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THE ERYTHRO CONFIGURATION OF THE REACTION PRODUCTS FROM CYCLOHEXANONE ENAMINES AND β-NITROSTYRENES

A.Risaliti, M.Forchiassin and E.Valentin
Institute of Chemistry, University of Trieste
Trieste, Italy

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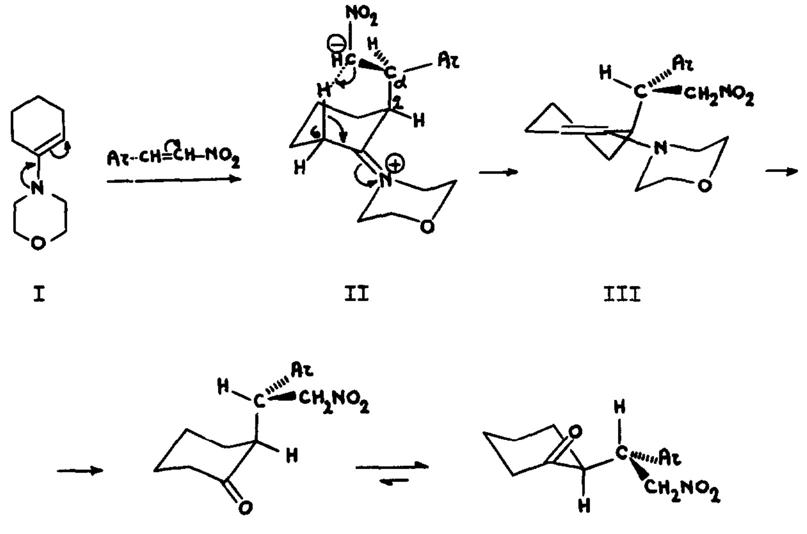
In previous works it was observed that the structure of the reaction products of cyclohexanone enamines with electrophilic reagents depends on the steric requirements of the reagents themselves. Thus, when bulky groups are attached to the electrophilic carbon atom, the formation of less substituted enamines is favoured (1,2). Moreover, with suitable electrophiles it is possible also to obtain several stereoisomers, for in the reaction products more than one asymmetric center can be originated (3). In some of these cases, however, in accordance with the mechanism proposed for the above reactions, a stereospecific course with formation of a sole stereoisomer was expected. This occurs, for instance, in the reaction of cyclohexanone enamines with β-nitrostyrene, where only one of the two possible diastereoisomers was obtained (2). To this one the erythro configuration was assigned on the basis of the following stereochemical considerations.



I II III

IVa IVe

(Ar = C_6H_5, p-Br-C_6H_4)

In considering the reaction to be a two steps process, involving a dipolar intermediate, it can be seen that the more stable conformation for such an intermediate is II, where the cyclohexane ring is in a chair form with the substituent in 2 position axially oriented. In this structure the rotation around the C_2-C_α bond is strongly restricted, because the Ar bulky group interferes with the cyclohexane ring. Therefore such a group must be arranged in the anti conformation with respect to the same ring. Consequently the carbon atom bearing the negative charge is near to the axial hydrogen atom at the 6 position. The intramolecular transfer of this hydrogen affords the less substituted alkylated enamine III. This mechanism is determining the configuration of both C_2 and C_α atoms and can account for the formation of the sole stereoisomer III. The same configuration must be found obviously in the ketone IV. It can be seen that this configuration is erythro type. In fact, if the molecule IV is viewed along the direction of the bond linking the asymmetric C_2 and C_α atoms, the two sets of identical (H atoms) or like substituents (CH_2 bonded to NO_2 group and CH_2 of the cyclohexanone ring) are trans to each other (*).

In order to confirm the stereochemistry proposed for the above reaction, 1-N-morpholino-cyclohexene was allowed to react with p-bromo-β-nitrostyrene. The enamine III (Ar = p-Br-C_6H_4), m.p. 111-113° (from ligroine) was obtained in 95% yield. Anal. Calcd. for $C_{18}H_{23}BrN_2O_3$: C 54.69; H 5.86; N 7.08. Found: C 54.71; H 5.78; N 7.17. I.R. (KBr): 1646 cm^{-1} (C=C-N); 1550 and 1378 cm^{-1} (NO_2).

The acidic hydrolysis of III (Ar = p-Br-C_6H_4) gave the corresponding ketone IV, m.p. 108-110° (from ethanol) in 90% yield. Anal. Calcd. for $C_{14}H_{16}BrNO_3$: C 51.55; H 4.94; N 4.29. Found: C 51.74; H 4.82; N 4.28. I.R. (KBr): 1706 cm^{-1}(C=O); 1552 and 1384 cm^{-1}(NO_2).

(*) The threo type configuration of the dipolar intermediate, from which too the less substituted enamine could be obtained by intramolecular protonic transfer, is very unfavoured for the steric interference of C_6H_5 group with the cyclohexane ring.

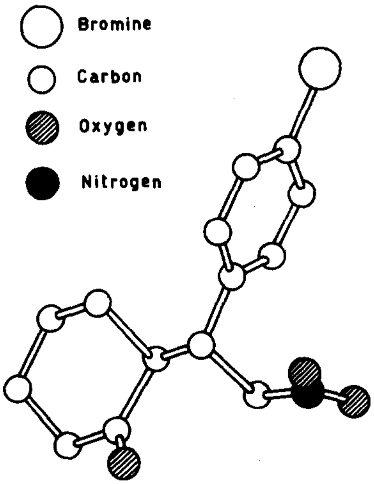


FIG.1
A view of the molecule of the compound IV as it exists in the crystal

The X-ray analysis of the crystal structure of IV (Ar = *p*-Br-C_6H_4) was carried out (4). From the results of this analysis it was established that the cyclohexanone ring is in a chair conformation, the bond C_2-C_α is equatorially oriented and, according to our hypothesis, the molecule has the *erythro* configuration (IVe), Fig.1.

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