

Comparison of the Basic Strength of Solid Catalysts in the Synthesis of 2-Styrylbenzoxazoles under Microwave, Ultrasonic Irradiations and Solvent Free Conditions

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Abstract: Condensation of 2-methyl benzoxazole with aromatic aldehydes was carried out over a number of solid base catalysts under microwave, ultrasonic irradiation and solvent free conditions. NaNH₂ supported on alumina in solvent free condition without microwave and ultrasound irradiation presented the most active base for the condensation.

Keywords: Heterogeneous catalysis, KF-alumina; CsNaX Zeolit, Microwave, Ultra Sound, 2-Styryl benzoxazoles

Introduction

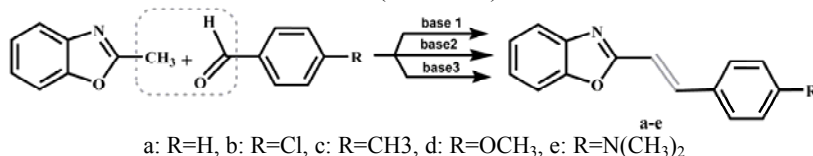
2-Styryl benzoxazoles are prepared via condensation of 2-methylbenzoxazole with aromatic aldehydes in presence of different catalysts and methods¹⁻². These compounds have diverse biological activities such as antiviral³, antisecretory⁴ and different applications such as optical brightener⁵ and dyes⁶. Basic catalysts are suitable in synthesis of styryl benzoxazoles and considering the fact that replacing the liquid bases with solid base catalysts leads to cleaner reactions with high yield, high reaction rate, easy separation and purification of the products, utilization of such bases means saving in cost and energy. Therefore, such solid bases are frequently used in many chemical reactions. KF-alumina⁷, zeolites⁸ and NaNH₂-alumina⁹ are efficient bases of this type.

KF/alumina was introduced by Clark⁷ and has been applied as catalyst to a variety of reactions and Ando and coworkers concluded that the fluoride ions and hydroxyl groups are the source of the strong basicity¹⁰. Advantage of the strongly basic nature of KF/Al₂O₃, has allowed it to replace organic bases in a number of reactions including Suzuki couplings¹¹, condensations¹², epoxidations¹³, diazotizations¹⁴, Sonogashira couplings¹⁵, Knoevenagel reactions¹⁶ and *etc.*

The catalytic activities of basic zeolites have been also reported also in early 1970s by yashima *et al*¹⁷ and they have concluded that oxygen ions in the zeolite framework are responsible for weak basic effect of this catalyst. In alkali ion-exchanged zeolites, the basic strength was added and controlled by selecting the exchanged cation and the type of zeolite^{8, 17-18}. The high activities are caused by the generation of strong basic sites by addition of alkali ions which are located in the zeolite cavities in the form of alkali oxides. Today, zeolite X has many applications for a high ion exchange capacity and large pore size which make this zeolite as a high-cation exchange material¹⁹. The post-synthesis modification of NaX zeolite is carried out by conventional ion-exchange technique, using 5 wt.% of aqueous solutions of chloride salts of K, Rb and Cs. The basicity of NaX zeolite is added from Na to Cs (as a non framework cations) directly reflecting on the extent of basicity of cations. The zeolites are used in many reactions such as Knoevenagel reactions²⁰, condensations²¹ and Henry reactions²².

Alkali amides present excellent bases in organic synthesis and Alkali amides supported on alumina have led to the emergence of very effective solid base catalysts that have been used in many reactions such as alken isomeration²³⁻²⁴, vinyl byciclohepten isomerization²⁴ and Dimerization²⁴.

On the other hand, the application of microwave²⁵ and ultra sonic irradiations²⁶ in reactions using heterogeneous catalysts or supports especially in solvent-free conditions is a promising method due to the short reaction times, purer products, minimized waste and good yields. Herein we have reported the application of KF-alumina and CsNaX zeolite in synthesis of 2-styryl benzoxazoles under microwave oven and ultrasound conditions in presence of solvents and in solvent-free conditions and also NaNH₂ supported on alumina and NaX zeolite in solvent-free conditions (Scheme 1).



Scheme 1. Base 1: KF/alumina, base 2: CsNaX zeolite, base 3: NaNH₂

Experimental

All commercially available chemicals were purchased from Merck and Aldrich Company and used as received. Melting points were measured using Barnstead Electro thermal. Ultrasonic apparatus was POWER SONIC 405. The microwave oven used, was LG MOD MC-838 WR.

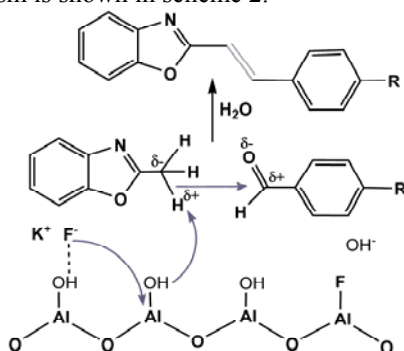
Chemistry

The condensation of 2-methylbenzoxazole (**1**) with substituted benzaldehydes (**2**) has been carried out in the presence of KF/Al₂O₃, CsNaX zeolite under microwave and ultrasound irradiations in solvent free and solvent conditions and NaNH₂ supported on alumina and NaX zeolite (Scheme 1). The products were obtained in good yield and identified by comparison of their physical and spectroscopic data with those reported in literature¹⁻². The results are summarized in Table 1.

General procedures for the preparation of 2-styryl benzoxazoles using KF-basic alumina

A mixture of aqueous solution of KF (0.6 g, 10 mmole KF in 10 mL H₂O) and basic alumina (1 g) was stirred at room temperature for 30 min. The mixture was then concentrated to dryness under vacuum and kept at 150 °C for 30 min. This mixture was transferred to a

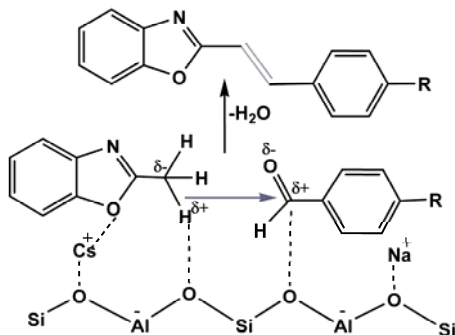
pestle and DMSO or DMF (2 mmole) and 2-methyl benzoxazole (1 mmole, 0.13 mL) were added and the mixture was well ground for 5 min. Finally, aldehyde (1.05 mmole) was added to the mixture and ground for 2 min. The mixture was then exposed to microwave irradiation (600 W) or ultrasonic irradiation. After completion of the reaction, the mixture was cooled down and extracted with 15 mL acetone or ethyl acetate. After filtration of the solid support and removal of the solvent the product was purified by recrystallization from ethanol/H₂O. The mechanism is shown in scheme 2.



Scheme 2. The mechanism of condensation of 2-methylbenzoxazole with aromatic aldehydes in presence of KF-basic alumina

General procedures for the Preparation of 2-styryl benzoxazoles using zeolite

NaX Zeolite was prepared hydrothermally from Na₂O, SiO₂, Al₂O₃ and H₂O, according to the literature²⁷⁻²⁸. The CsNaX was prepared conventionally by ion exchange of NaX powder with 5 wt. % cesium chloride solution at 100 °C for 12 h. The aqueous salt solution was taken in the proportion of 15 mL g⁻¹ of zeolite for exchange reaction. The solid was filtered by vacuum system and washed with distilled water to remove chloride ions. The solid was again dried in an air oven maintained at 100 °C for 10 h and stored for later use. The CsNaX zeolite (1 g) was transferred to a pestle and DMSO or DMF (2 mmole) and 2-methyl benzoxazole (1 mmole, 0.13 mL) were added. The mixture was then ground for 5 min. Finally, aldehyde (1.05 mmole) was added to the mixture and was ground again for 2 min. The mixture was then exposed microwave irradiation or ultrasonic irradiation. After completion of the reaction, the products were isolated and purified according to the method mentioned above. The mechanism is shown in Scheme 3.



Scheme 3. The mechanism of condensation of 2-methylbenzoxazole with aromatic aldehydes in presence of CsNaX zeolite

General procedures for the preparation of 2-styryl benzoxazoles using NaNH₂ supported on alumina or NaX zeolite

2-Methyl benzoxazole (1 mmole, 0.13 mL) and basic alumina or NaX zeolite support (1 g) was transferred to a pestle and well was ground using a mortar for 5 min. Sodium amide (0.19 g, 5 mmole) was then added under inert atmosphere (N₂) and ground and the aldehyde (1.05 mmole) was immediately added and the mixture was ground again about 30-40 second until the color of mixture is completely changed. After completion of the reaction, the compounds obtained by this method were isolated and purified according to the procedure mentioned.

Results and Discussion

Condensation of 2-methyl benzoxazole with aromatic aldehydes has been facilitated with KF/Al₂O₃ and NaX zeolite in conjunction with microwave and ultrasound under various conditions in presence of DMSO or DMF and in solvent free condition. Also, NaNH₂ supported on alumina and NaX zeolite were used as the heterogeneous bases. The results are summarized in Table 1.

Table 1. The comparison of yield and reaction time for the synthesis of 2-styryl benzoxazoles in different conditions

Comp	KF-basic alumina / Microwave irradiation						KF-basic alumina / Ultrasound irradiation						NaNH ₂ -basic alumina	
	React ion	Yield %	React ion	Yield %	React ion	Yield %	React ion	Yield %	React ion	Yield %	React ion	Yield %	React ion	Yield %
	time (s)	DMS O	time (s)	DMF (s)	time (s)	(sf) ^a	time, min	DMS O	time, min	DMF min	time, min	(sf)	time (s)	(sf) ^a
a	40	88	150	82	360	62	20	68	20	68	55	50	30	90
b	40	90	150	83	360	65	20	68	20	70	55	50	30	91
c	45	92	170	88	480	70	20	71	25	70	60	55	35	95
d	45	92	170	85	480	65	20	69	25	67	60	46	35	92
e	45	87	182	82	480	68	25	65	30	65	60	46	35	90
Comp	CsNaX zeolites / Microwave irradiation						CsNaX zeolites / Ultrasound irradiation						NaNH ₂ -NaXzeolite	
	React ion	Yield %	React ion	Yield %	React ion	Yield %	React ion	Yield %	React ion	Yield %	React ion	Yield %	React ion	Yield %
	time (s)	DMS O	time (s)	DMF (s)	time (s)	(sf) ^a	time, min	DMS O	time, min	DMF min	time, min	(sf)	time (s)	(sf) ^a
a	120	71	200	69	600	50	25	59	30	60	70	35	35	86
b	120	78	200	73	600	52	25	63	30	61	70	35	35	88
c	180	75	250	75	700	52	30	64	30	65	80	33	40	89
d	180	78	250	75	700	49	30	60	35	60	80	37	40	86
e	200	75	280	69	700	45	35	60	35	55	80	32	40	85

a : Solvent free

As Table 1 shows, the application of microwave irradiation in addition to KF/Al₂O₃ provides higher yield and shorter reaction time compared to CsNaX zeolite and under ultrasonic irradiation. On the other hand, KF/Al₂O₃ under microwave irradiation in presence of DMSO gave the best results which could be due to the utilization of microwave irradiation power and DMSO as polar solvent. The main absorption occurs between microwaves and the polar molecules of the solvent and energy transfer occur from solvent to

reaction mixture and the reactants²⁹. Whereas the lowest results obtained under solvent free conditions in the presence of KF/Al₂O₃ and CsNaX zeolite. It is apparent that under ultrasound condition the reaction is completed in longer period of time indicating that the ultrasound irradiation has less power than microwave irradiation in this reaction.

The reactions carried out in solvent free conditions are considered more environmentally friendly. Two solvent-free reactions were carried out using NaNH₂ loaded on alumina and NaX zeolite presented good results. Both of these reactions were easy to conduct and took place in a short time, without the need to use microwave or ultrasound irradiation. The reaction could be further explored in other condensation reactions such as aldol and Michael addition.

In conclusion, condensation of 2-methyl benzoxazole with aromatic aldehydes was carried out over a number of solid base catalysts under microwave, ultrasonic irradiation and solvent free conditions. NaNH₂ supported on alumina in solvent free condition without microwave and ultrasound irradiation presented the most active base for the condensation.

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