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# SYNTHESIS AND REACTIVITY OF EXO- AND ENDO-5-SUBSTITUTED BICYCLO[2.1.0]PENTANES

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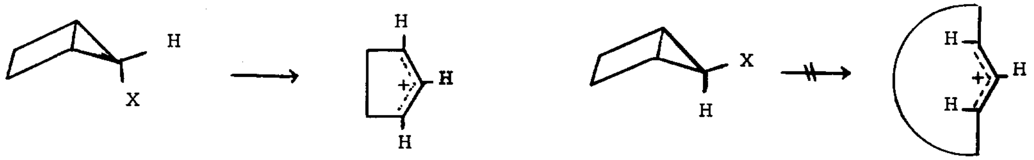
In the solvolysis of cyclopropyl systems, theoretical calculations have predicted (1) and experimental work has verified (2) that substituents trans to the leaving group prefer an outward disrotatory motion. Application of this concept to (n + 3)-substituted bicyclo[n.1.0]alkyl systems, where n is small (e.g. 2, 3, or 4) suggests the endo compounds should solvolyze more rapidly than their exo-epimers (3). We felt that this epimeric reactivity difference might be maximized in the bicyclo[2.1.0]pentyl series where the favored mode



I a, X = OH
b, X = $OCH_2C_6H_5$
c, X = OPNB

II a, X = OH
b, X = $OCH_2C_6H_5$
c, X = OPNB

for disrotatory opening of the endo-epimer I would involve considerable relief of the strain energy present in the starting material (approx. 54.1 kcal/mole (4)).‡ The solvolysis of the exo-epimer might be expected to proceed very slowly since a concerted ring-opening ionization process is disfavored. Indeed, the solvolytic reactivity of exo-bicyclo[3.1.0]hex-6-yl triflate ranks it as the least reactive secondary system recorded (5).

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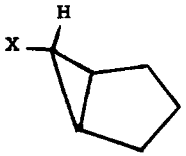
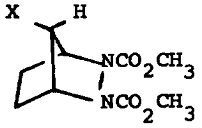
‡ Ring opening of bicyclo[2.1.0]pentane to the corresponding diradical would release approx. 50.5 kcal/mole (4). Some fraction of this must be released in achieving the transition state for solvolysis.

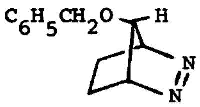
To achieve our synthetic goals, the previously reported (6) 2,3-dicarbomethoxy-anti-2,3-diazabicyclo[2.2.1]heptan-7-ol (IVa) was benzylated. The corresponding benzyl ether, IV b, was converted into the diaza benzyl ether V, which upon photolysis afforded an 85:15 mixture of *exo*- and *endo*-5-benzyloxybicyclo[2.1.0]pentanes, respectively. The *exo*-benzyl ether IIb was separated and cleaved to the corresponding alcohol with sodium/liquid ammonia.



III



IV a, X = OH
b, X = $OCH_2C_6H_5$



V

The kinetic data for the *exo* OPNB IIc is summarized in the following table.

Solvolytic Reactivity of (n + 3)-Substituted Bicyclo[n.1.0]pentanes[a]

| Compound | Solvent | Temp, °C | k, $sec^{-1}$ |
|---|---|---|---|
| IIc | 80% aq. acetone | 75.4±0.2 | (3.14±0.16)x$10^{-6}$ |
| IIc | 80% aq. acetone | 95.0±0.2 | (2.98±0.14)x$10^{-5}$ |
| IIc | 80% aq. acetone | 25.0 | 2.6 x$10^{-9}$[b] |
| IIc | 60% aq. acetone | 95.0±0.2 | (3.25±0.14)x$10^{-5}$ |
| IIc | acetic acid | 25.0 | 2.6 x$10^{-9}$[c] |
| III-OPNB | acetic acid | 25.0 | *ca.* $10^{-27}$[d] |
| IIc | bromobenzene-$d_5$ | 75.5° | 3.4 x$10^{-6}$[e] |
| IIb | bromobenzene-$d_5$ | 135° | *ca.* $10^{-4}$[f] |
| IIc | 80% aq. acetone | 135° | 1.6 x$10^{-3}$[b] |

(a) Determined titrimetrically unless otherwise noted. (b) Extrapolated from kinetic data at 75.4° and 95°. (c) Since no significant change in rate is observed with change in solvent polarity, this rate constant is estimated from the datum in 80% aq. acetone at 25°. (d) Estimated by assuming a OTs/OPNB rate ratio of $10^{10}$ (S. Winstein, M. Shavatsky, C. Norton and R. B. Woodward, J. Amer. Chem. Soc., 77, 4183 (1955), and data in reference 7) and a OTf/OTs rate ratio of $10^5$ (5). (e) Determined by nmr. (f) Instantaneous rate constant determined after *ca.* one half-life.

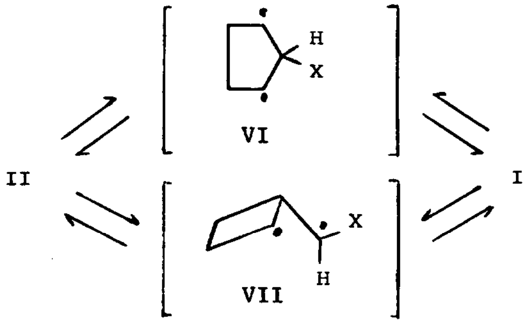
There are two striking features which emerge from the tabulated data. The solvolysis of *exo*-OPNB IIc is, within experimental error, independent of solvent polarity (cf., data in bromobenzene-$d_5$, 60% and 80% aqueous acetone).

By comparison, anti-bicyclo[2.2.1]hept-2-ene-7-ol p-nitrobenzoate exhibits a nineteen-fold rate acceleration in going from 80% to 60% aqueous acetone (7). More remarkably, acetolysis of exo-OPNB IIc exceeds that of III-OPNB by a rate factor of ca. $10^{18}$!

The above results suggest that IIc and III-OPNB undergo solvolysis by different mechanistic pathways and, moreover, that the rate-limiting step for IIc does not involve charge separation. These considerations are embodied in the following suggested scheme.

In accord with this picture, the rate constant (measured at 135° by an nmr technique) for the transformation of exo-benzyl ether IIb into its endo-epimer, determined in bromobenzene-$d_5$, only differs from the corresponding rate constant for IIc in 80% aqueous acetone by a small factor (i.e., ca. 10). Also, the endo-derivatives (i.e. I) are much more reactive than their exo-counterparts. Warming a solution of endo- and exo- acetates in carbon tetrachloride at 60° for 15 minutes resulted in the complete isomerization of the endo-acetates to 3-acetoxycyclopentene whereas the exo-acetate remained unchanged.‡

A plausible intermediate for the conversion of exo-derivatives into their endo-counterparts is the 1,3-diradical formed by severing the $C_1$-$C_4$ bond in II; however, the activation energy we obtain from our kinetic data (Ea = 29.2 kcal/mole) is considerably less than that reported by Chesick (9) (Ea = 38.9 kcal/mole) for an analogous



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‡ The formation of 3-cyclopentenyl derivatives from I or II may also be viewed as a concerted [$\sigma^2s$ + $\sigma^2a$] process (9).

reaction involving 2-methylbicyclo[2.1.0]pentane, or those reported by Jorgensen and co-workers (10) (Ea ~ 33-36 kcal/mole) for systems where the diradical is expected to be stabilized by bridgehead substitution (11). Thus, either the 5-substituent is exhibiting a special effect which stabilizes the transition state for the formation of the 1,3-diradical VI (12, 13), or the reaction may proceed by cleavage of the $C_1$-$C_5$ bond (10) to afford a different 1,3-diradical i.e., VII). This point is under investigation (14).

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