g. of Florisil. Elution with 100 ml. of 20% and 30 ml. of 50% ethyl acetate–benzene gave 49 mg. (74%) of II which, after one crystallization from methylene chloride–petroleum ether, gave 39 mg., m.p. 168.5–170°, identical by infrared spectrum and mixture melting point with II obtained by photoirradiation of IA.

Heating 13 mg. of XV in a sealed, evacuated capillary for 15 min. at 215° gave material exhibiting infrared and ultraviolet spectra identical with those of IC.

Photoirradiation of $\Delta^{4,6}$-Cholestadien-3-one (ID). Photodimer XVI. A. In Petroleum Ether.—A solution of 518 mg. of $\Delta^{4,6}$-cholestadien-3-one[30] (ID) in 15 ml. of petroleum ether was irradiated for 1.75 hr. at 3–4°. The solid which precipitated was filtered to give 247 mg. (48%) of dimer XVI, m.p. 175–177°. The yield could be raised to 79% by successive crop taking and reirradiation. The analytical sample was obtained by crystallization from ethyl acetate, m.p. 174.5–175°; $\lambda_{max}^{cyclohexane}$ 243 $m\mu$ (ϵ 10,600); λ_{max}^{KBr} 5.93, 5.98, 6.25 μ; $[\alpha]^{26}D$ +37°; lit.[3] λ_{max}^{alc} 258 $m\mu$ (ϵ 9100); $\lambda_{max}^{CHCl_3}$ 5.91, 6.02, 6.21 μ; $\lambda_{max}^{CCl_4}$ 5.89, 5.97, 6.23 μ; lit.[17] m.p. 173–174°, 179–180°; $[\alpha]D$ +37°.

Anal. Calcd. for $C_{54}H_{84}O_2$: C, 84.75; H, 11.07; mol. wt., 765. Found: C, 84.55; H, 10.93; mol. wt., 730.

Heating 16 mg. of XVI in a sealed capillary at 215° for 15 min. gave an oil, λ_{max} 284 $m\mu$ (ϵ 25,200), identical with ID by comparison of infrared spectra.

B. In Benzene–Dioxane Solution.—A solution of 206 mg. of ID in 5.4 ml. of 1:1 benzene–dioxane was irradiated for 5.5 hr. The solution remained clear. After removal of solvent under reduced pressure, the residue was chromatographed on 10 g. of Florisil. Elution with 800 ml. of 1% ethyl acetate–benzene yielded 87 mg. of starting material. Elution with 600 ml. of 3% ethyl acetate–benzene afforded 36 mg. (18%) of XVI. One crystallization from methylene chloride–ethyl acetate gave 18 mg., m.p. 172.5–173°; mixture melting point with product from the petroleum ether reaction, 172.5–173°. Infrared spectra were identical.

Reversibility of Photodimerization of IA.—A solution of 480 mg. of dimer II in 14 ml. of 1:1 benzene–dioxane was irradiated for 12.5 hr. The clear solution was concentrated under reduced pressure and the residue, λ_{max} 284 $m\mu$ (ϵ 11,800), chromatographed on 21 g. of Florisil as described for the photoirradiation of IA to give 46% of IA, m.p. 135–136°, and 38% of II, m.p. 167–169°. Identity was further established by comparisons of infrared spectra.

Photostationary States.—Solutions of IA (0.1 *M*) or II (0.05 *M*) in 1:1 benzene–dioxane were immersed in a water bath having a Pyrex window and irradiated until ultraviolet spectra of samples from each solution were identical. Compositions were calculated from the extinction coefficients of the monomer at 280 $m\mu$ (ϵ 26,900) correcting for the relatively weak absorption (ϵ 5200) of dimer at this wave length. At 3–4°, 15 hr. were required to attain equilibrium; the product of irradiation of IA contained 29% IA and 71% II, the product from II contained 28% IA and 72% II. At 27–28° equilibrium was attained in 3 hr.,[31] the compositions were 31% IA and 69% II in both cases.

Acknowledgment.—Financial support from the Squibb Institute for Medical Research is gratefully acknowledged. N.m.r. spectra were determined by Miss P. Zwitkowitz.

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[30] A. L. Wilds and C. Djerassi, *J. Am. Chem. Soc.*, **68**, 1712 (1946). Use of the chloranil oxidation procedure as described for IB afforded ID in 65% yield.

[31] The considerable differences in duration of reaction may have been due to relative age of the lamp in the two sets of experiments.

Perhydroindanone Derivatives. IV. The 1,1a,4,4a-Tetrahydrofluoren-9-one System[1a]

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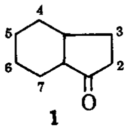
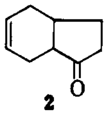
The *cis*-fused isomer (the more stable) of 8-methyl-1,1a,4,4a-tetrahydrofluoren-9-one (**3**) has been synthesized and found to give primarily the *cis*-fused product **4** on alkylation. Several possible routes to the 2-keto hexahydrofluorenone system **20** have been explored and a satisfactory preparative route is described.

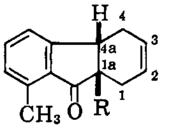
Upon finding[2] that the relative stability of the *cis* isomer of perhydroindan-1-one (**1**, 75% *cis* at equilibrium) could be diminished by the introduction of a double bond at the 5–6-position (as in **2**, 53% *cis* at equilibrium), it became of interest to learn whether the alkylation of the tetrahydrofluorenone system **3** would lead to a mixture of the *cis* and *trans* ring-fused products **4** and **5** rather than only (or at least very largely) a *cis*-fused product such as **6** obtained from alkylation of the hexahydrofluorenone **7**.[3] The realization of such a nonstereoselective alkylation appeared to offer a possible route to intermediates useful for the synthesis of both allogibberic acid (*trans* B–C ring fusion) and epiallogibberic acid (*cis* B–C ring fusion) without requiring inversion of a center at some later stage.[4]



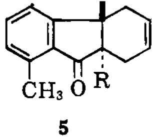
1



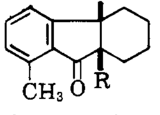
2



3, R = H
4, R = CH_2CO_2Me



5



6, R = CH_2CO_2Me
7, R = H

To examine this question the tetrahydrofluorenone **3** was prepared as indicated in Chart I following a sequence previously applied to 1-indanone.[5] Since a preliminary attempt to prepare the Diels–Alder adduct **10** led to a complex mixture (*cf.* ref. 5), we modified the procedure to generate the very reactive indenone **11** in the presence of excess butadiene. A single crystalline adduct **3** was isolated from this Diels–Alder reaction. This material was stable to refluxing methanolic sodium methoxide although these

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[1] (a) Supported in part by Grant No. G-25214 from the National Science Foundation; (b) National Institutes of Health Predoctoral Fellow, 1960–1963.

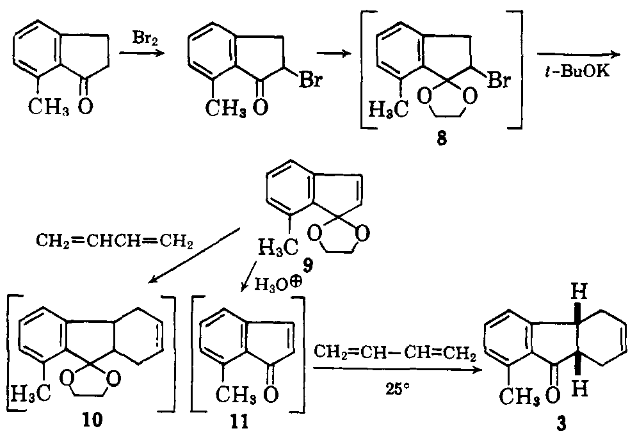
[2] H. O. House and G. Rasmusson, *J. Org. Chem.*, **28**, 31 (1963).

[3] H. O. House, V. Paragamian, and D. J. Wluka, *J. Am. Chem. Soc.*, **82**, 2561 (1960); **83**, 2714 (1961).

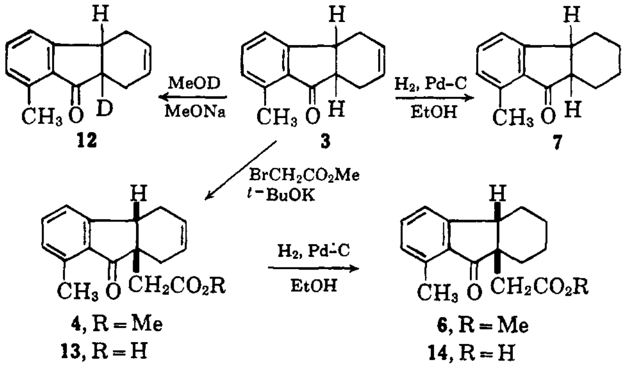
[4] For one method, albeit a circuitous one, of effecting this inversion in the system **4**, see H. O. House, R. G. Carlson, H. Müller, A. W. Noltes, and C. D. Slater, *ibid.*, **84**, 2614 (1962).

[5] H. O. House, V. Paragamian, R. S. Ro, and D. J. Wluka, *ibid.*, **82**, 1452, 1457 (1960).

CHART I



conditions were sufficiently vigorous to remove the proton α to the carbonyl function as demonstrated by conversion to the monodeuterated derivative **12**. Consequently, the product **3** is the more stable epimer in this series. The conclusion that the product **3** should possess the indicated *cis* stereochemistry by virtue of having been produced by a Diels–Alder reaction[6] is rendered equivocal because of the formation of the product in the presence of very dilute aqueous acid which could have epimerized an initially formed product. Several attempts to isolate the pure indenone **11** in order to remove this ambiguity led only to polymeric material. However, several additional facts indicate strongly that the *cis* stereochemical assignment is correct. Catalytic hydrogenation of **3** under conditions which permitted the reduction[2] of the tetrahydroindanone **2** to **1** without significant epimerization produced the hexahydrofluorenone **7** previously assigned[3] the indicated *cis* configuration. Furthermore, examination of the n.m.r. spectra of **3** and **12** indicates that coupling between the proton at C-4a and each of the protons at C-4 as well as the proton at C-1a is 6–7 c.p.s. in each case. This observation suggests either that each of the three dihedral angles H–C$_{(4a)}$–C$_{(1a)}$–H and H–C$_{(4a)}$–C$_{(4)}$–H (for each C-4 proton) is approximately 30° or that one of the dihedral angles is approximately 30°, one is approximately 150°, and the third dihedral angle is either 30° or 150°.[7]



Examination of molecular models indicates that at least two conformations (a twisted boat or a chair cyclohexene ring) of the *cis*-tetrahydrofluorenone **3** are possible which would be consistent with such a combination of dihedral angles. However, it appears very difficult to reconcile the observed coupling constants with the dihedral angles (about 60°, 150°, and 180° as estimated from Dreiding models) present in the conformationally rigid 8-methyl-*trans*-1,1a,4,4a-tetrahydrofluoren-9-one. Our data are, therefore, in best agreement with the interpretation that the *cis* ring fusion in the tetrahydrofluorenone system **3** is more stable than the *trans* ring fusion as was previously found for the 1,1a,2,3,4,4a-hexahydrofluoren-9-one system.[5,8]

The alkylation of the tetrahydrofluorenone (**3**) produced primarily the ester **4** with a *cis* ring fusion as demonstrated by hydrogenation and subsequent hydrolysis to the previously known[3] *cis* acid **14**. In addition to the major alkylation product, the *cis* keto ester **4**, a minor product was formed in this reaction which had spectral properties similar to the *cis* ester **4** suggesting that it may be the corresponding keto ester having a *trans* ring fusion. However, we were unable to isolate a pure sample of this minor product to permit complete characterization. In any case, alkylation of the tetrahydrofluorenone system **3** does not offer a useful route to a *trans*-fused hexahydrofluorenone.

Several additional routes to a hexahydrofluorenone **6** having an oxygen substituent at C-2 (*cf.* ref. 4) have been examined. The results of these studies are summarized in Chart II. Of importance to our further synthetic work was the fact that, although cleavage of the diketone lactone **19** with zinc and acetic acid or calcium and liquid ammonia occurred very slowly, presumably because the acyloxy function occupied an equatorial position,[4,9] the reduction to form **20** was readily achieved with chromous chloride.[10]

With the *cis* keto ester **20** in hand, it was of interest to explore the possibility[11] that partial conversion of the *cis*-fused ester **20** to the *trans*-fused isomer **23** might be achieved by reaction of **20** with refluxing methanolic sodium methoxide to form the intermediate triketone

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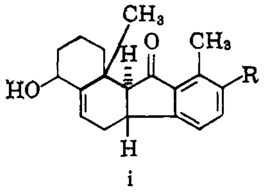
[6] J. G. Martin and R. K. Hill, *Chem. Rev.*, **61**, 537 (1961).

[7] L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p. 87.

[8] D. M. Bailey, D. P. G. Hamon, and, W. S. Johnson [*Tetrahedron Letters*, **No. 9**, 555 (1963)] have found the tetrahydrofluorenone system present in 11-ketoveratramine (i) to be more stable in the configuration having a *trans* fusion of the 5- and 6-membered rings. Since this system is analogous to the tetrahydrofluorenone (**3**) except for the presence of substituents at positions corresponding to C-1 and C-2 in **3**, we believe that the predominant factor stabilizing the *trans* isomer of 11-ketoveratramine is these substituents. The importance of a substituent in determining the position of the *cis–trans* equilibrium in a perhydroindanone system **1** is pointed up clearly in the effect of a 7-methyl substituent (ref. 2).



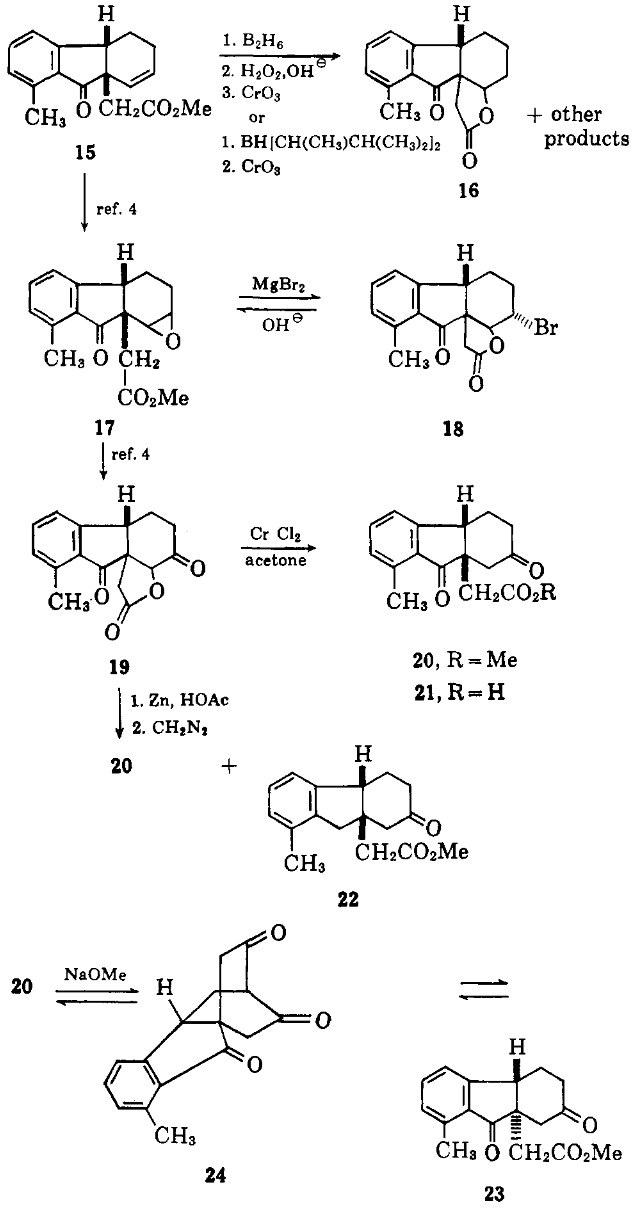
i

[9] The cleavage of an acyloxy group or a halogen atom α to a carbonyl function by a dissolving metal reduction has generally been found to occur more rapidly if the substituent being cleaved occupies (or can occupy) an axial position. For examples and discussion, see (a) F. Sondheimer, S. Kaufmann, J. Romo, H. Martinez, and G. Rosenkrantz, *J. Am. Chem. Soc.*, **75**, 4712 (1953); (b) R. S. Rosenfeld and T. F. Gallagher, *ibid.*, **77**, 4367 (1955); (c) J. H. Chapman, J. Elks, G. H. Phillipps, and L. J. Wyman, *J. Chem. Soc.*, 4344 (1956).

[10] (a) G. Rosenkranz, O. Mancera, J. Gatica, and C. Djerassi, *J. Am. Chem. Soc.*, **72**, 4077 (1950); (b) W. Cole and P. L. Julian, *J. Org. Chem.*, **19**, 131 (1954); (c) D. H. R. Barton and J. T. Pinhey, *Proc. Chem. Soc.*, 279 (1960); (d) D. H. R. Barton, T. Miki, and J. T. Pinhey, *ibid.*, 112 (1962); (e) G. Büchi and J. H. E. Loewenthal, *ibid.*, 280 (1962).

[11] (a) J. F. Grove and T. P. C. Mulholland, *J. Chem. Soc.*, 3007 (1960); (b) B. E. Cross, J. R. Hanson, L. H. Briggs, R. C. Cambie, and P. S. Rutledge, *Proc. Chem. Soc.*, 17 (1963).

CHART II



24 followed by conversion to either 20 or 23. However, this procedure led only to recovery of the ester 20 and the corresponding acid 21 with no second component being isolated even after a 48-hr. reaction period. Therefore, it seems probable that the equilibrium position between the *cis* and *trans* keto esters (*i.e.*, 20 and 23) favors the *cis*-fused product 20 as was noted previously[11a] with similarly constituted degradation products of allogibberic acid and epiallogibberic acid.

Experimental[12]

2-Bromo-7-methylindanone.—To a cold (0°) solution of 14.36 g. (0.0982 mole) of 7-methylindanone[2] in 1.1 l. of ether was added, dropwise and with stirring over a 45-min. period, 15.70 g. (0.0983 mole) of bromine. The resulting solution was allowed to warm to room temperature and then washed with aqueous sodium bicarbonate, dried, and concentrated. Crystallization of the semisolid residue from an ether-petroleum ether (b.p. 30–60°) mixture afforded 15.14 g. (68.5%) of the bromo ketone as pale yellow needles, m.p. 45–48°. Recrystallization afforded the pure bromo ketone, m.p. 47.5–49°; with infrared absorption[13] at 1722 cm.$^{-1}$ (C=O); ultraviolet maxima[14] at 258 mμ (ϵ 13,400) and 303 (2320); and n.m.r. peaks[13] at 7.42 τ (3H singlet, Ar-CH_3), a multiplet in the region 6.0–7.0 (2H, >CH_2), a series of four peaks centered at 5.52 (1H, >CH–Br), and a complex multiplet in the region 2.4–3.1 (3H, aryl C–H).

Anal. Calcd. for $C_{10}H_9BrO$: C, 53.36; H, 4.03; Br, 35.51. Found: C, 53.13; H, 4.05; Br, 35.57.

The Ethylene Ketal (9) of 7-Methylindenone.—A solution of 12.00 g. (0.0534 mole) of the bromo ketone, 100 mg. of *p*-toluenesulfonic acid, and 5.00 g. (0.0798 mole) of ethylene glycol in 150 ml. of benzene was refluxed with continuous separation of water for 1 week, additional 5.00-g. portions of ethylene glycol being added after 42 and 114 hr. At this time the infrared spectrum of the reaction mixture exhibited only weak carbonyl absorption. The mixture was washed with aqueous sodium bicarbonate, dried, and concentrated to leave the crude bromo ketal 8 as a brown liquid. A solution of this crude ketal in 25 ml. of *t*-butyl alcohol was added, dropwise and with stirring over a 10-min. period, to a solution of potassium *t*-butoxide prepared from 3.12 g. (0.08 g.-atom) of potassium and 50 ml. of *t*-butyl alcohol. The resulting mixture was stirred at room temperature under a nitrogen atmosphere for 5 hr. and then poured into ice–water and extracted with ether. After the ethereal extract had been washed with water, dried, and concentrated, distillation of the residue, first through a shortpath still (5.636 g., b.p. 97–105° at 0.1 mm.) and then through a Holtzmann column, separated 4.368 g. (43.4%) of the ketal, b.p. 86–88° (0.24 mm.). Upon redistillation of a portion of this material, the distillate crystallized as white prisms, m.p. 68–69°, which could be recrystallized from hexane. In a subsequent preparation from 20.0 g. (0.137 mole) of the indanone where the crude bromo ketone was used without purification, the yield of the indenone ketal 9, m.p. 67–68.5°, was 14.62 g. (55% based on the indanone). The product, which has no infrared absorption[13] in the 3- or 6-μ region attributable to hydroxyl or carbonyl functions, exhibits ultraviolet maxima[14] at 219 mμ (ϵ 29,000), 226 (25,000), 278 (2640), 287 (shoulder 2330), 300 (1840), and 311 (shoulder 1390); with n.m.r. peaks[13] at 7.68 τ (3H singlet, Ar-CH_3), a multiplet centered at 5.88 (4H, -OCH_2-CH_2O-), a pair of doublets (J = 5.5 c.p.s.) centered at 3.91 and 3.49 (2H, vinyl C–H), and a multiplet in the region 2.7–3.3 (3H, aryl C–H).

Anal. Calcd. for $C_{12}H_{12}O_2$: C, 76.57; H, 6.43; mol. wt., 188. Found: C, 76.50; H, 6.55; mol. wt., 188 (mass spectrum).

8-Methyl-1,1a,4,4a-tetrahydrofluoren-9-one (3).—Into a cold (−5 to 0°) solution of 5.00 g. (0.0266 mole) of ketal 9 and 5 ml. of water in 25 ml. of tetrahydrofuran was distilled, through a tube containing molecular sieves, 14 g. (0.27 mole) of 1,3-butadiene. The resulting solution was cooled in a Dry Ice–acetone bath, 3 drops of concentrated hydrochloric acid was added, and then the flask was stoppered and stirred at room temperature for 8 days. The excess butadiene was allowed to evaporate from the resulting mixture, 50 ml. of saturated, aqueous sodium chloride solution was added, and the mixture was extracted with ether. The ethereal extract was washed with aqueous sodium bicarbonate, dried, and concentrated to leave 5.05 g. of yellow oil which solidified on standing. Distillation through a shortpath still separated 3.80 g. of the tetrahydrofluorenone 3, b.p. 118–128° (0.1 mm.), which was recrystallized from pentane to give 3.27 g. (62.5%) of the ketone as white prisms, m.p. 48.5–50.5°. An additional crystallization raised the melting point to 50–51°. The product has infrared absorption[13] at 1705 cm.$^{-1}$ (C=O); ultraviolet maxima[14] at 250 mμ (ϵ 12,050) and 298 (2510); and a series of n.m.r. peaks[15] in the region 2.4–3.0 τ (3H, aryl C–H), as well as a multiplet centered at 4.17 (2H, vinyl C–H), a singlet at 7.37 (3H, aryl CH_3), a complex series of peaks in the region 7.0–8.0 (5H), and a quadruplet of broad peaks (half-band widths 3–5 c.p.s., peak positions 204, 212, 218 and 225 c.p.s. from tetramethylsilane) centered at 6.42 (1H, benzylic C–H).

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(12) All melting points are corrected and all boiling points are uncorrected. Unless otherwise stated magnesium sulfate was employed as a drying agent. The infrared spectra were determined with either a Baird, Model B, or a Perkin-Elmer, Model 21, infrared recording spectrophotometer fitted with a sodium chloride prism. The ultraviolet spectra were determined with a Cary recording spectrophotometer, Model 14. The n.m.r. spectra were determined at 60 Mc. with a Varian, Model A-60, n.m.r. spectrometer. The mass spectra were obtained with a CEC, Model 21-130, mass spectrometer. The microanalyses were performed by Dr. S. M. Nagy and his associates and by the Scandinavian Microanalytical Laboratory.

(13) Determined in carbon tetrachloride solution.

(14) Determined in 95% ethanol solution.

(15) Determined as a solution in deuteriochloroform.

Anal. Calcd. for $C_{14}H_{14}O$: C, 84.81; H, 7.12; mol. wt., 198. Found: C, 84.73; H, 7.17; mol. wt., 198 (mass spectrum).

A solution of 196 mg. (0.99 mmole) of the tetrahydrofluorenone **3** in the methanolic sodium methoxide prepared from 60 mg. (2.61 mg.-atoms) of sodium and 5 ml. of deuteriomethanol was refluxed for 3.5 hr. and then concentrated under reduced pressure. An additional 5-ml. portion of deuteriomethanol was added and the resulting solution was refluxed for 7.5 hr. and then poured into a mixture of pentane and deuterium oxide. After the pentane extract had been dried and concentrated, the residual oil (198 mg.) was crystallized from pentane to separate 116 mg. (59%) of the deuterated tetrahydrofluorenone **12** as pale yellow prisms, m.p. 49–51°. The material which did not depress the melting point of the starting ketone **3** and had the same R_f value on thin layer chromatography,[16] contained 17% d_0, 75% d_1, and 8% d_2 species. The deuterated ketone **12** has an n.m.r. spectrum[16] which differs from the spectrum of the undeuterated ketone **3** in lacking a complex multiplet attributable to one proton in the region 7.0–7.3 τ (C–H α to carbonyl) and in having a triplet (rather than a quartet) of broad peaks (half-band widths 3–4 c.p.s., peak positions 207, 213 and 219 c.p.s. from tetramethylsilane) centered at 6.43 (1H, benzylic C–H).

Hydrogenation of the Tetrahydrofluorenone 3.—A solution of 167 mg. (0.844 mmole) of the unsaturated ketone **3** in 8 ml. of ethanol was hydrogenated over 25 mg. of a 5% palladium-on-carbon catalyst at 27° and atmospheric pressure. After the hydrogen uptake (21.1 ml. or 1.01 equiv.) ceased (1 hr.), the mixture was filtered, and concentrated to leave 157 mg. (93%) of the hexahydrofluorenone **7** as a colorless oil which crystallized when cooled. Recrystallization from pentane separated 88 mg. (53%) of the pure ketone **7** as white prisms, m.p. 34–35°. The infrared spectra[13] of both the crude and recrystallized products are identical with the spectrum of a previously described[3] sample of *cis*-ketone **7**.

Alkylation of the Tetrahydrofluorenone 3.—A solution of 1.629 g. (8.21 mmoles) of the ketone **3** in the potassium *t*-butoxide solution obtained from 1.28 g. (32.8 mg.-atoms) of potassium and 35 ml. of *t*-butyl alcohol was refluxed for 10 min. and then cooled and treated, dropwise and with stirring over a 15-min. period, with 5.00 g. (32.7 mmoles) of methyl bromoacetate. The resulting mixture was refluxed for 5 min. and then concentrated, diluted with water, neutralized by the addition of a few drops of hydrochloric acid, and extracted with ether. After the ethereal extract had been dried and concentrated the residual brown oil (2.689 g.) was dissolved in a mixture of 1.0 g. (0.25 mole) of sodium hydroxide, 10 ml. of water, and 25 ml. of methanol. The resulting solution was refluxed for 11 hr., cooled, diluted with saturated aqueous sodium chloride solution, and extracted with ether. After acidification of the aqueous phase and extraction with ether, the ethereal solution was washed with water, dried, and concentrated. The crude acidic product (1.896 g.), which contained[16] one major component (acid **13**) and one minor component, was esterified with ethereal diazomethane to give 1.580 g. of crude ester **4**[16,17] (containing one major and one minor component) as a pale yellow oil. A combination of chromatography on silica gel and recrystallization from methanol separated 845 mg. (39%) of the major component,[17] ester **4** as pale yellow prisms, m.p. 69–71°. Recrystallization raised the melting point to 73–74°. The product has infrared absorption[13] at 1735 cm.$^{-1}$ (ester C=O) and 1705; ultraviolet maxima[14] at 250 mμ (ϵ 12,400) and 299 (2540); and a series of n.m.r. peaks[13] in the region 2.3–3.2 τ (3H, aryl CH), a multiplet centered at 4.28 (2H, vinyl C–H), a singlet at 6.45 (3H, OCH_3) superimposed on a multiplet (1H, benzylic CH), and a complex series of peaks in the region 7.2–7.9 (9H, aryl CH_3 and three CH_2 groups).

Anal. Calcd. for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.54; H, 6.77.

The mother liquors remaining after this separation contained[17] approximately 90% of ester **4** (first eluted) and approximately 10% of a second component (second eluted) which may be the *trans* isomer corresponding to ester **4**. However, repeated efforts to separate a pure sample of the minor component served only to yield small quantities of an approximately equal mixture of ester **4** and the second product. The infrared spectrum of this mixture resembled closely the spectrum of the pure ester **4**.

Hydrogenation of the Unsaturated Ester 4.—A solution of 200 mg. (0.744 mmole) of ester **4** in 10 ml. of ethanol was hydrogenated over 30 mg. of a 5% palladium-on-carbon catalyst at 25° and atmospheric pressure. After the hydrogen uptake (18.3 ml. on 1.01 equiv.) had ceased (25 min.), the solution was filtered and concentrated to leave 202 mg. of colorless oil whose infrared spectrum[13] was identical with the spectrum of previously described[3] ester **6**. Crystallization from aqueous ethanol afforded 163 mg. (81%) of one crystalline form of ester **6**, m.p. 74–76°. Since this material tends to crystallize as a mixture of crystalline forms[3] which complicated comparison of samples, a solution of 100 mg. (0.364 mmole) of ester **6** and 310 mg. of 85% potassium hydroxide in a mixture of 4 ml. of methanol and 2 ml. of water was refluxed for 4.5 hr., then diluted with water, and extracted with ether. After the aqueous phase had been acidified and extracted with ether, this ethereal extract was dried and concentrated. Recrystallization of the residual solid (106 mg.) from an ethyl acetate–hexane mixture gave 61 mg. (65%) of the keto acid **14** as white prisms, m.p. 140.5–141.5°, which was identified by a mixture melting point determination and by comparison of infrared spectra[18] and thin layer chromatograms.[16]

Reaction of the Epoxy Keto Ester 17 with Magnesium Bromide.—To a solution of 500 mg. (1.74 mmoles) of epoxide **17**[4] in 25 ml. of benzene was added 1.7 ml. of an ethereal solution containing 5.22 mmoles of anhydrous magnesium bromide (from ethylene dibromide and magnesium). The resulting mixture was refluxed for 11 hr. and then diluted with benzene and washed with saturated aqueous ammonium sulfate. The benzene layer was dried and concentrated to leave 576 mg. of a pale yellow solid which gave a positive test for halogen and showed only one spot on thin layer chromatography.[16] Recrystallization from methanol gave 398 mg. (68.3%) of the bromo lactone **18** as white needles, m.p. 181.5–183.5°, which melted at 183–183.5° after recrystallization. The product has infrared absorption[19] at 1778 cm.$^{-1}$ (γ-lactone C=O) and 1704 (C=O) with ultraviolet maxima[14] at 252 mμ (ϵ 13,500) and 300 (2300).

Anal. Calcd. for $C_{16}H_{15}BrO_3$: C, 57.33; H, 4.51; Br, 23.84. Found: C, 57.11; H, 4.61; Br, 24.30.

A mixture of 200 mg. (0.597 mmole) of the bromo lactone **18**, 350 mg. (8.75 mmoles) of sodium hydroxide, 2 ml. of methanol, and 10 ml. of water was stirred at room temperature until solution was complete (30 hr.) and then successively extracted with ether, cooled, acidified to pH 3 with hydrochloric acid, and again extracted with ether. The final ethereal extracts were dried and concentrated and the residual solid (210 mg.) was esterified with ethereal diazomethane. After appropriate manipulations, crystallization of the resulting neutral product from methanol gave 114 mg. (66%) of the epoxy ester **17**, m.p. 101–103°, identified with an authentic sample by a mixture melting point determination and by comparison of infrared spectra and thin layer chromatograms.

Reaction of the Unsaturated Ester 15 with Diborane.—Subsequent preparations of the previously described[4] unsaturated ester **15** yielded a different crystalline form of the material as white prisms, m.p. 82.5–84° (lit.[4] m.p. 70.1–71°), which has infrared absorption[13] and thin layer chromatographic behavior identical with the material melting at 70.1–71°.

Anal. Calcd. for $C_{17}H_{18}O_3$: C, 75.53; H, 6.71. Found: C, 75.65; H, 6.72.

A cold (0°) solution containing 3.87 mmoles of diborane in 10 ml. of tetrahydrofuran was added to 2.00 g. (7.32 mmoles) of the unsaturated ester **15** and the resulting solution was stirred, under nitrogen, for 3 hr. at 0° and for an additional 2 hr. at room temperature. The reaction mixture was treated successively with 0.5 ml. of water, 10 ml. of 3 *N* aqueous sodium hydroxide and, after cooling to 0°, 10 ml. of 30% aqueous hydrogen peroxide. The mixture was then stirred at 0° for 3 hr. and at room temperature for 5 hr. An additional 5 ml. of 3 *N* aqueous sodium hydroxide was added and the reaction mixture was refluxed for 2 hr., then diluted with water, and extracted with ether. After the ethereal extract had been dried and concentrated, the residual oil (1.509 g.) was found to contain[16] at least four components. The infrared spectrum of the material indicated essentially complete reduction of the ester function. To a solution of 1.25 g. of this neutral material in 35 ml. of 90% aqueous acetic acid was added, dropwise and with stirring, 6 ml. of a 2.67 *M* solution of chromium trioxide in aqueous sulfuric acid. The reaction mixture was stirred

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[16] A thin layer chromatographic plate coated with silica gel was employed for this analysis.

[17] A gas chromatography column packed with General Electric Silicone No. SE30 suspended on ground firebrick was employed for this analysis.

[18] Determined in chloroform solution.

[19] Determined as a suspension in a potassium bromide pellet.

for 3 hr. at room temperature and then treated with a few drops of methanol, concentrated under reduced pressure, diluted with aqueous ammonium sulfate, and extracted with ether. The ethereal extract was washed with aqueous sodium bicarbonate, dried, and concentrated to leave 954 mg. of white solid containing[16] two components, lactone **16** and a second unidentified material, in approximately equal amounts. Fractional crystallization from methanol separated 354 mg. (23%) of the pure lactone **16**, m.p. 130–131.5°, identified with a subsequently described sample by a mixture melting point determination and comparison of infrared spectra. No other pure material was isolated from either the neutral or acidic portions of the reaction products.

In another experiment, 9.00 ml. of a tetrahydrofuran solution containing 8.51 mmoles of diborane was treated with 1.158 g. (17.02 mmoles) of 2-methyl-2-butene to prepare di(3-methyl-2-butyl)borane.[20] After this solution had been stirred at 0° for 3 hr., it was added to a solution of 2.00 g. (7.40 mmoles) of the unsaturated ester **15** in 5 ml. of tetrahydrofuran. The resulting solution was stirred for 2 hr. at 0° and 20 hr. at room temperature. The mixture was treated successively with 2 ml. of water and a solution of 4.90 g. of sodium dichromate hexahydrate and 3 ml. of concentrated sulfuric acid in 25 ml. of water, and then stirred for 30 min. at 0° and at room temperature for 5 hr. After the reaction mixture had been diluted with aqueous ammonium sulfate and extracted with ether, the ethereal extract was washed with aqueous sodium bicarbonate, dried, and concentrated. The crude neutral oil (1.943 g.) contained[16] two major products, the lactone **16** and a second unidentified material, as well as some starting material. A solution of the neutral product in 75 ml. of ether was stirred with a solution of 4.0 g. of sodium hydroxide in 50 ml. of water for 45 min. at room temperature to selectively saponify part of the γ-lactone **16**. Acidification of the aqueous layer followed by appropriate manipulation afforded 287 mg. (16%) of the crude lactone **16**, m.p. 128–131°, which was recrystallized from aqueous methanol to give 210 mg. of the pure lactone as white needles, m.p. 131.2–132.2°. This product has infrared absorption[18] at 1775 and 1760 (shoulder) cm.$^{-1}$ (γ-lactone C=O) and at 1705 (C=O); ultraviolet maxima[14] at 252 mμ (ϵ 12,800) and 300 (2320); and a series of n.m.r. peaks[15] in the region 2.3–3.0 τ (3H, aryl C–H) as well as a multiplet centered at 5.04 (1H, CH–O), a singlet at 7.35 (3H, aryl CH_3), a multiplet centered at 6.79 (1H, benzylic C–H), a pair of doublets (J = 17 c.p.s.) centered at approximately 7.1 and 7.6 (2H, CH_2 of lactone), and complex absorption in the region 7.6–8.9.

Anal. Calcd. for $C_{16}H_{16}O_3$: C, 74.98; H, 6.29. Found: C, 74.87; H, 6.31.

Reductive Cleavage of the Diketone Lactone 19. A. With Zinc and Acetic Acid.—A mixture of 1.092 g. (4.03 mmoles) of lactone **19**, 2.00 g. of zinc dust, 3 ml. of water, and 30 ml. of acetic acid was refluxed with stirring for 7 hr. at which time all the zinc had dissolved. An additional 2.05-g. portion of zinc was added and refluxing and stirring were continued for an additional 14 hr. The resulting mixture was filtered and the filtrate was concentrated under reduced pressure, diluted with aqueous ammonium sulfate, and extracted with ether. The ethereal extract was washed with aqueous sodium bicarbonate, dried, and concentrated to leave 309 mg. of neutral oil which contained[16] at least five components, one of which corresponded in R_f value to the starting material. The aqueous bicarbonate layer was acidified, saturated with ammonium sulfate, and extracted with ether. After this ether solution had been dried and concentrated, the crude acidic fraction (1.408 g.) was esterified with ethereal diazomethane to give, after appropriate manipulation, 812 mg. of a neutral oil which contained two major components, **20** and **22**. After an involved sequence of chromatography and fractional crystallization, a small amount of the keto ester **20** was separated from ether at low temperatures as white prisms, m.p. 93–94° The product has infrared absorption[18] at 1710 cm.$^{-1}$ (C=O) with a shoulder at *ca.* 1725 (ester C=O); ultraviolet maxima[14] at 252 mμ (ϵ 12,900) and 300 (2320); and a series of n.m.r. peaks[15] in the region 2.3–2.9 τ (3H, aryl C–H) with a singlet at 6.39 (3H, O–CH_3) superimposed on a multiplet (1H, benzylic C–H), and a single peak at 7.33 (8H, aryl CH_3 and two –CH_2– groups next to multiple bonds), as well as complex absorption in the region 7.4–8.2

Anal. Calcd. for $C_{17}H_{18}O_4$: C, 71.31; H, 6.34. Found: C, 71.22; H, 6.40.

The combined mother liquors from this separation were subjected to preparative thin layer chromatography on silica gel to separate the second component, the keto ester **22**, which crystallized from an ether–petroleum ether mixture as white prisms, m.p. 81–82°. This product has infrared absorption[18] at 1710 cm.$^{-1}$ (C=O) and 1725 (ester C=O) with no absorption in the 3-μ region indicative of a hydroxyl function. The product has weak ultraviolet maxima[14] at 265 mμ (ϵ 494) and 273 (454).

Anal. Calcd. for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.94; H, 7.42.

B. With Chromium(II) Chloride.—To a solution of 3.680 g. (13.6 mmoles) of keto lactone **19** in 200 ml. of acetone was added the aqueous solution of chromium(II) chloride prepared from 15.0 g. (56.2 mmoles) of chromium(III) chloride hexahydrate by reduction with zinc amalgam.[10a] After the resulting solution had been stirred at room temperature under a carbon dioxide atmosphere for 5 hr., the mixture was concentrated under reduced pressure, diluted with aqueous sodium chloride, and extracted with ether. The ethereal extract was washed with aqueous sodium bicarbonate, dried, and concentrated to leave 3.130 g. of the crude acid **21** as a white solid which was esterified with ethereal diazomethane. Recrystallization of the resulting crude ester (3.099 g.) from an ethyl acetate–hexane mixture afforded 2.509 g. (65%) of the pure keto ester **20** as white prisms, m.p. 92.5–94°. This product was identified with the previously described sample by a mixture melting point determination and comparison of infrared spectra.

Treatment of the Diketo Ester 20 with Sodium Methoxide.—A solution of 300 mg. (1.05 mmoles) of diketo ester **20** in methanolic sodium methoxide, prepared from 5 ml. of methanol and 60 mg. (2.6 mg.-atoms) of sodium was refluxed for 48 hr. The neutral product separated from 1-ml. aliquots withdrawn from this refluxing solution after 2 and 8 hr. exhibited only a single peak on gas chromatography[17] corresponding in retention time to the starting ester **20**. The solution remaining after 48 hr. was diluted with ether and washed with aqueous sodium bicarbonate. The crude acid, isolated from the aqueous extract in the usual way, was esterified with diazomethane and, after recombination with material removed as 1-ml. aliquots, the crude ester (277 mg.) was distilled in a short-path still (180-200° at 0.05, mm.) to separate 179 mg. (59.7%) of the crude ester **20** as a yellow oil which crystallized on standing, m.p. 82–86°. This crude product, which has infrared absorption[18] and behavior on thin–layer[16] and gas chromatography[17] identical with the starting diketo ester, was recrystallized from a hexane–ethyl acetate mixture to separate 109 mg. (36.4%) of the pure diketo ester **20** 91.5–93°, which was identified by a mixture melting point determination.

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(20) H. C. Brown and G. Zweifel, *J. Am. Chem. Soc.*, **83**, 1241 (1961).