(only the stronger bands were observed) was inconsistent with the presence of either *cis*- or *trans*-1-methyl-2-ethylcyclopentane,[16] but was consistent with that of a mixture containing 50% or more *trans*-1-methyl-3-ethylcyclopentane[17] together with an unknown component, presumably the *cis* isomer. Gas chromatography on a column of 10% squalane on Columpak showed 92% of the sample under one peak, with all of the contaminants higher-boiling materials except for 0.1%. Most hydrocarbons boiling higher than the 1-methyl-3-ethylcyclopentanes have higher refractive indices, so the value found for the present material may be considered a probable upper limit. In addition, the infrared spectrum showed changes only in weak bands in going from the lowest-boiling to highest-boiling distillation fractions, indicating that the bulk of the material had a uniform boiling point and that substances changing the refractive index from one cut to the next were impurities, not major constituents. The sample described above was redistilled in a spinning band column at a reflux ratio of 40:1 and a center cut taken, b.p. (± 0.5°) 121.2°, $n^{25}D$ 1.4170, d^{25}_4 0.7614. Gas chromatography on a column of 25% cyanoethyl glyceryl ether on Columpak, indicated that 94% of the material was under one peak, three higher-boiling major impurities (2%, 3% and 1%) were present, and lower-boiling impurities amounted to 0.1%. Thus, the observed physical constants exclude *trans*-1-methyl-2-ethylcyclopentane, but are consistent with those of a mixture containing largely *trans*- probably mixed with some *cis*-1-methyl-3-ethylcyclopentane.

7-Methylene-1,3,5-cycloheptatriene (XII).—A distilled mixture of pyrolysis products containing approximately 71% V and 25% VI, was passed over approximately 20 ml. of heated catalyst at reduced pressure and trapped at −75°. Dehydrogenation of this crude mixture of methylenecycloheptadienes at 530° (2 mm.) over 1% platinum-on-granular charcoal catalyst that had been treated with alkaline hydrogen peroxide yielded a bright red solution having absorption maxima at 600, 550 and 500 mμ. Comparison with the extinction coefficients determined by Doering and Wiley[7] indicated that the concentration of methylenecycloheptatriene was 0.03%. In another experiment, 1. g. of crude mixture of methylenecycloheptadienes was dehydrogenated at 610° (1 mm.) and collected in a solution of 1 ml. of dimethylacetylene-dicarboxylate in 10 ml. of tetrahydrofuran. Then the methylene-cycloheptatriene was converted to 1,2-bis-(methoxycarbonyl)-azulene by the method of Doering and Wiley.[7] The azulene was partially purified by chromatography, and the yield was estimated to be 0.1% on the basis of the ultraviolet spectrum. Dehydrogenation of the crude mixture of methylenecycloheptadienes at 490° (1 mm.) over chromia–alumina catalyst that had been treated with methanolic potassium hydroxide yielded red solutions which faded very rapidly. Addition of pentane to the product precipitated a white polymer, presumably poly-(methylenecyclo-heptatriene), in 18% yield. An attempt to get a carbon and hydrogen analysis failed because the polymer exploded in the combustion tube, probably because of formation of peroxides. When a solution of 0.5 g. of the crude mixture of methylene-cycloheptadienes in 2 ml. of pyridine was passed over the alkali-treated chromia–alumina catalyst at 490° (1 mm.), the methylene-cycloheptatriene formed was stabilized somewhat. In this case, the yield of monomer, as determined spectroscopically, was 0.9%, and the yield of polymeric product was about the same as in the absence of pyridine. Pyrolysis of 5-methylenebicyclo-[2.2.1]-hept-2-ene (I) over the 1% platinum-on-charcoal catalyst at 650–675° (2 mm.) yielded a 0.1% solution of methylenecycloheptatriene. The yield of methylenecycloheptatriene from the usual pyrolysis of the hydrocarbon I over a Vycor or carbon surface appeared to be about 0.05%.

Acknowledgment.—We wish to thank Dr. D. W. Wiley of this Laboratory for many helpful discussions on the chemistry of methylenecycloheptatriene and methylenecycloheptadienes.

WILMINGTON, DEL.

(16) G. Chiurdoglu and A. Guillemonat, *Bull. soc. chim. France*, [5] **5**, 1328 (1938).

(17) P. A. Bazhulin, A. V. Koperina, A. L. Liberman, V. A. Ovodova and B. A. Kazanskii, *Bull. Acad. Sci. U.S.S.R., Div. Chem. Sci. S.S.R.*, 607 (1954) (Engl. translation).

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, CORNELL UNIVERSITY, ITHACA, N. Y.]

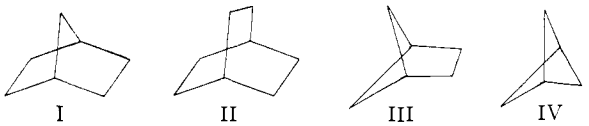
Highly Strained Bicyclic Systems. I. The Synthesis of Some Bicyclo[2,1,1]hexanes of Known Stereochemistry[1]

BY JERROLD MEINWALD[2] AND PAUL G. GASSMAN[3]

RECEIVED OCTOBER 31, 1959

The stereospecific synthesis of a series of 2-substituted bicyclo[2,1,1]hexanes, starting from (±)-α-pinene, is described.

Introduction.—Chemical investigations of the bicyclo[2,2,1]heptanes (I) have led to some of the most interesting discoveries in the classical area of natural products as well as in the field of physical organic chemistry.[4] All of the possible types of monosubstituted derivatives of I are known; each has some unique, characteristic behavior. In addition, olefinic and aromatic variants of I have been the subject of much recent attention.[4]



I II III IV

A good deal of the unusual chemistry associated with the bicyclo[2,2,1]heptyl system may be attributed ultimately to the strain incorporated in the rigid, bridged carbon skeleton; the analogously constituted but less strained bicyclo[2,2,2]-octanes (II) show much more classical behavior. In this context, a study of the synthesis, properties and reactions of the bicyclo[2,1,1]hexanes (III) and bicyclo[1,1,1]pentanes (IV) should be of special significance, since these molecules must be considerably more strained than I itself. It is remarkable that no systematic effort to study the chemistry of these systems seems to have been made, although compounds with carbon skeleton III have been prepared in a few instances. With

(1) A portion of this work was presented at the Boston Meeting of the American Chemical Society, April 5–10, 1959; Abstracts of Papers Presented, p. 14-O.

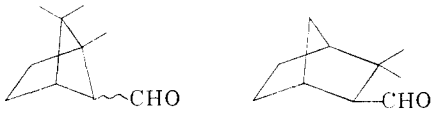
(2) Fellow of the Alfred P. Sloan Foundation.

(3) National Science Foundation Coöperative Fellow, 1959–1960.

(4) For an interesting historical survey of this field see L. Ruzicka in A. Todd's "Perspectives in Organic Chemistry," Interscience Publishers, Inc., New York, N. Y., 1956, pp. 265–314. See also S. Winstein, M. Shatavsky, C. Norton and R. B. Woodward, THIS JOURNAL, **77**, 4183 (1955); S. Winstein and M. Shatavsky, *ibid.*, **78**, 592 (1956); S. Winstein and E. T. Stafford, *ibid.*, **79**, 505 (1957); J. Meinwald, H. Nozaki and G. A. Wiley, *ibid.*, **79**, 5597 (1957); J. Meinwald and G. A. Wiley, *ibid.*, **80**, 3667 (1958).

this background in mind, we have undertaken a study of some of these highly strained molecules.

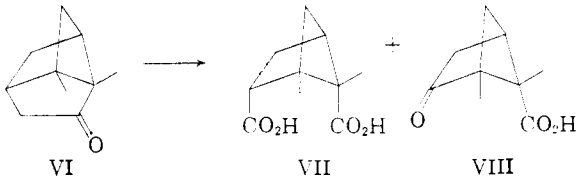
What is perhaps the earliest literature reference to the bicyclo[2,1,1]hexane system is to be found in a 1900 paper by Bredt and Jagelki, who assigned structure Va to camphenilanaldehyde, and similar structures to some closely related derivatives.[5]



Va Vb

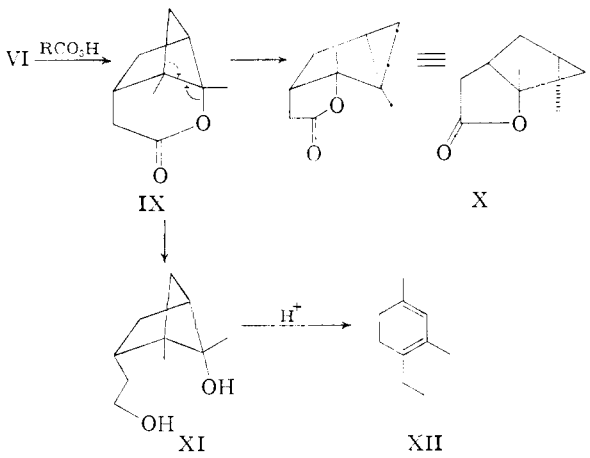
Bredt corrected these structures to the presently accepted ones (based on a bicyclo[2,2,1]heptane nucleus as shown in formula Vb) in a subsequent publication.[6]

The first investigator to have had an *authentic* bicyclo[2,1,1]hexane in hand seems to have been Sernagiotto,[7] who obtained the acids VII and VIII as oxidative degradation products of carvonecamphor (VI), which is obtained in low yield by the solar irradiation of carvone.[8] Since the correct structures for VI, VII and VIII were firmly estab-



VI VII VIII

lished only recently, in a brilliant study by Büchi and Goldman,[9] it is not surprising that these compounds have evaded extensive investigation. It should be pointed out, however, that an intriguing foreshadowing of the chemistry of these bicyclic molecules has been provided by Büchi and Goldman's work.[9] Thus, the lactone IX, prepared by Baeyer–Villiger oxidation of VI, rearranges readily to the bicyclo[3,1,0]hexane derivative X. Another interesting example of an even more deep-seated rearrangement in this series is provided by the glycol XI, obtained by lithium aluminum hydride reduction of IX, which gives rise to



(5) J. Bredt and W. Jagelki, *Ann.*, **310**, 112 (1900).

(6) See footnote on p. 57 of J. Bredt, *ibid.*, **366**, 1 (1909); see also G. Komppa and O. Komppa, *Ber.*, **69**, 2606 (1936).

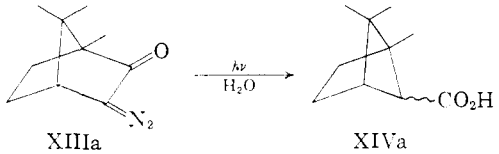
(7) E. Sernagiotto, *Gazz. chim. ital.*, **48**, 52 (1918); **47**, 153 (1917).

(8) G. Ciamician and P. Silber, *Ber.*, **41**, 1928 (1908).

(9) G. Büchi and I. M. Goldman, THIS JOURNAL, **79**, 4741 (1957).

1,3-dimethyl-4-ethylbenzene (XII) on treatment with acid. Although plausible mechanisms, in one case involving a non-classical carbonium ion intermediate, have been put forward for these reactions,[9] it would be interesting to learn much more about the details of the behavior of these systems, preferably using as simple compounds as possible.

Aside from the work related to carvonecamphor, the only published method for entry into the bicyclo[2,1,1]hexane system was provided, in 1955, by the ingenious work of Horner and Spietschka,[10] who found that photolysis of diazocamphor (XIIIa) brought about a Wolff rearrangement and yielded the ring-contracted acid XIVa. Actually, the photolysis of XIIIa had been reported some thirty

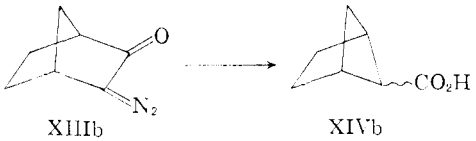


XIIIa XIVa

years earlier by Bredig.[11] Since Bredig, a physical chemist, was interested only in the possibility of obtaining an *optically active product* by the photolysis of an *optically inactive precursor* (±XIIIa), using circularly-polarized ultraviolet light, and since his reaction mixtures failed to develop any optical activity during the nitrogen evolution, his work along these lines was abandoned without characterization of the reaction products.

Only a small amount of preliminary work has been reported to date on further reactions of Horner and Spietschka's acid. The successful degradation of XIVa, in low yield, to the corresponding amine *via* a photochemical Curtius reaction, has been carried out. An acid isomeric with XIVa was obtained in an attempted bromination reaction. Other attempts to study the chemistry or stereochemistry of this series of compounds have been unrewarding,[10,12] perhaps because of the severe crowding of the functional group by the nearby methyl functions.

Finally, it should be mentioned that Colby[13] has recently applied Horner's technique to the ring-contraction of diazonorcamphor (XIIIb), and has thus prepared a bicyclo[2,1,1]hexane-5-carboxylic acid (XIVb) of unknown configuration. No further work with this acid has been reported.



XIIIb XIVb

It is clear that Horner's work has opened up a satisfactory route to bicyclo[2,1,1]hexanes *bearing functional groups on a one-carbon bridge*, which could be of general value. We have set out in the present work to develop a method for the preparation of a series of derivatives of III with *functional groups of known configuration on the two-carbon*

(10) L. Horner and E. Spietschka, *Ber.*, **88**, 934 (1955).

(11) G. Bredig, *Angew. Chem.*, **36**, 456 (1923).

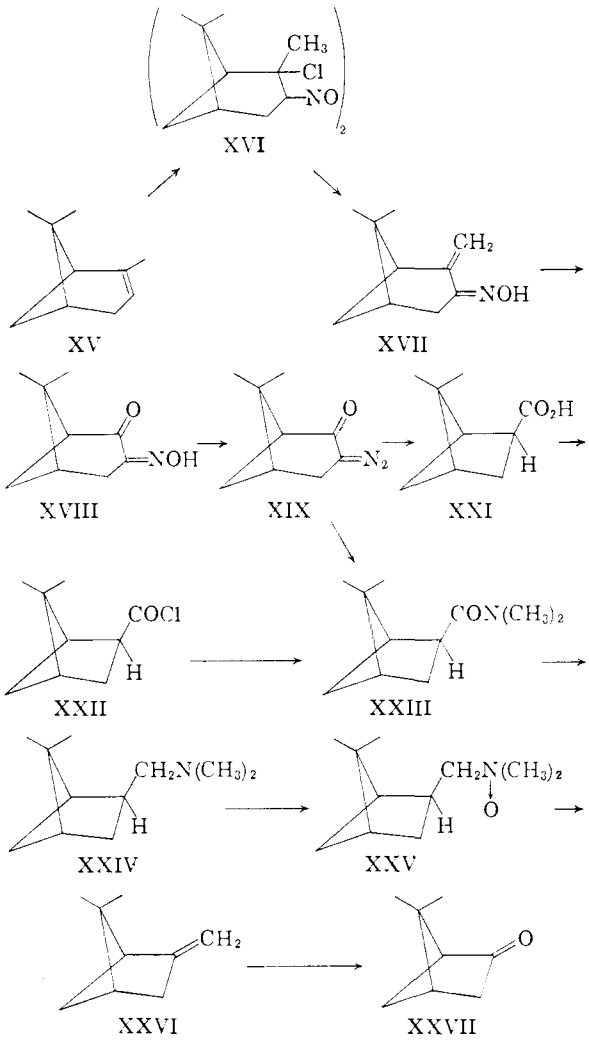
(12) Unpublished results of P. G. Gassman.

(13) T. H. Colby, Doctoral Dissertation submitted to University of Washington, 1957.

bridge. The details of this synthetic work are reported below.

Discussion.—α-Pinene (XV) serves as a particularly appropriate starting material for the preparation of bicyclo[2,1,1]hexanes, since in a formal sense all that is required is the removal of one carbon atom from the three-carbon bridge. The pathway for the removal of this carbon atom is outlined in Chart 1.

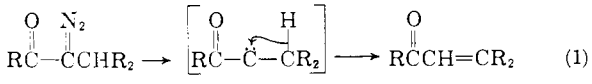
Chart I



Addition of nitrosyl chloride to XV gave (±)-α-pinene nitrosochloride (XVI), as previously described.[14] Although the excellent yields reported in the literature for this step could not be duplicated, the curious observation that the best yields are obtained with (±)-α-pinene[15] could be confirmed.

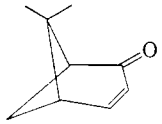
Dehydrohalogenation of XVI to give nitrosopinene (XVII) had been carried out in 50% yield in the presence of sodium ethoxide.[16] The use of sodium *t*-butoxide to bring about this elimination reaction resulted in an improvement of the yield to 80–90%. The conversion of XVII to an *oil*, presumed to be isonitrosonopinone (XVIII), by direct ozonolysis, has been reported.[17] By modification of the published procedure, XVIII could be isolated as a crystalline, analytically pure solid, m.p. 155°, for the first time. The conversion of XVIII into the cyclic diazo ketone XIX was accomplished by treatment with chloramine solution. This little-known technique, discovered by Forster in 1915,[18] and recently resurrected and exploited by Cava,[19,20] gave the desired product in 85% yield. 3-Diazonopinone was found to be a mobile, bright-yellow liquid, showing characteristic infrared absorption at 4.69 and 5.96 μ.[19]

The success of the projected bicyclo[2,1,1]-hexane synthesis, in analogy to the Horner synthesis, depended on our being able to bring about a Wolff rearrangement of 3-diazonopinone to give a ring-contracted acid. Franzen has made the generalization in a recent publication[21] that the Wolff rearrangement usually proceeds poorly, if at all, in cases where a simple hydride shift would allow the formation of an α,β-unsaturated ketone without rearrangement of the carbon skeleton (see eq. 1). The Horner ring-contraction of di-



(1)

azocamphor would be expected to succeed on this basis, since its structural features make this alternate route an impossibility. In the case of 3-diazonopinone, however, the formation of an unrearranged, unsaturated ketone (XX) might be easily possible. There were, nevertheless, grounds



XX

for optimism even in this case, since both Cava[19] and Kirmse[22] have provided examples independently of successful ring contractions in cases where hydride shifts provided reasonable alternative reaction paths.

In the actual event, 3-diazonopinone was recovered unchanged under the normal, heterogeneous, Wolff rearrangement conditions.[23] However, irradiation of XIX in aqueous dioxane solution, contained in a Pyrex vessel and using Sylvania "Blacklite" fluorescent tubes as a light source, gave the ring-contracted acid XXI in 68% yield. The stereochemistry of this acid was assigned on the basis of an argument which is presented below.

Irradiation of XIX in anhydrous ethyl ether containing dimethylamine gave the corresponding

(14) H. Rupe, *Helv. Chim. Acta*, **4**, 149 (1921).

(15) For a brief discussion of this observation see Elsevier's "Encyclopedia of Organic Chemistry," Vol. 12A, Elsevier Publishing Co., Inc., New York, N. Y., 1948, p. 517.

(16) G. Vitte, *C. A.*, **28**, 472 (1934).

(17) L. Ruzicka and H. Trebler, *Helv. Chim. Acta*, **4**, 566 (1921).

(18) M. O. Forster, *J. Chem. Soc.*, **107**, 260 (1915).

(19) M. P. Cava, R. L. Litle and D. R. Napier, THIS JOURNAL, **80**, 2257 (1958).

(20) For a brief discussion of the mechanism of this reaction, see J. Meinwald, P. G. Gassman and E. G. Miller, *ibid.*, **81**, 4751 (1959).

(21) V. Franzen, *Ann.*, **602**, 199 (1957).

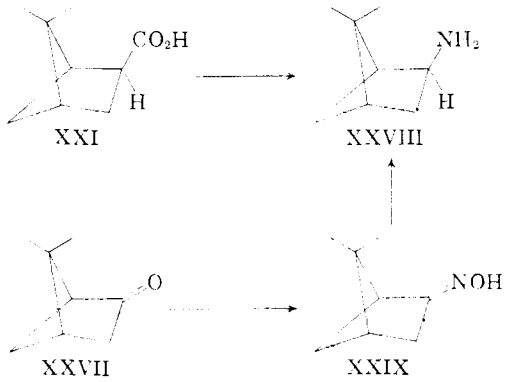
(22) W. Kirmse, *Angew. Chem.*, **69**, 106 (1957).

(23) A normal procedure, employing silver oxide as catalyst as described in ref. 21, was followed.

amide XXIII, which was reduced smoothly to the expected amine XXIV by the action of lithium aluminum hydride. The same amide XXIII was readily obtained from the acid itself XXI *via* the corresponding acid chloride XXII. Oxidation of XXIV with hydrogen peroxide yielded the N-oxide XXV, which gave rise to the exocyclic olefin XXVI when subjected to pyrolysis[24] at 120–125°. The degradation of this exocyclic olefin to the corresponding ketone XXVII was accomplished smoothly, following the permanganate–periodate procedure of Lemieux.[25] The over-all yield from α-pinene to 5,5-dimethylbicyclo[2,1,1]hexan-2-one (XXVII) as outlined in Chart 1 was about 3.8%.

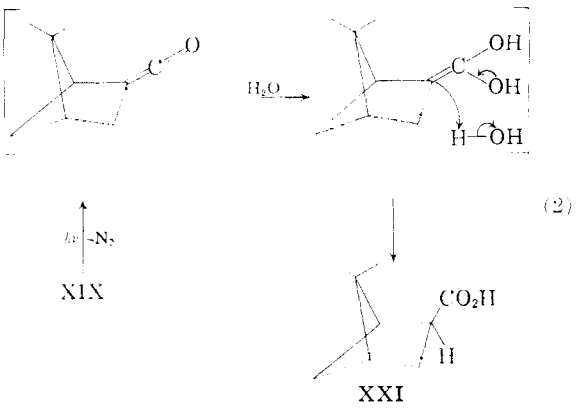
With the aim of being able to assign the proper stereochemistry to the compounds in this sequence, attempts to study the epimerization of the acid XXI were made. No conclusive results were obtained from this direct approach; however, the problem was solved in a more indirect way as shown in Chart 2. Thus XXI was subjected to the Schmidt

Chart 2



degradation, which gave rise to the corresponding amine XXVIII, presumably with retention of configuration.[26] *The same amine* was obtained by conversion of the ketone XXVII to its oxime XXIX followed by lithium aluminum hydride reduction. On the assumption that this reduction would involve hydride donation from the less hindered side of the oxime (*i.e.*, *trans* to the *gem*-dimethyl bridge), XXVIII should have its amino group in the *more hindered position*. It therefore follows that the acid originally obtained in the photolytic reaction had its carboxyl group *cis* to the *gem*-dimethyl bridge. (We would like to suggest that substituents in this stereochemical series be arbitrarily designated as having the β-configuration, in analogy to the convention used for the steroids, triterpenes and the tropane alkaloids.[27] Substituents *cis* to the unsubstituted one-carbon bridge would then be referred to as α-substituents.)

The conclusion that the photolysis product XXI has a β-carboxyl group is of some interest, although it cannot be said to be unexpected. This result would simply imply that in the formation of the acid from the corresponding ketene, the hydrogen α- to the carboxyl group is donated from the less hindered side of the bicyclic molecule, giving a kinetically controlled product,[28] as shown in eq. 2.



(2)

The reaction sequence from 5,5-dimethylbicyclo[2,1,1]hexane-2β-carboxylic acid (XXI) to 5,5-dimethylbicyclo[2,1,1]hexan-2-one (XXVII), involving six steps, proved to be somewhat cumbersome for the preparation of sizable quantities of ketonic product. Since XXVII was sought as a key intermediate for the preparation of the 2α- and 2β-alcohols and amines, as well as for possible further contraction to a bicyclo[1,1,1]pentane derivative, a shorter degradation path was highly desirable. A useful solution to this problem was found in the direct oxidation of the acid XXI, using a strongly alkaline solution of potassium permanganate. The use of this reagent for oxidation of acids has been reported,[9] and the stereochemistry of the conversion of the norbornane-2-carboxylic acids to the corresponding α-hydroxy acids has been studied recently by Kwart.[29] We have found that this reagent converts XXI into a *mixture* of the crystalline α-hydroxy acid XXX and the desired ketone, in about 59 and 24% yield, respectively. The hydroxy acid is smoothly oxidized to the ketone by the use of chromic acid in glacial acetic acid or, preferably, using sodium bismuthate.[30] Thus, this one and a half step sequence, summarized in Chart 3, replaced the original N-oxide pyrolysis route for routine preparative work.

The stereochemistry of XXX was proved to involve 2α-hydroxyl and 2β-carboxyl groups by esterification with diazomethane to give XXXI, followed by lithium aluminum hydride reduction to the glycol XXXII. Oxidation of 2-methylene-5,5-bicyclo[2,1,1]hexane (XXVI) with osmium tetroxide, which should certainly be expected to involve hydroxylation from the less hindered (*i.e.*, α) side, gave an authentic sample of 2α-hydroxy-2β-hydroxymethylbicyclo[2,1,1]hexane (XXXII), identical in all respects with the product obtained

(24) For a recent reference to this technique, developed largely by A. C. Cope, see A. C. Cope, E. Ciganek and N. A. LeBel, THIS JOURNAL, **81**, 2799 (1959).

(25) R. U. Lemieux and E. von Rudloff, *Can. J. Chem.*, **33**, 1701 (1955).

(26) A. Campbell and J. Kenyon, *J. Chem. Soc.*, 25 (1946).

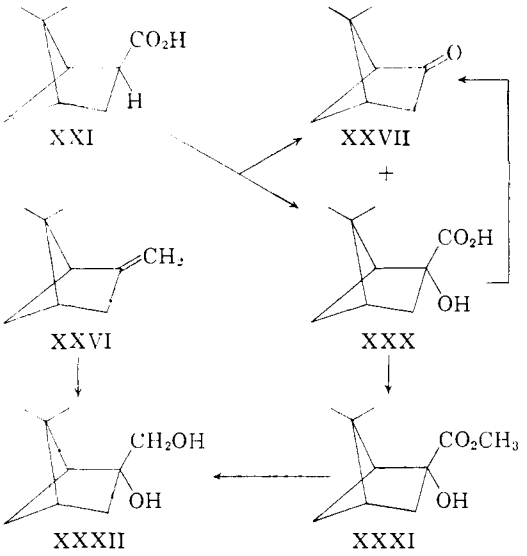
(27) The application of this type of nomenclature system to bicyclic molecules was first proposed by G. Fodor and K. Nádor, *ibid.*, 721 (1953), and has now been widely adopted.

(28) For a leading reference to the discussion of processes of this type, see H. E. Zimmerman and T. W. Cutshall, THIS JOURNAL, **81**, 4305 (1959).

(29) H. Kwart and G. D. Null, Abstracts of Papers presented at 131st Meeting of Am. Chem. Soc., April 7–12, 1957, p. 86-O. We are indebted to Professor H. Kwart for providing us with details of this study in advance of full publication.

(30) W. Rigby, *J. Chem. Soc.*, 1907 (1950).

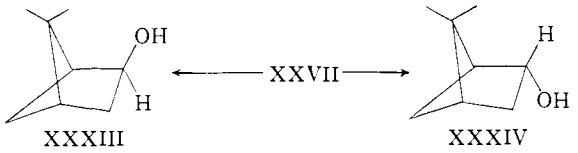
CHART 3



from the hydroxy acid. This was confirmed when samples of XXXII prepared by the two routes were found to give identical mono-*p*-nitrobenzoate esters.

It is interesting to note in passing that the permanganate oxidation of XXI must have involved delivery of the hydroxyl group from the less hindered side of the bicyclic molecule. This conclusion is in accord with the results of Kwart,[29] who found that both the *exo* and *endo* forms of norbornane-2-carboxylic acid gave rise, under comparable reaction conditions, to 2-*exo*-hydroxybicyclo[2,2,1]-heptane-2-*endo*-carboxylic acid.

In order to be able ultimately to study the solvolysis behavior of 2-substituted bicyclo[2,1,1]-hexanes, the 2-keto compound was reduced to the two possible alcohols. Reduction with lithium aluminum hydride gave an alcohol XXXIII, assigned the β-configuration on the basis of greater ease of hydride donor approach to the hindered keto group from the α-side of the substrate. Sodium–ethanol reduction of XXVII gave a product which should be at least predominantly the α-alcohol XXXIV, since this should be by far the



more stable of the two possible epimers. The infrared spectrum of the β-alcohol, obtained by lithium aluminum hydride reduction, shows it to be free of any appreciable amount of α-isomer. The sodium–alcohol reduction product, however, may contain a small amount of the β-isomer. Work is now in progress to prepare pure tosylates of these two alcohols, and we hope soon to be able to report on the solvolytic properties of these systems as well as on the deamination reactions of the corresponding amines.

Acknowledgment.—This work was supported in part by a research grant from the National Science Foundation. This support is acknowledged with pleasure.

Experimental

α-Pinene Nitrosochloride (XVI).—α-Pinene ($\alpha^{25}D$ +16.6°, obtained from the Brothers Chemical Co. and used without purification) was treated with nitrosyl chloride according to the method of Rupe[14] to give (±)-α-pinene nitrosochloride, m.p. 111.0–111.5° (lit. 107–108°),[14,15] in 40% yield. Several attempts at varying the procedure to increase the yield were unrewarding.

Nitrosopinene (XVII).—One hundred grams (0.5 mole) of XVI was gradually added to a solution of 16.5 g. of sodium in 1 kg. of dry *t*-butyl alcohol. Considerable refluxing occurred upon addition. When the addition was completed, the solution was refluxed for 15 minutes and then gradually added to an ice-cold solution of 0.5 l. of glacial acetic acid in 6 l. of water, which had been seeded with 1 g. of nitrosopinene to prevent oiling. The solution was stirred for 1 hour and the white precipitate which had formed was collected by filtration and washed with 200 ml. of ice-cold 30–60° petroleum ether. The air-dried product, m.p. 131–132° (lit.[16] 132°), weighed 64.7 g. (79%).

Omitting the wash with petroleum ether gave 75.0 g. of product (91%), m.p. 125–129°. This material was sufficiently pure for utilization in the next step.

Isonitrosonopinone (XVIII).—A solution of 45 g. (0.273 mole) of XVII in 1.575 l. of chloroform was ozonized at 0° in portions of 175 ml. each. These portions were recombined and the mixture was added to 200 ml. of water; the immiscible layers were stirred vigorously overnight. The chloroform was evaporated under reduced pressure and the oily residue was extracted repeatedly with several portions of boiling water. Evaporation of the aqueous solution yielded a white crystalline solid, which on sublimation gave 24.7 g. (54%) of XVIII, m.p. 155.0–155.5°; infrared spectrum (Nujol): 3.12, 5.80, 6.14 μ.

Anal. Calcd. for $C_9H_{11}NO_2$: C, 64.65; H, 7.84; N, 8.38. Found: C, 64.67; H, 7.89; N, 8.36.

Slow crystallization from water yielded a stable monohydrate, m.p. 100–105° dec.; infrared spectrum (Nujol) same as that of XVIII with the exception of an extra peak in the vicinity of 3.00 μ.

Anal. Calcd. for $C_9H_{15}NO_3$: C, 58.36; H, 8.16; N, 7.56. Found: C, 58.63; H, 7.99; N, 7.79.

A more convenient method for the preparation of XVIII involved ozonolysis of XVII in methanol at −70 to −80°. The reaction mixture is worked up by hydrolysis with water, followed by evaporation of the methanol and extraction of the aqueous solution with ether. The organic solvent is removed under reduced pressure and the solid residue is washed with 30–60° petroleum ether and air-dried. Sublimation of the dried product give a 45–50% yield of XVIII, m.p. 150–154°.

3-Diazonopinone (XIX).—Twenty grams of finely ground XVIII was dissolved in a minimum amount of concentrated, aqueous sodium hydroxide solution, and the volume of the solution was brought to 1.1 liters. The solution was cooled to 0°, and 45 ml. of 15 *N* NH_4OH was added, followed by dropwise addition of 530 ml. of 5.25% sodium hypochlorite solution (Clorox) over a 1-hour period. The solution was then stirred at 0° for 30 minutes.

The reaction mixture was extracted with 30–60° petroleum ether by stirring vigorously with three 600-ml. portions of this solvent for 2-, 2- and 12-hour periods. The combined extracts were dried over anhydrous magnesium sulfate, and the solvent was distilled off under reduced pressure to give 16.6 g. (85%) of a mobile yellow oil; infrared spectrum (neat): 4.69, 5.96 μ.

5,5-Dimethylbicyclo[2,1,1]hexane-2β-carboxylic Acid (XXI).—A solution of 6.73 g. of XIX in a mixture of 220 ml. of spectrograde *p*-dioxane and 55 ml. of water was irradiated in a Pyrex vessel, using a bank of eight 15-watt Sylvania "Blacklite" fluorescent tubes, for 190 hours. The solvent was distilled off under reduced pressure, and the residue was taken up in sodium carbonate solution. The resultant solution was extracted with ether, and the aqueous layer was warmed gently under reduced pressure to remove any remaining traces of organic solvent. The aqueous layer was then filtered, cooled, and acidified with dilute hydrochloric acid. The white precipitate which formed was collected by filtration and air-dried to give 4.25 g. (68%) of XXI. Recrystallization from acetic acid–water gave an analytical sample, m.p. 77.2–77.5°; infrared spectrum ($CHCl_3$):

3.20, 5.90 μ. This acid was saturated to bromine and potassium permanganate tests carried out under the usual conditions.

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.40; H, 9.20.

5,5-Dimethylbicyclo[2,1,1]hexane-2β-dimethylcarboxamide (XXII). A.—Dimethylamine was bubbled into a solution of 8.38 g. of XIX in 400 ml. of anhydrous ethyl ether until the volume reached 440 ml. The resulting solution was irradiated with ultraviolet light for 20 days in a Pyrex vessel equipped with a cooling coil to maintain the temperature at 10–15°. The solvent was evaporated under reduced pressure, and the residue was dissolved in hexane and washed with water. The hexane was allowed to evaporate and the residue was sublimed twice to give 5.53 g. (60%) of XXII, m.p. 59–60°; infrared (neat): 6.05 μ. Recrystallization from hexane followed by sublimation gave an analytical sample, m.p. 60–60.5°.

Anal. Calcd. for $C_{11}H_{19}NO$: C, 72.88; H, 10.56; N, 7.73. Found: C, 72.96; H, 10.66; N, 7.66.

B.—A solution of 5.00 g. of XXI and 10.0 g. of thionyl chloride in 50 ml. of dry benzene was refluxed for 2 hours. The benzene–thionyl chloride was distilled off, 25 ml. of dry benzene was added, and about 15 ml. of this solvent was removed again by distillation. The residual acid chloride was diluted to 50 ml. with dry ether, and dimethylamine was bubbled into the solution. The dimethylamine hydrochloride was removed by filtration, and the benzene was evaporated under reduced pressure. The residue was sublimed to give 5.45 g. (93%) of XXIII, m.p. 57–59°.

2β-Dimethylaminomethyl-5,5-dimethylbicyclo[2,1,1]hexane (XXIV).—A solution of 7.20 g. of XXIII in 40 ml. of anhydrous ether was added dropwise over a 1-hour period to a stirred suspension of 3.00 g. of lithium aluminum hydride in 75 ml. of anhydrous ether. The reaction mixture was stirred at room temperature for 18 hours, cooled to 0°, and quenched by dropwise addition of 12.0 g. of water. The resultant mixture was stirred vigorously for 3 hours and then filtered. The precipitated salts were washed thoroughly with ether, and the combined ether extract was dried over anhydrous magnesium sulfate. Evaporation of the ether followed by fractional distillation of the residue gave 5.75 g. (87%) of XXIV, b.p. 83–85° (19 mm.), n^{30}_D 1.4630; infrared spectrum (neat): no absorption in the region 2.8–3.0 or 5.8–6.1 μ.

Anal. Calcd. for $C_{11}H_{21}N$: C, 78.97; H, 12.65; N, 8.37. Found: C, 79.26; H, 12.65; N, 8.26.

A picrate of XXIV was prepared in absolute ethanol. Four recrystallizations from absolute ethanol gave a product, m.p. 132.5–133°.

Anal. Calcd. for $C_{17}H_{24}N_4O_7$: C, 51.50; H, 6.14; N, 14.14. Found: C, 51.56; H, 6.22; N, 14.18.

2β-Dimethylaminomethyl-5,5-dimethylbicyclo[2,1,1]hexane N-Oxide (XXV).—To a solution of 6.40 g. of XXIV in 10 ml. of anhydrous methyl alcohol was added, with stirring and cooling, 12 ml. of 30% hydrogen peroxide. After stirring for an additional 8 hours, a further 2-ml. portion of hydrogen peroxide was added, and the solution was allowed to stand 16 hours longer. A small amount of platinum black was added, and the mixture was stirred for 24 hours to destroy the excess hydrogen peroxide. The solution was then filtered and the solvent evaporated off in a stream of dry air.

A picrate of the residual N-oxide XXV was prepared in 95% ethanol. Two recrystallizations from absolute ethanol gave an analytical sample as long yellow needles, m.p. 142.5–143°.

Anal. Calcd. for $C_{17}H_{24}N_4O_8$: C, 49.51; H, 5.86; N, 13.59. Found: C, 49.73; H, 5.97; N, 13.43.

2-Methylene-5,5-dimethylbicyclo[2,1,1]hexane (XXVI).—The N-oxide prepared from 6.40 g. of XXV was pyrolyzed at 120–125° under a vacuum of 56 mm. The pyrolysis products were condensed in a trap which had been cooled in an ice–salt-bath to −7°. The trapped material was diluted with ether, and washed with water until the aqueous solution showed no signs of basicity. The ethereal solution was dried over anhydrous magnesium sulfate, filtered, and the ether distilled off. The residue was fractionally distilled to give 3.30 g. (70.6%) of XXVI, b.p. 70–71° (96 mm.), n^{28}_D 1.4611; infrared spectrum (neat): 6.02, 11.50μ. These two peaks vanish when XXVI is allowed to react with bromine in carbon tetrachloride.

Anal. Calcd. for C_9H_{14}: C, 88.45; H, 11.55. Found: C, 88.69; H, 11.55.

5,5-Dimethylbicyclo[2,1,1]hexan-2-one (XXVII).—A mixture of 2.20 g. of XXVI, 14.0 g. of potassium periodate, 0.50 g. of potassium permanganate and 20.0 g. of potassium carbonate in 200 ml. of water was shaken vigorously for 16 hours. The organic material was extracted with ether, and the ethereal solution was dried over anhydrous magnesium sulfate. After filtration of the drying agent, the ether was removed and the residue fractionally distilled to give 1.31 g. (59%) of XXVII, b.p. 85–87° (40 mm.), n^{29}_D 1.4581; infrared spectrum (neat): 5.69 μ. This material was redistilled to give an analytical sample, b.p. 89–90° (47 mm.), n^{25}_D 1.4612.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.56; H, 9.69.

A 2,4-dinitrophenylhydrazone of XXVII was prepared in the usual way. This derivative was recrystallized from 95% ethanol four times to give a pure sample, m.p. 130.5–131°.

Anal. Calcd. for $C_{14}H_{16}N_4O_4$: C, 55.25; H, 5.30; N, 18.41. Found: C, 55.10; H, 5.31; N, 18.70.

2β-Amino-5,5-dimethylbicyclo[2,1,1]hexane (XXVIII).—To a mixture of 5.00 g. of XXI, 100 ml. of concentrated sulfuric acid and 250 ml. of chloroform was added with vigorous stirring, at 45–50°, 7.00 g. of sodium azide. The addition occupied a 30-minute period. The resultant mixture was stirred at 50–55° for 1.5 hours, cooled, diluted by the addition of ice, and made basic with dilute sodium hydroxide solution. The reaction mixture was then extracted with ether and the ethereal extracts washed with water. The organic solution was extracted with dilute hydrochloric acid and the acidic layer was warmed gently under reduced pressure to remove any remaining traces of organic solvent. After filtering and cooling, the acidic solution was made basic with dilute sodium hydroxide solution and extracted with ether. After drying over potassium hydroxide pellets, the ether was evaporated under reduced pressure and the residue was fractionally distilled to give 2.50 g. (61%) of XXVIII, b.p. 84–86° (67 mm.), n^{25}_D 1.4750; infrared spectrum (neat): 3.05, 6.13μ. The amine had a very offensive odor. It was not analyzed due to the very rapid formation of a solid carbonate when exposed to air.

A *p*-nitrobenzamide of XXVIII was prepared in the usual way in benzene solution. Three recrystallizations from aqueous ethanol gave an analytical sample as silky, white needles, m.p. 158.5–159.0°.

Anal. Calcd. for $C_{15}H_{18}N_2O_3$: C, 65.67; H, 6.61; N, 10.21. Found: C, 65.45; H, 6.45; N, 10.44.

5,5-Dimethylbicyclo[2,1,1]hexan-2-one Oxime (XXIX).—A mixture of 1.52 g. of XXVII, 1.05 g. of hydroxylamine hydrochloride, 5.25 g. of potassium hydroxide and 35 ml. of 95% ethyl alcohol was refluxed for 2 hours. The reaction mixture was diluted with 100 ml. of water, acidified with dilute hydrochloric acid, and extracted immediately with ether. The ethereal solution was dried over anhydrous magnesium sulfate, filtered, and the ether distilled off under reduced pressure. The residue was fractionally distilled to give 1.33 g. (78%) of XXIX, b.p. 86–87° (1.8 mm.), n^{27}_D 1.5032; infrared spectrum (neat): 3.12, 5.92, 10.75 μ.

Anal. Calcd. for $C_8H_{13}NO$: C, 69.03; H, 9.41; N, 10.06. Found: C, 69.05; H, 9.52; N, 9.91.

2β-Amino-5,5-dimethylbicyclo[2,1,1]hexane (XXVIII).—A solution of 1.15 g. of XXIX in 10 ml. of anhydrous ether was added dropwise to a stirred suspension of 1.20 g. of lithium aluminum hydride in 15 ml. of anhydrous ether. This reaction mixture was refluxed for 51 hours. After cooling to 0° in an ice-bath, the suspension was hydrolyzed by dropwise addition of 4.80 g. of water, followed by stirring for 30 minutes. The solution was filtered and the precipitated inorganic salts were washed thoroughly with ether. The combined filtrates were dried over anhydrous sodium carbonate, filtered, and the ether distilled off. The residue was fractionally distilled to give 0.30 g. of starting material and 0.50 g. (66% based on unrecovered oxime) of XXVIII, b.p. 87–88° (67 mm.), n^{20}_D 1.4741; infrared spectrum (neat): identical with that of the amine obtained from XXI by the Schmidt reaction.

A *p*-nitrobenzamide was prepared; it melted at 157–158° after one recrystallization from ethanol–water. A mixture melting point with *p*-nitrobenzamide of amine XXVIII obtained stereospecifically from XXI was undepressed (157–158°).

5,5-Dimethylbicyclo[2,1,1]hexan-2-one (XXVII) and 5,5-Dimethylbicyclo[2,1,1]hexan - 2α - ol - 2β - carboxylic Acid (XXX).—A mixture of 12.0 g. of XXI, 21.0 g. of potassium permanganate and 54.0 g. of potassium hydroxide was dissolved in 170 ml. of water. This solution was stirred with 150 ml. of 60–70° petroleum ether and the resulting emulsion was heated to 50–55° for 19 hours. The solution was cooled, and sulfur dioxide was bubbled into the reaction mixture to reduce the excess potassium permanganate. The resultant solution was diluted with about 200 ml. of water and 150 ml. of 30–60° petroleum ether, and the precipitated manganese dioxide was removed by filtration. The immiscible layers were then separated.

The organic layer was dried over anhydrous magnesium sulfate and concentrated to a volume of 10 ml. Fractional distillation of this material gave 2.30 g. (24%) of pure XXVII.

The aqueous layer was acidified with dilute hydrochloric acid and extracted with ether. The ethereal solution was dried over anhydrous magnesium sulfate, filtered, and evaporated under reduced pressure to give 7.82 g. (59%) of XXX, m.p. 104–106°; infrared spectrum (Nujol): 3.00, 3.12, 5.92 μ. Recrystallization from benzene or carbon tetrachloride raised the melting point to 117–118°, but this dropped to 104–106° after standing several hours.

5,5-Dimethylbicyclo[2,1,1]hexan-2-one (XXVII).—To a solution of 2.12 g. of XXX in 25 ml. of water was added 4.12 g. of sodium bismuthate (85% purity). A solution of 4.00 g. of 85% phosphorous acid in 1 ml. of water was added dropwise over a 20-minute period, with vigorous stirring. Stirring was continued and the temperature was gradually raised to 45° over a 4-hour period, and then maintained at 45–50° for 12 hours. The reaction mixture was cooled and extracted with ether, which was then washed thoroughly with dilute sodium bicarbonate solution. The ethereal solution was dried over anhydrous magnesium sulfate, filtered, and the ether removed under reduced pressure. Fractional distillation of the residue gave 1.07 g. (69%) of pure XXVII, b.p. 91–92° (46 mm.).

5,5 - Dimethylbicyclo[2,1,1]hexan - 2α - ol - 2β - carboxylic Acid Methyl Ester (XXXI).—An ethereal solution of diazomethane was added dropwise to 1.50 g. of XXX in 10 ml. of ether until the color remained on addition of more reagent. The slight excess of diazomethane was destroyed by the addition of a very dilute solution of acetic acid in ether until the solution was colorless. The organic solution was dried over anhydrous magnesium sulfate, filtered, and the ether distilled off. The residue was fractionally distilled to yield 1.28 g. (79%) of XXXI, b.p. 100–102° (2 mm.), $n^{27}D$ 1.4743; infrared spectrum (neat), 2.95, 5.82 μ.

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.26; H, 8.95.

The 2α-Hydroxy-2β-hydroxymethyl-5,5-dimethylbicyclo[2,1,1]hexane (XXXII).—A solution of 1.00 g. of XXXI in 15 ml. of anhydrous ether was added dropwise at 0° to a stirred suspension of 0.70 g. of lithium aluminum hydride in 15 ml. of anhydrous ether. When the addition was complete, the reaction mixture was stirred at room temperature for 12 hours. It was then cooled to 0° and 2.80 g. of water was added dropwise with vigorous stirring. The precipitated inorganic salts were removed by filtration and washed with anhydrous ether. The ethereal filtrate was dried over anhydrous magnesium sulfate, filtered, and the ether distilled off under reduced pressure. Distillation of the residue gave 0.77 g. (84%) of XXXII, b.p. 108–109° (1.9 mm.), $n^{24}D$ 1.4972; infrared spectrum (neat): 3.05, 9.69 μ.

Anal. Calcd. for $C_9H_{16}O_2$: C, 69.19; H, 10.32. Found: C, 68.98; H, 10.25.

A mono-*p*-nitrobenzoate was prepared in the usual fashion. Two recrystallizations from hexane gave an analytical sample as small, glistening plates, m.p. 98.5–99°.

Anal. Calcd. for $C_{16}H_{19}NO_5$: C, 62.94; H, 6.27. Found: C, 62.93; H, 6.24.

2α-Hydroxy-2β-hydroxymethyl-5,5-dimethylbicyclo[2,1,1]hexane (XXXII).—One gram of osmium tetroxide in 25 ml. of purified dioxane was added to a solution of 0.48 g. of XXVI in 5 ml. of purified dioxane. The reaction mixture was stirred in the dark for 4 days at room temperature. The osmic ester was decomposed by bubbling hydrogen sulfide into the reaction mixture with cooling and stirring. The precipitated inorganic material was removed by filtration, and the solvent was removed on a rotating flash evaporator. Fractional distillation of the residue gave 0.24 g. (39%) of XXXII, b.p. 108–109° (1.9 mm.), $n^{27}D$ 1.4970; infrared spectrum (neat) identical to that of the diol XXXII prepared *via* hydride reduction of the α-hydroxy acid XXX.

A mono-*p*-nitrobenzoate was prepared (m.p. 94–95°) which gave no depression on mixed melting (m.m.p. 96–97°) with the *p*-nitrobenzoate of the diol prepared from the α-hydroxy acid (m.p. 98–98.5°).

5,5-Dimethylbicyclo[2,1,1]hexan-2β-ol (XXXIII).—A solution of 0.76 g. of XXVII in 10 ml. of anhydrous ethyl ether was added dropwise, at 0°, to a stirred suspension of 0.12 g. of lithium aluminum hydride in 10 ml. of anhydrous ethyl ether. The reaction mixture was stirred at 0° for 2 hours, and was then hydrolyzed by dropwise addition of 0.47 g. of water, followed by stirring at 0° for 30 minutes. The resulting reaction mixture was filtered, and the precipitated salts were washed thoroughly with ether. The filtrate was dried over anhydrous sodium sulfate, filtered, and the ether distilled off under reduced pressure. The residue was fractionally distilled to give 0.67 g. (86%) of XXXIII, b.p. 90–92° (25 mm.), $n^{23}D$ 1.4757; infrared spectrum (neat): 3.00, 9.86 μ.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.38; H, 11.06.

A phenylurethan of XXXIII was prepared in the usual way. Two recrystallizations from hexane gave an analytical sample, m.p. 95–96°.

Anal. Calcd. for $C_{15}H_{19}NO_3$: C, 73.44; H, 7.81; N, 5.71. Found: C, 73.55; H, 7.58; N, 5.69.

5,5-Dimethylbicyclo[2,1,1]hexan-2α-ol (XXXIV).—To a solution of 0.90 g. of XXVII in 15 ml. of 95% ethanol was added, with vigorous stirring, 1.85 g. of sodium (in small, clean-faced pieces) at a rate sufficient to maintain gentle refluxing. When the addition was complete, the solution was diluted with 5 ml. of 50% ethanol and refluxed for 1 hour. The reaction mixture was allowed to cool. It was then diluted with 15 ml. of water, saturated with ammonium chloride, and extracted with two 30-ml. portions of ether. The combined ethereal extracts were dried over anhydrous magnesium sulfate, filtered, and the ether distilled off under reduced pressure. Fractional distillation of the residue gave 0.62 g. (68%) of XXXIV, b.p. 91–92° (23 mm). Redistillation gave an analytical sample, $n^{21}D$ 1.4753; infrared spectrum (neat): 3.00, 9.60 μ.

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.38; H, 11.06.