treatment (no aliquots were taken after 2 half-lives). Of the 15 kinetic points taken, one or two were rejected after a hand plot. Three infinity points were averaged. The correlation coefficient, slope, and least-squares standard deviation were calculated as before.[1]

Kinetics of Exchange of 3-Methyl-1-phenyl-2-butanone (7).—To a clean, dry 5-mm nmr tube was added approximately 30 mg of 3-methyl-1-phenyl-2-butanone and a measured amount of methanol-*O*-*d* (Diaprep, minimum 99% isotopic purity). The solution was analyzed at the appropriate temperature by a Varian A-60 nmr spectrometer equipped with a V-6040 variable temperature attachment. The probe was cooled with either an ice–water bath or Dry Ice–acetone bath, and temperature was checked periodically by lowering a calibrated thermometer into the probe to sample level. Temperature 25 and 0° were held to within 0.2° throughout all runs. After tuning, a full spectrum was taken and several additional scans were made on the dimethyl doublet 135 Hz upfield from the methyl resonance of the solvent. The tube was removed and the correct amount of 2.2 *M* sodium methoxide in methanol-*O*-*d* was added to achieve the desired base concentration and a total volume of 0.500 ml. The tube was capped, shaken, and replaced in the probe. After temperature equilibration, repetitive scans were taken on the upfield dimethyl signal. The instrument was periodically retuned and calibration samples (see below) were run.

Analysis of the scans of the dimethyl group for the amount of deuterium incorporation in the methine position was carried out by measuring line lengths of the two peaks of the doublet, together with that of the inner triplet (displayed as a broad singlet), correcting for the lack of base line separation for the doublet of the protio component, correcting for the relative widths of the individual peaks, and calibrating the corrected peak heights with three known standard mixtures (see below). These base line and line width corrections on the standard mixtures gave calibration curves which were nearly linear and had a slope of near unity. The mole fraction of unexchanged material before calibration is expressed as

$$[\mathrm{H}] = \frac{L_1 + L_2}{(L_1 + L_2)(1 - a) + L_3 b}$$

where L_1, L_2, L_3 refer to the line lengths of the low- and high-field lines of the doublet for the protio and inner triplet for the deuterio compounds, respectively, a is $L_3/L_1 + L_2$ prior to introduction of base, and b is $(2WH_3/L_3)/(WH_1/L_1 + WH_2/L_2)$. WH is the width at half-height measured for a given peak. Both a and b are constant throughout a run; b is calculated from data on lines 1 and 2 at $t = 0$ and line 3 at $t = \infty$. The infinity value of [H] was calculated from the equilibrium amounts of H in three positions in the ketone and one position in the solvent (1% H present originally). This treatment was adequate for all runs taken; the value $(L_1 + L_2)(1 - a) + L_3 b$ was uniform throughout a run indicating that the six-proton signal remained at a constant overall intensity despite changes in line shape. No runs was carried out to more than 2 half-lives beyond which L_1 and L_2 would be uncorrected for contributions from line 3.

Calibration samples were prepared by individually weighing pure protio and 97.5% isotopically pure trideuterio ketone (see below) into a single pan of a Cahn Model M-10 electrobalance. The mixtures were each dissolved in methanol and placed in separate nmr tubes. The mixtures contained 0.253, 0.397, and 0.672 of three atoms of deuterium after correction for the protio impurity in the deuterio component and the molecular weight difference between the components. A calibration curve was constructed for each run.

The calibrated mole fractions for protio ketone were used in the usual first-order treatment. A least-squares slope and standard deviations were obtained from a program[22] on a Wang 700 calculator.

The two runs each at 37.5 and 0° were at substantially different methoxide ion concentrations, showing that the reaction was first order in base.

3-Methyl-1-phenyl-1,1,3-trideuterio-2-butanone.—To 200 mg of partially deuterated 3-methyl-1-phenyl-2-butanone was added 1 ml of methanol-*O*-*d* and 0.02 ml of methanol-*O*-*d*–2.2 *M* sodium methoxide. The mixture was capped and left 10 hr at room temperature, then concentrated under reduced pressure. Fresh methanol-*O*-*d* was added, and the mixture was allowed to stand for an additional 10 hr. An equivalent amount of acetic acid-*O*-*d* was added, and the product was chromatographed after concentration under reduced pressure. Fractions eluted with 0.5–1.0% ether in hexane (120 mg, 60%) were analyzed by nmr in 0.022 *M* dichloromethane in carbon tetrachloride. Integration of the benzyl protons of the pure ketone *vs.* the dichloromethane showed 97.5% deuterium incorporation.

(22) This program was kindly supplied by Dr. T. G. Mecca.

Favorskii Rearrangements. IX. Stereochemistry of the Reaction with 2-Bromo-4-methyl-4-phenylcyclohexanone

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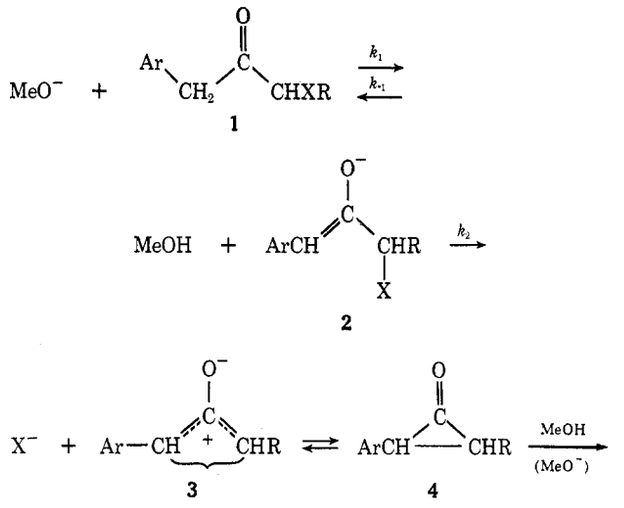
In the reaction of 2-chlorocyclohexanone or 2-bromo-5-methyl-5-phenylcyclohexanone (cis or trans) with NaOMe in MeOH the yield of Favorskii ester has been found to increase markedly at the expense of α-methoxyoxirane and α-methoxy ketone products on increasing the methoxide concentration. 2-Chloro- and 2-bromo-4-methyl-4-phenylcyclohexanones (**6**) are much less subject to this concentration effect, 40% yield of Favorskii ester being obtained even at low ($\sim 10^{-5}$ *M*) methoxide concentrations. The ratio of stereoisomeric esters formed from **6** was found to be *reversed* in going from low to high (2 *M*) methoxide concentrations. This result is rationalized in terms of equilibrating dipolar ion and cyclopropanone intermediates.

Previous papers in this series have provided evidence which points to the following mechanism for the Favorskii rearrangement, as applied to the $ArCH_2COCHXR$ (**1**) system with NaOMe in MeOH.[2]

The reversibility of the first step in the reaction sequence (*i.e.*, $k_{-1} \gg k_2$) was demonstrated for **1** with Ar = Ph and R = H by deuterium exchange and a large k^{Br}/k^{Cl} leaving group effect.[2c] (Similar evidence was also obtained for reversible carbanion formation in 2-halo-4,4-disubstituted cyclohexanones.[2a]) Ionization of the halogen from enolate ion **2** to form dipolar ion **3** was indicated by a large negative ρ (*ca.* −5) for this step with R = H, a sizable positive salt effect, and a strong rate acceleration by increasing the ionizing power of the solvent,[2b,c] Furthermore, a change in R from H to Me caused a marked rate acceleration, as expected in an ionization mechanism.[2d] In fact, the increase in k_2 was large enough to change the mecha-

(1) Abstracted in part from Ph.D. Dissertation of J. G. Strong, Northwestern University, 1968.

(2) (a) F. G. Bordwell, R. R. Frame, R. G. Scamehorn, J. G. Strong, and S. Meyerson, *J. Amer. Chem. Soc.*, **89**, 6704 (1967); (b) F. G. Bordwell and R. G. Scamehorn, *ibid.*, **90**, 6751 (1968); (c) F. G. Bordwell, R. G. Scamehorn, and W. R. Springer, *ibid.*, **91**, 2087 (1969); (d) F. G. Bordwell and M. W. Carlson, *ibid.*, **92**, 3370 (1970); (e) F. G. Bordwell and M. W. Carlson, *ibid.*, **92**, 3377 (1970); (f) F. G. Bordwell and R. G. Scamehorn, *ibid.*, **93**, 3410 (1971); (g) F. G. Bordwell and J. Almy, *J. Org. Chem.*, **38**, 575 (1973).



ArCH$_2$CHRCO$_2$Me

5

nism by making $k_2 \gg k_{-1}$, which was indicated by the absence of deuterium exchange, a k^{Br}/k^{Cl} rate ratio near 1.0 and a positive rather than a negative ρ in the ArCH$_2$COCHXCH$_3$ system.[2d] Evidence supporting the postulate of a dipolar ion intermediate was obtained from reactions of Ph$_2$CClCOCH$_3$ and Ph$_2$CHCOCH$_2$Cl. These isomers gave nearly quantitative yields of the same Favorskii ester with 0.05 M NaOCH$_3$, but with very dilute NaOMe ($\sim 10^{-5}$ M) 1-phenyl-2-indanone was formed in appreciable yields as a by-product.[2f] The formation of identical indanone/ester ratios (1.0:1.6) from the two substrates points to a common intermediate believed to be a dipolar ion, comparable in structure to **3**. This dipolar ion is presumably in equilibrium with the corresponding cyclopropanone.[3] The dipolar ion cyclizes (slowly) to the indanone, but at high methoxide ion concentrations the cyclopropanone reacts rapidly to form the ester to the exclusion of the indanone.[2f]

Additional evidence for a dipolar ion intermediate in Favorskii reactions can be deduced from the loss of stereospecificity of the reaction of 1-chloro-*cis*-1-acetyl-2-methylcyclohexane when carried out with NaOMe in MeOH in contrast to the stereospecificity observed with NaOMe in 1,2-dimethoxyethane.[5] On the other hand, it now appears that the formation of α-methoxy ketone by-products derived from reactions of α-halo ketones with NaOMe in MeOH *cannot* be used as evidence for the presence of dipolar ion intermediate as was formerly supposed.[6] These by-products arise instead from the methanolysis of enol allylic halide intermediates.[2e]

The present paper presents additional evidence for the above mechanistic scheme as deduced from a study of the stereochemistry of the reaction of 2-bromo-4-methyl-4-phenylcyclohexanone (**6**) and *cis*- and *trans*-2-bromo-5-methyl-5-phenylcyclohexanones (**7**) with NaOMe in MeOH.

(3) Recent calculations of R. Hoffmann, *J. Amer. Chem. Soc.*, **90**, 1475 (1968), indicate that the dipolar ion would be favored at equilibrium relative to either the cyclopropanone or allene oxide. [See, however, A. Liberles, A. Greenberg, and A. Lesk, *J. Amer. Chem. Soc.*, **94**, 8685 (1972).] In methanol solution the cyclopropanone would be expected to exist principally as its hemi methyl ketal.[4]

(4) N. J. Turro and W. B. Hammond, *ibid.*, **87**, 3258 (1965).

(5) H. O. House and W. F. Gilmore, *ibid.*, **83**, 3980 (1961).

(6) A. W. Fort, *ibid.*, **84**, 2620, 2625 (1962).

TABLE I

EFFECT OF SODIUM METHOXIDE CONCENTRATION ON PRODUCT DISTRIBUTION FROM 2-HALOCYCLOHEXANONES

α-Halocyclohexanone	[NaOMe], M	% ester	% hydroxy ketal	% ether
2-Chlorocyclohexanone	$\sim 10^{-5}$ [a]	3	62	28
	0.05	10		
	1.0	33		
	2.0	49	47	0
	3.5[b]	75[b]		
2-Bromo-4-methyl-4-phenylcyclohexanone (**6**)	$\sim 10^{-5}$ [a]	40	36	15
	2	55	37	0
2-Bromo-5-methyl-5-phenylcyclohexanone (**7**)	0.05	9		
	1.0	22–24		
	2.0	69		

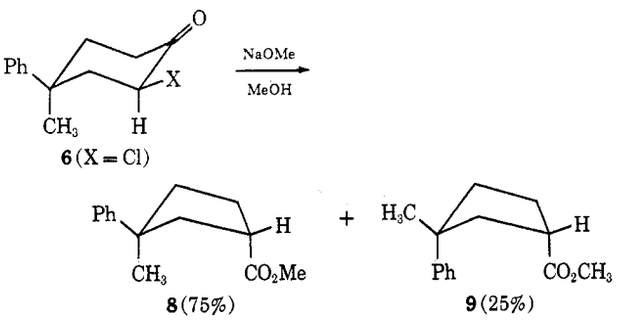
[a] Methoxide added slowly to α-halo ketone. [b] $C_6H_5CH_2ONa$ in $C_6H_5CH_2OH$; results of G. Stork and I. J. Borowitz, *J. Amer. Chem. Soc.*, **82**, 4307 (1960).

Results

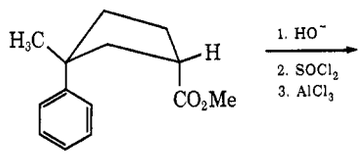
The striking variation in products frequently observed for the reaction of α-halo ketones with low *vs.* high concentrations of sodium methoxide[2b,d-g,6] prompted a study of this type with 2-chlorocyclohexanone, and with **6** and **7** (Table I).

The marked increase in yield of ester with increased [NaOMe] for 2-chlorocyclohexanone and for 2-bromo-5-methyl-5-phenylcyclohexanone (**7**) is similar to earlier observations. The increased yield can be attributed partly to a positive salt effect favoring ionization of halide ion from the enolate ion, which leads to an increased rate of ester formation. Earlier work has established the reality of such a salt effect and has indicated that the principal side reaction, *i.e.*, methoxyoxirane formation, is not subject to a comparable salt effect.[2b] As a consequence, with increased [NaOMe] the yield of ester increases at the expense of hydroxy methyl ketal (derived from the methoxyoxirane).[2b] The yield of ester also increases at the expense of ether (*i.e.*, methoxy ketone) formation, because at high methoxide concentrations the enol allylic halide, which is the precursor of the ether, is largely converted into enolate ion, which forms ester.[2e] Note that the behavior of 2-bromo-4-methyl-4-phenylcyclohexanone (**6**) differs in that ketal formation is not disfavored relative to ester formation at high methoxide concentrations (Table I).

The reaction of chloride **6** with 0.2 M NaOMe in MeOH gave a 53% yield of a mixture of two isomeric esters (**8** and **9**) in a 3:1 ratio. The esters were not isomerized under the reaction conditions, but prolonged (165 hr) reflux with 1 M NaOMe changed the ratio of **8**/**9** from 75:25 to 55:45.



Structure assignments were made to **8** and **9** by conversion of the mixture of esters into a mixture of acid chlorides, **8b** and **9b** (*via* the acids **8a** and **9a**), which was treated with aluminum chloride to form 59% of bicyclic ketone **10** and 25% of a pure acid (recovered **8a**). Examination of molecular models shows that cyclization to form **10** can occur readily with **9b** in which the phenyl and carboxyl chloride groups are cis, but is impossible with **8b** where these groups are trans.



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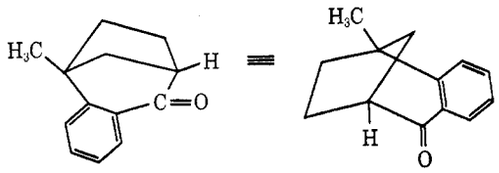

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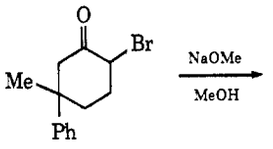
The yield of **10** was greater than that expected on the basis of the amount of ester **9** present in the mixture (vpc analysis), indicating that some of the acid chloride derived from **8** had epimerized during the reaction. This was confirmed by subjecting the recovered acid (**8a**) to the synthetic sequence; 25% of **10** was produced thereby and 45% of acid **8a** was recovered.

When the reaction of **6** (X = Br) was carried out at low methoxide concentrations, the same two esters were obtained (40% yield), but in an *inverse ratio* (**8**/**9** = 1:3). A similar ratio was obtained (in very low yield) by debromination of 2,6-dibromo-4-methyl-4-phenylcyclohexanone in methanol using a zinc–copper couple.

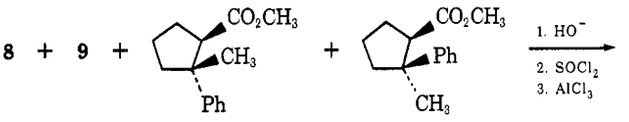
Reaction of *either cis*- or *trans*-2-bromo-5-methyl-5-phenylcyclohexanone (**7**) with NaOMe in MeOH gave a mixture of four products, esters **8** and **9** plus two new esters (**11** and **12**). The ester distribution (**8**/**9**/**11**/**12**) with 0.05 *M* NaOMe was 57:6:14:23, but with 2 *M* NaOMe this changed to 45:7:9:39. In other words, at higher methoxide concentrations the percentage of **12** appears to increase (and the percentage of **9** also appears to increase slightly) at the expense of **8** and **11**. The ester distribution of **8**/**9**/**11**/**12** obtained after equilibration was 26:24:28:22. Application to this mixture of the synthetic sequence leading to ring closure gave bicyclic ketone **10** and a new ketone **13**, the structure of which was assigned on the basis of its ir and nmr spectra. Ketone **13** must, for steric reasons, be derived from ester **12** in which the phenyl and methyl carboxylate groups are cis to one another.

Discussion

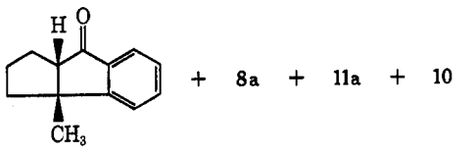
The difference in response of the 2-halo-4-methyl-4-phenyl- and 2-halo-5-methyl-5-phenylcyclohexanones (**6** and **7**, respectively) to variations in methoxide concentration is striking. With **6** formation of high yields of ester product even at low methoxide ion concentrations indicates the importance of the 1,3-diaxial effect in curbing side reactions, particularly in preventing the halogen atom from assuming the axial position most



7 (cis or trans)



11 **12**



13

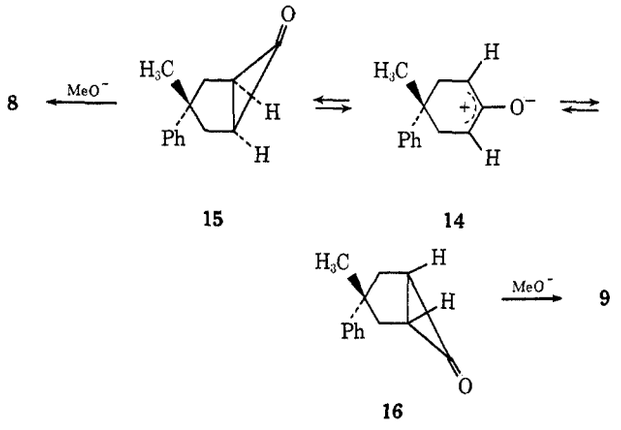
suitable for epoxy ether formation.[2a] Such 1,3-diaxial effects are absent in **7** and 2-chlorocyclohexanone. The twofold slower rate of ester formation for **6** relative to 2-chlorocyclohexanone[2a] might be construed as evidence for a small 1,3-diaxial effect in loss of halide ion from the enolate ion (*i.e.*, ionization of axial halogen), but the rate difference could equally well result from a smaller concentration of enolate ion derived from **6**.

The evidence obtained does not indicate whether an equatorial or axial halogen is ejected during the reaction. In example **6** an intramolecular SN2-type displacement, such as Loftfield suggested,[7] would lead to inversion of configuration if the halogen is equatorial, and retention of configuration if it is axial. The major product from **6**, ester **8**, is the result of retention of configuration or presumed displacement of axial halogen. In example *cis*-**7** an intramolecular SN2-type displacement of axial halogen would be expected to afford ester **9**, whereas ester **8** is the major product. The formation of the same products from *cis*- and *trans*-**7** indicates that epimerization at the halogen-bearing carbon may occur. Thus to accommodate the SN2 mechanism example **6** would rearrange through an axial halogen to give a major product **8**, and examples *cis*- and *trans*-**7** would equilibrate and then rearrange through an equatorial halogen to give a major product **8**.

A more likely mechanism, however, is one where ionization from **6** occurs first to give a dipolar ion (**14**) which then undergoes a disrotatory ring closure in either of two ways to give cyclopropanones **15** and **16**. According to this mechanism the product stereochemistry is determined after release of the halide ion, which would account for the similar product distribution from **6** and *cis*- or *trans*-**7**.

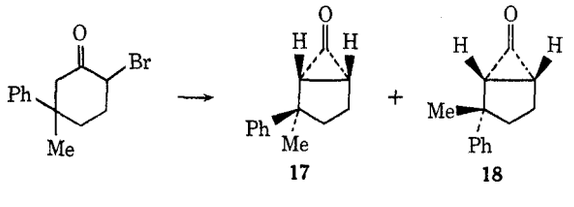
At low methoxide concentrations the major product is ester **9**, which is derived from **16** (or its hemiketal[4]). In 2 *M* NaOMe the major product is, however, ester **8**. One possible rationalization of these results is that cyclopropanone **15** is formed more rapidly than **16** and that in the presence of high methoxide concentrations **15** and **16** both react very rapidly with methoxide ion, making the product composition controlled by the

(7) R. B. Loftfield, *J. Amer. Chem. Soc.*, **73**, 4707 (1951).



rate of their formation. At very low methoxide concentrations, on the other hand, there is time to establish the **15** ⇄ **16** equilibrium prior to ester formation; the product distribution under these conditions is controlled by this equilibrium position, as well as by the rate constants for the reactions of **15** and **16** (or their hemi methyl ketals) with methoxide ion. One would not expect, *a priori*, that **16** would be favored over **15** at equilibrium, but it might react fast enough with methoxide ion to make **9** the favored product. Since the reversal in product distribution from 3:1 to 1:3 corresponds to only a small difference in rates and/or equilibria (*ca.* 1.3 kcal/mol at 25°), it does not appear practical to speculate further on the reasons for this reversal at this time. The significant point is that the ratio *does change*, indicating that more than one intermediate is present and that they are being interconverted. This result is consistent with the mechanism outlined in the introduction wherein a dipolar ion is formed and is converted (reversibly at least under some conditions) into a cyclopropanone intermediate.

Formation of four esters from *cis*- or *trans*-**7** must be a consequence of the formation of two cyclopropanones, **17** and **18**, each of which can be cleaved by



methoxide–methanol to give two products. Cyclopropanone **17**, in which the phenyl and carbonyl groups are trans will give **8** and **11**, and cyclopropanone **18** will give **9** and **12**. Changing from 0.05 to 2 *M* NaOMe evidently increases the yield of **18** at the expense of **17**, since the proportions of **9** and **12** increase at the expense of **8** and **11**. This is the same trend as was noted in the reactions of **6**, and a similar explanation can be offered. It is not clear, however, why the ratios of **9**/**12** and **8**/**11** change with changing base concentration.

Equilibration of the ester mixture from **7** for 286 hr gave a slightly different ratio of **8**/**9** than was obtained from equilibration of the ester mixture derived from **6** for 165 hr. This no doubt reflects the difficulty of reaching equilibrium.

Experimental Section[8]

Favorskii Rearrangement of 2-Chloro-4-methyl-*cis*-4-phenylcyclohexanone (6, X = Cl).—A solution of 1.26 g (5.63 mmol) of **6** (X = Cl)[2a] in 37.5 ml of methanol was mixed with 50 ml of 0.193 *M* sodium methoxide in methanol at 0° and allowed to remain at that temperature for 20 hr (2 half-lives). The excess base was neutralized with 20 ml of 0.5 *M* nitric acid, and the products were extracted with ether (2 × 100 ml). The ether layer was washed with 5% bicarbonate (2 × 75 ml) and with saturated brine (2 × 75 ml), dried over magnesium sulfate, and concentrated. The residue was adsorbed onto a slurry-packed (4% ether in hexane) silica gel (200 g) column (45 × 3.3 cm) and eluted with 1000 ml each of 4, 5, and 7% ether in hexane. The 250-ml fractions 4, 5, 6, and 7 contained 0.65 g (2.97 mmol; 53%) of a mixture of methyl 3-methyl-3-phenylcyclopentane-1-carboxylates (**8** and **9**). Analysis by glpc using a 7-ft copper tube (0.25 in.) packed with 8% Carbowax 20 M on Gas Chromasorb W operated at 155° and 80 ml/min helium flow rate indicated a trans (**8**) to cis (**9**) isomer ratio of 3:1.

Examination by nmr revealed that the chemical shift (1.29 ppm) of the three 3-methyl hydrogens of **8** was downfield by 5 Hz from those of **9**. A ratio of the integrated intensities of each absorption confirmed the 3:1 ratio. Spectroscopic measurements were consistent with the assigned structure: λ_{max}^{film} 5.77 (s), 8.30, and 8.51 (s, doublet) μ: $\delta_{TMS}^{CCl_4}$ 7.25 (5 H), 3.59 (3 H), 3.10–2.65 (7 H), 1.29 and 1.20 (3 H, two singlets): mass spectrum *m/e* 218, molecular ion.

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.93; H, 8.27.

Reaction of 2-Bromo-4-methyl-*cis*-4-phenylcyclohexanone (6, X = Br) by the Inverse Addition of Sodium Methoxide in Methanol.—A solution of 8.3 mmol (10% excess) of sodium methoxide in 100 ml of methanol was added over 5 hr to a stirred solution of 2.0 g (7.5 mmol) of **6** (X = Br)[2a] in 200 ml of methanol. The solution stood for 18 hr before a few drops of glacial acetic acid were added, and 200 ml of methanol was distilled through a Vigreux column. The concentrate was poured into 75 ml of saturated brine, and the products were extracted into pentane (4 × 100 ml). The extracts were combined, washed with saturated bicarbonate (2 × 50 ml) and with saturated brine, dried over magnesium sulfate, and concentrated. The residue was applied to a slurry-packed (3% ether in hexane) silica gel (70 g) column and eluted with 2 l. of 3% and 1 l. each of 10, 25, 50, and 100% ether in hexane. Fractions (250 ml) 3 and 4 contained 0.66 g (3.03 mmol; 40%) of a mixture of methyl 3-methyl-3-phenylcyclopentane-1-carboxylates. Analysis by glpc as above indicated a trans (**8**) to cis (**9**) isomer ratio of 1:3. Fractions 11 and 12 contained 0.25 g (1.15 mmol; 15%) of 2-methoxy-4-methyl-*cis*-4-phenylcyclohexanone. Rechromatography followed by bulb-to-bulb distillation, bp ~110° (0.2 mm), afforded an analytical sample: λ_{max}^{film} 5.75 (s), 8.4–9.3 (m, broad) μ; $\delta_{TMS}^{CCl_4}$ 7.8–7.4 (5 H), 3.5 (1 H, doublet of doublets, J_{ae} = 4.2 Hz, J_{aa} = 14.5 Hz), 3.46 (3 H, singlet), 3.1–1.7 (6 H, multiplet), 1.31 (3 H, singlet).

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.21; H, 8.15.

Chromatography fractions 14–17 contained 0.68 g (2.72 mmol; 36%) of 2-hydroxy-4-methyl-4-phenylcyclohexanone dimethyl ketal: λ_{max}^{film} 2.84 (m), 8.5–9.7 (s) μ: $\delta_{TMS}^{CCl_4}$ 7.8–7.3 (5 H), 4.2–3.8 (1 H), 3.35 and 3.42 (6 H, two 3 H singlets), 2.4–1.5 (7 H), 1.26 (3 H, singlet).

A portion of the α-hydroxy ketal was dissolved in methanol and stirred with a few drops of concentrated hydrochloric acid for 30 min. The products were extracted into 50:50 mixture of ether and hexane, and the organic solution was water-washed, dried, and concentrated. The residue crystallized while standing for 2 days. Recrystallization from chloroform–methanol afforded an analytical sample: mp 293° dec; λ_{max}^{KBr} 2.89 (m), 8.90, 9.06, and 9.45 (s). This material was too insoluble to give a clear nmr spectrum, but no methoxy bands of a dilute chloroform solution of the above was observed. This compound is assigned

(8) Melting points were determined on a Fisher-Johns melting point apparatus and are uncorrected. Analyses were performed by Micro-Tech Laboratories, Skokie, Ill. Infrared spectra were taken on a Beckman IR-5 spectrophotometer. Nmr spectra were measured on a Varian A-60 using tetramethylsilane as an internal reference. Determinations of rearrangement product mixtures were carried out on an F & M Model 5752A gas chromatograph equipped with a thermoconductivity cell and a Disc Chart Integrator Model 227.

the structure of a dihemiketal resulting from the dimerization of 2-hydroxy-4-methyl-4-phenylcyclohexanone.

Anal. Calcd for $C_{26}H_{32}O_4$: C, 76.44; H, 7.90. Found: C, 76.28; H, 7.93.

Reaction of 2-Bromo-4-methyl-*cis*-4-phenylcyclohexanone (6, X = Br) with 2.0 *M* Sodium Methoxide in Methanol.—A 1.0 g (3.75 mmol) portion of 6 (X = Br)[2a] was added with stirring to a 0°, 100 ml solution of 2.0 *M* sodium methoxide in methanol. The solution was stirred at 0° for 40 min before 15 g (>0.2 mol) of glacial acetic acid was added. The resulting slurry was poured into 75 ml of saturated brine, and the products were extracted into pentane (5 × 75 ml). The extracts were combined, washed with saturated bicarbonate (2 × 50 ml) and with saturated brine (1 × 50 ml), dried over magnesium sulfate, and concentrated. The residue was applied to a slurry-packed (3% ether in hexane) silica gel (70 g) column and eluted as above. Isolated was 0.46 g (2.1 mmol; 56%) of a mixture of the esters **8** and **9** in a ratio of 3:1 as determined by glpc. Also eluted from the silica gel column was 0.35 g (1.4 mmol; 37%) of 2-hydroxy-4-methyl-4-phenylcyclohexanone dimethyl ketal identical with that above. There was no 2-methoxy-4-methyl-*cis*-4-phenylcyclohexanone detected.

Equilibration of Methyl 3-Methyl-3-phenylcyclopentane-1-carboxylates (8 and 9) by Sodium Methoxide in Methanol.—A solution of 2.0 g (9.16 mmol) of a mixture containing 70% of **8** and 30% of **9** in 40 ml of methanol was refluxed, moisture excluded, with 0.1 mol of sodium methoxide in 60 ml of methanol. Portions of 10 ml were withdrawn at 25-hr intervals: the esters were isolated; and the ratio of isomers was determined by nmr. After 165 hr there was no change in the isomer ratio. The remainder of the mixture was processed in the usual fashion; nmr and glpc analyses indicated the equilibrium mixture to be 55% of **8** and 45% of **9**.

Stereochemical Assignments for Methyl 3-Methyl-*trans*-3-phenylcyclopentane-1-carboxylate (8) and Methyl 3-Methyl-*cis*-3-phenylcyclopentane-1-carboxylate (9).—A mixture of 1.55 g (7.59 mmol) of the isomeric carboxylic acids (56% trans and 44% cis)[9] derived from the respective esters (**8** and **9**) by basic hydrolysis were converted into their acid chlorides by reaction with excess thionyl chloride. The acid chlorides were dissolved in 200 ml of dry carbon disulfide, and 2.48 g (17.8 mmol) of aluminum chloride was added portionwise over 30 min to the stirred, 0° solution. The mixture was stirred at 0° for 90 min and then at room temperature for 40 min. The contents were poured onto 200 ml of crushed ice, and the aqueous layer was extracted thoroughly with ether. The extracts were combined, concentrated to 100 ml, and extracted with 5% sodium bicarbonate (4 × 75 ml). The ether layer was dried over magnesium sulfate and concentrated. The neutral material was applied to a slurry-packed (5% ether in hexane) silica gel (200 g) column (48 × 3.5 cm) and eluted with 1000 ml each of 5, 6, 10, and 15% ether in hexane. Fractions (250 ml) 7, 8, and 9 contained 0.84 g (4.54 mmol) of 2,3-benzo-1-methylbicyclo-[3.2.1]oct-2-en-4-one (**10**). Evaporative distillation (bp ~95° at 0.05 mm) followed by crystallization from pentane afforded an analytical sample: mp 30.5–31.0°, λ_{max}^{film} 5.92 (s) μ: $\delta_{TMS}^{CCl_4}$ 8.15 and 8.05 (1 H, two triplets), 7.62–7.15 (3 H, multiplet), 3.08 (1 H, broad triplet), 2.38–1.38 (10 H, multiplet).

Anal. Calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 84.00; H, 7.75.

The compound gave a colorless oxime, mp 138–139°.

Anal. Calcd for $C_{13}H_{15}NO$: C, 77.58; H, 7.51. Found: C, 77.55; H, 7.70.

The bicarbonate wash solutions were combined and neutralized with hydrochloric acid. The liberated carboxylic acid was extracted into ether, and the ether solution was dried and concentrated to yield 0.39 g (1.90 mmol) of 3-methyl-*trans*-3-phenylcyclopentane-1-carboxylic acid (**8a**). A small quantity of this acid was converted into its methyl ester with diazomethane, and the ester corresponded to **8** by infrared and nmr spectroscopy and by glpc retention time. The trans acid was purified by chromatography and recrystallized from ethanol–water, mp 42.5–44°.

Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.56; H, 7.88.

In order to confirm that the acid chloride derived from **8** has partially isomerized to that from **9** during reaction with aluminum chloride, the acid chloride from 0.4 g (2.0 mmol) of **8a** was dissolved in 70 ml of dry carbon disulfide and allowed to react with 0.86 g (6.2 mmol) of aluminum chloride as above. Isolation of the products gave 0.19 g (0.93 mmol) of the nonisomerized trans acid and 92 mg (0.50 mmol) of the tetralone **10**. This result indicates a 25% conversion of the trans into the cis acid chloride as compared with a 29% conversion in the first experiment.

***cis*-2,6-Dibromo-4-methyl-*cis*-4-phenylcyclohexanone.**—A solution of 16.6 g (0.104 mol) of bromine and 8.5 g (0.104 mol) of sodium acetate in 80 ml glacial acetic acid was added dropwise over 60 min to a stirred solution of 10.0 g (0.053 mol) of 4-methyl-4-phenylcyclohexanone[2a] in 100 ml acetic acid. Following the disappearance of bromine, the mixture was poured into 200 ml saturated brine, and the products were extracted with ether (3 × 100 ml). The ethereal solution was washed with 5% bicarbonate until all acetic acid was removed and with saturated brine, dried over magnesium sulfate, and concentrated. The remaining residue was applied to a slurry-packed (4% ether in hexane) silica gel (500 g) column (93 × 3 cm) and eluted with 1000 ml each of 4, 5, 6, and 8 ether in hexane. Fractions (500 ml) 5, 6, 7, and 8 contained, after recrystallization from benzene–hexane, 7.93 g (0.023 mmol; 44%) of *cis*-2,6-dibromo-4-methyl-*cis*-4-phenylcyclohexanone: mp 128–129°; λ_{max}^{KBr} 5.73 (s) μ; $\delta_{TMS}^{CDCl_3}$ 7.58 (5 H, broad), 4.68 (2 H, doublet of doublets, J_{ae} = 5 Hz, J_{aa} = 14.5 Hz), 3.31 and 2.37 (4 H, centers of multiplets), 1.29 (3 H, singlet).

Anal. Calcd for $C_{13}H_{14}OBr$: C, 45.12; H, 4.08. Found: C, 45.21; H, 4.07.

Reaction of *cis*-2,6-Dibromo-4-methyl-*cis*-4-phenylcyclohexanone with Zinc–Copper Couple in Methanol.—A suspension of zinc–copper couple prepared from 2.9 g (44 g-atoms) of powdered zinc and 2% cupric sulfate was added with 200 ml of methanol to 5.0 g (14.4 mmol) of dibromide in 200 ml of methanol. The mixture was stirred under reflux for 14 hr. The mixture was filtered through diatomaceous earth, and the filtrate plus washings were concentrated. The residue was dissolved in ether, and the ethereal layer was washed with 5% hydrochloric acid and with saturated brine, dried over magnesium sulfate, and concentrated. Chromatography on silica gel (150 g) gave by elution with 3% ether in hexane 66 mg (0.31 mmol; 2%) of the esters **8** and **9**. The ratio of isomers was determined by glpc to be 36% of **8** and 64% of **9**. Further elution (5% ether in hexane) of the column gave 0.24 g (1.27 mmol) of 4-methyl-4-phenylcyclohexanone, identified by comparison with an authentic sample.[2a] The other six products (by glpc) were unidentified.

Reaction of 2-Bromo-5-methyl-*cis*-5-phenylcyclohexanone (7a) with 5.0 × 10^{-2} *M* Sodium Methoxide in Methanol.—A 20-ml portion of 0.2 *M* sodium methoxide in methanol at 0° was added to 0.79 g (2.96 mmol) of **7a**[10] in 60 ml of methanol at 0°. The mixture was swirled and allowed to stand for 80 min (10 half-lives). A 4.0-ml solution of 0.25 *M* nitric acid was added, and the mixture was concentrated. The products were extracted into ether (2 × 75 ml), and the ether layer was washed with water (2 × 50 ml), with 5% sodium bicarbonate (1 × 50 ml), and with saturated brine (there were no carboxylic acids in the aqueous washings), dried over magnesium sulfate, and concentrated. The residue was chromatographed over 70 g of silica gel using 3% ether in hexane. The 250-ml fractions 2 and 3 contained 57 mg (0.26 mmol; 9%) of a mixture of carboxylic esters. Analysis by glpc using a 10-ft copper tube (0.25 in) packed with 10% Carbowax 20M on 60–80 Gas Chromasorb W operated at 175° and 35 ml/min helium flow rate revealed the isomer distribution in order of their elution as 23% of **12**, 14% of **11**, 57% of **8**, and 6% of **9**.

These esters were further purified by evaporative distillation (~80° at 0.1 mm) to yield an analytical sample.

Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 77.30; H, 8.44.

Reaction of 2-Bromo-5-methyl-*trans*-5-phenylcyclohexanone (7b) with 5.0 × 10^{-2} *M* Sodium Methoxide in Methanol.—The procedure for the reaction of 0.79 g (2.96 mmol) of **7b** (88% of **7b** and 12% of **7a**)[10] in 60 ml of methanol with 20 ml of 0.2 *M* sodium methoxide was the same as that described for **7a**. The reaction was terminated after 80 min (10 half-lives). The product isolated after chromatography weighed 51 mg (0.23 mmol, 9%) and was identical by glpc, infrared, and nmr to that

(9) By nmr analysis; the 3-methyl protons were found to be equally shielded by the carbomethoxy and carboxyl groups (δ 1.22 and 1.31 ppm).

(10) F. G. Bordwell, R. R. Frame, and J. G. Strong, *J. Org. Chem.*, **33**, 3385 (1968).

from **7a**. The distribution of isomers was 25% of **12**, 14% of **11**, 56% of **8**, and 5% of **9**.

Reaction of 2-Bromo-5-methyl-*cis*-5-phenylcyclohexanone (7a) with 1.0 *M* Sodium Methoxide in Methanol.—A 50-ml portion of 1.2 *M* sodium methoxide was cooled to 0° and added with stirring to 0.5 g (1.87 mmole) of **7a** in 10 ml of methanol. The reaction was maintained at 0° for 20 min before a solution of nitric acid (4.5 ml) in water was added. The products were extracted into ether, and the ether solution was washed with 5% bicarbonate (there were no carboxylic acids present) and with saturated brine, dried over magnesium sulfate, and concentrated. Elution of the residue over 70 g of silica gel with 3% ether in hexane gave 90 mg (0.41 mmol, 22%) of a mixture of carboxylic esters composed of (by glpc) 27% of **12**, 11% of **11**, 56% of **8**, and 6% of **9**.

Reaction of 2-Bromo-5-methyl-*trans*-5-phenylcyclohexanone (7b) with 1.0 *M* Sodium Methoxide in Methanol.—The same procedure as for the reaction of **7a** with 1.0 *M* sodium methoxide was employed for the reaction of 0.5 g (1.87 mmol) of 68% **7b** and 32% **7a** in 10 ml of methanol with 50 ml of 1.2 *M* sodium methoxide. Chromatography on silica gel yielded 110 mg (0.50 mmol, 24%) of Favorskii esters. Glpc analysis showed the product distribution as 26% of **12**, 11% of **11**, 56% of **8**, and 7% of **9**.

Reaction of 2-Bromo-5-methyl-*cis*-5-phenylcyclohexanone (7a) with 2.0 *M* Sodium Methoxide in Methanol.—A cooled, 50-ml solution of 2.4 *M* sodium methoxide in methanol was mixed at 0° with a 10 ml methanolic solution of 0.5 g (1.87 mmol) of **7a**. The remainder of the procedure followed that for the reaction of **7a** in 1.0 *M* sodium methoxide. The product esters weighed 0.28 g (1.28 mmol; 69%) and had an isomer distribution of 39% of **12**, 9% of **11**, 45% of **8**, and 7% of **9**.

Reaction of 2-Bromo-5-methyl-*trans*-5-phenylcyclohexanone (7b) with 2.0 *M* Sodium Methoxide in Methanol.—A solution of 0.5 g (1.87 mmol) of 68% **7b** and 32% **7a** in 10 ml of methanol was mixed at 0° with 50 ml of 2.4 *M* sodium methoxide in the manner as for **7a**. Termination and isolation as above gave 0.28 g (1.30 mmol; 69%) of Favorskii esters. Analysis by glpc revealed an isomer distribution of 39% of **12**, 9% of **11**, 45% of **8**, and 7% of **9**.

Equilibration of Methyl 2-Methyl-2-phenylcyclopentane-1-carboxylates (11 and 12) by Sodium Methoxide in Methanol.—A solution of 1.32 g (6.05 mmol) of a mixture containing 34% of **12**, 9% of **11**, 50% of **8**, and 7% of **9** in 40 ml of methanol was stirred at 0° for 1 hr with 0.1 mol of sodium methoxide. A 20-ml portion was withdrawn, the esters were isolated, and the distribution of isomers was determined by glpc. There had been no change in the isomer ratios, indicating that these products were stable under normal Favorskii conditions. The remaining solution was heated to reflux, and 10-ml portions were withdrawn after intervals of 154, 217, and 286 hr. After 286 hr, there was no change in the isomer ratios. The reaction mixture was processed in the usual fashion and a glpc analyses placed the equilibrium at 24% of **9**, 22% of **12**, 26% of **8**, and 28% of **11**.

Stereochemical Assignments for Methyl 2-Methyl-*cis*-2-phenylcyclopentane-1-carboxylate (12) and Methyl 2-Methyl-*trans*-2-phenylcyclopentane-1-carboxylate (11).—A mixture of 1.02 g (5.0 mmol) of the isomeric carboxylic acids derived from the respective esters (22% of **12**, 12% of **11**, 57% of **8**, and 9% of **9**) by basic hydrolysis were converted into their acid chlorides by reflux with excess thionyl chloride. The acid chlorides were dissolved in 110 ml of dry carbon disulfide, and the solution was cooled to −15°. Solid aluminum chloride (1.4 g, 10.5 mmol) was added over 15 min, and the mixture was stirred for 1 hr at −15° and at room temperature for 20 min. The mixture was poured onto 50 ml of ice, and the products were absorbed into ether (4 × 50 ml). The organic layers were combined, washed with dilute acid, and concentrated. The residue was dissolved in ether, and the solution was washed with 5% sodium bicarbonate (5 × 50 ml) and with saturated brine, dried over magnesium sulfate, and concentrated. The neutral material was adsorbed onto 70 g of silica gel and eluted with 1 l. of 2% and 4 l. of 4% ether in hexane. Fractions (250 ml) 8 and 9 contained 0.28 g (1.52 mmol) of 47% 2,3-benzo-1-methyl-*cis*-bicyclo[3.3.0]oct-2-en-4-one (**13**) and 53% 2,3-benzo-1-methylbicyclo[3.2.1]oct-2-en-4-one (**10**). These isomeric ketones were separated by collection of the eluted samples from a 10-ft 10% Carbowax 20M column operated at 160° with a helium flow rate of 35 ml/min. The tetralone (**10**) was identical with that previously isolated. The infrared and nmr spectra were consistent with the assigned structure for the *cis*-bicyclooctenone (**13**): λ_{max}^{film} 5.86 (s) μ: $\delta_{TMS}^{CCl_4}$ 8.15 and 8.05 (1 H, two triplets), 7.70–7.15 (3 H, multiplet), 2.60 (1 H, multiplet), 2.30–1.30 (10 H, multiplet).

Anal. Calcd for $C_{13}H_{14}O$: C, 83.83; H, 7.58. Found: C, 83.81; H, 7.60.

The solutions from the bicarbonate extractions were combined and neutralized with hydrochloric acid. The liberated acids were extracted into ether, and the ether solution was dried and concentrated to give 0.36 g (1.76 mmol). These acids were readily converted into their methyl esters with diazomethane, and the esters corresponded to **8** and **11** by infrared and nmr spectroscopy and by glpc retention time.

Yield of Methyl Cyclopentanecarboxylate (20) from 2-Chlorocyclohexanone (19) with Increasing Concentrations of Sodium Methoxide in Methanol. A.—A solution of 8.3 mmol (10% excess) of sodium methoxide in 100 ml of methanol was added over 6 hr to a stirred solution of 1.0 g (7.5 mmol) of distilled (bp 84–85°, 7.0 mm) 2-chlorocyclohexanone (**19**) in 200 ml of methanol. The solution was allowed to stand for 18 hr before a few drops of glacial acetic acid was added. Methanol (200 ml) was removed by distillation through a Vigreux column, and the concentrate was poured into 100 ml of saturated brine. The products were extracted into pentane (5 × 75 ml), and the extracts were combined, washed with saturated bicarbonate (3 × 50 ml) and with saturated brine (1 × 50 ml), dried over magnesium sulfate, and concentrated to ~2–3 ml by distillation of the pentane through a Vigreux column. The residue was diluted to 5.0 ml with chloroform in a volumetric flask. Measured volumes of the chloroform solution were injected into a 10-ft copper tube packed with 10% Carbowax 20M on Gas Chromasorb W operated at 120° with a helium flow rate of 35 ml/min. The yield of methyl cyclopentanecarboxylate (**20**), 3%, was calculated from the integrated peak area using a 0.214 *M* chloroform solution of prepared **20**[11] as a standard.

The other products could not be accurately analyzed by glpc because of their decomposition and interconversion during the analysis.

B.—A solution of 1.0 g (7.5 mmol) of **19** in 100 ml of methanol was added to a stirred solution of 15 mmol of sodium methoxide in 200 ml of methanol. The reaction was terminated after 12 hr by the addition of 0.48 g (8.0 mmol) of glacial acetic acid in 10 ml of methanol. The reaction mixture was processed, the products were isolated, and the yield of **20** (10%) was determined in the manner as above.

C.—A solution of 1.0 g (7.5 mmol) of **19** in 50 ml of methanol was added to a stirred solution of 0.1 mol of sodium methoxide in 50 ml of methanol. The cloudy suspension was stirred for 40 min before 6.0 g (0.1 mol) of glacial acetic acid was added. The mixture was poured into 100 ml of saturated brine, and the organic products were extracted into pentane (5 × 75 ml). The pentane extracts were processed and the yield of **20** (33%) was determined as above.

D.—A 100-ml portion of 2.0 *M* sodium methoxide in methanol was added to 1.0 g (7.50 mmol) of **19**, and the cloudy solution was stirred for 30 min. Glacial acetic acid (15 g, >0.2 mol) was added, and isolation as described in part C was followed. Analysis by glpc indicated a 49% yield of **20**.

Reaction of 2-Chlorocyclohexanone (19) by the Inverse Addition of Sodium Methoxide in Methanol.—A 100-ml solution of 0.413 *M* sodium methoxide in methanol was added over 6 hr to a stirred solution of 5.0 g (37.5 mmol) of **19** in 200 ml of methanol. The solution stood for 18 hr before excess glacial acetic acid was added. Methanol (250 ml) was removed by distillation through a Vigreux column and by distillation of 40 ml through a microware column packed with glass helices. The concentrate was applied to a slurry-packed (10% ether in hexane) silica gel (250 g) column and eluted with 1.0 l. each of 10, 15, and 25% ether in hexane with 2.0 l. of 50% ether in hexane and with 1.0 l. each of ether and chloroform. Fractions (250 ml) 14–19 contained 4.8 g of a mixture of 2-methoxycyclohexanone and 2-hydroxycyclohexanone dimethyl ketal. This mixture was rechromatographed as above, and fractions 14 and 15 contained 0.70 g (5.5 mmol; 15%) of 2-methoxycyclohexanone, identical with a prepared authentic sample,[12] and fractions 16–22 contained 3.74 g (23.3 mmol; 62%) of 2-hydroxycyclohexanone

(11) D. W. Goheen and W. R. Vaughan, "Organic Syntheses," Collect. Vol. IV, Wiley, New York, N. Y., 1963, p 594.

(12) H. Adkins, R. M. Elofson, A. G. Rossow, and C. C. Robinson, *J. Amer. Chem. Soc.*, **71**, 3622 (1949).

dimethyl ketal identical with that reported.[13] The α-hydroxy ketal gave a colorless 3,5-dinitrobenzoate, mp 97–98° (lit.[13] 97–98°).

Also when a small crystal of *p*-toluenesulfonic acid was added to 1.5 g (9.4 mmol) of the hydroxy ketal, and the mixture was allowed to remain at room temperature for 24 hr, a crystalline material weighing 1.1 g (4.1 mmol, 87%) was isolated and identified as dodecahydro-4a,9a-dimethoxydibenzo-*p*-dioxin, mp 167–168° (lit.[14] mp 165°).

Reaction of 2-Chlorocyclohexanone (19) with 2.0 *M* Sodium Methoxide in Methanol.—A 100-ml solution of 2.0 *M* sodium methoxide in methanol was added to 5.0 g (37.5 mmol) of **19**, and the cloudy mixture was stirred for 45 min. The mixture was cooled, and 15 g (>0.2 mol) of glacial acetic acid in 50 ml of methanol was added. Methanol (100 ml) was removed by distillation through a Vigreux column. The moist solid that remained was mixed with 200 ml of pentane, and the inorganic precipitate was removed by filtration. The filter cake was washed several times with pentane, and the filtrate was concentrated by the distillations of pentane through a Vigreux column and methanol (40 ml) through a microware column packed with glass helices. The residue was applied to a slurry-packed (10% ether in hexane) silica gel (250 g) column and eluted as in the above experiment. Fractions (250 ml) 12–16 contained 2.83 g (17.7 mmol; 47%) of 2-hydroxycyclohexanone dimethyl ketal identical with that described above. There was no 2-methoxycyclohexanone detected.

(13) C. L. Stevens and J. Tazuma, *J. Amer. Chem. Soc.*, **76**, 715 (1954).
(14) M. Bergman and M. Gierth, *Justus Liebigs Ann. Chem.*, **448**, 48 (1926); R. Criegee and W. Schnorrenberg, *ibid.*, **560**, 144 (1948).

Registry No.—6 (X = Cl), 19054-51-4; 6 (X = Br), 19209-96-2; **7a**, 17245-79-3; **7b**, 17245-80-6; **8**, 37107-95-2; **8a**, 37107-96-3; **9**, 37107-97-4; **10**, 37107-98-5; **10** oxime, 37111-95-8; **11**, 37107-99-6; **12**, 37108-00-2; **13**, 37108-01-3; **17**, 37108-02-4; **19**, 822-87-7; 2-methoxy-4-methyl-*cis*-4-phenylcyclohexanone, 37108-03-5; 2-hydroxy-4-methyl-4-phenylcyclohexanone dimethyl ketal, 37111-97-0; 2-hydroxy-4-methyl-4-phenylcyclohexanone dimer, 37164-32-2.

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Ivalbatin, a New Xanthanolide from *Iva Dealbata*[1a]

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Ivalbatin, a new xanthanolide, has been isolated from *Iva dealbata* Gray and its gross structure established as **2**. The stereochemistry of ivalbin and ivalbatin is discussed and formulas **23** (stereochemistry at C-2 still uncertain) and **26** (stereochemistry at C-6 questionable) are derived.

In an earlier communication[2] we derived a gross structure for ivalbin (**1**), a crystalline xanthanolide from *Iva dealbata* Gray. In the present paper we report isolation and structure determination of a second new xanthanolide (**2**) from *Iva dealbata*, which we have named ivalbatin, and discuss the stereochemistry of ivalbin and ivalbatin. For the former, formula **23** is deduced, although the stereochemistry at C-2 remains uncertain, for the latter formula **26**, with the stereochemistry at C-6 still in doubt.

As ivalbatin was obtained as an unstable oil and polymerized rapidly, it was purified by immediate conversion into the crystalline acetate **3**, $C_{17}H_{22}O_5$. The yield of **3**, based on the crude chloroform extract, was 16.8%, twice the amount of ivalbin; hence, ivalbatin is the major sesquiterpene lactone of this species.

Ivalbatin had $[\alpha]^{24}D$ −84°, uv end absorption at 210 nm (ε 13,400) and ir bands at 3450 (OH), 1755 (γ-lactone), 1705 (ketone), and 1655 cm^{-1} (C=C). A comparison of the nmr spectra of **2** and **3** revealed only one significant change, signals at 3.65 (>CHOH) and 3.40 ppm (>CHOH) being replaced by signals at 4.80 (>CHOAc) and 2.11 ppm (>CHOCOCH$_3$), respectively. Hence formula $C_{15}H_{20}O_4$ containing a secondary alcohol group could be assigned to ivalbatin. Other functional groups of **3** were the following: conjugated lactone as evidenced by ir bands at 1755 and 1655 cm^{-1}, uv end absorption at 209 nm (ε 13,800), and an nmr signal

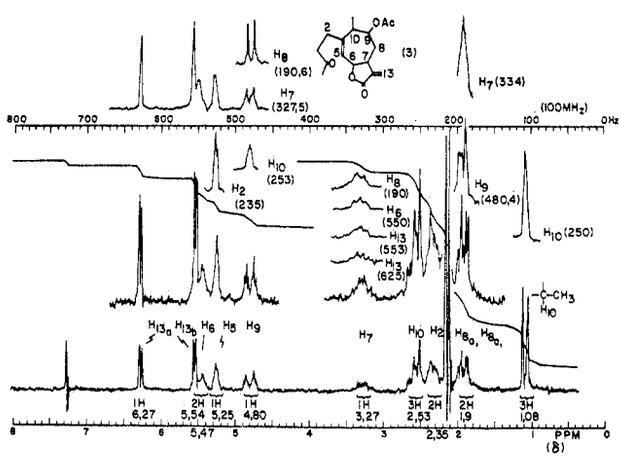

Figure 1.—Nmr spectrum and spin decoupling of acetylivalbatin (**3**).

characteristic of hydrogen under lactone at 5.47 ppm (Figure 1); methyl ketone (iodoform test, ir band at 1720 cm^{-1}, nmr signal at 2.17 ppm); secondary methyl (three-proton doublet at 1.08 ppm); trisubstituted double bond (one-proton broadened singlet at 5.25 ppm); and an exocyclic methylene group conjugated with the lactone group (two one-proton doublets at 5.54 and 6.27 ppm).

The presence of the exocyclic methylene group was confirmed by ozonolysis of **3** which yielded formaldehyde. Treatment of **3** with sodium borohydride gave an alcohol **4** which polymerized on standing and was converted into a diacetate **5** ($C_{19}H_{28}O_6$) (see Scheme I). The latter was not identical with diacetyldihydro-

(1) (a) Paper XIV: Constituents of *Iva* Species. For paper XIII, see G. D. Anderson, R. S. McEwen, and W. Herz, *Tetrahedron Lett.*, 4423 (1972). (b) Osaka University. (c) Florida State University. Work supported in part by a grant from the U. S. Public Health Service (CA-13121).
(2) W. Herz, H. Chikamatsu, N. Viswanathan, and V. Sudarsanam, *J. Org. Chem.*, **32**, 682 (1967).