cycloöctanecarboxaldehyde 2,4-dinitrophenylhydrazone. The infrared spectrum of a sample from a similar reaction was essentially identical with that of authentic cycloöctanecarboxaldehyde 2,4-dinitrophenylhydrazone.

1-Hydroxycycloöctane-1-methanol Isopropylidene Ketal.—A 0.596-g. quantity of crude glycol from fractions VI and VII was stirred for 23.5 hr. with 4.01 g. of anhydrous copper sulfate in 200 ml. of reagent grade acetone[17] (previously dried with copper sulfate). After filtration and removal of the solvent, the residue, 0.644 g., was chromatographed on 20 g. of neutral activity I alumina, with 20 fractions of 50 ml. each being collected. A total of 0.579 g. of crude isopropylidene ketal was eluted with pentane, and a small amount of unreacted glycol (0.035–0.040 g.) was recovered.

A portion of the isopropylidene ketal was purified by distillation in a short-path still at 10 mm. (bath temperature 109–135°), n^{25}D 1.4617.

Anal. Calcd. for $C_{12}H_{22}O_2$: C, 72.68; H, 11.18. Found: C, 72.45; H, 11.28.

Treatment of 1-Cycloöctene-1-methanol (III) with Formic Acid.—To 200 ml. of formic acid (98–100%) was added with stirring in a nitrogen atmosphere 19.6 g. of 1-cycloöctene-1-methanol (III) during 4 min. The last traces of alcohol were rinsed in with an additional 35 ml. of formic acid. The mixture was stirred for 1 hr. at 22–25°, added to 400 ml. of water, and extracted with one 400-ml. and two 200-ml. portions of ether. The combined extracts were washed with two 200-ml. portions of water and five 200-ml. portions of saturated sodium bicarbonate solution. The solvent was removed by distillation at atmospheric pressure, and the residue was treated overnight with 20 g. of sodium hydroxide dissolved in 100 ml. of methanol and 40 ml. of water. A portion of the methanol was removed under reduced pressure, and then the mixture was added to 400 ml. of water and extracted with three 300-ml. portions of ether, saturated sodium chloride solution (20 ml.) being added. The combined extracts were dried over magnesium sulfate. After removal of the solvent, the residue was distilled through a 30 × 0.5-cm. spinning band column, yielding in five fractions a total of 16.6 g. containing 1.25 g. of 2-methylenecycloöctanol (IV) and 14.47 g. of recovered III, in addition to several minor components, the amounts being estimated from the areas of the peaks of gas chromatography. The first three fractions (1.45 g.) which were highly enriched in compound IV were combined and chromatographed on 75 g. of neutral activity I alumina, and there were obtained several fractions which were more highly enriched in IV. Complete isolation of IV was effected by gas chromatography on silicone oil at 182–184°. An analytical sample was obtained by this method, n^{25}D 1.4954.

Anal. Calcd. for $C_9H_{16}O$: C, 77.09; H, 11.50. Found: C, 77.08; H, 11.54.

This sample of IV was identical (infrared spectrum) with authentic 2-methylenecycloöctanol and with IV obtained from the solvolysis of methylenecycloöctane oxide. Its phenylurethan, m.p. 97.5–98.5° (hot-stage), was undepressed in mixed m.p. with a sample of the phenylurethan of IV from the solvolysis of methylenecycloöctane oxide.

Compound V, isolated from the first three distillation fractions in 8.5-mg. quantity by gas chromatography on silicone oil at 182–194°, had a retention time similar to that of V in the solvolysis product mixture of methylenecyclooctane oxide. Its infrared spectrum had medium strength bands at 3360, 1430, 1055 and 987 cm.$^{-1}$, and a weak band at 1365 cm.$^{-1}$. On treatment with phenylisocyanate an oil formed which failed to crystallize.

Conversion of 2-Methylenecycloöctanol (IV) to 2-Methylenecycloöct-1-yl Acetate (VI).—2-Methylenecycloöctanol (IV) (0.251 g.), isolated from the reaction of 1-cycloöctene-1-methanol (III) with formic acid, was allowed to stand for 24.3 hr. at room temperature with 0.406 g. of acetic anhydride and 2.5 ml. of pyridine. The reaction mixture was added to 5 ml. of water and extracted with three 10-ml. portions of ether. The combined extracts were washed with one 10-ml. portion of water, three 5-ml. portions of cold 5% hydrochloric acid, and two 5-ml. portions of water, and dried over magnesium sulfate. The crude weight was 0.294 g. (89%). The crude material was combined with 0.032 g. from an earlier preparation, and purified by chromatography on neutral activity I alumina, yielding 0.236 g. of 2-methylenecycloöct-1-yl acetate (VI). An analytical sample was purified by gas chromatography on silicone oil at 187°, n^{25}D 1.4690. The infrared spectrum and the retention time on gas chromatography were essentially identical with those of authentic 2-methylenecycloöct-1-yl acetate.

Anal. Calcd. for $C_{11}H_{18}O_2$: C, 72.49; H, 9.96. Found: C, 72.62; H, 9.90.

Acid Treatment of 2-Methylenecycloöct-1-yl Acetate (VI).[18]—2-Methylenecycloöct-1-yl acetate (VI), 0.02 ml., was treated with 0.2 ml. of deoxygenated glacial acetic acid containing 0.25% *p*-toluenesulfonic acid in a nitrogen-filled vial for 48 hours at room temperature. The reaction mixture was then added to 2.2 ml. of 25% aqueous potassium carbonate solution. Ether was added and the mixture was agitated. Then 2.2 ml. of water was added and the mixture again agitated, and the ether layer separated. The aqueous layer was extracted twice more with ether, and the combined extracts were dried over magnesium sulfate. Gas chromatography of the product on silicone oil at 187° showed three components; the first (0.3%) was not identified, but is probably not an acetate because of its short retention time. The second (89.8%) corresponded in retention time to that of the starting material. A small amount was collected by gas chromatography, and was identified as 2-methylenecycloöct-1-yl acetate by comparison of its infrared spectrum with that of an authentic specimen. The third material (9.9%) corresponded approximately in retention time to that of 1-cycloöctene-1-methyl acetate, and addition of an authentic sample of the latter to the mixture produced no additional peaks.

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

Highly Strained Bicyclic Systems. II. The Synthesis of Optically Active 2α- and 2β-Amino and Hydroxy Bicyclo[2,1,1]hexanes

BY JERROLD MEINWALD[1] AND PAUL G. GASSMAN[2]

RECEIVED MARCH 14, 1960

Stereospecific syntheses leading from (−)-β-pinene to (−)-5,5-dimethylbicyclo[2,1,1]hexan-2β-ol, (−)-5,5-dimethylbicyclo[2,1,1]hexan-2α-ol, (−)-2β-amino-5,5-dimethylbicyclo[2,1,1]hexane and (+)-2α-amino-5,5-dimethylbicyclo[2,1,1]hexane are described. The key step in the synthesis of compounds in the 2α-series is the epimerization of (−)-5,5-dimethylbicyclo[2,1,1]hexane-2β-carboxylic acid. The success of this epimerization confirms the stereochemistry of all of the compounds described above.

Introduction.—In a recent publication,[3] we have described the synthesis of a number of *racemic*, 2-substituted bicyclo[2,1,1]hexanes of known stereochemistry. It appears desirable, for a variety of reasons, to have available for study *optically active* compounds of this type with the general formula I, bearing hydroxyl and amino groups in both the α- and β-configurations.[4] These compounds should be of particular value, for example, in helping to

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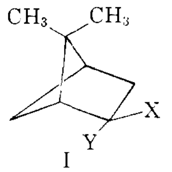
[1] Alfred P. Sloan Foundation Fellow.

[2] National Science Foundation Coöperative Fellow, 1959–1960.

[3] J. Meinwald and P. G. Gassman, THIS JOURNAL, **82**, 2857 (1960).

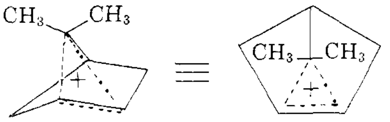
[4] In reference 3, a β-designation is suggested for any substituent *cis* to the *gem*-dimethyl group.



I

Ia, X = NH_2, Y = H
Ib, X = H, Y = NH_2
Ic, X = OH, Y = H
Id, X = H, Y = OH

determine whether or not the symmetrical, bridged, ion II plays a role in reactions such as the solvolysis of the tosylate of Id, or the deamination of the amine Ib

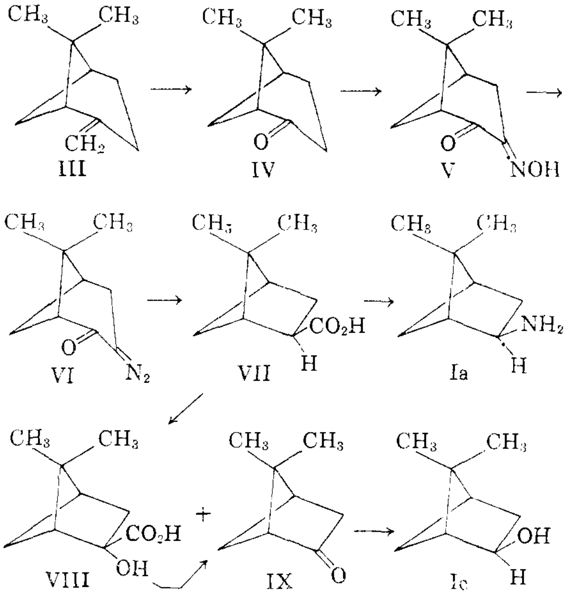


II

It was a special limiting feature of our original synthetic scheme starting from α-pinene[3] that only racemic products could be obtained, since α-pinene nitrosochloride, a key intermediate, is readily available only in its racemic form. Rather than carrying out tedious resolutions on our previously characterized intermediates, we have exploited a somewhat modified route to the bicyclo[2,1,1]hexanes, starting from (−)-β-pinene (III). We would like to report in this paper the details of the new route, which permits retention of the asymmetry conveniently provided by Nature.

Discussion.—The initial step in the new synthetic sequence, outlined in Chart 1, involved ozonolysis of (−)-β-pinene (III) to give (+)-nopinone (IV) in 67% yield. Condensation of IV with isoamyl nitrite, using potassium *t*-butoxide in dry *t*-butyl alcohol under carefully controlled conditions, gave the desired (+)-oximino-ketone V in 87% yield. (The preparation of (±)-V *via* a three-step sequence starting from α-pinene has been discussed in our earlier publication.[3]) Chloramine diazotization[5] of V gave the corresponding diazo-ketone VI as a bright yellow oil in about 80-85% yield. Irradiation of this material in aqueous dioxane, using Sylvania "Blacklite" sources, gave about 65% yields of (−)-5,5-dimethylbicyclo-[2,1,1]hexane-2β-carboxylic acid (VII). Schmidt degradation of this acid gave an excellent conversion to (−)-2β-amino-5,5-dimethylbicyclo[2,1,1]-hexane (Ia), a mobile, colorless liquid which was characterized as its *p*-nitrobenzamide. For the preparation of the corresponding optically active 2β-alcohol Ic, permanganate oxidation of (−)-VII gave the (−)-α-hydroxy-β-acid VIII, accompanied by some (+)-5,5-dimethylbicyclo[2,1,1]hexan-2-one (IX). Sodium bismuthate cleaved VIII readily to give additional (+)-IX. Finally, lithium aluminum hydride reduction of the (+)-ketone gave the desired (−)-5,5-dimethylbicyclo[2,1,1]-hexan-2β-ol (Ic) quantitatively. Both the (−)-β-amine (Ia) and the (−)-β-alcohol (Ic) were shown, by vapor phase chromatography, to be free of contamination by the epimeric α-isomers.

CHART 1



The preparation of pure substances belonging to the 2α-series proved to be somewhat more of a problem. Thus, sodium-alcohol reduction of the (+)-ketone IX gave an analytically pure alcohol which, however, was readily resolved by vapor phase chromatography on a polyethylene glycol-glass bead column into *two* components, present in a 2:1 ratio. Although the *major* constituent of this mixture appeared to be the desired 2α-alcohol Id, the second component was the previously characterized 2β-alcohol Ic. Since this reduction did not proceed with the requisite specificity,[6] epimerization of the readily available 2β-alcohol Ic was investigated. Refluxing Ic with a solution of aluminum isopropoxide in isopropyl alcohol containing 1% of acetone for an eight-day period, however, was shown by vapor phase chromatography to give a product which was not quite half epimerized.[7] This technique looked particularly unpromising since the recovery was only 65%, and other contaminants were present in the product. Although it would appear from the consideration of models that this result can hardly reflect the equilibrium position for the α and β-alcohols, it does show that the equilibrium is approached in this system only at a very low rate, making the procedure unpromising for preparative purposes Extrapolating from these observations, the likelihood of obtaining pure 2α-amine Ib by sodium-alcohol reduction of the oxime of ketone IX did not seem especially great. Finally, no simple technique for the separation of mixtures of either epimeric alcohols or amines on a preparative scale was available. In view of these difficulties, both anticipated and real, more direct and reliable routes to the 2α-oriented alcohol and amine were sought. The results of this search are summarized in Chart 2.

Since the synthesis of the desired compounds from the as yet unknown 2α-carboxylic acid XI

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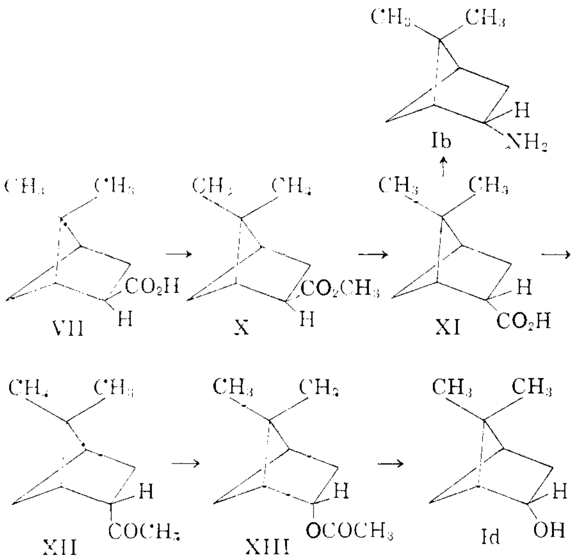
[5] For a leading reference, see J. Meinwald, P. G. Gassman and E. G. Miller, THIS JOURNAL, **81**, 4751 (1959).

[6] For a recent discussion of the breakdown of the usually employed generalizations (D. H. R. Barton, *J. Chem. Soc.*, 1027 (1953), see K. D. Hardy and R. J. Wicker, THIS JOURNAL, **80**, 640 (1958)).

[7] For a recent example of the use of this technique see A. A. Youseff, M. E. Baum and H. M. Walborsky, *ibid.*, **81**, 4709 (1959).

CHART 2

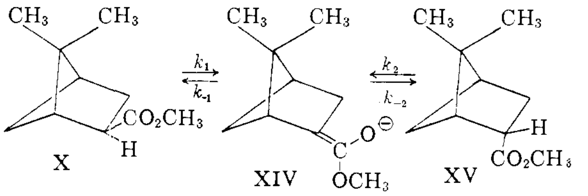


might be anticipated to be straightforward, an effort was made to epimerize the readily available (−)-2β-carboxylic acid VII. Initial experiments in this direction were all discouraging,[8] although it seemed that non-bonded interaction between a 2β-carboxyl substituent and the *syn*-methyl group at C_5 would cause the 2α-epimer to be greatly favored at equilibrium. Thus, refluxing of VII with thionyl chloride[9] in benzene for seven days, followed by hydrolysis, gave only an impure sample of starting material. Several attempts at chromatography of the recovered product failed to yield any of the desired, new isomer. Esterification of VII, using diazomethane, and subsequent treatment of the ester X with a catalytic amount of sodium methoxide in refluxing absolute methanol for six days gave essentially unchanged β-methyl ester.[10] These findings were so contrary to expectation that they seemed to cast doubt on the correctness of the assignment of the β-configuration to the original acid VII. However, an observation made by Dr. Arthur Lewis while working with a related series of compounds provided a technique for accomplishing the β → α conversion. Lewis had observed that a methyl ester which had obstinately resisted epimerization during prolonged boiling with sodium methoxide in methanol was efficiently epimerized *during subsequent hydrolysis* with aqueous alcohol sodium hydroxide! Since the original acid was completely stable to strong base, it must be concluded that inversion was so rapid under these conditions as to compete favorably with ester hydrolysis. It would appear that the conditions normally selected for ester saponification are particularly favorable for equilibration of the ester with its enolate anion.

With these results in mind, the (−)-β-methyl ester X was saponified with aqueous alcoholic potassium hydroxide. The acid obtained showed a broader and considerably lower melting point range (m.p. 30–35°) than the original acid (m.p. 83.0–83.5°), and several new bands made their appearance in the infrared spectrum. (These new absorption bands could also be detected, in much lower intensity, in the crude thionyl chloride "epimerization product" mentioned earlier.) Repeated esterification and saponification gave a sharper melting product (m.p. 30–32°) which might have been taken for the desired pure α-acid XI were it not for the retention in its infrared spectrum, in reduced intensity, of all of the bands characteristic of the starting material VII. Three further esterification–saponification cycles finally yielded pure (+)-5,5-dimethylbicyclo[2,1,1]hexane-2α-carboxylic acid (XI) (m.p. 55.0–55.5°) in 35% over-all yield. This procedure, obviously unsatisfactory for preparative work, could be greatly simplified. Refluxing the β-methyl ester X with three molar equivalents of sodium ethoxide (about the amount of base used in the saponification experiments) in absolute ethanol (to achieve a higher temperature than was obtained in methanol) for three days, followed by dilution with water and continued heating to effect hydrolysis, gave a 74% yield of epimerized acid XI in one experimental operation.

That the acid obtained in this way was simply the 2α-epimer, and not some more complex rearrangement product, was demonstrated by a vigorous oxidation using alkaline permanganate. Under these conditions, XI proved much more stable than its epimer VII, as might be expected because of the greatly increased steric hindrance to attack at the remaining hydrogen atom at C_2. Nevertheless, XI was oxidized to a small extent to (+)-5,5-dimethylbicyclo[2,1,1]hexane-2-one (IX), identical with the product obtained by oxidation of VII. It should be noted at this point that these epimerization studies not only provide a convenient source of the required starting material for syntheses in the 2α-series, but also serve to confirm the assignment of the β-configuration to VII, made earlier on more indirect evidence.[3]

The failure of the initial epimerization experiments would seem to find its simplest explanation in terms of the kinetic scheme outline below. In order to understand the slow attainment of equilibrium, it need only be assumed that the intermediate enolate anion XIV returns to the *less* stable β-ester X more readily than to the α-ester XV, *i.e.*, $k_{-1} > k_{-2}$. This seems to be entirely reasonable



on the basis of steric shielding of the β-side of XIV by the *gem*-dimethyl group, which would direct a proton donor to attack from the α-side. Experimental support for this suggestion is provided by the fact that the β-acid VII is formed preferentially from the corresponding ketene in its photolytic

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(8) The participation of Mr. John Emory Morris in this part of our work is acknowledged with pleasure.

(9) This technique, described by A. Burger and W. L. Yost, THIS JOURNAL, **70**, 2198 (1948), has also been employed successfully by E. N. Trachtenberg and G. Odian, *ibid.*, **80**, 4015 (1958).

(10) For a recent example of this type of procedure see G. W. Eigenmann and R. T. Arnold, *ibid.*, **81**, 3440 (1959).

synthesis. The *kinetic* preference of the enolate anion for return to the β-ester is easily reconciled with the thermodynamic preference for α-ester, which requires only that $(k_1k_{-2}/k_2k_{-1}) > 1$, as long as $k_1 >> k_2$. This would imply that enolization of the α-isomer is very much slower than that of the β-isomer, a conclusion which again finds a ready stereochemical rationalization in terms of relative hindrance to base attack at the C_2-proton. It is interesting to note that this type of "kinetic interference" with the attainment of equilibrium must be expected to be quite a general phenomenon, and to be one which would attain greater importance as the position of the equilibrium involved becomes more and more one-sided.[11]

Continuing with our synthetic objectives, the (+)-2α-acid XI was treated with methyllithium to give the (+)-methyl ketone XII. Bayer–Villiger oxidation[12] of XII, using trifluoroperacetic acid, gave a mixture of the expected acetate XIII and the corresponding trifluoroacetate. Reduction of this mixture with lithium aluminum hydride gave the expected (−)-2α-alcohol Id, free of 2β-epimer.

The (+)-2α-amine Ib was obtained in excellent yield by Schmidt degradation of XI. The product was shown to be free of the 2β-epimer by vapor phase chromatography. With this step complete, the way is opened for studies of the reactions of these simple, 2-substituted bicyclo[2,1,1]hexanes.

Acknowledgment.—The support of this work by a research grant from the National Science Foundation is acknowledged with pleasure.

Experimental

Melting points and boiling points are uncorrected. All optical rotations were taken in absolute ethanol unless otherwise stated. Microanalyses were performed by the Schwarzkopf Microanalytical Laboratory, Woodside 77, N.Y.

(+)-Nopinone (IV).[13]—A solution of 20.0 g. of (−)-β-pinene (III) in 180 ml. of absolute methanol was exhaustively ozonized at −70 to −80°. The ozonized solution was then added to a vigorously stirred mixture of 150 ml. of absolute methanol, 40 ml. of glacial acetic acid and 80 g. of sodium iodide. The resulting iodine colored solution was stirred for 4 hours and diluted with a liter of water. Sodium bisulfite was added until the color of the iodine disappeared; this was followed by the addition of sodium carbonate until the solution was basic. The reaction mixture was then extracted with 800 ml. of diethyl ether, and the ethereal extract was dried over anhydrous magnesium sulfate. The drying agent was removed by filtration and the solvent was distilled under reduced pressure. The residue was fractionally distilled to give 13.7 g. (67%) of IV, b.p. 83–86° (12 mm.), $n^{20}\text{D}$ 1.4802 (lit.[13] 1.4798), $[\alpha]^{25}\text{D}$ +18.4° (lit.[13] +18.5°).

(+)-Isonitrosonopinone (V).—Fifty grams of IV was added dropwise to a stirred solution of 15.75 g. of potassium in 500 ml. of purified *t*-butyl alcohol. This solution was cooled until the solvent began to crystallize, and was stirred for 20 minutes. The reaction mixture was then cooled to 0° and 44.50 g. of isoamyl nitrite was added, followed after an additional 20 minutes of stirring by 100 ml. of dry 30–60° petroleum ether. The resulting solution was stirred at 0° for 2.5 hours, diluted with 500 ml. of 30–60° petroleum ether, and extracted with 250 ml. of water. The aqueous layer was washed thoroughly with 30–60° petroleum ether, cooled to 0° and acidified with dilute hydrochloric acid. The precipitate which formed was collected by filtration and air-dried to give 50.02 g. of V, m.p. 172–174°. Extraction of the filtrate with ether yielded an additional 2.40 g. of product, giving an over-all yield of 52.42 g. (87%). Sublimation of the crude product gave analytically pure material, m.p. 175–176°, $[\alpha]^{25}\text{D}$ +27.5° (*c* 10.0), +27.9° (*c* 6.0).

Anal. Calcd. for $C_9H_{11}NO_2$: C, 64.65; H, 7.84; N, 8.38. Found: C, 64.74; H, 7.81; N, 8.27.

3-Diazonopinone (VI) was prepared as previously described[3] by treatment of the corresponding oximinoketone V with chloramine. Typical yields were in the range of 80–85%.

(−)-5,5-Dimethylbicyclo[2,1,1]hexane-2β-carboxylic Acid (VII).—The photochemical ring contraction of VI was carried out as described earlier[3] to give a product of m.p. 83.0–83.5°, $[\alpha]^{25}\text{D}$ −59.1° (*c* 9.0), −59.8° (*c* 16.1), in *ca.* 65% yield.

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.17; H, 8.97.

(−)-2β-Amino-5,5-dimethylbicyclo[2,1,1]hexane (Ia).—Five grams of VII was treated with sodium azide under the usual Schmidt reaction conditions,[3] giving 3.49 g. (86%) of pure 2β-amine Ia, b.p. 90–92° (71 mm.), $n^{25}\text{D}$ 1.4741, $[\alpha]^{25}\text{D}$ −31.7° (c 12.1), −31.2° (c 5.5). Because of the pronounced tendency of this amine to form a carbonate on exposure to the atmosphere, it was characterized as its *p*-nitrobenzamide, which was prepared in the usual way. Two recrystallizations from ethanol–water gave an analytical sample as fine, colorless needles, m.p. 128–129°.

Anal. Calcd. for $C_{15}H_{18}N_2O_3$: C, 65.67; H, 6.61; N, 10.21. Found: C, 65.90; H, 6.80; N, 10.15.

(+)-5,5-Dimethylbicyclo[2,1,1]hexan-2-one (IX) and (−)-5,5-Dimethylbicyclo[2,1,1]hexan-2α-ol-2β-carboxylic Acid (VIII).—The ring contracted acid VII was oxidized by the method previously developed[3] to give a 56% yield of VIII and a 29% yield of ketone IX, b.p. 91–92° (45 mm.), $n^{26}\text{D}$ 1.4608, $[\alpha]^{25}\text{D}$ + 120.2° (neat), +120.5° (*c* 1.8), d^{25} 0.957.

Anal. Calcd. for $C_8H_{12}O$: C, 77.37; H, 9.74. Found: C, 77.38; H, 9.90.

A 2,4-dinitrophenylhydrazone was prepared in the usual way. Three recrystallizations from ethanol gave long, yellow-orange needles, m.p. 155.5–156.0°.

Anal. Calcd. for $C_{14}H_{16}N_4O_4$: C, 55.25; H, 5.30; N, 18.41. Found: C, 55.50; H, 5.54; N, 18.62.

Two recrystallizations of the hydroxy acid VIII from benzene gave an analytical sample as fine, colorless needles, m.p. 107–108°, $[\alpha]^{25}\text{D}$ −61.0° (*c* 4.7), −61.7° (*c* 7.5). As previously described,[3] VIII could be oxidized to IX in 75% yield by treatment with sodium bismuthate.

Anal. Calcd. for $C_9H_{14}O_3$: C, 63.51; H, 8.29. Found: C, 63.77; H, 8.26.

(−)-5,5-Dimethylbicyclo[2,1,1]hexan-2β-ol (Ic).—A solution of 2.00 g. of IX in 25 ml. of anhydrous ether was added dropwise to a stirred suspension of 0.45 g. of lithium aluminum hydride in 10 ml. of anhydrous ether at 0°. After stirring for 1.5 hours at 0°, the mixture was hydrolyzed by dropwise addition of 1.80 g. of water. The reaction mixture was filtered and the ethereal solution was dried over anhydrous magnesium sulfate. After filtration to remove the drying agent, the solvent was distilled under reduced pressure and the residue fractionally distilled to give 1.96 g. (97%) of the expected alcohol Ic, b.p. 91–92° (24 mm.), m.p. 20–21°, $n^{26}\text{D}$ 1.4759, $[\alpha]^{25}\text{D}$ −8.66° (neat), −7.7° (*c* 10), d^{25} 0.954.

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[11] An alternative view of the slow epimerization might be that the initial enolization of X is unusually slow. This assumption seems unlikely, however, since no special factors leading to resistance to enolization are apparent. In fact, the presence of the *gem*-dimethyl group at C_5 might be expected to provide steric acceleration to this enolization, which would reduce the non-bonded interactions between the C_2 and C_5 substituents. An isotope exchange experiment would provide a ready distinction between these two possibilities.

[12] The Bayer–Villiger oxidation is well known to proceed with retention of configuration. For a leading reference see C. H. Hassall in R. Adams, "Organic Reactions," Vol. 9, John Wiley and Sons, Inc., New York, N. Y., 1957, pp. 73–106.

[13] For a convenient review of the absolute configurations of terpenes, see A. J. Birch. *Ann. Rep.*, **47**, 191 (1950). The formulas used in this paper correspond to the correct absolute configurations, based on the known correspondence of (−)-β-pinene to (−)-α-pinene (see "Elsevier's Encyclopedia of Organic Chemistry," Vol. 12A, Elsevier Publishing Co., Inc., New York, N. Y., 1948, pp. 454, 455, 467 and 510).

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.28; H, 11.03.

A *p*-nitrobenzoate was prepared in the usual way. Two recrystallizations from ethanol gave long, colorless needles, m.p. 87.0–87.5°.

Anal. Calcd. for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.68; H, 6.49; N, 5.07.

Reduction of 5,5-Dimethylbicyclo[2,1,1]hexan-2-one with Sodium and Alcohol.—The reaction of 0.96 g. of IX in 15 ml. of 95% ethanol with 1.85 g. of sodium over a 3-hour period gave 0.64 g. (67%) of product, b.p. 91–92° (23 mm.). This product was shown by vapor phase chromatography to be a mixture of 35% β-alcohol Ic and 65% α-alcohol Id.

Attempted Epimerization of 5,5-Dimethylbicyclo[2,1,1]-hexan-2β-ol with Aluminum Isopropoxide.—Treatment of Ic with aluminum isopropoxide in anhydrous isopropyl alcohol containing 1% acetone for 8 days at reflux temperatures gave a 75% yield of a mixture of the epimeric alcohols which was shown by vapor phase chromatography to be only 45% epimerized.

(–)-5,5-Dimethylbicyclo[2,1,1]hexane-2β-carboxylic Acid Methyl Ester (X).—An ethereal solution of diazomethane was added dropwise to an ethereal solution of 10.00 g. of VII until the color of the diazomethane persisted. The reaction mixture was dried over anhydrous magnesium sulfate, filtered, and the solvent removed on a flash evaporator. The residue was fractionally distilled to give 10.47 g. (96%) of X, b.p. 90–91° (15 mm), $n^{24}\mathrm{D}$ 1.4611, $[\alpha]^{25}\mathrm{D}$ –61.5° (*c* 8.5), –61.6° (*c* 11.1).

Anal. Calcd. for $C_{10}H_{16}O_2$: C, 71.39; H, 9.59. Found: C, 71.17; H, 9.77.

The (+)-5,5-Dimethylbicyclo[2,1,1]hexane-2α-carboxylic Acid (XI).—To a solution of 5.00 g. of sodium in 150 ml. of freshly prepared absolute ethanol was added 10.31 g. of X. This solution was refluxed for 64 hours; 75 ml. of water was added dropwise and the resulting solution was refluxed for 6 hours. The reaction mixture was diluted with an additional 75 ml. of water and thoroughly extracted with ether. The aqueous solution was acidified with diluted hydrochloric acid and the white precipitate which formed was collected by filtration and air-dried. The crude product weighed 6.99 g. (74%), m.p. 54–55°. Sublimation gave an analytical sample, m.p. 55.0–55.5°, $[\alpha]^{25}\mathrm{D}$ +2.4 (*c* 6.2).

Anal. Calcd. for $C_9H_{14}O_2$: C, 70.10; H, 9.15. Found: C, 70.24; H, 9.11.

Oxidation of (+)-5,5-Dimethylbicyclo[2,1,1]hexane-2α-carboxylic Acid (XI).—In a preliminary experiment, 1 g. of XI was treated with 1.75 g. of potassium permanganate and 4.50 g. of potassium hydroxide in 14 ml. of water. This solution was covered with 12.5 ml. of 60–70° petroleum ether and stirred vigorously in a closed system at 50–55° for 25 hours. This reaction mixture was cooled and diluted. The excess potassium permanganate was destroyed with sulfur dioxide. The precipitated manganese dioxide was removed by filtration and the layers were separated.

On acidification with dilute hydrochloric acid, the aqueous layer gave 0.76 g. of the starting acid XI.

The organic layer was dried over anhydrous magnesium sulfate, filtered, and the solvent removed to give a residue which on fractional distillation gave 90 mg. of ketone, b.p. 90–91°, (45 mm.), infrared spectrum identical to that of IX. A 2,4-dinitrophenylhydrazone (m.p. 151–154°) was prepared, which gave no depression on mixed melting with the derivative of the authentic ketone IX (m.m.p. 152–154°).

(+)-2α-Acetyl-5,5-dimethylbicyclo[2,1,1]hexane (XII).—Methyllithium was prepared by adding 11.0 g. of methyl iodide in 35 ml. of anhydrous ether to a stirred suspension of 1.58 g. of lithium ribbon in 35 ml. of anhydrous ether at a rate necessary to maintain mild refluxing.

The resultant solution of methyllithium was added dropwise to a stirred solution of 3.0 g. of XI in 40 ml. of anhydrous ether, the addition taking one hour. After stirring an additional hour, the reaction mixture was poured into 75 g. of crushed ice. The ethereal solution was removed, dried over anhydrous magnesium sulfate, filtered and the solvent removed under reduced pressure. The residue was fractionally distilled to give 2.75 g. of crude XII, estimated on the basis of gas-chromatographic analysis to contain 1.97 g. (67% over-all yield) of the desired ketone. This material was chromatographed on neutral alumina to remove the small amount of alcoholic product, and redistilled to give an analytical sample of XII, b.p. 90–91° (15 mm.), $n^{25}\mathrm{D}$ 1.4651, $[\alpha]^{25}\mathrm{D}$ +38.7° (*c* 4.1).

Anal. Calcd. for $C_{10}H_{16}O$: C, 78.89; H, 10.59. Found: C, 78.93; H, 10.45.

(–)-5,5-Dimethylbicyclo[2,1,1]hexan-2α-ol (Id).—A solution of trifluoroperacetic acid was prepared by mixing 1.7 ml. of trifluoroacetic anhydride with 0.26 ml. of 90% hydrogen peroxide in 3.3 ml. of methylene chloride.[14]

The resulting peracid solution was added dropwise to a stirred solution of 0.80 g. of XII, 3.90 g. of anhydrous dibasic sodium phosphate and 10 ml. of methylene chloride. The reaction mixture was refluxed for 1.5 hours, filtered, and the inorganic salts washed thoroughly with methylene chloride. The filtrate was dried over anhydrous magnesium sulfate, filtered and the solvent distilled off. Infrared analysis of the residue indicated that only about 60% of the ketone had been converted to the acetate.

The total reaction product was recycled by dissolving it in 10 ml. of methylene chloride to which 3.90 g. of anhydrous dibasic sodium phosphate had been added. The trifluoroperacetic acid obtained from 2.32 ml. of trifluoroacetic anhydride, 0.40 ml. of 90% hydrogen peroxide and 2.2 ml. of methylene chloride was added dropwise. Refluxing was maintained for 6.5 hours. The solution was cooled, filtered and the filter cake washed thoroughly with solvent. The solution was dried over anhydrous magnesium sulfate, filtered, and the solvent distilled off to give 0.80 g. of acetate (containing some trifluoroacetate, as indicated by infrared absorption at 5.60 μ as well as 5.78 μ).

The crude acetate was dissolved in 7 ml. of anhydrous ether and added dropwise to a stirred suspension of 0.80 g. of lithium aluminum hydride in 20 ml. of anhydrous ether. After stirring at room temperature for 5 hours, the reaction mixture was cooled to 0° and quenched by the dropwise addition of 3.20 g. of water. The hydrolyzed mixture was stirred for 0.5 hour and the precipitated salts were removed by filtration. The salts were washed thoroughly with anhydrous ether and the combined filtrates were dried over anhydrous magnesium sulfate. The drying agent was removed by filtration and the solvent was evaporated under reduced pressure to give a colorless liquid which on distillation gave 0.46 g. of Id (70% based on XII), b.p. 96–97° (25 mm.), $n^{25}\mathrm{D}$ 1.4739, $[\alpha]^{25}\mathrm{D}$ –3.0° (*c* 2.1).

Anal. Calcd. for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.29; H, 11.19.

A *p*-nitrobenzoate was prepared in pyridine solution. Two recrystallizations from ethanol–water gave an analytical sample, m.p. 77.0–77.5°.

Anal. Calcd. for $C_{15}H_{17}NO_4$: C, 65.44; H, 6.22; N, 5.09. Found: C, 65.41; H, 6.44; N, 4.82.

(+)-2α-Amino-5,5-dimethylbicyclo[2,1,1]hexane (Ib).—Finely powdered sodium azide (5.25 g.) was added in small portions to a vigorously stirred dispersion of 3.60 g. of XI, 75 ml. of concentrated sulfuric acid and 180 ml. of chloroform. During the addition, which took 0.5 hour, the temperature of the reaction mixture was maintained at 45–50°. After stirring for an additional 2 hours, the acid solution was diluted by the careful addition of ice, made basic with aqueous sodium hydroxide (while keeping the temperature below 25°) and extracted with chloroform. The chloroform solution was thoroughly extracted with dilute hydrochloric acid solution which in turn was made basic with dilute sodium hydroxide solution. The alkaline reaction mixture was extracted with ether and the ethereal solution dried over potassium hydroxide pellets. After standing overnight, the ether layer was decanted and the ether removed under reduced pressure. Fractional distillation of the remaining liquid produced 2.77 g. (95%) of the α-amine Ib, b.p. 93–94° (70 mm.), $n^{25}\mathrm{D}$ 1.4738, $[\alpha]^{25}\mathrm{D}$ +13.7° (*c* 8.6). Due to rapid formation of a carbonate, the amine itself was not analyzed.

A *p*-nitrobenzamide was prepared in pyridine–benzene solution. Two recrystallizations from ethanol-water gave small, colorless plates, m.p. 143.0–143.5°.

Anal. Calcd. for $C_{15}H_{18}N_2O_3$: C, 65.67; H, 6.61; N, 10.21. Found: C, 65.64; H, 6.58; N, 10.48.

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[14] W. D. Emmons and G. B. Lucas, THIS JOURNAL, **77**, 2287 (1955).

Vapor Phase Chromatography.—Gas chromatography was carried out using a standard Perkin–Elmer vapor fractometer model 154 B equipped with a $^1/_4'' \times 6'$ aluminum column packed with 0.5% polyethylene glycol 400 on glass beads. Helium was used as carrier gas, flowing at a rate of 50 cc. per minute. The results are tabulated below. The resolution in the cases of epimeric pairs of compounds was quite good.

Compound	Column temp., °C.	Retention time, min.	Purity
Ia	112	2.90	>99.5%
Ib	112	3.75	>99.5%
Ic	125	6.00	No detectable impurity
Id	125	6.65	No detectable impurity
XII	143	3.00	No detectable impurity

[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF CALIFORNIA AT LOS ANGELES]

Neighboring Carbon and Hydrogen. XXXIV. Interaction of Non-conjugated Chromophores[1]

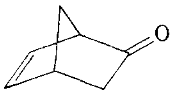
BY C. F. WILCOX, JR.,[2] S. WINSTEIN AND W. G. McMILLAN

RECEIVED AUGUST 3, 1959

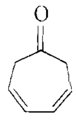
Three of the common semi-empirical wave-mechanical methods have been applied to the problem of interaction of non-conjugated chromophores in bicycloheptadiene and bicyclooctatriene. The simple LCAO model, as well as the more refined models of Pariser and Parr and Longuet-Higgins, agree in describing the ground state of bicycloheptadiene as the classical Kekulé structure, the predicted delocalization energy being zero. Similarly, bicyclooctatriene is predicted to have no homoconjugative stabilization. Bicycloheptadiene shows ultraviolet absorption at longer wave length than does bicycloheptene, the shift being accounted for almost quantitatively by the two refined models, and only poorly by the simple LCAO model.

It is known that π-electron systems situated beta to a developing carbonium ion center can significantly influence the course and rate of reaction.[3] This anchimeric acceleration of rate has been ascribed to delocalization of the electron cloud of the neighboring π-electron substituent in the rate-determining step and calculations with the simple LCAO model lead to stabilization energies in accord with experiment and also indicate the geometrical factors leading to maximum interaction.[4]

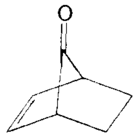
Another somewhat analogous[3d,4] manifestation of π-electron interaction is the modification of characteristic ultraviolet absorption spectra by neighboring π-electron systems.[5] The consequences of this interaction are not readily predictable. In some cases, *e.g.*, the $n \rightarrow \pi^*$ carbonyl band of bicycloheptene-5-one (I),[6] the characteristic absorption is shifted to longer wave lengths and in other cases, *e.g.*, the carbonyl band of cyclohepta-1,3-diene-6-one (II),[7] the wave length remains unchanged and the intensity increases. A hypsochromic shift of the carbonyl band has been observed with bicycloheptene-7-one (III).[8]



I

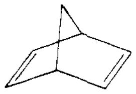


II

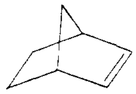


III

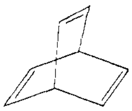
The alterations of the characteristic spectra of rigid bicyclic systems with non-adjacent but interacting chromophores have not received explicit theoretical treatment.[8a] In the present paper, an attempt has been made to apply three of the common semi-empirical methods to this problem of non-adjacent chromophores using bicycloheptadiene (IV) and bicycloheptene (V) as a model system. The predicted absorption spectrum of the unknown bicyclooctatriene (VI) is also presented.



IV



V



VI

Results.—In contrast with the intense ultraviolet absorption of bicycloheptene (V) at 195 mμ and butadiene at 210 mμ, bicycloheptadiene (IV) in ethanol has weak peaks at 205 mμ (ϵ 2,100), 214 mμ (ϵ 1,480), 220 mμ (ϵ 870) and a shoulder at 230 mμ (ϵ 200). These three peaks were not sharp but their definition was enhanced when the solution was cooled to 3°. In the vapor, bicycloheptadiene showed considerable fine structure (see Table I) with no less than 17 sharp bands from 226 to 199 mμ. The energy spacing of these bands was constant at 381 cm.$^{-1}$ within experimental error. There was some indication of higher energy spacing, but its definition was lost in the maze of sharply rising peaks. At wave lengths below 198 mμ the absorption increased sharply.

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[1] We are indebted to the late Martin Shatavsky for preliminary work, in 1951, on the ultraviolet and infrared spectra of bicycloheptadiene and the isolation of the 1:2 diene-silver nitrate complex from addition of diene to concentrated aqueous silver nitrate. The 1:1 complex has recently been reported by J. G. Traynham and J. R. Olechowski [THIS JOURNAL, **81**, 571 (1959)] from addition of diene to 1 *M* silver nitrate.

[2] National Science Foundation Predoctoral Fellow, 1952–1953, 1954–1955.

[3] *E.g.*, (a) S. Winstein and R. Adams, THIS JOURNAL, **70**, 838 (1948); (b) S. Winstein and A. H. Schlesinger, *ibid.*, **70**, 3528 (1948); (c) S. Winstein, H. M. Walborsky and K. C. Schreiber, *ibid.*, **72**, 5795 (1950); (d) S. Winstein, M. Brown, K. C. Schreiber and A. H. Schlesinger, *ibid.*, **74**, 1140 (1952); (e) S. Winstein, M. Shatavsky, C. Norton and R. B. Woodward, *ibid.*, **77**, 4183 (1955); (f) S. Winstein and M. Shatavsky, *ibid.*, **78**, 592 (1956).

[4] M. Simonetta and S. Winstein, *ibid.*, **76**, 18 (1954).

[5] *E.g.*, P. D. Bartlett and E. S. Lewis, *ibid.*, **72**, 1005 (1950); E. A. Braude, *et al.*, *J. Chem. Soc.*, 607, 1902 (1949).

[6] P. D. Bartlett and B. E. Tate, THIS JOURNAL, **78**, 2473 (1956).

[7] J. Meinwald, S. L. Emerman, N. C. Yang and G. Büchi, *ibid.*, **77**, 4401 (1955).

[8] C. J. Norton, Ph.D. Dissertation, Harvard Univ., 1955.

[8a] NOTE ADDED IN PROOF.—A very recent exception is the paper by H. Labhart and G. Wagnière [*Helv. Chim. Acta*, **42**, 2219 (1959)] who have given a simplified treatment of β,γ-unsaturated ketones such as I.