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# STERIC EFFECTS IN BICYCLIC RING SYSTEMS. II. ANGLE STRAIN AND NON-BONDING REPULSION IN BASE-CATALYZED DEUTERIUM EXCHANGE OF BICYCLIC KETONES[1]

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It has been found that rates of base-catalyzed deuterium exchange of bicyclic ketones[2,3,4] and bicyclic nitriles[5] are a sensitive probe for the chemical consequences of structural variation. Results reported herein for exchange of bicyclo[2.1.1]hexan-2-one (1) and bicyclo[2.2.2]octan-2-one (2), when compared to the corresponding rates for bicyclo[2.2.1]heptan-2-one (3), establish that angle strain (I-strain) and non-bonded van der Waals repulsion (F-strain) are major contributors to the rate differences. Results on methyl-substituted bicycloheptyl derivatives reported in Part III[6] indicate that torsional strain[7] has an indeterminate influence. Hybridization effects[8] are not detected in these reactions but may still be operative. The rates of exchange are collected in Table I and relative rates are illustrated in Figure I.

The large decrease in rate of 1[9] relative to exo-3 ($k_{rel}$= 9,000) is attributable to the angle strain in 1 making generation of a new $sp^2$ carbon in the enolate (or enol) transition state more difficult. The non-bonded repulsions from the adjacent one-carbon bridges should be approximately the same. Similar reasoning can account for the enhanced rate of 2 relative to endo-3. The hybridization of the exchanging carbon in the more strained rings would favor the opposite trend in reactivity, as evidenced by the order of exchange of the cycloalkanes with base ($C_6$:$C_5$:$C_4$:$C_3$ = 1.00:5.72:28:7.0 x $10^4$).[8]

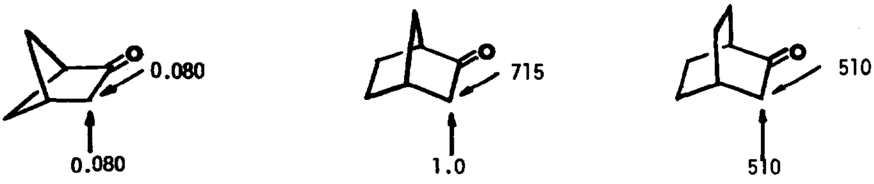
The comparison of 2 relative to exo-3 illustrates that despite the more favorable bond angle in 2, the non-bonded repulsions of an adjacent two-carbon bridge in 2 relative to the one-carbon bridge on the exo-face of 3 makes the rates of exchange comparable. The greater steric hindrance on the endo face of the bicyclo[2.2.1]heptyl system is well documented for a variety of kinetic and

Table I. Second-Order Rate Constants of NaOD-Catalyzed Deuterium Exchange of Ketones at 25.0° in 2:1 Dioxane-$D_2O$[a].

| Ketone | | $k_2$(l. mol$^{-1}$ sec$^{-1}$) |
|---|---|---|
| Bicyclo[2.1.1]hexan-2-one (1) | | $1.23 \times 10^{-5}$ |
| Bicyclo[2.2.2]octan-2-one (2) | | $7.88 \times 10^{-2}$ |
| Bicyclo[2.2.1]hexan-2-one (3) | exo | $5.48 \times 10^{-2}$ |
| | endo | $7.67 \times 10^{-5}$ |

[a] Rates were obtained as in Ref. 1 by observing the decrease in the non-labeled parent ion peak by mass spectrometry.

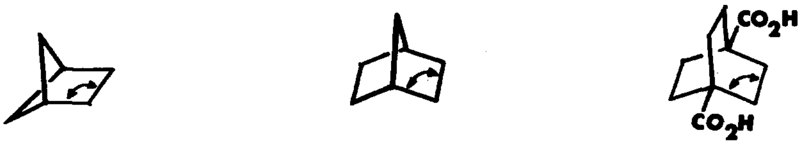
Figure I. Relative Rates of NaOD-Catalyzed Deuterium Exchange of Ketones at 25.0° in 2:1 Dioxane-$D_2O$.[b,c]



1 (1758)[d]  3 (1751)[e]  2 (1731)[e]

[b] Per equivalent H relative to endo-3; [c] Ketone stretching frequency (cm$^{-1}$) in parenthesis; [d] Ref. 10b; [e] Ref. 13

Figure II. Measured Bond Angles of Bicyclic Compounds.



100.5°[f,g]  103.0°[f,h] 104.3°[f,i]  110°[j]

[f] Electron diffraction; [g] Ref. 14; [h] Ref. 15a; [i] Ref. 15b; [j] X-ray, Ref. 16.

equilibrium properties. For example, hydroboration of bicyclo[2.2.1]heptene gives a preference for exo attack of 200,[11] whereas the norbornyl radical abstracts chlorine from a variety of donors with an exo preference of 2 to 42.[12]

There have been several examinations of the correlation of chemical reactivity with the interrelated physical properties of bond angles, ketone stretching frequencies, nmr coupling constants, and hybridization.[8,13] For example, a relationship has been observed between rates of solvolysis of secondary sulfonates and stretching frequencies of the corresponding ketones.[13a] It was proposed by Foote[13a] that "It should be possible to extend the correlation to other types of reaction involving tetrahedral ground states and trigonal transition states (or vice versa)". Ketone enolizations fulfill this criterion and inspection of the rates and carbonyl stretching frequencies (Fig. I) show that the expected trend is observed, although the fact that there are two distinguishable rates for **3** require that a more sophisticated treatment that includes other factors such as non-bonded interactions will be needed to quantitatively account for the results. Such a treatment has been utilized by Schleyer for the sulfonate solvolyses[13b] but will be deferred in the present case until realistic estimates of the transition state structures and the interactions therein can be made.[17] This will be particularly complex in the present case because of the large role no doubt played by solvation.

Ideally the angle strain in these reactions, which involve conversion of molecules with one sp$^2$ carbon to an intermediate with two such carbons, would be evaluated from the precise geometries of the ketones and the transition states. Unfortunately, these geometries have not been experimentally determined for any of these structures, but some relevent bond angles for the parent saturated ring systems are given in Table II. As expected these follow the trend of the ketone frequencies but are insufficient to quantitatively correlate the data.

In summary, angle strain and non-bonded repulsions have been shown to have dominant influences on the rates of base-catalyzed deuterium exchange in bicyclic ketones, while hybridization effects are overshadowed.

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