3 hr., 1.94 moles/mole after 6 hr., and 2.33 moles/mole after 24 hr.

Methyl 2-Acetamido-4,6-O-benzylidene-2,3-dideoxy-α-D-mannopyranoside (XXIX).—The blocked amide (XXII), 2.54 g. (5.91 mmoles), was desulfurized with 25 g. of Raney nickel[15] according to the procedure described for the preparation of XXXII. The residue was extracted with hot petroleum ether (b.p. 88–90°) and the insoluble portion was partitioned between 15 ml. of benzene and 15 ml. of water. The aqueous extract was evaporated *in vacuo*, affording 0.96 g. of a colorless sirup (XXX) whose infrared spectrum showed the amide carbonyl at 6.02 μ and essentially no phenyl absorption in the 13–14.5-μ region.

The methanolysis of 0.74 g. of crude XXX, carried out as described for the preparation of XXXIII, gave 0.29 g. of the very hygroscopic salt (XXXI) which showed essentially no infared amide absorption.

Anal. Calcd. for $C_7H_{16}ClNO_4$: C, 39.4; H, 7.55; N, 6.56; Cl, 16.6. Found: C, 39.2; H, 8.27; N, 5.66; Cl, 14.7.

On titration with periodate, the product showed the consumption of 0.74 mole/mole after 1 hr. and 3 hr., 0.81 mole/mole after 6 hr., and 1.12 moles/mole after 24 hr.

The benzene extract from the XXII desulfurization residue was evaporated *in vacuo* affording 0.63 g. of a white foam which was crystallized from isopropyl alcohol–petroleum ether (b.p. 30–60°) to give 0.24 g. of white needles, m.p. 162–173°. Two recrystallizations from ethyl acetate–petroleum ether (30–60°) yielded 0.15 g. of the analytical sample of XXIX, m.p. 169–171°; $\lambda_{max(\mu)}^{Nujol}$ 3.07 (NH), 6.10 (amide C=O).

Anal. Calcd. for $C_{16}H_{21}NO_5$: C, 62.5; H, 6.88; N, 4.56. Found: C, 63.1, H, 7.29; H, 4.47.

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The Reaction of 9-Chloro-*trans*-1-decalone with Methoxide Ion[1]

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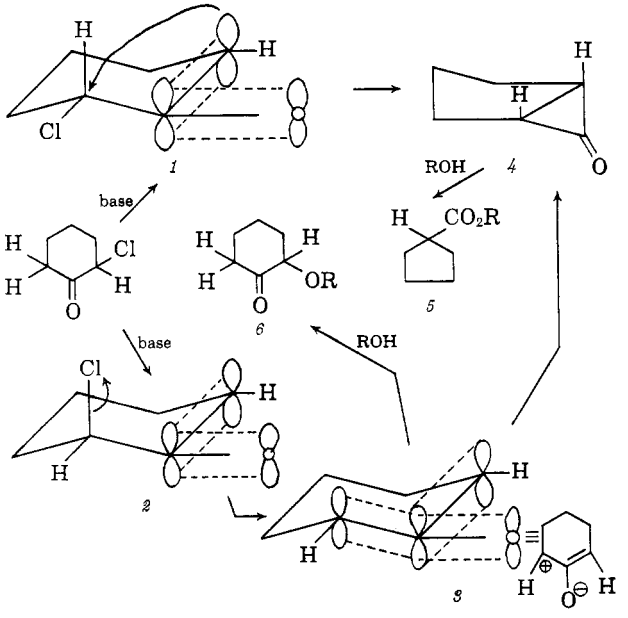
The reaction of 9-chloro-*trans*-1-decalone (**12**) with methanolic sodium methoxide yielded as the major products a mixture of 9-methoxy-*trans*-1-decalone (**14**), 9-methoxy-*cis*-1-decalone (**13**), and 2-methoxy-*trans*-1-decalone (**15**). The relationship of this reaction to the Favorskii rearrangement is discussed.

Previous studies of the Favorskii rearrangement[2] suggested that the reaction of α-halo ketones with bases to remove an α′-hydrogen atom could be followed either by an intramolecular S_N2 displacement (as in **1**) with inversion of configuration at the α-carbon atom[3] or by loss of halide ion (as in **2**) to form a zwitterionic intermediate **3** Although intervention of an intermediate such as **3** did not preclude a subsequent nonstereospecific Favorskii rearrangement—*e.g.*, the formation of **5**—in cases previously studied,[2a] it was clear that conditions favoring this intermediate **3** also favored the formation of solvolysis products such as **6**. In considering the applicability of these observations to the α-halocyclohexanone system, we have been led to the hypothesis that in order to maintain continuous *pi* orbital overlap the ionization **2** should be favored by an axial halogen atom and the displacement **1** should be favored by an equatorial halogen atom. Thus, the ionization process **2** should be enhanced not only by an increase in solvent polarity,[2a] but also by the presence of a halogen atom fixed in an axial conformation. Support for this idea is found in the reaction of several 9-α-halo-11-keto steroids (partial structure **7** necessarily containing an axial halogen atom) with alcoholic bases to yield 12-α-alkoxy ketones **8** rather than Favorskii rearrangement products.[4] The corresponding reaction with a 5-α-halo-6-keto steroid (partial structure **9**) was also reported to yield not a Favorskii product, but rather the 5-β-hydroxy ketone **10**.[5] The reported[3,6] failure of 2-chloro-2-methylcyclohexanone (**11**) to undergo a Favorskii rearrangement, only 2-hydroxy-2-methylcyclohexanone being isolated, may well be attributable to the same stereoelectronic effect since in this ketone both conformational factors[7] and dipole repulsion between the C=O bond and the C—Cl bond should favor the conformation **11** containing an axial chlorine atom.



(1) This research has been supported in part by a research grant from the Solvay Process Division of the Allied Chemical Corp. and in part by grant no. 594-A from the Petroleum Research Fund.

(2) (a) See H. O. House and W. F. Gilmore, *J. Am. Chem. Soc.*, **83**, 3972, 3980 (1961), and references cited therein, particularly (b) R. B. Loftfield, *ibid.*, **73**, 4707 (1951), and (c) J. G. Burr and M. J. S. Dewar, *J. Chem. Soc.*, 1201 (1954).

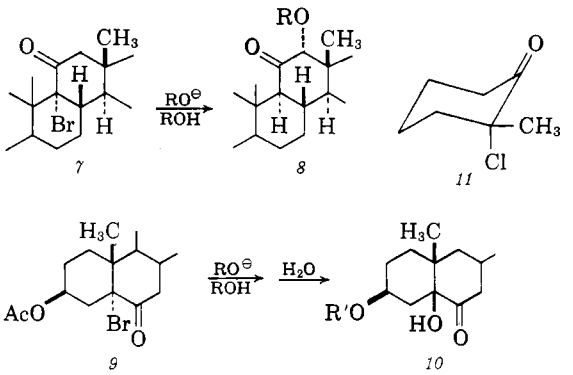
(3) G. Stork and I. J. Borowitz, *J. Am. Chem. Soc.*, **82**, 4307 (1960).

(4) (a) J. S. G. Cox, *J. Chem. Soc.*, 4508 (1960); (b) P. A. Diassi and R. M. Palmere, *J. Org. Chem.*, **26**, 5240 (1961).

(5) A. T. Rowland, *ibid.*, **27**, 1135 (1962). This product is suggested to arise from an intermediate epoxy ether (see ref. 6a).

(6) (a) A. S. Kende, *Org. Reactions*, **11**, 261 (1960); (b) M. Mousseron, F. Winternitz, and R. Jacquier, *Bull. soc. chim. France*, [5] **14**, 83 (1947).

(7) The free-energy differences between axial and equatorial conformations of a chlorine atom and a methyl group are 0.3 to 0.5 kcal./mole and 1.5 to 1.9 kcal./mole, respectively. E. L. Eliel, "Stereochemistry of Carbon Compounds," McGraw-Hill Book Co., Inc., New York, N. Y., 1962.



Although one might be tempted to conclude from these data that the energy barriers[2c] associated with the displacement process **1** or with the transformation **3** → **4** in a cyclohexanone system are so large that formation of the bicyclo[3.1.0] system **4** and, subsequently, the Favorskii product **5** is prohibited, this conclusion is clearly not valid since certain α-halocyclohexanones[2b] do yield Favorskii rearrangement products. Furthermore, the rearrangement of piperitone oxide[2a] to form Favorskii products in either a stereospecific or a nonstereospecific manner depending on reaction conditions indicates that the energy of neither transformation **1** → **4** nor **3** → **4** is prohibitively high. However, the aforementioned studies of the systems **7**, **9**, and **11** do suggest that reaction of the intermediate **3** with solvent (to form **6**) is more favorable than closure to the strained bicyclic system **4**. Since other structural features present in **7** and **9** might be imagined to hinder formation of a cyclopropanone and since the material balances reported from reactions of **7**, **9** and **11** certainly did not exclude the formation of substantial amounts of other products, it seemed advisable to investigate this question further. For this purpose we have studied the reaction of methanolic sodium methoxide with 9-chloro-*trans*-1-decalone (**12**),[8] a ketone possessing an unambiguously axial α-halogen atom with a minimum of structural complexity.

The results of this study (Chart I) indicate that primarily solvolysis products **13**, **14**, and **15** (the latter is not necessarily a kinetically controlled product) are formed from the chloro ketone **12** under conditions which afford good yields of Favorskii products from acyclic tertiary α-chloro ketones[2a] in a nonstereospecific rearrangement. These results are most readily explained by supposing that the zwittereonic intermediate (as in **3**) formed from ketone **12**, either because of the strain associated with closure to a bicyclo[3.1.0] system (as in **4**) or because of steric accessibility to attack by solvent, undergoes primarily reaction with solvent whereas the previously studied[2a] acyclic and conformationally mobile analog of **3** yields primarily a mixture of stereoisomeric cyclopropanones and, subsequently, Favorskii products.

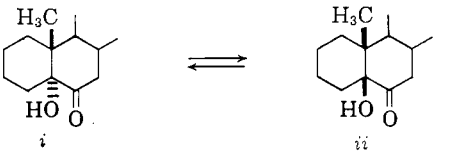
In order to learn whether formation of the enolate anion—*e.g.*, **2**—was much more rapid than loss of chloride ion—*e.g.*, **3**— the reaction was run to partial completion in methanol-d_1. Since the chloro ketone **12** recovered contained no appreciable enrichment in deuterium, we conclude that the formation of the enolate anion is either rate-determining or at least comparable in rate with the subsequent loss of chloride ion. In accord with our tentative conclusion[2] that chloride ion is lost from the enolate anion—*e.g.*, **2**—rather than from the free enol (the conjugate acid of **2**) is the fact that the chloro ketone **12** reacts more slowly in methanol solution in the absence of base; in the presence of added acid the reaction is also slower and product mixtures of different composition are formed. However, these observations by no means rigorously exclude the intermediacy of the enol. Since the 9-methoxy ketones **13** and **14** constitute the major fraction of the product mixture, the suggestion of Cox[4a] that an SN2 reaction—*i.e.*, **16**—may account for the reaction forming an alkoxy ketone is inappropriate for the chloro ketone **12**. As noted previously,[2] we see no compelling reason to invoke the explanation in other cases. The possible formation of the 9-methoxy ketone **13** (inversion at C-9) by an SN2 reaction between the chloro ketone **12** and methoxide ion appears most improbable in view of the tertiary nature of this alkyl chloride.

The stereochemical relationships between the various methoxy ketones were established by the reactions summarized in Chart I. The stereochemical assignments for the 9-substituted decalones **13**, **14**, **18**, and **19** follow both from the various spectra of these products (see Experimental) and from the equilibration of the two hydroxy ketones **18** and **19** (presumably *via* intermediate **20**) indicating that the *cis* isomer **18** and the *trans* isomer **19** are of comparable stability.[9] The structure of the epimeric 2-methoxy-1-decalones **15** and **17** follow from their spectral properties (see Experimental) and from a demonstration that only two hydrogen atoms are replaced by deuterium when the ketones **15** and **17** are treated with methanol-d_1 and base. The stereochemical assignments are based on the fact that base-catalyzed equilibration of either compound produces a mixture in which **15** (with a *trans*-decalin ring fusion and an equatorial substituent) and the ketone **17** (with a *trans*-decalin ring fusion and an axial substituent) are the predominate components with **15** being more stable than **17**.

In view of the fact that no appreciable quantity of either of the hydroxy ketones **18** and **19** was formed from the chloro ketone **12**, we were led to consider what factor might account for the apparently very different behavior[5] of the bromo ketone **9** (which gave the hydroxy ketone **10** as the only isolated product). Since our previous studies[2] indicated that the slight changes in reaction conditions (potassium hydroxide in methanol, sodium ethoxide in ethanol) almost certainly were not responsible for this differ-

(8) H. O. House and H. W. Thompson, *J. Org. Chem.*, **26**, 3729 (1961).

(9) Y. Mazur and M. Nussim, *Tetrahedron Letters*, No. **22**, 817 (1961). In this study α- and β-5-hydroxy-6-keto steroids (**i** and **ii**) were equilibrated in refluxing methanolic potassium hydroxide. The equilibrium mixture



i *ii*

contained 92% of the *cis* isomer **ii**, the increased stability of the *cis* isomer being attributed to formation of a strong hydrogen bond. In our series **18** and **19**, the relative stability of the *cis* isomer (54–67% at equilibrium) is less overwhelming. This result is not unexpected, since the angular methyl group present in **i** and **ii** reduces the difference in energy between the *cis*- and *trans*-decalin systems present (see ref. 7).

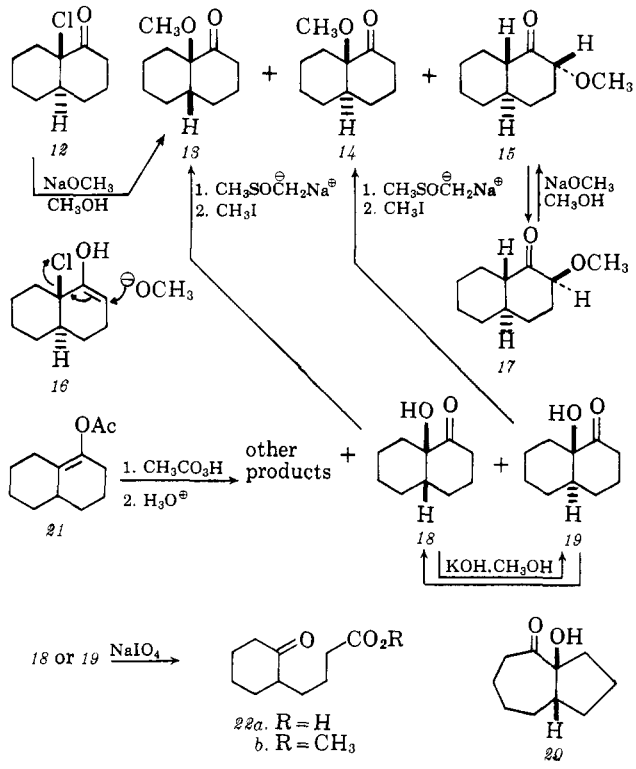
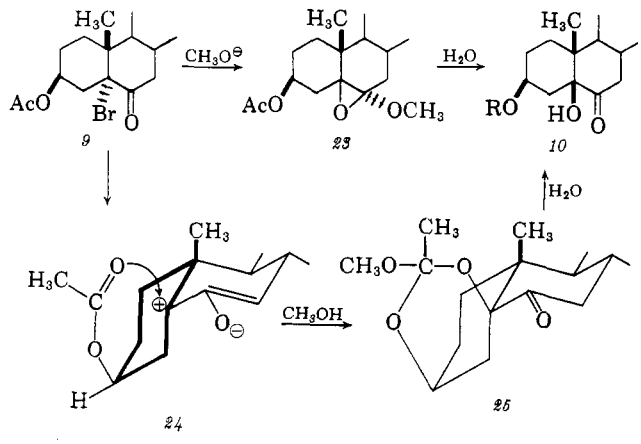


Chart I

ence, the most reasonable explanation appeared to lie in the presence of some structural feature present in **9** but not **12**. Rowland had argued[5] that the bromo ketone **9** was first coverted to the epoxy ether **23**[6a] and subsequently during the isolation process to the hydroxy ketone **10**. The fact that the 5β-hydroxy compound **10** was isolated was offered as stereochemical evidence for this reaction path. However, the finding[9] that the reaction conditions employed might suffice to interconvert the 5α- and 5β-hydroxy compounds renders this stereochemical evidence equivocal at best. Furthermore, we have been unable to discern any reason why the sequence **9** → **23** → **10** should be substantially more important with the ketone **9** than with the ketone **12**. We are, therefore, led to the conclusion that the differing behavior of the bromo ketone **9** is to be attributed to the presence of the 3β-acetoxyl function and suggest the reaction path **9** → **24** **25** → **10** in which the intermediate zwitterion **24** reacts intramolecularly with the acetoxy function more rapidly than it is attacked by solvent.



Experimental[10]

Reaction of 9-Chloro-*trans*-1-decalone (12) with Sodium Methoxide.—To a solution of sodium methoxide, prepared from 700 mg. (30.5 mg.-atoms) of sodium and 35 ml. of methanol, was added 999.5 mg. (5.38 mmoles) of 9-chloro-*trans*-1-decalone,[8] m.p. 39.5–41.5°. The solution, from which sodium chloride began to separate after a few seconds, was allowed to stand at room temperature for 12 hr. and then diluted with water and extracted with an ether–petroleum ether mixture. After concentration of the organic extract, the residual liquid (*ca.* 1 g.) was found to contain,[11] in order of elution, the *trans*-9-methoxy ketone **14** (30%), the *cis*-9-methoxy ketone **13** (27%), and the 2-methoxy ketone **15** (25%) as well as a number of minor components. Each of the three major components was collected[11] and redistilled in a short-path still. The *trans*-9-methoxy ketone **14**, b.p. 65–75° (0.65 mm.) $n^{25}D$ 1.4818, m.p. 23°, has infrared absorption[12] at 1713 cm.$^{-1}$ (C=O), an ultraviolet maximum[13] at 305.5 mμ (ε 40) and n.m.r. absorption[12] at 6.95 τ (singlet, 3H, O—CH_3) with complex absorption in the region 7.0–9.0 τ and no absorption at lower field than 6.8 τ.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96; mol. wt., 182. Found: C, 72.41; H, 10.01; mol. wt., 182 (mass spectrum).

The *cis*-9-methoxy ketone **13**, b.p. 65–75° (0.65 mm.), $n^{25}D$ 1.4851, m.p. 20°, has infrared absorption[12] at 1710 cm.$^{-1}$ (C=O), an ultraviolet maximum[13] at 301 mμ (ε 33) and n.m.r. absorption[12] at 6.91 τ (singlet, 3H, OCH_3) with complex absorption in the region 7.0 to 9.0 τ and no absorption at lower field than 6.8 τ.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96; mol. wt. 182. Found: C, 72.66; H, 9.98; mol. wt., 182 (mass spectrum).

Attempts to collect the 2-methoxy ketone **15** at relatively high column temperatures resulted in partial epimerization of ketone **15** to ketone **17**. Each of these two products was collected[11] at sufficiently low temperature to prevent epimerization and then distilled in a short-path still. The 2-methoxy ketone **15** (eluted second), b.p. 80–95° (0.55 mm.), m.p. 45–47°, has infrared absorption[12] at 1724 cm.$^{-1}$ (C=O). The ultraviolet absorption was obscured by the presence of traces of octalones (<2%) which we were unable to remove. The product has n.m.r. absorption[11] at 6.42 τ (1H, multiplet with splitting pattern not discernible but with a half-band width of approximately 20 c.p.s. as expected for an axial proton, >CH—O) and at 6.66 τ (3H, singlet, CH_3O) with complex absorption in the region 7.5 to 9.0 τ.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96; mol. wt., 182. Found: C, 72.50; H, 9.87; mol. wt., 182 (mass spectrum).

The 2-methoxy ketone **17** (first eluted), b.p. 70–85° (0.6 mm.), has infrared absorption[12] at 1715 cm.$^{-1}$ (C=O), an ultraviolet maximum[13] at 304.5 mμ (ε 50) and n.m.r. absorption[12] at 6.64 τ (1H, multiplet, splitting pattern not discernible but with a half-band width of approximately 5 c.p.s. as expected for an equatorial proton, >CH—O) and at 6.78 τ (3H, singlet, CH_3O) with complex absorption in the region 7.5 to 9.0 τ.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96; mol. wt., 182. Found: C, 72.41; H, 9.88; mol. wt., 182 (mass spectrum).

A solution of each of the pure 2-methoxy ketones **15** and **17** in methanolic sodium methoxide was refluxed for 10 hr. under nitrogen and then the neutral material was recovered in the usual way. Analysis[11] of each crude product indicated the

(10) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated magnesium sulfate was employed as a drying agent. The infrared spectra were determined with either a Baird, Model B, or a Perkin–Elmer, Model 21, infrared recording spectrophotometer fitted with a sodium chloride prism. The ultraviolet spectra were determined with a Cary recording spectrophotometer, Model 11. The n.m.r. spectra were determined at 60 Mc. with a Varian, Model A-60, n.m.r. spectrometer. The mass spectra were obtained with a CEC, Model 21-130, mass spectrometer. The microanalyses were performed by Dr. S. M. Nagy and his associates and by the Scandinavian Microanalytical Laboratory.

(11) A gas chromatography column packed with Dow Corning silicone fluid, no. 710, suspended on ground firebrick was employed for this separation.

(12) Determined in carbon tetrachloride solution.

(13) Determined in 95% ethanol solution.

presence of 68% of the 2-methoxy ketone **15**, 11% of the 2-methoxy ketone **17** and 22% of a mixture of other components. A solution of 0.035 ml. of a mixture of the methoxy ketones **15** and **17** in methanolic sodium methoxide, prepared from 30 mg. (1.3 mg.-atoms) of sodium and 2.25 ml. of methanol-d_1, was refluxed under nitrogen for 10 hr. and then mixed with 15 ml. of deuterium oxide and 135 mg. (1.3 mmoles) of acetic anhydride (the pH of the final solution was 5–6). After the mixture had been extracted with an ether–petroleum ether mixture, the extract was concentrated. A sample of the 2-methoxy ketone **15**, collected,[11] and analyzed by mass spectrometry, was found to contain 8% d_0 species, 40% d_1 species, 52% d_2 species, and <1% d_3 species.

In subsequent reactions of the 9-chlorodecalone **12** with methanolic sodium methoxide run as previously described, the reaction was found to be complete in less than 1 min. at room temperature. A solution of 50.3 mg. (0.27 mmole) of the chloro ketone **12** in methanolic sodium methoxide, prepared from 20 mg. (0.87 mg.-atom) of sodium and 4.6 ml. of methanol-d_1, was swirled for 30 sec. and then quenched by the addition of a solution of 74 mg. (0.70 mmole) of acetic anhydride in 15 ml. of deuterium oxide. The crude organic product, recovered in the usual way, was found to contain 35% of the starting chloro ketone **12** as well as the methoxy decalones **13** (20%), **14** (21%), and **15** (7%). A sample of the chloro ketone **12** collected[11] from the mixture was found by mass spectrometric analysis to contain less than 5% of deuterium-containing species. After a solution of 100 mg. of the chloro ketone **12** and 10 mg. of *p*-toluenesulfonic acid in 3 ml. of methanol had been refluxed under nitrogen for 1 hr., the recovered product contained[11] a mixture of the unchanged chloro ketone (28%) and a component tentatively identified as $\Delta^{9,10}$-octal-1-one[8] (63%). After a mixture of 93.3 mg. (0.5 mmole) of the chloro ketone **12**, 240 mg. (2.86 mmoles) of sodium bicarbonate and 3.5 ml. of methanol had been stirred at room temperature for 96 hr., the recovered organic product contained[11] the unchanged chloro ketone **12** (66%) and the methoxy ketones **13** (10%), **14** (11%), and **15** (4%).

The 9-Hydroxy-1-decalones 18 and 19.—After a sample of 1-acetoxy-$\Delta^{1,9}$-octalin (**21**) had been converted to a mixture of octalones and accompanying by-products as previously described,[8] the $\Delta^{8,9}$-octal-1-one was separated from the mixture by extraction with pyrrolidine[14] and residual material was separated from lower boiling components and then chromatographed on Woelm, activity no. 3, alumina. The later fractions from the chromatograph, eluted with ether–hexane mixtures, contained[11] mixtures of the hydroxy ketones **18** and **19**. The minor component, *cis*-9-hydroxy-1-decalone (**18**, the first isomer eluted from the gas chromatograph), was collected and recrystallized from petroleum ether to separate the pure hydroxy ketone **18** as white prisms, m.p. 61–64°, identified with the previously described[8] sample, m.p. 62.5–63.5° by a mixed melting-point determination and comparison of infrared spectra. The product, which has an ultraviolet maximum[13] at 287.5 mμ (ϵ 34.5) and infrared absorption[12] at 3485 cm.$^{-1}$ (assoc. O—H) and 1708 cm.$^{-1}$ (C=O), shows evidence of intramolecular hydrogen bonding, consistent with the assigned stereochemistry,[9] since the band at 3485 cm.$^{-1}$, attributable to an associated hydroxyl function, is not replaced by a band at higher frequency as the solution is diluted.[15] The n.m.r. spectrum[16] of the material has a singlet at 6.09 τ (6.33 τ in carbon tetrachloride, 1H, O—H) and complex absorption in the region 7.2 to 9.0 τ.

The major component from the alumina chromatograph, *trans*-9-hydroxy-1-decalone (**19**, eluted second from the gas chromatograph) was isolated by fractional crystallization from pentane as white crystals, m.p. 38–44.5°. Sublimation (60–75° at 0.65 mm.) raised the melting point to 44–45°. The product has an ultraviolet maximum[13] at 300 mμ (ϵ 32.6) with infrared bands[12] at 3610 cm.$^{-1}$ (unassoc. O—H), at 3490 cm.$^{-1}$ (assoc. O—H), and at 1705 cm.$^{-1}$ (C=O). As the solution is diluted the relative intensity of the peak[15] at 3610 cm.$^{-1}$ increases indicating the lack of favorable geometry for intramolecular hydrogen bond formation.[9] The n.m.r. spectrum[16] has a singlet at 6.97 τ (O—H) superimposed on a multiplet in the region 6.9 to 7.2 τ (possibly the axial proton at C-2)[17] and complex absorption in the region 7.7 to 9.0 τ.

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59; mol. wt., 168. Found: C, 71.21; H, 9.77; mol. wt., 168 (mass spectrum).

After a solution of 47.9 mg. of the *trans*-hydroxy ketone **19** in methanolic sodium methoxide, prepared from 208 mg. of sodium and 5 ml. of methanol, had been refluxed under nitrogen for 24.5 hr, the product was isolated in the usual way. The product mixture contained[11] 62% of the *trans* isomer **19** and 38% of the *cis* isomer **18**. A collected[11] sample of the *cis* isomer was identified both from its retention time and from its infrared spectrum. From a comparable reaction in which a solution of the *trans*-9-hydroxy ketone **19** in 17% methanolic potassium hydroxide was refluxed for 21.5 hr., the resulting mixture of 9-hydroxy ketones contained 46% of the *trans* isomer **19** and 54% of the *cis* isomer **18**. An equilibration starting with the pure *cis* isomer **18** afforded a mixture containing 33% of the *trans* isomer **19** and 67% of the *cis* isomer **18**. Because of competing side reactions more complete equilibrations of the hydroxy ketones **18** and **19** were not practical.

A solution of 100 mg. (0.595 mmole) of the *cis*-hydroxy ketone **18** and 160 mg. (0.75 mmole) of sodium periodate in 4 ml. of 50% aqueous methanol was allowed to stand at room temperature for 26 hr. and then diluted with water and extracted with ether. After the extract had been concentrated, crystallization of the residue from petroleum ether afforded 27.8 mg. (25.4%) of 4-(2-ketocyclohexyl)butyric acid (**22a**) as white plates, m.p. 55–58° (lit.,[18] 57.5–59.5°),[19] whose melting point was not depressed by mixing with the subsequently described authentic sample. A 36.9-mg. sample of the keto acid **22a** derived form the *cis*-hydroxy ketone **18** was esterified as subsequently described to yield 36.2 mg. (91%) of the crude methyl ester **22b**, b.p. 105–110° (0.8 mm.), from which a pure sample of the ester was collected[11] and identified with the subsequently described sample by comparison of retention times, infrared spectra, and mass spectra.

Similarly, reaction of 100 mg. (0.595 mmoles) of the *trans*-hydroxy ketone **19** with 161.5 mg. (0.75 mmole) of sodium periodate in aqueous methanol for 18 hr. at room temperature yielded, after purification, 95.0 mg. (86.5%) of the keto acid **22a**, m.p. 60–62°. Esterification of a 78.2-mg. sample of this acid produced 65 mg. (77%) of the keto ester **22b**, b.p. 95–100° (0.27 mm.), which was identified as previously described.

An authentic sample of the keto acid **22a** was obtained as a by-product from the oxidation of a mixture of 1-decalols with chromic acid.[8] The keto acid, which crystallized from petroleum ether as white plates, m.p. 60.5–61.5°, has an ultraviolet maximum[13] at 287 mμ (ϵ 22.5) with broad infrared absorption[12] in the region 3400–2600 cm.$^{-1}$ (assoc. O—H) and a peak at 1705 cm.$^{-1}$, (C=O of ketone and carboxyl functions). A solution of 200.5 mg. (1.09 mmoles) of the keto acid **22a** and 3 drops of sulfuric acid in 3 ml. of methanol was refluxed for 1 hr. and then cooled and treated with excess aqueous sodium bicarbonate. The resulting mixture was extracted with ether and the extract was concentrated and distilled to separate 200 mg. (93%) of the crude methyl ester **22b** which contained[11] 10% of a minor component. The pure ester **22b**, b.p. 95° (0.2 mm.), n^{25}D 1.4635 (lit.,[20] n^{20}D 1.4762), was obtained by collection from the gas chromatograph and redistillation. The product has infrared absorption[12] at 1735 cm.$^{-1}$ (ester C=O) and at 1708 cm.$^{-1}$ (C=O).

Anal. Calcd. for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15; mol. wt., 198. Found: C, 66.69; H, 9.20; mol. wt., 198 (mass spectrum).

An authentic sample of pure[11] methyl 3-(2-ketocyclohexyl)-propionate, b.p. 114–115° (1.5 mm.), n^{25}D 1.4662 [lit.,[19] 135–137° (11 mm.), n^{20}D 1.4640], prepared by Dr. Harry Babad in our laboratories has infrared absorption[12] at 1735 cm.$^{-1}$ (ester C=O)

(14) H. O. House and H. W. Thompson, *J. Org. Chem.*, in press.

(15) A Baird infrared spectrophotometer equipped with a calcium fluoride prism was employed for this measurement.

(16) Determined as a solution in deuteriochloroform.

(17) See S. Brownstein, *J. Am. Chem. Soc.*, **81**, 1606 (1959). Similarly, the n.m.r. spectrum[12] of the chloro ketone **12** has a multiplet centered at 6.87 τ [1H, pattern consistent with coupling with the equatorial C-2 proton (J = 13 c.p.s.) and the two protons at C-3] as well as complex absorption in the region 7.5 to 9.0 τ.

(18) W. Herz, *J. Org. Chem.*, **22**, 630 (1957).

(19) Since the keto acid **22a** melts very close to its next lower homolog 3-(2-ketocyclohexyl) propionic acid [reported m.p. 64–66°, M. Häring and T. Wagner-Jauregg, *Helv. Chim. Acta*, **40**, 852 (1957)] and the infrared spectra of the two acids are not particularly distinctive, further characterization of the keto acid **22a** was considered appropriate.

(20) A. I. Kamneva and A. I. Efimenkova, *Trudy Moskv. Khim.-Tekhnol. Inst. im. D. I. Mendeleeva*, No. **25**, 38 (1957); *Chem. Abstr.*, **52**, 14571 (1958). There is question as to the correctness of this assigned structure since the authors report the semicarbazone of the acid **22a** to melt at 252°, whereas others (ref. 17) report values in the range 185–189°.

TABLE I

CARBONYL ABSORPTION MAXIMA IN THE INFRARED AND ULTRAVIOLET

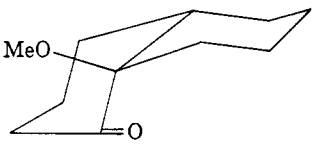
Compound	$\nu_{C=O}^{CCl_4}$, cm.$^{-1}$	λ_{max}^{EtOH}, mμ	Conformation of alpha electronegative substituent
trans-1-Decalone	1711	286.5 (ε 26.6)	
trans-9-Chloro-1-decalone (**12**), m.p. 40–41°	1723	300.5 (ε 45)	Axial
trans-9-Methoxy-1-decalone (**14**), m.p. 23°	1713	305.5 (ε 40)	Axial
cis-9-Methoxy-1-decalone (**13**), m.p. 20°	1710	301 (ε 33)	Axial
cis-2-Methoxy-*trans*-1-decalone (**15**), m.p. 45–47°	1724	...	Equatorial
trans-2-Methoxy-*trans*-1-decalone (**17**), liquid	1715	304.5 (ε 50)	Axial
cis-9-Hydroxy-1-decalone (**18**), m.p. 62.5–63.5	1708	287.5 (ε 34.5)	Presumably equatorial, intramolecular hydrogen bonding occurs
trans-9-Hydroxy-1-decalone (**19**), m.p. 44–45°	1705	300 (ε 32.6)	Axial, intermolecular hydrogen bonding occurs
cis-2-Hydroxy-*trans*-1-decalone (**12** in ref. 8), m.p. 76–76.7°	1712	275 (ε 38)	Presumably equatorial, hydrogen bonding occurs
cis-2-Acetoxy-*trans*-1-decalone (**9** in ref. 8), m.p. 72.5–73.5°	1730	284.5 (ε 29.3)	Equatorial

and at 1708 cm.$^{-1}$ (C=O) as well as many similarities to the methyl ester **22b** in the fingerprint region. However, the two homologous keto esters are readily distinguished by their mass spectra.

A solution containing 5.22 mmoles of the sodium derivative[21] of dimethyl sulfoxide was prepared from 179.6 mg. (7.5 mmoles) of sodium hydride, 18 ml. of dry (distilled from a mixture containing triphenylmethylsodium) dimethyl sulfoxide, and 2 mg. of triphenylmethane.[22] A solution of 84 mg. (0.5 mmole) of the *trans*-hydroxy ketone **19** in 0.85 ml. of ether was added to 2.0 ml. (0.58 mmole) of the dimethyl sulfoxide solution and then 2.75 g. (19.2 mmoles) of methyl iodide was added promptly. After the resulting mixture had been allowed to stand for 24 hr., it was diluted with water and extracted with petroleum ether. Concentration of the extract followed by distillation separated 71.4 mg. of colorless liquid, b.p. 70–85° (0.45 mm.), which contained[11] at least six components including the *trans*-methoxy ketone **14** (36%). A sample of the *trans*-methoxy ketone **14** was collected[11] and identified by comparison of its infrared spectrum with the spectrum of the previously described material.

The same alkylation precedure was applied to 168 mg. (1.0 mmole) of the *cis*-hydroxy ketone **18**, 1.0 mmole of the sodium derivative of dimethyl sulfoxide, 4.45 ml. of dimethyl sulfoxide, and 9.1 g. (64.2 mmoles) of methyl iodide being employed. From the crude reaction mixture which contained at least six components including the *cis*-methoxy ketone **13** (11%), a sample of the *cis*-methoxy ketone **13** was obtained by successive collection from two columns.[11,23] Although gas chromatography on two columns indicated that the collected sample was homogeneous and had the same retention time as the previously described methoxy ketone **13**, both the infrared and mass spectra of the collected sample indicated the presence of a minor component which we were unable to remove. Thus, the infrared spectra of the two samples were identical except for the presence of four additional weak bands (less than 15% of the intensity of the C=O stretching band or the C—H stretching band) at 1380, 1360, 975, and 910 cm.$^{-1}$ in the spectrum of the collected sample. The mass spectrum of the collected sample has peaks not present in the pure *cis*-methoxy ketone **13** at m/e 196 and 168; the relative intensities of the peaks at m/e 182 (molecular ion of **13**) and at m/e 196 (presumably the molecular ion of the contaminant) are in the ratio 100:32. Comparison of the thin layer chromatograms of the pure methoxy ketone **13** and the collected sample (employing both alumina and silica gel coatings) indicated that the collected sample contained primarily the methoxy ketone **13** accompanied by a contaminant. Thus, all of our data are in accord with the presence in the collected sample of the methoxy ketone **13** accompanied by small amounts of a second component, possibly the C-methyl derivative of the methoxy ketone **13**.

Spectroscopic Properties.—The positions of carbonyl absorption in the infrared and ultraviolet, summarized in Table I, indicate that the predominant conformations[7,24] of the compounds listed are in accord with the stereochemical assignments made. The data indicate that compound **13** exists predominately in the conformation shown in formula **13a**.



13a

(21) E. J. Corey and M. Chaykovsky, *J. Am. Chem. Soc.*, **84**, 866 (1962).

(22) The triphenylmethane was added as an indicator. The solution was standardized by titrating a 2-ml. aliquot with diisopropyl ketone until the red color was discharged.

(23) A column packed with 20 M Carbowax suspended on ground firebrick was employed for this separation.

(24) L. F. Fieser and M. Fieser, "Steroids," Reinhold Publishing Corp., New York, N. Y., 1959, pp. 175–176.