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STEREOCHEMISTRY OF THE BASE CATALYZED KETONIZATION OF THE BIRDCAGE ALCOHOL

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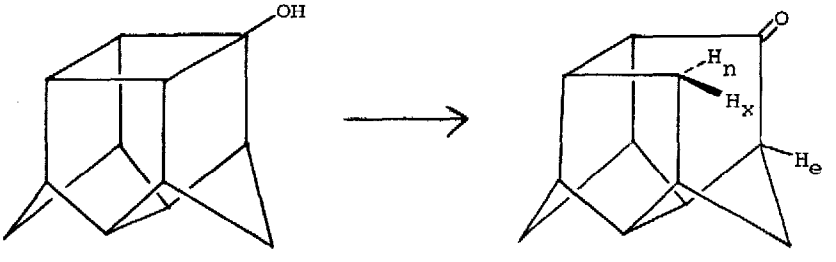
In 1965 Howe and Winstein[1a] and Fukunaga[1b] reported the base catalyzed cleavage of the birdcage alcohol (1) to the half-caged ketone (2). The stereochemistry observed in the base catalyzed ketonization of cyclopropanols[2] led Winstein and Howe to conjecture that the transformation of 1 to 2 proceeds with inversion of configuration, the solvent delivering the exo proton (H_x) in 2.



1 2

More recently, however, we[3] and others[4] have found that polycyclic alcohols which do not contain cyclopropanol rings undergo base catalyzed cleavage with very nearly complete retention of configuration. Because of our continuing interest in this carbon-carbon bond cleavage reaction, we undertook the study of the stereochemistry of deuterium incorporation into 2 when 1 is treated with base in deuterated alcohol solvents.

Heating 1 in $(CH_3)_3COD$,[5] 1M in $(CH_3)_3OK$, for 48 hr at 100° converted it to 2, which was purified by sublimation. The pmr spectrum showed the upfield doublet for H_n in 2[1] to be greatly reduced in size;[6] and only a very small singlet appeared, corresponding to collapse of the doublet for H_n by deuterium incorporation at H_x. Although it was thus clear that deuterium had been preferentially incorporated at H_n, it was impossible to determine accurately the quantitative preference for the retention over the inversion pathway, since there are no other signals in the pmr spectrum of 2 that correspond to a small integral number of protons. Moreover, the mass spectrum of the product showed that it contained two atoms of deuterium. Control experiments established that incorporation of the second deuterium atom was reversible and did not occur at H_x or H_n; nevertheless it seemed desirable to ascertain at which carbon reversible exchange was occuring. Therefore, the half-cage ketone (2) was reduced to the endo half-cage alcohol,[1a] and the resonances in the $Eu(fod)_3$ shifted pmr spectrum of the all-protio alcohol were assigned on the basis of the lanthanide induced shifts and decoupling studies. The $Eu(fod)_3$ shifted pmr spectrum of endo alcohol-d_2, obtained from the opening of 1 in $(CH_3)_3COD$ followed by reduction of the half-cage ketone product, showed the exchangeable proton in 2 to be H_e. More important, repeated careful integration indicated that the opening of the birdcage alcohol proceeds with 95 ± 3% retention of configuration in $(CH_3)_3COD$.

Cram's studies on the base catalyzed cleavage of acyclic alcohols have demonstrated that in tert-butanol retention is the usual result.[7] Consequently,

we also carried out the opening of 1 in ethylene glycol, a solvent in which inversion predominates with acyclic alcohols.[7] Heating the birdcage alcohol in ethylene glycol, 1M in potassium glycolate, at 200° for 20 hr did not give 2, but instead led to the isolation of its reduction product, the endo half-cage alcohol. A control experiment showed that under these conditions the half-cage ketone is itself reduced to this alcohol. Further evidence for the intermediacy of 2 is provided by the fact that from the opening of 1 in $(CH_2OD)_2$,[8] endo alcohol-d_2 was isolated. Its Eu(Fod)$_3$ shifted pmr spectrum showed the absence of protium at the position corresponding to H_e in 2, suggesting that 1 opens to 2, which exchanges this proton prior to being reduced by hydride transfer from the glycolate. Repeated careful integration of the shifted spectrum indicated that 90 ± 3% of the remaining deuterium corresponds to H_n in 2, establishing that retention is the preferred pathway for the opening of 1 in ethylene glycol as well as in tert-butanol.

The finding that retention of configuration is the outcome, independent of solvent, in the base catalyzed ketonization of the birdcage alcohol serves to further establish the generality of this stereochemical reaction path for polycyclic molecules not containing cyclopropanol rings. The origin of this preference for retention has, thus far, only been speculated upon.[3,4,9] Indeed, it is not even clear whether the base catalyzed cleavage of these polycyclic alcohols involves the rate determining formation of a carbanion that is subsequently protonated (S_E1 mechanism), or whether a proton is involved in the rate determining step (S_E2 mechanism). Experiments designed to distinguish between S_E1 and S_E2 pathways are currently underway in this laboratory.

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