

An Improved Method for the Synthesis of Flavanones

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Abstract—An isomerization of 2'-hydroxychalcones into the corresponding flavanones in ethanol in the presence of triethylamine is described.

Key words: *chalcone, flavanone, isomerization, synthesis*

Flavanones, 2,3-dihydroflavones, attract the attention of researchers as physiologically active substances with a diverse spectrum of activities. Cholagogues, hepatoprotectors, antiphlogistics, and compounds with other valuable medicinal properties are among them.

Flavanones are usually obtained by the isomerization of 2'-hydroxychalcones in acidic or alkaline media. The methods of 2'-hydroxychalcone isomerization into the corresponding flavanones by the use of hot ethanol; diluted alkali; sulfuric, hydrochloric, or phosphoric acid are known. Methanolic hydrogen chloride, sodium acetate, and ion exchanger Amberlist [1] are also used for this purpose. Pyridine, glacial acetic acid, *n*-butylamine, and silica gel with adsorbed concentrated sulfuric acid, ethylenediamine, or hydroxylamine hydro-

chloride are also used sometimes [2–6]. However, the conditions that displace the equilibrium to flavanones are impossible to predict.

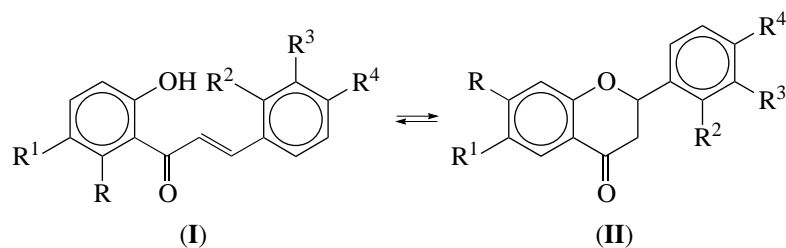
Here we report the isomerization of some 2'-hydroxychalcones into the corresponding flavanones in ethanol in the presence of triethylamine.

When refluxed in ethanol in the presence of triethylamine, chalcones (**I**) are transformed into the corresponding flavanones (**II**) for 2 h in good yields (60–85%). The chalcones containing electronodonor or electronoacceptor substituents in position 5', as well as those with no substituents were obtained in the highest yields. They were purified to homogeneous state by crystallization or fractional crystallization (table).

Characteristics of flavanones (**IIa**)–(**IIm**)

Compound	Yield, %	Mp, °C	Empirical formula	Crystallization solvent
(IIa)	47.6	76–78	C ₁₅ H ₁₂ O ₂	EtOH
(IIb)	69.4	109–110	C ₁₇ H ₁₆ O ₃	EtOH
(IIc)	72.1	76–77	C ₁₅ H ₁₁ FO ₂	EtOH
(IId)	78.5	96–97	C ₁₅ H ₁₁ ClO ₂	EtOH
(IIe)	73.3	76–78	C ₁₇ H ₁₄ O ₄	EtOH
(IIf)	75.2	94–95	C ₁₆ H ₁₄ O ₃	MeOH
(IIg)	58.8	97–98	C ₁₆ H ₁₄ O ₃	EtOH
(IIh)	85.2	127–128	C ₁₆ H ₁₂ O ₄	MeOH
(IIi)	73.3	108–109	C ₁₇ H ₁₄ O ₄	MeOH
(IIj)	82.3	180–181	C ₁₈ H ₁₆ O ₅	MeOH
(IIk)	79.8	120–121	C ₁₇ H ₁₃ FO ₄	MeOH
(IIl)	81.7	115–116	C ₁₇ H ₁₃ ClO ₄	MeOH
(IIm)	84.1	121–122	C ₁₇ H ₁₃ BrO ₄	AcOEt/petroleum ether

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- a: $R = R^1 = R^2 = R^3 = R^4 = H$,
b: $R = R^2 = R^3 = H$, $R^1 = CH_3$, $R^4 = OCH_3$,
c: $R = R^2 = R^3 = R^4 = H$, $R^1 = F$,
d: $R = R^2 = R^3 = R^4 = H$, $R^1 = Cl$,
e: $R = R^2 = H$, $R^1 = CH_3$, $R^3 = R^4 = -OCH_2CH_2O-$,
f: $R = R^2 = R^3 = R^4 = H$, $R^1 = OCH_3$,
g: $R = R^1 = R^2 = R^3 = H$, $R^4 = OCH_3$,

- h: $R = R^1 = R^2 = H$, $R^3 = R^4 = -OCH_2O-$,
i: $R = R^1 = R^2 = H$, $R^3 = R^4 = -OCH_2CH_2O-$,
j: $R = R^2 = H$, $R^1 = OCH_3$, $R^3 = R^4 = -OCH_2CH_2O-$,
k: $R = R^2 = H$, $R^1 = F$, $R^3 = R^4 = -OCH_2CH_2O-$,
l: $R = R^2 = H$, $R^1 = Cl$, $R^3 = R^4 = -OCH_2CH_2O-$,
m: $R = R^2 = H$, $R^1 = Br$, $R^3 = R^4 = -OCH_2CH_2O-$.

Scheme.

The structures and the compositions of the flavanones were confirmed by elemental analysis, melting points of mixed samples, TLC, and chemical transformations.

Thus, we suggested an improved and efficient method for obtaining flavanones and studied the effect of substituents in rings A and B on the isomerization course and the yields of target products.

EXPERIMENTAL

The reactions were monitored and the purities of resulting compounds were checked by TLC on pre-coated Silufol UV-254 plates. As an eluent, a 9 : 1 benzene–ethanol mixture was used. The data of elemental analyses of all the compounds corresponded to the calculated values.

General procedure of the chalcone (Ia)–(Im) isomerization into flavanones (IIa)–(IIm). A solution of the corresponding 2'-hydroxychalcone (2 mmol) and

triethylamine (0.28 ml, 2 mmol) in ethanol (25 ml) was refluxed for 2–3 h and poured out into cold water containing 1 ml of 10% hydrochloric acid. The precipitated solid was filtered, washed with water, and crystallized from an appropriate solvent (see table).

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