[CONTRIBUTION FROM THE WHITMORE LABORATORY OF THE COLLEGE OF CHEMISTRY AND PHYSICS, THE PENNSYLVANIA STATE UNIVERSITY]

The Synthesis and Dehydration of 7-Hydroxyspiro[5.6]dodecane, a Neopentyl System

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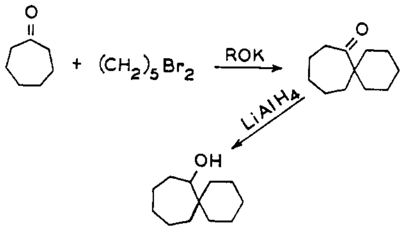
Rearrangements of α-hydroxyspiranols must lead to changes in ring size. The preparation of 7-hydroxyspiro[5.6]dodecane has been improved and its dehydration with four typical dehydration catalysts has been studied. In all cases the two major products were shown to be cyclohexylcyclohexene and spiro[5.6]-7-dodecene (or a position isomer thereof). Conformational analysis suggests that the course of the reaction is determined solely on steric grounds and that it can be rationalized by a comparison of the free energies of the various transition states.

Dehydrations of α-hydroxyspiranes are of interest for two reasons. First, these spiranols are unique in that they contain neopentyl systems which are completely incorporated into two fused alicyclic rings. Any rearrangements which occur must therefore result in changes of ring size. Consequently, dehydrations of these systems, unlike aliphatic neopentyl alcohols, afford an opportunity to study the effect of ring size and conformation of the resulting rearrangements. Second, the rearrangements of these compounds might provide new synthetic routes to otherwise difficultly obtainable fused ring systems. The few studies which have been made have been briefly reviewed.[3]

The dehydration of 7-hydroxyspiro[5.6]dodecane (I) has previously been attempted by Jacquier and Christol[4] and Christol, Jacquier, and Mousseron.[5] These workers treated the spiranol with polyphosphoric acid and obtained only a small amount of cyclohexylcyclohexene (IX) and unchanged alcohol. In addition, the spiranol was reported to be unaffected by twice its weight of zinc chloride at 140°. In contrast to these observations, Laber[6] has reported that the spiranol I is easily dehydrated by zinc chloride, giving an 80% yield of IX. Because of these surprising results and because of the aforementioned possible application of the dehydrations of such spiranols to the synthesis of otherwise difficultly obtainable fused ring systems, it appeared desirable to study the preparation and dehydration of 7-hydroxyspiro[5.6]dodecane.

The spiranol was prepared as follows:



I

7-Ketospiro[5.6]dodecane was prepared in approximately 45% yield by a modification of the method of Mousseron.[7] However, the spiranone could not be purified by fractional distillation. Analysis of the middle fractions by both infrared spectrophotometry and vapor phase chromatography indicated that olefinic and ketonic impurities on the order of 15–20% were present. Attempts to isolate and characterize these impurities were unsuccessful due to the complexity of the reaction product.

The crude ketone was purified both by elution chromatography and by regeneration from the semicarbazone (45% yield). The latter method proved to be the more convenient for the purification of large amounts of the crude ketone. Even though the semicarbazone could not be obtained in high purity because of contamination by isomeric ketones, the regenerated material was easily purified by fractional distillation. This purification technique, together with modifications described in the Experimental, constitute what is probably the best available procedure for the preparation of this compound.

The crude ketone was reduced directly to the desired spiranol with lithium aluminum hydride. Only 28.4% of high purity spiranol was obtained, the remainder being contaminated by olefinic impurities.

The spiranol was dehydrated using four catalysts: anhydrous alumina, concentrated sulfuric acid, zinc chloride, and boron trifluoride etherate. The olefins were distilled and analyzed by vapor phase chromatography. The results are summarized in Table I.

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(2) Taken in part from the dissertation submitted by P. A. Naro in partial fulfillment of the requirements for the Ph.D. degree at The Pennsylvania State University.

(3) P. A. Naro and J. A. Dixon, *J. Am. Chem. Soc.*, **81**, 1681 (1959).

(4) R. Jacquier and H. Christol, *Bull. soc. chim. France*, 556 (1954).

(5) H. Christol, R. Jacquier, and M. Mousseron, *Bull. soc. chim. France*, 346 (1957).

(6) G. Laber, *Ann.*, **588**, 79 (1954).

(7) M. Mousseron, R. Jacquier, and H. Christol, *Bull. soc. chim. France*, 346 (1957).

TABLE I

RESULTS OF THE DEHYDRATIONS OF 7-HYDROXYSPIRO[5.6]DODECANE

		Percentage Yield				
Catalyst	Reaction Temp.	Olefin product	Component A, cyclohexyl-cyclohexene	Component B, spiro[5.6]-7-dodecene (VIII)	Component C	Other
Boron trifluoride	25	90	83.4	14.2	1.0	1.4
Sulfuric acid	100	92	61.3	37.9	0.8	0
Zinc chloride	130	93	77.7	21.5	0	0.8
Alumina	350	84	51.1	42.9	4.7	1.3

The olefins from these dehydrations could not be separated by fractional distillation. However, A and B, the two main components, were isolated in high purity in a preparatory vapor-phase chromatography apparatus similar to one described by Anderson.[8]

Component A was the principal product in all of the dehydrations. It was found to be identical in all respects to an authentic sample of cyclohexylcyclohexene prepared by the method of Signaigo and Cramer.[9]

Component B, the only other major component, was hydrogenated to a compound whose infrared spectrum was identical to that of spiro[5.6]dodecane, prepared by Wolff-Kishner reduction of the corresponding ketone. The olefin was therefore spiro[5.6]-7-dodecene (VIII) or a position isomer thereof.

Component C could not be isolated and was therefore not identified. Laber,[6] who also dehydrated the spiranol I, observed a transitory blue color while preparing the nitrosochloride of his product. He attributed this color to the presence of traces of bicyclo[0.5.5]-1(7)-dodecene (VI). Although a blue color was also noted in this research, the same effect was observed when the nitrosochloride of pure cyclohexylcyclohexene was prepared. There is therefore no real evidence that component C might be VI.

Trace amounts of other components of shorter retention times were sometimes observed in the chromatography traces but these could not be isolated or identified.

The products and intermediates which might reasonably be expected from the dehydration are illustrated in Fig. 1. The fact that only two major products were actually found suggested that the transition state conformation of the spiranol might be important. Accordingly, the relative energies of the axial and equatorial isomers of the spiranol in all of its four possible ring conformations have been estimated. Results indicate that the hydroxyl group in the axial isomer is not always more hindered than the equatorial since the latter encounter skew interactions with the cyclohexane ring. In all cases the energy differences between the two were within the range 0.8–2.4 kcal. Such a small energy difference will not be important in determining the course of a reaction provided that the barrier to interconversion is small compared to the energy of activation.

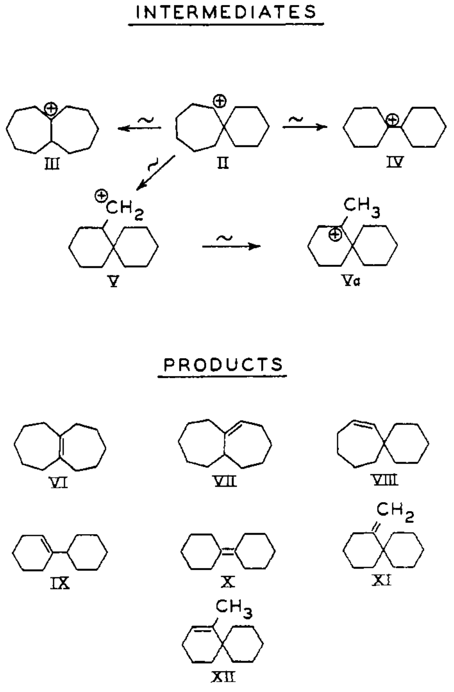

Figure 1

Examination of molecular models suggests that at least two transition states are possible for each isomer (Fig. 2). Thus, the axial may yield A and B while the equatorial may lead to C and D. (In these figures the rear atom is the C_7-atom and the R-groups refer to the rest of the ring involved.) Transition state C generates the unlikely intermediate V which involves a change from a secondary carbonium ion to a primary one. State A, which leads to VIII, would therefore be expected to predominate. On the other hand, any energy differences between B and D are not immediately obvious. Although both would lead to intermediates involving tertiary carbonium ions,

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[8] B. C. Anderson, E. I. du Pont de Nemours and Company, private communication.

[9] F. K. Signaigo and P. L. Cramer, *J. Am. Chem. Soc.*, 55, 3326 (1933).

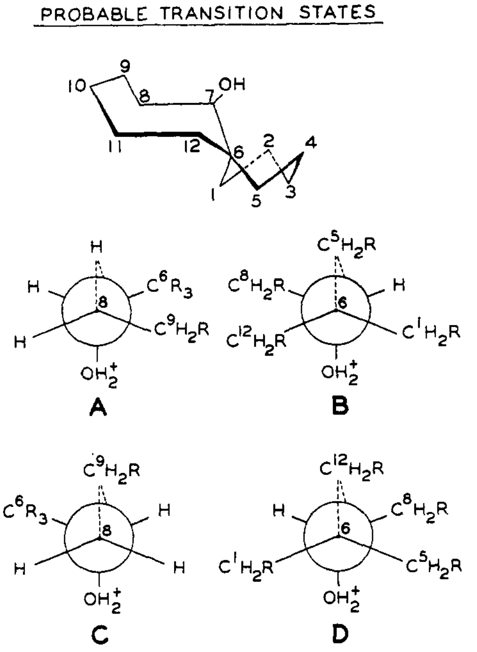

FIGURE 2

the intermediate generated by B (III) would be much less stable than that generated by D (IV) because of the great distortion of the two seven-membered rings caused by the necessary planar sp^2 state of the bridgehead atom. Because of this strain, transition state D would be expected to predominate and to yield cyclohexylcyclohexene (IX), which is observed.

In view of the foregoing it is not surprising that the predominant products in the dehydration are VIII and IX. However, it is interesting to note that the product distribution in the sulfuric acid-catalyzed dehydration very closely approaches that found in the alumina dehydration. In a previous study[3] involving the dehydration of 6-hydroxyspiro[4.5]decane, no normal product was found in the sulfuric acid-catalyzed dehydration while the use of alumina gave 42% of the normal olefin. As the same experimental techniques were used in both studies, the results suggest that for 6-hydroxyspiro[4.5]decane the transition state free energy for the axial isomer is less than that of the equatorial isomer ($F^{\ddagger}_{ax} < F^{\ddagger}_{eq}$), while for the present case the reverse is true ($F^{\ddagger}_{eq} \leqq F^{\ddagger}_{ax}$).

It is noteworthy that the dehydrations of both 7-hydroxyspiro[5.6]dodecane and 6-hydroxyspiro-[4.5]decane[3] represent examples of reaction courses determined purely on steric grounds. Further work is planned in which it will be determined whether or not these reaction courses are sensitive to temperature.

EXPERIMENTAL[10]

Preparation of 7-ketospiro[5.6]dodecane. Into a carefully dried, nitrogen-filled flask equipped with a stirrer and condenser were placed 1 kg. (13.5 moles) of anhydrous *t*-butyl alcohol and 82.1 g. (2.1 moles) of potassium.[11] The mixture was stirred for 8 hr. under nitrogen and the resulting clear water-white solution was distilled to dryness under reduced pressure. To the resulting white salt were added 2 l. of anhydrous toluene, 112 g. (1 mole) of cycloheptanone, and 230 g. (1 mole) of 1,5-dibromopentane. The mixture was refluxed for 73 hr. The resulting brown solution was treated with 200 ml. of water and 400 ml. of a 10% hydrochloric acid solution and cooled to room temperature. The organic layer was separated and the aqueous layer extracted three times with ether. The original layer and the extracts were combined, washed with 5% sodium bicarbonate solution, and dried over anhydrous sodium sulfate. Removal of the ether followed by distillation of the dark residue yielded 133 g. of crude product, b.p. 83° (3 mm.), n_D^{25} 1.4749–1.4880. Attempts to purify the crude spiranone by fractional distillation through a spinning band column[12] were unsuccessful. Fortunately, the crude product could be used directly in the synthesis of 7-hydroxyspiro[5.6]dodecane as described below.

Analyses of the crude ketone by vapor phase chromatography and by infrared spectroscopy indicated that it contained 15–20% of olefinic impurities. The material was purified by regeneration from the semicarbazone. From 250 g. of the crude product there was obtained 161 g. (47%) of the semicarbazone, m.p. 186–204°. All attempts to purify the derivative further by recrystallization failed. Hydrolysis with 10% hydrochloric acid followed by fractional distillation yielded 112.1 g. (96%) of high purity spiranone, b.p. 100° (2.3 mm.), n_D^{25} 1.4922, n_D^{20} 1.4939, d_4^{20} 0.9897, M_D 53.25 (calcd.), 53.02 (found).

The 2,4-dinitrophenylhydrazone was prepared in the usual way,[13a] m.p. 117–118°.

Anal. Calcd. for $C_{18}H_{24}N_4O_4$: N, 15.55. Found: N, 15.54.

Preparation of 7-Hydroxyspiro[5.6]dodecane. A solution of 105 g. of crude 7-ketospiro[5.6]dodecane in 500 ml. of anhydrous ether was slowly added to a refluxing slurry of 11.0 g. (0.29 mole) of lithium aluminum hydride in 1 l. of anhydrous ether (nitrogen atmosphere). After addition was complete the mixture was refluxed for 1 hr. and the excess hydride was decomposed by dropwise addition of 58.2 g. (0.61 mole) of ethyl acetate. The resulting mixture was hydrolyzed with 10% sodium hydroxide solution and the ethereal solution was decanted. The solid residue was extracted three times with ether and the combined material was dried over anhydrous sodium sulfate. Removal of the ether followed by fractional distillation of the residue through a spinning band column[12] yielded 29.8 g. (28.4%) of high purity spiranol, b.p. 151° (20 mm.), n_D^{25} 1.5082, n_D^{20} 1.5103, d_4^{20} 1.0059, M_D 54.77 (calcd.), 54.23 (found). The 3,5-dinitrobenzoate was prepared,[13b] m.p. 104.3–105.2°.

Anal. Calcd. for $C_{12}H_{22}O$: C, 79.06; H, 12.17. Found: C, 78.63; H, 11.90.

Dehydration over alumina. The apparatus used consisted of a horizontal 36-inch, 30 mm. i.d. Pyrex tube with three separately controlled heating sections. The alumina (4–8 mesh, Alorco) was activated by heating overnight at 450° in a stream of nitrogen. The spiranol (20 g., 0.11 mole) was added to the tube at a rate of about 20 drops/min. while maintaining the three sections at 250, 300, and 350°,

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[10] All melting points are uncorrected. Microanalyses were performed by Galbraith Microanalytical Laboratories, Knoxville, Tenn.

[11] W. S. Johnson and G. H. Daub, *Organic Reactions*, Wiley, New York, 1951, Vol. VI, p. 42.

[12] This column is manufactured by the Nester-Faust Co., Exton, Pa. The packed section is 36 inches long with an internal diameter of 11 mm. The band is a spiral of 300 mesh stainless steel screen.

[13a] R. L. Shriner and R. C. Fuson, *Identification of Organic Compounds*, Wiley, New York, 1954, p. 171. (b) p. 165.

respectively. After all of the material had been added to the tube, a slow stream of nitrogen was passed through to sweep out any remaining olefins and water. A total of 17.6 g. (88%) of material was collected. The remainder of the products remained on the alumina as a black deposit. The organic material was taken up in ether and dried over anhydrous copper sulfate. Distillation yielded 15.2 g. (84%) of olefins, b.p. 40–43° (0.2 mm.), n_D^{25} 1.4955.

Dehydration with sulfuric acid. A solution of 5.00 g. (0.027 mole) of 7-hydroxyspiro[5.6]dodecane and 1 drop of concentrated sulfuric acid was heated to 100°, at which point the olefins and water distilled. The distillate was taken up in ether and dried over anhydrous copper sulfate. The ether and then the olefins were distilled to yield 4.13 g. (92%) of product, b.p. 50–60° (0.5 mm.), n_D^{25} 1.4948.

The nitroso chloride[3] was prepared and crystallized as pale blue crystals, but three recrystallizations from large volumes of acetone yielded only white needles, m.p. 141.5–142.5°. A mixed melting point taken with a sample of the nitroso chloride of cyclohexylcyclohexene, prepared by the method of Signaigo and Cramer,[9] was not depressed.

Dehydration with zinc chloride. A mixture of 5.00 g. (0.037 mole) of freshly fused zinc chloride and 5.00 g. (0.027 mole) of 7-hydroxyspiro[5.6]dodecane was heated at 135° for 1 hr. at 130 mm. pressure. The resulting paste was treated with 5 ml. of water and extracted three times with ether. The combined extracts were dried over anhydrous copper sulfate and distilled to yield 4.20 g. (93%) of olefin product, b.p. 78–80° (1 mm.), n_D^{25} 1.4942.

Dehydration with boron trifluoride etherate. A solution of 5.00 g. (0.027 mole) of 7-hydroxyspiro[5.6]dodecane and 10 ml. of boron trifluoride etherate was stirred at room temperature for 4.5 hr. The reaction mixture was treated with 50 ml. of water and the yellow upper layer was separated. The aqueous layer was extracted three times with hexane and the combined material was washed with dilute bicarbonate solution and dried over anhydrous copper sulfate. Distillation yielded 1.20 g. (25.2%) of unchanged spiranol and 3.00 g. (90%, based on spiranol actually dehydrated) of olefins, b.p. 70–80° (1 mm.), n_D^{25} 1.4941.

Analyses. All olefin analyses were made in an Aerograph instrument[14] at 150° using a helium flow rate of 90 ml./min. The column consisted of a 12-foot length of 0.25-inch o.d. copper tubing packed with 30% 1,2,3-tris(β-cyanoethoxy)-propane[15] on 30–60 mesh firebrick. This absorbent, suggested by Anderson,[8] had excellent selectivity for these olefin mixtures.

Acknowledgment. The authors express their appreciation to the American Petroleum Institute and to the Esso Research and Engineering Company for the funds which helped to support this research.

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[14] Obtained from Wilkens Instrument and Research, Inc., Berkeley, Calif.

[15] H. A. Bruson and T. W. Reiner, *J. Am. Chem. Soc.*, **65**, 27 (1943); H. A. Bruson, U. S. Patent 2,401,607 (*Chem. Abstr.*, **40**, 5450 (1946)).

[CONTRIBUTION FROM THE NAVAL STORES RESEARCH STATION[1]]

The Thermal Isomerization of Palustric Acid

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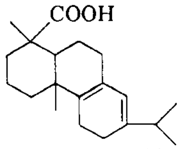
The thermal isomerization of palustric acid was studied at 170 and 200°. Spectrographic and chromatographic examination of the isomerizates showed that abietic and neoabietic acid accounted for all of the detectable products. The formation of abietic acid was favored in this isomerization over the formation of neoabietic acid. The isomerization was found to be a first-order reaction with respect to the palustric acid. Palustric acid was shown to be more stable to heat than levopimaric acid and less stable than neoabietic acid. Methyl palustrate underwent only a slight change on prolonged heating at 200°.

A series of thermal and acid isomerizations was started in this Laboratory on the abietic-type acids in oleoresin and rosin—namely, levopimaric acid,[2,3] neoabietic acid,[4] and palustric acid. Palustric acid, the most recently isolated acid, is one of the major constituents of pine oleoresin and rosin[5]. The structure of this acid was recently established by Schuller, *et al.*[6]:



Palustric acid

This paper describes a study of the thermal isomerization of pure palustric acid at 170 and 200°. Samples of palustric acid were heated in sealed evacuated tubes over a period of twenty-four hours and the progress of the isomerization followed by obtaining the specific rotation, ultraviolet absorption spectrum and chromatographic analysis of each sample. At both temperatures the isomerization product seemed to approach an equilibrium mixture of approximately 13% palustric acid, 80% abietic acid, and 7% neoabietic acid. Palustric acid has a half-life of about four hours at 170°.

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[1] One of the laboratories of the Southern Utilization Research and Development Division, Agricultural Research Service, U. S. Department of Agriculture.

[2] V. M. Loeblich, D. E. Baldwin, R. T. O'Connor, and R. V. Lawrence, *J. Am. Chem. Soc.*, **77**, 6311 (1955).

[3] D. E. Baldwin, V. M. Loeblich, and R. V. Lawrence, *J. Am. Chem. Soc.*, **78**, 2015 (1956).

[4] V. M. Loeblich and R. V. Lawrence, *J. Am. Chem.*, **79**, 1497 (1957).

[5] V. M. Loeblich, D. E. Baldwin, and R. V. Lawrence, *J. Am. Chem. Soc.*, **77**, 2823 (1955).

[6] W. H. Schuller, R. N. Moore, and R. V. Lawrence, *J. Am. Chem. Soc.*, **82**, 1734 (1960).