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THE REACTION OF CYCLOHEXANONE ENAMINES WITH 2-NITROPROPENE AND PHENYL VINYL SULFONE

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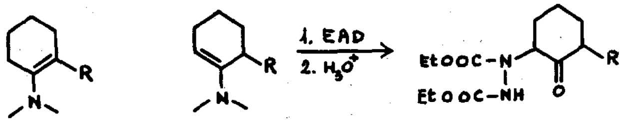
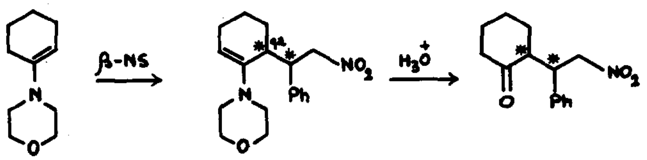
It is known that enamines of cycloalkanones undergo C-alkylation with electrophilic olefins to form, after hydrolysis, the corresponding 2-substituted ketones (1). We found an analogous behaviour with other dienophiles, as for instance ethyl azodicarboxylate (2). In these reactions two isomeric enamines, the more substituted (I) and the less substituted one (II), can be formed. The structure of the less substituted enamine (II) can be established by n.m.r. spectroscopy and/or by reaction with ethyl azodicarboxylate (EAD) and subsequent hydrolysis leading to the 2,6-disubstituted derivative (III) (2).



I   II   III

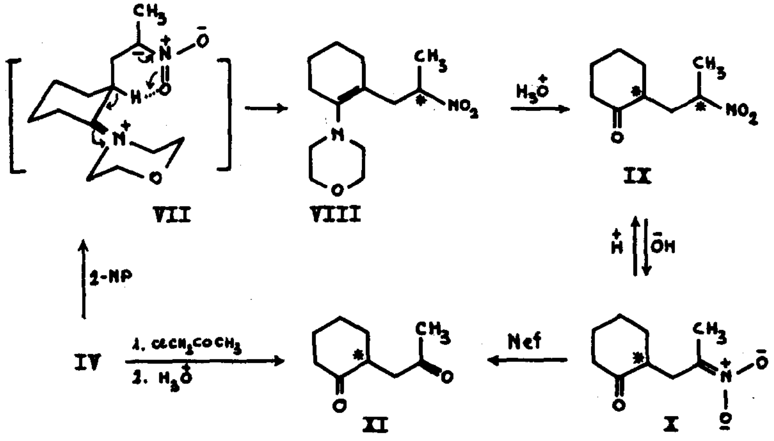
We assumed, from inspection of molecular models, that the preferred formation of one of the two possible isomeric enamines must depend on the nature of the dienophile. Thus, the presence of hindering groups at the electrophilic carbon atom should favour the less substituted isomer. Actually, we have demonstrated (3) that the enamine obtained from the reaction of 1-N-morpholino-cyclohexene (IV) and β-nitrostyrene (β-NS) has the structure V (4), with the substituent in the quasi-axial orientation. On the basis of similar stereochemical reasons, it was expected that the hydrolysis of V would result in the formation of only one of the two possible diastereoisomeric ketones (5). Indeed, a single product VI was obtained to which the *erythro* configuration was assigned (3).



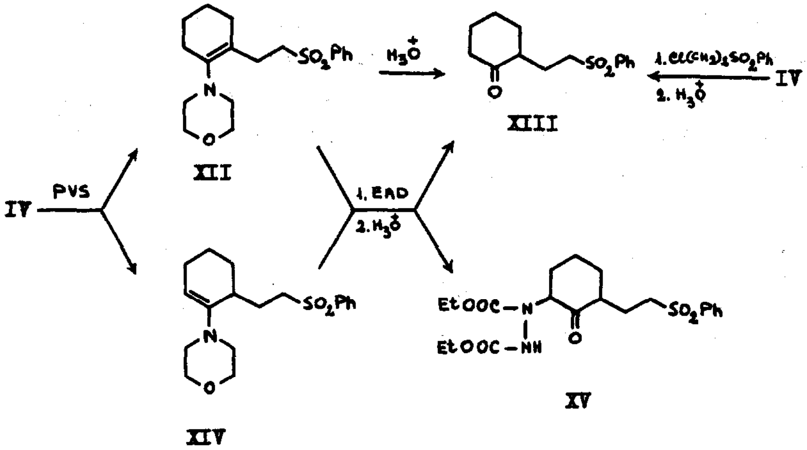
IV V VI

In order to confirm our assumption, we have pursued this problem further. We have examined then 2-nitropropene (2-NP), as reagent bearing no substituent at the electrophilic carbon atom. In this case the most stable conformation for the intermediate of the reaction with 1-N-morpholino-cyclohexene should be VII. In accord with this hypothesis, the more substituted enamine VIII was obtained as major product (m.p. 64-5°, 78% yield); its structure followed from analytical results, i.r. spectral data (C=C stretching) and its failure to react with ethyl azodicarboxylate. Hydrolysis of VIII gave 2-(β-nitropropyl)-cyclohexanone (IX) (b.p., 125-30°, semicarbazone m.p. 150°).

Gas chromatographic analysis indicated the material to be a mixture about 1:1 of two diastereoisomers, as would be expected. Indeed, the sodium salt formed from IX gave by Nef reaction the sole diketone XI and regenerated on acidification the same starting mixture IX.



Similarly behaves phenyl vinyl sulfone (PVS) in the reaction with enamine IV. Even in this case the main product (68% yield) was the more substituted enamine XII (m.p. 101-02°). The structure XII was assigned on the basis of analytical and n.m.r. spectral data (no absorption for vinyl proton, while a band at 6.78τ of area 2 corresponding to $-CH_2SO_2-$ group was present) and chemical behaviour (no reaction with ethyl azodicarboxylate). Hydrolysis of XII produced the 2-(β-phenylsulfonyl)ethylcyclohexanone (XIII) (m.p. 71-2°), also obtained from IV by alkylation with β-chloroethyl phenyl sulfone, followed by hydrolysis.



The enamine XII is not the sole product of the above reaction, but also the less substituted one (XIV) was formed. This isomer was not isolated and its presence was identified by treatment of the reaction mixture with ethyl azodicarboxylate. After acidic hydrolysis at room temperature, beside the monosubstituted ketone XIII (68% yield), the 2,6-disubstituted ketone XV (m.p. 140°, 23% yield) was obtained . It must be originated unambiguously from the less substituted enamine XIV. The compound XV by refluxing in acidic medium was converted to an isomeric product (m.p. 105°); this result seems to indicate a possible <u>cis</u>-<u>trans</u> isomerism.

References

1) G.Stork, A.Brizzolara, H.Landesman, J.Smuszkovicz and R. Terrell, J.Am.Chem.Soc. 85, 207 (1963).

2) A.Risaliti and L.Marchetti, Ann.Chimica 53, 718 (1963); ibid. 55, 635 (1965).

3) A.Risaliti, L.Marchetti and M.Forchiassin, Ann.Chimica 56, (1966) in press.

4) Very recently M.E.Kuehne and L.Foley [J.Org.Chem. 30. 4280 (1965)] refer the reaction of enamines with nitro olefins and report the preparation of compounds V and VI. Their results are in agreement with those we found.

5) In formulae V, VI, VIII, IX, X and XI the asymmetric carbon atoms are starred.