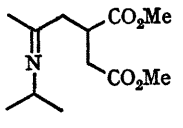
Addition of the Enamine Tautomers of Ketimines to Dimethyl Maleate

By MICHEL PFAU* and CATHERINE RIBIÈRE

[*Laboratoire de Chimie de l'École Normale Supérieure, 24 rue Lhomond, 75-Paris (5e), France*]

Summary Aliphatic imines add to dimethyl maleate *via* their enamine tautomers, which are shown to exist in equilibrium with the imine by deuterium-exchange n.m.r. spectroscopy.

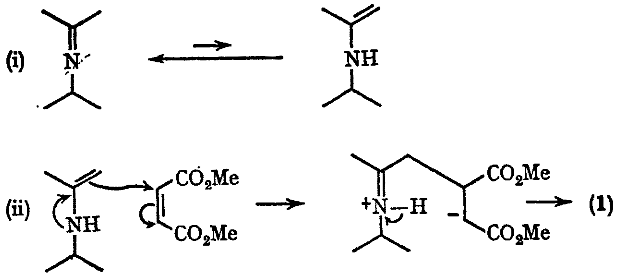
DURING research into the photochemical addition of imines to $\alpha\beta$-unsaturated esters,[1] it appeared that there was a competitive non-photochemical addition. At ordinary temperatures this reaction is very slow but, for example, if an equimolecular solution of *N*-isopropylideneisopropylamine and dimethyl maleate is heated in refluxing benzene or dioxan (without catalyst) the addition compound (**1**) ($E_{0\cdot 2}$ 95°) is isolated in 86% yield;† the corresponding diesterketone is obtained upon hydrolysis. Two patents[3] describe examples of ketimine additions to acrylonitrile in an autoclave in presence of hydroquinone, with or without catalyst, and the addition of an aldimine with methyl vinyl sulphone to give a similar product has been described.[4]



(1)

No mechanism was given for this type of addition.

It seemed to us that a rational mechanism could be the following:



The enamine consumed in reaction (ii) (the classical reaction of true enamines,[5] but with migration of the nitrogen-bonded hydrogen in this case) would allow a complete displacement of equilibrium (i) to the right.

A survey of the literature revealed no demonstration of an equilibrium such as (i) with imines whose enamine tautomers are not stabilized by conjugation, with one exception[6] where the authors suppose the existence of an enamine form in equilibrium with *N*-cyclohexylidenecyclohexylamine on the basis of the observation of an i.r. absorption at 3·08 μm attributed to N–H.

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† Satisfactory elemental analysis and spectra (i.r., n.m.r., mass) were obtained with all new compounds; they will be reported in the full paper.[2]

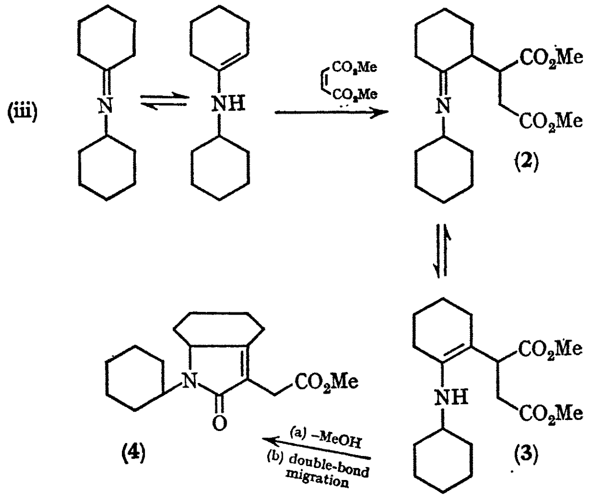
To test the validity of the hypothesis of an imine–enamine[‡] equilibrium of the type (i), n.m.r. spectra of *N*-isopropylideneisopropylamine were recorded at ordinary temperatures, in CH_3OH and CH_3OD. In this latter solvent, an immediate suppression of the signals corresponding to the two methyls (magnetically nonequivalent) located on the double bond which appear at δ 1·94 and 2·01 p.p.m. in non-deuteriated methanol was observed. These results show that at equilibrium the imine is almost the exclusive form (no vinyl hydrogen was detected in methanol at ordinary temperature) but that the six hydrogen atoms of these methyl groups are exchanged very rapidly *via* the enamine form.

The formation of compound (**1**) in good yield is interesting because, in this particular case, Stork's method cannot be applied because of the difficulty in obtaining enamines with methyl ketones.[5]

With *N*-cyclohexylidenecyclohexylamine and dimethyl maleate the compound (**2**) was not isolated, but instead, the compound (**4**) was obtained.

As indicated in equation (iii), we can assume that since the addition compound (**2**) is also in equilibrium with the enamine (**3**), the latter reacts in this instance *via* its secondary amine group to cyclize with one of the carboxylates. In the experimental conditions used for the isolation of (**1**), no lactamization took place.

From a synthetic point of view it seems that this method, employing readily available imines,[8] can find many applications by the reaction of the double bond and/or the secondary amino-group of the enamine form. In the full paper[2] we shall mention other examples, particularly cases where other simple methods leading to the same results are not applicable.



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[‡] We recently reported a study on the imine and enamine tautomeric forms of the addition products resulting from hydrazines and dimethyl acetylenedicarboxylate.[7]

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