PYRIMIDONE DERIVATIVES AS EFFECTIVE ACID CAPTORS
A METHOD FOR THE PREPARATION OF CARBOXAMIDES

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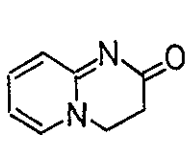
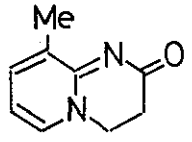
The equimolar reactions of carboxylic acids and amines with 1-methyl-2-chloropyridinium salt in the presence of 3,4-dihydro-9-methyl-2H-pyrido[1,2-a] pyrimidin-2-one(II) or 3,4-dihydro-3,9-dimethyl-2H-pyrido[1,2-a]-pyrimidin-2-one(III) afforded the corresponding carboxamides in high yields.

A convenient method for the preparation of carboxamides by equimolar reactions of carboxylic acids and amines with 1-methyl-2-halopyridinium salts and tri-n-butylamine has been reported from our laboratory[1]. In these reactions, tri-n-butylamine is completely consumed in the final stage, however, the reaction medium is rather basic in the initial stage. After screening effective acid captors with lower basicity than tri-n-butylamine, pyrimidone(I) was found to be an effective acid captors in the carboxylic ester formation by using 2-halopyridinium salt as a coupling reagent[2]. However, carboxamides were isolated with the utmost 60% yields by using

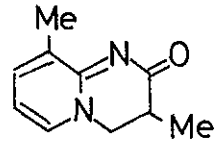
2-halopyridinium salt and I as coupling reagents[3]. During the course of our continuing investigation on the development of new effective acid captors, we have found that two derivatives of I, 3,4-dihydro-9-methyl-2H-pyrido[1,2-a]pyrimidin-2-one(II)[4] or 3,4-dihydro-3,9-dimethyl-2H-pyrido[1,2-a]-pyrimidin-2-one(III)[4], act as very effective acid captors.



I

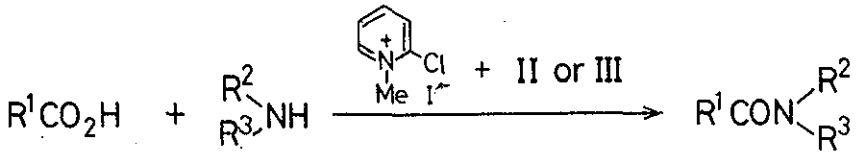


II



III

In this paper the usefulness of pyrimidone derivatives, II or III, in the preparation of carboxamides according to the reaction shown in the following equation, is described.



In a general procedure, to a mixture of 1-methyl-2-chloropyridinium iodide (308 mg, 1.2 m mol) and pyrimidone II or III (388 mg or 404 mg, respectively, 2.4 m mol) is added an acetonitrile solution (18 ml) of a carboxylic acid (1 m mol) and an amine (1 m mol) at room temperature under an argon atmosphere, and the reaction mixture is stirred at room temperature for 4 hr. After evaporation of the solvent under reduced pressure the residue is separated by silica gel thin layer chromatography to give a carboxamide.

In a similar manner, various carboxamides were prepared in high yields as listed in the Table.

Table

Preparation of Carboxamides

Carboxylic Acid	Amin		Isolated Yield %	
R^1	R^2	R^3	pyrimidone (II)	pyrimidone (III)
$C_6H_5CH_2$	n-C_4H_9	H	98	quant
$C_6H_5CH_2$	i-C_3H_7	i-C_3H_7	87	
$C_6H_5CH_2$	C_6H_5	H	99	99
$C_6H_5CH_2$	C_6H_5	CH_3	88	
$C_6H_5CH_2$	t-C_4H_9	H	89	89
$C_6H_5CH_2$	n-C_8H_{17}	H	92	
$C_6H_5CH_2CH_2$	t-C_4H_9	H	90	
$C_6H_5CH_2CH_2$	C_6H_5	H	quant	quant
$C_6H_5CH_2CH_2$	$C_6H_5CH_2$	CH_3	93*	84
$C_6H_5CH_2CH_2$	C_6H_5	CH_3	90	
C_6H_5	n-C_4H_9	H	quant	
C_6H_5	$C_6H_5CH_2$	CH_3	82	
C_6H_5	t-C_4H_9	H	96*	
C_6H_5	C_6H_5	H	79*	82
C_6H_5	C_6H_5	CH_3	82	
CH_3CH_2	$C_6H_5CH_2$	CH_3	80	

*refluxed for 2 hrs.

It should be noted that, by the use of pyrimidone derivatives, II or III, as an acid captor, various carboxamides are obtained in high yields under rather weakly basic condition.

REFERENCES

1. E. Bald, K. Saigo, and T. Mukaiyama, Chem. Lett., 1975 1163.
2. T. Mukaiyama, H. Toda, and S. Kobayashi, ibid., 1976, 13.
3. T. Mukaiyama, Y. Aikawa, and S. Kobayashi, ibid., 1976, 57.
4. Pyrimidone (II) or (III) was prepared from 2-aminopicoline and ethyl acrylate or ethyl methacrylate, respectively, in the same procedure for pyrimidone (I)[5].
5. R. Adams and I. J. Pachter, J. Amer. Chem. Soc., 1952, 74, 5491.

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