7 ml of anhydrous ether, was added 300 mg of 2-(3-butenyl)-4,4-dimethylcyclohexanone (**8**) in 5 ml of anhydrous ether. The reaction was stirred at room temperature under a nitrogen atmosphere for 24 hr, then poured into a dilute, ice-cold acetic acid solution. The aqueous portion was extracted five times with ether. The combined ether fractions were washed (water, bicarbonate, and brine), dried over $MgSO_4$, and concentrated on a rotary evaporator to yield 273 mg of crude alcohol. Evaporative distillation (0.3 mm, 70°) provided 254 mg of a 3:1 mixture of axial and equatorial alcohols. The alcohols could be separated by preparative thin layer chromatography.

The major isomer had nmr (CCl_4, 100 MHz) δ 0.84 and 0.90 (s, 3 H each, geminal methyls), 1.13 (s, 3 H, C-1 methyl), 4.84–5.08 (m, 2 H, $-CH{=}CH_2$), and 5.52–6.00 ppm (m, 1 H, $-CH{=}CH_2$); ir (film) 3450, 1640, and 915 cm^{-1}.

The minor isomer had nmr (CCl_4, 100 MHz) δ 0.90 and 0.92 (s, 3 H each, geminal methyls), 0.99 (s, 3 H, C-1 methyl), 4.82–5.10 (m, 2 H, $-CH{=}CH_2$), and 5.57–6.00 ppm (m, 1 H, $-CH{=}CH_2$); ir (film) 3375, 1635, and 920 cm^{-1}.

Cyclization Studies. A. Cyclization with Formic Acid.—A 60-mg sample of the mixture of alcohols described above was dissolved in 6 ml of anhydrous formic acid and stirred at room temperature for 3 hr. The solution was poured into water and extracted four times with ether. The combined ether fractions were washed (water, bicarbonate, and brine), dried over $MgSO_4$, and concentrated on a rotary evaporator to yield 57 mg of product.

The crude material was hydrolyzed by addition to a stirred solution of lithium aluminum hydride in ether and stirring for 30 min. Then 2 ml of methanol and 2 ml of 10% sodium hydroxide solution were added carefully. The mixture was stirred for 5 min, filtered, and concentrated. The crude material was oxidized in the normal manner with Jones reagent in acetone.[6] Evaporative distillation (0.25 mm, 72°) gave 28 mg of ketonic product: nmr (CCl_4, 100 MHz) δ 0.93 (d, $J = \sim 1$ Hz, 3 H, C-9 methyl),[10] 0.96 and 0.97 ppm (s, 3 H each, geminal methyls); ir (film) 1700 cm^{-1}. Analysis by gas chromatography on SE-30 or Carbowax columns showed only one significant peak.

Careful examination of the nmr spectrum showed a small peak at δ 0.74 ppm. This peak can be attributed to the C-9 methyl of *trans*-6,6,9-trimethyl-2-decalone.[10]

Cyclization of either of the individual isomers of alcohol **6** gave results indistinguishable from cyclization of the mixture.

B. Cyclization in Deuterioformic Acid.—A 31-mg sample of alcohol **6** was dissolved in 1 ml of deuterioformic acid. The mixture was stirred for 4 hr, and the product was isolated and converted into the trimethyldecalone in the manner described above. The mass spectrum of the product showed *m/e* (rel intensity) 194 (P, 22.5), 195 (P + 1, 100), 196 (P + 2, 41.9), and 197 (P + 3, 17.3). Correction for natural isotopic abundances indicates deuterium incorporation in 86% of the product (49% d_1, 26% d_2, and 11% d_3).

***cis*-6,6,9-Trimethyl-2-decalone (9).**—A mixture of 50 mg of cuprous bromide and 0.7 ml of 1.4 *M* methylmagnesium iodide in ether was diluted to 5 ml with anhydrous ether. Then 110 mg (0.625 mmol) of 6,6-dimethyl-$\Delta^{1,9}$-2-decalone (**10**) in 5 ml of ether was added. The reaction was stirred at room temperature for 2 hr and poured onto an ice–acetic acid mixture. The aqueous portion was extracted five times with ether, and the combined ether fractions were washed (water, bicarbonate, and brine), dried over $MgSO_4$, and concentrated on a rotary evaporator to yield 96 mg of crude product. Preparative tlc and evaporative distillation (0.25 mm) gave 61 mg of authentic *cis*-6,6,9-trimethyl-2-decalone. *Anal.* Calcd for $C_{13}H_{22}O$: *m/e* 194.16719 (M^+). Found: *m/e* 194.16706. The ir and nmr spectra were identical with those obtained from material prepared by cyclization.

Acknowledgment.—We thank the Robert A. Welch Foundation and the National Institute of Arthritis and Metabolic Diseases for support of this research.

Registry No.—*cis*-**6**, 42271-36-3; *trans*-**6**, 42271-37-4; **8**, 38481-13-9; **9**, 42271-39-6; **10**, 4044-27-3.

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[10] The C-9 methyl groups of *cis*- and *trans*-9-methyl-2-decalone show absorption at δ 0.97 and 0.78 ppm, respectively.[11] The C-9 methyl of *cis*-9-methyl-2-decalone has also been observed as a doublet.[12]

[11] W. S. Johnson, P. J. Neustaedter, and K. K. Schmiegel, *J. Amer. Chem. Soc.*, **87**, 5148 (1965).

[12] M. J. T. Robinson, *Tetrahedron Lett.*, 1685 (1965).

Lithium Dimethylcuprate Reaction with Oxygen-Substituted Epoxides[1]

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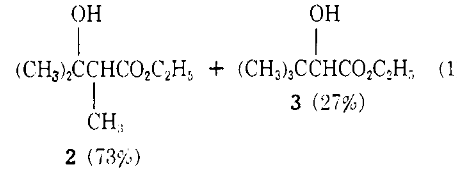
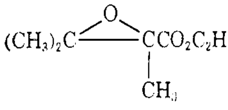
Recent work[2-4] has shown that lithium dimethylcuprate is superior to other organometallic reagents for the nucleophilic opening of epoxides. It was of interest to determine whether adjacent oxygen functions would exert a directive influence on the course of this reaction of the sort observed, *e.g.*, in the Simmons–Smith methylenation. We report here the results obtained with various substituted epoxides.

Johnson and coworkers[2] have reported that the reaction of lithium dimethylcuprate with ethyl 2,3-epoxybutyrate gives α-methylated product in good yield. We have extended this study to include the more highly substituted glycidic esters **1** and **4**. As shown in eq 1,





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the reaction of **1** (overall yield 68%) shows only low regioselectivity, even though the formation of **3** formally requires substitution at a tertiary center. Interestingly, **4**, in which both epoxy centers are tertiary, failed to react at all with the organocopper reagent even under more forcing conditions. These results are difficult to interpret mechanistically, but indicate that the degree of selectivity observed in the simpler system[2] will not prove to be a generally useful feature of the reaction of glycidic esters.

As examples of other oxygen-substituted epoxides, 3-hydroxycyclohexene oxide and its derivative methyl ether and acetate were also subjected to lithium dimethylcuprate treatment. The cis and trans alcohols (**5** and **8**) both gave rapid gas evolution (methane) followed by slower attack of the oxirane ring; the reaction must therefore involve an intermediate O-metalated species. As shown in eq 2 and 3, these reactions exhibit completely stereospecific anti opening of the oxirane ring, with moderate regioselectivity suggesting preferred diaxial opening through the half-chair con-

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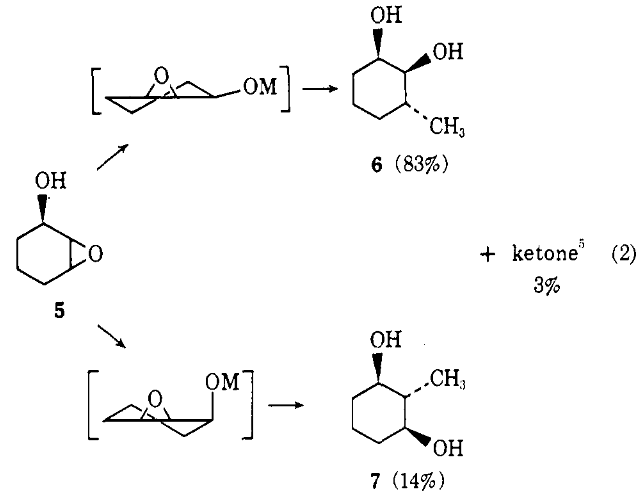
[1] Support in part by the donors of the Petroleum Research Fund, administered by the American Chemical Society, is gratefully acknowledged.

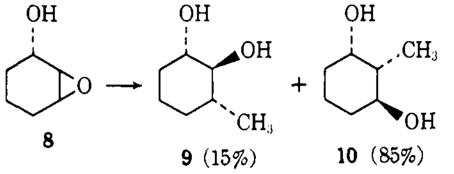
[2] R. W. Herr, D. M. Wieland, and C. R. Johnson, *J. Amer. Chem. Soc.*, **92**, 3813 (1970).

[3] R. W. Herr and C. R. Johnson, *J. Amer. Chem. Soc.*, **92**, 4979 (1970).

[4] J. Staroscik and B. Rickborn, *J. Amer. Chem. Soc.*, **93**, 3046 (1971).



5 → **6** (83%) + **7** (14%) (2)

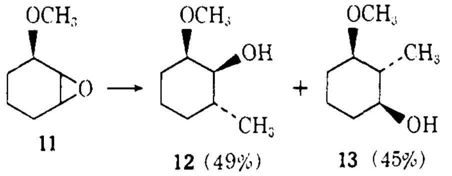


8 → **9** (15%) + **10** (85%) (3)

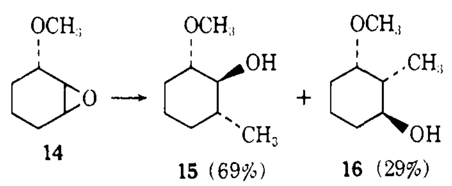
formers in which the 3 substituent prefers the pseudoequatorial position.

The change in preference for attack at carbons 1 and 2 in the cis,trans pair **5** and **8** suggests that neither inductive nor other specific directive influences play a major role in these reactions. However, it was noted that the trans isomer **8** reacted more slowly than the cis material **5**.

The methyl ethers **11** and **14** show even lower regioselectivity (eq 4 and 5) than the alcohols, resembling in this respect the reactions of these materials with lithium aluminum hydride.[6] The trans ether **14** again reacted more slowly with lithium dimethylcuprate than cis **11**.

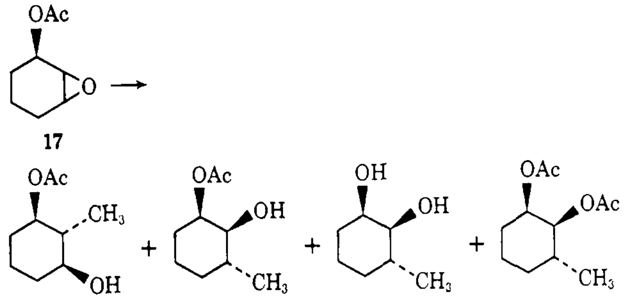


11 → **12** (49%) + **13** (45%) + ketone 6% (4)



14 → **15** (69%) + **16** (29%) + ketone 2% (5)

Only the cis isomer of the acetate, **17**, was examined, and this exhibited somewhat higher regioselectivity than the alcohol **5**. In this system the results were complicated by transesterification during the reaction leading to a mixture of diols and diacetates; analysis was accomplished by conversion of the mixture to the diacetate derivatives.



17 → **18** (7%) + **19** (30%) + **20** (33%) + **21** (30%) (6)

In summary, the results with various oxygen-substituted epoxides in the reaction with lithium dimethylcuprate suggest that no specific directive influences are to be expected, and product distribution will largely be the result of conformational control.

Experimental Section

The glycidic esters[7] **1** and **4** and epoxides[6] **5**, **8**, **11**, and **14** have all been reported previously. Compound **17** was prepared from the alcohol **5** by treatment with acetic anhydride in pyridine.

The lithium dimethylcuprate solutions were prepared by the method of Gilman,[8] using cuprous thiocyanate. The epoxides were added dropwise at −5°, and reaction progress was followed by vpc analysis of aliquots. The mixtures were quenched by adding a small amount of water and filtering. All reactions were carried out with approximately 3 mol of lithium dimethylcuprate/mol of epoxide.

The crude reaction mixtures were subjected to vpc analysis and then distilled (short path) to obtain overall yields. Further vpc analysis showed no significant fractionation; the percentages shown in the equations in the discussion section are the vpc-determined compositions of the distilled materials (*i.e.*, normalized yields.)

After 20 min, compound **1** gave an isolated 68% yield of material consisting of 73% ethyl 3-hydroxy-2,3-dimethylbutanoate[9] (**2**), nmr δ 1.1–1.5 (m, 12), 2.35 (q, J = 7 Hz, 1), 3.0 (OH), and 4.12 ppm (q, J = 7 Hz, 2), ir 870, 950, 1095, 1130–1210, 1730, 3200–3600 cm^{-1}, and 27% ethyl 2-hydroxy-3,3-dimethylbutanoate[10] (**3**), nmr δ 1.22 (s, 9), 1.27 (t, J = 7 Hz, 3), 2.37 (s, 1), 3.27 (OH), 4.11 ppm (q, J = 7 Hz, 2), ir 910, 1035, 1200, 1730, 3200–3600 cm^{-1}.

Ethyl trimethylglycidate (**4**) failed to react with the organocuprate when treated for 2 hr at −5° followed by 2 hr at 25°. Starting material was recovered in good yield.

cis-2,3-Epoxycyclohexanol (**5**) after 2 hr at −8° and subsequent conversion to the diacetate derivative[11] gave 70% of a mixture, bp 72–75° (0.7 Torr). The major product proved to be *cis*-2-hydroxy-*trans*-3-methylcyclohexanol (**6**), diacetate nmr δ 0.91 (d, J = 7 Hz, 3), 1.0–2.1 (m, 7), 1.98 and 2.03 (two s, 3 each), 4.46 (d of d, J = 1.4, 10.0 Hz, 1), and 5.19 ppm (m, 1). The minor adduct was **7**, diacetate nmr δ 0.90 (d, J = 7 Hz, 3), 0.9–2.1 (m, 7), 2.01 (s, 6), and 4.50 (t of d, J = 4.7, 11 Hz, 2).

trans-2,3-Epoxycyclohexanol (**8**) after 21.5 hr with gradual warming from −5 to 10° overnight, followed by conversion to the acetate derivative, gave 70% of a mixture, bp 92–97° (2 Torr). A significant amount (12.5%) of the acetate from unreacted starting material was obtained, with the remainder consisting of 15% of the diacetate of *trans*-2-hydroxy-*cis*-3-methylcyclohexanol (**9**), nmr δ 0.90 (d, J = 7 Hz, 3), 0.9–2.1 (m, 7), 1.99 and 2.00 (two s, 3 each), and 4.5–4.8 ppm (m, 2), and 85% of the diacetate of *trans*-3-hydroxy-*cis*-2-methylcyclohexanol (**10**), nmr δ 0.89 (d, J = 7 Hz, 3), 1.2–2.2 (m, 7), 2.01 and 2.08

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[5] Epoxide-carbonyl rearrangement is a commonly observed side reaction in the lithium dimethylcuprate treatment of epoxides. For example, cyclohexene oxide gives roughly 20% of cyclohexanone.[2] In the present study these materials were not completely characterized, but appeared at short vpc retention times and exhibited carbonyl ir absorptions.

[6] B. C. Hartman and B. Rickborn, *J. Org. Chem.*, **37**, 4246 (1972).

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[8] H. Gilman, R. G. Jones, and L. A. Woods, *J. Org. Chem.*, **17**, 1630 (1952).

[9] S. Landa, Y. Szebenyi, O. Weisser, and J. Mastecky, *Acta Chim. Acad. Sci. Hung.*, **29**, 237 (1961).

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[11] R. U. Lemieux, R. K. Kullnig, and R. Y. Moir, *J. Amer. Chem. Soc.*, **80**, 2237 (1958); R. U. Lemieux, R. K. Kulling, H. G. Bernstein, and W. G. Schneider, *ibid.*, **80**, 6098 (1958).

(two s, 3 each), 4.72 (t of d, J = 4.5, 10.0 Hz, 1), and 5.10 ppm (m, 1).

The cis epoxy ether **11** reacted very rapidly (1 min) to give the product distribution shown in eq 4 in overall 95% yield. The acetate of **12** had nmr δ 0.85 (d, J = 7 Hz, 3), 0.9–2.1 (m, 7), 2.02 (s, 3), 3.31 (s, 3), 3.48 (m, 1), and 4.38 ppm (d of d, J = 1.4, 10.1 Hz, 1). The acetate of **13** had nmr δ 0.97 (d, J = 7 Hz, 3), 0.9–2.3 (m, 7), 1.98 (s, 3), 2.75 (t of d, J = 4.7, 11 Hz, 1), 3.31 (s, 3), and 4.38 ppm (t of d, J = 4.7, 11 Hz, 1).

The trans epoxy ether **14** after 3 hr at −5° and 2.5 hr at 25° gave 83% of a mixture having the composition shown in eq 5. The acetate of **15** had nmr δ 0.90 (d, J = 7 Hz, 3), 0.9–2.2 (m, 7), 2.00 (s, 3), 3.01 (m, 1), 3.22 (s, 3), and 4.48 (t, J = 10 Hz, 1). The acetate of **16** had δ 0.94 (d, J = 7 Hz, 3), 0.9–2.1 (m, 7), 1.96 (s, 3), 3.29 (s, 3), 3.33 (m, 1), and 4.74 ppm (t of d, J = 4.3 and 10.0 Hz, 1).

cis-2,3-Epoxycyclohexyl acetate (**17**) after 40 min at −7° gave 89% of a mixture containing 6% unreacted **17**, 29% of **6**[12] (identical with material formed in eq 2), 7% of a compound assumed to be **18** (see below), and 59% of an approximately equal mixture (by nmr, unresolved by vpc) of **19** and **21**.

This mixture was treated with acetic anhydride in pyridine, giving 93% of **6** diacetate and 7% of **7** diacetate. Combining these data allowed the determination of the product distribution shown in eq 6.

The stereospecific trans opening of the epoxide ring by lithium dimethylcuprate was evident from the mutually exclusive formation of products in, *e.g.*, eq 2 (and 6) *vs.* 3 and 4 *vs.* 5.

Registry No.—**1**, 5369-63-1; **2**, 34849-39-3; **3**, 42282-48-4; **5**, 26828-72-8; **6** diacetate, 42282-50-8; **7** diacetate, 42282-51-9; **8**, 26828-73-9; **9** diacetate, 42282-53-1; **10** diacetate, 42282-54-2; **11**, 17208-68-3; **12** acetate, 42282-56-4; **13** acetate, 42282-57-5; **14**, 2699-17-4; **15** acetate, 42282-59-7; **16** acetate, 42282-60-0; lithium dimethylcuprate, 15681-48-8.

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Dehydrochlorination–Decarbonylation of 2-Chloro-1,3-dicarbonyl Compounds, a Method for Ring Contraction

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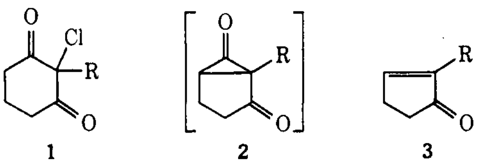
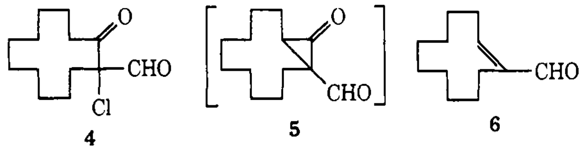
Treatment of 2-chloro-2-alkylcyclohexane-1,3-diones (**1**) with sodium carbonate in hot xylene leads to 2-alkylcyclopentenones (**3**). This new method for the construction of cyclopentenones was used in efficient syntheses of methyl jasmonate and jasmone.[1] It was applied subsequently in the preparation of other cyclopentenones on the way to prostaglandins.[2,3] To survey the applicability of the new reaction, we investigated the behavior of an α-chloro-β-ketoaldehyde and two α-chloro-β-keto esters.



1 2 3

Chlorination of 2-formylcyclododecanone with *tert*-butyl hypochlorite in chloroform solution gave the crystalline chloride **4**, whose reaction with suspended sodium carbonate in boiling xylene was slow, requiring 45 hr. The resulting cycloundecene-1-carboxaldehyde (**6**) was separated from minor amounts of 2-chlorocyclododecanone by chromatography.

tert-Butyl hypochlorite served again in the chlorination of 2-carbomethoxycyclohexanone. The resulting chloride **7** (84%) on dehydrochlorination–decarbonylation with sodium carbonate in hot xylene afforded 1-carbomethoxycyclopentene (**9**) in 71% yield.



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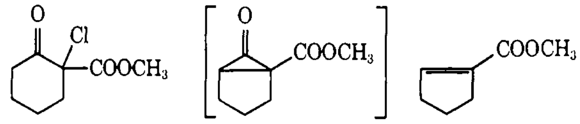

7 8 9

To study the behavior of an aliphatic α-chloro-β-keto ester, compound **10** was prepared by standard procedures. When a solution of **10** was heated in xylene over sodium carbonate, gas evolution ceased in 6 hr. Owing to the air sensitivity of some of the products, the isolation of four pure substances by chromatography was accompanied by heavy losses. The least polar, liquid material was identified as methyl (*E*)-2-phenylcinnamate (**23**, 6%) by hydrolysis to the known carboxylic acid **24**. It was followed by crystalline 1-phenyl-2-indanone (**19**, 21%). The more polar fractions contained 2-methoxy-5-oxo-3,4-diphenyl-2,5-dihydrofuran (**22**, 5%) and 2-methoxy-4-oxo-3,5-diphenyl-4,5-dihydrofuran (**16**, 14%) whose structures were deduced from spectral properties (see Experimental Section).

The products observed in the dehydrochlorination–decarbonylation of the three cyclic chlorides **1**, **4**, and **7** appear to originate from the cyclopropanones **2**, **5**, and **8** by thermal, nonconcerted elimination of carbon monoxide. Earlier work on the pyrolysis of 2-acetoxy-1,3-cyclohexanediones[4] and medium-ring 2-acetoxy ketones[5] as well as investigations on the thermolysis of 3-cyclopropyl-3-oxopropanoates[6] support this hypothesis. Thermally allowed, energetically more favorable disrotatory ring opening of these cyclopropanones to the corresponding cis–cis oxyallyl dipoles,[7] if it occurs, is nonproductive and reversible.[8] An entirely different situation prevails in the aliphatic case **10**. Two of the four phenyl-stabilized oxyallyl ions **12–15**, produced either directly from the enolate by ionization or, less likely, by disrotatory ring opening of the two diastereomeric cyclopropanones **11**, can cyclize to the

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[8] Compare the facile thermal racemization of optically active *trans*-2,3-di-*tert*-butylcyclopropanone with its slow decarbonylation: D. B. Sclove, J. F. Pazos, R. L. Camp, and F. D. Greene, *J. Amer. Chem. Soc.*, **92**, 7488 (1970).