192.5–194°. The analytical sample was prepared by repeated crystallization from the same solvent, m.p. 194°, $[\alpha]^{27}D$ +17.5° (chloroform) (lit.[4] m.p. 193–194°, $[\alpha]D$ +20° (dioxane)).

Anal. Calcd. for $C_{28}H_{50}O_2$: C, 80.32; H, 12.06. Found: C, 80.16; H, 12.22.

6β-Methylcholestan-3β,6α-diol Monoacetate (IIb).—To a solution containing 6.375 g. (15.22 moles) of 6β-methylcholestan-3β,6α-diol (IIa) dissolved in 60 ml. of anhydrous pyridine was added 40 ml. of acetic anhydride. Reaction was allowed to proceed for 1 hour at steam-plate temperatures. After cooling to room temperature, the reaction mixture was poured into ice-water, and the resulting solid material was filtered, washed exhaustively with water and dried, furnishing 6.794 g. (95.5%) of crude 6β-methylcholestan-3β,6α-diol monoacetate (IIb), m.p. 161–161.75° (lit.[4] m.p. 166°). The crude monoester was used in the succeeding synthetic step without further purification.

6-Methylcholesteryl Acetate (IIIb). **A. By the Action of Phosphorus Oxychloride in Pyridine.**—To a solution containing 155 mg. of 6β-methylcholestan-3β,6α-diol monoacetate (IIb) in 2 ml. of anhydrous pyridine was added 2 ml. of phosphorus oxychloride. The reaction mixture was allowed to stand overnight at room temperature, was diluted with anhydrous ether, and the excess phosphorus oxychloride was decomposed by the dropwise addition of water. The water layer was removed and the ethereal solution was washed successively with fresh water, 10% sodium bicarbonate, and again with fresh water. The ethereal solution was dried over anhydrous potassium carbonate, filtered, and most of the solvent was evaporated. Crystallization was effected from ether–ethanol–water, furnishing 49 mg. (33%) of 6-methylcholesteryl acetate (IIIb), m.p. 112.5–113° (lit.[4] m.p. 115.5–116.5°).

B. By the Action of *p*-Toluenesulfonic Acid in Acetic Acid.—To a solution containing 6.794 g. (14.51 mmoles) of 6β-methylcholestan-3β,6α-diol monoacetate (IIb) dissolved in 370 ml. of acetic acid was added 503 mg. of *p*-toluenesulfonic acid monohydrate. The mixture was heated under reflux for 25 minutes, and then cooled to room temperature and diluted with water until crystallization ensued, yielding 5.694 g. (87.4%) of 6-methylcholesteryl acetate (IIIb), m.p. 112–113.75°. This material was saponified without further purification. A mixture melting point with the material obtained by dehydration with phosphorus oxychloride was not depressed.

6-Methylcholesterol (IIIa).—6-Methylcholesteryl acetate (IIIb) (5.394 g., 12.2 mmoles) was dissolved in 200 ml. of 95% aqueous ethanol containing 4.0 g. of potassium hydroxide. The reaction mixture was heated under reflux for 40 minutes and then diluted with water to crystallization. On cooling, the crystalline material was filtered, washed with *ca.* 30 ml. of 50% aqueous ethanol, and dried, yielding 4.444 g. (90.9%) of crude 6-methylcholesterol (IIIa), m.p. 144.5–145.25°. The analytical sample was prepared by repeated crystallization from ethanol–water, m.p. 144.5–145.25°, $[\alpha]^{30}D$ −46.4° (chloroform), $[\alpha]^{27}D$ −43.2° (9:1 dioxane–water) (lit.[4] m.p. 138.5–140.5°, $[\alpha]D$ −36.8° (dioxane); lit.[2] m.p. 134.5–135°).

Anal. Calcd. for $C_{28}H_{48}O$: C, 83.93; H, 12.06. Found: C, 83.70; H, 12.28.

6-Methylcholesteryl *p*-Toluenesulfonate (IIIc).—A solution containing 4.082 g. (9.74 mmoles) of 6β-methylcholestan-3β,6α-diol (IIa) and 3.177 g. (16.7 mmoles) of *p*-toluenesulfonyl chloride in 25 ml. of anhydrous pyridine was allowed to stand at room temperature for 44 hours. A magnetic stirring bar was placed in the flask and to this reaction mixture (containing crystals of pyridine hydrochloride), cooled to 0°, was added dropwise 10.0 ml. of thionyl chloride with stirring and continued cooling. After the addition was complete (*ca.* 10 minutes) the reaction mixture was diluted with large quantities of anhydrous ether and excess thionyl chloride was decomposed by the dropwise addition of water. This water layer was removed and the ethereal solution was washed twice with fresh water, dried over potassium carbonate, and filtered.

The solution was concentrated to about 25 ml. *in vacuo*, acetone was added, and more solvent was removed *in vacuo*. On cooling to −80°, a white crystalline material separated and was filtered off. Repeated concentration of the mother liquor and subsequent cooling furnished a second and a third crop. These combined crops after drying weighed 4.686 g. (86.5%) and had m.p. 126.5–130.5° dec. The analytical sample was prepared by crystallization from pentane at −80° $[\alpha]^{27}D$ −43.5° (chloroform).

Anal. Calcd. for $C_{35}H_{54}SO_3$: C, 75.76; H, 9.81. Found: C, 76.40; H, 10.48.

Some preparations of this ester showed discoloration on standing at room temperature for two or three days. The decomposition appears to be autocatalytic. The melting points of the various preparations of this ester were erratic, some fairly pure samples decomposing before melting below 100°.

Acknowledgments.—This work was supported in part by a generous grant from the du Pont Co. The microanalyses were performed by Mrs. C. S. Yeh, and the nuclear magnetic resonance spectra were run by Mr. Ben Shoulders of the University of Illinois.

LAFAYETTE, INDIANA

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF WAYNE STATE UNIVERSITY]

Optical Rotatory Dispersion Studies. XVI.[1] Synthesis and Conformation of Optically Active Octalones and Decalones[2]

BY CARL DJERASSI AND D. MARSHALL[3]

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Collidine dehydrobromination of (−)-2-bromo-*trans*-9-methyl-3-decalone (IV) afforded (+)-Δ^1-*trans*-9-methyl-3-octalone (V) and (−)-Δ^4-9-methyl-3-octalone (VI), whose rotatory dispersion curves are similar to those of Δ^1-cholesten-3-one and Δ^4-cholesten-3-one, respectively. The dispersion curve of (−)-*cis*-9-methyl-3-decalone (VII), obtained by catalytic hydrogenation of (−)-Δ^4-9-methyl-3-octalone (VI), indicates that such *cis*-decalones and 3-keto-5β-steroids exist in the same conformation. The same statement also can be made about the conformations of *trans*-10-methyl-1-decalone (XI) and 4-keto-5α-steroids, such as cholestan-4-one (XV). The rotatory dispersion results indicate, however, that this does not appear to be the case with coprostan-4-one (XIV) and (−)-*cis*-10-methyl-1-decalone (X), the exclusive product of hydrogenation of (+)-Δ^8-10-methyl-1-octalone (VIII). The latter, in turn, was synthesized by an application of the "hetero-Δ^1-steroid rearrangement" from (−)-2-bromo-*trans*-9-methyl-3-decalone (IV). The conformational distortion produced by a 6,7-double bond or a 4,4-*gem*-dimethyl grouping is also illustrated by rotatory dispersion measurements of appropriate, optically active, bicyclic model compounds.

(1) Paper XV, C. Djerassi, O. Halpern, V. Halpern, O. Schindler and C. Tamm, *Helv. Chim. Acta*, **41**, 250 (1958).

(2) Supported by a research grant (No. CY-2919), from the National Cancer Institute of the National Institutes of Health, U. S. Public Health Service.

(3) Postdoctorate research fellow, 1956–1957.

One of the important applications of the rotatory dispersion method developed in this Laboratory[4] has been the determination of the absolute configuration[5,6] of cyclic ketones by comparison of rotatory dispersion curves with suitable models of established absolute configuration. Among the most suitable models are steroids, whose absolute configuration with respect to D-glyceraldehyde is known[7] and their use is predicated on the assumption that the characteristic shape of any given ketonic rotatory dispersion curve, and in particular the sign of the Cotton effect,[8] is governed principally by the conformation and stereochemistry of the *bicyclic environment* around the carbonyl group. A considerable number of examples have been offered[5] in support of this premise, but it has also been pointed out that there exist some striking exceptions—9-methyl-1-decalones *vs.* 1-ketosteroids[1,9]—where the rest of the polycyclic system of the steroid model makes an important and undefined[10] contribution. A very likely and at least partially correct explanation of this apparent anomaly will be discussed in detail below and involves possible conformational differences between certain bicyclic systems and the more rigid steroid molecule. In order to strengthen the scope of our rotatory dispersion approach to absolute configuration as well as to uncover possible exceptions, it was necessary to synthesize certain key bicyclic ketones of *known absolute configuration* and to determine their rotatory dispersion curves. The details of the synthetic and dispersion work are summarized in the present communication.

Synthetic Studies.—The synthesis of a few optically active decalones and hydrindanones, together with their rotatory dispersion curves, has already been reported[5a,11] and a secure assignment of absolute configuration was made possible in each case by commencing with the resolved bicyclic ketone I[12] (or its antipode) which had been transformed by the Monsanto group[13] using the Harvard steroid synthesis[14] to known steroids, thus establishing the absolute configuration of the starting ketone I. Since the purpose of the present work was to make available a series of optically active, pure octalones and decalones, a synthetic scheme—derived *in toto* by analogy to known steroid transformations—was devised which employed one common starting material (IV) and which was not necessarily the most efficient one from the standpoint of yields.

A very generous amount of the ketone I[12] was kindly furnished by Dr. W. S. Knowles[15] and this was converted by the literature procedure[12,14] into II and hydrogenated[5a,11] with platinum oxide in methanol solution to (−)-*trans*-9-methyl-3-decalone (III). Bromination in glacial acetic acid provided (−)-2-bromo-*trans*-9-methyl-3-decalone (IV)[16] which represented the key substance for this investigation. The site of substitution of the bromine atom at C-2 already had been established earlier[11] in the (+)-series and is thus in full accord with the results recorded in the steroid field.[17,18] Since it had been observed[19] that dehydrobromination of 2α-bromocholestan-3-one (XII) with collidine yields in addition to the expected[20] Δ^1-cholesten-3-one approximately 20% of Δ^4-cholesten-3-one, it was hoped that both Δ^1-*trans*-9-methyl-3-octalone (V) and Δ^4-9-methyl-3-octalone (VI) would be produced in a similar reaction with IV. In point of fact, such a collidine dehydrobromination with *dl*-IV has already been carried out by Yanagita and co-workers[21] who isolated (by distillation) only one product—Δ^4-9-methyl-3-octalone (VI)—with an ultraviolet absorption maximum at 236 mμ. Actually, such an ultraviolet absorption is too low for the Δ^4-3-ketone VI and rather suggestive[19] of a mixture of Δ^1-(V) and Δ^4-(VI) isomers (the same comment also applies to the results reported[18] in the *cis* series). When this dehydrobromination was repeated in our laboratory and the crude product purified (as in the steroid series[19]) by careful chromatography and spectrophotometric examination of the various eluates, it was indeed found that the results closely paralleled those in the steroid field and that the principal product was the expected Δ^1-*trans*-9-metyl-3-octalone (V) (λ_{max}^{EtOH} 229 mμ) accompanied by some Δ^4-9-methyl-3-octalone (VI) (λ_{max}^{EtOH} 240 mμ). The ultraviolet absorption spectra of the respective 2,4-dinitrophenylhydrazones were in excellent agreement with

(4) *Cf.* C. Djerassi, *Bull. soc. chim. France*, 741 (1957).

(5) For pertinent examples see: (a) C. Djerassi, R. Riniker and B. Riniker, THIS JOURNAL, **78**, 6362 (1956); (b) C. Djerassi and W. Klyne, *Chemistry & Industry*, 988 (1956); (c) C. Djerassi and D. Marshall, *Tetrahedron*, **1**, 238 (1957); (d) C. Djerassi, J. Osiecki and W. Herz, *J. Org. Chem.*, **22**, 1361 (1957).

(6) An alternate rotatory dispersion approach, applicable to axial α-halocyclohexanones, has been described by C. Djerassi and W. Klyne (THIS JOURNAL, **79**, 1506 (1957)) and does not require any model compounds of known absolute configuration.

(7) W. G. Dauben, D. F. Dickel, O. Jeger and V. Prelog, *Helv. Chim. Acta*, **36**, 325 (1953); B. Riniker, D. Arigoni and O. Jeger, *ibid.*, **37**, 345 (1954); M. Viscontini and P. Miglioretto, *ibid.*, **38**, 930 (1955); J. W. Cornforth, I. Youhotsky and G. Popjak, *Nature*, **173**, 536 (1954).

(8) For nomenclature of rotatory dispersion results and recording of experimental data see C. Djerassi and W. Klyne, *Proc. Chem. Soc.*, 55 (1957).

(9) C. Djerassi, W. Closson and A. E. Lippman, THIS JOURNAL, **78**, 3163 (1956).

(10) A possible analysis of this contribution has been mentioned in a lecture by W. Klyne at the XVI International Congress of Pure and Applied Chemistry, Paris, 1957 (for abstract see W. Klyne and C. Djerassi, *Angew. Chem.*, **69**, 683 (1957)).

(11) See also B. Riniker, J. Kalvoda, D. Arigoni, A. Fürst, O. Jeger, A. M. Gold and R. B. Woodward, THIS JOURNAL, **76**, 312 (1954).

(12) A. J. Speziale, J. A. Stephens and Q. E. Thompson, *ibid.*, **76**, 5011 (1954).

(13) L. B. Barkley, M. W. Farrar, W. S. Knowles, H. Raffelson and Q. E. Thompson, *ibid.*, **76**, 5014 (1954); L. B. Barkley, M. W. Farrar, W. S. Knowles and H. Raffelson, *ibid.*, **76**, 5017 (1954).

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

(15) We are greatly indebted to Dr. W. S. Knowles (Monsanto Chemical Co., St. Louis, Mo.) for this very valuable gift.

(16) The bromination of the *dl*-form of III (ref. 21) as well as of the (+)-antipode (ref. 11) already has been reported.

(17) A. Butenandt and A. Wolff, *Ber.*, **68**, 2091 (1935).

(18) On the other hand, such analogy cannot be carried over to the *cis* series since coprostan-3-one gives a 4-bromo derivative while M. Yanagita and K. Yamakawa (*J. Org. Chem.*, **22**, 291 (1957)) report that monobromination of *dl-cis*-9-methyl-3-decalone (VII) occurs at C-2. The recorded ultraviolet absorption maximum of the Δ^1-3-keto-dinitrophenylhydrazone is unusual (362 mμ) and the reaction merits reinvestigation.

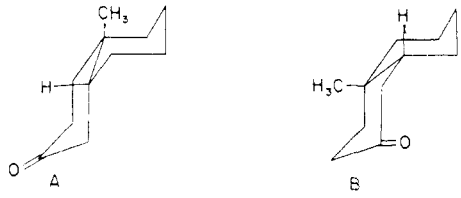
(19) C. Djerassi and C. R. Scholz, THIS JOURNAL, **69**, 2404 (1947).

(20) A. Butenandt, L. Mamoli, H. Dannenberg, L. W. Masch and J. Paland, *Ber.*, **72**, 1617 (1939).

(21) M. Yanagita and A. Tahara, *J. Org. Chem.*, **18**, 792 (1953); M. Yanagita and K. Yamakawa, *ibid.*, **21**, 500 (1956).

those reported for analogous steroids[22] and the 2,4-dinitrophenylhydrazone of Δ^1-*trans*-9-methyl-3-octalone (V) could also be obtained directly in high yield by Mattox–Kendall dehydrobromination[23] of IV,[24] since this reaction is known[25] to be free of rearrangements in the case of 2-bromocholestan-3-one (XII). Cleavage of this 2,4-dinitrophenylhydrazone by a modification[26] of the Demaecker–Martin procedure[27] regenerated Δ^1-*trans*-9-methyl-3-octalone (V), identical with the product of the chromatographed collidine dehydrobromination. From a preparative standpoint, the best route to Δ^4-9-methyl-3-octalone (VI) involves Mannich base condensation[28] with 2-methylcyclohexanone, but for our purposes this approach could not be used since the resulting racemate of VI would have to be resolved and no rigorous information concerning the absolute configuration of the resolved material would be available. On the other hand, the above-described dehydrobromination procedure has the advantage of providing products of known absolute configuration and a three-step sequence from the doubly unsaturated ketone II leads to three important bicyclic analogs (III, V, VI) of cholestan-3-one, Δ^1-cholesten-3-one and Δ^4-cholesten-3-one which represent key compounds for rotatory dispersion work. A fourth substance, optically active *cis*-9-methyl-3-decalone (VII), was of particular interest and was prepared by catalytic hydrogenation of the Δ^4-3-ketone VI as has already been reported[28,29] for the racemate of VI. While there is little question that the conformations of *trans*-9-methyl-3-decalone (III) and 3-ketoallosteroids (*e. g.*, cholestan-3-one) are identical, this does not necessarily apply to the *cis* series, where two all-chair conformations (A and B) are possible[30] for the decalone VII, while A (representing rings A and B of a steroid) is necessarily favored in 3-keto-5β-steroids (*e. g.*, coprostan-3-one) because of the additional B/C *trans* juncture. The rotatory dispersion (*vide infra*) of an optically active *cis*-9-methyl-3-decalone (VII) should, therefore, be of considerable value in settling this point.

In the above four bicyclic model compounds, III, V, VI and VII, the carbonyl group is not adjacent to an asymmetric center and the main factor to be considered in evaluating the rotatory dispersion curves is the predominance of a given conformer in solution. Of intrinsic interest as well as



A B

pertinent to some synthetic work currently under way in our laboratory in the sesquiterpene series was the extension of rotatory dispersion measurements to bicyclic ketones with carbonyl groups adjacent to an invertible ring juncture. In addition to the conformational factor, there enters the question of relative stability of *cis*- and *trans*-decalones[31] and consequently there was undertaken the synthesis of optically active *cis*- and *trans*-10-methyl-1-decalone (X and XI).

In choosing a suitable synthetic path, it was again necessary to consider the ultimate objective of obtaining a pure substance of known absolute configuration. In that connection, it appeared particularly attractive to examine the applicability of the "hetero-Δ^1-steroid rearrangement" to the decalone system, since, if successful, this would offer a short route to three bicyclic analogs of Δ^5-cholesten-4-one (XIII), coprostan-4-one (XIV) and cholestan-4-one (XV). As shown by Butenandt and Ruhenstroth-Bauer,[32] treatment of 2α-bromo-3-ketosteroids, such as 2α-bromocholestan-3-one (XII), with potassium acetate in acetic acid at 200° results in rearrangement with formation of "hetero-Δ^1-cholestenone" which was subsequently identified as Δ^5-cholesten-4-one (XIII). While the yield is only fair (27%),[33] this represents one of the simplest ways of shifting a carbonyl group from position 3 to 4 in a 5α-steroid. Careful catalytic hydrogenation[5a] of XIII affords pure coprostan-4-one (XIV) which can be isomerized irreversibly to cholestan-4-one (XV), thus making available 4-ketosteroids with the *cis* as well as *trans* orientation. The mechanism of the "hetero-Δ^1-steroid rearrangement" is only incompletely understood[34] and its application to non-steroid systems has not been investigated. Furthermore, the extension of this rearrangement to decalones would be of considerable utility in synthetic work in the eremophilone (XXV) series which is currently in progress in our laboratory.

Preliminary experiments dealing with the action of potassium acetate in acetic acid at 200° upon 2-bromo-*trans*-9-methyl-3-decalone (IV) indicated that the principal product was a crystalline ketol acetate, which by analogy to the steroids[34] must be 2- or 4-acetoxy-*trans*-9-methyl-3-decalone (IX). In order to simplify the chromatographic separation of this acetate from the desired unsaturated ketone VIII, the crude reaction mixture was first saponified, thus increasing greatly the difference in polarity of the products. Chromatography then

(22) C. Djerassi and E. Ryan, THIS JOURNAL, **71**, 1000 (1949).

(23) V. R. Mattox and E. C. Kendall, *ibid.*, **70**, 882 (1948), and later papers.

(24) The reaction of (+)-IV with 2,4-dinitrophenylhydrazine has already been reported briefly by Riniker, *et al.*, in a preliminary communication (ref. 11).

(25) C. Djerassi, THIS JOURNAL, **71**, 1003 (1949).

(26) C. Djerassi, A. Bowers, R. Hodges and B. Riniker, *ibid.*, **78**, 1733 (1956).

(27) J. Demaecker and R. H. Martin, *Nature*, **173**, 266 (1954).

(28) E. C. du Feu, F. J. McQuillin and R. Robinson, *J. Chem. Soc.*, 53 (1937).

(29) A mixture of *cis*-(VII) and *trans*-(III) decalones is produced but the *cis* isomer, being crystalline, can be separated readily. A quantitative estimation of the proportion of isomers formed in this hydrogenation has been accomplished recently by Sondheimer and Rosenthal (ref. 38).

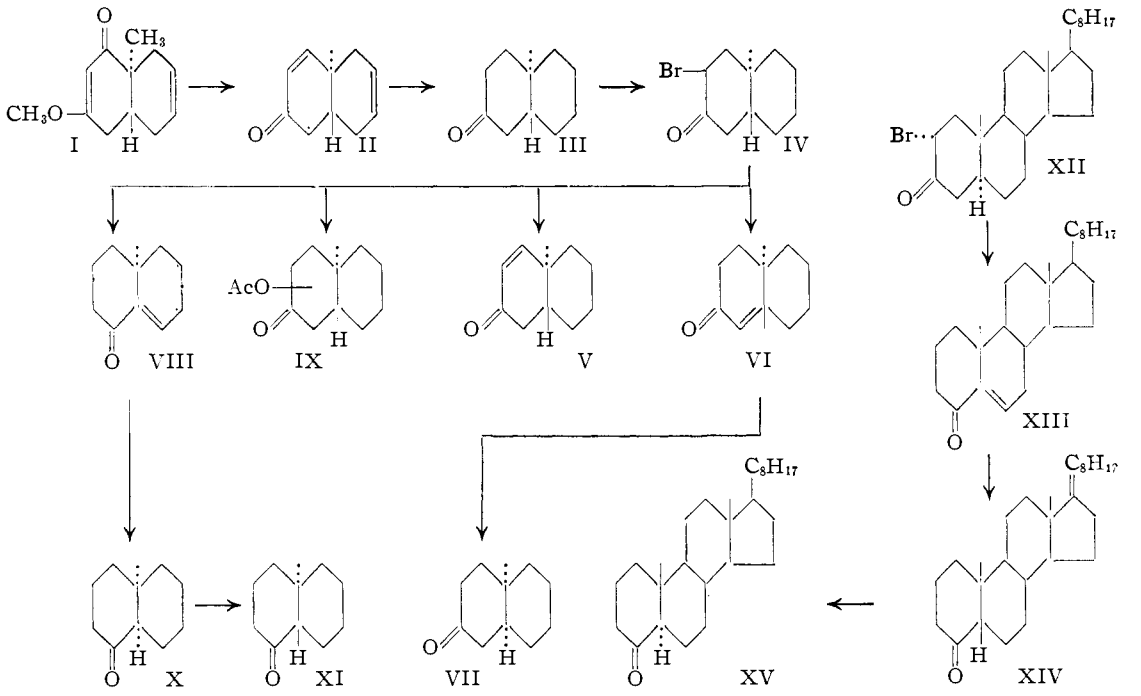
(30) See W. Klyne, "Progress in Stereochemistry," Academic Press, Inc., New York, N. Y., 1954, chapter 2; W. G. Dauben and K. S. Pitzer in M. S. Newman "Steric Effects in Organic Chemistry," John Wiley and Sons, Inc., New York, N. Y., 1956, p. 28.

(31) For pertinent summary see N. L. Allinger, *J. Org. Chem.*, **21**, 915 (1956).

(32) A. Butenandt and G. Ruhenstroth-Bauer, *Ber.*, **77**, 397 (1944), and earlier papers.

(33) Unpublished model experiment by Dr. B. Riniker in this Laboratory.

(34) See L. F. Fieser and M. Romero, THIS JOURNAL, **75**, 4716 (1953).



afforded in 28% yield an unsaturated ketone, whose infrared and particularly ultraviolet absorption spectrum (typical of cisoid enone) clearly showed that it was the required unsaturated ketone VIII and that the "hetero-Δ^1-steroid rearrangement" also can be used with decalones. The ketone was sensitive to air oxidation, strongly reminiscent of eremophilone (XXV)[35] which possesses the same chromophoric system, and consequently it was immediately hydrogenated by the procedure[36] employed successfully[5a] for the conversion of Δ^5-cholesten-4-one (XIII) to coprostan-4-one (XIV). The resulting reduction product was almost certainly stereochemically homogeneous, as pointed out below in a discussion of the relevant dispersion curves, and we are tentatively assigning[37] to it the *cis*-10-methyl-1-decalone (X) structure by analogy to the course of the steroid hydrogenation.[5a] The rotatory dispersion results, outlined below, do not offer an unequivocal answer. Alkali or acid treatment of X leads to a new isomer—whose rotatory dispersion (see Fig. 5) shows an inverted Cotton effect—which is probably not stereochemically pure[38] but which must consist predominantly of the other isomer, *trans*-10-methyl-1-decalone (XI). Neither X nor XI afforded a sharp melting 2,4-dinitrophenylhydrazone and this most likely was due to conversion to an equilibrium mixture[38] of the two isomers under the conditions of hydrazone formation.

Rotatory Dispersion Results.—The rotatory dispersion curves of the two octalones V and VI are reproduced in Fig. 1 and both of them show the fine structure in the 350–400 mμ region which has been attributed[39] to the unsaturated carbonyl moiety. The curve of Δ^1-*trans*-9-methyl-3-octalone (V) closely resembles[40] that[39] of Δ^1-cholesten-3-one even to the extent that the first peak (respectively trough) is more intense than the second one. It is interesting to note that Δ^4-9-methyl-3-octalone (VI) exhibits a curve, which is somewhat different from that of Δ^4-cholesten-3-one[39] since it never crosses the zero axis and this has also been observed[5d] with Prelog and Acklin's[41] Δ^4-9-methyl-8-hydroxy-3-octalone (XVI). Nevertheless the gross shape and in particular the sign of the multiple Cotton effect[8] curve is sufficiently similar to that of Δ^4-3-ketosteroids so that such curves can be used safely for purposes of absolute configuration determinations.[5a,5d]

The shape (and often even sign) of the rotatory dispersion curve of a given ketone is characteristic of the location of the carbonyl chromophore in a certain asymmetric environment. Since changes in conformation of rings clearly affect the asymmetry of the system, it can be expected that this will reflect itself in alterations of the dispersion curve; and optical rotatory dispersion can, there-

(35) A. E. Bradfield, A. R. Penfold and J. L. Simonsen, *J. Chem. Soc.*, 2744 (1932).

(36) Other workers (ref. 32 and D. N. Jones, J. R. Lewis, C. W. Shoppee and G. H. R. Summers, *ibid.*, 2876 (1955)) have used conditions which led directly to cholestan-4-one (XV), probably by rearrangement of the initially formed coprostan-4-one (XIV).

(37) Great caution has to be exercised in this case in drawing stereochemical conclusions from analogy to related systems, since additional substituents play an important role (see for instance D. F. Grant and D. Rogers, *Chemistry & Industry*, 278 (1956)). A striking case in point is the hydrogenation of eremophilone (XXV) (see ref. 5a) which will be discussed in detail in a future paper dealing also with transformations in the hydroxydihydroeremophilone series (R. Mauli, unpublished experiments).

(38) F. Sondheimer and D. Rosenthal (THIS JOURNAL, **80**, 3995 (1958)), utilizing a completely different synthetic sequence in the *dl*-series, have shown that 10-methyl-1-decalone forms an equilibrium mixture consisting of 40% *cis* (X) and 60% *trans* (XI) isomers. We are greatly indebted to Dr. Sondheimer for informing us of his results prior to publication.

(39) A. E. Lippman, E. W. Foltz and C. Djerassi, *ibid.*, **77**, 4354 (1955).

(40) The curves are, of course, roughly mirror images since the compounds are of enantiomeric types as indicated in the structural formulas which are intended to indicate actual absolute configurations using the steroid system.

(41) V. Prelog and W. Acklin, *Helv. Chim. Acta*, **39**, 748 (1956).

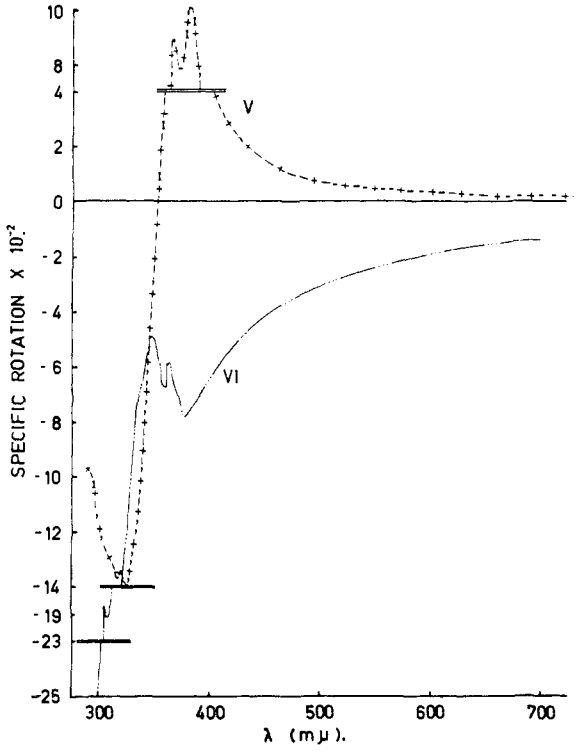


Fig. 1.—Optical rotatory dispersion curves (dioxane solution) of Δ^1-*trans*-9-methyl-3-octalone (V) and Δ^4-9-methyl-3-octalone (VI).

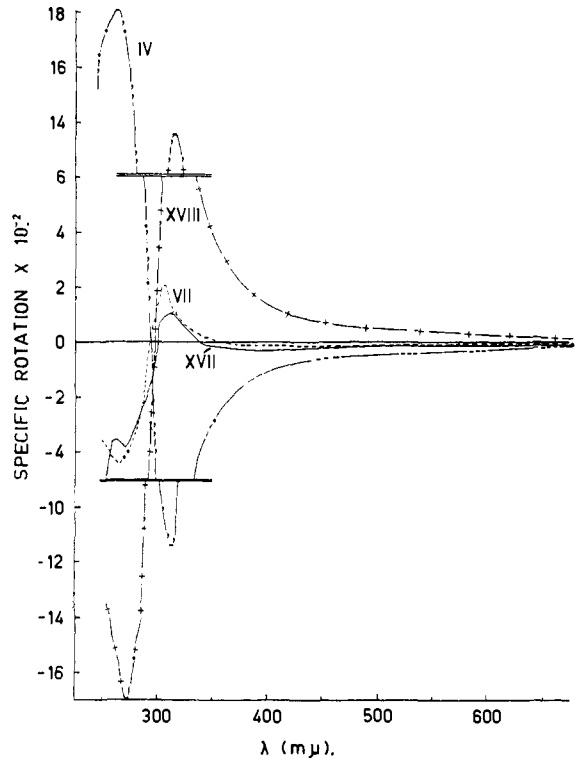


Fig. 2.—Optical rotatory dispersion curves (methanol solution) of 2-bromo-*trans*-9-methyl-3-decalone (IV), *cis*-9-methyl-3-decalone (VII), *cis*-9-methyl-8-methoxycarbonyl-3-decalone (XVII) and *cis*-9-methyl-1-decalone (XVIII).

fore, be used as a sensitive tool[42] for the detection of even minor conformational changes. A case in point is illustrated in Fig. 2 which contains the rotatory dispersion curves of the above-described *cis*-9-methyl-3-decalone (VII) and of *cis*-9-methyl-8-methoxycarbonyl-3-decalone (XVII) derived from cevine.[43] The two curves are sufficiently similar so that it can be assumed safely that both of these *cis*-decalones (VII, XVII) possess the same conformation (A or B), a statement which could not have been made *a priori* since depending upon its orientation the additional C-8 substituent could well have favored the alternate conformation. Furthermore, the shape[44] of their rotatory dispersion curves is very similar to that of 3-keto-5β-steroids,[45] such as coprostan-3-one, which exists in conformation A (rings A and B of the steroid) rather than conformation B due to the restriction imposed by the additional *trans* B/C juncture. The question has been raised[46] whether *cis*-decalones, because of increased conformational mobility,[30] may not exist in a conformation different from that of 3-keto-5β-steroids and our rotatory dispersion results strongly suggest that form A correctly represents *cis*-9-methyl-3-decalones such as VII and XVII.[47]

Two additional examples are collected in Fig. 2. The first refers to the rotatory dispersion curve of (−)-2-bromo-*trans*-9-methyl-3-decalone (IV) and it bears the same relation—both with respect to amplitude and to position of peak and trough—to (−)-*trans*-9-methyl-3-decalone (III)[5a] as has been reported[48] for the pair cholestan-3-one and 2α-bromocholestan-3-one (XII). The generalizations concerning the effect of axial and equatorial halogen atoms made in the steroid series[48] would appear, therefore, to be equally applicable to bicyclic ketones.[49] The other curve shown in Fig. 2 corresponds to *cis*-9-methyl-1-decalone (XVIII)[43] and is characterized by a positive Cotton effect curve as is the corresponding *trans* isomer[5a] as well as certain hydrogenation products[5a] of ψ-santonin. Since the steric course of the hydrogenation of ψ-santonin has not been established definitely,[50] the fact that the sign of the Cotton effect in simple[51] 9-methyl-1-decalones is not affected by the stereochemistry at C-10 strengthens our earlier assign-

(42) This subject is covered in detail in paper XVII of this series, Djerassi, *et al.*, THIS JOURNAL, **80**, 4001 (1958).

(43) F. Gautschi, O. Jeger, V. Prelog and R. B. Woodward, *Helv. Chim. Acta*, **37**, 2280 (1954).

(44) In the present paper we are only considering gross similarities in shape. More precise quantitative comparisons based on molecular rotatory dispersion curves (see ref. 10) and conclusions to be drawn from them will be considered in a future paper.

(45) C. Djerassi and W. Closson, THIS JOURNAL, **78**, 3761 (1956).

(46) (a) W. Klyne, *Experientia*, **12**, 119 (1956); (b) see, for instance, R. B. Turner, W. R. Meador and R. E. Winkler, THIS JOURNAL, **79**, 4122 (1957).

(47) It should be appreciated that certain axial substituents (based on conformation A) may change the picture completely and favor form B in order to relieve non-bonded interactions (see ref. 30).

(48) C. Djerassi, J. Osiecki, R. Riniker and B. Riniker, THIS JOURNAL, **80**, 1216 (1958).

(49) Additional examples have been secured during synthetic studies (F. X. Markley and L. Zalkow, unpublished work) directed toward eremophilone (XXV) and these will form the subject of a separate communication.

(50) A *trans* ring fusion has been suggested by N. M. Chopra, W. Cocker, J. T. Edward, T. B. H. McMurray and E. R. Stuart, *J. Chem. Soc.*, 1828 (1956).

(51) Substitution at C-2 can change the picture radically and this is illustrated in paper XVII of this series.

ment[5a] of the absolute configuration of ψ-santonin.

As demonstrated elsewhere,[42] introduction of axial methyl groups in an adjacent or vinylogous position to a ketone can produce marked rotatory dispersion changes and this is particularly pronounced in 4,4-dimethyl-3-keto-5α-steroids or triterpenes, where such a structural modification actually results in an inversion of the sign of the Cotton effect. Since interaction between the angular methyl group and one of the methyl groups at C-4 is *not* responsible[42] for this remarkable effect, it was of very considerable interest to examine the situation in the decalone series. Fortunately, this was made possible by the recent synthesis[52] of optically active Δ^6-*trans*-4,4,9-trimethyl-3-octalol (XIX), whose absolute configuration was established as depicted in XIX since it was derived from the bicyclic ketone I.[12,14] Oxidation of XIX with the Jones reagent[53] afforded the octalone XXI, while catalytic hydrogenation produced the decalol XX and oxidation led to the desired *trans*-4,4,9-trimethyl-3-decalone (XXII). The rotatory dispersions (Fig. 3) of both ketones (XXI, XXII) are

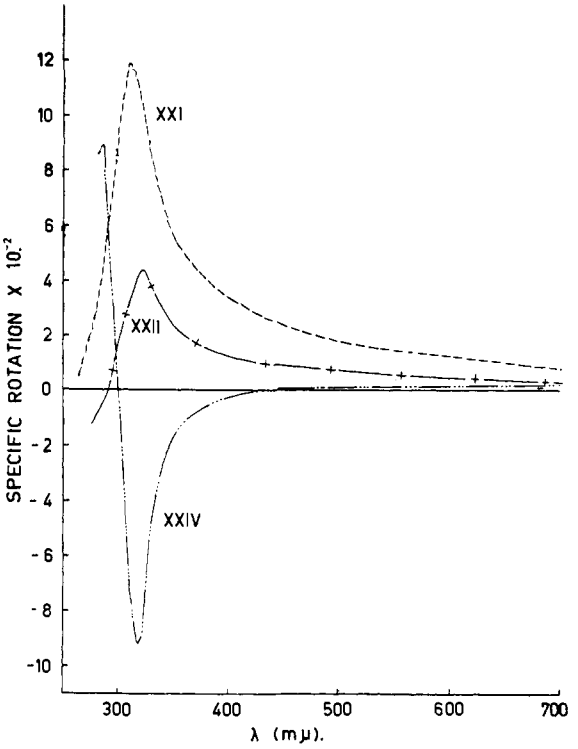


Fig. 3.—Optical rotatory dispersion curves of Δ^6-*trans*-4,4,9-trimethyl-3-octalone (XXI) (methanol), *trans*-4,4,9-trimethyl-3-decalone (XXII) (methanol) and *trans*-5,9-dimethyl-3-decalone (XXIV) (dioxane).

characterized by a positive Cotton effect curve in contrast to the negative one[5a] of *trans*-9-methyl-3-decalone (III) thus showing the operation of the same conformational factor[42] due to the *gem*-dimethyl grouping which causes the inversion of the Cotton effect in polycyclic systems. Furthermore, the marked amplitude differences between the octalone XXI and the decalone XXII can be attributed to the conformational distortion produced by the 6,7-double bond. This becomes particularly noticeable in the presence of a 1,2-double bond as can be judged by a comparison of the rotatory dispersion curve (Fig. 4) of the un-

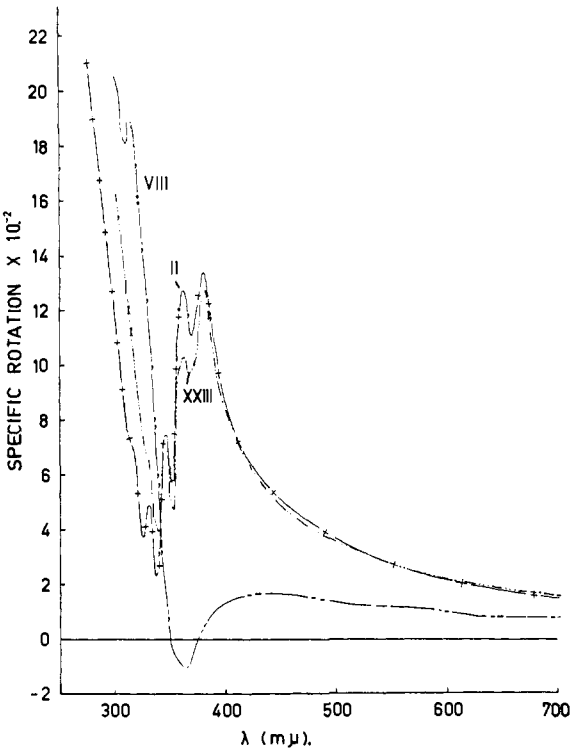


Fig. 4.—Optical rotatory dispersion curves (dioxane solution) of (+)-*trans*-3-keto-9-methyl-$\Delta^{1,6}$-hexahydronaphthalene (II), Δ^8-10-methyl-1-octalone (VIII) and *trans*-3-keto-4,4,9-trimethyl-$\Delta^{1,6}$-hexahydronaphthalene (XXIII).

saturated ketone II[54] with its remarkable wealth of fine structure and the comparatively simple curve (Fig. 1) of Δ^1-*trans*-9-methyl-3-octalone (V). In the hexahydronaphthalene ketones (II, XXIII), the presence of a *gem*-dimethyl function plays essentially no role as can be seen in Fig. 4 where the dispersion curve of the 4,4,9-trimethyl ketone XXIII[52] is reproduced. The presence of a methyl group in the second ring, as in *trans*-5,9-dimethyl-3-decalone (XXIV),[55] produces no striking effect, but the amplitude of its rotatory dispersion curve (Fig. 2) is reduced as compared to *trans*-9-methyl-3-decalone (III)[5a] and this we attribute to some steric interference between the equatorial 5-methyl function and the hydrogen atoms at C-4.

One of the chief reasons for synthesizing Δ^8-10-methyl-1-octalone (VIII) was to support our earlier assignment[5a] of the absolute configuration of eremophilone (XXV) which was based on a com-

(52) R. B. Woodward, *et al.*, to be published. We are deeply indebted to Prof. R. B. Woodward (Harvard University) for a generous gift of this substance.

(53) K. Bowden, I. M. Heilbron, E. R. H. Jones and B. C. L. Weedon, *J. Chem. Soc.*, 39 (1946), and later papers.

(54) See C. Djerassi, R. Riniker and B. Riniker, THIS JOURNAL, **78**, 6377 (1956), where the dispersion curve of its antipode is reproduced in three different solvents.

(55) B. Riniker, D. Sc. thesis, Eidgenössische Technische Hochschule, Zurich, 1955, p. 48. The sample was obtained through the courtesy of Prof. O. Jeger (E. T. H., Zurich).

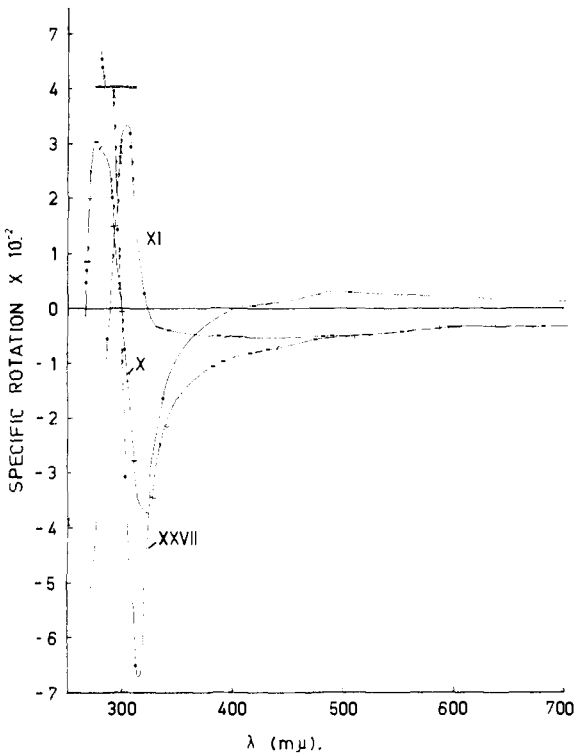


Fig. 5.—Optical rotatory dispersion curves of *cis*-10-methyl-1-decalone (X) (methanol), *trans*-10-methyl-1-decalone (XI) (methanol) and β-5-(*trans*-2,5-dimethyl-6-carboxy-1-decalone)-propionic acid (XXVII) (dioxane).

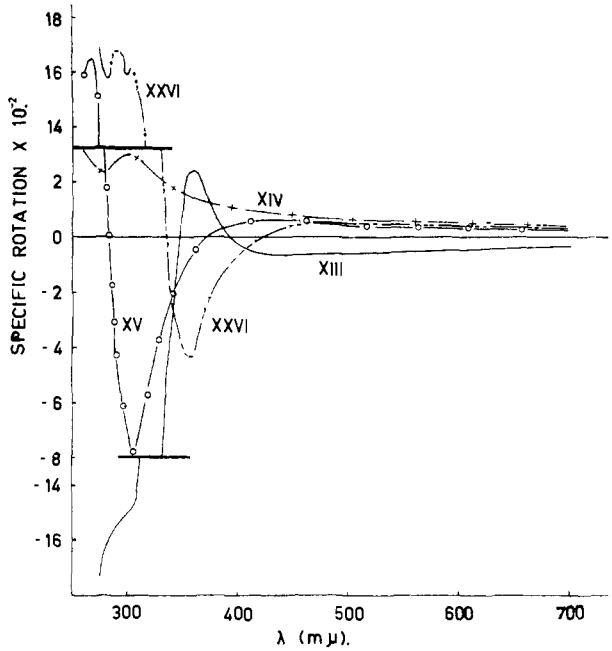


Fig. 6.—Optical rotatory dispersion curves of Δ⁵-cholesten-4-one (XIII) (dioxane), coprostan-4-one (XIV) (methanol), cholestan-4-one (XV) (methanol) and Δ⁴-cholesten-6-one (XXVI) (dioxane).

parison of its rotatory dispersion curve with those of Δ⁴-cholestene-6-one (XXVI) and Δ⁵-cholestene-4-one (XIII). The octalone VIII represents the fundamental unsubstituted eremophilone skeleton and its rotatory dispersion curve (Fig. 4) strongly resembles that of Δ⁴-cholesten-6-one (XXVI) and is roughly antipodal to that of Δ⁵-cholesten-4-one (XIII) (Fig. 6). While the curve[5a] of eremophilone (XXV) itself is shifted considerably toward more negative rotation values (which may be due to the additional substituents), its shape is on the whole similar to the curve of Δ⁸-10-methyl-1-octalone (VIII), thus strengthening the original[5a] absolute configuration proposal.

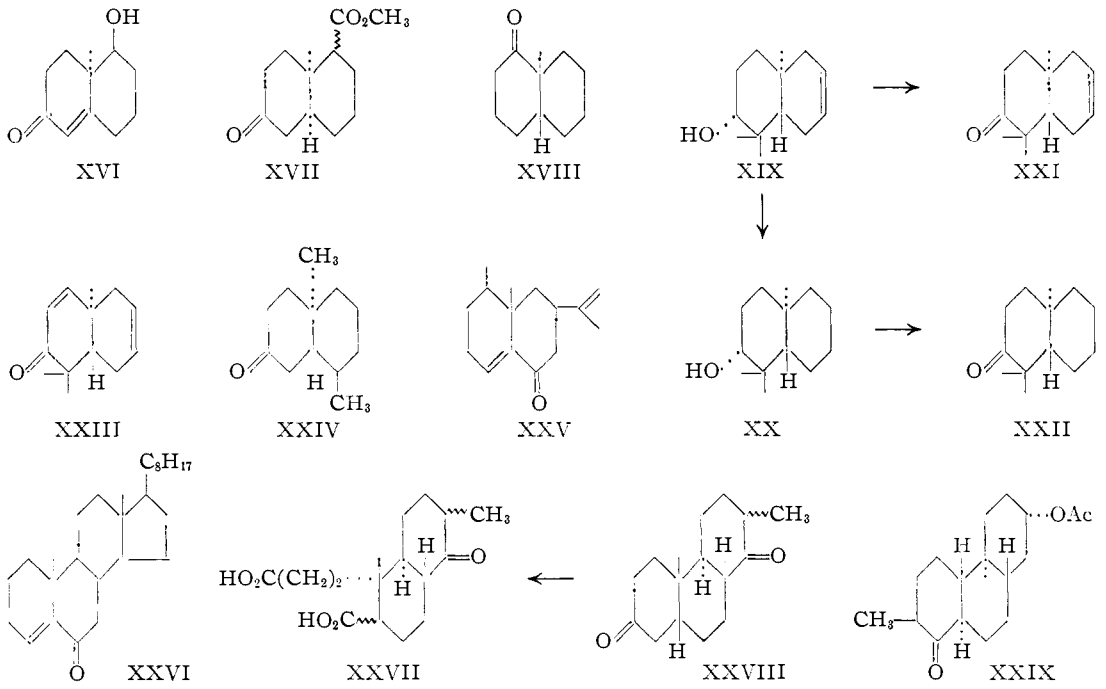
Attention already has been called[56] to the fact that cholestan-6-one, coprostan-6-one and cholestan-4-one (XV) all exhibit negative single Cotton effect curves while coprostan-4-one (XIV) shows a positive one. For purposes of orientation, the dispersion curves of the last two ketones are again reproduced in Fig. 6 and it is clear[56] that 4-keto- and 6-ketosteroids should not be considered as enantiomeric ring types.[57] As a result, it was of very considerable interest to measure the rotatory dispersion curves of the bicyclic analogs, *cis*- (X) and *trans*- (XI) 10-methyl-1-decalone and these are reproduced in Fig. 5. The hydrogenation product of Δ⁸-10-methyl-1-octalone (VIII) has been assigned (*vide supra*) tentatively[37] the *cis* configuration X and the stereochemical purity of the substance (irrespective of whether it is *cis* or *trans*) is suggested by the virtually symmetrical character (around the zero rotation line) of its rotatory dispersion curve (Fig. 5). While alkali or acid treatment of the initial hydrogenation product X probably leads to an equilibrium mixture,[38] the rotatory dispersion curve of this isomerization product clearly shows that the other isomer XI must have an opposite Cotton effect.

A comparison of the rotatory dispersion curve (Fig. 6) of cholestan-4-one (XV) (containing a terminal *trans*-10-methyl-1-decalone system) with that of *trans*-10-methyl-1-decalone (XI) is probably valid since both can be expected to exist in substantially the same all-chair conformation. In view of the fact that our synthetic decalone XI possesses the opposite absolute configuration from the steroids, its Cotton effect curve should be roughly enantiomeric to that of cholestan-4-one (XV) and an inspection of Figs. 5 and 6 bears this out. Consequently, we feel justified in assuming that the major product of the alkali or acid isomerization in the 10-methyl-1-decalone series is the *trans* isomer XI from which it follows that the initial hydrogenation product of VIII should be *cis*-10-methyl-1-decalone (X).

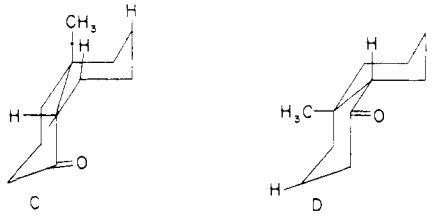
On the other hand, we do not believe that at the present time a valid rotatory dispersion comparison can be carried out between coprostan-4-one (XIV) and *cis*-10-methyl-1-decalone (X). Just as with *cis*-9-methyl-3-decalone (VII), which can exist in two all-chair conformations (A and B), two conformations (C and D) are also possible for *cis*-10-methyl-1-decalone (X) (for further discussion see ref. 46a). While in the former, the difference between forms A and B is a very subtle one in the absence of additional substitution, this is not necessarily the case in the 1-decalone series where con-

(56) See footnote 52 in ref. 5a.

(57) For definition and application to molecular rotation difference calculations see W. Klyne, *J. Chem. Soc.*, 2916 (1952).



former D exhibits one less axial methyl-hydrogen interference than C. It is very likely, therefore, that *cis*-10-methyl-1-decalone (X) exists largely in conformation D while steroids such as coprostan-4-one (XIV) assume (as far as rings A and B are concerned) conformation C because of the restraint toward conformational mobility imposed by the additional *trans* B/C juncture.



Since a stereochemical assignment, based on rotatory dispersion comparisons, seems only possible in the *trans* series, it is desirable to collect additional examples which would strengthen the above arguments. A possible case in point is the dibasic acid XXVII,[58] obtained by ring opening of the perhydrophenanthrene diketone XXVIII, which in turn was derived from the well-known Köster–Logemann ketone.[59] Unfortunately, the keto-dibasic acid XXVII suffers from a disadvantage which places dispersion comparisons on somewhat tenuous grounds. The substance lacks an angular methyl group which would tend to stabilize[60] the *trans* ring juncture present in the starting material XXVIII, but there exists some doubt about the stereochemistry at C-2 and C-6. If these invertible centers have been converted to the equatorial orientations during the degradation, then the dibasic acid XXVII represents a satisfactory rotatory dispersion model for a *trans*-decalone. On the other hand, if the substituents at both centers are still axial then it is quite possible that the *cis*-decalone system is more stable and that inversion of the ring juncture might have occurred. With this reservation in mind, it should be noted that the rotatory dispersion curves (Fig. 5) of the dibasic acid XXVII and *trans*-10-methyl-1-decalone (XI) are of mirror image type, which would be expected if the stereochemistry of their ring junctures is correct as indicated in the structural formulas.

An even better example is provided by the tricyclic ketone XXIX, whose stereochemistry is known[61] already and which exhibits[5b,62] a negative Cotton effect curve. Since the absolute configuration of the *trans*-decalone system of XXIX is opposite to that of our synthetic ketone XI, their respective rotatory dispersion curves should be antipodal in nature and this is actually the case.

Acknowledgment.—We are grateful to Dr. W. Klyne, Postgraduate Medical School, London, for stimulating correspondence.

Experimental[63]

(−)-2-Bromo-*trans*-9-methyl-3-decalone (IV).[16]—A solution of 3.7 g. of (+)-*trans*-3-keto-9-methyl-$\Delta^{1,6}$-hexahydronaphthalene (II)[12,15] in 40 cc. of methanol was hydrogenated at room temperature and atmospheric pressure with 300 mg. of platinum oxide catalyst. Hydrogen up-take, corresponding to two equivalents, ceased in less than 2 hr. and

(58) We are grateful to Prof. O. Jeger (E. T. H., Zurich) for providing this specimen.

(59) H. Köster and W. Logemann, *Ber.*, **73**, 298 (1940).

(60) In the absence of additional substituents, α-decalones lacking an angular methyl group are considerably more stable in the *trans* form (see W. Hückel and E. Brinkmann, *Ann.*, **441**, 21 (1925); R. B. Turner, THIS JOURNAL, **74**, 2118 (1952)).

(61) J. R. Billeter and K. Miescher, *Helv. Chim. Acta*, **33**, 388 (1950).

(62) Compound III in ref. 5b.

(63) Melting points were determined on the Kofler block while boiling points are uncorrected. We are indebted to Mrs. V. Halpern for most of the rotatory dispersion measurements; leading references to the experimental procedure and errors are given in ref. 5 and 54. The ultraviolet and infrared spectral determinations are due to Mrs. Dolores Phillips and the microanalyses to Dr. A. Bernhardt, Mülheim, Germany.

after filtration of the catalyst the solvent was removed through a small column and (−)-*trans*-9-methyl-3-decalone (III)[58] was distilled; yield, 3.65 g., b.p. 130° at 17 mm.

A stirred, cold solution of 4.0 g. of the ketone III in 30 cc. of glacial acetic acid was treated dropwise with 4.0 g. of bromine in 30 cc. of acetic acid. After stirring for an additional 30 min. at room temperature, water was added and the precipitate of the bromo ketone IV was collected and washed well with water. Recrystallization from dilute acetone and sublimation at 95° and 0.05 mm. furnished 4.12 g. of colorless needles exhibiting m.p. 137–139°, $[\alpha]D$ −21° ($CHCl_3$); $\lambda_{max}^{CS_2}$ 5.72 μ (as compared to 5.80 μ for III), λ_{max}^{EtOH} 284 mμ, ε 29 (as compared to λ_{max}^{EtOH} 284 mμ, ε 20 for III); R.D. (Fig. 2) in methanol (*c* 0.135): $[\alpha]_{700}$ −10°, $[\alpha]_{589}$ −21°, $[\alpha]_{312.5}$ −1140°, $[\alpha]_{265}$ +1815°, $[\alpha]_{245}$ +1510°.

Anal. Calcd. for $C_{11}H_{17}BrO$: C, 53.88; H, 6.98; Br, 32.65. Found: C, 54.02; H, 6.72; Br, 32.74.

Dehydrobromination of (−)-2-Bromo-*trans*-9-methyl-3-decalone (IV). (a) With γ-Collidine.—A solution of 3.32 g. of the bromoketone IV in 25 cc. of γ-collidine[64] was heated under reflux for 20 min. in an atmosphere of nitrogen and the quantitatively precipitated collidine hydrobromide was filtered and washed with much ether. The filtrate was diluted with more ether and then washed repeatedly with dilute hydrochloric acid followed by potassium carbonate solution and water, dried and evaporated. The resulting oil (1.85 g.), dissolved in hexane, was chromatographed on 200 g. of Fisher activated alumina. Elution with benzene and benzene–ether (9:1) afforded fractions with λ_{max}^{EtOH} 228–229 mμ and these were combined to give 1.0 g. of (+)-Δ¹-*trans*-9-methyl-3-octalone (V), which distilled at a bath temperature of 150° and 18 mm.; $\lambda_{max}^{liquid\ film}$ 5.92 μ, λ_{max}^{EtOH} 229 mμ, ε 9500; R.D. (Fig. 1) in dioxane (*c* 0.086): $[\alpha]_{700}$ +20°, $[\alpha]_{586}$ +40°, $[\alpha]_{390}$ + 1020°, $[\alpha]_{370}$ +788°, $[\alpha]_{365}$ +898°, $[\alpha]_{322.5}$ −1400°, $[\alpha]_{317.5}$ −1340°, $[\alpha]_{315}$ −1370°, $[\alpha]_{285}$ −968°.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.83; O, 9.74. Found: C, 80.37; H, 10.03; O, 9.94.

The 2,4-dinitrophenylhydrazone[65] was crystallized from methanol–chloroform whereupon it showed m.p. 191–192°, $\lambda_{max}^{CHCl_3}$ 381 mμ, ε 27600.

Anal. Calcd. for $C_{17}H_{20}N_4O_4$: C, 59.29; H, 5.85. Found: C, 59.11; H, 5.80.

Further development of the chromatogram column and combination of those fractions (eluted with benzene–ether 8:2 and 7:3) exhibiting ultraviolet absorption at 240 mμ yielded 210 mg. of (−)-Δ⁴-9-methyl-3-octalone (VI), which was distilled at a bath temperature of 155° and 17 mm.: $\lambda_{max}^{liquid\ film}$ 5.98μ, λ_{max}^{EtOH} 240 mμ, ε 16200; R.D. (Fig. 1) in dioxane (*c* 0.075): $[\alpha]_{700}$ −139°, $[\alpha]_{589}$ −196°, $[\alpha]_{375}$ −785°, $[\alpha]_{365}$ −641°, $[\alpha]_{362.5}$ −587°, $[\alpha]_{357.5-360}$ −670°, $[\alpha]_{347.5}$ −487°, $[\alpha]_{307.5}$ −1920°, $[\alpha]_{305}$ −1870°, $[\alpha]_{290}$ −3290°.

The 2,4-dinitrophenylhydrazone crystallized as red microplates from methanol–chloroform and exhibited m.p. 176–177°, $\lambda_{max}^{CHCl_3}$ 391 mμ, ε 28500.

Anal. Calcd. for $C_{17}H_{20}N_4O_4$: C, 59.29; H, 5.85; N, 16.27. Found: C, 58.84; H, 6.03; N, 16.15.

(b) With 2,4-Dinitrophenylhydrazine.—The bromo ketone acid IV (150 mg.) in 3 cc. of glacial acetic was heated on the steam-bath with an equal weight of 2,4-dinitrophenylhydrazine for 10 min. in a current of nitrogen. After standing for 2 hr., 103 mg. of (+)-Δ¹-*trans*-9-methyl-3-octalone 2,4-dinitrophenylhydrazone, m.p. 184–186°, was filtered off and an additional 30 mg. (m.p. 185–188°) could be secured by dilution of the filtrate with water and recrystallization from ethanol–chloroform. The melting point was not depressed upon admixture with the 2,4-dinitrophenylhydrazone of the collidine dehydrobromination product.

In order to regenerate the unsaturated ketone, 90 mg. of the 2,4-dinitrophenylhydrazone was heated under reflux for 45 min. with 40 cc. of acetone and 1 cc. of concd. hydrochloric acid. After cooling, a solution of 0.75 g. of stannous chloride in 0.75 cc. of concd. hydrochloric acid was added, followed by 2 cc. of water and the mixture was heated under reflux for 30 min. in an atmosphere of nitrogen. Dilution with 100 cc. of water, extraction with pentane, washing of the extract with dilute hydrochloric acid until colorless, evaporation of the solvent and distillation of the residual oil at a bath temperature of 150° and 18 mm. afforded 45 mg. of (+)-Δ¹-*trans*-9-methyl-3-octalone (V), λ_{max}^{EtOH} 228 mμ, ε 9300.

(−)-*cis*-9-Methyl-3-decalone (VII).—The catalytic hydrogenation of 110 mg. of (−)-Δ⁴-9-methyl-3-decalone (VI) in 35 cc. of methanol with 14 mg. of 2% palladized charcoal was complete in less than 30 min., at which time ultraviolet spectral measurement of an aliquot showed the presence of only a trace of α,β-unsaturated ketone. Filtration of the catalyst and evaporation of the filtrate to dryness left a semi-solid residue which upon several low temperature crystallizations from pentane yielded 30 mg. of the *cis*-decalone, m.p. 62–63°, $\lambda_{max}^{liquid\ film}$ 5.80 μ; R.D. (Fig. 2) in methanol (*c* 0.05): $[\alpha]_{700}$ −28°, $[\alpha]_{589}$ −6°, $[\alpha]_{550}$ −20°, $[\alpha]_{307.5}$ +208°, $[\alpha]_{267.5}$ −442°, $[\alpha]_{250}$ −352°.

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.92. Found: C, 79.03; H, 10.98.

Reaction of Potassium Acetate with (−)-2-Bromo-*trans*-9-methyl-3-decalone (IV).—The bromoketone IV (500 mg.) was heated in a sealed tube for 6 hr. at 200° with 5.3 g. of freshly fused potassium acetate and 25 cc. of glacial acetic acid and then diluted with water. Extraction with ether, washing with dilute potassium carbonate solution and water, drying and evaporating left 360 mg. of semi-solid which was separated into two fractions by distillation; (a) 81 mg., b.p. 130–140° at 15 mm.; (b) 140 mg., b.p. 175–180° at 15 mm. The higher boiling fraction solidified on cooling and after crystallization from ether–pentane and sublimation at 120° and 0.3 mm. led to colorless needles of (−)-x-acetoxy-*trans*-9-methyl-3-decalone (IX), m.p. 132–134°, $\lambda_{max}^{liquid\ film}$ 5.72 and 5.88 μ; R.D. in methanol (*c* 0.098 and 0.02 below 285 mμ): $[\alpha]_{700}$ −64°, $[\alpha]_{589}$ −134°, $[\alpha]_{307.5}$ −2461°, $[\alpha]_{270}$ +1954°, $[\alpha]_{265}$ +699°.

Anal. Calcd. for $C_{13}H_{22}O_3$: C, 69.61; H, 8.99; O, 21.40. Found: C, 69.49; H, 9.00; O, 21.76.

The desired α,β-unsaturated ketone VIII could be separated from the above acetate only by wasteful chromatography and consequently the following modification was introduced. The reaction mixture from 2.0 g. of bromoketone IV, 21.2 g. of potassium acetate and 100 cc. of glacial acetic acid after being heated for 20 hr. at 200° was processed as above except that the resulting neutral product (1.4 g.) was stirred in an atmosphere of nitrogen for 3 hr. at 50° with 2.0 g. of potassium carbonate and 25 cc. of dilute methanol. After pouring into water, extracting with ether, evaporating and chromatographing the residue (1.2 g.) on 100 g. of Fisher alumina (deactivated by shaking a hexane suspension with 3 cc. of 10% aqueous acetic acid), elution with hexane–benzene (1:1) gave 370 mg. (28%) of (+)-Δ⁸-10-methyl-1-octalone (VIII). After purification by repeated chromatography and distillation at 115° and 14 mm., there was isolated 116 mg. of the pure octalone VIII, $\lambda_{max}^{liquid\ film}$ 5.90 and 6.11 μ, λ_{max}^{EtOH} 240 mμ, ε 6400; R.D. (Fig. 4) in dioxane (*c* 0.173): $[\alpha]_{700}$ +80°, $[\alpha]_{589}$ +102°, $[\alpha]_{450-425}$ +163–162° (broad peak), $[\alpha]_{261.5}$ −94°, $[\alpha]_{312.5}$ +1874°, $[\alpha]_{310}$ +1810°, $[\alpha]_{300}$ +2040°.

Anal. Calcd. for $C_{11}H_{16}O$: C, 80.44; H, 9.83. Found: C, 79.96; H, 9.21.

The ketone was quite unstable and on standing in air at room temperature it turned to a yellow resin.

Hydrogenation of (+)-Δ⁸-10-Methyl-1-octalone (VIII).—The freshly prepared unsaturated ketone VIII (160 mg.) was hydrogenated in methanol (30 cc.) using 10% palladized charcoal catalyst (30 mg.) at room temperature and atmospheric pressure. Hydrogen up-take corresponding to one equivalent was complete within 15 min., at which time no more gas was consumed. After filtering the catalyst and removing the solvent, distillation at a bath temperature of 110–115° and 16 mm. yielded 125 mg. of (−)-*cis*-10-methyl-1-decalone (X), $\lambda_{max}^{liquid\ film}$ 5.82 μ; R.D. (Fig. 5) in methanol (*c* 0.10): $[\alpha]_{700}$ −33°, $[\alpha]_{589}$ −39°, $[\alpha]_{322.5}$ −371°, $[\alpha]_{275}$ +305°, $[\alpha]_{265}$ −90°.

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.92. Found: C, 79.71; H, 10.82.

Attempts to prepare a pure 2,4-dinitrophenylhydrazone failed, probably due to equilibration.[38]

A product, containing the identical amount[38] of *trans*-10-methyl-1-decalone (XI) as judged by coincidence of rotatory dispersion curves, was obtained when the *cis*-decalone

(64) Purchased from Schweizerische Teerindustrie, A. G., Pratteln (Switzerland), since synthetic γ-collidine gave inferior results.

(65) The corresponding derivative of the (−)-antipode has been mentioned by Riniker, *et al.* (ref. 11), who report m.p. 193–194°.

X (80 mg.) was heated under reflux with 1 cc. each of methanol and 2 *N* hydrochloric acid for 1 hr. or for 20 min. with 4 cc. of 5% methanolic potassium hydroxide solution. The isomerization product was purified by distillation at 105–110° at 15 mm., whereupon it exhibited $\lambda_{max}^{liquid\ film}$ 5.81 μ; R.D. (Fig. 5) in methanol (*c* 0.097): $[\alpha]_{700}$ −38°, $[\alpha]_{589}$ −33°, $[\alpha]_{400-375}$ −51° (broad trough), $[\alpha]_{305}$ +335°, $[\alpha]_{265}$ −565°.

Anal. Calcd. for $C_{11}H_{18}O$: C, 79.46; H, 10.92; O, 9.62. Found: C, 79.72; H, 10.82; O, 9.22.

(+)-Δ^6-*trans*-**4,4,9-Trimethyl-3-octalone (XXI).**—To an ice-cold solution of 300 mg. of (+)-Δ^6-*trans*-4,4,9-trimethyl-3-octalol (XIX)[52] in 5 cc. of acetone was added dropwise 0.4 cc. of 8 *N* chromic acid solution.[53] After standing for 3 minutes, the solution was poured into 60 cc. of water and extracted well with ether to yield, after washing, drying and evaporating, 290 mg. of oil. Chromatography on 15 g. of Merck acid-washed alumina and elution with hexane–benzene (4:6) furnished 280 mg., which was distilled at a bath temperature of 120–130° and 6 mm. to give 260 mg. of colorless oil, $\lambda_{max}^{liquid\ film}$ 5.85 and 6.01 μ; R.D. (Fig. 3) in methanol (*c* 0.104): $[\alpha]_{700}$ +71°, $[\alpha]_{589}$ +133°, $[\alpha]_{310}$ +1190°, $[\alpha]_{265}$ +43°. The analytical sample was broken in transit and no new analysis was secured. The 2,4-dinitrophenylhydrazone was recrystallized several times from methanol–chloroform and was obtained as a yellow-orange micro-crystalline powder, m.p. 147.5–149°.

Anal. Calcd. for $C_{19}H_{24}N_4O_4$: C, 61.27; H, 6.48. Found: C, 61.48; H, 6.23.

(+)-*trans*-**4,4,9-Trimethyl-3-decalone (XXII).**—The trimethyloctalol XIX[52] (400 mg.) was hydrogenated with platinum oxide in 5 cc. of ethanol in a microhydrogenation apparatus. After consumption of 50 cc. of hydrogen (calcd. 54 cc.), the catalyst was filtered, the solvent removed and the solid residue was recrystallized from aqueous methanol and sublimed at 70° and 0.1 mm. to give 367 mg. of colorless needles of (+)-*trans*-4,4,9-trimethyl-3-decalol (XX), m.p. 87–89°, $[\alpha]_D$ +78° (*c* 0.3 in dioxane). This alcohol, just like the octalol XIX, showed a positive plain dispersion curve rising to about 250° at 275 mμ.

Anal. Calcd. for $C_{13}H_{24}O$: C, 79.53; H, 12.32. Found: C, 79.58; H, 12.28.

The above decalol XX (310 mg.) was oxidized exactly as described above for the oxidation of the octalol XIX and afforded after chromatographic purification and distillation at 100° and 2 mm., 268 mg. of (+)-*trans*-4,4,9-trimethyl-3-decalone (XXII), $\lambda_{max}^{liquid\ film}$ 5.82 μ; R.D. (Fig. 3) in methanol (*c* 0.154): $[\alpha]_{700}$ +27°, $[\alpha]_{589}$ +49°, $[\alpha]_{320}$ +438°, $[\alpha]_{275}$ −133°.

Anal. Calcd. for $C_{13}H_{22}O$: C, 80.35; H, 11.41. Found: C, 80.03; H, 10.93.

The 2,4-dinitrophenylhydrazone crystallized as orange leaflets, m.p. 158–159° from methanol–chloroform.

Anal. Calcd. for $C_{19}H_{26}N_4O_4$: C, 60.94; H, 7.00; N, 14.96; O, 17.09. Found: C, 60.50; H, 6.69; N, 15.11; 0.17.22.

(−)-*cis*-**9-Methyl-8-methoxycarbonyl-3-decalone (XVII),**[43] R.D. (Fig. 2) in methanol (*c* 0.091): $[\alpha]_{700}$ −15°, $[\alpha]_{589}$ −11°, $[\alpha]_{400}$ −31°, $[\alpha]_{312.5}$ +104°, $[\alpha]_{270}$ −374°, $[\alpha]_{260}$ −352°, $[\alpha]_{255}$ −569°.

(+)-*cis*-**9-Methyl-1-decalone (XVIII),**[49] R.D. (Fig. 2) in methanol (*c* 0.0566): $[\alpha]_{700}$ +5°, $[\alpha]_{589}$ +16°, $[\alpha]_{312.5}$ +1350°, $[\alpha]_{275}$ −1695°, $[\alpha]_{255}$ −1345°.

trans-**5,9-Dimethyl-3-decalone (XXIV),**[55] R.D. (Fig. 3) in dioxane (*c* 0.159): $[\alpha]_{700}$ +24°, $[\alpha]_{589}$ +20°, $[\alpha]_{317.5}$ −915°, $[\alpha]_{255}$ +897°, $[\alpha]_{280}$ +860°.

(+)-*trans*-**3-Keto-9-methyl-$\Delta^{1,6}$-hexahydronaphthalene (II),**[12,54] R.D. (Fig. 4) in dioxane (*c* 0.059): $[\alpha]_{700}$ +149°, $[\alpha]_{589}$ +220°, $[\alpha]_{380}$ +1340°, $[\alpha]_{370}$ +1105°, $[\alpha]_{362.5}$ +1270°, $[\alpha]_{351.25}$ +575°, $[\alpha]_{337.5}$ +228°, $[\alpha]_{331.25}$ +497°, $[\alpha]_{325}$ +363°, $[\alpha]_{275}$ +2130°.

(+)-*trans*-**3-Keto-4,4,9-trimethyl-$\Delta^{1,6}$-hexahydronaphthalene (XXIII),**[52] R.D. (Fig. 4) in dioxane (*c* 0.151 (700–345 mμ), 0.033 (350–300 mμ)): $[\alpha]_{700}$ +150°, $[\alpha]_{589}$ +228°, $[\alpha]_{390}$ +1265°, $[\alpha]_{365}$ +966°, $[\alpha]_{360}$ +1030°, $[\alpha]_{350}$ +454°, $[\alpha]_{345}$ +700°, $[\alpha]_{337.5}$ +391°, $[\alpha]_{300}$ +1615°; R.D. in octane (*c* 0.137 (700–350 mμ), 0.029 (375–320 mμ)): $[\alpha]_{700}$ +152°, $[\alpha]_{589}$ +224°, $[\alpha]_{385}$ +1215°, $[\alpha]_{375}$ +785°, $[\alpha]_{365}$ +1520°, $[\alpha]_{355}$ +445°, $[\alpha]_{350}$ +817°, $[\alpha]_{342.5}$ +328°, $[\alpha]_{332.5}$ +915°, $[\alpha]_{327.5}$ +770°, $[\alpha]_{320}$ +1140°.

β-**5-(*trans*-2,5-Dimethyl-6-carboxy-1-decalone)-propionic acid (XXVII),**[58] R.D. (Fig. 5) in dioxane (*c* 0.10): $[\alpha]_{700}$ +12°, $[\alpha]_{589}$ +26°, $[\alpha]_{500}$ +34°, $[\alpha]_{315}$ −670°, $[\alpha]_{280}$ +670°.

DETROIT, MICH.

[CONTRIBUTION FROM THE DANIEL SIEFF RESEARCH INSTITUTE, THE WEIZMANN INSTITUTE OF SCIENCE]

Syntheses in the Terpene Series. VI.[1] Synthesis of 10-Methyl-1-decalone. The Stereochemical Stability Relationship in the 9-Methyldecalin Series

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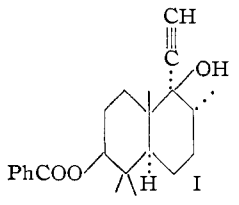
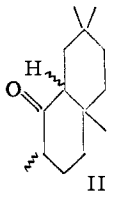
2,7,7,10-Tetramethyl-1-decalone (II) is required as an intermediate for the synthesis of pentacyclic triterpenes. As a model, 10-methyl-1-decalone has been synthesized from 10-methyl-$\Delta^{1(9)}$-octal-2-one (VII) by a four-step sequence. This ketone was obtained as an equilibrium mixture which has been shown to contain 40% of the *cis* isomer XII and 60% of the *trans* isomer XIII, through conversion to a mixture of the *cis* and *trans* isomers of 9-methyldecalin. On the other hand, the reduction of 10-methyl-$\Delta^{1(9)}$-octal-2-one (VII) with lithium in liquid ammonia was found to give a saturated ketone containing at least 95% of *trans*-10-methyl-2-decalone (XXIV). The significance of these results in connection with the stereochemical stability relationship in the 9-methyl-decalin series is discussed.

In the previous paper of this series,[1] the stereospecific synthesis of 1,1,6α,10β-tetramethyl-5α-ethynyl-*trans*-decalin-2β,5β-diol 2-monobenzoate (I) was described. This compound appears to be a potentially useful building block for the construction of the pentacyclic triterpenes. For instance condensation with 2,7,7,10-tetramethyl-1-decalone (II), preferably the *cis*-decalin isomer, will give an acetylenic 1,4-glycol which should be convertible to substances belonging to the β-amyrin group of triterpenes. It was for this reason that we were interested in developing a synthesis of derivatives of 10-methyl-1-decalone of type II.





Besides being of synthetic importance, 10-methyl-1-decalone derivatives of type II are of interest in connection with the question whether the *cis* or the *trans* isomer will be the more stable.

(1) For Part V, see F. Sondheimer and D. Elad, THIS JOURNAL, **80**, 1967 (1958).

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