II. *Anal.* Calcd for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02. Found: C, 63.74; H,7.93.

When the photolysis was done in CCl_4 with a slight molar excess of CH_3OD, the ester was not obtained; other products formed very slowly.

3,6-Dimethyl-6-acetoxycyclohexa-2,4-dienone, from 2,5-dimethylphenol and lead tetraacetate,[50] was purified for elemental and spectral analyses by glpc. The nmr spectrum had a broad singlet at τ 3.9 (2), a broad multiplet at 4.1 (1), 7.95 (d, 3, J = 1 Hz), 8.0 (s, 3), and 8.73 (s, 3); infrared bands at 3020 w, 2980 w, 2920 w, 1745 s, 1670 s, 1575 w, 1440 m, 1400 m, 1365 m, 1315 w, 1245 s, 1215 m, 1165 m, 1115 w, 1070 s, 1015 m, and 865 w cm^{-1}; $\lambda_{max}^{CH_3OH}$ 300 mμ (ϵ 4 × 10^3). *Anal.* Calcd for $C_{10}H_{12}O_3$: C, 66.65; H, 6.71. Found: C, 66.77; H, 6.90.

Photolysis of 3,6-Dimethyl-6-acetoxycyclohexa-2,4-dienone. A 50-mg sample of the cyclohexadienone, purified by glpc, was dissolved in 0.4 ml of CCl_4 and 15 μl of CH_3OD. At the end of 10 min of photolysis, approximately one-third of the starting material had been converted to a new compound as estimated by nmr and glpc analyses. The product had $\lambda_{max}^{CH_3OH}$ 241 mμ (ϵ 6 × 10^3); infrared bands at 2950 m, 1750 sh, 1735 s, 1620 w, 1515 m, 1430 m, 1365 m, 1200 s, 1140 m, 980 (broad), 910 w, and 720 s (broad) cm^{-1}; parent peak at *m/e* 213 (calcd for $C_{11}H_{15}DO_4$: 213) (61%), 212 (38%), 171 (P − 42) (100%), and 170 (80%). The nmr data are in Table II.

(50) W. Metlesics, E. Schinzel, H. Vilcsek, and F. Wessely, *Monatsh. Chem.*, **88**, 1069 (1957).

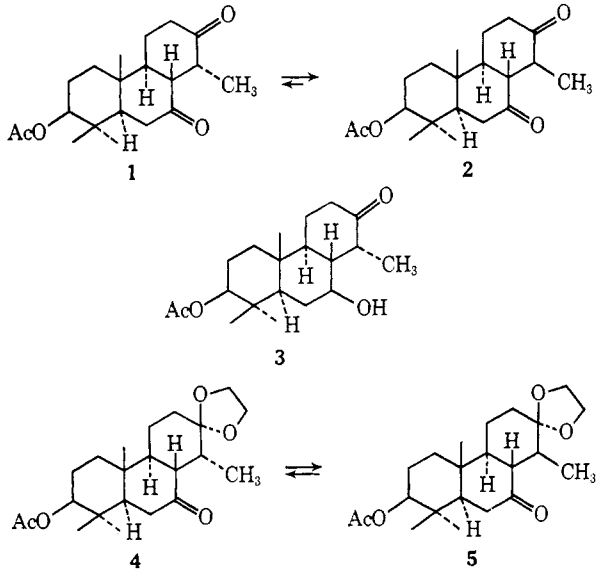
Stereochemical Investigations of Methyl Epimerization in Derivatives of 1-Methyl-*trans*-decalin[1]

Richard B. Turner, R. B. Miller, and Jeen-Lee Lin

Contribution from the Department of Chemistry, Rice University, Houston, Texas 77001. *Received May 11, 1968*

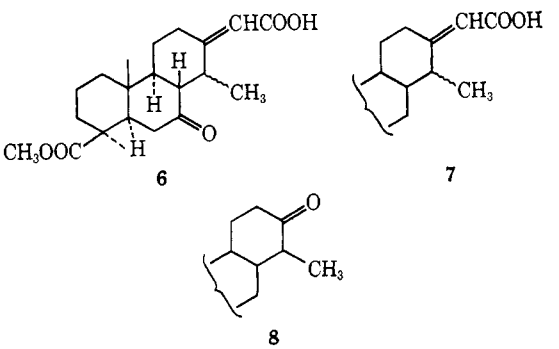
Abstract: It has been established that in both 1-methyl-*trans*-decalone-2 and 1-methyl-*trans*-decalin-2,8-dione the thermodynamically favored orientation of the methyl group is equatorial. The thermodynamically unstable axial epimers have been prepared, and equilibration studies have been carried out with various hydroxy and ketal derivatives. The literature statement that 4β-methylcholestan-3-one is not epimerized to 4α-methylcholestan-3-one is incorrect.

Some time ago, in connection with a study of the chemistry and synthesis of cassaic acid, we observed that the diketone **1**, obtained by ozonolysis of cassaic acid acetate methyl ester, is thermodynamically unstable with respect to the methyl epimer **2**.[2] It was noted further that hydroxy ketone **3** is stable under enolizing conditions and that ketal ketones **4** and **5** furnish an equilibrium mixture on treatment with *p*-toluenesulfonic acid in benzene, which consists of approximately equal amounts of the two epimers.



The stereochemistry assigned to the ring C methyl group in compounds of this series was based upon the thought that steric repulsions involving the ketal function in the pair **4** and **5** might serve to destabilize the methyl configuration favored in **2** if that group were equatorial, but not if it possessed an axial orientation. The stability of **3** was attributed to the fact that epimerization of the methyl group in this compound would result in an energetically unfavorable 1,3 methyl–hydroxyl interaction.

During the period in which this work was in progress, arguments in support of opposite assignments to the methyl group analogously situated in various derivatives of cassamic acid (**6**) were presented by Chapman, Jaques, Mathieson, and Arya.[3] In view of structural



(1) This work was supported by the Robert A. Welch Foundation and in part by the National Science Foundation.

(2) R. B. Turner, E. Herzog, R. B. Morin, and A. Riebel, *Tetrahedron Lett.*, No. 2, 7 (1959); R. B. Turner, O. Burchardt, E. Herzog, R. B. Morin, A. Riebel, and J. M. Sanders, *J. Amer. Chem. Soc.*, **88**, 1766 (1966).

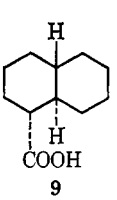
(3) G. T. Chapman, B. Jaques, D. W. Mathieson, and V. P. Arya, *J. Chem. Soc.*, 4010 (1963).

correlations which have been established between cassaic and cassamic acids,[4] the implication of the British work was that our sterochemical designations were incorrect. The main point of contention arose from the observation that cassamic acid (**6**) undergoes Clemmensen reduction to furnish a deoxo derivative **7**, which is further convertible by ozonolysis into a monoketone **8**. This latter product is base stable and shows optical rotatory dispersion properties compatible with the equatorial methyl configuration indicted. The possibility of methyl inversion in the steps leading from **5** to **8** was not considered, and an equatorial (β) configuration was hence assigned to the methyl group of cassamic acid. Since the diketone epimerization **2** to **3** was also observed in corresponding products derived from cassamic acid, this transformation was regarded as an equatorial (β) to axial (α) change.

In commenting on the apparent reversal of stability order in passing from the monoketone to the diketone series, Chapman, Mathieson, *et al.*, noted that if enolization in the monoketone **8** took place in a directionally specific sense (away from the methyl substituent), then epimerization could not occur. The report of Beton, Halsall, Jones, and Phillips[5] that 4β-methylcholestanone is not transformed into the 4α epimer under enolizing conditions was cited in this connection. This argument appeared to us to lack force with respect to questions involving equilibria, and further comment on this problem will be found in a subsequent paragraph.

The stereochemical uncertainties outlined above and the more important questions of the generality and synthetic usefulness of transformations involving compounds of type **1**–**5** prompted us to undertake a more extended examination of the problem in simpler compounds of known stereochemistry. It is worth noting that in the meantime the stereochemistry of derivatives **1**–**5** and of cassaic acid itself, has been established with certainty[6–8] and is in agreement with our earlier tentative suggestions.[2]

For purposes of the present investigation the *trans*-decalin carboxylic acids **9** and **10** were chosen as reference compounds, since both these substances and the corresponding *cis*-fused isomers had been thoroughly studied from the stereochemical point of view.[9,10] The two acids were reduced with lithium



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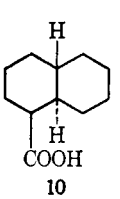

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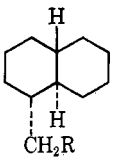
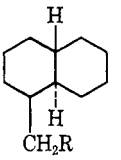
aluminum hydride to the corresponding primary alcohols **11a** and **12a**, which could be reoxidized to the parent acids, and which on treatment with *p*-toluenesulfonyl chloride and pyridine afforded *p*-toluenesulfonoxy derivatives **11b** and **12b**. Reduction of the latter compounds with lithium aluminum hydride gave hydrocarbons **11c** and **12c** accompanied by some



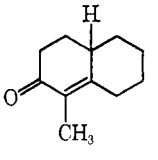
11a, R = OH
b, R = OTs
c, R = H



12a, R = OH
b, R = OTs
c, R = H

alcohol produced by hydride attack on sulfur.[11] The hydrocarbons showed only minor differences in the infrared, but the nmr spectrum of **11c** showed a broad singlet in the methyl region whereas the methyl signal in **12c** appeared as a poorly resolved doublet. The compounds were readily differentiated by vapor phase chromatography and by their mass spectral fragmentation patterns.[12]

1-Methyl-$\Delta^{1(9)}$-octalone-2 (**13**)[13] was next reduced with sodium in liquid ammonia, and afforded a crystalline alcohol **14a** as the only isolated product. The stereochemistry assigned to the methyl group and ring fusion in this substance was based on the observation



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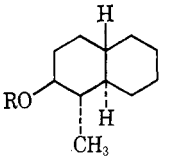
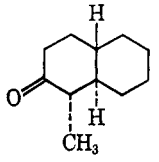


14a, R = H
b, R = Ts

that conversion into the corresponding *p*-toluenesulfonoxy derivative followed by lithium aluminum hydride reduction furnished a single hydrocarbon identical in all respects with reference compound **11c**.

Oxidation of **14a** with chromium trioxide in acetic acid afforded the ketone **15**. Reduction of the latter substance with lithium aluminum hydride furnished a mixture of epimeric alcohols **14a** and **16** in a ratio of 3:1, whereas the same two alcohols were produced in



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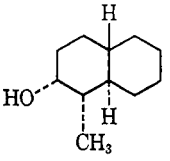


16

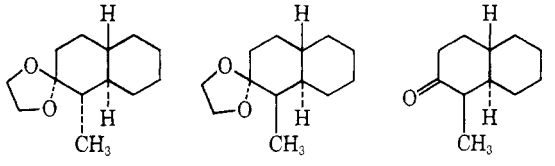
a 1:4 ratio by catalytic hydrogenation (Pt). Ketone **15** was obtained as the sole product of oxidation of alcohol **16**. The stereochemistry (*trans*-fused, equatorial methyl) of ketone **15** is thereby established.

(4) V. P. Arya and B. G. Engel, *Helv. Chim. Acta*, **44**, 1650 (1961).
(5) J. L. Beton, T. G. Halsall, E. R. H. Jones, and P. C. Phillips, *J. Chem. Soc.*, 753 (1957).
(6) H. Hauth, D. Stauffacher, P. Niklaus, and A. Melera, *Helv. Chim. Acta*, **48**, 1087 (1965).
(7) K. Mori and M. Matsui, *Tetrahedron*, **22**, 2883 (1966).
(8) R. L. Clarke, S. J. Daum, P. E. Shaw, and R. Kullnig, *J. Amer. Chem. Soc.*, **88**, 5865 (1966).
(9) W. G. Dauben, R. C. Tweit, and C. Mannerskantz, *ibid.*, **76**, 4420 (1954).
(10) I. N. Nazarov, V. F. Kucherov, and G. M. Segal, *Izv. Akad. Nauk SSSR, Otd. Khim. Nauk*, 1215 (1956).
(11) H. Schmid and P. Karrer, *Helv. Chim. Acta*, **32**, 1371 (1949); G. W. Kenner and M. A. Murray, *J. Chem. Soc.*, 406 (1950).
(12) Both **11c** and **12c** showed parent molecule ion peaks at *m/e* 152. The second significant peak in the mass spectrum of **11c** appeared at *m/e* 137 corresponding to the loss of 15 mass units (methyl), whereas the spectrum of **12c** was characterized by an ion of mass 146.
(13) G. Stork, A. Brizzolara, H. Landesman, J. Smuszkowicz, and R. Terrell, *J. Amer. Chem. Soc.*, **85**, 207 (1963).

When ketone **15** was exposed for prolonged periods to the action of sodium methoxide in methanol, chromatographically pure starting material was recovered. This experiment was then repeated with deuteriomethanol (CH_3OD) as the solvent. The mass spectrum of the product obtained in this way revealed parent peaks at M + 2 and M + 3 corresponding to about 18% of the former and 82% of the latter species. We conclude, therefore, that the equatorial arrangement of the methyl group in **15** is thermodynamically preferred. Further evidence on this point is given below.

Since Dauben[14] has reported instances where stereochemical equilibria are markedly influenced by exchange of tetrahedral for trigonal carbon atoms within the molecule, examination of the alkoxide-catalyzed equilibrium behavior of alcohols **14a** and **16** was a matter of interest. The mechanism of alcohol equilibration under these conditions has been shown to involve a ketonic intermediate,[15] and hence equilibration at both the hydroxyl and methyl centers in **14a** and **16** could be anticipated. The two alcohols were accordingly treated in sealed tubes at 170° with sodium butoxide in 1-butanol containing a small amount of benzophenone. Equilibrium was established slowly but was essentially complete after 144 hr. Vapor chromatographic analysis of the reaction products revealed mixtures containing 73% of **14a** and 27% of **16**, and 70% of **14a** and 30% of **16**, when **14a** and **16** were employed as starting materials, respectively. No methyl epimers were produced in amounts sufficient for chromatographic detection. It follows that in the alcohols as well as in ketone **15** an equatorial orientation of the methyl group is favored over the alternate axial arrangement. Stereochemical assignments to the hydroxyl groups in **14a** and **16** are based upon the equilibrium data cited above.

Attention was next directed toward the behavior of the ethylene ketal of ketone (**15**). This substance (**17**) was readily obtained by treatment of the ketone with ethylene glycol in benzene containing traces of *p*-toluenesulfonic acid. When a purified sample of **17** was heated in refluxing benzene for 24 hr with

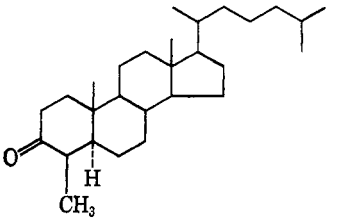


17 **18** **19**

larger amounts of *p*-toluenesulfonic acid, equilibrium with a second ketal (**18**) was established, the ratio being 3.3:1 in favor of **17**. Isolation of **18** by preparative vapor phase chromatography afforded material which gave the same ratio of products on acid-catalyzed equilibration. It is evident, therefore, that incorporation of the ethylene ketal function results in significant destabilization of the equatorial methyl group.

Of special interest is the fact that whereas cleavage of ketal **17** by exchange with acetone yields ketone **15** exclusively, similar cleavage of **18** furnishes a mixture of **15** and the epimer **19** in a ratio of 3:7. The cleavage reactions cannot, therefore, involve exclusively a common intermediate. Ketone **19** is quantitatively converted into **15** on treatment with base, and affords, on lithium aluminum hydride reduction, a mixture of two alcohols (reoxidizable to starting ketone) which differ in chromatographic retention time from compounds **14a** and **16**.

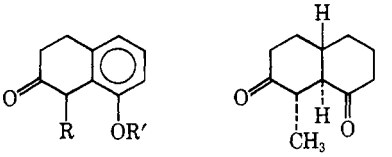
Mention has already been made of experiments by Jones and his associates[5] which suggested that 4β-methylcholestan-3-one (**20**) is not converted into 4α-methylcholestan-3-one under enolizing conditions. This conclusion is in direct opposition to experience



20

with the model ketone **19**, and a reexamination of the point was thus undertaken. Our procedure for preparation of **20** differed from that of the English group, and involved reaction of methyllithium with 3α,4α-epoxycholestane[16] followed by oxidation of the resulting 3α-hydroxy-4β-methylcholestane. The product did not melt particularly sharply (132–136°; lit.[5] mp 125–127°), but was smoothly isomerized by sodium methoxide into the known 4α-methylcholestan-3-one, mp 121–123°. Although it is not possible to point directly to the discrepancy in the earlier work, it is not unlikely that the particular sample employed in the previous epimerization study was in fact cholestanone-3 (mp 129°), which could easily have been isolated from the reaction sequence that was utilized for preparation of **20**.

We turn now to experiments carried out in the diketone series. Preparation of the appropriate compound **22** was readily accomplished by enamine methylation of 8-methoxy-2-tetralone (**21a**) and cleavage of the ether function in the resulting product **21b** to



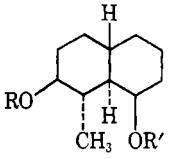
21a, R = H; R′ = OCH_3
b, R = CH_3; R′ = OCH_3
c, R = CH_3; R′ = H

22

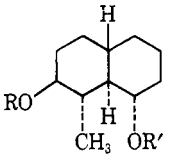
8-hydroxy-1-methyl-2-tetralone (**21c**). Catalytic hydrogenation of the latter substance furnished a mixture of stereoisomeric diols which was then oxidized directly to the diketone stage. The presence of two components in this product was demonstrated by vapor chromatography, but equilibration of the mixture with sodium methoxide furnished a single, pure compound to which structure **22** is assigned. Methoxide-catalyzed equilibration of **22** in deuteriomethanol led to the incorporation of six deuterium atoms (mass spectral analysis).

(14) W. G. Dauben, G. A. Boswell, W. Templeton, and J. W. McFarland, *J. Amer. Chem. Soc.*, **85**, 2302 (1963).
(15) W. von E. Doering and T. C. Aschner, *ibid.*, **71**, 838 (1949).
(16) A. Fürst and R. Scotoni, *Helv. Chim. Acta*, **36**, 1332 (1953).

The stereochemistry of diketone **22** was established unambiguously as follows. Lithium aluminum hydride reduction yielded a mixture of four diols, from which two crystalline isomers, **23a** and **24a**, were isolated in pure form by chromatography on alumina. Both substances, as well as the residual unresolved mixture of the two remaining diols, could be reoxidized to the starting diketone **22**. Acetylation of **23a** with 1 molar equiv of acetic anhydride in pyridine afforded a

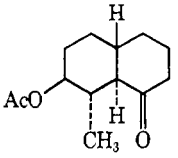


23a, R = R′ = H
b, R = Ac; R′ = H
c, R = R′ = Ac
d, R = H; R′ = Ac



24a, R = R′ = H
b, R = R′ = Ac
c, R = H; R′ = Ac

monoacetate **23b**, which was oxidized to the corresponding acetoxy ketone **25**. Clemmensen reduction of the latter compound yielded the monoalcohol **14a** which had been correlated previously with reference hydrocarbon **11c**. Alternatively routine transformations of diol **23a** through the diacetate **23c** and monoacetate **23d** led to keto acetate **26a** and keto alcohol **26b**. The latter substance was smoothly converted into the corresponding ketal and thence into keto ketal **27**, which upon Wolff–Kishner reduction furnished a product identical in all respects with ketal **17**.



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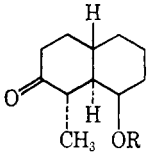
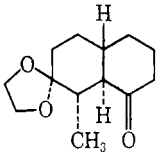
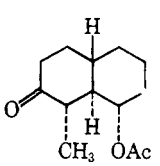


26a, R = Ac
b, R = H

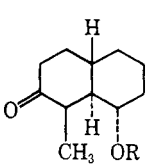


27

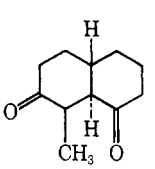
Identity of diols **23a** and **24a** with respect to configuration at four of the five asymmetric centers was established by the fact that reduction of keto acetate **25** with lithium and methanol in liquid ammonia furnished the two diols in approximately equal amounts. The question of the orientation of the second (C-8) hydroxyl group in the two epimers was resolved in the following manner. Acetylation of **24a** yielded a diacetate **24b**, convertible into monoacetate **24c** by partial saponification. Oxidation of **24c** then furnished a keto acetate **28** which was not identical with keto acetate **25**. Treatment of the new keto acetate **28** with sodium methoxide in methanol yielded a keto alcohol as expected, but reactylation of this material did not give back the starting keto acetate **28**. Instead



28



29a, R = H
b, R = Ac



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a third keto acetate **29b** was obtained, and it follows that epimerization of the methyl group accompanies saponification of **28** to **29a**. This conclusion is supported by two lines of evidence.

Conversion of keto alcohol **29a** into the corresponding *p*-toluenesulfonoxy derivative followed by lithium aluminum hydride reduction furnished a mixture of two monohydroxy derivatives which showed the same retention times on vapor chromatography as did the components of the mixture obtained by lithium aluminum hydride reduction of **19**. A stronger argument is provided by the observation that oxidation of **29a** yielded a diketone **30**, nonidentical with, but readily epimerized into, diketone **22** by the action of base. The sequence of reactions **22** → **24a** → **24c** → **28** → **29a** → **30** therefore constitutes a route for conversion of the thermodynamically stable to the thermodynamically unstable diketone. The epimerization which occurs in the transformation of **28** into **29a** furthermore permits assignment of stereochemistry to the C-8 hydroxyl function in compounds of this series, since this change is plausible only if the configuration in **28** is that indicated. We conclude, finally, that the changes first observed in derivatives of cassaic acid are general ones which may be expected to have useful synthetic applications.

Experimental Section[17]

Preparation of *anti-trans*-1-Hydroxymethyldecahydronaphthalene (11a). A fourfold excess of lithium aluminumhydride was added to a solution of 210 mg of *anti-trans*-decahydro-1-naphthoic acid (**9**)[10] in 25 ml of dry ether, and the resulting slurry was stirred for 5 hr at room temperature. After decomposition of the excess lithium aluminum hydride, the reaction mixture was acidified with 1 *N* hydrochloric acid, and the product was isolated by ether extraction. The combined ether layers were washed with water and saturated sodium chloride solution. After drying over anhydrous magnesium sulfate, the solvent was removed yielding 190 mg of residual oil, $\lambda_{max}^{CCl_4}$ 2.80 μ. Reoxidation of this product by the Jones procedure[18] furnished material identical with the starting acid.

The corresponding ***p*-toluenesulfonate 11b** was prepared as a derivative by reaction of the alcohol (190 mg) with 220 mg of *p*-toluenesulfonyl chloride in 7 ml of dry pyridine. After 17 hr the product was isolated in the usual way and afforded, after evaporation of solvent, 273 mg of crude crystalline material. Recrystallization from petroleum ether (bp 30–60°) gave a pure sample, 195 mg, mp 74.5–75.0°.

Anal. Calcd for $C_{18}H_{26}O_3S$: C, 67.04; H, 8.13; S, 9.94. Found: C, 67.22; H, 8.24; S, 9.92.

Preparation of *anti-trans*-1-Methyldecahydronaphthalene (11c). A sample (1.6 g) of *p*-toluenesulfonate **11b** was dissolved in anhydrous ether and was treated with a fourfold excess of lithium aluminum hydride for 24 hr with stirring. The product was isolated in the standard way and was filtered through a Florisil column in 200 ml of petroleum ether. Further elution with ether furnished 255 mg of alcohol **11a**. Removal of the petroleum ether gave 506 mg of hydrocarbon **11c** which was chromatographically homogeneous in a 20% Ucon 50HB260 on 60–80 mesh Chromosorb P column. The mass spectrum[19] showed the molecular ion peak at *m/e* 152 and the highest molecular weight fragment peak at *m/e* 137. The nmr spectrum revealed methyl absorption as a broad singlet at δ 0.89 ppm from tetramethylsilane.

Preparation of *syn-trans*-1-Hydroxymethyldecahydronaphthalene (12a). A 240-mg sample of methyl ester, derived by treatment of *syn-trans*-decahydronaphthoic acid (mp 126–127°) with ethereal diazomethane, was reduced with lithium aluminum hydride by the procedure described for preparation of **11a**. The crude product was

(17) Infrared and nmr spectra were taken routinely on samples prepared in the course of this investigation.
(18) K. Bowden, I. M. Heilbron, E. R. H. Jones, and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946).
(19) We are indebted to Professor J. L. Franklin for this result.

chromatographed on Florisil and was further purified by recrystallization from petroleum ether; yield 170 mg, mp 58.5–59.0°.

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.98. Found: C, 78.43; H, 11.83.

Reoxidization of this substance gave *syn-trans*-decahydronaphthoic acid.

Preparation of *syn-trans*-1-Methyldecahydronaphthalene (12c). A solution of 190 mg of alcohol **12a** in 8 ml of dry pyridine was treated with 250 mg of *p*-toluenesulfonyl chloride for 72 hr at room temperature. The crude product (228 mg) was subjected to sublimation to remove unreacted starting material (55 mg), and the residual oily *p*-toluenesulfonate which failed to crystallize was employed directly for lithium aluminum hydride reduction (see procedure above). In this way there was obtained after filtration through Florisil, 24 mg of hydrocarbon **12c**. The parent peak in the mass spectrum appeared at *m/e* 152 with fragment peaks at *m/e* 146, 137, and 131. The retention time on vpc was differentiated by about 2 min from that of hydrocarbon **11c**. The nmr spectrum showed a poorly resolved methyl doublet centered at δ 0.85.

Preparation of *trans-anti-trans*-2-Hydroxy-1-methyldecahydronaphthalene (14a). A solution of 7.09 g of 1-methyl-$\Delta^{1(9)}$-octalone-2 (**13**)[13] in 140 ml of ethanol was cooled in a Dry Ice–acetone bath. Liquid ammonia (200 ml) was then condensed in the reaction vessel, and sodium metal was added slowly in small pieces at a rate sufficient to maintain a blue color. At the end of 4.5 hr the cooling bath was removed, and the ammonia was allowed to evaporate. Dilution with water and extraction with ether furnished an organic phase which was washed successively with dilute sulfuric acid, water, dilute sodium bicarbonate, water, and saturated sodium chloride solution. After drying over anhydrous magnesium sulfate, the solvent was removed, and the residue was sublimed under aspirator vacuum; yield 4.42 g, mp 55–57°.

Anal. Calcd for $C_{11}H_{20}O$: C, 78.51; H, 11.97. Found: C, 78.53; H, 11.88.

The 3,5-dinitrobenzoate prepared as a derivative melted at 162–164° (from methanol).

Anal. Calcd for $C_{18}H_{22}N_2O_6$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.32; H, 6.10; N, 7.56.

Conversion of Alcohol 14a into the *p*-Toluenesulfonoxy Derivative 14b. To a solution of 345 mg of alcohol **14a** in 15 ml of anhydrous pyridine, 644 mg of *p*-toluenesulfonyl chloride was added. The reaction mixture was allowed to stand at room temperature for 5 days, at the end of which time ice, ether, and dilute sodium hydroxide solution were added. The ether layer was washed with water and saturated sodium chloride, and after filtering through anhydrous magnesium sulfate, the solvent was removed under reduced pressure. The crude product, 494 mg, was crystallized twice from ligroin, mp 100–100.5°.

Anal. Calcd for $C_{18}H_{26}O_3S$: C, 67.04; H, 8.12; S, 9.94. Found: C, 67.00; H, 8.16; S, 9.94.

Preparation of *anti-trans*-1-Methyldecahydronaphthalene (11c) from Tosylate 14b. Lithium aluminum hydride (242 mg) was suspended in 9 ml of anhydrous ether, and 347 mg of tosylate **14b** was added. The mixture was stirred at room temperature for 40 hr, at the end of which time the excess lithium aluminum hydride was destroyed by careful addition of ethanol. Addition of sulfuric acid followed by ether extraction gave an organic phase which was washed successively with water, dilute sodium hydroxide, water, and saturated sodium chloride solution. After drying over anhydrous magnesium sulfate, the solvent was evaporated, and the residue was taken up in petroleum ether and filtered through an alumina column. In this way 66 mg of hydrocarbon was obtained that proved to be identical (infrared, nmr, vpc, mass spectral analysis) with an authentic sample of *ani-trans*-1-methyldecalin (**11c**).

Elution of the alumina with ether afforded 45 mg of alcohol **14a**.

Preparation of *anti-trans*-1-Methyldecalone-2 (15). A 3.42-g sample of alcohol **14a** in 30 ml of acetic acid was treated with 2.18 g of chromium trioxide in dilute acetic acid. After 30 min at 10° and 3 hr at room temperature, the bulk of the acetic acid was removed under reduced pressure. The product was isolated by water dilution and ether extraction. After the usual washing and drying procedures, the solvent was removed furnishing 2.8 g of ketone **15**, $\lambda_{max}^{CS_2}$ 5.83 μ, which showed a single symmetrical peak on vapor chromatography and a methyl doublet at δ 0.9 in the nmr.

The liquid ketone was converted into a yellow dinitrophenylhydrazone, mp 187.5–189° (from ethyl acetate), for identification purposes.

Anal. Calcd for $C_{17}H_{22}N_4O_4$: C, 58.94; H, 6.40; N, 16.17. Found: C, 58.72; H, 6.43; N, 16.25.

Base-Catalyzed Equilibration and Deuterium Exchange of Ketone 15. A solution consisting of 68 mg of ketone **15** and 108 mg of sodium methoxide in 5 ml of methanol was allowed to stand at room temperature for 22 hr. At the end of this time the product (60 mg) was isolated by standard procedures. The material proved to be identical in all respects with the starting ketone **15**.

When a 70-mg sample of ketone was treated in the above manner, with the exception that CH_3OD was substituted for methanol solvent, the product (59 mg) showed only a broad singlet at δ 0.95 in the nmr. The mass spectrum indicated the presence of 82% of a species *m/e* 169 (M + 3) and 18% of a species *m/e* 168 (M + 2).

Lithium Aluminum Hydride Reduction of Ketone 15. An excess of lithium aluminum hydride was added to a solution of 208 mg of ketone **15** in 15 ml of dry ether, and the resulting mixture was stirred at room temperature for 27 hr. The product (161 mg) was isolated by standard procedures and showed two peaks (ratio 1:3) in vapor chromatography. The material was then chromatographed on alumina, activity II–III. Elution with petroleum ether–benzene (8:2) furnished 30 mg of amorphous alcohol **16**, which yielded a crystalline 3,5-dinitrobenzoate, mp 123–125°.

Anal. Calcd for $C_{18}H_{22}N_2O_6$: C, 59.66; H, 6.12; N, 7.73. Found: C, 59.58; H, 6.15; N, 7.96.

Elution of the chromatographic column with petroleum ether–benzene (1:1) gave 95 mg of crystalline product identical in all respects with alcohol **14a**.

Chromium Trioxide Oxidation of Alcohol 16. A solution of 80 mg of alcohol **16** in acetic acid was oxidized with chromium trioxide according to the procedure outlined for oxidation of the epimer **14a**. There was obtained 60 mg of product that was indistinguishable from ketone **15** by infrared, nmr, and vapor chromatographic analysis.

Sodium Butoxide Catalyzed Equilibration of Alcohols 14a and 16. A solution of 90 mg of alcohol **14a** in 3 ml of dry 1-butanol was added to a solution prepared by dissolving 310 mg of sodium metal in 4 ml of dry 1-butanol. Benzophenone, 9 mg, was added, and the mixture was sealed under vacuum in a glass tube which was immersed in a metal bath at 165–170° for 144 hr. At the end of this time the tube was cooled, and the contents were diluted with water and extracted with ether. The ether solution was thoroughly washed with water and with saturated sodium chloride. After drying over anhydrous magnesium sulfate, the solvent was removed and the residue was analyzed by vapor chromatography. Two major peaks with retention times identical with those of alcohols **14a** and **16** appeared with an integrated ratio of 2.7:1. Chromatography on alumina furnished 46 mg of pure **14a**, 19 mg of **16**, and 8 mg of unidentified material.

The procedure was repeated with alcohol **16** as starting material. There was obtained in this experiment 31 mg of **14a** and 13 mg of **16**.

Preparation of Ketal 17. A solution of 2.40 g of ketone **15** in 40 ml of ethylene glycol was treated with 180 mg of *p*-toluenesulfonic acid. The mixture was heated to reflux under a water separator until the collection of water had ceased (about 6 hr). The solution was then cooled, diluted with ether, and washed successively with dilute sodium hydroxide, water, and saturated sodium chloride solution. Filtration through anhydrous magnesium sulfate and evaporation of the filtrate afforded 2.62 g of ketal **17**, which showed no carbonyl absorption in the infrared. The nmr spectrum contained a methyl doublet centered at δ 0.9 and a multiplet at δ 3.9 (ketal methylene groups). Vapor chromatographic analysis showed that the sample was essentially pure, although contamination by traces of ketal **18** was indicated.

Equilibration of Ketals 17 and 18. A 2.53-g sample of ketal **17** was dissolved in 45 ml of dry benzene, and 120 mg of *p*-toluenesulfonic acid was added. The resulting solution was heated under reflux for 24 hr. At the end of this time the product was isolated as described in the preceding experiment. The nmr spectrum of the crude product showed two methyl doublets centered at δ 0.9 and at 1.0, respectively.

Preparative gas phase chromatography yielded 930 mg of ketal **17** and 280 mg of a second ketal **18**. The infrared spectra of the two samples showed marked differences.

Equilibration of ketal **18** in 4 ml of benzene containing 1 mg of *p*-toluenesulfonic acid was carried out as described above. Vapor chromatographic and nmr analyses indicated substantially the same product ratio as that obtained when ketal **17** was employed as starting material.

Cleavage of Ketal 18. A 245-mg sample of ketal **18** was dissolved in 6 ml of acetone, and 15 mg of *p*-toluenesulfonic acid was added.

The mixture was allowed to stand at room temperature for 10 hr. The bulk of the solvent was then removed on a nitrogen stream without external heating, and the residue was taken up in ether and washed with water and saturated sodium chloride solution. After drying over anhydrous magnesium sulfate, the ether was removed at low temperature. The residue, 170 mg, $\lambda_{max}^{CS_2}$ 5.83 μ, was subjected to vapor chromatographic analysis which showed two major components in a ratio of 2.3:1. The minor constituent was identified as ketone **15**. Preparative separation afforded the major product, ketone **19**, in pure form. The nmr spectrum contained a methyl doublet at δ 1.0.

Base-Catalyzed Equilibration of Ketone 19. A 6-mg sample of ketone **19** was dissolved in 2 ml of methanol, and 22 mg of sodium methoxide was added. The reaction mixture was allowed to stand at room temperature for 20 hr, at the end of which time the product was isolated by routine methods. The material was identified as essentially pure ketone **15** by infrared and vapor chromatographic analysis.

Lithium Aluminum Hydride Reduction of Ketone 19. Ketone **19**, 40 mg, was dissolved in 10 ml of anhydrous ether to which an excess of lithium aluminum hydride was added. The resulting mixture was stirred at room temperature for 21 hr. The product, 38 mg, was isolated by ether extraction followed by the usual washing and drying procedures. Vpc analysis of the crude material $\lambda_{max}^{CS_2}$ 2.78 μ, indicated the presence of two alcohols which were well differentiated in retention time from alcohols **14a** and **16**.

Reoxidation of the alcohol mixture with chromium trioxide–acetic acid afforded 3 mg of material that was identified as ketone **19**.

Preparation of 4β-Methylcholestan-3-one (20). 3α,4α-Epoxycholestane (193 mg), mp 116–117°, prepared by the literature procedure[16] and showing infrared characteristics identical with the published data,[20] was treated with 20 ml (excess) of an ethereal solution containing methyllithium. The reaction mixture was heated under reflux for a period of 3 days, at the end of which time the excess reagent was destroyed by addition of water. The ethereal solution was washed with water, and after drying and evaporation of the solvent, 159 mg of crude material was obtained which showed hydroxyl absorption in the infrared. Chromatography on alumina furnished 70 mg of starting epoxide and 70 mg of 4β-methylcholestan-3α-ol, mp 138–141°.

The alcohol fraction (46 mg) was taken up directly in 2 ml of acetic acid, and 14 mg of chromium trioxide in a few drops of water was added. After 4 hr at room temperature, the product was isolated by routine procedures; yield 37 mg, mp 130–135°, $\lambda_{max}^{CS_2}$ 5.83 μ. Recrystallization from ether–petroleum ether gave a sample melting at 132–136°. A mixture melting point with cholestan-3-one was depressed to 104–122°.

Epimerization of 4β-Methylcholestan-3-one (20). 4β-Methylcholestan-3-one (**20**), 34 mg, was dissolved in 2 ml of methanol and 50 mg of sodium methoxide was added. After standing for 8 hr at room temperature, the reaction mixture was diluted with water, and the product was isolated by ether extraction. The crude product thus obtained was chromatographed on alumina yielding a fraction (26 mg) melting at 114–120°. Recrystallization from ether–petroleum ether afforded a pure sample of 4α-methylcholestan-3-one, mp 121–123°. This material did not depress the melting point of an authentic specimen, whereas mixture melting points with compound **20** and with cholestan-3-one were depressed to 102–116° and 114–123°, respectively.

Preparation of the Ethylene Ketal of 8-Methoxy-2-tetralone. To a mixture of 1 g of 8-methoxy-2-tetralone,[21] 2 ml of ethylene glycol, and 10 ml of benzene, a catalytic amount of *p*-toluenesulfonic acid was added. The solution was heated to reflux temperature under a water separator for 5 hr. At the end of this time ether was added, and the mixture was washed with dilute sodium hydroxide, water, and saturated sodium chloride. Evaporation of the solvent afforded crude material which was recrystallized from ether–petroleum ether; yield 1.02 g, mp 51.5–52°.

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.93; H, 7.33.

Preparation of the Ethylene Ketal of 8-Methoxy-1-methyl-2-tetralone. A 530-mg sample of 8-methoxy-1-methyl-2-tetralone (**21b**), obtained by standard enamine methylation of 8-methoxy-2-tetralone (**21a**),[22] was converted into the corresponding ethylene ketal by the procedure of the preceding experiment. The product, 585 mg, melted at 61.5–62.0° after recrystallization from petroleum ether.

Anal. Calcd for $C_{14}H_{18}O_3$: C, 71.77; H, 7.74. Found: C, 71.82; H, 7.75.

Preparation of 8-Hydroxy-1-methyl-2-tetralone (21c). A solution of 4.5 g of 8-methoxy-1-methyl-2-tetralone in 150 ml of glacial acetic acid was heated to reflux temperature under an atmosphere of nitrogen. Freshly distilled, constant boiling hydriodic acid, 20 ml, was added, and refluxing was continued for 90 min. The reaction mixture was then rapidly cooled and diluted with 250 ml of water containing a small amount of sodium bisulfite. The product was taken into ether and was finally isolated by base extraction. Acidification of the alkaline solution and ether extraction gave 3.51 g of crude phenolic material which was distilled in a Hickman tube at 0.01 mm pressure and a bath temperature of 130°. In this way there was obtained 1.64 g of 8-hydroxy-1-methyl-2-tetralone, which slowly crystallized on standing. Recrystallization from ether–petroleum ether afforded material melting at 95.5–96.5°, $\lambda_{max}^{CH_2Cl_2}$ 2.81 and 5.82 μ. The compound is sensitive to air and darkened rapidly on exposure to the atmosphere.

The corresponding ethylene ketal was prepared as a derivative by the procedure described for the preparation of the ethylene ketal of 8-methoxy-2-tetralone. Sublimation and recrystallization from ether–petroleum ether gave a sample melting at 149.5–150.0°, $\lambda_{max}^{CH_2Cl_2}$ 2.81 μ.

Anal. Calcd for $C_{13}H_{16}O_3$: C, 70.89; H, 7.32. Found: C, 70.93; H, 7.32.

Cleavage of the ketal function by exchange with acetone and *p*-toluenesulfonic acid gave material identical in all respects with the keto phenol **21c**.

Preparation of *anti-trans*-1-Methyl-2,8-decalindione (22). 8-Hydroxy-1-methyl-2-tetralone (**21c**), 462 mg, and platinum oxide catalyst, 250 mg, in 10 ml of glacial acetic acid were stirred in a hydrogen atomsphere for 24 hr. The hydrogenation product was isolated in the normal way and was filtered through an alumina column (activity II–III). The ether eluates afforded 317 mg of diol mixture, which was taken up directly in 50 ml of acetone. Jones' reagent (1.4 ml) was added, and the reaction mixture was stirred for 3 min. Water was then added, and the mixture was extracted three times with ether. The combined ether fractions were washed thoroughly with water, and saturated sodium chloride solution. After drying over anhydrous magnesium sulfate, the solvent was evaporated, and the resulting diketone, 276 mg, was analyzed by vapor chromatography. The material exhibited two peaks of approximately equal area with retention times of 15.5 and 20.5 min on an SE 30 column.

The diketone mixture was next dissolved in 10 ml of absolute methanol, and 100 mg of sodium methoxide was added. After standing at room temperature (nitrogen atmosphere) for 24 hr, the product was isolated by water dilution and ether extraction. Chromatography on alumina afforded 220 mg of liquid *anti-trans*-1-methyl-2,8-decalindione (**22**), which was homogeneous as indicated by vapor chromatography (retention time 15.5 min); methyl doublet at δ 0.92.

The sample for analysis was prepared by preparative vapor chromatography followed by flash distillation.

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95. Found: C, 73.19; H, 9.03.

Deuterium Exchange in *anti-trans*-1-Methyl-2,8-Decalindione (22). A solution of 60 mg of sodium metal in 5 ml of deuteriomethanol (CH_3OD) was treated with 50 mg of diketone **22**. After standing at room temperature under nitrogen for 24 hr, the product was isolated by water dilution and ether extraction. There was obtained 48 mg of liquid residue which showed the parent ion peak at *m/e* 186 (M + 6). The nmr spectrum showed a methyl singlet at δ 0.92.

Lithium Aluminum Hydride Reduction of *anti-trans*-1-Methyl-2,8-decalindione (22). Lithium aluminum hydride, 500 mg, was added to a solution containing 1.0 g of diketone **22** in 100 ml of anhydrous ether. The mixture was stirred overnight at room temperature, and the excess lithium aluminum hydride was then destroyed by the addition of wet ether followed by water and dilute hydrochloric acid. The crude product (1.05 g), obtained by ether extraction and the usual washing and drying procedures, was chromatographed on alumina (activity III). There was obtained in this

(20) H. Günthard, H. Heusser, and A. Fürst, *Helv. Chim. Acta*, **36**, 1900 (1953).

(21) P. A. Robins and J. Walker, *J. Chem. Soc.*, 409 (1958).

(22) D. A. H. Taylor, *West Afr. J. Biol. Appl. Chem.*, 7 (2), 14 (1963); *Chem. Abstr.*, **61**, 588 (1964).

way 488 mg of diol **23a**, 270 mg of diol **24a**, and 213 mg of an amorphous mixture of the two remaining epimeric diols (vpc analysis).

Recrystallization of diol **23a** from ether–petroleum ether furnished a pure sample, mp 147.5–148.5°.

Anal. Calcd for $C_{11}H_{20}O_2$: C, 71.70; H, 10.94. Found: C, 71.51; H, 10.71.

The diacetate **23c** melted at 73.0–73.5° (from petroleum ether).

Anal. Calcd for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01. Found: C, 67.06; H, 9.01.

Recrystallization of diol **24a** from ether–petroleum ether afforded material melting at 141.0–141.5°.

Anal. Found: C, 71.72; H, 10.84.

The corresponding diacetate **24b** melted at 53.0–54.0° (from petroleum ether).

Anal. Found: C, 67.22; H, 9.16.

Preparation of Monoacetate 23b. To a solution of 122 mg of diol **23a** there was added 0.7 ml of a solutlon containing 1 ml of acetic anhydride in 9 ml of benzene. The mixture was allowed to stand at room temperature for 19 hr, and was then poured onto ice and extracted with ether. The ether phase was washed successively with water, dilute hydrochloric acid, water, dilute sodium hydroxide, and saturated sodium chloride solution, and was finally filtered through anhydrous magnesium sulfate. Evaporation of the solvent and chromatography of the residual crude product (120 mg) on alumina furnished 15 mg of a starting diol **23a** and 97 mg of monoacetate **23b**, mp 109–109.5°, $\lambda_{max}^{CS_2}$ 2.80, 5.78, and 8.00 μ (from ether–petroleum ether).

Anal. Calcd for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 69.07; H, 9.81.

Preparation of Monoacetate 23d. A sample of diacetate **23c**, 295 mg, was dissolved in 200 ml of methanol, and 1.25 g of potassium hydroxide was added. The mixture was heated under reflux for 1.25 hr and was then poured onto ice and extracted with ether. The usual washing and drying procedures gave 270 mg of crude material which was chromatographed on alumina (activity III). In this way 46 mg of diol **23a** and 184 mg of monoacetate **23d** were obtained. Recrystallization of the monoacetate from ether–petroleum ether gave a sample melting at 80.0–80.5°, $\lambda_{max}^{CS_2}$ 2.80, 5.78, and 8.14 μ.

Anal. Found: C, 68.97; H, 9.81.

Preparation of Monoacetate 24c. A 70-mg sample of diacetate **24b** was partially hydrolyzed by heating for 40 min in a refluxing solution of 50 ml of methanol containing 320 mg of potassium hydroxide. The product, 58 mg, was isolated as indicated in the preceding experiment. Chromatography on alumina furnished 14 mg of diol **24a** and 32 mg of monoacetate **24c**, which, after recrystallization from ether–petroleum ether, melted at 78.5–79.0°, $\lambda_{max}^{CS_2}$ 2.80, 5.78, and 8.00 μ.

Anal. Found: C, 68.95; H, 9.70.

Preparation of Keto Acetate 25. A solution of 89 mg of monoacetate **23b** in 5 ml of acetone was treated with 0.17 ml of Jones' reagent. After a reaction period of 2 min the product, 86 mg, was isolated in the usual way. Recrystallization from petroleum ether afforded a pure sample, mp 87.0–87.5°, $\lambda_{max}^{CS_2}$ 5.78, 5.83, and 8.00 μ.

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.76; H, 9.18.

Clemmensen Reduction of Keto Acetate 25. A mixture of 8 mg of keto acetate **25**, 300 mg of amalgamated zinc, and 1 ml of concentrated hydrochloric acid was heated under reflux for 3.5 hr. Dilution with water and extraction with ether furnished an organic phase which was thoroughly washed with water and saturated sodium chloride solution. After drying over anhydrous magnesium sulfate the solvent was removed, and the crude product was filtered through an alumina column. Sublimation of the alcohol fraction afforded 4 mg of crystalline material, mp 59–62°, that did not depress the melting point of alcohol **14a**. The infrared spectra and vapor chromatographic retention times of the two samples were likewise identical.

Preparation of Keto Acetate 26a. A solution of 184 mg of monoacetate **23d** in 20 ml of acetone was oxidized with 0.33 ml of Jones' reagent as indicated above for monoacetate **23b**. The product, 175 mg, melted at 64.0–64.5° after recrystallization from petroleum ether; $\lambda_{max}^{CS_2}$ 5.78, 5.83, and 8.05 μ.

Anal. Found: C, 69.82; H, 8.99.

Methoxide-Catalyzed Methanolysis of Keto Acetate 26a. To 5 ml of methanol in which 20 mg of sodium metal had been dissolved, 40 mg of keto acetate **26a** was added. The reaction mixture was allowed to stand at room temperature for 24 hr and was then diluted with water and extracted with ether. The combined ether extracts were washed with water and saturated sodium chloride, filtered through anhydrous magnesium sulfate, and concentrated to dryness. Recrystallization of the residue from ether–petroleum ether afforded pure keto alcohol **26b**, mp 72.0–72.5°, $\lambda_{max}^{CH_2Cl_2}$ 2.80 and 5.83 μ.

Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.45; H, 9.80.

Acetylation of this material gave back a compound identical in all respects with the starting keto acetate **26a**.

Repetition of the methanolysis experiment with CH_3OD as solvent furnished a product which showed a parent ion peak at *m/e* 185 (M + 3) in the mass spectrum.

Jones oxidation of **26b** afforded diketone **22**. Compound **26b** was also converted into the corresponding **ethylene ketal** by standard procedures. This material failed to crystallize, but showed the expected molecular ion peak at *m/e* 226 in the mass spectrum.

Preparation of Ethylene Ketal 27. A 65-mg sample of the ketal derived above from hydroxy ketone **26b** was treated with 30 mg of chromium trioxide in 2 ml of pyridine. The reaction mixture was stirred at room temperature for 12 hr, and was then diluted with ether. The combined ether extracts were washed with water until neutral and with saturated sodium chloride solution. Filtration through anhydrous magnesium sulfate and evaporation of the solvent furnished 60 mg of crude material which was chromatographed on basic alumina. The resulting product failed to crystallize. The mass spectrum showed the parent peak at *m/e* 224.

Wolff–Kishner Reduction of Ketal 27. To a solution of 16 mg of compound **27** in 5 ml of ethylene glycol there was added 1 ml of hydrazine hydrate and 200 mg of potassium hydroxide. The mixture was heated under a water-cooled reflux condenser for 9 hr at 105° and for a further 9 hr at 180° with the cooling water shut off. The solution was finally cooled, diluted with water, and extracted with ether. After the usual washing and drying procedures, the solvent was removed, and the oily residue was analyzed by vapor chromatography and infrared spectroscopy. The product proved to be identical by these criteria with ketal **17**.

Preparation of Keto Acetate 28. A solution of 90 mg of hydroxy acetate **24c** in 10 ml of acetone was oxidized with 0.17 ml of Jones' reagent according to the procedure employed for oxidation of compound **23b**. The crude product, 82 mg, crystallized on standing and was recrystallized from petroleum ether, mp 57.5–58°, $\lambda_{max}^{CS_2}$ 5.78, 5.83, 8.01 μ.

Anal. Calcd for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.39; H, 8.82.

Epimerization of Keto Acetate 28. A 40-mg sample of keto acetate **28** was added to 5 ml of methanol in which 20 mg of sodium metal had been dissolved. The mixture was allowed to stand at room temperature for 24 hr, and the product was then isolated as described for the case of the similar treatment of compound **26a**. The material (**29a**) obtained in this way failed to crystallize, and was acetylated directly with acetic anhydride and pyridine. The resulting keto acetate, **29b**, mp 88.5–89.0°, $\lambda_{max}^{CS_2}$ 5.78, 5.83, and 8.05 μ (from petroleum ether), differed markedly from keto acetate **28** in the infrared.

Anal. Found: C, 69.52; H, 9.30.

Preparation and Equilibration of Diketone 30. Oxidation of 15 mg of keto alcohol **29a** by 0.04 ml of Jones' reagent in 5 ml of acetone was carried out by the standard procedure (see above). The amorphous product, $\lambda_{max}^{CS_2}$ 5.83 μ, showed a single peak on vapor chromatography. The material differed from diketone **22** in both infrared and vapor chromatographic characteristics. The nmr spectrum showed a methyl doublet (J = 7 cps) centered at δ 1.10.

The product was taken up in 5 ml of methanol in which 2 mg of sodium metal had been dissolved. After 24 hr at room temperature (nitrogen atmosphere), the product was isolated by water dilution and ether extraction. The ether solution was dried over anhydrous magnesium sulfate and evaporated to dryness. The residue (12 mg) proved to be identical with diketone **22** as judged by the criteria of vpc retention time and by infrared and nmr spectra.