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A NOVEL CONVENIENT ONE STEP PYRIMIDINE SYNTHESIS

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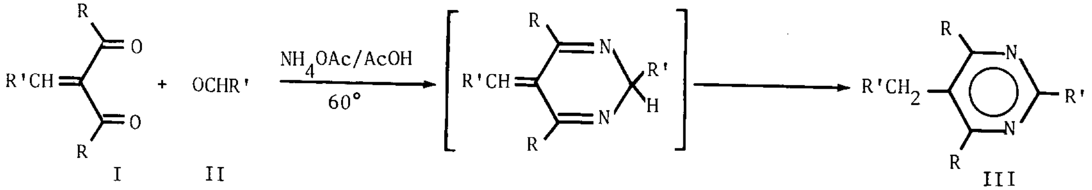
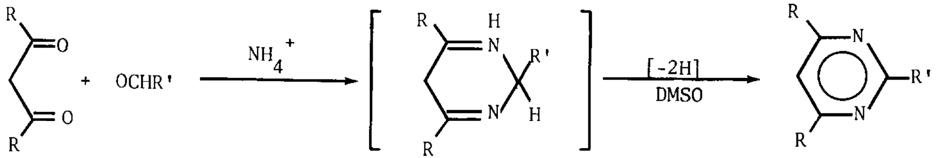
A new method for the preparation of pyrimidines by condensation of β-dicarbonyl compounds, ammonium salts and carbonyl containing substances has been developed.

An attractive approach to the synthesis of 1,2-dihydropyrimidines bearing alkyl or aryl groups consists of the reaction of β-dicarbonyl compounds, ammonium salts and carbonyl containing substances. 1,2-Dihydropyrimidines containing gem-dialkyl groups attached to the saturated carbon in position 2 of the pyrimidine ring have been prepared.[1-3] These compounds are stable to further oxidation to pyrimidines because of the gem-disubstitution. New routes to pyrimidines via the corresponding dihydropyrimidines, where the substituents do not prevent, but rather favour subsequent dehydrogenation (intramolecular disproportion) have been described:[4]



I II III

In the course of our studies on the synthesis of dihydropyrimidines which might be subsequently oxidized to pyrimidines, we have found a convenient new method for the direct preparation of pyrimidines. The reaction takes place when β-dicarbonyl compounds are treated with aldehydes and ammonium salts under oxidating conditions:



IV II V

In a typical experiment, to 8 g of anhydrous ammonium acetate was added a solution of 0.01 mole IV and II each, in 8 ml of dry dimethylsulfoxide containing 2 ml of glacial acetic acid.[5] The mixture was heated to 80-90°C and dry air was bubbled through it. The progress of reaction was monitored by thin layer chromatography (TLC) on silica gel plates. After 10-12 hours, the reaction mixture was cooled,[6] mixed with chloroform and washed with water. Evaporation of the dried chloroform extract followed by column chromatography on silica gel afforded the corresponding pyrimidines.

Table 1. Yields and Melting Points Data for Pyrimidines V

Reactants	Product V		Yield	M.p. (°C)	
II and IV	R	R'	(%)*	solvent	lit.
a. 1,1,3,3-Tetramethoxypropane benzaldehyde	H	C_6H_5	12	38-39 (hexane)	37.5-38.5[7]
b. Acetylacetone benzaldehyde	CH_3	C_6H_5	17	82-83 (C_2H_5OH)	81-83[8]
c. Dibenzoylmethane benzaldehyde	C_6H_5	C_6H_5	47	185-187 (CH_3COOH)	185-187[9]
d. Dibenzoylmethane 4-methoxybenzaldehyde	C_6H_5	$4\text{-}CH_3O\text{-}C_6H_4$	32	130-131 (hexane)	
e. Dibenzoylmethane 2-naphthaldehyde	C_6H_5	$2\text{-}C_{10}H_7$	29	154-155 (hexane)	

*Yield after isolation. Each product was fully characterized by chromatographic behaviour, UV, IR, ^1H-NMR and high resolution mass-spectral analysis or by comparison with an authentical sample.

In all reactions where β-diketones were used, the intermediate compounds I, which were prepared independently by condensation of IV and II, were detected by TLC. Traces of pyrimidine III were observed in the reaction of acetylacetone with benzaldehyde. In the course of the reactions of dibenzoylmethane with 4-methoxybenzaldehyde and 2-naphtaldehyde, in addition to the products described in Table 1,we also isolated small amounts of 2,6-di(4'-methoxyphenyl)-4-phenyl- and 2,6-di(2'-naphthyl)-4-phenylpyrimidine, respectively, whose formation may be rationalized by the reaction of the α,β-unsaturated carbonyl fragment of compound **I**, rather than the β-dicarbonyl fragment[4]. An analogous observation has been made by Ruhemann[10].

From the viewpoint of facile one-pot synthesis of a variety pyrimidines from readily available compounds the present method is expected to be useful in small scale as well as in industrial processes.

References and Notes

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5. The yields were considerably better in the presence of a small amount of glacial acetic acid, but no attempts of optimization have been made to date.
6. In the case of 2,4,6-triphenylpyrimidine (Vc) a crystalline product was obtained.
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