

Protonation and Deprotonation of Enamines. A Convenient Way of Separating Isomeric Enamines Obtained from Methyl Isopropyl Ketone and Morpholine

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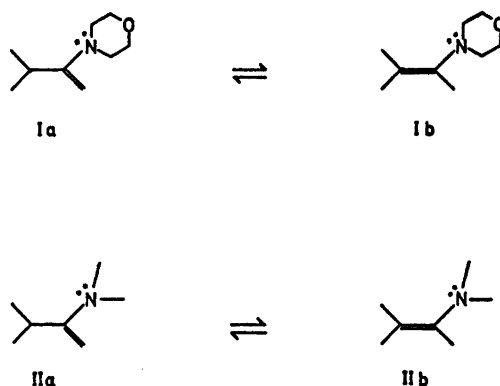
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Enamines from methyl isopropyl ketone were converted to the corresponding immonium salts using hydrogen chloride or trifluoroacetic acid. The salts were characterized by their ^1H NMR, ^{13}C NMR and mass spectra. The morpholine immonium salt is readily deprotonated to the least substituted enamine isomer by treatment with sterically hindered base. By careful dosage of acid the most substituted morpholine enamine isomer can be left unreacted in solution, and can easily be separated from the other isomer. A convenient procedure for this separation is described.

Preparation of enamines from unsymmetric ketones usually affords mixtures of tautomeric enamines. In some cases it is possible to obtain one isomer in a pure state, using titanium tetrachloride and a hydrocarbon solvent.¹ The yield using this method is moderate due to the conditions necessary for avoiding rearrangement of the kinetically favoured product. Immonium salts may be intermediates in the formation of an enamine from a ketone and a secondary amine. The aim of the present investigation is to study if proton abstraction from the immonium salt primarily yields one isomer, *viz* the same isomer as using titanium tetrachloride and *excess* of secondary amine. Model substances were the morpholino and dimethyl-amino enamines from methyl isopropyl ketone (Scheme 1).

RESULTS AND DISCUSSION

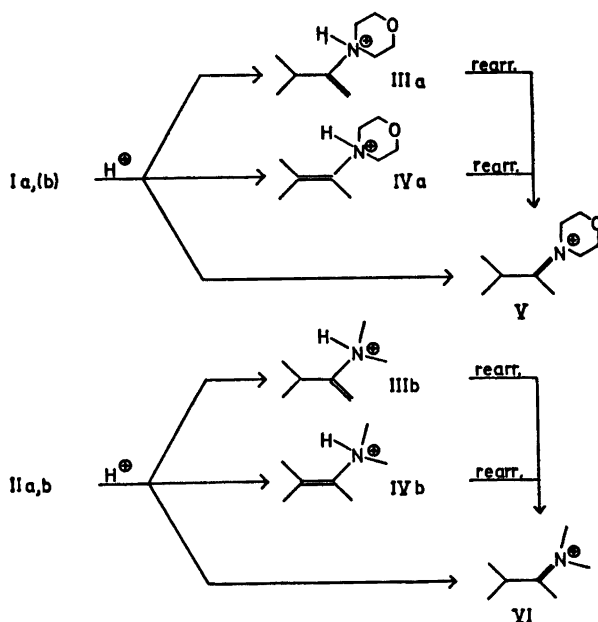
The enamines in dry pentane were treated with hydrogen chloride at -78 and 0°C , or



Scheme 1.

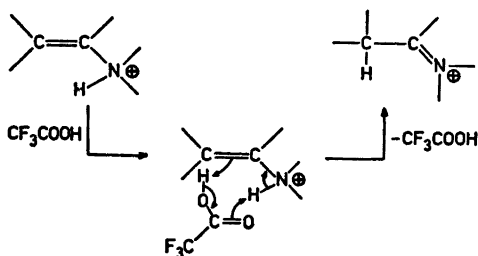
with trifluoroacetic acid at 0°C . White crystals precipitated when dry hydrogen chloride was bubbled through the enamine solution. As reported before,² they were found to be a mixture of β -C and N-protonated species (IIIa, IIIb, IVa, IVb, V, VI). The crystals were isolated and kept in a desiccator at room temperature. After 7–10 days a complete rearrangement was found to have taken place (NMR) (Scheme 2). Using trifluoroacetic acid only β -C-protonated species (V, VI) were obtained. This difference in behaviour may lie in bifunctional catalysis by trifluoroacetic acid on the nitrogen to carbon transfer (Scheme 3).

The immonium salts were characterized by their spectra. Some features of the ^1H NMR spectra ought to be mentioned. The morpholine appeared as a broad multiplet at δ 4.4–3.9 in the immonium salts and not as two distinct



Scheme 2.

multiplets, as in the free enamine. A general downfield shift of 0.2–1.5 ppm was observed in the immonium salts compared with the corresponding enamines. In the ^{13}C NMR spectra a resonance signal at δ 195.0–194.5 was observed, and is assigned to $C=N^+$ in the immonium structure. The resonance signal from the parent ketone $C=O$ carbon appeared at lower field. Samples of the immonium salts, partially hydrolyzed to the ketone, showed both signals. It was not possible to obtain mass spectra of the immonium salts due to early decomposition in the instrument. The largest fragments were the corresponding enaminic molecule ions.



Scheme 3.

The immonium chlorides (V , VI) were quite stable, and could be stored in a desiccator for months at room temperature without decomposition. This is in striking contrast to the immonium salts from aldehyde enamines and enamines from cyclic ketones.²⁻⁵ Immonium trifluoroacetates (V , VI) were less stable and decomposed on standing.

Surprisingly, the most substituted isomer Ib could be readily separated in a pure state from a mixture of Ia and Ib . This was done simply by introducing hydrogen chloride or trifluoroacetic acid in an amount equivalent to the less substituted isomer Ia . Mass spectra analysis was performed on immonium salts and supernatant liquid consisting of Ib in dry pentane, from experiments using deuterium chloride or trifluoroacetic acid- d_1 . A considerable deuterium incorporation was found in the immonium salts, but could not be detected in Ib . This indicates that no conversion of Ia to Ib via the immonium salt occurs during the reaction. The method for separation described here was not successful for separation of IIa from IIb . A more laborious method for separating Ia from a mixture has been re-

ported previously, using 1,3-dipolar cycloaddition.⁶

The isolated immonium salts were dissolved in chloroform or suspended in pentane and treated with an equivalent amount of diisopropylamine. The morpholine immonium salt V was completely deprotonated to Ia, and no trace of Ib could be detected in the ¹H NMR spectrum. The dimethylamine immonium salt VI yielded a mixture of IIa and IIb under the same reaction conditions. Sterically less hindered bases, e.g. trimethylamine and triethylamine, showed less selectivity, yielding isomeric mixtures of both morpholine and dimethylamino enamines.

EXPERIMENTAL

¹H NMR spectra were recorded on a JEOL-C 60 HL spectrometer, and the ¹³C NMR spectra were obtained using a JEOL PFT-60 HL spectrometer. Deuterated chloroform was used as solvent (ca. 1 M solutions) using TMS as an internal standard. Mass spectra were obtained on a LKB-9000 mass spectrometer. The enamines were prepared according to White and Weingarten.¹

Immonium chlorides were prepared by bubbling a slow stream of dry gaseous hydrogen chloride through a solution of the enamines in dry pentane at -78 °C. The precipitated salt was collected by filtration under nitrogen.

Deuterium chloride was prepared by adding D₂SO₄ to a calculated amount of dry potassium chloride.

Immonium trifluoroacetates were prepared by adding an equivalent amount of trifluoroacetic acid dissolved in dry pentane to a solution of the enamine in dry pentane at 0 °C. The precipitate was recovered as above.

Separation of Ib. A typical procedure was: 3.1 g (0.02 mol) of a mixture of Ia and Ib (1:1) was treated with 225 ml (0.01 mol) of gaseous hydrogen chloride as above. After filtration, the filtrate was evaporated *in vacuo*, yielding 1.3 g (84 %) of Ib in a pure state.

Separation of Ia from a mixture using trifluoroacetic acid. To 7.2 g of a mixture of Ia and Ib (6:1) in dry pentane was added 4.6 g (0.04 mol) of trifluoroacetic acid in 50 ml of dry pentane with stirring at 0 °C. The immonium salt separated as an oil, which crystallized on scratching. The supernatant liquid was decanted and the residue washed with a small portion of cooled pentane. The combined pentane solutions were evaporated *in vacuo* yielding 0.9 g (88 %) of Ib. The immonium salt was suspended in 150 ml of cooled pentane, and 4.1 g (0.04 mol) of diisopropylamine in 10 ml of cooled pentane was added with

stirring at 0 °C. The reaction was complete within 1 h. The precipitated diisopropylammonium trifluoroacetate was removed by filtration and the filtrate was evaporated *in vacuo* yielding 4.5 g (73 %) of Ia. No trace of Ib could be detected by NMR.

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