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A NEW METHOD OF SYNTHESIS OF DIHYDROPYRIDONES
REACTION OF AROMATIC KETIMINES WITH ACRYLIC ESTERS

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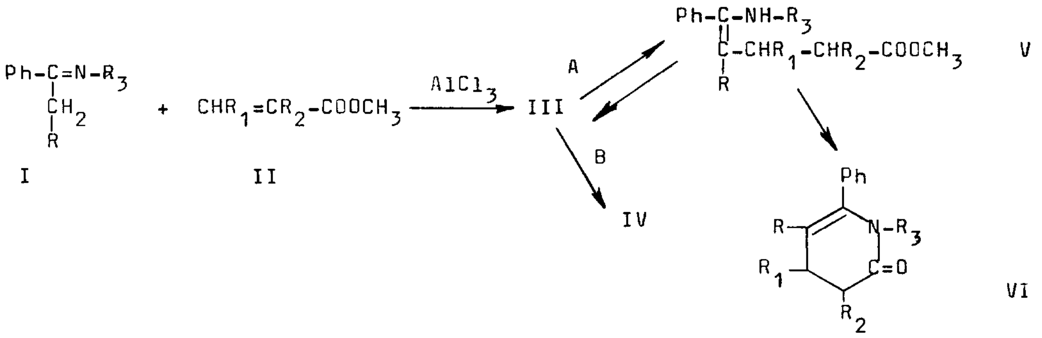
In our studies directed towards the development of new synthetic methods for the production of heterocyclic compounds, we have investigated the reaction of Schiff bases derived from aromatic ketones (acetophenone and propiophenone) with acrylic esters, in the presence of $AlCl_3$ as catalyst. In an earlier paper$^{(1)}$ a report was made on the synthesis of cyclic amidines, obtained by the reaction of Schiff bases with acrylic nitriles.

When acrylic esters are used instead of the corresponding nitriles, in the case of a Michael addition, the reactions in competition are expected to be:



The first step is the formation of a mono-adduct III by reaction of I+II. By addition of II to III, IV, a di-, or tri-addition compound, is obtained through step B, or otherwise III is in equilibrium with V, which gives VI by intramolecular condensation, with elimination of methanol (step A).

In the room-temperature reaction of I ($R=H,CH_3$) with II ($R_1=H,CH_3$), using $AlCl_3$ as catalyst, in molecular ratio 1:1:1, reaction time one hr., and in some cases in yields of over 80%, the corresponding dihydropyridone VI is obtained as the only product, i.e., the reaction proceeds by the step A.$^{(2)}$

Under the same reaction conditions, using methyl cinnamate as reagent II, no reaction is observed. This anomaly may be caused by steric and electronic effects$^{(3)}$. Under more vigorous conditions (heating to 80°C; reaction time 24 hr.), the corresponding dihydropyridone is formed, in about 30% yield.$^{(4)}$

In the reaction of I+II+$AlCl_3$ in molecular ratio 1:10:1, at room temperature, the reaction also proceeds through step A.

The reaction goes exclusively via B, when the phenyl group linked to the N atom of the Schiff base is replaced by an aliphatic group, such as cyclohexyl. This fact can be explained by displacement of the equilibrium ($III \rightleftarrows V$) in the direction of III, or by the lower acidity of the enamine H atom, which would impede the condensation reaction, or possibly, because of the sum of both effects.(5)

Products of reaction and yields are shown in the following table:

molar ratio 1:1:1

R	R_1	R_2	R_3	VI		IV	
				%	M.p., ºC	%	
H	H	H	Ph	85	140-2		
H	H	CH_3	Ph	55	139-40		
CH_3	H	H	Ph	85	144-5		
CH_3	H	CH_3	Ph	60	103-5		
H	Ph	H	Ph	30	118		
CH_3	Ph	H	Ph	25	98-100		
H	H	H	C_6H_{11}	-	-	70	K_p0,001, 150ºC*
CH_3	H	H	C_6H_{11}	-	-	60	K_p0,001, 145ºC*

*Results obtained for molecular ratio 1:10:1

The elemental analyses, molecular weight, and also IR, and NMR spectra, agree in all cases with the structures indicated.

NOTES AND REFERENCES

(1) V. Gómez Aranda, J. Barluenga and V. Gotor, Tetrahedron Letters, 2819 (1973).

(2) In the absence of the catalyst, no reaction is observed, even at the boiling temperature of the corresponding esters.

(3) The chemistry of alkenes, edited by Saul Patai, The Hebrew University Jerusalem Israel (1964).

(4) When acrylic acid is used as, the electrophilic olefin, products resulting from the polymerization of the acid are obtained.

(5) Cyclic amidines cannot be obtained by reaction of Schiff bases with acrylic nitriles when the group bound to the ketimine nitrogen atom is cyclohexyl.