mediately and was collected on a sintered glass funnel and washed with acetic acid and anhydrous ether. The tropylium perchlorate (infrared spectrum identical with authentic material) collected in this way amounted to 115.4 mg. (90%). The filtrate and acetic acid wash was added to a solution of 129.6 mg. (0.655 mmole) of 2,4-dinitrophenylhydrazone in glacial acetic acid. The solution lightened in color while standing overnight. The 1-(2,4-dinitrophenyl)-3,5-dimethylpyrazole was isolated by dilution with a large volume of water. After recrystallization from aqueous ethanol it amounted to 128.9 mg. (73%), m.p. and m.m.p. with authentic material prepared from acetylacetone, 122.5–123.0°.

Fragmentation of Tropylacetone.—A solution of 140.0 mg. (0.945 mmole) of tropylacetone in 5.0 ml. of glacial acetic acid was treated with 0.15 ml. (*ca.* 1.8 mmoles) of 70% perchloric acid. The first appearance of crystals occurred in about 12 minutes. After three hours, 107.9 mg. (53.5%) of tropylium perchlorate was collected by filtration. The filtrate was mixed with 2,4-dinitrophenylhydrazine solution, but no acetone 2,4-dinitrophenylhydrazone was isolated.

The fragmentation reactions of tropylacetylacetone and of tropylacetone were also conducted in dilute solution in acetonitrile and the products detected spectroscopically. A solution of tropylacetylacetone ($6.51 \times 10^{-4} M$) in acetonitrile showed essentially unchanged absorption from that shown in ethanol. Perchloric acid was added to a concentration of $6.23 \times 10^{-3} M$ and the resulting mixture diluted 10:1. The spectrum now observed was, within experimental error, that calculated for an equimolar solution of tropylium perchlorate (λ_{max} 275 mμ, log ε 3.64; λ_{infl} 268.5 and 280.5 mμ, log ε 3.52 and 3.60; λ_{min} 245 mμ, log ε 2.57) and acetylacetone (λ_{max} 273 mμ, log ε 3.82) in perchloric acid solution. Spectra of a solution $5.40 \times 10^{-4} M$ in tropylacetone and $1.05 \times 10^{-3} M$ in perchloric acid changed with time; spectra taken within 10 minutes showed only partial loss of tropyl absorption and partial appearance of tropylium absorption; after an hour the spectrum had the appearance of that of pure tropylium ion, though the extinction coefficients had not yet attained the proper magnitude. The series of spectra exhibited three isosbestic points, at 239 mμ (log ε 3.30), 267 mμ (log ε 3.48) and *ca.* 289 mμ (log ε *ca.* 3.06), indicating that the reaction involved only two light absorbing species, the tropylium ion and tropylacetone.[15]

Tropylacetylacetone and Ferric Chloride Solution.—Tropylacetylacetone slowly develops a wine-red color with alcoholic ferric chloride. Spectrophotometric comparison of the colors was made imprecise by the interfering color of the ferric chloride itself. Difference curves between the spectra of the ferric chloride solution and the tropylacetylacetone-ferric chloride mixture gave a maximum at 495 ± 20 mμ. A similar procedure with acetylacetone gave a maximum at 490 ± 15 mμ. Absorption of the species in solution was too strong to be able to detect absorption due to the seven-membered ring species in the ultraviolet. It was not possible, then, to obtain proof that tropylium loss accompanied enolization, but on the assumption that tropylacetylacetone enolate–ferric chloride complex would absorb at a significantly different wave length from acetylacetone enolate-ferric chloride complex itself, the coincidence of maxima is indicative of tropylium loss.

Base-induced retro-Claisen Reaction of Tropylacetylacetone.—A few milligrams of tropylacetylacetone was shaken vigorously with 10% sodium hydroxide solution. The solid slowly dissolved and gave rise to an oily suspension. Some 95% ethanol was added to increase mutual solubility and the mixture shaken some more. The mixture was acidified with concentrated sulfuric acid and poured into an ethanol solution of 2,4-dinitrophenylhydrazine. The yellow precipitate which formed almost immediately was collected and recrystallized from ethanol–ethyl acetate, m.p. and m.m.p. with the tropylacetone 2,4-dinitrophenylhydrazone described above, 171–172°.

Infrared Spectra.—Infrared spectra of the compounds reported here and a few other tropilidene derivatives already in the literature were taken during the course of this investigation. Certain bands were found to be characteristic of the tropilidene nucleus.

Strong bands appeared in the 685–705 and the 735–755 cm.$^{-1}$ regions in the twenty-two cases examined. Another band, always sharp, usually strong, but sometimes only medium in intensity, could be observed in the 1358–1410 cm.$^{-1}$ region in all these cases. Ditropyl shows weak bands at 1688, 1771, 1880 and 1935 cm.$^{-1}$. Bands in these general regions (1685–1694, 1740–1777, 1850–1895 and 1905–1940 cm.$^{-1}$, respectively) were exhibited by the majority of the compounds investigated, though in several cases these absorptions were obscured by neighboring strong absorptions due to carbonyl groups or were too weak to detect under the conditions used. Benzenoid compounds show similar weak absorption in this region. The tropilidene derivatives, however, do not absorb characteristically near 1500 and 1600 cm.$^{-1}$ and so can be readily distinguished from benzene derivatives.

Ditropyl,[3] ditropyl ether,[1] tropyl methyl ether[1] and tropyl cyclopentadiene[5] showed absorption near 2800 cm.$^{-1}$, probably due to the C–H stretching frequency of the hydrogen on the saturated carbon of the tropilidene nucleus. This band is obscured by other C–H stretching bands under ordinary conditions in the other compounds, but it can be detected by use of lithium fluoride optics as was done in the case of ethyl tropylacetate and 1-tropyl-2-methyl-2-propanol which showed this absorption near 2760 cm.$^{-1}$.

LOS ANGELES, CALIF.

(15) W. West in Weissberger's "Technique of Organic Chemistry," Vol. IX, Interscience Publishers, Inc., New York, N. Y. 1956, p. 68.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY, UNIVERSITY OF NEW SOUTH WALES]

Glycol Fission in Rigid Systems. I. The Camphane-2,3-diols[1]

BY S. J. ANGYAL AND R. J. YOUNG

RECEIVED MARCH 6, 1959

The four diastereomeric camphane-2,3-diols—all having the skeletal configuration of (+)-camphor—have been prepared. Hydrogenation of camphorquinone gave mainly the 2-*exo*,3-*exo*-isomer; the 2-*exo*,3-*endo*-diol was obtained from 3-*endo*-hydroxycamphor, and the 2-*endo*,3-*exo*-diol from 2-*endo*-hydroxyepicamphor, by hydrogenation; in both cases camphane-2-*endo*,3-*endo*-diol is also formed.

The *cis*-diols react very rapidly, the *trans*-diols very slowly, with lead tetraacetate, phenyl iodosoacetate and periodic acid, indicating the importance of the relative positions of the oxygen atoms in glycol fission.

Dimler and his co-workers[2,3] have shown that 1,6-anhydro-β-D-glucofuranose and 1,6-anhydro-α-D-galactofuranose are resistant to the action of sodium metaperiodate, periodic acid and lead tetraacetate although each compound contains a vicinal glycol group. The fact that the two hydroxyl groups are *trans*-situated in five-membered rings does not, in itself, explain the non-occurrence of the usual glycol fission since *trans*-cyclopentane-1,2-diol[4] and L-threitan[5] (*trans*-tetrahydrofuran-3,4-diol) react under these circum-

(1) Presented before the Division of Organic Chemistry, 132nd National A.C.S. Meeting, New York, N. Y., September 11, 1957. Abstracted from part of the Ph.D. thesis of R. J. Young, Sydney, 1958.

(2) R. J. Dimler, H. A. Davis and G. E. Hilbert, THIS JOURNAL, **68**, 1377 (1946).

(3) B. H. Alexander, R. J. Dimler and C. L. Mehltretter, *ibid.*, **73**, 4658 (1951).

(4) (a) R. Criegee, E. Buchner and W. Walther, *Ber.*, **73**, 571 (1940); (b) V. C. Bulgrin, *J. Phys. Chem.*, **61**, 702 (1957).

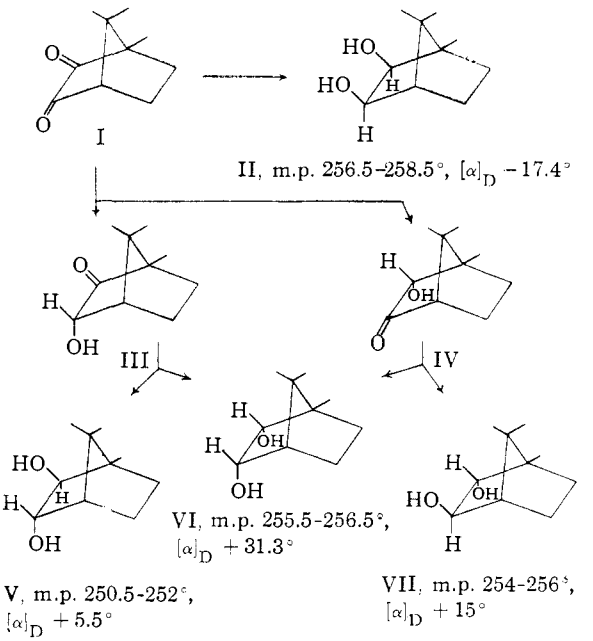
(5) H. Klosterman and F. Smith, THIS JOURNAL, **74**, 5336 (1952).

stances. Dimler[6] suggested that the reduced flexibility of the five-membered ring in his compounds—owing to its fusion with another ring—causes the hydroxyl groups to be held close to a projected valency angle[7] of 120°, too far apart for easy formation of cyclic intermediates with periodate or lead tetraacetate.[8]

To ascertain whether this explanation is valid, the glycol fission of some other rigid glycols has been investigated. The camphane-2,3-diols were chosen as the first objects of this study because the system of two fused five-membered rings in camphane is more rigid than that in Dimler's anhydro-sugars. All the four diastereomeric glycols[9] were prepared and investigated (in Dimler's case the two *cis*-diastereomers are not yet known). Rupe and his co-workers[10,11] have described three camphane-2,3-diols, but only one was sufficiently characterized by conversion into derivatives. The other two are now shown to have been mixtures. The purity of the camphanediols cannot be established from their behavior on melting because they do not depress each other's melting points. They are not readily separated by crystallization or by chromatography but the *cis* isomers can be separated from the *trans* compounds by formation of acetonides[11] or, as it is now shown, by steam distillation: the *cis* isomers, which are internally hydrogen bonded (see below), are much more volatile. The diols were characterized by their optical rotation and by conversion into *p*-nitrobenzoates.

All the compounds were prepared from (+)-camphor. Since there is no generally recognized convention for specifying the configuration of camphane derivatives, it is necessary to state here that *all the compounds described in this paper have the same skeletal configuration as (+)-camphor.*

The 2-*exo*,3-*exo*-Isomer II.[12]—Rupe and co-workers[10,11] have hydrogenated camphane-2,3-dione (I, "camphorquinone") over a nickel catalyst to a mixture of glycols. The main component of this mixture, separated as the acetonide, was a *cis*-glycol, $[\alpha]_D$ −17.7°, which was characterized as the cyclic sulfite, the mono- and the di-*p*-nitrobenzoate. Reduction of camphorquinone by lithium aluminum hydride[13] gave the same *cis*-glycol in superior yield. The 2-*exo*,3-*exo* configuration II is assigned to this glycol since hydrogenation of camphor[14] and epicamphor,[15] or their reduction by lithium aluminum hydride,[16] is known to give predominantly the *exo*-alcohols.



The 2-*endo*,3-*endo*-Isomer VI.—Manasse[17] found that reduction of camphorquinone by zinc dust in acetic acid produced two isomeric hydroxyketones. The structure of one was established, by another method of preparation,[18] as that of 3-hydroxycamphor, and the other was shown by prolonged investigations of Bredt and co-workers[19] to be a 2-hydroxyepicamphor. The configuration of the hydroxy groups in these compounds was not known with certainty. Manasse[17] found that further reduction of the mixture of the hydroxyketones by sodium in ethanol gave a white crystalline solid, $[\alpha]_D$ +12.3°, which had the composition of camphanediol. Rupe and Thommen[11] showed that it was a mixture and that removal, as the isopropylidene compound, of a small amount of *cis*-diol (which was not further studied) left a *trans*-diol with $[\alpha]_D$ + 9.8°.

These experiments were repeated by us and the *cis*-diol was isolated through the isopropylidene derivative and purified as the di-*p*-nitrobenzoate. The small proportion of *cis*-diol present makes the purification difficult; the diol is better prepared by hydrogenation of hydroxycamphor (see below). It was different from the 2-*exo*,3-*exo*-isomer, hence it was assigned the 2-*endo*,3-*endo* configuration. This assignment is in accord with its preparation since camphor gives predominantly,[20] and epi-

(6) R. J. Dimler, *Advances in Carbohydrate Chem.*, **7**, 37 (1952).

(7) The projected hydroxyl valency angle is defined as the angle between the carbon–oxygen bonds projected onto a plane perpendicular to the carbon–carbon axis; see R. E. Reeves, *Advances in Carbohydrate Chem.*, **6**, 107 (1951).

(8) See discussion in the following paper. The carbohydrate literature contains two other instances of vicinal glycols not cleaved by periodate: 7-β-(4,6-*O*-benzylidene-D-glucopyranosyl)-theophilline [W. E. Harvey, J. J. Michalski and A. R. Todd, *J. Chem. Soc.*, 2273 (1951)] and methyl α-D-glucoside 4,6-(phenyl phosphate) [J. Baddiley, J. G. Buchanan and L. Szabo, *ibid.*, 3828 (1954)]; these cases are not explained by the above postulate because the *trans*-1,2-diol groups are in six-membered rings and therefore the projected valency angle is about 60°. The resistance to glycol fission may here be caused by steric hindrance.

(9) Eight stereoisomers of camphane-2,3-diol are possible, comprising four pairs of enantiomers; the four glycols described in this paper represent one of each pair.

(10) H. Rupe and F. Müller, *Helv. Chim. Acta*, **24**, 265E (1941).

(11) H. Rupe and W. Thommen, *ibid.*, **30**, 933 (1947).

(12) The formulas are written in their correct absolute configuration [K. Freudenberg and W. Lwowski, *Ann.*, **587**, 213 (1954); **594**, 76 (1955); A. Fredga and J. K. Mietinnen, *Acta Chem. Scand.*, **1**, 371 (1947)].

(13) L. W. Trevoy and W. G. Brown, THIS JOURNAL, **71**, 1675 (1949).

(14) G. Vavon and P. Peignier, *Bull. soc. chim. France*, [4] **39**, 924 (1926).

(15) M. Lipp and E. Bund, *Ber.*, **68**, 249 (1935).

(16) S. Beckmann and R. Mezger, *Chem. Ber.*, **89**, 2738 (1956).

(17) O. Manasse, *Ber.*, **30**, 659 (1897); **35**, 3811 (1902).

(18) A. Lapworth and E. M. Chapman, *J. Chem. Soc.*, **79**, 377 (1901).

(19) (a) J. Bredt and H. Ahrens, *J. prakt. Chem.*, [2] **112**, 273 (1926); J. Bredt, *ibid.*, [2] **121**, 153 (1929); (b) J. Bredt and M. Bredt-Savelsberg, *Ber.*, **62**, 2214 (1929); J. Bredt and M. Fisher, *J. prakt. Chem.*, [2] **131**, 49 (1931).

(20) E. Beckman, *ibid.*, [2] **55**, 31 (1897).

camphor exclusively,[21] the *endo*-alcohol on reduction with sodium in ethanol.

The *trans*-Diols.—Rupe and Thommen[11] regarded the *trans*-diol, $[\alpha]_D$ +9.8°, obtained from the sodium–ethanol reduction of the hydroxycamphors as a pure compound. In our hands the rotation was usually lower (about 8°) but esterification gave, in good yield, a di-*p*-nitrobenzoate, m.p. 154.5°, from which the glycol could be recovered with a rotation of +10°. For a while it was thought that one of the *trans*-diols had been obtained; however, chromatography of the diol gave fractions of varying rotations and, when the pure *trans*-diols became known, it transpired that the di-*p*-nitrobenzoate, m.p. 154.5°, was a 1:1 molecular compound of the two *trans*-diol di-*p*-nitrobenzoates.

A glance at the structures (V and VII) of the *trans*-diols shows that, but for the presence of a methyl group on C1, they would be enantiomers. Molecular compounds of such "nearly enantiomers" have been called quasi-racemates by Fredga[22] who has done much work on them. In the present case, the quasi-racemate has a higher melting point and lower solubility than its components; consequently, mixtures of the *p*-nitrobenzoates of the *trans*-diols could not be separated by crystallization but yielded the quasi-racemate as the first product; the diol in excess could be isolated from the mother liquors.

In order to obtain the two *trans*-diols, the hydrogenation of the hydroxyketones was studied. Rupe and Müller,[10] working at 100 atm. pressure, obtained a glycol of approx. $[\alpha]_D$ +26°—presumably a mixture—from either hydroxyketone. We found that slow hydrogenation at atmospheric pressure gave mainly *trans*-diol, while faster reaction resulted in increasing proportions of *cis*-isomer. The products of the hydrogenation of 3-hydroxycamphor were separated by acetonide formation: camphane-2-*endo*,3-*endo*-diol (VI) and a *trans*-diol were obtained. Since fast hydrogenation of a ketone (in contrast to the sodium–ethanol reduction) does not usually cause epimerization of an adjacent hydroxyl group, formation of VI indicates that 3-hydroxy-camphor has the *endo* configuration III. The *trans*-glycol, $[\alpha]_D$ +5.5°, then must be the 2-*exo*,3-*endo*-isomer V. Hydrogenation of 2-hydroxyepicamphor gave a *trans*-diol, $[\alpha]_D$ +15°, which must be the 2-*endo*,-3-*exo* isomer VII. Formation of this isomer proves that the hydroxyl group in 2-hydroxyepicamphor also has the *endo* configuration IV.

It appears then that the best methods for obtaining the individual glycols are as follows: the 2-*exo*,3-*exo*-diol by reduction of camphorquinone with lithium aluminum hydride; the 2-*endo*,3-*endo*-diol by fast catalytic hydrogenation of the mixture of hydroxycamphor and -epicamphor; the 2-*exo*,3-*endo*- and the 2-*endo*,3-*exo*-diols by slow hydrogenation of 3-hydroxycamphor and 2-hydroxyepicamphor, respectively.

(21) J. Bredt and W. H. Perkin, *J. Chem. Soc.*, **103**, 2182 (1913).

(22) A. Fredga in "Thé Svedberg Anniversary Volume," Almquist and Wiksells, Stockholm, 1944, p. 261; for a review, see W. Klyne, "Progress in Stereochemistry," Academic Press, Inc., New York, N. Y., 1954, Vol. I, p. 201.

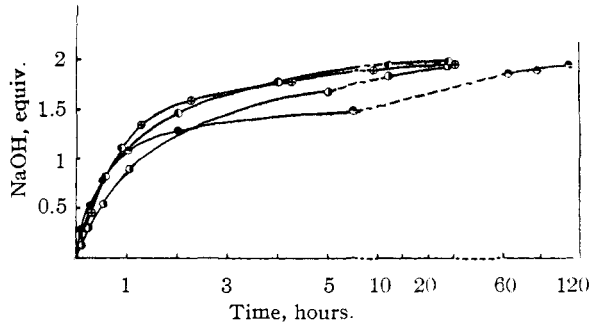


Fig. 1.—Hydrolysis of the camphane-2,3-diol diacetates: ⊕, camphane-2-*endo*,3-*exo*-diol; ◐, -2-*endo*,3-*endo*-diol; ◑, -2-*exo*,3-*exo*-diol; ●, -2-*exo*,3-*endo*-diol.

Assignment of Configurations.—The configurations tentatively assigned on the basis of the methods of preparation were confirmed by studying the relative hydrolysis rates of the diol diacetates. Lipp and Bund[15] compared the alkaline hydrolyses of the acetates of borneol, epiborneol, isoborneol and isoepiborneol and found that the order of rates was 3-*endo* > 2-*endo* > 3-*exo* >>> 2-*exo*, the latter position being strongly hindered by the two methyl groups at C1 and C7. Our results obtained with the diol diacetates are shown in Fig. 1. Of the two *trans*-glycols, the hydrolysis of the 2-*exo*,3-*endo*-isomer slows down considerably and takes a long time to become complete, confirming the presence of the hindered 2-*exo*-hydroxyl group. Of the two *cis*-glycols, the hydrolysis of the *exo*-isomer is slower, again confirming the configuration previously assigned; but here there is no drop in the rate after the consumption of one mole of alkali. Presumably, the acetyl group on C2 migrates to C3—the *cis* configuration being favorable for such a reaction—and is therefore hydrolyzed without being subject to steric hindrance. The hindered nature of the 2-hydroxyl group in the *exo*,*exo*-diol is shown by the fact that it gives a mono-*p*-nitrobenzoate under conditions which lead to the formation of the di-*p*-nitrobenzoates with the other diols.

The diols can be equilibrated by the use of sodium in ethanol at 180°, the resulting mixture containing approx. 45% of the 2-*endo*,3-*endo*, 40% of the 2-*exo*,3-*endo* and 15% of the 2-*endo*,3-*exo* isomer. The sodium–ethanol reduction of the hydroxyketones gives a similar[23] mixture. The *exo*,*exo*-diol was not detected in either case; with both hydroxyl groups on the hindered side, it would be the thermodynamically least stable isomer.

In the two *cis*-diols the presence of a strong intramolecular hydrogen bond is shown by the elegant method of Kuhn.[24] In very dilute carbon tetrachloride solution, the infrared spectra of glycols show two hydroxyl bands: one near 3630 cm.$^{-1}$ due to free OH groups and one at a lower frequency due to intramolecularly bonded OH. The value of the difference, $\Delta\nu$, between the two frequencies increases as the length of the hydrogen bond

(23) J. J. Umland and B. W. Williams [*J. Org. Chem.*, **21**, 1302 (1956); *cf.* also K. D. Hardy and R. J. Wicker, THIS JOURNAL, **80**, 640 (1958)] have shown that sodium–alcohol reduction of ketones does not always give the equilibrium mixture of alcohols.

(24) L. P. Kuhn, THIS JOURNAL, **74**, 2492 (1952); **76**, 4323 (1954).

TABLE I

RATES OF REACTION WITH GLYCOL-SPLITTING REAGENTS

Compound, diol	Lead tetraacetate T, °C.	Lead tetraacetate k^a	Phenyliodosoacetate T, °C.	Phenyliodosoacetate k^a	Periodic acid T, °C.	Periodic acid pH	Periodic acid k^b
Camphane-2-*exo*,3-*exo*- (II)	20	>25000	25	85	0	10.45	135
Camphane-2-*endo*,3-*endo*- (VI)	20	>25000	25	170	0	10.45	109
Camphane-2-*exo*,3-*endo*- (V)	50	0.37	80	0.020[c]	80	2.12[d]	0.53
Camphane-2-*endo*,3-*exo*- (VII)	50	0.38	80	[e]	80	2.12[d]	0.45
cis-Cyclopentane-1,2-	20	>40000[f]			0	4–5	Too fast[g]
trans-Cyclopentane-1,2-	20	12.8[f]			25.2	4–5	82.2[g]

[a] k is in mole^{-1} l. min.$^{-1}$ in glacial acetic acid. [b] k is in mole^{-1} l. min.$^{-1}$ in water at concentrations given in the Experimental part. [c] The reaction rate fell away from a second-order equation after *ca.* 40% completion. [d] Measured at 25°. [e] The reaction was about as fast as that of V but did not fit the second-order equation satisfactorily. [f] R. Criegee, E. Büchner and W. Walther, *Ber.*, **73**, 571 (1940). [g] V. C. Bulgrin, *J. Phys. Chem.*, **61**, 702 (1957).

decreases. The $\Delta\nu$ values for the 2-*exo*,3-*exo*- and the 2-*endo*,3-*endo*-diols, 96 and 95 cm.$^{-1}$, respectively, are similar to the $\Delta\nu$ values 103 and 102 cm.$^{-1}$ reported[25] for the corresponding norcamphanediols. These values indicate that the O–H distances[26] in these hydrogen bonds are considerably shorter than that in *cis*-cyclopentane-1,2-diol ($\Delta\nu$ 61 cm.$^{-1}$); they confirm the view that in these rigid *cis*-glycols the hydroxyl groups are entirely eclipsed whereas the cyclopentane ring, being somewhat puckered, allows the repulsion between the hydroxyl groups to twist them apart.[25]

The Rate of Glycol Fission.—Second-order rate constants for the reactions of the four diols with lead tetraacetate, phenyliodosoacetate and periodic acid are shown in Table I, together with data for the cyclopentane-1,2-diols. The reactions of the *cis*-glycols are very fast; only approximate constants could be determined for the lead tetraacetate oxidation, and, in order to obtain reproducible figures, the periodate reaction had to be measured at 0° and in acid solution (in which periodate oxidations are slower than at higher pH's). On the other hand, the reactions of the *trans*-camphanediols at room temperature were too slow to be measured; the constants were determined at elevated temperatures. These reactions are considerably slower than those of *trans*-cyclopentane-1,2-diol. Since the four camphanediols differ in no other respect than in their stereochemistry, the data support Dimler's hypothesis[6] that the unreactivity of the *trans*-diols is caused by a large and rigidly held distance between the two oxygen atoms.[27]

Experimental[28]

All melting points are corrected; those of the diols were determined in sealed tubes with fairly fast heating (since these m.p.'s vary with the rate of heating). Specific rotations were measured at room temperature. Peter Spence Grade H alumina was used for chromatography. Light petroleum had b.p. 40–60°.

(+)-Camphorquinone, prepared according to Evans, *et al.*,[29] was always contaminated by some camphor; it was purified by chromatography in benzene, only the yellow fractions being collected, followed by crystallization from benzene. It had m.p. 199°.

Hydrogenation of (+)-Camphorquinone.—Camphorquinone was hydrogenated in ethanol with Raney nickel W2[30] and W4[31] catalysts at atmospheric pressure, and with W2 catalyst at 45 atmospheres.[10] The crude reaction mixtures had $[\alpha]_D$ −2, −6 and −10°, respectively (*c* 3 in EtOH), and gave, by separation as its acetonide,[10] (−)-camphane-2-*exo*,3-*exo*-diol (II) in 32, 55 and 70% yield, respectively. After several recrystallizations from light petroleum at −40° it had m.p. 256.5–258.5°, $[\alpha]_D$ −17.4° (*c* 6 in EtOH). Rupe and Thommen[11] reported m.p. 253–255°, $[\alpha]^{20}_D$ −17.7°.

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.65. Found: C, 70.25; H, 10.65.

The glycol (0.11 g.) and *p*-nitrobenzoyl chloride (0.25 g.), dissolved in anhydrous pyridine (2 ml.), were allowed to stand at room temperature for 72 hr. Water was then added and the precipitated solid (0.134 g., 66%) was collected by filtration. Crystallization from light petroleum and sublimation at 140–160° (2 mm.) gave needles of the mono-*p*-nitrobenzoate, m.p. 128–129°. Rupe and Thommen[11] reported m.p. 129–130°.

The glycol (2.64 g.) and *p*-nitrobenzoyl chloride (7.1 g.), dissolved in anhydrous pyridine (25 ml.), were heated on the steam-bath for 15 minutes, then allowed to stand overnight. The solid obtained by the addition of ice was filtered off and crystallized from chloroform–ethanol to give needles (4.4 g., 61%) of the di-*p*-nitrobenzoate, m.p. 197.5–198.5°. Rupe and Thommen[11] reported m.p. 191–192°, $[\alpha]^{20}_D$ −21.1° (*c* 4.6 in ethanol).[32]

Rupe and Thommen[11] reported that the *trans*-glycol mixture remaining after removal of the *cis* isomers as acetonides had a rotation of +17.7°; this is hard to interpret since neither of the *trans*-diols has such high rotation. In our experiments the crude *trans* mixture had $[\alpha]_D$ values ranging from +6.5 to +8.5°, and it was found to consist mostly of the 2-*exo*,3-*exo*-isomer; after treatment with *p*-nitrobenzoyl chloride, the quasi-racemic di-*p*-nitrobenzoate of the two *trans*-glycols and the di-*p*-nitrobenzoate of camphane-2-*exo*,3-*endo*-diol were isolated.

Reduction of (+)-Camphorquinone with Lithium Aluminum Hydride.—(+)-Camphorquinone (1.0 g.) in anhydrous ether (10 ml.) was added with shaking to a slurry of lithium aluminum hydride (0.25 g.) in anhydrous ether (15 ml.) and the mixture was heated under reflux for 1 hr. Excess hydride was decomposed by the addition of moist ether and the precipitate removed by filtration. Evaporation of the dried solvent left a solid (1.0 g.), $[\alpha]_D$ −16° (*c* 1.8 in EtOH); steam distillation (500 ml. of distillate) gave camphane-2-*exo*,3-*exo*-diol (0.94 g., 93%), $[\alpha]_D$ −17° (*c* 1 in EtOH), without further purification. The non-volatile *trans*-glycol

(25) H. Kwart and W. G. Vosburgh, THIS JOURNAL, **76**, 5400 (1954). In a recent paper, H. Kwart and G. C. Gatos (*ibid.*, **80**, 881 (1958)] reported $\Delta\nu$ 91 cm.$^{-1}$ for camphane-2-*exo*,3-*exo*-diol.

(26) We have refrained from calculating the lengths of the hydrogen bonds from the $\Delta\nu$ values by the equation given by Kuhn.[24] We regard it as inaccurate since it is based on the assumption of fully eclipsed hydroxyl groups in *cis*-cyclopentane-1,2-diol ($\Delta\nu$ 61 cm.$^{-1}$); it would be more correct to make this assumption for the *cis*-norcamphanediols ($\Delta\nu$ 102 cm.$^{-1}$).

(27) After completion of this work Dr. Tsuneichi Takeshita (Ota-ku, Tokyo, Japan) has kindly informed us that he has also synthesized and characterized the four camphanediols.

(28) Microanalyses were performed by Dr. E. Challen and Mr. D. Weeden. Infrared spectra were taken by Mr. I. Reece.

(29) W. C. Evans, J. M. Ridgion and J. L. Simonsen, *J. Chem. Soc.*, 137 (1934).

(30) R. Mozingo, "Organic Syntheses," Coll. Vol. III, John Wiley and Sons, Inc., New York, N. Y., 1955, p. 181.

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(32) Rupe and Thommen were unable to carry out the esterification in pyridine; they obtained the di-*p*-nitrobenzoate, in a maximum yield of 5%, by heating the glycol with an excess of *p*-nitrobenzoyl chloride.

(0.05 g.), extracted by ether, gave on esterification 15 mg. of impure (+)-camphane-2-*endo*,3-*exo*-diol di-*p*-nitrobenzoate, m.p. 148–150°, $[\alpha]_D$ −98° (*c* 0.2 in $CHCl_3$).

Hydrogenation of (+)-3-*endo*-Hydroxycamphor (III).—Hydroxycamphor and hydroxyepicamphor were prepared and separated according to Bredt.[19a] (+)-3-*endo*-Hydroxycamphor (29.9 g.) was dissolved in ethanol (200 ml.) and shaken with Raney nickel (W2) catalyst (20 g.) in hydrogen at a pressure of 115 atm. for 3 hr. at room temperature and then for 15 minutes at 50°. Removal of the catalyst and solvent gave a solid (29.6 g.), $[\alpha]_D$ +19.4° (*c* 6 in EtOH), which on boiling with sulfuric acid (2 drops) and anhydrous acetone (200 ml.) for 2 hr. and distillation, gave a yellow liquid, b.p. 33–60° (1.5 mm.) (12.9 g., mainly condensation products of acetone) and a pale yellow oil (22 g.), b.p. 60–80° (2 mm.). The yellow oil was chromatographed in light petroleum on alumina; distillation of the eluate gave the isopropylidene derivative (13.2 g., 40%), b.p. 70–74° (2 mm.). It was hydrolyzed with boiling 50% acetic acid (100 ml.); working up gave a yellow oily solid (10 g.) from which slow sublimation at atmospheric pressure and 100° removed the oil and left a pale yellow solid (5.5 g.). Recrystallization at −40° from light petroleum gave the (+)-2-*endo*,3-*endo*-glycol as plates, $[\alpha]_D$ +27° (*c* 6.9 in EtOH).

The plates (1.45 g.) and *p*-nitrobenzoyl chloride (3.87 g.) were dissolved in anhydrous pyridine (30 ml.) and set aside at room temperature for 76 hr. The oil produced on addition of water was taken up in chloroform; removal of the dried solvent left a solid (3.62 g., 82%); recrystallization from chloroform–light petroleum or ethanol gave (+)-camphane-2-*endo*,3-*endo*-diol di-*p*-nitrobenzoate as needles, m.p. 170°, $[\alpha]_D$ +32.7° (*c* 6 in EtOH).

Anal. Calcd. for $C_{24}H_{24}O_8N_2$: C, 61.55; H, 5.15; N, 6.0. Found: C, 61.7; H, 5.2; N, 6.1.

The di-*p*-nitrobenzoate (1.3 g.) was heated under reflux with 5% methanolic potassium hydroxide (25 ml.) for 2 hr. Addition of water and extraction with ether gave a yellow solid (0.44 g., 93%) which on recrystallization from light petroleum at −40° yielded (+)-**camphane-2-*endo*,3-*endo*-diol** as plates, m.p. 255.5–256.5°, $[\alpha]_D$ +31.3° (*c* 6 in EtOH). The diol is very soluble even in light petroleum and crystallization is accompanied by heavy losses. It is better purified by sublimation at 110° (2 mm.).

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.65. Found: C, 70.65; H, 10.5.

The distillation residue left after removal of the isopropylidene derivative had $[\alpha]_D$ +5.8° (*c* 6.6 in EtOH) after recrystallization from benzene. This solid (4 g.) and *p*-nitrobenzoyl chloride (10.4 g.), dissolved in anhydrous pyridine (70 ml.), were allowed to stand at room temperature for 167 hr. Addition of water gave an oil, and working up in the usual manner produced a gum (9.32 g., 85%). Recrystallization from ethanol gave (+)-camphane-2-*exo*,3-*endo*-diol di-*p*-nitrobenzoate as needles, m.p. 128–129°, $[\alpha]_D$ +134.5° (*c* 6 in EtOH).

Anal. Calcd. for $C_{24}H_{24}O_8N_2$: C, 61.55; H, 5.15; N, 6.0. Found: C, 61.45; H, 5.35; N, 6.0.

Hydrolysis of the di-*p*-nitrobenzoate (5.5 g.) by heating under reflux with 5% methanolic potassium hydroxide for 3 hr. gave a pale yellow solid (1.84 g., 93%); recrystallization from benzene yielded (+)-**camphane-2-*exo*,3-*endo*-diol** as needles, m.p. 250.5–252°, $[\alpha]_D$ +5.5° (*c* 3 in EtOH).

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.65. Found: C, 70.55; H, 10.45.

A hydrogenation with W2 Raney nickel at atmospheric pressure required 12 hr. and gave a glycol mixture of $[\alpha]_D$ +6.7° (*c* 6 in EtOH), corresponding to 95% 2-*exo*,3-*endo*-glycol.

Hydrogenation of (+)-2-*endo*-Hydroxyepicamphor (IV).—2-*endo*-Hydroxyepicamphor (30 g.) in ethanol (300 ml.) was shaken with Raney nickel (W2) catalyst until 1 mole of hydrogen was taken up (22 hr.). Removal of the catalyst and the solvent left a solid, $[\alpha]_D$ +17.1° (*c* 6 in EtOH). A sample was twice crystallized from benzene and then had $[\alpha]_D$ +15° (*c* 6 in EtOH); esterification of 0.69 g. with *p*-nitrobenzoyl chloride (1.84 g.) in anhydrous pyridine (20 ml.) at room temperature for 65 hr., gave an oily product (1.86 g.) which on two crystallizations from ethanol yielded (+)-camphane-2-*endo*,3-*exo*-diol di-*p*-nitrobenzoate as needles, m.p. 151.5° (soften at 149.5°), $[\alpha]_D$ −114.8°, (*c* 6 in $CHCl_3$).

Anal. Calcd. for $C_{24}H_{24}O_8N_2$: C, 61.55; H, 5.15; N, 6.0. Found: C, 61.35; H, 5.45; N, 6.0.

The ester (0.64 g.) was heated under reflux with 5% methanolic potassium hydroxide (15 ml.) for 2 hr. Working up gave a solid (0.2 g., 85%) which on recrystallization from benzene–light petroleum gave (+)-**camphane-2-*endo*,3-*exo*-diol** as needles, m.p. 254–256°, $[\alpha]_D$ +15° (*c* 1.5 in EtOH).

Anal. Calcd. for $C_{10}H_{18}O_2$: C, 70.55; H, 10.65. Found: C, 70.55; H, 10.6.

The bulk of the crude hydrogenation mixture was worked up in a different way. In order to ensure complete removal of *cis*-glycol, a solution of sodium metaperiodate (1.3 g.) in water (50 ml.) was added to a solution of the crude hydrogenation product (11 g.) in ethanol. After 0.5 hr., aqueous potassium iodide solution was added, and the mixture extracted with chloroform; the extract was washed with sodium thiosulfate and water. Removal of the dried solvent left the *trans*-glycol, $[\alpha]_D$ +14° (*c* 1.4 in EtOH). Esterification of 0.37 g. with *p*-nitrobenzoyl chloride (0.98 g.) in anhydrous pyridine (3 ml.) and working up in the usual manner yielded a solid (1.02 g.) which on recrystallization from ethanol gave (+)-camphane-2-*endo*,3-*exo*-diol di-*p*-nitrobenzoate as needles, m.p. 150° (soften at 146°), $[\alpha]_D$ −113° (*c* 0.7 in $CHCl_3$).

Sodium–Ethanol Reduction of the Hydroxyketones.—A mixture (30.9 g.) of hydroxycamphor and hydroxyepicamphor, obtained by the reduction of (+)-camphor with zinc and acetic acid,[19a] was refluxed in anhydrous ethanol (540 ml.) while sodium (42 g.) was added in small pieces. When all the sodium had dissolved, most of the solvent was removed and the residue diluted with water. The product (22.5 g.) was extracted with ether and had $[\alpha]_D$ +14.7° (*c* 6 in EtOH). It was twice acetonated, as described above, and the distilled isopropylidene derivative, which contained much solid glycol, was redistilled to give two fractions: (i) b.p. 28–40° (1–2 mm.), (ii) b.p. 58–64° (1–2 mm.), 3.66 g., 13%. The second fraction was heated under reflux with 20% acetic acid (30 ml.) for 2 hr. Working up as usual left a dark oily solid (2 g.) from which slow sublimation at 100° at atmospheric pressure removed most of the oil. Sublimation at 120–130° (2 mm.) gave pale yellow plates (1.03 g.) of (+)-camphane-2-*endo*,3-*endo*-diol, $[\alpha]_D$ +26.3° (*c* 6 in EtOH). The dinitrobenzoate had m.p. 170–170.5°.

The *trans*-glycol remaining after removal of the isopropylidene derivative was sublimed at 120–140° (0.1 mm.) and then had $[\alpha]_D$ +10.5° (6.45 g.). To remove any *cis*-glycol still present it was dissolved in ethanol (100 ml.), a solution of sodium metaperiodate (1.2 g.) in water (50 ml.) was added and the mixture set aside at room temperature. After 0.5 hr. the mixture was diluted with much water and extracted with ether; the extract was washed with saturated sodium bisulfite solution and evaporated to leave a solid (5.0 g.), $[\alpha]_D$ + 8.7° (*c* 6 in EtOH). Esterification gave a di-*p*-nitrobenzoate, m.p. 148–153.5°, $[\alpha]_D$ +51.7° (*c* 6 in $CHCl_3$). After 3 recrystallizations the m.p. became constant at 154–154.5°, but it required 18 crystallizations (from different solvents) to reach the constant rotation, $[\alpha]_D$ + 10.5°, or the quasi-racemate.

The Quasi-racemic Di-*p*-nitrobenzoate.—A mixture of equal quantities (0.05 g.) of the di-*p*-nitrobenzoates of (+)-camphane-2-*exo*,3-*endo*-diol and (+)-camphane-2-*endo*,3-*exo*-diol was dissolved in ethanol and the solution cooled; brown prisms, m.p. 154°, $[\alpha]_D$ +11° (*c* 1 in EtOH), separated. A mixture of approximately equal amounts of the two esters softened at 120°, immediately solidified into prisms and melted at 152–154°.

The m.p. of the *trans*-glycols showed no depression on admixture, but a mixture of the *trans*-glycols always crystallized in plates whereas the pure *trans*-glycols crystallized in needles; it is possible therefore that the free glycols also form a quasi-racemate.

Equilibration of the Diols with Sodium.—A *trans*-glycol mixture (2.2 g.), $[\alpha]_D$ +7°, and a solution of sodium (2.5 g.) in anhydrous ethanol (45 ml.) were heated in a sealed tube for 63 hr. at 180°. The solution was concentrated, diluted with water and extracted with ether. Evaporation of the dried solvent left a solid (1.92 g.), $[\alpha]_D$ +18° (*c* 2 in EtOH). Sulfuric acid (1 drop) was added to a solution of the solid in anhydrous acetone (11 ml.) and the mixture was heated under reflux for 2 hr. Working up in the usual manner and distillation of the resultant liquid gave the isopropylidene derivative, b.p. 88–92° (2 mm.). The residue was

treated with acetone and sulfuric acid a second time. The combined isopropylidene derivatives (0.86 g., 41%) were heated under reflux with 50% acetic acid (14 ml.) for 2 hr. and the resulting yellow oily solid (0.66 g.) was treated with *p*-nitrobenzoyl chloride (1.5 g.) in anhydrous pyridine (10 ml.) for 2 days: (+)-camphane-2-*endo*,3-*endo*-diol di-*p*-nitrobenzoate, m.p. 169.5–170.5°, $[\alpha]_D$ +28.5° (*c* 0.4 in $CHCl_3$), was obtained.

The dark residue (0.67 g.) from the distillation of the isopropylidene derivative was sublimed at 120° (1 mm.) to give a colorless, crystalline solid (0.53 g.), $[\alpha]_D$ +8° (*c* 1. 4in EtOH). Esterification gave a crude di-*p*-nitrobenzoate (1.37 g., 93%), $[\alpha]_D$ +69° (*c* 1.3 in $CHCl_3$) from which—by crystallization from ethanol—the quasi-racemic di-*p*-nitrobenzoate (0.9 g.), m.p. 152–154°, and (+)-camphane-2-*exo*,3-*endo*-diol di-*p*-nitrobenzoate, m.p. 123–125°, were isolated.

The Camphane-2,3-diol Diacetates.—Each diol (2.2 g.) was heated with acetic anhydride (20 ml.) and anhydrous sodium acetate (1 g.) for 6 hr. on a steam-bath. After cooling, the solution was diluted with water, extracted with ether, the solvent dried (Na_2SO_4) and evaporated, and the residue distilled to give the diacetate as a colorless oil. Crude yields, b.p.'s, $[\alpha]_D$ values in ethanol, and analyses were: (−)-2-*exo*,3-*exo*: 79%, 140–145° (5.5 mm.), −10° (*c* 3); C, 66.15; H, 8.65; (+)-2-*endo*,3-*endo*: 86%, 98° (0.5 mm.), +39° (*c* 4); C, 66.3; H, 8.85; (+)-2-*endo*,3-*exo*: 96%, 89–90° (0.4 mm.), +26° (*c* 4); C, 66.35; H, 9.0; (+)-2-*exo*,3-*endo*: 75%, 94° (0.6 mm.), 0° (*c* 2); C, 66.35; H, 8.8. Calcd. for $C_{14}H_{22}O_4$: C, 66.1; H, 8.7.

Comparative Rates of Hydrolysis of the Camphane-2,3-diol Diacetates.—Solutions (0.025 *M*) of the diacetates were used. The required amount of the diacetate was weighed into a 100-ml. volumetric flask, dissolved in 75% ethanol (v./v.) and immersed, together with a *N* solution of sodium hydroxide, in a constant temperature bath at 22.5° (±0.3) (except for the 2-*exo*,3-*endo*-isomer which was treated at 25°). After 0.5 hr., 5 ml. of the sodium hydroxide solution was added to the solution of the diacetate and the mixture diluted to the mark. At time intervals 10-ml. aliquots were removed, cooled in a Dry Ice–ethanol mixture and titrated with standard hydrochloric acid. The results are shown in Fig. 1.

Hydrogen Bonds.—Infrared spectra were taken and evaluated according to Kuhn's method.[24] The carbon tetrachloride used as the solvent was distilled over P_2O_5 and stored over P_2O_5. The measurements were made with a Perkin-Elmer double-beam recording spectrophotometer equipped with a quartz prism, on solutions less than 0.005 *M* in 2- and 4-cm. cells. Hydroxy bands were found at the following frequencies: 2-*exo*,3-*exo*: 3641 and 3545 cm.$^{-1}$, 2-*endo*,3-*endo*: 3635 and 3540 cm.$^{-1}$, 2-*exo*,3-*endo*: 3631 cm.$^{-1}$ and 2-*endo*,3-*exo*: 3628 cm.$^{-1}$.

Kinetic Runs. (a) **Lead Tetraacetate and Phenyl Iodosoacetate.**—Acetic acid was successively treated with chromic oxide and boron triacetate.[33] Runs with the *cis*-glycols were carried out in "Dreischenkelrohr"[34] tubes using Criegee's fast method. Solutions (5 ml. of each) of the diols (0.0005 − 0.001 *M*) and the oxidizing agent (0.0125 − 0.02 *M*) in glacial acetic acid were placed in each of the lower bulbs of the "Dreischenkelrohr." Ten ml. of "stopping solution" (50 g. of potassium iodide and 250 g. of sodium acetate in 1 l. of water) was placed in the side bulb. After 15 min. in the thermostat, the reaction solutions were mixed and, at a definite time, the "stopping solution" was added. The liberated iodine was titrated with 0.02 *N* thiosulfate solution.

The *trans*-glycols (*ca.* 1.5 × 10^{-4} mole) were weighed into a 50-ml. volumetric flask and, after thermostating, were dissolved in the solution of the oxidizing agent (0.0125–0.02 *M*). At intervals, 5-ml. aliquots were added to 10 ml. of stopping solution and titrated as above. Blank titrations were always run.

(b) **Periodate.**—The following buffer solutions were used: (i) *p*H 10.45: 0.1 *N* hydrochloric acid (100 ml.) and sodium carbonate (5.301 g.) in 1 l. of water; (ii) *p*H 2.12: *N* sodium acetate (200 ml.) and *N* hydrochloric acid (200 ml.) diluted with water to 1 l. The ionic strength was maintained constant by dissolving sufficient sodium nitrate in each buffer to make it 0.2 *M*. Solutions of sodium metaperiodate (0.001 *M*), which were also 0.2 *M* in sodium nitrate, were made up in the same buffers. The glycols were dissolved in ethanol (1 vol.) and the solution diluted with buffer (9 vols.).

Runs with the *cis*-diols (*p*H 10.45) were made in the "Dreischenkelrohr" as described above. The "stopping solution" was *M* in potassium iodide and *M* in sodium hydrogen carbonate; 0.0016 *N* arsenite solution was used for the titrations. The initial concentration of the glycols was 0.00128 *M* and that of periodate, 0.000585 *M*.

Solutions of the *trans*-glycols (*p*H 2.12) were made up to 50 ml. and, at intervals, 5-ml. aliquots were removed. The "stopping solution" (10 ml.) was 0.1 *N* hydrochloric acid containing a few crystals of potassium iodide. The liberated iodine was titrated with 0.007 *N* thiosulfate solution. The initial glycol concentration was 0.00123 *M* and that of periodate, 0.00077 *M*.

The rate constants were calculated as described by Cordner and Pausacker.[35]

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[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF MERCK & CO., INC.]

Reaction of Diazomethane with Δ^{16}-20-Keto Steroids[1]

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The reaction of 3α-acetoxy-Δ^{11}-pregnene-11,20-dione with diazomethane and the products formed consequent to pyrolysis of the intermediate pyrazoline derivative are discussed.

The reaction of diazomethane with Δ^{16}-20-keto steroids was first studied by Wettstein[2] who prepared the pyrazoline derivatives corresponding to 16-dehydropregnenolone, its acetate and 16-dehydroprogesterone. The major product formed from the pyrolysis of these derivatives was formulated by Wettstein as a 16-methyl-16-dehydro-20-keto system and this structure has received unequivocal confirmation recently from the work of Romo, Lepe and Romero.[3] In this connection, these authors demonstrated the identity of the major compound from the pyrazoline pyrolysis with the product obtained from kryptogenin on treatment with methyl Grignard with subsequent side chain degradation. They found further that the same compound was obtained by bromination and dehydrobromination of the 16-methyl-20-ketone produced from the corresponding 16-dehydro-20-ketone with methyl Grignard. Wettstein also

(1) Presented at the Meeting-in-Miniature of the North Jersey Section of the American Chemical Society on January 26, 1959.

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