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$A^{(1,3)}$ STRAIN FACTORS IN THE HYDROBROMINATION OF CYCLOHEXENECARBOXYLIC ACID

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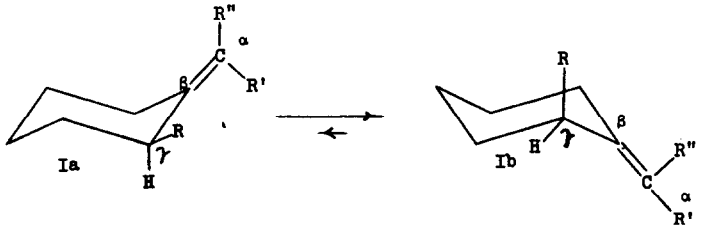
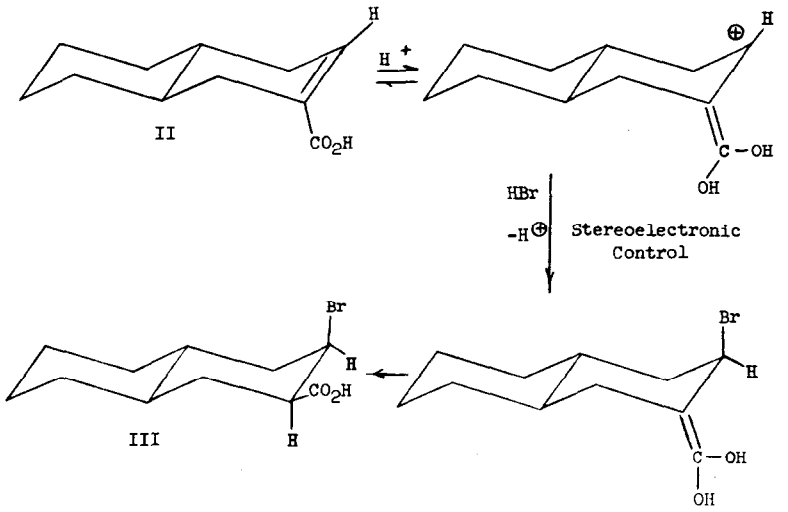
A stereochemical theorem has been recently postulated by Johnson and Malhotra (1) to account for steric factors affecting the preferred conformation of an intermediate possessing a γ-substituted exocyclic double bond in a mobile six-membered ring. In contrast to an earlier interpretation by Zimmerman (2), they feel that the equilibrium between Ia and Ib should lie to the right if R and R' are medium or large in size. The important consequence of this theory, if valid, is that the most stable conformation possesses an axial substituent. The steric interference

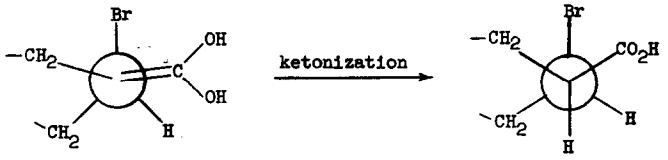


between R and R' in conformer Ia is referred to (1) as $A^{(1,3)}$ strain and preliminary evidence has been provided by Johnson et al (3a-c) which supports this interpretation.

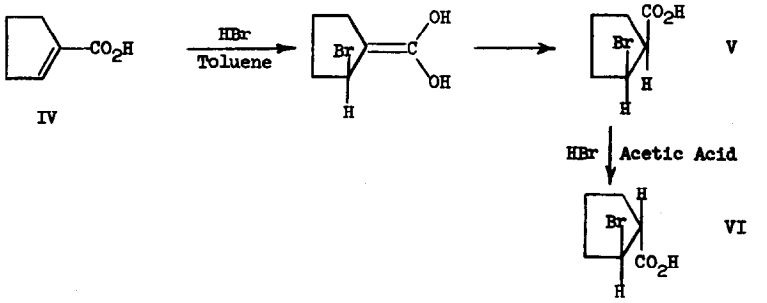
We wish to draw attention to our studies in the hydrobromination of α, ß-unsaturated cyclohexenecarboxylic acids (4) which we believe provide another reaction type which can be best interpreted in terms of the $A^{(1,3)}$ strain theory. Furthermore, these results substantiate, for our case, the basic assumption that the product controlling step can be governed by a sterically controlled attack anti to the axial substituent in the conformation corresponding to Ib. We have established that the kinetically controlled hydrobromination in toluene of trans-Δ^{2}-octalin-2-carboxylic acid (II) leads to trans-axial-3-bromodecalin-equat-2-carboxylic acid (III) and have postulated the mechanism indicated below. The intermediate bromo acid-enol is necessarily rigid (cannot undergo a conformational flip) and corresponds to the preferred conformation in



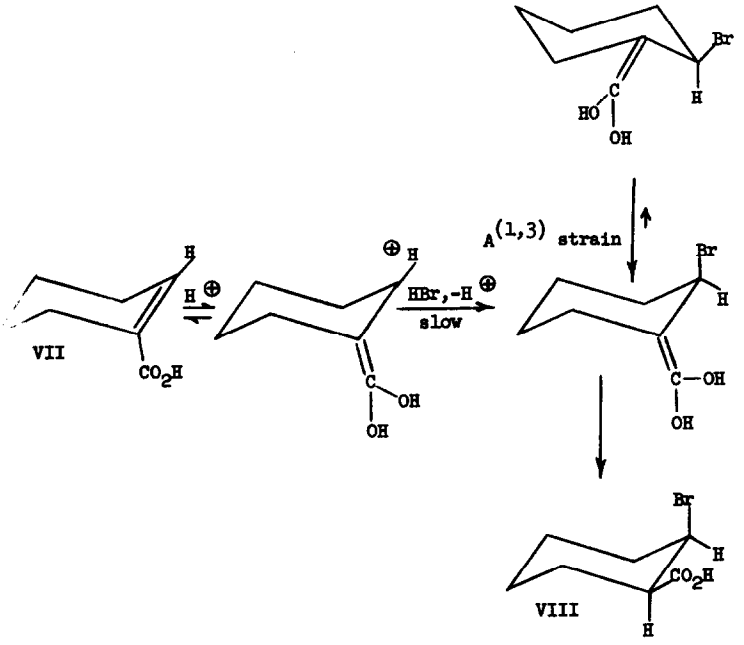
the $A^{(1,3)}$ strain theory for an exocyclic enol in a mobile cyclohexane system where R' = OH and R = Br. Similar results were obtained with bicyclo[3.2.1]oct-2-ene-2-carboxylic acid (4) and in neither case could the diaxial isomer be detected. It appears that the proton transfer in the ketonization step is best accounted for in terms of steric effects where the proton transferring agent approaches the bromo acid-enol opposite the bulky bromine. Similar arguments were assumed by Johnson and Malhotra (3c) to account for the stereochemistry of several reactions in mobile cyclohexane systems previously studied by Zimmerman (2).



The importance of steric control in the ketonization process can be more strikingly observed in the addition of hydrogen bromide in toluene to cyclopentenecarboxylic acid (IV) (5). The initial hydrobromide is cis-2-bromocyclopentanecarboxylic acid (V) which is readily converted to the trans isomer (VI) under epimerizing conditions (HBr in acetic acid).



With the above considerations in mind, we feel our mechanism for the net trans addition of hydrogen bromide to cyclohexenecarboxylic acid (VII) (4) should be modified as outlined below. In contrast to our earlier interpretation (4), we now suggest that cis-2-bromocyclohexanecarboxylic



acid (VIII) arises from a sterically controlled ketonization of the intermediate bromo acid-enol with an axial bromine. We originally (4) believed VIII was derived from the other conformation using Zimmerman's arguments (2). Again the cis isomer VIII can be converted to the corresponding trans product under epimerizing conditions, indicating that the initial process is kinetically controlled.

It is important to note that the product controlling step leading to the bromo acid VIII from either ground state conformation of the six-membered bromo acid-enol can best be interpreted in terms of a sterically controlled ketonization. Hence even this modified interpretation in terms of $A^{(1,3)}$ strain factors is consistent with the basic hypothesis as outlined by Zimmerman.[2]

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