# Acetolysis of *exo*- and *endo*-Bicyclo[3.3.1]nonan-3-yl Toluenesulphonates

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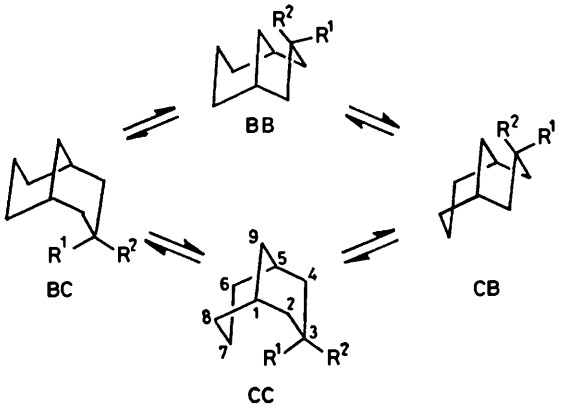
The rate constants for buffered acetolysis at 25° of *exo*- and *endo*-bicyclo[3.3.1]nonan-3-yl toluenesulphonates (2a and b) have been found to be $5.78 \times 10^{-5}$ and $5.96 \times 10^{-4}$ $s^{-1}$, respectively. The value found for (2b) differs from that given in an earlier report. Activation parameters are reported. The major product in both cases is bicyclo[3.3.1]non-2-ene. The bicyclo[3.3.1]nonan-3-yl acetate formed in the acetolysis of (2a) shows excess of retained stereochemistry. By use of a deuterium-labelled substrate the total amount of 3,7-hydride shift occurring in the reaction of (2a) has been found to be 5.9%, with the largest proportion of rearrangement (20.8%) appearing in the acetate of retained configuration. Empirical force field calculations on *exo*- and *endo*-bicyclo[3.3.1]nonan-3-ols (3a and b) and on the bicyclo[3.3.1]nonan-3-yl cation have been used to elucidate a possible course of reaction.

BICYCLO[3.3.1]NONANE and its derivatives have been interesting subjects for conformational analysis.[1] The skeleton contains mutually 1,3-bridged six-membered rings and a 1,5-methylene-bridged cyclo-octane ring. *X*-Ray crystallographic studies of derivatives [2] have shown that these adopt a twin-chair conformation in the solid state, and a recent electron diffraction study of the parent hydrocarbon [3] has shown that this is also the preferred conformation (1a-CC) in the gas phase. The




(1a) $R^1 = R^2 = H$
(2a) $R^1 = H$, $R^2 = OTs$ (2b) $R^1 = OTs$, $R^2 = H$
(3a) $R^1 = H$, $R^2 = OH$ (3b) $R^1 = OH$, $R^2 = H$
(4a) $R^1 = H$, $R^2 = CO_2Me$ (4b) $R^1 = CO_2Me$, $R^2 = H$

two chair-form cyclohexanes are flattened somewhat so that the internuclear angles between carbons are significantly increased over their 'normal' (cyclohexane) values. If the molecule is viewed as a methylene-bridged cyclo-octane, then the eight-membered ring has adopted a conformation reminiscent of the saddle form of cyclo-octane.[4]

Parker *et al.*[5] have recently determined the heat of combustion of the hydrocarbon and have thus estimated its strain to be *ca.* 10 kcal $mol^{-1}$, in fair agreement with the results of empirical force field calculations.[6] A considerable part of the total strain is attributable to the non-bonded interaction between the *endo*-hydrogens at the 3- and 7-positions, or to distortions of the molecular framework to relieve this interaction. Dreiding models (which do not allow for deformation of internuclear angles) place these hydrogens in van der Waals contact.

Other conformations are open to the molecule. Either or both of the cyclohexane rings can flip to give a chair-boat (1a-CB) or twin-boat (1a-BB) conformation. Empirical force field calculations on the hydrocarbon show that these conformations are more strained than the twin-chair conformation by 2.5 and 5.7 kcal $mol^{-1}$ respectively.[6] Conformations containing a chair-form cyclohexane are rigid with respect to twisting distortions which would remove the mirror plane of symmetry through C-3, C-7, and C-9, but the twin-boat form is flexible and could relax to a twin-twist boat form. The chair-boat and twin-boat conformations contain eight-membered rings approximating to the chair-boat and crown conformations of cyclo-octane itself.[4]

*exo*- and *endo*-3-Substituents modify these conformational preferences somewhat. An *exo*-3-substituent would be oriented equatorially with respect to the substituted six-membered ring and would emphasize the preference of that ring for the chair conformation. An *endo*-3-substituent would be oriented axially with respect to a chair-form cyclohexane moiety, and the resultant 1,3-diaxial and exacerbated 3,7-nonbonded interaction would destabilize the twin-chair form of substituted bicyclo[3.3.1]nonane.

These conformational preferences should be reflected in reactions which effectively remove the substituents, and we have investigated the acetolysis of *exo*- and *endo*-bicyclo[3.3.1]nonan-3-yl tosylates (2a and b) [7] in the hope that the results would afford further insight into the solvolytic reactivity of conformationally restricted cyclohexanes [8] and cyclo-octanes.[9]

*The Substrates.*—The epimeric alcohols (3a and b) were prepared by published methods.[10] The *exo*-alcohol (3a) is the major product of reduction of bicyclo[3.3.1]-nonan-3-one under equilibrating conditions. The n.m.r. spectrum of the alcohol has already been discussed, and is entirely consistent with the alcohol having the twin-chair (3a-CC) conformation. In particular the C-3 methine proton shows the characteristic pattern of coupling of a proton oriented axially with respect to a

cyclohexane ring. The n.m.r. spectrum of this alcohol shows no temperature dependence. The *endo*-alcohol (3b), the major product of metal hydride reduction of bicyclo[3.3.1]nonan-3-one,[10] has been shown to exist as a mixture of conformational isomers, with the chair-boat conformer (3b-CB) being the major component of the mixture at room temperature.[11]

Equilibration studies on the alcohols [12] (3a and b) and on the carboxylic acid esters [13] (4a and b) have shown the *exo*-epimers to be the more stable by 2.5 (94°) and 2.7 (20°) kcal mol$^{-1}$, respectively. The relative stabilities appear to be insensitive to the nature of the substituents (despite the difference in their *A* values [14]), and it has been suggested that the difference in stabilities of the epimers is largely a reflection of the skeletal changes involved in the equilibrium.[13]

We have used the empirical force field method to further investigate the conformations of the alcohols (3a and b). Calculations using Allinger's 1972 force field [15] gave the results illustrated in Figure 1.

Global minima were found for the epimers corresponding to the twin-chair structure (3a-CC) for the *exo*-epimer and for the chair-boat (3b-CB) of the *endo*-epimer. Other conformations represent local minima. In all cases, only minimal distortions from the represented structures with the mirror plane through C-3, C-7, and C-9 (neglecting hydroxy hydrogen) were found. The relative ordering of the energies of the epimers and their conformations is in qualitative but not quantitative agreement with the results of the experimental studies cited above. The difference in strain between the ground states of the epimeric alcohols is only 1.1 kcal mol$^{-1}$, too low to be considered in good agreement with the equilibrium results. In fact this is the same as the change in strain calculated for the twin-chair to chair–boat change in the hydrocarbon itself, when the Allinger force field is used and is lower than that found using Schleyer's force field.[6] The increase in strain for the conformational change within *endo*-alcohol going from (3b-CB) to (3b-CC), on the other hand appears to be too large to be consistent with the n.m.r. studies.

The reasons for the difference in results of Schleyer's and Allinger's force fields have already been discussed,[6] and Allinger [16] has already pointed out that his oxygen force field is not yet as reliable as its hydrocarbon counterpart. It is to be expected that the newer force fields [17] would give better agreement with experiment.

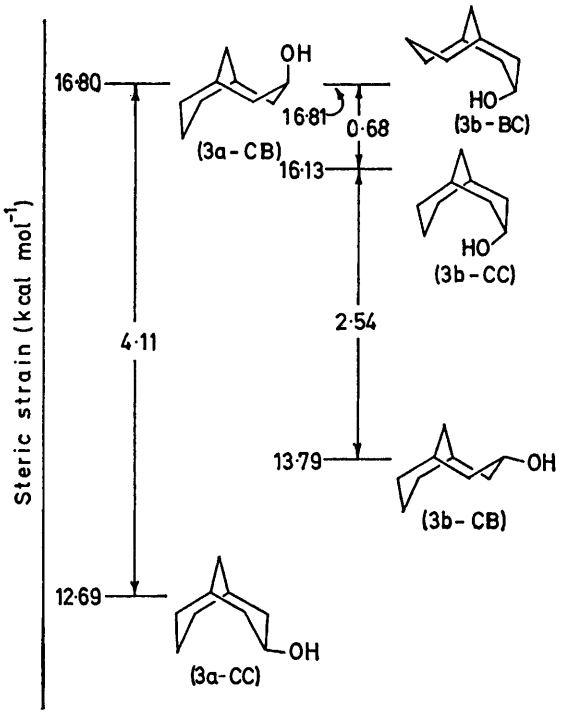



FIGURE 1 Relative strains of conformational isomers of *exo*- and *endo*-bicyclo[3.3.1]nonan-3-ol calculated by Allinger force field

The tosylate esters of the alcohols, prepared by the Tipson procedure,[18] were both nicely crystalline solids with sharp m.p.s (decomposition). The *endo*-tosylate (2b) was extremely sensitive to heat and moisture, and precautions were taken accordingly (see Experimental section).

*Solvolyses.*—Solvolyses in buffered acetic acid were

TABLE 1

Kinetic data for buffered acetolysis of *exo*- and *endo*-bicyclo[3.3.1]nonan-3-yl tosylates (2a and b)

| Substrate | $T$/°C | $k$/s$^{-1}$ | $k_{rel}$ | $\Delta H^{\ddagger}$/kcal mol$^{-1}$ | $\Delta S^{\ddagger}_{298}$/cal mol$^{-1}$ K$^{-1}$ [40] |
|---|---|---|---|---|---|
| (2a) [a] | 25 | 5.78 (±0.08) × 10$^{-5}$ | 1.2 × 10$^{3}$ | 22.24 (±0.06) | −3.34 (−0.21) |
| | 50 | 1.15 (±0.06) × 10$^{-3}$ | | | |
| | 70 | 9.25 (±0.41) × 10$^{-3}$ | | $\Delta G^{\ddagger}_{298}$ 23.24 (±0.12) kcal mol$^{-1}$ | |
| | 80 | 2.31 (±0.90) × 10$^{-3}$ | | | |
| (2b) [a] | 21.0 | 3.77 (±0.17) × 10$^{-4}$ | | | |
| | 25.1 | 5.96 (±0.11) × 10$^{-4}$ | 1.2 × 10$^{4}$ | 21.03 (±0.34) | −2.8 (±1.12) |
| | 26.2 | 7.13 (±0.32) × 10$^{-4}$ | | | |
| | 31.1 | 1.26 (±0.06) × 10$^{-3}$ | | $\Delta G^{\ddagger}_{298}$ 21.85 (±0.67) kcal mol$^{-1}$ | |
| | 34.8 | 1.96 (±0.07) × 10$^{-3}$ | | | |
| Cyclohexyl [b] | 25 | 4.88 × 10$^{-8}$ | 1.0 | | |
| Cyclo-octyl [b] | 25 | 2.82 × 10$^{-5}$ | 5.8 × 10$^{2}$ | | |
| *exo*-Bicyclo[3.2.1]octan-3-yl [c] | 25 | 4.87 × 10$^{-7}$ | 1.0 × 10$^{1}$ | | |
| *endo*-Bicyclo[3.2.1]octan-3-yl [c] | 25 | 5.32 × 10$^{-6}$ | 1.1 × 10$^{2}$ | | |

[a] This work. [b] Taken from ref. 20a. [c] Taken from ref. 20b.

monitored spectrophotometrically [19] and both epimers gave good first-order kinetics. The rate data, and some comparative data from other sources [20] are presented in Table 1.

In separate larger scale reactions the products of buffered acetolyses at 50° were identified. The olefin

DISCUSSION

It is evident from Table 1 that these are reactive substrates, being $10^3$—$10^4$ faster than cyclohexyl, and more than twice as reactive as cyclo-octyl tosylate. Rate enhancements in solvolysis of medium-ring substrates have been attributed primarily to relief of

TABLE 2

Products of buffered acetolysis of *exo*- and *endo*-bicyclo[3.3.1]nonan-3-yl tosylates (2a and b) at 50°

| | Products (%) | | | |
|---|---|---|---|---|
| Substrate tosylate | Olefin, bicyclo[3.3.1]non-2-ene | Acetates, *exo*- and *endo*-bicyclo[3.3.1]nonan-3-yl | | Unidentified |
| *exo*-Bicyclo[3.3.1]nonan-3-yl (2a) | 95 | 3.0 | 1.9 | 0.2 |
| *endo*-Bicyclo[3.3.1]nonan-3-yl (2b) | 89.5 | 6.6 | 2.8 | |

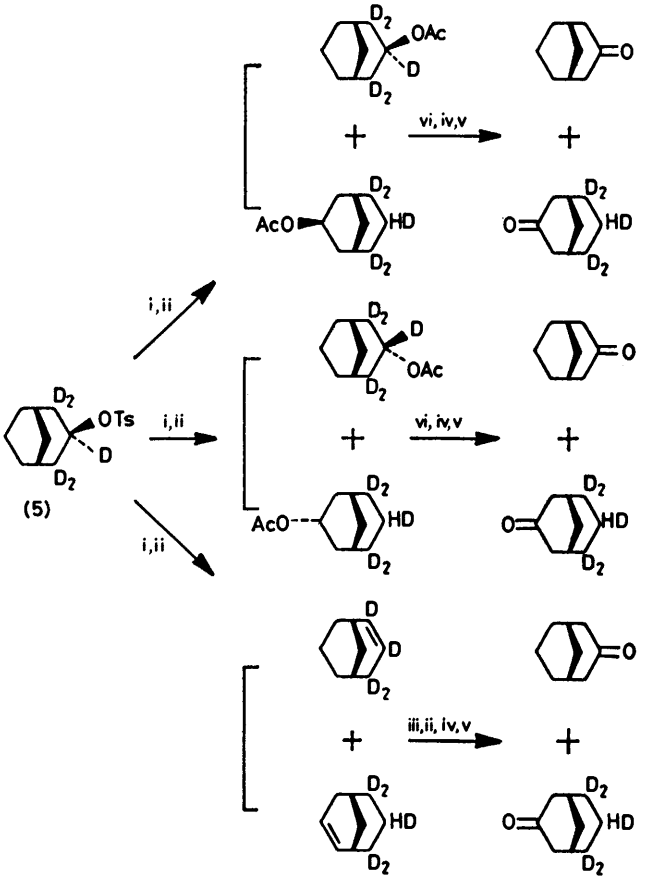
product, in both cases, could be isolated and identified by spectroscopic comparison with authentic material. The acetates were identified by g.l.c. comparison and cross-injection with authentic samples of possible products arising from direct displacement, 1,2-hydride shift, or combination of 1,2-hydride shift and Wagner–Meerwein rearrangement, namely, *exo*- and *endo*-bicyclo[3.3.1]nonan-3-yl acetates, *exo*- and *endo*-bicyclo[3.3.1]nonan-2-yl acetates,[12] *exo*- and *endo*-bicyclo[3.2.2]nonan-6-yl acetates,[21] and *exo*- and *endo*-bicyclo[4.2.1]nonan-2-yl acetates.[22]

The g.l.c. comparison allowed assignment of one of the product acetates as *exo*-bicyclo[3.3.1]nonan-3-yl acetate, which gave a peak well resolved from all other acetates. The second acetate was not well resolved and coinjected with *endo*-bicyclo[3.3.1]nonan-3-yl, *exo*-, and *endo*-bicyclo[4.2.1]nonan-2-yl acetates. The acetates were therefore isolated by preparative g.l.c., converted into the corresponding ketones, and subjected to mass spectroscopic comparison with authentic samples of the four authentic bicyclic ketones, confirming that both acetate products were derived from bicyclo[3.3.1]nonanone. The product distributions are summarized in Table 2.

The amounts of 3,7-hydride shift occurring in the solvolysis of *exo*-tosylate (2a) were determined using an adaptation of the method used by Cope and Gale [23] to determine 1,5-hydride shift in the acetolyses of cyclo-octyl arenesulphonates. The pentadeuteriated *exo*-3-alcohol (5a) was prepared from bicyclo[3.3.1]nonan-3-one by base-catalysed deuterium exchange, followed by reduction with sodium–ether–$D_2O$. Preparative scale buffered acetolyses of the tosylate ester gave an olefin–acetate mixture which was separated and the olefin and acetates were then converted separately to the corresponding bicyclo[3.3.1]nonan-3-ones by the methods indicated in the Scheme.

The ketones were then resubjected to base catalysed exchange conditions with water ($H_2O$), then analysed for deuterium content by mass spectrometry. Any material containing five deuterium atoms per molecule should only arise from material which suffered 3,7-hydride shift (or equivalent multiple shifts) in the course of the solvolysis reaction. The results are summarized in Table 3.

high ground state strain on ionization,[27] and recent experimental studies on the solvolysis of cyclo-octyl tosylate support this view.[28] The most obvious steric interaction relieved on ionization is indeed the 3,7-




SCHEME Reagents: i, buffered acetic acid; ii, g.l.c. separation; iii, $BH_3$ followed by alkaline hydrogen peroxide; iv, Jones oxidation; v, $OH^-$–$H_2O$; vi, $LiAlH_4$

non-bonded interaction, and empirical force field calculations on the hydrocarbon and the 3-cation (*i.e.* $H^-$ is taken as a model leaving group), using the Schleyer force field,[26] shows the 3-cation to be less strained by 2.5 kcal $mol^{-1}$. This number is certainly too low, as hydride ($H^-$) is not the best steric model for the leaving

TABLE 3

Products of buffered acetolysis of *exo*-2,2,3,4,4-pentadeuteriobicyclo[3.3.1]nonan-3-yl tosylate (30°)

| Product | Unrearranged (%) | Rearranged (%) | Rearrangement in product (%) |
|---|---|---|---|
| Bicyclo[3.3.1]non-3-ene | 76.4 | 2.8 | 3.4 |
| *exo*-Bicyclo[3.3.1]-nonan-3-yl acetate | 10.0 | 2.6 | 20.8 |
| *endo*-Bicyclo[3.3.1]-nonan-3-yl acetate | 6.9 | 0.5 | 6.8 |
| Total product * | 93.3 | 5.9 | 5.9 |

* 0.8% of an unidentified acetate was also found.

group ($OTs^-$). We restrict our comments, at this stage, to noting that the observed rate enhancements could easily be accounted for on the basis of relief of ground state strain.

Before we discuss other points, we must note that our rate data for the *endo*-3-tosylate (2b) disagrees with the value of $k_{25}$ of $7.4 \times 10^{-5}$ $s^{-1}$ reported earlier by Eakin *et al.*,[7] and is inconsistent with the value $k_{25}$ $22.5 \times 10^{-5}$ $s^{-1}$ reported by Schaefer and Flegal [26] for acetolysis of the brosylate. Combination of our data with that of Schaefer would give an extremely unusual brosylate : tosylate rate ratio of only 0.4.[22] Agreement for the *exo*-tosylate, however, is good, and, with Schaefer's data for the *exo*-brosylate gives a brosylate : tosylate rate ratio of 3.8, a value for which there is ample precedent.[22]

The fact that the rates found for the *endo*-tosylate and brosylate in the earlier work are so close to the rates for their *exo*-epimers ($k_{endo}/k_{exo} = 1.22$ for the tosylates and 1.07 for the brosylates) points to a possible reason for the difference between the results we present here and the earlier data. The *endo*-alcohol (3b), prepared by metal hydride reduction of bicyclo[3.3.1]nonan-3-one contains *ca.* 5% of its *exo*-epimer. We have found that attempted tosylation and recrystallization of the 95 : 5 mixture results in eventual isolation of the *exo*-3-tosylate, the *endo*-3-tosylate being thermally unstable and selectively decomposed under the conditions of recrystallization. We think it possible that the earlier workers, in fact, measured solvolysis rates of the *exo*-3-tosylate or brosylate in the belief that they were working with the *endo*-epimers.

In this work, the *endo*-3-alcohol was purified by preparative g.l.c. (as its acetate) prior to conversion to its tosylate ester. The *endo*-alcohol used was greater than 99.95% pure and certainly contained no detectable (0.01%) epimeric material.

Our rate data gives an *endo* : *exo* ratio of 10.5 which is close to the ratio found in the solvolyses of the related bicyclo[3.2.1]octan-3-yl tosylates,[22] and is in the same sense as axial : equatorial leaving group rate ratios found in other conformationally restricted cyclohexanes.[8]

Whiting has commented [27] that a large body of data on the solvolyses of cyclohexyl (and acylic) arenesulphonates, including β-deuterium isotope effects,[28] can be explained by a strong stereoelectronic preference for a leaving group to be anticoplanar to a β-hydrogen in the ionization process. The observed ratio is consistent with this view, being a reflection of the difference in the ground state energies and the conformational energies required to achieve this favoured condition.

If conformational behaviour of the *endo*-3-alcohol is taken as representative of its tosylate, then the *endo*-3-tosylate has the substituted ring in a boat conformation (2b-CB) (in which there are no β-hydrogen anticoplanar to the leaving group) in its ground state conformation. However, a flip of the substituted ring places the tosylate axial with respect to a chair-form cyclohexane (2b-CC) in which there are anticoplanar β-hydrogens. The n.m.r. data [11] on the alcohol, though not quantitative, suggests the free energy difference between these two conformations is unlikely to be >1 kcal $mol^{-1}$. The *exo*-3-tosylate with a twin-chair conformation (2a-CC) can only

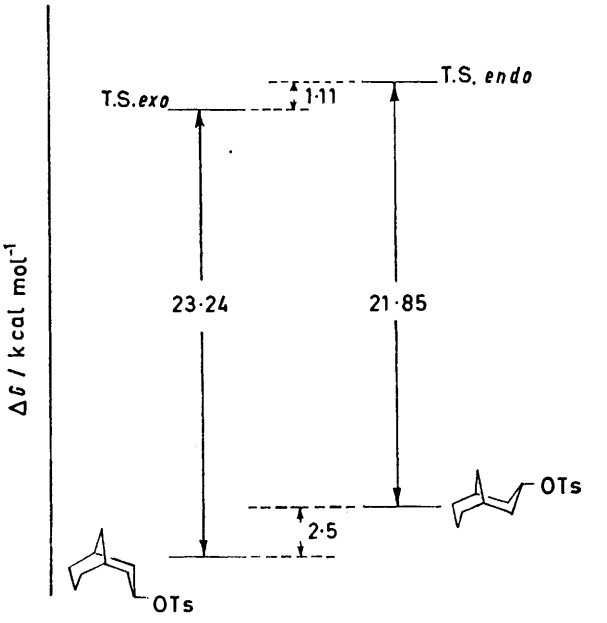



FIGURE 2 Free energy relationships in the acetolysis of *exo*- and *endo*-bicyclo[3.3.1]nonan-3-yl tosylates

achieve the anticoplanar arrangement of leaving group and β-hydrogen by a ring flip of the substituted ring to a boat conformation (2a-CB). In strain terms, the force field calculations suggest this process is endothermic by 4.1 kcal $mol^{-1}$, and the free energy change is likely to be similar.

In fact, combination of the observed activation energies with the stability data from equilibration of the alcohols (see Figure 2) suggests that the transition state for solvolysis of the *exo*-tosylate is *ca.* 1 kcal $mol^{-1}$ more stable than that for the *endo*-epimer. The size of this difference is very close to the combined experimental errors in the data used to derive it, and we hesitate to put much weight on it. Nevertheless, the possibility of a small rate enhancement in the *exo*-tosylate (perhaps due to anchimeric assistance) or rate depression in the *endo*-tosylate [perhaps due to steric hindrance to ionization from the twin-chair conformation (2b-CC)] cannot be eliminated on the basis of the kinetic data alone, and

we raise this point again in discussion of the product data.

Bicyclo[3.3.1]non-2-ene is the major product of acetolysis of both tosylates; no rearranged olefins were detected. The high proportion of olefin in the products (95% from the *exo*-tosylate and 91% from the *endo*-tosylate) can be rationalized in terms of relief of 3,7-non-bonded interaction. Solvent capture of cationic intermediates would re-establish this unfavourable interaction. The acetate from the *endo*-tosylate shows overall inversion of configuration. The absence of some rearrangement is remarkable in view of the results from the acetolysis of other simple arenesulphonates.[29] Recently Maskill and Banks [30] have demonstrated the presence of rearranged products in the acetolysis of the closely related bicyclo[3.2.1]heptan-3-yl tosylates.

The acetate products from the *exo*-tosylate show excess of retained configuration, in contrast to the high inversion found in almost all other simple cyclohexyl derivatives.[27] Although we have argued that ionization in the *exo*-tosylate takes place from a chair–boat form, it is difficult to reconcile this with the excess of retained acetate. It is possible that some reaction directly from the ground state twin-chair conformation could give rise to retained acetate since, in this conformation, the 7-methylene is positioned to shield the reactive centre at the 3-position from rearside solvent attack. Cyclohexanes with 'locked' equatorial leaving groups are extremely unreactive,[31] but in this case reaction from the twin-chair conformation, with formation of a trigonal centre at the 3-position, would provide an alternative to conformational change as a means of relieving the 3,7-non-bonded interaction.

Earlier workers [7,26] have discussed the possibility of ionization with participation of the *endo*-7-hydrogen leading to rate enhancements in the solvolyses of the *exo*-tosylate, but our finding of a 'normal' *endo* : *exo* rate ratio shows any enhancements must be small. However, Stehelin *et al.*[32] have shown that, in the ethanolysis of *exo*-bicyclo[3.3.1]nonan-3-yl tosylates carrying *exo*-7-substituents, rates and amount of 3,7-hydride shift in the products increase rapidly when the *exo*-7-substituent is cation-stabilizing. These authors point out that this result is consistent with inreasing σ-C–H participation by the *endo*-7-hydrogen. The *endo* : *exo* rate ratios were not presented in these studies but could have been most informative.

The total amount of 3,7-hydride shift found in the products of acetolyses of the *exo*-tosylate is only 5.9%, much less than the corresponding 50% found in the acetolysis of the cyclo-octyl substrate.[23] The retained configuration acetate shows the largest proportion of rearranged material. The product assigned as *endo*-bicyclo[3.3.1]nonan-3-yl acetate also shows 6.8% rearrangement.

Whether 3,7-hydride transfer accompanies ionization, or occurs in a subsequent step, the distances between the 3- and 7-positions of the bicyclo[3.3.1]nonane skeleton are such that hydride transfer could only occur when the skeleton adopts the twin-chair conformation. This situation could arise most simply by reaction directly from the twin-chair ground state, and if this were the only process giving rise to rearranged product, then the figure of 5.9% would also represent a minimum for the fraction of the reaction proceeding in this way. Alternatively reaction from the chair–boat conformation (2a-CB) could give a cationic intermediate (presumably an ion-pair) which could undergo conformational change to a twin-chair ion and hence also give rise to rearranged product. Evidence has been presented [33] that the lifetimes of simple acyclic carbonium ions in acetic acid are short relative to time for rotation about carbon–carbon single bonds, but the barrier for the boat-to-chair conversion in the intermediates from acetolyses of the bicyclo[3.3.1]nonan-3-yl tosylates could be substantially lower than that for rotation in acyclic carbonium ions. Conformational studies [34] on simple six-membered rings containing a single trigonal centre do not give information as to the size of the barrier, as monocyclic derivatives need not pass through a boat form with the trigonal centre at the 'bow' position, as would be the case in the bicyclo[3.3.1]nonane derivatives. In the absence of pertinent experimental data we have examined conformations of the bicyclo[3.3.1]nonan-3-yl cation using Schleyer's cation force field.

The results show an interesting difference in behaviour between the cation and its parent hydrocarbon (see Figure 2). The hydrocarbon shows two distinct energy minima, the lower associated with the twin-chair conformation (1-CC), and a second 2.58 kcal $mol^{-1}$ higher in energy associated with the chair-boat (1-CB). The size of the energy barrier between these was estimated by constraining C(1)–C(4) to planarity and allowing relaxation of all other atoms. Within thse constraints the 'transition state' for the ring flip lies 1.91 kcal $mol^{-1}$ above the chair–boat form. Similar treatment of the 3-cation, however, shows only a single minimum with a structure approximating to the twin-chair form. No second minimum was found corresponding to a chair–boat cation. The changes are conveniently represented by a plot of strain against the C(1)—C(4) torsion angle.

The absence of any second energy minimum in the cation is a result of the very low torsional barrier about bonds to trigonal centres.[6] Use of the same force field with the 1-methylpropyl cation through the same range of torsion angles gives an energy difference between $\phi_{1\text{-}2\text{-}3\text{-}4} = 40$ and $\phi = 0°$ (eclipsed) of only 0.51 kcal $mol^{-1}$ and when the s-butyl fragment is incorporated in the bicyclo[3.3.1]nonane framework, this small barrier is more than overcome by other interactions such as the eclipsing of groups along the C(1)—C(2) and C(4)—C(5) bonds in the chair–boat conformation. Although the force field calculations refer to gas-phase structures, and the structures of intermediates in solution are not well defined, the results point to a difference between the acyclic and bicyclic cations, and show it is not necessary to postulate any reaction from the twin-chair conformer to explain the observed rearrangement.

Activation energies for solvent capture and hydride transfer in these molecules must be finely balanced,[35] so that small changes in conformational energies can have large effects on products distributions.[36] We expect to comment in detail on this aspect in a later paper.

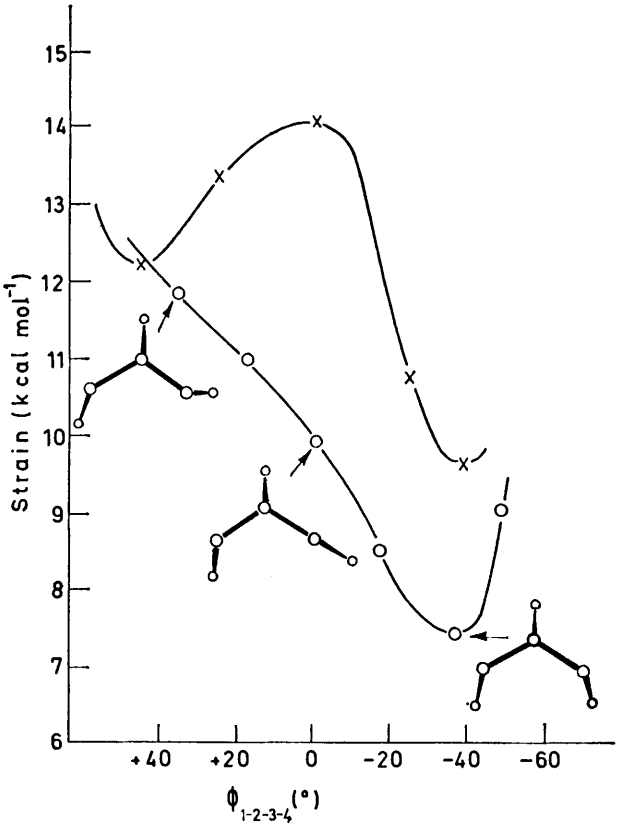



FIGURE 3 Variation of strain for twin-chair to chair-boat conformational change in bicyclo[3.3.1]nonane and the bicyclo-[3.3.1]nonan-3-yl cation calculated by the Schleyer force field: ×, hydrocarbon; ○, cation

## EXPERIMENTAL

I.r. spectra were taken for carbon tetrachloride solutions on Perkin-Elmer 157G or 457G spectrophotometers. N.m.r. spectra were determined for carbon tetrachloride solutions, with tetramethylsilane as internal reference, on a Perkin-Elmer R32 spectrometer at 90 MHz. Mass spectra were determined with an M.S. 902 instrument (P.C.M.U. Harwell).

Routine g.l.c. analyses were run on a Perkin-Elmer F-11 instrument on a 2 m × $\frac{1}{8}$ in stainless steel column with a 5% FFAP on Chromosorb G packing (carrier gas $N_2$; inlet pressure 20 lb $in^{-2}$; 150°). Silica gel $GF_{254}$ was used for both analytical and preparative t.l.c. (elution with 60 : 40 v/v ether–light petroleum). Preparative g.l.c. separations were run on a Varian 700 using a 12 ft × $\frac{3}{8}$ in column packed with 10% Carbowax on Chromosorb A (column temperature 150°; flow rate 180 ml $N_2$ per $min^{-1}$). Force field calculations were run on a CDC 7600 at UMRCC using an adapted version of the Princeton STRAIN program.

exo-*Bicyclo*[3.3.1]*nonan-3-ol* (3a).—The method described by Eakin[37] was used. Ethyl acetoacetate (8.12 g) and cyclohexenone (5 g) were added to a solution of sodium (1.2 g) in dry methanol, and the mixture was heated under reflux under nitrogen for 72 h. A solution of potassium hydroxide (7.82 g) in water (90 ml) was then added, and the mixture was refluxed for a further 12 h. The cooled mixture was then extracted with methylene chloride and the combined extracts were washed once with brine, dried ($Na_2SO_4$), and evaporated under reduced pressure to give 1-*hydroxybicyclo*[3.3.1]*nonan-3-one* which recrystallised from ether as needles (4 g), m.p. 191—193°; $\nu_{max.}$ ($CCl_4$) 3 602, 1 712, 1 151, 1 110, 1 080, and 1 007 $cm^{-1}$; δ($CCl_4$) 1.55 (5 H, m), 1.85 (3 H, m), 2.32 (2 H, m), 2.42 (3 H, m), and 3.85 (1 H, s) (Found: C, 69.8; H, 8.8. $C_9H_{14}O_2$ requires C, 70.1; H, 9.15%).

A solution of 1-hydroxybicyclo[3.3.1]nonan-3-one (4 g) in ether (250 ml) was added dropwise to phosphorus tribromide (8 g) in ether (50 ml) and the mixture heated under reflux for 1 h. The cooled solution was poured onto ice, the organic layer separated, washed with water and saturated sodium hydrogencarbonate solution, dried ($Na_2SO_4$), and evaporated under reduced pressure to give 1-bromobicyclo[3.3.1]nonan-3-one (6.8 g) as a light tan solid, m.p. 83.4—83.5°.

The crude bromoketone (5.0 g) dissolved in dry t-butyl alcohol (25 ml) and ether (50 ml) was added slowly to a stirred solution of lithium (2.5 g) in liquid ammonia (250 ml). The mixture was left for 3 h under reflux, then methanol was added until the blue colour was discharged. After evaporation of the ammonia, enough water was added to dissolve the solids, and the organic layer was separated, dried ($Na_2SO_4$), and evaporated under reduced pressure to give a light yellow solid. Sublimation under reduced pressure, and recrystallisation from light petroleum gave exo-*bicyclo*[3.3.1]*nonan-3-ol* (1.6 g), m.p. 96—97°, $\nu_{max.}$ 3 630, 1 475, 1 045, 1 005, and 981 $cm^{-1}$; δ 1.2—2.2 (14 H, m), 3.6 (1 H, s), 4.3 (1 H, 9 lines, $J_{AX}$ 11.0, $J_{BX}$ 6 Hz) (Found: C, 77.0; H, 11.4. $C_9H_{16}O$ requires C, 77.1; H, 11.5%).

G.l.c. analysis of the acetate of this alcohol showed it to contain $<1.0\%$ of its epimeric alcohol.

*Bicyclo*[3.3.1]*nonan-3-one*.—A solution of Jones reagent was added dropwise to a solution of *exo*-bicyclo[3.3.1]-nonan-3-ol (1 g) in acetone (30 ml) at 10° until the red colour of $Cr^{6+}$ persisted for longer than 5 min. The supernatant liquid was then decanted from the chromium salts, dried ($Na_2SO_4$), and evaporated. The residue was taken up in light petroleum, filtered through a wad of silica, and evaporated to give the crude ketone as a white amorphous solid. Sublimation gave material (0.8 g) identical in all spectroscopic and chromatographic respects to a sample of bicyclo[3.3.1]nonan-3-one prepared by the method of Hall *et al.*[38]

endo-*Bicyclo*[3.3.1]*nonan-3-ol*.—A solution of bicyclo-[3.3.1]nonan-3-one (0.2 g) in ether (5 ml) was added to a stirred suspension of lithium aluminium hydride (0.05 g) in ether (20 ml), and heated under reflux for 1 h. Excess of lithium aluminium hydride was then destroyed by cautious addition of saturated, aqueous sodium sulphate. The ether layer was decanted, dried ($Na_2SO_4$), and evaporated to give a crystalline solid (0.18 g) which was recrystallised from light petroleum as needles, m.p. 122—123°; $\nu_{max.}$ 3 623, 1 468, 1 110, 1 056, 1 022, 1 012, 962, and 931 $cm^{-1}$; δ 0.8—2.2 (14 H, unresolved), 2.7 (1 H, s), 3.88 (1 H, complex m) (Found: C, 76.8; H, 11.5. Calc. for $C_9H_{14}O$: C, 77.1; H, 11.5%).

Analysis of the acetate of this alcohol by g.l.c. showed it to

be contaminated by *ca.* 4% of its *exo*-epimer, which was not removed by recrystallisation. The bulk of the material was therefore acetylated and the *endo*-acetate purified by preparative g.l.c. The alcohol was recovered by cleavage of the acetate with lithium aluminium hydride.

*Acetylation Procedure.*—The appropriate alcohol (0.2 g) was dissolved in pyridine (2 ml) and acetic anhydride (0.5 ml) added. After standing at room temperature for 12 h, a chip of ice was added and the mixture was diluted with water and extracted with light petroleum. The extracts were washed with saturated aqueous copper sulphate solution and water, dried ($Na_2SO_4$), and evaporated to give the acetates as clear viscous oils.

*Tosylation Procedure.*—The Tipson [18] method was used with minor modification. Toluene-*p*-sulphonyl chloride (0.2 g) was added to a cooled solution (0°) of the alcohol (0.1 g) in pyridine (5 ml), the mixture shaken until solution was complete, then allowed to stand for 24 h at 0°. A chip of ice was added, and the mixture stirred at 0° for 10 min. The mixture was then poured into ice–water (50 ml) and extracted with precooled ether (0°). The extracts were washed sequentially with saturated copper sulphate solution, water, and saturated aqueous sodium hydrogencarbonate, all reagents having been precooled to 0°. The extracts were dried ($Na_2SO_4$) and evaporated under reduced pressure at $<10°$. The residue was taken up in the minimum amount of 1 : 1 v/v ether–light petroleum without heating and then cooled to −40° for crystallisation. Recrystallisation in the same manner gave the *exo*-tosylate (3a) as plates, m.p. 58.5—59°, and the *endo*-tosylate (3b), m.p. 49.5°, both samples showing $\lambda_{max.}$ 273, 267, 263, and 256 nm. They were stored at −15°. The samples decomposed readily at room temperature and it was not possible to obtain analytical data.

*Kinetics.*—A stock solution of 0.2M-sodium acetate in glacial acetic acid was used as a reaction medium. The buffered acetic acid (2 ml) was pipetted into stoppered 1 cm u.v. cells which were placed in the thermostatted cell block of a Gilford S2400 spectrophotometer. The cells were allowed to equilibrate for at least 30 min before substrate was added. The change in absorbance (relative to a solvent blank) at 273 nm was monitored as a function of time. Rates were calculated from 20—30 points on the curve up to at least three half-lives, and first-order rate constants were calculated using a non-linear least squares curve-fitting procedure.[39] Temperatures were steady to ±0.02° over the course of a kinetic run.

*Product Analyses.*—A solution of the tosylate [0.25 g in the case of (2a) and 0.1 g in the case of (2b)] in glacial acetic acid (10 ml of 0.5M in sodium acetate to which 1% of acetic anhydride was added) was placed in a stoppered flask and thermostatted at 50° for 24 h. The cooled mixture was poured onto ice–water (50 ml), extracted with pentane (2 × 10 ml), and the combined extracts washed once with water, then with saturated sodium hydrogencarbonate solution until no further carbon dioxide evolution was observed. The pentane solution was then dried ($Na_2SO_4$) and examined by g.l.c. on a 50 m × 0.02 in stainless steel WCOT column with a Carbowax 1540 coating (flow rate 2.5 ml $N_2$ $min^{-1}$; 140°). Under these conditions the products from both epimeric tosylates gave three peaks, one of short retention time (olefin) and two of longer (acetates). Cross injection of authentic samples of possible products (see text) allowed unequivocal identification of one of the acetate peaks as *exo*-bicyclo[3.3.1]nonan-3-yl acetate. This peak was well resolved from all other acetates. The second acetate peak coinjected with *endo*-bicyclo[3.3.1]nonan-3-yl acetate but resolution was not sufficient to rule out the possibility of this material being *exo*- or *endo*-bicyclo[4.2.1]-nonan-2-yl acetate. Resolution of the acetate mixture was not as good on either FFAP or TCEP columns. Relative detector responses were determined using a known mixture of bicyclo[3.3.1]non-2-ene and the *endo*- and *exo*-acetates. Peak areas were determined by photocopying the traces and cutting and weighing the peak. The olefin product was isolated after the g.l.c. examination by preparative g.l.c. and identified as bicyclo[3.3.1]non-2-ene by spectroscopic comparison with an authentic sample. The acetates, also isolated by preparative g.l.c., were converted into the corresponding ketones by cleavage with ethereal lithium aluminium hydride and oxidation with Jones reagent. Mass spectroscopic comparison with authentic ketone samples showed that the acetates to be derived either from bicyclo[3.3.1]nonan-3- or -2-one. Product stability to the reaction conditions was established by resubjecting the mixture to buffered acetolysis at 50° for 72 h. Standard work-up and g.l.c. examination showed no new peaks and no change in the peak ratios.

exo-2,2,3,4,4-*Pentadeuteriobicyclo*[3.3.1]*nonan*-3-*ol* (5a).—Bicyclo[3.3.1]nonan-3-one (2 g) was dissolved in dioxan (20 ml)–deuterium oxide (20 ml), to which sodium (0.5 g) had been added. The mixture was sealed in a Pyrex glass tube and heated at 100° for 72 h. The cooled tube was then opened, the contents poured into ice–water (50 ml), and extracted with light petroleum (3 × 20 ml). The combined extracts were dried ($Na_2SO_4$), and evaporated to yield the crude deuteriated ketone, which was resubjected twice to the same exchange conditions. The ketone was finally purified by sublimation at 80° at aspirator pressure to give 2,2,4,4-tetradeuteriobicyclo[3.3.1]nonan-3-one (1.75 g), identical in its g.l.c. behaviour to undeuteriated material. The i.r. spectrum showed a peak at 2 100 $cm^{-1}$ (C–D stretch). Mass spectral analysis of the ketone showed $^2H_0$ and $^2H_1$ (<1%), $^2H_2$ (1%), $^2H_3$ (12%), and $^2H_4$ (87%).

The tetradeuteriated ketone was dissolved in dry ether (30 ml) and deuterium oxide (0.2 ml) added. A small piece of sodium (0.1 g) was added and the mixture was stirred under nitrogen until reaction ceased. More deuterium oxide (0.2 ml) was added, and further reaction took place until all the sodium was consumed. Alternate addition of sodium and deuterium oxide was continued until g.l.c. analysis of the reaction mixture showed all the ketone had been converted. The mixture was then washed with water, the organic layer separated, dried ($Na_2SO_4$), and evaporated to yield the crude deuteriated alcohol. Recrystallization from ether gave *exo*-2,2,3,4,4-pentadeuteriobicyclo[3.3.1]nonan-3-ol (1.4 g), m.p. 190°; $\nu_{max.}$ 3 600, 2 220, and 2 120 $cm^{-1}$ (C–D stretch); δ 1.2—2.2 (9.5 H, complex pattern) and 3.7 (1 H, s). The region at δ 4.3 where the alcohol methine signal would be expected showed no signal. Mass spectral analysis of the trimethylsilyl ether of the alcohol gave $^2H_0$, $^2H_1$, and $^2H_2$ (<1%), $^2H_3$ (1%), $^2H_4$ (12%), and $^2H_5$ (88%). G.l.c. analysis of the acetylated alcohol showed it to be contaminated with 2.5% of the *endo*-epimer.

*Acetolysis of* exo-2,2,3,4,4-*Pentadeuteriobicyclo*[3.3.1]*nonan*-3-*yl Tosylate.*—The tosylate (2.5 g) and buffered acetic acid (50 ml of 0.5M in NaOAc, 1% in acetic anhydride) were placed in a stoppered flask which was then placed in a thermostatted (30°) water bath. After 150 h the flask was

cooled, the contents poured into ice–water (200 ml), and extracted with pentane (4 × 25 ml portions). The combined extracts were washed with saturated aqueous sodium hydrogencarbonate solution, dried ($Na_2SO_4$), then examined by g.l.c. on a 2 m × ⅛ in 5% FFAP column. The following components (in order of increasing retention time) were identified by cross-injection with authentic samples: bicyclo[3.3.1]non-2-ene, *exo*-3-bicyclo[3.3.1]nonan-3-yl acetate, and *endo*-3-bicyclo[3.3.1]nonan-3-yl acetate. A fourth minor component of longer retention time was also found but was not identified. These four peaks gave peak areas in a ratio of 37.3 : 1.91 : 1.01 : 0.12 (average of three runs). Detector response was calibrated against a mixture of known composition prepared from authentic samples of the identified components. The corrected molar ratios for the known components were 79.2 : 12.6 : 7.5. The pentane solution was then evaporated to an oil and applied to a short silica column. Elution with light petroleum gave the olefin and elution with ether gave the acetate mixture.

The acetates were then separated by preparative g.l.c. on the Carbowax column and separately cleaved with lithium aluminium hydride and oxidized with Jones reagent to bicyclo[3.3.1]nonan-3-one before resubjection to base catalysed exchange conditions (see preparation of deuteriated alcohol) using water in place of deuterium oxide. The ketones were then analysed for deuterium content by mass spectroscopy. That from the *exo*-acetate gave $^2H_0$ (72%), $^2H_1$ (3%), $^2H_2$ (2%), $^2H_3$ (1%), $^2H_4$ (2%), and $^2H_5$ (18%). That from the *endo*-acetate gave $^2H_0$ (87%), $^2H_1$ (2%), $^2H_2$ (2%), $^2H_3$ (1%), $^2H_4$ (1%), and $^2H_5$ (7%).

The olefin was converted to a mixture of *exo*-bicyclo-[3.3.1]nonan-3- and -2-ol by standard hydroboration and alkaline hydrogen peroxide oxidation. The alcohol mixture was acetylated and the bicyclo[3.3.1]nonan-3-yl acetate isolated by preparative g.l.c. before conversion as before into bicyclo[3.3.1]nonan-3-one and subjection to exchange conditions. Analysis for deuterium content of this olefin derived ketone gave $^2H_0$ (84%), $^2H_1$ (9%), $^2H_2$ (2%), $^2H_3$ (1%), $^2H_4$ (0%), and $^2H_5$ (3%).

The product ratios given in Table 3 have been adjusted for incomplete deuteriation of substrate.

exo- *and* endo-*bicyclo*[3.3.1]*nonan-2-yl acetates* were prepared by reduction of the 2-ketone and acetylation according to published method.[12]

exo- *and* endo-*bicyclo*[3.2.2]*nonan-6-yl acetates* were prepared by method of Penrose.[21]

exo- *and* endo-*Bicyclo*[4.2.1]*nonan-2-ols*.—The alcohols were a generous gift from Professor G. Klein, Tubingen.

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