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PREPARATION AND REACTIVITY OF BRIDGE-SUBSTITUTED BICYCLO[3.2.1]-OCTYL AND BICYCLO[3.3.1]NONYL TOLUENESULFONATES

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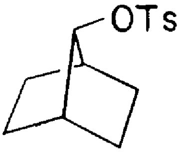
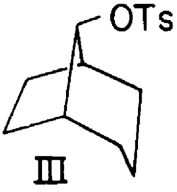
Abstract—*Endo*- and *exo*-bicyclo[3.2.1]octyl-8-tosylate (III and IV) and bicyclo[3.3.1]nonyl-9-tosylate (V) have been prepared by a novel synthetic sequence. In acetolysis, the relative rates are: III, $7·8 \times 10^{-5}$; IV, $6·1 \times 10^{-1}$; V, 3·0; for comparison, the rate of norbornyl-7-tosylate (I) is $9·1 \times 10^{-8}$, and that of cyclohexyl tosylate (II) is 1·00. The solvolyses of IV and V are anchimerically accelerated. V is shown to undergo ion-pair return during solvolysis to *cis-trans*-hydrindyl-4-tosylate (XXIII). The relatively low rates of acetolysis of III and I are a result of internal angle strain at the carbon atom bearing the leaving group.

SATURATED derivatives of norbornane substituted at the 7-position are well known for their unreactivity in solvolysis.[1] For instance, norbornyl-7-tosylate (toluenesulfonate) (I) undergoes acetolysis at a rate seven powers of ten slower than that of cyclohexyl tosylate (II).[1b,e] Several widely differing explanations which have been offered for this lack of reactivity[1a,c,e] have been discussed by Schleyer and Nicholas.[2] In order to assess the relative importance of the factors influencing reactivity, we have synthesized

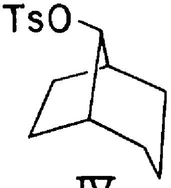


I

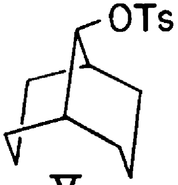
II



III



IV



V

[1a] J. D. Roberts, F. O. Johnson and R. A. Carboni, *J. Amer. Chem. Soc.* **76**, 5692 (1954); [b] S. Winstein, M. Shatavsky, C. Norton and R. B. Woodward, *Ibid.* **77**, 4183 (1955); [c] W. G. Woods, R. A. Carboni and J. D. Roberts, *Ibid.* **78**, 5653 (1956); [d] S. Winstein and M. Shatavsky, *Ibid.* **78**, 592 (1956); [e] C. J. Norton, Ph.D. Thesis, Harvard, 1955.

[2] P. v. R. Schleyer and R. D. Nicholas, *J. Amer. Chem. Soc.* **83**, 182 (1961).

and solvolyzed three homologues of norbornyl-7-tosylate: *endo*- and *exo*-bicyclo-[3.2.1]octyl-8-tosylate[3] (III and IV) and bicyclo[3.3.1]nonyl-9-tosylate (V). These compounds retain many of the unusual geometrical features of the norbornane system, but are considerably less strained. V is nearly strainless, and III and IV are intermediate in strain between I and V.

Synthesis of the bicyclic compounds

A very convenient route to bicyclo[3.2.1]octane and bicyclo[3.3.1]nonane derivatives was developed from the aminoketones VI and VII, which are readily made in good yields by condensation of the enamines derived from cyclopentanone and cyclohexanone with acrolein.[4] The aminoketones were converted to the N-oxides of the corresponding ethylene ketals and pyrolyzed to yield Δ^2-bicyclo[3.2.1]octene-8-ethylene ketal (VIII, 30–50%) and Δ^2-bicyclo[3.3.1]nonene-9-ethylene ketal (IX, 40–60%). Each ketal was hydrolyzed to the corresponding unsaturated ketone (X and XI), which was hydrogenated to the saturated ketone (XII[3,5] and XIII).[6] Reduction of bicyclo[3.2.1]octan-8-one with either sodium borohydride in methanol or hydrogen on platinum in acetic acid[3] gave *endo*-bicyclo[3.2.1]octan-8-ol[3,5,7] (XIV), uncontaminated by the *exo* isomer[3,5,7] XV). Bicyclo[3.3.1]nonan-9-one (XIII) was reduced with sodium borohydride to bicyclo[3.3.1]nonan-9-ol (XVI). In both the bicyclooctane and bicyclononane series, the hydrolysis and reduction steps were conveniently combined by hydrogenating VIII or IX over platinum in aqueous acetic acid containing a little hydrochloric acid to give XIV or XVI directly and in excellent yields.

Although reduction of XII with several reagents and reductions of X followed by hydrogenation gave mixtures of *exo* and *endo* saturated alcohols consisting of at most 36 per cent of the *exo* isomer (see Experimental), acetolysis of *endo*-bicyclo[3.2.1]-octyl-8-tosylate (III) was found to give satisfactory yields of *exo* acetate, which was saponified to give XV.

The bicyclo[3.2.1]octan-8-ols were identical with samples prepared by Cope *et al.*, who have unambiguously assigned their configurations.[3,5,7] The structure of the previously unknown bicyclo[3.3.1]nonan-9-ol (XVI) was inferred from its empirical formula and those of derivatives, its IR and NMR spectra, its mode of synthesis, and analogy with the bicyclooctane series. In addition, bicyclo[3.3.1]nonan-9-one (XIII) was reduced to the known[8] bicyclo[3.3.1]nonane; XIII has since been prepared by a different route.[9]

The synthetic routes described above are summarized in Fig. 1, and represent the first simple and convenient preparation of bridge-substituted bicyclo[3.2.1]octanes and [3.3.1]nonanes.

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[3] A. C. Cope, J. M. Grisar and P. E. Peterson, *J. Amer. Chem. Soc.* **82**, 4299 (1960).

[4a] G. Stork and H. K. Landesman, *J. Amer. Chem. Soc.* **78**, 5129 (1956); [b] G. Stork, *16th National Organic Chemistry Symposium* of the American Chemical Society, *Abstracts* p. 44 (1959).

[5] We are indebted to A. C. Cope and S. Moon for supplying samples, IR spectra, and gas chromatographic data for many compounds in the bicyclo[3.2.1] and [3.3.0]octane series.

[6] Formation of the semicarbazones from both X and XII was unusually difficult, indicating a marked preference by the bicyclo[3.2.1]octane system for tetrahedral rather than trigonal hybridization at the 8-position. The reasons for this preference are discussed below.

[7] A. C. Cope, S. Moon, C. H. Park and G. L. Woo, *J. Amer. Chem. Soc.* **84**, 4865 (1962).

[8a] A. C. Cope and M. E. Synerholm, *J. Amer. Chem. Soc.* **72**, 5228 (1950); [b] H. Meerwein, F. Kiel, G. Klösgen and E. Schoch, *J. Prakt. Chem.* **104**, 161 (1922).

[9] D. M. Bailey, J. E. Bowers and C. D. Gutsche, *J. Org. Chem.* **28**, 610 (1963).

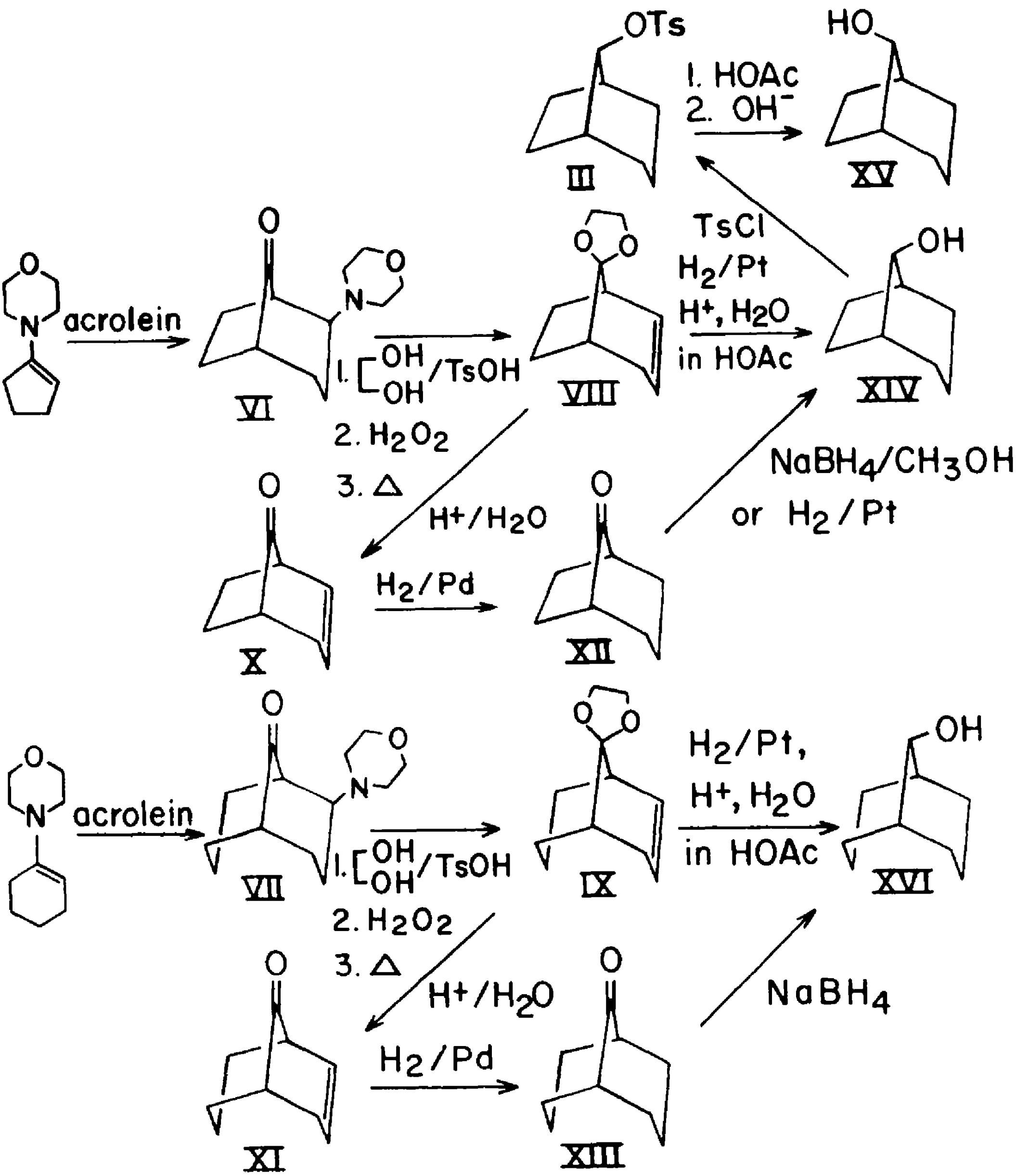

FIG. 1. Synthetic route to the bicyclic alcohols.

Acetolysis of the bicyclic tosylates

1. *Kinetics.* The results of the kinetic studies are summarized in Table 1. *endo*-Bicyclo[3.2.1]octyl-8-tosylate (III) reacted very slowly, with first-order kinetics. *exo*-Bicyclo[3.2.1]octyl-8-tosylate (IV) and bicyclo[3.3.1]nonyl-9-tosylate (V) reacted much faster, with a rate which increased by a factor of roughly three during solvolysis, becoming constant after the reaction was roughly 30% complete. Table 2 gives the instantaneous rate constant for acetolysis of bicyclononyl tosylate as a

TABLE 1. RATES OF ACETOLYSIS OF THE BICYCLIC TOSYLATES

Tosylate	T	ROTs, M	KOAc, M	$k \times 10^5$ sec^{-1} [a]	ΔH‡, kcal.	ΔS‡, e.u.
III	140°	0·09	0·099	$2·27 \pm 0·02$[b]		
	120°	0·09	0·099	$0·300 \pm 0·003$[c]		
	145°	0·019	—	$2·76$[d]		
	25°	0·09	0·099	$5·2 \pm 2·0 \times 10^{-7}$[e]	$31·9 \pm 0·6$	$-3·5 \pm 1·9$
IV	100°	0·09	0·099	$45·5 + 1·5$[c,f]		
	75°	0·09	0·099	$3·16 \pm 0·02$[c,f]		
	75°	0·02	—	$2·49$[d,f]		
	25°	0·09	0·099	$4·2 \pm 0·6 \times 10^{-3}$[e]	$26·8 \pm 0·6$	$-2·6 \pm 2·4$
V	85°	0·09	0·099	$50·2 \pm 0·2$[c,f]		
	65°	0·09	0·099	$5·05 \pm 0·02$[c,f]		
	65°	0·02	—	$4·22$[d,f]		
	25°	0·09	0·099	$2·0 + 0·3 \times 10^{-2}$[e]	$27·2 + 0·6$	$2·0 \pm 1·6$

[a] measured graphically.
[b] average of three runs.
[c] average of two runs.
[d] one run
[e] extrapolated from data at other temperatures.
[f] not first-order; final rate.

function of time. None of the tosylates showed a large salt effect, the rates in 0·1 molar potassium acetate being faster than those in pure acetic acid by a factor of about 1·3 in each case.

2. *Products.* The products of the acetolyses were complex mixtures, summarized in Fig. 2. The individual components of each product mixture were separated by gas chromatography (after saponification in the case of the acetates).[10]

The compounds in the C_8 series were identified by comparison of IR spectra, gas chromatographic retention times, and in some cases, melting points of derivatives, with those of authentic samples.[3,5,11] The hexahydroindenes were characterized by IR

TABLE 2. ACETOLYSIS OF 0·09 M BICYCLONONYL TOSYLATE AT
65·0°, 0·099 M KOAc

t, sec	$1 - \left[\dfrac{\text{Mo(KOAc)} - \text{M(KOAc)}}{\text{Mo(ROTs)}}\right]$	$k_{\text{inst}} \times 10^5$, sec^{-1} [a]
000	1·000	1·9
1800	0·964	2·5
3600	0·922	3·3
5400	0·859	3·8
9720	0·728	4·5
10800	0·686	5·0
13320	0·609	5·0
14400	0·575	5·0
16920	0·511	5·0
19450	0·447	5·0
27000	0·309	5·0
37800	0·178	5·0

[a] determined graphically by taking the slope of the tangent to the line through the experimental points on a ln conc. *vs.* time plot.

and NMR spectra, and by elemental analysis. *cis*-Δ^4-Hexahydroindene (XVII) was oxidized to *cis*-2-carboxycyclopentanepropionic acid.[12] The IR spectrum[13] of Δ^8-hexahydroindene (XVIII) and the melting point of its unstable dibromide[13,14] were identical to those reported in the literature. The three hydrindan-4-ols were compared by means of IR spectra, relative retention times, and melting points of derivatives with samples whose preparation and configurational assignments are described below.

Two hydrindan-4-ols had been reported,[12a,b] and their configurations had been tentatively assigned.[15] One isomer, the predominant product of hydrogenation of indan-4-ol,[12b] is readily purified by means of the insoluble potassium salt of its acid phthalate;[12a] as diazotization of a hydrindylamine produced this alcohol along with much *cis*-Δ^4-hexahydroindene (XVII),[12a,16] the ring junction of this alcohol is undoubtedly also *cis*. The *cis-cis* configuration (XIX) was assigned to this alcohol by Dauben on the basis of analogy between a number of reactions in the hydrindane and decalin series.[15] A second alcohol was reportedly produced in almost pure state by treating XIX with sodium in refluxing decalin;[12a] this alcohol was assigned the *cis-trans* configuration (XX).[15]

In order to verify the configurational assignments and to learn the structure of the third acetate produced in the acetolysis of bicyclononyl tosylate, it was necessary to repeat and extend some of the earlier work, which had been done without an adequate method of separating the alcohol mixtures. Fig. 3 summarizes the reactions carried out, and the composition of the product mixtures (determined by gas-chromatographic separation[10] and measurement of the IR spectra of the isolated components).

Hydrogenation of indan-4-ol (Reaction 1) produced a mixture of four alcohols. The major product could be purified by precipitation of the potassium salt of its acid phthalate (the procedure of Hückel[12a]); the resulting phthalate was recrystallized and saponified to yield a gas-chromatographically pure alcohol (A). The acid phthalate of A had the same melting point as that reported for the phthalate of the alcohol prepared in this way[12a] and assigned[15] the *cis-cis* configuration (XIX).

Oxidation of pure A gave a ketone which could be reduced with lithium aluminum hydride to give a mixture which contained only A and a small amount of a second alcohol (B); (Reaction 2). Equilibration of A with aluminum isopropoxide in isopropanol containing acetone[18] (Reaction 3) again gave a mixture containing only A and B; B predominated in this mixture. Equilibration of pure B under the same conditions (Reaction 4) produced an almost identical product mixture.

Reactions 2–4 establish that A and B are epimers, of which B is the more stable; A and B must have the *cis* ring junction (see above). Models indicate that the *cis-cis*

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[10] Tris-(2-cyanoethoxy)propane (TCEP) was the only stationary phase found useful for separation of the alcohol mixtures.[11]

[11] A. C. Cope and P. E. Peterson, *J. Amer. Chem. Soc.* **81**, 1643 (1959).

[12a] W. Hückel, R. Schlüter, W. Doll and F. Reimer, *Liebigs Ann.* **530**, 166 (1937); [b] W. Hückel and E. Goth, *Ber. Dtsch. Chem. Ges.* **67**, 2104 (1934); [c] A. H. Cook and R. P. Linstead, *J. Chem. Soc.* 946 (1934).

[13] P. E. Fuchs, Ph.D. Thesis, Harvard (1955).

[14] R. Criegee and H. Zogel, *Chem. Ber.* **84**, 215 (1951).

[15] W. G. Dauben and J. Jiu, *J. Amer. Chem. Soc.* **76**, 4426 (1954).

[16] The *cis* ring junction of XVII was shown unambiguously by a series of interconversions.[12b,17]

[17] W. Hückel and H. Friedrich, *Liebigs Ann.* **451**, 132 (1927).

[18] E. L. Eliel and R. S. Ro, *J. Amer. Chem. Soc.* **79**, 5992 (1957).

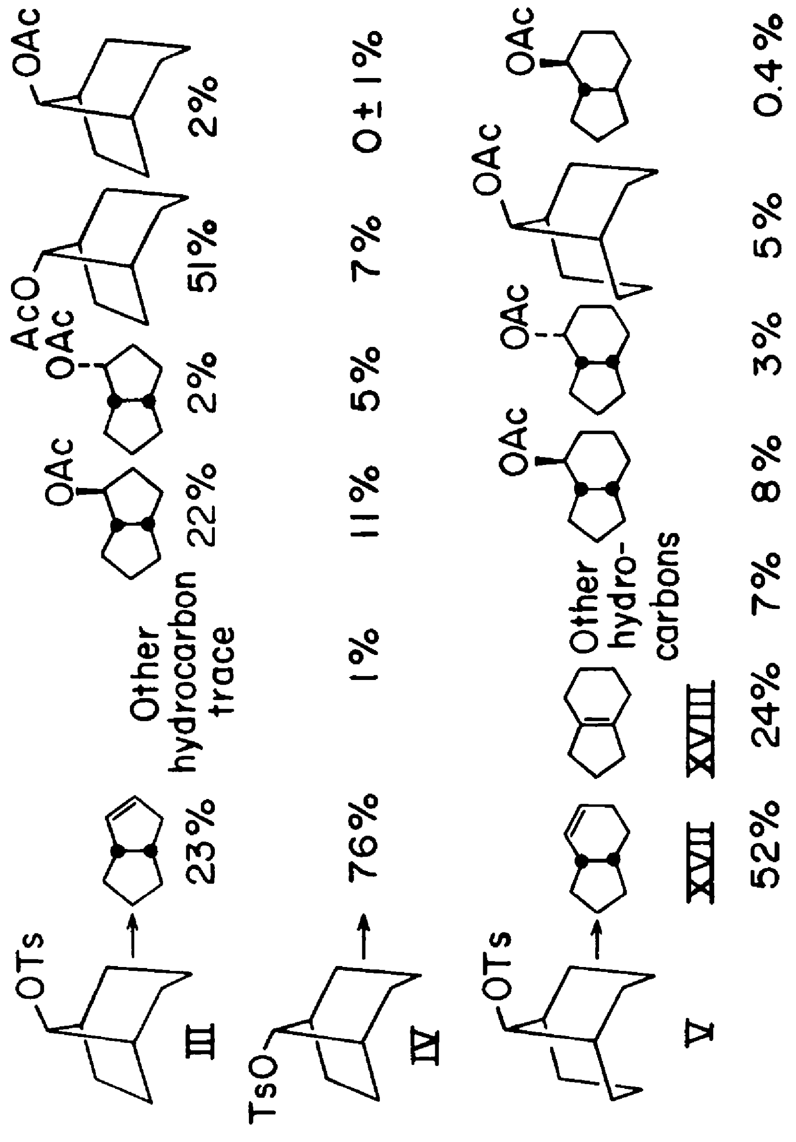


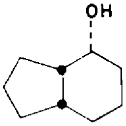
Fig. 2. Products from the acetolyses

alcohol has the more serious non-bonded interactions and would be expected to be less stable. On the basis of these arguments, A is *cis-cis*-hydrindan-4-ol (XIX) in agreement with the previous assignment,[15] and B is the *cis-trans* epimer (XX).

	Reaction	Per cent of component in alcohol mixture[a]			
		A	B	C	D
1.	Indan-4-ol $\xrightarrow[HOAc]{H_2/Pt}$ (mixture 1)	68	7	1	20[b]
2.	A $\xrightarrow[HOAc]{CrO_3}$ *cis*-Ketone $\xrightarrow{LAH}$	89	11	—	—
3.	A $\xrightarrow[iprOH, acetone]{Al(Oipr)_3}$	32	68	—	—
4.	B $\xrightarrow[iprOH, acetone]{Al(Oipr)_3}$	28	72	—	—
5.	Mixture 1 $\xrightarrow[reflux]{Na/decalin}$	20	32	38	6[b]
6.	*cis*-Ketone $\xrightarrow[iprOH]{Na}$	38	38	20	4
7.	*cis*-Ketone $\xrightarrow[CH_3OH]{NaOCH_3}$ $\xrightarrow{LAH}$	68	9	16	6

Structure assigned:

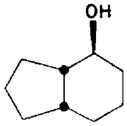
A



cis-cis

XIX

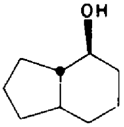
B



cis-trans

XX

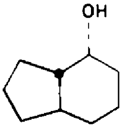
C



trans-trans

XXI

D



trans-cis

XXII

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[a] Determined by gas chromatography. As alcohols A and B were poorly resolved, their relative proportions are somewhat less certain than those of the other alcohols.

[b] Traces of unidentified components and large amounts of hydrocarbons were also present.

FIG. 3. Reactions and products in the hydrindane series.

Refluxing the crude mixture from the hydrogenation of indan-4-ol with sodium in decalin (Reaction 5) produced a mixture from which it was not possible to isolate a pure product: when the acid phthalate was made from the product mixture and treated by the procedure reported[12a] to yield the phthalate of the alcohol assigned[15] the *cis-trans* configuration (XX), the isolated material, although it had the reported[12a] melting point, proved to be a gross mixture whose composition and melting point were unchanged by further recrystallization. The composition of the alcohol mixture from Reaction 5 indicates that the ring junction is equilibrated by sodium in refluxing decalin, since the total amount of *trans* alcohols doubles during the reaction.

Reduction of *cis*-hydrindan-4-one with sodium in isopropanol (a reaction which produces predominantly the more stable epimer[19]), gave a mixture in which all four hydrindanols were present (Reaction 6); of the *trans* pair, the one produced in larger amount (C) was also the one produced in larger amount in the sodium in decalin reaction (5) and is thus the more stable of the two. This must be the equatorial *trans-trans* isomer (XXI); its epimer (D, produced in larger amount in the hydrogenation of indan-4-ol) must then be the axial *trans-cis* isomer (XXII).

Treatment of *cis*-hydrindan-4-one with sodium methoxide in methanol produced an inseparable mixture of *cis* and *trans* ketones; reduction of this mixture with lithium aluminum hydride (Reaction 7) produced a mixture of *cis* and *trans* alcohols; the two *cis* alcohols were produced in the same relative amounts as in Reaction 2 (reduction of the pure *cis* ketone); 22% of the total product consisted of *trans* alcohols; thus the ketone mixture must also have been 22% *trans*. Of the *trans* alcohols, the equatorial *trans-trans* isomer predominated.

The kinetics and products of acetolysis of bicyclo[3.3.1]nonyl-9-tosylate (V) and *exo*-bicyclo[3.2.1]octyl-8-tosylate (IV) suggest that some process such as ion-pair return is occurring.[20] In order to gain an understanding of the solvolysis mechanism, *cis-trans*-hydrindyl-4-tosylate (XXIII), the most likely product of return from bicyclononyl tosylate, was prepared and solvolyzed.

Pure *cis-cis*-hydrindan-4-ol (XIX) was prepared via the potassium salt of its acid phthalate.[12a] Equilibration of XIX (Reaction 4, Fig. 3) gave a mixture of 68% *cis-trans* (XX) and 32% *cis-cis* (XIX) alcohols. The acid phthalate of XIX was removed from the phthalate of the mixture by precipitation of the potassium salt.[12a] The soluble fraction was acidified and recrystallized to constant melting point, then saponified to give the *cis-trans* alcohol, which contained approximately 2·2% of *cis-cis* (XIX) and 0·8% of *trans-trans* (XXI) alcohols. The tosylate of this mixture was recrystallized to constant melting point for the kinetic and product studies.[21] For comparison, the rates of acetolysis of the *cis-cis* tosylate (XXIV) and the *trans-trans* tosylate (XXV)[22] were also determined. The rates are summarized in Table 3.

The acetolysis rate of *cis-trans*-hydrindyl tosylate (XXIII) was constant for the first 80% reaction, at which time a slight downward drift became apparent. This drift was somewhat greater than the experimental error (which is rather large in the region 75 to 95% reaction) and is probably real; its significance is discussed below. XXIV and XXV solvolyzed with first-order kinetics.

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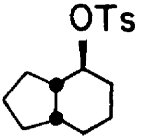
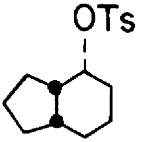
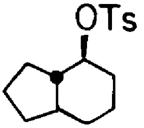
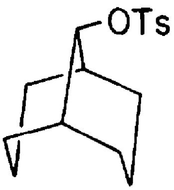
[19] D. H. R. Barton, *J. Chem. Soc.* 1027 (1953).

[20] S. Winstein, F. Gadient, E. T. Stafford and P. E. Klinedinst Jr., *J. Amer. Chem. Soc.* **80**, 5895 (1958): internal return occurs in the acetolysis of norbornyl-7-tosylate.

[21] The tosylate thus prepared was shown by kinetic analysis to be free of *cis-cis* tosylate, but could have contained small amounts of *trans-trans* tosylate. This point is discussed below.

[22] Made by preparing the phthalate of the crude sodium–decalin reflux mixture (Reaction 5, Fig. 3), recrystallizing to constant m.p., saponifying and tosylating, and recrystallizing the tosylate to constant m.p. Kinetic analysis showed the tosylate thus prepared to be essentially free of either of the much more reactive *cis* tosylates.

TABLE 3. ACETOLYSIS RATES OF THE HYDRINDYL TOSYLATES (65·0°)

Tosylate	ROTs, M	KOAc, M	$k \times 10^6$ sec^{-1}[a]
 XXIII	0·07	0·094	20·4 ± 0·1[b,c]
 XXIV	0·07	0·099	85·3[d]
 XXV	0·07	0·099	1·49[d]
 V	0·09	0·099	5·05 ± 0·02[b,e]

[a] measured graphically. [b] average of two runs.
[c] first order to 80% reaction; then slight downward drift.
[d] one run. [e] final rate constant.

The products of acetolysis of *cis-trans*-hydrindyl tosylate consisted of 98% hydrocarbons and 2% acetates. The hydrocarbons were separated by gas chromatography and identified by their IR spectra and relative retention times as *cis*-Δ^4-hexahydroindene (XVII, 54%) and Δ^8-hexahydroindene (XVIII, 32%); in addition, two unidentified hydrocarbons were produced (10 and 4%). Because of the very small amounts available, the acetates could not be identified; at least three were present, as shown by gas chromatography. The products of acetolysis of *cis-cis* (XXIV) and *trans-trans* (XXV) tosylates were not investigated in detail; the product from XXIV was largely hydrocarbon;[23] that from XXV was mainly acetate.

Discussion of the experimental results

The observed kinetic behavior of bicyclo[3.3.1]nonyl-9-tosylate (V) and *cis-trans*-hydrindyl-4-tosylate (XXIII) suggests that each tosylate returns partly to the

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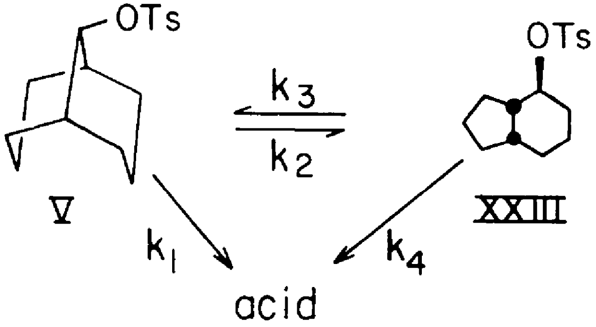
[23] A recent study of the acetolysis of XXIV reports 98% hydrocarbon product, of which 68% was the trisubstituted $\Delta^{4,9}$-hexahydroindene: R. A. Spenger, Ph.D. Thesis, University of Wisconsin (1962); *Dissertation Abstracts* **22**, 3412 (1962).

other in the course of acetolysis. Such a reaction has been shown to occur in the case of the solvolysis of bicyclo[2.2.2]octyl-2-tosylate and axial-bicyclo[3.2.1]octyl-2-tosylate.[24] This scheme will now be examined in detail.



The integrated rate equations for the general scheme

$$\begin{tikzcd}
A \arrow[r, shift left, "k_2"] \arrow[dr, "k_1"'] & B \arrow[l, shift left, "k_3"] \arrow[d, "k_4"] \\
& C
\end{tikzcd}$$

with the boundary conditions A(0) = A0, B(0) = O, C(0) = 0 are:[25]

$$\frac{A}{A_0} = \frac{(\lambda_1 e^{-\lambda_1 t} - \lambda_2 e^{-\lambda_2 t}) + (k_3 + k_4)(e^{-\lambda_2 t} - e^{-\lambda_1 t})}{\lambda_1 - \lambda_2} \tag{1}$$

$$\frac{B}{A_0} = \frac{k_2(e^{-\lambda_2 t} - e^{-\lambda_1 t})}{\lambda_1 - \lambda_2} \tag{2}$$

$$x = \frac{1 - C}{A_0} = \frac{\lambda_1 - k_1}{\lambda_1 - \lambda_2} e^{-\lambda_2 t} - \frac{\lambda_2 - k_1}{\lambda_1 - \lambda_2} e^{-\lambda_1 t} \tag{3}$$

where

$$\lambda_1 + \lambda_2 = k_1 + k_2 + k_3 + k_4 \tag{4}$$

$$\lambda_1 \lambda_2 = k_1 k_3 + k_1 k_4 + k_2 k_4 \tag{5}$$

From the experimental data it is possible to evaluate three of the parameters in the above equations with reasonable accuracy; a fourth can then be chosen to give the best fit for the solvolysis curves of the two tosylates. The procedure used is the following. First, the final rate constant for acetolysis of bicyclononyl tosylate is accurately known, since most of the reaction proceeds at this rate. This constant is equal to λ_2 in Equation 3, if λ_2 is allowed to be smaller than λ_1.[26] Second, if the

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[24] H. L. Goering and M. F. Sloan, *J. Amer. Chem. Soc.* **83**, 1992 (1961).

[25] P. D. Bartlett, C. E. Dills and H. G. Richey, Jr., *J. Amer. Chem. Soc.* **82**, 5414 (1960). We are indebted to Professor Bartlett and Dr. C. Perrin for discussion of these equations and their implications.

[26] The equations are symmetrical in λ_1 and λ_2; the final rate is equal to the one chosen to be smaller, as can be verified by taking $\lim_{t \to \infty} \left[\frac{-d \ln x}{dt}\right]$ from Eq. 3.

straight final portion of the acetolysis curve for bicyclononyl tosylate is extrapolated to zero time, the intercept is equal to the logarithm of the coefficient of the first term in Equation 3, which is the dominant term at long times.[27] Third, the initial rate for acetolysis of *cis-trans*-hydrindyl tosylate (easily determined, since the initial straight portion is long) is equal to k_4.[28]

The above three parameters were evaluated, and several different values for k_1 (which may be roughly estimated from the initial slope of the bicyclononyl tosylate curve) were selected and the remaining parameters calculated. Table 4 shows the variation of the various rate constants with different choices of k_1.

TABLE 4. VALUES OF RATE PARAMETERS CALCULATED FROM EQUATIONS 1–5

$\lambda_2 = 5{\cdot}05 \times 10^{-5}\ \text{sec}^{-1}$ $\qquad \dfrac{\lambda_1 - k_1}{\lambda_1 - \lambda_2} = 1{\cdot}189$ $\qquad k_4 = 20{\cdot}4 \times 10^{-5}\ \text{sec}^{-1}$

$k_1 \times 10^5\ \text{sec}^{-1}$	$\lambda_1 \times 10^5\ \text{sec}^{-1}$	$k_2 \times 10^5\ \text{sec}^{-1}$	$k_3 \times 10^5\ \text{sec}^{-1}$
1·80	22·2	3·47	0·153
1·94	21·4	3·28	0·083
2·00	21·1	3·18	0·064
2·08	20·7	3·03	0·022
2·165	20·4	2·89	0·000

All values listed in Table 4 give plots which fit the bicyclononyl tosylate acetolysis data well (as they should, since λ_2 is always the observed final slope, and k_1, the initial slope, is varied only over narrow limits); see Fig. 4. The data for *cis-trans*-hydrindyl tosylate are fitted within the experimental error by either $k_1 = 2{\cdot}00$ or $2{\cdot}08 \times 10^{-5}\ \text{sec}^{-1}$ (Fig. 5). Note that if $k_1 = 2{\cdot}165\ \text{sec}^{-1}$, *cis-trans*-hydrindyl tosylate would solvolyze with first-order kinetics, and the return to bicyclononyl tosylate would not occur. Unfortunately, the various sets of rate constants begin to give appreciably different rate plots for *cis-trans*-hydrindyl tosylate only in the region of 90% reaction, where the experimental error becomes large. A particular difficulty with accurate measurement of the acetolysis rate of *cis-trans*-hydrindyl tosylate is that the presence of only a few tenths of a per cent of the relatively inert *trans-trans* isomer (XXV) would also cause a slight downward drift in the experimental rate constant as the time becomes large; thus it is entirely possible that all of the deviation from first-order kinetics is due to the presence of traces of this isomer, which is extremely difficult to remove completely. In any case, however, it is clear that the rate of return from *cis-trans*-hydrindyl to bicyclononyl tosylate (or any other less reactive tosylate such as XXV) is extremely small, that is, $k_3 < 0{\cdot}064 \times 10^{-5}\ \text{sec}^{-1}$, which is less than 0·3% of k_4, the rate of product formation from the hydrindyl tosylate.

The amounts of each tosylate present at any time in the acetolysis reaction, starting from either, can easily be calculated from the tabulated values of the rate parameters. Determination of the actual composition of recovered mixtures proved to be difficult, since both recovered mixtures and synthetic mixtures of bicyclononyl

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[27] This parameter is accurately measurable because the final straight portion of the solvolysis plot for bicyclononyl tosylate is long.

[28] $\lim\limits_{t \to \infty} \left[\dfrac{-d \ln x}{dt}\right] = k_{\text{initial}} = k_4$ where $B(0) = B_0$, $A(0) = 0$, $C(0) = 0$.

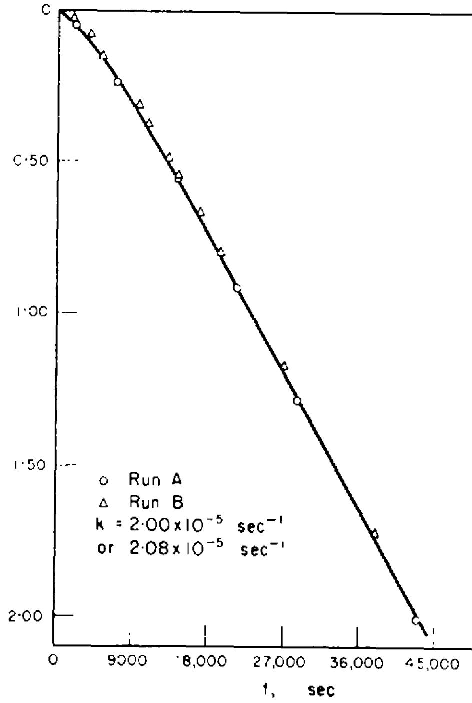

FIG. 4. Calculated acetolysis curves for bicyclononyl tosylate and experimental data (65°).

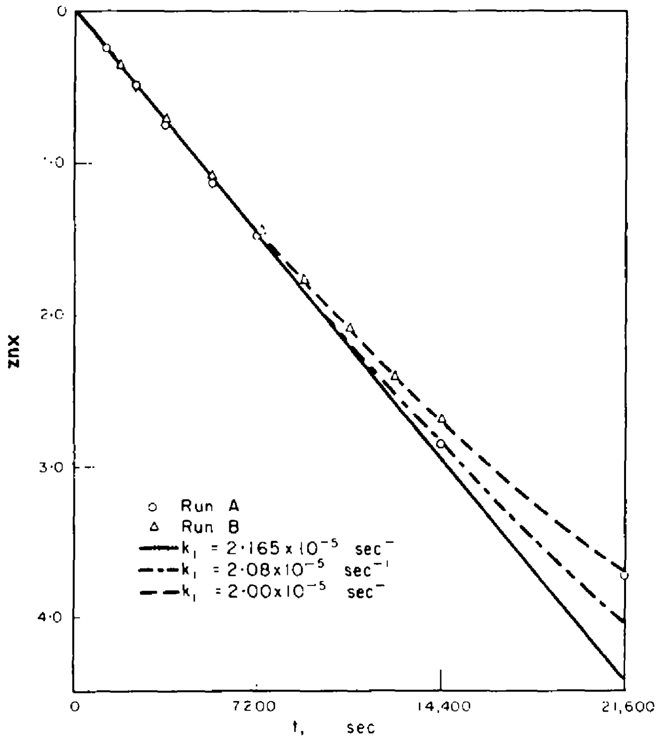

FIG. 5. Calculated acetolysis curves for *cis-trans*-hydrindyl tosylate and experimental data (65°).

and *cis-trans*-hydrindyl tosylates had IR spectra identical to that of pure bicyclononyl tosylate and could not be separated by fractional crystallization or chromatography. It was finally possible to determine the compositions of the mixtures by NMR spectroscopy; as the spectra were not completely resolved, however, the compositions are accurate only to about 3%. *trans-trans* Tosylate would have been detectable in the IR spectra of the recovered mixtures had it been present.

Pure bicyclononyl tosylate was acetolyzed for 3·2 hours, a time sufficient to reach the steady-state composition; the tosylate was recovered and lyophilized to remove hydrocarbon and acetate products; removal was complete, as shown by the IR and NMR spectra. The tosylate thus recovered had a NMR spectrum and melting point identical to those of a mixture of 84% bicyclononyl and 16% *cis-trans*-hydrindyl tosylates. The acetolysis of a sample of the tosylate mixture recovered after the steady-state composition had been reached followed the first order rate law.

Determination of the composition of recovered tosylate from the acetolysis of *cis-trans*-hydrindyl tosylate was very difficult, since the reaction had to be carried to at least 98% completion to permit even a chance of detecting bicyclononyl tosylate.

TABLE 5. CALCULATED AND OBSERVED COMPOSITIONS OF RECOVERED TOSYLATE MIXTURES

Starting tosylate	$k_3 \times 10^5$ sec^{-1}	Reaction time, hr	Bicyclononyl	Composition of recovered tosylate, %	*cis-trans* Hydrindyl	Calculated total tosylate remaining, % of initial
Bicyclononyl	0·064	3·2	84·3	V	15·7	65
Bicyclononyl	0·022	3·2	85·8	V	14·2	65
Bicyclononyl	0·000	3·2	86·3	V	13·7	65
Bicyclononyl (observed)	—	3·2	84 ± 3	V (obs.)	16 ± 3	
cis-trans-	0·064	8·0	70	XXIII	30	1·1
Hydrindyl	0·022	8·0	50	XXIII	50	0·6
Hydrindyl	0·000	8·0	0	XXIII (obs.)	100	0·3
Hydrindyl (observed)	—	8·0	<50		>50	∼0·5

The tosylate recovered after eight hours and recrystallized once from pentane had a melting point slightly lower than that of pure *cis-trans*-hydrindyl tosylate (and the same solubility and crystallization behavior), and therefore could not have contained large amounts of the less-soluble and higher-melting bicyclononyl tosylate. NMR spectroscopy could not be used with the available quantities of material. Calculated and observed compositions of tosylate recovered from the acetolysis of bicyclononyl and *cis-trans*-hydrindyl tosylates are listed in Table 5. The figures are consistent with the postulated reaction mechanism, and suggest that the upper limit on k_3 should be reduced to $0{\cdot}02 \times 10^{-6}$ sec^{-1} or below. Fig. 6 summarizes the most probable rate constants for each of the reactions in the proposed scheme.

The kinetic behavior and the products of acetolysis of *exo*-bicyclo[3.2.1]octyl-8-tosylate (IV) parallel almost exactly those of bicyclo[3.3.1]nonyl-9-tosylate (V). Unfortunately, IV is less readily accessible than V, and the corresponding product of ion-pair return, *cis-trans*-bicyclo[3.3.0]octyl-2-tosylate, can be made only with

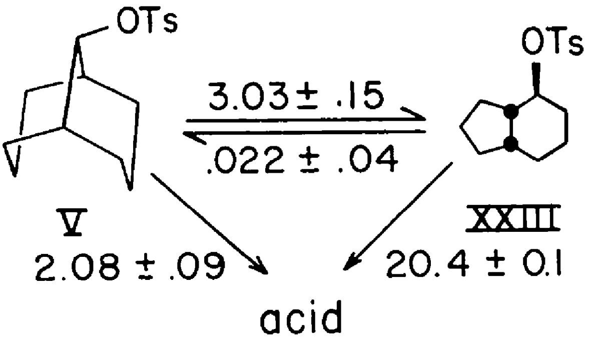

Fig. 6. Most probable rate constants ($\times 10^6$ sec^{-1}) for acetolysis of the tosylates at 65°.

difficulty.[3] It was therefore not possible to investigate the mechanism of solvolysis of IV in the same detail as that of V; it seems likely, however, that the two mechanisms are quite similar.

The relative acetolysis rates of the three bridged bicyclic tosylates III, IV, and V are summarized in Table 6 with some other relevant rates from the literature. The most striking feature of the data is the trend in the rates. Norbornyl-7-tosylate (I) reacts extremely slowly; *endo*-bicyclo[3.2.1]octyl-8-tosylate (III) much faster, but still very slowly; adamantyl-2-tosylate (XXVI), *exo*-bicyclo[3.2.1]octyl-8-tosylate (IV), and bicyclo[3.3.1]nonyl-9-tosylate (V) all solvolyze at rates not far different from that of cyclohexyl tosylate (II). Furthermore, III, which reacts with first-order kinetics with predominant inversion of configuration, has a rate very much slower than that of its epimer, IV, which reacts with a drifting rate and predominant rearrangement, all the unrearranged product being of retained configuration.[29] In the same way, XXVI, which on acetolysis produces only 2-adamantyl acetate with first-order kinetics,[2] has a smaller rate than the closely related V, which reacts with a drifting rate to give largely rearranged product.

Both with regard to products and in kinetic behavior, IV and V behave in a very similar fashion. This behavior provides a further argument in favor of the configuration assigned[3,7] to III and IV, since the arrangement of atoms behind the leaving group, identical in IV and V, would be expected to control carbon participation. Rearrangement of the two-carbon bridge in either I or III would give an ion having some of the strain of a four-membered ring; if XXVI were to rearrange, the favorable adamantane geometry would be lost, and the ion would be badly strained. Rearrangement of the three-carbon bridges of IV and V, on the other hand, produces no obvious increase in strain and may cause strain relief. The kinetic data imply that the rates of acetolysis of IV and V are anchimerically accelerated by carbon participation; there is no evidence for acceleration in the rates of I, II, III, or XXVI.

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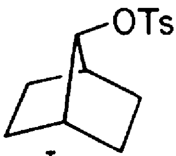
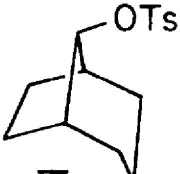
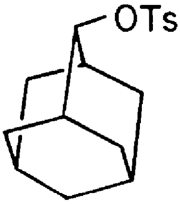
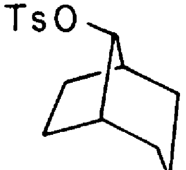
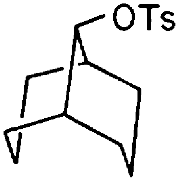
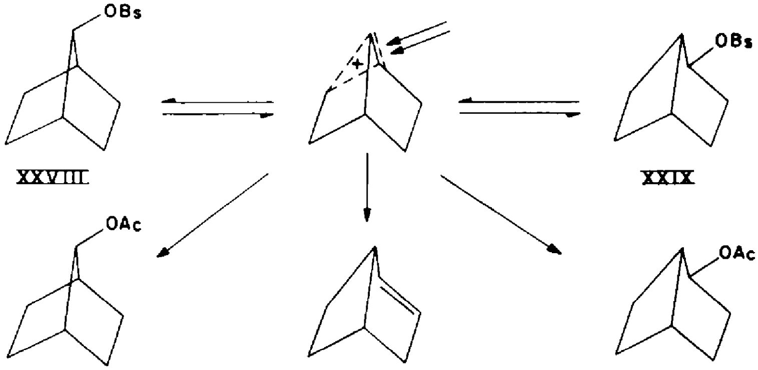
[29] The solvolytic behavior of III and IV is closely paralleled by that of the corresponding Δ^3-bicyclo [3.2.1]octenyl-8-tosylates, where the rate of the *anti* (*exo*) isomer shows an anchimeric acceleration of five powers of ten compared to the inert *syn* (*endo*) isomer: see N. A. LeBel and L. A. Spurlock, *Tetrahedron* **20**, 215 (1964). We are indebted to Professor LeBel for an advance copy of his manuscript. The solvolytic behavior of *endo*-bicyclo[3.2.1]octyl-8-bromide has also been reported and is analogous in product and rate to the behavior of III: N. A. LeBel, J. E. Huber, and L. H. Zalkow, *J. Amer. Chem. Soc.* **84**, 2226 (1962).

TABLE 6. RATES AND PRODUCTS OF ACETOLYSIS OF TOSYLATES

Compound	Relative rate, 25°	Product description	Reference
 I	$9{\cdot}1 \times 10^{-8}$	Mainly unrearranged, small amount rearranged, mostly acetate.	1[b,c] 20
 III	$7{\cdot}8 \times 10^{-5}$	Mainly unrearranged and inverted, trace retained; much rearranged, mostly acetates.	
 XXVI	$6{\cdot}6 \times 10^{-2}$	Entirely unrearranged.	2
 IV	$6{\cdot}1 \times 10^{-1}$ (final rate)	Mainly rearranged, mostly olefin, some acetates; small amount unrearranged, entirely retained.	
 V	$3{\cdot}0$ (final rate)	Mainly rearranged, mostly olefin, some acetates; small amount unrearranged.	
 II	(1·00)	Mainly olefin, some acetate	30

[30a] J. D. Roberts and V. C. Chambers, *J. Amer. Chem. Soc.* 73, 5034 (1951); [b] S. Winstein, B. K. Morse, E. Grunwald, H. W. Jones, J. Corse, D. Trifan and H. Marshall, *Ibid.* 74, 1127 (1952); [c] H. C. Brown and G. Ham, *Ibid.* 78, 2735 (1956).

The non-classical ion XXVII could be intermediate between V and *cis-trans*-hydrindyl tosylate (XXIII), and an analogous ion between *exo*-bicyclo[3.2.1]octyl-8-tosylate (IV) and the corresponding rearranged tosylate. Such ions would conveniently account for the observed rate accelerations and for the stereospecific formation of *exo*-bicyclo[3.2.1]octyl-8-acetate from IV (although the bicyclo[3.2.1]-octane system has a known preference for *exo* attack at the 8-position[3]). These ions, however, are not sufficient to account for all the products, since non-classical ions would be expected to react stereospecifically with solvent (as, for example, in the interconversion of norbornyl-7-brosylate (XXVIII) and *cis-trans*-bicyclo[3.2.0]heptyl-2-brosylate (bromobenzenesulfonate XXIX[20]). The formation of *cis-cis*-hydrindyl acetate and hydride-shift products in the bicyclononane series, and of *cis-cis*-bicyclo-[3.3.0]octyl-2-acetate in the bicyclooctane series, clearly requires other ions, such as XXX and XXXI in the bicyclo nonane series, and an ion corresponding to XXX in the bicyclooctane series.[31] The traces of *trans-trans*-hydrindyl acetate might arise from a second hydride shift to the ion XXXII (unlikely, since a tertiary ion would have to yield a secondary one), or via a new bridged ion, XXXIII.



XXVIII

XXIX

The above scheme is the simplest which can account for the observed products, if the usual assumption is made that the non-classical ion XXVII can react with solvent only from the side opposite to the bridging group. A similar scheme has recently been proposed to account for the lack of stereospecificity in the deamination of the 2-aminomethylnorbornanes, and in the acetolysis of the corresponding brosylates.[32]

The various factors which could contribute to the unreactivity of norbornyl-7-tosylate (I) have been lucidly reviewed and discussed by Schleyer and Nicholas in the light of the solvolysis data on adamantyl-2-tosylate; they reached the conclusion that the only important factor is the small angle at the 7-position in norbornane.[2] In compounds where the C—C—C angle at the leaving group is constrained to be less than the normal tetrahedral angle, reactions in which the transition state is normally of nearly trigonal hybridization should be very slow, since there should be a large

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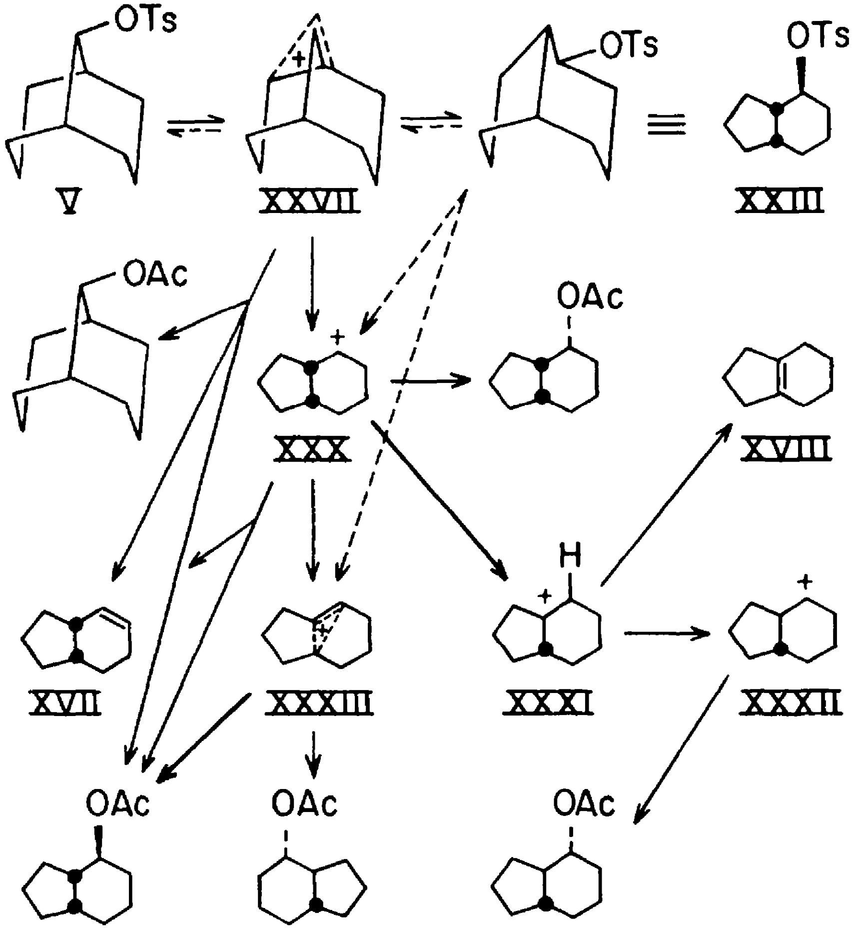
[31] Behavior very similar to that of bicyclo[3.3.1]nonyl-9-tosylate and of *cis-trans*-hydrindyl tosylate in solvolysis has recently been observed in the acetolysis of arenesulfonates of *anti*-3-oxabicyclo-[3.3.1]nonan-9-ol and *trans*-6-hydroxy-*cis*-3-oxabicyclo[4.3.0]nonane. L. J. Dolby and M. J. Schwarz, *J. Org. Chem.* **28,** 1456 (1963).

[32a] J. A. Berson and P. Reynolds-Warnhoff, *J. Amer. Chem. Soc.* **84,** 682 (1962); [b] J. A. Berson, P. Reynolds-Warnhoff and D. Willner, *18th National Organic Symposium* of the American Chemical Society, *Abstracts* p. 23 (1963).



increase in the total angle strain (I-strain[33]) in the transition state as compared to the ground state. The bridge angle in norbornane is known to be about 96°,[34] which is 13° less than the normal tetrahedral angle and 24° less than the normal trigonal angle. In bicyclo[3.2.1]octane the angle has not been measured, but models show that some constraint is present, although considerably less than in norbornane.[35] In adamantane a tetrahedral angle is unstrained, but a trigonal atom is somewhat constricted, which causes adamantyl tosylate to solvolyze more slowly than cyclohexyl tosylate, where both ground and transition states are virtually strainless.[2,36] The rate of *endo*-bicyclo [3.2.1]octyl-8-tosylate is intermediate between that of norbornyl and adamantyl tosylates, just as would be predicted if angle strain is the most important factor governing reactivity in this series. Neither the rate of adamantyl tosylate nor that of

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[33] H. C. Brown, *J. Chem. Soc.* 1248 (1956).

[34a] A. F. Berndt, Ph.D. Thesis, California Institute of Technology (1957); [b] C. H. Wong, Ph.D. Thesis, California Institute of Technology (1957).

[35] The angle at the 8-position of bicyclooctane has been calculated to be intermediate between that of norbornane and that of adamantane: J. B. Hendrickson, private communication. See J. B. Hendrickson, *J. Amer. Chem. Soc.* **83**, 4537 (1961).

[36] The progression of strain in tetrahedrally and trigonally hybridized derivatives of the above series

bicyclooctyl tosylate would have been predicted by any of the previous explanations — —steric inhibition of hyperconjugation[1a,c] or of solvation,[1c,e] or conformational hindrance to ionization.

Streitwieser has suggested that in systems where bond angles are less than normal, rehybridization takes place such that the carbon-carbon bonds receive an unusual amount of p-character, thus making partial localization of a p-orbital in the transition state more difficult.[38] The C_{13}—H coupling constant at the 7-position of norbornadiene (which has a C—C—C angle nearly the same as that in norbornane[1c,34]) indicates that there is indeed a marked increase in s-character in the C—H bonds,[39] implying increased p-character in the C—C bonds.[40] The angle strain and hybridization descriptions are probably equivalent,[41] and both rationalize the data equally well.

EXPERIMENTAL

M.p.s are corrected; b.p.s are uncorrected. Microanalyses were by Scandinavian Microanalytical Laboratory, Copenhagen; by A. Bernhardt, Max-Planck Institut, Mülheim (Ruhr); and by C. Daesslé, Montreal.

Aminoketones VI *and* VII

2-N-Morpholinobicyclo[3.2.1]octan-8-one (VI) and 2-N-morpholinobicyclo[3.3.1]nonan-9-one (VII) were prepared by the method of Stork[4] from the redistilled morpholine enamines, made respectively from cyclopentanone and cyclohexanone by the procedure of Hünig.[42] VI (76%) had b.p.$_{0\cdot2}$ 127–140°, n_D^{25} 1·5176 and $\lambda_{c=o}$ (CHCl$_3$) 5·72 μ; VII (64%) had b.p.$_1$ 141–147°, n_D^{25} 1·5182 and $\lambda_{c=o}$(CHCl$_3$) 5·84 μ.[43] Both VI and VII (viscous pale yellow oils, rapidly darkened by exposure to air) were easily prepared in kilogram quantities. Attempts to eliminate the morpholino group directly from the aminoketones were only partly successful: Δ^2-bicyclo[3.3.1]nonen-9-one (XI) was formed in roughly 25% yield on pyrolysis of the N-oxide of VII, but Δ^2-bicyclo[3.2.1]octen-8-one (X) was not formed from the N-oxide of VI. As the pyrolysis of the corresponding ketal-N-oxides was found to proceed smoothly, attempts to improve the direct route were abandoned.

Ketals of VI *and* VII

The ethylene ketals were made from aminoketones VI and VII by the following procedure. One mole of the aminoketone was dissolved in 10 moles ethylene glycol, and 1·1 moles

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of compounds is illustrated by the ease of formation of semicarbazones from the ketones, a reaction in which a tetrahedral intermediate must be dehydrated to form the trigonal product.[37] Norton observed that 7-norbornanone does not form a semicarbazone at all under the normal conditions (and even forms a stable hydrate);[1e] bicyclo[3.2.1]octan-8-one requires several days for complete semicarbazone formation; in unstrained compounds and in bicyclo[3.3.1]nonan-9-one, where the angle must be the same as in adamantanone, the reaction is very much faster.

[37] W. P. Jencks, *J. Amer. Chem. Soc.* **81**, 475 (1959).

[38] A. Streitwieser, Jr., *Chem. Revs.* **56**, 571 (1956).

[39] N. Muller and D. E. Pritchard, *J. Chem. Phys.* **31**, 768, 1471 (1959).

[40] C. S. Foote, *Tetrahedron Letters* No. 9, 579 (1963).

[41] Norton's similar argument was based on the idea that the C—C bond shortening which would be expected in the transition state to a carbonium ion would be resisted more in strained systems than in unstrained ones.[1e] It is difficult to separate bond shortening, angle strain, and hybridization factors.

[42a] S. Hünig, E. Benzing, and E. Lücke, *Chem. Ber.* **90**, 2833 (1957); [b] S. Hünig and W. Lendle, *Ibid.* **93**, 909 (1960).

[43] A satisfactory elemental analysis for this compound is described in D. M. Gale, Ph.D. Thesis, Massachusetts Institute of Technology (1963).

toluenesulfonic acid monohydrate[44] were added. The solution was heated to 80–85° for 2 hr, then cooled and poured into a well-stirred solution of 3 moles KOH in 1 l. ice water. The suspension was diluted with water to 3 l. and extracted continuously overnight with ether. The ether was washed twice with an equal volume of water and once with brine, then evaporated. The residue was distilled, yielding the pure ketal. The ketal was prepared in this way from VI in 85% yield, and had b.p.$_{0\cdot2}$ 114–122°, n_D^{25} 1·5130; that from VII was obtained in 81% yield and had b.p.$_{0\cdot5}$ 134–138°.[43] Both *ketals* were very viscous pale yellow oils, which exhibited complex absorption near 10 μ in the IR; both had only a trace of absorption in the carbonyl region.

Δ^2-*Bicyclo*[3.2.1]*octen-8-ethylene ketal* (VIII)

The aminoketal prepared from VI, 373 g (1·48 moles), was dissolved in 800 ml methanol to which 360 g (3·2 moles) 30% H_2O_2 were added. As reaction at room temp proved to be extremely slow, the solution was refluxed until it became neutral to pH 6·6–8·0 indicator paper (6 hr). After the solution had cooled, platinum black was added to decompose excess peroxide and the solution stirred for 2 days and filtered. After removal of solvent and most of the water (65°, 11 mm), the residue, crystalline N-oxide, was pyrolyzed[45] in two portions at 150° and 1 mm. The product which had distilled into a Dry-ice-cooled trap was dissolved in ether and extracted with 6 N HCl, 10% Na_2CO_3 aq., and with water and brine. After the solvent had been removed, the residue was distilled, yielding 77 g (0·46 mole, 31%) Δ^2-*bicyclo*[3.2.1]*octen-8-ethylene ketal* (VIII), a colorless oil of b.p.$_{12}$ 97–102°, which had significant IR absorption bands at 3·30 μ, 6·10 μ, 9–10 μ (complex), 14·5 μ and 14·9 μ. An analytical sample was purified by gas chromatography (Found: C, 72·52; H, 8·47. $C_{10}H_{14}O_2$ requires: C, 72·26; H, 8·49%). The yield of this reaction decreased with increasing reaction scale; small-scale reactions gave yields of over 50%.

Δ^2-*Bicyclo*[3.2.1]*octen-8-one* (X)

Δ^2-Bicyclo[3.2.1]octen-8-ethylene ketal (VIII), 5·0 g (0·030 mole), 30 ml 2 N HCl, and 20 ml methanol were refluxed 2 hr. The solution was cooled, poured into 50 ml water, and extracted 3 times with ether. The combined ether extracts were washed 3 times with water and once with brine, then dried ($CaCl_2$). Evaporation of the ether and distillation of the residue with a short-path still (130°, 25 mm) gave 3·1 g (0·025 mole, 85%) Δ^2-*bicyclo*[3.2.1]*octen-8-one* (X), contaminated with much ketal. The ketone was liquid, even after purification by gas chromatography, and had significant IR bands (CCl_4) at 3·30 μ, 5·77 μ, 6·10 μ, 14·45 μ and 15·00 μ.

The formation of the semicarbazone by the usual procedure required 6 hr for completion. The flat needles were recrystallized from ethanol–water to a constant m.p. of 189·2–190·2°.

The 2,4-dinitrophenylhydrazone was made by the usual procedure and recrystallized from ethyl acetate–ethanol to a constant m.p. of 176·4–177·2°. (Found: C, 55·71; H, 4·84; N, 18·05. $C_{14}H_{14}N_4O_4$ requires: C, 55·62; H, 4·67; N, 18·54%).

Bicyclo[3.2.1]*octane-8-one* (XII)

Crude Δ^2-bicyclo[3.2.1]octen-8-one, 0·6 g (4·9 mmoles), was hydrogenated on a platinum catalyst in 10 ml methanol. After the uptake of 5 mmoles hydrogen, the reaction became very slow. The solution was filtered and the solvent evaporated, yielding a solid product which was sublimed. The yield was 0·35 g (2·8 mmoles, 58%) of crystalline solid, contaminated with a considerable amount of the oily ketal. A sample was purified by gas chromatography, and had m.p. 140–141° (reported for bicyclo[3.2.1]octan-8-one: 141·5–143·2°,[8] 134–136°[46]). The IR spectrum of the product was identical with that of an authentic sample;[5] the two samples were not separated by gas chromatography.

The formation of the semicarbazone was complete only after 3 days at room temp; the product was recrystallized to the constant m.p. of 189·8–190·5°d (reported:[46] 183–184°). The 2,4-dinitrophenylhydrazone formed instantly; after recrystallization, the flat needles had the constant m.p.

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[44] Use of less than one mole of acid produced no conversion.

[45] A. C. Cope, T. T. Foster, and P. H. Towle, *J. Amer. Chem. Soc.* **71**, 3929 (1949). In two large-scale pyrolyses, control of the reaction was lost and decomposition became quite violent.

[46] R. Mayer, G. Wenschuh and W. Töpelmann, *Chem. Ber.* **91**, 1616 (1958).

175·4–176·2° (reported:[46] 175–176°); the m.p. of a mixture with an authentic sample[5] of m.p. 175–175·4° was 175·3–175·8°. (Found: C, 55·35; H, 5·37; N, 18·17. Calc. for $C_{14}H_{16}N_4O_4$: C, 55·25; H, 5·30; N, 18·41%).

Reductions of X *and* XII

The following reductions were carried out in a search for a route to *exo*-bicyclo[3.2.1]octan-8-ol (XV). The product mixtures, containing varying amounts of *endo* and *exo* alcohols (XIV and XV), were analyzed by gas chromatography; at 95° on a six-foot column of 20% TCEP on Chromosorb W,[10] XIV has a relative retention time of 107, and XV, 100. The results were confirmed by examination of the IR spectra of the mixtures: XII has bands at 9·08 μ, 9·45 μ, and 9·70 μ, which clearly differentiate it from XV, which has bands at 9·10 μ, 9·28 μ and 9·63 μ.

I. *Reductions of bicyclo*[3.2.1]*octan-8-one* (XII)

a. Repetition of the reported[8] reductions of XII with platinum in acetic acid, and with $NaBH_4$ in pyridine confirmed that the former reagent produced exclusively *endo* alcohol (XIV), and that the latter produced a 64:36 mixture of XIV and XV.

b. Bicyclo[3.2.1]octan-8-one (XII), 2·0 g (0·016 mole) and 300 mg (8·1 mmoles) $NaBH_4$ were allowed to react in 50% aq. methanol at 0° for 10 hr. The solution was diluted and extracted with ether; the extracts were washed with water and brine and filtered through $MgSO_4$. Evaporation of the ether gave pure *endo*-bicyclo[3.2.1]octan-8-ol (XIV); no trace of the *exo* isomer was detected.

II. *Reductions of* Δ^2*-bicyclo*[3.2.1]*octen-8-one* (X)

Δ^2-Bicyclo[3.2.1]octen-8-one (X) was reduced with a number of reagents; the crude products from the reductions were hydrogenated with platinum and acetic acid, the amount of hydrogen required for saturation of the double bond being absorbed in each case.

a. *With sodium borohydride in methanol.* Δ^2-Bicyclo[3.2.1]octen-8-one (X), 0·5 g (4·1 mmoles) and 60 mg (1·6 mmoles) $NaBH_4$ were allowed to stand overnight in 14 ml 50% aq methanol. Water was added, and the solution extracted 3 times with ether; the ether extracts were washed twice with water and evaporated. The product, after hydrogenation, was a mixture of 76% *endo* and 24% *exo*-bicyclo[3.2.1]octan-8-ol (XIV and XV).

b. *With sodium borohydride in pyridine.* Δ^2-Bicyclo[3.2.1]octen-8-one (X), 200 mg (1·6 mmoles), and 100 mg $NaBH_4$ (2·7 mmoles) were heated on the steam bath in 13 ml dry pyridine for 20 hr. After the reaction mixture had cooled, 10 ml 5% NaOH aq. were added. The solution was stirred for 2 hr at room temp, poured into water, and extracted twice with ether. The ether extracts were washed 3 times with 6 N HCl, once each with water, 5% $NaHCO_3$ aq., and brine, then dried (Na_2SO_4). The product, after hydrogenation, was shown by its IR spectrum to consist largely of *endo*-bicyclo-[3.2.1]octan-8-ol.

c. *With sodium in isopropanol.* Δ^2-Bicyclo[3.2.1]octen-8-one (X), 1·0 g (8·2 mmoles), was dissolved in 25 ml isopropanol, and the solution heated to reflux. Clean sodium, 1·0 g (0·043 moles) was added in small pieces during 5 min. The solution was refluxed until all the sodium had reacted (10 min), then poured into water and extracted with ether. The extracts were washed with water and brine, dried ($MgSO_4$) and evaporated. Hydrogenation of the product gave a 70:30 mixture of *endo-* and *exo*-bicyclo[3.2.1]octan-8-ols (XIV and XV).

endo-*Bicyclo*[3.2.1]*octan-8-ol* (XIV)

The following procedure allowed the most convenient preparation of XIV. Δ^2-Bicyclo[3.2.1]-octen-8-ethylene ketal (VIII), 77 g (0·46 mole), was dissolved in 300 ml acetic acid containing 50 ml water and 2 ml conc. HCl. The solution was hydrogenated (Parr apparatus at 3 atm); after a total uptake of 0·78 moles of hydrogen (85% of that required for complete reduction of the double bond and the ketone), the reaction ceased. Addition of fresh catalyst caused only slight further uptake. The solution was filtered, poured into 750 ml water and extracted with pentane. The pentane was distilled off through a short Vigreux column (to avoid losses of the volatile alcohol), and the residue dissolved in 100 ml methanol with 10 g (0·18 mole) KOH. The solution was refluxed 1 hr to saponify any acetate, then cooled, poured into water, and extracted with pentane. The pentane extracts were washed with water and brine, and filtered through $MgSO_4$. The pentane was distilled off through a Vigreux column, and the residue sublimed to give 50·0 g (0·40 mole, 87%) of soft crystals of *endo*-bicyclo[3.2.1]octane-8-ol (XIV). The *exo* isomer was shown to be absent by gas chromatography and IR spectroscopy.

A sample of the alcohol was recrystallized from pentane to the constant m.p. of 200·2–201·0° (reported:[8] 199–200·5°).

The tosylate (III) was made in 74% yield by the method of Tipson;[47] two recrystallizations from ligroin gave a constant m.p. of 75·4–76·2° (reported:[8] 75·7–76·1°). The saponification equivalent, from an infinity titer in the acetolysis, was 282·5 g (calc: 280·4 g).

Acetolysis of endo-*bicyclo*[3.2.1]*octyl-8-tosylate* (III)

A solution of 1·0 g (3·6 mmoles) *endo*-bicyclo[3.2.1]octyl-8-tosylate (III) and 5·0 ml of a 1 M solution (in dry acetic acid) of potassium acetate was diluted to 50 ml with dry acetic acid and heated to 150° for 30 hr (10 half lives). The reaction mixture, which contained a considerable amount of dark, insoluble material, was poured into water and extracted with pentane. The pentane extracts were washed with water and filtered through $CaCl_2$. A small sample of the pentane solution was analysed by gas chromatography (silicone oil, 131°) and found to contain, besides solvent, a mixture of a hydrocarbon (23%) and acetates (77%). A sample of the hydrocarbon was collected from the gas chromatograph and had a relative retention time and IR spectrum identical to those of a sample of *cis*-Δ^2-bicyclo[3.3.0]octene produced in the acetolysis of *exo*-bicyclo[3.2.1]octyl-8-tosylate (IV) and described more fully below. Traces of an unidentified hydrocarbon were also formed.

The pentane was evaporated from the remainder of the extracts and the residue dissolved in a solution of 1·0 g (0·017 mole) KOH in 10 ml methanol. The solution was refluxed for 1 hr and poured into water. The resulting mixture was extracted with pentane; the pentane extracts were washed with water and filtered through $CaCl_2$. The pentane was distilled off through a Vigreux column; the alcohols in the residue were separated by gas chromatography (TCEP column,[10] 95°) and identified by comparison of relative retention times and IR spectra with those of authentic samples.[5] The alcohols present and their relative amounts (based on total acetolysis product) were: *exo*-bicyclo[3.2.1]octan-8-ol (XV, 51%, rel. ret. time 100); *cis-trans*-bicyclo[3.3.0]octan-2-ol (21·8%, rel. ret. time 93, not separated by gas chromatography from an authentic sample[5]); *cis-cis*-bicyclo[3.3.0]octan-2-ol (2·2%, rel. ret. time 80); and *endo*-bicyclo[3.2.1]octan-8-ol (XIV, approx. 2%, rel. ret. time 107, poorly resolved from XV).

exo-*Bicyclo*[3.2.1]*octan-8-ol* (XV)

Although XV could be prepared by acetolysis of the *endo* tosylate, the usual reaction conditions required inconveniently long reflux periods; the following procedure shortened the reaction times considerably.

To a solution (b.p. 180°) of 280 g (2·9 moles) potassium acetate in 250 ml (4·3 moles) acetic acid were added 21 g (0·075 mole) *endo*-bicyclo[3.2.1]octyl-8-tosylate (III). The solution was refluxed for 2 hr, then cooled and poured into water. The solution was extracted with pentane, and the pentane extracts washed with water and evaporated. The residue was dissolved in 50 ml methanol containing 5 g (0·089 mole) KOH, and the solution refluxed 1 hr. The solution was poured into water and extracted with pentane; the pentane extracts were washed with water and filtered through Na_2SO_4. The pentane was distilled off through a Vigreux column, and the residue sublimed to yield 6·0 g (0·048 mole, 64% crude yield) of a solid alcohol mixture which was shown by gas chromatography to contain 71% of the desired *exo*-bicyclo[3.2.1]octan-8-ol (XV). Further purification was most simply accomplished by recrystallization of the tosylate.

A sample of the sublimate was recrystallized from pentane to the constant m.p. 192·2–192·5° (reported[8] for XV: 191·2–192·4). The material was shown to be identical to an authentic sample[5] of XV by means of its IR spectrum and gas chromatographic behavior.

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[47] R. S. Tipson, *J. Org. Chem.* **9**, 235 (1944).

The tosylate (IV) was made from 5·65 g (0·045 mole) of the crude sublimate by Tipson's procedure,[47] and recrystallized from ligroin to yield 7·25 g (0·026 mole, 58%), with the constant m.p. 77·4–78·6° (reported[8] 78·4–79·0°). The saponification equivalent (from an infinity titer in the acetolysis) was 282·5 g (calc 280·4 g).

A sample of recrystallized *exo* alcohol (149 mg, 1·2 mmoles) was oxidized with 108 mg (1·1 mmole) chromic anhydride in 2·0 ml pyridine. The product was extracted from aqueous acid with pentane; the pentane was washed with acid and water, and evaporated. The IR spectrum of the sublimed product showed it to consist of bicyclo[3.2.1]octan-8-one, together with a small amount of starting alcohol.

Acetolysis of exo-*bicyclo*[3.2.1]*octyl-8-tosylate* (IV)

exo-Bicyclo[3.2.1]octyl-8-tosylate (IV), 2·55 g (9·1 mmoles), and 10 ml 1·0 M potassium acetate solution were dissolved in 90 ml acetic acid. The solution was heated to 100° for 3 hr (roughly 7 half-lives). The reaction mixture was cooled, poured into water, and extracted with pentane. The pentane extracts were washed with water. A sample of the pentane solution was shown by gas chromatography (silicone oil, 120°) to be a mixture of 77% hydrocarbons and 23% acetates. The pentane was distilled off through a Vigreux column, and the residue distilled to give a hydrocarbon and an acetate fraction.

I. *The hydrocarbon fraction.* The hydrocarbon fraction, which distilled at a bath temp of 125° at 1 atm, weighed 605 mg (5·6 mmoles, 62%). Gas chromatography (silicone oil, 55°) showed the fraction to consist of two hydrocarbons: one (rel. ret. time 100) made up 98·5% of the mixture; the other (rel. ret. time 112) made up only 1·5%, and was not further investigated.

The major component of the hydrocarbon mixture had an IR spectrum identical to that of *cis*-Δ^2-bicyclo[3.3.0]octene.[6,11] The NMR spectrum of this hydrocarbon had a complex peak at 4·25 τ, with an area corresponding to two hydrogens.

A sample of the hydrocarbon was purified for analysis by gas chromatography (Found: C, 88·41; H, 11·17. Calc. for C_8H_{12}: C, 88·82; H, 11·18%).

The hydrocarbon fraction (170 mg, 1·6 mmoles, crude *cis*-Δ^2-bicyclo[3.3.0]octene) was stirred overnight with 85 mg (0·67 mmoles) K_2CO_3 in 65 ml (equiv. to 1·6 mmoles) of a solution of 20·9 g $NaIO_4$ and 250 mg $KMnO_4$ in 1 l. water (Lemieux' reagent[48]). A few ml 10% Na_2CO_3 were added to the solution, which was then extracted with pentane. The aqueous layer was acidified and extracted with ether; the ether was washed with brine and evaporated. The residue, 130 mg (0·76 mmole, 47%) *cis*-cyclopentane-1-carboxy-2-acetic acid, was recrystallized from benzene-ligroin to the constant m.p. of 91–94° (reported: 89°,[12c] 91–93·5° [11]). The dianilide melted at 232–234° (reported:[12c] 234°).

II. *The acetate fraction.* The acetate fraction from the acetolysis distilled at 12 mm and a bath temp of 140° (218 mg, 1·3 mmoles, 14%). Of this fraction 137 mg (0·82 mmoles) were refluxed for 1 hr in 3 ml methanol containing 2 pellets KOH. The reaction mixture was poured into water and extracted with pentane. The extracts were washed with water and filtered through cotton. The pentane was distilled off through a Vigreux column, and the alcohol mixture separated by gas chromatography[10] into its components, identified by comparison of IR spectra and relative retention times with those of authentic samples.[5] The relative amounts are based on total acetolysis product. The components were identified as: *cis-trans*-bicyclo[3.3.0]octan-2-ol (10·8%, rel. ret. time 95, not separated from an authentic sample by gas chromatography); *exo*-bicyclo[3.2.1]octan-8-ol (XV, 7·1%, rel. ret. time 100, not separated from authentic material); and *cis-cis*-bicyclo[3.3.0]-octan-2-ol (5·3%, rel. ret. time 83); no *endo*-bicyclo[3.2.1]octan-8-ol was detected, although as much as 1% might have escaped detection, as this alcohol is not well resolved from the *exo* isomer.

Δ^2-*Bicyclo*[3.3.1]*nonen-9-ethylene ketal* (IX)

To 194 g (0·73 mole) ethylene ketal prepared from 2-N-morpholinobicyclo[3.3.1]nonan-9-one (VII) were added an equal volume methanol and 120 g (1·05 mole) 30% H_2O_2. The solution was refluxed 2 hr,[49] and 110 g (0·97 mole) additional peroxide added. The solution was again refluxed 2 hr, then cooled to room temp, stirred for 2 days with platinum black, and filtered. The solvent

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[48] R. U. Lemieux and E. von Rudloff, *Can. J. Chem.* **33**, 1701, 1710 (1955).

[49] The reaction is extremely slow at room temperature.

was removed at 80° in vacuum. The residue, the N-oxide (which slowly crystallized), was pyrolyzed for 2 hr at 140–150° (oil bath) and 1 mm, then at 160° for a further hr. The distillate was poured into 6 N HCl and extracted with ether; the extract was washed with dil. HCl, 10% Na_2CO_3 aq., and water. The ether was evaporated and the residue distilled, yielding 69 g (0·38 mole, 53%) of *Δ^2-bicyclo*[3.3.1]*nonen-9-ethylene ketal*, a colorless oil, b.p.$_{12}$ 98–109°. The IR spectrum had significant bands at 3·54, 6·07, 8–10 (complex) and 14·30 μ. A sample was purified by gas chromatography. (Found: C, 73·24; H, 8·86; $C_{11}H_{16}O_2$ requires: C, 73·30; H, 8·95%).

Δ^2-*Bicyclo*[3.3.1]*nonen-9-one* (XI)

Δ^2-Bicyclo[3.3.1]nonen-9-ethylene ketal (IX), 0·50 g (2·8 mmoles), was dissolved in 4 ml methanol and 2 ml water, and one drop conc. HCl was added. The solution was allowed to stand 3 days, then poured into 5 ml water and extracted with ether. The ether was washed with bicarbonate, water and brine, dried (Na_2SO_4), and evaporated. The crude product, which contained considerable ketal, weighed 0·39 g (2·8 mmoles, 100%). A sample was purified by gas chromatography to give soft crystals with m.p. 98–99°. The IR spectrum (CCl_4) had significant bands at 3·27, 5·77, 6·07, 14·40 and 14·60 μ. *Δ^2-Bicyclo*[3.3.1]*nonen-9-one* could also be made in 25% yield by direct pyrolysis of the N-oxide of aminoketone VII. The semicarbazone (which formed at a normal rate) was recrystallized from ethanol–water to give colorless needles with the constant m.p. 201–201·5°. (Found: C, 61·71; H, 7·50; N, 21·68; $C_{10}H_{15}N_3O$ requires: C, 67·15; H, 7·82; N, 21·75%).

The 2,4-dinitrophenylhydrazone was recrystallized from ethyl acetate–ethanol to give orange needles of constant m.p. 194·5–195·6°. (Found: C, 56·82; H, 4·87; N, 17·82; $C_{15}H_{16}N_{11}O_7$ requires: C, 56·95; H, 5·10; N, 17·71%).

Bicyclo[3.3.1]*nonan-9-one* (XIII)[9]

Crude Δ^2-bicyclo[3.3.1]nonen-9-one, 8·0 g (0·059 mole), was hydrogenated (palladium–charcoal) in methanol. After slightly more than 0·059 mole hydrogen had been taken up, the solution was filtered, the methanol evaporated, and the residue sublimed (80°/12 mm) to give 6·7 g (0·048 mole, 82%) of colorless waxy crystals of *bicyclo*[3.3.1]*nonan-9-one*. A sample purified by gas chromatography had m.p. 155–158·5°. The IR spectrum had $\lambda_{c=o}$ 5·80 μ (CCl_4).

The semicarbazone (which formed at a normal rate) was recrystallized from ethanol–water to give colorless plates with the constant m.p. 202·5–203·2°d. The 2,4-dinitrophenylhydrazone was recrystallized from ethyl acetate–ethanol to the constant m.p. 191·8–192·3° (orange prisms; Found: C, 56·83; H, 5·48; N, 17·57. $C_{15}H_{18}N_4O_4$ requires: C, 56·59; H, 5·70; N, 17·60%).

Bicyclo[3.3.1]*nonane*

Bicyclo[3.3.1]nonan-9-one (XIII) was reduced by the procedure used by Cope[8a] to reduce the 1-bromo derivative to bicyclo[3.3.1]nonane. A mixture of 1·8 g (0·013 moles) XIII, 20 ml conc. HCl and 15 g Zn amalgam was refluxed 2 hr. The solution was extracted with pentane, the pentane washed with conc. H_2SO_4 and 10% Na_2CO_3 aq., then filtered through $MgSO_4$. The pentane was evaporated, the residue sublimed, and the product recrystallized twice from methanol, to give soft crystals of bicyclo[3.3.1]nonane, m.p. 143–144·5° (reported:[8] 145–146°).

Bicyclo[3.3.1]*nonan*-9-ol (XVI)

Crude bicyclo[3.3.1]nonan-9-one (XIII), 13·0 g (0·096 mole), was allowed to stand overnight in 100 ml methanol containing 30 ml water and 1·1 g (0·12 equiv) $NaHB_4$. 200 ml water were added, and the precipitated product was collected and sublimed, yielding 10·75 g (0·077 mole, 80%) *bicyclo*-[3.3.1]*nonan-9-ol*, which was recrystallized from ligroin to give large, somewhat soft plates, m.p. 207–208·2°. (Found: C, 76·94; H, 11·16. $C_9H_{16}O$ requires: C, 77·09; H, 11·50%).

The 3,5-dinitrobenzoate was recrystallized to a constant m.p. of 145.5–146.5°. (Found: C, 57·61; H, 5·26; N, 8·54. $C_{16}H_{18}N_2O_6$ requires: C, 57·48; H, 5·43; N, 8·38%).

The tosylate V, made by the procedure of Tipson,[47] was recrystallized from ligroin to give a

69% yield of large spars with the constant m.p. 92–93°. (Found: C, 65·13; H, 7·62; S, 10·85; sapon. equiv., from an infinity titer in the acetolysis, 296·0. $C_{16}H_{22}O_3S$ requires: C, 65·29; H, 7·53; S, 10·87; sapon. equiv. 294·4).

The most convenient procedure for the preparation of the alcohol XVI was the following: Δ^2-Bicyclo[3.3.1]nonen-9-ethylene ketal (IX), 30 g (0·165 mole), was dissolved in 120 ml acetic acid containing 30 ml water and 2 ml 6 N HCl. The solution was hydrogenated (3 atm) over platinum oxide. After 2 hr, 0·33 moles hydrogen (the amount required for reduction of double bond and ketone) had been taken up, and reaction ceased. The solution was filtered, poured into water, and extracted with ether; the ether was washed with 10% Na_2CO_3 aq. and evaporated. The residue was dissolved in 50 ml methanol containing 5 g (0·09 mole) KOH, and the solution refluxed 1 hr (to saponify any acetate), then cooled, poured into water, and extracted with ether. The ether was washed with water, 100 ml ligroin were added, and the solution was washed with brine and filtered. The ether was distilled off, and the solution allowed to crystallize, yielding two crops of pure bicyclo[3.3.1]nonan-9-ol, 18 g (0·128 mole, 78%), m.p. 207–208°.

Acetolysis of bicyclo[3.3.1]*nonyl-9-tosylate* (V)

Bicyclo[3.3.1]nonyl-9-tosylate (V), 20 g (0·068 mole), was dissolved in 1 l. glacial acetic acid, containing 6·9 g (0·071 mole) potassium acetate, and the solution was heated to 80–85° for 6 hr (8–11 half-lives). The reaction mixture was allowed to cool, then poured into 2 l. water and extracted continuously overnight with pentane. The pentane solution was washed with water and 10% Na_2CO_3 aq., and filtered through $CaCl_2$. A small sample of this solution was shown by gas chromatography to contain (besides solvent) a mixture of 83 ± 2% hydrocarbons and 17 ± 2% acetates.

The pentane was distilled from the bulk of the solution through a Vigreux column, and the residue was distilled (from a trace of $CaCO_3$) to give 2 fractions, one (hydrocarbons) b.p.$_{12}$ 44–45°, 6·19 g (0·0507 mole, 75% for C_9H_{14}), and the second (acetates) of b.p.$_{12}$ 96–97°, 1·84 g (0·0101 mole, 15% for $C_{11}H_{18}O_2$).

I. *The hydrocarbon fraction.* Gas chromatography (silicone oil, 65°) of the hydrocarbon fraction showed the presence of 3 partially-resolved components with the following relative retention times: 85 (51 ± 2% of total acetolysis product, *cis*-Δ^4-hexahydroindene, XVII), 93 (7 ± 2%, unidentified) and 100 (25 ± 2%, Δ^8-hexahydroindene, XVIII). Analytical samples of the first and third components were collected. (Found: C, 88·54; H, 11·35; C, 88·52; H, 11·47. Calc. for C_9H_{14}: C, 88·45; H, 11·55%). A preparative gas chromatograph[50] was used to obtain larger samples of the first and third components for the chemical studies reported below.

The first component (XVII) had significant IR bands (CS_2) at 3·33, 6·05, 13·62, 14·17, and 14·71 μ; the NMR spectrum had a peak at 4·43 τ with an area corresponding to two protons.

Oxidation of 96 mg (0·79 mmoles) of the first hydrocarbon with 31 ml of a solution of 20·9 g $NaIO_4$ and 250 mg $KMnO_4$ in 1 l. water (Lemieux' reagent[48]) containing 40 mg (0·35 mmole) K_2CO_3 gave a light-colored solution after 36 hr; a few ml of 10% Na_2CO_3 were added, and the solution was extracted with pentane. The aqueous layer was acidified and extracted 4 times with ether. The extracts were washed with dil. HCl and evaporated. The residue crystallized very slowly to give 62 mg (0·33 mmole, 42%) of rosettes of tiny colorless needles of *cis*-cyclopentane-1-carboxy-2-propionic acid; recrystallization from benzene–ligroin gave the constant m.p. 99–100° (reported:[12] 101°); the dianilide had m.p. 183–190° (reported:[12a] 190°).

The third component of the hydrocarbon fraction had no IR bands in the regions 3·29–3·35 or 14–15 μ, and no NMR absorption below 7·04 τ. The IR spectrum was identical to that of Δ^8-hexahydroindene[18] (XVIII). Bromination of a few mg in CCl_4 was carried out at 0°; the bromine was decolorized instantly. The m.p. of the unstable dibromide was determined by allowing a drop of the bromination solution to evaporate on a microscope slide, then taking the m.p. of the resulting crystals on a micro hot stage before they decomposed. The m.p. thus determined was 56–59°d (reported: 57–60°d;[14] 61–63°d[18]).

II. *The acetate fraction.* The distilled acetate fraction from the acetolysis of bicyclo[3.3.1]nonyl-9-tosylate (0·65 g, 3·6 mmoles) was refluxed 1 hr in 5 ml methanol containing 0·5 g (9 mmoles) KOH. The solution was poured into water and extracted with ether; the ether was washed with water and brine and dried (Na_2SO_4). The solution was filtered, the ether distilled off, and the residue

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[50] Designed and built by Dr. G. O. Dudek. We are grateful to Dr. Dudek for assistance.

distilled to give 412 mg (2·95 mmoles, 82%) of a liquid alcohol mixture. This mixture was separated by gas chromatography into 4 components, which were collected and identified by comparison of their IR spectra and relative retention times with those of samples whose preparation and properties are described in a subsequent section. Each of the isolated components was not separated from a corresponding authentic sample by gas chromatography. Percentages are based on total acetolysis product. The components were trans-trans-*hydrindan-4-ol* (XXI; 0·4%), *cis-trans*-hydrindan-4-ol (XX, 8·4%, acid phthalate m.p. 151–153°), *cis-cis*-hydrindan-4-ol (XIX, 3·1%, acid phthalate m.p. 132–135°, mixture with acid phthalate of XIX (m.p. 133–134°) melted 132–134°), and bicyclo-[3.3.1]nonan-9-ol (XVI, 5·0%, m.p. 205–207°, mixture with XVI of m.p. 207–208° melted 206·5–207·5°).

Both bicyclo[3.3.1]nonyl-9-acetate and *cis*-Δ^4-hexahydroindene were recovered unchanged after having been subjected to the acetolysis conditions.

Recovery of unsolvolyzed tosylate after partial acetolysis of V

Bicyclo[3.3.1]nonyl-9-tosylate, 250 mg (0·85 mmoles), was dissolved in 12·5 ml dry acetic acid containing 1·6 ml of 0·78 N potassium acetate and heated to 65·0° for 3·2 hr (a time calculated to be sufficient to reach the equilibrium tosylate mixture). The solution was cooled, poured into water and extracted with benzene. The benzene solution was washed with water and filtered through $MgSO_4$; the solution was lyophilized at 0·005 mm and $-20°$ for 6 hr, then at room temp for 1 hr. The crystalline residue was free of acetate and hydrocarbon products (as shown by the IR spectrum) and melted at 78–88° (m.p. of pure V is 92–93°). Neither the IR spectrum of the product nor that of a synthetic mixture of 84% V and 16% *cis-trans*-hydrindyl-4-tosylate (XXIII), m.p. 78–88°, was distinguishable from that of pure bicyclo[3.3.1]nonyl-9-tosylate. The product could not have contained appreciable amounts of *trans-trans*-tosylate, as this would have been detectable in the IR spectrum. The NMR spectrum of the product mixture was identical to that of a synthetic mixture of 84% V and 16% XXIII, and differed from that of pure V (broad peak centered at 8·24 τ) and of pure XXIII (somewhat sharper peak centered at 8·45 τ). Unfortunately, the spectra of the two tosylates overlap, preventing accurate determination of the composition of mixtures. Separation of the mixture was attempted by chromatography on alumina, by paper chromatography, and by thin-layer chromatography on silica gel, as well as by fractional crystallization. All methods failed, either because of decomposition of the tosylates, or because of difficulties in the detection of minor components. A sample of the recovered tosylate mixture was found to solvolyze with first-order kinetics.

Hydrogenation of indan-4-ol

Indan-4-ol, 33 g (0·25 mole), was hydrogenated with platinum oxide in 100 ml acetic acid containing 1 ml conc. HCl. The mixture took up 0·75 mole hydrogen in 2 days at room temp and 3 atm; addition of fresh catalyst caused no further uptake. The reaction mixture was filtered, poured into water, and extracted with pentane. After one washing with 10% KOH aq., the pentane was evaporated and the residue taken up in 50 ml methanol. Potassium hydroxide, 10 g (0·18 mole), was added and the solution refluxed 1 hr to saponify acetates. The reaction mixture was poured into water and extracted with pentane; the extracts were dried, and the pentane was evaporated. The residue was distilled to give two fractions: hydrocarbons, b.p.$_{11}$ 51–54°, 10·7 g (0·086 mole, 34·5%, not further investigated) and alcohols, b.p.$_{12}$ 99–102°, (reported:[12b] 107–109°), 19·0 g (0·136 mole, 55%).

The alcohol fraction was shown by gas chromatography to consist of a mixture of at least 5 components; the major one (68%) had a rel. ret. time (on a six-foot column of 20% TCEP on Chromosorb W at 115°) of 92 (bicyclo[3.3.1]nonan-9-ol = 100). This alcohol was assigned the structure of *cis-cis*-hydrindan-4-ol (XIX) on the basis of arguments set forth in the discussion section. The other alcohols present in this mixture had assigned structures and relative retention times as follows: *cis-trans*-hydrindan-4-ol (XX, 7%, 87), *trans-trans*-hydrindan-4-ol (XXI, 1·4%, 71), trans-cis-*hydrindan-4-ol* (XXII, 20%, 55, IR band at 9·36 μ), and an unidentified compound (3%, 74).

cis-cis-*Hydrindan-4-ol* (XIX)

The major product of the hydrogenation was purified as follows (procedure of Hückel[12a]): 12·5 g of the alcohol fraction (0·089 mole) were heated with 13·2 g (0·089 mole) phthalic anhydride for 5 hr at 150° (sealed tube). The product was taken up in 20 ml ether and stirred with 50 ml 15%

KOH aq. for 10 min; the insoluble potassium phthalate of XIX precipitated and was collected and washed with ether and ice water. The salt was shaken with ether and 6 N HCl; the ether layer was separated and the aqueous layer extracted with additional ether. The combined ether extracts were washed with water and brine, then dried (Na_2SO_4) and filtered. Benzene was added and the ether distilled off; ligroin was then added and the solution allowed to crystallize, yielding 8·9 g (0·031 mole, 52%, based on XIX in the alcohol mixture) of the acid phthalate of XX, m.p. 133–134·4° (reported:[12a] 134°) after one further recrystallization. This material was added to 25 ml methanol containing 5 g (0·12 mole) NaOH and the suspension refluxed 2 hr. The reaction mixture was poured into water and extracted with pentane. The extracts were washed with water, dried (Na_2SO_4) and evaporated, yielding 3·9 g (0·028 mole, 90%) *cis-cis*-hydrindan-4-ol, a viscous oil which was at least 98% pure as shown by gas chromatography and by its IR spectrum, which has distinctive bands at 9·37, 9·55 and 9·90 μ. The rel. ret. time on TCEP is 92 (bicyclo[3.3.1]nonan-9-ol = 100).

The tosylate (XXIV) was made and recrystallized from ligroin to a const. m.p. 78–79°d (reported[51] 79–80°), and was not stable at room temp for more than a few days. The saponification equivalent (from an infinity titer in the acetolysis) was 299 (calc: 294·4).

A sample of the tosylate was subjected to acetolysis with excess acetate at 65·0° for 10 half-lives; the product proved to be almost exclusively hydrocarbons,[52] which were not further investigated.

cis-trans-*Hydrindan-4-ol* (XX)

Purified *cis-cis* alcohol (XIX), 8·5 g (0·061 mole), was refluxed 48 hr in 39 ml isopropanol containing 4·7 g aluminum isopropoxide and 1 ml acetone. The solution was poured into 6 N HCl and extracted with pentane. The pentane was washed with 6 N HCl and water, filtered through $MgSO_4$ and evaporated to give 7·7 g (0·055 mole, 91%) of an oily alcohol mixture which gas chromatography showed to consist of 32% XIX and 68% *cis-trans*-hydrindan-4-ol. This mixture was refluxed 4 hr in 100 ml dry pyridine containing 11 g (0·074 mole) phthalic anhydride, then cooled and poured into iced dil. HCl, and extracted with ether. The ether solution was washed with water, then stirred 15 min at 0° with a solution of 8·2 g (0·15 mole) KOH in 32 g water. The precipitated potassium phthalate (of XIX) was filtered off and washed once with ice water; the aqueous filtrate and washings were washed twice with ether, then acidified and extracted with ether. The ether extracts were washed with water and brine and filtered through Na_2SO_4. Benzene was added and the ether distilled off; ligroin was added and the solution allowed to crystallize. The crude product was recrystallized 3 times from benzene–ligroin to a const. m.p. of 149–150°; the yield was 5·5 g (0·022 moles, 60%, based on XX in the alcohol mixture).

A solution of 4·0 g (0·016 moles) of the acid phthalate in 30 ml methanol was refluxed 4 hr with 6 g KOH, then poured into water and extracted with pentane. The pentane was washed with water, filtered through $MgSO_4$, and evaporated to yield 1·6 g (0·012 moles, 72%) of *cis-trans*-hydrindan-4-ol (XX), a viscous oil. Gas chromatography of this alcohol on a 150 ft TCEP capillary column[52] indicated that the alcohol contained 0·8% *trans-trans* and 2·2% *cis-cis* alcohols. XX has characteristic IR bands at 9·33, 9·65 (shoulder) and 9·79 μ. The tosylate (XXIII) was made in 81% yield and was recrystallized to a const. m.p. of 57·2–57·5° (reported:[51] 53–54°). A sample of 75 mg of *cis-trans* alcohol (XX) was equilibrated under the above conditions with aluminum isopropoxide; gas chromatography showed the product mixture to contain (after work-up) 72% *cis-trans* and 28% *cis-cis* alcohols (XX and XIX).

Acetolysis of cis-trans-*hydrindyl-4-tosylate* (XXIII)

A solution of 0·230 g (0·78 mmole) *cis-trans*-hydrindyl-4-tosylate (XXIII) in 9 ml dry acetic acid and 0·9 ml 1·0 N potassium acetate solution was heated in a sealed ampoule to 65° for 16 hr (more than 10 half-lives), then cooled, poured into water, and extracted with pentane. The pentane extracts were washed with water and filtered through $CaCl_2$. The pentane was distilled off through a Vigreux column. The product was shown by gas chromatography to consist of a mixture of about 2% of an acetate mixture (not further investigated) and 98% of a hydrocarbon mixture. The hydrocarbons

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[51] W. Hückel, H. Havekoss, K. Kumetat, D. Ullman, and W. Doll, *Liebigs Ann.* **533**, 128 (1938).

[52] We are grateful to Professor J. Berson for this analysis.

were *cis*-Δ^4-hexahydroindene (45 ± 3%) and Δ^8-hexahydroindene (34 ± 3%) (identified by their rel. ret. times and IR spectra). Two other hydrocarbons (14% and 7%) were also present, but were not identified.

Recovery of tosylate from acetolysis of XXIII

cis-trans-Hydrindyl tosylate (XXIII), 0·865 g (2·9 mmoles), was dissolved with 4·0 ml 0·78 N potassium acetate solution in 28 ml acetic acid. The solution was heated to 65·0° for 8·0 hr, then cooled, poured into water, and extracted with pentane. The pentane was washed with water and evaporated; the residue was pumped at 0·05 mm for 4 hr. The product remaining at the end of this period was an oil, weighing 25 mg, which still smelled of acetate. This material was dissolved in a small amount of pentane and cooled to −20°. The crystals which formed weighed 7·5 mg and had m.p. 49–52°. One further recrystallization gave 4·3 mg (0·5%) melting 53–54°; the IR spectrum of this material was identical to that of pure XXIII; however, bicyclo[3.3.1]nonyl-9-tosylate would not have been detected. The mother liquor from the second crystallization was concentrated and yielded a second crop of less than 1 mg of crystals, m.p. 48–51°; the IR spectrum of these crystals was also identical to that of pure XXIII. There is no evidence for the presence of any bicyclo[3.3.1]-nonyl-9-tosylate. XXV would have been detected, but was absent.

cis-*Hydrindan-4-one*

Pure *cis-cis*-hydrindan-4-ol (XIX), 405 mg (2·9 mmoles), was dissolved in 5 ml acetic acid; 320 mg (3·2 mmoles) chromic anhydride in 0·25 ml water and 5·0 ml acetic acid were added dropwise over 45 min (the solution was kept cool enough so that part of the solvent was always frozen). The solution was then stirred 4 hr at room temp, poured into water and extracted with pentane. The pentane was washed with water and evaporated, leaving 280 mg (2·0 mmoles, 70%) of *cis*-hydrindan-4-one, shown by its gas chromatogram and IR spectrum to be contaminated with 2% of XIX; *trans* ketone could not have been detected by gas chromatography, but was shown to be absent by the results of the reductions reported below.

Reductions of cis-*hydrindan-4-one*

The products of the following reductions were identified only by their relative retention times (TCEP, 120°).

I. *With lithium aluminum hydride. cis*-Hydrindan-4-one, 50 mg, was stirred with excess $LiAlH_4$ in dry ether for 2 hr. Sodium hydroxide solution was added, the ether layer separated, and the aqueous layer extracted with pentane. The combined organic extracts were washed with 6 N HCl and water, and evaporated. The product was 89% *cis-cis* (XIX, rel. ret. time 92) and 11% *cis-trans* (XX, rel. ret. time 88) hydrindan-4-ol. No *trans* alcohols were present.

II. *With sodium in isopropanol. cis*-Hydrindan-4-one (50 mg) was reduced with a six-fold excess of clean sodium in 5 ml isopropanol. The solution was poured into water and extracted with pentane; the pentane was washed with water. Gas chromatography of the pentane solution showed the product to consist of *cis-cis* (XIX, 38%), *cis-trans* (XX, 38%), *trans-trans* (XXI, 20%) and *trans-cis* (XXII, 4%) hydrindan-4-ol, rel. ret. times 92, 88, 71, and 56, respectively.

III. *Equilibration with methoxide, followed by reduction with lithium aluminum hydride.* A solution of 19 mg of the *cis* ketone in methanol with a few mg sodium methoxide was refluxed 2 hr, then poured into water. The solution was extracted with pentane and the pentane washed with water and evaporated. Gas chromatography showed that the *cis* and *trans* ketones were not separated (TCEP). The equilibration mixture was reduced with $LiAlH_4$ by the procedure used in Section I (above). The product consisted of *cis-cis* (XIX, 68%), *cis-trans* (XX, 9%), *trans-trans* (XXI, 16%) and *trans-cis* (XXII, 6%) hydrindan-4-ol, rel. ret. times 92, 86, 70, and 54, respectively.

Equilibration of hydrogenated indan-4-ol with sodium in decalin

A portion of the alcohol fraction from the hydrogenation of indan-4-ol, 2·0 g (0·014 mole), was dissolved in 5 ml decalin (purified by washing with H_2SO_4 and distillation under N_2); 400 mg clean Na (0·017 mole) were added, and the solution refluxed for 8 hr under N_2. The solution was cooled and excess Na decomposed; the resulting mixture was poured into water and extracted with ether. The ether was washed with water and brine and dried ($MgSO_4$), then evaporated, and the residual decalin solution analyzed by gas chromatography. The principal alcohol produced was *trans-trans*-hydrindan-4-ol (XXI, 38%, acid phthalate m.p. 156–157°, IR bands at 9·09, 9·44, 9·68, and 9·84 μ, rel. ret. time 72 on TCEP). Other components of the mixture were *cis-trans* (XX, 32%, 88), *cis-cis* (XIX, 20%, 92) and *trans-cis* (XXII, 6%, 54) hydrindan-4-ol, as well as an unidentified component (4%, 56).[53]

The acid phthalate was made directly from 9 g (0·064 mole) of a similarly prepared mixture by heating with an equal weight of phthalic anhydride to 140° for 4 hr. The reaction mixture was cooled and ligroin added; the product was recrystallized twice from benzene to yield 6·2 g acid phthalate (0·022 mole, 30%) with the m.p. 145–147°. Of this, 6·0 g (0·021 mole) were refluxed 1 hr with excess KOH in aq. methanol. The solution was poured into water and extracted with ether; the ether was washed with Na_2CO_3 aq., water, and brine, and dried (Na_2SO_4). The ether was evaporated to yield 2·8 g (0·020 mole, 95%) of an oily alcohol mixture, which gas chromatography showed to consist of *trans-trans* (XXI, 63%, rel. ret. time 73), *cis-trans* (XX, 23%, 88) and *cis-cis* (XIX, 12%, 92) hydrindan-4-ol, in addition to 1·6% of an unidentified compound (rel. ret. time 58).

From this mixture, the tosylate was made in 50% yield and recrystallized to a const. m.p. of 99–100°. This material was much less soluble than either of the *cis* tosylates, and was probably pure *trans-trans* tosylate (XXV). The acetolysis gave good first-order kinetics, indicating absence of more than small amounts of either of the much more reactive *cis*-tosylates.

PROPERTIES OF THE HYDRINDAN-4-OLS

Compound	Rel. ret. time (TCEP)	Acid phthalate m.p.	Tosylate m.p.	Characteristic infra-red bands. (Strongest underlined)
cis-cis (XIX)	92	133–134·4°	78–79°d	9·40, $\underline{9{\cdot}47}$, 9·91 μ
cis-trans (XX)	87	149–150° [a]	57·0–57·5°	$\underline{9{\cdot}36}$, 9·65 w, 9·82 μ
trans-trans (XXI)	71	156–157° [a]	99–100°	9·10, $\underline{9{\cdot}44}$, 9·68, 9·86 μ
trans-cis (XXII)	55	—	—	$\underline{9{\cdot}36}$ μ

[a] a mixture of 80% of the phthalate of XX and 20% of the phthalate of XXI melted sharply at 143·5–144·5°; neither the m.p. of the phthalate mixture nor its composition was changed by recrystallization. Other mixtures displayed similar behavior and m.p.s between 146° and 150°.

Kinetics. The acetolysis procedure followed for the kinetic runs was essentially that of Winstein[54] and Norton.[16] In most runs excess potassium acetate was present; it was back-titrated using standard perchloric acid solution with crystal violet as indicator. Runs with no acetate were followed by titration with sodium acetate solution. A typical run is reproduced below.

endo-Bicyclo[3.2.1]octyl-8-tosylate (III), 1·2669 g (4·5 mmoles), was dissolved in 5·00 ml of a 0·993M potassium acetate solution in dry acetic acid, and the solution diluted to 50·00 ml with dry acetic acid. Aliquots were sealed in ampoules which were placed in a constant temp bath regulated at 140·00 ± 0·02°; at intervals ampoules were withdrawn from the bath, cooled and opened; 5·00 ml of the solution were titrated with 0·1054N perchloric acid solution.

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[53] This reaction was reported to yield the pure epimer of the alcohol assigned the *cis-cis* structure (reported m.p. of acid phthalate: 146°).[19c] It seems likely that the alcohol previously reported and assigned the *cis-trans* structure XX[15] was a mixture of XX and *trans-trans* alcohol (XXI). The table is included for convenient reference.

[54] S. Winstein, C. Hanson and E. Grunwald, *J. Amer. Chem. Soc.* **70**, 812 (1948).

t, sec	ml $HClO_4$- (ml $HClO_4)_0$	$-\ln \frac{[ROTs]}{[ROTs]_0}$
000	0·000	0·000
7560	0·738	0·189
18000	1·498	0·431
27400	2·028	0·641
73800	3·493	1·693
79200	3·588	1·820
84600	3·685	1·942
90000	3·723	2·033
95400	3·798	2·180

k_1 (calculated graphically) = $2{\cdot}28 \times 10^{-5}$ sec^{-1}

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