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Zeolite: An Efficient Catalyst for the Synthesis of Various Heterocyclic Compounds.

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Abstract : A novel heterogeneous catalytic method to synthesize various heterocyclic compounds of biological interest, aminobenzisothiazole **[2a-h]** and 1,3-thiazine derivatives **[4, 6]**, using an environmentally attractive solid catalyst, zeolite, is described. © 1997 Elsevier Science Ltd.

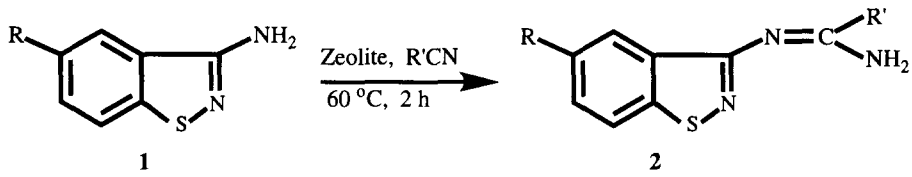
Zeolites as catalysts have received considerable attention in recent years due to their characteristic properties such as transition-state shape and size selectivity involving 1Å level precision, acidity and thermal stability.[1] In recent years, there has been a tremendous upsurge of interest in various organic transformations mediated by zeolites, and we have exploited the catalytic potential of zeolites for various organic transformations.[2] Hitherto no report is available in the literature in which a zeolite is employed to promote the synthesis of heterocyclic compounds.

In this communication, we wish to report a mild, convenient and heterogeneous catalytic methodology for the synthesis of various heterocyclic compounds using large pore zeolites like HYZeolite, HEMT and HZeolite beta. However the results with H-Mordenite and HZSM-5 (Si/Al=45), medium pore zeolites, gave the desired products in low yield. The zeolites were synthesized according to the reported procedure.[3] Prior to use the zeolites were activated by heating it at 500 °C in a current of air for 5 h.

Amidines are the nitrogen analogues of carboxylic acids and are part of several compounds of biological interest.[4] Vicini *et al.* have synthesized various amidinobenzisothiazole derivatives using Lewis acids, *e.g.* $SnCl_4$ and $AlCl_3$, and studied their pharmacological properties.[5,6]

The 3-aminobenzisothiazoles were synthesized as reported elsewere.[7] In a typical experiment, a mixture of the 3-aminobenzisothiazole **1a** (0.25 g), an excess of freshly distilled acetonitrile (15 mL) and HYZeolite (2.0 g) was heated at 60 °C for 2 h under stirring. The progress of the reaction was monitored by TLC. After 2 h the zeolite was filtered off and the solvent was evaporated to afford the product **2a** , which was further purified by column chromatography using hexane/ethyl acetate (Yield: 85%). The results with other substrates are summarized in Table 1. This method was successfully applied to other zeolites and the results are listed in Table 1.

Another example were zeolite can be used as a versatile catalyst is in the cyclocondensation reaction of various



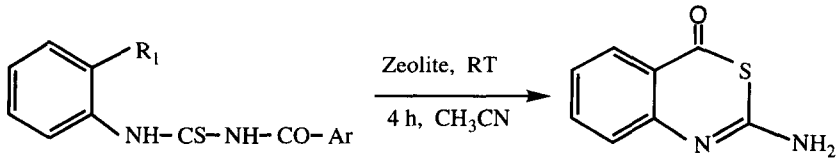
1 2

Table 1. Comparison of the yields of **[2a-h]** over various zeolites. T = 60 °C, t = 2 h.

Substrates			Products [a]	Yield [b]		
	R	R'		HY-Zeolite	HEMT	HZeolite beta
1a	H	CH_3	**2a**	85	78	72
1b	CH_3	CH_3	**2b**	87	84	69
1c	H	C_6H_5	**2c**	81	80	64
1d	CH_3	C_6H_5	**2d**	82	77	62
1e	H	CH_2Cl	**2e**	90	87	74
1f	CH_3	CH_2Cl	**2f**	92	86	70
1g	H	Cyclopentyl	**2g**	78	71	60
1h	CH_3	Cyclopentyl	**2h**	75	70	63

[a] all products were characterized by their IR, ^{1}HNMR and Mass Spectra and are in agreement with the reported data .[5,6] [b] yield of isolated pure products.

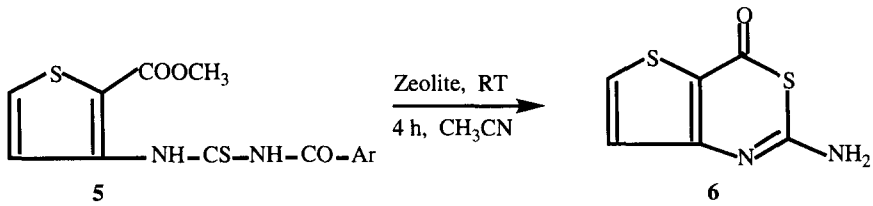
methyl 2-benzoyl thioureidobenzoate and methyl 3-aroyl thioureido-2-thiophenecarboxylate derivatives. Hetero- and carbo cyclic thioureas containing a neighboring carboxy, alkoxy carbonyl or carbonitrile function are an important class of starting compounds for the synthesis of heterocyclic compounds.[8] Gutschow *et al.* studied the cyclocondensation reaction of various methyl 2-benzoyl thioureidobenzoate and methyl 3-aroyl thioureido-2-thiophenecarboxylate derivatives in presence of concentrated sulfuric acid.[9] Depending on the reaction conditions, treatment of **3b** with concentrated sulfuric acid affords 2-amino-3,1-benzothiazin-4-one at higher temperature and



3 4

2-benzoylamino-3,1-benzothiazin-4-one at room temperature. But over zeolites **[4,6]** was the only product formed from **[3a-c & 5a-b]** both at room temperature and at 60 °C. At 60 °C, over HYZeolite **3a** was converted to **4** in 94% yield at 4 h.

The starting materials **[3a-c & 5a-b]** were synthesized according to the reported procedure.[9] A mixture of **3a** (0.28 g) and HY-Zeolite (2.0 g) in dry acetonitrile (50 mL) was stirred at room temperature for 4 h in a round bottom flask. Then it was poured into a mixture of ice cold water and sodium hydrogen carbonate. The precipitate of **4** was filtered and recrystalized from ethyl acetate/acetonitrile mixture (88%). The compounds **[3b, 3c, 5a & 5b]** were also underwent the cyclocondensation reaction over various zeolites to **[4, 6]** and the results are summarized in Table 2.



5 **6**

Table 2. The yields of cyclocondensation products [**4, 6**] over different zeolites. T = r.t, t = 4 h

Substates	Products [a]	Yield [b]		
		HY-Zeolite	HEMT	HZeolite beta
3a : R_1 = COOH Ar = Ph	**4**	88	82	76
3b : R_1= $COOCH_3$ Ar = Ph	**4**	94	89	75
3c : R_1 = $COOCH_3$ Ar = (4-CH_3) Ph	**4**	85	73	68
5a : Ar = Ph	**6**	81	84	79
5b : Ar = (4-CH_3) Ph	**6**	84	75	65

[a] all products were characterized by their IR, ^{1}HNMR and Mass spectra and are in agreement with reported data.[9] [b] yield of isolated pure products.

The observed efficient performance of HYZeolite may be attributed to its large pore opening (0.74 nm), three dimensional channel system and higher concentration of acid sites and the low yields of desired products over HZSM-5 may be due to the small pore opening (0.56 nm).[10] The present procedure for the synthesis of amidino benzisothiazoles and 1,3-thiazines are clean and workup procedure is exceedingly simple, only involving the filtration of zeolite and removal of the solvent to obtain the product in high state of purity. The recovered zeolite can be reactivated for reuse by heating it at 500 °C in the presence of air.

The superiority of zeolites over conventional methods can be clearly visualized in the replacement of the corro-

sive and polluting acid catalysts by the more environmentally attractive zeolites and high yield of amidinobenzisothiazoles and 1,3-thiazine derivatives. In this connection our methodology for the synthesis of various amidinobenzisothiazoles and 1,3-thiazine derivatives is noteworthy.

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