pared with $\lambda_0$ for the solvent in question. For example, for the nitro group in chloroform solvent

$$B = 515 - 577 = -62 \text{ m}\mu; \quad A = 577^2/515^2 - 1 = 0.255$$

The $\bar{B}$'s and $\bar{A}$'s are average values calculated by least squares from all pertinent experimental data in Table II. Thus, for the nitro group in chloroform solvent, $\bar{B}$ and $\bar{A}$ are calculated from the experimental $\lambda_{max}$'s for azulene and for the mononitro, dinitro, monobromo, dibromo and bromonitro derivatives.

The calculated $\lambda_{max}$'s based on these empirical $B$'s, $A$'s, $\bar{B}$'s and $\bar{A}$'s are obviously empirical also. Naturally, over-all, the $\lambda_{max}$'s calculated from the $\bar{B}$'s and $\bar{A}$'s agree better with the experimental $\lambda_{max}$'s than do the $\lambda_{max}$'s calculated from the $B$'s and $A$'s.

Equation 3 or 4 might be obtained by considering the $\pi$-electron system of azulene, or the center of gravity of the $\pi$-electrons,[10] as a simple harmonic oscillator, for which the frequency of absorbed light would be given by an equation of the type[11]

$$\bar{\nu} = \sqrt{\frac{k}{m}} \Big/ 2\pi c \qquad (5)$$

If, in the azulene system, the mass $m$ of the oscillator may be considered constant, and if 1- and 3-substituents increase or decrease $k$ in a simple additive fashion, then equation 5 leads directly to equation 3 or 4.

For the discrepancies between the experimental values of $\lambda_{max}$ and the values calculated on the basis of equation 3 or 4, the same reasons may be advanced, of course, as for the discrepancies resulting from the use of equation 1.

**Effects of Solvent.**—Table I shows that, as compared with the saturated hydrocarbons, the more polar solvent, chloroform, markedly increases the hypsochromic effect of $m$-directing groups but decreases the bathochromic effect of $o,p$-directing groups.

As expected, chloroform (as well as alcohol) also tends to destroy the fine structure exhibited by the spectra of many of these compounds in alkane solutions. Chloroform is preferable, however, in the respect that some of the substituted azulenes, such as the dinitro compound, are readily soluble in chloroform but practically insoluble in saturated hydrocarbons.

(10) *Cf.* W. T. Simpson, *J. Chem. Phys.*, **16**, 1124 (1948).

(11) *Cf.* G. N. Lewis, *Chem. Revs.*, **25**, 273 (1939); also K. Hirayama, THIS JOURNAL, **77**, 373 (1955).

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# Sterol Models. I. 3a-Methyl-*cis*- and -*trans*-hexahydroindans and their -3a-Methyl-$d_3$ Analogs[1]

BY RICHARD L. KRONENTHAL[2] AND ERNEST I. BECKER[3]

The independent and unequivocal syntheses of 3a-methyl-*cis*- and -*trans*-hexahydroindan and several of their deuteromethyl analogs have been achieved through stereospecific reactions. Through a Diels–Alder synthesis, a methoxycarbonyl group was locked into the *cis*-configuration at the angular position of a tetrahydroindan and transformed, *via* the saturated angular ester, hydroxymethyl and corresponding tosylate of the latter, to the desired 3a-methyl-*cis*-hexahydroindan. By employing the appropriate combinations of lithium aluminum hydride and lithium aluminum deuteride, the mono-, di- and trideuteromethyl-*cis*-hexahydroindans also were obtained. 3a-Methyl-*trans*-hexahydroindan was attained through 4a-ethoxycarbonyl-*trans*-3,4,4a,5,6,7,8,8a-octahydro-2-[1H]-naphthalenone. After the oxo group was converted to the corresponding dioxolane, the angular ester was reduced to the hydroxymethyl group and then to the angular methyl group through the tosylate and benzyl thioether. After hydrolysis of the dioxolane, the resulting methyldecalone was oxidatively cleaved, recyclized to the corresponding hydrindanones and finally reduced to 3a-methyl-*trans*-hexahydroindan. By starting with the dioxolane ester and using lithium aluminum deuteride and deuterated Raney nickel, the corresponding deuterium containing analogs were obtained.

## Introduction

Until it was shown in the present work that butadiene could be made to undergo an unequivocal *cis*-addition to a cyclopentenodienophile resulting in an angularly substituted *cis*-tetrahydroindan, no direct stereospecific synthesis of a *cis*- or a *trans*-hexahydroindan containing a substituent only at 3a- had been reported.[4] In almost all other

routes described in the literature,[5-8] both isomers may be formed with one usually predominating. Because the ultimate aim of the present work was to obtain compounds for infrared studies and because infrared determinations are, in general, sensitive enough to be affected by small amounts of impurities, the previously available route to the

(1) (a) This work was supported by the National Institutes of Health, Grant G-3124. (b) Presented in part at the 127th Meeting of the American Chemical Society, March 29–April 7, 1955, Cincinnati, Ohio, Abstracts, 49-N.

(2) Taken from the Dissertation submitted to the Graduate Faculty of the Polytechnic Institute of Brooklyn in partial fulfillment of the requirements for the degree of Doctor of Philosophy, 1955.

(3) To whom inquiries should be directed.

(4) Stereospecific syntheses of more highly substituted hexahydroin-

dans have been accomplished; *cf.* E. Dane, J. Schmitt and C. Rautenstrauch, *Ann.*, **532**, 29 (1937), and W. Bockemuller, U. S. Patent 2,179,809; *C. A.*, **34**, 1823 (1940).
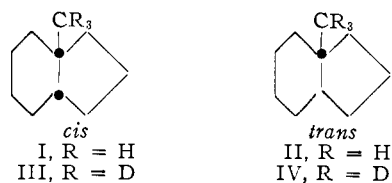
(5) For earlier references, see E. Josephy and F. Radt, "Elsevier's Encyclopaedia of Organic Chemistry," Vol. XIIA, p. 105 ff.

(6) W. E. Bachmann and E. K. Raunio, THIS JOURNAL, **72**, 2530 (1950).

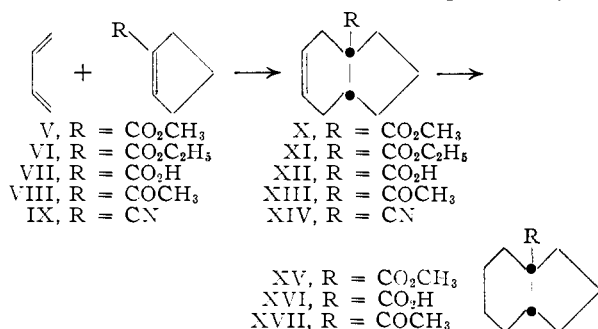(7) C. A. Grob and J. A. Rumpf, *Helv. Chim. Acta*, **37**, 1479 (1954).

(8) D. K. Banerjee and P. R. Schafer, THIS JOURNAL, **72**, 1931 (1950).

3a-methylhexahydroindans (I, II) was felt to be unsatisfactory.



cis
I, R = H
III, R = D

trans
II, R = H
IV, R = D

### The cis-Series

The experimental approach to 3a-methyl-cis-hexahydroindan (I) and its deuteromethyl analogs was based on the Diels–Alder reaction. The necessary electrophilic group of the dienophile served as the potential methyl group, vital in light of the projected deuterium syntheses. In addition, this group is stereochemically fixed at the ring fusion by virtue of the known cis-addition of the diene to the dienophile.[9] Methyl cyclopenten-1-yl ketone (VIII) when heated with butadiene was converted to the adduct XIII which, upon catalytic



V, R = CO₂CH₃
VI, R = CO₂C₂H₅
VII, R = CO₂H
VIII, R = COCH₃
IX, R = CN

X, R = CO₂CH₃
XI, R = CO₂C₂H₅
XII, R = CO₂H
XIII, R = COCH₃
XIV, R = CN

XV, R = CO₂CH₃
XVI, R = CO₂H
XVII, R = COCH₃

hydrogenation afforded XVII. Hypochlorite oxidation of XVII followed by esterification with diazomethane produced the acid XVI and its methyl ester XV, respectively. Both of these compounds (XV and XVI) were, however, also directly available in good yield by employing cyclopenten-1-carboxylic acid (VII) or its methyl ester V in the Diels–Alder synthesis with butadiene, followed by catalytic hydrogenation of the adduct.

Cyclopenten-1-carbonitrile (IX) was also heated with butadiene at 200°. Pure XIV never was isolated.

V and IX were prepared by a method modeled after a procedure[10] for the corresponding cyclohexane derivatives. Cyclopentanone cyanohydrin was prepared from the sodium bisulfite adduct of cyclopentanone. Acetylation followed by pyrolysis afforded cyclopenten-1-carbonitrile which underwent either alcoholysis or hydrolysis and esterification to methyl cyclopenten-1-carboxylate (V).

Methyl cyclopenten-1-yl ketone (VIII) was prepared by the direct acetylation of cyclopentene under Friedel–Crafts conditions.

An alternate route to XII has been devised[11] employing 2-ethoxycarbonylcyclopentanone as the starting material. This was converted to VI in 68% yield by catalytic hydrogenation followed by

dehydration. The Diels–Alder synthesis with butadiene afforded XI, saponification of which yielded XII.

The reduction of XV to a 3a-hydroxymethyl-cis-hexahydroindan (XVIII) with lithium aluminum hydride (LAH) initiated the stepwise conversion of the angular ester to a methyl group. It was then proposed to convert XVIII to the corresponding alkyl halide XIX. Hydrolysis of the



CO₂CH₃        CH₂OH        CH₂R
XV            XVIII        XIX
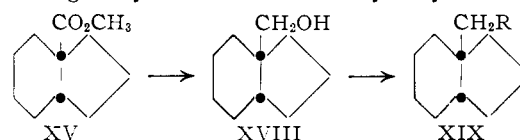
Grignard derivative of XIX would then afford I. However, treatment of the alcohol with thionyl



XVIII  →(1, SOCl₂ / 2, Δ)→  (structure)  →(1, Mg / 2, H₂O)→ XIX
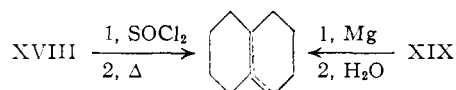
chloride in carbon tetrachloride caused the formation of what is thought to be a relatively stable sulfite ester.[12,13] Attempted distillation of the sulfite ester caused a rearrangement of the neopentyl system to a hydronaphthalene structure. Analysis of the rearranged material agreed with that for an octalin. Absence of a band at 1380 cm.⁻¹ indicated no methyl group. This substance added bromine, decolorized permanganate solutions and was dehydrogenated to naphthalene by hot sulfur. However, attempts to isolate a crystalline dibromide or a nitroso chloride failed. On this basis, the product might possibly be a mixture of octalins or a bicyclic isomer.

The desired halide XIX was finally prepared by a slightly modified procedure[14] for converting neopentyl alcohol to neopentyl bromide. Phosphorus-(III) bromide and quinoline in bromobenzene converted XVIII to XIX (R = Br). That rearrangement to a hydronaphthalene derivative, e.g., 4a-bromodecahydronaphthalene, did not occur here is indicated by the inertness of the angular bromide toward Grignard formation,[15] a reaction which XIX easily underwent. Although an analytically pure sample was never obtained, the redistilled bromide reacted readily with magnesium in anhydrous ether. Hydrolysis of the Grignard complex resulted in a product identical to that obtained in the rearrangement of XVIII and not in the expected 3a-methylhexahydroindan.

Successful reduction of the angular hydroxymethyl group to the hydrocarbon was finally realized through the sequence XVIII → XX → I. Conversion of the alcohol to XX proceeded smoothly in cold pyridine. Displacement of the



CH₂OTs        CH₃
XVIII →       XX            I

(9) M. C. Kloetzel, "Organic Reactions," Vol. IV, edited by R. Adams, John Wiley and Sons, Inc., New York, N. Y., 1948, pp. 10 ff.

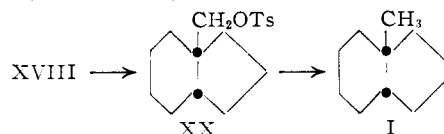(10) E. R. Burns, D. T. Jones and P. D. Ritchie, J. Chem. Soc., 400 (1935).

(11) This procedure was developed and carried out in the laboratory of Professor Ernest L. Eliel of the University of Notre Dame.

(12) W. Gerrard, A. Nechvatal and B. M. Wilson, J. Chem. Soc., 2088 (1950).

(13) W. Gerrard and P. Tolcher, ibid., 3640 (1954).

(14) L. H. Sommer, H. D. Blankman and P. C. Miller, THIS JOURNAL, 73, 3542 (1951).

(15) G. R. Clemo and J. Ormston, J. Chem. Soc., 1778 (1932).

tosylate by LAH[16] resulted in good yields of stereochemically pure I.

The synthesis of 3a-methyl-$d_3$-hexahydroindan (III) was achieved with equal facility by employing lithium aluminum deuteride (LAD) in both the

XV $\xrightarrow{\text{LAD}}$ XXI → XXIV

XXI → (LAD) → III

XXIV $\downarrow$ LAH → XXIII

XX $\xrightarrow{\text{LAD}}$ XXII
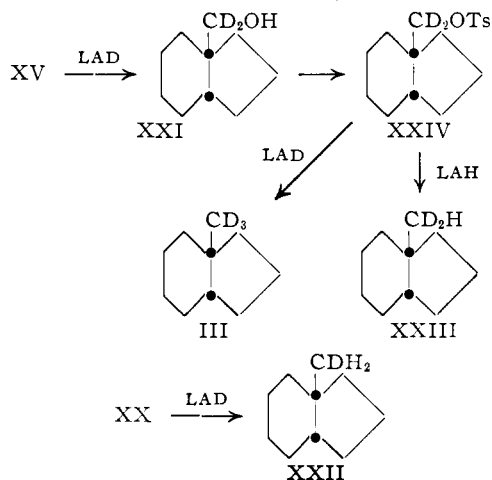
reduction of the ester and in the displacement of the tosylate. The mono- and di-deuteromethyl compounds, XXII and XXIII, respectively, were also prepared by employing the appropriate combinations of LAH and LAD (see diagram above). A stereochemically unequivocal series of four successively deuterated 3a-methyl-cis-hexahydroindans was thus obtained.

### The trans-Series

Several unsuccessful attempts at the synthesis of 3a-methyl-trans-hexahydroindan (V) were made. Treatment of the cis-isomer with aluminum chloride isomerized it to a material possessing a methyl group but whose infrared spectrum was later shown to be different from the actual trans-isomer. Most probable structures for this substance are 1-methyl-spiro[4,4]nonane or a non-angular methylhydrindan.

In view of Linstead's plausible hypothesis[17] that there is a steric factor arising from the angular group which prevents the molecule from facing the catalyst in any position other than that which results in the trans-isomer, it was felt that compounds of the type XXV would most likely undergo hydrogenation in such a manner as to give the trans-configuration at the ring fusion. Two separate experimental approaches were attempted for the synthesis of XXV. They were equally unfruitful. The Diels–Alder reaction employing ethyl 2-

XXV
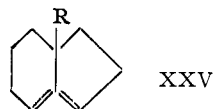
acetoxycyclopenten-1-carboxylate (XXVI) and ethyl 2-chlorocyclopenten-1-carboxylate (XXVII) as dienophiles failed to give adducts. An attempt to convert XV to XXV through the tertiary bromide with N-bromosuccinimide met with a similar fate.

(16) Cf. H. Schmid and P. Karrer, Helv. Chim. Acta, **32**, 1371 (1949).

(17) R. P. Linstead, W. v. E. Doering, S. B. Davis, P. Levine and R. R. Whetstone, This Journal, **64**, 1985 (1942).

It had been suggested[18] that catalytic hydrogenation transformed XXVIII to the cis-decahydronaphthalenone derivative XXIX. On this basis, an attempt was made to obtain the more stable trans-isomer XXX through a chemical reduction.

XXVIII + →

XXVIII → cis, XXIX; trans, XXX
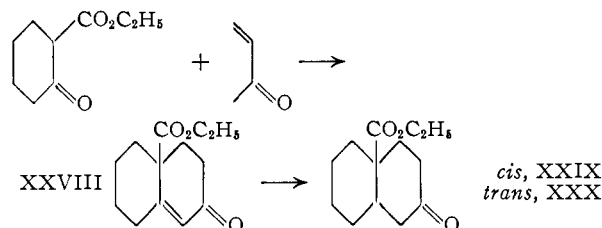
XXVIII was found to react rapidly with two equivalents of lithium in an anhydrous ammonia–ether system yielding a mixture of hydroxy and keto esters.[19] Chromic acid oxidation of this mixture afforded what was probably a mixture of the cis- and trans-isomers XXIX and XXX. This route to XXX was quickly abandoned with the report[20,21] that the product of catalytic hydrogenation of XXVIII was predominantly the trans- and not the cis-isomer.

At this point two routes seemed open for reaching 3a-methyl-trans-hexahydroindan. The first, requiring oxidative ring opening of XXX, failed when hot nitric acid did not produce a pure diacid,

XXX → →

→ =O → XXXI
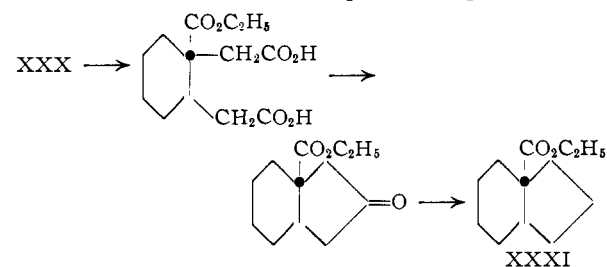
the precursor of XXXI. The ultimately successful synthesis involved the protection of the ketone function of XXX through its dioxolane derivative, while reductive operations on the ester outlined in Chart I converted the ester to a methyl group. The dioxolane (XXXII) was prepared in excellent yield through an acid-catalyzed exchange reaction with 2,2-ethylenedioxybutane.[24] Although LAH readily converted XXXII to the alcohol XXXIII, presumably steric factors prohibited its use in the displacement of the corresponding tosylate derivative XXXIV in order ultimately to obtain XXXV[21]; the tosylate was, however, readily converted to the corresponding benzyl thioether[18,25] which underwent hydrogenolysis over nickel and then acid

(18) A. S. Hussey, H. P. Liao and R. H. Baker, ibid., **75**, 4727 (1953).

(19) Cf. E. E. van Tamelen and W. C. Proost, Jr., ibid., **76**, 3632 (1954).

(20) A. S. Hussey and R. H. Baker, private communication, April 3, 1955.

(21) M. Idelson, Ph.D. Dissertation, Polytechnic Institute of Brooklyn, 1955. Other investigators have independently reported the same conclusion.[22,23]

(22) W. G. Dauben, R. C. Tweit and R. L. MacLean, This Journal, **77**, 48 (1955).

(23) A. S. Dreiding and A. J. Tomasewski, ibid., **77**, 168 (1955).

(24) H. J. Dauben, Jr., B. Löken and H. J. Ringold, ibid., **76**, 1359 (1954).

(25) F. G. Bordwell, B. M. Pitt and M. Knell, ibid., **73**, 5004 (1951).

CHART I
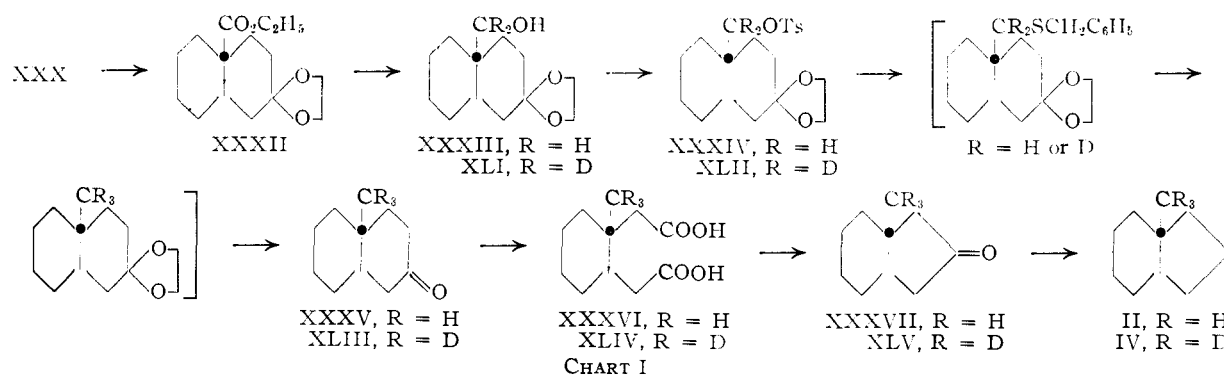


hydrolysis to afford **XXXV**, a previously known compound.[26] Although the boiling point of **XXXV** agreed well with that recorded in the literature, there was an unexplained difference in the refractive index.

Refluxing concentrated nitric acid effectively oxidized **XXXV** to a dicarboxylic acid in 50% yield. Concurrently, this oxidation had also been reported to give the same diacetic acid.[27] Oxidation to the diacetic acid (**XXXVI**) rather than to the propionic-carboxylic acid (**XXXVIII**) was essential since the latter would, on cyclization to the hexahydroindanone (**XXXIX**), give rise to an enolizable angular hydrogen. The latter could
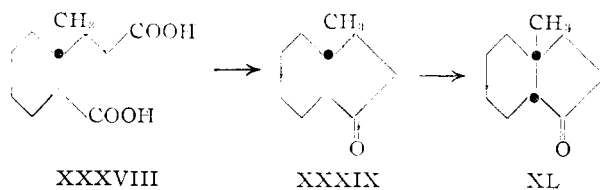
almost certainly be expected to revert to the more stable cis-configuration **XL**, either during the cyclization or during the subsequent reduction to the hydrocarbon. That such enolization and isomerization does not occur is evidenced by the complete absence of strong absorption bands occurring in the infrared spectrum of **I** from the corresponding spectrum of **II** derived from **XXXV** (see Fig. 1).

It should be mentioned that a dibasic acid obtained by an oxidative cleavage of the 3-carboxy derivative of **XXXV** has been characterized and reported in the literature[28] as being **XXXVI** or **XXXVIII** or its cis-isomer, no specific assignment having been made. On the basis of the evidence cited above, the assignment of structure **XXXVI** to this acid seems most justifiable. A mixed melting point determination with **XXXVI** and its authentic cis-isomer (prepared by the oxidation of the known 4a-methyl-cis-3,4,4a,5,6,7,8,8a-octahydro-2-[1H]-naphthalenone) was strongly depressed, obviating any possibility that **XXXVI** might have the cis-configuration.[24,29]

Pyrolytic cyclization of **XXXVI** with barium oxide at 315–320° produced **XXXVII** which was isolated as its semicarbazone. Crystallization followed by regeneration and distillation afforded the pure free ketone **XXXVII** which resisted Clemmensen reduction under conditions only slightly modified from those reported for the reduction of the corresponding cis-isomer.[29] However, **XXXVII** easily was converted to **II** by the Huang-Minlon modification of the Wolff–Kishner reduction.[30]

The corresponding deuteromethyl hydrocarbon **IV** was prepared by employing LAD in the reduction of **XXXII** to **XLI** and deuterated sponge nickel catalyst in the cleavage of the thioether. For a reason not understood, the conversion of **XLII** to **XLIII** proceeded in poor yield when compared with the analogous experiment in the hydrogen series. However, the recovery of a substantial amount of what was believed to be the ketone corresponding to **XLII** seemed to indicate that the benzyl thioether had not been formed in high yield. All other transformations were accomplished in a manner identical to those employed for the hydrogen analogs as shown in Chart I.

## Experimental[31]

**Ethyl 2-Acetoxycyclopenten-1-carboxylate (XXVI).**—Directions for the preparation of ethyl acetoxycrotonate[32] were followed. Acetyl chloride (57.5 g., 0.73 mole) was added to a solution of 78.5 g. (0.50 mole) of 2-ethoxycarbonylcyclopentanone in 79 g. (1.0 mole) of redistilled pyridine. The mixture was allowed to stand for two days. It was then diluted with ether, filtered and the filtrate was washed with two 300-ml. portions of 10% sodium hydroxide, two 300-ml. portions of 10% sulfuric acid and finally with water. The ethereal solution was dried, concentrated and distilled, yielding 76 g. (0.38 mole, 77%) of **XXVI**, b.p. 134° (20 mm.), $n^{23}D$ 1.4596, $d^{23}{}_4$ 1.0434 (reported[33] 130° (17 mm.)).

*Anal.* Calcd. for $C_{10}H_{14}O_4$: C, 60.59; H, 7.12; $R^{23}D$ 49.02. Found: C, 60.24; H, 7.24; $R^{23}D$ 51.99.

**Attempted Diels–Alder Reaction with XXVI and XXVII.**[34]—Both **XXVI** and **XXVII** were heated with an excess of butadiene at 200° in a stainless steel autoclave. After 24 hr., each mixture was distilled, but no appreciable amount of high-boiling material which might have been adduct was obtained.

**Methyl** cis-3a,4,7,7a-Tetrahydroindan-3a-yl **Ketone (XIII).**—A sealed Carius tube containing 47.5 g. (0.43 mole)

(26) R. B. Woodward, F. Sondheimer, D. Taub, K. Heusler and W. M. McLamore, THIS JOURNAL, **74**, 4223 (1952).

(27) B. Riniker, J. Kalvoda, D. Arigoni, A. Fürst, O. Jeger, A. M. Gold and R. B. Woodward, *ibid.*, **76**, 313 (1954).

(28) A. S. Dreiding and A. J. Tomasewski, *J. Org. Chem.*, **19**, 241 (1954).

(29) A. P. Linstead, A. F. Millidge and A. L. Walpole, *J. Chem. Soc.*, 140 (1937).

(30) Huang-Minlon, THIS JOURNAL, **71**, 3302 (1949).

(31) Unless otherwise stated, melting points are corrected, boiling points are not. All organic solutions were dried with anhydrous magnesium sulfate. Microanalyses were performed by Dr. K. Ritter, Basel, Switzerland, deuterium analyses by Mr. B. Arison, Merck and Co., Rahway, N. J. Infrared spectra were recorded on a Perkin–Elmer Infrared Spectrophotometer Model 21.

(32) L. Claisen and E. Haase, *Ber.*, **33**, 1242 (1900).

(33) H. Gault and L. Daltroff, *Compt. rend.*, **209**, 997 (1939).

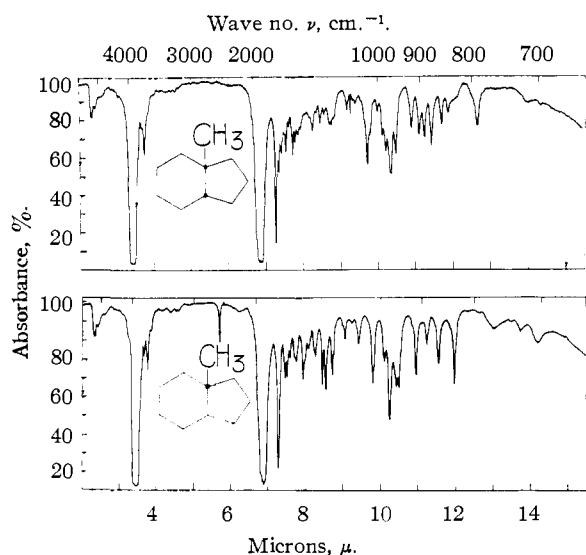(34) W. S. Rapson and R. Robinson, *J. Chem. Soc.*, 1540 (1935).

Fig. 1.—Infrared spectra of 3a-methyl-*cis*-hexahydroindan
and of 3a-methyl-*trans*-hexahydroindan.

of VIII[35] (b.p. 48–50° (10 mm.)) and 50 g. (0.92 mole) of
freshly distilled butadiene was heated at 200° for 24 hr.
Distillation yielded a forerun weighing 23.3 g., b.p. 28–50°
(9 mm.), which consisted mainly of vinylcyclohexene and
unreacted VIII. A second fraction, 20 g., b.p. 70–115° (9
mm.), was separated from an undistillable polymeric residue.
Fractionation of the high boiling material afforded 16 g.
(0.098 mole, 23%) of XIII, b.p. 78–78.2° (2.4 mm.), $n^{25}$D
1.4890, $d^{25}_4$ 0.9865, which decolorized a solution of bromine in
carbon tetrachloride without evolution of hydrogen bromide
and discharged the purple color of alkaline potassium per-
manganate solution.

*Anal.* Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.82; $R^{25}$D
48.14. Found: C, 80.58; H, 9.95; $R^{25}$D 48.05.

The **2,4-dinitrophenylhydrazone** of XIII was prepared by
refluxing the ketone with an excess of 2,4-dinitrophenylhy-
drazine in acidified 95% ethanol for 15 minutes. The small
yellow needles which formed on cooling were recrystallized
three times from absolute ethanol and once from petroleum
ether (b.p. 90–100°), m.p. 130.5–131°.

*Anal.* Calcd. for $C_{17}H_{20}N_4O_4$: C, 59.29; H, 5.85; N,
16.27. Found: C, 59.09; C, 5.89; N, 16.20.

**Methyl *cis*-Hexahydroindan-3a-yl Ketone (XVII).**—A
solution of 11.2 g. (0.068 mole) of XIII in 30 ml. of absolute
ethanol was hydrogenated over Raney nickel catalyst[36] at
room temperature. The hydrogenation required 10 minutes
for completion, at an initial pressure of 3 atmospheres.
Distillation of the filtered solution yielded 11 g. (0.066 mole,
97%) of XVII, b.p. 77° (3 mm.), $n^{25}$D 1.4789, $d^{25}_4$ 0.9723.

*Anal.* Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.91; $R^{25}$D
48.61. Found: C, 79.47; H, 11.03; $R^{25}$D 48.48.

**Methyl *cis*-3a,4,7,7a-Tetrahydroindan-3a-carboxylate (X).**
—A mixture of 153 g. (1.12 moles) of V and 400 ml. (240 g.,
4.44 moles) of freshly distilled butadiene was heated at 200°
in a stainless steel hydrogenation bomb for 24 hr. The re-
sulting light yellow liquid was rapidly distilled under vac-
uum from polymer and redistilled through a fractionating
column.[32] A forerun of low boiling vinylcyclohexene was
followed by 45 g. (0.33 mole) of V, b.p. 74° (24 mm.) and
117 g. (0.65 mole, 75%) of X, b.p. 119–120° (23 mm.),
$n^{25}$D 1.4837; $d^{25}_4$ 1.0413.

*Anal.* Calcd. for $C_{11}H_{16}O_2$: C, 73.30; H, 8.95; $R^{25}$D
49.78. Found: C, 73.10; H, 8.94; $R^{25}$D 49.49.

***cis*-3a,4,7,7a-Tetrahydroindan-3a-carboxylic Acid (XIII).**
**A.**—A solution containing 11.2 (0.10 mole) of VII[37] in 30

(35) W. S. Rapson and R. Robinson, *J. Chem. Soc.*, 1285 (1935);
b.p. 75–78° (22 mm.).

(36) R. Mozingo in "Organic Syntheses," Coll. Vol. III, edited by
E. C. Horning, John Wiley and Sons, Inc., New York, N. Y., 1955, p.
181.

(37) R. P. Linstead and A. H. Cook, *J. Chem. Soc.*, 956 (1934).

ml. (18 g., 0.33 mole) of freshly distilled butadiene was
heated at 200° for 24 hr. in a stainless steel autoclave. Upon
cooling the resulting mixture, 8.5 g. (0.05 mole, 50%) of
XII was deposited as white needles, which were dissolved in
10% sodium hydroxide. The alkaline solution was ex-
tracted with benzene followed by ether, heated on the steam-
bath for 30 minutes, cooled and acidified with concentrated
hydrochloric acid. The free acid was collected and dried
overnight under vacuum over barium oxide, m.p. 77.5–
78.5°. Three crystallizations, effected by dissolving the
acid in warm glacial acetic acid, adding water until the solu-
tion became saturated and slowly cooling, raised the melting
point to 80.0–80.5°.

*Anal.* Calcd. for $C_{10}H_{14}O_2$: C, 72.26; H, 8.49; neut.
equiv., 166.2. Found: C, 71.64; H, 8.41; neut. equiv.,
167.9.

**B.**[11]—Following a procedure described by Adkins[38] for the
reduction of ethyl acetoacetate, 156 g. (1.0 mole) of 2-
ethoxycarbonylcyclopentanone,[39] dissolved in 300 ml. of
absolute ethanol, was hydrogenated in a stainless steel
bomb at 125° and 1200–1500 p.s.i. in the presence of 5 g. of
Raney nickel. One mole of hydrogen was taken up in about
2.5 hr. Filtration, concentration and distillation of the prod-
uct gave 125 g. (0.79 mole, 79%) of 2-ethoxycarbonylcyclo-
pentanol collected at 72–73° (1.4 mm.) (reported[40] 110–
111° (12 mm.)), $n^{25}$D 1.4549.

The *p*-**toluenesulfonate**, prepared by means of *p*-toluene-
sulfonyl chloride in cold pyridine, melted at 111–113°.

*Anal.* Calcd. for $C_{15}H_{20}O_5S$: C, 57.67; H, 6.45. Found:
C, 57.84; H, 6.88.

The above alcohol was converted to VI by the following
procedure, which was the best of several tried. To an ice-
cold solution of 50 g. (0.317 mole) of 2-ethoxycarbonylcyclo-
pentanol in 140 ml. of pyridine was added 66 g. (0.346 mole)
of *p*-toluenesulfonyl chloride in small portions. The mix-
ture was then refluxed for 3 hr., cooled and poured into 500
ml. of ice-cold 0.4 *N* hydrochloric acid. The resulting oil
was separated from the water layer and the latter extracted
three times with ether. The combined oil and ether layer
was dried over anhydrous sodium sulfate, filtered, concen-
trated and distilled, to yield 38.1 g. (0.272 mole, 86%) of VI,
b.p. 73–74° (13 mm.), $n^{25}$D 1.4594 (reported[41] b.p. 75° (10
mm.)).

To obtain the dicyclic ester XI a stainless steel bomb was
charged with 18.9 g. (0.135 mole) of VII and 30 g. (0.55
mole) of liquid butadiene, sealed and heated with rocking at
200° for 25 hr. After cooling, the contents of the bomb was
dissolved in ether and flash-distilled at water-pump vacuum
to free it from polymeric material. Fractionation of the dis-
tillate yielded 10.1 g. of XI, b.p. 108° (10 mm.), $n^{25}$D
1.4775. An additional 0.6 g. could be recovered by steam
distillation of the original polymeric residue bringing the
total yield to 41%. Saponification of the ester with aque-
ous alcoholic potassium hydroxide followed by acidification
gave the corresponding acid (XII), m.p. 79–80°.

***cis*-Hexahydroindan-3a-carboxylic Acid (XVI). A. From
XVII.**—A mixture of 200 g. (2.3 mole) of potassium hypo-
chlorite in 1.5 l. of water and 95 g. (0.57 mole) of XVII was
heated with stirring at 65° until no hypochlorite remained
(acidified potassium iodide test). The cooled, alkaline solu-
tion was extracted twice with ether and the combined ex-
tracts were evaporated. The residue, which consisted
mainly of unreacted XVII, was again treated with hypo-
chlorite solution as before, a total of four passes through the
hypochlorite being required. The combined aqueous solu-
tions were freed from excess hypochlorite with solid sodium
bisulfite, acidified with concentrated hydrochloric acid and
extracted twice. After drying, the ether was removed and
the residue distilled to give 30.2 g. (0.18 mole, 32%) of
XVI, b.p. 129.5° (3 mm.), $n^{25}$D 1.4885. The acid is dif-
ficultly crystallized from methanol–water mixtures yielding a
white, waxy solid, m.p. 43.5–45.5°.

**B. From XII.**—Two and three-tenths grams (0.014 mole)
of XII was dissolved in 50 ml. of methanol and hydrogenated
over Raney nickel catalyst at about 3 atmospheres pressure.

(38) H. Adkins, R. Connor and H. Cramer, THIS JOURNAL, **52**,
5192 (1930).

(39) P. S. Pinkney, "Organic Syntheses," Coll. Vol. II, edited by
A. H. Blatt, John Wiley and Sons, Inc., New York, N. Y., 1943, p. 116.

(40) W. Dieckmann, *Ann.*, **317**, 64 (1901).

(41) A. H. Cook and R. P. Linstead, *J. Chem. Soc.*, 959 (1934).

When absorption ceased, the solvent was removed from the filtered mixture and the residue distilled to give 1.5 g. (0.009 mole, 64%) of an oil, b.p. 118–119° (1–2 mm.). Recrystallization from acetic acid–water mixtures gave an analytical sample melting at 49°.

*Anal.* Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59; neut. equiv., 168.2. Found: C, 70.95; H, 9.31; neut. equiv., 169.5.

**Methyl *cis*-Hexahydroindan-3a-carboxylate (XV). A. From XVI.**—A solution of 31 g. (0.18 mole) of XVI in 1 l. of absolute ether was cooled to 0° and 20 g. (0.48 mole) of diazomethane[42] dissolved in 300 ml. of absolute ether was added. Distillation of the residue, after removing the ether, afforded 27 g. (0.15 mole, 83%) of XV, b.p. 86° (4 mm.), $n^{25}$D 1.4701, $d^{25}_4$ 1.0156.

*Anal.* Calcd. for $C_{11}H_{18}O_2$: $R^{25}$D 50.25. Found: $R^{25}$D 50.08.

**B. From X.**—Two hundred and seventy grams (1.5 moles) of X was dissolved in 300 ml. of methanol and hydrogenated batchwise, at three atmospheres, over Raney nickel catalyst.[36] The pooled solutions were freed of solvent and distilled to yield 266 g. (1.46 mole, 97.5%) of XV, b.p. 115–117° (most at 116°) (20 mm.).

*Anal.* Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.57; H, 9.87.

**3a-Hydroxymethyl-*cis*-hexahydroindan (XVIII).**—In a flask protected from moisture a suspension of 5 g. (0.13 mole) of LAH in 150 ml. of anhydrous ether was refluxed with stirring for 3 hr. A solution of 45 g. (0.25 mole) of XV in 100 ml. of anhydrous ether was then added at such a rate that gentle reflux ensued. After the addition was complete, the mixture was refluxed for 3 hr. and allowed to stand overnight. Excess hydride was decomposed with wet ether followed by 100 ml. of saturated aqueous ammonium chloride. After separating the ether phase and extracting the aqueous layer with three 50-ml. portions of fresh ether, the combined organic solutions were washed five times with water and dried. Removal of the ether followed by distillation at reduced pressure gave 36.5 g. (0.24 mole, 96%) of XVIII, b.p. 84° (2 mm.), $n^{25}$D 1.4921; $d^{25}_4$ 0.9861, which solidified on standing, m.p. 29.5–30.5°.

*Anal.* Calcd. for $C_{10}H_{18}O$: C, 77.87; H, 11.76; $R^{25}$D 45.51. Found: C, 77.68; H, 11.57; $R^{25}$D 45.39.

**The 3,5-dinitrobenzoate** of XVIII was prepared from the alcohol and 3,5-dinitrobenzoyl chloride. The ester was washed with sodium carbonate and crystallized five times from 95% ethanol after treatment with Nuchar; m.p. 88.0–88.5°.

*Anal.* Calcd. for $C_{17}H_{20}N_2O_6$: C, 58.61; H, 5.79; N, 8.04. Found: C, 58.68; H, 5.89; N, 8.12.

**3a-Hydroxymethyl-$d_2$-*cis*-hexahydroindan (XXI).**—To a stirred solution of 13.02 g. (0.31 mole) of LAD in 400 ml. of anhydrous ether was slowly added 82.77 g. (0.455 mole) of XV in an equal volume of ether. After refluxing for 30 hr. and standing at room temperature for 2.5 days, the excess LAD was destroyed with ethyl acetate. Hydrolysis was effected as for XVIII. The aqueous phase was extracted four times with 50-ml. portions of ether and the combined organic layers were washed with dilute sodium bicarbonate and water. Drying, concentration and two successive distillations afforded 55 g. (0.35 mole, 77%) of XXI, b.p. 79° (1 mm.), which solidified in the receiver, m.p. 29.5–30.5°.

*Anal.* Calcd. for $C_{10}H_{16}D_2O$: C, 76.92; H+D as H, 11.75. Found: C, 77.12; H+D as H, 11.58.

**$p$-Toluenesulfonate of 3a-Hydroxymethyl-*cis*-hexahydroindan (XX).**—Recrystallized (from hexane) $p$-toluenesulfonyl chloride (33 g., 0.173 mole) was added to a cold solution of 24.5 g. (0.159 mole) of XVIII in 160 ml. of pyridine previously fractionated from calcium hydride. After standing for three days in the refrigerator, the mixture was poured onto excess ice. The solid was washed with dilute hydrochloric acid and water. After three crystallizations from absolute ethanol (saturation at 25° and filtration at −80°), the analytical sample melted at 37.5–38°. One crystallization of the crude tosylate gave 47 g. (0.153 mole, 96%) of XX, m.p. 37.0–37.5°.

*Anal.* Calcd. for $C_{17}H_{24}O_3S$: C, 66.20; H, 7.84; S, 10.39. Found: C, 66.13; H, 7.65; S, 10.28.

**$p$-Toluenesulfonate of 3a-Hydroxymethyl-$d_2$-*cis*-hexahydroindan (XXIV).**—This material was prepared in 87% yield by the procedure described for XX. The melting point of the analytical sample was 37.5–38.5°.

*Anal.* Calcd. for $C_{17}H_{22}D_2O_3S$: C, 65.77; H+D as H, 7.87; S, 10.33. Found: C, 66.13; H+D as H, 7.96; S, 10.30.

**3a-Bromomethyl-*cis*-hexahydroindan (XIX).**—To an ice-cold solution of 16.26 g. (0.06 mole) of phosphorus(III) bromide in 8.39 g. (0.065 mole) of redistilled quinoline was added 9.24 g. (0.06 mole) of XVIII dissolved in 30 g. of bromobenzene. The reaction temperature was kept below 25° during the addition. After the temperature ceased to rise spontaneously, the mixture was refluxed overnight, cooled, poured into water and filtered. The filtrate was extracted twice with ether and the combined extracts (100 ml.) were washed twice with 10% hydrochloric acid followed by saturated sodium bicarbonate until the washings were alkaline. After washing with water and drying, distillation afforded 8.5 g. of crude XIX, redistillation of which yielded 7 g. (0.032 mole, 54%) of XIX, b.p. 66° (0.8 mm.), $n^{25}$D 1.5162, $d^{25}_4$ 1.2735. This compound did not give analytically correct results for C and H, possibly resulting from the ease with which it loses hydrogen bromide.

*Anal.* Calcd. for $C_{10}H_{17}Br$: C, 55.30; H, 7.89; $R^{25}$D 51.75. Found: C, 57.42; H, 8.24; $R^{25}$D 51.52.

**"Octalin." A. From XVIII.**—A solution of 5.1 g. (0.033 mole) of XVIII in 20 ml. of carbon tetrachloride was slowly added to an ice-cold solution of 4.76 g. (0.04 mole) of purified thionyl chloride[43] in 30 ml. of carbon tetrachloride. After the initial reaction had subsided, the mixture was refluxed for 2 hr., cooled, poured onto ice, washed with saturated aqueous sodium bicarbonate until alkaline and dried. After the solvent was removed, the residue was slowly heated to 290° yielding 3.5 g. of distillate. Two redistillations, the last from sodium, afforded 2 g. (0.015 mole, 45%) of "octalin," b.p. 68° (7.5 mm.), $n^{20}$D 1.4955. Literature constants for $\Delta^{4a,8a}$-octahydronaphthalene are b.p. 74° (13 mm.), $n^{20}$D 1.4984.[44]

*Anal.* Calcd. for $C_{10}H_{16}$: C, 88.16; H, 11.84. Found: C, 88.08; H, 11.97.

**B.**—To a suspension of 2.84 g. (0.12 mole) of magnesium in 50 ml. of anhydrous ether was added slowly 12.8 g. (0.059 mole) of XIX, dissolved in 20 ml. of anhydrous ether. After the addition of halide had been completed, reflux was continued for 1.5 hr. Hydrolysis of the Grignard complex was effected with 11.5 ml. of water followed by dilute hydrochloric acid. The aqueous phase was extracted with fresh ether, and the combined organic layers were washed with dilute sodium bicarbonate, water, dried and concentrated. Distillation of the residue afforded 6 g. (0.044 mole, 75%) of crude "octalin," b.p. 69–100° (15–19 mm.).

**Conversion of Octalin to Naphthalene.**—A 1.2-g. sample of pure "octalin" was heated at 275° with 4.6 g. of sulfur. Hydrogen sulfide was evolved and after about 100 mg. of crystals had sublimed into the condenser, the reaction was stopped. The sublimate was twice crystallized from ethanol–water; m.p. 79°. Upon admixture with an authentic sample of naphthalene the melting point was not depressed.

**3a-Methyl-*cis*-hexahydroindan (I).**—A mixture of 17 g. (0.056 mole) of XX and 2.0 g. (0.054 mole) of LAH in 150 ml. of anhydrous ether was refluxed for 48 hr. The excess hydride was destroyed with ethyl acetate and hydrolysis was effected with 10% sulfuric acid. The aqueous phase was extracted once with fresh ether which was combined with the organic layer and washed once with water, three times with 50-ml. portions of 10% sodium hydroxide, with 20% hydrochloric acid until acid and with half-saturated sodium bicarbonate until the washings remained alkaline. Distillation of the dried solution yielded 6.1 g. (0.044 mole, 78%) of crude I, b.p. 70–72° (20 mm.), $n^{25}$D 1.4702. Sixteen grams of this material was dissolved in $n$-hexane which had been previously freed of olefins with concentrated sulfuric acid, washed, dried and fractionated, b.p. 68–70°. The hexane solution was shaken with fresh portions of concentrated sulfuric acid until no yellow color was developed within 20 min-

(42) F. Arndt, "Organic Syntheses," Coll. Vol. II, edited by A. H. Blatt, John Wiley and Sons, Inc., New York, N. Y., 1943. p. 165.

(43) L. F. Fieser, "Experiments in Organic Chemistry," 3rd Ed., D. C. Heath and Co., New York, N. Y., 1955, p. 345.

(44) A. Zlatkis and E. A. Smith, *Can. J. Chem.*, 29, 162 (1951).

utes in succeeding aliquots. After being washed successively with water, saturated sodium bicarbonate and distilled water, the solution was dried and stripped of solvent in the steam-bath. Distillation of the residue from sodium under an atmosphere of nitrogen afforded 10.5 g. of I, b.p. 69–70° (21 mm.), which was finally redistilled at 765 mm., b.p. 176°, m.p. 16–17°, $n^{25}$D 1.4671, $d^{25}_4$ 0.8756.

*Anal.* Calcd. for $C_{10}H_{18}$: C, 86.88; H, 13.12; $R^{25}$D 43.98. Found: C, 87.02; H, 13.24; $R^{25}$D, 43.82.

**3a-Methyl-$d_1$-*cis*-hexahydroindan (XXII).**—A solution of 11.3 g. (0.036 mole) of XX and 1.624 g. (0.038 mole) of LAD in 100 ml. of anhydrous ether was refluxed for eight days and worked up as described for I, except that the distillation prior to the sulfuric acid treatment was omitted. The final distillation afforded 2.5 g. (0.018 mole, 49%) of XXII, b.p. 70° (20 mm.), $n^{25}$D 1.4672, $d^{25}_4$ 0.8798.

*Anal.* Calcd. for $C_{10}H_{17}$D: C, 86.24; H+D as H, 13.10; D/H+D, 5.55; $R^{25}$D 43.98. Found: C, 86.82; H+D as H, 13.02; D/H+D, 4.85 ± 0.07 (87.5%); $R^{25}$D 43.94.

**3a-Methyl-$d_2$-*cis*-hexahydroindan (XXIII).**—Employing the procedure used for the preparation of XXII, 1.6 g. (0.042 mole) of LAH and 11.3 g. (0.035 mole) of XXIV were refluxed for three days in 100 ml. of anhydrous ether. Workup of the reaction mixture yielded 3.5 g. (0.025 mole, 70%) of XXIII, b.p. 70–71° (22 mm.), $n^{25}$D 1.4666, $d^{25}_4$ 0.8868.

*Anal.* Calcd. for $C_{10}H_{16}D_2$: C, 85.63; H+D as H, 13.08; D/H+D, 11.11; $R^{25}$D 43.98. Found: C, 85.53; H+D as H, 13.08; D/H+D, 10.50 ± 0.15 (94.5%); $R^{25}$D 43.94.

**3a-Methyl-$d_3$-*cis*-hexahydroindan (III).**—A mixture of 3.248 g. (0.076 mole) of LAD and 22.6 g. (0.073 mole) of XXIV was refluxed for one week in 250 ml. of anhydrous ether and thence treated as described for XXII. There resulted 6.5 g. (0.046 mole, 64%) of III, b.p. 69° (19 mm.), $n^{25}$D 1.4668, $d^{25}_4$ 0.8923.

*Anal.* Calcd. for $C_{10}H_{15}D_3$: C, 85.02; H+D as H, 13.08; D/H+D, 16.67; $R^{25}$D 43.98. Found: C, 84.86; 84.84; H+D as H, 13.00; 13.08; D/H+D, 15.1 ± 0.2 (90.5%) $R^{25}$D, 43.86.

**Isomerization of 3a-Methyl-*cis*-hexahydroindan (I).**—Approximately 200 mg. of freshly sublimed anhydrous aluminum chloride was added to 2.5 g. (0.018 mole) of IV contained in a tightly stoppered flask. The mixture was allowed to stand for 24 hr. at room temperature during which time the refractive index fell from $n^{25}$D 1.4673 to $n^{25}$D 1.4627. There was no further change on standing over the catalyst for an additional day. The hydrocarbon was decanted and distilled from sodium affording 1.9 g. (0.014 mole, 78%) of product, b.p. 56–57° (11 mm.), $n^{25}$D 1.4621.

*Anal.* Calcd. for $C_{10}H_{18}$: C, 86.88; H, 13.12. Found: C, 86.75; H, 13.15.

**4a-Ethoxycarbonyl-*trans*-3,4,4a,5,6,7,8,8a-octahydro-2-(1H)-naphthalenone (XXX).**—Two hundred and sixty-two grams (1.0 mole) of XXVIII, b.p. 100–139° (2 mm.), $n^{22}$D 1.5141, prepared in 68% yield by the procedure of Idelson[21] was hydrogenated over 2.0 g. of 5% palladium on charcoal in 300 ml. of absolute ethanol containing 10 g. of calcium carbonate. Fractionation of the resulting mixture gave 175 g. of XXX, b.p. 110–118° (0.75 mm.) (most boiling at 117–118°), $n^{25.5}$D 1.4828 [reported 100° (0.5 mm.)[21]; 125–132° (1 mm.),[45] 146–148° (2 mm.),[18] $n^{25}$D 1.4790[21]; $n^{25}$D 1.4801[18]; $n^{25}$D 1.5070[45]].

**4a-Ethoxycarbonyl-2,2-ethylenedioxy-*trans*-decahydronaphthalene (XXXII).**—A solution of 187.5 g. (0.71 mole) of XXX in 475 g. (4.1 moles) of 2-ethylenedioxybutane[24] containing 3 g. of p-toluenesulfonic acid was refluxed for 30 minutes and then slowly distilled through a fractionating column.[39] Methyl ethyl ketone (69 ml., b.p. 79–80°) was first collected. An intermediate fraction of 30 ml., b.p. 81–117°, was followed by 150 ml. of 2-ethylenedioxybutane, b.p. 117–117.5°. The residue, after cooling, was poured into 450 g. of benzene, and the mixture was washed with 100 ml. of dilute sodium bicarbonate and then with water. After drying, the solvent was removed, and distillation of the concentrate yielded 216.5 g. (0.695 mole, 98%) of XXXII, b.p. 122–137° (0.3–1.2 mm.), $n^{25}$D 1.4854. Two additional distillations afforded an analytical sample, b.p. 119–120° (0.4 mm.), $n^{25}$D 1.4854 (reported[45] b.p. 115–122° (0.2 mm.), $n^{23}$D 1.4850).

*Anal.* Calcd. for $C_{15}H_{24}O_4$; C, 67.13; H, 9.02. Found: C, 67.11; H, 8.97.

**2,2-Ethylenedioxy-*trans*-4a-decahydronaphthalenemethanol (XXXIII).**—One hundred grams (0.37 mole) of XXXII dissolved in 130 ml. of anhydrous ether was added slowly to a solution of 13.9 g. (0.366 mole) of LAH in 100 ml. of ether. The mixture was refluxed with stirring for two days. The excess hydride was destroyed with ethyl acetate and the complex was hydrolyzed with water. After extracting the aqueous phase with ether, the combined organic solutions were washed with water, dried, concentrated and distilled, yielding 65 g. (0.288 mole, 77%) of XXXIII, b.p. 137° (0.55 mm.), $n^{25}$D 1.5122 (reported[45] b.p. 135–136° (0.2 mm.)). Yields of nearly 90% have been obtained in other runs.

*Anal.* Calcd. for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80. Found: C, 68.81, 69.05; H, 9.63, 9.92.

**2,2-Ethylenedioxy-*trans*-4a-decahydronaphthalenemethanol-$d_2$ (XLI).**—A mixture of 100 g. (0.375 mole) of XXXII in 50 ml. of anhydrous ether was added slowly to a solution of 11.4 g. (0.27 mole) of LAD in 100 ml. of ether. The reaction mixture was refluxed with stirring for eight days. Treatment with excess ethyl acetate was followed by cautious (at first) dilution to 2 l. with water which was then extracted three times with fresh ether. After adding 1 ml. of pyridine, the combined extracts were washed with water, dried and concentrated. Distillation of the residue afforded 76.5 g. (0.335 mole, 92%) of XLI, b.p. 137–140° (0.7 mm.). A sample was redistilled for analysis, b.p. 136° (0.7 mm.).

*Anal.* Calcd. for $C_{13}H_{20}D_2O_3$: C, 68.38; H+D as H, 9.81; D/H+D, 9.1. Found: C, 68.39; H+D as H, 9.82; D/H+D, 8.6 ± 0.1.

**p-Toluenesulfonate of 2,2-Ethylenedioxy-*trans*-4a-deca-hydronaphthalenemethanol (XXXIV).**—To a cooled solution of 56.5 g. (0.25 mole) of XXXIII in 200 ml. of fractionated anhydrous pyridine was added 52.5 g. (0.28 mole) of recrystallized p-toluenesulfonyl chloride. After standing for two days at room temperature, the mixture was poured into 1 l. of ice-water and the resulting crystalline tosylate, after drying in air (94 g., m.p. 96–108°, sinter at 92°), was recrystallized from ethanol yielding 82.5 g. (0.22 mole, 87%) of XXXIV, m.p. 104–110°. Two crystallizations from benzene, three from methanol and one from petroleum ether (b.p. 30–40°)-benzene afforded the analytical sample, m.p. 115.5–116°.

*Anal.* Calcd. for $C_{20}H_{28}O_5S$: C, 63.13; H, 7.42; S, 8.43. Found: C, 63.28; H, 7.55; S, 8.36.

**p-Toluenesulfonate of 2,2-Ethylenedioxy-*trans*-4a-deca-hydronaphthalenemethanol-$d_2$ (XLII).**—Starting with 68.4 g. (0.30 mole) of XLI and 63 g. (0.40 mole) of p-toluenesulfonyl chloride, XLII was obtained in 89% yield, m.p. 104–107°. Crystallization once from ethanol, three times from methanol and finally from petroleum ether (b.p. 30–40°)-benzene (3:1) gave the analytical sample, m.p. 115.5–116.0°.

*Anal.* Calcd. for $C_{20}H_{26}D_2O_5S$: C, 62.80; H+D as H, 7.43; S, 8.38; D/H+D, 7.14. Found: C, 63.18; H+D as H, 7.57; S, 8.35; D/H+D, 6.8 ± 0.1.

**4a-Methyl-*trans*-3,4,4a,5,6,7,8,8a-octahydro-2(1H)-naphthalenone (XXXV).**—Recrystallized XXXIV (79.8 g., 0.21 mole) was added to a solution of sodium mercaptide (from 8.4 g. of sodium and 42 ml. of α-toluenethiol in 400 ml. of methyl carbitol).[18] After refluxing for 4 hr. and cooling (sodium p-toluenesulfonate precipitates), the mixture was poured into 2 l. of water and extracted three times with 300-ml. portions of ether. The combined extracts were washed twice with 200 ml. of 10% sodium hydroxide and twice with the same volume of water and dried. After the ether was removed on the steam-bath, the residual benzyl thioether was added to 1.2 l. of 95% ethanol containing about 500 g. of sponge nickel[46] which previously had been prepared by washing with water until neutral followed by three washes with 95% ethanol. After the last alcohol treatment, the nickel was shaken with hydrogen at a pressure of three atmospheres for 1 hr.

After refluxing with stirring for 40 hr., the nickel slurry was filtered cautiously (pyrophoric), and the solids were leached twice with 250-ml. portions of boiling ethanol. The

(45) A. S. Dreiding and A. J. Tomasewski, THIS JOURNAL, **77**, 411 (1955).

(46) The sponge nickel catalyst (Lot No. K-00538-1) was obtained from the Davison Chemical Corporation, Baltimore 3, Md.

filtrate was distilled through a column until a volume of about 500 ml. remained whereupon 10 ml. of 1:1 hydrochloric acid–water were added, and the concentration was continued until about 150 ml. remained. This residue was poured into 800 ml. of water and extracted with three 100-ml. portions of Skellysolve A. The combined extracts were washed with half-saturated sodium bicarbonate, then water, dried and concentrated. Distillation of the residue afforded 25.5 g. (0.15 mole, 75%) of XXXV, b.p. 132–140° (18 mm.), $n^{25}$D 1.4929. For analysis a sample was redistilled, b.p. 136° (20 mm.) and $n^{25}$D 1.4903 (reported b.p. 130° (20 mm.)[26]; b.p. 140–150° (10 mm.)[45]; $n^{24}$D 1.4862[26]; $n^{24}$D 1.4872[45]).

*Anal.* Calcd. for $C_{11}H_{18}O$: C, 79.45; H, 10.91. Found: C, 79.12; H, 10.85.

**4a-Methyl-$d_3$-trans-3,4,4a,5,6,7,8,8a-octahydro-2(1H)-naphthalenone (XLIII).**—Deuterated sponge nickel was prepared as follows. About 1 kg. of nickel–water slurry[46] containing approximately 50% solids was washed in a stream of tap water overnight. The neutral catalyst was then washed three times with distilled water followed by three washings with 95% ethanol. This was followed by successive washings with dry dioxane (a centrifuge facilitated this process) until the supernatant liquid showed a negligible reaction with a clean metallic sodium surface. The final centrifugation yielded 475 g. of nickel–dioxane slurry which was considered to be 95% nickel (450 g. nickel). This was suspended in 750 ml. of dry dioxane in a 3-l. flask and shaken with a total of 50 l. of deuterium (99.8% $D_2$).[47] The spent deuterium was flushed with nitrogen and replaced after each 12 hr. of shaking for 12 days (144 hr., 12 hr. shaking per day). The exchange was carried out at an average partial pressure of deuterium of approximately 125 cm.

To a solution of sodium benzyl mercaptide from 52 ml. (0.44 mole) of α-toluenethiol and 10.2 g. (0.44 mole) of sodium in 480 ml. of methyl carbitol was added 99 g. (0.26 mole) of XLII. The mixture was refluxed for 4.5 hr. and allowed to stand overnight under anhydrous conditions. The crude benzyl thioether was oiled out by diluting with 2.5 l. of water which was extracted three times with 300-ml. portions of ether. The combined organic layers were washed twice with 250 ml. of 10% sodium hydroxide and finally with two 500-ml. portions of water. After drying, the solvent was removed yielding 99 g. of crude oil which, along with 10 g. of deuterium oxide was immediately added to the deuterated nickel and refluxed for 40 hr., care being taken to exclude atmospheric moisture. The nickel was removed by filtration and washed thoroughly with fresh dioxane. The solvent was distilled through a column until a volume of 250 ml. remained. Benzene (75 ml.) was now added and then distilled to about 175 ml. to remove traces of water. At this point, 22 ml. of 1:2 hydrochloric acid was added and the mixture was refluxed for 0.5 hr., cooled, poured into 1.5 l. of water and extracted three times with 150-ml. portions of petroleum ether (b.p. 30–40°). The combined extracts were washed with half-saturated sodium bicarbonate, then water and dried. Removal of the solvent afforded 47.8 g. (0.14 mole) of the p-toluenesulfonate of 4a-hydroxymethyl-$d_2$-trans-3,4,4a,5,6,7,8,8a-octahydro-2-[1H]-naphthalenone along with 8.7 g. (0.05 mole, 42%) of XLIII, b.p. 132–144° (21 mm.), neither of which was further purified or characterized.

**trans-Methylcyclohexane-1,2-diacetic Acid (XXXVI).**—A suspension of 250 mg. of vanadium(V) oxide in 230 ml. of concentrated nitric acid was heated to reflux. The source of heat was removed and 23.2 g. (0.14 mole) of XXXV was added as rapidly as possible (about 10 minutes). After the addition, boiling was continued for two minutes whereupon 100 ml. of water was added and the mixture was refluxed for 1 hr. and then cooled in ice. The crystallized acid was collected (20 g., m.p. 172–180°) and recrystallized from 120 ml. of 50% aqueous acetic acid yielding 15 g. (0.07 mole, 50%) of XXXVI, m.p. 192–194°. On admixture with authentic cis-1-methylcyclohexane-1,2-diacetic acid, the melting point was strongly depressed. Crystallization from water yielded colorless needles, m.p. 196.5–197.5° (reported[27] m.p. 194–195.5°).

*Anal.* Calcd. for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: 61.64; H, 8.55.

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(47) Procedure of N. A. Khan, *Science*, **117**, 130 (1953).

**trans-1-Methyl-$d_3$-cyclohexane-1,2-diacetic Acid (XLIV).** —The directions for preparing XXXVI were followed. Eight and one-half grams (0.05 mole) of XLIII was oxidized in 85 ml. of concentrated nitric acid containing 100 mg. of vanadium(V) oxide. After the addition of 35 ml. of water and final cooling, the acid crystallized, m.p. 174–178°. Recrystallization from a water–acetic acid mixture afforded 4.75 g. (0.022 mole, 44%) of XLIV, m.p. 193–194°.

*Anal.* Calcd. for $C_{11}H_{15}D_3O_4$: C, 60.80; H+D as H, 8.52; D/H+D, 16.7. Found: C, 60.77; H+D as H. 8.37; D/H +D, 14.9 ± 0.2.

**3a-Methyl-trans-2-hexahydroindanone (XXXVII).**—The dicarboxylic acid (XXXVI) (14 g., 0.067 mole) was heated to 315–328° with 750 mg. of barium hydroxide. The distillate was poured into 300 ml. of water which was extracted three times with ether. The residue remaining after the ether was distilled and taken up in 100 ml. of hot 50% ethanol to which was added a mixture of 10 g. of semicarbazide hydrochloride and 15 g. of sodium acetate. Within ten seconds, the mixture solidified. Crystallization of the semicarbazone from 600 ml. of 95% ethanol afforded 7.9 g. (57%) from the acid) of glistening white flakes with varying decomposition points.[48] The analytical sample was recrystallized from methanol. The melting point is given and followed by the temperature of inserting the thermometer into the bath: 228–228.5° dec. (25°); 236–236.5° dec. (228.5°); 240–240.5° dec. (238.5°).

*Anal.* Calcd. for $C_{11}H_{19}N_3O$: C, 63.13; H, 9.15; N, 20.08. Found: C, 63.14; H, 9.10; N, 20.08.

The ketone was regenerated by heating 7.65 g. (0.39 mole) of recrystallized semicarbazone with 10 ml. of benzene and 10 ml. of 1:1 aqueous hydrochloric acid to 60° until the solid was completely dissolved. The aqueous phase was then separated, extracted with fresh benzene and the combined benzene solutions were washed with dilute sodium bicarbonate, then water. Concentration at atmospheric pressure followed by distillation gave 4.85 g. (0.032 mole, 82%) of XXXVII, b.p. 109–110° (20 mm.), $n^{25}$D 1.4794.

**3a-Methyl-$d_3$-trans-hexahydroindanone (XLV).**—Two batches of 2.75 g. (0.021 mole) each of XLIV were heated at 310–320° with 100 mg. of barium hydroxide. The combined distillates were taken up in petroleum ether (b.p. 30–40°), washed with dilute sodium bicarbonate and water, dried and distilled to give 1.5 g. (0.0097 mole, 46%) of XLV, b.p. 110–112° (21 mm.), $n^{25}$D 1.4768.

The semicarbazone of XLV was prepared and recrystallized three times from methanol; m.p. 240° (inserted in bath at 238.5°).

*Anal.* Calcd. for $C_{11}H_{16}D_3N_3O$: D/H+D, 15.8. Found: D/H, 12.9 ± 0.3.

**3a-Methyl-trans-2-hexahydroindan (II).**—Clemmensen reduction of 3.3 g. of XXXVII (7 hr. refluxing with 30 g. of amalgamated zinc in 30 ml. of glacial acetic acid and 30 ml. (15 ml. initially followed by three portions of 5 ml. each) of concentrated hydrochloric acid) yielded, on steam distillation, extraction of the distillate petroleum ether (b.p. 30–40°) and redistillation of the dried extract, 90% of the starting ketone (XXXVII).

Simple modifications of this procedure, e.g., longer reaction time, increased amounts of hydrochloric acid and of zinc gave the same result in two other experiments.

A mixture of 2.0 g. (0.013 mole) of XXXVII, 2.3 g. (0.042 mole) of 85% potassium hydroxide, 1.7 ml. (0.033 mole) of 85% hydrazine hydrate in 15 ml. of diethylene glycol was refluxed for 4 hr. and then distilled until the flask temperature reached 190°.[30] The residue was diluted with twice its volume of water and extracted three times with 10-ml. portions of petroleum ether (b.p. 30–40°). The extracts were combined with the distillate and washed thoroughly with water, concentrated sulfuric acid (until the acid was no longer discolored), water, saturated sodium bicarbonate and finally with water. The solution was dried and concentrated. Distillation from sodium afforded 1.1 g. (0.008 mole, 61%) of II, b.p. 74° (20 mm.). Redistillation gave material of the same boiling point, $n^{25}$D 1.4672, $d^{25}_4$ 0.8756.

*Anal.* Calcd. for $C_{10}H_{18}$: C, 86.88; H, 13.12; $R^{25}$D, 43.98. Found: C, 86.91; H, 13.11; $R^{25}$D, 43.80.

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(48) According to Linstead[49] this material melts at 238–239°.
(49) D. C. Hibbit and R. P. Linstead, *J. Chem. Soc.*, 470 (1936).

**3a-Methyl-$d_3$-trans-hexahydroindan (IV).**—The Clemmensen conditions described for the reduction of XXXVII were duplicated for the reduction of XLV. The attempt was equally unsuccessful.

Using the procedure described immediately above, 0.95 g. (6.0 mole) of XLV, 1.2 g. of 85% potassium hydroxide and 0.9 ml. of hydrazine hydrate (85%) in 8 ml. of diethylene glycol gave 0.48 g. (3.0 mole, 51%) of IV, b.p. 70° (21 mm.), $n^{25}$D 1.4669, $d^{25}_4$ 0.8923.

*Anal.* Calcd. for $C_{10}H_{15}D_3$: C, 85.02; H, 13.08; D/H+D, 16.7; $R^{25}$D 43.98. Found: C, 85.33; H, 13.27; D/H+D, 15.8 ± 0.2; $R^{25}$D, 43.92.

**Reduction of XXVIII to XXIX and XXX with Lithium in Anhydrous Ammonia.**—In a 2-l. flask insulated with rock wool and equipped with a mercury sealed stirrer, Dry Ice condenser protected with a soda lime drying tube, dropping funnel and nitrogen inlet were placed 500 ml. of anhydrous ammonia, and 55.56 g. (0.25 mole) of XXVIII (b.p. 146–149°(1.5 mm.)) dissolved in 100 ml. of anhydrous ether. Ten and one-half grams (1.5 atoms) of lithium was added in small pieces over 0.5 hr. The usual blue color of alkali metal-ammonia solutions became evident only after an amount in excess of two equivalents of lithium had dissolved. The solution was stirred for 1 hr. after the addition of the metal, whereupon 81 g. of absolute ethanol was added dropwise over a period of 75 minutes followed by 70 g. of ammonium chloride. The ammonia was then allowed to evaporate rapidly, the residue being treated with 250 ml. of ether and 100 ml. of water. A water-cooled condenser was utilized while the mixture was cautiously acidified with dilute (2:1) hydrochloric acid. The complete operation through the acidification was carried out with stirring under a slow stream of dry nitrogen. The aqueous phase from the acidified mixture was removed and extracted three times

with 100-ml. portions of ether which were combined with the original organic layer and washed once with 50 ml. of water followed by half-saturated sodium bicarbonate solution until alkaline to litmus. The ethereal solution was dried, concentrated on the steam-bath and finally distilled. The product boiling between 115–155° (0.3–1.0 mm.) was collected and weighed 31.5 g. This material was definitely composed of two substances easily separable by fractionation. However, infrared spectra showed the lower-boiling material to be mainly ketonic while the higher-boiling fraction was strongly hydroxylic and that little, if any, starting material was present. The distillate was dissolved in 70 ml. of acetic acid and added dropwise while cooling in ice to 13.8 g. of chromium(VI) oxide dissolved in 280 ml. of acetic acid containing 7 ml. of water at such a rate that the temperature did not rise above 30°. The mixture was allowed to stand at room temperature for 1 hr., then 40 ml. of ethanol was added. After standing an additional 15 minutes, the mixture was poured into 1 liter of water and extracted four times with 100-ml. portions of petroleum ether (b.p. 30–40°). The combined extracts were washed with water, half-saturated sodium bicarbonate solution until the washings were alkaline to litmus, dried and concentrated on the steam-bath. Vacuum distillation resulted in 17.7 g. (0.08 mole, 32%) of the mixture of XXIX and XXX, b.p. 120–123° (1.2 mm.).

*Anal.* Calcd. for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99. Found: C, 69.75; H, 8.91.

From 1.12 g. of this product, 0.5 g. (38%) of **semicarbazone** was obtained. Two recrystallizations from 95% ethanol raised the melting point to 163–164.5° dec.

*Anal.* Calcd. for $C_{14}H_{23}N_3O_3$: C, 59.76; H, 8.24; N, 14.94. Found: C, 60.14; H, 8.23; N, 15.01.

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# Heterocyclic Analogs of the Estrogenic Steroid Hormones. I. Synthesis of a Thiophene Analog of 3-Desoxyisoequilenin[1,2]

BY ROBERT J. COLLINS AND ELLIS V. BROWN[3]

A thiophene analog of 3-desoxyisoequilenin has been prepared. The required intermediate, 4-keto-1,2,3,4-tetrahydrodibenzothiophene, was prepared both by a modification of the synthesis of Buu-Hoi and Cagniant and by a new route. Application to this material of an equilenin synthesis of Johnson gave the desired final compound. Along with the structural proof inherent in the synthesis both chemical and spectrophotometric evidence were considered. In the course of this work two new fused ring systems have been prepared for which are proposed both systematic and trivial names.

Replacement of the benzene ring in many physiologically active compounds by heterocyclic rings often has led to interesting variations in activity and sometimes to antimetabolite behavior. Applications of this approach to the estrogenic hormones have been limited to the synthetic estrogens,[4] and although several active estrogens have been produced, no effective hormonal antagonists have been obtained.

As part of a general program to prepare hetero-

cyclic analogs of estrogenic steroid hormones, we have undertaken to prepare a 3-desoxyequilenin analog in which a thiophene ring replaces the benzene "B" ring, cis and trans-16-cyclopentano[c]-10,11,12,13,14,15-hexahydro-12-methyldibenzothiophene. The hitherto unknown cyclopentano-[c]dibenzothiophene system has been tentatively assigned a numbering system which resembles that of the steroid hormones.



Of the three excellent syntheses of the equilenins which are available,[5] all beginning with a sub-
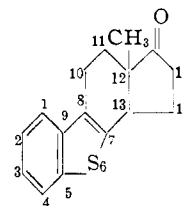
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(2) Presented at the 125th meeting of the American Chemical Society, Kansas City, March, 1954. After this paper had been submitted to the JOURNAL, an abstract of a paper presented at the 42nd Session of the Indian Science Congress, Baroda, January, 1955, came to our attention. This paper by R. B. Mitra and B. D. Tilak (*J. Sci. Ind. Research*, **14B**, 132 (1955)) reaches the same conclusions as our work except that the 154.5° melting reduction product is reported to be the thiophene analog of 3-desoxyequilenin.

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(4) N. P. Buu-Hoi and H. Hoan, *J. Org. Chem.*, **17**, 350 (1952); W. P. Biggerstaff and O. L. Stafford, THIS JOURNAL, **74**, 419 (1952); J. Sice and M. Mednick, *ibid.*, **75**, 1628 (1953).

(5) (a) W. E. Bachmann, W. Cole and A. L. Wilds, *ibid.*, **62**, 824 (1940); (b) W. S. Johnson, J. W. Petersen and C. D. Gutsche, *ibid.*, **69**, 2924 (1947); (c) W. S. Johnson and V. L. Stromberg, *ibid.*, **72**, 505 (1950).