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FLASH VACUUM THERMOLYSIS OF 2-ISOPROPYL OXAZOLIDINES. MECHANISM OF THE TAUTOMERISM BETWEEN AZOMETHINE YLID, AZIRIDINE AND ENAMINE

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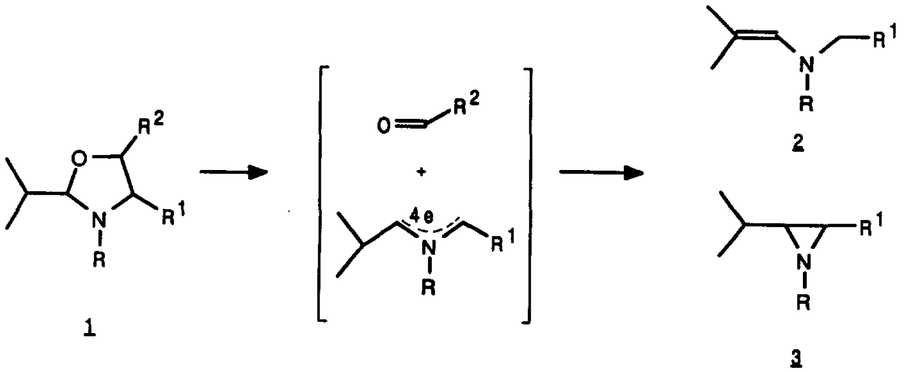
Abstract: Depending on the nature of the substitution of 2-isopropyl oxazolidines and the Flash Vacuum Thermolysis conditions, aziridines and/or enamines are recovered through the azomethine ylid formed in situ Studies with deuterium labelled molecules give arguments for a concerted process in the gas phase.

Tautomerism of azomethine ylids to enamines has been mentioned previously in the literature(1-8); only one paper was devoted to the thermal generation of azomethine ylids from stable enamines(8). Recently we have reported that azomethine ylids can be generated by retrocycloaddition of oxazolidines as well in the liquid phase by thermolysis, as in the gas phase by Flash Vacuum Thermolysis(FVT) (9-11). In the absence of a better dipolarophile than the carbonyl one, thermolysis of oxazolidines left the starting material unchanged whereas FVT gave rise to aziridines.

We report in this paper results from the FVT of 2-isopropyl oxazolidines 1 which lead to either enamines 2 or aziridines 3 , or a mixture of 2 + 3(scheme 1).



Scheme 1

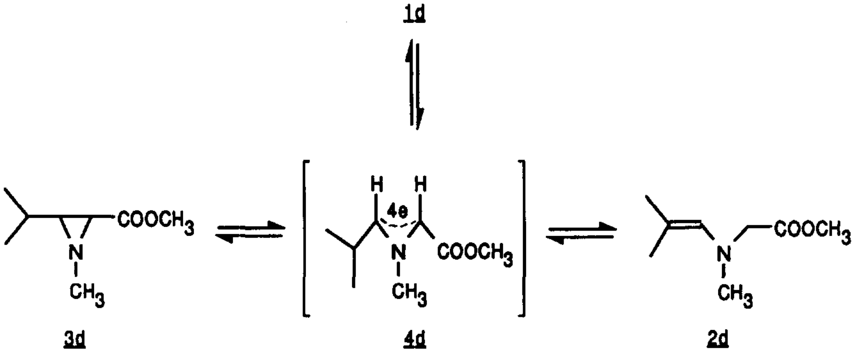
Several factors are of importance on the course of the reaction. The temperature does not influence the ratio 2/3 in many cases, except for 1d; on the other hand, it has a marked effect on the conversion ratio. Temperatures reported in Table 1 are those for which the transformation was found to be optimum. With 1d, depending on the temperature 2d or 3d are recovered. Oxazolidines 1a and 1b lead to a mixture of enamine and aziridine, while only aziridine 3c is obtained from 1c as a mixture of both diastereomers, whatever the temperature. The nature of the substituent attached to the nitrogen influences mainly the ratio between enamine and aziridine. The nature of the group attached to C-4 seems to be of importance. At the higher temperature reaction, the presence of an electron-withdrawing group transforms 1d specifically into enamine 2d; when a methyl replaces the ester group, the aziridine alone is obtained and, with H, both enamine and aziridine are formed.

Table 1

1	R	R^1	R^2	T° C		2	3	C%
a	CH3	H	H	600	50	33		83
b	Ph	"	"	625	7	48		56
c	CH3	CH3	Ph	550	-	68		100
d	"	COOCH3	"	450	-	34		68
d	"	"	"	550	75	-		100

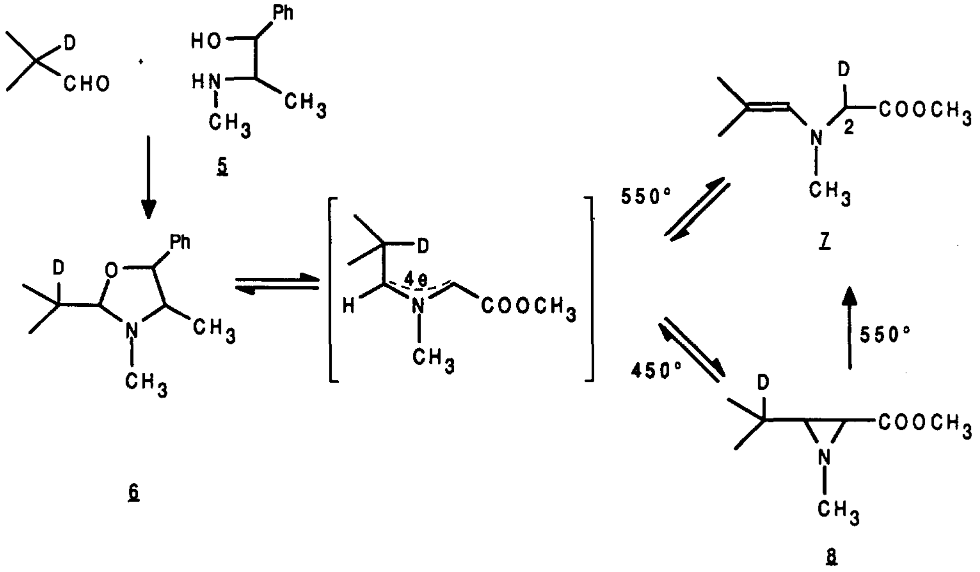
C% = conversion ratio of oxazolidine

The fact that, with 1d, the enamine and the aziridine can be obtained specifically at different temperatures, rises the question of the reversibility of a such reaction.Pure aziridine 3d gives rise quantitatively to enamine 2d when the FVT is performed at 550°C, which means that azomethine ylid 4d can be the common intermediate for one hand lead to either 2d or 3d depending on the temperature and for one other hand is the intermediate for the specific transformation of 3d to 2d (scheme 2).



Scheme 2

The formation of enamine 2d from azomethine ylid 4d can proceed from a formal [1,4]-sigmatropic shift of hydrogen(1, 2, 5, 6); involving a 6e process located on 5 centers(12). To check this mechanism, we have synthesized C-2 deuterated isobutyraldehyde and condensed it with aminoalcool 5; oxazolidine 6 was obtained in good yield. The FVT of 6 at 450° and 550°C led to aziridine 8 and enamine 7 respectively, specifically deuterated as shown on scheme 3. The FVT of aziridine 8 at 550°C produced enamine 7. In all cases deuterium was specifically attached to the C-2 of 7.

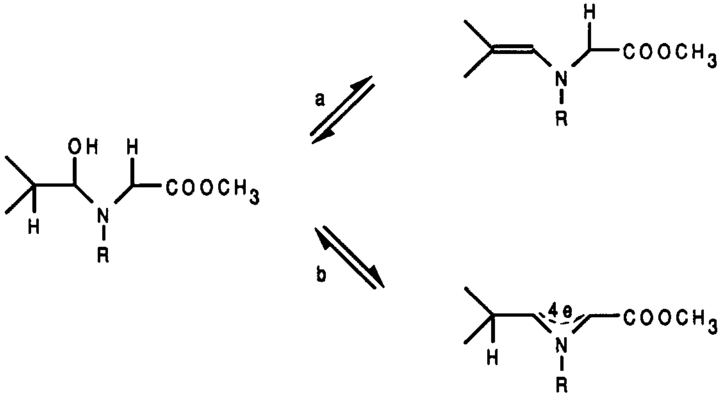


Scheme 3

To confirm, in this case, the reversibility of the equilibrium between enamine and azomethine ylid, we have synthesized enamine 2d. It does not react at room temperature with dimethyl fumarate but reacts at the reflux of toluene, leading to the expected pyrrolidine 9 as a mixture of diastereomers. At room temperature, with molecular sieves in the dichloromethane, when a mixture of isobutyraldehyde and methyl sarcosinate is reacted with dimethyl fumarate, pyrrolidine 9 is recovered as the major product with a small amount of enamine 2d (9/1).

The fact that, at room temperature, enamine 2d does not react with dimethyl fumarate whereas a mixture of isobutyraldehyde and methyl sarcosinate does, is in agreement with the formation of an azomethine ylid in the course of the formation of enamine.

The mechanism of formation of enamines by the condensation of secondary amines with carbonyl compounds can proceed through either the classic water -elimination(way a) or the azomethine ylid(way b) depending mainly from the protons acidities(scheme 4).



Scheme 4

In conclusion, we describe a new tautomerism between azomethine ylid, aziridine and enamine. In the gas phase, a concerted migration of hydrogen can occur, and finally the azomethine ylid can play the role of an intermediate, even at room temperature, for the condensation of aldehydes and secondary amines, leading to enamine.

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