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# MIGRATION OF A CARBOXAMIDO GROUP WITH PARTICIPATION BY AMIDE NITROGEN

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Although molecular rearrangements in the fully carbocyclic bicyclo [2.2.1] heptyl and bicyclo [2.2.2] octyl series are well known,(1) there are few analogies to be found in those systems containing atoms other than carbon.* In addition, although neighboring group participation by amino groups is well known, (3) participation by an amide nitrogen under other than basic conditions appears to be without precedent.

We wish to report the rearrangement of a 2-azabicyclo [2.2.2] octane derivative to a 2-azabicyclo [3.2.1] octane under mild solvolytic conditions. In addition to being a rather unusual migration of an amide group, this rearrangement appears to be the first example of neighboring group participation by amide nitrogen in other than strongly basic media.**

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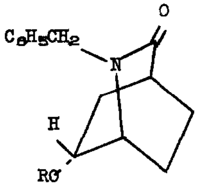
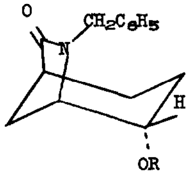
* A notable exception is the racemization of L-(+)-2-α-tropanol(2). This reaction, however, proceeds with participation of an amino group, a type of interaction for which there is considerable precedent.

** A number of examples of reactions where participation of the nitrogen atom in the ambident anion derived from an amide in strong base are known (Ref. 3b), and participation by amide oxygen is well known (Ref. 3).

When 2-benzyl-3-oxo-6-endo-tosyloxy-2-azabicyclo [2.2.2] octane,*** m.p. 152-154°, was heated (Reflux, two hours) in acetic acid sodium acetate, two acetates were obtained. The minor product, m.p. 124-125° (33%) was the endo-acetate (Ic) (6) and the major product of the mixture (67%) was 2-benzyl-3-oxo-7-endo-acetoxy-2-azabicyclo [3.2.1] octane, m.p. 92-94°. By both thin layer and gas chromatography these are the only products of the solvolysis, and the overall yield is 97%. The structure of (IIa) was confirmed by its infrared spectrum ( $\lambda^{KBr}_{max}$ 5.78, 5.96$\mu$ , versus 5.78 and 6.06$\mu$ for Ic), and the n.m.r. spectrum which showed the equatorial proton at C-7 as a rather narrow multiplet at 4.80 $\delta$ . The balance of the n.m.r. spectrum, with the exception of the high field methylene region was quite similar to that of the unrearranged acetate. In all these compounds the benzyl protons appear as an AB pattern(J=14-15 cps) and further evidence for the structure of IIa is found in the



Ia) R=$SO_2C_7H_7$
b) R=H
c) R=$COCH_3$



IIa) R=$COCH_3$
b) R=H
c) R=$SO_2C_7H_7$

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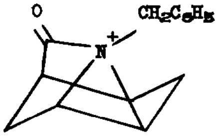
*** This compound was prepared by the reaction of the corresponding alcohol (Ib), m.p. 97-99°, with tosyl chloride-pyridine. The azabicyclooctanol was prepared by the route employed in the synthesis of desethylibogamine(4). Satisfactory analytical data were obtained for all new compounds and all compounds were characterized by infrared and nuclear magnetic resonance spectroscopy. The prefixes endo and exo are arbitrarily assigned to describe the relation of the substituent to the nitrogen bridge.

fact that $\Delta\delta$ for these protons in both the acetate and corresponding alcohol is the same. Mechanistic considerations also demand that the compound has the stereochemistry assigned. The rearranged acetate was further characterized by hydrolysis to the alcohol and oxidation to the corresponding ketone, ($\lambda^{KBr}_{max}$ 5.84, 5.92$\mu$) m.p. 73-75° which was different from the ketone, m.p. 98-99° ($\lambda^{KBr}_{max}$ 5,84, 6.10$\mu$) obtained by oxidizing Ib.

The tosylate from the bicyclo [3.2.1] octanol (IIc) m.p. 85-86°, also gave a mixture of Ic and IIa in a ratio of 1:2. Either tosylate (Ia or IIc) on heating to 170° gave a mixture of the two tosylates in a ratio of <u>ca</u>. 5 to 1 with the bicyclo [3.2.1] octanol derivative as the major product.

The above rearrangement, the observed retention of configuration in the acetates, and the interconversion of tosylates Ia and IIc appear to demand that the reactions of Ia and IIc proceed <u>via</u> a common intermediate. The species which best agrees with these data is an acylaziridinium ion (III).



III

Conversion of either tosylate to III, followed by attack of an appropriate nucleophile at either of the reactive sites on the carbocyclic ring gives the products observed in these reactions.

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