). The aqueous solution was extracted with ether (20 ml, three times) and the combined ether extract was washed with water, dried (Na_2SO_4), and evaporated *in vacuo* to dryness. The crystalline residue was chromatographed on silica gel with a mixture of chloroform, acetone, and ethanol (96:4:1, vol) to give 37 mg (39%) of crystals. Recrystallization of the product from ethanol gave cholesterol (23 mg).

Registry No.—**1**, 20071-52-7; **2**, 20071-53-8; **4**, 28180-56-5; **5**, 10191-01-2; **6**, 10215-89-1; **8**, 20071-51-6; **9**, 20071-54-9; **10**, 13017-11-3; **11**, 28180-62-3; **12**, 28180-63-4; **14**, 28291-99-8; **15**, 28180-64-5; **16**, 20230-31-3; **18**, 28312-59-6; **19**, 28180-66-7; styrene oxide, 96-09-3; *cis*-stilbene oxide, 1689-71-0; *trans*-stilbene oxide, 1439-07-2; 1-octene oxide, 2984-50-1; 2-*cis*-octene oxide, 23024-54-6; 2-*trans*-octene oxide, 28180-70-3; 3-*cis*-octene oxide, 28180-71-4; 3-*trans*-octene oxide, 28180-72-5; 4-*cis*-octene oxide, 1439-06-1; 4-*trans*-octene oxide, 1689-70-9.

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The Acetylation of Cyclononene

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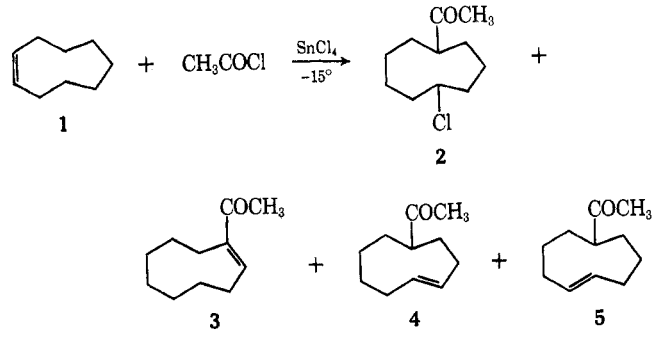
The acetylation of *cis*-cyclononene with acetyl chloride in the presence of stannic chloride yields 50–60% of 1-acetyl-5-chlorocyclononane and ~20% of 4- and 5-acetylcyclononenes, the products of 1,5-transannular hydride transfer. Use of acetic anhydride–trifluoroacetic acid gave similar results. Acetylation in the presence of active aluminum chloride led to ring contraction, with six- and seven-membered ring compounds being formed. The major (35%) product was shown to be a chloro derivative of 1-acetyl-4-isopropylcyclohexane. The other products are chlorine-bearing derivatives of 4-ethyl-1-acetylcycloheptane and, possibly, 4- or 5-methyl-1-acetylcyclooctane.

The Lewis acid catalyzed acylation of cyclic olefins and polyolefins containing seven- and eight-membered rings, including cycloheptene,[2] cycloheptatriene,[3] cyclooctene,[4,5] and 1,3- and 1,5-cyclooctadiene,[6] has been the subject of considerable recent investigation. Transannular hydride transfers were frequently observed as well as ring contraction and ring-bridging reactions. Thus, acetylation of cyclooctene in the presence of stannic chloride or added deactivated aluminum chloride gave predominantly 1-acetyl-4-chlorocyclooctane, the product of a sequence of steps which includes a 1,5-transannular hydride transfer.[5,6] When fresh, active aluminum chloride was employed, the acetylation gave a mixture of 1-acetyl-4-chloro-4-ethylcyclohexane and 1-acetyl-4-methylcycloheptane, products of ring-contraction reactions. Since of the medium rings, the nine-membered ring appears to possess the most severe transannular interactions,[7] it was considered worthwhile to extend our previous investigations to nine-membered ring olefins. We present herewith the results of our studies on the acetylation of *cis*-cyclononene.

Results

Our initial experiments were of acetylations employing acetyl chloride in the presence of stannic chloride, performed in methylene chloride as solvent. This system might, by analogy with cyclooctene, favor the formation of products resulting from transannular hydride transfer, with ring-contraction and bridging reactions being avoided. In fact, acetylation of *cis*-cyclononene (**1**) in the presence of stannic chloride in methylene chloride at −15° gave as the major product 1-acetyl-5-chlorocyclononane (**2**, 42–55%) and a mixture of 1-, 4-, and 5-acetylcyclononene (**3**, **4**, and **5**, 20–25%). The yields were erratic and depend particularly on the purity of the catalyst. Larger amounts of the unsaturated ketones **3** and **4** were obtained when stannic chloride from a freshly opened bottle was used. The structures of **2**, **3**, **4**, and **5** were assigned initially on the bases of analytical and spectral data. The mass spectrum of chloro ketone **2** showed molecular ion peaks at *m/e* 202 and 204; its infrared spectrum displayed bands for a



saturated ketone function at 1709 cm^{-1}. The nmr spectrum of **2** exhibited, *inter alia*, a one-hydrogen multiplet at τ 5.83 attributable to the hydrogen on the chlorine-bearing carbon (C-5) and an acetyl methyl singlet at τ 7.85; no signals in the τ 8.6–9.2 region which might be attributable to *C*-methyl groups were present. The lower boiling fraction from the acetylation of **1** showed two partially resolved peaks on several gas chromatography columns. The infrared spectrum

(1) NDEA Fellow, 1965–1968.
(2) (a) N. Jones, H. T. Taylor, and E. Rudd, *J. Chem. Soc.*, 1342 (1961); (b) L. Rand and R. J. Dolinski, *J. Org. Chem.*, **31**, 3063 (1966).
(3) J. A. Blair and C. J. Tate, *Chem. Commun.*, 1506 (1969).
(4) T. S. Cantrell, *J. Org. Chem.*, **32**, 1669 (1967).
(5) J. K. Groves and N. Jones, *J. Chem. Soc. C*, 1718 (1969).
(6) T. S. Cantrell and B. L. Strasser, *J. Org. Chem.*, **36**, 670 (1971).
(7) V. Prelog, "Perspectives in Organic Chemistry," A. R. Todd, Ed., Wiley–Interscience, New York, N. Y., 1956.