tan-3-one (43), and 2α-bromo-5α,6β-dichlorocholestan-3-one (44) were prepared by the procedure of Jacquesy and Levisalles.[29]

Acknowledgments. We are grateful for samples supplied by Professors W. G. Dauben, J. A. Marshall, and A. R. Katritzky and Dr. D. K. Phillips. This research was supported by grants from the Public Health Service (GM 10224-03 and AM 05014-04) and the Petroleum Research Fund of the American Chemical Society. The n.m.r. spectra were run, through the courtesy of the University of Massachusetts, on a Varian A-60 spectrometer located at that institution.

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A Conformational Analysis of the Favorskii Rearrangement[1]

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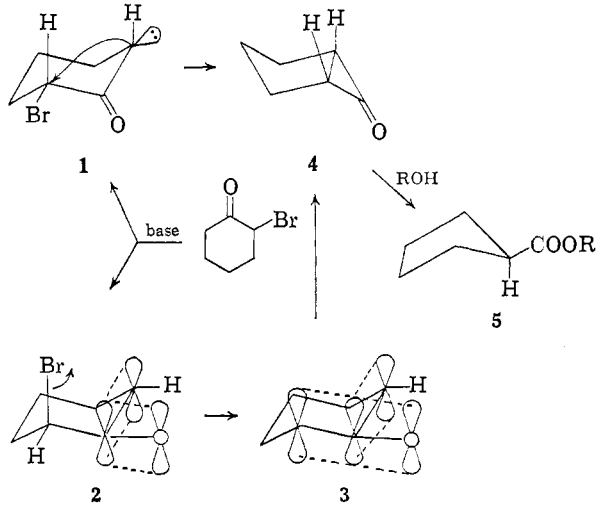
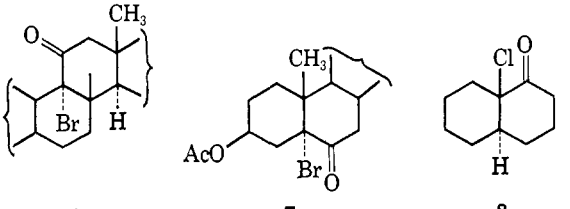
Contribution from the Department of Medicinal Chemistry, School of Pharmacy, University of Kansas, Lawrence, Kansas. *Received August 25, 1965*

Abstract: In an attempt to elucidate the steric requirements of the Favorskii rearrangement, 3-a-bromo-*trans*-2-decalone (**11a**), 3-e-bromo-*trans*-2-decalone (**11e**), and 2-e-bromo-9-methyl-*trans*-3-decalone (**12**) were subjected to Favorskii rearrangement conditions in both polar and nonpolar solvents. The axial compound, **11a**, gave no rearrangement product in either solvent, whereas the equatorial compounds, **11e** and **12**, rearranged on treatment with sodium ethoxide in polar and nonpolar solvents. Evidence disputing the necessity of proposing a "zwitterion mechanism" in polar solvents is given.

The Favorskii rearrangement, the skeletal rearrangement of α-halogenated ketones in the presence of nucleophilic agents, has been reviewed by Kende.[2] Previous evidence suggested that the reaction proceeded through a "cyclopropanone intermediate," [3] which formed directly without involvement of an intermediate dipolar ion.[4] Recent studies have implied that the nature of the intermediate is solvent dependent with a cyclopropanone intermediate being facilitated by nonpolar solvents and a "zwitterion intermediate" by polar solvents.[5-7] The cyclopropanone intermediate could result from abstraction of the α′ hydrogen of an α-halo ketone, followed by an intramolecular backside displacement with inversion of configuration at the α-carbon atom. Such a displacement would require an equatorial halogen in the case of cyclic systems, as shown for α-bromocyclohexanone (**1**). The zwitterion intermediate would result from base abstraction of the α′ hydrogen followed by ionization of the halogen at the α-carbon atom. The ionization would be favored by an axial halogen as shown in **2**. When 3α,20β-dibenzoyloxy-9α-bromo-5β-pregnan-11-one (partial structure **6**),[8] 5α-bromocholestan-3β-ol-6-one acetate (partial structure **7**),[9] and 9-chloro-*trans*-1-decalone (**8**)[7] were treated with base in polar solvents, no Favorskii rearrangement products were found. The strain of the bicyclic system **4** was given as the reason for the absence of rearrangement.[7] Although no example of a rearrangement can be found with systems possessing a fixed axial halogen, the zwitterion intermediate, but not the cyclopropanone intermediate, can account for the loss of stereospecificity found when piperitone oxide (**9**) and 1-chloro-*cis*-1-acetyl-2-methylcyclohexanone (**10**) undergo rearrangement in polar media.[5,6] Several examples of successful Favorskii rearrangements have been reported in conformationally rigid systems which possess an equatorial halogen.[10-12]





(1) Taken in part from the dissertation presented by Odd Kristiansen, June 1962, to the Graduate School of the University of Kansas in partial fulfillment of the requirements for the Doctor of Philosophy Degree.
(2) A. S. Kende, *Org. Reactions*, **11**, 261 (1960).
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(11) N. Pappas and H. R. Nace, *J. Am. Chem. Soc.*, **81**, 4556 (1959).
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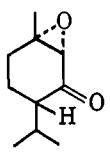

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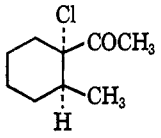

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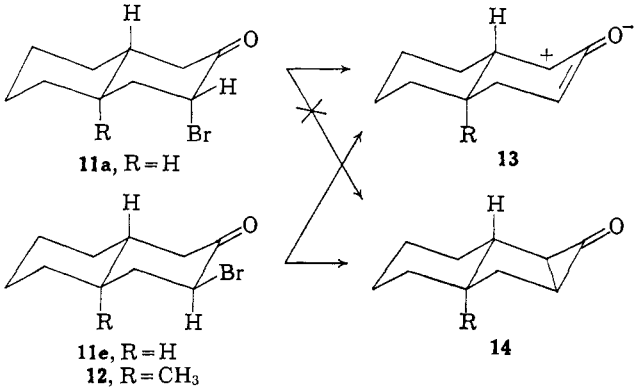
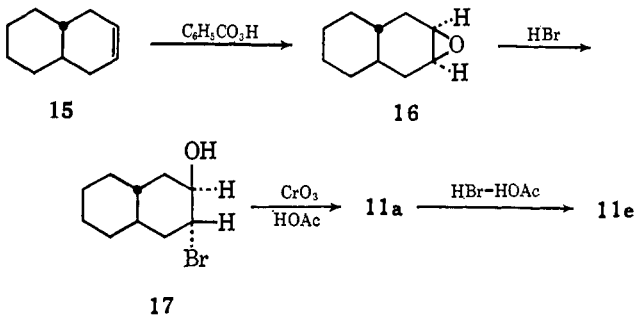
In an attempt to clarify the importance of the conformation of the α halogen and also in an attempt to furnish information on the nature of the intermediate, the axial and equatorial isomers of 3-bromo-*trans*-2-decalone (**11a** and **11e**) and 2-e-bromo-9-methyl-*trans*-3-decalone (**12**) were prepared and submitted to Favorskii conditions in polar solvent (ethanol) and nonpolar solvent (1,2-dimethoxyethane). If formation of a cyclopropanone intermediate occurs by an intramolecular backside displacement, it is expected that only the isomer with the equatorial halogen substituent **11e** and **12** will give rearranged product, by means of intermediate **14**. If, conversely, the zwitterion mechanism is operative, loss of halide ion by ionization to yield **13** is possible with **11a**, **11e**, and **12**, but only in polar media. On a steric basis the axial isomer might be expected to form the zwitterion at a faster rate than the equatorial isomer. If both mechanisms are operative, only **11a** in nonpolar media would not give the expected rearrangement products.



11a, R = H
11e, R = H
12, R = CH_3
13
14

The starting point for the synthesis of bromo ketones **11a** and **11e** was *trans*-Δ^2-octalin (**15**) which was converted to 2,3-epoxy-*trans*-decalin (**16**) with perbenzoic acid in chloroform.[13] The latter (**16**) was treated with hydrobromic acid to give the bromohydrin **17**, which was oxidized with chromium trioxide in acetic acid to give 3-a-bromo-*trans*-2-decalone (**11a**).[14,15] The equatorial isomer **11e** was prepared by isomerization of the axial isomer using catalytic amounts of hydrobromic acid in acetic acid. The axial halo ketone **11a** was distinguished from its equatorial counterpart by infrared, ultraviolet, and nuclear magnetic resonance spectroscopy (Table I).

Sodium ethoxide was used as the reagent for effecting the rearrangement both in the polar solvent, ethanol, and in the nonpolar solvent, 1,2-dimethoxyethane. On attempting the rearrangement of 3-a-bromo-*trans*-2-decalone (**11a**) in polar solvent and examination of the neutral fraction by gas–liquid chromatography (g.l.c.), three peaks were found.[16] The components were separated and one of the peaks was found to be composed of 3-e-hydroxy-*trans*-2-decalone (**19**, 50–55%), isolated usually as the dimer *trans*-A/B,*trans*-D/E-5a,12a-dihydroxy-6,13-dioxaperhydropentacene (**23**),



15 16 17 **11a** **11e**

Table I

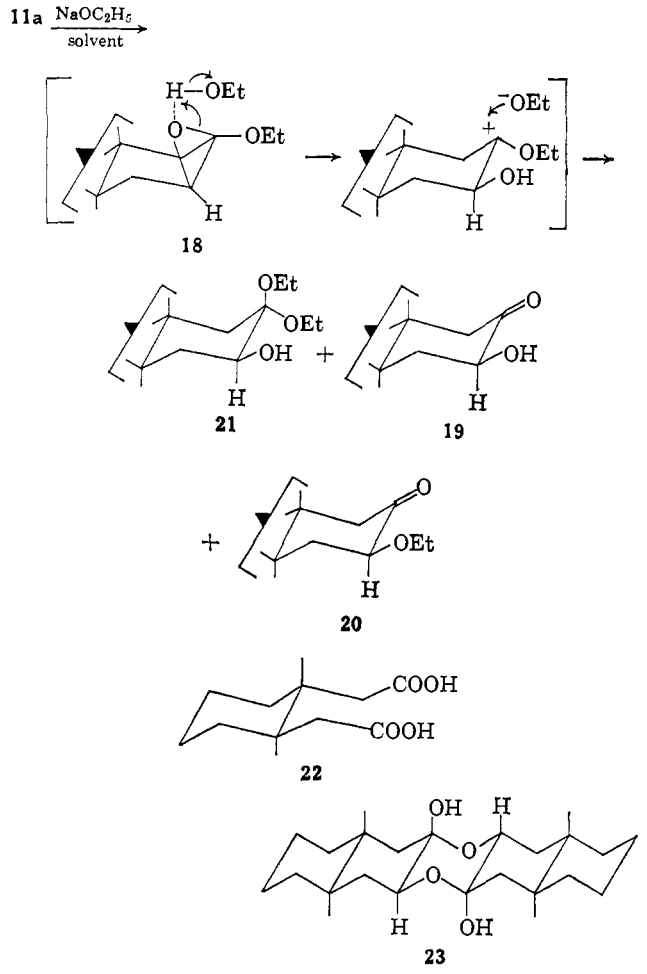
Compound	Infrared C=O absorption, μ	Ultraviolet.[a,b] λ_{max}, Å. (ϵ)	N.m.r.,[c] δ (p.p.m.)
3-a-Bromo-*trans*-2-decalone	5.83	3105 (104)	4.40 (J = 5 c.p.s.)
3-e-Bromo-*trans*-2-decalone	5.79	2868 (28)	4.72 (J = 19 c.p.s.)

[a] Recorded in isooctane solution. [b] O. Kristiansen, E. E. Smissman, and E. M. Kosower, *J. Pharm. Sci.*, **53**, 1283 (1965). [c] Recorded in carbon tetrachloride.

and 3-e-ethoxy-*trans*-2-decalone (**20**, 5–10%). A second was identified as 3-e-hydroxy-2,2-diethoxy-*trans*-decalin (**21**). This material was present in varying amounts and usually upon standing or on chromatography was hydrolyzed to the α-ketol **19**. The third peak was never isolated in a pure form but appeared to be dimeric (5–10%), probably composed of 2 moles of **20**.

Several acidic products were isolated, but the only material present in substantial amounts was 1,2-*trans*-cyclohexanediacetic acid (**22**, 15–20%). Dicarboxylic acids which result from similar ring openings have been reported in the case of α-2-bromo-3-keto steroids.[8,10] It has been suggested that the ring opening may arise from a reverse acyloin-type reaction. Earlier work has demonstrated that 3-hydroxy-*trans*-2-decalone (**19**) can be converted to the dicarboxylic acid **22** by treatment with base.[17] The neutral side products can be accounted for in the following manner. The hydroxyketal **21** and the ketol **19** may have resulted from base attack on the carbonyl followed by displacement of the axial halogen by the oxygen anion which would lead to the epoxide **18**. Opening of the epoxide through a solvolytic intermediate, rather than attack by base, would lead to equatorial hydroxyls in **19** and **21**. Ketols which result from similar epoxides have been reported in other systems.[7] Compound **20** may originate by direct displacement of the halogen by base, but also may be the result of base attack on the epoxide **18** followed by isomerization. Both **19** and **20** could

(13) W. S. Johnson, V. J. Bauer, J. L. Margrave, M. S. Frisch, L. H. Dreger, and W. H. Hubbard, *J. Am. Chem. Soc.*, **83**, 606 (1961).
(14) D. H. R. Barton, D. A. Lewis, and J. F. McGhie, *J. Chem. Soc.*, 2907 (1957).
(15) J. Fajkos and F. Sorm, *Chem. Listy*, **52**, 2115 (1958); *Chem. Abstr.*, **53**, 5342 (1959).
(16) Obtained with dual 4-ft. columns packed with 20% SE-30 suspended on 80–100 mesh Gas Chrom P.
(17) M. Stoll and J. Hulstkamp, *Helv. Chim. Acta*, **30**, 1815 (1947); E. Lehmann and B. Krätschell, *Ber.*, **67**, 1867 (1934).

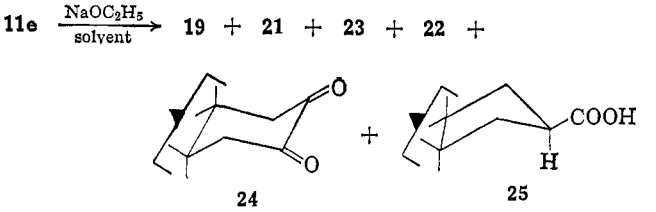


isomerize readily and due to the symmetry of the resulting enediol in the enolization of **19** one cannot be positive that the carbonyl is located at the carbon which originally possessed the ketonic function. The possibility also exists that **19** may have been derived from **18** during the isolation procedure. This could occur by base attack on **18** to give the axial isomer of ketol **19**, followed by isomerization.

When the rearrangement of the axial isomer **11a** was attempted in nonpolar solvent the α-ketol, **19** (50–60%) along with a material which could not be identified (<10%), were the only neutral products obtained. Once again several acidic materials were present, but the only acid found in more than 1% yield was the dicarboxylic acid, **22** (20–30%). With the axial bromo ketone **11a** no Favorskii product could be obtained utilizing either a polar or nonpolar solvent system.

When the equatorial bromo ketone **11e** was treated with sodium ethoxide in ethanol, followed by hydrolysis, an acidic mixture, which consisted of the dicarboxylic acid **22**, *trans*-decalin-2,3-dione (**24**), and *trans*-hexahydroindane-2-carboxylic acid (**25**, 11–13%), was produced. Only the latter compound was a product of the Favorskii rearrangement, while the dione **24** was a product of oxidation and was the precursor to the dicarboxylic acid **22**. The neutral products in this case consisted of 3-e-hydroxy-*trans*-2-decalone (**19**, 10–15%), isolated as its dimer **23**, and the α-hydroxyketal **21** (50–55%). The presence of the neutral products suggest that a considerable amount of isomerization may have occurred at the α carbon prior to reaction. This was verified by the fact that deuterium was found to exchange with the proton at the 3-position of the equatorial bromo ketone **11e** before exchanging with those at the 1-position. The instability of the equatorial isomer **11e** was also observed when the rearrangement was attempted in nonpolar solvent.

The equatorial bromo ketone **11e**, on base treatment utilizing a nonpolar solvent, afforded the same neutral products obtained on the treatment of the axial isomer **11a**, under the same conditions, α-ketol **19** (45%) and the same unknown (10–15%). Two acids were found, one of which was the dicarboxylic acid **22** (22%), and the other was the Favorskii acid **25** (13%).

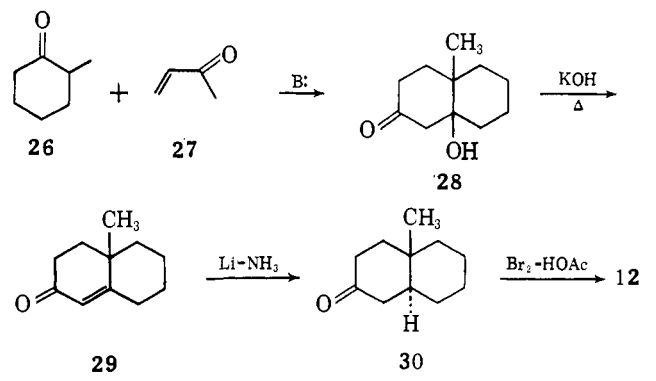


Similar results were obtained utilizing the axial and equatorial 3-chloro-*trans*-2-decalones in polar solvent.

The results reported above suggest that in the case of the 3-halo-*trans*-2-decalones the cyclopropanone mechanism is operative. If the zwitterion mechanism was functioning, hexahydroindancarboxylic acid (**25**) should have been detected when the axial bromo ketone **11a** was treated with base in polar solvent. With the equatorial compound **11e**, rearrangement does occur, but oxidation and isomerization to **11a** followed by displacement and/or epoxide formation are competing reactions. Since the rearrangement of **11e** was successful in polar and nonpolar solvents to an equal extent, it appears that the rearrangement is not dependent on solvent polarity.

Since the isomerization of the equatorial α-halodecalone **11e** to the axial isomer **11a** was responsible for the low yield of rearrangement product, a system which could not isomerize, under rearrangement conditions, 2-e-bromo-9-methyl-*trans*-3-decalone (**12**), was investigated. The steric interaction between an axial bromine at the 2-position and the 9-methyl group is much greater than the electronic dipole effect between the carbonyl and equatorial halogen in **12**.[18]

The bromo ketone **12** was prepared by starting with 2-methylcyclohexanone (**26**) and the methyl vinyl ketone (**27**) according to the procedure of Marshall and Fanta.[19] *cis*-10-Methyl-2-decalon-9-ol (**28**), re-



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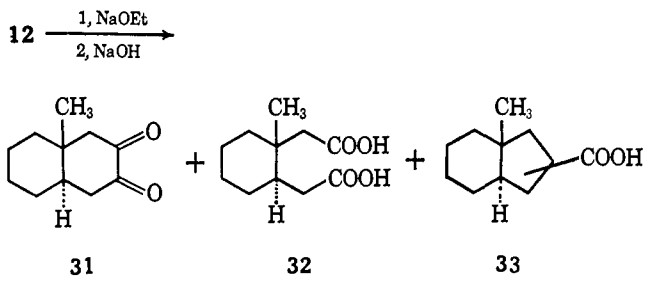
(19) J. A. Marshall and W. I. Fanta, *ibid.*, **29**, 2501 (1964).

sulting from the base-catalyzed Robinson annealation, was dehydrated readily with potassium hydroxide to methyl-1(9)-octalone-2 (**29**).[19] A lithium–ammonia reduction of this material gave the desired 10-methyl-*trans*-2-decalone (**30**),[20] which upon bromination gave the bromo ketone **12**.[21]

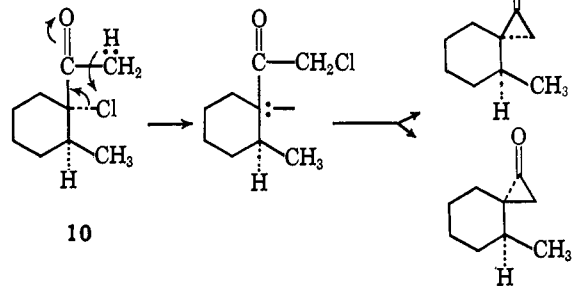
When 2-e-bromo-9-methyl-*trans*-3-decalone (**12**) was treated with sodium ethoxide in ethanol and followed by hydrolysis, three acidic products were isolated. The products were 9-methyl-*trans*-decalin-2,3-dione (**31**, 20%), 1-methyl-*trans*-cyclohexane-1,2-diacetic acid (**32**, 22%), and *trans*-hexahydro-7a-methylindancarboxylic acid (**33**, 38%). When the bromo ketone **12** was treated with sodium ethoxide in 1,2-dimethoxyethane, the same three products were isolated: 10% dione **31**, 17% dicarboxylic acid **32**, and 44% Favorskii acid **33**.



31 **32** **33**

The results of this study with the halo-*trans*-decalones (**11a**, **11e**, **12**) disputes the role of the zwitterion intermediate as an active participant in the Favorskii rearrangement.

The need for such an intermediate originated with the inability to explain the nonstereospecific results found when piperitone oxide (**9**) and 1-chloro-*cis*-1-acetyl-2-methylcyclohexanone (**10**) were treated with base in a



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polar solvent.[5,6] Examination of models of α,β-epoxy ketones, such as **9**, indicates that the oxide cannot attain a true equatorial position as can an α-bromo ketone. Such a deviation from Favorskii requirements may effect profoundly the course of reaction of such systems and as previously suggested might cause the rearrangement of oxides to proceed by an entirely different mechanism[5] from that of a classical Favorskii rearrangement. It would appear that further studies on α,β-epoxy ketones are necessary before accepting their similarity to α-bromo ketones in this reaction.

On examination of the nonstereospecificity in the rearrangement of **10**, the proposal has been made by Wendler and co-workers that isomerization of the α-halo ketone may occur prior to rearrangement.[22] This would mean transfer of the halogen to the acetate methyl followed by formation of the cyclopropanone. As stated by House and Gilmore,[6] "a rigorous disproof of this idea would appear to be exceedingly difficult."

From this study it can be concluded that the cyclopropanone intermediate is compatible with our findings, while the zwitterion intermediate is not. While the zwitterion intermediate need not be invoked in our case, more extensive studies are necessary before proposing such an intermediate as a general intermediate in the Favorskii rearrangement in polar solvents.

Experimental Section[23]

2,3-Epoxy-*trans*-decalin (16). To a cold (0°) solution of 18 g. (0.13 mole) of perbenzoic acid in 320 ml. of chloroform, was added 16.24 g. (0.119 mole) of *trans*-Δ^2-octalin.[18] The solution was maintained at 6° for 4 days, then extracted with cold 10% aqueous sodium hydroxide, washed with water, and dried over anhydrous sodium sulfate. The solvent was removed and the oil was distilled at 88–91° (0.2 mm.) to give 11.24 g. (62%) of **16**.

***trans*-3-Bromo-2-decalol (17).** A mixture of 1.09 g. (0.0072 mole) of **16**, 30 ml. of 40% hydrobromic acid solution, and 75 ml. of chloroform was shaken for 30 min.[14] The combined chloroform layers were dried over anhydrous sodium sulfate. After filtration and evaporation of the solvent, 1.67 g. (99%) of **17** was recovered: m.p. 75–77°, 86–87° after recrystallization from acetone; n.m.r. δ 2.25 (1 H, peak half-width 15 c.p.s.) a broad absorption between 1.00 and 2.10 (14 H); infrared (KBr) 3.05 (broad), 6.95 (m), and 7.00 μ. *Anal.* Calcd. for $C_{10}H_{17}BrO$: C, 51.53; H, 7.34. Found: C, 51.77; H, 7.44.

3-a-Bromo-*trans*-2-decalone (11a). To a cold solution of 1.50 g. (0.015 mole) of chromium trioxide dissolved in a minimum amount of water and 25 ml. of glacial acetic acid was added 3.00 g. (0.013 mole) of **17**. The mixture was maintained at 25° and stirred occasionally for 24 hr.[15] Several drops of methanol was added to destroy the excess chromium trioxide and the mixture extracted with three 50-ml. portions of ether. The combined ether layers were extracted with three 50-ml. portions of water and allowed to react with 50 ml. of saturated sodium bicarbonate solution. The ether layer was removed, and the bicarbonate layer was extracted with two 50-ml. portions of ether. The ether layers were combined and dried over anhydrous magnesium sulfate. After removal of the solvent, 2.756 g. (93%) of the desired bromo ketone **11a** was isolated: $n^{23}D$ 1.5190; ultraviolet $\lambda_{max}^{CH_3OH}$ 307 mμ (ϵ 103); infrared (KBr) 5.83 (s) μ; n.m.r. (benzene) δ 4.34 (1 H, broad multiplet which was essentially a doublet of doublets, peak half-width 5 c.p.s.), 0.7 to 2.30 (14 H, broad band). The compound gave a yellow 2,4-dinitrophenylhydrazone, m.p. 171.5–172°. *Anal.* Calcd. for $C_{16}H_{20}N_4O_5$: C, 55.16; H, 5.80; N, 16.09. Found: C, 55.54; H, 6.21; N, 15.62.

A second, deep red 2,4-dinitrophenylhydrazone, m.p. 221–222°, was formed after further treatment with warm 2,4-dinitrophenylhydrazine reagent.

3-e-Bromo-*trans*-2-decalone (11e). Five drops of 30–32% hydrobromic acid in acetic acid was added to 1.50 g. (0.0065 mole) of **11a**. The mixture was allowed to stand until it became crystalline. Recrystallization was performed using petroleum ether (b.p. 63–68°). The crystals were filtered and the mother liquor was concentrated to an oil which again crystallized on standing. This was recrystallized a second time. A total of 864 mg. (58%) of **11e** was isolated: m.p. 91.5–92°; ultraviolet $\lambda_{max}^{CH_3OH}$ 283 mμ (ϵ 31.4); infrared (KBr) 5.81 (s) μ; n.m.r. δ 4.72 (1 H, broad multiplet, peak half-width 19 c.p.s.), 0.8 to 2.8 (14 H, broad band).

(20) M. Yanagita, K. Yamakawa, A. Tahara, and H. Ogura, *J. Org. Chem.*, 20, 1767 (1955).

(21) M. Yanagita and A. Tahara, *ibid.*, 18, 792 (1953).

(22) N. L. Wendler, R. P. Graber, and G. G. Hazen, *Tetrahedron*, 3, 144 (1958).

(23) Melting points were obtained on either a Thomas-Hoover Unimelt or a Kofler micro hot stage and are corrected. Infrared data were recorded on Beckman IR5 and IR8 spectrophotometers and the ultraviolet data were recorded on Cary 11 and Cary 14 spectrophotometers. N.m.r. data were recorded on a Varian Associates Model A-60 spectrophotometer using tetramethylsilane as the internal standard. All n.m.r. spectra were recorded in CCl_4 unless otherwise stated. Gas chromatographic data were obtained on F and M 500 and 810 research chromatographs. Elemental analyses were performed by Drs. G. Weiler and F. B. Strauss, Oxford, England, and the Huffman Microanalytical Laboratories, Wheatridge, Colo.

Anal. Calcd. for $C_{10}H_{15}BrO$: C, 51.96; H, 6.49. Found: C, 51.93; H, 6.57.

Reaction of 3-a-Bromo-*trans*-2-decalone (11a) with Sodium Ethoxide in Ethanol. A solution of 2.399 g. (0.010 mole) of axial bromo ketone **11a** in 10 ml. of ethanol was added in portions during a period of 30 min. to a stirred solution of sodium ethoxide, prepared from 712 mg. (0.031 g.-atom) of sodium and 50 ml. of ethanol. The reaction mixture was stirred for 45 min. at 50°. After addition of 100 ml. of water, the solution was extracted with four 60-ml. portions of diethyl ether. The combined ether layers were dried over anhydrous magnesium sulfate (ether extract I). The aqueous phase was acidified with 10% hydrochloric acid and extracted with ether (ether extract II). Ether extract II was dried over anhydrous magnesium sulfate.

Evaporation of the solvent from ether extract I gave 1.355 g. of an oil. Gas–liquid partition chromatography (g.l.p.c.) showed three peaks.[16] The oil was chromatographed on silica gel (Brinkman, 0.05–0.20 mm.) and eluted with chloroform. The first fraction consisted of 102 mg. of a sweet-smelling oil, which by infrared and n.m.r. spectroscopy proved to be 3-e-ethoxy-*trans*-2-decalone (**20**): infrared (liquid film) 5.78 (s), 6.90 (s), doublet 8.49, 8.64 μ; n.m.r. δ 4.20 (2 H, quartet J = 7.1 c.p.s.), 3.56 (1 H, broad quartet J = 7 c.p.s.), 1.0 to 2.4 (17 H, broad band). The compound gave a yellow 2,4-dinitrophenylhydrazone in the cold, m.p. 168–168.5°. *Anal.* Calcd. for $C_{18}H_{24}N_4O_5$: C, 57.43; H, 6.42; N, 14.88. Found: C, 57.13; H, 6.52; N, 15.06.

When treated with more reagent while on the steam bath, a second, deep red derivative was formed, m.p. 224–226°, which did not cause depression on mixture melting point with the 2,4-DNP of haloketone **11e**. A white, solid material amounting to 149 mg. was obtained: m.p. 75–80°; after recrystallization from petroleum ether (b.p. 63–68°), m.p. 82° (lit.[24] m.p. 82°); infrared (KBr) 2.93 (m), 5.85 (s) μ. The next 566 mg. was an oil which still showed three peaks by g.l.p.c., but the next 366 mg. was **19**, m.p. 82°. When the mixture of oils was chromatographed a second time on silica gel, **19** was found to be eluted from the column at two different times. This was due to hydrolysis of 3-e-hydroxy-2,2-diethoxy-*trans*-decalin (**21**) to the ketol **19** by the silica gel. A total 849 mg. of α-ketol, **19**, was isolated. The material responsible for the third peak on gas chromatography amounted to 117 mg., but could not be purified sufficiently for analysis: infrared (liquid film) 2.90 (w), 5.81 (s), doublet 8.78, 8.95 μ; n.m.r. δ 3.45 (2 H, quartet, J = 7.2 c.p.s.), 3.85 (3–4 H, three broad singlets), 1.20 (3 H, triplet superimposed on broad band), 1.0 to 2.45 (26–28 H, broad band). Since this peak is found on chromatography of the reaction mixture from the treatment of the ketol **19** with ethanol and *p*-toluenesulfonic acid (see below), it appears that the unknown is a dimer of the ketol **19** plus an ethoxy group.

Evaporation of the solvent from ether extract II led to a residue of 646 mg. Chromatography on silica gel (Brinkman) resulted in isolation of an additional 116 mg. of the ketol, **19**, and 332 mg. of *trans*-1,2-cyclohexanediacetic acid (**22**), m.p. 165° (lit.[24] m.p. 167°).

Reaction of 3-a-Bromo-*trans*-2-decalone (11a) with Sodium Ethoxide in 1,2-Dimethoxyethane. To a suspension of sodium ethoxide, prepared by the addition of 0.545 g. (0.024 g.-atom) of sodium to 3.824 g. (0.083 mole) of ethanol in 50 ml. of refluxing 1,2-dimethoxyethane (previously distilled from sodium hydride) was added 1.503 g. (0.0065 mole) of **11a** dissolved in 20 ml. of 1,2-dimethoxyethane. A cloudy mixture resulted immediately, but the mixture was allowed to stir at room temperature for 18 hr. The solvent then was removed on a flash evaporator, and water was added to the residue. The water layer was extracted with diethyl ether, and the extract was dried over anhydrous magnesium sulfate (ether extract I). The water layer was acidified with 10% hydrochloric acid and extracted with ether. The combined ether extracts were dried over anhydrous magnesium sulfate (ether extract II).

After evaporation of the solvent from ether extract I, 514 mg. of oil remained. G.l.p.c. showed this material to be composed of 90% (462 mg.) α-ketol **19** and 10% (51 mg.) of an unknown. The unknown was purified by chromatography on aluminum oxide (Merck, regular): infrared (liquid film) 2.90 (w), 9.09 to 9.40 (m) μ; n.m.r. δ 2.55 (1 H, broad singlet), 3.0 to 4.0 (5 H, broad multiplet), 0.8 to 2.20 (24 H, broad band). The elemental analysis was inconclusive.

Evaporation of the ether from ether extract II produced 790 mg. of an orange semisolid. Addition of chloroform led to the precipitation of 134 mg. of dicarboxylic acid **22**. The remaining oil partially dissolved in sodium bicarbonate, and the remainder was dissolved in ether. The ether layer was found to contain 130 mg. of oil which consisted of 90% (117 mg.) α-ketol **19** and 10% (13 mg.) of the unknown reported above. The aqueous layer was acidified and extracted with ether. Evaporation of the ether followed by chromatography of the residue on silica gel (Brinkman) resulted in recovery of an additional 217 mg. of dicarboxylic acid **22**.

Reaction of 3-e-Bromo-*trans*-2-decalone (11e) with Sodium Ethoxide in Ethanol. A sample of 1.2 g. (0.0052 mole) of equatorial bromo ketone **11e** was added over a period of 30 min. to a stirred ethanolic solution of sodium ethoxide, prepared from 0.5 g. (0.022 g.-atom) of sodium and 40 ml. of ethanol. The mixture was stirred for an additional 90 min. at 30°. The ethanol was evaporated under vacuum and replaced by 40 ml. of water. The aqueous suspension was refluxed for 3 hr. before it was extracted with ether (ether extract I). The aqueous phase was acidified with 10% hydrochloric acid and once more extracted with ether (ether extract II). Ether extract II was washed with water and dried over magnesium sulfate. After removal of solvent, a residue of 209 mg. was obtained. Acid **25** was isolated after purification by partition chromatography on a silicic acid–indicator (bromocresol blue) column.[25] The yield was 97 mg. (11%). In a later experiment the yield was increased to 13%. Further purification by rechromatography on a regular silicic acid column yielded a solid material: m.p. 35–36° (lit.[26] 40°); infrared (liquid film) 5.88 (s), 6.90 and 7.05 (m doublet) μ; n.m.r. δ 12.28 (1 H, singlet) 2.88 (1 H, broad multiplet, peak half-width 25 c.p.s.), 0.8 to 2.5 (14 H, broad band). *Anal.* Calcd. for $C_{10}H_{16}O_2$: C, 70.20; H, 9.59. Found: C, 70.64; H, 9.46.

A sample of hexahydroindancarboxylic acid (**25**) was degraded[27] with sodium azide and sulfuric acid to an amine which was characterized as 2-aminohexahydroindane by its derivative with benzoyl chloride, m.p. 136.5–137.5 (lit.[28] 140°).

The second component of the acidic fraction was a solid, m.p. 165°, which was discarboxylic acid **22**. In another experiment a third acidic material was isolated in small quantities. This material was dione **24** which gave a positive ferric chloride test; infrared ($CHCl_3$) 2.89 (w), 5.85 (w), 5.98 (s) μ.[24]

Ether extract I was chromatographed on an aluminum oxide column (Merck, regular) after evaporation of solvent. The main fraction which was eluted with a mixture of three parts of benzene and one part of ether consisted of 741 mg. of a solid, white material **21**: m.p. 40–42°; infrared (KBr) 2.8 (w), 2.95 (w) μ; n.m.r. δ 3.68 (5 H, broad multiplet), 0.9 to 2.20 (21 H, broad band, which contained two sets of triplets centered at 1.15 and 1.18, J = 7.2 c.p.s.) (benzene), 0.6 to 2.50 (21 H, broad band which contained a broad singlet at 2.35 and two sets of triplets centered at 1.14 and 1.16, J = 7.2 c.p.s.), 3.77 (4 H, broad quartet, J = 6.5 c.p.s.), 3.41 (1 H, doublet of doublet, broad, J = 3.5 and 6.5 c.p.s.). Under forcing conditions, the substance gave a deep red 2,4-dinitrophenylhydrazone derivative, m.p. 223–226°, which showed no depression on mixture melting point with the 2,4-dinitrophenylhydrazones prepared from **11e**. *Anal.* Calcd. for $C_{14}H_{26}O_3$: C, 69.67; H, 10.44. Found: C, 70.10; H, 10.87.

When ether extract I was allowed to stand for some time prior to chromatography, a solid appeared which was the dimer of α-ketol **19**. The dimer **23** had m.p. 129–130° (lit.[24] 122–123°), infrared (KBr) 2.90, no C=O stretch.

Reaction of 3-e-Bromo-*trans*-2-decalone (11e) with Sodium Ethoxide in 1,2-Dimethoxyethane. To a suspension of sodium ethoxide, prepared by the reaction of 0.461 g. (0.020 g.-atom) of sodium with 3.008 g. (0.066 mole) of ethanol in 50 ml. of refluxing 1,2-dimethoxyethane (previously distilled from sodium hydride), was added 1.514 g. (0.0066 mole) of bromo ketone **11e** dissolved in 1,2-dimethoxyethane. The reaction mixture was stirred at 25° for 18 hr. The 1,2-dimethoxyethane was removed under vacuum, and 75 ml. of water was added. The aqueous layer was extracted with ether, and the ether extracts were dried over magnesium sulfate (ether extract I). The aqueous phase was acidified with 10% hydrochloric acid and extracted with ether (ether extract II). The combined extracts were dried over magnesium sulfate.

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After removal of the solvent from ether extract I, a residue of 658 mg. was obtained. This mixture was analyzed by g.l.p.c. and was found to consist of 72% (475 mg.) of **19**, 18% (118 mg.) of the unknown found when **11a** was treated with base in nonpolar solvent.

Ether extract II, after removal of the solvent, gave a residue amounting to 875 mg. Upon standing 192 mg. of **22**, m.p. 159–162°, was obtained. The remaining oil was chromatographed on silica gel (Brinkman) using chloroform as the eluting solvent. The first fractions consisted of 142 mg. (13%) of **25**. A second component, amounting to 98 mg., was acid **22**.

Reaction of 3-e-Hydroxy-*trans*-2-decalone (19) with Ethanol and *p*-Toluenesulfonic Acid. To a solution of 10 mg. of *p*-toluenesulfonic acid dissolved in 15 ml. of dry benzene and 3 ml. of ethanol was added 227 mg. of **19**. The flask was fitted with a Dean–Stark trap and condenser and refluxed for 2 hr. The reaction mixture was analyzed by g.l.p.c.[16] Detectable quantities of **19**, **21**, and the unknown which was present after attempted rearrangement of the axial bromo ketone **11a** were obtained.

Deuterium Exchange with 3-e-Bromo-*trans*-2-decalone (11e). A sample of **11e** was dissolved in carbon tetrachloride and placed in an n.m.r. tube. An initial spectrum was taken and then 1 ml. of NaOD in D_2O was added and spectra were taken at intervals. The peak centered at δ 4.70 decreased slowly but upon heating at 100° the peak size decreased rapidly. After 45 min., 70% of the absorption had disappeared but g.l.p.c. analysis indicated that 88% of the bromo ketone was still present.

Deuterium Exchange with 3-a-Bromo-*trans*-2-decalone (11a). Using the same procedure as above, a sample of **11a** was studied. After 60 min. the peak at δ 4.40 had decreased by 40–50%, but g.l.p.c. analysis showed that 40% of the reaction mixture was α-ketol **19** and 60% was **11a**.

***cis*-10-Methyl-2-decalon-9-ol (28).** To a solution of 3 ml. of 3 *N* ethanolic sodium ethoxide in 56 g. (0.5 mole) of 2-methylcyclohexanone (**26**) (Aldrich Chemical Co.) maintained at −10° and stirred under a nitrogen atmosphere was added 35 g. (0.5 mole) of methylvinyl ketone (**27**) (Aldrich Chemical Co.) over a 6-hr. interval. Using the reported isolation procedure, 28 g. (31%) of **28** was isolated: m.p. 115–118° (lit.[19] 124–125°); infrared (KBr) 2.97 (s), 5.84 (s) μ; n.m.r. ($CDCl_3$) δ 1.13 (3 H, singlet), 1.60 to 2.90 (15 H, multiplet). The mother liquor contained 18 g. (32%) of **26**.

10-Methyl-1(9)-octalone-2 (29). As reported by Marshall and Fanta,[19] steam distillation of **28** from a 10% potassium hydroxide solution resulted in 99% yield of **29**: infrared ($CHCl_3$) 6.00 (s) μ; ultraviolet λ_{max}^{EtOH} 239 mμ; n.m.r. δ 5.72 (1 H, singlet), 1.28 (3 H, singlet), 1.40 to 2.6 (12 H, broad band).

10-Methyl-*trans*-2-decalone (30). Using a procedure similar to that of Yanagita and co-workers,[20] 8.0 g. (0.049 mole) of **29**, dissolved in dry diethyl ether, was added to 300 ml. of liquid ammonia, cooled in an acetone–solid CO_2 bath. To this suspension was added 2.044 g. (0.294 g.-atom) of lithium. The addition of lithium required 2 hr. and the reaction mixture was allowed to stir for an additional 2 hr. The excess lithium was destroyed by addition of an excess of ammonium chloride. The ammonia was allowed to evaporate and water was added. The aqueous layer was extracted several times with ether. The combined ether layers were washed with water and dried over magnesium sulfate. Removal of the solvent left a residue, 6.85 g. of an oil. G.l.p.c. analysis[16] showed the oil to be 66% (4.75 g.) of **30** and 33% (2.37 g.) of **29**. The components of the oil were separated by chromatography on 200 g. of silica gel (Brinkman) using chloroform as the eluting solvent. The oil showed infrared carbonyl absorption at 5.85 μ.

2-e-Bromo-9-methyl-*trans*-3-decalone (12). Using the procedure of Yanagita and Tahara,[21] 4.85 g. (0.03 mole) of bromine dissolved in 20 ml. of glacial acetic acid was added slowly to an ice-cold solution of 5.035 g. (0.03 mole) of **30** in 25 ml. of acetic acid and yielded 2.27 g. (30%) of **12**: m.p. 101–102° (lit.[21] 101–102°); infrared (KBr) 5.81 (s) μ; n.m.r. δ 4.83 (1 H, doublet of doublets, J = 7 and 13 c.p.s.), 1.15 (3 H singlet superimposed on a broad band), 1.0 to 2.6 (13 H, broad band); ultraviolet $\lambda_{max}^{CH_3OH}$ 283 mμ. The yield was far below that reported by the authors.[21]

Reaction of 2-e-Bromo-9-methyl-*trans*-3-decalone (12) with Sodium Ethoxide in Ethanol. To a solution of sodium ethoxide in ethanol, prepared by addition of 2.03 g. (0.088 g.-atom) of sodium to 50 ml. of ethanol, was added 2.16 g. (0.0088 mole) of **12**. The mixture was stirred at 25° for 25 hr. and the isolation procedure as previously reported for **11e** was followed, including hydrolysis before extraction.

After removal of the solvent from ether extract II, 1.566 g. of an oil was obtained. Thin layer chromatography (t.l.c.) on silica gel G (Brinkman), using benzene as the solvent, showed the presence of three compounds with R_f values of 0.0, 0.138, and 0.250. The oil was chromatographed on silica gel (Brinkman) using benzene as the solvent. The first few fractions from the column (176 mg.) consisted of dione **31**; infrared (liquid film) 5.85 (s), 5.95 (s) μ; ultraviolet $\lambda_{max}^{CH_3OH}$ 267 mμ. The oxime was prepared, m.p. 237–240°, after recrystallization from ethanol and water 232–232.5° dec. *Anal.* Calcd. for $C_{11}H_{18}N_2O_2$: C, 62.83; H, 8.63; N, 13.32. Found: C, 62.79; H, 8.83; N, 13.01.

The second component from the column was *trans*-hexahydro-7a-methylindancarboxylic acid (**33**, 459 mg.): infrared (liquid film) 5.83 (s) μ; n.m.r. δ 11.55 (1 H, broad singlet), 0.78 (3 H, singlet), 1.0 to 2.1 (14 H, broad band); $n^{25}D$ 1.4890. *Anal.* Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.37; H, 9.79.

The final component was removed using benzene–acetone (7:3) and was dicarboxylic acid **32** (424 mg.): m.p. 190° (lit.[29] m.p. 194–195°); infrared (KBr) 2.90 (m), 3.75 (m and broad), 5.89 (s), 7.70 (s) μ.

Removal of the solvent from ether extract I afforded 332 mg. of an oil. Analysis by g.l.p.c.,[16] showed this oil to consist of 40% (133 mg.) of dione **31**, 44% (146 mg.) of Favorskii acid **33**, and 16% (53 mg.) of an unknown.

Reaction of 2-e-Bromo-9-methyl-*trans*-3-decalone (12) with Sodium Ethoxide in 1,2-Dimethoxyethane. To a suspension of sodium ethoxide in 50 ml. of 1,2-dimethoxyethane, prepared by addition of 1.412 g. (0.061 g.-atom) of sodium to an excess of ethanol followed by evaporation of nearly all of the ethanol and the addition of the 1,2-dimethoxyethane (previous distilled from sodium hydride), was added 1.529 g. (0.0062 mole) of **12**. The reaction mixture was cooled during addition and allowed to stir at 25° for 23 hr. The reaction mixture was treated in the manner previously reported for **11e**, including hydrolysis prior to extraction.

After removal of the solvent from ether extract I, a residue of 79 mg. was obtained. Analysis by g.l.p.c.,[16] showed the residue to be composed of 52% (41 mg.) of dione **31**, 35% (27 mg.) of acid **33**, and 13% (10 mg.) of an unknown. From ether extract II, after chromatography on silica gel as reported previously, 79 mg. of dione **31**, 470 mg. of acid **33**, and 227 mg. of dicarboxylic acid **32** were recovered.

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