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DETERMINATION BY CHEMICAL METHODS OF THE MIXTURE COMPOSITION OF ENAMINES FROM 2-SUBSTITUTED CYCLOALKANONES

F.P.Colonna, M.Forchiassin, A.Risaliti and E.Valentin
Istituto di Chimica, Università di Trieste
34127 Trieste, Italy

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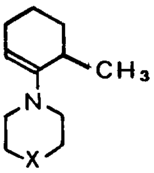
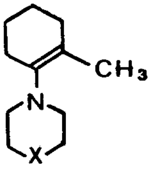
The mixture composition of isomeric enamines from 2-substituted cycloalkanones is usually determined by physical methods, essentially by NMR spectroscopy. By this technique it was shown that the pyrrolidine enamine of 2-methylcyclohexanone consists almost exclusively of the isomer IIIa (1).



Ia, IIa, IIIa

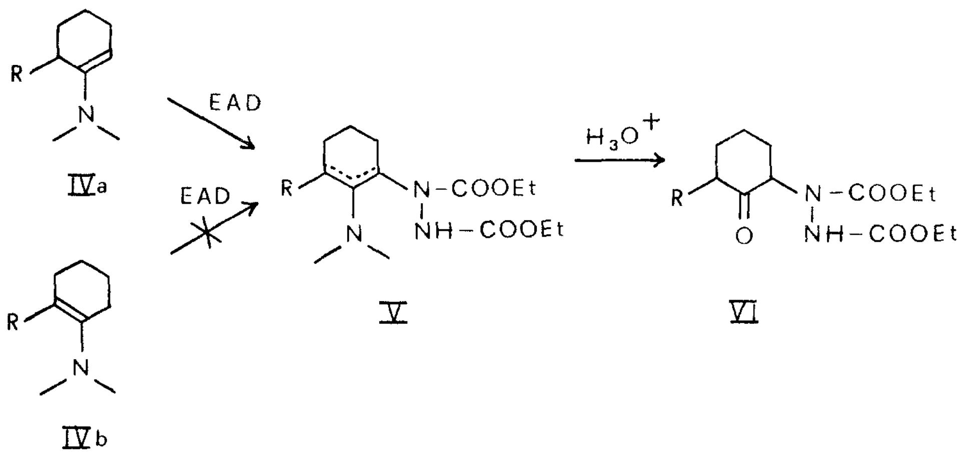


Ib, IIb, IIIb

I : X = O ; II : X = CH_2 ; III : X = −

Deuterium isotope studies on the hydrolysis of this enamine led to the same conclusion (2). Recent NMR spectroscopy investigations (3) gave the following isomeric compositions of morpholine, piperidine and pyrrolidine enamines of 2-methylcyclohexanone : Ia/Ib = 52/48; IIa/IIb = 46/54; IIIa/IIIb = 90/10. These values are in accordance with those found by other authors (4).

In previous works (5,6,7) we have reported that also the reaction with ethyl azodicarboxylate (EAD) can be used for determining the composition of mixtures of 2- and 6-substituted cycloalkanone enamines, since the less substituted isomers IVa react quantitatively, yielding the corresponding 2,6-disubstituted derivatives V and VI. This procedure is correct, provided that no isomerization of IVb into IVa occurs during the reaction.



In order to compare the physical with the chemical method, 2-methylcyclohexanone enamine mixtures were allowed to react with EAD. Compound VI ($R = CH_3$) (8) [m.p. 103-104°, IR (nujol) : 3288 cm^{-1} (NH), 1752-1718-1709-1689 cm^{-1} (CO)] was isolated in 49%, 47% and 81% yield from the mixtures I, II and III respectively. The reactions went to completion within 72 hr and had to be carried out under controlled conditions, to prevent the temperature from raising above 5°. In fact at higher temperatures the yields of VI changed substantially. Quantitative isolation of VI could be obtained by cromatography on SiO_2 column, eluting with benzene-acetone (380:5).

Analogous results were observed in the reactions with phenyl isocyanate (9) carried out in the cold. Actually, after removal of the unchanged phenyl isocyanate with morpholine and subsequent hydrolysis, 2-methyl-6-phenylcarbamyl-cyclohexanone (10) [m.p. 118-120°, IR (nujol) : 3287 cm^{-1} (NH) , 1698-1651-1545 cm^{-1} (CO)] was isolated in 51%, 42% and 78% yield from the mixtures I, II and III respectively.

Thus, it appears that the results obtained by the chemical methods are practically in agreement with those furnished by the physical ones.

To confirm that, during the reactions the more substituted enamines do not isomerize into the less substituted ones, pure Ib (IR and NMR) was isolated (4) from the isomeric enamine mixture and allowed to react with ethyl azodicarboxylate and phenyl isocyanate. In both cases no traces of the corresponding 2,6-disubstituted cycloalkanones were detected.

This result is of intrinsic interest since it indicates that neither spontaneous equilibrium exists between the less and the more substituted enamines, nor an equilibration occurs between them, at least under the above mentioned reaction conditions.

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