The ultraviolet spectrum in 95% ethanol showed λ_{max} 262 mμ (log ε 4.07); λ_{max} 262.5 mμ (log ε 4.03[3] and 4.10[31]) for I.

Some of the signals and coupling constants for the nmr spectrum of XIII are recorded in Table I. In addition there were five aromatic hydrogens as a multiplet centered at *ca.* 7.25 ppm and the remaining four hydrogens at 1.0–2.0 ppm.

7-*syn*-Chloro-3-*endo*-phenyl-2-*exo*-norbornanol (XV).—The procedure was similar to that employed by Collins, Cheema, Werth, and Benjamin[6] for the preparation of III. From 7.20 g (0.0352 mole) of XIII there was obtained 3.24 g (42.8% yield) of a colorless oil [bp 148–152° (1.6 mm)] which could not be crystallized from a variety of solvents.

In very dilute carbon tetrachloride solution XV showed absorption at 3589 and 3621 cm^{-1} in the infrared with relative intensities of *ca.* 2:1.

Some of the signals and coupling constants for the nmr spectrum of XV are recorded in Table I. In addition there were five aromatic hyrogens (7.17 ppm), hydroxyl hydrogen (2.91 ppm), and remaining four hydrogens (0.9–1.7 ppm).

The tosylate (XVa) was prepared in the usual manner in 94% yield and gave mp 108–108.5°.

Anal. Calcd for $C_{20}H_{21}ClO_3S$: C, 63.74; H, 5.58. Found: C, 63.24; H, 5.86.

(31) The presence of some 1-phenylnortricyclene impurity reduces the absorption intensity. The log ε of 4.10 is for a sample practically devoid of 1-phenylnortricyclene.

The pertinent signals and coupling constants for the nmr spectrum of XVa are recorded in Table I.

Registry No.—I, 4237-08-5; II, 953-59-3; III, 944-56-9; IIIa, 10561-82-7; IIIb, 10561-83-8; IV, 10381-59-6; IVa, 10472-58-9; IVb, 10472-59-0; V, 10561-84-9; Va, 10561-85-0; Vb, 10561-86-1; VI, 10472-45-4; VIa, 10472-63-6; VIb, 10472-44-3; VIII, 10472-46-5; XII, 10472-47-6; XIII, 10472-48-7; XV, 10472-49-8; XVa, 10472-41-0; *exo*-norbornanol, 497-37-0; *exo*-norbornanol *p*-nitrobenzoate, 10472-43-2; *endo*-norbornanol, 497-36-9; *endo*-norbornanol *p*-nitrobenzoate, 10472-51-2; 2-phenylnorbornane-2,3-*cis*-*exo*-diol, 1135-59-7.

Acknowledgment.—We are indebted to Mr. Louis Joris, Chemistry Department, Princeton University, for the determination of the O–H stretching vibrations in dilute carbon tetrachloride solutions. Also, we are grateful to Dr. Ben M. Benjamin, Oak Ridge National Laboratories, for valuable discussions concerning interpretation of some of the nmr spectra.

Perhydroindan Derivatives. VII. Stereochemistry of Bridgehead Alkylation[1a]

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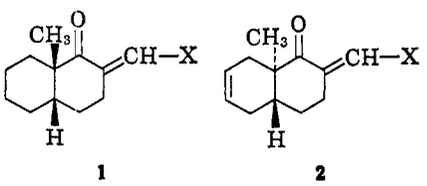
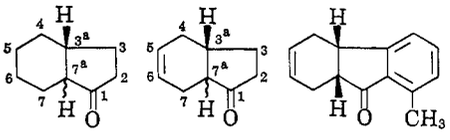
Solutions of the lithium enolate anions **8** (from **4**) and **9** (from **3**) were prepared from the corresponding enol acetates and then were alkylated with methyl bromoacetate. The monoalkylated product from the saturated ketone **3** contained more than 98% of the stereoisomer **17a** with a *cis* ring fusion. The corresponding ketone **4** with a $\Delta^{5,6}$ double bond gave monoalkylated product which contained 96% of the *cis* fused isomer **14a** and 4% of the *trans* fused isomer **15**. A comparable mixture of stereoisomers (mainly **14a**) was obtained from alkylation of the unsaturated ketone **6** and subsequent cleavage of the blocking group.

Earlier studies[2,3] demonstrated that the normal predominance of a *cis* fused product (*e.g.*, **1**) from the methylation of a suitably blocked 1-decalone derivative could be altered by the introduction of $\Delta^{6,7}$ double bond so that the major alkylated product became the *trans* fused isomer (*e.g.*, **2**). The introduction of an analogously located $\Delta^{5,6}$ double bond into the perhydroindanone system increased the equilibrium concentration of the *trans* isomer from 25% for the saturated ketone **3** to 47% for the olefinic ketone **4**.[4] These two observations suggested that the synthetic problem of obtaining a *trans* fused perhydroindan derivative from the alkylation of the ketone **3** at position 7a might be solved by alkylation of the unsaturated ketone **4**. We have explored this possibility earlier by alkylating the enolate anion derived from the tetrahydrofluorenone **5** with methyl bromoacetate;[4b]



1 **2**



3 **4** **5**

in this case the major alkylated product was found to be the *cis* isomer but a minor, uncharacterized product (possibly the *trans* isomer) was also obtained. However, this result did not provide an unambiguous answer to our question because the fused aromatic ring present in ketone **5** altered the relative stabilities of the two modes of ring fusion so that the *cis* fused isomer **5** was substantially more stable than the corresponding *trans* isomer.[4b]

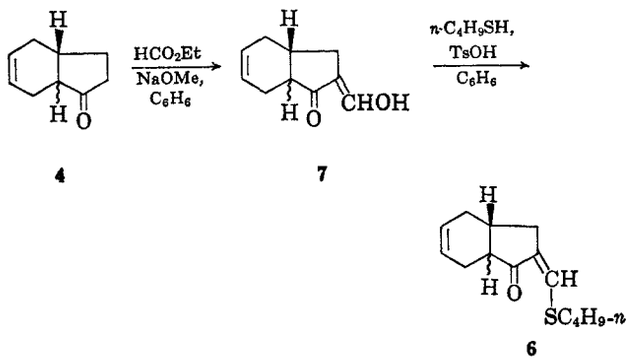
To explore the question of alkylation stereochemistry further, we have now studied the alkylation with methyl bromoacetate of the appropriate enolate anions derived from the unsubstituted ketones **3** and **4** as well as the derivative **6** of the ketone **4** substituted with a thiobutylmethylene blocking group.[2b]

(1) (a) This research has been supported by a grant from the National Science Foundation (No. GP-5685); (b) National Institutes of Health Predoctoral Fellow, 1964–1966.

(2) (a) W. S. Johnson, D. S. Allen, Jr., R. R. Hindersinn, G. N. Sausen, and R. Pappo, *J. Am. Chem. Soc.*, **84**, 2181 (1962); (b) R. E. Ireland and J. A. Marshall, *J. Org. Chem.*, **27**, 1615, 1620 (1962).

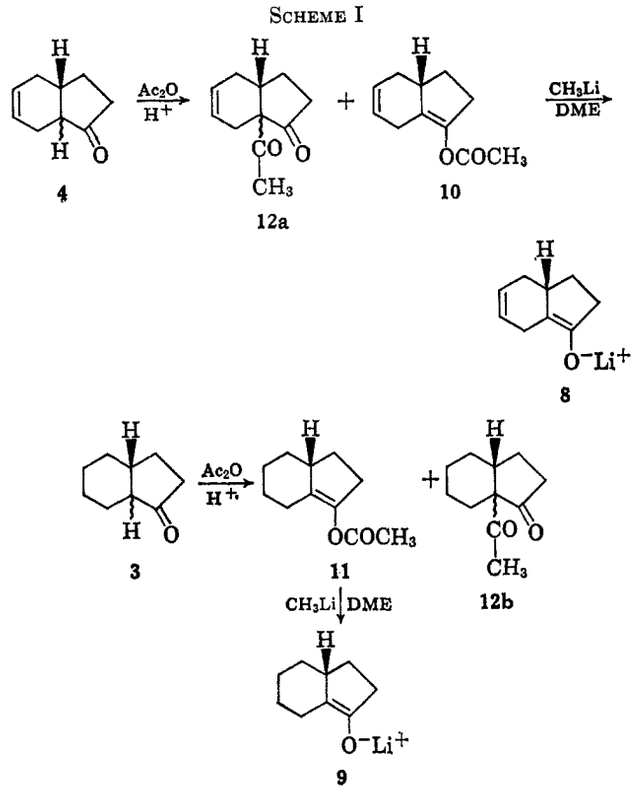
(3) For general reviews of the stereochemistry of enolate alkylation, see (a) J. M. Conia, *Record Chem. Progr. Kresge-Hooker Sci. Lib.*, **24**, 43 (1963); (b) L. Velluz, J. Valls, and G. Nomine, *Angew. Chem. Intern. Ed. Engl.*, **4**, 181 (1965).

(4) (a) H. O. House and G. H. Rasmusson, *J. Org. Chem.*, **28**, 31 (1963); (b) H. O. House and R. G. Carlson, *ibid.*, **29**, 74 (1964).

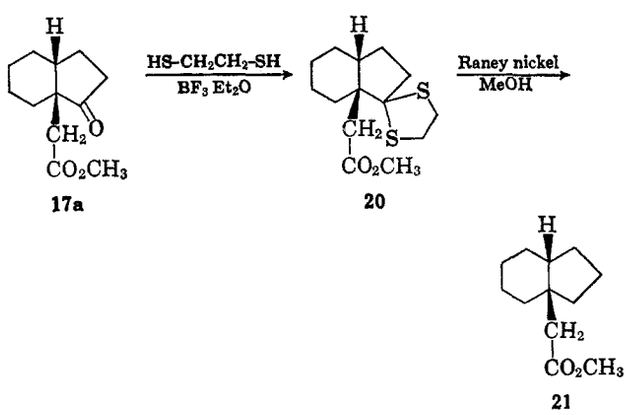


To obtain solutions of the enolate anions **8** and **9** uncontaminated with structurally isomeric enolates, each of the ketones **3** and **4** was converted to the more highly substituted (and hence more stable) enol acetate **10** or **11** (Scheme I). Subsequent reaction of **10** and **11** with 2 equiv of methyllithium[5] in 1,2-dimethoxyethane (DME) afforded solutions of the desired enolate anions **8** and **9**. Each of the lithium enolates **8** and **9**

SCHEME I



as well as the potassium enolate derived from ketone **6** was alkylated with methyl bromoacetate as summarized in Scheme II. The monoalkylated products **14a** + **15** and **17**, were isolated in yields of 58 and 60%, respectively; the mixture of stereoisomeric keto esters **14a** and **15** was isolated in an over-all yield of 28% from alkylation of the thiobutyl derivative **6** and subsequent cleavage of the blocking group. The predominant unsaturated alkylation products **13** and **14** were interrelated and converted to the major saturated product **17**. The dialkylated products **16** and **18** were interrelated and shown to have the same stereochemical arrangement at the bridgehead as the monoalkylated product **17**. The keto ester **17** was converted *via* the dithio ketal **20** to the known[6] *cis*-perhydroindan derivative **21**. These results allow us to conclude that alkylation of each of the ketones **3**, **4**, and **6** at position 7a leads to the predominant formation of a *cis* fused perhydroindanone derivative. A minor product **15** (4% of the monoalkylated product) formed in the alkylation of the unsaturated ketone **4** was hydrogenated to the corresponding saturated keto ester **19** (Scheme II). Although we have no rigorous structure proof for these minor products, their spectroscopic properties leave little doubt but that they are the indicated *trans* fused isomers. Therefore, it appears that the presence of a $\Delta^{5,6}$ double bond in the perhydroindan-1-one system does enhance slightly the amount of *trans* fused alkylated product formed but this structural change alone is insufficient to make the *trans* fused ketone the major product.



We explored several other potential routes to the *trans* fused isomer **19** which are summarized in Scheme III. Alkylation of the α,β-unsaturated ketone **22** afforded the β,γ-unsaturated keto ester **23**. Hydrogenation of either the keto ester **23** or the derived lactone **24**[7] led to *cis* fused products. The possibility of photoisomerism[8] of the keto ester **17a** was also examined. However, the major product formed from irradiation of the keto ester **17a** was not the *trans*-keto ester **19** but rather a material whose spectroscopic properties suggested that it was the unsaturated aldehyde **26**.

Experimental Section[9]

Preparation of the Hexahydroindanones 3 and the Tetrahydroindanones 4 and 22.—The $\Delta^{5,6}$-tetrahydroindanones **4** were

(5) H. O. House and B. M. Trost, *J. Org. Chem.*, **30**, 1341, 2502 (1965).

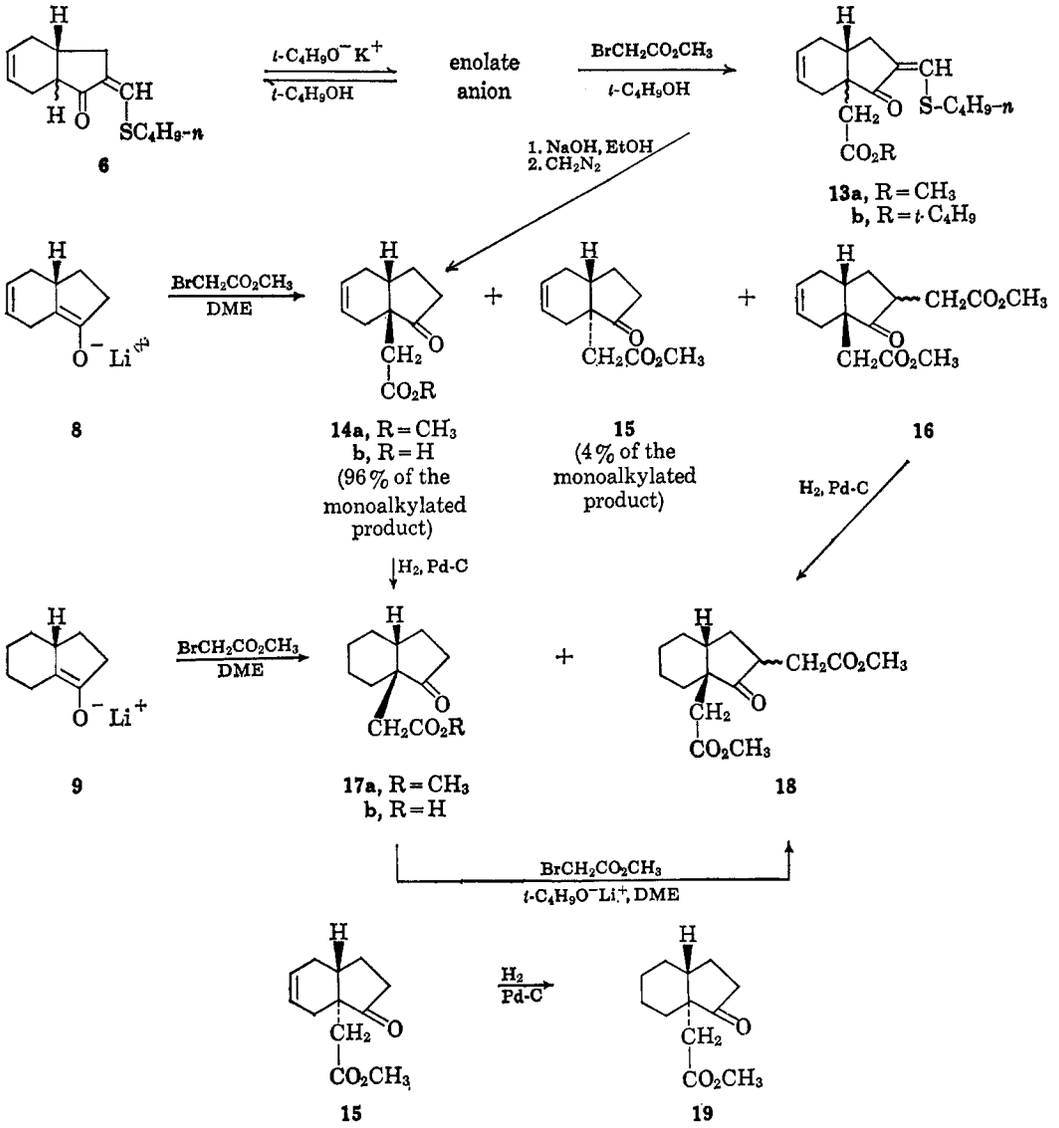
(6) H. O. House, S. G. Boots, and V. K. Jones, *ibid.*, **30**, 2519 (1965).

(7) This procedure was investigated because of other work [H. O. House, R. G. Carlson, H. Müller, A. W. Noltes, and C. D. Slater, *J. Am. Chem. Soc.*, **84**, 2614 (1962)] in which a relatively rigid γ-lactone system served to direct the incoming hydrogen to the opposite side of the molecule and yield a *trans* fused perhydroindan derivative.

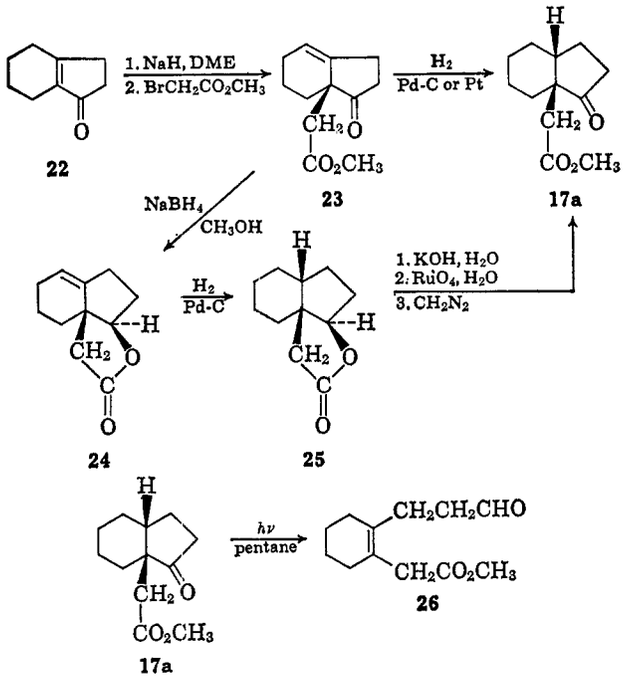
(8) H. Wehrli and K. Schaffner [*Helv. Chim. Acta*, **45**, 385 (1962)] have reported the successful photochemical interconversion of *cis* fused and *trans* fused perhydroindan derivatives in the steroid series.

(9) 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 a Perkin-Elmer, Model 237, infrared recording spectrophotometer fitted with a grating. The ultraviolet spectra were determined with a Cary recording spectrophotometer, Model 14. The nuclear magnetic resonance (nmr) spectra were determined at 60 Mc with a Varian, Model A-60, nmr spectrometer. The chemical shift values are expressed either in cycles per second or δ values (parts per million) relative to a tetramethylsilane internal standard. 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.

SCHEME II



SCHEME III



prepared from cyclopentenone as previously described[4a] and pure samples of the *cis* and *trans* isomers were collected[10] and identified with the previously described samples by comparison of infrared spectra. In subsequent work, mixtures containing approximately equal amounts of these two stereoisomers were employed. The Stobbe condensation product obtained from cyclohexanone and diethylsuccinate[11] was converted to the tetrahydroindanone **22** [bp 122° at 19 mm, $n^{24.9}$D 1.5299 (lit.[11b] 83.5–85° at 2 mm, n^{18}D 1.5260)] as previously described.[4a,11] An ethanol solution of the tetrahydroindanone **22** was hydrogenated[4a] over a 5% palladium-on-carbon catalyst to yield the *cis*[10]-perhydroindanone **3** [bp 98° at 20 mm, $n^{24.9}$D 1.4825 (lit.[11b] bp 72–73° at 6 mm, n^{25}D 1.4813)]. Alternatively, a solution of 9.88 g (0.075 mole) of 1-indanone in 50 ml of acetic acid was hydrogenated at room temperature and under 4 atm of hydrogen pressure over 4.97 g of a 5% rhodium-on-alumina catalyst.[12] The hydrogen uptake (0.318 mole) ceased after 75 min and the crude, neutral product (8.78 g of colorless liquid) was separated in the usual manner. A solution of this crude product, which contained[10] a mixture of perhydroindanols (*ca.* 85%), perhydroindanone **3** (*ca.* 5%), and unidentified hydrocarbons (*ca.* 10%),

(10) A gas chromatography column packed with silicone fluid, no. 710, suspended on Chromosorb P was employed for this analysis.

(11) (a) W. S. Johnson, C. E. Davis, R. H. Hunt, and G. Stork, *J. Am. Chem. Soc.*, **70**, 3021 (1948); (b) D. W. Mathieson, *J. Chem. Soc.*, 3248 (1953).

(12) The relatively large amount of catalyst used could be recovered and reused in subsequent hydrogenations. See A. I. Meyers, W. Beverung, and G. Garcia-Munoz, *J. Org. Chem.*, **29**, 3427 (1964).

in 200 ml of acetone was cooled in an ice bath and treated with 11.1 ml of 8 *N* chromic acid.[13] After the mixture had been stirred for 15 min, the excess oxidant was destroyed by the addition of isopropyl alcohol and the reaction mixture was filtered and concentrated. Distillation of the residual liquid afforded 7.58 g (73%) of the crude perhydroindanone **3**, bp 82–106° (16 mm). Although this product contained[10] some perhydroindanol (*ca.* 15%) and some hydrocarbon, it was sufficiently pure for use in the subsequently described enol acetate preparation.

Preparation of the Thiobutylmethylene Ketone 6.—A mixture of 650 ml of benzene, 22.9 g (0.521 mole) of sodium methoxide, 39.7 g (0.920 mole) of ethyl formate, and 17.94 g (0.129 mole) of the tetrahydroindanone **4** was allowed to stand, at room temperature and under a nitrogen atmosphere, with occasional swirling for 21 hr. The resulting mixture was poured into 400 ml of ice water and the organic phase was separated and washed with aqueous 5% sodium hydroxide. After the combined aqueous solutions had been acidified and extracted with ether, the ethereal extract was concentrated; the crude hydroxymethylene compound **7** was allowed to react with excess copper(II) acetate in aqueous methanol. The resulting copper chelate was collected and washed with hexane to leave 20.14 g (90%) of green solid, mp 172–185° dec. Recrystallization from a benzene–methanol mixture afforded the copper chelate as a green solid, mp 180–183° dec, with infrared absorption[14] at 1485 and 1610 cm^{-1} (enolate of a 1,3-dicarbonyl compound) and ultraviolet maxima[15] at 214 mμ (ε 7780), 257 (10,900), 314.5 (20,800), and 333 (sh, 11,100). A 9.69-g sample of this copper chelate was shaken with a mixture of aqueous 10% sulfuric acid and ether to regenerate the hydroxymethylene compound **7**, recovered from the ether phase as 7.75 g (96%) of yellow semisolid material which darkened rapidly on exposure to air. A solution of 7.75 g (0.051 mole) of the crude hydroxymethylene ketone **7**, 5.13 g (0.057 mole) of butanethiol, and 10 mg of *p*-toluenesulfonic acid in 130 ml of benzene was refluxed under a nitrogen atmosphere with continuous separation of water for 5 hr. The resulting solution was concentrated and the residual oil was partitioned between ether and aqueous sodium bicarbonate. After the ethereal phase had been washed with water, dried, and concentrated, distillation of the residue separated 8.61 (72%) of the thiobutylmethylene derivative **6** as a yellow oil [bp 140–151° (0.5–0.8 mm)], which is presumably a mixture of stereoisomers. A portion of the product was crystallized from petroleum ether (bp 30–60°) at Dry-Ice temperatures and the resulting solid (mp 30–38°) was chromatographed on Florisil and then repeatedly recrystallized from petroleum ether. One stereoisomer of the thiobutylmethylene ketone **6** was obtained as fine white prisms, mp 50.5–51.5°. The product has infrared absorption[16] at 1710 (conjugated C=O in a five-membered ring), 1655 (unconjugated C=C), and 1595 cm^{-1} (conjugated C=C), with an ultraviolet maximum[15] at 309 mμ (ε 20,800). The nmr spectrum[16] has a triplet (J = 1.8 cps) of partially resolved multiplets at δ 7.29 (1 H, C=CHS) with a multiplet at 5.63 (2 H, vinyl CH), a triplet (J = 6.8 cps) at 2.86 (2 H, SCH_2), a broad multiplet at *ca.* 2.3 (6 H, allylic CH), and a complex multiplet in the region 0.9–2.2 (9 H, aliphatic CH).

Anal. Calcd for $C_{14}H_{20}OS$: C, 71.14; H, 8.53; S, 13.53; mol wt, 236. Found: C, 70.90; H, 8.54; S, 13.44; mol wt, 236 (mass spectrum).

Preparation of the Enol Acetates 10 and 11.—A solution of 23.59 g (0.173 mole) of the tetrahydroindanone **4**, 50 ml of acetic anhydride, and 0.3 ml of aqueous 70% perchloric acid in 150 ml of carbon tetrachloride was stirred at room temperature and under a nitrogen atmosphere for 30 min and then diluted with ether. This solution was mixed with aqueous sodium bicarbonate and additional quantities of solid sodium bicarbonate were added until carbon dioxide evolution ceased. The organic layer was separated, combined with the ethereal extract of the aqueous layer, washed with aqueous sodium chloride, dried, and concentrated. Distillation of the residual liquid separated 24.30 g of pale yellow liquid, boiling at or below 123° (5 mm), which contained (in order of increasing retention time)[10] the starting ketones **4** (*ca.* 30%), the enol acetate **10** (*ca.* 65%), and a higher boiling component believed to be the diketone **12a** (*ca.* 5%).[17] Fractional distillation with a 40-cm spinning-band column separated fractions, bp 109–110° (6 mm), $n^{27.5}D$ 1.5000, which contained[10] the pure enol acetate **10**. Redistillation afforded an analytical sample, bp 116° (7 mm), $n^{27}D$ 1.5018, with infrared absorption[16] at 1765 (enol ester C=O), 1715 (enol ester C=C), and 1655 cm^{-1} (C=C) and a weak ultraviolet maximum[15] at 312 mμ (ε 129) as well as intense end absorption. The product has nmr absorption[16] at δ 5.65 (2 H multiplet, vinyl CH) and 2.10 (3 H, singlet, CH_3CO) as well as broad absorption in the region δ 1.3–2.8 (9 H, aliphatic CH).

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92; mol wt, 178. Found: C, 73.85; H, 7.78; mol wt, 178 (mass spectrum).

The higher boiling fractions, bp 127° (16 mm), from the above distillation afforded a crystalline solid which was recrystallized from methanol to separate a product believed to be the diketone **12a** as white cubes, mp 73–74.5°. The product has infrared absorption[14] at 1740 (C=O in a five-membered ring) and 1705 cm^{-1} (C=O) with weak end absorption (ε 1490 at 210 mμ) in the ultraviolet.[15] The nmr spectrum[18] has peaks at δ 5.59 (2 H multiplet, vinyl CH) and 2.13 (3 H singlet, $COCH_3$) as well as broad absorption in the region δ 1.3–3.0 (9 H, aliphatic CH). The mass spectrum exhibits a molecular ion peak at *m/e* 178 with a very abundant fragment peak at *m/e* 135 corresponding to the loss of $CH_3C{\equiv}O^+$. This fragmentation is characteristic of methyl ketones and differs from the abundant fragment peak at *m/e* 136 (loss of $CH_2{=}C{=}O$) in the spectrum of the isomeric enol acetate **10**.

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92. Found: C, 73.86; H, 7.91.

When a solution of 4.06 g (0.030 mole) of the unsaturated ketone **4** and 57 mg of *p*-toluenesulfonic acid in 9.18 g (0.090 mole) of acetic anhydride was refluxed for 5 hr with continuous distillation of acetic acid and then subjected to the same isolation procedure described above, the distillation fractions [4.10 g (77%), bp 110–129° (18 mm), $n^{24.4}D$ 1.4971–1.4988] contained[10] the same enol acetate **10** accompanied by *ca.* 10% of the starting ketones. This procedure yielded little, if any, of the C-acylated product **12a**.

A solution of 23.58 g (0.171 mole) of the perhydroindanones **3**, 50 ml of acetic anhydride, and 0.3 ml of aqueous 70% perchloric acid in 150 ml of carbon tetrachloride was stirred at room temperature and under a nitrogen atmosphere for 1 hr and then subjected to the previously described isolation procedure. The distilled product [28.28 g, bp 82–107° (5 mm)] contained[19] (in order of increasing retention time) the starting ketone **3** (*ca.* 5%), the enol acetate **11** (*ca.* 70%), and a product believed to be the diketone **12b** (*ca.* 25%).[17] Fractional distillation with a 40-cm spinning-band column separated the pure enol acetate **11** [bp 103° (6 mm), $n^{11}d$ 1.4832] with infrared absorption[16] at 1765 (enol ester C=O) and 1710 cm^{-1} (enol ester C=C) and an nmr[11] singlet at δ 2.08 (CH_3CO) superimposed on complex absorption in the region δ 1.4–2.6 (aliphatic CH).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95; mol wt, 180. Found: C, 73.00; H, 8.90; mol wt, 180 (mass spectrum).

Higher boiling fractions [bp 132–134° (10 mm)] from the fractional distillation contained[10] a compound believed to be the diketone **12b** with infrared absorption[16] at 1740 (C=O in a five-membered ring) and 1705 cm^{-1} (C=O). The sample has an nmr[16] singlet at δ 2.08 (CH_3CO) superimposed on complex absorption in the region δ 1.1–2.9 (aliphatic CH).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95; mol wt, 180. Found: C, 73.34; H, 8.98; mol wt, 180 (mass spectrum).

In an alternative procedure, a mixture of 4.10 g (0.030 mole) of the perhydro ketone **3**, 51 mg of *p*-toluenesulfonic acid, and 9.69 g (0.095 mole) of acetic anhydride was refluxed for 5 hr with continuous distillation of acetic acid. An additional 3.09 g (0.030 mole) of acetic anhydride was added and heating was continued for an additional 3 hr. After the crude product had been isolated as previously described, fractional distillation through a Holzmann column separated 4.19 g (78%) of fractions [bp 116–139° (19 mm), $n^{24.5}D$ 1.4794–1.4849] which contained[10] the enol acetate **11** accompanied by 3–8% of the starting ketone **3**. Little, if any, of the diketone **12b** was produced by this procedure.

(13) D. C. Kleinfelter and P. von R. Schleyer, *Org. Syn.*, **42**, 79 (1962).

(14) Determined as a solution in chloroform.

(15) Determined as a solution in 95% ethanol.

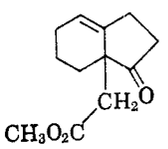
(16) Determined as a solution in carbon tetrachloride.

(17) The amount of C-acylated product formed was found to vary from run to run suggesting that it was formed by acid-catalyzed rearrangement of the initially formed enol acetate. See C. R. Hauser, F. W. Swamer, and J. T. Adams, *Org. Reactions*, **8**, 59 (1954).

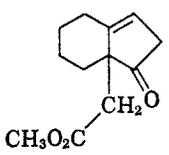
(18) Determined as a solution in deuteriochloroform.

(19) A gas chromatography column packed with Carbowax 20 M suspended on Chromosorb P was employed for this analysis.

Alkylation of the Tetrahydroindanone 22.—A 1.44-g (*ca.* 0.03 mole) sample of sodium hydride dispersion was washed with several portions of petroleum ether to remove the mineral oil and then suspended in 30 ml of 1,2-dimethoxyethane. To this mixture was added 0.23 g (0.003 mole) of *t*-butyl alcohol.[20] The resulting mixture was warmed to 65–70° and then a solution of 3.02 g (0.0222 mole) of the ketone **22** in 20 ml of 1,2-dimethoxyethane was added, dropwise and with stirring, over a 1.25-hr period, during which time the volume of evolved hydrogen was followed. When the addition was complete, the mixture was stirred at 65–70° for an additional 1 hr. The total amount of evolved hydrogen was 511 ml (corrected value) corresponding to 1.04 equiv of hydrogen. The resulting solution of the enolate anion was cooled to 20° (some enolate precipitated at this temperature) and 5.24 g (0.0342 mole) of methyl bromoacetate was added in one portion with stirring. After the resulting mixture had been stirred for 5 min, it was poured into aqueous 1 *M* hydrochloric acid. The ethereal extract of the resulting mixture was washed successively with aqueous sodium bicarbonate and aqueous sodium chloride and then dried and concentrated. The residual crude product, which contained[21] the keto ester **23** accompanied by at least three less volatile components, was chromatographed on 150 g of Florisil; the keto ester **23**, eluted with benzene–ether mixtures, amounted to 1.82 g (40%) of colorless liquid. Samples for characterization were collected from the gas chromatograph.[21] The product has infrared absorption[16] at 1745 (C=O) and 1675 cm^{-1} (weak, C=C) with nmr peaks[16] at δ 5.56 (1 H broad, one-half band width $\cong$ 8 cps, vinyl CH), 3.52 (3 H singlet, OCH_3), and 2.39 (2 H singlet, CH_2CO_2R) as well as broad absorption in the region δ 1.1–2.8 (10 H, aliphatic CH). The absence of additional relatively low-field absorption indicates that this product is correctly formulated as **23** rather than the alternative structure **27** which would be expected to



23



27

have additional low-field absorption attributable to the protons at C-2.[22] The mass spectrum has a molecular ion peak at *m/e* 208 with abundant fragment peaks at *m/e* 135 ($M - CH_2CO_2CH_3$), 91, and 74 ($CH_2{=}C{<}^{OH}_{OCH_3}$)$^+$.

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74. Found: C, 69.07; H, 7.75.

A solution of 225 mg (1.1 mmole) of the keto ester **23** in 10 ml of ethanol was hydrogenated at room temperature and atmospheric pressure over 40 mg of 5% palladium-on-carbon catalyst. The hydrogen uptake (26.5 ml or 1.08 equiv) was complete after 1.1 hr. The crude product (209 mg) recovered contained[19] the *cis*-keto ester **17a**, a collected sample of which was identified with the subsequently described sample by comparison of infrared spectra. Similarly, the hydrogenation of a solution of 234 mg (1.2 mmoles) of the keto ester **23** in 10 ml of ethanol over the catalyst obtained from 85 mg of platinum oxide was complete (hydrogen uptake 27.9 ml or 1.06 equiv) in 15 min and yielded a crude product (239 mg) which contained the *cis*-keto ester **17a**. Short-path distillation (100–130° at 0.1 mm) separated 214 mg (90%) of the keto ester **17a** which was identified with the subsequently described sample by comparison of infrared and nmr spectra.

Preparation of the Lactones 24 and 25.—A solution of 1.24 g (59.7 mmoles) of the keto ester **23** and 0.30 g (81 mmoles) of sodium borohydride in 22 ml of methanol was cooled in an ice bath and stirred for 2 hr. The resulting solution was acidified (pH $\sim$ 1), concentrated under reduced pressure, and redissolved in ether. The ethereal solution was washed successively with aqueous sodium bicarbonate and aqueous sodium chloride and then dried and concentrated. Short-path distillation (70–170° at 0.1 mm) of the crude residue (0.87 g) afforded 0.70 g (66%) of the unsaturated lactone **24** as a colorless liquid. The product has infrared absorption[16] at 1780 cm^{-1} (γ-lactone C=O) with nmr peaks[16] at δ 5.37 (1 H broad, one-half band width $\cong$ 7 cps, vinyl CH), 4.49 (1 H, pair of doublets, peak separations 5.5 and 2.0 cps, >CHO), and 2.40 (2 H singlet, CH_2CO), as well as broad absorption in the region δ 1.1–2.5 (10 H, aliphatic CH).

Anal. Calcd for $C_{11}H_{14}O_2$: C, 74.13; H, 7.92; mol wt, 178. Found: C, 73.84; H, 7.91; mol wt, 178 (mass spectrum).

Samples (155–202 mg) of the unsaturated lactone **24** were dissolved in 10 ml of ethanol and hydrogenated at atmospheric pressure and room temperature over either a 5% palladium-on-carbon catalyst or the catalyst from platinum oxide. Both relatively large (*e.g.*, 86 mg) and relatively small (*e.g.*, 4–26 mg) amounts of catalyst were employed since the amount of catalyst had been found important in other studies.[7] However, in all cases the crude products (yields >90%) exhibited only a single peak on gas chromatography. The nmr spectra of the products obtained on short-path distillation (yields 80–95%) all corresponded to the nmr spectrum of the pure *cis*-lactone **25**. The distilled product solidified and was recrystallized from hexane to separate the pure lactone **25** as white prisms, mp 63–66°. The product has infrared absorption[16] at 1780 cm^{-1} (γ-lactone C=O) with an nmr multiplet[16] centered at δ 4.32 (1 H, >CHO) as well as broad absorption in the region δ 1.1–2.1 (13 H, aliphatic CH) and a partially resolved AB pattern (J = 17 cps) with the chemical shift values estimated to be at δ 2.20 and 2.48 (2 H, CH_2CO).

Anal. Calcd for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95; mol wt, 180. Found: C, 73.48; H, 8.95; mol wt, 180 (mass spectrum).

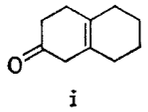
A mixture of 203 mg (1.13 mmoles) of the lactone **25**, 87 mg (1.3 mmoles) of potassium hydroxide, and 5 ml of water was stirred at room temperature for 6 hr at which time saponification was complete and a homogeneous mixture (pH $\sim$ 10) was obtained. The addition of several drops of acetic acid gave a solution of pH $\sim$ 5 which was then cooled in an ice bath and treated with a solution of ruthenium tetroxide (from 1.46 mmoles of ruthenium dioxide)[23] in 10 ml of carbon tetrachloride. After the mixture had been shaken for 5 min it was filtered and the filtrate was made basic with aqueous sodium hydroxide and washed with carbon tetrachloride. The aqueous phase was acidified and extracted with ether to separate 132 mg (60%) of the crude keto acid **17b**, mp 87–98°. Esterification with excess ethereal diazomethane afforded 128 mg (57%) of the *cis*-keto ester **17a** which was identified with the subsequently described sample by comparison of gas chromatographic retention times and infrared spectra.

Alkylation of the Tetrahydroindanone 4.—An ether solution containing 23 mmoles of methyllithium was concentrated to dryness under reduced pressure and the methyllithium was redissolved in 100 ml of 1,2-dimethoxyethane containing *ca.* 1 mg of triphenylmethane. To the resulting solution was added, dropwise with stirring under a nitrogen atmosphere, the enol acetate **10** (1.89 g or 10.6 mmoles) until the red color of the triphenylmethyl anion was almost completely discharged. The resulting solution of the enolate anion **8** was cooled in an ice bath and treated with 5.17 g (33.8 mmoles) of methyl bromoacetate. After the solution had been stirred for 30 sec, 50 ml of aqueous 1 *M* hydrochloric acid was added. The ethereal extract of the mixture was washed successively with aqueous sodium bicarbonate and aqueous sodium chloride and then dried and concentrated. The crude product (4.28 g of yellow oil) contained[19,21] in addition to low molecular weight materials the following components (listed in order of elution): the unalkylated ketones **4**, *ca.* 3%; the *cis*-keto ester **14a**, *ca.* 73%; the *trans*-

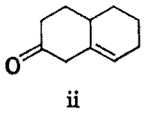
(20) The reaction of sodium hydride with the ketone (followed by measuring the volume of liberated hydrogen) was very slow in the absence of added *t*-butyl alcohol. This addition of 10 mole % *t*-butyl alcohol to catalyze ketone–sodium hydride reactions appears to be a more generally useful technique than the commonly recommended procedure of adding several drops of ethanol. For example, see W. S. Johnson and G. H. Daub, *Org. Reactions*, **6**, 1 (1951).

(21) A gas chromatography column packed with silicone gum, SE-30, suspended on Chromosorb P was employed for this analysis.

(22) For example the C-1 signal for octalones i and ii is centered at *ca.* δ 2.9. H. O. House, B. M. Trost, R. W. Magin, R. G. Carlson, R. W. Franck, and G. H. Rasmusson, *J. Org. Chem.*, **30**, 2513 (1965).



i



ii

(23) The ruthenium tetroxide was prepared by the oxidation of the black hydrate of ruthenium dioxide with excess aqueous sodium periodate. The resulting yellow solution was extracted with carbon tetrachloride. See P. J. Beynon, P. M. Collins, P. T. Doganges, and W. G. Overend, *J. Chem. Soc., Sect. C*, 1131 (1966).

keto ester **15**, *ca.* 6%; and the dialkylated product **16**, *ca.* 18%. Subsequent runs, done for analytical purposes, followed the same general reaction procedure except that weighed amounts of acenaphthene were added to the crude product as an internal standard for gas chromatographic analysis and the chromatography columns[19,21] were calibrated with known mixtures of collected samples. For a reaction employing 1.9 moles of alkylating agent/mole of enolate anion with a reaction time of 30 sec at 0°, the calculated yields were 46% **4**, 41% **14a**, 2% **15**, and 8% **16**. When 2.9 moles of methyl bromoacetate/mole of enolate anion was employed with a reaction time of 1.0 min at 0°, the calculated yields were 19% **4**, 51% **14a**, 2% **15**, and 15% **16**. In both runs the monoalkylated product contained 96% of the *cis* isomer **14a** and 4% of the *trans* isomer **15**. The crude product from the above preparative run was chromatographed on 150 g of Florisil. The earlier fractions (1.27 g or 58% yield of colorless liquid), eluted with benzene–ether mixtures, contained the monoalkylated products **14a** and **15**. The later fractions (0.29 g or 10% yield of colorless liquid), eluted with benzene ether mixtures, contained the dialkylated product(s) **16**. A 1.33-g (6.4 mmoles) sample of the monoalkylated products was mixed with a solution of 0.50 g (7.7 mmoles) of potassium hydroxide in 15 ml of methanol and the resulting solution was stirred at room temperature for 23 hr. After the mixture had been concentrated, diluted with water, and extracted with ether, it was acidified and again extracted with ether. The crude acid (0.91 g or 74%) obtained from the final ether extract was recrystallized from a benzene–petroleum ether mixture to separate the pure acid **14b** as white prisms, mp 114–115.8°. This product has infrared absorption[16] at 1745 (C=O in a five-membered ring), 1710 (carboxyl C=O), and 1655 cm^{-1} (C=C) with an ultraviolet maximum[15] at 278 mμ (ε 51). The nmr spectrum[18] has peaks at δ 11.25 (1 H, COOH) and 5.73 (2 H multiplet, vinyl CH) with broad absorption in the region δ 1.2–3.0 (11 H, aliphatic CH).

Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.02; H, 7.27. Found: C, 67.86; H, 7.31.

A sample of this crystalline acid was esterified with excess ethereal diazomethane to yield the keto ester **14a** as a colorless liquid, $n^{26}D$ 1.4958. This product was identified with a sample of the keto ester **14a** collected[19] from an alkylation reaction mixture. The product has infrared absorption[16] at 1745 (C=O of ester and of a cyclopentanone derivative) and 1660 cm^{-1} (C=C) with nmr peaks[16] at δ 5.61 (2 H multiplet, vinyl CH) and 3.57 (3 H singlet, OCH_3) as well as complex absorption in the region δ 1.2–2.9 (11 H, aliphatic CH).

Anal. Calcd for $C_{12}H_{16}O_3$: C, 69.21; H, 7.74; mol wt, 208. Found: C, 68.96; H, 7.71; mol wt, 208 (mass spectrum).

The mother liquors remaining after the keto acid **14b** had been crystallized from the crude monoalkylated product were concentrated and chromatographed on silicic acid. The fraction eluted with benzene–ether mixtures partially solidified and was recrystallized from a benzene–petroleum ether to remove an additional crop of the major keto acid **14b**. The residual acid from the mother liquors was esterified with excess ethereal diazomethane to yield 97 mg of a yellow oil which contained[19] approximately equal amounts of the *cis*- (**14a**) and *trans*- (**15**) keto esters. A collected sample of the *cis* isomer (first eluted) was identified with the previously described sample of keto ester **14a** by comparison of infrared spectra. A collected[19] sample of the *trans* isomer **15** has infrared absorption[16] at 1745 (C=O of ester and cyclopentanone derivative) and 1635 cm^{-1} (C=C) with nmr absorption[24] at δ 5.64 (2 H multiplet, vinyl CH) and 3.52 (3 H singlet, OCH_3) as well as complex absorption in the region δ 1.2–2.9 (11 H, aliphatic CH). The mass spectrum of the sample exhibits a molecular ion peak at *m/e* 208 with abundant fragment peaks at *m/e* 135, 134, 92, 91, 79, 77, and 39. This mass spectrum is similar to the spectrum observed for the *cis*-keto ester **14a**.

The remaining 35 mg of the mixture of keto esters **14a** and **15** was dissolved in 2 ml of ethanol and hydrogenated at room temperature and atmospheric pressure over the catalyst from 10 mg of platinum oxide. The hydrogen uptake (1 mole equiv) had ceased after 30 min. The solution was filtered and concentrated to leave 30 mg of yellow oil which contained[19] approximately equal amounts of the *cis*-keto ester **17a** (first eluted) and the *trans*-keto ester **19** (eluted second). A collected sample of the *cis* isomer **17a** was identified with a subsequent sample by comparison of infrared spectra. A collected[19] sample of the *trans* isomer **19** has infrared absorption[16] at 1745 (C=O of ester and cyclopentanone derivative) with an nmr singlet[24] singlet at δ 3.86 (3 H, OCH_3) as well as complex absorption in the region δ 1.2–3.2 (15 H, aliphatic CH). The mass spectrum of the *trans* isomer exhibits a molecular ion peak at *m/e* 210 with abundant fragment peaks at *m/e* 137, 94, 79, 74, 41 and 39; this spectrum resembles closely the mass spectrum of the subsequently described *cis* isomer **17a**. Further characterization of the *trans*-keto esters **15** and **19** was not possible with the amounts of material available.

In additional experiments performed to interrelate the saturated and unsaturated alkylation products, a solution of 489 mg (2.5 mmoles) of the unsaturated acid **14b** in 20 ml of ethanol was hydrogenated at room temperature and atmospheric pressure over 54 mg of a 30% palladium-on-carbon catalyst. After 3.75 hr the hydrogen uptake (59.4 ml or 1.06 equiv) ceased and the reaction mixture was filtered and concentrated. The residual crude acid (480 mg) was chromatographed on silicic acid. The fractions eluted with benzene–ether mixtures were combined and recrystallized from a benzene–petroleum ether mixture to separate 405 mg (81%) of the keto acid **17b** which was identified with the subsequently described sample by a mixture melting point determination and by comparison of the infrared and ultraviolet spectra of the two samples. Similarly the hydrogenation of a solution of 579 mg (2.78 mmoles) of the keto ester **14a** in 20 ml of ethanol over 89 mg of a 30% palladium-on-carbon catalyst resulted in the uptake of 1.06 equiv of hydrogen over a 130-min period. The resulting product, 520 mg (87%) of colorless oil, was identified with the subsequently described sample of the keto ester **17a** by comparison of gas chromatographic retention times and infrared spectra.

The chromatographic fraction from the alkylation of the tetrahydroindan **4** which contained the crude liquid dialkylation product **16** had infrared absorption[14] at 1735 (br, C=O of ester and cyclopentanone derivative) and 1650 cm^{-1} (weak, C=C) with nmr absorption[18] at δ 5.61 (2 H multiplet, vinyl CH), 3.66 (3 H singlet, OCH_3), and 3.59 (3 H singlet, OCH_3), as well as complex absorption in the region δ 1.0–3.1 (aliphatic CH). A solution of 290 mg (1.04 mmole) of this keto diester **16** in 10 ml of ethanol was hydrogenated at room temperature and atmospheric pressure over 36 mg of a 30% palladium-on-carbon catalyst. The hydrogen uptake (23.8 ml or 1.04 equiv) was complete after 1 hr and the reaction mixture was filtered and concentrated. The residual oil (224 mg) which solidified on standing was recrystallized from methanol to separate 72 mg of one stereoisomer of the keto diester **18** as white prisms, mp 95–98°. This material was identified with the subsequently described sample **18** by a mixture melting point determination and by comparison of infrared spectra.

Alkylation of the Perhydroindanone 3.—Following the previously described procedure a solution of 30 mmoles of methyllithium in 60 ml of 1,2-dimethoxyethane was treated with 2.52 g (14.0 mmoles) of the enol acetate **11**. After the enolate solution had been cooled in an ice bath, 5.75 g (37.6 mmoles) of methyl bromoacetate was added. The resulting mixture was stirred for 30 sec, quenched by the addition of 50 ml of aqueous 1 *M* hydrochloric acid, and then subjected to the previously described isolation procedure. The crude product (4.13 g of yellow liquid) contained[21] (in addition to low boiling components), the monoalkylated ketone **17a** (*ca.* 65%) and the dialkylated product **18** (*ca.* 35%). In subsequent analytical runs the same reaction procedure was used and weighed amounts of acenaphthene were added to the crude reaction products as internal standards. The mixtures were analyzed by gas chromatography,[19,21] employing apparatus previously calibrated with known mixtures of collected materials. For a reaction employing 1.9 moles of alkylating agent/mole of enolate anion with a reaction time of 30 sec at 0° the calculated yields of products (listed in order of elution)[19,21] were **3**, 29%; **17a**, 54%; and **18**, 6%. Employing the same reaction time and temperature with 3.8 moles of alkylating agent/mole of enolate, the calculated yields were **3**, 8%; **17a**, 48%; and **18**, 28%. A reaction for 1 min at 0° employing 2.6 moles of alkylating agent/mole of enolate gave the following calculated yields: **3**, 12%; **17a**, 60%; and **18**, 20%. In none of these cases did we detect a peak which could be identified as the previously described *trans* monoalkylated product **19** which would be eluted[19] after the *cis* isomer **17a**. We, therefore, conclude that at least 98% of the monoalkylated product is the *cis* isomer **17a**.

(24) Determined as a pure liquid.

The crude monoalkylated product from the preparative alkylation described above was chromatographed on 150 g of Florisil to separate 1.76 g (60%) of the crude monoalkylation product **17a** as a colorless oil from early fractions eluted with ether–benzene mixtures. Later fractions eluted with ether–benzene mixtures afforded 0.72 g (22%) of the crude dialkylated product **18** as an oil which solidified on standing. The dialkylation product was recrystallized several times from methanol to separate one pure stereoisomer of the keto diester **18** as white prisms, mp 98–99.5°. This product has infrared absorption[14] at 1735 cm^{-1} (C=O of ester and cyclopentanone derivative) with nmr peaks[18] at δ 3.81 (3 H, OCH_3) and 3.73 (3 H, OCH_3) as well as complex absorption in the region δ 1.1–3.2 (16 H, aliphatic CH).

Anal. Calcd for $C_{15}H_{22}O_5$: C, 63.81; H, 7.85. Found: C, 63.66; H, 7.86.

The crude monoalkylated product **17a** from the above chromatography was saponified by stirring a 1.76-g (8.4 mmoles) sample of the keto ester with a solution of 0.60 g (9 mmoles) of potassium hydroxide in 15 ml of methanol for 32 hr. After separation of a neutral fraction, the crude acid was isolated in the usual way as 1.40 g (85%) of a light brown oil which solidified on standing. This material was chromatographed on silicic acid and the major fraction (1.19 g or 72.5%) eluted with a benzene–ether mixture was recrystallized from a benzene–petroleum ether mixture to separate the pure keto acid **17b** as white prisms, mp 100.5–102.5°. The product has infrared absorption[16] at 1740 (C=O of a cyclopentanone derivative) and 1710 cm^{-1} (carboxyl C=O) with an ultraviolet maximum[15] at 282 mμ (ϵ 39). The nmr spectrum[18] has peaks at δ 11.30 (1 H, COOH) and 2.75 (2 H singlet, CH_2CO) as well as complex absorption in the region δ 1.0–2.8 (13 H, aliphatic CH).

Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.43; H, 8.30.

A 973-mg sample of the keto acid **17b** was esterified with excess ethereal diazomethane. The crude product (1.06 g of colorless oil) solidified on standing and was recrystallized from petroleum ether at Dry Ice temperatures. The pure keto ester **17a** separated as fine white crystals, mp 39–40.5°. The keto ester **17a** has infrared absorption[16] at 1740 (C=O of an ester and cyclopentanone derivative) with nmr absorption[18] at δ 3.52 (3 H singlet, OCH_3) and 2.48 (2 H singlet CH_2CO) as well as complex absorption in the region δ 1.0–2.5 (aliphatic CH).

Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.63; mol wt, 210. Found: C, 68.32; H, 8.67; mol wt, 210 (mass spectrum).

To a cold (0°) solution of 2.24 mmoles of lithium *t*-butoxide (from *t*-butyl alcohol and methyllithium) in 12 ml of 1,2-dimethoxyethane was added a solution of 389 mg (1.85 mmoles) of the keto ester **17a** and 365 mg (2.38 mmoles) of methyl bromoacetate in 3 ml of 1,2-dimethoxyethane. The resulting solution was stirred for 1 min and then quenched by the addition of 25 ml of aqueous 1 *M* hydrochloric acid. The ether extract of the resulting mixture was washed successively with aqueous sodium bicarbonate and aqueous sodium chloride and then dried and concentrated. The residual oil (614 mg) which contained[21] *ca.* 65% of the starting keto ester **17a** and *ca.* 35% of the keto diester **18** was chromatographed on Florisil. The latter fractions eluted with benzene–ether mixtures afforded 134 mg (25%) of the crude crystalline keto diester **18**. Recrystallization of this sample from methanol separated the keto diester **18** as white prisms (mp 95.5–99.5°) which were identified with the previously described sample by comparison of infrared spectra.

A solution of 450 mg (2.14 mmoles) of the keto ester **17a** in 210 ml of hexane was placed in an irradiation vessel, purged with nitrogen, and then irradiated with the light from a 450-w high-pressure mercury lamp. Aliquots of the solution were removed and analyzed periodially.[19] A new component of slightly shorter retention time than the *cis* ester **17a** was produced, the transformation being essentially complete after 60 min. At no point during the irradiation was there evidence for the presence of the *trans* ester **19** which has a longer retention time than the starting *cis* isomer **17a**. The remaining irradiation mixture was concentrated and the residual yellow liquid (368 mg) was distilled in a short-path still to separate 183 mg (41%) of colorless liquid which contained[19] primarily a single component believed to be the aldehyde **26**. Collected[19] samples of this material had infrared absorption[16] at 2725 (aldehyde CH), 1740 (br, C=O of an aldehyde and an ester), and 1660 cm^{-1} (weak, C=C) with nmr peaks[16] at δ 9.62 (1 H multiplet, aldehyde C—H), 3.59 (3 H singlet, OCH_3), and 2.95 (2 H singlet, $C{=}CCH_2CO$) as well as complex absorption in the region δ 1.2–2.6 (12 H, aliphatic CH). The mass spectrum lacks a molecular ion peak, the highest mass peak being formed at *m/e* 194 ($M^+ - 18$). The spectrum has abundant fragment peaks at *m/e* 107, 93, 91, 79, 74, 44 (base peak) 41, and 39.

Reduction of the Keto Ester 17a.—A solution of 859 mg (4.1 mmoles) of the keto ester **17a** and 1.5 ml of 1,2-ethanethiol in 3.0 ml of ether containing 1.0 ml of boron trifluoride etherate was stirred at room temperature for 30 min. The resulting mixture was partitioned between water and methylene chloride and the organic layer was washed successively with aqueous 10% sodium hydroxide and aqueous sodium chloride. After the organic solution had been dried and concentrated, the residual crude solid (1.02 g) was chromatographed on 50 g of Florisil. The fractions (550 mg or 48%) eluted with benzene contained[25] the pure ketal **20** and further quantities were obtained by fractional crystallization of earlier chromatographic fractions. Recrystallization from cyclohexane and from cyclohexane–petroleum ether mixtures afforded the pure dithio ketal **20** as white needles, mp 73.5–74.5°. The product has infrared absorption[16] at 1735 cm^{-1} (ester C=O) with nmr peaks[16] at δ 3.53 (3 H singlet, OCH_3), 3.20 (4 H multiplet, CH_2S), and 2.53 (2 H singlet, CH_2CO), as well as a complex multiplet in the region δ 1.1–2.7 (13 H, aliphatic CH).

Anal. Calcd for $C_{14}H_{22}O_2S_2$: C, 58.73; H, 7.75; S, 22.35. Found: C, 58.62; H, 7.77; S, 22.31.

A mixture of 260 mg (0.90 mmole) of the dithio ketal **20**, 5.7 g of commercial Raney nickel catalyst, and 30 ml of methanol was refluxed with stirring for 4 hr and then cooled and filtered. The filtrate was concentrated, taken up in ether, dried, and concentrated to leave 165 mg (90%) of pale yellow liquid which contained[21] low-boiling components and the *cis* ester **21**. A collected[21] sample was identified with a previously described[6] authentic sample of the *cis* ester **21** by comparison of gas chromatographic retention times, infrared spectra, mass spectra, and nmr spectra.

Alkylation of the Thiobutylmethylene Ketone 6.—To a solution of potassium *t*-butoxide, prepared from 1.27 g (32.6 mg-atoms) of potassium and 50 ml of *t*-butyl alcohol, was added 2.49 g (10.6 mmoles) of the ketone **6**. After this solution had been stirred for 5 min under a nitrogen atmosphere, 6.45 g (42.2 mmoles) of methyl bromoacetate was added and the resulting mixture was stirred at room temperature for 1 hr and then concentrated under reduced pressure. The residue was partitioned between water and ether and the organic layer was washed successively with aqueous sodium bicarbonate and aqueous sodium chloride and then dried and concentrated. Distillation of the residue in a short-path still (215° bath temperature and 0.25 mm) afforded 2.57 g of yellow liquid which was mixed with a solution of 5.0 g of sodium hydroxide in 50 ml of aqueous ethanol (1:9, v/v). The resulting solution was refluxed under a nitrogen atmosphere for 37 hr[26] and then cooled and partitioned between water and ether. The aqueous phase was acidified, extracted with ether, and this ethereal extract was washed with aqueous sodium bicarbonate. After the aqueous bicarbonate solutions had been acidified and extracted with ether, this ethereal solution was washed with aqueous sodium chloride, dried, and concentrated to leave 1.75 g of crude acid as a yellow liquid. Esterification with excess ethereal diazomethane afforded 1.62 g of crude methyl ester which contained[21] (in order of increasing retention time) the thiobutyl ether **28a** (*ca.* 33%), the *cis*-keto ester **14a**

$$n\text{-}C_4H_9SCH_2CO_2R$$

28a, R = CH_3
b, R = H

(*ca.* 64%), and the *trans*-keto ester **15** (*ca.* 3%). A subsequent run utilized the same reaction procedure except that the final crude ester was mixed with a weighed amount of acenaphthene for gas chromatographic analysis.[19] The calculated yields of alkylated products were 45% **14a** and 3.5% **15**. The average composition of the monoalkylated product was 94% of the *cis* isomer **14a** and 6% of the *trans* isomer **15**.

The crude product from a preparative alkylation was chromatographed on Florisil to separate 0.40 g of the thiobutyl ether **28a** eluted in the early benzene–ether fractions and 0.62 g

(25) A thin layer chromatographic plate coated with silicic acid and eluted with benzene–ether mixtures was employed for this analysis.

(26) We found this procedure to be superior to the use of either a solution of potassium hydroxide in refluxing aqueous diethylene glycol or a solution of hydrochloric acid in refluxing methanol for the cleavage of the thiobutylmethylene blocking group. Compare ref 2b, and Z. Valenta, K. Wiesner, and C. M. Wong, *Tetrahedron Letters*, No. 36, 2437 (1964).

(28%) of the monoalkylated products **14a** (*ca.* 88%) and **15** (*ca.* 12%) eluted in the later benzene–ether fractions. Fractional distillation of the crude product from a comparable preparative run separated a fraction [bp 36° (0.13 mm), $n^{24.3}$D 1.4651; lit.[27] bp 85° (10 mm), n^{25}D 1.4590] which contained[10] primarily the thiobutyl ether **28a**. The fractions [bp 83–100° (0.1 mm), $n^{24.3}$D 1.4899–1.4927] from this distillation contained[10] 80–90% of the monoalkylated products **14a** and **15** accompanied by minor quantities of several lower boiling components. A collected[10] sample of the thiobutyl ether **28a** has infrared absorption[16] at 1740 cm^{-1} (ester C=O) with nmr peaks[16] at δ 3.71 (3 H, OCH_3) and 3.10 (2 H, SCH_2CO) with multiplets in the regions δ 2.4–2.8 (2 H, CH_2S) and 0.8–1.8 (7 H, aliphatic CH). The mass spectrum has a molecular ion peak at *m/e* 162 with abundant fragment peaks at *m/e* 89 (n-$C_4H_9S^+$), 74 $[CH_2{=}C(OH)OCH_3]^+$, 61, 55, 47, 45, and 41. This thiobutyl ether **28a** is apparently found during alkaline cleavage of the blocking group by reaction of the liberated butyl mercaptide anion with the excess methyl bromoacetate present. A collected[19] sample of the *cis*-keto ester **14a** was identified with the previously described sample by comparison of infrared and mass spectra. The small amount of *trans* isomer present was identified only by its gas chromatographic retention time.[19]

In subsequent experiments, the same alkylation procedure was followed but the crude product was investigated prior to cleavage of the blocking group. From reaction of a solution of 2.02 g (8.6 mmoles) of the ketone **6** in 50 ml of *t*-butyl alcohol with 34.5 mmoles of potassium *t*-butoxide followed by 5.54 g (36.2 mmoles) of methyl bromoacetate the crude neutral alkylated product consisted of 4.91 g of an orange oil. Successive chromatography on Florisil and on neutral alumina (activity grade III) separated a number of low boiling fractions from 1.55 g of liquid fractions which contained[28] mixtures of the methyl and *t*-butyl esters **13a** and **b**. Additional chromatography on neutral alumina (activity grade III) separated 241 mg of an early fraction, eluted with benzene–hexane mixtures, which contained[28] primarily the crude *t*-butyl ester **13b**. This sample has infrared absorption[16] at 1720 (br, ester and ketone C=O) and 1595 cm^{-1} (conjugated C=C) with an ultraviolet maximum[15] at 310 mμ (ϵ 16,500). The material has nmr absorption[16] at δ 7.26 (1 H multiplet, C=CHS), 5.60 (2 H multiplet, vinyl CH), and 1.38 [singlet, $(CH_3)_3CO$], as well as complex absorption in the region δ 0.8–3.1 (aliphatic CH). A later fraction (449 mg) from the chromatography, also eluted with benzene–hexane mixtures, contained mainly the methyl ester **13a**. Short-path distillation of this fraction afforded the methyl ester **13a** as a pale yellow liquid with infrared absorption[16] at 1740 (ester C=O), 1710 (C=O of a conjugated cyclopentanone derivative) and 1590 cm^{-1} (conjugated C=C) and an ultraviolet maximum[15] at 309.5 mμ (ϵ 20,600). The sample has nmr peaks[16] at δ 7.31 (1 H multiplet, C=CHS), 5.66 (2 H multiplet, vinyl CH), 3.58 (3 H singlet, OCH_3), and 2.87 (2 H triplet with J = 7 cps, CH_2S), as well as complex absorption in the region δ 0.8–2.6 (16 H, aliphatic CH). Although the general appearance of the nmr spectrum of this sample would suggest that it contains only the *cis* fused tetrahydroindan stereoisomer, we have no way to exclude the possibility that the *trans* fused stereoisomer is also present.

Anal. Calcd for $C_{17}H_{24}O_3S$: C, 66.21; H, 7.85; S, 10.26. Found: C, 66.40; H, 7.94; S, 10.45.

In an additional alkylation experiment, an aliquot of the crude alkylation product was mixed with a weighed amount of triphenylmethane as an internal standard and analyzed by gas chromatography.[11] The calculated yields of products were 1% starting ketone **6** and 31% methyl ester **13a**.[29] The remainder of the crude alkylated product was treated with potassium hydroxide in aqueous ethanol to remove the blocking group. An aliquot of this final product (after reesterification with diazomethane) was mixed with a weighed amount of acenaphthene and analyzed by gas chromatography.[19] The calculated yields were 35% *cis* isomer **14a** and 2% *trans* isomer **15**.

Registry No.—**6**, 10308-96-0; **10**, 10308-97-1; **11**, 10308-98-2; **12a**, 10308-99-3; **12b**, 10309-00-9; **13a**, 10309-01-0; **13b**, 10309-02-1; **14a**, 10309-03-2; **14b**, 10309-04-3; **15**, 10309-05-4; **16**, 10309-06-5; **17a**, 10309-07-6; **17b**, 10309-08-7; **18**, 10315-72-7; **19**, 10309-09-8; **20**, 10309-10-1; **23**, 10309-11-2; **24**, 10309-12-3; **25**, 10309-13-4; **28a**, 10309-14-5.

(27) Y. Uyeda and E. E. Reid, *J. Am. Chem. Soc.*, **42**, 2385 (1920).

(28) Thin layer chromatography plates coated with alumina and eluted with benzene–ether mixtures were employed for this analysis.

(29) The *t*-butyl ester **13b** could not be successfully eluted from our gas chromatography equipment apparently because of decomposition in the inlet system or on the column. The reason for the apparent low yield of alkylated products arises from the fact that the crude alkylated product contains both the methyl and *t*-butyl esters **13** but only the methyl ester fraction is being measured in this analysis.

Alane Reductions of 1-Phenylcyclopentene Oxide

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The title compound has been reduced by alane prepared from lithium aluminum hydride ($LiAlH_4$) and aluminum chloride in ether, according to Eliel and Ashby, or from $LiAlH_4$ and sulfuric acid in tetrahydrofuran, as described by Brown, with similar results. Three types of reaction occur, depending on ratios of reactants and order of addition, when alane-d_3 is used: excess alane gives *cis*-2-phenylcyclopentanol-2-*d* mainly; when alane-d_3 is added in great deficiency, *cis*- and *trans*-2-phenylcyclopentanol-1-*d* are the main products. A mechanistic rationale for these reactions is presented.

Several groups of investigators, notably Nystrom, *et al.*,[2] and Eliel and co-workers[3] have investigated the reducing properties of "mixed hydride" reagents, prepared from various ratios of lithium aluminum hydride ($LiAlH_4$) and aluminum chloride. These reagents can reduce aryl carbonyl groups to methylene groups[2] and react with unsymmetrical epoxides in several ways,[3] depending on which ratios of the two reagents are used, as illustrated in Scheme I.[3] The structures and position of deuterium in the products indicate whether rearrangement occurs during reduction but the stereochemical aspects of the epoxide ring opening cannot be determined from the acyclic products obtained. Recently, Ashby[4] has shown that the actual reducing agent obtained from $LiAlH_4$–$^1/_3AlCl_3$ is alane, whereas $LiAlH_4$–$3AlCl_3$ produces dichloroalane, $AlHCl_2$. Realizing that the latter reagent is a stronger Lewis acid and weaker hydride donor than AlH_3, Ashby rationalized[4] earlier results of Eliel[3] in terms of initially formed epoxide–alane complexes that col-

(1) Alfred P. Sloan Foundation Fellow, 1963–1967.

(2) R. F. Nystrom and C. R. A. Berger, *J. Am. Chem. Soc.*, **80**, 2896 (1958).

(3) E. L. Eliel, *Rec. Chem. Progr.*, **22**, 129 (1961); M. Rerick and E. L. Eliel, *J. Am. Chem. Soc.*, **84**, 2356 (1962).

(4) E. C. Ashby and J. Prather, *ibid.*, **88**, 729 (1966).