

Articles

Stereoselective Crossed-Aldol Condensation of Hetarylmethyl Ketones with Aromatic Aldehydes in Water : Synthesis of (2*E*)-3-Aryl-1-hetarylprop-2-en-1-ones

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Aldol condensation of 2-acetylthiophene, 2-acetylpyrrole and 2-acetylpyridine with different aromatic aldehydes were carried out in water in heterogeneous phases in the presence of cetyltrimethylammonium bromide as cationic surfactant at room temperature. All the reactions occur in a short time with excellent yields of stereoselective hetarylpropanones in water as environmental friendly solvent.

Key Words : Crossed-Aldol, Hetarylpropanones, Chalcones, Synthesis in water

Introduction

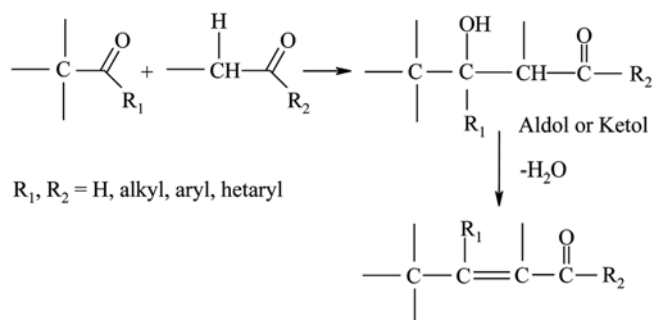
Chalcones are α,β -unsaturated ketones and they have great existence in the plant kingdom. It is well known that most of natural or synthetic chalcones are highly biologically active with a great pharmaceutical and medicinal applications.¹ Recently they are used as anti-AIDS agents,² cytotoxic with antiangiogenic activity,^{3,4} antimalarial,^{5,6} anti-inflammatory^{7,8} and antitumor.^{9,10}

The U.S. Environmental Protection Agency (EPA) has suggested a drastic reduction of using of more than ten of hazard common organic solvents in the industrial production of chemicals. We are dealing in this paper a cleaner and safe production of high yield of stereoselective hetarylchalcones as an important biologically active compounds in water as a cheap solvent and environmental friendly reaction medium.

Recently, water is an attractive medium for many organic reactions.¹¹ The important advantageous of aqueous medium with respect to organic solvents are less expensive, healthy, safe and environmentally friendly. Also, it allows the pH control and the use of surfactants as micro aggregates.

The hydrophobic effect and the large cohesive energy of water are considered to be the main factors responsible for increasing reactivity and selectivity of the reactions.^{12,13}

Mixed or crossed aldol condensation is a base-catalyzed



addition of different aldehydes and ketones one of them must contain at least one α -hydrogen to give an aldol or ketol which are dehydrated to α,β -unsaturated aldehydes or ketones.

The classical reaction conditions of aldol condensation are NaOH solution in hydroalcoholic medium which are, often, yielded a mixture of (*E*) and (*Z*) chalcones.^{14,15}

Recently, aldol reaction can, also, be carried out in an aqueous medium in the presence of catalysts to increase molecular aggregations and stereoselectivity.¹⁶⁻¹⁹ It is considered cleaner conditions of the production of some known and unknown chalcones.

Results and Discussion

We extended the previous investigations¹⁶⁻¹⁹ to carbon-carbon bond formation and we focus in this paper the crossed-aldol condensation of some hetarylmethyl ketones with a variety of different aromatic aldehydes in water at room temperature and in the presence of cetyltrimethylammonium bromide (CTABr) as the proper cationic surfactant for the synthesis of (2*E*)-3-aryl-1-hetarylprop-2-en-1-ones in an excellent yields with high stereoselectivity. Analytical gas chromatography proved that, only, *E*-isomers of isolated propanones were detected. The ¹H-NMR coupling constants (*J*) of C2-H and C3-H of the isolated hetarylpropanones are in the range of 15.5-16.0 Hz which are characteristic to *E*-propanones.

We are expected that the synthesized hetarylpropanones might have a biological and medicinal activities in analogous to the biologically active amino chalcones,⁹ quinoliny chalcones and some ferrocenyl chalcone.⁵

Efficient stirring of an equimolar amount of 2-hetaryl methyl ketones (**1**, **3**, **5**) and aromatic aldehydes in aqueous NaOH solution and in the presence of cetyltrimethylammonium bromide (CTABr) as surfactant at room temper-