Ionic Reactions in Bicyclic Systems. VII. Solvolysis of Optically Active *exo*-Bicyclo[3.2.1]octan-2-yl and Bicyclo[2.2.2]octan-2-yl *p*-Toluenesulfonate[1]

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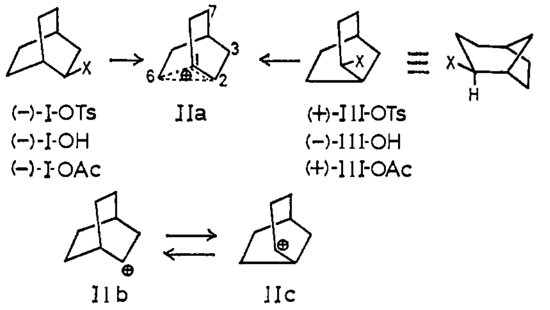
Abstract: Solvolysis of bicyclo[2.2.2]octan-2-yl (I-OTs) and *exo*-bicyclo[3.2.1]octan-2-yl *p*-toluenesulfonates (III-OTs) gives binary mixtures of [2.2.2] and *exo*-[3.2.1] isomers. Optical purities of both isomers have been determined for acetolysis and hydrolysis (80% acetone) of optically active I-OTs and III-OTs. Both isomers in the product are optically active; however, some activity is lost and in all cases the [2.2.2] isomer (47–78% optically pure) is less optically pure than the *exo*-[3.2.1] isomer (63–88% optically pure). Acetolysis gives products of lower optical purity than solvolysis in 80% acetone. The partial loss of optical configuration is thought to result from racemization of the asymmetric nonclassical ion IIa by reversible opening to the symmetrical [2.2.2] classical ion IIb. The latter intermediate is thought to be the origin of the excess racemic [2.2.2] isomer in the product. Hydride shifts may also contribute to the racemization of IIa.

This paper reports a kinetic and stereochemical investigation of the solvolysis of optically active bicyclo[2.2.2]octan-2-yl (I-OTs) and *exo*-bicyclo[3.2.1]octan-2-yl *p*-toluenesulfonates (III-OTs). In the preceding paper, it was shown that these isomers are related to the same carbonium ion system; configurational compositions of solvolysis products derived from I-OTs and III-OTs (binary mixtures of [2.2.2] and *exo*-[3.2.1] isomers) are indistinguishable. The purpose of this phase of our investigation was to obtain information about the stereochemistry and symmetry properties of this carbonium ion system.



In this system one can distinguish between the nonclassical carbonium ion IIa and a set of equilibrating classical ions (IIb ⇄ IIc) on the basis of symmetry. The nonclassical structure IIa is asymmetric and if this is the only intermediate, retention of optical configuration would be expected. Hydride shifts (*e.g.*, 6,2 or 3,2) or reversible opening to the symmetrical classical ion IIb in competition with solvent capture could result in partial racemization of IIa and thus optical purities of the products would not necessarily be the same as that of the substrate. However, in any case, if IIa is the only product-forming intermediate the [2.2.2] isomer (capture at C_2) and the *exo*-[3.2.1] isomer (capture at C_1) would have the same optical purity. Also, if IIa is the initially formed intermediate from both I-OTs and III-OTs, the optical purities of products would be the same for both substrates.

On the other hand, loss of optical configuration would be expected if the carbonium ion system consists of equilibrating classical ions (IIb ⇄ IIc) because this is a symmetrical system—in IIb the 1,8 and 1,6 bonds are equivalent and rearrangement to IIc would give the enantiomers at equal rates. Since the product composition is the same for I-OTs and III-OTs[3] equilibration would have to be rapid relative to solvent capture, which means that for both isomers the symmetrical classical ion IIb would be an intermediate for all of the product. The possibility of asymmetry being preserved by a twist or "propeller" conformation of IIb or by the presence of the departing anion will be considered later.

In a related study, Walborsky and coworkers[4] investigated the acetolysis of optically active bicyclo[2.2.2]octan-2-yl *p*-bromobenzenesulfonate (I-OBs). The [2.2.2] isomer I in the product was formed with 47% retention of optical configuration. As has been recognized,[4-8] preservation of optical configuration in this system is strong evidence for the asymmetric nonclassical intermediate. The *exo*-[3.2.1] isomer III was also optically active; however, relative rotations for I and III were not known and thus the optical purity of this isomer could not be determined. In the present work we have determined the optical purities of both isomers in the product for acetolysis and hydrolysis (80% acetone) of optically active I-OTs and III-OTs.

Results and Discussion

Optically active bicyclo[2.2.2]octan-2-ol (I-OH) was obtained by catalytic hydrogenation (10% palladium on carbon) of active *endo*-bicyclo[2.2.2]oct-5-en-2-ol (IV).[9] The optically active *exo*-bicyclo[3.2.1]octan-2-yl

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[2] National Science Foundation Predoctoral Fellow, 1962–1964.

[3] H. L. Goering and G. N. Fickes, *J. Am. Chem. Soc.*, **90**, 2856 (1968).

[4] H. M. Walborsky, J. Webb, and C. G. Pitt, *J. Org. Chem.*, **28**, 3214 (1963).

[5] N. C. Deno, *Progr. Phys. Org. Chem.*, **2**, 146 (1964).

[6] G. D. Sargent, *Quart. Rev.* (London), 20, 301 (1966).

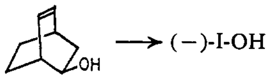
[7] J. A. Berson and P. Reynolds-Warnhoff, *J. Am. Chem. Soc.*, **86**, 595 (1964).

[8] J. A. Berson and D. Willner, *ibid.*, **86**, 609 (1964).

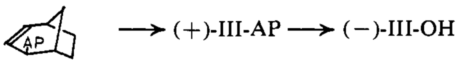
[9] H. L. Goering and D. L. Towns, *ibid.*, **85**, 2295 (1963).

system III was prepared in a similar manner from active *exo*-bicyclo[3.2.1]oct-3-en-2-yl acid phthalate (V).[9]

Rotations and optical purities of the [2.2.2] and *exo*-[3.2.1] isomers I and III were correlated as follows. Specific rotations of the unsaturated [2.2.2] and *exo*-[3.2.1] isomers IV and V were determined by an isotope dilution method in an earlier investigation.[9] Thus, specific rotations of I and III can be determined by correlation with IV and V. Hydrogenation of (+)-IV,[10] $[\alpha]^{25}\mathrm{D}$ 27.8°[11] (38% optically pure), gave (−)-I-OH, $[\alpha]^{25}\mathrm{D}$ −12.0°. This corresponds to $[\alpha]^{25}\mathrm{D}$ 32° and $[\alpha]^{25}_{365}$ 103° for optically pure I-OH. The change in rotation for conversion of IV to I-OH was reproducible and in good agreement with the report[12] that hydrogenation of (+)-IV, $[\alpha]^{23}\mathrm{D}$ 68.2°, gives (−)-I-OH, $[\alpha]^{21}\mathrm{D}$ −28.0°.[12] An independent determination of the rotation of the [2.2.2] system I by the isotope dilution method gave $[\alpha]^{25}\mathrm{D}$ 22.2° for I-AP. This corresponds to $[\alpha]^{25}\mathrm{D}$ 30° for I-OH which is in fair agreement with the value obtained by correlation with IV. We consider the latter to be more reliable because the resolution is easier and rotations are over two times higher for the unsaturated system, and thus uncertainties in the isotope dilution determinations should be smaller than for the saturated system.

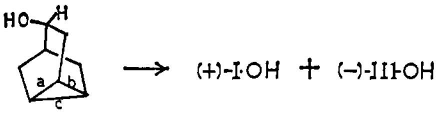


(+)-IV



(+)-V

Catalytic reduction of (+)-*exo*-bicyclo[3.2.1]oct-3-en-2-yl acid phthalate (V), $[\alpha]^{24}\mathrm{D}$ 234° (100% optically pure),[9] gave (+)-III-AP, $[\alpha]^{25}\mathrm{D}$ 20.7°, which when saponified gave (−)-III-OH, $[\alpha]^{25}\mathrm{D}$ −16.9°,[11] −14.0° (95% ethanol), $[\alpha]^{25}_{365}$ −54.5°. In a duplicate experiment (−)-III-OH, $[\alpha]^{25}\mathrm{D}$ −16.8°, was obtained. Presumably these samples of (+)-V and (−)-III-OH were optically pure. The unsaturated acid phthalate V can be resolved readily to constant rotation and this material has been shown to be optically pure.[9] Racemization during hydrogenation seems unlikely because the results are reproducible and it was shown earlier[13] that reduction of the unsaturated acid phthalate V and acetate of the same optical purity gives the corresponding saturated compounds having the same optical purities. From the present correlations the ratio of rotations ($[\alpha]\mathrm{D}$) for I/III is 32°/17° = 1.88[11] which is the value that was used to calculate the relative optical purities in the product studies described below. This value is in excellent agreement with that recently determined by Berson and coworkers[14] by an independent method which involves catalytic hydrogenation of the tricyclooctanol VI. Hydrogenation of (+)-VI gives a mixture of (+)-I-OH (cleavage c) and (−)-III-OH (cleavage b) together with a minor amount of *endo*-[3.2.1] alcohol, (−)-VII-OH (cleavage a). The ratio of rotations of I-OH and III-OH isolated from the mixture by gc was 1.87.



(+)-VI

The *exo*-[3.2.1] system III was also correlated with the *endo*-[3.2.1] system VII by the method described by Berson and Reynolds-Warnhoff[7] which involves conversion of the epimeric alcohols III-OH and VII-OH to bicyclo[3.2.1]octan-2-one (VIII). Chromic acid oxidation[15] of (−)-III-OH, $[\alpha]^{25}\mathrm{D}$ −16.4°, −13.6° (95% ethanol), $[\alpha]^{25}_{365}$ −52.7°, gave (+)-VIII, $[\alpha]^{25}\mathrm{D}$ 130°, $[\alpha]^{25}_{365}$ 646°,[11] and oxidation of (−)-VII-OH, $[\alpha]^{25}\mathrm{D}$ −19.2°, 24.7° (95% ethanol), $[\alpha]^{25}_{365}$ −49.4°, gave (−)-VIII, $[\alpha]^{25}\mathrm{D}$ −120°, $[\alpha]^{25}_{365}$ −593°.[11] Under these conditions there is no rearrangement of the *exo*-[3.2.1] alcohol III-OH to the [2.2.2] isomer, which shows that carbonium ion intermediates are not involved. Thus it seems unlikely that the *endo*-[3.2.1] alcohol VII-OH undergoes any racemization because this isomer is less reactive than the *exo* isomer.[16] From this correlation the ratio of rotations ($[\alpha]\mathrm{D}$) for VII-OH/III-OH is 1.27 for chloroform and 1.91 for 95% ethanol. This gives a value of 1.27 × 16.9° = 21.5° for the rotation of *endo*-[3.2.1] alcohol IV-OH. In other work[16] (−)-IV-OH, $[\alpha]^{25}\mathrm{D}$ −22.1°, was prepared. The present correlation indicates that this sample was optically pure.

(+)-VII-OH (+)-VIII

Optically active bicyclo[2.2.2]octan-2-yl (I-OTs) and *exo*-bicyclo[3.2.1]octan-2-yl *p*-toluenesulfonates (III-OTs) were prepared from the corresponding active alcohols. Recrystallization of these derivatives results in optical fractionation. For example, recrystallization of (+)-I-OTs, $[\alpha]^{25}_{365}$ 6.11°, from an ether–pentane mixtute gave material having $[\alpha]^{25}_{365}$ 5.38°. Similarly, recrystallization of (−)-III-OTs, $[\alpha]^{25}_{365}$ −26.1°, gave (−)-III-OTs, $[\alpha]_{365}$ −25.5°. The samples of active I-OTs and III-OTs used in the product studies were not recrystallized and thus presumably had the same optical purities as the alcohols from which they were derived. Infrared spectra of these materials were indistinguishable from those of analytical samples and there was no evidence of contamination by unreacted alcohol.

Kinetic Studies. In an earlier investigation[17] it was found that I-OTs and III-OTs are interconverted by ion-pair return during solvolysis. Equilibration of the two isomers is reached by about 35% solvolysis in acetic acid and the I-OTs/III-OTs steady-state ratio is about 0.5. Starting with the more reactive I-OTs the instantaneous solvolytic rate constant drops until the I-OTs/III-OTs steady-state ratio is reached, after which the first-order constant remains steady. With the less reactive *exo*-[3.2.1] isomer III-OTs the rate constant drifts up, as the more reactive [2.2.2] isomer accumulates, until the steady-state value is reached.

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(10) Structural formulas correspond to the correct absolute configurations (see ref 8).

(11) Rotations are for chloroform solutions unless otherwise noted.

(12) K. Mislow and J. G. Berger, *J. Am. Chem. Soc.*, **84**, 1956 (1962).

(13) H. L. Goering and U. Mayer, *ibid.*, **86**, 3753 (1964).

(14) J. A. Berson, private communication.

(15) H. C. Brown and C. P. Garg, *J. Am. Chem. Soc.*, 83, 2952 (1961).

(16) H. L. Goering and G. N. Fickes, *ibid.*, **90**, 2848 (1968).

(17) H. L. Goering and M. F. Sloan, *ibid.*, **83**, 1992 (1961).

In the present work we have examined the rates of acetolysis of optically active I-OTs and III-OTs polarimetrically. For acetolysis of (−)-I-OTs plots of log ($\alpha_t - \alpha_\infty$) *vs.* time (α_t is the angle at time t and α_∞ is the final angle) show an initial steep rise due to accumulation of (+)-III-OTs. After reaching a maximum the plot becomes linear and good first-order behavior is observed. The linear relationship begins at about 40% solvolysis which shows that the I-OTs/III-OTs steady-state ratio is reached at this point.

Similar behavior is observed with (+)-III-OTs. In this case the initial disturbance in the logrithmic plot is a slight depression (because of accumulating (−)-I-OTs) after which the plot becomes linear (at about 35% solvolysis). The present results are in excellent agreement with earlier estimates[13] of the time required to reach steady-state conditions for acetolysis of I-OTs and III-OTs.

The integrated first-order rate constants for mutarotation (k_α) of equilibrium mixtures derived from both isomers are presented in Table I. In these cases the zero point was taken after equilibration was complete (about 50% solvolysis) and rate constants were determined using the integrated equation for a first-order reaction. These runs were followed to about 90% completion and no trends in the rate constant were observed. The values of k_α in the table are averages of 9 (for I-OTs) and 14 (for III-OTs) individual determinations. The observed change in angle for this part of the reaction was 0.7° for I-OTs and >1° for III-OTs. Rotations could be measured to about 0.003° and thus reactions could be followed with good precision as indicated by the small average deviations. In these experiments, and in the product studies, anhydrous acetic acid was used and a slight excess of sodium acetate was present. Under these conditions the solvolysis products are optically stable.

Table I. Polarimetric (k_α) and Titrimetric (k_t) First-Order Rate Constants for Acetolysis of Equilibrium Mixture of Bicyclo[2.2.2]octan-2-yl (I-OTs) and *exo*-Bicyclo[3.2.1]octan-2-yl *p*-Toluenesulfonates (III-OTs) at 48.86°

Starting ester	10^5k_α, sec^{-1}	10^5k_t,[a] sec^{-1}	k_α/k_t
I-OTs	$6.46 \pm 0.05^{b,c}$	$5.72 \pm 0.03^{b,d}$	1.13
III-OTs	6.49 ± 0.03^{d}	5.64 ± 0.03^{d}	1.15

[a] Initial ester concentration 0.057 *M*. [b] Indicated uncertainties are average deviations of individual determinations within a run. [c] Sodium acetate concentration 0.067 *M*. [d] Sodium acetate concentration 0.063 *M*.

As expected, polarimetric constants (k_α) are the same for steady-state mixtures derived from optically active I-OTs and III-OTs. However, k_α is about 20% higher than the reported[17] titrimetric constant (k_t) for this portion of the reaction. To determine if this discrepancy is real or results from slightly different experimental conditions the titrimetric constants were redetermined for the same conditions as the polarimetric experiments including solvent batch. Zero-point titers were taken at about 50% solvolysis, *i.e.*, after equilibration of the isomers, and rate constants were determined from ten appropriately spaced titrations. The titrimetric constants (k_t), starting with I-OTs and III-OTs, are included in Table I. In each case the constants were steady and the values are in good agreement with those reported earlier.[17] As shown in Table I, k_α is about 14% larger than k_t. This difference is reproducible and observed for both isomers. For this reason we feel confident that the discrepancy between k_α and k_t (about 25 times larger than the average deviation) is real. This is an important result in connection with the product studies because it shows that about 12% of the original optical activity of the substrate is lost prior to solvolysis—as has been shown by Winstein and Trifan,[18] in such a case the fractions of ester that solvolyze prior and subsequent to racemization are k_t/k_α and $(k_\alpha - k_t)/k_t$, respectively, or, to put it another way, the I-OTs $\rightleftharpoons$ III-OTs equilibration resulting from ion-pair return is accompanied by partial loss of optical activity. Possible ways in which optical configuration might be lost at this stage of the reaction are discussed below.

Product Studies. Optically active I-OTs and III-OTs of known optical purity were solvolyzed in glacial acetic acid containing 0.03 *M* sodium acetate and 80% (by volume) aqueous acetone containing 0.03 *M* pyridine; in each case the substrate concentration was ~0.025 *M*. Conditions for the acetolysis experiments were the same as for the kinetic experiments summarized in Table I. Except for the pyridine, conditions for hydrolysis in 80% acetone were also the same as for an earlier kinetic study.[17] In all cases products were isolated after ten half-lives.

Acetolysis products were saponified with methanolic potassium hydroxide, and the resulting mixtures of I-OH and III-OH were separated by preparative gc. Configurational compositions of alcohol mixtures derived from solvolysis products were determined by capillary gc and found to be indistinguishable from those reported in the previous paper.

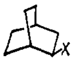
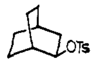
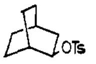
Capillary gc gave complete resolution of the alcohol mixtures; however, with the preparative column the I-OH and III-OH peaks overlapped and repetitive gc was necessary to separate the isomers. After three or four passes the isomers were obtained with from traces to about 8% intracontamination. Infrared spectra of the purest samples were indistinguishable from those of authentic racemic samples. Control experiments showed that both isomers are optically stable under the reaction conditions.

For each separation, optical rotations and configurational compositions (capillary gc) were determined for partially separated binary mixtures as well as for the purest samples. From these rotations and compositions the rotations of the pure isomers can be determined. Rotations calculated for the pure isomers were generally with 3% of the observed value for the purest sample and the maximum difference was 5%. The small amount of *endo*-[3.2.1] isomer VII resulting from acetolysis (~0.5% of the product)[3] could not be separated from the [2.2.2] isomer and as a result the I-OH derived from the acetolysis product was contaminated with from 0.6 to 2.2% VII-OH. This isomer is thought to result from rearrangement (leakage) of the [2.2.2]-*exo*-[3.2.1] ion II to the symmetrical *endo*-[3.2.1] nonclassical ion[8,16] and thus is presumably racemic. Rotations were corrected for this contaminant by assuming it to be an inactive diluent.

(18) S. Winstein and D. Trifan, *J. Am. Chem. Soc.*, 74, 1154 (1952).

Optical purities of I-OH and III-OH derived from solvolysis products, relative to those of the substrates, are shown in Table II. The first value for each entry is the observed optical purity and the value in parentheses has been corrected for racemization of the substrate prior to solvolysis, or, to put it another way, the first value is relative to the initial optical purity of the substrate and the value in parentheses is relative to the average optical purity of the substrate. The latter corresponds to the retention of configuration for that part of the reaction following generation of a capturable intermediate.

Table II. Optical Purities of Solvolysis Products Derived from Optically Active Bicyclo[2.2.2]octan-2-yl (I-OTs) and *exo*-Bicyclo[3.2.1]octan-2-yl *p*-Toluenesulfonates (III-OTs)

		Optical purity, %	
			
		A. Acetolysis (48.86°),[a, b] X = OAc	
	→	47 (53)	63 (72)
	→	52 (59)	68 (77)
		B. 80% Acetone (48.86°),[a,c] X = OH	
	→	73 (78)	87 (93)
	→	78 (83)	88 (94)

[a] Substrate concentration ~0.06 *M*. [b] Solvent contained a 10% molar excess of sodium acetate. [c] Solvent contained a 10% molar excess of pyridine.

Average optical purities of substrates were estimated as follows. For a substrate that undergoes simultaneous first-order racemization and solvolysis the average optical purity for complete solvolysis is k_t/k_α times the initial value.[18] Table I shows that for acetolysis $k_t/k_\alpha = 0.88$ for that part of the reaction after equilibration of the isomers is complete. The average optical purity would be a little lower for III-OTs than for I-OTs because of the higher initial rate of solvolysis of the latter.[17] However, the difference would be small because most of the reaction occurs after equilibration, and the value calculated from k_α and k_t (88% of original value) should be a good approximation for both isomers.

Polarimetric and titrimetric rate constants are not available for solvolysis in 80% acetone. However, for solvolysis of the *endo*-[3.2.1] isomer VII-OTs the return-to-capture ratio $(k_\alpha - k_t)/k_t$ is about half as large in 80% acetone as in acetic acid.[16] We assume that I-OTs and III-OTs will show similar behavior and that the return-to-capture ratio will be reduced about 50% in 80% acetone. Providing that racemization associated with return is reduced by a similar amount the average optical purities for 80% acetone will be about 94% of the original value.

Each result in Table II is the second of two independent determinations. These are considered to be more reliable than the first experiments because larger amounts of material were used and larger samples of the alcohols were isolated. The results of the first experiments were in good agreement with those in the table; optical purities were within three percentage units. Thus the values in the tables are considered to be reproducible to within three percentage units. For all of the experiments initial optical purities were well over 50%. Optical purities of I-OH derived from I-OTs and of III-OH derived from III-OTs are obtained by direct comparison of rotations of these alcohols with those of the alcohols from which the substrates were prepared. Thus uncertainties in configurational or rotational correlations are not involved in these determinations. On the other hand, the ratio of rotations for I and III is needed to determine the relative optical purities of I-OH derived from III-OTs and of III-OH derived from I-OTs. Thus these values are subject to uncertainties in the ratio of rotations for I/III. We believe this ratio is reliable to within 5% and that the values in Table II for these four cases are reliable to within 5% of the amount indicated.

The results for acetolysis of I-OTs are in close agreement with those reported by Walborsky and coworkers[4] for acetolysis of I-OBs at 50°. They report the same retention of configuration for the [2.2.2] isomer (47%), and their rotation for the *exo*-[3.2.1] isomer corresponds to an optical purity of 57%.

The data in Table II show that the products are optically active; however, some activity is lost. The total preservation of optical configuration for solvent capture varies from 62%[19] for acetolysis of I-OTs to 87%[19] for solvolysis of III-OTs in 80% acetone. The data suggest that the partial loss of configuration (in addition to that associated with ion-pair return) results from racemization of an asymmetric intermediate in competition with solvent capture. This is indicated by the greater preservation of activity in the more nucleophilic solvent, 80% acetone.

Clearly the carbonium ion system is (at least for the most part) asymmetric. We feel that the observed preservation of asymmetry cannot be accounted for in terms of equilibrating classical ions (IIb $\rightleftarrows$ IIc) because, as indicated above, this equilibration corresponds to a symmetrical system.

It has been suggested[5] that in this system equilibrating classical ions might give products with retention of configuration as a result of a directive influence of the counterion. There are several major difficulties with this proposal. There is evidence that the presence or location of a counterion has no effect on the partitioning or stereoselective *exo* capture at C_1—the product distribution is the same when the intermediate is generated by the σ,[3] π,[20] and ring-expansion routes.[8] A corollary of this is that the observed optical results are independent of the presence or location of the counterion and there is direct evidence that this is the case. Berson and Willner[8] have observed that the amounts of configuration retained in the two isomers when the intermediate is generated from optically active *exo*-2-norbornylcarbinylamine by the ring-expansion route are very similar to those observed in the present work. Clearly deamination of *exo*-2-norbornylcarbinylamine

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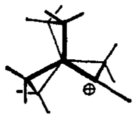
[19] These values are obtained from the isomeric compositions of the solvolysis products (54% I for acetolysis and 57% I for 80% acetone)[8] and the optical purities in Table II, *e.g.*, retention of optical configuration for acetolysis of I-OTs is (0.54 × 53) + (0.46 × 72) = 62%.

[20] S. Winstein and P. Carter, *J. Am. Chem. Soc.*, **83**, 4485 (1961).

and ionization of I-OTs or III-OTs cannot give the same ion-pair intermediate. It should also be noted that if the counterion had any effect on the stereochemistry of capture of equilibrating classical ions the opposite stereochemical result (excess inversion instead of retention) would be expected. In all relevant cases that we are aware of in which the counterion has an effect on the stereochemistry of capture of a classical carbonium ion for solvolysis of secondary alkyl arenesulfonates the result is excess inversion, and this is the situation for cyclic[21a] and acyclic[21b,c] systems.

The possibility that a set of equilibrating classical ions might retain asymmetry as a result of IIa having a twist conformation (IX) should also be considered. In this case preservation of optical configuration would require (a) that bond making and breaking occur almost exclusively on one of the two almost equivalent sides of C_2 (otherwise there would be crossover of enantiomers in the ionization and capture steps), and (b) a high barrier for conformational equilibration (racemization) of IX relative to that for solvent capture. Both of these requirements seem improbable. It is not apparent from steric and torsional considerations why ionization of twist conformers of I-OTs and solvent capture of IX would be sufficiently stereoselective to give the observed retention of optical configuration. Moreover, the barrier for racemization of IX would not be expected to be large enough to preserve most of the optical configuration. As has been noted,[3,6] in this system the windshield-wiper effect[22] does not provide a satisfactory explanation for the retention of optical configuration.



IX

For these reasons we feel that retention of optical configuration indicates that the asymmetric nonclassical ion IIa is involved. However, it is clear that IIa is not the only product-forming intermediate because for both substrates, the optical purity of the *exo*-[3.2.1] isomer III is higher than that of the [2.2.2] isomer I, or, to put it another way, in each case there is excess racemic I in the product.

There is also an indication that products derived from I-OTs may be less active than products from III-OTs: about 8% (for acetolysis) and 4% (80% acetone).[23] However, we cannot be sure of this because these differences are very sensitive to the ratio of rotations for I/III (1.88) used to calculate relative optical purities of the two systems. A ratio 6% larger than that used in the calculations gives optical purities of products from the two isomers that are within the limits of reproducibility—in this case the spread in optical purities for the two isomers in the product is increased. A slight excess loss of configuration for solvolysis of I-OTs could result from parallel assisted and unassisted ionizations to give IIa and IIb, respectively. From the similar product composition and optical purities for III-OTs and I-OTs it seems that, at most, unassisted ionization is involved to only a small extent.

In any event, it is clear that optical purities of products must be very similar for I-OTs and III-OTs because in each case most of the product is derived from the same equilibrium mixture. The solvolytic behavior of I-OTs and III-OTs is summarized by

$$\begin{tikzcd}
\text{IOTs} \arrow[rr, shift left, "k_1"] \arrow[dr, "k_3"'] & & \text{IIIOTs} \arrow[ll, shift left, "k_2"] \arrow[dl, "k_4"] \\
& \text{products} &
\end{tikzcd}$$

In an earlier investigation of acetolysis at 50°, k_3 and k_4 were determined from initial rates of solvolysis and k_1 and k_2 were estimated from the rate of approach to the III-OTs/I-OTs steady-state ratio.[17] Regardless of mechanism, starting with I-OTs the amount that passes through III-OTs is $100[k_1/(k_1 + k_3)] \approx 65\%$ ($\sim$35% solvolyzes directly) or the amount equilibrated prior to solvolysis is $100(k_1 + k_2)/(k_1 + k_2 + k_3) \approx 75\%$. Similarly, when one starts with III-OTs, $100[k_2/(k_2 + k_4)] \approx 60\%$ is converted to I-OTs ($\sim$40% solvolyzes directly) or $100(k_1 + k_2)/(k_1 + k_2 + k_4) \approx 80\%$ is equilibrated prior to solvolysis. Any difference in solvolytic behavior would have to be in the fraction of solvolysis that occurs prior to equilibration; for acetolysis this is $\sim$20% for III-OTs and $\sim$25% for I-OTs.

About one-fourth of the total loss of optical configuration results from racemization of the substrate prior to solvolysis and the rest is associated with solvent capture. There are several transformations, for which there are precedents in related systems, that would result in loss of configuration at one or both of these stages of the reaction.

For example, acetolysis of optically active 2-octyl *p*-toluenesulfonate is accompanied by racemization of the unsolvolyzed ester.[21c] A similar process (inversion of C_2) would result in racemization of I-OTs and thus of the I-OTs $\rightleftharpoons$ III-OTs equilibrium mixture. Racemization of the 2-octyl ester is thought[21c] to result from a displacement by toluenesulfonate ion (from the acid produced by the reaction) on an ion-pair intermediate with inversion of configuration. In any case, racemization evidently involves exchange with external toluenesulfonate ion with inversion at C_2. Such a process seems improbable in the present system because the same stereochemistry would be expected for exchange (capture by toluenesulfonate ion) as for solvent capture. In the 2-octyl system, solvolysis involves almost complete inversion of configuration.[21b,c] However, in the present case, solvent capture proceeds with predominating retention and there is no apparent reason why capture by an external toluenesulfonate ion should proceed with inversion. It seems more likely that racemization of the substrate is intramolecular and results from racemization of an ion-pair intermediate.

In IIa, 3,2- and 6,2-hydride shifts would result in interconversion of enantiomers and a 6,1-hydride shift would give a symmetrical ion. There is recent evidence[24] that 6,2-hydride shifts are not involved in this system and racemization by a reversible 6,1-hydride

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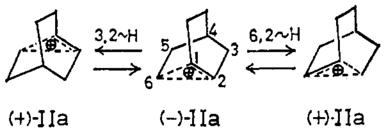
(21) (a) S. Winstein and N. J. Holness, *J. Am. Chem. Soc.*, **77**, 5562 (1955); (b) R. A. Sneen, *et al.*, *ibid.*, **87**, 292 (1965); **88**, 2593 (1966); (c) A. Streitwieser, *et al.*, *ibid.*, **87**, 3682, 3686 (1965).

(22) H. C. Brown, K. J. Morgan, and F. J. Chloupek, *ibid.*, **87**, 2137 (1965).

(23) The data in Table II correspond to 62 and 84% retention of activity[19] for solvolysis of I-OTs in acetic acid and 80% acetone, respectively. The corresponding values for III-OTs are 67 and 87%.

(24) J. A. Berson and M. S. Poonian, *J. Am. Chem. Soc.*, **88**, 170 (1966).

shift can also be ruled out. This shift leads to the carbonium ion related to the *exo*-bicyclo[3.2.1]octan-6-yl system. The latter has been shown[25] to give different products from those obtained from I-OTs and III-OTs. A 7,1-hydride shift in IIa (or IIc) also results in interconversion of enantiomers. It has been shown[7] that this shift does not occur in the *endo*-[3.2.1] system and from this it seems unlikely that it is involved in the present case.

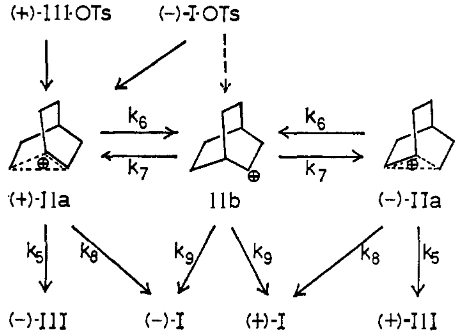


A 3,2-hydride shift in the initially formed ion-pair intermediate is a plausible mechanism for the racemization associated with ion-pair return. This shift, followed by ion-pair return with the usual stereochemical consequences, results in racemization of the substrate. If this hydride shift competes with ion-pair return it must also compete with the slower solvent capture and contribute to the loss of configuration at that stage of the reaction.

A probable mechanism for racemization of the carbonium ion system in competition with solvent capture is the reversible opening of IIa to the symmetrical [2.2.2] classical ion IIb.[8] It is questionable if this process is involved in the racemization associated with ion-pair return because this would require a migration of the toluenesulfonate ion to the opposite side of C_2. We are not aware of any cases in which this type of intramolecular inversion accompanies acetolysis of secondary alkyl arylsulfonates.

The present results are accommodated by the mechanism shown in Chart I. This scheme accounts for (a) predominating retention of configuration in both isomers; (b) racemization of an asymmetric intermediate in competition with solvent capture; (c) excess racemic [2.2.2] isomer I in the product starting with either isomer; and (d) similar, if not identical, product compositions for I-OTs and III-OTs.

Chart I



According to this scheme, ionization of I-OTs and III-OTs gives the asymmetric nonclassical ion IIa. The possibility of a small amount of parallel unassisted ionization of I-OTs to give IIb is indicated by a dashed arrow. This is included because of the indication that the product may be a little less active when starting with I-OTs than when starting with III-OTs. Presumably unassisted ionization would lead to racemic products—it is conceivable that this could give rise to [2.2.2] isomer with excess inversion (*cf.* stereochemistry of solvolysis of 2-octyl arenesulfonates[21b,c]) which would lead to excess racemic [2.2.2] isomer in the product. To fit the results in Table II to the scheme in Chart I requires that IIb is for the most part converted to racemic IIa (*i.e.*, $k_7/k_9 > 1$) and thus a small amount of entry at this point would not necessarily cause a detectable difference in product compositions for I-OTs and III-OTs. Only product-forming intermediates are indicated in Chart I and the loss of configuration that occurs prior to generation of capturable intermediates is not included. Also, the possibility that a 3,2-hydride shift in IIa may contribute to the racemization in competition with capture is not indicated.

The main feature of this mechanism is the involvement of the nonclassical and classical [2.2.2] ions IIa and IIb as product-forming intermediates. This was first proposed by Berson and Willner[8] for reasons similar to those involved in the present work. According to this interpretation, loss of configuration results from reversible opening of IIa to give IIb, and the latter is the origin of the excess racemic [2.2.2] isomer in the product. This is consistent with the observation that less activity is lost and there is less excess [2.2.2] isomer in the product for solvolysis in the more nucleophilic 80% acetone.

The excess racemic [2.2.2] isomer in the product could also result from a displacement reaction superimposed on the carbonium ion process. Formation of a small amount of the [2.2.2] isomer (~8% for acetolysis and ~5% for 80% acetone) by nucleophilic attack by solvent on I-OTs with inversion of configuration would lead to the observed results. In this connection, it should be recalled that most of the substrate equilibrates prior to solvolysis and thus similar results would be expected starting with either isomer. We believe that the excess racemic [2.2.2] isomer is derived from IIb as indicated in Chart I and does not result from a concurrent displacement with inversion because less of this material is formed in the more nucleophilic solvent, 80% acetone, than in acetic acid.

Experimental Section[11,26]

Optically Active Bicyclo[2.2.2]octan-2-ol (I-OH). The active [2.2.2] system I was obtained by catalytic hydrogenation[12] of optically active *endo*-bicyclo[2.2.2]oct-5-en-2-ol (IV) or the acid phthalate derivative.[9] In a typical experiment, 1.47 g of (+)-IV, $[\alpha]^{25}\text{D}$ 52.7°, mp 166–168° [28] (containing ~6% of the *exo* isomer) was hydrogenated[12] in 25 ml of absolute ethanol over 0.3 g of 10% palladium-on-carbon catalyst. Hydrogen uptake was rapid. Removal of the catalyst and solvent gave 1.45 g (98% yield) of (−)-I-OH, mp 220–222°, $[\alpha]^{25}\text{D}$ −24.5°, $[\alpha]^{25}_{365}$ −79.0.[12,28] This product was shown to be homogeneous by capillary gc.

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[25] Unpublished work by Dr. T. Padmanathan.

[26] Optical rotations were determined with an O. C. Rudolph and Sons Model 80 high-precision polarimeter equipped with a photoelectric attachment and oscillating polarizer. Readings were reproducible to within 0.003°. In all cases, infrared spectra of optically active compounds were indistinguishable from those of authentic racemic samples. Characteristic infrared bands for the bicyclic alcohols and their corresponding *p*-toluenesulfonate derivatives have been reported earlier in ref 17, 27, and H. L. Goering and M. F. Sloan, *J. Am. Chem. Soc.*, **83** 1397 (1961).

[27] H. L. Goering, R. W. Greiner, and M. F. Sloan, *ibid.*, **83**, 1391 (1961).

[28] Bicyclic alcohols and ketones were purified by sublimation (90°, aspirator pressure) prior to determination of rotations and melting points. Samples were sealed in capillaries for the melting-point determinations.

In another experiment a pure sample of (+)-IV, mp 167–168°, $[\alpha]^{25}_{\mathrm{D}}$ 27.8° (37.8% optically pure[9]), was converted to (−)-I-OH, $[\alpha]^{24}_{\mathrm{D}}$ −12.0°, mp 220–222°, by the method described above. This shows that optically pure I-OH has $[\alpha]^{25}_{\mathrm{D}}$ 32° and $[\alpha]^{25}_{365}$ 102°.[11]

(−)-Bicyclo[2.2.2]octan-2-yl Acetate (I-OAc). To correlate rotations of I-OH and I-OAc, 0.3 g of (−)-I-OH, $[\alpha]^{24}_{\mathrm{D}}$ −12.0°, was heated in 1.5 ml of freshly distilled acetic anhydride with 155 mg of anhydrous sodium acetate. The mixture was diluted with water and extracted with pentane. The extract was washed with 5% potassium carbonate solution and dried over sodium sulfate. Removal of the pentane gave 347 mg (88%) of colorless liquid acetate which was shown to be homogeneous (gc) and had $[\alpha]^{25}_{\mathrm{D}}$ −7.56°, $[\alpha]^{25}_{365}$ −25.4°. This material was derived from 38% optically pure I-OH which indicates that I-OAc has $[\alpha]^{25}_{\mathrm{D}}$ 20°.

Optically Active Bicyclo[2.2.2]octan-2-yl *p*-Toluenesulfonate (I-OTs). Active I-OH was converted to the *p*-toluenesulfonate derivative by a standard procedure described earlier.[27] The crude product was thoroughly dried under reduced pressure to remove all volatile contaminants. To avoid optical fractionation the samples used in the product studies were not recrystallized. The crude product was shown to be free of unreacted alcohol by infrared analysis of all of the fractions and residues resulting from fractional recrystallization. In a typical experiment (+)-I-OH, $[\alpha]^{25}_{\mathrm{D}}$ 24.6°, gave (+)-I-OTs, $[\alpha]^{25}_{\mathrm{D}}$ 6.11°,[11] mp 53.5–55°. Since the I-OH was 78% optically pure presumably the rotation of I-OTs is $[\alpha]^{25}_{\mathrm{D}}$ 7.8°. Recrystallization of the above (+)-I-OTs from pentane lowered the rotation to $[\alpha]^{25}_{\mathrm{D}}$ 5.38°.

Anal. Calcd for $C_{15}H_{20}O_3S$: C, 64.25; H, 7.19. Found: C, 64.30; H, 7.19.

Optically Active *exo*-Bicyclo[3.2.1]octan-2-ol (III-OH) and Derivatives. Optically pure (+)-*exo*-bicyclo[3.2.1]oct-3-en-2-yl acid phthalate (V), mp 83.7–85.2°, $[\alpha]^{24}_{\mathrm{D}}$ 234°, was prepared as described earlier.[9] Additional recrystallizations of this material did not result in any change in melting point or rotation. Reduction[12] of the above acid phthalate gave (+)-*exo*-bicyclo[3.2.1]octan-2-yl acid phthalate (III-AP), mp 108.8–110.0°, $[\alpha]^{25}_{\mathrm{D}}$ 20.7°.

Anal. Calcd for $C_{16}H_{18}O_4$: C, 70.06; H, 6.61. Found: C, 69.81; H, 6.62.

The above (+)-III-AP was saponified by refluxing in 1.5 *M* methanolic potassium hydroxide for 2.5 hr. After cooling, the solution was diluted with four volumes of water and extracted with pentane for 24 hr with a continuous extractor. Removal of the solvent from the dried extract (Na_2SO_4) gave (−)-*exo*-bicyclo[3.2.1]-octan-2-ol (III-OH), mp 198–200°, $[\alpha]^{25}_{\mathrm{D}}$ −16.9°,[11] −14.0° (*c* 1.2, 95% ethanol), $[\alpha]^{25}_{365}$ −54.5°. Capillary gc showed that this material did not contain any of the unsaturated alcohol; the only contaminant was a trace (∼0.1%) of the *endo* isomer VII-OH.

Anal. Calcd for $C_8H_{14}O$: C, 76.14; H, 11.18. Found: C, 76.04; H, 11.26.

Since the above (−)-III-OH was derived from optically pure (+)-V, presumably it also is optically pure. A duplicate experiment gave (−)-III-OH, $[\alpha]^{25}_{\mathrm{D}}$ −16.8°.

(+)-*exo*-Bicyclo[3.2.1]octan-2-yl acetate (III-OAc) was prepared from (−)-III-OH, $[\alpha]^{25}_{\mathrm{D}}$ −11.3°, by the method described above for acylation of I-OH. This gave liquid (+)-III-OAc, $[\alpha]^{25}_{\mathrm{D}}$ 0.485°.

Optically active III-OH was converted to the *p*-toluenesulfonate derivative as described above for the [2.2.2] isomer. In a typical case (−)-III-OH, mp 198–200°, $[\alpha]^{25}_{\mathrm{D}}$ −16.4°, $[\alpha]^{25}_{365}$ −53.2°, gave crude (+)-*exo*-bicyclo[3.2.1]octan-2-yl *p*-toluenesulfonate (III-OTs), mp 41–42°, $[\alpha]^{25}_{\mathrm{D}}$ 10.0°, $[\alpha]^{25}_{365}$ 31.5°. To avoid optical fractionation the samples used in the product studies were not recrystallized. These samples were shown not to contain unreacted alcohol by infrared analysis of various fractions and residues obtained by fractional recrystallization. An analytical sample was purified by one recrystallization from an ether–pentane mixture.

Anal. Calcd for $C_{15}H_{20}O_3S$: C, 64.25; H, 7.19. Found: C, 64.36; H, 7.20.

Kinetic Experiments. Anhydrous acetic acid was prepared as described earlier.[16] Reaction mixtures containing 0.057 *M* toluenesulfonate and 0.67 *M* sodium acetate in 100-ml volumetric flasks were placed in a 48.86° thermostat. After sufficient time for equilibration of the esters (270 min starting with I-OTs and 380 min starting with III-OTs) the rate constants for acetolysis were determined as described earlier.[17]

Polarimetric rates were determined for the same conditions and concentrations as the titrimetric rates. Zero-point readings were taken after equilibration of the esters (about 270 min), and the rate constants were determined[16] from the rate of change of optical activity. The optically active products are stable under these conditions and thus the infinity readings were constant. Results of the kinetic experiments are summarized in Table I.

Product Studies. A. Acetolysis. A 50-ml solution of 1.00 g (0.0036 mol) of (+)-I-OTs, $[\alpha]^{24}_{365}$ 6.11° (derived from 78% optically pure (+)-I-OH), and 0.325 g (0.0040 mol) of anhydrous sodium acetate in anhydrous acetic acid[16] was sealed in an ampoule and heated at 48.86° for 44 hr (greater than ten half-lives for acetolysis). The reaction mixture was added to 200 ml of water and extracted with pentane for 24 hr with a continuous extractor. The extract was washed three times with 5% aqueous potassium carbonate. After drying (Na_2SO_4), the pentane was removed by distillation and the residual acetate was saponified by refluxing in 10 ml of 1.5 *M* methanolic potassium hydroxide for 3 hr. The solution was diluted with 100 ml of water and extracted with pentane for 36 hr. Removal of the solvent left 0.385 g (86% yield) of a solid white residue consisting of 53.7% I-OH, 45.9% III-OH, and 0.4% VII-OH, $[\alpha]^{24}_{365}$ 36.9°.

This mixture was separated by preparative gc. After an initial separation into two fractions, the first fraction was recycled three times and the second fraction was recycled once. After sublimation of the first fraction, 29.4 mg of alcohol was obtained which consisted of 97.6% III-OH and 2.4% I-OH and had $[\alpha]^{25}_{365}$ 27.2°. Sublimation of the second fraction gave 66 mg of alcohol which consisted of 94.2% I-OH, 5.2% III-OH, and 0.6% VII-OH, $[\alpha]^{25}_{365}$ 37.1°. A third sample of alcohol, 27.1 mg, obtained by combining, miscellaneous fractions consisted of 56.9% I-OH and 43.1% IIa, $[\alpha]^{25}_{365}$ 33.0°. From these data it can be determined that the I-OH had $[\alpha]^{25}_{365}$ 37.9° (37% optically pure) and the III-OH had $[\alpha]^{25}_{365}$ 27° (49.5% optically pure).

Acetolysis of (−)-III-OTs, $[\alpha]^{24}_{365}$ −26.1° (derived from 87% optically pure (+)-III-OH), was investigated in a similar manner. The results of these experiments are presented in part A of Table II.

In control experiments it was found that optically active I-OAc and III-OAc are optically stable under conditions of the product studies and isolation.

B. Solvolysis in 80% Aqueous Acetone. In a typical experiment a 50-ml solution of 0.800 g (0.00286 mol) of (+)-I-OTs, $[\alpha]^{24}_{365}$ 5.09° (derived from 70% optically pure (+)-I-OH), and 0.2616 g (0.0033 mol) of pyridine in 80% aqueous acetone[16] was sealed in an ampoule and placed in a 48.86° thermostat for 45 hr (more than ten half-lives for solvolysis). About 25 ml of acetone was removed under reduced pressure which caused part of the product to separate. The residual mixture was diluted with 100 ml of water, and the resulting solution was extracted with pentane for 18 hr. The extract was washed three times with cold 2% hydrochloric acid, two times with 5% aqueous potassium carbonate, and then with water. After drying (Na_2SO_4), the solvent was removed by distillation. The slightly yellow residue, 300 mg (83% yield), consisted of 57.2% I-OH and 42.8% III-OH and had $[\alpha]^{24}_{365}$ 44.6°. This mixture was separated into three fractions as described above. The first 9.9 mg consisted of 91.2% III-OH and 8.8% I-OH and had $[\alpha]^{25}_{365}$ 35.1°, the second, 24.8 mg, consisted of 95.9% I-OH and 4.1% III-OH and had $[\alpha]^{25}_{365}$ 52.0°, and the third consisted of 68.5% I-OH and 31.5% III-OH and had $[\alpha]^{25}_{365}$ 46.1°.[11,27] From these data it can be determined that the [2.2.2] isomer I-OH in the product had $[\alpha]^{25}_{365}$ 52.8° (51.3% optically pure) and the *exo*-[3.2.1] isomer III-OH had $[\alpha]^{25}_{365}$ 33.4° (61.3% optically pure).

The products resulting from solvolysis of (−)-III-OTs, $[\alpha]^{24}_{365}$ −17.5° (derived from 56% optically pure (+)-III-OH), were investigated in a similar manner. The results of these experiments are presented in part B of Table II.

Control experiments showed that optically active I-OH and III-OH are optically stable under the conditions of the product studies.

Separation of I-OH and III-OH by Gas Chromatography. Compositions of mixtures of bicyclooctyl alcohols were determined by capillary gas chromatography as described in the previous paper. Mixtures of I-OH and III-OH derived from the solvolysis products were separated with a 10-ft, $^3/_8$ in. column packed with 20% TCEP on acid-washed Chromosorb P. Best results were obtained with on-column injection and temperature programming of 50 to 130° and a helium flow rate of 120 cc/min. The alcohol peaks overlapped; however, the separations outlined above could be obtained by using 60–90-mg injections and separating the mixture into two main fractions consisting of about 60–70% III-OH and 80–90% I-OH. Recycling these fractions two or three times gave III-OH from 92 to 97% pure and I-OH from 95 to 99% pure.

Control experiments showed that active I-OH and III-OH are optically and structurally stable under the conditions of the separation.