[CONTRIBUTION FROM THE CHEMICAL LABORATORIES OF COLUMBIA UNIVERSITY]

THE OPTICAL ISOMERS OF *cis*-9-METHYL-1-DECALONE

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The synthesis of compounds possessing the carbon skeleton of steroids has been the object of many important publications in recent years. In all cases except the total synthesis of the four possible equilenin isomers by Bachmann, Cole, and Wilds (1), the question of optical isomerism was either ignored or postponed to a later stage in the proposed synthesis.

Inasmuch as the aim of all these investigations was without exception the comparison of some one synthetic steroid with the corresponding natural compound and, since the natural compounds in all cases are optically active, the ultimate comparison, which at the same time would represent an absolute structure proof, can never be achieved unless the synthetic compound is a pure substance stereochemically. This concerns not only *cis-trans* isomerism in rings and substituents, but also optical isomerism with respect to every center of asymmetry. The stereochemical problem is simplified if the syntheses are performed on stereochemically homogeneous perhydronaphthalenes.

It was therefore attempted to synthesize such an optically active perhydronaphthalene derivative containing an angular methyl group and possessing a structure that would permit further synthetic operations. The compound chosen for this purpose was 9-methyl-1-decalone, reported in impure form as its semicarbazone by Chuang, Tien, and Ma (2), and as relatively pure, probably *cis* form, by Elliot and Linstead (3). The reason for choosing this particular compound was twofold: firstly, the angular methyl group at C_9 gives dissymmetry to the molecule, in addition to being a general characteristic of all steroids and, secondly, its method of synthesis outlined in flow-sheet A, as well as the method reported by Elliot and Linstead, can be repeated using 9-methyl-1-decalone, instead of methylcyclohexanone as starting material. The procedure could thus be applied to the synthesis of perhydrophenanthrenes or cyclopentenophenanthrenes.

Since rather large amounts of 9-methyl-1-decalone were necessary for the steps outlined in flow-sheet B, it was decided to check all methods re-

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ported in the literature and, if possible, improve them, since good yields were of utmost importance.

All reported methods center around the preparation of methylcyclohexenylbutyric acid (VI), which is cyclized according to the Darzens reaction as modified by Cook and Lawrence (4) to the corresponding chloro ketone (VII) which, after removal of hydrochloric acid, yields the unsaturated ketones (VIII) and (X). The yields in this cyclization are very good and the problem is therefore primarily the preparation of the substituted butyric acid. Since the method outlined by Elliot and Linstead (3) for the preparation of this acid proved to be the most economical, an attempt was made to improve the over-all yields in those reactions. According to this method methylcyclohexenylbutyric acid is prepared by a Grignard reaction of pentenyl bromide (5-bromo-1-pentene) with methylcyclohexanone, permanganate oxidation of the resulting tertiary alcohol and dehydration of the hydroxy acid. Linstead's 60 to 70% yield in the Grignard reaction could not be duplicated, and considerable amounts of methylcyclohexanol were found in the reaction mixture. This formation of carbinols by Grignard reagents is in agreement with earlier observations that aliphatic magnesium bromides with moderately long chains have reducing properties (8, 9, 10). As noted by Elliot and Linstead (3), the dehydration of the hydroxy acid proceeds with formation also of a spiro-lactone, some of which isomerizes to the unsaturated acid on distillation. This spiro-lactone need not be discarded, since it can be converted into ethyl methyl cyclohexenylbutyrate in very good yield, by boiling with thionyl chloride in benzene solution and pouring the mixture into absolute ethyl alcohol. This procedure, usually applied to the splitting of γ-lactones (13), apparently is also applicable to δ-lactones. The resulting ester can be quantitatively saponified to the acid.

Simultaneously with the study of the reported methods, a new synthesis of this acid was attempted, which proved to be superior in ease of preparation as well as yield. The method developed consists mainly in an elongation of the side chain of methylcyclohexenylacetic acid by two successive Arndt-Eistert rearrangements.

Starting with methylcyclohexenylacetic acid, the ethyl ester of which was prepared as described by Chuang *et al.* (2), its acid chloride was reacted with diazomethane to give a liquid diazo ketone (IIa). Rearrangement of this diazo ketone with concentrated ammonium hydroxide solution in the presence of silver oxide gave an amide in yields not exceeding 20%. When rearranged in ethyl alcoholic solution, the ester (IV) was obtained in 40% yield, which did not represent any improvement over the direct rearrangement to the acid (III), using thiosulfate in aqueous solution as medium. In the former case, the yield of the final product (III) after saponification would hardly have exceeded 35%, the yield obtained in the direct rearrangement.

Methylcyclohexenylpropionic acid (III) was prepared by Chuang, Tien, and Ma (2), in their synthesis of 8-methyl-1-hydrindanone but, since these authors failed to report any physical constants other than the boiling point, the acid prepared by the Arndt-Eistert rearrangement was analyzed and the values found to correspond to the formula $C_{10}H_{10}O_2$. The dibromo compound reported by Chuang, Tien, and Ma (2) could not be obtained in crystalline form. The next higher homolog of this acid, the desired methylcyclohexenylbutyric acid (VI) was prepared from the propionic acid by a second diazo ketone rearrangement without isolation of any intermediates. Rearrangement to the amide or ester in this case was not tried, since the rearrangement to the acid proceeded easily with quite satisfactory yield.

In the ring closure to the chloro ketone (VII), the original procedure of Cook and Lawrence (4) was followed. These authors applied the reaction to the cyclization of cyclohexenylbutyric acid to 10-chloro-1-octalone. The subsequent removal of hydrochloric acid required more extensive investigation, since there was some doubt as to the purity of the product. The question of purity at this stage required particular attention since the success of all later steps was dependent on the purity of the starting material. Cook (4) reported the formation of an octalone and identified it as $\Delta^{9,10}$-1-octalone, originally reported by Hueckel and Naab (5). Their product was uniform, and it seems natural that removal of hydrochloric acid should proceed as indicated by them. Since in the case of methylcyclohexenylbutyric acid the formation of a C_9—C_{10} double bond is impossible, the product must be either $\Delta^{4,10}$ (VIII)- or $\Delta^{5,10}$ (IX)-9-methyl-1-octalone. With the exception of the carbonyl group, the chloro ketone is perfectly symmetrical, the latter group being too far removed to have any particular influence on the course of the reaction. One would therefore expect both octalones to be formed in this reaction.

Frequent distillations of the product failed to give consistent refractive indices, though correct analytical figures were obtained. Chuang, Tien, and Ma (2) reported the melting point 226–227° for the semicarbazone and left the question of the double bond open. They also reported an oxime melting at 99–100°. These constants could not be verified in this laboratory, and these derivatives were identified as mixtures of two semicarbazones and two oximes. Chuang's semicarbazone was found to be a mixture of semicarbazones melting at 228–229° and 168°, from which the octalones could be regenerated. The oximes formed by the usual procedure from the pure octalones, melted at 105° and 120° respectively. All attempts to determine the exact position of the double bond in the pure octalones failed. Oxidative cleavage of the double bond would produce, in either case, diketocarboxylic acids with the same empirical formulas. Oxidation of the octalones to dicarboxylic acids, followed by cleavage of the double bond should permit differentiation, but the two dicarboxylic acids could not be prepared.

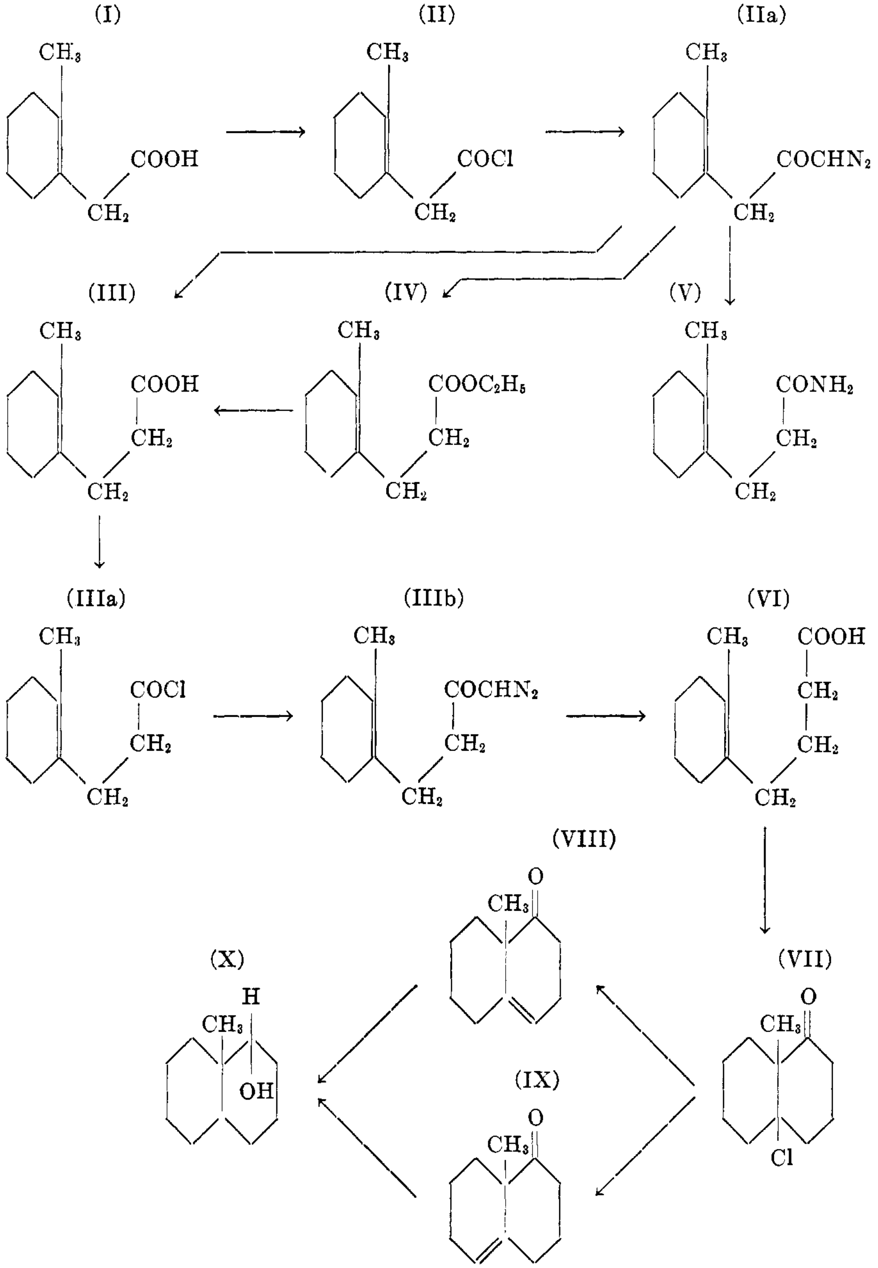
Hydrogenation of both octalones gave either 9-methyl-1-decalol (X) or 9-methyl-1-decalone (XI), depending on the quantity of catalyst used. With platinum oxide in acetic acid, in quantities exceeding one-tenth the amount of octalone, the hydrogenation could not be stopped at the ketone stage. Reduction of the carbonyl group seemed to take place at the same time. In order to ensure uniformity of the product, all the octalone was hydrogenated to the alcohol (X) which, after purification, was oxidized to the ketone (XI).

Purification of this ketone was effected by regeneration from its semicarbazone, m.p. 225°, which agrees with the value reported by Elliot and Linstead (3) for what they call the *cis* form. The next step, the conversion to the oxime, was somewhat complicated by the fact that the reaction of hydroxylamine hydrochloride yielded two oximes, m.p. 106° and 88°, probably the *syn* and *anti* forms (XII and XIII). Both oximes, when reduced in alkaline solution, similar to the procedure of Leroux (6), gave an amine which, on the basis of its analogy to decalylamine, we have designated as *cis*-9-methyl-1-decalylamine-B, for want of a better nomenclature (15). The exact position of the NH_2 group, or the hydrogen atom with respect to the angular methyl group is uncertain in either case (11). The epimeric amine, *cis*-9-methyl-1-decalylamine-A, was obtained by catalytic reduction of the two oximes of m.p. 105° and 120°.

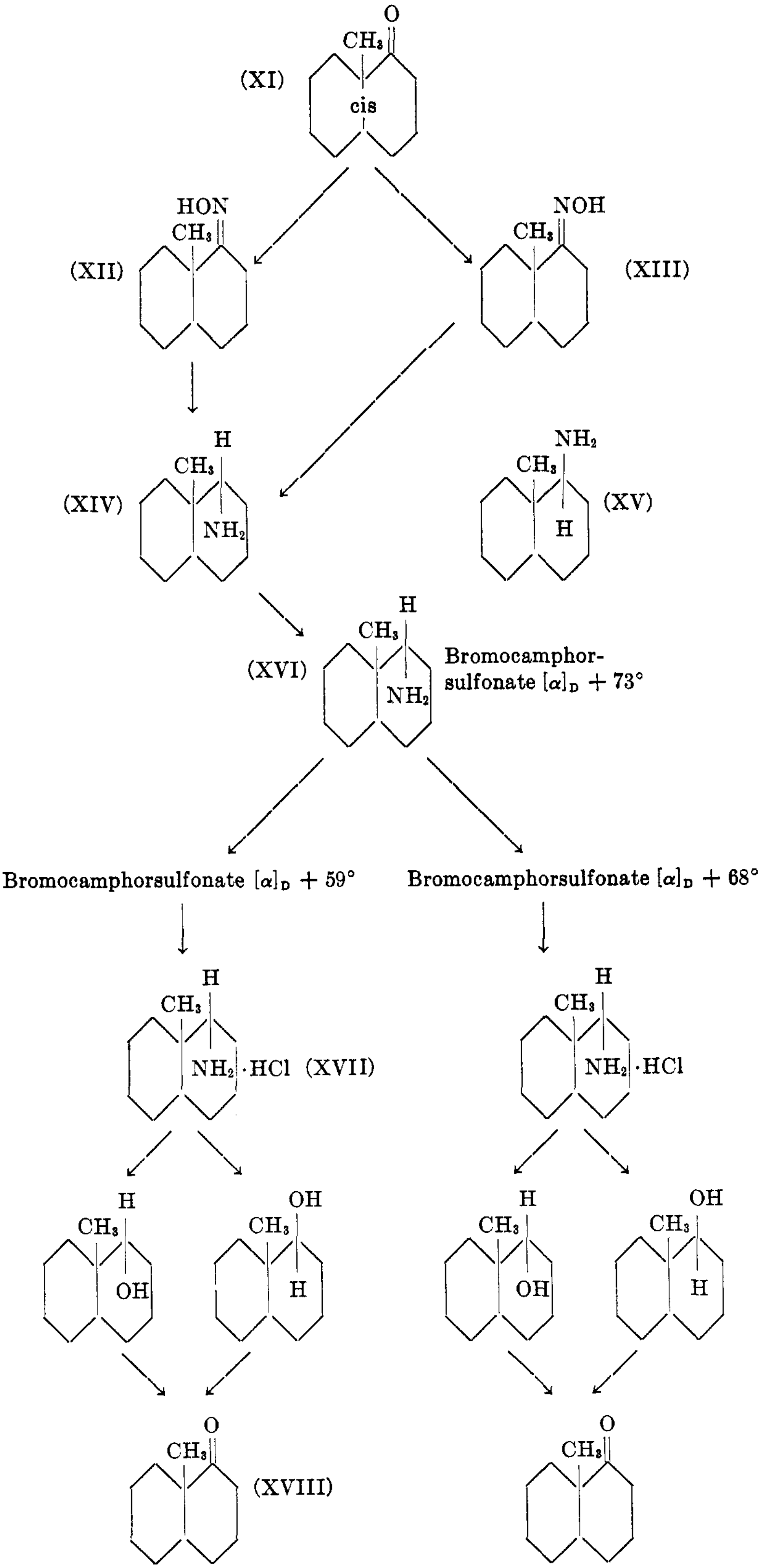
The latter route, although shorter, was found to be less satisfactory than the reduction of the saturated oxime, since the product, due to incomplete hydrogenation, was less uniform than in the former case. In either case, the products were purified through their benzoyl derivatives, melting at 158° and 142° respectively. The procedure followed in the preparation of the benzoyl derivatives, and the regeneration of the amines, was essentially the one described by Hueckel *et al.* (14).

Only the purest fraction of this *cis*-9-methyl-1-decalylamine-B (XIV) was used for the subsequent resolution into its optical isomers. Hueckel and Kuehn (7) reported a similar resolution of β-decalylamine using camphorsulfonic acid (Reychler's acid) as the optically active reagent. This acid was found to be unsuitable for the resolution of XIV, because of the excessive solubility of its salts. α-Bromo-π-camphorsulfonic acid, on the other hand, was found to form salts which were sufficiently difficultly soluble in dilute ethyl alcohol to be separated by a reasonable number of crystallizations.

Flow-Sheet A


(I)
CH₃
COOH
CH₂
(II)
CH₃
COCl
CH₂
(IIa)
CH₃
COCHN₂
CH₂
(III)
CH₃
COOH
CH₂
CH₂
(IV)
CH₃
COOC₂H₅
CH₂
CH₂
(V)
CH₃
CONH₂
CH₂
CH₂
(IIIa)
CH₃
COCl
CH₂
CH₂
(IIIb)
CH₃
COCHN₂
CH₂
CH₂
(VI)
CH₃
COOH
CH₂
CH₂
CH₂
(VIII)
O
CH₃
(X)
H
CH₃
OH
(VII)
O
CH₃
Cl
(IX)
O
CH₃

Flow Sheet B


(XI)
cis
(XII)
(XIII)
(XIV)
(XV)
(XVI)
Bromocamphorsulfonate [α]D + 73°
Bromocamphorsulfonate [α]D + 59°
Bromocamphorsulfonate [α]D + 68°
NH2·HCl (XVII)
NH2·HCl
(XVIII)

The amines, regenerated from the bromocamphorsulfonates were reacted with nitrous acid, to give a mixture of hydrocarbon and partially inverted alcohol. The hydrocarbon in each case was probably $\Delta^{1,2}$-9-methyloctalin and was not further investigated. The conversion to the alcohols seemed to proceed under partial inversion at C_1, since the mixtures obtained from the *d*- and *l*-amines could not be brought to equal and opposite rotation. However, the fact that oxidation of the dextro and levo mixture yielded *d*, and *l*-9-methyl-1-decalone in reasonably pure condition, indicated that the Walden inversion was confined to C_1 as indicated in flow-sheet B.

This fact is quite in agreement with the observations of Hueckel (15), that in the α B series inversion of the product takes place to a limited extent, although he was unable to isolate the inverted alcohol in pure form. The optical data herein reported do not necessarily prove that inversion has taken place, but certainly support Hueckel's statement. Furthermore, it may be taken as additional confirmation that the ring configuration is *cis* and not *trans*, since in the α B-*trans* series no inversion whatsoever occurred (15).

After oxidation of the alcohol mixture, the products were purified by means of their semicarbazones. These derivatives were found to have the same melting point, which was higher than that of the semicarbazone of the inactive ketone. Mixed melting points of these compounds in varying ratios indicated that the semicarbazone of the inactive ketone was a racemic mixture.

ACKNOWLEDGMENTS

Our thanks are due to Professor Charles O. Beckmann, of this University, for the use of his polarimeter; and to Mr. Saul Gottlieb, who carried out the analytical work herein recorded.

EXPERIMENTAL

(All melting points recorded are corrected.)

2-Methylcyclohexenylacetic acid (I). The ethyl ester of this acid was prepared according to the procedure of Chuang, Tien, and Ma (2). When saponified and worked up in the usual way, the acid boiled at 137–139°/10 mm. Previously reported boiling point is 151°/28 mm. (17).

2-Methylcyclohexenylacetylchloride (II). Fifty grams of cyclohexenylacetic acid was added drop by drop to 70 cc. of thionyl chloride over a period of one-half hour. The mixture was then heated to boiling on the steam-bath and refluxed for one-half hour. The excess of thionyl chloride was removed under reduced pressure and the residue distilled from a 200 cc. Claisen flask (the large flask was necessary because of strong foaming). The distillate was redistilled from a 50 cc. Claisen flask equipped with a short fractionating column. The fraction boiling at 86–89°/10 mm. was collected. Yield: 36 g.; d_4^{25} 1.065; n_D^{25} 1.4852; R_L found: 46.00, calc'd: 45.98.

Anal. Calc'd for $C_9H_{13}ClO$: Cl, 20.4. Found: Cl, 20.3.

β-(2-Methylcyclohexenyl)propionamide (V). An ether solution of diazomethane was prepared from 74 g. of nitrosomethylurea in the usual manner, using 500 cc. of absolute ether as solvent. This solution was cooled in ice and, while efficiently stirred, 35 g. of cyclohexenylacetyl chloride was added. As soon as the evolution of gases had ceased, the flask was placed in the ice-box overnight. The following day the precipitated polymethylenes were removed by filtration and the solution concentrated under reduced pressure. The residual diazo ketone (IIa) could not be crystallized and, due to its instability to light and heat, was worked up immediately.

Approximately 10 g. of the diazo ketone was dissolved in 75 cc. of dioxane, 30 cc. of 20% ammonium hydroxide solution, and 5 cc. of a 10% silver nitrate solution added, and the mixture heated on the steam-bath. After a few minutes the solution became cloudy and nitrogen was given off. The heating was continued for another hour, the reaction mixture decanted from the precipitated silver, poured upon ice and the product extracted with ether. The ether was dried, filtered, and evaporated. The residue crystallized on standing in the ice-box overnight. The crude crystalline material was purified by crystallization from benzene-petroleum ether mixtures; m.p. 135°.

Anal. Calc'd for $C_{10}H_{17}NO$: C, 71.9; H, 10.3.
Found: C, 72.0; H, 10.4.

Ethyl β-(2-methylcyclohexenyl)propionate (IV). Ten grams of the diazo ketone, prepared as described above, was dissolved in 150 cc. of absolute ethyl alcohol, a suspension of 10 g. of silver oxide added, and the mixture refluxed on the steam-bath. After refluxing for one hour, the solution became clear and the precipitated silver was filtered off. The alcohol in the filtrate was removed under reduced pressure and, after elimination of a small amount of water, the product was distilled under reduced pressure, b.p. 95-97°/10 mm.; yield, 4.5 g.

Anal. Calc'd for $C_{12}H_{20}O_2$: C, 73.4; H, 10.2.
Found: C, 73.2; H, 10.2.

β-(2-Methylcyclohexenyl)propionic acid (III). Thirty-two grams of diazo ketone, prepared as described above, was dissolved in 50 cc. of pure dioxane and added to a vigorously stirred solution of 35 g. of sodium thiosulfate in 400 cc. of water containing 30 g. of silver oxide in suspension. After stirring for one hour at room temperature, the reaction mixture was filtered through cotton, the filtrate acidified with nitric acid and the product isolated in the usual manner; b.p. 112–113°/14 mm.; yield, 33%.

Anal. Calc'd for $C_{10}H_{16}O_2$: C, 71.4; H, 9.5.
Found: C, 71.2; H, 9.5.

A lower-boiling fraction in this distillation was identified as the ethyl ester of this acid. Its formation was probably due to hydrolysis of the dioxane.

γ-(2-Methylcyclohexenyl)butyric acid (VI). Nine and two-tenths grams of methylcyclohexenylpropionic acid (III) was dissolved in 60 cc. of anhydrous ether, 4.5 g. of anhydrous pyridine added and the mixture cooled in ice. One molar equivalent of thionyl chloride (4.2 cc.) was then slowly added to the mixture. The pyridine hydrochloride first separated in white crystals, and later congealed to a yellow semisolid mass. After all the thionyl chloride had been added, a little anhydrous ether saturated with dry hydrogen chloride was added, to precipitate the excess of pyridine. The pyridine hydrochloride was centrifuged and washed once more with anhydrous ether. The ether solution was concentrated under reduced pressure at room temperature, and the residual acid chloride, a slightly yellow liquid, was brought into reaction with excess of diazomethane in the manner described above. The rearrangement to the butyric acid proceeded smoothly without the use of silver oxide. The product, 3.5 g., boiled at 166–167°/10 mm. and solidified in the side arm.

It was recrystallized from petroleum ether, and then melted at 43°. Elliot and Linstead reported the melting point 44°. Chuang, Tien, and Ma (2) do not give a melting point.

Ethyl γ-(2-methylcyclohexenyl)butyrate. Eleven grams of the pure spiro-lactone, b.p. 102–105°/1 mm., obtained as by-product in the dehydration of Linstead's hydroxybutyric acid, was dissolved in 50 cc. of dry benzene and refluxed on the steam-bath. Fourteen grams of thionyl chloride, dissolved in 25 cc. of dry benzene, was added from a dropping-funnel and the refluxing continued for 2 hours, the reaction mixture allowed to cool to room temperature and then poured into 200 cc. of absolute alcohol. This alcohol-benzene solution was warmed on the steam-bath for about 10 minutes, the solvents removed under reduced pressure and the residue distilled using a small fractionating column. Eight grams of pure ester, b.p. 77–78°/0.5 mm., was collected; n_D^{25} 1.4671; d_4^{25} 0.9680.

Anal. Calc'd for $C_{13}H_{22}O_2$: C, 74.3; H, 10.5.
Found: C, 74.5; H, 10.4.

If the refluxing of the reaction mixture was stopped after one hour, the resulting product was a mixture of about 30% unsaturated and 70% saturated ester.

The ester prepared by this procedure was saponified with 20% alcoholic potassium hydroxide solution and worked up in the usual manner. The acid distilled at 132–135°/2 mm. and, after recrystallization from petroleum ether, had the melting point of 43°, and was identical with the acid obtained by the diazo ketone rearrangement, dehydration of the hydroxy acid according to Linstead, as well as the acid obtained by isomerization of the spiro-lactone itself.

9-Methyl-1-octalone (VIII or IX). The cyclization of methylcyclohexenylbutyric acid was carried out exactly as described by Cook and Lawrence (4), without isolation of the intermediate chloro ketone (VII). All attempts to distill this ketone, contrary to the experience of Elliot and Linstead (3), failed since the compound decomposed even at 0.1 mm. pressure. The crude chloro ketone was therefore heated with dimethylaniline at 180° for 3 hours and the product distilled under reduced pressure. Repeated distillations failed to give a pure product as indicated by inconsistent refractive indices.

The first crude product, b.p. 85-95°/0.5 mm., dissolved in solvent alcohol, was added to a mixture of 2 parts of anhydrous sodium acetate and 1.5 parts of semicarbazide hydrochloride, with the requisite amount of water. After a period of about 10 or 15 minutes, a precipitate began to form. The reaction was brought to completion by heating the mixture on the steam-bath for about one hour and allowing it to stand in the ice-box overnight. The following day the semicarbazone was filtered off and recrystallized from dilute ethyl alcohol. Recrystallization was repeated until the precipitate showed the same melting point as the second crop obtained by concentration of the mother liquors. The pure compound melted at 228–229°.

Anal. Calc'd for $C_{12}H_{19}N_3O$: C, 65.2; H, 8.6.
Found: C, 65.5; H, 8.4.

Eight and two-tenths grams of the pure semicarbazone, m.p. 228–229°, was suspended in 200 cc. of 5% hydrochloric acid, stirred, and heated on the steam-bath for one-half hour. The ketone, which had formed as a colorless oil, was extracted with ether, the ether washed with sodium carbonate solution, and dried with magnesium sulfate. After filtration and removal of the solvent, the product was distilled under reduced pressure, b.p. 66–67°/0.5 mm.; n_D^{25} 1.5065; d_4^{25} 1.0054; R^L calc'd: 48.16, found: 48.6; yield, nearly that calculated.

Anal. Calc'd for $C_{11}H_{16}O$: C, 80.5; H, 9.75.
Found: C, 80.4; H, 9.88.

The product was a camphoraceous-smelling oil and exhibited all the properties of unsaturation. On standing for a month, it polymerized to a yellow resin. Since there existed the possibility of a shift of the double bond, a small sample of the compound was converted into its semicarbazone by the usual procedure; the crude derivative had the melting point 228°, indicating that no isomerization had taken place under the influence of hydrochloric acid.

Oxime. Eight hundred milligrams of the ketone was dissolved in 6 cc. of methanol and to this solution was added 1 g. of hydroxylamine hydrochloride and 1 g. of sodium acetate, dissolved in 3 cc. of water. Methanol was then added to the mixture until a clear solution was obtained. After a few minutes, a precipitate formed and, on standing overnight, the reaction was complete as indicated by the absence of the characteristic odor of the ketone. The oxime was filtered and recrystallized from dilute methyl alcohol; m.p. 105°.

Anal. Calc'd for $C_{11}H_{17}NO$: C, 73.7; H, 9.5.
Found: C, 73.9; H, 9.8.

There was some evidence of an isomeric oxime in the mother liquor, but it could not be isolated in pure form.

Isomeric 9-methyl-1-octalone (VIII or IX). The combined mother liquors of the semicarbazone (m.p. 228–229°) were diluted with water until cloudy, left standing for about a week, and the precipitate filtered off. After frequent recrystallization, from Skellysolve D (77–116° ligroin), a semicarbazone m.p. 168° was isolated.

Anal. Calc'd for $C_{12}H_{19}N_3O$: C, 65.2; H, 8.6.
Found: C, 65.5; H, 8.6.

This semicarbazone was decomposed as described for its isomer. The product distilled at 70–71°/0.5 mm.; n_D, 1.5084; d_4^{25} 1.0081. It was a colorless oil, in its properties and odor similar to the isomer (b.p. 66–67°/0.5 mm.).

Anal. Calc'd for $C_{11}H_{16}O$; C, 80.5; H, 9.7.
Found: C, 80.4; H, 9.9.

Oxime. This derivative was prepared from the ketone, using the same procedure as described above; m.p. 120° (from alcohol).

Anal. Calc'd for $C_{11}H_{17}NO$: C, 73.7; H, 9.5.
Found: C, 73.6; H, 9.8.

Oxidation experiments. (a) *Oxidation with hypobromite in pyridine solution.* The procedure followed was that described by Ladenburg, Chakravorty, and Wallis (18), for the oxidation of *i*-cholestanone-6 to α_1-*i*-cholestane-diacid-6,7.

Two grams of the octalone, freshly regenerated from its semicarbazone (m.p. 168°), was added to a solution of sodium hypobromite prepared by dissolving 10 g. of sodium hydroxide in 100 cc. of water followed by addition of 2.5 cc. of bromine. To this solution was added 75 cc. of pure pyridine and the mixture shaken for 25 hours. Two layers were formed; the upper pyridine layer was bright red and the aqueous layer colorless. The mixture was cooled in ice and slowly acidified with dilute (50%) sulfuric acid. When the mixture was acid to Congo red the red color disappeared. The acid products were then extracted with ether and attempts were made to purify the product or products in the usual way. Only resinous material could be isolated.

(b) *Nitrous acid reaction and rearrangement.* The procedure followed that reported by Levitz, Perlman, and Bogert (19) in the conversion of spirocyclohexane-1,1'-tetralone-4' to α,α-pentamethylenehomophthalic acid.

To an ice-cold and well-stirred mixture of 1 g. of freshly regenerated octalone, 2 cc. of freshly distilled butyl nitrite, and 2 cc. of glacial acetic acid, 3 cc. of concentrated nitric acid was added from a microburette. No reaction took place cold, and the mixture was slowly heated to 50° and allowed to remain at that temperature for 15 minutes. It was then placed in the ice-box and left standing for several days. No crystalline material formed, but the mixture separated into two layers. The lower layer was removed and a rearrangement attempted under the assumption that this material represented the crude isonitroso ketone. No definite acidic reaction product could be isolated.

The experiment was repeated and attempts made to crystallize the crude product. Standing in the ice-box for 11 months under petroleum ether, scratching, etc., did not produce crystallization.

cis-*9-Methyl-1-decalylamine-A* (XIV). The two unsaturated oximes, m.p. 105° and 120°, were reduced according to the following procedure: 200 mg. of each oxime was dissolved in 25 cc. of glacial acetic acid containing 95 mg. of reduced platinum oxide catalyst and shaken in hydrogen. The two compounds took up respectively 76.5 and 77.0 cc. of hydrogen in 9 hours. The calculated amount of hydrogen under the conditions was 82.3 cc. After removal of the catalyst by filtration, the acid was neutralized with 10% sodium hydroxide solution and the amine extracted with ether. After careful drying with anhydrous magnesium sulfate for two days, the amines were precipitated from the filtered solution with dry hydrogen chloride and recrystallized from acetone-alcohol mixtures.

Anal. Calc'd for $C_{11}H_{22}ClN$: C, 65.0; H, 10.8.
Found: C, 64.8; H, 11.0.

Benzoyl derivative. The amines were regenerated from their hydrochlorides with dilute sodium hydroxide solution and extracted with ether. The ether extracts were concentrated to about 3 cc. and 200 mg. of benzoic anhydride, dissolved in an equal amount of anhydrous ether, added. The benzoyl derivatives were crystallized by seeding, from dilute alcohol containing a little sodium bicarbonate, and then from pure alcohol. The two benzoyl derivatives showed the same melting point (142°) and gave no depression when mixed.

Anal. Calc'd for $C_{18}H_{25}NO$: C, 79.6; H, 9.2.
Found: C, 79.5; H, 9.0.

cis-*9-Methyl-1-decalol* (X). The octalone (2.133 g.), regenerated from the semicarbazone (m.p. 228–229°), was dissolved in 50 cc. of glacial acetic acid and hydrogenated using platinum oxide as catalyst. The compound took up 658.5 cc. of hydrogen in 90 minutes. No more hydrogen was taken up if the shaking was continued. The calculated amount of hydrogen for two moles under the conditions of the experiment was 651 cc. After removal of the catalyst by filtration, neutralization of the acid, and extraction with ether, drying, etc., the product was distilled under reduced pressure. The decalol was found to be a very viscous oil, with a camphoraceous odor which was even more pronounced than in the case of the ketone: b.p. 95°/1 mm.; n_D^{25} 1.5029; d_4^{25} 1.0000; R_L calc'd: 50.1, found: 49.8.

Anal. Calc'd for $C_{11}H_{20}O$: C, 78.5; H, 11.9.
Found: C, 78.6; H, 12.1.

3,5-Dinitrobenzoate. This ester was formed by interaction of the alcohol and 3,5-dinitrobenzoyl chloride in anhydrous pyridine solution. The reaction mixture was poured into ice-water, the precipitate filtered and recrystallized from 95% alcohol, m.p. 126°.

The octalone regenerated from the semicarbazone of m.p. 168° was similarly hydrogenated, and a dinitrobenzoate prepared from this product gave no depression with the ester of m.p. 126°.

Anal. Calc'd for $C_{18}H_{22}N_2O_6$: C, 59.7; H, 6.1; N, 7.7.
Found: C, 59.8; H, 6.1; N, 7.7.

Of these analytical figures, the C and H determinations were run on a dinitrobenzoate from the semicarbazone of m.p. 228–229°, and the N determination on the dinitrobenzoate from the semicarbazone of m.p. 168°.

cis-*9-Methyl-1-decalone* (XI). Five and five-tenths grams of pure *cis*-9-methyl-1-decalol was dissolved in 30 cc. of glacial acetic acid, and 2.6 g. of chromic anhydride dissolved in 10 cc. of water was added in small amounts. The solution was cooled and stirred for several hours, transferred to a larger vessel and steam distilled. Three hundred cubic centimeters of distillate was collected and the product, after extraction with ether and removal of the solvent, transformed into its semicarbazone by the usual procedure, and crystallized from alcohol, giving a product of m.p. 225°.

Anal. Calc'd for $C_{12}H_{21}N_3O$: C, 64.6; H, 9.4.
Found: C, 64.7; H, 9.5.

The ketone was regenerated from the semicarbazone by means of oxalic acid; b.p. 58.5°/0.7 mm.; n_D^{25} 1.4862; d_4^{25} 0.9820; R_L calc'd 48.63, found 48.61.

Elliot and Linstead (3) reported the following values: d_4^{16} 0.9958; n_D^{16} 1.4926; R_L calc'd 48.61, found 48.45.

Anal. Calc'd for $C_{11}H_{18}O$: C, 79.5; H, 10.8.
Found: C, 79.7; H, 11.0.

Oxime. Three and eight-tenths grams of pure *cis*-9-methyl-1-decalone was dissolved in 20 cc. of ethyl alcohol and to this solution was added 4 g. of hydroxylamine hydrochloride and 4 g. of anhydrous sodium acetate, dissolved in 10 cc. of water. Sufficient alcohol was then added to form a clear solution. After standing overnight, 2.5 g. of crystalline oxime had formed. This was filtered off and recrystallized from dilute alcohol, m.p. 106°.

Anal. Calc'd for $C_{11}H_{19}NO$: C, 72.9; H, 10.5.
Found: C, 73.1; H, 10.7.

The mother liquors of this oxime were concentrated at room temperature and the solution allowed to stand in the ice-box for several days. The crystalline precipitate was filtered off and recrystallized many times from very dilute alcohol, m.p. 88°.

Anal. Calc'd for $C_{11}H_{19}NO$: C, 72.9; H, 10.5.
Found: C, 72.7; H, 10.3.

In order to prove that these oximes were not derived from the possible presence of *trans*-9-methyl-1-decalone, both oximes were hydrolyzed by shaking with 20% oxalic acid and the products transformed into the semicarbazones. They proved to be identical, m.p. 225°, and identical with the original semicarbazone from which the ketone was prepared.

Hydrogenation of the 9-methyl octalone mixture to cis-*9-methyl-1-decalone.* Thirty grams of octalone mixture, regenerated from the mixed semicarbazones (m.p. 168° and 228–229°), was hydrogenated using 1 g. of reduced platinum oxide in 100 cc. of glacial acetic acid. Hydrogen was rapidly taken up during the first hour, at the end of which time 4500 cc. had been absorbed, and the shaking was continued for another 12 hours. A total of 4840 cc. of hydrogen was taken up. The calculated amount for one double bond was 4835 cc. The mixture was freed from the catalyst by filtration, the acetic acid neutralized with sodium hydroxide and sodium bicarbonate solutions, and the ketone isolated by steam distillation. The product was converted into its semicarbazone by the usual procedure, and proved to be identical with the compound obtained by oxidation of *cis*-9-methyl-1-decalol (X). After regeneration from its semicarbazone, 24.5 g. of the pure *cis*-9-methyl-1-decalone was obtained.

cis-*9-Methyl-1-decalylamine-B* (XIV). One and eight-tenths grams of the oxime, m.p. 106°, was dissolved in 40 cc. of absolute alcohol. To this solution was added 4 g. of metallic sodium in small pieces over a period of 2 hours, and the mixture was then heated under reflux until all the sodium had gone into solution. When cooled to room temperature, the solid mass was dissolved in water and the amine extracted with ether. After drying and removal of the ether, the amine was distilled under reduced pressure, b.p. 65-68°/1 mm. Determination of the density and refractive index, as well as an analysis, was omitted because of the strong tendency of this compound to take up carbon dioxide from the air with formation of carbonates.

The hydrochloride was prepared by precipitation from anhydrous ether solution with dry hydrogen chloride, and crystallization from acetone-alcohol mixtures.

Anal. Calc'd for $C_{11}H_{22}ClN$: C, 65.0; H, 10.8.
Found: C, 64.8; H, 10.9.

Benzoyl derivative. This derivative was prepared in exactly the same manner as already described for its epimer. Recrystallized from dilute ethyl alcohol, m.p. 158–159°.

Anal. Calc'd for $C_{18}H_{25}NO$: C, 79.6; H, 9.2.
Found: C, 79.7; H, 9.2.

The same procedure was repeated with the oxime m.p. 88°, and found to give the same amine as indicated by the identity of the benzoyl derivatives.

α-Bromo-π-camphorsulfonic acid. This acid was prepared according to the procedure of Regler and Hein (16), and purified through its ammonium and silver salts; yield 60%. A solution of 0.069 g. in 5 cc. water, 1 dm. tube, showed α_D + 1.08, [α_D] + 78.5°.

Resolution of the amines. Six and five-tenths grams of purest *cis*-9-methyl-1-decalylamine-B purified through its benzoyl derivative, m.p. 158–159°, according to the procedure of Hueckel (14), was dissolved in 20 cc. of absolute ethyl alcohol, and 12.1 g. of α-bromo-π-camphorsulfonic acid dissolved in 50 cc. of absolute ethyl alcohol was added. The solution was cooled in ice during the addition, since otherwise considerable ammonia was given off, indicating decomposition of the amine. The solution was allowed to stand in the ice-box overnight and was then concentrated under reduced pressure until the salt began to crystallize, when the mixture was transferred to a crystallizing dish and the solvent evaporated at room temperature. The crude salt had the specific rotation +73.5°.

This salt was recrystallized and fractionated in the usual triangle procedure. Both salts crystallized in long needles. The less soluble salt was first obtained in pure condition and was rather easily brought to constant rotation, yield 7.4 g; 0.392 g. in 5 cc. solution, 1 dm. tube, α_D +5.37°; $[\alpha_D]_{H_2O}$ + 68.8°.

The more soluble salt was obtained in pure form only after a great number of crystallizations and repeated seeding of its saturated solution with the less soluble salt; yield, 6.1 g; 0.277 g. in 5 cc. solution, 1 dm. tube, α_D +3.28°; $[\alpha_D]_{H_2O}$ + 59.2°.

The salts were dissolved in 10% sodium hydroxide solution and the free amine extracted with ether. After careful washing and drying with magnesium sulfate, the amines were precipitated as their hydrochlorides and excess of hydrochloric acid removed in a vacuum desiccator containing soda lime.

*(+)*cis*-9-Methyl-1-decalylamine-B.* Regenerated from the bromocamphorsulfonate, $[\alpha_D]_{H_2O}$ + 68.5°, it was transformed into its hydrochloride according to the procedure outlined above; 0.3532 g. in 5 cc. solution, 1 dm. tube, α_D +0.45°; $[\alpha_D]_{H_2O}$ +7.0°.

*(−)*cis*-9-Methyl-1-decalylamine-B.* Regenerated from the bromocamphorsulfonate, $[\alpha_D]_{H_2O}$ +59.2°, it was transformed into its hydrochloride as outlined above; 0.459 g. in 5 cc. solution, 1 dm. tube, α_D −0.59°; $[\alpha_D]_{H_2O}$ −6.9°.

(+)cis-*9-Methyl-1-decalone.* Two grams of the (+) amine, regenerated from its hydrochloride, was dissolved in 25 cc. of 10% acetic acid and 1 g. of sodium nitrite, dissolved in 3 cc. of water, added. The resulting green solution was kept at 50° until the reaction had died down and then heated on the steam-bath for about 3 hours. When cooled to room temperature, the product was extracted with ether, the ether extracts washed, and the ether removed on the steam-bath. The residual mixture of alcohol, hydrocarbon, and ester was saponified by refluxing on the steam-bath with alcoholic potassium hydroxide solution for 2 hours. The neutral constituents were worked up in the usual way and distilled under reduced pressure. The first fraction, consisting mostly of hydrocarbon, was neglected, and only the main fraction, boiling at 95-97°/1 mm., was collected. Its specific rotation was about +8° and, in the redistilled product, went up to about +11°; yield, 1.2 g. All this material was dissolved in 20 cc. of glacial acetic acid, and 600 mg. of chromic anhydride dissolved in 1 cc. of water was added. The mixture was allowed to stand at room temperature for an hour and was then steam distilled. Alcohol was added to the distillate until a clear solution was obtained, and the ketone was precipitated as the semicarbazone in the usual way. After repeated recrystallizations, this derivative melted at 228°. A mixed melting point with the inactive ketone in a ratio of 5:1 gave the melting point 226-227° and in a ratio of 1:1, 225-227°; 920 mg. of pure semicarbazone was obtained; 0.391 g. in 5 cc. solution, 1 dm. tube; α_D +0.09°; $[\alpha_D]_{EtOH}$ +1.1°.

The ketone was regenerated from the semicarbazone in the manner described above, and its boiling point was approximately 60°/1 mm.; 0.341 g. in 5 cc. solution, 1 dm. tube; α_D +0.29°; $[\alpha_D]_{EtOH}$ +4.2°.

(−)cis-*9-Methyl-1-decalone.* The conversion of the amine to the alcohol and the oxidation of this alcohol to the ketone, was carried out exactly as described for its epimer. The semicarbazone was much more difficult to bring to constant melting point, but reached the same value, 228°, after about 10 recrystallizations. Four grams of amine gave 1.1 g. of pure semicarbazone; 0.5440 g. in 5 cc. solution, 1 dm. tube, α_D −0.10°; $[\alpha_D]_{EtOH}$ −0.90°.

The ketone regenerated from the semicarbazone had approximately the same boiling point as its antipode, 60°/1 mm.; 0.4240 g. in 5 cc. solution, 1 dm. tube; α_D −0.33°; $[\alpha_D]_{EtOH}$ −3.9°.

SUMMARY

1. β-(2-Methylcyclohexenyl)propionic acid (III) and γ-(2-methylcyclohexenyl)butyric acid (VI) were prepared by a new method.

2. Removal of hydrochloric acid from 9-methyl-10-chloro-1-decalone (VII) proceeds with formation of two isomers: $\Delta^{4,10}$-, and $\Delta^{5,10}$-9-methyl-1-octalone (VIII and IX), both of which were isolated and characterized by derivatives. The exact position of the double bond in each of these ketones was not determined.

3. The two possible epimeric forms (XIV and XV) of *cis*-9-methyl-1-decalylamine were prepared and characterized by derivatives.

4. One of these amines (XV) was resolved into its optical antipodes (XVII) by means of α-bromo-π-camphorsulfonic acid.

5. The conversion of the *d*-, and *l*-amine with nitrous acid, was found to proceed with partial Walden Inversion at C_1, as indicated by the fact that

oxidation of the resulting mixture of alcohols yielded an optically pure ketone in each case (XVIII).

6. The semicarbazone of the inactive *cis*-9-methyl-1-decalone proved to be a racemic mixture, as shown by mixed melting points in varying ratios.

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