The Mechanism of the Prins Reaction. III. The Acetolysis of Arenesulfonates of *anti*-3-Oxabicyclo[3.3.1]nonan-9-ol and *trans*-6-Hydroxy-*cis*-3-oxabicyclo[4.3.0]nonane[1]

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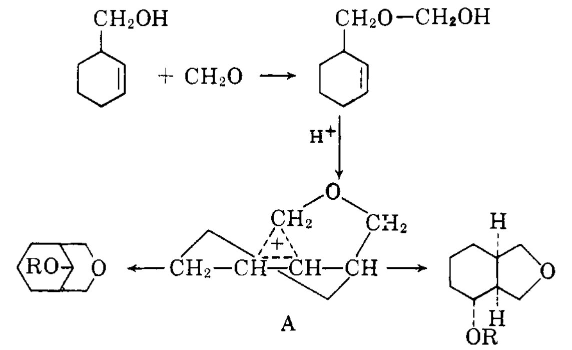
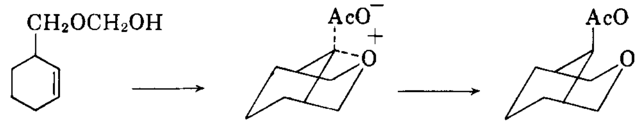
The acetolysis of arenesulfonates of both *anti*-3-oxabicyclo[3.3.1]nonan-9-ol and *trans*-6-hydroxy-*cis*-3-oxabicyclo [4.3.0]nonane gives the same products although in different yields. The acetates of the parent alcohols are formed in the same ratio in both cases. It is suggested that the formation of the bicyclic alcohols, 1 and 2, in the Prins reaction of cyclohexene and the solvolysis of their arenesulfonates proceeds by way of the nonclassical bridged ion A.

A recent study of the saponification products from the sulfuric acid-catalyzed reaction of cyclohexene and formaldehyde in acetic acid solution revealed the presence of a previously unreported compound, *trans*-6-hydroxy-*cis*-3-oxabicyclo[4.3.0]nonane.[2] It was suggested[2] that both this new alcohol and a previously reported isomer, *anti*-3-oxbicyclo[3.3.1]nonan-9-ol,[3] are formed from a single carbonium ion intermediate, A, derived from 3-hydroxymethylcyclohexene *via* the hemiformal. It was established earlier that the acetate of 3-hydroxymethylcyclohexene is among the products of the Prins reaction of cyclohexene.[3]



1. R = H
1a. R = Ac
2. R = H
2a. R = Ac

Blomquist and Wolinsky[3] have offered a mechanism for the formation of the acetate of *anti*-3-oxabicyclo-[3.3.1]nonan-9-ol involving a four-membered oxonium ion derived from the hemiformal of 3-hydroxymethylcyclohexene.



1a

Since both mechanisms assume that the bicyclic acetates, **1a** and **2a**, are formed from 3-hydroxymethylcyclohexene, we first examined the reaction of 3-hydroxymethylcyclohexene under the conditions of the Prins reaction used in previous studies.[2,3] The acetate of 3-oxabicyclo[3.3.1]nonan-9-ol, **1a**, was obtained in 22% yield, the acetate of *trans*-6-hydroxy-*cis*-3-bicyclo[4.3.0]nonane was obtained in 8% yield and the bicyclic olefin, *cis*-3-oxabicyclo[4.3.0]-6-nonene, was isolated in 40% yield. In addition, there was formed a quantity of unidentified high boiling material. The yields were determined by vapor phase chromatography of the distilled reaction products and the compounds were identified by comparison of their retention times and infrared spectra with those of authentic samples. A portion of the products was saponified and the alcohols were identified similarly by vapor phase chromatography and infrared spectroscopy. This evidence provides firm support for the assumption that the bicyclic acetates, **1a** and **2a**, arise from 3-hydroxymethylcyclohexene.

We have undertaken an investigation of the acetolysis of arenesulfonates of 3-oxabicyclo[3.3.1]nonan-9-ol and *trans*-6-hydroxy-*cis*-3-oxabicyclo[4.3.0]nonane to obtain evidence regarding the mechanism of their formation in the Prins reaction. It was anticipated that the solvolysis would proceed through the intermediate or intermediates involved in their formation and this would be discernible in the nature and distribution of the solvolysis products. The results of the solvolysis studies are summarized in Table I. The values in parenthesis refer to the corresponding alcohols in the case of the substitution products. The discrepancies in the analyses before and after saponification are undoubtedly caused by the difficulty of extracting the alcohols from aqueous solution.

The products from the solvolyses were examined by vapor phase chromatography and infrared spectroscopy. A control experiment indicated that the acetate–olefin mixture was stable under the reaction conditions but some of the olefin was lost in the isolation procedure. The reproducibility of the vapor phase chromatographic analysis was about ±2%. We did not find conditions for separating the *cis*- and *trans*-6-hydroxy-*cis*-3-oxabicyclo[4.3.0]nonanes (**2a** and **3a**) or their acetates by vapor phase chromatography. The analysis was carried out for both the acetates and the alcohols by comparing the infrared spectra of the mixtures isolated by vapor phase chromatography with mixtures of known composition. In all cases the infrared spectra of the product *anti*-3-oxabicyclo[3.3.1]-nonan-9-ol and its acetate were identical with those of authentic samples. The *anti*-3-oxabicyclo[3.3.1]nonan-9-ol and *trans*-6-hydroxy-*cis*-3-oxabicyclo[4.3.0]-nonane (containing *ca.* 10% of the all *cis*-isomer) obtained from the solvolysis of the tosylate of *anti*-3-oxabicyclo[3.3.1]nonan-9-ol were characterized as crystalline derivatives identical in all respect with authentic samples. The acetolysis of arenesulfonates of both alcohols produced some unidentified material with the longest retention time on vapor phase chromatography.

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[1] Supported by the Petroleum Research Fund of the American Chemical Society, grant no. 915-A4.

[2] L. J. Dolby, *J. Org. Chem.*, **27**, 2971 (1962).

[3] A. T. Blomquist and J. Wolinsky, *J. Am. Chem. Soc.*, **79**, 6025 (1957).

TABLE I

PRODUCTS OF ACETOLYSIS[a] OF ARENESULFONATES OF *anti*-3-OXABICYCLO[3.3.1]NONAN-9-OL AND *trans*-6-HYDROXY-*cis*-3-OXABICYCLO-[4.3.0]NONANE

Arenesulfonate	*cis*-3-Oxabicyclo-[4.3.0]-6-nonene,[b] %	*anti*-9-Acetoxy-3-oxabicyclo[3.3.1]-nonane, 1a, %	*trans*-6-Acetoxy-*cis*-3-oxabicyclo-[4.3.0]nonane, 2a, %	*cis*-6-Acetoxy-*cis*-3-oxabicyclo-[4.3.0]nonane, 3a, %	Unidentified, %
Tosylate of 1	53	20	20	2	5
	(71)	(14)	(12)	(1)	(2)
p-Nitrobenzenesulfonate of 1	55	17	19	2	8
p-Nitrobenzenesulfonate of 2[c]	43	11	12	18	16
	(70)	(8)	(7)	(10)	(6)

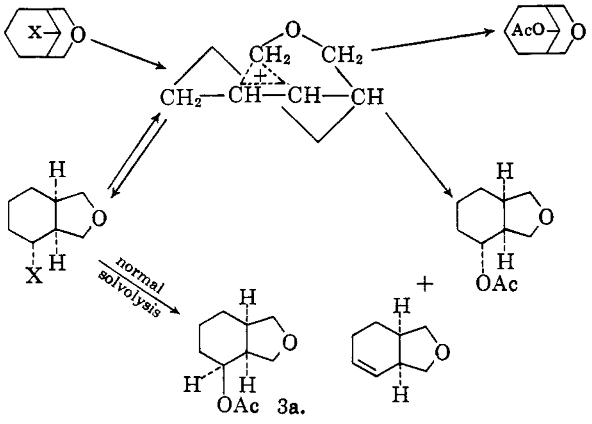
[a] All solvolyses were carried out in 0.2 *M* sodium acetate in reagent grade acetic acid at about 100°. [b] The olefin was contaminated with small amounts of materials (<5%) with almost identical retention times on vapor phase chromatography. [c] A second small-scale run gave a similar product distribution except that there was less unidentified material found.

The infrared spectrum of this material suggests a saturated acetate structure.

A sample of *cis*-3-oxabicyclo[4.3.0]-6-nonene was prepared by the phosphoric acid-catalyzed dehydration of 3-oxabicyclo[3.3.1]nonan-9-ol (1). The physical properties of the olefin prepared in the present investigation are in good agreement with those of the material isolated previously from the Prins reaction of cyclohexene.[3] Additional evidence for the position of the double bond was obtained from the proton magnetic resonance spectrum.[4] The spectrum shows three areas of absorption: peaks in the region 3.3–4.3 τ values corresponding to two protons, peaks in the region of 5.4–6.4 τ values corresponding to four protons, and peaks in the range of 6.7–8.2 τ values corresponding to six protons. The spectrum was not analyzed in detail, but the absorption at 3.3–4.3 τ provides good evidence for two vinyl protons consistent with the *cis*-3-oxabicyclo[4.3.0]-6-nonene structure. The peaks at 5.4–6.4 τ are ascribed to protons adjacent to the oxygen of the tetrahydrofuran ring.[5]

Interestingly, the acid-catalyzed dehydration of the 3-oxabicyclo[3.3.1]nonan-9-ol produced some formaldehyde, isolated as the 2,4-dinitrophenylhydrazone. The formaldehyde probably is liberated by essentially the reverse of the reaction leading to the formation of the bicyclic alcohol.

The product distributions from the acetolyses of the arensulfonates of the isomeric alcohols lead us to propose the following reaction scheme.



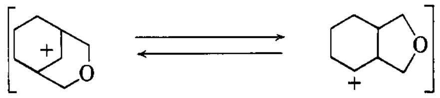
X = Arenesulfonate

The product studies indicate that the 6-acetoxy-*cis*-3-oxabicyclo[4.3.0]nonane obtained from the solvolysis of the *p*-nitrobenzenesulfonate of *trans*-6-hydroxy-*cis*-3-oxabicyclo[4.3.0]nonane contains about 60% of the all *cis* isomer, the product of normal solvolysis with inversion. The relatively large fraction (40%) of retention of configuration in this material is not the result of a normal solvolysis. For example, the substitution products from the methanolysis of *trans*-2-methylcyclohexyl tosylate show 86% inversion, 8% retention of configuration, and 6% rearrangement product, 1-methyl-1-methoxycyclohexane.[6]

It is interesting that acetolysis of arenesulfonates of *anti*-3-oxabicyclo-[3.3.1]nonan-9-ol also produces some *cis*-6-acetoxy-*cis*-3-oxabicyclo[4.3.0]nonane. We suggest that this product arises by isomerization of the arenesulfonate of the *anti*-3-oxabicyclo[3.3.1]nonan-9-ol *via* the bridged ion A to the 3-oxabicyclo[4.3.0]nonane arenesulfonate followed by normal solvolysis. It is not clear whether the olefin is formed from the bridged ion A or a normal solvolytic pathway.

It is significant that the same products are formed from arenesulfonates of both bicyclic alcohols, **1** and **2**. However, the most important piece of evidence for the intervention of the common intermediate, A, is that the acetates of retained configuration, **1a** and **2a**, were formed in the same ratio, within experimental error, in both cases.

It should be pointed out that the results can be accommodated by replacing intermediate A with a pair of rapidly equilibrating classical carbonium ions.



Either hypothesis readily accounts for the formation of the same products from arenesulfonates of both alcohols and is consistent with the large fraction of retention of configuration found in both cases.

Experimental[7]

The Sulfuric Acid-Catalyzed Reaction of 3-Hydroxymethylcyclohexene and Formaldehyde in Acetic Acid Solution.[8]—

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[4] The proton magnetic resonance spectrum was determined in carbon tetrachloride solution with a Varian HR-60 operating at 60 mc.

[5] L. M. Jackman, "Applications of Nuclear Magnetic Resonance Spectroscopy in Organic Chemistry," Pergamon Press, New York, N. Y., 1959, p. 55.

[6] W. Hückel, R. Bross, O. Fechtig, H. Feltkamp, S. Geiger, M. Hanack, M. Heinzel, A. Hubele, J. Kurz, M. Maier, D. Maucher, G. Näher, R. Neidlein, and R. B. Rashingkar, *Ann.*, **624**, 208 (1959).

[7] All melting points and boiling points are uncorrected; distillations were carried out using a 65-cm. modified Podbielniak tantalum spiral column. Microanalyses are by Pascher and Pascher Microanalytical Laboratory, Bonn, Germany. Infrared spectra were determined with a Beckman IR-7 infrared spectrophotometer.

[8] The authors are indebted to Mr. David R. Rosencrantz for carrying out this reaction.

To a stirred solution of 1.83 g. of paraformaldehyde, 5 ml. of glacial acetic acid, and 1 drop of concentrated sulfuric acid at 50° was added slowly a solution of 5.0 g. of 3-hydroxymethylcyclohexanol and 5 ml. of acetic acid. The resulting solution was heated at 70° for 2 hr. with stirring. The reaction mixture was diluted with water, neutralized with sodium carbonate, and extracted with chloroform. Fractional distillation of the product afforded 6.11 g. of material collected in three fractions. The first fraction, 2.20 g. (*ca.* 40%), b.p. 50–83° (13 mm.), $n^{25}\mathrm{D}$ 1.4675, was predominantly *cis*-3-oxabicyclo[4.3.0]-6-nonene, identified from its retention time on vapor phase chromatography and the infrared spectrum of a sample purified by vapor phase chromatography. The second fraction, 2.45 g., b.p. 98–125° (13 mm.), $n^{25}\mathrm{D}$ 1.4850, was found by vapor phase chromatography and infrared spectroscopy to be a mixture of the acetates of 3-oxabicyclo[4.3.0]nonane (**2a**) in the ratio of 3:1. The yield of the acetate of 3-oxabicyclo[3.3.1]nonan-9-ol is 22% and the yield of the acetate of *trans*-6-hydroxy-*cis*-3-oxabicyclo[4.3.0]nonane is 8%. The third fraction, 1.36 g., b.p. 110–130° (0.25 mm.), $n^{25}\mathrm{D}$ 1.4928, did not contain any of the compounds previously identified and was not investigated further.

A 1.0-g. sample of the second fraction was saponified with methanolic sodium hydroxide. The reaction mixture was diluted with water and extracted with chloroform. The chloroform was distilled and the residue was subjected to vapor phase chromatography. Both 3-oxabicyclo[3.3.1]nonan-9-ol and *trans*-6-hydroxy-*cis*-3-oxabicyclo[4.3.0]nonane were identified by their retention times and the infrared spectra of collected samples.

***cis*-3-Oxabicyclo[4.3.0]-6-nonene.**—A 14.0-g. sample of 3-oxabicyclo[3.3.1]nonan-9-ol and 2.0 ml. of 85% phosphoric acid were distilled at atmospheric pressure to yield crude *cis*-3-oxabicyclo[4.3.0]-6-nonene, b.p. 150–190°. The crude product was taken up in ether, washed with water, and dried over potassium carbonate. Fractionation of the residue yielded 7.0 g. (57%) of *cis*-2-oxabicyclo[4.3.0]-6-nonene, b.p. 79–82° (20 mm.), $n^{25}\mathrm{D}$ 1.4871 [lit.[3] b.p. 83–84° (35 mm.), $n^{25}\mathrm{D}$ 1.4876].

The aqueous wash was treated with 2,4-dinitrophenylhydrazine solution. The precipitate, 0.1706 g. (1%), was identified as formaldehyde 2,4-dinitrophenylhydrazone, m.p. 166–167°, undepressed upon mixture with an authentic sample. The infrared spectrum was also identical with that of authentic formaldehyde 2,4-dinitrophenylhydrazone.

***trans*-6-Acetoxy-*cis*-3-oxabicyclo[4.3.0]nonane.**—A small sample of *trans*-6-hydroxy-*cis*-3-oxabicyclo[4.3.0]nonane was acetylated with acetic anhydride and a drop of perchloric acid. The crude acetate was purified by vapor phase chromatography as described previously. The analytical sample showed $n^{25}\mathrm{D}$ 1.4709.

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 65.18; H, 8.64.

***cis*-6-Acetoxy-*cis*-3-oxabicyclo[4.3.0]nonane** was prepared from *cis*-6-hydroxy-*cis*-3-oxabicyclo[4.3.0]nonane as described for *trans*-6-acetoxy-*cis*-3-oxabicyclo[4.3.0]nonane and showed the same refractive index, $n^{25}\mathrm{D}$ 1.4709, and retention time on vapor phase chromatography.

Anal. Calcd. for $C_{10}H_{16}O_3$: C, 65.19; H, 8.75. Found: C, 64.99; H, 8.76.

Acetolysis of the Tosylate of 3-Oxabicyclo[3.3.1]nonan-9-ol.—The tosylate of 3-oxabicyclo[3.3.1]nonan-9-ol, m.p. 103–104° (lit.[3] m.p. 105–106°), was prepared by treating the alcohol with *p*-toluenesulfonylchloride in pyridine solution. A 13.950-g. sample of the tosylate, 300 ml. of reagent grade acetic acid, and 5.00 g. of sodium acetate were placed in a round-bottomed flask and heated on the steam bath for 24 hr. The cooled mixture was diluted with 900 ml. of water and the acetic acid was neutralized with solid sodium carbonate. The reaction mixture was extracted five times with ether and the combined extracts were washed with water then dried over sodium sulfate. The ether was flash distilled and the residue was examined by vapor phase chromatography using a 5-ft. column of 20% Carbowax 20M on firebrick at 200°. The vapor phase chromatogram showed four main peaks with retention times of 5 min., 15 min., 23 min., and 27 min. The retention times of the first three compounds corresponded to the retention times of authentic samples of *cis*-3-oxabicyclo[4.3.0]-6-nonene and the acetates of 3-oxabicyclo[3.3.1]nonan-9-ol and *trans*-6-hydroxybicyclo[4.3.0]nonane. The fourth peak was unidentified. Samples of each peak effluent were collected from several runs. The infrared spectra of the first two components eluted were identical with those of authentic samples of *cis*-3-oxabicyclo[4.3.0]-6-nonene and *anti*-9-acetoxy-3-oxabicyclo[3.3.1]nonane, respectively. The third peak proved to be a mixture of *cis*- and *trans*-6-acetoxy-*cis*-3-oxabicyclo[4.3.0]nonane which by infrared analysis was found to contain 10% of the all *cis* isomer.

It was assumed that the area under each peak is directly proportional to the mole fraction of that component in the mixture and the yield of each compound is recorded in Table I.

The remainder of the reaction products was dissolved in a solution of 50 ml. of methanol, 20 ml. of water, and 5 g. of sodium hydroxide and stored overnight. The solution was diluted with water and continuously extracted with ether. The ether was distilled and the residue was examined by vapor phase chromatography, using a 5-ft. column of 20% Carbowax 20M on firebrick at 200°. The vapor phase chromatogram showed four peaks with retention times of 5 min., 28 min., 37 min., and 41 min. The retention times of the first three peaks eluted are identical with the retention times of *cis*-3-oxabicyclo[4.3.0]-6-nonene, 3-oxabicyclo[3.3.1]nonan-9-ol and 6-hydroxy-*cis*-3-oxabicyclo[4.3.0]nonane, respectively. The fourth peak at a longer retention time was not identified. Samples of the first three components were collected from multiple injections and the infrared spectra of the first two were identical with those of *cis*-3-oxabicyclo[4.3.0]-6-nonene and *anti*-3-oxabicyclo[4.3.1]nonan-9-ol, respectively. The third component was found by infrared analysis to be *trans*-6-hydroxy-*cis*-3-oxabicyclo[4.3.0]nonane containing 10% of the all *cis* isomer.

A sample of the *anti*-3-oxabicyclo[3.3.1]nonan-9-ol collected by vapor phase chromatography was converted to the tosylate which was identical in all respects with an authentic sample.

A sample of the *trans*-6-hydroxy-*cis*-3-oxabicyclo[4.3.0]nonane similarly was converted to the *p*-nitrobenzenesulfonate which was identical with an authentic sample.[2]

Acetolysis of the *p*-Nitrobenzenesulfonate of *anti*-3-Oxabicyclo[3.3.1]nonan-9-ol.—The *p*-nitrobenzenesulfonate of *anti*-3-oxabicyclo[3.3.1]nonan-9-ol was prepared in the usual manner and crystallized from benzene–petroleum ether. The analytical sample melted at 133–135°.

Anal. Calcd. for $C_{14}H_{17}NO_6S$: C, 51.36; H, 5.23; N, 4.27. Found: C, 50.96; H, 5.10; N, 4.33.

The acetolysis of a sample of the *p*-nitrobenzenesulfonate was carried out as described for the acetolysis of the tosylate and the product mixture was analyzed by vapor phase chromatography and infrared spectroscopy. The product distribution is recorded in Table I.

Acetolysis of the *p*-Nitrobenzenesulfonate of *trans*-6-Hydroxy-*cis*-3-oxabicyclo[4.3.0]nonane.—A 5.4-g. sample of the *p*-nitrobenzenesulfonate[2] was solvolyzed and the products were analyzed as described for the solvolysis of the tosylate of *anti*-3-oxabicyclo[3.3.1]nonan-9-ol. The product distribution is recorded in Table I. A sample of the unidentified component was obtained by vapor phase chromatography and its infrared spectrum showed peaks at 1735 cm.$^{-1}$ and 1250 cm.$^{-1}$ ascribed to an acetate group. There was no absorption near 1600 cm.$^{-1}$ which could be attributed to a double bond.

The crude reaction mixture was saponified and examined by vapor phase chromatography and infrared spectroscopy as previously described. These results are recorded in Table I.

A second run gave similar results except that the amount of unidentified product was somewhat less.

Control Experiments on the Stability of the Products and the Isolation Procedure.—A mixture of *cis*-3-oxabicyclo[4.3.0]-non-6-ene and the acetates of *anti*-3-oxabicyclo[3.3.1]nonan-9-ol and *trans*-6-hydroxy[4.3.0]nonane was prepared and analyzed by vapor phase chromatography. It was found to contain 43% of the olefin, 19% of the acetate of *anti*-3-oxabicyclo[3.3.1]nonan-9-ol, and 38% of the acetate of *trans*-6-hydroxy-*cis*-3-oxa bicyclo[4.3.0]nonane. The mixture was dissolved in 0.1 *M* sodium acetate in acetic acid. A portion of the solution was worked up immediately and analyzed by vapor phase chromatography. The crude material was found to consist of 37% of the olefin, 22% of the acetate of *anti*-3-oxabicyclo[3.3.1]nonan-9-ol, and 41% of the acetate of *trans*-6-hydroxy-*cis*-3-oxabicyclo-[4.3.0]nonane. The remainder of the acetic acid solution of the mixture was heated on the steam bath for 24 hr. and worked up. The mixture was found to contain 36% of the olefin, 22% of the acetate of *anti*-3-oxabicyclo[3.3.1]nonan-9-ol, and 42% of the acetate of *trans*-6-hydroxy-*cis*-3-oxabicyclo[4.3.0]nonane.